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AN EXAMINATION OF AGONIST AND ANTAGONIST MOTOR UNIT FIRING PROPERTIES

A DISSERTATION APPROVED FOR THE
DEPARTMENT OF HEALTH AND EXERCISE SCIENCE

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"If I have seen further it is only by standing on the shoulders of giants"

– Isaac Newton, Feb. 15 1676

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ABSTRACT

The interactions between opposing muscle (i.e. agonist and antagonist) groups can be extremely complex, task-dependent, and are still poorly understood. To identify possible origins of the coordination between antagonistic muscle groups, the common or shared sources of neural input need to be understood. The assessment and manipulation of motor unit firing properties, such as synchronization, can provide information regarding the common inputs to opposing muscles. **PURPOSE:** The purpose of this study was to introduce various interventions to systematically manipulate both agonist and antagonist motor unit firing properties, and obtain a better understanding of the interactions between the two. **METHODS:** Muscle activity was detected from the biceps brachii ("agonist") and the triceps brachii ("antagonist") during isometric forearm flexions. The signals from these muscles were decomposed into individual motor unit action potential trains. Subsequently, various firing properties such as mean firing rate, recruitment threshold, and synchronization were calculated. On two separate visits, either the agonist or antagonist muscle was fatigued. During another two visits, either the agonist or antagonist muscle underwent 18 minutes of prolonged stretching, which has been shown to significantly desensitize proprioceptors. **RESULTS:** During co-activation, the antagonist demonstrated significant motor unit synchronization, but to a lesser extent when compared to the agonist. The antagonist also exhibited a substantially smaller recruitment threshold range and higher average firing rates. Fatigue of the agonist did not show any changes to antagonist motor unit firing

properties, despite a significant increase in co-activation. Fatigue of the antagonists produced effects on the motor unit behavior of the agonist, such as decreased motor unit synchronization. It was suggested that group III and IV muscle afferents originating from the antagonist were responsible for the change to the agonist. The stretching interventions provided some mixed results, often providing non-uniform changes across motor unit types. For example, agonist low-threshold motor unit pairs demonstrated an increase in short-term synchronization after agonist stretching, but the high-threshold motor unit pairs exhibited a decrease in synchronization. Future studies to help answer follow-up questions were suggested.

1. INTRODUCTION

1.1. Introduction

In 1662, René Descartes published[81] his perceptive observations regarding the coordinated interactions between opposing muscles. Since then, hundreds of studies have further examined these complex interactions. The primary muscle responsible for an action or movement is referred to as the *agonist*, and the muscle that opposes that action or movement is referred to as the *antagonist*. For example, during a leg extension exercise, the quadriceps femoris muscle group is the agonist (i.e. primary mover), and the hamstrings group is the antagonist (since their primary function is to flex the leg). The coordinated interactions between the agonist and antagonist muscles can be extremely complex. It has been demonstrated by several studies [257-259] that during specific situations, agonist activation is accompanied by antagonist relaxation, or inhibition. This contraction-relaxation phenomenon is often referred to as reciprocal innervation[257], or reciprocal inhibition[120, 221]. However, there are other conditions where the opposing muscles (i.e. antagonists) are involuntarily active [230, 292], albeit to a lesser extent than the agonist. This phenomenon of dual contraction is referred to as antagonist coactivation. Antagonist coactivation seems to be more common during voluntary movements[292], especially those under weighted or high-velocity conditions[8, 300]. Furthermore, under conditions of load-bearing isometric contractions, it may be beneficial or necessary to intentionally activate both agonist and antagonist muscles.

This intentional activation of both muscle groups is referred to as voluntary co-contraction.

One of the original hypotheses[207] describing the purpose of antagonist coactivation suggested that it served solely as a protective mechanism. Since activation of an antagonist muscle reduces the torque produced at a joint (by opposing the force produced by the agonist), its purpose was thought to prevent muscle/tendon tearing or injury from over-exertion[214]. However, antagonist coactivation has been shown to be present at even very low force-levels. In fact, golgi tendon organs, one of the mechanisms behind antagonist coactivation, has been shown[27] to respond to the twitches of a single motor unit. These findings have led to the development of new hypotheses to describe its purpose. One of the most common hypotheses to date is that antagonist coactivation serves to increase joint stability[16].

Furthermore, the underlying mechanisms responsible for antagonistic interactions have yet to be fully understood. To identify the possible origins of the coordination between opposing muscle groups, the common or shared sources of neural input to each muscle's α–motor neuron pool must first be understood. Some of these common sources, as well as their potential influence on agonists and antagonists, are listed below and summarized in Figure 1:

Common Sources of Input to Agonist and Antagonist motor neuron pools:

- Central descending drive
    - On agonist: Excitation
    - On antagonist: Either excitation or inhibition (situation dependent)
- Agonist Muscle Spindles (group Ia and II afferents)
    - On agonist: Excitation (termed “autogenic excitation”)
    - On antagonist: Inhibition (termed “reciprocal inhibition”)
- Agonist Golgi Tendon Organs (group Ib afferents)
    - On agonist: Situation dependent
        - Typical response: Inhibition (termed “autogenic inhibition”)
        - Response during co-contraction: Excitation
    - On antagonist: Excitation (termed “reciprocal excitation”)
- Agonist Renshaw Cells (RC)
    - On agonist: Inhibition (termed “recurrent inhibition”)
    - On antagonist: Disinhibition (termed “reciprocal disinhibition”) by inhibiting the Ia inhibitory interneurons
- Nociceptors, chemoceptors, and mechanoreceptors (group III and IV afferents)
    - On agonist: Either excitation or inhibition (situation-dependent)
    - On antagonist: Either excitation or inhibition (situation-dependent)
- Antagonist Muscle Spindles (group Ia and II afferents)
    - On agonist: Inhibition (termed “reciprocal inhibition”)
    - On antagonist: Excitation (termed “autogenic excitation”)

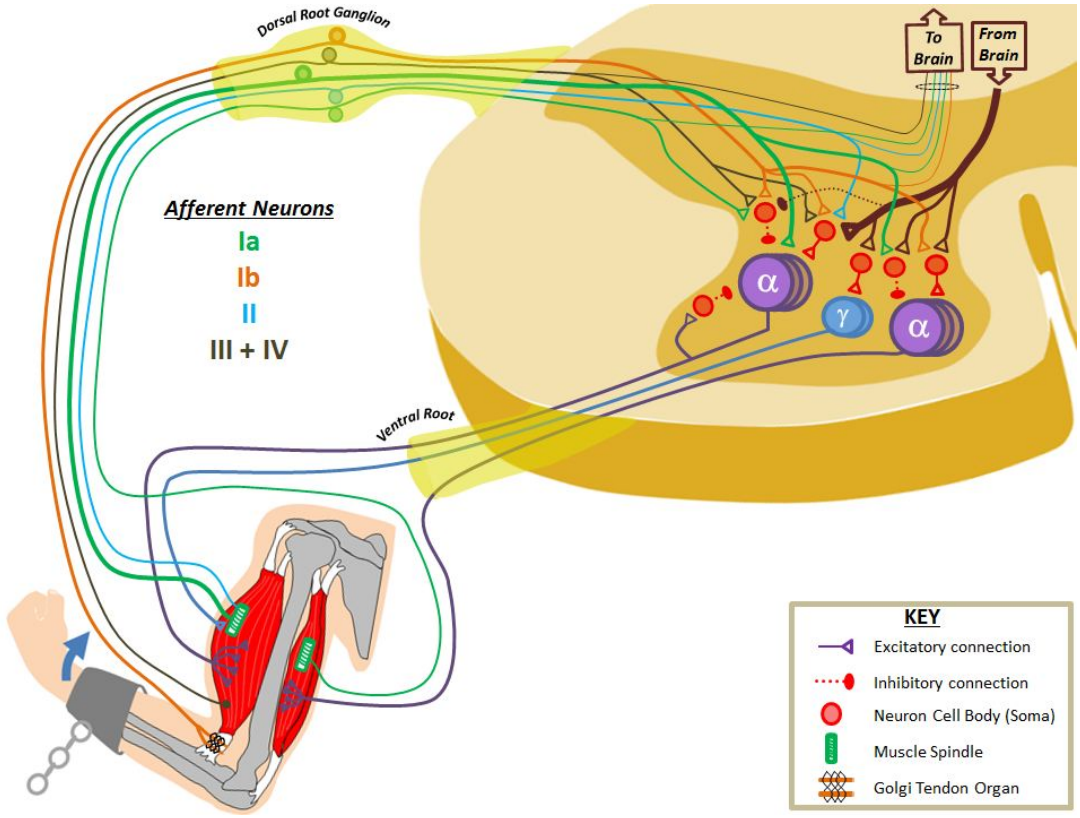

Figure 1 – Summary of common inputs that affect the interactions between agonist and antagonist muscles. **α** = α-motor neuron pool; γ = γ-motor neuron pool. Not illustrated: Shared Ia/Ib excitatory interneurons; commissural interneurons from contralateral afferent and efferent sources; central pattern generator interneurons active during rhythmic alternating movements, such as gait or cycling; Renshaw cell disinhibition of antagonist inhibitory interneurons

As previously mentioned, these interactions are very situation dependent. Any changes to the movement, force level, fatigue-level, or structural integrity of the muscle can lead to changes in the way that the agonist and antagonist interact. Most studies have used surface electromyography (EMG) to investigate the coordination between agonist and antagonist muscle groups. However, to understand the underlying mechanisms of these interactions, more studies need to be performed at either the motor neuron or motor unit level. One assessment tool that could be quite useful in this regard is the calculation of motor unit synchronization. Motor unit synchronization is the tendency for motor units from the same muscle to fire with dependent latencies relative to each other more often than would be expected if the motor units were independent. In short, motor units fire together more often than would be expected from chance alone. The mostly widely accepted hypothesis for the cause of synchronization is shared or common inputs to the motor units[56, 247]. So, if two motor units both receive excitatory post-synaptic potentials from the same source at the same time, the probability that the two motor units fire simultaneously increases[34]. These shared inputs that lead to synchronization can be central (e.g. descending drive from the brain) or peripheral (e.g. afferent input from the proprioceptors) in origin. Thus, examining changes in synchronization of motor units in agonist and antagonist muscles could provide insight into activity at their common inputs (summarized in Figure 1). Furthermore, rapid changes in the firing times (or rates) of motor units can provide important information about the inputs as well[294]. For example, if a motor unit gets a sudden influx of inhibitory

impulses (e.g. from a golgi tendon organ), the result would be a decrease in the firing times for that motor unit (i.e. it would take longer to produce each action potential).

Another useful tool that could provide insight of the interactions between agonists and antagonists is the systematic manipulation of the common inputs (e.g. proprioceptors). For example, prolonged stretching of a muscle has been shown to significantly depress or attenuate the peripheral feedback from the proprioceptors[12]. It has been hypothesized [12, 125, 129] that prolonged stretching leads to plastic deformation (i.e. elongation) of the muscle connective tissue, causing laxity in the muscle spindles, which significantly desensitizes them. Under some extreme stretching conditions, Golgi Tendon Organs may be temporarily desensitized as well[146]. Therefore, recording motor unit activity after prolonged stretching could provide insight into how the agonist and antagonist would interact *without* the common input from the proprioceptors.

Local muscular fatigue of either the agonist or antagonist muscle is yet another tool that could provide information regarding the muscle's common inputs. Fatiguing a muscle causes decreases in motor unit firing rates and recruitment thresholds[127], changes in the activity of the muscle spindles, chemoreceptors[25] (which detect metabolic accumulates and changes in O_2/CO_2 levels), nociceptors[272], and increases in antagonist coactivation[234]. Assessing fatigue-induced and/or stretch-induced changes in the synchronization and firing rates of

agonist and antagonist motor units could provide an assortment of new, intriguing information about the coordination between the two muscles.

1.2. Purpose of the Study

Despite the completion of hundreds of studies, there is still a very poor understanding of how antagonist muscles behave, and how they interact with agonists during different situations. Therefore, the purpose of this study was to use two different interventions to systematically manipulate both agonist and antagonist motor unit firing properties.

1.3. Research Questions

This study had the potential to provide new information about the interactions between agonist and antagonist muscles. The following 12 research questions were those that had the potential to be answered by the present study and that *had not* yet been answered in the literature:

- Does the antagonist muscle demonstrate significant levels of motor unit synchronization?
    - If so, how will the degree of synchronization in the antagonist be affected by:
        - fatigue of the agonist?
        - removal of the agonist spindle input (from prolonged stretching)?

- Does fatigue of the antagonist alter:
    - the motor unit firing properties of the agonist?
    - the level of antagonist coactivation during subsequent agonist contractions?
    - the amount of force the agonist is able to produce?

- How will fatigue of the agonist affect:
    - the motor unit firing properties of the antagonist (during coactivation)?

- How will the removal of agonist spindle input (from prolonged stretching) affect:
    - the motor unit firing properties of the agonist (including synchronization)?
    - the motor unit firing properties of the antagonist?

- How will the removal of antagonist spindle input (from prolonged stretching) affect:
    - the motor unit firing properties of the agonist (including synchronization)?
    - the level of antagonist coactivation during subsequent agonist contractions?
    - the amount of force the agonist is able to produce?

1.4. Hypotheses

- The antagonist muscle will demonstrate significant levels of motor unit synchronization.

- Fatigue of the antagonist will not significantly alter the motor unit firing properties of the agonist.
- Fatigue of the antagonist will lead to a decrease in the magnitude of antagonist coactivation during subsequent agonist contractions.
- Fatigue of the antagonist will lead to an increase in the force that the agonist is able to produce.
- Fatigue of the agonist will lead to increased antagonist coactivation, and potentially increased antagonist motor unit firing rates.
- Fatigue of the agonist will lead to increases in the magnitude of synchronization in the antagonist.
- Removal of agonist spindle input (from prolonged stretching) will decrease the agonist motor unit firing rates, but increase the level of motor unit synchronization.
- Removal of agonist spindle input (from prolonged stretching) may increase the antagonist motor unit firing rates.
    - This resultant effect of the prolonged stretching were highly dependent on whether the stretch is sufficient enough to also desensitize the GTOs (in addition to desensitizing the spindles).
- Removal of the agonist spindle input (from prolonged stretching) will lead to increases in the magnitude of synchronization in the antagonist.
- Removal of antagonist spindle input (from prolonged stretching) will not significantly alter the motor unit firing properties of the agonist, including the level of synchronization.
- Removal of antagonist spindle input (from prolonged stretching) will decrease the level of antagonist coactivation during subsequent agonist contractions.
- Removal of antagonist spindle input (from prolonged stretching) will increase the amount of force that the agonist is able to produce.

1.5. Significance of the Study

This study enhanced our understanding of the interactions between opposing muscles. The prolonged stretching-induced attenuation of the proprioceptive response had the potential to reveal the central versus peripheral contributions to motor unit synchronization and antagonist coactivation. In addition to the improved understanding of the interactions between antagonist muscles, these results had the potential for clinical and practical applications as well. For example, it has been hypothesized that the severe distal limb tremor often associated with progressed stages of Parkinson's disease[14, 59, 83, 197] or paretic stroke[29, 233] is caused by extreme levels of motor unit synchronization and spastic antagonist coactivation. Therefore, if this study shows the ability to reduce synchronization and antagonist coactivation through the use of prolonged stretching, then that may introduce a possible therapeutic intervention for future clinical studies.

It was also been hypothesized that fatigue of the antagonist will lead to decreased antagonist coactivation and increased force production during subsequent contractions. If that hypothesis were to hold true, then it opens up the potential for future studies to examine the prospective improvement of some human performance variables (e.g. strength, power, etc.) through the use of antagonist pre-fatigue.

1.6. Delimitations

The following were the delimitations for this study:

1. Approximately 15-30 males and females were needed to complete this investigation.
2. Participants had to be between 18 and 35 years of age.
3. All participants had to be healthy, and free of neuromuscular disease as self-reported on a questionnaire.
4. The participants only performed voluntary contractions.
5. Only one group of antagonistic muscles was assessed (i.e. only the biceps brachii and triceps brachii).

1.7. Limitations

1. Participants responded to either a posted flyer or classroom visit by the investigator and chose to enroll on a volunteer basis. Therefore, the process of subject selection was not truly random.
2. The technology and equipment used to assess motor unit firing properties has many restrictions, including:
    a. Contractions must be isometric

b. The force profile must be trapezoidal in shape, characterized by a linear increase in force, a steady force hold, and then a linear decrease.

c. Contractions must be short in duration (under 45 seconds)

3. Since only voluntary contractions were used, changes to spindle afferent function could not be directly tested or confirmed via the Hoffman-reflex (H-reflex), which requires the use of electrical stimulation.

4. The higher force levels used in this study led to shorter action potential trains than is demonstrated in most of the literature.

1.8. Assumptions

1. Subjects accurately and honestly answered the health questionnaire.

2. Maximal effort was given on each maximal contraction.

3. The EMG and motor unit variables detected at the sensors accurately represented the behavior of the whole muscle.

4. The efficacy of the prolonged stretching can be accurately determined by changes in the maximal force production.

1.9. Threats to validity

The following were the potential threats to validity and the actions that were taken to prevent them:

1. *Intra-subject variability* – it is difficult for subjects to perform consistently on multiple visits to the laboratory
    a. To account for this threat, only within-day comparisons are made. Each intervention had its own pre- and post-tests within the same visit.
2. *Efficacy of the prolonged stretching*
    a. Since the stretching was intended to cause temporary changes to the muscle fiber's length-tension relationship, the efficacy should be visible by decreases in maximal force production
3. *Order effect* – Tracing the force template requires a certain degree of skill. Consequently, there is a learning effect to the contractions being performed. Therefore, the subjects were likely better at tracing the force template on the last visit than they were on the first.
    a. The subjects underwent a familiarization session prior to the intervention visits to help remove the learning effect.
    b. The order of the 4 intervention visits was randomized.

2. REVIEW OF LITERATURE

The review of literature is organized in a study-by-study manner and has 5 subsections (labeled 2.1-2.5). The article summaries are provided in chronological order within each subsection. A brief summary of each component is provided at the end of that section.

2.1. Agonist/Antagonist Interaction and Peripheral Feedback

Bell, 1823 [20]

A short passage in an early Anatomy and Physiology textbook may very well have provided the first insight into the neural control of opposing muscles. Remarkably, from experiments of his own and with little to no literature on the subject, the author stated:

> "The nerves have been considered so generally as instruments for stimulating the muscles, without thought of their acting in the opposite capacity, that some additional illustration may be necessary here. Through the nerves is established the connection between the muscles, not only that connection by which muscles combine to one effort, but also that relation between the classes of muscles by which the one relaxes and the other contracts. I appended a weight to a tendon of an extensor muscle, which gently stretched it and drew out the muscle; and I found that the contraction of the opponent flexor was attended with a descent of the weight, which indicated the relaxation of the extensor."

This short passage, as credited by Sherrington[255], is truly noteworthy because it may be the first mention of a neural interaction between antagonistic muscles. Previous works[81, 308], going as far back as a book written by René

Descartes in 1662[81], described the interactions between antagonistic muscles, but this Bell passage may have been the first to suggest a neural mechanism.

Kölliker, 1862 [172]

The purpose of this study was to identify the termination of nerves onto muscles. The main relevant contribution of this study to the present one is the finding of bundles of intrafusal fibers within the muscle. Following motor neurons to the fibers, it was observed that there were separated bundles of 3-10 fibers each. These would later be identified as muscle spindle receptors.

Sherrington, 1892-1909 [253-268]

Over the course of 18 years, Sir Charles Sherrington published and/or presented several seminal papers on the relationships between reflexes and antagonistic muscles. In the first paper[253], Sherrington observed, for the first time in the literature, that the afferent response from a knee tendon tap originated from within the same muscle that "jerks". Later work[256] attributed the origin of this afferent response to the spindles embedded within the muscle. Prior to that realization, there was only minor, unfounded speculation[167] that muscle spindles may have had a sensory function. Within that original paper[253] Sherrington also discovered an antagonistic interaction between the quadriceps and hamstrings. He observed that the knee-jerk reflex is facilitated when the hamstrings are relaxed, and

that tension on the hamstrings has a depressing effect on the reflex. Since he was able to reproduce this depressing effect at multiple joint angles (by manually applying tension to the hamstrings), it was concluded that this interaction was more than simply mechanical and that there had to be a neural component to this depressive effect as well. Sherrington then went on to demonstrate the reciprocal innervation of antagonistic muscles [255, 257, 258]; that is the active contraction of one muscle is accompanied by a relaxation of its mechanical opponent. In Sherrington's sixth note[260] on the phenomenon, he introduced the term "muscular sense"; which involved sensory organs in muscles, tendons, and joints which were largely affected by various limb positions. This is often credited as the first documentation in the scientific literature of the proprioceptive phenomenon often referred to as "kinesthetic sense". Sherrington later[262] went on to note that the magnitude of the "extensor-thrust" reflex could be altered if preceded by a prolonged flexion reflex. An initial flexor reflex caused the extensor reflex to be heightened, faster (i.e. shorter latency), and persist for a longer duration. However, during a flexion reflex, the extensor reflex is temporarily inhibited. He concluded that an agonist contraction immediately elicits an antagonist inhibition, but is eventually followed with a phase of super-excitability for the antagonist. In short, the after-effect is in the opposite direction to the initial primary effect. These alternating reflexes were proposed to be important for canine or feline locomotion (the animals used for many of these experiments).

Ruffini, 1898 [237]

The purpose of this study was to explore the micro-anatomy of the cat muscle spindles. The main relevant contribution of this study to the present one is the histological evidence of two types of nerve endings on the spindles. These would later be identified as group Ia and group II afferents.

Tilney and Pike, 1925 [292]

The objective of this study was to determine the possible role of the cerebellum in the coordination between antagonistic muscles. This work was especially concerned with the interactions that occur during voluntary movements (as opposed to the reflex work performed by Sherrington). Tilney and Pike considered their work to be follow-up experiments to that originally performed by Beaunis[17] and Demeny[78], which were also during voluntary movements. Unlike Sherrington's experiments, Beaunis and Demeny both found simultaneous activation of antagonistic muscles[17, 78]. Similar to their findings, Tilney and Pike demonstrated that the antagonists coactivated [when recording EMG from the biceps brachii (BB) and triceps brachii (TB)]. In fact, they were unable to reproduce Sherrington's reciprocal inhibition in all trials. However, they also recognized that despite both opposing muscles being activated, the level of activation was not equal. The authors stated that every movement has a dominant element (i.e. agonist) and a check, or moderator element (i.e. antagonist), and even

though the dominant element was always greater than the check element, they were always proportional (i.e. constant ratio). To determine the cerebellar role in these interactions, the cerebellum of monkeys and cats were systematically removed in varying proportions. These lesions had a disorganizing effect, leading to a disassociation between antagonistic muscles. In short, these cerebellar lesions led to the appearance of the contraction-relaxation phenomenon described by Sherrington (i.e. reciprocal innervation). However, it should be noted that the author's observation may have been an artifact of their myographic tracings, and they suggested that the falling force curve of an antagonist muscle does not necessarily imply relaxation (a rising force curve does, however, imply contraction). It was concluded[(292)] that both antagonistic muscles contract, albeit to different degrees, during a voluntary movement, and the coordination between them is influenced, at least in part, by the cerebellum.

Matthews, 1933 [(201)]

The aim of this extensive study was to further explore the nerve endings in mammalian muscles (primarily cats and guinea-pigs). The most relevant finding from these many subexperiments was the observation that spindles have a much higher-frequency response to rapid stretch than when the stretch is slower or static.

Levine and Kabat, 1952 [182]

The aim of this study was to examine the coordination of muscular activity during voluntary movement. The author's results seemed to conflict the reciprocal innervation described by Sherrington [257-268] during his reflex studies (i.e. involuntary). Specifically, the authors found that Sherrington's findings of antagonist inactivity held true during unresisted voluntary movement. However, when resistance to the agonist was applied, the antagonist became active (i.e. coactivation). It was concluded[182] that during voluntary movement in humans, antagonist coactivation seemed to be the rule rather than the exception.

Eldred et al., 1953 [91]

The aim of this investigation was to explore the potential supraspinal control of muscle spindles. This was an important paper as their demonstration of γ-motor neuron influence over spindle responses and their servo-control mechanism theory[207] influenced many later studies.

Hufschmidt and Hufschmidt, 1954 [148]

The purpose of this study was to examine the simultaneous responses of antagonistic muscles to a given stimulus. The subjects started the experiment by producing a sustained low-force contraction of the biceps brachii. They were then instructed to switch to a contraction of the triceps brachii as quickly as possible in

response to a tactile stimulus. Interestingly, the authors found that inhibition of the biceps preceded the reaction of the triceps by 50 msec. In short, antagonist inhibition preceded agonist activation during the sensory-motor reaction. The authors also concluded that the long 50 msec latency demonstrated that the reciprocal inhibition was of supraspinal, rather than spinal origin. They deducted, from previous literature, that afferent conduction time to the cortex was about 18 msec, with an efferent conduction time of approximately 12 msec, thereby leaving an estimated 20 msec for cortical integration.

Eccles et al., 1957 [86, 87]

These two studies were integral in understanding the excitatory and inhibitory effects of group Ia, Ib, and II afferent responses on the entire α-motor neuron pool. The observed effects on agonist and antagonists are discussed elsewhere in this dissertation (see section 2.1.1). However, these studies also demonstrated excitatory afferent projections to synergistic muscles.

Person, 1958 [230]

The aim of this study was to examine the effects of developing a new motor habit on the coordination of an antagonistic muscle. While recording EMG signals from the BB and TB muscles, Person[230] found considerable coactivation of antagonistic muscles during a novel alternating, rhythmic task. Interestingly,

training in the task led to the disappearance of this coactivation and the development of antagonist rest periods. It was concluded[230] that coordination of antagonistic muscles plays an important role in the development of a new motor habit.

Matthews, 1962 [202]

The purpose of this study was to explore the fusimotor (i.e. "γ") innervation of muscle spindles. This was the first paper to acknowledge two separate fusimotor types: dynamic and static. Many later studies referred to these fusimotor axon types as γ-dynamic and γ-static. The γ-dynamic axons innervate nuclear bag fibers, and the γ-static axons innervate nuclear chain fibers.

Jansen and Rudjord, 1964; Houk and Henneman, 1967 [145, 153]

These two studies, together, made an important contribution to the understanding of Golgi tendon organs (GTO) mechanics. Both investigations demonstrated that GTOs respond strongly to active force production, but weakly to passive stretching, even if held to an equitable tension. However, the reason for this preferential selectivity to active contractile tension is still unknown.

Patton and Mortensen, 1971 [227]

The purpose of this study was to further examine the reciprocal activity of opposing muscles. EMG signals were detected from the BB and TB during various weighted and unweighted forearm flexions and extensions. The authors found a continuum of reciprocal activity that varied greatly. Unresisted forearm flexions demonstrated the contraction-relaxation phenomenon described by Sherrington's[257] reciprocal innervation. Forearm extensions, or any movement with a resistance, led to a coactivation of the antagonist, as described by Tilney and Pike[292]. The authors[227] suggested that flexion and extension are opposite but not equal movements. Since extensors are typically involved in posture and stance, it is suggested that coactivation is more the rule than the exception. However, flexors are suggested to be more of a mobilizing, or skill muscle group and, therefore, less likely to induce coactivation.

Mendell and Henneman, 1971 [206]

The purpose of this study was to determine the location, density, and distribution of Ia terminals on homonymous α-motor neurons. This study would drastically change the way in which spindle responses were understood. The authors found that each individual Ia afferent neuron projects at least once to virtually every homonymous α-motor neuron. The authors continually stimulated a Ia afferent neuron and systematically explored how many α-motor neurons

demonstrated a resultant excitatory post-synaptic potential (EPSP). One afferent was typically able to elicit an EPSP in > 90% of the α-motor neurons. Unfortunately, antagonist α-motor neurons were not investigated. However, these results demonstrated why the stretch reflex is one of the most powerful reflexes in mammalian muscle.

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Vallbo, 1971 [297]

The aim of this study was to examine the time difference between the onset of motor unit activity and spindle afferent activity during voluntary isometric contractions. Both sustained contractions and fast-rise twitches were examined. Spindle activity occurred after the onset of motor unit activity in 95% of the tests conducted during sustained contractions. Approximately 70% of those observations showed a delay between 0 and 500 msec (median = 227 msec). Furthermore, spindle activity was maintained during the sustained contraction, and in some instances, continued shortly after the cessation of motor unit activity. During twitches, motor unit activity preceded spindle afferent activity in 99.15% of all observations. The authors concluded that fusimotor and skeletomotor outputs are controlled in the spinal cord simultaneously. In other words, the γ-motor neurons responsible for controlling spindle sensitivity are coactivated along with the alpha-motor neuron pool.

Goodwin et al., 1972 [123]

This study was an extensive series of experiments in which the authors were able to systematically confirm Sherrington's theory of "muscle sense". Vibration of the muscle elicited illusions of movement in the subjects. These vibrations were thought to activate both spindles and GTOs. It was suggested, therefore, that spindles contribute to the sense of position and movement in limbs, a finding that was later confirmed by Gandevia's research [112]. Paralyzation of joint afferents did not significantly affect limb position awareness. The authors[123] suggested that corollary discharges[273], or efference copies[298], were responsible for the compensation (i.e. motor collaterals traveling back upstream to provide information on the intended movement).

Tanaka, 1974 [278]

Prior to this study, reciprocal disynaptic Ia inhibitory pathways had been demonstrated in the spinal cord of cat[149]. The purpose of this investigation was to determine if the pathway exists during voluntary movements in man. Tanaka[278] tested the H-reflex of the triceps surae muscle group (plantarflexors) both at rest and during voluntary ankle movements. He found that active dorsiflexion (i.e. contraction of the opposing muscles) depressed the H-reflex in the triceps surae. No such effect was found during rest. Furthermore, the very short latency (1.7 msec) suggested a disynaptic connection. He also found that the threshold for the

occurrence of Ia inhibition of the antagonists was lower during stronger voluntary dorsiflexions. This suggests that activity of the Ia inhibitory pathway is higher during stronger contractions of the antagonist. This strong relationship between agonist α-motor neuron activity and reciprocal Ia inhibitory interneuron activity led Tanaka to suggest that the underlying mechanism is primarily central. Corticospinal tract fibers originating from the motor cortex connect not only monosynaptically with α- and γ-motor neurons, but also with Ia inhibitory interneurons.

Burke et al., 1976 [41]

The purpose of this study was to examine differences in synaptic strength from short-latency pathways to type-identified motor units. Intracellular recordings and stimulation were performed in anaesthetized cats. The authors found that the amplitudes of monosynaptic EPSPs (i.e. group Ia afferents) were related to motor unit type, and were inversely correlated with force. Therefore, the lower-force producing slow-twitch motor units received stronger synaptic inputs from spindle afferents than fast-twitch motor units.

Angel, 1977 [8]

The purpose of this investigation was to determine if the antagonist coactivation exhibited during rapid arm movements was due to: (a) a pre-determined central motor program, (b) peripheral feedback and long-loop reflexes,

or (c) a combination of a central motor program and peripheral modulation. During contractions in which the limb was not allowed to move, the antagonist demonstrated little to no coactivation. Therefore, coactivation is, at least in part, affected by peripheral feedback from the limb. However, there are times that antagonist activity precedes the onset of movement, which is suggestive of a central component as well. Consequently, the author[8] concluded that antagonist coactivation during rapid arm movements was the result of the initiation of a pre-existing central motor program that can be stopped or altered in response to proprioceptive feedback.

Binder et al., 1977 [27]

The purpose of this study was to determine the potential responses of GTOs to single motor units. The results were interesting in that GTOs depolarized in response to the twitch of a single motor unit. This finding helped change the former opinion that GTOs were high-threshold sensors designed simply to help detect danger from excessive forces.

Kudina, 1980 [176]

The purpose of this study was to examine the effects of electrical nerve stimulation and tendon taps on antagonist motor unit firings in the gastrocnemius, soleus, and tibialis anterior. The electrical stimulation of a nerve demonstrated a

clear inhibitory effect, as evidenced by a decrease in the firing probability within a histogram. Conversely, tendon taps showed an excitatory effect on antagonist muscles. As an explanation, the author discussed the fact that Eccles et al.[86] demonstrated that excitatory collaterals of the agonist Ia afferents have been shown to connect monosynaptically with the antagonist. In regards to the more common inhibitory response of Ia afferents (as demonstrated by electrical stimulation), the author found that the effect of the reciprocal inhibitory volley on the antagonist interpulse intervals depended on when the volley occurred. The inhibitory volley only lengthened the motor neuron's interpulse interval when it arrived close to when the next firing was supposed to occur. Inhibition that occurred early or in the middle of the interpulse intervals had no effect on it.

Smith, 1981 [270]

This publication was a review paper and therefore, will not be thoroughly summarized. However, the author did present something novel, and of particular relevance to the current study. The author compiled a list of the various situations that dictate whether the antagonist will coactivate or receive reciprocal inhibition:

Situations favoring reciprocal inhibition of the antagonist:

1. When external resistance prevents displacement or shortening by the agonists, the antagonists relax. One important exception is in isometric prehension.

2. Rhythmic motor processes such as locomotion, mastication, respiration, etc. During these processes, opposing muscles tend to alternate in activation.
3. Antagonistic muscles also usually alternate activity during low-velocity voluntary limb displacements without a load.

Situations favoring antagonist coactivation:

1. When muscular tension or limb position must be precisely monitored without load
2. In higher velocity limb displacements, or under loaded conditions, antagonists contract strongly to decelerate the limb (after a short, initial period of inactivity)
3. Isometric prehension of the hand

Humphrey and Reed, 1983 [150]

The aim of this study was to examine cortical control systems of antagonistic muscles for movement and joint stiffness in primates. The results from the study supported the hypothesis that cocontraction of opposing muscles leads to a significant increase in joint stiffness (see their fig. 15). In addition, the study showed that the flexor and extensor areas in the motor cortex overlap, and the active area during cocontraction of both muscle groups has a separate center, but overlaps with both of the original areas. Stimulation of this latter area resulted in simultaneous activation of both flexor and extensor α-motor neurons.

Hagbarth et al., 1986 [133]

The purpose of this study was to determine if the loss in dorsiflexion power in result to a chemical γ-fiber block was due to a decrease in excitatory spindle input to α-motor neurons. After the peroneal nerve block, motor unit firing rates of the tibialis anterior were lower and more irregular (during max efforts). Vibration placed over the antagonist muscle further reduced agonist motor unit firing rates. Conversely, vibration or stretches of the agonist during maximal efforts increased motor unit firing rates. It should be noted that the vibration and stretch interventions were over a very short period of time (e.g. 2 sec) and should not be compared with the neuromuscular effects from more prolonged durations. The authors[133] concluded that the loss in power was, at least in part, due to the γ-loop interruption. It was suggested that the γ-loop interruption lowered autogenic excitation to the α-motor neurons.

De Luca and Mambrito, 1987 [65]

The purpose of this study was to examine motor unit firing rate properties within and among antagonistic muscles. Motor unit firings were detected from the flexor pollicis longus and extensor pollicis longus muscles, which are responsible for control of the interphalangeal joint of the thumb. The subjects performed force varying contractions in both directions (flexion and then extension) as well as zero-force contractions in which both muscles were co-contracting. Motor unit firing

rates were strongly cross-correlated at a zero time shift, supporting the hypothesis of common drive. Firing rate comparisons between opposing muscles during co-contraction also showed common drive, but to a lesser magnitude than within each muscle contracting separately (i.e. smaller r value). The authors suggested that the central nervous system may control the motor units for both opposing muscles as if they were one pool when the two muscles are performing the same task (i.e. co-contraction).

Baratta et al., 1988 [16]

The aim of this study was to examine the role of antagonist coactivation in maintaining joint stability at the knee. EMG signals were detected from the quadriceps and hamstring muscle groups during slow ($15°\cdot s^{-1}$), isokinetic leg extensions. When antagonist EMG amplitude was normalized to joint angle, it was inversely related to moment arm variations across joint angle. The authors concluded that the antagonist exerts a constant opposing torque throughout the range of motion, which suggests that it may play an important role in maintaining knee joint stability. It should be noted, however, that the antagonist has been shown to have multiple phases during rapid movements (for review, see Smith[270]). Therefore, the applicability of the slow isokinetic contractions applied in this study may have some limitations.

Carolan and Cafarelli, 1992 [43]

The purpose of this study was to examine training-induced changes in antagonist coactivation. Untrained young males performed 8 weeks of unilateral isometric leg extension training (3 days per week). EMG signals were detected from the vastus lateralis (VL) and biceps femoris (BF) pre- and post-training. Interestingly, antagonist coactivation decreased by 20% in the trained leg after just 1 week of training, and by 13% in the untrained leg. The authors speculated that these changes in coactivation could have been due to alterations to Renshaw Cells, GTOs, and/or descending motor pathways.

Neilsen and Kagamihara, 1992 [221]

The objective of this study was to examine how disynaptic Ia reciprocal inhibition was controlled during simultaneous activation of antagonistic muscles (i.e. co-contraction). EMG signals were detected from the soleus and tibialis anterior (TA). Reciprocal inhibition was found during plantarflexion and co-contraction, but not during dorsiflexion. The degree of inhibition became progressively smaller during increasing plantarflexion. Disynaptic reciprocal inhibition was found to be decreased after ischaemic block of the peripheral feedback. The authors argued that their results suggested a central command modulation of the Ia inhibitory pathways. However, their conclusion seems fairly

speculative and tenuous, since it was an alteration to the peripheral feedback that led to the changes.

Psek and Cafarelli, 1993 [234]

The purpose of this study was to investigate agonist and antagonist behavior during two separate agonist-fatiguing protocols. Surface EMG sensors were placed on the VL and BF muscles. The subjects repeated submaximal, isometric leg extensions at either 30% (7 sec. on/3 sec. off cycles) or 70% (3 sec. on/ 7 sec. off cycles) of the MVC. The average BF coactivation during extension MVC was approximately 15% of BF maximal EMG amplitude (from flexion MVC). Maximal extension force decreased 29% in the low-intensity fatigue protocol (30% cycles) and 17% in the high-intensity protocol (70% cycles). During the high-intensity protocol, BF coactivation significantly increased relative to pre-fatigue. Post-test flexor MVCs revealed that the BF did not fatigue from the agonist fatiguing protocol. The authors estimated that at the end of the fatiguing protocol, approximately 11% of the extensor force was being wasted just to offset the opposing force of coactivation. The EMG signals from the VL and BF were highly correlated ($r = 0.96$) during fatigue, which the author's interpreted to be "consistent with the notion of a centrally mediated common drive to an agonist-antagonist pair."

Nielsen and Kagamihara, 1994 [223]

The purpose of this investigation was to examine the magnitude of motor unit synchronization in the TA during dorsiflexion, the soleus during plantarflexion, and to compare them to the amount of synchrony between the two muscles during a simultaneous cocontraction. The TA and soleus muscles each showed a significant amount of synchrony when they acted as an agonist, although the level in the TA was higher. Synchrony was even higher within each muscle during cocontraction. Between muscles, only 4 of 30 motor unit pairs (one TA, one soleus) showed synchrony during cocontraction. In addition, another 4 pairs demonstrated central troughs (i.e. anti-synchronization). Unfortunately, within-muscle synchronization was not reported when a muscle was in a true antagonist role (e.g. TA during plantarflexion). The authors also compared motor unit synchronization across different interelectrode distances. The larger the distance between the recording sites, the smaller the magnitude of synchronization.

Gibbs et al., 1994 [121]

The purpose of this study was to examine the degree of motor unit synchronization between antagonistic muscles during co-contraction. Indwelling EMG signals were detected from multiple antagonistic muscle groups (TA + SOL; BB + TB; IFDS + IEDC). The results demonstrated central troughs, instead of peaks, in their cross-correlation histograms. The authors interpreted this

phenomenon as “anti-synchronization”. It was proposed that antagonistic muscles may share common inputs, but those inputs could be excitatory to one muscle and inhibitory to another, thereby leading to a decrease in the probability of the two motor units firing simultaneously.

Amiridis et al., 1996 [7]

The objective of this study was to compare the level of antagonist coactivation during isokinetic leg extensions in sedentary and highly-skilled individuals. The highly-skilled group consisted of national and international level high-jumpers. EMG signals were detected from the vastus medialis (VM), VL, and semitendonosus (ST) muscles. The interesting contribution to the literature from this study is that they included eccentric muscle actions. The authors found that ST coactivation during eccentric muscle actions was significantly lower than that during concentric muscle actions. In addition, ST coactivation was significantly lower in the highly-skilled group compared to the sedentary group for both concentric and eccentric muscle actions.

Jarić et al., 1997 [154]

The purpose of this study was to investigate the effects of agonist and antagonist muscle fatigue on the performance of rapid movements (i.e. acceleration and deceleration). Two separate trials were conducted: one in which the forearm

flexors were fatigued, and one in which the forearm extensors were fatigued. Both flexion and extension were tested prior to and immediately following fatigue during each trial. Fatigue of each muscle group particularly affected the movement phase in which that group accelerated a limb (i.e. agonist role). The authors concluded that although the antagonist fatigue did result in performance impairment, agonist fatigue had a greater influence on movement velocity.

Weir et al., 1998 [300]

The purpose of this study was to examine the effects of agonist fatigue and speed of movement on antagonist coactivation. EMG signals were detected from the VL and BF muscles during 50 maximal isokinetic leg extensions. The contractions occurred at $100°\cdot s^{-1}$ during one visit and $250°\cdot s^{-1}$ during another. Hamstring EMG amplitude decreased with fatigue at both speeds. However, when normalized to force, hamstring coactivation actually increased with fatigue. In addition, coactivation was greater at the faster movement speed.

Burke et al., 1999 [39]

The aim of this study was to assess agonist force immediately following a maximal contraction of the antagonists. All possible combinations of slow speed, fast speed, and isometric contractions for both the agonist and the antagonist were examined. A double-acting concentric dynamometer was used to simulate the

horizontal seated row and bench press. Performance of fast-speed antagonist contractions significantly increased peak force of an ensuing fast agonist contraction. No combination involving isometric or slow antagonist contractions altered the succeeding effort of the agonist. The authors attributed the facilitation to activation of the stretch-shortening cycle. Furthermore, since a fast antagonist contraction did not influence slow or isometric agonist performance, it was suggested that the observed changes were primarily due to utilization of stored elastic energy, with little to no neural contribution (i.e. stretch reflex).

Burnett et al., 2000 [42]

Since it has been proposed that the level of antagonist coactivation is a mechanism to control the speed and stability of a movement, the purpose of this study was to see if coactivation was related to force steadiness. EMG signals were recorded from the first dorsal interosseous (FDI) and second palmar interosseus (SPI) during submaximal abductions of the first digit (2.5 - 75% MVC). The results showed little to no association between antagonist coactivation and force steadiness. The Pearson correlation coefficients were not reported, but their figure 4 demonstrated a wide distribution of data points, indicating a very poor association.

Kellis and Kellis, 2001 [162]

The objective of this study was to examine agonist and antagonist EMG amplitude during a reciprocal isokinetic fatigue test of the leg flexors and extensors (at $60°\cdot s^{-1}$). EMG signals were detected from the VM, VL, and BF muscles. During leg extensions, VM and VL EMG amplitude increased toward the top of the range of motion, but showed no changes during the initial part of the contractions. BF EMG amplitude increased with fatigue during leg flexions. Interestingly, there were no changes in EMG amplitude for any of the muscles when they acted as an antagonist.

Mullany et al., 2002 [216]

The purpose of this study was to examine the common drive between antagonistic muscles during fatigue. Surface EMG signals were detected from the VM, VL, rectus femoris (RF), and BF during isometric knee extensions to failure at 25%, 50%, 75%, and 100% MVC (each on a different visit). The VM, VL, and BF demonstrated similar patterns of response with fatigue, which were increasing EMG amplitudes until failure at submaximal intensities, and decreasing EMG amplitudes until failure during the maximal bout. The authors concluded that the similarities were due to the antagonistic muscles sharing a common motor neuron pool. It was also noted, as a potential limitation, that cross-talk between electrodes could have produced similar results. However, the relatively large interelectrode distances led

the authors to conclude that it was not an issue, and was instead suggestive of common drive.

Patikas et al., 2002 [226]

The aim of this study was to examine agonist and antagonist EMG amplitude changes during fatigue. Repeated maximal plantarflexions were performed until maximal torque diminished to 50% of the initial, baseline value. EMG amplitude was collected from the soleus (agonist) and TA (antagonist) muscles. Soleus EMG activity significantly decreased to 66% of baseline values with the fatiguing protocol. Antagonist (TA) EMG amplitude decreased as well, but the change was non-significant. Consequently, the decreased rate of decline in the antagonist led to an increase in the antagonist/agonist EMG ratio after fatigue. The authors concluded that such a change in this ratio implies that the relative opposing torque from the antagonist was higher after fatigue.

Beltman et al., 2003 [22]

The aim of this study was to examine the effects of antagonist pre-fatigue on subsequent agonist torque. The authors reported that leg extensor MVC, EMG amplitude, and voluntary activation were unaffected by a preceding leg flexion fatigue protocol. In addition, the leg flexion fatigue did not influence the level of

leg flexor coactivation during the subsequent leg extension tests. It should be noted that these results contradict those from other studies [106].

Gribble et al., 2003 [126]

The purpose of this investigation was to examine the possible relationship between antagonist coactivation and movement accuracy in multi-joint arm movements. EMG signals were recorded from 7 muscles that crossed either the elbow joint, shoulder joint, or both. As the size of the visual feedback target provided to the subject decreased, the level of antagonist coactivation increased. The authors concluded that antagonist coactivation was an intentional neural strategy used to facilitate multi-joint arm movement accuracy.

Maynard and Ebben, 2003 [203]

The goal of this study was to examine the effects of antagonist prefatigue on agonist and antagonist EMG activity, as well as isokinetic peak torque and power. The quadriceps (agonist) and hamstrings (antagonist) were assessed during maximal isokinetic leg extensions in 20 Division I wrestlers. Antagonist fatigue was induced in the hamstrings by 5 maximal isokinetic leg flexions. Interestingly, there was a 1.7% decrease in peak leg extension torque and an 11% decrease in peak power after the prefatigued condition (compared to a non-fatigued condition). Prefatigue also caused a 25% increase in coactivation (EMG amplitude) during subsequent leg

extensions while leading to no changes in agonist EMG amplitude. The authors concluded that antagonist prefatigue has a facilitative effect on the antagonist during subsequent agonist contractions, thereby decreasing agonist performance. However, no possible physiological mechanisms were provided to explain their results. Reservations, about the conclusions, exist since it is more likely that the very short duration leg extension set (5 reps) led to potentiation (post-activation potentiation) of the hamstring muscles, rather than actually fatiguing them.

Hassani et al., 2006 [137]

This study served as a follow-up study to the Kellis and Kellis investigation[162] previously described. The new addition was the inclusion of a submaximal fatigue protocol. During submaximal testing, antagonist EMG amplitude (of the BF during leg extensions) initially demonstrated a significant increase and then a subsequent decrease. It should be noted, however, that the latter decrease only served to return the muscle back to its original levels (i.e. antagonist EMG amplitude did not decrease below baseline).

Kotzamanidis, 2006 [175]

The objective of this study was to examine if fatigue of an agonist muscle also caused fatigue to the antagonist. EMG signals were detected from the VM and VL (agonists) and BF (antagonist) muscles during isokinetic leg extensions at $60°\cdot s^{-}$

[1]. The results demonstrated no change in antagonist (BF) torque or EMG amplitude (when tested as an agonist) following fatigue of the agonist muscles (VM and VL). In other words, a fatiguing protocol performed on the leg extensors does not affect leg flexion torque.

Martin et al., 2006 [195]

The purpose of this study was to examine the effects of group III and IV muscle afferents from agonist or antagonist muscles on their motor neuron pools. Surface EMG signals were recorded from the biceps brachii and triceps brachii during electrically evoked potentials of the corticospinal tract at the cervicomedullary junction (CMEPs). The evoked potentials in the triceps were inhibited after bicep fatigue, but the potentials in the biceps were facilitated after tricep fatigue. The authors concluded that fatigue-sensitive afferents have different effects on flexors than they do on extensors.

Geertsen et al., 2008 [118]

The objective of this study was to compare the degree of disynaptic reciprocal inhibition of soleus motor neurons before and after 4 weeks of explosive strength training. Reciprocal inhibition was assessed by depression of the antagonist H-reflex. It has already been shown in multiple studies [43, 134, 230] that antagonist coactivation decreases with skill or strength training. This study adds a

potential mechanism for why that adaptation occurs. The results showed that disynaptic reciprocal inhibition of the antagonist increased from 6% to 22% after training. This increased inhibition of the antagonist helps explain the reduced coactivation that is commonly demonstrated.

Lévénez et al., 2008 [181]

The purpose of this study was to investigate the control mechanisms of antagonist coactivation at the cortical and spinal levels during a fatiguing contraction. Potentials evoked from the motor cortex (MEPs), the corticospinal tract (CMEPs), and brachial plexus (H-reflex and M-wave) were recorded from the triceps brachii during forearm flexions to help distinguish between spinal and supraspinal contributions to coactivation. Both MEP and CMEP in the triceps brachii increased linearly with fatigue. Conversely, the H-reflex increased during the early stages, but declined to 65% of its initial value by the end of fatigue. The authors concluded that peripheral excitatory drive by itself cannot mediate the level of antagonist coactivation during sustained contractions. Rather, coactivation is mediated by supraspinal mechanisms. Of additional interest to this dissertation is the fact that the authors[181] demonstrated no change in isometric forearm extension strength after fatigue of the forearm flexors.

Geertsen et al., 2010 [119]

The aim of this study was to assess soleus MEPs [elicited by Transcranial magnetic stimulation (TMS)] prior to and at the onset of plantar- and dorsiflexion (i.e. in both the agonist and antagonist roles). As an agonist, soleus MEPs were significantly facilitated when TMS was applied 50 ms prior to the onset of plantarflexion. Interestingly, they were also facilitated prior to onset of dorsiflexion (but to a lesser extent). Comparisons of MEPs and CMEPs suggest that the antagonist facilitation was occurring at subcortical levels. The authors suggested that the simultaneous activation of both the agonist and antagonist may be useful for making quick changes in movement direction.

Kuruganti et al., 2011 [179]

The objective of this study was to determine if antagonist coactivation played a role in the bilateral force deficit (i.e. bilateral force is less than the summed unilateral forces). Antagonist coactivation, as assessed by EMG amplitude of the hamstrings, was similar during bilateral and unilateral leg extensions. This implies that alterations in antagonist coactivation are not responsible for the bilateral deficit.

Tillin et al., 2011 [291]

The purpose of this study was to examine the agonist and antagonist neural adaptations that occur with 4 weeks of unilateral resistance training. The authors

found increased agonist activation in the trained leg and decreased antagonist coactivation in both legs. The results of training studies, such as this one, are intriguing from a mechanistic point of view because they demonstrate that the interactions between agonists and antagonists can be altered. It is currently unknown whether the underlying mechanisms causing this decrease in coactivation are of a peripheral (i.e. desensitized GTOs) or central (i.e. decreased descending drive) origin.

Haruno et al., 2012 [136]

The purpose of this study was to examine the role of higher-order control over the level of co-contraction. Functional MRI of the brain was performed during isometric hand contractions (at the wrist). Conditions were either alternating flexion/extension (i.e. reciprocal activation), or co-contraction. The authors found that blood oxygen level-dependent (BOLD) activity in the caudo-dorsal premotor cortex (PMd), primary motor cortex (M1), cerebellum (CB), and supplementary motor area (SMA) were correlated with torque (during flexion/extension conditions). BOLD activity in the ventral premotor cortex (PMv), M1, SMA, and putamen were correlated with averaged EMG amplitude during co-contraction. It was concluded that the CNS can use distinct processes to coordinate muscles, and different centers of the premotor cortex can be used for either reciprocal activation or co-contraction.

2.1.1 Summary of "Agonist/Antagonist Interaction and Peripheral Feedback"

The coordinated interactions between agonist and antagonist muscle groups can be extremely complex. This coordination between opposing muscles depends on the integration of multiple shared inputs, which can be central or peripheral in origin. The central inputs can be supraspinal in origin, consisting of various descending pathways, or from solely within the spine, such as Renshaw cells[88, 235] and central pattern generator (CPG) interneuron networks[46]. The supraspinal pathways can lead to either excitation or inhibition of the antagonist depending on the situation, and are regulated by the motor cortex[150, 181, 278], cerebellum[107, 292, 305], and other premotor areas[136]. Renshaw cells inhibit neighboring α-motor neurons[235] and the Ia inhibitory interneurons projecting to the antagonist α-motor neurons[214]. The peripheral inputs include muscle spindles (group Ia and II afferent), golgi tendon organs (group Ib afferent), and various smaller group III and IV afferents (such as chemoreceptors, nociceptors, and mechanoreceptors). Group Ia afferent neurons both mono- and disynaptically excite the agonist α-motor neurons, and disynaptically inhibit the antagonist α-motor neurons[87, 278]. They have a dynamic response and are more sensitive to quick lengthening of the muscle than to slow or static conditions [201]. Group II afferent neurons disynaptically excite the agonist α-motor neurons, and don't appear to have any appreciable connections to the antagonist. Group Ib afferent neurons can both disynaptically inhibit or excite the agonist α-motor neurons[87]. They synapse more strongly with Ib inhibitory interneurons, and therefore, that is the default response. However,

during situations requiring intentional co-contraction, the Ib inhibitory interneurons are inhibited by the CNS (disinhibition) and the lesser, Ib excitatory interneurons prevail[214]. Interestingly, group Ib afferents are significantly more sensitive to tension in the tendon from contraction than from passive stretch, even if the tension in the tendon is equitable [145, 146, 153]. In fact, GTOs are sensitive enough to contractile forces to respond to the twitch of a single motor unit[27, 145]. The group Ib afferents also disynaptically excite the antagonist α-motor neurons[87], facilitating antagonist coactivation or co-contraction. To add further complexity, the disynaptic Ia and Ib excitatory pathways can actually share the same excitatory interneurons[152]. Small afferent nociceptors, in response to pain, lead to polysynaptic inhibition of the agonist α-motor neurons and excitation of the antagonist α-motor neurons[272]. The small cutaneous mechanoreceptors, sensitive to touch or pressure, can elicit flexion or extension reflexes[262], or even a complex series of excitation-inhibition-excitation cycles [115]. The role of agonist or antagonist in these instances is relative to the task being performed. Chemoreceptors, which are sensitive to changes in O_2, CO_2, and/or metabolic accumulates, can lead to inhibition of the agonist α-motor neurons[25]. Whether or not the chemoreceptors affect the antagonist is unknown. Furthermore, central and peripheral sources of input are not independent processes. The CNS can regulate the Ia afferents (presynaptic inhibition), Ib inhibitory interneurons, and Ia inhibitory interneurons[118, 222, 236]. Peripheral afferents also ascend to the brain and affect subsequent motor commands via long-loop reflexes[116]. The integration of all these

complex shared inputs ultimately regulates the coordination between agonist and antagonist muscle groups. Various input combinations can lead to either antagonist inhibition, coactivation, co-contraction, or even a preprogrammed pattern consisting of multiple phases[8].

2.2. Motor Unit Firing Properties

Liddell and Sherrington, 1925 [183]

The purpose of this study was to examine the inhibitory relaxation that occurs due to stimulation of an ipsilateral afferent nerve. The experiments themselves are actually not directly relevant to the present study. However, this paper was important because it was the first to recognize that a motor neuron and all of the fibers that it innervates behave as a single entity. Accordingly, Liddell and Sherrington are credited with being the first to use the term *motor unit*.

Adrian and Bronk, 1929 [5]

The purpose of this study was to examine the firing properties of motor neurons. This investigation was the first to detect action potentials from a single motor unit[85]. An important contribution from Adrian and Bronk[5] comes from their statement, “the gradation of force is brought about by changes in the discharge

frequency in each fibre and also by changes in the number of fibres in action" (p.137). Thus, this study was the first to recognize the two primary ways to increase force production: recruit motor units and increase their firing rates.

Denny-Brown and Pennybacker, 1938 [80]

The purpose of this study was to examine the EMG and force outputs produced from involuntary twitching. This study was the first to demonstrate an orderly recruitment of motor units. The authors discovered that during any voluntary movement the same motor units were always the first to discharge, and there was a consistent sequence of recruitment as intensity increased. Furthermore, they recognized a difference in the size of the motor units in the ordered recruitment (size was assessed by the innervation ratio). Denny-Brown and Pennybacker stated (p.324),

> "The early motor units in normal gradual voluntary contraction are always in our experience small ones (Fig.11). The larger and more powerful motor units, each controlling many more muscle fibres, enter contraction late."

This observation was astounding for their time, and to this day is still the accepted understanding of the process for motor unit recruitment.

Gilson and Mills, 1941 [122]

The purpose of this study was to examine motor unit firing properties during low-intensity voluntary efforts. An important finding was that the consistency of the amplitude of single motor unit action potentials, regardless of the intensity of the contraction. The authors noted that increases in spike amplitude were due to either spatial changes in the relation of the electrode to the detected fibers, or the summation of multiple motor unit action potentials. It was concluded that force is modulated by recruitment of new motor units and changes in their firing rates, rather than their amplitude. Therefore, this observation, in conjunction with those made by Denny-Brown and Pennymaker[80] as well as Adrian and Forbes[4], demonstrate the beginning of the "all-or-none" principle of motor unit activation.

Bigland and Lippold, 1954 [26]

The goal of this investigation was to detect human motor unit action potentials to further examine the relationship between firing rate and force. Fine wire EMG signals were detected from two small muscles of the hand: adductor pollicis and abductor digiti minimi. Maximal and submaximal electrical stimulations were applied to the ulnar nerve. By progressively increasing the stimulation frequency in a step-like fashion from 0 to 100 Hz, the authors found that force increased linearly with stimulation frequency until around 35-45 Hz. Once 35-45 Hz had been reached, tension plateaued or slightly decreased. Due to this

plateau, the authors concluded that 35-45 pulses per second (pps) was probably the maximal firing rate for most motor units. They also noticed that the lowest threshold motor units (< 5% MVC) demonstrated the lowest initial firing rates, but also showed a greater firing rate range than high-threshold motor units.

Henneman, 1957 [138]

The purpose of this study was to examine the intensity of stimulation required to elicit discharges in motor neurons of varying sizes. Neuron size was determined by the size of the action potential produced, which linearly related to axon diameter[98, 117]. Henneman[138] found that motor neurons can be graded by their susceptibility to firing. In short, smaller neurons required a lower stimulation intensity to elicit firings (i.e. lower threshold), and the threshold of the neurons increased progressively with neuron size. It should be noted that it does not appear (judging by the lack of citation) that Henneman was aware of the size-dependent finding previously reported by Denny-Brown and Pennymaker[80].

Henneman et al., 1965 [139-141]

Eight years after his initial findings[138], Henneman and his colleagues published a series of papers further describing the relationship between a neuron's size and its firing properties. The purpose of the third and most influential paper [139] was two-fold: (a) to determine if motor neuron excitability is source-dependent,

or if motor neurons respond to all excitability the same, regardless of the source; and (b) to see if neuron size also dictates its susceptibility to inhibition. In regards to the first question, the authors found that the susceptibility of a neuron to discharge was size-dependent, regardless of the source of excitation (e.g. stretch reflex, flexor reflex, electrical stimulation, etc.). Furthermore, there was a size-dependent effect on a neuron's susceptibility to inhibition, although the relationship was opposite to the excitation relationship (the larger the neuron, the more susceptible it was to inhibition). However, it should be noted that the authors' measure of "inhibitibility" was to examine the order in which cells were silenced by inhibitory stimulation. Therefore, the true finding is that neurons that are recruited later are derecruited earlier (i.e. recruitment threshold = derecruitment threshold).

Clamann, 1970 [48]

The aim of this study was to examine the motor unit firing properties of the BB and abductor pollicis brevis (APB) as they relate to isometric tension. Action potential trains were detected with fine-wire electrodes. The indwelling recordings from the BB were at various depths from 0.5 – 2.5 cm. The results showed that higher threshold motor units had a lower firing rate and smaller firing rate ranges than lower threshold motor units. Interestingly, Clamann also found that the higher threshold motor units tended to be located superficially (0.5 – 1.0 cm deep) and the low threshold motor units were deeper within the muscle (1.0 – 2.5 cm).

Milner-Brown et al., 1973 [209-211]

In 1973, Milner-Brown, Stein, and Yemm published a series of three papers examining motor unit properties during voluntary isometric contractions. Amazingly, Stein's laboratory developed a spike-triggered averaging technique that allowed for the calculation of the contractile properties of individual motor units[210]. Specifically, they were able to determine the relative contribution of twitch force from each additionally recruited motor unit. This development allowed for the first direct evidence of the size principle, which was performed in the FDI. Their Figure 3 [211] demonstrated a highly linear positive relationship between a motor unit's recruitment threshold and the amount of force it is able to produce (all correlation coefficients were > 0.8). They also observed [211] that although the higher threshold motor units can generate more force, "the contribution of recruitment to increases in voluntary force declines at higher force levels" (p.359). They subsequently concluded that, at higher force levels, increases in firing rate (i.e. rate coding) was the dominant mechanism for continuing to increase voluntary force [209].

Gydikov and Kosarov, 1974 [131]

The objective of this study was to examine the relationship between BB motor unit firing rates and force, and how that relationship is affected by motor unit recruitment threshold, size, and susceptibility to fatigue. The authors divided motor units into two classifications[130] based on firing patterns: tonic and phasic. They

found that the tonic motor units, which are small and low-threshold, increase firing rate with force and then plateau, and are resistant to fatigue. The phasic motor units, which are large and high-threshold, continued to demonstrate increases in firing rate with force (i.e. no plateau), and were very fatigable.

Stephens and Usherwood, 1977 [274]

The aim of this investigation was to examine the contractile properties and fatiguability of various motor units from the FDI. The authors were able to reproduce a recruitment threshold versus twitch force relationship that was very similar to that reported by Milner-Brown et al.[211]. The results suggested that lower-threshold motor units had longer contraction times and were more fatigue-resistant than higher-threshold motor units. These results supported the findings from Gydikov and Kosarov[131].

Lüscher et al., 1979 [187]

Previous work from Henneman's laboratory[138, 139] had demonstrated that a motor neuron's susceptibility to discharge was dependent on its size. However, the reason for this was still unknown. The purpose of this study was to determine if terminal branching of group Ia afferent inputs could be the mechanism underlying the size principle. The authors' found that afferent impulses from Ia fibers invade small motor neurons more completely than the extensive branching that occurs with

larger motor neurons. This means that an action potential traveling down a Ia fiber will result in the activation of a higher percentage of terminal endings on small motor neurons. The more efficient activation, in turn, produces a larger EPSP to the smaller motor neuron and "accounts for their greater susceptibility to discharge" (pg. 859). The authors suggested that the soma size of a motor neuron may be a factor in the degree of branching from an approaching Ia fiber.

Kukulka and Clamann, 1981 [177]

The purpose of this study was to examine the relative contribution of firing rate changes and motor unit recruitment to isometric force production in the BB and adductor pollicis muscles. Fine wire EMG signals were detected from the muscles during isometric step contractions up to 100% MVC. The two muscles exhibited very different recruitment profiles. Approximately 47% of the BB's detected motor units were active at 30% MVC, 67% were active by 40% MVC, and recruitment of additional motor units continued up to 88% MVC. Conversely, 41% of the adductor pollicis' detected motor units were recruited by 10% MVC, 86% were active by 30% MVC, and all of the motor units were recruited by 50% MVC. Additional increases in force beyond the point of full motor unit recruitment were presumed to be due to increases in firing rates. Therefore, it was concluded that small, distal muscles of the hand rely more on firing rate changes for their force modulation, while larger, proximal muscles rely more on motor unit recruitment.

Belanger and McComas, 1981 [19]

The objective of this study was to compare the percentage voluntary motor unit activations of the plantarflexors and dorsiflexors with the interpolated twitch technique. The subjects consistently demonstrated complete activation (100% recruitment of available motor units) of the tibialis anterior (TA) muscle. However, the plantarflexors were more difficult to fully activate. Estimations from their Figure 3 suggested that the subjects were able to voluntarily activate approximately 92% of their available plantarflexor motor units (i.e. the superimposed twitch increased maximal force by approximately 8%). The authors suggested that differences in percentage voluntary activation might be due to differences in the relative contributions of Ia spindle afferents and descending pathways to each muscle's synaptic input (i.e. the TA relies more on descending pathways and less on Ia afferents than the plantarflexors).

De Luca et al., 1982 [62]

The purpose of this investigation was to examine the control of motor unit behavior during linearly force-varying contractions. Needle EMG signals were detected from the deltoid and FDI muscles during separate triangular contractions (i.e. ramp-up then ramp-down) up to 40% and 80% MVC. The results showed that, at any given submaximal force level, the firing rates of earlier recruited motor units were higher than those of later recruited motor units. This pattern of motor unit

behavior would later[67] be described as the onion-skin phenomenon. Furthermore, the initial firing rates at recruitment were higher than the firing rates at derecruitment. Lastly, due to between-muscle differences in the way firing rates increased with force, the authors concluded that the deltoid muscle relies more on motor unit recruitment to generate additional force, while the FDI is more dependent on firing rate changes.

De Luca et al., 1982 [63]

The purpose of this study was to investigate how changes in individual motor unit firing rates can be controlled to produce precise changes in force. The same methods as a previous study[62] were used. Interestingly, the authors found that the firing rates of small, slow-twitch motor units decreased during the ramp-down in force prior to the decrease in the large, fast-twitch motor unit's firing rates. Additionally, the authors suggested that small variations in force (i.e. force steadiness) were due to all of the motor neurons for a muscle being subject to the same common drive.

ter Haar Romeny et al., 1982 [287]

The purpose of this study was to investigate the motor unit recruitment properties of a multifunctional muscle during different tasks. The muscle examined was the BB, which is both a flexor and a supinator of the forearm. The same motor

units were recorded during isometric forearm flexion, isometric supination, or a combination of both. Some units could only be activated during one of the tasks. However, most of them were recruited during all 3 trials. Motor units with a high-threshold during flexion demonstrated a lower threshold while simultaneously supinating. Conversely, motor units that were low-threshold during flexion were harder to recruit during the combined task. The authors concluded that motor units in a multifunctional muscle are recruited when a linear combination of exerted forces exceeded a certain threshold. On a methodological note, the author's cutoff between low- and high-threshold motor units (2.5 N·m flexion) equated to approximately 3.5% MVC[288].

Bellemare et al., 1983 [21]

The purpose of this study was to measure individual motor unit firing rates during MVCs for the BB, adductor pollicis, and soleus muscles. Prior to this investigation, most studies were limited to 75-80% MVC for single motor unit recordings. The results showed significantly higher mean motor unit firing rates in the BB (31.1 Hz) and adductor pollicis (29.9 Hz) muscles than in the soleus (10.7 Hz). The authors suggested that the between-muscle differences could be representative of the fiber type composition differences. Furthermore, it was suggested that, during a voluntary effort, the firing rate for a motor unit will never exceed the minimum required to produce maximum force.

Binder et al., 1983 [28]

The purpose of this study was to examine which was more highly correlated with the order of motor unit recruitment: motor unit size, or motor unit type. The authors compared the axonal conduction velocities (CV) of soleus motor neurons of the same histological composition to their order of recruitment. The results showed, that in the absence of different motor neuron types, neuron size (defined by axonal CV) was highly correlated with the order in which the neuron was recruited. It should be noted, however, that motor neurons of different histological types were not compared. To completely test their hypothesis, the authors should have also determined the recruitment order of neurons of similar CVs, but different compositions (although this is potentially very difficult to find).

ter Haar Romeny et al., 1984 [288]

The authors had previously shown that the recruitment thresholds of motor units from multifunctional muscles varied based on the task[287]. The purpose of this study was to determine if those varying task-oriented motor units differed in their location within the long head of the biceps brachii. The authors found that motor units that are only active during flexion were located laterally, while the units that are active only during supination were located medially. Units whose threshold depended on a linear combination of exerted forces were located medially, and those that behaved nonlinearly were located centrally. The authors proposed a

somatotopic model of synaptic inputs to the motor units of the biceps brachii (demonstrated by their Figure 7).

Broman et al., 1985 [32]

The purpose of this investigation was to examine the interactions between motor unit recruitment and firing rate changes with increases in force production. Needle EMG signals were recorded from the TA and FDI muscles. The authors demonstrated that recruitment of a new motor unit leads to slight decreases in the firing rates of the already active motor units. They suggested that this mechanism's purpose is to allow for smooth force production by avoiding sudden jumps in force that would occur when a new motor unit is recruited. The authors proposed that this mechanism is due to the Ia afferent loop and Renshaw cell recurrent inhibition.

Thomas et al., 1987 [289]

The purpose of this paper was to determine if there was ordered recruitment of motor units during a dynamic movement. Needle EMG signals were detected from the FDI and APB muscles during isometric contractions and repeated scissor movements. The isometric contractions were performed first to identify motor units, as well as their recruitment thresholds and twitch amplitudes. Using that information, the same motor units were identified during the scissor movements. The results showed that recruitment during the scissor movements was ordered by

increasing twitch size. Any deviations from an orderly recruitment were primarily between motor units of similar thresholds (see their Fig. 8).

Kamen and De Luca, 1989 [156]

During a previous study, De Luca et al.[62] had demonstrated that the order of motor unit recruitment was maintained (but in reverse) for derecruitment. However, that study was performed in young, healthy individuals. The purpose of this investigation was to share some observations found in older individuals. The authors demonstrated an unusual firing pattern in a 63 year old subject in which some of the later recruited motor units were also among the last to be derecruited (i.e. no reversal of order). Possible mechanisms for this phenomenon, such as differences in antagonist coactivation or active reinnervation of motor units were discussed. However, ultimately the authors were unable to provide an explanation for the unusual firing patterns.

Nardone et al., 1989 [217]

The objective of this study was to determine if the typical ordered recruitment of motor units was exhibited during eccentric muscle actions. EMG signals were recorded from the gastrocnemius and soleus muscles during eccentric muscle actions in an apparatus that was weighted to have full dorsiflexion as the natural position. Therefore, after performing a plantarflexion, the plantarflexors

performed an eccentric muscle action simply by releasing the plantarflexion tension. Since the machine was moving the foot into dorsiflexion, activation of the dorsiflexors was unnecessary. Interestingly, the authors found that the gradual deactivation of the plantarflexors to induce the lengthening was characterized by a derecruitment of the low-threshold, slow-twitch (defined by half-relaxation time) motor units. Instead, the high-threshold, fast-twitch motor units were the ones that remained active during the lengthening. However, the authors were unable to propose a possible mechanism for this selective recruitment of high-threshold motor units.

Tax et al., 1989 [282]

The purpose of this study was to compare the motor unit recruitment properties of the BB during dynamic and isometric muscle actions at varying velocities and force levels. The results demonstrated that the order of motor unit recruitment was the same for both dynamic and isometric muscle actions. However, there were still significant differences between the motor control strategies used for the two muscle action types. The dynamic muscle actions were characterized by lower recruitment thresholds and higher initial firing rates than the isometric muscle actions. It was concluded that the manner in which the CNS controls motor units is task-dependent.

Gandevia et al., 1990 [109]

The aim of this study was to investigate the firing properties of motor neurons that innervate muscles in a deafferented hand. Microelectrodes were inserted into the ulnar nerve to record from the axons of motor neurons. The hand was then blocked distal to the microelectrodes by use of local anesthetic. Despite the absence of afferent feedback, subjects were still able to recruit and sustain motor neuron activity, although the coefficients of variations for the interpulse intervals were higher than normal. During attempted MVCs, mean firing rates were significantly lower than normal, demonstrating the facilitatory influence of peripheral afferents on motor neurons. During sustained efforts, mean firing rates did not decrease over time as is typically shown with fatigue. This suggests that there could be a disfacilitation from afferents that occurs over time in fatiguing contractions.

Cope and Clark, 1991 [53]

The purpose of this study was to examine the ability of various motor unit properties to predict recruitment order in the decerebrate cat. Twitch contraction time was the best predictor, demonstrating a 94% agreement in rank order with recruitment order. Axonal conduction velocity (87%), tetanic tension (84%) and fatigue index (75%) were also significant predictors. It should be noted, however, that, due to the condition of the cat (i.e. decerebrate), all of the motor units were

assessed during a stretch reflex or electrical nerve stimulation. Therefore, it is unknown how well these variables would predict recruitment order under voluntary conditions.

Masuda and De Luca, 1991 [198]

The purpose of this study was to further investigate the relationship between motor unit recruitment threshold and muscle fiber action potential conduction velocity (CV). Needle EMG electrodes were inserted into the TA to detect the action potentials from single motor units, and a linear surface electrode array was used to assess CV. The authors found that the conduction velocity of the muscle increased with the recruitment of each additional motor unit (during linearly increasing isometric force). Two conclusions were drawn: (a) the higher the last recruited motor unit's threshold is, the higher the muscle's CV, and (b) the higher the motor unit's threshold, the more it contributes to the muscle's CV.

Fallentin et al., 1993 [101]

The objective of this study was to examine motor unit recruitment patterns during prolonged isometric contractions of the forearm flexors. Fine wire electrodes were inserted in the BB muscle during the isometric contractions, which equated to approximately 10-40% MVC. During sustained contractions at 10% MVC, the authors witnessed motor unit rotation, which is a phenomenon where initially active

motor units get replaced by newly recruited units. However, no motor unit rotation was exhibited during sustained contractions at 40% MVC.

Macefield et al., 1993 [190]

The purpose of this study was to quantify the contributions of muscle afferent feedback to motor neuron firing rates. Action potentials from individual motor axons in the common peroneal nerve were detected with and without afferent feedback. Acute deafferentiation was achieved by anaesthetic block of the nerve 5-7 cm distal to the recording site. Mean firing rates of deafferented motor axons were ~10 Hz and ~6 Hz lower than normal during maximal (18.6 to 28.2 Hz) and half-maximal (10.8 to 16.5 Hz) efforts, respectively. Typically, motor neuron firing rates tend to decrease with fatigue during sustained maximal contractions.[25, 109, 194] However, in this study[190], after the first 5 sec of a prolonged MVC, the deafferented motor neurons maintained their firing rates. This suggests that afferents have an integral role in the progressive decrease in motor neuron firing rates during fatigue. Finally, it was concluded that muscle afferents can increase the excitatory drive to the motor neuron pool by approximately one-third.

De Luca and Erim, 1994 [67]

This review paper made two important contributions to the literature. First, it introduced the "onion-skin" model to help explain the relationship between mean

motor unit firing rate and recruitment threshold. Second, it introduced a simple hydraulic model to summarize the CNS's regulation of motor unit firing rates (see their Fig. 4). Specifically, the hydraulic model demonstrated how the level of excitation from common drive can control how many motor units are recruited, as well as their firing rates.

De Luca et al., 1996 [68]

Previous studies which had examined motor unit firing rates during constant-force contractions observed either gradual decreases with time[231], gradual increases[199, 200], or increasing instability[224]. Therefore, the purpose of this study was to assess the direction of motor unit firing rate changes during constant-force contractions, and to determine if they differed across motor units of varying recruitment thresholds. Needle EMG signals were recorded from the FDI and TA during the initial experiment and from 5 separate hand muscles during extensions of the hand in a second subexperiment. The results showed that the motor unit firing rates decreased during the first 8-15 sec of an isometric constant force contraction. Furthermore, higher-threshold motor units demonstrated a greater decrease in firing rate during this period than the lower-threshold motor units. Since the force remained constant, the authors had difficulty explaining the possible compensatory mechanism that could account for the decreased firing rates. No additional recruitment was observed during the contractions. The second subexperiment failed to demonstrate any antagonist compensatory mechanism. The authors concluded

that Kernell's "late-adaptation phenomenon"[164] could explain the results, but more evidence would be needed to support this conclusion.

Erim et al., 1996 [97]

The purpose of this study was to further examine the relationship between motor unit recruitment and firing rate. Needle EMG signals were detected from the TA during isometric muscle actions that slowly increased to MVC. The authors demonstrated a weak, positive relationship between a motor unit's initial firing rate and its recruitment threshold. However, the strength of the association was not reported (i.e. no correlation coefficient). Interestingly, the firing rates of all the motor units, regardless of their recruitment threshold, converged to similar values at MVC.

Tansey and Botterman, 1996 [279-281]

The purpose of these three papers was to compare recruitment and firing rate properties for motor units with different physiological and histochemical profiles. Cat gastrocnemius motor units were categorized according to Burke's[40] four-type classification system: slow-twitch (S), fast-twitch fatigue-resistant (FR), fast-twitch fatigue-intermediate (FI), and fast-twitch fatigable (FF). During electrical stimulation at 40% maximal tetanic tension, 100% of S, 95% of FR, 86% of FI, and 49% of FF motor units were active. Motor unit recruitment was in the predicted

order (S > FR > FI > FF) for 93% of the pairs. The authors found faster firing rates (48.4 pps) among fast-twitch motor units than in S (27.8 pps), but no differences were found between the fast-twitch motor units. It should be noted that these firing rate patterns conflict with those found in voluntary conditions in man[62, 63, 67, 68].

Gandevia et al., 1999 [111]

The aim of this study was to explore the possibility that voluntary contractions induce changes at subcortical levels within the motor pathways from M1 to the α-motor neuron. MEPs and CMEPs were detected with EMG to assess changes in motor neuron firing properties immediately following voluntary contractions. Amplitude responses to CMEPs reduced to approximately a third of baseline values immediately following voluntary isometric contractions lasting 10 sec (see their Fig. 6). Furthermore, a similar depression was found in MEPs after the voluntary contraction. These reductions lasted approximately 2 minutes and were eventually followed by a longer-lasting potentiation of the responses. A satisfactory explanation for these acute neural adaptations was not provided.

Kamen and Du, 1999 [159]

The objective of this study was to further examine the interaction between motor unit recruitment and firing rate in the modulation of force. Needle EMG signals were detected from the FDI during slow, triangular isometric muscle actions

up to 40% MVC. Contrary to what was found by Broman et al.[32] and later again by Westgaard and De Luca[304], this study did not demonstrate decreases in motor unit firing rates when a new motor unit was recruited. The authors concluded that there is no short-term disfacilitation of previously active motor units to effect precise regulation of force.

Westgaard and De Luca, 1999 [303]

The purpose of this study was to examine motor unit behavior during long, sustained contractions. Motor unit firings were recorded from the trapezius muscle during sustained contractions at approximately 4% MVC. During the first few minutes of the contraction, the motor unit firing rates remained quite stable. However, low-threshold motor units became inactive after a few minutes and were substituted by new motor units with a higher threshold. Occasionally, the original motor units that had been substituted would become active again towards the end of the contraction. The authors suggested that this motor unit rotation is a mechanism to protect motor units from excessive fatigue during sustained contractions.

Sohn et al., 2000 [272]

The purpose of this study was to examine the effects of muscle pain on motor unit firing properties. Fine-wire EMG signals were recorded from the masseter muscle before and during the pain stimulus, which was induced by

intramuscular Capsaicin injection. The authors found that the stimulation of nociceptors (group III and IV afferents) led to an inhibition of motor unit firing. Specifically, mean firing rates were lower at any given isometric force level during the pain condition when compared to baseline. Surprisingly, despite the inhibition, no changes in recruitment threshold were observed. However, that was likely due to recruitment threshold being a relative measure of force, and not an absolute measure of excitation (e.g. electrical stimulation). Furthermore, the order of recruitment was maintained during the pain condition.

De Luca and Erim, 2002 [69]

The purpose of this study was to determine if common drive existed within synergistic muscles. Needle EMG signals were recorded from the ECRL and ECU muscles during isometric hand extensions at 20-30% MVC. Cross-correlations of mean motor unit firing rates were used to assess common drive. The cross-correlations revealed the presence of common drive between synergistic muscles. However, the magnitude of the common drive was less than is typically observed from motor units within the same muscle. The authors suggested that, in some conditions, the CNS treats synergistic muscles as a single functional unit.

Grande and Cafarelli, 2003 [124]

The purpose of this study was to determine if the stimulation of Ia afferents via vibration would alter motor unit firing properties. This was first performed with reflexes and then subsequently during voluntary contractions to determine how the vibration affected already active motor units. VL motor unit recruitment thresholds and firing rates both decreased during reflex contractions following patellar tendon vibration. During the voluntary contractions, bursts of vibration led to brief reductions in the firing rates, as well as the recruitment of additional motor units (see their Fig. 4D). It was concluded that Ia afferents modulate motor neuron firing rates and recruitment properties. The authors also suggested that the initial burst from Ia afferents is important in activating a muscle from the relaxed state.

Taylor et al., 2003 [284]

The objective of this investigation was to identify the motor unit firing properties that are responsible for fluctuations in force. Surface EMG signals were detected from the FDI during abduction of the index finger. The experimental results were compared to computer simulations based on Fuglevand's model of recruitment and rate coding[108]. The model also included varying levels of motor unit synchronization. Despite attempting multiple simulated combinations of recruitment and rate coding, the authors were unable to adequately replicate the coefficient of variation for force that was observed in the experimental trials,

especially at the higher force levels (above 50% MVC). Adding synchronization to the model did not seem to alter the coefficients of variation. The authors suggested that motor unit synchronization may dampen the effects of firing rate variability on force fluctuations.

Tracy et al., 2005 [293]

The purpose of this study was to explore the relationship between motor unit firing rate variability and force fluctuations for both young and older adults. Fine-wire EMG signals were detected from the FDI during steady-force isometric muscle actions at various force levels. Variability for motor unit firing rates and force were measured as the coefficient of variation. The coefficient of variation for firing rates was significantly higher in older adults than in the young subjects. There was a positive, but weak relationship between coefficient of variation for firing rate and coefficient of variation for force ($r^2 = 0.20$). These results were interpreted by the authors as evidence that the variation in firing rates contributes significantly to increased motor variability and force fluctuations with aging.

Knight and Kamen, 2008 [171]

The objective of this study was to investigate the relationship between voluntary activation and maximal motor unit firing rates in both young and old subjects. The authors were attempting to identify the reason that electrical

stimulation increases force production. They hypothesized that the inability to produce maximal force voluntarily was due to either incomplete recruitment, suboptimal firing rates, or a combination of both. They found that the additional force (beyond MVC) from an interpolated twitch was significantly correlated with maximal firing rates ($r = -0.62$). In addition, voluntary activation level was correlated with maximal firing rates at $r = 0.68$ (also statistically significant). The authors concluded that maximal firing rate was an important factor limiting maximal force production.

De Luca et al., 2009 [71]

The purpose of this study was to examine the effects of motor unit recruitment and proprioceptive feedback on common drive. Four muscles, all with varying levels of spindle densities, were investigated (TA, trapezius, FDI, and VL). The results showed a strong, negative relationship between the correlation coefficient of motor unit firing rates (i.e. magnitude of common drive) and the muscle's spindle density ($r = -0.942$). The authors concluded that common drive originates in the CNS and is reduced by the proprioceptive feedback from muscle spindles and GTOs.

De Luca and Hostage, 2010 [72]

The purpose of this study was to characterize the relationship between motor unit recruitment threshold and mean firing rates during voluntary isometric contractions and to formulize that behavior. Surface EMG signals from three separate muscles (VL, FDI, TA), exhibiting varying maximal recruitment ranges, were detected at 20, 50, 80, and 100% MVC and decomposed into the constituent motor unit action potential trains. The linearity of the relationship (defined by R^2) between mean firing rate and recruitment threshold was much higher for individual subjects than it was for the group. Pooling motor units from multiple subjects together reduced the R^2. Therefore, the R^2 should be determined individually for each contraction, and then averaged with other R^2 values. The authors found that the slope of the relationship becomes less negative (i.e. flatter) as the target force level (as a %MVC) increases (Figure 6-A). They go on to describe this as an "operating point" which is the magnitude of the slope for the mean firing rate vs. recruitment threshold relationship. Essentially, this operating point decreases monotonically relative to excitation. The operating point differs slightly between subjects, but substantially between muscles. Of particular interest to the methods of the present dissertation, the authors note in Appendix 2 that the subject's ability to match the force template had a significant influence on the group analysis. If a subject was unable to reach and sustain the target force, then their motor units would have slightly lower firing rates and therefore, pull the group regression downward.

De Luca and Contessa, 2012 [73]

Despite De Luca's previous findings[62, 72] regarding the relationship between motor unit firing rates and recruitment threshold, there was still some disparity in the literature[89, 165, 166] regarding the direction of that relationship. The aim of this study was to settle this controversy and propose a model that describes motor unit firing behavior. Surface EMG signals were detected from the VL and FDI muscles during trapezoidal isometric muscle actions of varying force levels and ramp speeds. The signals were then decomposed into their constituent motor unit action potential trains and analyzed. The first test was to determine if the decomposition algorithm introduced any bias. The investigators took a decomposed signal, randomized the firing occurrences, reconstructed it with added noise, and decomposed it again. The randomized signal did not demonstrate the characteristics of the onion-skin model, which showed that no bias was introduced by the algorithm. The authors observed that motor unit firing rates increased as a negative exponential function as force increased. They also found that the rate of rise of the firing rate trajectories were similar, regardless of the speed of the force ramp. Finally, and most importantly, the authors provided overwhelming evidence of the hierarchical control scheme that governs motor unit behavior, and demonstrated that the firing rates of earlier recruited motor units were higher than those of the later recruited motor units.

De Luca and Kline, 2012 [74]

The purpose of this paper was to perform a meta-analysis of the literature to explore potential relationships between the firing rates and recruitment thresholds of a motor unit, and the spindle properties of various muscles. A weak, inverse relationship was found between the average mean firing rate of a muscle (grand mean of all motor units) and the number of spindles within the muscle. The relationship became more negative and linear at higher force levels. Conversely, there was little to no relationship at very low force levels (i.e., 1-10% MVC). It has been established in the literature that, during slowly increasing isometric contractions, the firing rates of already activated motor neurons temporarily decrease slightly with the recruitment of each additional motor neuron. The authors proposed a model that the decrease in firing rate is due to the slackening of the muscle spindles, therefore reducing the excitation they provide the motor neurons. Since each spindle synapses with each motor neuron in the pool for that muscle, the authors conclude that differences in the total number of spindles are a major factor for why muscles have varying firing rates. According to their model, muscles with a low number of spindles (e.g., FDI) have higher firing rates and a small range of recruitment. Alternatively, muscles with lower firing rates and a large range of recruitment (e.g., VL) behave that way because of the muscle's large number of spindles.

2.2.1 Summary of "Motor Unit Firing Properties"

Thanks to the work performed by Liddell and Sherrington[183], we now know that a motor neuron and all of the skeletal muscle fibers that it innervates behave as a single entity, or as a *motor unit*. Since this observation, the understanding of how movement and force are regulated has increased exponentially. One action potential in the neuron always leads to one action potential in each muscle fiber that it innervates. The reason this advanced the field of neuromuscular physiology so much is because the recording of single muscle fiber activity can now be assumed to be reflective of the activity of the motor neuron itself. This finding, in conjunction with others [4, 80, 122], led to the eventual acceptance of the *all-or-none* principle.

During this same period, Adrian and Bronk[5] made the observation that the gradation of force could be accomplished by two separate, but related mechanisms: recruitment of motor units and changes in their firing rates. Both an increase in firing rate and the recruitment of an additional motor unit can lead to increases in force production. The separate work of Sherrington and Adrian was so influential in our understanding of the function of neurons that they shared the Nobel Prize for Physiology or Medicine in 1932. Later work[80] out of the laboratory of Denny-Brown, a former student of Sherrington's, further extended the understanding of motor unit recruitment introduced by Adrian. It was discovered that there was an orderly recruitment of motor units, and that the order was dependent on the motor unit's size. The smaller motor units, as assessed by innervation ratio, were always the earliest to become active, and the large powerful motor units typically entered

later[80]. Elwood Henneman[138-140] enhanced this concept even further with the discovery that a neuron's action potential threshold was highly dependent on the size of the soma. Therefore, the orderly recruitment presented by Denny-Brown could be explained by the observation that the smaller motor units (both in soma size and innervation ratio) were more susceptible to discharge, and therefore were always recruited early in a contraction. Unfortunately, Denny-Brown's findings went fairly unnoticed, and the size principle of motor unit recruitment is often credited to Henneman's work 19 years later.

The next advancement came from Milner-Brown et al.[211], whom provided the first direct evidence of the size principle. They developed a technique to measure the tension produced by single motor units, and showed a strong positive relationship between a motor unit's recruitment threshold and the amount of force it can produce. Subsequent work demonstrated additional differences between motor units of varying size, such as the amplitude of the action potential, the size and speed of the resultant twitch, the axonal conduction velocity, the firing rates and the susceptibility to fatigue[53, 89, 131, 209, 274]. The understanding of the relationship between a motor unit's recruitment threshold and its mean firing rate at any given force level has been greatly advanced by the work of Carlo De Luca and his colleagues[32, 62-64, 68, 72, 73, 97]. His work has demonstrated that earlier recruited motor units exhibit higher firing rates, and the gradual recruitment of each additional motor unit is characterized by progressively lower firing rates. This observation has been termed the *onion skin phenomenon* [67] and can be seen in Figure 5-B (section

3.3.8). However, despite this initial separation, the firing rates of all motor units, regardless of recruitment threshold, converge to similar values at MVC[97]. Another important contribution from De Luca's lab is the concept that all the motor units in a given pool receive the same common drive[63, 67] from the brain, and it is the properties of each individual motor unit that dictates how it responds to that drive. This alleviates the CNS from having to control each individual motor unit separately.

It has also been demonstrated that not every muscle uses rate coding and recruitment in the same way to control force[62, 177]. Smaller, more distal muscles that are typically associated with fine motor control, such as the muscles of the hand, are characterized by a relatively short recruitment range (e.g. all of the motor units are recruited by 50% MVC) and have to rely more on firing rate modulation (i.e. rate coding) to control force. Conversely, the larger more proximal muscles associated with powerful gross movements have a greater number of motor units and rely more heavily on recruitment to increase force (some larger muscles may recruit new motor units all the way up to 100% MVC).

Currently, one of the more interesting topics regarding motor unit firing properties regards the relative contributions from central and peripheral inputs. Work out of the lab of Simon Gandevia[109, 190] has suggested that muscle afferents can contribute up to one-third of the excitatory drive to the α-motor neuron pool. Deafferentation by chemical block significantly reduces motor unit firing rates. De Luca et al. has gone a step further and has hypothesized[74] that differences in the

total number of spindles embedded within a muscle may explain the between-muscle differences in recruitment range.

2.3. Motor Unit Synchronization

Piper, 1912 [232]

In 1912, Hans Piper published a book, titled *Elektrophysiologie menschlicher Muskeln* that described a series of his experiments. One of his more interesting findings was the observation of background oscillation in the EMG signal. This low amplitude oscillation was typically around 50 Hz and has often been credited[33, 299] as the original evidence of a synchronizing input to muscles.

Adrian and Bronk, 1929 [5]

This paper described the findings from a series of experiments that examined the frequency of motor neuron discharge during reflex and voluntary contractions in humans. In one experiment, the authors discovered that the EMG response to the flexion reflex consisted of large primary waves that recurred with the frequency of stimulation, along with some smaller, secondary waves. It was concluded that each primary wave was due to a "synchronous volley of impulses in many motor fibres evoked by the corresponding volley of impulses in the afferent nerve" (pg. 140-

141). The issue was not discussed any further as the paper's main focus was individual neuron behavior. Nonetheless, this may be the first investigation to propose that large oscillations, such as those found by Piper [232], might be due to the synchronization of multiple motor units.

Hoff et al., 1934 [144]

Immediately following a tendon-jerk (e.g., knee jerk reflex) is a silent period in which there is a cessation of action potentials from the muscle. The hypothesis to explain this silent period is that the afferent excitatory impulses from the reflex stimulation lead to a synchronous discharge of the motor neurons. Due to the motor neurons being synchronously discharged, there is a quiescent period that lasts a time period equal to that between their normal firings (from the neuron's normal refractory period). Hoff et al.[144] tested this hypothesis on decerebrate cats. The silent periods of the motor neurons were equal to the length of the neuron's discharge rate, regardless of the duration of time between the tendon tap and the previous discharge (i.e., regardless of when the next firing was supposed to occur). Therefore, it was concluded that the efferent volley from the tendon jerk reset the rhythm of all active motor neurons, subsequently leading to a silent period.

Buchthal and Clemmesen, 1941 [36]

The purpose of this investigation was to differentiate between the two major types of muscular atrophy: neurogenic and myogenic (named after their origin). The authors found that synchronous discharges of two separate motor units (detected with two needle electrodes) were short-lasting in normal, healthy subjects, but were much more prominent in subjects with muscular atrophy (and rigidity). In addition, subjects with neurogenic atrophy showed "single oscillations" in the action potentials thereby indicating a much larger degree of synchronous activity than patients with myogenic atrophy. This issue was further investigated in later studies [37, 38].

Renshaw, 1941 [235]

In this investigation, Renshaw found that antidromic impulses sent up a motor neuron have an inhibitory effect on the discharges of neighboring motor neurons. One of his proposed mechanisms (shown in his Fig. 6D) was the existence of an interneuron that receives input from axon collaterals of motor neurons and has an inhibitory effect on neighboring neurons. The existence of this interneuron was confirmed later by Eccles et al. [88] in 1954 and was referred to as a "Renshaw cell" for the first time. This is important because later studies [66, 135] have proposed that Renshaw cells, and the "recurrent inhibition" that they cause, are one of the potential mechanisms underlying synchronization between motor units. Conversely,

other studies [3, 35, 192] have suggested that Renshaw cell activity actually has a desynchronizing input on the neighboring motor neurons.

Arvanitaki, 1942 [9]

The purpose of this study was to examine potential non-synaptic interactions between neurons. Single neurons were prepared from dissection of the visceral ganglia of Aplysia (large sea slugs). Arvanitaki[9] termed the axonal areas of interest "ephapses", which are non-synaptic points of contact between two neurons. Interestingly, she found that an inactive neuron placed in close proximity to an active neuron weregin to fire in phase with the active one. Furthermore, two separate active neurons that are brought closer together will start to fire together, only to revert back to their independent rhythms following separation. This finding was proposed as one of the mechanisms underlying neuron synchronization.

Buchthal and Madsen, 1950 [38]

The purpose of this study was to investigate the occurrence of synchronization in normal muscles and in pareses of central and peripheral origin. This is the first investigation to attempt to quantify the magnitude of synchronous activity. Motor unit recordings were taken from the biceps brachii in 20 healthy subjects as well as in 258 patients suffering from atrophy of either central or peripheral origin. The incidence of points that were synchronized as a percentage of

the total points investigated was used to quantify synchronization (i.e. the percentage of firings that were synchronized). The contractions were held at an intensity that provided firing rates of 3-12 pulses per sec, which corresponded to approximately 4% MVC. In the normal, healthy subjects, an average of 18% of the firings were synchronized (within 10 ms). For the patients suffering from atrophy of a peripheral origin (e.g. traumatic lesion or compression of a peripheral nerve), synchronization was the same or lower than the normal subjects. However, synchronization was much higher (approximately 59% of firings were synchronized) in patients suffering from atrophy of central origin (e.g. amyotrophic lateral sclerosis, spinal muscular dystrophy, etc.). These results suggested that peripheral mechanisms had larger contributions to the synchronization between motor units than central mechanisms.

Bigland and Lippold, 1954 [26]

The major findings of this study were discussed previously, in section 2.2 (pg. 45). As a small added note, Bigland and Lippold[26] briefly mentioned the synchronization of motor unit firings. During their typical responses, the discharges seemed to be mostly asynchronous. However, if the muscle was already fatigued, then the synchrony became more apparent, and tremor was observed at approximately the same frequency as the groupings of action potentials (14 per sec).

Taylor, 1962 [283]

A subexperiment within a larger study was performed in response to the suggestion by Lippold et al. [184] that motor unit synchronization was a result of the self-oscillation in stretch-reflex arcs. In contrast to Lippold et al.'s hypothesis, Taylor[283] demonstrated no change in the grouping of motor unit firings following acute deafferentation in anaesthetized cats. These results suggested that synchronization relies more on central mechanisms and that reflex feedback is not a significant contributor (or at least is not a necessary contributor).

Woodward and Goldsmith, 1964 [310]

The purpose of this monograph was to introduce a new quantitative analysis for industry quality control measures. The authors presented the cumulative sum technique, which is used to detect trends in a long string of data. Fourteen years later, Peter Ellaway proposed [92, 93] the application of this technique to neurophysiology research. A complete description of this analysis, especially as it applies to neurological data, is provided on pg 85-86.

Perkel et al., 1967 [228, 229]

The purpose of these two papers was to introduce various statistical procedures for analyzing neuronal action potential trains. The first paper[228] discussed the use of post-stimulus-time histograms (PSTH) to estimate probability

distributions in single spike trains. The PSTH estimated the firing probability of a neuron as a function of time (starting at the onset of stimulation). The second paper[229], which was more relevant to the synchronization literature, discussed techniques that could be used to determine if two separate action potential trains were independent or dependent processes. This paper was the first introduction to cross-interval and cross-correlation histograms (the cross-interval histogram were utilized in this study) and to describe how various types of interactions between two neurons could affect these histograms.

Bryant Jr. et al., 1973 [34]

The purpose of this study was to examine the correlations between neuronal discharges of *Afdysia californica* (a sea slug). This animal was investigated because of the simplicity of the neural network, containing many common monosynaptic pathways. This study is of particular interest because it demonstrated that when two neurons have a common presynaptic input of the same sign (i.e., both EPSPs or both IPSPs), the probability of the two neurons firing simultaneously is significantly increased.

Milner-Brown et al., 1975 [212]

This study was actually a collection of three separate experiments designed to further understand the importance of motor unit synchronization in force

production, as well as trying to identify the potential underlying mechanisms. The authors used a unique method for quantifying synchronization. They detected both surface and indwelling EMG signals from the FDI. For each single motor unit discharge, a brief epoch encompassing that time point was also selected from the rectified surface EMG, and the two signals were compared. If the surface EMG signal showed a peak that was greater than what would be expected from a single motor unit, then it was presumed that other motor units were firing at that precise time as well (i.e. synchronized). The ratio between the amplitudes from the surface EMG and single motor unit recordings were, therefore, used as a synchronization ratio. In the authors' first experiment, it was shown that weightlifters exhibited a significantly greater synchronization ratio than the control subjects. In their second experiment, the authors had 4 subjects undergo a 6-week training program with their non-dominant hand. The synchronization ratio significantly increased after the 6-weeks of training. In the third experiment, reflex responses were compared between weightlifters and control subjects. There were no group differences in the early reflexes (e.g. M-wave and H-reflex). However, there was a significant difference in the late reflexes (V_2 and V_3), which are believed to be long-loop supraspinal reflexes. The authors therefore concluded that the training adaptations that led to the increase in motor unit synchronization were likely caused by changes in supraspinal pathways. It should be noted that the method used by the authors for quantifying synchronization was later questioned for its accuracy[312].

Mori, 1975 [215]

The purpose of this study was to examine the entrainment (see Appendix B for definition) of motor unit discharges as a neuronal mechanism underlying force oscillations and synchronization. The author demonstrated that when one motor unit maintains a stable firing rate (10 pps in this study), the oscillations in force and other motor unit firing rates follow. In essence, the stationary motor unit acts as a pacemaker that alters the natural firing properties of the homonymous motor units. This finding raises a serious methodological question regarding studies that investigate synchronization using methods that control for motor unit firing rate.

Shiavi and Negin, 1975 [269]

The purpose of this investigation was to determine if simultaneously active motor units are centrally regulated together, or if they are independent processes. Fine-wire electrodes were used to detect motor unit action potential trains from the TA during low-intensity isometric dorsiflexions. Individual motor unit interpulse intervals were analyzed, as were cross-interval histograms for each motor unit pair. The authors were unable to find any significant interaction between simultaneously active motor units, and they therefore concluded that the motor units fired independently of each other. To explain the ability to produce smooth force contractions, despite independent motor unit control, the authors suggested a

regulatory effect of the viscoelastic properties of the muscle. It should be noted that these studies contradict the more observed finding of common drive[67].

Dietz et al., 1976 [84]

The objective of this investigation was to further explore the amount of motor unit synchronization that occurs during voluntary contractions. Motor unit spike train pairs were recorded from within the FDI muscle, as well as between synergists (gastrocnemius and soleus). Cross-correlation analyses revealed a strong tendency towards synchronization, and the majority of motor unit pairs exhibited a single, central peak in the cross-correlogram at a latency of 0 ms. Furthermore, motor unit synchronization seemed to be equally pronounced in the hand and leg muscles.

Sears and Stagg, 1976 [247]

This was one of the first papers to hypothesize that if two motor neurons share a common presynaptic input, then an excitatory potential from that shared input would momentarily increase the probability of firing in both neurons. The aim of this study was to examine the potential presence of short-term synchronization among motor neurons. Intracellular recordings were made from external intercostal motor neurons in 10 anaesthetized cats and 1 conscious human subject. The subsequent post-stimulus spike histograms were compared to MUAPT histograms

(from indwelling EMG). The intercostal muscles were chosen because they are divided into well-defined sectors. Thus, multiple neurons, which would share the same nerve filament leading to them, could be detected within the same segment. The general form of the motor unit histograms was similar to the neuronal data, with the exception of having slightly wider peaks. Furthermore, the primary peak extended to ±3 msec, which supports the hypothesis of short-term synchrony being due to common presynaptic connectivity.

Adam et al., 1978 [3]

The purpose of this study was to explore the regulatory role of the Renshaw cell pathways on the interactions between motor neurons. Two motor neuron spike trains were simultaneously recorded from 19 adult decerebrate cats, cross-correlated, and constructed into histograms. Renshaw cell activity was blocked by injection of atropine sulfate and mecamylamine[307]. Cross-correlation histograms from before and after Renshaw cell blockage were then compared. After the blockage injection, the strength of the correlation between spike trains increased (i.e., they became more synchronized). It was concluded that normal Renshaw cell activity has a desynchronizing effect on its neighboring motor neurons.

Ellaway, 1978 [93]

The purpose of this paper was to introduce the cumulative sum technique[310] to the medical and neurophysiology fields as a simple method for detecting trends in histograms. The simplicity of the technique lies in the fact that it requires nothing more than addition and subtraction. In short, a reference value (k) is successively subtracted from each data point on the histogram (x_1, x_2, …, x_n). New data points (S_1, S_2, …, S_n) are created by adding up these differences consecutively:

$$S_1 = (x_1 - k)$$
$$S_2 = (x_1 - k) + (x_2 - k)$$
$$S_n = (x_1 - k) + (x_2 - k)\ldots + (x_n - k)$$

Phases of change are indicated by changes in slope, and the value of the slope is the difference between the mean level of the period and the reference value. This allows trends to be detected that would normally be obscured by normal fluctuations in the histograms. After this paper introduced the cumulative sum method to the neurophysiology field, there have been hundreds of studies that have applied this technique.

Allum et al., 1982 [6]

The purpose of this study was to examine the magnitude of the correlation between adjacent pairs of precentral neurons in the hand region of the brain whose discharges exhibited a co-variation with isometric force. Cross-correlograms

revealed sharp peaks or troughs. Furthermore, these peaks or troughs were at short latencies, suggesting a common monosynaptic input. The authors proposed that afferents from the ventrolateral nucleus of the thalamus, which branch within the motor cortex before exciting pyramidal tract neurons monosynaptically[82], could have been the common input responsible for the synchronized discharges. There are conflicting findings within the literature on whether motor neuron synchronization is primarily of central or peripheral origin. Therefore, this study is important because it demonstrates that neurons in the brain (i.e., central origin) can exhibit synchronization before descending and activating α–motor neurons.

Kirkwood et al., 1982 [169]

The authors examined cat external intercostal motor neuron firing latencies under varying levels of anesthesia. The results indicated that almost every post-stimulus histogram demonstrated a central peak. However, the time course for this peak showed considerable variation. As a result, the authors developed three classification systems to describe the varying levels of motor neuron synchrony: (a) short-term synchronization, characterized by a narrow, central peak extending to ±3-5 msec; broad peak synchronization, which showed a wider peak extending to ±20 msec; and a high-frequency oscillation, which oscillated from 60-120 Hz. This is one of the first studies to identify the potentials for different forms of synchrony and attempt to classify them.

Dengler et al., 1984 [79]

The aim of this study was to examine the temporal distribution of motor unit synchronization. Motor unit firings were recorded from the FDI during submaximal (5-15% MVC) isometric contractions. Interestingly, it was found that synchronous discharges between two motor units were not uniformly distributed throughout the contraction. Instead, the synchronies tended to form clusters consisting of several sequential events. The authors suggested that the clustering may have been a by-product of the similar characteristics of the observed motor neurons. Since they were all low-threshold (<15% MVC), it can be assumed that the motor neurons were of similar soma size, and therefore had similar membrane potential characteristics.

Ellaway and Murthy, 1985 [94, 95]

The purpose of these two studies was to examine the degree of synchronization between pairs of γ-motor neurons and, if present, to determine its origin. The ratio (k') of total firings within the peak of the cross-correlation histogram over the number of firings expected by chance was used to assess synchronization. The authors found a significant amount of synchrony between γ-motor neurons, and observed a negative curvilinear relationship between k' and motor neuron firing rate (when firing rate was expressed on a logarithmic scale). Interestingly, strong synchronization was not observed between the static and dynamic γ-motor neurons. The authors were unable to determine the precise origin

of the common inputs, but did suggest that it could have been from afferents that entered the spinal cord at the same segment level as the motor neuron pool.

Connell et al., 1986 [50]

The degree of short-term synchronization between semitendinosus α- and γ-motor neurons was tested by inducing the flexion reflex (firm squeeze of ipsilateral heel) in the decerebrate cat. To quantify the magnitude of synchrony, a ratio *k′* was calculated as the sum of the counts (Σx) in the *n* bins constituting the peaks from a cross-correlation histogram, divided by the number of counts expected in that period by chance alone ($n \times m$). The ratio was higher when the average frequency of motor neuron discharge was low (see their Fig.7). In addition to the relative size (*k′*), the peak width also became larger at low frequencies. The primary finding of this paper was that heterologous (α/γ) pairings of motor neurons had a weaker degree of synchrony compared to either type of homologous pairing (α/α or γ/γ). The authors hypothesized that the α-motor neurons that demonstrated short-term synchrony with γ-motor neurons were, in fact, β-motor neurons (neurons that innervate both extrafusal and intrafusal muscle fibers).

Davey et al., 1986 [58]

The purpose of this study was to introduce a statistical approach for detecting a change in the CUSUM of a peristimulus time histogram (PSTH)[93]. The authors demonstrated that setting significance levels at 3 standard deviations of the CUSUM provided the best fit for detecting change. This method would work well over a wide range of coefficients of variation. However, it should be noted that the PSTH is assessing changes from resting levels that occur due to a stimulus. Therefore, the CUSUM from a PSTH would differ from the zero-mean CUSUM in the present study.

Wiegner and Wierzbicka, 1987 [306]

The purpose of this study was to introduce a new index that allows for identification of short-term synchronization. This index differs from k' in that it included the variance of the histogram in the calculation. The authors also found that the critical value for significance was dependent on the width of the peak.

Baker et al., 1988 [13]

This study examined motor unit activity from a 'deafferented' man. The patient had a functional loss of afferents below the neck and demonstrated a complete lack of perception to touch, pressure, proprioception or kinaesthesia. Nevertheless, the patient still exhibited the presence of short-term synchrony

between motor unit firings. Similar to the findings of Taylor[283], it was concluded that central inputs alone were sufficient to induce motor unit synchronization.

Davey and Ellaway, 1988 [60]

The purpose of this study was to explore the role of the brain stem and cerebellum in the synchronization of γ-motor neurons. Various areas of the cat were systematically sectioned. Decerebration (with intact spinal cord) led to the absence of synchronization. Section of the medial part of the dorsolateral funiculus (within the spinal cord) led to irregular, but synchronized firings. Subsequent administration of the monoamine neurotransmitters dopamine and/or serotonin led to a significant reduction in synchrony (and firing variability). The authors concluded that a "monoaminergic pathway descending in the dorsolateral funiculus from the brainstem controls synchrony of γ-motor neurons". It should be noted, however, that this is still a broad statement, as this area within the spinal cord encompasses parts of the corticospinal, rubrospinal, reticulospinal, and raphespinal tracts.

Powers, 1989 [233]

The objective of this study was to determine if there was synchronization between motor units from synergistic muscles in both normal and paretic stroke subjects. Needle EMG signals were used to detect motor unit firings from the

biceps brachii, brachialis, and brachioradialis during isometric forearm flexion. Significant motor unit synchronization was observed approximately 44% of the time in normal subjects. Paretic patients demonstrated wider, longer duration central peaks in cross-correlation histograms (see their Fig. 2). The authors concluded that synergistic muscles exhibit between-muscle synchronization.

Smith and Fetz, 1989 [271]

The purpose of this investigation was to examine the effects of synchronization between primate motor cortex (M1) neurons on post-spike facilitation of muscles and motor units. The finding most relevant to the present dissertation is the initial demonstration that M1 neurons exhibit significant synchronization before synapsing with α-motor neurons. Therefore, synchronization has to be, at least in part, of a central origin.

Datta and Stephens, 1990 [56]

The purpose of this study was to examine short-term synchronization in the FDI and determine if it is affected by the motor unit recruitment threshold. Subjects were required to contract so that both motor units fired with each other at a target frequency of 10 impulses per second. Motor units were separated into two groups: low-threshold and high-threshold. In many of the cases, high threshold motor units were considered to be anything > 0.5 N, which in comparison to other studies[249,

[251], may equate to as little as 1-2% MVC. To quantify synchrony, the area of central peak in the cumulative sum was expressed as a percentage of the control area. Synchronization ranged from 8 – 485% using this method. The strength of synchronization was found to be inversely related to the difference between the two recruitment thresholds. Synchronization was higher when the two motor units had similar recruitment thresholds.

Bremner et al., 1991 [30, 31]

The purpose of these experiments was to assess the level of synchronization within and between different finger muscles. Needle EMG signals were detected from six separate hand muscles during weak, isometric contractions. Approximately 88% of the cases where significant synchronization occurred were characterized by a narrow, central peak in the cross-correlation histogram within 5 ms of time zero. Across all of the muscles, synchronization was present 68 - 100% of the time. Short-term synchronization was also present between all possible combinations of finger muscles. The results also showed greater motor unit synchronization in the FDI during finger extension than abduction. It was concluded that the level of synchronization between motor units was task-dependent.

Datta et al., 1991 [57]

The purpose of this study was to examine the CNS pathways underlying motor unit synchronization. Two needle electrodes were used to detect separate single motor unit action potential trains from the FDI, gastrocnemius, and TA muscles in 18 normal subjects, and 7 patients who had suffered a stroke anywhere between 3 and 32 weeks prior. The results from the normal subjects were characterized by the commonly observed single peak in the cross-interval histogram around time zero, with a peak width of 12.1 ms. A subject with a contralateral parietal haemorrhage exhibited less synchronization, and a much broader peak (47.9 ms) compared to the normal subject. Another subject with a cervical spinal lesion exhibited even less synchronization. Some of their figures (e.g. figures 4 and 5) demonstrated a rightward shift of the peak (i.e. not at time zero), which was easily discernible with the cumulative sum technique. The authors[57] suggested that the contralateral cerebral cortex, as well as the cervical spinal cord, must be intact and functioning properly for the generation of short-term motor unit synchronization.

Lytton and Sejnowski, 1991 [188]

The aim of this study was to use computer simulations to determine whether or not inhibitory interneurons could lead to synchronization of post-synaptic cells. The authors found that phase-locking in the post-synaptic cells started to occur if only 20% of the IPSPs were synchronized. In comparison, 40% synchronization of

EPSPs was required to cause phase-locking. IPSPs showed a modulatory effect, which typically delayed the firing of the neurons, but could also increase the firing rate over a limited range depending on the timing of the IPSP. The occasional increase in firing rate, which was unexpected, occurred when the IPSP arrived during the hyperpolarization of the soma. The IPSPs essentially reduced or interrupted the hyperpolarization phase, making subsequent firing more likely. Nonetheless, the expected response of an IPSP delaying soma firing was more typical. The important contribution of this study was the demonstration that inhibitory neurotransmitters (e.g. GABA) can lead to synchronization of the post-synaptic neurons.

Kamen and De Luca, 1992 [157]

The purpose of this study was to determine if the phenomenon of common drive, a phase-locking oscillation of motor unit firing rates, would differ in a muscle with no detectable muscle spindles. Motor unit firings were detected from the orbicularis oris inferior (OOI) muscle of 4 healthy subjects. The authors found a greater variability in the cross-correlations of the OOI when compared to normal values from the FDI. Of particular interest is that the OOI exhibited significant synchronization of its motor unit firings at a latency within ±3-4 ms (i.e., short-term synchronization). This evidence suggests that muscle spindles are not necessary for common drive or motor unit synchrony. However, it should be noted that some

doubt was raised on whether or not the OOI is completely devoid of spindles. McClean[204] has demonstrated that stretch reflexes can be evoked from the OOI.

Kamen et al., 1992 [158]

The purpose of this study was to determine if common drive, a phase-locking oscillation of motor unit firing rates, differed between the same muscle of the dominant and non-dominant hands. Motor unit firings were detected from the FDI muscle of both hands in 12 healthy subjects. Greater mean firing rate cross-correlations (i.e. more common drive) were found between the motor units of the dominant hand when compared to the non-dominant hand. The authors suggested that a central site is primarily responsible for the lateralization of common drive.

Nordstrom et al., 1992 [225]

The purpose of this study was to examine the relationship between motor unit firing patterns and the magnitude of synchronization from five separate indices. The authors found small, yet significant, relationships between motor unit firing rate and each synchronization index (r^2 ranged from 0.11-0.27). This is of particular interest because one of their indices is the one that were used in the present investigation (designated as index "E"). The r^2 for that index was 0.11. It was concluded that all of the conventional indices are sensitive to motor unit firing rate, which compromises their usefulness. In turn, the authors presented a model with a

new index called common input strength (CIS), which they claim is independent of firing rates. However, closer inspection of CIS introduces a potential drawback. The CIS is calculated by taking the extra events (i.e. the number of synchronized firings beyond what would be expected from chance) and normalizing it to the duration of the contraction. This suggestion introduces a dilemma, as the number of extra events that occur within a particular time period for a motor unit pair with high firing rates should, hypothetically, be much higher than a pair with lower firing rates, simply due to the higher number of total firings within the period. To remove the effects of the number of firings within the time period (i.e. firing rate), the extra events should be normalized to the total number of firings that occurred within the epoch. However, this normalization is the precise method that the authors concluded was dependent on firing rates. The reason for the contradiction between theoretical supposition and the authors' hypothesis is puzzling and should be investigated further. In short, the authors' evidence (e.g. very low r^2) does not appear sufficient to support their interpretations.

Davey et al., 1993 [61]

The purpose of this study was to examine the primary and secondary peaks in synchronization histograms in multiple muscles that are subject to different degrees of recurrent inhibitory feedback. Motor unit trains were detected from the EDC and TA muscles during weak, voluntary isometric contractions (estimated to be less than 15% MVC). Both muscles demonstrated typical, primary central

peaks. However, the TA consistently exhibited a secondary peak centered around 52 ms, which was absent in the EDC records. Furthermore, coherence analysis of the TA EMG signals demonstrated peaks in the 17-24 Hz range, which matches closely with the lag interval of the histogram (52 ms lag = 19.2 Hz). The authors suggested that there was a rhythmic modulation of motor unit firings in the TA due to the muscle's higher representation of recurrent inhibition, while the lack of a secondary peak in the EDC was likely due to that muscle's reduced recurrent inhibition.

De Luca et al., 1993 [66]

The purpose of this investigation was to examine the characteristics associated with motor unit synchronization including how to quantify it, between-muscle differences, and potential relationships with recruitment threshold. Needle EMG signals from six separate muscles recorded during sustained contractions at 30% MVC were decomposed into motor unit action potential trains. Recurrence times were accumulated using Perkel's[229] cross-interval histogram method. If there was a significant peak in the cross-interval histogram, synchronization was quantified as the number of additional firings (i.e. extra events) within the peak beyond what would be expected by chance (i.e. mean of the histogram) normalized to the total number of firings[185]. The confidence interval for determining whether or not a peak was significant was dependent on the width of the peak[306]. These methods, with the exception of the peak width-dependent significant level, were

used to assess synchronization during this dissertation. The authors[66] observed occurrences of both short- (-6 to 6 ms) and long-term synchronization (8 to 76 ms). The long-term peaks were significantly lower than the central peaks. Approximately 91% of the synchronized firings were characterized by short bursts of firings (1 to 2), with a few cases of bursts of up to 10 firings. Larger muscles also demonstrated lower levels of synchronization than smaller muscles. No relationship between recruitment threshold and synchronization was observed. The authors suggested that the fairly low levels of synchronization were in disagreement with the common input theory, and that it is likely that natural oscillations within the CNS was the cause for these low levels.

Farmer et al., 1993 [103]

The purpose of this study was to determine the frequency contents of the common synaptic inputs to motor neurons. Two separate needle electrodes were inserted into either the FDI or SDI to detect motor unit action potential trains during weak voluntary isometric contractions. Firings from separate motor unit pairs were cross-correlated and compared to coherence analysis. The coherence analysis demonstrated significant relationships between motor unit firings in the frequency ranges of 1-12 Hz and 16-32 Hz. Interestingly, a small subexperiment demonstrated little change to the dominant frequency ranges in a clinically deafferented patient. The authors also had the subjects voluntarily oscillate the level of isometric force

that they produced. Significant coherence was detected at the same frequency values as the force oscillations (i.e. demonstrating entrainment).

Schmied et al., 1993 [244]

The purpose of this study was to examine potential relationships between the level of motor unit synchronization and the contractile properties of the motor units. The most relevant finding from this study was that subjects could voluntarily alter the level of synchronization. Along with using visual and audio firing feedback to the subjects, the authors added feedback "clicks" triggered by synchronized firings. An attempt to increase or decrease the rate of the clicks altered the level of synchronization to the muscles. In conjunction with the results of Mori[215], this study provided further support against the use of auditory feedback to regulate motor unit firing rate.

Schmied et al., 1994 [245]

The purpose of this study was to examine potential relationships between the level of motor neuron synchronization and handedness (dominant vs. non-dominant) or motor unit type (defined by recruitment threshold and twitch rise time). The dominant arm exhibited a higher occurrence of significant synchronization, as well as larger peaks, than the non-dominant arm. The authors also found higher levels of

synchronization in fast twitch fibers than in slow, but it should be noted that their cutoff threshold for determining fast vs. slow-twitch motor units was quite low.

Conway et al., 1995 [52]

The purpose of this study was to determine if there was synchronization between the motor cortex (M1) firings and motor unit firings. Magnetoencephalographic (MEG) and FDI EMG signals were detected simultaneously during sustained voluntary contractions. Coherence between the two signals demonstrated a peak in the 13 to 35 Hz range (i.e. beta range). The authors concluded that synchronized motor cortex activity was coupled with the frequencies displayed by the motor units.

Türker et al., 1996 [296]

The objective of this investigation was to determine whether there was a statistically significant change in a motor neuron's firing rate around the time of synchronous discharge. Action potential trains were recorded from masseter and TB motor unit pairs during weak isometric contractions. Peri-spike frequencygrams were constructed by plotting the instantaneous firing rates from one motor unit aligned with the latency of the closest firing from the other motor unit. The cumulative sum technique was applied to the peri-spike frequencygram to detect trends. Calculating the slope of the cumulative sum during a given period of

interest (e.g. -6 to 6 ms) allows for the estimation of the net post-synaptic potential (nPSP). The nPSP provides the sign of any changes from the common inputs (i.e. either excitatory or inhibitory) during that period. This assessment were used in this dissertation (see section 3.3.9). The authors found that about half (48 of 93) of the motor unit pairs demonstrated a significant increase in firing rate in the synchronized firings.

Semmler et al., 1997 [248]

The purpose of this study was to examine the potential relationship between short-term synchronization and common drive in the FDI. Cross-correlation of motor unit action potential trains and the cumulative sum technique were used to quantify synchronization. Cross-correlation of motor unit firing rate curves was used for common drive analysis. Synchronization, as quantified by CIS, demonstrated a very weak ($r^2 = 0.06$) relationship with the strength of the common drive. The authors thereby concluded that common drive and short-term synchronization originate from separate mechanisms.

Semmler and Nordstrom, 1998 [249]

The objective of this study was to examine motor unit synchronization and force tremor in skill-, strength- and un-trained individuals. Indwelling electrodes were inserted into the FDI to detect motor unit action potential trains during very

weak (2 to 11% MVC) voluntary isometric contractions. Interestingly, the authors found significantly greater synchronization in strength-trained individuals than skill-trained musicians or untrained subjects. Furthermore, the skill-trained musicians demonstrated the lowest amounts of synchronization. These results strongly supported the hypothesis that synchronization could be used as a neural strategy to either increase force, or improve fine motor control, depending on the habitual demands placed on the muscles.

Baker et al., 1999 [15]

In this investigation, local field potentials (LFPs) and pyramidal tract neuron firings were recorded from the primary motor cortex of monkeys during a precision grip task. EMG signals were also recorded from the contralateral hand and forearm muscles. This study described 3 separate findings that were of particular interest to this dissertation. First, the LFPs showed oscillatory synchronization in the 20-30 Hz range, which supports the findings of Allum et al.[6] whom also demonstrated central synchronization. Second, the synchronization was highly task-dependent, being present during a steady, isometric grip task, but absent during the movement phases. This phenomenon was described as 'event-related desynchronization'. Third, the authors constructed a computer model (see their Figure 5) demonstrating that synchronization of descending command can lead to increased force production. Of additional importance is that this model also revealed another potential purpose of synchronization; a synchronized common drive requires a lower firing rate to

produce the same amount of force as an asynchronous common drive. In other words, synchronization allows the CNS to be more efficient.

Kakuda et al., 1999 [155]

The purpose of this study was to examine motor unit coherence during slow, voluntary movements of the wrist. Intramuscular EMG signals were recorded from the extensor carpi radialis brevis during low-torque (~1.5% MVC), slow wrist movements. Coherence showed a broad peak in the 6-12 Hz range (centered around 10 Hz) in 83% of the motor unit pairs, with a smaller peak below 5 Hz (2-4 Hz range). The authors suggested that there may be different underlying mechanisms behind the common modulation at 2-4 Hz and 6-12 Hz. They concluded, from past studies[301, 302], that peripheral input, such as the stretch reflex, could not be responsible for the 6-12 Hz modulation, but the closed-loops had the potential to oscillate in the 2-4 Hz range.

Semmler and Nordstrom, 1999 [250]

The purpose of this study was to compare a surface EMG technique for quantifying motor unit synchronization with the more common cross-correlation method (which requires action potential trains). This surface EMG method was the same technique first introduced by Milner-Brown et al.[212], and later questioned by Yue et al.[312]. No significant correlation between the two methods was found (r^2

=0.04) during isometric contractions performed by the FDI. The authors concluded that methodological issues with the surface EMG technique significantly limit its accuracy and usefulness.

Huesler, 2000 [147]

This study consisted of a series of subexperiments examining the levels of motor unit synchronization for 15 hand muscles during a precision grip task. In contrast to the findings of others (e.g. Kamen and Roy[160]), the authors[147] found that motor unit synchronization was higher, and more common at lower force levels than at higher ones. They also found that synchronization was highest among motor unit pairs with similar recruitment thresholds. Additionally, motor units from the same muscle exhibited more synchronization than those from separate muscles (i.e. synergists). Of relevance to this dissertation is the fact that the authors provided force feedback to the subjects, recognizing that many past studies may have biased their synchronization analyses by providing feedback of motor unit firings.

Kamen and Roy, 2000 [160]

The purpose of this study was to determine if there was a difference in the degree of motor unit synchronization between young (mean of 28 yrs) and elderly (mean of 75 yrs) subjects. Intramuscular EMG signals were recorded from the FDI during isometric abductions at 50% and 100% MVC. A CUSUM of a cross-

correlogram was used to identify significant peaks of synchronization, and five separate measures were used to quantify their magnitude. The elderly had a longer IPI (i.e., shorter MFR) than the younger subjects. There were no significant differences between groups for synchronization at either 50% or 100% MVC. Synchronization appeared to be higher at 100% MVC than at 50% MVC for both groups. However, no statistics were provided for this comparison. Additionally, little to no relationship ($r = -0.14$) was found between the magnitude of synchronization and the difference in recruitment threshold between the motor units. In other words, motor unit pairs of similar recruitment thresholds were not more likely to be synchronized than pairs with a large discrepancy in recruitment threshold.

Yao et al., 2000 [311]

The purpose of this study was to determine if motor unit synchronization had an effect on isometric force and the amplitude of the surface EMG signal. All signals were generated by computer simulations. The authors found increases in EMG amplitude from moderate (65%) and high (130% increase in EMG amplitude) levels of synchronization (when compared to the no-synchronization condition). Synchronization had no effect on the average level of force, but did seem to alter force steadiness.

Kleine et al., 2001 [170]

The purpose of this study was to examine the potential influence of motor neuron synchronization on surface EMG median frequency and its dependence on electrode position. The hypothesis was tested with a computer simulation model and partially confirmed with experimental data on the BB. The authors found that increases in synchronization decreased the EMG median frequency when the sensors were placed between the innervation zone and the tendon, but not when placed above the innervation zone.

Türker and Powers, 2001 [294]

The aim of this study was to compare the effects of common excitatory and inhibitory inputs on synchronization. Sections of rat brain stem were repetitively stimulated by injecting current along with superimposed noise. The authors found that both excitatory and inhibitory common inputs led to synchronous discharge, which was revealed as a central peak in a cross-correlation histogram. Interestingly, the histograms from a common excitatory input showed larger and narrower central peaks than the histograms from an inhibitory origin, which were smaller and wider. As expected, peri-spike frequencygrams (i.e. histograms of firing rates, or frequencies) revealed an increase in motor neuron discharge rates around time zero for the excitatory inputs. However, inhibitory-based synchronization led to little or no changes in the frequencygram at time zero (see top tracings in author's Fig. 9).

The authors concluded that peri-spike frequencygrams cannot be used to definitively discriminate net excitation from net inhibition. However, this interpretation does not necessarily match what the authors showed. Even though the responses from the two sources of input did not behave as predicted (more so with the net inhibitory input), the fact that they had different responses at all suggests an ability to distinguish the net sign of the common input. It is clear from this study that the use of a peri-spike frequencygram for this purpose does have its limitations. Nevertheless, when restricted to the area of the histogram's center, this method can still be used for a rough estimate of the net sign for the common input.

Türker and Powers, 2002 [295]

The purpose of this study was to compare the various synchronization indices and their dependencies on motor neuron discharge rate. In strong contrast to the findings of Nordstrom et al.[225], the authors found that synchronization, when produced by high-frequency small EPSPs, had no significant relationship with firing rate if the index was normalized to the total number of counts (or counts by chance). Additionally, they found that the common input strength (CIS) index suggested by Nordstrom et al.[225] demonstrated a significant negative correlation ($r = 0.564$, $p < 0.001$) with the product interpulse interval (i.e. firing rates). The authors[295] concluded that synchronization should be quantified by dividing the counts by the total number of counts in one or both action potential trains.

Kidgell et al., 2006 [168]

The aim of this study was to determine if 4-8 weeks of isometric FDI strength training altered the strength of motor unit synchronization. Using the common input strength index (from cross-correlation), motor unit synchronization did not change following training. Coherence z scores were also uninfluenced by training. These findings conflict with previous results from Milner-Brown et al.[212], which found that motor unit synchrony increased with training. However, the authors contended that it has been demonstrated[312] that the methods used by Milner-Brown et al.[212] had several limitations. Therefore, they asserted that strength training does not increase the synchronization between motor unit firings. However, it should be noted that the authors used audio firing rate feedback during their motor unit recordings, which can artificially increase the levels of synchronization[215]. In addition, the motor unit firings were recorded at very low force levels (≈8-9% MVC). If correlated motor unit activity is an important element in the production of force, then it is possible that adaptations to this neural component might not be appropriately expressed at such low force levels. Finally, the Milner-Brown et al.[212] study that was not criticized by the authors[168] is not the only study to demonstrate training-induced increases in synchronization[75, 243].

Mellor and Hodges, 2006 [205]

The purpose of this study was to determine if knee joint angle had an effect on motor unit synchronization between the VL and VM muscles. Single motor unit action potential trains were recorded from the VL and VM separately at knee joint angles of 120°, 150°, and 180°. There were no significant differences in the degrees of motor unit synchronization between the VL and VM across the 3 joint angles. The authors concluded that the between-muscle neural coordination between the two muscles is consistent throughout the knee's range of motion.

Christou et al., 2007 [47]

The purpose of this investigation was to determine if motor unit pairs exhibiting different firing rates (i.e. dissimilar recruitment thresholds) also exhibit varying levels of motor unit synchronization. The CIS and k' indices, as well as coherence analysis, were utilized as measures of synchronization. In contrast to the findings of Türker and Powers[295], the authors[47] found no relationship between mean interpusle interval (for the motor unit pair) and the CIS index. Additionally, they found a weak positive relationship ($r^2 = 0.20$) between mean interpulse interval and the k' index. In combination with the coherence analysis, it was suggested that differences in firing rates across motor unit pairs can modulate synchronization at frequencies less than 15 Hz.

Keenan et al., 2007 [161]

The purpose of this study was to determine if cross-correlation of two surface EMG signals was sensitive to the degree of synchronization within and across muscles. Signals were simulated with a volume conduction model that systematically manipulated muscle size, excitation level, fat thickness, skin conductivity, and motor unit conduction velocity. The cross-correlation index exhibited a positive relationship with the degree of synchronization. However, the index's sensitivity to synchrony varied widely across different muscle types. In other words, the above listed parameters that were included in the model (other than synchrony), which vary across muscles, influenced the cross-correlation index's sensitivity to represent motor unit synchronization.

Contessa et al., 2009 [51]

The aim of this study was to explore potential relationships between common drive, motor unit synchronization, force steadiness, and endurance time (i.e. fatigue). Indwelling EMG signals were collected from the VL during sustained isometric contractions of the leg extensors, decomposed and analyzed. De Luca et al.'s[66] method of quantifying synchronization was used. The authors found that force steadiness decreased (i.e. increased coefficient of variation in force) across time. Common drive also increased with endurance time. Surprisingly, no changes

in synchronization were observed. The authors also found no relationship between synchronization and force steadiness.

Negro and Farina, 2011 [219]

This study used a computational model of an α-motor neuron pool to investigate the influence of various common inputs. The authors demonstrated that oscillations originating in the motor cortex and descending down the corticospinal tract lead to oscillations of the same frequencies in the motor neurons. However, a second input that is common to all of the motor neuron pool would have a desynchronizing effect. It would theoretically lead to a decorrelation between cortical and motor outputs. It is possible that afferent projections to the motor neuron pool could have this effect.

DeFreitas et al., In review [76]

The purpose of this study was to explore potential differences in synchronization between low- and high-threshold motor unit pairs at relatively high levels of force. Surface EMG signals were detected from the VL during isometric leg extensions, decomposed, and analyzed. The authors found that high-threshold motor unit pairs demonstrated significantly more synchronization than low-threshold pairs. It was suggested that low- and high-threshold motor units may possess differences in the varying degrees of common inputs.

2.3.1 Summary of "Motor Unit Synchronization"

The phenomenon of motor unit synchronization has been a topic of much debate. Within the scientific community, there seems to be little agreement on the degree of synchronization present during voluntary contractions, its origin, its purpose, and even how to quantify it. The most commonly accepted hypothesis for the underlying mechanisms of synchronization is the presence of shared, presynaptic inputs to the motor neurons. However, the origin and relative contributions of these common inputs are still poorly understood. It has been demonstrated that in the absence of volition, or central drive, peripheral afferent input by itself is sufficient to synchronize the motor neuron pool (as elicited by reflex)[144]. However, it has also been shown that motor unit synchronization can still occur following chemical[283] or clinical[13] deafferentation. Therefore, both central and peripheral inputs, when acting alone, are sufficient to produce synchronization. It is the relative contributions to synchronization from central and peripheral inputs during voluntary contractions in healthy humans that remain unknown. Furthermore, it has been suggested that while synchronized oscillations are descending down central pathways, other inputs to the motor neuron pool, such as Renshaw cells[3, 35, 192] or peripheral afferents[219], can have a desynchronizing effect.

Another debate is whether or not the synchronization of motor units is an intentional strategy that can be manipulated by the CNS. It has been demonstrated[15] that a synchronized motor neuron pool can produce more force

than an unsynchronized pool. Additionally, a synchronized descending drive can produce the same amount of force using a lower frequency drive (i.e be more efficient). Furthermore, it has been demonstrated[160] that synchronization is greater during high force contractions than low force ones. However, if synchronization is indeed an intentional strategy to increase force, it withstands that there should be an appropriate adaptation to habitually producing high levels of force (i.e. strength training). The results from training studies have been inconclusive to this point, showing both increases[75, 212, 243] and no change[168] following training. In support of the potential adaptation, multiple studies [104, 249, 252] have demonstrated increased levels of synchronization in strength trained individuals when compared to either untrained and/or skill-trained individuals.

There also seems to be disagreement on the way that motor unit synchronization should be quantified. Nordstrom et al.[225] suggested that some of the original quantification methods used were inappropriately dependent on motor unit firing rates. They went on to suggest a new technique, called common input strength (CIS) that they consider to be independent of changes in firing rates. However, CIS might actually be more dependent on changes to firing rates than the previous methods. Additionally, Milner-Brown et al.[212] introduced a surface EMG technique to quantify synchronization. However, it has since been suggested[250, 312] that the accuracy of Milner-Brown et al.'s[212] method has many limitations. Nevertheless, other surface EMG techniques have also been introduced[77, 246].

It should also be noted that many other variables have since been introduced to further understand motor unit synchronization, such as common drive, coherence, and estimated net post-synaptic potentials (nPSPs). Cross-correlation of motor unit firing rates provides an estimation of the common drive between them[18, 69]. Coherence analysis provides the frequency bands that are demonstrating the most synchronization. Applying the CUSUM technique to a peri-spike frequencygram allows for an estimation of the net sign (i.e excitatory or inhibitory) leading to synchronization. This analysis may provide insight on the relative contributions from the common inputs to motor unit synchronization.

2.4. Effects of Fatigue on Neuromuscular Function

Cobb and Forbes, 1923 [49]

This is one of the first documented studies on human muscle fatigue during voluntary contractions. The purpose of this study was to examine changes in EMG signals from fatigue of the hand flexors. Their first two observations were that the frequency of the EMG signals decreased and the amplitude increased over time during repeated contractions. They also found that, given enough rest, the values returned to baseline. The authors concluded that the fatigue takes place at the neuromuscular junction.

Edwards and Lippold, 1956 [90]

The purpose of this study was to examine the EMG amplitude vs. force relationship during fatigue. Surface EMG signals were detected from soleus during step contractions before and after sustained isometric contractions at 25% MVC. The EMG amplitude at each force level was higher after fatigue than before. The authors concluded that increases in EMG amplitude were representative of increases in motor unit recruitment to compensate for the decrease in force capabilities of the already active motor units.

Kuroda et al., 1970 [178]

The purpose of this study was to describe the relationships between O_2 consumption, EMG amplitude from the quadriceps femoris, and isometric leg extension force. Interestingly, the authors found the each of the relationships (i.e. EMG-Force, Force-O_2, O_2-EMG) were characterized by an initial linear phase followed by an exponential increase. The authors concluded that fatigue could be avoided by limiting contraction periods to one half of the exhaustion time.

Komi and Viitasalo, 1977 [173]

The purpose of this study was to investigate the electrical and metabolic aspects of fatigue before and after repeated bouts of either concentric or eccentric contractions (40 reps). EMG and muscle glycogen were measured from the

quadriceps femoris, as well as serum creatine kinase and lactate. EMG activity increased immediately after both concentric and eccentric work, but showed a greater change after eccentric. Furthermore, eccentric work resulted in large changes in motor unit action potential shapes, while no such change seemed to occur from the concentric bout. Muscle glycogen levels decreased after both bouts, but were not depleted in either. Interestingly, glycogen levels were still depressed 2 days later. Looking at all the variables, the authors interpreted these findings as an indication that eccentric work was more fatiguing than concentric work.

Asmussen and Mazin, 1978 [11]

The purpose of this study was to assess if physically or mentally diverting activities improved recovery from fatigue. The subjects would perform exhaustive bicep curls, take a 2 minute pause, and then continue with the work bout. The authors showed that the amount of work that could be performed was higher when diverting activities were performed during the pause (versus quiet resting). Blood flow measurements were also assessed to determine if there was a circulatory factor involved. However, there were no blood flow increases with the diverting activity. Therefore, it was concluded that recovery after local muscle fatigue is influenced by a central nervous factor.

Asmussen and Mazin, 1978 [10]

This study was part of the same investigation listed in the above study[11]. To add on to the diverting activity findings, the authors also discovered that the volume of work that could be performed before failure was dependent on whether the subject's had their eyes open or closed. The eyes opened condition showed a great work production than eyes closed. Furthermore, patellar tendon reflexes were potentiated when the eyes were opened, possibly showing enhanced central arousal. In addition, closing the eyes may have an inhibitory effect on the stretch reflex.

Komi and Tesch, 1979 [174]

This study examined the effects of fatigue on isokinetic leg extension torque, VL EMG amplitude, and mean power frequency (MPF). Biopsies of the VL were taken to relate the findings to fiber-type composition. The authors showed that individuals with a greater proportion of fast-twitch muscle fibers demonstrated higher peak torque, but also exhibited a greater percent decline with repeated contractions. That same group demonstrated a significant decrease in EMG amplitude and MPF during fatigue. The individuals with a greater percentage of slow twitch fibers demonstrated similar, but attenuated, non-significant effects.

Grimby et al., 1981 [127]

The purpose of this study was to determine the discharge properties of low- (tonic) and high-frequency (phasic) motor units during sustained MVCs. The prolonged maximal efforts led to a decrease in motor unit firing rates and total recruitment (i.e. number of motor units activated). The authors found that some motor units decreased their threshold with fatigue, while others increased. They went on to suggest that higher threshold motor units increase their threshold to protect from excessive exhaustion.

Bigland-Ritchie et al., 1983 [23]

This paper examined motor unit firing rates during sustained MVCs in the adductor pollicis. The authors demonstrated that motor unit firing rates dropped from 27 pps to 15 pps within the first 60 seconds. Interestingly, they also suggested that the motor units with the highest initial firing rates showed the greatest percent decline with fatigue.

Nelson and Hutton, 1985 [220]

The objective of this study was to examine the dynamic and static responses of muscle spindles to stretch and vibration before and after electrically-induced fatigue. Isolated cat gastrocnemius was stimulated until tetanic tension reached 50-60% of baseline. Resting spindle activity, as well as responses to stretch and

vibration, increased after fatigue. This increased activity led to a decrease in the response latency. The authors hypothesized that the purpose of this increased activity was to increase joint stiffness. It should be noted that these results conflict with later findings, which assessed voluntary fatigue in humans[189], although those spindle recordings were during isometric contraction, and not in response to stretch, as was the case in this study.

Sandercock et al., 1985 [242]

The aim of this study was to examine potential changes to the amplitude and duration of single motor unit action potentials during fatigue. Indwelling EMG signals were recorded from the cat gastrocnemius during repetitive electrical stimulation at 10 or 80 Hz. The low-frequency fatigue led to depressed force recovery and a poor correlation with action potential changes. However, the high-frequency fatigue caused the changes in action potentials to be correlated with changes in tension. The authors concluded that EMG should only be used to assess high-frequency fatigue, and is unreliable during low-frequency fatigue.

Bigland-Ritchie et al., 1986 [25]

The purpose of this study was to compare the recovery of motor neuron firing rates following fatigue with and without normal blood supply to the muscle. Under normal conditions, motor neuron firing rates decreased with fatigue from a

sustained MVC, but fully recovered within 3 minutes. However, when blood flow was cutoff to induce ischemia, there was no recovery 3 minutes post-fatigue. The authors suggest that motor neuron firing rates may be regulated by a peripheral reflex originating in response to fatigue-induced changes within the muscle, such as group III and IV metabolic chemoreceptors.

Hutton and Nelson, 1986 [151]

The purpose of this study was to examine the effects of fatigue on the stretch sensitivity of GTOs (and group Ib afferent response). Cat gastrocnemius muscles were fatigued by electrical stimulation to 50-60% of pre-fatigue peak tension. After fatigue, the group Ib afferent responses to stretch were greatly diminished and slower (i.e. longer latencies), if not completely eliminated. In a subexperiment, applying vibration demonstrated the possibility of a post-excitation depression at the level of the receptor. Interestingly, this GTO response to fatigue is the opposite of what the authors previously found in the muscle spindles [220].

Woods et al., 1986 [309]

This study is a follow-up investigation to two previously described studies [24, 25]. It was already demonstrated that motor neuron firing rates decline during sustained MVCs, and that their recovery depends on blood supply. The purpose of this study was to determine if those fatigue-induced changes to motor neurons are

the result of an inhibitory reflex. The authors found that well-motivated subjects showed no decrease in % voluntary activation or evoked M-wave amplitude. They concluded that the lack of firing rate recovery during ischemic conditions is not due to failure of neuromuscular transmission, which in turn, supports the possibility of an inhibitory reflex.

Maton and Gamet, 1989 [200]

The aim of this study was to examine the motor unit firing properties of the biceps brachii and brachioradialis (synergistic muscles) during a sustained submaximal (20-30% MVC) isometric contraction (sustained until fatigued). New motor units were continually recruited throughout the contraction as the muscles became increasingly fatigued. The firing rates of the first recruited motor units either increased slightly or remained stable. However, it was shown that their recruitment thresholds were decreased after the fatiguing contraction. Some of the newly recruited motor units started off as intermittent, bursting activity which increased in frequency over time and eventually progressed to continuous firing. The authors concluded that motor unit recruitment is the primary compensatory mechanism in maintaining force during a sustained, fatiguing contraction.

Garland and McComas, 1990 [113]

The purpose of this study was to examine motor neuron excitability, as elicited by H-reflex, during fatiguing conditions. Fatigue was induced by ischaemia (pressure cuff) and electrical stimulation (at 15Hz). Torque and EMG activity of the soleus muscle decreased with fatigue. M-wave did not significantly change, but the H-reflex was significantly reduced. These results demonstrate a decrease in motor neuron excitability with fatigue.

Garland, 1991 [114]

This was a follow-up study to the Garland and McComas study[113] previously described. The purpose of this study was to see if the depressed motor neuron excitability demonstrated in their previous work was due to reflex inhibition from small diameter afferents (e.g. group III and IV). The authors applied a compression block to the sciatic nerve, which has a large blocking effect on large afferents, but leaves small afferents relatively unaffected. The compression led to a decrease in torque and EMG amplitude. Subsequent fatigue decreased these variables further. The M-wave and superimposed interpolated twitches remained fairly consistent, indicating no change in peripheral excitability or descending drive. The author concluded that the reduced motor neuron excitability was likely due to reflex inhibition originating from small group III and IV afferents, which would have been unaffected by the compression block.

Macefield et al., 1991 [189]

The purpose of this study was to examine afferent receptor discharge activity during sustained contractions. Afferent fibers (mostly of spindle origin, but a few from GTOs) were recorded from a microelectrode embedded in the common peroneal nerve. The firing rate of most of the spindle afferents progressively declined during over time during the sustained contraction. Within 30 sec., the firing rates had decreased to 66%. Due to the necessity to recruit additional motor units to sustain the desired force levels, EMG amplitude increased over time. Therefore, EMG amplitude was inversely related to spindle firing rates. The motor unit firing rates also decreased with fatigue. The authors suggested that it was due to the progressive disfacilitation of α-motor neurons from the spindles. Of the four GTO afferents recorded, two showed a firing rate decay over time, while the other two maintained their firing rates.

Psek and Cafarelli, 1993 [234]

Refer to section *2.1 Agonist/Antagonist Interaction*; pg 27

Fallentin et al., 1993 [101]

Refer to section *2.2 Motor Unit Firing Properties*; pg 59

Cupido et al., 1996 [55]

The objective of this study was to investigate the effects of repeated excitation on the M-wave (i.e. compound action potential) in the biceps brachii. Continuous indirect stimulation led to a 100% increase in M-wave area, and a 50% increase in M-wave size (i.e. mean peak-to-peak amplitude). The enlarged M-wave was sustained when stimulated with a rate of 10Hz, but gradually declined at a stimulation rate of 20 Hz. Mean muscle fiber conduction velocity decreased by more than 50% and then increased above the resting value during recovery.

Taylor et al., and Gandevia et al., 1996 [110, 286]

The objective of these studies was to determine if central fatigue occurred during sustained MVCs. EMG signals were detected from the BB during M1 and muscle stimulation. The increment in force from the superimposed twitches increased with fatigue due to a decrease in the relative contribution from voluntary activation. Tendon vibration during MVCs demonstrated there was no influence from spindle afferents. The author's concluded that central fatigue was present in the higher centers upstream of M1 (i.e. premotor), and that the drive to the M1 area was reduced.

Miller et al., 1996 [208]

The objective of this study was to examine motor unit behavior in the TB during a submaximal (~17% MVC) fatigue protocol. During fatigue, the phenomenon of motor unit substitutions (i.e. new motor units recruited) was demonstrated. Each new motor unit recruited had a higher recruitment threshold than the previously active motor units. The firing rate changes were inconsistent (some increased, some decreased) with fatigue. The authors speculated that peripheral feedback from the fatigued muscles may have led to changes in the motor neuron discharge properties. However, it should be noted that without any reflex measurements, the authors couldn't truly distinguish between central and peripheral influences. Also, despite the fact that their fatigue protocol involved alternating forearm flexions and extensions, the authors did not include any information of the TB motor unit discharge properties when it was acting as an antagonist (i.e. during flexion).

Esposito et al., 1998 [99]

The purpose of this study was to examine changes to EMG and mechanomyographic (MMG) signals from the BB during sustained isometric contractions at 80% MVC. During fatigue, there was a decrease in EMG mean frequency, MMG amplitude, and force. There was also an increase in EMG amplitude, and MMG mean frequency. Additional tests 10 minutes after fatigue

showed recovery to the EMG variables, but continued alteration to the MMG variables. The authors concluded that high-threshold, highly fatigable motor units may still not be available for recruitment 10 minutes after a sustained, high force bout of fatigue.

Kent-Braun, 1999 [163]

The purpose of this study was to estimate and quantify the central and peripheral contributions to fatigue. Subjects sustained an isometric MVC of the dorsiflexors for approximately 4 minutes. The fatiguing protocol caused isometric MVC and stimulated tetanic forces to decrease by 78% and 67%, respectively. Decreases in measures of central activation (e.g. central activation ratio) suggest that central fatigue occurred. Changes in intramuscular pH [as measured by magnetic resonance spectroscopy (MRS)] demonstrated peripheral fatigue, as would be expected. The author estimated that central factors were responsible for 20% of the overall fatigue, with intramuscular factors (i.e. peripheral) being accountable for the remainder.

Carpentier et al., 2001 [44]

The purpose of this study was to examine changes in motor unit behavior during fatigue in the FDI muscle. Intermittent 10-s isometric muscle actions were held at 50% MVC until the force level could no longer be achieved. Motor units

that were recruited below 25% MVC were considered to be low-threshold and those recruited above 25% MVC were designated as high-threshold. The recruitment threshold for all of the motor units decreased with fatigue (they were recruited earlier in the fatigued state). Interestingly, the high-threshold motor units showed an expected decrease in force after fatigue whereas the low-threshold motor units actually showed an increase in force after fatigue. The authors also had a few subjects perform a short, 15-s stretch of the FDI after the fatiguing protocol and then retested a small group of motor units. The low-threshold motor units showed a significant decrease in force immediately after the stretch and had their recruitment thresholds "reset" back to their original, pre-fatigue values. Conversely, the high-threshold motor units showed no change after the short stretch. Additionally, the author's data confirmed prior findings [96, 186, 200] that excitatory central drive increases during fatiguing tasks despite the fact that motor unit firing rates decrease [68, 200, 231].

Zhang and Rymer, 2001 [314]

The purpose of this study was to examine the effects of fatigue on the intrinsic and reflex actions of the forearm extensors. Fatigue was induced with intermittent submaximal isometric contractions. The duty cycle was 10 sec., with 6 sec. of contraction and 4 sec. of relaxation. Each contraction was held at approximately 60% of MVC. Stretch reflex gains were broken down into static and dynamic components. Intrinsic variables included joint stiffness and viscosity.

After fatigue, joint stiffness was reduced and viscosity was higher. Furthermore, static stretch reflex gain decreased with fatigue. Consequently, it was suggested that dynamic reflexes contributed relatively more torque after fatigue. In addition, the authors proposed that the increased relative contributions from dynamic stretch reflexes after fatigue compensate for the reduced intrinsic stiffness.

Adam and De Luca, 2003 [1, 2]

The purpose of these two studies was to examine motor unit recruitment and firing rate properties during fatigue. EMG signals were detected from the VL during isometric contractions sustained at 20% MVC. The authors found that fatigue was characterized by a decrease in motor unit recruitment thresholds, recruitment of additional motor units, and no deviations in the recruitment order. Interestingly, the firing rates demonstrated an initial decrease after 10-20 s, but eventually increased. The authors attribute the initial decrease in firing rate to temporary potentiation, and the eventual increased firing rate and additional recruitment to an increase in central excitatory drive to the motor unit pool.

Lévénez et al., 2005 [180]

The purpose of this study was to examine spinal reflexes and antagonist coactivation during a fatiguing contraction. Surface EMG signals were detected from the TA, soleus, and gastrocnemius muscles during isometric dorsiflexions. M-

wave and H-reflex responses of the antagonists were assessed during and after fatigue. During the first 20% of the fatiguing contraction, antagonist motor neuron excitability increased approximately 150%. However, the antagonist motor neuron excitability subsequently decreased to approximately 70% of the pre-fatigue values. Interestingly, the H-reflex response did not mirror changes to EMG amplitude. The authors concluded that modulation of antagonist H-reflex during agonist fatigue was due to presynaptic inhibition, which is both peripherally and centrally mediated.

Contessa et al., 2009 [51]

Refer to section *2.3 Motor Unit Synchronization*; pg 111

Farina et al., 2009 [102]

This paper compared the changes in motor unit firing properties and conduction velocity during repeated, low-force isometric contractions. The motor units that were active the most during the contractions (> 70% of the time) demonstrated decreases in their action potential conduction velocity. Those same units also showed increases in their recruitment and derecruitment thresholds. Conversely, the less active motor units exhibited decreased thresholds and no changes in conduction velocity.

Tanaka et al., 2011 [277]

The purpose of this study was to examine the central regulatory mechanism of physical fatigue. Magnetoencephalographic (MEG) signals were detected while the subjects performed repetitive maximal isometric grips of the dominant hand every second. During one condition, the subjects could see their hand perform the task. During a second visit, a Ramachandran mirror box was used over the dominant hand to reflect an image of the resting, non-dominant hand. Therefore, the mirror box made it look as if both hands were resting. Perception of fatigue increased over time during the first condition. However, perceived fatigue did not change in the mirror box condition. MEG analysis showed that β-band event related desynchronization (ERD) levels in movement-evoked fields decreased with fatigue in the no-mirror box condition, and remained unaltered with the use of the box. The authors concluded that their findings demonstrated neural evidence of central inhibition and that the visual feedback system was involved in the central mechanism regulating motor output.

Stock et al., 2012 [276]

The purpose of this study was to examine the effects of fatigue on the relationship between motor unit firing rate and recruitment threshold. Surface EMG signals were detected from the VL and VM during isometric leg extensions at 50% MVC pre and post fatigue. Fatigue was elicited by ten, 10-sec. MVCs over the

course of 200 sec. The EMG signals were decomposed into individual motor unit action potential trains. The slopes of the relationship between motor unit firing rate and recruitment threshold increased after fatigue, along with a decrease in the y-intercepts. Average firing rates also decreased after fatigue. The authors concluded that the change in linear slope coefficients with fatigue was due to the recruitment of higher threshold motor units.

2.4.1 Summary of the "Effects of Fatigue on Neuromuscular Function"

Fatigue can be defined as a state of exhaustion, or a loss of strength or endurance. Although, there is no universally accepted definition of fatigue due to its complexity. It can be affected by both central and peripheral factors, and the neuromuscular response to fatigue is highly dependent on the type of fatiguing task. During sustained MVCs, there is a decrease in force, EMG amplitude, EMG mean frequency, and motor unit firing rates[23]. Performing sustained MVCs can also lead to decreased motor neuron excitability[163], spindle firing rates[189], and GTO responses to stretch[151]. The task's effects on motor unit recruitment thresholds are still debatable as they have shown to both increase and decrease[127]. During sustained submaximal contractions, EMG amplitude increases[90]. This is because, during a sustained submaximal contraction, new motor units are recruited and substituted in to maintain the same force level after the fatigue of the previously active motor units[1, 2, 200, 208, 303]. Additionally, this type of fatigue may lead to decreases in motor unit recruitment threshold[1, 200]. Fatigue caused by repetitive

electrical stimulation can cause decreased motor neuron excitability[113] and conduction velocity[55]. Intermittent voluntary contractions can lead to decreased recruitment thresholds[44], average firing rates[276], conduction velocity[102] and joint stiffness[314]. This type of fatigue can also increase the viscosity of the muscle[314].

Many studies have demonstrated evidence of central fatigue[110, 163, 286]. Kent-Braun[163] even went as far as to estimate that central fatigue was responsible for 20% of the overall observed fatigue after sustained MVCs. Furthermore, there may be a perceptual or mental component to fatigue and/or recovery. Multiple studies[11, 275] have demonstrated that mentally diverting activities improves recovery after fatigue and Tanaka[277] showed that the perception of fatigue is reduced if the hand performing the task appears to be resting. Clearly, the effects of fatigue on neuromuscular function are still poorly understood, can originate from multiple sources, and are extremely complex.

2.5. Effects of Stretching on Neuromuscular Function

Mark et al., 1968 [193]

The purpose of this study was to examine the effect of passive stretching of the calf muscles on their H-reflex response. The authors had the subjects perform a Jendrassik's maneuver (see glossary) to assess the reflex uninhibited. They found that a maintained stretch of the muscles reduces motor neuron excitability. This

would suggest that perhaps plastic deformation from a prolonged stretch might have the same effect.

Houk et al., 1971 [146]

The objective of this study was to assess the necessary stimulus to elicit a GTO response. Cat calf muscles were passively stretched and the responses of GTOs were recorded. Only in the last 10% of the physiological range of motion did GTOs start to respond. They also found that GTOs were sensitive to length changes from within the previous minute. The authors concluded that, without the use of active contraction, a very strong stimulus is required to initiate GTOs. This may provide insight into the difficulty of desensitizing GTOs with prolonged stretching.

Gydikov and Tankov, 1977 [132]

The purpose of this study was to examine the transient processes of the instantaneous firing rates of low-threshold motor units in the biceps brachii. Motor unit firings were recorded during various conditions, such as loaded stretch and balanced unloading (i.e. loads to both agonist and antagonist). This investigation showed that instantaneous firing rates are sensitive to changes in the condition of the muscle. The authors[132] also suggested that the changes in firing rates of the agonist were dependent on the degree of activity in the antagonist.

Guissard et al., 1988 [128]

The aim of this study was to examine changes in motor neuron excitability after static stretches of the human soleus muscle. Tendon and H-reflexes were recorded during static stretches of varying degrees (i.e. multiple joint angles). The comparison of relative changes in both reflexes allowed the authors to identify the contribution of the spindles to the observed changes. Each static stretch was maintained for approximately 30 seconds. Static stretching resulted in a significant decrease in motor neuron excitability (i.e. attenuated H-reflex) and an even greater relative decrease in the tendon tap reflex. The authors concluded that the muscle spindles (Ia) were less sensitive in the stretched position and that there was additional inhibition of the motor neuron pool. This inhibition may have been directly from golgi tendon organs (Ib), muscle spindle secondary afferents (II) or potentially an indirect depression by Ia presynaptic inhibition of Ia afferents.

Taylor et al., 1990 [285]

The objective of this study was to characterize the viscoelastic properties of a muscle-tendon unit. EDL and TA muscle-tendon units from white rabbits were clamped and mechanically stretched. Stress relaxation curves revealed that the most significant changes occur in the first 12 to 18 seconds. From a practical standpoint, this means that a muscle shouldn't be held at a constant length. Instead, the stretch should be held with a constant force so that the length continues to slowly increase

throughout. The authors also found that a minimal amount of stretching (at least 4 repetitions) was effective in eliciting most of the muscle-tendon unit lengthening.

Magnusson et al., 1996 [191]

This study examined the mechanical and electrical responses of the hamstrings to prolonged stretching, and whether or not a pre-isometric contraction altered those affects. The authors found that the viscoelastic and EMG response was unaffected by the isometric contraction. This suggests that the pre- and post-stretching MVCs utilized in this dissertation will not affect the responses from the prolonged stretching.

Avela et al., 1999 [12]

The purpose of this study was to see if direct fatigue effects on the muscle spindle itself could be demonstrated by applying repetitive passive stretches (for up to an hour). Each stretch itself was very short (1.5 cycles/second). After the repeated stretches, MVC decreased by 23% and stretch reflex sensitivity (peak-to-peak amplitude) decreased by 85%. The author's primary conclusion was that the stretch-induced decrease in force and H-reflex was due to a reduction in excitatory drive from large, Ia afferents onto the α-motor neuron pool. This decreased drive was likely from a decrease in the resting discharge of the spindle receptors (due to the increased compliance).

Fowles et al., 2000 [105]

The objective of this study was to assess prolonged stretching-induced changes in strength performance. The plantar flexors were passively stretched to the maximal position tolerable without pain. Thirteen stretches were performed for 2 minutes 15 seconds each, for a total of 30 minutes. MVC decreased by 28% immediately following the stretch and slowly began to recover. One hour after the stretch there was still a 9% decrease in maximal strength. Using twitch interpolation, motor unit activation was significantly depressed immediately post-stretching, but had recovered within 15 minutes. The author's had estimated the neural and mechanical contributions to the stretch-induced force loss. Immediate post-stretch, the majority (≈57%) of force decrement was due to reduced motor unit activation (i.e. neural). This also held true for 5-minutes post, but ceased by 15 minutes post. For 15 to 60 minutes post, a reduced muscle force generating capacity was the primary contributor to the remaining force decrements. The author's hypothesized that the mechanisms affecting the force-generating abilities after stretch were due to changes in the length-tension relationship and/or plastic deformation of connective tissue.

Evetovich et al., 2003 [100]

The purpose of this study was to determine if torque, EMG, or MMG during concentric isokinetic muscle actions were acutely effected by a static stretching bout

of the biceps brachii. The biceps were stretched for 12 times for 30 seconds each with 15 seconds of rest between each set. The 12 stretch sets were a rotation of 3 separate stretches. On a separate visit, the same subjects performed the same isokinetic muscle actions without stretching beforehand. The isokinetic torque after the stretching protocol was significantly lower than the non-stretching visit at both slow ($30°\cdot s^{-1}$) and fast ($270°\cdot s^{-1}$) velocities. It was suggested that the decrease in torque was due to a decrease in muscular stiffness (as demonstrated by a decrease in maximal MMG amplitude) without any neural changes (as shown by no change in maximal EMG amplitude). The author's concluded that acute bouts of static stretching are detrimental to athletic performance.

Ryan et al., 2008 [239]

The objective of this study was to examine the recovery time course of musculotendinous stiffness (MTS) to passive stretching trials of varying durations. The varying durations were 2, 4, and 8 min. of passive, static stretching of the plantar flexors which were performed in 30 second repetitions. MTS decreased immediately after each condition. The 2-min. stretching trial showed a recovery in MTS within 10 min. The 4 and 8 min. trials took 20 minutes to return to baseline.

Ryan et al., 2008 [238]

The aim of this study was to examine the effect and recovery of 3 duration-varying stretching protocols on neuromuscular function in the plantar flexors. The durations differed from most prolonged stretching studies as these trials were of more practical durations (2, 4, and 8 min.). Torque decreased immediately after each trial, but did not significantly differ from a control trial. EMG amplitude remained unaltered for all conditions. Only the 4 and 8 min. stretch duration trials showed decreases in peak twitch torque and rate of twitch torque development, but were not sufficient to alter voluntary force production. Range of motion increased for all conditions, but had returned to baseline within 10 minutes. The authors concluded that practical durations of static stretching do not exhibit a detrimental influence on performance.

Cè et al., 2008 [45]

The purpose of this study was to determine if post-activation potentiation (PAP) and conduction velocity (CV) were affected by an acute bout of stretching. MVCs were tested prior to and immediately after passive stretches (5×45 s) of the biceps brachii. CV and peak torque increased from pre to post in the control condition (no stretches), but showed no change in the stretch trial. It was concluded that the acute bout of passive stretching blunted the typical effects of PAP.

Costa et al., 2009 [54]

The purpose of this study was to examine the effects of prolonged stretching of the hamstrings on the hamstrings-to-quadriceps ratio and EMG amplitude. This study was particularly relevant to this dissertation because surface EMG signals were detected pre- and post-stretching in the agonist and antagonist muscles during both leg extension and flexion. The subjects underwent approximately 19 minutes of stretching. During leg flexion (agonist was stretched), antagonist coactivation of the quadriceps increased slightly. During leg extension, peak torque increased, and antagonist coactivation of the hamstrings (the stretched muscle) decreased. It should be noted that there was a 10 minute break between the last stretch and the post-testing.

Ryan et al., 2009 [240]

The purpose of this study was to determine the minimum number of passive stretches necessary to alter musculotendinous stiffness. The subjects underwent a series of multiple 30-sec passive, constant-torque stretches of the plantarflexors. Interestingly, the authors found that only two bouts of 30-sec stretches was enough to reduce musculotendinous stiffness.

Herda et al., 2009 [142]

The aim of this study was to examine the acute effects of prolonged passive stretching and vibration on neuromuscular function. Peak torque, percent voluntary activation, peak twitch torque, passive range of motion, musculotendinous stiffness, EMG amplitude, and MMG amplitude of the medial gastrocnemius and soleus muscles were recorded before and immediately after each condition (including a control trial). The stretching protocol was similar to the one performed by Fowles et al. [105] (135 second sets, 5 seconds of rest in-between sets) with the exception of 4 less sets (i.e. 20 minutes under stretch instead of 30). For vibration, a percussion hammer was attached to the Achilles tendon for 20 minutes at a frequency of 70 Hz. Both the stretch (-10%) and vibration (-5%) trials resulted in significant decreases in peak torque. Percent voluntary activation did not significantly change, but EMG amplitude declined for both conditions. Passive range of motion showed a significant increase after stretch, but no change with vibration. Likewise, musculotendinous stiffness showed a significant decrease after stretch, but no change with vibration.

Sandberg et al., 2012 [241]

The purpose of this study was to examine the acute effects of antagonist stretching on vertical jump, torque, and EMG amplitude. The hamstrings underwent 3 sets of 30 second passive stretching with 20 seconds of rest in-between each one.

Antagonist (hamstring) stretching led to an increase in leg extension torque and vertical jump height. There were no changes in EMG amplitude. It should be noted that, in an attempt to stretch the thigh flexors, an antagonist for vertical jump, the authors stretched the rectus femoris, which is also an agonist for leg extension (it crosses both the hip and knee joints).

2.5.1 Summary of the "Effects of Stretching on Neuromuscular Function"

It has been hypothesized that when a muscle is passively stretched for a prolonged period of time, it leads to a plastic deformation of the connective tissue, thereby elongating all of the fibers within. The resting length of the both the extrafusal and intrafusal fibers increase, which significantly desensitizes the responses from muscle spindles[128]. Consequently, the H-reflex and tendon tap reflex become attenuated[128]. In fact, repetitive stretching can decrease stretch-reflex sensitivity by up to 85%[12]. Reduction to the spindle's sensitivity could also reduce the excitatory drive from large Ia afferents to the α-motor neuron pool, thereby leading to a decrease in EMG amplitude[142]. However, stretch-induced changes to the muscle are not always associated with changes in EMG amplitude[100, 238]. Under conditions of high-intensity stretching, a GTO response can also be elicited[146]. Hypothetically, it might be possible to desensitize the GTOs if a stretch is intense enough and of long enough duration. Either way, it is clear that the spindle responses are greatly diminished after prolonged stretching. Therefore, it is hereby proposed that having a muscle undergo periods of prolonged stretching

could be used as a method for examining neuromuscular function without the input from spindles, and possibly even GTOs. Such an intervention might be a simple, yet effect tool to help in discriminating the inputs underlying agonist/antagonist interactions and/or mechanisms for motor unit synchronization.

3. METHODS

3.1. Participants

Seventeen healthy, college-aged (18-35 yr olds) men and women volunteered for this investigation. All subjects completed an informed consent, a pre-exercise health and exercise status questionnaire, and indicated no current or recent neuromuscular or musculoskeletal problems to their dominant shoulder, elbow, or wrist. This study was approved by the University's Institutional Review Board prior to data collection.

3.2. Research Design

The study required 5 separate visits to the lab. The first visit consisted of maximal voluntary contraction (MVC) testing of the forearm flexors and extensors, and familiarization with the testing procedures. A separate visit involved an exercise protocol designed to fatigue the agonist muscle group. The primary muscles of interest were the biceps brachii (BB) (agonist; "flexors") and the triceps brachii (TB) (antagonist; "extensors"). They were referred to in the summary below as "flexors" and "extensors". Another visit involved the same fatiguing protocol, but for the antagonists. The final 2 visits consisted of prolonged stretching of the agonist or the antagonist. Below is a summary of each visit:

1. First Visit (in order):
   1.1. Three MVCs of the Flexors
   1.2. Three MVCs of the Extensors
   1.3. Familiarization:
      - practice the submaximal ramp contractions with visual feedback of force

2. Agonist-Fatigue Visit (in order):
   2.1. Pre-Test:
      - Three 20-s, submaximal contractions of the Flexors
      - Pre-Fatigue MVC of the Extensors
      - Pre-Fatigue MVC of the Flexors
   2.2. Fatigue of the *Flexors*:
      - Intermittent 10-s contractions at 70% MVC
   2.3. Post-Test:
      - Three 20-s, submaximal contractions of the Flexors
      - Post-Fatigue MVC of the Flexors
      - Post-Fatigue MVC of the Extensors

3. Antagonist-Fatigue Visit (in order):
   3.1. Pre-Test:
      - Three 20-s, submaximal contractions of the Flexors
      - Pre-Fatigue MVC of the Flexors
      - Pre-Fatigue MVC of the Extensors
   3.2. Fatigue of the *Extensors*:
      - Intermittent 10-s contractions at 70% MVC
   3.3. Post-Test:
      - Three 20-s, submaximal contractions of the Flexors
      - Post-Fatigue MVC of the Extensors
      - Post-Fatigue MVC of the Flexors

4. Agonist-Stretch Visit (in order):
   4.1. Pre-Test:

- Three 20-s, submaximal contractions of the Flexors
- Pre-Stretch MVC of the Flexors
- Pre-Stretch MVC of the Extensors

4.2. Prolonged stretch of the Flexors:

- Twelve 100-s cycles interspersed with 15-s of rest (20 min. total)

4.3. Post- Agonist Stretch Test:

- Three 20-s, submaximal contractions of the Flexors
- Post-Stretch MVC of the Flexors
- Post-Stretch MVC of the Extensors

5. Antagonist-Stretch Visit (in order):

5.1. Pre-Test:

- Three 20-s, submaximal contractions of the Flexors
- Pre-Stretch MVC of the Extensors
- Pre-Stretch MVC of the Flexors

5.2. Prolonged stretch of the Extensors:

- Twelve 100-s cycles interspersed with 15-s of rest (20 min. total)

5.3. Post- Antagonist Stretch Test:

- Three 20-s, submaximal contractions of the Flexors
- Post-Stretch MVC of the Extensors
- Post-Stretch MVC of the Flexors

Please refer to the Data Collection Form in Appendix C to see a visual representation of the study design. Visits 2-5 were completed in a randomized order and separated by a minimum of 48 hours.

3.3. Instrumentation and Procedures

3.3.1 Isometric Strength Assessment

The subjects were seated at a table with their dominant arm placed in a custom-built, isometric strength testing apparatus. The arm was flexed 90° at the shoulder with the elbow resting on a soft pad. The forearm was flexed 90° at the elbow and a soft cuff was secured around the participant's wrist. The cuff was secured to the apparatus perpendicular to the forearm with a load cell (Model SSM-AJ-500, Interface Inc., Scottsdale, AZ) to measure isometric force (N). Forearm flexion force wasmeasured when the subject is facing the apparatus, and forearm extension force was measured when the subject is facing away from the apparatus (see Figure 2). Following a warm-up of four, 15 sec. submaximal isometric muscle actions at approximately 50% MVC, the subjects performed three, 5-s MVCs of the flexors and three, 5-s MVCs of the extensors. Each MVC was separated by 2-3 minutes of rest, and the highest force value from the three trials was designated as the subject's MVC for that muscle group.

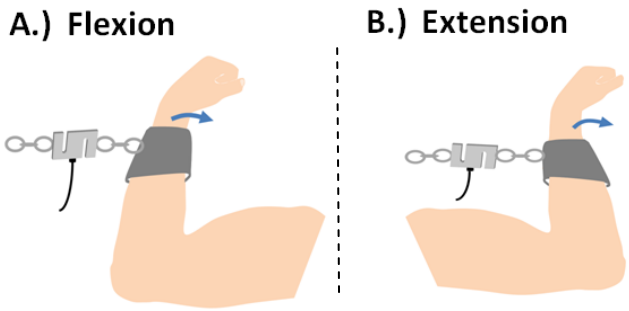


Figure 2 - A.) Testing setup for isometric strength of the forearm flexors. **B.)** Testing setup for isometric strength of the forearm extensors

3.3.2 Submaximal Muscle Actions

Submaximal, isometric trapezoid muscle actions were performed at 60% of the subject's pre-testing MVC (see Figure 3). The trapezoid required a linear force increase from 0% to 60% MVC over a period of 6-s, a constant force hold at 60% MVC for 10-s, and a linear force decrease from 60% MVC to 0% over a 4-s period (total time = 20-s). Visual feedback of the real-time force level was provided to the subjects along with a target template of the trapezoid. This feedback helped minimize error and ensure that the subject is as close to the target force template as possible. The extended duration of the ramp-up and constant-hold portions of the trapezoid were planned with special considerations for the motor unit recruitment (see section 3.3.7), synchronization (section 3.3.8), and synaptic potential (section 3.3.9) analyses.

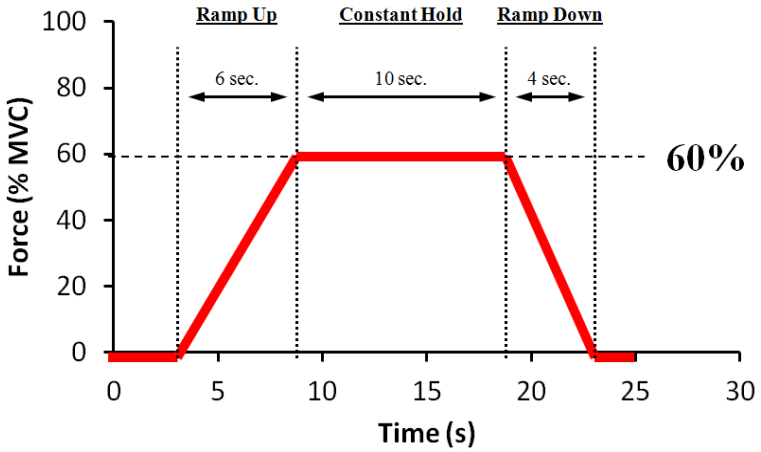


Figure 3 - An example of the trapezoid template used for submaximal the isometric muscle actions. Visual feedback of the subject's real-time force level was overlayed on the screen as the subject attempts to match the template.

3.3.3 Fatiguing Protocol

Local muscular fatigue was induced with intermittent, submaximal contractions, each held at 70% MVC for 10-s and interspersed with 5-s rest periods. The MVCs were retested each minute throughout the protocol to track the development of fatigue. The protocol continued until the subject can no longer achieve 70% of the pre-fatigue MVC. This protocol was designed with two special considerations in mind: a.) to assure that each subject was fatigued to the same magnitude (slightly below 70% MVC), and b.) to assure that each subject could still complete the necessary trapezoidal contractions at 60% MVC during the post-test.

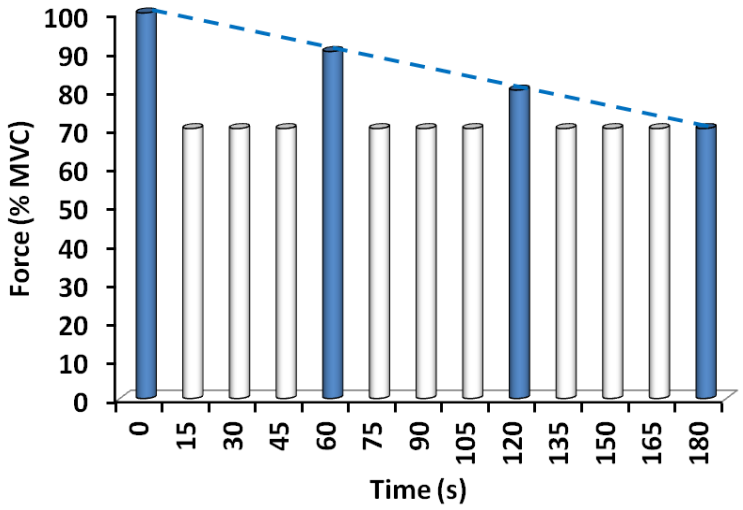


Figure 4 - Fatigue Protocol. Fatigue was induced with intermittent submaximal contractions, each held at 70% MVC for 10-s (empty columns) and interspersed with 5-s of rest. MVCs were retested each minute throughout the protocol (dark columns) to track the development of fatigue. The protocol ended when the subject has difficulty reaching 70% of the pre-fatigue MVC.

3.3.4 Stretching Protocol

The biceps brachii and triceps brachii muscles underwent prolonged stretching during two separate visits. The subjects performed 12 total, 100-s stretches for a total of 20 minutes under stretch, with 15-s rest periods between each stretch cycle. Stretches that were used for the BB and TB can be found in Tables 1 and 2, respectively. The stretches that were used varied slightly for each subject depending on which ones provided the best stretch for that individual, as based on their verbal feedback.

Table 1 – Stretches for the Biceps Brachii (BB) muscle

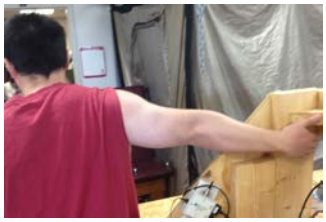
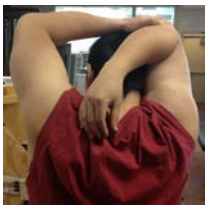
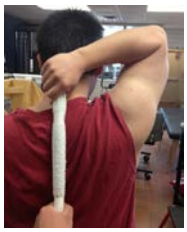
A.)		Reaching backwards, posteriorly abduct the dominant arm, keeping it perpendicular to the trunk. The forearm should be supinated so that the thumb is pointing superiorly. The subject grabbed the frame of the testing apparatus and rotated their trunk away from their arm until a sufficient stretch was felt.
B.)		Reaching backwards, posteriorly abduct the dominant arm, keeping it perpendicular to the trunk. The forearm should be pronated so that the thumb is pointing inferiorly. The subject grabbed the frame of the testing apparatus and rotated their trunk away from their arm until a sufficient stretch was felt.
C.)		With the dominant arm fully extended, the subject supinated and hyperextend the hand, using the force of a solid surface (e.g. ground, table, etc.) to apply the stretch.

Table 2 – Stretches for the Triceps Brachii (TB) muscle

A.)		Flex the dominant arm to at least 180° at the shoulder joint. Flex the forearm so that the hand is resting on the upper back. With the non-dominant hand, pull downward on the dominant elbow until a stretch is felt in the TB.
		Other variations of this stretch include applying the resistance with a towel pulled from below, or manual resistance applied from the investigator.
B.)		Reaching forwards, flex the dominant arm to at least 90° at the shoulder joint and extend the forearm. While grasping onto an immovable object (e.g. doorframe, testing apparatus, etc.), drop the bodyweight backwards until a stretch is felt in the shoulders and TB muscles.

3.3.5 Electromyography

Four separate surface electromyographic (EMG) sensors were placed on the subject's dominant arm during visits 2-5. Two sensors detected EMG from the biceps brachii, and the other two detected signals from the triceps brachii. One of the sensors on each muscle was a bipolar electrode (DE-2.1; Delsys, Inc., Boston, MA) with a 1 cm interelectrode distance. The second sensor for each muscle was a

specialized 5-pin square array (Delsys, Inc., Boston, MA) designed specifically for the motor unit decomposition analyses. The EMG sensors were placed on the BB in accordance with specific recommendations for use with the decomposition analyses[313], which is approximately over the belly of the muscle. The EMG sensors for the TB was placed in accordance with specific recommendations from the SENIAM project[143], which corresponds to 2 finger lengths medial from the center of the line (i.e. 50% of the distance) between the acromion process and the olecranon. Sensor locations were traced with a permanent marker to assure consistent placement between visits. A reference electrode (Dermatrode, American Imex, Irvine, CA) was placed on the spinous process of the C7 vertebrate at the inferior portion of the neck. Prior to electrode placement, the surface of the skin for the sensor sites was prepared in accordance with the procedures described in the surface EMG decomposition user's manual (reference). Specifically, the skin was shaved, cleansed with rubbing alcohol, and touched repeatedly with hypo-allergenic tape to remove dead skin. The 5-pin sensor was also lightly dabbed with an alcohol pad to moisten the tips. The sensors were then firmly secured to the skin with hypo-allergenic surgical tape.

3.3.6 Signal Processing

The analog EMG signals were collected with a modified Bagnoli desktop EMG system (Delsys Inc, Boston, MA). The EMG signals from the 5-pin sensor were analog high-pass filtered (cutoff frequency = 100 Hz), low-pass filtered (cutoff frequency = 9,500 Hz), and sampled at 20 kHz. The EMG signals were then digitally band-pass filtered (8^{th}-order Butterworth; cut-offs of 250 and 2000 Hz) prior to decomposition (see section 3.3.7). The EMG signals from the bipolar electrodes were analog band-passed filtered with cutoffs of 20 and 450 Hz. The amplitude of each EMG signal was assessed as the root-mean-square (RMS; V) and normalized to the value obtained during that muscle group's MVC.

3.3.7 EMG Decomposition

The raw EMG signals from the 5-pin sensor were decomposed into their constituent motor unit action potential trains (MUAPTs) using the Precision Decomposition (PD) III algorithm recently described by De Luca et al.[70] and improved by Nawab et al.[218]. The MUAPTs were then tested for accuracy using the Decompose-Synthesize-Decompose-Compare (DSDC) test described by De Luca and Contessa [73]. To reduce the potential influence of false positive and false negative firings, any motor unit that did not demonstrate an accuracy of 90.0% or greater was eliminated from further analyses. Any motor unit that did not demonstrate an accuracy of 95.0% or greater was eliminated from synchronization

analyses. Figure 5-A shows an example of the firings for 21 motor units detected from the VL during a trapezoid muscle action up to 80% MVC [76]. Mean firing rate and recruitment threshold was also calculated for each motor unit. Recruitment threshold was defined as the force level (%MVC) at which the motor unit first started firing, and were obtained from the individual motor unit firings, not the mean firing rates. Mean firing rate curves were computed for each MUAPT by low-pass filtering the impulse train with a 1-s unit-area Hanning window. Low-threshold motor units were those recruited below 30% MVC, with motor units recruited at or above 30% MVC designated as high-threshold. Previously used cutoffs to distinguish between low- and high-threshold motor units have been 20% MVC [290] , 25% MVC [1, 44, 274] and 30% MVC [131]. Furthermore, it has been demonstrated that the biceps brachii, which has maximal motor unit recruitment ranges up to 90-95% MVC [177], has recruited close to 50% (23 of 49) of its motor units at 30% MVC [177].

3.3.8 Motor Unit Synchronization

The synchronization between the firings of motor unit pairs were examined by constructing cross-interval histograms in accordance with the technique first applied by De Luca et al.[66] and later by Contessa et al.[51]. The cross-interval histograms (see Figure 5-D) were constructed from each possible unique pairing of MUAPTs by measuring only the first-order forward and backward recurrence times (see Figure 5-C). The firings used for this analysis were pulled from the center,

approximately flat portion of the mean firing rate plot (Figure 5-B) for each motor unit. When the flat portion of a motor unit's mean firing rate is selected, the same portion was pulled from all previous motor units for comparison. For example, after selecting the appropriate firings from motor unit # 4's mean firing rate plot, the same portion was pulled from motor units 1-3 for comparison (i.e., 4 vs. 3, 4 vs. 2, and 4 vs. 1). A separate portion was then selected for motor unit 5 for comparisons of 5 vs. 4, 5 vs. 3, etc. The analyses were performed using these descending-order comparisons because the region of stable mean firing rates gets progressively smaller with increases in recruitment threshold (see Figure 5-B). For any given motor unit pair, the motor unit with the lowest number of firings in the selected region was designated as the reference motor unit. The second was designated as the test motor unit. For each motor unit comparison, two separate cross-interval histograms were constructed: one with the original, observed firings, and a second in which the firings of the reference motor unit are randomly shuffled. The shuffled histogram represents the between-firing latencies if the two motor units are completely independent of each other (i.e., no common synaptic inputs). The width of the histograms were limited to ± the mean interpulse interval for the reference motor unit (e.g. histogram x-axis ranges from -50 to 50 ms for a reference motor unit with an interpulse interval of 50 ms). A 95% confidence interval (CI) was calculated for the shuffled histogram and then overlaid on top of the observed histogram. Any peaks in the observed histogram that fall below the 95% CI was considered to have occurred from chance and any peaks that exceed the CI was

subsequently considered significant. In other words, the peak is considered to have more synchronous firings at that latency than could be expected from chance alone. The magnitude of synchronization of the significant peaks was then calculated using the "Sync Index" (%) described by De Luca et al. [66]. In short, the Sync Index is the percentage of extra events (i.e. percentage of firings beyond what would be expected from chance alone) normalized to the number of firings in the reference motor unit. With short-term synchronization being of particular interest in this study, a separate short-term Sync Index was also calculated maintaining the entire histogram as total area, but only considering the significant peaks that occur between -6 and 6 ms. If no peaks exceed the 95% CI, then the resulting Sync Index was 0% (i.e. no synchronization is present). The short-term Sync Indexes from each of the motor unit pairs within a single contraction were pooled together and averaged. This allowed the synchronization for a single contraction to be expressed as a single value (i.e. average short term Sync Index).

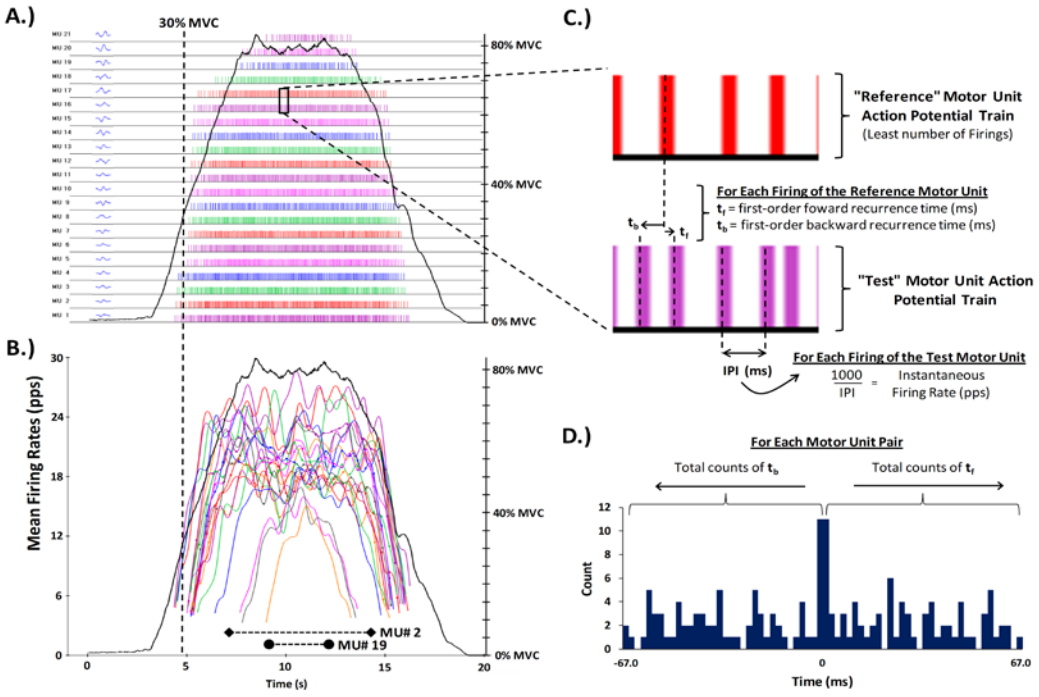


Figure 5 - A: The individual motor unit action potential trains during the isometric, trapezoid muscle action. Each vertical bar represents a motor unit firing. The solid black line is the subject's force output. **B:** The mean firing rate curves for each of the motor units depicted in A. The horizontal dashed line with the diamond ends represents the region of firings that was used for subsequent analysis for motor unit 2. The horizontal dashed line with the circles represents the same region for motor unit 19. The vertical dashed line represents the cutoff (30% MVC) between low- and high- threshold motor units. In this particular muscle action there were only four motor units that were designated as low-threshold. **C:** Visual depiction of the first-order forward and backward recurrence times used to construct a cross-interval histogram (**D**). The interpulse intervals (IPIs) of the test motor unit are used to calculate instantaneous firing rates (pulses per second). Reproduced from DeFreitas et al.[76]

3.3.9 Estimation of Net Post-Synaptic Potentials

Within each motor unit comparison, instantaneous firing rates (IFRs; pulses per second) were calculated for each firing of the test motor unit by dividing 1,000 by the interpulse interval (IPI; ms) leading up to the firing. The IFR of each firing was then plotted against when that firing occurs in time relative to the closest firing of the reference motor unit to construct a peri-spike frequencygram[296]. The IFRs in the peri-spike frequencygram are sorted into ascending order by their value on the x-axis (e.g., sorted from firings occurring near -50 ms to 0 ms to 50 ms in relation to the reference motor unit). A cumulative sum (CUSUM) was then computed after sorting the peri-spike frequencygram (see Figure 6-A+B). In short, the CUSUM creates a series of new data points by comparing each of the original data points to a reference value, and then summing it to the previous points[93] (see pg 85-86 for a summary). In the present study, the original data points were the IFRs of the test motor unit, and the reference value was the mean firing rate. If two motor units are near their firing threshold, then a common excitatory post-synaptic potential would bring both motor units closer to firing, and, consequently, decrease the interpulse interval. In turn, a common inhibitory input would cause both motor units to increase the IPI (i.e. take longer to reach firing threshold). Therefore, an increase in the slope of the CUSUM would signify that consecutive firings of the motor unit were firing above its mean firing rate (i.e. it was reaching threshold earlier than typical). Such an outcome would suggest that the two motor units shared a common excitatory input. On the other hand, a decrease in the CUSUM would be suggestive

of a common inhibitory input to the two motor units, causing both to delay their firings. To quantify the estimated net post-synaptic potentials (nPSPs) during periods of short-term synchronization, a linear slope wascalculated for the CUSUM of the firings that were within 6 ms of a reference motor unit firing (see Figure 6-D). Since the IFRs were sorted along the x-axis of the peri-spike frequencygram, all of the test motor unit firings that occurred within 6 ms of a reference motor unit firing were consecutive data points in the CUSUM, regardless of when they occurred in the original muscle action. As a result, a positive slope would signify excitatory inputs that led to short-term synchronization between the motor unit pair, and a negative slope would suggest that inhibitory inputs led to the synchronization.

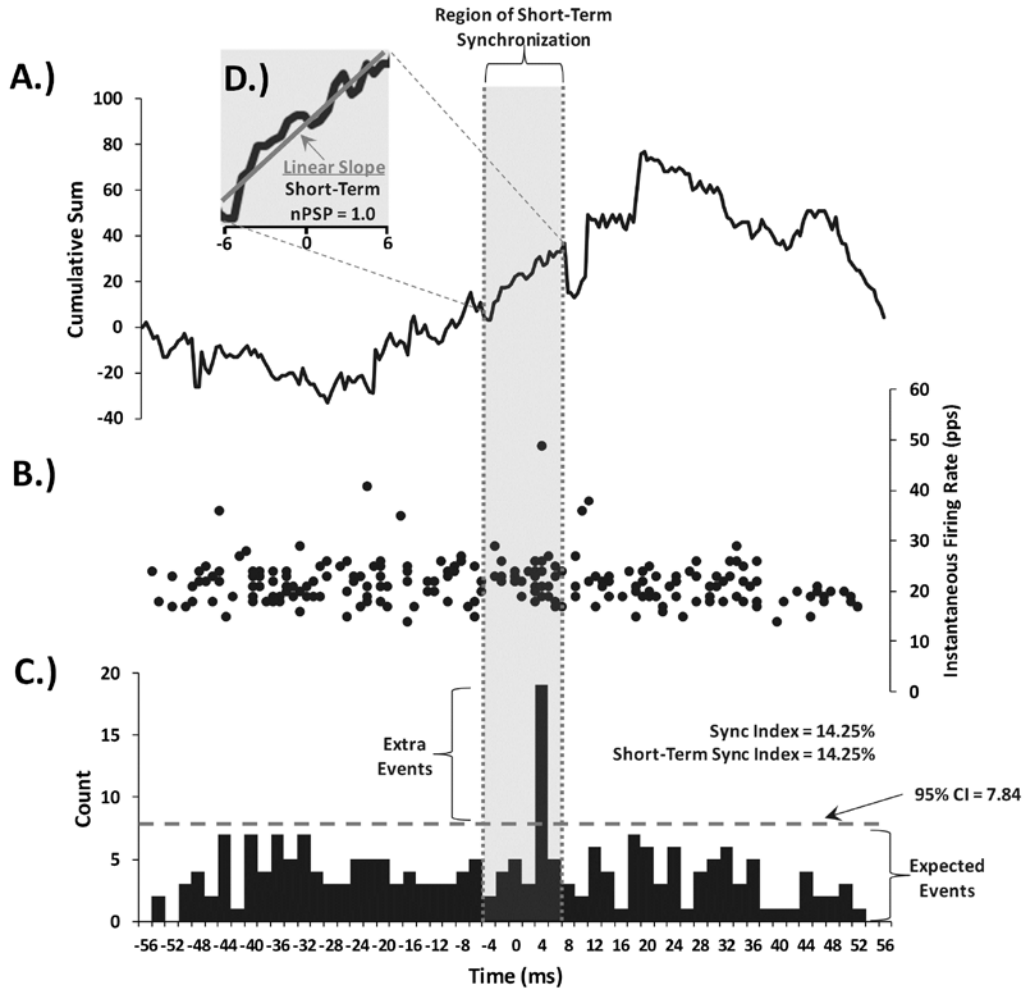


Figure 6 - At the bottom is an example cross-interval histogram (**C**) from a pair of low-threshold motor units. The magnitude of synchronization was calculated as the Sync Index. The vertical shaded area depicts the region of short-term synchronization (-6 to 6 ms). Significant peaks are those that exceed the 95% confidence interval (CI). The peri-spike frequencygram (**B**) contains the instantaneous firing rate (IFR; pulses per second) of each firing of the test motor unit plotted against when that firing occurred in time relative to the firing of the reference motor unit. The cumulative sum (CUSUM) technique (**A**) was then applied to the peri-spike frequencygram to detect trends. The net post-synaptic potential (nPSP) for the firings that happened to be short-term synchronized with the other motor unit was estimated by taking a linear slope of the CUSUM within the short-term region (**D**). In the above example, each firing within that short-term region is occurring, on average, 1.0 pulse per second faster than the motor unit's mean firing rate (nPSP = 1.0). That increased firing rate for the synchronized firings would be due to an increase from a common excitatory input. Reproduced from DeFreitas et al.[76]

3.4. Statistical Analyses

Mean motor unit firing rate (MFR) and recruitment threshold (RT) relationships for each contraction were analyzed using linear regression to obtain the regression coefficients (i.e. slope and y-intercept). Linear regression was also applied to the pooled motor unit data (pooled across all of the subjects). Next, ten separate 2-way (contraction [pre and post] × condition [agonist-fatigue, antagonist-fatigue, agonist-stretch, and antagonist-stretch]; "within-within") repeated measures analysis of variance (ANOVAs) were performed. The ten dependent variables were flexor force, extensor force, antagonist coactivation, and force steadiness, as well as average mean firing rate, average short-term sync index, and average nPSP for both the biceps and triceps brachii muscles. When appropriate, follow-up analyses included paired samples t-tests. An alpha level of 0.05 was used as the starting value to determine statistical significance for all comparisons. However, a Bonferroni correction was performed based on the number of follow-up t-tests that were necessary (0.05 divided by the number of t-tests). Effect size (ES) was assessed and reported using Cohen's d (mean difference divided by the pooled standard deviation).

4. RESULTS

4.1. Descriptives

Seventeen subjects participated in this investigation. Thirteen of the participants were males (mean ± SD: age = 25.4 ± 3.2 yrs, height = 1.82 ± 0.05 m, weight = 90.3 ± 12.8 kg) and four were females (mean ± SD: age = 25.4 ± 2.7 yrs, height = 1.64 ± 0.03 m, weight = 64.2 ± 4.1 kg). Sixteen of the participants completed all 5 visits, and one performed 4 of the 5 total visits. Accuracy tests were performed on the motor units detected from the biceps brachii and triceps brachii from each contraction. Only motor units that met at least the 90% accuracy criterion were analyzed. After having detected 6,458 total motor units, 5,360 motor units met the 90% accuracy criterion and were used for further analyses (3,708 motor units from the biceps brachii, and 1,652 motor units from the triceps brachii). From those motor units, 94,689 unique pairs were used for synchronization and nPSP analyses (67,529 pairs for the biceps brachii, and 27,160 pairs for the triceps brachii). However, since the synchronization analyses used individual firings, and not simply mean firing rates, a stricter accuracy criterion was required. Only pairs in which both motor units had at least 95% accuracy were kept for further analysis. Due to the strict accuracy criteria, there were many instances in which entire contractions had to be eliminated from analysis (due to an insufficient number of accurate motor units). Of those original 94,689 unique motor unit pairs, 36,789 of the pairs met the stricter accuracy criterion. All 10 repeated measures ANOVAs showed a significant interaction. Therefore, 40 follow-up t-tests were performed

(pre vs. post for each of the 10 variables for each of the 4 conditions). To avoid a family-wise, compounded Type I error from the multiple t-tests, the alpha level was Bonferroni corrected and adjusted to 0.00125 (0.05/40).

4.2. Effects of Agonist Fatigue on Neuromuscular Function

All seventeen participants completed this visit. In all, 1,471 motor units were used for analysis; 964 from the biceps brachii (465 pre-fatigue and 499 post-fatigue), and 507 from the triceps brachii (259 pre-fatigue and 248 post-fatigue). From these motor units, 10,550 unique pairs were used for synchronization analysis; 7,797 from the biceps brachii (3,595 pre-fatigue and 4,202 post-fatigue), and 2,753 from the triceps brachii (1,598 pre-fatigue and 1,155 post-fatigue). The force and EMG results are shown in Figure 7. Averaged mean firing rates, short-term synchronization, and nPSPs are shown in Figure 8. The pooled MFR/Recruitment Threshold relationships can be seen in Figure 9. Figure 10 shows the pooled Short-term Sync Index/Mean Recruitment Threshold relationships.

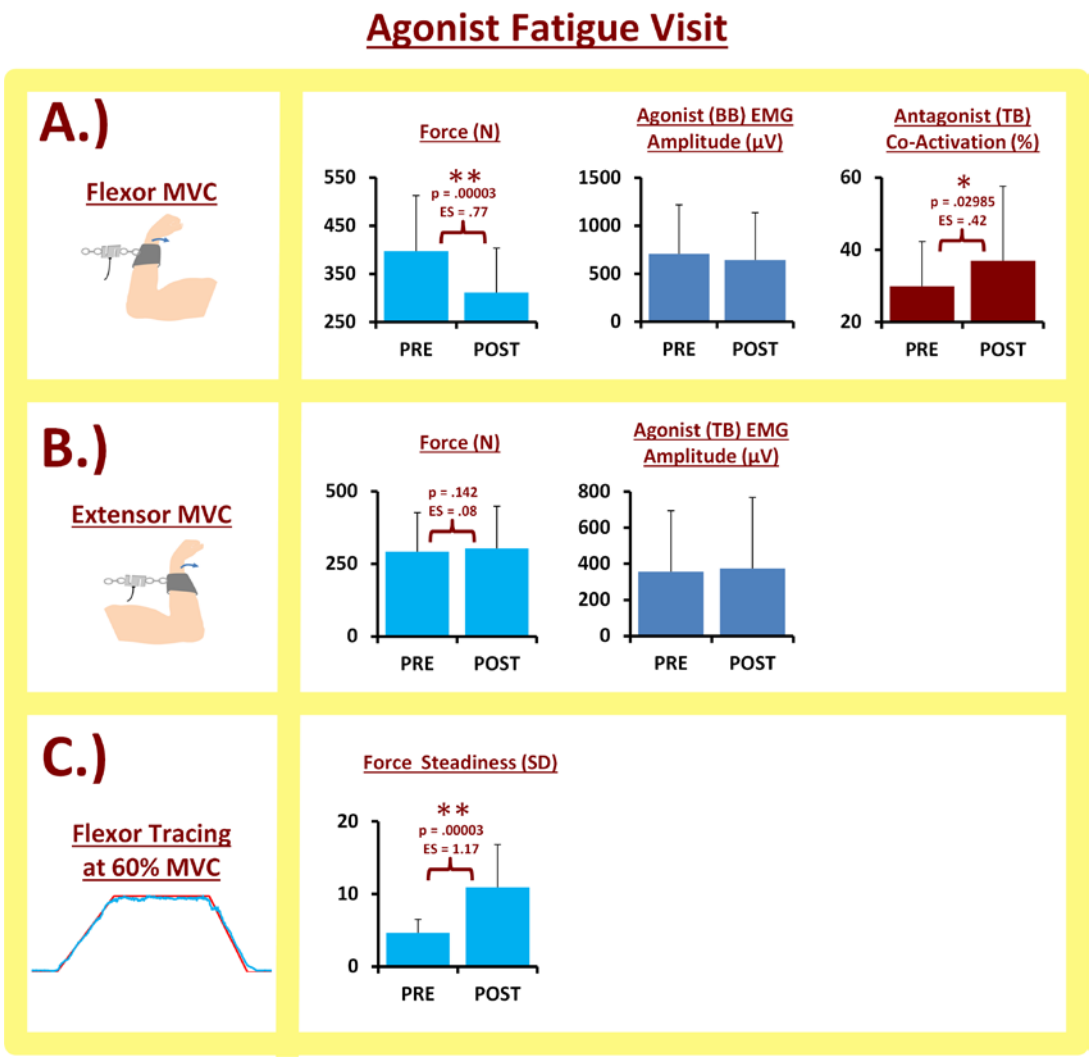


Figure 7 – Force and electromyography (EMG) variables before and after fatigue of the agonist muscle. MVC = maximal voluntary contraction, BB = biceps brachii, TB = triceps brachii, N = Newtons, SD = standard deviation, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

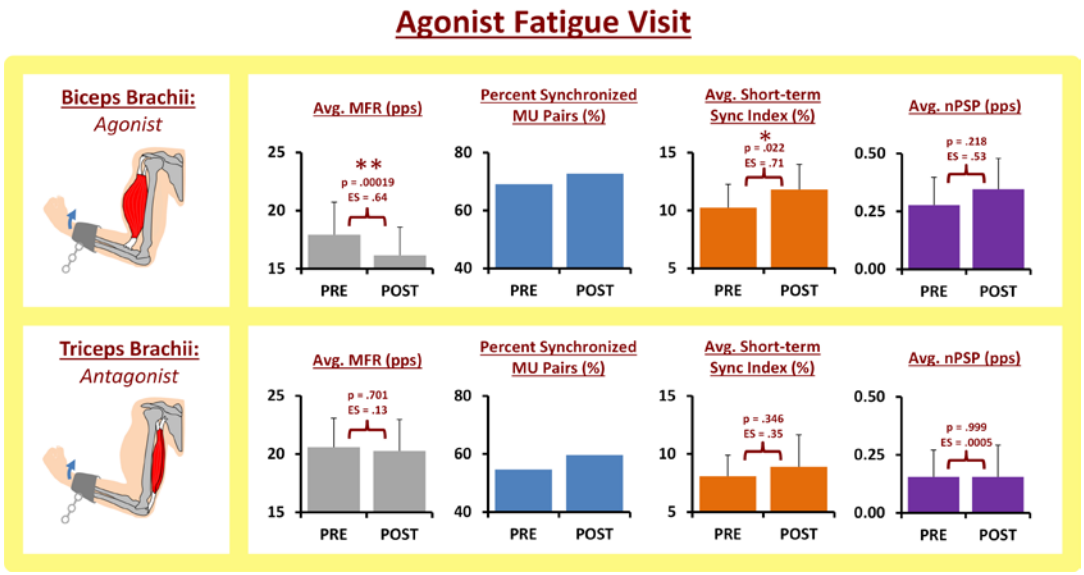


Figure 8 – Average motor unit variables before and after fatigue of the agonist muscle. Avg. = Average, MFR = Mean Firing Rate, nPSP = net post-synaptic potential, pps = pulses per second, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

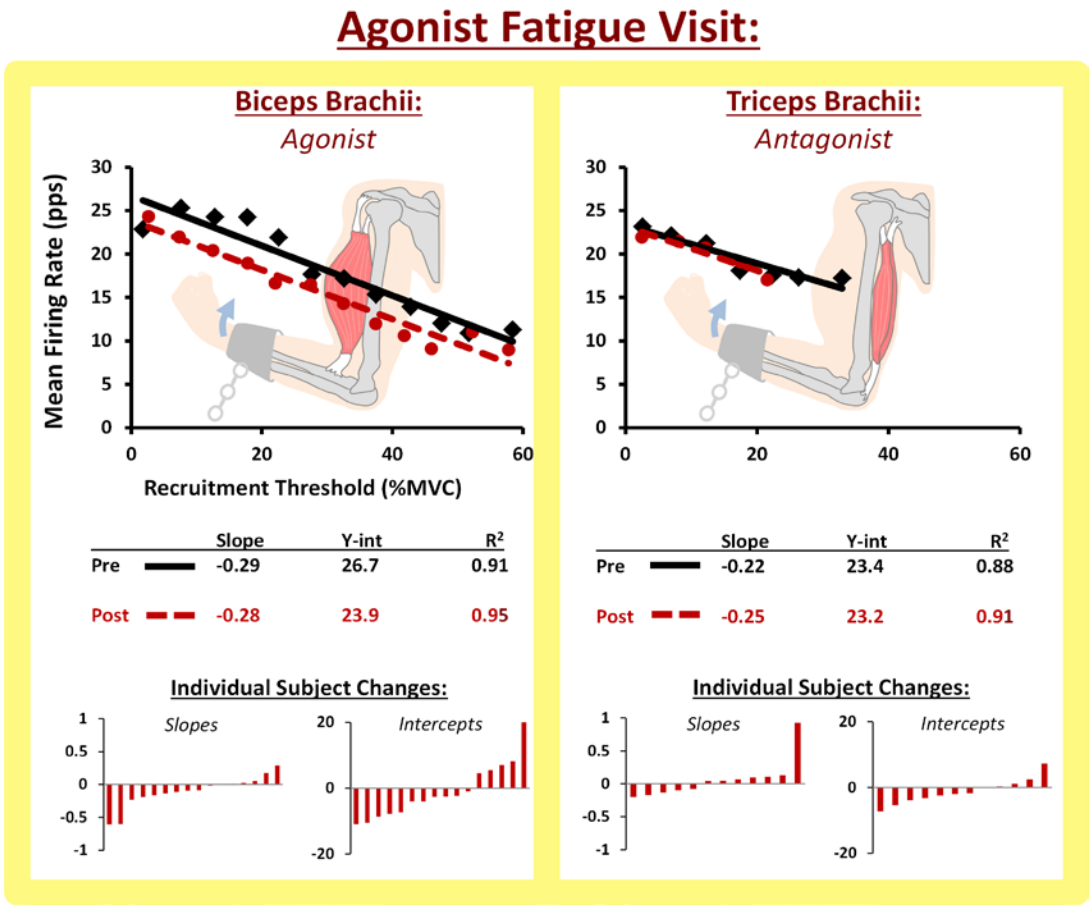


Figure 9 – Mean Firing Rate /Recruitment Threshold relationships before and after fatigue of the agonist muscle. The figures in the top row are pooled from all of the subject's motor units and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction, pps = pulses per second

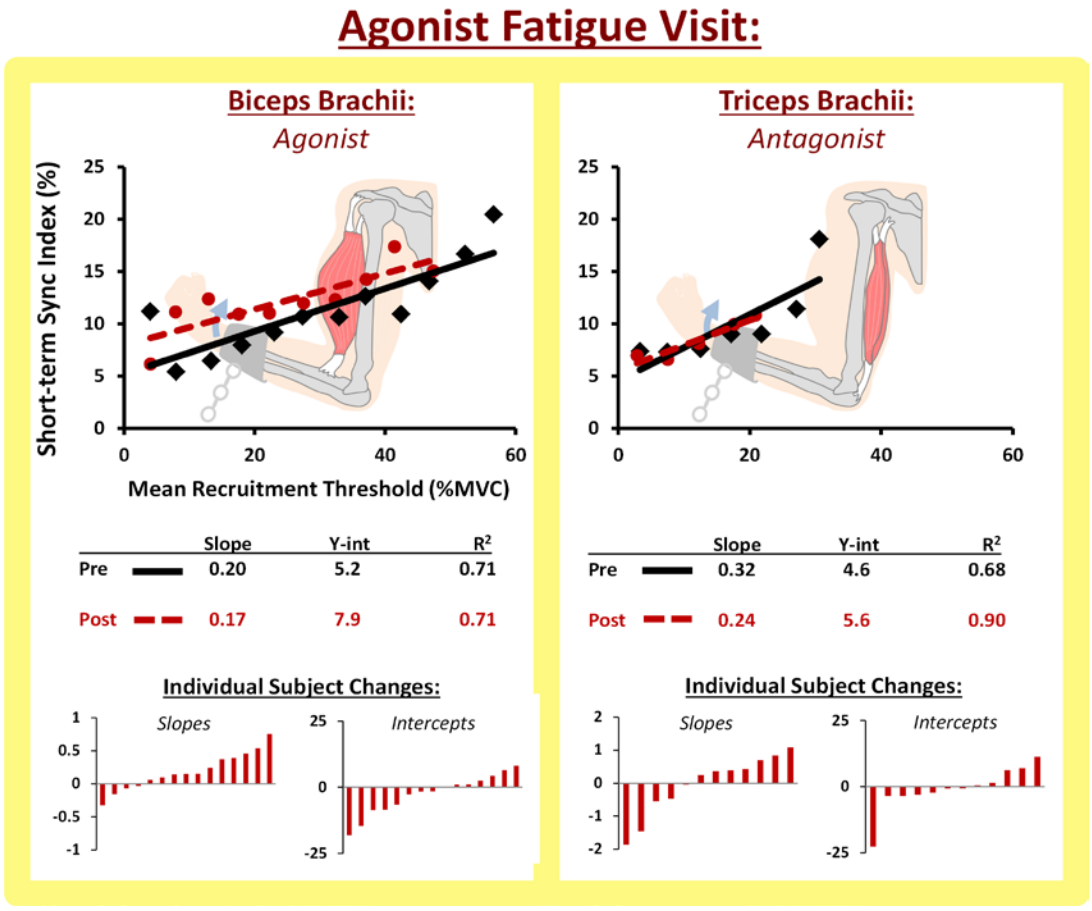


Figure 10 – Short-term Synchronization Index /Mean Recruitment Threshold relationships before and after fatigue of the agonist muscle. The figures in the top row are pooled from motor unit pairs from all of the subjects and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction

4.3. Effects of Antagonist Fatigue on Neuromuscular Function

Sixteen of the participants completed this visit. In all, 1,216 motor units were used for analysis; 900 from the biceps brachii (471pre-fatigue and 429 post-fatigue), and 316 from the triceps brachii (162 pre-fatigue and 154 post-fatigue). From these motor units, 8,492 unique pairs were used for synchronization analysis; 7,296 from the biceps brachii (4,105 pre-fatigue and 3,191 post-fatigue), and 1,196 pairs from the triceps brachii (650 pre-fatigue and 546 post-fatigue). The force and EMG results are shown in Figure 11. Averaged mean firing rates, short-term synchronization, and nPSPs are shown in Figure 12. The pooled MFR/Recruitment Threshold relationships can be seen in Figure 13. Figure 14 shows the pooled Short-term Sync Index/Mean Recruitment Threshold relationships.

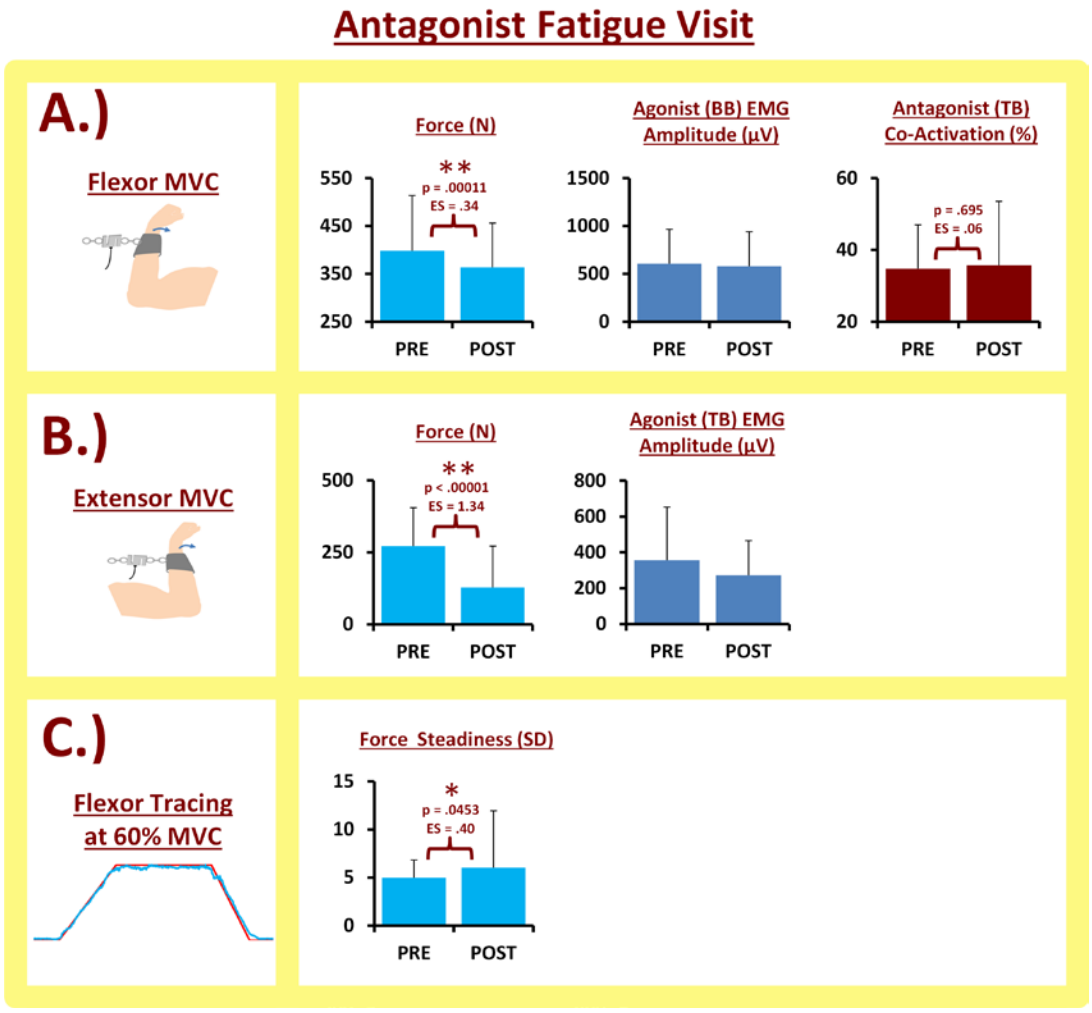


Figure 11 – Force and electromyography (EMG) variables before and after fatigue of the antagonist muscle. MVC = maximal voluntary contraction, BB = biceps brachii, TB = triceps brachii, N = Newtons, SD = standard deviation, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

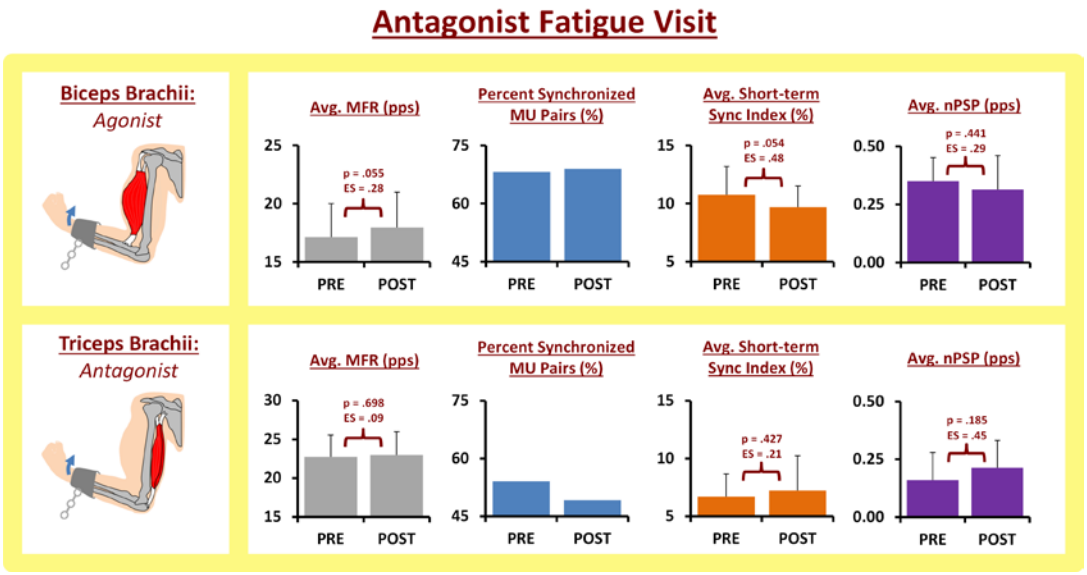


Figure 12 – Average motor unit variables before and after fatigue of the antagonist muscle. Avg. = Average, MFR = Mean Firing Rate, nPSP = net post-synaptic potential, pps = pulses per second, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

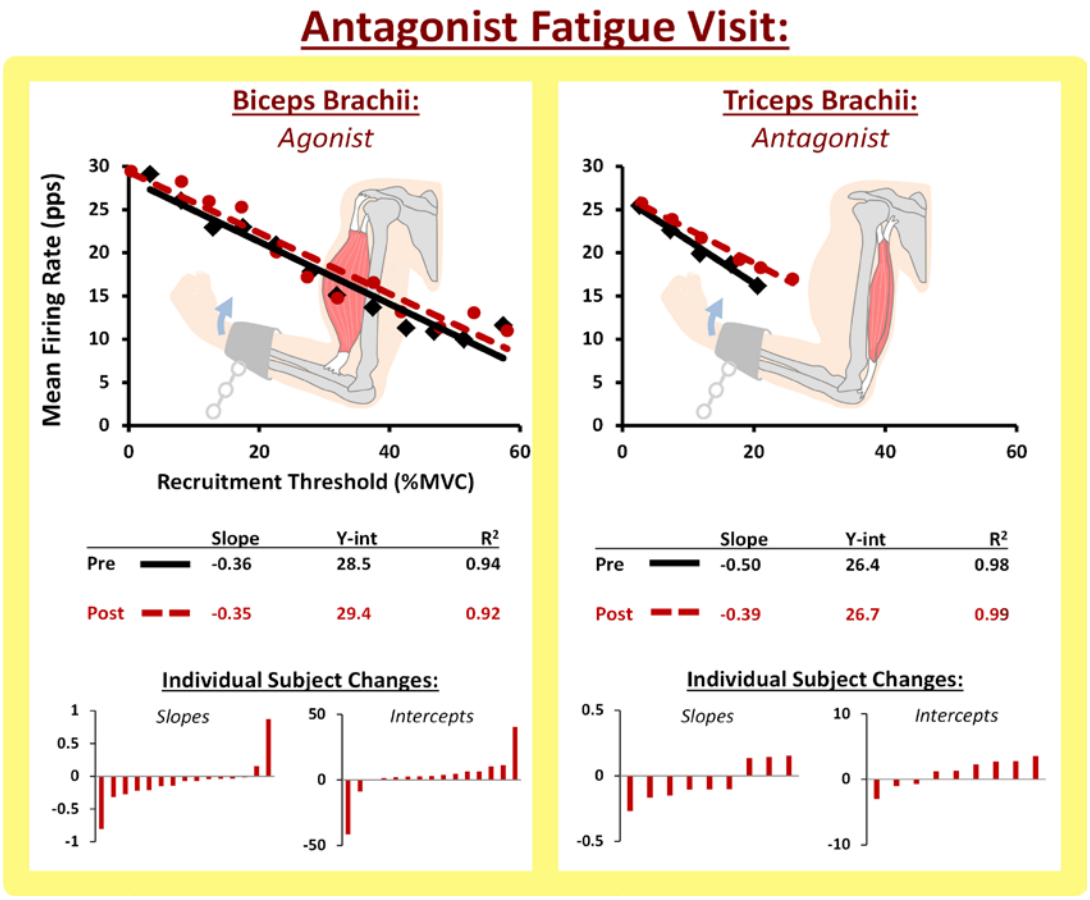


Figure 13 – Mean Firing Rate /Recruitment Threshold relationships before and after fatigue of the antagonist muscle. The figures in the top row are pooled from all of the subject's motor units and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction, pps = pulses per second.

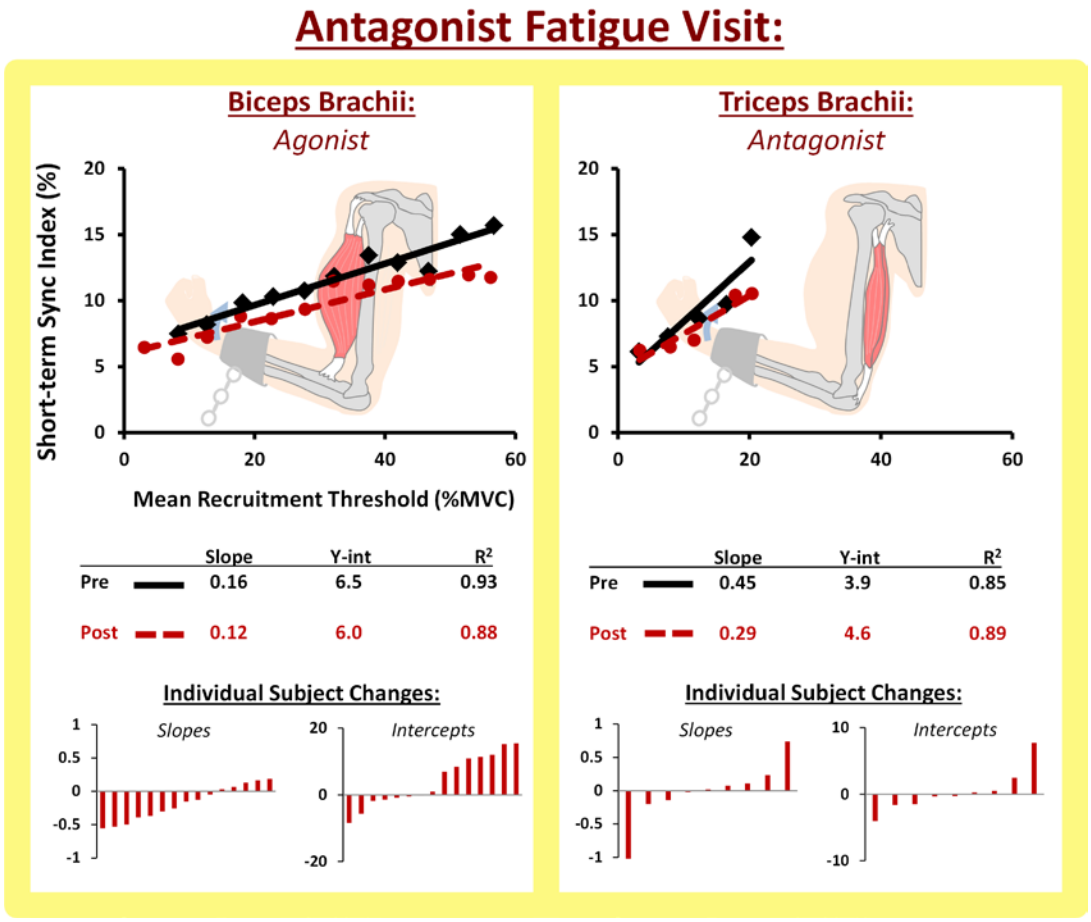


Figure 14 – Short-term Synchronization Index /Mean Recruitment Threshold relationships before and after fatigue of the antagonist muscle. The figures in the top row are pooled from motor unit pairs from all of the subjects and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction

4.4. Effects of Prolonged Agonist Stretch on Neuromuscular Function

All seventeen participants completed this visit. In all, 1,424 motor units were used for analysis; 962 from the biceps brachii (488 pre-fatigue and 474 post-fatigue), and 462 from the triceps brachii (238 pre-fatigue and 224 post-fatigue). From these motor units, 9,921 unique pairs were used for synchronization analysis; 7,697 from the biceps brachii (4,055 pre-fatigue and 3,642 post-fatigue), and 2,224 from the triceps brachii (1,067 pre-fatigue and 1,157 post-fatigue). The force and EMG results are shown in Figure 15. Averaged mean firing rates, short-term synchronization, and nPSPs are shown in Figure 16. The pooled MFR/Recruitment Threshold relationships can be seen in Figure 17. Figure 18 shows the pooled Short-term Sync Index/Mean Recruitment Threshold relationships.

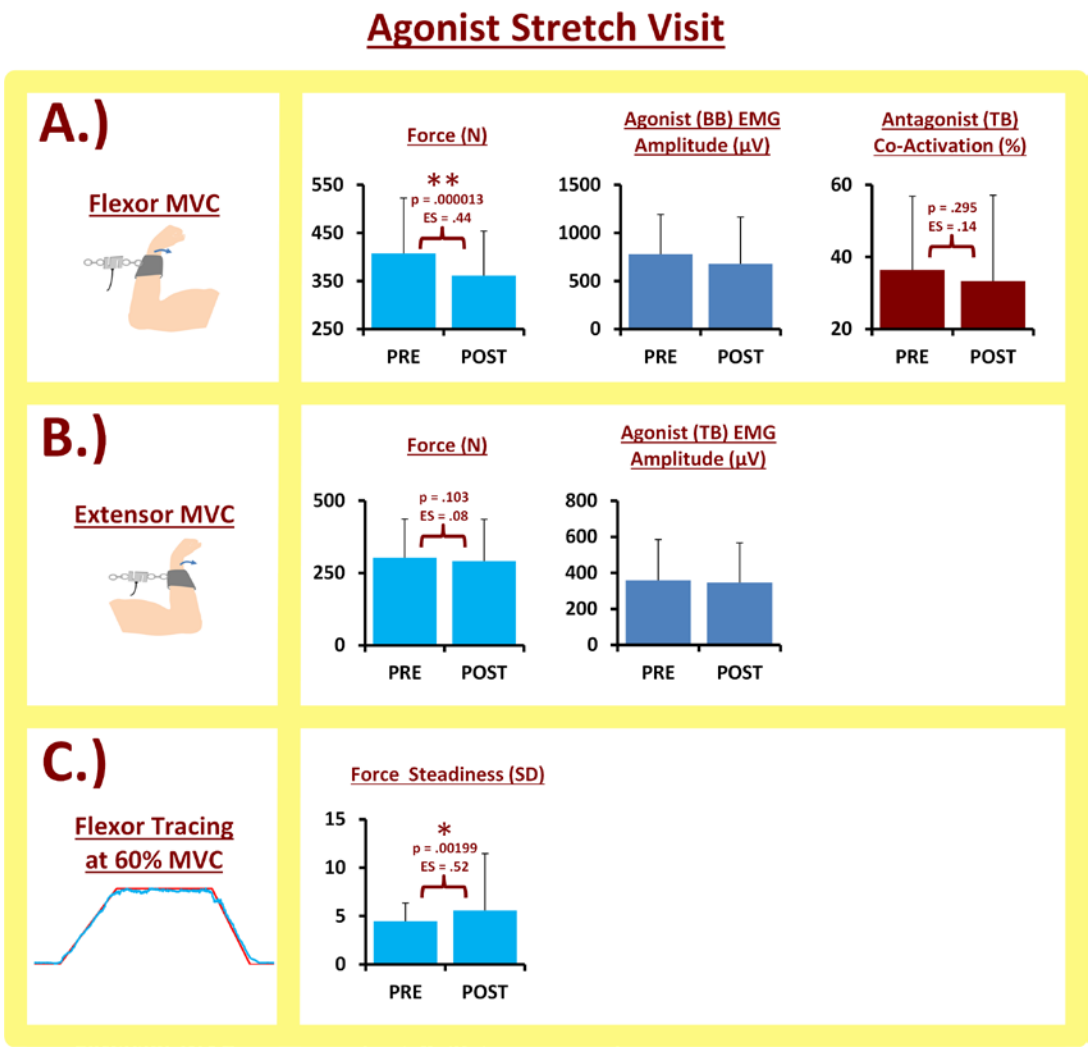


Figure 15 – Force and electromyography (EMG) variables before and after prolonged stretching of the agonist muscle. MVC = maximal voluntary contraction, BB = biceps brachii, TB = triceps brachii, N = Newtons, SD = standard deviation, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

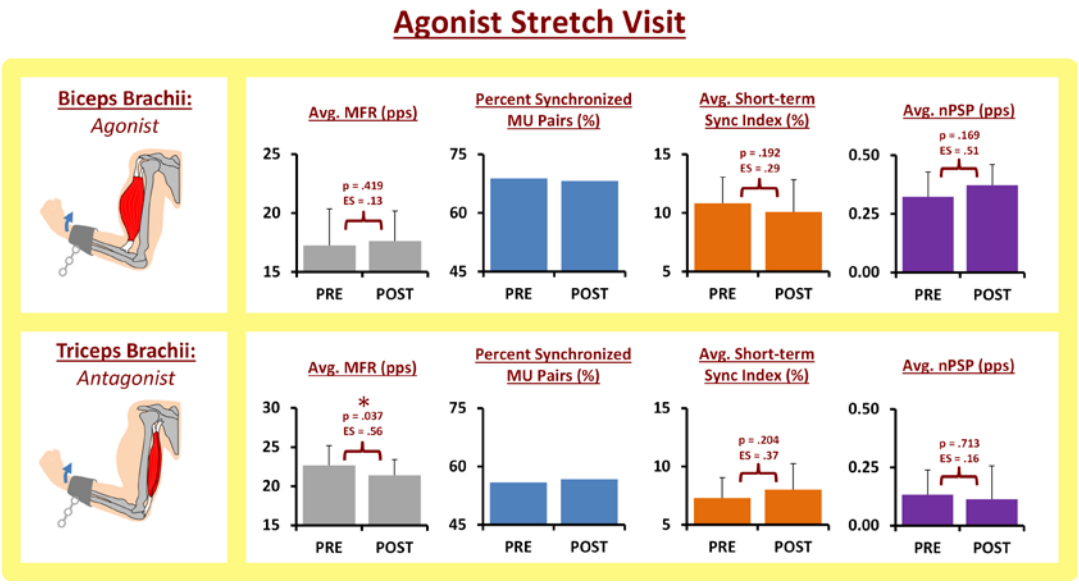


Figure 16 – Average motor unit variables before and after prolonged stretching of the agonist muscle. Avg. = Average, MFR = Mean Firing Rate, nPSP = net post-synaptic potential, pps = pulses per second, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

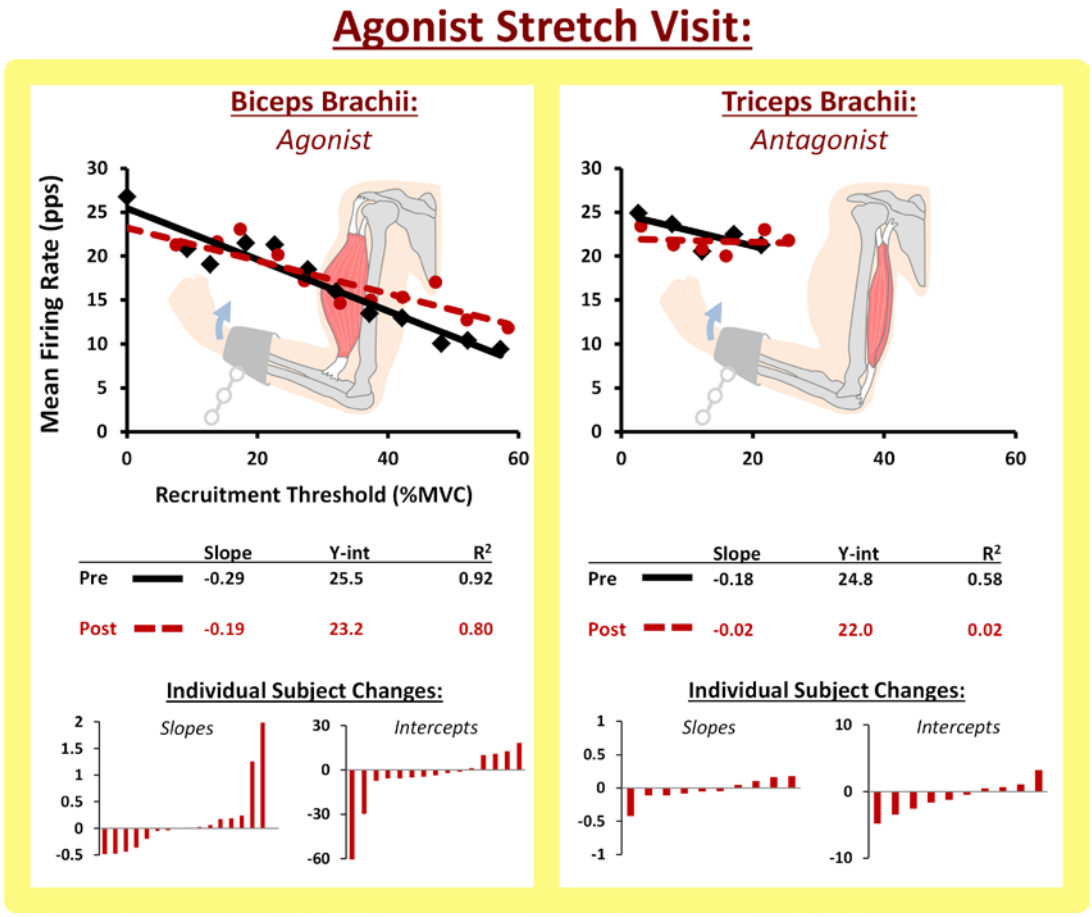


Figure 17 – Mean Firing Rate /Recruitment Threshold relationships before and after prolonged stretching of the agonist muscle. The figures in the top row are pooled from all of the subject's motor units and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction, pps = pulses per second.

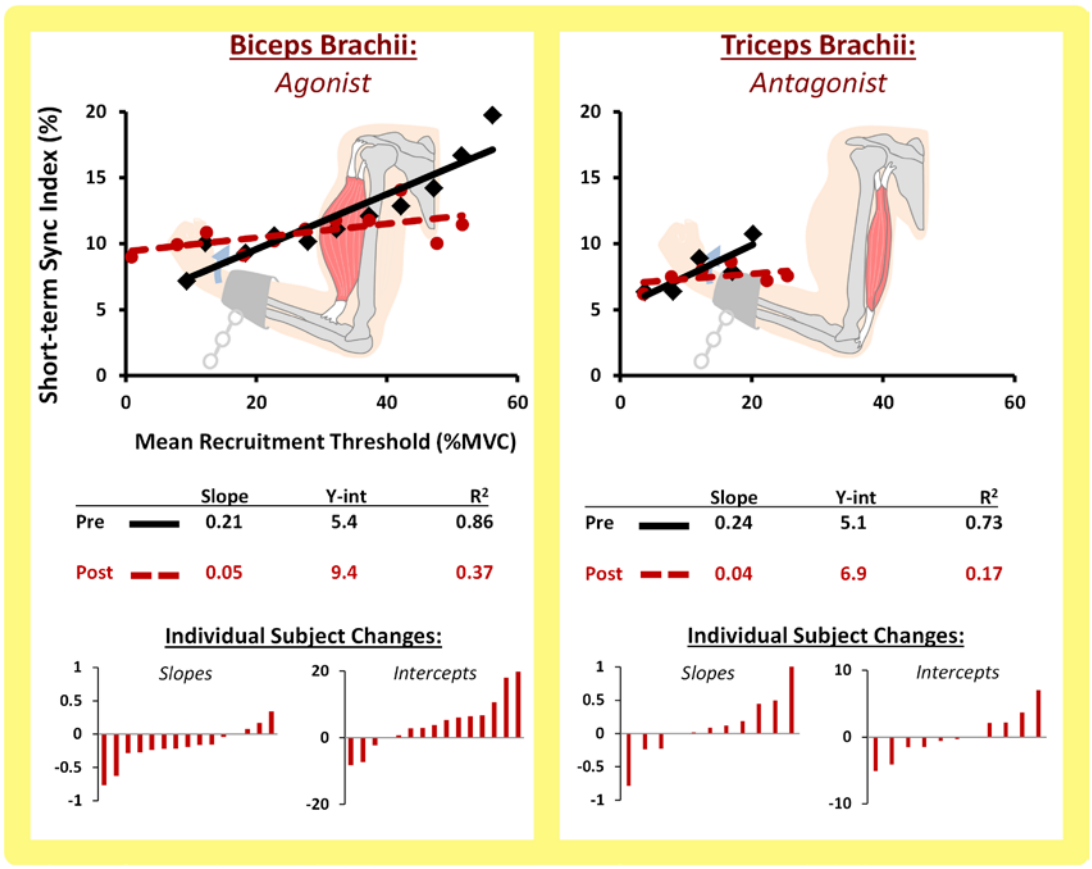


Figure 18 – Short-term Synchronization Index /Mean Recruitment Threshold relationships before and after prolonged stretching of the agonist muscle. The figures in the top row are pooled from motor unit pairs from all of the subjects and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction

4.5. Effects of Prolonged Antagonist Stretch on Neuromuscular Function

All seventeen participants completed this visit. In all, 1,249 motor units were used for analysis; 882 from the biceps brachii (446 pre-fatigue and 436 post-fatigue), and 367 from the triceps brachii (183 pre-fatigue and 184 post-fatigue). From these motor units, 7,826 unique pairs were used for synchronization analysis; 6,386 from the biceps brachii (3,176 pre-fatigue and 3,210 post-fatigue), and 1,440 from the triceps brachii (661 pre-fatigue and 779 post-fatigue). The force and EMG results are shown in Figure 19. Averaged mean firing rates, short-term synchronization, and nPSPs are shown in Figure 20. The pooled MFR/Recruitment Threshold relationships can be seen in Figure 21. Figure 22 shows the pooled Short-term Sync Index/Mean Recruitment Threshold relationships.

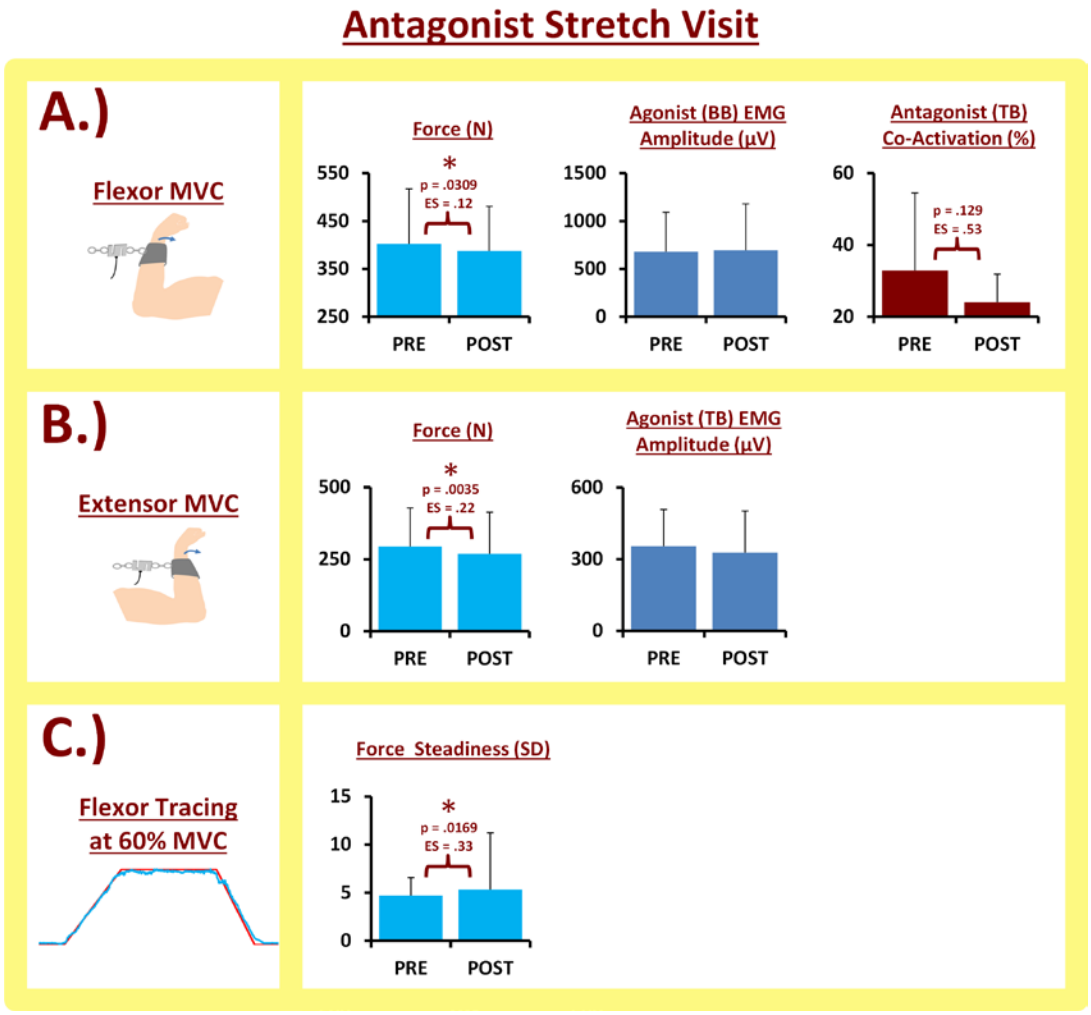


Figure 19 – Force and electromyography (EMG) variables before and after prolonged stretching of the antagonist muscle. MVC = maximal voluntary contraction, BB = biceps brachii, TB = triceps brachii, N = Newtons, SD = standard deviation, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

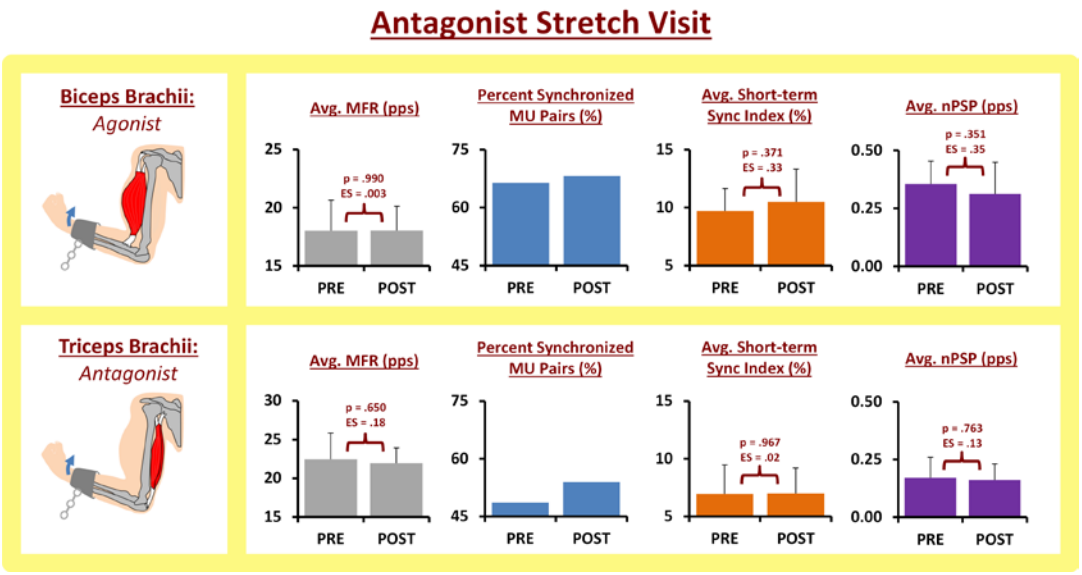


Figure 20 – Average motor unit variables before and after prolonged stretching of the antagonist muscle. Avg. = Average, MFR = Mean Firing Rate, nPSP = net post-synaptic potential, pps = pulses per second, ES = effect size. One asterisk signifies that the p-value was below 0.05. Two asterisks signifies that the p-value was below the Bonferroni corrected value of 0.00125.

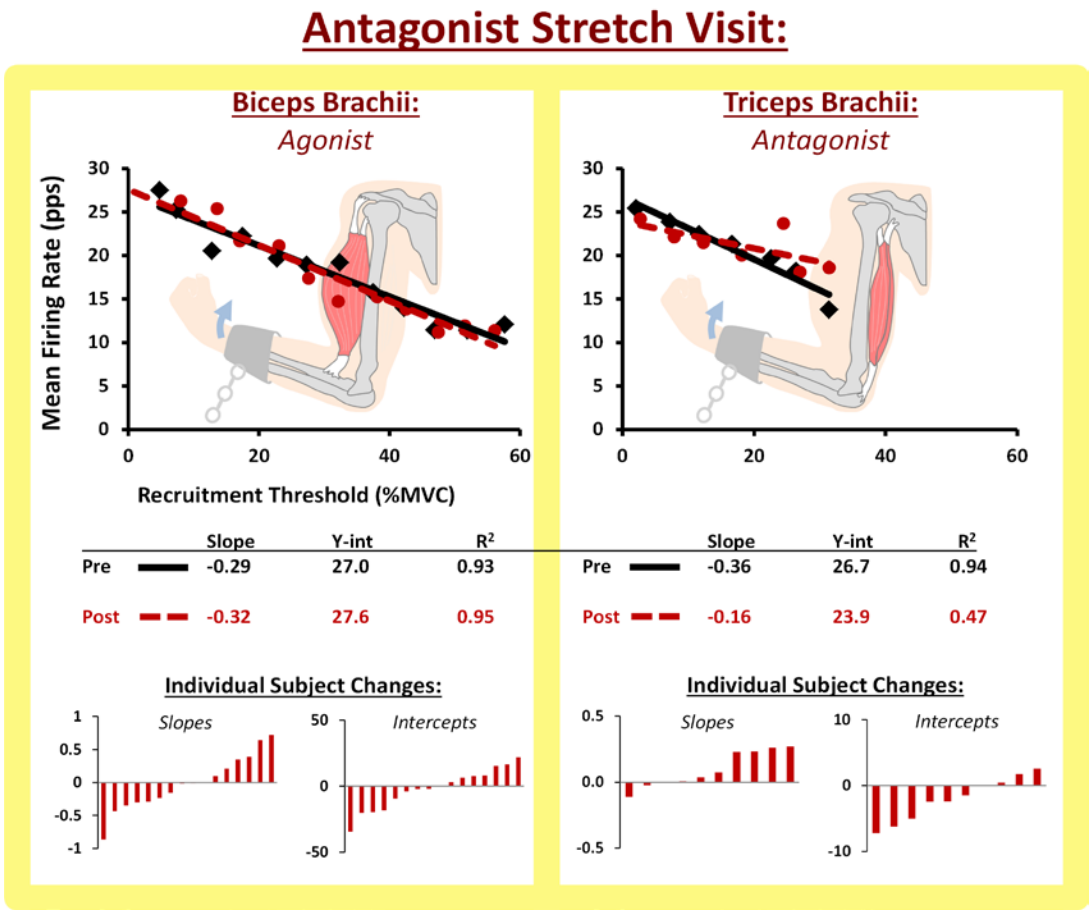


Figure 21 – Mean Firing Rate /Recruitment Threshold relationships before and after prolonged stretching of the antagonist muscle. The figures in the top row are pooled from all of the subject's motor units and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction, pps = pulses per second.

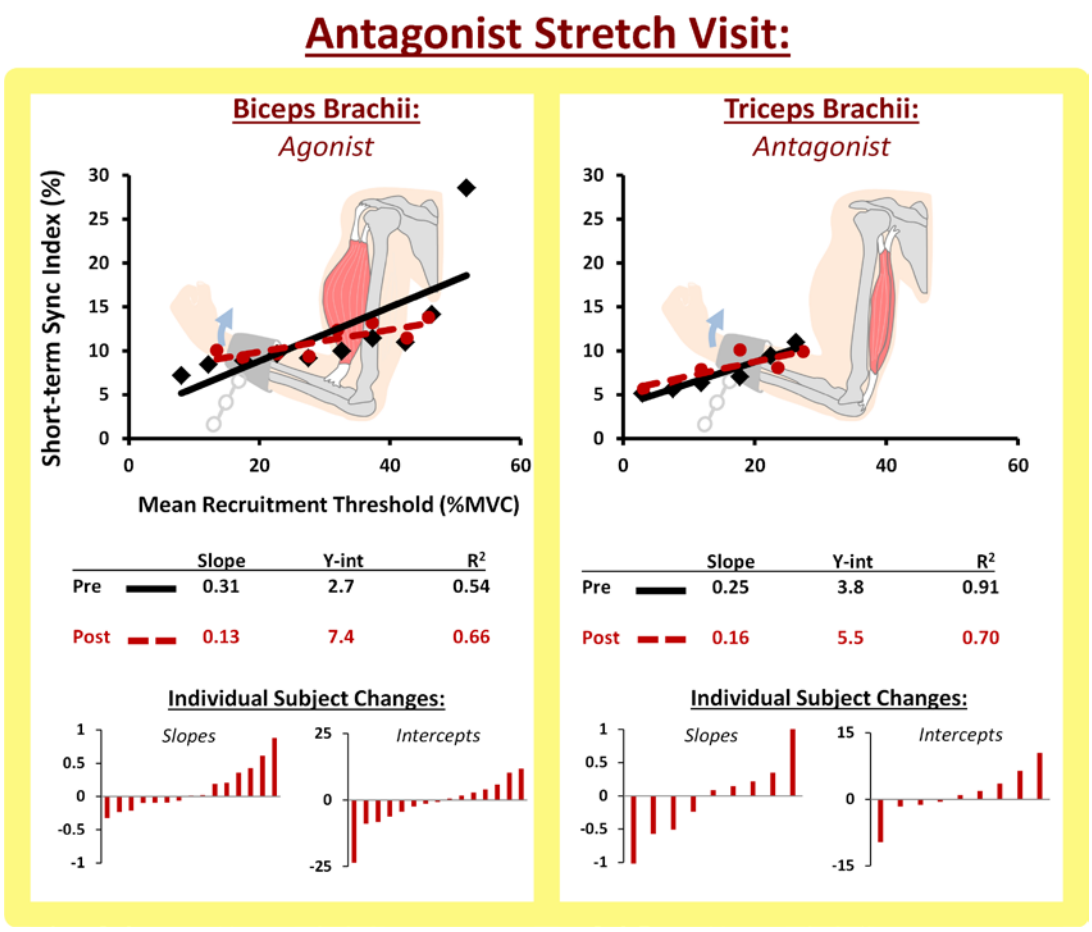


Figure 22 – Short-term Synchronization Index /Mean Recruitment Threshold relationships before and after prolonged stretching of the antagonist muscle. The figures in the top row are pooled from motor unit pairs from all of the subjects and averaged in 5% intervals. The tables in the second row show the regression coefficients from the lines in the top figures. The bottom row shows the individual patterns of response. MVC = Maximal voluntary contraction.

5. DISCUSSION

5.1. Implications and Significance

The focus of this investigation was to examine the changes that occur in agonist and antagonist motor unit firing properties due to fatigue and stretching. The first observation was that antagonist motor unit firing properties during coactivation differed from those of agonist motor units. The MFR/RT plots demonstrated a considerably smaller recruitment threshold range in the antagonists, as well as higher firing rates. However, the higher firing rates might simply be an artifact of the small recruitment threshold range (i.e. more low-threshold motor units, which have higher firing rates). Furthermore, the antagonist motor units demonstrated significant levels of short-term synchronization, but to a lesser extent than was exhibited by the agonist motor units. Across the four pre-testing sessions, approximately 66-69% of the agonist motor unit pairs demonstrated significant short-term synchronization compared to 48-56% of the antagonist motor unit pairs. Additionally, the average short-term synchronization index for agonist motor units was 10.4% compared to 7.3% in the antagonist motor units.

The effects from agonist fatigue were as hypothesized, with one exception. This predictability is a reflection of the fact that more work has been performed examining motor unit function in response to agonist fatigue than of the other interventions administered in the present study. Consistent with previous findings during agonist fatigue, the present investigation showed that antagonist coactivation

increased[234], force steadiness was reduced[51, 213], the average firing rate of agonist motor units decreased[276], and short-term synchronization increased[26]. The significant decrease in average agonist motor unit firing rates was likely due to changes in recruitment thresholds. As lower-threshold motor units become fatigued, progressively higher-threshold motor units are recruited to aid in maintaining force[303]. Since motor unit firing rates progressively decrease with increases in recruitment threshold (e.g. see MFR/RT plots), this additional recruitment of higher-threshold motor units would cause a decrease in the average firing rate. This additional recruitment could also help explain the increases in synchronization since higher-threshold motor unit pairs exhibited greater levels of synchronization than lower-threshold motor unit pairs (e.g. see Sync Index/Mean RT plots).

Interestingly, despite the increase in coactivation, agonist fatigue had no effect on the antagonist motor unit firing properties. This was an unexpected outcome and the hypothesis that antagonist motor unit firing rates would increase was not supported by the data. The finding of an increase in EMG amplitude without changes to the motor unit firing properties is interesting. The EMG sensors remained attached to the skin for the duration of each visit, so it is unlikely that any methodological or technical differences could have affected the signal's amplitude. It has been shown that agonist muscle spindle afferents, which have an inhibitory effect on the antagonist[86], progressively decrease their firing rates with fatigue[189]. A decrease in the inhibition to the antagonist motor units would have an excitatory-like effect and may have increased the number of antagonist motor units that were

active. Hypothetically, it is possible that the lower firing rates of newly recruited, higher-threshold motor units could offset an increase in the firing rates of the previously active motor units; thereby causing no change in the average firing rates. However, an increase in recruitment threshold should have been accompanied by an increase in synchronization, and it was not. Furthermore, whether possible or not, there is an inherent discomfort in providing a physiological justification for why a variable did *not* change, regardless of how unexpected it was. Despite the significant change in coactivation, the possibility that agonist fatigue simply had no effect on antagonist motor unit firing properties cannot be disregarded. Additional research in this area is definitely needed.

The effects of the antagonist fatigue provided many interesting results. The most surprising finding was that it did not affect coactivation of the antagonist. None of the agonist or antagonist motor unit firing properties showed significant changes. The flexor MVC significantly decreased, which was not in support of my hypothesis. Although, it is important to note that the MVC was performed *after* the flexor force tracings. Therefore, it is possible that there was some agonist fatigue occurring by the time the MVC was performed. The agonist MFR/RT plot (Figure 13; left side) appears to show overlapping pre- and post-fatigue regression lines with very few differences. However, it can't be ignored that 12 of the 15 subjects (80%) used for that analysis exhibited a decreased linear slope coefficient and increased y-intercept after antagonist fatigue. The slopes of the pooled Sync Index/Mean RT relationships (Figure 14) also seemed to get flatter after the intervention. This

would suggest that agonist motor unit pairs were less synchronized after antagonist fatigue. Nine of the 14 subjects used for this analysis demonstrated similar responses to the pooled data. However, the finding is contradicted some by the lack of a significant change in the average short-term sync index ($p = .054$, ES = .48). Nevertheless, the effect size is large enough to support the conclusions of the pooled data and suggests the lack of significance in the averaged data may have been due to being slightly underpowered. It has been suggested[76, 219] that an increase in the number of sources a motor neuron receives input from can lower the levels of synchronization. The common drive that motor neurons receive from the brain is highly synchronized, and the addition of any secondary inputs, regardless of their level of synchrony independently, can have a desynchronizing effect on the motor neuron[219]. Therefore, it is possible that fatigue of the antagonist muscle stimulates an afferent pathway that (a) synapses with the agonist motor neuron pool, and (b) was not active prior to the fatigue. The best candidate for a neural pathway meeting those conditions would be group III and IV muscle afferents originating from the antagonists. Group III and IV afferents are known to respond to fatigue and the metabolic products of fatigue[25, 195, 196]. In support of this hypothesis, Martin et al.[195] found that there was facilitation to the flexor motor neuron pool after fatiguing extensor contractions.

As expected, the prolonged agonist stretch significantly decreased flexor MVC force. Unexpectedly, however, none of the agonist motor unit firing properties showed significant stretch-induced changes. For the antagonist, only the

average firing rate exhibited a change, and that decrease only met the 0.05 alpha level, not the Bonferroni corrected value (0.00125). The agonist Sync Index/Mean RT plot (Figure 18; left side) provided some interesting information. As hypothesized, the low-threshold motor unit pairs demonstrated greater levels of synchronization after the prolonged stretching. The unanticipated finding was that the high-threshold motor units did not follow the same pattern, instead exhibiting a stretch-induced decrease in synchronization. This lead to a much flatter slope after the stretch; a pattern shared by 73% (11 of 15) of the subjects used for this analysis. The lack of a decrease in agonist motor unit firing rates combined with the decreased synchronization among high-threshold motor unit pairs raises an important question: did the prolonged stretching intervention serve its purpose and desensitize the muscle spindles? At the very least, the efficacy of the intervention should at least introduce reservations. By itself, the partial rejection of the hypothesis predicting an increase in synchronization would not be enough to question the efficacy of the intervention (sometimes hypotheses are just wrong). However, the intervention also failed to support previous findings, such as decreased agonist motor unit firing rates[190]. In hindsight, this investigation could have been improved by the inclusion of a reflex measure to directly assess the spindle afferent function.

The prolonged antagonist stretching intervention produced mixed results in regards to supporting or rejecting the hypotheses. As predicted, stretching the antagonist did not alter agonist motor unit firing properties; nor did it affect

synchronization in the agonist. Both extensor ($p = .0035$) and flexor ($p = .031$) MVCs decreased, but neither met the Bonferroni corrected alpha value. Once again, it is important to note that the MVC was performed *after* the flexor force tracings. Therefore, it is possible that fatigue affected the flexor MVC. Antagonist coactivation decreased from 33% to 24%, but this change was not significant. Another surprise was that the averaged motor unit properties of the antagonist were unaffected by the prolonged stretch. Interestingly, the MFR/RT relationship during coactivation (Figure 21; right side) became flatter (i.e. the slope became less negative and the y-intercept decreased) after the stretching. The firing rates of the low-threshold motor units decreased while the higher-threshold motor unit firing rates increased. Unfortunately, the reasons for these non-uniform changes across motor unit types are unknown.

5.2. Limitations

For individuals who are unfamiliar with motor unit decomposition and/or synchronization research, it is very difficult to fully appreciate the massive amount of data associated with the variables, as well as how much time is required to analyze each signal. For example, almost 17 billion (16,940,160,000) data points were collected and analyzed during this investigation. While data collection only took two months, it took a very fast, new computer approximately 6 months of running 12-16 hours/day, 7 days/week, to analyze the signals (and sometimes two computers were analyzing data simultaneously). In total, it took over 3500 hours of

analysis just to get the variables before any statistics could be performed. The point of this summary is that the nature of the data and analysis is, in itself, a limitation. Due to the time commitment required, the investigator has to be very cautious of how many variables, analyses, and even subjects to include in the study. For this reason, the analyses of some variables can be underpowered, while those for others can be overpowered. Thus, I feel that inclusion of some type of effect size measure along with the significance testing is essential with this type of research.

An additional limitation imposed by the decomposition system is the types of contractions that can be performed. The algorithm can only decompose short (< 45 seconds), isometric contractions. The limitation from this time restriction cannot be overlooked. The ability to decompose long signals would have greatly improved the study. Longer contractions would have allowed individual motor units to be tracked along the fatigue protocols.

Another limitation is the inescapable order effect to the contractions. If the MVCs were performed first during pre- and post-tests, then they may have affected the motor unit firing properties during subsequent force tracings. However, performing the three tracings first may have caused fatigue and affected the MVC values. I had to prioritize my data and I chose to perform the tracings first. In essence, the motor unit data were more important than the strength data.

As already discussed, other limitations include the efficacy of the stretching protocol, as well as the lack of a reflex measurement. The magnitudes of the stretches were up to the participants and were rated subjectively. It is quite possible

that some of the subjects did not perform a sufficient stretch. Furthermore, the inclusion of a reflex measure could have directly assessed whether the stretching interventions had their intended effects (i.e. desensitized spindle responses).

5.3. Future Research Needs

As is typically the case, attaining the answers to the research questions in the present investigation has only led to more questions. Such is the nature of experimental research. One of the more interesting questions arose from the agonist fatigue findings. A significant increase in antagonist coactivation was found despite no changes to the antagonist motor unit firing properties. This finding proves difficult to satisfactorily explain solely from this study's data. Therefore, further research is needed examining antagonist motor unit activity during agonist fatigue.

The small recruitment threshold range exhibited by the antagonist also raised an interesting question; are any high-threshold motor units recruited during co-activation? Future studies should examine motor unit behavior during antagonist coactivation from higher force contractions than those performed in the present study (i.e. > 60% MVC). Furthermore, the behavior of the antagonist motor units should be compared to the motor unit behavior of the same muscle when it acts as an agonist (at the same relative level based on % max EMG).

Lastly, although the stretching data provided some interesting preliminary results, this area requires significantly more work. Multiple studies[74, 190] have

suggested that spindle afferents play an important role in voluntary motor control. Therefore, more studies need to perform interventions that influence spindle function (e.g. chemical block, prolonged stretching, vibration) while examining agonist and antagonist motor unit responses. As previously mentioned, future studies should be sure to incorporate a reflex measure (either mechanical or electrical) to assess the efficacy of the intervention.

CONCLUSIONS

This study provided many new findings regarding the interactions between opposing muscles. Firstly, during co-activation, the antagonist muscle demonstrated a much smaller recruitment threshold range than the agonist. The antagonist muscle also exhibited significant levels of short-term synchronization between its motor units, but less so than the motor units of the agonist. Interestingly, fatigue of the agonist had no significant effects on antagonist motor unit behavior, despite an increase in co-activation.

The evidence from the present study also seems to support the existence of a neural pathway that (a) synapses with the agonist motor neuron pool, and (b) is stimulated by fatigue of the antagonist. The existence of this pathway was reflected by decreases in agonist motor unit synchronization as well as increases in agonist

firing rates. It was suggested that group III and IV muscle afferents originating from the antagonists were the pathway responsible for the changes to the agonist.

The results from the prolonged stretching interventions produced mixed results. One of the more unexpected findings was non-uniform changes across motor unit types. It was suggested that the prolonged stretching may not have been as effective at desensitizing the muscle spindles as originally hoped and that future studies should incorporate additional measures.

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APPENDIX A - ABBREVIATIONS

ACh = Acetylcholine

ANOVA = Analysis of Variance

AP = Action Potential

APB = Abductor Pollicis Brevis muscle

BB = Biceps Brachii muscle

CI = Confidence Interval

CIS = Common Input Strength

CMEP = Cervicomedullary Motor Evoked Potentials

CNS = Central Nervous System

CoV = Coefficient of Variation

CPG = Central Pattern Generator

CUSUM = Cumulative Sum

CV = Conduction Velocity

ECR = Extensor Carpi Radialis muscle

EDL = Extensor Digitorum Longus muscle

EMG = Electromyography

EPL = Extensor Pollicis Longus muscle

EPSP = Excitatory Post-Synaptic Potentials

ES = Effect Size

FCR = Flexor Carpi Radialis muscle

FCU = Flexor Carpi Ulnaris muscle

FDI = First Dorsal Interosseous muscle

FDS = Flexor Digitorum Superfialis muscle

FPL = Flexor Pollicis Longus muscle

GTO = Golgi Tendon Organ

IEDC = Index Extensor Digitorum Communis

IFDS = Index Flexor Digitorum Sublimis muscle

IPI = Interpulse Interval

IPSP = Inhibitory Post-Synaptic Potentials

LFP = Local Field Potentials

M1 = Motor Cortex area of the brain

MEG = Magnetoencephalography

MEP = Motor Evoked Potentials

MFR = Mean Firing Rate

MMG = Mechanomyography

MRS = Magnetic Resonance Spectroscopy

MTS = Musculotendinous Stiffness

MUAPT = Motor Unit Action Potential Train

MVC = Maximal Voluntary Contraction

nPSP = Estimated Net Post-Synaptic Potential

OOI = Orbicularis Oris Inferior muscle

PAP = Post-Activation Potentiation

PSTH = Post-Stimulus (or Peri-) Time Histogram

RT = Recruitment Threshold

SD = Standard Deviation

SPI = Second Palmar Interosseus muscle

ST = Semitendonosus muscle

TA = Tibialis Anterior muscle

TB = Triceps Brachii muscle

TMS = Transcranial Magnetic Stimulation

VL = Vastus Lateralis muscle

VM = Vastus Medialis muscle

APPENDIX B - GLOSSARY

Action Potential (AP) = a short-lasting event in which a neuron's electrical membrane potential rapidly increases and then decreases. An AP, once initiated, begins at the axon hillock (also called "initial segment") and rapidly spreads down the membrane of the axon, eventually reaching the terminal branches and causing the release of a neurotransmitter. The amplitude (in voltage) of an AP for a given neuron is considered to be constant. Note: APs are also often referred to as "firings", "spikes", "pulses", or "discharges"

Afferent = conveying towards a center. Afferent neurons are sensory neurons that carry nerve impulses from receptors in the periphery (e.g. muscles, tendons, skin, etc…) towards the central nervous system (Antonym: Efferent)

Agonist = the primary muscle responsible for an action (Antonym: Antagonist)

All-or-None Principle = the principle, or law, stating that a stimulus to a neuron must be strong enough to reach threshold to trigger an action potential. Once threshold is achieved, the action potential, in its entirety, is propagated. Weaker or stronger stimuli cannot alter the amplitude of an action potential. Consequently, the propagation of an action potential down an axon will always result in the same response. In the case of a motor neuron, an action potential always results in the activation of all of the muscle fibers that it innervates.

Alpha (α)-Motor Neuron = an efferent neuron that originates from the anterior horn of the spinal cord and innervates extrafusal muscle fibers

Antagonist = a muscle that opposes the action produced by the agonist

Antagonist Coactivation = Simultaneous activation of the antagonist muscle during an agonist contraction. The coactivation is not intentional and has both central and peripheral origins (peripheral origin is by the stimulation of agonist golgi tendon organs and/or antagonist muscle spindles).

Antidromic conduction = the conduction of a neural impulse backward from a receptor in the midportion of an axon traveling upstream towards the soma. It is an unnatural phenomenon and may be produced experimentally.

Autogenic Excitation = Self-generating excitation that feeds back to the origin. For example, the stimulation of a muscle spindle will lead to excitation of the same muscle that the spindle originated from. Note: older literature sometimes refers to this as "autogenetic" excitation.

Autogenic Inhibition = Self-generating inhibition that feeds back to the origin. For example, contraction of a muscle will stimulate the GTO's within that muscles tendon. This stimulation will lead to inhibition of the same muscle that the GTO responded to. Note: older literature sometimes refers to this as "autogenetic" inhibition.

Beta (β)-Motor Neuron = an efferent neuron that originates from the anterior horn of the spinal cord and innervates both extrafusal and intrafusal muscle fibers. β-motor neurons are, in essence, a hybrid of both α- and γ-motor neurons.

Central Activation Ratio = A measure of central activation which requires both a voluntary contraction (MVC) as well as an electrical stimulation. It is measured as MVC÷(MVC + superimposed tetanic force).

Chemoreceptors = a sensory nerve cell activated by chemical stimuli. In the case of the muscle, chemoreceptors can respond to changes in O_2, CO_2, or even the accumulation of metabolites, such as during fatigue.

Co-contraction = Simultaneous activation of two or more muscles. The muscles are typically either synergists or oppose each other. If they are opposing muscles, then this differs from coactivation because during co-contraction each muscle is intentionally contracted. There is no true agonist or antagonist role for muscles involved in a co-contraction. Note: some of the older literature sometimes refers to antagonist coactivation as "co-contraction".

Concentric = A muscle action in which the muscle shortens while generating force.

Contralateral = pertaining to, or originating in, the opposite side of a point of reference, such as a point on a body.

Decerebration = the process of removing the brain or of cutting the brainstem above the level of the red nucleus, thus eliminating cerebral function.

Eccentric = A muscle action in which the muscle lengthens while generating force.

Efferent = conveying away from a center. Efferent neurons are motor or "effector" neurons that carry nerve impulses away from the central nervous system to effectors, such as muscles or glands. (Antonym: Afferent)

Electromyography (EMG) = the electrical recording of muscle action potentials. The data are obtained by applying surface electrodes or by inserting an indwelling electrode into the muscle and observing electric activity.

Entrainment = the process whereby two interacting oscillating systems, which have different periods when they function independently, assume a common period. This, therefore, creates a synchrony. For example, this "frequency mimicking" is clearly demonstrated when the brain's dominant EEG frequency tends to change towards the frequency of a dominant external stimulus (such as auditory tones).

Ephapse = a point of lateral contact between two neurons across which impulses may be transmitted directly through the cell membranes rather than across a synapse. Referred to as "ephaptic transmission". Unmyelinated neurons are significantly more susceptible to this type of close-contact, unintended transmission.

Excitatory Post-Synaptic Potentials (EPSPs) = a positive increase in a neuron's membrane potential due to a neurotransmitter released from another neuron (the pre-synaptic neuron). A large influx of EPSPs in a short period of time will lead to an action potential in the post-synaptic neuron.

Extrafusal fibers = the standard skeletal muscle fibers that are innervated by α–motor neurons. The term is used to distinguish from intrafusal fibers.

Fatigue = a state of exhaustion or a loss of strength or endurance

Gamma (γ)-Motor Neuron = an efferent neuron that originates from the anterior horn of the spinal cord and innervates intrafusal muscle fibers

Golgi Tendon Organs (GTO) = mechanoreceptors embedded within the tendons of mammalian muscles. GTOs are responsible for detecting length changes in the tendon. Stimulation of GTOs typically occur during high-force concentric muscle actions but can also occur from intense muscle stretches. GTOs stimulate type Ib afferent neurons.

Heteronymous Motor Neurons = motor neurons supplying muscles other than the one from which the afferent impulses originate. Afferent impulses from one muscle can have an excitatory or inhibitory effect on other muscles, which are typically either synergists or antagonists. (Antonym: Homonymous)

Homonymous Motor Neurons = motor neurons supplying the same muscle from which afferent impulses originate. (Antonym: Heteronymous)

Inhibitory Post-Synaptic Potentials (IPSPs) = a negative decrease in a neuron's membrane potential due to a neurotransmitter released from another neuron. IPSPs cause the membrane potential of the post-synaptic neuron to be farther from threshold.

Innervation Ratio = the average number of fibers per motor unit for a given muscle. E.g. rectus lateralis muscle (eye) = 5 fibers per motor unit; gastrocnemius muscle = 1,934 fibers per motor unit

Interneuron = a small neuron whose axon and dendrites lie entirely within the CNS and whose function is to relay impulses within the CNS.

Interpolated Twitch = the introduction of an electrical stimulation to an active voluntary contraction. During an MVC, a supramaximal stimulation is administered. If an additional twitch is present, then the subject was unable to recruit all of their motor units during the MVC.

Interpulse interval (IPI) = the observed times between firings. Note: often called interspike interval (ISI) as well

Intrafusal fibers = the skeletal muscle fibers within a muscle spindle. Intrafusal fibers are innervated by γ–motor neurons.

Ipsilateral = pertaining to, or originating in, the same side of a point of reference, such as a point on a body.

Isometric = A muscle action that generates force without a change in muscle length (i.e., no visible change in joint angle).

Jendrassik's maneuver = a distracting maneuver in which the patient hooks the flexed fingers of the two hands together and forcibly tries to pull them apart. This is used to distract the patient, thereby overcoming the common voluntary suppression of reflexes.

Kinesthetic sense = an ability to be aware of muscular movement and position. By providing information through receptors originating in muscles, tendons, joints, and other body parts, the kinesthetic sense helps control and coordinate activities such as walking.

Mechanoreceptors = any sensory nerve ending that responds to mechanical stimuli, such as touch, pressure, sound, and muscular contractions.

Motor Unit = an α–motor neuron and all of the muscle fibers that it innervates.

Motor Unit Action Potential Train (MUAPT) = a temporal sequence of action potentials generated by a single motor unit

Nociceptors = pain receptors that stimulate type IV afferent neurons. Nociceptors have an inhibitory effect on the central drive to motor neurons.

Prehension = the use of the hands to grasp, pick up objects, or pinch

Proprioceptor = any sensory nerve ending, such as those located in muscles, tendons, joints, and the vestibular apparatus, that responds to stimuli originating from within the body related to movement and spatial position.

Post-Activation Potentiation (PAP) = an increase in muscle force production of subsequent contractions immediately following an initial submaximal or maximal contraction

Rate Coding = the manipulation of a neuron's firing rate. E.g. increases in muscular force can be achieved by increasing the firing rates of the active motor units.

Reciprocal Excitation = Excitation of antagonistic muscles. This excitation is what leads to antagonist coactivation. For example, contraction of a muscle will stimulate the GTO's within that muscles tendon. This stimulation will lead to excitation of the antagonist. It should be noted, however, that reciprocal excitation can also originate from the motor cortex.

Reciprocal Inhibition = Inhibition of antagonist muscles to accommodate contraction on the other side of the joint (i.e. agonist). For example, the stimulation of a muscle spindle will lead to inhibition of the antagonist. It should be noted, however, that reciprocal inhibition can also originate from the motor cortex.

Recurrent Inhibition = an inhibitory pathway that turns back so as to reverse direction on itself, therefore creating a feedback circuit. Within the CNS, this most regularly occurs through the Renshaw cell pathway. Small branches, known as collaterals, split off from the motor axon and excite an interneuron, known as a Renshaw cell. The Renshaw cell then releases an inhibitory neurotransmitter (i.e. IPSPs) back on the originating and neighboring motor neurons. It is believed to have a stabilizing effect on the motor neuron pool preventing rapid, repeated firing.

Recruitment = the activation of an additional motor unit(s)

Recruitment Range = the relative level of force to which a muscle can recruit additional motor units. E.g. some small muscles have all of their motor units recruited by 50% MVC, while other, larger, muscles have the ability to recruit all the way up to 100% MVC.

Recruitment Threshold (RT) = The force level at which a motor unit is activated. In the present study, RTs are normalized by expressing them in relative terms (as a % of MVC).

Renshaw Cells = small interneurons that act as feedback circuit on α-motor neurons. Axon collaterals from α-motor neurons excite the interneuron, which in turn, releases IPSPs on the dendrites of the original and neighboring α-motor neurons.

Safety Factor = the measure of excess of released neurotransmitter (the amount beyond that required to initiate an action potential). E.g. the synaptic connection between a group Ia spindle afferent neuron and an α-motor neuron has a negative safety factor, because an action potential in the presynaptic neuron does not cause enough neurotransmitter release to elicit a post-synaptic action potential (Σ of EPSPs < threshold); however, the synaptic connection between an α-motor neuron and the muscle fibers (i.e. neuromuscular junction) has a very high safety factor because an action potential in the α-motor neuron always releases more than enough neurotransmitter (ACh) to elicit an action potential in the muscle fibers.

Size Principle = the orderly recruitment of motor units from smallest to largest as demand increases.

Soma = the cell body of a neuron

Spike-Triggered Average (STA) = a technique allowing visualization of an event that occurs regularly after an identifiable trigger (e.g. motor unit action potential) but is otherwise obscured by noise. The relevant signal becomes evident with averaging of a large number of triggered events.

Spindle = a fusiform organ arranged in parallel between extrafusal muscle fibers which acts as a mechanoreceptor. Spindles are responsible for detecting changes in muscle length. The 2 types of sensory neurons stimulated by spindles are referred to as type Ia and type II afferent fibers.

Strength = the maximal amount of force or tension a muscle or muscle group can exert against a resistance in a single effort

Stretch reflex = a reflex characterized by a muscular contraction in direct response to the stimulation of the muscles spindle receptors. Note: also called myotatic reflex.

Synapse = the region at which a nerve impulse passes from one neuron to another through the action of a neurotransmitter.

Synchronization = the tendency for two neurons to fire with dependent latencies relative to each other more often than would be expected if they were to fire randomly, but independently. E.g. motor units fire together more often than would be expected from chance alone. The mostly widely accepted hypothesis for the cause of synchronization is shared or common inputs to the neurons, although in some instances, ephaptic transmission can also be a cause.

Synergist = a muscle that assists another muscle to accomplish a movement

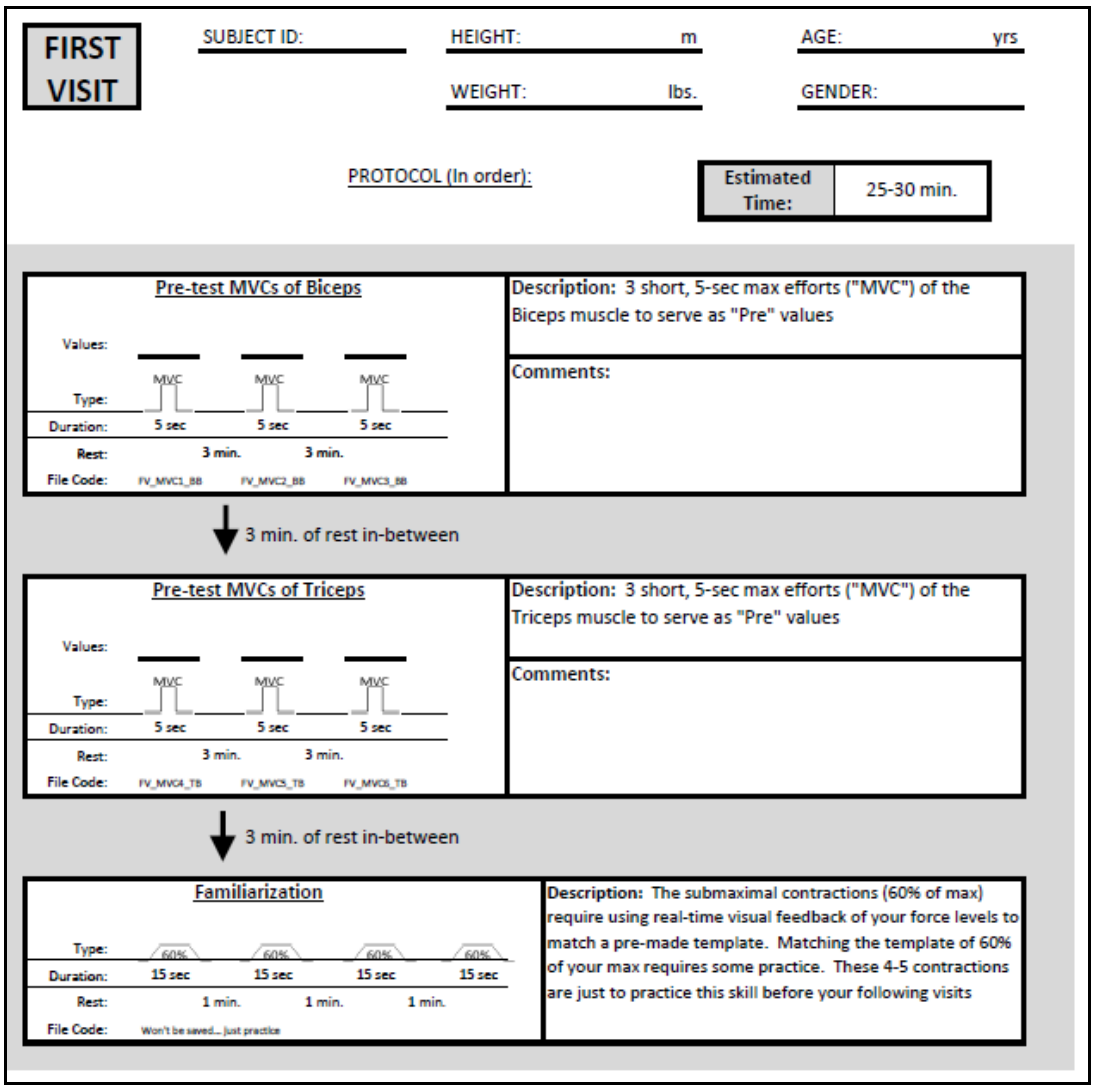
Tetanus = prolonged contraction of a muscle resulting from a series of motor impulses following one another too rapidly to permit intervening relaxation of the muscle

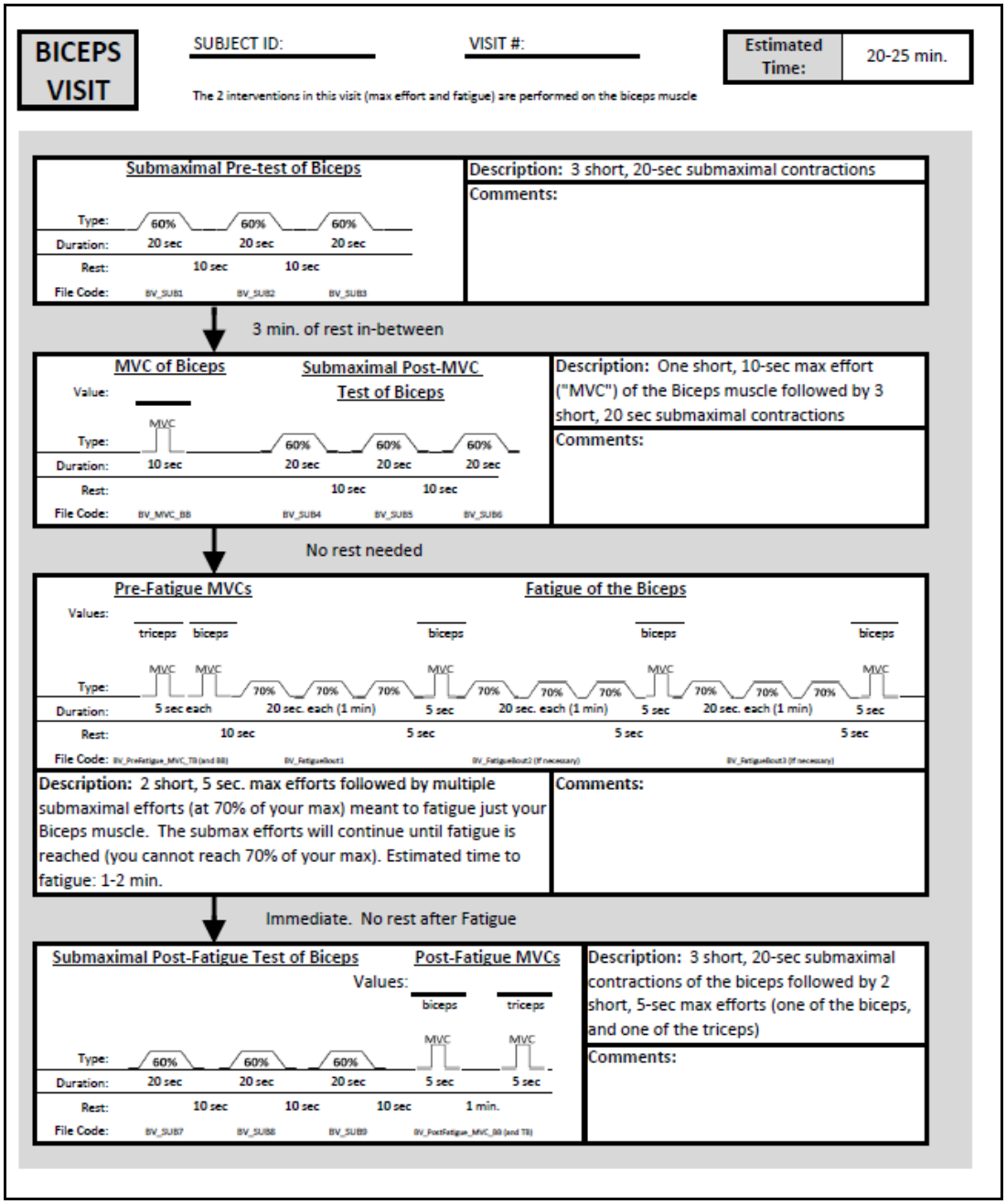
Threshold = the precise voltage that causes the voltage-gated ion channels in a neuron's membrane to open. The opening of these channels leads to an action potential. Note: often called "critical firing level"

Twitch = a short, spastic contraction of a motor unit

APPENDIX C – DATA COLLECTION PACKET

This packet contains five separate forms; one for each visit to the laboratory. It provided a visual aid in understanding the study design, and was used during the informed consent process.




BICEPS VISIT
SUBJECT ID:
VISIT #:
Estimated Time:
20-25 min.
The 2 interventions in this visit (max effort and fatigue) are performed on the biceps muscle
Submaximal Pre-test of Biceps
Type:
Duration:
Rest:
File Code:
60%
20 sec
10 sec
Description: 3 short, 20-sec submaximal contractions
Comments:
3 min. of rest in-between
MVC of Biceps
Submaximal Post-MVC Test of Biceps
Value:
MVC
10 sec
Description: One short, 10-sec max effort ("MVC") of the Biceps muscle followed by 3 short, 20 sec submaximal contractions
Comments:
No rest needed
Pre-Fatigue MVCs
Fatigue of the Biceps
Values:
triceps
biceps
70%
5 sec each
20 sec. each (1 min)
5 sec
Description: 2 short, 5 sec. max efforts followed by multiple submaximal efforts (at 70% of your max) meant to fatigue just your Biceps muscle. The submax efforts will continue until fatigue is reached (you cannot reach 70% of your max). Estimated time to fatigue: 1-2 min.
Comments:
Immediate. No rest after Fatigue
Submaximal Post-Fatigue Test of Biceps
Post-Fatigue MVCs
1 min.
Description: 3 short, 20-sec submaximal contractions of the biceps followed by 2 short, 5-sec max efforts (one of the biceps, and one of the triceps)
Comments:

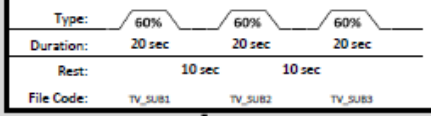
TRICEPS VISIT

SUBJECT ID: _____ VISIT #: _____

Estimated Time:	20-25 min.

The 2 interventions in this visit (max effort and fatigue) are performed on the triceps muscle

Submaximal Pre-test of Biceps

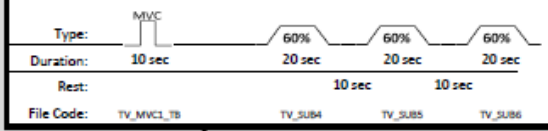


Description: 3 short, 20-sec submaximal contractions

Comments:

3 min. of rest in-between

MVC of Triceps **Submaximal Post-MVC Test of Biceps**

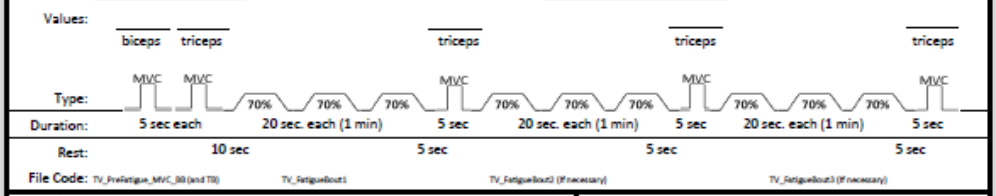


Description: One short, 10-sec max effort ("MVC") of the Triceps muscle followed by 3 short, 20 sec submax efforts of the Biceps

Comments:

No rest needed

Pre-Fatigue MVCs **Fatigue of the Triceps**

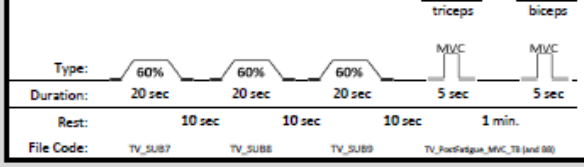


Description: 2 short, 5 sec. max efforts followed by multiple submaximal efforts (at 70% of your max) meant to fatigue just your Triceps muscle. The submax efforts will continue until fatigue is reached (when you can no longer reach 70% of your max). Estimated time to fatigue: 1-2 min.

Comments:

Immediate. No rest after Fatigue

Submaximal Post-Fatigue Test of Biceps **Post-Fatigue MVCs**



Description: 3 short, 20-sec submaximal contractions of the biceps followed by 2 short, 5-sec max efforts (one of the triceps, and one of the biceps)

Comments:

BICEP STRETCH VISIT

SUBJECT ID: _____ VISIT #: _____

Estimated Time:	30-35 min.

The intervention in this visit will be a stretch of the biceps muscle

Submaximal Pre-test of Biceps — **Pre-Stretch MVCs**

Values: biceps _____ triceps _____

Type:	60%	60%	60%	MVC	MVC
Duration:	20 sec	20 sec	20 sec	5 sec	5 sec
Rest:	10 sec	10 sec	10 sec	1 min.	
File Code:	BSV_SUB1	BSV_SUB2	BSV_SUB3	BSV_PreStretch_MVC_BB (and TB)	

Description: 3 short, 20-sec submaximal contractions of the biceps followed by 2 short, 5-sec max efforts (one of the biceps, and one of the triceps)

Comments:

↓

Stretching of the Biceps muscle Duration: 20 min.

Description: You will perform 12 total 100-sec stretches of the biceps muscle for a total of about 20 minutes. It will consist of 100-sec followed by 15-sec of rest. You will cycle between 3 different stretches.

Comments:

↓

Immediate. No rest after Stretch

Submaximal Post-Stretch Test on Biceps — **Post-Stretch MVCs**

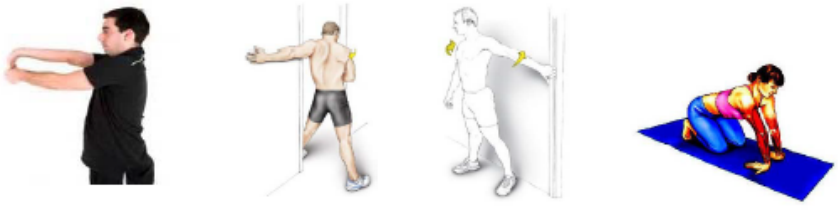
Values: biceps _____ triceps _____

Type:	60%	60%	60%	MVC	MVC
Duration:	20 sec	20 sec	20 sec	5 sec	5 sec
Rest:	10 sec	10 sec	10 sec	1 min.	
File Code:	BSV_SUB4	BSV_SUB5	BSV_SUB6	BSV_PostStretch_MVC_BB (and TB)	

Description: 3 short, 20-sec submaximal contractions of the biceps followed by 2 short, 5-sec max efforts (one of the biceps, and one of the triceps)

Comments:

Possible Stretches of the Biceps – The 3 used will depend on which ones work best for you



TRICEP STRETCH VISIT

SUBJECT ID: _____ VISIT #: _____

Estimated Time:	30-35 min.

The intervention in this visit will be a stretch of the triceps muscle

Submaximal Pre-test of Biceps — **Post-Stretch MVCs**

Values: triceps _____ biceps _____

Type:	60%	60%	60%	MVC	MVC
Duration:	20 sec	20 sec	20 sec	5 sec	5 sec
Rest:		10 sec	10 sec	1 min.	1 min.
File Code:	TSV_SUB1	TSV_SUB2	TSV_SUB3	TSV_PreStretch_MVC_TB (and BB)	

Description: 3 short, 20-sec submaximal contractions of the biceps followed by 2 short, 5-sec max efforts (one of the biceps, and one of the triceps)

Comments:

↓

Stretching of the Triceps muscle Duration: 20 min.

Description: You will perform 12 total 100-sec stretches of the triceps muscle for a total of about 20 minutes. It will consist of 100-sec followed by 15-sec of rest. You will cycle between 3 different stretches.

Comments:

↓ Immediate. No rest after Stretch

Submaximal Post-Stretch Test on Biceps — **Post-Stretch MVCs**

Values: triceps _____ biceps _____

Type:	60%	60%	60%	MVC	MVC
Duration:	20 sec	20 sec	20 sec	5 sec	5 sec
Rest:		10 sec	10 sec	1 min.	1 min.
File Code:	TSV_SUB4	TSV_SUB5	TSV_SUB6	TSV_PostStretch_MVC_TB (and BB)	

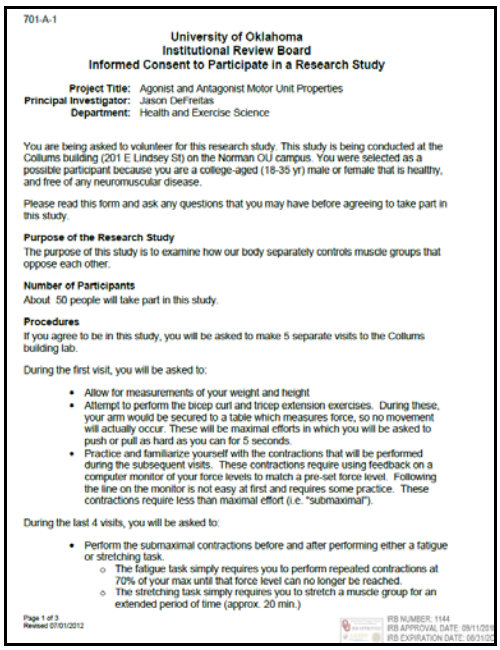
Description: 3 short, 20-sec submaximal contractions of the biceps followed by a 2 short, 5-sec max efforts (one of the biceps, and one of the triceps)

Comments:

Possible Stretches of the Triceps



APPENDIX D – INFORMED CONSENT



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University of Oklahoma
Institutional Review Board
Informed Consent to Participate in a Research Study

Project Title: Agonist and Antagonist Motor Unit Properties
Principal Investigator: Jason DeFreitas
Department: Health and Exercise Science

You are being asked to volunteer for this research study. This study is being conducted at the Collums building (201 E Lindsey St) on the Norman OU campus. You were selected as a possible participant because you are a college-aged (18-35 yr) male or female that is healthy, and free of any neuromuscular disease.

Please read this form and ask any questions that you may have before agreeing to take part in this study.

Purpose of the Research Study
The purpose of this study is to examine how our body separately controls muscle groups that oppose each other.

Number of Participants
About 50 people will take part in this study.

Procedures
If you agree to be in this study, you will be asked to make 5 separate visits to the Collums building lab.

During the first visit, you will be asked to:

- Allow for measurements of your weight and height
- Attempt to perform the bicep curl and tricep extension exercises. During these, your arm would be secured to a table which measures force, so no movement will actually occur. These will be maximal efforts in which you will be asked to push or pull as hard as you can for 5 seconds.
- Practice and familiarize yourself with the contractions that will be performed during the subsequent visits. These contractions require using feedback on a computer monitor of your force levels to match a pre-set force level. Following the line on the monitor is not easy at first and requires some practice. These contractions require less than maximal effort (i.e. "submaximal").

During the last 4 visits, you will be asked to:

- Perform the submaximal contractions before and after performing either a fatigue or stretching task.
  - The fatigue task simply requires you to perform repeated contractions at 70% of your max until that force level can no longer be reached.
  - The stretching task simply requires you to stretch a muscle group for an extended period of time (approx. 20 min.)

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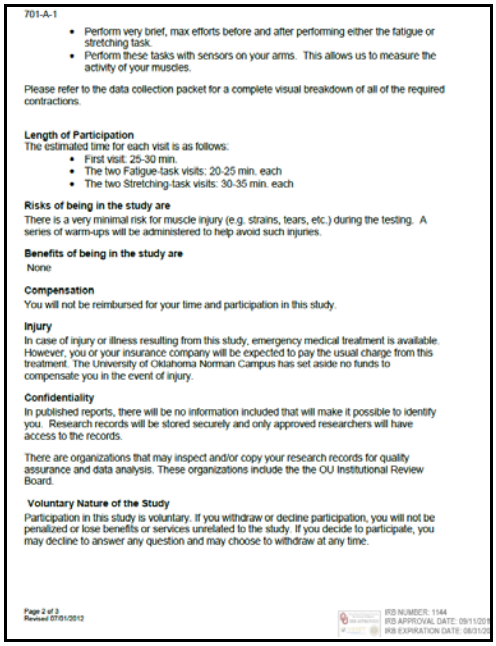
Revised 07/01/2012

IRB NUMBER: 1144
IRB APPROVAL DATE: 09/11/201
IRB EXPIRATION DATE: 08/31/20



701-A-1

- Perform very brief, max efforts before and after performing either the fatigue or stretching task.
- Perform these tasks with sensors on your arms. This allows us to measure the activity of your muscles.

Please refer to the data collection packet for a complete visual breakdown of all of the required contractions.

Length of Participation
The estimated time for each visit is as follows:

- First visit: 25-30 min.
- The two Fatigue-task visits: 20-25 min. each
- The two Stretching-task visits: 30-35 min. each

Risks of being in the study are
There is a very minimal risk for muscle injury (e.g. strains, tears, etc.) during the testing. A series of warm-ups will be administered to help avoid such injuries.

Benefits of being in the study are
None

Compensation
You will not be reimbursed for your time and participation in this study.

Injury
In case of injury or illness resulting from this study, 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.

Confidentiality
In published reports, there will be no information included that will make it possible to identify you. Research records will be stored securely and only approved researchers will have access to the records.

There are organizations that may inspect and/or copy your research records for quality assurance and data analysis. These organizations include the the OU Institutional Review Board.

Voluntary Nature of the Study
Participation in this study is voluntary. If you withdraw or decline participation, you will not be penalized or lose benefits or services unrelated to the study. If you decide to participate, you may decline to answer any question and may choose to withdraw at any time.

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Revised 07/01/2012

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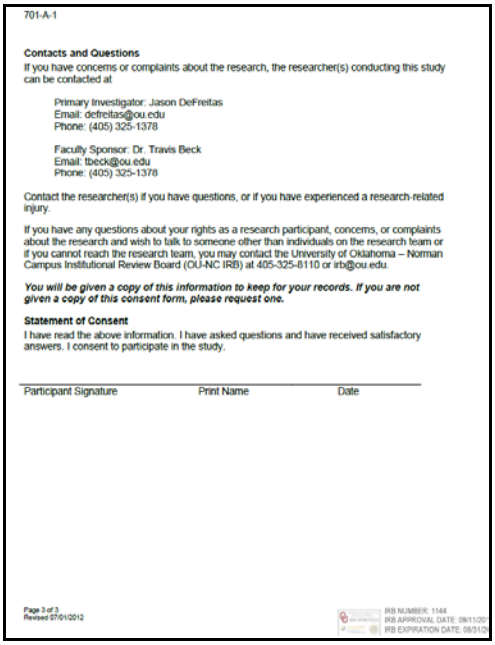

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Contacts and Questions
If you have concerns or complaints about the research, the researcher(s) conducting this study can be contacted at

Primary Investigator: Jason DeFreitas
Email: defreitas@ou.edu
Phone: (405) 325-1378

Faculty Sponsor: Dr. Travis Beck
Email: tbeck@ou.edu
Phone: (405) 325-1378

Contact the researcher(s) if you have questions, or if you have experienced a research-related injury.

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

You will be given a copy of this information to keep for your records. If you are not given a copy of this consent form, please request one.

Statement of Consent
I have read the above information. I have asked questions and have received satisfactory answers. I consent to participate in the study.

Participant Signature Print Name Date

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IRB NUMBER: 1144
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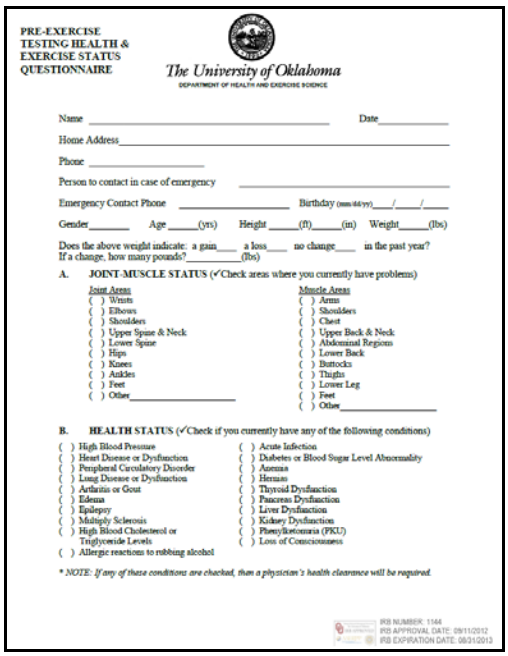
APPENDIX E – PRE-EXERCISE HEALTH QUESTIONNAIRE



PRE-EXERCISE TESTING HEALTH & EXERCISE STATUS QUESTIONNAIRE

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	Muscle Areas
( ) Wrists	( ) Arms
( ) Elbows	( ) Shoulders
( ) Shoulders	( ) Chest
( ) Upper Spine & Neck	( ) Upper Back & Neck
( ) Lower Spine	( ) Abdominal Regions
( ) Hips	( ) Lower Back
( ) Knees	( ) Buttocks
( ) Ankles	( ) Thighs
( ) Feet	( ) Lower Leg
( ) Other_____	( ) Feet
	( ) Other_____

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

( ) High Blood Pressure	( ) Acute Infection
( ) Heart Disease or Dysfunction	( ) Diabetes or Blood Sugar Level Abnormality
( ) Peripheral Circulatory Disorder	( ) Anemias
( ) Lung Disease or Dysfunction	( ) Hernias
( ) Arthritis or Gout	( ) Thyroid Dysfunction
( ) Edema	( ) Pancreas Dysfunction
( ) Epilepsy	( ) Liver Dysfunction
( ) Multiple Sclerosis	( ) Kidney Dysfunction
( ) High Blood Cholesterol or Triglyceride Levels	( ) Phenylketonuria (PKU)
	( ) Loss of Consciousness
( ) Allergic reactions to rubbing alcohol	

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

IRB NUMBER: 1144
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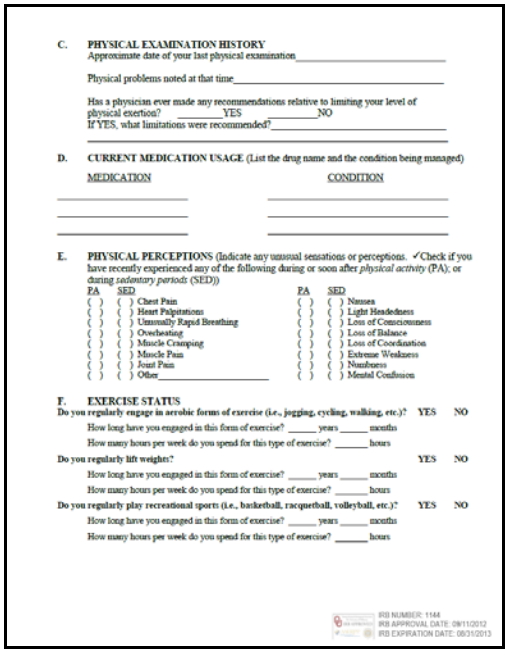

C. PHYSICAL EXAMINATION HISTORY
Approximate date of your last physical examination_____

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		PA	SED	
( )	( )	Chest Pain	( )	( )	Nausea
( )	( )	Heart Palpitations	( )	( )	Light Headedness
( )	( )	Unusually Rapid Breathing	( )	( )	Loss of Consciousness
( )	( )	Overheating	( )	( )	Loss of Balance
( )	( )	Muscle Cramping	( )	( )	Loss of Coordination
( )	( )	Muscle Pain	( )	( )	Extreme Weakness
( )	( )	Joint Pain	( )	( )	Numbness
( )	( )	Other_____	( )	( )	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

IRB NUMBER: 1144
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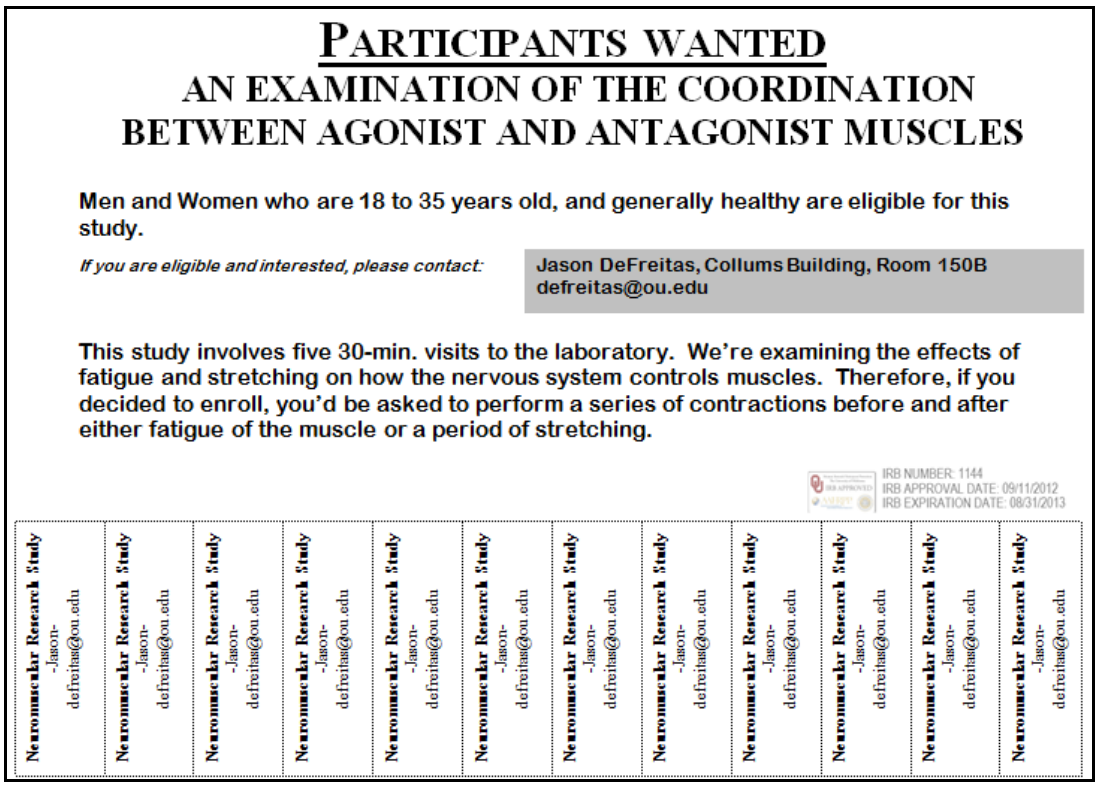
APPENDIX F – RECRUITMENT FLYER



PARTICIPANTS WANTED

AN EXAMINATION OF THE COORDINATION BETWEEN AGONIST AND ANTAGONIST MUSCLES

Men and Women who are 18 to 35 years old, and generally healthy are eligible for this study.

If you are eligible and interested, please contact:

Jason DeFreitas, Collums Building, Room 150B
defreitas@ou.edu

This study involves five 30-min. visits to the laboratory. We're examining the effects of fatigue and stretching on how the nervous system controls muscles. Therefore, if you decided to enroll, you'd be asked to perform a series of contractions before and after either fatigue of the muscle or a period of stretching.

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