The Influence of Sex and Pain Catastrophizing on Conditioned Pain Modulation in Athletes

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ABSTRACT

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Context: Recent findings suggests that athletes have enhance pain modulatory systems compared to non-athletes, despite being constantly subjected to painful stimuli through training and competition. Measurements such as conditioned pain modulation (CPM) is one test that we can use to compare modulatory pain processes. CPM has been shown to be different in non-athlete males and females, but to our knowledge, no study has examined the sex differences in CPM in athletes. In addition, psychological factors, including pain catastrophizing, may explain why athletes perceive and express pain differently. **Objective**: To compare the sex differences in pain ratings, pressure pain threshold (PPT), and cardiovascular variables in athletes during a CPM protocol; and to determine influence of pain catastrophizing and other psychological factors with pain and cardiovascular variables recorded during a CPM protocol. **Design**: Cross-sectional design. **Setting**: Laboratory. **Participants**: 120 athletes (60 females) from various sports participated in this study. **Main Outcome Measures**: We measured catastrophizing using the Pain Catastrophizing Scale and pain using an 11-point numeric pain rating scale. CPM was measured using pressure pain threshold (PPT), which was measured on the thenar eminence and tibialis anterior before and after a cold pressor test (CPT). **Results**: During the CPT, participants experienced increases in subjective pain ratings, but pain intensity did not differ between males and females. We observed increases in PPT measures following the CPT in males and females, but males displayed higher PPT measures than females at pre- and post-CPT. In addition, we did

not identify a relationship between any psychological factors and subjective pain ratings during the CPT. **Conclusions**: Our results suggest that psychological factors do not influence pain perception during a CPT and that male athletes present greater PPT measures than female athletes.

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LIST OF ABBREVIATIONS

QST – Quantitative Sensory Test

CPM – Conditioned Pain Modulation

PPT – Pressure Pain Threshold

CPT – Cold Pressor Test

PCS – Pain Catastrophizing Scale

AFAQ – Athlete Fear Avoidance Questionnaire

STAI – State-Trait Anxiety Inventory

HR – Heart Rate

SBP – Systolic Blood Pressure

DBP – Diastolic Blood Pressure

LITERATURE REVIEW

Conditioned Pain Modulation

Conditioned Pain Modulation (CPM) is a measurement used to reflect the endogenous pain modulatory system.[1] The endogenous pain pathways regulate competing faciliatory and inhibitory mechanisms of an incoming signal from the periphery to the brain.[1] This means that the endogenous pain pathways dictate how an individual perceives a noxious (painful) stimulus. We can measure CPM phenomenon by assessing the changes in pain sensitivity or perception of a test stimulus that is applied before and in the presence of a conditioning stimulus (see Figure 1).[2] While CPM is a relatively robust measure, factors such as individual and methodological protocols can account for the considerable interindividual variation in humans.[3-6]

The following section will briefly review the underlying mechanisms of CPM, the different methodological approaches that can be used to test CPM, and how CPM differs in various populations.

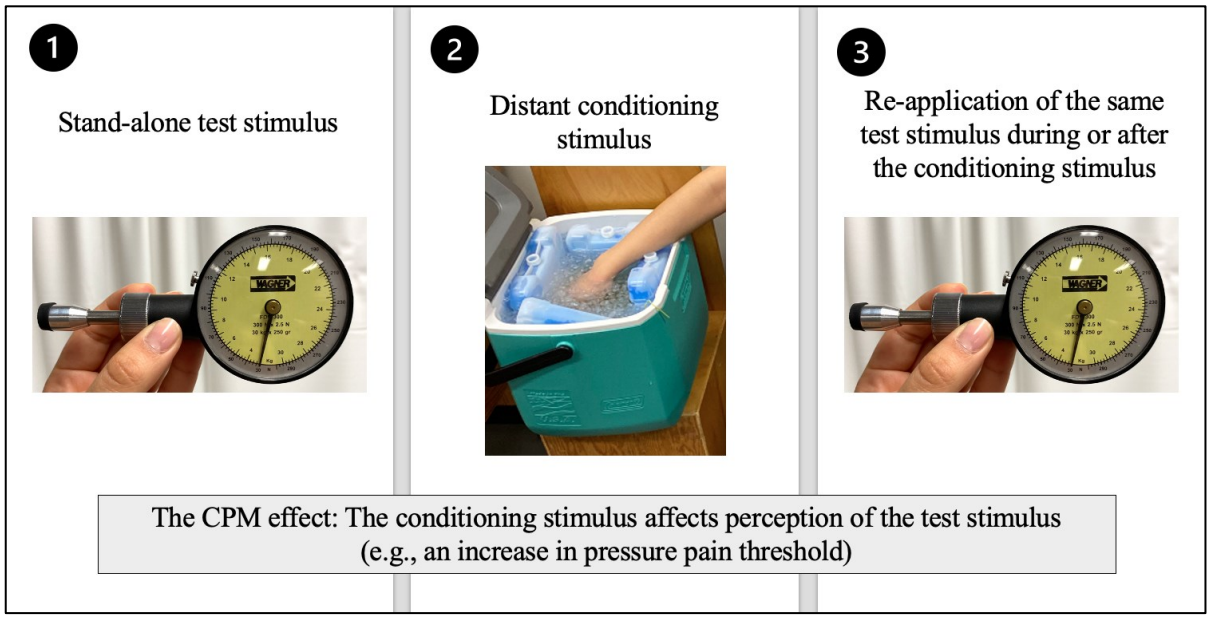

Figure 1 – Illustration of the CPM phenomenon

Mechanism of Conditioned Pain Modulation

Conditioned pain modulation is based on the concept called diffuse noxious inhibitory control (DNIC), which was proposed by Le Bars and colleagues when studying anesthetized rats.[7] The researchers found that different stimuli (e.g., pinch, heat, mechanical pressure, etc.) would inhibit dorsal horn unit activity when another noxious stimulus was applied, causing a wide-spread inhibitory effect over the rats body.[7] Le Bars et al. believed that DNIC modulated spinal nociceptive processing through ascending and descending influences, which was termed the spino-bulbo-spinal loop.[7,8] Neuroimaging research has found brain structures such as the periaqueductal grey, the rostral ventromedial medulla, and the subnucleus reticularis dorsalis to be active during pain modulation.[9] In humans, CPM appears to involve both the spino-bulbo-spinal-loop and top-down influences from higher brain centres (e.g., distraction and attention) that involve the above mentioned brain structures.[1,2]

Measuring Conditioned Pain Modulation

Thus far, a standard testing protocol or calculation does not exist to measure CPM.[3,4] In experimental settings, for example, measures employed to assess CPM vary across laboratories based on the available resources (i.e., the pain modalities available) and the population of interest (i.e., healthy versus patient participants). However, once the population and modalities used to test CPM are selected, laboratories must decide on what test paradigm to use (i.e., sequential or parallel paradigm), the type of modality used for the TS and CS, the duration of each test (i.e., how long the TS and CS are), and test-pain parameters (i.e., pain threshold versus pain tolerance).[3,4]

In 2015, a panel of experts created a CPM testing guideline.[10] It was recommended that 1) the use of mechanical or thermal stimuli that is tested on two separate areas of the body; 2) the intensity of the TS should be moderate and should be determined in an ascending fashion

(discontinued at pain level 40) or as a fixed intensity; 3) CPM should be measured twice with a 10-minute break between each stimulus; 4) the intensity of the CS should be mild to moderate (>20/100 pain level) and should be a thermal or mechanical stimulus; and 5) CPM should be calculated by reporting physical units (e.g., temperature) as $TS_{Pre} - TS_{Post}$ and subjective ratings (e.g., numerical pain ratings for a fixed temperature) as $TS_{Post} - TS_{Pre}$.

In a recent systematic review, the cold pressor test (CPT), which is a cold thermal stimulus, was reported as the most commonly used conditioning stimulus to measure CPM.[4] The CPT is a reliable and non-invasive measure that mimics the effects of chronic pain,[6,11] and has been used in patient, healthy, and athletic populations.[4,5,12] In most cases, individuals submerge a hand or foot into a bath of cold water. The cold temperature of the water stimulates afferent sensory pathways in the body, which induces a sympathetic response and increases heart rate and blood pressure.[13,14] Participants' tolerance to a CPT seems to be time and temperature dependent. In one study with a sample of 31 healthy adults (10 females), CPM was only induced by a 60-second CPT set to 12°C ($p = .003$), but not for temperatures at 15°C ($p = .139$) or 18°C ($p = .0.249$).[15] In another study, among 26 healthy adults (14 females), the influence of temperature on pain tolerance and intensity during a CPT was assessed.[11] Results demonstrated that water temperatures 5°C and 7°C allowed participants to keep their hand in the cold water for longer (measure of tolerance) than a temperature of 1°C (both at level of $p < .05$). Moreover, water temperature at 1°C yield significantly greater pain intensity on the visual analog scale than pain rating 3°C ($p < .001$), 5°C ($p < .01$) and 7°C ($p < .01$).[11]

In the same systematic review by Kennedy et al. (mentioned above),[4] pressure pain threshold (PPT) was reported as the most used test stimulus, followed by thermal heat. PPT can be measured using a handheld or computerized algometer to evaluate deep mechanical

sensitivity.[16] PPT represents the minimum amount of pressure required before an individual first detects a painful pressure sensation.[16] When measuring deep mechanical sensitivity, PPT has demonstrated good to excellent reliability, in comparison to pressure pain tolerance (the maximum amount of pressure a person can tolerate) as retest reliability is reported as poor to fair.[17] CPM is suggested to vary based on the methods and measures used,[4,5,18] including testing sites for PPT.[19] For example, in a sample of 12 healthy males, a CPT elicited a significantly higher CPM effect when PPT was used as the test stimulus, especially when it was measured over the tibialis anterior in comparison to the masseter and the forearm (both at level of $p <$ .001).[19] However, the interpretations of the current study should be taken with caution as the study has a small sample size and includes males only.

Conditioned pain modulation is often measured using two paradigms – a sequential or a parallel paradigm. The sequential paradigm is when the test stimulus is measured before and immediately after the conditioning stimulus; whereas the parallel paradigm is when the test stimulus is measured before and during the conditioning stimulus.[10] Evidence suggests that the CPM effect gradually diminishes with time; therefore, the parallel paradigm is thought to yield a more substantial CPM responses.[3,6] In one study, after an ischemic arm test and CPT, inhibition of PPT remained significant at 10 minutes (p = .026 versus p = .023, respectively) post-CPT but returned to baseline by 15 minutes post-CPT.[6] However, some suggest that the parallel paradigm may provoke biases such as distraction, and therefore, is currently recommended to use the sequential paradigm when measuring CPM.[10]

The Clinical Significance of Conditioned Pain Modulation

Conditioned pain modulation has been explored extensively in healthy and patient populations. Previous studies have found that patients suffering acute and chronic conditions

have dysfunctional CPM[5] – meaning they experience less pain analgesia (pain relief) when the test stimulus is re-tested in the presence of the conditioning stimulus. The clinical significance of using CPM as a measure of pain state is that it can shed light on the descending pain modulatory pathways ability to activate endogenous analgesia, which is shown to be important for pain chronification in rats.[20] Furthermore, dysfunction to pain modulatory pathways is suggested to contribute to the development and maintenance of central sensitization and which could explain the arise of various pain conditions.[21]

Conditioned Pain Modulation in Athletes

Athletes dedicate a substantial amount of time and effort to training and competition, which can involve hours of considerable pain and psychological stress. Frequent exposure to painful stimuli through training and competition may explain why athletes are reported to be less sensitive to experimental pain.[22-27] According to recent but limited data, CPM appears to be more efficient in athletes than non-athletes.[28-30] However, the literature is inconsistent.[30-32] In a systematic review and meta-analysis conducted by McDougall and colleagues, results revealed no significant difference in CPM between athletes and non-athletes.[12] The investigators reported high heterogeneity between the identified studies, emphasizing the difficulty of comparing CPM in athletes and non-athletes due to different methods used to measure CPM and variation in the amount of time athletes spent training.

A study of 19 triathletes and 17 non-athletes conducted by Geva and Defrin used a fixed noxious heat (VAS pain level 7/10) as the test stimulus and a noxious 30-second CPT (12°C) to compare the CPM effect.[28] Results demonstrated that triathletes exhibit more significant decreases in perceived pain than non-athletes (triathletes: 6.8 ± 1.0 to 3.8 ± 2.3, $p < .0001$; non-athletes: 7.0 ± 1.5 to 5.5 ± 2.0, $p < .05$), and thus presented a greater CPM effect than non-

athletes (3.0 ± 2.3 versus 1.5 ± 2.3, $p < .05$). Similarly, Flood et al., compared the CPM effect in athletes and non-athletes using PPT as the test stimulus and a noxious 4-minute CPT (2 ± 1°C) and found athletes to report more pain relief after the CPT than non-athletes (change in PPT scores: 1.19 ± 1.12 versus 0.30 ± 1.04 kg, $p < .05$; respectively).[29] Results from a correlation analysis did not indicate an association between CPM in athletes and self-reported hours of training/physical exercise hour spent training ($r_\tau = .05$, $p > .05$). In addition, CPM in athletes was not correlated with the number of training/physical exercise sessions per week ($r_\tau = .25$, $p > .05$). In contrast, investigators found the opposite relationship to occur between training/physical exercise sessions per week and CPM in non-athletes, whereby the more time spent training reduced the efficiency of CPM in non-athletes ($r_\tau = -.44$, $p < .05$).

Longitudinal studies on groups of athletes demonstrate increases in pain tolerance throughout a sports season/physical exercise training.[25,26] For example, pain tolerance induced by ischemic pain increased throughout a swimming season among 30 (14 females) national swimmers but decreased shortly after the swimming season was over.[25] Although these studies do not measure CPM, it may suggest that high continuous training/physical exercise levels may modulate pain processes. Further investigation on the effects of training/physical exercise on CPM in athletes is needed.

To our knowledge, only one research group reported healthy non-athletes presenting significantly better-CPM effects than elite endurance athletes ($p = .02$).[31] Athletes presented small effect sizes ($d = .14$) in response to the CPM protocol, where tonic heat pain was applied before and after a 2-minute CPT (12 ± 0.2°C). Non-athletes presented moderate effect sizes ($d = .55$) in response to the CPM protocol. Tesarz et al. suggest that the exposure to pain that athletes experience may cause decreases in the DNIC system's ability to inhibit pain when further

stimulated.[31] Furthermore, the athletes included in this study trained far less (9.6 ± 3.5 hours per week) compared to studies that demonstrated enhanced pain modulation in athletes.[28-30] The interpretations of the current study should be taken with caution due to the testing parameters used and the participants included in the study. More research is needed to understand how the amount of training may influence pain modulation in both athlete and non-athlete groups.

The type of sport played by athletes seems to also impact pain modulation. Assa and colleagues examined the different CPM responses between 19 endurance athletes, 17 strength athletes, and 17 non-athletic controls.[30] A noxious heat stimulus was used to test heat pain threshold and tolerance and CPM (measured by applying 2 minutes of heat before and during a 30-second CPT). Endurance-based athletes perceived the noxious heat stimulus to be less painful (2.7 ± 2 VAS units) than the strength-based athletes and non-athletes did ([strength-based athletes]: -1.1 ± 2.5 and [non-athletes]: -1.49 ± 1.9 VAS units, $p < .05$ for both), with the latter presenting similar scores.[30] However, the strength-based athletes had higher heat pain thresholds than both the endurance athletes and controls ($p < 0.05$ for both), while the endurance athletes had higher heat pain tolerances than the strength athletes and controls ($p < .001$ for both). The authors suggest that the nature of the sport (aerobic versus anaerobic) may influence pain modulatory mechanisms.[30] Pettersen et al. found endurance-based athletes (e.g., cross-country skiers) to tolerate a CPT longer than soccer players (179.67 0.90 and 113.90 71.54 seconds).[24] They suggest that sports with longer sustaining physically intense efforts (e.g., ultramarathon runners and triathletes) may allow these athletes to tolerate more pain.[24] This may explain why Assa et al. found endurance-based athletes to have experienced more pain inhibition than the other groups[30]; however, more research is needed to support these findings.

Based on the literature reviewed in this section, it appears that athletes modulate and response differently than non-athletes.[22,24-26,28-30] Researchers debate whether enhanced pain modulation in athletes is something that athletes are born with or something that is acquired through training.[29,30] Evidence suggests that the time spent training may influence the DNIC system's ability to inhibit pain.[28] In addition, the type of training (e.g., endurance based training versus strength based training) may also be relevant to how athletes perceive pain.[24,30] Furthermore, factors such as coping strategies, team culture, ability to ignore pain, and psychological factors may also contribute to the multifaceted relationship athletes have with pain.[24,33] Enhanced endogenous pain pathways in athletes may act as a *double-edged sword* – on one end, better-CPM may allow athletes to tolerate the physical demand and associated pain. On the other end, injuries may increase, as well as the chronicity of the injury, if athletes cannot recognize pain. Therefore, understanding how the endogenous pain pathway works in athletes may affect how physicians and therapists develop training and rehabilitation programs for athletes.

Pain Catastrophizing

Pain catastrophizing is described as an amplified negative response towards anticipated or an actual painful experience.[34] Pain catastrophizing is often characterized in individuals who magnify the threat of a pain and ruminate about it, which can manifest itself into a sense of helplessness.[34-36] Studies have shown that catastrophizing is a robust and reliable predictor and correlate of negative pain experiences.[35,37] For example, high catastrophizers tend to report greater pain intensities, emotional distress, and pain severity, than non-catastrophizers.[34,35,38]

Theoretical and Physiological Mechanisms of Pain Catastrophizing

Early conceptualization of pain catastrophizing was first noted in patients suffering from depression and anxiety disorders.[39,40] Chaves and Brown later described patients' responses to dental procedures as an exaggerated fearful response to a painful stimulus.[41] However, investigators could not empirically quantify pain catastrophizing as no standardized method existed.[36] The Coping Pain Strategies Questionnaire was among the first self-assessment tools to measure pain catastrophizing.[42] Sullivan et al. expanded on this work by developing the Pain Catastrophizing Scale (PCS), a psychometric self-reporting tool that evaluates elements related to catastrophizing, such as magnification, rumination, and helplessness.[34] The PCS was considered an inclusive assessment tool compared to the Coping Pain Strategies Questionnaire[36], as the latter only examined aspects of catastrophizing, such as helplessness and negativity in pain.[42]

The underlying mechanisms of pain catastrophizing are described by various theoretical conceptualizes, including attention bias theory, communal coping theory, and the appraisal theory.[36] Pain catastrophizing can be considered an attention bias since it prioritizes pain-related information.[36] Pain catastrophizing can also be describe as a communal coping strategy, where unconscious coping strategies are employed to solicit physical or emotional support from others, which can reinforce pain-related behaviour.[36] Some investigators refer to pain catastrophizing as an appraisal process where high levels of helplessness will affect an individual's ability to rationalize and cope with pain.[23,35]

Pain Catastrophizing in Athletes

The relationship between catastrophizing and pain is unclear in athletes. Sullivan and colleagues were the first to suggest a difference in catastrophizing levels between 44 varsity

basketball and rugby athletes (63.7% female) and 54 non-athletes (50% female).[23] Participants completed the PCS before performing a 1-minute CPT (2 - 4°C) and rated their pain on a pain rating scale. At baseline, athletes catastrophized less than (17.1 ± 7.3) non-athletes (20.0 ± 9.1), with group differences almost significant ($p < .06$). Athletes also experienced less pain than non-athletes (5.7 ± 1.6 versus 7.0 ± 1.7, respectively); however, the correlation between pain ratings and catastrophizing ranged from weak to moderate for both groups ([athletes]: r = .30, $p < .05$ versus [non-athletes]: r = .43, $p < .01$). Sullivan et al. argue that the lack of correlational strength between pain ratings and catastrophizing in the athlete group may be due to frequent exposure to cold stimuli (e.g., ice).[23]

One part of the Assa et al. study compared heat-pain threshold and tolerance with pain catastrophizing scores among endurance athletes, strength athletes, and non-athletic controls.[30] At baseline, pain catastrophizing scores were not significantly different among the three groups (17.3 ± 7.5 [endurance athletes] versus 17.0 ± 8.2 [strength-athletes] versus 20.8 ± 11.7 [non-athletes], $p = 0.3$). Interestingly, only strength athletes' heat-pain threshold and heat-pain tolerance scores were correlated with pain catastrophizing ($p < 0.05$). These findings suggest that pain catastrophizing may be lower in certain athletic groups, particularly those who engage in strength-based sports.[30]

In a longitudinal study on groups of contact athletes, investigators compared cold pressor tolerance and catastrophizing scores between athletes who attended all practices and games (labelled as participating athletes) to other athletes that did not have perfect attendance (labelled as non-participating athletes).[26] All athletes completed a catastrophizing questionnaire before submerging their hand in a bath of cold water (2-3°C) water for as long as they could (with a 5-minute limit) at pre-season (0-month), mid-season (4-months) and end of the season (8-months).

By the end of the season, participating athletes had lower pain catastrophizing scores than non-participating athletes ($p < 0.0001$).[26] Long-term exposure to pain through training and competition may cause changes to pain processes at the conceptual level.[30] One limitation is that the catastrophizing pain scores recorded in this study cannot be compared to others because the investigators used the Sports Inventory for Pain rather than the PCS.

Our laboratory has previously reported a relationship between pain catastrophizing with cardiovascular reactivity induced by a CPT.[14] Lentini et al. assessed changes in HR, systolic blood pressure, and diastolic blood pressure during a CPT in a group of 36 male contact athletes.[14] High catastrophizing athletes reported greater pain ratings during the CPT ($r = 0.397$, $p = 0.02$). Additionally, PCS scores were moderately correlated with the change in HR during ($r = 0.437$, $p = 0.008$) the cold pressor, with a linear regression indicating peak pain and catastrophizing accounted for 29.2% of the variance in HR change.[14]

Although athletes may catastrophize less than non-athletes, none of the studies mentioned have demonstrated statistically significant differences.[23,30] Catastrophizing has been associated with higher pain intensities, greater pain severity, and increases in emotional distress in the presence of anticipation of a painful event,[34,35,38] which are possible outcomes that may affect athletes. For example, Mannes et al. found that retired National Football League (NFL) players, who catastrophized more, had greater odds of reporting pain interference, moderate-severe depressive symptoms, and lower quality of life.[43] Tripp and colleagues followed-up with 49 athletes 1 year post ACL reconstruction and reported pain catastrophizing scores to be negatively correlated with athletes confidence and actual return to sport.[44] Not addressing the potential consequences of pain catastrophizing in athletes could threaten their well-being and return to sport if they are injured.

RATIONALE

Athletes have a complex relationship with pain, and psychosocial variables like pain catastrophizing can complicate their experiences with pain further. CPM is a good measure to assess the human body's natural ability to inhibit pain. However, previous research on CPM in athletes is inconsistent, with some studies reporting enhanced pain modulation in athletes,[28-30] while others demonstrate no differences between athletes and non-athletes.[12] In addition, some literature suggest athletes catastrophize less about pain than non-athletes.[23,30] Nevertheless, studies present non-statistically significant trends toward less catastrophizing in athletic populations,[30] or do not use standardized self-report assessment tools to measure catastrophizing.[26] Pain is an integral part of sports.[23] Understanding the relationship between pain catastrophizing and pain perception will allow for further insight into the determining factors of pain in athletes. It will also provide important information on how pain catastrophizing and other psychological factors can be used as potential intervention tools for training and rehabilitation.

OBJECTIVES & HYPOTHESE

The objectives of this thesis were to:

1. Examine and compare the sex differences in pain ratings, pressure pain threshold, and cardiovascular variables.
2. Investigate the relationship between psychological factors, pain ratings, and cardiovascular variables during the cold pressor test.

We hypothesized:

1. Females would experience more pain than males during the cold pressor test, females would present fewer changes in pressure pain threshold measures than males, and males would present greater changes in cardiovascular reactivity than females during the cold pressor test.
2. Increased levels of catastrophizing, fear avoidance, and anxiety would be positively correlated with pain experienced during the cold pressor test; and greater changes in heart rate, systolic blood pressure, and diastolic blood pressure would be positively correlated with pain experienced during the cold pressor test.

METHODS

Study Design

This was a pre-post-study design using data (from day one of a two-day study) that examined the influence of ibuprofen and a placebo on CPM in athletes from Concordia University. This study was approved by the Human Research Ethics Committee (HREC) of Concordia University (Certificate Number: 30015224). All participants provided written informed consent.

Sample

A non-probabilistic convenience sample of female and male athletes from various sporting backgrounds volunteered in this study. We recruit athletes from Concordia University's Department of Recreation and Athletics and students who reported being an athlete for a provincial/national sports team. Participants were recruited through announcements at varsity sports practices, posters around campus, and through word of mouth. Prospective participants were excluded if they were smokers, prescribed medication that could alter cardiovascular function, had existing pathologies to the hands (e.g., Reynaud's disease), bruises or any other lesions to hands, or reported having an injury at the time of testing. Participants were excluded if resting HR was above 99 beats/min, systolic blood pressure ≥ 140 millimetres per mercury (mmHg), and diastolic blood pressure ≥ 90 mmHg.

Measures

Subjective Pain Ratings

Subjective pain ratings were measured using an 11-point numeric rating scale (NRS) for pain. The NRS is a valid and reliable self-assessment tool commonly used to assess pain in clinical settings.[45] Anchors for the NRS range from 0 to 10, with 0 indicating, "no pain at

all" and 10 indicating, "the worst pain imaginable." We used the highest score from each time period in our CPM protocol to represent participants' subjective pain ratings.

Pressure Pain Threshold

Pressure pain threshold (PPT) was measured on the left thenar eminence and the left tibialis anterior to assess deep mechanical sensitivity (see Figure 2). Participants were seated on a chair with their left hand rested on a table in a supinated position, while both feet were flat on the floor (knee was bent at a 90° angle). A 300 newton (N) gage handheld algometer (Wagner Instruments., Greenwich, CT) with a 1cm^2 circular rubber was used to apply increasing amounts of force (~1 N/sec) over the left thenar eminence and tibialis anterior. The muscle belly of each test site was marked so PPT testing could be repeated. Pressure was applied gradually, and participants were instructed to notify researchers when they first perceived the pressure change to a painful sensation. PPT was measured twice, alternating between each site, and was performed before and after the cold pressor test. PPT is regarded as the most used test stimulus in CPM protocols,[4] and found to be a reliable measurement in athletes with patellar tendinopathy.[46]

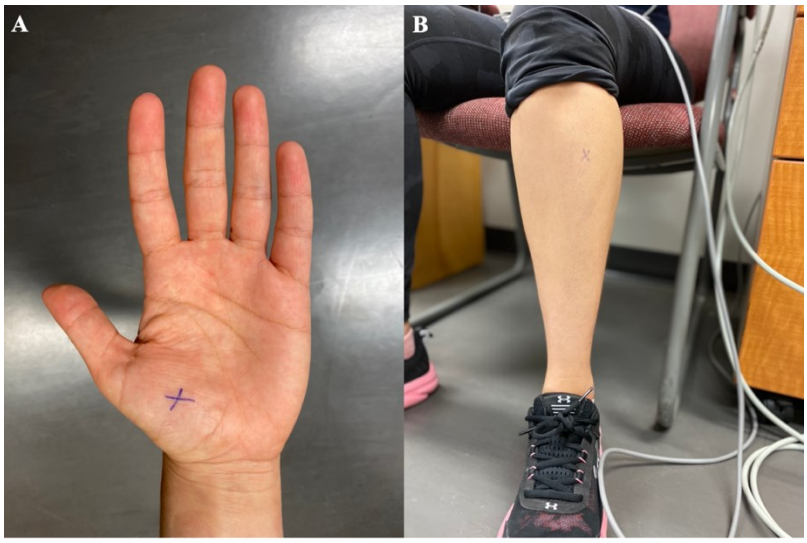

Figure 2 – Image displaying the anatomical testing sites for PPT measurement. PPT was measured on the left thenar eminence (A) and left tibialis anterior (B).

Cold Pressor Test

We used 3-minute cold pressor test (CPT) as the conditioning stimulus in our CPM protocol. A plastic cooler was lined with ice packs and filled with ice and water to maintain water temperatures between 2 – 3 ± 1°C. The water was not circulated, and participants were blinded to the temperature of the water. We checked the temperature of the water every 5-minutes for the first 15 minutes of the CPM protocol to ensure consistency in water temperature. Participants were instructed to remain seated throughout the CPT and to submerge their right hand in the plastic cooler (1 cm above the wrist line). Participants were asked to avoid making a fist with their hand and moving their hand in the water and to keep their hand in the cold water for the duration of the test; however, they were told that they could take their hand out at any point if the water became intolerable or if they began to feel unwell. The CPT is regarded as the most commonly used conditioning stimulus in CPM protocols.[4]

Conditioned Pain Modulation Paradigm

Conditioned pain modulation (CPM) was measured using a sequential paradigm, which is when the test stimulus is measures before and immediately after the conditioning stimulus.[10] An expert panel in 2015 recommended the use of the sequential paradigm over the parallel paradigm (this is when the test stimulus is re-tested at the same time as the conditioning stimulus) to mitigate biases such as distraction.[10] To calculate the CPM effect, we subtracted pre-CPT PPT measures from post-CPT PPT measures (e.g., $PPT_{after} - PPT_{before}$). According to a recent systematic review and meta-analysis, CPM protocols were found to have the highest intra-session reliability when PPT was used as the test stimulus and ischemic pain or a CPT was used as the conditioning stimulus in healthy pain-free individuals (Intraclass correlation coefficient [ICC] = .64).[18]

Cardiovascular Measures

Heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) was measured using the EDAN iM50 Patient Monitor (EDAN Instruments, Inc., Shenzhen, China) during the initial screening period and throughout our CPM protocol. Previous studies have linked cardiovascular reactivity to experimentally induced pain.[13,14] The EDAN iM50 Patient Monitor is a medical-grade device with a 3-lead echocardiogram (ECG) attachment and an automatic blood pressure cuff. Participants were asked to remove their shirts or wear a sports bra/tank top during electrode placement. An alcohol swab was used to clean the sites where the 3-lead ECG was placed. Two electrodes were placed below the distal end of both clavicles, while the third was placed inferior to the 12th left rib (as shown in Figure 3). The blood pressure cuff was placed on the upper left arm 2-3 cm above the antecubital space. Cardiovascular measures were average based on the period they were recorded during our CPM protocol (see Figure 5).

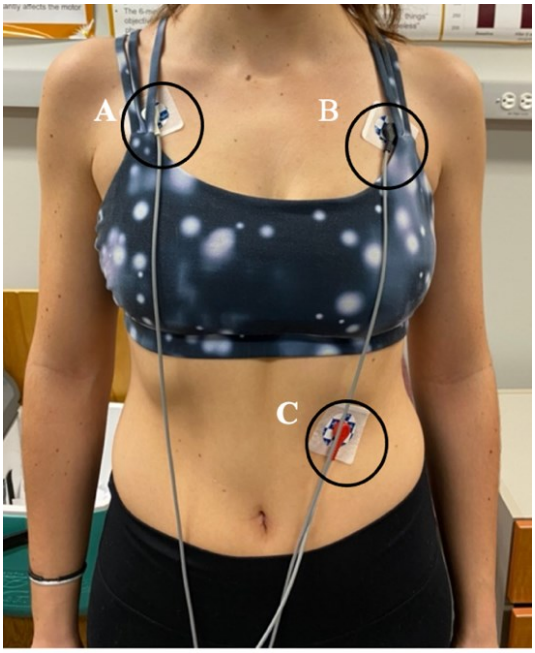

Figure 3 – Image demonstrating the placement of 3-lead ECG for HR measurement during the experiment. Electrodes were placed on the distal end of the right (A) and left (B) clavicle and the hypogastrium, inferior to the 12th left rib (C).

Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS; see Appendix) is a 13-item self-report assessment tool that was designed to assess catastrophic thinking towards anticipated or actual pain.[34] The PCS includes a 5-point Likert scale that ranges from 0, indicating "not at all," and 4, indicating "all the time." Items on the PCS are categorized into three subscales used to describe the components of catastrophic thinking/behaviour: Magnification, rumination, and helplessness. A total possible score on the PCS ranges from 0 to 52, with higher scores suggesting greater catastrophic thinking.[34] Moreover, the PCS has been shown to have excellent internal reliability ($\alpha = .87$) in athletic populations.[23]

Athlete Fear Avoidance Questionnaire

The Athlete Fear Avoidance Questionnaire (AFAQ; see Appendix) is a 10-items self-report tool designed to measure athletes' fear avoidance behaviour towards a sport-related injury.[47] Each item on the AFAQ is scored on a 5-point Likert scale, with 1 indicating, "not at all" and 5 indicating, "completely agree." AFAQ scores range from 10 to 50, with higher scores suggesting that an athlete is presenting fear avoidant behaviour towards a sustained sport-related injury.[47] The AFAQ is found to have high internal consistency ($\alpha = .805$) in athletic populations.[47]

State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory (STAI; see Appendix) is a 40-item self-assessment tool that was designed to assess two types of anxiety – state and trait anxiety. State anxiety represents an individual's emotional state at the time of assessment, while trait anxiety measures general anxious behaviour.[48] The STAI is divided into two 20-item questionnaires scored on a 4-point Likert scale. Each item on the STAI-State (STAI-S) scale ranges from 1 indicating, "not at

all," and 4, indicating "very much." The STAI-Trait (STAI-T) scale ranges from 1 being, "almost never" and 4 being, "almost always." A total possible score on the STAI ranges from 20 to 80, with higher scores indicating greater state or trait anxiety symptoms.[48] The STAI is noted for having high internal consistency both state (α = .91) and trait (α = .89) anxiety subscales in the general population.[49]

Procedure

All visits were performed in the same laboratory and led by at least one of the two graduate students (i.e., primary investigators) with the assistance from two undergraduate research assistants.

To ensure consistency in our experimental reporting's, all participants were asked to refrain from engaging in physical activity/training and consuming alcohol, caffeine, nicotine, or cannabis 12 hours before visiting the laboratory. All participants confirmed adhering to this request. We provided participants with a brief outline of our study before they read the consent document. Once informed consent was provided, we administered a demographic questionnaire to determine eligibility and gather participant characteristics data. Participants then filled the psychological questionnaires, including the PCS, AFAQ, and STAI. Participants were then instructed to sit with their back against a chair, with feet flat on the floor uncrossed, with their left hand resting on a table. Next, baseline cardiovascular (performed right before the CPM protocol started) measures were obtained using the EDAN iM50 Patient Monitor, which was left on for cardiovascular assessment during the experiment. We then debriefed participants before beginning the CPM test.

We used a script (see Appendix) to ensure consistency in the instructions delivered during all PPT measurements and during the CPT. The CPM protocol took 25 minutes to

complete and was divided into four periods: a 10-minute pre-CPT (baseline) period, a 2-minute anticipation period, a 3-minute CPT, and a 10-minute post-CPT (recovery) period. An illustration of the CPM protocol is presented in Figure 5. During the pre-CPT period, the first PPT measurement was performed at minute 8. At minute 10, the cooler filled with water was placed on the participant's right side, but participants were instructed not to submerge their hand in the water. A 2-minute period of rest was implemented to minimize the effects of anticipation before starting the CPT. The anticipatory period was adapted from a previous study to ensure that HR, SBP, and DBP reflected baseline measures and were not elevated due to a stress response from the CPT.[14] Of note, our analysis did not include any cardiovascular values from the 2-minute anticipatory period. At minute 12, participants were instructed to submerge their right hand into the cold water, which was the start of the CPT. At minute 15 (end of CPT), participants were instructed to remove their hand from the water, and PPT was immediately re-tested at the same assessment sites. Participants were then instructed to remain seated for another 10 minutes (minutes 15 to 25), so we could monitor cardiovascular variables.

We recorded subjective pain ratings and cardiovascular variables throughout the CPM protocol. We asked participants to rate their pain every 5 minutes during the CPM protocol. HR was recorded in 30 second intervals, while blood pressure was recorded every 3 minutes. During the CPT, blood pressure and subjective pain ratings were recorded more frequently (~90 seconds) to account for the short duration of the test.

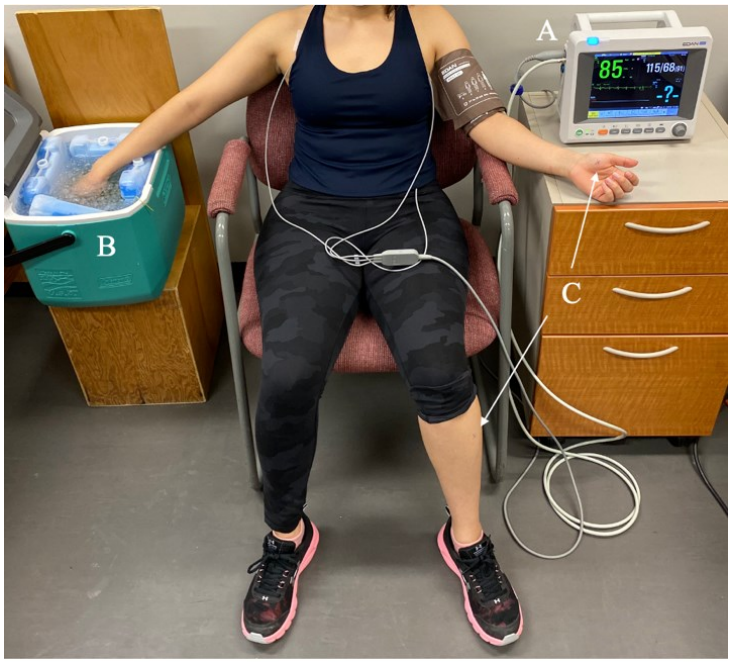

Figure 4 – Image demonstrating the CPT set-up. Cardiovascular measures were recorded using the EDAN iM50 Patient Monitor (A) while a cooler lined with ice packs (B) and a pressure algometer (C) was used to measure PPT on the left thenar eminence and the left tibialis anterior.

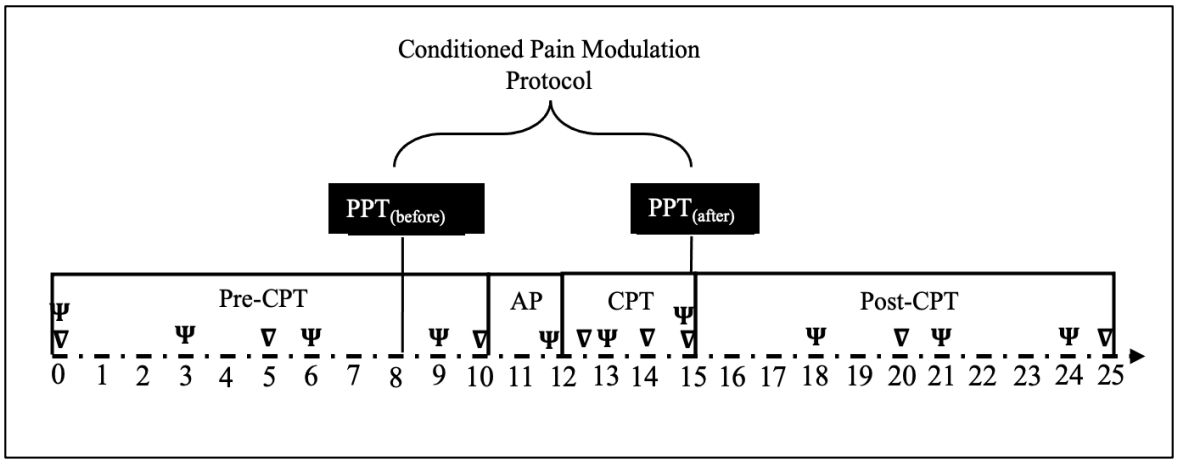

Figure 5 – Illustration of the experiment timeline. This experiment involved a 10-minute pre-CPT period, a 2-minute anticipatory period, a 3-minute CPT, and a 10-minute post-CPT period. Subjective pain ratings (∇) were recorded every 5 minutes throughout the experiment. HR (represented by the dotted line) was recorded every 30 seconds. SBP and DBP (Ψ) were recorded every 3 minutes.

STATISTICAL ANALYSIS

All statistical analyses were performed in SPSS v. 29.0 (SPSS, Inc., Chicago, IL). Means and standard deviations were calculated for all participant characteristics, cardiovascular variables, and pain-related outcomes.

Unpaired t-tests were used to examine and compare sex differences in participant characteristics. We also used unpaired t-tests to compare sex differences in PPT measures for each testing site (thenar eminence and tibialis anterior). Paired t-tests were also used to examine and compare within-group differences between pre- and post-CPT PPT measures among males and females. Separate two-way repeated measures Analyses of Variances (ANOVAs) were performed to examine and compare the sex differences in pain ratings and cardiovascular variables across all time points during the CPM protocol (pre-, during, and post-CPT). It is important to note that for most comparisons, we did not look at the sex main effect because it was important for us to be able to see how the CPT effect the variables of interest between the pre-CPT and post-CPT period. Based on our initial analyses, pain ratings, HR, and SBP violated the homogeneity-of-variance-of-differences (i.e., Sphericity); therefore, degrees of freedom and F-statistic were reported using the Greenhouse-Geisser correction. DBP did not violate Sphericity, therefore the data was reported assuming Sphericity. A post-hoc Bonferroni correction was performed only for variables with a $p < .05$.

In addition, an exploratory Pearson's correlation coefficients matrix was used to examine the relationship between psychological questionnaires (PCS, AFAQ, STAI), pain ratings, and cardiovascular measures (HR, SBP, and DBP), and during the CPT. We referenced Cohen's interpretations of Pearson's r for all correlation analyses.[50]

RESULTS

Study Enrollment

A total of 126 participants were approached to participate in this study. Six participants were excluded including: two because they could not tolerate the cold water during the CPT (pain ratings: 7/10 and 10/10), and another two because they rated their pain as 0/10. These individuals were excluded from our data analysis since the CPT needed to be painful enough to affect participants' perception of the PPT measurements. One participant (n = 1) fainted during the CPT and was withdrawn from the study. Lastly, one athlete (n =1) experienced an adverse reaction to the CPT, but we could not determine if it was because of a physiological or psychological response, so their data was not included in our analysis. Therefore, 120 participants were included in our final data analysis (see Figure 6).

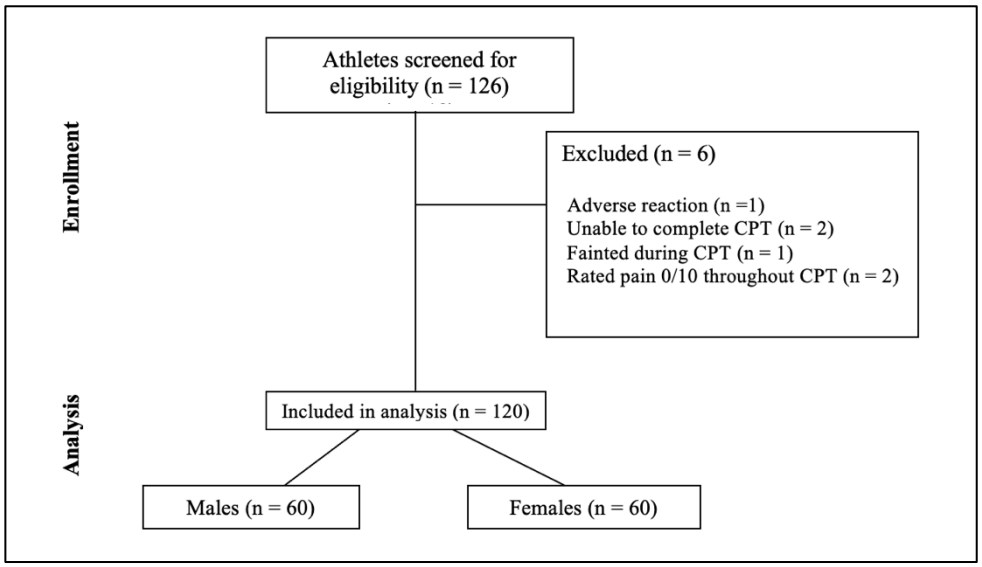

Figure 6 – Flow diagram showing participant enrollment. *Note*. CPT = Cold pressor test.

Participant Characteristics

Measures	All (n = 120)	Male (n = 60)	Female (n = 60)
Age, y	22.7 ± 2.4	22.9 ± 2.2	22.5 ± 2.5
Height, cm	172.1 ± 11.0	179.3 ± 9.6	164.8 ± 6.7*
Mass, kg	77.1 ± 18.8	89.2 ± 18.2	65.0 ± 9.2**
Body Mass Index, kg/m^2	25.9 ± 4.9	27.8 ± 5.7	23.9 ± 3.0**
Pain Catastrophizing Scale	15.9 ± 8.8	15.4 ± 8.5	16.4 ± 9.1
Athlete Fear Avoidance Questionnaire	23.7 ± 6.6	23.0 ± 6.3	24.5 ± 6.8
State-Trait Anxiety Inventory			
State	47.1 ± 4.3	48.1 ± 3.4	46.2 ± 4.9
Trait	46.4 ± 5.5	45.5 ± 5.1	47.4 ± 5.8
Cardiovascular measures			
Heart rate, beats/min	67.4 ± 11.3	66.7 ± 11.3	68.0 ± 11.3
Systolic blood pressure, mm Hg	120.6 ± 14.3	128.8 ± 13.2	112.3 ± 9.8 *
Diastolic blood pressure, mm Hg	69.5 ± 9.6	72.7 ± 10.2	66.4 ± 7.8
Sport Type			
Rugby	29	11	18
Wrestling	9	4	5
Soccer	23	9	14
Synchronized figure skating	3	-	3
Football	23	23	-
Flag football	2	-	2
Triathlon	4	3	1
Boxing	1	-	1
Basketball	18	8	10
Hockey	6	-	6
Baseball	2	2	-
No. Training sessions per week	6.56 ± 2.15	6.4 ± 1.9	6.7 ± 2.4
No. Training hours per week	13.26 ± 4.33	13.2 ± 4.6	13.3 ± 4.1

Table 1 – Participant characteristics (mean ± SD).
* = $p < .05$ difference between males and females
** = $p < .001$ difference between males and females

Participant characteristics for male and female athletes are presented in Table 1. Female athletes were significantly shorter (t = -9.582, $p = .029$, 164.8 ± 6.7 cm) than male athletes (179.3 ± 9.6 cm), with an average of 4.5 cm (95% CI:-17.51, -11.50) less height. Female athletes also weighed significantly less (t = -9.199, $p < .001$, 65.0 ± 9.2 kg) compared to male athletes (89.2 ± 18.2 kg), with an average of 24.2 kg (95% CI: -29.44, -18.98) less weight. In addition, female athletes' mean body index (BMI) was significantly less (t = -4.707, $p < .001$, 23.9 ± 3.0

kg/m^2) in comparison to male athletes (27.8 ± 5.7 kg/m^2), with an average of 3.89 kg/m^2 (95% CI: -5.53, -2.25). There was no significant difference in age, PCS scores, AFAQ scores, STAI scores, or HR between the sexes. Furthermore, female athletes' baseline SBP was significantly less (t = -7.772; p = .017, 112.3 ± 9.8 mmHg) than male athletes (128.8 ± 13.2 mmHg), with an average of 16.5 mmHg (95% CI: -20.75, -12.32). There was no significant difference in DBP, number of training sessions per week or number of training hours per week between the sexes.

Subjective Pain Ratings

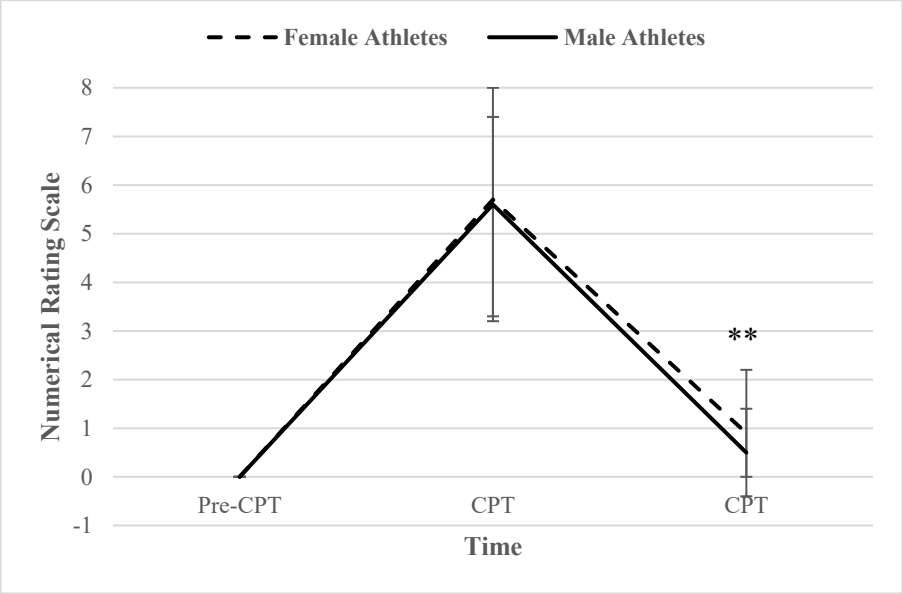

Figure 7 – Subjective pain ratings pre, during, and post-CPT in male and female athletes. For subjective pain ratings, a repeated measure ANOVA revealed a main effect for time; (F(1.453, 171.428) = 729.747, p < .001). No time x sex interaction was observed; F(1.453, 171.428) = .734, p = .441); *Note*. ** = p < .001 difference across all-time points.

The results of the ANOVA for peak pain ratings in male and female athletes are presented in Figure 7. The ANOVA revealed a main effect of time; F(1.453, 171.428) = 729.747, p < .001, reflecting the increase in pain ratings during the CPT (0.0 ± 0.0 to 5.6 ± 2.1), followed by a decrease throughout the post-CPT period (5.6 ± 2.1 to 0.7 ± 1.1). We did not observe a time x sex interaction; F(1.453, 171.428) = .734, p = .441, indicating that pain ratings for males and

females were similar over time ([male athletes]: 0.0 ± 0.0 to 5.6 ± 2.4 to 0.5 ± 0.9 versus [female athletes]: 0.0 ± 0.0 to 5.7 ± 1.7 to 0.9 ± 1.3).

Cardiovascular Measures

Heart Rate

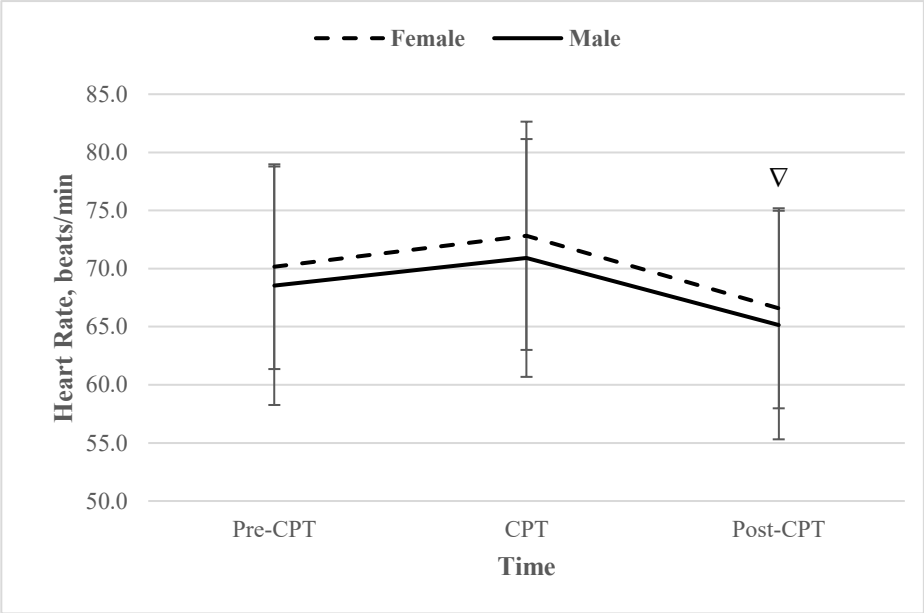

Figure 8 – Average values for HR pre-, during, and post-CPT in male and female athletes. For HR, a repeated measure ANOVA indicated a main effect for time; F(1.525, 179.905) = 85.724, $p < .001$). No time x sex interaction was observed; F(1.525, 179.905) = .134, $p = .818$); *Note*. ∇ = p < .001 difference between each point.

The results of the ANOVA for HR in male and female athletes are presented in Figure 8. The ANOVA indicated a main effect of time; F(1.525, 179.905) = 85.724, $p < .001$, reflecting the increase in HR during CPT (69.3 ± 9.6 to 71.9 ± 10.0 beats/min), followed by a decrease throughout the post-CPT period (71.9 ± 10.0 to 65.9 ± 9.2 beats/min). In addition, the ANOVA did not exhibit a time x sex interaction; F(1.525, 179.905) = .134, $p = .818$, suggesting that HR for males and females were similar over time ([male athletes]: 68.5 ± 10.3 to 70.9 ± 10.2 to 65.1 ± 9.8 versus [female athletes]: 68.5 ± 10.3 to 70.9 ± 10.2 to 65.1 ± 9.8 beats/min).

Systolic Blood Pressure

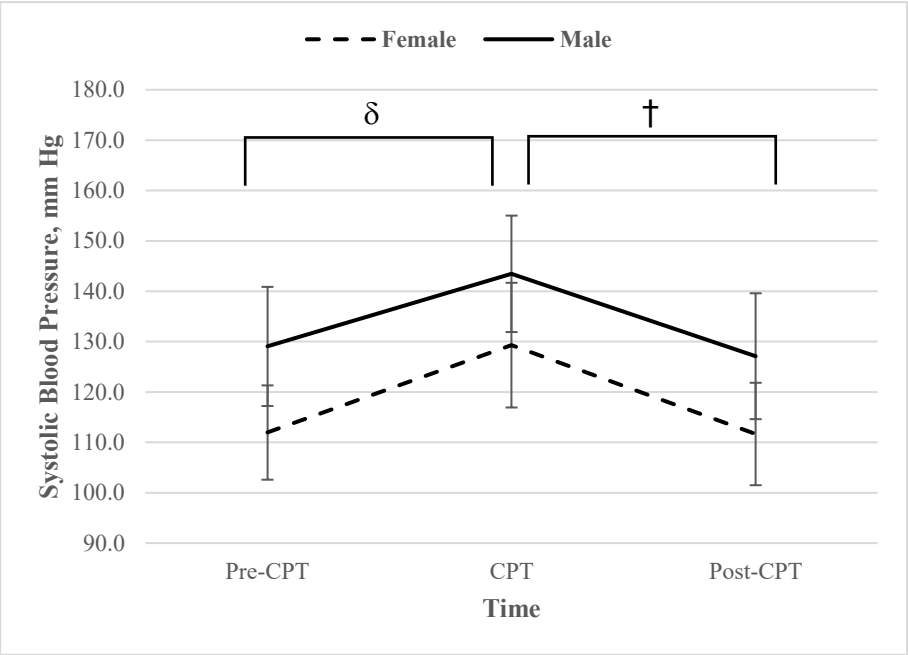

Figure 9 – Average values for SBP pre, during, and post-CPT in male and female athletes. For SBP, a repeated measure ANOVA revealed a main effect for time; F(1.688, 199.141) = 296.478; $p < .001$). No time x sex interaction was observed; F(1.688, 199.141) = 1.768, $p = .179$); *Note*. δ = $p < .001$ difference between pre-CPT and during CPT SBP values; † = $p < .001$ difference between during CPT and post-CPT SBP values.

The results of the ANOVA for SBP in male and female athletes are presented in Figure 9. The ANOVA demonstrated a main effect of time; (F(1.688, 199.141) = 296.478; $p < .001$), reflecting an increase in SBP during the CPT (120.5 ± 13.6 to 136.4 ± 13.9 mmHg), followed by a decrease throughout the CPT period (136.4 ± 13.9 to 119.4 ± 13.7 mm Hg). However, SBP at pre- and post-CPT was not significantly different (120.5 ± 13.6 versus 119.4 ± 13.7 mm Hg, $p = .188$). Moreover, the ANOVA did not detect a time x sex interaction; F(1.688, 199.141) = *1.768,* $p = .179$, suggesting that SBP was similar between sexes ([male athletes]: 129.0 ± 11.8 to 143.5 ± 11.6 to 127.1 ± 12.5 versus [female athletes]: 112.0 ± 9.4 to 126.1 ± 12.4 to 111.7 ± 10.2 mmHg).

Diastolic Blood Pressure

The results of the ANOVA for DBP in male and female athletes are presented in Figure 10. The ANOVA revealed a main effect of time; $F(2, 236) = 263.436$; $p < .001$), showing an increase in DBP during the (69.8 ± 8.6 to 85.6 ± 11.2 mmHg), followed by a significant decrease throughout the post-CPT period (85.6 ± 11.2 to 70.3 ± 11.0 mmHg). However, DBP at pre- and post-CPT was not different (69.8 ± 8.6 versus 70.3 ± 11.0 mmHg, $p = 1.0$). Unlike SBP, we observed a time x sex interaction; $F(2, 236) = 3.709$; $p = .026$. Male athletes exhibited greater DBP reactivity to the CPT relative to female athletes and returned to baseline values ([male athletes]: 72.3 ± 8.9 to 88.6 ± 11.1 to 71.2 ± 9.5 versus [female athletes]: 67.3 ± 7.6 to 82.6 ± 10.5 to 69.3 ± 12.2 mmHg).

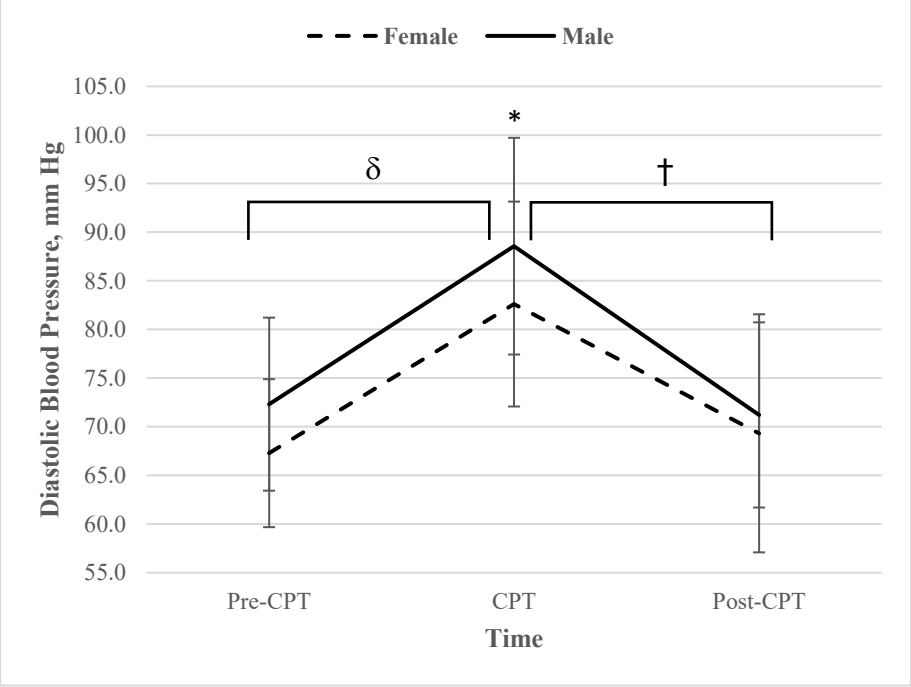

Figure 10 – Average values for DBP pre-, during, and post-CPT in male and female athletes. For DBP, a repeated measure ANOVA indicated a main effect for time; ($F(2, 236) = 263.436$; $p < .001$). Similarly, a time x sex interaction was observed; ($F(2, 236) = 3.709$; $p = .026$). *Note*. δ = $p < .001$ difference between pre-CPT and during CPT SBP values; † = $p < .001$ difference between during CPT and post-CPT SBP values; * = $p < .05$ difference between males and females.

Correlation Analysis

Measures	Pain Catastrophizing Scale	Athlete Fear Avoidance Questionnaire	State-Trait Anxiety Inventory		Cardiovascular Variables			Pain during the CPT
			State	Trait	Heart Rate	Systolic Blood Pressure	Diastolic Blood Pressure	
Pain Catastrophizing Scale	1	.485[b]	.084	.351[b]	-.032	-.031	-.063	.165
Athlete Fear Avoidance Questionnaire		1	.117	.229[a]	.104	.027	.034	.111
State-Trait Anxiety Inventory								
State			1	.121	-.057	.16	.041	.078
Trait				1	.035	-.103	-.071	.135
Cardiovascular Variables								
Heart Rate					1	.078	.129	0.163
Systolic Blood Pressure						1	.784[b]	0.017
Diastolic Blood Pressure							1	0.133
Pain during the CPT								1

Table 2. Correlations among catastrophizing, fear-avoidance, state and trait anxiety, cardiovascular measures, and pain during cold pressor test in athletes.

[a] $p < .05$ correlation

[b] $p < .001$ correlation

The Relationship Between Psychological Factors and Pain During the CPT

We examined the relationship between psychological factors and pain during the CPT (see Table 2). There were no significant correlations between PCS scores (r = .165, p = .071), AFAQ Scores (r = .111, p = .229), and STAI ([State]: r = .078, p = .398; [Trait]: r = .135, p = .142).

The Relationship Between Cardiovascular Measures and Pain During the CPT

We explored the relationship between cardiovascular measures recorded during the CPT and pain during the CPT (Table 2). There were no significant correlations between average HR values (r = .163, p = .075), SBP values (r = .017, p = .853), and DBP values (r = .133, p = .149), with pain during the CPT.

Sex Differences in Pressure Pain Threshold

Figure 11 presents the changes in PPT before and after the CPT in male and female athletes and includes pain ratings across the CPT. As mentioned above, athletes subjective pain ratings increased during the CPT, followed by a decrease throughout the post-CPT period. However, pain ratings were not different between male and female athletes across all time points.

Thenar Eminence

There was a significant increase in female athletes' PPT measures over the thenar eminence (t = -3.019, p = .004, 70.2 ± 24.8 to 74.7 ± 24.3 N), with an increase by 4.5 N (95% CI: -7.54, -3.019). Likewise, there was a significant increase in male athletes' PPT measures over the thenar eminence (t = -5.08, p < .001, 98.0 ± 31.6 to 107.9 ± 35.6 N), with an increase by 9.9 N (95% CI: -13.84, -6.02).

Independent t-tests compared PPT measures over the thenar eminence between male and female athletes (see Figure 12). Male athletes presented greater post-CPT PPT measures (t = -

5.97; p = .033, 107.9 ± 35.6 N) than female athletes (74.7 ± 24.3 N), with an average of 33.2 N (95% CI: -44.17, -22.14). No significant differences were found for pre-CPT PPT measures between the sexes ([male athletes]: 98.0 ± 31.6 versus [female athletes]: 70.2 ± 24.8, p = 0.73) .

Tibialis Anterior

There was a significant increase in female athletes' PPT measures over the tibialis anterior (t = -4.48, p < .001, 94.3 ± 28.6 to 104.5 ± 32.5 N), with an increase by 10.2 N (95% CI: -14.74, -5.64) Males also displayed a significant increase in PPT measures over the tibialis anterior (t = -3.36, p = .001, 127.1 ± 47.0 to 137.8 ± 50.9 N), with an increase by 10.7 (95% CI: -17.05, -4.33).

Independent t-tests compared PPT measures over the tibialis anterior between male and female athletes (see Figure 12). Male athletes exhibited greater pre-CPT PPT measures (t = -4.617; p = .001, 127.1 ± 47.0) than female athletes (94.3 ± 28.6), with an increase of 32.8 N (95% CI: -46.91, -18.79). Furthermore, male athletes had greater post-CPT PPT measures (t = -4.271; p = .003, 137.8 ± 50.9 N) compared to female athletes (104.5 ± 32.5 N), with an increase of 33.3 N (95% CI: -48.78, -17.84).

Sex Differences in CPM

In our study, we calculated the change in PPT to determine the CPM effect in male and female athletes. Male athletes exhibited a significantly greater CPM effect when PPT was measured over the thenar eminence (t = -2.191, p = .039, 9.9 ± 15.1) in comparison to female athletes (4.5 ± 11.6), with an increase by 5.4 N (95% CI: -10.28, -.517). In addition, male athletes also displayed a greater CPM effect when PPT was measured over the tibialis anterior (t = -.128, p = .05, 10.7 ± 24.6) than female athletes (10.2 ± 17.6), with an increase by 0.5 N (95% CI: -8.25, 7.25)

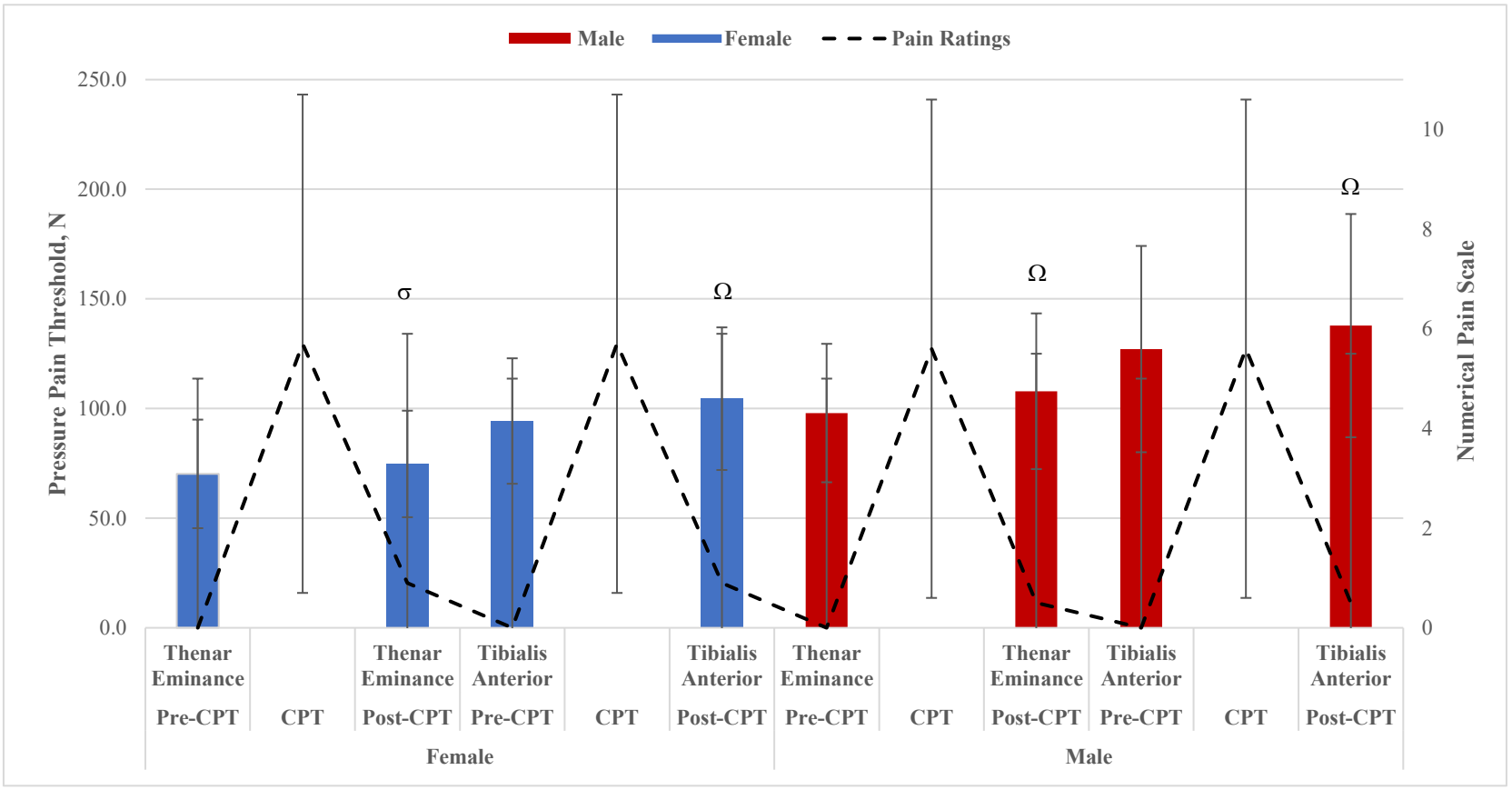

Figure 11 – Subjective pain ratings and PPT pre- to post-CPT in male and female athletes. Peak subjective pain ratings were similar in male and female athletes during the CPT (Figure 7). *However,* PPT measurements over the thenar eminence increased from pre- to post-CPT in male ($t = -5.084$, $p < .001$) and female ($t = -3.019$, $p = .004$) athletes. PPT measurements over the tibialis anterior also increased from pre- to post-CPT in male ($t = -3.36$, $p = .001$) and female ($t = -4.48$, $p < .001$) athletes. *Note*. σ $p < .05$ difference in PPT measures from pre-CPT to post-CPT; Ω $p < .001$ difference in PPT measures from pre-CPT to post-CPT.

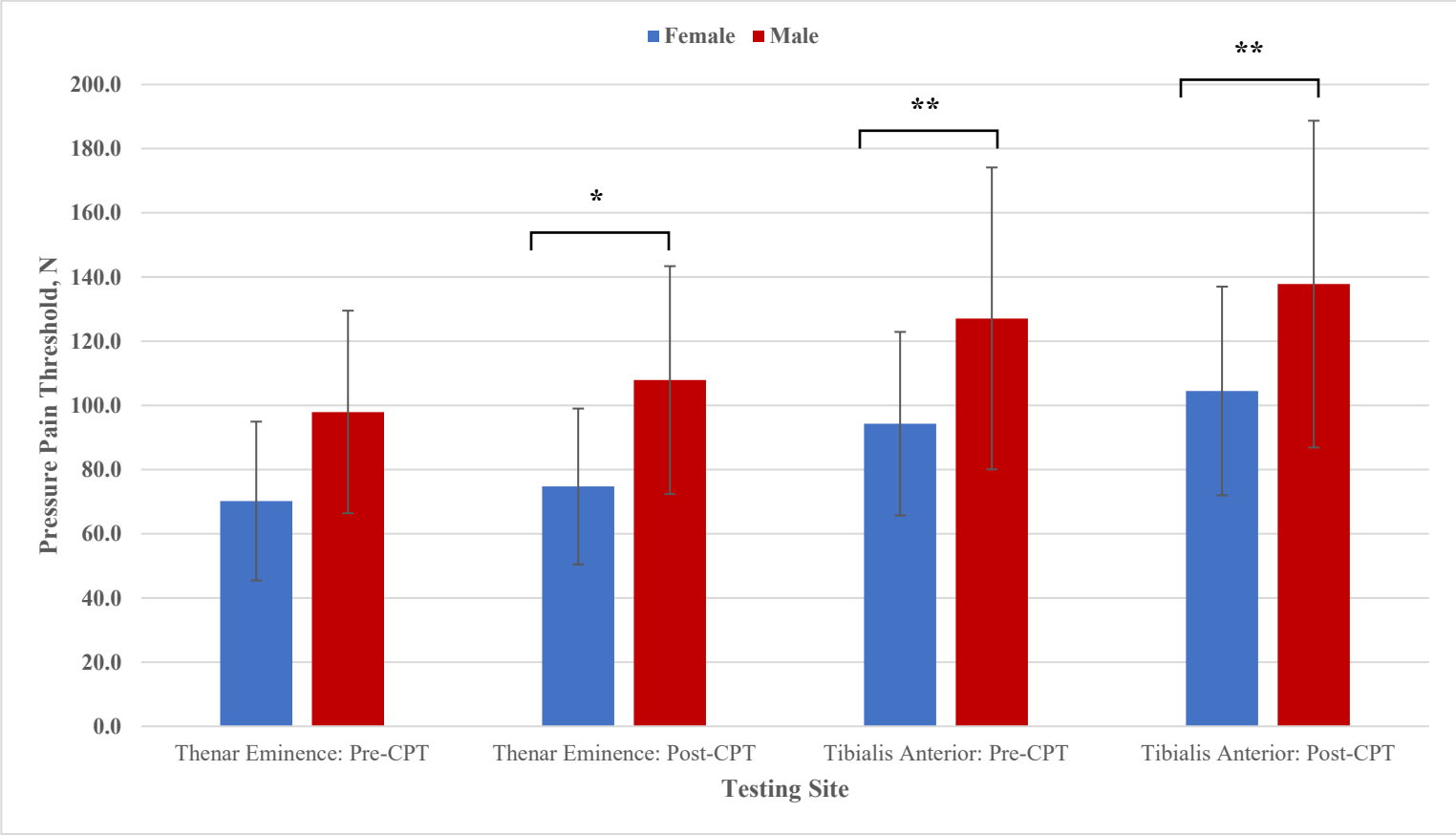

Figure 12. Sex differences for PPT pre- and post-CPT in athletes. PPT measurements over the thenar eminence pre-CPT did not differ between sexes (t = -5.360, p = .073); however, males PPT measurement post-CPT was greater than females (t = -5.97; p = .033). Moreover, males PPT measures was greater at pre-CPT (t = -4.617; p = .001) and post-CPT (t = -4.271; p = .003) in comparison to females. *Note*. * = p < .05 difference between males and females; ** p < .001 difference between males and females.

DISCUSSION

This study aimed to 1) examine and compare the sex differences in athletes pain ratings, PPT, and cardiovascular variables during the CPT, and 2) investigate the relationship between psychological factors with athletes' pain during the CPT and cardiovascular measures. The key finding from this study is that males and females presented increases in PPT measures from pre-CPT to post-CPT, but overall, males had greater PPT measures than females. The CPT caused an increase in subjective pain ratings in males and females; however, the pain experienced was similar between the sexes. Furthermore, results from this study demonstrated that psychological factors did not influence pain experienced during our CPM protocol or influence cardiovascular variables.

It is hard to tell if males and females respond differently to pain. Several reviews have documented sex differences in pain at the clinical and experimental level.[51-55] However, the underlying mechanisms responsible for how males and females perceive and respond to pain still remains unclear. Some suggest that the type of coping strategies people use could explain how males and females perceive and express pain differently.[53,54] Others propose that beliefs on masculinity and femininity can influence pain responses in experimental and clinical settings.[54,56] Biological influences has also been found to impact pain perception,[54] including fluctuations in hormones during the female menstrual cycle or when using contraceptives.[53,57,58] Even though we may never know what causes sex differences in pain perception, women are more often diagnosed with musculoskeletal conditions related to chronic pain,[53,59] and present more psychological distress when confronted with a painful stimulus,[52,60]

In a few studies, investigators have examined sex differences in response to experimental pain in athlete populations. Previously, Manning and Fillingim performed a 1°C CPT in a sample

of 24 (12 female) collegiate-level athletes.[27] Female athletes displayed greater pain ratings during threshold ([female athletes]: 4.56 ± 2.02 versus [male athletes]: 3.79 ± 1.67) and tolerance ([female athlete]: 6.78 ± 1.93 versus [male athletes]: 6.24 ± 2.54) measures compared to male athletes, but the differences were not significant. Although the previous study had large effect sizes for sex differences (threshold, d = .81; tolerance, d = .80), the authors suggest that their results may not have been statistically significant because of their small sample size. Of note, we examined peak pain responses during 3-minute CPT. Peak pain is the most amount of pain the participant experienced during a pre-determined noxious stimulus, which is different from pain tolerance. Like Manning and Fillingim, our male and female athletes presented almost identical peak pain ratings during the CPT and were not statistically different. Other studies have demonstrated similar findings in non-athlete and patient groups.[57,61] Researchers suggest that the inconclusive results may be attributed to poor methodologic design and a lack of power due to insufficient sample sizes.

In agreement with our hypothesis, we also noted our male athletes presented higher PPT measures than females, which is consistent with other research.[16,62] Chesterton et al. showed that females displayed lower PPT measures in the first dorsal interosseous muscle than males, and it was repeatedly maintained within one hour of initial testing.[62] Some suggest that that males have thicker muscle and subcutaneous tissues than females,[16] which could affect the pressure pain detection from the handheld pressure algometer. Another possible explanation could be that males do not want to respond to the pressure pain as quickly as females based on traditional gender expectations that males should be able to endure more pain.[56]

In the last decade, researchers have investigated the differences in CPM between athletes and non-athletes.[28-31] The majority of these studies have included males exclusively, with few

mixing female participants into the groups. For our CPM comparison between males and females, males had a greater change in PPT at the thenar eminence compared to females, but not at the tibialis anterior site. If the change was greater in males at both sites, we could conclude that the CPM was better in male athletes, but this was not what we found. Measuring changes in CPM between groups is challenging due to the various conditioning and test stimuli that previous researchers have chosen to use.[4,5,12,63] A previous systematic review reported CPM responses to be greater in males, but only when reporting changes in pain ratings or pain thresholds.[63] The investigators suggested that CPM responses are dependent on methodological approaches and the modalities used, which has been recommended elsewhere.[4,5,63] Future studies should examine the sex differences in CPM responses in athletes and use reliable pain modalities and methodological approaches when testing CPM.

Psychological factors such as catastrophizing, fear avoidance, and anxiety may explain athletes' perception of experimental pain. Nevertheless, our results indicate no correlation between the aforementioned psychological factors and pain during the CPT. Studies assessing the associations between catastrophizing and pain outcomes are somewhat inconsistent. While evidence on pain catastrophizing demonstrates its robust ability to predict experimental-based pain outcomes (e.g., pain threshold, pain tolerance, and subjective pain ratings) during a CPT, other findings suggest that pain catastrophizing may correlate stronger with qualitative aspects of pain such as clinical outcomes of pain.[34,60,64] For example, in a sample of 59 (24 females) shoulder pain patients, George and Hirsh investigated the relationship between fear of pain and catastrophizing with shoulder pain intensity (measured on the Brief Pain Inventory) and pain intensity (pain ratings, pain threshold, pain tolerance) during a 3-minute CPT (2°C).[64] Results from a multivariate regression model demonstrated that only fear of pain contributed to the

variance in experimental pain sensitivity, whereas sex and pain catastrophizing contributed to variance in clinical pain outcomes. Although our study only investigated healthy uninjured athletes (at the time of testing) and pain during a CPT, the previous study may partly explain why the correlation between PCS scores and pain during the CPT was insignificant.

Contrary to our findings, previous studies have shown significant correlations between catastrophizing and pain during a CPT in athletes. The results from the correlation analysis in these studies should be interpreted carefully as the relationship between catastrophizing and pain during the CPT varied from weak to moderate.[14,23] One consideration could be the timing of when psychological questionnaires are administered to participants. Pain catastrophizing, for example, is often conceptualized as a trait-like variable and may require a prompt, such as the threat of a painful stimulus, for catastrophic behaviour to be initiated.[36] Questionnaires like PCS may require individuals (e.g., our pain-free athletes) to reflect on events that previously happened to activate the full cognitive and affective responses to painful stimuli. Dixon et al. examined PCS scores before and after a CPT in 203 university students (112 females). Instructions were modified when the PCS was re-administered post-CPT so that participants would think about the pain they experienced during the CPT. Results demonstrated that post-CPT PCS scores were positively correlated to pain ratings and negatively correlated to CPT tolerance; however, pre-CPT PCS was not correlated to pain ratings or CPT tolerance.[65] Similarly, our participant's pre-CPT PCS scores were not correlated to pain ratings during the CPT, and perhaps administering the PCS after our CPT would have yielded different results. Another possible reason we did not observe a correlation between PCS scores and pain ratings during the CPT could be that our athletes did not perceive the cold water as a threatening stimulus.

Investigators have previously explored the relationship between pain and PCS sub-scales. In a sample of 54 athletes, Sullivan et al. found that PCS sub-scales such as rumination and helplessness were correlated to pain ratings during a CPT, while magnification was not correlated to pain ratings.[23] Magnification is the tendency to magnify the threat of a potentially noxious stimulus. Perhaps for athletes, the CPT is not as threatening as other experimental pain modalities or pain experienced on the field or court because of their exposure to cold therapy from sport-related injuries (ice water and ice packs are generally used to alleviate pain and inflammation). We asked all participants to report previous experience using ice or full-body cold immersions since studies have shown that whole-body cold immersions can influence a CPT.[66,67] To our knowledge, none of the athletes reported using ice or cold-water immersions regularly around the time of our study; as such, we do not suspect this would affect our results.

We also investigated the relationship between fear avoidance, anxiety, and pain during the CPT. Our athletes' AFAQ score was 23.7 ± 6.6 and was not correlated to pain during the CPT. Our athlete AFAQ score is similar to other varsity athletes with various sporting backgrounds (23.7± 6.98).[47] Fear-avoidance and decreased physical function are often linked in groups of injured athletes.[68] We may not have observed a correlation between our athletes' AFAQ scores and pain during the CPT, possibly due to the nature of the AFAQ. The AFAQ is designed to assess pain-related fear among injured athletes.[47] Questions in this self-assessment tool are positioned in the context of an injury; for example, item 5 states, "I believe my current injury has jeopardized my future athletic abilities."[47] Participants in our study may not have been able to relate to the statements on the AFAQ because all of our participants were injury and pain-free at the time of our study. Regarding anxiety, our athletes' STAI scores were 47.1 ± 4.3 for STAI-S and 46.4 ± 5.5 for STAI-T. Similar to findings by Lentini et al. who reported no

associations between pain during a CPT and STAI-S (46.9 ± 3.2, r = .132, $p > .05$) and STAI-T (46.7 ± 3.1, r = .103, $p > .05$) scores.[14] Anxiety is thought to explain why athletes experience more pain in the face of a noxious stimulus, but results from our study and Lentini and colleagues suggest otherwise.

To the best of our knowledge, this is the first study to examine and compare sex differences and the influence of psychological factors on CPM among a large sample of university athletes. Our study had an equal representation of males and females, unlike other studies that tested CPM in athlete populations, with their samples predominately male participants. However, our study did have some limitations. It was only possible to measure blood pressure every 90 seconds, so we could only get three measurements total during the cold pressor test. Second, we were unable to control for what stage in the menstrual cycle our female participants were in. Some studies have found associations between pain and the different phases of the menstrual cycle, with increased sensitivity to various pain modalities during the luteal phase and increases in CPM analgesia during the ovulatory phase.[57,58] It is hard to track the phases of the menstrual cycle without performing blood draws. We attempted to calculate the different phases of the menstrual cycle that each female athlete was in during testing. We found that 50% of the female cohort reported being on a hormonal contraceptive and reported either irregular periods or not having one at all (e.g., amenorrhea). Symptoms such as amenorrhea is common among female athletes since they typically have low body fat.[69] In some women, their menstrual cycle can be affected when using contraceptives, which has been reported to influence pain perception.[53] The remaining 50% were either not able to provide exact dates of when their period took place or reported irregular periods as well, which made it difficult to pinpoint the exact phase of their menstrual cycle. Therefore, it was hard for us to know if the phase of the

menstrual cycle may have mitigated our female participant's results. Future studies could use blood draws or record basal body temperature measurements to determine the ovulatory phase of the participants. Lastly, the sex of the researchers can influence the pain responses for the participants. Some studies suggest that males are less likely to report pain to female researchers in comparison to male researchers.[70] In our study the two primary researchers were female and we had two male research assistants to help offset this challenge. But the male assistants were not present for every participant.

Conclusion

This study aimed examine and compare sex differences and determine the influence of pain catastrophizing and other psychological factors on CPM in athletes. Although we did not identify a relationship between psychological factors and pain, the key findings from this study were that male and female athletes experience similar levels of pain during a CPT, and that male athletes displayed greater PPT measures pre- and post-CPT compared to female athletes. Future research should use different modalities when measuring the relationship between psychological factors and CPM in athletes as certain pain modalities may be similar to what they are exposed to in their sport. In addition, future studies testing CPM in female athletes should implement rigorous methodological approaches to account for the fluctuation of the menstrual cycle, which could affect their perception of pain.

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APPENDIX

Ψ

PCS-EN

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

Updated 11/11

UNIVERSITÉ Concordia UNIVERSITY

Name: **Sport:** **Date:**

Athletic Fear Avoidance Questionnaire (AFAQ)

Instructions: We are interested in your feelings or thoughts when in pain as a result of a sport injury. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are in pain due to a sports injury.

Rating	1	2	3	4	5
Meaning	Not at all	To a slight degree	To a moderate degree	To a great degree	Completely agree

Statement	Rating
1. I will never be able to play as I did before my injury	
2. I am worried about my role with the team changing	
3. I am worried about what other people will think of me if I don't perform at the same level	
4. I am not sure what my injury is	
5. I believe that my current injury has jeopardized my future athletic abilities	
6. I am not comfortable going back to play until I am 100%	
7. People don't understand how serious my injury is	
8. I don't know if I am ready to play	
9. I worry if I go back to play too soon I will make my injury worse	
10. When my pain is intense, I worry that my injury is a very serious one	

ANNEX 2 -STAI QUESTIONNAIRE

Self-evaluation questionnaire of the "State-Trait Anxiety Inventory – State" (STAI-S)

Name:_____Date:_____Year:_____

INSTRUCTIONS: Some statements that people have used to describe their feelings are given below. Read each statement and then circle the response option to the right to indicate how you feel right now, that is, at this moment. Do not spend too much time on any one statement, but give the answer which seems to describe your present feelings best.

Not at all --------- 1
Somewhat ------- 2
Moderately ------ 3
Very much ------- 4

1. I feel calm	1	2	3	4
2. I feel secure	1	2	3	4
3. I am tense	1	2	3	4
4. I am regretful	1	2	3	4
5. I feel at ease	1	2	3	4
6. I feel upset	1	2	3	4
7. I am currently worried about possible misfortunes	1	2	3	4
8. I feel rested	1	2	3	4
9. I feel anxious	1	2	3	4
10. I feel comfortable	1	2	3	4
11. I feel self-confident	1	2	3	4
12. I feel nervous	1	2	3	4
13. I am jittery	1	2	3	4
14. I feel "high-strung"	1	2	3	4
15. I am relaxed	1	2	3	4
16. I feel content	1	2	3	4
17. I am worried	1	2	3	4
18. I feel overexcited and rattled	1	2	3	4
19. I feel joyful	1	2	3	4
20. I feel fine	1	2	3	4

ANNEX 2 -STAI QUESTIONNAIRE

Self-evaluation questionnaire of the "State-Trait Anxiety Inventory – Trait" (STAI-T)

Name:_____Date:_____Year:_____

INSTRUCTIONS: Some statements that people have used to describe their feelings are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on a single statement, but give the answer that comes closest to how you generally feel.

Almost never ------- 1
Sometimes ---------- 2
Often ---------- 3
Almost always ----- 4

1. I feel fine	1	2	3	4
2. I tire quickly	1	2	3	4
3. I feel like crying	1	2	3	4
4. I wish I could be as happy as others seem to be	1	2	3	4
5. I am losing opportunities because I cannot make decisions fast	1	2	3	4
6. I feel rested	1	2	3	4
7. I am calm	1	2	3	4
8. I feel that difficulties are piling up in such a way that I cannot overcome them	1	2	3	4
9. I worry too much about things that do not really matter	1	2	3	4
10. I am happy	1	2	3	4
11. I am inclined to take things hard	1	2	3	4
12. I lack self-confidence	1	2	3	4
13. I feel secure	1	2	3	4
14. I try to avoid facing a crisis or difficulty	1	2	3	4
15. I feel blue	1	2	3	4
16. I am content	1	2	3	4
17. Some unimportant thoughts run through my mind and bother me	1	2	3	4
18. I take disappointments so keenly that I cannot get them out of my mind	1	2	3	4
19. I am a steady person	1	2	3	4
20. I become tense and upset when I think about my current concerns	1	2	3	4

Introduction:

To ensure the wording is the same for all participants, I will be reading all the instructions to you aloud.

Humans have a natural occurring pain reducing mechanism which can be measured experimentally using a protocol called conditioned pain modulation. Athletes are commonly thought to experience pain differently than non-athletes possibly because they are frequently exposed to painful stimuli through training and competition. Our lab is interested in any factors that can affect conditioned pain modulation in athletes so that we can better understand pain experienced by athletes to improve treatments in the future.

For this study, you will be asked to visit our lab **1** OR**2** time(s) to assess conditioned pain modulation. At the first visit, we will also ask you fill out a series of questionnaires that will assess psychological factors that can influence pain. Then we will measure point tenderness using a pressure measuring device. Then you will complete a cold pressor test which involves you submerging your hand in a cold-water bath. After the cold-water bath, we will re-test the point tenderness. The point tenderness and cold pressor tests will be the only measures repeated in the subsequent visits.

Before we begin, you will need to read the consent form. The consent form contains an in-depth description about the study. If you have any questions while you are reading the document, please do not hesitate to ask. If you choose to consent, we will ask you to sign the document.

PAUSE – GIVE PARTICIPANTS CONSENT FORM

Now that the consent form is signed, we can begin the study with a general health screening document in which you will complete to ensure you are eligible for this study. Answer the questions as best as you can and let us know if you have any questions or need clarifications on a question.

PAUSE – ADMINISTER DEMOGRAPHIC QUESTIONNAIRE

Thank you for completing the eligibility questionnaire. While we go over this document, you will complete the Athlete Fear Avoidance Questionnaire, the State-Trait Anxiety Inventory, and the Pain Catastrophizing Questionnaire. It is important that you answer each question honestly. These questionnaires will be anonymized and sealed in envelopes, so no-one will be able to identify your results. This includes your coaches and athletic staff.

Carefully read the instructions for each questionnaire and pay attention to the scales, as they are unique to each document. If you have any questions, do not hesitate to ask.

HANDOUT QUESTIONNAIRES ONE AT A TIME

Protocol:

To make sure these tests are always performed in the same manner, the instructions will be read to you aloud. If you have not understood the instructions, please feel free to immediately ask for clarification. We cannot discuss the nature of these tests during this current session and the next, but we are happy to share your results with you at the end of the study.

The testing procedure takes 25 minutes. During this time, we will periodically measure your heart rate and blood pressure. Please note that the blood pressure cuff with inflate multiple times throughout the study. We will also ask you to rate any pain in your left and right arm on a scale of 0 to 10 multiple times, with 0 being no pain and 10 being the worst pain imaginable.

PPT (READ AT MINUTE 7):

We will test your ability to feel pressure pain above the muscle. We will press this pressure measuring device against the muscles on your hand and on your shin two times each. Please say 'now' as soon as the sensation of pressure changes towards pain. This is not a test of tolerance, but rather your first sensation of discomfort. This will be done once now and repeated later in the procedure after the CPT. Before we begin, please rate any pain in your left and left shin on a scale of 0 to 10, with 0 being no pain and 10 being the worst pain imaginable.

MEASURE PPT AT MINUTE 8

BRING WATER AT 10 AND EXPLAIN CPT AT 10.5 MINUTES

CPT:

We will soon begin the CPT. Please do not put your hand in the water until I tell you. For this test, we will ask you to submerge your right hand in the water, up to the wrist. Please keep your hand open and avoid touching the walls of the container. I will ask you to rate your pain 3 times during the test, using a scale of 0 to 10 with 0 being no pain and 10 being the worst pain imaginable. Most people can tolerate this test without any problems, but if you wish to stop, you can take your hand out. After the cold pressor test is complete, we will repeat the pressure test. Please leave your left arm in the same position.