No significant effect of caffeine on five kilometer running performance after muscle damage

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Abstract: Caffeine has documented hypoalgesic effects during exercise. However, there is a lack of research focusing on caffeine's potential analgesic effects to ameliorate delayed onset muscle soreness. A placebo controlled randomized cross-over trial was carried out to determine if 5 mg/kg of body weight (mg/kgBW) of caffeine attenuates muscle pain and improves 5 k running performance following delayed onset muscle soreness. Prior to participating, eleven runners (9 male; 2 female; age, 24.5 ± 6.3 years; height, 173.6 ± 7.8 cm; body mass, 66.3 ± 7.5 kg; BMI, 23.18 kg/m^2 ± 1.6; VO$_{2max}$ 61.0 ± 6.1 ml/kg/min^{-1}), were asked to discontinue supplement use for 72 hours and abstain from caffeine consumption for 48 hours. Participants performed a 30-minute downhill run on a treadmill set at −10% grade at 70% VO$_{2max}$ to induce delayed onset of muscle soreness. Participants then returned 48 hours after to complete a 5 k time trial run where they consumed either 5 mg/kgBW of caffeine or a placebo. Rate of perceived exertion and heart rate were taken every two minutes during the trial. There was no detectable statistical difference between 5 k performance between caffeine (1074.9 ± 119.7 sec) or placebo (1053.8 ± 86.8 sec) (p = .41). Algometer readings were similar between both treatments for muscle soreness in the rectus femoris (p = .791) and the vastus medialis oblique (p = .371). Muscle soreness ratings were found to be greater in the caffeine condition compared to the placebo condition (p = .030). There was no effect of treatment on rating of perceived exertion between conditions (p = .574). The present study suggests that caffeine is not effective at reducing muscle soreness, rating of perceived exertion, or improving running performance in a time trial in the presence of muscle soreness.

Keywords: Caffeine supplementation, delayed onset muscle soreness, downhill running, performance enhancement

Introduction

Caffeine is widely used in sport and has been shown to have many beneficial physiological and psychological effects [1]. Caffeine is a central nervous system stimulant that regardless of mode, intensity, or duration results in an alteration in participants' perceptual response during exercise testing [2]. Recent studies have demonstrated that caffeine ingestion prior to aerobic bouts of exercise has positive ergogenic effects by delaying fatigue and increasing time to exhaustion [3, 4]. In addition, caffeine is an adenosine receptor antagonist and has a documented exercise-related hypoalgesic effect [5, 6]. Recent research has shown that caffeine ingestion prior to exercise results in decreased pain perception [7, 8]. An analysis of the efficacy of caffeine on reducing muscle pain during submaximal aerobic exercise demonstrated that relatively moderate caffeine doses (5 mg/kg

of body weight) attenuate leg pain [9]. Therefore, the body of literature that suggests that caffeine supplementation (between 5–10 mg/kgBW) has hypoalgesic effects on the sensation of pain serves as the foundation for this current investigation.

Caffeine administration exceeding 3 mg/kg of body weight (mg/kgBW) has also been shown to improve aerobic performance [10]. More specifically, doses ranging from 3–13 mg/kgBW improve exercise performance by a magnitude of 0.41 SD [2]. Duncan et al. [8] provided data on eleven resistance trained individuals who ingested a caffeinated solution (5 mg kg^{-1}) in a cross-over experimental study consisting of four resistance movements at 60% one repetition maximum. Results indicated that participants completed a significantly greater number of repetitions prior to failure, irrespective of exercise, in the presence of caffeine (p = 0.0001) and their overall

perception of effort was significantly lower (p = 0.03). Furthermore, Graham, Hibbert, and Sathasivam [11] investigated the effects of caffeine on a performance trial (85% VO_{2Max} to exhaustion in conditioned runners) where participants ingested either caffeine capsules plus water, regular coffee, decaffeinated coffee, decaffeinated coffee plus caffeine in a capsular form, or a placebo an hour before activity. Results indicated that performance was significantly improved with the caffeine capsule as compared to the other four treatments. As a whole, there have been inconsistent performance results in experimental caffeine studies which may be the result of differences in dosage, timing of ingestion, mode of exercise, subject population, and the acute nature of individual studies.

According to Doherty and Smith [12], caffeine reduces the rating of perceived exertion (RPE) during exercise which may account for the subsequent ergogenic effects on performance. RPE has been used primarily as an undifferentiated rating of perceived effort [13, 14]. When RPE is differentiated, three central nervous system factors of motivation, aversion, and drive determine overall perception of effort. Cardiorespiratory factors (heart rate, ventilation frequency, and depth) determine chest perception of effort. Local factors (strain, force sensation, and fatigue of the working muscles) determine the legs' perception of effort. It has been stated that caffeine has a small but significant effect on 5 k times of well-trained and recreational runners (n = 30), improving by 1.0 and 1.1% respectively (90% CI 0.4–1.6), when assessed during an outdoor 5 k time trial [15]. However, few studies have examined how caffeine affects human performance during delayed onset of muscle soreness (DOMS) and pain between 24 and 48 hours after a muscle damaging downhill run on a subsequent 5 km time trial performance [16].

Despite the available literature on the hypoalgesic and ergogenic effects of caffeine, there is currently a lack of research focusing specifically on the effectiveness of caffeine following DOMS-inducing exercise on subsequent exercise performance and the attenuation of muscle pain. Delayed onset muscle soreness continues to increase post exercise with peaks between 24 and 48 hours and is the main cause of decline in physical performance for both athletes and non-athletes [17]. A single bout of downhill running (lasting approximately 30 minutes) has also been shown to elicit DOMS in trained runners after approximately 48 hours. This population observed increased HR and increased ventilation rates as well as decreased stride length as a result [18]. Due to the associated pain, discomfort, and malperformance, DOMS prevention and treatment are of great interest to coaches, fitness instructors and therapists. The current literature concerning DOMS management has identified supplementation as a potential treatment method [17]. Therefore, the purpose of this study was to determine if 5 mg/kgBW of caffeine a) attenuates muscle pain following a 5 km running time trial completed in subjects with muscle soreness and b) improves 5 km running performance and reduces RPE following exercise-induced muscle soreness.

Subjects and methods

Experimental design

The relative effectiveness of caffeine on 5 km running performance and measures of muscle soreness following downhill running was examined in a randomized, double-blind, repeated-measures crossover design with participants serving as their own controls. Performance, reduction of RPE, and subjective measures of muscle soreness were assessed. Moderately trained (regional level runners) and triathletes accustomed to high-intensity exercise were tested to improve sensitivity and the external validity of the study. Participants performed the protocol on two occasions with at least three weeks in between trials to allow time for muscle soreness to disperse. Participants were asked to discontinue all supplement use for at least 72 hours prior to participating. Furthermore, participants abstained from caffeine consumption 48 hours prior to testing. Participants in this study regularly consumed an average of 2.4 mg of caffeine per day. Evidence suggests that a complete caffeine withdrawal can be achieved within 24–48 hours [19].

Participants

Eleven runners (9 male; 2 female; age, 24.5 ± 6.3 years; height, 173.6 ± 7.8 cm; body mass, 66.3 ± 7.5 kg; BMI, 23.18 kg/m^2 ± 1.6; VO_{2max} 61.0 ± 6.1 ml/kg/min^{-1}) were recruited to participate in this study. All participants provided informed consent and were free to withdraw from the study at any time. The subjects were moderately trained regional level runners and triathletes accustomed to high-intensity exercise were eligible if the following criteria were met: minimum of two years of involvement in endurance sports, a minimum of six training hours/week and between the ages of 19–40 years old. Exclusion criteria consisted of participants with the presence of significant or unstable acute or chronic medical conditions. The number of selected participants was based on an *a priori* power analysis conducted using G*Power software. Based on data from recent articles [20, 37 ((**author: ref 37 is cited here. Please check & suggest if this ref can be renumbered so as to arrange ref citation in sequential order))], a one-tailed alpha-level of 0.05 power analysis indicated the need for

nine participants. Participants were instructed to avoid exercise for 24 hours prior to reporting to the lab, and reported to the lab without any signs of muscle soreness. Upon arrival, participants were fully informed of the purpose and associated risks, and written informed consent was obtained. Participants were not advised with regard to the nature or direction of the hypotheses. Age (years), height (cm) and mass (kg) were recorded, and body fat percentage was estimated using Lange skinfold calipers (Cambridge, MD, USA) and a 3-site method (chest, abdomen, thigh) [21].

All procedures were approved by the Central Washington University Institutional Review Board. Before the study, participants were informed of the study purpose, along with any associated risks and benefits. In accordance with the university institutional review board and the Declaration of Helsinki, participants gave their written informed consent and completed a health history questionnaire before the first test session. Each participant arrived at the lab after an eight-hour overnight fast and having abstained from caffeine for 48 hours and alcohol for a minimum of 24 hours. Participants were also instructed to refrain from exercise for 24 hours prior to testing. Participants reported no muscle soreness prior to beginning the study, and creatine kinase levels for all participants were within acceptable levels (<190 u/L).

Each participant performed an introductory testing and familiarization session and two separate trials (three total sessions). The study consisted of an exercise session followed by a 48-hour rest period and a 5 k time trial. There was a three-week washout period and then the protocol was repeated with the other treatment (Figure 1).

Maximal oxygen consumption (VO$_{2max}$)

Maximal oxygen consumption (VO$_{2max}$) was determined during an incremental exercise test to volitional fatigue on a treadmill (Barimill treadmill, Woodway, Waukesha, WI). Participants were fitted with a heart rate (HR) monitor transmitter (Polar, Stamford, CN, USA) at the level of the sternum. Expired air was directed through a one-way valve (Hans Rudolf, KC, MO) and plastic tubing was connected to a metabolic cart (Parvo Medics' TrueOne® 2400, UT, USA), which was calibrated prior to each test with a known gas composition. A 4-L precision syringe (Hans Rudolph, Kansas City, MO, USA) was utilized to calibrate the system for measurement of ventilation. Test termination criteria aligned with those suggested by ACSM for VO$_{2max}$ testing [22]. Criteria for achievement of VO$_{2max}$ were: a) RPE $\geq$ 19, b) RER $\geq$ 1.1, c) plateau of VO$_2$ with increased workload, and d) > 85% of age-predicted maximum HR [23]. Two or more of these four criteria were met by all participants.
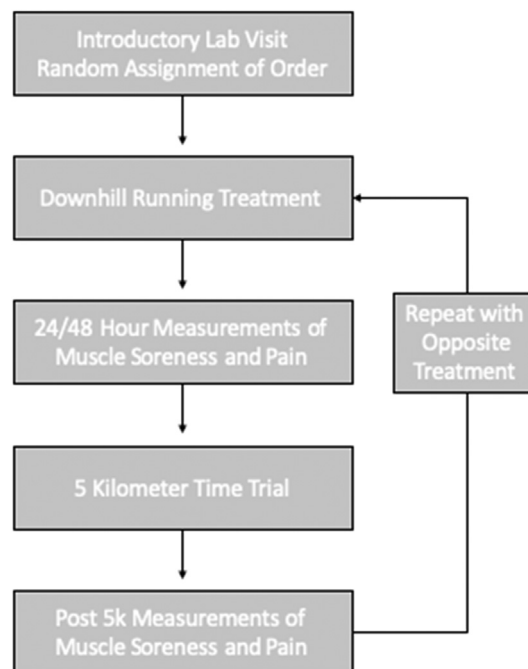

Figure 1. Description of experimental protocol.

Downhill running trial

Downhill running at a −10% grade was utilized in order to induce muscle soreness [24]. The downhill runs were completed on a commercial treadmill (Barimill treadmill, Woodway, Waukesha, WI) that was modified to allow for a −10% grade. Participants completed a 5-minute warm-up at 0% grade on a treadmill. After the warm-up, the treadmill was declined to a −10% grade and the speed was adjusted to elicit 70% of their VO$_{2max}$ determined by oxygen uptake to allow the subject to exercise at a constant "steady-state" where physiological variables (heart rate and oxygen requirements) remained stable. This intensity was maintained for 30-minutes. Heart rate was monitored continuously, and rate of perceived exertion was assessed every 2 minutes.

5 k running time trial

Subjects returned to the lab 48 hours after the downhill running session to perform a 5 k running time trial. Participants completed a five-minute warm-up on the treadmill at a self-selected pace. Participants were verbally encouraged to run at a maximal effort and were able to select their pace. RPE (Rating of Perceived Exertion – Borg 6–20) [25] and HR (heart rate; Polar, Electro Inc Finland) were taken every two minutes during the trial. Termination criteria for the testing session included if the participant requested to stop for any reason [26] or if the participant exhibited any evidence of

heat illness, such as chills, nausea, or confusion. In order to determine the individuals performance in this trial the time in seconds was recorded when the participant traveled a distance of 5 kilomteres on the treadmill.

Treatment

One hour prior to the 5 k running time trial, participants consumed either 5 mg/kgBW caffeine (CAFF) capsule (equivalent to no more than 3 cups of coffee) [10, 11] or a placebo pill (PLB) along with 400 ml (~2 cups) of water. Participants waited in the lab until the exercise session began. Trial two was repeated after the three-week wash out period with the opposite treatment.

Measurements

Subjective measurements of muscle soreness were assessed using a 10 cm visual analog scale [27] with anchor points "no pain at all" at the left end and "unbearable pain" at the right end. This measure was completed four times: immediately following downhill running, 24 hours post downhill running, 48 hours post downhill running (pre-5 k), and 48 hours post downhill running (post-5 k). Session RPE [25] was assessed 30 minutes after the 5 k running trial. Muscle pain was assessed using a Force Algometer (Wagner Pain Test Model FPK Algometer) [28]. Measurements were made at the rectus femoris (RF) and vastus medialis oblique (VMO). All measurements were reported in kilograms of force (kgf). Force was applied via the probe through a 1 cm diameter head until the participant indicated pain or discomfort. At this point the force value (kgf) was recorded. Muscle pain was measured at immediately following the downhill run, 24 hours post, 48 hours post (pre-5 K), and 48 hours post (post-5 K).

Statistical analysis

Basic descriptive characteristics were computed for the participants (Table 1). Mean values for RPE, pain, and HR were computed for each treatment (CAFF, PLB). Examination of normality of data was undertaken using Shapiro-Wilk analysis, no measures were found to significantly deviate from a normal distribution (W > 0.8, $p > .09$). Data was examined for documentation of muscle soreness and pain during the first 48 hours of the trials to determine if DOMS was present. Following this analysis, repeated measures ANOVA analyses were used to determine the change in muscle soreness and pain from the end of the downhill run to the post 5 k time trial period. Additionally, changes in HR and RPE were examined using 2 × 2 repeated-measures ANOVA (treatment × time).

Table 1. Participant characteristics ($n = 11$)

Characteristic	Mean ± standard deviation
Female ($n = 2$)	
Height (cm)	169.0 ± 5.6
Body mass (kg)	61.7 ± 0.4
VO$_2$ max (ml/kg × min)	56.9 ± 1.1
BMI (kg/m^2)	21.6 ± 0.9
Male ($n = 9$)	
Height (cm)	178.1 ± 7.3
Body mass (kg)	70.8 ± 7.3
VO$_2$ max (ml/kg × min)	65.1 ± 5.7
BMI (kg/m^2)	23.3 ± 1.7

Bonferroni post hoc tests were conducted on ANOVA results. Finally, time trial performance in seconds was examined between trials using a paired samples t-test. All statistical analyses were performed using IBM SPSS Statistical Package (v26).

Results

Muscle soreness

Muscle soreness was evaluated using a repeated measures ANOVA at the following time points (post, 24 hours, 48 hours, post 5 k) to determine the effects of the treatment on measures of muscle soreness. There was no significant effect for time ($F = 1.129$, $p = .364$), and no interaction of time × treatment ($F = 2.886$, $p = .064$). There was a significant effect of treatment ($F = 7.937$, $p = .030$), indicating that muscle soreness was approximately 1.18 units higher in the caffeine condition compared to the placebo condition.

Muscle pain

Muscle pain was evaluated using a repeated measures ANOVA at the following time points (post, 24 hours, 48 hours, post 5 k) for two muscles to observe the effects of treatment on the attenuation of muscle pain. For the vastus medialis, the ANOVA did not reveal a significant main effect for treatment ($F = .936$, $p = .371$) nor a significant interaction of time × treatment ($F = .399$, $p = .755$). There was a significant effect of time ($F = 3.386$, $p = .041$), and Bonferroni post hoc pairwise comparisons revealed one significant pair: muscle pain was significantly higher at the 24 hour mark compared to post 5 k (mean difference .886 kg/cm^2, $p = .034$).

For the rectus femoris, the ANOVA did not reveal a significant effect for treatment ($F = .077$, $p = .791$) or time ($F = 2.912$, $p = .063$), nor a significant interaction of

Table 2. Muscle soreness scores

Subject #	Post downhill (CAFF)	Post downhill (PLB)	24 h CAFF	24 h PLB	48 h CAFF	48 h PLB	5 k CAFF	5 k PLB
1	4.25	4.15			3.30	3.20		4.20
2	2.10	4.50		6.05	6.60	6.85	5.65	7.60
3	5.90	6.20	6.00	5.20	4.95	6.50	5.05	4.10
4	5.90	5.40	6.75	6.25	7.70	4.95	7.55	5.70
5	6.65	2.65	7.90	4.80	7.85	4.40	4.60	2.40
6	6.50	7.30	5.90	6.20	6.80	5.10	8.20	6.90
7	2.40	2.60		5.00		2.00		4.20
8	1.90	1.60	3.10			6.20	3.50	3.80
9	5.40	5.60	6.40	5.00	5.90	3.10	6.40	4.40
10	0.90	1.50	4.10	2.40	2.00	0.60	5.40	1.70
11	1.30	2.60	3.90	3.30	2.60	0.80	0.70	1.20

CAFF: Caffeine; PLB: Placebo. Muscle soreness was assessed using a 10 cm Visual Analogue Scale.

Table 3. Vastus medialis pain (in kgf)

Subject #	Post downhill (CAFF)	Post downhill (PLB)	24 h CAFF	24 h PLB	48 h CAFF	48 h PLB	5 k CAFF	5 k PLB
1		2.86		2.30	6.00			
2	4.00	4.60			4.20	3.50	3.90	
3	4.60	3.30	4.00	4.10	4.40	3.10	3.40	2.70
4	4.30	3.40	3.50	3.60	3.90	4.30	3.20	4.40
5	3.40	3.60	5.00	2.80	3.00	3.70	2.50	2.30
6	4.60	4.20	5.20	3.60	4.60	2.80	4.50	2.40
7	6.00	4.50		5.00		5.70		6.10
8	3.50	2.80	2.60			2.20	2.80	2.60
9	7.00	4.00	4.60	4.60	3.60	4.30	3.00	4.00
10	5.80	4.90	6.00	7.00	7.00	6.40	5.00	6.60
11	4.00	3.60	4.50	5.40	3.40	3.90	3.80	3.70

CAFF: Caffeine; PLB: Placebo. Muscle pain was assessed using a Force Algometer (Wagner Pain Test Model FPK Algometer).

time × treatment ($F = 1.467$, $p = .271$). **((authors please check position of tables and add references to table 2, 3 and 4 in text))**

Time trial performance

Time trial performances by treatment were evaluated via paired samples t-test. The results did not reveal a significant change ($t = 0.86$, $p = 0.41$) in time trial performance by treatment (CAFF: 1074.9 ± 119.7 sec vs PLB: 1053.8 ± 86.8 sec) (Table 5).

RPE and HR

As participants did not all complete all stages of the downhill running trial, RPE and HR values were assessed at the first measurement time (2 min) and the final value was taken at the final trial each participant completed. A 2 × 2 repeated-measures ANOVA determined there to be no effect by treatment ($F = .338$, $p = .574$), and no interaction by time × treatment ($F = .362$, $p = .561$) on RPE. There was a significant effect by time ($F = 115.703$, $p < .001$), in which participant RPE was higher at their final stage compared to the initial measurement (Figure 2). There was a significant effect of time ($F = 270.478$, $p < .001$) and treatment ($F = 16.647$, $p = .003$) on participant HR, in which participant HR was increased during the final stage of their trial compared to the beginning stage, and was increased in the caffeine condition compared to the placebo condition. There was no significant interaction of time × treatment ($F = 1.256$, $p = .291$). Session RPE was unable to be collected from all participants, and has been excluded from statistical analysis.

Discussion

The aim of the present study was to investigate the influence of caffeine (5 mg/kgBW) on a 5 k running time trial, muscle soreness, and perceived exertion following a

Table 4. Rectus femoris pain (in kgf)

Subject #	Post downhill (CAFF)	Post downhill (PLB)	24 h CAFF	24 h PLB	48 h CAFF	48 h PLB	5 k CAFF	5 k PLB
1		2.70		5.10	6.90			
2	4.10	4.40			5.70	4.10	4.50	
3	7.90	3.70	5.40	4.80	5.00	3.20	3.50	3.20
4	4.20	4.44	6.50	5.10	5.70	4.50	5.00	5.10
5	4.50	4.60	5.00	6.00	4.20	4.60	3.00	4.10
6	4.70	3.70	5.20	3.60	5.40	3.10	5.00	2.30
7	7.00	7.00		7.00		7.00		6.10
8	4.40	3.80	3.50			2.80	4.20	5.20
9	4.30	5.20	5.10	6.50	5.00	4.90	5.50	5.30
10	6.40	6.00	6.50	7.00	6.70	6.40	7.00	6.60
11	4.80	6.40	3.00	7.00	3.90	5.50	3.90	5.30

CAFF: Caffeine; PLB: Placebo. Muscle pain was assessed using a Force Algometer (Wagner Pain Test Model FPK Algometer.

Table 5. 5 k Times

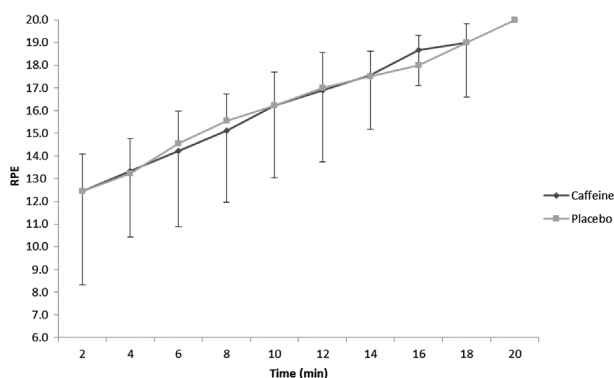| Subject #	Sex	Placebo 5 k Time (sec)	Caffeine 5 k time (sec)	Change from placebo (sec)
Subject 1	M	1036	939	−97
Subject 2	M	1025	1080	+55
Subject 3	M	945	944	−1
Subject 4	M	980	1030	+50
Subject 5	M	1129	1089	−40
Subject 6	M	991	1005	+14
Subject 7	M	1215	1226	+11
Subject 8	M	952	947	−5
Subject 9	M	1118	1066	−52
Subject 10	F	1136	1230	+94
Subject 11	F	1065	1268	+206
Mean (SD)		1053.8 (86.8)	1074.9 (119.7)	21.4 (81.1)

Figure 2. Rate of perceived exertion (RPE) during 5 k time trial obtained via the Borg RPE scale. Subjects ($n = 11$) returned to the lab 48 hours after the downhill running session to perform a 5 k running time trial.

thirty-minute muscle damaging bout of downhill running at 70% VO_{2max}. While the data do clearly indicate that the protocol produced DOMS in the subject, there were no statistically significant effects of CAFF on performance, muscle pain, visual analogue scores or RPE. Previous experiments have reported no reduction in quadriceps muscle pain ratings after ingestion of low doses of caffeine (1, 2, 3 mg/kgBW) during 15 minutes of high intensity cycling exercise in males who were low to moderate caffeine users [29]. However, it should be noted that the pain intensity ratings were lower than those reported in the current study. It is plausible that this is due to the magnitude of eccentric loading of the current protocol. Additional research might investigate a dose response to caffeine on muscle pain during high-intensity exercise in individuals who differ in habitual caffeine consumption.

Emerging evidence suggests that moderate to large doses of caffeine are associated with a reduction in pain rating during moderate to high intensity cycling exercise in low and high caffeine consuming individuals [6]. In the low-dose caffeine group, researchers observed a significant decrease in pain intensity in the caffeine condition using a visual analog scale ($p = .036$). In the present study, however,

visual analog scale measurements were not significantly different between CAFF and PLB groups. There are two potential explanations for this finding. One suggestion is that the dosage of caffeine provided was not sufficient to elicit reductions in muscular pain perception. Another suggestion is that the bout of exercise was not strenuous enough to elicit sufficient amounts of muscular pain, which would cause the CAFF condition to appear ineffective. Future studies should observe the effects of larger doses of caffeine on muscular pain reduction, and the effects of a moderate caffeine dose on muscular pain following a more strenuous bout of exercise.

Previous research suggests that caffeine's principle mechanism of action has an ergogenic effect on endurance performance, muscle glycogen expenditure, decreased perception of effort, and free fatty acid mobilization [30–34]. High intensity aerobic activity such as a 5 k time trial relies primarily on intramuscular glycogen stores; therefore, ATP production to fuel such an activity would be limited from mobilized free fatty acid oxidation, and adequate from individuals consuming a regular diet. However, the effects of caffeine as an ergogenic agent are not entirely understood. While under many circumstances, moderate to large doses of caffeine have been shown to improve endurance running performance, this is not always the case. Some studies have suggested that exercising in conditions of moderate to high heat stress does not elicit ergogenic benefits from caffeine [35, 36]. While some studies suggest that the dosage of caffeine used in the present study (5 mg/kgBW) is a hypoalgesic dose following intense exercise (80% VO_{2max}) [37], it is possible that the bout of exercise in the present study was insufficient to elicit this hypoalgesic response. The question of whether hypoalgesia is partially responsible for the ergogenic properties of caffeine is not entirely understood, and warrants further investigation.

It is important to acknowledge the strengths and limitations of the current research. To avoid potential differences in physiological responses that might occur as a result of caffeine supplementation a randomized, double-blind, repeated measures crossover design with participants serving as their own controls was implemented. The present study also controlled for the half-life of caffeine by incorporating a three-week washout period before the protocol was repeated with the other treatment. Limitations for the present work include sample size, limited number of female participants, lack of a true baseline measurement of muscle soreness and pain, training age and status of the participants may impact generalizability of the findings. Finally it should be noted that the participants were not caffeine naïve and did consume roughly 2.4 mg per kg of body weight of caffeine daily.

The discrepancies in the findings could indicate a potential genetic factor as the underlying modulator of caffeine's effect on RPE. Caffeine is absorbed rapidly and wholly from the gastrointestinal tract and metabolised by cytochrome P-450 enzymes, which are the rate-limiting step for plasma clearance. The P-450 1A2 enzyme is coded for by the CYP1A2 gene, and is the primary enzyme which demethylates caffeine into dimethylxanthine metabolites [38]. It has been estimated that variants of the CYP1A2 gene account for 90% of the metabolism of caffeine in humans [39]. A particular A/C substitution within that gene has previously been shown to modulate caffeine metabolism as well as the influence of caffeine on exercise performance [40]. In short, carriers of the C allele metabolise caffeine more slowly than those with the A/A genotype, and would thus be more likely to be affected by caffeine supplementation.

The present study does expand the understanding of caffeine as applied to muscle endurance, as the data also suggests that caffeine is not an effective analgesic during exercise performed in a state of DOMS. Future studies should evaluate whether caffeine plays a role in reducing muscle soreness, pain, and improving 5 k performance time following more extreme bouts of exercise. One suggestion from the present study would be to examine the impact of caffeine on exercise analgesia closer to the time period of greatest muscle soreness. The data from the present study suggests that with downhill running a peak soreness is achieved closer to 24 hours, rather than at 48 hours. Additionally, future research should evaluate the perception of pain during the bout of exercise undertaken with muscle soreness rather than just at the conclusion.

Conclusion

The present study suggests that a caffeine dosage of 5 mg/kgBW is not sufficient to reduce muscular pain, soreness, or RPE, or improve performance during a 5 km time trial following a bout of exercise inducing DOMS. It's possible that caffeine may show an ergogenic or hypoalgesic effect following a more strenuous bout of exercise, or in greater doses. Professionals and athletes should look to alternative methods to increase performance and/or reduce discomfort associated with these types of activities.

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Conflicts of interest
The authors declare that there are no conflicts of interest.

Authorship
AMA created the study design. BF conducted the literature review. MFB and AMT were involved in data collection. DB, RCP and KKP analyzed the data. MAS, AJ and LWJ developed the manuscript.

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