The effects of localized fatigue in the knee extensors on crank power and muscle activation

by

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ABSTRACT

Maximal power output during cycling exercise relies on the production of maximal force from the lower limb muscles, through their coordinated activation by the central nervous system. Larger levels of crank power are produced during the downstroke phase of the pedal cycle where the knee extensor muscles are highly activated and produce large levels of joint power. Reductions in force-generating capacity of the knee extensors resulting from fatiguing cycling exercises have been linked with a reduction in the ability of individuals to produce crank power and alterations in muscle coordination. However, fatigue induced by cycling exercises is likely to reduce the force-generating capacities of the other lower limb muscles, making it impossible to identify the effect of fatigue in the knee extensors on crank power production and muscle coordination. Isolated reductions in force-generating capacity of the knee extensors have been observed following single-joint exercises requiring repeated contractions of this muscle group.

To date, it is unknown how a unilateral single joint exercise effects power production during a bilateral movement. The aim of this study was to investigate the effect of repeated contractions of the left knee extensor muscles on the production of crank power and the activation of the locomotor muscles of both lower limbs during bilateral maximal cycling exercise.

A group of twelve young healthy adults performed a maximal 6-s cycling exercise before and ~1min after a series of isometric contractions of the left knee extensors (20% of maximal force) that continued until their maximal voluntary force (MVF) was reduced by 50%. We observed a substantial reduction of MVF of the left knee extensors (-48 ± 11 %, $p<0.001$) after completion of the series of unilateral isometric contractions. The reduction in force-generating capacity in the left knee extensors was associated with peripheral fatigue (resting evoked force was reduced by 27 ± 21 %, $p<0.001$) and central fatigue (voluntary activation reduced by 23 ± 12 %, $p<0.001$). No significant changes in MVF of the right knee extensors were observed after the end of the left knee extension exercise, although there was a tendency to increase (baseline: 693 ± 196N vs. post: 735 ± 194 N, $p=0.05$). During sprint cycling, crank power transmitted to the left crank during the downstroke phase was reduced by 12.1 ± 7.2 % ($p<0.001$), while peak EMG was reduced by 6 ± 16 % for *vastus medialis* normalized to M-wave and by 5 ± 19 % for *rectus femoris* ($p<0.05$) following the reduction of the force-generating capacity of the left knee extensors. We also observed a decrease in power transmitted to the left crank during the upstroke phase (-25.0 ± 15.4 %, $p<0.001$), but also reductions in power

transmitted to the right crank during both the downstroke (-6 ± 3 %, $p<0.001$) and the upstroke phases (-13.5 ± 9.0 %, $p<0.001$). Interestingly, peak EMG for the right *vastus lateralis* was reduced (-5 ± 16 %, $p<0.05$) during the maximal cycling exercise performed after the series of isometric contractions of the left knee extensors. Our results show that completion of a series of unilateral and submaximal voluntary contractions of the knee extensors led to bilateral reductions in the power transmitted to the cranks during both phases of the pedal cycle, during which the knee extensors are either agonists (i.e. downstroke phase) or antagonists (i.e. upstroke phase). In conclusion, the findings from this study indicate that unilateral fatigue of a single muscle group can reduce power production from non-fatigued muscles during complex and bilateral movements.

STUDENT DECLARATION

"I, Rosie Bourke, declare that the Masters thesis entitled The Effects of Localized Fatigue in the Knee Extensors on Crank Power and Muscle Activation is no more than 60,000 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 

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CHAPTER 1. INTRODUCTION

The performance of everyday multi-joint movements, such as walking up stairs, running or rising from a chair, requires the coordinated activation of many muscles, acting on numerous joints. The specific activation of individual muscles within a movement however, is continuously adjusted by the CNS so we can successfully complete these tasks. Adjustments of muscle coordination are essential so that we can adapt to perturbations or constraints (e.g. loss of muscle function) that may be imposed on a movement (109). Exercise-induced fatigue has been used as a means to perturb the movement to assess changes in muscle coordination and the effects on performance during dynamic bilateral exercises.

Fatigue itself presents a very complex phenomenon as there are many underlying mechanisms acting on various central and peripheral sites, that lead to a reversible reduction in the force-generating capacity of exercising muscles (3, 73). The type of exercise performed influences the processes effecting muscle function and consequently how long fatigue may persist (28, 96, 163). Single-joint isometric exercises can be used to induce isolated fatigue and identify contributions of central and peripheral mechanisms.

Cycling exercises can be used as a model to safely study the effect of perturbations on coordination during a locomotor task, as kinematics and external resistance can be controlled. Because a large portion of propulsive forces are generated by the knee extensors over the downstroke phase of the pedal cycle (63, 117) reducing the force-generating capacity of the knee extensors should induce a substantial perturbation that may require adjustment of muscle coordination. But as yet, fatigue has not been isolated to this muscle group so the effects of a reduction in force-generating capacity solely in the knee extensors is unknown. Further to this, with fatigue isolated to one muscle group, the activation and force-generating capacity of other non-exercising muscles, within the ipsilateral and contralateral limbs, can also be affected (84, 120).

Therefore, the objective of this study was to investigate how the perturbation caused by a unilateral reduction in force-generating capacity of a primary power-producing muscle group effects the performance and coordination during a bilateral locomotor

exercise. Repeated, isometric knee extension exercises were used to induce isolated fatigue in the knee extensors, while electrical stimulation of the femoral nerve was also used to quantify the central and peripheral components of the induced fatigue. Crank power transmitted to both cranks during downstroke and upstroke phases of the pedal cycle were measured during maximal cycling exercise to assess intra- and inter-limb effects of the unilateral perturbation. As unilateral fatigue in the knee extensors can impact the activation and force-generating capacity of the homologous muscle group in the non-exercised limb, maximal voluntary force of the contralateral knee extensors was also measured to assess any 'cross-over' of fatigue.

A loss of force-generating capacity in a specific muscle group can result from not only fatigue, but also injury, surgery or disease (e.g. stroke, osteoarthritis). The effect of isolated fatigue in one muscle group has been previously assessed on the performance of single-joint, static and unilateral tasks (9, 167). However, little is known about the effect of isolated fatigue in one muscle group on power production and movement control during dynamic and bilateral exercises such as cycling, which relate to many types of movements that are performed on a daily basis (e.g. walking/ running). The results of this study could provide useful information to clinicians when assessing muscle function or prescribing rehabilitation exercises, as a loss of force-generating capacity in one muscle group could affect the activity of other muscle groups and consequently impact on bilateral task performance that is more applicable to daily functionality.

CHAPTER 2. REVIEW OF LITERATURE

2.1 Power production during cycling exercise

The power produced at the cranks during cycling exercise results from the combination of the force applied to the pedals and angular velocity of the cranks – cadence. During maximal sprint cycling, the relationships between force and velocity (F-V) and power and cadence (P-C) have been well established and consistently reproduced (50, 53, 54, 78, 155, 156). The F-V relationship shows crank torque decreases as cadence increases (155, 156), modelled by 2nd order polynomials to better describe the approximately linear relationship (10, 180). The parabolic P-C relationship has typically been modelled with a quadratic equation, however, more recently 3rd order polynomials have been shown to provide a better goodness of fit (180). The apex of the P-C relationship represents the maximal anaerobic power (P_{max}) an individual can produce, which correlates to the maximal force-generating capacity of the knee extensor muscles (54). From extrapolation of the P-C relationship, P_{max} occurs at a single optimal cadence (C_{opt}) (commonly between 110-130RPM) (77, 118, 155). However, the relationship also describes cadence-specific maximal power (77), i.e. there is a maximal power value that can be produced for a given cadence.

P_{max} measured over a complete pedal cycle was shown to relate to P_{max} generated over two phases of the pedal cycle – downstroke and upstroke (50). The majority of the power (~73%) is produced during the downstroke phase of the pedal cycle (defined as 30° to 150° of the pedal cycle in this study), when tested across a range of cadences (80-170 RPM) (50). While the upstroke phase (defined as 210° to 330° of the pedal cycle in this study) accounts for ~10% of P_{max} at 80 RPM with a negative contribution (-3.3 ± 6.2 %) at 170 RPM. The large positive contribution of the propulsive forces during the downstroke (extension phase) and lower amplitude, sometimes negative, contribution during the upstroke (flexion phase) to power output is consistently observed during cycling exercise across maximal and submaximal intensities (63, 70, 117, 185). As exercise intensity increases however, alterations in pedalling strategy have been seen where a more positive contribution of force occurs during the upstroke, with the largest upstroke force contributions occurring during sprint cycling (154, 185). In addition, Elmer et al. (2011) found the ratio between the time of extension phase to

time of flexion phase (i.e. duty cycle) increased during maximal cycling compared to submaximal cycling over a range of intensities (250 – 850 W). In line with this, when manipulating the length of the extension phase during one-legged cycling, Martin et al. (2002) reported increased power production when extension accounted for 58% of the cycle time, compared to 42% or 50% of cycle time. The increased power is thought to be due to a greater amount of time in the portion of the pedal cycle where the primary power producing muscles are in the shortening phase and can produce work (11). Given the dependence on the extension phase to produce power, any perturbations to force production during the downstroke is likely to reduce power production calculated over a full pedal cycle.

2.1.1 Joint powers in cycling exercise

The major power-producing muscles involved in cycling are those crossing the hip, knee and ankle, with knee extension power providing a sizable portion of the total power output across submaximal (39 – 60 % between 120 and 850 W) (63, 69) and maximal intensities (~41%) (63, 117, 122), linking with the correlation between P_{max} and maximal knee extensor force-generating capacity (54). Along with knee extension, hip extension power provides a substantial amount of the total power (63, 117), with Ericson (1988) reporting combined knee and hip extension accounting for ~70% of the total positive work (70). Knee flexion has also been shown to provide a significant amount of power throughout the pedal cycle, as well as important contributions from ankle flexion and extension and smaller contributions from hip flexion (16, 63, 117, 122). However, the absolute power and relative contributions of these joint powers vary as a function of exercise intensity (34, 63, 128). As intensity increases and becomes maximal a number of authors have found hip extension and knee flexion power become more important (63, 122). Accompanying these findings, it has been shown that increasing exercise intensity (at a constant pedalling rate) led to an increase in effective forces (tangential force) applied to the pedals, particularly during the upstroke/ flexion phase of the pedal cycle (105, 185). During maximal cycling exercise force is more effectively applied to the pedal during both the downstroke and, relatively, even more so in the upstroke, when compared to submaximal exercise (128). These findings have been related to an intensity dependent adjustment in the coordinated activity of the major muscles involved in cycling exercise (52, 152). At high/ maximal intensities, the

knee flexor muscles are more highly activated to allow greater effective force application to the pedals, increasing power production. However, at submaximal intensities this strategy appears to increase metabolic demand, reducing gross efficiency (105, 152). Likewise, as exercises intensity increases the involvement of the upper body increases, to transfer power across the hip, which is associated with reduced efficiency (63). It seems that the system adjusts the relative contributions of the lower limb muscles according to the preferred outcome, i.e. maximise power output at high intensities and maximise efficiency at submaximal intensities.

2.1.2 Muscle coordination during cycling exercise

Effective application of force to the pedals requires the coordinated activity of the major power-producing lower limb muscles throughout the pedal cycle, which is sensitive to changes in exercise conditions such as body position, intensity and fatigue (33, 49, 51, 90, 185). In line with the prominent knee and hip extension joint powers during the downstroke, the uni-articular knee extensor muscles; *vastus lateralis* and *vastus medialis* (VL and VM; VAS) and hip extensors *gluteus maximus* (GMAX) are most active during the propulsive downstroke phase of the pedal cycle, with the onset of activity occurring just before top dead centre (TDC) (37, 92, 143, 151, 152, 173). The relative activation level of VAS muscles is considered as maximal during maximal cycling exercise (52, 152), highlighting their importance in power production. During the flexion phase of the pedal cycle, intuitively, the bi-articular knee and hip flexor muscles; *hamstrings* (HAM) and *rectus femoris* (RF), respectively, are activated. However, they are also active for a large portion of the extension phase (37, 52, 90, 144, 170, 171, 183). The paradoxical activity of these antagonist muscles can be explained by the functional role of uni-articular versus bi-articular muscles (170, 172).

Computational studies have shown a significant portion of power produced over the extension phase of maximal cycling exercise, is generated by the uni-articular knee extensors. Much of this power acts to accelerate the limb and only a relatively small portion is applied directly to the crank (144, 183). During this extension phase high levels of activity are also seen in the ankle plantarflexors; *gastrocnemius lateralis* and *medialis* (GAS) and *soleus* (SOL) (52). But the power produced by these muscles applied directly to the crank, calculated through inverse dynamics, is much lower

compared to the knee extensors (184). The bi-articular ankle plantarflexors (GAS) largely contribute to the tangential crank force by transferring the power produced by the uni-articular knee extensors (132, 183). As described by van Ingen Schenau et al. (1994) the role of the uni-articular muscles is primary power producers, while bi-articular muscles are activated to facilitate the transfer of power across the joints to the crank.

The coordinated activation of the lower limb muscles during cycling exercise has been shown to be largely consistent across varied cycling exercises (90, 91, 132). As a result, numerous studies have identified muscle synergies within the pedalling movement (41, 91, 132, 143). Findings show that individual muscles and muscle groups that contribute to the same action (e.g. extension/flexion) share a common neural drive, to minimise the complexity of a movement for the central nervous system (CNS) (39, 92, 107, 157, 169).

2.1.2.1 Muscle synergies

While different studies varied slightly in the portion of the crank cycle where muscle activity was grouped, synergistic activity between the lower limb muscles has been identified during the downstroke phase, upstroke phase and transitioning phases between downstroke and upstroke (91, 132, 143). Using electromyography (EMG), the power produced over the downstroke can be accounted for by 2 synergies: 1) uni-articular VAS and GMAX in the initial stages and 2) bi-articular HAM, GAS and uni-articular SOL active during the second half of the downstroke. Initially the uni-articular VAS and GMAX are active to generate large forces, while the bi-articular HAM and GAS are activated later to transfer the force across the knee and ankle joints and effectively directed onto the pedal, to maximise the tangential component of the force. During the upstroke phase and transitioning between the two phases, forces of lower magnitude, compared to the downstroke, are produced by HAM which are partly transmitted directly to the crank. The remainder of the force from HAM transmitted to the cranks is facilitated by the ankle plantarflexors (GAS and SOL). In the latter stages of the upstroke and transitioning back to the downstroke, force produced by the hip flexors (RF) is able to be transferred to the crank through the activation of the ankle dorsiflexors (*tibialis anterior*, TA).

Across different motor tasks, synergistic activity has been shown to be robust when perturbations are introduced to the task constraints however, slight variations in muscle activity and force application can be observed across pedal cycles between and within individuals (40, 143, 168). Due to the large number of muscles and joints involved in dynamic exercises, such as cycling, the many degrees of freedom allows the CNS countless ways of manipulating the contribution of the different muscles to perform the same task (18, 19). Referred to originally by Bernstein (1967) as 'motor redundancy', Latash (2000) has described how this 'problem' of redundancy is advantageous to the system to deal with disruptions to the movement and adapt to changing conditions. During cycling exercise, adjustments in the level and timing of activation between synergies and individual muscles within a synergy, have been seen in conjunction with changes in task demands (e.g. cadence and power output) (91, 143, 176). While this may be the case, it is yet to be seen how the system might adapt if the perturbation to the task was isolated to a single muscle group. With the many degrees of freedom involved in cycling exercise it seems the system has the ability to adapt and compensate. But during maximal cycling exercise, theoretically the muscles are already maximally activated in their optimal timing of activation to produce maximal power (151).

Evidence has also been put forward suggesting that during some motor tasks, muscle activity can be preferentially influenced by the specific task (task-orientated), not just a pre-set control mechanism by the CNS (65, 106, 169). In a study by Enders et al. (2013), they demonstrated that with increased load (300 versus 150 W) the variability in muscle activity between pedal cycles for an individual reduces. The explanation behind the finding was put down to a reduction in the solution space as the task demand increased. Following Bernstein's observation of motor redundancy, there are multiple ways to perform the same task, considered a reflection of the flexibility and adaptability of the motor control system (131). When specific constraints are imposed on the performance of a task however (e.g. performed as quickly as possible), rather than just achieving the end goal, the amount of solutions available within the musculoskeletal system are reduced (86). During cycling exercise, if the end goal is restricted from power production – to *maximal* power production, then the solution space would be reduced and consequently, a reduction in variability of muscle activation patterns would also be observed. Introducing a perturbation to a maximal cycling task however, e.g.

reduced force-generating capacity in one muscle group, would seemingly increase variability in the execution (e.g. muscle coordination) as the system tries to adapt. However, the limited solution space, as the muscles are already maximally activated, suggests a lack of adaptability, likely effecting the result – i.e. reduced maximal power output.

2.1.2.2 Inter-limb muscle coordination

During bilateral cycling exercise it is apparent that along with coordinated *intra*-limb muscle activation, considerable *inter*-limb coordinated activity is involved, in particular between contralateral extension and flexion phases (164, 165). When comparing EMG activity between submaximal bilateral and unilateral cycling exercise, Ting et al. (1998) reported during unilateral cycling exercise, integrated EMG increased in the flexor muscles by 59% for HAM, 43% for RF and 70% for TA, compared to the bilateral condition. This was despite external load applied to the contralateral pedal during unilateral cycling that matched the loading during bilateral pedalling (i.e. task mechanics were identical in the unilateral and bilateral conditions). The findings supported the idea of an inhibitory pathway between extensor activation and modulation of contralateral flexor activity. In a separate study, the same group also reported during unilateral cycling exercise, RF and TA activity can also be impacted with rhythmic contralateral extensor force generation and movement (164). In a similar way, Kautz et al. (2002) demonstrated activity of the bi-articular RF and knee flexors, is highly effected by sensorimotor feedback from the contralateral limb, during transition phases of the pedal cycle. However, they reported that during unilateral cycling, the execution of posterior and anterior transition phases by HAM and RF increased when extension and flexion forces were generated by the contralateral limb (through rhythmic isometric extensions), as opposed to being inhibited. From the combined findings, a common neuronal input to the two lower limbs during bilateral locomotor exercise suggests that muscle activation is regulated according to the sensorimotor state of the contralateral limb, effecting the performance of the task.

When a unilateral perturbation was introduced to locomotor exercise performed bilaterally (adding a load to one limb during treadmill walking), it was found, that the system adapted by predominantly adjusting coordination between the limbs (inter-limb)

compared to changes in coordination within the effected limb (intra-limb) (82). Suggesting that, intra-limb coordination is more tightly constrained and the system more readily modifies coordination between limbs than within the effected limb. A similar finding was presented by Reisman et al. (2005) assessing adaptations to split-belt treadmill walking. They reported that when the velocity of the treadmill for one leg increased, locomotion was maintained primarily due to changes in inter-limb coordination. From the findings, the authors highlighted the ability of the CNS to independently modify inter-limb coordination without impacting on intra-limb coordination. The effect of isolated unilateral fatigue on the performance of bilateral, dynamic exercise is largely unexplored and could provide valuable insight into *inter*- and *intra*-limb muscle coordination strategies.

2.1.2.3 Changes in muscle coordination associated with locomotor fatigue

When cycling exercises are performed at submaximal intensities the muscles are not fully activated, so the system has room to adjust the level of activation or timing of activation of the lower limb muscles to achieve the same power output (52, 152). During constant load submaximal cycling exercises studies have shown that over-time, while power output is maintained, the activity of some of the muscles is adjusted, primarily to compensate for fatigue (45, 46, 51). For example, Dorel (2009) found when cycling at 80% of maximal power tolerated (327 ± 23 W) for as long as possible, the effective forces applied to the pedals during the downstroke and through bottom dead centre (transitioning to the upstroke) significantly increased towards the end of the exercise. These changes were met with a change in the timing of EMG activity in VAS and GAS, as well as the ankle dorsiflexors - TA, who all shifted forward (i.e. occurred later) in the pedal cycle (by 4° for VAS and 7°- 9° for GAS and TA). EMG amplitude significantly increased in GMAX and HAM in the last 25% of exercise, which the authors have suggested is to compensate for potential fatigue that may have occurred in the knee extensors (51). In a similar protocol (triathletes maintaining 355 ± 23 W to failure), Diefenthaeler et al., (2012) found normal and tangential pedal forces increased, and cadence decreased as the exercise progressed. Accompanying the mechanical alterations, relative muscle activity of the hip and knee extensors (GMAX, VL and VM) increased, along with the hip flexors (RF) until task end. Ankle dorsiflexor, TA, activity also tended to increase throughout the exercise however, not significantly.

When cycling exercises are performed at maximal intensities, the task objective is not only to produce power, but the highest amount of power as possible. Presumably, to produce maximal power the system is already working in the single most effective coordinative strategy (144, 181, 182). Consequently, there is theoretically very limited, if any, solutions available to adjust pedalling strategy during maximal cycling exercises. Studies assessing muscle coordination have shown that changes can occur in the EMG activity, however unlike submaximal cycling exercise, the subjects are unable to maintain power output (32, 87, 145). For example, Hautier et al. (2000) (15 x 5-s repeated sprints with 25-s rest in between) and Racinais et al. (2007) (10 x 6-s sprints with 30-s rest between) reported that while force and power decreased as subjects repeat sprints, VAS activation remained unchanged. However, activity of the bi-articular HAM decreased over the series of sprints, reducing co-activation between the pair of muscles. From these results, the authors proposed that the force-generating capacity of VAS was reduced, therefore less force was required from HAM to transfer to the pedal so its activity is adjusted accordingly. Billaut et al., (2005) found after 10 x 6-s sprints (with 30-s recovery) the level of VAS and HAM activity was unchanged as power output decreased in the latter repetitions, but the onset of HAM activity shifted earlier in the pedal cycle in response to likely impairment in VAS force-generating capacity. In the study from Racinais et al., (2007) while they reported VAS activity remained unchanged between sprint repetitions, within each sprint variability in activation occurred between the early pedal cycles (cycle 2 and 3), which are considered to coincide with maximal power production (119). Billaut et al., (2005) showed that within sprints, the participants were unable to reach the same cadence for corresponding pedal cycles between sprint 1 and sprint 10. Additionally, in this study, along with Hautier et al., (2000), the maximal power produced in the later sprints was occurring at a lower cadence, and later in the sprint cycles. A limitation of these studies is that the relation between fatigue and reduction in power output may be inaccurate, as power is directly influenced by cadence.

The parabolic relationship between power and cadence means that, in a fatigue-free condition, when cadence is above or below that of optimal (C_{opt}), power output will be less than maximal (P_{max}), despite a maximal effort. From this relationship, every

cadence value has its own corresponding theoretical maximal power that can be achieved. Following this, power output between two cycling conditions may differ as a consequence of cadence, as opposed to force-generating capacity, as a given amount of force generated and transmitted to the pedals will result in a lower power output as cadence diverts further from optimal (either above or below). When considering the effects of fatigue, the relative reductions in power output will be influenced by the ability of an individual to accelerate the flywheel. When assessing alterations in sprint cycling with variable cadence, Gardner et al. (2009) highlighted the importance of taking into account this relationship, and provided an elegant solution for quantifying changes in power with fatigue. They calculated a 'pedaling rate index', which compared the power values obtained during a fatigued sprint to the power achieved at the same pedalling rate in a non-fatigued sprint. Using this method, the effect of fatigue directly on power output can be assessed, without cadence as a confounding factor (77). From the P-C calculations by Dorel et al. (2010), power output also significantly varies between phases of the cycle. To more accurately quantify power, individual P-C relationships, describing cadence-specific power, were calculated in this study for the downstroke and upstroke phases of the pedal cycle as well as for the left and right cranks separately. To the best of our knowledge this is the first study to quantify the relative changes in crank power with fatigue, specific to cadence, phase and side.

2.1.2.4 Changes in muscle coordination associated with fatigue in the knee extensors

While changes in pedalling strategy associated with a reduction in knee extensor force-generating capacity have been demonstrated in maximal and submaximal cycling, fatigue was induced by the cycling exercise itself, where it is likely fatigue in other muscles may have also occurred. This has been shown by Decorte et al. (2012), who intermittently measured maximal voluntary force (MVF) of the knee flexors as well as extensors, during a cycling task to failure at 80% of maximal power output. Knee extensor force was significantly reduced from 40% of total exercise time and continued to decline until failure. While not significant, knee flexor MVF also showed a progressive fall throughout the exercise until failure. In conjunction with MVF reductions, EMG from the knee extensors (VL and RF) and knee flexors, had significantly increased by 60% of exercise duration and continued to increase until

exercise completion. These combined observations could suggest that activity in both the knee extensors and flexors is increased in part due to muscular fatigue. As well as an attempt by the CNS to adjust intermuscular coordination as the increase in knee extensor activation was not sufficient to compensate for the reduction in force-generating capacity. Additionally, Elmer, et al. (2012) demonstrated that reductions in joint-specific power in sprint cycling, following a 10-min time trial, are not uniform, highlighting that different muscle groups are effected differently with fatigue in cycling (64). The effects of fatigue that has been isolated to the knee extensors on power output, muscle coordination and pedal forces during maximal cycling exercise is yet to be examined. Bieuzen et al. (2008) conducted a study investigating the effects of prior concentric (CC) and eccentric (ECC) knee extension contractions on constant load cycling. Knee extensor MVC force was reduced by ~18% after CC and ~16% after ECC with MVC EMG reduced for VL and HAM following only ECC. In a 10-min constant-load cycling exercise undertaken at 277 ± 27 W, significant increases in RF, VL and BF EMG where reported following the CC exercise, but not in the ECC condition. The CC exercise appears to cause force reduction at the muscular level resulting in increased neural drive to maintain power output, while ECC conversely, likely resulted in central fatigue, where neural drive to the muscles reduced. However, EMG was only recorded from VL, RF and BF so the contribution of other lower limb muscles is unknown, which are important for understanding pedalling strategy, due to the synergistic behaviour of the lower limb muscles (90, 143, 171). Furthermore, the reduction in knee extensor force (16 – 18 %) may have been insufficient to force the system to adjust motor command. Hence, a more comprehensive investigation into the effect of a high level of isolated fatigue in the knee extensors on cycling performance is yet to be undertaken.

2.2 Fatigue

Fatigue presents a complex phenomenon involving a large number of physiological pathways and mechanisms, whose interactions are still not fully understood (1, 3, 71, 73, 162, 163). Fatigue has commonly been defined as “any reduction in the force generating capacity of the total neuromuscular system regardless of the force required in any given situation” (29). While the net result of fatigue, *in vivo*, is typically identified by a measurable reduction in maximal force output of a specific muscle or muscle group (29, 73, 141), the mechanisms behind the loss of force can occur at

numerous sites along the neural pathway and excitation-contraction (E-C) coupling process within the muscle. Depending on the site of impairment fatigue can be categorized as either peripheral - occurring at or distal to the neuromuscular junction (NMJ) (transmission failure of neural signal, or failure of the muscle to respond to neural excitation) or central – proximal to the NMJ (failure of excitation of motoneurons) (25, 27, 73, 159).

2.2.1 Peripheral fatigue

The site of peripheral fatigue can be broken down into neuromuscular transmission failure (fatigue at the neuromuscular junction) or failure of excitation-contraction (E-C) coupling (22, 25, 159). While evidence of neuromuscular transmission failure exists, its involvement in fatigue following exercise in humans has been debated and argued to be negligible (25, 27, 58, 123). In light of this, the observed reduction in force with fatigue has been more readily attributed to failure of E-C coupling (3, 23, 71, 108). It has been well documented that repeated activation of the muscle fibre can lead to failure of any number of the mechanisms involved in the E-C coupling process. For example; 1) failure of excitation, (effecting the transmission of the AP along the sarcolemma and T-tubules), 2) reduced Ca^{2+} release from the sarcoplasmic reticulum (SR), 3) reduced Ca^{2+} sensitivity of myofibrillar proteins, 4) myofibrillar fatigue and 5) reduced Ca^{2+} re-uptake by SR (3, 58, 71) have all been identified as possible causes for impairment of E-C coupling.

2.2.1.1 High- and low-frequency fatigue

Since the work of Mosso in 1904, electrical stimulation has been widely used to characterise fatigue and identify where along the chain of events in E-C coupling impairments may have occurred (21, 97, 126, 129). By adjusting the frequency of stimulation distinct features of fatigue have been able to be identified (26, 61, 96). By comparing the ratio of force evoked from low frequency stimulation [below fusion frequency, 10 - 20 Hz (125)] to high-frequency stimulation [i.e. above fusion frequency, 50 – 100 Hz (125)] the predominance of high-frequency fatigue (increase in ratio) or low-frequency fatigue (reduction in the ratio) can be assessed.

High-frequency fatigue is characterised by a rapid recovery of force (within seconds) following reduction in stimulation frequency (97), associated with failure of excitation, disrupting AP propagation along the surface membrane (26). During *in vivo* human testing, reduced amplitude and lengthened duration of the compound muscle action potential (M-wave) shape of the fatigued muscle is associated with high-frequency fatigue, indicating altered transmission of the action potential (27, 96). Low-frequency fatigue is characterised by a slow recovery (59, 60), lasting hours or even days (13, 96), associated with a reduction in $[Ca^{2+}]_i$ released from the SR (89, 177) or damage to the central portion of the muscle fibre due to over-extension of the end sarcomeres during fatigue (98).

The gold standard for quantifying fatigue in human studies is tetanic stimulation. However, this can be quite painful and uncomfortable for subjects (125). Alternatively, doublet stimulations have been recommended as a surrogate, commonly at intensities of 100Hz (high frequency) and 10Hz (low frequency) (174, 179). A reduction in the size of the high frequency potentiated doublet resting evoked force represents the level of peripheral fatigue credited to impaired calcium kinetics within the cell, while changes in M-wave shape indicates impairment to cell membrane excitability. A reduction in the ratio of the size of the low frequency doublet to the high frequency doublet evoked force (10Hz:100Hz ratio) gives a measure of the prevalence of low-frequency fatigue (59, 126).

2.2.2 Central fatigue

The amount of force produced during a voluntary contraction, is the result of the number of motor units recruited and the discharge frequency of the motoneurons, controlled by the CNS (22, 31, 121). As peripheral fatigue develops, muscle contraction and relaxation slows and it has been observed that firing rates of the motoneurons are also reduced (115), with no reduction in M wave amplitude (i.e. normal AP conduction) (24, 178). Central fatigue arises with a decline in the number of motor units recruited and/ or when firing rates fall below what is necessary to produce maximal force, as voluntary activation is reduced (75). The mechanisms behind central fatigue in exercising humans aren't as well understood as those in peripheral fatigue (67, 72), but are known to occur at the spinal level or supraspinal segments (73, 75).

2.2.2.1 Central fatigue at the spinal level

Central fatigue at the spinal level is believed to be associated with afferent feedback from large-diameter, group Ia (spindles) and Ib (Golgi tendon organs) and small diameter group III and group IV afferents (73, 80). Increased activation of these small diameter afferents is commonly implicated in the decline of motoneuron excitability (5, 30, 79, 80, 138), likely through reflex inhibition.

2.2.2.2 Central fatigue at the supraspinal level

Evidence also exists of increased afferent firing indirectly attenuating cortical drive (110). At the supraspinal level, central fatigue describes the reduction in muscle activation owing to reduced output from the motor cortex. In human studies, suboptimal drive originating at the supraspinal level can be assessed using transcranial magnetic stimulation (TMS) (15, 74). Pin-pointing the interaction between, and exact mechanisms behind central fatigue may still be a working progress (73, 163). However, functionally, the occurrence of reduced central drive has been proposed as a protective measure against catastrophic failure of muscle contraction. For example, central fatigue is believed to regulate the amount of peripheral fatigue developed in the muscle to within a tolerable limit (based on feedback from group III/IV afferents) - preventing a state of complete failure or damage to the structures involved (1, 147) (5, 7, 146). In the present study TMS was not used, as such the mechanisms leading to central fatigue were not explored. Only the occurrence of central fatigue, differentiated from peripheral fatigue, using the twitch interpolation technique (ITT) was able to be assessed.

2.2.2.3 Interpolated twitch technique and voluntary activation

First described by Merton (1954), ITT involves electrical stimulation of the peripheral nerve to measure the level of voluntary activation (VA) to the fatigued muscle/group (123). A high intensity stimulus is delivered to the nerve while the subject performs a maximal voluntary contraction. An increment in force from the superimposed stimulus, above what is generated voluntarily, indicates submaximal recruitment of motor units (supraspinal) or suboptimal discharge rates (spinal level) (75). It has been well documented in numerous muscle groups (e.g. ankle plantarflexors (17), elbow flexors (4), adductor pollicis (88) and abdominal muscles (160)) that VA is less than 100% (i.e.

not maximally activated during voluntarily contraction) (67, 73). In the knee extensors the average VA from a number of studies using ITT, has been measured between ~90-96%, ranging from 87 - 99% (12, 44, 94, 114, 116, 127, 133, 136, 140).

The validity and value of ITT in assessing the existence of central fatigue has been repeatedly presented (36, 76, 140, 161) and similarly to high- and low-frequency fatigue assessment, the recommendation for ITT is to use high frequency paired pulses (i.e.100Hz) (55, 125, 126, 140). While supramaximal trains are the gold standard, this type of stimulation over a maximal voluntary contraction could potentially lead to cramping and in rare cases even injury has been reported (25). Hence for the comfort of the subject, high frequency doublets are advised (126). .

2.2.3 Fatigue in the knee extensors

While central and peripheral fatigue has been evident to occur within seconds during maximal sustained contractions (163), progression of fatigue during submaximal contractions varies with the exercise modality. For example, the development of fatigue at the various peripheral and central sites can differ between isometric vs. dynamic (i.e. concentric/ eccentric) contractions and intermittent vs. sustained contractions (28, 68, 101, 163, 175).

Looking at fatigue in the knee extensors, a study from Morel et al. (2014) found after 20 sets of isometric and concentric (30°/s and 240°/s) knee extension exercises, isometric contractions presented a larger reduction in VA and smaller reduction in resting twitch force compared to concentric exercise performed at low velocity, indicating a greater contribution of central fatigue following the isometric exercise. Likewise, Kay et al. (2000) reported greater central fatigue (from reduced MVC EMG) following maximal isometric contractions compared to concentric and also found a greater reduction in force at the end of exercise in the isometric condition (101). Following the results from maximal isometric contractions, Neyroud et al. (2012) reported that fatigue following submaximal isometric contractions (20% of MVC force) was also mostly related to central (and motivational) deficits. In their review Place et al. (2010) compared the results from numerous studies assessing fatigue in the knee extensors following sustained, isometric contractions between 15-80% of MVC, and

suggested that central fatigue becomes more influential in contractions performed at <30% of MVC force. When recovery time was compared between submaximal isometric knee extension exercise performed at different intensities (20%, 40% and 80% of MVC force), Rodriquez et al. (1993) reported that the lower the intensity, the longer it took for the participant to recover their MVC force (i.e. slowest recovery following 20% contraction) (150). Based on these findings it seems that substantial and long lasting fatigue can be induced in the knee extensors following sustained, low-intensity isometric contractions. The reduction in force-generating capacity is also likely to be associated with a high level of central fatigue, which could be confirmed by utilizing the ITT with high frequency doublets (126).

It has also been observed, more notably during isometric contractions, that as fatigue develops a progressive recruitment of other muscles can occur (73). Interestingly, the additional muscles recruited may provide no assistance to the action of the fatiguing muscle group (e.g. activation of the contralateral muscle group) (47). This phenomenon has been shown to occur in the absence of peripheral feedback, and is likely the result of a spread of excitation within the motor cortex (73).

2.2.4 Cross-over effect of fatigue

Numerous studies have suggested that central perturbations induced by fatiguing exercise in an isolated muscle group can lead to performance reductions in non-exercised muscles. This result has been shown between homologous and heterologous muscle groups (85, 100, 120) (83, 103, 104). As well as between ipsilateral and contralateral muscle groups (85, 100, 102, 103, 120, 148). The effect has been suggested to be muscle specific with lower limb muscles, in particular knee extensors, more susceptible to performance decrements than upper body muscle groups (85). Specifically looking at the knee extensors, when unilateral fatiguing exercises have been performed, a reduction in force-generating capacity was seen in the contralateral knee extensors (100, 120). The cause of the cross-over is believed to be primarily centrally mediated, as evidenced by a reduction in non-exercised knee extensor activation following contralateral knee extensor fatigue (48, 85, 120, 148).

The explanation for the cross-over is the inhibitory action of the group III/IV afferents, stimulated by fatigue in the exercising muscle, reducing motoneuron output to other muscles (8, 48, 148, 158, 166). While it is difficult to dissociate the prevailing mechanisms at work, there presents a case for both spinal (reflex inhibition) (48) and supraspinal (reduced cortical output) (102, 166), sites of impairment. There has also been evidence of a reduction in activation in non-exercised knee extensors following unilateral fatigue in the contralateral knee extensors, with no change in MVC force (148). Not all studies are in agreement about the occurrence of this 'cross-over effect' with numerous studies reporting no change in knee extensor force or activation of the contralateral limb following unilateral fatigue (9, 102). And to the contrary, Todd et al. (2003) suggested that the performance of unilateral sustained MVCs in the elbow flexors may incite a systemic response that aids in recovery of the rested limb and improves endurance performance in subsequent MVC efforts (166).

Given the discrepancy of these findings, it is important to assess the force-generating capacity of non-exercised muscle groups following single-joint exercises, as fatigue isolated to one muscle group could have potential implications on the performance of multi-joint, dynamic exercises, such as cycling, where multiple agonist/antagonists muscle groups are involved.

2.3 Effects of unilateral fatigue on performance of multi-joint exercises

While a number of studies have investigated the effects of isolated fatigue on non-exercised muscles during static and single-joint exercises (i.e. MVC), fewer studies have reported the effects during a dynamic, multi-joint task. Using cycling exercise, Elmer et al. (2013) assessed the effects of a 10-minute single-leg cycling time trial (TT) task on maximal power production (P_{max}) during a single-leg 4-5s sprint of the fatigued ipsilateral limb and rested contralateral limb (62). When testing the fatigued limb, the TT exercise resulted in a 22 ± 3 % decrease in P_{max}, 30-s post exercise completion. However, the results failed to reveal any cross-over effect on P_{max} in the rested limb. In this study a multi-joint exercise was used for the fatiguing protocol, meaning it is likely

that global fatigue of the lower limb muscles was induced and the effects of isolated fatigue in the knee extensors during the dynamic performance test are unknown.

2.3.1 Isolated fatigue in cycling exercise

To introduce a perturbation to a single muscle group significant enough to challenge the system, a substantial reduction in the force-generating capacity with long-lasting effects will need to be induced. While distinct variations in muscle activity are apparent between individuals during cycling exercise (35, 92), it is well established through EMG, mechanical and simulated studies that the knee extensors are highly influential in the amount of power able to be produced during both, maximal and submaximal exercise (2, 52, 63, 69, 81, 132, 183). It follows that a substantial reduction in the force-generating capacity of the knee extensors is likely to impact on power production and coordination of the lower limb muscles. While hip extension also contributes significantly to crank power (63, 117), it is difficult to isolate fatigue in this muscle group and subsequently test the force-generating capacity without contributions from other muscles. In light of this, practically, it is ideal to target the knee extensors and furthermore, they are a commonly studied muscle group in fatiguing and cycling exercises (6, 14, 20, 42, 45, 93, 111, 113).

The degree of reduced force-generating capacity and time of recovery is dependent on the type of exercise being performed, namely the intensity, duration and work-to-rest ratio involved (28, 68, 135, 139, 163). Typically, in the knee extensors isometric contractions performed at low intensity, for a sustained duration and high work-to-rest ratio, can induce large reductions in force-generating capacity, which can persist for prolonged periods (73, 163). As proposed by Bieuzen et al. (2008) the type of fatigue induced in the knee extensor muscles may determine the solution space available and how the system adapts, i.e. muscular fatigue increased muscle activity, while central fatigue led to reduced cadence (20). Using sustained isometric contractions, a high level of fatigue will be able to be induced and having them performed at low intensity (20% of MVC) should promote low-frequency fatigue, prolonging the effects of knee extensor force-generating capacity. This type of exercise is also typically associated with central fatigue, which is believed to be primarily responsible for the cross-over effect of fatigue in the contralateral limb (84, 141, 150, 163).

2.3.2 Effects of unilateral fatigue on cycling performance

Reducing the force-generating capacity of a primary power producing muscle during cycling exercise would intuitively impair the ability of the system to produce power. In order to maintain power output, it follows that the activity of other muscles will need to be altered to compensate. As discussed earlier, sprint cycling poses a more complex problem to the CNS as the solution space is reduced compared to submaximal cycling and alternate coordination strategies may not be available within the ipsilateral or contralateral limb.

From the synergies identified by Raasch and Zajac (1999) and Hug et al. (2010), VAS are active with ipsilateral GMAX to produce the majority of force during the downstroke phase. With reduced contribution from VAS, maintaining power output during the propulsive downstroke phase may lead to a heavier contribution of GMAX. However, theoretically all muscles are already operating maximally during sprint cycling exercise (151) so it is unlikely GMAX could compensate during the downstroke. The ability of the system to produce power during the upstroke phase of the pedal cycle is seemingly unimpaired. While typically substantially less force is produced over the upstroke compared to the downstroke, propulsive forces of lower amplitude are transferred to the crank through the activation of the hip and knee flexors, RF and HAM respectively, and ankle dorsiflexors, TA. During sprint cycling Dorel et al. (2012) showed peak TA EMG was 76% of isometric maximal activation, while BF and SM reached 71% and 60%, respectively. These values may be misleading however, as when normalized to isometric maximal voluntary EMG, this does not necessarily reflect the activation capacity during cycling exercise (151). During submaximal cycling exercise there is still room for the CNS to increase the activation of these muscles during the upstroke, however, this may not be the case for maximal cycling exercise. This strategy was reported during a fatiguing submaximal cycling exercise by Dorel et al. (2009), when cycling to failure at 80% of maximal power tolerated. EMG activity in GMAX, BF, SM and RF at the end of the exercise, compared to the start, suggested pedalling adaptations to increase knee and hip flexion power by actively pulling up on the pedal as well as increasing extension power through the hip on the ipsilateral side. By isolating fatigue to the knee extensors, however, RF will also be

fatigued and likely to a greater level than VAS due to the high percentage of type II muscle fibres typically found in this muscle (~62% in RF and ~53% in VAS) (95). Also, activation of the knee flexors may be effected by the unilateral fatiguing exercise (102) which could impact on their ability to produce force.

Alternatively, with the novelty of this study implementing isolated unilateral fatigue of the knee extensors during cycling exercise, the CNS may be lead to increase muscle activity during the coinciding flexion phase of the contralateral limb to assist crank propulsion. As well as potentially increasing activation during the contralateral extension phase to maintain power output over the total crank cycle. But, as discussed above, presumably, the system is limited in alternate strategies during sprint cycling. Additionally, the coordinated coupling identified in the inter-limb agonist-antagonist pairs (164, 165) could limit the ability of the system to independently adjust muscle activation of the two lower limbs. With changes in activity of the muscles throughout the pedal cycle it is anticipated that alterations in the forces applied to the pedals will follow and consequently impact the effectiveness of the adopted strategy (185).

While numerous studies have presented changes in muscle activity following fatigue in the knee extensors, not all have incorporated neuromuscular testing to quantify the magnitude of fatigue in this muscle group t. Using neuromuscular testing Decorte et al. (2012) demonstrated that cycling to failure at 80% of maximal power output induced significant central (VA reduced by ~6%) and peripheral fatigue (resting twitch force reduced by ~45% of baseline) in the knee extensors. With this, an increase in BF EMG activity was reported, suggesting increased knee flexion during the pedal cycle relating to fatigue in the knee extensors. Similarly, the reduction in knee extensor force was correlated with increased EMG activity (approximately doubled from baseline) in RF, a bi-articular hip flexor, but it is likely that this increase may be due to a high level of fatigue developing in RF. The findings of this study are limited by the absence of EMG recordings from GMAX and the ankle plantarflexors and dorsiflexors (GAS, SOL and TA). Referring to the identified synergies (92, 143), BF is activated with GAS and SOL whose main function is to transfer power from GMAX and VAS to the pedal. Given that GMAX, BF and SM activity has been altered with knee extensor fatigue it is likely that activation of the ankle plantarflexors will also be effected. This is evidenced by results from Dorel et al. (2009) during submaximal cycling exercise and O'Bryan et al.

(2014) during a 30-s maximal sprint, where towards the end of the exercise GAS activation was significantly decreased. But again, these studies did not include neuromuscular testing so the effects cannot be definitively associated with the level of fatigue in the knee extensors. Without including EMG activity from both lower leg and upper leg muscles and utilising neuromuscular testing it cannot conclusively be said what the effects are of fatigue of the knee extensors on muscle coordination, pedal forces and ultimately crank power. The study from O'Bryan et al. (2014), was previously done in this laboratory and the current study aims to extend on this work by investigating how muscle coordination and crank power is altered during a maximal cycling sprint when a known level of fatigue is isolated to the knee extensors prior to cycling exercise. Additionally, if the maximal cycling exercise time is reduced (i.e. from 30-s to 6-s) fatigue occurring in other lower limb muscles as a result of the cycling exercise is limited, so mechanical and EMG changes can be more closely related to knee extensor fatigue. Inducing fatigue unilaterally in the knee extensors will also provide some insight into inter-limb changes in muscle coordination and power output, along with intra-limb changes discussed by O'Bryan et al. (2014).

The aims of this study were therefore to investigate the effects of a known level of fatigue in the unilateral knee extensors on;

- Production of crank power from the ipsilateral and contralateral sides during the downstroke and upstroke phases of the pedal cycle
- Forces applied to the pedals and activation of the muscles in the ipsilateral and contralateral sides during maximal sprint cycling

With a substantial loss of unilateral force-generating capacity in the knee extensors it is hypothesised that crank power during the downstroke phase from the ipsilateral limb will be significantly reduced, along with a reduction in peak EMG of the ipsilateral knee extensors (VL, VM and RF). It is not expected that the unilateral fatiguing knee extension exercise will impact on the IMVC force or peak EMG of the contralateral knee extensors. As the participants are performing a maximal cycling exercise, we do not expect to see increased power during the upstroke on the ipsilateral side, or either downstroke or upstroke from the contralateral side to try and compensate. Additionally, as the lower limb muscles are theoretically maximally activated during sprint cycling,

it is anticipated that EMG activity from the lower limb muscles (other than ipsilateral VL, VM or RF) will be similar during the maximal cycling exercise, before and after the unilateral fatiguing exercise. We do expect that the perturbation introduced by the unilateral knee extension fatigue will increase the variability of the force and EMG profiles, as the participants try to adapt to the loss of force-generating capacity in a major power-producing muscle group during an all-out cycling exercise.

CHAPTER 3. METHODS

3.1 Participants

12 recreationally active males (n = 9, 28.2 ± 3.3 yrs, 83.3 ± 15.4 kg, 183.0 ± 6.4 cm) and females (n = 3, 27.7 ± 1.5 yrs, 67.6 ± 4.8 kg, 171.1 ± 3.3 cm) participated in this study. Participants were recruited from Victoria University and the wider community through flyer advertisements. All participants were involved in at least one sport or exercise session per week. Before giving their informed consent, all testing procedures and associated risks were fully explained and the participants were asked to complete a risk factor assessment questionnaire to screen for health risks and other exclusion criteria, which included; cardio and respiratory conditions and lower limb injuries that occurred within 3 months of the trial, or involved structural damage (i.e. knee surgery). Ethical approval was given by the Victoria University Human Research Ethics Committee (Application ID: HRE15 – 041) and the study was conducted in accordance with the Declaration of Helsinki.

3.2 Study design

Participants were required to complete 3 separate testing sessions, conducted in the muscle function laboratory at Victoria University, Footscray Park campus. Testing sessions were performed at the same time of day, between at least 1 and no more than 10 days apart. Participants were asked to refrain from strenuous exercise in the 24 hours prior to testing (see Figure 3.1 for overview). During *session 1,* participants were familiarised with the fatiguing unilateral knee extension exercise and electrical stimulation of the left femoral nerve to be performed in *session 3*. This session was also used for screening, to ensure the fatiguing unilateral knee extension protocol could induce the required reduction in knee extensor force in each of the subjects. *Session 2* involved a force-velocity test on a bike ergometer to characterise the population and determine the external resistance for the maximal cycling exercise performed in *session 3,* before undergoing a familiarisation of the cycling exercise. The main testing session, *session 3,* required participants to perform a maximal cycling exercise before and immediately after, a fatiguing isometric unilateral knee extension exercise (FAT_{ISO}). From this session, the effects of isolated, unilateral knee extension exercise on power production and muscle activation during maximal cycling were investigated.

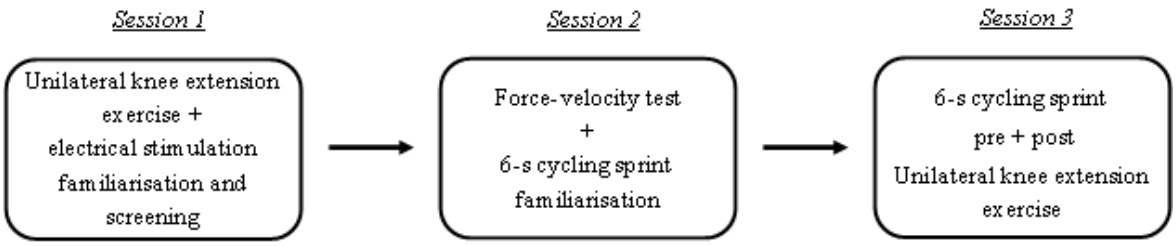


Figure 3.1: Protocol overview.

3.3 Equipment

3.3.1 Force measurements

All knee extension exercises, including force and electrical stimulation measurements, were performed seated on a dynamometer (Cybex, CSMi, Stoughton, USA) with a hip and knee angle of 90°. The Cybex was fitted with straps that fastened across participants' chest and shoulders, as well as a Velcro strap secured across the hips, to limit involvement from other muscles during voluntary and electrically induced knee extensions.

3.3.1.1 Left knee extensor force

Force from the left knee extensors was measured through a load cell (AMS-1 S Type, AWE, Ingleburn, Australia), supported by a custom-built frame connected to the base of the Cybex. Participants wore a padded ankle strap that clipped onto a steel rod, forming a rigid connection with the load cell (Figure 3.2). The frame was constructed with multiple height adjustments to accommodate different leg lengths of the participants, to allow a horizontal connection between the ankle and load cell. The force trace was recorded and stored, through the EMG software (detailed in 3.3.2) to allow synchronized force and EMG recordings. Force data from the load cell was amplified (gain = 500) and digitized online at a sampling rate of 1500Hz.

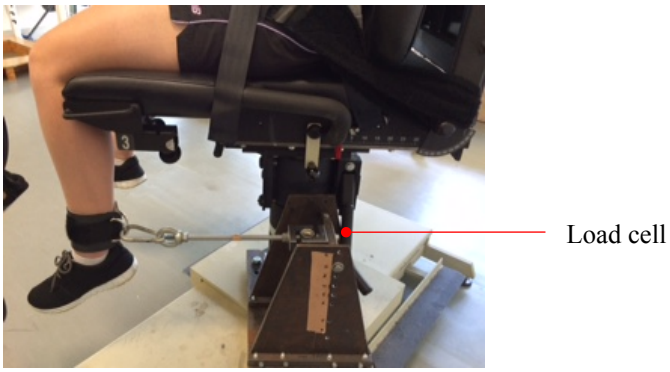


Figure 3.2: Cybex set-up for knee extension exercises with the left leg. The load cell used for force measurements and was supported by a custom-built frame.

3.3.1.2 Right knee extensor force

Due to equipment restrictions, only one load cell was available during testing, so participants performed maximal isometric knee extensions with the right leg against a fixed lever arm connected to the Cybex. Torque was measured from the right knee extensors through the Cybex software and digitized online at a sampling rate of 100Hz. The torque data was stored in the Cybex software and later converted to force by dividing by the length of the lever arm (m). The axis of rotation was aligned with the lateral femoral condyle, with the arm positioned just above the right ankle. Due to set-up limitations, the lever arm extended across the left and right legs, so to avoid impacting on the left leg, the lever arm was set to a knee angle of 80° for the right leg (0° = full extension).

3.3.2 Electromyography (EMG)

EMG activity was recorded wirelessly (Telemyo DTS, Noraxon USA Inc., Scottsdale, AZ) from *vastus lateralis* (VL), *vastus medialis* (VM), *rectus femoris* (RF) and *biceps femoris* (HAM) on both the left and right legs. From the left leg only; *gluteus maximus* (GMAX), *tibialis anterior* (TA), *lateral gastrocnemius* (GAS) and *soleus* (SOL) were also recorded (Figure 3.3). The additional distal muscles were unable to be recorded from the right leg due to the number of recording channels in the EMG system. The signals were digitized in real time at a sampling rate of 1500Hz and stored using the Noraxon software (MyoResearch XP Master Edition, V1.08.27, Noraxon USA Inc., Scottsdale, AZ). Dual surface electrodes of 10mm diameter and inter-electrode distance of 20mm (Noraxon dual electrodes, Noraxon USA Inc., Scottsdale, AZ) were positioned across the direction of the muscle fibres over the belly of the muscle, identified by palpation. The electrode sites were prepared by shaving, lightly abrading and cleaning the skin with an alcohol swab to reduce impedance before applying the self-adhesive electrodes.

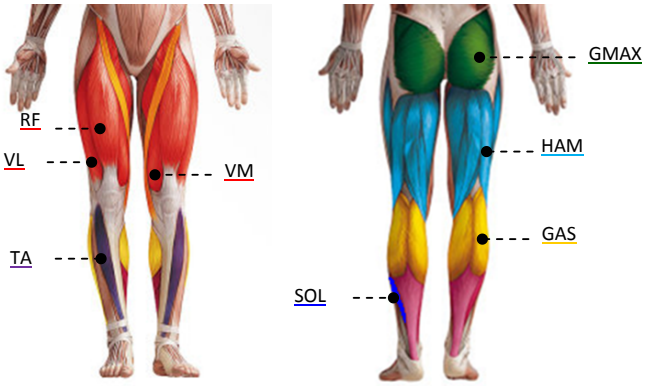


Figure 3.3: Surface EMG recorded from lower limb muscles. Vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF), and biceps femoris (HAM) were recorded from both the left and right legs. Gluteus maximus (GMAX), tibialis anterior (TA), lateral gastrocnemius (GAS) and soleus (SOL) were recorded form the left leg only.

3.3.3 Electrical stimulation

Electrical stimulation was performed using a high-voltage stimulator (Digitimer DS7, Hertfordshire, UK). A square self-adhesive anode (5cm x 9cm) was positioned in the left gluteal fold and a ball probe cathode was pressed over the femoral nerve during stimulations. 100Hz high-frequency doublet stimulations were used to assess voluntary activation and resting evoked force of the left quadriceps (140). 10Hz low-frequency stimulations were also administered to assess the prevalence of low-frequency fatigue (174) (calculation outlined in section 3.4.1). Additionally, VL and VM compound action potentials (M-waves) were obtained from the 10Hz doublets. At the time of testing, we did not have equipment available to perform electrical stimulation on the right femoral nerve as well as the left side, so these measurements were only made for the left quadriceps.

3.3.4 Bike ergometer

All cycling exercises were performed on a custom-built bike ergometer fitted with 172.5mm instrumented cranks (Axis, Carole Park, Australia) and 11-speed hub gearing system (Shimano Alfine SG-S700, Osaka, Japan). Crank angle, tangential torque and radial forces applied to the left and right pedals were recorded at 100Hz using Axis software (Swift Performance Equipment, Australia). Instantaneous total power output and cadence were displayed in real-time on a laptop computer connected to the cranks. At the beginning of each testing session a static calibration of the instrumented cranks

connected to the software was performed. The bike was fitted with clipless pedals (Shimano PD-R540 SPD-SL, Osaka, Japan) and participants were provided with cleated bike shoes (Shimano SH-R064, Osaka, Japan). Vertical and horizontal adjustments of the seat and handlebars were made for each participant and recorded so the bike was set-up with the same dimensions during each session.

3.4 Data processing

3.4.1 Force measurements

Force data from the knee extensors was analysed using motion capture software (Visual 3D, v5 C-Motion Inc., Germantown, USA). Raw force traces were lowpass filtered (Butterworth 30Hz). Maximal voluntary force (MVF) from the right and left knee extensors was measured from 3-s isometric maximal voluntary contractions (IMVC). MVF was then calculated as the average force over a 250ms window, 125ms either side of the instantaneous peak force. In the left leg, if the peak force occurred within 125ms of the electrical stimulus artefact, MVF was taken over the 250ms period before the artefact. Baseline MVF from the left and right knee extensors was considered as the highest value from 3 baseline measurements. Real-time processing was used to normalize the left knee extensor force signal to the highest baseline MVF measurement within the testing session. At the end of the sessions, raw force traces were exported from the EMG software and re-normalized to the MVF calculated from the filtered force trace in the software for further analysis.

During the baseline and final MVF measurements of the left knee extensors, voluntary activation was calculated from a 100Hz doublet stimulation superimposed over the contraction when a plateau in MVF was seen. The superimposed twitch force (SIT) was calculated by subtracting the force at the time the stimulus was delivered, from the peak increment in force from the stimulus. Following the IMVC resting 100Hz and 10Hz doublets were delivered, 3-s apart, in a randomized order over the left femoral nerve (Figure 3.4). Resting potentiated evoked force (R_{EF}) was calculated from the peak 100Hz evoked force. At baseline, R_{EF} was reported as the highest value from three trials. Voluntary activation (%VA) of the left quadriceps was calculated from the SIT and R_{EF} using the equation; $\%VA = 100 \times [1 - (SIT/R_{EF})]$ (161). On occasion, the superimposed stimulus was delivered after the peak force was reached and had started

to decline. To account for this, a correction was applied whereby %VA = [1 - (SIT × voluntary force just before SIT/maximal voluntary force)/ R_{EF}] × 100 (140). To assess the prevalence of low-frequency fatigue, the ratio between the 10Hz and 100Hz peak evoked force (10:100) was calculated (174).

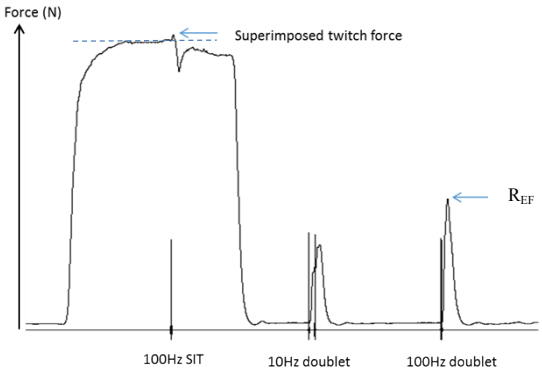


Figure 3.4: Force trace from 1 participant of an isometric maximal voluntary contraction (IMVC) of the left knee extensors. A 100Hz doublet stimulation was delivered over the contraction to record the superimposed twitch force. 100Hz doublet and 10Hz doublets were given at rest to measure resting evoked force (R_{EF} and 10:100 calculation) and maximal M-waves from VL and VM (via 10Hz doublet).

During FAT_{ISO}, the average force of each submaximal contraction (target 20% of MVF) was calculated over the time period when normalized force was above 17%. i.e. the start of the contraction, where force was increasing to 20%, and the end of the contraction, where force was decreasing from 20% to relaxation, were not included (Figure 3.5).

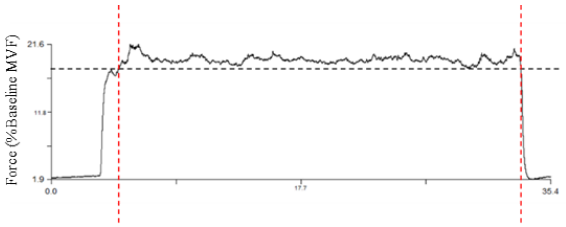


Figure 3.5: Force trace from 1 participant during a submaximal sustained isometric contraction with the left leg. The average force was measured when the normalized force was above 17% of MVF, indicated by the grey dashed line (target was 20%).

3.4.2 Electrical stimulation

The optimal stimulation site and supramaximal stimulus intensity were determined at the beginning of the session. To find the optimal site, single stimuli of low intensity (60mA) were delivered to multiple sites over the femoral nerve. The site corresponding

to the largest twitch force was determined as the optimal stimulation site and was marked in pen to be used throughout the session. To determine the supramaximal stimulus intensity a recruitment curve was performed. Two, single stimuli were given at 20mA and then at increasing 10mA increments, until a plateau was reached in the twitch force (i.e. no further increase in twitch response despite an increase in stimulus intensity) (Figure 3.6). The maximal intensity was confirmed by a plateau in maximal M-wave amplitude of VL and VM. The supramaximal intensity was calculated as 130% of the maximal intensity and used for the remainder of the session (group average = 181 ± 53mA). This intensity was chosen as it has been shown that stimulating at 150% of maximal intensity can cause considerable discomfort for participants with doublet stimulations. Additionally, it can increase antagonist co-activation of the hamstrings. While stimulating at 120% yielded similar measures of voluntary activation and resting twitch force as the 150% intensity, but was more tolerable (134). It was also noted that decreasing intensity (100% of maximal) can lead to an over estimation of peripheral fatigue (reduced R_{EF}). Hence, 130% supramaximal intensity was used to minimise discomfort to the participants, as well as minimise error in the R_{EF} measurement.

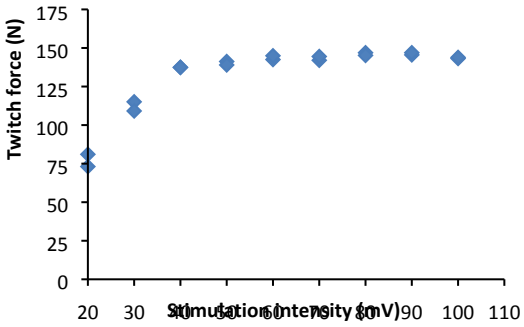


Figure 3.6: Recruitment curve from 1 participant.

3.4.3 Mechanical cycling data

Mechanical data recorded during cycling exercise was analysed using motion capture software (Visual 3D v5, C-Motion, Inc., Germantown, USA). Raw torque and radial force (F_{rad}) signals were lowpass filtered (Butterworth 10Hz). Tangential force (F_{tan}) was calculated from the measured torque signal (N.m) / crank length (0.1725m). Total force (F_{tot}) applied to the left and right pedals was calculated from tangential and radial forces for the left and right cranks;

$$F_{tot} = \sqrt{F_{tan}{}^2 + F_{rad}{}^2}$$

Within the software, crank position was identified when the crank passed top dead centre (TDC) and bottom dead centre (BDC) and the time between the events was calculated as cycle duration (s). Cadence was calculated over a full pedal cycle for the left (LTDC-LTDC) and right cranks (RTDC-RTDC) for analysis of the force-velocity test in *session 2,* using the formula;

$$cadence\ (RPM) = \frac{60}{cycle\ duration\ (s)}$$

For *sessions 2* and *3*, cadence was calculated over the downstroke (TDC – BDC) and upstroke (BDC-TDC) phases of the pedal cycle for the left and right cranks;

$$cadence\ (RPM) = \frac{30}{cycle\ duration\ (s)}$$

As the cranks are mechanically coupled, left downstroke cadence is also right upstroke cadence and left upstroke cadence is also right downstroke cadence. For simplicity, the cadence results for *session 3* are reported for the left and right downstroke phases. i.e. left downstroke cadence also refers to right upstroke cadence and right downstroke cadence also refers to left upstroke cadence.

Power was calculated over a full pedal cycle ($P_{0\text{-}360°}$) for *session 2*, from the total of both cranks and for the left and right cranks separately, using the average torque;

$$P_{0-360°} = \frac{torque\ (N.m)\ \times 2\pi}{cycle\ duration\ (s)}$$

Power from the left and right cranks separately was calculated over the downstroke ($P_{0\text{-}180°}$) and upstroke ($P_{180\text{-}360°}$) phases of the pedal cycle for *session 2* and *3*, from the equation;

$$P_{180°} = \frac{torque\ (N.m)\ \times \pi}{cycle\ duration\ (s)}$$

3.4.3.1 Force-velocity test (session 2)

The data was analysed during the session to plot crank power vs. cadence points of each full pedal cycle from the combined sprints (Figure 3.7A). Separate plots were created

for the left crank, right crank and total (left + right cranks). For each plot, the maximal power value at each 5RPM cadence interval (i.e. maximal power between; 0-5RPM, 5-10RPM, 10-15RPM…, -200RPM) was selected. Using 3rd order polynomial regression, individual power-cadence (P-C) relationships were described from the selected maximal points (10, 180) (Figure 3.7B). From the equation of the modelled relationships, the power value at the apex was extrapolated and reported as maximal power (P_{max}) and the corresponding cadence value reported as optimal cadence (C_{opt}) (Figure 3.7B). P_{max} was normalized to body mass (W/kg) for each participant to characterise the population. Torque-cadence (T-C) relationships were described using 2nd order quadratic polynomial regressions from the maximal torque values corresponding to the maximal P-C points selected (Figure 3.7C). From the modelled T-C relationship, torque intercept (T_0, i.e. where cadence = 0) and cadence intercept (C_0, i.e. where torque = 0) values were extrapolated to characterise the population.

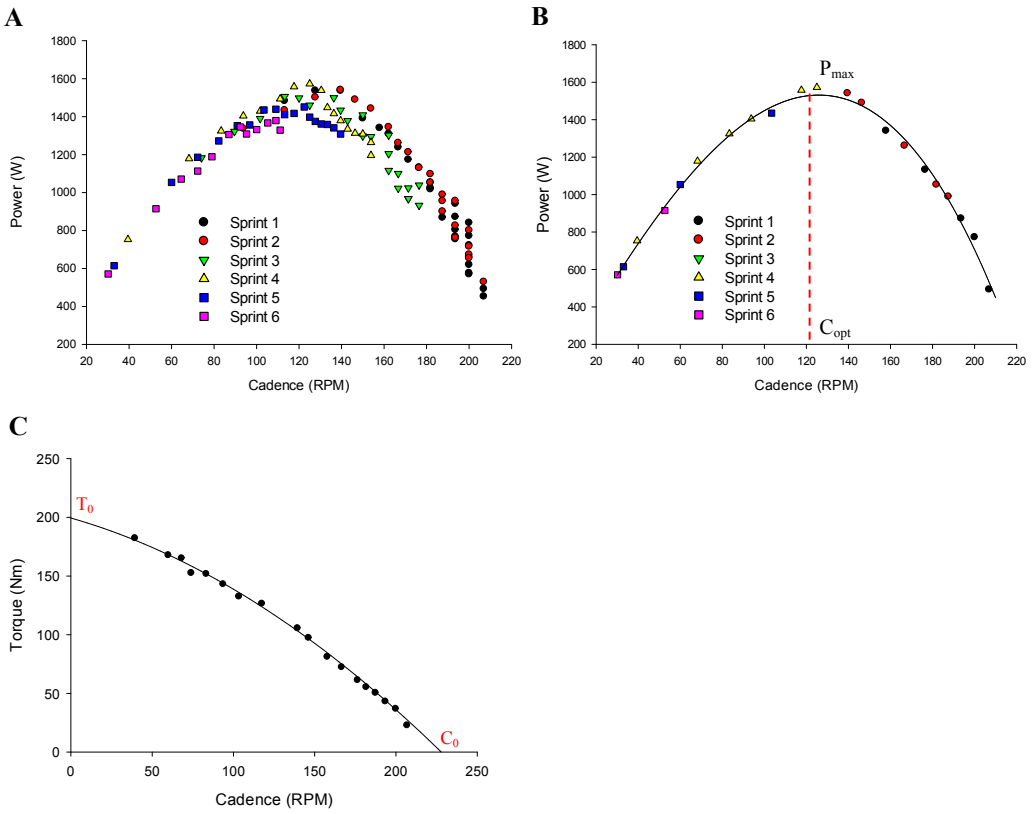


Figure 3.7: Calculation of maximal P-C and T-C relationships for 1 participant. A) All power vs. cadence data points from each sprint performed during the F-V test. B) Modelled P-C relationship using 3rd order polynomial regression from the maximal power values selected at each cadence interval. Dashed red line; C_{opt} corresponding to P_{max}. C) Maximal T-C relationship. Maximal torque is extrapolated from the curve where torque intercepts, i.e. cadence = 0 (T_0). Maximal cadence is extrapolated from the curve where cadence intercepts, i.e. torque = 0 (C_0).

Post testing, maximal P-C and T-C relationships were also calculated for the separate phases of the pedal cycle (downstroke and upstroke) and for both the left and right sides. As power is effected by variations in cadence, these relationships were used to describe the theoretical maximal power each participant could produce for a specific cadence. Additionally, power varies with the different phases of the pedal cycle (i.e. downstroke power is much higher than upstroke) and also between the left and right sides, so the maximal P-C relationships are able to calculate power specific to side, phase and cadence during maximal cycling exercise. To the best of our knowledge this is the first study to use this methodology and will allow us to more accurately relate changes in unilateral knee extensor force with changes in crank power. The power produced during *session 3* was quantified relative to the maximal cadence-, side- and phase-specific power (calculation outlined below). Total power over each full pedal cycle was calculated from the sum of the downstroke and upstroke maximal power. The contribution of power produced during each phase (i.e. downstroke vs. upstroke) was then expressed as percentage of the total power over a full pedal cycle.

Linear regression was used to correlate MVF of the left knee extensors at baseline during *session* 3 with; P_{max} and T_0 calculated over the downstroke from the left crank. Linear regression was also used to calculate the correlation between the reduction in MVF (% from baseline) of the left knee extensors in *session 1,* and the reduction in left crank power (%) over the downstroke phase during maximal cycling exercise after FAT_{ISO} in *session 3*. This was to see if individuals who recovered more quickly after the knee extension exercise also had less of a reduction in power during cycling exercise after the knee extension exercise.

3.4.3.2 Maximal cycling exercise (session 3)

During *session 3*, data from the maximal cycling exercise was analysed from the first 6 pedal cycles, starting with the left crank at top dead centre (LTDC). Force (F_{tan} and F_{tot}) recordings during maximal cycling were time normalized to create profiles of the first 6 pedal cycles for the left and right cranks separately (LTDC = 0/100%, RTDC = 50%). An average force profile from the 6 cycles was created for each participant. Peak F_{tan} and F_{tot} was reported from the profiles of the individual cycles. The percentage of the pedal cycle (%cycle) where the peak force occurred was reported from the average

profile. Cross-correlation coefficients (r_{xy}) were calculated to measure if there was a shift in the time domain (% of pedal cycle) of the average force profiles between baseline and post FAT_{ISO}. This technique has been used to provide a more objective measure of changes in profiles, as it takes into account the shape of the profile. This method can detect more subtle variations in the shape of the profile as well as the timing of the EMG burst (51, 112). r_{xy} was calculated for F_{tan} and F_{tot} for the left and right cranks using the equation from Li and Caldwell (1999);

$$r_{xy}(k) = \frac{c_{xy}(k)}{\sqrt{c_{xx}(0)c_{yy}(0)}}$$

where;

$$c_{xy}(k) = \begin{cases} \sum_{t=1}^{N-k} (x_t - \bar{x})(y_{t+k} - \bar{y}) + \sum_{t=N-k+1}^{N} (x_t - \bar{x})(y_{t-N+k} - \bar{y}) & k = 1, 2, \ldots, (N-1) \\ \sum_{t=1}^{N} (x_t - \bar{x})(y_t - \bar{y}) & k = 0 \end{cases}$$

$$c_{xx}(0) = \sum_{t=1}^{N} (x_t - \bar{x})^2$$

$$c_{yy}(0) = \sum_{t=1}^{N} (y_t - \bar{y})^2$$

For the analysis;

x= the time series of data from the baseline profile

y = the corresponding time series profile after FAT_{ISO}

N = the number of data points for each series

k = the time shift of the series after FAT_{ISO} with respect to the baseline series (i.e. % of pedal cycle).

The correlation when k = 0, $r_{xy}(0)$, indicates how closely the force profiles match between the maximal cycling exercises at baseline and after FAT_{ISO}. r_{xy} values were

calculated with k values between -25 and +25. The k value returning the highest r_{xy} indicates the % of pedal cycle the profile from the cycling exercise performed after FAT_{ISO} had shifted compared to the baseline sprint. Negative k values indicate a shift later (to the right of the profile) and positive k values indicate a shift earlier (to the left) in the pedal cycle (Figure 3.8). The 95% confidence interval of the highest cross-correlation value, $r_{xy}(k)$, was calculated as per the calculations from Li and Caldwell (1999);

$$\left(\frac{e^{2h_1}-1}{e^{2h_1}+1}, \frac{e^{2h_2}-1}{e^{2h_2}+1}\right)$$

Where; $h_1 = \frac{1}{2}\ln\left(\frac{1+r_{xy}}{1-r_{xy}}\right) - 1.96/\sqrt{N-3}$, and $h_2 = \frac{1}{2}\ln\left(\frac{1+r_{xy}}{1-r_{xy}}\right) + 1.96/\sqrt{N-3}$

The 95% CI was used to determine if the k value was significant, as detailed in the Li and Caldwell paper (112).

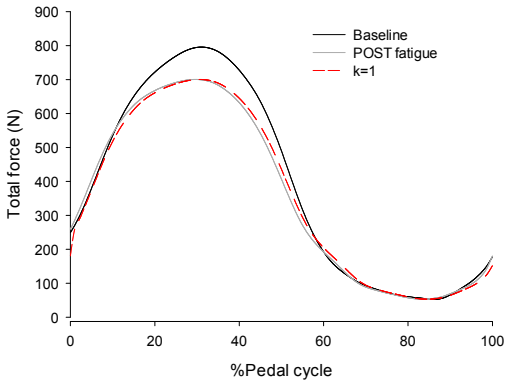


Figure 3.8: Calculation of cross-correlation coefficient of the left crank total force (F_{tot}). Solid line = average F_{tot} profile before the knee extension exercise (baseline), grey line = average F_{tot} profile after the knee extension exercise. Max r_{xy} occurred when k = 1, i.e. Post knee extension exercise profile shifted 1% earlier in the pedal cycle with respect to the baseline profile. Red dashed line = transposed post knee extension exercise profile when k= 1.

Intra-individual variability of the tangential and total force profiles was assessed by calculating the variance ratio (VR) (151), using the equation;

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

Where; $\overline{X} = \frac{1}{k}\Sigma_{i=1}^{k}\overline{X}_i$

VR was calculated between the force profiles from the 6 cycles during the maximal cycling exercises, performed before and after FAT_{ISO} for each participant.

Power output measured over each cycle of the maximal cycling exercises performed during *session 3* was expressed in percentage of the fatigue free P-C relationship modelled during *session 2*. The relative power was used to verify the sprint performed before FAT_{ISO} (baseline sprint) was maximal. More importantly it was also used to quantify crank power during the maximal cycling exercises specific to cadence, side and phase of the pedal cycle. Relative power (%) was calculated for the downstroke and upstroke phases and for the left and right cranks. Each power value from the 6 cycles was compared to the corresponding power value at the same cadence from the maximal P-C relationship (Figure 3.9). The percentage difference between the measured power value from *session 3* and the modelled power value from *session 2* was calculated for each cycle (77). The average difference from the 6 cycles was reported as relative power (%).

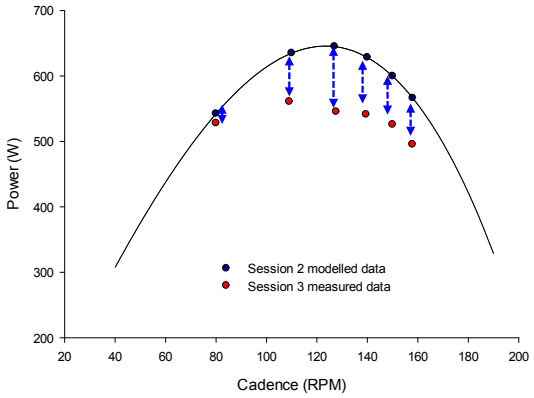


Figure 3.9: Calculation of relative power (%) from the left crank of 1 participant. Blue arrows indicate the difference calculated between the maximal fatigue-free power from *session 2* (black circles) and the measured power during *session 3* (red circles).

3.4.4 EMG

All EMG data was analysed post testing using the Visual 3D software, except the M-wave traces from VL and VM electrical stimulation, which were analysed using different software (Spike2 v7.13, Cambridge Electronic Design Limited, Cambridge, England).

3.4.4.1 M-waves

M-waves elicited from the second pulse of the 10Hz doublet were analysed and reported (153). Maximal M-wave peak-to-peak amplitude (M_{max}, mV), peak-to-peak duration ($M_{dur,}$ ms) and area under the positive and negative curves (M_{area}, mV·s) were calculated for VL and VM of the left leg (Figure 3.10).

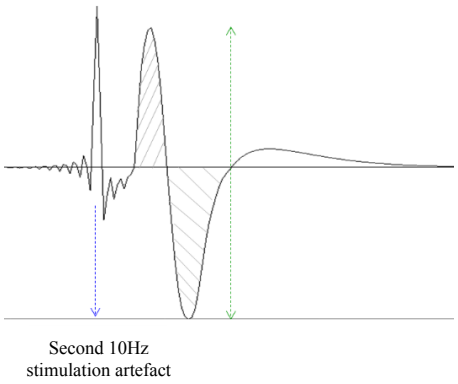


Figure 3.10: M-wave trace from the left VM of 1 participant. M_{max} was calculated between the positive and negative peaks (green dashed arrow). M_{area} was calculated within the shaded areas.

Raw EMG signals from the knee extension and cycling exercises were highpass filtered (20Hz), lowpass filtered (500Hz), full wave rectified and further lowpass filtered (7Hz) to create linear envelopes.

3.4.4.2 Unilateral knee extension exercise (FAT_{ISO})

Peak EMG during IMVCs was calculated over a 250ms period corresponding to peak force for the knee extensors (VL, VM and RF) and knee flexors (HAM). During FAT_{ISO} with the left leg, average EMG from VL, VM, RF and HAM was measured over the time period when normalized force was above 17%, corresponding to the force measurement (described in 3.4.1). VL and VM EMG from the left leg was normalized to M_{max} to account for peripheral factors and better quantify a reduction in central drive (125). EMG for VL, VM, RF and HAM from right leg, along with RF and HAM from the left leg were normalized to peak IMVC EMG. Knee flexor MVF was unable to be measured, hence, HAM EMG was normalized to the maximal EMG during knee extension IMVC.

3.4.4.3 Maximal cycling exercise

During *session 3*, data from the maximal cycling exercises was analysed from the first 6 cycles, starting from LTDC. EMG recordings from all the left and right leg muscles were time normalized to create profiles over the first 6 pedal cycles (LTDC = 0/100%, RTDC = 50%). An average profile was created for each muscle and each participant. VL and VM EMG during the maximal cycling exercises were normalized to M_{max} from the corresponding baseline or post FAT_{ISO} M-wave measurement. EMG from the other muscles were normalized to the peak EMG from the sprint profiles. Peak EMG was reported as the average of the peaks from the 6 individual profiles for each participant. The percentage of the pedal cycle (%cycle) where the peak occurred was reported from the average profile. To measure if there was a shift in the time domain (% of pedal cycle) of the EMG profiles after FAT_{ISO} compared to baseline, cross-correlation coefficients (r_{xy}) were calculated for all muscles from the equation outlined above in 3.4.3.2. For reporting the results, the muscles were classified as 'downstroke' or 'upstroke' muscles depending on where the peak activation occurred. The downstroke muscles consisted of; VL, VM, RF, HAM, GMAX, GAS and SOL. Peak RF activation from the profiles appear to be during the upstroke, but are classified as downstroke muscles accounting for electromechanical delay. Only TA is considered as an upstroke muscle.

Intra-individual variability for each of the left and right leg muscles was assessed using the VR equation described above (see 3.4.3.2). VR was calculated between the 6 individual cycles during the baseline sprint and the sprint post FAT_{ISO}, to assess within-subject variability of muscle activation.

3.5 Experimental design

3.5.1 Session 1: Evaluation of knee extensor function

21 individuals completed this session, assessing MVF and resistance to fatigue of the knee extensors for each individual. During this session, participants were familiarised with electrical stimulation of the left femoral nerve, IMVC of the left and right knee extensors and FAT_{ISO} (Figure 3.11).

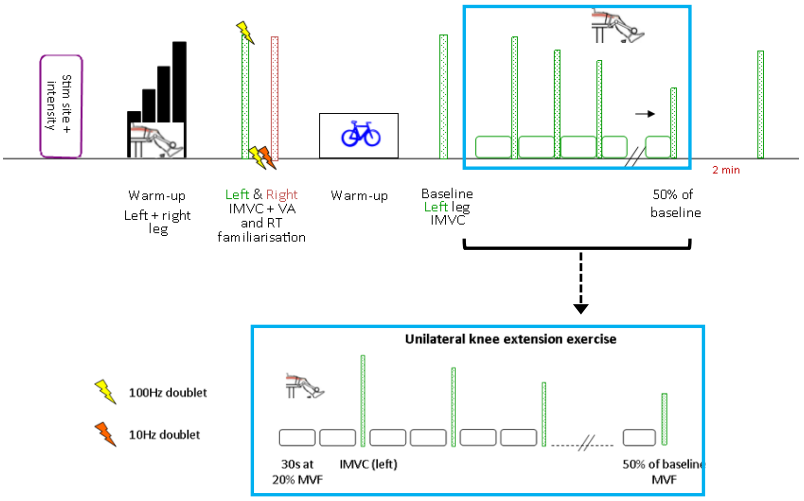


Figure 3.11: Session 1 overview. The unilateral knee extension exercise (enlarged in the blue box) was performed with the left leg. Participants were required to repeat sustained isometric contractions at 20% of their MVF for 30s. After every second submaximal contraction MVF was measured, the exercise continued until MVF was reduced to 50% of baseline.

Participants were first familiarised with electrical stimulation of the left leg femoral nerve via a recruitment curve (described above 3.4.2), before completing a warm-up of the left and right knee extensors individually. The warm-up consisted of two, 4-s isometric contractions at: 25%, 50%, 75% and 100% of the participants' perceived maximal effort. They were then taken through the testing procedures for voluntary activation (via SIT), resting potentiated evoked force and M-waves from the left VL and VM. During *session 1* and *3*, MVF and evoked force from the left and right legs was performed in the order of;

- left IMVC + SIT,
- resting 100Hz and 10Hz doublets in a randomized order
- right IMVC (Figure 3.11)

Before FAT_{ISO} participants completed a standardized cycling warm-up consisting of;

- 2min at 80 - 120W and 80-90RPM
- 2min at 120 - 145W and 80-90RPM
- 2min at 145 - 190W and 80-90RPM
- 6s rolling start sprint from 80RPM at low resistance,
- 2min at 120 – 145W and 80-90RPM
- 6s stationary start sprint against a low resistance
- 2min at 120W and 80-90RPM

MVF measurements were recorded before and after the cycling warm-up to ensure no fatigue had been induced in the knee extensors by the warm-up.

Participants then undertook FAT_{ISO}, performed with the left leg. Prior to the exercise baseline MVF was recorded from the left leg to normalize the force signal in real-time. FAT_{ISO} involved repeated, sustained, submaximal contractions with a high work-to-rest ratio to induce long-lasting fatigue in the knee extensors. Participants were required to repeat sets of; 2 × 30-s isometric contractions with 5-s rest in between, followed by a 3-s IMVC of the left knee extensors (Figure 3.11). The 30-s contractions were sustained at 20% of the baseline IMVC force, with visual feedback of the force trace provided on a television monitor. The sets were repeated until the MVF was 50% of baseline on two consecutive IMVCs. Once this had been reached IMVC force was measured again, 2-minutes after the exercise to track the recovery of MVF to estimate the level of fatigue at the beginning of the cycling exercise in *session 3*. We anticipated it would take 1 – 2 minutes for participants to transfer from the Cybex to the bike during *session 3*, so allowed a 2-minute transfer period. If, after 30 sustained contractions (including 15 IMVCs) the participant's IMVC force was still >55% of baseline, they were excluded from the study. Of the 21 individuals who completed this session, 4 were excluded based on this criterion.

3.5.2 Session 2: Evaluation of lower limb function during maximal cycling.

17 subjects completed this session, after 4 were excluded following session 1, which consisted of a force-velocity (F-V) test, to determine individual P-C and T-C relationships, and familiarisation of the maximal cycling exercise performed in *session 3* (Figure 3.12). A standardised cycling warm-up (described in *session 1*) was performed at the beginning of the session.

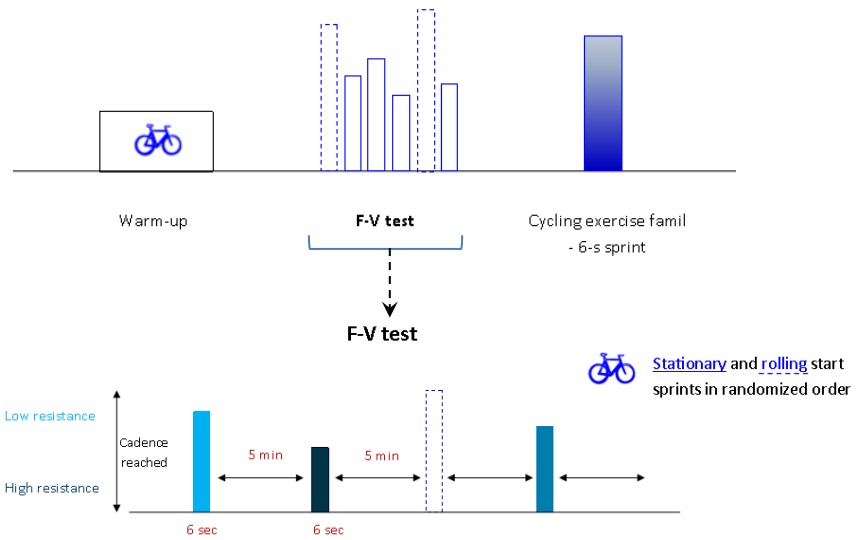


Figure 3.12: Session 2 overview. During the F-V test the external resistance was adjusted for rolling and stationary start sprints to cover the individual's maximal cadence range. Stationary start sprints (filled bars) with high resistance (darker blue) and low resistance (lighter blue) covered the lower cadence range. Top end cadence was reached from rolling start sprints (dashed bar) at low resistance (light blue).

The F-V test consisted of a series of five to seven, 6-s sprints initiated from either a rolling start or stationary start against varied resistances. During the sprints participants were instructed to reach the highest cadence they could as quickly as possible, keeping their hands on the drops of the handlebars and remaining seated. Verbal encouragement was given to the participants throughout each sprint. During rolling start sprints participants gradually increased their cadence to the required cadence (10, 20, 40, 70 or 90 RPM) while pedalling against a very low resistance, before stopping pedalling and being counted in "3, 2, 1 – GO!" to start the sprint. 5-min of passive rest was given between each sprint to minimize fatigue (151). Power-cadence values from each sprint were extracted during the 5-minute rest periods so at the end of the test the maximal P-C relationship from the combined sprints had been modelled (described in 3.4.3.1). Additionally, P-C relationships of the individual sprints performed from a stationary start were calculated. Based on these relationships, the resistance of the sprint that resulted in the most similar curve to the maximal P-C relationship was selected for the maximal cycling exercise in *session 3*. The maximal cycling exercise involved a 6-s maximal sprint from a stationary start. During the exercise participants had to remain seated with their hands on the drops of the handlebars.

3.5.3 Session 3: Main testing session (Effect of unilateral knee extensor fatigue on crank power and muscle activity)

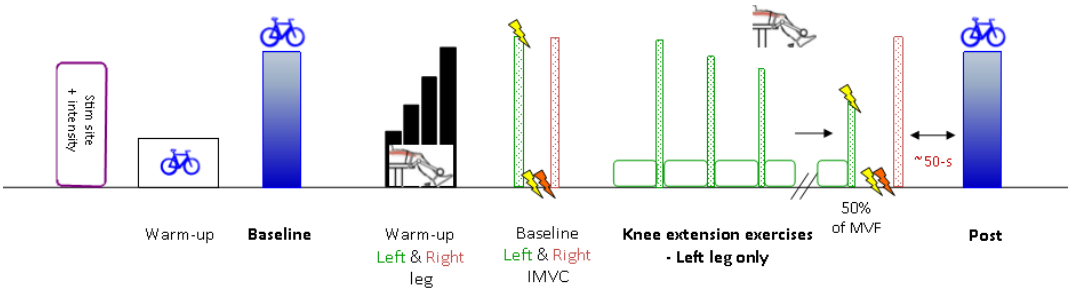


Figure 3.13: Session 3 overview. Participants performed a maximal 6-s cycling sprint before (Baseline) and after (Post) a unilateral fatiguing knee extension exercise with the left leg.

Following *session 2*, three subjects dropped out leaving 14 individuals who completed the final session. Data from two of these subjects had to be excluded, so the results of 12 individuals were analysed for this study. This session consisted of a 6-s cycling sprint performed before (baseline) and after FAT_{ISO}, to assess the effects of unilateral isolated knee extensor fatigue on power production and muscle coordination during maximal cycling exercise (Figure 3.13).

As described in *session 2*, the maximal cycling exercise was a 6-s stationary-start sprint. The short duration, maximal exercise was selected to minimise fatigue occurring in the lower limb muscles, so any changes in muscle coordination and power output after FAT_{ISO}, compared to baseline, could be associated with fatigue in the left knee extensors. At the start of the session the standardised cycling warm-up was performed (described in *session 1*) before undergoing the baseline maximal cycling exercise. All sprints started with the left crank just behind LTDC.

After the knee extension warm-up (described in session 1), three baseline MVF measurements of the left and right knee extensors were recorded prior to FAT_{ISO}, along with baseline VA, R_{EF} and M-wave recordings from the left knee extensors. FAT_{ISO} (described in *session 1*) was then undertaken with the left leg, until the MVF of the knee extensors was reduced to 50% of baseline on two consecutive IMVCs. Final MVF, VA, R_{EF} and M-wave measurements from the left knee extensors were taken from the second IMVC where MVF was 50% of baseline. The final MVF of the right knee extensors was measured immediately (3-s) after the left knee extensors measurements.

At the end of FAT_{ISO} participants were helped off the Cybex and onto the bike as quickly as possible to begin the post knee extension maximal cycling exercise. The participants were assisted to minimise the time between the final IMCV and the cycling exercise (mean = 49 ± 10-s) however, this delay was unavoidable.

3.6 Statistics

All statistical analysis was performed using commercially available software (IBM SPSS Statistics Version 22.0, IBM Corp. Armonk, NY). Shapiro-Wilk test was used to test normality of the data. For non-normally distributed data, Log(10) and square root transformations were performed. Mauchly's test was used to ensure sphericity had not been violated. Significance was considered for p-values <0.05. All values are reported as mean ± standard deviation (S.D.).

3.6.1 Unilateral knee extension exercise (FAT_{ISO}) variables

Two-way ANOVA with repeated measures was used to investigate time (baseline vs. post FAT_{ISO}), side (left vs. right), and interaction (time × side) effects on MVF of the knee extensors and peak EMG of VL, VM, RF and HAM from the left and right sides. This analysis was also used to test main and interaction effects of time (baseline vs. post FAT_{ISO}) and session (*session 1* vs. *session 3*) on MVF of the left knee extensors. Two-way repeated measures ANOVA was used to assess time (baseline vs. post FAT_{ISO}), muscle (VL vs. VM) and interaction (time × muscle) effects for M-wave characteristics; M_{max}, M_{area} and M_{dur}. Where significant effects were seen post hoc analysis was performed using Bonferroni corrections for all tests.

One-way ANOVA with repeated measures was used to assess a time effect on MFV during *session 1* between; baseline vs. post FAT_{ISO} vs. 2-min post FAT_{ISO} measurements. One-way ANOVA with repeated measures determined a time effect (baseline vs. post FAT_{ISO}) on %VA, RT, 10:100, IMVC VL/M_{max} and IMVC VM/M_{max} in the left knee extensors. As well as a time effect between the first submaximal contraction and the final contraction of FAT_{ISO}, for average VL, VM, RF and HAM EMG from the left leg.

3.6.2 Maximal cycling exercise variables

Three-way ANOVA with repeated measures was used to investigate main effects of time (baseline vs. post FAT_{ISO}), side (left vs. right), phase (downstroke vs. upstroke) and interaction effects (time × side × phase) for absolute power (W) and relative power (%). Two-way ANOVA with repeated measures was used to investigate time (baseline vs. post FAT_{ISO}), side (left vs. right), and interaction (time × side) effects for average, initial and final downstroke cadence. For the left and right sides separately, two-way repeated measures ANOVA was also used to assess main and interaction effects of time (baseline vs. post FAT_{ISO}) and phase (downstroke vs. upstroke) on crank torque, absolute power (W) and relative power (%). Two-way ANOVA with repeated measures was used to assess side (left vs. right), phase (downstroke vs. upstroke) and interaction effects (side × phase) on P_{max} (absolute and normalized to body mass), C_{opt}, T_0 and C_0 from the force-velocity test. As well as the percentage of total power over a full pedal cycle contributed by the downstroke and upstroke phases. Where significant effects were seen post hoc analysis was performed using Bonferroni corrections for all tests.

Linear regression analysis was used to determine correlations between; MVF and P_{max} over the downstroke, as well as MVC and T_0 over the downstroke for the left and right sides. As well as the correlation between the change in MVF 2-min post $FAT_{ISO}$and change in power (%) during maximal cycling post $FAT_{ISO}$for the left side only.

One-way ANOVA with repeated measures was used to assess a time effect (baseline vs. post FAT_{ISO}) on the following variables extracted during the maximal cycling exercise; peak force (F_{tan} and F_{tot}), %cycle of peak force, peak EMG as well as intra-individual variability (VR) of force and EMG profiles.

CHAPTER 4. RESULTS

4.1 Knee extensor evaluation

4.1.1 Knee extensor function (session 1)

At baseline, average MVF of the left knee extensors was 642 ± 185 N. During FAT_{ISO} participants completed an average of 17 ± 7 sustained contractions. At the end of exercise, average left knee extensor MVF was 328 ± 108 N (50.2 ± 6.8 % of baseline, $p<0.01$). MVF measured 2-min after FAT_{ISO} was different to both values measured immediately after the end of the exercise ($p<0.005$) and before the start of the exercise (473 ± 137 N, 74.1 ± 7.2 % of baseline, $p<0.001$) (Figure 4.1).

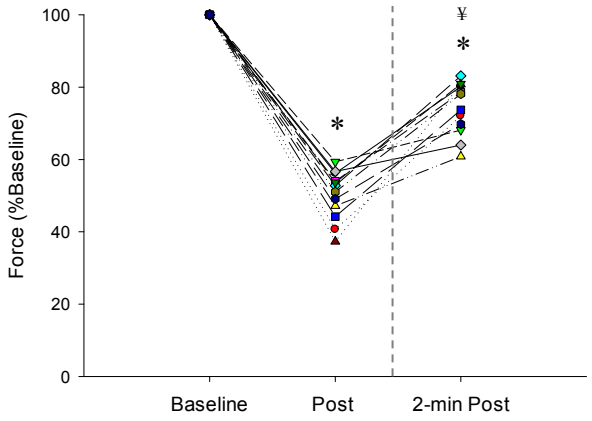


Figure 4.1:Individual maximal voluntary force of the left knee extensors during *session 1*. Measurements were made at baseline, immediately after the exercise (Post) and 2 minutes after the end of the exercise (2-min Post). Dashed vertical line indicates the time when the maximal cycling exercise would have started in *session 3* (Post + ~49s). *Significantly different from baseline. ¥ Significantly different from Post.

4.1.2 Lower limb function during maximal cycling (session 2)

From the combined sprints, F-V data was calculated over 133 ± 15 cycles for each participant over an average cadence ranging from a minimum of 33 ± 6 RPM to a maximum of 188 ± 15 RPM over a full pedal cycle. The key variables extrapolated from the F-V test are reported in Table 4.1. P_{max} normalized to body mass from the total (left + right) cranks was 14.7 ± 2.1 W/kg over a full pedal cycle. Average P_{max} over the downstroke from the left crank was higher than the right crank (13.4 ± 1.8 vs. 12.9 ± 1.6 W/kg, $p<0.05$). Over the upstroke phase, average P_{max} was not different ($p=0.134$) between the left (2.2 ± 0.8 W/kg) and right (2.3 ± 0.9 W/kg) sides. There was a phase effect ($p<0.001$) on crank power produced over a full pedal cycle, as 85.7 ± 3.8 % of

total power was produced over the downstroke and 14.2 ± 3.8 % was produced over the upstroke. From the left crank, power over the downstroke accounted for 86.4 ± 3.6 % of the total, while power over the upstroke contributed 13.6 ± 3.6 % ($p<0.05$). From the right crank, power over the downstroke made up 85.0 ± 4.2 % of the total power, while power over the upstroke contributed 15.0 ± 4.2 % ($p<0.05$).

Table 4.1: Population characteristics from the force-velocity test during *session 2*. P-C variables are reported from the individual power-cadence relationships calculated over the downstroke phase, upstroke phase and from the left and right sides separately. T-C variables are from the individual torque-cadence relationships. Total = left + right cranks. Values are reported as mean ± S.D.

Population characteristics from Force-Velocity test						
		Total	***Left crank***		***Right crank***	
		Full cycle	*Downstroke*	*Upstroke*	*Downstroke*	*Upstroke*
P-C	**P_{max} (W)**	1171 ± 286	1071 ± 265	173 ± 74	1020 ± 234	184 ± 75
	C_{opt} (RPM)	122 ± 9	130 ± 10	109 ± 17	126 ± 10	100 ± 13
	r^2	0.989 ± 0.007	0.999 ± 0.001	0.994 ± 0.010	0.999 ± 0.000	0.990 ± 0.012
	SEE (W)	23.12 ± 10.07	23.42 ± 8.05	7.18 ± 2.88	23.98 ± 7.91	13.16 ± 9.07
T-C	**T_0 (N.m)**	142 ± 40	124 ± 25	20 ± 16	126 ± 26	31 ± 16
	C_0 (RPM)	216 ± 13	233 ± 15	185 ± 24	226 ± 16	183 ± 27
	r^2	0.997 ± 0.001	0.993 ± 0.006	0.986 ± 0.023	0.993 ± 0.004	0.981 ± 0.025
	SEE (N.m)	2.14 ± 0.71	2.28 ± 0.99	0.59 ± 0.22	2.33 ± 1.00	1.25 ± 0.60

4.1.3 Correlation between knee extensor function and maximal cycling

Maximal power (P_{max}) calculated over the downstroke phase was positively correlated with MVF of the knee extensors, in both the left ($r = 0.849$, $R^2 = 0.722$, $p<0.001$) and right ($r = 0.908$, $R^2 = 0.825$, $p<0.001$) sides (Figure 4.2A). Knee extensor MVF was not correlated with downstroke T_0 in the left ($r = 0.539$, $R^2 = 0.290$, $p = 0.07$) or right ($r = 0.534$, $R^2 = 0.286$, $p = 0.07$) sides (Figure 4.2B).

A **B**

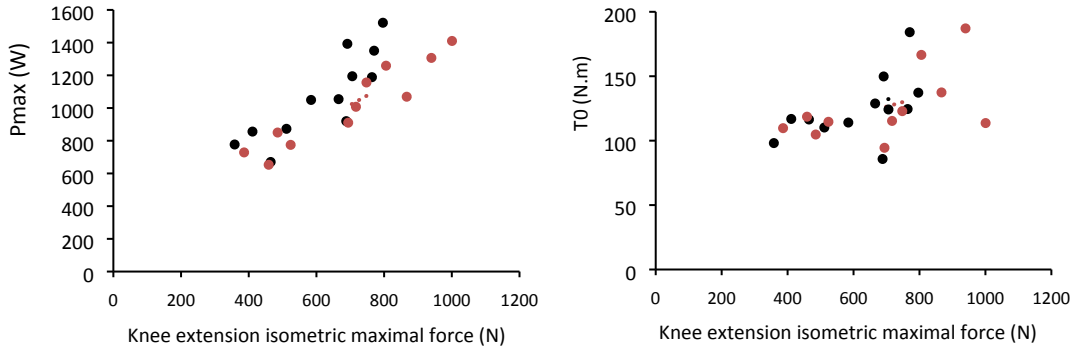


Figure 4.2: Correlations between isometric MVF and extrapolated maximal fatigue-free power (A) and torque intercept (B) over the downstroke phase of the pedal cycle, from the left (black) and right (red) knee extensors.

4.2 Unilateral fatigue in the left knee extensors and maximal cycling exercise

4.2.1 Main findings

4.2.1.1 Knee extensor function

At baseline during *session 3*, left MVF was less than the right side ($p<0.05$). Post FAT_{ISO}, MVF on the left side was reduced compared to baseline (618 ± 149 vs. 292 ± 85 N, $p<0.001$), while MVF of the right knee extensors did not change (693 ± 196 vs. 735 ± 194 N, $p > 0.05$) (see Figure 4.3).

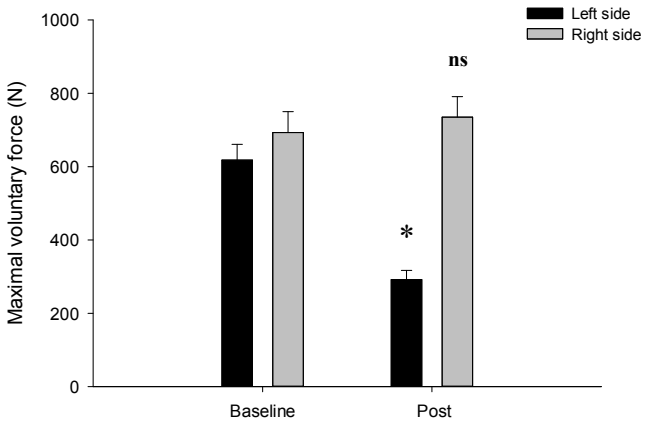


Figure 4.3:Maximal voluntary knee extensor force from the left (black bars) and right (grey bars) knee extensors at baseline and after the unilateral knee extension exercise (Post). Values are shown as mean ± SEM. *Significant difference from baseline for the left side, right side not significant (ns).

4.2.1.2 Maximal cycling exercise performance

Three-way ANOVA analysis of absolute crank power revealed at baseline, downstroke power from the left crank was less than the right crank (875 ± 312 vs. 915 ± 218 W, $p<0.05$), but not different between the two sides for upstroke power (left: 143 ± 69 vs. right: 139 ± 61 W, $p>0.05$). Post FAT_{ISO}, power from the left crank was less than the right crank over the downstroke (777 ± 311 vs. 867 ± 223 W, $p<0.001$) and upstroke (111 ± 65 vs. 122 ± 58 W, $p<0.01$). Post hoc analysis revealed absolute crank power over the downstroke phase reduced in both the left (-99 ± 27 W, $p<0.001$) and right cranks (-47 ± 21 W, $p<0.001$) after FAT_{ISO} performed with the left leg. The magnitude of reduction in absolute power over the downstroke was greater in the left crank compared to the right crank ($p<0.001$). Over the upstroke phase, power was reduced in the left crank (-32 ± 11 W, $p<0.001$) and also the right crank (-17 ± 9 W, $p<0.001$), with a greater reduction seen in the left crank ($p<0.005$) (see Figure 4.4).

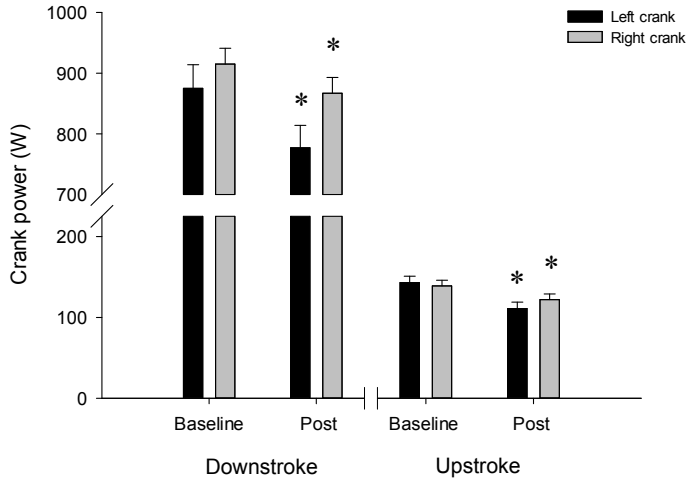


Figure 4.4: Average absolute power (W) over the downstroke and upstroke phases from the left crank (black bars) and right crank (grey bars), at baseline and after the unilateral knee extension exercise (Post). *Significant difference from baseline for individual sides revealed by post hoc tests.

A higher cadence was reached at baseline compared to post FAT_{ISO} ($p<0.001$) and cadence was lower on the left side compared to the right ($p<0.001$). There was no interaction effect on cadence ($p>0.05$) (Figure 4.5).

§ §

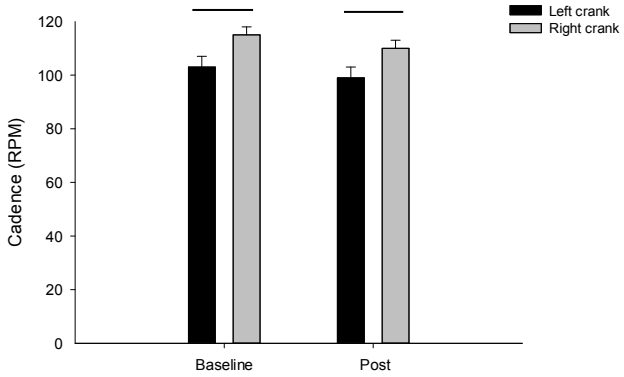


Figure 4.5: Average downstroke cadence from the left crank (black bars) and right crank (grey bars) during the baseline maximal cycling exercise and after the unilateral knee extension exercise (Post). § significant difference between left and right sides (side effect) revealed by post hoc tests at baseline and post knee extension exercise.

For power relative to cadence-, side- and phase, main effects of time (pre: 92 ± 3 vs. post: 80 ± 4 %, $p<0.001$), side (left: 83 ± 4 vs. right: 89 ± 3 %, $p<0.001$) and phase (downstroke: 91 ± 2 vs. upstroke: 80 ± 5 %, $p<0.001$) were observed. A time × side × phase effect was observed ($p<0.05$) (Figure 4.6), with post hoc tests showing at baseline, power was not different between the left and right sides over the downstroke (left: 95 ± 5 vs. right: 96 ± 4 %, $p>0.05$) or upstroke (left: 89 ± 12 vs. right: 90 ± 14 %, $p>0.05$) phases. Relative downstroke power at baseline was higher than upstroke power on the left side (95 ± 5 vs. 89 ± 12 %, $p<0.001$) and right side (96 ± 4 vs. 90 ± 14 %, $p<0.01$). After FAT_{ISO}, post hoc tests revealed, relative power decreased from baseline in both the left crank (-10 ± 7 %, $p<0.001$) and the right crank (-5 ± 15 %, $p<0.001$), with left crank relative power decreasing more than the right crank ($p<0.001$). Similarly, relative crank power over the upstroke was reduced in the left (-23 ± 13 %, $p<0.001$) and right cranks (-13 ± 8 %, $p<0.001$), decreasing more on the left side compared to the right crank after FAT_{ISO} ($p<0.001$).

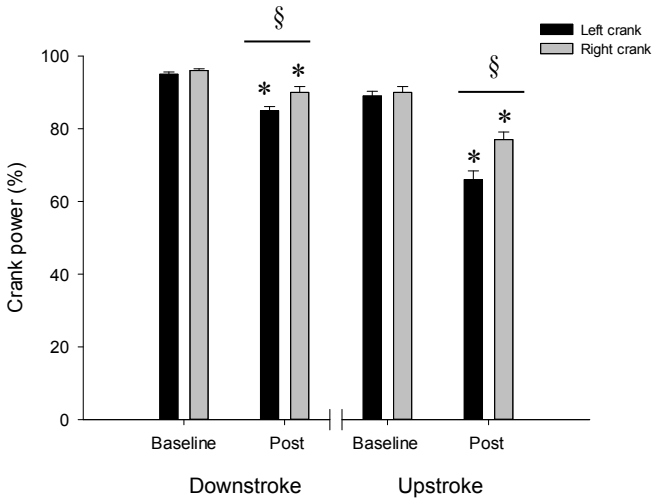


Figure 4.6: Average cadence- side- and phase-specific power (%) over the downstroke and upstroke phases of the maximal cycling exercises. Measured from the left crank (black bars) and right crank (grey bars) at baseline and after the unilateral knee extension exercise (Post). Mean ± SEM shown. Interaction effects (time × side × phase) are indicated by; § significant difference between left and right sides. *Significant difference from baseline for individual sides.

4.2.2 Ipsilateral limb

4.2.2.1 Unilateral knee extension exercise (FAT_{ISO})

Participants completed an average of 17 ± 9 sustained, submaximal contractions with the left leg during FAT_{ISO}. Average force of the submaximal contractions was 19.4 ± 0.4 % of baseline MVF. At the end of the exercise MVF was reduced to 48.2 ± 10.9 % of baseline ($p<0.001$). Two-way ANOVA (session × time) showed a main effect of time ($p<0.001$) on MVF (pre: 630 ± 45 vs. post: 310 ± 24 N), but no session ($p = 0.297$) or interaction ($p = 0.698$) effects.

4.2.2.1.1 Peripheral fatigue

At the end of FAT_{ISO}, R_{EF} had decreased by 27.4 ± 21% of baseline (279.8 ± 67.4 *vs.* 195.0 ± 59.7 N, $p<0.01$) and 10:100 had reduced by 17.8 ± 11.3 % ($p<0.005$) of baseline (Figure 4.7). M_{max} and M_{dur} were not different at the end of the exercise compared to baseline, for both VL and VM. An interaction effect ($p<0.05$) was seen for M_{area}, where a 7.9 ± 8.9 % ($p<0.05$) reduction in M_{area} occurred in VM compared to baseline, but did not change for VL (M-wave characteristics reported in Table 4.2).

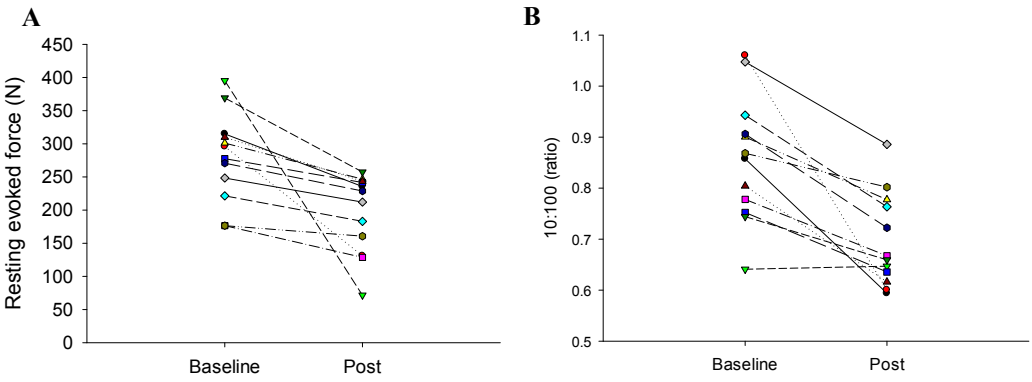


Figure 4.7:Peripheral changes in the left knee extensors Individual changes in (A) resting evoked force and (B) the ratio between the low- and high-frequency doublet evoked force (10:100) measured at baseline and immediately after the unilateral knee extension exercise (Post). Error bars show SEM.

Table 4.2: M-wave characteristics from VL and VM of the left knee extensors measured at baseline and following the unilateral knee extension exercise (Post). Values are reported as mean ± S.D. * Significantly different from baseline.

M-wave characteristics				
	VL		*VM*	
	Baseline	*Post*	*Baseline*	*Post*
Amplitude (mV)	13.4 ± 5.0	13.3 ± 5.3	15.0 ± 4.3	14.0 ± 3.9
Duration (msec)	7.7 ± 2.0	7.6 ± 2.3	6.4 ± 1.6	6.2 ± 1.6
Area (mV·s)	0.76 ± 0.33	0.72 ± 0.32	0.84 ± 0.43	0.78 ± 0.37*

During FAT_{ISO}, average EMG increased from the first sustained contraction to the final contraction of the exercise in VL ($p<0.05$), VM ($p<0.05$) and RF ($p<0.05$) (Figure 4.8). Average HAM EMG also increased ($p<0.01$) in the final submaximal contraction.

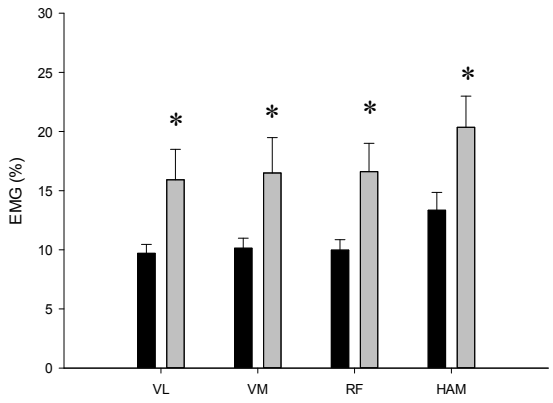


Figure 4.8: Average EMG from the left thigh muscles during the first (black bars) and final (grey bars) 30-s submaximal contractions of the knee extension exercise. Values are shown as mean ± SEM. *Significant difference between baseline and post. Note: HAM normalized to maximal EMG during maximal isometric knee extension contraction.

4.2.2.1.2 Central fatigue

%VA of the left knee extensors was reduced ($p<0.005$) following FAT_{ISO}, from 91.8 ± 3.6 % at baseline to 68.7 ± 12.4 %. Peak EMG during IMVC decreased in VL/M_{max} (-34.0 ± 20.0 %, $p<0.001$), VM/M_{max} (-25.6 ± 21.4 %, $p<0.005$) and RF (-35.7 ± 20.5 %, $p<0.005$) after FAT_{ISO}. HAM EMG during IMVC at the end of FAT_{ISO} decreased by 21.0 ± 19.6 % ($p<0.05$) (see Figure 4.10).

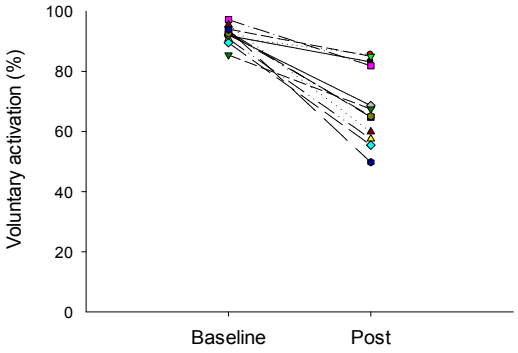


Figure 4.9:Voluntary activation of the left knee extensors Individual measurements of voluntary activation from the left knee extensors at baseline and immediately after the unilateral knee extension exercise (Post). *Significant difference between baseline and post.

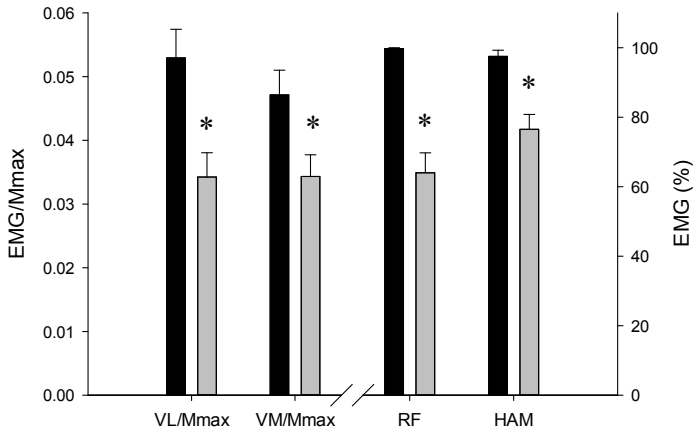


Figure 4.10: IMVC EMG from the left thigh muscles at baseline (black bars) and after the knee extension exercise (grey bars). VL and VM normalized to M_{max}. Values are shown as mean ± SEM. *Significant difference between baseline and post.

4.2.2.2 Maximal cycling exercise

4.2.2.2.1 Mechanical

Two-way ANOVA revealed initial downstroke cadence on the left side decreased from 33 ± 4 to 31 ± 3 RPM ($p<0.01$) and final cadence decreased from 143 ± 7 to 138 ± 7

RPM ($p<0.001$) after FAT_{ISO}. There was also a side effect on initial ($p<0.001$) and final ($p<0.001$) downstroke cadence. Due to the instructions given to the participants (i.e. starting with left crank at TDC), cadence was lower on the left side at the start (left: 32 ± 3 vs. right: 64 ± 5 RPM) and end (left: 141 ± 7 vs. right: 145 ± 7 RPM) of the sprint. There was no interaction effect ($p>0.05$) for initial or final cadence (Figure 4.11).

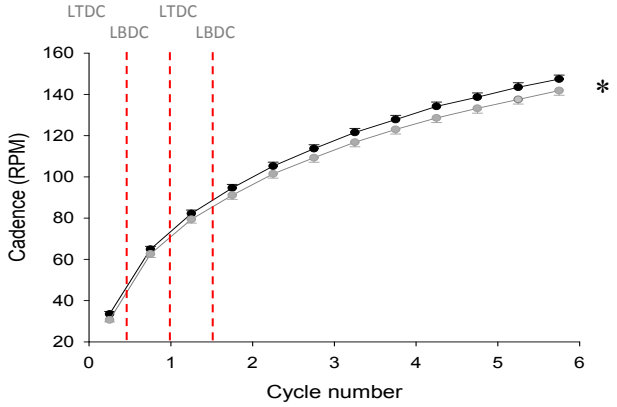


Figure 4.11: Average cadence calculated over 6 pedal cycles during the baseline (black) and post knee extension exercise (grey) sprints. Left downstroke cadence was calculated between LTDC – LBDC. Right downstroke cadence was calculated between LBDC – LTDC. Mean values ± SEM shown. *Average relative power over the 6 cycles was significantly reduced from baseline.

Post hoc tests revealed torque over the downstroke from the left crank reduced from 86 ± 10 to 79 ± 10 N.m post FAT_{ISO}, a greater reduction than torque over the upstroke ($p<0.001$). Over the upstroke, average torque from the left crank reduced from 12 ± 3 N.m at baseline to 10 ± 3 N.m ($p<0.001$) after FAT_{ISO} (Figure 4.12).

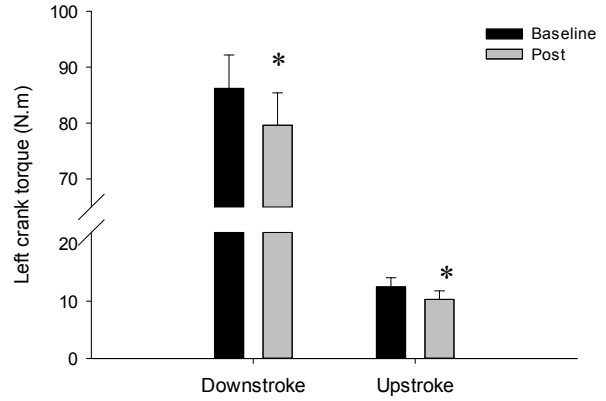


Figure 4.12: Average torque from the left crank calculated over the downstroke and upstroke phases during the baseline (black bars) and post knee extension exercise (grey bars) sprints. Mean values ± SEM shown. * Average torque significantly different from baseline.

Two-way ANOVA analysis of absolute power from the left crank showed main effects of time (pre: 509 ± 73 vs. post: 444 ± 71 W, $p<0.001$) and phase (826 ± 127 vs. 127 ± 27 W, $p<0.001$). Over the downstroke phase power was reduced from 875 ± 205 to 777 ± 311 W ($p<0.001$) after FAT_{ISO}. Absolute power over the upstroke was reduced from 143 ± 69 to 111 ± 65 W ($p<0.001$) post FAT_{ISO} (Figure 4.4 and Figure 4.13). An interaction effect (time × phase, $p<0.001$) was also seen, with post hoc analysis showing a greater reduction in absolute power occurred over the downstroke (-99 ± 27 W) compared to the upstroke (-32 ± 11 W).

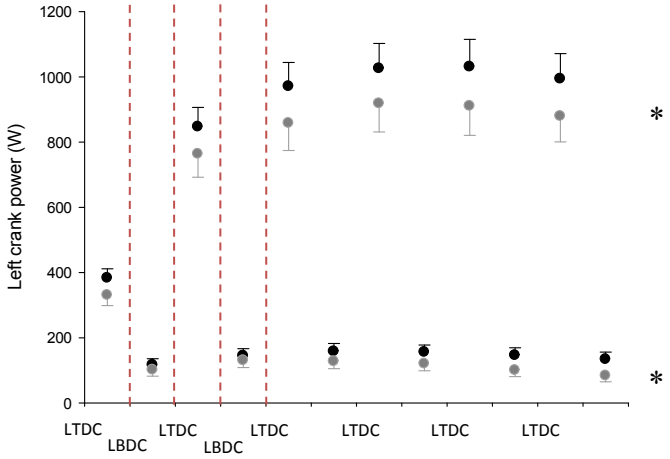


Figure 4.13: Average left crank power calculated over the downstroke (LTDC - LBDC) and upstroke (LBDC - LTDC) for each cycle , during the baseline sprint (black circles) and post knee extension exercise maximal cycling exercise (grey circles). Mean values ± SEM shown. *Average relative power over the 6 cycles was significantly reduced from baseline.

Two-way ANOVA analysis on relative power from the left crank showed main effects of time (pre: 91.8 ± 2.5 vs. post: 75.1 ± 5.2 %, $p<0.001$) and phase (downstroke: 89.7 ± 2.7 vs. upstroke: 77.1 ± 5.4 %). Relative power over the downstroke in the left crank was reduced from 95 ± 5 to 85 ± 9 % following FAT_{ISO} ($p<0.001$) (Figure 4.6 and Figure 4.14). An interaction effect (time × phase) ($p<0.001$) on relative power was also seen, with post hoc tests showing a larger reduction in relative power occurring over the upstroke phase (-22.7 ± 12.8 %) compared to the downstroke phase (-10.1 ± 6.7 %). Relative crank power over the upstroke reduced from 89 ± 12 % at baseline to 66 ± 20 % ($p<0.001$) after FAT_{ISO}.

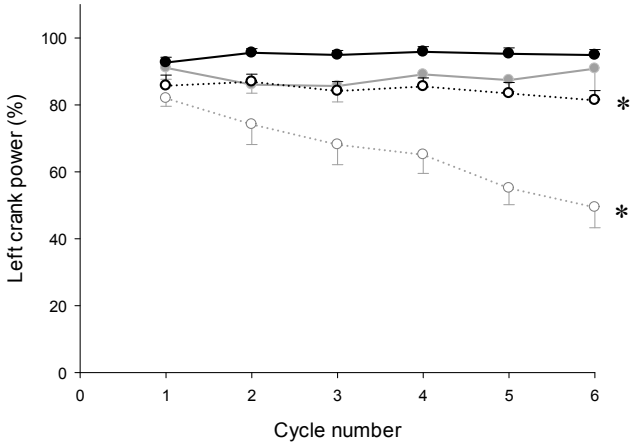


Figure 4.14: Average relative power (%) from the left crank measured during the downstroke (black lines) and upstroke (grey lines) for each cycle at baseline (solid lines and filled circles) and after the knee extension exercise (dotted lines and unfilled circles). Mean ± SEM shown. *Average relative power over the 6 cycles was significantly reduced from baseline.

The magnitude of reduction in relative crank power measured from the left crank during the downstroke phase, was not correlated with the reduction in MVF of the left knee extensors measured 2-min post FAT_{ISO} ($r = 0.070$, $R^2 = 0.005$, $p = 0.828$) (Figure 4.15).

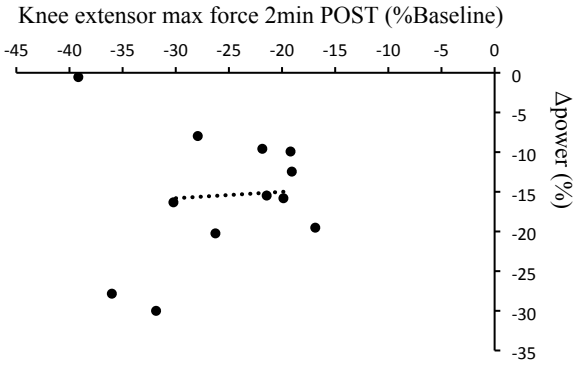


Figure 4.15: Correlation between the reduction in MVF 2-min post unilateral knee extension exercise (from *session 1)* and the reduction in relative power (%) post knee extension exercise during *session 3* for the left knee extensors.

Compared to baseline, peak $F_{tan,}$ and F_{tot} decreased by 9.9 ± 5.9 % ($p<0.001$) and 11.8 ± 7.1 % ($p<0.005$) following FAT_{ISO}. There was no time effect on %cycle where peak force occurred for F_{tan} (28 ± 2 % in both sprints, $p=0.341$) or F_{tot} (32 ± 4 vs. 30 ± 5 %, $p=0.091$) (Figure 4.16). Cross-correlation coefficient, r_{xy}, showed no alteration in the profile of F_{tan}, i.e. $k = 0$. For F_{tot}, $k = 1$, suggesting a shift in F_{tot} applied to the pedals 1% earlier in the pedal cycle after FAT_{ISO} compared to baseline.

VR of left crank F_{tan} profiles increased from 0.217 ± 0.068 to 0.250 ± 0.065 ($p<0.05$) post FAT_{ISO}. There was no interaction effect (side × phase, $p=0.198$). VR of left F_{tot} profiles increased from 0.201 ± 0.069 to 0.251 ± 0.072 ($p<0.005$) following FAT_{ISO}. Post hoc tests revealed VR of F_{tot} profiles had a larger increase in the left crank compared to the right crank ($p<0.005$).

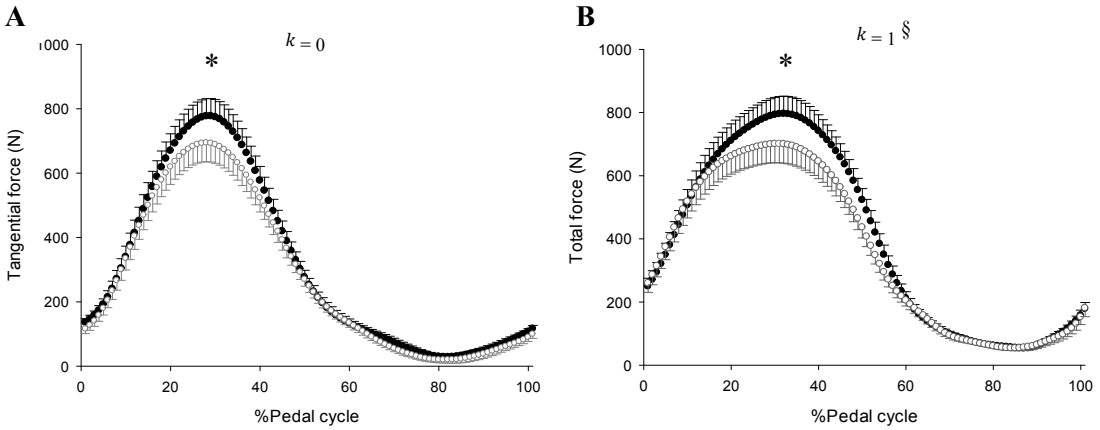
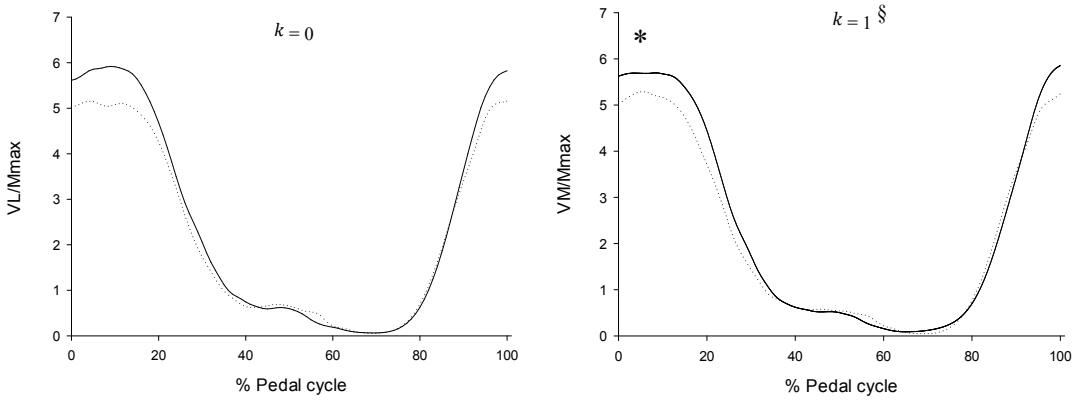


Figure 4.16: Average force profiles from the left crank during maximal cycling. Tangential (A), and total force (B) measured over a full pedal cycle from LTDC- LTDC during maximal cycling at baseline (black circles) and maximal cycling after the fatiguing knee extension exercise (open grey circles). Mean values ± SEM shown. *Peak force significantly different from baseline to post knee extension exercise. § significant *k* value (i.e. significant shift in force profile).



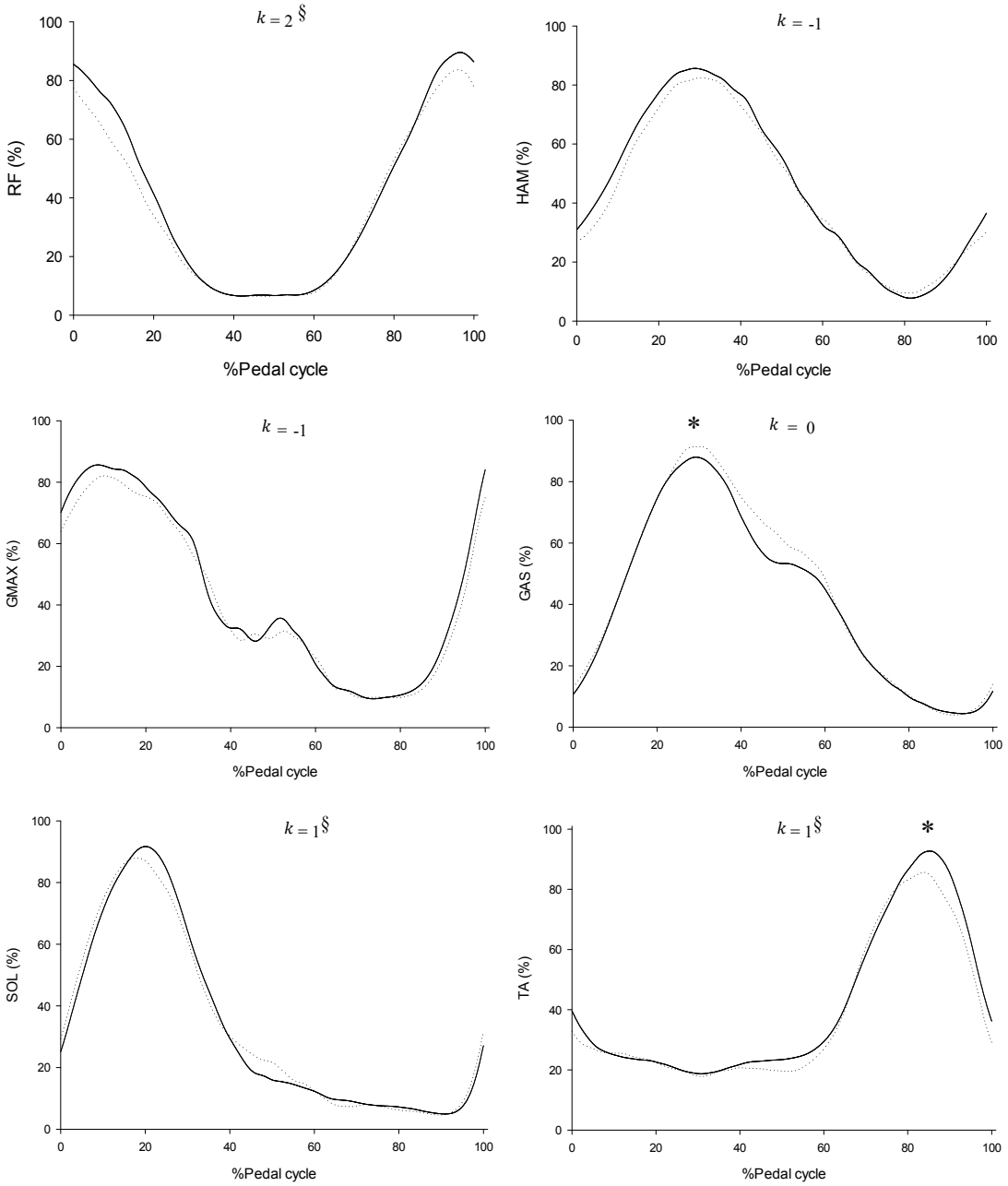


Figure 4.17: Average EMG profiles over a full cycle (LTDC – LTDC) from the left leg before (solid lines) and after (dashed lines) the knee extension exercise. Downstroke muscles; vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF), hamstrings (HAM), gluteus maximus (GMAX), soleus (SOL) and gastrocnemius lateralis (GAS). Upstroke muscle; tibialis anterior (TA). *Peak EMG significantly different from baseline to post knee extension exercise. § significant k value (i.e. significant shift in EMG profile).

4.2.2.2.2 EMG

There was a time effect on peak EMG in the left knee extensor muscles for VM/M_{max} (-5.5 ± 15.9 %, $p<0.05$) but not in VL/M_{max}. Of the other downstroke muscles in the left leg, peak EMG decreased in RF (-4.9 ± 19.0 %, $p<0.005$) and increased in GAS

(+10.5 ± 17.70 %, $p<0.01$) compared to baseline. There was no time effect on HAM, GMAX or SOL peak EMG (all $p>0.05$). Similarly, there was no change in %cycle of the peak EMG for any of the downstroke muscles (Figure 4.17). During the upstroke phase, EMG for TA decreased after FAT_{ISO} (-6.6 ± 15.0 %, $p<0.05$). The %cycle of peak TA EMG was not different between baseline and post FAT_{ISO} (Figure 4.17).

r_{xy} showed small but significant variations in time domain for VM by 1% (i.e. $k = 1$), RF by 2%, SOL by 1% and TA by 1% earlier in the pedal cycle. During the upstroke, TA profile shifted earlier in the pedal cycle by 1% after FAT_{ISO} compared to baseline. k values for the other muscles were not significant (see Figure 4.17 for all values).

Intra-individual variability increased in GAS ($p<0.05$), SOL ($p<0.05$) and RF ($p<0.05$), shown by an increase in VR post FAT_{ISO}. VR was unchanged for the other muscles ($p>0.05$). VR for all muscles is presented in **Table 4.3**.

Table 4.3: Intra-individual variability (VR) values for EMG profiles from the left leg during maximal cycling. VR was calculated for each participant from the 6 cycles analysed during the sprint. Values are reported as mean ± S.D. *Significantly different from baseline.

VR - Left leg EMG profiles		
	Baseline	*Post*
VL	0.265 ± 0.08	0.278 ± 0.067
VM	0.233 ± 0.056	0.282 ± 0.061
RF	0.252 ± 0.085	0.295 ± 0.081*
HAM	0.404 ± 0.101	0.474 ± 0.111
GMAX	0.592 ± 0.104	0.608 ± 0.090
GAS	0.262 ± 0.060	0.292 ± 0.055*
SOL	0.252 ± 0.072	0.322 ± 0.084*
TA	0.307 ± 0.080	0.316 ± 0.097

4.2.3 Contralateral limb

4.2.3.1 Unilateral knee extension exercise, FAT_{ISO}

MVF of the right knee extensors was not different over time (Figure 4.3). Post hoc analysis revealed right VL EMG during IMVC was reduced by 8.2 ± 18.5 % ($p<0.05$) post FAT_{ISO}. EMG during IMVC was not different between baseline and post FAT_{ISO} for VM, RF and HAM (Figure 4.18).

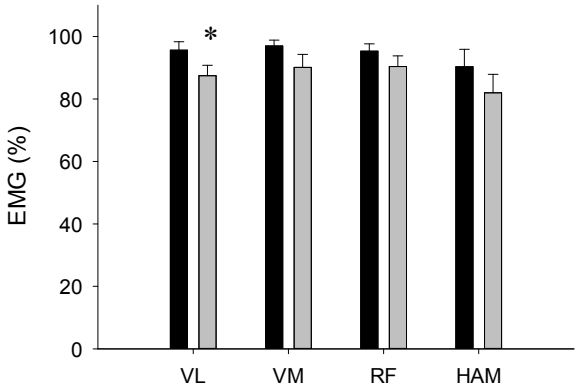


Figure 4.18:IMVC EMG from the right thigh muscles at baseline (black bars) and after the knee extension exercise (grey bars). Values are shown as mean ± SEM. *Significant difference between baseline and post.

4.2.3.2 Maximal cycling exercise

4.2.3.2.1 Mechanical

Initial cadence from the right side was reduced from 65 ± 5 to 63 ± 5 RPM post FAT_{ISO}. Final cadence was also reduced from 147 ± 6 to 142 ± 7 RPM ($p<0.001$) (Figure 4.11). Following completion of FAT_{ISO} right crank torque over the downstroke decreased from 80 ± 9 to 78 ± 9 N.m ($p<0.005$). During the upstroke, torque reduced from 15 ± 5 to 14 ± 5 N.m ($p<0.001$) (Figure 4.19). There was no interaction effect ($p>0.05$).

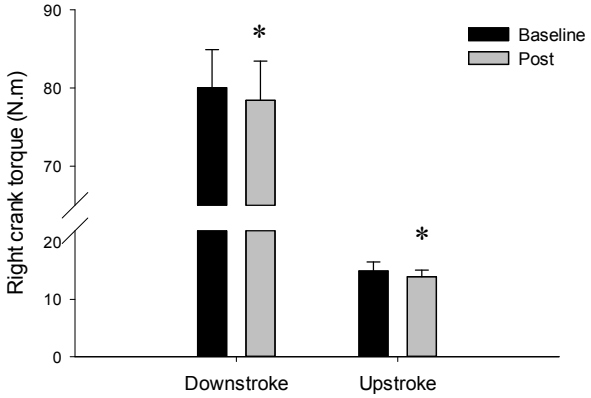


Figure 4.19: Average torque from the right crank calculated over the downstroke and upstroke phases during the baseline (black bars) and post knee extension exercise (grey bars) sprints. Mean values ± SEM shown. *Average torque significantly different from baseline.

A time effect was seen on absolute power from the right crank (pre: 527 ± 21 vs. post: 494 ± 21 W, $p<0.001$), as well as a phase effect (downstroke: 891 ± 90 vs. upstroke: 130 ± 24 W, $p<0.001$). Crank power was reduced over the downstroke from 915 ± 90 to 867 ± 91 W ($p<0.001$) and over the upstroke from 139 ± 25 to 122 ± 24 W ($p<0.001$) after FAT_{ISO}. An interaction effect was also observed ($p<0.001$), with post hoc analysis revealing a greater reduction in crank power over the downstroke (-47 ± 21 W) compared to power over the upstroke (-17 ± 9 W) ($p<0.001$) (Figure 4.4 and Figure 4.20).

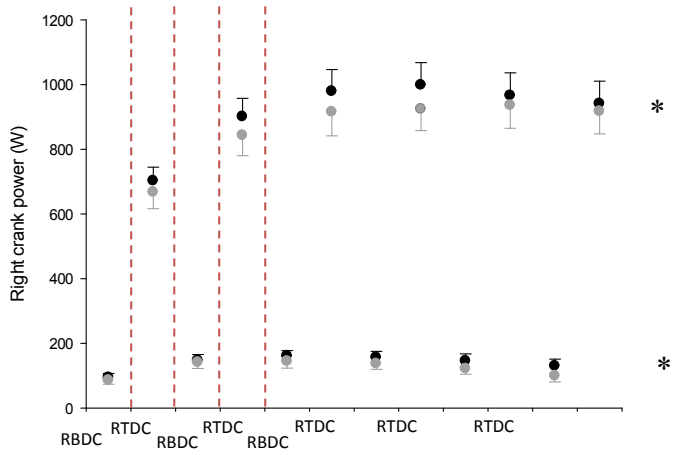


Figure 4.20: Average power (W) from the right crank calculated over the downstroke (RTDC - RBDC) and upstroke (RBDC - RTDC) for each cycle during maximal cycling exercises at baseline (black circles) and post knee extension exercise (grey circles). Mean ± SEM values shown. *Average relative power over the 6 cycles was significantly reduced from baseline.

Main effects of time (pre: 94 ± 3 vs. post: 84 ± 4 %, $p<0.001$), phase (downstroke: 93 ± 2 vs. upstroke: 84 ± 6 %, $p<0.001$) and interaction effects ($p<0.001$) were seen for relative power from the right crank. Over the downstroke, relative crank power reduced from 96 ± 4 to 91 ± 5 % ($p<0.005$) post FAT_{ISO}. Over the upstroke relative crank power reduced from 90 ± 14 to 77 ± 18 % ($p<0.001$). Post hoc tests showed relative crank power reduced more over the upstroke than the downstroke phase (-12.7 ± 7.8 vs. -5.2 ± 2.9 %, $p<0.001$)
Figure 4.6 and Figure 4.21).

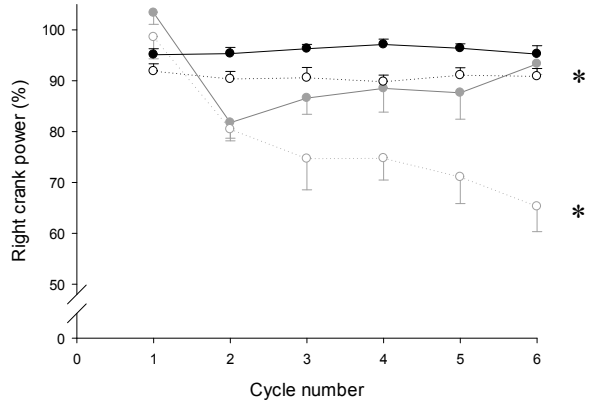


Figure 4.21: Average relative power (%) from the right crank measured during the downstroke (black lines) and upstroke (grey lines) for each cycle at baseline (solid lines and filled circles) and after the knee extension exercise (dotted lines and unfilled circles). Mean ± SEM. *Average relative power over the 6 cycles was significantly reduced from baseline.

After FAT_{ISO} peak $F_{tan,}$ decreased from 810 ± 208 to 770 ± 212 N (-5.3 ± 2.6 %, $p<0.001$). Peak F_{tot} also decreased from 909 ± 194 to 868 ± 208 N (-4.9 ± 3.8 %, $p<0.005$) as illustrated in Figure 4.22.

Peak F_{tan} shifted later in the pedal cycle ($p<0.05$) after the fatiguing exercise, from 79 ± 2 % of the cycle at baseline to 80 ± 2 %. The %cycle where peak F_{tot} occurred was not different between baseline and post exercise. r_{xy}, showed no alterations in F_{tan} profiles, or F_{tot} profiles as $k = 0$ for both (Figure 4.22).

Intra-individual variability (VR) of the tangential force profiles increased from 0.147 ± 0.052 to 0.163 ± 0.059 ($p<0.005$) following FAT_{ISO}. VR of the total force profiles also increased from 0.119 ± 0.055 to 0.138 ± 0.066 ($p<0.05$) after FAT_{ISO}.

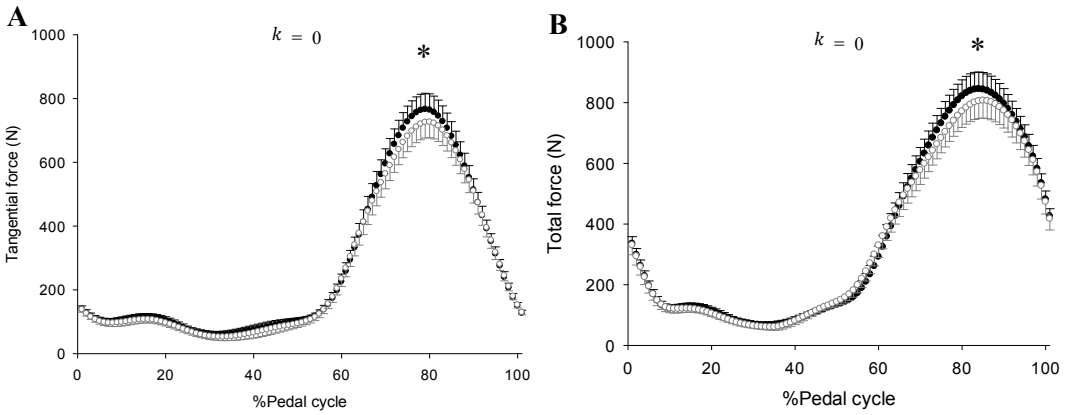


Figure 4.22: Average force profiles from the right crank during maximal cycling. Tangential (A), and total force (B) measured over a full pedal cycle from LTDC- LTDC during maximal cycling at baseline (black circles) and maximal cycling after the fatiguing knee extension exercise (open grey circles). Mean values ± SEM shown. *Peak force significantly different from baseline to post knee extension exercise.

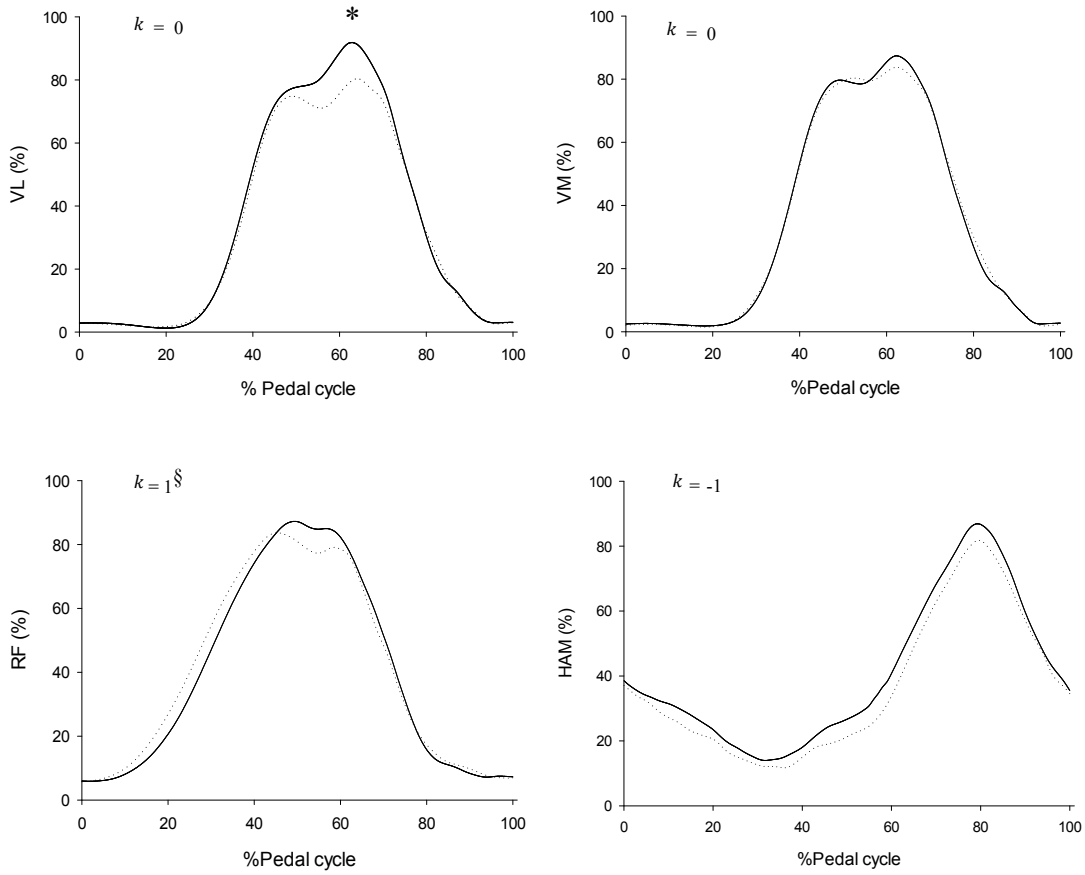


Figure 4.23: Average EMG profiles over a full cycle (LTDC – LTDC) from the right thigh muscles before (solid lines) and after (dashed lines) the knee extension exercise. From muscles active during the downstroke; vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF) and hamstrings (HAM). *Peak EMG significantly different from baseline to post knee extension exercise. § significant k value (i.e. significant shift in EMG profile).

4.2.3.2.2 EMG

EMG was reduced in VL (-4.9 ± 15.9 %, $p<0.05$), but was not different in VM or RF compared to baseline (Figure 4.23). There was also no time effect on HAM EMG. The %cycle of peak RF occurred earlier in the pedal cycle by 5.2 ± 8.1 % ($p<0.05$) after FAT_{ISO}. There was no change in %cycle for VL, VM or HAM.

Cross correlation (r_{xy}), showed an average significant shift earlier in the pedal cycle for right RF by 1%. *k* values for VL, VM and HAM were not significant (see Figure 4.23 for all *k* values).

Intra-individual differences between pedal cycles increased in RF activation ($p<0.01$) following FAT_{ISO}, there was no change in VR for VL, VM or HAM (Table 4.4).

Table 4.4: Intra-individual variability (VR) values for EMG profiles from the right leg during maximal cycling. VR was calculated for each participant from the 6 cycles analysed during the sprint. Values are reported as mean ± S.D. *Significantly different from baseline.

VR – Right leg EMG profiles		
	Baseline	*Post*
VL	0.316 ± 0.068	0.333 ± 0.069
VM	0.298 ± 0.064	0.344 ± 0.097
RF	0.341 ± 0.064	0.380 ± 0.068*
HAM	0.330 ± 0.105	0.366 ± 0.160

CHAPTER 5. DISCUSSION

The main aim of this study was to reduce the force-generating capacity of the knee extensors of one leg and assess how crank power production and muscle activation were effected in both the ipsilateral and contralateral sides, during bilateral maximal cycling exercise. It was anticipated with fatigue in the left knee extensors, crank power over the downstroke would be affected more than over the upstroke phase of the left crank. Also, power from the left crank would be affected more than the right crank.

Our results show that unilateral repeated, isometric and submaximal contractions of the knee extensors led to ~52% reduction in force-generating capacity. During subsequent maximal cycling exercise, average cadence was reduced (pre:109 ± 14 vs. post:105 ± 14 RPM, $p<0.001$). Unilateral fatigue in the left knee extensors translated to a reduction in absolute crank power over the downstroke phase on the left side, where the knee extensors contribute a large amount of power (63, 117, 122). Interestingly, absolute crank power produced over the upstroke phase of the pedal cycle, where the knee extensors are predominantly inactive (152), was also reduced on the left side. Despite no change in MVF of the right knee extensors, the absolute power produced from the right crank over the downstroke was also reduced after fatigue in the left knee extensors, with a decrease in right VL activity. Absolute crank power was also reduced over the upstroke from the non-fatigued right side, following fatigue in the left knee extensors. The magnitude of reduction in absolute power varied between the downstroke and upstroke phases (-73 ± 20 vs. -25 ± 9 W, $p<0.001$) as well as between the left and right sides (-65 ± 17 vs. -32 ± 13 W, $p<0.001$). When relative crank power was calculated in reference to the maximal power produced at a given cadence, side and phase, we observed that relative power over the upstroke was reduced to a greater extent than the downstroke, for both the left (-22.7 ± 12.8 vs. -10.1 ± 6.7 %, $p<0.001$) and right sides (-12.7 ± 7.8 vs. -5.2 ± 2.9 %, $p<0.001$). At the end of the unilateral knee extension exercise MVF of the right knee extensors was unchanged, however VL EMG in the right leg was reduced during the cycling exercise, along with the reduction in crank power. Overall, this study found when the force-generating capacity of a major power-producing muscle group, active during the downstroke phase, is reduced only on one side, the ability of the system to produce maximal power is impacted over both phases of the cycle and on both sides.

5.1 Knee extensor function and lower limb function during cycling exercise

To the best of our knowledge this is the first study to calculate fatigue during maximal cycling exercise in reference to the individual power-cadence relationships obtained for the left and right cranks separately, as well as for the upstroke and downstroke phases of the pedal cycle. From the fatigue-free calculations, we can clearly see the importance of the downstroke phase in generating crank power. From the left crank, downstroke power contributed 85.6 ± 4.5% of total power over a full pedal cycle, while upstroke power contributed 14.4 ± 4.5%. Similarly, from the right crank, downstroke power contributed 85.0 ± 4.2%, while upstroke power contributed 15.0 ± 4.2%. We found that maximal voluntary force of the knee extensors in both the left and right sides was correlated with maximal crank power transmitted to the respective left and right cranks, specifically over the downstroke phase of the pedal cycle (Figure 4.2). This is in agreement with the findings from Driss et al. (2002) however, in their study F-V characteristics were estimated from the total power of both cranks and over a full pedal cycle. Comparing the results, we found a stronger correlation for the left ($r = 0.85$ vs. $r = 0.66$) and right sides ($r = 0.85$ vs. $r = 0.66$), showing MVF of the knee extensors is more highly correlated to crank power specific to the phase of the pedal cycle they are active.

Using the fatigue-free P-C relationships, we are able to quantify the power produced during the baseline sprint in *session 3* relative to each individual's fatigue-free maximal power and confirmed that the participants had produced a maximal sprint effort (98.6 ± 3.1%) in the fatigue-free cycling exercise before the unilateral knee extension exercise.

5.2 Unilateral knee extensor fatigue and maximal cycling exercise

At the end of the fatiguing unilateral knee extension exercise there was less than 1-min between the MVF measurements and the start of the maximal cycling exercise as participants transferred from the Cybex to the bike ergometer. This unavoidable delay presents a limitation of the study as it could allow for recovery in the knee extensors.

From the measurements obtained during *session 1*, average MVF was still significantly reduced to 74 ± 7% of baseline 2-minutes post the fatiguing unilateral knee extension exercise (Figure 4.1). Initially we anticipated the time to transfer from the Cybex to the bike may take up to 2-minutes but found the participants could transfer within 1-minute so decided to instruct the participants to transfer as quickly as possible to minimise recovery. Given there was no difference in MVF at baseline and at the end of the exercise between sessions *1* and *3*, we can be confident that the force-generating capacity of the knee extensors at that start of the maximal cycling exercise, post FAT_{ISO}, was still reduced between ~48% and 74% of baseline MVF. In addition, the significant reduction in the ratio of the resting doublet evoked force (10:100; -17.8 ± 11.3 %, Figure 4.7) indicates the prevalence of low-frequency fatigue. Following submaximal sustained isometric contractions with the knee extensors (60-s at 50% MVF), the ratio of low- to high-frequency stimulations has been shown to be still significantly reduced 27-minutes post exercise and at the same time MVF was still reduced to ~85% of baseline (43). With sustained isometric contractions at 20% of MVF in the knee extensors, same intensity as this study, it has been reported that MVF was still significantly reduced 10-minutes post exercise to ~90% of MVF (150).

With significant fatigue in the left knee extensors we were able to see that a unilateral reduction in the force-generating capacity isolated to one muscle group, effects crank power in both the left and right sides and over both the downstroke and upstroke phases. At the beginning and the end of the maximal cycling exercise, participants were also unable to reach the same cadence compared to baseline with a reduction in the initial (-3 ± 3 RPM) and final cadence values (-6 ± 4 RPM) (Figure 4.11).

5.2.1 Downstroke

5.2.1.1 Ipsilateral limb

From the fatigue-free correlation between MVF and P_{max} over the downstroke it was expected that with such a large reduction in knee extensor force-generating capacity, crank power during the downstroke phase of the pedal cycle would be effected on the ipsilateral side. This was clearly demonstrated by the reduction in absolute crank power (-99 ± 27 W, $p<0.001$) (Figure 4.4) and relative power specific to the left crank over the downstroke phase (-10 ± 7 %, $p<0.001$) (Figure 4.6). We did not see a correlation

(r = 0.07) between the reduction in MVF 2-min post the knee extension exercise in *session 1* and the reduction in relative power (Figure 4.15). However, there is an apparent outlier in the data, that when excluded, a trend is observed.

With the high level of peripheral fatigue exhibited at the beginning of the maximal cycling exercise, seen by the reduction in R_{EF} (-27.4 ± 21 %) (Figure 4.7), the associated increase in metabolites would impact the contractile properties of the exercising muscles. In particular, increased P_i and acidosis effecting maximal force per cross-bridge cycle and increased ADP known to effect the shortening velocity of the muscle fibres (38, 124). As the maximal exercise began from a stationary start, with the left crank at top dead centre, the reduction in cadence from the initial left downstroke illustrates a reduced ability of the participants to overcome the inertia of the flywheel compared to the non-fatigued state, as maximal force applied to the pedal is reduced with fatigue in the knee extensors. This effect is carried throughout the maximal exercise as the cadence during subsequent downstroke cycles is reduced comparative to the baseline sprint (Figure 4.11), which may be indicative of reduced shortening velocity in the primary power-producing knee extensors, due to increased ADP, restricting the maximal velocity the participants would be able to reach.

Over the downstroke phase, average torque from the left crank was reduced (-7 ± 2 N.m) and the participants weren't able to produce the same peak effective force (F_{tan}) or total force (F_{tot}) during the downstroke phase, coinciding with knee extensor activity. Following the assumption that during maximal cycling, there is a very limited solution space for effectively applying force to the pedals to reach the maximal power possible (65, 144) a reduction in the force-generating capacity of a major power-producing muscle group would most likely result in a reduction in force applied to the pedals as, seemingly, there are no adequate compensation strategies. Cross-correlation calculations showed a significant shift in the shape of the total force applied to the pedals with fatigue in the knee extensors, however this was only by 1% earlier (k = 1) in the pedal cycle which could be considered negligible (Figure 4.16).

We also found that intra-individual variability (VR) increased for the tangential and total force profiles following the knee extension exercise. This indicates that a reduction in MVF of the knee extensors impacts on the ability of the system to consistently

transmit force to the pedal between pedal cycles. The results also showed that VR increased more for the total force profiles in the ipsilateral limb than the contralateral limb. This could be the result of the CNS nervous system trying to modify the intra-limb strategy in the effected limb to adapt to the reduction in force. Or it may be representative of the system trying to still maintain the optimal pedalling strategy required for maximal power production, but with reduced force-generating capacity in a main power-producing muscle group, the other lower limb muscles are unable to transfer the reduced force onto the pedal as consistently.

At the end of the knee extension exercise activation of the knee extensor muscles (%VA; -23 ± 12 %, Figure 4.9) and peak EMG activity (VL/M_{max}; -34 ± 20 %, VM/M_{max}; 26 ± 21 %, RF; -35.7 ± 20.5 %, Figure 4.10) significantly reduced which translated to a reduction in peak EMG during the cycling exercise for VM (VM/M_{max} -6 ± 16 %, $p<0.005$) and RF (-5 ± 19 %, $p<0.005$). While a significant reduction in IMVC VL activity was evident following the knee extension exercise, peak activity during the maximal cycling exercise of VL normalized to M_{max} was not significantly different between sprints. The delay between the knee extension and cycling exercises could explain this observation for VL, as some recovery in the activation may have occurred. These results suggest that the reduction in force seen during maximal cycling post knee extension exercise resulted from a combination of reduced activation from the CNS (for VM and potentially RF) and an impairment of E-C coupling within the muscles. Along with a reduction in peak EMG, cross-correlation also calculated a small shift in EMG patterns for VM (1%, $k = 1$) and RF (2%, $k = 2$) earlier in the pedalling cycle, which could explain the 1% shift in total force patterns, but is not a significant change in the context of the whole exercise.

Reductions in knee extensor activity have been documented in previous studies, during repeated and sustained sprint cycling, with reductions in ankle plantarflexors, GAS also reported (87, 137). This reduction in EMG from the bi-articular ankle plantarflexors is not thought to be fatigue related, but instead, linked to a reduction in force generated by the uni-articular muscles, due to fatigue in these proximal muscles. Therefore, reducing the amount of force to be transferred to the pedal, so GAS activity is adjusted accordingly (87). In our study, we assume there is also no fatigue induced in GAS between the baseline and post knee extension exercise sprint, however, with significant

reductions in knee extensor MVF our results show an increase in peak GAS EMG activity. As these muscles only contribute a small amount of the total energy they produce directly to the crank (184), it is unlikely that this would be an attempt by the CNS to increase force from GAS to compensate for force reduction in the knee extensors. This may instead be in response to the slight shift in activation of VM and RF. Along with GAS, uni-articular SOL activity is also associated with transferring force generated by the proximal muscles from the limb to the pedals as part of the extensor synergy (184). While peak EMG of SOL was unchanged, we did observe a shift in SOL EMG profiles by 1% (k = 1) earlier in the cycle, similar to VM and RF. This could reflect the CNS adjusting the activity of SOL to match the changes in knee extensor activity with fatigue and maintain the effective application of force to the pedal.

The calculation of VR showed that intra-individual variability in SOL and GAS was also increased with prior fatigue in the knee extensors. The increase in VR indicates that when knee extensor MVF was reduced, ankle plantarflexor activity was more varied between each pedal cycle. Taken with the increase in peak GAS EMG and shift in SOL, this could be a marker of the CNS trying to adapt to a significant perturbation (i.e. reduction in a major power-producing muscle) on the coordinated transfer of force between the lower limb muscles to the pedal.

A significant increase in VR was also seen for RF in the left leg, along with a reduction in peak RF EMG and 2% earlier shift in the cycle (k = 2). This could be linked to the large amount of peripheral and central fatigue induced in the left knee extensors following the unilateral knee extension exercise. However, VR in VM and VL profiles was not significantly different between baseline and post knee extension exercise. Unlike the uni-articular VAS, who are active solely to generate force, the bi-articular RF is implicated in coordinating the transfer of energy between the hip and knee (66, 172, 184). Along with VAS, the uni-articular hip extensors, GMAX are primary power-producers. Following fatiguing knee extension exercises the force-generating capacity of uni-articular GMAX was presumably unimpeded and given that the level of activity in GMAX did not change, it is likely the same amount of force was generated by this powerful muscle group during cycling pre- and post- knee extension exercise. Fatigue in RF, however, could mean the power that is produced by the non-fatigued GMAX

would not be able to be as effectively transferred across the hip to the limb and subsequently to the pedal. Moreover, RF has been shown to fatigue at a higher rate compared to the uni-articular VAS muscles during submaximal isometric contractions (56). Excessive levels of fatigue in RF could substantially impact on their ability to transfer force from GMAX to the limb and ultimately impact on the power production during the downstroke of the pedal cycle. The increased variability in VR from RF, along with the slightly earlier shift in profile, may be an indication of the CNS trying to adjust RF activation to still transfer force as effectively as possible.

Along with reductions in knee extensor activity, adjustments in knee flexor activity have also been reported, by a reduction in peak HAM EMG (87) and a shift within the pedal cycle of knee flexor activity (32). During maximal cycling exercise, the large contribution from the uni-articular VAS muscles to crank power also relies on the coordinated activation of the bi-articular knee flexors to redirect the force to be effectively transmitted to the pedal (144, 173). Hautier, et al. (2000) proposed that the reduction in knee flexor activity observed in their study was in response to reduced knee extensor activation due to fatigue in these muscles. With isolated pre-fatigue in the knee extensors in the present study, the same adjustments in HAM activation were not seen i.e. no reduction in peak EMG or shift in pedal cycle of the profile. As the novelty of this study was isolating fatigue in the knee extensors, the disparity between our results and these findings may be related to fatigue induced by cycling exercise having a global effect on the force-generating capacity of the lower limb muscles. Therefore, the changes in HAM activity may not solely reflect fatigue in the knee extensors, but a combined effect of fatigue occurring in other muscles involved in the repeated cycling task. Additionally, over the upstroke phase considerable relative knee flexion joint power is produced during sprint cycling (63, 117) which could also support fatigue occurring in the knee flexors. With no significant changes in HAM activity seen in our results, we presume fatigue had not been induced in the knee flexors. However, some fatigue may have been induced in the knee flexors during the knee extension exercise. Antagonist co-activation has previously been observed during submaximal knee extension contractions (142), which was also observed in the present study by increased HAM EMG during the submaximal contractions of the knee extension exercise (71 ± 77% from the first contraction to the final contraction, Figure 4.8). In addition, it has been shown through spectral analysis that significant fatigue, observed from a shift in

median frequency of the EMG signal, was experienced by the antagonist hamstring muscles following sustained knee extension contractions to the limit of endurance (56, 130). This could suggest that the lack of change in HAM EMG during maximal cycling may be related to peripheral fatigue in the knee flexors prior to the sprint, requiring a higher level of activation in the hamstrings to maintain effective transfer of force from the knee extensors. However, unfortunately MVF of the knee flexors could not be obtained during this study, so any changes in activity are unable to be related to a loss of force-generating capacity.

From the results, fatigue-free power during the downstroke phase of the pedal cycle, is unable to be reproduced when the force-generating capacity of the knee extensors is reduced. The changes in intra-limb coordination appear to only be adapted at the ankle muscles, which are involved in transferring force to the pedals. Suggesting during maximal cycling exercise, the CNS cannot adapt muscle activity to compensate for reduced power in the knee extensors.

5.2.1.2 Contralateral limb

With the force-generating capacity of the knee extensors in the right leg unaffected after fatiguing exercises with the left knee extensors, the correlation between MVF of the knee extensors and downstroke P_{max} would suggest that power production over the downstroke on the contralateral side would be unaffected. Our results showed that, to the contrary, absolute power was reduced (-47 ± 21 W, $p<0.001$) in the non-exercised right side and was reduced relative to maximal cadence- side- and phase-specific power (-5 ± 15 %, $p<0.005$). Additionally, the initial, final and average cadence measured over the downstroke of the right crank was also reduced with fatigue in the left knee extensors revealing a reduced ability to accelerate.

As the cycling exercises began with a downstroke of the left crank the reduction in the initial right downstroke cadence may be a result of decreased initial cadence from the left side. This could also explain the reduction in average and final cadence, as all right downstroke cycles are preceded by a reduced left downstroke cadence, due to fatigue in the left knee extensors. At the time of testing only one force transducer was available so unfortunately electrical stimulation was not performed on the right femoral nerve as

such, evoked force measurements were unable to be recorded. But given the right leg was rested during the knee extension exercise it is unlikely any peripheral fatigue occurred so, seemingly force produced per cross-bridge cycle or impaired shortening velocity would not influence cadence on the right side. Conversely, we observed a reduction in both the peak effective (tangential) force (-5 ± 3 %, $p<0.001$) and total force (-5 ± 4 %, $p<0.005$) transmitted to the right pedal, along with a reduction in crank torque (-2 ± 1 N.m, $p<0.005$). This may have contributed to the reduced ability of the participants to accelerate the flywheel.

Further to this, intra-individual variability of both the tangential and total force profiles increased with fatigue in the left knee extensors. Despite the force-generating capacity of the right lower limb muscles presumably unaffected, force appears to be less consistently applied to the right pedal between the pedal cycles. This could represent an *intra*-limb adjustment of the system due to a cross-over effect of fatigue to the right limb, or potentially an *inter*-limb adaptation to the reduced force in the left knee extensors. Given it is unlikely that peripheral fatigue would have developed in the right knee extensors, a reduction in pedal forces is most likely due to a reduction in central drive. At the end of the knee extension exercise IMVC EMG was reduced in VL (-8 ± 19 %, $p<0.05$) and peak EMG during the subsequent maximal cycling exercise was also reduced in VL (-5 ± 16 %, $p<0.05$). The reduction in central drive to the non-exercised VL may be the result of increased firing from group III/IV afferents in the left knee extensors that led to a reduction of cortical drive. In a study by Todd et al. (2003), after fatiguing, alternating unilateral MVCs of the elbow flexors, they found that maximal torque was maintained but a slight reduction in activation occurred. Using TMS to assess motor-evoked potentials and voluntary activation, they attributed the finding to a reduced ability of motor cortical output to maximally drive the muscles.

Although MVF of the right knee extensors did not show any reductions immediately after the knee extension, the reduction seen in crank power over the downstroke from the right side may be due to the type of task being performed. Previous studies assessing cross-over of fatigue to non-exercised muscles have found that the effects were only evident after multiple fatiguing contractions with the exercised and non-exercised muscle groups (48, 83, 166). In our study the significant fatigue induced in the left knee extensors may not have affected the rested right knee extensors during the single-joint

IMVCs, but inhibited central drive with the repeated activation of the right knee extensors during maximal cycling. Alternatively, based on previous findings, where unilateral perturbations were imposed during treadmill walking (82, 149), the reduction in power transmitted to the right crank could reflect an inter-limb coordination strategy used by the CNS. As the force-generating capacity of the contralateral right knee extensors in our study was unaffected following the fatiguing knee extension exercise, the reduction in power could be a consequence of the system trying to match that of the left leg to maintain a smooth pedalling technique to maximise total power output over the pedal cycle.

For the most part EMG activity in the right leg was unchanged between the two sprints, however, post knee extension exercise, peak EMG of RF occurred 5 ± 8 % ($p<0.05$) earlier in the pedal cycle (Figure 4.23), with a shift in the profile of RF activation 1% earlier, shown by cross-correlation ($k = 1$). While RF is highly activated during the downstroke peak activity occurs close to TDC (52, 151) to transition the crank into the downstroke phase. Earlier activation of RF could be related to the reduction in downstroke power in the left leg, resulting in less propulsive force at the onset of RF activation in the right leg, that would normally assist pushing the mechanically coupled cranks through the vertical top and bottom dead centres. As the cycling exercise was maximal, theoretically the level of RF activation can only be marginally increased as maximal EMG levels have been reported during maximal cycling exercises (151). The earlier onset of activity may be an adjustment by the CNS to compensate for the reduction in downstroke power from the left side to allow a smooth transition of the pedals from flexion to extension in the right pedal and extension to flexion in the left pedal. In a study from Kautz et al. (2002) they demonstrated that the activity of the bi-articular RF and knee flexors involved in transition phases of the pedal cycle is highly effected by sensorimotor feedback of force generated by the contralateral limb. In our study, the reduced force and earlier shift in VM and RF activation during extension in the left side may have triggered an adjustment in RF activation via the proposed neural inter-limb pathway (99), affecting force transfer and consequently power delivered to the crank.

Intra- individual variability of RF was also increased in the right leg, which could be related to the functional role of RF as a bi-articular muscle (172, 173). The increased

variability could be representative of the system relying on adjustments of bi-articular RF activity to optimize inter-limb coordination with contralateral fatigue. Unfortunately, we were limited in the number of muscles we could record EMG activity from, so without quantifying the activation of GMAX and the synergistic lower limb GAS and SOL muscles in the contralateral right leg, it is difficult to definitively comment on intra-limb coordination modifications over the downstroke phase of the right leg that may have led to the reductions in force and power output.

5.2.2 Upstroke

Given the bi-functional role of RF as a knee extensor and hip flexor, it seems likely that alterations in RF activation, in both the left and right sides, could affect force production over the upstroke of the pedal as well as the downstroke, where flexor muscles are active.

5.2.2.1 Ipsilateral limb

The large reduction in MVF, %VA and R_{EF} in the left knee extensors, imply that the force-generating capacity of bi-articular RF in the left leg was significantly impaired at the end of the knee extension exercise. Although much lower in magnitude compared to the downstroke (seen by the phase effect on absolute power; 858 ± 105 vs. 128 ± 25 W, $p<0.001$), propulsive forces during the upstroke phase are associated with knee and hip flexion power generated by the bi-articular knee flexors (HAM) and in the later stages, hip flexor muscles (RF) (63). Intuitively, fatiguing the knee extensors would seemingly have a larger effect on power produced during the downstroke (extension) phase, but interestingly our results show that the reduction in relative power, specific to cadence, side and phase, was reduced to a greater extent over the upstroke phase in the left crank (-23 ± 13 vs. -10 ± 7 %, $p<0.001$). Which was mirrored by the relative reductions in crank torque over the upstroke compared to the downstroke (-20.6 ± 15.1 vs. -8.3 ± 5.3 %, $p<0.001$), suggesting the amount of force transmitted to the pedals was also reduced, leading to reduced power output.

To effectively transfer flexion power onto the pedal, ankle dorsiflexors TA, are activated with RF over the later stages of the upstroke, assisting the transition of the crank into the downstroke phase (144). Peak EMG of TA in the left leg decreased by 7

± 15 % ($p<0.05$) after the knee extension exercise and the profile of EMG activation shifted 1% earlier in the cycle ($k = 1$). The reduction in TA is highly unlikely the result of fatigue induced in this muscle group, as such, the changes in activity are most likely linked to an adaptation of muscle coordination by the CNS. The reduction in force-generating capacity of RF following the knee extension exercise, along with the reduction in RF EMG amplitude during the cycling exercise, suggest there would be less flexion forces over the upstroke needing to be transmitted to the pedal. As a result, TA activation may have been reduced to maintain coordinated activation between the flexion muscles groups. Which would also relate the 1% shift earlier in TA activation, to coincide with the 1% earlier shift in RF activation.

The possible fatigue that may have been induced in HAM by the knee extension exercise, along with the presumably high levels of central and peripheral fatigue in RF from the knee extension exercise, increasing power during the upstroke phase to compensate for reduced power production during the downstroke might not have been a solution for the system. On the contrary, it seems more plausible that power during the upstroke would be reduced in conjunction with the downstroke power, as indicated by our results.

Although relative power had a greater reduction over the upstroke compared to the downstroke, in absolute terms, the magnitude of reduction was small compared to the reduction in power over the downstroke (-31± 11 vs. -99 ± 27 W). From a performance and functional stand point, the reduction in downstroke power had a larger impact on the overall performance produced during maximal cycling exercise. This is highlighted in the results, as for both the left and right sides, power over the downstroke represents ~86% of total crank power over a full pedal cycle, compared to ~15% from the upstroke ($p<0.001$).

5.2.2.2 Contralateral limb

In a surprising alignment with the left side, relative crank power was also reduced in the non-exercised right limb over the upstroke phase (-14 ± 9 %, $p<0.001$) and by a larger amount than the downstroke phase (-5 ± 15 %, $p<0.001$). Torque generated at the crank was also reduced over the upstroke on the right side (15 ± 5 vs. 14 ± 5 N.m,

$p<0.001$) however, the absolute difference was only ~1N.m. As the perturbation imposed on the left knee extensors resulted in a reduction in left crank power over the downstroke, the system could potentially try to limit the overall reduction in performance by increasing upstroke power in the non-fatigued contralateral limb. However, this doesn't appear to be the case. Of the major muscles involved in generating flexion power, we did not observe any increase in RF or HAM activity during the cycling exercise after fatiguing the left knee extensors. While HAM activity remained unchanged, there was a shift in peak RF activity earlier in the pedal cycle, occurring in the later stages of the upstroke phase and an increase in variability of RF activity between cycles was also observed. As discussed earlier, this may be associated with alterations in transitioning the crank between phases and effectively transmitting force to the pedals at the beginning of the downstroke, due to reduced downstroke power from the left crank. But it may also have impacted on the force transmitted to the pedal over the upstroke, leading to the reduction in power. Due to set-up restrictions EMG activity of TA from the right leg could not be recorded, so it is difficult to speculate how the variation in RF activity impacted on the synergistic coordination of the right limb and consequently the transfer of force to the right pedal during the upstroke phase.

As mentioned above, the force-generating capacity in the contralateral knee and hip flexors is presumed to be unimpaired during post knee extension exercise cycling, so the reduction in power is unlikely the result of fatigue in the flexor muscles. From the studies by Kautz et al. (2002) and Ting et al. (1998), antagonist knee and hip flexor activity appear to be regulated according to the sensorimotor state of the contralateral knee extensors. Ting et al. (1998) found that with passive or voluntary extension in the contralateral knee extensors, HAM activity over the coinciding upstroke was reduced. Kautz et al. (2002) found that increased contralateral force led to increased bi-articular activity, in particular RF and TA. This could associate the reduction in power over the upstroke from the right crank, occurring in response to the reduction in downstroke power from the left crank. However, in our case, activation levels of the non-exercised right knee flexors showed no change in amplitude, while the fatigued left knee extensors VM and RF activation reduced. This would relate more closely with Ting et al. (2000) who demonstrated a reciprocal relationship between the contralateral agonist/antagonist muscle groups. But again, with no changes in amplitude of HAM and RF activation as

well as the absence of TA activation in our study, it is difficult to comment on the causes and underlying intra-limb mechanisms that may have effected contralateral power production during the upstroke. Furthermore, in these studies the cycling exercise was submaximal. As the cycling exercise in this study was maximal there was probably limited opportunities for the CNS to adjust muscle coordination.

With the hamstrings and hip flexors (RF) the prominent muscles involved in the upstroke phase of the cycle, the lack of compensation observed in the contralateral flexion phase could be considered as further confirmation of the functional role of the bi-articular muscles in transferring power and as such, have a limited capacity to assist in power production (144, 170, 173, 184).

5.3 Summary, implications and future directions

5.3.1 Summary

From the results, we found that a unilateral reduction in force-generating capacity of major power-producing muscles, active over one phase of the cycle, results in a reduction in crank power from both the ipsilateral and contralateral sides and throughout both the upstroke and downstroke phases. It appears that, as hypothesised, during maximal bilateral cycling exercise, with an impairment induced unilaterally, there are very limited solutions available for the CNS to combat the perturbation and maintain power output. The CNS doesn't seem to be afforded much intra- or inter-limb solutions to compensate for unilateral perturbations, presumably as the muscles are already maximally activated. Consequently, the changes in muscle activation that were seen in the ipsilateral limb (VM, RF, GAS and TA), were only marginal in the time domain (1-2% of the pedal cycle). As the adaptations were seen in GAS and TA, this most likely related to adjusting to reduced force to be transmitted to the pedals, rather than trying to generate additional force from the ankle plantarflexors (i.e. increased GAS activity) to compensate for knee extensor force reduction. As such, the reduction in unilateral force-generating capacity in the knee extensors, a major power producing muscle, results in a loss of crank power over both the downstroke and upstroke phases. On the contralateral side, aside from a slight shift in peak RF, intra-limb coordination in the non-fatigued right limb was largely unadjusted, further suggesting that during

maximal bilateral exercise both sides are already performing in their optimal strategy and cannot compensate for contralateral force reduction.

Having said that, the reduction in relative downstroke power was ~10%, while knee-extensor force was reduced to 48% of MVF immediately after the knee extension exercise and presumably still <74% at the start of the cycling exercise. From the results of studies utilising inverse dynamics and computer modelling, knee extension power during maximal cycling contributes ~41% of total power (63, 117, 122). Based on the combined results, while maximal power is unable to be maintained in the ipsilateral limb, the system is seemingly able to minimise losses without drastic changes in coordination. The findings in this study seem to differ from other studies assessing muscle coordination changes in fatiguing sprint cycling (mainly changes in HAM activity and reductions in GAS). However, this can be explained by the novelty of our study, which suggests that when fatigue is isolated in the knee extensors prior to cycling exercise, the system adapts differently to fatigue induced by the cycling exercise, which would be likely to induce fatigue in the other lower limb muscles involved.

Our results from the knee extension exercise show that, during maximal single-joint exercises the force-generating capacity of the knee extensors in the non-exercised limb was not affected by substantial peripheral and central fatigue in the contralateral muscle group. Our results do support previous findings that some cross over effect of central fatigue can occur with submaximal sustained isometric contractions. The fact that MVF was not changed, but maximal power output during cycling exercise was reduced may be a consequence of the type of exercise being performed. As previously noted, cross-over effects of fatigue may be more likely to occur during repeated maximal efforts rather than a single IMVC (84).

5.3.2 Implications

The novelty of this study is that we were able to investigate how bilateral dynamic exercise is affected by a reduction in the force-generating capacity, isolated to a major power-producing muscle group. The main finding that crank power was reduced on both the ipsilateral and contralateral sides as a result of fatigue in the knee extensors may have implications for future research, as well as in clinical settings. For research

involving cycling exercise in particular, the results suggest that when investigating changes in muscle activation with fatigue, it is important to consider fatigue that may be induced in other lower limb muscles, not just the knee extensors. Previously reported changes in muscle activation (e.g. ankle plantar flexors and knee flexors) (87) have been associated with fatigue in the knee extensors, however, we did not see the same changes when fatigue was isolated to the knee extensors, which may mean that these changes also result from fatigue in other muscles. Although, we were unable to evaluate MVF of the other muscles so we cannot confirm if fatigue had occurred in other muscles. The finding that contralateral VL activation was reduced following repeated knee extension exercises may have implications for other studies assessing muscle activation using bilateral and dynamic exercises, as fatigue in one muscle group could influence the level of activation in other muscles on the contralateral side.

From a clinical perspective, the loss of force-generating capacity in a muscle group can present as a result of numerous diseases, pathological conditions or as a result of injury. The results of this study could be useful for clinicians in assessing muscle function and implementing rehabilitation programs, as a reduction in function of one muscle group could have effects on the activation of other muscles and the ability of the patient to effectively coordinate bilateral tasks.

5.3.3 Future directions

The limitations of the present study need to be considered when interpreting the results. One limitation associated with the knee extension exercise was that we were not able to quantify maximal voluntary force in the knee flexors. As knee extension exercises can increase knee flexor activation leading to a greater rate of fatigue in this muscle group (57, 142), it is possible that the fatiguing knee extension protocol used in the present study also induced fatigue in the knee flexors. Which may have contributed to the reductions in crank power observed during the subsequent cycling exercise. But as we could not measure maximal voluntary force in this muscle group we don't know if fatigue occurred in the knee flexors. Another limitation is our inability to measure resting and superimposed evoked force, voluntary activation and M-waves in the non-exercised right knee extensors. We observed a reduction in VL EMG during IMVC but we could not study if there was any central fatigue. To further develop the findings from

this study, future studies would focus more specifically on the cross-over of fatigue using single-joint knee extension and flexion exercises. As well as quantify voluntary activation, resting evoked force and M-waves from both knee extensors. In addition, using repeated contractions or sustained contractions following the perturbations to assess non-exercised muscle function, as single maximal voluntary force efforts may not be sufficient to uncover any effects. As we only observed rather minor changes in muscle coordination during the cycling sprint following the knee extension exercise, the level of peripheral and/ or central fatigue that was induced may not have been sufficient to require the system to adjust muscle activity. Future studies where a higher level of fatigue in the knee extensors is achieved may be necessary to uncover adaptations in muscle coordination that might occur during cycling exercise with reduced unilateral force-generating capacity in the knee extensors.

A measurement limitation of the cycling exercise was we were unable to obtain EMG recordings of the distal lower limb muscles on the right leg (GAS, SOL and TA). As a result, it is difficult to comment on changes in the intra-limb coordination of the right leg, leading to a reduction in crank power. A methodological limitation of testing cycling performance is the delay between transferring from the chair, following knee extension exercises, to the bike ergometer to begin the maximal cycling exercise. As stated above, for future studies a more focused investigation on the cross-over of fatigue would be undertaken first. Assessment of muscle coordination using cycling exercise would then be investigated in separate sessions or a follow-up study, once more is known about the cross-over effect of fatigue between different muscles groups (e.g. agonist/antagonist and ipsilateral/contralateral muscles) as well as the pattern of recovery following single-joint exercises.

CHAPTER 6. CONCLUSION

The results of this study show that a unilateral reduction in force-generating capacity of one muscle group, can impact performance on both the ipsilateral and contralateral sides during maximal bilateral locomotor exercise. The lack of compensation for fatigue in the left knee extensors, by increasing crank power during the right downstroke and upstroke phases or left upstroke phase, is not surprising as the cycling exercise was maximal. The reduction in crank power during the left upstroke as well as the downstroke and upstroke phases from the right crank could be due to some central cross-over of fatigue from the left knee extensors. This may also be related to a strategy by the CNS to optimize the smoothness of the movement in response to a reduction in maximal force-generating capacity of the left knee extensors.

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