Development of a Mathematical Model of a Lower Leg Muscle to Determine How Muscle Cramps are Formed and Sustained

(Technical Paper)

The Significance of Pain in Pregnant Women Caused by Muscle Cramps and Other Pregnancy Symptoms

(STS Paper)

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Introduction

How can muscle cramps be better understood to improve the lives of pregnant women and other patients?

An estimated 60% of adults experience muscle cramps, and an estimated 40-50% of pregnant women experience severe nocturnal leg cramps, however the limited research in this area has failed to validate a mechanism of cramp formation (Giuriato et al., 2018). The cases of muscle cramps are widely varied, making it difficult to draw conclusions on causes and treatment without investigating the mechanics of muscle components and how they interact with one another. Due to the complexity of muscles and the existence of more pressing research into life-threatening diseases, muscle cramps have been left largely under-researched{Citation}.

A muscle cramp is defined as "an involuntary contraction of a muscle that occurs suddenly and does not relax (*Muscle Cramps - OrthoInfo - AAOS*, n.d.)." These contractions can occur in any skeletal muscle but are seen most commonly in leg muscles such as the calf and quadricep. Currently, healthcare professionals and researchers are unsure of what causes cramps, though there is some speculation surrounding dehydration or factors involving exercise as potential causes. They can last anywhere from a few seconds to 15 minutes with the potential for post-cramp symptoms, and some patients experience pain in the muscle for hours after the cramp subsides, while others experience no effects after the release of the cramp (*Leg Cramps at Night: Causes, Pain Relief & Prevention*, n.d.). Muscle cramps also frequently impair function while they occur, potentially endangering those in physically demanding situations such as swimming or hiking where continuous muscle function is necessary.

Since the mechanism of muscle cramps is unknown, researchers cannot completely validate underlying causes, but there are some conditions and medications that have displayed correlations to cramps, such as medications that treat hypertension or heart disease (*Healthy Aging: Muscle Cramps & Spasms | MUSC Health | Charleston SC*, n.d.). There is also a phenomenon called secondary leg cramps, referring to cramps that occur as a symptom of other more serious conditions like diabetes, amyotrophic lateral sclerosis, and congestive heart failure (*Leg Cramps at Night: Causes, Pain Relief & Prevention*, n.d.). Investigating the connection between these diseases and muscle cramps could lead to increased accuracy in diagnosis and potentially improved treatment timelines for life threatening conditions, but this is currently not feasible as there is such a lack of knowledge surrounding muscle cramps. Pregnancy is also commonly listed as a cause of muscle cramps, but generally no information about why pregnant women may experience muscle cramps or how to prevent them is given, making this yet another symptom that pregnant women have to endure with little to no explanation or treatment (Mathur et al., 2021). The intention of the technical work is to create and validate a mathematical model representing the mechanics of muscle contraction and feedback and use the model to test multiple hypotheses of how cramps are initiated, sustained, and released. The intention of the STS research is to investigate how pregnancy-related pains are viewed in the medical field currently and describe how the attitude towards and treatment of these symptoms needs to change.

Technical Discussion

What is the underlying mechanism of muscle cramps that causes them to be initiated, sustained, and released?

The muscle is comprised of muscle fibers, muscle spindles, and Golgi tendon organs, and acts based on information from the central nervous system and feedback from its components. The muscle spindle is an intrafusal fiber positioned between extrafusal (contractile) fibers that senses muscle length and rate of change of this length, producing afferent nerve firing in response. Muscle spindles send excitatory signals that induce muscle contraction (*Mathematical Models of Proprioceptors. I. Control and Transduction in the Muscle Spindle,* n.d.). The Golgi tendon organ (GTO) is positioned between the muscle fibers and the tendon and is comprised of tendon fibers, innervated collagen, and bypassing collagen. The GTO stretches when muscle contraction occurs, triggering pressure sensitive nerve endings found on the innervated collagen which send inhibitory signals that stop or reduce muscle contraction (*Mathematical Models of Proprioceptors. II. Structure and Function of the Golgi Tendon Organ*, n.d.).

One of the most accurate and relevant depictions of the muscle currently is the Hill-type muscle model, which describes a muscle as a combination of four elements: contractile, parallel elastic, series elastic, and serial damping. It can be used to predict passive and active muscle forces based on mathematical expressions corresponding to mechanical elements in the model such as springs and dashpots. The model as a whole represents the muscle tendon complex and serves as a macroscopic view of muscle contraction, focus on mechanical responses but not modeling neurological feedback created by components within the muscle (Göktepe et al., 2014). Therefore, the Hill model cannot represent muscle cramps, which we believe will be explained by investigating the muscle spindle, Golgi tendon organs, and the afferent firing produced by each of them.

The computational model that we aim to build will be created in python, using mathematic expressions to quantify the responses of each element within the muscle spindle and

Golgi tendon organ. The model will be comprised of a file representing the muscle spindle, equipped with functions that represent each internal component and its response to muscle length and velocity of stretch or contraction, as well as a file representing the Golgi tendon organ, including similar functions. The model will also bring in elements of the Hill-type muscle model, combining mechanical responses with neurological responses to create a comprehensive model of the muscle. Once the model is complete, it will be validated against data collected from cat and human cramp studies.

Using the model that accurately represents a correctly functioning muscle, we will design tests for three main hypotheses describing the mechanism of muscle cramps that we developed based on our current knowledge. The spatial disconnect hypothesis claims that firing occurs from a motor neuron and creates a local contraction, but the motor unit is only connected to a muscle spindle, not a Golgi tendon organ. This leads to a positive feedback loop created by excitatory feedback from the muscle spindle, with a lack of inhibitory feedback from the Golgi tendon organ. The Golgi offloading hypothesis is based on the stretch and contraction of the calf muscle during walking. In this hypothesis, complete unloading of the calf muscle removes tension from the Golgi tendon organ, so while the muscle spindle continues to produce excitatory feedback, the Golgi tendon organ no longer produces inhibitory feedback, resulting in sustained contraction. Finally, the Golgi tendon organ adaptation hypothesis describes a Golgi tendon organ that produces a response as long as stimulation persists, but when repeatedly loaded and unloaded over a brief period of time, sends a lower frequency response, which reduces the overall inhibitory feedback. We will assess each of these hypotheses using the model by altering the structure of the model, specifically the connections between the components, to represent the assumptions made in the hypothesis. Then, using the altered version of the model, we will run

trials using input given in electrically induced cramps and compare the resulting "contraction" of the model with the muscle contraction of the induced cramp. If the model output accurately reflects experimental data, it can be concluded that the hypothesis represented by the model is an accurate description of muscle cramps.

STS Discussion

How should healthcare professionals and medical scientists place importance on the pain of pregnant women?

It is often casually stated that "women have a higher pain tolerance than men." This is a seemingly harmless phrase describing the way men and women relate to their pain, but it perpetuates the subconscious narrative that the pain of women needs to be treated less aggressively than that of men. As people with significant biological differences, men and women do experience pain differently. Some studies site hormonal differences and structural differences in the central nervous system as factors affecting the perception of pain among women and men, and a greater sensory receptor density in women is believed to increase the sensitivity of women's skin when compared to men's (Smith, 2002). However, the underlying biology that shapes human sensory experience is often not considered when treating pain differently between the sexes. Even though women have a higher incidence for reporting pain, they are treated less frequently and less aggressively than their male counterparts. The complaints are seen as emotional, where the complaints of men in pain are seen as logical and valued more highly. The aforementioned statement comparing the pain tolerance of men and women is accepted most likely because women are better at managing the pain they experience. Studies have shown that while women do not on average have a higher pain tolerance than men, they do have more and healthier coping mechanisms that better equip them to endure pain (Smith, 2002). If this is true,

then women are experiencing the same or greater levels of pain than men but are treated less due to their ability to continue functioning even in times of significant pain.

My STS research will focus on the pain women experience related to pregnancy and the response of the healthcare system to said pain. I plan to investigate how pregnancy related pains are treated and examine the perceived significance of women's pain by comparing advancements in medicine targeting pain in men and women. I will assess how women's pain is valued and understood by asking the question: Is women's pain ignored, or seen as less important than men's pain? This research will focus specifically on the healthcare system in the United States as it pertains to pain related to pregnancy and will provide valuable information for the discussion of women's rights in healthcare at large.

The significance of this research is displayed in the results of pain associated with pregnancy. Research has shown that most pregnant women experience moderately severe pain, most frequently in the lower back, pelvic girdle, or abdomen, during pregnancy, and that pregnancy-related pain is linked to postpartum depression. In a study of women up to eleven years postpartum, these researchers found that women who experienced moderate to severe pain during their pregnancy had higher rates of depression (Mathur et al., 2021). This displays the lasting mental effects that pregnancy-related pains can have on women.

Conclusion

This technical project will result in a computer model of a muscle that accurately describes the mechanism of cramps. The medical field will gain an understanding of how muscle cramps are initiated and sustained, and this information may be used to advance prevention and treatment of muscle cramps in a number of ways. Most notably, the discovery of how cramps are

formed will open a field of research likely leading to the development of a systemic or local drug that prevents or relieves cramps. This could be administered to pregnant women who experience a number of severe nocturnal leg cramps, thus reducing the pain they experience during pregnancy. It would also be beneficial for patients who are prone to cramps, preventing long term muscle pain. The STS research will present an analysis of how pregnancy-related pains are viewed and treated in the medical field, along with a plan for reform to increase the respect for pregnant women and the pain they experience, increase the autonomy of pregnant women, and improve the experience of pregnancy.

Resources

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