**Title:** **Implications of the Cross Education Phenomenon on Rehabilitation and Training**

**Abstract:** The mechanism responsible for the cross education phenomenon, which is the transfer of strength and mobility into a non-active limb by training the opposing limb, is still unclear. Several mechanisms exist to describe cross education happening at different levels within the body. There is significant data suggesting that it is a neural mechanism that occurs within the higher centers of the brain. As a result, this research project focuses on identifying and understanding the brain and muscular mechanisms responsible for cross education effects during physical and mental practice on the trained limb through a study of participants over several weeks. The use of electromyography and electroencephalography will measure changes in muscle activation and within the brain regions, respectively, to assess the benefits of the training program. The findings from this research will inform researchers and clinicians on the effectiveness of these training interventions and will provide valuable insight to establish innovative rehabilitation practices for individuals recovering from conditions such as stroke, multiple sclerosis, and immobilization in clinical settings.

**Personal Statement:** When I was a kid, I fell in love with playing the violin. I carried it on my back everywhere I went, never to leave it behind. Competing, traveling, and sharing music with communities that could not experience the power of such beautiful sounds was my life for nine beautiful years. Amidst the excitement of my musical journey, I began to notice uncomfortable aches occurring within my body. As one can imagine, holding a violin is a very unnatural body position. I later began to develop pain and discomfort in my left shoulder, back, and neck, weakness on the dominant side of my body, and muscle size imbalances.

Practicing music eventually became cumbersome for any great length of time. Wanting to find answers to my problems, I turned to the internet. All the blogs, articles, and websites I came across suggested one common solution—physical exercise and stretching. Although music and sports were on the opposite sides of the spectrum, I reluctantly decided to try something new and go to my community recreational center for the first time. I completed my first workout ever and I had never felt so sore and exhausted in my life. However, I felt unbelievably amazing afterwards. I went back the following day and the day after, and so on. Eventually, I became stronger; my muscles ached less. My movements were less stiff and rigid. Not only did my performance in the gym improve, but so did my violin performance Soon after, I began researching about how muscles functioned, developed, and recovered which quickly evolved into a new passion: understanding the human body.

I had this insatiable thirst to find information about the human body. I searched everywhere for answers, reading anything I could get my hands on about the subject and finding experts to point me in the right direction. I accepted every opportunity that presented itself to me which gave me the privilege to shadow local physicians, participate in an internship through the University of Tennessee Youth Leadership Medical Forum twice, and attend The People to People national medical conference at John Hopkins University. The more experiences and skills I acquired about the body, the more aware I became about health and illness around the world.

Even after these unforgettable experiences, I still felt unsatisfied. As a result, I decided that the next step for me was to make a difference in the world. I did my high school senior capstone research project on Neglected Tropical Diseases in third world countries. I presented in front of my school, brought awareness to my community, and raised over seven hundred dollars to cure over 1,400 people with the seven most common tropical diseases.

My first two years at Elon have only encouraged me to pursue and learn more about medicine. After having the opportunity to take courses such as anatomy, physiology, exercise science practicum, and neuromotor control, my love for medicine has only been reassured. In addition, I was offered the chance to enroll in the EMT extracurricular course at Elon, which led me to receiving my North Carolina State EMT certification.

Medicine and health are topics that are near and dear to my heart because these are issues that will forever directly or indirectly affect everyone, regardless if rich, poor, strong, weak, etc. The Lumen Prize would allow me to conduct extensive research on the human body by providing the resources to do so. It will further my passion for medicine and give me the techniques to explore these burning questions I have as part of my professional development. It will allow me to spread awareness and collaborate with professionals and experts at national conferences as I become immersed in the health field. Most importantly, this project will allow me to be able to begin giving back to the community as I continue on the path of medicine and eventually doctorhood.

**Focus:**

Imagine being a sprinter who has injured their right leg and has been instructed to not apply any pressure on it. During several weeks of recovery, muscle strength and function in the compromised leg declines. Despite this setback, there may be ways to minimize atrophy and speed up recovery. Physical exercise on the left leg, as well as imagined contractions, can not only strengthen and increase function of the mobile leg, but also provide the same benefits indirectly to the immobilized leg (Yue, 1992). Recovery from a musculoskeletal injury can require ample time and costly surgical procedures. Sports, physically demanding jobs, accidents, and health events such as stroke are common causes of incidents resulting in immobilized limbs. Typical consequences from immobilization include loss of muscle function, strength, and mobility in the affected limb. However, it may be possible to reduce the immobilization period, make recovery more effective, and preserve strength in the limb thanks to a concept known as cross education. Cross education of muscles – the phenomenon in which training one limb leads to improvement in strength, mobility, and activation in the opposing untrained limb – has been observed for over a century in the field of exercise science (Lee, 2007). The implications and impact of cross education is immense in areas such as rehabilitation for patients with debilitating, immobilizing, or limb degenerative medical conditions. Cross education is not age or gender limited and can occur in small or large muscle groups through voluntary contractions, electrical stimulation, or imagined contractions of the active limb (Lee, 2007). The observation of these contralateral effects has been documented in studies involving healthy individuals and those recovering from conditions such as a stroke, multiple sclerosis, and immobilization. In recent research trials, strength gains on the immobilized limb have been observed between 3-77% of initial strength, depending on which muscle groups are targeted and the degree of training (Hendy, 2012). In other experimental studies, previously immobile limbs have regained movement by training the opposing side, such as dorsiflexors in stroke victims (Dragert, 2013). There are measured improvements in muscle strength through cross education of muscles; however, how these increases are transferred from one side of the body to the other is still unknown. Therefore, the focus of this project is to better understand the mechanisms of the cross education phenomenon as it relates to muscular function to provide information on improving rehabilitation and strength training practices. This central focus sits at the intersection of neuromotor control and biomechanics – between how the brain and neurons control and learn movement patterns and the actual performance of those movements.

There are competing mechanistic theories that describe cross education as adaptations that occur at the muscular, spinal, or cortical levels within the body. At the muscular level, it has been proposed that muscle hypertrophy, a change in enzyme concentration, or a change in contractile protein composition of the non-active limb should occur while training the opposing limb (Carroll, 2006). However, a recent review did not support these large-muscle adaptations in the non-active limb; instead it was proposed that smaller-muscle adaptations that are still undetectable could be contributing to the phenomenon (Carroll, 2006). Alternatively, the spinal cord mechanism posits that adaptations in motor spinal circuitry allow for these increases to transfer over from the trained limb into the untrained limb (Hendy, 2012). Nevertheless, there is still much that is unknown about how complex nerve circuitry within the spinal cord interact with each other when relaying messages throughout the body (Carroll, 2006). Additionally, testing the spinal cord mechanism requires invasive techniques, such as inserting electrodes into the spinal cord (Hendy, 2012). As a result, the impact it possesses in relation to cross education is very limited, but it is suggested that multiple spinal pathways do contribute to some degree.

The muscular and spinal theories likely contribute to some aspect of cross education, but a cortical mechanism, which has been observed consistently, better explains this phenomenon (Hendy, 2012). The higher centers of the brain are responsible for synthesizing sensory information, cognitive drive, and motor function through the innumerable connections within and between brain regions (Munn, 2005). The brain also possesses the ability to undergo cortical reorganization to compensate or tailor to changes within the body. For example, the brain may develop alternative muscle activation patterns to successfully throw a ball if a person no longer has control over all five fingers on their hand. The brain is hardwired to receive, integrate, and transmit signals across its different sites, so it is theorized that motor neurons branching from the motor cortex are being projected onto bilateral motor neurons even during unilateral training. In other words, the brain sends signals for planning and executing movements to the arm being trained as well as the untrained arm. Not only is this possible through physical training, but also through mental practice. A study showcased mental contractions on one side altering central motor programming, activation, and communication between the brain and muscle by increasing muscle force generation on both sides of the body by mentally contracting one side (Yue, 1992). Due to findings in previous literature and feasibility of measuring changes in the brain and muscle through noninvasive techniques, this project will focus on identifying and understanding the cortical and muscular mechanisms responsible for contralateral effects during unilateral and mental practice on the trained limb.

 By combining measurements of brain activity with muscle activity and movement patterns, it will be possible to get a holistic view of how the brain plans and executes movement. This can then be applied to create better rehabilitation and training techniques by targeting specific neural and muscular mechanisms to improve outcomes.

**Scholarly Process**:

The first stage of this research project will consist of familiarizing myself with the use and interpretation of electromyography (EMG) and electroencephalography (EEG) data. I have already started this process through self-guided tutorials of the EEG equipment and will continue throughout this spring semester. Additionally, Dr. Wittstein will assist me in using EMG, seeking out potential workshops or tutorials in the region to attend, and working through the manufacturers’ training material. By the end of the semester, I will have the confidence to use EMG and EEG to measure the electrical activity in both the muscles and brain, respectively.

During the second stage of the research project, I will use EEG and EMG equipment this summer SURE program to do a pilot study consisting of healthy, young adults. By using both EMG and EEG, it will be possible to observe contributions of the two mechanisms, cortical and muscular, simultaneously through brain and muscle activation. The responses will be recorded for a weight training intervention, in which participants would be asked to perform a simple exercise, such as a bicep curl, on each individual side and both sides together. Once the data is collected, it will be analyzed to identify which brain regions are being stimulated during the exercises, as well as the amount of muscle activation. This second stage will provide practical experience with the equipment in addition to baseline data from a training intervention to compare to my main study.

The next stage of this project entails utilizing both EEG and EMG once more in a larger study consisting of multiple testing groups over several weeks of participation. The study would involve participants split amongst a control, a weight lifting, and a mental practice group throughout my junior year to assess muscular and neural changes of the cross education effect. The control group would receive no weight lifting or mental practice intervention. The weight lifting participants would receive a weight training intervention, such as a bicep curl on one arm. The mental practice group would receive a mental exercise on visualized bicep contractions on one arm. The EMG equipment would be used to measure the change of muscle activation over time on the inactive limb, while EEG would track cortical responses of brain regions over time. After summarizing the data, we would be able to infer unique contributions of muscular and cortical mechanisms to the cross education phenomenon.

In the final stage of this project, we plan to collaborate with physical therapy or other health professionals to see how cross education can be applied in a rehabilitation setting. In this scenario we would work with faculty and students from the College of Health Sciences to determine an appropriate patient group (e.g., ankle injury, knee injury, stroke, etc.) and develop a component for rehabilitation that uses either mental or physical practice to improve patient outcomes. This final stage will allow us to evaluate the effectiveness of using cross education in real-life settings.

**Proposed Products:**

The primary product of this project is scholarly work in the form of formal research presentations and manuscript preparation. Additionally, this work may result in the creation of training techniques for physical rehabilitation.

During the Summer of 2018, I would present the results of my pilot study at the end of SURE. In the Fall of 2018, I would propose my research on contralateral effects for my honors thesis. To further my intellectual curiosity, I would attend conferences such as the ACSM national conference or Society for Neuroscience during my junior year to better my understanding of conducting and presenting research professionally.

Initial findings from my research project would be presented at SURF in the Spring of 2019. In addition, I plan to present my research at SEACSM regional conference in 2020 to receive feedback by experts in my area of research. In the end of Spring 2020, when my research is fully completed, I will be preparing and submitting manuscripts to a disciplinary journal such as American Journal of Sports Science and Medicine to formally publish my findings.

**Feasibility Statement:**

Many of the products and testing equipment needed for this project are available through the exercise science department, such as EMG, EEG, and weights. Some minor consumable products (i.e. electrodes, conducting gel, etc.) may need to be purchased to support this project. Additionally, there may be an opportunity to update software and hardware.

In order for this project to be feasible, there are specific skills I will need to learn such as operating the EMG and EEG equipment. Some of these skills will be self-taught through online and printed tutorials. I will also seek the guidance of experienced Elon faculty, such as Dr. Wittstein and Dr. Bixby from exercise science. There may also be an opportunity to learn these techniques through local tutorials or workshops on EMG and EEG data collection and analysis. To improve my skill and confidence with this equipment, I will use this equipment during my SURE project of 2018 in a small-scale pilot study.

 I have courses on taken anatomy, physiology, and neuromotor control which have given me a solid foundation on the interactions between human body development, structure, and central nervous system communication. I have also taken several honors courses in which I received extensive training on how to synthesize and communicate research.

One of the challenges to overcome during my research is the recruitment of a sizeable number of participants on campus to take part in a monitored five to six-week study. As a result, I intend to use some of the Lumen prize funding to help recruit participants for the study. Accommodating for a large sample size will also be challenging, which is why Dr. Wittstein and I will also be working on coordinating schedules with participants to schedule convenient testing times that will be scaffolded throughout the year. Another obstacle will be monitoring activities in the participants’ lives done outside of the study that could affect results, such as participating in a fitness program during the study. These concerning factors and conditions will be addressed within a waiver before participants are selected. In regards to the applied study, Dr. Wittstein has previously collaborated with faculty in Physical Therapy Education and has positive relationships with other regional institutions. These connections will be vital in order to devise and implement an intervention in a real clinical setting.

**References:**

Carroll, T. J., Herbert, R. D., Munn, J., Lee, M., & Gandevia, S. C. (2006). Contralateral effects of unilateral strength training: Evidence and possible mechanisms. Journal of applied physiology, 101(5), 1514-1522.

Dragert, K., & Zehr, E. P. (2013). High-intensity unilateral dorsiflexor resistance training results in bilateral neuromuscular plasticity after stroke. Experimental Brain Research, 225(1), 93–104. https://doi.org/10.1007/s00221-012-3351-x.

Hendy, A. M., Spittle, M., & Kidgell, D. J. (2012). Cross education and immobilization: Mechanisms and implications for injury rehabilitation. Journal of Science and Medicine in Sport; Belconnen, 15(2), 94–101.

Lee, M., & Carroll, T. J. (2007). Cross education. Sports Medicine, 37(1), 1–14. https://doi.org/10.2165/00007256-200737010-00001

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Yue, G., & Cole, K. J. (1992). Strength increases from the motor program: comparison of training with maximal voluntary and imagined muscle contractions. Journal of neurophysiology, 67(5), 1114-1123.

**Timeline:**

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|  | **Proposed Experiences** | **Proposed Product(s)** |
| **Summer 2018** | Participate in SURE at Elon University -conduct pilot study -operate EEG and EMG equipment | SURE research presentation |
| **Fall 2018** | IRB proposal submissionHNR 498- 2 s.h.  -operate EMG and EEG equipment -begin testing on participants for main study | Honors Thesis Proposal IRB proposal accepted |
| **Winter 2019** | Abroad | None |
| **Spring 2019** | HNR 498 – 2 s.h. -complete testing on participants for main study -data analysis -consult with clinicians for applied study | Data collection and analysisSURF Presentation |
| **Summer 2019** | Participate in SURE at Elon University -complete data analysis -initiate applied studyAttend Progress in Motor Control National conference | SURE research presentationData collection and analysis |
| **Fall 2019** | HNR 498 – 2 s.h. -begin writing Honors Thesis -continue applied intervention study with clinicians  | SEACSM conference abstractData and observation collection from intervention study |
| **Winter 2020** | Continue writing honors thesis  | Complete Honors Thesis |
| **Spring 2020** | HNR 498 – 2 s.h. -attend at SEACSM conference  -draft manuscripts | Honors Thesis DefensePresent at SEACSMSubmit Manuscripts to *Journal of American College Health*, *American Journal of Sports Medicine*, *American Journal of Sports Science and Medicine, American Physiology Society* |

**Budget:**

Participation Incentives

* 21 participants ($100.00)

Total **$2100.00**

Equipment

* Miscellaneous supplies

-electrode gel $2.50x

-disposable stickers $0.50x

Total **$100.00**

Conferences/Workshops

* Society for Neuroscience Conference (4 days San Diego, CA) based on 2018

-$900.00 hotel

-$350.00 attendance fee

-$170.00 food

-$530.00 airfare and shuttle $1950.00

* SEACSM Conference (3 days Chattanooga, TN) based on 2018

-$650.00 hotel

-$15.00 membership

-$100.00 attendance fee

-$100.00 booth fee

-$160.00 food

 -$200.00 gas $1225.00

Total **$3175.00**

Tuition

* Fall 2018-Spring 2019 $7312.50
* Fall 2019-Spring 2020 $7312.50

Total **$14625.00**

**Total $20000.00**