ASSOCIATION BETWEEN ACTIVE MOTOR THRESHOLD, ELECTROMYOGRAPHIC ONSET TIMES, AND GROUND REACTION FORCE RATE OF LOADING DURING GAIT IN PATIENTS WITH ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

Justin Fegley

A thesis submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Arts in the Exercise and Sport Science in the College of Arts and Sciences

Chapel Hill
2015

Approved by:

Brian Pietrosimone

Troy Blackburn

Matthew Harkey

ABSTRACT

Justin Fegley: Association Between Active Motor Threshold, Electromyographic Onset Times, and Ground Reaction Force Rate of Loading During Gait in Patients with Anterior Cruciate Ligament Reconstruction
(Under the direction of Brian Pietrosimone)

Previous studies have found that anterior cruciate ligament reconstructed (ACL-R), individuals demonstrate altered corticospinal excitability, quadriceps activation, and vertical ground reaction force (vGRF) loading rates during walking gait. Altered corticospinal excitability may influence the onset of quadriceps activity in preparation for heel strike, which could lead to an increased vGRF rate of loading. The purpose of this study was to determine the association between corticospinal excitability and vGRF rate of loading and quadriceps electromyography activity onset times during walking gait in ACL-R individuals. Individuals in this study participated in two testing sessions separated by at least one week. This study found a significant negative association between corticospinal excitability and vGRF rate of loading but no association between corticospinal excitability and quadriceps EMG onset times. The results of this study suggest that ACL-R individuals with higher corticospinal excitability have higher vGRF during walking gait.

TABLE OF CONTENTS

ABSTRACT iii
TABLE OF CONTENTS iv
CHAPTER 1: INTRODUCTION 1
1.1 ACL Injury and Osteoarthritis 1
1.2 ACL Functional Anatomy 2
1.3 Linking Corticospinal Excitability and Gait 2
1.4 Effect of Corticospinal Excitability on EMG Onset Times and vGRF Loading Rates 5
CHAPTER 2: LITERATURE REVIEW 6
2.1 Anatomical Significance of the ACL 6
2.2 Risk of ACL Injury 7
2.3 Risk of Osteoarthritis Following ACL Injury 8
2.4 Quadriceps Activation Following ACL Injury 10
2.5 Corticospinal Excitability and Transcranial Magnetic Stimulation 11
2.6 Gait Adaptations 14
2.7 Basics of Electromyography 16
2.8 Ground Reaction Forces 18
CHAPTER 3: METHODS 21
3.1 Study Design 21
3.2 Participants 21
3.3 Instrumentation 22
3.4 Procedures 23
3.5 Outcome Measures 23
3.6 Statistical Analysis 26
CHAPTER 4: RESULTS 27
CHAPTER 5: DISCUSSION 30

5.1 Summary of Findings 30
5.3 Steady State Gait and AMT 32
5.4 AMT and EMG Onset Times 33
5.5 Clinical Relevance 35
5.6 Limitations 36
5.7 Future Research 37
5.8 Conclusion 38
REFERENCES 40

CHAPTER 1: INTRODUCTION

1.1 ACL Injury and Osteoarthritis

Approximately 250,000 individuals sustain anterior cruciate ligament (ACL) rupture in the United States each year;[1] leading to about 100,000 ACL reconstructions (ACL-R) being performed each year.[2] Injury to the ACL can lead to pain, swelling, and rotational instability[3,4] and loss of quadriceps function following injury.[5] It has been demonstrated that following ACL-R there is decreased activation of the quadriceps due to arthrogenic muscle inhibition (AMI).[6,7] AMI has been historically described as a continuous reflexive inhibition that results in decreased activation of muscles surrounding an injured joint, and is considered a protective mechanism to prevent pain and further damage.[7] Quadriceps AMI results in muscle weakness and altered neuromuscular activation patterns,[8] due to an inability to achieve full muscular activation. Quadriceps muscle weakness and neuromuscular activation deficits can lead to altered lower extremity kinematics, therefore causing irregular load distribution across the knee that can lead to damage to the articular cartilage.[8] Even following surgical ACL-R, there is still an increased risk of developing osteoarthritis (OA). Current estimates suggest that rupturing the ACL leads to OA 5-20 years following injury.[9] Since ACL injuries primarily occur in young, active individuals, this suggests that the symptoms of OA may begin to present at a prematurely young age.[9] The early onset of OA after injury to the ACL presents a clinical problem because treatment strategies, such as total knee arthroplasty (TKA), used to treat older patients with OA are not appropriate for these younger patients.[9] Although TKA may be appropriate for those over the age of 65, the risk of implant loosening and revision is more than 3-fold higher than those

under the age of 65 because of the higher activity levels typically sought by a younger age group.[10] All of this suggests that we need to determine the extent of deficits following injury, in order to properly restore function before the onset of OA.

1.2 ACL Functional Anatomy

The ACL is composed of mechanoreceptors that provide information about joint position to the central nervous system to aid in coordinating movement with surrounding musculature.[11] Therefore, injury to the ACL can disrupt the natural afferent feedback to the central nervous system, which can affect normal knee joint function. Decreased quadriceps activation following ACL injury may be the cause of lasting weakness and kinetic changes during gait,[12] which may lead to a decreased energy attenuation capability of the quadriceps during joint loading. ACL-R patients that display quadriceps dysfunction have demonstrated decreased knee flexion angles during heel strike and throughout the stance phases of gait.[12] In theory, a weak quadriceps from persistent AMI reduces the ability to generate force and provide eccentric control to the knee joint during the loading phases of gait.[6] The inability of the knee joint dynamic stabilizers to diminish impact forces during gait may be a contributor of cartilage damage.[11]

1.3 Linking Corticospinal Excitability and Gait

While previous literature has focused on how spinal reflex alterations may contribute to decreased voluntary quadriceps activation, it has been demonstrated that altered corticospinal excitability may play a role in decreasing quadriceps excitability.[13] Transcranial magnetic stimulation (TMS) is a useful, non-invasive tool for studying the human brain.[14] A pulse magnetic field created by the TMS machine creates current flow in the brain and can temporarily excite or inhibit specific areas.[14] In fact, TMS of the motor cortex can produce activity in the peripheral musculature.[14] TMS can be used to quantify corticospinal excitability in the

quadriceps by applying a magnetic stimulus onto the region of the motor cortex that generates a motor evoked potential (MEP) in the targeted muscle group.[15] Active motor threshold (AMT) (a measure of corticospinal excitability), defined as the TMS required to produce a measureable motor evoked potential (MEP),[15] has been found to be higher in patients following ACL-R.[16] In a person with a higher AMT, a greater percentage of the maximal TMS intensity output is required to excite the primary motor cortex to cause a motor response in a particular muscle.

Following ACL injury decreased quadriceps activation can affect gait patterns.[12,17,18-20] Some patients display a quadriceps avoidance gait pattern following ACL-R.[12,17] Quadriceps avoidance gait is defined as a reduction in the knee extensor moment during the gait cycle.[21] The quadriceps are responsible for generating the knee extensor moment early in stance phase of gait, and an isolated reduction in quadriceps force may lead to a smaller knee extensor moment.[22] Furthermore, following ACL injury it was found that subjects also walk with decreased knee flexion angles,[12,18-20] and therefore exhibited a "stiffer" knee, or more extended knee, during the stance phase of gait. Weak quadriceps have a decreased ability to control knee joint loading eccentrically during the loading phase of gait, thereby exposing joint surfaces to unusual and excessive joint loading, which in turn could lead to joint degeneration.[23,24] Furthermore, it has been demonstrated that patients with OA of the medial knee compartment initiated ground contact with a more extended knee joint and displayed increased axial loading rate when compared to the matched controls.[25] It was also found that subjects with OA of the knee activate their quadriceps significantly later in the gait cycle (ie closer to foot strike) than their asymptomatic matched controls. Liikavainio et al[26] found that lower activation of the vatus medialis in patients with OA of the knee is associated with the presence of heel strike transient, which is a kinetic biomechanical marker that may indicate an increases rate of loading across the

lower extremity. Furthermore, patients with both unilateral and bilateral tibiofemoral OA display quadriceps activation deficits.[27] Subjects with knee OA have demonstrated that they have altered quadriceps activation, which can lead to an increased loading rate at the knee, as the quadriceps are not able to fully dissipate the vGRF. The quadriceps are a knee extensor for open chain activities, while the quadriceps act eccentrically to control knee flexion during the stance phase of gait.[12] Following injury to the ACL, patients are also found to have decreased activation of the quadriceps.[12,28] Voluntary quadriceps activation deficits have been attributed in part to the impairment of the central nervous system's ability to fully (> 95%), volitionally activate the muscle, which is termed central activation failure or arthrogenic muscle inhibition (AMI).[29-32] The central activation ratio (CAR) and AMT of the quadriceps can be used to measure the voluntary activation of a muscle[33,34] by measuring the recruitment and firing of motor units.[32] As mentioned before, patients who have undergone ACL-R demonstrate a higher quadriceps AMT, which indicates that they require more stimulus to produce a motor response (i.e. decreased activation).[13] Numerous studies have also demonstrated that following injury to the ACL, patients have an increased risk for the development of early onset knee OA.[9,35-40] ACL injured patients display altered quadriceps activation[17,20] which is also observed in elderly patients with knee OA;[26,41,42] thereby suggesting that persistent quadriceps activation deficits may be a predisposing factor that influences knee OA development following ACL injury.[41] It has also been found that knee OA patients demonstrate altered quadriceps electromyographic (EMG) activity during gait[42] and stair walking,[26,43] and patients who have had an ACL injury display altered quadriceps EMG activity during walking gait.[20] These findings suggest that not only do activation deficits occur in tasks requiring maximal effort (voluntary activation assessments) but quadriceps activation alterations may occur in submaximal activities of daily living such as gait.

1.4 Effect of Corticospinal Excitability on EMG Onset Times and vGRF Loading Rates

Following ACL-R, the decreased corticospinal excitability, may lead to altered quadriceps EMG onset times. The altered quadriceps onset time may occur because the primary motor cortex must reach a higher threshold before it can send a descending action potential to activate the quadriceps. The altered quadriceps EMG onset times may alter the quadriceps' ability to control the vGRF rate of loading that occurs during ground contact of walking gait. It has been found that following ACL injury there is altered loading that occurs about the knee joint which can lead to the development of OA.[44] From all of this, it can be inferred that decreased corticospinal excitability may be a predisposing factor for the premature onset of OA following ACL-R. Therefore, the purpose of this study is to determine the associations between quadriceps AMT, electromyographic (EMG) onset times, and ground reaction force (GRF) rate of loading during gait in patients with ACL-R.

CHAPTER 2: LITERATURE REVIEW

2.1 Anatomical Significance of the ACL

The anterior cruciate ligament (ACL) is very important for providing stability to the knee joint. The ACL serves as the main restraint to anterior tibial translation, while also providing much of the rotational stability to the knee.[45] The ACL does not heal following rupture and repair is not feasible, so reconstruction of the ligament is generally the operative choice.[46] Many athletic events require high, speed pivot-shift actions about the knee joint; an ACL deficient (ACL-D) knee will render these tasks very difficult for most individuals.. ACL reconstruction (ACL-R) is largely effective for restoring anterior and rotational stability to the knee, which is why most active individuals choose to undergo reconstruction.[47]

The ACL not only serves to provide stability to the knee, it also provides neural input to the central nervous system. The ACL and the knee capsule is composed of mechanoreceptors, such as free nerve endings, Ruffini endings, Golgi tendon organs, and Pacinian corpuscles which provide sensory information back to the central nervous system for communication with the muscle.[11,48,49] In fact, the ACL is abundantly innervated, and neural components make up about 1% of the total area of the ligament.[50] Furthermore, a study investigating the contribution of the ACL in joint repositioning tasks found that individuals who were ACL-D were less capable of reproducing a knee joint angle during a joint repositioning task compared to those who had healthy knees.[11] Baumeister et al[51] also found that following ACL-R, subjects reproduced target joint angles with greater error compared to the control in a joint repositioning task. Furthermore, it has been hypothesized that the decreased sensory information caused by

damage to the ACL mechanoreceptors may not have an impact on alpha motor function, however, alterations in afferent signals from joint receptors directly affect the gamma motor neuron system.[52,53] The gamma motor neuron are responsible for adjusting the shortening of intrafusal fibers of the muscle spindles, thus affecting their ability to produce muscle contractions.[54] Deficits in the gamma loop system have been found in patients following ACL injury following continuous stimulation of the patellar tendon.[52,53,55-57] All of this suggests that the ACL is an important component that provides proprioceptive information about the knee joint to the central nervous system. With ACL injury, proprioceptive capabilities about the knee joint may be compromised, therefore affecting the structures that surround the knee joint.

2.2 Risk of ACL Injury

A recent survey has demonstrated that 35 million kids between the ages of 5-18 compete in organized sports each year in the United States,[58] leading to numerous adolescents being injured each year while competing in organized sporting events. A 2008 study found that 1383 knee injuries were reported during 3,551,131 athlete exposures, for a knee injury rate of 3.89 per 10,000 athlete exposures.[59] Furthermore, surgery was required for 16.8% of the reported knee injuries, and the most common reason for surgery was complete ligament tears .[59]

The ACL injury is the most common complete ligament injury of the knee.[60] Each year there are 250,000 ACL ruptures in young athletes ages 15-25 years[1], and 100,000 ACL reconstructions.[2] In fact, this age group comprises more than 50% of those who sustain an ACL injury.[10] Following ACL injury; there are both acute and chronic consequences. The acute consequences following ACL injury are pain, swelling, loss of function, and rotational instability. Fortunately, ACL-R and a comprehensive rehabilitation program has been shown to be effective in reestablishing rotational stability of the knee.[2] Even though ACL-R is beneficial

in helping active individuals return to their activity levels with rotational stability, studies have shown that even following ACL-R patients are not able compete at their pre-injury levels,[61] and there is still an increased risk of developing OA,[9,35-40] which is the most serious chronic consequence of concern.

2.3 Risk of Osteoarthritis Following ACL Injury

Tibiofemoral OA is the most commonly reported disability affecting Americans over the age of 55.[8] OA is a disease characterized by the failure of the synovial joint.[62] OA occurs when the equilibrium between the breakdown and repair of joint tissues becomes unbalanced, often as a result of mechanical loads exceeding the limits that can be tolerated.[63] It is characterized by progressive cartilage loss, subchondral bone remodeling, osteophyte formation, and synovial inflammation, which may result in joint pain and increased disability.[64] According to Kellgren and Lawrence,[65] radiographic OA includes the following: formation of osteophytes on the joint margins, periarticular ossicles, narrowing of joint cartilage, small pseudocystic areas with sclerotic walls usually in the subchondral bone, and altered bone end shapes. OA is typically divided into five grades using the Kellgren-Lawrence (KL) scale, with 0 being no radiographic evidence of OA and 4 being severe.[65] Recently, evidence has emerged that injuries to the ACL increases the risk of developing knee OA.[9,35-40] In a follow-up study of female soccer players who had suffered an ACL injury 12 years prior, 82% had radiographic changes in their knee.[9] Since injuries to the ACL typically occur in young, active individuals, there is an increased risk of developing knee OA at a younger age. Estimates suggest that injuring the ACL will lead to the development of OA 5-20 years following injury, therefore, aging the knee by several years.[36] OA is a disease that typically affects elderly individuals, but younger individuals who have had traumatic knee injuries may show signs of OA that are similar to those who are older.[66] Luc et

al[66] found that by the second decade following ACL injury, those who choose to undergo ACL-R, nearly half will develop OA, while those who remain ACL-D, about one third will develop OA. Keeping these estimates in mind and remembering that injuries to the ACL typically occur in the younger population, symptoms of OA will appear in patients in their 20's or 30's.[8] This very early onset of OA is of clinical significance because this is a time when high demands from physical activity, work, and activities of daily living are still required of the joints. With patients developing OA earlier in their life, they will have to live longer with this disease, which can put them at risk for the development of other problems due to their decreased activity levels. With the decreased activity levels, the patients will be more prone to becoming obese which will predispose them to the development of other chronic diseases such as heart disease.[67]

As stated previously, ACL-R is beneficial in reestablishing rotational stability to the knee [68,69], however, there is still an elevated risk of developing OA.[9,35-40] Despite following standard ACL-R rehabilitation programs and being cleared to return to full activity by an orthopedic surgeon, patients are still developing signs and symptoms of OA at an accelerated rate following ACL injuries. Although the exact mechanism for the development of OA following ACL injury is not fully understood, a proposed mechanism is lingering quadriceps dysfunction.[5,41,70-72] Quadriceps dysfunction can be characterized as persistent weakness, reduced voluntary activation, and functional quadriceps asymmetries.[73] The quadriceps eccentrically contracts during weight acceptance of gait to allow loads to be transferred appropriately across the knee joint.[12] It has been shown that patients with lower quadriceps strength have displayed increased symptoms of OA.[38,74] As stated earlier, the quadriceps are important for controlling the loads that cross the knee joint during dynamic lower extremity activities. Therefore, they help to ensure that the total load and the rate of loading across the knee joint are appropriately

controlled. Andriacchi et al[44] also found that with knee injuries, there may be a shift in the contact patterns on the joint surfaces at the knee, which may cause surfaces that were once unloaded to become loaded and surfaces that were once loaded to become unloaded. It was found that subjects with OA of the medial knee compartment made initial ground contact with the knee in a more extended position, and an increased axial loading rate was recorded. Patients with OA of the knee typically display quadriceps activation deficits, and as stated earlier, the quadriceps are essential for controlling the rate of loading across the knee. Lingering quadriceps dysfunction may subject the knee to altered loading patterns and increased loading rates, which may lead to the premature onset of OA. These studies suggest that quadriceps weakness can lead to diminished abilities to attenuate joint loading across the knee joint, which in turn can lead to degeneration of the articular cartilage.

2.4 Quadriceps Activation Following ACL Injury

Several studies demonstrated that following ACL injury, there is decreased activation of quadriceps, even following ACL-R. Deficits in quadriceps strength and activation are of the major concerns following ACL-R.[5,12,41,70-73] One of the proposed mechanisms for the decreased activation of the quadriceps following ACL injury is arthrogenic muscle inhibition (AMI).[8,75-77] AMI is a continuous reflexive inhibition that results in decreased activation of uninjured muscles surrounding an injured joint.[7] AMI is initially considered to be a protective mechanism to prevent pain and further damage,[7] however, sustained quadriceps AMI will cause prolonged weakness and altered neuromuscular activation patterns.[8] AMI has been found to impede rehabilitation following knee injury, due to a decreased activation of the quadriceps.[75,76]

During weight acceptance in gait, the limb will support the entire weight of the body, and through knee flexion controlled by eccentric contraction of the quadriceps the forces

crossing the knee joint will be attenuated.[12] With decreased activation of the quadriceps, the patient will be unable to fully attenuate the forces placed on the knee joint during ambulation, because the quadriceps are unable to optimally eccentrically contract, therefore, decreasing their ability to control knee flexion which will lead to increased impulsive loading across the knee. These forces will then be placed across the joint surface. Following ACL injury decreased voluntary quadriceps strength predicted 61% of the self- reported disability.[70] Quadriceps strength is the ability to develop maximal force, while quadriceps activation is the ability of the alpha motor neuron pool to fully activate the quadriceps and can be measure by CAR.[33,34] Therefore, an inability to fully activate the quadriceps will lead to decreased quadriceps strength values. Furthermore, decreased quadriceps activation has been linked to the development of OA in the knee.[41] In a study that examined quadriceps activation and radiographic OA in subjects who had undergone ACL revision surgery, it was shown that quadriceps activation failure was a risk factor for the development of OA.[41] The study shows that altered quadriceps activation may be a risk factor for the onset of OA. With activation deficits, the quadriceps will not be able to control the rate of loading across the knee to their fullest potential, which could subject the articular cartilage to loads that exceed the tolerable limits of the tissue.

2.5 Corticospinal Excitability and Transcranial Magnetic Stimulation

Recent studies have demonstrated that quadriceps dysfunction following ACL injury may be the result of altered neural input.[13,51,70,78] These findings suggest that the decreased quadriceps activation may be the result of alterations to the central mechanisms and not injury to the muscle. Lepley et al.[13,79] found that patients following ACL-R demonstrated lower corticospinal excitability of the quadriceps compared to the uninjured limb. Corticospinal excitability is the ability of the corticospinal tract to receive and respond to stimulus. Corticospinal excitability is

quantified as active motor threshold (AMT), which is defined as the lowest transcranial magnetic stimulation (TMS) stimulus required to produce a measurable motor response [motor evoked potential (MEP) >100μV].[15] A higher AMT corresponds to a lower corticospinal excitability, because this indicates that the motor neurons must receive a higher amount of stimulus before they can properly activate a specific muscle group. TMS is a useful tool to measure the corticospinal excitability of a particular muscle group through activation the stimulation of brain tissue from a rapidly changing magnetic field delivered from a coil placed over the scalp.[80-82] Stimulation of the contralateral primary motor cortex introduces an electrical stimulus in the neural tissue which causes depolarization of neurons that is transmitted by the corticospinal tract to the contralateral peripheral muscle where a motor response can be recorded.[6,82,83] AMT and amplitudes of MEPs are both outcomes measures of interest to measure corticospinal excitability.[84-86] AMT is useful in providing information about a core region of neurons in the muscle representation of the motor cortex[83], whereas MEP amplitude can be used to examine overall corticospinal excitability.[87] MEPs provide information regarding the functionality of the central nervous system and are frequently measured for diagnostic and therapeutic purposes.[88] TMS uses an exogenous magnetic stimulus applied to the contralateral motor cortex to elicit a muscle contraction. TMS provides a non-invasive way of assessing central nervous system motor pathways in humans.[15] Originally, transcranial electrical stimulation was used to stimulate areas of the motor cortex, but transcranial electrical stimulation was painful since it stimulated nerve fibers in the scalp.[14] However, with TMS a magnetic stimulus is applied to the region of the motor cortex that generates a MEP in the periphery and excites corresponding descending corticospinal tracts that project to motor neurons within the targeted musculature.[14]

ACL-R patients present with a higher AMT, which is representative of lower corticospinal excitability because more stimulus was required to evoke a motor response in the quadriceps.[13] It was also found that patients, who had sustained an ACL injury, displayed lower resting motor thresholds in the hemisphere contralateral to the injured limb.[78] This suggests that there is change in the excitability quadriceps musculature.[78] Furthermore, Lepley et al,[13] found that subjects who had undergone ACL-R and who were classified as having a low quadriceps strength value, demonstrated higher AMT values, which indicates altered quadriceps activation. This suggests that lingering quadriceps weakness following ACL-R was be due to a neural deficit, rather than a deficit to the muscle itself. It was also found that elderly subjects displayed less corticospinal excitability than younger subjects and subsequently had higher reaction times during a choice reaction time task.[89] Even though this study did not specifically look at the quadriceps, it could be indicative of quadriceps function following ACL-R. Following ACL-R, patients may have decreased quadriceps corticospinal excitability, which could be a predisposing factor for quadriceps dysfunction. The decreased corticospinal excitability may lead to higher reaction times for quadriceps activation in preparation for dynamic activities. This higher reaction time could alter the quadriceps ability to control lower extremity loading during dynamic activities, which may lead to altered loading about the knee. The results of these studies show that patients following ACL-R , who have been cleared to return to play, may have lower corticospinal excitability of the quadriceps, which may suggest that standard rehabilitation techniques are not adequate in restoring neuromuscular function. In fact, techniques that target rehabilitating corticospinal excitability may be necessary to fully restore quadriceps function following ACL injury.

2.6 Gait Adaptations

The quadriceps is an important muscle group for controlling joint loading about the knee during dynamic activities. Greater eccentric control of the quadriceps will increase knee flexion angle, which will aid in diminishing the forces that cross the knee.[12] Therefore, those with non-pathological knees and normally functioning quadriceps will display greater internal knee extensor moments in their gait patterns.[12] Following ACL injury, it has been found that subjects will alter their gait mechanics.[12,18,22,90] People with knee instability will alter their gait patterns through reduced knee flexion and internal knee extensor moments.[18,22] Contraction of the quadriceps during the gait cycle has been shown to cause anterior tibial translation, which could initiate an episode of "giving way" in a person who is ACL-D, which may be another mechanism why there is decreased quadriceps activation following ACL injury.[91] These altered gait patterns, including decreased knee flexion angle, can exist for up to five years following surgery.[92]

Studies have shown that ACL injured participants display lower EMG activity of the quadriceps during the gait cycle.[12,17] ACL injured participants display a "quadriceps avoidance" gait pattern following injury,[12,17] which results in decreased activity of the quadriceps during the gait cycle, in order to reduce anterior tibial translation.[93] The eccentric contraction of the quadriceps is important during the normal gait cycle to help decrease the rate at which forces cross the knee joint.[12] Therefore, with decreased quadriceps activity during the gait cycle, patients are unable to fully dissipate the forces that cross the knee joint. Prior to ACL-R and six weeks post-ACL-R, subjects displayed a quadriceps avoidance gait pattern.[17] Normal gait patterns were not re-established on average until eight months following surgery.[17] Furthermore, subjects who had weak quadriceps following ACL-R were found to have gait patterns that were

similar to those who were ACL-D,[12] indicating that restoring joint stability does not fully restore function.

ACL injured participants display decreased knee flexion angles during gait, and therefore exhibited a "stiff" knee during the gait cycle.[12,18,19] A coper is an ACL-D person who can maintain high activity levels without experiencing episodes of instability, loss of function, or weakness.[94] Copers are able to return to pre-injury levels without reconstructive surgery.[94] Non-copers and those with weak quadriceps following ACL-R were found to have decreased knee extensor moments and knee flexion angles during the gait cycle, indicating that there is decreased eccentric quadriceps activity.[12,19] Muscle forces are a major determining factor as to how loads will be distributed across a joint's surface.[8] For example, the quadriceps are important shock absorbers, and they function to help dissipate loads across the knee joint.[8] Isolated quadriceps weakness and activation deficits are capable of altering dynamic loading conditions as shown through increased vertical ground reaction forces and smaller knee flexion angles.[95] Radin et al[96] have shown that repetitive impulsive loading, application of loads across the knee at a high rate, in the hind limb of rabbits resulted in degeneration of articular cartilage. With the quadriceps not functioning to their fullest potential as shock absorbers, the knee joint may be subjected to greater loading rates during dynamic activities. Patients with knee OA have been found to have altered quadriceps activation and gait biomechanics. Subjects with symptomatic OA were found to have a decreased quadriceps rate of force development (RFD) when compared to healthy controls, indicating that impairments in rapid force generation are more profound in older adults with OA.[97] RFD is defined as the amount of force produced over a given amount of time.[98] It can be utilized to evaluate the ability to generate muscle force rapidly.[99] Quadriceps RFD is an important component of physical function, as it was found to correlate more strongly

than maximal quadriceps strength with activities of daily living.[100] Quadriceps RFD is likely important for knee joint function and stability.[97] Another study showed that subjects with asymptomatic OA had decreased EMG amplitudes, or less activation, of the vastus medialis (VM) during the swing phase of gate.[26] The subjects also demonstrated greater ground reaction forces during the tasks, especially with stair descent.[26] The results of these studies suggest that adequate quadriceps function in preparation for heel strike in an important factor for successful weight acceptance during gait. Impairments to the quadriceps may decrease one's ability to fully dissipate the impulsive loading that occurs across the knee joint during the normal gait cycle, which could be a predisposing factor for the development of OA.

2.7 Basics of Electromyography

Electromyography is an experimental technique used for recording and analyzing electrical activity of the skeletal musculature.[101] Surface EMG is also an effective tool for measuring quadriceps activity during the gait cycle, and it can provide insight about quadriceps function following ACL injury. Following ACL injury, subjects were found to have decreased quadriceps EMG amplitudes during weight acceptance of the walking gait cycle.[20] It was found that non-copers had lower EMG amplitudes in the vastus medialis and vastus lateralis on the injured limb when compared to the uninjured limb.[20] Previous studies have also examined quadriceps EMG activity during the gait cycle of patients with OA.[26,42] Liikavainio et al[26] measured bilateral muscle activity of the vastus medialis, vastus lateralis, biceps femoris, and the medial gastrocnemius during walking and stair ascent/descent in subjects with asymptomatic knee OA. The study found that subjects with a heel strike transient (HST) had 43.5% lower activity in the vastus medialis prior to heel strike during maximal walking speeds.[26] HST is described as a distinctive, sharp peak in the GRF.[102] It was found that those displaying a HST

during the gait cycle have a delay in quadriceps EMG activity.[103] In fact, those with a HST were found to have lower EMG amplitude of both the vastus medialis and vastus lateralis during normal and maximal speed walking, but only the EMG amplitude of the vastus medialis during maximal speed walking was found to be significantly different.[26] As stated earlier, subjects with ACL injury display quadriceps dysfunction, which may be a predisposing factor for these altered gait mechanics. This is of clinical concern because this decreased quadriceps function during the gait cycle may be an explanation for the development of OA at the knee.

It was also found that subjects with OA of the knee have delayed activation of the quadriceps during stair descent.[43] When compared to their matched, healthy controls, the patients with OA activated their quadriceps significantly later during the task in preparation for ground contact.[43] This study suggests that OA of the knee may be associated with altered neural control of the quadriceps. As mentioned several times previously, patients who have undergone ACL-R demonstrate quadriceps activation deficits, which have also been found in subjects with OA of the knee. This all suggests that the quadriceps activation deficits that exist following ACL injury may be a predisposing factor for the development of post-traumatic OA.

Metcalfe et al[42] examined the bilateral EMG activity of the vastus medialis, vastus lateralis, semitendinosus, and biceps femoris during walking gait in subjects who had predominately medial tibiofemoral arthritis and were on the waiting list for knee replacement. They used the data from the EMG to calculate muscular co-contraction index of the quadriceps and hamstrings.[42] A high value indicated a strong simultaneous contraction of the quadriceps and hamstrings.[42] The subjects with OA displayed higher co-contraction indexes compared to the control subjects.[42] As stated earlier, non-copers displayed higher co-contractions in the injured limb compared to the uninjured limb.[20] This strategy leads to a "stiff" knee gait and could prove

to be potentially harmful to the articular cartilage.[20] Increased co-contraction of the quadriceps and hamstrings may further contribute to joint loading and speed up the rate of articular cartilage degeneration.[20] Following ACL injury, patients may display EMG patterns that are similar to those who suffer from OA of the knee. This suggests that ACL injury is a predisposing factor for the development of OA at the knee.

2.8 Ground Reaction Forces

The measurement of vertical ground reaction force (vGRF) is a beneficial tool to measure the force that is applied to the ground during dynamic activities, which have the potential to travel to the knee. Previous studies have evaluated the vGRF that occur during the gait cycle in subjects who have knee pathologies.[12,26,104] Hunt et al[104] investigated measures of impact loading during walking (rate of loading and HST occurrence) in individuals with knee OA. The study found that patients with more severe OA tended to display a higher frequency of a HST and greater maximal loading rates when compared to patients with less severe OA.[104] Metcalfe et al[42] examined the effects of knee OA on lower extremity biomechanics. In the study, it was found that subjects with knee OA tended to have greater knee adduction moment impulses on both the affected and unaffected limbs when compared to healthy controls.[42] A study by Mundermann et al[25] observed the gait changes that occur in patients of medial knee OA. The patients with medial knee OA made initial ground contact with the knee in a more extended position than those of the control group.[25] This was more pronounced in patients with more severe OA than those with less severe OA.[25] Furthermore, following heel strike, the ground reaction forces in all patients with OA were higher than those of the control group.[25] The patients with OA also displayed a loading rate that was higher than that of the control group.[25] The OA patients in this study made initial ground contact with the knee in a more extended position, which suggests that there is an

alteration to the normal knee extensor moment, which is indicative of quadriceps dysfunction. With an alteration of the knee extensor mechanism, the quadriceps of the patients with OA were most likely unable to fully attenuate the forces that were acting upon the knee joint. Noehren et al[105] also found that females who have undergone ACL-R display long-term gait deviations. The study found that those who had undergone ACL-R had significantly greater initial impact force and average loading rate during a walking gait trial.[105] With patients developing quadriceps activation deficits following ACL injury that are usually not fully addressed with reconstruction and standard rehabilitation, it can be inferred that these activation deficits can lead to higher loading rates about the knee joint following injury. With higher loading rates about the knee joint following injury, the articular cartilage in the patients' knee will be subjected to non-normal mechanical stresses, which could lead to structural changes.

Lewek et al[12] used force plates and motion analysis software to examine the knee extensor moments in ACL injured and control subjects. A reduced knee extensor moment is defined as a "quadriceps avoidance" gait pattern,[106] which could represent a decrease in quadriceps activity or an increase in flexor activity provided by the hamstrings.[107] The subjects used in this study were categorized into ACL strong (quadriceps strength of 90% or more in the involved limb compared to the uninvolved limb), ACL weak (quadriceps strength of 80% or less in the involved limb compared to the uninvolved limb), ACL-D, and uninjured.[12] The results of the study showed that uninjured and the ACL strong group had greater knee extensor moment, indicating that they had greater contributions from the knee extensors during the gait cycle.[12] A decreased knee extensor moment has been correlated with a "stiff knee" gait pattern, which has the potential to lead to arthritic changes to the knee joint over time.[12,18,19] Liikavainio et al[26] also used force plates to study the GRF and loading rate in subjects with asymptomatic OA. During

the study, the subjects walked on a 15 meter level walkway with a 10 meter force platform in the middle, and they also walked up a set of stairs which also contained force plates.[26] The study found that loading rate was greatest during maximal speed walking, and the greatest GRF occurred during stair descent.[26] The study also found that there was an association between lower pre-activity of the vastus medialis with a clear heel strike transient under normal conditions, which indicates that there was a sharp rise in the vGRF during the gait cycle.[26] Patients who have sustained an injury to the ACL and patients with OA of the knee display altered knee extensor mechanisms and quadriceps activation. With altered knee extensor moments and quadriceps activation deficits there can be altered loading rates about the knee joint. This shows that injury to the ACL may be a predisposing factor for the development of OA at the knee.

CHAPTER 3: METHODS

3.1 Study Design

A descriptive laboratory study was utilized.[108] The study investigated the association between quadriceps corticospinal excitability and quadriceps EMG onset times during a walking gait trial in preparation for heel strike, and quadriceps corticospinal excitability and rate of vGRF loading during the stance phase of gait. Gait analysis occurred during the first testing session and corticospinal excitability analysis occurred during the second testing session. The individuals in this study completed both sessions with at least one week separating the two sessions. Both sessions occurred during the same time of day.

3.2 Participants

All participants were between the ages of 18 and 40 with a history of unilateral ACL-R. The participants' graft type was limitied to patellar tendon (PT) or hamstring tendon (HT) autografts. Participants that had received allografts or other types of autografts were excluded from this study. Participants were required to be at least six months post-ACL-R and cleared by a physcian to return to physical activity with no restrictions. The individuals were physically active, paricipating in at least 20 minutes of physical activty three times a week, and did not have a history of ACL graft rupture or ACL revision surgery. Participants did not have a history of an injury to either leg within the six months prior to participation, a history of knee OA or current symptoms related to knee OA (ie pain, swelling, and stiffness). Participants were excluded from the study if they had a history of neurological disorders that included the following: stroke, multiple sclerosis, amyotrophic lateral sclerosis (Lou Gehrig's Disease), diabetic neuropathy,

epilepsy, traumatic brain injury resulting in loss of consciousness, concussion within the last six months, cranial neural surgery, and balance disorders. Futhermore, participants were excluded from the study if they met any of the following criteria: pregnant during the study, currently using a pacemaker or other implantable eletronic device, history of cardiac arrythmia, psychiatric disorder, cancer in the brain or thigh musculature, histroy of any cardiac condition, and/or implanted metallic objects. All participants provided informed constent approved by the institutional review board at the University of North Carolina at Chapel Hill (UNC-CH) prior to participating in this study.

UNC-CH students and employees were recruited as part of a convenience sample. The individuals were notified via the informed consent document that their employment or academic status would not be affected byparticipation or lack of particpation in this study. ACL-R patients were also recruited from UNC Orthopedics (Jeff Spang, MD and Robert Creighton, MD) following successful completion of the prescribed rehabilitation protocol, and they were notified via the informed consent document that their clinical care will not be influenced by their partcipation or lack thereof.

3.3 Instrumentation

Transcranial Magnetic Stimulation

The Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., Stoughton MA, USA) was used for patient positioning and to measure torque for TMS testing. The Magstim Bistim (Magstim Company, Wales, UK) with a double-cone coil was used to estimate corticospinal excitability by eliciting motor evoked potentials in the quadriceps. A BIOPAC MP 150 (BIOPAC Systems Inc., Goleta CA, USA) was used to convert analog electromyographic signal to digital signal (used in corticospinal testing), which was used for data processing. A

MacBook Pro with Acqknowledge Software (Biopac Systems Inc., Goleta CA, USA) was used to collect and record the peak-to-peak amplitude of motor evoked potentials during the TMS testing.

Gait

The Vicon Nexus motion analysis system (Vicon Motion Systems, Oxford, UK) was used for collection of kinetic data from a force plate (model 4060-NC, Bertec Corp, Columbus OH) that was used to measure the participants' vGRF during the stance phase of gait. Surface EMG elctrodes (Bagnoli 8, Delsys, Boston MA) were used to identify the onset of the quadriceps in preparation for heel strike during the gait cycle. Timing Gaits (TF100, Trac Tronix, Lenexa, KS) were used to ensure that the participants were walking at a consistent gait speed during the trials.

3.4 Procedures

Participants in this study reported to the Sports Medicine Research Laboratory for session one where outcome measures for gait assesment were tested during a two hour period. All participants also reported to the Neuromuscular Research Laboratory for session two where outcome measures for corticospinal excitability were tested during a three hour period. Session one and session two were separated by at least one week.

3.5 Outcome Measures

Gait Assessment and EMG Analysis

EMG analysis was collected during the same session as the kinetic analysis. Subjects walked forward along a 10 foot walkway at a comfortable, self-selected speed. Kinetic data from the force plate were sampled at 1200Hz. The vGRFs were normalized to bodyweight, and the data were filtered with a fourth order, low pass Butterworth filter at 75Hz. Initial heel strike was defined as the instant when the vGRF exceeded 20N. The loading rate of the vGRF was defined

at the time from initial heel strike to peak vGRF. For this study, the first 50% of stance phase was analyzed At least five practice trials were performed to determine the average preferred speed and to ensure that subjects could consistently strike a force plate mounted in the walkway with the test limb without noticeably altering their gait pattern. Gait speed was monitored via an infrared timing system (TF100, Trac Tronix, Lenexa, KS) to ensure that each trial was within ±5% of the preferred speed. The subjects performed five valid trails from which the following variables were measured.

Techniques similiar to those utilized by Lindstrom et al[109] were utilized for quadricpes EMG analysis. EMG data were sampled at 1200Hz, common mode rejection ratio of 92dB, and input impedance of >10Ω//0.2pF. Electrode placement sites over the vastus medialis were shaved, lightly abraded, and cleansed with alcohol pads to improve adhesion to the skin and signal quality. EMG electrodes (Bagnoli 8, Delsys, Boston MA) were secured via hypoallergenic tape over the vastus medialis. The electrodes were preamplified with a gain of 10 and with an interelectrode distance of 10 millimeters. EMG data was rectified, filtered, and analyzed. The EMG data were bandpassed filtered (20-350Hz) and notch filtered at 60Hz. Root mean square (rms) smoothing was conducted at 25ms for the EMG readings. Analysis was concerned with the EMG onset times of the quadriceps in the affected limb during swing phase of the gait cycle in preparation for heel strike. A time epoch of 416ms (500 data point samples) was sampled from the middle of a 3 second static standing trial and utilized to determine the resting EMG activity of the quadriceps to be used for baseline value. The quadriceps were considered "on" when EMG activity was at least two standard deviations above the baseline for a duration of at least 30 milliseconds.[109] The time between the beginning of muscle activity and heel strike during gait

was used as our outcome measure. The EMG data were post-processed using custom written software (Labview, National Instruments, Austin, TX).

Corticospinal Excitability

Corticospinal excitability was quantified using AMT which was collected with TMS. Motor evoked potentials (MEPs) were elicited using the magnetic stimulator with an attached double cone coil (Magstim Bistim,Magstim Company, Wales, UK). The intensity of magnetic stimulation never exceeded two Tesla. The Bistim works by applying a brief, non-painful magnetic stimulus over the motor cortex that can be utilized as a non-invasive technique to assess corticospinal excitability of the quadriceps. Participants were positioned in the dynamometer with knee and hip joints positioned at 90 and 85 degrees of flexion respectively. Bilateral chest and lap restraints were used to secure the participants into the dynamometer to limit excess motion. The distal shank of the tested limb was secured to the dynamometer using a velcro strap. First, quadricep MVICs were measured for each limb. The subjects were instructed to extend their knee at their maximum ability into the dynamometer while they were provided verbal encouragment.[110] The peak torque that was obtained was recorded as the MVIC for that trial. The participants continued this process for a minimum of three trials or until their peak torque plateaued. The participants were provided with at least sixty seconds of rest between attempts. MEPs were measured in the vastus medials(VM) via surface EMG electrodes. The area over the collection site was shaved, debrided, and cleaned with an alcohol pad. A lyrca swim cap with a 1x1cm grid was placed over the participants' to determine the optimal stimulating area. The grid included two lines: one running from the nose to the occiput (separating the hemispheres of the brain) and one running from the apex of one ear to the other (bisecting the sagittal line). The intersection of these two lines is the vertex of the skull, and was

used as a reference point of the motor cortex.[111] To produce a MEP in the quadriceps, the TMS coil was placed over the contralateral motor cortex by an investigator, and the participants produced a quadriceps contraction that was 5% of their MVIC while the TMS was applied to the desired location. The coil was moved systematically along the swim cap grid: first by moving medial to lateral than anterior to posterior in one centimeter increments until the largest MEP response was found, which was termed the optimal stimulating area. A computer screen depiciting real time feedback of the participants' torque output was used to ensure that the participants were extending their knees with a torque that was equal to 5% of their quadriceps MVIC. AMT was considered the lowest TMS intensity that is required to produce a measurable MEP ($\geq$ 100μV) in the contralateral quadriceps musculature in 5 out of 10 trials.

3.6 Statistical Analysis

Mean and standard deviation for age, height, weight, time since injury, time since surgery were determined before the primary analysis. Prior to the primary analyses, we evaluated if AMT, EMG onset times, and vGRF rate of loading were normally distributed using a Shapiro Wilk Test for normality. The Shapiro Wilk Test showed that AMT and vGRF rate of loading were normally distributed, and AMT and EMG onset times were not normally distributed. Therefore, a Pearson Product Moment was used to analyze the correlation between AMT and vGRF rate of loading, and Spearman Rho rank order was used to analyze the correlation between AMT and EMG onset times.Associations for the current study were described as negligible (0.0-0.3), low (0.3-0.5), moderate (0.5-0.7), high (0.7-0.9), and very high (0.9-1.0).[112] The level of significance was set *a priori* at $P \leq 0.05$ for all inferential statistics, which were evaluated using SPSS 19.1 statistical software.

CHAPTER 4: RESULTS

Eighteen participants, with a history of unilateral ACL-R participated in this study (Table 1). EMG onset measurements and AMT were collect and analyzed on a total of 10 participats, while AMT and vGRF rate of loading were collected and analyzed for 12 participants (Table 2). Eight participants did not have EMG onset data because the EMG signal was insufficient, and six participants did not have AMT measurements because they did not attend a second testing session, therefore, only ten participant were included in the EMG onset and AMT correlation, and tweleve subjects were included in the vGRF rate of loading and AMT correlation. The results of the Shapiro Wilk test demonstrated that AMT ($W=0.883$, $p=0.095$) and vGRF rate of loading ($W=0.946$, $p=0.584$) were normally distributed but EMG onset times were not normally distributed ($W=0.803$, $p=0.016$). Therefore, a Pearson Product moment correlation was utilized to determine asscoaition between vGRF rate of loading and AMT, and a Spearman Rho rank order correlation was utilized for the correlation between EMG onset and AMT.

Association Between AMT and vGRF Rate of Loading

There was a significant negative association between AMT and vGRF rate of loading ($r= - 0.654$, $n=12$, $p=0.021$; see and Figure 1), indicating that ACL-R individuals with higher AMT demonstrated lower vGRF rate of loading. Therefore ACL-R individuals with higher corticospinal excitability also had a higher vGRF rate of loading.

Correlation Between AMT and Quadriceps EMG Onset Time

There was no significant correlation between AMT and EMG onset times (ρ= -0.134, n=10, p=0.713; see Figure 2). The outliers in this association were originally removed from analysis, however, it did not change the results of the analysis, therefore, the outlier was retained in the final analysis.

Table 1. Average demographics of all participants

Number	**Age(years)**	**Height(cm)**	**Weight(kg)**	**Time Since Injury (months)**	**Time Since Surgery (months)**
18 (15 F, 3 M)	21.44±2.75	168.17±10.69	75.11±18.54	44±45.61	43.44±43.94

Table 2. Average demographics of participants included for analysis

Number	**Age(years)**	**Height(cm)**	**Weight(kg)**	**Time Since Injury(months)**	**Time Since Surgery (months)**
12 (11 F, 1 M)	21.83±3.27	166.99±12.03	76.75±21.96	50.75±51.41	49.25±50.92

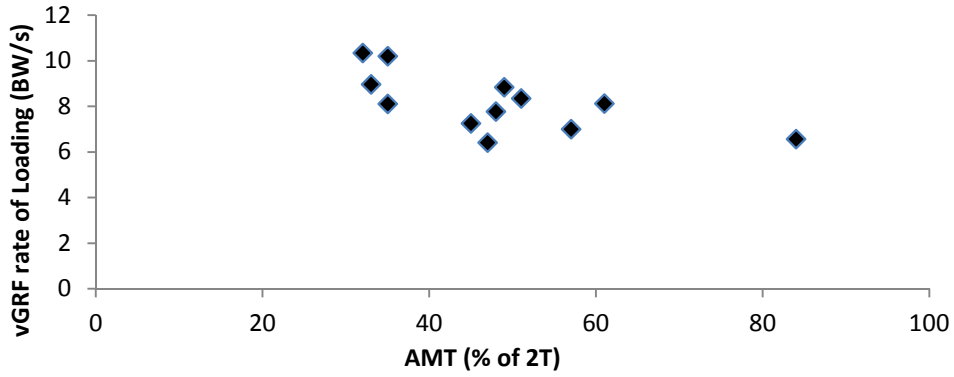

Figure 1. Correlation between AMT and vGRF Rate of Loading

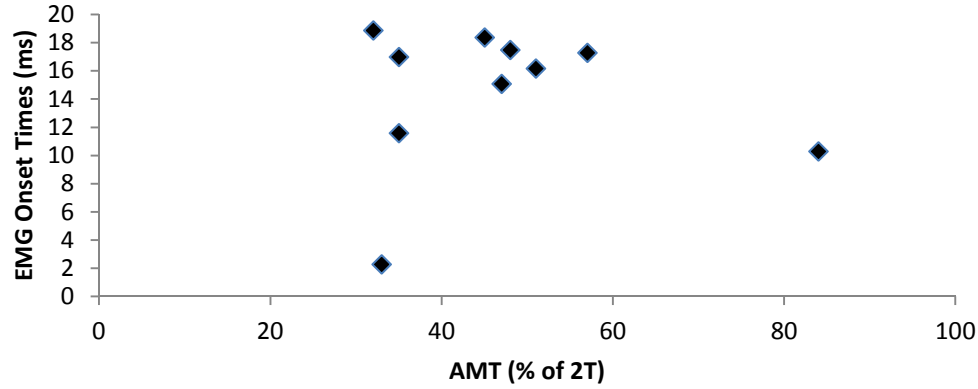

Figure 2. Correlation between AMT and EMG Onset Times

CHAPTER 5: DISCUSSION

5.1 Summary of Findings

The main findings of the current study were that: 1) a higher AMT was associated with a lower vGRF rate of loading during a walking gait trial and 2) there was no association between AMT and quadriceps EMG onset times. The findings of the current study were not consistant with our *a priori* experimental hypothesis. We expected that individuals with a higher AMT would have a higher vGRF rate of loading during a walking gait trial. Also, it was hypothesized that individuals with a higher AMT would display a shorter time interval between quadriceps EMG onset and intial ground contact during a walking gait trial. Our findings suggest that AMT may not influence quadriceps EMG onset times in steady state gait, however, more corticospinal excitability may be associated with greater vGRF rate of loading during walking gait.

5.2 AMT and vGRF Rate of Loading

As stated previously, it was expected that those individuals with a lower AMT would have longer duration between quadriceps EMG onset and heel strike, as well as a lower vGRF loading rate. Previous research has demonstrated that many patients display persistent quadriceps alterations following ACL-R.[5,6,16,51,70,72,78] Specifically, it was found that participants who had undergone ACL-R displayed a higher quadriceps AMT in the reconstructed limb than the unaffected limb,[16] which potentially suggests the presence of quadriceps corticospinal excitability deficits. We hypothesized that a higher AMT would lead to greater vGRF rate of loading becuase the quadriceps' ability to control knee joint loading is potentially decreased. Furthermore, higher vGRF loading rates have been observed in participants with knee OA,[25,104]

and altered vGRF loading rates have also been observed in individuals who have sustained ACL injury as well.[105] Lower vGRF loading rates during walking tasks may be desired because forces are gradually being applied across the knee rather than rapidly. Rapid vGRF loading rates could lead to the premature development of OA. Also previous research has found that quadriceps EMG activity is altered following ACL injury [12,17,20] and in patients with knee OA.[26,42]. However, it has also been found that ACL injured patients display decreased loading of the injured than the healthy limb.[113]It is well understood that normal loading is essential for cartilage health, therefore, unloading of weight bearing cartilage can lead to deteriorations in cartilage health.[44]Even though this unloading of the injured limb may be a protective mechanism, it may lead to non-normal loading patterns about the knee joint which could lead to the early progression of OA.

The current study suggests that the participants with higher corticospinal excitability may be utilizing their other lower extremity muscles to better to attenuate the vGRF than those with lower corticospinal excitability. It is understood that during locomotion there is dynamic coordination of trunk and lower extremity musculature.[114] This current study only examined the quadricpes activity during a walking gait trial, when in fact the muscles of the lower limb and hip are active during these trials. Perhaps these muscles were more active in those with higher corticospinal excitability to help attenuate the vGRFs. Past research has shown that those with lower quadriceps strength had higher loading rates during walking gait.[115] With lower quadriceps strength, the participants may have had lower excitability, and may not have been able to attenuate the vGRF during gait adequatley. Therefore, individuals with a higher quadriceps corticospinal excitability may display greater vGRF loading rate, however, they may be better able to attenuate the vGRF compared to those with lower corticospinal excitability. Also, this

study did not examine knee extensor moments during walking gait. Previous studies have found that knee extensor moments are reduced following ACL injury, which suggest that the quadricpes are not activating properly during the walking gait cylce.[12,18,22,90,92] Knee extensor moments may provide more insight of the quadriceps are working during the walking gait cycle. A reduced knee extensor moment may be a compensation for lower corticospinal excitability, or the reduced knee extensor moment may be caused by the lower corticospinal excitability. Even though, the participants with higher corticospinal excitability displayed greater vGRF loading rates, they may have normal knee extensor moments which allow them to fully attenuate the vGRF during walking gait. Future studies should consider examining the association between knee extensor moments, AMT, and vGRF loading rates.

5.3 Steady State Gait and AMT

Outcomes during steady state gait may not relate to corticospinal excitability because the rythmic nature of walking may not require high levels of corticomotor excitability. The outcomes we looked at may be more indicative of spinal pathways. Central pattern generators (CPGs) are neural circuits that generate periodic motor commands for rnythmic movements such as locomotion.[116] Although the anatomical details for CPGs are not fully understood, the motor commands have been shown to originate from the spinal cord.[117] Previous research in cats has shown that recovery to the CPGs is possible when a spinal cord lesion is present.[118,119] In both studies,[118,119] the cats had spinal cord lesions manually done by the researchers; the first at T10-T11 was a partial lesion and the second was a complete lesion at the T13-L1 level. The two lesion procedures were separated by a time window that varied between the cats. The two studies found that with locomotive training[118] and without locomotive training[119] the cats were able to display hindlimb locomotive patterns. This suggests that with spinal cord injury the CPGs have

the ability to reorganize to allow for locomotion. Even though the subjects in our study did not have spinal cord injuries, reorganization of the CPGs may explain why AMT is not correlated with EMG onset times and why lower AMT is correlated with higher vGRF rate of loading during walking gait. The CPGs may have reorganized at the level of the spinal cord in the individuals with higher AMT values to allow them to maintain normal gait patterns. Even though the participants with lower corticospinal excitability may have a deficit in the motor cortex, the CPGs in their spinal cord modulate gait patterns that influence the normal vGRF loading rates and EMG onset times during steady state gait. This reorganization may explain why the individuals with less corticospinal excitability did not display greater vGRF rate of loading or prolonged quadriceps EMG onset times during walking gait.

5.4 AMT and EMG Onset Times

As stated earlier, it was expected that a lower AMT would be correlated with longer time between EMG onset and heel strike. This was expected because a lower AMT means that the quadriceps are more excitable, which could suggest that they activate sooner during the gait cylce in preparation for heel strike. This would be a desireable situation because this shows that the corticospinal tract is able to adequatley activate the quadriceps in a timely manner to prepare for heel strike. This early activation of the quadriceps may help to control the vGRF rate of loading that occurs about the knee joint. However, this current study has shown that AMT is not correlated with longer quadriceps EMG onset times. Younger individuals tend to have greater corticospinal excitability and subsequently better reaction time than older participants.[89] However, authors of a previous study concluded that when the participants in both age groups were matched with individuals in their respective age group (young with young and old with old), there was no significant correlation between corticospinal excitability and reaction time.[89]

This is interesting to note becuase this may help to explain why there was no correlation between AMT and quadricpes EMG onset times. Eventhough some individuals may have a higher AMT, they may still have the ability to fully activate their quadriceps in a timely manner to prepare for heel strike during the walking gait cycle. Since it appears that age may affect both corticospinal excitability and reaction time, some individuals with lower corticospinal excitability may still have the ability to activate their quadriceps in a timely manner to prepare for heel strike during the stance phase of gait. The reduced corticospinal excitability may not hinder the ability to activate the quadriceps in preparation for heel strike, therefore, allowing for optimal strategy to attenuate the vGRF occuring at heel strike.

Even though AMT may be altered following ACL injury, individuals who have sustained an ACL injury may have involuntarily developed different neural pathways in their CNS to help compensate for different levels of corticospinal excitability. Previous authors have concluded that there is decreased proprioceptive information in the injured joint following ACL injury, which may lead the CNS to compensate for the decreased input from the proprioceptors through reorganization of the CNS and altered neuromuscular activity.[120-122] Previous research has also shown that following ACL injury there is decreased activation in certain cortical areas and increased activation in other cortical areas.[123] These alterations included diminished activation in several sensorimotor areas and increased activation in the pre-supplementary motor area, posterior secondary somatosensory area, and posterior inferior temporal gyrus.[121] These increases and decreases in activation that occur in several areas of the CNS following ACL injury suggest that even though neural deficits are present following ACL injury, the CNS may upregulate activation in the uninhibited cortical areas to compensate for decreased excitability in the primary motor cortex. Even though having less corticospinal excitability suggests that ACL

injured individuals have deficits in their motor cortex, their CNS may have reorganzied to combat this deficiency to allow them to complete typical tasks. This may help to explain why there is no correlation between AMT and quadricpes EMG onset times. Even though high thresholds may exist in their primary motor cortex, the CNS in these ACL injured patients may have reorganized to allow for earlier activation of their quadriceps during walking gait.

5.5 Clinical Relevance

It is well accepted that gait retraining programs are a vital component of ACL-R rehabilitation protocols.[12,124-126] Furthermore, gait adaptations following ACL-R have been found to be associated with low patient satisfaction as well.[127] It has been shown that individuals who receive specialized gait retraining interventions following ACL injury display better rehabilitative outcomes that those who do not receive gait retraining interventions.[124,128] One study involved perturbation training in conjunction with quadriceps strengthening for gait retraining[128] and the other consisted of feedback training in the form of force driven harmonic oscillators (FDHOs).[124] These studies suggest that even though an individual sustained an ACL injury, he/she is able to obtain normal walking gait patterns when compared to healthy participants. This is promising because although an individual has sustained an ACL injury, with gait retraining and proper rehabilitation, they can return to their pre-injured gait pattern. It was expected that the individuals with greater corticospinal excitability would have lower vGRF rate of loading, however, our study showed that lower AMT values were correlated with greater vGRF rate of loading. This could suggest that the individuals with greater corticospinal excitability are more receptive to gait retraining. Even though the individuals with lower AMT values tended to display greater vGRF rate of loading during walking gait, they may have responded better to gait retraining strategies than the individuals with higher AMT values.

Despite displaying higher loading rates, the individuals with greater corticospinal excitability may have responded better to the gait retraining interventions the underwent and, therefore, obtained walking kinematics that were similar to their pre-injury values.

5.6 Limitations

Our analysis was originally supposed to include eighteen participants, however, some patients were unable to report for session two of the study, and some did not have EMG onset data, so these individuals were removed from the analysis. Only twelve subjects were included in the analysis, which is a small sample size for a study such as this. There was also a wide range of time from surgery for the individuals in this study (10-163 months). The differences in time from surgery may have had an affect on the outcome measures. Those who had a longer time from surgery may have had a longer time to develop their walking gait patterns, and therefore may have had lower vGRF loading rates and faster EMG onset times in preparation for heel strike than those that had undergone surgery closer to the study. A larger cohort of ACL-R individuals with a less variable time post ACL-R may need to be collected to determine the impact of time post injury on the association between EMG onset times and vGRF loading rates. Another limitation was the simplicity of the walking gait trial. Cyclic walking gait trials may not be a good indicator of vGRF rate of loading and EMG onset times when compared to more complex tasks such as stair walking, gait initiation, running, change of direction, or landing from a jump.These more complex activities do not access the CPGs, therefore, they may provide more insight regarding quadriceps EMG onset and vGRF rate of loading. The method for obtaining baseline quadriceps EMG activity may have also been a limitation. Only one static trial was taken for each subject, which may not have truly captured the baseline quadriceps EMG values.

The swing phase of the gait cycle could have also been used to record baseline EMG values for the quadriceps.

5.7 Future Research

Future studies can expand on the current study by including an analysis of the uninjured limb or by including a control group. Perhaps if a control group was included in this study, we would have been able to determine how the vGRF rate of loading, quadriceps EMG onest, and corticospinal excitbality of ACL-R individuals differed compared to healthy individuals. We did not associate AMT and knee extensor moment outcome measures during walking gait. Previous studies have reported the presence of altered knee extensor moments in those who have sustained ACL injuries[12,18,22,90,92] Knee extensor moments may provide more insight about quadriceps function following ACL injury, and it may better explain the vGRF loading rate that occurs at heel strike. Previous research in ACL-D non-copers has shown that these individuals display lower quadricpes EMG amplitudes on the injured limb during weight acceptance of the walking gait cylce.[20] The current study observed EMG onset times in preparation for heel strike, however, future studies could consider observing both quadriceps EMG onset times in prepartation for heel strike and EMG amplitudes during weight acceptance. Future studies should also consider examining the association between AMT and outcome measures asscoiated with gait initiation. Gait initiation appears to be a centrally programmed function,[129] therefore, individuals with less corticospinal excitability may have alterations during gait initiation than those with greater corticospinal excitability. Perhaps there is greater loading rates during the initial steps of gait initiation in those who have lower corticospinal excitability. Over time these increased loading rates may lead to knee joint degeneration. Individuals in this could have also been separated based on time from injury and time from surgery. Evidence has shown that

quadriceps strength deficits are present six months following ACL-R and tend to lessen as time progresses.[130] Separating the individuals in this study into groups based on time since surgery may be a better representation of AMT, vGRF rate of loading, and quadriceps EMG onset times. This study only examined walking gait trials; future studies should consider examining quadriceps EMG onset times and vGRF rate of loading during more complex tasks such as stair walking, obstacle navigations, running, change of direction, or landing from a jump. Research has shown that vGRF loading rates increase during stair walking[26] and vGRF are greater during running when compared to walking.[131] The above studies[26,129] indicate that walking gait trials may not fully capture the biomechanical adaptations that occur following ACL-R. The tasks of obstacle navigation, change of direction, and landing from a jump also require conscious thought, therefore, the individuals with lower lower corticospinal excitability may display greater loading rates. Over time the higher loading rates that occur during these tasks may lead to knee joint degeneration. Futhermore, it was shown that individuals that undergo ACL-R have a greater relative risk of developing knee OA than those who choose to remain ACL-D.[60] Individuals undergoing ACL-R tend to return to their previous level of activity (ie athletics), while those who remain ACL-D modify there activity levels. Athletic events require higher intenstity actions than walking, so if the ACL-R individual has lingering quadriceps deficits, they may develop OA at an accelerated rate than an individual that has chosen to modify their activies.

5.8 Conclusion

This study found that there is a signifcant negative correlation between AMT and vGRF rate of loading during a walking gait trial, which means that individulas with higher corticospinal excitability display higher loading rates and individuals with lower corticospinal excitability display lower loading rates. Furthermore, there was no association between AMT and quadriceps

EMG onset times during a walking gait trial. Therefore, lower corticospinal excitability is not associated with longer quadriceps EMG onset times or lower vGRF loading rates during a walking gait trial in individuals who have undergone unilateral ACL-R.

REFERENCES

1. Griffin LY, Albohm MJ, Arendt EA, et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. *The American journal of sports medicine.* Sep 2006;34(9):1512-1532.

2. Csintalan RP, Inacio MC, Funahashi TT. Incidence rate of anterior cruciate ligament reconstructions. *The Permanente journal.* Summer 2008;12(3):17-21.

3. Scanlan SF, Chaudhari AM, Dyrby CO, Andriacchi TP. Differences in tibial rotation during walking in ACL reconstructed and healthy contralateral knees. *Journal of biomechanics.* Jun 18 2010;43(9):1817-1822.

4. Nakamura S, Kobayashi M, Asano T, Arai R, Nakagawa Y, Nakamura T. Image-matching technique can detect rotational and AP instabilities in chronic ACL-deficient knees. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* Dec 2011;19 Suppl 1:S69-76.

5. Chmielewski TL, Stackhouse S, Axe MJ, Snyder-Mackler L. A prospective analysis of incidence and severity of quadriceps inhibition in a consecutive sample of 100 patients with complete acute anterior cruciate ligament rupture. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Sep 2004;22(5):925-930.

6. Hart JM, Pietrosimone B, Hertel J, Ingersoll CD. Quadriceps activation following knee injuries: a systematic review. *Journal of athletic training.* Jan-Feb 2010;45(1):87-97.

7. Hopkins JT IC. arthrogenic muscle inhibition: a limiting factor in joint rehabilitation. *Journal of Sport and Rehabilitation.* 2000;9:135-159.

8. Palmieri-Smith RM, Thomas AC. A neuromuscular mechanism of posttraumatic osteoarthritis associated with ACL injury. *Exercise and sport sciences reviews.* Jul 2009;37(3):147-153.

9. Lohmander LS, Ostenberg A, Englund M, Roos H. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury. *Arthritis and rheumatism.* Oct 2004;50(10):3145-3152.

10. Knutson K, Lewold S, Robertsson O, Lidgren L. The Swedish knee arthroplasty register. A nation-wide study of 30,003 knees 1976-1992. *Acta orthopaedica Scandinavica.* Aug 1994;65(4):375-386.

11. Adachi N, Ochi M, Uchio Y, Iwasa J, Ryoke K, Kuriwaka M. Mechanoreceptors in the anterior cruciate ligament contribute to the joint position sense. *Acta orthopaedica Scandinavica.* Jun 2002;73(3):330-334.

12. Lewek M, Rudolph K, Axe M, Snyder-Mackler L. The effect of insufficient quadriceps strength on gait after anterior cruciate ligament reconstruction. *Clinical biomechanics (Bristol, Avon).* Jan 2002;17(1):56-63.

13. Lepley AS, Ericksen HM, Sohn DH, Pietrosimone BG. Contributions of neural excitability and voluntary activation to quadriceps muscle strength following anterior cruciate ligament reconstruction. *The Knee.* Jun 2014;21(3):736-742.

14. Hallet M. Transcranial magnetic stimulation and the human brain. *Nature.* 2000;2000.

15. Plowman-Prine EK, Triggs WJ, Malcolm MP, Rosenbek JC. Reliability of transcranial magnetic stimulation for mapping swallowing musculature in the human motor cortex. *Clinical neurophysiology : official journal of the International Federation of Clinical Neurophysiology.* Oct 2008;119(10):2298-2303.

16. Pietrosimone BG, Lepley AS, Ericksen HM, Clements A, Sohn DH, Gribble PA. Neural Excitability Alterations After Anterior Cruciate Ligament Reconstruction. *Journal of athletic training.* Apr 6 2015.

17. Knoll Z, Kiss RM, Kocsis L. Gait adaptation in ACL deficient patients before and after anterior cruciate ligament reconstruction surgery. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology.* Jun 2004;14(3):287-294.

18. Rudolph KS, Eastlack ME, Axe MJ, Snyder-Mackler L. 1998 Basmajian Student Award Paper: Movement patterns after anterior cruciate ligament injury: a comparison of patients who compensate well for the injury and those who require operative stabilization. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology.* Dec 1998;8(6):349-362.

19. Alkjaer T, Simonsen EB, Jorgensen U, Dyhre-Poulsen P. Evaluation of the walking pattern in two types of patients with anterior cruciate ligament deficiency: copers and non-copers. *European journal of applied physiology.* May 2003;89(3-4):301-308.

20. Hurd WJ, Snyder-Mackler L. Knee instability after acute ACL rupture affects movement patterns during the mid-stance phase of gait. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Oct 2007;25(10):1369-1377.

21. Berchuck M, Andriacchi TP, Bach BR, Reider B. Gait adaptations by patients who have a deficient anterior cruciate ligament. *The Journal of bone and joint surgery. American volume.* Jul 1990;72(6):871-877.

22. Gardinier ES, Manal K, Buchanan TS, Snyder-Mackler L. Gait and neuromuscular asymmetries after acute anterior cruciate ligament rupture. *Medicine and science in sports and exercise.* Aug 2012;44(8):1490-1496.

23. Herzog W, Longino D, Clark A. The role of muscles in joint adaptation and degeneration. *Langenbeck's archives of surgery / Deutsche Gesellschaft fur Chirurgie.* Oct 2003;388(5):305-315.

24. Hurley MV. The role of muscle weakness in the pathogenesis of osteoarthritis. *Rheumatic diseases clinics of North America.* May 1999;25(2):283-298, vi.

25. Mundermann A, Dyrby CO, Andriacchi TP. Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. *Arthritis and rheumatism.* Sep 2005;52(9):2835-2844.

26. Liikavainio T, Isolehto J, Helminen HJ, et al. Loading and gait symmetry during level and stair walking in asymptomatic subjects with knee osteoarthritis: importance of quadriceps femoris in reducing impact force during heel strike? *The Knee.* Jun 2007;14(3):231-238.

27. Pietrosimone BG, Hertel J, Ingersoll CD, Hart JM, Saliba SA. Voluntary quadriceps activation deficits in patients with tibiofemoral osteoarthritis: a meta-analysis. *PM & R : the journal of injury, function, and rehabilitation.* Feb 2011;3(2):153-162; quiz 162.

28. Otzel DM, Chow JW, Tillman MD. Long-term deficits in quadriceps strength and activation following anterior cruciate ligament reconstruction. *Physical therapy in sport : official journal of the Association of Chartered Physiotherapists in Sports Medicine.* Feb 21 2014.

29. Hassan BS, Mockett S, Doherty M. Static postural sway, proprioception, and maximal voluntary quadriceps contraction in patients with knee osteoarthritis and normal control subjects. *Annals of the rheumatic diseases.* Jun 2001;60(6):612-618.

30. Hurley MV. The effects of joint damage on muscle function, proprioception and rehabilitation. *Manual therapy.* Feb 1997;2(1):11-17.

31. O'Reilly SC, Jones A, Muir KR, Doherty M. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. *Annals of the rheumatic diseases.* Oct 1998;57(10):588-594.

32. Stackhouse SK, Dean JC, Lee SC, Binder-MacLeod SA. Measurement of central activation failure of the quadriceps femoris in healthy adults. *Muscle & nerve.* Nov 2000;23(11):1706-1712.

33. Lewek MD, Rudolph KS, Snyder-Mackler L. Quadriceps femoris muscle weakness and activation failure in patients with symptomatic knee osteoarthritis. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Jan 2004;22(1):110-115.

34. Hart JM, Fritz JM, Kerrigan DC, Saliba EN, Gansneder BM, Ingersoll CD. Reduced quadriceps activation after lumbar paraspinal fatiguing exercise. *Journal of athletic training.* Jan-Mar 2006;41(1):79-86.

35. Keays SL, Newcombe PA, Bullock-Saxton JE, Bullock MI, Keays AC. Factors involved in the development of osteoarthritis after anterior cruciate ligament surgery. *The American journal of sports medicine.* Mar 2010;38(3):455-463.

36. Roos EM. Joint injury causes knee osteoarthritis in young adults. *Current opinion in rheumatology.* Mar 2005;17(2):195-200.

37. von Porat A, Roos EM, Roos H. High prevalence of osteoarthritis 14 years after an anterior cruciate ligament tear in male soccer players: a study of radiographic and patient relevant outcomes. *Annals of the rheumatic diseases.* Mar 2004;63(3):269-273.

38. Slemenda C, Brandt KD, Heilman DK, et al. Quadriceps weakness and osteoarthritis of the knee. *Annals of internal medicine.* Jul 15 1997;127(2):97-104.

39. Strand T, Molster A, Hordvik M, Krukhaug Y. Long-term follow-up after primary repair of the anterior cruciate ligament: clinical and radiological evaluation 15-23 years postoperatively. *Archives of orthopaedic and trauma surgery.* May 2005;125(4):217-221.

40. Struewer J, Frangen TM, Ishaque B, et al. Knee function and prevalence of osteoarthritis after isolated anterior cruciate ligament reconstruction using bone-patellar tendon-bone graft: long-term follow-up. *International orthopaedics.* Jan 2012;36(1):171-177.

41. Hart JM, Turman KA, Diduch DR, Hart JA, Miller MD. Quadriceps muscle activation and radiographic osteoarthritis following ACL revision. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* Apr 2011;19(4):634-640.

42. Metcalfe AJ, Stewart C, Postans N, Dodds AL, Holt CA, Roberts AP. The effect of osteoarthritis of the knee on the biomechanics of other joints in the lower limbs. *The bone & joint journal.* Mar 2013;95-b(3):348-353.

43. Hinman RS, Bennell KL, Metcalf BR, Crossley KM. Delayed onset of quadriceps activity and altered knee joint kinematics during stair stepping in individuals with knee osteoarthritis. *Archives of physical medicine and rehabilitation.* Aug 2002;83(8):1080-1086.

44. Andriacchi TP, Koo S, Scanlan SF. Gait mechanics influence healthy cartilage morphology and osteoarthritis of the knee. *The Journal of bone and joint surgery. American volume.* Feb 2009;91 Suppl 1:95-101.

45. Butler DL, Noyes FR, Grood ES. Ligamentous restraints to anterior-posterior drawer in the human knee. A biomechanical study. *The Journal of bone and joint surgery. American volume.* Mar 1980;62(2):259-270.

46. Kiapour AM, Murray MM. Basic science of anterior cruciate ligament injury and repair. *Bone & joint research.* 2014;3(2):20-31.

47. Smith MA, Smith WT, Kosko P. Anterior cruciate ligament tears: reconstruction and rehabilitation. *Orthopaedic nursing / National Association of Orthopaedic Nurses.* Jan-Feb 2014;33(1):14-24.

48. Schultz RA, Miller DC, Kerr CS, Micheli L. Mechanoreceptors in human cruciate ligaments. A histological study. *The Journal of bone and joint surgery. American volume.* Sep 1984;66(7):1072-1076.

49. Zimny ML. Mechanoreceptors in articular tissues. *The American journal of anatomy.* May 1988;182(1):16-32.

50. Schutte MJ, Dabezies EJ, Zimny ML, Happel LT. Neural anatomy of the human anterior cruciate ligament. *The Journal of bone and joint surgery. American volume.* Feb 1987;69(2):243-247.

51. Baumeister J, Reinecke K, Weiss M. Changed cortical activity after anterior cruciate ligament reconstruction in a joint position paradigm: an EEG study. *Scandinavian journal of medicine & science in sports.* Aug 2008;18(4):473-484.

52. Konishi Y, Fukubayashi T, Takeshita D. Mechanism of quadriceps femoris muscle weakness in patients with anterior cruciate ligament reconstruction. *Scandinavian journal of medicine & science in sports.* Dec 2002;12(6):371-375.

53. Konishi Y, Fukubayashi T, Takeshita D. Possible mechanism of quadriceps femoris weakness in patients with ruptured anterior cruciate ligament. *Medicine and science in sports and exercise.* Sep 2002;34(9):1414-1418.

54. Ingersoll CD, Grindstaff TL, Pietrosimone BG, Hart JM. Neuromuscular consequences of anterior cruciate ligament injury. *Clinics in sports medicine.* Jul 2008;27(3):383-404, vii.

55. Kostogiannis I, Ageberg E, Neuman P, Dahlberg L, Friden T, Roos H. Activity level and subjective knee function 15 years after anterior cruciate ligament injury: a prospective, longitudinal study of nonreconstructed patients. *The American journal of sports medicine.* Jul 2007;35(7):1135-1143.

56. Konishi Y, Konishi H, Fukubayashi T. Gamma loop dysfunction in quadriceps on the contralateral side in patients with ruptured ACL. *Medicine and science in sports and exercise.* Jun 2003;35(6):897-900.

57. Richardson MS, Cramer JT, Bemben DA, Shehab RL, Glover J, Bemben MG. Effects of age and ACL reconstruction on quadriceps gamma loop function. *Journal of geriatric physical therapy (2001).* 2006;29(1):28-34.

58. Commission MAS. Youth Sports Statistics. 2013; http://www.statisticbrain.com/youth-sports-statistics/, 2014.

59. Ingram JG, Fields SK, Yard EE, Comstock RD. Epidemiology of knee injuries among boys and girls in US high school athletics. *The American journal of sports medicine.* Jun 2008;36(6):1116-1122.

60. Ajuied A, Wong F, Smith C, et al. Anterior Cruciate Ligament Injury and Radiologic Progression of Knee Osteoarthritis: A Systematic Review and Meta-analysis. *The American journal of sports medicine.* Nov 8 2013.

61. Dunn WR, Spindler KP. Predictors of activity level 2 years after anterior cruciate ligament reconstruction (ACLR): a Multicenter Orthopaedic Outcomes Network (MOON) ACLR cohort study. *The American journal of sports medicine.* Oct 2010;38(10):2040-2050.

62. Nuki G. Osteoarthritis: a problem of joint failure. *Zeitschrift fur Rheumatologie.* Jun 1999;58(3):142-147.

63. Eyre DR. Collagens and cartilage matrix homeostasis. *Clinical orthopaedics and related research.* Oct 2004(427 Suppl):S118-122.

64. Hunter DJ. Osteoarthritis. *Best practice & research. Clinical rheumatology.* Dec 2011;25(6):801-814.

65. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Annals of the rheumatic diseases.* Dec 1957;16(4):494-502.

66. Luc BA GP, Pietrosimone B. Osteoarthritis Prevalence Following ACL Injury & Reconstruction: A Numbers Needed to Treat Analysis. *Journal of Athletic Training. In Press.* 2014.

67. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. *Comprehensive Physiology.* Apr 2012;2(2):1143-1211.

68. Kim HS, Seon JK, Jo AR. Current Trends in Anterior Cruciate Ligament Reconstruction. *Knee surgery & related research.* Dec 2013;25(4):165-173.

69. Ardern CL, Webster KE, Taylor NF, Feller JA. Return to sport following anterior cruciate ligament reconstruction surgery: a systematic review and meta-analysis of the state of play. *British journal of sports medicine.* Jun 2011;45(7):596-606.

70. Pietrosimone BG, Lepley AS, Ericksen HM, Gribble PA, Levine J. Quadriceps strength and corticospinal excitability as predictors of disability after anterior cruciate ligament reconstruction. *Journal of sport rehabilitation.* Feb 2013;22(1):1-6.

71. Drechsler WI, Cramp MC, Scott OM. Changes in muscle strength and EMG median frequency after anterior cruciate ligament reconstruction. *European journal of applied physiology.* Dec 2006;98(6):613-623.

72. Urbach D, Nebelung W, Becker R, Awiszus F. Effects of reconstruction of the anterior cruciate ligament on voluntary activation of quadriceps femoris a prospective twitch interpolation study. *The Journal of bone and joint surgery. British volume.* Nov 2001;83(8):1104-1110.

73. Kuenze CM, Hertel J, Weltman A, Diduch D, Saliba SA, Hart JM. Persistent neuromuscular and corticomotor quadriceps asymmetry after anterior cruciate ligament reconstruction. *Journal of athletic training.* Mar 2015;50(3):303-312.

74. Elboim-Gabyzon M, Rozen N, Laufer Y. Quadriceps femoris muscle fatigue in patients with knee osteoarthritis. *Clinical interventions in aging.* 2013;8:1071-1077.

75. Palmieri RM, Weltman A, Edwards JE, et al. Pre-synaptic modulation of quadriceps arthrogenic muscle inhibition. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* Jul 2005;13(5):370-376.

76. Rice DA, McNair PJ. Quadriceps arthrogenic muscle inhibition: neural mechanisms and treatment perspectives. *Seminars in arthritis and rheumatism.* Dec 2010;40(3):250-266.

77. Rice DA, McNair PJ, Lewis GN. Mechanisms of quadriceps muscle weakness in knee joint osteoarthritis: the effects of prolonged vibration on torque and muscle activation in osteoarthritic and healthy control subjects. *Arthritis research & therapy.* 2011;13(5):R151.

78. Heroux ME, Tremblay F. Corticomotor excitability associated with unilateral knee dysfunction secondary to anterior cruciate ligament injury. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* Sep 2006;14(9):823-833.

79. Lepley AS, Gribble PA, Thomas AC, Tevald MA, Sohn DH, Pietrosimone BG. Quadriceps neural alterations in anterior cruciate ligament reconstructed patients: A 6-month longitudinal investigation. *Scandinavian journal of medicine & science in sports.* Feb 18 2015.

80. Corneal SF, Butler AJ, Wolf SL. Intra- and intersubject reliability of abductor pollicis brevis muscle motor map characteristics with transcranial magnetic stimulation. *Archives of physical medicine and rehabilitation.* Aug 2005;86(8):1670-1675.

81. Zehr EP. Considerations for use of the Hoffmann reflex in exercise studies. *European journal of applied physiology.* Apr 2002;86(6):455-468.

82. Barker AT, Jalinous R, Freeston IL. Non-invasive magnetic stimulation of human motor cortex. *Lancet.* May 11 1985;1(8437):1106-1107.

83. Chen R. Studies of human motor physiology with transcranial magnetic stimulation. *Muscle & nerve. Supplement.* 2000;9:S26-32.

84. Lefebvre R, Pepin A, Louis PF, Boucher JP. Reliability of the motor evoked potentials elicited through magnetic stimulation at three sites. *Journal of manipulative and physiological therapeutics.* Feb 2004;27(2):97-102.

85. Martin PG, Hudson AL, Gandevia SC, Taylor JL. Reproducible measurement of human motoneuron excitability with magnetic stimulation of the corticospinal tract. *Journal of neurophysiology.* Jul 2009;102(1):606-613.

86. Goodall S, Romer LM, Ross EZ. Voluntary activation of human knee extensors measured using transcranial magnetic stimulation. *Experimental physiology.* Sep 2009;94(9):995-1004.

87. van Hedel HJ, Murer C, Dietz V, Curt A. The amplitude of lower leg motor evoked potentials is a reliable measure when controlled for torque and motor task. *Journal of neurology.* Aug 2007;254(8):1089-1098.

88. Cuypers K, Thijs H, Meesen RL. Optimization of the transcranial magnetic stimulation protocol by defining a reliable estimate for corticospinal excitability. *PloS one.* 2014;9(1):e86380.

89. Cuypers K, Thijs H, Duque J, Swinnen SP, Levin O, Meesen RL. Age-related differences in corticospinal excitability during a choice reaction time task. *Age (Dordrecht, Netherlands).* Oct 2013;35(5):1705-1719.

90. Hart JM, Ko JW, Konold T, Pietrosimone B. Sagittal plane knee joint moments following anterior cruciate ligament injury and reconstruction: a systematic review. *Clinical biomechanics (Bristol, Avon).* May 2010;25(4):277-283.

91. Hirokawa S, Solomonow M, Lu Y, Lou ZP, D'Ambrosia R. Anterior-posterior and rotational displacement of the tibia elicited by quadriceps contraction. *The American journal of sports medicine.* May-Jun 1992;20(3):299-306.

92. Gokeler A, Benjaminse A, van Eck CF, Webster KE, Schot L, Otten E. Return of normal gait as an outcome measurement in acl reconstructed patients. A systematic review. *International journal of sports physical therapy.* Aug 2013;8(4):441-451.

93. Wexler G, Hurwitz DE, Bush-Joseph CA, Andriacchi TP, Bach BR, Jr. Functional gait adaptations in patients with anterior cruciate ligament deficiency over time. *Clinical orthopaedics and related research.* Mar 1998(348):166-175.

94. Daniel DM, Stone ML, Dobson BE, Fithian DC, Rossman DJ, Kaufman KR. Fate of the ACL-injured patient. A prospective outcome study. *The American journal of sports medicine.* Sep-Oct 1994;22(5):632-644.

95. Palmieri-Smith RM, Kreinbrink J, Ashton-Miller JA, Wojtys EM. Quadriceps inhibition induced by an experimental knee joint effusion affects knee joint mechanics during a single-legged drop landing. *The American journal of sports medicine.* Aug 2007;35(8):1269-1275.

96. Radin EL, Martin RB, Burr DB, Caterson B, Boyd RD, Goodwin C. Effects of mechanical loading on the tissues of the rabbit knee. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* 1984;2(3):221-234.

97. Winters JD, Rudolph KS. Quadriceps rate of force development affects gait and function in people with knee osteoarthritis. *European journal of applied physiology.* Feb 2014;114(2):273-284.

98. Aagaard P, Simonsen EB, Andersen JL, Magnusson P, Dyhre-Poulsen P. Increased rate of force development and neural drive of human skeletal muscle following resistance training. *Journal of applied physiology (Bethesda, Md. : 1985).* Oct 2002;93(4):1318-1326.

99. Oliveira FB, Oliveira AS, Rizatto GF, Denadai BS. Resistance training for explosive and maximal strength: effects on early and late rate of force development. *Journal of sports science & medicine.* 2013;12(3):402-408.

100. Maffiuletti NA, Bizzini M, Widler K, Munzinger U. Asymmetry in quadriceps rate of force development as a functional outcome measure in TKA. *Clinical orthopaedics and related research.* Jan 2010;468(1):191-198.

101. Kamen G. Electromyographic Kinesiology. *Research Methods in Biomechanics*. Champaign, IL: Human Kinetics Publ.; 2004.

102. L. RE, M W, K Y. The heel strike transient, its relationship with the angular velocity of the shank, and effects of quadriceps paralysis. *Advances in bioengineering. New York: American Society of Mechanical Engineering.* 1986:121-123.

103. Verdini F, Marcucci M, Benedetti MG, Leo T. Identification and characterisation of heel strike transient. *Gait & posture.* Aug 2006;24(1):77-84.

104. Hunt MA, Hinman RS, Metcalf BR, et al. Quadriceps strength is not related to gait impact loading in knee osteoarthritis. *The Knee.* Aug 2010;17(4):296-302.

105. Noehren B, Wilson H, Miller C, Lattermann C. Long-term gait deviations in anterior cruciate ligament-reconstructed females. *Medicine and science in sports and exercise.* Jul 2013;45(7):1340-1347.

106. Berchuck M AT, Bach BR, Reider B. Gait adapta- tions by patients who have a deficient anterior cruciate ligament. *J Bone Joint Surg Am A* 1990;72:871-877.

107. Andriacchi TP BD. Functional testing in the anterior cruciate ligament-deficient knee. *Clin Orthop.* 1993;288:40-47.

108. Hertel J. Keep it simple: study design nomenclature in research article abstracts. *Journal of athletic training.* May-Jun 2010;45(3):213-214.

109. Lindstrom M, Fellander-Tsai L, Wredmark T, Henriksson M. Adaptations of gait and muscle activation in chronic ACL deficiency. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA.* Jan 2010;18(1):106-114.

110. Pietrosimone BG, Ingersoll CD. Focal knee joint cooling increases the quadriceps central activation ratio. *Journal of sports sciences.* Jun 2009;27(8):873-879.

111. Norte GE, Pietrosimone BG, Hart JM, Hertel J, Ingersoll CD. Relationship between transcranial magnetic stimulation and percutaneous electrical stimulation in determining the quadriceps central activation ratio. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists.* Dec 2010;89(12):986-996.

112. Mukaka MM. Statistics corner: A guide to appropriate use of correlation coefficient in medical research. *Malawi medical journal : the journal of Medical Association of Malawi.* Sep 2012;24(3):69-71.

113. Gardinier ES, Manal K, Buchanan TS, Snyder-Mackler L. Altered loading in the injured knee after ACL rupture. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Mar 2013;31(3):458-464.

114. Hagio S, Fukuda M, Kouzaki M. Identification of muscle synergies associated with gait transition in humans. *Frontiers in human neuroscience.* 2015;9:48.

115. Mikesky AE, Meyer A, Thompson KL. Relationship between quadriceps strength and rate of loading during gait in women. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Mar 2000;18(2):171-175.

116. Kuo AD. The relative roles of feedforward and feedback in the control of rhythmic movements. *Motor control.* Apr 2002;6(2):129-145.

117. Grillner S, Wallen P. Central pattern generators for locomotion, with special reference to vertebrates. *Annual review of neuroscience.* 1985;8:233-261.

118. Barriere G, Leblond H, Provencher J, Rossignol S. Prominent role of the spinal central pattern generator in the recovery of locomotion after partial spinal cord injuries. *The Journal of neuroscience : the official journal of the Society for Neuroscience.* Apr 9 2008;28(15):3976-3987.

119. Martinez M, Delivet-Mongrain H, Leblond H, Rossignol S. Recovery of hindlimb locomotion after incomplete spinal cord injury in the cat involves spontaneous compensatory changes within the spinal locomotor circuitry. *Journal of neurophysiology.* Oct 2011;106(4):1969-1984.

120. Valeriani M, Restuccia D, Di Lazzaro V, Franceschi F, Fabbriciani C, Tonali P. Clinical and neurophysiological abnormalities before and after reconstruction of the anterior cruciate ligament of the knee. *Acta neurologica Scandinavica.* May 1999;99(5):303-307.

121. Courtney C, Rine RM, Kroll P. Central somatosensory changes and altered muscle synergies in subjects with anterior cruciate ligament deficiency. *Gait & posture.* Aug 2005;22(1):69-74.

122. Valeriani M, Restuccia D, Di Lazzaro V, Franceschi F, Fabbriciani C, Tonali P. Central nervous system modifications in patients with lesion of the anterior cruciate ligament of the knee. *Brain : a journal of neurology.* Oct 1996;119 (Pt 5):1751-1762.

123. Kapreli E, Athanasopoulos S, Gliatis J, et al. Anterior cruciate ligament deficiency causes brain plasticity: a functional MRI study. *The American journal of sports medicine.* Dec 2009;37(12):2419-2426.

124. Decker MJ, Torry MR, Noonan TJ, Sterett WI, Steadman JR. Gait retraining after anterior cruciate ligament reconstruction. *Archives of physical medicine and rehabilitation.* May 2004;85(5):848-856.

125. Adams D, Logerstedt DS, Hunter-Giordano A, Axe MJ, Snyder-Mackler L. Current concepts for anterior cruciate ligament reconstruction: a criterion-based rehabilitation progression. *The Journal of orthopaedic and sports physical therapy.* Jul 2012;42(7):601-614.

126. Wilk KE, Macrina LC, Cain EL, Dugas JR, Andrews JR. Recent advances in the rehabilitation of anterior cruciate ligament injuries. *The Journal of orthopaedic and sports physical therapy.* Mar 2012;42(3):153-171.

127. Kocher MS, Steadman JR, Briggs K, Zurakowski D, Sterett WI, Hawkins RJ. Determinants of patient satisfaction with outcome after anterior cruciate ligament reconstruction. *The Journal of bone and joint surgery. American volume.* Sep 2002;84-a(9):1560-1572.

128. Hartigan E, Axe MJ, Snyder-Mackler L. Perturbation training prior to ACL reconstruction improves gait asymmetries in non-copers. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society.* Jun 2009;27(6):724-729.

129. Brunt D, Lafferty MJ, McKeon A, Goode B, Mulhausen C, Polk P. Invariant characteristics of gait initiation. *American journal of physical medicine & rehabilitation / Association of Academic Physiatrists.* Aug 1991;70(4):206-212.

130. Palmieri-Smith RM, Thomas AC, Wojtys EM. Maximizing quadriceps strength after ACL reconstruction. *Clinics in sports medicine.* Jul 2008;27(3):405-424, vii-ix.

131. Keller TS, Weisberger AM, Ray JL, Hasan SS, Shiavi RG, Spengler DM. Relationship between vertical ground reaction force and speed during walking, slow jogging, and running. *Clinical biomechanics (Bristol, Avon).* Jul 1996;11(5):253-259.