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Factors influencing serum caffeine concentrations following caffeine ingestion

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ABSTRACT

Objectives: To determine whether differences in training status, body composition and/or habitual caffeine intake influenced serum caffeine concentrations following caffeine ingestion.
Design: Single-blind.
Methods: Trained cyclists/triathletes ($n = 14$) and active ($n = 14$) males consumed 6 mg kg^{-1} anhydrous caffeine. Peak, total and time to peak serum caffeine concentrations were determined from venous blood samples at baseline and 6 time-points over 4 h following intake. Body composition was assessed by dual energy X-ray absorptiometry and habitual caffeine intake by a questionnaire.
Results: Trained cyclists/triathletes had 16% lower peak caffeine concentrations following caffeine ingestion compared to active individuals, although this was not statistically significant ($p = 0.066$). There was no significant difference between trained cyclists/triathletes and active males in total ($p = 0.131$) or time to peak ($p = 0.249$) serum caffeine concentrations. Fat mass was significantly associated with total ($r = 0.427$, $p = 0.038$) but not peak ($r = 0.343$, $p = 0.101$) or time to peak serum caffeine concentration ($\beta = 0.00008$, $p = 0.961$). There were no associations between habitual caffeine intake and peak, total or time to peak serum caffeine concentrations.
Conclusions: Following caffeine ingestion three findings from the study were evident: (1) endurance-trained athletes trended towards lower peak caffeine concentrations compared to active males; (2) higher fat mass was associated with higher concentrations of caffeine in the blood over 4 h, and (3) habitual caffeine intake does not appear to influence serum caffeine concentrations. Identification of the optimal conditions to ensure peak availability of caffeine within the blood and/or overcoming some of the variation in how individuals respond to caffeine requires consideration of the training status and body composition of the athlete.

1. Introduction

Most investigations examining the potential for caffeine to improve exercise performance have used a dose of 3–6 mg kg^{-1} caffeine, that is administered 1 h pre-exercise based on the assumption that (i) peak circulating levels are achieved 1 h following ingestion, and (ii) performing exercise whilst at peak levels will provide the greatest ergogenic benefit.[1–3] Studies that have investigated larger doses of caffeine (≥9 mg kg^{-1}) have reported evidence of potential side effects, including impaired reaction time, alertness, gastrointestinal distress, dizziness, anxiety, irritability and an inability to concentrate, which may negate any stimulatory effect of caffeine on performance.[4–6] Moreover, consumption at such high doses may be difficult to achieve through dietary sources or energy drinks. Therefore, the identification of the smallest ergogenic dose for athletic populations is important, however this may vary between individuals if caffeine metabolism is influenced by many different factors. Balogh et al.,[7] reported a distribution of variance in caffeine elimination of 21.4% for within-individual variations and 78.6% for between-individual variations. These reported within- and between-individual variations compare reasonably well with similar studies[8,9]. Thus, identification of factors with the potential to influence caffeine absorption, its appearance and subsequent clearance in the blood may, in part at least, overcome some of the variation in how individuals respond to caffeine intake.

There is some support within the literature for the existence of differing responses to caffeine with training status, including increased resting metabolic rate and epinephrine release[10] and swimming velocity[11] in trained versus untrained individuals. Collomp et al.,[11] investigated the influence of specific training on

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performance benefits from 250 mg caffeine (~4.3 mg kg^{-1} body mass) supplementation; an ~3% significant improvement in 100 m swimming velocity was reported in trained swimmers (n = 7) but not untrained swimmers (n = 7) following caffeine ingestion.[11] Whether differences in training status also result in subsequent variations in concentrations of caffeine in the blood following caffeine ingestion is yet to be investigated.

Individual variations in fat mass (FM) and fat-free mass have been suggested to contribute to the diverse absorption and appearance rates of several drugs, including caffeine.[12,13] A hepatically metabolised drug, caffeine's highly lipophilic nature permits transportation to various areas of the body and can affect several physiological systems.[14] Of the numerous studies that have examined caffeine and performance, only one[13] has compared dosage relative to body composition; obese individuals (>30% body fat; n = 3) had significantly higher absorption rates, lower elimination rates and longer serum half-life than lean (<15% body fat; n = 3) participants. The small sample size was a limitation of the study; however, caffeine dosing models that are based on total body mass, irrespective of body composition, may provide less consistent serum caffeine responses among participants and potentially more variability in the ergogenic response. This is important as greater variability in the ergogenic response makes it harder to detect subtle differences in studies with relatively small participant numbers.

It has also been suggested that chronic caffeine ingestion may dampen the erogenic effect of caffeine on exercise due to stimulation and up-regulation of the CYP1A2 system, adenosine receptors and/or receptor mediated activity.[15] Frequent high-dose caffeine intake may result in rapid desensitisation, which in turn, requires the need for even higher doses to elicit an effect.[6] Bell and McLellan[16] reported caffeine had a greater and longer lasting effect on performance in non-users (<50 mg week^{-1}) compared with users (≥300 mg day^{-1}); the overall magnitude of the ergogenic effect (measured as time to exhaustion) was 19% for users and 28% for non-users. In contrast, Tarnopolsky and Cupido[17] and Wiles et al.,[18] failed to find any relationship between caffeine habits and performance when investigating muscle force development and 1500 m running capacity, respectively. Neither Tarnopolsky and Cupido[17] or Wiles et al.,[18] measured caffeine concentrations in the blood, making comparisons among caffeine habit studies difficult. Therefore, individual adjustment of the dosage in the context of habitual intake may be important to athletic performance, however the research to date is inconclusive.

The purpose of the present study was to investigate the relationships between training status, body composition and habitual caffeine intake with serum caffeine concentrations. It was hypothesised that trained athletes would have higher peak serum caffeine concentrations following caffeine ingestion compared with active individuals. It was also hypothesised that higher serum caffeine concentrations would be found in (i) participants with higher FM, and (ii) individuals who habitually consume lower concentrations of caffeine in their diet. Affirmation of these hypotheses would allow future studies and practical applications of caffeine dosing to contribute to reduced individual variation and improved consistency and optimisation of ergogenic effects.

2. Methods

Trained male cyclists and triathletes (n = 14) and active males (n = 14) aged 18–40 years volunteered to participate in the study. The following eligibility criteria were used for the trained male cyclists/triathletes: (a) high maximal aerobic power (VO_2max >60 mL kg^{-1} min^{-1}); (b) cycled competitively for >1 season; and (c) consistently trained at high volume and intensity for >6 months. The active male participants were required to meet physical activity guidelines (>150 min week^{-1}) but not be currently nor previously involved in regular, high volume and/or intensity endurance training. Participants were excluded from the study if they reported any current disease state that may affect participation, were currently being treated with a diuretic, had donated blood within the previous 3 months, smoked cigarettes regularly or had quit smoking in the last 6 months, or were regularly exposed to environmental tobacco smoke.

Participants were required to: (a) consume a high carbohydrate meal the night before testing; (b) fast overnight (≥12 h); (c) refrain from caffeine consumption (including substances that potentially affect the metabolism of caffeine e.g. cruciferous vegetables, charcoal broiled beef, aspirin and cimetidine) and alcohol for 48 h; and (d) maintain a hydrated state. In addition, participants were required to abstain from high intensity physical activity for 24 h prior to each trial with light training permitted until midday on the day prior to testing. The research study was approved by an ethics committee of The University of Queensland (approval project #2010000074) and all participants provided informed consent.

On arrival at the laboratory, a urine sample was collected and osmolality was measured using a vapour pressure osmometer (Wescor 5500XR, Logan, UT) to assess hydration status. Participants completed the Active Australia Self-Report Physical Activity Measure,[19] a modified Sports Medicine Australia screening questionnaire and a caffeine consumption questionnaire. Prior to administration of the individually-filled caffeine capsules (6 mg kg^{-1} anhydrous caffeine) (Sigma–Aldrich) blood was sampled for the measurement of serum caffeine concentration to ensure compliance. Venous blood was subsequently sampled from an antecubital vein at 30, 60, 90, 120, 180 and 240 min following caffeine consumption. During the 4 h caffeine profiling period, 250 mL h^{-1} of water was provided to participants. Following the caffeine profiling, participants completed a graded cycle ergometer test on an electronically-braked cycle ergometer (Lode Excalibur Sport, Lode B.V., Groningen, Netherlands) to confirm that the maximal aerobic power (VO_2max) of the trained cyclists/triathletes was comparable with previous studies involving highly trained endurance athletes. VO_2max was recorded as the highest VO_2 reading averaged over two consecutive readings. The order of testing was chosen to minimise inconvenience to the participants whilst avoiding any influence of exercise on the main outcome, caffeine concentrations.

Blood samples were allowed to clot in 1.3 mL serum tubes (Sarstedt micro tube z) then centrifuged at 5500 × g at 4 °C for 10 min. Serum was removed and placed into separate 0.6 mL storage tubes. Each serum sample was frozen at −80 °C until later analysis. Serum samples were analysed according to the protocol previously described by our laboratory.[20] The intra-assay coefficient of variation (CV) for caffeine was 4.6% (analysis of 20 duplicate samples pooled containing 35 ± 17 μmol L^{-1} caffeine).

Height and body mass were measured for determination of body mass index (BMI). Bone mineral-free lean mass (LM), FM and % body fat was derived by dual energy X-ray absorptiometry (DXA, Hologic QDR Discovery, MA, USA). The DXA operator was blinded to group allocations. Two participants were unwilling to participate in the DXA scanning. The CV in our laboratory for LM, FM and % body fat are 0.3, 0.9 and 0.9%, respectively.

Data were analysed using Microsoft Excel 2007 and SPSS (version 15.0, SPSS, Inc., IL, USA). Normality of the distribution for outcome measures was tested using the Kolmogorov-Smirnov test. Analyses included standard descriptive statistics, Pearson correlation, independent t-tests, and analysis of covariance to examine the differences between groups for peak and total caffeine concentrations controlling for age. Partial correlation was undertaken to examine the relationships between peak and total serum