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Effect of Unaccustomed Eccentric Exercise on Motor Unit Firing Characteristics and the Contralateral Repeated Bout Effect: A Pilot Study

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EFFECT OF UNACCUSTOMED ECCENTRIC EXERCISE ON MOTOR UNIT FIRING CHARACTERISTICS AND THE CONTRALATERAL REPEATED BOUT EFFECT: A PILOT STUDY

by

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ABSTRACT

Introduction: Eccentric exercise elicits considerable muscle damage. If a bout of unilateral eccentric exercise is repeated on the ipsilateral or contralateral limb, a repeated bout effect (RBE) may be observed where muscle damage is attenuated. **Purpose:** To examine whether a RBE exists following repeated bouts of damaging eccentric exercise in the ipsilateral and contralateral limbs, and assess changes to motor unit firing characteristics in both limbs following recovery from an initial bout. **Methods:** Sixteen untrained men were randomized into exercise (EX) or control (CON) groups. EX performed eccentric exercise of the elbow flexors on the dominant (ipsilateral) limb and repeated the exercise protocol on both ipsilateral and contralateral limbs fourteen days later. Range of motion (ROM), proximal and distal measures of muscle soreness (pVAS/dVAS) and pain-pressure threshold (pPPT/dPPT), maximal isometric torque (MVIC), rate of torque development (RTD) at 50ms (RTD_{50}), 100ms (RTD_{100}), 200ms (RTD_{200}), and peak RTD (RTD_{peak}) were assessed at baseline (BL), immediately-post (IP), and at twenty-four (24H) and seventy-two hours (72H) post-exercise in EX and CON. Motor unit (MU) firing characteristics were assessed in both limbs via decomposition of surface electromyography (EMG) signals collected during submaximal ramp contractions at 50% and 80% MVIC. **Results:** Changes in ROM and RTD_{200} indicated a RBE in both limbs, whereas changes in MVIC and RTD_{100} indicated a RBE in the ipsilateral limb only. Changes in RTD_{50}, RTD_{peak}, pPPT, or dPPT did not support a RBE. Increases in the slopes of both the mean firing rate vs. recruitment threshold and the action potential amplitude vs. recruitment threshold relationships at 80% MVIC were noted between bouts for the ipsilateral limb in EX, but not the contralateral limb.

Conclusions: Results of this study provide support for a RBE in both limbs, whereas alterations to MU firing characteristics were noted in the ipsilateral limb only.

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LIST OF ACRONYMS/ABBREVIATIONS

24H	Twenty-four hours post-exercise
72H	Seventy-two hours post-exercise
ANOVA	Analysis of variance
BIA	Bioelectrical impedance analysis
BL	Baseline
CON	Control group
CV	Coefficient of variation
DOMS	Delayed-onset muscle soreness
dPPT	Distal pain-pressure threshold
dVAS	Distal muscle soreness
ECC1	Initial eccentric exercise bout
ECC1-CL	Contralateral limb during ECC1
ECC1-IL	Ipsilateral limb during ECC1
ECC2-CL	Contralateral limb during ECC2
ECC2-IL	Ipsilateral limb during ECC2
EIMD	Exercise-induced muscle damage
EMG	Electromyography
EX	Exercise group
FAM	Familiarization session
FAM1	Initial familiarization session
FAM2	Second familiarization session
ICC	Intraclass correlation
IP	Immediately post-exercise
EPIC	Exercise Physiology Intervention and Collaboration
MATLAB	Matrix laboratory
MFR	Mean firing rate

MHAQ	Medical history and activity questionnaire
MU	Motor unit
MUAPT	Motor unit action potential train
MVIC	Maximal voluntary isometric contraction
NF-κB	Nuclear factor-kappa B
NSAID	Non-steroidal anti-inflammatory drug
PAR-Q+	Physical activity readiness questionnaire
pPPT	Proximal pain-pressure threshold
pVAS	Proximal muscle soreness
RMS	Root mean squared
ROM	Range of motion
RT	Recruitment threshold
RTD	Rate of torque development
RTD_{50}	Rate of torque development at 50 ms
RTD_{100}	Rate of torque development at 100 ms
RTD_{200}	Rate of torque development at 200 ms
RTD_{peak}	Peak rate of torque development
SD	Standard deviation
SEM	Standard error of the measurement
sEMG	Surface electromyography
SPSS	Statistical package for the social sciences
TMS	Transcranial magnetic stimulation
USG	Urine specific gravity
VAS	Visual analog scale

CHAPTER 1: INTRODUCTION

A novel bout of high-intensity exercise may result in damage to muscle fibers, which presents as Z-disc streaming and dysregulation of cytoskeletal proteins (Friden & Lieber, 2001). This structural damage will likely result in the development of muscular soreness of the involved muscle, along with functional decrements such as losses in strength and range of motion (Howatson & van Someren, 2007; Jamurtas et al., 2005). This damage response appears to primarily be related to the performance of eccentric contractions in which the muscle must produce force while lengthening (Asmussen, 1956; Clarkson & Hubal, 2002). In response to the initial exercise stimulus, a rapid adaptation process occurs that results in an attenuation of muscle damage if the exercise is repeated, a phenomenon known as the repeated bout effect (T. Chen et al., 2007; McHugh, 2003). This adaptation may be due, in part, to changes to neural factors, including increases in corticospinal drive and alterations to recruitment patterns of exercised muscle (T. Chen, 2003; Goodall et al., 2017; Hight et al., 2017). Previous research indicates that high threshold motor units are preferentially recruited during eccentric exercise and more susceptible to damage (Friden et al., 1983; Macaluso et al., 2012; Macgregor & Hunter, 2018; Nardone et al., 1989). However, if exercise is repeated, changes in muscular excitation and activation consistent with increased firing of lower-threshold motor units has been repeatedly observed (T. Chen, 2003; Hight et al., 2017; Howatson et al., 2007; Starbuck & Eston, 2012; Tsuchiya et al., 2018). Consistent with this, increased motor unit synchronization and common drive have been shown to increase for up to seven days following damaging eccentric exercise (Dartnall et al., 2011; Macgregor & Hunter, 2018). These adaptations may improve the

efficiency of motor unit recruitment, allowing for a more equitable distribution of stress across active fibers, resulting in an attenuation of damage.

Further evidence has shown that muscular adaptation may not be entirely dependent upon the presence of damage during an initial bout of exercise, indicating that central adaptations may underly the repeated bout effect (T. Chen et al., 2013). Indeed, attenuations in damage indicators have been observed following a myriad of non-damaging exercise bouts, including isometric contractions (Tseng et al., 2016) as well as low-intensity eccentrics (H.-L. Chen et al., 2012; T. Chen et al., 2013). Research has also shown that protective effects are conferred upon the homologous muscle of the contralateral limb for up to four weeks (T. Chen et al., 2016; T. Chen, Lin, Chen, Lai, et al., 2018; T. Chen, Lin, Chen, Yu, et al., 2018; Howatson & van Someren, 2007). The transfer of protective effects to the contralateral limb is reported to be approximately 50% of that observed when the same limb performs both exercise bouts (T. Chen, Lin, Chen, Yu, et al., 2018). While the contralateral repeated bout effect is believed to be primarily neural in nature, evidence to support this claim thus far is limited. Previous research has observed functional decrements to the contralateral limb following unaccustomed eccentrics in addition to pain desensitization following a repeated bout of exercise in the contralateral limb (Hedayatpour et al., 2018; Hosseinzadeh et al., 2015). It has also been shown that muscle activation may favor increased recruitment of low-threshold motor units to sustain similar workloads during a repeated bout performed on the contralateral limb (Starbuck & Eston, 2012; Tsuchiya et al., 2018). Together, this suggests that neural adaptations occur following unaccustomed eccentric exercise that facilitate increased recruitment of lower-threshold motor units to meet force demands, and that these adaptations may be transferred to the contralateral limb.

While current evidence seems to suggest an alteration in recruitment strategy following a bout of exercise occurs on the same limb, evidence supporting contralateral transfer of these adaptations is limited. Additionally, the relationship between alterations in recruitment strategy and the subsequent attenuation of markers of muscle damage following a second bout of exercise have not been assessed. Therefore, the purpose of the current study was to examine whether a repeated bout effect exists following repeated bouts of damaging eccentric exercise in the ipsilateral and contralateral limbs. A secondary purpose of this study was to assess changes to motor unit firing characteristics in both limbs following recovery from an initial bout.

CHAPTER 2: REVIEW OF LITERATURE

Introduction

Following a bout of unaccustomed eccentric exercise, skeletal muscle displays marked structural abnormalities such as Z-disc streaming indicating damage to muscle fibers (Friden & Lieber, 2001). Myofibrillar damage is accompanied by reductions in muscular function (e.g. reduced force production capacity, range of motion losses, increased soreness, and mechanical hyperalgesia) as well as increased concentrations of intramuscular proteins in the blood (Clarkson & Hubal, 2002). Following a novel bout of damaging exercise, a rapid adaptation occurs such that if an exercise of a similar magnitude is repeated, the appearance of damage will be markedly less; this phenomenon is referred to as the repeated bout effect (K. Nosaka & Clarkson, 1995). Adaptations for the repeated bout effect have been postulated to be the result of a combination of mechanical remodeling, biochemical signaling, and neural mechanisms (Hyldahl et al., 2017). Neural mechanisms underlying the repeated bout effect may include adaptations within the central nervous system, such as increased corticospinal excitability, as well as alterations to recruitment patterns of active musculature improving the efficiency of force production (Goodall et al., 2017; Hight et al., 2017). Further, recent evidence also seems to suggest that protective effects may be transferred to the homologous muscle of the contralateral limb following damaging exercise (Starbuck & Eston, 2012). Presumably, this contralateral repeated bout effect would be the result of neural mechanisms, as the muscle exercised during the repeated bout did not receive a prior damaging stimulus (Hyldahl et al., 2017). Previous research has provided support for alterations to muscular activation and pain-sensitive reflexes in the contralateral limb following a repeated bout (Hosseinzadeh et al., 2015; Starbuck & Eston,

2012). Since the late 19th century, it has been observed that strength increases as a result of unilateral training experience a cross-education effect, where the untrained limb also displays increased strength following training (Carr et al., 2019; Moritani & DeVries, 1979; Scripture et al., 1894). Cross-education of strength has been observed to be the result of enhanced communication between hemispheres of the brain (Hortobágyi et al., 2011; Ruddy & Carson, 2013). Therefore, it is possible that the contralateral repeated bout effect presents a response to acute exercise that mimics the long-term effects of unilateral resistance training in terms of neural adaptations. However, while changes to the surface electromyogram during repeated eccentric contractions on a contralateral limb have been evaluated (Starbuck & Eston, 2012), alterations to motor unit recruitment strategies extracted from surface electromyographic measures have not been evaluated on a contralateral limb. Investigation of these mechanisms has potential to provide insight into the time course of specific neural adaptations that occur with resistance training as well as highlight therapeutic strategies that may enhance recovery following prolonged immobilization resulting in detraining of one limb.

Exercise-Induced Muscle Damage

Exercise-induced muscle damage (EIMD) is defined as disruption to skeletal muscle ultrastructure resulting from unaccustomed stress (Friden & Lieber, 2001). At the cellular level, EIMD is usually characterized by the presence of Z-disc streaming as well as alterations to staining pattern of structural filaments such as desmin (Friden & Lieber, 1992). One of the earliest observations of disruption to sarcomeric structure following eccentric exercise reported that sarcomeres adjacent to affected Z-discs displayed a disorganized structure as well (Friden et al., 1983). Previous research has indicated that in response to EIMD, desmin translocates

towards the outer portion of the sarcolemma as part of myofibrillar remodeling (Yu et al., 2004). Desmin primarily functions as an anchoring filament, serving to maintain the relative position of adjacent Z-discs (Clarkson & Hubal, 2002). Therefore, disruptions to desmin following damaging exercise may produce an unstable sarcomeric structure, further contributing to the damaged appearance of adjacent sarcomeres. Yu and colleagues (2003) observed that lesions to the myofibrillar membrane typically appear between two and eight days following unaccustomed eccentric exercise, and that these damaged fibers may be broadly divided into two subcategories: 1) myofibrils that stain positive for desmin and actin, but negative for structural proteins such as titin, nebulin, and α-actinin, and 2) myofibrils which stain strongly for desmin and actin and also containing supernumerary sarcomeres. It is hypothesized that this reflects different stages of the repair process, whereby severely damaged sarcomeres display a strain-induced loss of structural protein (e.g. titin, nebulin, α-actinin) early in the adaptation process, but as new sarcomeres are inserted into existing myofibrils, concentrations of desmin and actin are increased. This would seem to support the notion that following damaging exercise, new sarcomeres are formed as part of the regeneration process in order to improve the efficiency of force production if subjected to subsequent stress.

Early observations of damaging exercise reported that exercise-induced muscle damage was higher when the muscle was contracting eccentrically (i.e. producing force while lengthening) than concentric contractions (Friden et al., 1983). One of the explanations for the localization of damage to specific sites within the muscle states that sarcomeres within a myofibril have non-uniform resting lengths, resulting in increased damage to overstretched sarcomeres and less damage to sarcomeres with a shorter resting length (Morgan & Proske, 2004). Shellock and colleagues (1991) reported a greater magnitude of muscle damage following

eccentric contractions than if the same quantity of work was performed concentrically. This is also indirectly supported by observations from several studies indicating that increased muscle pain sensitivity in response to damage is localized to specific regions within the muscle (Delfa de la Morena et al., 2013; Hosseinzadeh et al., 2013). Previous research has also observed that the magnitude of muscle damage may be fiber type dependent; that is to say, muscles with a greater percentage of fast-twitch fibers (and therefore a higher capacity for tension) likely experience a greater magnitude of exercise-induced muscle damage when subjected to the same volume of eccentric exercise (Choi & Widrick, 2010; Friden et al., 1983; Macaluso et al., 2012). Choi & Widrick (2010) reported that following chemical activation of skinned muscle fibers, hybrid IIa/IIx fibers experienced a significant amount of damage, while Type I and IIa fibers were less affected. More recent research using a plyometric damaging protocol *in vivo* reported a significantly greater magnitude of muscle damage following exercise in Type II muscle fibers (Macaluso et al., 2012). However, while muscle damage responses appear to be fiber-type specific, they do not appear to be influenced by genetic differences (Gulbin & Gaffney, 2002). A recently published review article by Lieber (2018) proposed two mechanisms for this fiber-type specific damage response: 1) during maximal eccentric contractions, fast glycolytic muscle fibers become depleted of glycogen, resulting in a diminished ATP regeneration capacity and enter a high-rigor state, making them more susceptible to mechanical stress; or 2) this diminished ATP regenerating capacity results in an inability of myofibrillar mitochondria to buffer intracellular calcium, resulting in an increase in intracellular calcium and activating cellular proteases, leading to breakdown of structural proteins.

Another important consideration for the interpretation of the magnitude of damage following eccentric exercise is the muscle group utilized during the exercise protocol. It has been

repeatedly observed that muscle groups that regularly undergo submaximal eccentric contractions as a result of locomotion (i.e. the knee extensors) are less susceptible to muscle damage than muscle groups that are naïve to eccentric contractions if subjected to similar volumes of exercise (Huang et al., 2019; Jamurtas et al., 2005; Saka et al., 2009). Jamurtas and colleagues (2005) reported that when both the elbow flexors and knee extensors were subjected to six sets of 10 maximal eccentric repetitions, muscle soreness and range of motion were similar between muscle groups; however, creatine kinase, myoglobin, and muscle strength as measured by both eccentric peak torque and isometric peak torque were depressed to a much greater extent for up to 96 hours post-exercise in the elbow flexors than in the knee extensors.

Muscle Soreness and Pain Sensitivity

One of the ways in which exercise-induced muscle damage has been non-invasively quantified previously is through the magnitude of soreness that develops following the exercise bout (Clarkson et al., 1992). Pioneering research by Asmussen (1956) observed that when individuals completed a bout of eccentric exercise, considerable soreness developed. However, despite a more rapid rate of fatigue when performing concentric exercise, soreness was not observed. The authors therefore ascribed the development of soreness to mechanical rather than metabolic factors, as shortening of muscle is a much more metabolically intensive process and produces greater accumulation of metabolites as a result (Durand et al., 2003; Lieber, 2018). Similarly, it has been frequently observed that following unaccustomed eccentric exercise, muscles develop increased soreness and sensitivity to pain that peaks within 48-72 hours post-exercise and subsides within one week (T. Chen, 2003; T. Chen et al., 2016, 2019; T. Chen, Lin, Chen, Yu, et al., 2018; Harmsen et al., 2019; Hedayatpour et al., 2018; Maeo et al., 2018; Starbuck & Eston, 2012).

While the cause of the development of soreness is likely multifaceted, recent evidence suggests that the onset may result from production of neurotrophic factors related to the release of bradykinin, which increases sensitivity of afferent nerve endings and results in mechanical hyperalgesia (i.e. pain in response to mechanical stimuli; Mizumura & Taguchi, 2016). In particular, it is currently thought that prostaglandin E2 interacts with group IV afferent nerve endings to induce mechanical sensitization of fascia surrounding muscle fibers, resulting in a reduced threshold for pain in response to a pressure stimulus following eccentric exercise (Alvarez et al., 2010; Gibson et al., 2009). Previous research has indicated that although muscular soreness and pain-pressure thresholds change similarly in response to muscle damage, the responses are unrelated to each other, which may indicate different underlying mechanisms (Lau et al., 2015c; Muanjai et al., 2019). For example, while muscular soreness is likely related to the onset of an inflammatory cascade, alterations in pain-pressure threshold may be related to inflammation, alterations to sensory feedback, and mechanical changes (Muanjai et al., 2019; Peake et al., 2017). Support for altered sensory feedback include that attenuations in pain-pressure threshold as well as nociceptive withdrawal reflexes as a result of eccentric damage are transferred to the contralateral limb (Hosseinzadeh et al., 2015).

While the development of DOMS has long been used as an indicator of the magnitude of damage experienced as a result of exercise, previous research has called this practice into question because of its relatively poor correlation with both myofibrillar damage and muscular function following mechanical injury (K. Nosaka et al., 2002; Warren et al., 1999). Nosaka and colleagues (2002) evaluated the relationship with measures of soreness using a visual analog scale when muscles were palpated, passively flexed, or passively extended following eccentric exercise at various volume-loads, and other indirect indicators of exercise-induced muscle

damage. They observed that although other damage indicators increased concomitantly with the volume of exercise performed, soreness did not appear to sufficiently reflect these changes, with the exception of measurement during the passive extension condition. This may be related to increased sensitivity in structures responsible for passive tension (Hosseinzadeh et al., 2013; Lau et al., 2015a, 2015c). Further, soreness and pain-pressure threshold development in response to exercise have consistently been shown to be highly localized to specific regions of the exercised muscle (Delfa de la Morena et al., 2013; Hosseinzadeh et al., 2013, 2015). Taken together, previous research supports the use of muscle soreness and pain-pressure mapping at multiple sites to provide insight into changes in inflammatory processes as well as neuromechanical alterations of pain perception in response to the development of damage.

Range of Motion (ROM)

Another non-invasive measure frequently used to make inferences about the magnitude of exercise-induced muscle damage are observed decrements to the range of motion (ROM) about a joint following damaging exercise (Clarkson et al., 1992). Range of motion assessment provides a practical, non-invasive means of assessment of muscular function that seems to occur in phase with the development of exercise-induced muscle damage. ROM is typically assessed using a manual goniometer to assess the flexed and relaxed angles of the joint, then calculating the difference between the average of these two measurements (Barroso et al., 2010; T. Chen et al., 2016, 2019; T. Chen, Lin, Chen, Yu, et al., 2018; T. Chen, Lin, Lai, Chen, et al., 2018; Lau et al., 2015b). It has been proposed that a joint angle measured while contracting through a full range of motion provides an indication of the muscles ability to actively shorten, the relaxed joint angle provides an indication of the resting muscular stiffness (Clarkson et al., 1992; Muanjai et al., 2019). It is possible that impaired range of motion throughout the recovery process relate to

structural alterations to skeletal muscle and surrounding connective tissue causing a short-term change in the resting length of the muscle. For example, it has been observed that following eccentric exercise, alterations to mechanical properties of muscle result in increased stiffness that persist for several days (Harmsen et al., 2019; Hunter et al., 2012; Lau et al., 2015b; Muanjai et al., 2019; Xu et al., 2019). This may indicate that short term functional decrements are related to changes within muscular and connective tissues that persist throughout the recovery period following damage.

Maximal Isometric Force

Another method commonly used to assess the magnitude of exercise-induced muscle damage involves assessment of the muscle's ability to actively produce force (Warren et al., 1999). Previous research has quantified maximal isometric force in a variety of ways, including eccentric peak torque (Hortobágyi et al., 1998), concentric peak torque (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018), and isometric torque assessed during a maximal voluntary isometric contraction (Deschenes et al., 2000; Gordon et al., 2017), and may be further characterized by the use of isokinetic or isotonic testing (Coratella & Bertinato, 2015; Hortobágyi et al., 1998). Previous research has reported that immediately following an unaccustomed bout of eccentric exercise, isometric torque declines and does not fully recover for up to seven days after the initial bout (Barroso et al., 2010; Byrne et al., 2001; Lau et al., 2015b; Maeo et al., 2018; Muanjai et al., 2019). A commonly cited review by Warren, Lowe, & Armstrong (1999) advocated the use of a maximal voluntary isometric contraction as the gold standard of damage assessment because it is a reliable measure of functional decrements that result from eccentric muscle damage that persists over the entire course of the damage and regeneration process. Additionally, it has been observed that while changes in other non-invasive

measures of exercise-induced muscle damage do not correlate well with each other, all commonly used measures correlate with changes in maximal isometric force (Damas et al., 2016). While other research has reported a shorter time course from recovery, these studies have typically included either physically active or trained individuals However, conflicting research has observed a recovery of isometric torque that lasts for between 48-72 hours (Chan et al., 2012; Coratella & Bertinato, 2015; Falvo et al., 2009). Therefore, it is possible that the inclusion of individuals who may be physically active but are not specifically untrained may influence the duration of the recovery process following damage.

Previous research has observed that maximal voluntary concentric torque of both the elbow flexors and knee extensors remain depressed for up to 5 days following damaging eccentric exercise (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018). The magnitude of strength loss following eccentric exercise has also been shown previously to be related to pre-exercise muscle stiffness (Xu et al., 2019). This would seem to indicate that part of the losses in strength following eccentrics are related to disruptions in efficient force transmission along fascia as well as disruptions to contractile machinery. Indeed, alterations to muscular stiffness have been observed alongside reductions in maximal isometric force (Hunter et al., 2012). Therefore, maximal isometric and isokinetic contractions used to assess changes in strength following damaging eccentrics provide valuable non-invasive measures of recovery of contractile tissue as well as changes in muscular stiffness tied to a functional outcome.

Rate of Force Development

The rate at which force is developed at the onset of contraction has also been used to evaluate neuromuscular changes in response to eccentric exercise (Farup et al., 2016; Hunter et

al., 2012; Jenkins et al., 2014; Macgregor & Hunter, 2018; Peñailillo et al., 2015). Early-phase measures of rate of force development, such as those measured up to 100 ms after force onset, may provide a reliable measure for understanding neuromuscular consequences of damage due to their relationship with the behavior of active motor units (Farup et al., 2016; Van Cutsem et al., 1998; Vecchio et al., 2019). The first study to investigate the effect of damaging eccentric exercise of the elbow flexors on rate of force development at 10, 50, and 100 ms observed decrements following exercise that persisted for up to 48 hours (Jenkins et al., 2014; Peñailillo et al., 2015). However, when assessed over later phases, such as between 200-300 ms, rate of force development more closely reflects differences in mechanical properties of series elastic components and cross-bridge kinetics, and as such, more closely follows the recovery of maximal isometric force (Edman & Josephson, 2007). Jenkins and colleagues (2014) observed that both rate of force development at 200 ms and peak torque were significantly depressed beyond 72 hours post-exercise. Similar results were observed for rate of force development at 300 ms, which was reduced for 72 hours following exercise, while peak torque was only reduced up to 48 hours (Macgregor & Hunter, 2018). While not typical, other studies have also noted depressions in rate of force development for six days or longer (Farup et al., 2016; Hunter et al., 2012).

In support of findings indicated by rate of force development impairments following eccentric exercise, decrements to neuromuscular function have been also been observed within the electromyographic signal following eccentric exercise (Deschenes et al., 2000; Ye et al., 2015). Due to the mechanical stress exerted on the sarcolemma as a result of eccentric exercise, it has been proposed that the velocity of action potential propagation along the sarcolemma may be impaired throughout the recovery process (Nasrabadi et al., 2018; Ochi et al., 2020). Previous

research has indicated a relationship between changes in rate of force development and changes within the EMG signal following eccentric exercise, indicating reductions in neural drive to active muscle (Farup et al., 2016). Indeed, previous research has indicated that muscle fiber conduction velocity impairments following eccentric damage is dependent upon the extent of damage sustained (Bazzucchi et al, 2019). This mechanical disruption seems to also result in short-term excitation-contraction uncoupling representing a dissociation between the delivery of excitation to a muscle and the subsequent development of tension (Choi & Widrick, 2010; Howatson, 2010; Ingalls et al., 1998; Muanjai et al., 2020). Therefore, the measurement of rate of force development provides a unique indicator for assessing the structural and neural determinants of force loss following eccentric exercise.

Factors Influencing the Magnitude of Damage

Previous research has indicated that the degree of muscle damage experienced in response to the same volume of eccentric exercise is also partially dependent upon the muscle group that performs the exercise bout (T. Chen et al., 2019). While slight differences could arise from differences in methodology, including the volume of exercise performed, definition of untrained, and follow up time points, discrepancies in magnitude are largely believed to be the result of the frequency with which a given muscle experiences submaximal eccentric contractions as part of daily activities. For example, it has been observed that the muscle group that experiences the lowest degree of muscle damage is the knee extensors, which regularly experience low-intensity eccentric muscle actions as part of locomotion (T. Chen et al., 2019). Previous research by Chen and colleagues (2018) observed a significantly lower degree of muscle damage of the knee extensors when compared to the elbow flexors, even when the knee

extensors performed double the volume of the elbow flexors. This is also observed to a smaller degree in the trunk musculature, including the latissimus dorsi, erector spinae, and abdominis muscles (T. Chen et al., 2019).

Another important consideration for the magnitude of damage observed is the method of inducing damage. Previous research has utilized a variety of methods to elicit muscle damage, with mixed results. These methods have included eccentric-biased dynamic exercise (Zourdos et al., 2015), eccentric cycling (Mavropalias et al., 2020), traditional resistance training (Falvo et al., 2009; Gordon et al., 2017), and downhill running (Eston et al., 1996). However, the majority of studies have utilized single-joint, eccentric-only isokinetic exercise performed at maximal intensity (T. Chen et al., 2019; T. Chen, Lin, Lai, Chen, et al., 2018; Huang et al., 2019; Ye et al., 2015). Somewhat paradoxically, previous research has indicated that the extent of muscle damage appears to be related to the amount of maximal eccentric work performed rather than the amount of total work performed (Chapman et al., 2008; Mavropalias et al., 2020; Kazunori Nosaka et al., 2002). Therefore, it seems that the magnitude of muscle damage is dependent upon the type of exercise performed, the volume of eccentric exercise, the intensity at which the exercise is performed, and the muscle group performing the exercise.

Repeated Bout Effect

It has long been understood that some of the earliest adaptations to resistance training are neural in nature (Moritani & DeVries, 1979). Previous research has consistently observed that after a single bout of unaccustomed eccentric or isometric exercise, adaptations take place that result in significantly attenuated measures of damage following a secondary exercise bout completed within several days or weeks (Chan et al., 2012; T. Chen et al., 2007, 2016, 2019; T.

Chen, Lin, Chen, Yu, et al., 2018; Hortobágyi et al., 1998; Lau et al., 2015b). This phenomenon has come to be referred to within the literature as the repeated bout effect (Hyldahl et al., 2017; Hyldahl & Hubal, 2014; McHugh, 2003). In a recent review published by Hyldahl and colleagues (2017), it was proposed that this rapid adaptation is likely multifaceted and includes adaptations such as reorganization of the extracellular matrix, alterations to mechanical properties of skeletal muscle and surrounding connective tissue improving the equitable distribution and efficient transmission of force, changes to biochemical signaling patterns increasing the robustness of the response to damage, and alterations to neural recruitment patterns which lead to a more equitable distribution of force output over a greater number of agonist muscle fibers. Each of these proposed mechanisms will be discussed, with particular focus given to proposed neural adaptations.

The observed protective effects following a primary bout of exercise differ not only in their time course and theoretical underpinnings, but also in the observed length of their adaptation. While it is consistently reported that protective effects last between two and six weeks, one study has also reported that damage may be attenuated for approximately six to nine months (K. Nosaka et al., 2001). Nosaka and colleagues (2001) evaluated measures of muscle damage following a damaging upper body exercise bout that was repeated at either six, nine, or twelve months following the initial bout. The results of this study indicate that maximal isometric force recovered significantly more quickly following a repeated bout completed up to nine months after the initial exercise, but changes in circumference and soreness measures were only attenuated at six months. Additionally, it appears as though range of motion decrements did not change over the course of six or nine months but were significantly greater at twelve months.

This seems to highlight the specificity of the repeated bout effect to the measure of damage employed, which may be a function of the underlying mechanism of adaptation.

Previous research has also observed repeated bout effects on isokinetic exercise following an initial bout of a variety of isotonic exercise protocols, indicating that adaptations are relatively nonspecific to the type, intensity, and volume of eccentric exercise performed in the initial bout (H.-L. Chen et al., 2012; T. Chen, 2003; T. Chen et al., 2010, 2013, 2019; Eston et al., 1996; Lavender & Nosaka, 2008; Tseng et al., 2016; Zourdos et al., 2015). However, the literature has consistently reported that if concentric contractions are performed prior to the secondary bout of eccentrics, the muscle appears to become more susceptible to damage during the eccentric bout (Gleeson, 2003; Margaritelis et al., 2015; K. Nosaka & Clarkson, 1997).

Extracellular Matrix Remodeling

In a recently published review article, adaptations within the extracellular matrix were outlined as a primary contributing adaptation to the repeated bout effect (Hyldahl et al., 2017). The extracellular matrix provides a source of passive stiffness, which may reduce skeletal muscle from subsequent injury due to lower average force requirements by myofibers to accomplish similar amounts of mechanical work (Hyldahl et al., 2017). Hyldahl and colleagues (2015) performed global transcriptome analysis in order to evaluate alterations to signaling transcripts in exercised and non-exercised vastus lateralis muscles following ten sets of 10 eccentric contractions at an angular velocity of 35 degrees per second in 35 healthy, untrained subjects. They reported a significant increase in Tenascin-C immunoreactivity two days after the initial bout, which was returned to baseline at 27 days. Additionally, this increase was blunted two days after a secondary bout. Further, increases in collagen I, III, and IV transcripts were not initially

evident at 2 days postexercise, but were all significantly elevated at 27 days. One significant limitation of this study, however, was that although these transcripts were not elevated two days after the secondary bout, measures were not taken 27 days after the secondary bout. Tenascin-C is responsible for the de-adhesion of muscle tissue to the basement membrane, which may contribute to post-exercise force loss (Hyldahl et al., 2015). Changes to extracellular matrix encoding proteins were related to force loss on the first bout, indirectly supporting the hypothesis that this remodeling process introduces short-term reductions in force that eventually contribute to protective effects during a secondary bout. This is in agreement with other research published in this field (Mackey et al., 2011). Mackey and colleagues (2011) performed electrically stimulated contractions of the gastrocnemius for 30 minute periods during repeated bouts separated by one month. This study reported that when Tenascin C immunoreactivity was assessed following the repeated bout, the percent of total area was significantly lower than was observed during the control bout. Additionally, this study observed that collagen types I and III were upregulated to a greater extent following the repeated bout than the initial bout, which occurred at approximately the same time frame as the follow-up analysis that reported similar observations by Hyldahl and colleagues (2015). The results of these studies seem to suggest that in response to damaging exercise, de-adhesion of the extracellular matrix and upregulation of collagen proteins contributes to muscle regeneration and increased passive stiffness, reducing requirements of skeletal muscle if subjected to a similar bout of exercise.

Mechanical Tissue Adaptations

If such an amplification of tissue-encoding proteins is evident following the initial bout of exercise, it seems plausible that this may result in adaptations to tissue mechanics that ultimately improve the efficient distribution and transmission of force during a subsequent

exercise bout on the same limb. Frequently, adaptations to tissue have been evaluated using non-invasive measures such as alterations to the joint angle at which maximum force output is achieved during an isokinetic contraction (T. Chen et al., 2007; McHugh, 2003) as well as differences in the displacement of the muscle-tendon complex over the course of the damaging bout as measured through B-mode ultrasonography (Lau et al., 2015b). Both of these measures are used as a way to non-invasively provide information regarding changes to the series elastic element of skeletal muscle following damaging eccentric exercise. This is a means of providing inferences regarding adaptations to both connective tissue as well as changes to the number of sarcomeres in series. In fact, it has been previously suggested by Chen and colleagues that the time course of the shift in these measures may provide a specific indication on the type of adaptations taking place, where short term shifts in the optimum angle are reflective of sarcomere disruption and exercise-induced muscle damage magnitude, while long-term shifts are likely indicative of an increase in the number of sarcomeres in series, which could theoretically improve force transmission at longer muscle lengths. Likewise, previous research by Lau and colleagues (2015) observed reduced myotendinous displacement of the biceps brachii over the course of ten sets of eccentric contractions, increasing musculotendinous stiffness, improving the transmission of force from active sarcomeres, and reducing damage incurred as a result of a similar number of contractions. Previous research has also assessed changes to the rate of torque development following repeated bouts of exercise with mixed results, which may indicate the presence of both neural and mechanical adaptations following repeated bouts (Mavropalias et al., 2020; Peñailillo et al., 2015).

However, the notion of sarcomerogenesis in response to an acute bout, and thus, as an explanation for the repeated bout effect, has been challenged in recent literature (Hoffman et al.,

2016; Pincheira et al., 2018). Each of these studies evaluated changes in fascicle length-torque curves of the medial gastrocnemius in response to an eccentric exercise bout and reported no changes in muscle mechanical behavior during a repeated bout separated by seven days from the initial bout. These studies also serve to highlight the potential of muscle specificity in understanding the repeated bout effect. Previous studies have reported that the magnitude of the protective effect, and indeed, the extent of damage itself, is specific to the muscle used (T. Chen et al., 2019). It has been proposed that lower body musculature that is regularly exposed to submaximal eccentric motion during walking may display lower susceptibility to exercise-induced muscle damage and a lower overall protection from damage than upper body muscles such as the biceps brachii (T. Chen, Lin, Chen, Yu, et al., 2018). Presumably, this would extend to the gastrocnemius muscle, which is heavily involved in propulsion during walking. Additionally, it is possible that in muscles such as the gastrocnemius, which have relatively long, compliant tendons, more protection is conferred through adaptations within local connective tissue rather than sarcomerogenesis. This may partially explain discrepancies in findings between these and other studies, as these are the only two published studies which have used the gastrocnemius.

Biochemical Signaling Patterns

Damaging eccentric exercise results in necrosis of myofibers and subsequent inflammatory response to remove cellular debris, resulting in the development of secondary damage to the injured muscle (Tidball & Villalta, 2010). This is primarily mediated by the transmigration of neutrophils and monocytes to the damaged tissue, which then initiate a pro-inflammatory response (Peake et al., 2017). Among these responses are processes mediated by nuclear factor-kappa B (NF-κB), which then increases expression of proinflammatory proteins

such as monocyte chemoattractant protein-1 and interleukin-6 (Pahl, 1999). Therefore, it is plausible that reductions in these proinflammatory proteins may partially mediate the repeated bout effect by reducing the magnitude of secondary damage. This may theoretically provide a mechanism for reduced soreness (lower infiltration of monocytes, lower sensitivity of afferent nerve endings), reductions in muscle force output (less damage to myofibers, improved transmission of force), and lower leakage of intracellular proteins such as creatine kinase (lower secondary damage, less permeability of cellular membrane to leaking of intracellular components). There seems to be some support for this within the literature. Pizza and colleagues (1996) reported a reduction in leukocyte receptors within the bloodstream following a secondary bout of exercise. Likewise, this same group also reported significantly lower numbers of circulating neutrophils following a secondary bout of exercise (F. Pizza et al., 2001). Lastly, Smith and colleagues (2007) reported significant attenuations of MCP-1 and IL-6 following a secondary bout of damaging exercise, as well as a significant increase in the production of anti-inflammatory IL-10. Further, previous research by Xin and colleagues (2014) reported significant reductions of NF-κB binding activity following a secondary bout, which would seem to indicate a less robust signaling response for the amplification of damage following completion of a secondary bout on the contralateral limb. However, a systemic response such as this would likely confer protective effects to muscles other than the injured muscle and contralateral homologous muscle, however, as will be discussed in subsequent sections, this has currently not been observed to be the case.

Neural Adaptations

Following a bout of unaccustomed exercise, the majority of muscle damage is sustained by Type II muscle fibers (Friden et al., 1983; Macaluso et al., 2012). This results in changes to

neuromuscular recruitment strategies favoring lower recruitment of high-threshold motor units that persists throughout recovery (Macgregor & Hunter, 2018; Nardone et al., 1989; Ye et al., 2015). Similar changes have been observed prior to a repeated bout of eccentric exercise once the muscle has fully recovered (Hight et al., 2017). This would seem to indicate that in response to muscle damage, high-threshold motor units display impaired excitability, and to compensate for losses in force output, a greater degree of central drive to low-threshold motor units results in earlier recruitment and increased mean firing rates (Ye et al., 2015). However, in response to this challenge, the neuromuscular systems adapt to favor increased recruitment of lower-threshold motor units to more efficiently distribute force across the active muscle should the exercise be repeated (Hight et al., 2017; Starbuck & Eston, 2012; Tsuchiya et al., 2018). Neural adaptations that may partially explain enhanced excitability of the motor unit pool include increased corticospinal excitability (Goodall et al., 2017), alterations to inhibitory circuitry following pain and damage (Alhassani et al., 2019; Hosseinzadeh et al., 2013, 2015; Pitman & Semmler, 2012), reduced antagonist co-activation (Dartnall et al., 2011; Hight et al., 2017), and increases in motor unit synchronization at low force thresholds (Dartnall et al., 2011). Previous research has indicated that low-threshold motor units display lower levels of short term synchronization than high-threshold motor units, possibly attributable to increased input from afferent feedback (Defreitas et al., 2014). If the motoneuron pool becomes more excitable in response to a single bout of exercise and inhibitory feedback is reduced, it is plausible that low-threshold motor units are synchronized to a greater degree, providing a more efficient distribution of force production among low-threshold motor units and reducing overall requirement for activation of high-threshold motor units on a subsequent bout.

Previous research has indicated that during a repeated bout of eccentric exercise, median power frequency of the EMG spectrum is reduced as well as earlier recruitment and higher mean firing rates of active motor units (Dartnall et al., 2011; Hight et al., 2017; Starbuck & Eston, 2012). Hight and colleagues (2017) observed a steeper slope in the regression line for the relationship between mean firing rate and recruitment threshold of active motor units during contractions at 80% MVIC, indicating increased firing rates and reduced recruitment threshold of active motor units. Interestingly, similar changes were not observed during contractions at 50% MVIC, which may indicate a specificity of adaptation within high-threshold motor units. Previous research has indicated that in response to experimental muscle pain, high-threshold motor units are recruited earlier and discharge more frequently (Martinez-Valdes et al., 2020). This would seem to indirectly support the notion that during the early stages of eccentric exercise, high-threshold motor units are recruited to meet force demands, resulting in preferential damage to those types of motor units. However, throughout the recovery process and as a protective mechanism against similar insult, a greater proportion of force output is derived from increased firing of low-threshold motor units (Hight et al., 2017; Starbuck & Eston, 2012).

Another method for evaluation of changes in recruitment strategy following repeated eccentrics include changes in the electromyographic (EMG) signal. While studies have reported changes in EMG signal parameters during a repeated bout of exercise, findings are inconsistent (T. Chen, 2003; Falvo et al., 2009; Hortobágyi et al., 1998; Nasrabadi et al., 2018; Pincheira et al., 2018; Starbuck & Eston, 2012; Tesch et al., 1990). In general, measures of changes in EMG amplitude have indicated no change across time or between bouts in response to eccentrics (T. Chen, 2003; Falvo et al., 2009; Pincheira et al., 2018; Starbuck & Eston, 2012; Tesch et al., 1990). However, reductions in median power frequency during repeated bouts of eccentrics have

been repeatedly observed (T. Chen, 2003; Pincheira et al., 2018; Starbuck & Eston, 2012). Reductions in EMG median power frequency in response to repeated eccentric bouts have typically been attributed to either increased recruitment of low-threshold motor units or increased conduction velocity indicating faster propagation of action potentials along the sarcolemma (Nasrabadi et al., 2018; Starbuck & Eston, 2012). Taken together, these findings support the notion of alterations to neural recruitment strategies that may facilitate a more efficient transfer of force on subsequent bouts, resulting in less damage.

Neural adaptations to an unaccustomed bout may also include adaptations within intracortical, corticospinal, or spinal inhibitory networks, resulting in changes to activation characteristics on a repeated bout (Goodall et al., 2017; Prasartwuth et al., 2019; Škarabot et al., 2019). Previous research has indicated that following unaccustomed eccentrics, motor corticospinal drive is compromised, but this response is attenuated following a repeated bout (Goodall et al., 2017). While Goodall and colleagues did not observe significant alterations to inhibitory responses, other studies have observed attenuated reductions in corticospinal silent period duration during a repeated bout, indicative of better maintenance of inhibitory networks following a repeated bout (Škarabot et al., 2019). This has been further supported by previous research observing changes to pain sensitivity and nociceptive withdrawal reflexes following a repeated bout of eccentrics (Hosseinzadeh et al., 2013, 2015; Lau et al., 2015a). Therefore, neural adaptations to repeated bouts of eccentric exercise include enhanced neural drive to active muscles, earlier recruitment of the motor unit pool and increased firing rates of active motor units, attenuated reductions in corticospinal inhibition following a repeated bout, and desensitization of nociceptive afferents resulting in lower sensitivity to painful stimuli following

a repeated bout (Dartnall et al., 2011; Goodall et al., 2017; Hight et al., 2017; Hosseinzadeh et al., 2013, 2015; Lau et al., 2015a; Škarabot et al., 2019).

Neural Adaptations to Short-term Resistance Training

Neural adaptations may occur very early in the adaptation response, following short-term or even acute exposure to a stimulus (Alhassani et al., 2019; Goodall et al., 2017; Martinez-Valdes et al., 2020; Prasartwuth et al., 2019; Schabrun et al., 2016). It is well known that musculoskeletal pain, as may be seen following damaging eccentric exercise, reduces function of the affected limb; however, some degree of this impairment is transferred to the contralateral limb (Halperin et al., 2014; Hedayatpour et al., 2018). Presumably, this transfer of functional decrements to an uninjured homologous muscle would necessarily be the result of adaptations to the central nervous system resulting in increased communication and transfer of information between hemispheres of the brain. Previous research by Alhassani and colleagues (2019) sought to further examine this phenomenon by assessing changes to measures of interhemispheric inhibition in response to musculoskeletal pain induced by hypertonic saline injection into the first dorsal interosseous muscle. Interhemispheric inhibition was measured via motor evoked potentials to both the involved and uninvolved motor cortex using transcranial magnetic stimulation before pain was induced, as well as immediately after and 30 minutes after pain had been completely resolved. The results of this study indicated that hypertonic saline injection resulted in significant reductions in corticomotor excitability and interhemispheric inhibition that persisted for 30 minutes after the resolution of muscle pain, and was moderately correlated with the degree of reported muscle pain in the affected limb.

Previous research has also indicated that a single bout of damaging eccentric exercise results in a rapid adaptation response that results in increased corticospinal excitability during a repeated bout performed on the same limb (Goodall et al., 2017). Interestingly, this study also reported reductions in resting twitch measures that persisted for up to seven days, which is in line with previous research evaluated using tensiomyography (Harmsen et al., 2019) and electromechanical delay (Howatson, 2010). This would seem to further support the idea of excitation-contraction uncoupling in response to eccentric exercise induced muscle damage (Ingalls et al., 1998; Muanjai et al., 2020). Interestingly, Goodall and colleagues (2017) reported that although potentiated twitch force was higher in bout 2, changes in resting twitch force were not significantly different between bouts. This study evaluated measures of voluntary activation using both motor point and motor cortex stimulation, and reported that although voluntary activation using motor point stimulation was unchanged between the first and second bouts of damaging exercise, motor cortex stimulation resulted in attenuated reductions in voluntary activation following the 2nd bout of exercise and a faster recovery. The authors state that this may indicate that reductions in maximal voluntary contraction force are the combined result of persistent central fatigue as well as suboptimal motor output from the cortical regions.

Recent research has also indicated that the intensity of exercise may influence the magnitude of central adaptations experienced in response to an acute bout (Andrews et al., 2019). Andrews and colleagues (2019) evaluated changes to synaptic plasticity, as measured by changes to corticomotor excitability, short- and long-interval intracortical inhibition, and intracortical facilitation using repetitive transcranial magnetic stimulation as well as intermittent theta burst stimulation, in response to either moderate intensity continuous exercise or high-

intensity interval exercise. This study reported increases in corticomotor excitability, short-interval intracortical inhibition, and the intracortical facilitation ratio following high-intensity interval exercise compared to the rest condition. However, several limitations should be noted for this study, including a small (n=20), heterogeneous sample of recreationally active males and females between the ages of 21-64 years old. Second, the interval training was matched to the continuous training based on total exercise duration, not overall workload, which resulted in significantly greater exercise workload completed during the high-intensity interval training sessions. This study measured changes in TMS variables using the first dorsal interosseous muscle for EMG assessment, but performed a lower body cycling protocol for each exercise session. Lastly, because cycling largely consists of concentric contractions, it is not known exactly how the results from this study may apply to a study using unilateral eccentric exercise. While speculative, the results of this study seem to indicate that changes to synaptic plasticity following exercise are largely intensity-dependent, which may indicate that eccentric exercise results in greater synaptic plasticity than concentric exercise (i.e. cycling).

Cross-Education of Strength

The cross-education of strength is a well-characterized phenomenon in which a muscle experiences an increase in strength in response to prolonged training of the contralateral, homologous limb (Boyes et al., 2017; Carr et al., 2019). Original observations of the cross-education effect date to the late 19th century, when Scripture and colleagues (1894) reported that following 13 days of unilateral hand training, the contralateral hand increased strength to a slightly lesser degree than the trained hand. In light of these results, the authors state that it appears that the transfer of skill to an untrained limb appears to be of neural origin. Further, recent research has observed that in response to two weeks of isometric exercise, maximal

voluntary isometric force as well as late-phase rate of force development were significantly increased in the untrained arm, while early phase rate of force development was significantly increased after three weeks of training (Carr et al., 2019). Additionally, it has been repeatedly observed that unilateral training results in significantly increased rate of EMG rise during isometric contractions of the untrained limb, which may be indicative of increased motor unit activity at contraction onset (Carr et al., 2019; Ruddy et al., 2016). Shifts in motor unit activity toward increased activity of low-threshold motor units have been reported in response to an acute eccentric bout, but have currently not been evaluated on a contralateral limb following an acute bout of exercise (Hight et al., 2017).

More recent support for this hypothesis have stated that the mechanisms responsible for the cross-education effect are believed to be primarily neural in nature (Ruddy & Carson, 2013). In this review, two potential mechanisms for the neural cross-transfer of skill acquisition are elucidated: the bilateral access and cross-activation hypotheses. The bilateral access hypothesis states that unilateral task training results in the generation of motor engrams that are then stored in a common repository that is accessible by both hemispheres of the brain, allowing the contralateral limb to also experience a learning effect, and this hypothesis tends to be more closely associated with fine motor skill acquisition. On the other hand, the cross-activation hypothesis states that although motor activity is lateralized within the motor cortex, unilateral activity also results in a small degree of activation of the contralateral motor cortex, inducing neuroplastic effects. This hypothesis tends to be more closely associated with high-intensity activity (i.e. maximal eccentric exercise). Changes to corticomotor excitability have also been observed in response to 4 weeks of high-load resistance training (Kidgell et al., 2011). Kidgell and colleagues (2011) reported that following eccentric-concentric training of the elbow flexors

using unilateral dumbbell exercise, participants displayed a 28% increase in maximal elbow flexor strength as well as approximately a 30% increase in corticomotor excitability as measured from TMS at three different intensities. An interesting finding of this study was that these increases also experienced a degree of transfer to the contralateral, untrained arm, indicating that strength training may increase corticomotor excitability even in muscles that do not receive a mechanical stimulus. While these findings may appear in contrast to the observations of Ruddy and colleagues (2016), it is important to note that this study utilized a ballistic wrist flexion exercise protocol, compared to the dumbbell elbow flexor exercise used by Ruddy et al., which may partially explain the discrepancy in findings.

The studies mentioned above support the notion that unilateral resistance training may produce increases in muscular strength in an untrained limb through neural mechanisms. However, it appears that increases in strength may take as long as two weeks of training to manifest in an untrained limb. In response to a single eccentric exercise bout, it has been observed that protective effects against subsequent damage are transferred to the homologous muscle of the contralateral limb as well (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018; Howatson & van Someren, 2007; Starbuck & Eston, 2012). This contralateral repeated bout effect is hypothesized to be primarily the result of neural adaptations that are transferred to the contralateral limb, but this has largely gone unexplored (Hyldahl et al., 2017).

Contralateral Repeated Bout Effect

Perhaps some of the most compelling evidence of the occurrence of the role of neural adaptations following an unaccustomed bout of exercise are that previous research has reported that protective effects are conferred to the homologous muscle of the contralateral limb, which

has subsequently come to be known within the literature as the contralateral repeated bout effect (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018; T. Chen, Lin, Lai, Chen, et al., 2018; Connolly et al., 2002; Howatson & van Someren, 2007; Starbuck & Eston, 2012; Xin et al., 2014). The first study to investigate potential cross-transfer of protective effects was published by Connolly and colleagues (2002). This study utilized a step-up protocol in which participants were asked to step onto a 46 cm step with one leg before lowering themselves onto the ground with the other leg at a cadence of 15 steps per minute, and repeating the same protocol using the opposite leg two weeks later. Indicators of damage used in this study included measures of soreness, tenderness, and decrease in isometric force. Results from this study indicated that tenderness and strength responses were not significantly different between bouts. However, it is important to note that this study utilized a dynamic exercise protocol on a step of moderate height, and the authors make no mention of what was done to correct the effects of fatigue over the course of the 20 minute exercise protocol. Further, this is the only study published on contralateral transfer effects that has not employed an ipsilateral control group from which to make comparisons, calling into question the effect of performing concentric and eccentric exercise simultaneously. Therefore, it is possible that the lack of observed differences may be due to the experimental protocol employed. Additionally, no mention was made as to the training status of the participants, which is particularly important for cross-transfer of the lower limbs. Subsequent studies in this area have consistently reported protective effects between limbs. For example, Howatson & van Someren (2007) reported that following a damaging bout of isokinetic exercise on the contralateral limb, multiple damage indicators were significantly lower in the contralateral group (i.e. creatine kinase, muscle soreness, isometric force) than following the initial bout on the opposite limb. The authors further speculate that the observed differences

between the contralateral and ipsilateral groups suggest a differential adaptation, as differences following a bout of the ipsilateral limb include cellular, mechanical, and neural adaptations (as outlined in Hyldahl et al., 2017), while the contralateral limb experiences no mechanical disruption as a result of the initial bout and presumably doesn't receive the local cellular adaptations that the initially exercised limb does. These observations have since been supported in subsequent research, with contralateral protective effects observed following damaging eccentric exercise in both the elbow flexors (T. Chen et al., 2016) and knee extensors (T. Chen, Lin, Chen, Yu, et al., 2018), with the time course for adaptations ranging from as little as one day following the initial bout of exercise to as long as four weeks. Previous research has observed changes to neuromuscular parameters in the contralateral limb as a result of unaccustomed eccentrics, including attenuated sensitivity to nociceptive reflexes as well as reduced median power frequency of the EMG signal (Hosseinzadeh et al., 2015; Starbuck & Eston, 2012). Importantly, each of these studies also noted no significant differences between responses in ipsilateral and contralateral limbs during the repeated bout, indicating the potential for a neural mechanism that is shared at either the spinal or supraspinal level, rather than through peripheral mechanisms.

Previous research has also indicated that the contralateral repeated bout effect may be partially explained by alterations to the inflammatory response (Xin et al., 2014). While at face value this would seem to indicate the cross-transfer of inflammatory effects from the initial bout, it is important to note that because the inflammatory response is a feature of primary damage to skeletal muscle following eccentric exercise, and damage indicators were reduced during the repeated bout, it is somewhat unsurprising that measures of inflammation were lower during the repeated bout, as there was likely less damage to the myofibrillar ultrastructure. This finding also

does not preclude the presence of a neural transfer mechanism, as it is possible that neural adaptations preceded the development of inflammation during the repeated bout. To date, the only study to directly investigate potential neural adaptations as a mechanism for contralateral protective effects on repeated bouts of eccentrics was conducted by Starbuck & Eston (Starbuck & Eston, 2012). This study utilized an elbow flexor damage model in which untrained participants were required to complete 60 eccentric contractions at an angular velocity of $30°\cdot s^{-1}$ separated by two weeks. Measures of muscle damage included isometric strength loss, muscle soreness assessed during active flexion and extension, and the resting arm angle. Additionally, surface electromyography was assessed using the median power frequency and peak EMG amplitude from EMG signals collected from the biceps brachii. The results of this study indicated that both groups (contralateral and ipsilateral) displayed a significant reduction in median power frequency during bout 2 compared to bout 1, with no significant differences between groups. Interestingly, the authors suggest that the lack of difference in EMG amplitude is indicative of a similar number of motor units recruited, which, taken in concert with the reductions in median power frequency, would seem to suggest an increased reliance on low threshold motor units, as has been suggested previously (Enoka, 1996; Warren et al., 2000). Furthermore, some of the more compelling evidence that the contralateral repeated bout effect is likely caused in large part by an intensity-dependent centrally mediated mechanism is the observation of previous studies which have reported that short-term protective effects may be observed in both the ipsilateral and contralateral limb even when the initial bout of exercise consists of isometric contractions not performed in sufficient quantity so as to cause damage (T. Chen, Lin, Chen, Lai, et al., 2018; Tseng et al., 2016). As a matter of fact, Chen and colleagues (2018) reported that two maximal voluntary isometric contractions performed up to 4 days prior

to a subsequent bout of damaging eccentric exercise resulted in significantly lower measures of damage compared to a group that received no isometric bout.

Research Questions

Does unaccustomed eccentric exercise result in a protective effect following a repeated bout on the ipsilateral and contralateral limbs?

Does unaccustomed eccentric exercise result in alterations to motor unit firing characteristics prior to a repeated bout of exercise on either the ipsilateral or contralateral limb?

Do changes to motor unit firing characteristics following an unaccustomed bout of eccentric exercise relate to changes in muscle damage indicators following a repeated bout of eccentric exercise on either the ipsilateral or contralateral limb?

Hypotheses

It is hypothesized that an unaccustomed bout of eccentric exercise will result in a rapid adaptation response resulting in reductions in measures of exercise-induced muscle damage following a repeated bout of eccentric exercise on both the ipsilateral and contralateral limbs.

It is hypothesized that unaccustomed eccentric exercise results in alterations to motor unit firing characteristics observed prior to a repeated bout of eccentric exercise on both ipsilateral and contralateral limbs.

It is hypothesized that a moderate relationship will be observed between changes in motor unit firing characteristics between an initial and repeated bout and reductions in indices of muscle damage observed following the performance of a repeated bout on the ipsilateral and contralateral limbs.

CHAPTER 3: METHODOLOGY

Participants

A total of 20 untrained male participants between the ages of 18 and 35 were enrolled in this study. Of the original sample, one participant in the control group was removed due to non-compliance with the study protocol, and four were lost to follow-up due to COVID-19 related lab shutdowns. A total of 15 participants completed the study protocol. This study was approved by the University of Central Florida Institutional Review Board (ID#: STUDY00000740). Following an explanation of all procedures, risks and benefits, each participant provided his written informed consent prior to participation in this study. Participants were required to be free from disease or physical limitations as determined by medical health and activity questionnaire (MHAQ) and physical activity readiness questionnaire (PAR-Q+), and having participated in no upper body resistance training during the past 6 months. Participants currently taking anabolic steroids or any other ergogenic aid (e.g., creatine, beta alanine, branched chain amino acids, etc.), currently taking over the counter or prescription medication (e.g. NSAIDs), or who were otherwise unwilling or unable to comply with the research protocol were excluded from the study. Participants were randomly assigned to either an exercise group (EX; n=9; height: 173.4 ± 8.4; mass: 76.8 ± 9.1; age: 21.1 ± 2.5; %body fat: 23.0 ± 6.9) or control group (CON; n=6; height: 181.4 ± 6.9; mass: 82.1 ± 17.1; age: 21.7 ± 2.2; %body fat: 18.5 ± 7.8).

Procedures and Design

This study utilized a randomized, counterbalanced, parallel group design. Each participant completed a total of eight visits to the Exercise Physiology Intervention and Collaboration (EPIC) Lab. During the first visit, participants provided written informed consent

and completed an MHQ, and PARQ+. Participants also completed the first of two familiarization (FAM) sessions. Participants were provided with instruction and a demonstration on how to perform maximal voluntary isometric contractions and submaximal trapezoidal muscle actions using visual feedback on a computer monitor. Participants were also provided instruction on how to perform the damaging eccentric exercise protocol (FAM1). Participants did not complete any isometric or eccentric muscle actions during the first session in order to minimize potential protective effects of low load or isometric contractions (Lavender & Nosaka, 2008; Tseng et al., 2016). However, participants observed a member of the research team performing all assessments. At least 24 hours later, participants reported back to the EPIC Lab for visit 2. Visit 2 consisted of anthropometrics, body composition analysis via bioelectrical impedance analysis (BIA), and a second familiarization session (FAM2). Hydration status was tested prior to BIA analysis to ensure adequate hydration. For FAM2, participants completed maximal voluntary isometric contractions (MVIC), and submaximal trapezoidal muscle actions up to 50% and 80% of MVIC on both limbs. Seven days after the completion of FAM2, participants returned for visit 3 where baseline (BL) measures of range of motion (ROM), pain pressure threshold (PPT), muscle soreness using a visual analog scale (VAS), and maximal voluntary isometric contractions (MVIC) were assessed, followed by trapezoidal contractions at 50% and 80% MVIC. Participants assigned to EX then completed a bout of eccentric exercise designed to elicit muscle damage of the elbow flexors on the dominant arm (ECC1). ROM, PPT, VAS and MVIC assessments were repeated immediately post-exercise (IP), twenty-four (24H) and seventy-two hours (72H) later (visits 4 and 5, respectively). Fourteen days later (±1 day), participants returned for visit 6 where the same exercise bout was repeated on both the dominant (i.e. ipsilateral) and non-dominant (i.e. contralateral) elbow flexors in a randomized order (ECC2-IL

and ECC2-CL, respectively). CON completed all testing assessments but did not complete the eccentric exercise bout. ROM, PPT, VAS and MVIC assessments were completed prior to both repeated bouts, while trapezoidal contractions at 50% and 80% MVIC were completed on both limbs prior to the initial repeated bout only. The second repeated bout occurred 30 minutes after the completion of the first repeated bout. ROM, PPT, VAS and MVIC assessments were repeated immediately following each repeated bout, and at twenty-four (24H) and seventy-two hours (72H) post-exercise (visits 7 and 8, respectively). Rate of torque development (RTD) at 50 ms (RTD_{50}), 100 ms (RTD_{100}), 200 ms (RTD_{200}), and peak RTD (RTD_{peak}) were extracted from each MVIC. Participants were asked to avoid caffeine and alcohol consumption for a minimum of 24 hours prior to all assessments. Additionally, all assessments were completed at the same time of day (±1 hour) as ECC1. A timeline of the study procedures is presented in Figure 1.

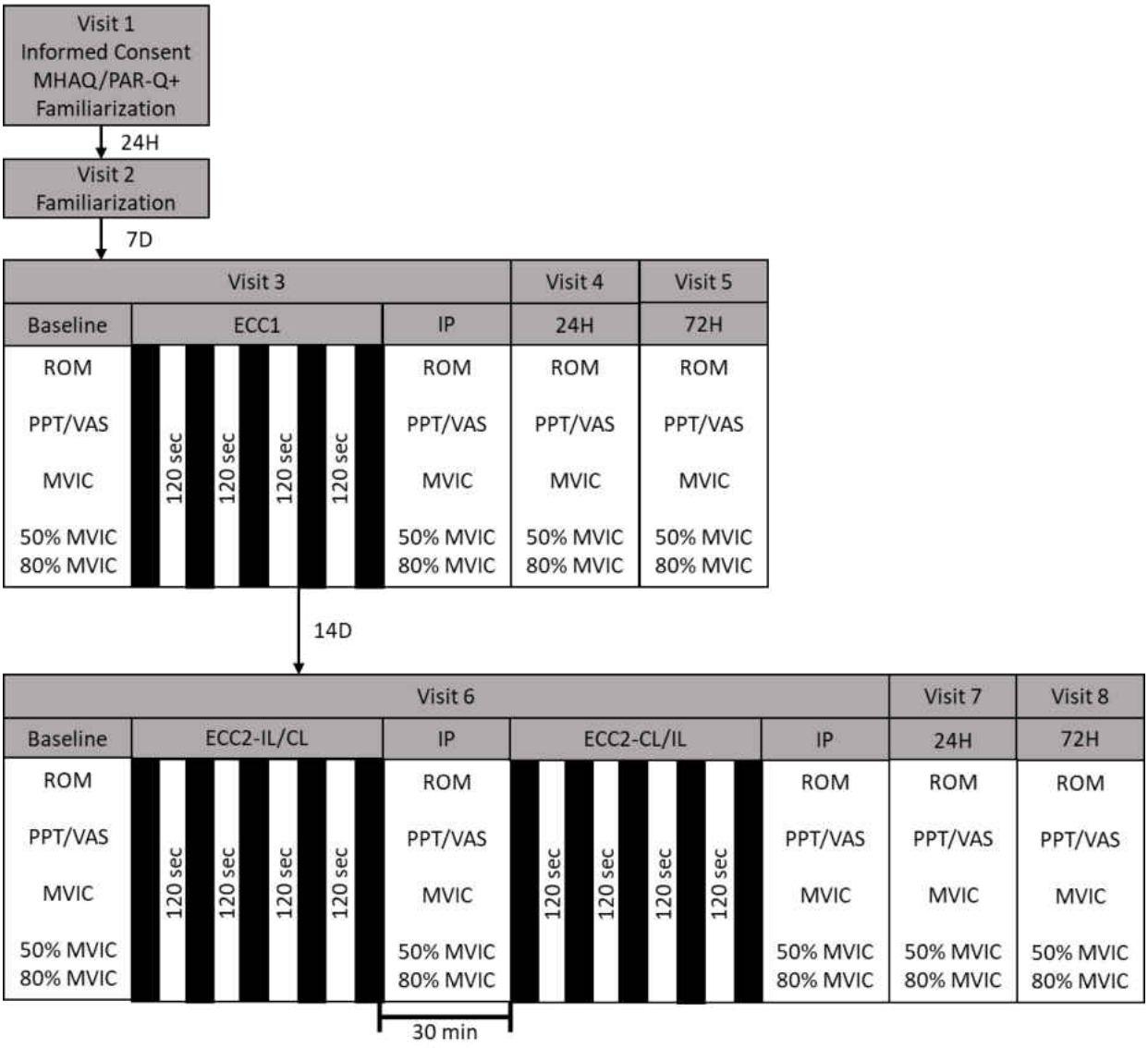


Figure 1. Illustration of study design.

MHAQ = Medical history and activity questionnaire; PAR-Q+ = Physical activity readiness questionnaire; ROM = Range of motion; PPT = pain-pressure threshold; VAS = visual analog scale; MVIC = maximal voluntary isometric contraction; ECC1 = initial eccentric exercise bout, ECC2-IL = repeated bout on ipsilateral arm, ECC2-CL=repeated bout on contralateral arm; IP = immediately post-exercise; 24H = 24 hours post-exercise; 72H = 72 hours post-exercise.

Hydration Status

Prior to the assessment of body composition, urine specific gravity via refractometry was assessed to determine hydration status (USG; Human Urine Refractometer, MISCO

Refractometer, Cleveland, OH, USA). To be considered adequately hydrated and permitted to continue with body composition testing, participants were asked to provide a urine sample in a sterile container. A drop of urine was placed on the refractometer for the determination of urine osmolarity, and participants were considered euhydrated if urine specific gravity was ≤1.020. If the participant was not properly hydrated at the time of assessment, they were asked to drink water until proper hydration was achieved, or their visit was rescheduled.

Body Composition Assessment

Anthropometric and body composition measurements were completed during visit 2 prior to FAM2. Body mass (±0.1 kg) and height (±0.1 cm) were determined using a Health-O-Meter Professional scale (Model 500 KL, Pelstar, Alsip, IL, USA). Body composition was assessed using bioelectrical impedance analysis (BIA; Inbody 770, Inbody Co., LTD, Seoul, SK). Participants were asked to report to the laboratory a minimum of four hours fasted and in a euhydrated state. After removing their shoes along with any jewelry, participants were asked to wipe the palms of their hands as well as the soles of their feet prior to placing their feet onto electrodes mounted within the base of the BIA system. Participants were instructed to lift the hand electrodes out of their mounting handles and stay as still as possible with their arms fully extended and sufficiently abducted to prevent contact of the upper arm with the torso during the assessment.

Range of Motion (ROM)

ROM was evaluated using a manual goniometer. Participants were asked to stand with their arm unsupported and let their arm hang by their side in a supinated position. A semi-permanent marker was used to mark the lateral epicondyle of the humerus, the acromion process

of the scapula, and the styloid process of the radius. Participants were then asked to fully flex the arm by touching their palm to their shoulder while simultaneously keeping their elbow at their side. Three measurements were taken, and both the mean flexed elbow joint angle and mean relaxed elbow joint angle were calculated from these measurements. Elbow joint ROM was determined as the difference between the mean relaxed and flexed elbow angles. Elbow range of motion measurements demonstrated a high degree of reliability ($ICC_{3,1}$=0.84, SEM=3.97 degrees).

Muscle Soreness (VAS) and Pain-Pressure Threshold (PPT)

The magnitude of muscle soreness was assessed using a VAS consisting of a 100-mm line with the far left (0-mm) hash mark representing "no pain" and the far right (100-mm) hash mark representing "very, very painful". Subjects were asked to indicate their level of soreness by marking an X on the line while an investigator provided a standardized reference stimulus through palpation of the mid-belly (proximal) as well as the distal portion of the biceps brachii using a pressure algometer (FPX 10; Wagner Instruments, Greenwich, CT, USA). The probe head of the algometer was placed perpendicular to the middle and distal sites of the elbow flexors, and pressure was applied at a rate of approximately 1 kg per second until the participant reported the first feeling of noticeable pain, at which point the algometer was removed from the skin. Pressure readings were obtained at a sampling rate of 100 Hz. PPT was defined as the highest force recorded prior to the development of noticeable pain. Both proximal and distal PPT measurements demonstrated a high degree of reliability (proximal PPT: $ICC_{3,1}$= 0.90, SEM=0.71 N/cm^2; distal PPT: $ICC_{3,1}$= 0.93, SEM=0.83 N/cm^2).

Maximal Voluntary Isometric Contraction (MVIC) Torque

Participants were seated in an isokinetic dynamometer (Biodex System 4, Biodex Medical Systems, Inc., Shirley, NY, USA) and secured to the chair using two shoulder straps as well as a pelvic strap secured across the hips for the assessment of isometric strength during a MVIC of the elbow flexors. The upper arm was supported by an arm rest with the shoulder at 45° of shoulder flexion from anatomical position. Chair and dynamometer settings were adjusted for each participant to properly align the axis of rotation of the lever arm with the lateral epicondyle of the humerus and maintained consistent for all isometric assessments. All maximal and submaximal torque testing was completed at 90° of elbow flexion with the wrist supinated. Participants completed a standardized warm-up consisting of three 10-second contractions at approximately 50% of self-perceived MVIC, with 10 seconds of rest provided in between each contraction. Participants were then allowed 60 seconds of rest before completing three 5-second MVICs with 3 minutes of rest between each attempt. MVIC was defined as the highest 500-ms epoch during the completion of the three isometric contractions and was used to standardize the submaximal testing among participants. Torque signals were sampled at 1,926 Hz using a differential amplifier (Delsys Trigno, Delsys, Inc., Natick, MA, USA) and filtered using a fourth order low-pass Butterworth filter at 150 Hz, which is consistent with previously published recommendations for the collection and analysis of torque signals (Thompson, 2019). RTD was measured as the slope of the torque-time curve at 50-, 100-, and 200- ms from the onset of isometric torque production, as well as RTD_{peak}. The onset of torque was determined using a manual onset technique in which the amplitude of the baseline signal was estimated from plots of torque data and torque onset was established as the point in which a visual deviation from the baseline mean above the amplitude of the baseline signal was observed. Torque onset and all

RTD variables were determined using custom-written MATLAB programs (MATLAB 2019a, Mathworks, Inc., Natick, MA, USA). MVICs which demonstrated a significant deviation from rest prior to onset were not used for analysis. All RTD variables and MVICs demonstrated a high degree of reliability (RTD_{50}: $ICC_{3,1}$=0.91, SEM=168.35 N*m/s; RTD_{100}: $ICC_{3,1}$=0.95, SEM=91.73 N*m/s; RTD_{200}: $ICC_{3,1}$=0.96, SEM=39.71 N*m/s; RTD_{peak}: $ICC_{3,1}$=0.86, SEM=281.35 N*m/s; MVIC: $ICC_{3,1}$=0.91, SEM=8.76 N*m).

Submaximal Muscle Actions

Participants were familiarized with submaximal muscle actions seven days before the completion of the first eccentric exercise bout. Familiarization consisted of completion of an MVIC of the ipsilateral arm followed by submaximal trapezoidal muscle actions at 50% and 80% MVIC, which was then repeated on the contralateral arm. Immediately prior to each damaging exercise bout, MVIC and submaximal muscle actions were completed on the ipsilateral (ECC1-IL and ECC2-IL) and contralateral (ECC1-CL and ECC2-CL) limbs. In order to evaluate MU firing characteristics, surface electromyography signals were collected during the completion of submaximal muscle actions at 50% and 80% MVIC of the limb performing the contraction. Prior to testing, participants were provided with a demonstration of both the 50% and 80% submaximal isometric trapezoidal contractions with visual feedback for familiarization. Isometric trapezoidal contractions consisted of participants increasing isometric torque in a controlled manner from 0-50% MVIC over the course of five seconds, maintaining 50% MVIC for 10-seconds, and then decreasing isometric torque in a controlled manner from 50-0% MVIC in five seconds. The total contraction time for 50% MVIC muscle actions was 20 seconds. Immediately after completion of the 50% MVIC muscle actions, a similar protocol was

completed at an isometric torque output of 80% MVIC. Participants increased isometric torque from 0-80% MVIC in six seconds, maintained a torque output of 80% MVIC for four seconds, and steadily decreased isometric torque from 80-0% MVIC in six seconds. The total time per contraction at 80% MVIC was 16 seconds. Visual feedback of the real-time torque output was provided alongside a template showing the target torque output for the duration of the contraction. Participants were instructed to maintain their torque output as close as possible to the target torque template. Torque steadiness was defined as the two second period with the smallest coefficient of variation ([CV]; [SD/mean] x 100) during the period of constant torque production during the submaximal muscle actions. Torque steadiness was calculated using a custom-written MATLAB program (MATLAB 2019a, Mathworks, Inc., Natick, MA, USA) and was used to evaluate mean firing rate characteristics during submaximal muscle actions following EMG decomposition procedures.

Surface EMG Signal Recording

Surface electromyographic (sEMG) signals were recorded from the biceps brachii during each submaximal muscle actions using a Trigno 16-channel wireless EMG system (Delsys, Inc., Natick, MA, USA). Prior to the placement of EMG electrodes, the skin was shaved with a medical razor and dead skin cells as well as other debris were removed with hypo-allergenic tape, followed by cleaning with an isopropyl alcohol wipe. MU firing characteristics of the biceps brachii were evaluated during submaximal muscle actions immediately following the completion of MVIC assessment using surface electromyography. A surface sensor array consisting of four pin electrodes with an interelectrode distance of 5 mm was placed at 2/3 of the distance between the medial acromion and the fossa cubit, with an active reference electrode

placed on the brachioradialis. Electrodes were firmly secured to the skin using medical tape and traced with semi-permanent marker to ensure consistency of placement between exercise bouts. Surface EMG signal quality was verified prior to the beginning of submaximal muscle actions through completion of a submaximal trapezoidal contraction at 20% MVIC (i.e. line interference <1.0, signal-to-noise ratio >3.0, and baseline noise <2.0 μV RMS). In the event that signal quality checks were not acceptable, investigators performed additional skin conditioning procedures (e.g. shaving, reapplication of alcohol, etc.).

Surface EMG Signal Decomposition

Four filtered sEMG signals were collected at a sampling rate of 2,222 Hz and decomposed into their constituent motor unit action potential trains (MUAPTs). These trains were used to calculate a time-varying firing rate curve for each detected MU. Firing rate curves were smoothed with a 1-s Hanning filter and selected from the 2-s portion of the constant-torque portion of the submaximal muscle actions with the lowest torque CV, as determined by custom-written lab software (MATLAB 2019a; Mathworks, Inc., Natick, MA, USA). High-threshold motor units that were not active during the entire 2-s portion of the complete firing rate curve were not considered for subsequent analysis. Recruitment threshold (RT), defined as the relative torque at which the MU first discharged, and mean firing rate (MFR), defined as the average number of pulses per second during the 2-s steadiness portion in each individual MUs firing curve were calculated for each validated MU. Slope coefficients and y-intercepts were calculated for each participant before each eccentric exercise bout. MUs not validated with an accuracy of at least 90% were not considered for analysis. Additionally, contractions in which less than five active motor units were decomposed with an accuracy of at least 90% were removed from

consideration for subsequent analysis. Contractions with a range of RTs for all detected MUs of less than 10% were also removed from consideration.

Additionally, following decomposition, individual MUs identified at each relative intensity during the submaximal muscle actions (e.g. 50% MVIC and 80% MVIC) were separated into two separate motor unit "bins" based upon their recruitment threshold. For 50% MVIC contractions, bin 1 included all MUs recruited up to 25% MVIC, while bin 2 included all MUs recruited above 25% MVIC. For 80% MVIC contractions, bin 1 included all MUs recruited up to 40% MVIC, while bin 2 included all MUs recruited above 40% MVIC. The mean firing rate of all identified MUs within each bin was calculated and used for subsequent analysis. Additionally, from each of four unique action potential waveform templates, the peak-to-peak amplitude values were averaged to calculate motor unit action potential amplitude. Subsequently, slope coefficients and y-intercepts were calculated for the relationship between motor unit action potential amplitude and recruitment threshold.

Eccentric Exercise Bout

The eccentric exercise bout was completed on an isokinetic dynamometer seven days after the completion of MVIC and submaximal muscle action familiarization sessions (i.e. visit 2). The eccentric exercise protocol was conducted by a member of the research team. The shoulder joint angle was standardized as 45° of flexion with 0° of abduction. Participants were asked to grasp a hand bar attached to the lever arm on the dynamometer with the wrist in a supinated position. Five sets of 6 maximal eccentric repetitions were completed at an angular velocity of 0.53 rad·s^{-1} (30°·s^{-1}). Each contraction proceeded from a flexed (1.58 rad; 90°) to a completely extended (0 rad; 0°) position over the course of 3 seconds while the participant

maximally contracted against the movement of the lever arm. Following completion of each eccentric contraction, the lever arm was passively returned to the start position at a velocity of 0.17 rad·s^{-1} (10°·s^{-1}). Two minutes of rest were provided in between each set. During the completion of each contraction, participants were given standardized verbal encouragement to maximally resist the movement of the lever arm. Fourteen days later, this eccentric exercise bout was repeated on both the ipsilateral and contralateral arm.

Statistical Analysis

A three-way mixed design analysis of variance (ANOVA) [group (exercise vs. control) x bout (ECC1 vs. ECC2-IL vs. ECC2-CL) x time (BL vs. IP vs. 24H vs. 72H)] was used to assess differences in ROM, PPT, VAS, MVIC and RTD. In the event that a three-way interaction was observed, follow up two-way mixed ANOVAs were used to assess between group differences over time for each level of bout [group (2) x time (4)], between bout differences over time for each level of group [bout (3) x time (4)] and between group differences within each bout for each level of time [group (2) x bout (3)] with a Bonferroni correction to adjust for multiple comparisons where applicable. All data was assessed for normality using the Shapiro-Wilk test for each treatment group independently and homogeneity of variance was assessed using Levene's test. Data were treated as normally distributed if the majority of time points for a given dependent variable were normally distributed. If the assumption of sphericity was violated, a Greenhouse-Geisser correction was applied. Differences in linear slope coefficients and y-intercepts for mean firing rate vs. recruitment threshold and action potential amplitude vs. recruitment threshold were assessed using two-way mixed ANOVAs (group x bout) in the ipsilateral and contralateral limbs at both contraction intensities (50% and 80% MVIC).

Differences in the mean firing rate of motor units identified within each recruitment threshold bin within each group were assessed using separate two-way mixed ANOVAs within each level of limb (ipsilateral vs. contralateral) and bin at each contraction intensity [50% MVIC (0-25% MVIC and between 25-50% MVIC) and 80% MVIC (0-40% MVIC and between 40-80% MVIC)] for 50% MVIC [group (2) x bout (2)] and 80% MVIC [group (2) x bout (2)], respectively. Main effects and interaction effects for ANOVAs were interpreted using partial eta squared (η^2_p) effect size in accordance with thresholds established by Cohen (1988): small effect (0.01-0.058), medium effect (0.059-0.137) and large effect (>0.138). All hypothesis tests were interpreted based on whether an effect was determined to be meaningful rather than significant, as determined by a moderate effect size ($\eta^2_p \geq 0.059$). In the event that a two-way interaction or main effect was observed, interpretations were made based on the magnitude of estimated effects and their associated 95% confidence intervals using Hedges' *g* effect size estimates corrected for small sample sizes. Hedges g was calculated using the following equation to correct for small sample sizes according to Hedges and Holkin (1985):

$$g = \left(\frac{Mex - Mcon}{SDpooled}\right)\left(\frac{N-3}{N-2.25}\right)\sqrt{\frac{N-2}{N}}, \quad (1)$$

Where M_{ex} is the mean for the exercise group and M_{con} is the mean for the control group. Effect sizes were interpreted in accordance with Cohen (1992) at the following thresholds: negligible effect (0-0.2), small effect (0.21-0.5), medium effect (0.51-0.8), and large effect (≥0.81). Effect sizes and associated 95% confidence intervals were calculated in R version 3.5.3 using the 'effsize' package (Torchiano, 2020). Pearson product moment correlations were used to assess the relationship between BL changes in MU firing characteristics between initial and

repeated bouts and changes from BL to 24H and 72H, respectively, following each repeated bout. Correlations were interpreted as negligible (≤0.1), small (0.1-0.3), moderate (0.31-0.5), or large (≥0.51) in accordance with Cohen (1988). Unless otherwise noted, all statistical analysis was performed using IBM SPSS Statistical Analysis Software version 25 (IBM, Armonk, NY, USA).

CHAPTER 4: RESULTS

Range of Motion

No outliers were detected for ROM at any time point. All ROM data was normally distributed except for at 24H in the exercise group during ECC2-IL (*SW*=0.821; *df*=8; *p*=0.048) and at BL in the control group during ECC2-IL (*SW*=0.762; *df*=5; *p*=0.039).

A group x bout x time interaction was observed for ROM ($F_{6,78}$=1.030; *p*=0.403; η^2_p=0.073). Follow-up analysis revealed a group x bout interaction at 72H ($F_{2,26}$= 2.024; p= 0.173; η^2_p= 0.135). Large effects were noted for between group differences in ROM at 72H during all three bouts. No group x bout interactions were noted at BL ($F_{2,26}$= 0.047; *p*= 0.954; η^2_p= 0.004), IP ($F_{2,26}$=0.216; *p*= 0.808; η^2_p= 0.016), or 24H ($F_{2,26}$= 0.153; *p*= 0.859; η^2_p= 0.012). However, main effects of group were observed at IP ($F_{1,13}$=14.108; *p*=0.002; η^2_p= 0.520), and 24H ($F_{1,13}$=13.232; *p*=0.003; η^2_p= 0.504). When collapsed across bout, large effects for between group differences were noted at both IP and 24H. A main effect of group was not observed at BL ($F_{1,13}$= 0.108; *p*=0.748; η^2_p= 0.008). Pairwise comparisons between groups across levels of bout and time are presented in Table 1. Changes in ROM across time are presented in Figure 2.

Table 1. Between-group differences (EX vs. CON) in ROM at each time point during ECC1, ECC2-IL, and ECC2-CL.

Time	Effect	F	η^2_p	Bout	p	g	95% CI (Lower)	95% CI (Upper)
BL	Group	0.108	0.008	-	0.748	-0.153	-0.757	0.450
IP	Group	14.108	0.520	-	0.002	-1.890	-2.610	-1.170
24H	Group	13.232	0.504	-	0.003	-1.730	-2.430	-1.030
72H	Group x bout	2.024	0.135	ECC1	0.030	-1.210	-2.370	-0.046
				ECC2-IL	0.125	-0.813	-1.930	0.300
				ECC2-CL	0.274	-0.566	-1.660	0.526

EX = exercise group; CON = control group; ROM = range of motion; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise. η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Where a main effect of group is noted, negative g indicates greater ROM in control group at corresponding time point. Where a group x bout interaction is noted, negative g indicates greater ROM in control group during corresponding bout and time point.

A group x time interaction was observed for ROM during ECC1 ($F_{3,39}$=10.591; p<0.001; η^2_p= 0.449), ECC2-IL ($F_{3,39}$=17.645; p<0.001; η^2_p= 0.576), and ECC2-CL ($F_{3,39}$=11.143; p<0.001; η^2_p= 0.462). In the exercise group, main effects of time were observed during ECC1 ($F_{3,24}$=21.555; p<0.001; η^2_p= 0.729), ECC2-IL ($F_{3,24}$=33.653; p<0.001; η^2_p= 0.808) and ECC2-CL ($F_{3,24}$=17.527; p<0.0001; η^2_p= 0.687). During ECC1, large effects for differences in ROM were noted at IP, 24H, and 72H relative to BL, while a negligible effect was noted at 24H relative to IP. A small effect was noted at 72H relative to IP and 24H. During ECC2-IL, large effects were noted at IP and 24H relative to BL, and at 72H relative to both IP and 24H, while a small effect was noted at 24H relative to IP. During ECC2-CL, large effects were noted at IP and 24H relative to BL, while medium effects were noted at 72H relative to BL, IP, and 24H. The effect for difference in ROM at 24H relative to IP during ECC2-CL was negligible.

In the control group, main effects of time were observed during ECC2-IL ($F_{3,15}$=1.179; p=0.351; η^2_p= 0.191) and ECC2-CL ($F_{3,15}$=0.721; p=0.555; η^2_p=0.126); Follow up analysis indicated that differences in ROM during ECC2-IL were negligible at 24H and 72H relative to BL, as well as at 24H relative to IP and 72H relative to 24H. Small effects were observed for differences in ROM at IP relative to BL, and at 72H relative to IP. During ECC2-CL, negligible effects were observed for changes in range of motion at IP and 24H relative to BL as well as 24H relative to IP. Additionally, small effects were noted at 72H relative to BL, IP, and 24H. No main effect of time was observed in the control group during ECC1 ($F_{3,15}$= 0.216; p= 0.883; η^2_p= 0.042). Pairwise comparisons for each two-way interaction are presented in Table 2.

Table 2. Within-group differences in ROM across time points during ECC1, ECC2-IL, and ECC2-CL.

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC1	Group x time	10.591	0.449	Exercise	<0.001 (0.729)	BL vs. IP	0.002	-1.650	-2.570	-0.727
						BL vs. 24H	0.002	-1.330	-1.950	-0.706
						BL vs. 72H	0.009	-1.080	-1.680	-0.473
						IP vs. 24H	1.000	0.023	-0.306	0.351
						IP vs. 72H	0.153	0.491	0.089	0.892
						24H vs. 72H	0.319	0.422	0.010	0.834
				Control	0.883 (0.042)	-	-			
ECC2-IL	Group x time	17.645	0.576	Exercise	<0.001 (0.808)	BL vs. IP	0.001	-1.380	-1.950	-0.820
						BL vs. 24H	0.001	-1.180	-1.670	-0.688
						BL vs. 72H	0.404	-0.297	-0.601	0.007
						IP vs. 24H	0.001	0.320	0.084	0.555
						IP vs. 72H	0.110	1.130	0.601	1.650
						24H vs. 72H	0.002	1.020	0.587	1.440
				Control	0.351 (0.191)	BL vs. IP	1.000	0.035	-0.108	0.178
						BL vs. 24H	0.258	0.119	0.020	0.218
						BL vs. 72H	1.000	0.228	-0.215	0.670
						IP vs. 24H	0.663	0.147	-0.023	0.318
						IP vs. 72H	1.000	0.201	-0.238	0.640
						24H vs. 72H	1.000	0.077	-0.307	0.462

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC2-CL	Group x time	11.143	0.462	Exercise	<0.001 (0.687)	BL vs. IP	0.009	-1.350	-2.190	-0.509
						BL vs. 24H	0.002	-1.310	-1.950	-0.672
						BL vs. 72H	0.083	-0.604	-1.050	-0.160
						IP vs. 24H	1.000	0.133	-0.303	0.569
						IP vs. 72H	0.053	0.779	0.231	1.330
						24H vs. 72H	0.001	0.700	0.442	0.958
				Control	0.555 (0.126)	BL vs. IP	1.000	0.083	-0.093	0.259
						BL vs. 24H	1.000	-0.016	-0.226	0.195
						BL vs. 72H	1.000	-0.092	-0.406	0.223
						IP vs. 24H	1.000	-0.105	-0.363	0.152
						IP vs. 72H	1.000	-0.175	-0.546	0.196
						24H vs. 72H	1.000	-0.065	-0.255	0.126

EX = exercise group; CON = control group; ROM = range of motion; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; η^2_p> 0.059 indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater ROM relative to preceding time point in corresponding group and bout. Negative g indicates lower ROM relative to preceding time point in corresponding group and bout.

Bout x time interactions were observed for ROM in both the exercise ($F_{6,48}$=2.809; p=0.020; η^2_p= 0.260) and control group ($F_{6,30}$=1.082; p=0.395; η^2_p= 0.178). In the exercise group, main effects of bout were observed at BL ($F_{2,16}$=1.235; p= 0.317; η^2_p= 0.134), IP ($F_{2,16}$=1.915; p=0.180; η^2_p= 0.193), 24H ($F_{2,16}$=3.641; p=0.050; η^2_p= 0.313) and 72H ($F_{2,16}$= 8.328; p=0.003; η^2_p= 0.510). A small effect was noted between ECC1 and ECC2-CL; however, effects for all other between bout comparisons at BL were negligible. A small effect was noted between ECC1 and ECC2-IL at IP; however, effects for all other between bout comparisons at IP were negligible. At 24H, medium and small effects were noted between ECC1 and ECC2-IL, and ECC1 and ECC2-CL, respectively, while the effect between ECC2-IL and ECC2-CL at 24H was negligible. At 72H, large and medium effects were noted between ECC1 and ECC2-IL and between ECC1 and ECC2-CL, respectively, while the effect between ECC2-IL and ECC2-CL at 72H was negligible.

In the control group, main effects of bout were observed at BL ($F_{2,10}$=0.636; p=0.550; η^2_p= 0.113), IP ($F_{2,10}$=0.804; p=0.474; η^2_p= 0.139), 24H ($F_{2,10}$= 2.519; p=0.130; η^2_p= 0.335) and 72H ($F_{2,10}$=2.821; p=0.107; η^2_p= 0.361). At BL, a negligible effect was noted for differences in ROM between ECC1 and ECC2-IL, while the effects between ECC1 and ECC2-CL, and between ECC2-IL and ECC2-CL were small. At IP, negligible effects were noted between ECC1 and ECC2-IL and between ECC2-IL and ECC2-CL, while a small effect was noted between ECC1 and ECC2-CL. At 24H, a medium effect was noted between ECC1 and ECC2-IL, while small and negligible effects were noted between ECC1 and ECC2-CL, and ECC2-IL and ECC2-CL, respectively. At 72H, a small effect was noted between ECC1 and ECC2-IL. Effects for all other between bout comparisons at 72H were negligible. Pairwise comparisons for each two-way interaction are presented in Table 3.

Table 3. Within-group differences in ROM across bouts at BL, IP, 24H, and 72H.

Group	Effect	F	η^2_p	Time	p (η^2_p)	Bout	p	g	95% CI (Lower)	95% CI (Upper)
EX	Bout x time	2.809	0.260	BL	0.317 (0.134)	ECC1 vs. ECC2-IL	1.000	0.184	-0.283	0.650
						ECC1 vs. ECC2-CL	0.632	0.378	-0.231	0.988
						ECC2-IL vs. ECC2-CL	1.000	0.115	-0.149	0.379
				IP	0.180 (0.193)	ECC1 vs. ECC2-IL	1.000	0.030	-0.203	0.262
						ECC1 vs. ECC2-CL	0.570	0.301	-0.155	0.758
						ECC2-IL vs. ECC2-CL	0.407	0.249	-0.074	0.573
				24H	0.050 (0.313)	ECC1 vs. ECC2-IL	0.172	0.503	-0.007	1.010
						ECC1 vs. ECC2-CL	0.250	0.420	-0.049	0.890
						ECC2-IL vs. ECC2-CL	1.000	-0.071	-0.400	0.257
				72H	0.003 (0.510)	ECC1 vs. ECC2-IL	0.021	0.950	0.279	1.620
						ECC1 vs. ECC2-CL	0.119	0.730	0.020	1.440
						ECC2-IL vs. ECC2-CL	0.578	-0.170	-0.424	0.085
CON	Bout x time	1.082	0.178	BL	0.550 (0.113)	ECC1 vs. ECC2-IL	1.000	0.372	-0.561	1.310
						ECC1 vs. ECC2-CL	1.000	0.321	-0.533	1.170
						ECC2-IL vs. ECC2-CL	1.000	0.043	-0.354	0.440
				IP	0.474 (0.139)	ECC1 vs. ECC2-IL	1.000	0.211	-0.376	0.798
						ECC1 vs. ECC2-CL	1.000	0.260	-0.357	0.877
						ECC2-IL vs. ECC2-CL	1.000	0.081	-0.143	0.305
				24H	0.130 (0.335)	ECC1 vs. ECC2-IL	0.308	0.592	-0.125	1.310
						ECC1 vs. ECC2-CL	0.642	0.319	-0.193	0.832
						ECC2-IL vs. ECC2-CL	1.000	-0.114	-0.441	0.214
				72H	0.003 (0.510)	ECC1 vs. ECC2-IL	0.211	0.384	-0.002	0.771
						ECC1 vs. ECC2-CL	1.000	0.105	-0.312	0.522
						ECC2-IL vs. ECC2-CL	0.168	-0.193	-0.369	-0.018

EX = exercise group; CON = control group; ROM = range of motion; ECC1= initial exercise bout; ECC2-IL= repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater ROM relative to preceding bout for corresponding time point and group. Negative g indicates lower ROM relative to preceding bout for corresponding time point and group.

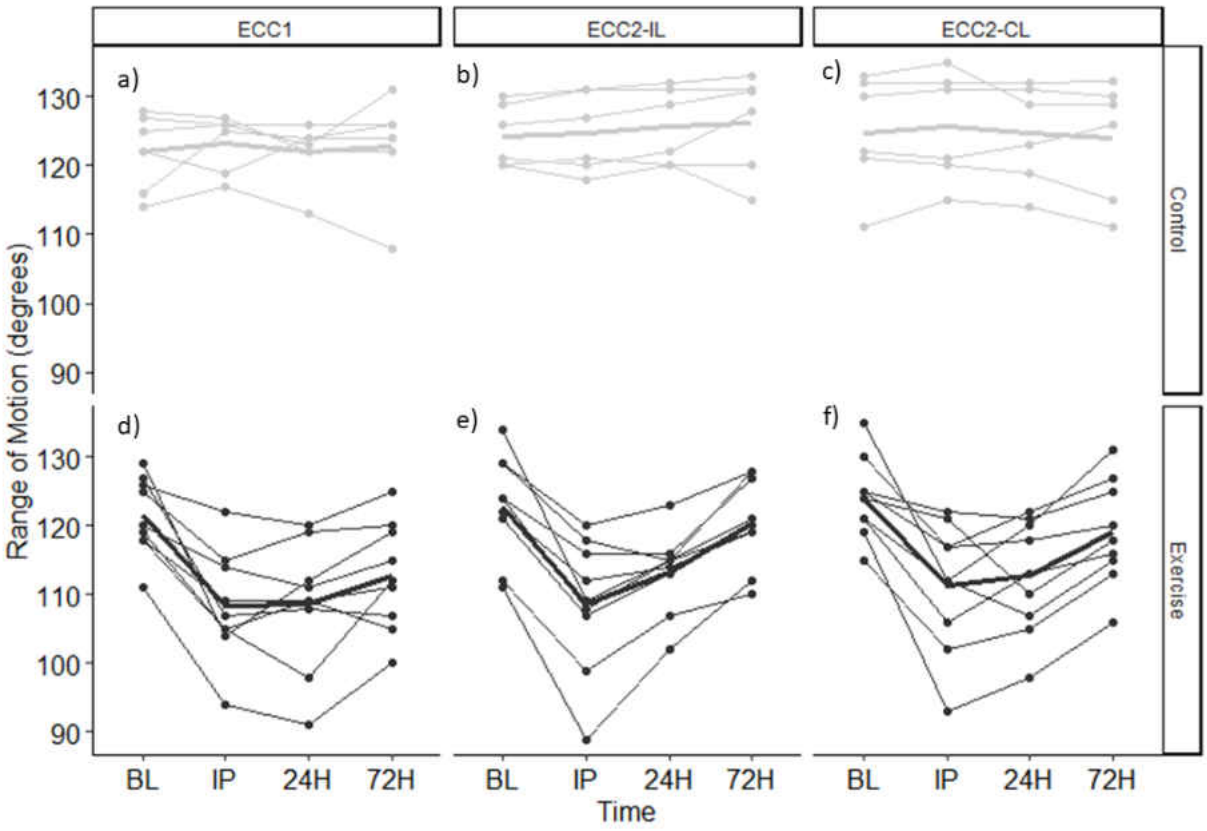


Figure 2.Changes in range of motion across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Proximal Soreness (pVAS)

No outliers were detected for pVAS at any time point. All pVAS data were normally distributed except for at BL (SW=0.768; df=5; p=0.043) and 24H (SW=0.759; df=5; p=0.036) in the control group during ECC2-IL, and at IP (SW=0.692; df=5; p=0.008) and 24H (SW=0.750; df=5; p=0.030) in the control group during ECC2-CL.

No group x bout x time interaction was observed for pVAS ($F_{3.280,42.638}$=0.268; p= 0.864; η^2_p= 0.020). However, a group x time interaction was observed ($F_{3,39}$= 4.383; p= 0.009; η^2_p=

0.252). In the exercise group, a main effect of time was observed ($F_{3,24}$= 0.734; p= 0.542; η^2_p= 0.084). When collapsed across bout, small effects were noted for differences in pVAS at IP and 72H relative to BL and at 24H and 72H relative to IP, while a medium effect was noted at 24H relative to BL. A negligible effect was noted at 72H relative to 24H. No main effect of time was observed for pVAS in the control group ($F_{3,15}$= 0.300; p= 0.825; η^2_p= 0.057).

Analyses of between group comparisons collapsed across bout revealed a small effect at BL, medium effects at IP and 24H, and a large effect at 72H. Pairwise comparisons within each group across time as well as between-group comparisons at each time point are presented in Table 4. Changes in pVAS across time are presented in Figure 3.

Table 4. Within-group differences in pVAS across time points.

Effect	F	η^2_p	Group	Time	p	g	95% CI (Lower)	95% CI (Upper)
Group x time	4.383	0.252	EX	BL vs. IP	1.000	0.217	0.055	0.378
				BL vs. 24H	1.000	0.572	0.391	0.754
				BL vs. 72H	1.000	0.451	0.273	0.628
				IP vs. 24H	1.000	0.388	0.211	0.564
				IP vs. 72H	1.000	0.246	0.078	0.414
				24H vs. 72H	1.000	-0.121	-0.244	0.001
			CON	BL vs. IP	-			
				BL vs. 24H	-			
				BL vs. 72H	-			
				IP vs. 24H	-			
				IP vs. 72H	-			
				24H vs. 72H	-			
			EX vs. CON	BL	0.582	0.293	-0.313	0.899
				IP	0.342	0.481	-0.130	1.090
				24H	0.280	0.755	0.131	1.380
				72H	0.285	0.804	0.178	1.430

EX = exercise group; CON = control group; pVAS = proximal soreness; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise. η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater proximal soreness relative to preceding time point in corresponding group or in exercise relative to control when collapsed across bout. Negative g indicates lower proximal soreness relative to preceding time point in corresponding group or in exercise relative to control when collapsed across bout.

No bout x time ($F_{3.280,42.638}$= 0.637; p= 0.609; η^2_p= 0.047) or group x bout ($F_{2,26}$= 0.060; p= 0.942; η^2_p= 0.058) interactions were observed. However, main effects of bout ($F_{2,26}$= 1.681; p= 0.206; η^2_p= 0.115) and group ($F_{1,13}$= 1.317; p=0.272; η^2_p= 0.092) were observed. When collapsed across bout and time, a medium effect was noted for differences in proximal soreness between groups. When collapsed across group and time, effects for all comparisons between bouts were negligible. Pairwise comparisons for main effects of group and bout are presented in Table 5.

Table 5. Differences in pVAS between groups (EX vs. CON) and bouts.

Effect	F	p (η^2_p)	Comparison	p	g	95% CI (Lower)	95% CI (Upper)
Group	1.317	0.272 (0.092)	EX vs. CON	0.272	0.590	0.285	0.895
Bout	1.681	0.206 (0.115)	ECC1 vs. ECC2-IL	1.000	-0.167	-0.292	-0.043
			ECC1 vs. ECC2-CL	1.000	-0.082	-0.220	0.056
			ECC2-IL vs. ECC2-CL	1.000	0.068	-0.015	0.151

EX = exercise group; CON = control group; pVAS = proximal soreness; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Where a main effect of group is noted, positive g indicates greater pVAS in exercise group at corresponding time point. Where a main effect of bout is noted, negative g indicates lower pVAS relative to preceding bout.

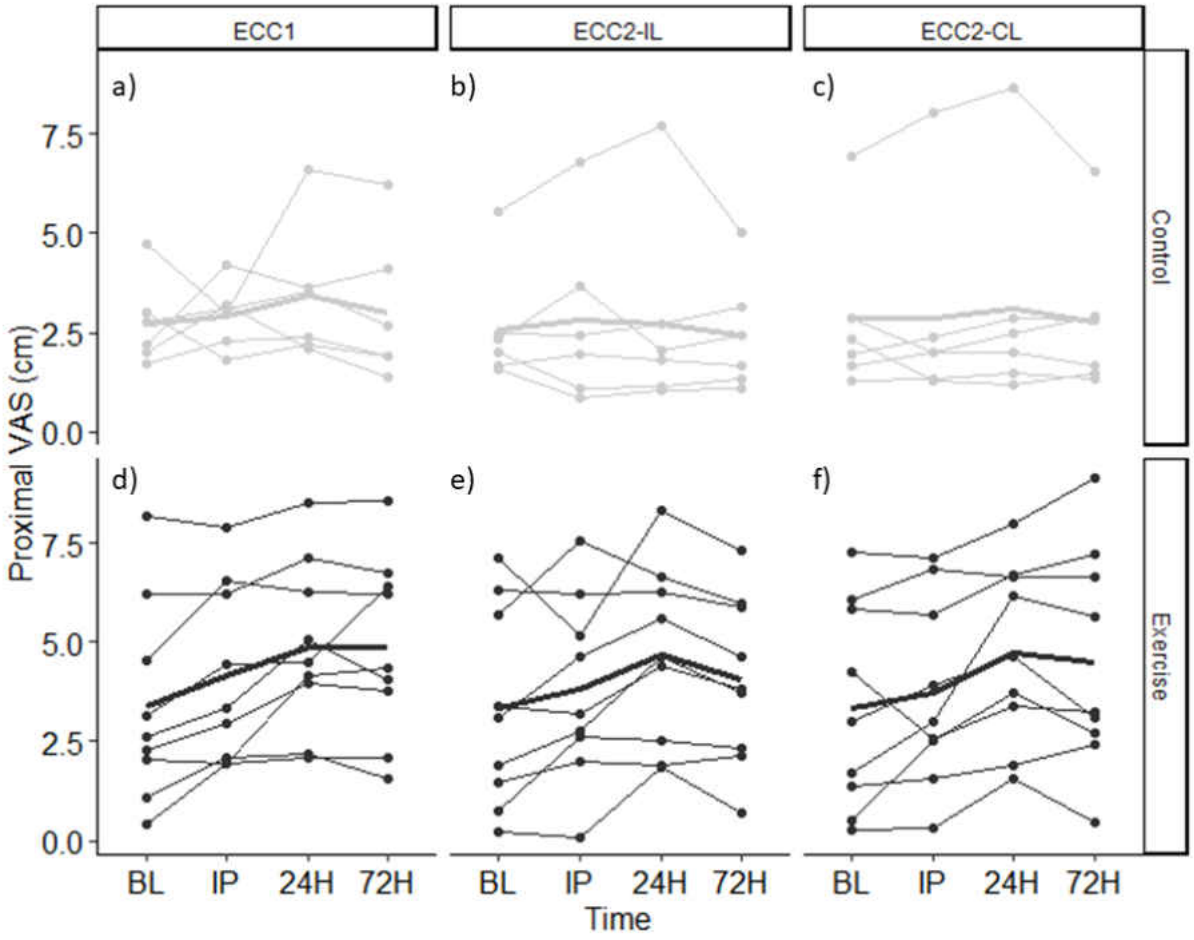


Figure 3. Changes in proximal soreness (pVAS) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Distal Soreness (dVAS)

No outliers were detected for dVAS at any time point. All distal soreness data were normally distributed except for in the control group at BL (*SW*=0.746; *df*=5; *p*=0.027) and IP (*SW*=0.773; *df*=5; *p*=0.048) during ECC2-IL and ECC2-CL, respectively.

No group x bout x time interaction was observed ($F_{6,78}$= 1.009; p= 0.783; η^2_p= 0.039). However, a group x time interaction was observed for dVAS ($F_{3,39}$= 1.577; p= 0.210; η^2_p= 0.108). In the exercise group, a main effect of time was observed ($F_{1.595,12.762}$= 7.643; p= 0.009; η^2_p= 0.489). When collapsed across bout, small effects were noted for differences in dVAS at IP, 24H, and 72H relative to BL. Small effects were also noted for differences at 24H relative to IP and 72H relative to 24H, while a negligible effect was noted at 72H relative to IP.

In the control group, a main effect of time was also observed ($F_{3,15}$= 1.578; p= 0.236; η^2_p= 0.240). When collapsed across bout, a small effect was noted for differences at 24H relative to BL. However, comparisons between all other time points were negligible.

Analyses of between group comparisons collapsed across bout revealed a small effect at BL and medium effects at IP, 24H, and 72H. Pairwise comparisons within each group across time as well as between groups at each time point are presented in Table 6. Changes in dVAS across time are presented in Figure 4.

Table 6. Differences in dVAS across time and between groups (EX vs. CON).

Effect	F	η^2_p	Group	Time	p	g	95% CI (Lower)	95% CI (Upper)
Group x time	1.577	0.108	EX	BL vs. IP	0.052	0.248	0.128	0.371
				BL vs. 24H	0.012	0.458	0.296	0.621
				BL vs. 72H	0.413	0.262	0.101	0.423
				IP vs. 24H	0.351	0.216	0.056	0.375
				IP vs. 72H	1.000	0.009	-0.152	0.172
				24H vs. 72H	0.011	-0.203	-0.308	-0.098
			CON	BL vs. IP	1.000	0.116	-0.104	0.336
				BL vs. 24H	1.000	0.201	0.032	0.370
				BL vs. 72H	1.000	0.022	-0.139	0.183
				IP vs. 24H	1.000	0.104	-0.026	0.235
				IP vs. 72H	1.000	-0.094	-0.285	0.097
				24H vs. 72H	0.622	-0.169	-0.285	-0.053
			EX vs. CON	BL	0.582	0.298	-0.308	0.904
				IP	0.342	0.515	-0.098	1.130
				24H	0.280	0.595	-0.020	1.210
				72H	0.285	0.593	-0.023	1.210

EX = exercise group; CON = control group; dVAS = distal soreness; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater dVAS relative to preceding time point in corresponding group or greater dVAS in exercise compared to control at same time point when collapsed across bout. Negative g indicates lower dVAS relative to preceding time point in corresponding group or greater dVAS in control group compared to exercise group when collapsed across bout.

A bout x time interaction was also observed for dVAS ($F_{6,78}$= 1.009; p= 0.426; η^2_p= 0.072). When collapsed across group, small effects were noted for differences in dVAS at IP, 24H, and 72H relative to BL during ECC1. During ECC2-IL, a small effect was noted at 24H relative to BL, while a small effect was noted for differences at 24H relative to IP during ECC2-CL. All other effects for comparisons between time points within each bout were negligible. No group x bout interaction was observed for dVAS ($F_{2,26}$= 0.278; p= 0.760; η^2_p= 0.021). Pairwise comparisons between time points within each bout are presented in Table 7.

Table 7. Differences in dVAS across time within ECC1, ECC2-IL, and ECC2-CL.

Effect	F	η^2_p	Bout	Time	p	g	95% CI (Lower)	95% CI (Upper)
Bout x time	1.009	0.072	ECC1	BL vs. IP	0.091	0.349	0.108	0.590
				BL vs. 24H	<0.001	0.428	0.273	0.584
				BL vs. 72H	0.179	0.259	0.055	0.464
				IP vs. 24H	1.000	0.090	-0.125	0.305
				IP vs. 72H	1.000	-0.078	-0.315	0.159
				24H vs. 72H	0.190	-0.169	-0.309	-0.030
			ECC2-IL	BL vs. IP	0.705	0.141	-0.009	0.290
				BL vs. 24H	0.151	0.285	0.071	0.499
				BL vs. 72H	1.000	0.078	-0.101	0.257
				IP vs. 24H	0.843	0.146	-0.039	0.331
				IP vs. 72H	1.000	-0.069	-0.243	0.104
				24H vs. 72H	0.030	-0.198	-0.316	-0.080
			ECC2-CL	BL vs. IP	1.000	0.117	-0.048	0.281
				BL vs. 24H	0.113	0.350	0.097	0.603
				BL vs. 72H	1.000	0.183	-0.048	0.414
				IP vs. 24H	0.042	0.236	0.088	0.383
				IP vs. 72H	1.000	0.068	-0.119	0.256
				24H vs. 72H	0.238	-0.171	-0.310	-0.032

dVAS = distal soreness; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; η^2_p > 0.059 indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater dVAS relative to preceding time point in corresponding bout when collapsed across group. Negative g indicates lower dVAS relative to preceding time point in corresponding bout when collapsed across group.

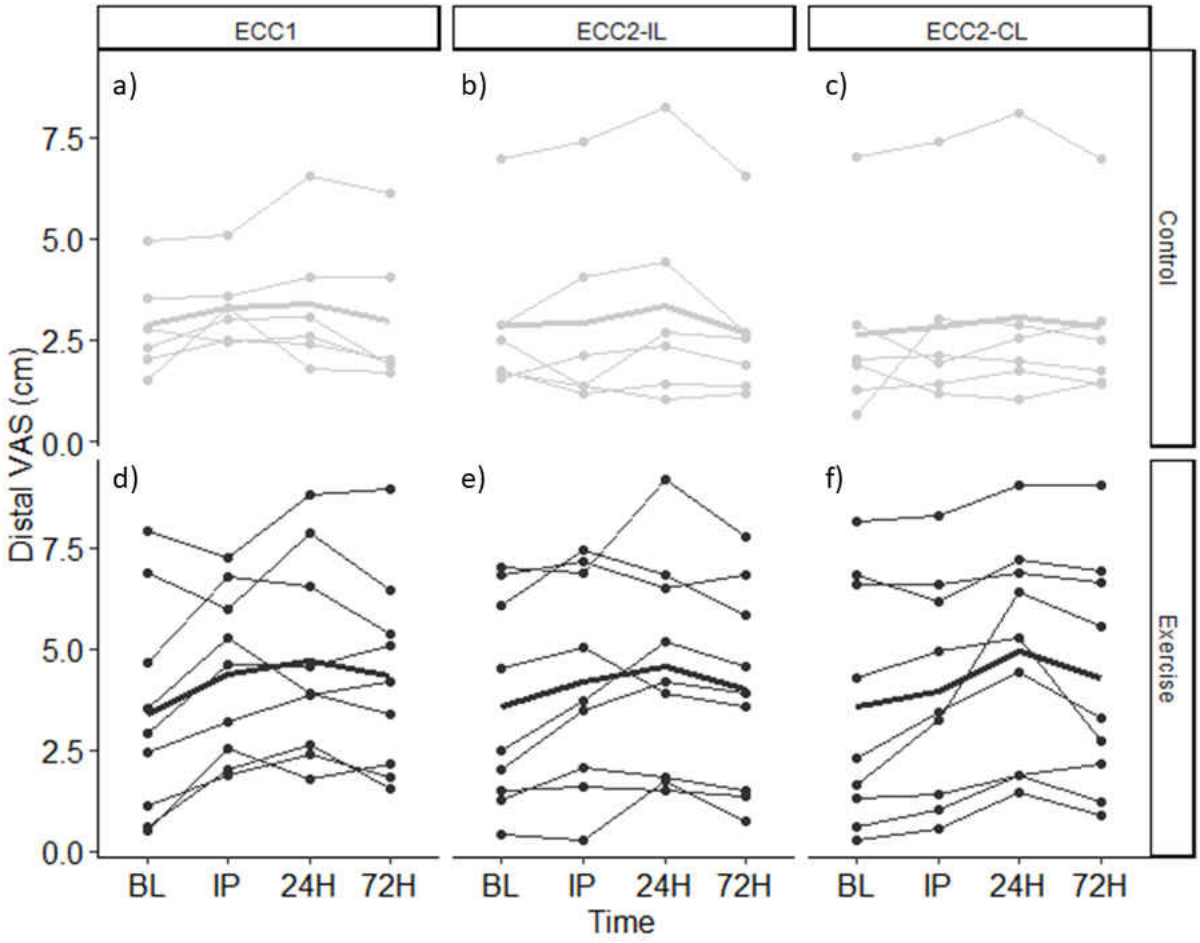


Figure 4. Changes in distal soreness (dVAS) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Proximal Pain-Pressure Threshold (pPPT)

Two outliers with studentized residuals of 3.02 and 3.04 were detected at BL and IP time points in the control group during ECC2-IL. All pPPT data were normally distributed except for at IP (*SW*=0.818; *df*=8; *p*=0.044) and 72H (*SW*=0.800; *df*= 8; *p*=0.028) in the exercise group during ECC2-CL.

No group x bout x time interaction was observed for pPPT ($F_{6,66}$= 0.431; p=0.856; η^2_p= 0.038). However, a group x time interaction was observed ($F_{3,33}$= 2.500; p=0.077; η^2_p= 0.185). Within the exercise group, a main effect of time was observed ($F_{1.465,10.253}$= 14.463; p=0.002; η^2_p= 0.674). When collapsed across bout, a medium effect was noted for differences at 24H relative to BL, while small effects were noted for differences at 24H relative to IP and 72H relative to 24H. However, comparisons between all other time points within the exercise group were negligible.

Within the control group, a main effect of time was also observed ($F_{3,12}$= 0.634; p= 0.607; η^2_p= 0.137). However, when collapsed across bout, comparisons between time points were negligible. When comparing between groups across time points, medium effects were noted for differences at IP, 24H, and 72H, while a small effect was noted at BL. Pairwise comparisons between groups across levels of time are presented in Table 8. Changes in pPPT across time are presented in Figure 5.

Table 8. Differences in pPPT across time and between groups (EX vs. CON).

Effect	F	η^2_p	Group	Time	p	g	95% CI (Lower)	95% CI (Upper)
Group x time	2.500	0.185	EX	BL vs. IP	0.006	-0.165	-0.358	0.028
				BL vs. 24H	<0.001	-0.512	-0.690	-0.334
				BL vs. 72H	0.473	-0.166	-0.389	0.056
				IP vs. 24H	<0.001	-0.395	-0.598	-0.193
				IP vs. 72H	1.000	-0.047	-0.268	0.174
				24H vs. 72H	0.119	0.279	0.131	0.427
			CON	BL vs. IP	0.898	-0.040	-0.202	0.121
				BL vs. 24H	0.387	-0.057	-0.190	0.077
				BL vs. 72H	1.000	0.052	-0.178	0.282
				IP vs. 24H	1.000	-0.019	-0.171	0.133
				IP vs. 72H	1.000	0.088	-0.100	0.276
				24H vs. 72H	1.000	0.137	-0.082	0.357
			EX vs. CON	BL	0.169	-0.462	-1.070	0.149
				IP	0.127	-0.673	-1.300	-0.049
				24H	0.078	-0.814	-1.440	-0.188
				72H	0.106	-0.625	-1.250	0.003

EX = Exercise Group; CON = Control Group; pPPT = proximal pain-pressure threshold; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater pPPT relative to preceding time point in corresponding group or greater pPPT in exercise compared to control at same time point when collapsed across bout. Negative g indicates lower pPPT relative to preceding time point in corresponding group or greater pPPT in control group compared to exercise group when collapsed across bout.

A bout x time interaction was also observed for pPPT ($F_{6,66}$= 1.174; p= 0.331; η^2_p= 0.096). When collapsed across group, small effects were noted for differences at 24H relative to BL and 72H relative to 24H in ECC2-IL. However, negligible effects were noted for all other comparisons across time. During ECC2-CL, small effects were noted for differences at 24H relative to BL and IP as well as 72H relative to 24H. Negligible effects were noted for all comparisons across time within ECC1. No group x bout interaction was observed ($F_{2,22}$= 0.236; p=0.792; η^2_p= 0.021). Pairwise comparisons between time points within each bout are presented in Table 9.

Table 9. Differences in pPPT across time during ECC1, ECC2-IL, and ECC2-CL.

Effect	F	η^2_p	Bout	Time	p	g	95% CI (Lower)	95% CI (Upper)
Bout x time	1.174	0.096	ECC1	BL vs. IP	1.000	-0.059	-0.288	0.170
				BL vs. 24H	0.077	-0.186	-0.406	0.034
				BL vs. 72H	0.068	-0.051	-0.350	0.248
				IP vs. 24H	1.000	-0.132	-0.306	0.042
				IP vs. 72H	1.000	-0.001	-0.211	0.210
				24H vs. 72H	1.000	0.112	-0.094	0.317
			ECC2-IL	BL vs. IP	1.000	-0.063	-0.240	0.113
				BL vs. 24H	0.007	-0.201	-0.341	-0.060
				BL vs. 72H	1.000	0.028	-0.119	0.174
				IP vs. 24H	0.867	-0.120	-0.323	0.083
				IP vs. 72H	1.000	0.093	-0.100	0.285
				24H vs. 72H	0.116	0.272	0.102	0.442
			ECC2-CL	BL vs. IP	1.000	-0.131	-0.290	0.028
				BL vs. 24H	0.007	-0.396	-0.607	-0.184
				BL vs. 72H	1.000	-0.183	-0.480	0.114
				IP vs. 24H	0.151	-0.239	-0.431	-0.048
				IP vs. 72H	1.000	-0.032	-0.267	0.203
				24H vs. 72H	0.870	0.226	-0.019	0.471

pPPT = proximal pain pressure threshold; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater pPPT relative to preceding time point in corresponding bout when collapsed across group. Negative g indicates lower pPPT relative to preceding time point in corresponding bout when collapsed across group.

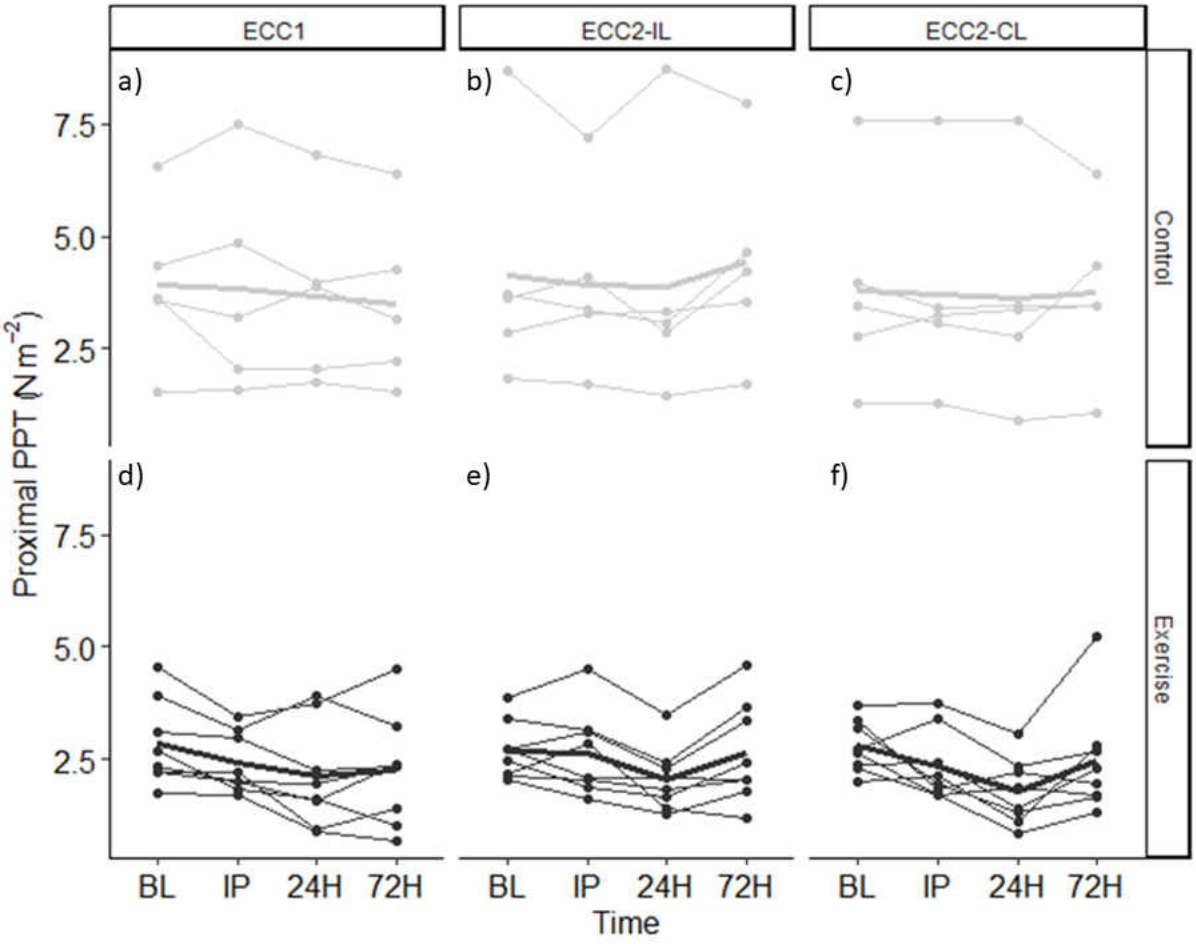


Figure 5. Changes in proximal pain-pressure threshold (pPPT) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Distal Pain-Pressure Threshold (dPPT)

No outliers were detected for dPPT at any time point. All distal PPT data were normally distributed except for at BL (*SW*=0.806; *df*=8; *p*=0.034) in the exercise group during ECC2-CL.

No group x bout x time interaction was observed ($F_{3.008,\ 39.101}$= 0.477; *p*= 0.701; η^2_p= 0.035). However, a group x time interaction was observed for dPPT ($F_{1,752,\ 22.870}$= 1.840; *p*= 0.185; η^2_p= 0.124). In the exercise group, a main effect of time was observed ($F_{3,24}$= 6.530; *p*=

0.002; η^2_p= 0.449). When collapsed across bout, small effects were noted for differences in dPPT at 24H relative to BL and IP as well as 72H relative to 24H. However, comparisons between all other time points were negligible.

In the control group, a main effect of time was also observed ($F_{1.317, 6.585}$= 1.376; p=0.297; η^2_p= 0.216). When collapsed across bout, small effects were noted for differences at 72H relative to IP and 24H. However, comparisons between all other time points were negligible.

Analysis of between group comparisons collapsed across bout revealed medium effects for differences between groups at BL and 72H, while a large effect was noted for between group differences at 24H. A small effect was noted for between group differences at IP. Pairwise comparisons between groups across levels of time are presented in Table 10. Changes in dPPT across time are presented in Figure 6.

Table 10. Within and between-group differences (EX vs. CON) in dPPT across time points.

Effect	F	η^2_p	Group	Time	p	g	95% CI (Lower)	95% CI (Upper)
Group x time	1.84	0.124	EX	BL vs. IP	1.000	-0.041	-0.198	0.115
				BL vs. 24H	0.006	-0.410	-0.608	-0.211
				BL vs. 72H	1.000	-0.056	-0.270	0.158
				IP vs. 24H	0.003	-0.368	-0.542	-0.192
				IP vs. 72H	1.000	-0.017	-0.215	0.180
				24H vs. 72H	0.133	0.310	0.168	0.452
			CON	BL vs. IP	0.207	-0.153	-0.308	0.003
				BL vs. 24H	1.000	-0.129	-0.307	0.050
				BL vs. 72H	1.000	0.069	-0.157	0.294
				IP vs. 24H	1.000	0.029	-0.089	0.147
				IP vs. 72H	1.000	0.222	-0.039	0.482
				24H vs. 72H	0.906	0.200	-0.007	0.407
			EX vs. CON	BL	0.230	-0.639	-1.260	-0.022
				IP	0.378	-0.479	-1.090	0.132
				24H	0.117	-0.879	-1.510	-0.249
				72H	0.176	-0.740	-1.360	-0.118

EX = exercise group; CON = control group; dPPT = distal pain-pressure threshold; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater proximal soreness relative to preceding time point in corresponding group or in exercise relative to control when collapsed across bout. Negative g indicates lower proximal soreness relative to preceding time point in corresponding group or in exercise relative to control when collapsed across bout.

A group x bout interaction was also observed for dPPT ($F_{1.417, 18.416}$= 0.977; p= 0.367; η^2_p= 0.070). In the exercise group, a main effect of bout was observed ($F_{2,16}$=1.000; p=0.390; η^2_p= 0.111). However, when collapsed across time, negligible effects were noted for differences between bouts. In the control group, a main effect of bout was also observed ($F_{1.123, 5.617}$= 1.219; p=0.324; η^2_p= 0.196). When collapsed across time, a small effect was noted for differences between ECC1 and ECC2-IL, while negligible effects were noted for differences between all other bout comparisons. A bout x time interaction was not observed for dPPT ($F_{3.008, 39.101}$= 0.339; p= 0.798; η^2_p= 0.025). Pairwise bout comparisons within each group are presented in Table 11.

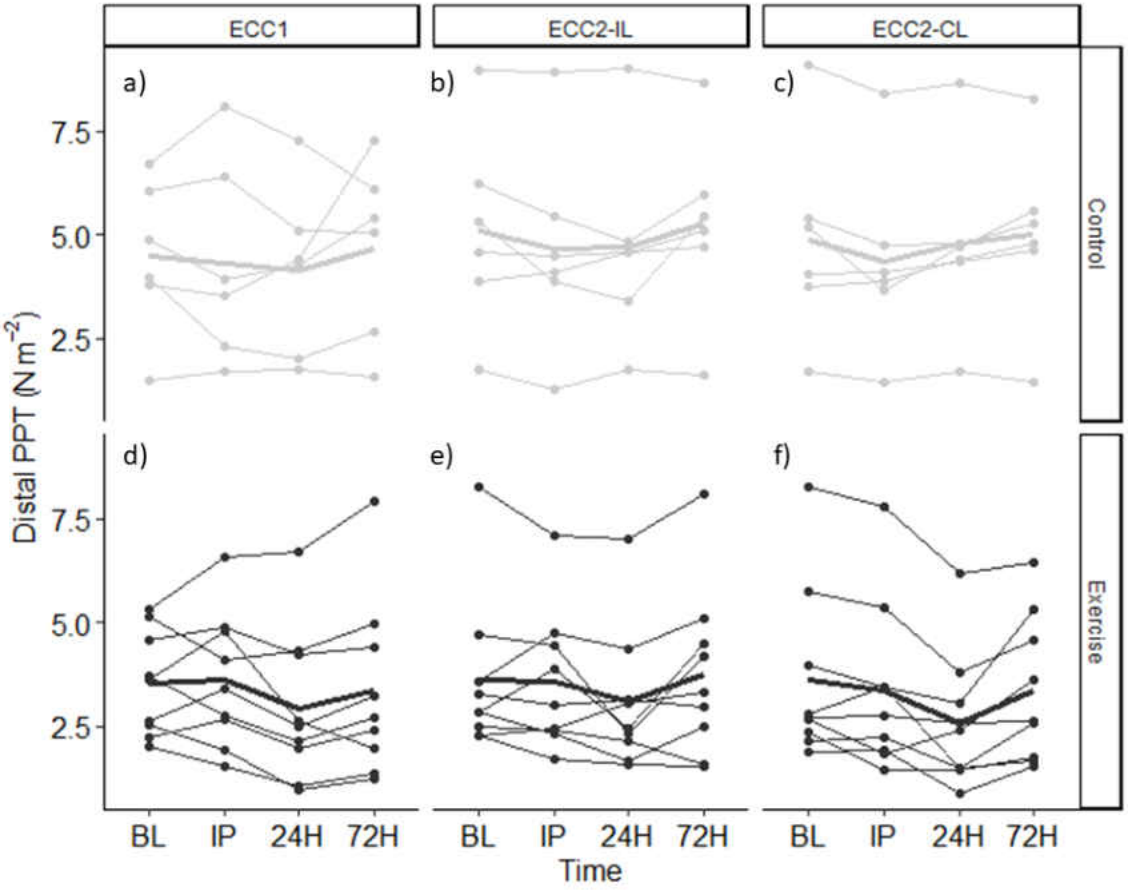


Figure 6. Changes in distal pain-pressure threshold (dPPT) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Table 11. Within-group differences in dPPT during ECC1, ECC2-IL, and ECC2-CL.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.977	0.070	EX	ECC1 vs. ECC2-IL	1.000	0.078	-0.108	0.264
				ECC1 vs. ECC2-CL	1.000	-0.070	-0.238	0.092
				ECC2-IL vs. ECC2-CL	0.533	-0.150	-0.289	-0.003
			CON	ECC1 vs. ECC2-IL	0.837	0.236	0.001	0.470
				ECC1 vs. ECC2-CL	1.000	0.159	-0.068	0.386
				ECC2-IL vs. ECC2-CL	0.635	-0.080	-0.156	-0.001

EX = Exercise Group; CON = Control Group; dPPT = distal pain pressure threshold; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons when collapsed across time. Positive g indicates greater dPPT in repeated bout compared to ECC1, or in ECC2-CL compared to ECC2-IL when collapsed across time.

Maximal Voluntary Isometric Contraction Torque

No outliers were detected for maximal voluntary isometric contraction torque at any time point. Data were normally distributed at all time points except for in the exercise group at 24H during ECC1 (SW= 0.791; df=8; p=0.023).

A group x bout x time interaction was noted for MVIC torque ($F_{6,78}$= 1.488; p= 0.242; η^2_p= 0.103). Follow up analysis revealed group x bout interactions at BL ($F_{2,26}$=2.146; p= 0.137, η^2_p= 0.142), IP ($F_{2,26}$= 0.850; p=0.401; η^2_p= 0.061) and 24H ($F_{2,26}$= 1.268; p=0.298; η^2_p= 0.089). Large effects were noted for between group differences in MVIC torque at BL during ECC1 and ECC2-IL, while the effect for between group differences at BL during ECC2-CL was small. At IP and 24H, large effects were noted for between group differences in MVIC torque during all three bouts. No group x bout interaction was observed at 72H ($F_{2,26}$=0.472; p=0.629; η^2_p= 0.035). However, a main effect of group was observed ($F_{1,13}$=7.795; p= 0.015; η^2_p= 0.375). When collapsed across bout, a large effect for between group differences in MVIC torque was noted. Pairwise comparisons between groups across levels of bout and time are presented in Table 12. Changes in MVIC torque are presented in Figure 7.

Table 12. Between-group differences (EX vs. CON) in MVIC torque at each time point during ECC1, ECC2-IL, and ECC2-CL.

Time	Effect	F	η^2_p	Bout	p	g	95% CI (Lower)	95% CI (Upper)
BL	Group x bout	2.146	0.142	ECC1	0.078	-0.948	-2.080	0.180
				ECC2-IL	0.046	-1.090	-2.240	0.053
				ECC2-CL	0.372	-0.458	-1.540	0.627
IP	Group x bout	0.850	0.061	ECC1	<0.001	-2.530	-3.960	-1.110
				ECC2-IL	0.001	-2.120	-3.450	-0.790
				ECC2-CL	0.010	-1.500	-2.710	-0.291
24H	Group x bout	1.268	0.089	ECC1	0.001	-2.180	-3.520	-0.835
				ECC2-IL	0.569	-1.350	-2.530	-0.165
				ECC2-CL	0.037	-1.150	-2.300	0.003
72H	Group	7.795	0.375	-	0.015	-1.267	-1.926	-0.609

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL= repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Where a main effect of group is noted, negative g indicates greater MVIC torque in control group at corresponding time point. Where a group x bout interaction is noted, negative g indicates greater MVIC torque in control group during corresponding bout and time point.

A group x time interaction was observed for MVIC torque during ECC1 ($F_{3,39}$= 4.170; p= 0.012; η^2_p= 0.243), ECC2-IL ($F_{3,39}$= 1.375; p= 0.266; η^2_p= 0.096), and ECC2-CL ($F_{3,39}$= 3.157; p= 0.035; η^2_p= 0.195). In the exercise group, main effects of time were observed during ECC1 ($F_{3,24}$= 26.579; p< 0.001; η^2_p= 0.769), ECC2-IL ($F_{3,24}$= 30.447; p< 0.001; η^2_p= 0.792) and ECC2-CL ($F_{3,24}$= 7.921; p= 0.001; η^2_p= 0.498). During ECC1, large effects for differences in MVIC torque were noted at IP and 24H relative to BL, as well at 72H relative to IP. Medium effects were noted at 72H relative to BL and 24H, while a negligible effect was noted at 24H relative to IP. During ECC2-IL, large effects were noted at IP relative to BL, as well as at 24H and 72H relative to IP. Small effects were noted at 24H relative to BL and at 72H relative to 24H, and a negligible effect was noted at 72H relative to BL. During ECC2-CL, large effects were noted at IP and 24H relative to BL, as well as at 72H relative to IP and 24H, while a small effect was noted at 72H relative to BL. Lastly, a negligible difference in MVIC torque was noted at 24H relative to IP.

In the control group, main effects of time were observed during ECC1 ($F_{3,15}$= 0.611; p= 0.618; η^2_p= 0.109), ECC2-IL ($F_{3,15}$= 0.738; p= 0.434; η^2_p= 0.129), and ECC2-CL ($F_{3,15}$= 3.696; p= 0.101; η^2_p= 0.425). Small effects were noted for differences in MVIC torque at 72H relative to IP and 24H during ECC1, at IP relative to BL and at 72H relative to IP during ECC2-IL, and at 72H relative to BL, IP, and 24H during ECC2-CL. All other changes across time during ECC1, ECC2-IL and ECC2-CL were negligible. Pairwise comparisons between groups across levels of time and bout are presented in Table 13.

Table 13. Within-group differences in MVIC torque across time points during ECC1, ECC2-IL, and ECC2-CL.

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC1	Group x time	4.170	0.243	EX	<0.001 (0.769)	BL vs. IP	<0.001	-1.850	-2.640	-1.070
						BL vs. 24H	0.002	-1.690	-2.610	-0.771
						BL vs. 72H	0.079	-0.712	-1.250	-0.179
						IP vs. 24H	1.000	0.150	-0.305	0.605
						IP vs 72H	0.028	0.890	0.315	1.470
						24H vs. 72H	0.001	0.687	0.428	0.947
				CON	0.618 (0.109)	BL vs. IP	1.000	-0.179	-0.494	0.137
						BL vs. 24H	1.000	-0.196	-0.489	0.097
						BL vs. 72H	1.000	0.058	-0.410	0.526
						IP vs. 24H	1.000	-0.004	-0.373	0.364
						IP vs 72H	1.000	0.225	-0.439	0.888
						24H vs. 72H	1.000	0.228	-0.430	0.886
ECC2-IL	Group x time	1.375	0.096	EX	<0.001 (0.792)	BL vs. IP	<0.001	-1.250	-1.670	-0.841
						BL vs. 24H	0.026	-0.481	-0.755	-0.207
						BL vs. 72H	1.000	-0.161	-0.461	0.139
						IP vs. 24H	<0.001	0.804	0.592	1.020
						IP vs 72H	0.002	1.220	0.632	1.820
						24H vs. 72H	0.401	0.347	-0.010	0.705
				CON	0.434 (0.129)	BL vs. IP	0.139	-0.324	-0.553	-0.095
						BL vs. 24H	1.000	-0.096	-0.529	0.336
						BL vs. 72H	1.000	-0.096	-0.408	0.216
						IP vs. 24H	1.000	0.195	-0.091	0.481
						IP vs 72H	0.625	0.246	-0.034	0.526
						24H vs. 72H	1.000	0.008	-0.264	0.279

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC2-CL	Group x time	3.157	0.195	EX	0.001 (0.498)	BL vs. IP	0.003	-2.280	-3.870	-0.686
						BL vs. 24H	0.057	-1.560	-3.020	-0.105
						BL vs. 72H	1.000	-0.473	-1.580	0.631
						IP vs. 24H	1.000	0.153	-0.677	0.982
						IP vs 72H	0.143	1.170	0.015	2.320
						24H vs. 72H	0.111	0.857	0.136	1.580
				CON	0.101 (0.425)	BL vs. IP	1.000	-0.080	-0.383	0.222
						BL vs. 24H	1.000	-0.021	-0.362	0.319
						BL vs. 72H	0.957	0.275	-0.103	0.653
						IP vs. 24H	1.000	0.020	-0.047	0.087
						IP vs 72H	0.032	0.267	0.138	0.397
						24H vs. 72H	0.004	0.296	0.208	0.385

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater MVIC torque relative to preceding time point in corresponding group and bout. Negative g indicates lower MVIC torque relative to preceding time point in corresponding group and bout.

Bout x time interactions were observed for MVIC torque in both the exercise ($F_{6,48}$= 1.962; p=0.090; η^2_p= 0.197) and control group ($F_{6,30}$=0.440; p=0.846; η^2_p= 0.081). In the exercise group, a main effect of bout was noted at 24H ($F_{2,16}$= 2.654; p=0.101; η^2_p= 0.249). Large and medium effects were noted at 24H for differences in MVIC torque between ECC1 and ECC2-IL, and between ECC2-IL and ECC2-CL, respectively, while differences between ECC1 and ECC2-CL at 24H were negligible. No main effects of bout were observed at BL ($F_{2,16}$=0.131; p=0.878; η^2_p= 0.016), IP ($F_{2,16}$= 0.390; p= 0.683; η^2_p= 0.046) or 72H ($F_{2,16}$= 0.406; p=0.569; η^2_p= 0.048) in the exercise group.

In the control group, main effects of bout were observed at BL ($F_{2,10}$=3.860; p=0.057; η^2_p= 0.436) and IP ($F_{2,10}$= 0.608; p= 0.563; η^2_p= 0.108). Small effects were noted at BL for differences in MVIC torque between ECC1 and ECC2-CL, and between ECC2-IL and ECC2-CL, while the difference between ECC1 and ECC2-IL was negligible. At IP, negligible effects were noted between ECC1 and ECC2-IL and between ECC2-IL and ECC2-CL, while a small effect was noted between ECC1 and ECC2-CL. No main effects of bout were observed in the control group at 24H ($F_{2,10}$= 0.223; p=0.804; η^2_p= 0.043) or 72H ($F_{2,10}$= 0.215; p=0.679; η^2_p= 0.041). Pairwise comparisons within groups across levels of time and bout are presented in Table 14.

Table 14. Within-group differences in MVIC torque across bouts at BL, IP, 24H, and 72H.

Group	Effect	F	η^2_p	Time	p (η^2_p)	Bout	p	g	95% CI (Lower)	95% CI (Upper)
EX	Bout x time	1.962	0.197	BL	0.878 (0.016)	-	-	-	-	-
				IP	0.683 (0.046)	-	-	-	-	-
				24H	0.101 (0.249)	ECC1 vs. ECC2-IL	0.020	0.899	0.278	1.520
						ECC1 vs. ECC2-CL	1.000	0.095	-1.060	1.250
						ECC2-IL vs. ECC2-CL	0.361	-0.782	-1.870	0.308
				72H	0.569 (0.048)	-	-	-	-	-
CON	Bout x time	0.440	0.081	BL	0.057 (0.436)	ECC1 vs. ECC2-IL	1.000	0.041	-0.182	0.264
						ECC1 vs. ECC2-CL	0.385	-0.362	-0.820	0.095
						ECC2-IL vs. ECC2-CL	0.178	-0.400	-0.780	-0.019
				IP	0.563 (0.108)	ECC1 vs. ECC2-IL	1.000	-0.125	-0.599	0.349
						ECC1 vs. ECC2-CL	1.000	-0.259	-0.987	0.470
						ECC2-IL vs. ECC2-CL	1.000	-0.137	-0.521	0.248
				24H	0.804 (0.043)	-	-	-	-	-
				72H	0.679 (0.041)	-	-	-	-	-

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater MVIC torque relative to preceding bout for corresponding time point and group. Negative g indicates lower MVIC torque relative to preceding bout for corresponding time point and group.

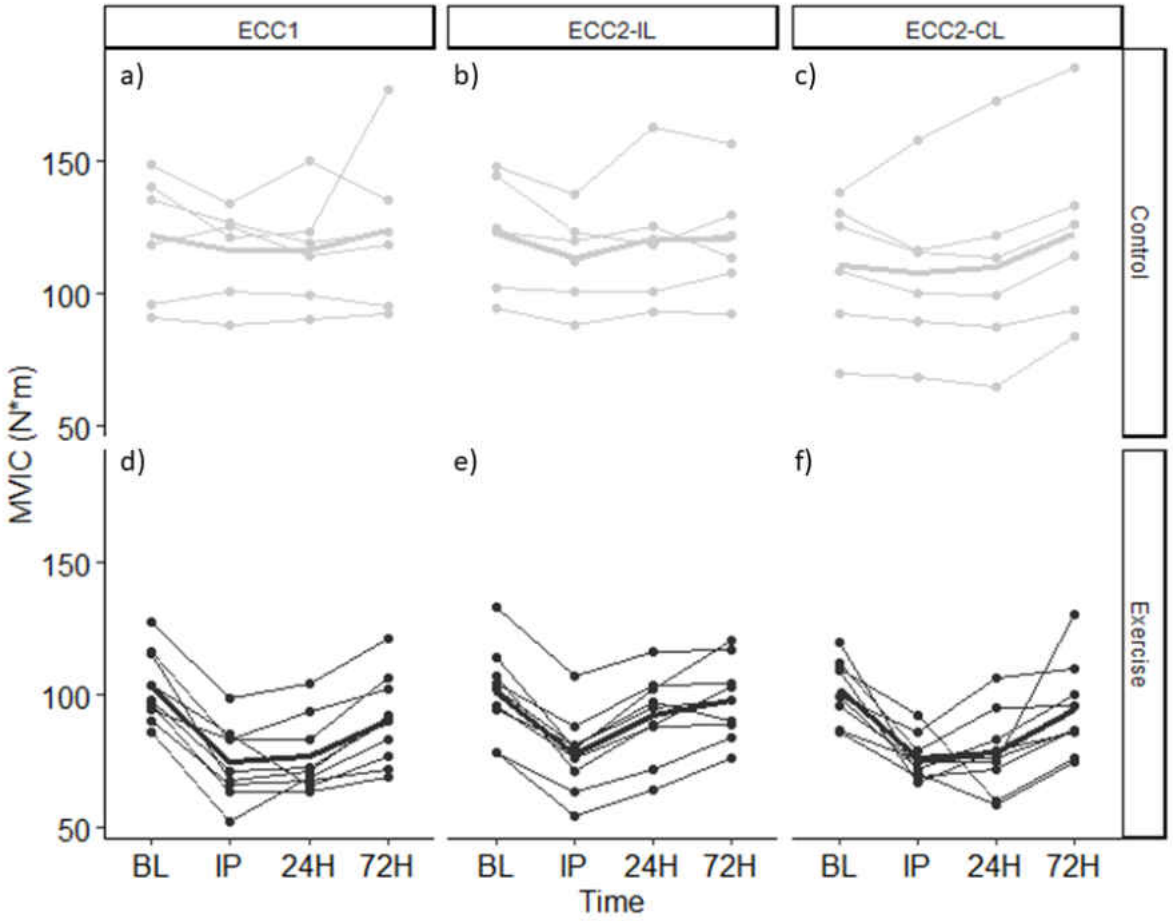


Figure 7. Changes in maximal voluntary isometric contraction (MVIC) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Rate of Torque Development at 50 ms (RTD_{50})

No outliers were detected for RTD_{50} at any time point. All RTD_{50} data were normally distributed except for at BL in both the exercise (*SW*=0.808; *df*=9; *p*=0.025) and control group (*SW*=0.754; *df*=6; *p*=0.022) during ECC2-IL.

No group x bout x time interaction was observed ($F_{6,78}$= 0.730; *p*= 0.626; η^2_p= 0.053). However, a group x time interaction was observed ($F_{3,39}$= 2.245; *p*= 0.098; η^2_p= 0.147). In the

exercise group, a main effect of time was observed ($F_{3,24}$= 4.364; p= 0.014; η^2_p= 0.353). When collapsed across bout, small effects were observed for differences in RTD_{50} at IP and 24H relative to BL. However, comparisons between all other time points were negligible. In the control group, a main effect of time was not observed ($F_{3,15}$= 0.245; p= 0.864; η^2_p= 0.047).

Analysis of between group comparisons collapsed across bout revealed medium effects at IP, 24H, and 72H, while a small effect was noted for differences between groups at BL. Pairwise comparisons between groups across levels of time are presented in Table 15. Changes in RTD_{50} across time are presented in Figure 8.

Table 15. Within-group differences in RTD_{50} across time points.

Effect	F	η^2_p	Group	Time	p	g	95% CI (Lower)	95% CI (Upper)
Group x time	2.245	0.147	EX	BL vs. IP	0.072	-0.323	-0.665	0.017
				BL vs. 24H	1.000	-0.213	-0.552	0.128
				BL vs. 72H	1.000	-0.155	-0.485	0.174
				IP vs. 24H	0.197	0.120	-0.178	0.419
				IP vs. 72H	0.206	0.185	-0.122	0.492
				24H vs. 72H	1.000	0.062	-0.126	0.251
			CON	BL vs. IP	1.000	-0.264	-0.602	0.075
				BL vs. 24H	1.000	-0.067	-0.439	0.306
				BL vs. 72H	1.000	0.041	-0.296	0.379
				IP vs. 24H	1.000	0.228	-0.184	0.640
				IP vs. 72H	1.000	0.354	-0.061	0.769
				24H vs. 72H	1.000	0.126	-0.099	0.350
			EX vs. CON	BL	0.347	-0.417	-1.030	0.192
				IP	0.005	-0.545	-1.160	0.069
				24H	0.186	-0.652	-1.270	-0.033
				72H	0.171	-0.727	-1.350	-0.105

EX = Exercise Group; CON = Control Group; RTD_{50} = rate of torque development at 50ms; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{50} relative to preceding time point in corresponding group or in exercise relative to control when collapsed across bout. Negative g indicates lower RTD_{50} relative to preceding time point in corresponding group or in exercise relative to control.

A group x bout interaction was also observed for RTD_{50} ($F_{2,26}$= 1.250; p= 0.303; η^2_p= 0.088). A main effect of bout was not observed in the exercise group ($F_{2,16}$=0.265; p= 0.771; η^2_p= 0.032). However, a main effect of bout was observed in the control group ($F_{2,10}$=1.290; p= 0.317; η^2_p= 205). When collapsed across time in the control group, a small effect was noted for differences in ECC1 compared to ECC2-IL. However, negligible effects were noted for comparisons between other bouts. No bout x time interaction was observed for RTD_{50} ($F_{6,78}$= 0.702; p= 0.649; η^2_p= 0.051). Pairwise bout comparisons within each group are presented in Table 16.

Table 16. Within-group differences in RTD_{50} during ECC1, ECC2-IL, and ECC2-CL.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	1.250	0.088	EX	-				
			CON	ECC1 vs. ECC2-IL	0.348	0.342	-0.004	0.687
				ECC1 vs. ECC2-CL	0.984	0.199	-0.196	0.594
				ECC2-IL vs. ECC2-CL	1.000	-0.114	-0.355	0.128

EX = Exercise Group; CON = Control Group; RTD_{50} = rate of torque development at 50ms; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{50} in repeated bout compared to ECC1, or in ECC2-CL compared to ECC2-IL when collapsed across time.

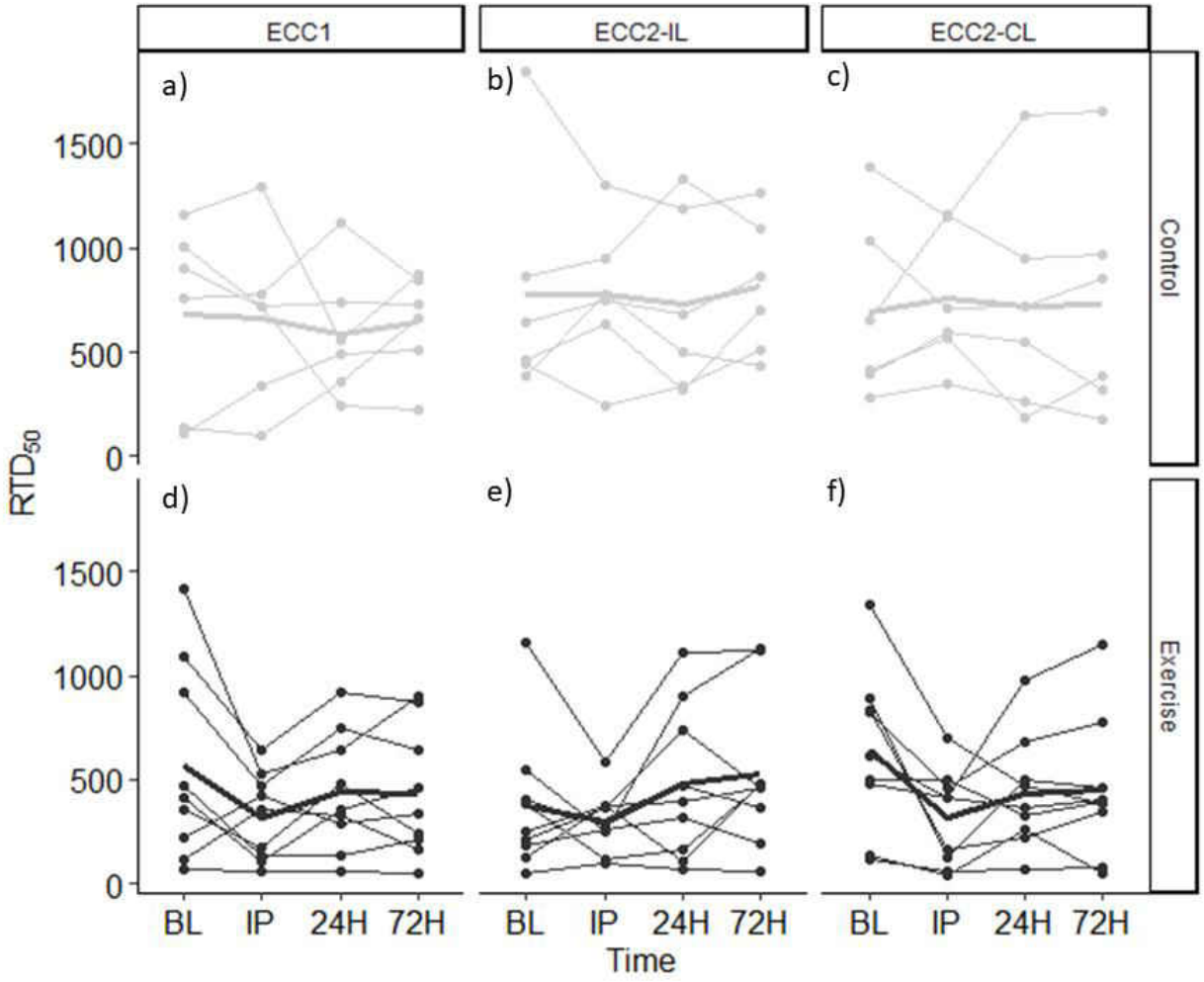


Figure 8. Changes in rate of torque development at 50 ms (RTD_{50}) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Rate of Torque Development at 100 ms (RTD_{100})

No outliers were detected for RTD_{100} at any time point. All RTD_{100} data were normally distributed except for at IP in the control group during ECC2-CL (*SW*=0.767; *df*=6; *p*=0.029).

A group x bout x time interaction was observed for RTD_{100} ($F_{6,78}$= 1.423; *p*= 0.247; η^2_p= 0.099). Follow up analysis revealed group x bout interactions at BL ($F_{2,26}$= 1.767; *p*= 0.191; η^2_p=

0.120) and 24H ($F_{2,26}$= 0.844; p= 0.441; η^2_p= 0.061). Small and medium effects were noted for between group differences in RTD_{100} at BL during ECC1 and ECC2-IL, respectively, while a negligible effect was noted during ECC2-CL. At 24H, large effects were noted for between group differences in RTD_{100} during all three bouts. No group x bout interactions were observed at IP ($F_{2,26}$= 0.349; p=0.709; η^2_p= 0.026) or 72H ($F_{2,26}$= 0.087; p= 0.917; η^2_p= 0.007). However, main effects of group were observed at IP ($F_{1,13}$= 10.642; p= 0.006; η^2_p= 0.450) and 72H ($F_{1,13}$= 1.853; p= 0.197; η^2_p= 0.125). When collapsed across bout, medium effects for between-group differences in RTD_{100} were noted at both IP and 72H. Pairwise comparisons between groups across levels of bout and time are presented in Table 17. Changes in RTD_{100} across time are presented in Figure 9.

Table 17. Between-group differences (EX vs. CON) in RTD_{100} at each time point during ECC1, ECC2-IL, and ECC2-CL.

Time	Effect	F	η^2_p	Bout	p	g	95% CI (Lower)	95% CI (Upper)
BL	Group x bout	1.767	0.120	ECC1	0.379	-0.451	-1.540	0.633
				ECC2-IL	0.172	-0.718	-1.820	0.387
				ECC2-CL	0.872	0.082	-0.990	1.150
IP	Group	10.642	0.450	-	0.006	-0.578	-1.190	0.037
24H	Group x bout	0.844	0.061	ECC1	0.111	-0.849	-1.970	0.268
				ECC2-IL	0.274	-0.566	-1.660	0.526
				ECC2-CL	0.034	-1.180	-2.330	-0.019
72H	Group	1.853	0.125	-	0.197	-0.678	-1.300	-0.059

EX = Exercise Group; CON = Control Group; RTD_{100} = rate of torque development at 100ms; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL= repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Where a main effect of group is noted, negative g indicates greater RTD_{100} in control group at corresponding time point. Where a group x bout interaction is noted, negative g indicates greater RTD_{100} in control group during corresponding bout and time point.

A group x time interaction was observed during ECC2-IL ($F_{3,39}$= 1.775; p=0.168; η^2_p= 0.120) and ECC2-CL ($F_{3,39}$= 6.161; p=0.002; η^2_p= 0.322). In the exercise group, main effects of time were observed for ECC2-IL ($F_{3,24}$= 5.281; p= 0.006; η^2_p= 0.398) and ECC2-CL ($F_{3,24}$= 6.627; p=0.002; η^2_p= 0.453). During ECC2-IL, small effects were noted for differences in RTD_{100} at IP and 72H relative to BL, while small effects were noted at 24H and 72H relative to IP, and at 72H relative to 24H. A negligible effect was noted at 24H compared to BL. During ECC2-CL, a large effect was noted at IP relative to BL, while medium effects were noted at 24H and 72H relative to BL and IP. Small and negligible effects were noted at 24H relative to IP and 72H relative to 24H, respectively.

In the control group, a main effect of time was observed during ECC2-CL ($F_{3,15}$= 1.459; p= 0.266; η^2_p= 0.226). Small effects were noted for differences in RTD_{100} at IP and 24H relative to BL, and at 72H relative to 24H. All other changes across time during ECC2-CL were negligible. No main effect of time was observed in the control group during ECC2-IL ($F_{3,15}$= 0.224; p= 0.878; η^2_p= 0.043). No group x time interaction ($F_{3,39}$= 0.459; p= 0.713; η^2_p= 0.034) or main effect of time ($F_{3,39}$= 0.688; p= 0.565; η^2_p= 0.050) were observed for RTD_{100} during ECC1. Pairwise comparisons between bouts across each level of group and time are presented in Table 18.

Table 18. Within-group differences in RTD_{100} across time points during ECC1, ECC2-IL, and ECC2-CL.

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC1	Time	0.459	0.034	-	-	-	-			
ECC2-IL	Group x time	1.775	0.120	EX	0.006 (0.398)	BL vs. IP	1.000	-0.205	-0.529	0.119
						BL vs. 24H	1.000	0.099	-0.135	0.332
						BL vs. 72H	0.117	0.357	0.089	0.626
						IP vs. 24H	0.295	0.228	0.017	0.439
						IP vs. 72H	0.071	0.382	0.123	0.640
						24H vs. 72H	0.685	0.267	-0.058	0.593
				CON	0.878 (0.043)	-	-			
ECC2-CL	Group x time	6.161	0.322	EX	0.002 (0.453)	BL vs. IP	0.016	-1.130	-1.850	-0.413
						BL vs. 24H	0.188	-0.773	-1.490	-0.056
						BL vs. 72H	0.478	-0.663	-1.440	0.110
						IP vs. 24H	1.000	0.435	-0.264	1.130
						IP vs. 72H	0.525	0.567	-0.098	1.230
						24H vs. 72H	1.000	0.125	-0.145	0.395
				CON	0.266 (0.226)	BL vs. IP	1.000	0.347	-0.331	1.030
						BL vs. 24H	1.000	0.404	-0.224	1.030
						BL vs. 72H	1.000	0.134	-0.163	0.432
						IP vs. 24H	1.000	0.063	-0.270	0.397
						IP vs. 72H	1.000	-0.183	-0.620	0.255
						24H vs. 72H	1.000	-0.213	-0.581	0.154

EX = Exercise Group; CON = Control Group; RTD_{100} = rate of torque development at 100ms; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP=immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{100} relative to preceding time point in corresponding group and bout. Negative g indicates lower RTD_{100} relative to preceding time point in corresponding group and bout.

Bout x time interactions were observed for RTD_{100} in both the exercise ($F_{6,48}$= 2.662; p= 0.026; η^2_p= 0.250) and control group ($F_{6,30}$= 0.426; p= 0.856; η^2_p= 0.079). In the exercise group, main effects of bout were observed at BL ($F_{2,16}$= 2.532; p= 0.111; η^2_p= 0.240), 24H ($F_{2,16}$= 0.903; p= 0.425; η^2_p= 0.101), and 72H ($F_{2,16}$= 4.436; p= 0.029; η^2_p= 0.357). Small and medium effects were noted at BL for differences in RTD_{100} between ECC1 and ECC2-CL, and between ECC2-IL and ECC2-CL, respectively, while differences between ECC1 and ECC2-IL at BL were negligible. A small effect was noted between ECC1 and ECC2-IL at 24H, while effects for all other between bout comparisons at 24H were negligible. At 72H, small effects were noted between ECC1 and ECC2-IL, and between ECC2-IL and ECC2-CL, while differences between ECC1 and ECC2-CL were negligible. No main effect of bout was observed in the exercise group at IP ($F_{2,16}$= 0.096; p= 0.909; η^2_p= 0.012).

In the control group, main effects of bout were observed at 24H ($F_{2,10}$= 1.136; p= 0.359; η^2_p= 0.185) and 72H ($F_{2,10}$= 0.665; p= 0.536; η^2_p= 0.117). At 24H, medium and small effects were noted for differences in RTD_{100} between ECC1 and ECC2-CL, and between ECC2-IL and ECC2-CL, respectively, while differences between ECC1 and ECC2-IL at 24H were negligible. At 72H, a small effect was noted between ECC1 and ECC2-IL, while effects for all other bout comparisons were negligible. No main effects of bout were observed in the control group at BL ($F_{2,10}$= 0.208; p= 0.816; η^2_p= 0.040) or IP ($F_{2,10}$= 0.204; p= 0.819; η^2_p= 0.039). Pairwise comparisons for each group across levels of time and bout are presented in Table 19.

Table 19. Within-group differences in RTD_{100} across bouts at BL, IP, 24H, and 72H.

Group	Effect	F	η^2_p	Time	p (η^2_p)	Bout	p	g	95% CI (Lower)	95% CI (Upper)
EX	Bout x time	2.662	0.250	BL	0.111 (0.240)	ECC1 vs. ECC2-IL	1.000	-0.171	-0.562	0.220
						ECC1 vs. ECC2-CL	0.570	0.393	-0.211	0.997
						ECC2-IL vs. ECC2-CL	0.285	0.609	-0.133	1.350
				IP	0.909 (0.012)	-	-			
				24H	0.425 (0.101)	ECC1 vs. ECC2-IL	0.972	0.276	-0.292	0.844
						ECC1 vs. ECC2-CL	1.000	0.157	-0.307	0.621
						ECC2-IL vs. ECC2-CL	1.000	-0.124	-0.396	0.148
				72H	0.029 (0.357)	ECC1 vs. ECC2-IL	0.097	0.309	0.050	0.569
						ECC1 vs. ECC2-CL	1.000	0.104	-0.174	0.381
						ECC2-IL vs. ECC2-CL	0.198	-0.249	-0.501	0.003
CON	Bout x time	0.426	0.079	BL	0.816 (0.040)	-	-			
				IP	0.819 (0.039)	-	-			
				24H	0.359 (0.185)	ECC1 vs. ECC2-IL	1.000	0.099	-0.552	0.933
						ECC1 vs. ECC2-CL	0.727	0.642	-0.432	1.510
						ECC2-IL vs. ECC2-CL	0.812	0.297	-0.195	0.666
				72H	0.536 (0.117)	ECC1 vs. ECC2-IL	0.837	0.405	-0.368	1.180
						ECC1 vs. ECC2-CL	1.000	0.169	-0.576	0.914
						ECC2-IL vs. ECC2-CL	1.000	-0.130	-0.560	0.300

EX = Exercise Group; CON = Control Group; RTD_{100} = rate of torque development at 100ms; ECC1= initial exercise bout; ECC2-IL= repeated bout on ipsilateral arm; ECC2-CL= repeated bout on contralateral arm; BL= baseline; IP=immediately post-exercise; 24H= twenty-four hours post-exercise; 72H=seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{100} relative to preceding bout for corresponding time point and group. Negative g indicates lower RTD_{100} relative to preceding bout for corresponding time point and group.

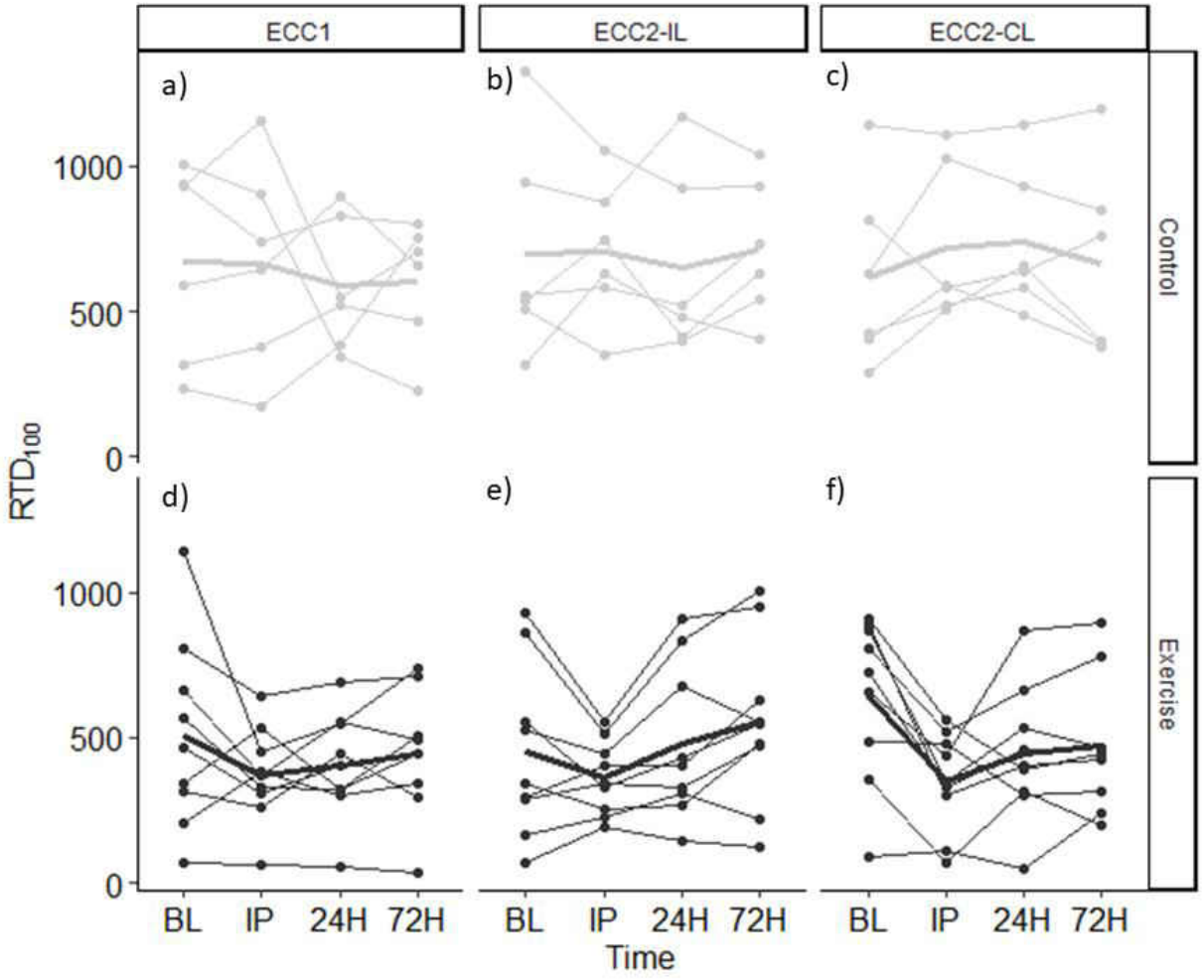


Figure 9. Changes in rate of torque development at 100 ms (RTD_{100}) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Rate of Torque Development at 200 ms (RTD_{200})

No outliers were detected for RTD_{200} at any time point. All RTD_{200} data were normally distributed except for at 24H in exercise group during ECC1 (*SW*=0.769; *df*=9; *p*=0.009).

A group x bout x time interaction was observed for RTD_{200} ($F_{6,78}$= 1.496; *p*= 0.190; η^2_p= 0.103). Follow up analysis revealed a group x bout interaction at BL ($F_{2,26}$= 1.846; *p*= 0.178;

η^2_p= 0.124), 24H ($F_{2,26}$= 2.081; p= 0.145; η^2_p= 0.138), and 72H ($F_{2,26}$= 0.981; p= 0.389; η^2_p= 0.070). Medium effects were noted for the between-group differences in RTD_{200} at BL during ECC1 and ECC2-IL, while the effect for between group differences at BL during ECC2-CL was negligible. At 24H, large effects were noted during ECC1 and ECC2-CL, while a medium effect was noted during ECC2-IL. At 72H, large effects were noted during ECC1 and ECC2-CL, while a medium effect was noted during ECC2-IL. No group x bout interaction was observed at IP ($F_{2,26}$= 0.053; p= 0.949; η^2_p= 0.004); however, a main effect of group was observed ($F_{1,13}$= 11.631; p= 0.005; η^2_p= 0.472). When collapsed across bout, a small effect was noted for between group differences at IP. Pairwise comparisons between groups across levels of bout and time are presented in Table 20. Changes in RTD_{200} across time are presented in Figure 10.

Table 20. Between-group differences (EX vs. CON) in RTD_{200} at each time point during ECC1, ECC2-IL, and ECC2-CL.

Time	Effect	F	η^2_p	Bout	p	g	95% CI (Lower)	95% CI (Upper)
BL	Group x bout	1.846	0.103	ECC1	0.200	-0.670	-1.770	0.431
				ECC2-IL	0.212	-0.652	-1.750	0.447
				ECC2-CL	0.904	0.061	-1.010	1.130
IP	Group	11.361	0.472	-	0.005	-0.478	-1.090	0.133
24H	Group x bout	2.081	0.138	ECC1	0.009	-1.530	-2.740	-0.316
				ECC2-IL	0.206	-0.660	-1.760	0.439
				ECC2-CL	0.009	-1.520	-2.730	-0.305
72H	Group x bout	0.981	0.070	ECC1	0.077	-0.951	-2.080	0.177
				ECC2-IL	0.315	-0.518	-1.610	0.571
				ECC2-CL	0.026	-1.250	-2.410	-0.080

EX = Exercise Group; CON = Control Group; RTD_{200} = rate of torque development at 200ms; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Where a main effect of group is noted, negative g indicates greater RTD_{200} in control group at corresponding time point. Where a group x bout interaction is noted, negative g indicates greater RTD_{200} in control group during corresponding bout and time point.

A group x time interaction was observed for RTD_{200} during ECC2-IL ($F_{3,39}$= 1.775; p= 0.168; η^2_p= 0.120) and ECC2-CL ($F_{3,39}$= 6.177; p= 0.002; η^2_p= 0.322). In the exercise group, main effects of time were observed during ECC2-IL ($F_{3,24}$= 4.942; p=0.008; η^2_p= 0.382) and ECC2-CL ($F_{3,24}$= 7.844; p= 0.001; η^2_p= 0.495). During ECC2-IL, medium effects were noted for differences in RTD_{200} at 24H and 72H relative to IP, while small effects were noted at IP relative to BL, and at 72H relative to 24H. Negligible effects were noted at 24H and 72H relative to BL. During ECC2-CL, large effects were noted for differences in RTD_{200} at IP and 24H relative to BL, while medium effects were noted at 72H relative to BL and IP. Small and negligible effects were noted at 72H relative to 24H, and at 24H relative to IP, respectively.

In the control group, main effects of time were observed during ECC2-IL ($F_{3,15}$= 0.416; p= 0.744; η^2_p= 0.077) and ECC2-CL ($F_{3,15}$= 0.995; p= 0.422; η^2_p= 0.166). During ECC2-IL, all effects for differences in RTD_{200} between time points were negligible. During ECC2-CL, small effects were noted for differences in RTD_{200} at IP, 24H, and 72H relative to BL, while effects for all other comparisons between time points were negligible. No group x time interaction was observed for ECC1 ($F_{3,39}$= 0.427; p= 0.735; η^2_p= 0.032). However, a main effect of time was observed ($F_{3,39}$= 1.619; p= 0.201; η^2_p= 0.111). When collapsed across group, a medium effect was noted for differences in RTD_{200} at 24H relative to BL, while small effects were noted at IP and 72H relative to BL, and at 72H relative to 24H. Effects for differences in RTD200 at 24H and 72H compared to IP were negligible. Pairwise comparisons between bouts across each level of group and time are presented in Table 21.

Table 21. Within-group differences in RTD_{200} across time points during ECC1, ECC2-IL, and ECC2-CL.

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC1	Time	1.619	0.111	-	-	BL vs. IP	0.349	-0.367	-0.701	-0.033
						BL vs. 24H	0.120	-0.516	-0.904	-0.128
						BL vs. 72H	1.000	-0.232	-0.738	0.273
						IP vs. 24H	1.000	-0.082	-0.428	0.264
						IP vs 72H	1.000	0.149	-0.387	0.684
						24H vs. 72H	1.000	0.263	-0.155	0.681
ECC2-IL	Group x time	1.775	0.120	EX	0.008 (0.382)	BL vs. IP	0.461	-0.379	-0.789	0.031
						BL vs. 24H	1.000	-0.038	-0.444	0.367
						BL vs. 72H	1.000	0.161	-0.144	0.467
						IP vs. 24H	0.016	0.522	0.247	0.796
						IP vs 72H	0.047	0.546	0.194	0.898
						24H vs. 72H	0.970	0.213	-0.083	0.508
				CON	0.744 (0.077)	BL vs. IP	1.000	-0.093	-0.512	0.326
						BL vs. 24H	1.000	-0.192	-0.529	0.146
						BL vs. 72H	1.000	-0.043	-0.496	0.409
						IP vs. 24H	1.000	-0.123	-0.629	0.384
						IP vs 72H	1.000	0.078	-0.623	0.778
						24H vs. 72H	1.000	0.186	-0.163	0.534
ECC2-CL	Group x time	6.177	0.322	EX	0.001 (0.495)	BL vs. IP	0.019	-1.070	-1.760	-0.384
						BL vs. 24H	0.032	-0.852	-1.410	-0.295
						BL vs. 72H	0.333	-0.663	-1.360	0.031
						IP vs. 24H	1.000	0.195	-0.374	0.765
						IP vs 72H	0.638	0.506	-0.120	1.130
						24H vs. 72H	0.876	0.243	-0.081	0.567
				CON	0.422 (0.166)	BL vs. IP	1.000	0.269	-0.296	0.835
						BL vs. 24H	1.000	0.388	-0.393	1.170
						BL vs. 72H	1.000	0.368	-0.277	1.010
						IP vs. 24H	1.000	0.079	-0.317	0.475
						IP vs 72H	1.000	0.094	-0.429	0.617
						24H vs. 72H	1.000	-0.001	-0.555	0.552

EX = Exercise Group; CON = Control Group; RTD_{200} = rate of torque development at 200ms; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{200} relative to preceding time point in corresponding group and bout. Negative g indicates lower RTD_{200} relative to preceding time point in corresponding group and bout.

Bout x time interactions were observed for RTD_{200} in both the exercise ($F_{6,48}$= 2.275; p=0.052; η^2_p= 0.221) and control group ($F_{6,30}$= 0.405; p=0.870; η^2_p= 0.075). In the exercise group, main effects of bout were observed at BL ($F_{2,16}$= 2.525; p= 0.111; η^2_p= 0.240) 24H ($F_{2,16}$= 5.541; p= 0.015; η^2_p= 0.409), and 72H ($F_{2,16}$= 3.045; p= 0.076; η^2_p= 0.276). Effects for all between bout comparisons at BL and 72H were small. A medium effect was noted between ECC1 and ECC2-IL at 24H, while effects for differences between ECC1 and ECC2-CL, and between ECC2-IL and ECC2-CL were small. No main effect of bout was observed in the exercise group at IP ($F_{2,16}$= 0.296; p= 0.748; η^2_p= 0.036).

In the control group, a main effect of bout was observed at 24H ($F_{2,10}$= 1.261; p= 0.325; η^2_p= 0.201). Medium and small effects were noted for differences in RTD_{200} between ECC1 and ECC2-CL, and between ECC2-IL and ECC2-CL, respectively, while a negligible effect was noted between ECC1 and ECC2-IL. No main effects of bout were observed in the control group at BL ($F_{2,10}$= 0.270; p= 0.769; η^2_p= 0.051), IP ($F_{2,10}$= 0.082; p= 0.922; η^2_p= 0.016), or 72H ($F_{2,10}$= 0.174; p= 0.843; η^2_p= 0.034). Pairwise comparisons for each two-way interaction are presented in Table 22.

Table 22. Within-group differences in RTD_{200} across bouts at BL, IP, 24H, and 72H.

Group	Effect	F	η^2_p	Time	p (η^2_p)	Bout	p	g	95% CI (Lower)	95% CI (Upper)
EX	Bout x time	2.275	0.221	BL	0.111 (0.240)	ECC1 vs. ECC2-IL	1.000	-0.046	-0.550	0.457
						ECC1 vs. ECC2-CL	0.180	0.479	-0.011	0.970
						ECC2-IL vs. ECC2-CL	0.339	0.484	-0.125	1.090
				IP	0.748 (0.036)	-	-			
				24H	0.015 (0.409)	ECC1 vs. ECC2-IL	0.046	0.750	0.165	1.330
						ECC1 vs. ECC2-CL	0.519	0.310	-0.140	0.759
						ECC2-IL vs. ECC2-CL	0.170	-0.281	-0.554	-0.008
				72H	0.076 (0.276)	ECC1 vs. ECC2-IL	0.059	0.483	0.111	0.855
						ECC1 vs. ECC2-CL	1.000	0.239	-0.272	0.750
						ECC2-IL vs. ECC2-CL	0.684	-0.280	-0.742	0.183
CON	Bout x time	0.405	0.075	BL	0.769 (0.051)	-	-			
				IP	0.922 (0.016)	-	-			
				24H	0.325 (0.201)	ECC1 vs. ECC2-IL	1.000	0.099	-0.608	0.805
						ECC1 vs. ECC2-CL	0.653	0.642	-0.473	1.760
						ECC2-IL vs. ECC2-CL	0.676	0.297	-0.192	0.786
				72H	0.843 (0.034)	-	-			

EX = Exercise Group; CON = Control Group; RTD_{200} = rate of torque development at 200ms; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{200} relative to preceding bout for corresponding time point and group. Negative g indicates lower RTD_{200} relative to preceding bout for corresponding time point and group.

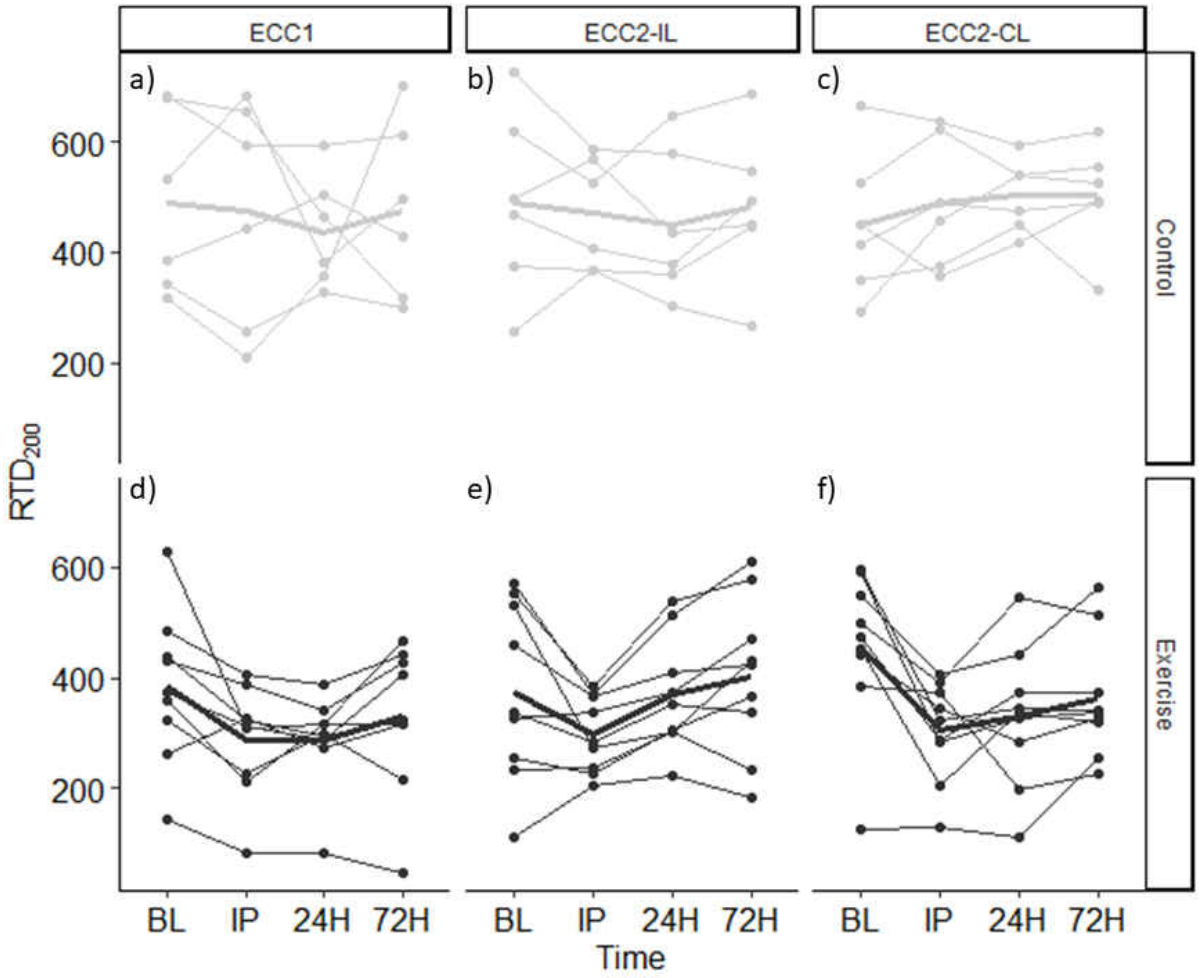


Figure 10. Changes in rate of torque development at 200 ms (RTD_{200}) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Peak Rate of Torque Development (RTD_{peak})

No outliers were detected for RTD_{peak} at any time point. All RTD_{peak} data were normally distributed except for at BL in the exercise group (*SW*=0.802; *df*=9; *p*=0.022) and 24H in the control group (*SW*=0.757; *df*=6; *p*=0.023) during ECC1, at BL (*SW*=0.762; *df*=6; *p*=0.026) and 24H (*SW*=0.775; *df*=6; *p*=0.034) in the control group during ECC2-IL, at 24H (*SW*=0.737; *df*=6;

p=0.015) in the control group during ECC2-CL, and at 72H in the exercise group (SW=0.750; df=9 ;p=0.005) and control group (SW=0.766; df=6; p=0.028) during ECC2-CL.

A group x bout x time interaction was observed for RTD_{peak} ($F_{1.950, 25.355}$= 1.376; p=0.271; η^2_p= 0.096). Follow-up analysis revealed a group x bout interaction at BL ($F_{2,26}$= 0.850; p=0.439; η^2_p=0.061), IP($F_{2,26}$= 1.614; p=0.218; η^2_p= 0.110), and 72H ($F_{1.160,15.086}$=1.602; p=0.228; η^2_p= 0.110). A medium effect was noted for between group differences at BL during ECC2-IL. However, negligible effects were noted for between group differences during ECC1 and ECC2-CL. Large effects were noted for between group differences at IP during all three bouts. Medium effects were noted for between group differences at 72H during ECC1 and ECC2-IL, while a large effect was noted during ECC2-CL. A group x bout interaction was not observed at 24H ($F_{1.382, 17.967}$= 0.496; p=0.550; η^2_p= 0.037). However, a main effect of group was observed at 24H ($F_{1,13}$=4.166; p=0.062; η^2_p= 0.243). When collapsed across bout, a medium effect was noted for between group differences at 24H. Pairwise comparisons between groups across levels of bout and time are presented in Table 23. Changes in RTD_{peak} across time are presented in Figure 11.

Table 23. Between-group differences (EX vs. CON) in RTD_{peak} at each time point during ECC1, ECC2-IL, and ECC2-CL.

Time	Effect	F	η^2_p	Bout	p	g	95% CI (Lower)	95% CI (Upper)
BL	Group x bout	0.85	0.061	ECC1	0.831	-0.108	-1.180	0.964
				ECC2-IL	0.256	-0.589	-1.680	0.505
				ECC2-CL	0.907	0.059	-1.010	1.130
IP	Group x bout	1.614	0.110	ECC1	0.047	-1.090	-2.240	0.054
				ECC2-IL	0.005	-1.670	-2.910	-0.436
				ECC2-CL	0.017	-1.360	-2.540	-0.173
24H	Group	4.166	0.243	-	0.119	-0.628	-1.250	-0.011
72H	Group x bout	1.602	0.110	ECC1	0.239	-0.612	-1.710	0.483
				ECC2-IL	0.189	-0.688	-1.800	0.413
				ECC2-CL	0.128	-0.807	-1.920	0.306

EX = Exercise Group; CON = Control Group; RTD_{peak} = peak rate of torque development; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates effect is present; g = Hedges g effect size for comparisons. Where a main effect of group is noted, negative g indicates greater RTD_{peak} in control group at corresponding time point. Where a group x bout interaction is noted, negative g indicates greater RTD_{peak} in control group during corresponding bout and time point.

Group x time interactions were observed for ECC2-IL ($F_{3,39}$= 1.617; p=0.201; η^2_p= 0.111) and ECC2-CL ($F_{1.606, 20.873}$= 3.465; p=0.059; η^2_p= 0.210). In the exercise group, effects of time were observed during ECC2-IL ($F_{1.686,13.491}$=4.228; p=0.043; η^2_p= 0.346) and ECC2-CL ($F_{1.263,10.108}$=3.293; p=0.093; η^2_p= 0.292). During ECC2-IL, small effects were noted at IP relative to BL, 24H and 72H relative to IP, and 72H relative to 24H. negligible effects were noted for 72H and 24H relative to BL. During ECC2-CL, a main effect of time was observed in the exercise group. Medium effects were noted for differences at IP, 24H, and 72H relative to BL, while small effects were noted for differences at 24H and 72H relative to IP. Negligible effects were noted for differences at 72H relative to 24H.

A main effect of time was also observed in the control group for ECC2-CL ($F_{3,15}$=1.661; p=0.218; η^2_p= 0.249). Small effects were noted for differences at IP, 24H, and 72H relative to BL; however, effects for all other comparisons between time points were negligible. A main effect of time was not observed during ECC2-IL in the control group ($F_{3,15}$=0.188; p=0.903; η^2_p= 0.036).

A group x time interaction was not observed for ECC1 ($F_{2.019, 26.248}$= 0.675; p=0.519; η^2_p= 0.049). However, a main effect of time was observed for ECC1 ($F_{2.019, 26.248}$= 1.401; p= 0.264; η^2_p= 0.097). When collapsed across group, small effects were noted for differences at IP and 24H relative to BL as well as 72H relative to IP. Negligible effects were noted for differences between all other time points. Pairwise comparisons between bouts across each level of group and time are presented in Table 24.

Table 24. Within-group differences in RTD_{peak} across time points during ECC1, ECC2-IL, and ECC2-CL.

Bout	Effect	F	η^2_p	Group	p (η^2_p)	Time	p	g	95% CI (Lower)	95% CI (Upper)
ECC1	Time	1.401	0.097	-	-	BL vs. IP	0.640	-0.332	-0.583	-0.082
						BL vs. 24H	1.000	-0.207	-0.480	0.067
						BL vs. 72H	1.000	-0.011	-0.276	0.255
						IP vs. 24H	1.000	0.145	-0.063	0.353
						IP vs 72H	1.000	0.282	0.080	0.484
						24H vs. 72H	1.000	0.160	0.023	0.297
ECC2-IL	Group x time	1.617	0.111	Exercise	0.043 (0.346)	BL vs. IP	1.000	-0.209	-0.510	0.091
						BL vs. 24H	1.000	0.024	-0.155	0.202
						BL vs. 72H	0.741	0.190	-0.046	0.427
						IP vs. 24H	0.324	0.277	0.012	0.542
						IP vs 72H	0.070	0.300	0.100	0.499
						24H vs. 72H	1.000	0.201	-0.108	0.511
				Control	0.903 (0.036)	-				
ECC2-CL	Group x time	3.465	0.210	Exercise	0.093 (0.292)	BL vs. IP	0.077	-0.523	-0.894	-0.152
						BL vs. 24H	0.718	-0.638	-1.490	0.213
						BL vs. 72H	1.000	-0.525	-1.420	0.374
						IP vs. 24H	1.000	0.307	-0.372	0.985
						IP vs 72H	1.000	0.431	-0.313	1.180
						24H vs. 72H	0.853	0.123	-0.038	0.284
				Control	0.218 (0.249)	BL vs. IP	1.000	0.241	-0.144	0.626
						BL vs. 24H	1.000	0.254	-0.135	0.642
						BL vs. 72H	1.000	0.234	-0.119	0.587
						IP vs. 24H	1.000	0.030	-0.134	0.195
						IP vs 72H	1.000	0.050	-0.054	0.155
						24H vs. 72H	1.000	0.041	-0.040	0.122

EX = Exercise Group; CON = Control Group; RTD_{peak} = peak rate of torque development; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{peak} relative to preceding time point in corresponding group and bout. Negative g indicates lower RTD_{peak} relative to preceding time point in corresponding group and bout.

Bout x time interactions were observed for both the exercise ($F_{1.403,11.221}$= 1.263; p=0.304; η^2_p= 0.136) and control ($F_{6,30}$= 0.646; p= 0.693; η^2_p= 0.114) groups. In the exercise group, effects of bout were observed at BL ($F_{2,16}$= 1.159; p= 0.339; η^2_p= 0.127) and 72H ($F_{2,16}$= 1.317; p= 0.296; η^2_p= 0.141). At BL, a small effect was noted for differences between ECC1 and ECC2-IL, while a medium effect was noted for differences between ECC2-IL and ECC2-CL. However, the effect for the comparison between ECC1 and ECC2-CL was negligible. At 72H, negligible effects were noted for comparisons between all bouts. Effects of bout were not observed at IP ($F_{2,16}$= 0.076; p=0.927; η^2_p= 0.009) or 24H ($F_{2,16}$= 0.459; p= 0.640; η^2_p= 0.054).

In the control group, effects of bout were observed at IP ($F_{2,10}$=1.623; p= 0.245; η^2_p= 0.245), 24H ($F_{2,10}$=0.398; p=0.682; η^2_p= 0.074), and 72H ($F_{1.116,5.579}$=0.919; p=0.390; η^2_p= 0.155). At IP, small effects were noted for differences in RTD_{peak} between ECC1 and ECC2-IL and between ECC1 and ECC2-CL; however, negligible effects were noted between ECC2-IL and ECC2-CL. While small effects were noted for differences between ECC1 and ECC2-CL and between ECC2-IL and ECC2-CL at 24H, negligible effects were noted for differences between ECC1 and ECC2-IL. Small effects were noted for differences between ECC1 and ECC2-IL and between ECC1 and ECC2-CL, whilenegligible effects were noted for differences between ECC2-IL and ECC2-CL at 72H. No effect of bout was observed at BL ($F_{2,10}$=0.071; p= 0.932; η^2_p= 0.014). Pairwise comparisons for each group across levels of bout and time are presented in Table 25.

Table 25. Within-group differences in RTD_{peak} across bouts at BL, IP, 24H, and 72H.

Group	Effect	F	η^2_p	Time	p (η^2_p)	Bout	p	g	95% CI (Lower)	95% CI (Upper)
EX	Bout x time	1.263	0.136	BL	0.339 (0.127)	ECC1 vs. ECC2-IL	0.262	-0.246	-0.026	0.518
						ECC1 vs. ECC2-CL	1.000	-0.120	-0.874	0.634
						ECC2-IL vs. ECC2-CL	0.654	-0.529	-1.430	0.367
				IP	0.927 (0.009)	-				
				24H	0.640 (0.054)	-				
				72H	0.296 (0.141)	ECC1 vs. ECC2-IL	0.756	-0.154	-0.421	0.112
						ECC1 vs. ECC2-CL	1.000	-0.025	-0.247	0.296
						ECC2-IL vs. ECC2-CL	0.372	-0.186	-0.045	0.417
CON	Bout x time	0.646	0.114	BL	0.932 (0.014)	-				
				IP	0.245 (0.245)	ECC1 vs. ECC2-IL	0.529	0.297	-0.726	0.133
						ECC1 vs. ECC2-CL	0.723	0.328	-0.892	0.236
						ECC2-IL vs. ECC2-CL	1.000	0.074	-0.367	0.219
				24H	0.682 (0.074)	ECC1 vs. ECC2-IL	1.000	0.125	-1.150	0.901
						ECC1 vs. ECC2-CL	1.000	0.341	-1.510	0.831
						ECC2-IL vs. ECC2-CL	1.000	0.210	-0.707	0.287
				72H	0.390 (0.155)	ECC1 vs. ECC2-IL	1.000	0.244	-1.040	0.553
						ECC1 vs. ECC2-CL	1.000	0.361	-1.200	0.476
						ECC2-IL vs. ECC2-CL	1.000	0.177	-0.598	0.245

EX = Exercise Group; CON = Control Group; RTD_{peak} = peak rate of torque development; ECC1 = initial exercise bout; ECC2-IL = repeated bout on ipsilateral arm; ECC2-CL = repeated bout on contralateral arm; BL = baseline; IP = immediately post-exercise; 24H = twenty-four hours post-exercise; 72H = seventy-two hours post-exercise; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates greater RTD_{peak} relative to preceding bout for corresponding time point and group. Negative g indicates lower RTD_{peak} relative to preceding bout for corresponding time point and group.

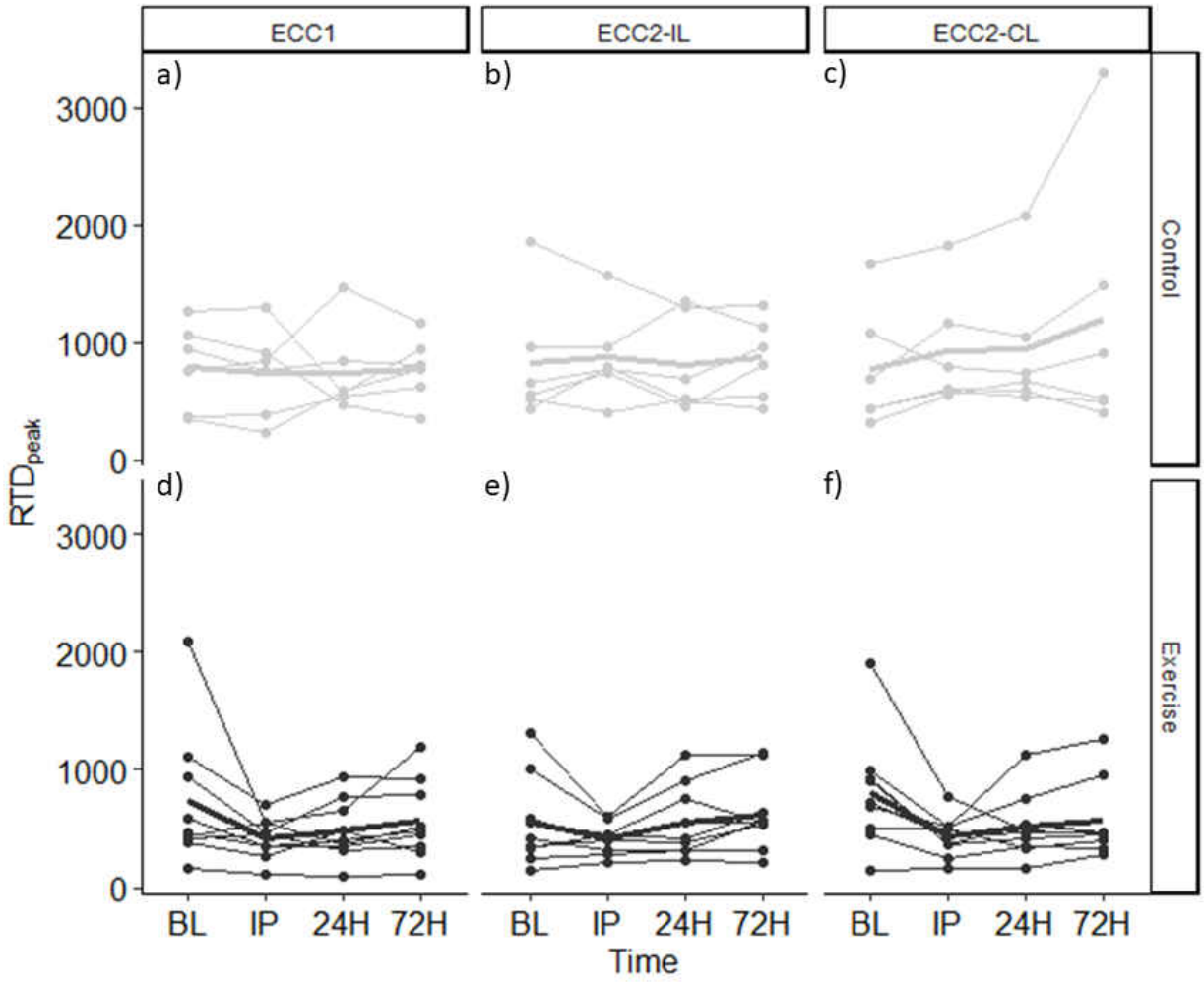


Figure 11.Changes in peak rate of torque development (RTD_{peak}) across time.

Solid lines indicate group means at each time point. a) ECC1, control group; b) ECC2-IL, control group; c) ECC2-CL, control group; d) ECC1 exercise group; e) ECC2-IL, exercise group; f) ECC2-CL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

Motor Unit Decomposition Accuracy at 50% MVIC

For isometric contractions at 50% MVIC, the total number of motor units meeting the accuracy threshold of 90% relative to total number of motor units identified within each bout are as follows: ECC1-IL (80 of 218, exercise: k=54, n=6; control k=26, n=3), ECC2-IL (76 of 189, exercise: k=45, n=6; control k=31, n=3), ECC1-CL (96 of 245, exercise: k=48, n=6; control k=48 n=5), ECC2-CL (95 of 225, exercise: k=54, n=6; control k=41, n=5), where k is equal to

the number of motor units analyzed in each group and n is equal to the number of participants used for analysis. Because of differences in the number of identified motor units between limbs as well as between bins, effects of bin and limb could not be evaluated. Therefore, group x bout interactions were assessed for each level of bin and limb.

Mean Firing Rate vs. Recruitment Threshold Slope at 50% MVIC

Individual and mean regression lines for the mean firing rate vs. recruitment threshold slope in the ipsilateral and contralateral limb are presented in Figures 12 and 13, respectively. In the ipsilateral limb, a group x bout interaction was observed ($F_{1,7}$=0.754; p=0.414; η^2_p=0.097). In both the exercise and control groups, small effects were noted for differences between ECC1-IL and ECC2-IL. Additionally, large effects were noted for between group differences during ECC1-IL, while small effects were noted during ECC2-IL. Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 26.

A group x bout interaction was not observed in the contralateral limb ($F_{1,9}$=0.010; p=0.922; η^2_p= 0.001). Main effects of group ($F_{1,9}$=0.001; p=0.979; η^2_p=0.000) and bout ($F_{1,9}$=0.001; p=0.973; η^2_p=0.000) were also not observed in the contralateral limb.

Table 26. Pairwise comparisons for differences in mean firing rate vs. recruitment threshold slope at 50% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.315	0.348	-0.368	1.060
			CON	ECC1-IL vs. ECC2-IL	0.364	0.301	-0.432	1.030
			EX vs. CON	ECC1-IL	0.138	0.960	-0.456	2.380
			EX vs. CON	ECC2-IL	0.497	0.381	-0.832	1.600

EX = Exercise Group; CON = Control Group; ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL = baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates lower slope relative to preceding bout or higher slope in control than exercise. Negative g indicates higher slope relative to preceding bout or higher slope in exercise than control.

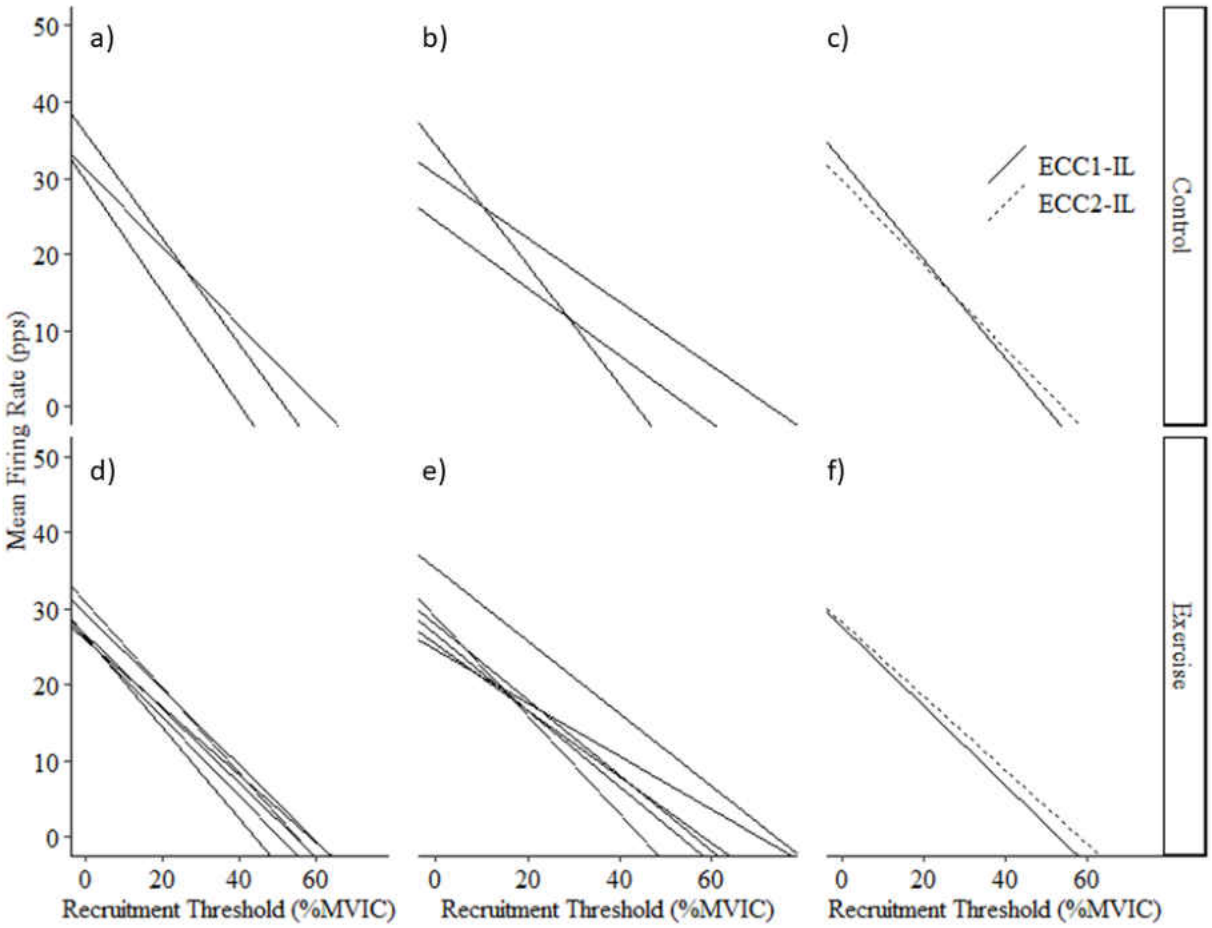


Figure 12.Individual and group trendlines for the mean firing rate vs. recruitment threshold relationship at 50% MVIC.

a) ECC1-IL, control group; b) ECC2-IL, control group; c) group means for ECC1-IL and ECC2-IL, control group; d) ECC1-IL exercise group; e) ECC2-IL, exercise group; f) group means for ECC1-IL and ECC2-IL, exercise group. ECC1-IL=initial exercise bout on ipsilateral limb; ECC2-IL=repeated exercise bout in ipsilateral limb.

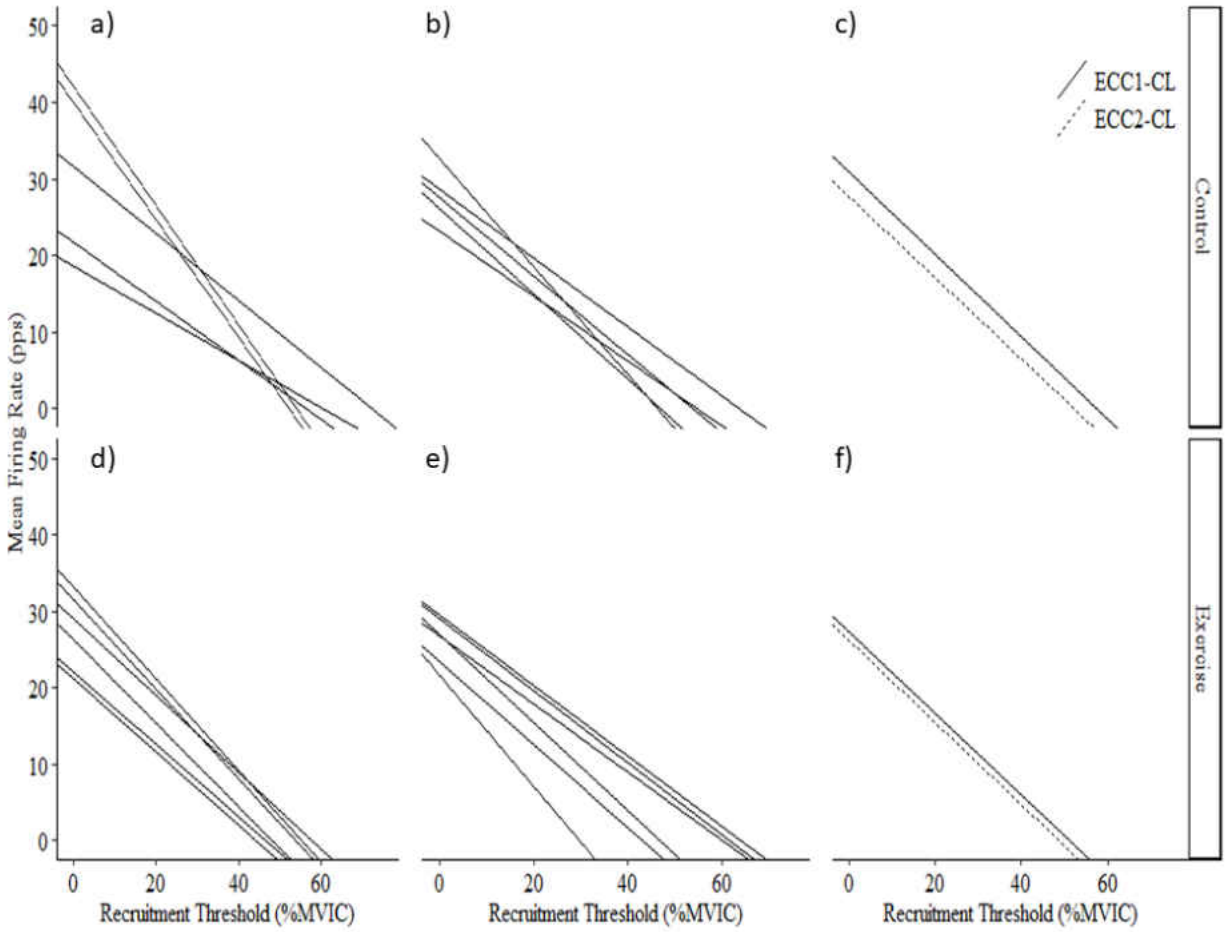


Figure 13. Individual and group trendlines for the mean firing rate vs. recruitment threshold relationship at 50% MVIC.

a) ECC1-CL, control group; b) ECC2-CL, control group; c) group means for ECC1-CL and ECC2-CL, control group; d) ECC1-CL, exercise group; e) ECC2-CL, exercise group; f) group means for ECC1-CL and ECC2-CL, exercise group. ECC1-CL=initial exercise bout on the contralateral limb; ECC2-CL=repeated exercise bout on the contralateral limb.

Mean Firing Rate vs. Recruitment Threshold y-intercept at 50% MVIC

A group x bout interaction was observed in the ipsilateral limb ($F_{1,7}$=0.736; p=0.419; η^2_p= 0.095). Negligible and small effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise and control groups, respectively, while large and medium effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL,

respectively. Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 27. No group x bout interaction was observed in the contralateral limb ($F_{1,9}$= 0.244; p= 0.633; η^2_p= 0.026). However, main effects of group ($F_{1,9}$=0.731; p=0.415; η^2_p=0.075) and bout ($F_{1,9}$=0.975; p=0.349; η^2_p=0.098) were observed. When collapsed across bout, small effects were noted for differences between groups. When collapsed across group, small effects were also noted for differences between bouts. Follow up analysis for group and bout effects are presented in Table 28.

Table 27. Pairwise comparisons for differences in mean firing rate vs. recruitment threshold y-intercept at 50% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.710	0.132	-0.617	0.880
			CON	ECC1-IL vs. ECC2-IL	0.636	-0.364	-2.250	1.520
			EX vs. CON	ECC1-IL	0.249	-0.802	-2.350	0.743
			EX vs. CON	ECC2-IL	0.388	-0.528	-1.860	0.798

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL = baseline measurement during ECC1 on ipsilateral limb; ECC2-IL = baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise.

Table 28.Between-group (EX vs. CON) and bout comparison for differences in mean firing rate vs. recruitment threshold y-intercept at 50% MVIC between groups and bouts.

Effect	p	g	95% CI (Lower)	95% CI (Upper)
Group	0.349	-0.394	-1.210	0.419
Bout	0.415	0.328	-0.478	1.130

η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control in the contralateral arm. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise in the contralateral arm.

Action Potential Amplitude vs. Recruitment Threshold Slope at 50% MVIC

Individual and mean regression lines for the action potential amplitude vs. recruitment threshold slope in the ipsilateral and contralateral limb are presented in Figures 3 and 4, respectively. A group x bout interaction was observed in the ipsilateral limb ($F_{1,7}$=1.098; p=0.330; η^2_p= 0.136). Small effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in both the exercise group and control group, while small and negligible effects were noted for between group differences (EX vs. CON) during ECC1-IL and ECC2-IL, respectively. Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 29.

No group x bout interaction ($F_{1,9}$=0.158; p=0.701; η^2_p=0.017), main effect of group ($F_{1,9}$=0.456; p=0.516; η^2_p=0.048) or main effect of bout ($F_{1,9}$=0.027; p=0.874; η^2_p=0.003) were observed in the contralateral limb.

Table 29. Pairwise comparisons for differences in action potential amplitude vs. recruitment threshold slope at 50% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.296	-0.306	-0.903	0.291
			CON	ECC1-IL vs. ECC2-IL	0.020	-0.438	-0.620	-0.256
			EX vs. CON	ECC1-IL	0.500	-0.412	-1.770	0.946
			EX vs. CON	ECC2-IL	0.733	-0.190	-1.400	1.020

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL= baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; η^2_p > 0.059 indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher slope relative to preceding bout or higher slope in exercise than control. Negative g indicates lower slope relative to preceding bout or higher slope in control than exercise.

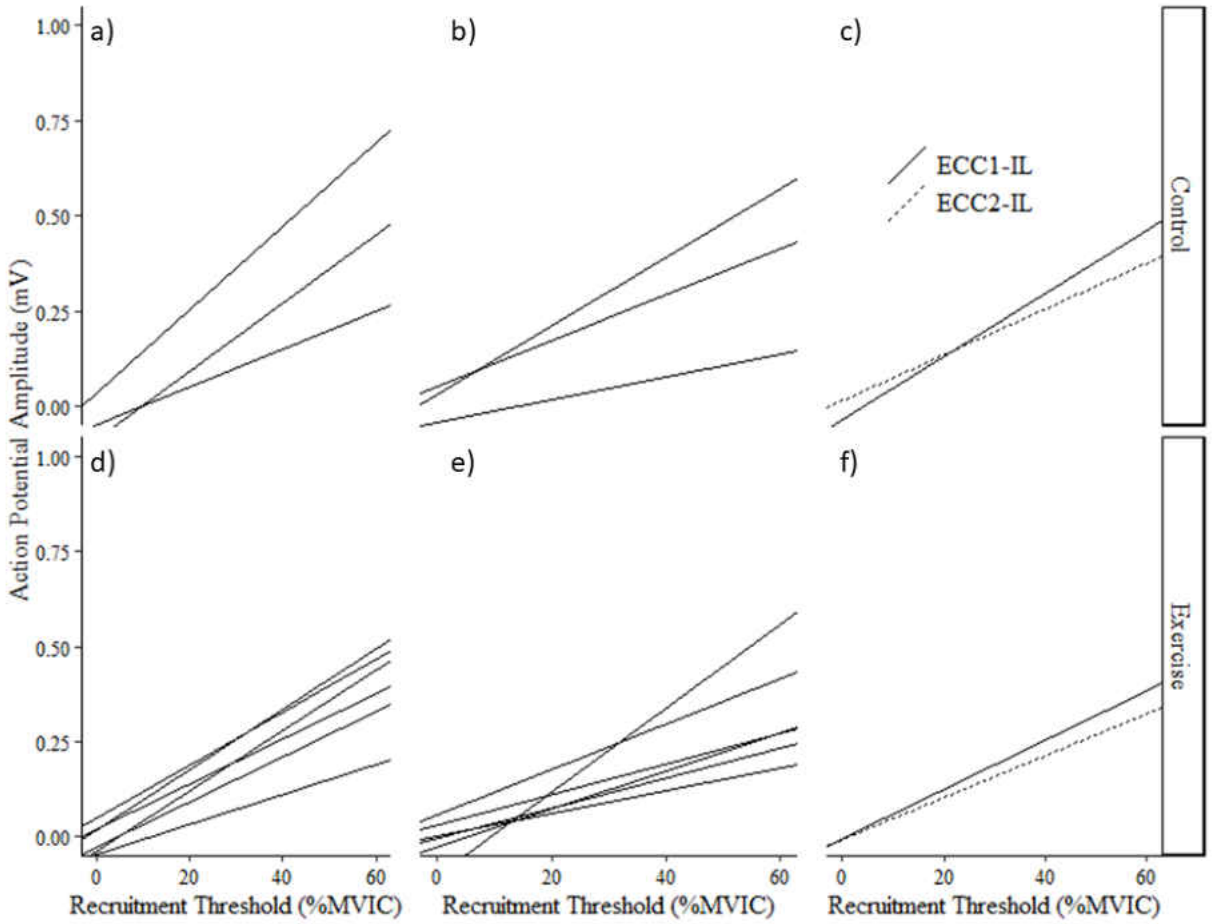


Figure 14. Individual and group trendlines for the action potential amplitude vs. recruitment threshold relationship at 50% MVIC on the ipsilateral side.

a) ECC1, control group; b) ECC2-IL, control group; c) group means for ECC1-IL and ECC2-IL, control group; d) ECC1-IL, exercise group; e) ECC2-IL, exercise group; f) group means for ECC1-IL and ECC2-IL, exercise group. ECC1-IL=initial exercise bout; ECC2-IL=repeated exercise bout.

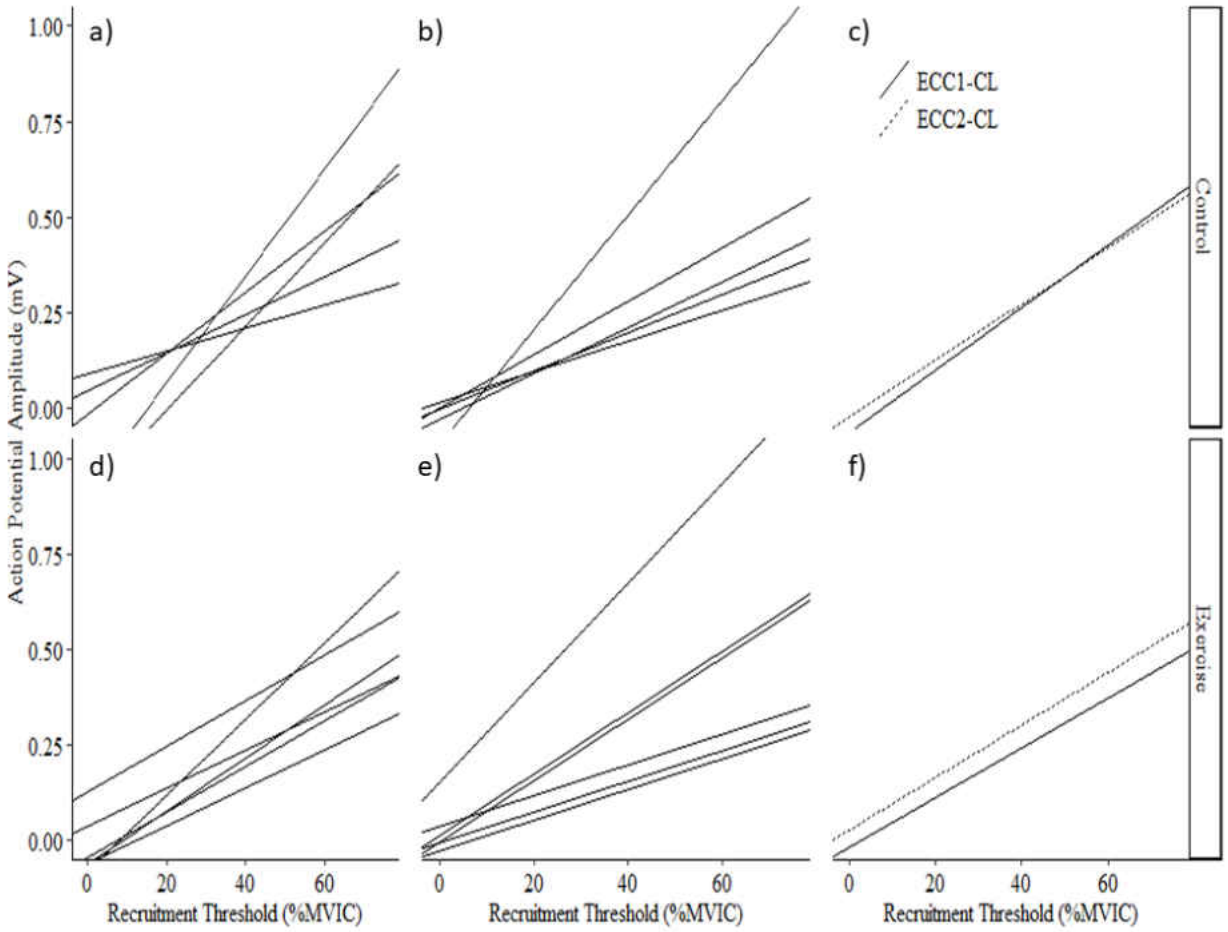


Figure 15. Individual and group trendlines for the action potential amplitude vs. recruitment threshold relationship at 50% MVIC on the contralateral side.

a) ECC1-CL, control group; b) ECC2-CL, control group; c) group means for ECC1-CL and ECC2-CL, control group; d) ECC1-CL, exercise group; e) ECC2-CL, exercise group; f) group means for ECC1-CL and ECC2-CL, exercise group. ECC1-CL=initial exercise bout; ECC2-CL=repeated exercise bout.

Action Potential Amplitude vs. Recruitment Threshold y-intercept at 50% MVIC

A group x bout interaction was observed in the ipsilateral limb ($F_{1,7}$=1.644; p=0.241; η^2_p= 0.190). Negligible and small effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise and control groups, respectively, while small and negligible effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL,

respectively. Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 30.

No group x bout interaction was observed in the contralateral limb ($F_{1,9}$=0.001; p=0.981; η^2_p=0.000). However, main effects of group ($F_{1,9}$=1.336; p=0278; η^2_p=0.129) and bout ($F_{1,9}$=1.592; p=0.239; η^2_p=0.150) were observed. When collapsed across bout, small effects were noted for differences between groups. Similarly, when collapsed across group, small effects were noted for differences between bouts. Follow up analysis for group and bout effects are presented in Table 31.

Table 30. Pairwise comparisons for differences in action potential amplitude vs. recruitment threshold y-intercept at 50% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.949	-0.020	-0.674	0.635
			CON	ECC1-IL vs. ECC2-IL	0.399	0.496	-0.876	1.870
			EX vs. CON	ECC1-IL	0.602	0.316	-1.040	1.670
			EX vs. CON	ECC2-IL	0.867	0.093	-1.110	1.300

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL= baseline measurement during ECC2 on ipsilateral limb. ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL= baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise.

Table 31. Between-group (EX vs. CON) and bout comparison for differences in action potential amplitude vs. recruitment threshold y-intercept at 50% MVIC between groups and bouts.

Effect	p	g	95% CI (Lower)	95% CI (Upper)
Group	0.278	0.473	-0.344	1.290
Bout	0.239	-0.387	-1.200	0.421

η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control in the contralateral arm. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise in the contralateral arm.

50% MVIC Bin Analysis

No group x bout interactions were observed in the ipsilateral limb for bin 1 ($F_{1,6}$=0.028; p=0.873; η^2_p= 0.005) or bin 2 ($F_{1,7}$=0.187; p=0.678; η^2_p= 0.026). However, a main effect of group was observed for bin 1 in the ipsilateral limb ($F_{1,6}$=4.208; p=0.086; η^2_p=0.412). When collapsed across bout, a small effect was noted for differences between groups. No main effect of group was observed for bin 2 in the ipsilateral limb ($F_{1,7}$=0.001; p=0.979; η^2_p=0.000). Further, no main effects of bout were observed for bin 1 ($F_{1,6}$=0.120; p=0.741; η^2_p=0.020) or bin 2 ($F_{1,7}$=0.179; p=0.685; η^2_p=0.025) in the ipsilateral limb.

A group x bout interaction was observed for bin 2 in the contralateral limb ($F_{1,7}$=2.166; p=0.185; η^2_p=0.236). Small and medium effects were noted for between bout comparisons (ECC1-CL vs. ECC2-CL) in the exercise group and control groups, respectively, while medium and small effects were noted for between group comparisons (EX vs. CON) during ECC1-CL and ECC2-CL, respectively. No group x bout interaction ($F_{1,9}$=0.330; p=0.579; η^2_p=0.035), main effect of group ($F_{1,9}$=0.490; p=0.502; η^2_p=0.052) or main effect of bout ($F_{1,9}$=0.057; p=0.817; η^2_p=0.006) were observed in the contralateral limb for bin 1.

Motor Unit Decomposition Accuracy at 80% MVIC

For isometric contractions at 80% MVIC, the total number of motor units meeting the accuracy threshold of 90% relative to number motor units identified within each bout are as follows: ECC1-IL (102 of 247, exercise: k=66, n=7; control k=36, n=4), ECC2-IL (96 of 227, exercise: k=61, n=7; control k=35, n=4), ECC1-CL (120 of 216, exercise: k=67, n=6; control k=53, n=4), ECC2-CL (101 of 233, exercise: k=60, n=6; control k=41, n=4), where k is equal to the number of motor units analyzed in each group and n is equal to the number of participants

used for analysis. Because of differences in the number of identified motor units between limbs as well as between bins, effects of bin and limb could not be evaluated. Therefore, group x bout interactions were assessed for each level of bin and limb.

Mean Firing Rate vs. Recruitment Threshold Slope at 80% MVIC

Individual and mean regression lines for the mean firing rate vs. recruitment threshold slope in the ipsilateral and contralateral limb are presented in Figures 16 and 17, respectively. A group x bout interaction was observed in the ipsilateral limb ($F_{1,10}$=0.844; p=0.380; η^2_p=0.078). Small and negligible effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise group and control groups, respectively, while small and large effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL, respectively Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 32. No group x bout interaction ($F_{1,11}$=0.004; p=0.54; η^2_p= 0.000), main effect of group ($F_{1,11}$=0.100; p=0.758; η^2_p=0.009) or main effect of bout ($F_{1,11}$=0.037; p=0.850; η^2_p=0.003) was observed in the contralateral limb.

Table 32. Pairwise comparisons for differences in mean firing rate vs. recruitment threshold slope at 80% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.526	-0.311	-1.330	0.712
			CON	ECC1-IL vs. ECC2-IL	0.560	0.087	-0.239	0.412
			EX vs. CON	ECC1-IL	0.538	0.320	-0.788	1.430
			EX vs. CON	ECC2-IL	0.145	-0.894	-2.210	0.420

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL = baseline measurement during ECC1 on ipsilateral limb; ECC2-IL = baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates lower slope relative to preceding bout or higher slope in control than exercise. Negative g indicates higher slope relative to preceding bout or higher slope in exercise than control.

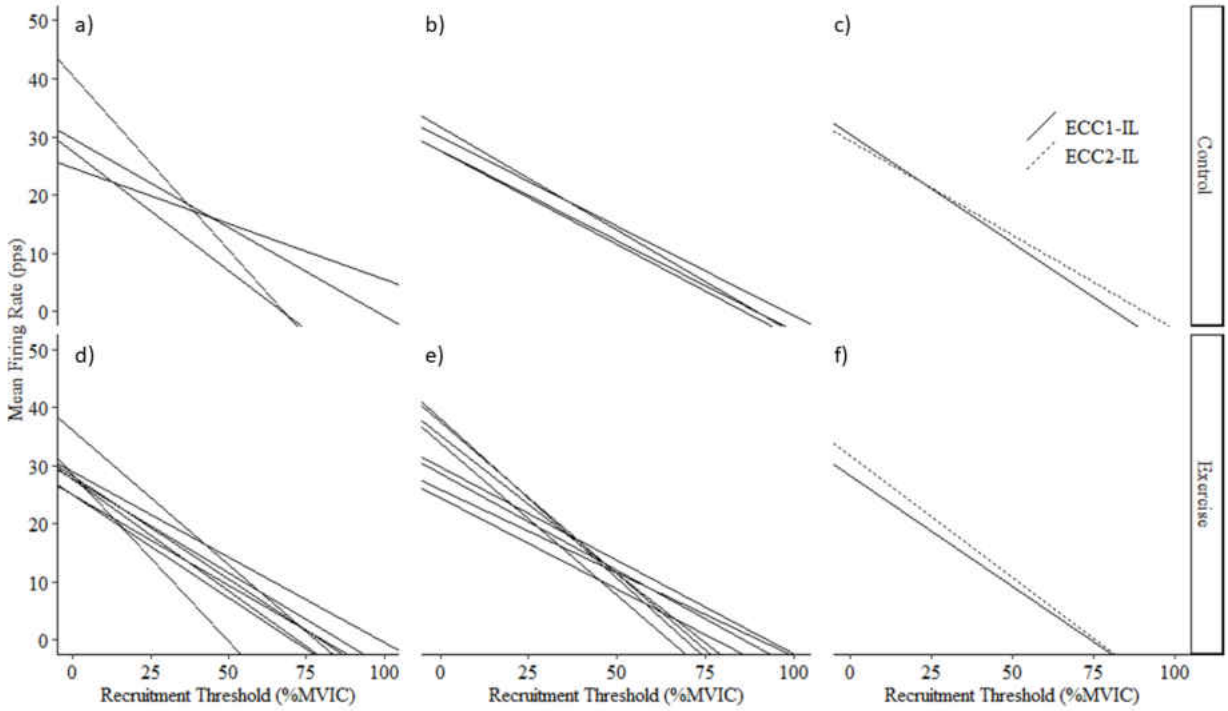


Figure 16. Individual and group trendlines for the mean firing rate vs. recruitment threshold relationship at 80% MVIC on the ipsilateral side.

a) ECC1, control group; b) ECC2-IL, control group; c) group means for ECC1-IL and ECC2-IL, control group; d) ECC1-IL, exercise group; e) ECC2-IL, exercise group; f) group means for ECC1-IL and ECC2-IL, exercise group. ECC1-IL=initial exercise bout; ECC2-IL=repeated exercise bout.

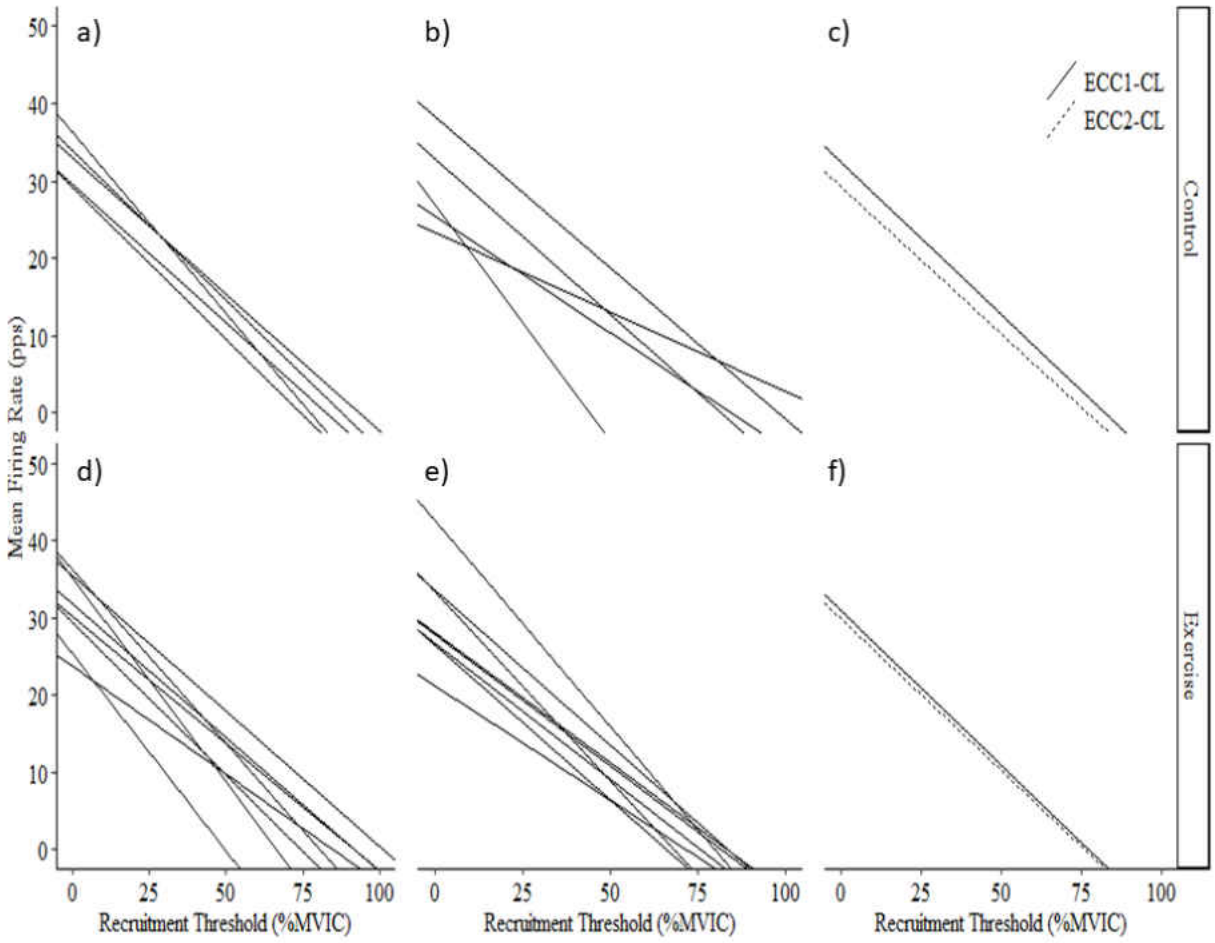


Figure 17. Individual and group trendlines for the mean firing rate vs. recruitment threshold relationship at 80% MVIC on the contralateral side.

a) ECC1-CL, control group; b) ECC2-CL, control group; c) group means for ECC1-CL and ECC2-CL, control group; d) ECC1-CL, exercise group; e) ECC2-CL, exercise group; f) group means for ECC1-CL and ECC2-CL, exercise group. ECC1-CL=initial exercise bout; ECC2-CL=repeated exercise bout.

Mean Firing Rate vs. Recruitment Threshold y-intercept at 80% MVIC

A group x bout interaction was observed in the ipsilateral limb ($F_{1,10}$=1.829; p=0.206; η^2_p=0.155). Medium and negligible effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise group and control groups, respectively, while medium and small effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL,

respectively. Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 33.

No group x bout interaction ($F_{1,11}$=0.416; p=0.532; η^2_p=0.036) or main effect of group ($F_{1,11}$=0.031; p=0.863; η^2_p=0.003) was observed in the contralateral limb. However, a main effect of bout was observed ($F_{1,11}$=1.510; p=0.245; η^2_p=0.121). When collapsed across group, a small effect was noted for differences between bouts. Follow up analysis for group effect are presented in Table 34.

Table 33. Pairwise comparisons for differences in mean firing rate vs. recruitment threshold y-intercept at 80% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.131	0.677	-0.265	1.620
			CON	ECC1-IL vs. ECC2-IL	0.687	-0.060	-0.394	0.273
			EX vs. CON	ECC1-IL	0.300	-0.547	-1.670	0.574
			EX vs. CON	ECC2-IL	0.406	0.490	-0.786	1.770

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL= baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; η^2_p > 0.059 indicates observed effect; g = Hedges g effect size for comparisons . Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise.

Table 34. Between-group (EX vs. CON) comparison for differences in mean firing rate vs. recruitment threshold y-intercept at 80% MVIC between groups and bouts.

Effect	p	g	95% CI (Lower)	95% CI (Upper)
Group	0.863	0.460	-0.306	1.230

η^2_p = partial eta squared effect size; η^2_p > 0.059 indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control in the contralateral arm. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise in the contralateral arm.

Action Potential Amplitude vs. Recruitment Threshold Slope at 80% MVIC

Individual and mean regression lines for the action potential amplitude vs. recruitment threshold slope at 80% MVIC in the ipsilateral and contralateral limb are presented in Figures 18 and 19, respectively. A group x bout interaction was observed in the ipsilateral limb ($F_{1,10}$=2.148; p=0.173; η^2_p=0.177). Small and negligible effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise group and control groups, respectively, while medium and negligible effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL, respectively. Pairwise comparisons for within-group comparisons across levels of time as well as between-group comparisons at each level of time are presented in Table 35.

No group x bout interaction ($F_{1,11}$=0.004; p=0.951; η^2_p=0.000) or main effect of bout ($F_{1,11}$=0.081; p=0.781; η^2_p=0.007) was observed in the contralateral limb. A main effect of group was observed ($F_{1,11}$=0.960; p=0.348; η^2_p=0.080). When collapsed across bout, a small effect was noted for differences between groups. Follow up analysis for group effect are presented in Table 36.

Table 35. Pairwise comparisons for differences in action potential amplitude vs recruitment threshold slope at 80% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.551	0.226	-0.558	1.010
			CON	ECC1-IL vs. ECC2-IL	0.337	-0.125	-0.394	0.144
			EX vs. CON	ECC1-IL	0.314	-0.532	-1.650	0.589
			EX vs. CON	ECC2-IL	0.840	0.117	-1.140	1.380

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL= baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; η^2_p > 0.059 indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher slope relative to preceding bout or higher slope in exercise than control. Negative g indicates lower slope relative to preceding bout or higher slope in control than exercise.

Table 36. Between-group (EX vs. CON) comparison for differences in action potential amplitude vs. recruitment threshold slope at 80% MVIC in the contralateral arm.

Effect	p	g	95% CI (Lower)	95% CI (Upper)
Group	0.348	-0.414	-1.19	0.366

η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control in the contralateral arm. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise in the contralateral arm.

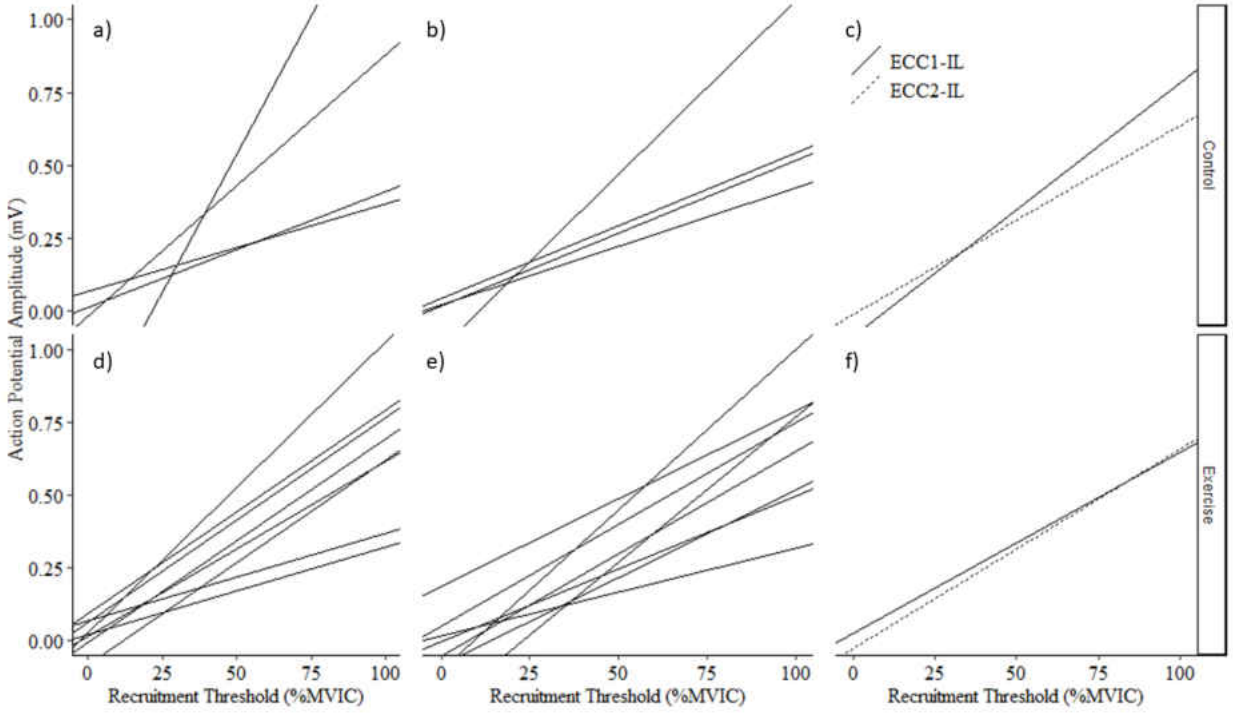


Figure 18. Individual and group trendlines for the action potential amplitude vs. recruitment threshold relationship at 80% MVIC on the ipsilateral side.

a) ECC1, control group; b) ECC2-IL, control group; c) group means for ECC1-IL and ECC2-IL, control group; d) ECC1-IL, exercise group; e) ECC2-IL, exercise group; f) group means for ECC1-IL and ECC2-IL, exercise group. ECC1-IL=initial exercise bout; ECC2-IL=repeated exercise bout.

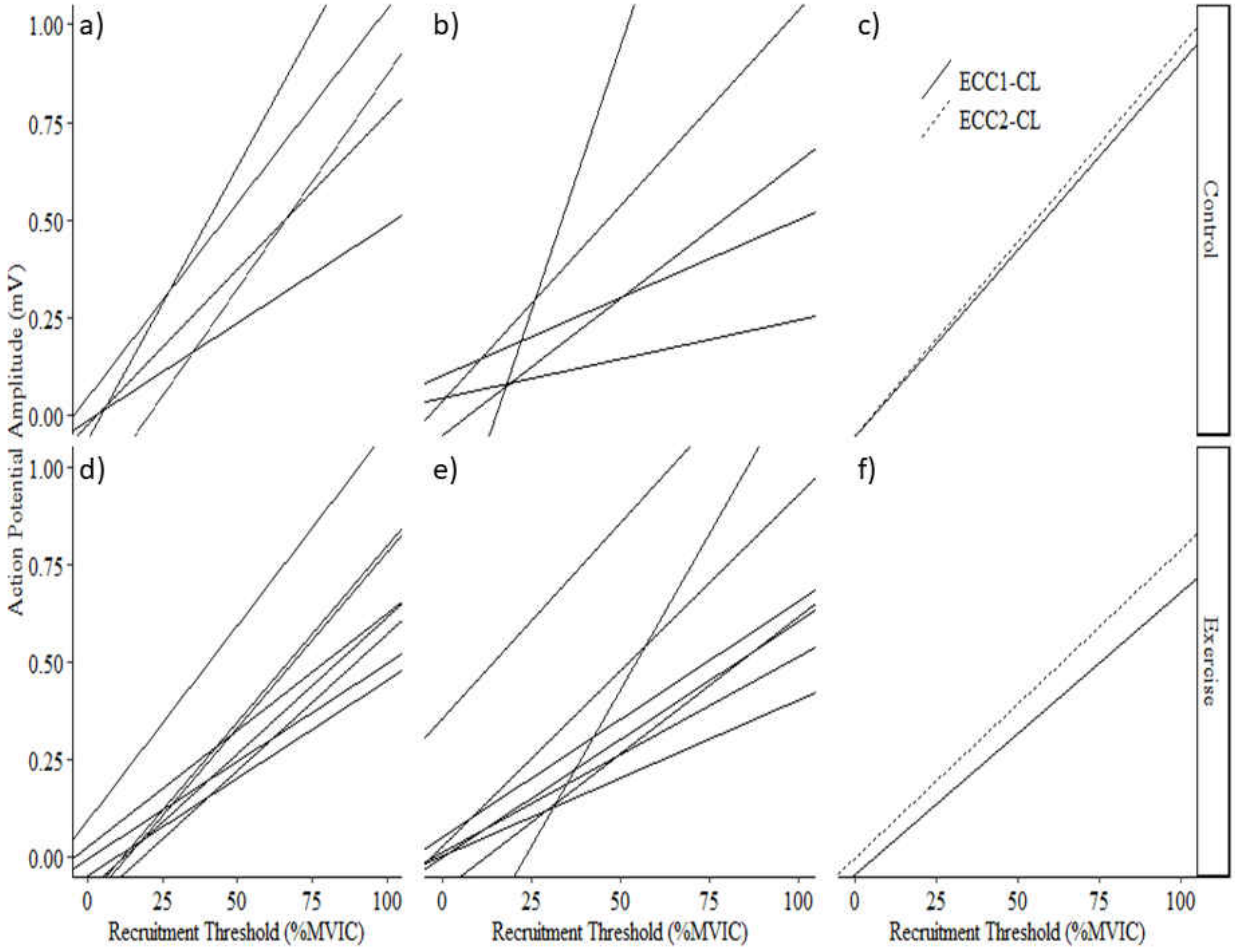


Figure 19. Individual and group trendlines for the action potential amplitude vs. recruitment threshold relationship at 80% MVIC on the contralateral side.

a) ECC1-CL, control group; b) ECC2-CL, control group; c) group means for ECC1-CL and ECC2-CL, control group; d) ECC1-CL, exercise group; e) ECC2-CL, exercise group; f) group means for ECC1-CL and ECC2-CL, exercise group. ECC1-CL=initial exercise bout; ECC2-CL=repeated exercise bout.

Action Potential Amplitude vs. Recruitment Threshold y-intercept at 80% MVIC

A group x bout interaction was observed in the ipsilateral limb ($F_{1,10}$=2.731; p=0.129; η^2_p= 0.215). Small and negligible effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise group and control groups, respectively, while medium and negligible

effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL, respectively. Pairwise comparisons for the group x time interaction are presented in Table 37.

No group x bout interaction ($F_{1,11}$=0.164; p=0.693; η^2_p=0.015), or main effects of group ($F_{1,11}$=0.216; p=0.651; η^2_p=0.019) or bout ($F_{1,11}$=0.186; p=0.675; η^2_p=0.017) were observed in the contralateral limb.

Table 37. Pairwise comparisons for differences in action potential amplitude vs. recruitment threshold y-intercept at 80% MVIC between groups and bouts.

Effect	F	η^2_p	Group	Bout	p	g	95% CI (Lower)	95% CI (Upper)
Group x bout	0.754	0.097	EX	ECC1-IL vs. ECC2-IL	0.247	-0.454	-1.260	0.357
			CON	ECC1-IL vs. ECC2-IL	0.376	0.109	-0.148	0.366
			EX vs. CON	ECC1-IL	0.196	0.693	-0.440	1.830
			EX vs. CON	ECC2-IL	0.836	-0.120	-1.380	1.140

EX = Exercise Group; CON = Control Group; MVIC = maximal voluntary isometric contraction; ECC1-IL= baseline measurement during ECC1 on ipsilateral limb; ECC2-IL= baseline measurement during ECC2 on ipsilateral limb; η^2_p = partial eta squared effect size; $\eta^2_p > 0.059$ indicates observed effect; g = Hedges g effect size for comparisons. Positive g indicates higher y-intercept relative to preceding bout or higher y-intercept in exercise than control. Negative g indicates lower y-intercept relative to preceding bout or higher y-intercept in control than exercise.

80% MVIC Bin Analysis

A group x bout interaction was observed for bin 1 ($F_{1,9}$=0.679; p=0.431; η^2_p=0.070) and bin 2 ($F_{1,9}$=1.594; p=0.238; η^2_p=0.151) in the ipsilateral limb. In bin 1, small and medium effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise group and control groups, respectively, while negligible and medium effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL, respectively.

In bin 2, medium and small effects were noted for between bout comparisons (ECC1-IL vs. ECC2-IL) in the exercise group and control groups, respectively, while large and small

effects were noted for between group comparisons (EX vs. CON) during ECC1-IL and ECC2-IL, respectively.

A group x bout interaction was also observed for bin 1 ($F_{1,8}$=0.823; p=0.391; η^2_p=0.093) and bin 2 ($F_{1,8}$=1.893; p=0.206; η^2_p=0.191) in the contralateral limb. In bin 1, small effects were noted for between bout comparisons (ECC1-CL vs. ECC2-CL) in both the exercise group and control groups, respectively, while large and negligible effects were noted for between group comparisons (EX vs. CON) during ECC1-CL and ECC2-CL, respectively.

In bin 2, large and negligible effects were noted for between bout comparisons (ECC1-CL vs. ECC2-CL) in both the exercise group and control groups, respectively, while negligible and medium effects were noted for between group comparisons (EX vs. CON) during ECC1-CL and ECC2-CL, respectively.

Association between Changes in Motor Unit Firing Characteristic Relationships and Muscle Damage Indicators

The change in ROM from BL to 24H during ECC2-IL was significantly related with the change in action potential amplitude vs. recruitment threshold slope at 50% MVIC in the ipsilateral arm (r=-0.751; p=0.020). Changes in RTD_{100} at 72H following ECC2-CL were significantly related to changes in the mean firing rate vs. recruitment threshold slope at 50% MVIC in the contralateral arm (r=-0.613; p=0.045). The change in dVAS at 72H following ECC2-CL was significantly related to changes in the mean firing rate vs. recruitment threshold slope at 80% MVIC in the contralateral arm (r=-0.582; p=0.037). Changes in MVIC at 72H following ECC2-IL were significantly related to changes in the action potential amplitude vs. recruitment threshold slope at 80% MVIC in the ipsilateral arm (r=0.629; p=0.028). However, no

other significant relationships were noted between changes in damage variables and changes in motor unit firing characteristics between bouts.

CHAPTER 5: DISCUSSION

The results of this study provide support for a RBE in both the ipsilateral and contralateral limbs following repeated bouts of eccentric exercise of the biceps brachii, although the magnitude of the effect appears to be greater in the ipsilateral limb. Small to large effects were noted for ROM and RTD_{200} in both limbs in EX, indicating enhanced recovery during repeated bouts when compared to corresponding time points during ECC1. Magnitude of effects for ROM generally increased as recovery progressed in both limbs, while effects for differences in RTD200 were generally more consistent, ranging from small to medium throughout recovery. In contrast, changes in RTD_{100} and MVIC in EX provide support for a RBE in the ipsilateral limb only, as evidenced by small and large effects in the ipsilateral limb compared to negligible effects in the contralateral limb. Small effects for decreases in the slope of the mean firing rate vs. recruitment threshold relationship at 50% MVIC were also observed, indicating that MUs were recruited over a wider range of recruitment thresholds in EX during ECC2-IL compared to ECC1-IL. Similar results were noted in the ipsilateral limb for changes in the action potential amplitude vs. recruitment threshold slope at 50% MVIC, indicating smaller amplitude MUs were recruited later during the submaximal contractions. During contractions at 80% MVIC, small increases in the slope of the mean firing rate vs. recruitment threshold relationship were noted in EX, indicating earlier recruitment of high-threshold MUs in ECC2-IL compared to ECC1-IL. This was further supported by medium increases in the y-intercept between bouts in EX, indicating increases in the average firing rate of active MUs as a result of prior eccentric exercise. Small effects were also noted for increases in average firing rates of high threshold MUs in the ipsilateral limb in EX, while large effects were noted for decreases in the

contralateral limb. However, no differences in MU firing characteristic regression coefficients were noted at 50% or 80% MVIC for the contralateral limb, suggesting that adaptations to high-threshold MUs arising from an initial bout of eccentric exercise in the ipsilateral limb are not transferred to the contralateral limb during a repeated bout. Our results do not provide support for the notion that altered MU firing characteristics influence changes in recovery responses during repeated bouts, since significant relationships between the two variables were not observed. Finally, while muscle soreness and pain sensitivity increased in proximal and distal sites following eccentric exercise, a RBE was not observed in either limb.

Decreases in ROM were noted following all three bouts in EX when compared to CON. However, a more rapid rate of recovery was observed in EX during both ECC2-IL and ECC2-CL when compared to ECC1, particularly at 24H and 72H as indicated by medium and large between bout effects, respectively. Notably, negligible differences in ROM were observed between ECC2-IL and ECC2-CL, suggesting that the magnitude of effect was similar between limbs. Our findings with respect to ROM are consistent with previous studies indicating the presence of a RBE in both limbs following a single bout of unilateral exercise (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018; Starbuck & Eston, 2012; Tsuchiya et al., 2018). However, the majority of studies examining ROM have also reported differences in the magnitude of the RBE between limbs, which we did not observe (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018; Howatson & van Someren, 2007; Starbuck & Eston, 2012). It should be noted that each of these studies utilized a between subjects repeated bout design in which subjects were assigned to perform the repeated bout on either the ipsilateral or contralateral limb only, preventing a direct comparison in recovery between limbs within subjects. To our knowledge, only one other study has utilized a within subject's design when examining RBEs on

ROM. Their findings provide support for a RBE in both limbs with no differences in recovery between limbs, which is consistent with our findings (Tsuchiya et al., 2018).

Changes in RTD_{200} also appeared to indicate an ipsilateral and contralateral RBE. While previous research has evaluated the sensitivity of RTD to eccentric exercise-induced muscle damage (Farup et al., 2016; Jenkins et al., 2014; Macgregor & Hunter, 2018), only one study has investigated RBEs of RTD measures (Peñailillo et al., 2015). These authors reported a significant correlation between declines in RTD_{200} and declines in MVIC torque, which is in agreement with research indicating that late-phase RTD measures tend to follow a similar recovery pattern as MVIC (Jenkins et al., 2014; Macgregor & Hunter, 2018). However, the current study is the first to investigate contralateral adaptations to RTD following repeated bouts. Changes in MVIC torque and RTD_{100} in the present study provide support for a RBE in the ipsilateral limb, but not the contralateral limb. Our findings are consistent with a number of previous studies that report enhanced recovery of MVIC torque following a repeated bout on the ipsilateral limb (T. Chen et al., 2007; Hosseinzadeh et al., 2015; Howatson et al., 2007; Howatson & van Someren, 2007; Lau et al., 2015b; Starbuck & Eston, 2012; Tsuchiya et al., 2018; Xin et al., 2014), but are in contrast to others reporting no differences in recovery of MVIC torque between initial and repeated bouts (Connolly et al., 2002). The reason for this finding is unclear; however, it is possible that fatigue resulting from completion of both repeated exercise bouts on the same day produced disparate impairments in recovery between ipsilateral and contralateral limbs. Previous research indicates that eccentric muscle damage results in modest reductions in MVIC torque in the contralateral limb that persist for at least 48 hours post-exercise (Hedayatpour et al., 2018). Although we provided thirty minutes of recovery between the repeated bouts, it is possible that MVIC torque was reduced in both limbs following the initial repeated bout, which may have

influenced recovery. Additionally, despite randomizing the order of repeated bouts, it is possible that the ipsilateral limb may have been influenced to a lesser extent since the ipsilateral RBE is also reported to be moderated by mechanical, neural, inflammatory, and extracellular matrix adaptations. The contralateral RBE on the other hand would depend primarily upon neural adaptations since it was not subjected to the initial bout (Hyldahl et al., 2017). While speculative, it is also possible that this transfer of fatigue only occurs from the dominant to the non-dominant limb rather than from the non-dominant to the dominant. Other studies implementing exercise interventions in both limbs on the same day during repeated bouts report either small or non-significant differences in MVIC recovery (Connolly et al., 2002; Tsuchiya et al., 2018). Warren and colleagues (1999) advocated the use of MVIC as the gold-standard of non-invasive muscle damage assessment. However, we suggest that the potential influence of the transfer of damage between limbs should be considered when assessing contralateral RBEs. While the potential for cross-over effects of other damage markers following eccentrics should not be discounted, to date only MVIC has been investigated (Hedayatpour et al., 2018).

In the present study, RTD_{100} appeared to recover more rapidly following ECC2-IL when compared to ECC1, although the effect was small. This is consistent with previous research demonstrating modest reductions in RTD_{100} that are recovered by 24H (Jenkins et al., 2014; Peñailillo et al., 2015). Early-phase RTD measures (e.g. RTD_{50}, RTD_{100}, and RTD_{peak}) are primarily related to efficient activation of the MU pool (Del Vecchio et al., 2019; Edman & Josephson, 2007). Therefore, attenuation of declines in early-phase RTD measures following a repeated bout of exercise would presumably be related to increased efficiency in the delivery of efferent motor signals to activated muscle, though this has not been directly assessed. In contrast, while RTD_{50} and RTD_{peak} were reduced following eccentric exercise, RTD_{50} appeared to recover

by 72H while RTD_{peak} did not, regardless of bout. This is consistent with previous reports indicating that RTD_{peak} may not be fully recovered by 72H (Farup et al., 2016; Jenkins et al., 2014). Additionally, symptoms of neuromuscular disturbance may be present for up to ten days post-exercise, long after other damage indicators have recovered (Deschenes et al., 2000; Farup et al., 2016; Howatson, 2010). Alterations to voluntary activation and inhibitory networks appear to occur as part of the RBE, although they are likely a modest contributor to adaptation (Goodall et al., 2017; Škarabot et al., 2019). Therefore, it is possible that recovery of early-phase RTD measures are modest and may not be transferred to the contralateral limb. Taken together, these results provide preliminary evidence for a RBE related to more rapid recovery of contractile mechanisms as a result of prior eccentric exercise. However, future research should consider performing repeated bouts across multiple days to minimize potentially deleterious effects on the contralateral limb.

We observed small decreases in the slopes of the regression lines for both mean firing rate vs. recruitment threshold and action potential amplitude vs. recruitment threshold at 50% MVIC. Previous research has not evaluated changes in the action potential amplitude vs. recruitment threshold relationship in response to repeated bouts. However, it is possible that decreases in the slope of the action potential amplitude vs. recruitment threshold relationship at 50% MVIC represents a shift towards a more equitable recruitment of low action potential amplitude MUs over a wider range of recruitment thresholds. This may indicate a learning effect from isometric exercise as opposed to an exercise induced change in slope, since similar changes were observed for both EX and CON groups. Previous research has postulated that neural adaptations underlying the contralateral RBE may be the result of increased recruitment of low-threshold MUs (Starbuck & Eston, 2012; Tsuchiya et al., 2018). Small shifts in linear slope

coefficients and y-intercepts observed at 50% MVIC in the present study are consistent with effects reported in previous studies showing nonsignificant findings, suggesting effects for these shifts may be of little practical significance (Hight et al., 2017). Therefore, while some studies have postulated increased low-threshold MU recruitment as a mechanism for the RBE (Starbuck & Eston, 2012; Tsuchiya et al., 2018), our findings and those of others do not support this (Hight et al., 2017). The reason for this discrepancy may be related to methodological considerations regarding the way in which inferences were made about muscular activation strategies. Previously mentioned studies reporting increased low-threshold MU recruitment have assessed activation strategies during or immediately after the performance of the maximal eccentric bout, while Hight and colleagues performed isometric contractions at 50% MVIC prior to exercise. Research suggests that recruitment of biceps brachii MUs is continuous up to 88% MVIC, relying more heavily on recruitment of new MUs rather than increased firing rate of already active MUs (Kukulka & Clamann, 1981). Because of the difference in the nature of these contractions (i.e. maximal vs. submaximal), they likely reflect different proportions of the MU pool. Therefore, it seems that adaptations within low-threshold MUs may not be the result of decreased recruitment threshold, but rather increased firing rate at high force output to offset lower overall activation of high-threshold MUs. While the bin analysis in the present study indicates a shift towards increased mean firing rate of MUs recruited above 25% MVIC in the contralateral limb, it is not known why this was observed. Previous research has reported no changes within bins of MUs for the ipsilateral limb between bouts at 50% MVIC. Therefore, it seems unlikely that changes would be observed in the contralateral but not ipsilateral limb (Hight et al., 2017). However, this should be further investigated in future research.

Results from the 80% MVIC contractions appear to indicate that high threshold MUs were recruited earlier and fired faster following unaccustomed eccentric exercise. Analysis of regression coefficients seem to indicate that changes to MU firing behavior in the contralateral limb were not observed as a result of an initial bout of eccentric exercise; however, when MUs were grouped into bins as a function of their recruitment threshold, changes in MU firing behavior in the contralateral limb were noted. These findings are in agreement with previous research indicating lower recruitment thresholds and increased firing rate of active MUs in response to a prior bout of eccentric exercise (Dartnall et al., 2011; Hight et al., 2017). During eccentric contractions, high-threshold MUs appear to be selectively recruited (Nardone et al., 1989) leading to a greater magnitude of muscle damage compared to low-threshold motor units (Friden et al., 1983; Macaluso et al., 2012; Macgregor & Hunter, 2018). Additionally, low- and high threshold MUs appear to respond differentially to muscular pain, indicating the potential for disparate recovery responses following damaging exercise (Martinez-Valdes et al., 2020). Previous research shows that conduction velocity along active motor units are decreased and firing rates of low-threshold MU are increased following muscle damage (Hedayatpour et al., 2009; Macgregor & Hunter, 2018; Nasrabadi et al., 2018; Ochi et al., 2020; Ye et al., 2015). This indicates a compensatory mechanism whereby damage results in impaired activation of high-threshold MUs, and stronger neural drive is delivered throughout recovery to maintain contraction force via increased recruitment of low-threshold MUs (Macgregor & Hunter, 2018; Ye et al., 2015). While increased firing rates of low-threshold MUs have typically not been observed prior to repeated bouts when using low-level contraction forces (Hight et al., 2017), shifts in activation strategies towards more rapid recruitment of the motor unit pool have been observed in both limbs while performing maximal efforts during repeated bouts (Starbuck &

Eston, 2012; Tsuchiya et al., 2018). A similar relationship has been observed when evaluating a greater proportion of the motor unit pool (i.e. 80% MVIC) prior to a repeated bout (Hight et al., 2017), which is in agreement with our findings in the ipsilateral limb. This is further supported by the increase in the action potential amplitude vs. recruitment threshold slope observed in the ipsilateral limb at 80% MVIC in the present study, which suggests that MUs with large action potential amplitudes were recruited at lower force outputs. It is worth mentioning that the slope coefficient of the action potential amplitude vs. recruitment threshold relationship has been observed to increase in response to training, and is strongly correlated with increases in muscle cross-sectional area (Pope et al., 2016). However, it seems unlikely that this would be the cause of the shifts observed in the present study since participants only performed a single bout of exercise. The likely explanation therefore seems to be that similar MUs were recruited at lower force outputs. While the bin widths used in the bin analysis do not allow for more detailed evaluation of shifts, increases in the mean firing rate of both bins in the ipsilateral limb indirectly support this. Because of the inverse relationship between firing rate and recruitment threshold (De Luca & Contessa, 2012), increases in the mean firing rate within a bin may indicate an earlier recruitment resulting in higher mean firing rate at the same absolute force. Nevertheless, lower firing rates were noted prior to the repeated bout of the contralateral limb. While the specific mechanism behind the observed changes in the contralateral limb are unclear, previous research has indicated that both corticospinal drive and inhibitory mechanisms are better maintained following repeated bouts (Goodall et al., 2017; Škarabot et al., 2019). Following an initial bout of unaccustomed exercise, nociceptors also become desensitized in both the ipsilateral and contralateral limb, resulting in a lower sensation of pain following a repeated bout (Hosseinzadeh et al., 2015). Therefore, it is plausible that changes to motor unit firing

characteristics of the contralateral limb are the result of adaptations to both central and peripheral mechanisms that lead to improvements in the efficiency of muscular contractions following unaccustomed eccentric exercise. These mechanisms should be further addressed in future research.

Our results also indicate that muscle soreness was elevated at 24H and 72H relative to BL and IP in the exercise group, regardless of bout, with medium and large effects for increases in soreness at proximal and distal sites respectively, compared to the control group. However, between bout comparisons were negligible in both groups and associated confidence intervals were small, indicating little to no change in soreness responses following repeated bouts. This is in contrast to previous research which has indicated an attenuation of soreness following repeated bouts in both ipsilateral and contralateral limbs (T. Chen et al., 2016; T. Chen, Lin, Chen, Yu, et al., 2018; Connolly et al., 2002; Hosseinzadeh et al., 2013; Howatson & van Someren, 2007; Starbuck & Eston, 2012). One potential explanation for this discrepancy is the difference in the way muscular soreness was assessed in the current study. The vast majority of previous studies have evaluated muscle soreness using visual analog scale measures in response to a palpation stimulus (T. Chen, 2003; T. Chen et al., 2007, 2016; T. Chen, Lin, Chen, Yu, et al., 2018; Connolly et al., 2002; Hosseinzadeh et al., 2013; Muthalib et al., 2011). In contrast, the current study asked participants to complete soreness measurements in response to the stimulus of a pain-pressure threshold assessment. It is plausible that changes in PPT following eccentric exercise influenced responses to soreness measurements. Regardless of bout, PPT at both sites was lowest in the exercise group at 24H, while all other time points were not different from BL. On the other hand, negligible differences were noted across the majority of time points in the control group, with medium to large differences between groups at all follow-up time points.

This indicates that although the eccentric bout effectively elicited mechanical hyperalgesia indicative of muscle damage, RBEs were not noted for either limb. Several studies have reported RBEs for pain-pressure threshold (Delfa de la Morena et al., 2013; Hosseinzadeh et al., 2013, 2015; Lau et al., 2015a; Pincheira et al., 2018). However, this is not a consistent finding within the literature (Muanjai et al., 2019). Muanjai and colleagues (2019) observed that although pain-pressure thresholds were different across time, they were not significantly attenuated during a repeated bout. An interesting note regarding this study was that participants observed significantly reduced pain in response to stretch, which may indicate an adaptation within muscle mechanical properties rather than afferent feedback loops within the mechanoreceptive systems. Additionally, the majority of studies reporting a RBE used other muscle groups, such as the tibialis anterior (Hosseinzadeh et al., 2013, 2015), gastrocnemius (Pincheira et al., 2018), or forearm flexors (Delfa de la Morena et al., 2013), suggesting a possible role of muscle specificity in adaptations to pain sensitivity. Previous research has indicated that the primary site of development of exercise-induced pain sensitivity is within the fascia (Lau et al., 2015a). Therefore, muscles with longer tendons which rely on passive torque generation to a larger extent, such as the gastrocnemius or tibialis anterior, may be more susceptible to adaptations to mechanical hyperalgesia. All available studies reporting adaptations to pain pressure threshold also utilized damaging protocols with a higher exercise volume than utilized in the current study, suggesting that pain sensitivity adaptations may require extensive muscle damage. Future research should consider providing a standardized stimulus for pain assessment.

There are a number of limitations to the present study that should be addressed. First, we assessed muscular soreness via visual analog scale in response to a non-standardized stimulus (i.e. pain-pressure threshold stimulus). This may have confounded the observed results for

soreness measurements, as these two variables may change in a non-linear fashion in relation to one another (Lau et al., 2015c). Second, while asking participants to perform repeated bouts on both ipsilateral and contralateral limbs allowed for direct comparison of the responses following the initial bout on the dominant limb, it is not known whether performing these bouts within 30 minutes of each other may have resulted in transfer of fatigue to the contralateral limb. To mitigate this, future research should investigate performing repeated bouts on each limb on separate days to minimize effects of fatigue from the initial bout. Third, performance of submaximal isometric ramp contractions was not randomized or normalized to the ECC1 MVIC, which may have shifted motor unit recruitment relationships if MVIC was different between ECC1 and ECC2 due to contractions being performed at a different absolute intensity. Future research should consider performing two sets of contractions normalized to ECC1 and ECC2 MVIC, respectively. Lastly, limitations inherent to the use of the isokinetic dynamometer may have affected our results. It is possible that the use of a handled implement during both isometric testing and isokinetic exercise may have influenced the development of exercise-induced muscle damage specific to the biceps brachii. Previous research has used an adjustable hook-and-loop fastener secured about the wrist to isolate the elbow flexor muscles and minimize the influence of wrist position during performance of these tests, which was not used in the current study (Lau et al., 2015b). The use of a handled dynamometer limb may also have allowed for greater freedom of movement, changing the loading pattern of active muscles. Finally, studies that have reported significant, sustained losses in RTD in conjunction with RBEs have been measured using load cells (Jenkins et al., 2014; Peñailillo et al., 2015), whereas our study and others reporting no RBEs (Mavropalias et al., 2020) utilized an isokinetic dynamometer for assessment of early-phase RTD. A recently published review indicates that load cells may minimize baseline

noise in comparison to commercial dynamometers and are therefore preferable if very early-phase RTD measures are of interest (Maffiuletti et al., 2016). Future studies should examine changes in RTD_{peak} following repeated bouts using load cells over a longer time scale to allow for a full recovery response to be observed. Randomizing the order in which ramp contractions are performed and normalizing to pre-test MVICs to more effectively compare differences between bouts might also be considered. The use of a single-blind protocol in which investigators performing muscle damage assessment are blinded to group assignment (i.e. treatment vs control) may also be prudent. Additionally, it is possible that correlations between some of the observed damage responses and changes in motor unit firing characteristics may have violated the assumptions of the Pearson correlation, particularly the assumption of homoscedasticity.

A number of limitations were introduced as a result of the small sample size obtained in the current study. For example, the limited number of observations prevented the assessment of the effect of order in which repeated bouts were performed. Additionally, all motor unit analyses were performed on a subset of completed subjects because for a number of subjects, an insufficient number of motor units were decomposed with sufficient accuracy, resulting in no data for that subject. This further prevented the assessment of both interlimb differences for all dependent variables obtained from the decomposed EMG signal as well as differences between bins at each relative contraction intensity during the submaximal muscle actions. Therefore, to maximize the number of observations within each level of group and bout, effects of limb were not assessed for any of the EMG variables assessed and effects of bin were not assessed for the bin analysis. For all damage variables, all subjects had repeated observations, allowing for assessments of interlimb differences. The small sample size also resulted in low statistical power

to assess effects of interest using hypothesis tests. Therefore, we limited our primary interpretations to those made based on the observed effect sizes rather than hypothesis tests. This was done to identify potential effects of interest for further evaluation in future research; however, because of this, the generalizability of findings beyond the current sample should be interpreted with caution.

In conclusion, the results of this pilot study support the presence of ipsilateral and contralateral repeated bout effects using non-invasive measures of muscle damage. Additionally, motor unit behavior assessed prior to the start of each eccentric bout indicated earlier recruitment and increased firing of high-threshold motor units in the ipsilateral limb, while changes to the contralateral limb were less clear. This provides further evidence that the repeated bout effect may be partially mediated through neural mechanisms, though future research should further investigate mechanisms for the contralateral repeated bout effect.

APPENDIX A: UCF IRB APPROVAL LETTER

UNIVERSITY OF CENTRAL FLORIDA

Institutional Review Board
FWA00000351
IRB00001138Office of Research
12201 Research Parkway
Orlando, FL 32826-3246

APPROVAL

August 6, 2019

Dear Adam Wells:

On 8/6/2019, the IRB reviewed the following submission:

Type of Review:	Initial Study
Title:	Effect of Unaccustomed Eccentric Exercise on Motor Unit Firing Characteristics and the Contralateral Repeated Bout Effect
Investigator:	Adam Wells
IRB ID:	STUDY00000740
Funding:	None
Grant ID:	None
IND, IDE, or HDE:	None
Documents Reviewed:	• Consent, Category: Consent Form; • Flyer, Category: Recruitment Materials; • MHQ, Category: Survey / Questionnaire; • PAR-Q+, Category: Survey / Questionnaire; • Protocol, Category: IRB Protocol; • VAS, Category: Test Instruments;

The IRB approved the protocol on 8/6/2019.

In conducting this protocol, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system.

If you have any questions, please contact the UCF IRB at 407-823-2901 or irb@ucf.edu. Please include your project title and IRB number in all correspondence with this office.

Sincerely,

Racine Jacques, Ph.D.
Designated Reviewer

APPENDIX B: UCF IRB COVERAGE LETTER

UNIVERSITY OF CENTRAL FLORIDA

Institutional Review Board
FWA00000351
IRB00001138, IRB00012110
Office of Research
12201 Research Parkway
Orlando, FL 32826-3246

Memorandum

To: Nicholas Coker

From: UCF Institutional Review Board (IRB)

Date: June 2, 2020

Re: IRB Coverage

The IRB reviewed the information related to your dissertation *EFFECT OF UNACCUSTOMED ECCENTRIC EXERCISE ON MOTOR UNIT FIRING CHARACTERISTICS AND THE CONTRALATERAL REPEATED BOUT EFFECT: A PILOT STUDY*

Your project data is covered under the following protocol previously approved by the IRB. You are listed as a Co-Investigator on the study and your use of the data is consistent with the the protocol.

IRB study name	IRB Approval Number
Effect of Unaccustomed Eccentric Exercise on Motor Unit Firing Characteristics and the Contralateral Repeated Bout Effect	STUDY00000740

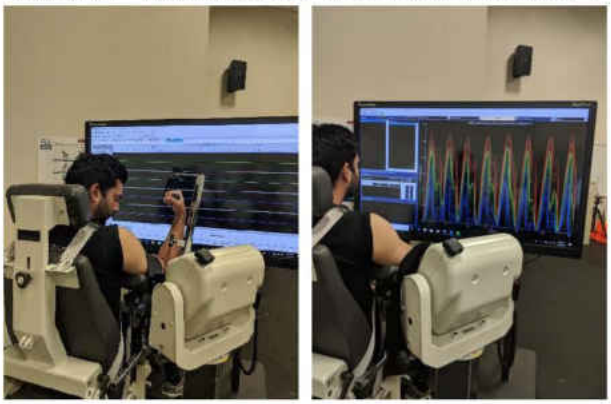
If you have any questions, please contact the UCF IRB irb@ucf.edu.

Sincerely,

Racine Jacques, Ph.D.
IRB Specialist

APPENDIX C: STUDY RECRUITMENT FLYER

RESEARCH PARTICIPANTS NEEDED
FOR A STUDY SEEKING TO EVALUATE EARLY ADAPTATIONS TO EXERCISE



Researchers at the University of Central Florida's Institute of Exercise Physiology and Rehabilitation Science are seeking to evaluate changes in muscle function after a new upper body exercise stimulus is performed, and how this may relate to changes in how muscles are recruited.

Who is eligible?

Males between the ages of 18 and 35 years old who have not performed upper body resistance training within the last six months.

What will you be asked to do?

Complete 8 visits to the Human Performance Lab (11.5 hours total), which includes:

- Informed consent, Medical History Questionnaire, Physical Activity Readiness Questionnaire (PAR-Q+), and familiarization trials
- Body composition
- Two sessions consisting of assessment of muscle function and muscle recruitment characteristics followed by an exercise session intended to reduce muscle function
- Follow-up assessments of muscle function 24- and 72-hours post-exercise

To learn more, contact Nick Coker at 407-823-2809 or n.coker0418@knights.ucf.edu

This research is conducted under the direction of Adam J. Wells, Ph.D., School of Kinesiology and Physical Therapy and has been reviewed and approved by the UCF Institutional Review Board.

UCF Human Performance Lab 12494 University Blvd. Education Complex Room 172 Orlando, FL 32828

APPENDIX D: INFORMED CONSENT

UNIVERSITY OF CENTRAL FLORIDA

Title of research study: Effect of Unaccustomed Eccentric Exercise on Motor Unit Firing Characteristics and the Contralateral Repeated Bout Effect

Investigator: *Adam J. Wells, PhD, CSCS*D*

Co-Investigator: *Nicholas Coker, PhD ABD, CSCS, CISSN*

Key Information: The following is a short summary of this study to help you decide whether or not you would like to participate. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you are an apparently healthy male between the ages of 18 and 35 who has not done upper-body resistance training for at least six months. Additionally, you are not currently be taking any ergogenic aids (e.g. creatine, beta-alanine, etc.), anabolic steroids, or over-the-counter or prescription medications or supplements that may influence the appearance of muscle damage and the recovery response (e.g. NSAIDs, whey protein, etc.).

Why is this research being done?

When beginning a new exercise program, individuals typically become sore and experience a loss in muscle function. However, if the same exercise is repeated within a few weeks, less soreness develops and the muscle maintains most of its functional capacity. This is known as the repeated bout effect. These changes that occur after a repeated bout of exercise also may be transferred to the same muscle on the opposite limb, a process which is likely the result of changes within the nervous system. The purpose of this study will be to investigate the extent to which neural adaptations may explain the transfer of the repeated bout effect between limbs.

How long will the research last and what will I need to do?

In order to participate in this study, you will be asked to complete eight visits to the UCF Strength and Conditioning Laboratory over the course of approximately four weeks. These visits will include various assessments of upper body muscle activation strategies, damage, and strength on your right and left sides. The first visit will consist of filling out paperwork required for enrollment as well as a demonstration of some of the force production tasks that you will be asked to perform. Twenty-four and 72 hours after visit 3 (visits four and five), you will be asked to report to the Strength and Conditioning Laboratory to complete follow-up assessment of muscle damage, including measures of range of motion, soreness, pain-pressure threshold, and maximal voluntary isometric contractions of the limb that completed the exercise bout. Two weeks after the completion of visit 3, you will be asked to report to the Strength and Conditioning Laboratory to repeat this resistance exercise session on both limbs as well as assessment of muscle function. Visits seven and eight will occur 24 and 72 hours after the completion of visit 6, respectively, and will consist of follow-up assessments of muscle function on each arm.

More detailed information about the study procedures can be found under ***"What happens if I say yes, I want to be in this research?"***

University of Central Florida IRB
IRB Number: MOD00000472
IRB Approval Date: 9/19/2019

Is there any way being in this study could be bad for me?

Participation in this study includes the same risks associated with regular physical activity and resistance training of the upper body as well as risks associated with shaving. These risks include temporary muscle soreness and fatigue as well as minor musculoskeletal injuries (e.g. muscle strains, joint sprains). Additionally, there are risks associated with the skin preparation prior to EMG electrode placement. Your skin will be shaved to remove any skin and excess hair, hypoallergenic tape will be placed on the skin to remove any remaining debris, and the site will be cleansed with rubbing alcohol. Risks associated with skin preparation for surface EMG recordings include slight irritation at the site of electrode placement as a result of shaving and abrading the skin, and may include red, dry skin at the preparation site.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me?"***

Will being in this study help me in any way?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, possible benefits to others include an increased understanding of how the body may adapt to a new exercise stimulus, and whether these adaptations are transferred to the opposite limb. This has potential to benefit those beginning a new exercise program as well as clinical populations that may not have full functional capacity of both limbs.

What happens if I do not want to be in this research?

Your participation in this study is voluntary. You are free to withdraw your consent and discontinue participation in this study at any time without prejudice or penalty. Your decision to participate or not participate in this study will in no way affect your continued enrollment, grades, employment or your relationship with UCF or the individuals who may have an interest in this study. Your alternative to participating in this research study is to not participate.

Detailed Information: The following is more detailed information about this study in addition to the information listed above.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team: Nicholas Coker (Co-Investigator) at (407) 823-2809 or by email at n.coker0418@knights.ucf.edu, or Dr. Adam Wells (Principal Investigator) at (407) 823-3906 or by email at adam.wells@ucf.edu.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at 407-823-2901or irb@ucf.edu if:

University of Central Florida IRB
IRB Number: MOD00000472
IRB Approval Date: 9/19/2019

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

How many people will be studied?

We expect 50 people will be in this research study.

What happens if I say yes, I want to be in this research?

1. You will be asked to report to the University of Central Florida's Institute of Exercise Physiology and Rehabilitation Sciences eight times over the course of approximately four weeks. The first visit will include filling out paperwork to determine your eligibility as well as a familiarization trial where the research team will demonstrate some of the strength-based tasks you will be asked to do. At least one day later, you will be asked to report to the Strength and Conditioning Laboratory for visit two, in which you will be asked to complete assessments of hydration status, body composition, and height and weight, as well as familiarization with maximal and submaximal isometric muscle contractions. The third visit will include baseline assessments of your elbow range of motion, muscle soreness, pain perception, arm strength, and muscle firing characteristics during a low-level contraction task before completing an exercise session designed to cause muscle damage on your dominant arm. After this session, your range of motion, soreness, pain perception, and arm strength will be assessed again. Twenty-four and 72 hours later, you will come back to the laboratory to repeat the measurements of range of motion, soreness, pain perception, and muscle strength. Two weeks after the first exercise session, you will come back to the laboratory to repeat the exercise session on both arms in a random order. Range of motion, muscle soreness, pain perception, arm strength, and muscle firing characteristics will be repeated on both arms before completing the exercise session on either your dominant or non-dominant arm. After completing the exercise session, follow-up assessments of muscle damage will be completed. Thirty minutes after the first session is completed, you will repeat the exercise session on the opposite arm and complete follow-up damage assessments on this arm. You will then be asked to return to the laboratory twenty-four and 72 hours later for assessment of muscle damage.
2. Visit Two: The second visit will consist of measures of height, weight, hydration status, and familiarizations of muscular strength and control measurements of right and left arm muscles. This visit should last approximately two hours.

1. Hydration status- Prior to arrival to the laboratory, you will be asked to not consume caffeine or alcohol for at least 24 hours and to drink enough water to be normally hydrated. Before arriving to the laboratory, please avoid drinking excessive amounts of water. Upon arrival to the laboratory, you will be asked to provide a small urine sample. From this sample, a small drop of urine will be used to assess your current level of hydration. If you are not properly hydrated at the time of assessment, you will be asked to drink water and provide another urine sample until properly hydrated. If you arrive in a dehydrated state and are instructed to consume additional

water, a waiting period of 30 minutes will begin after you achieve proper hydration before you are able to continue on with the rest of the assessments. There are no risks associated with the measurement of hydration status.

2. Anthropometrics: Your height and weight will be determined using a clinical scale and mounted stadiometer.
3. Body composition: Body composition will be assessed via bioelectrical impedance analysis (BIA). You will be asked to arrive to the laboratory at least 4 hours fasted as well as abstain from caffeine and alcohol for at least 24 hours prior to testing. Prior to body composition assessment, you will be asked to remove their footwear, socks, and any jewelry. You will then be asked to wipe the soles of your feet as well as palm of your hands using a sterile alcohol wipe before stepping onto the platform of the BIA device. A small electrical current will be sent through your body in order to measure impedance. This procedure carries no inherent risk of participation and will take approximately two minutes to complete.
4. Maximal voluntary isometric contraction (MVIC): Your arm strength will be assessed using maximal voluntary isometric contractions performed on a medical strength testing device. You will be seated in a chair and secured using straps across your shoulders and waist. You will then be asked to complete a standardized warm-up consisting of three 10-second contractions at approximately 50% of self-perceived maximal strength, with ten seconds of rest provided in between contractions. You will then be provided with 60 seconds of rest before testing of maximal arm strength will begin. Three 5-second MVICs will be completed on each limb with 3 minutes of rest provided between each attempt. Standardized instruction will be provided prior to the start of MVIC assessment, and verbal encouragement will be provided throughout each trial. The risks associated with isometric exercise are the same as those associated with regular physical activity, and include risks of muscle soreness, pains, and slight risks of muscular and joint strains.
5. Submaximal muscle actions: after maximal strength assessments, you will be asked to complete familiarization trials consisting of three submaximal trapezoidal muscle actions at 50% and 80% MVIC on a medical strength testing device on each limb. During 50% and 80% submaximal trapezoidal contractions, you will be asked to slowly increase the force you are producing with your arm to trace a red line that will appear on a screen in front of you. In following this red line, you will increase force for a period of time, hold your force output steady for between four and 10 seconds, and then steadily decrease your force output back to zero. Three minutes of rest will be provided between each contraction. You will be asked to repeat this on your opposite limb as well. The risks associated with isometric exercise are the same as those associated with regular physical activity, and include risks of muscle soreness, pains, and slight risks of muscular and joint strains.

3. Visit Three: Visit three will consist of baseline assessments of muscle damage indicators, including range of motion, soreness, pain-pressure threshold of the involved limb, and maximal voluntary isometric contraction assessments of both limbs. Additionally, submaximal muscle actions as outlined in visit 2 will be performed on both arms with surface electromyography recordings completed during performance of the submaximal muscle actions of the limb that will be used for the repeated bout. After completion of submaximal muscle action

recordings, a damaging eccentric exercise bout will be completed on either the dominant or non-dominant arm, and indicators of muscle damage will be assessed again immediately post-exercise. This visit will last approximately two hours.

1. Range of motion: Range of motion will be evaluated using a manual goniometer. You will be asked to stand with your arm unsupported and hanging by your side with your palm facing forward. A semi-permanent marker will be used to make marks on your arm at the shoulder, elbow, and wrist. You will then be asked to fully flex the arm by touching your palm to their shoulder while simultaneously keeping your elbow at your side. Three measurements each will be taken at the point of resting extension and maximal flexion.
2. Visual Analog Scale: Your current level of muscle soreness will be assessed using a visual analog scale consisting of a 100-mm line with the far left (0-mm) hash mark representing "no pain" and the far right (100-mm) hash mark representing "very, very painful". You will be asked to indicate your level of soreness by marking an X on the line while an investigator provides a standardized reference stimulus at 60% and 80% of the distance along the belly of your biceps brachii muscle using a pressure algometer.
3. Pain-Pressure Threshold: Pain-pressure threshold will be assessed using a pressure algometer placed perpendicular to two sites along the belly of the biceps brachii and applying a consistent pressure until you inform investigators that that the stimulus has become painful.
4. Surface Electromyography (EMG): Surface EMG measures will be collected during the performance of submaximal muscle actions of both limbs using a surface EMG sensor. Before investigators apply the EMG electrodes, your skin will be shaved with a medical razor and dead skin cells and other debris will be removed with hypo-allergenic tape, followed by cleaning with an isopropyl alcohol wipe. Electrodes will be firmly secured to your skin using medical tape and traced with a permanent marker to ensure consistency of placement between exercise bouts. Surface EMG measures will be assessed immediately prior to each eccentric exercise bout, following the completion of MVIC measurements.
5. Eccentric exercise bout: following completion of submaximal muscle actions, the eccentric exercise bout will commence. You will be asked to grasp a hand bar attached to the lever arm on the dynamometer with your palm facing upwards. You will be asked to complete five sets of six maximal repetitions while resisting the dynamometer arm on the way down and relaxing as the arm returns to the top. Each contraction will last for three seconds and will move through a 90 degree range of motion, followed by a 9 second period where the arm is returned to the starting point and you will be asked to relax. Two minutes of rest will be provided between each set. During the completion of each contraction, you will be encouraged to maximally resist the movement of the lever arm. The risks associated with eccentric exercise are the same as those associated with regular physical activity, and include risks of muscle soreness, pains, and slight risks of muscular and joint strains.

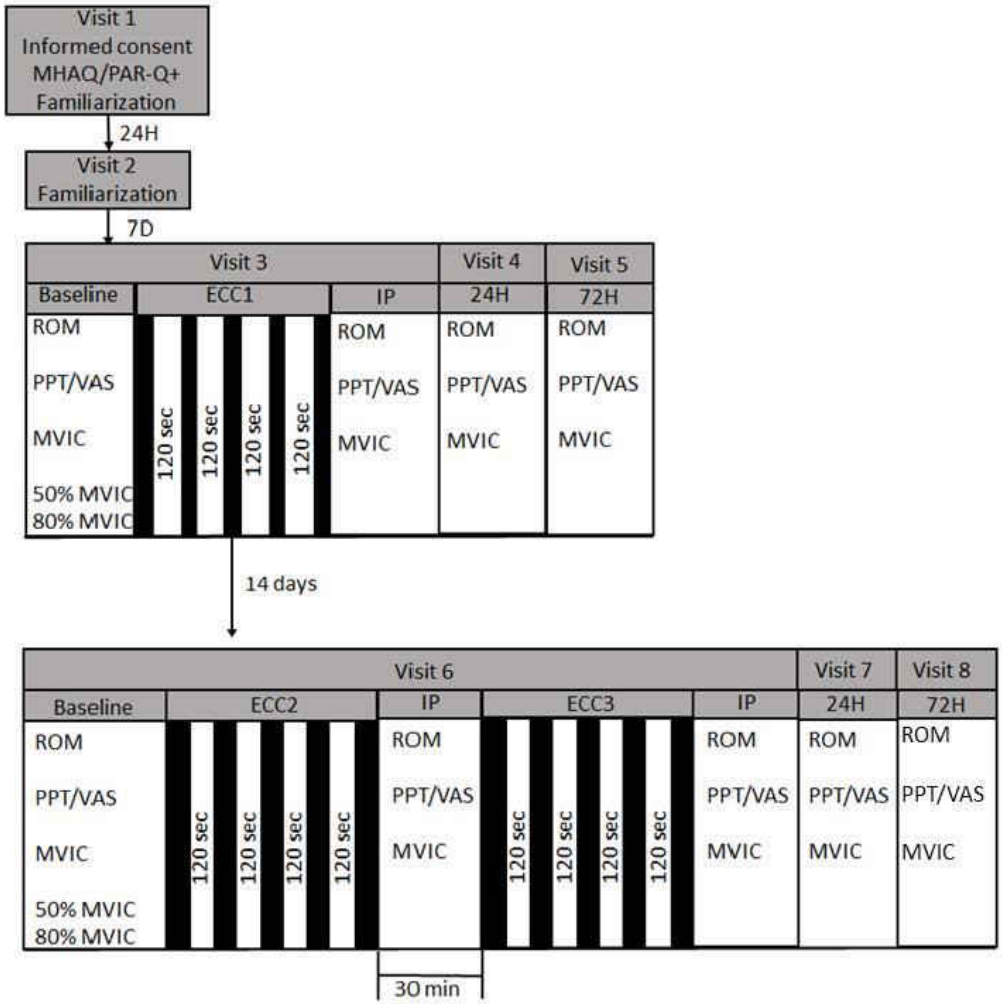
4. Visits 4 and 5: For visits 4 and 5, you will arrive to the laboratory and complete assessments of muscle damage, including range of motion, muscle soreness, pain-pressure threshold, and maximal voluntary isometric contraction of the

tested limb as described above. These visits are expected to last approximately 30 minutes each.

5. Visit 6: Visit 6 will consist of baseline assessments of muscle damage and muscle activation characteristics for both limbs as outlined in visit 3. You will then complete a repeated bout on either the same arm used in visit three [ipsilateral repeated bout (RB-IL)] or the opposite arm [contralateral repeated bout (RB-CL)]. Which arm will be used for this exercise session will be decided randomly, similar to flipping a coin. Immediately after the first repeated bout, follow-up assessments of muscle damage will be performed on the involved limb only. Thirty minutes after the completion of this bout, a second repeated bout will be performed on your other limb. After this bout is completed, follow-up assessments of damage will be performed on the involved limb. Prior to either of the eccentric exercise bouts, muscle activation characteristics will be assessed on both limbs in the order in which the repeated bouts will be completed. This visit is expected to last approximately three hours.

Visit 7 and 8: Visits 7 and 8 will be identical to procedures for visits 4-7, consisting of measures of muscle damage, including range of motion, muscle soreness, pain-pressure threshold, and maximal voluntary isometric contraction of both limbs as described above. Each of these visits is expected to last approximately one hour. Your total time commitment for involvement in this study should be approximately 11.5 hours over eight total visits.

6.



The devices involved in this study are listed below and will be used per the FDA approved use only:

1. Scale (Health-O-Meter professional scale, patient weighing scale, model 500KL, Pelstar, Alsip, IL, USA)
2. A BIA device (Inbody 770, body composition analysis, Inbody, Cerritos, CA, USA)
3. Surface EMG electrodes (Delsys Trigno Galileo, surface EMG decomposition, Delsys, Inc., Natick, MA, USA)
4. Pressure algometer (Wagner Force10, pain-pressure threshold, Wagner Instruments, Greenwich, CT, USA)

5. Isokinetic dynamometer (Biodex System4, eccentric/isometric exercise, Biodex Medical Systems, Shirley, NY, USA)

The order in which you complete the repeated exercise bouts during visit 6 will be chosen by chance, like flipping a coin. Neither you nor the study doctor will choose the order in which you complete the exercise bouts. You will have an equal chance of being assigned to complete the first repeated bout on either your dominant or non-dominant arm.

What happens if I say yes, but I change my mind later?

You can leave the research at any time it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can remove you from the study schedule. Discontinuation of participation can occur at any time. You have the right to discontinue participation without penalty, regardless of the status of the study. If you decide to leave the study, your data will not be included in the final analysis for publication. Data that is collected prior to withdrawal from the study will be discarded and not used or distributed to anyone.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this organization. All paperwork related to this study will be stored in a locked cabinet during and following the investigation, and all electronically-entered data will be saved in an encrypted file. Your participant folder and data files will be marked with an ID number to protect against a breach of confidentiality; your name and ID number will be stored separately. Access to research-related data, paperwork, and records will be limited to appropriate research personnel only. All records will be destroyed after 5 years

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include inability to adhere to the research protocol, failure to adhere to any requirements, or failure to complete all visits. We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

If you need medical care because of taking part in this research study, contact the investigator and medical care will be made available. Generally, this care will be billed to you, your insurance, or other third party. The Institute of Exercise Physiology and Rehabilitation Sciences at the University of Central Florida has no program to pay for medical care for research-related injury.

If you believe you have been injured during participation in this research project, you may file a claim with UCF Environmental Health and Safety, Risk and Insurance Office, P.O. Box 163500, Orlando, FL 32816-3500, (407) 823-6300. The University of Central Florida is an agency of the State of Florida for purposes of sovereign immunity and the university's and the state's liability for personal injury or property damage is extremely limited under Florida law. Accordingly, the university's and the state's ability to compensate you for any personal injury or property damage suffered during this research project is very limited.

No individual results will be published or shared with any third person or party, including the study sponsor. Individual results will remain confidential and only be relayed to participants upon request following the conclusion of all data collection and analyses.

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

APPENDIX E: MEDICAL HISTORY QUESTIONNAIRE

Human Performance Laboratory
University of Central Florida

Confidential Medical and Activity History Questionnaire (MHQ)

Participant #_____

When was your last physical examination? _____

1. List any medications, herbals or supplements you currently take or have taken the last month:

Medication	Reason for medication
_____	_____
_____	_____
_____	_____
_____	_____

2. Are you allergic to any medications? If yes, please list medications and reaction.

3. Please list any allergies, including food allergies that you may have?

4. Have you ever been hospitalized? If yes, please explain.

Year of hospitalization	Reason
_____	_____
_____	_____
_____	_____

5. Illnesses and other Health Issues

List any chronic (long-term) illnesses that have caused you to seek medical care.

6. Have you undergone major surgery within the previous 16 weeks? If yes, please explain.

7. Have you ever had (or do you have now) active malignant disease or cancer. If yes, please explain.

8. Have you ever had (or do you have scheduled) any procedure Iodine, Barium, or Nuclear Medicine Isotopes? (CT and PET scans are examples) If yes, please specify the date of the procedure.

Have you ever had (or do you have now) any of the following? Please circle questions that you do not know the answer to.

Cystic fibrosis	yes	no
Water retention problems	yes	no
Epilepsy	yes	no
Convulsions	yes	no
Dizziness/fainting/unconsciousness	yes	no
Chronic headaches	yes	no
Chronic cough	yes	no
Chronic sinus problem	yes	no
High cholesterol	yes	no
Rheumatic fever	yes	no
Chronic bronchitis	yes	no
Tuberculosis (positive skin test)	yes	no
Yellow jaundice	yes	no
Anemia	yes	no
Anorexia nervosa	yes	no
Bulimia	yes	no
Stomach/intestinal problems	yes	no
Arthritis	yes	no
Back pain	yes	no
Cardiovascular Disease		
Peripheral vascular disease	yes	no
Cerebrovascular disease	yes	no
Coronary artery disease	yes	no
Aortic stenosis	yes	no
Atrial fibrillation	yes	no
Poorly controlled hypertension	yes	no
Heart pacemaker	yes	no
Heart murmur	yes	no

Pulmonary disease		
Chronic obstructive pulmonary disease	yes	no
Asthma	yes	no
Interstitial lung disease	yes	no
Emphysema	yes	no
Metabolic disorder		
Diabetes mellitus (type 1, type 2)	yes	no
Diabetes insipidus	yes	no

Any others (specify):_____

_____

_____

_____

Do you smoke cigarettes or use any other tobacco products?	yes	no
Do you have a history of drug or alcohol dependency?	yes	no
Has your doctor ever said you have a heart condition and that you should only do physical activity recommended by a doctor?	yes	no
Do you feel any pain in your chest when you do physical activity?	yes	no
Are you ever bothered by racing of your heart?	yes	no
Do you ever notice abnormal or skipped heartbeats?	yes	no
Do you ever have any arm or jaw discomfort, nausea, or vomiting associated with cardiac symptoms?	yes	no
Do you ever have difficulty breathing?	yes	no
Do you ever experience shortness of breath?	yes	no
Do you lose your balance because of dizziness or		

do you ever lose consciousness?	yes	no
Have you ever had any tingling or numbness in your arms or legs?	yes	no
Has a member of your family or close relative died of heart problems or sudden death before the age of 50?	yes	no
Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?	yes	no
Do you have a bone or joint problem that could be made worse by a change in your physical activity?	yes	no
Have you ever used performance enhancing drugs (i.e. anabolic steroids)?	yes	no
Has a health care practitioner ever denied or restricted your participation in sports for any problem	yes	no

If yes, please explain: _____

_____

Do you know any other reason why you should not do physical activity? yes no

If yes, please explain: _____

I have answered these questions honestly and have provided all past and present health and exercise information to the bestof my knowledge.

YES [ ] NO [ ]

_____

Date

APPENDIX F: PHYSICAL ACTIVITY READINESS QUESTIONNAIRE

2017 PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

The health benefits of regular physical activity are clear; more people should engage in physical activity every day of the week. Participating in physical activity is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

GENERAL HEALTH QUESTIONS

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	**YES**	**NO**
1) Has your doctor ever said that you have a heart condition ☐ OR high blood pressure ☐?	☐	☐
2) Do you feel pain in your chest at rest, during your daily activities of living, **OR** when you do physical activity?	☐	☐
3) Do you lose balance because of dizziness **OR** have you lost consciousness in the last 12 months? Please answer **NO** if your dizziness was associated with over-breathing (including during vigorous exercise).	☐	☐
4) Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? **PLEASE LIST CONDITION(S) HERE:** _____	☐	☐
5) Are you currently taking prescribed medications for a chronic medical condition? **PLEASE LIST CONDITION(S) AND MEDICATIONS HERE:** _____	☐	☐
6) Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer **NO** if you had a problem in the past, but it ***does not limit your current ability*** to be physically active. **PLEASE LIST CONDITION(S) HERE:** _____	☐	☐
7) Has your doctor ever said that you should only do medically supervised physical activity?	☐	☐

☑ **If you answered NO to all of the questions above, you are cleared for physical activity.**
Go to Page 4 to sign the PARTICIPANT DECLARATION. You do not need to complete Pages 2 and 3.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow International Physical Activity Guidelines for your age (www.who.int/dietphysicalactivity/en/).
- You may take part in a health and fitness appraisal.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.
- If you have any further questions, contact a qualified exercise professional.

If you answered YES to one or more of the questions above, COMPLETE PAGES 2 AND 3.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at **www.eparmedx.com** before becoming more physically active.
- Your health changes - answer the questions on Pages 2 and 3 of this document and/or talk to your doctor or a qualified exercise professional before continuing with any physical activity program.

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FOLLOW-UP QUESTIONS ABOUT YOUR MEDICAL CONDITION(S)

1. Do you have Arthritis, Osteoporosis, or Back Problems?

If the above condition(s) is/are present, answer questions 1a-1c — If **NO** ☐ go to question 2

1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	YES ☐ NO ☐
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	YES ☐ NO ☐

2. Do you currently have Cancer of any kind?

If the above condition(s) is/are present, answer questions 2a-2b — If **NO** ☐ go to question 3

2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and/or neck?	YES ☐ NO ☐
2b.	Are you currently receiving cancer therapy (such as chemotheraphy or radiotherapy)?	YES ☐ NO ☐

3. Do you have a Heart or Cardiovascular Condition? *This includes Coronary Artery Disease, Heart Failure, Diagnosed Abnormality of Heart Rhythm*

If the above condition(s) is/are present, answer questions 3a-3d — If **NO** ☐ go to question 4

3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
3b.	Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)	YES ☐ NO ☐
3c.	Do you have chronic heart failure?	YES ☐ NO ☐
3d.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	YES ☐ NO ☐

4. Do you have High Blood Pressure?

If the above condition(s) is/are present, answer questions 4a-4b — If **NO** ☐ go to question 5

4a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
4b.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer **YES** if you do not know your resting blood pressure)	YES ☐ NO ☐

5. Do you have any Metabolic Conditions? *This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes*

If the above condition(s) is/are present, answer questions 5a-5e — If **NO** ☐ go to question 6

5a.	Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician-prescribed therapies?	YES ☐ NO ☐
5b.	Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness.	YES ☐ NO ☐
5c.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, **OR** the sensation in your toes and feet?	YES ☐ NO ☐
5d.	Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)?	YES ☐ NO ☐
5e.	Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future?	YES ☐ NO ☐

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6. Do you have any Mental Health Problems or Learning Difficulties? *This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome*

If the above condition(s) is/are present, answer questions 6a-6b — If **NO** ☐ go to question 7

6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
6b.	Do you have Down Syndrome **AND** back problems affecting nerves or muscles?	YES ☐ NO ☐

7. Do you have a Respiratory Disease? *This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure*

If the above condition(s) is/are present, answer questions 7a-7d — If **NO** ☐ go to question 8

7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
7b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	YES ☐ NO ☐
7c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	YES ☐ NO ☐
7d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	YES ☐ NO ☐

8. Do you have a Spinal Cord Injury? *This includes Tetraplegia and Paraplegia*

If the above condition(s) is/are present, answer questions 8a-8c — If **NO** ☐ go to question 9

8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
8b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	YES ☐ NO ☐
8c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	YES ☐ NO ☐

9. Have you had a Stroke? *This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event*

If the above condition(s) is/are present, answer questions 9a-9c — If **NO** ☐ go to question 10

9a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
9b.	Do you have any impairment in walking or mobility?	YES ☐ NO ☐
9c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	YES ☐ NO ☐

10. Do you have any other medical condition not listed above or do you have two or more medical conditions?

If you have other medical conditions, answer questions 10a-10c — If **NO** ☐ read the Page 4 recommendations

10a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months?	YES ☐ NO ☐
10b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	YES ☐ NO ☐
10c.	Do you currently live with two or more medical conditions?	YES ☐ NO ☐

PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE: _____

_____

GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.

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If you answered NO to all of the follow-up questions about your medical condition, you are ready to become more physically active - sign the PARTICIPANT DECLARATION below:

- It is advised that you consult a qualified exercise professional to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually - 20 to 60 minutes of low to moderate intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate intensity physical activity per week.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.

If you answered **YES** to **one or more of the follow-up questions** about your medical condition:

You should seek further information before becoming more physically active or engaging in a fitness appraisal. You should complete the specially designed online screening and exercise recommendations program - the **ePARmed-X+ at www.eparmedx.com** and/or visit a qualified exercise professional to work through the ePARmed-X+ and for further information.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ **at www.eparmedx.com** before becoming more physically active.
- Your health changes - talk to your doctor or qualified exercise professional before continuing with any physical activity program.

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The authors, the PAR-Q+ Collaboration, partner organizations, and their agents assume no liability for persons who undertake physical activity and/or make use of the PAR-Q+ or ePARmed-X+. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.

PARTICIPANT DECLARATION

- All persons who have completed the PAR-Q+ please read and sign the declaration below.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that a Trustee (such as my employer, community/fitness centre, health care provider, or other designate) may retain a copy of this form for their records. In these instances, the Trustee will be required to adhere to local, national, and international guidelines regarding the storage of personal health information ensuring that the Trustee maintains the privacy of the information and does not misuse or wrongfully disclose such information.

NAME _____ DATE _____

SIGNATURE _____ WITNESS _____

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER _____

For more information, please contact
www.eparmedx.com
Email: eparmedx@gmail.com

Citation for PAR-Q+
Warburton DER, Jamnik VK, Bredin SSD, and Gledhill N on behalf of the PAR-Q+ Collaboration. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and Electronic Physical Activity Readiness Medical Examination (ePARmed-X+). Health & Fitness Journal of Canada 4(2):3-23, 2011.

The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+ Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or the BC Ministry of Health Services.

Key References

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01-01-2017

APPENDIX G: VISUAL ANALOG SCALE

Subject #:_____ **Visit #:** 3 4 5 6 7 8

Date: _____

Dominant [ ] Nondominant [ ] **Right [ ] Left [ ]**

The following questions are designed to assess your feelings of soreness in response to a pressure stimulus. After each application of the probe, please mark an X across the line at the spot that best describes the level of soreness you experienced.

Proximal 1
My level of soreness is

No pain _____ Very, very painful

Distal 1
My level of soreness is

No pain _____ Very, very painful

Proximal 2
My level of soreness is

No pain _____ Very, very painful

Distal 2
My level of soreness is

No pain _____ Very, very painful

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