The Effects of Transcranial Direct Current Stimulation on Quadriceps Muscle Function in Individuals with a History of Anterior Cruciate Ligament Reconstruction

Justin L. Rush
justin.rush@uconn.edu

Recommended Citation
https://opencommons.uconn.edu/gs_theses/1380
The Effects of Transcranial Direct Current Stimulation on Quadriceps Muscle Function in Individuals with a History of Anterior Cruciate Ligament Reconstruction

Justin Rush

B.S., Westfield State University 2017

A Thesis
Submitted in Partial Fulfillment of the Requirements for the Degree of Masters of Science
At the
University of Connecticut
2019
The Effects of Transcranial Direct Current Stimulation on Patients with a History of Anterior Cruciate Ligament Reconstruction

Presented By

Justin Rush, B.S.

Major Advisor:

Adam S. Lepley

Associate Advisor:

Lindsey K. Lepley

Associate Advisor:

Lindsay J. DiStefano

University of Connecticut
2019
Acknowledgements

Dr. DiStefano – Thank you for taking the time to be a part of my committee. All of the input you provided was extremely helpful. You really walked me through a lot of my results and had me interpret them from a different view. I greatly appreciate all of your help and I look forward to seeing what you and Emma have in store for your future research!

Eastern – Thank you to all of the Eastern staff that welcomed me with open arms over the last year. You allowed me to get the professional experience I wanted while simultaneously developing great relationships with all of my fellow colleagues. I am very happy I got to spend the last year with such an awesome staff! I will truly miss working with everyone!

Julie and Steve – Over the last two years, you both have really taken me under your wings. You both showed me the ropes in the lab and really helped shaped me into the growing researcher in am today. You both were very patient with me and always pointed me in the right direction when I needed some guidance. Hopefully we can all collaborate in the future and make an impact in our field together.

Emma – Thank you for being my best friend in this program! With a whopping cohort of two students we didn’t really have a choice but to get as close as we did. I knew I could always count on you whenever I needed someone to talk to and could count on you for genuinely honest advice. It is going to be hard to find a replacement for you out in Toledo, but I know we will always have a great friendship for years to come!

Dr. Lindsey Lepley – Thank you for being such an awesome co-advisor over the last couple years. You always knew what to say to give me an extra push when I needed it. I always felt very comfortable discussing anything with you academically or personally. You are one of the smartest people I have had the pleasure of working with and the University of Michigan is very lucky to be adding such a clever mind to their research team. I am looking forward to our paths crossing again!

Dr. Adam Lepley – I have learned so much from you since I started at UConn. I cannot thank you enough for all of your help and I don’t know where I would be without your guidance and support. You completely understood that I was essentially starting from scratch in the field of research and you were more than patient with me. I never was afraid to express my feelings about different aspects of this project and you always made me feel like my input was wanted and valuable. You are a great mentor to me and I know I can reach out to you for advice in the future. I know that we can look back on this project and be proud of what we have done together! Thank you for EVERYTHING!
# TABLE OF CONTENTS

**CHAPTER I: REVIEW OF LITERATURE**

I.a. Anterior Cruciate Ligament Tears

I.b. Clinical Outcomes Following Anterior Cruciate Ligament Reconstruction

I.c. Quadriceps Strength Deficits After ACL Tear/Reconstruction

I.d. Transcranial Direct Current Stimulation

I.e. Conclusion of Literature Review

**REFERENCES**

**CHAPTER II: INTRODUCTION**

**CHAPTER III: METHODS**

Participants

Protocol

Quadriceps Strength Testing and Volitional Activation

Electromyographic (EMG) Testing

Self-Reported Questionnaires

Transcranial Direct Current Stimulation

Statistical Analyses

**CHAPTER IV: RESULTS**

**CHAPTER V: DISCUSSION**

Limitations

Conclusions

**APPENDIX**
CHAPTER I: REVIEW OF LITERATURE

1.a. Anterior Cruciate Ligament Tears

Anterior cruciate ligament (ACL) injuries are among the most common sports related injuries. Each year, there are an estimated 80,000 to 250,000 ACL injuries that occur.\(^1\) In the United States, every 84 per 100,000 (and 78 per 100,000 in Sweden) people will suffer trauma to the ACL.\(^1,2\) Young athletes from the age of 15-25 compose up to 50% of ACL injuries each year.\(^1\) In a study composed by Dragoo et al 2012, data was collected on the prevalence of ACL injury during the 2004-2005 and 2008-2009 National Collegiate Athletic Association football.\(^3\) In NCAA football alone, there were 318 ACL injuries during these two seasons.\(^3\) This specific injury occurred in 1.42 incidences for every 10,000 athletic exposures.\(^3\) Injury rates during games were 8.06 injuries per 10,000 athletic exposures.\(^3\) The majority of ACL injuries have a non-contact mechanism. The common mechanism of injury is produced with a non-contact valgus force combined with an internal rotation of the tibia.\(^4\) The patient will usually report a “pop” when the injury occurs. The early occurrence of swelling and inability to continue participation in the game or practice are key signs an ACL injury.\(^5\) In some cases, athletes do not need to get surgical intervention right away. Acute management of an ACL tear can focus on reducing the swelling within the joint with the RICE (rest, ice, compression, and elevation) technique and non-steroidal anti-inflammatory drugs, regaining normal range of motion of the knee joint, developing quadriceps control, and restoring normal gait patterns.\(^5\) All of these treatments for a non-surgical patient can take on average two to four weeks from the time of injury.\(^5\) Surgical treatment is indicated if the patient has a sensation of instability in normal activities of daily living, or
wants to resume activities that involve cutting and pivoting. Currently, there has been worldwide acceptance of arthroscopically assisted ACL reconstruction (ACLR) with the use of tendon grafts. Currently, hamstring-tendons (semitendinosus), bone-patellar-tendon-bone complexes and quadriceps tendon-bone complexes are frequently used grafts. The procedure consists of using the grafts through tunnels drilled into the tibia and femur at insertion point of the ACL to approximate normal anatomy, with the goal of eliminating ACL instability. Every year, there are about 100,000 reconstructions reported. In Sweden, approximately 36% of males and 37% of females underwent the reconstructive surgery. Of these reconstruction patients, 48% of them were under the age of 30 years old.

1.b. Clinical Outcomes Following Anterior Cruciate Ligament Reconstruction

Return to Sport and Re-injury Outcomes

After reconstruction surgery of the ACL, the patient outcomes tend to vary in terms of rehabilitation and return to sport. In the athletic population, 82% of the patients who undergo ACLR return to sport participation. However, only 63% of the patients return to pre-injury level of sport participation, and only 44% return to participation in competitive sports. In a study conducted by Burland et al, the investigation team attempted to examine the psychosocial factors that influence an individual's decision to return to sport after at least 1 year after ACL. These authors concluded that a decision to return to sport is influenced by the participants' lack of confidence, self-limiting factors, expectations about recovery, and intrinsic personal characteristics.
Returning to sport at pre-injury competition level is the main goal with rehabilitation. However, returning to competitive sport involving side stepping, pivoting, or jumping can lead to increased risk of re-injury. In a study by Salmon et al, 612 patients were studied after being treated with ACLR. Out of this large cohort, 72 (11.7%) of the patients had suffered a graft rupture or a contralateral injury to their ACL. Salmon et al, identified that there was a higher risk of a graft tear with a contact mechanism of injury where are just retuning to cutting and jumping sports put the contralateral knee at a greater risk of tearing the patients ACL. Also, an additional 12% of the patients that were examined had a repeat ACL injury within the first five years after ACLR.

Other studies have taken interest into factors that help predict a second ACL injury after the initial ACLR. However, there still seems to be some ambiguity to the main factors that influence a second tear. A second ACL tear can either occur on the same side or on the contralateral side after ACLR. There have been discussions about which type of tear occurs more often and how long after surgery the tear occurs. In a previous study, there was a comparison of ACLR patients that visited a specialist two years after the surgery. There was an even split between the contralateral tears and the ipsilateral tears, each making up 3% of the disrupted ACL population. In another study, there was a longer follow-up period of five years, which showed to have a greater disruption of the contralateral knee. This study showed that over the extended period of time, there was about double the amount of contralateral ACL injuries compared to the ipsilateral graft injuries. Wright et al found that over the
course of five years, there was an annual rate of 1.69 ACL tears in the population that was examined.\textsuperscript{12}

Following a second ACL tear, the patient has the option to undergo revision surgery. In a study by Yabroudi et al, predictors for revision surgery were detected after primary ACLR.\textsuperscript{9} Yabroudi et al found that younger individuals at the time of the primary ACLR and ACLR with an allograft were predicted to have an increased risk of revision surgery.\textsuperscript{9} Also returning to a competitive baseline activity and having initial double-bundle ACLR had been shown to increase the risk of having revision surgery.\textsuperscript{9}

Following ACLR, there is lack of consensus on return to play guidelines, leaving ambiguity on when the patient can return-to-sport/activity. However, even after the patient is cleared to participate, there are usually complications. The patient’s return to pre-injury activity level has a relatively low rate, but there is still a gap on why there are such poor return rates.\textsuperscript{6,13} The return-to-play decision has to be made by the athlete/patient in the situation even if a physician clears them. Ardern et al found that of the 503 patients examined in the study, 335 patients (66.6\%) did not attempt to go back to their full competitive level of sport.\textsuperscript{6} The decision to return to sport was based on the patient’s knee function and also other factors that take up time such as work and family matters.\textsuperscript{6} Also, the patient reports their signs and symptoms to their physician’s after surgery as well to get a measure of knee function during every day activity.

\textbf{Self-Reported Outcomes}

Self-reported outcomes are an important part of communication between the patient and physician. The data presented by these assessments can help with measuring knee function, while also identifying early development of conditions such as
symptomatic signs of post-traumatic osteoarthritis. A common evaluation tool used by researchers and clinicians is the International Knee Documentation Committee Evaluation Form (IKDC). This specific tool is used to detect any improvement or deterioration in symptoms, function, and sport activity after a knee injury and knee surgery such as ACLR. This self-reported outcome measure can be used for injuries such as ligamentous and meniscal injuries, articular cartilage lesions, and patellofemoral pain. Other studies have also used the Knee Injury and Osteoarthristis Outcome Score (KOOS) to assess self-reported knee function. This scoring system is used to measure the patients' opinions about their knee and associated problems over short- and long-term follow-ups, and it's major benefit and distinction is that it provides five subscales of 1.) pain, 2.) other symptoms, 3.) functions in activities of daily living (ADL), 4.) functions in sport and recreation, and 5.) knee-related quality of life (QOL). Visual analog scales (VAS) have widely been used to as another measure to help patients subjectively rank pain symptoms involved with the injury. The VAS is highly reliable and has been used in a number of studies. The scale is usually scored from one to ten (one being no pain and ten being extreme pain). These subjective measures are all used frequently in ACLR research.

**Post-Traumatic Osteoarthritis**

Post-traumatic osteoarthritis (PTOA) development has been thoroughly studied in patients that have had a previous ACLR. PTOA has been associated with risk factors such as age, obesity, smoking, and major knee injuries. Injuries such as ACL rupture and meniscal tears are common knee injuries that influence the development of PTOA. Other predictors have been discovered by Li et al, who was
looking into development of PTOA after ACLR. They were able to categorize the predictors into preoperative variables and intraoperative variables. The preoperative variables consisted of increased BMI, prior medial and lateral meniscectomy, and increased time from injury to surgery. The intraoperative variables consisted of presence of grade 2 or greater medial patellar chondrosis and medial meniscectomy.

ACLR has been used as the primary treatment for a ruptured ACL. The goals of the reconstruction are to restore knee joint stability, allow the patients to return to pre-injury activities, and prevent the development of post-traumatic knee osteoarthritis. However, even with the reconstruction surgery and months of aggressive rehabilitation, PTOA rates are still relatively high as time progresses. In a study by Strewer et al, there was an assessment of knee function and the prevalence of PTOA during a long-term follow-up. Thirteen years after ACLR, patients went to a follow-up and the assessment was based on the IKDC score. On the long-term follow-up, 23.3% of the patients had an abnormal knee condition and 5.5% of the patients had a severe abnormal condition according to the IKDC assessment score. 20% of the evaluated population ended up developing symptoms of PTOA.

Similarly to the Strewer study, Oiestad et al conducted a prospective study that assessed the knee function and prevalence of PTOA at a 10 to 15 year follow-up after ACLR. In the 10 to 15 year follow-up, 74% of the participants presented with a Kellgren and Lawrence grade of two or higher. 47% if the participants were categorized as having symptomatic and radiographic knee PTOA. Further data shows that 80% of subjects that have combined injury (ACL injury with medial collateral ligament injury and/or meniscal injury and/or chondral lesions) have a higher prevalence of
radiographic PTOA in comparison with subjects with isolated ACL injury (60% prevalence of PTOA).\textsuperscript{27} This study concluded that although there is an improvement in knee function 10 to 15 years after ACLR, there was still a high prevalence of PTOA in the population that was studied.

Luc et al also wanted to compare the prevalence of PTOA in subjects who had ruptured their ACL and also had the reconstruction done with subjects who were just ACL deficient and did not follow through with the reconstruction using a systematic review technique. This study revealed that the ACLR group had a slight increase in patients with OA (44%) in comparison to the ACL deficient group (37%).\textsuperscript{24} Also the ACLR group was 1.73 times more likely to develop PTOA than the ACL deficient group.\textsuperscript{24} This investigation proposes that although ACLR is effective in restoring joint stability, it may not be the most efficient treatment in decreasing the likelihood of PTOA if there is an isolated ACL injury.

**Biomechanical Changes Following ACLR**

Following an ACL injury or ACLR, there are many changes observed at the knee. The evaluation of biomechanics is an important part of a rehabilitation program. Studies have investigated the changes in biomechanics during various tasks after ACLR.\textsuperscript{4,28-31} Slater et al, used a meta-analysis and a systematic review to examine the change in gait biomechanics in patients who were ACL deficient, patients who had undergone the ACLR, and healthy controls.\textsuperscript{31} The ACL deficient group and the ACLR group both demonstrated large deficits in peak knee angles in all planes in comparison to the healthy controls, indicating that these patients use smaller ranges of motion during ambulation.\textsuperscript{31}
Butler et al. were also interested in investigating walking mechanics after ACLR.\textsuperscript{28} This study examined the internal knee moments and joint angles of the individuals who had undergone ACLR.\textsuperscript{28} The participants were on average $5.3 \pm 4.4$ years post ACLR during this study. Individuals in the ACL injured group exhibited a 21\% larger knee abduction moment than the control group, which was significantly different.\textsuperscript{28} This increase could suggest a greater risk for PTOA development and may provide a mechanism behind the early onset of PTOA seen in ACLR populations.\textsuperscript{28} Understanding the gait patterns in ACLR patients is important for examining the biomechanics changes after ACL injury and reconstruction.

Biomechanics have been evaluated for ACLR patients in other everyday activities as well. Stair walking is a challenge for some ACL patients due to the extensive hip and knee flexion needed to climb up the stairs and also the ability to have quadriceps control during stair descent. Lepley et al. longitudinally examined the stair walking biomechanics in patients who had suffered ACL injury.\textsuperscript{29} Participants again were assessed at the pre-surgery level and again at 6 months post-surgery. During stair descent, ACL injured patients had smaller knee extension moments in their injured limb compared to the uninjured limb and healthy control group.\textsuperscript{29} During stair ascent, the ACL injured group demonstrated less knee flexion and also used less total sagittal plane knee motion than the uninjured group.\textsuperscript{29} Again, this data indicates that these patients are adopting new biomechanical strategies to complete similar everyday tasks, which could have profound implications for PTOA development by changing the osteokinematics of the tibiofemoral joint. Interestingly, Lepley et al observed that the
deficits in the knee biomechanics were still persistent despite 6-months of extensive knee rehabilitation and even after being cleared for unrestricted activity.

The consistent deficits in knee joint biomechanics in the studies suggest that rehabilitation plans and assessment plans are not adequately identifying the dysfunctional movement patterns. Even with the surgical and therapeutic intervention, the standard of care still does not address the deficits. These deficits persisted even after individuals have been cleared for unrestrictive activity even though the patient is not demonstrating optimal biomechanical profiles.

**Quadriceps Strength Deficits**

Quadriceps muscle dysfunction is a common and persistent impairment observed following ACL injury, which likely has profound effects on recovery, as muscle strength is known to influence self-reported outcomes and can attenuate joint forces during dynamic activity. In fact, there is still ambiguity whether the individuals who suffer an ACL tear can return to 100% limb function even after a full rehabilitation protocol. In a systematic review constructed by Hart et al, quadriceps activation was assessed in multiple populations. The study investigated the prevalence of quadriceps activation deficits after acute knee injury or surgery in ACL deficient patients, ACLR patients, and anterior knee pain patients. Full activation of the quadriceps was determined if the calculated central activation ratio was 95% or higher. The ACL deficient group had an overall mean quadriceps activation of 87.3% in the involved limb and 89.1% activation in the uninvolved limb in the 352 participants. The ACLR group had an overall mean activation of 86.5% in the involved side and 84.0% in the contralateral side in 99 participants. Lastly, the anterior knee pain group had a mean activation of 78.6% on
the injured limb and 77.7% on the uninvolved limb.\textsuperscript{32} This study showed that even though these participants were cleared to return to activity, there were still clinically meaningful deficits in the quadriceps activation. However, although there were deficits still in each group, the ACLR group did show to have an overall improvement meaning that it is still the best treatment for ACL injury.

During ACLR, surgeons use a femoral nerve blockade to enhance post-operative pain control.\textsuperscript{33,34} However, this technique has been shown to prolong the return of quadriceps strength and causing a delay in return to pre-injury level of activity.\textsuperscript{33} Christensen et al, used an alternative adductor canal blockade to try to prevent the prolonged deficits of the quadriceps muscles\textsuperscript{33}. The results showed that there was more of a deficit in the adductor canal blockade in comparison to the femoral nerve blockade by 7.5%.\textsuperscript{33} Researchers are continuing to look for alternatives to help prevent the prolonged deficits in quadriceps strength.

Previous literature has used similar techniques to measure quadriceps strength before ACLR and after the athlete has been cleared to return to activity. When measuring strength, the investigators have used an isokinetic dynamometer assessment.\textsuperscript{19,35-41} The dynamometer allows for the research group to test maximal voluntary isometric contractions (MVIC) bilaterally before and after ACLR. The dynamometer is also used to help quantify the quadriceps muscle activation using the superimposed burst technique. During MVIC collections, torque is produced from the participant extending the knee. Once the torque no longer increases, that number is collected as the MVIC. Previous literature suggests that muscle strength in the injured limb is deficient when compared to the contralateral side after calculating
measurements from the isokinetic dynamometer.\textsuperscript{33,36,37} Torque variability has also been shown to be greater in ACLR groups in comparison to healthy controls.\textsuperscript{38} Peak torque with knee extension has been shown to occur earlier within the range of motion in the injured muscles even when the peak torque and quadriceps to hamstring ratio was not statistically significant.\textsuperscript{40} Although there is an abundance of research stating the quadriceps muscle has lost strength, there is still no clear answer to why there is such a loss in voluntary muscle activation.

1.c. Quadriceps Strength Deficits After ACL Tear/Reconstruction

As mentioned above, muscle function is assessed clinically using muscle strength outcomes. However, there are multiple underlying factors to muscle strength, such as morphological and neural considerations, and therefore muscle weakness following joint injury can be multifaceted. Following ACL injury, changes to these factors have been shown to affect the muscle’s ability to continue to function normally.

Muscle Atrophy

After ACL injury, physical changes in the morphological properties of the quadriceps muscle are known to occur. Over time, the quadriceps muscles atrophy, or reduce in cross sectional size, and lose muscle tone after the injury to the ligament.\textsuperscript{42} Although this is a common effect from an ACL injury, the origin in which the atrophy comes from is still unknown and its contribution to muscle weakness is still up for debate.\textsuperscript{43} Previous theories suggested that quadriceps atrophy results from the discontinued use of the limb for an extended period of time. For example, the atrophy can result from decrease in exercise from the lack of participation in sport or possibly
from immobilizing the knee joint after the injury.\textsuperscript{43} However, quadriceps atrophy is present in patients despite extensive therapeutic rehabilitation and regardless if patients return to sport or not, suggesting other underlying factors to muscle atrophy, such as neural inhibition.

Peripheral changes in quadriceps muscle morphology, quantified via cross sectional area, have been correlated to quadriceps strength following ACLR,\textsuperscript{44-46} with correlation coefficients as high as 0.75-0.81.\textsuperscript{44,46} In a study by Thomas et al, atrophy and muscle activation failure were examined after ACLR to see if they had any correlation with quadriceps weakness.\textsuperscript{47} The study had revealed that the cross sectional area of the muscle group was strongly related to the muscle strength six months after ACLR.\textsuperscript{47} The cross sectional area in the injured limb was much less than the unaffected limb and there was a significantly less strength differential in the injured limb.\textsuperscript{47} Similarly, Krishnan et al.\textsuperscript{48} demonstrated that peripheral changes in muscle, and not neural activation (voluntary activation), were primarily contributing to chronic quadriceps weakness (R\textsuperscript{2} = 0.71). However, this investigation utilized electrically evoked knee extension torque at rest to assess morphology, and therefore did not directly assess the morphological characteristics of the muscle. Conversely, Williams et al.\textsuperscript{45} observed that both quadriceps morphological structure (cross sectional area) and neural activity (voluntary activation) collectively accounted for 62\% of the variance in muscle strength following ACL injury. These studies reveal that there is a relationship between the quadriceps weakness after ACLR and muscle atrophy, even after six months of strenuous rehabilitation, and that underlying neural changes may influence this relationship.
Changes in Neural Activity

Immediately following ACL injury, there are already changes occurring that can affect neural activity. Methodological assessments of neural activity include the central activation ratio (CAR) and electromyography (EMG). These tools are important because they help quantify the deficits of neural activity in the injured limb. There are two major motor generating neural pathways that help with quadriceps muscle contractions and quadriceps function that are affected after injury. These two pathways are corticospinal and spinal-reflex pathways.

Before discussing the neural pathways, it is important to understand gross measures of neural activity assessed via CAR and EMG. Researchers are continuing to look for data about the changes in neural activity after the ACL has been ruptured and after it has been reconstructed. One of the most important changes that have been revealed from previous studies is the gross change in muscle activation. CAR has been used in many investigations in order to calculate how much the participant can voluntarily activate their quadriceps muscles while also giving an estimate of the motor neurons that can be used to help fire the muscle.\textsuperscript{32,35,37,47,49-51} CAR is collected using an electrically induced superimposed-burst technique that occurs during the contraction of the quadriceps. The CAR can be calculated using a specific equation. The force generated during an MVIC without the stimulus is divided by the total force generated with the stimulus (superimposed-burst).\textsuperscript{52} The equation is as follows: $\text{CAR} = \frac{F_{\text{MVIC}}}{(F_{\text{MVIC}} + F_{\text{SIB}})}$.\textsuperscript{52}

When collecting CAR, EMG is commonly used at the same time to help add additional information regarding the neural activity during quadriceps muscle
contractions. EMG is a method of assessing neural activity during dynamic tasks such as strength assessments on a dynamometer, or walking, running and jumping tasks. Studies have previously looked at EMG values in the quadriceps muscle group to try to simulate neural changes after there is a structural or functional change in the involved joint. For example, Torry et al, had a goal to describe the changes in neural activity and knee joint kinematics when the knee is induced with intra-articular effusion. Of the 13 participants, 10 subjects experienced inhibition of the vastus lateralis after the effusion was injected within the joint capsule. These results could play an important role in ACLR research because joint effusion is common after ACLR. This research explained that although there cannot be a direct link to the muscle inhibition, however, there were reductions in vastus medialis and lateralis activity with the knee joint effusion. This study could be a baseline when comparing functional capabilities of pathological groups who exhibit knee joint injury.

Although gross assessments of EMG and CAR are great tools to use when measuring neural activity, they do not show where the deficits are coming from. Investigations are continuing to be conducted to try to discover where the neural deficits are coming from in the neural pathways. Again, the two major motor generating neural pathways are the corticospinal and spinal-reflexive pathways. The corticospinal pathway is the pathway that originates at the motor cortex of the brain and sends voluntary descending signals to the muscle of interest via the corticospinal tract to initiate voluntary movement. The spinal-reflexive pathway relies on an outside stimulus to stimulate mechanoreceptors that send afferent information towards the CNS. The signal will then synapse across to the efferent pathway, bypassing descending motor control,
and resulting in the reflexive, involuntary contraction of a muscle. Deficits in the excitability of both of these pathways have been found following ACL injury and ACLR.\textsuperscript{18,32,34,51,55,57-60}

The changes in neural activity following injury are beginning to be explored more in knee injury research. Although investigators have been discovering the effects of ACL rupture and reconstruction, the cause of these negative effects is still unclear. Many researchers are suggesting that arthrogenic muscle inhibition (AMI) is responsible for the lack of quadriceps activation and strength post-ACL injury. AMI is the diminished ability to reflexively contract the muscle even if it is not damaged.\textsuperscript{57} It is a presynaptic, ongoing reflex inhibition of the muscle surrounding a joint after there is some sort of damage to the structures of the involved joint.\textsuperscript{57} The information from the joint decreases the ability to recruit motoneurons, which then decreases force production of any contraction coming from the motoneuron pool.\textsuperscript{57} Initially, AMI seems like a natural reaction to injury, as a protective mechanism to prohibit muscle contraction and prevent further damage to the joint.\textsuperscript{57} However, in the rehabilitation setting, AMI must be addressed or even stopped to help the injured individual return back to their pre-injury activities.\textsuperscript{32,57}

Because AMI affects the recruitment from the motoneuron pool, Hoffmann reflex (H-reflex) is used to measure the quadriceps spinal-reflexive excitability.\textsuperscript{50,51} The H-reflex uses both presynaptic and postsynaptic central nervous system inhibitory mechanisms, and provides the percentage of the motoneuron pool that can be activated.\textsuperscript{42} Transcranial magnetic stimulation (TMS) is also used to determine the effects of AMI, however at the corticospinal level. This is used to determine the active
motor threshold and the amplitude of motor evoked potentials elicited at 120% of the active motor threshold.\textsuperscript{50,51} Lkeley et al, conducted a 6 month longitudinal study to assess the change in spinal-reflexive excitability and corticospinal excitability after ACLR.\textsuperscript{51} The participants were tested on three separate occasions: 1.) Pre-surgery 2.) 2-weeks post-surgery 3.) 6-months post-surgery.\textsuperscript{51} The results showed that spinal-reflex excitability (H-reflex) in the injured limb was lower than the healthy controls before surgery and 2-weeks post-surgery.\textsuperscript{51} However, at the 6-month post-surgery follow-up, the spinal-reflex excitability had increased higher than the pre-surgery values.\textsuperscript{51} The corticospinal excitability measures were not different between the ACLR limbs and the healthy control limbs at the pre-surgery and 2-weeks post-surgery data collections. At the 6-month follow-up, both of the limbs of the ACLR patients had higher active motor thresholds.\textsuperscript{51} Higher active motor threshold values means that there is a decrease in corticospinal excitability. The decrease in corticospinal excitability may continue to progress the further the patients are from their injury.\textsuperscript{51} This study concluded that the spinal-reflex excitability is deficient in the early stages of injury but then resolve anywhere between 2-weeks and 6-months post-surgery.\textsuperscript{51} Although the spinal-reflexive deficits return to normal, corticospinal excitability begins to decrease at any point of time between the 2-weeks and the 6-months post-surgery.\textsuperscript{51}

Pietrosimone et al, also assessed the changes in spinal-reflex and corticospinal excitability in ACLR and uninjured participants and also compared the neural excitability in the ACLR patients who had acceptable levels of voluntary quadriceps activation.\textsuperscript{50} The time after surgery was on average 48.10± 36.17 months.\textsuperscript{50} The investigators found that H-reflex was bilaterally higher in the ACLR group than in the control group.\textsuperscript{50} This
study suggested that maintaining a higher H-reflex bilaterally could be used as a strategy to maintain voluntary activation in the effected quadriceps muscle group.\textsuperscript{50} Pietrosimone et al. also found similar results to the Lepley et al. longitudinal study in regards to the corticospinal excitability values. Greater active motor thresholds were found in the uninjured limb of the ACLR group and also in the ACLR limb in comparison to the uninjured control group.\textsuperscript{50} The higher active motor thresholds shows that even years after the ACLR, corticomotor deficits were still present.\textsuperscript{50} Because there are still deficits with the corticospinal excitability long after the injury, researchers believe that there is a piece missing in current rehabilitative programs for ACLR patients that need to be addressed in order to restore optimal outcomes.

**SUMMARY/DISCUSSION OF CORTICOSPINAL CHANGES**

Peripheral joint injury results in central nervous system reorganization at both the spinal and cortical levels.\textsuperscript{61} The reorganization of the corticospinal pathways is causing neuromuscular deficits following joint injury, and the effects are lasting for a considerable amount of time.\textsuperscript{51,61} Without the proper function of these pathways, the ability to properly contract peripheral muscle groups, such as the quadriceps muscles, decreases.\textsuperscript{60} The voluntary muscle contraction strength is determined by the amount of motor neurons recruited by the primary motor cortex. The change in corticospinal activity alters the ability to recruit from the motor neuron pool resulting in a weaker muscle contraction and less voluntary muscle activation.\textsuperscript{60-62}

To measure the motor cortex excitability, transcranial magnetic stimulation (TMS) has been used as a tool to investigate the alterations of the primary motor cortex and the functional integrity and excitability of descending motor pathways to control muscle
following joint injury. Studies using TMS revealed asymmetries in resting motor thresholds of the corticospinal pathways in individuals with ACL injury, with the threshold lower on the ACL-injured limb compared bilaterally. The decrease in threshold requires a need for an increase of stimulus in order to achieve an optimal muscle contraction. Therefore, the injured joint loses activation and strength of the surrounding muscle due to the changes in corticospinal pathways and activity. The change in these pathways causes a decrease in motor neuron recruitment in the primary motor cortex resulting in a weaker muscle contraction. Individuals suffering from joint injury such as an ACL rupture experience these deficits because of the reorganization of the central nervous system, especially at the corticospinal level.

**Failures with Current Rehabilitation**

ACLR rehabilitation programs focus largely on quadriceps function returning to its pre-injury levels. However, there is a piece that seems to be missing due to the continuous findings of corticospinal excitability and strength deficits even after the patient is cleared to return to activity. Some deficits can exceed 20% of strength and activation of the quadriceps muscle 6-months post-ACLR. As previously stated, AMI prevents the quadriceps muscles from returning to their full potential. Because of these lasting deficits, the patient is still at risk even after return to activity, and roughly 40-50% do not return to their pre-injury activity levels. If the patients do return to activity, they risk either graft failure, or possibly injury to the contralateral limb, with approximately 20-30% of patients sustaining a second ACL injury. The rehabilitation teams seem to be doing as much as they can to return the patient to activity with therapeutic exercise. However, the strength and functional gains are still lacking, leading investigators to
believe that the deficits go further than the injured joint. The lack of corticospinal activity gives researchers an idea of changes occurring both within the joint and also in the brain, and a modifiable target to address during rehabilitation.

1.d. Transcranial Direct Current Stimulation

As more evidence is exposed about how after lower extremity injury, changes in the brain occur; new techniques are being studied to treat these changes in brain activity. Transcranial direct current stimulation (tDCS) is commonly used in treating neurologically impaired patients (ex. Parkinson’s disease, stroke, etc.), however represents a promising new approach to treating patients with different musculoskeletal conditions such as, PTOA or total knee arthroplasty.\textsuperscript{23,65} tDCS involves direct currents that are being delivered through rubber electrodes.\textsuperscript{66} In most studies, the current strength is delivered between 1 and 2 milliamps.\textsuperscript{66} This current strength is strong enough to induce physiological and cognitive effects and is proven to be safe to use.\textsuperscript{66} The positioning of the electrodes determines the direction of the current and efficacy of tDCS which can help stimulate cortical excitability.\textsuperscript{66} While tDCS is in effect, the cortical excitability can be increased or decreased depending on if anodal or cathodal tDCS is being performed.\textsuperscript{66}

The electrode placement is traditionally attached to the surface of the scalp above the primary motor cortex in the majority of studies reviewed.\textsuperscript{22,23,41,65,67} Weak currents are then applied to the scalp to help directly stimulate the motor cortex potentially increasing neural excitability and also decreasing pain signals. The placement over the motor cortex is to help increase responsiveness to motor training by
directing more neural input to increase muscle activity. This can create greater gains in muscle activity and strength when tDCS is combined with exercise.

**Does tDCS Work?**

The use of tDCS has been shown to work in a variety of settings. Many investigations that have been completed have been in support of using tDCS in many different populations. Previous literature has experimented using tDCS in groups with PTOA, knee arthroplasty, previous history of stroke, and also in healthy athletic populations.\textsuperscript{23,41,65} tDCS has been investigated to see if the treatment can be used as a pain reducer, a way to accelerated learning ability, and as a tool to increase muscle strength.

After surgery, many patients are given medication to help with pain. Pain medication can be very addictive and too much of the medication can cause serious consequences. Borckardt et al conducted a study of using tDCS as a pain reducer in place of postsurgical opioids in total knee arthroplasty patients.\textsuperscript{65} The investigation had four different sessions of anodal tDCS stimulation over the motor cortex and a cathodal stimulation of the right prefrontal cortex.\textsuperscript{65} There was a significant difference in amount of pain medication taken between the two groups. The sham group had taken an average of 12.3mg during the period of testing whereas the tDCS group had taken an average of 6.6mg.\textsuperscript{65} Although there were no differences in VAS pain or mood ratings, the tDCS group reported that the unpleasantness of their pain was significantly lower after the treatment.\textsuperscript{65} This study suggests that tDCS could potentially have an important role with managing acute and chronic pain.\textsuperscript{65} More research needs to be done in this field in order to make a less ambiguous conclusion.
A patient suffering from PTOA experiences chronic pain as the condition develops over time. As the pain increases the function of the affected joint decreases. Chang et al, experimented the use of tDCS in the OA population to see if the stimulation was safe and useful in decreasing pain and increasing the joint function. The investigation team used anodal tDCS to increase the excitability to the motor cortex combined with exercise therapy to help alter the sensory input from the periphery by modifying muscle control. Both the research team and the participants were blinded to whether the participants were receiving active tDCS or a sham trial. The measures collected for this study consisted of a visual analogue scale and different forms of pain mechanisms (pressure pain thresholds, heat pain thresholds, conditioned pain modulation, and nociceptive flexor withdrawal reflex). Of the 25 returning participants after baseline testing, it was shown that the active tDCS group benefited from the treatment. Pain reduction in the active tDCS group was double that observed in the sham group. Physical function of the involved knee was also improved based on what the patient was reporting. Chang et al concluded that the use of tDCS is safe and is shown to be beneficial in this population. Because of the pain reducing characteristics that tDCS provides by increasing the excitability in the corticospinal pathway, the device may have benefits in other settings and other patient populations, such as ACLR patients.

Stimulation to the motor cortex has also been believed to enhance motor skill and learning ability. Reis et al conducted a study where participants received tDCS and then were later tested on their knowledge of a specific novel and were assessed on a motor skill task. The objective of this study was to see how long the effects of anodal
tDCS would last without continued treatment. Similarly to other studies, there were two groups, one group receiving the tDCS and the other receiving a sham trial. The tDCS group exhibited greater total skill learning than the sham group. However, the ability to retain the skill that was learned during the training sessions decreased as the time increased in between the follow-ups. Therefore, tDCS could possibly be used for short-term learning and skill retention but the ability to continue learning at that same level decreases as time without treatment increases.

Previous research has looked into the effects of tDCS on muscle strength after receiving the treatment. Washabaugh et al wanted to try to increase the force generation of the thigh muscles in healthy, able-bodies adults, after the use of tDCS. Knee flexion and knee extension strength were both assessed using a Biodex isokinetic dynamometer to collect MVIC after being treated with tDCS. This study revealed that the tDCS treatment aids excitability-increasing effects creating a larger voluntary contraction during knee extension. The effects were thought to be isolated to the muscle groups that were involved with the task.

Another study wanted to increase the time to exhaustion in the quadriceps muscle group after the use of tDCS. Angius et al, had the participants come into the lab on five separate occasions to be tested. The participants each had to do a control, a placebo, a cephalic, and extra-cephalic testing session after being familiarized. Transcranial magnetic stimulation, EMG, tDCS, MVICs, and time to exhaustion tests were all completed during each trial. This study found that when the anodal electrode was over the left primary motor cortex and the cathodal electrode was placed over the shoulder (extra-cephalic testing), there was a longer time to exhaustion than any of the
other conditions.\textsuperscript{69} Cortical excitability increased only when at exhaustion.\textsuperscript{69} The investigation concludes that there was a greater increase in isometric endurance performance of the lower limb when using the extra-cephalic shoulder combination in comparison to just the cephalic electrode placement.

Vargus et al, investigated the effects of tDCS in the athletic population. The researchers were trying to determine if tDCS increased the isometric muscle strength of quadriceps in high school soccer players.\textsuperscript{41} The participants and the research team were both blinded to whether the participants were being treated with the tDCS or if they were a part of a sham trial.\textsuperscript{41} Each treatment was twenty minutes long and muscle strength was assessed at different time points (immediately pre-treatment, during the treatment, 30-minutes post-treatment, and 60-minutes post-treatment).\textsuperscript{41} It was concluded that MVIC was increased in the dominant limb of the athlete and continued to increase as time after treatment increased (5.2\% increase during tDCS, 6.3\% increase 30-minutes post-tDCS, and 9.4\% increase 60-minutes post-tDCS).\textsuperscript{41} This study was suggested that tDCS could also accelerate the process of recovery after surgeries or lesions.\textsuperscript{41}

**tDCS and Anterior Crucitate Ligament Reconstruction Patients**

The use of tDCS in a rehabilitation setting has been suggested but not widely used due to continuous research being done on the device. As previously stated, ACL injury causes strength and quadriceps activation deficits and rehabilitation protocols do not fully address these negative effects. More research is supporting the idea that there are changes in spinal-reflex and corticospinal excitability after the injury to the joint. Corticospinal excitability deficits seem to be lasting longer throughout the rehabilitation
process and even after the patients were cleared for return to activity. Using the tDCS device could potentially fill in the gaps of rehabilitation programs where they are not appropriately addressing deficits in the injured joint. ACLR patients also struggle with pain after surgery, throughout rehabilitation, and sometimes years after the reconstruction. tDCS has been used as a pain reducer and could potentially help with decrease pain levels in this specific population.

    tDCS has the ability to increase or decrease cortical excitability. Again, corticospinal excitability is still deficient in ACLR patients even after the injured athlete is cleared to return to sport. By using the tDCS device, the motor cortex will be directly stimulated and can help increase the corticospinal excitability, as has been demonstrated in a variety of other patient populations outlined above. Therefore, tDCS could help with muscle activation in the injured limb, which potentially could reduce recovery time. Also, tDCS was used in other populations to help increase strength. Patients with ACLR lack a significant amount of quadriceps strength after injury. tDCS has been shown to benefit other populations in increasing strength and tDCS could possibly recreate those same effects in the ACLR population.

    By directly stimulating the motor cortex with tDCS, we believe significant improvements in muscle function will occur and possibly help reverse the affects of AMI. By combining the use of EMG, an isometric dynamometer, superimposed burst, and tDCS together, we can assess the muscle activation and strength before and after tDCS treatment protocols in ACLR patients.
1.e. Conclusion of Literature Review

ACL injury is a very common injury in the sports population. There are lasting deficits even after the patients are cleared to return to activity. The lack of muscle and joint function in this population causes the athletes to become unable to return to previous levels of competition or return to competitive sport at all, and can lead to long term complications such as PTOA. With the use of tDCS, we believe there will be an increase in quadriceps strength and activation, resulting in positive outcomes in the rehabilitation setting. tDCS may have the ability to enhance rehabilitation to help reduce the strength deficits in ACLR population.

The purpose of this investigation is to determine if tDCS application over the primary motor cortex will immediately improve quadriceps muscle activity, muscle strength, and self-reported levels of pain in patients with a history of ACLR. We hypothesize that the participants will see an immediate increase in muscle strength and activity, along with decreases in self-reported levels of pain.
REFERENCES


CHAPTER II: INTRODUCTION

Approximately 80,000 to 250,000 anterior cruciate ligament (ACL) injuries occur annually in the United States.\textsuperscript{1} Unfortunately, many of these patients experience poor long-term outcomes following ACL reconstruction (ACLR), such as re-injury rates that exceed 20\%,\textsuperscript{2} and post-traumatic osteoarthritis development that occurs within 15 years following surgery\textsuperscript{3-6}. Quadriceps muscle weakness, which is ubiquitous following injury, has been attributed as a major factor in limiting restoration of clinical function.\textsuperscript{7-9}

Although ACLR rehabilitation programs already largely focus on restoring quadriceps strength,\textsuperscript{7,9} recent reviews have demonstrated that strength deficits can exceed 20\% of the contralateral limb even after formalized rehabilitation has finished.\textsuperscript{7} Identifying innovative and evidence-based techniques to restore quadriceps muscle function is imperative to improving long term outcomes in these patients.

Alterations in the excitability of peripheral and central nervous system pathways are hypothesized to contribute to quadriceps dysfunction following ACLR. Pain, swelling, and loss of mechanoreception from the joint can lead to altered afferent signals and poor somatosensation, which can negatively impair motor control.\textsuperscript{8,10-17} Evidence supporting this hypothesis stems from alterations that have been discovered in corticospinal excitability and brain activation following ACLR, highlighted by an inefficiency to generate and transmit action potentials from the motor cortex to the quadriceps muscle.\textsuperscript{8} Importantly, the excitability of the motor cortex is not only affected early in the injury process, but can persist for years following ACLR, likely contributing to prolonged deficits in muscle strength and neuromuscular function in these patients.\textsuperscript{8,18} The reorganization of the corticospinal pathway can have implications on
the downstream recruitment of alpha-motor neurons from the motor cortex, resulting in decreased voluntary muscle activation and strength.\textsuperscript{17-19}

During traditional ACLR rehabilitation, underlying corticospinal alterations that influence muscle strength are left unaddressed, which limits the effectiveness of the exercises performed. Transcranial direct current stimulation (tDCS) is a non-invasive method of electrically stimulating segments of the brain to help increase cortical activity and excitability.\textsuperscript{20} Although tDCS has historically been used in the rehabilitation field to treat neurologically impaired patients (ex. Stroke, Parkinson’s disease, etc.), it has recently shown promise in improving muscle strength, and decreasing pain and opioid use, in individuals with musculoskeletal conditions such as osteoarthritis and total knee arthroplasty.\textsuperscript{21,22} Theoretically, excitability of the areas directly below the electrodes can be manipulated which may potentially increase neural activity to the peripheral muscle being used. As mentioned above, ACLR patients exhibit deficits in excitability of the motor cortex, therefore, ACLR patients may benefit from an increase in corticospinal activation during exercise via tDCS, as well as potential reductions in pain, allowing for greater levels of peripheral muscle activation to be used and thus optimizing the benefits from the exercises being performed.\textsuperscript{22,23}

Therefore, the purpose of this study was to use a randomized cross-over design to determine if a single treatment of tDCS would improve quadriceps muscle activity and reduce self-reported levels of pain and function during exercise in participants with a history of ACLR. We hypothesized that tDCS would improve quadriceps muscle activity and reduce pain in participants with a history of ACLR.
CHAPTER III: METHODS

Participants

This study consisted of 10 participants, (5 male/5 female, 22.9yrs±4.23 176.57±12.01cm, 80.87±16.86 kg, 68.1±39.37 months since ACLR) (Table 1). To be included, participants reported history of a unilateral ACLR and were a minimum of 6 months post-reconstruction with full clearance for return to activity/sport by their physician. Participants were excluded from the study if the participant had experienced any of the following: a knee surgery prior to the ACLR; lower extremity injury within the last 6 months other than the current ACLR; heart condition; history of stroke, cranial neurosurgery, migraines, cancer in the brain, or a psychiatric or neurological disorder; taking medications that alter neural activity; intracranial metal clips; cochlear implants or other electronic devices implanted; a current pregnancy; known balance disorder, or vertigo; any active skin infections; or an allergy to adhesive tape. All participants provided written, informed consent prior to enrollment. The Institutional Review Board at the University of Connecticut approved all procedures.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age</th>
<th>Height</th>
<th>Mass</th>
<th>Months Post-Op</th>
<th>Injured Limb (1=R, 2=L)</th>
<th>Sex</th>
<th>Graft (PT=Patellar tendon, HS=Hamstring)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HALO 1</td>
<td>26</td>
<td>180.34</td>
<td>77.11</td>
<td>64</td>
<td>1</td>
<td>Female</td>
<td>PT</td>
</tr>
<tr>
<td>HALO 2</td>
<td>19</td>
<td>172.72</td>
<td>77.11</td>
<td>79</td>
<td>2</td>
<td>Female</td>
<td>PT</td>
</tr>
<tr>
<td>HALO 3</td>
<td>21</td>
<td>170.68</td>
<td>59.87</td>
<td>28</td>
<td>1</td>
<td>Female</td>
<td>PT</td>
</tr>
<tr>
<td>HALO 4</td>
<td>19</td>
<td>177.8</td>
<td>83.91</td>
<td>11</td>
<td>1</td>
<td>Male</td>
<td>PT</td>
</tr>
<tr>
<td>HALO 5</td>
<td>19</td>
<td>182.88</td>
<td>98.88</td>
<td>38</td>
<td>1</td>
<td>Male</td>
<td>HS</td>
</tr>
<tr>
<td>HALO 6</td>
<td>26</td>
<td>175.25</td>
<td>79.37</td>
<td>66</td>
<td>2</td>
<td>Male</td>
<td>PT</td>
</tr>
<tr>
<td>HALO 7</td>
<td>20</td>
<td>203.2</td>
<td>106.59</td>
<td>61</td>
<td>1</td>
<td>Male</td>
<td>PT</td>
</tr>
<tr>
<td>HALO 8</td>
<td>23</td>
<td>180.33</td>
<td>98.88</td>
<td>77</td>
<td>1</td>
<td>Male</td>
<td>HS</td>
</tr>
<tr>
<td>HALO 9</td>
<td>24</td>
<td>160.02</td>
<td>54.43</td>
<td>111</td>
<td>2</td>
<td>Female</td>
<td>HS</td>
</tr>
<tr>
<td>HALO 10</td>
<td>32</td>
<td>162.56</td>
<td>72.57</td>
<td>146</td>
<td>2</td>
<td>Female</td>
<td>HS</td>
</tr>
<tr>
<td>Averages</td>
<td></td>
<td>22.9</td>
<td>176.57</td>
<td>80.873</td>
<td>68.1</td>
<td>6R/4L</td>
<td>5M/SF</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>4.23</td>
<td>12.02</td>
<td>16.86</td>
<td>39.37</td>
<td></td>
<td>6 Patellar Tendon/4 Hamstring</td>
</tr>
</tbody>
</table>

Table 1: Demographics
Protocol

This cross-over study consisted of a familiarization session and two separate test sessions. During the familiarization session, participants were positioned on an isokinetic dynamometer (Biodex System 4, Biodex Medical Systems, Shirley, NY) in the same position as they would be during the testing session, as explained below. Participants were also able to wear and become familiar with tDCS stimulation unit (Halo Sport, Halo Neuroscience, San Francisco, CA).

The two subsequent test sessions randomly consisted of an active tDCS stimulation session, and a sham session with no stimulation during the walking period. The order of testing was as follows: a baseline assessment, the treatment condition (active tDCS or sham), and a post-test assessment (Figure 1). During test sessions, all outcome measures were collected bilaterally for all participants.

Quadriceps Strength Testing and Volitional Activation

Isometric strength was assessed using an isokinetic dynamometer by collecting the participant’s maximal voluntary force of the quadriceps muscles. Participants were instructed to sit on the dynamometer and were positioned in 90° of trunk flexion and 90° of knee flexion (Figure 2a). Restrictive straps were secured at the lap and over the shoulder of each participant to control accessory movement during the knee extension task. The tibia, just proximal to the ankle joint, was secured to a pad on the arm of the dynamometer with Velcro straps. Participants were instructed to cross their arms over the chest during all contractions to avoid unwanted upper extremity involvement in the task. Once correctly positioned on the dynamometer, the participants were asked to perform a series of submaximal isometric quadriceps contractions in which they were
attempting to extend their knee at 25, 50, and 75% of their perceived maximal effort. Additionally, participants received submaximal electrical stimulation at 25, 50 and 75% of the maximal 150 volts (100ms train of 10 stimuli, at 100 pps, with a pulse duration of 0.6 ms, and a 0.01 ms pulse delay via the Grass S48 dual channel electrical stimulation unit with an SIU8T isolation unit attached [Grass Products, Natus Neurology]). Participants then performed practice maximal contractions (without electrical stimulation) until the investigator and subject were confident that a maximal effort was being put forth. Participants then performed three maximal voluntary isometric contractions (MVIC) with visual feedback and verbal encouragement with at least 60 seconds between trials, in which the average of the three MVIC trials were used to quantify muscle strength. When each participant reached a plateau in torque output, the supramaximal electrical stimulation was triggered, which contracted any muscle not voluntarily contracted by the participant. This procedure was used to test both limbs.

The central activation ratio (CAR) was used to quantify the amount of quadriceps activation failure. To determine the CAR, the subject’s peak torque generated immediately prior to the delivery of the electrical stimulus was divided by the peak torque generated as a result of the electrical stimulus (superimposed burst torque) (Figure 2.b.). The average of the three trials was used for analysis.

Electromyographic (EMG) Testing

During all muscle strength testing, EMG signals were collected in order to assess alterations in muscle activity. The bellies of the distal vastus medialis (VM) and lateralis (VL) were shaved and cleaned with isopropyl alcohol prior to attaching the electrodes
(Dual EMG Electrodes [4cm x 2.2cm], Noraxon Inc., Scottsdale, AZ, US, Desktop DTS, Noraxon Inc.) (Figure 3). EMG signals were band-passed filtered 10 to 1000 Hz and subsequently processed using a root-mean-square algorithm with a 50-millisecond moving window. Dynamic EMG collected during the contractions were normalized to the peak muscle activity that occurs during the pre and post testing.

Self-Reported Questionnaires

At both the baseline and post-testing time points for each session, the participants were asked to complete questionnaires pertaining to their knee pain, knee function, and overall activity. The International Knee Documentation Committee (IKDC) Self-Reported Questionnaire, Visual Analog Scale, and Knee Injury Osteoarthritis Outcome Score (KOOS) were used to assess self-reported knee function. The KOOS allowed for investigation into five subscales of self-reported function: pain, disease-specific symptoms, activities of daily living, sport and recreation function, and knee-related quality of life. For this investigation, we focused on pain (KOOS Pn) and disease specific symptom scores (KOOS Sx).

Transcranial Direct Current Stimulation (tDCS)

The device tested was designed as a headset similar to noise canceling headphones with primer attachments to fit along the headset (Halo Sport tDCS, Halo Neuroscience, San Francisco, CA) (Figure 4). The participants were familiarized with the tDCS unit prior to their first testing session. In accordance with manufacture instructions, prior to the application of tDCS, the investigator thoroughly wet the primers prior to connecting them to the headset. The participants were instructed to place the headset directly over the motor cortex area as directed by the investigator, which was
estimated using anatomical landmarks of straight lines vertically in the sagittal (using nose and occiput) and frontal (using tragus to tragus) planes. The investigator controlled the headset with the software application, which specifically showed where the primers needed more contact with the head and then was adjusted so that the headset correctly covered all necessary portions of the treatment area. The application did not allow for tDCS stimulation unless there was appropriate contact with the participant’s head.

Once the primers were in complete contact with the participant’s head, the stimulation session began. Based on manufacturer specifications, the intensity of the signals could reach a maximum of 2.2mA. However, the application simplified intensity on a scale from 1 (0mA) to 10 (2.2mA). At the start of the treatment, the intensity was preset to 5 and could be manually adjusted by the investigator to the participant’s comfort. The stimulation intensity was documented for each testing session.

The tDCS device also allowed for a sham condition, in which the device was used but no electrical stimulation was delivered through the primers. It was explained to the participant that they may or may not feel a sensation from the device during the sham condition. The order in which the sham or stimulation condition was received was randomized. During both the stimulation and sham condition, the participant completed a 20-minute warm-up of walking on the treadmill at 2.0mph at a 1% incline.

**Statistical Analyses**

All statistical analyses were performed using SPSS statistics software, version 24. Separate 2 x 2 repeated measures analysis of variance (RM ANOVA) (time x condition) were used to determine significant differences between time and condition for
all outcome measures (percent maximum EMG, MVIC, CAR, KOOS Sx, KOOS Pn). Bonferroni post hoc analyses were conducted in the presence of a significant main effect. Additionally, percent change scores \( \text{Change Score} = \left( \frac{\text{POST} - \text{PRE}}{\text{PRE}} \right) \times 100 \) and Cohen’s d effect sizes with 95% confidence intervals were calculated for all variables. Paired samples t-tests were conducted on change scores between the tDCS and sham conditions. Alpha level was set \textit{a priori} at \( P \leq 0.05 \).

\textbf{CHAPTER IV: RESULTS}

A significant main effect of time was discovered for VM \( (F_{9,1} = 11.931, P = 0.007) \) and VL EMG \( (F_{9,1} = 9.132, P = 0.014) \), indicating that regardless of condition, EMG activity decreased from pre to post for each session. During the tDCS session, VM EMG activity decreased 12.1\% \( (d = -0.88; \text{CI} = -1.80, 0.04) \), whereas VM EMG activity decreased 18.9\% \( (d = -1.75, \text{CI} = -2.77, -0.72) \) during the sham condition. No significant difference was detected for the change in VM EMG during the tDCS and sham conditions \( (t = 1.07, P = 0.313) \) (Figure 5.a.-5.b.). Percent maximum VL EMG activity presented a decrease by 14.8\% in the active tDCS trial \( (d = -0.65; \text{CI} = -1.55, 0.25) \), whereas in the sham condition, there was a decrease in activity by 25.9\% \( (d = -1.82; \text{CI} = -2.86, -0.78) \). No significant difference was detected for the change in VL EMG during the tDCS and sham conditions \( (t = 1.232, P = 0.249) \) (Figure 6.a.-6.b.).

A significant main effect for time \( (F_{9,1} = 5.343, P = 0.046) \) and condition \( (F_{9,1} = 12.268, P = 0.007) \) was discovered for isometric strength indicating that regardless of the condition or the time point, there was a change in torque production. During active tDCS, strength decreased 8.9\% \( (d = -0.41; \text{CI} = -1.29, 0.48) \), whereas torque decreased
10.1% ($d = -0.42; CI = -1.31, 0.47$) during the sham condition. No significant difference was detected for the change in isometric strength during the tDCS and sham conditions ($t = 0.336, P = 0.745$) (Figure 7.a.-7.b.). There were no significant interactions or main effects discovered for CAR. CAR decreased 5.03% during the active tDCS trials ($d = -0.50; CI = -1.39, 0.39$) and 5.5% during the sham condition ($d = -0.49; CI = -1.38, 0.40$). No significant difference was detected for the change in voluntary activation during the tDCS and sham conditions ($t = -0.278, P = 0.787$) (Figure 8.a.-8.b.).

A significant time main effect ($F_{9,1} = 15.499, P = 0.044$) revealed that KOOS Sx decreased regardless of condition. There was an increase in KOOS Sx outcome scores in after both the tDCS condition, 4.7% ($d = 0.21; CI = -0.67, 1.09$), and the sham condition, 3.1% ($d = 0.15; CI = -0.72, 1.03$). No significant difference was detected for the change in KOOS Sx during the tDCS and sham conditions ($t = 1.929, P = 0.086$) (Figure 9.a.-9.b.). KOOS Pn displayed significant time and condition main effects (Time: $F_{9,1} = 15.499, P= 0.044$; Condition: $F_{9,1} = 6.106, P = 0.036$). KOOS Pn also displayed increases in outcome scores after both conditions. After the tDCS condition there was a 2.8% increase ($d = 0.36; CI = -0.52, 1.25$) and a 0.6% increase after the sham condition ($d = 0.07; CI = -0.81, 0.94$). No significant difference was detected for the change in KOOS Pn outcome score during the tDCS and sham conditions ($t = 0.756, P = 0.469$) (Figure 10.a.-10.b.).

**CHAPTER V: DISCUSSION**

The purpose of this study was to use a randomized cross-over design to determine if a single treatment of tDCS would improve quadriceps muscle activity and
reduce levels of pain during exercise in participants with a history of ACLR. The investigation discovered that there were no differences in quadriceps muscle activity or any self-reported outcomes when comparing active tDCS and sham treatments. EMG activity in both the VM and VL muscles were lower post-treatment (active or sham) with no differences between conditions. Decreased quadriceps strength and voluntary activation were also present in both the active tDCS and sham conditions when observing the pre and post time points. There were no differences in subjective scoring for the KOOS Pn and KOOS Sx.

EMG activity significantly declined following the 20-minute treadmill walking exercise for both the tDCS and sham conditions, however no interaction effect was discovered, indicating that tDCS had no effect on EMG activity. The decrease in EMG activity was surprising to the investigators, as we did not expect 20 minutes of walking to result in a decline of muscle activity. This may speak to the increased fatigability of the quadriceps muscle following ACLR, even during low demand task such as walking.\textsuperscript{24,25} Even with a decline in EMG activity from the walking session, we still believed that tDCS would be protective to the EMG decline comparative to the sham session. Thus, our results are contrary to our hypothesis, as we had believed that tDCS would increase muscle activity from pre to post treatment (or preserve muscle activity), allowing for more muscle activation to be available during exercise. Although not statistically significant, it should be noted that when observing change scores and effect sizes from pre and post measurements, there is less of an average decline in percent maximum EMG activity in the tDCS compared to the sham treatment for both the VM (tDCS = 12.1% decrease; sham = 18.9% decrease; $d = 0.41$; CI = -0.47, 1.30) and VL.
(tDCS = 14.8% decrease; sham = 25.9% decrease; $d = 0.47$, CI: -0.41, 1.36). This potentially means that the tDCS group is becoming more neurally efficient or is fatiguing less quickly in comparison to the sham group. A study by Cogiamanian et al, 2007, used EMG as a measurement in a fatiguing trial using maximal isometric contractions for the elbow flexors in a healthy population. It was shown that immediately after the tDCS treatment, EMG activation was significantly higher in both the polarization group and control group at the post-condition measurements, indicating that tDCS had no effect on the change in EMG activation compared to the control group, which is consistent with our findings.

Similar to our EMG outcomes, tDCS did not have a significant effect on isometric muscle strength, voluntary activation, or patient reported outcomes of pain and symptoms. We hypothesized tDCS might have worked in the ACLR population because of the direct stimulation over the primary motor cortex. The motor cortex stores pyramidal cells that are responsible for activating alpha motor neurons which directly simulates muscle during voluntary contractions. Theoretically, by increasing the motor cortex excitability with direct electrical stimulation, there should have been an increase in muscular strength immediately after the tDCS was delivered due to the increased activity of the alpha motor neurons. Similarly to Cogniamian and colleagues, Angius et al, 2016 also investigated the effects of different tDCS electrode locations on lower limb isometric exercise and endurance time. Muscle strength decreased significantly after the endurance trials but the rate of perceived exhaustion and time to exhaustion were significantly longer ($P > 0.05$) with this electrode placement that included left motor cortex and above the right shoulder. It is possible that this electrode placement by
Angius et al, in contrast to the stimulation location used our study, is more beneficial for seeing gains. However, more investigations is needed to understand the electrode placement on patient outcomes.

Vargas et al\textsuperscript{28}, examined the effects of tDCS on MVICs of the quadriceps in a healthy group of soccer players. This study included an active and a sham session while measuring five different MVICs at different time points post-tDCS/sham condition. When compared with the sham tDCS, the active tDCS improved MVIC during the tDCS, 30-minutes post-tDCS, and 60-minutes post-tDCS by 5.2\%, 6.3\%, and 9.4\% in the dominant limb.\textsuperscript{28} Unlike Vargas and colleagues,\textsuperscript{28} isometric strength values decreased for the tDCS (8.9\% decrease) and sham (10.1\% decrease) conditions after 20-minutes of walking on a treadmill ($d = .12; CI = -0.76, 1.00$). This decrease in torque may be the result from the active recovery following the pre-testing. A study conducted by Zarrouk et al,\textsuperscript{29} compared recovery strategies after peak torque trials during isokinetic contractions of the quadriceps muscles. Peak torque and EMG data were both collected to see the effects of passive recovery, active recovery, and electromyostimulation recovery after the fatiguing task.\textsuperscript{29} The investigators provided evidence that the active recovery sessions resulted in a greater deficit in peak torque for isokinetic contractions at 60, 120, and 180°/sec.\textsuperscript{29} Also, following the active recovery, there were deficits in EMG activity levels when compared to the passive rest and electromyostimulation rest.\textsuperscript{29} Based on these results, we may have had a similar experience with our trials. The active recovery in between testing sessions may have fatigued our participants resulting in deficits in both isometric strength and EMG activity. For future experiments, there should potentially be two sessions observing active and passive recovery in
between the sham and active tDCS conditions.

We also expected to see an improvement in subjective scores after the tDCS condition. When observing the change scores and effect sizes for KOOS Pn ($d = 0.41$; CI = -0.48, 1.30; tDCS = 2.8% increase, sham = 0.6% increase) and KOOS Sx ($d = 0.52$; CI = -0.37, 1.41; tDCS = 4.7% increase, sham = 3.1% increase) there was an increase from the pre and post measurements. However, the subjective scores for pain and osteoarthritis symptoms represented a time main effect, which infers that regardless of the condition, there was going to be a change in scores. The slight improvement of these scores may be a result of the 20-minutes of treadmill walking. Exercise as a symptom management provides evidence-based treatment while also providing similar, if not better, effects in comparison to other medical treatments. Therefore, it would make sense to see a slight improvement in scores even with this short bout of exercise.

Significant interactions or effects were potentially not found because only one trial of tDCS was performed. Previous literature has been presented suggesting that after ACLR, the central nervous system becomes remodeled after a certain time period. Due to this reorganization, there is a lack of communication between the CNS and the muscles surrounding the reconstructed joint. The increased neuroplasticity results in higher activation in other parts of the brain outside of the motor cortex (anterior cingulate gyrus, inferior frontal gyrus, etc.) in order to complete specific functional tasks. These changes in the neural pathways have been shown to exist up to 6-years post-ACLR. Our participants were on ranged from 11-months to 12-years post-ACLR. Due to the persistent restructuring in the pathways, we believe that one
session of tDCS was not enough to reverse the effects of the pathway alterations. Previous tDCS studies have used multiple treatment sessions of active tDCS where they saw beneficial effects resulting from the treatment.\textsuperscript{21,22} Also, we collected gross measurements of torque and EMG data. We may have been able to find a significant effect if we used more sensitive outcome measures such as transcranial magnetic stimulation (TMS) to detect any immediate changes in corticospinal excitability. TMS has been used in studies noting neuromuscular changes in ACLR patients because of the corticospinal changes post-surgery.\textsuperscript{8,13,15,16,25,31-34} Although the tDCS unit may not have shown any peripheral effects, there still could have been an increase of activity within the motor cortex. TMS would have allowed for us to obtain pre and post measurements of corticospinal excitability.

\textit{Limitations}

A limitation of this present study is that we did not know the exact intensity of the stimulation to the motor cortex. Although the product has its own scale of intensity (1-10), there is no algorithm provided to help determine the exact milliamps used to stimulate the brain. Our investigation team was also not able to determine the depth of stimulation of the motor cortex. The area of the motor cortex directly responsible for quadriceps muscle function is located slightly deeper than the rest of the active areas. In future studies, electroencephalography could be used to help determine the depth of penetration of the motor cortex after an active tDCS trial. This was a single-blinded experiment, so the investigator knew which condition the participants were receiving for each session. This may have created some unintentional bias which then could result in less external motivation exhibited by the investigation team. Lastly, there was no
specific method for finding the motor cortex to ensure that the stimulation was constantly targeting the desired area of the brain. We could have measured from the tip of the nose to the base of the occiput and from left and right external auditory meatus to pinpoint the exact location of the motor cortex. In future studies, a more exact approach should be used to ensure the optimal location of the tDCS unit over the motor cortex.

Conclusions

The results of this investigation suggested that there was a decline in EMG activity as well as isometric strength whether participants received active tDCS or a sham condition. Also, isometric strength was shown to change no matter what time point the data was collected at. Subjective scores were shown to increase between pre and post conditions and was not dependent on the condition. No significant interactions were detected between time and condition for individuals with ACLR following active tDCS. Future research needs to observe the effects of tDCS at different time points on multiple testing sessions. More sensitive measures, such as TMS, should be collected to determine if tDCS has any effect on corticospinal excitability.
APPENDIX

Figure 1: Testing Protocol

**Testing Protocol:**
Baseline Testing: Isometric strength (MVIC), voluntary activation (CAR), electromyographic activity (EMG), and Knee Injury and Osteoarthritis Outcome Score for pain and symptoms.
Condition: Active transcranial direct current stimulation or sham condition used for each participant while walking on the treadmill for 20-minutes.
Post-Testing: Repeat of baseline testing outcome measures.
Figure 2.a.) Positioning for MVIC testing. Figure 2.b.) Central Activation Ratio testing.

Figure 2.a.)

Figure 2.b.)

Figure 2b: Visual representation of the super-imposed burst (SIB) technique to determine the voluntary activation of the quadriceps, including the equation to find the percent of quadriceps activation. The maximal voluntary isometric contraction (MVIC) was divided by the torque produced with the SIB.
Figure 3.) EMG sensor and stimulation pad placement
Figure 5.a.) Represents the group averages of VM EMG activity at pre and post testing for each condition. The * represents a significant (p < 0.05) time main effect inferring that there is a change in VM EMG activity regardless of the condition present during the trial. The percentages represent the change score from pre to post testing. Figure 5.b) Represents the change in VM EMG for each individual participant at pre and post testing sessions.

**Figure 5.a.)**

![Bar chart](image)

\[ d = .41; -.47, 1.30; \Delta \text{ Score tDCS} = -12.1\%; \Delta \text{ Score Sham} = -18.9\% \text{ (t=} 1.03, P= 0.313) \]

**Figure 5.b.)**

![Graph](image)
Figure 6.a.) Represents the group averages of VL EMG activity at pre and post testing for each condition. The * represents a significant (p < 0.05) time main effect inferring that there is a change in VL EMG activity regardless of the condition present during the trial. The percentages represent the change score from pre to post testing. 5.b) Represents the change in VL EMG for each individual participant at pre and post testing sessions.

$d= 0.47; -0.41, 1.36; \Delta \text{ Score tDCS}= -14.8\%; \Delta \text{ Score Sham}= -25.9\%
(t= 1.323, P=0.249)
Figure 7.6) Represents the group averages of isometric strength at pre and post testing for each condition. The * represents a significant (p < 0.05) time main effect inferring that there is a change in isometric strength regardless of the condition present during the trial. The percentages represent the change score from pre to post testing. 7.7b) Represents the change in isometric strength for each individual participant at pre and post testing sessions.

**Figure 7.6a)**

![Graph showing isometric strength averages](image)

\[ d = 0.12; -0.76, 1.00; \Delta \text{Score tDCS} = -8.9\%; \Delta \text{Score Sham} = -10.1\% (t=0.336, P=0.745) \]

**Figure 7.7b)**

![Graph showing individual change scores](image)
Figure 8.a.) Represents the group averages of percent voluntary activation at pre and post testing for each condition. The percentages represent the change score from pre to post testing. 8.b.) Represents the change in voluntary activation for each individual participant at pre and post testing sessions.

**Figure 8.a.)**

Central Activation Ratio: Reconstructed Limb

![Graph showing Central Activation Ratio: Reconstructed Limb with bars for CAR_tDCS and CAR_Sham, with annotations for d= -0.12; -0.99, 0.76; Δ Score tDCS = -5.03% Δ Score Sham = -5.5% (t=-0.278, P= 0.787)]

**Figure 8.b.)**

Central Activation Ratio: Reconstructed Limb

![Graph showing Central Activation Ratio: Reconstructed Limb with lines for tDCS and Sham groups, with annotations for tDCS and Sham Group Means]
Figure 9.a.) Represents the group averages of KOOS Pn score at pre and post testing for each condition. The * represents a significant (p < 0.05) time main effect inferring that there is a change in KOOS Pn score activity regardless of the condition present during the trial. The percentages represent the change score from pre to post testing. 9.b) Represents the change in KOOS Pn for each individual participant at pre and post testing sessions.

![KOOS Pain Score Graph](image)

\[ d = .41; -0.48, 1.30; \ \Delta \text{Score} \text{tDCS}= 2.8\% \ \Delta \text{Score Sham}= 0.6\% (t=0.756, P=0.469) \]

Figure 9.b.)
Figure 10.a.) Represents the group averages of KOOS Sx score at pre and post testing for each condition. The * represents a significant (p < 0.05) time main effect inferring that there is a change in KOOS Sx score regardless of the condition present during the trial. The percentages represent the change score from pre to post testing. 10.b) Represents the change in KOOS Sx for each individual participant at pre and post testing sessions.

![KOOS Symptom Scores](image)

\[ d = 0.52; -0.37, 1.41; \Delta \text{ Score tDCS} = 4.7\% \quad \Delta \text{ Score Sham} = 3.1\% \ (t=1.929, \ P=0.086) \]

Figure 10.b.)

![Knee Injury and Osteoarthritis Outcome Score: Pain](image)
REFERENCES


