Marginal Effects of a Large Caffeine Dose on Heat Balance During Exercise-Heat Stress

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The use of caffeine supplements in athletic and military populations has increased in recent years. Excessive caffeine consumption in conjunction with exercise in a hot environment may predispose individuals to heat illness. **Purpose:** To examine heat balance induced by a large dose of caffeine during exercise in a hot environment. **Methods:** Ten men, not heat acclimated and not habitual caffeine users, consumed either caffeine (CAF; 9 mg/kg) or placebo (PLA) before performing cycle-ergometer exercise for 30 min at 50% VO\textsubscript{2peak} in a 40 °C, 25% relative humidity environment while body temperature (core and skin) and ratings of thermal comfort (TC) were monitored. Heat-exchange variables were calculated using partitional calorimetry and thermometry. **Results:** Mean body temperature ($T_b$) was higher ($p < .05$) with CAF (37.18 ± 0.15 °C) than with PLA (36.93 ± 0.15 °C) at the start of exercise. Heat production was slightly higher (~8 W, $p < .05$) with CAF. There were no differences in heat storage, dry heat gains, TC, or $T_b$ during exercise. **Conclusions:** A caffeine dose of 9 mg/kg does not appreciably alter heat balance during work in a hot environment. The small increase in $T_b$ observed with CAF was undetected by the participants and is unlikely to increase physiological strain sufficiently to affect endurance performance or risk of heat illness.

**Keywords:** body temperature, thermoregulation, epinephrine

Caffeine is a central-nervous-system stimulant found in ordinary foods and beverages. It is also a popular additive to energy drinks, energy gels, and chewing gums targeted toward athletes and U.S. military personnel, for whom caffeine is one of the most commonly used dietary supplements (Lieberman, Stavinoha, McGraw, & Sigrist, 2008; Maughan, Depiesse, & Geyer, 2007). Although caffeine is among few recognized legitimate ergogenic aids (American College of Sports Medicine, 2009), it does not appear to enhance exercise performance in a hot environment (Del Coso, Estavez, & Mora-Rodriguez, 2008; as reviewed in Ely & Cheuvront, 2010) unless combined with other known ergogenic aids such as carbohydrate-electrolyte beverages (Cureton et al., 2007). It is even possible that augmented heat production associated with caffeine use (Lin, Chandra, & Liu, 1980) might contribute to the absence of an ergogenic effect or even increase the risk of heat illness. Athletic training, competition, and present-day military conflicts often occur in very hot environments, and the risk and incidence of heat illness remain a serious threat to the optimal health and performance of both populations (Carter et al., 2005; Howe & Boden, 2007; Lee-Chiong & Stitt, 1995; Numneley & Reardon, 2002). It is unknown whether heavy caffeine use among those exposed to hot environments affects their susceptibility to heat illness.

Several studies have investigated the effects of caffeine on thermal responses to temperate and warm environments and found that caffeine doses of 5–7.5 mg/kg did not produce significant changes in core body temperature during exercise when the air temperature was less than 30 °C (Andersen & Hickey, 1994; Daniels, Mole, Shaffrath, & Stebbins, 1998; Dunagan, Greenleaf, & Cisar, 1998; Falk et al., 1990). Caffeine doses as high as 10 mg/kg, although not altering core body temperature during exercise in a temperate environment (21 °C), have been noted to lower skin temperatures, possibly as a result of peripheral vasoconstriction driven by enhanced epinephrine release (Dunagan et al., 1998). Peripheral vasoconstriction in a hot environment could potentially interfere with heat loss, increase core body temperature, and increase individual susceptibility to heat illness. However, Stebbins, Daniels, and Lewis (2001) reported that active vasodilation may override caffeine’s vasoconstrictor activity at moderate doses (6 mg/kg) during exercise in hotter environments (35 °C). It remains unsettled whether more extreme caffeine intakes such as those that produce a positive National Collegiate Athletic Association (NCAA) urine drug test (15 μg/ml) or those associated with adverse effects such as nausea, nervousness, headache, or “jitters” (Fredholm, Battig, Holmen, Nehlig, & Svartau, 1999; Lamarine, 1994) would alter this outcome in hotter environments. The amount of dietary caffeine necessary to produce these effects varies with an individual’s size, metabolism, and urine output (Birkett & Miners, 1991) but is in the range of 10 mg/kg (Fredholm et al., 1999;
Lamarine, 1994). Caffeine intakes in this range were previously banned by the International Association of Athletics Federations, but the caffeine restriction (12 μg/ml urine) in drug testing was lifted in 2003.

The purpose of this study was to examine gross body-temperature changes and heat balance of individuals given a single, large dose of caffeine during exercise in a very hot, dry environment. The testing of a large caffeine dose, just below the threshold for adverse affects and NCAA drug-testing compliance, in the most susceptible, non-heat-acclimated, and caffeine-naïve volunteers is a worst-case-scenario test of caffeine’s potential to increase thermal strain. We hypothesized that caffeine would not significantly alter heat balance or heat strain and thus impart no additional risk of developing heat illness.

Methods

Subjects

Volunteers were provided informational briefings and gave voluntary, informed written consent to participate. Investigators adhered to AR 70–25 and U.S. Army Medical Research and Materiel Command Regulation 70–25 on the use of volunteers in research, and the appropriate institutional review boards approved this study. Ten men, not heat acclimated and not habitual caffeine users (mean ± SD: age 23 ± 6 years, body mass 77.5 ± 10 kg, height 178 ± 6 cm, body fat 12% ± 7%; range: age 23 [18–37] years, body mass 77.5 [64.2–94.8] kg, height 178 [169–188] cm, body fat 12% [7–19%]) volunteered for this study. Subjects were healthy, with no history of heat illness, and moderately fit (peak oxygen uptake [VO2peak] 45.2 [40.5–55.2] ml · kg⁻¹ · min⁻¹).

Volunteers consumed low to moderate amounts of caffeine on an irregular basis as determined using a caffeine-intake questionnaire (mean daily caffeine intake of 64 [11–109] mg/day). Although volunteers did not consume caffeine on a daily basis and were therefore unlikely to be habituated to its effects, caffeine abstinence was required for a 4-day washout period before testing (Fisher, McMurray, Berry, Mar, & Forsythe, 1986). Volunteers were asked to refrain from heavy physical activity and alcohol consumption for 24 hr before testing. They consumed either caffeine (9 mg/kg body mass; 585–855 mg caffeine for 65- to 95-kg individuals) or placebo (microcrystalline cellulose) with a standardized breakfast 90 min before exercise. The study treatments were double-blind and counterbalanced and separated by 5–14 days. All experiments were conducted at the same time of day to control for circadian fluctuations in body temperature and other biological variables.

Preliminary Testing

VO2peak was measured in all volunteers using an incremental protocol on a cycle ergometer (Lode Excalibur Sport, Lode, Groningen, The Netherlands) with continuous gas-exchange measurements (True-Max, Parvo-Medics, Sandy, UT). Subjects cycled at approximately 60 rpm while workload was increased 20 W every minute until volitional fatigue. The workload for constant-load cycling was calculated based on the VO2peak test and validated during 2 weeks of familiarization sessions to elicit 50% of VO2peak. During the 2 weeks preceding the study, nude body mass (WSI-600, Mettler Toledo, Columbus, OH, accuracy ±50 g) and urine specific gravity (USG; 1110400A TS Meter, AO Reichert Scientific Instruments, Buffalo, NY) were measured each morning to determine a reliable baseline euhydrated body mass for each subject.

Experimental Testing

Volunteers consumed 2.0 L of carbohydrate-electrolyte beverage the night before each testing session. Nude body mass and first-void USG were obtained the morning of the testing session after an overnight fast to ensure that subjects began the trials in a euhydrated state (USG < 1.02, body mass ± 1% of baseline; American College of Sports Medicine et al., 2007). Baseline blood samples were taken and analyzed for plasma epinephrine and caffeine to confirm compliance with 4-day caffeine abstinence. Volunteers then consumed a standardized meal consisting of four small energy bars (total energy = 557 kcal; 78% carbohydrate, 18% fat, 4% protein) and several gelatin-coated capsules with ~500 ml water. The capsules delivered either USP anhydrous caffeine (9 mg/kg body mass) or microcrystalline cellulose. Each capsule was formulated (Compounded Solutions in Pharmacy, LLC, Monroe, CT) to contain 5–200 mg of caffeine for precision dosing.

One hour after meal consumption, volunteers had a second blood sample taken and were instrumented for measures of heart rate (Polar a3, Polar Electro Inc, Woodbury, NY), mean weighted skin temperature (YSI, Yellow Springs, OH; Ramanathan, 1964), and rectal temperature via a telemetric temperature sensor (Jonah core body temperature capsule, Mini Mitter Inc., Bend, OR) inserted 8–10 cm beyond the anal sphincter (Keneffick et al., 2009). They then entered the testing environment (40 °C, 25% relative humidity) and, after fully instrumented assessment of body mass, remained seated for a 20-min stabilization period. At the completion of the stabilization period, they performed 30 min of constant-load cycle ergometry at 50% VO2peak intensity. The combination of work and environmental heat loads was selected to produce a hot but compensable heat stress (Gagge & Gonzalez, 1996) analogous to both slow-paced desert maneuvers (military) and competitive exercise in cooler environments (athletes). Drinking was not permitted during exercise. Instrumented body mass was measured again immediately after steady-state-exercise completion and used to estimate whole-body sweat losses. Sweat volume was determined from the change in body mass, assuming that 1 ml of sweat was equal to 1 g of lost mass, expressed per unit of time (L/hr). VO2, expired ventilation, and respiratory rate were assessed after the initial 15 min of steady-state exercise using an automated system (TrueMax, ParvoMedics, Sandy, UT). All other physiological measures were recorded at 5-min intervals. Ratings of thermal comfort were also measured.
every 5 min using a continuum scale between the verbal anchors comfortable and unbearably hot. Immediately after exercise, a third and final blood sample was taken.

Mean body temperature ($T_b$) was calculated (Gagge & Gonzalez, 1996) using .9 and .1 as weighting coefficients for rectal temperature and mean weighted skin temperature. Heat storage was calculated using thermometry rather than calorimetry because of calorimetry’s inability to precisely measure evaporative sweat losses ($E_{sk}$) and thus solve the equation for heat storage. Instead, the solution to $E_{sk}$ was derived after applying a correction to thermometric heat storage (Snellen, 1966). Any remaining error compared with calorimetry (Jay et al., 2007) was assumed equal between trials. Heat production and dry heat exchange were calculated for each subject using classical partitional calorimetry. Sweat evaporative efficiency was calculated from the ratio of $E_{sk}$ to measured sweat rate, expressed as a percentage. All equations used are described in detail elsewhere (Gagge & Gonzalez 1996).

**Blood Analysis**

Venous blood samples were collected from a superficial antecubital vein after an overnight fast (baseline) after volunteers had been quietly seated for a 15-min stabilization period with arm position standardized. This sample was drawn immediately after the first morning body mass and urinary measurement. The second 10-ml sample was drawn 1 hr after breakfast and caffeine or placebo pills had been ingested, and subjects were again seated quietly for 15 min before sample collection. The third 10-ml sample was drawn immediately postexercise, while the volunteer remained seated on the cycle ergometer.

Plasma caffeine levels were determined from blood collected in a no-additive tube and held on ice for 30 min before centrifugation and freezing. Analysis was performed using a Beckman Coulter DXC 600 Pro and EMIT reagents for caffeine (Dade-Behring Diagnostics, Deerfield, IL). An additional vial of blood was collected in a heparinized tube and frozen for analysis. The blood was analyzed for epinephrine using high-performance liquid chromatography. Caffeine and epinephrine analyses were performed by Pennington Biomedical Research Center (Baton Rouge, LA).

**Statistics**

Group comparisons between caffeine and placebo for heat balance and metabolic variables were made using paired $t$ tests. A two-way repeated-measures ANOVA was used to determine any Group × Time interactions for body temperature and perceptual ratings during exercise. $F$ values were corrected for sphericity where appropriate, and Tukey’s post hoc tests were used when main or interaction effects were observed. A sample size of 10 volunteers was large enough (Tran, 1997) to detect meaningful differences in physiological variables, defined a priori as an effect size (signal-to-noise ratio) >1.0. All data are reported as mean ± SD. Significance was accepted at $p < .05$.

**Results**

Subjects were euhydrated (morning nude body mass within 1% of baseline, first-void USG ≤ 1.02) and compliant with the 4-day caffeine abstinence before the start of each testing day. Baseline body mass, USG, and starting plasma caffeine levels are summarized in Table 1. Peak plasma caffeine levels were reached postexercise in the caffeine group (14.1 [8.2–19.5] μg/ml plasma) and corresponded with an estimated urine concentration of 10.8 (6.3–15.0) μg/ml urine (Birkett & Miners, 1991), at or below the threshold for NCAA drug-testing compliance. As expected, plasma caffeine levels did not change over the course of the placebo trial.

Despite identical exercise workloads (118 ± 12 W) between trials, $VO_2$ was significantly higher with caffeine (1.81 ± 0.14 L/min) than with placebo (1.77 ± 0.14 L/min), primarily driven by an increased expired ventilation in the caffeine group (49.6 ± 5.0 vs. placebo 46.0 ± 5.9 ml/min; $p < .05$). As a result, the percentage of $VO_2$peak during exercise was also slightly but significantly higher in the caffeine group (52% ± 2% vs. placebo 51% ± 2%; $p < .05$). There were no differences in respiratory rate between treatments (caffeine 25.7 ± 5.4, placebo 24.7 ± 5.3 breaths/min, $p > .05$). Heat production was 260 W/m² during the caffeine trial and 253 W/m² during the placebo trial. Therefore, heat production was ~3% higher with caffeine than with placebo ($p < .05$), principally because of the higher $VO_2$ (Gagge & Gonzalez, 1996). All heat-balance data are detailed in Table 2. Sweating rate (and

### Table 1 Summary of Baseline Hydration Status and Compliance With Caffeine Abstinence

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<thead>
<tr>
<th></th>
<th>Caffeine</th>
<th>Placebo</th>
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<tr>
<td>% baseline body mass</td>
<td>+0.6 ± 1.1</td>
<td>+0.4 ± 1.0</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>1.013 ± 0.007</td>
<td>1.016 ± 0.006</td>
</tr>
<tr>
<td>Plasma caffeine (μg/ml)</td>
<td>0.1 ± 0.1</td>
<td>0.1 ± 0.1</td>
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### Table 2 Summary of Heat-Balance Calculations and Mean Body-Temperature Changes in Caffeine and Placebo Trials During Exercise

<table>
<thead>
<tr>
<th></th>
<th>Caffeine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat production (W/m²)</td>
<td>260.2 ± 29.0*</td>
<td>252.6 ± 25.4</td>
</tr>
<tr>
<td>Heat storage (W/m²)</td>
<td>77.2 ± 6.8</td>
<td>76.6 ± 11.5</td>
</tr>
<tr>
<td>Dry heat gain (W/m²)</td>
<td>24.7 ± 1.8</td>
<td>25.7 ± 2.8</td>
</tr>
<tr>
<td>Evaporative heat loss (W/m²)</td>
<td>207.7 ± 30.3</td>
<td>201.7 ± 37.1</td>
</tr>
<tr>
<td>Evaporative efficiency (%)</td>
<td>81.1 ± 13.8</td>
<td>83.7 ± 7.7</td>
</tr>
<tr>
<td>Δ$T_b$ (°C)</td>
<td>0.60 ± 0.10</td>
<td>0.59 ± 0.15</td>
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*Significantly different ($p < .05$) than placebo.
therefore also efficiency) could only be determined for 9 subjects because of measurement error; all other data represent measures from all 10 subjects. Dry heat gain and heat storage did not differ between caffeine and placebo conditions over the 30 min of exercise (Table 2). Sweating rates were modest (caffeine 0.73 ± 0.10 L/hr; \( p > .05 \)), and evaporative cooling and efficiency were similar between treatments.

\( T_b \) and thermal comfort increased similarly with both caffeine and placebo throughout the 30 min of exercise (Figure 1). \( T_b \) was higher at the start of the caffeine trial (37.18 ± 0.15 °C) than with placebo (36.93 ± 0.15 °C) and remained elevated by ~0.25 °C throughout exercise (\( p < .05 \); main effect of treatment; Figure 1[B]). The change in \( T_b \) over the 30 min of exercise was not different between trials (mean [95% CI] caffeine: 0.60 [0.54–0.66] °C; placebo: 0.59 [0.50–0.68] °C). The difference in \( T_b \) between trials for each volunteer (\( T_b \) caffeine – \( T_b \) placebo) was also nonsignificant (mean = 0.01, effect size = 0.08, 95% CI = –0.08 to 0.10) and well within biological variability and equipment sensitivity. Note that thermal comfort also did not differ between groups at any time point (Figure 1[A]). Thus, subjects did not perceive the small elevation in \( T_b \) during the caffeine trial.

Heart rates were similar across time and averaged 75% ± 6% and 76% ± 6% of estimated maximum heart rate during exercise in the caffeine and placebo trials, respectively. Baseline epinephrine values were low (54 ± 58 pg/ml), and no differences were found between treatments. Plasma epinephrine was elevated pre- and postexercise in the caffeine trial (mean [range]: 48 [18–133] pg/ml preexercise to 206 [63–536] pg/ml postexercise) compared with placebo (mean [range]: 27 [14–53] pg/ml preexercise to 117 [28–242] pg/ml postexercise, \( p < .05 \)). The fourfold magnitude of increase in plasma epinephrine pre- to postexercise was similar between groups.

**Discussion**

Caffeine is among the most widely used supplements in athletic (Maughan et al., 2007) and military populations (Lieberman et al., 2008) and is generally recognized as safe in doses <10 mg/kg (Committee on Military Nutrition Research & Institute of Medicine, 2001). The primary finding of this investigation is that in the unlikely situation that a non-heat-acclimated, nonhabitual caffeine user consumed 9 mg/kg caffeine before or during exercise in a hot, dry environment, only minor shifts in heat balance would occur. A 9-mg/kg dose of caffeine increased basal body temperature, oxygen consumption, and heat production during moderate continuous work in a hot environment compared with placebo. The increased basal body temperature was marginal and was not perceived by volunteers. In addition, the increase in body temperature of 0.25 °C is well within the day-to-day variability of core body temperature (<0.30 °C; Consolazio, Johnson, & Pecora, 1963).

The small but significant upward shift in mean \( T_b \) (+ 0.25 °C) at rest in the caffeine trial persisted over the course of the 30-min exercise bout (Figure 1B). This shift was likely the result of an increased resting energy expenditure (REE) during the 90 min between caffeine administration and testing. A 7–16% increase in REE has been previously reported for caffeine doses ranging from 5 to 10 mg/kg (Acheson et al., 2004; Acheson, Zahorska-Markiewicz, Pittet, Anantharaman, & Jequier, 1980; Engels, Wirth, Celik, & Dorsey, 1999). Heightened sympathetic nervous activity (evidenced by elevated epinephrine levels after caffeine administration) may account for the increased REE, the 2% increase in VO\(_2\), and the increased ventilatory response with caffeine (Acheson et al., 2004; Powers, Dodd, Woodyard, & Mangum, 1986; Robertson et al., 1978). The magnitude of VO\(_2\) increase with caffeine at fixed workloads was similar to that found in previously published work (Engels et al., 1999). Although statistically significant, the practical importance of this increase in VO\(_2\) is marginal.

The intentional use of non-heat-acclimated and nonhabitual caffeine users likely exacerbated any deleterious effects of caffeine in the heat (Nunneley & Reardon, 2002; Fisher et al., 1986). The average caffeine intake in the United States is considerably higher than in our subjects (average intake in U.S. intake 106–170 mg/day versus ~64 mg/day in our subjects; Knight, Knight, Mitchell, & Zepp, 2004), and competitive athletes and military personnel may have even higher intakes. A higher habitual caffeine intake would blunt the caffeine response (Fisher et al., 1986); therefore, the increased metabolic heat production seen in the current study would likely be even smaller.
Note that caffeine appeared in no way to interfere with dry heat gains or evaporative heat losses. Although skin blood flow was not measured in this study, the similar dry heat gains between caffeine and placebo trials are in direct agreement with previous findings (Stebbins et al., 2001). There is also evidence that caffeine could even augment temperature regulation, either directly or indirectly, by stimulating sweat-gland activity through elevated epinephrine levels (Sato, 1977). Although epinephrine levels were higher with caffeine than placebo during exercise, whole-body sweating rates and evaporative efficiency were similar between treatments. It remains possible that elevated epinephrine levels could enhance the onset or sensitivity of the local sweating response but go undetected by gross measures of whole-body sweating. Careful investigation of a local sweating response may better elucidate caffeine-induced shifts in sweating and determine whether the ample evaporative capacity of a hot, dry environment allows body heat storage to remain in balance. In contrast, the added basal heat load from caffeine administration might simply be small enough that ordinary heat-loss effector responses were sufficiently robust to balance heat gain, resulting in no net differences in whole-body heat storage. Considering the accumulating evidence that moderate and habitual caffeine intakes do not increase the risk of fluid and electrolyte imbalances (Armstrong et al., 2005), the consumption of caffeine at levels of 9 mg/kg or less should be considered safe in hot, dry environments.

**Conclusion**

A large caffeine intake (9 mg/kg), given as an acute dose to non-heat-acclimated, caffeine-naïve volunteers, increased body heat production at rest and during exercise in a hot, dry environment. However, the magnitude of the increase in heat production was small and heat losses appeared unaffected. As a result, elevations in mean body temperature were marginal, physiologically unimportant, and unlikely to predispose athletes or military personnel to an increased risk of heat illness.

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**References**


