Examining Changes in Pain Sensitivity Following 8 Minutes of Cycling at Varying Exercise Intensities

Brandi B. Antonio
University of Central Florida

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EXAMINING CHANGES IN PAIN SENSITIVITY FOLLOWING 8 MINUTES OF CYCLING AT VARYING EXERCISE INTENSITIES

by

BRANDI BURDS ANTONIO
B.A., Wartburg College, 2022

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the School of Kinesiology and Rehabilitation Sciences in the College of Health Professions and Sciences at the University of Central Florida Orlando, Florida

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ABSTRACT

This study assessed the effect of an eight-minute cycling intervention using varying intensities on exercise-induced hypoalgesia (EIH). Generally, current research examines EIH using protocols that last for more than 10 minutes and reach 75% of an individual's VO2 peak. The main objective of this study was to examine the effect of varying intensities on pressure pain threshold (PPT) and heat pain threshold (HPT) at the thigh and forearm, tested pre- and post-cycling intervention.

Healthy male participants (n=16) performed a graded exercise test on a cycle ergometer to establish their peak power output (PPO). In subsequent visits, participants completed five different 8-minute cycling interventions, with intensities randomly assigned to one of three counterbalanced orders. HPT and PPT were applied to the thigh and forearm two times before and after each cycling intervention.

Additionally, there was a notable effect of intensity on PPT in the thigh, with significant changes at intensities of 90% (p = 0.024) and 100% (p = 0.003). In the forearm, repeated measures ANOVA indicated that there was no significant interaction or main effect for intensity and time. Similarly, for HPT, the analysis did not show significant interaction or main effects for both intensity and location.

This study was the first to examine EIH using an 8-minute cycling intervention on a cycling ergometer at individualized intensities. Higher intensity cycling sessions generated EIH locally in the thigh using PPT. This intervention appeared to target the nociceptors activated by mechanical, rather than thermal stimuli, further highlighting the multi-faceted nature of EIH. A
short but high intensity cycling intervention may have clinical relevance, as it can provide an intervention to reduce localized pain immediately after exercise using a pressure pain stimulus.
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LIST OF ABBREVIATIONS

EIH: exercise-induced hypoalgesia

HPT: heat pain threshold

HRR: heart rate reserve

PPT: pressure pain threshold
CHAPTER ONE: INTRODUCTION

Pain perception, a dynamic and multi-faceted process, is altered during and after various forms of exercise (Koltyn, 2002; Tomschi et al., 2023; Vaegter & Jones, 2020). Aerobic, resistance, and isometric exercise consistently produce exercise-induced hypoalgesia (EIH) in healthy individuals, with moderate effects observed during aerobic exercise (Naugle et al., 2012). EIH is an acute reduction in the perception of pain (decreased pain ratings or a lessening of pain sensitivity) after a bout of exercise (Tomschi et al., 2022). The measurement of EIH may involve the application of a noxious stimulus—often a pressure, thermal, or mechanical modality—before and after exercise (Rice et al., 2019).

Understanding and utilizing EIH can result in practical and beneficial applications. It has been estimated that 20% of individuals in the United States experience chronic pain (Rice et al., 2019; Yong et al.) and physical inactivity is a risk factor for pain development (Ray et al., 2023; Sluka et al., 2018). EIH can be induced in as little as one session (Vaegter & Jones, 2020), and populations participating in moderate levels of physical activity have lower levels of musculoskeletal pain (Landmark et al., 2011; Landmark et al., 2013; Sluka et al., 2018). Therefore, physical activity can be recommended as a treatment for various pain conditions (Sluka et al., 2018). Consequently, physical activity and exercise may provide benefits in pain perception.

The reduction in pain caused by EIH stems from mechanisms that affect the central nervous system. Pain perception occurs when peripheral nociceptors, located in the muscle (Stacey, 1969), are activated and begin conduction through the A-delta and C fibers (Markenson, 1996). This signal travels to the dorsal root ganglion of the spinal cord, and then up the
spinothalamic tract to the thalamus (Markenson, 1996). From there, thalamic neurons connect to the somatosensory cortex, signaling the location, intensity, and quality of acute pain (Markenson, 1996).

The most prominent mechanism of EIH is the opioid hypothesis (Rice et al., 2019), which suggests that the activation of the endogenous opioid system leads to EIH by releasing endogenous opioids throughout the body (Koltyn et al., 2014). Specifically, the concentration of beta-endorphins, a type of opioid, has been shown to increase after exercise (Koltyn et al., 2014; Thoren et al., 1990). Beta-endorphins bind to opioid receptors, resulting in the inhibition of tachykinin release, a protein involved in pain transmission (Sprouse-Blum et al., 2010). Similarly, exercise releases endogenous cannabinoids, which affect how the central nervous system processes pain and may result in analgesia (Koltyn et al., 2014). There are several other proposed mechanisms of EIH, including an increase in blood pressure associated with exercise, reduced central nervous system sensitivity, immune system changes, and changes in psychological factors following exercise (Vaegter & Jones, 2020). However, the exact mechanism underlying EIH remains largely unknown (Koltyn et al., 2014; Vaegter & Jones, 2020).

Quantitative sensory testing provides an indirect measure of centrally mediated pain processing, which can provide insight into the analgesic effect of exercise (Baehr et al., 2022). Both the intensity and duration of aerobic exercise should be considered when examining the effectiveness of EIH (Tomschi et al., 2023). It appears that EIH can last up to 30 minutes (Kemppainen, Pertovaara, et al., 1990; Rice et al., 2019; Tomschi et al., 2022), is induced after exercise for at least ten minutes and exceeds 75% of one’s VO2 peak (Naugle et al., 2012; Tomschi et al., 2023). The population performing exercise also affects the EIH response, as
individuals with chronic pain may have a reduced response or experience EIH and an increase in pain following exercise (Vaegter & Jones, 2020). However, in pain-free populations, a dose-response relationship has been proposed to exist between exercise intensity and EIH, implying that as intensity increases, so does the magnitude of EIH (Hoffman et al., 2004; Micalos & Arendt-Nielsen, 2016; Naugle et al., 2012; Tomschi et al., 2022; Vaegter & Jones, 2020). This was determined by Naugle et al. (2012) when examining several studies comparing the pain pressure threshold (PPT) to aerobic exercise intensity. However, because this conclusion was drawn from the results of only four studies, more research must examine the intensity of aerobic exercise and EIH to further build upon this hypothesis (Naugle et al., 2012). There are currently mixed results regarding the prevalence of EIH following aerobic exercise (Tomschi et al., 2022), but these differences may result from the variety of exercise intensities being performed (Tomschi et al., 2023). The ideal intensity for inducing EIH remains unknown (Naugle et al., 2012; Tomschi et al., 2022). Aerobic exercise performed at a moderate to high intensity has been shown to elicit EIH (Vaegter & Jones, 2020). Hoffman et al. (2004) observed this, finding changes in PPT following treadmill running at 75% of VO2 peak for 30 minutes, while no change was observed at 75% of VO2 peak for 10 minutes, or 50% VO2 peak for 30 minutes (Hoffman et al., 2004). Similarly, exercise at 75% of the heart rate reserve (HRR) has been shown to increase PPT, whereas exercise at 50% of HRR caused no changes (Naugle et al., 2014).

EIH has been demonstrated after cycling through increases in pressure pain threshold at the local exercising muscle, the quadricep (Vaegter et al., 2019). However, EIH has also been generated at both local and remote sites in various investigations utilizing aerobic exercise on a cycle ergometer (Vaegter et al., 2018; Vaegter et al., 2014). Furthermore, whether local or remote
exercise-induced hypoalgesia occurs may be related to the intensity of the exercise (Naugle et al., 2014). Results have been equivocal when looking at local or systemic changes in EIH. For example, Jones et al reported an increase in both the thigh and the hand after five minutes of intense cycling, determined by an RPE greater than 17 (Jones, Taylor, et al., 2017). However, this study also utilized blood flow restriction in the thigh. However, Gomolka et al found an increase in thigh PPT after 2 separate 15-minute cycling sessions, and an increase in back PPT after only one of the sessions (Gomolka et al., 2019), perhaps indicating a local EIH response after cycling.

Various studies have examined EIH following exercise using a cycle ergometer. Naugle et al. (2012) observed changes in PPT following cycling for 25 minutes at 70% HRR or 50% HRR; however, the largest changes were seen after the higher intensity. Similarly, in a study by Kodesh et al. (2014), participants cycled at 70% HRR for 30 min or performed intervals of $4 \times 4$ min at 85% HRR with 2 min at 60% HRR. Following both interventions, heat pain threshold increased, yet by a larger magnitude after interval exercise (Kodesh & Weissman-Fogel, 2014). In a study by Tomschi et al. (2023), participants cycled at 75% of the peak power output, but for durations of 30, 45, and 60 min. Despite the differences in duration, none of these sessions elicited a different change in pain sensitivity, leading to the conclusion that intensity may be more important than duration when attempting to induce EIH (Tomschi et al., 2023).

Due to the potential clinical application of EIH (Naugle et al., 2012), it is beneficial to utilize an intervention that is accessible to many different populations, such as cycle ergometry. Currently, research using a cycle ergometer often implements interventions between 25-60 minutes (Kodesh & Weissman-Fogel, 2014; Naugle et al., 2014; Tomschi et al., 2023; Tomschi et al., 2022) at various percentages of VO2 peak or HRR. On the other hand, research that utilizes 8-minute cycling interventions have used a fixed wattage independent of one’s fitness level.
(Kemppainen, Paalasmaa, et al., 1990; Kemppainen et al., 1986; Pertovaara et al., 1984). Thus, it would be beneficial to utilize a shorter and more accessible intervention, in which the intensity is dependent on an individual’s fitness level. In addition, utilizing a shorter, standardized 8-minute cycling session versus longer individualized protocols can increase feasibility and adherence when translating the cycling intervention into various settings and populations. The use of an eight-minute cycling intervention at a prescribed individualized intensity can be useful for different populations and needs to be further understood. Therefore, the objective of this study was to assess how EIH is affected by an eight-minute cycling intervention with varying intensities in healthy men.
CHAPTER TWO: METHODS

Experimental Design

A recent study by Eustis and Henry (Eustis, 2023) examined the effects of PPT testing on the thighs before and after 10 minutes of cycling on an ergometer. The power output during cycling was set at 50% of the VO2 peak, which was the lowest intensity used in the current study. The researchers found a significant increase in PPT (t33 = -4.306, p<0.001) among 34 healthy adults. To determine an appropriate sample size based on the findings of Eustis and Henry, we used the G*Power software. With a desired statistical power of 0.80, a significance level of $\alpha = 0.05$, and an effect size of 0.74, a sample size of 17 participants was determined. Therefore, our study employed an experimental randomized design with recreationally active male participants who regularly participated in aerobic exercise. These participants attended six sessions, each spaced at least 48 h apart.

During the initial session, participants were screened for safety and familiarized with the sensory testing procedures (heat and pressure pain thresholds). This was followed by a graded exercise test using a cycle ergometer to assess VO2 peak and peak power output (PPO). Sessions 2-6 took place at least 48 h apart and involved PPT and HPT tests conducted before and after a cycling session. In each session, participants cycled at 70 revolutions per minute (RPM) at intensities of 50%, 70%, 80%, 90%, or 100% of the PPO achieved during the graded exercise test. To minimize potential order effects, the participants were randomly assigned (using a randomizer program) to one of three counterbalanced condition orders: 1) 50%, 70%, 80%, 90%, and 100%; 2) 100%, 90%, 80%, 70%, and 50%; and 3) 80%, 90%, 50%, 100%, and 70%. Participants were unaware of the order of intensities they received and were blinded to the
intensity during each visit. PPT and HPT tests were conducted before and after each cycling session.

**Participants**

The study recruited healthy male participants aged 18 to 30 years who were physically active and engaged in exercise at least 3-4 times per week. Prior to inclusion in the study, these individuals completed the Physical Activity Readiness Questionnaire (PAR-Q) to ensure suitability for participation. To prevent any potential interference with cycling performance or pain perception, participants were instructed to abstain from intense exercise for 24 h prior to each visit. Additionally, they were asked to maintain a consistent diet and refrain from consuming food or caffeine for three hours prior to each visit. All participants visited at the same time of day for all seven visits. The study protocol was reviewed and approved by the Institutional Review Board at the University of Central Florida. The participants were fully informed about the study procedures and provided informed consent prior to their participation. Various recruitment methods, such as flyers, posters, information sheets, notices, and online advertisements, were employed to recruit participants from the University of Central Florida campus and surrounding areas.

**Measurements**

**Anthropometric Measurements**

Participants’ body weight, height, and body composition were assessed. Height was measured using a stadiometer (Health-o-meter Professional Patient Weighing Scale, Model 500 KL, Pelstar, Alsip, IL, USA), while body composition and weight were determined using bioelectrical impedance analysis device (InBody 770, Biospace Co, Ltd. Seoul, Korea).
Surveys

Physical Activity Readiness Questionnaire (PAR-Q)

The PAR-Q evaluates the presence of risk factors during physical activity and considers the family history and disease severity. A questionnaire was used to determine whether the participants could safely engage in physical activity. If a participant answered affirmatively to any of the questions, they were excluded from the study and advised to consult a physician.

Sensitivity Testing

All the sensitivity tests were performed by the same researcher to avoid inter-rater differences. The participants were familiarized with each test before the actual trial. Furthermore, the assigned counterbalanced order was randomized and not controlled by the researchers. However, the researchers were aware of each participant’s assigned counterbalanced order because they had to input the intensity into the bike and onto the data collection sheet.

Pressure Pain Threshold (PPT)

The participants completed a familiarization trial of the PPT during the first visit, before the VO2 peak test was conducted. The trial test was completed one time, only during the first visit, and the subsequent trials were conducted immediately after. Participants were seated with their thighs supported. A computerized pressure algometer (AlgoMed, Ramat Yishai, Israel) with a rubber tip of diameter 1 cm was applied at a constant rate of 1 kPa/s. For the PPT, participants were instructed to say ‘stop’ or press a button connected to the algometer when the sensation first changed from pressure to pain (pain threshold). The stimulus was then stopped immediately. Participants then rated the pain experienced during threshold testing using the Numeric Pain Rating Scale. This was completed twice for both the dominant forearm, 8 cm from the elbow, and thigh, halfway between the anterior superior iliac spine and patella.
**Heat Pain Threshold (HPT)**

The participants completed a familiarization trial for the HPT before testing during the first visit, before the VO2 peak test was conducted. The trial test was completed one time, and only during the first session; the subsequent trials were conducted immediately after. Participants were provided with a 2 × 1 inch thermode attached to a TCS-II (QST.Lab, Strasbourg, France). The thermode increased from a baseline of 32 °C at a rate of 1 °C/s to a maximum of 50 °C. The participants were instructed to indicate when the sensation first changed from warmth to pain (pain threshold) by pressing a button. Once the button was pressed, the temperature stopped increasing and quickly returned to a baseline temperature of 32 °C. This procedure was completed twice on the dominant forearm (8 cm distal to the elbow crease) and twice on the dominant thigh (halfway between the anterior superior iliac spine (ASIS) and the top of the patella), and the average was taken for both. Each trial was separated by a 1-minute break.

**Determination of VO2peak**

All participants performed a graded exercise test on a cycle ergometer (Lode, Corival cpet, Groningen, The Netherlands) to determine VO2peak and PPO. Before testing, each participant was fitted with a heart rate monitor (chest strap and sensor; Polar H10, Polar Electro Oy, Kempele, Finland) to record their heart rate. The seat height was adjusted for each participant and kept constant at each visit. This was adjusted to allow the participant to maintain a slight bend in the knee when reaching full extension while pedaling. The pedals were also equipped with Velcro straps that were tightened around the participants’ shoes to minimize movement between the shoe and the pedal. Participants completed a five-minute warm-up on a cycle ergometer at a self-selected intensity and cadence. The test consisted of 2-minute stages, beginning at an initial workload of 50 watts (W), then 100 W, followed by an increase of 30 W
every 2 min until the participants could no longer maintain 70 RPM (Beltz et al., 2016; Spriet, 2007). The VO2peak was determined to be the highest value achieved during the last completed stage of the test. Open-circuit spirometry was used to estimate VO2peak with a calibrated metabolic cart (True One 2400® Metabolic Measurement System, Parvo-Medics Inc., Sandy, UT) by sampling and analyzing breath-by-breath expired gases. The metabolic cart software continuously recorded ventilation and expired gases with averages every 15s, calculated VO2, and determined the VO2peak value. The PPO, measured in watts, was the highest power output achieved during the last completed stage.

8-Min Cycling Intensity Protocol

During visits 2-6, the participants were randomly assigned to one of three counterbalanced orders of cycling intensity, as previously described. Each visit was separated by at least 2-3 days (Hoffman et al., 2004; Tomschi et al., 2022). All participants began with a warm-up on a cycle ergometer at a self-selected cadence. The participants then cycled for 8 min at 70 rpm and a power output of 50%, 70%, 80%, 90%, or 100% of the PPO, based on VO2 peak data obtained during visit 1 while pedaling at 70 rpm. Participants also wore a Polar heart rate monitor to record their heart rate. The seat height was adjusted to match the previously recorded height from the graded exercise test during visit one for each participant.

Participants completed PPT and HPT before and after cycling during visits 2-6. This was performed twice, before and after on the dominant forearm and thigh.

Statistical Analyses

Descriptive statistics were computed to determine participant demographics. The data were prepared by initially averaging the threshold tests for the HPT and PPT at each site.
Subsequently, the average values were normalized to the baseline values using percent relative change scores ([\(\text{post} - \text{pre}\) / \(\text{pre}\) \(\times 100\)]) for analysis. The data were subjected to analysis using repeated measures ANOVAs with a 5 (condition: 50\%, 70\%, 80\%, 90\%, 100\%) \(\times\) 2 (site: forearm, thigh) design to ascertain whether the change scores exhibited significant differences between intensities and sites. In addition, a 5 (condition: 50\%, 70\%, 80\%, 90\%, 100\%) \(\times\) 2 (time: Pre, Post) repeated measures ANOVA was conducted to investigate PPT and HPT in the thigh and forearm individually at different intensities. The objective of this analysis was to determine whether the pre- and post-exercise values displayed significant changes at each intensity level for the forearm or thigh. A Type I error rate of less than or equal to 5\% (p\(\leq\)0.05) was regarded as statistically significant for all analyses. If the sphericity assumptions were violated, the Greenhouse-Geiser correction was applied as necessary. For effect size, the partial eta squared (\(\eta^2\)) statistic was calculated according to Green et al (2000). A \(\eta^2\) of 0.01, 0.06, and 0.14 represents small, medium, and large effect sizes, respectively. All models and comparisons were computed using SPSS Statistics (Version 18.0, SPSS Inc., Chicago, Ill, USA) and Microsoft Excel (version 2007, Microsoft Corporation; Microsoft Network, LLC, Richmond, WA, USA).
CHAPTER THREE: RESULTS

Description of Participants

The descriptive statistics of the participants are presented in Table 1. Sixteen participants successfully completed all sessions and were included in the subsequent statistical analysis. Of the 21 participants recruited, five were unable to schedule all 7 visits required to complete the study. Notably, eight participants successfully completed the 8-minute cycling session at 100% intensity level. The average completion time of this session was 6.5 minutes. Kemppainen et al. used a similar workload duration of 8-10 minutes, but at a consistent workload for each participant (100, 200, 250, 300 W). However, they set the pedal frequency to 50 RPM, whereas our current protocol utilized a pedal frequency of 70 RPM. This disparity in pedal frequency could potentially account for the observed discrepancy in cycling time between our study and the findings of Kemppainen et al (1990).

Pressure Pain Threshold Results

The PPT data, including the means and standard deviations, are presented in Table 2. A 5 × 2 repeated measures ANOVA was conducted to analyze the PPT at five levels of intensity (50, 70, 80, 90, and 100) and two locations (thigh and forearm). Sphericity was confirmed using Mauchly's test (p = 0.778). The results indicated no significant interaction (F(3.286, 49.291) = 1.296, p = 0.282, partial η² = 0.080) or main effect for intensity (F(3.549, 53.229) = 2.286, p = 0.079, partial η² = 0.132). However, the main effect of location was statistically significant (F(1,15) = 6.125, p = 0.026, partial η² = 0.290). Bonferroni-corrected post hoc tests revealed significant mean differences in the PPT between the thigh and forearm at 100% (p = 0.018) and 90% (p = 0.024) intensity levels, as depicted in Figure 2.
A separate intensity-by-time repeated measures ANOVA was conducted specifically for thigh PPT at different intensities, supporting the assumption of sphericity (p = 0.07). There was a significant effect of intensity (F(4, 60) = 3.676, p = 0.010, partial η² = 0.197), with Bonferroni post hoc tests indicating significant changes in PPT at intensities of 90% (p = 0.024) and 100% (p = 0.003). In contrast, for the location of the forearm, repeated measures ANOVA revealed no significant interaction (F(4, 60) = 0.317, p = 0.866, partial η² = 0.021), or main effects for "intensity" (p = 0.082) and "time" (p = 0.085).

**Heat Pain Threshold Results**

The means and standard deviations of HPT are shown in Table 3. A repeated measures ANOVA was conducted on the HPT data to examine the interaction between intensity and location. The assumption of sphericity was confirmed (p = 0.102); however, the analysis revealed no significant interaction (F(4,60) = 1.972, p = 0.110, partial η² = 0.116), no significant main effect for intensity (F(4, 60) = 0.354, p = 0.851, partial η² = 0.023), and no main effect for location (F(1, 15) = 2.121, p = 0.166, partial η² = 0.124).
CHAPTER FOUR: DISCUSSION

The main objective of this study was to examine the impact of an 8-minute cycling intervention on exercise-induced hypoalgesia (EIH) in healthy men, focusing specifically on the thigh (local) and forearm (remote). The cycling intervention varied in intensity, ranging from 50% to 100% of each participant's peak power output, as established by the graded exercise VO\textsubscript{2} peak test (range: 75–320 W). The results indicated a significant difference in pressure pain threshold (PPT) between the thigh and forearm (Figure 2), which is consistent with prior research (Micalos & Arendt-Nielsen, 2016). Furthermore, PPT in the thigh demonstrated an increase after 90% and 100% PPO cycling sessions (Figure 3), thereby illustrating a dose-response relationship between exercise intensity and EIH (Naugle et al., 2012; Tomschi et al., 2022; Vaegter & Jones, 2020). No significant effects on the heat pain threshold were observed after any of the cycling intensities, which corroborates with the existing literature (Jones et al., 2019).

Local Increases in PPT

As mentioned above, PPT increased locally following higher-intensity cycling. Similarly, in their study using isometric exercise, Mais et al. observed an increase in PPT at local muscle sites, whereas no such increase was observed at remote sites (2023). Belavy et al. further supported this phenomenon through a comprehensive review, suggesting that exercises targeting local sites are more effective in reducing pain, quantified by measuring pain sensitivity with a pressure algometer, than those targeting remote sites (2021).

Similarly, Gomolka et al. assessed PPT after two separate 15-minute cycling sessions in 30 healthy adults and observed a significant increase in PPT at the thigh in both sessions and at
the back in one session, which may suggest that local, rather than remote, PPT is elicited after cycling (2019). Likewise, Vaegter et al. discovered that after 15 minutes of cycling at lactate threshold, PPT of the thigh significantly increased locally in 34 healthy subjects (average age: 25.3 years), but it did not increase remotely in the trapezius (2019). All these similar findings to the current study suggest localized EIH in the thigh following various cycling interventions in similar populations to that of the present study, although none were as short as the 8-minute intervention used in this investigation.

**Local and Systemic Increases in PPT**

In contrast to our results and the findings of the studies described previously, some investigations have reported both local and systemic increases in pressure pain threshold. Jones et al. found a significant increase in PPT in both legs and arms after 5 minutes of high intensity (RPE greater than 17) cycling in 36 healthy participants (mean age of 22.1 years). PPT was applied to the rectus femoris for the leg site, and on the first dorsal interosseous muscles of both the arms. However, this study utilized blood flow restriction (BFR) applied peripherally to one arm, perhaps accounting for the difference in PPT at remote exercise sites (Jones, Taylor, et al., 2017). Furthermore, these participants were described as undergraduate students who did not regularly participate in moderate- or high-intensity exercise. In our investigation, inclusion criteria required participants to regularly engage in exercise. Considering the discrepancies in PPT results between the two studies, differences in methods (use or no use of BFR) and population (active vs. inactive populations) may affect the presence of EIH. Therefore, the results of the current study may only be applicable to our specific population, healthy, college-aged men, and our intervention, eight minutes of cycling at various intensities.
In another investigation by Niwa et al, the researchers found an increase in PPT at all assessment sites after exercise (2022). This study examined different intensities of aerobic exercise (using a stationary cycle ergometer) and their effects on exercise-induced hypoalgesia, albeit the exercise was longer in duration (30 minutes) than our current investigation. Intensities included 30% HRR, 50% HRR, and 70% HRR. Additionally, while an increase in PPT occurred at all sites after exercise, a dose-response relationship still existed; higher-intensity exercise elicited a greater magnitude of EIH (Niwa et al., 2022). The effective lower-intensity exercise in this study may be due to the longer duration of the protocol, compared to the current study which used an eight-minute protocol.

**Intensity and PPT**

As mentioned above, the current research study utilized a short, eight-minute cycling intervention with various intensities, and hypoalgesia was found after the higher-intensity bouts. Albeit using a longer investigation than our current one, Koltyn et al. utilized a thirty-minute cycling intervention at 75% of the participants’ VO2 max, and pressure pain threshold was significantly higher after the exercise condition (1996). Additionally, Hoffman et al. had participants perform treadmill exercise for 10 minutes (75% VO2 max) and 30 minutes (50% and 75% VO2 max) (2004). They assessed hypoalgesia through pressure pain threshold ratings after completing the exercise bouts. Ultimately, they discovered that pain ratings decreased after the 30 minute session at 75% of VO2 max, but not after any of the other sessions. These results, in addition to our findings, may indicate that both intensity and duration play pivotal roles when attempting to elicit exercise-induced hypoalgesia.

In contrast to our findings, van Weerdenburg et al. conducted a study involving three interventions: 20 min of aerobic cycling, 12 min of isometric knee extension, or a deep breathing
exercise. They observed no hypoalgesic effect in the 15 healthy participants who performed either aerobic or isometric exercises (van Weerdenburg et al., 2016). Unlike our current investigation, their study determined the intensity of cycling based on age-predicted maximum heart rate, rather than using a set wattage or intensity on the cycle ergometer. Furthermore, they tested pain via visceral stimulation, pressure algometry, and conditioned pain modulation. No hypoalgesia was present after the visceral or pressure modalities (van Weerdenburg et al., 2016). Interestingly, the set cycling intensity in their study corresponded to 60-80% of the participants' VO2 max, which is lower than the intensity (90-100%) we found in our study to induce EIH.

**Lack of Findings in Heat Pain Threshold**

The absence of significant impacts on HPT in the current study is consistent with the results reported by Jones et al. In their study, they observed an increase in PPT after exercise (either 15 minutes of cycling at 60-70% HRR or a comparable 'light activity'), while HPT was not affected (Jones et al., 2019). In another investigation by Black et al., it was observed that the pressure pain threshold increased after 10 and 15 minutes of cycling, while the HPT only increased after the 15-minute exercise session and not the shorter, more intense session (2016). Additionally, this study sought to investigate the effects of caffeine ingestion on EIH. However, their results indicated that caffeine did not alter EIH after cycling (Black et al., 2016).

Similarly, Ruble et al. found no significant changes in thermal sensitivity or pain thresholds after 30 minutes of aerobic exercise on the treadmill performed at 75% of VO2 max (2005). One important factor that may influence the EIH response to both pressure pain and heat pain is the duration and area of the stimulus application, as both can affect sensitivity and pain thresholds (Graven-Nielsen et al., 2015; Yarnitsky & Ochoa, 1990). Jones' study and the present research used similar stimulus application durations, approximately 6-10 seconds (2019). Albeit
only in heat pain threshold, Yarnitsky et al discovered that pain threshold decreased as the rate of
the temperature rise increased (1990). Therefore, it would be important to note the duration of
the heat stimulus application in any investigation.

Vaegter et al. found that submaximal isometric exercise increased tolerance to pressure
pain but did not affect the pressure pain threshold or the heat pain threshold (2017). However,
Vaegter's study used computer-controlled cuff algometry to test pressure pain, whereas our study
used a handheld pressure algometer. The use of cuff algometry targets a larger range of skin
tissue and may induce ischemic pain, potentially leading to different results in different studies
(Jones et al., 2019).

Results may have differed between the pressure and heat stimuli due to the two types of
nociceptors, A-delta and C fibers, activated by the exercise intervention. While both A-delta and
C-fibers detect mechanical and heat sensitivity, they both have different thresholds required for
nociception (Dubin & Patapoutian, 2010). In a review published by Dubin and Patapoutian, they
concluded that C-fibers detect heat between 39 degrees and 51 degrees Celsius, while A-fiber
nociceptors detect heat from 43 to 47 degrees Celsius (2010). Therefore, the heat pain may have
been predominately dominated by C-fibers, rather than A-fibers. Both A-delta and C-fibers are
activated by muscle contractions in exercise, albeit perhaps in different ratios.

Additional Factors Affecting EIH

Additional influences on EIH following exercise may result from participants’ education
regarding the topic itself. For example, in an investigation by Jones et al., 20 participants
received education about EIH or general education about exercise and pain, and then the PPT
was measured before and after 20 minutes of cycling (2017). PPT showed a greater increase in
the intervention group (EIH education), which may indicate that participants’ previous
knowledge and expectations can affect the results of EIH investigations. This relates to the current study, as participants may have been affected by their previous knowledge of the topic. As the study drew from various populations, some may have already had background knowledge about EIH.

Naugle et al. conducted a study and found that younger adults experience more EIH compared to older adults, in which their average age was 63.7 years (2016). The average age of young adults in the study was 21.7 years, which is very similar to our mean age of 22 years. Therefore, our research agrees with Naugle’s investigation, and perhaps may be one of the reasons why EIH was generated in our population after certain intensities. In addition, the age of the participants in Nguy’s investigation, which was described above, may have affected their EIH response to the various forms of exercise (2019).

Limitations

The limitations of this current investigation are multi-faceted. First, the sample size and the demographics of the participants could be a limiting factor. For example, the sample was restricted to healthy, young men (mean age of 22 years old) between the ages of 18 and 45 years. Therefore, the results of the study may not be applicable to a broader population, such as an elderly population or a female population. Furthermore, the varied fitness level of participants (average VO2 peak value of 38.1 mL/kg/min; range of 27.6-51.5) could have elicited different responses to the different cycling intensities. While all pain testing was conducted by one researcher, blinding was not done. Therefore, the researcher was aware of each cycling intensity during the visits. Factors such as sleep and daily nutrition were also not accounted for in this study, which could influence how the participants felt each visit.
Conclusion

The current study is the first to investigate the effect of an 8-minute cycling intervention on PPT and HPT. The cycling intervention utilized the following intensities in a counterbalanced order: 50, 70, 80, 90, 100% PPO. Significant mean differences were found between the forearm and thigh for PPT at 90% and 100% PPO, as well as for the pre- and post-thigh PPT values at the same intensities. In contrast, for the location of the forearm, repeated measures ANOVA revealed no significant interaction or main effects for intensity or time. For the heat pain test, analysis revealed no significant interaction, no significant main effect for intensity, and no main effect for location. Thus, this study highlighted the importance of intensity (90-100% PPO) on EIH, especially when utilizing a short, eight-minute cycling protocol. Additionally, it may indicate that this intervention targeted nociceptors that are activated by mechanical stimuli, rather than thermal stimuli, which emphasizes the multifarious nature of EIH. Further research should seek to investigate this protocol utilizing different populations, or perhaps using a different mode of aerobic exercise, such as a treadmill.
Figure 1: Timeline of Procedures

Visit 1
- Consent/ PAR-Q
- Sensory Familiarization and Testing
- Graded Exercise Test on Cycle Ergometer

Visits 2-6 (2-3 days between visits)
- Heat Pain and Pressure Pain Threshold Testing
- 8 minutes of cycling at either 50, 70, 80, 90, or 100% PPO (randomized, counterbalanced order)
- Heat Pain and Pressure Pain Threshold Testing Repeated
Figure 2: Percent change values in pressure pain threshold (PPT) at thigh and forearm sites for each cycling intensity (50, 70, 80, 90, and 100 of peak power output).
Figure 3: pre-and post- pressure pain threshold (PPT) values for the thigh site at each intensity.
Table 1: Participant Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>22 (2.2)</td>
<td>18-27</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>177.4 (6.2)</td>
<td>166.5-188.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.0 (6.7)</td>
<td>65.7-87.1</td>
</tr>
<tr>
<td>Skeletal Muscle Mass (kg)</td>
<td>37.3 (4.1)</td>
<td>30.4-43.5</td>
</tr>
<tr>
<td>% Fat</td>
<td>13.5 (5.3)</td>
<td>3-23.8</td>
</tr>
<tr>
<td>VO2 peak (mL/min/kg)</td>
<td>38.1 (7.0)</td>
<td>27.6-51.5</td>
</tr>
<tr>
<td>50% Power Output (W)</td>
<td>105.8 (21.3)</td>
<td>85-160</td>
</tr>
<tr>
<td>70% Power Output (W)</td>
<td>148.2 (29.8)</td>
<td>119-224</td>
</tr>
<tr>
<td>80% Power Output (W)</td>
<td>169.3 (34.0)</td>
<td>136-256</td>
</tr>
<tr>
<td>90% Power Output (W)</td>
<td>190.5 (38.3)</td>
<td>153-288</td>
</tr>
<tr>
<td>100% Power Output (W)</td>
<td>211.7 (42.5)</td>
<td>170-320</td>
</tr>
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</table>
Table 2: PPT Values Measured Pre and Post Exercise at Each Exercise Intensity for the Thigh and Forearm

<table>
<thead>
<tr>
<th></th>
<th>% peak power output</th>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thigh (kPa)</td>
<td>50</td>
<td>pre</td>
<td>688.7 (218.5)</td>
<td>374.4-1037.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>699.2 (227.7)</td>
<td>346.9-1154.9</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>pre</td>
<td>668.1 (155.9)</td>
<td>451.3-882.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>654.9 (202.8)</td>
<td>365.9-1071.2</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>pre</td>
<td>683.2 (215.6)</td>
<td>369.5-1171.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>712.1 (237.5)</td>
<td>389.1-1258.4</td>
</tr>
<tr>
<td></td>
<td>90</td>
<td>pre</td>
<td>643.9 (190.4)</td>
<td>382.7-1067.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>721.8 (185.9)</td>
<td>396.4-1042.2</td>
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<tr>
<td></td>
<td>100</td>
<td>pre</td>
<td>667.4 (145.8)</td>
<td>414.6-953.1</td>
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<tr>
<td></td>
<td></td>
<td>post</td>
<td>798.5 (260.2)</td>
<td>481.9-1500</td>
</tr>
<tr>
<td>Forearm (kPa)</td>
<td>50</td>
<td>pre</td>
<td>564.9 (238.0)</td>
<td>276.9-994.3</td>
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<tr>
<td></td>
<td></td>
<td>post</td>
<td>534.7 (189.4)</td>
<td>224.5-820.3</td>
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<tr>
<td></td>
<td>70</td>
<td>pre</td>
<td>541.5 (175.9)</td>
<td>285.7-872.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>515.7 (150.7)</td>
<td>309.2-768.3</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>pre</td>
<td>573.2 (175.6)</td>
<td>333.2-851.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>522.1 (156.4)</td>
<td>306.7-864.4</td>
</tr>
<tr>
<td></td>
<td>90</td>
<td>pre</td>
<td>606.2 (217.0)</td>
<td>256.3-1067.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>575.7 (169.6)</td>
<td>336.2-843.8</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>pre</td>
<td>566.3 (159.9)</td>
<td>305.3-808</td>
</tr>
<tr>
<td></td>
<td></td>
<td>post</td>
<td>553.2 (140.1)</td>
<td>309.2-762.5</td>
</tr>
</tbody>
</table>
Table 3: HPT Values Measured Pre and Post Exercise at Each Exercise Intensity for the Thigh and Forearm

<table>
<thead>
<tr>
<th>% VO2 peak power</th>
<th>Variable</th>
<th>Mean (SD)</th>
<th>Range</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thigh (℃)</td>
</tr>
<tr>
<td>50</td>
<td>pre</td>
<td>44.71 (2.06)</td>
<td>38.85-46.9</td>
</tr>
<tr>
<td></td>
<td>post</td>
<td>45.28 (0.99)</td>
<td>43.05-46.75</td>
</tr>
<tr>
<td>70</td>
<td>pre</td>
<td>45.18 (1.42)</td>
<td>40.95-47.4</td>
</tr>
<tr>
<td></td>
<td>post</td>
<td>45.24 (1.16)</td>
<td>41.55-46.45</td>
</tr>
<tr>
<td>80</td>
<td>pre</td>
<td>44.79 (1.72)</td>
<td>41.55-47.45</td>
</tr>
<tr>
<td></td>
<td>post</td>
<td>44.56 (0.84)</td>
<td>43.15-46.2</td>
</tr>
<tr>
<td>90</td>
<td>pre</td>
<td>45.05 (1.44)</td>
<td>43.1-47.8</td>
</tr>
<tr>
<td></td>
<td>post</td>
<td>44.89 (1.16)</td>
<td>42.7-46.5</td>
</tr>
<tr>
<td>100</td>
<td>pre</td>
<td>45.07 (1.33)</td>
<td>42-27.35</td>
</tr>
<tr>
<td></td>
<td>post</td>
<td>45.27 (1.46)</td>
<td>42.2-47.6</td>
</tr>
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</table>
March 20, 2023

Dear Brandi Antonio:

On 3/20/2023, the IRB reviewed the following submission:

<table>
<thead>
<tr>
<th>Type of Review</th>
<th>Initial Study</th>
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<tr>
<td>Title</td>
<td>A Proposed Test for Determining Physical Working Capacity at Pain Threshold Using Cycle Ergometry, and its Relationship to Other Physiological and Pain Threshold Measures</td>
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<tr>
<td>Investigator</td>
<td>Brandi Antonio</td>
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<tr>
<td>IRB ID</td>
<td>STU0706095107</td>
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<tr>
<td>Funding</td>
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Documents Reviewed:
- HRP-251- FORM - Faculty Advisor Scientific-Scholarly Review Attable form (1).pdf, Category: Faculty Research Approval
- Consent PWCT updated, Category: Consent Form
- FPQ-9 Questionnaire (1).docx, Category: Survey / Questionnaire
- Heat pain test.docx, Category: Other
- Heat pain tolerance instructions.docx, Category: Other
- Pain Grid Diagram.doc, Category: Other
- Pain Intensity Scale.docx, Category: Other
- Pain Scales.docx, Category: Other
- Pain-catastrophizing scale-questionnaire (1).pdf, Category: Survey / Questionnaire
- PSQI+.pdf, Category: Survey / Questionnaire
- PFSQ(10).pdf, Category: Survey / Questionnaire
- PRECTM.xls (1), Category: Survey / Questionnaire
- Pressure Pain Threshold.docx, Category: Other
- PWCT Flyer (1).pdf, Category: Recruitment Materials
- State-Trait-Anxiety-Inventory Survey.pdf, Category: Survey / Questionnaire
- Study 5107 Conditioned Pain Modulation Updated, Category: Other
The IRB approved the protocol on 3/20/2023.

In conducting this protocol, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system. Guidance on submitting Modifications and a Continuing Review or Administrative Check-in is detailed in the manual. If continuing review is required and approval is not granted before the expiration date, approval of this protocol expires on that date.

Use of the stamped version of the consent form is required. To document consent, use the consent documents that were approved and stamped by the IRB. Go to the Documents tab to download them.

When you have completed your research, please submit a Study Closure request so that IRB records will be accurate.

If you have any questions, please contact the UCF IRB at 407-623-2901 or irb@ucf.edu. Please include your project title and IRB number in all correspondence with this office.

Sincerely,

Kristin Roditi
Designated Reviewer
LIST OF REFERENCES

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https://doi.org/10.1016/j.neubiorev.2020.11.012


https://digitalcommons.wku.edu/ijesab/vol8/iss11/33


Jones, M. D., Valenzuela, T., Booth, J., Taylor, J. L., & Barry, B. K. (2017). Explicit Education About Exercise-Induced Hypoalgesia Influences Pain Responses to Acute Exercise in Healthy Adults: A Randomized Controlled Trial. (1528-8447 (Electronic)).


Naugle, K. M., Naugle, K. E., & Riley, J. L., 3rd. (2016). Reduced Modulation of Pain in Older Adults After Isometric and Aerobic Exercise. (1528-8447 (Electronic)).


https://doi.org/10.1002/ejp.901

https://doi.org/10.1097/PR9.0000000000000823

