UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

RELATIONSHIP AMONG SITE SPECIFIC FAT, LEAN MASS, AND PRESSURE PAIN SENSITIVITY

A THESIS

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

Degree of

MASTER OF SCIENCE

By

CAMERON LOHMAN
Norman, Oklahoma
2018

RELATIONSHIP AMONG SITE SPECIFIC FAT, LEAN MASS, AND PRESSURE PAIN SENSITIVITY

A THESIS APPROVED FOR THE
DEPARTMENT OF HEALTH AND EXERCISE SCIENCE

BY

_____
Dr. Christopher Black, Chair

_____
Dr. Michael Bemben

_____
Dr. Rebecca Larson

Acknowledgements

Dr. Black, I cannot express how thankful I am for the opportunity to learn under you. My time in your lab has pushed me to excel in ways I never imagined. You have created a love and desire for research, and did an amazing job showing the importance of the field and its benefits. You are an exceptional mentor and the fun yet challenging learning environment you created in lab is second to none. I am a better student and person because of your example, encouragement, and the learning experiences I obtained working under you. Thank you for taking a chance on me and I hope you enjoyed these past two years as much as I enjoyed them.

Dr. Larson and Dr. Bemben, Thank you for all the encouragement and critical feedback you provided for me. I am very thankful and fortunate you two were on my committee. Thank you for working with me during the recruiting process and allowing me access to your lab equipment. Dr. Larson, thank you for helping Dr. Black and I with DXA procedures and training me to be able to perform the tasks I needed. This thesis project would not have happened if it wasn't for you two!

All my lab mates, thank you for the good times and great conversations. I learned a lot from each of you and I hope you learned something from me as well. Jess, thank you specifically for helping with data collection. I know the summer was a lot, but you being flexible during the process was a huge help and weight off my shoulders. Thank you all!

My parents, thank you all for always encouraging and supporting me throughout my college experience. All the success I have achieved up to now is directly because of you! Thank you again and I love you.

Table of Contents

List of Figures

List of Tables

Abstract

Pain is an unpleasant sensory or emotional experience associated with tissue damage or the potential for tissue damage. Over the years, research has studied the relationship between pain and body composition (BC). **PURPOSE:** The purposes of this study were to investigate if there are any site specific differences in pressure pain threshold (PPT), if lean and fat mass correlate with PPT values in any way, and if the magnitude of a conditioned pain modulation (CPM) or exercise induced hypoalgesia (EIH) is affected by BC. **METHODS:** 30 female and 26 male participants 3 experimental visits. BC via DXA scans and muscle/fat thickness at the specific sites were assessed on the first visit. During the first visit, participants were also familiarized to the PPT protocol. The second visit consisted on a baseline PPT measurement followed by a CPM where participants placed their feet in an ice bath for 1 min. Once the CPM protocol was completed, PPTs were measured immediately after. Baseline PPTs were measured again for the third visit, followed by an EIH protocol. To produce and EIH response, participants held 25% of their maximal isometric knee extension till failure. PPTs were assessed immediately after exercise failure. A Spearman correlation coefficients were determined between BC values and baseline PPTs. Independent t-test was used to determine any gender differences, and a mixed factorial ANOVA was ran for CPM and EIH assessments. **RESULTS:** PPTs from the left forearm (LA) had no significant correlations for total body fat ($p = 0.85$), body fat percentage ($p = 0.20$), fat percentage within the limb ($p = 0.73$), fat mass within the limb ($p = 0.08$), fat thickness at the measured site ($p = 0.59$), or skin fold measurements at the site ($p = 0.71$). No significant relationship was found in the right forearm (RA) [total body fat ($p = 0.81$), body fat

percentage ($p = 0.24$), fat percentage within the limb ($p = 0.52$), fat mass within the limb ($p = 0.83$), fat thickness at the measured site ($p = 0.63$), or skin fold measurements ($p = 0.62$)] or the non-dominant leg (NDL) [total body fat ($p = 0.07$), body fat percentage ($p = 0.32$), fat mass within the limb ($p = 0.33$), fat thickness at the site ($p = 0.33$), or skin fold measurements ($p = 0.50$).The dominant limb's (DL) PPT did show a significant negative correlation with fat percentage within the limb ($p = 0.03$). The DL did not correlate with total body fat ($p = 0.90$), body fat percentage ($p = 0.104$), fat mass within the limb ($p = 0.42$), fat thickness at the measured site ($p=0.08$), or skin fold measurements ($p = 0.29$). LA and NDL had significant correlations with total bone free lean mass (LA: $p = 0.02$, NDL: $p \leq 0.001$), bone free lean mass at the limb (LA: $p = 0.02$, NDL: $p \leq 0.001$), and muscle thickness (LA: $p = 0.03$, NDL: $p = 0.026$). The DL had significant correlations for total bone free lean mass ($p \leq 0.001$) and bone free lean mass at the limb ($p \leq 0.001$), but not for muscle thickness ($p = 0.13$). The RA showed significant correlations with bone free lean mass at the limb ($p = 0.04$), but not total bone free lean mass ($p = 0.09$) or muscle thickness ($p = 0.26$). There were no significant correlations between any of the BC measurements and the magnitude of CPM response ($p > 0.05$). The EIH response significantly increased PPTs for all of the four measured sites ($p \leq 0.001$). The EIH responses did not correlate with any of the taken BC measurements for the LA or the DL ($p \geq 0.05$). The RA had a significant correlation with total body fat ($p = 0.04$), fat mass within the limb ($p = 0.03$), and skinfold measurements ($p = 0.03$); However, all other RA BC measurement did not ($p \geq 0.05$). No measures of BC correlated with the EIH response for the NDL ($p \geq 0.10$). The EIH responses for the NDL did not correlate with total bone free lean mass or bone free lean mass with in the limb ($p \geq 0.05$). The results did show

that the NDL muscle thickness was negatively correlated with the EIH response ($p = 0.04$). **CONCLUSION:** PPTs positively correlated with bone free lean mass and not fat mass, suggesting that bone free lean mass plays a role in individuals PPTs values. The CPM response showed no relationship with BC. Results did suggest a potential relationship between the EIH response and BC; however, further investigation is need to determine if a relationship exists.

Chapter I: Introduction

1.1: Introduction

Pain is an unpleasant sensory or emotional experience associated with tissue damage or the potential for tissue damage (Merskey & Bogduk, 1994). A study published in 2012 found that 100 million people in the United States were affected by persistent pain, and the annual health care cost of pain was roughly $600 billion (Gaskin & Richard, 2012). The annual cost of pain was found to be higher than the next six most costly diagnoses, with cardiovascular diseases costing the next highest at $309 billion per year (Gaskin & Richard, 2012). Individuals with moderate or severe pain spend ($4,000 or $7,000, respectively) more per year than individuals with no pain (Gaskin & Richard, 2012).

Pain is a complex sensation that aids in avoiding situations where tissue damage could occur and to help maintain homeostasis in the body (Christopher D Black, 2012; O'Connor & Cook, 1999). Psychological and physiological processes are both involved in the perception of pain (Christopher D Black, 2012; O'Connor & Cook, 1999). Pain is the brain's interpretation of sensory input, within the somatic nervous system, that are evoked by noxious stimuli (Gold & Gebhart, 2010). A noxious stimulus is a stimulus that is damaging or potentially damaging to the tissue where the stimulus is applied (O'Connor & Cook, 1999). The term nociception describes the activation, conduction, and transmission processes for nociceptors to a noxious stimulus (Gold & Gebhart, 2010). The two major types of nociceptors are A-delta fibers and C-fibers. A-delta fibers typically respond to pressure stimuli and C-fibers typically respond to electrical, thermal, and/or chemical stimuli; however, some nociceptors are polymodal—meaning they can

respond to multiple stimuli (Christopher D Black, 2012; O'Connor & Cook, 1999). A-delta fibers are thinly myelinated free nerve endings and typically have higher conduction velocities, while C-fibers are unmyelinated and have lower conductions velocities compared to the A-delta fibers (Black, 2012; Gold & Gebhart, 2010). When a noxious stimulus interacts with a nociceptor an electrical signal is generated. If the stimulus meets or exceeds the activation threshold for the nociceptor, the signal travels down the neuron to the dorsal horn of the spinal cord and then travels to different regions of the brain via interneurons and several spinal tracts (Gold & Gebhart, 2010)(O'Connor & Cook, 1999). A common method used to investigate nociception and pain sensitivity is to determine the minimum noxious stimulus required to be deemed "painful"; termed a pain threshold (Christopher D Black, 2012; O'Connor & Cook, 1999). Pain thresholds have been shown to vary widely among individuals due to factors such as sex, pain history, state-of-training, etc. (Naugle, Fillingim, & Riley, 2012) Sensitivity to pressure is one of the most common noxious stimuli whose threshold is examined—whereby an increasing amount of pressure is applied to a specific site until the pressure is painful, termed a pressure pain threshold (PPT) (O'Connor & Cook, 1999). Pain thresholds can also be assessed by applying either an electrical or thermal noxious stimulus—termed as electrical pain threshold (EPT) or thermal pain threshold (TPT) (O'Connor & Cook, 1999).

One emerging factor that has been shown to potentially influence pain thresholds is body composition (BC), specifically excess body fat. The results of previous research have varied when investigating the effects of BC on pain thresholds. This may, in part, be due to the methods used to assess BC. Body mass index (BMI) (Khimich, 1997; McKendall & Haier, 1983; Price, Asenjo, Christou, Backman, & Schweinhardt, 2013;

Tashani, Astita, Sharp, & Johnson, 2017; Zahorska-Markiewicz, Kucio, & Pyszkowska, 1983; Zahorska-Markiewicz, Zych, & Kucio, 1988) and waist-to-hip ratio (WHR) (Tashani et al., 2017), neither of which are true measures of BC, skinfold estimates (Tashani et al., 2017), and dual-energy x-ray scans (DXA) (Stolzman & Hoeger Bement, 2016) have all been used to estimate BC and/or body size. When pain thresholds were measured at the forearm to an electrical stimulus (Zahorska-Markiewicz et al., 1983, 1988) or pressure (Khimich, 1997), the results indicated that obese individuals (BMI > 30) were less sensitive to pain (i.e. have higher pain thresholds) compared to those classified as overweight or normal weight. When measured at the hand, obese individuals been shown to have either reduced PPTs (more sensitive to pain) or not differ among from overweight or normal weight individuals (McKendall & Haier, 1983; Price et al., 2013; Tashani et al., 2017). The single study that used DXA scans (Stolzman & Hoeger Bement, 2016) to objectively measure BC found no difference in PPT values assessed at the finger, nailbed, and deltoid muscle across different body composition categories. In a previous study from our lab (C. D. Black et al., 2017) and from unpublished observations from our lab (Schubert, 2017), we have observed an inverse relationship between body weight and PPT in the muscles of the forearm and quadriceps. As such it remains unclear the extent to which fat mass, fat-free mass, and/or adipose tissue thickness directly over the PPT assessment site affect pain sensitivity particularly to pressure stimuli.

Exercise-induced hypoalgesia (EIH) is a type of endogenous pain modulation where pain sensitivity is acutely decreased following a bout of exercise. EIH has been shown to occur in both the exercising limb(s) and at more distant/remote sites on the body (Crombie, Brellenthin, Hillard, & Koltyn, 2017; Koltyn & Umeda, 2007). EIH

occurs after aerobic, resistance, or isometric exercise and has been shown to last for up to 30 minutes (Crombie et al., 2017; Koltyn & Umeda, 2007; Vaegter, Handberg, & Graven-Nielsen, 2014). The exercises result in an EIH response from activation of endogenous pain inhibitory mechanisms, but the pathways that lead to pain this modulation are not entirely understood (Koltyn & Umeda, 2007). The endogenous opioid system is a suggested mechanism of EIH and is potentially activated by muscle contractions simulating the release of endogenous opioids. The endocannabinoid system is another potential mechanism of EIH (Crombie et al., 2017). Cannabinoid levels have been shown to rise during exercise and potentially interact with receptors in the brain to alter pain interpretations. Another possible mechanism for EIH is a phenomenon method termed conditioned pain modulation (CPM). CPM describes a process whereby the application of an initial painful stimulus (termed the conditioning stimulus) functions to reduce pain from a second stimulus (Ellingson, Koltyn, Kim, & Cook, 2014). This process is often termed "pain inhibits pain" and likely works by activating descending neural pathways that decrease the pain sensitivity to other applied noxious stimuli (Ellingson et al., 2014; Lemley, Hunter, & Bement, 2015). In this manner, pain experienced during exercise may function to "condition" the nervous system to future noxious stimuli. The magnitude of CPM has been shown to correlate with the magnitude of EIH (Lemley et al., 2015), suggesting they may function via similar mechanisms. The CPM response is often tested, independently of EIH, by placing a participant's hand or foot into an ice bath for up to a minute and then assess the change in their pain sensitivity. Interestingly, DXA assessed bone free lean mass (but not fat mass) has been shown to be positively correlated with the CPM response in adolescents—suggesting

body composition might plausibly affect the EIH response as well (Stolzman & Hoeger Bement, 2016). To the author's knowledge, no research has been performed to comparing whole-body and site-specific body composition with pain sensitivity, EIH, and CPM in college-aged adults.

1.2: Purpose of the Study:

The purpose of this study was to determine if a significant relationship exists between the sensitivity of several sites to pressure stimuli (assessed as PPTs) were related values with DXA assessed measure of body composition and site specific assessments of fat and muscle thickness. This study also sought to determine if a significant relationship existed for CPM and EIH with body composition measurements.

1.3: Research Questions

1. Will a significant relationship exist among resting pressure pain thresholds, assessed in both forearms and both quadriceps, and assessments of total body percent fat (via DXA), total body fat mass (via DXA), total body lean tissue mass (via DXA), assessment site specific fat thickness (via ultrasound), muscle thickness (via ultrasound), and site specific skinfold thickness?
2. Will a significant relationship exist among the conditioned pain modulation response, assessed in both forearms and both quadriceps, and assessments of total body percent fat (via DXA), total body fat mass (via DXA), total body lean tissue mass (via DXA), assessment site specific fat thickness (via ultrasound), muscle thickness (via ultrasound), and site specific skinfold thickness?
3. Will a significant relationship exist among the exercise-induced hypoalgesia response, assessed in both forearms and both quadriceps, and assessments of total

body percent fat (via DXA), total body fat mass (via DXA), total body lean tissue mass (via DXA), assessment site specific fat thickness (via ultrasound), muscle thickness (via ultrasound), and site specific skinfold thickness?

1.4: Sub-Questions

1. Do resting PPT, CPM, and EIH differ between men and women?
2. Does a relationship exist among PPT, CPM, EIH, and self-reported physical activity?

1.5: Hypotheses

1. A significant positive relationship will exist between resting PPT in both forearms and quadriceps and total body percent fat, fat mass, fat thickness, and skinfold thickness.
2. No significant relationship will exist between resting PPT in both forearms and quadriceps and lean tissue mass and muscle thickness.
3. A significant negative relationship will exist between CPM in both forearms and quadriceps and total body percent fat, fat mass, fat thickness, and skinfold thickness.
4. A significant positive relationship will exist between CPM in both forearms and quadriceps and lean tissue mass and muscle thickness.
5. A significant negative relationship will exist between EIH in both forearms and quadriceps and total body percent fat, fat mass, fat thickness, and skinfold thickness.
6. A significant positive relationship will exist between EIH in both forearms and quadriceps and lean tissue mass and muscle thickness.

1.6: Sub-Hypotheses

1. Women will have reduced resting PPTs compared to men
2. No differences will be observed between men and women in their CPM and EIH response.
3. A significant positive relationship will exist among resting PPTs, CPM, and EIH and total, moderate, and vigorous intensity physical activity.

1.7: Significance of the Study

Based on the author's knowledge, no research has looked at EIH and its relationship with BC; furthermore, CPM and its relationship with BC has only been studied in adolescents. This will be the first study that looks into the relationship between BC and both EIH and CPM in healthy adults.

1.8: Limitations

1. Participants will be between the ages of 18-30 with no prior medically diagnosed chronic pain and will be recruited within Norman, OK.
2. PPTs are subjective and cannot control for dishonest readings.
3. Participants will be asked to refrain from taking pain medication during the experiment, but the daily routines of the participants cannot be controlled.

1.9: Delimitations

1. Participants will be familiarized to PPT measurements, MVC protocols, and the EIH protocol to limit training effects.
2. Participants will complete questionnaires confirm they fit the criteria to participate in the experiment.

1.10: Assumptions

1. Subjects are without any symptoms of chronic pain.
2. Subjects are honest on the perception of the onset of pain.
3. Subjects will give maximal effort during MVC protocols.
4. The exercise protocol and method used for EIH and CPM are sufficient to produce the desired response.

1.11: Operational Definitions

1. **Algesia**: Sensitivity to noxious stimuli.
2. **Hypoalgesia**: A decrease in the perception of pain from noxious stimuli.
3. **Exercise-induced hypoalgesia**: A decrease in the perception of pain from noxious stimuli following a bout of exercise.
4. **Conditioned pain modulation**: A decrease in pain sensitivity to noxious stimuli by administering noxious stimuli to separate locations
5. **Physical activity**: Body movement that requires additional caloric expenditure
6. **Body fat percentage**: The percentage of total body composition that is fat.
7. **Total body fat mass**: The total amount of fat mass within an individual.
8. **Total body lean tissue mass**: The total amount of lean muscle mass within an individual.
9. **Muscle thickness**: The amount of muscle between the subcutaneous fat and bone at a given site.
10. **Subcutaneous fat thickness**: The amount of fat between the skin and muscle at a given site.

11. **Skin-fold thickness**: The width of subcutaneous fat and skin when measured by calipers.
12. **Pressure pain threshold**: The amount of pressure required to interpret stimuli as painful.

Chapter II: Review of Literature

2.1: Nociception

Pain, and the unique characteristics it has compared to the other 5 senses, has been studied quite frequently and thoroughly. As mentioned previously in chapter 1, the term nociception is used when describing a noxious stimulus and the pathways involved in the interpretation of the noxious stimulus to be painful. It is very important to remember that pain involves both physiological and mental interpretations following a noxious stimulus. Tracey and Mantyh (Tracey & Mantyh, 2007)discussed how emotion/mood, context, and cognitive awareness can affect the overall interpretation of a noxious stimulus, not just the physiological pathways used in a noxious interpretation. They concluded that the mental aspect of interpreting pain affects the descending neural pathway via different areas within the brain. The authors found evidence showing some areas of the brain either facilitate or inhibit nociception; furthermore, those areas of the brain are: periaqueductal gray, amygdala, frontal lobe, insula, hypothalamus, anterior cingulate cortex, nucleus cuneiformis, and the rostral ventromedial medulla.

On the more physiological aspect of nociception, multitude of research has identified mechanisms for both input and output signaling of pain [see (Christopher D Black, 2012; O'Connor & Cook, 1999) for review]. When a stimulus is applied to the muscle, it must reach a certain threshold to activate the nociceptors (either A-delta or C fibers). Once the fibers are activated, they transmit the signal to the dorsal root of the spinal cord where the signal is then transmitted (usually with the biochemical marker substance P) to the dorsal horn of the spinal cord. The signal will then travel to the supraspinal regions in the brain/brainstem for further interpretation where the above-

mentioned areas of the brain interact with the signal to affect the descending pathway through endogenous opioids; however, modulation of pain is not limited to the descending pathway alone. Black (2012) discussed the gate control theory that utilizes the activation of non-nociceptive fibers that act to diminish a noxious stimulus by inhibition of substance P in the spinal cord via interneurons (i.e. muscle massages).

Not only is the interpretation process of pain a complex system, but research has also shown the gender and age can influence pain sensitivity. Petrini et al. (Petrini, Matthiesen, & Arendt-Nielsen, 2015) published a study in 2015 that investigated the relationship between both age and gender and their potential effects on PPT values. 20 young adults (10 female) between the ages of 20-34 and 20 older adults (10 female) between the ages of 65-88 participated. All subjects were free from any diagnosed chronic pain and reported they were pain-free on the day of the experiment. A hand-held pressure algometer was placed on the left and right index fingers and the left and right trapezius muscles to measure PPT and pressure pain tolerance threshold (PPTT) (the point at which the pain is unbearable). The authors found PPT to be lower in older adults compared to younger adults. They concluded the reasons for their results were potentially reductions in endogenous pain inhibition and/or degenerative changes due to aging. Petrini et al. (Petrini et al., 2015) found gender differences in PPT only in the younger adults; furthermore, they concluded the differences could be due to biological, hormonal, or genetic factors. A review article by Riley et al. (Riley, Robinson, Wise, Myers, & Fillingim, 1998) published in 1998 found similar results in gender differences.

2.2: Exercise-Induced Hypoalgesia

EIH is a typical intervention to assess PTs, and there are a variety of exercise interventions that can produce EIH. Naugle et al published a review comparing various aerobic, isometric, and dynamic exercise protocols. The authors concluded that all three types of exercise can produce EIH. The responses to the exercise ranged from moderate to large depending on the type of exercise as well as duration; more specifically, they found isometric exercise to have larger effects when the protocol consisted of low intensities (25% of MVC) and longer durations (until failure) (Naugle et al., 2012). Hoeger et al. (Hoeger Bement, Dicapo, Rasiarmos, & Hunter, 2008) specifically looked at the dose responses for isometric exercises at varying intensities and durations. A total of 40 men and women, who were all healthy young adults with no neurological diseases, participated in the experiment. All subjects went through a familiarization day followed by 4 experimental days; furthermore, all the subjects were administered the same interventions. The exercise task was a static contraction of the elbow flexor muscles and pain measurements were assessed with a noxious pressure stimulus. The stimulus was applied on the middle of the right index finger with a pressure equal to 1 kg and was applied for two consecutive minutes. The subjects completed 4 different isometric exercises with pain measurements taken before and 30 min after the exercise intervention. The 4 exercises were 3 MVCs sustained for 2 secs, holding 25% of MVC until task failure, 25% of MVC for 2 min, and 80% of MVC until task failure. Hoeger et al found that pain thresholds had the greatest increases following 25% MVC until task failure, although the changes in increases were only significant between the two 25% exercises and not between task failure exercises (Hoeger Bement et al., 2008).

Research has also shown that EIH has a more general pain inhibition and not just the exercising muscle group. Kosek and Lundberg (Kosek & Lundberg, 2003) investigated the PPT changes in the quadriceps and infraspinatus muscles; furthermore, the authors recruited 24 males and females for the experiment. PPTs were measured before, during, and 30 min after the exercises. The measurements were taken at the exercising muscle, resting contralateral muscle, and resting distal muscle (either the quads or infraspinatus muscles) in that order. Subjects were seated in a chair for the quadriceps exercise, and they performed a full leg extension using their dominant leg with a 1kg weight attached to the ankle; furthermore, the subjects were instructed to hold the weight until task failure or until they made it through 10 rounds of PPT assessments. For static contractions at the infraspinatus, the subjects were instructed to hold a 0.5kg weight attached at the wrist 20 degrees off a pad while keeping the elbow (flexed at 90 degrees) resting on the pad. The subjects were required to hold that position until task failure or until 10 rounds of PPT assessments were completed. The authors found that EIH responses can be found not only in the exercising muscle but the contralateral and distal muscles as well. The exercising muscle had larger increases in PPTs suggesting that there is a localized response as well as a general response to EIH (Kosek & Lundberg, 2003).

A study done by Koltyn et al. (Koltyn, Brellenthin, Cook, Sehgal, & Hillard, 2014) investigated the mechanisms behind EIH. The authors recruited 30 males and 30 females to undergo thermal and pressure stimuli to induce a pain response as well as complete an isometric exercise protocol to produce EIH. The isometric exercise used a hand dynamometer to assess grip strength and required the subjects to hold 25% of their

individual MVC for 3 minutes to produce EIH and pain and thermal stimuli were applied to the forefinger and the thenar eminence, respectively. All subjects were divided into two groups; the control group received a placebo and the experimental group received an opioid antagonist pill, which the opioid antagonist would control the potentially endogenous opioid response in EIH. The authors also analyzed potential gender differences for EIH. The authors found no gender differences for EIH effects. They also found that, despite the administered opioid antagonist, a similar EIH response was seen for both the control and experimental groups; furthermore, they found an increase in circulating endocannabinoid concentrations that would suggest nonopioid mechanisms involved in EIH (Koltyn et al., 2014). A study by Crombie et al. (Crombie, Brellenthin, Hillard, & Koltyn, 2017) had results that supported Koltyn et al. (Koltyn et al., 2014) findings that suggested endocannabinoids to be a major mechanism for EIH and not the endogenous opioid response. The results from Crombie et al. (Crombie et al., 2017) further suggested that 2-arachidonoylglycerol (2-AG) and 2-oleoylglycerol (2-OG) are the primary endocannabinoids responsible for the nonopioid EIH response (Crombie et al., 2017).

2.3: Conditioned Pain Modulation

CPM is a highly used intervention when studying algesia and the responses of the descending neural pathway from a noxious stimulation. CPM decreases sensitively to a noxious stimulus by administering a separate noxious stimulus as a "distraction" stimulus. Due to the requirement of applying a noxious stimulus, research has suggested the CPM works through the descending neural pathway via the diffuse noxious inhibitory control (DNIC). Lewis et al. (Lewis, Heales, Rice, Rome, & McNair, 2012) even

investigated the reliability of certain CPM and found them to be highly reliable for investigating endogenous inhibitory pathway and mechanisms. The research shows CPM to lead to increases in PT during the administered stimulus and immediately after the stimulus is removed. In a methodology review article, Pud et al. (Pud, Granovsky, & Yarnitsky, 2009) discussed different ways to induce CPM. The research has yet to determine the relationship between the applied noxious conditioning stimulus with the testing noxious stimulus due to the varying ways to induce CPM. They determined the most common/effective administered noxious stimuli is a cold stimulus (i.e. a foot/hand submerged in ice water). The authors also concluded that a standard method needs to be developed to control for the varying methods used in the research. Pud et al. (Pud et al., 2009) published an article suggesting that CPM leads both a homotopic and heterotopic pain inhibition. The experiment induced CPM using a cold stimulus applied to the right fingers, and pain measurements were taken at both the left and right thenar eminence. The authors found decreases in pain sensitivity in both hands immediately after removing the cold stimulus. CPM is not to be confused with EIH, although both lead to increases in PT (Pud et al., 2009). A study by Vaegter et al. (Vaegter, Handberg, & Graven-Nielsen, 2014) investigated the similarities between EIH and CPM. The authors recruited 80 males and females to undergo CPM via cold stimuli, two aerobic EIH protocols, and 4 isometric protocol. All EIH protocols had varying intensities and durations and the cold stimuli required the subjects to submerge their foot in ice water for the CPM. The authors found increases in PT from CPM only happened during the administered cold stimulus, and EIH related PT increases had effects lasting 15 min post exercise (Vaegter et al., 2014). The findings suggest that CPM and EIH use different mechanisms for pain

inhibition; furthermore, results from an article by Ellingson et al. (Ellingson et al., 2014) supports Vaeger et al. (Vaegter et al., 2014) conclusion comparing EIH and CPM.

2.4: Body Composition

BC and its effects on nociception have been slightly investigated over the years and has led to very conflicting conclusions. A study (Mckendall & Haier, 1983) published in 1982 compared PTs between obese and nonobese subjects. Obesity itself was determined to be >130% of a person's ideal body weight, which was calculated based on height and weight. The authors used a pressure stimulus applied to the index finger to assess the PT values. They found that obese subjects were more sensitive to the stimulus than nonobese. They suggested the endogenous opiate system and its control in ingestive behaviors were potential reasons for obese subjects increased sensitivity (Mckendall & Haier, 1983). Less than a year later Zahorska et al. (Zahorskamarkiewicz, Kucio, & Pyszkowska, 1983) investigated PT values using electrical stimuli on the medial surface of the forearm and on the back of the arm; furthermore, only women were recruited for the study. This study found obese subjects to be less sensitive to the stimulus and also suggested the endogenous opiate system and its increased activity in obesity was a potential reason for the differences (Zahorskamarkiewicz et al., 1983) Zahorska et al published another study similar to the previous study, but a 4-week weight loss program was administered to half of the obese women. They found the obese group to be less sensitive, supporting the previous findings, and the 4-week weight loss program did not alter PTs for the obese women (Zahorska-Markiewicz et al., 1988). Khimich (Khimich, 1997) published an article in 1997 that used an increasing pressure stimulus placed on the forearm to assess PTs among 206 subjects. Khimich (Khimich, 1997)found obese

subjects to be less sensitive, which supports Zahorska et al's findings, and offered up the idea that obese subjects have a decreased quantity of nerve endings at the skin. In 2013, Price et al. (Price, Asenjo, Christou, Backman, & Schweinhardt, 2013) investigated thermal PTs in the abdomen, hand, and forehead to compare PT at sites with different amounts of excess fat; furthermore, the authors also measured PPTs on the hand and forehead. Price et al only found differences in sensitivity at the abdomen and no differences were shown for thermal or pressure thresholds at the hand or forehead. The authors concluded that PTs in obese subjects are less sensitive to noxious stimuli only at sites with higher amounts of excess fat (Price et al., 2013). Stolzman and Bement (Stolzman & Hoeger Bement, 2016) investigated the CPM response across different weight statuses in adolescents by assessing PPT at the deltoid muscle and nailbed in the hand. They recruited 56 subjects (24 obese/overweight and 37 normal weight) and DXA scans were used to better assess BC. The authors had the subjects place their foot in an ice water bath for the CPM and pain measurements were assessed while the CPM was administered. They found no differences in the PPT responses from the CPM among the three weight groups; furthermore, they found that bone free lean mass values at the deltoid to be positively associated with CPM and not fat mass values (Stolzman & Hoeger Bement, 2016). The most known recent study by Tashani et al. (Tashani, Astita, Sharp, & Johnson, 2017) measured thermal and pressure thresholds between obese, overweight, and normal subjects. Specifically, PPTs were assessed at the thenar eminence since it is a site will little excess fat differences across the three groups. The authors found obese subjects to be more sensitive to both the normal and overweight groups and

suggested different body sites will have different responses to noxious stimuli potentially due to underlying levels of fat deposits (Tashani et al., 2017).

Chapter III: Methodology

3.1: Introduction

All participants for this experiment were recruited from the University of Oklahoma and the extended area of Norman, OK. A total of 56 participants (30 women; 26 men), between the ages of 18-30, were recruited for the study. Participants were free from injuries and have not been diagnosed with a chronic pain disorder. Females confirmed they were not pregnant by completing a pregnancy test, and all included female participants were tested during the luteal phase of their menstrual cycle. All participants completed a physical activity readiness questionnaire (PAR-Q), the international physical activity questionnaire (IPAQ) (Craig et al., 2003), and two questionnaires related to pain perception; 1) the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995) and 2) the Pain Attitudes Questionnaire (PAQ) (Yong, Gibson, Horne, & Helme, 2001). All participants signed a consent form outlining the about the risk, benefits, and duration of the experiment prior to participation.

3.2: Experimental Design

Participants completed a total of 3 testing visits with each visit lasting roughly 30-40 minutes. Participants were asked to refrain from exercise before each visit and were ask to not take any over the counter or prescription pain medication during the study. On the first visit, participants completed the PAR-Q, IPAQ, PCS, PAQ, and signed the consent form at the start of the visit to determine if they meet eligibility qualifications. Female participants then completed a pregnancy test to confirm they were not pregnant. Next height and weight, ultrasound assessment of muscle and fat thickness and skinfolds measurements were taken at the PPT assessment sites. A whole-body DXA scan was then

completed. Finally, participants performed 3 MVCs with their dominant knee extensors and two assessments PPT at each assessment site (right and left vastus lateralis and right and left brachioradialis) were performed in order to familiarize the participants. During the second visit PPTs were initially determined followed by the participants placing their foot in an ice bath for 60 seconds. PPTs were then reassessed. During the third and final visit, an initial assessment of PPTs was again completed followed by isometric knee extension exercise performed at 25% of MVC until task failure. PPTs were then immediately re-measured.

3.3: DXA Scan

BC was determined with a whole body DXA scan (Lunar Prodigy Advance; GE-Medical Systems, Madison, WI) and corresponding analysis software (enCore 2011, version 13.60, GE-Healthcare, Madison, WI) according to the manufacturer's instructions. The same researcher performed and analyzed all the scans in accordance to the standard laboratory protocol. Custom regions of interest (ROI) boxes were draw for the four specific sites. The ROI area for the forearms spanned from the olecranon process on the ulna to the bottom of the radius. The ROI for the legs followed the inguinal line (cutting though the neck of the femur) to the bottom of the femur. Participants lay in a supine position with their arms resting against the sides of the body. A block was placed between their feet to provide better clarity for thigh composition during the scans. DXA equipment was calibrated on a daily basis following the protocol provided by the manufacturer.

3.4: Ultrasound Assessments of Muscle Thickness

Muscle and fat thickness for the four sites were determined using ultrasound equipment (FF sonic UF-750XT, Fukuda Denshi, Tokyo, JPN). The same researcher performed all thickness measurements and analyses for each of the four sites. The probe was placed perpendicular to the specific limb and the given image was frozen for further analysis. To prevent any compression of muscle or fat, at least 5mm of ultrasound gel was visible on the display screen. Muscle thickness was measured from the first onset of muscle tissue down to the bone and fat thickness was measured between the skin and first layer of muscle of the specific sites. Measurements were taken using the software within the ultrasound by drawing a direct line between the composition boundaries and recorded in mm.

3.5: Assessment of Pressure Pain Thresholds

An FDIX Force One Pressure Algometer (Wagner Instruments, Greenwich, CT) with a 1 cm diameter circular rubber interfaced with Medoc Algomed software (Medoc Ltd., Ramat Yishai, Israel) was used to assess PPT. Assessments were performed over the belly of the brachioradialis muscle (BR) of both forearms and the belly of both vastus lateralis (VL) muscles. Participants were seated in a comfortable chair with their feet flat on the ground, with their knees flexed at approximately 90° and their quadriceps relaxed. For assessments of BR PPT they remained in the same seated position, but extended their arms in front of them and rested it on a solid, flat surface. Marks were placed approximately 1 inch apart over the belly of each muscle to ensure similar algometer placement for each assessment throughout the study. Pressure was applied to the muscle at a rate of 50 kilopascals (kPa) per second with the algometer placed perpendicular to

the assessment site. Participants indicated when the pressure became painful (defined as the point at which the pressure first "hurt") by pressing a handheld button that stopped the data collection software and marked the pressure value. Two trials were performed at each assessment site and averaged as the criterion assessment of PPT. The site testing order was as follows: the left VL, right VL, right BR, and finally left BR. The order was repeated for the second trial.

To produce EIH, an isometric knee extension exercise protocol was performed using the dominant leg. The protocol consisted of a time-to- task failure exercise bout performed at 25% of each participant's MVC. The participants were seated with their dominant knee at 110 degrees (full leg extension being 180 degrees) for both the EIH and MVC protocols. The ankle of each leg was secured against the end of an immobile lever arm, with a force transducer attached perpendicular to the line of pull. The force transducer was connected to acknowledge Biopac software and force data were displayed and recorded. MVC was assessed by instructing participants to "kick" against the strap around their ankle as forcefully as possible while the experimenter provided verbal encouragement. Three efforts were completed with two minutes of rest in between each attempt; the highest value was used as MVC. During the time-to-task failure exercise bout, participants were able to see the required force value by a line marked in the Biopac program and participants were asked to contract with a force equal to the mark and maintain this force for as long as possible.

3.6: Statistical Analysis

All data were analyzed using SPSS version 24 (IBM Armonk, New York). Independent measures t-tests were performed to compared all measured variables for a

given arm or leg between men and women. A 2 (men vs women) x 4 (pain testing site; dominant leg, non-dominant leg, right arm, left arm) mixed factorial ANOVA was performed to examine differences in resting PPTs, CPM, and EIH between men and women among the testing sites. Significant interactions were followed up with one-way ANOVAs and post-hoc simple comparisons or main comparisons were made using a Bonferroni alpha correction. Bivariate relationships among body composition, PPT, CPM, EIH, physical activity, and pain attitudes and catastrophizing were examined by calculating a Spearman ρ (rho) correlation coefficient to account for non-normal distributions of pain and self-reported data. Statistical significance was set *a priori* at $\alpha < 0.05$.

Chapter 4: Results

A total of 56 (30 women; 26 men) participants completed the study. Table 1 shows participant characteristics.

4.1: Gender Differences in Participant Characteristics

Men were taller ($p = 0.0005$) and heavier ($p = 0.000004$) compared to women. No differences were observed in BMI ($p = 0.17$). Whole body DXA scans revealed women to have lower BMD ($p = 0.00005$) and lean tissue mass ($p < 0.00001$) as well as high percent body fat ($p < 0.00001$) and fat mass ($p = 0.02$).

Table 1 – Participant Characteristics by Sex

Measure	Female (n = 30)	Male (n = 26)	Total (n = 56)
Age (yr)	22.6 ± 2.6	23.3 ± 2.6	22.9 ± 2.6
Height (cm)	161 ± 28.3*	182 ± 6.1	170.8 ± 23.5
Weight (kg)	65.8 ± 12*	83.3 ± 13.5	73.9 ± 15.4
BMI (kg/m^2)	23.7 ± 3.7	25.1 ± 3.8	24.3 ± 3.8
BMD (g/cm^2)	1.201 ± 0.101*	1.320 ± 0.097	1.256 ± 0.115
DXA %Fat (%)	31.6 ± 7.9*	18.2 ± 8.3	25.4 ± 10.5
DXA Fat Mass (kg)	21.2 ± 8.5*	15.5 ± 9.5	18.5 ± 9.4
DXA Bone Free Lean Mass (kg)	40.2 ± 9.0*	64.3 ± 10.6	51.4 ± 15.5

BMI: Body mass index; BMD: Bone mineral density,*indicates a significant difference ($P < 0.05$) between female and male participants. Values are mean ± the SD

Tables 2-5 contain data for site-specific (Table 2 for the dominant leg, Table 3 for the Non-dominant leg, Table 4 for the right arm, and Table 5 for the left arm) body composition assessed from DXA and ultrasound as well as resting PPTs, CPM, and EIH at each site. In each limb women had lower BMD ($p < 0.05$), higher percent fat ($p < 0.05$), larger fat mass ($p < 0.05$), lower bone free lean mass ($p < 0.05$), greater subcutaneous fat thickness over the PPT site ($p < 0.05$), lower muscle thickness at the PPT site ($p < 0.05$), and a larger skin-fold thickness at the PPT site ($p < 0.05$) compared

to men. In the dominant leg, men were stronger ($p < 0.0001$), but endurance time to task failure at 25% of MVC did not differ between men and women ($p = 0.97$).

Table 2 – Dominant leg composition and pain sensitivity by sex

Measure	Female (n = 30)	Male (n = 26)	Total (n = 56)
Leg BMD (g/cm^2)	1.439 ± 0.126*	1.678 ± 0.158	1.550 ± 0.185
DXA %Fat (%)	42.6 ± 6.9*	24.1 ± 9.5	34.0 ± 12.3
DXA Fat Mass (kg)	3.7 ± 1.2*	2.5 ± 1.3	3.2 ± 1.4
DXA Bone Free Lean Mass (kg)	4.9 ± 0.9*	7.7 ± 1.3	6.2 ± 1.8
US Fat Thickness (mm)	9.8 ± 3.6*	4.1 ± 2.7	7.2 ± 4.3
US Muscle Thickness (mm)	40.9 ± 7.4*	48.8 ± 8.3	44.6 ± 8.7
Skin-fold Thickness (mm)	26.8 ± 10.3*	14.2 ± 7.4	21.0 ± 11.0
Knee Ext MVC (lbs)	66.9 ± 14.3*	102.7 ± 24.1	83.5 ± 26.4
TTF (sec)	203.4 ± 70.6	204.4 ± 124.4	203.9 ± 98.3
Resting PPT (kPa)	456.5 ± 193.0*	669.4 ± 244.2	555.3 ± 244.2
CPM (%)	15.0 ± 16.0	14.9 ± 21.9	15.0 ± 18.8
EIH (%)	41.8 ± 32.4	34.1 ± 29.2	38.2 ± 30.9

BMD: Bone mineral density; US: Ultrasound; Knee Ext MVC: Maximal voluntary contraction strength of the knee extensors; TTF: Time to task failure when holding 25% of MVC; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia. *indicates a significant difference ($P < 0.05$) between female and male participants. Values are mean ± the SD

Table 3 – Non-dominant leg composition and pain sensitivity by sex

Measure	Female (n = 30)	Male (n = 26)	Total (n = 56)
Leg BMD (g/cm^2)	1.472 ± 0.123*	1.680 ± 0.133	1.568 ± 0.164
DXA %Fat (%)	42.3 ± 6.6*	24.6 ± 10.3	34.1 ± 12.3
DXA Fat Mass (kg)	3.5 ± 1.3*	2.4 ± 1.2	3.0 ± 1.4
DXA Bone Free Lean Mass (kg)	4.7 ± 1.1*	7.6 ± 1.3	6.0 ± 1.9
US Fat Thickness (mm)	10.2 ± 3.6*	4.1 ± 3.1	7.4 ± 4.6
US Muscle Thickness (mm)	38.6 ± 5.8*	46.9 ± 7.6	42.5 ± 7.8
Skin-fold Thickness (mm)	26.9 ± 9.4*	14.3 ± 8.2	21.0 ± 10.8
Resting PPT (kPa)	426.1 ± 168.5*	608.0 ±232.0	510.5 ± 218.7
CPM (%)	21.4 ± 19.4	19.6 ± 12.6	20.5 ± 16.5
EIH (%)	26.6 ± 22.1*	13.9 ± 23.0	20.7 ± 23.2

BMD: Bone mineral density; US: Ultrasound; Knee Ext MVC: Maximal voluntary contraction strength of the knee extensors; TTF: Time to task failure when holding 25% of MVC; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia. *indicates a significant difference ($P < 0.05$) between female and male participants. Values are mean ± the SD

Table 4 – Right forearm composition and pain sensitivity by sex

Measure	Female (n = 30)	Male (n = 26)	Total (n = 56)
Forearm BMD (g/cm^2)	0.955 ± 0.126*	1.151 ± 0.124	1.046 ± 0.159
DXA %Fat (%)	18.1 ± 7.4*	8.1 ± 4.6	13.4 ± 8.0
DXA Fat Mass (kg)	0.19 ± 0.1*	0.14 ± 0.1	0.17 ± 0.1
DXA Bone Free Lean Mass (kg)	0.86 ± 0.1*	1.5 ± 0.3	1.2 ± 0.4
US Fat Thickness (mm)	4.8 ± 1.9*	2.2 ± 1.1	3.6 ± 2.0
US Muscle Thickness (mm)	20.6 ± 3.3*	26.7 ± 5.8	23.4 ± 5.5
Skin-fold Thickness (mm)	10.1 ± 3.4*	7.4 ± 3.0	8.9 ± 3.5
Resting PPT (kPa)	313.5 ± 134.9*	413.6 ± 159.6	359.9 ± 154.0
CPM (%)	14.1 ± 24.2	14.9 ± 30.2	14.5 ± 26.9
EIH (%)	17.3 ± 26.3	15.8 ± 21.0	16.6 ± 23.8

BMD: Bone mineral density; US: Ultrasound; Knee Ext MVC: Maximal voluntary contraction strength of the knee extensors; TTF: Time to task failure when holding 25% of MVC; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia. *indicates a significant difference ($P < 0.05$) between female and male participants. Values are means ± the SD

Table 5 – Left forearm composition and pain sensitivity by sex

Measure	Female (n = 30)	Male (n = 26)	Total (n = 56)
Forearm BMD (g/cm^2)	0.961 ± .0116*	1.193 ± 0.191	1.069 ± 0.193
DXA %Fat (%)	19.1 ± 7.4*	8.2 ± 4.6	14.0 ± 8.3
DXA Fat Mass (kg)	0.20 ± 0.1*	0.14 ± 0.1	0.17 ± 0.1
DXA Bone Free Lean Mass (kg)	0.82 ± 0.1*	1.5 ± 0.3	1.1 ± 0.4
US Fat Thickness (mm)	5.0 ± 2.0*	2.6 ± 1.8	3.8 ± 2.2
US Muscle Thickness (mm)	20.7 ± 3.6*	27.2 ± 5.8	23.7 ± 5.7
Skin-fold Thickness (mm)	10.6 ± 3.3*	7.7 ± 3.2	9.2 ± 3.6
Resting PPT (kPa)	297.7 ± 108.9*	396.3 ± 162.0	343.4 ± 143.7
CPM (%)	7.5 ± 26.5	11.7 ± 20.7	9.4 ± 23.5
EIH (%)	20.4 ± 29.4	16.4 ± 24.5	18.6 ± 27.1

BMD: Bone mineral density; US: Ultrasound; Knee Ext MVC: Maximal voluntary contraction strength of the knee extensors; TTF: Time to task failure when holding 25% of MVC; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia. *indicates a significant difference ($P < 0.05$) between female and male participants. Values are means ± the SD

A significant sex testing site interaction was found for resting PPT (Figure 1). Post-hoc analysis revealed women had lower PPTs at all four testing sites compared to men ($p \leq 0.01$ fpr each). In both men and women PPTs from the dominant leg were higher than the other 3 testing sites ($p \leq 0.008$ for each; Figure 1) and PPTs in both arms

were lower than those from both legs ($p \leq 0.001$ for each; Figure 1). No differences were observed in either men or women between the right and left arm ($p \geq 0.16$; Figure 1).

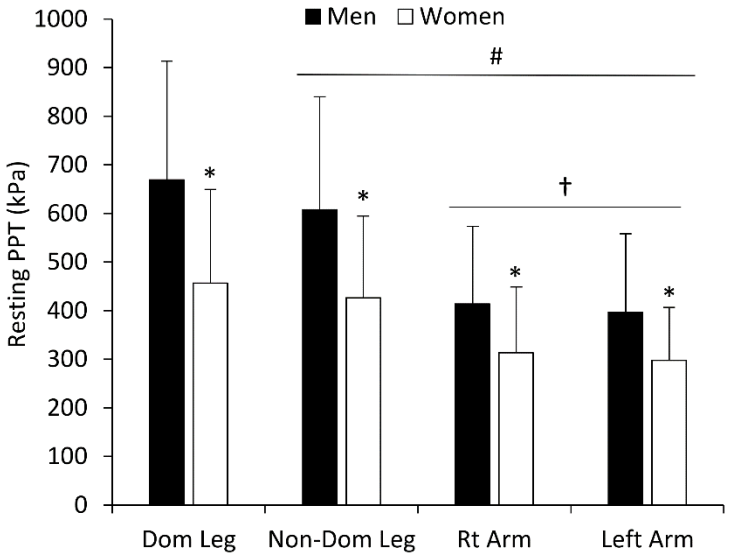

Figure 1 – Resting pressure pain thresholds across the 4 testing sites in men and women. *indicates a significant difference ($p < 0.05$) between men and women at that site. # indicates a significant ($p < 0.05$) difference in both men and women from the dominant leg. † indicates a significant difference from both legs in both men and women ($p < 0.05$). Values are mean ± SD.

The CPM response among testing sites and men and women are shown in Figure 2. The sex x testing site interaction was not significant ($p = 0.85$), nor was there a main effect for sex ($p = 0.84$). A main effect for testing site was found ($p = 0.049$). Follow-up analysis of main comparisons among testing sites revealed the CPM response was reduced in the left arm compared to the non-dominant leg ($p = 0.023$). No other differences were found.

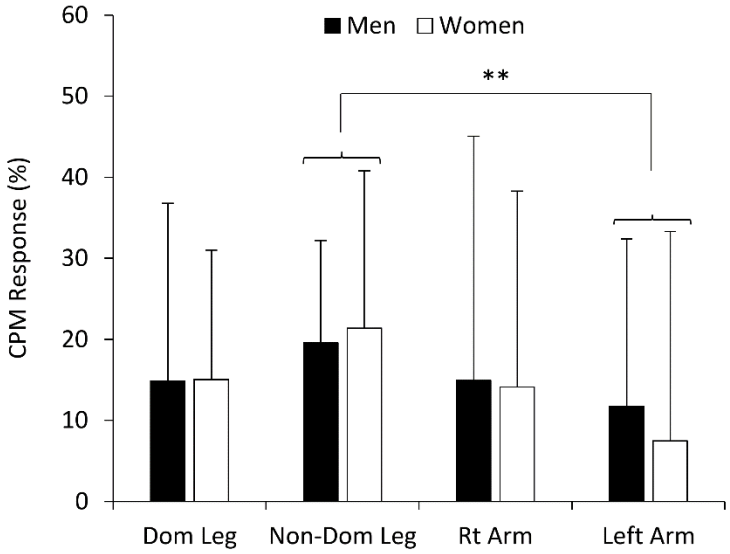

Figure 2 – CPM response (change in PPT from pre to post 1 minute of foot immersion in an ice bath) across the 4 testing sites in men and women. **indicates a significant difference (main comparison; $p < 0.05$) between testing sites. Values are mean ± SD.

The EIH response among testing sites and men and women are shown in Figure 3. The sex x testing site interaction was not significant ($p = 0.48$), nor was there a main effect for sex ($p = 0.23$). A main effect for testing site was found ($p < 0.001$). Follow-up analysis of main comparisons among testing sites revealed the EIH response was reduced in the non-dominant leg, right and left arms compared to the dominant leg ($p < 0.001$). No other differences were found.

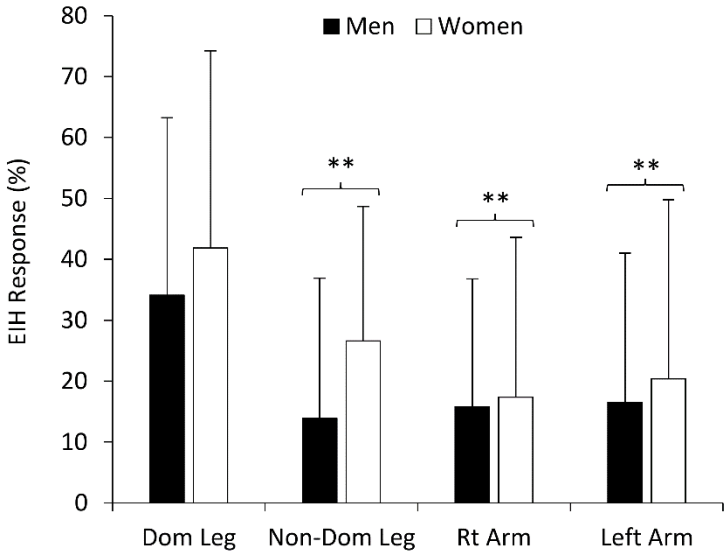

Figure 3 – EIH response (change in PPT from pre to post isometric exercise with the dominant leg) across the 4 testing sites in men and women. **indicates a significant difference (main comparison; $p < 0.05$) from the dominant leg. Values are mean ± SD.

Table 6 contains self-reported data on physical activity, pain catastrophizing, and pain attitudes. There were no significant difference between women and men for any dimension of the IPAQ ($p > 0.10$ for each). No differences were observed for any of the dimension of the PAQ between women and men as well ($p > 0.19$ for each). Additionally, women and men did not differ on the PCS ($p = 0.35$

Table 6 – Self-reported pain characteristics and physical activity by sex

Measure	Female (n = 30)	Male (n = 26)	Total (n = 56)
IPAQ Total (MET·min·wk^{-1})	6307.1 ± 5700.8	4826.4 ± 3163.5	5619.6 ± 4715.9
IPAQ Walking (MET·min·wk^{-1})	1776 ± 1516.2	1146.2 ± 1281.6	1483.6 ± 1435
IPAQ Moderate (MET·min·wk^{-1})	1542.1 ± 1845.3	1592.8 ± 1536.6	1565.7 ± 1693.9
IPAQ Vigorous (MET·min·wk^{-1})	3089.1 ± 3998.5	2087.3 ± 1736.8	2624 ± 3171
Pain Att: Stoic-Fortitude	16.8 ± 3.8	16.1 ± 4.4	16.5 ± 4.1
Pain Att: Stoic-Concealment	11.8 ± 3.1	11.3 ± 3.1	11.6 ± 3.0
Pain Att: Stoic-Superiority	14.0 ± 3.4	13.5 ± 3.6	13.8 ± 3.5
Pain Att: Cautious-Self Doubt	14.6 ± 4.2	13.3 ± 4.0	14.0 ± 4.1
Pain Att: Cautious-Reluctance	14.1 ± 3.2	13.0 ± 2.8	13.6 ± 3.0
Pain Catastrophizing	11.6 ± 8.1	13.9 ± 10.4	12.6 ± 9.2

IPAQ: International physical activity questionnaire; Pain Att: Pain attitudes questionnaire. Values are mean ± the SD

4.2: Relationship of Pain Sensitivity and Body Composition

Spearman's ρ correlation coefficients can be seen in Table 7. The measurements taken at the left forearm (LA) found no significant correlation between PPTs and total body fat ($p = 0.85$), body fat percentage ($p = 0.20$), fat percentage within the limb ($p = 0.73$), fat mass within the limb ($p = 0.08$), fat thickness at the measured site ($p = 0.59$), or skin fold measurements at the site ($p = 0.71$). The same results held true for both the right forearm (RA) (total body fat ($p = 0.81$), body fat percentage ($p = 0.24$), fat percentage within the limb ($p = 0.52$), fat mass within the limb ($p = 0.83$), fat thickness at the measured site ($p = 0.63$), or skin fold measurements ($p = 0.62$) and the non-dominant leg (NDL) (total body fat ($p = 0.07$), body fat percentage ($p = 0.32$), fat mass within the limb ($p = 0.33$), fat thickness at the site ($p = 0.33$), or skin fold measurements ($p = 0.50$; Table 7).The dominant limb's (DL) PPT did show a significant negative correlation with fat percentage within the limb ($p = 0.03$). The DL did not correlate with the other fat measurements [total body fat ($p = 0.90$), body fat percentage ($p = 0.104$), fat mass within

the limb ($p = 0.42$), fat thickness at the measured site ($p=0.08$), or skin fold measurements ($p = 0.29$)]. The Pearson's correlation coefficients can be seen in Table 7.

In regards to bone free lean mass composition, the LA and NDL had significant correlations with total bone free lean mass (LA: $p = 0.02$, NDL: $p \leq 0.001$), bone free lean mass at the limb (LA: $p = 0.02$, NDL: $p \leq 0.001$), and muscle thickness (LA: $p = 0.03$, NDL: $p = 0.026$). The DL had significant correlations for total bone free lean mass ($p \leq 0.001$) and bone free lean mass at the limb ($p \leq 0.001$), but not for muscle thickness ($p = 0.13$). The RA showed significant correlations with bone free lean mass at the limb ($p = 0.04$); However, no significant correlation was found between the RA and total bone free lean mass ($p = 0.09$) or muscle thickness ($p = 0.26$).

There were no significant correlations between any of the BC measurements and the magnitude of CPM response ($p > 0.05$; Table 7). The EIH response significantly increased PPTs for all of the four measured sites ($p \leq 0.001$). The EIH responses did not correlate with any of the taken BC measurements for the LA or the DL ($p \geq 0.05$). The RA had a significant correlation with total body fat ($p = 0.04$), fat mass within the limb ($p = 0.03$), and skinfold measurements ($p = 0.03$); However, no other BC measurement had a significant correlation with the RA ($p \geq 0.05$). No measures of body composition, in regards to fat mass, correlated with the EIH response for the NDL ($p \geq 0.10$). The EIH responses for the NDL did not correlate with total bone free lean mass or bone free lean mass with in the limb ($p \geq 0.05$). The results did show that the NDL muscle thickness was negatively correlated with the EIH response ($p = 0.04$).

Few relationships (shown in Table 8) were found among resting PPTs, CPM, EIH, and self-reported physical activity, dimensions of the pain attitudes questionnaire, and the pain catastrophizing scale. A positive relationship was found between PCS and the dominant leg CPM ($p < 0.001$), but not with any other pain variable. Stoic fortitude, a dimension of the PAQ, was positively correlated with EIH ($p < 0.05$ for each) in the dominant and non-dominant leg, but not in the arms. Stoic superiority was found to correlate with EIH in the right arm ($p < 0.05$), but not at any other site. The only significant relationship found among the physical activity data was that vigorous intensity exercise was positively correlated with EIH in the dominant leg ($p < 0.05$).

Table 7– Relationship among body composition variables and pain sensitivity

	DL PPT	DL CPM	DL EIH	NDL PPT	NDL CPM	NDL EIH	RA PPT	RA CPM	RA EIH	LA PPT	LA CPM	LA EIH
Weight (kg)	.44**	.05	-.07	.49**	-.17	-.24	.17	.06	.17	.24	.18	.08
BMI (kg/m^2)	.22	.10	.02	.31*	-.07	-.15	-.03	.10	.27*	.07	.23	.15
Tot %Fat	-.22	.13	.10	-.14	.05	.06	-.16	.06	.21	-.17	.24	.06
Tot Fat Mass (kg)	-.02	.12	.02	.08	.05	-.02	-.03	.07	.28*	-.03	.26	.09
Tot Bone Free Lean Mass (kg)	.47**	-.04	-.11	.45**	-.10	-.23	.23	.03	.01	.30*	-.01	.03
Limb %Fat	-.30*	.15	.16	-.16	-.02	.04	-.09	.05	.24	-.05	.13	.06
Limb Fat Mass (kg)	-.11	.18	.05	.04	-.00	-.01	.03	.11	.30*	.08	.21	.05
Limb Bone Free Lean Mass (kg)	.45**	.01	-.10	.43**	-.19	-.22	.28*	.04	-.01	.32*	.00	.05
Limb Fat Thickness (mm)	-.24	.15	.13	-.13	.02	.10	-.07	.01	.23	-.07	.17	.10
Limb Musc Thickness (mm)	.21	.13	-.23	.30*	-.03	-.27*	.15	-.11	.09	.30*	.09	-.01
Limb Skinfold (mm)	-.15	.12	.06	-.09	.10	.13	.07	.05	.29*	.05	.20	.13
Resting PPT (kPa)	--	-.03	.01	--	-.03	-.04	--	-.14	.03	--	.01	.14
CPM (%)		--	.11		--	.05		--	.01		--	.01
EIH (%)			--			--			--			--

BMI: Body mass index; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia.*indicates a significant correlation ($p < 0.05$). ** indicates a significant correlation ($p < 0.001$). Values are mean ± the SD

Table 8 – Relationship among self-reported pain characteristics and physical activity with pain sensitivity

	DL PPT	DL CPM	DL EIH	NDL PPT	NDL CPM	NDL EIH	RA PPT	RA CPM	RA EIH	LA PPT	LA CPM	LA EIH
PCS	.20	.35**	-.02	.15	.14	-.12	.12	-.08	-.22	.07	-.12	.13
PAQ SF	-.08	-.26	.31*	-.06	.18	.30*	.05	-.04	.25	.03	-.03	.00
PAQ SC	-.15	.00	-.08	-.14	.08	-.07	-.01	.07	-.06	-.11	.14	-.19
PAQ Sup	.13	-.16	.12	.19	.26	.08	.14	.06	.27*	.14	.15	.07
PAQ CSD	.13	.02	.13	.15	.12	.02	.17	.07	-.10	.13	.09	.04
PAQ CR	-.14	-.06	.10	-.09	.26	-.02	-.04	-.17	.19	-.05	-.09	.02
IPAQ Tot	-.04	-.09	.26	.00	.05	.18	-.12	.18	.21	-.10	.04	.20
IPAQ Walk	-.16	-.13	.20	-.09	.10	.15	-.21	-.07	.15	-.17	-.08	.16
IPAQ Mod	.06	-.06	.10	.03	.02	.09	.00	.01	.18	.06	.02	.08
IPAQ Vig	-.08	.04	.28*	-.02	.05	.13	-.08	.21	.21	-.08	.07	.17

PCS: Pain Catastrophizing Scale; PAQ: Pain Attitudes Questionnaire; SC: Stoic Fortitude; SC: Stoic Concealment; Sup: Stoic Superiority; CSD: Cautious Self Doubt; CR: Cautious Reluctance; IPAQ: International Physical Activity Questionnaire *indicates a significant correlation ($p < 0.05$). ** indicates a significant correlation ($p < 0.001$). Values are mean ± SD

4.3: Discussion

The results from this study suggest that unlike previous findings, total body and assessment site specific fat mass/thickness were not related to resting pressure pain sensitivity or pain modulatory function assessed via CPM and EIH. Interestingly, total body lean tissue mass and assessment site specific muscle thickness were positively correlated with resting PPT. Additionally, self-reported daily physical activity did not consistently correlate with resting pressure pain sensitivity or pain modulatory function—as has sometimes been shown in previous studies. As expected, significant differences were observed between men and women, with women exhibiting greater fat reduced lean/muscle compared to me, for most body composition measures. Women also exhibited lower PPTs at all testing sites compared to men.

Previous studies that assessed PPTs have found differing results when PPTs are compared among BMI groups. Mckendall et al. (1983) and Tashani et al (2017) found those classified as obese by BMI were more sensitive to pressure pain compared to normal or overweight individuals. However, Price et al (2013) found no differences in PPTs among BMI groups and Khimich et al (1997) actually reported obese individuals were less sensitive to pressure pain (i.e. had elevated PPTs compared to normal and overweight individuals). Our study found BMI did not correlate with resting PPTs at any testing site except for the non-dominant leg and only weakly so in the NDL. The participants in our study were on average normal based off of BMI, with only a small amount in the overweight and the obese categories. Past research had even amounts of participants among the three groups, and the lack of participants in the overweight and

obese categories in our study could be a potential reason why no significant correlation was found.

We hypothesized that total body fat percentage and mass as well as site-specific fat thickness and skinfold thickness would be positively related to resting PPT, but no relationships were found. Rather, our results suggest total body bone free lean mass and limb mass and limb muscle thickness were positively related to resting PPTs. Stolzman et al (2016) is the only other study, to our knowledge, that used DXA scans to assess BC. However, they did not examine the relationship among resting PPT and weight, BMI, or any DXA assessed measure of fat and lean tissue, but did not find any differences among groups in PPT when compared across BMI categories. Interestingly, the groups did not have significant differences in bone free lean mass composition which, based upon our results may explain the lack of differences in resting PPT.

The primary methodological issue/problem with BMI is that is does not account for how much fat or bone free lean mass individuals (or groups) have. The majority of past research has relied on BMI to classify individuals as obese—making the assumption that those with a higher BMI would have more excess fat mass. Tashani et al (2017) divided groups based upon BMI, but did use skinfolds to estimate percent body fat and found that the obese group did have a higher body fat percentage compared to the normal and overweight groups and that the obese exhibited lower PPTs. However, the amount of bone free lean mass for the participants was not estimated and therefore it is difficult to know if the obese group had a reduced bone free lean mass which might have driven the observed decrease in PPT. It is important to note that studies that assessed sensitivity to electrical stimuli (EPT) and thermal stimuli (TPT) have shown that fat mass may play a

role in pain sensitivity. Two studies that assessed EPT at the forearm found obese participants to be less sensitive to than a normal weight group (Zahorska-Markiewicz et al 1983, Zahorska-Markiewicz et al 1988). Additionally, Price et al (2013) found that an obese group had higher TPTs compared to a normal weight group when TPT was assessed on the abdomen (where presumably a higher amount of excess fat was present), but no differences were seen when TPTs were taken at the hand (minimal excess fat). Electrical and thermal stimuli are primarily sensed by cutaneous type IV nociceptors located in and around the skin whereas mechanical pressure preferentially acts on type III nociceptors which are often located deeper in skeletal muscle (Christopher D Black, 2012; O'Connor & Cook, 1999). Because of the differences in receptor location, greater subcutaneous fat may alter thermal and electrical sensitivity to a greater extent. Our findings that greater lean tissue mass and muscle thickness correlated with resting PPT (more muscle equated to higher PPTs) deserves further study. Pain sensitivity tends to increase with age and in certain clinical conditions which are often accompanied by loss of lean tissue mass.

This study also found that BC did not affect pain inhibitory function assessed via CPM and EIH. To our knowledge only one other study has assessed BC and its effects on CPM--Stolzman et al (2016) and no study has examined the effects of BC on the EIH response. For CPM Stolzman et al. (2016) found that DXA assessed bone free lean mass of the arm predicted 10% of the CPM magnitude response in the deltoid muscle of in adolescents. This finding is in contrast to the results of the present study where no relationship was observed between the CPM response at any site and any of the measures of body composition. The discrepancies for this might be due to the methodologies

between studies. Stolzman et al (2016) assessed PPTs while the participants had their in the ice bath, while this study assessed PPTs immediately post the ice bath. The different populations that were assessed might also have played a role in the difference responses as Stolzman assessed adolescents (12-17.5 years old) while this study tested college-aged adults. Perhaps the change(s) in lean tissue mass that typically occur during growth and maturation influence the CPM response. This study was the first study to investigate if BC affects the EIH response. No moderate-to-large or consistent relationships were found between the EIH response at any assessment site and our assessments of BC. A weak negative relationship was observed between EIH and muscle thickness in the non-dominant leg, but this was not observed at any other site. Limb skinfold thickness was also weakly correlated to EIH in the right arm, but again this was not found at any other testing site. The EIH response has been shown to be reduced with age (Lemley et al., 2015; Naugle & Riley, 2014) where bone free lean mass often decline with a corresponding increase in fat mass—suggesting a possible relationship, but this was not borne out in our findings.

Two other findings from our study are of note. First, it is interesting that the CPM and the EIH responses did not correlate as has been shown previously (Lemley et al., 2015). The study of Lemley et al. (2015) included young and older adults, who showed a reduced EIH and CPM response, perhaps aiding in their ability to find a statistical relationship. Previous work by Ellingson and colleagues (Ellingson et al., 2014) demonstrated that EIH can occur following exercise that is not painful—suggesting they may work via similar, but not identical mechanisms. Our findings support this idea. Secondly, we found that women exhibited lower PPTs than men. This is a widely

reported and consistent finding (Racine et al., 2012; Riley et al., 1998). Considerable previous work has focused on the role of estrogen, gender roles, and pain history in the observed differences (Racine et al., 2012). Our findings suggest the role of lean tissue mass may also contribute to the lower PPTs observed in women. This is an area that has not been explored previously.

Chapter V: Conclusion

We concluded that PPTs and its relation to BC is dependent on bone free lean mass and not fat mass measurements, which is the novel finding for this study. Higher values of total bone free lean mass suggested higher PPTs among the participants. The sites measured within each participant with higher bone free lean mass had higher PPTs. The hypothesis that fat mass composition positively relates to PPTs was rejected since no correlations were shown. Our second hypothesis, pertaining to bone free lean mass, was also rejected due to the positive correlations found between bone free lean mass and PPTs. We observed both a CPM and EIH response following our applied interventions. We did not observe and differences in the magnitude of responses between the varying BC measurements. That led us to reject our last hypotheses that fat mass composition negatively correlates and that bone free lean mass composition positively correlates with the magnitudes of response for CPM and EIH. The biggest limitation to this study is the time of day each visit was performed was not controlled for, future studies would benefit for controlling for this. Another limitation is the results only apply to noxious pressure stimuli and do not address BC and the potential thermal or electrical relationships. It would be interesting if future studies sought to assess potential difference for physical activity levels. Future studies should utilize more accurate BC measurements (i.e. DXA scans) to explore if bone free lean mass or fat mass has any effects on thermal or electrical pain thresholds and if the bone free lean mass trends with PPTs hold true across all ages.

Works Cited

Black, C. D. (2012). Muscle Pain During and Following Exercise. *The Oxford Handbook of Exercise Psychology*, 144.

Black, C. D., Huber, J. K., Ellingson, L. D., Ade, C. J., Taylor, E. L., Griffeth, E. M., . . . Sutterfield, S. L. (2017). Exercise-Induced Hypoalgesia Is Not Influenced by Physical Activity Type and Amount. *Med Sci Sports Exerc, 49*(5), 975-982. doi:10.1249/MSS.0000000000001186

Craig, C. L., Marshall, A. L., Sjostrom, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., . . . Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine and Science in Sports and Exercise, 35*(8), 1381-1395. doi:10.1249/01.Mss.0000078924.61453.Fb

Crombie, K. M., Brellenthin, A. G., Hillard, C. J., & Koltyn, K. F. (2017). Endocannabinoid and Opioid System Interactions in Exercise-Induced Hypoalgesia. *Pain Med*. doi:10.1093/pm/pnx058

Ellingson, L. D., Koltyn, K. F., Kim, J. S., & Cook, D. B. (2014). Does exercise induce hypoalgesia through conditioned pain modulation? *Psychophysiology, 51*(3), 267-276. doi:10.1111/psyp.12168

Gaskin, D. J., & Richard, P. (2012). The economic costs of pain in the United States. *J Pain, 13*(8), 715-724. doi:10.1016/j.jpain.2012.03.009

Hoeger Bement, M. K., Dicapo, J., Rasiarmos, R., & Hunter, S. K. (2008). Dose response of isometric contractions on pain perception in healthy adults. *Med Sci Sports Exerc, 40*(11), 1880-1889. doi:10.1249/MSS.0b013e31817eeecc

Khimich, S. (1997). Level of sensitivity of pain in patients with obesity. *Acta Chir Hung, 36*(1-4), 166-167.

Koltyn, K. F., Brellenthin, A. G., Cook, D. B., Sehgal, N., & Hillard, C. (2014). Mechanisms of exercise-induced hypoalgesia. *J Pain, 15*(12), 1294-1304. doi:10.1016/j.jpain.2014.09.006

Kosek, E., & Lundberg, L. (2003). Segmental and plurisegmental modulation of pressure pain thresholds during static muscle contractions in healthy individuals. *European Journal of Pain, 7*(3), 251-258. doi:10.1016/s1090-3801(02)00124-6

Lemley, K. J., Hunter, S. K., & Bement, M. K. (2015). Conditioned pain modulation predicts exercise-induced hypoalgesia in healthy adults. *Med Sci Sports Exerc, 47*(1), 176-184. doi:10.1249/MSS.0000000000000381

Lewis, G. N., Heales, L., Rice, D. A., Rome, K., & McNair, P. J. (2012). Reliability of the conditioned pain modulation paradigm to assess endogenous inhibitory pain pathways. *Pain Research & Management, 17*(2), 98-102. doi:Doi 10.1155/2012/610561

Mckendall, M. J., & Haier, R. J. (1983). Pain Sensitivity and Obesity. *Psychiatry Research, 8*(2), 119-125. doi:Doi 10.1016/0165-1781(83)90099-9

Naugle, K. M., Fillingim, R. B., & Riley, J. L., 3rd. (2012). A meta-analytic review of the hypoalgesic effects of exercise. *J Pain, 13*(12), 1139-1150. doi:10.1016/j.jpain.2012.09.006

Naugle, K. M., & Riley, J. L., 3rd. (2014). Self-reported physical activity predicts pain inhibitory and facilitatory function. *Med Sci Sports Exerc, 46*(3), 622-629. doi:10.1249/MSS.0b013e3182a69cf1

O'Connor, P. J., & Cook, D. B. (1999). Exercise and Pain: The Neurobiology, Measurement, and Laboratory Study of Pain in Relation to Exercise in Humans. *Exercise and Sport Sciences Reviews, 27*(1), 119-166.

Petrini, L., Matthiesen, S. T., & Arendt-Nielsen, L. (2015). The effect of age and gender on pressure pain thresholds and suprathreshold stimuli. *Perception, 44*(5), 587-596. doi:10.1068/p7847

Price, R. C., Asenjo, J. F., Christou, N. V., Backman, S. B., & Schweinhardt, P. (2013). The role of excess subcutaneous fat in pain and sensory sensitivity in obesity. *Eur J Pain, 17*(9), 1316-1326. doi:10.1002/j.1532-2149.2013.00315.x

Pud, D., Granovsky, Y., & Yarnitsky, D. (2009). The methodology of experimentally induced diffuse noxious inhibitory control (DNIC)-like effect in humans. *Pain, 144*(1-2), 16-19. doi:10.1016/j.pain.2009.02.015

Racine, M., Tousignant-Laflamme, Y., Kloda, L. A., Dion, D., Dupuis, G., & Choiniere, M. (2012). A systematic literature review of 10 years of research on sex/gender and experimental pain perception - part 1: are there really differences between women and men? *Pain, 153*(3), 602-618. doi:10.1016/j.pain.2011.11.025

Riley, J. L., Robinson, M. E., Wise, E. A., Myers, C. D., & Fillingim, R. B. (1998). Sex differences in the perception of noxious experimental stimuli: a meta-analysis. *Pain, 74*(2-3), 181-187. doi:Doi 10.1016/S0304-3959(97)00199-1

Stolzman, S., & Hoeger Bement, M. (2016).Lean mass predicts conditioned pain modulation in adolescents across weight status. *Eur J Pain, 20*(6), 967-976. doi:10.1002/ejp.821

Sullivan, M., Bishop, S., & Pivik, J. (1995). The pain catastrophizing scale: development and validation. *Psychological Assessment, 7*(4), 524-532.

Tashani, O. A., Astita, R., Sharp, D., & Johnson, M. I. (2017). Body mass index and distribution of body fat can influence sensory detection and pain sensitivity. *Eur J Pain, 21*(7), 1186-1196. doi:10.1002/ejp.1019

Tracey, I., & Mantyh, P. W. (2007). The cerebral signature for pain perception and its modulation. *Neuron, 55*(3), 377-391. doi:10.1016/j.neuron.2007.07.012

Vaegter, H. B., Handberg, G., & Graven-Nielsen, T. (2014). Similarities between exercise-induced hypoalgesia and conditioned pain modulation in humans. *Pain, 155*(1), 158-167. doi:10.1016/j.pain.2013.09.023

Yong, H. H., Gibson, S. J., Horne, D. J., & Helme, R. D. (2001). Development of a pain attitudes questionnaire to assess stoicism and cautiousness for possible age differences. *J Gerontol B Psychol Sci Soc Sci, 56*(5), P279-284.

Zahorskamarkiewicz, B., Kucio, C., & Pyszkowska, J. (1983). Obesity and Pain. *Human Nutrition-Clinical Nutrition, 37*(4), 307-310.

Zahorska-Markiewicz, B., Zych, P., & Kucio, C. (1988). Pain sensitivity in obesity. *Acta Physiol Pol, 39*(3), 183-187.

Appendix A: IRB Approval Letter

The UNIVERSITY of OKLAHOMA

Institutional Review Board for the Protection of Human Subjects

Initial Submission – Board Approval

Date: March 19, 2018

To: Christopher D Black, PhD

IRB#: 9025
Meeting Date: 03/05/2018
Approval Date: 03/17/2018
Expiration Date: 02/28/2019

Study Title: The Relationship Among Site Specific Fat, Lean Mass, and Pressure Pain Sensitivity

Reference Number: 676371

Study Status: Active - Open

At its regularly scheduled meeting the IRB reviewed the above-referenced research study. Study documents associated with this submission are listed on page 2 of this letter. To review and/or access the submission forms as well as the study documents approved for this submission, open this study from the *My Studies* option, click to open this study, look under Protocol Items to click on the current *Application*, *Informed Consent* and *Other Study Documents*.

If this study required routing through the Office of Research Administration (ORA), you may *not begin your study yet*, as per OUHSC Institutional policy, until the contract through ORA is finalized and signed.

As principal investigator of this research study, it is your responsibility to:

- Conduct the research study in a manner consistent with the requirements of the IRB and federal regulations at 45 CFR 46 and/or 21 CFR 50 and 56.
- Request approval from the IRB prior to implementing any/all modifications.
- Promptly report to the IRB any harm experienced by a participant that is both unanticipated and related per IRB Policy.
- Maintain accurate and complete study records for evaluation by the HRPP quality improvement program and if applicable, inspection by regulatory agencies and/or the study sponsor.
- Promptly submit continuing review documents to the IRB upon notification approximately 60 days prior to the expiration date indicated above.

In addition, it is your responsibility to obtain informed consent and research privacy authorization using the currently approved, stamped forms and retain all original, signed forms, if applicable.

If you have questions about this notification or using iRIS, contact the IRB at 405-271-2045 or irb@ouhsc.edu.

Sincerely,

Karen Beckman, MD
Chairperson, Institutional Review Board

Appendix B: Consent Form

Consent Form
University of Oklahoma Health Sciences Center (OUHSC)
University of Oklahoma – Norman Campus
The Relationship Among Site Specific Fat, Bone free lean mass, and Pressure Pain Sensitivity
Christopher Black, PhD

This is a research study. Research studies involve only individuals who choose to participate. Please take your time to make your decision. Discuss this with your family and friends.

Why Have I Been Asked To Participate In This Study?
You are being asked to take part in this study because you are a healthy young adult (18-30) without any chronic pain. Females: you are not pregnant.

Why Is This Study Being Done?
The purpose of this study is to compare the relationship between body composition and pain sensitivity

How Many People Will Take Part In The Study?
About 100 people will take part in this study. All visits will take place in the Sensory and Muscle Function Laboratory located in the Health and Exercise Science Department on the Norman campus.

What Is Involved In The Study?
If you agree to be in this research, you will be asked to visit the Sensory and Muscle Function lab within the Health and Exercise Science Department at the University of Oklahoma Norman Campus for 3 separate visits.
Visit 1:
Height, weight, and fat thickness measurements at the forearms and things will be taken. Fat thickness will be measured by ultrasound and skinfolds. DXA scans will also be taken and participants will provide a urine sample to check hydration status. Female participants will complete a pregnancy test before the DXA scans. Pressure pain thresholds (PPT) will be assessed at both forearms (brachioradialis muscles) and thighs (vastus lateralis muscles) for familiarization on the protocol. Following PPT, participants will complete 3 maximal leg extensions on their dominant leg while they are seated and their leg in tied in at the ankle.
Visit 2:
The second visit, PPT will again be assessed at both forearms and thighs. Participants will then place both feet in ice water at 2 degrees Celsius for 1 minute. PPT will be assessed immediately after and 15 minutes after the feet are removed from the ice water.
Visit 3:
The third visit, PPT will again be assessed at both forearms and thighs. Following the PPT assessment, participants will perform a leg extension with their dominant leg, while seated with the dominant leg secured at the ankle that is equal to 25% of their maximal

effort. Participants will hold that weight for as long as they can. PPT will again be assessed immediately after and 15 minutes after the 25% leg extension exercise.

How Long Will I Be In The Study?
We think that you will be in the study for 3 visits, each lasting roughly 30-45 minutes.

There may be anticipated circumstances under which your participation may be terminated by the investigator without regard to your consent.

- The researcher feels that it is in your medical best interest.
- It is deemed risky to test you based upon you're medical history.
- You fail to follow study requirements.

You can stop participating in this study at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

What Are The Risks of The Study?
If you participate in this research, you will be exposed to radiation from a DXA scan (a type of x-ray). The amount of radiation to which you will be exposed from one DXA scan is approximately less than 1% of the amount of radiation that we are exposed to each year from natural background sources of radiation. The risk of radiation exposure is cumulative over your lifetime.

Performing maximal effort leg extensions may cause some discomfort and the effort required to produce maximal force may be uncomfortable. You may experience some lightheadedness or nausea. There is also the risk for cardiovascular events when performing leg extensions. There may also be some discomfort during the pressure pain protocol which may cause some discomfort and possible reddening of the skin. Having fee submerged in ice water for extended period of time will lead to temporary discomfort. You will be closely monitored for any issues.

Are There Benefits to Taking Part in The Study?
If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope that the information learned from this study will benefit other patients with this disease in the future. You will learn your body composition as well as your level of sensitivity to pressure pain.

What Other Options Are There?
You may choose not to participate in the study.

What about Confidentiality?
Efforts will be made to keep your personal information confidential. You will not be identifiable by name or description in any reports or publications about this study. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if

required by law. You will be asked to sign a separate authorization form for use or sharing of your protected health information.

There are organizations outside the OUHSC that may inspect and/or copy your research records for quality assurance and data analysis. These organizations include the US Food & Drug Administration and other regulatory agencies. The OUHSC Human Research Participant Program office, the OUHSC Institutional Review Board, and the OUHSC Office of Compliance may also inspect and/or copy your research records for these purposes.

What Are the Costs?
There is no cost to you if you participate in this study.

Will I Be Paid For Participating in This Study?
You will be entered in a raffle for a gift card for your participation.

What if I am Injured or Become Ill While Participating in this Study?
In case of injury or illness resulting from this study, emergency medical treatment is available. However, you or your insurance company will be expected to pay the usual charge from this treatment. The University of Oklahoma-Norman and the University of Oklahoma Health Sciences Center have not set aside any funds to compensate you in the event of injury.

What Are My Rights As a Participant?
Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time. However, at certain times during the treatment, it may be harmful for you to withdraw, so please be sure to discuss leaving the study with the principal investigator or your regular doctor. You may discontinue your participation at any time without penalty or loss of benefits to which you are otherwise entitled.

We will provide you with any significant new findings developed during the course of the research that may affect your health, welfare, or willingness to continue your participation in this study.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study has completely finished. You consent to this temporary restriction.

Whom Do I Call If I have Questions or Problems?
If you have questions, concerns, or complaints about the study or have a research-related injury, contact Cameron Lohman at 580-318-4151 or cameron.l.lohman-1@ou.edu, or Christopher Black, PhD at 706-255-3750 or cblack@ou.edu.

If you cannot reach the Investigator or wish to speak to someone other than the investigator, contact the OUHSC Director, Office of Human Research Participant Protection, at 405-271-2045.

For questions about your rights as a research participant, contact the OUHSC Director, Office of Human Research Participant Protection at 405-271-2045.

Signature:
By signing this form, you are agreeing to participate in this research study under the conditions described. You have not given up any of your legal rights or released any individual or entity from liability for negligence. You have been given an opportunity to ask questions. You will be given a copy of this consent document.

I agree to participate in this study:

_____	_____	_____
PARTICIPANT SIGNATURE (age ≥18)	Printed Name	Date
_____	_____	_____
SIGNATURE OF PERSON OBTAINING CONSENT	Printed Name	Date

IRB Office Version Date: 09/21/2016

Appendix C: HIPPA

University of Oklahoma Health Sciences Center Research Privacy Form 1
PHI Research Authorization

AUTHORIZATION TO USE or SHARE
HEALTH INFORMATION THAT IDENTIFIES YOU FOR RESEARCH
An Informed Consent Document for Research Participation may also be required.
Form 2 must be used for research involving psychotherapy notes.

Title of Research Project: **The Relationship Among Site-Specific Fat, Lean Mass, and Pressure**

Pain Sensitivity

Leader of Research Team: **Christopher D. Black, PhD**

Address: **1401 Asp Avenue, #110 SFC, Norman, OK, 73019**

Phone Number**: 706-255-3750 (cell); 405-325-7668 (office)**

If you decide to sign this document, University of Oklahoma Health Sciences Center (OUHSC) researchers may use or share information that identifies you (protected health information) for their research. Protected health information will be called PHI in this document.

PHI To Be Used or Shared. Federal law requires that researchers get your permission (authorization) to use or share your PHI. If you give permission, the researchers may use or share with the people identified in this Authorization any PHI related to this research from your medical records and from any test results. Information used or shared may include all information relating to any tests, procedures, surveys, or interviews as outlined in the consent form; medical records and charts; name, address, telephone number, date of birth, race, government-issued identification numbers, and nothing else.

Purposes for Using or Sharing PHI. If you give permission, the researchers may use your PHI to assess pressure pain thresholds among participants with varying body compositions to determine the relationship among site-specific fat, bone free lean mass, and pressure pain sensitivity.

Other Use and Sharing of PHI. If you give permission, the researchers may also use your PHI to develop new procedures or commercial products. They may share your PHI with other researchers, the research sponsor and its agents, the OUHSC Institutional Review Board, auditors and inspectors who check the research, and government agencies such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (HHS), and when required by law. The researchers may also share your PHI with your physician and/or a University of Oklahoma physician in the event of a serious health risk or adverse event that occurs during the study.

Confidentiality. Although the researchers may report their findings in scientific journals or meetings, they will not identify you in their reports. The researchers will try to keep your information

[1] **Protected Health Information includes all identifiable information relating to any aspect of an individual's health whether past, present or future, created or maintained by a Covered Entity.**

confidential, but confidentiality is not guaranteed. The law does not require everyone receiving the information covered by this document to keep it confidential, so they could release it to others, and federal law may no longer protect it.

YOU UNDERSTAND THAT YOUR PROTECTED HEALTH INFORMATION MAY INCLUDE INFORMATION REGARDING A COMMUNICABLE OR NONCOMMUNICABLE DISEASE.

Voluntary Choice. The choice to give OUHSC researchers permission to use or share your PHI for their research is voluntary. It is completely up to you. No one can force you to give permission. However, you must give permission for OUHSC researchers to use or share your PHI if you want to participate in the research and, if you cancel your authorization, you can no longer participate in this study.

Refusing to give permission will not affect your ability to get routine treatment or health care unrelated to this study from OUHSC.

Canceling Permission. If you give the OUHSC researchers permission to use or share your PHI, you have a right to cancel your permission whenever you want. However, canceling your permission will not apply to information that the researchers have already used, relied on, or shared or to information necessary to maintain the reliability or integrity of this research.

End of Permission. Unless you cancel it, permission for OUHSC researchers to use or share your

PHI for their research will never end.

Contacting OUHSC: You may find out if your PHI has been shared, get a copy of your PHI, or cancel your permission at any time by writing to:

Privacy Official or Privacy Board

University of Oklahoma Health Sciences Center University of Oklahoma Health Sciences Center

PO Box 26901 PO Box 26901

Oklahoma City, OK 73190 Oklahoma City, OK 73190

If you have questions, call: (405) 271-2511 or (405) 271-2045.

Access to Information. You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study is completely finished. You consent to this temporary restriction.

Giving Permission. By signing this form, you give OUHSC and OUHSC's researchers led by the Research Team Leader permission to share your PHI for the research project listed at the top of this form.

University of Oklahoma Health Sciences Center Research Privacy Form 1

PHI Research Authorization

Patient/Participant Name (Print): _____

_____ _____

Signature of Patient-Participant Date or Parent if Participant is a minor

Or

_____ _____

Signature of Legal Representative** Date

**If signed by a Legal Representative of the Patient-Participant, provide a description of the relationship to the Patient-Participant and the authority to act as Legal Representative:

_____

OUHSC may ask you to produce evidence of your relationship.

A signed copy of this form must be given to the Patient-Participant or the Legal Representative at the time this signed form is provided to the researcher or his representative.

Appendix D: International Physical Activity Questionnaire

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

(October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

☐ Yes

☐ No ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

_____ **days per week**

☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

_____ **days per week**

☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ hours per day
_____ minutes per day

This is the end of the questionnaire, thank you for participating.

Appendix E: Physical Activity Readiness Questionnaire

Physical Activity Readiness Questionnaire - PAR-Q (revised 2002)

PAR-Q & YOU

(A Questionnaire for People Aged 15 to 69)

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

YES	NO		
☐	☐	1.	**Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?**
☐	☐	2.	**Do you feel pain in your chest when you do physical activity?**
☐	☐	3.	**In the past month, have you had chest pain when you were not doing physical activity?**
☐	☐	4.	**Do you lose your balance because of dizziness or do you ever lose consciousness?**
☐	☐	5.	**Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?**
☐	☐	6.	**Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?**
☐	☐	7.	**Do you know of any other reason why you should not do physical activity?**

If you answered

YES to one or more questions

Talk with your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

DELAY BECOMING MUCH MORE ACTIVE:

- if you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- if you are or may be pregnant – talk to your doctor before you start becoming more active.

PLEASE NOTE: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed Use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.

NOTE: If the PAR-Q is being given to a person before he or she participates in a physical activity program or a fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

NAME _____

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority) _____ WITNESS _____

Note: This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.

Appendix F: Menstrual History Questionnaire

Department of Health and Exercise Science
University of Oklahoma

MENSTRUAL HISTORY QUESTIONNAIRE

Participant ID:_____Date:_____

We are asking you to give us as complete a menstrual history as possible. All information is strictly confidential.

Are you pregnant (circle your response)

YES- Do not complete the rest of this form
NO- Continue to section A.

SECTION A: CURRENT MENSTRUAL STATUS

1. Approximately how many menstrual periods have you had during the past 12 months? (please circle what months you have had a period. This means from this time last year to the present month)

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

2. What is the usual length of your menstrual cycle (first day of your period to the next onset of your period)?

_____days. Today is day _____ of your present menstrual cycle.

3. When was the date of the onset of your last period?

4. When do you expect you next period?

5. What is the average length (number of days) of your menstrual flow? _____ days

How many of these days do you consider “heavy”?_____days

6. Do you take oral contraceptives or any other medication that includes estrogen and/or progesterone?

   If yes, how long have you been taking this medication?_____

   What is the brand name and dosage of this mediation?_____

Has this medication affected your menstrual cycle (regularity, length and amount of flow)? If yes, indicate changes.

Appendix G: Pain Attitudes Questionnaire

Participant #:_____ Testing Session:_____ Date:_____

Pain Attitudes Questionnaire–Revised

Instructions

Rate how much you agree or disagree with each statement below using a 1 – 5 scale; **where 1 is Strongly Disagree and 5 is Strongly Agree.**

1. I take a long time to decide whether a sensation is painful or not
   1 2 3 4 5

2. When I am in pain I should keep it to myself
   1 2 3 4 5

3. When a sensation is mild, I tend to not trust myself in deciding whether it is painful or not
   1 2 3 4 5

4. I keep a stiff upper lip when I am in pain
   1 2 3 4 5

5. I lack confidence in making judgments about whether a sensation is painful or not
   1 2 3 4 5

6. I think I can tolerate more pain than other people
   1 2 3 4 5

7. I need time to decide whether a sensation is painful or not
   1 2 3 4 5

8. I would rather not make a decision about pain when it is difficult to decide whether a sensation is painful or not
   1 2 3 4 5

9. I think I can control my pain better than other people
   1 2 3 4 5

10. I avoid making a decision about pain when I am not sure whether a sensation is considered painful or not

    1 2 3 4 5

11. I take great care to avoid labelling a sensation as painful unless I am very certain

    1 2 3 4 5

12. When I get odd sensations, I don't necessarily think they are painful

    1 2 3 4 5

13. I tend to be reluctant to label a sensation as painful unless I am very certain

    1 2 3 4 5

14. I am seldom emotional when in pain

    1 2 3 4 5

15. I do not see any good in complaining when I am in pain

    1 2 3 4 5

16. I go on as if nothing has happened when I am in pain

    1 2 3 4 5

17. I maintain my pride and keep a stiff upper lip when I am in pain

    1 2 3 4 5

18. I have good control over my pain compared to others

    1 2 3 4 5

19. I make light of pain; I refuse to get too serious about it when in pain

    1 2 3 4 5

20. Relative to other people, I am not as emotional when in pain

    1 2 3 4 5

21. I get on with life despite being in pain

    1 2 3 4 5

22. I hide my pain from others

    1 2 3 4 5

23. I think I can endure more pain than other people

1 2 3 4 5

24. I need to be absolutely certain a sensation is painful before I will label it as painful

1 2 3 4 5

Appendix H: Pain Catastrophizing Scale

PCS

Client No.: _____ Age: _____ Sex: M(__) F(__) Date: _____

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

0 – not at all **1** – to a slight degree **2** – to a moderate degree **3** – to a great degree **4** – all the time

When I'm in pain …

1. ☐ I worry all the time about whether the pain will end.
2. ☐ I feel I can't go on.
3. ☐ It's terrible and I think it's never going to get any better.
4. ☐ It's awful and I feel that it overwhelms me.
5. ☐ I feel I can't stand it anymore.
6. ☐ I become afraid that the pain will get worse.
7. ☐ I keep thinking of other painful events.
8. ☐ I anxiously want the pain to go away.
9. ☐ I can't seem to keep it out of my mind.
10. ☐ I keep thinking about how much it hurts.
11. ☐ I keep thinking about how badly I want the pain to stop.
12. ☐ There's nothing I can do to reduce the intensity of the pain.
13. ☐ I wonder whether something serious may happen.

_____

…Total

Appendix I: Email Recruitment Script

Email Recruitment

To whom it may concern,

Hello, my name is Cameron Lohman and I am a Masters student in the Department of Health and Exercise Science. Dr. Chris Black and I are looking for research participants for a study titled: *The Relationship Among Site-Specific Fat, Lean Mass and Pressure Pain Sensitivity*. We are conducting research looking at the relationship between body composition and pain thresholds. If you are between the ages of 18-30, we encourage you to participate.

Participation in this research includes completing the Physical Activity Readiness Questionnaire (PAR-Q), the International Physical Activity Questionnaire (IPAQ), and an informed consent, which will take 30-45 minutes. You will be required to come to our lab for a total of 3 visits to assess your body composition via a DXA scan and skin fold assessments and your pain thresholds will be examined by experimentally induced pain prior to and following isometric exercising and placing your feet in a cold-water bath. The visits will be roughly 30-45 minutes in length for a total time commitment of 2 hrs. and 15 min. If you have any questions or would like to participate, please contact me at 580-318-4151 or Cameron.L.Lohman-1@ou.edu, or Dr. Chris Black, Principal Investigator, at 705-255-3750 or cblack@ou.edu.

All the best,

Cameron Lohman

The University of Oklahoma is an equal opportunity institution. IRB 9025,

Appendix J: Additional Data Tables

Table 9 – Relationship among selected variables and pain sensitivity in the dominant leg

	Weight	BMI	Tot %Fat	Tot Fat Mass	Tot Bone Free Lean Mass	Leg %Fat	Leg Fat Mass	Leg Bone Free Lean Mass	Leg Fat Thickness	Leg Musc Thickness	Leg Skinfold	Resting PPT	CPM	EIH
Weight (kg)	--	.82**	-.02	.32*	.79**	-.23	.18	.79**	-.33*	.74**	-.19	.44**	.05	-.07
BMI (kg/m^2)		--	.39**	.64**	.39**	.19	.55**	.47**	.07	.69**	.19	.22	.10	.02
Tot %Fat			--	.91**	-.60**	.93**	.92**	-.51**	.85**	-.12	.83**	-.22	.13	.10
Tot Fat Mass (kg)				--	-.26	.78**	.96**	-.19	.68**	.14	.73**	-.02	.12	.02
Tot Bone Free Lean Mass (kg)					--	-.74**	-.39**	.93**	-.75**	.66**	-.63**	.47	-.04	-.11
Leg %Fat						--	.87**	-.66**	.94**	-.30*	.90**	-.30*	.15	.16
Leg Fat Mass (kg)							--	-.29*	.79**	.04	.82**	-.11	.18	.05
Leg Bone Free Lean Mass (kg)								--	-.69**	.68**	-.60**	.45**	.01	-.10
Leg Fat Thickness (mm)									--	-.39**	.91**	-.24	.15	.13
Leg Musc Thickness (mm)										--	-.23	.21	.13	-.23
Leg Skinfold (mm)											--	-.15	.12	.06
Resting PPT (kPa)												--	-.03	.01
CPM (%)													--	.11
EIH (%)														--

BMI: Body mass index; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia.*indicates a significant correlation ($p < 0.05$). ** indicates a significant correlation ($p < 0.001$).

Table 10 – Relationship among selected variables and pain sensitivity in the non-dominant leg

	Weight	BMI	Tot %Fat	Tot Fat Mass	Tot Bone Free Lean Mass	Leg %Fat	Leg Fat Mass	Leg Bone Free Lean Mass	Leg Fat Thickness	Leg Musc Thickness	Leg Skinfold	Resting PPT	CPM	EIH
Weight (kg)	--	.818**	-.02	.32*	.79**	-.20	.19	.79**	-.33*	.78**	-.18	.49**	-.17	-.24
BMI (kg/m^2)		--	.39**	.64**	.39**	.18	.53**	.41**	.09	.70**	.20	.31*	-.07	-.15
Tot %Fat			--	.92**	-.60**	.89**	.88**	-.57**	.84**	-.13	.82**	-.14	.05	.06
Tot Fat Mass (kg)				--	-.26	.75**	.92**	-.25	.67**	.15	.74**	.08	.05	-.02
Tot Bone Free Lean Mass (kg)					--	-.67**	-.36**	.97**	-.76**	.70**	-.61**	.45**	-.10	-.23
Leg %Fat						--	.76**	-.66**	.86**	-.31*	.81**	-.16	-.02	.04
Leg Fat Mass (kg)							--	-.30*	.75**	.08	.80**	.04	-.00	-.01
Leg Bone Free Lean Mass (kg)								--	-.75**	.73**	-.62**	.43**	-.19	-.22
Leg Fat Thickness (mm)									--	-.39**	.90**	-.13	.02	.10
Leg Musc Thickness (mm)										--	-.20	.30*	-.03	-.27*
Leg Skinfold (mm)											--	-.09	.10	.13
Resting PPT (kPa)												--	-.03	-.04
CPM (%)													--	.05
EIH (%)														--

BMI: Body mass index; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia.*indicates a significant correlation ($p < 0.05$). ** indicates a significant correlation ($p < 0.001$).

Table 11 – Relationship among selected variables and pain sensitivity in the left arm

	Weight	BMI	Tot %Fat	Tot Fat Mass	Tot Bone Free Lean Mass	Arm %Fat	Arm Fat Mass	Arm Bone Free Lean Mass	Arm Fat Thickness	Arm Musc Thickness	Arm Skinfold	Resting PPT	CPM	EIH
Weight (kg)	--	.82**	-.02	.32*	.79**	-.12	.27*	.74**	-.10	.62**	.13	.24	.18	.08
BMI (kg/m^2)		--	.39**	.64**	.39**	.29*	.58**	.36**	.24	.40**	.45**	.07	.23	.15
Tot %Fat			--	.92**	-.60**	.91**	.82**	-.60**	.78**	-.44**	.82**	-.17	.24	.06
Tot Fat Mass (kg)				--	-.26	.81**	.88**	-.28*	.69**	-.19	.82**	-.03	.26	.09
Tot Bone Free Lean Mass (kg)					--	-.62**	-.26	.96**	-.55**	.73**	-.38**	.30*	-.01	.03
Arm %Fat						--	.89**	-.66**	.84**	-.44**	.82**	-.05	.13	.06
Arm Fat Mass (kg)							--	-.28*	.73**	-.17	.80**	.08	.21	.05
Arm Bone Free Lean Mass (kg)								--	-.56**	.75**	-.39**	.32*	.00	.05
Arm Fat Thickness (mm)									--	-.35**	.75**	-.07	.17	.10
Arm Musc Thickness (mm)										--	-.17	.30*	.09	-.01
Arm Skinfold (mm)											--	.05	.20	.13
Resting PPT (kPa)												--	.01	.14
CPM (%)													--	.01
EIH (%)														--

BMI: Body mass index; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia.*indicates a significant correlation ($p < 0.05$). ** indicates a significant correlation ($p < 0.001$).

Table 12 – Relationship among selected variables and pain sensitivity in the right arm

	Weight	BMI	Tot %Fat	Tot Fat Mass	Tot Bone Free Lean Mass	Arm %Fat	Arm Fat Mass	Arm Bone Free Lean Mass	Arm Fat Thickness	Arm Musc Thickness	Arm Skinfold	Resting PPT	CPM	EIH
Weight (kg)	--	.82**	-.02	.32*	.79**	-.09	.31*	.75**	-.09	.63**	.13	.17	.06	.17
BMI (kg/m²)		--	.39**	.64**	.39**	.33*	.62**	.36**	.28*	.48**	.43**	-.03	.10	.27*
Tot %Fat			--	.92**	-.60**	.96**	.85**	-.60**	.87**	-.33*	.82**	-.16	.06	.21
Tot Fat Mass (kg)				--	-.26	.85**	.90**	-.27*	.76**	-.09	.82**	-.03	.07	.28*
Tot Bone Free Lean Mass (kg)					--	-.63**	-.25	.97**	-.59**	.67**	-.38**	.23	.03	.01
Arm %Fat						--	.89**	-.64**	.92**	-.34**	.85**	-.09	.05	.24
Arm Fat Mass (kg)							--	-.25	.81**	-.04	.84**	.03	.11	.30*
Arm Bone Free Lean Mass (kg)								--	-.61**	.69**	-.38**	.28*	.04	-.01
Arm Fat Thickness (mm)									--	-.31*	.84**	-.07	.01	.23
Arm Musc Thickness (mm)										--	-.09	.15	-.11	.09
Arm Skinfold (mm)											--	.07	.05	.29*
Resting PPT (kPa)												--	-.14	.03
CPM (%)													--	.01
EIH (%)														--

BMI: Body mass index; PPT: Pressure pain threshold; CPM: Conditioned pain modulation; EIH: Exercise-induced hypoalgesia.*indicates a significant correlation ($p < 0.05$). ** indicates a significant correlation ($p < 0.001$).