
EFFECT OF CAFFEINE ON PERCEIVED SORENESS AND FUNCTIONALITY FOLLOWING AN ENDURANCE CYCLING EVENT

AARON R. CALDWELL,¹ MATTHEW A. TUCKER,¹ CORY L. BUTTS,¹ BRENDON P. McDERMOTT,¹ JAKOB L. VINGREN,² LAURA J. KUNCES,³ ELAINE C. LEE,⁴ COLLEEN X. MUNOZ,^{4,5} KEITH H. WILLIAMSON,⁶ LAWRENCE E. ARMSTRONG,⁴ AND MATTHEW S. GANIO¹

¹Human Performance Laboratory, University of Arkansas, Fayetteville, Arkansas; ²Applied Physiology Laboratory, University of North Texas, Denton, Texas; ³EXOS, Phoenix, Arizona; ⁴Human Performance Lab, University of Connecticut, Storrs, Connecticut; ⁵University of Hartford, West Hartford, Connecticut; and ⁶Midwestern State University, Wichita Falls, Texas

ABSTRACT

Caldwell, AR, Tucker, MA, Butts, CL, McDermott, BP, Vingren, JL, Kunces, LJ, Lee, EC, Munoz, CX, Williamson, KH, Armstrong, LE, and Ganio, MS. Effect of caffeine on perceived soreness and functionality following an endurance cycling event. *J Strength Cond Res* 31(3): 638–643, 2017—Caffeine can reduce muscle pain during exercise; however, the efficacy of caffeine in improving muscle soreness and recovery from a demanding long-duration exercise bout has not been established. The purpose of this study was to investigate the effects of caffeine intake on ratings of perceived muscle soreness (RPMS) and perceived lower extremity functionality (LEF) following the completion of a 164-km endurance cycling event. Before and after cycling RPMS (1-to-6; 6 = severe soreness) and LEF (0-to-80; 80 = full functionality) were assessed by questionnaires. Subjects ingested 3 mg/kg body mass of caffeine or placebo pills in a randomized, double-blind fashion immediately after the ride and for the next 4 mornings (i.e., ~800 hours) and 3 afternoons (i.e., ~1200 hours). Before each ingestion, RPMS and LEF were assessed. Afternoon ratings of LEF were greater with caffeine ingestion the first day postride (65.0 ± 6.1 vs. 72.3 ± 6.7 ; for placebo and caffeine, respectively; $p = 0.04$), but at no other time points ($p > 0.05$). The caffeine group tended to have lower overall RPMS in the afternoon versus placebo (i.e., main effect of group; 1.1 ± 0.2 vs. 0.5 ± 0.2 ; $p = 0.09$). Afternoon RPMS for the legs was significantly lower in the caffeine group (main effect of caffeine; 1.3 ± 0.2 vs. 0.5 ± 0.3 ; $p = 0.05$). In conclusion, ingesting caffeine improved RPMS for the legs, but not LEF in the days following an endurance cycling event.

Address correspondence to Dr. Matthew S. Ganio, msganio@uark.edu.
31(3)/638–643

Journal of Strength and Conditioning Research
© 2016 National Strength and Conditioning Association

638 ^{the}Journal of Strength and Conditioning Research[™]

Athletes may benefit from ingesting caffeine in the days following an arduous exercise bout to relieve feelings of soreness and reduced functionality.

KEY WORDS pain, DOMS, recovery, supplement, hypoalgesia

INTRODUCTION

Novel or unaccustomed exercise, especially when long in duration, can cause microscopic tears in the muscle generally referred to as exercise-induced muscle damage. This leads to soreness anywhere from 1 to 7 days postexercise typically termed delayed-onset muscle soreness (DOMS) (4). Attenuating such soreness after exercise is important to optimize performance for athletes competing in multiday competitive events and/or completing high-intensity training multiple times a week. For strength and conditioning coaches, this can translate to athletes being able to maintain their training volume rather than adjusting training because of DOMS. Furthermore, the pain associated with DOMS can reduce the willingness or ability of individuals to exercise (18) while also reducing their perception of functionality when performing activities of daily living (12,16). Therefore, interventions that attenuate postexercise pain should be examined.

Despite the development of multiple strategies to prevent and reduce DOMS, there is no scientific consensus on the most effective strategy. Caffeine is an ergogenic aid commonly used to improve performance during endurance exercise and is legal to consume under National Collegiate Athletic Association (NCAA) and World Anti-Doping Agency (WADA) standards. Furthermore, a recent Cochrane Collaboration review concluded that caffeine was a healthy adjuvant to nonsteroidal anti-inflammatory drugs (NSAID) in the treatment of acute pain (6). This is likely because caffeine, as an adenosine receptor antagonist, helps block pain perception (17), and may explain why individuals who consume caffeine have reduced pain perception during exercise (7,13,14).

Oral caffeine intake may attenuate DOMS. For example, Maridakis et al. (11), observed reduced perceptions of pain for the 24–48 hours after eccentric quadriceps contractions in young women. This is reinforced by another study also reporting significantly lower muscle soreness 2-d after an exhaustive bout of biceps curls in young men when caffeine was ingested (8). These studies show that with single-joint exercise eliciting DOMS, caffeine is effective in attenuating pain (8,11). Much less is understood about the effect of caffeine on DOMS when whole-body exercise is performed.

The beneficial effects of caffeine on pain perception may be short-lived however, as it is removed from circulation fairly quickly (10). Studies have shown that some effects of caffeine can diminish after only 2–4 hours (19). Most investigations schedule caffeine ingestion 1 hour before exercise (8,11), to maximize blood caffeine concentrations for ergogenic effects *during* exercise or testing. The timing of ingestion postexercise to maximize an effect (e.g., reducing muscle soreness or pain) is not well defined, and has implications for how a strength and conditioning coach would recommend caffeine. It is possible that the primary mode of action of caffeine during recovery is analgesic in nature, such that any reduction in pain is directly related to blood levels of caffeine. Thus, caffeine ingestion should occur on several occasions throughout the day so that decreases in skeletal muscle soreness are maintained. It is also possible that caffeine acts to aid in recovery from exercise secondary to its analgesic effect. If this is the case, it is possible that a dose of caffeine leads to lower soreness levels later, when caffeine levels in the blood are reduced. Given these possibilities, we provided caffeine to subjects in the current study twice a day. Subjects rated muscle soreness once in the morning, before caffeine ingestion (i.e., when blood caffeine levels were low), and once midday (i.e., when blood caffeine levels were high).

Therefore, the purpose of this study was twofold. The first aim was to investigate the effects of caffeine on perceived functionality and soreness following a 164-km cycling event. Our secondary aim was to investigate if hypothesized effects of caffeine only occurred in the few hours after ingesting caffeine, or if the positive effects persisted (when circulating concentrations of caffeine were low), suggesting that caffeine has an effect on the injury-recovery process. Overall, this study could establish the use of caffeine in the management of soreness for athletes recovering from strenuous exercise. We hypothesized that caffeine would significantly reduce perceived soreness and improve lower extremity functionality (LEF) in the days following exercise, but only in the afternoon when caffeine levels were high.

METHODS

Experimental Approach to the Problem

To test our hypotheses healthy, experienced (i.e., prior participation in a 164-km cycling ride) male and female cyclists were recruited to participate in this double-blind,

placebo-controlled, between subjects repeated-measures design study. To examine the effects of caffeine ingestion on soreness and functionality, subjects who completed a 164-km recreational cycle ride were matched for body mass, age, and sex, and were randomly assigned to ingest caffeine or identical looking placebo pills after completion of the ride. To examine the effects of caffeine or placebo ingestion on DOMS and functionality during recovery, subjects continued ingesting caffeine or placebo twice a day, once in the early morning on waking and once at noon, for the next 3 days. Measures of perceived functionality and soreness were obtained before and after the ride, and in the morning and in the afternoon of the 3 subsequent days before ingesting pills. Morning and afternoon measures of functionality and soreness were separated to evaluate if the caffeine dosing schedule effected subjects perception of these 2 variables (see Statistical Analyses).

Subjects

Before participating, all participants were carefully informed about the study and signed an informed consent document that was approved by the local Institutional Review Board. All subjects who participated were adult (18 years or older) men ($n = 25$; 53 ± 10 years) and women ($n = 5$; 46 ± 11 years) who participated in the 2015 Hotter’N Hell Hundred (Wichita Falls, TX; August, 2015) 164-km bicycle ride. Table 1 details the subject characteristics. Before participating, subjects completed a medical history questionnaire, and a 7-day caffeine consumption recall. All subjects had previously completed at least one 164-km cycle ride. Subjects were not naive to caffeine consumption (i.e., mean ~ 230 mg of caffeine per day, equivalent to 1 standard cup of coffee), however subjects volunteered to abstain from their normal habitual caffeine intake for this study. Subjects who reported previous adverse events with caffeine were excluded.

Study Measures

LEF Scale. This questionnaire assesses subjective difficulty in completing 20 separate activities of daily living and exercise (2). On each question, participants rate the difficulty of each task on a 0-to-4 scale where 0 is an inability to perform and 4 is no difficulty completing the activity. This creates

TABLE 1. Subject characteristics.*

	Caffeine	Placebo
Age (y)	52.3 ± 9.2	51.1 ± 11.8
Sex (male/female)	10/2	15/3
Height (cm)	172.7 ± 6.8	171.6 ± 20.7
Body mass (kg)	80.8 ± 13.3	84.8 ± 15.1

*Values are given as mean ± SD.

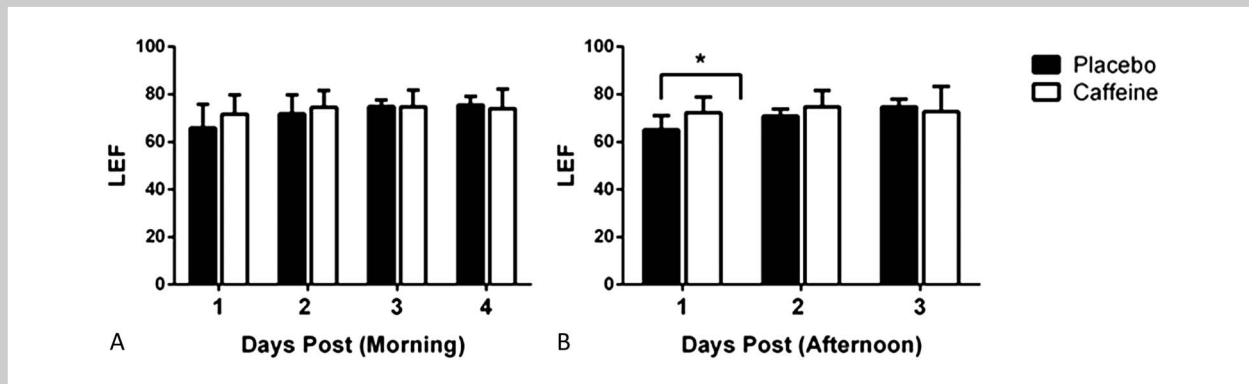


Figure 1. Mean (\pm SD) lower extremity functionality (LEF) when assessed in the (A) morning and (B) the afternoon, *Significant difference $p \leq 0.05$ between conditions.

a composite score of 0-to-80, where 80 equals full functionality. In the context of this study, this scale allowed us to determine if caffeine led to an improved perception of LEF among subjects ingesting caffeine following the 164-km ride. A change in this scale of 9 points or greater is considered clinically significant (2); therefore, only those who had a reduction in functionality of ≥ 9 following the cycling event

were included in the final analysis for LEF (see Statistical Analyses).

Rating of Perceived Muscle Soreness. Subjects were asked to rate their resting overall soreness (RPMS_{OVERALL}) and resting leg soreness (RPMS_{LEGS}) on a 1-to-6 scale, where 1 was the absence of soreness and 6 was severe pain that limited

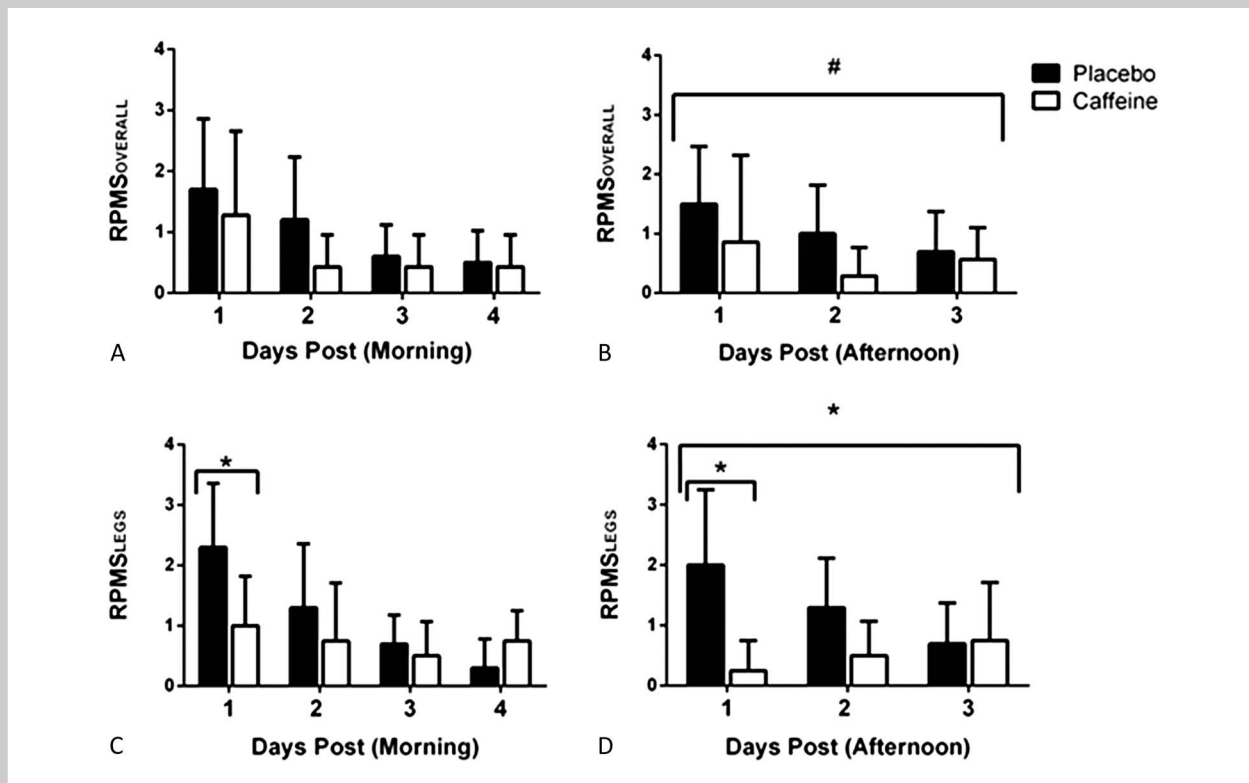


Figure 2. Mean (\pm SD) overall ratings of perceived muscle soreness (RPMS_{OVERALL}) when assessed in the (A) morning and (B) afternoon, and RPMS specifically in the legs (RPMS_{LEGS}) in the (C) morning and (D) afternoon. *Significant difference $p \leq 0.05$ between conditions, #Trend toward significance $p < 0.10$ between conditions. Brackets encompassing multiple days represent a main effect of treatment (see Results for details).

movement (3). Both localized pain, from the working muscles during cycling, and nonlocalized pain can be assessed by these 2 separate scales of soreness. Only those who experienced at least a 1-point increase in soreness were included in the final analysis for RPMS (see Statistical Analyses).

Procedures

Identical caffeine and placebo pills were prepared by a local pharmacy (Collier Compounding, Springdale, Arkansas) and consisted of caffeine anhydrous and inert microcrystallines, respectively. A researcher from a separate institution, who had no interaction with the subjects, coded the caffeine and placebo pills and assigned the proper dosing for each individual. Caffeine pills were packaged in 100 and 20 mg pills. Pills were provided in medical containers that were labeled with each time point of ingestion. Subjects ingested the pills in the mornings 1–4 days postride (700 or 800 hours) and in the afternoons on 1–3 days postride (1200 hours) after being prompted by e-mail and text message.

Immediately before and immediately after the 164-km cycle ride, subjects completed the LEF and RPMS questionnaires. Subjects were instructed to follow their normal dietary patterns during the ride and were not given any recommendations on ride, nutrition, hydration, or other strategies. After completing the postride questionnaires, subjects ingested their first set of pills, and were provided with their respective pill containers for the subsequent days. Subjects were prompted via e-mail and text messages to fill out the electronic questionnaires (i.e., Google Forms) and take the pills on the next 4 mornings and 3 afternoons at the same respective time each day. The fourth morning after the cycling event, subjects filled out 1 last set of questionnaires, but did not ingest caffeine or placebo pills.

Pill ingestion was confirmed on the questionnaires, and if the subjects answered that he or she did not ingest their assigned pills, they were prompted to give an explanation. Any subjects who were unable to continue supplementation were excluded from final data analysis. Subjects were asked about their outside caffeine intake with each questionnaire, and subjects who reported outside caffeine intake over 100 mg per day were excluded from the final analysis. Three subjects, all in the placebo group, reported outside caffeine and were excluded from the final analysis.

Statistical Analyses

Because the aim of this study was to investigate the effect of caffeine on recovery of functionality and improvements in soreness, subjects who did not experience decrements in their perceptual ratings of functionality (≥ 9 point decrease in LEF) or increases in soreness (≥ 1 point increase in RPMS) from before to immediately after the ride were excluded from final analysis. Fifteen subjects were included in the analysis of LEF (placebo = 8, caffeine = 7). A total of 17 subjects were included for RPMS_{OVERALL} (placebo = 10, caffeine = 7), and 14 subjects were included in the final

analysis of RPMS_{LEGS} (placebo = 10, caffeine = 4). To examine our hypothesis that caffeine would only have an effect in the afternoon, morning and afternoon assessments of RPMS and LEF were analyzed separately. Effects of caffeine and placebo on RPMS and LEF over time were assessed with a repeated-measurements analysis of variance with a pairwise Bonferroni correction after applying a between subjects' factor of group assignment. An analysis of covariance was used to adjust for differences in RPMS or LEF at postride (i.e., before caffeine or placebo administration). Data are presented as mean \pm *SD*. Significance was set at a $p \leq 0.05$ and a trend at a $p < 0.10$.

RESULTS

Subjects completed the 164-km cycle ride in 5.73 ± 0.05 hours with an average wet bulb globe temperature of $28.7 \pm 4.7^\circ$ C. During the ride, subjects, on average, ingested 44.0 ± 119 mg of caffeine. During the supplementation period postexercise, subjects in the caffeine group ingested 252 ± 34 mg (i.e., 3.0 mg/kg) at each dosing period.

Functionality

The caffeine group had significantly higher ratings of LEF on the first afternoon postride (i.e., after 24 hours; Figure 1, panel B; $p = 0.04$, but at no other time points or days $p > 0.05$).

Soreness

Morning measures of RPMS_{OVERALL} did not differ between caffeine and placebo groups ($p > 0.10$). However, the caffeine group tended to have lower RPMS_{OVERALL} when measured in the afternoon (i.e., main effect of group, $p = 0.09$; Figure 2, panel B), but there were no significant differences at individual time points ($p > 0.05$).

In the morning of the first day postride, the caffeine group had significantly lower RPMS_{LEGS} (Figure 2, panel C; $p = 0.04$). When measured in the afternoon, there was a main effect of caffeine to lower RPMS_{LEGS} (Figure 2, panel D; $p = 0.05$), and specifically on the first afternoon postride the caffeine group had lower RPMS than the placebo group (Figure 2; $p = 0.02$).

DISCUSSION

We examined the acute effectiveness of caffeine in reducing soreness and increasing functionality and whether these effects persisted 16–18 hours after approximately a 250-mg dose was ingested. After a 164-km cycling ride in the heat, caffeine ingestion significantly lowered leg muscle soreness during the 3 days of recovery. Furthermore, compared with placebo, the subjects consuming caffeine had increased functionality on the afternoon of the day after the ride. This study is in agreement with studies by Marikadis et al. (11) and Hurley et al. (8) demonstrating that caffeine can exert a hypoalgesic effect in individuals experiencing DOMS. However, this study, contrary to the aforementioned studies, used whole-body exercise versus single-joint exercise.

Previous studies have postulated that the adenosine receptor antagonism of caffeine is the primary method by which caffeine decreases pain perception (13). Adenosine receptors are involved in nociception, or the processing of pain stimuli. Further adenosine, a substance that can induce pain signals, is released in large amounts after exercise that produces an inflammatory response (5). When caffeine antagonizes (i.e., blocks) the adenosine receptor, pain signals are diminished because adenosine molecules are unable to bind. Therefore, it is reasonable to hypothesize that lower overall and leg RPMS in the caffeine group (Figure 2) is attributable to adenosine receptor antagonism. However, further research into the mechanisms behind the hypoalgesic effect of caffeine is necessary.

Measures of functionality (i.e., LEF) were assessed using a validated scale previously used by others when investigating recovery (12,16). It could be argued that muscle soreness affects LEF, and LEF may actually be a better measure, compared with RPMS, to determine how DOMS can affect perceived functional capacity across many activities of daily living (12). Specifically, increases in measures of muscle soreness usually occur with concurrent decrease in LEF (12). In the present study, we observed a significant difference in LEF between caffeine and placebo treatment (i.e., at one time point), whereas changes in RPMS were more apparent between treatments (Figures 1 and 2). This “mismatch” may be related to the relatively low RPMS on the first 4 days after the ride in the current study. Therefore, although subjects may have been sore, the level of soreness did not affect their LEF, and in turn caffeine did not have a large effect on LEF.

Similarly, our findings related to the effect of caffeine on RPMS and LEF were mild overall. Most subjects in the present study reported soreness immediately after the exercise bout as “a slight persistent pain.” To maximize any effect of caffeine, we only included individuals in the final analysis if they reported increased soreness or decreased functionality (See Methods). We believe that caffeine would have had a greater effect if larger increases in soreness and/or decreases in functionality had occurred after exercise. That being said, it is quite impressive that even mild levels of soreness were attenuated with caffeine in the days following a long-duration exercise bout (Figure 2). Future research exploring the influence of caffeine on to attenuate DOMS should attempt to replicate these findings using a rigorous muscle-damaging model such as downhill running (15).

The secondary aim of this study was to examine if the hypothesized effects of caffeine only occurred in the few hours after ingesting caffeine, or if the positive effects remained much later (when circulating concentrations of caffeine were low) (9). To test this, subjects in the present study rated their perceived feelings once in the morning, before caffeine ingestion (i.e., when blood caffeine levels were low) and once midday, after the morning ingestion (i.e., when blood caffeine levels were high). Thus, the questionnaires

were completed 16–18 hours and 3–4 hours after the last caffeine ingestion (morning and afternoon assessments, respectively). Morning ratings of LEF and RPMS (Figure 1, panel A; Figure 2, panels A and C) did not differ between caffeine and placebo groups, with 1 exception of $RPMS_{LEGS}$ being lower the first morning postride. This suggests that caffeine has a transient hypoalgesic effect and, although it may reduce soreness (see above), it is unlikely to directly aid in the recovery process of the damaged or sore muscles. Overall, the observed effect of caffeine in this study was seen in reducing soreness, and this effect is transient.

The present study includes some limitations that should be taken into consideration. First, subjects were not caffeine naive before starting the study. This could have dampened the effect of caffeine on these subjects (1), but while enrolled in the study, all subjects abstained from caffeine intake outside the pills they were assigned. This methodological control allowed us to independently test the effect of caffeine on perceived soreness and functionality.

Unfortunately, we do not have information about the subjects’ training history except that all subjects had previously completed at least one 164-km endurance cycling event. We are unaware of any evidence to suggest whether the period of training or training level differentially effects caffeine’s mechanism of action. However, future studies should examine this further.

PRACTICAL APPLICATIONS

Caffeine can be effective in reducing pain and improving functionality following muscle-damaging exercise. Furthermore, caffeine supplementation may be beneficial for those managing soreness following a muscle-damaging event, like a marathon, or unaccustomed stimulus such as starting a new exercise program. For example, it is well known that individuals starting a new exercise plan (e.g., resistance training, plyometrics, running, etc.) are often sore in the days following the initiation of these plans. Our data indicate that athletes can use caffeine consumption as part of their nutritional plan to enhance training and performance. Coaches in the field of strength and conditioning can recommend caffeine ingestion to individuals who are struggling with DOMS during training or competition. Furthermore, coaches should advise athletes to time the ingestion of caffeine to that they maximize the hypoalgesic effect. This should help athletes maintain training load or competitive performance, and reduce complaints about excessive soreness. However, coaches should cautiously advise athletes to maintain caffeine ingestion within those outlined by regulatory agencies such as the NCAA or WADA.

ACKNOWLEDGMENTS

The authors thank Collier Compounding, Springdale, Arkansas for formulating our placebo and caffeine pills. The results of the present study do not constitute endorsement of

caffeine use by the authors or the NSCA. Additionally, the authors thank the wonderful staff at the Hotter’N Hell 100. Without the help of their staff and space provided at the Wichita Falls Convention Center, this study would not have been possible. This study was funded by internal funds (i.e., no external funding was utilized). Laura Kunces, Ph.D. is employed by EXOS. There are no conflicts of interest to report. Source of Funding: Corresponding author’s internal money from the University of Arkansas.

REFERENCES

- Bell, DG and McLellan, TM. Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. *J Appl Physiol* (1985) 93: 1227–1234, 2002.
- Binkley, JM, Stratford, PW, Lott, SA, and Riddle, DL. The Lower Extremity Functional Scale (LEFS): Scale development, measurement properties, and clinical application. North American Orthopaedic Rehabilitation research Network. *Phys Ther* 79: 371–383, 1999.
- Braun, WA and Dutto, DJ. The effects of a single bout of downhill running and ensuing delayed onset of muscle soreness on running economy performed 48 h later. *Eur J Appl Physiol* 90: 29–34, 2003.
- Cleak, MJ and Eston, RG. Muscle soreness, swelling, stiffness and strength loss after intense eccentric exercise. *Br J Sports Med* 26: 267–272, 1992.
- Costa, F, Diedrich, A, Johnson, B, Sulur, P, Farley, G, and Biaggioni, I. Adenosine, a metabolic trigger of the exercise pressor reflex in humans. *Hypertension* 37: 917–922, 2001.
- Derry, CJ, Derry, S, and Moore, RA. Caffeine as an analgesic adjuvant for acute pain in adults. *Cochrane Database Syst Rev* CD009281, 2012.
- Gliottoni, RC, Meyers, JR, Arngrimsson, SA, Broglio, SP, and Motl, RW. Effect of caffeine on quadriceps muscle pain during acute cycling exercise in low versus high caffeine consumers. *Int J Sport Nutr Exerc Metab* 19: 150–161, 2009.
- Hurley, CF, Hatfield, DL, and Riebe, DA. The effect of caffeine ingestion on delayed onset muscle soreness. *J Strength Cond Res* 27: 3101–3109, 2013.
- Kamimori, GH, Karyekar, CS, Otterstetter, R, Cox, DS, Balkin, TJ, Belenky, GL, and Eddington, ND. The rate of absorption and relative bioavailability of caffeine administered in chewing gum versus capsules to normal healthy volunteers. *Int J Pharm* 234: 159–167, 2002.
- Magkos, F and Kavouras, SA. Caffeine use in sports, pharmacokinetics in man, and cellular mechanisms of action. *Crit Rev Food Sci Nutr* 45: 535–562, 2005.
- Maridakis, V, O’Connor, PJ, Dudley, GA, and McCully, KK. Caffeine attenuates delayed-onset muscle pain and force loss following eccentric exercise. *J Pain* 8: 237–243, 2007.
- McBrier, NM, Vairo, GL, Bagshaw, D, Lekan, JM, Bordi, PL, and Kris-Etherton, PM. Cocoa-based protein and carbohydrate drink decreases perceived soreness after exhaustive aerobic exercise: A pragmatic preliminary analysis. *J Strength Cond Res* 24: 2203–2210, 2010.
- Motl, RW, O’Connor, PJ, and Dishman, RK. Effect of caffeine on perceptions of leg muscle pain during moderate intensity cycling exercise. *J Pain* 4: 316–321, 2003.
- Motl, RW, O’Connor, PJ, Tubandt, L, Puetz, T, and Ely, MR. Effect of caffeine on leg muscle pain during cycling exercise among females. *Med Sci Sports Exerc* 38: 598–604, 2006.
- Paulsen, G, Mikkelsen, UR, Raastad, T, and Peake, JM. Leucocytes, cytokines and satellite cells: What role do they play in muscle damage and regeneration following eccentric exercise? *Exerc Immunol Rev* 18: 42–97, 2012.
- Peschek, K, Pritchett, R, Bergman, E, and Pritchett, K. The effects of acute post exercise consumption of two cocoa-based beverages with varying flavanol content on indices of muscle recovery following downhill treadmill running. *Nutrients* 6: 50–62, 2014.
- Sawynok, J. Adenosine receptor targets for pain. *Neuroscience* 338: 1–18, 2016.
- Trost, Z, France, CR, and Thomas, JS. Pain-related fear and avoidance of physical exertion following delayed-onset muscle soreness. *Pain* 152: 1540–1547, 2011.
- Wesensten, NJ, Killgore, WD, and Balkin, TJ. Performance and alertness effects of caffeine, dextroamphetamine, and modafinil during sleep deprivation. *J Sleep Res* 14: 255–266, 2005.