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# AN EXAMINATION OF NON-LOCAL MUSCLE FATIGUE IN UPPER AND LOWER LIMBS

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# AN EXAMINATION OF NON-LOCAL MUSCLE FATIGUE IN UPPER AND LOWER LIMBS

A DISSERTATION APPROVED FOR THE
DEPARTMENT OF HEALTH AND EXERCISE SCIENCE

BY

Dr. Travis W. Beck, Chair

Dr. Michael G. Bemben

Dr. Rebecca D. Larson

Dr. Carl J. Ade

Dr. Howard M. Crowson

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# Abstract

Non-local muscle fatigue (NLMF) is a phenomenon that has been described and examined extensively in literature. Traditionally, interventions have been applied in the unilateral limb to examine the potential short-term “cross-over” fatigue and long-term “cross education” effects in the contralateral limb. More recently, an emphasis is placed on the examination of unrelated heterogonous muscle groups after fatiguing the unilateral muscle groups (e.g. fatiguing upper limb and examining the motor performance of distal and unrelated lower limb muscles, or vice versa), as evidence was shown that the motor performance could be impaired in the non-exercised muscles. **PURPOSE:** To examine the possible changes in the neuromuscular properties and motor control strategies of both the contralateral homogenous and non-related heterogonous muscles following fatiguing exercise interventions on the unilateral muscle groups. **METHODS:** Eighteen subjects voluntarily participated in this 5-visit investigation. After the first visit as familiarization, subjects went through 4 separate randomly sequenced experimental visits, during which fatiguing interventions and testing were applied on different limbs (fatigue the right forearm flexors and test the left forearm flexors; fatigue the right forearm flexors and test the left leg extensors; fatigue the right leg extensors and test the left forearm flexors; fatigue the right leg extensors and test the left forearm flexors). Maximal isometric strength, force fluctuations during submaximal contraction, as well as surface electromyographic (EMG) signals were collected before and after the fatiguing interventions. In addition, surface EMG signals from the submaximal contractions were decomposed into individual motor unit action potential trains, and linear regression analysis was used to examine the relationship between motor unit mean firing rate and recruitment threshold. **RESULTS:** There was a significant decrease in maximal isometric strength in the non-exercised forearm flexors, but not in the non-exercised leg extensors. Consistent with this finding, the force became less steady during submaximal contractions in the non-exercised forearm flexors. However, the decreased motor performance was not accompanied with a decline in the EMG amplitude or altered motor control strategies. **CONCLUSIONS:** Six sets of 30-s maximal isometric contractions performed in the right forearm flexors and right leg extensors induced non-local muscle fatigue in the non-exercised left forearm flexors, but not in the leg extensors. Due to non-local muscle fatigue, the subjects' ability to maintain a steady constant force was impaired. Contradicting to the prevailing explanations of the NLMF, the EMG data from our study does not necessarily support the "central fatigue" mechanism, due to the lack of evidence of changes in EMG parameters and motor unit activity from the non-exercised biceps brachii. On the other hand, although the motor performance of the non-exercised left extensors was not affected by the fatiguing interventions, fatiguing upper body muscle vs. lower body muscle seemed to have differential effects on the motor unit firing behaviors from the non-exercised vastus lateralis. However, this difference was probably too small to induce significant changes in motor performance.

# Chapter 1: Introduction

In 1894, Scripture and colleagues (Scripture *et al.*, 1894) published a report that described two interesting experiments they had performed at the Yale Psychological Laboratory. In the first experiment, the research participant was asked to insert a needle into a hole with very small diameter for the purpose of measuring hand movement accuracy. The subject performed this task 20 times with the left hand on the first day, and half of the trials were successful. On the following 10 consecutive days, the subject practiced the same task only with the right hand 200 times per day. Surprisingly, with the gradual improvements of right hand movement accuracy, the research participant was able to insert the needle into the hole with her left hand (which received no training in movement accuracy) with a successful rate of 76% at the end of the experiment. The second experiment was performed by a separate research participant. This experiment required the participant to perform 10 maximal squeezing contractions against a rubber bulb with the right hand every day. In addition to the obvious grip strength improvement in the right hand, a 43% increase in grip strength of the left hand was also observed at the end of the experiment, which was due to the "indirect practice", according to the authors. In this report, the term "cross-education" was first introduced. Specifically, this term suggests that training one side of the body improves motor performance on the other side of the body. The same effect is sometimes termed "cross-over effect", "cross-transfer effect" or "contralateral training effect" (Carroll *et al.*, 2006).

Over the years, researchers have continued to study the "cross-education effect" by examining the effects of unilateral resistance training on strength of the contralateral limb (Carroll *et al.*, 2006). Meanwhile, a great emphasis has been placed on investigating the underlying mechanisms that contribute to the “cross-education” phenomenon. Specifically, numerous acute research studies have been conducted to examine the effects of different interventions (e.g. fatigue, stretching, etc.…) on motor control of the contralateral non-exercised limb.

One of the most important factors that is believed to influence the contralateral non-exercised motor control is “central fatigue”. Different from peripheral fatigue, which describes the fatigue within the muscles, central fatigue is generally defined as the decrease in central drive to the motor neurons (Gandevia, 2001). In addition, central fatigue is also hypothesized to modulate the planning and execution of motor tasks of the contralateral non-exercised muscle groups. Many researchers have examined the influences of fatiguing unilateral muscles on the neuromuscular responses of the contralateral homologous muscles (Todd *et al.*, 2003; Ratty *et al.*, 2006; Martin & Rattey, 2007; Paillard *et al.*, 2010; Doix *et al.*, 2013; Kawamoto *et al.*, 2014; Arora *et al.*, 2015; Kennedy *et al.*, 2015). Generally speaking, central fatigue can cross over to the contralateral non-exercised limb; however, controversial results on the basic force production were reported (Halperin *et al.*, 2015).

More recently, a small number of research studies (Takahashi *et al.*, 2011; Kennedy *et al.*, 2013; Halperin *et al.*, 2014a; Halperin *et al.*, 2014b; Kennedy *et al.*, 2015) have been conducted to examine the motor performance on the unrelated heterogonous muscle groups after fatiguing the unilateral muscle groups (e.g. fatiguing upper limb and examining the motor performance of distal and unrelated lower limb muscles, or vice versa). These findings were interesting, as the motor performance of the unrelated heterogonous muscle groups could be affected under certain conditions (muscle contraction type, exercise volume, muscle groups examined, and so on) (Halperin *et al.*, 2015). Thus, these results suggest that central fatigue created by a unilateral limb exercise would not only affect the motor performance of its contralateral homologous muscle groups, but can also cross over to and/or influence the motor performance of the unrelated, heterogonous muscle groups. Therefore, the term “non-local muscle fatigue” (NLMF) has been used to describe the temporary deficit in motor performance (mainly muscular strength) of non-exercised muscle groups that could be located contralateral and/or superior or inferior to the fatigued muscle group (Halperin *et al.*, 2015).

Many studies that examined central fatigue have used techniques such as transcranial magnetic stimulation (TMS) to test the effects of a fatiguing muscle contraction on motor cortex activity such as corticospinal and corticocortical excitability in the exercised and non-exercised muscles (Takahashi *et al.*, 2011). In addition, electrical nerve stimulation has been used to assess the level of voluntary muscle activation (VA) to quantify the contribution of central fatigue to the decrease in maximal force production (Belanger & McComas, 1981; Behm *et al.*, 1996). However, very limited research has been done to examine the control properties of the motor neurons that innervate the contralateral homologous muscles or heterogonous muscles. Specifically, since a decreased central drive to these muscles has been reported following fatigue of the unilateral muscles, it would be interesting to examine whether the control strategies of the motor units would be altered.

In addition to the methods/techniques mentioned above (TMS and electrical nerve stimulation), surface electromyography (EMG) has also been used extensively in research and clinical settings as a non-invasive technique for examining the summation of motor unit action potentials under the pick-up area of the electrodes (De Luca, 1997; Farina *et al.*, 2004). Specifically, many studies from our laboratory have used surface EMG amplitude and/or center frequency parameters to examine possible changes in various muscle activation parameters following different exercise interventions. For example, an increase in EMG amplitude is associated with increased net motor unit activity, which can be achieved by the recruitment of higher threshold motor units, the increase in the firing rate of the active motor units, or a combination of both (Farina *et al.*, 2004). On the other hand, a shift in EMG center frequency toward lower frequencies following certain exercise interventions (e.g. eccentric exercise) may suggest muscle fatigue or a selective damage to fast-twitch muscle fibers (Ye *et al.*, 2015b). Therefore, surface EMG serves as a good candidate for examining motor control strategies under various conditions.

A limitation of using surface EMG to examine motor control strategies is that this technique only provides a global measure of motor unit activity. Thus, research studies that focus on investigating individual motor unit behavior may not benefit by using traditional surface EMG. Other methods, such as intramuscular microelectrode recordings for single motor unit firing properties have been used to directly examine the firing behavior of individual motor units (Lindsley, 1935; Bigland & Lippold, 1954). However, the disadvantages of these methods include the fact that they are invasive, they only pick up the activities of a few motor units, and they are restricted to low level muscle contractions. Recent developments in surface EMG decomposition technology have greatly improved the ability to examine motor control strategies (Lindsley, 1935; Bigland & Lippold, 1954; Kleine *et al.*, 2000; Merletti *et al.*, 2003; De Luca *et al.*, 2006; Kleine *et al.*, 2007; Merletti *et al.*, 2008). Specifically, the surface EMG decomposition technology developed by De Luca's group (De Luca *et al.*, 2006) allows researchers to examine the activities of up to 40 motor units from almost any level of specified isometric constant force (De Luca *et al.*, 2006; De Luca & Hostage, 2010). Moreover, this decomposition algorithm has been proven to be valid (Hu *et al.*, 2013a, 2014b) and accurate (Nawab *et al.*, 2010; De Luca & Nawab, 2011; Hu *et al.*, 2014a). Thus, with this high accuracy and large motor unit yield, this technology can serve as a good candidate to examine and motor control strategies.

However, it is important to point out that, with the current surface EMG decomposition technology, it is impossible to track the changes in variables (e.g. recruitment threshold, firing rate) of a specific single motor unit during separate isometric contractions. Thus, the relationship between average motor unit firing rate and recruitment threshold from the output of the surface EMG decomposition has been used to examine the control strategies from a sample of the entire motor neuron pool (De Luca & Hostage, 2010). Specifically, the inverse relationship between recruitment threshold and the firing rate represents an "operating point" for the motor neuron pool in response to different levels of excitation (De Luca & Hostage, 2010; De Luca & Contessa, 2012). For example, as force output increases, the slope of the linear regression line of this relationship becomes progressively flatter (less negative), suggesting that higher threshold motor units are recruited to achieve a higher force output. In addition, an increased y-intercept without any change in the slope of the linear regression line indicates an increased average firing rate for all the detected motor units (De Luca & Hostage, 2010). This relationship has also been used to examine motor control strategies with different training modes (endurance vs. resistance-trained) (Herda *et al.*, 2015), before and after certain interventions such as isometric fatiguing exercise (Stock *et al.*, 2012), dynamic exercise (concentric vs. eccentric exercise) (Ye *et al.*, 2015a), prolonged stretching (Ye *et al.*, 2015c), and resistance training programs (Beck *et al.*, 2011b; Stock & Thompson, 2014).

To date, no research study has investigated the acute effects of fatiguing a unilateral muscle group on the motor control strategies of the contralateral homologous or unrelated heterogonous muscle group. Considering central fatigue can potentially transfer to the contralateral muscle group or unrelated heterogonous muscle groups, it is interesting to examine how the nervous system compensates for the possible decrements in motor performance.

## 1.1. Purpose of the Study

The purpose of this study was to use the surface EMG as well as a complicated EMG decomposition technique to examine the neuromuscular properties and motor control strategies of both the contralateral homogenous and non-related heterogonous muscles following fatiguing exercise interventions on the unilateral muscle groups.

### 1.2. Research Questions

1. Does fatiguing the unilateral muscle group decrease the maximal strength of the contralateral homologous and/or heterogonous muscles?
2. Does fatiguing the unilateral muscle group alter the force steadiness of the contralateral homologous and/or heterogonous muscles during submaximal isometric contractions?
3. Does fatiguing the unilateral muscle group alter the surface EMG amplitude and/or mean frequency of the contralateral homologous and/or heterogonous muscles during maximal and submaximal isometric contractions?
4. Does fatiguing the unilateral muscle group alter the operation (the relationship between motor unit recruitment threshold and firing rate) of the motor neuron pool of the contralateral homologous and/or heterogonous muscles?
5. Does fatiguing the unilateral muscle group alter the common modulation (common drive) from the central nervous system to the motor neuron pool of the contralateral homologous and/or heterogonous muscles?

### 1.3. Hypotheses

1. I hypothesize that fatiguing the unilateral muscle group can decrease the maximal strength of the contralateral homologous muscle and the heterogonous muscle.

2. I hypothesize that fatiguing the unilateral muscle group can deteriorate the force steadiness of the contralateral homologous muscle and the heterogonous muscle during submaximal isometric contractions.
3. I hypothesize that fatiguing the unilateral muscle group can decrease the surface EMG amplitude and mean frequency of the contralateral homologous muscle and the heterogonous muscle during maximal isometric contractions but increase the surface EMG amplitude and mean frequency during submaximal isometric contractions.
4. I hypothesize that fatiguing the unilateral muscle group can alter the operation (the relationship between motor unit recruitment threshold and firing rate) of the motor neuron pool of the contralateral homologous muscle and the heterogonous muscle (making the slope of the linear regression line more flat and the y-intercept greater).
5. I hypothesize that fatiguing the unilateral muscle group can increase the common modulation (common drive) from the central nervous system to the motor neuron pool of the contralateral homologous muscle and the heterogonous muscle.

## 1.4. Definition of Terms

1. Action Potential: a short-lasting event in which the electrical membrane potential of a cell rapidly rises and falls, following a consistent trajectory.

2. Central Fatigue: a progressive reduction in voluntary activation of muscle during exercise. It can also be defined as a decrease in the central drive to the motor neurons.
3. Common Drive: the common modulation from the central nervous system to motor neuron pool to regulate force production.
4. Concentric: a muscle action that involves the production of force while the muscle is shortening.
5. Contralateral: occurring on, affecting, or acting in conjunction with a part on the opposite side of the body.
6. Cross-education/Contralateral Training Effect: the phenomenon whereby training one side of the body increases the strength of muscles on the other side of the body.
7. Eccentric: a muscle action that involves the production of force while the muscle is lengthening.
8. Electromyography: an electrodiagnostic medicine technique for evaluating and recording the electrical activity produced by skeletal muscles.
9. Heterogonous: incommensurable through being of different kinds, degrees, or dimensions.
10. Homologous: having the same relation, relative position, or structure, in particular.
11. Ipsilateral: situated or appearing on or affecting the same side of the body.

12. Isometric: a muscle action involving tension production without movement at the joint or shortening of the muscle fibers; also known as static muscle action.
13. Maximal Voluntary Contraction: an isometric muscle action in which the subject provides as much effort as possible.
14. Motor Unit: a motor neuron and all of the muscle fibers it innervates.
15. Motor Unit Action Potential Train (MUAPT): a temporal sequence of action potentials generated by a single motor unit.
16. Motor Unit Recruitment: the activation of additional motor units to accomplish an increase in contractile strength in a muscle.
17. Motor Unit Recruitment Threshold: the force level where a motor unit is activated. It can be normalized by expressing them in relative terms (e.g. % of MVC in the current study).
18. Motor Unit Firing Rate/Discharging Frequency: the frequency that a motor neuron sends nerve impulses to the muscle fibers it innervates; it is usually expresses as pulse per second (PPS).
19. Muscle Fatigue: an exercise-induced reduction in maximal voluntary muscle force; also defined as the inability of maintain the desired or expected force. Muscle fatigue has peripheral and central causes.
20. Non-local Muscle Fatigue: a temporary deficit in performance of non-exercised muscle groups that could be located contralateral, or ipsilateral, as well as inferior or superior to the fatigued muscle groups.

21. Peripheral Fatigue: fatigue produced by changes at or distal to the neuromuscular junction.
22. Unilateral: occurring on, performed on, or affecting one side of the body or one of its parts.
23. Voluntary Activation: level of voluntary drive during an effort. It is also a measure of central fatigue that can be quantified by measuring the additional force produced by neuromuscular stimulation performed during a maximal voluntary contraction (MVC).

## 1.5. Abbreviations

1. ANOVA = Analysis of Variance
2. BB = Biceps Brachii Muscle
3. CI = Confidence Interval
4. CNS = Central Nervous System
5. Dominant = DOM
6. EMG = Electromyography
7. ES = Effect Size
8. FR = Firing Rate
9. ICC = Intraclass Correlation Coefficient
10. MEP = Motor Evoked Potentials
11. MNF = Mean Frequency
12. MVC = Maximal Voluntary Contraction
13. MUAPT = Motor Unit Action Potential Train

14. NLMF = Non-local Muscle Fatigue

15. POST = Post-Test

16. PRE = Pre-Test

17. RT = Recruitment Threshold

18. SD = Standard Deviation

19. TMS = Transcranial Magnetic Stimulation

20. VL = Vastus Lateralis Muscle

## 1.6. Delimitations

The following are the delimitations for this study:

1. Approximately 20 participants were needed to complete this investigation, based on a power analysis of ß = 0.8.
2. Participants had to be between the age of 18 and 40 years.
3. All participants had to complete a health history questionnaire and a written statement of informed consent prior to any testing.
4. All participants had to be healthy and free from any current or ongoing neuromuscular diseases. In addition, they could not have any injuries on their shoulders, elbows, wrists, hands, hips, knees, and ankles within the past 6 months.
5. The participants only performed voluntary contractions.

## 1.7. Limitations

The following are the limitations for this study:

1. Participants were mainly recruited via the following 2 ways: 1) participants responded to posted recruitment flyers, and 2) the investigator advertised the study in several departmental classes so the interested volunteers were selected. Therefore, the process of subject selection was not truly random.
2. The technique and equipment that were used to examine motor unit firing properties have the following restrictions and limitations:
   a. The muscle contractions had to be isometric.
   b. The force profile had to be trapezoidal in shape (subjects had to increase the force linearly to a target force level, held the force as steady as possible, and then decreased the force linearly).
   c. There was a duration restriction for the contraction (less than 45 seconds) due to the limitation of the computer's memory.
3. Since voluntary contractions were used, the contribution of the central fatigue to overall muscle fatigue developed during fatiguing exercises could not be quantified, which requires the use of electrical stimulation.

## 1.8. Assumptions

1. Participants actually and honestly answered the questions from the health questionnaire.
2. Participants gave their true maximal effort during each maximal contraction.
3. All equipment functioned properly during all testing sessions.
4. The EMG and motor unit variables detected at the sensors accurately represented the behavior of the whole muscle.

# Chapter 2. Review of Literature

The review of literature is organized in a study-by-study manner, and it has 4 subsections (labeled 2.1-2.4). The article summaries are provided in a chronological order within each subsection. At the end of each subsection (except subsection 2.1), a brief summary was provided.

## 2.1. Maximal Exercise-Induced Central Fatigue

Since examining and quantifying central fatigue is not the primary purpose of the dissertation project, this subsection will only list a small amount of papers that are important and essential to understand central fatigue. Specific emphasis will be placed on maximal isometric voluntary contraction (MVC)-induced central fatigue, because the isometric MVC will be used as an intervention to examine the "cross-over" effect in this study. Thus, review article Gandevia (2001) will be briefly introduced to cover the basic information about central fatigue. As an important research study, Kent-Braum (Kent-Braun, 1999) was able to quantify the contributions from different sites (central vs. peripheral) to muscle fatigue. The summary of this subsection will not be provided because Gandevia (2011) review article serves as a good candidate for the summary.

### *Kent-Braum (1999)*

This is a classic study that quantified central and peripheral contributions to muscle fatiguing during a prolonged maximal voluntary contraction (MVC). To induce muscle fatigue, nine healthy subjects performed a sustained MVC of their ankle dorsiflexor muscles for 4 minutes. Voluntary muscle fatigue was quantified as the percent decline in MVC during the sustained exercise. Changes in central activation were also quantified by calculating the central activation ration (CAR = MVC/ (MVC + superimposed tetanic force) during the exercise. In addition, intracellular pH and $H_2PO_4^-$ were measured to quantify the contribution from peripheral factors. During the entire exercise, voluntary force reduced by 78%. Accompanied with this force reduction was the depression in CAR (16%). Therefore, central fatigue contributed about 20% to the muscular fatigue during a high intensity prolonged contraction.

### *Gandevia (2001)*

This review article focused on the contributions of central factors in human muscle fatigue. After a brief historical review, the author introduced the definitions of several key terms. Peripheral fatigue refers to “exercise-induced process that lead to a reduction in force production and that occur at or distal to the neuromuscular junction.” While central fatigue refers to the fatigue that occurs more proximal and can be defined as “a progressive exercise-induced failure of voluntary activation of the muscle.” A common means to quantify the central fatigue is through examining the voluntary activation (VA), which refers to the level of voluntary drive to the motor neuron pool of the exercised muscle. The voluntary activation level is usually reported as a ratio of force generated during a maximal voluntary contraction (MVC) over the force generated during a MVC with a superimposed twitch stimulus delivered. If central fatigue occurs, this ratio should decrease. The measurement of voluntary activation, however, does not provide more detailed information on where exactly the fatigue occurs (e.g. in motor cortex or in the spinal cord). Generally speaking, central fatigue can be attributed to supraspinal (occurs in motor cortex) and/or spinal (occurs in spinal cord) mechanisms. To quantify supraspinal fatigue, a technique called transcranial magnetic stimulation (TMS) is often used to examine the motor drive developed from the motor cortex (also known as motor-evoked potentials (MEPs)) during fatiguing exercise. On the other hand, central fatigue that occurs at a spinal level can be influenced by proprioceptive input from muscle spindles, Golgi tendon organs, and so on. These factors do play important roles affecting firing rates of active motor neurons.

## 2.2. Effects of Exercise on Contralateral Homologous Neuromuscular Function

*Bonata et al. (Bonato et al., 1996)*

This study is one of the earlier studies that used transcranial magnetic stimulation (TMS) to examine the possible effects of exercise on the excitability of the activated and non-activated primary motor cortex (MI). Nine subjects performed repetitive abduction-adduction exercise with their right thumbs as fast as possible for one minute. Motor-evoked potentials (MEPs) from the non-exercised muscles started to decline after 5 minutes of the exercise, and reached a significant level from 10 to 20 minutes following the exercise. This experiment suggested that a depression in MI excitability can occur in the non-activated hemisphere after fatiguing exercise performed in the opposite limb muscles.

*Zijdewind et al. (Zijdewind et al., 1998)*

This study examined the influence of a voluntary fatiguing contraction on the motor performance of the contralateral muscle. The researchers had subjects perform submaximal isometric contractions (30% MVC) to failure (could not maintain the designated force for consecutive 5 seconds) with their right first dorsal interosseous (FDI), and then perform the same exercise on the left side. During the submaximal isometric muscle actions, subjects gave their perceived level of effort on a scale from 0 to 10 in every 30 seconds. In addition, three superimposed twitch-stimuli, three superimposed twitch-stimuli with an MVC, and three twitch stimuli during a 3-4 seconds rest were delivered during the submaximal isometric contraction in every 30 seconds. The fatiguing submaximal isometric exercise lasted 582 ± 248 seconds in the right side of the FDI muscle. With the decline of the MVC during the fatiguing contraction, relative amplitude of MVC-superimposed twitches gradually increased, which indicated that there was a gradual decline in maximal voluntary activation of the muscle. These variables in the following left hand fatiguing test were not significantly different with the ones from the right hand, suggesting the absence of "cross-over" of central fatigue effects in the contralateral hand.

*Grabiner and Owings (Grabiner & Owings, 1999)*

This study examined unilateral and contralateral strength responses following performing either 75 isokinetic concentric or eccentric MVC with the unilateral knee extensors. Both protocols caused significant strength losses in the unilateral limb, with the greater fatigue induced by concentric protocol when compared to eccentric exercise. The concentric exercise did not alter the contralateral maximal force output. Surprisingly, the eccentric protocol significantly increased contralateral eccentric MVC moment. No EMG data was reported in this study. This is the only study that showed a bout of exercise protocol can induce an increase in maximal strength in the contralateral limb.

*Todd et al. (Todd et al., 2003)*

The purpose of this study was to investigate the “cross-over” effect on contralateral neuromuscular performance by using transcranial magnetic stimulation (TMS). Ten subjects performed two different fatiguing protocols: “alternating protocol”, during which they did four consecutive 1-minute sustained elbow flexion MVCs (unilateral-contralateral-unilateral-contralateral); and “unilateral intermittent protocol”, during which they performed two 1-minute MVCs with their unilateral elbow flexors with one-minute rest provided between the contractions. During all MVCs, TMS was applied. The authors found that when the 1-minute rest interval was replaced with the contralateral elbow flexor MVC, voluntary activation significantly decreased in the 2nd unilateral elbow flexion MVC. However, voluntary strength or EMG responses to TMS were not altered. These results suggested that although fatiguing the unilateral elbow flexor can induce the “cross-over” effect, the impact to maximal motor performance was not functionally significant.

*Humphry et al. (Humphry et al., 2004)*

By using transcranial magnetic stimulation (TMS), the authors examined whether a reduction in corticospinal excitability would be transferred to the non-excised contralateral muscles following two fatiguing protocols with different exercise durations. During the first session (long-duration), the subjects performed biceps curls with a 3.5-kg weight to exhaustion. During the second session (short-duration), the subjects performed the same biceps curling protocol but only with the duration of 25% of the time to exhaustion (based on the results from the first session). Motor-evoked potentials (MEPs) were assessed before and after both sessions. Depressed MEPs were only observed in the contralateral non-exercised biceps following the long-duration exercise, but not short-duration exercise. In addition, after examining the impact of this depressed MEP to motor performance, the authors found that the functional motor performance was not affected (no reduction in MVC, and no changes in reaction time and movement times) in the contralateral non-exercised muscles.

### *Rattey et al. (Ratty et al., 2006)*

This one-visit study directly examined the effects of fatiguing the unilateral leg extensors on the strength and surface EMG variables of the contralateral leg extensors. Thirteen men and fifteen women performed a 100-s sustained MVC of their dominant legs. Although the voluntary activation of the non-dominant contralateral leg extensor significantly decreased (8.7%), there were no significant decreases in isometric MVC, twitch force, as well as the compound action potential (M-wave). The importance of this study is that it suggested that central mediated mechanisms seem to be the only contributor to fatigue in the non-exercised contralateral muscle.

### *Martin and Rattey (Martin & Rattey, 2007)*

This experiment and the one in Rattey et al. (2006) were both part of the same research study. The purpose of this study was to examine the gender differences with regards to contralateral motor performance following a bout of unilateral fatigue exercise. Sixteen young adults (8 men and 8 women) participated in the first phase of the study, which involved fatiguing the dominant leg extensors and testing the same muscle. Fifteen adults (7 men and 8 women) participated the second phase of the study, which involved fatiguing the dominant leg extensors but testing the contralateral non-dominant muscles. The fatiguing intervention (100-second sustained MVC) induced greater strength losses in both unilateral and contralateral limbs for men when compared to women. In addition, accompanied with the strength decrements were the reduced voluntary activation in both genders, but with greater deficits for men than women. This study is important as it was the first to show the gender differences in unilateral and contralateral maximal motor performance following the fatiguing intervention in unilateral muscle groups.

### *Regueme et al. (Regueme et al., 2007)*

This study examined contralateral maximal motor performance following a bout of unilateral exhaustive stretch-shortening cycle exercise of the triceps surae muscle group. Before, immediately after, and 2 days after the 30 unilateral exhaustive rebounds, isometric MVC and 10 drop jumps (DJs) were measured for the exercised leg, non-exercised leg, and both legs. Maximal strength and DJ performance were not altered for the non-exercised leg in any time points after the exhaustive rebound exercise.

### *Strang et al. (Strang et al., 2009)*

The purpose of this investigation was to examine whether anticipatory postural adjustments (APAs) alter in non-exercised contralateral muscles following the fatiguing exercise in unilateral muscles. After 7 sets of 20 repetitions of maximal concentric knee flexion/extension exercise in a dynamometer, isometric MVCs were performed with quadriceps and hamstring muscles in both unilateral and contralateral sides. The exercise intervention did not induce fatigue in the contralateral muscles, but there were earlier APA onsets in the contralateral muscles, which thought to be compensating for the fatigue-induced disturbance in postural stability.

*Paillard et al. (Paillard et al., 2010)*

This investigation was designed to examine whether contralateral unipedal postural control deteriorates following either unilateral muscle stimulation or isometric voluntary contractions. Fifteen healthy young men went through two separate experimental sessions: voluntary quadriceps femoris contractions, and electrical stimulation of the quadriceps femoris. The fatiguing protocol was 10 sets of 50 repetitions at 10% of the peak torque for both conditions. Before and after each intervention, isometric MVC and unipedal postural control were examined. Specifically, the subjects were asked to stand on a platform with their contralateral feet and with eyes closed for the postural test (dependent variables: the body sway area, and the spectral power density of the recorded body sway signals in three dimensions). Isometric strength of the contralateral non-exercised muscle was not affected by either voluntary contractions or electrical stimulation intervention. However, the body sway areas significantly increased following both conditions. Therefore, the “crossed-over” fatigue can disturb postural control after both stimulated and voluntary contractions.

*Doix et al. (Doix et al., 2013)*

This study aimed to investigate the time course of the cross-over effect of muscle fatigue on the non-exercised contralateral knee extensors. Fifteen healthy young men performed 2 bouts of 100-second maximal isometric unilateral knee extensions. Before, between two bouts of fatiguing exercise, and after the fatiguing exercise, neuromuscular functions (torque, normalized EMG amplitude, and voluntary activation) of both exercised and non-exercised contralateral knee extensors were examined. While the fatiguing intervention kept impairing the ability to produce maximal force on the unilateral limb following, the cross-over effect of fatigue was only observed after the 2nd bout of fatiguing exercise. In addition, significant correlation between the torque decline and the decrease in voluntary activation was also found. This study is important, as it partially solved the disagreement regarding the existence of cross-over effect of muscle fatigue in contralateral non-exercised muscles.

*Kawamoto et al. (Kawamoto et al., 2014)*

The purpose of this investigation was to examine the acute effects of performing different intensities (medium vs. high) of unilateral fatiguing dynamic knee extension exercise on the motor performance of the contralateral knee extensors. Before and after three different separate fatiguing conditions (control vs. 4 sets of 40% MVC to failure vs. 4 sets of 70% MVC to failure), the isometric MVC and the submaximal endurance test (70 % MVC) were performed on the contralateral knee extensors. Both medium and high intensity fatiguing protocols significantly decreased the maximal strength of the contralateral knee extensors, but the decrements were not specific to any condition. Accompanied with the strength decrease was the significant decreases in the force development in the first 100ms (F100) during the isometric MVC following both 40% and 70% MVC fatiguing protocols, with 70% condition induced greater decrement than 40% condition did. Although there was no significant difference for the endurance time among all three conditions, the force steadiness tended to be impaired following both 40% and 70% MVC fatiguing protocols.

### *Ye et al. (Ye et al., 2014a)*

This study investigated the isometric strength and EMG responses in unilateral and contralateral elbow flexors after fatiguing unilateral elbow flexors with concentric vs. eccentric exercise intervention. The subjects in this study were resistance-trained (n = 25). The fatiguing interventions were randomized in separate experimental visits: 6 sets of 10 repetitions of maximal concentric exercise or eccentric exercise on an isokinetic dynamometer. Before and after the exercise intervention, isometric strength and the amplitude of surface EMG were examined during isometric MVCs. Significant decrease in isometric strength was reported in both unilateral (36%) and contralateral (4%) elbow flexors. In addition, normalized EMG amplitude also decreased in both limbs (unilateral: 21%; contralateral: 7%). However, the decrements of both isometric strength and EMG amplitude were not specific to the exercise condition (concentric vs. eccentric).

*Summary*

Over the last two decades, many research studies have examined the “cross-over” effect on non-exercised contralateral muscles. Most studies agree that central fatigue-induced “cross-over” effect does exist because of the depression of the motor-evoked potentials (MEPs) as well as the reduced voluntary activation (VA) for the contralateral muscles following a bout of fatiguing exercise in the unilateral side. This “cross-over” also seems to have a clear effect on fine motor control (force steadiness and postural control) in the contralateral muscles. When measuring such effect from the perspective of the contralateral motor performance, however, many factors need to be considered. Specifically, the intensity, the duration, and the volume of the fatiguing exercise can play important roles affecting the contralateral motor functional performance. These factors therefore explain the contradicting results from different research studies, especially for the contralateral maximal motor performance (maximal strength). Based on the studies reviewed in this section, contralateral strength deficit would likely to occur in the situation where the intensity of the fatiguing exercise is high or even maximal, the duration is long enough, and with exercise performed with the isometric muscle action mode. In addition, more than one bout of long duration isometric MVCs may be needed to elicit the central fatigue-induced force deficit in the contralateral muscles.

## 2.3. Effects of Exercise on Unrelated Heterogonous Neuromuscular Function

*Takahashi et al. (Takahashi et al., 2011)*

The purpose of this study was to examine if fatiguing lower limb would affect the cortical excitability in the non-exercised upper limb muscles (biceps brachii (BB) and first dorsal interosseous (FDI)). Subjects performed 3 sets of exhaustive 5-minute leg press at their 50% MVC. Before, immediately after, and during the recovery period at 5, 10, 15, 20, and 30 minutes after the fatiguing protocol, motor-evoked potentials (MEPs), short interval intracortical inhibition (SICI), and intracortical facilitation (ICF) were measured in BB and FDI. Both MEPs and SICI were depressed for up to 20 minutes in both non-exercised muscles, suggesting that fatiguing large lower limb muscle group would affect the excitability of both SICI and the corticospinal projection to the non-exercised upper limb muscles.

### *Kennedy et al. (Kennedy et al., 2013)*

The aim of this study was to investigate the effects of two different types (maximal (100% MVC) vs. submaximal (30% MVC)) of bilateral forearm muscle fatiguing protocol on the neuromuscular function of the unrelated plantar-flexors muscles. MVC, voluntary activation (VA), and twitch torque were measured from the plantar-flexor muscles before and after each fatiguing protocol. Both protocols caused decreases in the MVC and the level of VA of the plantar-flexor muscles. However, the treatment effect of maximal fatiguing protocol was significantly greater than that following the submaximal fatiguing protocol.

### *Halperin et al. (Halperin et al., 2014a)*

The aim of this study was to examine if 5 sets of fatiguing bilateral dynamic knee extension to failure would induce nonlocal fatigue in unrelated muscles (dominant elbow flexors). In addition, this study also examined if nonlocal fatigue would occur after the fatiguing protocol in a single MVC performance (directly measuring muscle fatigue) vs. 12 repeated MVCs with short rest periods (measuring fatigue resistance/strength endurance). Before and after the fatiguing intervention, force and EMG amplitude of the dominant elbow flexor were measured during the MVC. The main finding of this experiment was that nonlocal fatigue was not seen during the single MVC testing, but the elbow flexors' fatigue resistance decreased (decreased force output in the last 5 MVCs when compared to the control condition) following the fatiguing intervention.

*Halperin et al. (Halperin et al., 2014b)*

Following the previous study (Halperin et al. 2014a), the same group of researchers conducted another two similar experiments to examine nonlocal cross-over fatigue responses between different muscle groups. Specifically, the three major purposes of these experiments were: 1) to examine if nonlocal cross-over fatigue would occur in 2 different non-fatigued muscle groups (non-dominant elbow flexor vs. non-dominant knee extensor) following fatiguing the same muscle (unilateral dominant quadriceps or heterogonous elbow flexors); 2) to examine if nonlocal cross-over effects measured in the same target muscles would differ after fatiguing different muscle groups (fatigue unilateral dominant quadriceps and test the contralateral quadriceps or heterogonous elbow flexors vs. fatigue unilateral dominant elbow flexors and test the contralateral elbow flexors and heterogonous quadriceps); and 3) to examine if the nonlocal crossover effects would differ between a single MVC performance after the fatiguing protocol and during a strength endurance protocol (12 MVCs). Force, EMG, and voluntary activation (VA) were measured before and after the fatiguing interventions. The results showed that the rested knee extensors demonstrated nonlocal effects no matter which muscle was fatigued. However, the elbow-flexors remained unchanged in terms of force, EMG, and VA responses following both fatiguing interventions.

### *Marchetti et al. (Marchetti et al., 2014)*

Although this study did not use fatiguing protocol to examine neuromuscular function in the nonrelated/nonlocal muscles, as an important exercise intervention used in many research studies, static-stretching on the upper limb did affect neuromuscular function in nonrelated/nonlocal lower body muscles. The aim of this study was to examine the acute effects of upper limb stretching on the maximal concentric jump performance. Twenty-five resistance-trained men performed 10 sets of 30 seconds static stretches on their shoulder joints. Before and after the stretching intervention, subjects performed maximal concentric jump tasks, during which vertical ground reaction forces, surface EMG of gastrocnemius lateralis (GL) and vastus lateralis (VL) were recorded. The stretching intervention induced a significant decrease in peak force and a significant increase in peak propulsion duration. However, the integrated EMG values for both GL and VL muscles were not affected.

*Summary*

The effects of fatiguing exercise on unrelated heterogonous muscle performance were not examined until recent years. Based on the results from Takahashi et al. (2011), it is clear that fatiguing exercise could affect the excitability of motor cortex that projecting the nonrelated heterogonous muscles. However, this effect on the motor performance of the heterogonous muscles was unclear. Later studies with different fatiguing interventions suggested that the “heterogonous muscle cross-over” effect is condition specific. For example, factors such as the intensity of the fatiguing contraction, as well as which muscle groups are fatigued seem to play important roles influencing the motor performance of the non-related heterogonous muscles.

## 2.4. Examining Motor Control Strategies through EMG Decomposition

This subsection will start with some basic motor unit control properties based on some EMG decomposition studies in the early 1980s. These studies (De Luca *et al.*, 1982b, a; De Luca, 1985) will demonstrate in a nutshell how voluntary force is controlled by the modulation of the recruitment of motor units and/or the rate of firings of the motor unit. With this basic information, an emphasis will be placed on the application of using surface EMG decomposition technique to examine motor control strategies under different conditions.

*De Luca et al. (De Luca et al., 1982a)*

Along with De Luca et al. (1982b), this is one of the earlier studies that De Luca and his colleagues used decomposition algorithm (early model, relatively low number of motor units yield) to examine the motor control strategies under voluntary contractions. Thirteen adult males (4 normal subjects, 3 long-distance swimmer representing endurance-trained individuals, 3 elite powerlifters representing resistance-trained individuals, and 3 world-class pianists who possessed very fine motor control) participated in this investigation. EMG signals were recorded via a single bipolar needle electrode during triangular isometric contractions (40% MVC and 80% MVC) of the first dorsal interosseous (FDI) and deltoid muscles. In addition, subjects were also asked to produce these contractions with three different force rates (10, 20, and 40% MVC/second). The decomposition algorithm was able to decompose 2 to 8 motor units that were simultaneously recruited during triangular contractions.

Motor units tended to decruit at slight higher forces than their recruitment threshold. Counterintuitively, accompanied with this phenomenon is the reduced motor unit firing rate from recruitment to decruitment. The authors explained this interesting observation by using the “potentiation” mechanism: after repetitive stimulation, the potentiation of motor unit twitch tension can occur, which requires a reduced discharging frequency and/or less number of recruited motor units to maintain the designated force.

When compared FDI vs. deltoid, the mechanisms of force generation were different. Specifically, the FDI largely relies on adjusting firing rates of the motor units (narrow recruitment threshold range), which is capable of producing smooth and accurate force. On the other hand, the deltoid muscle mainly relies on the recruitment of motor units (wide recruitment threshold range) to increase the force production, which is essential for gross movements that require high force level.

Finally, the authors examined the relationship between motor unit recruitment and firing rate. Specifically, higher-threshold motor unis tend to firing at lower frequencies, while the lower-threshold motor units tend to fire at higher frequencies. In fact, this observation was the earliest indication of the “motor neuron pool operating point” as well as the foundation of “onion-skin” scheme, which will be mentioned and reviewed in the later literature of this subsection.

### *De Luca et al. (De Luca et al., 1982b)*

Continuing from De Luca et al. (1982a), this paper mainly discussed the common modulation from the central nervous system (CNS) to motor units in a motor neuron pool. To examine the common drive (common modulation), the authors cross-correlated the firing-rate record of each active motor unit to the force output during the same contraction interval. In addition, the firing-rate record of each active motor unit was also cross-correlated with other concurrently active motor units one by one. In addition to the triangular contractions mentioned in De Luca (1982a), subjects were also asked to perform two constant force contractions (30% and 60% MVC).

Force fluctuations always existed during the two constant force contractions. In addition, small and similar firing-rate fluctuations were found in all recorded motor units. The cross-correlation results showed that the motor unit firing rate fluctuations were almost mirrored the force output with time delays (motor unit firing rate fluctuation led to force fluctuation). In addition, the firing rate records of concurrently active motor units were also highly correlated with each other ($r > 0.6$) at both 30% and

60% MVC. Although the term “common drive” was not presented in the paper, it was the earliest publication that described this general idea and the underlying mechanisms.

### *De Luca (De Luca, 1985)*

This is a review paper generally described two concepts: the common drive and the motor unit firing rate vs. recruitment threshold interaction.

According to the author, “…the unison behavior of the firing rates of motor units, both as a function of time and force, has been termed the common drive. Its existence indicates that the nervous system does not control the firing rates of motor units individually. Instead, it acts on the pool of the homonymous motor neurons in a uniform fashion. Thus, a demand for modulation of the force output of a muscle may be represented as a modulation of the excitation and/or inhibition on the motor neuron pool. (p. 126)”

Later in the paper, the author mentioned that “this interaction between recruitment and firing rate provides an apparently simple strategy for providing smooth force output”. In the last paragraph of this paper, the author summarized: “…recruitment is the more basic mode of force generation. The behavior of the firing rate is to some extent moulded by the performance required from the muscle and the number of motor units which comprise the muscle. It appears that the nervous system is constructed to “balance” the contribution of firing rate control and recruitment control, so as to enhance the smoothness of the force output of the muscle.”

### *De Luca and Erim (De Luca & Erim, 1994)*

This is another review work on common drive. In addition to strengthening the concept presented in De Luca (1985), the authors also mentioned “onion-skin” phenomenon (during isometric contractions, the firing rates of earlier recruited motor units are greater than those of later recruited motor units). Specifically, this phenomenon/motor control strategy exists for a reason: the neuromuscular system is not necessarily designed to maximize the force output, but to “optimize some combination of force and duration over which the force is sustained (p. 301).” Generally speaking, it is very important to have a common modulation (common drive) from the central nervous system to motor units in a motor neuron pool to execute this strategy.

### *De Luca and Erim (De Luca & Erim, 2002)*

The purpose of this study was to examine the possible interaction of motor units from a pair of synergists (extensor carpi radialis longus (ECRL) and extensor carpi ulnaris (ECU)) during wrist extensions. Intramuscular EMG signals from the trapezoid submaximal isometric contractions (20-30% MVC) were decomposed into motor unit action potentials (MUAPs). To quantify common drive, correlations between the firing rate fluctuations of paired active motor units were examined. Based on the results, common drive exists between motor units from two synergists. Therefore, it was suggested by the authors that the central nervous system (CNS) considers the synergists as a functional unit.

### *De Luca et al. (De Luca et al., 2006)*

This technical paper is a milestone of surface EMG decomposition technique. The authors described an early version of surface EMG decomposition technique. Back in 2006, the accuracy of this algorithm was 75 to 91%, which was not considered high based on today's perspective. In addition, only up to 6 motor unit action potential trains (MUAPTs) were decomposed according to the authors, which was tremendously low when compared to 30-40 motor units that can be decomposed through today's more advanced surface EMG decomposition. In the paper, the authors also described all the technical details.

### *De Luca and Hostage (De Luca & Hostage, 2010)*

The first study that used surface EMG decomposition technique to examine the relationship between firing rate and recruitment threshold of motor neurons during voluntary isometric contractions. The authors utilized this relationship to examine the motor control strategies in different muscles (the vastus lateralis, the tibialis anterior, and the first dorsal interosseous) at various force levels (20%, 50%, 80%, and 100% of MVC). They found that motor units of these muscles acted similarly (the linear regression lines gradually became flatter) when the subjects gradually generated higher force levels. The results indicated that there was an inverse relationship between the average motor unit firing rate and the recruitment threshold for each muscle at each force level. In addition, it was suggested that "the firing rate versus recruitment threshold line describes an 'operating point' of the motor neuron pool that shifts in response to excitation". This relationship is very important in examining motor control strategy.

*Nawab et al. (Nawab et al., 2010)*

In this technical paper, the authors described some important characteristics and advantages of surface EMG decomposition technique. Specifically, the noninvasive surface EMG decomposition technology developed by De Luca's group (De Luca et al. 2006) allows researchers to decompose up to 40 motor units based on their firings of motor unit action potential trains (MUAPTs) from any levels of specified isometric constant force contractions. In addition, the average accuracy of all the firings of the MUAPTs was 92.5%.

*Beck et al. (Beck et al., 2011a)*

The purpose of this study was to examine the effects an 8-week isometric leg extension resistance training program on the relationship between motor unit firing rate and recruitment threshold. Before and after the training program, 11 untrained men performed strength testing as well as trapezoid submaximal isometric muscle action (80% MVC). Surface EMG signals from the vastus lateralis (VL) were decomposed for analysis. Linear regression analysis was used to examine the relationship between motor unit firing rate and recruitment threshold. Although subjects' leg extension strength significantly improved, the slope coefficient and y-intercept of the linear regression line did not change, which suggested that resistance training did not affect the motor unit firing properties during high intensity submaximal contractions.

*Beck et al. (Beck et al., 2011b)*

The purpose of this study was to examine the effects of an 8-week isometric leg extension resistance training program on force steadiness and common drive for the vastus lateralis (VL) muscle. The data from this study is part of the same experiment from the one that has been described above *(Beck et al., 2011a)*. The training program did not change either force steadiness or common drive to motor units.

*Beck et al. (Beck et al., 2012a)*

The purpose of this study was to examine the effects of a bout of eccentric exercise on common drive. Eleven men performed 6 sets of 10 repetitions of eccentric isokinetic muscle actions of the forearm flexors. Before and after the exercise intervention, they also performed trapezoid isometric muscle actions (50% MVC), during which surface EMG signals were recorded from the biceps brachii muscle. After decomposing the EMG signals to individual motor unit action potential trains (MUAPTs), common drive to motor units was quantified. The results suggested that eccentric exercise does not affect common drive to motor units in the biceps brachii.

*Beck et al. (Beck et al., 2012b)*

The purpose of this study was to examine the effects of fatigue intermuscular common drive to motor units in the vastus lateralis (VL) and vastus medialis (VM) muscles. Fourteen subjects performed ten 10-second MVCs with their knee extensors. Before and after the fatiguing intervention, subjects performed trapezoid submaximal isometric contractions (50% MVC). Surface EMG signals from the vastus lateralis (VL) and vastus medialis (VM) were decomposed into motor unit action potential trains

(MUAPTs). The common drive was quantified for both muscles before and after the fatiguing intervention. The results suggested that fatigue does not affect intermuscular common drive.

*De Luca and Contessa (De Luca & Contessa, 2012)*

This paper proposed a simple model which describes the firing behavior of a set of motor neurons in a pool regulating voluntary isometric contractions: at any time and force level, the firing rate of a recruited motor unit is inversely related to the recruitment threshold of this motor unit. This strategy is efficient and economical for human motor system, as it reduces the fatigue of later-recruited higher force-twitch motor units.

*De Luca and Kline (De Luca & Kline, 2012)*

This is a meta-analysis which examined the influence of the number of muscle spindles on the relationships of the motor unit firing rate and recruitment threshold range (maximal recruitment threshold). Muscles with a relatively larger number of spindles tend to maintain consistently smaller firing rate increments, but with a relatively broader recruitment threshold range. In contrast, muscles with a relatively smaller number of spindles tend to have large increments in firing rates, but with a relatively narrower recruitment threshold range.

*Stock et al. (Stock et al., 2012)*

This study examined the acute effects of fatiguing exercise on the relationship between motor unit firing rate and recruitment threshold. The data from this study is part of the same experiment from the one that has been described earlier (*Beck et al. 2012 International Journal of Neuroscience*). Linear regression analyses showed that the slope and y-intercept of the VL significant increased and decreased, respectively. However, these variables did not alter for the VM. The data suggested that higher threshold motor units were recruited for the compensation of force deficit for the VL. In addition, the VM may be slightly more resistant to fatigue, which was the reason why the relationship did not change.

### *Zaheer et al. (Zaheer et al., 2012)*

In this technical paper, the authors investigated the influences of factors such as the sensor placement and skinfold thickness on the number of identified motor unit action potential trains (MUAPTs) in biceps brachii, vastus lateralis, rectus femoris, hamstrings, gastrocnemius, soleus, and tibialis anterior muscles. To summarize, the preferred sensor placement should be located between the center and tendious areas of the muscle. The signal-to-noise ratio of the detected surface EMG positively affects the motor unit yield. In addition, the authors recommended 3 as a minimal requirement of signal-to-noise ratio for obtaining a reliable motor unit yield.

### *Hu et al. (Hu et al., 2013b)*

The purpose of this study was to use the surface EMG decomposition technique (De Luca et al. 2006; Nawab et al. 2010) to examine Henneman’s Size Principle in a large pool of motor units during a single voluntary contraction task. The authors also examined the relationship between motor unit firing rates as a function of motor unit action potential (MUAP) size during a steady-state isometric force task. The size/amplitude of the MUAP was extracted from the recorded surface EMG signals using spike-triggered averaging (STA) template estimation method. In addition, the MUAP estimates derived from STA method were compared with the ones derived from surface EMG decomposition method. Consistent with “Size Principle”, the results showed that a pool of simultaneously recorded motor unis increased in an orderly fashion with increasing recruitment force. In addition, firing rate of smaller units was generally higher than that of the larger units, which was in agreement with the “onion-skin” property.

### *Hu et al. (Hu et al., 2013a)*

The purpose of this study was to use the spike triggered averaging (STA) analysis to assess the validity of surface EMG decomposition technique developed by De Luca et al. (2006). This study is important for the validity of surface EMG decomposition, as it was from an independent group other than De Luca and his colleagues. Based on the results the authors provided, the surface EMG decomposition algorithms developed by De Luca et al. (2006) are valid.

### *Herda and Cooper (Herda & Cooper, 2014)*

This case study examined motor unit control properties of the vastus lateralis (VL) in 2 healthy and 1 individual who acquired acute poliomyelitis (PO). All subjects performed submaximal isometric trapezoid contraction from 20% to 90% of their MVCs in 10% increments. Surface EMG signals recorded during these contractions were decomposed into individual motor unit action potential trains (MUAPTs). The individual who had PO had significantly lower motor unit recruitment threshold and lower firing rates at recruitment. In addition, the PO patient also had significantly lower peaking motor unit firing rates. When examining the relationship between motor unit recruitment and decruitment, the PO patient also showed different values when compared to healthy subjects, with significant longer duration of motor unit activity during force contractions.

### *Hu et al. (Hu et al., 2014b)*

Although the authors did not use surface EMG decomposition algorithm, this simulation study compared two different motor unit control paradigms during force generation: the “onion-skin” paradigm (lower threshold motor units have higher firing rates than those of higher threshold motor units), and the reverse “onion-skin” paradigm. Based on the simulation results, the authors suggested that the “onion-skin” paradigm is beneficial at different levels of voluntary force generation.

### *Hu et al. (Hu et al., 2014a)*

The purpose of this study was to assess the accuracy of a surface EMG decomposition algorithm (developed by De Luca et al. (2006)) during low levels of muscle contraction in first dorsal interosseous (FDI) muscle. This study confirmed that the accuracy of this decomposition algorithm is generally high, with approximately 95%.

### *Stock and Thompson (Stock & Thompson, 2014)*

The purpose of this study was to examine the effects of 10 weeks of barbell deadlift training on motor unit firing properties for the vastus lateralis (VL) and vastus medialis (VM) muscles during medium level force contraction (50% MVC). Fifteen untrained men were assigned to the training group, and 9 men were assigned to the control group. Before and after training, knee extension strength, force steadiness, as well as the relationship between motor unit firing rate and recruitment threshold was examined. Although the training improved subjects' knee extension strength, the force steadiness and the relationship between motor unit firing rate and recruitment threshold were not altered. These results suggested that strength training does not affect the motor unit firing properties during submaximal contractions, which was in agreement with a paper reviewed earlier (Beck *et al.*, 2011b).

### *Ye et al. (Ye et al., 2014b)*

The authors examined the acute effects of concentric vs. eccentric exercise on force steadiness and common drive from the central nervous system (CNS) to motor neuron pool. Seventeen resistance-trained men performed 6 sets of 10 repetitions of maximal concentric or eccentric exercise with their forearm flexors on separate visits. Before and after the exercise interventions, subjects performed submaximal trapezoid isometric contractions (40% MVC). Force steadiness and common drive were quantified in the flat area of the trapezoid contractions. Although force losses following both exercise interventions were similar, eccentric exercise intervention induced greater force fluctuations. Accompanied with the deteriorated force fluctuations was the increased common drive to motor units following the eccentric exercise, but not after the concentric exercise. Therefore, the increased common drive following the eccentric exercise played an important role influencing the force steadiness.

### *De Luca and Contessa (De Luca & Contessa, 2015)*

This is a continuation from the work of De Luca and Contessa (2012). The purpose of this study was to prove that the “onion-skin” scheme is more advantageous than the “after-hyperpolarization (AHP)” scheme (note: unlike the “onion-skin” scheme, AHP scheme generally suggests that high-threshold motor neurons have greater firing rates than low-threshold ones, which favors the maximization of muscle force). Using a mathematical model, the authors examined the firing rate characteristics of motor units as a function of increasing input excitation to the motor neuron pool of the first dossal interosseous (FDI) and vastus lateralis (VL) muscles. The results suggested that the “onion-skin” scheme allows generating force more quickly and more smoothly. Although this scheme does not favor the maximization of muscle force, it balances a combination of force and duration, which is more important in evolutionary survival.

### *Herda et al. (Herda et al., 2015)*

The purpose of this study was to examine motor control properties of resistance-trained (RT) vs. endurance-trained (ET) individuals. Five RT and five ET performed submaximal trapezoid isometric muscle actions at 40% and 70% of their leg extension MVCs. Surface EMG from the vastus lateralis muscles were decomposed into motor unit action potential trains (MUAPTs). The relationship between motor unit recruitment and decruitment, as well as the relationship between motor unit firing rate and recruitment were examined via linear regression analyses. The y-intercepts of the relationship between motor unit recruitment threshold and firing rate for the ET were greater than the RT in both contraction intensities. In addition, the slopes of the relationship between motor unit recruitment threshold and decruitment threshold for the RT were greater than the ET in both contraction intensities. These results suggested the training-related differences in the motor control strategies of the vastus lateralis between the RT and ET.

*Ye et al. (Ye et al., 2015a)*

The author used the relationship between motor unit firing rate and recruitment threshold to examine motor control strategies following different dynamic exercises (concentric vs. eccentric). Fifteen men who were not accustomed to eccentric exercise performed 6 sets of 10 repetitions of maximal concentric or eccentric exercise in a dynamometer in two separate visits. Between and after the exercise intervention, surface EMG decomposition technique was used to decompose EMG signals from the trapezoid submaximal (40% MVC) isometric contractions. Linear regression analysis was used to examine the relationship between motor unit firing rate and recruitment threshold. There were no significant changes in linear regression slope coefficient and y-intercept following the concentric exercise. But the mean slope coefficient and y-intercept significantly decreased and increased, respectively. These results suggested that after eccentric exercise, fast-twitch muscle fibers are likely to be damaged, which potentially alters the motor control strategy: increasing the firing rate of low-threshold motor units may be more important than recruiting high-threshold motor units to compensate for the exercise-induced force deficit.

### *Summary*

The basic motor control strategies during voluntary isometric contractions were summarized in De Luca (1982a; b) and De Luca (1985). In general, the interaction between the recruitment of new motor units and the adjustment of motor unit firing rate can be best described as the “onion-skin” phenomenon: during isometric contractions, the firing rates of earlier recruited motor units are greater than those of later recruited motor units. Therefore, this phenomenon can be examined by performing the linear regression analysis for the relationship between motor unit firing rate and recruitment threshold. In fact, this relationship indicates an “operating point” of the examined motor neuron pool, which is one of the dependent variables of this study.

The central nervous system (CNS) does not regulates motor unit firings individually, but as a fashion of sending a common modulation to the active motor units. Such strategy relieves the burden of the nervous system. It also explains why force production always fluctuates during voluntary contractions. Therefore, as another important dependent variable, changes in common drive serves as a good candidate to explaining the possible changes in force fluctuations under certain conditions.

With the development of a novel surface EMG decomposition algorithm (De Luca *et al.*, 2006; Nawab *et al.*, 2010), examining large number of concurrently active motor units from a motor neuron pool is possible. This algorithm has been proved to be valid and accurate by independent researchers (Hu *et al.*, 2013a, 2014a). Therefore, using this surface decomposition algorithm becomes a promising means to examine motor unit control properties under certain interventions.

# Chapter 3. Methods

## 3.1. Subjects

Eighteen subjects participated in this investigation. Prior to any experimental testing, each subject completed an informed consent and a pre-exercise health and exercise status questionnaire, which indicated no current or recent neuromuscular or musculoskeletal disorders. All experimental procedures for this investigation were approved by the University of Oklahoma Institutional Review Board (No. 5820) for the Protection of Human Subjects.

## 3.2. Research Design

This study used a within-subjects repeated-measures design. Five separate visits to the laboratory was required to complete this investigation. Between consecutive visits, a minimum of 48 hours of rest was provided. Figure 1 describes the design of this investigation. The first visit was the familiarization visit, during which the subjects were familiarized with the testing procedures. The next four visits (Visits 2-5) were conducted in a randomized fashion as follows: Fatiguing unilateral upper body limb muscle (right forearm flexors)-Testing contralateral homologous muscle (left forearm flexors) Visit (Arm-Arm Visit); Fatiguing unilateral upper body limb muscle (right forearm flexors)-Testing unrelated lower body heterogonous muscle (left leg extensors) Visit (Arm-Leg Visit); Fatiguing unilateral lower body limb muscle (right leg extensors)-Testing contralateral homologous (left leg extensors) Visit (Leg-Leg Visit); and Fatiguing unilateral lower body limb muscle (right leg extensors)-Testing unrelated upper body heterogonous muscle (left forearm flexors) Visit (Leg-Arm Visit). In this particular study, the fatiguing interventions were always performed at the right side of the subjects' limbs, and the testing was always performed at the left side of the subjects' limbs.

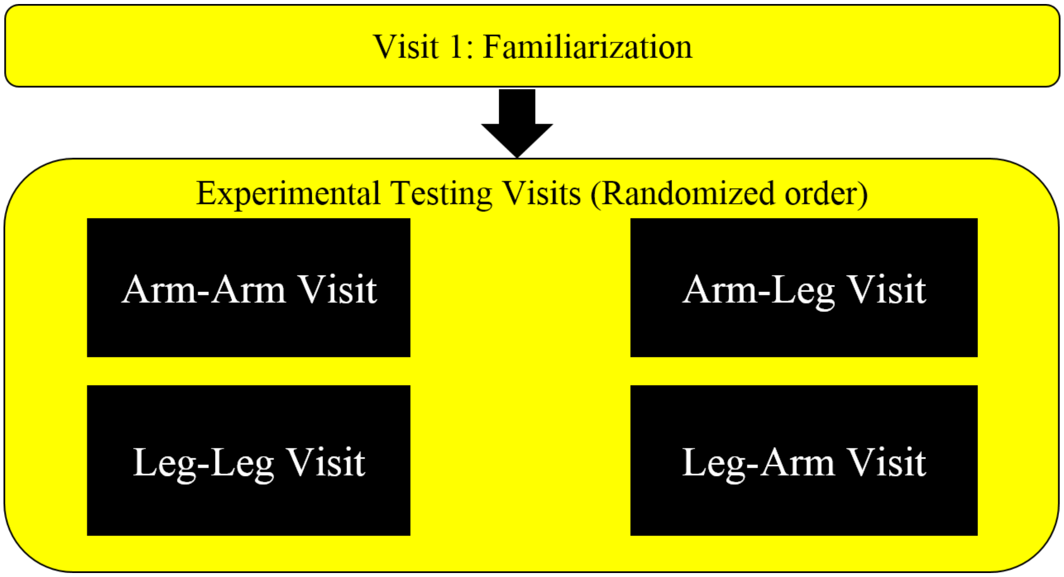

**Figure 1. Experimental Design of the Investigation**

## 3.3. Experimental Procedures

### *Familiarization Visit*

Prior to the four experimental testing visits, the subjects came to the laboratory and participated in a familiarization session. The purpose of this visit is to familiarize the subjects with all the experimental procedures, as well as to minimize the influence of a learning effect on each dependent variable.

Upon arrival, each subject was first instructed to sit in front of a custom-built table designed for isometric testing of the forearm flexors. The investigator then positioned the elbow of the subject's left arm into a U-shaped pad and put the wrist through a padded cuff that is connected to a load cell (Model SSM-AJ-500; Interface, Scottsdale, AZ) (Figure 2). Adjustments for seat height and the length of the cuff around the wrist were made to ensure that the subject's arm and forearm are at a 90° elbow joint angle. The investigators then recorded the seat height and the length of the cuff to make sure the subject would have the same position for testing during the experimental testing visits. With the palm supinated, the subjects were told to perform several submaximal isometric forearm flexion muscle actions for the purpose of a warm-up. Then they performed three 5-s isometric MVCs for the measurement of the isometric strength of their forearm flexors. With a 1-minute rest following the isometric strength testing, the subjects then practiced several submaximal trapezoid isometric elbow flexion muscle actions where they increased the force output linearly from 0% to 50% of the pre-determined MVC in 5 seconds, held the force output constant at 50% MVC for 10 seconds, and then gradually decreased the force output to 0 % MVC in 5 seconds. The subjects were provided with a visual template of their force production during these submaximal trapezoid muscle actions, and they practiced this type of contraction several times until they are able to trace the force profile smoothly and comfortably (Figure 3). Following the 50% MVC practice, the subjects were required to practice another submaximal trapezoid isometric muscle action with a different contraction intensity-80% MVC. The practice was similar to the 50% MVC submaximal trapezoid contraction, but with the subjects gradually increasing the force output linearly from 0% to 80% of the pre-determined MVC in 8 seconds, holding the force output constant at 80% MVC for 8 seconds, and then gradually decreasing the force output to 0 % MVC in 8 seconds. After a 1-minute rest period, the subjects were asked to perform a 30-s isometric MVC on their right arm for the purpose of practicing the elbow flexion fatiguing protocol. Five minutes of rest following the procedures stated above, subjects were asked to repeat the isometric MVCs, as well as the submaximal trapezoidal isometric contractions at 50% and 80% of the previously established MVC on their left forearm flexors.

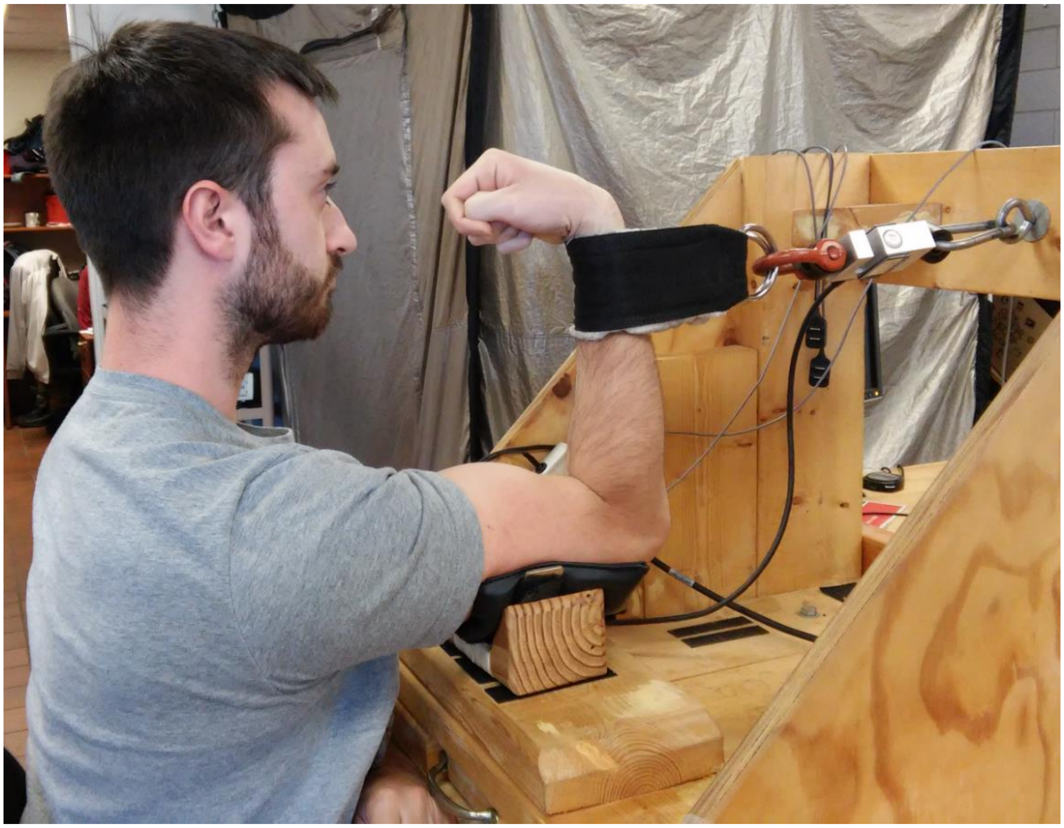

**Figure 2. A Subject Performing Isometric Forearm Flexion Exercise**

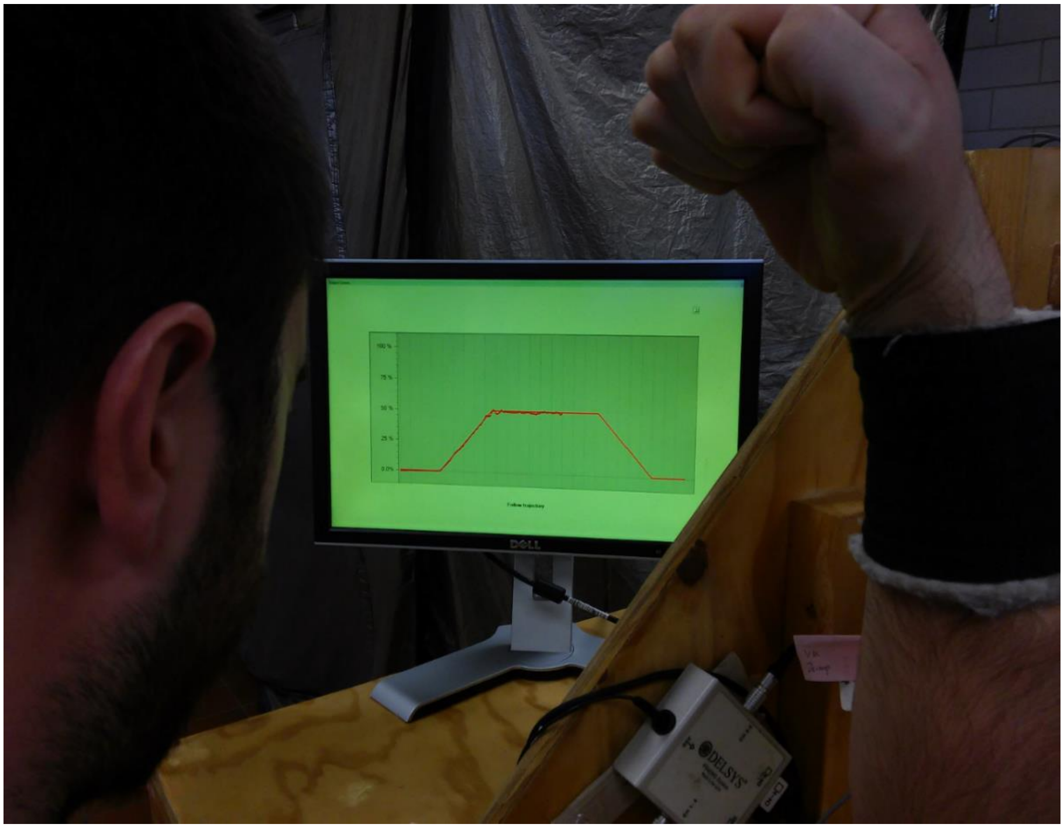

**Figure 3. A Subject Performing Submaximal Trapezoid Isometric Contraction with Force Profile Presented**

During the same visit, the subjects also practiced all the isometric tests on their knee extensors. Specifically, they sat on a lower body isometric strength testing apparatus comfortably with the ankle inserted into a padded cuff which is connected to a load cell (Model SSM-AJ-500; Interface, Scottsdale, AZ) (Figure 4). The subjects performed isometric strength testing and practiced the submaximal trapezoidal isometric contractions (50% and 80% MVC) with their left knee extensors. Following the practice of a 30-second isometric MVC on their right leg extensors, the subjects finished the familiarization visit with repeating the isometric MVCs, as well as the submaximal trapezoidal isometric contractions at 50% and 80% of the previously established MVC on their left knee extensors.

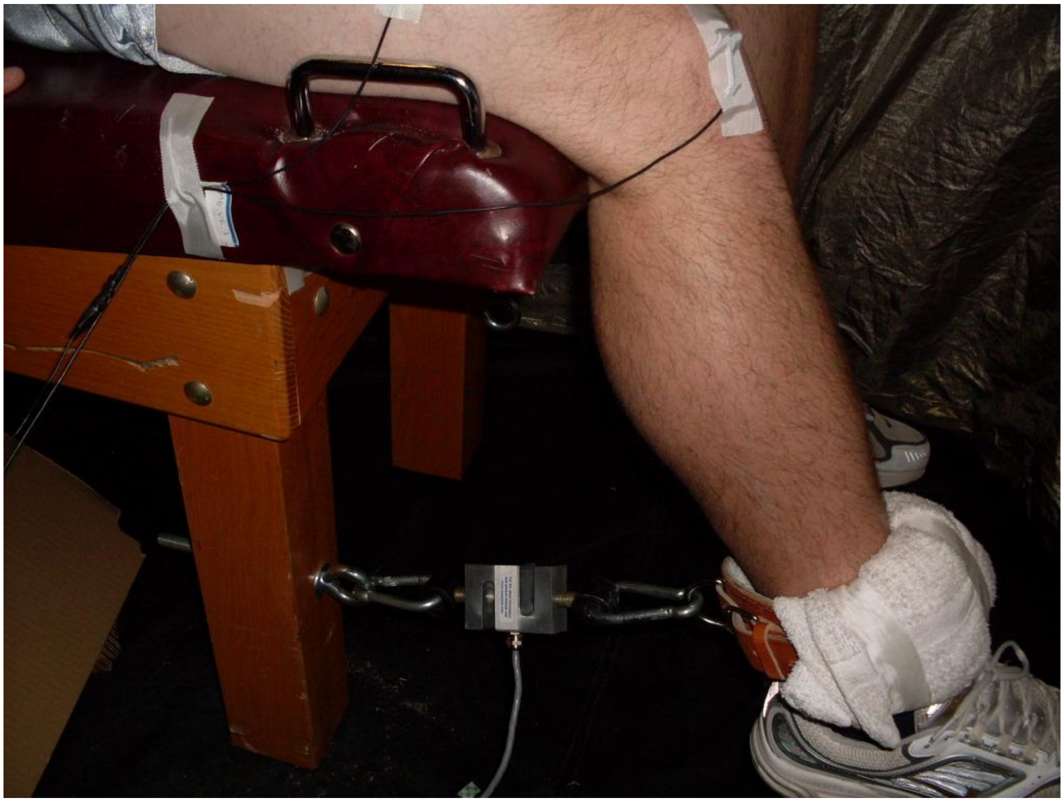

**Figure 4. A Demonstration of Isometric Leg Extension Exercise**

### *Experimental Testing Visits*

After a minimum of 48 hours following the familiarization visit, the subjects returned to the laboratory for one of the four experimental testing sessions. Specifically, following is a summary of the experimental testing procedures of each visit. Figure 5 depicts the experimental procedure during the Arm-Arm Visit.

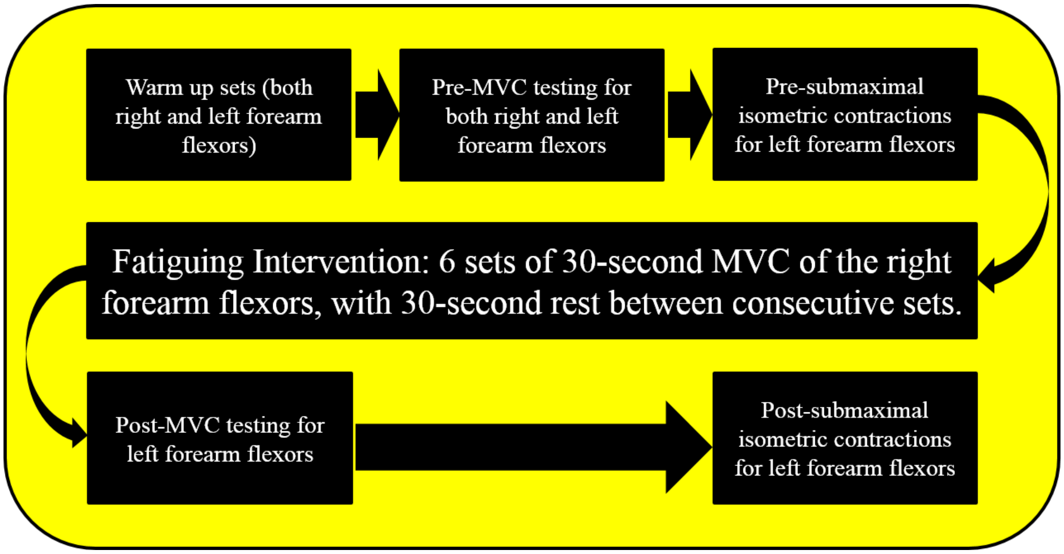

**Figure 5. An Example of Arm-Arm Visit Experimental Procedure**

Arm-Arm Visit (in order):

1. Pre-Testing
    a. Warm up both forearm flexors with approximately 50% of subjects' perceived MVCs
    b. Perform three 5-second MVCs of the right forearm flexors (30-second rest between consecutive MVCs)
    c. Perform three 5-second MVCs of the left forearm flexors (30-second rest between consecutive MVCs)
    d. One minute after, perform two submaximal isometric trapezoidal muscle actions of the left forearm flexors for each contraction intensity (50% and 80% MVC) (30-second rest was provided between two trapezoidal contractions at 50% MVC, and 45-second rest was provided between trapezoidal contractions at 80% MVC)
2. Fatiguing Intervention: Perform 6 sets of 30-second MVC of the right forearm flexors, with 30-second rest between consecutive fatiguing sets
3. Post-Testing
    a. Immediately following the fatiguing intervention, perform two MVCs of the left forearm flexors (30-second rest between consecutive MVCs)
    b. Perform two submaximal isometric trapezoidal muscle actions of the left forearm flexors for each contraction intensity (50% and 80% of the Pre-MVC) (30-second rest was provided between two trapezoidal contractions at 50% MVC, and 45-second rest was provided between trapezoidal contractions at 80% MVC)

Arm-Leg Visit:

The protocol for this visit was identical to Arm-Arm Visit with the only difference being that the left knee extensors were tested instead of the left forearm flexors.

Leg-Leg Visit:

1. Pre-Testing
    a. Warm up both leg extensors with approximately 50% of subjects' perceived MVCs
    b. Perform three 5-second MVCs of the right leg extensors (30-second rest between consecutive MVCs)
    c. One minute after, perform three 5-second MVCs of the left forearm flexors (30-second rest between consecutive MVCs)
    d. One minute after, perform two submaximal isometric trapezoidal muscle actions of the left leg extensors for each contraction intensity (50% and 80% of the Pre-MVC) (30-second rest was provided between two trapezoidal contractions at 50% MVC, and 45-second rest was provided between trapezoidal contractions at 80% MVC)
2. Fatiguing Intervention: Perform 6 sets of 30-second MVC of the right leg extensors, with 30-second rest between consecutive fatiguing sets.
3. Post-Testing

a. Immediately following the fatiguing intervention, subjects performed two 5-second MVCs of the left leg extensors (30-second rest between consecutive MVCs).
b. One minute after, perform two submaximal isometric trapezoidal muscle actions of the left leg extensors for each contraction intensity (50% and 80% of the Pre-MVC) (30-second rest was provided between two trapezoidal contractions at 50% MVC, and 45-second rest was provided between trapezoidal contractions at 80% MVC)

Leg-Arm Visit:

The protocol for this visit was identical to Leg-Leg Visit with the only difference being that the left forearm flexors were tested instead of the left leg extensors.

### 3.4. Measurements

#### *Force Measurements*

During both Pre- and Post-isometric strength testing in all four experimental testing visits, force was detected by the tension applied to the load cell (Model SSM-AJ-500; Interface, Scottsdale, AZ). The force signal was digitized with a 12-bit analog-to-digital converter (National Instruments, Austin, TX) and stored in a personal computer (Dell Optiplex 755, Round Rock, TX) for further analyses. For each force signal, the maximal force output was selected from the highest one-second portion of the five-second isometric MVC.

### *Surface EMG Signal Recording*

Different surface EMG sensors were placed on the primary muscles of the subjects' testing limbs. One of the sensors on the muscle was a bipolar electrode (DE 2.1 Single Differential Surface EMG Sensor, Delsys, Inc., Natick, MA; 10 mm interelectrode distance). This sensor recorded EMG signals during all PRE- and POST-testing MVCs, as well as the submaximal trapezoidal isometric contractions. The other sensor was a specialized 5-pin surface array (dEMG sensor, Delsys, Inc., Natick, MA), which is designed for the motor unit decomposition. This special sensor array consists of five cylindrical probes (0.5-mm diameter), which are located at the center and the corners of a 5 × 5-mm square (Figure 6). Four separate bipolar EMG signals were detected by the pairwise differentiation of the five electrodes. This sensor only recorded EMG signals during the submaximal trapezoidal isometric contractions. Both sensors were placed on the left biceps brachii during the Arm-Arm Visit and Leg-Arm Visit, and on the left vastus lateralis and left vastus medialis during the Arm-Leg Visit and Leg-Leg Visit, according to the electrode placement recommendations from the SENIAM project. Sensors locations were traced with a permanent marker to assure consistent placement between visits. A reference electrode (5.08 cm diameter Dermatrode HE-R, American Imex, Irvine, CA) was placed over the 7th cervical vertebrae (C7) during data collection. Prior to detecting any EMG signals, all skin sites were shaved with a razor and cleansed with rubbing alcohol. In addition, all the surface EMG sensors were firmly secured to the skin with adhesive tape.

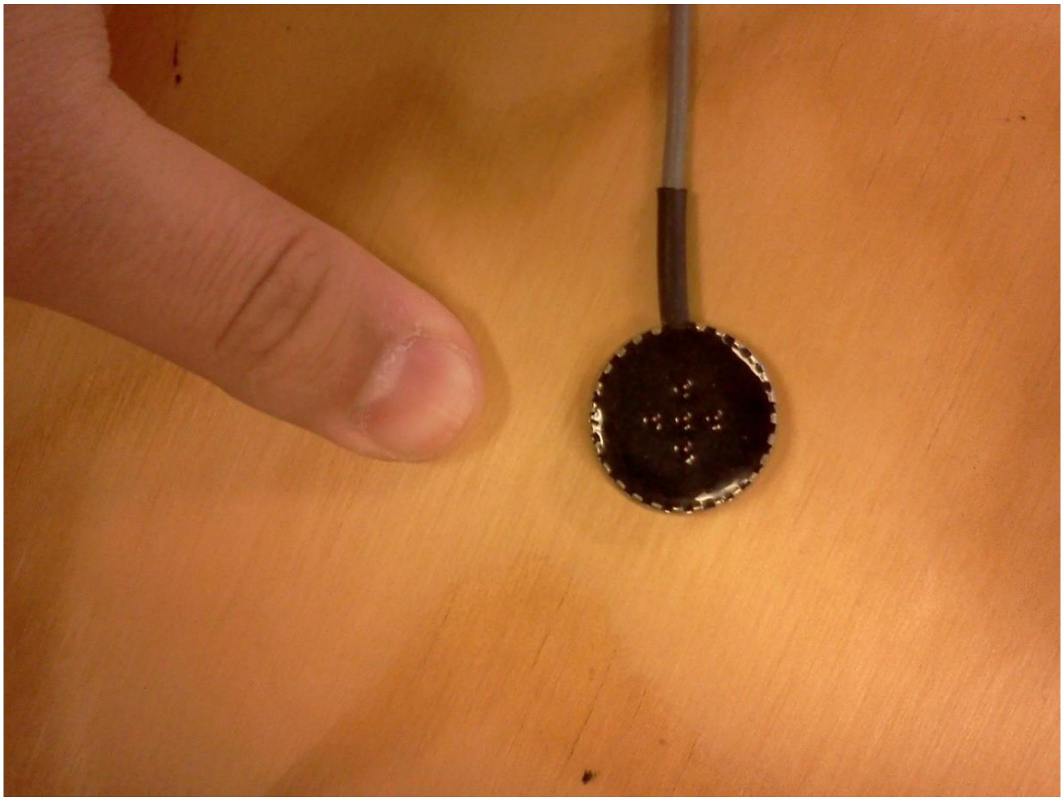

**Figure 6. The 5 x 5-mm Decomposition EMG Sensor Next to A Thumb**

### *Surface EMG Signal Processing and Decomposition*

The analog EMG signals were collected with a modified Bagnoli 16-channel desktop EMG system (Delsys, Inc., Boston, MA). The EMG signals from the bipolar electrodes were preamplified (gain=1000) with the Bagnoli 16-channel EMG system, and filtered with high and low pass filters set at 20 Hz and 450 Hz, respectively. The EMG signals were then digitized at a sampling rate of 20000 samples per second with a 12-bit analog-to-digital converter (National Instruments, Austin, TX) and stored in a personal computer (Dell Optiplex 755, Round Rock, TX) for subsequent analyses. Specifically, the amplitude (root-mean-square (RMS)) and the mean frequency (MNF) of each recorded EMG signal were calculated, and then normalized as a percentage of the values obtained during that muscle's MVC.

The EMG signals from the 5-pin sensor were analog high-pass filtered (cutoff frequency = 100 Hz), low-pass filtered (cutoff frequency = 9500 Hz), and sampled at 20000 Hz. The EMG signals were then digitally band-pass filtered (8th -order Butterworth; cut-offs of 250 and 2000 Hz) prior to decomposition.

After acquisition, the four separate filtered bipolar EMG signals were decomposed into the constituent motor unit action potential trains (MUAPTs) by the Precision Decomposition III algorithm (EMGWorks 4.0 Analysis, Delsys, Inc., Boston, MA) (De Luca *et al.*, 2006; Nawab *et al.*, 2010). Using the same algorithm, the shape of each action potential was identified and assigned to the individual motor units. When all the motor units are decomposed, the accuracy test was performed by using the Decompose-Synthesize-Decompose-Compare (DSDC) test described by Nawab et al.

(2010). In this study, only motor units that can be decomposed with > 90% accuracy were included for data analysis.

## 3.5. Data Analyses

### *Force Steadiness*

Force steadiness is quantified by calculating the force fluctuations: the coefficient of variation (CV = standard deviation ÷ mean × 100%) of the force output from the mid 6-second portion (middle flat portion of the force output during 50% or 80% MVC) of each submaximal trapezoid isometric muscle action.

### *The Relationship between Motor Unit Recruitment Threshold and Mean Firing Rate*

After the decomposition of motor units from the EMG signals, the firing rates of each motor unit were plotted as a function of time and smoothed with a 2-second Hanning window filter (Figure 7). In addition, the recruitment threshold of each detected motor unit was calculated as the percentage of the Pre-MVC. The dEMG Analysis software (Delsys Inc., Natick, MA) was then used to analyze the relationship between motor unit recruitment threshold and mean firing rates. Specifically, this relationship was examined using linear regression analysis. With this analysis, each submaximal trapezoidal isometric contraction yielded a linear regression slope coefficient (% MVC/PPS), as well as a y-intercept (PPS).

### *The Relationship between Motor Unit Recruitment Threshold and Decruitment Threshold*

Using the same dEMG Analysis software (Delsys Inc., Natick, MA), linear regression analysis was used again to examine the relationship between motor unit recruitment threshold and decruitment threshold. With this analysis, each submaximal trapezoidal isometric contraction will yield a linear regression slope coefficient (% MVC/% MVC), as well as a y-intercept (%MVC).

### *Common Drive from the CNS to the Motor Neuron Pool*

After the decomposition of motor units from the EMG signals, the average firing rates will also be plotted as a function of time and smoothed with a 400-ms Hanning window, which was originally described by De Luca et al. (De Luca *et al.,* 1982b). Common drive was calculated by cross-correlating the plateau regions of the mean firing rate curves between concurrently active motor units (Beck *et al.,* 2011b; 2012a; Ye *et al.,* 2014b). Extra care was taken to ensure that the plateau regions of the mean firing rate curves selected for common drive calculation exactly match the regions that are selected for calculating the force steadiness. In this study, all possible combinations of motor units were cross-correlated with one another. For example, if 20 motor units are decomposed from one trapezoid isometric muscle action, then 190 (20 × 19 ÷ 2) separate cross-correlations will be performed, thereby generating 190 peak cross-correlation coefficients ($0 < r < 1.0$).

The common drive was then examined based on the distributions of the peak cross-correlation coefficients. To better visualize the distributions, total numbers of occurrence for peak cross-correlation coefficients at different ranges ($r = 0.0$-$0.2$, 0.2-0.4, and 0.4-0.7) was counted. However, since a different number of motor units were detected during different trapezoid isometric muscle actions, the total pairs of cross-correlations were also different. Thus, to compare the common drive between different fatiguing interventions and between different time points, we normalized the occurrence frequency for peak cross-correlation coefficients (normalized occurrence frequency for peak cross-correlation coefficients = number of occurrence for peak cross-correlation coefficients at the specific range ÷ total number of peak cross-correlation coefficients × 100%) (Ye *et al.*, 2014b). For example, if 100 out of 400 peak cross-correlation coefficients fall into the 0.3-0.5 range, then the normalized occurrence frequency for peak cross-correlation coefficients corresponding to the 0.3-0.5 range would be 25%.

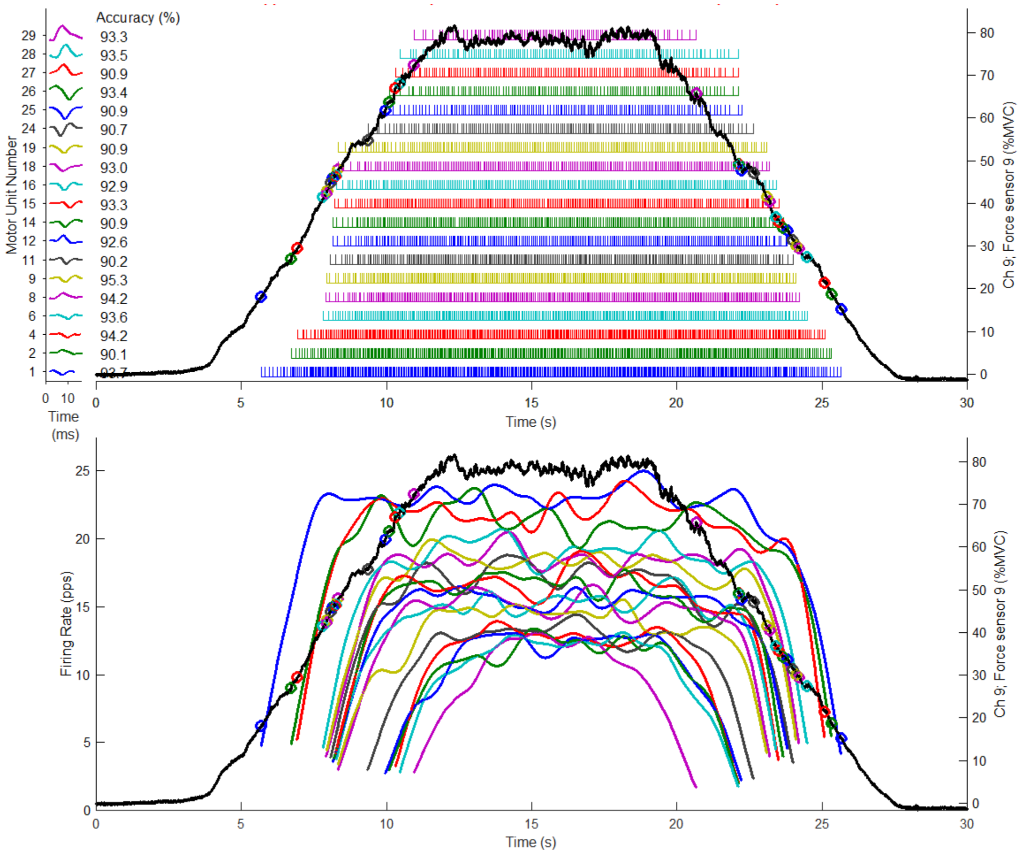

**Figure 7. An Example of Motor Unit Decomposition Output**

### 3.6. Statistical Analyses

Separate 2-way (time [Pre vs. Post] × condition [Arm-Arm vs. Leg-Arm]) repeated measures analyses of variance (ANOVAs) were performed to examine the effects of fatiguing different muscles on the isometric strength as well as the normalized EMG parameters (amplitude and MNF) of the non-exercised left forearm flexors during the isometric strength testing. In addition, the same statistical analyses were also applied to Arm-Leg and Leg-Leg visits to examine the effects of fatiguing different muscles on the isometric strength as well as the normalized EMG parameters (amplitude and MNF) of the non-exercised left leg extensors.

To analyze dependent variables (the force steadiness, the normalized EMG amplitude, the normalized EMG mean frequency, the linear regression slope coefficient for the relationship between mean motor unit firing rate (MFR) and recruitment threshold, as well as the y-intercept for the relationship between mean motor unit firing rate (MFR) and recruitment threshold) during the mid-portion of the submaximal trapezoid isometric contraction, separate 3-way (time [PRE vs. POST] × contraction intensity [50% vs. 80% MVC] × condition [Arm-Arm vs. Leg-Arm]) repeated ANOVAs were performed. Similarly, same statistical analyses were applied to Arm-Leg and Leg-Leg visits. When appropriate, follow-up analyses included 2-way repeated measures ANOVAs as well as paired samples t-tests. All statistical tests were conducted using statistical software (IBM SPSS Statistics 19.0, IBM, Armonk, NY) with alpha set at 0.05. Effect size (ES) were calculated using Cohen’s d to examine the magnitude of treatment effects (time, condition, and contraction intensity) when necessary.

# Chapter 4. Results

## 4.1. Descriptives

Eighteen subjects participated in this study. One of the subjects dropped out of the program after the second visit of the investigation. Therefore, the data for the rest 17 subjects was used for statistical analyses. Of these 17 subjects, 12 were males (mean ± SD: age = 26.1 ± 3.9 yrs, height = 177.5 ± 5.9 cm, weight = 85.7 ± 12.6 kg) and 5 were females (mean ± SD: age = 27.6 ± 1.7 yrs, height = 154.6 ± 4.2 cm, weight = 58.4 ± 11.2 kg). Sixteen of the participants completed all 5 visits, and one performed 3 of the 5 total visits due to a knee injury.

## 4.2. Isometric Strength

*Reliability*

The maximal isometric strength values for the left forearm flexors among three visits (Familiarization vs. Arm-Arm vs. Leg-Arm) were reliable, with r = 0.76 for the intraclass correlation coefficient model (3, 1) ($ICC_{3,1}$) (Weir, 2005). In addition, the isometric strength values were not significantly different among three visits ($p = 0.235$). The maximal isometric strength values for the left knee extensors among three visits (Familiarization vs. Arm-Leg vs. Leg-Leg) were also reliable, with the $ICC_{3,1} = 0.96$. In addition, the isometric strength values were not significantly different among three visits ($p = 0.442$).

### *Non-exercised Forearm Flexors (Left)*

Figure 8 shows the percent changes of isometric strength in each individual subject. The results from the 2-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm]) mixed factorial ANOVA indicated that there was no significant time × condition interaction. However, there was a main effect for time. When collapsed across the condition, the follow-up paired-samples t-test showed that after the fatiguing interventions, the isometric strength of the left forearm flexor significantly decreased (mean ± SE: Pre vs. Post = 392.098 ± 31.811 vs. 368.103 ± 30.145 N, $p = 0.002$).

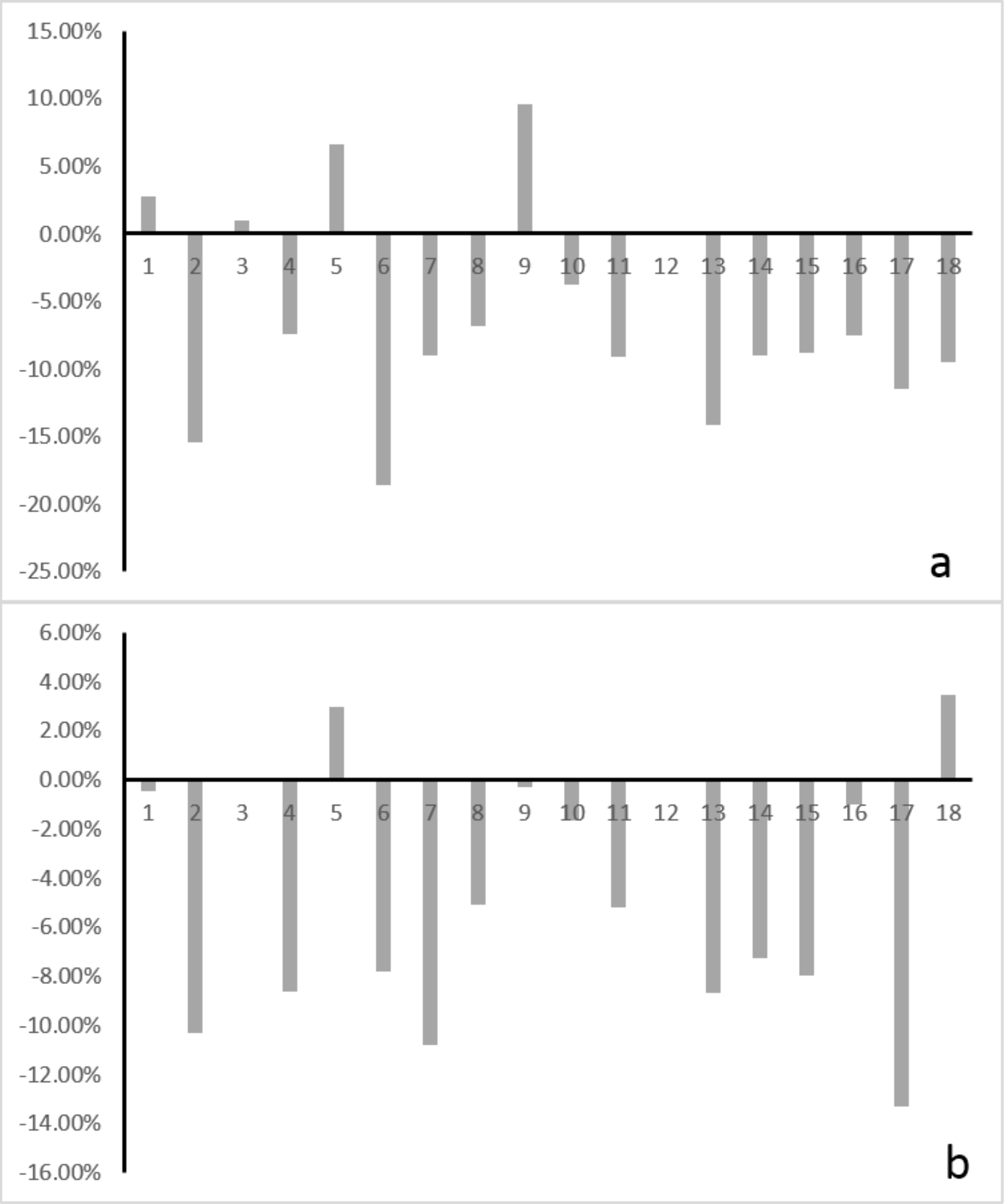

**Figure 8. Individual Responses of Non-Exercised Forearm Flexor Isometric Strength**

### *Non-exercised Leg Extensors (Left)*

Figure 9 shows the percent changes of isometric strength in each individual subject. The results from the 2-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg]) mixed factorial ANOVA indicated that there were no significant time × condition interaction as well as the main effects for both time and condition.

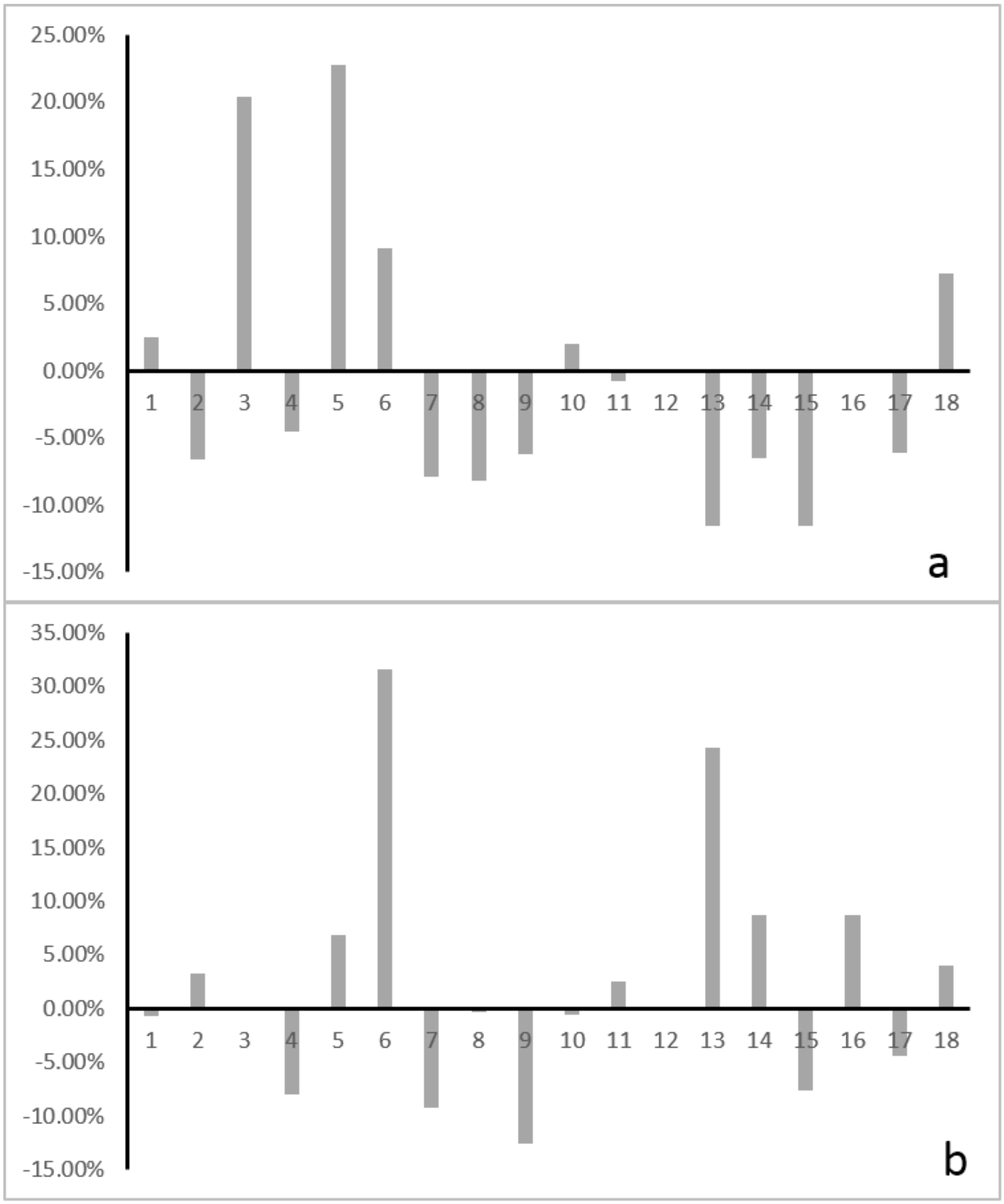

**Figure 9. Individual Responses of Non-Exercised Leg Extensor Isometric Strength**

To further look into the NLMF effects in terms of isometric strength performance, we calculated the effect sizes of isometric strength changes during all four experimental testing visits (Table 1).

**Table 1. The Effect Sizes (Cohen's *d*) For the Changes of Isometric Strength**

95% CI around mean difference and effect size (Cohen's *d*) values of the isometric strength before (Pre) and after (Post) the fatiguing interventions. *

| 95% CI (mean ± 1.96 SD) | Cohen's *d* | Magnitude of effect |
|---|---|---|
| Isometric Strength (N) | | |
| (Arm-Arm) Pre vs. Post: -24.98 ± 58.28 | 0.20 | Small |
| (Leg-Arm) Pre vs. Post: -21.17 ± 59.78 | 0.16 | Small |
| (Arm-Leg) Pre vs. Post: -8.14 ± 132.55 | 0.03 | Trivial |
| (Leg-Leg) Pre vs. Post: 10.69 ± 122.27 | 0.04 | Trivial |

* CI = confidence interval; SD = standard deviation; Pre = before exercise intervention; Post = after exercise intervention.

### 4.3. Force Steadiness

*Non-exercised Forearm Flexors (Left)*

The results from the 3-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm] × intensity [50% vs. 80%MVC] mixed factorial ANOVA indicated that there were no 3-way or 2-way interactions. However, there was a main effect for time (F = 5.670, p = 0.005, $\eta^2 = 0.42$). When collapsed across the contraction intensity and the condition, the follow-up test included a paired-samples t-tests for comparing the CV of the force output before and after the fatiguing interventions. Based on the result, the force fluctuations significantly went up following the fatiguing intervention (mean ± SE: Pre vs. Post = 2.060 ± 0.128% vs. 2.39 ± 0.153%, p = 0.005; Figure 10).

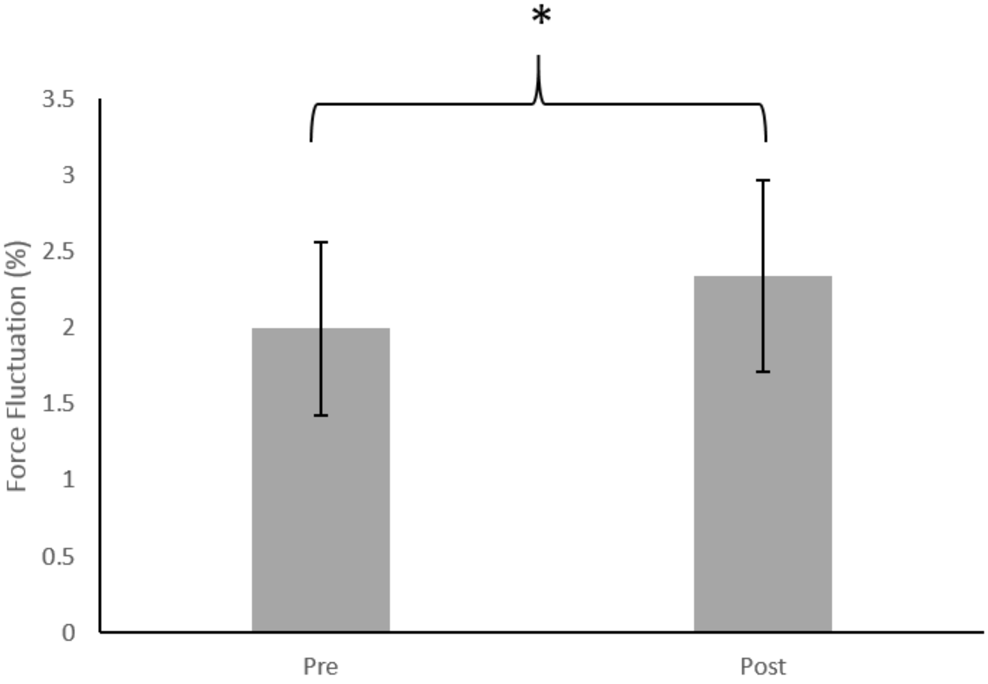

**Figure 10. Average Force Fluctuation of Non-Exercise Forearm Flexors**

*Non-exercised Leg Extensors (Left)*

The results from the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] mixed factorial ANOVA indicated that there were no 3-way interaction, 2-way interactions, as well as main effects.

## 4.4. Normalized EMG Amplitude

*Non-exercised Forearm Flexor (Biceps Brachii) (Left)*

The results from the 2-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm]) repeated measures ANOVA indicated that there was no significant 2-way interaction as well as main effects for the normalized EMG amplitude during the isometric MVC before and after 2 different fatiguing interventions.

For the normalized EMG amplitude during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, however, there was a main effect for intensity ($F = 89.496$, $p < 0.001$, $\eta^2 = 0.844$).

*Non-exercised Leg Extensors (Left Vastus Lateralis (VL))*

The results from the 2-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg]) repeated measures ANOVA indicated that there was no significant 2-way interaction as well as main effects for the normalized EMG amplitude during the isometric MVC before and after 2 different fatiguing interventions.

For the normalized EMG amplitude during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there was no significant 3-way interaction, 2-way interactions, however, there was a main effect for intensity (F = 208.983, $p < 0.001$, $\eta^2 = 0.933$).

*Non-exercised Leg Extensors (Left Vastus Medialis (VM))*

The results from the 2-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg]) repeated measures ANOVA indicated that there was no significant 2-way interaction as well as main effects for the normalized EMG amplitude during the isometric MVC before and after 2 different fatiguing interventions.

For the normalized EMG amplitude during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Control vs. Arm-Leg vs. Leg-Leg] × intensity [50%MVC vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, however, there was a main effect for intensity (F = 195.107, $p < 0.001$, $\eta^2 = 0.929$).

### 4.5. Normalized EMG Mean Frequency (MNF)

*Non-exercised Forearm Flexor (Biceps Brachii) (Left)*

The results from the 2-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm]) repeated measures ANOVA indicated that there were no significant 2-way interaction as well as main effects for the normalized EMG MNF during the isometric MVC before and after 2 different fatiguing interventions.

For the normalized EMG MNF during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, however, there was a main effect for intensity (F = 10.822, p = 0.005, $\eta^2 = 0.419$).

*Non-exercised Leg Extensors (Left Vastus Lateralis (VL))*

The results from the 2-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg]) repeated measures ANOVA indicated that there was no significant 2-way interaction, however, there was a main effect for time. When collapsed across the condition, the follow-up test showed that the normalized EMG MNF for the VL muscle significantly increased following fatiguing interventions (mean ± SD: Pre vs. Post = 100 ± 0% vs. 106.4 ± 2.4%, p = 0.017; Figure 11a).

For the normalized EMG MNF during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, as well as main effects.

*Non-exercised Leg Extensors (Left Vastus Medialis (VM))*

The results from the 2-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg]) repeated measures ANOVA indicated that there was no significant 2-way interaction, however, there was a main effect for time. When collapsed across the condition, the follow-up test showed that the normalized EMG MNF for the VM muscle significantly increased following fatiguing interventions (mean ± SD: Pre vs. Post = 100 ± 0% vs. 104.7 ± 2.0%, p = 0.030; Figure 11b).

For the normalized EMG MNF during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, as well as main effects.

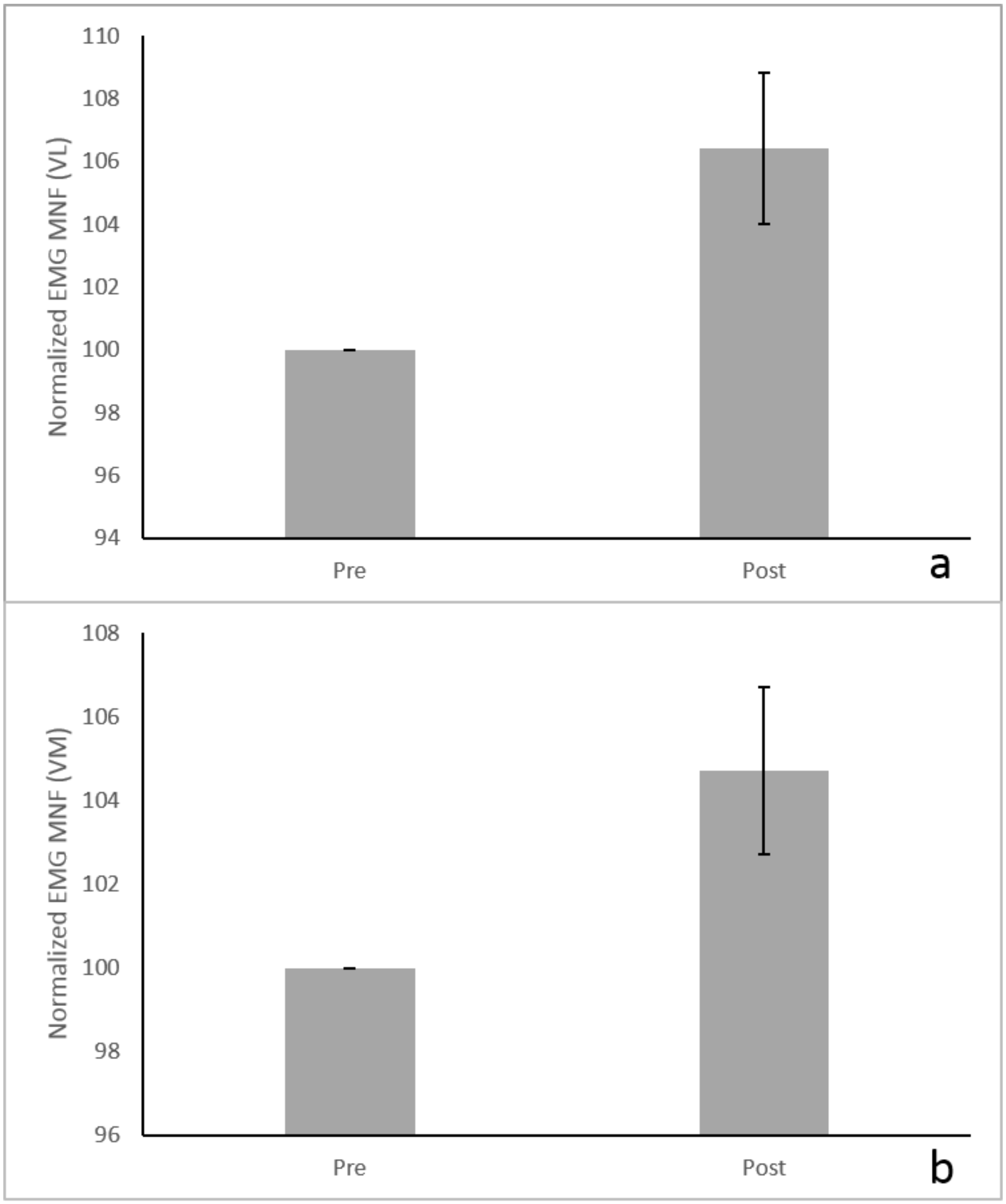

**Figure 11. Average Normalized EMG Mean Frequency Responses of Non-Exercised Leg Extensors**

## 4.6. Motor Unit Firing Behavior

### *The Relationship between Motor Unit Recruitment Threshold and Mean Firing Rate*

Figure 12 shows an example of the linear regression lines for the relationship between motor unit recruitment threshold and mean firing rate of the non-exercise biceps brachii muscle before the fatiguing intervention. Tables 2, 3, and 4 list individual responses of the linear slope coefficient and the y-intercepts of the relationship before and after each fatiguing intervention for the biceps brachii, vastus lateralis, and vastus medialis, respectively.

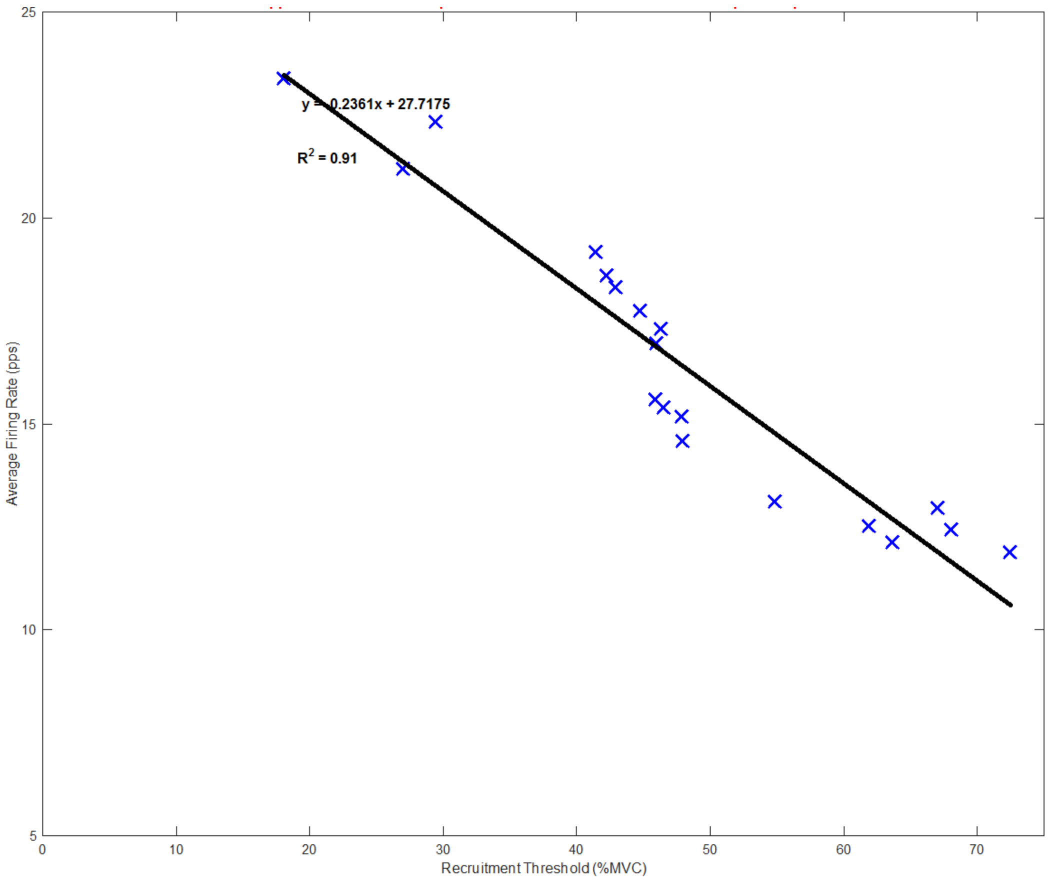

**Figure 12. An Example of the Linear Regression Line of the Relationship between Motor Unit Average Firing Rate and Recruitment Threshold**

### *Non-exercised Forearm Flexor (Biceps Brachii) (Left)*

For the slopes of the linear regression lines of the relationship between motor unit recruitment threshold and mean firing rates during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, as well as main effects.

For the y-intercepts of the linear regression lines, the 3-way (time [PRE vs. POST] × condition [Arm-Arm vs. Leg-Arm] × intensity [50% vs. 80%MVC] repeated measures ANOVA indicated that there were no significant 3-way interaction, 2-way interactions, however, there was a main effect for intensity for bicep brachii muscle ($F = 25.545$, $p < 0.001$, $\eta^2 = 0.630$).

**Table 2. Linear Regression Analysis for the Relationship between Motor Unit Mean Firing Rate and Recruitment Threshold for the Biceps Brachii Muscle***

| | | | Pre-Fatigue | | Post-Fatigue | |
|---|---|---|---|---|---|---|
| Arm-Arm Visit | 50% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.4224 | 28.0298 | -0.4182 | 27.6577 |
| | | SD | 0.1587 | 6.9307 | 0.2138 | 8.7431 |
| | 80% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.4102 | 34.0640 | -0.5745 | 37.8153 |
| | | SD | 0.2129 | 10.5344 | 0.4629 | 14.0338 |
| | | | Pre-Fatigue | | Post-Fatigue | |
| Leg-Arm Visit | 50% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.4622 | 28.6206 | -0.4626 | 27.7935 |
| | | SD | 0.2887 | 10.2824 | 0.2049 | 7.2665 |
| | 80% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.5215 | 36.6651 | -0.4447 | 34.8302 |
| | | SD | 0.2543 | 9.5508 | 0.1579 | 8.7824 |

* Mean and Standard Deviation (SD) of the linear slope coefficients (Slope) (pps/%MVC) and y-intercepts (y-int) (pps) of the linear regression lines for the relationship between motor unit mean firing rate and recruitment threshold (MFR vs. RT) before (Pre) and after (Post) fatiguing interventions for biceps brachii muscle during Arm-Arm Visit and Leg-Arm Visit at 50% and 80% maximal voluntary contraction (MVC) contraction intensities.

### *Non-exercised Leg Extensors (Left Vastus Lateralis (VL))*

For the slopes of the linear regression lines of the relationship between motor unit recruitment threshold and mean firing rates during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there was no significant 3-way interaction, however, there was a 2-way condition by intensity interaction ($F = 6.610$, $p = 0.033$, $\eta^2 = 0.452$). After collapsing across time, the follow-up 2-way ([Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC]) repeated measures ANOVA test indicated that there were main effects for both condition ($F = 17.142$, $p = 0.002$, $\eta^2 = 0.632$) and intensity ($F = 26.117$, $p < 0.001$, $\eta^2 = 0.723$). When collapsed across intensity, the slope of the linear regression line during Arm-Leg Visit was significantly greater (more flat) than that during Leg-Leg visit (mean ± SE: Arm-Leg Visit vs. Leg-Leg Visit = -0.495 ± 0.072 vs. -0.823 ± 0.097, $p = 0.002$). In addition, the slope during the 80% MVC was significantly greater (more flat) than that during the 50% MVC contraction intensity (mean ± SD: 50%MVC vs. 80%MVC = -0.776 ± 0.085 vs. -0.542 ± 0.074, $p < 0.001$).

For the y-intercepts of the linear regression lines, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA indicated that there were no significant 3-way interaction, 2-way interactions, as well as main effects.

**Table 3. Linear Regression Analysis for the Relationship between Motor Unit Mean Firing Rate and Recruitment Threshold for the Vastus Lateralis Muscle***

| | | | Pre-Fatigue | | Post-Fatigue | |
|---|---|---|---|---|---|---|
| Arm-Leg Visit | 50% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.4533 | 27.7442 | -0.4762 | 25.2457 |
| | | SD | 0.1287 | 6.4724 | 0.1889 | 5.1678 |
| | 80% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.3427 | 28.1935 | -0.3207 | 27.6800 |
| | | SD | 0.1988 | 9.3408 | 0.1710 | 9.2465 |
| | | | Pre-Fatigue | | Post-Fatigue | |
| Leg-Leg Visit | 50% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.3835 | 25.9903 | -0.3972 | 26.5018 |
| | | SD | 0.1780 | 6.1212 | 0.1373 | 6.0305 |
| | 80% MVC | | Slope | y-int | Slope | y-int |
| | | Mean | -0.3623 | 30.5916 | -0.3214 | 30.0019 |
| | | SD | 0.2341 | 11.0183 | 0.1374 | 7.5998 |

*Mean and Standard Deviation (SD) of the linear slope coefficients (Slope) (pps/%MVC) and y-intercepts (y-int) (pps) of the linear regression lines for the relationship between motor unit mean firing rate and recruitment threshold (MFR vs. RT) before (Pre) and after (Post) fatiguing interventions for vastus lateralis muscle during Arm-Leg Visit and Leg-Leg Visit at 50% and 80% maximal voluntary contraction (MVC) contraction intensities.

*Non-exercised Leg Extensors (Left Vastus Medialis (VM))*

For the slopes of the linear regression lines of the relationship between motor unit recruitment threshold and mean firing rates during the plateau region of the trapezoidal submaximal contractions, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, as well as main effects.

For the y-intercepts of the linear regression lines, the 3-way (time [PRE vs. POST] × condition [Arm-Leg vs. Leg-Leg] × intensity [50% vs. 80%MVC] repeated measures ANOVA indicated that there were no significant 3-way interaction, 2-way interactions, however, there was a main effect for intensity ($F = 8.527$, $p = 0.013$, $\eta^2 = 0.415$).

**Table 4. Linear Regression Analysis for the Relationship between Motor Unit Mean Firing Rate and Recruitment Threshold for the Vastus Medialis Muscle***

| | | | Pre-Fatigue | | Post-Fatigue | |
|---|---|---|---|---|---|---|
| Arm-Leg Visit | 50% MVC | Subject | Slope | y-int | Slope | y-int |
| | | Mean | -0.4050 | 27.6158 | -0.4928 | 27.3336 |
| | | SD | 0.1210 | 4.2552 | 0.2914 | 7.3610 |
| | 80% MVC | Subject | Slope | y-int | Slope | y-int |
| | | Mean | -0.4357 | 32.2646 | -0.4175 | 31.5667 |
| | | SD | 0.1935 | 7.0455 | 0.2426 | 10.3231 |
| | | | Pre-Fatigue | | Post-Fatigue | |
| Leg-Leg Visit | 50% MVC | Subject | Slope | y-int | Slope | y-int |
| | | Mean | -0.4294 | 26.7181 | -0.4959 | 28.3167 |
| | | SD | 0.1658 | 3.7929 | 0.3319 | 6.3104 |
| | 80% MVC | Subject | Slope | y-int | Slope | y-int |
| | | Mean | -0.3888 | 31.3624 | -0.3647 | 30.0919 |
| | | SD | 0.1485 | 6.8228 | 0.1715 | 7.0553 |

* Mean and Standard Deviation (SD) of the linear slope coefficients (Slope) (pps/%MVC) and y-intercepts (y-int) (pps) of the linear regression lines for the relationship between motor unit mean firing rate and recruitment threshold (MFR vs. RT) before (Pre) and after (Post) fatiguing interventions for vastus lateralis muscle during Arm-Leg Visit and Leg-Leg Visit at 50% and 80% maximal voluntary contraction (MVC) contraction intensities.

### *The Relationship between Motor Unit Recruitment Threshold and Decruitment Threshold*

For the slopes of the linear regression lines of the relationship between motor unit recruitment threshold and mean firing rates during the plateau region of the trapezoidal submaximal contractions, the 3-way repeated measures ANOVA showed that there were no significant 3-way interaction, 2-way interactions, as well as main effects for all three muscles (non-exercised biceps brachii, non-exercised vastus lateralis, and non-exercised vastus medialis).

For the y-intercepts of the linear regression lines, the 3-way repeated measures ANOVA indicated that there were no significant 3-way interaction, 2-way interactions, as well as main effects for all three muscles (non-exercised biceps brachii, non-exercised vastus lateralis, and non-exercised vastus medialis).

### *Common Drive from the CNS to the Motor Neuron Pool*

The distributions of the peak cross-correlation coefficients from analyzed motor unit firings were not different before and after the fatiguing interventions, in all three muscles (non-exercised biceps brachii, non-exercised vastus lateralis, and non-exercised vastus medialis). Therefore, the common drive from the CNS to the motor neuron pool remained unchanged.

# Chapter 5. Discussion

## 5.1. Implications and Significance

The purpose of this investigation was to examine the phenomenon of "non-local muscle fatigue" after fatiguing different limb muscles (upper body vs. lower body). In addition, a more important purpose of this study was to explore the potential underlying mechanisms of this phenomenon by interpreting surface EMG recordings and the motor unit firing behaviors from sophisticated surface EMG decomposition techniques. The significances of the findings of this study are two folds: 1. It allows us to understand the possible pathway(s) of short term "cross-over fatigue" and long term "cross education" phenomenon; 2. It can potentially shed light to future neural rehabilitation research.

The first major finding of this study was that the "non-local muscle fatigue" (NLMF) phenomenon did exist, however, this NLMF effect was muscle group specific. Specifically, we found significant decreases of isometric strength in the upper body (non-exercised forearm flexors) following the fatiguing interventions, but this decline was not seen in the lower body (non-exercised knee extensors), thereby suggesting that the knee extensors are less susceptible to NLMF than the forearm flexors. This result is further supported by the effect sizes of the changes in the isometric strength of the testing muscles. According to the effect sizes, there are small effects of using forearm flexors as testing limb; on the other hand, testing knee extensors does not seem to have a NLMF effect. Although NLMF is a relatively new and popular topic, our investigation is not the first few examining this effect. According to a very recent systematic review, around 3/4 (23 of 30 measurements) of all performance outcome measurements of the lower limbs observed NLMF, whereas only about 1/3 (9 or 28 measurements) of all measurements testing the upper body observed evidence for NLMF (Halperin *et al.*, 2015). Although the majority of the research that have examined NLMF effect found decreased performance in the lower body, the different fatiguing protocols being used, the different training status of the participants, as well as the different measurements that being used for testing limbs might have potentially influenced the results. Therefore, the results of our investigation add evidences supporting the phenomenon of upper body NLMF.

An additional set of research questions we intended to answer when we designed this experiment are whether fatiguing 2 separate muscles (upper body vs. lower body) would affect the same rested non-exercised muscle, and whether fatiguing the same muscle would affect 2 separate muscles (upper body vs. lower body) differently. This set of research questions were intrigued by the work of Halperin et al. (Halperin *et al.*, 2014b), where the authors designed similar experiments and tried to answer the same research questions. Based on our results, we agree with Halperin et al. (Halperin *et al.*, 2014b) that the NLMF effect is not specific to the muscle being fatigued, but to the non-exercised muscles being tested. However, completely contradicting to the results from Halperin et al. (2014), in which the lower body (knee extensors) always demonstrated NLMF effects regardless of the muscle being fatigued, our results suggest that instead of the lower body muscle (knee extensors), the upper body muscle (forearm flexors) are always the one being affected by the fatiguing interventions conducted in either the upper limb (forearm flexors) or the lower limb (knee extensors). Obviously, some of the major factors that led to this discrepancy are the protocol used to elicit the fatiguing, as well as the ways how the NLMF were measured, as suggested by Halperin et al.

(Halperin *et al.*, 2015). Different from our fatiguing protocol, Halperin et al. (2014) had participants perform two 100-s MVCs, and tested the non-exercised muscle groups with single MVC for isometric strength followed by 12 intermittent MVCs (work to rest ratio: 5/10s) for strength endurance. Although the total fatiguing exercise durations were similar (2 × 100s = 200s vs. 6 × 30s = 180s), the different resting durations during two experiments (1× 60s = 60s vs. 5 × 30s = 150s) might have influenced the crossover effect of the NLMF.

Following the findings of isometric strength of the non-exercised limb muscles, the results of the force steadiness indicate that the subjects' ability to maintain a steady force during submaximal isometric contractions were impaired in the forearm flexors after fatiguing either contralateral homologous forearm flexor or non-related heterogonous leg extensors. However, this ability in the leg extensors was not affected by any fatiguing interventions. As an important measurement of human motor performance, force steadiness is related to functional performance such as balance, precision, and movement accuracy (Ye *et al.*, 2015b), and it is one of the variables that has been most intensively studied previously (Tracy *et al.*, 2005; Missenard *et al.*, 2009). Before discussing our finding, it is important to point out that the exact same absolute force was required to reach before and after the fatiguing interventions. Thus, with the presence of the NLMF effect in the non-exercise forearm flexors, the subjects had to generate a higher percentage of their post-fatiguing maximal isometric strength to achieve the desired force production. Therefore, it is not surprising to see that the amplitude of the force fluctuations increased in the forearm flexors, but not in the knee extensors, which presented a lack of evidence of the NLMF effect.

With the presence of the NLMF effect, a more important question is what underlying mechanism(s) is/are that could have caused this phenomenon. Using the surface EMG technique, we are able to examine the neural drive from the central nervous system to specific muscle groups before and after the fatiguing interventions. As mentioned earlier, the EMG amplitude is a global measurement of neural drive to a specific muscle. Therefore, a decrease of EMG amplitude during a maximal voluntary contraction potentially indicates the decreased descending voluntary drive from the supraspinal level or an inability of a-motoneuron pool at the spinal level to respond, which usually occurs at spinal level or a combination of both. In the current investigation, it is not surprising to see that the EMG amplitudes for both vastus lateralis (VL) and vastus medialis (VM) remained the same before and after the fatiguing intervention, which at least partially explained unchanged isometric strength of the leg extensors. However, the EMG amplitudes during the isometric MVC were not altered, indicating that the subjects were still able to maximally activate their forearm flexors, even though the isometric strength of the non-exercised forearm flexors decreased following the fatiguing interventions. This finding is contradicting to many studies that investigated the NLMF, including our previous study (Ye et al. 2014a), where there was a decline in the EMG amplitude in the non-exercised forearm flexors following the maximal isokinetic concentric or eccentric fatiguing intervention. Our finding of the unchanged EMG amplitude during isometric maximal contraction does not necessarily disprove the “central fatigue” mechanism, because as a major limitation of this investigation, the supraspinal and spinal excitabilities were not measured in the current study.

Another interesting finding of this study is that during the plateau region of the forearm flexion trapezoidal submaximal contractions, there is a discrepancy between the force fluctuation and EMG amplitude response. Specifically, we expected that with the increased force fluctuations, there would have been an increase in the EMG amplitude, because more force was needed to compensate for the NLMF-induced strength loss in the non-exercised forearm flexors. However, the EMG amplitude during the plateau region of the trapezoidal submaximal contractions did not change, indicating that the increased force fluctuations during the submaximal contractions was not related to the changes in central factors, but more likely the peripheral factors. Another possible explanation to this discrepancy is the nonlinear EMG-force relations in human skeletal muscles (Milner-Brown & Stein, 1975; Bigland-Ritchie, 1981; Woods & Bigland-Ritchie, 1983), where the increase of the EMG amplitude does not always perfectly match the force increment. In addition to the EMG amplitude, the frequency information of the surface EMG signals was also examined in this study. Specifically, the only finding is that the EMG MNF significantly increased in both VL and VM during the isometric MVC of the non-exercised leg extensors following the fatiguing interventions.

To examine the potential changes in the motor unit firing behavior at the spinal level, we utilized an advanced technique-the surface EMG decomposition. Although this technique does not allow us to track changes of a specific single motor neuron firing behavior, it demonstrates a general picture of how the motoneuron pool operates to generate force to accomplish certain motor tasks by examining the firing behavior of many motor units in one isometric contraction. Specifically, the relationship between average motor unit firing rate and recruitment threshold has been used to examine the motor control strategies (De Luca & Hostage, 2010). Based on our results, the y-intercepts of the relationship between average motor unit firing rate and recruitment threshold are different between different contraction intensities (50% vs. 80%MVC) for both biceps brachii and vastus medialis muscles. The finding of the significant differences of y-intercepts between different contraction intensities is in accordance with previous observations from our lab (Ye *et al.*, 2015c) as well as others (De Luca & Hostage, 2010). As explained in De Luca and Hostage (2010), an increased y-intercept without any change in the slope of the linear regression line indicates an increased average firing rate for all the detected motor units. Obviously, comparing to the contraction intensity at 50% MVC, maintaining a force level at 80% MVC definitely required motor neurons discharge at a higher frequency. However, for both biceps brachii and vastus medialis muscles, the slope coefficients of the linear regression lines did not change after the fatiguing interventions, suggesting that the overall motor control strategies remained the same. Since the inverse relationship between recruitment threshold and the firing rate represents an "operating point" for the motor neuron pool in response to different levels of excitation (De Luca and Hostage 2010; De Luca and Contessa 2012), we are confident that before and after the fatiguing interventions, the levels of excitation from the central nervous system to the non-exercised biceps brachii and vastus medialis stayed the same. Therefore, this observation indicates that the possible NLMF effect at least did not cross over at the spinal cord level.

Interestingly, the slope coefficients of the linear regression line differed between the Arm-Leg and Leg-Leg Visits for the vastus lateralis muscle, with the slope of the linear regression line during Arm-Leg Visit significantly greater (more flat) than that during the Leg-Leg visit. According to De Luca and Hostage (2010), the slope of the linear regression line becomes progressively more flat (less negative) as force output increases, suggesting that higher threshold motor units are recruited to achieve a higher force output. Therefore, this finding indicates that additional high-threshold motor units might have been recruited during the Arm-Leg Visit when comparing to the Leg-Leg Visit, suggesting that fatiguing the non-related forearm flexor might have influenced the motoneuron pool of the non-exercised vastus lateralis in a different way than fatiguing the contralateral leg extensor did. When compared the Arm-Leg and Leg-Leg Visits, the isometric strength of the leg extensors responded slightly different following the different fatiguing intervention. Specifically, the average isometric strength of the leg extensor tended to increase after fatiguing the contralateral leg extensors, while the average isometric strength of the leg extensor tended to decrease after fatiguing the non-related forearm flexor, even though both fatiguing interventions did not induce significant changes in the isometric strength of the non-exercised leg extensors. In fact, the increase of isometric strength of the leg extensors following the fatiguing intervention on its contralateral part was also observed in our pilot study prior to this investigation, where we had subjects perform 12 sets of 10-s isometric leg extension or 4 sets of 30-s isometric leg extension unilaterally, and found out that the isometric strength of the contralateral leg extensors increased in both conditions. In addition to our finding, a previous study also reported this unilateral lower body fatiguing exercise-induced muscular strength performance increase in the contralateral limb (Grabiner & Owings, 1999), where the authors had their subjects perform 75 unilateral maximal isokinetic eccentric exercise on their leg extensors, and found that the maximal eccentric strength increased in the contralateral leg extensors. Therefore, to the non-exercised leg extensors, fatiguing 2 different muscles (upper body vs. lower body) seem to have differential effects on the motor unit activity of the non-exercised vastus lateralis.

## 5.2. Conclusions

In conclusion, 6 sets of 30-s maximal isometric contractions performed in the right forearm flexors and right leg extensors induced non-local muscle fatigue in the non-exercised left forearm flexors, but not in the leg extensors. Due to non-local muscle fatigue, the subjects' ability to maintain a steady constant force was impaired. Contradicting to the prevailing explanations of the NLMF, the EMG data from our study does not necessarily support the "central fatigue" mechanism, due to the lack of evidence of changes in EMG parameters and motor unit activity from the non-exercised biceps brachii. On the other hand, although the motor performance of the non-exercised left extensors was not affected by the fatiguing interventions, fatiguing upper body muscle vs. lower body muscle seemed to have differential effects on the motor unit firing behaviors from the non-exercised vastus lateralis. However, this difference was probably too small to induce significant changes in motor performance.

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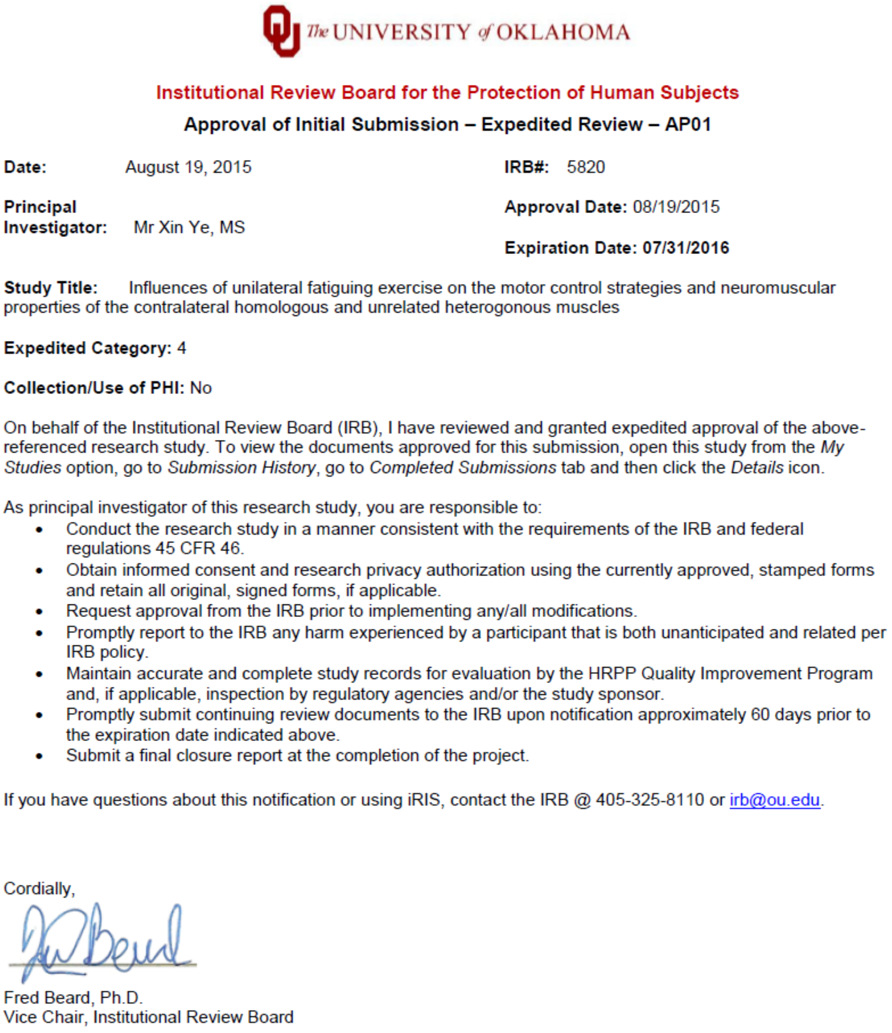
# Appendices

## Appendix A – Institutional Review Board Approval Letter



The UNIVERSITY of OKLAHOMA

**Institutional Review Board for the Protection of Human Subjects**

**Approval of Initial Submission – Expedited Review – AP01**

**Date:** August 19, 2015

**IRB#:** 5820

**Principal Investigator:** Mr Xin Ye, MS

**Approval Date:** 08/19/2015

**Expiration Date: 07/31/2016**

**Study Title:** Influences of unilateral fatiguing exercise on the motor control strategies and neuromuscular properties of the contralateral homologous and unrelated heterogonous muscles

**Expedited Category:** 4

**Collection/Use of PHI:** No

On behalf of the Institutional Review Board (IRB), I have reviewed and granted expedited approval of the above-referenced research study. To view the documents approved for this submission, open this study from the *My Studies* option, go to *Submission History*, go to *Completed Submissions* tab and then click the *Details* icon.

As principal investigator of this research study, you are responsible to:

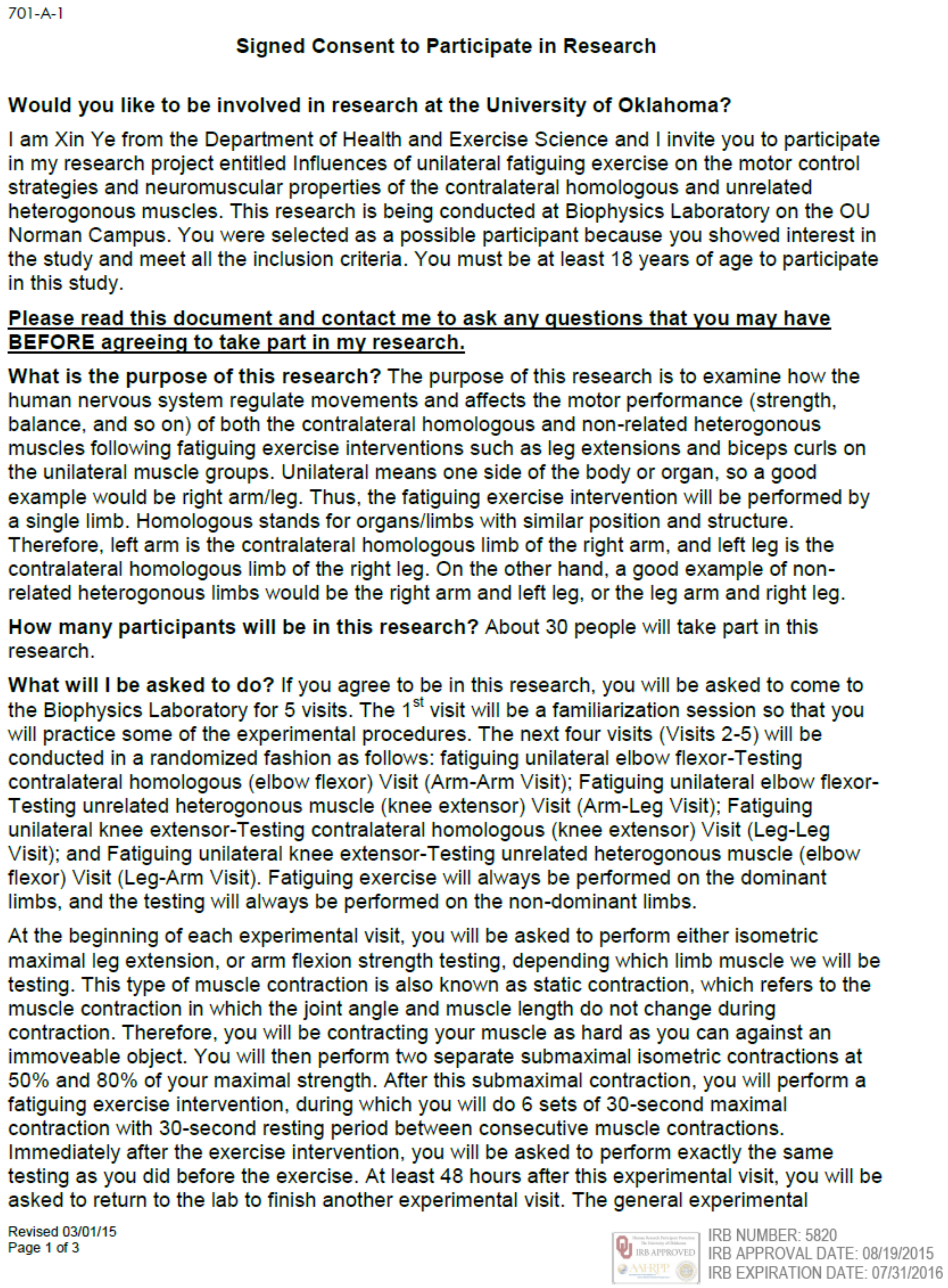
- Conduct the research study in a manner consistent with the requirements of the IRB and federal regulations 45 CFR 46.
- Obtain informed consent and research privacy authorization using the currently approved, stamped forms and retain all original, signed forms, if applicable.
- Request approval from the IRB prior to implementing any/all modifications.
- Promptly report to the IRB any harm experienced by a participant that is both unanticipated and related per IRB policy.
- Maintain accurate and complete study records for evaluation by the HRPP Quality Improvement Program and, if applicable, inspection by regulatory agencies and/or the study sponsor.
- Promptly submit continuing review documents to the IRB upon notification approximately 60 days prior to the expiration date indicated above.
- Submit a final closure report at the completion of the project.

If you have questions about this notification or using iRIS, contact the IRB @ 405-325-8110 or irb@ou.edu.

Cordially,

Fred Beard, Ph.D.
Vice Chair, Institutional Review Board

## Appendix B – Informed Consent



701-A-1

### Signed Consent to Participate in Research

**Would you like to be involved in research at the University of Oklahoma?**

I am Xin Ye from the Department of Health and Exercise Science and I invite you to participate in my research project entitled Influences of unilateral fatiguing exercise on the motor control strategies and neuromuscular properties of the contralateral homologous and unrelated heterogonous muscles. This research is being conducted at Biophysics Laboratory on the OU Norman Campus. You were selected as a possible participant because you showed interest in the study and meet all the inclusion criteria. You must be at least 18 years of age to participate in this study.

**Please read this document and contact me to ask any questions that you may have BEFORE agreeing to take part in my research.**

**What is the purpose of this research?** The purpose of this research is to examine how the human nervous system regulate movements and affects the motor performance (strength, balance, and so on) of both the contralateral homologous and non-related heterogonous muscles following fatiguing exercise interventions such as leg extensions and biceps curls on the unilateral muscle groups. Unilateral means one side of the body or organ, so a good example would be right arm/leg. Thus, the fatiguing exercise intervention will be performed by a single limb. Homologous stands for organs/limbs with similar position and structure. Therefore, left arm is the contralateral homologous limb of the right arm, and left leg is the contralateral homologous limb of the right leg. On the other hand, a good example of non-related heterogonous limbs would be the right arm and left leg, or the leg arm and right leg.

**How many participants will be in this research?** About 30 people will take part in this research.

**What will I be asked to do?** If you agree to be in this research, you will be asked to come to the Biophysics Laboratory for 5 visits. The 1st visit will be a familiarization session so that you will practice some of the experimental procedures. The next four visits (Visits 2-5) will be conducted in a randomized fashion as follows: fatiguing unilateral elbow flexor-Testing contralateral homologous (elbow flexor) Visit (Arm-Arm Visit); Fatiguing unilateral elbow flexor-Testing unrelated heterogonous muscle (knee extensor) Visit (Arm-Leg Visit); Fatiguing unilateral knee extensor-Testing contralateral homologous (knee extensor) Visit (Leg-Leg Visit); and Fatiguing unilateral knee extensor-Testing unrelated heterogonous muscle (elbow flexor) Visit (Leg-Arm Visit). Fatiguing exercise will always be performed on the dominant limbs, and the testing will always be performed on the non-dominant limbs.

At the beginning of each experimental visit, you will be asked to perform either isometric maximal leg extension, or arm flexion strength testing, depending which limb muscle we will be testing. This type of muscle contraction is also known as static contraction, which refers to the muscle contraction in which the joint angle and muscle length do not change during contraction. Therefore, you will be contracting your muscle as hard as you can against an immoveable object. You will then perform two separate submaximal isometric contractions at 50% and 80% of your maximal strength. After this submaximal contraction, you will perform a fatiguing exercise intervention, during which you will do 6 sets of 30-second maximal contraction with 30-second resting period between consecutive muscle contractions. Immediately after the exercise intervention, you will be asked to perform exactly the same testing as you did before the exercise. At least 48 hours after this experimental visit, you will be asked to return to the lab to finish another experimental visit. The general experimental

Revised 03/01/15
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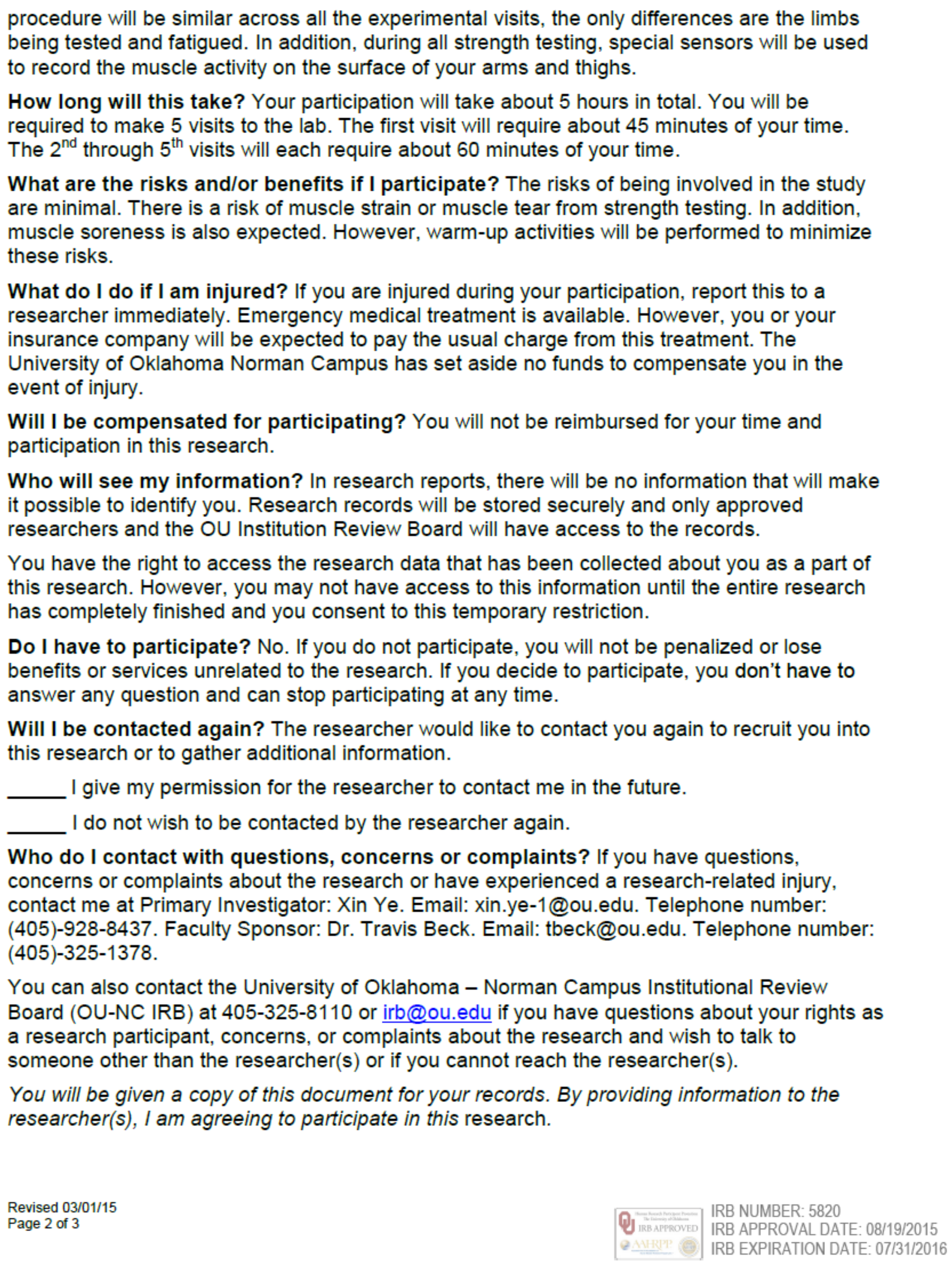

procedure will be similar across all the experimental visits, the only differences are the limbs being tested and fatigued. In addition, during all strength testing, special sensors will be used to record the muscle activity on the surface of your arms and thighs.

**How long will this take?** Your participation will take about 5 hours in total. You will be required to make 5 visits to the lab. The first visit will require about 45 minutes of your time. The 2nd through 5th visits will each require about 60 minutes of your time.

**What are the risks and/or benefits if I participate?** The risks of being involved in the study are minimal. There is a risk of muscle strain or muscle tear from strength testing. In addition, muscle soreness is also expected. However, warm-up activities will be performed to minimize these risks.

**What do I do if I am injured?** If you are injured during your participation, report this to a researcher immediately. Emergency medical treatment is available. However, you or your insurance company will be expected to pay the usual charge from this treatment. The University of Oklahoma Norman Campus has set aside no funds to compensate you in the event of injury.

**Will I be compensated for participating?** You will not be reimbursed for your time and participation in this research.

**Who will see my information?** In research reports, there will be no information that will make it possible to identify you. Research records will be stored securely and only approved researchers and the OU Institution Review Board will have access to the records.

You have the right to access the research data that has been collected about you as a part of this research. However, you may not have access to this information until the entire research has completely finished and you consent to this temporary restriction.

**Do I have to participate?** No. If you do not participate, you will not be penalized or lose benefits or services unrelated to the research. If you decide to participate, you **don't have to** answer any question and can stop participating at any time.

**Will I be contacted again?** The researcher would like to contact you again to recruit you into this research or to gather additional information.

_____ I give my permission for the researcher to contact me in the future.

_____ I do not wish to be contacted by the researcher again.

**Who do I contact with questions, concerns or complaints?** If you have questions, concerns or complaints about the research or have experienced a research-related injury, contact me at Primary Investigator: Xin Ye. Email: xin.ye-1@ou.edu. Telephone number: (405)-928-8437. Faculty Sponsor: Dr. Travis Beck. Email: tbeck@ou.edu. Telephone number: (405)-325-1378.

You can also contact the University of Oklahoma – Norman Campus Institutional Review Board (OU-NC IRB) at 405-325-8110 or irb@ou.edu if you have questions about your rights as a research participant, concerns, or complaints about the research and wish to talk to someone other than the researcher(s) or if you cannot reach the researcher(s).

*You will be given a copy of this document for your records. By providing information to the researcher(s), I am agreeing to participate in this* research.

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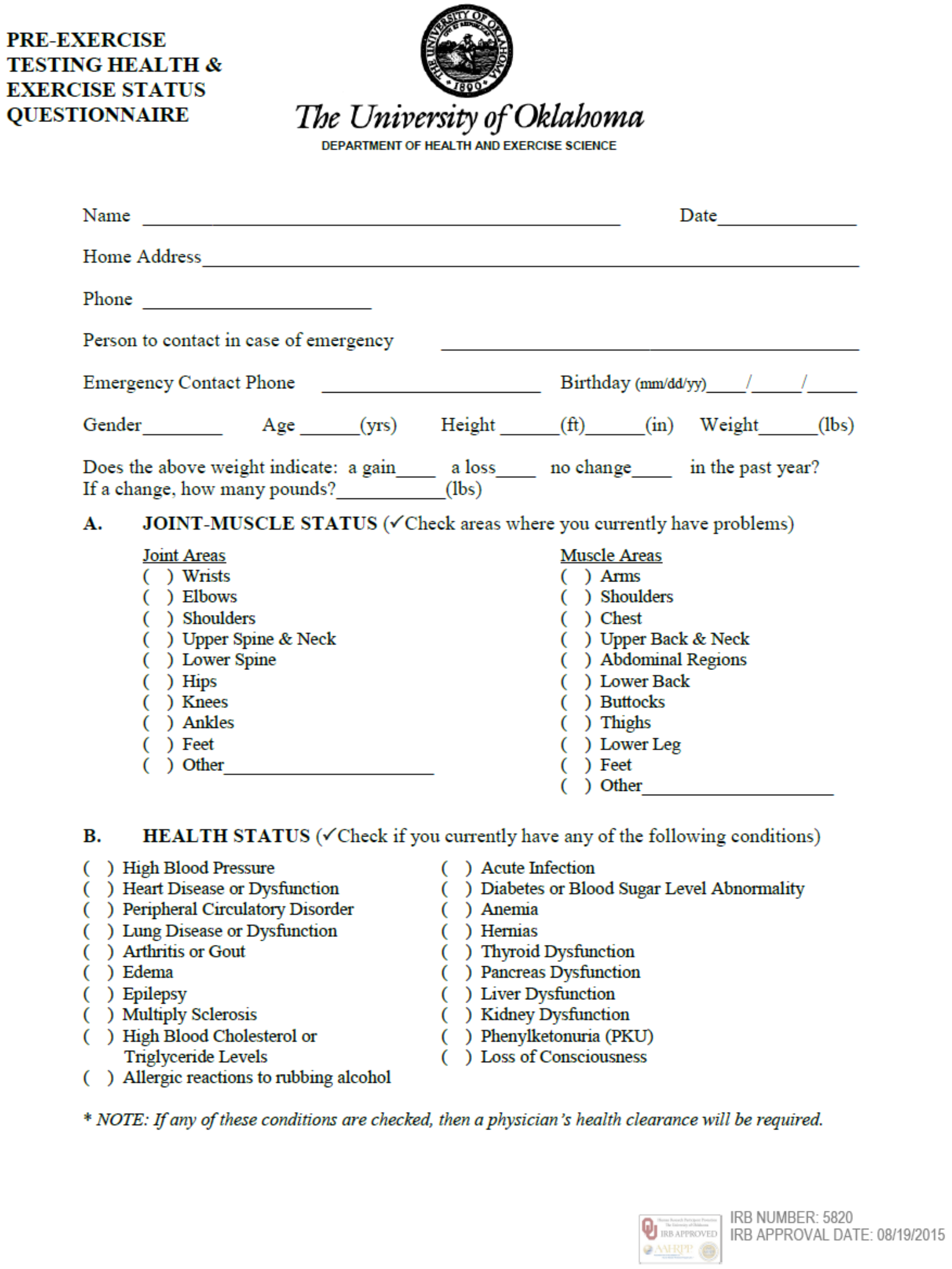
| | | |
|---|---|---|
| Participant Signature | Print Name | Date |
| Signature of Researcher Obtaining Consent | Print Name | Date |
| Signature of Witness (if applicable) | Print Name | Date |

# Appendix C – Pre-Exercise Health Questionnaire



**PRE-EXERCISE
TESTING HEALTH &
EXERCISE STATUS
QUESTIONNAIRE**

1890

The University of Oklahoma
DEPARTMENT OF HEALTH AND EXERCISE SCIENCE

Name ________________________________________ Date ____________

Home Address _______________________________________________________

Phone ____________________

Person to contact in case of emergency ________________________________

Emergency Contact Phone ___________________ Birthday (mm/dd/yy)____/_____/_____

Gender________ Age ______(yrs) Height ______(ft)______(in) Weight______(lbs)

Does the above weight indicate: a gain____ a loss____ no change____ in the past year?
If a change, how many pounds?___________(lbs)

**A.** **JOINT-MUSCLE STATUS** (✓Check areas where you currently have problems)

Joint Areas
( ) Wrists
( ) Elbows
( ) Shoulders
( ) Upper Spine & Neck
( ) Lower Spine
( ) Hips
( ) Knees
( ) Ankles
( ) Feet
( ) Other____________________

Muscle Areas
( ) Arms
( ) Shoulders
( ) Chest
( ) Upper Back & Neck
( ) Abdominal Regions
( ) Lower Back
( ) Buttocks
( ) Thighs
( ) Lower Leg
( ) Feet
( ) Other___________________

**B.** **HEALTH STATUS** (✓Check if you currently have any of the following conditions)

( ) High Blood Pressure
( ) Heart Disease or Dysfunction
( ) Peripheral Circulatory Disorder
( ) Lung Disease or Dysfunction
( ) Arthritis or Gout
( ) Edema
( ) Epilepsy
( ) Multiply Sclerosis
( ) High Blood Cholesterol or Triglyceride Levels
( ) Allergic reactions to rubbing alcohol

( ) Acute Infection
( ) Diabetes or Blood Sugar Level Abnormality
( ) Anemia
( ) Hernias
( ) Thyroid Dysfunction
( ) Pancreas Dysfunction
( ) Liver Dysfunction
( ) Kidney Dysfunction
( ) Phenylketonuria (PKU)
( ) Loss of Consciousness

** NOTE: If any of these conditions are checked, then a physician's health clearance will be required.*

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## C. PHYSICAL EXAMINATION HISTORY

Approximate date of your last physical examination______________________________

Physical problems noted at that time__________________________________________

Has a physician ever made any recommendations relative to limiting your level of physical exertion? _________YES _________NO

If YES, what limitations were recommended?____________________________________

______________________________________________________________________

## D. CURRENT MEDICATION USAGE (List the drug name and the condition being managed)

| MEDICATION | CONDITION |
|---|---|
| __________________________ | ____________________________________ |
| __________________________ | ____________________________________ |
| __________________________ | ____________________________________ |

## E. PHYSICAL PERCEPTIONS (Indicate any unusual sensations or perceptions. ✓Check if you have recently experienced any of the following during or soon after *physical activity* (PA); or during *sedentary periods* (SED))

PA SED
( ) ( ) Chest Pain
( ) ( ) Heart Palpitations
( ) ( ) Unusually Rapid Breathing
( ) ( ) Overheating
( ) ( ) Muscle Cramping
( ) ( ) Muscle Pain
( ) ( ) Joint Pain
( ) ( ) Other______________________

PA SED
( ) ( ) Nausea
( ) ( ) Light Headedness
( ) ( ) Loss of Consciousness
( ) ( ) Loss of Balance
( ) ( ) Loss of Coordination
( ) ( ) Extreme Weakness
( ) ( ) Numbness
( ) ( ) Mental Confusion

## F. EXERCISE STATUS

**Do you regularly engage in aerobic forms of exercise (i.e., jogging, cycling, walking, etc.)? YES NO**

How long have you engaged in this form of exercise? ______ years ______ months

How many hours per week do you spend for this type of exercise? _______ hours

**Do you regularly lift weights? YES NO**

How long have you engaged in this form of exercise? ______ years ______ months

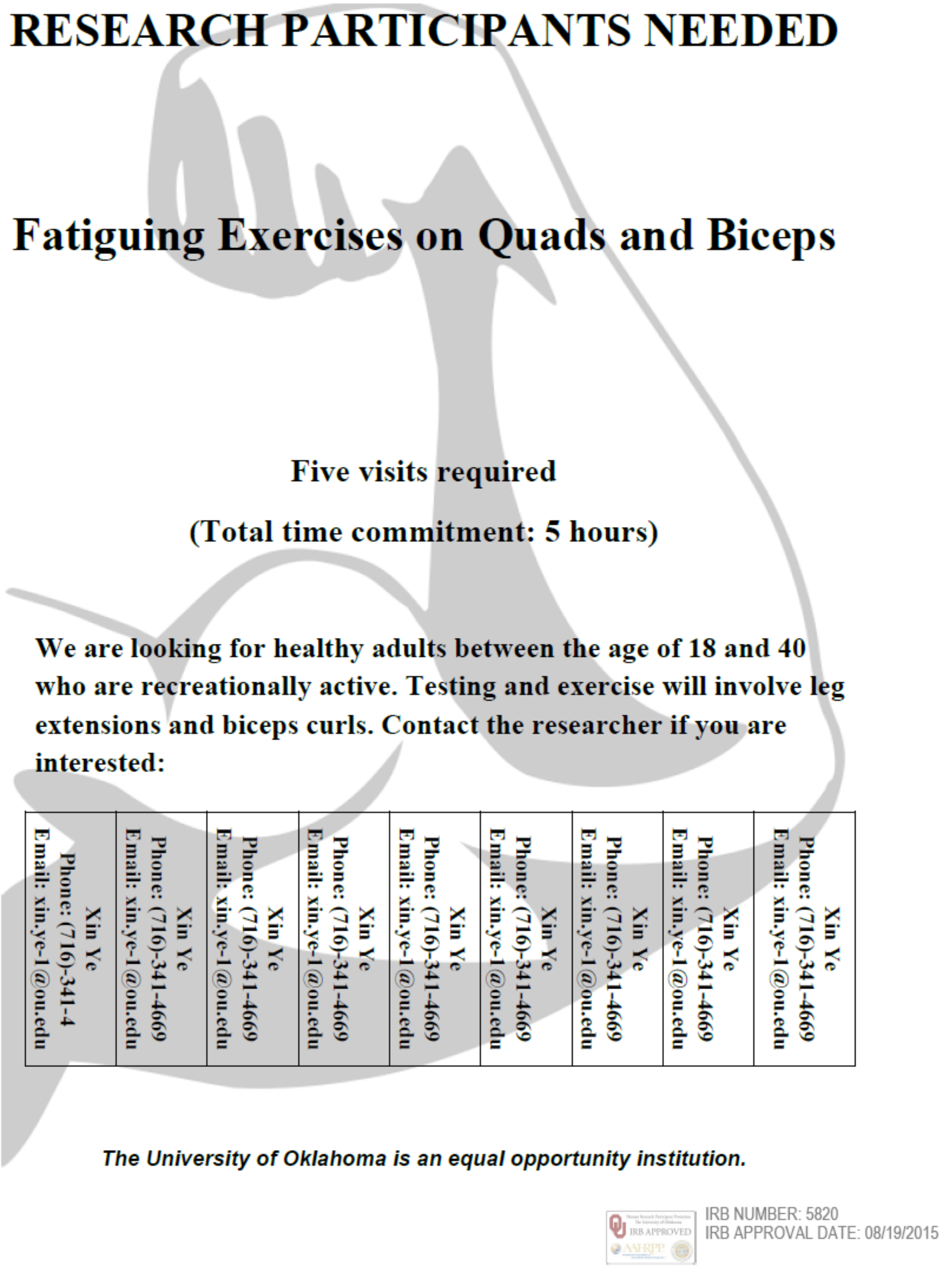
How many hours per week do you spend for this type of exercise? _______ hours

**Do you regularly play recreational sports (i.e., basketball, racquetball, volleyball, etc.)? YES NO**

How long have you engaged in this form of exercise? ______ years ______ months

How many hours per week do you spend for this type of exercise? _______ hours

**Appendix D – Recruitment Flyer**



# RESEARCH PARTICIPANTS NEEDED

## Fatiguing Exercises on Quads and Biceps

**Five visits required**

**(Total time commitment: 5 hours)**

**We are looking for healthy adults between the age of 18 and 40 who are recreationally active. Testing and exercise will involve leg extensions and biceps curls. Contact the researcher if you are interested:**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Xin Ye<br>Phone: (716)-341-4<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu | Xin Ye<br>Phone: (716)-341-4669<br>Email: xin.ye-1@ou.edu |

***The University of Oklahoma is an equal opportunity institution.***

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