# CONTRALATERAL EFFECTS OF ECCENTRIC EXERCISE AND DELAYED ONSET MUSCLE SORENESS (DOMS) OF THE PLANTAR FLEXORS: EVIDENCE OF CENTRAL MECHANISM INVOLVED

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Contralateral Effects of Eccentric Exercise and Delayed Onset Muscle Soreness (DOMS) of the Plantar Flexors: Evidence of Central Mechanism Involved

Field of Study: Exercise Physiology

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**CONTRALATERAL EFFECTS OF ECCENTRIC EXERCISE AND DELAYED ONSET MUSCLE SORENESS (DOMS) OF THE PLANTAR FLEXORS: EVIDENCE OF CENTRAL MECHANISM INVOLVED**


## ABSTRACT

Peripheral and central factors play important roles in the reduction of motor performance following a damaging eccentric exercise and delayed onset of muscle soreness (DOMS). Following this regime, contralateral limb could also be affected, however, the factors involved are inconclusive. The purpose of this study was to distinct contribution of peripheral and central factors following eccentric contraction and DOMS of the plantar flexors in both treated and contralateral homologous limb. Ten males (BMI = 25.08 ± 1.69 $kgm^{-2}$; age = 28.70 ± 4.24 years) were randomly assigned to experimental (DOM) or control (CON). The DOM group was treated with a damaging eccentric exercise, while CON rested. Plasma creatine kinase concentration (CK), visual analogue scale (VAS), muscle stiffness, maximal voluntary contraction (MVC) and voluntary activation (VA) were measured at pre, post-10 min, -24, -48, -72 hour, on both treated and contralateral limb. After the exercise, CK increased up-to post-48 hour, while VAS up-to post-72 hour compared to pre. Importantly, MVC was reduced at all-time points with greatest drop at post-24 hour (-16%), while VA affected up to post-48 hour with greatest drop at post-10 minute (-7%). Interestingly, a 'cross-over effect' was observed in the contralateral limb when VAS, MVC, and VA were negatively affected following the same pattern (time line) as in the treated limb (-13% peak MVC drop; -3.5% peak VA drop). These findings suggest a substantial central contribution to the drop in force especially immediately after the exercise and to a lesser extent the later part of DOMS in both treated and contralateral limb.



Keywords: Eccentric exercise, DOMS, Voluntary Activation, Pain.

**KESAN KONTRALATERAL LATIHAN EKSENTRIK DAN KESAKITAN MUSCLE ONSET (DOMS) PADA FLEKSI PLANTAR: BUKTI MEKANISME PUSAT TERLIBAT**

## ABSTRAK

Faktor periferi dan pusat memainkan peranan penting dalam penurunan prestasi motor berikutan senaman yang mencederakan tisu-tisu otot lalu mengakibatkan kelesuan otot (DOMS). Semasa DOMS, anggota badan kontralateral juga boleh terjejas, bagaimanapun, faktor-faktor yang menyumbang kepada fenomena ini adalah tidak konklusif. Kajian ini dijalankan untuk mengkaji faktor-faktor periferi dan pusat sejurus selepas kontraksi eksentrik dan DOMS pada 'plantar flexors' pada kedua-dua anggota badan homologus yang dilatih dan kontralateral. Sepuluh orang lelaki (BMI = 25.08 ± 1.69 $kgm^{-2}$; umur = 28.70 ± 4.24 tahun) diagaihkan secara rawak kepada kumpulan eksperimen (DOM) dan kawalan (CON). Kumpulan DOM membuat latihan kontraksi eksentrik, manakala kumpulan CON berehat sepenuhnya. Skala Analog Visual (VAS), kekejangan otot, pengenduran otot maksimum (MVC) dan peratus pengaktifan otot untuk pengecutan neural (VA) diukur pada pra, selepas 10 min, -24, -48, -72 jam, pada kedua-dua bahagian yang dilatih dan anggota kontralateral dan dalam pada masa yang sama mengukur 'plasma creatine kinase' (CK). Selepas latihan, CK meningkat secara signifikan sehingga pasca-48 jam, manakala VAS meningkat sehingga pasca-72 jam berbanding bacaan pada pra latihan. Seterusnya, MVC menurun secara signifikan sepanjang masa dengan kadar penurunan paling besar pada masa selepas 24 jam (-16%), sementara VA terjejas sehingga pasca-48 jam dengan penurunan paling signifikan pada pasca-10 minit (-7%). Di samping itu, 'cross-over effect' diperhatikan di bahagian anggota badan kontralateral apabila MVC, dan VA menurun dengan kadar yang selari (-13% puncak MVC; -3.5% VA). Penemuan ini mencadangkan sumbangan utama kepada penurunan prestasi motor yang ketara berlaku terutamanya akibat faktor pusat (central

drive) pasca latihan eksentrik dan seterusnya sehingga pada ketika DOMS kedua-dua anggota badan yang dilatih dan kontralateral megalami perubahan yang minimal.

Kata Kunci: Latihan eksentrik, DOMS, Pengecutan, Neural, Kesakitan.

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| | | |
|---|---|---|
| DOMS | : | Delayed Onset of Muscle Soreness |
| MVC | : | Maximal Voluntary Contractions |
| VA | : | Voluntary Activation |
| NMES | : | Neuromuscular Electrical Stimulation |
| RFD | : | Rate of Force Development |
| CoV | : | Coefficient of variation of the force |
| EMG | : | Electromyography |
| MVT | : | Maximal Voluntary Torque |
| SICI | : | Short-Interval Intracortical Inhibition |
| PAR-Q | : | Physical Activity Readiness Questionnaire |
| GPAQ | : | Global Physical Activity Questionnaire |
| BMI | : | Body Mass Index |
| SLCRs | : | Short-Latency Crossed Responses |

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# CHAPTER 1: INTRODUCTION

## 1.1 Delayed Onset of Muscle Soreness (DOMS)

### 1.1.1 Mechanism of DOMS

In general, maximum muscle contractions are often associated with muscle damage. Moreover, eccentric exercise and/or unaccustomed exercise can lead to extensive damage which is commonly experienced as muscle soreness (Evans & Cannon, 1991). Hough (1900) discovered that muscles became sore when subjects performed rhythmical contractions of the finger flexor muscles until fatigued. At the time of the contractions, the feeling of soreness was not reported, but its development and progression was observed 8 to 10 hours later and was most severe at 48 to 60 hours afterword (Cheung *et al*., 2003). Besides, an active lengthening overstretched sarcomeres lead to shift in optimal length for tension (Morgan *et al*., 1990). Further contraction leads to membrane damage (E-C Coupling Dysfunction) which gives rise to the passive tension and finally the fiber dies. Local inflammatory responses associated with tissue edema and soreness happens due to the breakdown of dead and dying cells (Proske & Morgan, 2001). Thus, following unaccustomed exercise, the delayed onset of muscle soreness, the feeling of pain and stiffness in the muscle that usually occur one to five days can negatively alter muscular performance from the voluntary effort reduction and also from the inevitable loss of capacity of the muscles to produce force affect muscular performance, both from voluntary effort reduction and from the inevitable loss of capacity of the muscles to produce force (Armstrong, 1984). Throughout the years the understanding on DOMS has expanded, however, with the advancement of recent technologies the multifactorial association of DOMS warrants further research particularly in areas of neuromuscular. These encompasses two main contributing factors of DOMS; firstly at the peripheral level, and secondly at central level.

### 1.1.2 Peripheral Factors Contributing to DOMS

Generally DOMS decreases movements, force productions (Armstrong, 1984; Clarkson, Nosaka, & Braun, 1992; Friden, Sjostrom, & Ekblom, 1983) and causes pain (Garrett, 1990; Smith, 1991). These effects are due to structural alterations of the Z-bands that have been damaged during the eccentric exercise. This observation was noted as the disorganisation of the Z-band material was prominent immediately following the eccentric exercise. The observation of the cross-striated band pattern indicates the mechanical changes originating from the myofibrillar Z-band, which exhibited streaming, broadening and at particular parts, total disruption. These changes could be seen in one tenth of the muscle fibres six day after the exercise. It is observed that type 2 fibres were notably affected in this study. (Friden et al., 1983; Schwane, Johnson, Vandenakker, & Armstrong, 1983) which directly increases and declines in circulating neutrophils which have been reported at comparable times to what typically occurs during classic, acute inflammation cause inflammation (Smith *et al*., 1994) which will in turn activate Type III and IV pain receptors, thus leading to the sensation of DOMS (O'Connor & Cook, 1999).

However, a study by Yu, Liu, Carlsson, Thornell, and Stal (2013), shown that the human soleus muscle was not as sensitive to the downstairs running movement (eccentric contraction) as animal muscles are to isolated eccentric exercise. More importantly, there were no sarcolemma damage at one hour post-exercise of downhill running, which indicates that the previous hypothesis that prior sarcolemma injuries trigger detrimental outcomes in muscles after eccentric exercise does not apply to the human soleus muscle. Consequently, the results refute the previous hypothesis of fibre swelling having a direct correlation to the symptoms of DOMS.

Ayles, Graven-Nielsen, and Gibson (2011) suggest a hypothesis that the large diameter of afferent neurons elevate DOMS effects, possibly via central mediated changes. This is because the convergent connection exists between how large the diameter of the neurons are to the nociceptive fibres of the dorsal horn of the spinal cord, both of which under typical conditions are latent.

### 1.1.3 Central Factors Contributing to DOMS

In more recent years, at the central level, impaired neural drive to the affected muscle from either cortical (including intracortical inhibitory interneurons) (Pitman, 2012) or/and spinal tracts (Vila cha, 2012; Prasartwuth, 2005) has been implicated. In addition, changes in the thresholds of the motor unit recruitment, discharge rates (Dartnall *et al*., 2009), motor unit conduction velocities (Hedayatpour *et al*., 2009), and synchronisation (Dartnall *et al*., 2008) have also provided evidence of central factor involvement. Furthermore, central factor involvement is substantiated by findings in the contralateral limb during DOMS of the trained limb, including (i) reduction in force and lower EMG amplitude (Hedayatpour, 2018) and (ii) short-latency cross responses (SLCR) of pain (Gervasio, 2018). However, there is lack of information on neural drive to the contralateral limb during DOMS of the trained limb. Voluntary activation (VA), which takes resting twitch into account, can provide reliable data on force generation which is essentially represented by the central drive to the motor neurons during a voluntary effort (Gandevia, 2001). To date, no studies have reported changes in VA in untrained limbs. Based on the evidences presented, it is believed that the nervous system contributes to the drop in force during DOMS, the precise mechanisms and pathways involved have yet to be fully established due to mix findings reported.

Thus, this study aims to assess the maximal voluntary contraction and voluntary activation and their associations with muscle soreness on both the ipsi/contralateral homologous limb of dorsi flexors. The drop in force and voluntary activation in the contralateral limb would suggest the central mechanisms are involved during DOMS. The expected outcomes of this study allows recovery strategies to overcome the central effect of DOMS.

## 1.2 Problem Statements

General ideas of peripheral contribution during DOMS have been widely explored. However, studies that focus on the effect of DOMS following eccentric exercise leading to the reduction in force are still inconclusive on the underlying mechanisms explaining this observation. In particular, the central contribution towards DOMS and its related outcomes i.e force reduction, has not been well established. Another possible mechanism associated with DOMS is the contralateral transfer of pain, contributed by the affected ipsilateral limb, implying neural involvements, which could also explain the reported reduction in force, however, lack of data to support this phenomenon.

## 1.3 Research Questions

- Can the published protocol to induce muscle damage be reproducible?
- What is the magnitude of force reduction following this protocol on plantar flexors? And is this effect also observed in the contralateral limb?
- Is the prognosis of DOMS can be associated with changes in muscle stiffness for both ipsi and contralateral exercised limb?
- Does the muscle damage marker CK in line with the drop in force? And do the values correlate with visual analogue rating?
- How clear is the contribution of the central drive to the drop in force?

- Is there a protective effect on the contralateral homologous limb during DOMS?

## 1.4 Research Aims and Objectives

The objectives of the present study are:

- To establish a protocol that induces delayed-onset muscle soreness (DOMS).
- To determine the fluctuation in force production following DOMS.
- To distinct peripheral and central mechanisms involved in DOMS by assessing the effect of DOMS in contralateral limb.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 Development of Delayed-Onset Muscle Soreness (DOMS) and its Attributes

Hough (1900) describes the phenomenon of DOMS that occur predominantly following lengthening (eccentric) contractions manifested in the muscle as pain and stiffness which developed 8-10 hours later, and is most severe after 48-60 hours. There are a few factors that contribute to the development of DOMS, generally these factors can be divided into peripheral and central involvements, which ultimately results in a general drop in force generation (Deschenes *et al.*, 2000; Sayers, Knight, & Clarkson, 2003).

Six theories have been postulated in the development of DOMS; lactic acid, muscle spasm, connective tissue damage, inflammation and acid reflux (Cheung, Hume, & Maxwell, 2003; Lewis, Ruby, & Bush-Joseph, 2012). The lactic acid theory depends on the notion that lactic acid continues to be produced even after the suspension of the exercise and this byproduct could cause the perceived pain during DOMS (Armstrong, 1984). However, there are also studies which found that damaging concentric exercise failed to produce the sensation of pain whilst lactic acid level has returned to the level it was at pre-exercise (Schwane, Watrous, Johnson, & Armstrong, 1983). Consequently, lactic acid could increase acutely after a bout of strenuous exercise. However it could not be related to the delayed pain during DOMS since no significant change is noted compared to baseline 1 hour post exercise (Cheung *et al.,* 2003).

Initially, the increase in resting muscle activity was believed to be associated with muscle spasm after an eccentric exercise. This phenomenon was then thought to be initiated by blood vessel compressions leading to ischemia and the accumulation of substances producing pain (Bobbert, Hollander, & Huijing, 1986). Later, using EMG recording during muscle soreness found a mix finding of increase in EMG and vice versa

using a bipolar and unipolar EMG method (Cheung *et al*., 2003). Thus the mix findings using EMG leads to an uncertainty in the cause which leads to DOMS.

Sheath around bundles of muscle fibers are formed by connective tissues. The structure and composition differs between various types of muscle fibres for instance, Type 1 muscle fibres are commonly known as slow twitch fibres display a more potent structure compared to that of the Type II (fast-twitch) fibres. Consequently, fast twitch muscle fibres may be seen to be increasingly susceptible to injuries which are stretch-induced. Muscle soreness would be the effect seen from the excessive pressure of the connective tissue. In support of this theory, a measurement of hydroxiproline (HP) and the hydroxylysine (HL) amino acids in urine indicate constituents of mature collagen. Overuse and or strain damage results in collagen degradation which in turn leads to the presence of HP and HL in the urine (Stauber, 1989). It is also noted that the HP and HL presence in the urine excretion may indicate either increase or decrease in collagen synthesis.

Hough (1900) was the first to suggest the association between muscle damage and muscle soreness. He found muscles became sore when the finger flexor muscles made continuous contraction until it fatigued. The soreness was focused on the sites where disruption of muscle tissues were reported after eccentric exercise, distinctly at the z-line. It was also observed that mechanical disruption to the structural elements showed an increase, particularly amongst the Type II fibers, which have the narrowest and weakest z-lines. When stimulated, the nociceptors, capillaries and musculotendinous junctions lead to a sensation of pain. This theory was further supported by the measurement of post-exercise blood enzyme. A key indicator of the permeability of the muscle membrane is creatine kinase (CK), which is discovered primarily in the skeletal and cardiac muscles. (Cleak & Eston, 1992). With CK being a precursor for muscle damage post-exercise and

during DOMS, the z-line disruption and sarcolemma damage will allow muscle enzymes such as CK to spread into the interstitial fluid. Although there are some discrepancies in the time of peaking between the muscle soreness and level of CK, this theory of muscle damage could be accepted as a partial theory explaining the sensation of DOMS (Cheung *et al*., 2003).

The theory of inflammation is based on the formation of edema and infiltration of inflammatory cells after repeated eccentric muscle action. The proteolytic enzymes in the muscle fibers cause cell structures to break down after injury. In relation to the rise in bradykinin, histamine and prostaglandins, monocytes and neutrophils are drawn to the injury site owing to the fast degradation of the damaged muscle tissue and connective tissues (Cheung *et al*., 2003). An inflow of protein-rich fluid (exudate) into the muscle via the increased permeability of narrow blood vessels following eccentric exercise soon follows (Smith, 1991). Both Smith (1991) and Armstrong (1984) have disputed that substances which sensitize the Type III and Type IV nerve endings within a 24-48 hour period are produced by monocytes which eventually converts to macrophages.

The assumption that calcium, generally stored in the sarcoplasmic reticulum accumulates in injured muscles following sarcolemma damage is the basis on the enzyme efflux theory which is suggested by Gulick and Kimura (1996). This is thought to lead to a cellular respiration inhibition. In addition, it is thought that the rise in calcium concentrations activates proteases and phospholipases that cause further sarcolemma injury. This results in an increase of muscle protein breakdown at the weakened z-lines and the occurrence of chemical stimulation of pain endings (Cheung *et al*., 2003).

An amalgamation of two or more of these factors synergistically exerts the effect of DOMS (Cheung *et al*., 2003) and most importantly, these lead to a drop in force (strength loss) for up to five days (Deschenes *et al*., 2000), however there are reports suggesting a

longer lasting effect of 7-10 days (Clarkson *et al*., 1992; Howell, Chleboun, & Conatser, 1993; Sayers & Clarkson, 2001). Specifically, few hypotheses have been put forth attributing to the drop in force; (i) a shift in the peak of the force-length curve to longer length is caused by weakened or overstretched sarcomeres (Saxton & Donnelly, 1996), (ii) reduced $Ca^{2+}$ release and reduced force caused by the changes in excitation-contraction coupling (Warren *et al*., 1993), (iii) the degeneration and the non-excitability of muscle fibers (McCully & Faulkner, 1986), and (iv) thick and thin filaments do not reinterdigitate (Morgan & Allen, 1999).

Apart from peripheral factors, the nervous systems are also shown to be involved in the development of DOMS and the subsequent drop in force. Evidences for this are shown in studies related to motor units where substantial changes in recruitment thresholds (Fuglevand, Winter, & Patla, 1993), discharge rates (De Luca, LeFever, McCue, & Xenakis, 1982), motor unit conduction velocities (Hedayatpour, Falla, Arendt-Nielsen, Vila-Cha, & Farina, 2009) and synchronisation (Keenan, Farina, Merletti, & Enoka, 2006), which are associated with DOMS (Semmler, 2014). These changes implicated in the motor units (which are the final common pathways) could have been contributed by higher centers (above motor units) and/or other associated feedback systems.

To justify these contributions, alterations to responses induced by neurophysiological techniques such as: H-reflex (Laurin, Dousset, Carrivale, Grelot, & Decherchi, 2012; Vila-Cha, Falla, Correia, & Farina, 2012), motor evoked potentials (MEPS) (Pitman & Semmler, 2012), M-wave (Pitman & Semmler, 2012; Semmler, Ebert, & Amarasena, 2013), and Central Activation Ratio (CAR) (Skurvydas, Brazaitis, Kamandulis, & Sipaviciene, 2010), as well as outcomes from twitch torque (Barss *et al*., 2014; Prasartwuth, Allen, Butler, Gandevia, & Taylor, 2006; Prasartwuth, Taylor, & Gandevia, 2005), and voluntary activation (Prasartwuth *et al.,* 2006; Prasartwuth *et al.,* 2005;

Skurvydas *et al*., 2010) have been reported. However from these studies no specific pathways and sites can be concluded due to different neurophysiological techniques employed, protocols and muscle groups used to induced DOMS, and time points measured following the eccentric exercise. Assessment of the central measures on the contralateral homologues limb would suggest the involvement and modulation of the neural component during DOMS in force drop.

## 2.2 Criterion measures of DOMS

### 2.2.1 Muscle damage marker (Creatine Kinase)

The presence of creatine kinase (CK) in the blood is commonly regarded as an indirect indicator of muscle damage. This has been shown to be helpful in the diagnosis of medical circumstances such as myocardial infarction, muscle dystrophy and brain disease (Baird, Graham, Baker, & Bickerstaff, 2012). In the general population, the baseline serum CK readings are between 35-175U / L.

### 2.2.2 Pain Scale

The difficulty in assessing and quantifying pain is one of the main factor that is influencing our understanding of muscle pain because of its subjective nature. Many authors have used Visual Analog Scale (VAS) to quantify musculoskeletal pain for DOMS assessment. Since without mechanical stimulus, DOMS is not felt, the process to quantify pain requires a standardized palpation. However, the method of how stimuli should be imposed to quantify pain level using a VAS is unclear, and presently there are no standardized protocols for stimulus application have been documented (Lau, Blazevich, Newton, Wu, & Nosaka, 2015).

### 2.2.3 Drop in Strength

Extended loss of strength after exercise is one of the most credible indirect indicators of human muscle damage. During exercise that does not generate muscle damage (e.g.,

concentric contractions), reduction in force immediately after the exercise session are only temporary and is restored in the subsequent few hours and it is generally considered to be due to metabolic or neural fatigue. Concentric protocols are used for strength loss of 10-30% immediately after exercise with strength returning to baseline within hours after exercise. Eccentric downhill running protocols are used for strength losses of 10-30 percent right after exercise, but with a longer recovery period (up to 24 hours after exercise). High-force eccentric exercise typically yields the highest degree of strength loss and the longest recovery times). When compared to pre-exercise values, these type of exercises (exercises consisting of maximal eccentric actions) can propagate up to 50-65% loss of force-generating capacity. These effects can typically last one to two weeks (Clarkson & Hubal, 2002).

### 2.2.4 Muscle stiffness

Mechanically, stiffness refers resistance of applied change in length. Increased risks of recurring soft-tissue injuries such as hamstring strains have been associated with relatively high stiffness in humans. It is also understood that stiffness is a causal factor in the efficiency of stretch-shortened cycle exercises. Since the primary priority of athletes is to stay free of accidents and to be at an ideal fitness rate, stiffness is an significant screening measure for physiotherapists, coaches, coaches and other sports professionals.

Myometer, an electronic device capable of recording various muscle tone features, is used to evaluate stiffness. The measurement and calculation of muscle stiffness by myometry is done by applying a small distress to the skin which is covering the muscles. Then an accelerometer is used to evaluate the muscle's discomfiture properties and calculates the muscle's stiffness using the damped natural oscillations shown by the muscle's recoil properties (Pruyn, Watsford, & Murphy, 2016).

## 2.3 Protocols Employed in Establishing DOMS

There are few modalities that can be used to perform eccentric exercises; isotonic, isokinetic and also eccentric-based exercise modalities. Isotonic exercise is executed by using body weight or accompanying external load against gravity (Isner-Horobeti *et al*., 2013). Generally the extent of muscle damage depends on gender, age, muscle type and also intensity of the exercise.

Among the exercise modalities used on triceps surae were in a study byGibson, Arendt-Nielsen, and Graven-Nielsen (2006), where participants are made to stand on a platform that is 13cm high, which is placed 45cm from the wall. Participants were advised not to support their trunk with their upper limbs while facing the wall, but to use their extended hands for stabilization. There was a foot bracket attached to the platform where they stood, which allowed the subjects to plantar-flex at the ankle in such a way that the middle and forefoot descended to the floor while the rear foot remained on the platform where the ankle joint was the rotation axis. The exercise leg was positioned with the foot on the bracket, the heel on the top of the platform and the middle and forefoot on the top. Once their positions are locked, the participants then lifted their contralateral limb off the platform by flexing the hip and knee, followed by a slow and regulated plantar-flexion movement of the ankle with its weight-bearing limb. Once in place, they lifted their contralateral limb off the platform by flexing the hip and knee and then conducted a slow-controlled plantar-flexion action of the ankle with their weight-bearing exercised limb, catalyzing the eccentric contraction of their anterior tibial muscle. After each repetition, the subjects are then required to re-establish the start position, this time with the other leg. Ten repetitions per set with 20 seconds rest between sets were performed. The participants continued the exercise for as long as it took them to not be able to walk on their heel while adequate ankle dorsiflexion is maintained. In general, 3 sets of 10 repetitions each with the fourth set consisting of only 5 to 10 repetitions each were required. Substantially

higher soreness ratings were recorded in Day 1 and Day 2 compared to Days 3 to 5 (Gibson *et al*., 2006). In another study by Ayles *et al*. (2011), using the same method found soreness ratings were higher 24 to 48 hours post exercise ($P < 0.05$), and baseline pressure pain threshold (PPTs) decreased post exercise ($P < 0.001$) at the muscle sites of the exercised legs. Both studies found significant soreness on tibialis anterior.

In this study muscle damage was induced by electrical stimulation whereby 40 tetanic contractions, evoked by electrical stimulation administered through two self-adhesive electrodes were performed by the subjects. This results in an immediate decline in MVC and a delayed decline in soleus muscle by 2 days (-29.8 ± 4.6%, $P < 0.001$; -13.0 ± 3.4%, $P < 0.05$ respectively). Similarly, V/Msup reduced immediately and 2 days after the session of neuromuscular electrical stimulation (NMES) (-43.3 ± 11.6%, $P < 0.05$; 35.3 ± 6.6%, $P < 0.05$). The delayed MVC and V-wave decreases happened at the same time as the muscle soreness peak ($P < 0.001$) (Laurin *et al*., 2012). This study found soreness and drop in force post exercise in soleus muscle.

In an isokinetic eccentric exercise study, participants engaged in 5 sets of 30 eccentric dorsiflexion contractions with each set separated by a 30-second interval and performed with a load of 80% MVC. Participants received visual velocity feedback and were told to resist while lowering the footplate over a one-second period through the 30 ° range of movement. The investigator then places the participant's back to the neutral ankle position over a period of 2 seconds. The dorsiflexes' measurements, both the voluntary and electrically-evoked were registered at baseline, during the fatigue protocol, immediately after each of the five sets and at 0.5 minute, 2 minute, 5 minute, 10 minute, 15-minute, 20-minute and 30-minute mark throughout the recovery period. It was noted that MVC torque decreased by 28% ($P < 0.05$) after the fatigue task and the muscles did not recover completely. Dorsiflexors voluntary activation was close (> 99%) during and after the fatigue task ($P > 0.05$) (Power, Dalton, Rice, & Vandervoort, 2010).

Many studies have used dorsiflexors as a model. However, the findings based on these models cannot be applied for other muscles. Thus in order to discern the features of muscle damage, it is optimal to use a distinct exercise model of a specific group of muscle and investigate the effect of eccentric exercise on that particular muscle. The susceptibility to exercise-induced muscle damage is affected by the difference in fiber type composition in the muscles since Type II is more susceptible than Type I fibers. (Friden *et al*., 1983).

Ideally using isokinetic machine testing would be the best in having a control muscle eccentric exercise and to quantify the drop in force right after. The ideal muscle group would be gastrocnemius due to its proportion of 50% fast twitch and 50 % slow twitch fiber (Edgerton, Smith, & Simpson, 1975).

## 2.4 Peripheral Factors Affecting DOMS

The study by Friden *et al*. (1983) was designed to obtain muscle biopsies from 12 males (25 ± 7 years old), all of whom suffered severe soreness in the muscles of the thighs between 18-72 hours after eccentric cycling. It was also shown that the knee extensor strength decreased at all angular velocities after exercise. However, a gradual increase, albeit at a slower rate at fastest contractions could be seen. The disturbances of the cross-striated band pattern originating from the myofibrillary z-band were also noted, showing both marked streaming, expansion and even complete disturbance in places. Type II fibers were found to be predominantly impaired, with disturbances occurring in each second to each third fiber for up to three days after exercise and six days after workout in one fifth of the fibers. The eccentric exercises are therefore attributed to muscle soreness and impacts on a mechanical and selective basis with regard to the fiber type that is the fine structure of the contractile apparatus (Friden *et al*., 1983).

Another study showed contradicting results. It was observed that DOMS caused by downstairs running did not lead to substantial sarcolemma injuries or crucial incendiary reactions in the soleus muscles. Consequently, the hypothesis of eccentric exercises that induce initial sarcolemma injuries that then trigger muscle fiber inflammation and necrosis does not appear to apply to the human soleus muscle. At 7-8 days post-exercise, the enlarged fiber size was interpreted as representing fiber swelling due to edema. It does not seem to be directly related to the etiology of DOMS as the swelling was not present at the time of maximal DOMS which was between 1.5 to 2.5 days after exercise (Yu *et al*., 2013). The results of this research seem to demonstrate that the sarcolemma of the human soleus muscle was not as susceptible to running downstairs as the exercise of the animal muscle (Komulainen, Takala, Kuipers, & Hesselink, 1998; Lehti, Kalliokoski, & Komulainen, 2007; Lieber, Thornell, & Friden, 1996; Lovering & De Deyne, 2004; McNeil & Khakee, 1992). More importantly, this study is able to disprove the previous notion that early sarcolemma injuries in human soleus muscles trigger further damaging responses in muscles after eccentric exercises as it did not show sarcolemma damage at one hour after downstairs running. The outcomes of all these studies seems to conclusively show that sarcolemma disruptions occur in a small number of exercised subjects regardless of how the voluntary eccentric exercise is performed (Yu *et al.*, 2013).

The mapping of the muscle with a calibrated probe after 48 hours could be seen in participants who had their triceps surae of one leg exercised eccentrically by walking backwards on a moving treadmill that is set at an incline. 5% Injection of sodium chloride into the sensitive leg site caused no more pain than injections into the untrained leg. This indicates that sensitization of nociceptors was not accountable. By applying controlled indentations to a sensitive region, pain could be exacerbated by 20-Hz to 80-Hz vibrations. Pain reduction was noted in unexercised muscles, indicating that the vibrations had the opposite effect. Pain thresholds were assessed before, during and after applying

a sciatic nerve stress block. The H reflex's disappearance and a weakened voluntary contraction, leaving unchanged painful heat and cold sensations, showed that the block only impacted large diameter nerve fibers. The pain threshold increased during the block. This conclusively proves that muscle mechanoreceptors, including muscle spindle which are considered to be the peripheral component of the muscle fiber, contribute to the soreness after eccentric exercises (Weerakkody, Whitehead, Canny, Gregory, & Proske, 2001).

A review by Proske and Morgan (2001) indicated that contracting muscles are forcibly extended and shortened in concentric exercises. Eccentric contractions slow or stop movements whereas concentric contractions initiate them. Untrained subjects who undergo eccentric exercises became stiff and sore the next day due to damage to the muscle fiber. Two possible initials are deemed to be liable for the subsequent damage; damage to the excitation-contraction coupling system and sarcomere level disruption. Other modifications can be seen after exercise; a decrease in active tension, a change in optimum duration for active tension and an increase in passive tension. These seem to favor sarcomere disruption as the starting point for the damage. In addition, there is proof of muscle sensory organs disruption and proprioception. Less damage is produced during a second period of exercise, conducted a week after the first bout. It is evident that an adaptation process has occurred. An increase in the sarcomere number in muscle fibers is one of the proposed mechanism for the adaptation process. He muscle's optimal length for active tension is a result of that. The possibility of clinical applications, such as protecting a muscle from major injuries caused by mild eccentric exercises, is increased by the ability of the muscle to adapt after the damage caused by eccentric exercises (Proske & Morgan, 2001).

Muscle damage associated with reduced ability to produce voluntary force and enhanced fiber permeability is caused by eccentric contractions. Cell depolarization that is supposed to affect the potential action of muscle cells propagation velocity is caused by modifications in the permeability of the fiber membrane. Hedayatpour et al. (2009) performed a research of muscle damage caused by eccentric contractions using multichannel surfaces and intramuscular fine wire on ten healthy males at 10% and 30 % of the maximum force after 60-second isometric contractions. In the study, signals from two locations of the right vastus medialis muscle were concurrently recorded. The maximal force showed a decrease of 26.1 ± 16.1% ($P < 0.0001$) at the 24-hour mark and remained at a reduced level of 23 ± 14.5% ($P < 0.0001$) 48 hours after exercise. The velocity of the motor unit also decreased ($P < 0.05$) by 7.7 ± 2.7 % (10 % MVC, proximal), 7.2 ± 2.8 % (10 % MVC, distal), 8.6 ± 3.8 percent (30% MVC, proximal), and 6.2 ± 1.5 % (30 % MVC, distal), respectively. Additionally, the velocity of motor unit conduction during the sustained contractions also showed a decrease over time, but at a faster rate when assessed 24 hours and 48 hours after exercise. These findings show that the electrophysiological membrane characteristics of the muscles are changed by muscle fiber damage caused by exercise (Hedayatpour *et al.*, 2009).

Another research investigated some of the physiological reactions such as biochemical immunological, functional and neuromuscular reactions associated with exercise-induced muscle damage in the untrained men's quadriceps muscle group. Maximal concentric and eccentric muscle actions at 0.53 rads $s^{-1}$ elicited muscle damage and soreness. Significant soreness ($P < 0.05$) appeared at 1, 2 and 3 days after muscle damage, while plasma creatine kinase, a muscle damage marker, was observed 3 and 5 days after muscle damage. Interleukin-Ib plasma concentrations improved dramatically within five minutes and remained high at 1, 2, 5 and 7 days after muscle damage. Maximum quadriceps isometric functions ($P < 0.05$) were impaired five days after muscle damage. Maximum

isokinetic performance was decreased at 1.09 rads $s^{-1}$ ($P < 0.05$) for 2 days after damage, with no substantial decreases at 3.14 rads $s^{-1}$. The quadriceps' average electrical activation (iEMG) was unchanged, but the rectus femoris' iEMG activity where soreness was targeted was significantly enhanced. During the 10-day post-insult inquiry period, neuromuscular effectiveness (torque / iEMG) was compromised. The neuromuscular perturbation persisted for at least ten days while other symptoms of exercise-induced muscle damage dissipated within seven days (Deschenes *et al*., 2000).

## 2.5 Neural/Central Factors Affecting DOMS

Voluntary force after eccentric exercise may be reduced and neural drive impaired by muscle damage. Motor cortex and motor nerve stimulation is used to examine the voluntary activation of elbow flexors to determine whether DOMS, which usually develops one day after exercise, reduces voluntary activation. Maximal voluntary isometric torque (MVC), twitch torque, muscle soreness and voluntary activation in eight subjects were measured at the following intervals: before, immediately after, 1, 2, 4 and 8 days after eccentric exercise. Twitch torques and measures of voluntary activation were derived using motor nerve stimulation and motor cortex stimulation. MVC was decreased by 38 ± 3% (mean ± SD, n = 8) by eccentric exercise. A reduction of 82 ± 6% was noted for the resting twitch when produced by motor nerve stimulation and a reduction of 47 ± 15% was noted for the estimated resting twitch produced by cortical stimulation. Both measures of resting twitch remain low while voluntary torque recovered after eight days. One to two days after exercise, muscle tenderness occurred and pain during contractions were felt on days 1-4. However, changes in voluntary activation did not follow this time course. A reduction of 19 ± 6% was noted for voluntary activation by nerve stimulation after exercise by the values were no different from the control values after two days.

Stimulation by the motor cortex, of the voluntary activation yielded no change by eccentric exercise. Increments in torque brought about by nerve and cortical stimulation during MVCs, behaved differently. The values produced by cortical stimulation decreased whereas the values produced by nerve stimulation tended to increase. These results demonstrate that the reduction of voluntary activation, not muscle soreness, leads to the early loss of eccentric force after exercise. The activation deficit resides in the motor cortex or at a spinal stage, which can be seen by the impairment of voluntary activation to nerve stimulation (Prasartwuth *et al*., 2005).

Racinais, Bringard, Puchaux, Noakes, and Perrey (2008) did a study to explore whether a non-exhausting workout of the plantar flexor muscles that generated muscle soreness would alter the modulation of the spinal cord and whether the development of muscle soreness would be associated with central motor control modulation. Ten healthy subjects undertaken a single round of backward downhill walking workout (duration 30 min, velocity 1 $ms^{-1}$, negative grade -25%, load 12% of body weight). After the exercise session, neuromuscular tests sessions [H-reflex, M-wave, maximal voluntary torque (MVT)] were performed. It was noted that there was a 15% reduction in MVT of the plantar flexors immediately after exercise. This could be ascribed in part to an adjustment in contractile features (-23% in electrically evoked mechanical twitch). However, even though contractile properties have significantly recovered within the first day, MVT failed to recover, even after three days. A reduction in voluntary muscle drive could be the cause of this delay. When there are no changes in the spinal modulation estimates from the H-reflex, the decrease in voluntary activation could be observed. These findings hint at the presence of muscle soreness being linked to the development of supraspinal modulation (Racinais *et al*., 2008).

The investigation of whether after a single bout of maximal eccentric muscle actions, a repeated bout effect is experienced and also to correlate the effect of such a protection to an ipsilateral control. 45 repetitions of maximal eccentric contraction of elbow flexors were performed by sixteen male subjects. The exercise using the same arm was repeated by the ipsilateral group (IL, n = 8) and the exercise using the contralateral arm (CL, n = 8) was repeated fourteen days later. The ipsilateral group found significant attenuation serum creatine kinase (CK), muscle soreness, maximal voluntary contraction (MVC) and range of motion (ROM) while a significant reduction in the repeated bout for CK, muscle soreness and MVC were observed in the CL group. Although further research is required, the findings of this study showed that neural mechanism plays a major role in the contralateral repeated bout effect (Howatson & van Someren, 2007).

The effects of quadriceps eccentric exercise and DOMS on both agonist / antagonist activity during a range of motor tasks have been investigated. Maximum voluntary contractions (MVC) and explosive knee extensor isometric contractions, to be followed by isometric contractions but at levels of 2.5, 5, 10, 15, 20 and 30% of MVC values from baseline measurements were performed by ten healthy male subjects, immediately after and in the 24hours following eccentric exercise of the quadriceps muscle group. The force of the knee extensors and the EMG surface of the vasti hamstring muscles were reported at the same time. Explosive isometric contractions resulting in the development of force frequency (RFD) were observed. The coefficient of variation of the force (CoV) was also estimated from contractions. The perceived pain intensity was evaluated by subjects 24 hours after exercise sessions found 4.1 ± 1.2 (score out of 10). It was observed that a reduction of the values of maximum RFD and MVC of the knee extensors (average across both time points: 19.1 ± 17.1% and 11.9 ± 9.8% respectively, $P < 0.05$), immediately post- and 24 hours after eccentric exercise, compared to the baseline values. After

eccentric exercise, it was noted that the CoV for force during the submaximal contractions were greater (up to 66% higher than baseline, $P < 0.001$) and remained high 24 hours after exercise during the presence of DOMS ($P < 0.01$). The EMG amplitude of the vasti muscles decreased immediately after exercise and was followed by an increase in antagonist muscles EMG for the explosive contractions only for the explosive and MVC tasks. However, force steadiness was reduced, followed by a general increase in EMG amplitude of the vasti muscles and further followed by an increase in antagonist muscle activity, but only at a higher force level (15% MVC). Maximal force, rate of force development and force steadiness of the knee extensors were reduced following eccentric exercise and subsequent DOMS of the quadriceps muscles. It is then followed by some adjustments of agonist and antagonist muscle activities (Vila-Chã, Hassanlouei, Farina, & Falla, 2011).

The impacts of eccentric muscle damage on the threshold force of recruitment and repetitive discharge traits of low-threshold motor units were explored. While electromyography (EMG) data were recorded from human biceps brachia and brachialis muscles, four tasks involving isometric contractions of elbow flexors were performed by ten subjects. Following were the tasks undertaken by the subjects: 1) maximal voluntary contraction (MVC); 2) constant force contractions at submaximal targets; 3) motor recruitment unit threshold; and 4) minimum motor unit discharge rate. On three separate days, before, during and after eccentric exercise of elbow flexor muscles, subjects undertook these tasks. There was a decline (42%) of MVC force immediately after exercise and it remained at a low value of 29% 24 hours later. This indicates muscle damage. Before eccentric exercise, the mean motor unit recruitment threshold for biceps brachia was 8.4 ± 4.2% MVC, (n = 34 and there was a reduction of 41% (5.0 ± 3.0% MVC, n = 34) immediately after exercise and a further reduction of 39% (5.2 ± 2.5% MVC, n = 34) 24 hours after exercise. However, in the brachialis muscle notable changes

were observed. With respect to the minimum tonic discharge rate, motor units in both muscles discharged 11 % faster (10.8 ± 2.0 vs. 9.7 ± 1.7 Hz) immediately after practice (n = 29) compared to before training (n = 32). Similarly, the minimum discharge rate in brachialis muscle immediately after exercise was greater (13.8 ± 3.1%) as compared to that before exercise (11.9 ± 3.1%) and 24 hours post-exercise (11.7 ± 2.4%). However, after exercise, there was no notable changes observed in the discharge rate variability of the biceps brachia motor units. These are clear indications that motor unit recruitment thresholds are altered by eccentric exercise for 24 hours, but the similar effects are not present in the different elbow flexor muscles (Dartnall, Rogasch, Nordstrom, & Semmler, 2009).

An investigation on the effects of repeated bouts of eccentric exercise on the modulation of neuromuscular disturbances was conducted. By using elbow flexors as preferred choice of eccentric exercise, the measurement of mavimal voluntary force, resting twitch force, muscle soreness, creatine kinase (CK) and voluntary activation (VA) using motor point and motor cortex stimulation at baseline, immediately after exercise and at 1, 2, 3, 4 and 7 days after exercise on two separate occasions, with a 3-week gap were taken. It was observed that after the first bout of exercise, significant muscle damage and fatigue were present. Besides that, there was a 35% reduction of MVC and that value remained low until 7 days after exercise. At 3 days and 4 days post-exercise, there was a peak in soreness and CL release respectively. At 7 days, resting twitch force remained at a drastically low reduction of 49%. Using the measurement with motor point and motor cortex stimulation, VA was at a reduced rate at 2 days and 3 days post-exercise. There was an attenuated soreness and CK release with a quick recovery of MVC and resting twitch force observed with a repeated bout effect (RBE). Following both bouts of exercise, there was a similar reduction of VA observed. However, there was a comparatively smaller reduction in, and a faster recovery of VA, measured using motor

cortical stimulation. It is suggested that the RBE may be due to the modification in motor corticospinal drive (Goodall *et al*., 2017).

## 2.6 Central Criterion Measures during DOMS

The neural drive from the brain to the muscle and the peripheral contractile function are the main factors that allows the generation of force in skeletal muscle. Any changes in either the neural drive or peripheral systems could bring about a variety of strength losses. By reducing the number of activated motor units or by decreasing the motor neuron firing rate, will lead to a decreased neural drive to the muscle (Gandevia, 2001). Comparison of neuromuscular functions in two groups of participants separated by greater to lower loss of strength after maximum elbow flexor lengthening actions were performed. This study's primary result shows that despite a large difference in voluntary function, central function (i.e., neural drive to muscle) was comparable among groups. Conversely, it was observed that there was a greater impairment of all measures of peripheral functions with greater voluntary strength loss, which is a clear indication that the mechanism for early loss of strength after lengthening actions is within the muscles and not within the muscle-activating central pathways (Hubal, Rubinstein, & Clarkson, 2007).

A rise in the coding speed of active motor units is the way in which the central nervous system compensates for the loss of muscle force output after maximum eccentric exercise. Additionally, the failure of the E-C coupling process at the sarcolemma level could partially explain the acute loss of force production in damaged muscles. The prolonged loss of force production, however, results from the impairment of the E C coupling method beyond the sarcolemma. This study found that there was a reduction in maximal voluntary force 21.3 ± 5.6% 2 hours and by 12.6 ± 11.1% 2 days post-exercise. It was

also found that the motor unit discharge rate was increased and mean muscle fibber conduction velocity was decreased, at the highest isometric contraction levels only (50 and 75% of MVC) at 2 hours post-exercise during DOMS (Piitulainen, Holobar, & Avela, 2012).

A significant drop in maximal voluntary isometric torque (MVC) immediately after eccentric exercise to the human elbow flexor muscles while motor stimulation and estimated resting twitch by cortical stimulation remained depressed for eight days. Evaluation of voluntary behavior by nerve stimulation dropped immediately following exercise but after two days showed no difference from the control values. Evaluation of voluntary behavior by stimulation of motor cortex was unchanged by exercise. Absolute torque gains brought about by nerve and cortical stimulation exhibited different behavior during MVCs. The gains brought about by nerve stimulation showed a loss whereas the gains brought about by cortical stimulation showed a raise. Early force loss after eccentric exercise is caused by voluntary activation after eccentric exercise and not due to muscle soreness. The deficiency in activation of the motor cortex at the spinal stage is suggested by the voluntary activation impairment to nerve stimulation and not by motor cortical stimulation (Prasartwuth *et al*., 2005).

Voluntary activation was considerably affected post exercise predominantly at 2 hours and up to 24 hours, especially at the shorter muscle lengths. The measured angle return to pre-recorded value while MVC, twitch torque and voluntary activation had not fully restored up until day 8. Thus it suggests that eccentric exercise causes a temporary changes in the optimal angle for MVCs and affects voluntary activation and it is dependent on length. Consequently, both central and peripheral variables seem to restrict muscle performance following eccentric injuries, with restrictions being particularly crucial at short lengths (Prasartwuth *et al*., 2006).

It is suggested that delayed-onset muscle soreness (DOMS) from eccentric exercise does not affect Short-Interval Intracortical Inhibition (SICI) due to the fact that SICI recovered two days after exercise in the presence of muscle pain and soreness. Eccentric muscle damage has extensive motor system-wide impacts that probably include modifications in the motor cortex due to these changes observed (Pitman & Semmler, 2012).

Changes in muscle activity during walking was induced by DOMS. Inter-limb communication during walking was affected by DOMS. This could be seen by the investigation of its effects on short-latency crossed responses (SLCRs). In two recording sessions, SLCRs were brought out by electrically stimulating the ipsilateral leg's tibial nerve and quantified in the contralateral gastrocnemius muscle. After the respondents (n 11) completed the eccentric exercises with the ipsilateral calf, the second recording session took place 24-36 hours later. A reduction in the magnitude of the spinally-mediated component of the SLCR in the contralateral gastrocnemius medialis was caused by DOMS. These results provide a great insight on the relationship between pain and motor control. The ability to maintain a dynamical stability during walking is greatly reduced due to the muscle pain affecting the spinal pathway, mediating inter-limb communication (Gervasio, Finocchietti, Stevenson, & Mrachacz-Kersting, 2018).

Central and peripheral neuromuscular fatigue-related parameters were studied by comparing concentric (CONC) and eccentric (ECC) exercises of the knee extensor muscles, and the first (ECC 1) and second (ECC 2) bouts of eccentric exercises. Twelve healthy male subjects performed three exercise bouts with a one-week separation between CONC and ECC 1 and a two-week separation between ECC 1 and ECC 2. Maximal voluntary isometric contractions (MVC) torque of at least 40% of the knee extensors were conducted until a reduction of 40% MVC was attained after exercise. MVC torque, central

(voluntary activation and normalised electromyographic activity), and peripheral neuromuscular indices (evoked torque and M-wave amplitude), and muscle soreness were assessed before (pre), immediately after (post), 1 hour, and 1– 4 days after exercise (D1, D2, D3, and D4). Voluntary activation showed a decrease immediately after ECC1 (-21.6%) and ECC2 (-21.1%), but not after CONC. Similar decrease was seen in electrically-evoked torques for the three conditions, but remained below the baseline at D1 only post-ECC1. These results corroborate that both the central and peripheral factors do contribute to the decrease of MVC after ECC 1 and ECC 2 but it was mostly because of the peripheral variables after concentric exercise (Souron, Nosaka, & Jubeau, 2018).

# CHAPTER 3: RESEARCH METHODOLOGY

## 3.1 Participants

Sample size (n = 10) participants were selected based on previous publications (Endoh *et al.,* 2005; Vila-Cha *et al.,* 2012; Goodall *et al*., 2017; Gervasio *et al*., 2018). They were healthy and moderately active male with not more than 150 minutes (5 days of 30 minutes) of physical activity in a week (age 28.70 ± 4.24 years old) determined using PAR-Q (refer appendix A) and GPAQ respectively, as well as no history of neuromuscular injuries were recruited in this study. All participants were right limb dominant determined using the lateral preferred inventory (Coren, 1993). The exercise protocol to induce DOMS were explained to all participants. The subjects then read and signed informed consent forms. The participants were asked to avoid using any medications for the duration of the study. This study was approved by the university's ethics committee (UM.TNC2/RC/H&E/UMREC-109).

## 3.2 Preliminary Measurements and Familiarisation

A stadiometer (Seca, UK) was used to measure participants' height and weight. A familiarisation session was carried out on using the isokinetic device (CSMI, Humac Norm, USA), performing a plantar flexion (eccentric exercise) and maximal voluntary isometric contraction (MVIC). Procedures to measure voluntary activation (VA) in both limb (dominant and non-dominant) were also demonstrated.

## 3.3 Study Design

This study employed a counter-balanced crossover experimental design where participants were randomly categorized to either the experimental (DOM) group or the control (CON) group. In the first leg, the DOM group were treated with a damaging eccentric exercise protocol on the plantar flexors using an isokinetic device, while the CON group rested. All participants completed a battery of tests comprising of

physiological (creatine kinase, VAS, muscle stiffness, and MVC) and neural (VA) on both treated and contralateral limb. After 4 weeks of wash out period, participants repeated an identical protocol to the first leg whereby participants who first treated in the DOM were now in CON and vice versa. All measures were taken at pre, post-10 minutes, 24, 48, 72 hours of DOM's induction.

### 3.4 Measures of Maximum Voluntary Contraction (MVC)

Participants were positioned on the isokinetic device in a prone position according to individual's comfort to maximize force production in a neutral position ($0^o$). Participants then performed a MVC lasting for 3-5 seconds and force produced was recorded. This was repeated 3 times with 3 minutes' rest in between contractions. Visual feedback of the torque and verbal encouragement were given by the same researcher to ensure consistency in the drive (Power *et al*., 2010).

### 3.5 Eccentric Exercise Protocol to Induce DOMS

Participants laid in prone position on a declined chair of an isokinetic device (Humac Norm, CSMI, USA) of which the calibration was adhered to the manufacturer's guidelines. A footplate was attached to the dynamometer to execute plantar flexion. The right foot was strapped tightly to the footplate with the lateral malleolus in line with the rotational axis of the dynamometer. Additional straps and tape were added to secure the foot, waist and thigh to minimize movements. The eccentric contractions started at 30° plantar flexion and ended at $0^o$ which is the neutral ankle angle, subsequently progressing through the range of motion of the angle. To reach the 30° angle of plantar flexion, an assisted concentric contraction was initially performed. Participants performed 5 sets of 30 eccentric plantar flexion contractions separated by 30 s at 80% MVC in isotonic mode adapted from (Power et al., 2010). Participants were instructed to counteract while the

footplate is being lowered through the 30° range of motion with visual feedback of their torque, time and repetition provided. (refer to appendix B)

### 3.6 Measures of Creatine Kinase

A finger-prick blood sample was obtained from the fourth finger and transferred on a creatine kinase (CK) test strip then immediately analyzed for CK concentration using a Reflotron blood-gas analyser (Reflotron, UK).

### 3.7 Measures of Visual Analogue Scale (VAS)

Visual Analog Scale (VAS) is a subjective evaluation of pain using a visual scale of 0 to 10 (horizontal line ranging from no pain on the left to extreme pain on the right). This was recorded while performing a 20% MVC of plantar flexion at pre, post-10 minutes, 24, 48 and 72 hours of DOM initiation (Racinais *et al.,* 2008).

### 3.8 Measures of Muscle Stiffness

Muscle stiffness measures; a Myoton-Pro (Myoton AS Tallinn, Estonia) were placed on the involved muscles (gastrocnemius and soleus) to measure stiffness. Reading from the myometry were noted for later analysis. To maintain consistency, assessment points were drawn using a water-proof ink, and identical points will be identified and measured on the second testing occasion. Myometry measurements were collected by holding the device right above the skin overlaying the assessment site. Once the desired position were identified, a mechanical impact (duration: 15 ms; force: 0.3 – 0.4 N) were delivered to the muscle by a mechanical probe, which caused the tissue to deform briefly. Subsequently, the resultant damped natural oscillations were recorded via an in-built accelerometer, sampled at 3200 Hz. Stiffness was calculated as the ratio between the force applied and the muscle deformation. Three consecutive measurements were taken at each site, with its mean value being used for analysis (Pruyn *et al*., 2016) (refer appendix E).

### 3.9 Measures of M-max

The surface of the sensor and the silver detection bars were wiped with isopropyl alcohol pad to remove residues. Then excessive hair from skin at the detection site were shaved followed by cleaning of the skin with isopropyl alcohol. Once the skin is dried a sensor was applied to the skin using a Delsys Adhesive Sensor Interface. To obtain an M-wave record, a wireless EMG self-adhesive electrodes (Ag-AgCl, 10-mm diameter; Delsys Trigno, Boston, MA, USA) were positioned on the medial gastrocnemius muscles (SENIAM) guidelines. The EMG signals were band-pass filtered at 20–450 Hz and the sampling rate was 2000 Hz. For EMG, the electrode placements for gastrocnemius was based the SENIAM guidelines (Stegeman & Hermens, 2007) using a standard EMG preparations (refer to appendix C).

### 3.10 Measures of Electrical Stimulation

The stimulation site for the tibial nerve at the popliteal fossa was located using a handheld stimulation probe, where the location with the highest M-wave response for a given current was the position selected for the placement of the cathode (5-mm diameter, Ag-AgCl, Meditrace), while the anode (Pals Platinum Neurostimulation Electrodes, Axelgaard, USA) was placed just proximal to the patella (lower region of the anterior thigh). A 200-μs pulse was delivered three times (at a 5–7-second interstimulus) by a constant-current stimulator (Digitimer Constant Current Stimulator, Model DS7AH, UK) beginning at 30 mA, followed by 5 mA increments until there was no further increase in EMG response in two consecutive sets, and the average value that first produced the plateau was established as Mmax. The currents used to obtain Mmax (refer to appendix D) ranged from 45 – 120 mA (Khong, Selvanayagam, Hamzah, & Yusof, 2018).

### 3.11 Torque Recordings

Voluntary activation (VA) is a measure of the central neural drive during a maximum contraction using the twitch interpolation technique via peripheral nerve stimulation. This measurement is compared to the resting twitch using the following equation [1 - (interpolated twitch/resting twitch)] x 100 (Merton, 1954). Here an electromyography (Delsys USA) recording was used to identify the maximum stimulation intensity required for the twitch interpolation at 120% of M-max stimulation intensity which was initially determined by a plateau in M-wave amplitude (45 – 120 mA). The same intensity was applied to identify the resting twitch. The participants were laid in the prone position on a dynamometer (HUMAC NORM, MA, USA) with their ankles at an anatomically zero position ($90^{o}$) and secured with straps. Then current ranging from 45 to 120 mA was used to stimulate the tibial nerve at MVC and 4 second post MVC (resting twitch).

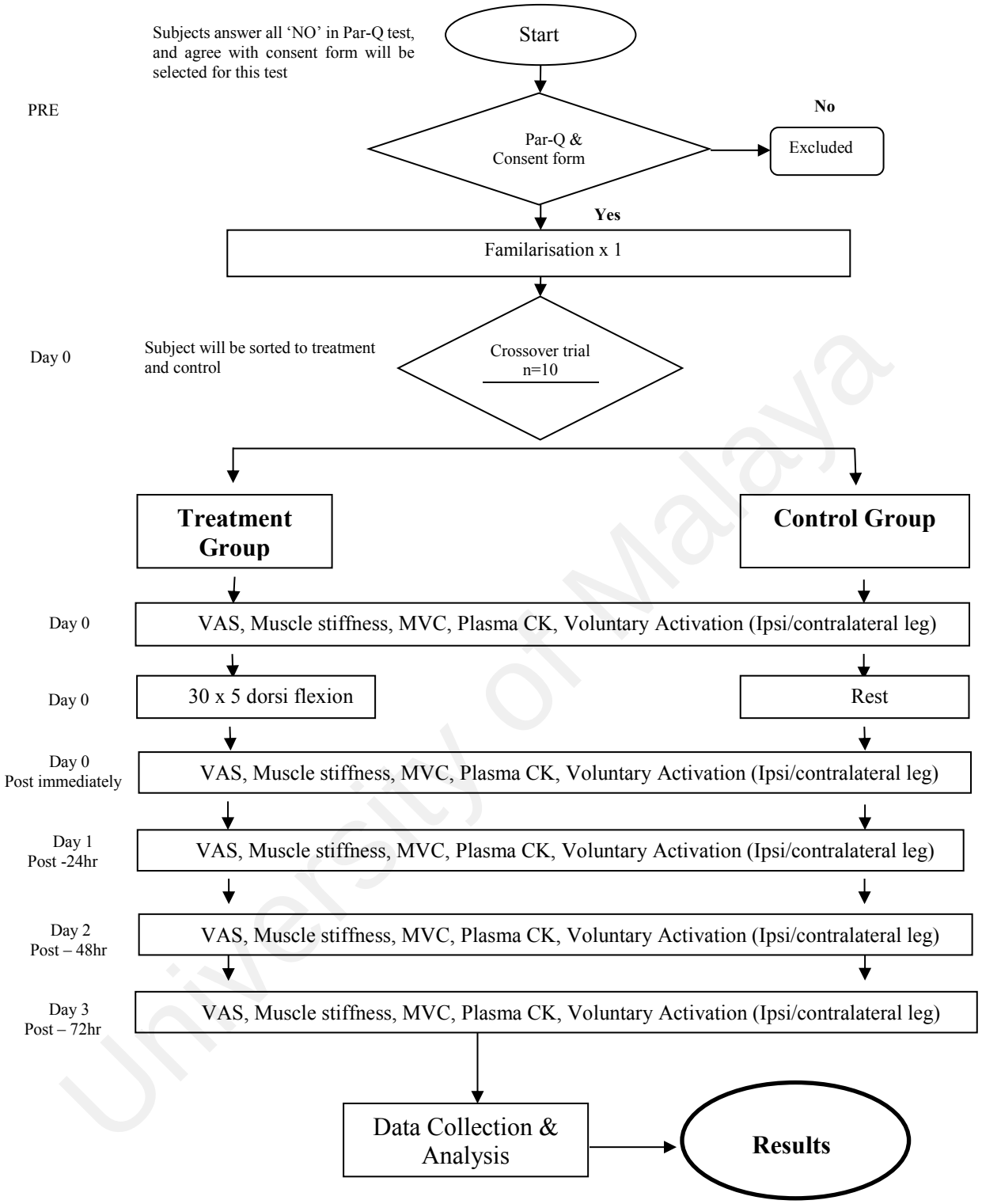
The degree of central activation, expressed as central activation ratio (CAR), was measured using the ratio of the voluntary force to the total force (including any force increment from the superimposition) as shown in Equation 3.1. A CAR of 1.0 indicates complete activation, whereas a CAR of less than 1.0 failure or inhibition (Khong *et al*., 2018).

$$CAR = MVC/ (MVC + Superimposed\ force) \qquad \textit{Equation 3.1}$$

### 3.12 Statistical Analysis

Force, CK, and neuromuscular/physiology data were analyzed using a three-way mixed model analysis as follows: treatment x time x site (2 x 5 x 2). Criterion measures observed to have a significant interaction were run with two-factor repeated measures analysis of variance (ANOVA) between treatment and time and side and time. All data were checked for assumptions of normality and were found to be normally distributed ($P > 0.05$). Statistical significance for all analyses was accepted as $P \leq 0.05$. Significant

effects identified by ANOVA were further analyzed using a Bonferroni post-hoc test between pairs. Data analysis was performed using Statistical Package for the Social Sciences (SPSS Inc.) version 22 for Windows.




VAS : Visual Analogue Scale
MVC : Maximal Voluntary Contraction
CK : Creatine Kinase

Figure 3.1 'flow chart' of subject's route throughout this experiment.

# CHAPTER 4: RESULTS

## 4.1 Anthropometric Measurements

Table 1 displays the body mass (kg), height (m) and body mass index (BMI: kg/m$^2$) of the participants. There was no significant difference between the experimental and control groups ($P > 0.05$).

Table 4.1 Anthropometric measures of the participants (mean ± SD; n = 10).

| Variable | Min - Max | Mean ± SD |
|---|---|---|
| Age (years) | 33 - 24 | 28.70 ± 4.24 |
| Body mass (kg) | 61 - 85 | 72.30 ± 6.53 |
| Height (m) | 1.63 – 1.75 | 1.70 ± 0.04 |
| Body mass index (kg/m$^2$) | 22.41 – 27.76 | 25.08 ± 1.69 |

## 4.2 Creatine Kinase

CK results are displayed in Figure 1. The analysis revealed a significant interaction F (4, 36) = 3.111, $P = 0.03$ (group x time). Between group differences were observed at post-10 minutes, 24 and 48 hours following initiation of DOMS ($P < 0.05$), however at 72 hour no significant difference was observed. Bonferroni post-hoc analyses demonstrated that the experimental group showed significant increase in CK level from pre to post-10 (~ 28%) minutes, 24 (~ 63%) and 48 (~ 40%) hours which indicates muscle damage. Meanwhile, no time effect was noted in the control group.

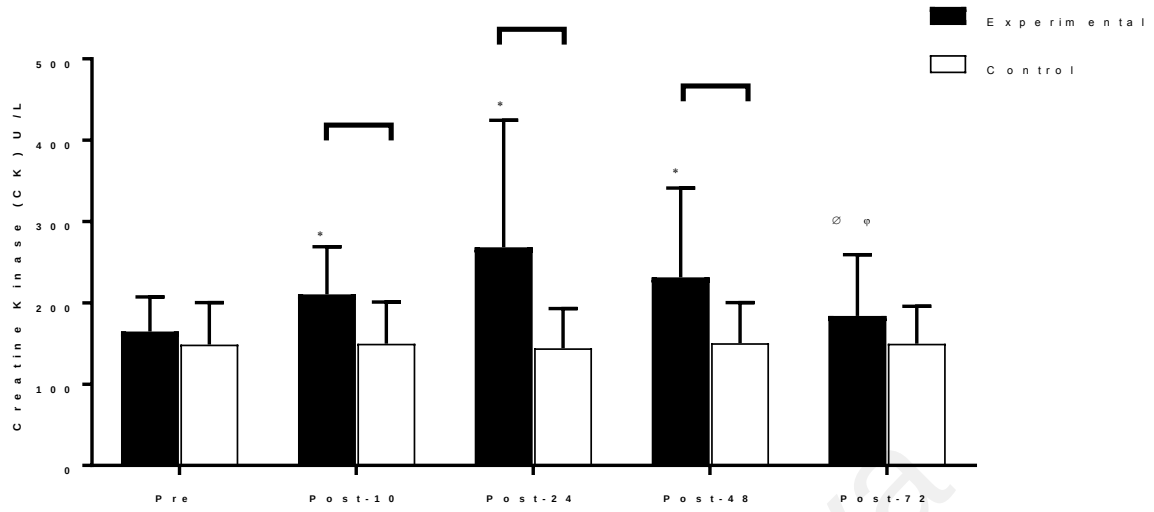



Figure 4.1 Time course change in creatine kinase (CK). * denotes significantly higher value compared to baseline (pre), ø denotes significant different from 24-h and ψ denotes significant different from 48-h ($P < 0.05$). Inverted bracket ( ⌐ ) shows the group difference.

## 4.3 Visual Analogue Scale

Muscle soreness (VAS) data are presented in Table 3. Data analysis revealed a group by time by side interaction effect F (4, 36) = 24.781, $P = 0.00$. Between group and site analysis showed significant interaction F (1, 9) = 63.39, $P = 0.00$ following initiation of DOMS in both trained and untrained limb compared to control. There were time effects in both trained and untrained limb of the experimental group at post-10 minutes, 24, 48 and 72 hours compared to pre ($P < 0.05$). In addition, there was also a significant site and time effect F (4, 90) = 3.93, $P = 0.006$, where the trained limb of experimental group showed higher VAS score compared to untrained limb.

## 4.4 Maximal Voluntary Contraction (MVC)

Analysis of MVC data showed significant interaction between group, time and side F (4, 36) = 4.942, $P = 0.003$. Between group and site analysis showed significant interaction F (1, 9) = 10.445, $P = 0.01$ following initiation of DOMS in both trained and untrained

limbs compared to control ($P < 0.05$). There were time effects in both trained and untrained limb of the experimental group at post-10 minutes, 24, 48 and 72 hours compared to pre ($P < 0.05$). However, no significant site and time effect, where both trained and untrained limb were equally affected.

### 4.5 Voluntary Activation (VA)

Analysis of VA data showed significant interactions between group, time and side $F(4, 36) = 6.734$, $P = 0.007$. Between group and site analysis showed significant interaction $F(1, 9) = 0.127$, $P = 0.014$ following initiation of DOMS in both trained and untrained limb compared to control ($P < 0.05$). There were time effects in both trained and untrained limb of the experimental group at post-10 minutes, 24 and 48 hours compared to pre ($P < 0.05$). However, no significant site and time effect, where both trained and untrained showed similar pattern of neural drive in treated limb.

### 4.6 Muscle Stiffness (Myometry)

No main interaction found, however, there was an increasing trend in muscle stiffness in experimental right limb following initiation of DOMS; 3% increase from pre to post and ~ 8% from pre to 24-h.

### 4.7 Resting Value, M-max and Central Activation Ratio (CAR)

There were no significant interactions between group, time and site for resting value, Mmax and central activation ratio.

Table 4.2 Criterion measures of the participants (mean ± SD; n = 10) in this cross-over study.

| **VAS** | | | | |
|---|---|---|---|---|
| Time | Experimental Right | Experimental Left | Control Right | Control left |
| Pre | 0.00 ± 0.00 | 0.00 ± 0.00 | 0.00 ± 0.00 | 0.00 ± 0.00 |
| Post 10 min | 4.00 ± 1.33* | 1.60 ± 0.84* | 0.10 ± 0.32 | 0.10 ± 0.32 |
| 24-h | 3.30 ± 1.06* | 1.60 ± 0.84* | 0.10 ± 0.32 | 0.10 ± 0.32 |
| 48-h | 2.60 ± 1.43* | 1.00 ± 1.05* | 0.00 ± 0.00 | 0.00 ± 0.00 |
| 72-h | 2.10 ± 1.37*, †, ‡, § | 0.60 ± 0.70*, †, ‡ | 0.00 ± 0.00 | 0.00 ± 0.00 |
| **MVC (Nm)** | | | | |
| Pre | 52.00 ± 25.97 | 46.90 ± 24.15 | 50.70 ± 24.82 | 45.50 ± 24.04 |
| Post 10 min | 43.50 ± 24.03* | 43.60 ± 23.00* | 51.70 ± 27.94 | 45.10 ± 24.10 |
| 24-h | 43.50 ± 24.01* | 40.60 ± 22.97* | 51.00 ± 29.61 | 45.70 ± 25.31 |
| 48-h | 44.70 ± 26.37* | 42.60 ± 23.57* | 50.00 ± 26.01 | 45.50 ± 23.95 |
| 72-h | 47.70 ± 28.27*, † | 41.60 ± 24.35* | 50.30 ± 28.56 | 45.30 ± 24.34 |
| **VA (%)** | | | | |
| Pre | 0.87 ± 0.01 | 0.86 ± 0.02 | 0.87 ± 0.01 | 0.85 ± 0.01 |
| Post 10 min | 0.81 ± 0.03* | 0.83 ± 0.02* | 0.88 ± 0.01 | 0.87 ± 0.01 |
| 24-h | 0.84 ± 0.02* | 0.84 ± 0.05* | 0.87 ± 0.01 | 0.86 ± 0.01 |
| 48-h | 0.85 ± 0.01*, †, ‡ | 0.84 ± 0.04* | 0.87 ± 0.01 | 0.85 ± 0.01 |
| 72-h | 0.86 ± 0.02 †, ‡ | 0.85 ± 0.04 ‡ | 0.87 ± 0.01 | 0.86 ± 0.01 |
| **Myoton (N/m)** | | | | |
| Pre | 426.43 ± 34.65 | 408.83 ± 47.14 | 422.50 ± 52.86 | 418.03 ± 83.15 |
| Post 10 min | 438.10 ± 36.62 | 411.63 ± 50.32 | 422.13 ± 54.12 | 424.23 ± 81.01 |
| 24-h | 462.66 ± 47.33 | 409.17 ± 54.26 | 428.63 ± 60.82 | 415.10 ± 76.42 |
| 48-h | 438.76 ± 49.36 | 406.43 ± 47.44 | 426.90 ± 61.21 | 417.90 ± 73.52 |
| 72-h | 409.30 ± 38.98 | 402.57 ± 41.97 | 429.55 ± 57.51 | 421.20 ± 70.20 |
| **Resting twitch** | | | | |
| Pre | 7.95 ± 2.96 | 9.22 ± 3.49 | 8.00 ± 1.86 | 7.55 ± 3.09 |
| Post 10 min | 8.92 ± 2.18 | 8.78 ± 2.90 | 8.03 ± 1.50 | 7.20 ± 2.75 |
| 24-h | 7.89 ± 2.90 | 8.07 ± 3.29 | 7.28 ± 2.79 | 8.46 ± 2.90 |
| 48-h | 7.29 ± 1.47 | 7.47 ± 2.01 | 7.56 ± 2.04 | 7.53 ± 2.73 |
| 72-h | 9.17 ± 3.82 | 7.34 ± 2.27 | 7.16 ± 2.13 | 6.92 ± 2.29 |
| **Mmax (mV)** | | | | |
| Pre | 4.49 ± 1.33 | 4.48 ± 1.56 | 5.06 ± 1.39 | 5.12 ± 1.89 |
| Post 10 min | 5.10 ± 2.09 | 4.32 ± 1.36 | 5.28 ± 2.00 | 4.94 ± 2.01 |
| 24-h | 4.70 ± 1.88 | 4.36 ± 1.05 | 4.85 ± 1.46 | 5.31 ± 2.12 |
| 48-h | 4.76 ± 2.12 | 4.43 ± 1.61 | 5.05 ± 1.37 | 5.11 ± 2.13 |
| 72-h | 4.72 ± 2.15 | 4.71 ± 1.81 | 5.29 ± 1.83 | 5.37 ± 2.04 |

Table 4.3 continued

| **CAR** | | | | |
|---|---|---|---|---|
| Time | Experimental Right | Experimental Left | Control Right | Control left |
| Pre | 0.97 ± 0.03 | 0.97 ± 0.03 | 0.98 ± 0.01 | 0.98 ± 0.01 |
| Post 10 min | 0.95 ± 0.06 | 0.96 ± 0.05 | 0.98 ± 0.01 | 0.98 ± 0.01 |
| 24-h | 0.96 ± 0.05 | 0.95 ± 0.06 | 0.98 ± 0.01 | 0.97 ± 0.01 |
| 48-h | 0.97 ± 0.03 | 0.97 ± 0.02 | 0.98 ± 0.01 | 0.97 ± 0.01 |
| 72-h | 0.97 ± 0.03 | 0.97 ± 0.02 | 0.98 ± 0.01 | 0.98 ± 0.01 |

Data were collected at baseline, post 10 minutes, 24, 48 and 72 hour post eccentric exercise of the gastrocnemius

* Significant difference from pre-value, † significant different from post-10 minutes, ‡ significant different from 24-h, § significant different from 4

# CHAPTER 5: DISCUSSION AND CONCLUSION

## 5.1 Overview

This study aimed at providing new insight on peripheral and central involvements following a damaging eccentric contraction of the plantar flexors in the treated dominant and contralateral non-dominant limb. This study made two major discoveries, first, DOMS adversely affects MVC of both limbs for up to 72 hours. Second, for up to 48 hours, the drop in MVC is accompanied by concomitant reductions in neural drive measured by motor nerve stimulation (VA). Interestingly, over the period of the experiment, similar pattern of changes in MVC and VA for both limbs was noted. These suggest that central adaptations which controls neural drive (following DOMS) affect both treated and contralateral limb similarly.

## 5.2 Peripheral Contribution to Eccentric Contraction and DOMS

Presently, there has no report of the effects of damaging eccentric exercise on plantar flexors of the dominant limb and its consequential effect on the contralateral homologous muscle group. In this study, in the treated dominant plantar flexors, a peak drop of 16.3% in MVC occurs after 24 hours following the initiation of DOMS. This is consistent with most studies where a peak drop in force production manifests 24 hours after initiation of DOMS (Cleak & Eston, 1992; Prasartwuth *et al*., 2005). The plausible causes for the drop in force are muscle structural damage and the sequelae of events that follow; stiffness (Avela & Komi, 1998), inflammation (Smith, 1991) and pain (Gervasio *et al*., 2018). Though not significant, an 8% increase in stiffness was observed during DOMS in the treated limb. Muscle damage changes stretch-reflex sensitivity through changes in the afferent inputs from the muscle spindle, Golgi tendon organ and group III and IV afferent nerve endings (Horita, Komi, Nicol, & Kyrolainen, 1999), which eventually disturbed (reduced) the muscle and joint stiffness and lead to the drop in performance (Avela & Komi, 1998). At cellular level, damaged myofibrils caused metabolic disturbances and

ion imbalances which increase activation of proteolytic enzymes leading to increased protein degradation and cell permeability (Baird *et al*., 2012). This allows extracellular $Ca^{2+}$ to enter triggering off a local injury contracture (Proske & Morgan, 2001) which cascade cell signaling events leading to inflammation (Smith *et al*., 1994; Tidball, 2005) and the consequent sensation of pain (Proske & Allen, 2005; Smith, 1991), which in turn affects force production (Sayers *et al*., 2003; Vila-Cha *et al*., 2012). These phenomena are supported by the increases in creatine kinase (CK) and visual analogue scale (VAS) post eccentric contraction in this study. CK were significantly high up to 48 hours and VAS were significantly high at all time points following the initiation of DOMS with averages of (CK) (268.22 ± 156.30) and VAS (3.30 ± 1.06) respectively at 24 hours (DOMS). Briefly, the protocol employed in this study is able to replicate the outcomes generally seen following a damaging eccentric contraction. It also appears that the outcomes could distinct acute fatiguing effect of the eccentric exercise and the effect of DOMS.

### 5.3 Central Contribution to Eccentric Contraction and DOMS

Besides the peripheral factors attributed to the drop in force following eccentric contraction and DOMS, central mechanisms are also involved. The neural drive to muscle i.e. voluntary activation (VA), estimated using nerve stimulation, provides evidence of central involvement (Merton, 1954; Prasartwuth *et al*., 2005). In this study, about 7% peak drop in VA was noted post-10 minutes after the eccentric exercise and remained low up to 48 hours in the treated limb. This indicates that there is a drop in 'central drive' towards the activated muscles. This phenomenon has also been observed in elbow flexors following an eccentric exercise, where VA remains low for 48 hours (Barss et al., 2014; Racinais *et al*., 2008). This observation is mainly due to the lack of change in the resting twitch in the treated limb, which insinuates larger difference in the interpolated twitch after the eccentric exercise. While using interpolated twitch alone with MVC (CAR) did

not reveal any changes. Hence, this reduction in VA implies failure to the drive the muscle at or above the point of stimulation. In a related study, supraspinal level has been suggested since the drop in VA is not accompanied by electrically evoked reflex (H-reflex) (Racinais *et al*., 2008). While, another study suggested, the sites involve were motor cortex and/or spinal level since the drop in VA is not accompanied by changes in cortical VA (Prasartwuth *et al*., 2005). On the other hand, Goodall *et al*. (2017) found reductions in VA and cortical VA with an increase in superimposed twitch (SIT) elicited by cortical stimulation, hence suggesting involvements of motor cortex and above. However, the results of these studies could be partially explained by the methods employed to elicit the muscle damage i.e. backward walking (Racinais *et al*., 2008), submaximal (30%) eccentric contraction (Prasartwuth *et al*., 2005) and maximal eccentric contraction (Goodall *et al.*, 2017). In addition, changes in motor unit recruitment thresholds (Dartnall *et al*., 2009), discharge rates (Piitulainen *et al*., 2012), motor unit conduction velocities (Hedayatpour *et al*., 2009) and synchronisation (Dartnall, Nordstrom, & Semmler, 2008) provide evidence of central involvement following an eccentric exercise. It appears that the variability in VA reductions following an eccentric exercise depends on the extend of the damaging protocol employed; 23% drop in VA when exercised up to 40% drop in MVC (Prasartwuth *et al*., 2005), and 12% drop in VA when exercised until 18% drop in MVC (Barss *et al.,* 2014) compared 7% drop in VA at 16% MVC in this study. In other words, central involvement is more prominent when greater force generating capacity is compromised.

As suggested earlier, the trend of recovery in VA observed at post-24 hours could also distinct acute fatiguing effect of eccentric exercise and DOMS. This observation has also been reported by few authors where VA showed a trend of recovery while MVC was at its lowest (Barss *et al*., 2014; Prasartwuth *et al*., 2005; Racinais *et al*., 2008). Furthermore, Souron *et al*. (2018) showed that the reduction in VA was only significant at post

eccentric exercise while MVC remained significant low up to 96 hours. In brief, both VAS and VA showed similar trend of recovery while MVC and CK were at their lowest suggest that during DOMS central involvement is less pronounced compared to peripheral factors.

### 5.4 Contralateral Homologous Limb and Cross-over Effect

In this study, it was found that following eccentric contraction and DOMS of the treated limb, "cross-over" effects on MVC, VAS and VA were observed in the contralateral homologous limb, though similar in pattern compared to the treated limb, these effects were less pronounced (significant group vs time interaction, $P < 0.05$). For MVC, there was a 7% drop at post-10 minute which further plummeted after 24 hours (13%) and remained significantly low up to 72 hours (11.3%). This cross-over effect in the contralateral limb during DOMS on MVC has only been recently reported in knee extensors (13.7% reduction in the contralateral limb) (Hedayatpour, Izanloo, & Falla, 2018). Dissimilar to the factors that contribute to the drop in force in the treated limb, the drop here could not be explained by structural changes, muscle stiffness and inflammation. In addition, there was also an increase in sensation of soreness (VAS) in the contralateral limb which peaked at post-10 minutes and 24 hours ($1.60 \pm 0.84$). Previously, this cross-over effect on muscle soreness following maximal eccentric contractions and DOMS has been reported in the elbow flexors (Howatson & van Someren, 2007) and knee extensors (Hedayatpour *et al*., 2018). It seems that the changes in MVC follow similar patterns to VAS and CK which indicate the reduction in force production is partially associated with alteration in neural drive due to pain threshold (Hedayatpour *et al*., 2018). The perception of pain within the injured muscle could alter cerebral motor plans (Svensson, Minoshima, Beydoun, Morrow, & Casey, 1997 ) which consequently reduces muscle performance of the contralateral limb (Halperin, Copithorne, & Behm, 2014). Mechanistically, it has been proposed that, nociceptor

sensitisation due to muscle injury leads to changes in muscle spindle afferent nerve fibres 24 h after eccentric exercise (Le Pera *et al*., 2001). Therefore, this cross-over drop of MVC is due to central factors and to a certain extent systemic changes affecting force generation. Damaged muscle fibres release immunomodulatory agents that could systemically affect the contralateral part of the body that could alter signaling pathways which in turn results in change in motor behavior (Dennis, 1998; Ruohonen *et al*., 2002). This phenomenon has also been shown in an animal model, where damage in cartilage releases inflammatory agents which induces protective mechanism (i.e. proteoglycan synthesis) in the contralateral knee joint (Homandberg, Kang, Zhang, Cole, & Williams, 2001).

The main evidence of central involvement is revealed when VA in the contralateral limb was also found to be affected by the eccentric contraction and DOMS of the treated limb, where to our knowledge is the first study to provide this information. VA reduction in the contralateral limb peaked at post-10 minutes (3.5%) and remained low up to 48 hours which is similar in pattern to the treated limb. Though VA was not measured, Hedayatpour *et al*. (2018) alluded that the drop in force in the contralateral limb to central involvement evidenced from the reduction in EMG activation. The findings of these studies is conclusive that central factors are involved in the drop in force in the contralateral limb following eccentric contraction and DOMS. In a different context, this cross-over effect is also present where reduction in VA alongside MVC observed immediately after fatiguing submaximal (Kennedy, Hug, Sveistrup, & Guevel, 2013; Todd, Petersen, Taylor, & Gandevia, 2003) and maximal contractions (Doix, Lefevre, & Colson, 2013; Kavanagh, Feldman, & Simmonds, 2016; Martin & Rattey, 2007). Interestingly, this cross-over fatigue effect is also seen from upper limb to non-homologous limb (lower limb) which affects VA and motor performance (Kennedy *et al*., 2013). The authors of these studies attributed the decline in motor performance to the

decline in neural drive of the contralateral limb to changes in motor cortex via inter hemispheric regulation through transcallosal pathways and/or spinal level. Based on all the evidences provided, the mechanisms underlying this cross-over phenomenon in fatigue could also explain similar observation following eccentric contraction and DOMS. It is plausible that the eccentric contraction and DOMS in the treated limb could (i) directly change the efficacy of the motor pathways to the contralateral limb, and (ii) alters a "common area" in the brain which regulates motor drive to both treated and contralateral limb (Howatson & van Someren, 2007; Zimmermann *et al*., 2012). On the other hand, these pathways have also been postulated enhanced after strength training (Carroll, Herbert, Munn, Lee, & Gandevia, 2006; Lee & Carroll, 2007). These potential underlying mechanisms, could also explain the drop in force both immediately and subsequent time points (at least up to 48 hours).

## 5.5 Limitation of study

There are few limitations in this study that are worth noting; (i) CK was the only muscle damaging variable used in this study, by adding more inflammatory variables would provide pertinent information on peripheral and systemic involvement following eccentric exercise and DOMS; and (ii) muscle stiffness was measured myometrically which is an indirect measure of muscle stiffness compared to imaging technique which limits the interpretation of this outcome.

## 5.6 Practical Application

This study showed a significant drop in force in ipsilateral and contralateral limb after an eccentric muscle contraction of the plantar flexors. The drop in force could last up to 72 hours in both limbs. Thus, an ideal therapeutic intervention must be given addressing both peripheral and central neural drive as this could enhance the recovery process. Importantly, the recovery modality should focus on both ipsilateral and contralateral

limbs, so that the affected athletes could return-to-play at their previous peak performances in shortest time possible.

## 5.7 Conclusions

In summary, the present study provides evidence of the reduction in force (MVC) and central activation (VA) and concomitant increase in pain score (VAS) in both treated and contralateral homologous plantar flexors following eccentric exercise and DOMS. While peripheral contribution is established, the findings of this study indicate significant role played by central factors leading to the drop in force. Interestingly, these central factors could distinct early (immediate after the cessation of exercise) and during DOMS, where maximum reduction in MVC was observed later than peak reduction of VA. In addition, similar pattern of outcomes was observed in the contralateral limb, indicating factors affecting the treated limb also played a role in the reduction of MVC observed.

**References**


Armstrong, R. B. (1984). Mechanisms of exercise-induced delayed onset muscular soreness: a brief review. *Medicine & Science in Sports & Exercise, 16*(6), 529-538.

Avela, J., & Komi, P.V. (1998). Reduced stretch reflex sensitivity and muscle stiffness after long-lasting stretch-shortening cycle exercise in humans. *European Journal of Applied Physiology 78*(5), 403-410.

Ayles, S., Graven-Nielsen, T., & Gibson, W. (2011). Vibration-induced afferent activity augments delayed onset muscle allodynia. *Journal of Pain, 12*(8), 884-891.

Baird, M. F., Graham, S. M., Baker, J. S., & Bickerstaff, G. F. (2012). Creatine-kinase- and exercise-related muscle damage implications for muscle performance and recovery. *Journal of Nutrition and Metabolism, 2012*, 960363.

Barss, T.S, Magnus, C.R.A, Clarke, N, Lanovaz, J.L, Chilibeck, P.D, Kontulainen, S.A, . . . Farthing, J.P. (2014). Velocity-specific strength recovery after a second bout of eccentric exercise. *Journal of Strength and Conditioning Research, 28*(2), 339-349.

Bobbert, M.F., Hollander, A.P., & Huijing, P.A. (1986). Factors in delayed onset muscular soreness of man. *Medicine & Science in Sports & Exercise 18*(1), 75-81.

Carroll, T. J., Herbert, R. D., Munn, J., Lee, M., & Gandevia, S. C. (2006). Contralateral effects of unilateral strength training: evidence and possible mechanisms. *Journal of Applied Physiology, 101*(5), 1514-1522.

Cheung, K., Hume, P.A., & Maxwell, L. (2003). Delayed Onset Muscle Soreness Treatment Strategies and Performance Factors. *Journal of Sports Medicine, 33*(2), 145-164.

Clarkson, P. M., & Hubal, M. J. (2002). Exercise-induced muscle damage in humans. *American Journal of Physical Medicine & Rehabilitation, 81*(11 Suppl), S52-69.

Clarkson, P. M., Nosaka, K. , & Braun, B. (1992). Muscle function after exercise-induced muscle damage and rapid adaptation. *Medicine & Science in Sports & Exercise, 24*(5), 512-520.

Cleak, M.J., & Eston, R.G. (1992). Muscle soreness, swelling, stiffness and strength loss after intense eccentric exercise. *British Journal of Sports Medicine 26*(4), 267-272.

Coren, S. (1993). The lateral preference inventory for measurement of handedness, footedness, eyedness, and earedness: Norms for young adults. *Bulletin of the Psychonomic Society, 31*(1), 1-3.

Dartnall, T. J., Nordstrom, M. A., & Semmler, J. G. (2008). Motor unit synchronization is increased in biceps brachii after exercise-induced damage to elbow flexor muscles. *Journal of Neurophysiology, 99*(2), 1008-1019.

Dartnall, T. J., Rogasch, N. C., Nordstrom, M. A., & Semmler, J. G. (2009). Eccentric muscle damage has variable effects on motor unit recruitment thresholds and discharge patterns in elbow flexor muscles. *Journal of Neurophysiology, 102*(1), 413-423.

De Luca, C. J., LeFever, R. S., McCue, M. P., & Xenakis, A. P. (1982). Control scheme governing concurrently active human motor units during voluntary contractions. *Journal of Physiology, 329*, 129-142.

Coyle, D. E. (1998). Partial peripheral nerve injury leads to activation of astroglia and microglia which parallels the development of allodynic behavior. *GLIA, 23(1),* 75–83.

Deschenes, M. R., Brewer, R. E., Bush, J. A., McCoy, R. W., Volek, J. S., & Kraemer, W. J. (2000). Neuromuscular disturbance outlasts other symptoms of exercise-induced muscle damage. *Journal of the Neurological Sciences, 174*(2), 92-99.

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

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

Endoh, T., Nakajima, T., Sakamoto, M., & Komiyama, T. (2005). Effects of Muscle Damage Induced by Eccentric Exercise on Muscle Fatigue. *Medicine & Science in Sports & Exercise, 37*(7), 1151-1156.

Evans, W. J., & Cannon, J. G. (1991). The metabolic effects of exercise-induced muscle damage. *Exercise and Sport Sciences Reviews, 19*, 99-125.

Friden, J., Sjostrom, M., & Ekblom, B. (1983). Myofibrillar damage following intense eccentric exercise in man. *International Journal of Sports Medicine, 4*(3), 170-176.

Fuglevand, A. J., Winter, D. A., & Patla, A. E. (1993). Models of recruitment and rate coding organization in motor-unit pools. *Journal of Neurophysiology, 70*(6), 2470-2488.

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

Garrett, W. E., Jr. (1990). Muscle strain injuries: clinical and basic aspects. *Medicine & Science in Sports & Exercise, 22*(4), 436-443.

Gervasio, S., Finocchietti, S., Stevenson, A. J. T., & Mrachacz-Kersting, N. (2018). Delayed muscle onset soreness in the gastrocnemius muscle attenuates the spinal

contribution to interlimb communication. *European Journal of Applied Physiology, 118*(11), 2393-2402.

Gibson, W., Arendt-Nielsen, L., & Graven-Nielsen, T. (2006). Delayed onset muscle soreness at tendon-bone junction and muscle tissue is associated with facilitated referred pain. *Experimental Brain Research, 174*(2), 351-360.

Goodall, S., Thomas, K., Barwood, M., Keane, K., Gonzalez, J. T., St Clair Gibson, A., & Howatson, G. (2017). Neuromuscular changes and the rapid adaptation following a bout of damaging eccentric exercise. *Acta Physiologica, 220*(4), 486-500.

Gulick, D. T., & Kimura, I. F. (1996). Delayed Onset Muscle Soreness: What is it and how do we treat it? *Journal of Sport Rehabilitation, 5*(3), 234-243.

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

Hedayatpour, N., Falla, D., Arendt-Nielsen, L., Vila-Cha, C., & Farina, D. (2009). Motor unit conduction velocity during sustained contraction after eccentric exercise. *Medicine & Science in Sports & Exercise, 41*(10), 1927-1933.

Hedayatpour, N., Izanloo, Z., & Falla, D. (2018). The effect of eccentric exercise and delayed onset muscle soreness on the homologous muscle of the contralateral limb. *Journal of Electromyography and Kinesiology, 41(4)*, 154-159.

Homandberg, G. A., Kang, Y., Zhang, J., Cole, A. A., & Williams, J. M. (2001). A single injection of fibronectin fragments into rabbit knee joints enhances catabolism in the articular cartilage followed by reparative responses but also induces systemic effects in the non-injected knee joints. *Osteoarthritis Cartilage, 9*(8), 673-683.

Horita, T., Komi, P. V., Nicol, C., & Kyrolainen, H. (1999). Effect of exhausting stretch-shortening cycle exercise on the time course of mechanical behaviour in the drop jump: possible role of muscle damage. *European Journal of Applied Physiology and Occupational Physiology, 79*(2), 160-167.

Hough, Theodore. (1900). Ergographic studies in muscular fatigue and soreness. *Journal of the Boston Society of Medical Sciences, 5*(3), 81-92.

Howatson, G., & van Someren, K. A. (2007). Evidence of a contralateral repeated bout effect after maximal eccentric contractions. *European Journal of Applied Physiology, 101*(2), 207-214.

Howell, J.N., Chleboun, G., & Conatser, R. (1993). Muscle stiffness, strength loss, swelling and soreness following exercise induced injury in humans. *Journal of Physiology, 464*, 183-196.

Hubal, M. J., Rubinstein, S. R., & Clarkson, P. M. (2007). Mechanisms of variability in strength loss after muscle-lengthening actions. *Medicine & Science in Sports & Exercise, 39*(3), 461-468.

Isner-Horobeti, M. E., Dufour, S. P., Vautravers, P., Geny, B., Coudeyre, E., & Richard, R. (2013). Eccentric exercise training: modalities, applications and perspectives. *Journal of Sports Medicine, 43*(6), 483-512.

Kavanagh, Justin J., Feldman, Matthew R., & Simmonds, Michael J. (2016). Maximal intermittent contractions of the first dorsal interosseous inhibits voluntary activation of the contralateral homologous muscle. *Journal of Neurophysiology, 116*(5), 2272-2280.

Keenan, K. G., Farina, D., Merletti, R., & Enoka, R. M. (2006). Amplitude cancellation reduces the size of motor unit potentials averaged from the surface EMG. *Journal of Applied Physiology, 100*(6), 1928-1937.

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.

Khong, T.K., Selvanayagam, V.S., Hamzah, S.H., & Yusof, A. (2018). The effect of quantity and quality of pre-exercise carbohydrate meals on central fatigue. *Journal of Applied Physiology*, 125(4), 1021-1029.

Komulainen, J., Takala, T. E., Kuipers, H., & Hesselink, M. K. (1998). The disruption of myofibre structures in rat skeletal muscle after forced lengthening contractions. *European Journal of Physiology, 436*(5), 735-741.

Lau, W. Y., Blazevich, A. J., Newton, M. J., Wu, S. S., & Nosaka, K. (2015). Assessment of Muscle Pain Induced by Elbow-Flexor Eccentric Exercise. *Journal of Athletic Training, 50*(11), 1140-1148.

Laurin, J., Dousset, E., Carrivale, R., Grelot, L., & Decherchi, P. (2012). Recovery pattern of motor reflex after a single bout of neuromuscular electrical stimulation session. *Scandinavian Journal of Science & Medicine in Sports, 22*(4), 534-544.

Le Pera, D., Graven-Nielsen, T., Valeriani, M., Oliviero, A., Di Lazzaro, V., Tonali, P. A., & Arendt-Nielsen, L. (2001). Inhibition of motor system excitability at cortical and spinal level by tonic muscle pain. *Clinical Neurophysiology, 112*(9), 1633-1641.

Lee, M., & Carroll, T. J. (2007). Possible mechanisms for the contralateral effects of unilateral resistance training. *Journal of Sports Medicine, 37*(1), 1-14.

Lehti, T. M., Kalliokoski, R., & Komulainen, J. (2007). Repeated bout effect on the cytoskeletal proteins titin, desmin, and dystrophin in rat skeletal muscle. *Journal of Muscle Research and Cell Motility, 28*(1), 39-47.

Lewis, P. B., Ruby, D., & Bush-Joseph, C. A. (2012). Muscle soreness and delayed-onset muscle soreness. *Clinical Journal of Sport Medicine, 31*(2), 255-262.

Lieber, R. L., Thornell, L. E., & Friden, J. (1996). Muscle cytoskeletal disruption occurs within the first 15 min of cyclic eccentric contraction. *Journal of Applied Physiology, 80*(1), 278-284.

Lovering, R. M., & De Deyne, P. G. (2004). Contractile function, sarcolemma integrity, and the loss of dystrophin after skeletal muscle eccentric contraction-induced injury. *American Journal of Physiology-Cell Physiology, 286*(2), C230-238.

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

McCully, K. K., & Faulkner, J. A. (1986). Characteristics of lengthening contractions associated with injury to skeletal muscle fibers. *Journal of Applied Physiology, 61*(1), 293-299.

McNeil, P. L., & Khakee, R. (1992). Disruptions of muscle fiber plasma membranes. Role in exercise-induced damage. *American Journal of Pathology, 140*(5), 1097-1109.

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

Morgan D.L. (1990). New insights into the behavior of muscle during active lengthening. *Biophysical Journal,* 57(2), 209-221.

Morgan, D. L., & Allen, D. G. (1999). Early events in stretch-induced muscle damage. *Journal of Applied Physiology, 87*(6), 2007-2015.

O'Connor, P. J., & Cook, D. B. (1999). Exercise and pain: the neurobiology, measurement, and laboratory study of pain in relation to exercise in humans. *Exercise and Sport Sciences Reviews, 27*, 119-166.

Piitulainen, H., Holobar, A., & Avela, J. (2012). Changes in motor unit characteristics after eccentric elbow flexor exercise. *Scandinavian Journal of Science & Medicine in Sports, 22*(3), 418-429.

Pitman, B. M., & Semmler, J. G. (2012). Reduced short-interval intracortical inhibition after eccentric muscle damage in human elbow flexor muscles. *Journal of Applied Physiology, 113*(6), 929-936.

Power, G.A., Dalton, B.H., Rice, C.L., & Vandervoort, A.A. (2010). Delayed recovery of velocity-dependent power loss following eccentric actions of the ankle dorsiflexors. *Journal of Applied Physiology, 109*(3), 669–676.

Prasartwuth, O., Allen, T. J., Butler, J. E., Gandevia, S. C., & Taylor, J. L. (2006). Length-dependent changes in voluntary activation, maximum voluntary torque and twitch responses after eccentric damage in humans. *Journal of Physiology, 571*(Pt 1), 243-252.

Prasartwuth, O., Taylor, J. L., & Gandevia, S. C. (2005). Maximal force, voluntary activation and muscle soreness after eccentric damage to human elbow flexor muscles. *Journal of Physiology, 567*(Pt 1), 337-348.

Proske, U., & Allen, T. J. (2005). Damage to skeletal muscle from eccentric exercise. *Exercise and Sport Sciences Reviews, 33*(2), 98–104.

Proske, U., & Morgan, D. L. (2001). Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. *Journal of Physiology, 537*(2), 333–345.

Pruyn, Elizabeth C., Watsford, Mark L., & Murphy, Aron J. (2016). Validity and reliability of three methods of stiffness assessment. *Journal of Sport and Health Science, 5*(4), 476-483.

Racinais, S., Bringard, A., Puchaux, K., Noakes, T. D., & Perrey, S. (2008). Modulation in voluntary neural drive in relation to muscle soreness. *European Journal of Applied Physiology, 102*(4), 439-446.

Ruohonen, S., Jagodi, M., Khademi, M., Taskinen, H.S., Ojala, P., Olsson, T., & Roytta, M. (2002). Contralateral non-operated nerve to transected rat sciatic nerve shows increased expression of IL-1h, TGF-h1, TNF-a, and IL-10. *Journal of Neuroimmunology, 132(1-2)*, 11-17.

Saxton, J. M., & Donnelly, A. E. (1996). Length-specific impairment of skeletal muscle contractile function after eccentric muscle actions in man. *Clinical Science (Lond), 90*(2), 119-125.

Sayers, S. P., & Clarkson, P. M. (2001). Force recovery after eccentric exercise in males and females. *European Journal of Applied Physiology, 84*(1-2), 122-126.

Sayers, S. P., Knight, C. A., & Clarkson, P. M. (2003). Neuromuscular variables affecting the magnitude of force loss after eccentric exercise. *Journal of Sports Science, 21*(5), 403-410.

Schwane, J. A., Johnson, S. R., Vandenakker, C. B., & Armstrong, R. B. (1983). Delayed-onset muscular soreness and plasma CPK and LDH activities after downhill running. *Medicine & Science in Sports & Exercise, 15*(1), 51-56.

Schwane, J. A., Watrous, B. G., Johnson, S. R., & Armstrong, R. B. (1983). Is lactic acid related to delayed-onset muscle soreness? *Physician and Sportsmedicine, 11*(3), 124-131.

Semmler, J. G. (2014). Motor unit activity after eccentric exercise and muscle damage in humans. *Acta Physiologica (Oxf), 210*(4), 754-767.

Semmler, J. G., Ebert, S. A., & Amarasena, J. (2013). Eccentric muscle damage increases intermuscular coherence during a fatiguing isometric contraction. *Acta Physiologica (Oxf), 208*(4), 362-375.

Skurvydas, A., Brazaitis, M., Kamandulis, S., & Sipaviciene, S. (2010). Peripheral and central fatigue after muscle-damaging exercise is muscle length dependent and inversely related. *Journal of Electromyography & Kinesiology, 20*(4), 655-660.

Smith, L.L. (1991). Acute inflammation: the underlying mechanism in delayed onset muscle soreness. *Medicine & Science in Sports & Exercise, 23*(5), 542-551.

Smith, L.L., Keating, M.N., Holbert, D., Spratt, D.J., McCammon, M.R., Smith, S.S., & Israel, R.G. (1994). The effects of athletic massage on delayed onset muscle

soreness, creatine kinase, and neutrophil count: a preliminary report. *Journal of Orthopaedic & Sports Physical Therapy, 19*(2), 93-99.

Souron, R., Nosaka, K., & Jubeau, M. (2018). Changes in central and peripheral neuromuscular fatigue indices after concentric versus eccentric contractions of the knee extensors. *European Journal of Applied Physiology, 118*(4), 805-816.

Stauber, W. T. (1989). Eccentric action of muscles: physiology, injury, and adaptation. *Exercise and Sport Sciences Reviews, 17(1)*, 157-185.

Stegeman, D., & Hermens, H. (2007). Standards for surface electromyography: The European project Surface EMG for non-invasive assessment of muscles (SENIAM). *http://www med uni-jena de/motorik/pdf/stegeman pdf* .

Svensson, P., Minoshima, S., Beydoun, A., Morrow, T.J., & Casey, K. L. (1997). Cerebral processing of acute skin and muscle pain in humans. *Journal of Neurophysiology, 78(1),* 450-460.

Tidball, J. G. (2005). Inflammatory processes in muscle injury and repair. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, 288*(2), R345-353.

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.

Vila-Cha, C., Falla, D., Correia, M. V. , & Farina, D. . (2012). Changes in H reflex and V wave following short-term endurance and strength training. *Journal of Applied Physiology, 112(1)*, 54-63.

Vila-Chã, C., Hassanlouei, H., Farina, D., & Falla, D. (2011). Eccentric exercise and delayed onset muscle soreness of the quadriceps induce adjustments in agonist–antagonist activity, which are dependent on the motor task. *Experimental Brain Research, 216*(3), 385-395.

Warren, G.L., D.A., Lowe, Hayes, D.A., Karwoski, C.J., Prior, B.M., & Armstrong, R. B. (1993). Excitation failure in eccentric contraction-induced injury of mouse soleus muscle. *Journal of Physiology, 468*, 487-499.

Weerakkody, N. S., Whitehead, N. P., Canny, B. J., Gregory, J. E., & Proske, U. (2001). Large-fiber mechanoreceptors contribute to muscle soreness after eccentric exercise. *Journal of Pain, 2*(4), 209-219.

Yu, J. G., Liu, J. X., Carlsson, L., Thornell, L. E., & Stal, P. S. (2013). Re-evaluation of sarcolemma injury and muscle swelling in human skeletal muscles after eccentric exercise. *PLoS One, 8*(4), e62056.

Zimmermann, K., Leidl, C., Kaschka, M., Carr, R. W., Terekhin, P., Handwerker, H. O., & Forster, C. (2012). Central projection of pain arising from delayed onset muscle soreness (DOMS) in human subjects. *PloS One, 7*(10), e47230.

## LIST OF PUBLICATIONS AND PAPERS PRESENTED

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