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Caffeine withdrawal and high-intensity endurance cycling performance

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Abstract
In this study, we investigated the impact of a controlled 4-day caffeine withdrawal period on the effect of an acute caffeine dose on endurance exercise performance. Twelve well-trained and familiarized male cyclists, who were caffeine consumers (from coffee and a range of other sources), were recruited for the study. A double-blind placebo-controlled cross-over design was employed, involving four experimental trials. Participants abstained from dietary caffeine sources for 4 days before the trials and ingested capsules (one in the morning and one in the afternoon) containing either placebo or caffeine (1.5 mg/kg body weight/day). On day 5, capsules containing placebo or caffeine (3 mg/kg body weight) were ingested 90 min before completing a time trial, equivalent to one hour of cycling at 75% peak sustainable power output. Hence the study was designed to incorporate placebo–placebo, placebo–caffeine, caffeine–placebo, and caffeine–caffeine conditions. Performance time was significantly improved after acute caffeine ingestion by 1:49 ± 1:41 min (3.0%, P = 0.021) following a withdrawal period (placebo–placebo vs. placebo–caffeine), and by 2:07 ± 1:28 min (3.6%, P = 0.002) following the non-withdrawal period (caffeine–placebo vs. caffeine–caffeine). No significant difference was detected between the two acute caffeine trials (placebo–caffeine vs. caffeine–caffeine). Average heart rate throughout exercise was significantly higher following acute caffeine administration compared with placebo. No differences were observed in ratings of perceived exertion between trials. A 3 mg/kg dose of caffeine significantly improves exercise performance irrespective of whether a 4-day withdrawal period is imposed on habitual caffeine users.

Keywords: Habitual, abstinence, acute dose, impact, ergogenic

Introduction
It is well established that caffeine elicits an ergogenic effect on endurance exercise performance (Doherty & Smith, 2004). Some attempts have been made to determine the optimal conditions of caffeine administration, predominantly focusing on factors such as the source of caffeine (Cox et al., 2002; Graham, Hibbert, & Sathasivam, 1998), the dose of caffeine (Cox et al., 2002; Graham & Spriet, 1995; Kovacs, Stegen, & Brouns, 1998), and the timing of caffeine intake relative to the performance task (Bell & McLellan, 2002; Cox et al., 2002). However, very few studies have investigated the importance of a period of caffeine withdrawal before administering an acute caffeine dose. Habitual caffeine consumption may result in the development of tolerance to the acute effects of caffeine (Robertson, Wade, Workman, Woosley, & Oates, 1981). Regular caffeine consumption can cause changes in the metabolic response to acute caffeine ingestion (Bangsbo, Jacobsen, Nordberg, Christensen, & Graham, 1992; Hetzler, Warhaftig-glynn, Thompson, Dowling, & Weltman, 1994; Van Soeren, Sathasivam, Spriet, & Graham, 1993) and hence may dampen the ergogenic potential of caffeine during exercise (Van Soeren & Graham, 1998). Alternatively, it is possible that performance improvements observed in studies may be a result of a rebound from withdrawal when an acute caffeine dose is administered, rather than a direct ergogenic effect of the caffeine dose. Therefore, it might be expected that caffeine tolerance will influence the outcome of research into the acute ergogenic effects of caffeine. To avoid the influence of caffeine tolerance, experiments investigating the acute effects of caffeine are often designed to include the administration of a withdrawal period preceding the acute caffeine dose. Many studies that have shown improved exercise performance with caffeine intake have imposed 12–48 h abstinence periods prior to administering the
across caffeine dose (as reviewed by Doherty & Smith, 2004), with some evidence suggesting that up to 4 days of withdrawal may be required to re-sensitize the body to the acute effects of caffeine (Fisher, McMurray, Berry, Mar, & Forsythe, 1986). However, in the only study to investigate the impact of an abstinence period on endurance exercise performance, Van Soeren and Graham (1998) demonstrated little impact of a caffeine withdrawal period on subsequent cycling performance.

Six “recreational” athletes who were high habitual caffeine users (761 ± 12 mg · day−1) participated in the study of Van Soeren and Graham (1998). Control of caffeine consumption during the non-withdrawal trials was lacking, with no plasma caffeine sampling completed to ensure compliance to the abstinence period and during non-withdrawal trials the participants were allowed to consume normal (and possibly varied) dietary caffeine up to the morning of the trial. The authors administered a moderate to high acute caffeine dose (6 mg · kg−1 body weight) before the participants completed a time-to-exhaustion exercise model. Time-to-exhaustion type tasks have been considered a less reliable and valid method of measuring endurance exercise performance compared with “time to complete a set amount of work” type tasks due to the high coefficient of variation (Jeukendrup, Saris, Brouns, & Kester, 1996).

Hence, the aim of the present study was to further investigate the effect of an acute moderate caffeine dose (3 mg · kg−1 body weight) on time trial performance following a 4-day controlled withdrawal period, in habitual caffeine consumers. It was hypothesized that caffeine-derived improvements in endurance performance would be greater following a 4-day controlled withdrawal from all dietary sources of caffeine compared with a trial without a caffeine withdrawal period.

Methods

Participants

Twelve well-trained male cyclists and triathletes (age 28.3 ± 5.8 years, weight 80.2 ± 6.6 kg, height 1.83 ± 0.04 m, peak VO2 63.7 ± 7.4 ml · kg−1 · min−1; mean ± s) who were training and/or competitively cycling at least three times a week volunteered to participate in the study. The reported habitual average caffeine intake of participants was equivalent to 240 ± 162 mg · day−1 (range 18–469). All participants were fully informed of the nature and possible risks of the study before providing their written informed consent. The investigation received approval from the Human Research Ethics Committee of Griffith University.

Experimental procedure

Each athlete visited the laboratory on seven occasions. The first visit involved a preliminary test to confirm the participants’ maximal exercise capacity. Each participant performed an incremental test to exhaustion (peak VO2 test) on an electromagnetically braked cycle ergometer (Lode Instruments, Groningen, Netherlands) to determine peak oxygen consumption (VO2) and peak sustainable power output. The peak VO2 test protocol and the methods used for determining peak VO2 and peak power output have been previously described (Desbrow, Minahan, & Leveritt, 2007). Briefly, each test began at 100 W and increased in 50-W increments every 5 min until exhaustion. During the peak VO2 test, which typically lasted between 30 and 35 min, expired air was analysed continuously by a calibrated metabolic measurement system (Medical Graphics, St. Paul, MN, USA).

Following the preliminary test, participants visited the laboratory a further two times to perform familiarization rides, allowing a practice of exercise trial conditions and to establish the individual linear factor used during the time trial. These sessions mimicked the experimental trial procedures with the exception of blood sample collections, and also allowed participants to establish a self-selected warm-up, which was replicated in all of the experimental trials.

Once familiar with the protocol, each athlete then undertook four experimental trials. The treatment conditions involved ingestion of placebo or caffeine for 4 days followed by acute administration of placebo or caffeine on trial day, corresponding to placebo–placebo, placebo–caffeine, caffeine–placebo, and caffeine–caffeine protocols. The trials were completed using a double-blind administration protocol and the four experimental treatments were randomized via an incomplete Latin square design. Participants were provided with two capsules containing either placebo (metamucil®) or a total of 1.5 mg caffeine per kilogram of body weight (provided as 3 mg · kg−1 body weight of caffeine citrate; Professional Compounding Chemists of Australia) for the 4 days preceding the trial and instructed to consume one capsule in the morning with breakfast and one capsule in the afternoon. This was followed by a fifth (test) day of placebo or 3 mg caffeine per kilogram of body weight (provided as 6 mg · kg−1 body weight of caffeine citrate; Professional Compounding Chemists of Australia) given in two capsules and ingested 90 min before completing the exercise test. Standard batch certificate of analysis indicates that the purity of caffeine used in this study was 47.3% in assay for caffeine and 51.4% in assay for citric acid. Each experimental trial
involved a cycling time trial that required participants to complete a set amount of work as fast as possible, equivalent to one hour of cycling at 75% peak power output.

Experimental trials were separated by at least 7 days and were conducted at the same time of the day in a stable laboratory environment (19 ± 2°C, 60–70% relative humidity). Participants were asked to refrain from consuming caffeine-containing substances for the duration of each treatment protocol and a list of products containing caffeine was provided. Participants were also asked to refrain from heavy training in the 24 h before each trial with any light training to be completed before 12.00 h on the day before the experimental trials. Compliance was verbally provided each morning, immediately before the experimental test.

During the 24 h immediately preceding each trial, participants were provided with a prepacked standard diet (energy = 200.2 ± 10.9 kJ · kg⁻¹ body weight, carbohydrate = 7.5 ± 0.4 g · kg⁻¹ body weight). On the morning of the trial, participants were also given an additional meal (energy = 43.3 ± 2.1 kJ · kg⁻¹ body weight, carbohydrate = 2.1 ± 0.1 g · kg⁻¹ body weight) that included a 600-ml commercial sports drink (Gatorade®), fruit bread, jam, and a Power Bar®. Food checklists were used to examine compliance. All dietary preparation and analysis was performed using Foodworks® Version 5.1, 2007 (Xyris Software, Australia) dietary analysis software.

On test day, participants arrived at the laboratory at approximately 05.30 h. On arrival, they were provided with breakfast and allowed 30 min to complete the meal. Immediately after breakfast a blood sample was taken and trial capsules were ingested with a small amount of water. Participants rested in the laboratory before mounting the cycle ergometer at ~07.10 h. A 20-min individually predetermined warm-up, which was replicated in each of the trials, was completed and participants were provided with 3 ml · kg⁻¹ body weight commercial sports drink (Gatorade®) to ingest during this period. A second blood sample was taken immediately after the warm-up and then participants mounted the cycle ergometer to initiate the time trial. The cycle ergometer was adjusted into a pedalling rate-dependent (linear) mode and participants were instructed to begin the testing phase in which they were required to complete a target amount of work as quickly as possible, as described by Jeukendrup et al. (1996). During the experimental trials, participants were provided with 3 ml · kg⁻¹ body weight of sports drink after completion of 30% and 60% of the total required workload. Throughout the time trial, elapsed time, subjective ratings of perceived exertion, and heart rates (Polar Electro, Kempele, Finland) were recorded at completion of each 10% interval of the total workload. Participants were informed of the amount of work completed at each interval but did not receive feedback on power or elapsed time.

At the end of each experimental trial, participants completed a questionnaire consisting of two open-ended statements asking them to identify the treatments received throughout the habituation period and immediately before the experimental trial. A third statement was also included, which asked the participants to report any symptoms experienced that were associated with treatment conditions. On completion of the study and all four experimental trials, participants completed a further questionnaire consisting of three statements, which asked them to again identify the order of treatment for all trials, nominate which treatment and trial they perceived was associated with their best time trial performance, and describe any factors that they believed prevented them from going faster in each of the trials.

A 5-ml blood sample was collected via venupuncture on the morning of day 3 of each treatment protocol after participants had ingested their capsules, to provide an indication of compliance with caffeine abstinence (compliance check #1). The exact timing for blood sample collection varied between participants due to individual scheduling and commitments. However, all sampling was completed between 08.00 and 11.00 h. In addition, 5-ml blood samples were collected following consumption of breakfast (compliance check #2), immediately before exercise, and immediately after the exercise trial. The samples were placed in tubes containing lithium heparin and centrifuged at 3000 rev · min⁻¹ for 10 min. The resultant plasma was stored at −84°C for subsequent analysis of caffeine. The quantitative analysis of caffeine was performed using an automated high-performance liquid chromatography system. These methods have been previously described (Desbrow, Minahan, Grant, & Leveritt, 2009). The calculated standard curves for caffeine were linear in the range from 1.0 to 10 μM and assay coefficients of variation of <5% were obtained for accuracy, repeatability, and intermediate precision studies. Samples preparation was achieved by protein precipitation using the following protocol: 100 μl serum + 300 μl methanol were mixed by vortexing for 30 s. Samples were centrifuged at 14000 rev · min⁻¹ for 30 min before being filtered through a 0.45-μm, 40-mm polytetrafluoroethylene Phenomenex syringe filter prior to injection. Samples of supernatant (25 μl) were injected into the high-performance liquid chromatography system in triplicate. The concentration of caffeine in samples was calculated by extrapolation from the
Statistical analysis

All statistical procedures were performed using SPSS for Windows, Version 17.0 (SPSS Inc., Chicago, IL). Statistical analysis of time-to-completion was conducted using a one-way repeated-measures analysis of variance (ANOVA). Plasma caffeine, heart rate, and ratings of perceived exertion were analysed using a two-way repeated-measures ANOVA. Post-hoc comparisons (Bonferroni) were performed where significant main effects were present. Data are presented as means ± standard deviations and statistical significance was set at $P \leq 0.05$. Cohen-type effect sizes (ES) were calculated for differences in time trial time between treatment protocols.

Results

No exercise was reported during the 18-h period before each trial and all participants verbally confirmed that they had refrained from heavy training in the 24 h before each experimental test.

Figure 1 shows concentrations of plasma caffeine taken on the four occasions throughout each treatment protocol. Complete caffeine abstinence was verbally reported for the 4 days of the withdrawal treatment protocols before each trial. Mean plasma caffeine concentrations were <1.0 µmol L$^{-1}$ on day −2 and following breakfast during the withdrawal treatments, supporting the verbal statements regarding compliance with caffeine withdrawal. Acute caffeine ingestion on test day resulted in significant increases in plasma caffeine concentrations throughout exercise ($P < 0.05$), with no difference between the placebo–caffeine and caffeine–caffeine trials.

The average amount of work completed by participants in each performance trial was $1040.85 ± 74$ kJ. Mean time trial results, average heart rate data, and average power output data for each performance trial are summarized in Table I. No differences in time were observed for caffeine–placebo vs. placebo–placebo and caffeine–caffeine vs. placebo–caffeine trials respectively, indicating no effect of withdrawal on exercise performance. Acute caffeine ingestion resulted in significant improvements in performance compared with placebo regardless of pre-trial treatment with a 3.6% difference between the caffeine–placebo and caffeine–caffeine trials ($P=0.002$, ES = 0.46) and a 3.0% difference between the placebo–placebo and placebo–caffeine trials ($P=0.021$, ES = 0.40). Twenty-one of 24 trials were faster when caffeine rather than placebo was administered on trial day, regardless of the pre-trial treatment condition. Caffeine ingestion resulted in a significantly higher average heart rate compared with placebo regardless of withdrawal, with a difference of $3 ± 1$ beats · min$^{-1}$ between the caffeine–caffeine and caffeine–placebo trials and a difference of $6 ± 2$ beats · min$^{-1}$ between the placebo–caffeine and placebo–placebo trials ($P < 0.05$). The participants’ ratings of perceived exertion increased over time during each exercise trial. There was no significant difference in ratings of perceived exertion between the treatment conditions at any stage throughout the exercise trials ($P > 0.05$). Mean perceived exertion data at the completion of exercise for all treatment protocols are shown in Table I.

Based on responses to the questionnaire regarding pre-trial and experimental trial protocols, a number of symptoms of withdrawal from caffeine were apparent. Only one participant reported having no symptoms during either of the withdrawal trials (placebo–placebo and placebo–caffeine), with the remaining 11 participants reporting symptoms in at least one of the withdrawal protocols (placebo–placebo or placebo–caffeine). Nine participants reported that they had headaches as a symptom, ranging from mild to severe in intensity during the 4-day withdrawal period of trials. In addition, eight participants reported some level of fatigue during the abstinence period, while five participants indicated that they were less focused and unmotivated during the withdrawal period.

In response to the non-withdrawal treatments (caffeine–caffeine and caffeine–placebo), most participants reported experiencing no symptoms, although four participants did report feeling more alert and “not as tired” during the caffeine–caffeine
treatment. The participants generally equated their best performances to having a good rhythm/cadence, being more mentally focused and motivated, and subjective sensations such as having more energy, being more alert, being less fatigued, and an overall sense of “feeling good” during the trial rides. On the other hand, participants reported factors that prevented them from improving their performance during the rides and which may have resulted in slower trial times, including feeling more fatigued, having less energy, and being less motivated when completing the exercise test.

One participant was able to correctly identify the complete order of their treatments at the time they occurred. There was considerable variability between the other participants, with one participant identifying three correct trial orders (caffeine–caffeine, placebo–caffeine, placebo–placebo), four participants identifying two correct trial orders (placebo–placebo, caffeine–caffeine; caffeine–placebo, caffeine–caffeine; caffeine–placebo, placebo–placebo; or placebo–caffeine, placebo–placebo), one participant identifying one correct trial order (caffeine–caffeine), and the remaining five participants unable to identify any of the trial orders in the post-trial guess at the time they occurred. Post-study questionnaires revealed that a further two participants were able to correctly identify the complete treatment order of trials. Six participants correctly identified their fastest time trial.

**Discussion**

To our knowledge, the present study is only the second to examine the impact of a controlled withdrawal period on the effect of acute caffeine administration on endurance exercise performance. The findings of the present study indicate that a 4-day withdrawal period from dietary caffeine has no impact on the ergogenic effect of a 3 mg · kg⁻¹ acute caffeine dose provided 90 min before commencing an endurance cycling task in which carbohydrate was readily available.

The present results are in accordance with the findings of Van Soeren and Graham (1998), who reported that variable periods of short-term withdrawal from dietary caffeine had no effect on the caffeine-induced enhancement of endurance cycling. Van Soeren and Graham (1998) enlisted six recreational athletes to complete a time-to-exhaustion cycle following 0, 2 or 4 days of caffeine withdrawal. In the current study, 12 trained athletes completed a more reliable and valid time trial performance task (Jeukendrup et al., 1996) following a controlled 4-day caffeine withdrawal period. However, taken collectively these results suggest that imposing a caffeine withdrawal period does not influence the ergogenic potential of an acute caffeine dose administered before a high-intensity endurance exercise task.

One explanation for the inability of a withdrawal period to influence the ergogenic potential of caffeine in the present study could be the habitual intakes of participants. Habitual caffeine use results in a tolerance to the effects of acute caffeine administration and it is proposed that at least 4 days of withdrawal from caffeine re-sensitizes an individual to the physiological effects of caffeine (Fisher et al., 1986). Caffeine withdrawal in the present study was associated with headaches, fatigue, loss of focus, and lack of motivation. Juliano and Griffiths (2004) have reported that symptoms such as headache, tiredness/fatigue, decreased energy/activeness, and decreased alertness/attentiveness are frequently described in studies assessing the features of caffeine withdrawal in humans. However, not all participants in the current study reported withdrawal symptoms and in those that did, the symptoms were often only mild in severity. Participants in this study had low to moderate habitual caffeine consumption (240 ± 162 mg · day⁻¹). It is possible that with low to moderate habitual caffeine consumption, the 4-day withdrawal period in this study was not able to elicit a severe enough withdrawal response. This might then explain why the withdrawal period was not able to potentiate the effect of an acute caffeine dose. However, Van Soeren and Graham (1998) enlisted participants that were high habitual caffeine users (761 ± 12 mg · day⁻¹). This suggests that there is no effect of a withdrawal period on the
impact of acute caffeine supplementation, irrespective of the caffeine consumption of habitual users.

Although the treatments were administered in a double-blind design, symptoms experienced may influence the ability of individuals to predict treatment status and knowledge of caffeine intake may influence performance. While many participants in this study reported some symptoms of caffeine withdrawal, it is interesting that only three of the 12 participants were able to correctly identify the complete treatment order of trials. The inability of participants to identify treatment orders suggests that the blinding was successful and that the results were not influenced by any prior knowledge of the treatment.

During exercise, caffeine ingestion resulted in a significant increase in mean heart rate compared with placebo, suggesting that participants were able to work at a higher percentage of their maximal heart rate during the caffeine trials. This is in line with the findings of Kovacs et al. (1998) and Bridge and Jones (2006), who also observed increases in heart rate during caffeine trials compared with placebo. The higher mean heart rate could be attributed to the direct effects of caffeine as a stimulant or the effects of caffeine on central perceptions of effort (Graham, 2001). Despite the increased mean heart rate, there were no consistent trends observed for perceived exertion data between any of the trials, or in relation to withdrawal. This suggests that caffeine enhanced the ability of participants to perform at higher workloads (305 W and 293 W for the caffeine–caffeine and caffeine–placebo trials respectively, $P = 0.004$; 301 W and 291 W for the placebo–caffeine and placebo–placebo trials respectively, $P = 0.009$) without a greater perception of effort. Doherty and Smith (2005) have suggested that this mechanism may explain the ergogenic effect of caffeine on exercise performance. If this was the mechanism responsible for performance improvement in the present study, it is apparent that the 4-day withdrawal period before caffeine administration did not significantly alter the mechanism’s dependent variable.

**Conclusion**

In this study, we investigated the effect of a controlled withdrawal period on the impact of an acute caffeine dose on endurance exercise performance in trained male cyclists. While an acute dose of caffeine enhanced exercise performance, an imposed 4-day withdrawal period from dietary caffeine did not enhance or reduce the effect of a 3 mg · kg$^{-1}$ acute caffeine dose on exercise performance. Therefore, acute caffeine supplementation positively effects exercise performance and provides an ergogenic benefit in regular caffeine users regardless of any withdrawal period.

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**References**


