AN ABSTRACT OF THE DISSERTATION OF

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Abstract approved:

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Mark A. Hoffman

Female athletes exhibit three- to six-fold greater incidence of noncontact anterior cruciate ligament (ACL) injury relative to their male counterparts. The increased risk appears to stem from interactions between several risk factors, that can roughly be categorized as anatomic, biomechanical, hormonal, and neuromuscular. Neuromuscular risk factors have recently gained a greater focus, and include differences in the timing and magnitude of activation of lower extremity and trunk musculature. In addition to neuromuscular risk factors, the incidence of ACL injury is not evenly distributed across the menstrual cycle, suggesting that hormonal fluctuations may influence neuromuscular control. Finally, it is known that even well-trained athletes experience decrements in performance and postural control when forced to attend to multiple sensory stimuli, which is common in many sports. PURPOSE: To explore neuromuscular differences in the ways healthy and ACL-injured women respond to a secondary task requiring fine motor control and sustained mental focus (typing task). Our investigation encompassed three broad aims. First, we sought to determine whether ACL-injured individuals demonstrated similar reflex profiles to healthy individuals, as well as to determine whether the ACL-involved limb was similar to its uninvolved counterpart. Our second aim was to determine whether the typing task resulted in attenuated Hoffmann (H) reflex amplitudes, and to investigate whether any observed changes were similar in healthy and ACL-injured groups. Finally, our third broad aim was to utilize more complex H reflex analysis techniques to determine whether differences in spinal excitability existed at different points in the menstrual cycle. METHODS: Thirty nine recreationally active women (20 with prior unilateral noncontact ACL injury: 24.0 ± 4.5 years; 23.8 ± 4.5 $kg \cdot m^{-2}$; 4.1 ± 2.6 years post-injury; 19 with no history of knee injury: 23.8 ± 4.5 years; 23.1 ± 2.3 $kg \cdot m^{-2}$) agreed to participate, and were tested during days 2-5 (follicular phase) of the menstrual cycle. A sub-set of this original group (n=8; 24.0 ± 4.8 years; 22.0 ± 2.1 $kg \cdot m^{-2}$) also agreed to return for a second testing session 24-96 hours after ovulation (early luteal phase), in order to assess H reflex differences across the menstrual cycle. During each testing session, H reflex testing was used to explore spinal-level control mechanisms of the lower extremity musculature under both Rest and Task conditions. In the control group, the dominant limb was tested (CON-D) while in the ACL group, both the uninvolved (ACL-UN) and involved (ACL-INV) limbs were assessed. Differences between groups (Control vs. ACL) and within-groups (ACL-UN vs. ACL-INV) were explored. RESULTS: At rest, H reflex parameters in ACL-INV were generally similar to ACL-UN and to CON-D. However, differences in presynaptic inhibition were apparent in ACL-INV that imply reduced reflex plasticity. During the typing task, both the Control and ACL groups experienced attenuated H reflex parameters. In the sub-set of participants who were tested twice during the menstrual cycle, a significant increase in presynaptic inhibition was observed during the early luteal phase compared to the follicular phase. CONCLUSION: While individuals with prior ACL injury display similar H reflex profiles to healthy individuals, the ACL-involved limb may demonstrate less reflex plasticity in response to environmental changes. This lack of plasticity may potentially increase the risk of re-injury. In addition, an upper extremity task requiring fine motor control and sustained mental focus attenuates the H reflex in both groups. This attenuation has implications for lower-extremity neuromuscular control in dual-task environments. Finally, the increase in presynaptic inhibition observed during the early luteal phase may provide insight into why ACL injuries are not evenly distributed across the menstrual cycle.

Spinal Reflex Control in Healthy and ACL-injured Women during a Distracting Task

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I understand that my dissertation will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my dissertation to any reader upon request.

Erica Taylor Perrier, Author

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CONTRIBUTION OF AUTHORS

Dr. Mark Hoffman was instrumental in the refining of the study design, editing of the manuscripts, and advice on statistical analysis. Dr. Mike Pavol also assisted with statistical analysis. Jeffrey Doeringer assisted in data collection and provided manuscript feedback.

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Chapter 1: Introduction

Noncontact rupture to the anterior cruciate ligament (ACL) is a catastrophic injury with consequences ranging from loss of a competitive season to the premature termination of an athlete's career. Furthermore, long-term consequences of ACL rupture include lingering deficits in strength, proprioception, and the increased risk of osteoarthritis (24, 35). Across levels of sport participation ranging from high school athletics to professional sports, women are three to six times more likely to suffer a noncontact ACL injury (14) than are men. There does not appear to be one key factor to explain the dramatic difference in injury rates; rather, it appears that an interactive combination of anatomic, biomechanical, neuromuscular and hormonal factors play a role in influencing injury risk (5). Anatomic factors such as femoral notch width and shape and ACL size are, practically speaking, unmodifiable (18). Neuromuscular control, however, has recently become an important area of focus, in part because of the development of neuromuscular training programs that can modify high-risk motor control patterns and reduce incidence of ACL injury (12, 26).

With respect to neuromuscular risk factors, there are several key differences between females and males. During dynamic movements such as landing and side-cutting, females tend to preferentially activate the knee extensors (quadriceps) compared to the hamstrings (10, 13). Moreover, females also tend to perform these movements with the knee more fully extended at ground contact (25). The result is an increase in anterior tibial translation without adequate posterior restraint from the hamstrings, leading to increased stress on the ACL. In addition to differences in magnitude of activation, there are also reported differences in the timing of muscle activation. Women tend to increase rectus femoris activity just prior to and after making ground contact (6, 22), which further exacerbates the functional imbalance between quadriceps and hamstring activation. Promising reductions in ACL injury rates have been reported in response to neuromuscular training programs. These training programs aim to address neuromuscular activation imbalances and correct risky movement patterns by teaching athletes to land with greater knee flexion and more input from the knee flexors (11). The key point is that clear neuromuscular differences have been identified between the sexes, and these differences are consistent with body mechanics that would increase loading of the ACL during dynamic movements. Moreover, the fact that ACL injury rates can be reduced with training is a strong indicator that more research is needed to understand the origins of these neuromuscular differences.

The ability of an athlete to maintain appropriate neuromuscular control during dynamic movements relies on both cortically-driven and reflex-mediated activity (31). Proprioceptive feedback from prime movers, stabilizers, and core postural muscles must be coordinated with visual and other sensory information about the playing environment, as well as with descending programming from the motor cortex. This complex interaction requires the integration and appropriate filtering of multiple sensory inputs, and is dependent upon both decision-making and movement planning in the cortex, as well as constant adjustments carried out in the spinal synapses. One way to assess spinal-level control of the lower extremity musculature is Hoffmann (H) reflex testing, which provides a window into the function of the central nervous system (CNS) in gating afferent feedback and regulating muscular activation. The H reflex, an analogue to the tendon-tap stretch reflex, is evoked by electrically stimulating Ia afferent fibers that synapse onto alpha motoneurons in the spinal cord. By modulating the intensity of the stimulus, reflex motor responses of varying intensities can be elicited. While the H reflex loop is monosynaptic, it is also modifiable by both segmental and supraspinal influences. Segmental influences arise from interneurons that project onto the synapse and carry afferent input from both homonymous and heteronymous muscle groups, which amplify and attenuate, respectively, the amplitude of the measured H reflex (28). Thus, the H reflex can be used to explore the level of spinal connectivity between muscle groups, as well as in response to various sensory stimuli.

In the context of ACL injury, the H reflex is an interesting tool for examining spinal-level control of the lower extremity because it can be modified by both task and environmental demands, and thus reflects the function of the CNS in modulating motor responses to sensory input. The H reflex is attenuated under conditions of task complexity, such as standing on an unstable surface, single-legged, or on a narrow beam (17, 23, 29). It is also attenuated during locomotion, such as walking, running, and arm cycling (3, 19, 37). Currently, little is known about H reflex profiles in ACL-injured individuals. Since differences in neuromuscular activation (both magnitude and timing) are risk factors for noncontact ACL rupture, exploring whether individuals with prior ACL injury demonstrate similar spinal-level control compared to ACL-intact individuals may help our understanding of the neural origins of these activation differences.

Athletes across many sports are required to perform complex tasks that require dividing their focus between multiple sensory stimuli on the playing field. This condition, known as dual-task processing, has been shown to negatively influence performance in motor tasks (2, 7, 15). This performance interference occurs regardless of whether the secondary task is verbal (2, 7) or motor (15). Specific to sports, skill performance declines under dual-task conditions. A study examining passing skills in rugby found that both highly-skilled and lower-skilled athletes experience performance decrements under dual-task conditions; however, less of a change was observed in the higher-skilled players (9). Moreover, even when individuals are highly trained in precise motor control, such as in highly-trained dancers, motor performance still suffers during a secondary task (21). One explanation for the observed performance reductions under dual-task conditions is that the brain has a limited capacity for processing inputs and that, past capacity, the amount of attention devoted to either task will be reduced (20). The fact that even highly-trained athletes experience this performance decrement suggests that attending to multiple sensory inputs on the playing field may compromise motor control, thereby increasing the likelihood of injury. In this context, assessing H reflex responses to a secondary task can illustrate whether neuromuscular control is modulated differently when attention is diverted from the muscles being assessed.

There is evidence that hormonal fluctuations associated with the menstrual cycle may impact neuromuscular control of the lower extremity (4). It has been well established that the incidence of ACL rupture is not consistent across the menstrual cycle, and that more ACL ruptures occur during the first half of the cycle (follicular phase through ovulation) compared to the second half (luteal phase) (27, 30, 36). This observation suggests that the monthly fluctuations in hormone concentrations may influence neuromuscular control. While some authors contend that differences in neuromuscular coordination, such as in the performance of motor tasks or in postural sway, exist across the cycle (4, 8), others have reported no effect of cycle phase on similar parameters (1). Overall, there currently is a lack of consensus of exactly how menstrual status affects ACL injury risk, although the evidence to suggest that menstrual cycle plays a role in ACL injury is substantial. While the H reflex has previously been reported not to vary with hormone concentration changes (16), we do know that the changes in circulating hormone concentrations that occur with the menstrual cycle affect several reflex measures including autonomic control of heart rate, pain thresholds, and the startle reflex (32-34). The fact that other reflex parameters are altered across the cycle suggests that there may exist differences in spinal reflex control, and that perhaps different H reflex analysis techniques may yield interesting results.

The broad purpose of this project was to explore neuromuscular differences in the ways ACL-intact ("healthy") and ACL-injured women respond to a secondary task requiring fine motor control and sustained mental focus (typing task). Hoffmann (H) reflex testing was used to explore spinal-level control mechanisms of the lower extremity musculature under both Rest and Task conditions. Differences between groups (healthy vs. ACL-injured women) and within-groups (ACL-involved vs. ACL-uninvolved limb) were explored for several purposes. First, little is known about H reflex profiles individuals who have suffered an ACL rupture and who have undergone reconstruction. Our first broad aim was to determine whether ACL-injured individuals demonstrated similar reflex profiles to healthy individuals with no knee injury, as well as to determine whether the ACL-involved limb was similar to its uninvolved counterpart. It was hypothesized that at rest, there would be little difference between the ACL and healthy groups. Our second broad aim was to determine whether the typing task resulted in attenuated H reflex amplitudes, and to investigate whether any observed changes were similar in healthy and ACL-injured groups. It was hypothesized that H reflex modulation in response to the typing task would differ between groups. Finally, our third broad aim was to utilize more complex H reflex analysis techniques to determine whether differences in spinal excitability existed at different points in the menstrual cycle, where it was hypothesized that differences in spinal excitability would be apparent across the menstrual cycle. These three aims are important in understanding how spinal-level control of the lower extremity is modulated in situations where attention is divided between multiple stimuli.

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Chapter 2: Literature Review

Introduction – Women, ACL Injury, and Neuromuscular Differences

Across all levels of sports participation, female athletes in sports including soccer, basketball, and volleyball experience greater incidence of noncontact ACL rupture than their male counterparts, with injury rates reported to be between two and six times higher than in comparable male athletic populations (26, 38). While the exact mechanisms behind increased injury risk are still unclear, the emerging picture is that women are at increased risk due to a number of integrated factors, including anatomic, biomechanical, neuromuscular, and hormonal risk factors (12). Together, risk factors from the various categories can increase the likelihood of an athlete adopting high-risk lower extremity alignment during landings, coined by Ireland as the "position of no return" (38). In this position, the foot is planted and pronated upon landing, combined with adduction at the hip, knee valgus, and tibial external rotation. The aggregate effect of this type of uncontrolled landing is a rapid forward shift of body weight over the knee, the inability of the knee flexors to protect the ACL from rapid anterior tibial translation, and finally, rapid loading of the ACL, resulting in rupture (38).

While many anatomic risk factors (such as ACL size, femoral notch size and shape, and intrinsic laxity) are not modifiable, four specific risk factors are at least partially modifiable: proprioception (balance and position sense), neuromuscular activation patterns, muscle order of firing, and acquired skills (38). The first of these factors, proprioceptive deficits, have mainly been studied following injury and reconstruction (2, 3, 17, 34, 41), in order to evaluate both surgical techniques and rehabilitation programs. Published studies have returned mixed evidence, with some reporting small, but persistent deficits in knee joint proprioception following ACL reconstruction (2, 17), and others reporting no lingering proprioceptive deficits (3, 34, 41), potentially as soon as six months following reconstruction (3). In a unique study, Zazulak et al. (64) prospectively evaluated 277 collegiate athletes (of whom 140 were female) in several proprioceptive tasks including postural control of the trunk after a sudden force release, as well as active trunk repositioning accuracy. They determined that female athletes who suffered a subsequent knee, ligament, or ACL injury demonstrated more lateral postural sway and performed worse on active trunk repositioning than the athletes who did not suffer an injury. The authors suggest that deficits in core stability can increase the risk of valgus positioning of the lower extremity, which may lead to increased stresses on the ACL.

Specific to neuromuscular activation patterns and muscle order of firing, sex differences have been reported while athletes perform during dynamic tasks. Quadriceps dominance (decreased ratio of hamstring to quadriceps activation) during dynamic motions such as landing and side-cutting has been reported in well-trained female athletes (23, 28). Moreover, women tend to perform tasks such as cross-cutting and side-cutting with less flexion at the knee joint compared to men (48). The combination of quadriceps dominance with less flexion at the knee joint results in an inability of the hamstrings to provide posterior restraint against anterior translation of the tibia during these actions. In addition, a recent study by Ford and colleagues (16) evaluated quadriceps and hamstrings electromyography (EMG) activity in female athletes during drop landings from varying heights. They found that as drop landing height increased, quadriceps EMG activity increased before ground contact, but without an accompanying increase in hamstrings activity. Thus, female athletes may be adopting worse strategies as they perform riskier maneuvers, further exacerbating activation imbalances between the extensors and flexors of the knee.

In addition to differences in magnitude of muscle activation, the timing of peak muscle activation may also differ between the sexes. Landry et al. (45) examined the amplitude and timing of leg muscle activation in young male and female soccer players during the pre-contact and early-stance phases of unanticipated side-cutting and cross-cutting. They found sex differences in both the amplitude and timing of muscle activation. Specifically, females' peak hamstring activation occurred earlier than males (pre-stance), with a reduction in hamstring activation upon ground contact. Conversely, males reached peak hamstring activation as ground contact approached. Females also increased rectus femoris activity as ground contact approached relative to their male counterparts for both maneuvers. The early peaking of hamstring activity in females combined with greater rectus femoris activity just prior to ground contact suggests that females may be more prone to increased loading of the ACL that results in increased stress. A more recent study by Ebben and colleagues (14) also examined the timing and activation of knee flexors and extensors during landing and side-cutting in males and females. In examining muscle activation post-ground contact, no sex differences were observed during drop landings; however, during the cutting maneuver, women displayed a longer burst of rectus femoris and vastus medialis activity than males (14). Both Ebben and Landry reported an increase in rectus femoris activity in women just before and during ground contact during a side-cutting maneuver, further supporting the hypothesis that women preferentially activate the knee extensors during dynamic movements.

The fourth factor that Ireland identified as a modifiable ACL risk factor was the notion of “acquired skills”. The importance of teaching athletes to land in a “get-down, knee flexed” position has been emphasized in several neuromuscular training programs (38). A meta-analysis by Hewett et al. (27) suggests that neuromuscular training programs are effective at reducing ACL injury rates. Common components of the successful injury prevention programs included plyometric training with an emphasis on technique, as well as a feedback component to reinforce correct landing technique, particularly the ability to land with a more flexed knee (27). The overall message to be taken away from the neuromuscular research is that women do appear to activate their knee flexors and extensors differently than men during dynamic tasks, that the activation differences are consistent with increased strain to the ACL, and that prevention programs that seek to modify these movement patterns reduce the incidence of ACL injury.

A discussion of neuromuscular activation patterns would not be complete without addressing the implications of hormonal fluctuations observed during the menstrual cycle. It is well established that significant variation in incidence of non-contact ACL injury exists across the menstrual cycle (4, 49, 50, 57, 63), suggesting that hormonal fluctuations may impact neuromuscular parameters leading to increased injury risk. A recent systematic review examining the relationship between menstrual cycle and ACL injury reported a significantly higher number of ACL injuries than expected during both the follicular and ovulatory phases of the menstrual cycle, with relatively fewer injuries than expected occurring in the luteal phase (29). Determining the causes of this increased risk has proven to be a challenge, as different studies have reported contradictory results. Friden et al. (18) examined neuromuscular coordination and knee joint kinesthesia (time to detect passive motion – TTDPM) at three points during the menstrual cycle (menstrual – days 3 to 5, ovulation – luteinizing hormone (LH) surge, premenstrual – 7 days after ovulation) over a three month period. The authors found that TTDPM (measured in degrees from movement onset) was significantly longer during the premenstrual phase compared with the menstrual or ovulatory phases. In a test of neuromuscular coordination (square-hop test), participants performed significantly better during the ovulatory phase than in the premenstrual or menstrual phases. Performance differences have also been reported across the menstrual cycle for lateral sway, with women experiencing greater lateral sway during the menstrual phase than during ovulation or early luteal phases (11). In contrast, Abt et al. reported no effect of menstrual cycle phase on neuromuscular parameters including single-leg postural stability and performance on a test of fine-motor skills (1). The lack of agreement within the current body of literature suggests that the interaction between hormonal fluctuations and neuromuscular control is complex, and may present subtle challenges to proper motor coordination at different points in the menstrual cycle.

Dynamic postural control during sport relies on both cortical and reflex control of lower extremity musculature (59). At the reflex level, there is evidence that menstrual cycle phase alters several sensorimotor reflex pathways, including the nociceptive flexion reflex (61) and the acoustic startle reflex (60), This suggests that at the spinal level, reflex feedback loops can be altered by cyclical hormone fluctuations. Therefore, investigating changes in spinal-level neuromuscular control may provide critical information to bridge the gap between monosynaptic reflex activity and complex, cortically-influenced measures of lower extremity motor control.

The Hoffmann reflex: assessing the "neural" in neuromuscular change

While the concept of neuromuscular control implies interaction between the central and peripheral nervous system and the musculature, the majority of research into neuromuscular control has involved the measurement of muscular parameters. Specifically, previous studies have used outcome measures such as degree of muscle activation via electromyography (13, 65) and timing of muscle activity during motor tasks such as cutting and landing (30, 45). While these measures certainly involve a neural component, the outcome measure – muscle activation – provides little information about activity at the afferent-efferent spinal synapses that influence muscular activation. Often overlooked is the neural component of neuromuscular control. The Hoffmann reflex (H reflex) is a measure that can be used to estimate spinal reflex excitability under varying conditions. Specifically, changes in the nervous system as a result of musculoskeletal injury, exercise, performance of motor tasks, and changes to the environment can be assessed using this measure (52). Essentially, the H reflex is an electrically-induced analogue to the monosynaptic stretch reflex – rapid stimulation of a sensory (afferent) nerve, either via rapid stretching of the muscle or via electrical stimulation, results in a reflexive contraction of the homonymous muscle. By varying the intensity of the electrical stimulation to the sensory nerve and observing the amplitude of the reflex response, information can be gleaned about the degree of neuromuscular connectivity in the system.

H reflex pathway

The H reflex is elicited by electrically stimulating a mixed peripheral nerve, thereby eliminating feedback from mechanoreceptors within the muscle and tendon (spindles and Golgi-tendon organs) (35, 52). The following is a description of the H reflex pathway for the soleus, a commonly-used muscle in H reflex testing (Fig. 1): electrical stimulation of the tibial nerve at the popliteal fossa activates Ia afferent fibers, resulting in neurotransmitter release at the Ia/aMN (alpha motoneuron) synapse in the spinal cord. The evoked efferent volley causes a brief contraction in the homonymous muscle (soleus), which is recorded using electromyography (EMG) (52, 67). The recorded twitch in the soleus is known as the H reflex.

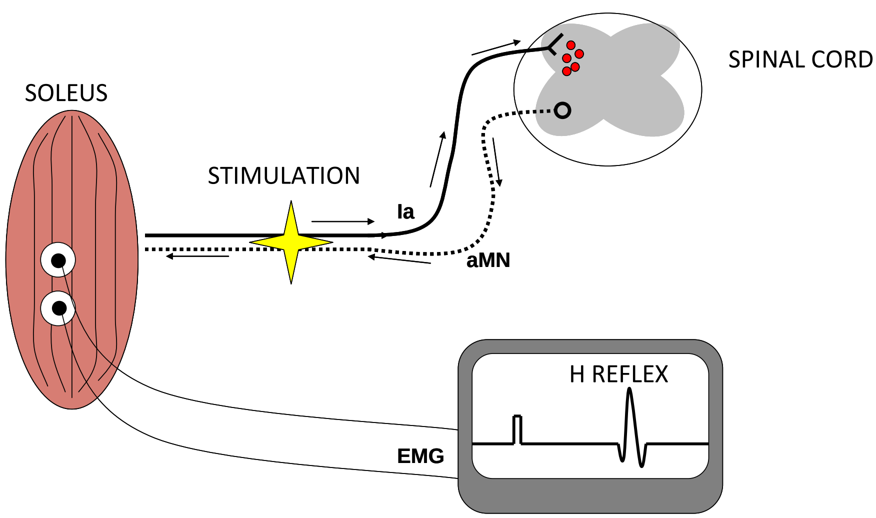

Fig. 2.1. Stimulation of a mixed peripheral nerve results in primary afferent (Ia) depolarization, neurotransmitter release at the Ia/aMN synapse, and subsequent activation of the homonymous aMN, culminating in a brief contraction at the soleus (as recorded by EMG).

At low stimulation intensities, the larger-diameter primary afferent (Ia) fibers are stimulated exclusively, and the resulting motor response in the soleus has a latency of approximately 30ms. As stimulation intensity increases, motor units are recruited in an orderly fashion according to the size principle, with smaller motor units recruited first and the larger motor units recruited last (67). Gradually increasing stimulus intensity also results in direct stimulation of the smaller diameter aMN fibers, giving rise to another, shorter-latency (~6 ms) waveform known as the M wave. The M wave represents direct stimulation of the muscle via volleys that travel down the aMN directly to the neuromuscular junction, bypassing the synaptic connection at the spinal cord. Because the largest diameter aMNs are recruited first, recruitment of motor units into the M wave follows a pattern that is opposite of the H reflex. Large motor units are recruited first, then moderate size motor units, and finally the smallest motor units are recruited into the M wave last (35) (Fig. 2).

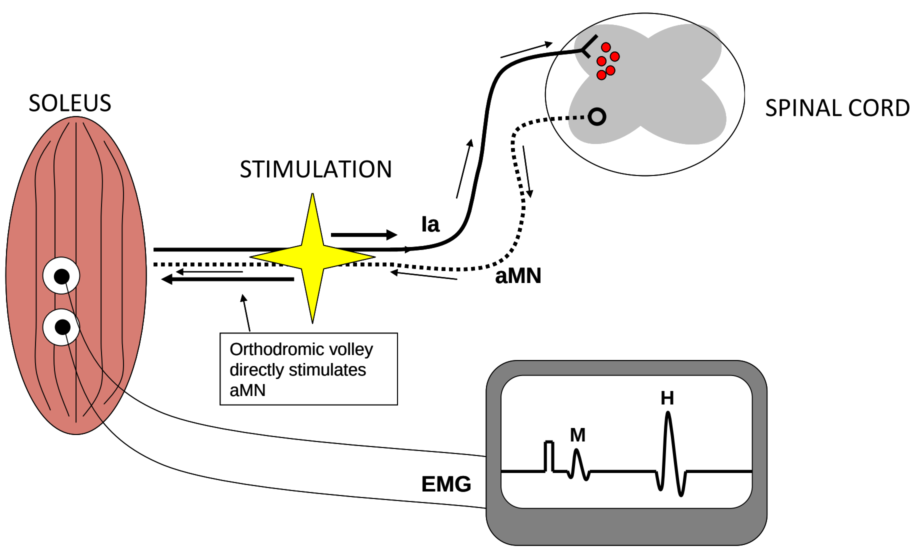

Fig. 2.2. Increased stimulation intensity depolarizes primary afferent fibers as well as aMN fiber directly. The volley travels directly to the neuromuscular junction, resulting in a very short latency (~6ms) waveform (M wave) in addition to the H reflex.

The Recruitment Curve

A recruitment curve (Fig. 3) is obtained by stimulating the mixed nerve at varying intensities ranging from the onset of a visible H reflex (H reflex threshold) through the largest obtainable M wave (Mmax). Low stimulation intensities that depolarize only afferent fibers will show an H reflex that gradually increases in size with increasing stimulation intensity. As stimulation intensity increases and the aMN is directly stimulated, an M wave will also appear. Both waveforms will gradually increase in size as stimulation intensity continues to be increased. However, directly stimulating the aMN also causes an antidromic volley to travel up the aMN towards the spinal cord and collide with the H reflex motor response that is travelling orthodromically down the aMN towards the muscle. This collision has the effect of reducing the magnitude of the measured H reflex. Ultimately, at high stimulation intensities that depolarize the entire aMN pool, the antidromic aMN volley will completely cancel out the H reflex, leaving only the M wave visible (Mmax) (52). Both waveforms can be graphed together as a function of stimulus intensity. The ascending portion of the H reflex curve has a sigmoid shape that levels off due to antidromic aMN volleys that attenuate the magnitude of the H reflex. Once the H reflex has reached its peak value (Hmax), the curve slowly descends and ultimately reaches zero, representing the point at which the entire H reflex is cancelled out by antidromic aMN volleys. The M wave is also a sigmoid shaped curve – the shallow initial portion of the curve represents the recruitment of the largest (but few in number) motor neurons, while the steep middle portion of the curve represents the recruitment of the moderate-sized (and numerous) motor neurons. The M curve levels off with the recruitment of the smallest motor neurons (35). When all aMN have been recruited, the M wave is said to have reached Mmax.

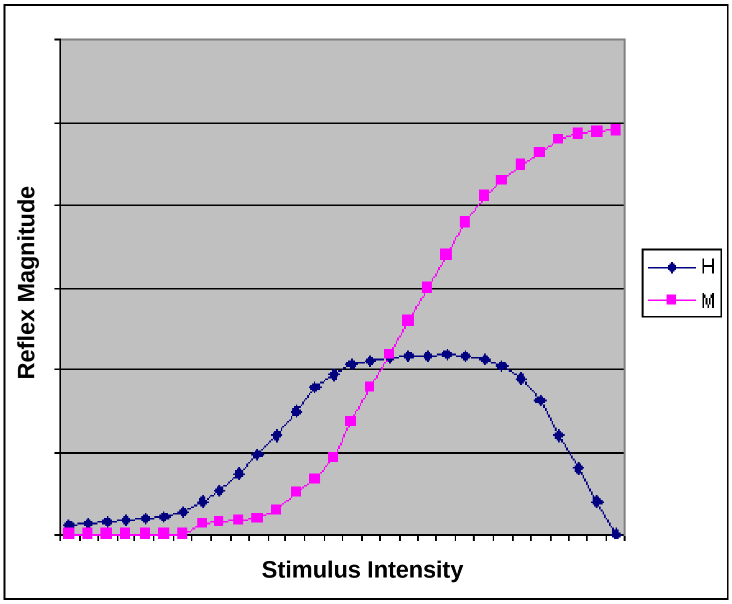

Fig. 3. Representation of the H reflex and M wave recruitment curves.

Interpreting H reflex measures:

Hmax

The peak-to-peak amplitude of the maximal H reflex that can be obtained under consistent environmental conditions, including the posture and "set" of the participant (67), is known as Hmax. Otherwise put, Hmax is a representation of the subset of the total MN pool that one can activate in a given state. Hmax is variable, and can be modulated by changing the participant's posture, level of anticipation, or activity – these modulations will be discussed in detail in the following paragraphs. One caveat is that the measured H reflex amplitude at Hmax may potentially be attenuated by antidromic volleys in the aMN. Thus, comparing Hmax under various conditions can provide information about the relative activation of the MN pool, but should not be considered to accurately represent an absolute percentage.

Mmax

Delivering a stimulation that is sufficient to directly activate all aMNs innervating the target muscle results in the complete disappearance of the H reflex and a plateau of the M wave with increased stimulus intensity. This measure is known as maximal muscle activation, or Mmax. Because Mmax represents activation of the entire MN pool (52), it is thought to be a relatively stable measure. Because of its purported stability, monitoring the size of the M wave can be used as a "quality control" measure during reflex testing: an increase or decrease in the size of the M wave with consistent stimulation most likely suggests that the position of the stimulating electrode has shifted (52). Some authors have questioned the stability of the M wave during longer-term experiments. Crone and colleagues (8) reported that with repeated stimulations, the amplitude of Mmax can decrease by a mean of 20%. However, this protocol involved obtaining a large number of Mmax measures (3 to 5 times every 3 minutes, for a period of 1-3 hours), which is unlikely to be necessary during the course of a single data collection. Palmieri et al. (51) reported high intersession reliability ($ICC_{soleus} = 0.95$) for Mmax obtained by recruitment curves over two consecutive days; this suggests that during the timeframe needed to obtain a recruitment curve, Mmax should indeed remain stable.

Hmax:Mmax ratio

Because Hmax is variable, both between individuals and across environmental and task conditions within individuals, one way to express Hmax for easy comparison is as a ratio to Mmax. This ratio represents the relative proportion of the total MN pool that can be activated in a given state (52). The Hmax:Mmax ratio (also referred to as the H:M ratio) is commonly used to compare two groups, such as explosively-trained and endurance-trained athletes (e.g., (47)), or to assess changes pre- and post-intervention (e.g., (62)). Both mathematically and conceptually, expressing Hmax as an H:M ratio represents one of the simplest ways to normalize raw Hmax values. As with raw Hmax amplitude, the problem of attenuation due to antidromic collisions applies. In addition, a second criticism of the Hmax:Mmax ratio is that it provides insight into motoneuron excitability at only a single point along the recruitment curve. This measure may therefore miss changes in the relationship between stimulus intensity and H reflex amplitude that occur at sub-maximal stimulation intensities, when only a small proportion of afferent fibers are stimulated. Thus, measures that take into account a broader segment of the recruitment curve may provide more robust information about motoneuron excitability.

Ascending slope

The shape of the H reflex curve is generally described as sigmoid. At its origin, the shape of the curve is the result of the orderly recruitment of aMNs according to the size principle. A short initial segment displays a shallow slope and reflects the recruitment of the smallest MNs. The middle ascending portion of the curve is relatively linear as larger MNs are recruited. The slope of the upper portion of the H reflex recruitment curve is attenuated due to antidromic volleys arising from the direct recruitment of MNs at higher stimulation intensities (M wave).

The linear slope of the ascending portion of the H reflex recruitment curve is representative of the sensitivity, or gain, in the system under the current environmental conditions. The "reflex gain" represents the changing rate of MN excitability as a function of changes in Ia input to the motoneuron pool (21), and is therefore representative of the input-to-output ratio between the sensory and motor fibers. A steep slope is suggestive of heightened sensitivity at the Ia-aMN synapse to small changes in stimulation intensity, while a shallow slope would suggest that the sensitivity at the synapse to small changes in stimulation intensity has been attenuated. Mechanisms for the modulation of H reflex slope (facilitation and inhibition) are discussed in the following section.

Compared to the Hmax:Mmax ratio, the slope of the H reflex recruitment curve may be a more robust measure of the connectivity between sensory and motor fibers for several reasons. First, the measured Hmax is attenuated by antidromic collisions associated with the M wave (24). In contrast, the linear portion of the ascending slope occurs with little or minimal M wave interference and is therefore not as likely to be influenced by antidromic activity (21). Second, because the linear ascending slope includes H reflexes obtained at a range of stimulation intensities, and because motor units are recruited in order from smallest to largest according to the Size Principle, the slope therefore targets different segments of the motoneuron pool. Both linear (20, 24) and sigmoid (43) equations have been used to describe the slope of the ascending portion of the H reflex recruitment curve. Klimstra et al. compared multiple mathematical models (linear, exponential, logarithmic, smoothing spline, polynomial, and sigmoid) and concluded that a sigmoid function provided the most accurate and sensitive method to determine the ascending slope of the recruitment curve (43). The use of linear regression to interpret the ascending slope was found to increase error at the foot (H threshold) and peak (H max) of the curve. However, the authors found that both the linear and sigmoid methods were effective in detecting differences in the middle portion of the H slope across multiple movement conditions. These findings suggest that while the accuracy and reliability of linear regression are compromised at the foot and peak of the regression curve, linear regression may be used to approximate the middle portion of the ascending slope, and provides researchers with a parameter of reflex gain that is simpler to obtain and easier to interpret as a measure of reflex gain.

Presynaptic Inhibition

The amplitude of the H reflex is a measure of motoneuron excitability that can be modulated by segmental and supraspinal influences, and has been demonstrated to vary with changes in task complexity. Afferent information at the synapse can be amplified or attenuated, thereby changing the magnitude of the motor response. In practice, this sensory “gating” is critical in filtering multiple inputs and mounting an environmentally appropriate response. This gating relies heavily on interneurons, which are typically inhibitory. When these inhibitory interneurons affect activity in the spinal cord and reduce the amplitude of the H reflex, the phenomenon is known as presynaptic inhibition (PI). Zehr (67) provides a good description of this phenomenon:

> Due to the direct synaptic connection of Ia afferents and alpha motoneurons it has been tempting for researchers to assume that the H reflex represents faithfully the excitability of the motoneuron pool under study. (…) However, the synaptic connection between Ia afferents and alpha motoneurons is itself subject to modification. (…) The important point is that it is dangerous to interpret changes in H-reflex size as changes in motoneuron excitability. The primary reason for this is the effect of presynaptic inhibition.

PI occurs due to the involvement of inhibitory interneurons that act to reduce neurotransmitter release at the synapse between the primary afferent fiber and its corresponding motoneuron (55). Contraction of an agonist muscle reduces PI to homonymous motoneurons, while increasing PI to heteronymous (antagonist) motoneurons, resulting in increased motor contrast between opposing muscle groups (53). The increase in PI to heteronymous motoneurons is known as “classical”, or extrinsic, PI (36). Prior activity can also result in depression of synaptic transmission between a primary afferent and a homonymous motoneuron: this is known as intrinsic PI or postactivation depression (36). PI at the Ia afferent-motoneuron spinal synapse occurs through the neurotransmitter gamma-aminobutyric acid (GABA), primarily via the activation of GABA-A receptors that are present on the afferent terminal (58). The resultant hyper-polarization of the cell membrane has an inhibitory effect and therefore reduces neurotransmitter release at the afferent terminal into the synapse (58).

Rudomin and Schmidt (55) argue that PI serves an essential function in filtering through the constant deluge of afferent feedback in order to concentrate on relevant inputs and suppress those “which are trivial to the organism at that moment.” Thus, PI may play an important role in maintaining appropriately-scaled responses to environmental cues. In the soleus, presynaptic inhibition is usually invoked via prior electric stimulation of the common peroneal (CP) nerve (7, 24, 37, 42, 66). Capaday and colleagues (7) reported that conditioning-test (C-T) intervals of 100-120 ms produced consistent PI in the soleus muscle, while others suggest C-T intervals of 80-120 ms are appropriate (67). A stimulus intensity of 1 to 1.5 times tibialis anterior (TA) motor threshold strongly targets CP Ia fibers that project to the soleus Ia terminals via interneurons (67). In inducing PI experimentally, Capaday argues that it is important to maintain a background level of EMG activity in order to minimize post-synaptic changes to the soleus motoneurons (6). Zehr also stresses the importance of eliciting the reflex under the same postural orientation and “set” of the subject (67). These precautions can help ensure that observed modulation of the H reflex can truly be attributed to PI due to CP-conditioning, and not to extraneous changes in the testing environment.

One way to conceptualize spinal excitability at the synapse is ultimately as the sum of all of the excitatory and inhibitory stimuli that are generated from segmental and supraspinal inputs. The degree of presynaptic inhibition that modulates spinal excitability is consistently being adjusted: PI is influenced by task and environmental context, as well as by locomotion. Specifically, task complexity and postural anxiety have both been found to increase PI. Hoffman and Koceja (33) found that both an unstable surface and lack of vision resulted in attenuated H reflex gain, and suggested that both visual and proprioceptive (cutaneous) sensory input play a role in modulating presynaptic inhibition. Later, a study by Pinar and colleagues supported these results, and also found that increasing postural anxiety by standing on one leg resulted in attenuated H reflex gain (54). Similarly, Llewellyn and colleagues (46) reported a 40% attenuation in H reflex gain when comparing treadmill and balance beam walking. Additionally, similar results have been reported when participants stand at the edge of a raised platform (56) and when performing a balancing task (42). It has also been reported that PI increases as an individual transitions from sitting to standing to walking (67). The overwhelming evidence in this area confirms that as tasks become more complex and require increasingly greater precision in motor control, PI increases in order to accommodate more subtle postural adjustments.

The Dual Task Paradigm and its applications to sport

Successful participation in many sports requires athletes to concurrently focus on several tasks – for example, receiving a pass in soccer while also paying attention to an approaching defender. Dividing one's attention between more than one task is referred to as dual-task processing, and has been shown to negatively influence performance in at least one of the simultaneous tasks (31). Specifically, reductions in the performance of motor tasks such as force production (15), movement speed (5) and reaction time (31) have been documented when individuals must concurrently perform a secondary task. This performance interference occurs regardless of whether the secondary task is verbal (5, 15) or motor (31) in nature. Studies examining sport-skill performance under dual-task conditions has shown that skill performance declines when a secondary task is incorporated. Specifically, a study of rugby passing skills revealed that highly-skilled athletes experience less of a performance decrement than lower-skilled players (22). A second study revealed that a concurrent mental task increased postural sway in highly-trained dancers (44). One theory for the reduction in performance relates to the brain's limited capacity for processing inputs. Once capacity is reached, the amount of attention devoted to one or more tasks will be reduced in order to accommodate competing inputs (40). In the context of noncontact ACL injury, it is theorized that attending to multiple sensory inputs on the playing field may compromise motor control, thereby increasing the likelihood of injury.

The H reflex is susceptible to attenuation as tasks become more complex (33, 42, 56). However, few studies have created environments in which the task was focused on motor control of the upper extremity, and the reflex effects were studied in the lower extremity. Given the incidence of ACL injury in sports such as basketball (38), which requires complex ball-handling maneuvers, the impact of upper-extremity tasks on lower extremity spinal-level control is of interest. The studies that have addressed upper-extremity tasks have typically involved rhythmic, repetitive arm movements. Specifically, Frigon et al. (19) examined the effects of arm cycling on lower-extremity (soleus) H reflex amplitude. They reported a decrease in soleus H reflex amplitude during cycling, suggesting an increase in lower-extremity PI during an upper-extremity task. More recent research suggests that the observed suppression of H reflex amplitude can persist up to 20 minutes after arm cycling is terminated (39), further supporting the idea that upper- and lower-extremity movements are coupled by a central neural mechanism. Frigon et al. reported that during arm cycling, soleus H reflex amplitude is modulated via a presynaptic pathway similar to CP nerve conditioning (19). The authors demonstrated this by manipulating the soleus H reflex with both sural and CP nerve conditioning. Sural nerve conditioning reduced the inhibition demonstrated during arm cycling, while CP nerve conditioning had the opposite effect, further increasing inhibition. The net additive effects of arm cycling and CP or sural nerve conditioning provide strong evidence that both mechanisms for reflex modulation proceed via a common presynaptic pathway. One disadvantage to the arm-cycling experimental model is that the movement is repetitive and predictable – therefore, less resources may be necessary to successfully perform the task. To date, little is known about H reflex attenuation during a task that is unrelated to locomotion and requires both fine motor control and sustained focus.

ACL Injury and H reflexes

There is a surprising lack of research investigating H reflex profiles in ACL-injured patients. A search of MEDLINE using the keywords “H reflex” or “Hoffmann reflex” and “ACL” revealed only 4 articles that measured H reflexes in ACL-injured patients, 2 of which (9, 10) were case studies/case series by the same group of authors with a total of only 3 participants. Héroux and colleagues (25) examined quadriceps Hmax in the injured and uninjured legs of 5 participants, and reported a trend (p=.07) towards a smaller Hmax in the injured leg. Hoffman and Koceja (32) reported no difference in the Hmax:Mmax ratio between the involved and uninvolved limbs following ACL reconstruction. However, the authors also reported in healthy (ACL-intact) individuals, the correlation between bilateral soleus Hmax:Mmax ratio was strong (r=.84), while in ACL-reconstructed patients the inter-limb correlation was weaker (r=.38). This suggests increased inter-limb variability in Hmax:Mmax ratio following ACL rupture and reconstruction. Given the scant body of literature examining H reflex profiles in ACL-injured participants, there is a need for further research to confirm or refute the reported Hmax:Mmax asymmetry between injured and uninjured legs.

Conclusion

The rate of ACL injury in female athletes compared to their male counterparts is striking. Many of the documented risk factors that may increase the risk of ACL injury relate to neuromuscular control of the trunk and lower extremity. These risk factors are of particular interest because unlike anatomic risk factors, they present the possibility that risky movement patterns may be able to be modified via neuromuscular training programs. From a neural perspective, there are many unanswered questions relating to spinal-level control of the lower extremity. The H reflex is a tool that can be used to explore how lower-extremity motor recruitment is controlled. Currently, little is known about H reflex profiles in individuals with ACL injury, either at rest or during a secondary task.

As individuals are presented with tasks of increasing complexity, presynaptic inhibition is known to increase. In sport, situations where athletes must attend to multiple sensory stimuli are common. Dual task processing often results in performance reductions in at least one task. In the area of athletics, there are few studies that have directly investigated the impact of dual task processing on performance. However, the studies that exist suggest that athletes' motor skill performance is adversely affected by the incorporation of a secondary task. Thus, there is certainly a rationale for exploring the effect of a secondary task on individuals who have suffered a prior noncontact ACL rupture, in order to determine whether spinal reflex modulation in this population is similar to healthy individuals with no history of knee injury. Finally, the documented relationship between incidence of ACL injury and menstrual cycle phase is currently unexplained, and a better understanding of spinal-level control across the menstrual cycle may help to understand why ACL injury rates are not consistent across the cycle.

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Chapter 3: Soleus Hoffmann reflexes after ACL reconstruction in involved and uninvolved limbs

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ABSTRACT

Little is known about H reflex parameters following ACL reconstruction. **PURPOSE**: to determine whether females with unilateral, reconstructed ACL tears demonstrate similarity in H reflex parameters in the involved and uninvolved limbs, as well as to compare ACL-reconstructed females with healthy, active females. **METHODS:** Thirty nine recreationally active women (20 with prior unilateral noncontact ACL injury: 24.0 ± 4.5 years; 23.8 ± 4.5 kg·m^{-2}; 4.1 ± 2.6 years post-injury; 19 with no history of knee injury: 23.8 ± 4.5 years; 23.1 ± 2.3 kg·m^{-2}) agreed to participate. All were free of neurological disorder or recent lower extremity injury. Unconditioned and Common Peroneal (CP)-conditioned H reflex recruitment curves were collected during days 2 and 5 of the menstrual cycle. In the Control group, the dominant limb (CON-D) was assessed; in the ACL group, both the uninvolved (ACL-UN) and involved (ACL-INV) limbs were tested. The dependent variables were Hmax:Mmax ratio (H:M), the linear ascending slope of the test and CP-conditioned recruitment curves ($Slope_{test}$ and $Slope_{CP}$), and the percent presynaptic inhibition (%PI) due to CP-conditioning. **RESULTS:** Comparisons were performed using independent-samples (for between-group) and paired-samples (for between-legs, ACL group) t-tests. There were no significant differences between any of the limbs for H:M, $Slope_{test}$ or $Slope_{CP}$ ($p > .05$). H reflex parameters in the ACL-UN and ACL-INV limbs, respectively, were: H:M: .69 ± .20 and .69 ± .18; $Slope_{test}$: 407 ± 199 and 427 ± 218; and $Slope_{CP}$: 374 ± 171 and 366 ± 231. In the Control group, H:M, $Slope_{test}$ and $Slope_{CP}$ were .59 ± .20, 363 ± 192, and 352 ± 190. In order to compare %PI, participants were grouped into Facilitators (%PI>0) and Inhibitors (%PI<0) based on the direction of change in H

reflex amplitude due to CP conditioning. Among Facilitators, there was a significant difference in %PI in ACL-INV (16.1±34.0%) compared to either ACL-UN (32.5 ± 27.4%; p=.046) or CON-D (43.1±19.2%; p=.049). There were no significant differences among Inhibitors (ACL-UN; ACL-INV; CON-D: -34.4±18.7%; -15.0±13.0%; -19.2±12.6%, respectively).

CONCLUSION: H reflex profiles were generally similar between the Control and ACL groups, and between limbs in the ACL group. After subjects were categorized as Facilitators or Inhibitors, among Facilitators, the ACL-INV limb displayed less reflex plasticity (i.e., a smaller magnitude of change) in response to CP conditioning. This may suggest a reduced ability to modulate spinal control of the lower extremity in response to changing environmental conditions.

Introduction

Female athletes experience a two to six time greater incidence of noncontact anterior cruciate ligament (ACL) rupture than their male counterparts (10, 17). This injury rate difference has been attributed to a multifactorial combination of at least some of the following factors; anatomical, biomechanical, neuromuscular, and hormonal (4). Of these factors, neuromuscular control has recently become an important area of focus, in part because of the development of neuromuscular training programs that can modify high-risk motor control patterns and reduce incidence of ACL injury (11, 24). With respect to neuromuscular risk factors, females demonstrate different neuromuscular control strategies than males during some athletic maneuvers (8, 12, 20), which may increase loading of the ACL in females and thus the likelihood of noncontact ACL rupture.

Specific neuromuscular sex differences have been reported in ACL-intact ("healthy") females compared with healthy males. Quadriceps dominance, in which the activation or magnitude of force production in the quadriceps is disproportionate to activation or force production in the hamstrings, occurs even in well-trained female athletes during landing and side-cutting (8, 12). This imbalance creates increased anterior shear forces on the tibia with respect to the femur, increasing the load on the ACL. One of the challenges in directly applying this research to ACL injury risk, however, is that neuromuscular sex differences were largely documented by comparing healthy females to healthy males. These cross-sectional studies cannot establish neuromuscular control differences as causing subsequent ACL injury.

Prospectively investigating neuromuscular contributors to ACL injury risk would result in a higher level of evidence, but is daunting due to the large number of people that need to be screened and the extensive follow-up period that would be required. A third study design option is to retrospectively study women who have sustained a previous ACL injury. Unfortunately, interpreting results is complicated by the fact that lingering deficits often occur even after ACL reconstruction. Specifically, deficits in proprioception and muscle function in both the involved and uninvolved limbs have been reported in women who have undergone ACL reconstruction (26, 29), suggesting that central nervous system (CNS) motor control differences persist despite ACL repair. This complicates researchers' ability to draw conclusions about neuromuscular control differences and ACL injury risk because the following question cannot adequately be answered: did neuromuscular control deficits exist *before* the ACL injury, or are the observed deficits a *result* of the injury?

In the context of ACL research, Hoffmann (H) reflex testing is a useful and currently under-utilized measure for investigating neuromuscular connectivity. The H reflex is an electrically-induced analogue to the tendon-tap reflex, and is evoked by directly stimulating afferent fibers in a peripheral nerve. The amplitude of the H reflex is a measure of motoneuron excitability and can be modulated by segmental and supraspinal influences. Thus, the amplitude of a "control" or "test" H reflex can be viewed as a baseline against which inhibitory or facilitatory influences can be compared (27). In the context of ACL injury risk and neuromuscular control, H reflex testing has the potential to illuminate differences in descending control of the lower extremity musculature in individuals with noncontact ACL injuries.

Healthy individuals generally demonstrate similar soleus H reflexes bilaterally (22). Similarly, it has been reported that no differences exist between the injured and uninjured legs of ACL reconstructed subjects. Specifically, Hoffman and Koceja (13) reported no difference in the Hmax:Mmax ratio between the involved and uninvolved limbs following ACL reconstruction. However, the authors also reported in healthy individuals, the correlation between bilateral soleus Hmax:Mmax ratio was strong ($r=.84$), while in ACL-reconstructed patients the inter-limb correlation was weaker ($r=.38$). This suggests increased inter-limb variability in Hmax:Mmax ratio following ACL rupture and reconstruction. While the Hmax:Mmax ratio is a common measure of the connectivity between the primary afferents and the motoneuron pool, one of the disadvantages of this variable is that it represents neuromuscular connectivity at one specific point in the motor pool with no consideration of specific inhibitory influences. Therefore, there is a need for a more robust characterization of bilateral spinal control mechanisms in individuals following ACL reconstruction.

Assessment of spinal level control of the lower extremity can contribute valuable information to the understanding of ACL injuries. In particular, measurement of inhibitory inputs to muscles of the leg may provide insight into the effects of ACL injury on spinal control. H reflex testing is one method of investigating spinal control mechanisms that may influence lower extremity neuromuscular control and ACL injury risk; however, we currently do not have a sufficiently broad characterization of bilateral soleus H reflexes following ACL reconstruction. Specifically, the impact of ACL injury and subsequent reconstruction on the H reflex recruitment curve is unknown. Moreover, the influence of ACL reconstruction on presynaptic inhibition has not been determined. The purpose of this study was to determine whether females with unilateral, reconstructed ACL tears demonstrate similarity in multiple H reflex parameters in the involved and uninvolved limbs, as well as to compare ACL-reconstructed females with healthy, active individuals with no history of knee injury.

Materials and Methods

Subjects

A total of 39 recreationally active women volunteered to participate. Twenty participants had sustained a unilateral noncontact ACL injury, repaired a minimum of 12 months prior to participation (mean ± SD age: 24.0 ± 4.5 years; Body Mass Index: 23.8 ± 4.5 $kg \cdot m^{-2}$; 4.1 ± 2.6 years post-injury). The control group consisted of nineteen healthy females who had no history of knee injury (23.8 ± 4.5 years; 23.1 ± 2.3 $kg \cdot m^{-2}$). All participants gave written informed consent and the study was approved by the university's institutional review board. In both groups, participants had no history of neurological disorder or recent (≤ 6 months) injury to the lower extremity. In order to control for potential effects of hormonal fluctuation on reflex measurements, all participants were tested between days 2 and 5 of their menstrual cycle. In the Control group, functional leg dominance was assessed using 3 tests: a step-up task, a ball kicking task, and a balance recovery task (14). The leg used for at least two of the 3 tasks was determined to be functionally dominant and was selected for testing. In the ACL-injured group, both the uninvolved and involved (reconstructed) limbs were tested, with limb testing order counterbalanced between participants.

Measurement Overview and Variables of Interest

Soleus H reflex recruitment curves were elicited for the dominant leg in the Control group (CON-D) and for both the uninvolved (ACL-UN) and involved (ACL-INV) limbs in the ACL-injured group. At each stimulation intensity, the soleus H reflex was also conditioned by stimulation of the common peroneal (CP) nerve in order to measure presynaptic inhibition (PI). The dependent variables were 1) the Hmax:Mmax ratio (H:M); the slope of the linear ascending portion of the H reflex recruitment curve using both 2) unconditioned ($Slope_{test}$) and 3) CP-conditioned ($Slope_{CP}$) stimuli; and 4) presynaptic inhibition (%PI) as determined by comparing peak-to-peak soleus H reflex amplitude with and without CP conditioning. Each measure is described in detail in the paragraphs following the reflex testing protocol.

Reflex testing protocol

On each leg, two unshielded 12mm stimulating electrodes were applied in positions to stimulate the tibial nerve (popliteal fossa) and the common peroneal (CP) nerve (posterior to the fibular head). Two dispersal pads (anodes) were attached to each leg: one on the anterior thigh proximal to the patella, and one on the lateral aspect of the lower leg approximately 10cm distal to the stimulating electrode to the common peroneal nerve. Lubricated bipolar Ag/AgCl surface electromyography (sEMG) electrodes were placed over the muscle belly of the soleus, as well as the lateral malleolus. An electrical stimulator (Model S88, Grass Instruments, Inc., Warwick, RI), connected to a stimulus isolation unit and constant current unit, was used to deliver the stimulus to elicit the H reflex. H reflex peak-to-peak amplitude was measured via sEMG at 2000Hz (MP100 Data Acquisition System and Acknowledge software v.3.9.1, Biopac Systems, Inc., Goleta, CA).

With electrodes in place, the participant was positioned in a reclining chair with the torso angled at approximately 110^o relative to the thigh, with the knee positioned in approximately 10^o of flexion and the lower leg supported on a padded ottoman. Square pulse stimulations (1 ms) were delivered approximately every 15-20 seconds, starting from below H reflex threshold and increasing in 0.01V increments until the peak-to-peak H reflex amplitude reached a plateau (Hmax). Maximal motor response (Mmax) was also determined. At each stimulation intensity, both an unconditioned test reflex and a CP-conditioned reflex were elicited. In this manner, two recruitment curves were collected simultaneously for each limb: one unconditioned or “test” recruitment curve, as well as a second recruitment curve where soleus H reflexes were conditioned with prior CP nerve stimulation. For CP nerve stimulation, intensity was set at the motor threshold for the tibialis anterior (TA), defined as the smallest stimulation that would result in a contraction of the TA, as determined by visible dorsiflexion of the ankle and palpation of the TA tendon. The selection of an 80ms latency between the delivery of the CP and tibial nerve stimuli, as well as a stimulation intensity set to motor threshold, has been previously reported to result in presynaptic inhibition (PI) to the soleus motoneurons (16, 31).

Recruitment curves were normalized to facilitate comparisons between individuals. On the x axis, stimulation intensity was normalized to the stimulus required to elicit a direct motor response (i.e., M threshold), in the manner described by Funase et al (6). On the y axis, H reflex peak-to-peak amplitude was normalized to the amplitude of the maximal M wave (Mmax).

Outcome Measures

Hmax:Mmax ratio (H:M): The maximal amplitude of the test H reflex, expressed relative to Mmax amplitude, is representative of the relative proportion of the motor unit pool able to be activated via the Ia reflex loop under given postural and environmental conditions. In this sense, the Hmax:Mmax ratio describes the relative "connectivity" of the synapse between the afferent (Ia) and efferent (α motoneuron) nerves in the spinal cord.

H slope ($Slope_{test}$ and $Slope_{CP}$): The ascending portion of the H reflex recruitment curve is sigmoid in shape, with toe and plateau segments connecting a relatively linear middle region. The linear slope of the ascending portion of the H reflex recruitment curve is representative of the sensitivity, or gain, in the system under the current environmental conditions. The "reflex gain" represents the changing rate of MN excitability as a function of changes in Ia input to the motoneuron pool (7), and is therefore representative of the connectivity between the sensory and motor fibers. To calculate H Slope, the linear ascending portion of the recruitment curve was isolated and its slope was obtained using least squares regression.

Presynaptic Inhibition (%PI). At a given stimulation intensity, the amplitude of the soleus H reflex can be modulated via presynaptic inhibition arising from prior CP nerve stimulation. The percent change in H reflex amplitude due to CP nerve stimulation was calculated at individual stimulus intensities by dividing the change in H reflex amplitude by its original, unconditioned amplitude and expressing the result as a percentage $[(H_{CP} – H_{TEST})/H_{TEST})*100]$. In order to minimize the volatility in H reflex amplitude often seen at the extreme low and high ends of the recruitment curve, the bottom and top 20% of evoked H reflex amplitudes were not included in this calculation. Using the percent change for each unconditioned-CP conditioned reflex pair, a mean change score was calculated. This mean change score was determined to represent percent presynaptic inhibition due to CP-conditioning (%PI). By convention, a decrease in H reflex amplitude due to CP-conditioning (%PI < 0) is defined as inhibition, whereas an increase in H amplitude (%PI > 0) represents facilitation.

Statistical Analysis

The chosen study design included both within-group (ACL-UN vs. ACL-INV) as well as a between-group (ACL vs. CON) comparison, leading us to conduct t-tests instead of ANOVA. The dependent variables were 1) Hmax:Mmax ratio (H:M); 2) the slope of the test reflex recruitment curve ($Slope_{test}$), 3) the slope of the CP-conditioned reflex recruitment curve ($Slope_{CP}$), and the 4) mean percent inhibition in the linear ascending portion of the recruitment curve (% PI). In order to assess reflex similarity between ACL-UN and ACL-INV, Pearson's correlation coefficients were calculated for all four dependent variables. Two participants in the ACL group were removed from analysis because of extreme (>3 standard deviations) facilitation due to CP conditioning. All analyses were carried out using SPSS for Windows, v. 18. For all statistical tests, the level of significance was set at $\alpha = .05$.

Results

The between-leg comparisons (CON-D vs. ACL-UN; CON-D vs. ACL-INV; ACL-UN vs. ACL-INV) showed no significant differences for H:M, $Slope_{test}$ or $Slope_{CP}$ ($p>.05$; Table 1; Figures 1 and 2). In the ACL group, paired-samples t-tests revealed H:M did not differ between the ACL-UN and ACL-INV limbs (.69 ± .20; .69 ± .18, respectively). Both $Slope_{test}$ and $Slope_{CP}$ were also similar (407 ± 199 vs. 427 ± 218; 374 ± 171 vs. 366 ± 231, respectively). Independent-samples t-tests revealed similar results when comparing each limb of the ACL group to the Control group (H:M, $Slope_{test}$ and $Slope_{CP}$: .59 ± .20, 363 ± 192, and 352 ± 190, respectively).

[FIGURES 1 AND 2 ABOUT HERE]

[TABLE 1 ABOUT HERE]

Because of the inherent variability in measurement of presynaptic inhibition, participants were grouped into Facilitators (%PI > 0; soleus H reflex amplitude increases with CP-conditioning) and Inhibitors (%PI < 0; soleus H reflex amplitude is attenuated by CP conditioning). Classification was based on the response observed in the dominant limb (Control group) or the uninvolved limb (ACL group). This classification resulted in a group of 20 Facilitators (n=11 ACL, 9 Control) and 17 Inhibitors (n=7 ACL, 10 Control). Following this grouping, % PI was compared in a similar manner to the previous dependent variables (CON-D vs. ACL-UN; CON-D vs. ACL-INV; ACL-UN vs. ACL-INV). Within the Facilitators, the ACL-involved limb was significantly different than either its contralateral limb or the Control group. %PI in ACL-INV (16.1±34.0%) was significantly less than %PI in ACL-UN (32.5 ± 27.4%; p=.046) or CON-D (43.1±19.2%; p=.049) (Table 2; Figure 3). Within the Inhibitors, no significant differences were observed between any limb pairs (ACL-UN; ACL-INV; CON-D: -34.4±18.7%; -15.0±13.0%; -19.2±12.6%, respectively).

[TABLE 2 ABOUT HERE]
[FIGURE 3 ABOUT HERE]

In the ACL-injured group, Pearson correlation coefficients revealed moderate correlations between the uninvolved and involved limbs for the following dependent variables: H:M (r=.63; p=.005). $Slope_{test}$ (r=.53; p=.02), %PI (r=.69; p=.002) (Figure 4).

[FIGURE 4 ABOUT HERE]

Discussion

The purpose of our study was to compare multiple soleus H reflex parameters (H:M, $Slope_{test}$, $Slope_{CP}$, %PI) in women who had previously torn their ACL and in women with no history of knee injury. With one exception, we found few significant differences in soleus H reflex profiles between limbs in the ACL group, or between the ACL and Control groups. These results suggest that in women who are at least 12 months post-reconstruction, many H reflex parameters at rest are similar in both the uninvolved and involved limbs, and do not differ from healthy controls. One area where significant differences emerged, however, was in the level of H reflex modulation in response to CP conditioning. In the participants classified as Facilitators, the degree of H reflex modulation was significantly limited in the ACL-involved limb, when compared to either the contralateral limb or the Control group.

Our finding that Hmax:Mmax ratios are not different between groups or between limbs in the ACL group confirms previous results reported by Hoffman and Koceja (13). In our study, at rest, the Hmax:Mmax ratio in the ACL-involved limb did not differ from either its contralateral limb or from a healthy control group. Hoffman and Kojeca's results, however, suggest that when comparing healthy participants to those with ACL reconstruction, there does appear to be a difference in the degree of bilateral reflex symmetry. Hoffman and Koceja reported a strong inter-limb correlation in Hmax:Mmax ratio in healthy individuals (r=.84), and a much weaker inter-limb correlation in individuals with ACL reconstruction (r=.38). In our study, the inter-limb correlation in Hmax:Mmax ratios in our ACL group was of moderate strength (r=.63). The difference between our findings and those previously reported may be due to the time between surgery and H reflex testing, as the participants in our study were tested much later after repair compared to the participants used by Hoffman and Koceja. Our ACL group participants were required to be a minimum of 12 months post-repair, and the average time between reconstruction and H reflex testing was over 4 years. In contrast, the ACL group tested by Hoffman and Koceja were an average of just 9.5 months after reconstruction. The aggregate of the findings of our study and the previous work suggests that acutely following ACL injury and reconstruction, there is a significant reduction in Hmax:Mmax bilateral symmetry, but that there may be a gradual return to symmetry over time. Our study participants may represent a midway point along the reflex recovery path. Whether individuals with ACL reconstruction eventually demonstrate bilateral symmetry equal to healthy individuals, and the time course for this progression, is unknown.

The use of the Hmax:Mmax ratio as a measure of motoneuron excitability is widespread, and was included in the current study in order to facilitate comparisons to previous work. (13). However, the measure also carries some limitations. First, the measured Hmax amplitude can be attenuated by antidromic collisions in the alpha motoneuron (7), and second, by definition, the Hmax:Mmax ratio provides information about connectivity at the synapse at only one point along the recruitment curve. We sought to improve upon current knowledge by evaluating two additional H reflex parameters: the slope of the ascending linear portion of the H reflex recruitment curve, and the percent presynaptic inhibition due to CP nerve stimulation. To our knowledge, these measures have not previously been assessed following ACL reconstruction. In the context of elucidating the neuromuscular causes and effects of ACL injury, both of these variables may be of interest. The ascending slope of the H reflex recruitment curve provides information about motoneuron excitability across the motoneuron pool, and is therefore a more global measure of neuromuscular connectivity at the spinal synapse. The linear ascending slope reflects the relationship between motoneuron recruitment and afferent input, and, in this sense, is a reflection of the size principle (7). The slope allows us to visualize the input/output relationship at the spinal synapse that is the result of the sum of facilitatory and inhibitory sensory inputs (7), and is therefore a representation of the excitability of the MN pool in a given environmental state. Comparing the slopes either bilaterally or between groups allows us to make inferences about how sensory information is "gated" in different groups. A very steep slope may suggest a very strong and potentially inappropriate motor response to mild afferent stimuli. The converse (mild motor response to strong afferent stimuli) may also be observed. Improperly scaled muscular responses may increase the risk of noncontact ACL rupture, particularly when paired with other existing risk factors such as impaired quadriceps-to-hamstring activation ratios. In our study, the slopes in the intact and reconstructed limbs were similar at rest. It is necessary to determine whether this similarity also exists during more complex situations, such as during motor tasks, selective attention conditions, or during locomotion, as these conditions may provide valuable insight into potential neuromuscular risk for ACL rupture.

We also tested the effect of reflex conditioning via common peroneal (CP) nerve stimulation. After participants were separated into facilitators (those who demonstrate an increase in soleus H reflex amplitude following CP conditioning) and inhibitors (those who demonstrate an attenuated soleus H reflex following CP conditioning), it became apparent that reflexes in the ACL-involved limb were modified to a lesser degree than the ACL-uninvolved or Control-dominant limbs in the facilitators (see Figure 3). Among facilitators, the change in reflex amplitude in the ACL-involved limb was significantly smaller than either the uninvolved limb or control group. In the inhibitors, the difference in the magnitude of change between the ACL-uninvolved and ACL-involved limbs was virtually identical to that seen in the facilitators, but not statistically significant. In examining Figure 3, the observation can be made that the Ia-alpha motoneuron spinal synapse in the ACL-involved limb is potentially less susceptible to presynaptic modulation than its uninvolved counterpart. This lack of plasticity in the reflex loop may indicate that neuromuscular control of the ACL-involved leg is less modifiable in response to the environmental context. As our study was retrospective, it cannot address whether the observed inter-limb differences may have predisposed the limb to injury. However, this finding suggests that residual differences in spinal control persist in the ACL-involved limb, long past reconstruction.

It is interesting to note that we observed atypical responses to CP conditioning in a high number of our participants. The deep branch of the CP innervates the tibialis anterior (TA) muscle, whose concentric action opposes the soleus-gastrocnemius complex. It is generally accepted that prior stimulation of the CP will result in reflex inhibition of the soleus via presynaptic pathways (2, 16). While the H reflex pathway is itself monosynaptic, it can be modulated both through segmental and supraspinal activity. Spinal interneurons project onto the synapse, modulating neurotransmitter release and changing the magnitude of the motor response. In the present study, we measured PI at rest using CP nerve stimulation, which is a common and widely-used technique (2, 9, 16, 19, 30). While individual responses to this reflex conditioning vary, in general CP conditioning results in an increase in PI (and a decrease in soleus H reflex amplitude) due to CP nerve stimulation. Interestingly, approximately half of our study participants demonstrated increased H reflex amplitudes (i.e., facilitation) in response to the conditioning stimulus. In the ACL-injured group in the intact limb, 61% (11 out of 18) demonstrated increased H reflex amplitudes when a conditioning stimulus to the CP was delivered 80ms prior to stimulating the tibial nerve. In the Healthy group, 47% (9 of 19) also exhibited a facilitation response. Correct placement of the stimulating electrode to the CP was verified both by a visible contraction of the TA and by palpation of the TA tendon. Moreover, on a subset of participants, surface EMG electrodes on the TA muscle belly further confirmed TA activity in response to the stimulating electrode, which was positioned just posterior to the fibular head. The proportion of our participants classified as facilitators is larger than the generally accepted neurophysiology would suggest. Zehr, in a review of H reflex methodology, suggests a conditioning stimulus intensity of 1.0-1.5 times the TA motor threshold, with a latency of 80-120 ms (31). Our stimulation intensity was set to the TA motor threshold, with a latency of 80 ms. While our methodology fell within the generally accepted range, it is conceivable that the high proportion of observed facilitators was a function of our reflex testing parameters, and had we selected a higher stimulation intensity and a slightly longer latency, the results may have been different.

There are some limitations to the generalizability of our study. First, H reflex measures were only taken at rest. While we were able to expand the remarkably small body of knowledge concerning H reflex profiles after ACL reconstruction, there is a need to determine how spinal control changes during settings that mimic some aspect of athletic activity, such as locomotion, motor control tasks, or dual-task or divided attention situations. Secondly, the females in our study demonstrated substantial variability in the time between reconstruction and study participation. With a range of 12 months to 9 years, it is certainly conceivable that restricting the participants to a narrower time frame may have elicited different results. Despite the limitations, there is a dearth of literature addressing H reflexes after ACL reconstruction. Therefore, our study takes an important first step towards establishing a baseline or reference for motoneuron excitability at rest. The results published here will help researchers make decisions regarding study design as well as provide a frame of reference for the similarity between groups and between legs at rest.

Because the H reflex is a useful tool to measure changes in descending spinal control under changing environmental conditions, such as increased postural anxiety (15, 19, 21, 28), locomotion (5, 18, 31), and mental imagery (1, 3, 23, 25), it may be employed to investigate or identify different neuromuscular control strategies in women who have experienced ACL injury. Knowing that women with prior ACL injury are not generally different from healthy controls at rest is a small, but important step towards investigating the modulation of spinal control mechanisms due to changes in experimental conditions.

Conclusion

At rest, H reflex parameters are generally similar between the uninvolved and involved limbs of females with unilateral noncontact ACL rupture, as well as compared with a healthy control group. The most obvious difference observed in this study was a blunted reflex modulation in the ACL-involved limb due to CP conditioning. However, this attenuated reflex modulation was observed in facilitators only. This general bilateral similarity suggests that similar interactions occur at the Ia-alpha motoneuron synapses for both the uninvolved and involved limbs. The observed similarities at rest pave the way for the H reflex to be used as a comparative tool in more active positions, such as standing and locomotion, to assess whether motor control during activity is similar in both groups and between limbs. Reflex profiles during locomotion or other motor tasks may be helpful in understanding neuromuscular control related to ACL injury.

Tables and Figures

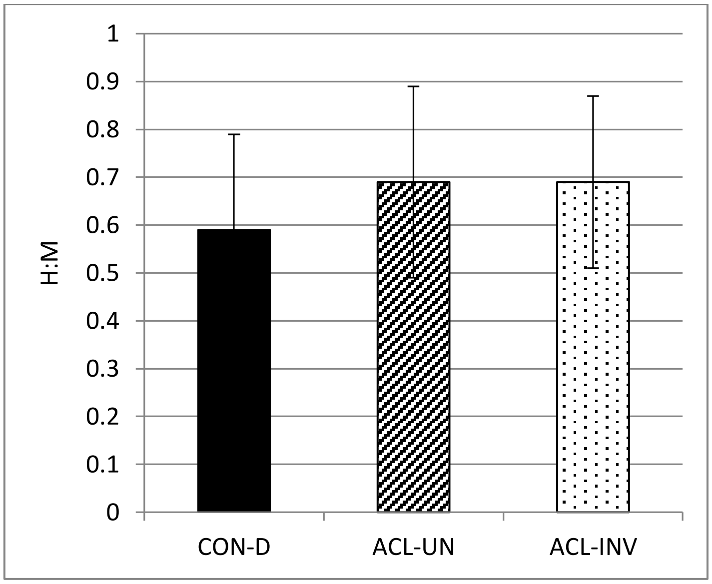


Fig. 3.1. **Hmax:Mmax ratios in CON-D, ACL-UN, and ACL-INV.** Hmax:Mmax ratios were not significantly different between groups or between limbs.

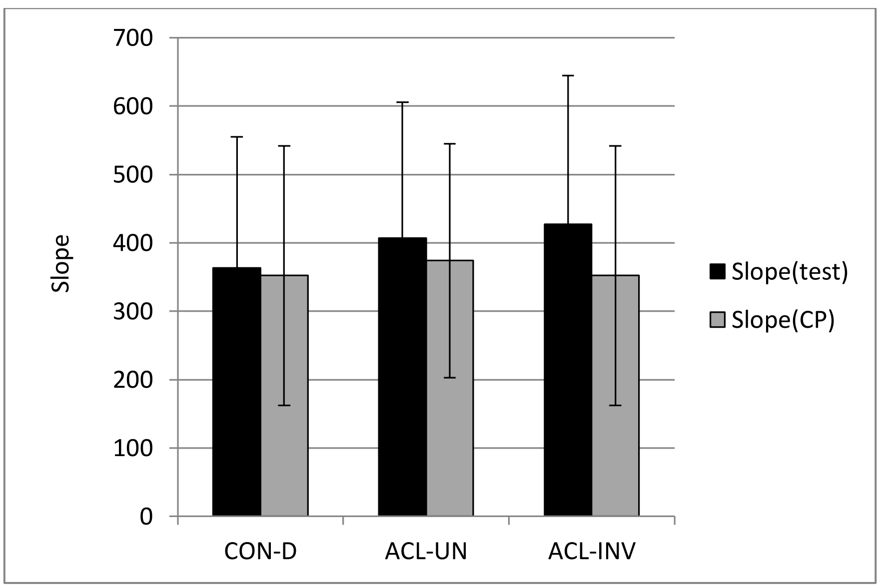


Fig. 3.2. **Slope$_{test}$ and Slope$_{CP}$ in CON-D, ACL-UN, and ACL-INV.** Neither the test (unconditioned) H slope or the CP-conditioned H slope was significantly different between groups or between limbs.

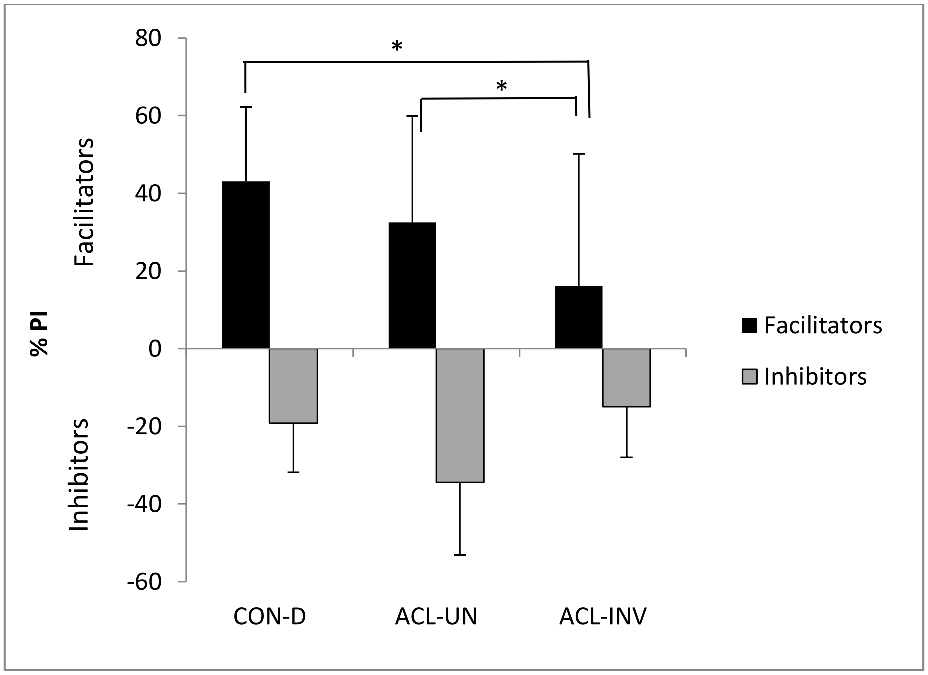
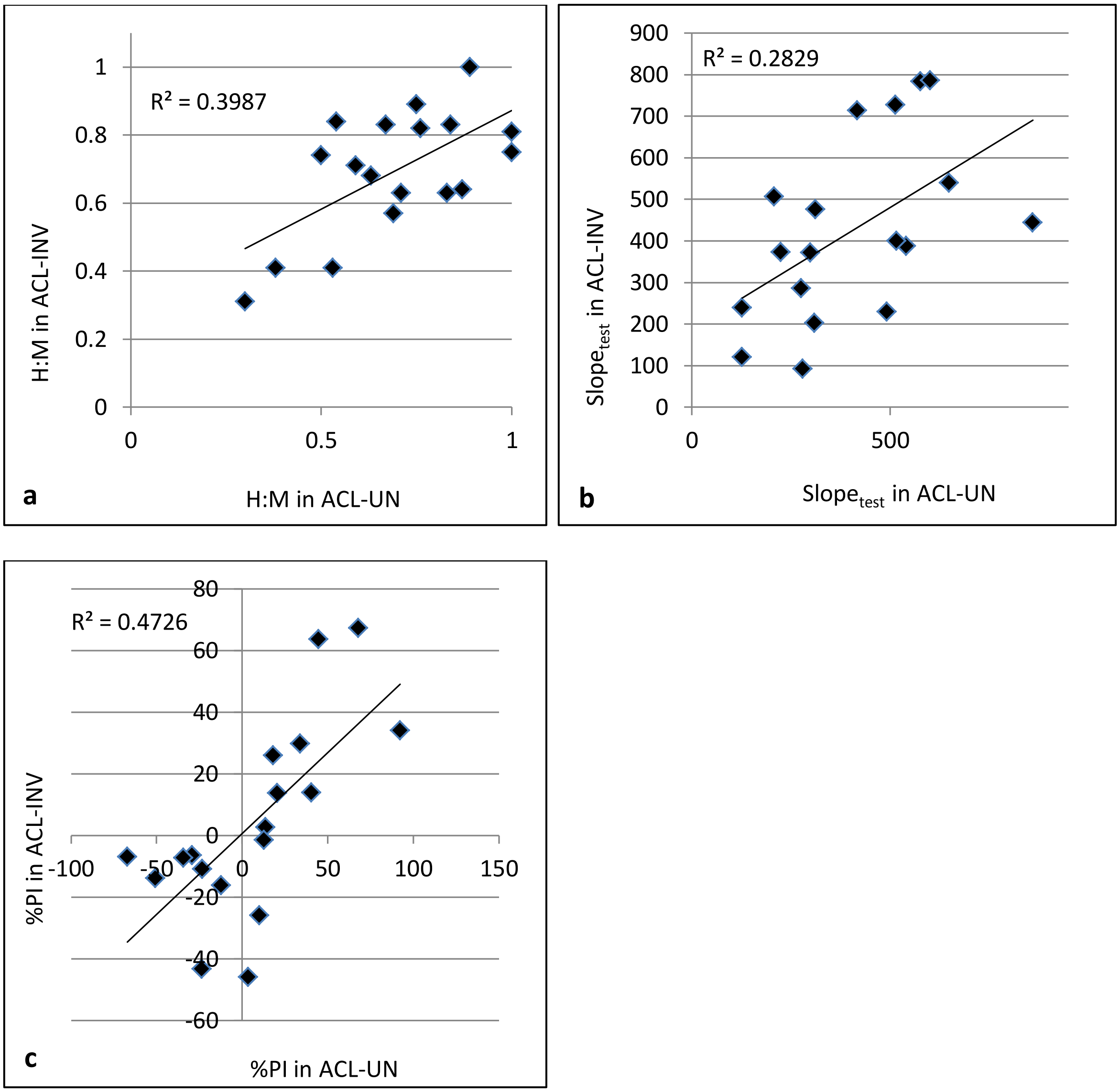


Fig. 3.3. **%PI in CON-D, ACL-UN, and ACL-INV, grouped into Facilitators and Inhibitors.** Among Facilitators, the ACL-involved limb showed a smaller degree of facilitation than either its contralateral limb or the Control group. Among Inhibitors, despite a similar numeric difference between the ACL-uninvolved and ACL-involved limbs, the difference was not significant.



<u>Fig. 3.4.</u> **The relationship between ACL-UN (x axis) and ACL-INV (y axis) for (a)H:M, (b)Slope$_{test}$, and (c)%PI.** Hmax:Mmax ratio, H slope (unconditioned), and % PI all demonstrate moderate-strength, positive correlations between limbs, suggesting that spinal reflexes are similar bilaterally in patients > 12 months post-ACL reconstruction.

Table 3.1. H:M ratios and Slopes for the uninvolved and involved limbs (ACL group) and the dominant limb (Control group).

	Mean ± SD			t-test p values		
Measure	ACL-UN	ACL-INV	CON-D	ACL-UN vs. ACL-INV	ACL-UN vs. CON-D	ACL-INV vs. CON-D
H:M	.69 ± .20	.69 ± .18	.59 ± .20	.98	.13	.11
$Slope_{test}$	407 ± 199	427 ± 218	363 ± 192	.69	.50	.35
$Slope_{CP}$	374 ± 171	366 ± 231	352 ± 190	.88	.71	.84

Table 3.2. Percent presynaptic inhibition in the uninvolved and involved limbs (ACL group) and in the dominant limb (Control group).

	Mean ± SD			t-test p values		
% PI	ACL-UN	ACL-INV	CON-D	ACL-UN vs. ACL-INV	ACL-UN vs. CON-D	ACL-INV vs. CON-D
Facilitators	32.5 ± 27.4%	16.1 ± 34.0%	43.1 ± 19.2%	.046	.34	.049
Inhibitors	-34.4 ± 18.7%	-15.0 ± 13.0%	-19.2 ± 12.6%	.10	.06	.51

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Chapter 4: Effects of task orientation and ACL injury status on soleus H reflex modulation

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ABSTRACT

Successful participation in sports requires athletes to attend to multiple sensory stimuli, which represents a dual-task paradigm. Differences in neurocognitive processing may influence ACL injury risk; however, it is unclear how a secondary task affects spinal reflex modulation. **PURPOSE**: To determine if performing an upper-extremity fine motor task would result in differential soleus H reflex modulation in women with a history of unilateral noncontact ACL injury compared to a healthy control group. **METHODS:** Thirty nine recreationally active women (20 with prior unilateral noncontact ACL injury: 24.0 ± 4.5 years; 23.8 ± 4.5 $kg \cdot m^{-2}$; 4.1 ± 2.6 years post-injury; 19 with no history of knee injury: 23.8 ± 4.5 years; 23.1 ± 2.3 $kg \cdot m^{-2}$) agreed to participate. All were free of neurological disorder or recent lower extremity injury. In the Control group, the dominant limb (CON-D) was assessed; in the ACL group, both the uninvolved (ACL-UN) and involved (ACL-INV) limbs were tested. Unconditioned (test) and Common Peroneal (CP)-conditioned H reflex recruitment curves were collected between days 2 and 5 of the menstrual cycle; and were elicited at rest (Rest) and while the participant performed a typing task (Task). The dependent variables were Hmax:Mmax ratio (H:M), the linear ascending slope of the test and CP-conditioned recruitment curves ($Slope_{test}$ and $Slope_{CP}$), the percent change in H reflex amplitude due to CP-conditioning (% $Change_{CP}$), and due to the typing task (% $Change_{TASK}$). **RESULTS:** Between groups (CON-D vs. ACL-UN), [2(Task) x 2(Group)] mixed model ANOVA revealed a significant main effect of Task on H:M, $Slope_{test}$ and $Slope_{CP}$ (p=.001; p=.002; p=.001, respectively). H:M and Slope were attenuated by the typing task. Within the ACL group (ACL-UN vs. ACL-INV),

[2(Task) x 2(Leg)] repeated-measurses ANOVA revealed a significant main effect of Task on $Slope_{test}$ and $Slope_{CP}$ ($p=.023$ and $p=.002$, respectively), but not on H:M ($p=.056$). The absolute value of % $Change_{TASK}$ was not different between groups (CON-D vs. ACL-UN; $p=.32$) nor within the ACL group (ACL-UN vs. ACL-INV; $p=.42$). Pearson's correlation assessing the relationship between the absolute value of % $Change_{CP}$ and % $Change_{TASK}$ revealed a moderate-strength relationship in the Control group ($r=.55$; $p=.01$), and no significant relationship in the ACL group (ACL-UN: $r=.03$; $p=.92$; ACL-INV: $r=.07$; $p=.78$).

CONCLUSION: The incorporation of a typing task requiring fine motor control and mental focus generally attenuated H reflex characteristics in both the Control and ACL groups, with the exception of Hmax:Mmax ratio, which was not attenuated in ACL-INV. There was no difference between groups or between legs in the percent change in H reflex amplitude due to typing. Attending to multiple sensory stimuli may alter spinal-level control mechanisms of lower extremity musculature.

Introduction

It is well-established that female athletes experience a greater incidence of noncontact anterior cruciate ligament (ACL) rupture than their male counterparts, with injury rates reported to be between two and six times higher than in comparable male athletic populations (7, 14). Historically, anatomical, biomechanical, neuromuscular, and hormonal risk factors have been thought to contribute to the risk for ACL injury (2). Recently, the idea of neurocognitive processing influence on noncontact ACL injury risk has been proposed (19). Participation in sport often involves concomitant focus on multiple sensory inputs – for example, the position and movement of both a ball and an opposing player – and therefore successful performance compels the athlete to simultaneously attend to various stimuli. This condition is referred to as dual-task processing, and has been shown to negatively influence performance in at least one of the simultaneous tasks (8). Specifically, reductions in the performance of motor tasks such as force production (3), movement speed (1) and reaction time (8) have been documented when individuals must concurrently perform a secondary task. This performance interference occurs regardless of whether the secondary task is verbal (1, 3) or motor (8) in nature. One theory for the reduction in performance relates to the brain's limited capacity for processing inputs. Once capacity is reached, the amount of attention devoted to one or more tasks will be reduced in order to accommodate competing inputs (16). In the context of noncontact ACL injury, it is theorized that attending to multiple sensory inputs on the playing field may compromise motor control, thereby increasing the likelihood of injury.

In comparison to the body of knowledge concerning anatomical, biomechanical, neuromuscular, and hormonal risk factors, there is a paucity of research into neurocognitive performance and ACL injury risk. In a unique study, Swanik et al (19) found that during the season following a baseline neurocognitive assessment, collegiate athletes who went on to suffer noncontact ACL injuries had scored worse on the test battery (IMPACT test), compared to matched controls. Specifically, performance impairments were noted in reaction time, processing speed, visual and verbal memory scores. Even small deficits in reaction time and processing speed, in particular, have the potential to alter an athlete's response to perturbations or unanticipated movement patterns, and may predispose athletes to injury.

While the performance deficits reported by Swanik et al. are in cortically-driven measures, the authors note that "maintaining dynamic restraint during complicated, high-velocity movements such as athletics is contingent on *both cortically programmed muscle preactivation and reflex-mediated contractions*"(19). One way to assess reflex-related control in the lower extremity musculature is Hoffmann (H) reflex testing. The H reflex is an electrically-induced analogue to the tendon-tap reflex, evoked by directly stimulating afferent nerve fibers, most commonly of the tibial nerve. This results in a monosynaptic reflex loop that is measured as a twitch in the soleus muscle. The amplitude of the H reflex is a measure of motoneuron excitability that can be modulated by segmental and supraspinal influences, and has been demonstrated to vary with changes in task complexity. Afferent information at the synapse can be amplified or attenuated, thereby changing the magnitude of the motor response. In practice, this sensory "gating" is critical in filtering multiple inputs and mounting an environmentally appropriate response. This gating relies heavily on interneurons, which are typically inhibitory. When these inhibitory interneurons affect activity in the spinal cord and reduce the amplitude of the H reflex, the phenomenon is known as presynaptic inhibition (PI). PI changes with variations in activity, as is evidenced by PI modulation that happens when an individual transitions from sitting to standing to walking (20). These changes in PI suggest that when tasks become more complex and require increasingly greater precision in motor control, PI increases in order to allow more subtle postural adjustments, and therefore plays an important role in spinal-level control of lower-extremity musculature. In sport, neuromuscular control of the lower extremity is constantly modulated by changes to the athlete's environment. The H reflex is a tool that can be used to investigate spinal control of lower extremity muscles and shed light on differences in spinal-level processing as individuals are exposed to tasks of varying levels of demand.

The purpose of this study was to determine if performing an upper-extremity fine motor task would result in differential soleus H reflex modulation in women with a history of unilateral noncontact ACL injury compared to a ACL-intact ("healthy") control group. To accomplish this purpose, we had three aims. Our first aim was to compare soleus H reflexes between groups (comparing our Control group to the uninvolved limb in our ACL group). Our second aim was to compare the involved and uninvolved limbs in the ACL group to determine whether inter-limb differences existed in reflex modulation. Finally, our third aim was to assess any reflex modulation to the secondary task ("task inhibition") and to compare any observed task inhibition to presynaptic inhibition due to common peroneal (CP) nerve conditioning.

Materials and Methods

Subjects

A total of 39 recreationally active women volunteered to participate. Twenty participants had sustained a unilateral noncontact ACL injury (mean ± SD age: 24.0 ± 4.5 years; Body Mass Index (BMI): 23.8 ± 4.5 $kg \cdot m^{-2}$; 4.1 ± 2.6 years post-injury). In order to meet inclusion criteria, the ACL rupture had to have occurred within the past ten years, with surgical repair occurring a minimum of 12 months prior to participation. The control group consisted of nineteen healthy females who had no history of knee injury (age: 23.8 ± 4.5 years; BMI: 23.1 ± 2.3 $kg \cdot m^{-2}$). All participants gave written informed consent and the study was approved by the university's institutional review board. In both groups, participants had no history of neurological disorder or recent (≤ 6 months) injury to the lower extremity. In order to control for potential effects of hormonal fluctuation on reflex measurements, all participants were tested between days 2 and 5 of their menstrual cycle. In the Control group, functional leg dominance was assessed using 3 tests: a step-up task, a ball kicking task, and a balance recovery task (11). The leg used for at least two of the 3 tasks was determined to be functionally dominant and was selected for testing. In the ACL-injured group, both the uninvolved and involved (reconstructed) limbs were tested, with limb testing order counterbalanced between participants.

Protocol Overview

Soleus H reflex recruitment curves were elicited for the dominant leg in the Control group (CON-D) and for both the uninvolved (ACL-UN) and involved (ACL-INV) limbs in the ACL-injured group. Recruitment curves were obtained under two task conditions: 1)while the participants were at rest ("Rest"), as well as 2) during a typing task ("Task") requiring fine motor control and sustained mental focus. At each stimulation intensity, the soleus H reflex was also conditioned by stimulation of the common peroneal (CP) nerve in order to measure presynaptic inhibition (PI). The typing task and nerve stimulation techniques are described in detail in the H reflex testing protocol.

H reflex testing

In the Control group, only the dominant limb was tested. In the ACL group, both legs were tested. On each leg, two unshielded 12mm stimulating electrodes were attached in positions to stimulate the tibial nerve (popliteal fossa) and the common peroneal (CP) nerve (posterior to the fibular head). Two dispersal pads (anodes) were placed on each leg: one on the anterior thigh proximal to the patella, and one on the lateral aspect of the lower leg approximately 10cm distal to the stimulating electrode to the common peroneal nerve. Lubricated bipolar Ag/AgCl surface electromyography (sEMG) electrodes were placed over the muscle belly of the soleus, as well as the lateral malleolus. An electrical stimulator (Model S88, Grass Instruments, Inc., Warwick, RI), connected to a stimulus isolation unit and constant current unit, was used to deliver the stimulus to elicit the H reflex. H reflex peak-to-peak amplitude was measured via sEMG at 2000Hz (MP100 Data Acquisition System and Acknowledge software v.3.9.1, Biopac systems, Inc., Goleta, CA).

With electrodes in place, the participant was positioned in a reclining chair with the torso angled at approximately 110^{o} relative to the thigh, with the knee positioned in approximately 10^{o} of flexion and the lower leg supported on a padded ottoman. Square pulse stimulations (1 ms) were delivered approximately every 15-20 seconds, starting from below H reflex threshold and increasing in 0.01V increments until the peak-to-peak H reflex amplitude reached a plateau (Hmax). Maximal motor response (Mmax) was also determined. At each stimulation intensity, both an unconditioned test reflex and a CP-conditioned reflex were elicited. In this manner, two recruitment curves were collected simultaneously for each limb: one unconditioned or “test” recruitment curve, as well as a second recruitment curve where soleus H reflexes were conditioned with prior CP nerve stimulation. CP nerve stimulation intensity was set at the motor threshold for the tibialis anterior (TA), defined as the smallest stimulation that would result in a palpable contraction. The 80ms latency between CP and tibial nerve stimulations and stimulation intensity have been previously reported to result in presynaptic inhibition (PI) to the soleus motoneurons (13, 20).

Once the procedures described above were completed with the participant at rest, the process was repeated with the addition of the secondary typing task. In this task condition, H reflexes were obtained while the participant was distracted by a laptop computer game (www.sense-lang.org). The typing game consisted of a continuous series of three character nonsense words containing only characters on the keyboard's home keys (e.g., "dfj adl s;k"). The task was selected because typing requires fine motor control of the upper extremity, as well as sustained mental focus. As in the rest trial, two recruitment curves (unconditioned, or "test"; and common-peroneal conditioned, or "CP") were obtained during this typing task.

Recruitment curves were normalized to facilitate comparisons between individuals. H reflex peak-to-peak amplitude was plotted on the y axis, with all measured H reflexes expressed as a percentage of the amplitude of the maximal M wave (Mmax). Stimulus intensity was plotted on the x axis and was normalized to the stimulus intensity required to elicit a direct motor response (i.e., M threshold), in the manner described by Funase et al (5).

Variable Selection

The study was a repeated-measures design with multiple independent variables (Group, Leg, Typing Task). As was noted, only the dominant leg of the subjects in the control group was tested compared to both legs (ACL-UN vs. ACL-INV) in the ACL-injured group. The independent variable of Typing Task had two levels (Rest vs. Task). The dependent variables were 1) Hmax:Mmax ratio (H:M); the linear ascending slope of the H reflex recruitment curve, under both the 2) test and 3) CP conditions ($Slope_{TEST}$ and $Slope_{CP}$), 4) the percent change in H reflex amplitude due to CP conditioning – otherwise known as presynaptic inhibition (% $Change_{CP}$), and 5) the percent change in H reflex amplitude due to the addition of the typing task – otherwise known as task inhibition (% $\text{Change}_{\text{TASK}}$). Each dependent variable is described in detail in the following paragraphs.

Hmax:Mmax ratio

The maximal amplitude of the test H reflex is expressed relative to Mmax amplitude. The Hmax:Mmax ratio represents the proportion of the motor unit pool able to be activated via the Ia reflex loop. In this sense, the Hmax:Mmax ratio describes the relative "connectivity" of the synapse between the afferent and efferent nerves in the spinal cord.

Slope: Between the toe region and the plateau region (when nearing Hmax), the ascending slope of the recruitment curve is approximately linear. The linear ascending portion of the recruitment curve was isolated and its slope was obtained using least squares regression. The steepness of the slope is representative of "reflex gain", as it represents the change in motoneuron recruitment as a function of increased Ia (afferent) stimulation (6).

% Change$_{CP}$ and % Change$_{TASK}$. The unconditioned (test) H reflex was conditioned in two ways. Segmental presynaptic inhibition was evoked via CP stimulation. Supraspinal inhibition was evoked via the incorporation of the typing task. Both calculations are described in the paragraphs that follow.

Presynaptic Inhibition (% Change$_{CP}$). At a given stimulation intensity, the amplitude of the soleus H reflex can be modulated via presynaptic inhibition arising from prior CP nerve stimulation. The percent change in H reflex amplitude due to CP nerve stimulation was calculated at individual stimulus intensities by dividing the change in H reflex amplitude by its original, unconditioned amplitude and expressing the result as a percentage [% Change$_{CP}$ = $\{(H_{CP} - H_{TEST})/H_{TEST}\}*100$]. In order to minimize the volatility in H reflex amplitude often seen at the extreme low and high ends of the recruitment curve, the bottom and top 20% of evoked H reflex amplitudes were not included in this calculation. Using the percent change for each unconditioned-CP conditioned reflex pair, a mean change score was calculated. This mean change score represents percent presynaptic inhibition due to CP-conditioning. By convention, a decrease in H amplitude (%PI < 0) represents inhibition, whereas an increase in H reflex amplitude due to CP-conditioning (%PI > 0) is defined as facilitation.

Task Inhibition (% Change$_{TASK}$). To determine the effect of the typing task, a similar process was used. The amplitude of the test H reflex in the rest condition was matched to the amplitude of the reflex obtained at the same stimulus intensity during typing [% Change$_{TASK}$ = $\{(H_{REST} - H_{TASK})/H_{REST}\}*100$]. Again the bottom and top 20% of evoked H reflex amplitudes were excluded from the calculation, and the same procedure as noted above was used to determine a mean change score from each Rest-Task H reflex pair. The same conventions specified above for inhibition and facilitation apply.

Statistical Analysis

Two participants were removed from analysis because of extreme (>3 standard deviations) facilitation due to CP conditioning. Since the comparisons of interest for our first two specific aims were both between Groups [Control-dominant limb (CON-D) vs. ACL-uninvolved limb (ACL-UN)] and within the ACL group [ACL-uninvolved vs. ACL-involved limb (ACL-INV)], separate ANOVA were performed. Specifically, when CON-D was compared to ACL-UN, a mixed model ANOVA was applied, and when ACL-UN was compared to ACL-INV, a repeated-measures ANOVA was used. For our third specific aim, exploring the differences and relationships between CP-induced presynaptic inhibition and task inhibition, t-tests (independent and paired, for between-group and within-group comparisons, respectively) as well as Pearson's correlation were utilitzed (SPSS for Windows, v. 18). For all statistical tests, level of significance was set at $\alpha = 0.05$.

Results

Our first aim was to determine whether females with a history of noncontact ACL rupture demonstrate different spinal reflexes than healthy females when performing a secondary task. To accomplish this aim, we compared H reflexes in the Control group, dominant limb (CON-D) to the ACL group, uninvolved limb (ACL-UN) (Table 1). The ACL-uninvolved limb was selected for the between-group comparison because it was considered to be the more faithful representation of the individual's "unaltered" neurophysiology.

Between-Groups Comparisons (CON-D vs. ACL-UN)

Hmax:Mmax ratio (H:M). A [2(Task) x 2(Group)] mixed model ANOVA was employed to compare H:M ratio in CON-D and ACL-UN. The results revealed a significant main effect of Typing Task ($p=.001$; Fig. 1), due to a decrease in H:M during the typing task. H:M in the Rest and Task conditions, respectively, were: CON-D: 0.59 ± 0.20 and $.52 \pm 0.22$; and ACL-UN: 0.69 ± 0.20 and 0.63 ± 0.20. There was no main effect of Group (CON-D: $.56 \pm .27$; ACL-UN: $.66 \pm .29$; $p=.13$), nor was there a significant Task*Group interaction ($p=.66$).

[FIGURE 1 ABOUT HERE]

[TABLE 1 ABOUT HERE]

Ascending H Slope. Between groups, a [2(Task) x 2(Group)] mixed measures ANOVA comparing CON-D and ACL-UN revealed a significant main effect of Task on $Slope_{TEST}$ ($p=.002$). $Slope_{TEST}$ decreased from 363 ± 192 at rest to 298 ± 176 during typing, and from 381 ± 169 to 317 ± 192 in CON-D and ACL-UN, respectively. There was no main effect of Group (331 ± 239 and 349 ± 253 for CON-D and ACL-UN, respectively, $p=.76$), and no Task*Group interaction ($p=.98$). A second [2(Task) x 2(Group)] mixed measures ANOVA was performed to compare $Slope_{CP}$ between groups. Again, there was a significant main effect of Task on $Slope_{CP}$ ($p=.001$) (Figure 2). In CON-D, $Slope_{CP}$ decreased from 352 ± 190 at rest to 310 ± 196 during typing. In ACL-UN, $Slope_{CP}$ dropped from 360 ± 165 at rest to 260

± 165 during the typing task. There was no main effect of group (p=.71) or Task*Group interaction (p=.13).

[FIGURE 2 ABOUT HERE]

Our second aim was to determine whether females within the ACL group demonstrated similar bilateral responses to the secondary task. To accomplish this aim, H reflexes in the uninvolved (ACL-UN) and involved (ACL-INV) limbs were compared.

Within-Groups Comparisons (ACL-UN vs. ACL-INV)

Hmax:Mmax ratio: The [2(Task) x 2(Leg)] repeated-measurses ANOVA comparing ACL-UN to ACL-INV revealed no significant main effect of Task (Rest: .69 ± .26, Typing Task: .64 ± .28; p=.056). In the ACL-INV limb, Hmax:Mmax ratio at Rest and during the Typing Task were .70 ± .19 and .66 ± .22, respectively. There was no main effect of Leg (ACL-UN: .66 ± .26; ACL-INV: .68 ± .27; p=.55) or Task*Leg interaction (p=.70).

Based on previous work in the area of task complexity (12, 17), the effect of task on Hmax:Mmax was expected. It was unclear as to why this effect was not demonstrated in the ACL group comparison of legs. Specifically, when ACL-UN was compared between-groups to CON-D, a significant main effect of task was observed. However, when ACL-UN was compared within the ACL group to ACL-INV, the main effect of task was not present. In order to further explore this contradiction, separate paired t-tests for ACL-UN and ACL-INV were performed to compare Hmax:Mmax at Rest and during the Typing Task. Results of the paired t-tests (Figure 3) revealed that Hmax:Mmax ratio in ACL-UN was significantly reduced during typing (p=.009), but that the Hmax:Mmax ratio in ACL-INV was not significantly impacted by the typing task (p=.31). This revealed that the ACL-INV limb behaved differently than both its contralateral counterpart (ACL-UN) as well as the healthy controls (CON-D), when using H:M as the dependent variable.

[FIGURE 3 ABOUT HERE]

Ascending H Slope: The unconditioned slope and the CP-conditioned slope were also compared between legs in the ACL group. Results of separate [2(Task) x 2(Leg)] repeated-measures ANOVA between ACL-UN and ACL-INV revealed a main effect of Task for both $Slope_{TEST}$ and $Slope_{CP}$ (p=.023 and p=.002, respectively; Figure 4). In ACL-INV, $Slope_{TEST}$ at rest and during the typing task were 426 ± 225 and 349 ± 205, while $Slope_{CP}$ at rest and during the typing task were 365 ± 238 and 330 ± 217, respectively. There was no main effect of Leg for $Slope_{TEST}$ or $Slope_{CP}$ (p=.42 and p=.47, respectively)or Task*Leg interaction (p=.79 and p=.09, respectively).

[FIGURE 4 ABOUT HERE]

Our third aim was to examine the nature of reflex modulation due to the typing task (“task inhibition”) and to compare any observed task inhibition to presynaptic inhibition due to CP conditioning. The test H reflex was conditioned in two ways: via segmental influence (CP conditioning – Presynaptic Inhibition) and via supraspinal influence (typing task – Task Inhibition). In examining Task Inhibition (% Change_{TASK}), initial inspection of the data revealed that individuals responded to the typing task in one of two ways: some individuals demonstrated a decrease in H reflex amplitude (i.e., inhibition), whereas an increase in H reflex amplitude (i.e., facilitation), was measured in others. This presented a challenge with regards to comparing the mean % Change_{TASK} between the Control and ACL groups, and between legs in the ACL group. Specifically, the mean % Change_{TASK} for the CON-D, ACL-UN, and ACL-INV limbs were 1.5 ± 37.4%, 1.3 ± 45.0%, and 15.0 ± 58.6%, respectively. To avoid the problem of "washing out" mean % Change by averaging positive and negative change scores, we focused on the magnitude, and not the direction, of change by looking at the absolute value of % Change_{TASK} (Table 2). First, we verified that there was no difference in the distribution of Facilitators and Inhibitors between the CON and ACL groups (Fisher's Exact Test; p=.50). Next, we compared the magnitude of reflex modulation due to Task by comparing the absolute value of % Change_{TASK} between groups (CON-D vs. ACL-UN) and within the ACL group (ACL-UN vs. ACL-INV). Between groups, an independent-samples t-test revealed no significant difference in the absolute value of % Change_{TASK} between CON-D (28.6 ± 23.2 %) and ACL-UN (36.6 ± 24.7 %; p=.32). Thus, there was no difference in task modulation between the Control and ACL groups. Within the ACL-group, a paired-samples t-test also revealed no significant difference (p=.42) in the absolute value of % Change_{TASK} between ACL-UN and ACL-INV (45.1 ± 38.9%).

Overall, there were neither between-group nor within-group differences in the magnitude of reflex modulation due to the typing task.

[TABLE 2 ABOUT HERE]

We also wanted to understand whether task inhibition (% $Change_{TASK}$) was mediated via a similar pathway to the presynaptic inhibition due to CP-conditioning (% $Change_{CP}$). In order to determine whether the two types of inhibition were related, Pearson's correlations were performed separately for each limb (CON-D, ACL-UN, and ACL-INV). In the Control group, Pearson's correlation revealed a very weak and insignificant relationship ($r=.06$; $p=.81$) between % $Change_{TASK}$ and % $Change_{CP}$. However, when the absolute value of the change scores were compared, thereby comparing magnitude but not direction, there was moderate strength relationship between the magnitude of H reflex change due to presynaptic and task inhibition ($r=.55$; $p=.01$; Figure 5). Thus, it appears that in the Control group, the magnitude of reflex modulation due to CP conditioning is related to the magnitude of reflex modulation due to task. Individuals with a large % change in H reflex amplitude due to CP conditioning were also likely to demonstrate a large % change in H reflex amplitude due to task.

[FIGURE 5 ABOUT HERE]

In the ACL group, Pearson's correlation revealed the relationships between % $Change_{TASK}$ and % $Change_{CP}$ in both legs were weak and not significant, regardless of whether raw or absolute values were compared (Pearson's r for absolute value of % $Change_{TASK}$ and % $Change_{CP}$: ACL-UN: r=.03; p=.92; ACL-INV: r=.07; p=.78). Thus, in the ACL group, there was no relationship between the magnitude of reflex modulation due to CP conditioning and reflex modulation due to the typing task.

Discussion

The main finding of our research was that a typing task requiring fine motor control of the upper extremity and sustained mental focus resulted in attenuated soleus Hmax:Mmax ratio and H slope. Two major comparisons were performed: between-groups comparisons were made between the Control group, dominant limb (CON-D) and the ACL group, uninvolved limb (ACL-UN), and within-group comparisons were made between ACL-UN and the contralateral, involved limb (ACL-INV). The between-groups comparisons revealed no differences in Hmax:Mmax ratio or linear ascending slope modulation between CON-D and ACL-UN. This suggests that both healthy and ACL-injured individuals demonstrate similar reflex attenuation when performing a secondary task. In contrast, the within-group comparisons revealed that the Hmax:Mmax ratio in the ACL-INV limb was not attenuated by the typing task, and was different than both its contralateral limb and the healthy control group. However, measures of H slope revealed that ACL-INV behaved similarly to the other limbs tested. The contradictory observations in ACL-INV between Hmax:Mmax and

H slope suggest that the selection of specific H reflex outcome measures may influence the results.

The Hmax:Mmax ratio is often used as a measure of motoneuron excitability (10, 18), because the maximal amplitude of the evoked H reflex represents the proportion of the total motoneuron pool that is able to be recruited via Ia stimulation in a given environmental state. In investigating the Hmax:Mmax ratio in the Control and ACL groups during the typing task, our results revealed that the ACL-involved limb behaved differently than its contralateral partner, and did not demonstrate an attenuated reflex response during the secondary task. If the Hmax:Mmax ratio was used as a sole outcome variable, this would lead to the conclusion that the ACL-involved limb does not modulate its reflex sensitivity in response to a secondary task, which could have implications for proper motor control during situations of divided attention. However, additional and potentially more robust H reflex parameters were also measured, which paint a different picture. In contrast to the Hmax:Mmax ratio, when the linear ascending slope of the recruitment curve (test and CP-conditioned) was analyzed, the ACL-involved limb did demonstrate significant H reflex attenuation with typing, and was not different than the contralateral, uninvolved limb or the Control-dominant limb. This suggests that the linear ascending slope may be a more robust measure of motoneuron excitability capable of assessing changes across a broader swath of the motoneuron pool.

The linear portion of the ascending slope of the recruitment curve may be more responsive to changes in spinal excitability across the motoneuron pool. Funase and colleagues (6) have described the H slope as essentially a reflection of the size principle of motor unit recruitment: a relationship between Ia spinal input and, consequently, the proportion of motoneurons recruited as a result. Further, they argue, modulation to H slope occurs via descending input from higher brain centers. Thus, changes to H slope may signal differences in descending spinal control that affect even the smaller motoneurons in the motoneuron pool. Dynamic postural control relies upon both cortically-driven and reflex-mediated muscle activation (19). Therefore, measuring H slope may allow us to detect alterations to the excitability of even low-threshold motor units, whose function is necessary for subtle adjustments to postural control.

There is little research on upper-extremity task processing and lower-extremity H reflex modulation. Prior work by Hoffman and Koceja revealed that task complexity (invoked by increasing postural anxiety) results in an attenuation of the H reflex (12). However, the methods used to increase complexity of the task (standing blindfolded and/or on an unstable surface) did not specifically target the upper extremity. Much of the previous work combining an upper extremity task with lower extremity H reflex assessment has involved rhythmic upper extremity motions associated with locomotion, such as flexion and extension of the shoulder during arm swinging or cycling (4, 9, 15). The modulation of soleus H reflexes in response to rhythmic movement of the upper extremity supports a neural link between upper and lower extremity motor control in order to maintain arm and leg coordination during locomotion. In the current study, the upper extremity task differed markedly from previous protocols, in that the upper-extremity typing task had no logical relationship to locomotion, involved fine motor control of the fingers, and required sustained mental focus. If an upper-extremity task not associated with locomotion can modulate lower extremity spinal control, this suggests that when the upper and lower extremities are performing separate tasks, the combined attentional demand may divert processing resources from closely regulating neuromuscular control of the lower extremity. If spinal-level control of the lower extremity musculature is altered by a competing upper-extremity task, potential changes to dynamic postural control may place the athlete at increased risk of injury during movements where appropriate control is critical, such as landing and cutting.

The mechanism that triggered attenuation of the soleus H reflex due to the upper extremity typing task is unknown. Frigon et al. previously demonstrated that during arm cycling, descending input due to arm movements likely modulates soleus H reflex amplitude via a presynaptic pathway similar to CP nerve conditioning (4). The authors supported this assertion by further manipulating the soleus H reflex with both sural and CP nerve conditioning. Sural nerve conditioning reduced the inhibition demonstrated during arm cycling, while CP nerve conditioning had the opposite effect, further increasing inhibition. The net additive effects of arm cycling and CP or sural nerve conditioning provide strong evidence that both mechanisms for reflex modulation proceed via a common presynaptic pathway. In the current study, we also compared inhibition due to the typing task with inhibition due to CP conditioning. In contrast to Frigon et al., our results suggest that reflex modulation due to the incorporation of a typing task may not occur via the same pathway. In the Control group, only the magnitude of change in H reflex amplitude due to typing was moderately related to the change observed with CP conditioning. However, in the

ACL group, there was no significant relationship between the change in H reflex amplitude due to typing and the change due to CP conditioning. Furthermore, responses to the typing task were varied, with some individuals demonstrating H reflex facilitation and some demonstrating H reflex inhibition. This suggests that unlike rhythmic arm cycling, an upper extremity task involving fine motor movement and sustained mental focus may modulate reflex amplitude via a more complex pathway.

One limitation to our approach is that the task we selected required both fine motor control and sustained mental focus. Thus, we cannot determine whether it was the cognitive load or the motor control required of typing that resulted in significant soleus H reflex depression. A second limitation was that the resting H reflex recruitment curves were always elicited prior to the typing task recruitment curves. Despite these limitation, the results open the door to the possibility that upper extremity fine motor movements not associated with locomotion also modulate lower extremity motoneuron excitability. In the context of sport and ACL injury, athletes attending to multiple inputs during a practice or game may compromise spinal-level control of lower extremity musculature, which may increase the likelihood of motor control error and injury.

Conclusion

In both healthy women and those with prior ACL rupture and repair, an upper extremity, fine motor typing task resulted in attenuation of the H reflex. The linear ascending slope of the recruitment curve was attenuated by the typing task in all three limbs tested: the Control group-dominant limb, and the uninvolved and involved limbs in the ACL group. The Hmax:Mmax ratio was only attenuated in the Control and ACL-uninvolved limbs, suggesting that the Hmax:Mmax ratio may not be an adequate measure to determine changes in spinal excitability. The pathway by which H reflex amplitude is modulated by a typing task is likely complex. It is conceivable that athletes attending to multiple sensory inputs may experience changes to spinal-level control of the lower extremity, which may increase the risk of noncontact ACL injury.

Tables and Figures

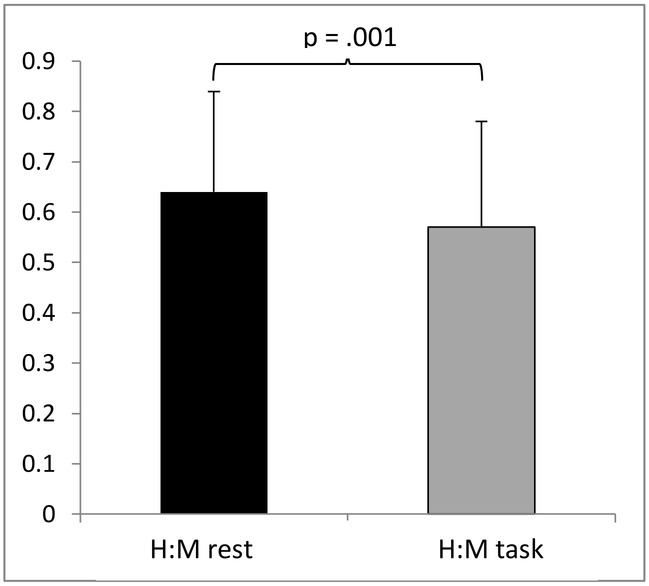

Fig. 4.1. **Main effect of Task on H:M.** There was a significant main effect of Task on Hmax:Mmax ratio on both CON-D and ACL-UN. Because there was no main effect of Group or Task*Group interaction, both limbs (CON-D and ACL-UN) are pooled.

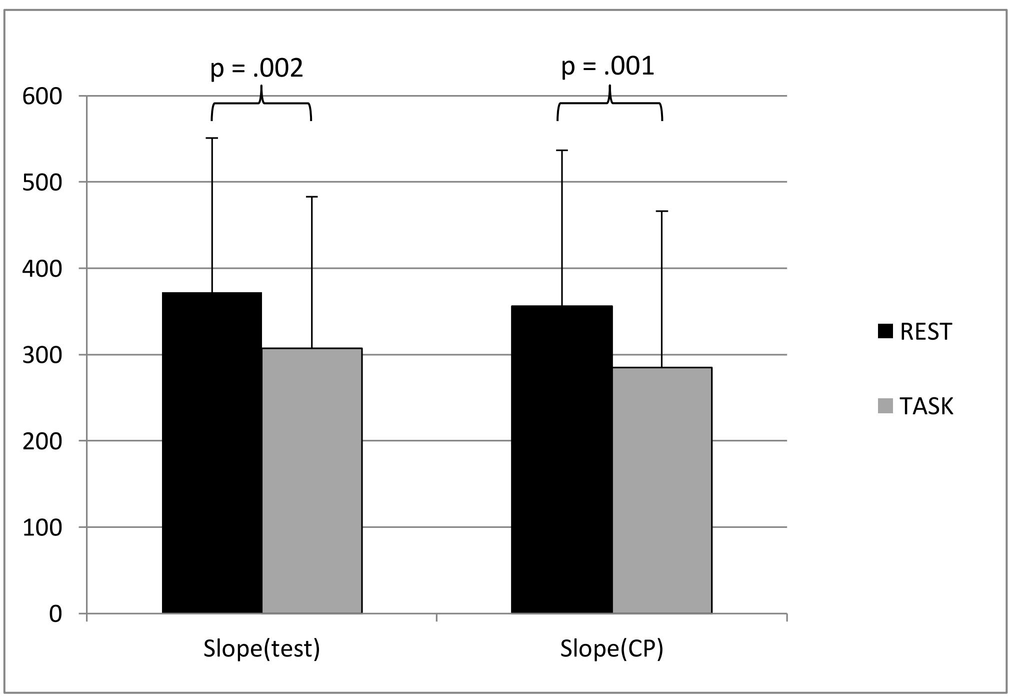

Fig. 4.2. **Main effect of Task on Slope$_{test}$ and Slope$_{CP}$.** Data for CON-D and ACL-UN are pooled. There were no significant main effects of Group or Task*Group interactions for either Slope(test) or Slope(CP).

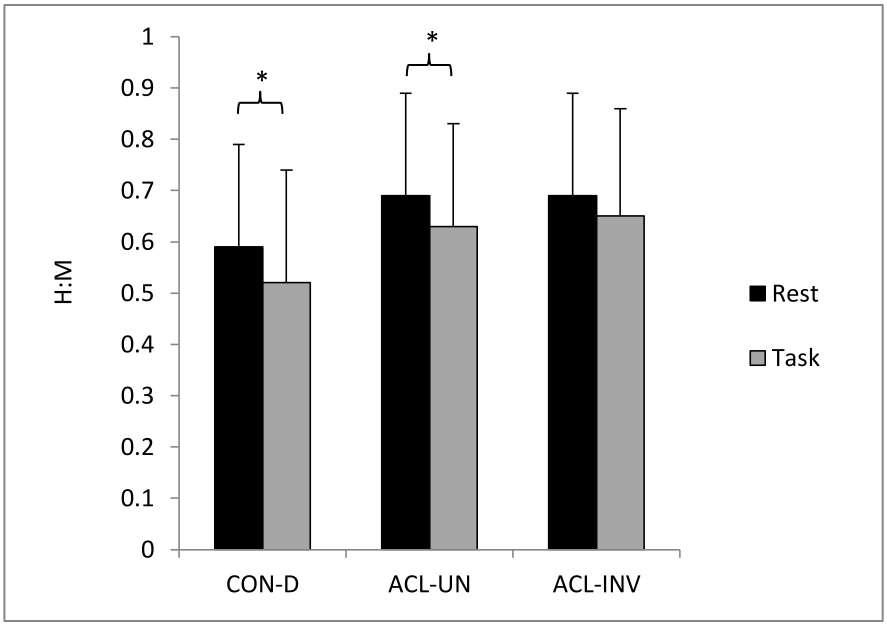

Fig. 4.3. **H:M in CON-D, ACL-UN, and ACL-INV at rest and during the typing task.** Hmax:Mmax ratio was significantly reduced in the Control-dominant and ACL-uninvolved limbs ($p<.05$), but not in the ACL-involved limb.

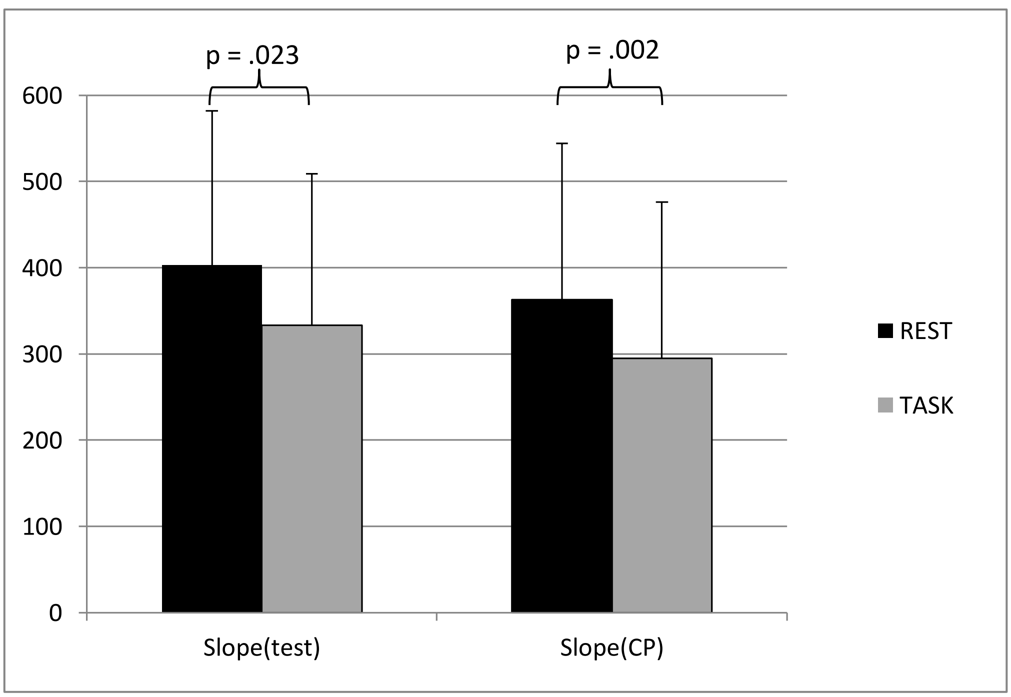

Fig. 4.4. **Main effect of Task on $\mathbf{Slope_{test}}$ and $\mathbf{Slope_{CP}}$.** Because there was no main effect of Leg or Task*Leg interaction, data for ACL-UN and ACL-INV are pooled.

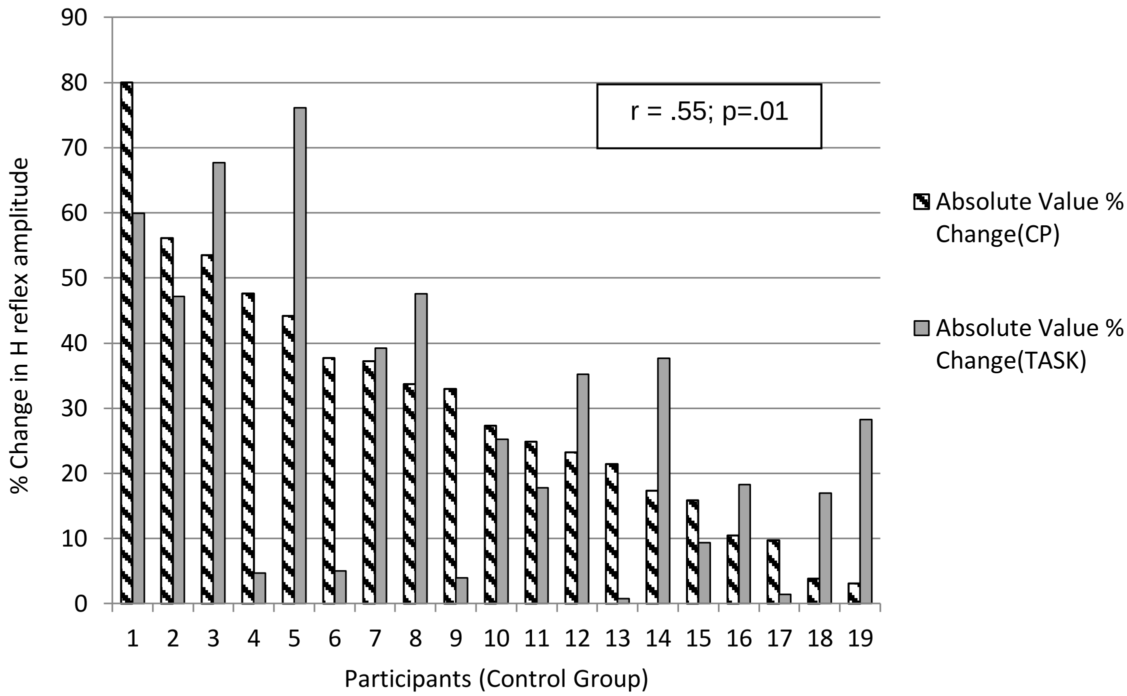

Fig. 4.5. **Absolute value of %Change$_{CP}$ and %Change$_{TASK}$ in Control group.**

Table 4.1. Mean ± SD for each limb tested (ACL-UN, ACL-INV, CON-D) during Rest and Task conditions.

	REST (Mean ± SD)			TASK (Mean ± SD)		
Measure	ACL-UN	ACL-INV	CON-D	ACL-UN	ACL-INV	CON-D
H:M*	.69 ± .20	.70 ± .19	.59 ± .20	.63 ± .20	.66 ± .22	.52 ± .22
$Slope_{test}$*	381 ± 169	426 ± 225	363 ± 192	317 ± 192	349 ± 205	298 ± 176
$Slope_{CP}$*	360 ± 165	365 ± 238	352 ± 190	260 ± 165	330 ± 217	310 ± 196

*denotes significant main effect of TASK (p<.05)

Table 4.2. Results of t-tests comparing % $Change_{task}$ for CON-D, ACL-UN, and ACL-INV limbs

	% Change(task) Mean ± SD			t-test p values	
	CON-D	ACL-UN	ACL-INV	ACL-UN vs. ACL-INV	ACL-UN vs. CON-D
Raw % change	1.5 ± 37.4	1.3 ± 45.0	15.0 ± 58.6	.34	.99
Abs. val. % change	28.6 ± 23.2	36.6 ± 24.7	45.1 ± 38.9	.42	.32

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Chapter 5: Effect of menstrual status on soleus Hoffmann reflex modulation

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ABSTRACT

Menstrual cycle phase alters several sensorimotor reflex pathways, but the impact of cycle phase on Hoffmann (H) reflex characteristics, specifically on presynaptic inhibition (PI), is not clear. **PURPOSE**: to investigate whether PI is affected by menstrual cycle phase. **METHODS:** Eight healthy females (mean ± SD age: 24.0 ± 4.8 years; BMI: 22.0 ± 2.1 kg·m^{-2}) consisting of subgroup of individuals who formed a larger cohort volunteered for the study. Participants were recreationally active and had no history of neurological disorder or recent injury to the lower extremity. Participants experienced regular monthly menstrual cycles and were not using any form of contraceptive that would preclude ovulation. Testing occurred during menses (follicular phase) and after ovulation (early luteal phase). Unconditioned and CP-conditioned H reflex recruitment curves were elicited at each testing session. Dependent variables were Hmax:Mmax ratio (H:M), the linear ascending portion of the recruitment curve slope, with and without CP conditioning ($Slope_{test}$ and $Slope_{CP}$), and presynaptic inhibition due to CP conditioning ($\%PI_{CP}$). **RESULTS:** Paired-samples t-tests revealed no significant difference in H:M (.58 ± .23 vs. .55 ± .20; p = .52), $Slope_{test}$ (366 ± 181 vs. 365 ± 227; p = .99) or $Slope_{CP}$ (360 ± 200 vs. 375 ± 237; p = .84), between the follicular and early luteal assessments, respectively. In contrast, $\%PI_{CP}$ was significantly different between the two cycle phases (17.6% ± 41.9% vs. -2.4% ± 34.6%; p = .011), suggesting an increase in presynaptic inhibition during the early luteal phase. **CONCLUSION:** While Hmax:Mmax ratio and Slope remained unchanged, presynaptic inhibition was significantly higher during the early luteal phase compared to the follicular phase. This suggests that spinal reflexes are

modifiable throughout the menstrual cycle. This may be due to changes in circulating hormone concentrations, specifically interactions between progesterone and the neurotransmitter GABA, which modulates presynaptic inhibition.

Introduction

The human menstrual cycle is characterized by rapid changes in steroid hormone levels, most notably estrogen and progesterone, and has been associated with changes in measures of both cognitive and physical performance. Cognitively, deficits in concentration (18), a decrease in energy (5), and reduced creativity (15) have been reported to occur as menses approach. Physically, one of the most striking findings has been that the incidence of ACL injury is higher during the first half of the menstrual cycle (2, 9, 20). Despite the cyclical fluctuation in injury rates, studies examining knee joint biomechanics suggest no significant differences exist across the menstrual cycle in multiple measures including knee kinematics and kinetics, anterior tibial shear force or quadriceps-to-hamstrings strength ratios (1, 4). Dynamic postural control during sport, however, relies on both cortical and reflex control of lower extremity musculature (24). Menstrual cycle phase has been reported to alter several sensorimotor reflex pathways, including the nociceptive flexion reflex (26) and the acoustic startle reflex (25). This suggests that spinal control mechanisms can be altered by cyclical hormone fluctuations. Therefore, investigating changes in spinal control of the lower extremity may provide critical information to bridge the gap between monosynaptic reflex activity and complex, cortically-influenced control during dynamic movements, and may provide useful information about the role of the menstrual cycle in noncontact ACL injury.

The Hoffmann (H) reflex is a monosynaptic reflex commonly used to evaluate motoneuron excitability under a given set of postural, task, and environmental conditions. The influence of menstrual cycle phase on H reflexes is uncertain. Hoffman et al. (10) compared soleus Hmax:Mmax ratio to estrogen and progesterone concentrations across the menstrual cycle and found no relationship between estrogen and progesterone fluctuations and Hmax:Mmax ratio, suggesting that the connectivity between afferent input and efferent output at the spinal synapse was not influenced by hormonal fluctuations associated with the menstrual cycle. However, while the H reflex is described as monosynaptic, in reality its amplitude is influenced by the actions of inhibitory interneurons that regulate activity at the level of the synapse in the spinal cord. This is known as presynaptic inhibition (PI). The amount of PI is consistently regulated to match an individual's environmental demands. Postural anxiety (e.g., standing on a high platform, eliminating visual input, standing on an unstable surface or a narrow beam) increases PI, reducing the magnitude of the H reflex (12, 14, 17, 23). Conversely, spinal excitability can also be increased: for example, when individuals imagine or see others performing a motor task, H reflexes are facilitated (3, 6, 19, 21). In the context of ACL injury, PI is important because it regulates the magnitude of the efferent (motor) response to a given afferent input. Cyclical changes in PI may result in improperly-scaled motor responses to changes in an individual's environmental context. Thus, the purpose of this study was to investigate whether PI is affected by menstrual cycle phase.

Materials and Methods

Subjects

Eight healthy females (mean ± SD age: 24.0 ± 4.8 years; BMI: 22.0 ± 2.1 kg·m^{-2}) volunteered for this study. This group of participants was a subgroup of individuals who formed a larger cohort that was studied only during the initial portion (follicular phase) of the menstrual cycle., and who agreed to be tested a second time following a positive ovulation test. All participants gave written informed consent and the study was approved by the university's institutional review board. Participants were recreationally active and had no history of neurological disorder or recent (≤ 6 months) injury to the lower extremity, wrist, or hand. In addition, participants experienced regular monthly menstrual cycles (defined as menstrual cycles that occurred monthly at regular, predictable intervals) and had not used any form of contraceptive that would preclude ovulation in the past six months. In order to determine whether menstrual cycle phase affected PI, all participants were tested on two occasions. The first test occurred between days 2 and 5 of their menstrual cycle (follicular phase). The second test occurred 24-96 hours following the luteinizing hormone (LH) surge, as detected by a commercially-available testing kit (early luteal phase). Functional leg dominance was assessed using 3 functional tests: the ball kick test, the step-up test, and the balance recovery test. Details of these procedures have been described by Hoffman et al. elsewhere (11). The leg used to perform at least 2 of the 3 tests was determined to be functionally dominant, and was selected for testing.

H reflex testing

Two unshielded 12mm stimulating electrodes were attached in positions to stimulate the tibial nerve (popliteal fossa) and the common peroneal (CP) nerve (posterior to the fibular head). Two dispersal pads (anodes) were attached: one on the anterior thigh proximal to the patella, and one on the lateral aspect of the lower leg approximately 10cm distal to the stimulating electrode to the common peroneal nerve. Lubricated bipolar Ag/AgCl surface electromyography (sEMG) electrodes were placed over the muscle belly of the soleus as well as the lateral malleolus. An electrical stimulator (Model S88, Grass Instruments, Inc., Warwick, RI), connected to a stimulus isolation unit and constant current unit, was used to deliver the stimulus to elicit the H reflex. H reflex peak-to-peak amplitude was measured via sEMG at 2000Hz (MP100 Data Acquisition System and Acknowledge software v.3.9.1, Biopac systems, Inc., Goleta, CA).

With electrodes in place, the participant was positioned in a reclining chair with the torso angled at approximately 110^{o} relative to the thigh, with the knee positioned in approximately 10^{o} of flexion and the lower leg supported on a padded ottoman. Square pulse stimulations (1 ms) were delivered approximately every 15-20 seconds, increasing in 0.01V increments until the peak-to-peak H reflex amplitude reached a plateau (Hmax). Maximal motor response (Mmax) was also determined. At each stimulus intensity, both an unconditioned (or “test”) and a conditioned stimulus were delivered. The conditioned stimulus was accomplished by prior (80ms) stimulation of the common peroneal (CP) nerve. In this manner, two recruitment curves were collected simultaneously for each limb: one unconditioned or “test” recruitment curve, as well as a second recruitment curve where soleus H reflexes were conditioned with prior CP nerve stimulation ("CP recruitment curve"). Stimulation intensity was set at the motor threshold for the tibialis anterior (TA), defined as the smallest stimulation that would result in a palpable contraction of the (TA). Both the latency (80ms) and stimulation intensity have been previously reported to increase presynaptic inhibition (PI) to the soleus motoneurons (13, 27).

Recruitment curves were normalized to facilitate comparisons between individuals. H reflex peak-to-peak amplitude was plotted on the y axis, with all measured H reflexes expressed as a percentage of the amplitude of the maximal M wave (Mmax). Stimulus intensity was plotted on the x axis and was normalized to the stimulus intensity required to elicit a direct motor response (i.e., M threshold), in the manner described by Funase et al (7).

Variables

The independent variable was cycle phase (Follicular vs. Early luteal). There were four dependent variables to characterize the H reflex response. The first was the ratio of the maximal unconditioned H reflex to the maximal motor response, or the Hmax:Mmax ratio (H:M). The second and third dependent variables were the linear ascending slopes of the Test and CP recruitment curves ($Slope_{test}$ and $Slope_{CP}$). The fourth dependent variable was presynaptic inhibition due to CP conditioning ($\%PI_{CP}$). All dependent variables are described in detail in the following paragraphs.

Hmax:Mmax ratio (H:M): The maximal H reflex, expressed relative to Mmax, is representative of the proportion of the motor unit pool able to be activated via an afferent reflex loop. In this sense, the Hmax:Mmax ratio describes the relative "connectivity" of afferent and efferent nerves at the spinal synapse.

Slope ($Slope_{test}$ and $Slope_{CP}$): Between the toe and plateau regions of the H reflex recruitment curve, the ascending slope of the recruitment curve is approximately linear. The linear ascending portion of the recruitment curve was visually determined and its slope was obtained using least squares regression. Assessing H slope may be a more robust indicator of motoneuron excitability than Hmax:Mmax ratio because the slope includes lower and higher-threshold MNs that represent different segments of the motoneuron pool. The steepness of the slope is representative of "reflex gain", as it represents the change in motoneuron recruitment as a function of increased Ia (afferent) stimulation (8).

Inhibition ($\%PI_{CP}$): The percent change in H reflex amplitude due to CP nerve stimulation was calculated at individual stimulus intensities by dividing the change in H reflex amplitude by its original, unconditioned amplitude and expressing the result as a percentage [$\%\ Change_{CP} = \{(H_{CP} - H_{TEST})/H_{TEST}\}*100$]. In order to minimize the volatility in H reflex amplitude often seen at the extreme low and high ends of the recruitment curve, the bottom and top 20% of evoked H reflex amplitudes were not included in this calculation. Using the percent change for each unconditioned-CP conditioned reflex pair, a mean change score was calculated. This mean change score was determined to represent percent presynaptic inhibition due to CP-conditioning (%PI). By convention, an increase in H reflex amplitude due to CP-conditioning (%PI > 0) is defined as facilitation, whereas a decrease in H amplitude (%PI < 0) represents inhibition.

Statistical Analysis: H reflex characteristics during the Follicular and Early luteal phases were compared using paired t-tests. All analyses were performed using SPSS v. 18 for Windows. For all statistical tests, level of significance was set at $\alpha = .05$.

Results

Paired-samples t-tests revealed no significant difference in Hmax:Mmax ratio (.58 ± .23 vs. .55 ± .20; p = .52), $Slope_{test}$ (366 ± 181 vs. 365 ± 227; p = .99) or $Slope_{CP}$ (360 ± 200 vs. 375 ± 237; p = .84), between the Follicular and Early luteal assessments, respectively (Table 1; Figure 1). However, presynaptic inhibition due to CP-conditioning was significantly different between the two cycle phases (17.6% ± 41.9% vs. -2.4% ± 34.6%; p = .011). All eight participants demonstrated increased inhibition during the Early luteal phase, compared to during the Follicular phase (Figure 2). The mean change in percent inhibition between the follicular and early luteal phases was 20.0 percentage points (range: 5.8 to 51.6 percentage points).

[TABLE 1 ABOUT HERE]

[FIGURE 1 ABOUT HERE]

[FIGURE 2 ABOUT HERE]

Discussion

The major finding of this study was that while Hmax:Mmax ratio and H Slope remained unchanged across both menstrual cycle phases, presynaptic inhibition due to CP conditioning is greater during the Early luteal phase than during the Follicular phase. This novel finding suggests that the technique used to measure the percent change in H reflex amplitude due to CP conditioning may be a more precise indicator than H slope or Hmax:Mmax ratio to determine changes to spinal control that occur across the menstrual cycle.

The finding that Hmax:Mmax ratio was not different across the menstrual cycle phases supports previous work by Hoffman et al., who reported that Hmax:Mmax was not related to estrogen and progesterone fluctuations across the menstrual cycle (10). The use of the Hmax:Mmax ratio as a measure of motoneuron excitability is commonplace, but also has some limitations. The Hmax:Mmax ratio is a measure of maximal motoneuron excitability and therefore provides information about a single point along the recruitment curve. In order to improve upon the evaluation of the entire H reflex recruitment curve, we examined two additional H reflex parameters: the slope of the ascending linear portion of the H reflex recruitment curve, and the percent presynaptic inhibition due to CP nerve stimulation. The ascending slope of the H reflex recruitment curve essentially reflects the size principle of motor unit recruitment, and therefore provides information about the excitability of both the smaller motoneurons that are recruited early, as well as the larger motoneurons that are recruited by larger stimuli. Despite the potential of this measure to elucidate differences across the motoneuron pool, the results of our study revealed that both the Test and CP-conditioned slopes showed no difference across cycle phases.

Our most notable finding was a significant increase in presynaptic inhibition during the Early Luteal phase in all eight participants. While there is considerable inter-individual variability, the Follicular phase is characterized by very low concentrations of estrogen and progesterone, while the Early luteal phase is characterized by higher concentrations of both hormones (22). Presynaptic inhibition is largely regulated by the neurotransmitter gamma-aminobutyric acid (GABA). Certain metabolites of progesterone interact with GABA-A receptors, thereby increasing presynaptic inhibition by reducing neurotransmitter release at the synaptic terminal (16). Thus, the increased inhibition observed during the Early luteal phase is consistent with this interaction between progesterone and GABA, as progesterone concentrations at this point in the cycle are elevated compared to the follicular phase.

Our finding that CP nerve-induced inhibition is increased during the Early luteal phase suggests that our method for calculating percent inhibition may be a useful measure to detect intra-cycle differences in spinal control of the lower extremity. One of the advantages of this measurement technique is that it compares the amplitude of the elicited reflex across a range of stimulus intensities. Instead of measuring the change in H reflex amplitude at a predetermined percentage of Hmax, we compared the change in H reflex amplitude for all H reflex pairs where the unconditioned H reflex amplitude fell between 20 and 80% of Hmax, therefore representing a large proportion of the motoneuron pool. In this manner, a more global sense of presynaptic inhibition across the motoneuron pool can be obtained.

In conclusion, common measures of H reflex plasticity such as Hmax:Mmax ratio and H slope may not be well-suited to detect differences in spinal control across the menstrual cycle. By examining changes in the magnitude of PI between cycle phases, we were able to demonstrate significant differences in spinal reflex modulation between the Follicular and Early luteal phases. The reason PI may be a good measure to examine menstrual cycle differences may be due to interactions between progesterone metabolites and GABA, a primary neurotransmitter regulating presynaptic inhibition.

Tables and Figures

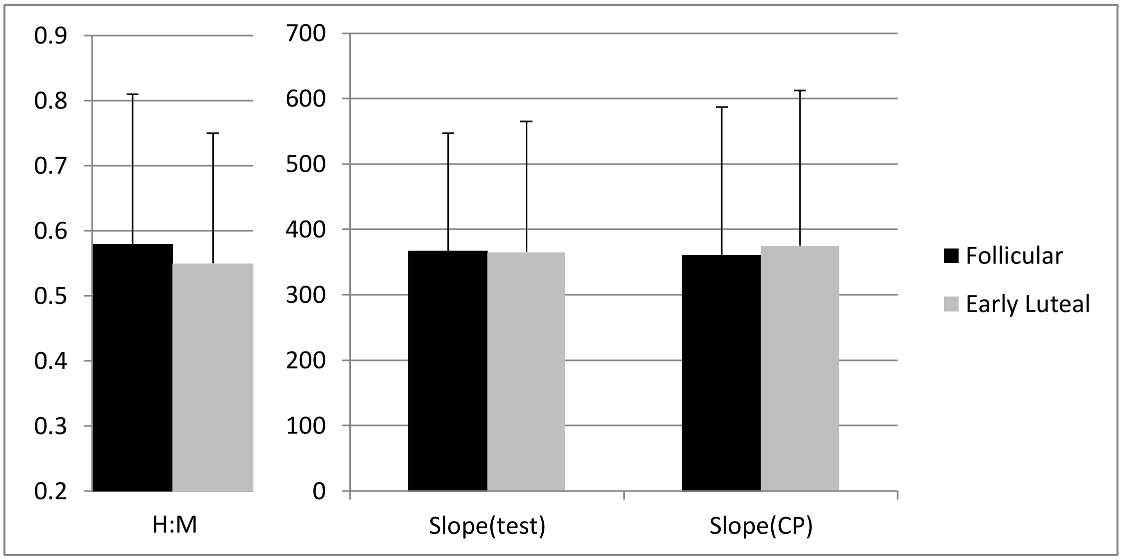

Fig. 5.1. **H:M, Slope$_{test}$, and Slope$_{CP}$ during the follicular and early luteal phases**. There were no significant differences across the menstrual cycle for any of these parameters.

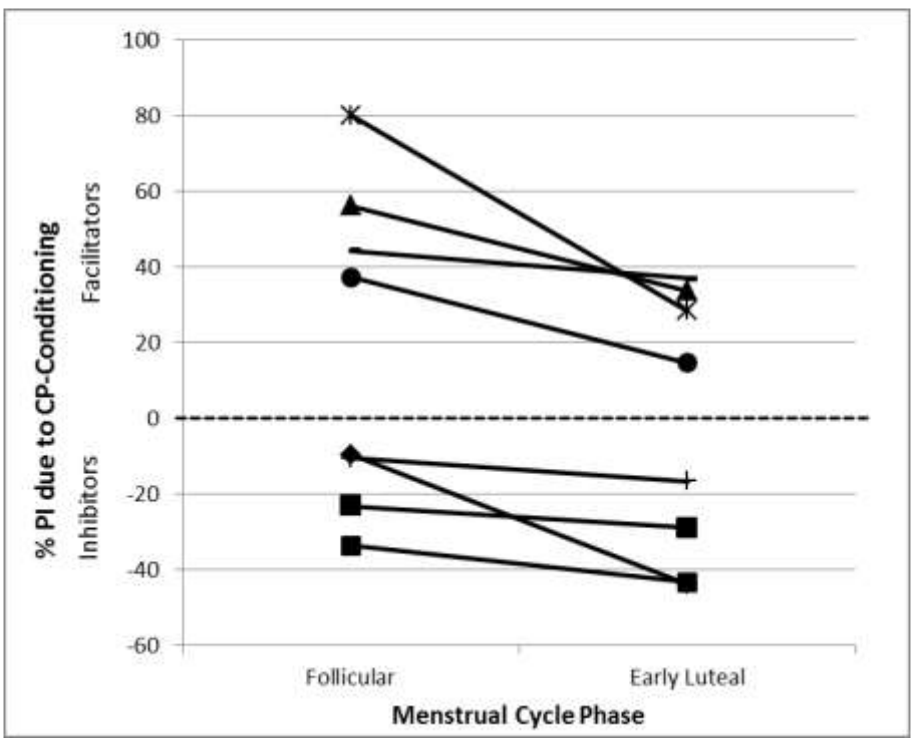

Fig. 5.2. **% PI during the follicular and early luteal phases.** Regardless of whether the participant was classified as a Facilitator or an Inhibitor, greater inhibition was present at ovulation (early luteal phase) compared to menses (follicular phase).

Table 5.1. Paired-samples t-tests comparing H reflex measures during the Follicular and Early Luteal phases

	Menstrual Phase (Mean ± SD)		
Measure	Follicular	Early Luteal	t-test p value
H:M	.58 ± .23	.55 ± .20	.52
$Slope_{test}$	366 ± 181	365 ± 227	.99
$Slope_{CP}$	360 ± 200	375 ± 237	.84
$\%PI_{CP}$	17.6% ± 41.9%	-2.4% ± 34.6%	.011

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Chapter 6: Conclusion

Female athletes experience a greater rate of noncontact ACL ruptures than their male counterparts, particularly in sports such as basketball and soccer. Among the multiple risk factors for ACL rupture that predispose women to greater injury rates, females demonstrate differences in neuromuscular activation patterns as well as differences in incidence of injury across the menstrual cycle. Moreover, as athletes attend to multiple sensory inputs, studies have shown that performance in sport-specific skill and postural control decline, suggesting that neuromuscular control of the lower extremity can be influenced by menstrual cycle phase as well as by the incorporation of a secondary task.

The broad purpose of this project was to explore neuromuscular differences in the ways healthy and ACL-injured women respond to a secondary task requiring fine motor control and sustained mental focus. Using Hoffmann (H) reflex testing to explore spinal-level control mechanisms of the soleus muscle, we investigated differences between healthy and ACL-injured females, as well as differences between the involved and uninvolved limbs in the ACL-injured group. Our project resulted in three broad research aims. Our first aim was to determine whether ACL-injured individuals demonstrated similar reflex profiles to healthy individuals with no knee injury, as well as to determine whether the ACL-involved limb was similar to its uninvolved counterpart. Our second aim was to determine whether the typing task resulted in attenuated H reflex amplitudes, and to investigate whether any observed changes were similar in healthy and ACL-injured groups. Finally, our third aim was to utilize more complex H reflex analysis techniques to determine whether differences in spinal excitability existed at different points in the menstrual cycle.

The results of our study revealed some important findings, summarized in the following paragraphs.

Our first aim was to compare resting H reflex profiles between the ACL-involved and ACL-uninvolved limbs, and compared to a healthy control group. The reason we chose to investigate these relationships is because very little is known about H reflexes in an ACL injured population. When comparing H reflex profiles at rest, there is generally similarity between the uninvolved and involved limbs of females with unilateral noncontact ACL rupture, as well as compared with a healthy control group. The most interesting finding was that when the test reflex was conditioned by common peroneal (CP) stimulation, the ACL-involved limb displays less reflex plasticity than either the uninvolved or healthy control limbs. In the context of ACL injury prevention, this finding is important because it implies that control of the ACL-involved leg is less modifiable in response to the environmental context. This may predispose this limb to further injury.

Our second aim was to determine whether the incorporation of a secondary typing task resulted in differential H reflex modulation in ACL-injured women and healthy controls. The rationale for this comparison was that differences in skill performance and postural control have been reported in well-trained athletes when a dual-task scenario is presented. The incorporation of a typing task requiring fine motor control of the upper extremity as well as sustained mental focus resulted in H reflex attenuation in both groups. This suggests that when attention is diverted to another task, spinal control of the lower extremity is altered. In evaluating several parameters of the H reflex, the linear ascending slope of the recruitment curve is a more robust assessment tool than Hmax:Mmax ratio, as it allows for assessment of changes in the sensory-input-to-motor-output relationship across a wide swatch of motor units, from small to large. This finding has important implications for athletes that must attend to multiple sensory inputs during game play.

Finally, our third objective was to determine whether H reflex parameters were influenced by menstrual cycle phase. We chose to pursue this question because other reflex pathways had previously been shown to be influenced by menstrual cycle phase, and because the incidence of ACL injury is not evenly distributed across the cycle. While assessing menstrual cycle fluctuations in H reflex parameters was not our primary objective, we had a subgroup of participants (n=8) who agreed to be re-tested following a positive ovulation test. This resulted in the ability to compare H reflex profiles from the Follicular (menses) and Early Luteal phases. The results revealed that presynaptic inhibition increases during the Early Luteal phase, and suggests that spinal reflexes are subject to modification by fluctuations in circulating hormone concentrations.

Overall, the results of our work are important because they establish that lower extremity spinal reflexes can be modulated by a non-locomotor task involving mental focus and fine motor control. In the context of sport, this finding is significant in that it implies that lower extremity neuromuscular control can be influenced by situations involving attention to multiple tasks. Future research should investigate spinal reflex modulation during sport-specific motor and attention-related tasks, as well as determine how dual task environments affect known neuromuscular risk parameters for ACL injury.

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Appendices

Appendix A – Institutional Review Board Documents

Institutional Review Board • Office of Research Integrity
B308 Kerr Administration Building, Corvallis, Oregon 97331-2140
Tel 541-737-8008 | Fax 541-737-3093 | IRB@oregonstate.edu
http://oregonstate.edu/research/ori/humansubjects.htm

INITIAL APPLICATION
Study Number: Assigned by Office

Study Title:	Effects of ACL Injury Status and Task Orientation on Spinal Reflex Modulation		
Principal Investigator:	Mark Hoffman		
email address:	mark.hoffman@oregonstate.edu	Telephone:	541-737-6787
College, Center, or Institute:	Health Human Sciences		
If "other", indicate college:			
Department:	Nutrition Exercise Sciences		
If "other", indicate department:			

Please email the completed application and all relevant attachments to IRB@oregonstate.edu

- File names for all attachments should include the last name of the Principal Investigator, document title, and version date. For example: Smith_Protocol_10272009.doc
- All attachments should include the last name of the Principal Investigator, document title, version date, and page number.
- Signature page must be mailed, faxed, or scanned and emailed to the IRB.

1. **In one paragraph or less, state your primary research question:** Little or no work has been done to investigate the specific mechanisms utilized by individuals to control the muscles when performing secondary tasks. This is especially of concern in individuals with prior ACL injury, where motor control during a secondary task may help explain some factors lead to injury. The purpose of this study is to investigate how prior ACL injury and task orientation affect spinal reflex modulation.

2. **Anticipated Level of Review**
See Review Level Determination form at http://oregonstate.edu/research/ori/forms/IRBreview.doc

☐ Exempt

☐ Expedited

☒ Full Board

3. **Sources of Support for this project (pending or awarded)**

☐ Internal Funding Source: _____
☐ External Funding Source: _____
☐ Source of material, equipment, drugs, supplements, or devices: _____
☒ None of the above

If funded, submit a copy of the grant or contract. If award is pending, submit as a project revision if and when funding or material is awarded.

4. **Ethics and Compliance Training**

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INITIAL APPLICATION
Study Number: Assigned by Office

All study team members involved in this project must receive training in the ethical use of human participants in research. Please refer to the Education Requirement Policy at: http://oregonstate.edu/research/ori/humansubjects.htm

Study Team Member(s)	Role in Project	email Address	Ethics Training Completed
Mark Hoffman	Principal Investigator	mark.hoffman@oregonstate.edu	☒ Yes ☐ No
Erica Perrier	Student Researcher	perriere@onid.orst.edu	☒ Yes ☐ No
Jeffrey Doeringer	Student Researcher	doerinje@onid.orst.edu	☒ Yes ☐ No
	Student Researcher		☐ Yes ☐ No
	Student Researcher		☐ Yes ☐ No
	Student Researcher		☐ Yes ☐ No
	Student Researcher		☐ Yes ☐ No
	Student Researcher		☐ Yes ☐ No

5. **Risk/Benefit Assessment for adults and/or children**
Minimal risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Adults	Children
☒ Minimal risk	☐ Minimal risk
☐ Greater than minimal risk	☐ Greater than minimal risk, but holds prospect of direct benefit to subjects
	☐ Greater than minimal risk; no prospect of direct benefit to subjects but likely to yield generalizable knowledge about the subject's disorder or condition
	☐ Research not otherwise approvable but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of the subjects

6. **Subject Population**

Total number (not a range) of subjects that will be enrolled over the life of the study: 60

Participant age range (check all that apply):

☐ 0-7: include parental consent form, unless seeking waiver

☐ 8-17: include assent form and parental consent, unless seeking waiver

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INITIAL APPLICATION
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☒ ≥18: include consent document or oral consent guide, unless seeking waiver of consent

Populations who may enroll in this research, even if they are not the target population (check all that apply):

☐ Adults lacking capacity to consent
☐ Pregnant women and fetuses
☐ Children in foster care or wards of the state
☒ OSU Students or employees
☐ Prisoners *(ineligible for exempt review)*

☐ Non-English speakers: If non-English speakers will be enrolled, provide details below regarding qualifications of the translator(s) and of the research staff or student(s) obtaining consent in a language other than English: ______

7. **If the research involves any of the following, check the appropriate box**

☐	Study of existing data	*Data must be "on the shelf" prior to conception of current study in order to be considered existing*
☐	Audio or video recording	*Consent document must indicate whether recording is optional or a required study activity. If optional, include an opt-in/opt-out section for subjects to initial*
☐	Deception	*Requires full board review*
☐	Radiation	*Complete attachment A. IRB will forward submission to Radiation Safety*
☐	Human biological materials	*Complete attachment B. IRB will forward submission to Biosafety*
☐	Microorganisms or Recombinant DNA	*IRB will forward submission to Biosafety*
☐	Sending or receiving biological materials	*Contact Technology Transfer regarding the potential need for a Material Transfer Agreement (541)737-4437*
☐	Using Chemical Carcinogens	*List of applicable chemicals: http://oregonstate.edu/ehs/carclist IRB will forward to Chemical Safety*
☐	Waiver of documentation (signature) of informed consent	*Include justification in protocol. See IRB website for INSTRUCTIONS FOR ORAL OF ALTERNATIVE CONSENT PROCESS*
☐	Waiver of informed consent	*Include justification in protocol*
☐	Translated documents	*Include material in English and translated into a language spoken by participants*

8. Research and/or recruitment sites

☐ If multi-center study, list all participating academic institution(s): ______
Submit IRB approvals from other sites
☐ Attached
☐ Pending

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☐ List all sites of research and/or recruitment. For example, schools, medical centers, tribal reservations, international sites, listservs, Registrars, etc.

Name(s) of other research site(s): ______
Provide letter(s) of support from appropriate authority at each site

Name(s) of other recruitment site(s): ______
If recruitment method involves more than an advertisement (newspaper classified, flier, listserv email), provide letter(s) of support from appropriate authority

9. **Attachments** *(check all that apply)*:

☒ Protocol (required)
☒ Consent Document(s)
☐ Assent Document(s)
☐ Attachment A: Radiation
☐ Attachment B: Human Materials
☐ Grant application or funding contract
☒ Recruiting tools (e.g., ad copy, flyers, letters)
☐ Test instruments (e.g., questionnaires, surveys)
☐ Material(s) in other languages
☐ External IRB Approvals
☐ Letters of support from external research sites
☐ Other: ______

10. **Will the study need to be registered with ClinicalTrials.gov?**

☐ **Yes** Applicable* Clinical Trials:

Trials of Drugs and Biologics: Controlled clinical investigations of a product subject to FDA regulation, other than Phase I investigations
Trials of Devices: Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies and pediatric postmarket surveillance
**NIH encourages registration of ALL trials whether required under the law or not.*
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html

☒ **No**

11. **Conflict of Interest:**

Federal Guidelines require assurances that there are no conflicts of interest in research projects that could affect the welfare of human subjects. If this study presents a potential conflict of interest, additional information will need to be provided to the IRB.

Examples of potential conflicts of interest in research involving human subjects may include, but are not limited to:

- A researcher or family member participates in research on a technology, process or product owned by a business in which the faculty member holds a financial interest.
- A researcher participates in research on a technology, process or product developed by that researcher.

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- A researcher or family member has a financial or other business interest in an entity which is supplying funding, materials, products, or equipment for the current research project.
- A researcher or family member serves on the Board of Directors of a business which is supplying funding, materials, products, or equipment for the current research project.
- A researcher receives consulting income from an entity that is funding the current research project.

Does any member of the study team, or any of their family members, have a financial or other business interest in the source(s) of funding, materials, or equipment related to this research study?

☒ No
☐ Yes – Please describe: ______

By signing below, I certify that the information contained in this application is accurate and complete. I understand that research involving human participants, including recruitment, may not begin until full approval has been granted by the IRB.

Name of Principal Investigator: ______________________________

Signature______________________________ Date______________
Principal Investigator

The signature page must be received by the IRB before review of the application will begin.

The signature page may be:

- **sent via mail to B308 Kerr**
- **faxed to the IRB at (541) 737-3093 or,**
- **scanned and sent via email**

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B308 Kerr Administration Building, Corvallis, Oregon 97331-2140
Tel 541-737-8008 | Fax 541-737-3093 | IRB@oregonstate.edu
http://oregonstate.edu/research/ori/humansubjects.htm

NOTIFICATION OF APPROVAL

March 23, 2010

Principal Investigator:	Mark Hoffman	Department:	Nutrition Exercise Sciences
Study Team Members:			
Student Researcher:	Erica Perrier, Jeffrey Doeringer		
Study Number:	4556		
Study Title:	Effects of ACL Injury Status and Task Orientation on Spinal Reflex Modulation		
Funding Source:	None		
Submission Type:	Initial Application received 02/17/2010		
Review Category:	Full Board	Category Number:	N/A
Waiver(s):	None	Number of Participants:	60
Risk level for children[1]:	N/A		

The above referenced study was reviewed and approved by the OSU Institutional Review Board (IRB).

Approval Date: 03/23/2010
Expiration Date: 03/22/2011

Annual continuing review applications are due at least 30 days prior to expiration date

Documents included in IRB approval:

- ☒ Protocol
- ☒ Consent forms
- ☐ Assent forms
- ☐ Grant/contract
- ☒ Recruiting tools
- ☐ Test instruments
- ☐ Attachment A: Radiation
- ☐ Letters of support
- ☐ External IRB approvals
- ☐ Translated documents
- ☐ Attachment B: Human materials
- ☐ Other:

☐ Project revisions:

Principal Investigator responsibilities for fulfilling the requirements of approval:

- All study team members should be kept informed of the status of the research.
- Any changes to the research must be submitted to the IRB for review and approval prior to the activation of the changes.
- Reports of unanticipated problems involving risks to participants or others must be submitted to the IRB within three calendar days.
- Only consent forms with a valid approval stamp may be presented to participants.
- Submit a continuing review application or final report to the IRB for review at least four weeks prior to the expiration date. Failure to submit a continuing review application prior to the expiration date will result in termination of the research, discontinuation of enrolled participants, and the submission of a new application to the IRB.

If you have any questions, please contact the IRB Office at IRB@oregonstate.edu or by phone at (541) 737-8008.

[1] Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by §§46.406 and 46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

IRB Form v. 01/08/2010

Department of Nutrition and Exercise Sciences
Oregon State University, 101 Milam Hall, Corvallis, Oregon 97331
Tel 541-737-2643 | **Fax** 541-737-2788

INFORMED CONSENT FORM

Project Title:	Effects of ACL Injury Status and Task Orientation on Spinal Reflex Modulation
Principal Investigator:	Mark Hoffman, PhD, ATC, Department of Nutrition and Exercise Sciences
Student Researcher:	Erica Perrier and Jeffrey Doeringer, Department of Nutrition and Exercise Sciences
Co-Investigator(s):	n/a
Sponsor:	n/a

1. WHAT IS THE PURPOSE OF THIS FORM?

This form contains information you will need to help you decide whether to be in this study or not. Please read the form carefully and ask the study team member(s) questions about anything that is not clear.

2. WHY IS THIS STUDY BEING DONE?

The purpose of this study is to evaluate possible differences in the way reflexes are affected by a task requiring precise movements and concentration, and to determine whether people with prior anterior cruciate ligament (ACL) injury have different reflexes. To test for these differences, your reflexes will be tested while you are resting and while you are performing a typing task on a laptop computer. Understanding the ways that reflexes are affected by a person's environment, including involvement in a task that requires your attention, may help researchers understand how humans control movement during tasks that demand different degrees of force and accuracy. These results will be used for the student researcher's dissertation as well as possible presentation and publication.

This study is being conducted for a dissertation.

Up to 60 participants will be invited to take part in this study.

3. WHY AM I BEING INVITED TO TAKE PART IN THIS STUDY?

You are being invited to take part in this study because you are between the ages of 18 and 35, have: 1) no current injury or illness, 2) had no lower extremity or back injury (strain, sprain, or fracture) in the previous six months, 3) have had no wrist or hand injury in the past six months; 4) are able to type on a keyboard using all four fingers and thumb on each hand; 5) exercise at least 30 minutes/day, 3 days/week; and 6) are currently menstruating (specifically, you are in days 2 through 5 of your menstrual cycle). If you have previously torn your ACL, you are being invited to take part in this study because you meet the criteria established above, in addition to having undergone arthroscopic surgery to repair your ACL in the past 10 years, but no more recently then one year ago from today.

If you have not previously torn your ACL, and have no condition that would preclude you from ovulating (e.g. use of oral contraceptives, patch, or injection in the past 6 months, or surgery that prevents you from ovulating), you will also be invited to take part in a second testing session approximately 2 weeks after the first testing session. If you choose not to take part in the second testing session, this will not affect your eligibility for the first part of the study. The second testing session will be similar to the first. The only difference is that you need to be within 4 days after ovulation to qualify. If you do choose to take part in the second testing session, you will be provided with an ovulation predictor kit and will be asked to call the study staff once you have a positive ovulation test. We will then schedule your second testing session within 4 days of your ovulation.

4. WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

The study activities include testing that will occur in the Sports Medicine and Disabilities Research Laboratory in the Women's Building on the campus of Oregon State University. You may request to stop at any point during the study. The following is a brief description of the testing session:

- Read and sign informed consent form (~15 minutes)
- Determination of height and weight (to assist the researchers in describing the range of individuals who participated in the study) (~2 minutes)
- Determination of leg dominance (~2 minutes)
  - You will be asked to kick a ball, step up onto a step, and recover from a small push from behind to determine your dominant leg.
- Take a one-minute typing test to see your typing speed (~3 minutes)
- Electrode placement (~5 minutes):
- A total of nine electrodes will be placed on your leg. If you have previously torn your ACL, nine electrodes will be placed on each leg. Five lubricated surface electrodes will be placed of your calf and shin muscles to monitor activity in your muscle. Two stimulating electrodes that deliver a small stimulation, which has been described as feeling similar to a "carpet shock", will be placed behind your knee and on the side of your knee. Two ground electrodes will also be attached, one above the front of your kneecap and another along the side of your leg. All areas of skin where electrodes will be placed will be shaved and cleaned with alcohol prior to application of the electrodes.
- Positioning in a reclining chair for testing (~3 minutes)
- You will sit on the reclining chair with your back slightly reclined, and your feet positioned on an attached ottoman.
- Elicitation of resting spinal reflex recruitment curves (~15 minutes per leg):

In this part of the study, you will receive approximately 60 stimulations . The stimulations will vary in intensity and we will be continually be asking you how you are feeling during the study. While seated, the stimulations of varying intensity will be applied to the back of your knee. There will be 15 seconds between each shock. Approximately 30 of the stimulations will consist of a single pulse to the back of the knee. For the other 30 stimulations, you will feel one pulse on the side of your knee and one on the back of your knee. Again, the stimulations have been described as feeling similar to a "carpet shock."

- Elicitation of motor-task spinal reflex recruitment curves (~15 minutes per leg):

While in the same position, you will go through the same 60 stimulations as described above, only this time, you will be playing a typing game using a laptop computer. The typing game consists of typing three-letter imaginary words.

- Cleanup (~5 minutes):
- Electrodes will be removed and testing is completed.
- Ovulation predictor kit and instructions for use will be given to you, if you qualify and are willing to participate in a second day of testing (~5 minutes)

Study duration: If you agree to take part in this study, your involvement will last for approximately 70 minutes if you do not have a prior ACL injury, and approximately 100 minutes if you do have a prior ACL injury. If you are eligible and choose to participate in the second round of testing, your total time commitment will be approximately doubled.

Future contact: We may contact you in the future for another similar study. You may ask us to stop contacting you at any time.

Study Results: Study results will not automatically be shared with subjects. If you are interested in the results, please contact the researcher via email for a summary of results.

5. WHAT ARE THE RISKS AND POSSIBLE DISCOMFORTS OF THIS STUDY?

The possible risks and/or discomforts associated with the being in the study include:

Reflex testing, while uncomfortable for some individuals, has relatively little risk. Some participants may experience dizziness, nausea, and fainting during or following the testing. If this occurs, immediately inform the researchers and testing will stop. Oregon State University and the researchers have no plan or fund to pay for medical treatment of research related injuries. If you think that you have been injured as a result of being in this study, please contact the researcher.

Anytime you are connected to a device that is attached to electrical current, there is a minimal risk of receiving a dangerous electrical shock. In this study, there are devices used to minimize this risk. There are two devices (stimulation isolation unit and constant current unit) placed in the circuit between you and the stimulator, which greatly decrease the chances of receiving a harmful shock. This type of nerve stimulation is common and considered to be safe for human subjects. In the unlikely event you receive a harmful shock, immediate steps will be taken to help you. First, the testing will be discontinued immediately and vital signs will be evaluated. You will be monitored, and if needed, the emergency response system will be contacted immediately via phone in the lab. All investigators are trained in CPR.

Email: The security and confidentiality of information sent by email cannot be guaranteed. Information sent by email can be intercepted, corrupted, lost, destroyed, arrive late or incomplete, or contain viruses.

6. WHAT HAPPENS IF I AM INJURED?

Oregon State University has no program to pay for research-related injuries. If you think that you have been injured as a result of being in this study, please contact the researcher immediately.

7. WHAT ARE THE BENEFITS OF THIS STUDY?

This study is not designed to benefit you directly. However, we hope, that in the future, other people might benefit from this study because we will have a better understanding of how movement is controlled during different tasks, and whether people with ACL injuries control movement differently.

8. WILL I BE PAID FOR BEING IN THIS STUDY?

You will not be paid for being in this research study.

9. WHO WILL SEE THE INFORMATION I GIVE?

The information you provide during this research study will be kept confidential to the extent permitted by law. Research records will be stored securely and only researchers will have access to the records. Federal regulatory agencies and the Oregon State University Institutional Review Board (a committee that reviews and approves research studies) may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

If the results of this project are published your identity will not be made public.

To help ensure confidentiality, we will code all data forms, files, and recordings without any identifiable participant information. All forms will be locked in a filing cabinet in a secured office.

10. WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THIS STUDY?

Participation in this study is voluntary. If you decide to participate, you are free to withdraw at any time without penalty. You will not be treated differently if you decide to stop taking part in the study. If you choose to withdraw from this project before it ends, the researchers may keep information collected about you and this information may be included in study reports.

11. WHO DO I CONTACT IF I HAVE QUESTIONS?

If you have any questions about this research project, please contact: Mark Hoffman, PhD, ATC at 541-737-6787 or by email at mark.hoffman@oregonstate.edu.

If you have questions about your rights or welfare as a participant, please contact the Oregon State University Institutional Review Board (IRB) Office, at (541) 737-8008 or by email at IRB@oregonstate.edu

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

12. WHAT DOES MY SIGNATURE ON THIS CONSENT FORM MEAN?

Your signature indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Participant's ID code: ___________

Participant's Name (printed): ____

______________________________________ ____________________________
(Signature of Participant) (Date)

______________________________________ ____________________________
(Signature of Person Obtaining Consent) (Date)

Appendix B – Data

Table A1. Raw data file

ID	Age	BMI	Dom_leg	Injured_leg	Yrs_post	Group	PI_Grouping	Mmax	Hmax_control	Hmax_typing	HM_ratio_control	HM_ratio_typing	H_slope_control	H1_slope_control	H_slope_typing	H1_slope_typing
ACL_01	21	19.4	0	0	3	1	0	17.7	10.4	9.7	0.59	0.55	299	317	208	208
ACL_02	25	21.3	0	0	5	1	1	14.8	7.4	6.4	0.50	0.43	208	99	237	98
ACL_03	24	22.9	0	1	8	1	0	9.2	2.8	3.3	0.30	0.36	127	106	127	107
ACL_04	22	21.6	0	0	2	1	1	12.7	4.8	4.9	0.38	0.39	127	132	149	122
ACL_05	24	22.9	0	1	4	1	1	9.2	5.8	5.4	0.63	0.59	276	323	250	257
ACL_06	24	37.9	0	1	4	1	0	3.8	2.9	2.8	0.76	0.74	577	621	307	232
ACL_07	21	21.8	0	1	3	1	0	14.4	10.0	9.6	0.69	0.67	492	473	560	346
ACL_08	22	32.1	0	0	9	1	0	4.77	2.0	1.9	0.42	0.39	122	154	142	184
ACL_09	18	19.4	0	0	2	1	0	9.2	6.9	6.5	0.75	0.71	312	398	135	127
ACL_10	22	25.1	0	1	1	1	0	4.7	4.7	4.4	1.00	0.94	649	367	388	246
ACL_11	18	22.2	0	0	2	1	1	7.4	6.2	5.2	0.84	0.70	601	623	555	628
ACL_12	22	23.7	0	1	2	1	1	9.1	2.0	1.2	0.22	0.13	89	217	50	215
ACL_13	30	22	0	1	3	1	1	7	5.8		0.83		860	616		
ACL_14	22	26.5	0	0	3	1	0	16.4	8.9	7.6	0.54	0.46	418	381	185	149
ACL_15	35	21	0	0	7	1	0	4.7	4.7	4.3	1.00	0.91	541	565	785	589
ACL_16	30	21	0	1	9	1	1	7.7	6.7	5.8	0.87	0.75	517	421	457	350
ACL_17	23	21.5	0	1	2	1	0	16.4	8.7	7.0	0.53	0.43	280	297	151	167
ACL_18	23	24.7	0	0	4	1	1	9.9	7.0	4.4	0.71	0.44	225	194	186	144
ACL_19	20	23.7	0	0	4	1	0	12.3	8.3	7.5	0.67	0.61	514	481	505	471
ACL_20	31	25.2	0	1	9	1	0	6.5	5.8	6.4	0.89	0.98	309	320	199	175
HEALTHY_01	24	23.5	0			0	1	11.1	8.4	6.9	0.76	0.62	609	548	639	724
HEALTHY_02	25	21.3	0			0	1	7.4	6.2	5.4	0.84	0.73	437	297	342	466
HEALTHY_03	31	22.9	1			0	0	6.5	4.2	4.5	0.64	0.69	379	397	326	356
HEALTHY_04	33	25.8	0			0	0	6.9	6.3	6.9	0.91	1.00	826	776	554	443
HEALTHY_05	23	22.5	0			0	1	8.95	6.2	6.4	0.69	0.72	402	424	502	336
HEALTHY_06	21	24.9	0			0	1	7.9	2.5	2.8	0.32	0.35	179	156	172	107
HEALTHY_07	19	24.7	0			0	0	9	5.1	3.3	0.57	0.37	290	252	178	171
HEALTHY_08	26	22.9	0			0	0	14.4	11.9	10.6	0.83	0.74	370	357	281	316
HEALTHY_10	19	24.1	0			0	1	11.5	2.2	1.7	0.19	0.15	79	57	95	71
HEALTHY_11	22	24.5	0			0	1	15.9	10.3	8.0	0.64	0.50	416	366	268	187
HEALTHY_12	21	19	0			0	0	11.1	7.2	2.9	0.65	0.26	248	250	92	97
HEALTHY_13	23	24.8	0			0	1	11.5	5.9	5.3	0.51	0.46	284	251	229	184
HEALTHY_14	21	23.6	0			0	1	5	3.3	3.4	0.66	0.68	614	681	557	761
HEALTHY_15	23	27.7	0			0	1	8.4	5.2	4.8	0.62	0.57	289	272	178	268
HEALTHY_16	22	23.5	0			0	0	17.8	8.5	7.6	0.48	0.43	156	215	166	190
HEALTHY_17	23	17.8	0			0	0	7.8	5.1	5.1	0.65	0.65	548	599	554	478
HEALTHY_18	18	22.1	0			0	0	8.4	5.5	2.9	0.65	0.35	426	419	177	368
HEALTHY_19	24	22.3	0			0	1	10.6	4.2	3.6	0.40	0.34	273	248	221	203
HEALTHY_20	34	21	1			0	0	12.6	3.1	3.2	0.25	0.25	78	119	134	175

ID	ACL_Mmax	ACL_Hmax_control	ACL_Hmax_typing	ACL_HM_ratio_control	ACL_HM_ratio_typing	ACL_H_slope_control	ACL_H1_slope_control	ACL_H_slope_typing	ACL_H1_slope_typing	OV_Mmax	OV_Hmax_control	OV_Hmax_typing	OV_HM_ratio_control	OV_HM_ratio_typing	OV_H_slope_control	OV_H1_slope_control	OV_H_slope_typing	OV_H1_slope_typing
ACL_01	10.2	7.2	8.8	0.71	0.86	372	431	409	429									
ACL_02	10.5	7.8	7.7	0.74	0.73	507	426	346	407									
ACL_03	5.9	1.8	2.0	0.31	0.34	121	108	121	127									
ACL_04	8.7	3.6	2.8	0.41	0.32	239	118	119	84									
ACL_05	5.0	3.4	4.9	0.68	0.98	286	217	451	383									
ACL_06	8.3	6.8	5.2	0.82	0.63	783	266	290	173									
ACL_07	10.5	6.0	6.1	0.57	0.58	230	187	237	214									
ACL_08	3.4	1.4	1.3	0.40	0.39	224	286	161	286									
ACL_09	6.2	5.5	4.3	0.89	0.69	476	821	745	856									
ACL_10	5.8	4.7	5.8	0.81	1.00	540	319	507	350									
ACL_11	4.7	3.9	3.3	0.83	0.70	786	893	723	622									
ACL_12	11.1	3.9	1.8	0.35	0.16	158	407	81	272									
ACL_13	9.8	6.2	6.2	0.63	0.63	444	373	440	185									
ACL_14	13.6	11.4	7.3	0.84	0.54	714	589	492	436									
ACL_15	9.2	6.9	8.2	0.75	0.89	388	379	329	338									
ACL_16	7.8	5.0	4.2	0.64	0.54	400	280	202	199									
ACL_17	9.3	3.8	3.6	0.41	0.39	93	113	96	91									
ACL_18	13.7	8.6	4.9	0.63	0.36	373	296	161	139									
ACL_19	11.1	9.2	8.1	0.83	0.73	727	599	539	610									
ACL_20	8.4	8.4	7.3	1.00	0.87	203	170	163	144									
HEALTHY_01																		
HEALTHY_02										6.4	5.1	4.5	0.80	0.70	754	599	430	451
HEALTHY_03																		
HEALTHY_04																		
HEALTHY_05																		
HEALTHY_06										15.2	3.2	3.1	0.21	0.20	99	58	106	66
HEALTHY_07																		
HEALTHY_08										13.9	8.8	8.1	0.63	0.58	601	700	630	583
HEALTHY_10																		
HEALTHY_11																		
HEALTHY_12																		
HEALTHY_13																		
HEALTHY_14										3.4	2.4	2.9	0.71	0.85	482	633	516	546
HEALTHY_15																		
HEALTHY_16																		
HEALTHY_17										4.7	3.2	2.0	0.68	0.43	333	341	334	222
HEALTHY_18										5.0	2.9	2.3	0.58	0.46	207	231	174	195
HEALTHY_19										16.2	6.5	7.1	0.40	0.44	234	228	222	202
HEALTHY_20										13.4	5.2	5.7	0.39	0.43	206	212	290	221

ID	Pct_PI_CP	Pct_Inhib_Task	ACL_Pct_PI_CP	ACL_Pct_Inhib_Task	OV_Pct_PI_CP	OV_Pct_Inhib_Task	ABS_CP_Inhibition	ABS_Task_Inhibition
ACL_01	44.6	64.3	63.6	7.3			44.6	64.3
ACL_02	-67.0	31.4	-7.0	126.7			67.0	31.4
ACL_03	33.9	33.9	29.7	-4.0			33.9	33.9
ACL_04	-23.4	-15.6	-10.9	-4.8			23.4	15.6
ACL_05	-50.8	-54.1	-13.8	99.6			50.8	54.1
ACL_06	3.6	14.5	-45.9	-40.8			3.6	14.5
ACL_07	13.6	85.0	2.6	31.4			13.6	85.0
ACL_08	49.0	31.2	180.2	-26.9			49.0	31.2
ACL_09	92.3	10.0	34.0	62.6			92.3	10.0
ACL_10	67.9	68.4	67.2	104.3			67.9	68.4
ACL_11	-29.2	-18.2	-6.4	-26.9			29.2	18.2
ACL_12	253.9	-23.3	157.3	-21.9			253.9	23.3
ACL_13	-23.7		-43.2	79.5			23.7	
ACL_14	10.0	-61.3	-25.9	-38.9			10.0	61.3
ACL_15	12.6	7.3	-1.4	69.5			12.6	7.3
ACL_16	-12.2	-57.1	-16.2	-83.9			12.2	57.1
ACL_17	18.2	-14.6	26.0	-19.1			18.2	14.6
ACL_18	-34.2	-44.1	-7.3	-20.0			34.2	44.1
ACL_19	40.6	-34.4	13.9	9.2			40.6	34.4
ACL_20	20.6	7.3	13.7	-17.0			20.6	7.3
HEALTHY_01	-3.8	-17.0					3.8	17.0
HEALTHY_02	-9.7	-1.4			-43.8	74.2	9.7	1.4
HEALTHY_03	24.9	-17.8					24.9	17.8
HEALTHY_04	27.3	-25.2					27.3	25.2
HEALTHY_05	-15.9	-9.4					15.9	9.4
HEALTHY_06	-33.7	47.6			-43.4	21.8	33.7	47.6
HEALTHY_07	17.3	-37.7					17.3	37.7
HEALTHY_08	56.1	47.2			33.6	80.6	56.1	47.2
HEALTHY_10	-21.4	0.8					21.4	0.8
HEALTHY_11	-33.0	-4.0					33.0	4.0
HEALTHY_12	53.5	-67.7					53.5	67.7
HEALTHY_13	-37.7	-5.0					37.7	5.0
HEALTHY_14	-23.2	35.2			-29.0	32.0	23.2	35.2
HEALTHY_15	-3.1	-28.3					3.1	28.3
HEALTHY_16	47.6	-4.7					47.6	4.7
HEALTHY_17	80.0	59.9			28.4	-32.8	80.0	59.9
HEALTHY_18	37.2	-39.2			14.6	2.8	37.2	39.2
HEALTHY_19	-10.5	18.3			-16.7	-1.9	10.5	18.3
HEALTHY_20	44.2	76.1			36.9	65.7	44.2	76.1

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Table A2. Results from paired (ACL-UN vs. ACL-INV) and independent-samples (ACL-UN vs. CON-D and ACL-INV vs. CON-D) t tests for the following dependent variables: Hmax:Mmax ratio, Slope(test), Slope(CP).

	Mean ± SD			t-test p values		
Measure	ACL-UN	ACL-INV	CON-D	ACL-UN vs. ACL-INV	ACL-UN vs. CON-D	ACL-INV vs. CON-D
H:M	.69 ± .20	.69 ± .18	.59 ± .20	.98	.13	.11
$Slope_{test}$	407 ± 199	427 ± 218	363 ± 192	.69	.50	.35
$Slope_{CP}$	374 ± 171	366 ± 231	352 ± 190	.88	.71	.84

Table A3: Results from t-tests comparing percent presynaptic inhibition due to CP conditioning in the uninvolved and involved limbs (ACL group) and in the dominant limb (Control group).

	Mean ± SD			t-test p values		
% PI	ACL-UN	ACL-INV	CON-D	ACL-UN vs. ACL-INV	ACL-UN vs. CON-D	ACL-INV vs. CON-D
Facilitators	32.5 ± 27.4%	16.1 ± 34.0%	43.1 ± 19.2%	.046	.34	.049
Inhibitors	-34.4 ± 18.7%	-15.0 ± 13.0%	-19.2 ± 12.6%	.10	.06	.51

Table A4. Pearson's correlation coefficients between ACL-INV and ACL-UN.

Dependent Variable	Pearson's r	p value
Hmax:Mmax	.63	.005
Slope(test)	.53	.023
Slope(CP)	.43	.08
% PI	.69	.002

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Table A5. Mean ± SD for all 3 legs (ACL-UN, ACL-INV, CON-D) during Rest and Task conditions

	REST (Mean ± SD)			TASK (Mean ± SD)		
Measure	ACL-UN	ACL-INV	CON-D	ACL-UN	ACL-INV	CON-D
H:M	.69 ± .20	.70 ± .19	.59 ± .20	.63 ± .20	.66 ± .22	.52 ± .22
$Slope_{test}$	381 ± 169	426 ± 225	363 ± 192	317 ± 192	349 ± 205	298 ± 176
$Slope_{CP}$	360 ± 165	365 ± 238	352 ± 190	260 ± 165	330 ± 217	310 ± 196

Table A6. Between-Group comparisons (CON-D vs. ACL-UN): [2(Task) x 2(Group)] mixed model ANOVA

Measure	Effect of Task p-value	Effect of Group p-value	Task*Group p-value
H:M	.001	.13	.66
$Slope_{test}$	.002	.76	.98
$Slope_{CP}$	.001	.71	.13

Table A7. Within-Group comparisons (ACL-UN vs. ACL-INV): [2(Task) x 2(Leg)] repeated-measures ANOVA

Measure	Effect of Task p-value	Effect of Leg p-value	Task*Leg p-value
H:M	.056	.55	.70
$Slope_{test}$	.023	.42	.79
$Slope_{CP}$	.002	.47	.09

Table A8. Paired t-tests comparing Hmax:Mmax ratio at Rest and during the Typing Task in ACL-UN and ACL-INV

Leg	Paired t-test p value
ACL-UN	.009
ACL-INV	.31

Table A9. Results of t-tests comparing % Change(task) for CON-D, ACL-UN, and ACL-INV limbs

	% Change(task) Mean ± SD			t-test p values	
	ACL-UN	ACL-INV	CON-D	ACL-UN vs. ACL-INV	ACL-UN vs. CON-D
Raw change score	1.3 ± 45.0	15.0 ± 58.6	1.5 ± 37.4	.34	.99
Abs. val. change score	36.6 ± 24.7	45.1 ± 38.9	28.6 ± 23.2	.42	.32

Table A10. Pearson's correlation coefficients comparing %Change(CP) to %Change(Task) in each limb. Both raw and absolute values of %Change were compared.

	Comparison of raw %Change(CP) to %Change(task)		Comparison of abs. val. %Change(CP) to %Change(task)	
Limb	Pearson's r	p value	Pearson's r	p value
CON-D	.06	.81	.55	.01
ACL-UN	.41	.10	.03	.92
ACL-INV	.21	.42	.07	.78

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Table A11. Paired-samples t-tests comparing H reflex measures during the Follicular and Early Luteal phases

	Menstrual Phase (Mean ± SD)		
Measure	Follicular	Early Luteal	t-test p value
H:M	.58 ± .23	.55 ± .20	.52
$Slope_{test}$	366 ± 181	365 ± 227	.99
$Slope_{CP}$	360 ± 200	375 ± 237	.84
%Change(CP)	17.6% ± 41.9%	-2.4% ± 34.6%	.011