

Effect of Caffeine on Leg-Muscle Pain During Intense Cycling Exercise: Possible Role of Anxiety Sensitivity

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This experiment examined the effect of a moderate dose of caffeine on perceptions of leg-muscle pain during a bout of high-intensity cycling exercise and the role of anxiety sensitivity in the hypoalgesic effect of caffeine on muscle pain during exercise. Sixteen college-age women ingested caffeine (5 mg/kg body weight) or a placebo and 1 hr later completed 30 min of cycling on an ergometer at 80% of peak aerobic capacity. The conditions were completed in a counterbalanced order, and perceptions of leg-muscle pain were recorded during the bouts of exercise. Caffeine resulted in a large reduction in leg-muscle pain-intensity ratings compared with placebo ($d = -0.95$), and the reduction in leg-muscle pain-intensity ratings was larger in those with lower anxiety-sensitivity scores than those with higher anxiety-sensitivity scores ($d = -1.28$ based on a difference in difference scores). The results support that caffeine ingestion has a large effect on reducing leg-muscle pain during high-intensity exercise, and the effect is moderated by anxiety sensitivity.

Keywords: adenosine, ergometry, hypoalgesia, physical activity

Acute exercise is a natural stimulus that can transiently, safely, and reliably produce muscle pain (Cook, Jackson, O'Connor, & Dishman, 2004; Cook, O'Connor, Eubanks, Smith, & Lee, 1997; Cook, O'Connor, Oliver, & Lee, 1998; O'Connor & Cook, 1999, 2001) that might generalize to the pain experienced by patients with chronic pain (Cook, 2006). Moderate- to high-intensity exercise results in transient, naturally occurring pain in the activated muscles (Cook et al., 1997). The pain is described as exhausting, intense, sharp, burning, tiring, cramping, pulling, and rasping (Cook et al.); the same descriptors have been used for characterizing clinical pain conditions including menstrual pain, arthritic pain, cancer pain, chronic back pain, and fibromyalgia (Cook). We further note that pain ratings during exercise are nearly 1 *SD* above the mean scores associated with other laboratory methods for inducing pain (Cook et al., 1997).

Acute exercise has been used as an experimental model for testing effects of caffeine ingestion on muscle pain (Motl, O'Connor, & Dishman, 2003; Motl, O'Connor, Tubandt, Puetz, & Ely, 2006; O'Connor, Motl, Broglio, & Ely, 2004).

Our first experiment indicated that ingesting a large dose of caffeine (10 mg/kg body weight) reduced quadriceps muscle pain intensity during moderate-intensity cycling in males (Motl et al., 2003). In a second experiment, ingesting a moderate (5 mg/kg body weight) and a large (10 mg/kg body weight) dose of caffeine dose-dependently reduced quadriceps muscle pain intensity during moderate-intensity cycling in males (O'Connor et al., 2004). The third experiment demonstrated that ingesting a moderate (5 mg/kg body weight) and a large (10 mg/kg body weight) dose of caffeine similarly reduced quadriceps muscle pain intensity during moderate-intensity cycling in females (Motl et al., 2006).

One limitation of previous research is that it only examined the effects of caffeine on muscle pain using moderate-intensity exercise (i.e., 60% of peak oxygen uptake [VO_{2peak}]). The hypoalgesic effect of caffeine on muscle pain during exercise could be extended by testing its effects using high-intensity exercise (i.e., 80% VO_{2peak}). This exercise stimulus would induce higher intensity pain in the activated muscles (Cook et al., 1997, 1998) and provide an additional test of caffeine-induced hypoalgesia during exercise. Another limitation is that previous research has not examined psychological factors that might account for individual variability in the effect of caffeine on muscle pain during exercise. Anxiety sensitivity is a personality trait characterized by the belief that the experience of anxiety or fear causes illness, embarrassment, or additional anxiety (Reiss, Peterson, Gursky, & McNally, 1986), and low anxiety sensitivity has been related to caffeine-induced hypoalgesia during a cold-pressor pain task in females (Keogh & Chaloner, 2002). Anxiety sensitivity might have a similar effect on caffeine-induced hypoalgesia during exercise. Accordingly, the current study examined the effect of caffeine on leg-muscle pain intensity during high-intensity (80% VO_{2peak}) cycling exercise in women and the role of anxiety sensitivity in the hypoalgesic effect of caffeine on muscle pain during exercise.

Methods

Participants

The methods were approved by the University of Illinois at Urbana-Champaign Institutional Review Board, and all participants provided written informed consent. Participants ($N = 16$) were nonsmoking college-age women of average body weight who reported low to moderate daily caffeine consumption (i.e., ≤ 200 mg/day) and no hypersensitivity to caffeine. Only nonsmokers of average body weight (i.e., BMI ≤ 25) were recruited to avoid the effects of cigarette smoking (Joeres et al., 1988) and obesity (Kamimori, Somani, Knowlton, & Perkins, 1987) on the rate of caffeine metabolism. Participants who reported low to moderate daily caffeine consumption were recruited to minimize tolerance of the effects of caffeine among habitual consumers of caffeine (Laska et al., 1984). Participants who reported no hypersensitivity to caffeine were recruited to minimize the potential for extreme anxiety reactions to caffeine ingestion (Charney, Galloway, & Heninger, 1984). The participants did not report taking pain or antidepressant medication. We did not consider anxiety sensitivity in our recruitment because there is minimal evidence for the idea that anxiety increases in association with an acute bout of exercise in people who are prone to anxiety or anxiety attacks (O'Connor, Raglin, & Martinsen, 2000).

We further note that all participants were regular exercisers with above-average fitness who were capable of undertaking and completing 30 min of high-intensity exercise. Selected participant characteristics are provided in Table 1.

Materials

Leg-Muscle Pain Ratings. Leg-muscle pain intensity was measured using a categorical scale with ratiolike properties (Cook et al., 2004, 1998). The categorical scale has 12 categories from 0 to 10: 0 = *no pain at all*, 0.5 = *very faint pain (just noticeable)*, 1 = *weak pain*, 2 = *mild pain*, 3 = *moderate pain*, 4 = *somewhat strong pain*, 5 = *strong pain*, 7 = *very strong pain*, and 10 = *extremely intense pain (almost unbearable)*. No verbal anchors are provided in association with numbers 6, 8, and 9. Prior research has demonstrated that scores from this scale are valid and reliable for assessing the perceived intensity of leg-muscle pain during exercise (Cook et al., 2004, 1998). The categorical scale was used in the current study both because of the evidence of its reliability and validity and because of its advantages over a visual analog scale applied during exercise (e.g., no physical mark needs to be made on a sheet of paper).

Anxiety-Sensitivity Index. The anxiety-sensitivity index contains 16 items that measure the possible negative consequences of experiencing anxiety, including additional anxiety, fear, illness, embarrassment, and loss of control (Reiss et al., 1986). The 16 items are rated on a 5-point scale on which 0 = *very little*, 1 = *a*

Table 1 Characteristics of the Overall and Subsamples Based on a Median Split of ASI Scores for the College-Age Female Volunteers

Characteristic	Overall sample	Lower ASI scores ($n = 8$)	Higher ASI scores ($n = 8$)
Age (years)	23.4 ± 3.9	23.6 ± 4.9	23.1 ± 2.8
Height (cm)	168.8 ± 7.0	168.9 ± 7.2	168.8 ± 7.3
Weight (kg)	60.1 ± 7.9	61.3 ± 6.1	58.9 ± 9.8
Body-mass index (kg/m ²)	21.1 ± 2.4	21.5 ± 1.9	21.6 ± 2.8
Daily caffeine consumed (mg/day)	50.5 ± 53.9	19.6 ± 24.9	81.4 ± 58.6
ASI	19.0 ± 8.4	12.6 ± 6.4	25.4 ± 4.4
Peak power output (W)	248.3 ± 30.8	255 ± 34.2	241.7 ± 27.7
VO _{2peak} (ml · kg ⁻¹ · min ⁻¹)	45.0 ± 4.9	44.7 ± 4.9	45.4 ± 5.2
HR _{peak} (beats/min)	183.1 ± 7.4	185.1 ± 7.7	180.9 ± 6.9
RER _{peak}	1.2 ± 0.1	1.24 ± 0.04	1.21 ± 0.1
RPE _{peak}	18.3 ± 1.2	18.3 ± 1.4	18.3 ± 1.2
Peak pain – intensity	6.5 ± 2.6	7.0 ± 2.3	5.9 ± 3.0

Note. Data presented as $M \pm SD$. ASI = anxiety-sensitivity index; VO_{2peak} = peak oxygen consumption; HR_{peak} = peak heart rate; RER_{peak} = peak respiratory-exchange ratio; RPE_{peak} = peak rating of perceived exertion. Independent-samples t tests indicated that there were statistically significant ($p < .05$) differences in ASI scores and daily caffeine consumed between groups of lower and higher ASI scores, but there are no other significant differences between groups in the variables included in the table.

little, 2 = *some*, 3 = *much*, and 4 = *very much*. An individual's anxiety-sensitivity score is the sum of the scores on the 16 items. Research has demonstrated that scores from this scale are valid and reliable for assessing individual differences in anxiety sensitivity (Reiss et al.).

Incremental Exercise Test. Participants performed an incremental exercise test on an electronically braked, computer-driven cycle ergometer (Lode BV, Groningen, The Netherlands) to measure $\text{VO}_{2\text{peak}}$. Initially, they were fitted to the cycle ergometer. The participants were then provided with standardized, tape-recorded instructions for correctly using the leg-muscle pain (Cook et al., 1997) and overall perceived-exertion (Borg, 1978) scales. The maximal-exercise test procedures were described by an investigator, and participant questions were answered. After inserting a mouthpiece for collecting expired gases, the participants performed a 5-min warm-up at 25 W. The initial work rate for the exercise test was 50 W, and the work rate continuously increased at a rate of 24 W/min until the participant reached volitional fatigue. Using an open-circuit spirometry system (TrueOne, Parvo Medics, Sandy, UT), ventilation, oxygen consumption (VO_2), carbon dioxide production, and respiratory-exchange ratio were measured every 20 s. Heart rate was continuously displayed using a Polar heart-rate monitor (Polar Electro Oy, Kempele, Finland). Heart rate, rating of perceived exertion, work rate, and perceptions of leg-muscle pain were recorded every minute during the test of $\text{VO}_{2\text{peak}}$. $\text{VO}_{2\text{peak}}$ was defined as the highest recorded VO_2 value when two of three criteria were satisfied: respiratory-exchange ratio ≥ 1.10 , peak heart rate within 10 beats/min of age-predicted maximum (i.e., ~ 1 SD), or peak rating of perceived exertion ≥ 18 .

Procedures

Participants had menses and were tested in the self-reported follicular phase of the menstrual cycle. Participants completed 1 day of preliminary testing and 2 days of experimental testing. The 2 days of experimental testing were separated by 1 week. Experimental testing was conducted in the morning (7 a.m. \pm 1 hr). Participants were asked to abstain from caffeine consumption for 1 week, alcohol consumption for 24 hr, and eating a meal and exercising for 12 hr before the experimental testing, consistent with procedures used in previous research (Motl et al., 2003, 2006; O'Connor et al., 2004).

Preliminary Day. Before incremental exercise testing, the participants completed a 7-day caffeine recall questionnaire (James, Bruce, Lader, & Scott, 1989), medical history questionnaire, and the anxiety-sensitivity index. The medical history questionnaire was used to identify contraindications to caffeine consumption and exercise testing. The incremental exercise test provided an opportunity for participants to experience and rate cycle-ergometry-induced leg-muscle pain throughout the full range of possible stimulus intensities.

Experimental Days. On the experimental days, the participants ingested capsules that contained caffeine (5 mg/kg body weight) or placebo with ~ 250 ml of water and then sat and read quietly. One hour after ingesting the capsules, a time that consistently has coincided with peak plasma caffeine concentrations (Charney et al., 1984; Kamimori et al., 1995, 1987; Kaplan et al., 1997), the participants walked to another room and performed 30 min of cycling on an ergometer at an intensity

of 80% $\text{VO}_{2\text{peak}}$. Participants' perception of leg-muscle pain intensity, work rate, and heart rate were recorded every 5 min during the submaximal exercise bouts. Expired gases were analyzed using open-circuit spirometry after 5, 15, and 25 min of exercise. Immediately after the expired gases were analyzed, an investigator adjusted the work rate so that each participant exercised at an intensity of approximately 80% $\text{VO}_{2\text{peak}}$ throughout the two bouts of exercise. All participants were asked to guess the order of drug administration after completing the last day of experimental testing.

Drug Delivery and Content. Caffeine (Caffeine Anhydrous, USP/NF, Gallipot, St. Paul, MN) and placebo were delivered in gelatin capsules (No. 1, Eli Lilly & Co., Indianapolis, IN). The dose of caffeine (5 mg/kg body weight) was moderate and equivalent to consuming approximately two and a half 8-oz cups of ground roasted coffee (Barone & Roberts, 1996). The dose of placebo was an equal number of gelatin capsules containing white, all-purpose flour. Caffeine was administered using a double-blind procedure to protect against possible participant and experimenter expectancy effects. The order of drug administration was counterbalanced.

Data Analysis

Descriptive statistics for the 16 participants are presented in text and tables as $M \pm SD$ and in figures as $M \pm SEM$. The leg-muscle pain-intensity, work-rate, and heart-rate data recorded during exercise were analyzed with 2 (drug: 5 mg/kg body weight caffeine and placebo) \times 6 (time: 5, 10, 15, 20, 25, and 30 min) repeated-measures ANOVAs based on the multivariate F statistic. The VO_2 data were analyzed with a 2 (drug: 5 mg/kg body weight caffeine and placebo) \times 3 (time: 5, 15, and 25 min) repeated-measures ANOVA based on the multivariate F statistic. The judgment of significance of the main effects and interaction in the repeated-measures ANOVA was based on the multivariate F statistic because it does not rely on the assumption of sphericity (Keselman, 1998). Effect sizes for F statistics were expressed as eta-squared (η^2). Effect sizes for mean differences were expressed as Cohen's d (Cohen, 1988), where the pooled SD was computed by accounting for the within-subjects correlation.

The effect of anxiety sensitivity on quadriceps muscle pain-intensity ratings during the caffeine condition was initially examined using bivariate and partial correlation analyses. With the bivariate correlation analysis, we examined the relationship between anxiety-sensitivity scores and change in average quadriceps muscle pain-intensity ratings in the caffeine session versus the placebo session (change = placebo – caffeine, with a larger value indicating a greater reduction in pain rating). With the partial correlation analysis, we examined the relationship between anxiety-sensitivity scores and average muscle pain-intensity ratings in the caffeine session, controlling for average muscle pain-intensity ratings in the placebo session. One last set of analyses involved dichotomizing individuals into two groups, those with lower or higher anxiety sensitivity, based on a median split of anxiety-sensitivity scores. We then examined the effect of anxiety sensitivity on quadriceps muscle pain-intensity ratings after caffeine and placebo ingestion using a mixed-model 2 (group: lower and higher anxiety sensitivity) \times 2 (drug: 5 mg/kg body weight caffeine and placebo) \times 6 (time: 5, 10, 15, 20, 25, and 30 min) ANOVA based on the multivariate F statistic. The judgment of significance

of the main effects and interactions in the mixed-model ANOVA was based on the multivariate F statistic because it does not rely on the assumption of sphericity (Keselman, 1998).

Results

Effect of Caffeine on Absolute and Relative Exercise Intensity

The work-rate and heart-rate data are presented in Figure 1. The 2×6 repeated-measures ANOVA indicated that there was not a statistically significant drug main effect on work rate, $F(1, 15) = 0.01, p = .94, \eta^2 = .00$, nor was there a statistically significant Drug \times Time interaction, $F(5, 11) = 0.01, p = .95, \eta^2 = .00$. Another 2×6 repeated-measures ANOVA indicated that there was not a statistically significant drug main effect, $F(1, 15) = 0.02, p = .89, \eta^2 = .00$, nor was there a statistically significant Drug \times Time interaction, $F(5, 11) = 0.43, p = .82, \eta^2 = .02$, on heart rate.

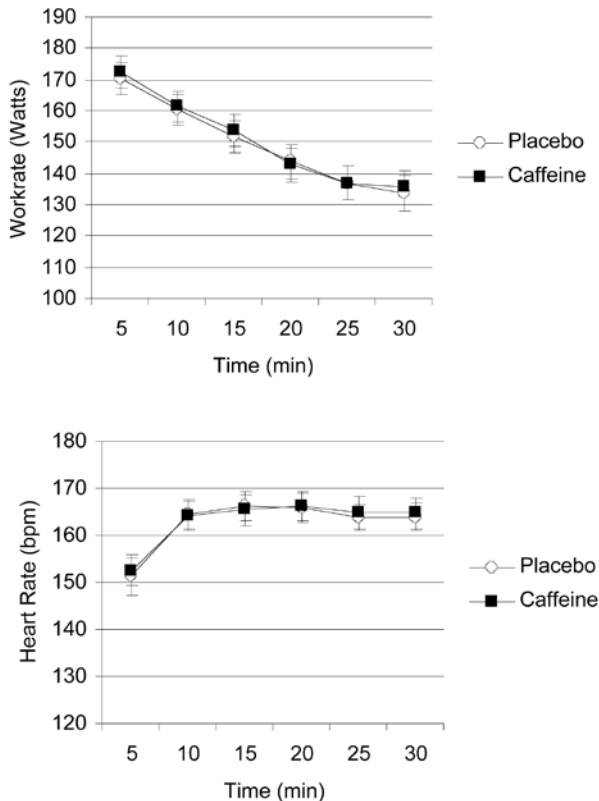


Figure 1 — Work-rate and heart-rate values recorded during 30 min of high-intensity cycling exercise ($80\% \text{VO}_{2\text{peak}}$). Values are $M \pm SE$.

The next analysis examined the effects of caffeine and placebo on VO_2 during the exercise session. The 2×3 repeated-measures ANOVA indicated that there was neither a statistically significant drug main effect, $F(1, 15) = 0.46, p = .51, \eta^2 = .03$, nor a statistically significant Drug \times Time interaction, $F(2, 14) = 0.11, p = .89, \eta^2 = .02$, on VO_2 . The mean VO_2 values during exercise after ingesting caffeine and placebo were 34.7 ± 3.0 and $34.9 \pm 3.4 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, respectively. Those VO_2 values represented relative exercise intensities of 77% $\text{VO}_{2\text{peak}}$ and 78% $\text{VO}_{2\text{peak}}$ for the caffeine and placebo conditions, respectively. These values were not statistically different based on a paired-sample t test, $t(15) = -0.63, p = .54$.

Effect of Caffeine on Ratings of Quadriceps Muscle Pain Intensity

The quadriceps muscle pain-intensity ratings recorded during the exercise sessions are provided in Figure 2. The 2×6 repeated-measures ANOVA indicated a significant drug main effect on pain-intensity ratings, $F(1, 15) = 14.24, p = .002, \eta^2 = .49$, but not a statistically significant Drug \times Time interaction, $F(5, 11) = 1.49, p = .27, \eta^2 = .40$. The mean pain-intensity scores during exercise after ingesting caffeine and placebo were 2.6 ± 1.5 and 3.8 ± 1.7 , respectively. Ingestion of caffeine resulted in a large reduction in leg-muscle pain-intensity ratings compared with the placebo ($d = -0.95$).

We performed an additional analysis that statistically tested for a possible order effect of drug administration on pain ratings during exercise. This was performed with order of drug administration coded as a between-subjects factor within a 2 (order of drug administration) \times 2 (drug) \times 6 (time) mixed-model ANOVA. There was not a significant main effect for order of drug administration, $F(1, 14) = 2.45, p = .14, \eta^2 = .15$, nor a significant Order of Drug Administration \times Drug interaction, $F(1, 14) = 0.59, p = .46, \eta^2 = .04$, but the drug main effect was still statistically significant, $F(1, 14) = 13.90, p = .002, \eta^2 = .50$. The statistical analysis, therefore, indicated that the effect of caffeine on leg-muscle pain during exercise was not caused by the order of caffeine and placebo administration.

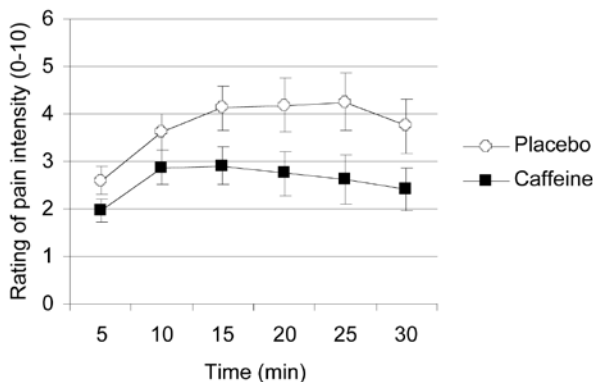


Figure 2 — Leg-muscle pain-intensity values recorded during 30 min of high-intensity cycling exercise ($80\% \text{VO}_{2\text{peak}}$). Values are $M \pm SE$.

Effect of Anxiety Sensitivity on Muscle Pain-Intensity Ratings

The bivariate correlation analysis indicated a negative correlation between anxiety-sensitivity scores and change in average quadriceps muscle pain-intensity ratings between caffeine and placebo conditions ($r = -.62, p = .01$), and this relationship was still significant when controlling for existing differences in daily caffeine consumption between individuals with lower and higher anxiety-sensitivity scores ($pr = -.53, p = .05$). This indicated that those with lower anxiety-sensitivity scores had a great reduction in muscle pain-intensity ratings during exercise after ingesting caffeine. The partial correlation analysis indicated a positive correlation between anxiety-sensitivity scores and average pain ratings in the caffeine condition, controlling for average pain ratings in the placebo condition ($pr = .55, p = .04$), and this relationship, too, was still significant when controlling for existing differences in daily caffeine consumption between individuals with lower and higher anxiety-sensitivity scores ($pr = -.50, p = .05$). This indicated that those with lower anxiety-sensitivity scores had lower muscle pain-intensity ratings during exercise after ingesting caffeine, and this relationship was relatively unaffected by differences in daily caffeine consumption between groups differing in anxiety sensitivity.

The last analysis was conducted to illustrate the effect of anxiety sensitivity on the hypoalgesia with caffeine during exercise and involved dichotomizing individuals into two groups, those with lower ($M = 12.6, SD = 6.4$) or higher ($M = 25.4, SD = 4.4$) anxiety-sensitivity scores, based on a median split of anxiety-sensitivity scores, and then performing a mixed-model 2 (group: lower and higher anxiety sensitivity) \times 2 (drug: 5 mg/kg body weight caffeine and placebo) \times 6 (time: 5, 10, 15, 20, 25, and 30 min) ANOVA on muscle pain-intensity ratings. The mixed-model ANOVA indicated a significant Group \times Drug interaction on pain-intensity ratings, $F(1, 14) = 5.24, p = .04, \eta^2 = .27$, but not a statistically significant Group \times Drug \times Time interaction, $F(5, 10) = 0.18, p = .97, \eta^2 = .08$. As illustrated in Figure 3,

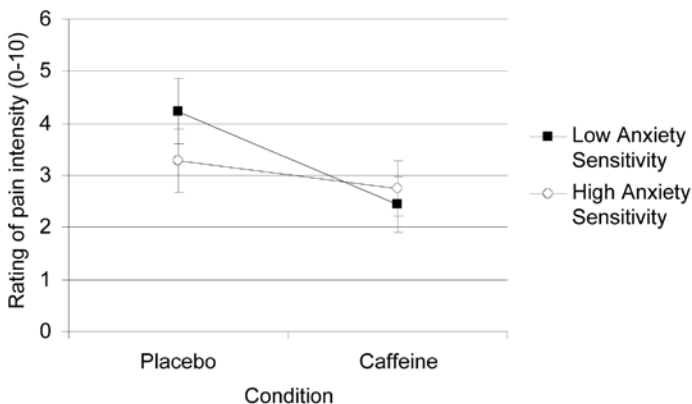


Figure 3 — Leg-muscle pain-intensity values recorded during 30 min of high-intensity cycling exercise ($80\% \text{VO}_{2\text{peak}}$) for those with lower and higher anxiety-sensitivity scores. Values are $M \pm SE$.

those with lower anxiety sensitivity had a larger reduction in quadriceps muscle pain-intensity ratings after caffeine ingestion compared with placebo than those with higher anxiety sensitivity ($d = -1.28$), and this difference was statistically significant, $t(14) = 2.30$, $p = .04$. Notably, there were no significant differences between groups in quadriceps muscle pain-intensity ratings for the placebo, $t(14) = 1.08$, $p = .30$, and caffeine, $t(14) = -0.40$, $p = .70$, conditions, and quadriceps muscle pain-intensity ratings were lower after caffeine ingestion than placebo for both those with lower anxiety-sensitivity scores, $t(7) = 3.48$, $p = .01$, and those with higher anxiety-sensitivity scores, $t(7) = 3.04$, $p = .02$.

Discussion

This experiment involved an examination of the effect of caffeine on naturally occurring quadriceps muscle pain during high-intensity cycling exercise in women and investigated the role of anxiety sensitivity in moderating the hypoalgesic effect of caffeine during exercise. Compared with placebo, the moderate dose of caffeine (i.e., 5 mg/kg body weight) had a significant and large hypoalgesic effect during cycling exercise, and the effect was larger for those with lower anxiety sensitivity than those with higher anxiety sensitivity. Notably, there were no differences in the absolute and relative intensities of the two exercise bouts. Hence, the women experienced a reduction in pain-intensity ratings in the quadriceps during high-intensity cycling after caffeine ingestion, and the effect was largest for those with lower anxiety sensitivity.

The current findings replicate and extend previous work on caffeine and naturally occurring muscle pain during exercise. Three previous experiments have demonstrated that ingesting large and moderate doses of caffeine reduced quadriceps muscle pain-intensity ratings during moderate-intensity cycling exercise in males and females (Motl et al., 2003, 2006; O'Connor et al., 2004). This study demonstrated that ingesting a moderate dose of caffeine reduced quadriceps muscle pain-intensity ratings during high-intensity cycling exercise in women. Of note, the high-intensity exercise did induce stronger quadriceps muscle pain-intensity ratings than reported in the placebo condition of previous studies that used moderate-intensity exercise. One previous study with females reported a mean quadriceps muscle pain-intensity rating in the placebo condition of 2.4 ± 1.1 (Motl et al., 2003), whereas we reported a mean rating in the placebo condition of 3.8 ± 1.7 . The difference of 1.4 units translates into a large difference in pain ratings between moderate- and high-intensity exercise ($d = 0.96$).

An additional novel feature of this study was its examination of the influence of anxiety sensitivity on the hypoalgesic effect of caffeine during cycling exercise. This study demonstrated that those with lower anxiety sensitivity had a significantly larger reduction in quadriceps muscle pain-intensity ratings after caffeine ingestion compared with placebo than those with higher anxiety sensitivity. Of note, quadriceps muscle pain-intensity ratings were lower after caffeine ingestion than after placebo for both groups of individuals with lower and higher anxiety sensitivity. Our findings are partially consistent with previous research that examined the effect of anxiety sensitivity on caffeine-induced hypoalgesia during a cold-pressor pain task in females (Keogh & Chaloner, 2002). That study indicated that low anxiety sensitivity was associated with an increase in pain threshold during a cold-pressor

pain task after caffeine ingestion compared with placebo; there were no effects of caffeine on pain threshold in those with medium or high anxiety sensitivity (Keogh & Chaloner). Therefore, the primary difference between our findings and those of previous research (Keogh & Chaloner) is that we observed an effect of caffeine on quadriceps muscle pain-intensity ratings in those with higher anxiety sensitivity, whereas previous research did not observe an effect of caffeine on pain threshold during a cold-pressor task in those with medium and high anxiety sensitivity.

Another difference is that previous research did not report a moderating role of anxiety sensitivity on sensory and affective components of pain associated with the cold-pressor task after caffeine ingestion (Keogh & Chaloner). The difference in findings of the effect of anxiety sensitivity on caffeine-induced hypoalgesia might be linked with the nature of the pain stimulus or the measurement of pain. This is further illustrated by the apparent, although likely not statistically significant based on low power, 1-point difference in pain ratings between the lower and higher anxiety-sensitive groups in the placebo condition in the current study. The women with lower anxiety sensitivity reported higher pain-intensity ratings during exercise in the placebo, whereas other research has demonstrated that women with higher anxiety sensitivity reported greater sensory pain during a cold-pressor task (Keogh & Birkby, 1999). The current study used exercise as a stimulus to produce pain and examined ratings of muscle pain intensity, whereas previous research used a cold-pressor pain task and measured pain threshold and tolerance, as well as the subjective experience of pain using the short form of the McGill Pain Questionnaire. Researchers might consider examining the precise conditions under which anxiety sensitivity moderates experimentally induced pain and the hypoalgesic effect of caffeine.

Although anxiety sensitivity did influence the effect of caffeine on muscle pain during exercise, we did not examine the mechanism underlying this moderator effect. One possibility is that the effect is mediated by a negative interpretive bias (Keogh & Cochrane, 2002; Keogh, Hamid, Hamid, & Ellery, 2004). That is, anxiety sensitivity might be related to pain responses because of the tendency of individuals to interpret bodily sensations in a negative manner (Keogh & Cochrane; Keogh et al., 2004). Indeed, with a cold-pressor task, individuals with high anxiety sensitivity exhibited a greater interpretive bias and reported more negative pain experiences than those low in anxiety sensitivity, and the tendency to misinterpret innocuous bodily sensations mediated the associations between anxiety sensitivity and affective pain experiences (Keogh & Cochrane). Perhaps individuals with higher anxiety sensitivity misinterpret bodily sensations associated with caffeine ingestion, and this misinterpretation influences pain responses associated with exercise after caffeine ingestion. Another possibility is that individuals with higher anxiety sensitivity exhibit greater negative psychological response during caffeine ingestion (Telch, Silverman, & Schmidt, 1996), and this influences the effect of caffeine on muscle pain during exercise in those with higher anxiety sensitivity.

The results of our study are consistent with experiments in humans that support caffeine's influence on ischemic muscle-contraction pain (Myers, Shaikh, & Zullo, 1997), pain induced by a cold-pressor task (Keogh & Witt, 2001), and eccentric-exercise-induced, delayed-onset muscle soreness (Maridakis, O'Connor, Dudley, & McCully, 2007). Indeed, one previous study reported that ingestion of 200 mg of

caffeine reduced pain-intensity ratings during artificially induced noxious muscle ischemia (Myers et al.). Another previous experiment reported that ingestion of 250 mg of caffeine increased pain threshold and pain tolerance during a cold-pressor task (Keogh & Witt). One final previous experiment reported that ingestion of 5 mg/kg body weight of caffeine produced a large reduction in pain-intensity ratings associated with eccentric-exercise-induced, delayed-onset muscle soreness (Maridakis et al.). Those findings combined with the consistent observation of caffeine-induced reductions in naturally occurring muscle pain during acute exercise suggest that caffeine has a hypoalgesic effect in humans under conditions of artificial and naturally occurring pain.

This study is not without limitations. One limitation involves the dose of caffeine and the efficacy of the double-blinding. As might be expected, 14 of the 16 participants correctly guessed the order of caffeine administration, and this likely undermined our double-blinding of caffeine versus placebo administration. Another limitation is that of the median split. Although our primary analysis involved bivariate and partial correlations with anxiety sensitivity as a continuous variable, the tertiary analysis included a median split based on anxiety-sensitivity scores. The two groups differed in mean anxiety-sensitivity scores, but there are potential problems associated with small sample bias and people in the lower anxiety-sensitivity group actually being moderate in anxiety sensitivity and vice versa.

Nevertheless, the results of this study add to the body of evidence that caffeine ingestion influences muscle pain during exercise and provides novel evidence that anxiety sensitivity moderates the magnitude of the effect. Further research should address the mechanisms underlying caffeine-induced hypoalgesia during acute exercise, as well as test the effect of varying doses of caffeine on muscle pain in males, habitual users of caffeine, and individuals with a variety of personality traits including anxiety sensitivity. Such inquiries will further highlight the effect of caffeine on naturally occurring muscle pain during acute exercise.

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