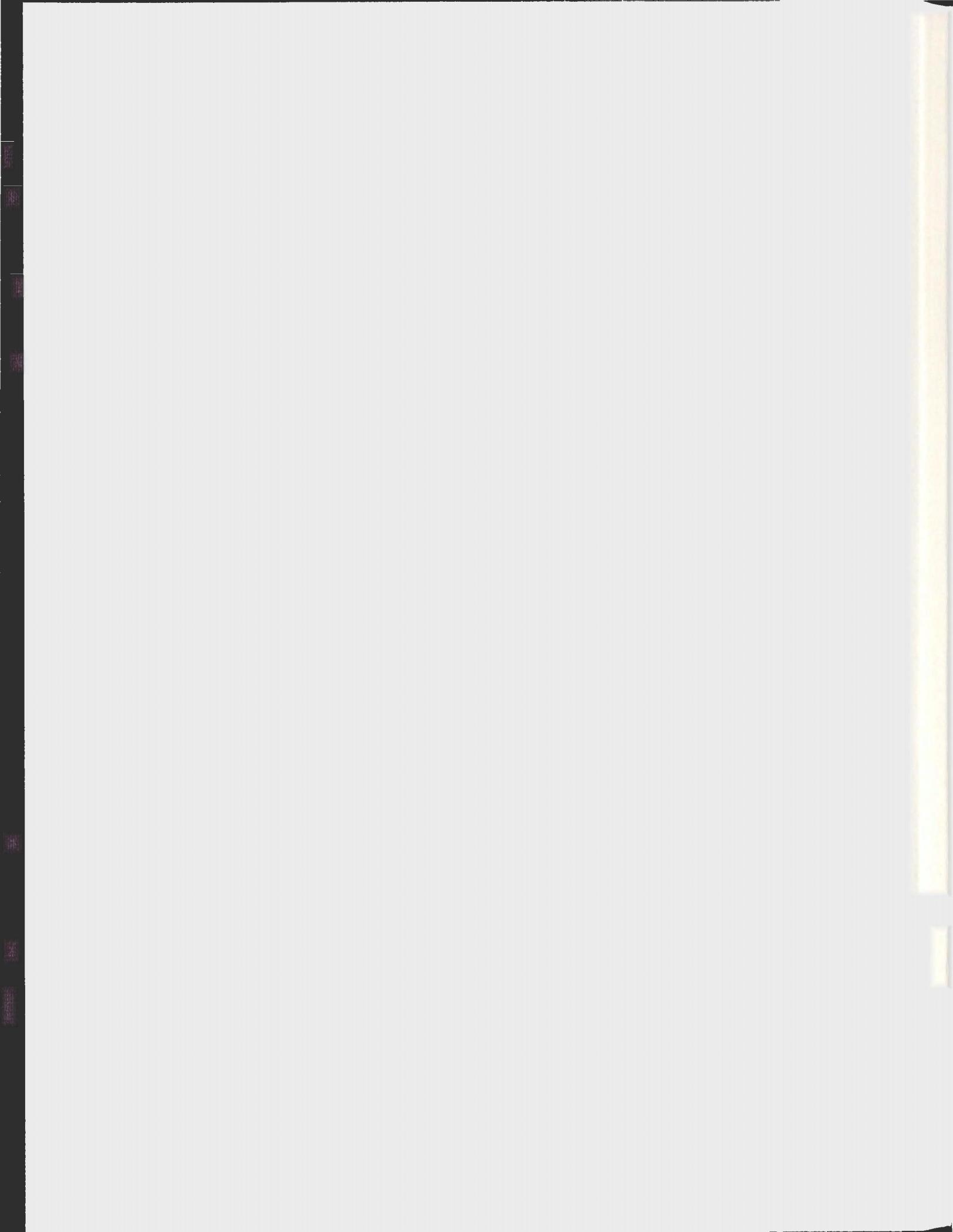


EFFECT OF CROSS-OVER FATIGUE ON POSTURE

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ABSTRACT

Research has shown that local fatigue occurring in an exercised limb can result in force loss in the same muscle of the non-exercised limb. This proposed cross-over effect of fatigue has been identified in muscles of the upper and lower limb and also in muscles that are not directly related to the fatigue (i.e. right quadriceps femoris fatigued and effects are noted in left and right biceps brachii and dorsal interosseous muscle). Studies published to date have also examined the effects of age and gender on cross-over fatigue. Not all studies, however, have confirmed the existence of cross-over fatigue in the non-exercised limb. The discrepancy in results (i.e. some studies finding cross-over fatigue and others not) may be attributed to the variety of outcome measures examined, the intensity at which the fatiguing contractions were performed, the type of fatiguing task and the specific muscle studied.

So far most studies have examined strength deficits created by this cross-over fatigue. Little attention has been paid to the effect of this type of fatigue on the body's ability to control movement. To the best of our knowledge there is only one study which has examined the effects of cross-over fatigue on balance. These researchers fatigued the quadriceps femoris on one side and measured balance of the non-fatigued leg during single leg standing pre- and post-fatigue protocol. Their study showed that balance, while standing on the non-exercised leg, was disturbed after the fatiguing protocol. At present it remains unknown whether these changes in non-exercised limb balance were due to the alterations in quadriceps femoris function or whether the fatigue affected the activation patterns and force production of other lower limb muscles. Based on this unanswered question this thesis aimed to replicate the previous balance related fatigue research, while adding a full analysis of lower limb muscle activity to assess how knee extensors fatigue on one side affected the non-exercised leg standing balance and muscle activation

patterns. The fatigue protocol incorporated 15 consecutive isometric contractions of 16 sec each, which were performed at 30% peak force for the dominant knee extensors. The experimental protocol consisted of pre-fatigue balance trials, warm-up exercises, maximum voluntary isometric contractions, fatigue protocol, and post-fatigue balance trials. The pre- and post-fatigue balance trials consisted of transition from double to single leg standing and single leg standing trials. The study found no cross-over fatigue effects and it is hypothesized that the intensity and the duration of the fatigue protocol incorporated in the present study might have accounted for the lack of cross-over fatigue effects.

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CO-AUTHORSHIP STATEMENT

Dr. Behm and Dr. Byrne have significantly contributed to this research study in various aspects. This includes contributing to the initial idea, formulating the design of the thesis proposal and the methods to carry out the research, supervising throughout the data collection, interpreting and analyzing the data and finally with the preparation of the manuscript.

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LIST OF ABBREVIATIONS

- AP - Anterio-posterior direction
- APA's - Anticipatory postural adjustments
- ATP - Adenosine triphosphate
- BoS - Base of support
- Ca⁺² - Calcium ion
- CoM - Center of mass
- CoP - Center of pressure
- CNS - Central nervous system
- EMG - Electromyography
- GM - Gastrocnemius medialis
- Gmax - Gluteus maximus
- Gmed - Gluteus medius
- iEMG - Integrated EMG
- GRF - Ground reaction forces
- Pi - Inorganic phosphate
- MVIC - Maximum voluntary isometric contraction
- ML - Medio-lateral direction
- PL - Peroneus longus
- RMS - Root mean square
- SD - Standard deviation
- TA - Tibialis anterior
- VM - Vastus medialis
- VL - Vastus lateralis
- VA - Voluntary activation

Chapter 1. INTRODUCTION

1.0 Overview

There are a variety of factors which are known to influence the ability of humans to generate purposeful, effective and efficient movements. These factors include attention, degree of proficiency with the motor skill, strength, endurance, flexibility, accuracy, speed and adaptability (Allen, 2007). In addition to these factors, fatigue has also been shown to affect the ability to perform motor tasks. As a consequence of fatigue, muscle properties such as action potential propagation, extracellular and intracellular ions and numerous intracellular metabolites may be affected (Allen et al., 1995). Additionally, a reduction in shortening velocity, slowing in the time course of relaxation (Fitt, 1994 and Allen et al., 1995) and reduction in force have been observed (Martin and Rattey, 2007). The decline in performance associated with muscular fatigue can be attributed to both peripheral (muscular) (Gandevia, 2001 and Taylor et al., 2000) and central (neural) factors (Boyas et al., 2011). Fatigue can also be either global or localized. The marathon runner at the end of a race will have full body fatigue while a person who has just completed a set of 20 repetitions of biceps curls will experience fatigue isolated primarily in the elbow flexors. In the case of a localized muscle, the effects of fatigue are easily recognized. The individual will experience a loss of force, typically indicated by a decrease in maximum voluntary isometric contraction (MVIC) (Bigland et al., 1995). In addition to this localized effects of fatigue, research has also shown that local fatigue occurring in one limb can result in a decrement in force production in the same muscle of the other non-fatigued side (Post et al., 2008).

This presence of cross-over fatigue has been identified in intrinsic hand muscles, (Zijdewind and Kernell, 2001), elbow flexors (Todd et al., 2003) and quadriceps femoris (Rattey et al., 2006, Mclean and Samorezov 2009 and Paillard et al., 2010). Studies published to date have also examined the effects of gender (Martin and Rattey, 2007) and

1.1 References

Allen, D. D. (2007). Proposing 6 dimensions within the construct of movement in the movement continuum theory. *Physical Therapy, 87*(7), 888-898. doi: 10.2522 /ptj.2006 0182.

Allen, D. G., Lannergren, J., & Westerblad, H. (1995). Muscle cell function during prolonged activity: Cellular mechanisms of fatigue. *Experimental Physiology, 80*(4), 497-527.

Berger, L. L., Regueme, S. C., & Forestier, N. (2010). Unilateral lower limb muscle fatigue induces bilateral effects on undisturbed stance and muscle EMG activities. *Journal of Electromyography and Kinesiology, 20*(5), 947-952. doi: 10.1016/j.jelekin.2009.09.006; 10.1016.

Bigland-Ritchie, B., Rice, C. L., Garland, S. J., & Walsh, M. L. (1995). Task-dependent factors in fatigue of human voluntary contractions. *Advances in Experimental Medicine and Biology, 384*, 361-380.

Boyas, S., & Guevel, A. (2011). Neuromuscular fatigue in healthy muscle: Underlying factors and adaptation mechanisms. *Annals of Physical and Rehabilitation Medicine, 54* (2), 88-108. doi: 10.1016/j.rehab.2011.01.001

Elmer, S. J., Amann, M., McDaniel, J., Martin, D. T., & Martin, J. C. (2013). Fatigue is specific to working muscles: No cross-over with single-leg cycling in trained cyclists. *European Journal of Applied Physiology, 113*(2), 479-488. doi: 10.1007/s00421 -012-24 55-0.

Enoka, R. M., & Stuart, D. G. (1992). Neurobiology of muscle fatigue. *Journal of Applied Physiology (Bethesda, Md.: 1985), 72*(5), 1631-1648.

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

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

Grabiner, M. D., & Owings, T. M. (1999). Effects of eccentrically and concentrically induced unilateral fatigue on the involved and uninvolved limbs. *Journal of Electromyography and Kinesiology 9*(3), 185-189.

Martin, P. G., & Rattey, J. (2007). Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. *Pflugers Archiv: European Journal of Physiology, 454*(6), 957-969. doi: 10.1007 /s00424-007-0243-1.

McLean, S. G., & Samorezov, J. E. (2009). Fatigue-induced ACL injury risk stems from a degradation in central control. *Medicine and Science in Sports and Exercise, 41*(8), 1661-1672. doi: 10.1249/MSS.0b013e31819ca07b.

Paillard, T., Chaubet, V., Maitre, J., Dumitrescu, M., & Borel, L. (2010). Disturbance of contralateral unipedal postural control after stimulated and voluntary contractions of the ipsilateral limb. *Neuroscience Research*, 68(4), 301-306. doi: 10.1016/j.neures. 2010.08.004.

Post, M., Bayrak, S., Kernell, D., & Zijdwind, I. (2008). Contralateral muscle activity and fatigue in the human first dorsal interosseous muscle. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 105(1), 70-82. doi: 10.1152/jappphysiol.01298.2007.

Rathey, J., Martin, P. G., Kay, D., Cannon, J., & Marino, F. E. (2006). Contralateral muscle fatigue in human quadriceps muscle: Evidence for a centrally mediated fatigue response and cross-over effect. *Pflugers Archiv: European Journal of Physiology*, 452(2), 199-207. doi: 10.1007/s00424-005-0027-4.

Regueme, S. C., Barthelemy, J., & Nicol, C. (2007). Exhaustive stretch-shortening cycle exercise: No contralateral effects on muscle activity in maximal motor performances. *Scandinavian Journal of Medicine & Science in Sports*, 17(5), 547-555. doi: 10.1111/j.1600-0838.2006.00614.x.

Shinohara, M., Keenan, K. G., & Enoka, R. M. (2003). Contralateral activity in a homologous hand muscle during voluntary contractions is greater in old adults. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 94(3), 966-974. doi: 10.1152/jappphysiol.00836.2002.

Taylor, J. L., Butler, J. E., & Gandevia, S. C. (2000). Changes in muscle afferents, motoneurons and motor drive during muscle fatigue. *European Journal of Applied Physiology*, 83(2-3), 106-115. doi: 10.1007/s004210000269.

Todd, G., Petersen, N. T., Taylor, J. L., & Gandevia, S. C. (2003). The effect of a contralateral contraction on maximal voluntary activation and central fatigue in elbow flexor muscles. *Experimental Brain Research*. 150(3), 308-313. doi: 10.1007/s00221-003-1379-7.

Zijdwind, I., & Kernell, D. (2001). Bilateral interactions during contractions of intrinsic hand muscles. *Journal of Neurophysiology*, 85(5), 1907-1913.

Zijdwind, I., Zwarts, M. J., & Kernell, D. (1998). Influence of a voluntary fatigue test on the contralateral homologous muscle in humans? *Neuroscience Letters*, 253(1), 41-44.

Chapter 2. REVIEW OF THE LITERATURE

2.0 What is fatigue?

Fatigue has been characterized in a variety of ways based on the task. Fatigue is sometimes described as an external measurable impairment in force, torque, power, or performance (Behm, 2004). Fatigue may be caused by frequent and persistent high intensity or maximal contractions and has been defined as a momentary drop off in functioning ability (Asmussen and Mazin, 1978), or a decline in the force generating capability of the muscle (Degens and Veerkamp, 1994). On the other hand, during prolonged contractions of submaximal intensity, fatigue may be observed as an augmentation in the apparent effort required to maintain the desired force (Enoka and Stuart, 1992). Regardless of its cause the effects of fatigue are well documented. Deficits in force production in the fatigued muscle (Degens and Veerkamp, 1994), decreased power (Behm, 2004), decreased firing frequency of the motoneurons (Bigland et al., 1983) and decreased muscle activity (Zijdewind et al., 1998) have been reported. Fatigue has also been shown to have negative effects on balance and stability (Paillard et al., (2010) and Paillard, 2012) indicating that fatigue can impact performance well beyond the specific or individual fatigued muscle. Fatigue is recognized to occur either in the periphery (i.e. distal to the neuromuscular junction) or centrally (spinal cord and brain).

2.1 Peripheral fatigue

Peripheral fatigue has been described as a task-dependent, exercise-induced attenuation in one's capability of producing the intended force (Bigland et al., 1995 and Gandevia et al., 1995). As described by Gandevia (2001), during motion the primary motor cortex causes an activation of the muscles via excitation of the motoneurons in the spinal cord. The axon of the motoneurons in the spinal cord, carry the action potentials to the

neuromuscular junction and then further transmission of action potentials to the muscle occur, leading to the muscle contraction. This contraction requires both mechanical and metabolic changes at the muscle level. Peripheral fatigue is thought to result due to these metabolic changes. Specifically a rise in inorganic phosphate (Pi) and a decrease in Ca^{2+} concentration have been found to play a role in decreasing the force capacity of the myofibril during fatigue (Boyas and Guevel, 2011). An increase in the amount of Pi has been shown to effect the force generating capacity of the myofibrils by affecting the sensitivity of myofibrils to calcium ion (Ca^{2+}) and thus affecting the cross-bridges (Westerblad et al., 2002). Also, the increase in Pi might affect the cycles involved in contraction-relaxation mechanism (coupling mechanism) (McLester, 1997), thus further contributing to fatigue. In addition to changes in Pi concentration, the decrease in force production during prolonged contractions is also due in part to a decrease in the concentration of Ca^{2+} (Van der Laarse et al., 1991). A muscle action potential travelling across to the t-tubule and then to the sarcolemma is required for the release of Ca^{2+} from the sarcoplasmic reticulum. In order for action potential propagation to continue a constant supply of energy from the hydrolysis of adenosine triphosphate (ATP) is required from the ATP driven Na^+/K^+ pump. As a result, a decline in the concentration of ATP during prolonged activity/fatigue may affect the activity of Na^+/K^+ pump and may alter the propagation of action potential, which will further affect the release of Ca^{2+} (Leppik et al., 2004).

Along with the amount of Ca^{2+} , the muscles' blood supply also plays an important role in regulating the force output (Sahlin et al., 1998). Blood supply is important because it ensures the muscle will get the required substrates and also help rid the muscle of waste metabolites. During contractions, however, blood vessels are compressed and as a result, muscles can sometimes become ischemic during isometric contraction. This may further

result in inadequate supply of oxygen and may even encourage more anaerobic pathways. Also, the inadequate supply of blood will result in the accumulation of metabolites such as Pi and H⁺ (responsible for the drop in force generating capacity) (Sjogaard et al., 1988).

2.2 Central fatigue

The factors described above are all thought to contribute directly to the occurrence of peripheral fatigue. On the other hand, central fatigue occurs due to events occurring proximal to the peripheral nerve. Central fatigue has been defined as an exercise-induced attenuation in the ability of the CNS to drive muscle maximally or can be characterised as a decline in the level of voluntary activation (VA) of a muscle (Taylor et al., 2006). The decrease in VA observed with central fatigue can involve any or all of the spinal and supraspinal mechanisms responsible for force production. As fatigue can occur due to the changes occurring either at the spinal cord or supraspinal levels, it is necessary to understand the adaptations that occur at these levels during fatigue.

Supraspinal fatigue has been identified by using transcranial magnetic stimulation (Sacco et al., 2000) and has been reported to be responsible for about 20-25% of the decrement in force with fatigue (Taylor et al., 2006). This force decrement might occur because of reduced excitatory signals provided by the motor cortex during prolonged exercise (Boyas and Guevel, 2011). The amount of brain neurotransmitters has also been associated with the decrease in excitation of the corticospinal descending tract. Increased concentration of certain brain neurotransmitters such as tryptophan (Newsholme and Blomstrand, 1995), γ -aminobutyric acid (GABA) (Tergau et al., 2000), acetylcholine (Conlay et al., 1992) and adenosine (Davis et al., 2003) during exercise have been found to affect supraspinal functioning, by decreasing the recruitment of motor units and further

resulting in central fatigue. The concentration of neurotransmitters and the muscle's force production ability have also been reported to decrease the activity of muscle afferents during fatiguing contraction, thus further leading to a decrease in cortical activity (supraspinal inhibition) (Gandevia, 2001).

In addition to possible supraspinal contributions to central fatigue, events occurring in the spinal cord can also contribute. There are five main factors hypothesized to be involved when fatigue occurs at the spinal level - motoneuron firing rate, small diameter muscle afferents (group III and IV), reflex induced muscle stiffness, feedback about intramuscular tension and renshaw cell inhibition (Gandevia, 2001; Boyas and Guevel, 2011). The details of the mechanisms surrounding each of these spinally linked mechanisms of central fatigue are beyond the scope of this review. The reader is directed to the review by Gandevia (2001) for details.

Clearly the reduction in force production observed during fatigue is a multi-factorial process. In all likelihood the occurrence of fatigue may involve both peripheral and central factors. The discussion above has focused on factors underlying the occurrence of local fatigue (i.e. prolonged quadriceps femoris contractions induces quadriceps femoris fatigue). In addition to this local fatigue, global effects of fatigue have also been observed. In the case of local muscle fatigue, one of the most common global effects is cross-over fatigue.

2.3 Cross-over fatigue

Cross-over fatigue results in a decrease in force production of the homologous muscle of the non-fatigued limb (Todd et al., 2003). Commonly it occurs involuntarily and in many cases goes unnoticed by an individual. Research examining cross-over fatigue has

examined its existence in upper and lower limbs, as well as attempted to quantify the time course of the muscle force deficits. Although inconclusive, there is some evidence to suggest that unilateral fatigue of lower limb muscles can negatively impact upper limb function (Takahashi et al., 2011) and vice-versa (Kennedy et al., 2013). This review will focus only on fatigue that crosses from lower limb to lower limb or upper limb to upper limb – the reader is referred to (Takahashi et al., 2011 and Kennedy et al., 2013) for details of cross-over fatigue that occurs between upper and lower limbs.

2.3.1 Upper limb cross-over fatigue

Only a few studies have focused on the effect of cross-over fatigue in the forearm flexors and intrinsic hand muscles (Todd et al., 2003; Post et al., 2008 and Zijdwind et al., 1998). Todd et al. (2003) examined the effect of a contralateral contraction on maximal voluntary activation and central fatigue for the elbow flexors using both alternating and unilateral intermittent muscle contractions. Their study demonstrated a 2.9% cross-over effect of central fatigue between limbs when four 1-min sustained maximum voluntary isometric contraction (MVICs) of the elbow flexors alternating between the left and right arms were performed. However, the unilateral intermittent contractions produced no cross-over fatigue. Post et al. (2008) observed an average decrease of 10% MVIC in the first dorsal interosseous muscle of the non-exercising hand, in a group of men and women after two different fatiguing protocols. These fatiguing protocols consisted of either two minutes of sustained MVIC or a submaximal intermittent exercise performed at 30% of MVIC, both of which were maintained until exhaustion. Their results suggested that maximal effort contraction may lead to a more marked decline in VA. They concluded that the central fatigue generated during a single-sided upper arm task was strong enough to decrease the force output in the non-exercised arm. Zijdwind et al. (1998) used 30%

MVIC contractions to fatigue the first dorsal interossei. Only minor cross-over effects of fatigue were found for the homologous contralateral muscle. From the aforementioned literature, it is clear that there is a disparity in the consistency of cross-over fatigue effects in the upper limb. Thus, further research is needed to illuminate this phenomena.

2.3.2 Lower limb cross-over fatigue

Evidence of cross-over fatigue in the lower limb has been reported (Rathey et al., 2006; Martin and Rathey, 2007; McLean and Samorezov, 2009; Berger et al., 2010 and Paillard et al., 2010). The study by Rathey et al. (2006) analysed the effect of unilateral voluntary muscular fatigue of quadriceps femoris on the contralateral limb. They found the force generating and peripheral parameters of fatigue (M-wave properties and the twitch torque) were unchanged for the non-exercised leg (MVIC was decreased but not significantly). Despite the lack of change in force, the VA and integrated electromyography of the quadriceps femoris were found to have declined significantly in the non-exercised leg after unilateral fatigue. Rathey et al. (2006) suggested that the central fatigue might have crossed to the non-exercised side, but did not disturb force generating ability. They concluded that the decrease in the maximum voluntary force in the fatigued limb may have been a combination of both peripheral and central changes, but on the non-exercised side it was just the central changes that contributed to the decrease. The other study by Martin and Rathey (2007) showed a significant average decrease in non-fatigued quadriceps femoris activation of about 9% in men and 3% in women after a 100-second sustained maximal isometric knee extension.

In addition to research that has identified cross-over fatigue, some research in this area has been unable to confirm the existence of such fatigue. For example Grabiner and Owings (1999) studied the effects of eccentrically and concentrically induced unilateral

fatigue of knee extensor on the fatigued and the non-fatigued limbs. Their study found the concentric MVIC force on the non-fatigued side did not change after the concentric fatigue protocol. When eccentric fatiguing contractions were performed, however, eccentric MVIC force on the non-fatigued side actually increased. The study suggested that the eccentric MVICs may be resistant to fatigue although further research is needed to confirm this. Regueme et al. (2007) studied a unilateral exhaustive rebound exercise incorporating calf muscles on a sledge apparatus. The study was unable to find the existence of cross-over effects after the exhaustive stretch-shortening type exercise. Similarly Elmer et al. (2013) concluded that high-intensity single-leg cycling did not compromise maximum cycling power for the contralateral limb and as well as for the maximum isometric handgrip force. Studies conducted by McLean and Samorezov, 2009; Berger et al., 2010 and Paillard et al., 2010 have also found evidence of cross-over fatigue in the form of disturbances in posture. The reader is referred to the posture section for more details on these studies.

Based on the literature the existence of cross-over fatigue can not be definitively confirmed. There have been a number of studies that have found evidence of its occurrence and others that have been unable to quantify any effects. The discrepancies in the literature can likely be explained by the variety of outcome measures examined, the type of fatiguing task incorporated, the intensity and the duration at which the fatiguing contractions were performed, and the specific muscle investigated (Enoka and Stuart, 1992, Zijdwind 1998; Rattey et al., 2006; Martin and Rattey, 2007; Paillard et al., 2010 and Elmer et al., 2013). Thus, more research is required in this area to better understand the mechanisms or factors responsible for causing such discrepancies.

2.3.3 Gender and cross-over fatigue

One of the reasons for the lack of consistency in research investigating cross-over fatigue may lie in the fact that there appears to be an effect of gender. Martin and Rattey (2007) have reported gender differences with respect to cross-over fatigue. After the sustained contractions of the dominant leg, Martin and Rattey (2007) reported that men experienced a greater decrement in voluntary force during fatigue (about 13%, compared to 8% in women) in the non-fatigued leg. Also greater deficits in non-fatigued quadriceps femoris activation were found in men as compared to women (about 9% versus 3%). Although this research seems to suggest that males are more susceptible to cross-over fatigue than females, the relationship is not straight forward, as Martin and Rattey (2007) suggested that differences in fatigue rates between males and females may have contributed to their results.

2.3.4 Posture and cross-over effect

Some authors have examined the effect of local muscle fatigue on postural control strategies and/or muscle activation during postural tasks when standing on the non-fatigued limb (McLean and Samorezov, 2009; Berger et al., 2010 and Paillard et al., 2010). McLean and Samorezov (2009) examined the effects of unilateral fatigue induced by single leg squats on non-fatigued limb performance during single-leg landing in elite female athletes. They reported that the non-fatigued limb exhibited an increased stance hip internal rotation moment. The study concluded that this increased moment occurred due to the effects of cross-over fatigue and might have occurred to counteract the deteriorating effects of fatigue on ligamentous injury during landing and have further led to promote beneficial postural adjustments. The study by Berger et al. (2010) analyzed the effects of unilateral ankle muscle fatigue on postural control. During the fatiguing

protocol, a sequence of 10 toe-lifts immediately followed by 10 knee flexions until exhaustion with the exercised leg was performed. These authors reported a decrease in the muscle activity of the tibialis anterior (TA) on the exercised side while finding increased activation in TA on the non-exercised leg. Also a trend toward a decrease in muscle activity of triceps surae was found in both legs. These alterations lead to an increase in the agonist/antagonist EMG ratio leading the authors to suggest that changes with the contralateral agonist/antagonist contractions could lower the risk of further injury of the fatigued muscles. These findings suggest that the effects of cross-over fatigue may extend beyond the homologous muscle. The other study in this context (Paillard et al., 2010) showed that ipsilateral fatigue not only affects force production on the non-fatigued side but it also affects the ability to complete a functional task like standing on one-leg on the non-fatigued side. These authors fatigued the quadriceps femoris muscle and compared postural stability pre- and post-fatigue while individuals stood on the non-fatigued limb with their eyes closed. Their results showed that individuals' postural stability, as quantified using center of pressure (CoP) measures, declined significantly when participants were asked to stand on the non-fatigued leg.

From the above literature, it is clear that the effects of cross-over fatigue are not just limited to the homologous muscle of the fatigued limb, but can have a substantial impact on the non-fatigued limb and posture as well. One interesting question arising from the literature is the mechanism by which unilateral fatigue of an isolated muscle impacts postural control. Although the work of both Paillard et al., 2010 and others (McLean and Samozov, 2009 and Berger et al., 2010) reported changes in postural control, they did not investigate the neuromuscular control strategy changes that lead to these alterations in posture. Specifically, it is surprising that cross-over fatigue in the quadriceps femoris (not an anti-gravity muscle) should have dramatic effects on posture

given the relatively small role the quadriceps femoris plays in quiet standing balance (Masani et al., 2013). As this thesis will probe the issue of the effects of unilateral quadriceps femoris fatigue on postural control, what follows is a brief review of the literature related to postural control.

2.4 Postural control

In order to study the effects of unilateral fatigue on postural control during quiet standing, it is important to have a general understanding of postural control and the strategies the body uses to maintain it. Postural control or balance during quiet standing is defined as one's ability to sustain the body's center of mass (CoM) within the base of support (BoS) (Winter, 1995). Although during quiet standing an individual may appear stationary, in reality they are undergoing postural sway. The reason for the continuous movement of the CoM remains unknown, and there is no consensus as to whether sway is beneficial or detrimental. Postural sway is defined as the continuous movement of body's CoM within the BoS (Winter et al., 1993). This continuous movement of CoM is controlled by CoP displacement, which is considered as a point of application of the net vertical ground reaction forces (GRF). This CoP displacement is further controlled by the activation of the muscles (gluteus medius (Gmed), TA, gastrocnemius medialis (GM), peroneus longus (PL)) (Van Deun et al., 2007). This is the reason why postural sway is commonly analyzed through the CoP displacement (Amiridis et al., 2003).

During daily activities, balance is continuously being challenged. Disturbance of balance might occur due to gravitational or other destabilizing forces acting on the body, or from environmental forces in contact with the body. There are two different movement strategies, fixed support or change in support that are used by individuals when they are exposed to a perturbation that threatens their stability (Horak, 1987). Fixed support

strategies can occur at the ankle or the hip. An ankle strategy attempts to compensate antero-posterior sway perturbations of the CoM by rotating the body around the ankle joint and some part of the hip strategy may also develop (Horak, 1987). The sagittal plane hip strategy involves the movement of the CoM by flexing or extending the hip joint. This happens when a person stands on a narrow BoS (heel-toe stance) or when the counterbalancing torque at the ankle joint is insufficient (Horak, 1987). On the other hand, change in support strategies involve a change in the size of the BoS. This can be carried out by taking a step with the feet or by reaching to grab something with the hands. This strategy ensures that the CoM remains in the now larger BoS support, therefore allowing the individual to remain balanced. It was once believed that the choice of strategy (i.e. fixed vs. change in support) depended upon the intensity of the postural disturbance (Horak, 1987). More recent literature (Maki and McIlory, 2006) has found that the choice of strategy is not based on the size of the perturbation but that there are many factors (i.e. BoS at the time of perturbation, any secondary tasks being undertaken, effects of previous perturbations, individual's perception of risk etc.) that contribute to it.

In addition to these reactive strategies that the body uses to maintain balance, the CNS also uses anticipatory reactions to help maintain postural control. These reactions, known as anticipatory postural adjustments (APA's) can occur in response to internally (Benvenuti et al., 1997) or externally created perturbations (Santos et al., 2010). As these perturbations have the potential to lead to changes in CoM position, the body must respond if balance is to be maintained. The unique aspect about APA's however is that the 'reaction' to the perturbation occurs before, or in anticipation of, the perturbation (Loram et al., 2005). The APA's serve two main functions (a) they minimize the displacement of CoM, by producing forces opposite to the direction of the applied force (Bouisset and Zattara, 1987) and (b) APA's also encourage carrying out of the voluntary

movements (Beraud and Gahery, 1995). The postural adjustments made with respect to the arm (Bouisset and Zattara, 1987) and during trunk movements (Oddsson, 1988) have been studied extensively.

2.4.1 The role of sensory information in maintenance of postural control

In order for the neuromuscular control system to be able to execute the strategies above and to maintain balance, it has to depend heavily on the information arising from sensory structures. In particular, sensory components such as vestibular, somatosensory and vision play an important role in controlling balance and posture (Horak, 2006). The vestibular system detects the changes in linear and angular acceleration of the head as well as detects the direction of gravity. On the other hand the somatosensory system detects the change in position and velocity of all body segments and as well as the direction of the gravity (Winter, 1995). The visual component has been found to play the most significant role in regulating postural stability.

2.4.2 The effect of vision on postural stability during quiet stance

Many researchers have reported a decrease in postural stability (observed as larger variability in CoP and as increased postural sway) in the absence of visual input (Oie et al., 2002; Speers et al., 2002, Corbeil et al., 2003 and Vuillerme et al. (2001, 2006). Vision also helps in minimizing the destabilizing effect that occurs due to fatigued muscle and also alleviates the effect of muscular fatigue on postural stability (Vuillerme et al., 2001). Corbeil et al. (2003) examined the involvement of vision in regulating postural control under muscular fatigue while individuals were in different stance situations. They found an increase in sway velocity with fatigue, for both eyes open and eyes closed conditions. Whereas when vision was provided, Vuillerme et al. (2001, 2006) found no or

very small change in postural sway with fatigue. The discrepancies between these two studies could be due to differences in the nature of muscle fatigue and various stances (single limb versus double limb stance) used by the authors. Vuillerme et al., (2001) showed that the availability of vision helps in controlling posture, which might have been affected as a consequence of calf muscle fatigue, suggesting that inputs from the sensory system played a significant role in controlling posture. Thus, from the above studies it can be concluded that removing vision affects balance irrespective of whether fatigue is present or not. Clearly based on the research outlined above, the absence of vision presents the neuromuscular control system with the increased challenges when it comes to maintaining balance. A similar challenge is posed by changes in BOS.

2.4.3 The effect of BoS on postural stability during quiet stance

Reductions in BoS have been shown to result in negative effects on postural stability particularly as task complexity is increased (Era et al., 2006). Matsuda et al. (2010) also reported standing on one leg as a less stable condition than standing on two legs. They examined the differences between CoP sway in one-legged and two-legged stances for typical male adults and male soccer players. Bisson et al. (2010) studied the effects of plantar flexor muscle fatigue on various postural tasks such as feet together, semi-tandem and single-leg stance on force plate. They found the CoP variation to be greater for the single limb stance and observed an increase in the postural sway variables as task difficulty increased.

In addition to examining the effects of size of BoS on balance, researchers have also examined how dynamic changes in size of BoS affect postural control. One such dynamic change is the transition from double to single limb support. This transition is essential for the beginning of the human locomotion (Carlsoo, 1966). There are many

other studies which have examined postural control during the transition from double to single support (Bisson et al., 2010, Matsuda et al., 2010, Mann et al., 1979, Rogers and Pai, 1990, Hughey and Fung, 2005). During the transition from double to single leg support, the decrease in BoS leads to displacement of the CoM. As the body's weight is supported on one limb during these kinds of transitions, adjustments in the postural control system are required to transfer the body's CoM to the new BoS. Rogers and Pai (1990) found the early recruitment of the Gmed of the flexing limb during the transition from double to single limb. Hughey and Fung, (2005) examined lower limb muscle activation during the transition from double to single leg stance. They found maximal activation of the adductor muscles occurred during limb unloading and activation of tensor fascia latae occurred during limb loading. These observed muscle activations likely reflect the mechanical adjustments required to overcome the change of CoM during the shifts occurring from double to single leg standing. Van Deun et al. (2007) studied the lower limb muscle activation during the transition from double to single leg standing in chronic ankle instability and control participants. The study found that the initiation of the muscle activity (Gmed, tensor fasciae latae, vastus lateralis medial hamstrings, TA, PL, and GM) in control participants occurred before the start of the transfer from double to single leg stance. Also, the study found that the control group was able to change the muscle recruitment order frequently for the eyes open and eyes closed condition. This signifies that the control group has the tendency to alter their muscle activation pattern as per the changing situation.

2.5 Fatigue and postural sway

Muscle fatigue affects postural stability by increasing static postural sway (Ledin et al., 2004). Studies have shown that muscular fatigue generated either at the trunk (Vuillerme

et al., 2008) or ankle (Vuillerme and Nougier, 2003) can result in deficits in postural stability. Studies have also shown that fatigue can negatively impact APAs (Morris and Allison, 2006) resulting in decreased stability. All of these effects are similar in that they occur in the muscle group that has been fatigued. Vuillerme et al. (2009) studied postural adjustments in response to unilateral hip abductor fatigue on the dominant leg with double-legged standing and found greater CoP displacements in the non-fatigued limb. This can be considered as an adaptive process, which might have occurred due to the weakened capability of the fatigued limb to control posture effectively. Allison and Henry (2002), studied the influence of trunk muscle fatigue and found early onset of APA in trunk muscles (transversus abdominis, internal oblique, rectus abdominis and external oblique and longissimus). Additionally their study suggested that this early onset of APAs may provide muscular contraction for a longer time, thus rendering more time for the critical force to reach a level required to maintain postural stability.

As discussed previously, however, the effect of fatigue on posture is not restricted to the fatigued muscles. Paillard et al. (2010) fatigued the quadriceps femoris on one side and measured postural control of the non-fatigued leg using a force plate during single leg standing before and after the completion of the fatiguing protocol. They showed that the ability to balance on the non-fatigued leg was disturbed after the fatiguing protocol. Confirmation of cross-over fatigue was supported by the increased CoP sway area, however no decrease in the values of MVIC of the contralateral quadriceps femoris were found. On the other hand, reduction in the MVIC of the ipsilateral quadriceps femoris was noted. The most interesting finding about this study was that by fatiguing the quadriceps femoris on one limb these authors were able to show deficits in standing balance on the other side. This occurred despite the fact that the quadriceps femoris is not a primary postural muscle during quiet standing (Masani et al., 2013). At present it remains

unknown as to whether these changes in balance performance of the non-fatigued limb were due to the alterations in quadriceps femoris function or whether the effects of fatigue were more global, affecting the activation patterns and force production of many other lower limb muscles. Thus, there is a need to examine the mechanisms responsible for affecting the postural control on the contralateral side.

2.6 Conclusions

The decrease in performance related to muscular fatigue can be attributed to both peripheral and central factors. The factors contributing to peripheral fatigue can range from altered concentration of H^+ , Pi and Ca^{+2} , impairments of Na^+/K^+ pump to the metabolic disruption sensed by the chemoreceptors. This metabolic fatigue sensed by chemoreceptors can relay information back to the CNS and lead to what is known as global or cross-over effects. A variety of studies have examined this cross-over effect of fatigue. Some of these have demonstrated the existence of cross-over fatigue while others have failed to find it. These discrepancies may depend on factors ranging from the type of muscle involved in the fatiguing protocol, intensity at which contractions were performed the experimental procedures to the dependency of muscle fatigue on the performed task. So far the evidence of cross-over fatigue has been reported with respect to upper body, lower body and age. The only study (Paillard et al., 2010) conducted so far with respect to posture was able to find changes in postural control. But the weakness of this study was that they did not examine changes in neuromuscular control resulting in these variations in posture. The study by Paillard et al. (2010) showed that balance performance of the non-fatigued leg was disturbed after the fatiguing protocol. Their research certainly provided added insight into the effects of fatigue on the non-fatigued leg. But at present it remains unknown whether those changes in the non-fatigued limb balance were due to

alterations in quadriceps femoris function or whether the fatigue affected the activation patterns and force of many other lower limb muscles. Thus, there is a need to examine the mechanisms, which could have led to the alterations in postural control of the non-fatigued side. Also, the appearance of the cross-over fatigue effect is not assured as the evidence from the literature is conflicting.

2.7 References

- Allison, G. T., & Henry, S. M. (2002). The influence of fatigue on trunk muscle responses to sudden arm movements, a pilot study. *Clinical Biomechanics (Bristol, Avon)*, 17(5), 414-417.
- Amiridis, I. G., Hatzitaki, V., & Arabatzi, F. (2003). Age-induced modifications of static postural control in humans. *Neuroscience Letters*, 350(3), 137-140.
- Asmussen, E., & Mazin, B. (1978). A central nervous component in local muscular fatigue. *European Journal of Applied Physiology and Occupational Physiology*, 38(1), 9-15.
- Behm, D. G. (2004). Force maintenance with submaximal fatiguing contractions. *Canadian Journal of Applied Physiology*, 29(3), 274-290.
- Benvenuti, F., Stanhope, S. J., Thomas, S. L., Panzer, V. P., & Hallett, M. (1997). Flexibility of anticipatory postural adjustments revealed by self-paced and reaction-time arm movements. *Brain Research*, 761(1), 59-70.
- Beraud, P., & Gahery, Y. (1995). Relationships between the force of voluntary leg movements and the associated postural adjustments. *Neuroscience Letters*, 194(3), 177-180.
- Berger, L. L., Regueme, S. C., & Forestier, N. (2010). Unilateral lower limb muscle fatigue induces bilateral effects on undisturbed stance and muscle EMG activities. *Journal of Electromyography and Kinesiology: Official Journal of the International Society of Electrophysiological Kinesiology*, 20(5), 947-952. doi: 10.1016/j.jelekin.2009.09.006.
- Bigland-Ritchie, B., Johansson, R., Lippold, O. C., Smith, S., & Woods, J. J. (1983). Changes in motoneurone firing rates during sustained maximal voluntary contractions. *The Journal of Physiology*, 340, 335-346.
- Bigland-Ritchie, B., Rice, C. L., Garland, S. J., & Walsh, M. L. (1995). Task-dependent factors in fatigue of human voluntary contractions. *Advances in Experimental Medicine and Biology*, 384, 361-380.
- Bisson, E. J., Chopra, S., Azzi, E., Morgan, A., & Bilodeau, M. (2010). Acute effects of fatigue of the plantarflexor muscles on different postural tasks. *Gait & Posture*, 32(4), 482-486. doi: 10.1016/j.gaitpost.2010.07.006.
- Bouisset, S., & Zattara, M. (1987). Biomechanical study of the programming of anticipatory postural adjustments associated with voluntary movement. *Journal of Biomechanics*, 20(8), 735-742.

Boyas, S., & Guevel, A. (2011). Neuromuscular fatigue in healthy muscle: Underlying factors and adaptation mechanisms. *Annals of Physical and Rehabilitation Medicine*, 54(2), 88-108. doi : 10.1016/j.rehab.2011.01.001.

Carlsoo, S. (1966). The initiation of walking. *Acta Anatomica*, 65(1), 1-9.

Conlay, L. A., Sabounjian, L. A., & Wurtman, R. J. (1992). Exercise and neuromodulators: Choline and acetylcholine in marathon runners. *International Journal of Sports Medicine*, 13 Suppl 1, S141-2. doi: 10.1055/s-2007-1024619.

Corbeil, P., Blouin, J. S., Begin, F., Nougier, V., & Teasdale, N. (2003). Perturbation of the postural control system induced by muscular fatigue. *Gait & Posture*, 18(2), 92-100.

Davis, J. M., Zhao, Z., Stock, H. S., Mehl, K. A., Buggy, J., & Hand, G. A. (2003). Central nervous system effects of caffeine and adenosine on fatigue. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, 284(2), R399-404. doi: 10.1152/ajpregu.00386.2002.

Degens, H., & Veerkamp, J. H. (1994). Changes in oxidative capacity and fatigue resistance in skeletal muscle. *The International Journal of Biochemistry*, 26(7), 871-878.

Elmer, S. J., Amann, M., McDaniel, J., Martin, D. T., & Martin, J. C. (2013). Fatigue is specific to working muscles: No cross-over with single-leg cycling in trained cyclists. *European Journal of Applied Physiology*, 113(2), 479-488. doi: 10.1007/s00421-012-2455-0.

Enoka, R. M., & Stuart, D. G. (1992). Neurobiology of muscle fatigue. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 72(5), 1631-1648.

Era, P., Sainio, P., Koskinen, S., Haavisto, P., Vaara, M., & Aromaa, A. (2006). Postural balance in a random sample of 7,979 subjects aged 30 years and over. *Gerontology*, 52(4), 204-213. doi: 10.1159/000093652.

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

Gandevia, S. C., Allen, G. M., & McKenzie, D. K. (1995). Central fatigue. Critical issues, quantification and practical implications. *Advances in Experimental Medicine and Biology*, 384, 281-294.

Grabiner, M. D., & Owings, T. M. (1999). Effects of eccentrically and concentrically induced unilateral fatigue on the involved and uninvolved limbs. *Journal of Electromyography and Kinesiology*, 9(3), 185-189.

Horak, F. B. (1987). Clinical measurement of postural control in adults. *Physical Therapy*, 67(12), 1881-1885.

Horak, F. B. (2006). Postural orientation and equilibrium: What do we need to know about neural control of balance to prevent falls? *Age and Ageing, 35 Suppl 2*, ii7-ii11. doi:10.1093/ageing/afl077.

Hughey, L. K., & Fung, J. (2005). Postural responses triggered by multidirectional leg lifts and surface tilts. *Experimental Brain Research, 165*(2), 152-166. doi: 10.1007/s00221-005-2295-9.

Kennedy, A., Hug, F., Sveistrup, H., & Guevel, A. (2013). Fatiguing handgrip exercise alters maximal force-generating capacity of plantar-flexors. *European Journal of Applied Physiology, 113*(3), 559-566. doi: 10.1007/s00421-012-2462-1.

Ledin, T., Fransson, P. A., & Magnusson, M. (2004). Effects of postural disturbances with fatigued triceps surae muscles or with 20% additional body weight. *Gait & Posture, 19*(2), 184-193. doi: 10.1016/S0966-6362(03)00061-4.

Leppik, J. A., Aughey, R. J., Medved, I., Fairweather, I., Carey, M. F., & McKenna, M. J. (2004). Prolonged exercise to fatigue in humans impairs skeletal muscle $\text{Na}^+\text{-K}^+\text{-ATPase}$ activity, sarcoplasmic reticulum Ca^{2+} release, and Ca^{2+} uptake. *Journal of Applied Physiology (Bethesda, Md.: 1985), 97*(4), 1414-1423. doi: 10.1152/jappphysiol.00964.2003.

Loram, I. D., Maganaris, C. N., & Lakie, M. (2005). Active, non-spring-like muscle movements in human postural sway: How might paradoxical changes in muscle length be produced? *The Journal of Physiology, 564*(Pt 1), 281-293. doi: 10.1113/jphysiol.2004.073437.

Maki, B. E., & McIlroy, W. E. (2006). Control of rapid limb movements for balance recovery: Age-related changes and implications for fall prevention. *Age and Ageing, 35 Suppl 2*, ii12-ii18. doi: 10.1093/ageing/afl078.

Mann, R. A., Hagy, J. L., White, V., & Liddell, D. (1979). The initiation of gait. *The Journal of Bone and Joint Surgery. American Volume, 61*(2), 232-239.

Martin, P. G., & Rattey, J. (2007). Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. *Pflugers Archiv: European Journal of Physiology, 454*(6), 957-969. doi: 10.1007/s00424-007-0243-1.

Masani, K., Sayenko, D. G., & Vette, A. H. (2013). What triggers the continuous muscle activity during upright standing? *Gait & Posture, 37*(1), 72-77. doi: 10.1016/j.gaitpost.2012.06.006.

Matsuda, S., Demura, S., & Demura, T. (2010). Examining differences between center of pressure sway in one-legged and two-legged stances for soccer players and typical adults. *Perceptual and Motor Skills, 110*(3 Pt 1), 751-760.

McLean, S. G., & Samorezov, J. E. (2009). Fatigue-induced ACL injury risk stems from a degradation in central control. *Medicine and Science in Sports and Exercise, 41*(8), 1661-1672. doi : 10.1249/MSS.0b013e31819ca07b.

- McLester, J. R., Jr. (1997). Muscle contraction and fatigue. the role of adenosine 5'-diphosphate and inorganic phosphate. *Sports Medicine (Auckland, N.Z.)*, 23(5), 287-305.
- Morris, S. L., & Allison, G. T. (2006). Effects of abdominal muscle fatigue on anticipatory postural adjustments associated with arm raising. *Gait & Posture*, 24(3), 342-348. doi: 10.1016/j.gaitpost.2005.10.011.
- Newsholme, E. A., & Blomstrand, E. (1995). Tryptophan, 5-hydroxytryptamine and a possible explanation for central fatigue. *Advances in Experimental Medicine and Biology*, 384, 315-320.
- Oddsson, L. (1988). Co-ordination of a simple voluntary multi-joint movement with postural demands: Trunk extension in standing man. *Acta Physiologica Scandinavica*, 134(1), 109-118.
- Oie, K. S., Kiemel, T., & Jeka, J. J. (2002). Multisensory fusion: Simultaneous re-weighting of vision and touch for the control of human posture. *Brain Research. Cognitive Brain Research*, 14(1), 164-176.
- Paillard, T., Chaubet, V., Maitre, J., Dumitrescu, M., & Borel, L. (2010). Disturbance of contralateral unipedal postural control after stimulated and voluntary contractions of the ipsilateral limb. *Neuroscience Research*, 68(4), 301-306. doi: 10.1016/j.neures.2010.08.004.
- Paillard, T. (2012). Effects of general and local fatigue on postural control: A review. *Neuroscience and Biobehavioral Reviews*, 36(1), 162-176. doi: 10.1016/j.neubiorev.2011.05.009.
- Post, M., Bayrak, S., Kernell, D., & Zijdwind, I. (2008). Contralateral muscle activity and fatigue in the human first dorsal interosseous muscle. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 105(1), 70-82. doi: 10.1152/jappphysiol.01298.2007.
- Rathey, J., Martin, P. G., Kay, D., Cannon, J., & Marino, F. E. (2006). Contralateral muscle fatigue in human quadriceps muscle: Evidence for a centrally mediated fatigue response and cross-over effect. *Pflugers Archiv: European Journal of Physiology*, 452(2), 199-207. doi: 10.1007/s00424-005-0027-4.
- Regueme, S. C., Barthelemy, J., & Nicol, C. (2007). Exhaustive stretch-shortening cycle exercise: No contralateral effects on muscle activity in maximal motor performances. *Scandinavian Journal of Medicine & Science in Sports*, 17(5), 547-555. doi: 10.1111/j.1600-0838.2006.00614.x.
- Rogers, M. W., & Pai, Y. C. (1990). Dynamic transitions in stance support accompanying leg flexion movements in man. *Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale*, 81(2), 398-402.
- Sacco, P., Thickbroom, G. W., Byrnes, M. L., & Mastaglia, F. L. (2000). Changes in corticomotor excitability after fatiguing muscle contractions. *Muscle & Nerve*, 23(12), 1840-1846.

- Sahlin, K., Tonkonogi, M., & Soderlund, K. (1998). Energy supply and muscle fatigue in humans. *Acta Physiologica Scandinavica*, *162*(3), 261-266.
- Santos, M. J., Kanekar, N., & Aruin, A. S. (2010). The role of anticipatory postural adjustments in compensatory control of posture: 2. biomechanical analysis. *Journal of Electromyography and Kinesiology: Official Journal of the International Society of Electrophysiological Kinesiology*, *20*(3), 398-405. doi: 10.1016/j.jelekin.2010.01.002.
- Sjogaard, G., Savard, G., & Juel, C. (1988). Muscle blood flow during isometric activity and its relation to muscle fatigue. *European Journal of Applied Physiology and Occupational Physiology*, *57*(3), 327-335.
- Speers, R. A., Kuo, A. D., & Horak, F. B. (2002). Contributions of altered sensation and feedback responses to changes in coordination of postural control due to aging. *Gait & Posture*, *16*(1), 20-30.
- Takahashi, K., Maruyama, A., Hirakoba, K., Maeda, M., Etoh, S., Kawahira, K., & Rothwell, J. C. (2011). Fatiguing intermittent lower limb exercise influences corticospinal and corticocortical excitability in the nonexercised upper limb. *Brain Stimulation*, *4*(2), 90-96. doi: 10.1016/j.brs.2010.07.001.
- Taylor, J. L., Todd, G., & Gandevia, S. C. (2006). Evidence for a supraspinal contribution to human muscle fatigue. *Clinical and Experimental Pharmacology & Physiology*, *33*(4), 400-405. doi: 10.1111/j.1440-1681.2006.04363.x.
- Tergau, F., Geese, R., Bauer, A., Baur, S., Paulus, W., & Reimers, C. D. (2000). Motor cortex fatigue in sports measured by transcranial magnetic double stimulation. *Medicine and Science in Sports and Exercise*, *32*(11), 1942-1948.
- Todd, G., Petersen, N. T., Taylor, J. L., & Gandevia, S. C. (2003). The effect of a contralateral contraction on maximal voluntary activation and central fatigue in elbow flexor muscles. *Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale*, *150*(3), 308-313. doi: 10.1007/s00221-003-1379-7.
- Van der Laarse, W. J., Lannergren, J., & Diegenbach, P. C. (1991). Resistance to fatigue of single muscle fibres from xenopus related to succinate dehydrogenase and myofibrillar ATPase activities. *Experimental Physiology*, *76*(4), 589-596.
- Van Deun, S., Staes, F. F., Stappaerts, K. H., Janssens, L., Levin, O., & Peers, K. K. (2007). Relationship of chronic ankle instability to muscle activation patterns during the transition from double-leg to single-leg stance. *The American Journal of Sports Medicine*, *35*(2), 274-281. doi: 10.1177/0363546506294470.
- Vuillerme, N., Burdet, C., Isableu, B., & Demetz, S. (2006). The magnitude of the effect of calf muscles fatigue on postural control during bipedal quiet standing with vision depends on the eye-visual target distance. *Gait & Posture*, *24*(2), 169-172. doi: 10.1016/j.gaitpost.2005.07.011.

Vuillerme, N., & Nougier, V. (2003). Effect of light finger touch on postural sway after lower-limb muscular fatigue. *Archives of Physical Medicine and Rehabilitation*, 84(10), 1560-1563.

Vuillerme, N., Nougier, V., & Prieur, J. M. (2001). Can vision compensate for a lower limbs muscular fatigue for controlling posture in humans? *Neuroscience Letters*, 308(2), 103-106.

Vuillerme, N., Pinsault, N., Chenu, O., Fleury, A., Payan, Y., & Demongeot, J. (2008). Postural destabilization induced by trunk extensor muscles fatigue is suppressed by use of a plantar pressure-based electro-tactile biofeedback. *European Journal of Applied Physiology*, 104(1), 119-125. doi: 10.1007/s00421-008-0768-9.

Vuillerme, N., Sporbert, C., & Pinsault, N. (2009). Postural adaptation to unilateral hip muscle fatigue during human bipedal standing. *Gait & Posture*, 30(1), 122-125. doi: 10.1016/j.gaitpost. 2009.03.004.

Westerblad, H., Allen, D. G., & Lannergren, J. (2002). Muscle fatigue: Lactic acid or inorganic phosphate the major cause? *News in Physiological Sciences: An International Journal of Physiology Produced Jointly by the International Union of Physiological Sciences and the American Physiological Society*, 17, 17-21.

Winter, D. A., MacKinnon, C. D., Ruder, G. K., & Wieman, C. (1993). An integrated EMG/biomechanical model of upper body balance and posture during human gait. *Progress in Brain Research*, 97, 359-367.

Winter, D.A. (1995). *A.B.C. (Anatomy, biomechanics and control) of Balance During Standing and Walking*. Waterloo Biomechanics. Waterloo, Ontario, Canada.

Zijdewind, I., Zwarts, M. J., & Kernell, D. (1998). Influence of a voluntary fatigue test on the contralateral homologous muscle in humans? *Neuroscience Letters*, 253(1), 41-44.

**Chapter 3. EFFECT OF UNILATERAL KNEE
EXTENSOR FATIGUE ON NON-FATIGUED
LIMB'S STANDING BALANCE, MUSCLE
FORCE AND ACTIVATION**

3.0 Abstract

Local fatigue occurring in one limb can result in decreased force production in the homologous muscle as well as in other muscles of the non-fatigued limb. Local fatigue has also been shown to influence balance. The objective of the present study was to examine the effect of unilateral knee extensor fatigue on the non-fatigued limb's standing balance, muscle force and activation. Sixteen healthy male subjects were recruited for the study. The experimental protocol consisted of pre-fatigue balance trials, warm-up exercises, maximum voluntary isometric contractions, knee extensors fatigue protocol, and post-fatigue balance trials. The fatigue protocol consisted of 15 consecutive isometric contractions of 16 s each, which were performed at 30% peak force for the dominant knee extensors muscle. These contractions continued until a 50% decrease in knee extensor force was observed. Pre- and post-fatigue balance assessment consisted of transition from double to single leg standing and also single leg standing trials, all of which were performed bilaterally and in randomized order. The study found no significant changes in the non-fatigued limb's muscle force, activation, muscle onset timing or the postural stability parameters. Results of this study suggest that the fatigue protocol did not result in any cross-over fatigue. While the lack of change in non-fatigued limb force production is in agreement with some of the previous literature in this area, the lack of effect on postural measures directly contradicts earlier work. It is hypothesized that discrepancies in the duration and the intensity of the fatigue protocol may have accounted for this discrepancy.

3.1 Introduction

Balance can be affected in diseases such as Parkinson disease (Schoneburg et al., 2013), multiple sclerosis (Dibble et al., 2013), injuries (Hertel, 2000), aging (Vellas et al., 1997) and during muscle fatigue (Kanekar et al., 2008; Bellew and Fenter, 2006). Muscular fatigue, which has been defined as "any exercise-induced reduction in the ability to exert muscle force or power, regardless of whether or not the task is sustained" (Bigland and Woods (1984), p. 691) is one of the many factors that can impair balance (Yaggie and Armstrong, 2004). Fatigue can be characterized by decreased force production of the fatigued muscle (Degens and Veerkamp, 1994), a reduction in the amplitude of muscle activation (Zijdewind et al., 1998), decrease in firing frequency of the motoneurons (Bigland et al., 1983) or decreased power (Behm, 2004). Muscle fatigue is also believed to affect joint position sense by increasing the threshold of muscle firing rate and by disrupting the afferent feedback, thereby impairing proprioceptive and kinesthetic feedback (Macefield, 1990; Gribble and Hertel, 2004).

Fatigue can be further characterized as peripheral or central. Peripheral fatigue occurs due to changes occurring distal to the peripheral nerve. On the other hand, central fatigue has been defined as an exercise-induced attenuation in the ability of the central nervous system (CNS) to drive muscle maximally or as a decline in voluntary muscle activation (Taylor et al., 2006). The effects of fatigue can either be localized or global (Rathey et al., 2006). Some research has shown that local fatigue occurring in one limb can result in decreased force production in the homologous muscle (Martin & Rathey, 2007) and as well as in the distant muscle (Takahashi et al., 2011, Kennedy et al., 2013) of the non-fatigued limb. This cross-over effect of fatigue has been identified for upper- (Humphry et al., 2004) and lower-limbs (Rathey et al., 2006; Martin & Rathey, 2007;

McLean & Samorezov, 2009; Paillard et al., 2010). Despite this evidence of cross-over fatigue the majority of studies have not found evidence of its occurrence (Zidjewind et al., 1998, Grabiner & Owings, 1999, Todd et al., 2003, Regueme et al., 2007, Strang et al., 2009, Place et al., 2004, Ross et al., 2007, Ross et al., 2010, Elmer et al., 2013). Hence there is a conflict in the literature that needs further exploration.

Aside from the cross-over effect of fatigue on muscle force, fatigue has also shown to negatively influence balance. There is only one study that has examined such effects of unilateral fatigue (Paillard et al., 2010). Paillard et al. (2010) demonstrated cross-over fatigue effects on balance reporting increased sway area of center of pressure (CoP), although no decrease in the non-fatigued quadriceps femoris maximum voluntary isometric contractions (MVIC) was noted.

Although Paillard et al. (2010) provided initial insight into the effects of unilateral fatigue on contralateral limb balance, it remains unknown whether the balance changes in the non-fatigued limb were due to alterations in quadriceps femoris function or whether the effects of the fatigue were more global, affecting the activation patterns and force production of many other lower limb muscles. Also, it is not clear how fatigue in a non-postural muscle such as the quadriceps femoris (Masani et al., 2013) could have such a profound effect on non-fatigue limb balance. Based on this, the main objective of this study was to examine the effect of unilateral knee extensor fatigue on non-fatigued limb's standing balance, muscle force and activation. From the results obtained by the Paillard et al. (2010), it was hypothesized that knee extensors fatigue would result in reduced balance while standing on the non-fatigued limb and would also affect muscle force and activation patterns in lower limb muscles.

3.2 Methodology

Participants

Sixteen healthy male subjects with a mean age 24.9 ± 5 years, mean height 183 ± 7.7 cm and mean weight 86.4 ± 10 kg were recruited for the study. Only individuals who engaged in lower body resistance exercise for at least 2 days/ week for a minimum of 20 minutes were recruited. Additionally, participants who had no history of balance disorders over the past 2 years, or neurological or musculoskeletal impairment / injury / medical conditions that might affect their postural stability were eligible to participate. This information was determined from the Physical Activity and Medical Questionnaire. The study was approved by the Interdisciplinary Committee on Ethics in Human Research.

Experimental Design

Procedure

Participants came to the lab for a single testing session. They were asked to complete the consent form and two questionnaires (PAR-Q and Physical Activity and Medical Questionnaire) to determine if they were able to take part in this study. Then the dominant leg of the participants was determined by asking them which leg they would use to kick a ball. In this study, fifteen out of sixteen participants were right leg dominant.

Participants were then fitted with bipolar surface electromyography (EMG) electrodes on their non-dominant leg. These electrodes were used to record muscle activity from eight lower limb muscles: tibialis anterior (TA), peroneus longus (PL), gastrocnemius medialis (GM), hamstrings, vastus lateralis (VL), vastus medialis (VM), gluteus maximus (Gmax) and gluteus medius (Gmed). Before electrode placement, skin surfaces were shaved, abraded using sand paper, and cleaned with alcohol to decrease the

resistance offered by dead surface skin and tissue oils. Disposable Ag/AgCl disc electrode (three cm in diameter) pairs (Kendall Medi-trace 100 series, Chikopee, MA) were placed between the respective motor point and the tendon of the muscle with an inter-electrode distance of 2 cm. Tape was applied over the electrodes to minimize any movement of the electrodes during the contractions. The ground electrode was secured at the distal one-third of the iliac crest on the dominant side. Electrodes were placed according to the recommendation of Criswell (2011). As Criswell didn't describe electrode placement for PL, these electrodes were placed over the muscle belly at the sight of the strongest signal intensity (4 cm lateral to the shin of tibia, and approximately one-third to one-fourth proximally the distance between the knee and the ankle). A Biopac Systems MEC 100 amplifier (Santa Barbara, CA), with an input impedance of 2m M Ω and common mode rejection ratio of >110 dB minimum (50/60 Hz) was used to collect all EMG. The signals were sampled at a rate of 2000 Hz and then digitized using a 12-bit analog-digital converter (BIOPAC MP 150).

The experimental protocol consisted of pre-fatigue balance trials, warm-up exercises, MVIC, fatigue protocol, and post-fatigue balance trials (See protocol outline in Figure 3.1). Prior to beginning this protocol, participants performed familiarization trials to become acquainted with the two-legged and single leg standing trials that would be used in the study. The stance width during natural two-legged standing was determined and was marked with surgical tape for reference. This stance was used as the starting point for all subsequent balance trials performed.

Pre- and post-fatigue balance assessment consisted of transition from double to single leg standing and also single leg standing trials. All balance trials were performed on both right and left sides using a randomized selection order. During all balance tests subjects stood on a force platform (AMTI, Watertown, MA, USA) which was connected

to a six channel amplifier and an analog-to-digital converter. The force plate recorded ground reaction forces (GRF) and moment of force along X, Y and Z axis.

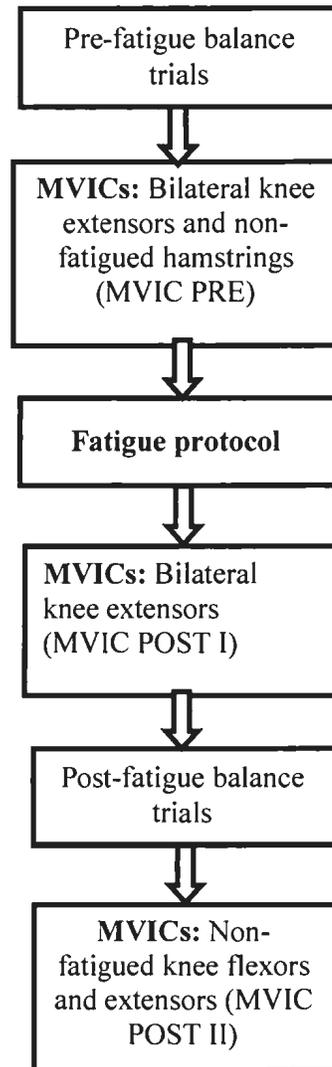


Figure 3.1: The general outline of the protocol involved in the study.

The signals were sampled at a rate of 2000 Hz. The initial stance position was the same for both the pre- and post-fatigue balance test: barefooted and weight evenly distributed across both feet. Participants were asked to stand in such a way that a single

foot was placed on the force plate. Also, they were instructed to stand naturally and try to maintain their balance. As stated above, two types of balance trials were performed – single leg standing and a transition from double to single leg standing. For the single leg standing balance trials, the participants were asked to stand on a single leg and once they were balanced they were asked to close their eyes. Once their eyes were closed they were asked to maintain their single leg stance for a period of 30 seconds. Data collection for these trials did not begin until the person was stable with their eyes closed. During this trial, they were also asked to place their little finger, on the side of their non-supporting limb, on the edge of a chair placed immediately adjacent to the force plate. They were instructed to use the chair for minimal support – this was done to ensure participants could maintain the full 30 seconds stance required for this condition. The position of the chair was marked with tape for reference and remained in the same position for all balance testing during that session. The participants were asked to stand such that the knee of the non-stance leg was flexed at an angle of about 45°. During trials where participants transitioned from double to single leg stance participants were asked to maintain an initial 3 seconds of double-leg stance and then shift as quickly as possible to single leg stance. Once they achieved a single leg stance, they were asked to maintain their balance for five seconds. For these double to single transition trials, they were asked to keep their eyes open and rest both hands on their hips. The trials where participants touched their foot to the floor or otherwise lost their balance were discarded and another trial was collected. Force plate and EMG data were recorded throughout all balance tests.

Maximum Voluntary Isometric Contractions (MVIC)

Following completion of the pre-fatigue balance test, participants were asked to perform a 5 minute warm-up on a cycle ergometer (1 kilo pound resistance at 70 revolutions per

minute). Next the MVICs for all eight muscles on the non-dominant side and quadriceps femoris/knee extensors on the dominant side (MVIC PRE) were performed. For all MVICs participants were asked to contract maximally against the resistance provided. For TA, participants were in supine lying position with their arms across the chest and were asked to perform maximum dorsiflexion against researcher's resistance. While in the same position participants were asked to produce maximal ankle eversion against researcher's resistance in order to elicit an MVIC from PL. For the GM, subjects were asked to stand in single limb stance on the non-dominant leg. Participants were then asked to perform a heel raise while using a chair to maintain balance. The researcher provided resistance to this motion by applying downward force on the participant's shoulders. For the MVIC of Gmax, participants lay prone and produced maximum hip extension while keeping their knee in flexion. For the Gmed participants were in a side lying position and were asked to produce a MVIC of their hip abductors. Muscle activation data recorded from these MVICs was used to normalize EMG collected during balance trials.

In addition to the MVICs described above, MVICs were also performed for knee extension and flexion. As force production in these muscles was used to assess the extent of fatigue in both dominant and non-dominant limbs, both muscle force and EMG were recorded during these trials (See Figure 3.2). For the knee flexors only data from the non-dominant limb was collected. Participants stood facing a bench with the non-dominant knee slightly bent and their foot touching the ground. Their ankle was inserted into a padded strap which was then attached to a Wheatstone bridge load cell through a high tension wire. They were asked to flex their knee as hard as possible against the strap for a period of four seconds. Knee extension MVICs were performed for both the dominant

and non-dominant leg. Participants sat on a bench with their hips and knees flexed at 90° and their chest, hips and upper legs restrained with straps. The participants were then asked to perform an isometric knee extension as hard as possible against the strap attached to a load cell for four seconds (while placing their arms across their chest). For all the MVICs, two trials each lasting four seconds were performed with a two minute rest between each trial. Verbal encouragement was provided throughout the collection of MVICs.

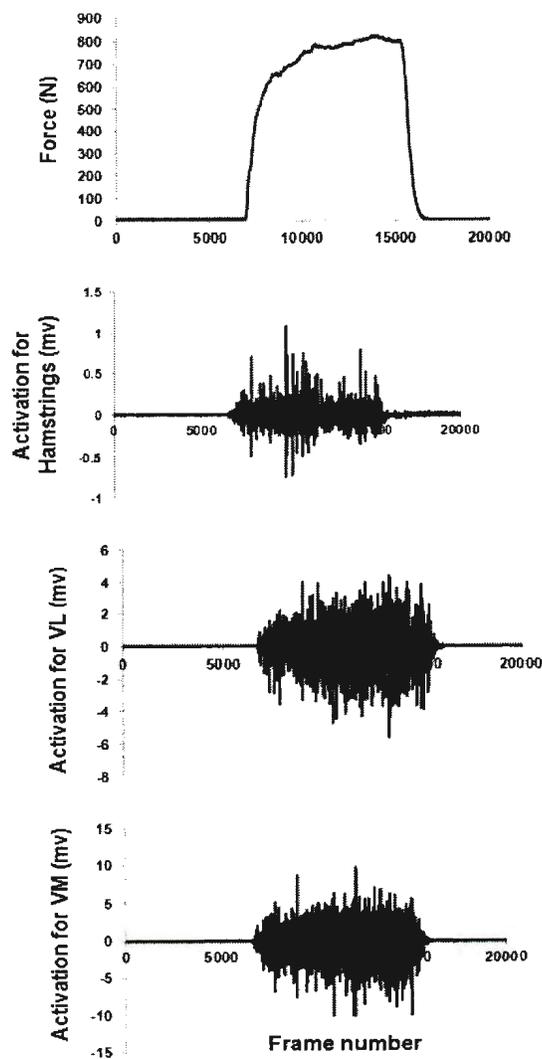


Figure 3.2: Force (top trace) and raw EMG signals of hamstrings, VL and VM recorded during MVIC of the non-fatigued knee extensors.

Fatigue Protocol

Following completion of the MVIC trials, the fatigue protocol was carried out. Participants remained in the position used for the knee extension MVIC with the same padded strap and load cell affixed to their dominant leg. Participants were then asked to perform an isometric knee extension contraction at 30% of peak MVIC force. In order to ensure force was maintained at the desired magnitude, subjects were provided with visual feedback of the generated force during their fatiguing tasks. The fatigue protocol consisted of 15 consecutive 16 s isometric knee extension contractions. Each contraction was followed by a 4 s recovery. Following the 15 contractions, an MVIC (MVIC POST I) was performed to assess the fatiguing effects. If force production had dropped by at least 50% of MVIC then fatigue was considered to have occurred and the isometric contractions were stopped. If fatigue had not occurred then the above procedure was repeated until a 50% reduction in force was observed. If volitional fatigue occurred during the 15 contractions (i.e. participants could not maintain the 30% MVIC force required) then participant's contractions were stopped and an MVIC (MVIC POST I) was performed. Once fatigue was determined to have occurred, a knee extension MVIC (MVIC POST I) was performed on the non-fatigued side to record any potential cross-over effect of the fatiguing contractions on the dominant side. This MVIC POST I was performed approximately 10 s after the completion of the fatigue trials.

Participants then immediately did the post-fatigue balance trials, which were performed similar to the pre-fatigue balance trials. Following these balance trials another series of non-fatigued limb knee extension (MVIC POST II) and flexion MVICs (MVIC POST II) were performed. This was done approximately 10 minutes from the end of the fatiguing protocol.

Data analysis

Force

Force data from the load cell was assessed to determine the effect of fatigue on both the fatigued and non-fatigued leg. This was performed by calculating peak force (N) and F100 (N) (MacDonald et al., 2013) during the knee extension MVIC trials. F100 was the force developed in the first 100 milliseconds of MVIC and was calculated for the time period where the first deflection of the baseline activity of force was observed to the period of initial 100 milliseconds of force developed. The MVIC with the highest peak force was used to assess both the effects of fatigue on force production and for the calculation of F100.

Ground reaction force data

All GRF data was processed using custom designed software (MATLAB 2013a; Visual Basic 6.0). Initial processing was done to determine CoP location in both the anterior-posterior (AP) and medio-lateral (ML) directions. This was done using formula as provided by Robertson et al. (2004). For the single leg standing trials a variety of sway parameters were determined in order to help quantify the effect of fatigue on postural stability. Details of the sway parameters calculated can be found in Table 3.1. Briefly, CoP velocity and length in the ML and AP directions were determined as were the total CoP length and mean sway velocity over the duration of the 30 s trial. In addition CoP range (AP and ML) and standard deviation (SD) were determined as was the total sway area. All measures were determined as per Bigelow (2008) with the exception of total sway area, which was calculated based on Duarte and Zatsiorsky (2002).

For trials where participants were asked to move from double to single leg standing, GRF data was used to determine when participants began to transition from

double to single leg standing. Motion onset was determined as per Sims and Brauer (2000). The start of motion was considered as the point of time when the vertical forces underneath the stepping leg dropped below the mean force - 3SD for more than 100 frames (Sims and Brauer, 2000). Mean and SD were determined over a 2 second period during the double leg stance portion of the trial (see Figure 3.3). This movement start time was considered time zero and was used as a reference point for all muscle onset times determined during this task as described below.

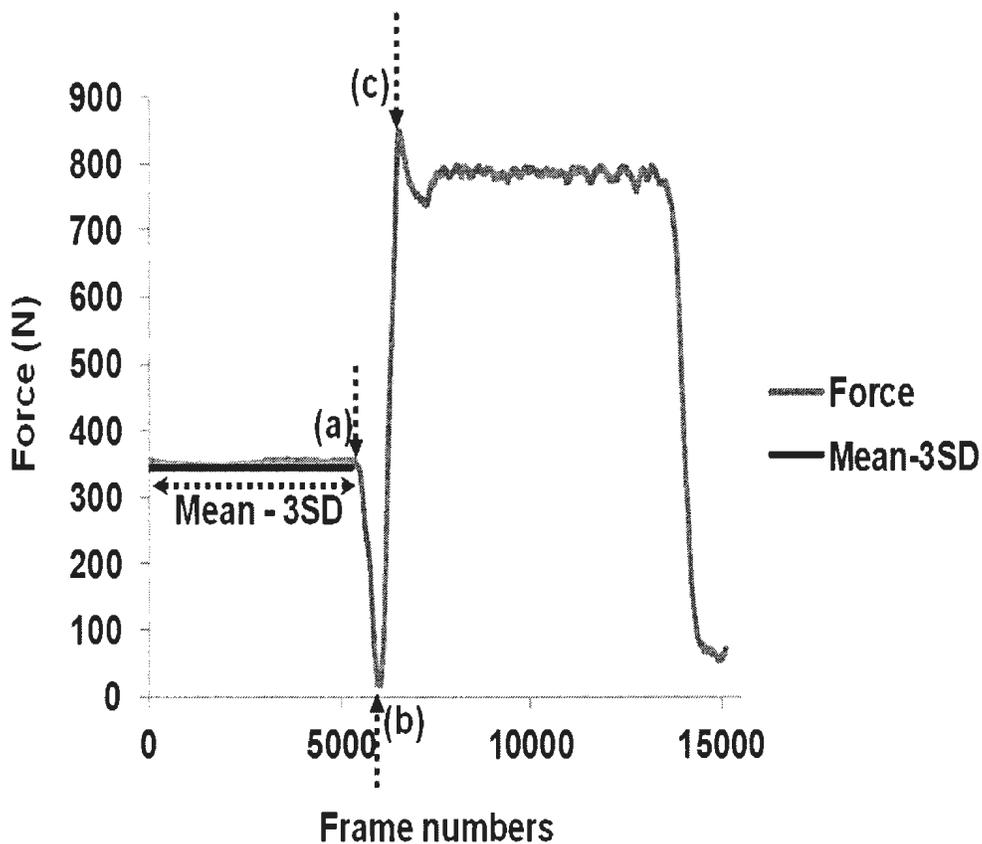


Figure 3.3: Figure depicting the vertical force during the double to single stance trials. Black horizontal and dotted horizontal line represents the mean - 3SD of the vertical force during double limb standing portion of the trial. (a) start of the motion as determined by when the vertical force was less than the (mean-3SD), (b) point at which the force becomes minimum and (c) point at which the transition from double to single limb stance was considered complete.

Table 3.1: Sway parameters used during single leg standing. m is meters and all other abbreviations are defined in the table.

Sway parameter	Formula	Units
Medial lateral range covered by CoP (Range _{ML})	$ (\text{CoP}_{ML})_{\text{max}} - (\text{CoP}_{ML})_{\text{min}} $, where $(\text{CoP}_{ML})_{\text{max}}$ and $(\text{CoP}_{ML})_{\text{min}}$ represents the maximum and minimum values attained by medial lateral CoP during single leg standing.	m
Anterior posterior range covered by CoP (Range _{AP})	$ (\text{CoP}_{AP})_{\text{max}} - (\text{CoP}_{AP})_{\text{min}} $, where $(\text{CoP}_{AP})_{\text{max}}$ and $(\text{CoP}_{AP})_{\text{min}}$ represents the maximum and minimum values attained by anterior posterior CoP during single leg standing.	m
Mean velocity (V_m)	$\frac{\sum_{n=1}^{N-1} \sqrt{((\text{CoP}_{ML})_{n+1} - (\text{CoP}_{ML})_n)^2 + ((\text{CoP}_{AP})_{n+1} - (\text{CoP}_{AP})_n)^2}}{T}$ Where, T is the total time period of the trial and n is the data point of interest.	m/sec
Average medial lateral velocity ($V_{m(ML)}$)	$\frac{\sum_{n=1}^{N-1} \{(\text{CoP}_{ML})_{n+1} - (\text{CoP}_{ML})_n\}}{T}$	m/sec
Average anterior posterior velocity ($V_{m(AP)}$)	$\frac{\sum_{n=1}^{N-1} \{(\text{CoP}_{AP})_{n+1} - (\text{CoP}_{AP})_n\}}{T}$	m/sec
Total distance travelled by CoP (L)	$\sqrt{((\text{CoP}_{ML})_{n+1} - (\text{CoP}_{ML})_n)^2 + ((\text{CoP}_{AP})_{n+1} - (\text{CoP}_{AP})_n)^2}$	m
Medial lateral CoP distance (Length _{ML})	$(\text{CoP}_{ML})_{n+1} - (\text{CoP}_{ML})_n$	m
Anterior posterior CoP distance (Length _{AP})	$(\text{CoP}_{AP})_{n+1} - (\text{CoP}_{AP})_n$	m
Root mean square of CoP (RMS)	$\sqrt{\frac{1}{T} \sum_{i=1}^T (\text{CoP}_i)^2}$, where $i = 1, 2, 3, 4, \dots, N$ and N is the total number of data points.	m

Electromyography

All EMG data was analyzed using custom designed software written in Visual Basic 6.0. Prior to analysis all EMG data was high pass filtered at 20 Hz to eliminate motion artifacts produced because of movement of the cables (De Luca et al., 2010). Following this filtering, all raw EMG signals were first normalized using data collected during the MVIC trials. A 50 millisecond moving window was used to determine root mean square (RMS) of MVIC EMG for each muscle. The peak RMS for each muscle was determined and was used to normalize all EMG data collected during the study. This amplitude normalized EMG was used for all calculations of EMG amplitude and on-set timing described below.

EMG Amplitude: EMG amplitude was quantified by calculating integrated EMG (iEMG, mv) (Behm et al., 2001) for all muscles during the single leg standing trials. For these trials amplitude normalized EMG was integrated over the full 30 sec duration of the trial. In addition iEMG was determined for hamstrings, VL and VM during non-fatigued limb knee extensors and hamstrings MVIC trials. The iEMG was calculated over a one sec period starting 0.5 sec before and ending 0.5 sec following the peak force attained during the MVIC trial. For trials where peak force occurred at the end (i.e. no 0.5 sec window existed after the peak was reached), iEMG was calculated using the one sec prior to the time when the peak force occurred.

Muscle activation timing: EMG collected during the double to single leg trials was used primarily to assess the effects of the fatiguing contractions on muscle onset timing. Muscle onset was determined based on the protocol established by Hodges and Bui (1996). As per these authors all data was first full wave rectified and was low pass filtered

at 50 Hz. The mean and SD of the EMG during the double leg stance portion of the trial was first determined over a 2 sec period. This 2 sec period was considered to represent quiet stance and therefore minimal muscle activity was observed. Muscle onset was determined to have occurred once the level of muscle activity exceeded the mean + 1SD for at least 100 milliseconds. As per Hodges and Bui (1996) muscle activity was determined using a 100 milliseconds moving average full-wave rectified and filtered signal (see Figure 3.4). All onset times were expressed with respect to the onset of motion as described above. Due to errors in the estimation of muscle onset times by the automated computer process all onset times were subsequently checked manually to ensure their accuracy. The individual doing the manual checking was blind to the trial condition to prevent any bias in assigning an onset time to each muscle.

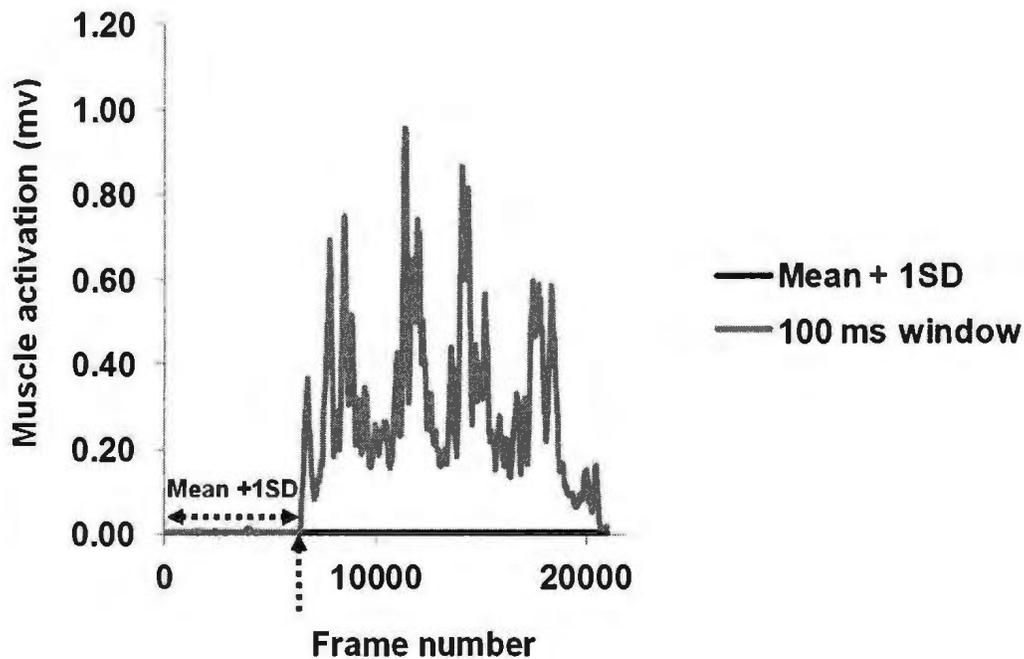


Figure 3.4: Figure depicting the EMG onset for TA during the transition from double to single limb stance on the non-dominant limb. Horizontal dotted line represents the mean + 1SD of the double limb stance TA muscle activation. EMG depicted was first full-wave rectified and high pass filtered. A 100 millisecond moving window was then used to calculate a moving average of the rectified and filtered EMG signal. Muscle onset was determined to have occurred once EMG exceeded the mean + 1SD (see text for more details and has been represented as vertical dotted line).

Statistical Analysis

A priori statistical power analysis was conducted which determined that approximately sixteen subjects would provide an alpha of $p < 0.01$ with a power of 0.8. The data was examined to assess differences in force, iEMG, muscle onsets and sway parameters prior to and following the fatigue protocol. Paired t-tests were used. Significant differences were detected at $p < 0.05$. To infer the magnitude of the outcomes, effect sizes (ES) were calculated (Cohen, 1990). The following formula was used to calculate the ES as per Cohen (1969):

Pre-post ES = $\frac{\text{Post mean} - \text{Pre mean}}{\text{Pre Standard Deviation}}$.

Cohen (1969) considered an ES of less than 0.2 as trivial, 0.2 - 0.41 as small, 0.41 - 0.70 as moderate and greater than 0.70 as large. As some of the data was not normally distributed, a Wilcoxon signed rank test was also performed.

3.3 Results

Force

Significant changes pre- and post-fatigue were detected for the fatigued side peak force ($p < 0.0001$ and F100 ($p = 0.04$)) (Figure 3.5 (A)). The peak force and F100 were significantly decreased by 44.82% (ES = 2.54, large) and 39.96% (ES = 0.59, moderate) respectively for the fatigued limb post-fatigue protocol (MVIC POST 1). There were no significant changes in peak force and F100 for the knee extensors on the non-fatigued limb (Figure 3.5(B)) when pre- and post-fatigue extensor force was compared. Although knee extensor force data was collected following the post-fatigue balance tests this data was not examined statistically due to the lack of difference found immediately post fatigue.

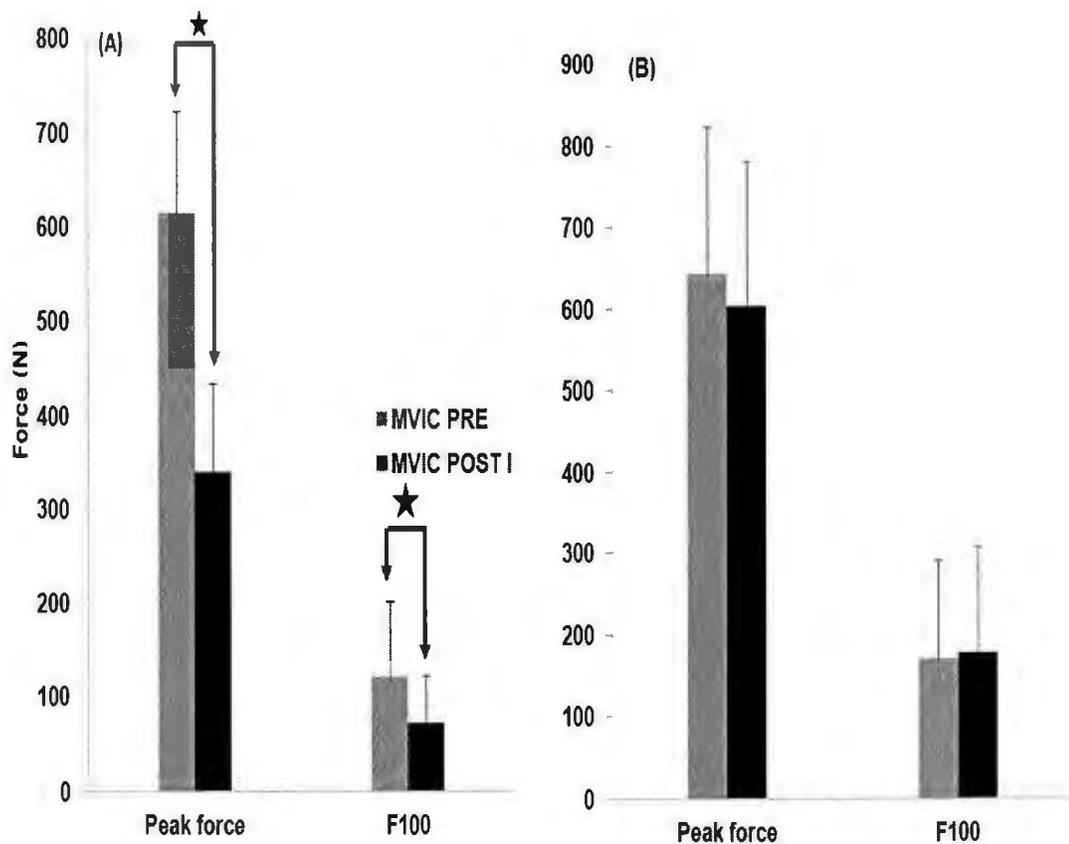


Figure 3.5: (A) Knee extension peak force and F100 (mean \pm SD) for the fatigued limb and (B) non-fatigued limb pre- (MVIC PRE) and post-fatigue (MVIC POST I) respectively.* represents statistical significance of $p < 0.05$ for post-fatigued versus pre-fatigued leg conditions.

iEMG

During both, the knee extensors and hamstrings MVICs on the non-fatigued side, fatigue had no effect on the magnitude of either hamstrings, VL or VM activation. Similarly no significant changes were observed in iEMG of these muscles during the pre- and post-fatigue single leg standing trials on the non-fatigued side (See Table 3.2).

Table 3.2: iEMG (mean (\pm SD)) of the non-fatigued limb during single limb standing pre- and post-fatigue. Units (task voltage/MVC voltage).s

Muscle	Pre non-fatigued leg	Post non-fatigued leg
TA [#]	1.07 \pm 0.83	0.94 \pm 0.56
PL	3.25 \pm 1.65	2.91 \pm 1.26
GM [#]	3.41 \pm 1.52	2.88 \pm 2.2
Hamstrings [#]	0.22 \pm 0.17	0.32 \pm 0.54
VL	0.53 \pm 0.46	0.47 \pm 0.39
VM [#]	0.34 \pm 0.38	0.25 \pm 0.28
Gmax [#]	0.19 \pm 0.15	0.22 \pm 0.14
Gmed	1.38 \pm 1.1	1.2 \pm 0.87

[#] denotes the variables which were not normally distributed and were analyzed using Wilcoxon rank test. The test revealed no significant results.

Double to single leg standing parameters

There were no significant changes with the pre- to post-fatigue muscle onsets during the transition from double to single leg standing on the non-fatigued side (Figure 3.6). Furthermore, prior to fatigue it took participants 0.43 sec to transition from double to single leg stance. This did not differ statistically from the 0.47 sec post-fatigue ($p = 0.4$).

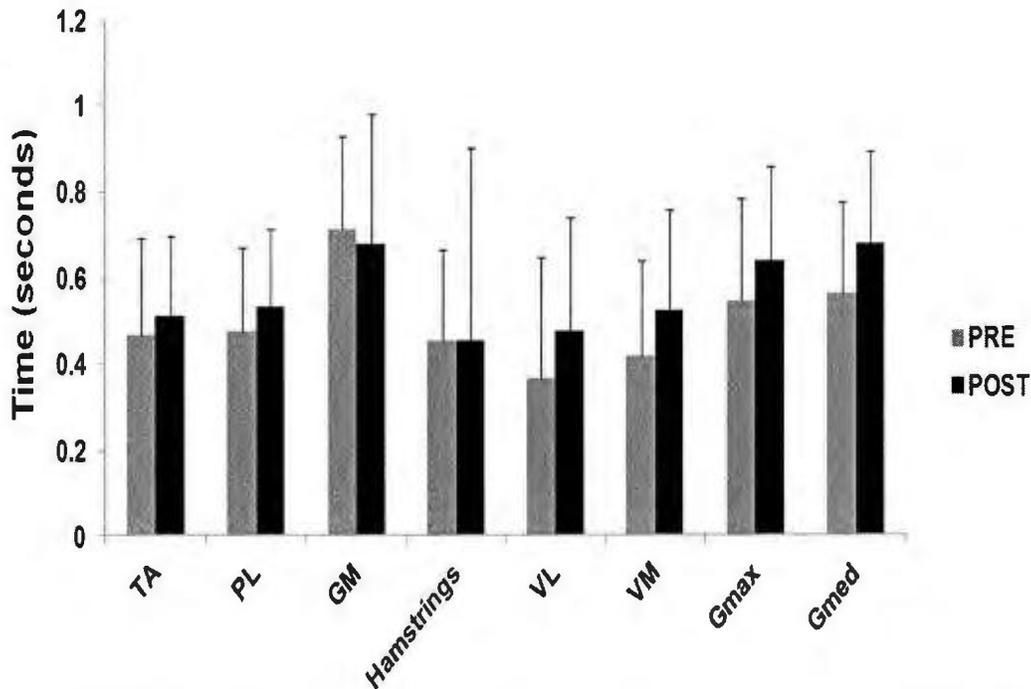


Figure 3.6: Muscle onset time estimated during the transition from double to single limb standing on the non-fatigued side. All times are reported with respect to the start of motion with positive times indicating muscle onset occurred after the start of motion. See text for details on how motion start was determined. The muscle onsets for TA, PL, GM, hamstrings, Gmax and Gmed were not normally distributed and were analyzed using Wilcoxon rank test. The test revealed no significant results.

Stability during single leg standing

On the fatigued side, the fatiguing protocol led to an increase in the total length covered by CoP, CoP_{AP}, CoP velocity and the total sway area. CoP length increased by 1.63% ($p = 0.002$) although the effect size (0.12) was trivial (Table 3.3). CoP_{AP} length (Table 3.3) and CoP velocity (Table 3.3) demonstrated similar trivial effect sizes (0.14 and 0.12 respectively) as they increased by 2.43% ($p = 0.007$) and 1.63% ($p = 0.002$) following the fatiguing contractions. Sway area demonstrated the largest increase at 27.89% ($p = 0.01$, ES = 0.66, moderate, Table 3.3). The only significant change observed on the non-fatigued side was the CoP_{ML} range which was 15.38% greater ($p = 0.04$, ES = 0.38, small) post-fatigue than pre-fatigue (Table 3.3). All other postural sway measures values remained unchanged following the fatigue protocol (see Table 3.3).

Table 3.3: The sway parameters (mean±SD) calculated during the single limb standing on the fatigued and the non-fatigued limb pre- and post-fatigue.

	Pre-fatigued leg	Post-fatigued leg	Pre non-fatigued leg	Post non-fatigued leg
Range _(AP) [#] (m)	0.05 ± 0.01	0.05 ± 0.02	0.05 ± 0.02	0.06 ± 0.02
Range _(ML) (m)	0.02 ± 0.01	0.02 ± 0.01	0.020247 ± 0.0083	0.023362 ± 0.0075**
V [#] (m/sec)	0.267442 ± 0.037	0.271804 ± 0.0365*	0.27 ± 0.03	0.28 ± 0.03
Length [#] (m)	8.02 ± 1.11	8.15 ± 1.1 *	8.2 ± 0.78	8.31 ± 0.92
Length _(AP) [#] (m)	5.35 ± 0.94	5.48 ± 0.99 *	5.45 ± 0.73	5.58 ± 0.78
Length _(ML) (m)	4.03 ± 0.56	4.1 ± 0.46	4.18 ± 0.55	4.17 ± 0.64
SD _{AP} [#] (m)	0.01 ± 0.002	0.01 ± 0.003	0.01 ± 0.002	0.01 ± 0.003
SD _{ML} (m)	0.004 ± 0.001	0.004 ± 0.002	0.004 ± 0.002	0.004 ± 0.001
Area (m ²)	457.61 ± 193.79	585.25 ± 341.82*	505.34 ± 295.55	596.85 ± 335.73
RMS [#] (m)	4.13x10 ⁻⁵ ± 1.05x10 ⁻⁵	4.29x10 ⁻⁵ ± 1.27x10 ⁻⁵	4.22x10 ⁻⁵ ± 1.06x10 ⁻⁵	4.67x10 ⁻⁵ ± 1.32x10 ⁻⁵

* Significant difference ($p < 0.05$) for fatigued leg pre- versus post-fatigue.

** Significant difference ($p < 0.05$) for non-fatigued leg pre- versus post-fatigue.

denotes the variables which were not normally distributed and were analyzed using Wilcoxon rank test. The test revealed no significant results.

3.4 Discussion

This study investigated the effect of unilateral knee extensor fatigue on standing balance, muscle force and activation in the non-fatigued limb. Muscle fatigue was induced by isometric knee extension contractions performed at 30% of MVICs. The most important findings of this study were the absence of any cross-over fatigue effects. More specifically, the non-fatigued limb showed no significant reductions in muscle force, activation or muscle onset timing and no disturbances in the postural stability parameters.

The aforementioned results contradict the study hypothesis. The significant decrease in the peak force and F100 with the fatigued limb clearly indicated that the fatigue protocol did lead to ipsilateral fatigue. However, the ipsilateral fatigue did not produce global effects in the form of cross-over fatigue in the non-fatigued limb. In the literature, cross-over fatigue effects have been observed as a decrease in voluntary muscle activation (VA) (Rathey et al., 2006), decrease in force (Martin & Rathey, 2007) and an increase in postural sway (Paillard et al., 2010) of the non-fatigued limb. The findings of the present study are similar to published studies that have found no evidence of cross-over force deficits associated with ipsilateral fatigue (Zidjewind et al., 1998, Grabiner & Owings, 1999, Todd et al., 2003, Regueme et al., 2007, Strang et al., 2009, Place et al., 2004, Ross et al., 2007, Ross et al., 2010, Elmer et al., 2013). The study by Zidjewind et al. (1998) used a very similar protocol with 30% MVICs regularly interrupted with MVICs and brief rest periods in the right first dorsal interosseus muscle (FDI) until failure and found no evidence of cross-over force deficits.

However, the present findings are in opposition to several studies that have reported cross-over fatigue effects (Rathey et al., 2006, Martin & Rathey, 2007). Rathey et al. (2006) and Martin and Rathey (2007) used a 100-s sustained MVIC of the dominant limb knee extensors to induce fatigue. Rathey et al. (2006) found a decrease in VA and iEMG in the contralateral limb and a decrease in MVIC which was not significant. However, Martin and Rathey (2007) found reductions in force and VA in the contralateral limb. One possible reason for the lack of agreement between Rathey's (2006) work and that of the present research may be related to the intensity of the fatiguing contraction used. In contrast to the work conducted by Rathey et al. (2006) and Martin and Rathey (2007), who used maximal contractions, fatiguing contractions were maintained at 30% MVIC (submaximal) in the present study. Cross-over fatigue is felt to depend upon the

intensity at which the isometric contractions are maintained (Kennedy et al., 2013) and is also thought to depend on the occurrence of central fatigue (Enoka and Duchateau, 2008). Work by Bigland et al. (1986) suggests that perhaps the intensity of contractions used in the present study may not have been sufficient to create the central changes required to see cross-over effects. Specifically, Bigland et al. (1986) used repeated voluntary submaximal contractions which were maintained at 30% MVIC to identify neuromuscular fatigue. The study reported decrease in force, however central activation was preserved suggesting that submaximal contractions, like those used in the present study, may not be sufficient to induce central changes. Similarly, Kennedy et al. (2013) concluded that the energy required to drive the muscle (forearm muscle) maximally might lead to more severe central alterations as compared to the submaximal contractions. Thus, the work conducted by Bigland et al. (1986) suggests that the submaximal intensity contractions (30% MVIC) in the present study might have led to a preservation of the central activation. This is in contrast to the work conducted by Rattey et al. (2006) and Martin and Rattey (2007), where the fatiguing contractions were maintained at MVIC and might have led to central changes. While this argument of intensity of contraction influencing the occurrence of cross-over fatigue makes sense based on the work of Bigland et al. (1986) but the other research suggests the relationship may not be as straight forward as this. For example Place et al. (2009) reported that low intensity sustained contractions are often related to central alterations, whereas maximal contractions have been related to peripheral changes. Clearly more work is necessary to delineate contraction intensities and durations related to central or global fatigue effects.

One of the primary reasons for undertaking this study was to expand the work of Paillard et al. (2010). The present study was designed to allow for a more detailed examination of non-fatigued limb muscle activation changes, in an effort to better

understand the mechanism underlying the postural control change that these authors demonstrated. The present study failed to show any cross-over effect of fatigue on standing balance – a direct contradiction of the results of Paillard et al. (2010). Evidence of cross-over fatigue was supported in the Paillard study (2010) by the increased CoP sway area, though there was no decrease in the non-fatigued quadriceps femoris MVIC force. The present study found no effect of ipsilateral fatigue on sway measures, force or muscle activation. These contradictory findings between Paillard et al. (2010) and the present study may be related to differences between the fatigue protocols. Contraction intensity differences between the protocols (10% versus 30% in the present study) might have been a factor. In the previous paragraph it was suggested that higher intensity contraction were needed to produce cross-over fatigue. Based on this, and the contraction used in the present study and the work of Paillard et al. (2010), it is surprising that Paillard et al. (2010) found cross-over effects. This suggests that there is likely some other mechanism, other than contraction intensity that needs to be explored. Examining the protocols used in this and the Paillard study (2010), an additional factor that has to be considered is the duration of the fatiguing contractions. In the present study, 15 consecutive contractions of 16 s each were executed at 30% peak force until a 50% decrease in force occurred. Paillard et al. (2010) utilized 10 sets of 50 repetitions at 10% peak torque resulting in a longer duration of contractions. Specifically, it was estimated that Paillard's (2010) protocol would have resulted in individuals contracting for approximately 33 minutes at 10% MVIC. In the present study, on average, individuals contracted for 3.5 minutes at 30% MVIC. It is possible that the difference in fatigue duration could be a factor that led to the contradictory results. Support for this hypothesis can be found in the work of Behm and St-Pierre (1997). These authors examined the effects of the duration of fatigue protocols on quadriceps femoris muscle activation

properties. They reported that longer duration protocols (approximately 19 minutes at 25% MVIC) differentially affected muscle activation properties when compared to shorter duration fatiguing contractions (approximately 4 minutes of 50% MVIC isometric contractions). Behm and colleagues (1997) suggested their results were indicative of greater central inhibitory (muscle inactivation) responses for the longer duration contractions. Rattey et al. (2006) have shown that such central responses can lead to reflex impulses at the medullar level which can potentially affect contralateral function. Similarly, Hortobagyi et al. (2003) have shown that disturbance in the homologous motor drive during prolonged fatiguing contractions can inhibit the contralateral motor pathway. Collectively these results suggest it is possible that the prolonged contractions in the Paillard et al. (2010) study had a greater capacity to alter contralateral muscle function leading to the alterations in posture on the non-fatigued limb post-fatigue. In the present study, the short fatigue protocol duration may not have been sufficient to induce changes in the contralateral limb. Replication of the present study, using a longer duration fatigue protocol, is required to confirm this hypothesis.

While a main area of interest of this study was to examine the cross-over effect of fatigue on postural control, the results also add to the body of knowledge on cross-over fatigue effects on muscle force production. This study is one of many (Zidjewind et al., 1998, Grabiner & Owings, 1999, Todd et al., 2003, Regueme and Nicol, 2007) that have failed to find an effect of ipsilateral fatigue on either contralateral force or muscle activation. As has been discussed above, it is hypothesized that the lack of evidence of cross-over fatigue may be related to either the duration of fatiguing contractions, the intensity of the contractions or in all likelihood some combination of the two. In order to understand how factors such as contraction intensity and duration can influence the presence or absence of cross-over fatigue, the inhibitory and excitatory effects of muscle

contraction must be understood. According to the motor outflow theory, ipsilateral voluntary muscle activation patterns are likely to cross-over to the non-fatigued homologous muscles (Post et al., 2008) through transcallosal connections (Bonato et al., 1996). Unilateral motor activity (unilateral knee extension incorporated in the present study) has been proposed to activate excitatory paths interconnecting the ipsilateral and contralateral primary motor cortex, referred to as motor irradiation (Zidjewind et al., 1998). However, the theory of default bilateral interaction states that throughout the unilateral contractions the activation of the non-targeted muscle group can be actively inhibited (Post et al., 2008). In the present study, it is possible that these competing inhibitory and facilitating effects might have balanced contralateral responses resulting in no significant changes in the force and postural sway parameters on the non-fatigued limb. Clearly, further research is needed to determine the exact mechanisms underlying the cross-over effects of fatigue and the factors that determine if and when it occurs.

3.5 Limitations

Limitations to the study include the use of only male participants. As a previous study by Martin and Rattey, (2007) has examined the effects of gender (Martin & Rattey, 2007) on cross-over fatigue, it would be interesting to understand the effects of cross-over fatigue on female population too. Also, the idea of placing the little finger on the edge of the chair during the single leg standing balance trials might be a factor that contributed to the lack of change in non-fatigued limb balance. Work by Bolton et al. (2011) has shown that even light finger pressure has the ability to alter postural sway. In the present study, however, the use of finger touch to assist with balance was maintained for all conditions and both limbs, thus the effect would be the same for all conditions. Based on this fact it

is felt that the results would have been unlikely to change even if the chair has not been used.

3.6 Conclusion

No evidence of reductions in force, muscle activation, muscle co-ordination or disturbance in the postural stability parameters were noted for the non-fatigued limb. However, significant changes were noted for the fatigued side with MVIC, CoP sway area, total length covered by CoP, CoP_{AP} length as well as the mean velocity covered by CoP. Posture can be dependent upon the extent and onset of muscle forces to compensate for disruptions to the CoG. It can be concluded that the lack of changes in non-fatigued force, F100 and stability parameters contributed to the lack of change in non-dominant postural sway parameters. Briefer fatigue duration than a previously published similar study (Paillard et al. 2010) or the use of submaximal intensity contractions as compared to MVIC (Rathey et al., 2006; Martin & Rathey, 2007) may have contributed to the lack of cross-over fatigue effects.

3.7 References

- Behm, D. G. (2004). Force maintenance with submaximal fatiguing contractions. *Canadian Journal of Applied Physiology*, 29(3), 274-290.
- Behm, D. G., Button, D. C., & Butt, J. C. (2001). Factors affecting force loss with prolonged stretching. *Canadian Journal of Applied Physiology*, 26(3), 261-272.
- Behm, D. G., & St-Pierre, D. M. (1997). Effects of fatigue duration and muscle type on voluntary and evoked contractile properties. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 82(5), 1654-1661.
- Bellew, J. W., & Fenter, P. C. (2006). Control of balance differs after knee or ankle fatigue in older women. *Archives of Physical Medicine and Rehabilitation*, 87(11), 1486-1489. doi: 10.1016/j.apmr.2006.08.020.
- Bigland-Ritchie, B., Cafarelli, E., & Vollestad, N. K. (1986). Fatigue of submaximal static contractions. *Acta Physiologica Scandinavica. Supplementum*, 556, 137-148.
- Bigland-Ritchie, B., Johansson, R., Lippold, O. C., Smith, S., & Woods, J. J. (1983). Changes in motoneurone firing rates during sustained maximal voluntary contractions. *The Journal of Physiology*, 340, 335-346.
- Bigland-Ritchie, B., & Woods, J. J. (1984). Changes in muscle contractile properties and neural control during human muscular fatigue. *Muscle & Nerve*, 7(9), 691-699. doi: 10.1002/mus.880 070902.
- Bigelow K.E. (2008). *Identification of key traditional and fractal postural sway parameters to develop a clinical protocol for fall risk assessment in older adults* (Doctoral dissertation). The Ohio State University, Columbus, Ohio, USA.
- Bolton, D. A., McIlroy, W. E., & Staines, W. R. (2011). The impact of light fingertip touch on haptic cortical processing during a standing balance task. *Experimental Brain Research* 212(2), 279-291. doi: 10.1007/s00 221-011-2728-6.

Bonato, C., Zanette, G., Manganotti, P., Tinazzi, M., Bongiovanni, G., Polo, A., & Fiaschi, A. (1996). 'Direct' and 'crossed' modulation of human motor cortex excitability following exercise. *Neuroscience Letters*, 216(2), 97-100.

Cohen J (1969). *Statistical Power Analysis for the Biomechanical Sciences*. First Edition. New York: Academic Press.

Cohen J (1990). Things I have learned (so far). *Am. Psych*, 45(12):1304-1312.

Criswell, E (2011). *Cram's introduction to surface electromyography*. Second Edition. Jones and Bartlett .

Degens, H., & Veerkamp, J. H. (1994). Changes in oxidative capacity and fatigue resistance in skeletal muscle. *The International Journal of Biochemistry*, 26(7), 871-878.

De Luca, C. J., Gilmore, L. D., Kuznetsov, M., & Roy, S. H. (2010). Filtering the surface EMG signal: Movement artifact and baseline noise contamination. *Journal of Biomechanics*, 43(8), 1573-1579. doi: 10.1016/j.jbiomech.2010.01.027.

Dibble, L. E., Lopez-Lennon, C., Lake, W., Hoffmeister, C., & Gappmaier, E. (2013). Utility of disease-specific measures and clinical balance tests in prediction of falls in persons with multiple sclerosis. *Journal of Neurologic Physical Therapy: JNPT*, doi: 10.1097/NPT.0b 013e31 82a18 460.

Duarte, M., & Zatsiorsky, V. M. (2002). Effects of body lean and visual information on the equilibrium maintenance during stance. *Experimental Brain Research*, 146(1), 60-69. doi: 10.1007/s00221-002-11 54-1.

Elmer, S. J., Amann, M., McDaniel, J., Martin, D. T., & Martin, J. C. (2013). Fatigue is specific to working muscles: No cross-over with single-leg cycling in trained cyclists. *European Journal of Applied Physiology*, 113(2), 479-488. doi: 10.1007/s00421-012-24 55-0.

Enoka, R. M., & Duchateau, J. (2008). Muscle fatigue: What, why and how it influences muscle function. *The Journal of Physiology*, 586(1), 11-23. doi: 10.1113 /jphysiol .2007. 139477.

Grabiner, M. D., & Owings, T. M. (1999). Effects of eccentrically and concentrically induced unilateral fatigue on the involved and uninvolved limbs. *Journal of Electromyography and Kinesiology*, 9(3), 185-189.

Gribble, P. A., & Hertel, J. (2004). Effect of lower-extremity muscle fatigue on postural control. *Archives of Physical Medicine and Rehabilitation*, 85(4), 589-592.

Hertel, J. (2000). Functional instability following lateral ankle sprain. *Sports Medicine (Auckland, N.Z.)*, 29(5), 361-371.

Hodges, P. W., & Bui, B. H. (1996). A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography. *Electroencephalography and Clinical Neurophysiology*, 101(6), 511-519.

Hortobagyi, T., Taylor, J. L., Petersen, N. T., Russell, G., & Gandevia, S. C. (2003). Changes in segmental and motor cortical output with contralateral muscle contractions and altered sensory inputs in humans. *Journal of Neurophysiology*, 90(4), 2451-2459. doi: 10.1152/jn.01001.2002.

Humphry, A. T., Lloyd-Davies, E. J., Teare, R. J., Williams, K. E., Strutton, P. H., & Davey, N. J. (2004). Specificity and functional impact of post-exercise depression of cortically evoked motor potentials in man. *European Journal of Applied Physiology*, 92(1-2), 211-218. doi: 10.1007/s00421-004-1082-9.

Kanekar, N., Santos, M. J., & Aruin, A. S. (2008). Anticipatory postural control following fatigue of postural and focal muscles. *Clinical Neurophysiology*, 119(10), 2304-2313. doi: 10.1016/j.clinph.2008.06.015.

Kennedy, A., Hug, F., Sveistrup, H., & Guevel, A. (2013). Fatiguing handgrip exercise alters maximal force-generating capacity of plantar-flexors. *European Journal of Applied Physiology*, 113(3), 559-566. doi: 10.1007/s00421-012-2462-1.

MacDonald GZ, Button DC, Drinkwater EJ, Behm DG (2013). Foam Rolling as a Recovery Tool Following an Intense Bout of Physical Activity. In press *Med Sci Sports Exerc*. doi: 10.1249 /MSS.0b013e3182a123db.

Macefield, G., Gandevia, S. C., & Burke, D. (1990). Perceptual responses to microstimulation of single afferents innervating joints, muscles and skin of the human hand. *The Journal of Physiology*, 429, 113-129.

Martin, P. G., & Rattey, J. (2007). Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. *Pflugers Archiv : European Journal of Physiology*, 454(6), 957-969. doi: 10.1007/s00424-007-0243-1.

Masani, K., Sayenko, D. G., & Vette, A. H. (2013). What triggers the continuous muscle activity during upright standing? *Gait & Posture*, 37(1), 72-77. doi: 10.1016/j.gaitpost.2012.06.006.

McLean, S. G., & Samorezov, J. E. (2009). Fatigue-induced ACL injury risk stems from a degradation in central control. *Medicine and Science in Sports and Exercise*, 41(8), 1661-1672. doi : 10.1249/MSS.0b013e31819ca07b.

Paillard, T., Chaubet, V., Maitre, J., Dumitrescu, M., & Borel, L. (2010). Disturbance of contralateral unipedal postural control after stimulated and voluntary contractions of the ipsilateral limb. *Neuroscience Research*, 68(4), 301-306. doi: 10.1016/j.neures.2010.08.004.

Place, N., Lepers, R., Deley, G., & Millet, G. Y. (2004). Time course of neuromuscular alterations during a prolonged running exercise. *Medicine and Science in Sports and Exercise*, 36(8), 1347-1356.

Post, M., Bayrak, S., Kernell, D., & Zijdwind, I. (2008). Contralateral muscle activity and fatigue in the human first dorsal interosseous muscle. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 105(1), 70-82. doi: 10.1152/jappphysiol.01298.2007.

Rattee, J., Martin, P. G., Kay, D., Cannon, J., & Marino, F. E. (2006). Contralateral muscle fatigue in human quadriceps muscle: Evidence for a centrally mediated fatigue response and cross-over effect. *Pflugers Archiv: European Journal of Physiology*, 452(2), 199-207. doi: 10.1007/s00424-005-0027-4.

Regueme, S.C., Barthelemy, J., & Nicol, C. (2007). Exhaustive stretch-shortening cycle exercise: No contralateral effects on muscle activity in maximal motor performances. *Scandinavian Journal of Medicine & Science in Sports*, 17(5), 547-555. doi: 10.1111/j.1600-0838.2006.00614.x.

Robertson DGE, Caldwell GE, Hamill J, Kamen G, Whittlesey SN (2004). Research Methods for Biomechanics. Champaign: Human Kinetics Publishers.

Ross, E. Z., Goodall, S., Stevens, A., & Harris, I. (2010). Time course of neuromuscular changes during running in well-trained subjects. *Medicine and Science in Sports and Exercise*, 42(6), 1184-1190. doi: 10.1249/MSS.0b013e3181c91f4e.

Ross, E. Z., Middleton, N., Shave, R., George, K., & Nowicky, A. (2007). Corticomotor excitability contributes to neuromuscular fatigue following marathon running in man. *Experimental Physiology*, 92(2), 417-426. doi: 10.1113/expphysiol.2006.035972.

Schoneburg, B., Mancini, M., Horak, F., & Nutt, J. G. (2013). Framework for understanding balance dysfunction in parkinson's disease. *Movement Disorders: Official Journal of the Movement Disorder Society*, doi: 10.1002/mds.25613; 10.1002/mds.25613.

Sims, K. J., & Brauer, S. G. (2000). A rapid upward step challenges medio-lateral postural stability. *Gait & Posture*, 12(3), 217-224.

Strang, A. J., Berg, W. P., & Hieronymus, M. (2009). Fatigue-induced early onset of anticipatory postural adjustments in non-fatigued muscles: Support for a centrally mediated adaptation. *Experimental Brain* 197(3) , 245-254. doi: 10.1007/s00221-009-1908-0.

Takahashi, K., Maruyama, A., Hirakoba, K., Maeda, M., Etoh, S., Kawahira, K., & Rothwell, J. C. (2011). Fatiguing intermittent lower limb exercise influences corticospinal and corticocortical excitability in the nonexercised upper limb. *Brain Stimulation*, 4(2), 90-96. doi: 10.1016 /j.brs.2010.07.001.

Taylor, J. L., Todd, G., & Gandevia, S. C. (2006). Evidence for a supraspinal contribution to human muscle fatigue. *Clinical and Experimental Pharmacology & Physiology*, 33(4), 400-405. doi: 10.1111/j.1440-1681.2006.04363.x.

Todd, G., Petersen, N. T., Taylor, J. L., & Gandevia, S. C. (2003). The effect of a contralateral contraction on maximal voluntary activation and central fatigue in elbow flexor muscles. *Experimental Brain* 150(3) , 308-313. doi: 10.1007/s00221-003-1379-7.

Vellas, B. J., Wayne, S. J., Romero, L., Baumgartner, R. N., Rubenstein, L. Z., & Garry, P. J. (1997). One-leg balance is an important predictor of injurious falls in older persons. *Journal of the American Geriatrics Society*, 45(6), 735-738.

Yaggie J, Armstrong WJ (2004) Effects of lower extremity fatigue on indices of balance. *J Sport Rehabil*, 13:312-322.

Zijdewind, I., Zwarts, M. J., & Kernell, D. (1998). Influence of a voluntary fatigue test on the contralateral homologous muscle in humans? *Neuroscience Letters*, 253(1), 41-44.



