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# The effects of caffeine ingestion on exercise-induced hypoalgesia: A pilot study

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## HIGHLIGHTS

- Exercise resulted in exercise-induced hypoalgesia to pressure and thermal stimuli.
- Ingestion of a 5 mg·kg$^{-1}$ dose of caffeine did not alter the hypoalgesic response.
- Caffeine ingestion did not alter "resting" pain sensitivity.

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## ABSTRACT

Exercise acutely reduces pain sensitivity, termed exercise-induced hypoalgesia (EIH). The mechanisms underlying EIH remain unclear. Caffeine, a non-specific adenosine receptor antagonist has been shown to attenuate EIH in animals—suggesting the involvement of the adenosinergic system. This pilot study investigated the effects of caffeine on pain sensitivity following cycling exercise in college-aged men. Pressure pain threshold (PPT) and thermal pain threshold (TPT) were assessed in thirteen low caffeine consuming men prior to ingestion of a counter-balanced 5 mg·kg$^{-1}$ dose of caffeine or a placebo (Pre), 60 min following ingestion (Post-In), and then following a 15 min bout of cycling exercise (Post-Ex) at an intensity eliciting a quadriceps muscle pain rating of 3 out of 10. Nine of the men completed follow-up testing which was identical except that the exercise consisted of 10 min of cycling eliciting a pain rating of 5 out of 10. Caffeine had no effect compared to placebo on PPT ($p \geq 0.15$) or TPT ($p \geq 0.41$) 60 min following ingestion and following exercise. PPT increased from 599 ± 176 kPa to 648 ± 202 kPa ($p = 0.009$) and from 578 ± 217 kPa to 666 ± 278 kPa ($p = 0.01$) following 15 and 10 min of cycling, respectively. TPT increased from 46.2 ± 2.9 °C to 46.8 ± 2.6 °C ($p = 0.008$) following the 15 min exercise bout, but did not change (46.4 ± 3.6 °C vs. 46.8 ± 3.3 °C; $p = 0.24$) following the shorter, higher intensity exercise bout. The results from this study indicate cycling exercise reduces pain sensitivity, especially to pressure stimuli. Caffeine ingestion did not alter the EIH response—suggesting adenosine may not play a prominent role in the EIH response in humans.



## 1. Introduction

Acute bouts of aerobic and resistance exercise have been shown to activate endogenous pain inhibitory systems and reduce pain sensitivity to noxious pressure, heat, and electrical stimuli (see for review [1–3]). This phenomenon is termed exercise-induced hypoalgesia (EIH). EIH remains mechanistically unresolved with evidence supporting generalized pain inhibition via the release of endogenous opioids [1,4] and endocannabinoids [5], elevations in blood pressure [6], and conditioned pain modulation (CPM) [7–9] as well as localized activation of afferent Aδ and C-fibers [10,11] in the contracting muscle(s). Recent findings [12] from an animal model of neuropathic pain have also implicated the adenosine system in reduced pain sensitivity following exercise. ATP and its metabolites ADP, AMP, and adenosine produce both anti- and pro-nociceptive actions primarily dependent on the receptor ($A_1$, $A_{2A}$, $A_{2B}$, or $A_3$) to which it binds [13]. Adenosine's anti-nociceptive actions following exercise appear to be through interactions with $A_1$ and $A_{2A}$ receptors [12]. Similarly, activation of adenosine receptors has been shown to play a role in the endogenous pain inhibitory effects following acupuncture [14,15], transcutaneous electrical nerve stimulation (TENS) [16], and vibration [17].

Caffeine is one of the most ubiquitously consumed (in foods and beverages) substances in the world with daily consumption ranging from ~170 to 220 mg·day$^{-1}$ in North America to ~400 mg·day$^{-1}$ in Scandinavian countries [18]. Caffeine is a non-specific adenosine receptor antagonist with similar affinity for all receptor types [19]. It has intrinsic (typically at very high doses; ≥25 mg·kg$^{-1}$ of body weight which would equate to ~2000 mg in a 70 kg adult male) anti-nociceptive actions [20] likely due to antagonism of $A_{2A}$ and $A_{2B}$ receptors. At lower

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doses (5–10 mg·kg$^{-1}$) caffeine ingestion has been shown to reduce muscle pain during exercise [21,22]. Additionally, caffeine has been shown to function as an adjuvant analgesic (at doses of ≥100 mg) when administered in combination with several common pain medications such as acetaminophen, aspirin, and ibuprofen [23]. Conversely, larger doses in the range of 3–10 mg·kg$^{-1}$ (~200–700 mg in a 70 kg adult male) have been shown to inhibit the anti-nociceptive effects of drugs such as acetaminophen [24], tramadol [25], and gabapentin [26]—likely due to antagonism of $A_1$ receptors. Moderate doses of caffeine have been shown to attenuate endogenous pain inhibition from acupuncture [15], TENS [16], and vibration [17], but to our knowledge its effects on EIH have not been tested. Thus, the purpose of this pilot study was to examine the effects of a moderate (5 mg·kg$^{-1}$) dose of caffeine on pressure and thermal pain thresholds following cycling exercise at moderate and heavy intensities. It was hypothesized caffeine ingestion would attenuate EIH compared to ingestion of a placebo.

## 2. Materials and methods

### 2.1. Participants

Participants were recruited as part of a larger study [27] aimed at determining the effects of caffeine ingestion not only on endogenous pain inhibition following exercise, but also on cycling exercise performance when exercise intensity was determined based upon ratings of muscle pain during exercise. Sixteen men (aged 22 ± 5 years, height 180 ± 4 cm, and weight 76.7 ± 6.8) who self-reported ingesting ≤40 mg of caffeine daily, being nonsmokers, being physically active (accumulating at least 150 min of moderate intensity activity per week), and having no contraindications to cycling exercise. All participants self-reported no history of clinical pain or the use of pain medications. Participants were asked to refrain from caffeine, nicotine, over-the-counter pain medication and exercise for 24 h prior to each testing session. Compliance with these instructions was confirmed by participants completing a 24-hour diet and exercise recall questionnaire prior to each testing session. Three participants did not complete all testing session—one due to the time commitment and two due to musculoskeletal injuries unrelated to the experimental procedures. A sample of 13 was sufficient to detect a small (0.31 SD) effect at a power of 0.80 and an alpha level of p ≤ 0.05 [28]. Nine of the 13 participants completed a second set of follow-up testing where they completed a shorter, but higher intensity cycling bout. A sample of 9 was sufficient to detect a moderate (0.49 SD) effect at a power of 0.80 and an alpha level of p ≤ 0.05 [28]. The study was powered in this manner as changes in pain sensitivity of ~0.50 SD are considered clinically meaningful [29]. All procedures were approved by a university institutional review board and participants provided written informed consent prior to testing.

### 2.2. Experimental approach

A randomized double-blind, placebo-controlled crossover design was employed with participants ingesting either a 5 mg·kg$^{-1}$ dose of caffeine or a placebo in a counter-balanced manner. Testing was performed at approximately the same time of day and participants self-reported consumption of a similar light meal (~50% carbohydrates, 30% fat, and 20% protein) 2 h prior to each testing session. Three familiarization sessions were performed in order for participants to become accustomed [30] to the exercise protocol and the assessment of pressure pain (PPT) and thermal (heat) thresholds (TPT) to improve the reliability of the assessments. Two experimental sessions (see Fig. 1) were performed (separated by 48–72 h) where PPT and TPT were assessed prior to caffeine/placebo ingestion (Baseline), 60 min following ingestion (Post-In), and immediately following 15 min of cycling (plus a graded, 8-min warm-up) exercise (Post-Ex). Three additional sessions were performed as part of the follow-up—another familiarization session, and two additional experimental sessions (separated by 48–72 h) where PPT and TPT were again assessed at Baseline, Post-In, and Post-Ex following caffeine/placebo ingestion. In the follow-up testing the cycling exercise consisted of 10 min of cycling (plus a 10-min graded warm-up).

### 2.3. Administration of caffeine and placebo

Participants consumed a commercially available caffeine supplement or a placebo 50 min prior to the beginning of exercise. A 400 mg dose of caffeine was administered by having participants consume two pills each containing 200 mg of caffeine. This yielded a caffeine of dose ranging from 4.8 to 5.3 mg·kg$^{-1}$ of body weight per participant (the mean among the 13 participants was 5.2 mg·kg$^{-1}$ of body weight) and was based upon previous studies examining the effects of a similar (~5 mg·kg$^{-1}$ of body weight) dose of caffeine on muscle pain [21,22]. Based upon previous findings [31] this dose likely resulted in plasma

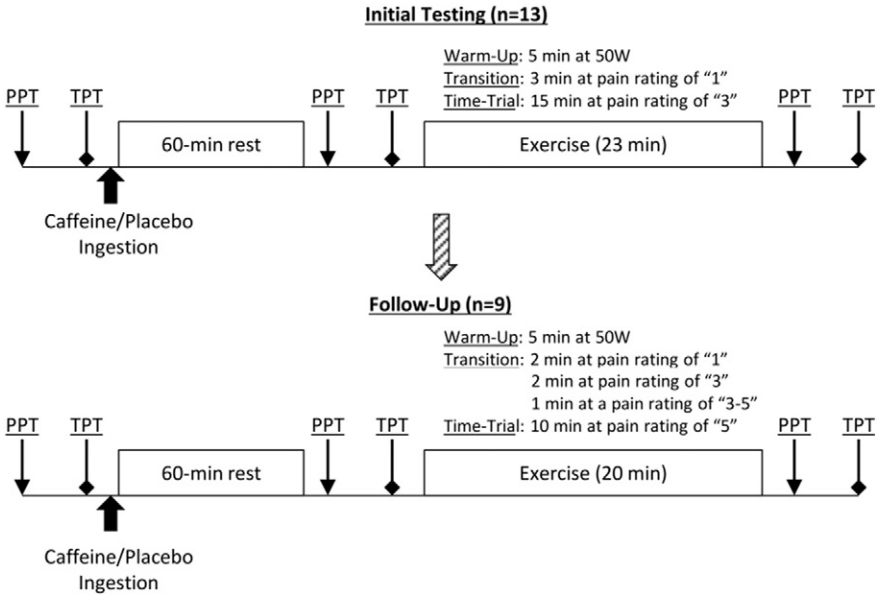


**Fig. 1.** Overview of experimental approach.