Women Experience the Same Ergogenic Response to Caffeine as Men

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Accepted for Publication: 2 January 2019
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This study was supported by The University of Queensland New Staff Research Start-Up Fund, Grant #2011001239. **Conflict of Interest:** The authors have no declared conflicts of interest. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine.
Abstract

Purpose: This study aimed to determine if 1) consumption of caffeine improves endurance cycling performance in women, and 2) sex differences exist in the magnitude of the ergogenic and plasma responses to caffeine supplementation.

Methods: Twenty-seven (11 women and 16 men) endurance-trained cyclists and triathletes participated in this randomized, double-blind, placebo-controlled, crossover study. Participants completed an incremental exercise test to exhaustion, two familiarization trials and two performance trials. Ninety minutes prior to the performance trials participants ingested opaque capsules containing either 3 mg·kg\(^{-1}\) body mass of anhydrous caffeine or a placebo. They then completed a set amount of work (75% of peak sustainable power output) in the fastest possible time. Plasma was sampled at baseline, pre- and post-exercise for caffeine. Strict standardization and verification of diet, hydration, training volume and intensity, and for women, contraceptive hormone phase was implemented.

Results: Performance time was significantly improved following caffeine administration in women (placebo: 3863±419s, caffeine: 3757±312s; p=0.03) and men (placebo: 3903±341s, caffeine: 3734±287s; p<0.001). The magnitude of performance improvement was similar for women [4.3% (0.4-8.2%); mean (95% CI)] and men [4.6% (2.3-6.8%)]. Plasma caffeine concentrations were similar between sexes before exercise, but significantly greater in women after exercise (p<0.001).

Conclusions: Ingestion of 3 mg·kg\(^{-1}\) body mass of caffeine enhanced endurance exercise performance in women. The magnitude of the performance enhancement observed in women was similar to that of men, despite significantly greater plasma caffeine concentrations following exercise in women. These results suggest the current recommendations for caffeine intake (i.e. 3-
6 mg·kg⁻¹ caffeine prior to exercise to enhance endurance performance), which are derived almost exclusively from studies on men, may also be applicable to women. **Key words:** Exercise Performance; Ergogenic aids; Central Nervous System Stimulants; Physiological Effects of Drugs; Sex differences
Introduction

The ergogenic potential of caffeine on endurance performance tasks lasting approximately 1h has been well documented and summarised in a number of reviews (1, 2). Studies investigating the effects of caffeine on endurance exercise performance have examined the influence of several factors on the ergogenic response including the dose (3), timing (4), environmental conditions (5) and method of ingestion (6). However, these studies exclusively used male participants. Indeed, <10% of the 435 participants from 21 studies included in a systematic review of the effect of caffeine on endurance time trial performance were women (1); whilst in a more recent systematic review of the effect of caffeine-containing energy drinks on physical performance in a variety of sport disciplines, female participants comprised <20% of the total sample of 634 participants (7). Evidently, research inclusive of female participants is warranted.

Results of studies investigating the effect of caffeine on exercise performance in women are mixed, with some studies reporting a significant ergogenic effect of caffeine (3-6 mg·kg\(^{-1}\) body mass; BM) (5, 8-11), whilst others report no effect when the same dose of caffeine was ingested (12-14). Variation in the ergogenic potential of caffeine among studies involving women may be explained, at least in part, by sex hormone status. Previous studies have demonstrated that endogenous and exogenous (e.g. oral contraceptives) female sex hormones have the potential to influence physiological responses to exercise (15-17) and exercise capacity (18, 19). Oral contraceptives, which are used with high prevalence (~50-70%) in young women from Western countries (20, 21), have also been found to affect the metabolism of caffeine following ingestion (22). Whether the reduced caffeine clearance rate in women taking oral contraceptives, and
subsequent increased accumulation of caffeine within the body, influences the ergogenic potential of caffeine has yet to be elucidated.

To date, no studies have directly compared the ergogenic effects of caffeine in women and men using the same exercise protocol. Lane et al. (10) reported similar improvements in cycling time trial performance after caffeinated chewing gum was ingested in groups of men and women. However, the cycling time trial protocol was different between sexes (men were required to cycle ~44 km and women ~29 km). Whilst this data provides some evidence that the ergogenic response may be similar in women and men, the different protocols make direct comparisons between groups problematic. In contrast, two separate studies, one with men (23) and the other with women (24), using the same exercise protocols reported different findings in relation to the dose-response effect of caffeine on rowing performance. Bruce et al. (23) investigated the effects of ingesting 6 and 9 mg·kg\(^{-1}\) BM doses of caffeine or a placebo on the performance of 8 well-trained male rowers in a 2000 m time trial (~7 min duration). These researchers reported a 1.2% improvement in performance with both doses. However, only a high dose (9 mg·kg\(^{-1}\) BM) was found to positively influence performance in women (24). Therefore, it is unclear whether caffeine exerts similar ergogenic effects in women and men.

This study aims to determine whether 1) consumption of caffeine improves endurance cycling performance in women, and 2) sex differences exist in the magnitude of the ergogenic and plasma responses to caffeine. To enable accurate results and comparisons between sexes, this study was conducted in trained, familiarised athletes under stringently controlled testing conditions, including timing of testing, sex hormone status, and hydration and dietary
standardisation procedures. Due to the similarities in both the training status of participants and the mode of exercise (cycling) employed between the current study and the study conducted by Lane et al. (10) it was hypothesized that 1) consumption of caffeine would improve endurance cycling performance in women, 2) the ergogenic effect would be similar between sexes, and 3) women would have higher post-exercise plasma caffeine concentrations compared to men.

Methods

Participants

Twenty-seven endurance-trained cyclists and triathletes (11 women and 16 men) were recruited to participate in this randomized, double-blind, placebo-controlled, crossover study. The inclusion criteria were as follows: (a) aged 18–45 years (b) raced competitively for at least one season; (c) consistently high training volume and intensity for at least the last two months; and (d) self-described satisfactory health status. Women were also required to be regularly taking an oral contraceptive pill for at least three months. Participants were excluded if they reported: (a) current injury or disease state that may affect participation, confirmed by completion of a modified Sports Medicine Australia Pre-Exercise Screening System (25); (b) currently taking diuretics or have been treated with diuretics within the previous 4 weeks; (c) allergies to heparin or latex; (d) donated blood within the previous 3 months; and (e) regular cigarette smoking, cessation within the last six months, or exposure to environmental tobacco smoke. All participants provided written informed consent; the study was approved by the Medical Research Ethics Committee of The University of Queensland and Human Research Ethics Committee of Griffith University, Queensland, Australia.
Pre-trial standardization

A standardized pre-packaged diet was provided for the 24 h preceding each experimental trial for women (180 kJ·kg\(^{-1}\) BM, providing 7 g·kg\(^{-1}\) BM of carbohydrates) and men (200 kJ·kg\(^{-1}\) BM, providing 7.5 g·kg\(^{-1}\) BM of carbohydrates). A pre-exercise meal (40 kJ·kg\(^{-1}\) BM, providing 1.5 g·kg\(^{-1}\) BM of carbohydrates for women; 42 kJ·kg\(^{-1}\) BM, providing 2 g·kg\(^{-1}\) BM of carbohydrates for men) was consumed 2 h before the commencement of each time trial. Dietary analysis software (FoodWorks®, Xyris Software, Australia) and the Nutrition Information Panels of each food item were used to ensure the foods selected for each participant met the carbohydrate and energy intake guidelines (26). Our previous experience has indicated that very high intakes of energy and carbohydrate are not as well tolerated by some women cyclists. Therefore, we aimed for slightly lower intake for women to keep the intake of carbohydrate and energy as consistent as possible within and between participants. To avoid any influence of circadian variance, experimental trials were performed at the same time of the day (mornings) and separated by $\geq$5 days to enable a wash-out period between each session.

On each day of testing, participants confirmed and signed written compliance with the pre-trial study requirements, including: (a) following a hydration protocol to minimise variation in pre-exercise hydration state; (b) following pre-trial dietary requirements involving completion of a food diary and avoiding consumption of substances that potentially affect the metabolism of caffeine for 24 h e.g. cruciferous vegetables, charcoal broiled beef, aspirin and cimetidine; (c) completing the habitual caffeine consumption questionnaire (27); (d) avoiding consumption of caffeine-containing substance/s, vigorous exercise and alcohol within 24 h of testing.
Contraceptive hormone phase

Women were asked to map their oral contraceptive use to indicate when active and inactive pills were consumed throughout the cycle, according to previously published methods (28). In the 4 weeks (i.e. 1 cycle) leading up to and during testing, women were asked to take the oral contraceptive at the same time each day, preferably before 20:00 each night, in order to minimise variability in exogenous hormone concentration at the time of testing. Testing for women taking monophasic and triphasic oral contraceptive formulations occurred in the high hormone phase (between days 15-28 and days 22-28 of the active pill phase, respectively), to optimise consistency of the hormone profile across the monophasic and triphasic pill types. Ovulation testing was performed to confirm cycle control by exogenous hormones. Participants were provided with a home urine ovulation detection kit (Discover ® 7-Day Pregnancy Planning kit, Church and Dwight Australia Pty Ltd.) and instructed to follow the directions on the packaging to perform the ovulation test for seven consecutive days during their cycle, prior to the testing sessions. Negative ovulation results over 7 consecutive days indicated efficacious exogenous control of ovarian hormones.

Preliminary testing

Participants attended the laboratory on three occasions prior to the experimental trials. The first visit involved medical screening, the completion of a habitual caffeine consumption questionnaire and an incremental exercise test to exhaustion on an electromagnetically-braked cycle ergometer (Lode Excalibur Sport, Lode, Groningen, The Netherlands), to determine participants’ individual peak aerobic capacity (\( \dot{V}O_{2\text{peak}} \)) and peak sustainable power output (PPO). The metabolic system’s (Medgraphic Ultima, MGC Diagnostics and Medisoft, USA) gas
analysers were calibrated as per the manufacturer’s instructions using a certified calibration standard gas mixture (BOC gases, Brisbane, Australia). The system pneumotach was also calibrated as per the manufacturer’s instructions using a 3 L calibration syringe (Hans Rudolph Inc., Shawnee, Kansas, USA). Participants began cycling at 100 W (women) and 150 W (men), with 15 W increments every 30 s until volitional fatigue. Expired air was sampled every 15 s and analysed according to the method described by Laursen et al. (29); \( \dot{V}O_2 \)peak was recorded as the highest \( \dot{V}O_2 \) reading averaged over two consecutive readings. Calibration readings were verified after each test. Laboratory visits two and three were familiarisation trials involving the full exercise protocol. Our laboratory has previously shown time trials to be highly reliable (coefficient of variation = 0.9 ± 0.7%) for trained male cyclists following a familiarisation trial (30). Two familiarisation sessions were performed to establish a self-selected warm-up and ensure the accurate calculation of individual linear factors. The participants’ linear factors were determined based on individual PPO and was initially chosen to enable 75% PPO to be achieved at ~100 rpm. The target amount of work was calculated according to the formula: Total work (J) = 0.75·PPO·3600

**Experimental trials**

Each participant completed two time trials, in a random order, under double-blinded conditions. The order of trials was randomized by a person independent from the study using a random number generating process.

Upon arrival at the laboratory, a urine sample was collected and osmolality measured to confirm euhydration using a vapour pressure osmometer (Wescor 5500XR, Logan, UT). If urine
osmolarity was ≥830 mosm, participants were required to consume water and provide a second urine sample before continuing with testing. Height and body mass were measured using a stadiometer (Seca, Birmingham, UK) and electronic scales (A&D Mercury, Pty Ltd, Thebarton, AUS), respectively, for the calculation of body mass index (BMI; kg·m\(^{-2}\)). A venous blood sample (5 mL) was collected from the antecubital vein using a 21 G needle into a lithium heparin-prepared vacutainer by a qualified phlebotomist. Ninety minutes before exercise, participants ingested opaque capsules containing either anhydrous caffeine (3 mg·kg\(^{-1}\) BM; Sigma-Aldrich) or a placebo containing approximately 400 mg of Metamucil\(^\circledR\) (100% psyllium husk fibre).

Participants completed the same self-selected warm up determined during the familiarisation trials in both time trials. Immediately prior to the commencement of the time trial and immediately after the completion of the time trial, additional venous blood samples (5 mL) were collected. Time trials required participants to complete the set amount of work as fast as possible. Subjective ratings of perceived exertion (RPE) and heart rate (HR) (Polar Electro, Kempele, Finland) were recorded after each 10% of total work throughout the time trial. Participants were able to view their HR, cadence and power output for the first 10% of each time trial; the only information available to participants for the remainder of the trial was total work percentage. Participants ingested 3 mL·kg\(^{-1}\) BM of 6% carbohydrate-electrolyte beverage during the warm-up, as well as upon completion of 30% and 60% of the target amount of work. Upon completion of all trials, participants attempted to identify the order of treatment for the trials, rate their confidence with this order and judge which trial they perceived to be their best performance.
Blood analysis

After each venipuncture, vacutainers were placed on ice for <2 h prior to centrifugation at 7000 x g at 5°C for 10 min. Plasma was removed, placed into separate storage tubes and stored at -80°C until later analysis. All samples were analysed for caffeine using an automated reversed-phase high-performance liquid chromatography system as outlined by Desbrow and colleagues (31). The intra-assay coefficient of variation for caffeine was 3.9% (analysis for 84 duplicate samples pooled containing 41 ± 18 μmol·L⁻¹ caffeine).

Statistical analysis

A sample size calculation indicated that to detect a 2% difference in performance (assuming 65 min to complete time trial = 80 s) with a SD of 85 s with alpha of 0.05 and 80% power, 11 participants would be required (paired t-test) (Power and Sample Size Software, Vanderbilt University, TN).

Analyses were performed using SPSS (version 22.0, SPSS, Inc., IL, USA). Normality of distribution for outcome measures was tested using the Shapiro-Wilk test. Where data were not normally distributed (i.e. VO₂peak, PPO, usual caffeine intake and female performance time) data were log transformed and rechecked for normality. Treatment, sex, and treatment x sex differences in performance time, RPE and HR values were analysed using two-way repeated measures analysis of variance. Where significant main effects were observed, pair-wise Bonferroni corrected comparisons were conducted to identify the nature of the differences. Paired sample t-tests were completed to determine whether plasma caffeine concentrations differed pre- to post-exercise for both sexes. Unpaired t-tests were completed to determine
whether there were sex differences in plasma caffeine concentrations. Pearson’s correlation coefficient analyses were completed to determine whether relationships existed between performance time and plasma caffeine concentrations. Significance was set at an alpha level of <0.05. All data are reported as mean ± SD, or median (interquartile range) for nonparametric analyses, as appropriate.

Results

Participant characteristics are presented in Table 1. Analysis indicated that women had significantly lower BM (p < 0.001), BMI (p = 0.014), $\dot{V}O_{2\text{peak}}$ (p = 0.001) and PPO (p < 0.001) compared to men. No significant differences in age (p = 0.318) or usual caffeine intake (p = 0.168) was observed between sexes. All participants included in the analysis confirmed compliance with pre-trial study requirements, including abstinence from substances that influence caffeine metabolism. All testing procedures for women occurred in the high hormone phase (between days 15-28) of the oral contraceptive pill cycle and all women had negative ovulation results throughout testing, demonstrating efficacious control of ovarian hormone fluctuations. Only one woman was taking a triphasic formulation, so no comparisons in the response to caffeine between women taking either monophasic or triphasic contraceptive pills were possible. All participants consumed the carbohydrate-electrolyte beverage during the warm-up and at 30% and 60% of the target amount of work in full.

Performance time

Performance results are displayed in Table 2. Results showed a significant main effect of treatment, with an average performance time improvement of 169 s [$F(1, 25) = 21.91, \ p <$
following caffeine compared to placebo. However, there was no significant main effect of sex [$F(1, 25) = 1.02, p = 0.32$], or sex x treatment interaction [$F(1, 25) = 0.001, p = 0.98$]. Percentage change in performance time was similar ($p = 0.88$) between men ($4.6 \pm 4.2\%$) and women ($4.3 \pm 5.8\%$) (Fig. 1).

**Rating of perceived exertion**

Results showed no main effect of treatment [$F(1, 24) = 0.50, p = 0.49$], indicating RPE did not significantly differ between the caffeine and placebo trials (Table 2). There was also no significant main effect of sex [$F(1,24) = 1.17, p = 0.96$] or a sex x treatment interaction [$F(1,24) = 1.36, p = 0.26$].

**Heart rate**

A significant main effect of treatment was observed, resulting in an average HR elevation of 6 bpm [$F(1/25), 29.21, p < 0.001$] in the caffeine trials compared to placebo (Table 2). There was no significant main effect of sex [$F(1/25), 0.003, p = 0.29$], however, a significant sex x treatment interaction [$F(1/25), 4.66, p = 0.04$] was observed. For men, average HR was significantly higher in the caffeine ($170 \pm 13$ bpm) trials compared to the placebo ($163 \pm 13$ bpm) trials ($t(15) = -5.60, p < 0.001$). There was also a significant difference in average HR between trials ($t(10) = -2.33, p = 0.04$) in women, with the average heart rate being $168 \pm 8.5$ bpm in the caffeine trials and $166 \pm 12.6$ bpm in the placebo trials.
Plasma caffeine concentrations

Pre-exercise plasma caffeine concentrations were not significantly different ($p = 0.41$) between men (22.6 ± 4.7 μmol·L$^{-1}$) and women (19.7 ± 8.5 μmol·L$^{-1}$) (Fig. 2). Post-exercise plasma caffeine concentrations were significantly higher ($p < 0.001$) in women (32.3 ± 4.7 μmol·L$^{-1}$) compared to men (23.0 ± 3.5 μmol·L$^{-1}$). A significant increase in plasma caffeine concentration was observed in women from pre- to post-exercise ($p = 0.008$); no significant difference between pre- and post-exercise caffeine concentrations was observed in men.

No significant relationship was observed between pre- or post-trial plasma caffeine concentration and percentage change in performance time with caffeine (compared to placebo) for women or men (all $p > 0.05$) (Fig. 3).

Blinding success and adverse events

There was no difference between sexes in the success of participant blinding; with 63.6% of women and 62.5% of men correctly identifying their trial. No participant reported adverse side effects during or after each testing session.

Discussion

This is the first study to directly compare the ergogenic response to caffeine using the same exercise protocol in women and men. Consistent with our hypothesis, the results suggest that caffeine enhances endurance cycling performance in women and the magnitude of this performance enhancement is similar to that observed in men. This occurred despite subtle differences in plasma caffeine concentrations and HR responses.
The present study showed that compared to placebo, cycling performance in women was improved by 4.3% when 3 mg·kg\(^{-1}\) BM of caffeine was ingested. This finding is consistent with the study by Lane et al. (10) who found significant improvements in endurance cycling performance in women after consumption of 3 mg·kg\(^{-1}\) BM of caffeine. In trained female soccer players, Lara et al. (32) demonstrated an improvement in the 1) average peak running speed during a sprint test, 2) total number of sprint bouts performed, 3) total running distance, and 4) total running distance covered at >18 km·h\(^{-1}\) with the ingestion of 3 mg·kg\(^{-1}\) BM of caffeine in the form of an energy drink, during a 2 x 40 min (including a 15-min half time) simulated game. In contrast, Anderson et al. (24) found mixed results in the rowing performance of competitive oarswomen, with significant improvements following 9 mg·kg\(^{-1}\) BM but not 6 mg·kg\(^{-1}\) BM of caffeine. Del Coso et al. (33) demonstrated that 3 mg·kg\(^{-1}\) BM of caffeine ingested in the form of an energy drink improved the running pace and increased the distance covered at a running speed of >18 km·h\(^{-1}\) in competitive female rugby players during a match competition. However, the maximal running speed during a repeated sprint test performed after competition was unaffected. Collectively, these studies highlight the variability in the ergogenic response to caffeine in women. The inconsistent outcomes reported among these studies may be due to the variable duration of exercise, or more likely, the potential influence of female sex hormones on performance measures. The present study was the first of its kind to use tight control and verification of sex hormone concentrations across testing sessions in female participants. Therefore, whilst other studies using female participants have reported mixed results, the ergogenic effects of caffeine observed in the current study with trained and familiarized athletes using an ecologically valid protocol under well-controlled experimental conditions, including sex
hormone status, carbohydrate availability and hydration status, suggest that caffeine is able to enhance endurance performance in women.

The present study demonstrated a significant improvement in endurance cycling performance for women (4.6%) and men (4.3%) with 3 mg·kg\(^{-1}\) BM of anhydrous caffeine, compared to placebo. This finding is similar to that of Lane et al. (10) who found between 3-4% improvement in cycling time trial performance in both women and men following 3 mg·kg\(^{-1}\) BM of caffeinated chewing gum compared to placebo. Lane et al. (10) found no sex difference in ergogenic response, however in this study men were required to cycle a greater time trial distance than the women. The results of the present study provide evidence that the ergogenic response of men and women to caffeine is similar when both sexes complete an identical exercise task. Therefore, despite the current recommendations for caffeine use to enhance performance being based almost exclusively on studies involving men (34), the results of the present investigation suggest that these recommendations may also be applicable to women.

Caffeine ingestion has been shown to elicit physiological changes in perceptual responses (RPE) (11), and HR variables (4), which may contribute to subsequent performance improvements (15). Caffeine is a potent adenosine A\(_1\) and/or A\(_2\alpha\) receptor antagonist that can alter perceptual responses during exercise (11). The present study showed no significant change in RPE between placebo or caffeine trials in either sex, despite an improvement in performance time. This suggests the enhancement in endurance performance during the caffeine trials occurred with no concurrent increase in perceptual response. These results support the findings by Astorino et al. (2) who found no significant change in RPE responses between caffeine and placebo trials in
men or women when undertaking a cycle to exhaustion protocol, similar to the protocol used within the current study. In a meta-analysis, Doherty and Smith (11) showed that RPE was likely to be reduced with caffeine ingestion prior to constant load exercise, whereas no difference in RPE between caffeine and placebo trials were observed in exercise to exhaustion protocols. As such, the present results indicate that despite participants performing at a higher intensity in the caffeine trial, their perception of effort did not concurrently increase.

Average HR increased following caffeine ingestion in the present study, in accordance with observations from previous studies (9, 11). The present study demonstrated that the consumption of caffeine elicited a significant increase in average HR values in both men and women. These results are in accordance with those found by Bridge & Jones (9) who demonstrated a mean HR increase of 1.9 ± 0.9 bpm in trained male participants during exercise after ingesting 3 mg·kg⁻¹ BM caffeine. In addition, Lara et al. (32) reported that average HR tended to be higher (~6 bpm) in caffeine trials compared to placebo trials in trained female soccer players, however these differences did not reach statistical significance. As performance time was similar between males and females, and there were no observed sex differences in HR responses, it appears that sex does not influence the effect of caffeine on heart rate.

The metabolism of caffeine is largely dependent on genetics (CYP1A2 isoform of cytochrome P450), with some evidence of downstream enzymatic differences between sexes (35). Supporting our hypothesis, significantly greater post-exercise plasma caffeine concentrations were found in women compared to men in the present study. Given that there was no significant difference in endurance exercise performance between women and men, these results suggest that the
differences in plasma caffeine concentrations did not influence the ergogenic potential of caffeine. This is consistent with Skinner et al. (4), who only demonstrated significantly faster endurance cycling time trial performance when caffeine was administered 1 h prior to exercise, rather than when peak caffeine concentration coincided with the onset of exercise. Therefore, optimizing concentrations of caffeine in the bloodstream may not be related to enhanced performance. Moreover, no significant correlation between the pre- or post-trial plasma caffeine concentrations and the improvement in performance was observed in either sex. Both these results provide further evidence to suggest the ergogenic potential of caffeine is unlikely to be influenced by the relative concentration of caffeine in the bloodstream in either sex.

**Limitations**

This study has several limitations worthy of comment. First, there was no measure of plasma volume, body composition (other than body mass before the time trials) or change in hydration status following the time trials; therefore, we were unable to determine whether differences in plasma volume, fat mass and/or lean mass among participants may have explained the observed differences in plasma caffeine concentrations between sexes following exercise. Second, whilst we matched participants for training volume, competitive history and age, and expected differences between sexes in body composition and exercise performance parameters, the women appear to be less trained than the men. Overall sex differences in VO$_{2}$peak may have influenced the effect of caffeine on performance outcomes, and should be further elucidated. Whilst there were no significant differences in usual caffeine intake between sexes, the mean usual caffeine intake of men was more than double that of women. There is a common assumption that compared to no or low usual caffeine intake, high usual caffeine intake reduces the ergogenic
potential of caffeine, and thus these individuals require greater acute doses of caffeine to maintain the ergogenic effect. However, this assumption is not supported by the available evidence (36), with previous studies suggesting usual caffeine intake does not influence serum caffeine concentrations, nor does it appear to affect the ergogenic potential of caffeine (37-39). The study’s relatively small sample size, in particular the small number of female participants, may have limited the ability to detect statistically significant changes in RPE and HR. Finally, whilst many studies have demonstrated ergogenic effects associated with caffeine ingestion, the possibility of known placebo effects associated with caffeine ingestion (40) must also be considered. Although the treatments were administered in a double-blind manner, the majority of participants (n = 14) correctly identified the placebo trials at the conclusion of the study. Hence there is the potential that the participant’s awareness of an ‘active’ intervention may have influenced subsequent performance. Nevertheless, the performance improvement of 4.3% for women, and 4.6% for men, after caffeine ingestion is somewhat greater than the magnitude of previously documented placebo effects (40).

In summary, this study has shown that caffeine ingestion can enhance endurance exercise performance in both women and men, and the magnitude of this performance enhancement is similar in both sexes. These results indicate that current recommendations for caffeine intake for endurance athletes, which are derived almost exclusively from studies on men only, may also be applicable to women.
Acknowledgements

This study was supported by The University of Queensland New Staff Research Start-Up Fund, Grant #2011001239. We would like to thank Amy Gibson, Hillary Mathison and Emily Neville for their assistance with data collection.

Conflict of Interest

The authors have no declared conflicts of interest. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The results of the present study do not constitute endorsement by the American College of Sports Medicine.
References


Figures

**Figure 1** Percentage change in performance time with caffeine relative to placebo in men and women. Positive values indicate improved performance. Values are mean±SD.

**Figure 2** Plasma caffeine concentrations pre- and post-exercise in men and women. Values are mean±SD. * denotes a significant difference between sexes ($p<0.001$); † denotes a significant difference pre- to post-exercise ($p=0.008$).

**Figure 3** Relationship between pre-trial (A) and post-trial (B) plasma caffeine concentration and percent difference in performance between caffeine and placebo trials. Positive values indicate improved performance with caffeine. Values are mean±SD.
Figure 1
Figure 2

[Diagram showing plasma caffeine concentration (μmol/L) before and after exercise for men and women, with a significant difference indicated.]
Figure 3

Performance Δ with caffeine (%)

Pre-trial plasma caffeine concentration (μmolL⁻¹)

Women
Men

\[ y = 0.1297x, r = 0.2102, p = 0.62 \]

\[ y = 0.0035x, r = 0.90713, p = 0.98 \]
Figure 3b
Table 1 Characteristics of participants undertaking caffeine and placebo cycling time trials

<table>
<thead>
<tr>
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<th>Women (n=11)</th>
<th>Men (n=16)</th>
<th>p-value</th>
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<tr>
<td>Age (years)</td>
<td>29.7 ± 5.3</td>
<td>32.6 ± 8.3</td>
<td>0.318</td>
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<tr>
<td>Body mass (kg)</td>
<td>59.5 ± 9.7</td>
<td>78.5 ± 6.0</td>
<td>0.001*</td>
</tr>
<tr>
<td>Body mass index (kg·m⁻²)</td>
<td>21.9 ± 2.7</td>
<td>24.0 ± 1.3</td>
<td>0.014*</td>
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<td>Usual caffeine intake (mg·day⁻¹)</td>
<td></td>
<td>253.1 ±</td>
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<td></td>
<td>122.1 ± 74.6</td>
<td>227.8 ±</td>
<td>0.168</td>
</tr>
<tr>
<td>Peak aerobic capacity (mL·kg⁻¹·min⁻¹)</td>
<td>51.9 ± 7.2</td>
<td>60.4 ± 4.1</td>
<td>0.001*</td>
</tr>
<tr>
<td>Peak power output (W)</td>
<td>234.9 ± 26.4</td>
<td>375.0 ±</td>
<td>0.001*</td>
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Data presented as mean±SD. * denotes a significant difference between sexes.
Table 2 Performance time, heart rate and rating of perceived exertion outcomes

<table>
<thead>
<tr>
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<th>Women</th>
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<td></td>
<td>Caffeine</td>
<td>Placebo</td>
<td>p-</td>
<td>Caffeine</td>
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<td>Caffeine</td>
<td>Placebo</td>
<td>p-</td>
<td>Caffeine</td>
<td>Placebo</td>
</tr>
<tr>
<td>Performance time (sec)</td>
<td>3757 (3720-4072)</td>
<td>3863 (3771-4320)</td>
<td>0.014</td>
<td>3734±287</td>
<td>3903±341</td>
<td>&lt;0.001</td>
<td>0.321</td>
<td></td>
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</tr>
<tr>
<td>Rating of perceived exertion score a</td>
<td>15.7±1.5</td>
<td>15.5±1.7</td>
<td>0.309</td>
<td>16.1±0.87</td>
<td>16.1±1.04</td>
<td>0.695</td>
<td>0.956</td>
<td></td>
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</tr>
<tr>
<td>Heart rate (beats per min)</td>
<td>168.2±8.5</td>
<td>165.5±10.2</td>
<td>0.042</td>
<td>169.8±12.6</td>
<td>163.4±12.7</td>
<td>&lt;0.001</td>
<td>0.290</td>
<td></td>
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</tr>
</tbody>
</table>

Values are mean±SD or median and interquartile range where appropriate. a n=24