Performance and metabolic responses to a high caffeine dose during prolonged exercise

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The present study examined whether a high caffeine dose improved running and cycling performance and altered substrate metabolism in well-trained runners. Seven trained competitive runners [maximal O_2 uptake (VO_2max) 72.6 ± 1.5 ml·kg⁻¹·min⁻¹] completed four randomized and double-blind exercise trials at ~85% VO_2max; two trials running to exhaustion and two trials cycling to exhaustion. Subjects ingested either placebo (PL, 9 mg/kg dextrose) or caffeine (CAF, 9 mg/kg) 1 h before exercise. Endurance times were increased (P < 0.05) after CAF ingestion during running (PL 49.2 ± 7.2 min, CAF 71.0 ± 11.0 min) and cycling (PL 39.2 ± 6.5 min, CAF 59.3 ± 9.9 min). Plasma epinephrine concentration [EPI] was increased (P < 0.05) with CAF before running (0.22 ± 0.02 vs. 0.44 ± 0.08 nM) and cycling (0.31 ± 0.06 vs. 0.45 ± 0.06 nM). CAF ingestion also increased [EPI] (P < 0.05) during exercise; PL and CAF values at 15 min were 1.23 ± 0.13 and 2.51 ± 0.33 nM for running and 1.24 ± 0.24 and 2.53 ± 0.32 nM for cycling. Similar results were obtained at exhaustion. Plasma norepinephrine was unaffected by [CAF] at rest and during exercise. CAF ingestion also had no effect on respiratory exchange ratio or plasma free fatty acid data at rest or during exercise. Plasma glycerol was elevated (P < 0.05) by CAF before exercise and at 15 min and exhaustion during running but only at exhaustion during cycling. Urinary [CAF] increased to 8.7 ± 1.2 and 10.0 ± 0.8 µg/ml after the running and cycling trials. These data demonstrate that CAF in high doses increases [EPI] and endurance performance during both running and cycling in elite runners, while urinary [CAF] is below the level accepted by the International Olympic Committee. However, it is unclear whether the enhanced endurance performance was due to increased fat utilization and muscle glycogen sparing.

THE WORK OF Costill and colleagues (9, 12, 16) has provided the major support for the theory of a positive ergogenic effect of caffeine ingestion during endurance exercise. They proposed that the effect is achieved by an elevation in catecholamines enhancing fat oxidation [either by increasing free fatty acid (FFA) mobilization or muscle triacylglycerol lipolysis]. This in turn would spare muscle glycogen, resulting in a prolonged time to exhaustion. The hypothesis remains unproven, and the subsequent research has produced conflicting results.

In the early studies from Costill's laboratory, only Esig et al. (12) were able to demonstrate significantly elevated [FFA] before exercise. Plasma [FFA] were elevated 1 h after caffeine ingestion in some of the more recent studies (6, 12, 24, 27, 28, 30) and unchanged in others (11, 19, 34). The failure to consistently demonstrate an increase in [FFA] may be due to increased uptake by the active muscle. However, many of these studies also found no change in respiratory exchange ratio (RER).

Although studies have frequently speculated that a key aspect of the response to caffeine ingestion is an elevation of plasma catecholamines, they have rarely been measured. In addition, as with other aspects of the response to caffeine, the few results are conflicting. Fisher et al. (13) reported increases in plasma norepinephrine and dopamine after 60 min of exercise after caffeine ingestion, while [FFA] were elevated and RER was lower only after 15 min of exercise. Tarnapolsky et al. (30) found no effect of caffeine on epinephrine, norepinephrine, and RER response during 90 min of exercise, although plasma [FFA] were elevated at 0 and 60 min. Recently, Graham et al. (15) found that caffeine selectively increased plasma epinephrine and [FFA] during mild prolonged exercise in the cold but had no effect on RER. Thus the performance, endocrine, and metabolic effects of caffeine ingestion and the validity of the hypothesis stated above are uncertain.

In an attempt to account for the confusion in this area, Conlee (8) recently listed a number of experimental factors that are important in these studies, including caffeine dose, type of exercise, exercise intensity, preexercise feedings, subject training status, previous caffeine use, and individual variation. Variation in these factors and/or failure to control for these factors may be responsible for the controversial results reported in this body of literature.

The hypothesis of this study was that a high dose of caffeine would elevate plasma epinephrine concentration at rest and during exercise but would not alter substrate utilization or enhance endurance performance during running and cycling in trained competitive runners.

METHODS

Subjects. One female and six male volunteers served as subjects for the experiment. All were well-trained distance runners, 19–38 yr old [28.3 ± 2.3 (SE) yr] with a weight of 56–83 kg (67.2 ± 3.4 kg). The average personal best for the group for 10 km of running was 31 min 36 s ± 36 s and 2 h 33 min ± 3 min for the five runners who had completed a marathon. The experimental procedures and possible risks of the study were explained to each subject both verbally and in writing. All subjects gave...
their informed consent, and the experiment was approved by the University's Ethics Committee.

Preexperimental protocol. Each subject reported to the laboratory on two occasions several days apart before the start of the experiment. On each day an incremental maximum \( \dot{V}_O_2 \) uptake test (\( \dot{V}_O_2 \text{max} \)) was performed either on a treadmill or cycle ergometer. After 30 min of rest, subjects exercised for 10–15 min at a power output designed to elicit \( \sim 85\% \dot{V}_O_2 \text{max} \). Mean \( \dot{V}_O_2 \text{max} \) values on the treadmill and cycle ergometer were 72.6 \( \pm \) 1.5 and 61.9 \( \pm \) 2.7 ml \( \cdot \) kg\(^{-1} \) \( \cdot \) min\(^{-1} \), respectively.

Subjects then reported to the laboratory four times, separated in most cases by 1 wk. For a given subject all trials were conducted at the same time of day. Each subject ran to exhaustion on two occasions and cycled to exhaustion on the other two occasions, after ingestion of either a placebo or caffeine (9 mg/kg body wt). The four trials were randomized and double blind. One subject did not participate in the cycling trials. The subjects were instructed to maintain their normal training programs throughout the duration of the study, and most incorporated the weekly test into their training program as a hard workout.

Caffeine consumption habits were not considered in the selection of subjects, inasmuch as elite running status was the major criterion for inclusion in the study. Two runners were definite caffeine users (450–720 mg/day), three consumed the equivalent of one cup of coffee per day (120–150 mg), and two were nonusers (\( \sim 20 \) mg/day). The subjects were asked to refrain from caffeine consumption in the 48 h preceding each trial.

Subjects were not asked to fast before the trials as in most previous studies, because this is not typical prerase preparation. They were instructed to eat in preparation for each trial as they would for a race. All subjects maintained proreal food diaries and consumed diets high in carbohydrate content that were similar before all trials in every subject. This was confirmed by analysis of all diets for total caloric content and carbohydrate consumption (10). This ensured that muscle, blood, and liver carbohydrate stores were optimal.

Experimental protocol. Before each trial subjects gave a urine sample and a catheter was placed percutaneously into a medial antecubital vein and a saline drip was started to maintain catheter patency. A resting blood sample was obtained, and subjects then consumed 9 mg/kg placebo (dextrose) or caffeine in capsule form along with water. One hour after ingestion of the capsules a second resting blood sample was taken and exercise began. Subjects ran or cycled to exhaustion at \( \sim 85\% \dot{V}_O_2 \text{max} \). Blood and expired gas samples were taken every 15 min and at exhaustion. All blood samples were taken when the subject was still exercising. During the trials, subjects were given no external cues regarding the duration of exercise and were verbally encouraged to exercise to exhaustion in all trials. A second urine sample was obtained within 15 min of completion of each trial. Before leaving the laboratory subjects completed a questionnaire asking if they believed they had received placebo or caffeine or could not tell and on what they based their answer. The results of the trials were not disclosed to the subjects or the investigators until completion of the entire study.

Analyses. Expired gas samples were analyzed for fractions of \( O_2 \) and \( CO_2 \) with an Applied Electrochemical S-3A \( O_2 \) analyzer and Sensor Medics LB-2 \( CO_2 \) detector, respectively. Expired volume was determined with a Parkinson-Cowan volumeter. The analyzers were calibrated with gases of known concentrations, previously determined by micro-Scholander technique. The volumeter was calibrated with a Tissot spirometer.

Blood samples were immediately separated into two aliquots; 3 ml were transferred to a nontreated tube for serum, and 7 ml were transferred to a sodium heparinized tube. Hematocrit was immediately measured in triplicate from the latter tube by use of high-speed centrifugation. Hemoconcentration occurred in all exercise samples, but there was no difference between caffeine and placebo trials. A 100-\( \mu \)l aliquot of heparinized blood was added to 500 \( \mu \)l of 0.3 M perchloric acid. A solution containing 120 \( \mu \)l of 0.24 M EGTA and reduced glutathione was then added to the remaining heparinized whole blood.

The EGTA- and glutathione-treated plasma was analyzed in duplicate for epinephrine and norepinephrine concentration by high-performance liquid chromatography (Waters) as described by Weiker et al. (32). The whole blood acid extracts were analyzed enzymatically in triplicate for lactate and glucose as described by Bergmeyer (3). Serum was analyzed enzymatically in triplicate for FFA (22) and glycerol (14).

Pre- and postexercise urine samples were analyzed by high-performance liquid chromatography HPLC at the National Institute of Scientific Research (Pointe-Claire, Quebec). This center is the Canadian center for doping control and is accredited by the International Olympic Committee (IOC).

Statistics. Statistical analysis of the data was complicated by the fact that each subject exercised for a different duration during running and cycling. Therefore, complete data sets were obtained only at -60, 0, 15, and 30 min and at exhaustion for placebo and caffeine trials during running (\( n = 7 \)) and cycling (\( n = 6 \)). Resting data during the running and cycling trials were analyzed for time (-60 vs. 0 min) and treatment (placebo vs. caffeine) effects by analysis of variance. Significant interactions between time and treatments were tested with a Duncan's multiple range test. Paired \( t \) tests were used to determine whether significant differences existed between placebo and caffeine variables at 15 and 30 min and at exhaustion in both the running and cycling trials. Significance was accepted at \( P \leq 0.05 \), and all data are means \( \pm \) SE.

RESULTS

The ingestion of 9 mg of caffeine per kilogram of body weight 1 h before exercise produced significant increases in exercise time to exhaustion. Running time to exhaustion increased from 49.2 \( \pm \) 7.2 min during the placebo trial to 71.0 \( \pm \) 11.0 min during the caffeine trial. Similar times for cycling to exhaustion were 39.2 \( \pm \) 6.5 min after placebo and 59.3 \( \pm \) 9.9 min after caffeine. Every subject increased exercise time to exhaustion during the caffeine trial both during running and cycling (Fig. 1).

Urinary caffeine concentrations after running and cy-
2294 PERFORMANCE AND METABOLIC RESPONSES TO CAFFEINE INGESTION

The RER at 15-30 min of exercise was 0.85-0.86 during placebo and 0.83-0.89 during caffeine (Table 1). Similar values at exhaustion were 0.84-0.86 and 0.83-0.88. Caffeine ingestion increased the plasma epinephrine concentration at rest and during running and cycling by approximately twofold (Fig. 2). In the placebo exercise trials, epinephrine concentration was constant during the 60 min of rest at ~0.25-0.30 nM and increased to ~1.25 and 1.70-2.00 nM at 15 min and exhaustion, respectively. In the 60 min after caffeine ingestion, plasma epinephrine concentration increased significantly from ~0.20-0.30 to ~0.45 nM. Exercise levels were also significantly greater after caffeine: ~2.50 nM at 15 min and ~4.10-4.60 nM at exhaustion.

There were no major effects of caffeine on plasma norepinephrine concentration (Fig. 3). Resting plasma [FFA] at rest or during exercise (Fig. 4). There were trends for a higher [FFA] at rest after caffeine, but large individual variation precluded significance. Resting plasma [glycerol] increased significantly during rest in both the running and cycling caffeine trials (Fig. 5). However, glycerol also increased significantly at rest in the cycling placebo trial. During running, plasma [glycerol] was significantly elevated at 15 min and at exhaustion after caffeine ingestion. In the cycling caffeine trial, a significant difference occurred only at exhaustion.

The ingestion of caffeine 1 h before running or cycling had no major impact on whole blood levels of glucose or lactate (Table 2). Blood lactate was significantly elevated in the cycling caffeine trial compared with placebo at all time points except exhaustion. In addition, blood lactate increased during the 60 min of rest before cycling in the placebo and caffeine trial.

<table>
<thead>
<tr>
<th>%VO₂_max</th>
<th>Running (n = 7)</th>
<th>Cycling (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>30 min</td>
<td>Exh</td>
</tr>
<tr>
<td>PL</td>
<td>81.1 ±1.9</td>
<td>84.5 ±1.9</td>
</tr>
<tr>
<td>CAF</td>
<td>79.1 ±2.3</td>
<td>84.1 ±2.0</td>
</tr>
<tr>
<td>RER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL</td>
<td>0.85 ±0.02</td>
<td>0.85 ±0.01</td>
</tr>
<tr>
<td>CAF</td>
<td>0.83 ±0.03</td>
<td>0.84 ±0.01</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjs. VO₂ max, maximal O₂ uptake; RER, respiratory exchange ratio; PL, placebo; CAF, caffeine; Exh, exhaustion.
PERFORMANCE AND METABOLIC RESPONSES TO CAFFEINE INGESTION

The trained runners were also tested on a cycle ergometer to determine whether differences between exercise modalities existed. Costill et al. (9) first reported an ergogenic effect of caffeine as trained cyclists exercised 20% longer at 80% \( \text{VO}_2\text{max} \) after the ingestion of 4.7 mg/kg of caffeine. A second study from the same laboratory reported a 7% increase in total work performed over 2 h of cycling at \( \sim 70\% \text{VO}_2\text{max} \) (16). Since this early work, only one field study involving skiing (2) and one laboratory study with runners (27) have substantiated the ergogenic effect of caffeine during prolonged endurance activities. However, two additional studies were unable to demonstrate a performance-enhancing effect during prolonged running (28) and cycling (5) in the laboratory. The enhanced performance in the present study is consistent with the above studies that measured improved time to exhaustion during cycling, running, and skiing at \( \sim 80\% \text{VO}_2\text{max} \) with control trial durations of 40–75 min (2, 9, 27). However, the magnitude of the performance increase was greater in the present study (44–51%) than in the earlier studies (2–32%), possibly because of the higher caffeine dose in this study (9.0 vs. 4.7 7.0 mg/kg). The results of the present study also demonstrated that the ergogenic
tent, refraining from caffeine intake 48 h before each trial, and incorporating the exercise trials into their weekly training as heavy workouts. The trained runners

The two major findings of the present study were the dramatic increases in exercise endurance performance and plasma epinephrine concentration after caffeine ingestion. Every subject exercised longer after caffeine ingestion during both the running and cycling trials. The magnitude of the ergogenic effect was large, being between 28 and 156% in all but one subject (Fig. 1). A high caffeine dose (9 mg/kg) was used in this study to maximize the chance for ergogenic performance and metabolic effects and to produce urinary caffeine levels just below the acceptable limits for competition as outlined by the IOC.

In addition to a high caffeine dose, the present study was also designed to control for a number of experimental factors that may have contributed to the controversial findings reported in the caffeine literature (8). A specific population of well-trained competitive runners was chosen as subjects because they were accustomed to exercising to exhaustion at high power outputs (85% \( \text{VO}_2\text{max} \)) in a competitive environment. Many previous studies used exercise intensities that were lower than experienced during competitive situations. The subjects also prepared for the exercise trials as if they were competitions by consuming pretrial diets high in carbohydrate con-
PERFORMANCE AND METABOLIC RESPONSES TO CAFFEINE INGESTION

The lack of a significant increase in plasma [FFA] in the present study is consistent with the results of Weir et al. (33), but this did not dampen the ergogenic effects of caffeine.

Other than the increase in performance time, the most striking finding of this study was the large caffeine-induced increase in plasma epinephrine, independent of norepinephrine. It is well documented that caffeine ingestion causes a specific elevation in epinephrine at rest (1,15,20,21,26), and it has been assumed to occur during exercise. Graham et al. (15) recently found a modest increase in epinephrine with caffeine ingestion (5 mg/kg) by noncaffeine users during mild exercise in the cold. In contrast, Tarnapolsky et al. (30) found no epinephrine response with a protocol similar to the present one: 6 mg/kg caffeine ingestion followed by 1 h of treadmill running at 80% \( \dot{V}O_2 \) max. The reason for the difference may be the lower dose in their study and/or the fact that their subjects consumed caffeine up until the day of the test, whereas our subjects had no caffeine for 48 h before testing.

The caffeine-induced rise in plasma epinephrine is independent of norepinephrine, suggesting that the caffeine is acting on the sympathetic nervous control of the adrenal medulla rather than generally increasing the activity of the sympathetic nervous system. It is known that the rise in plasma norepinephrine during exercise is

Effect of caffeine was independent of the exercise modality because all subjects exercised longer on the bicycle and treadmill after caffeine ingestion. Earlier investigations suggested that caffeine may have an ergogenic effect during cycling but not during running (6,19). However, these studies did not measure performance, and their conclusions were based on measurements of plasma substrate during exercise.

Fisher et al. (13) previously reported that 4 days without caffeine magnified the effects of caffeine in habitual users. The improved endurance in the present study was independent of habitual caffeine use, inasmuch as the two subjects who consumed 450–720 mg of caffeine per day responded in the same manner as the other five who consumed either 120–150 or <20 mg/day (Fig. 1). This may have been influenced by the users refraining from caffeine ingestion for 48 h before each trial.

Weir et al. (33) speculated that carbohydrate loading may negate the ergogenic effect of caffeine by dampening its fat-mobilizing effect, although they did not measure performance. They reported that 3 h after a carbohydrate meal (including 6.5 mg/kg caffeine), plasma [FFA] was attenuated when subjects were carbohydrate loaded vs. not carbohydrate loaded. The subjects in the present study loaded with carbohydrate-rich foods in the days and hours preceding the trials as they would for competitions. In spite of this, a very significant ergogenic effect was demonstrated in the present study, which may be related to the higher caffeine dose.

FIG. 4. Plasma free fatty acid (FFA) concentrations (means ± SE) during running (n = 7) and cycling (n = 6) to exhaustion after placebo or caffeine ingestion.

FIG. 5. Plasma glycerol responses (means ± SE) during running (n = 7) and cycling (n = 6) to exhaustion after placebo or caffeine ingestion. *Significantly different from placebo. †Significantly different from −60 min.
a reflection of the sympathetic discharge to the vascular bed of the active muscle (7, 29), and caffeine does not appear to influence this system. It may stimulate the adrenal medulla directly by enhancing the Ca\textsuperscript{2+} release (25) or indirectly via the central nervous system.

The increase in epinephrine concentration is a reflection of increased secretion rather than clearance (18). The caffeine effect was present at rest, but its stimulation of epinephrine secretion was greatly amplified during exercise. Others have also observed that epinephrine secretion during exercise is more sensitive when a second stimulus such as hypoglycemia, hypoxia, or hypercapnia is present (17, 31).

The results of the metabolic data were much less consistent than the endurance times and catecholamines. Portions of the metabolic data suggest that aspects of fat metabolism were enhanced after caffeine ingestion, but the data are equivocal. Plasma [FFA] increased at rest in both the running and cycling trials, but individual variation precluded any significant effects. Despite the high doses of caffeine, the FFA results in the present study are typical of the unpredictable responses found in many previous studies (6, 13, 19, 24, 28, 30). In three of the earlier studies reporting an ergogenic effect of caffeine (9, 16, 27), only Sasaski et al. (19) found a significant increase in [FFA] before exercise after caffeine ingestion. Plasma glycerol levels were elevated at rest and during exercise at 15 min and exhaustion after caffeine ingestion in the running trials but only at exhaustion in the cycling trials. Again these findings appear typical, inasmuch as some previous studies report caffeine-induced increases in plasma glycerol (9, 24) and others do not (16, 19).

It must be stated, however, that FFA measurements on blood taken from peripheral arm veins are not conclusive for assessing whether extramuscular fat oxidation was increased after caffeine ingestion. Plasma concentrations are a function of entry and removal from the plasma pool, and unchanging plasma levels do not rule out the possibility that turnover has increased. Studies with arterial and venous [FFA] and blood flow measurements across exercising muscle or FFA turnover studies are required to unequivocally determine whether increased extramuscular FFA uptake occurs after caffeine ingestion. A small increase in FFA uptake would translate into a significant change in substrate utilization due to the large energy yield of fat. In addition, as reported by Essig et al. (12), intramuscular FFA utilization increases after caffeine ingestion and may contribute more significantly than extramuscular FFA to enhanced fat oxidation. Their results suggest that caffeine may also exert a direct effect on the hormone-sensitive triacylglycerol lipase found in skeletal muscle, because it is believed to be responsible for the mobilization of endogenous FFA (23).

Examination of our RER data does not assist in understanding the metabolic events, inasmuch as no consistent changes with caffeine ingestion were found. The lack of significant changes is in agreement with many studies (6, 11, 19, 30) but at odds with others where a decreased RER was reported (9, 12, 16, 27). In the present study the correlation between pulmonary RER and muscle respiratory quotient must be questioned. At 85% VO\textsubscript{2max}, there may be disturbances in acid-base balance and the CO\textsubscript{2} stores may not be in a steady state. Thus a small shift in respiratory quotient may not be reflected in the RER when exercising at this intensity.

Furthermore it is unknown whether the proposed glyco- gen-sparing effect occurs throughout the exercise period. The only studies to examine the effect of caffeine ingestion on muscle glycogen used moderate nonexhaustive exercise and only reported data pre- and postexercise (11, 12). The data of Essig et al. (12) suggest that the glyco- gen-sparing effect occurs within the initial 30 min when exercising at 65–75% VO\textsubscript{2max}. It is known that muscle glycogenolysis is most rapid during the initial minutes of exercise (4), and thus even a transient reduction in the rate at this time could result in considerable glycogen sparing. If a transient reduction in glycogenolysis occurred in the caffeine trials, it may be unrealistic to expect significant RER differences between placebo and caffeine trials beyond 15–30 min of exercise in the present study, inasmuch as the rates of carbohydrate and fat utilization may not be different.

Although this study has resulted in performance and plasma epinephrine effects that are more distinct than previous investigations, it has not elucidated the nature of the underlying metabolic events. It is tempting to suggest that epinephrine is a key factor, and indeed it may be. However, it must be recognized that epinephrine can stimulate both lipolysis and glycogenolysis in adipocytes, liver, and muscle. Thus it is not possible to predict the outcome of an increase in epinephrine. If the caffeine metabolic effect is entirely due to epinephrine enhancing fat metabolism, then metabolic effects should be detected (e.g., glycerol and FFA increases and a decrease in RER) at rest and throughout the exercise. Because these are not consistently observed, we cannot provide insight

### Table 2: Whole blood lactate and glucose concentrations during running and cycling to exhaustion after placebo or caffeine ingestion

<table>
<thead>
<tr>
<th></th>
<th>-60 min</th>
<th>0 min</th>
<th>15 min</th>
<th>30 min</th>
<th>Exh</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Running (n = 7)</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Lactate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL</td>
<td>0.95±0.13</td>
<td>0.99±0.12</td>
<td>2.46±0.67</td>
<td>2.95±0.78</td>
<td>3.12±0.79</td>
</tr>
<tr>
<td>CAF</td>
<td>0.87±0.12</td>
<td>1.21±0.14</td>
<td>2.96±0.55</td>
<td>3.60±0.84</td>
<td>3.72±0.88</td>
</tr>
<tr>
<td>Glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PL</td>
<td>3.47±0.37</td>
<td>3.55±0.35</td>
<td>3.97±0.34</td>
<td>4.40±0.53</td>
<td>4.85±0.65</td>
</tr>
<tr>
<td>CAF</td>
<td>3.60±0.25</td>
<td>3.79±0.19</td>
<td>4.68±0.22</td>
<td>5.31±0.55</td>
<td>5.35±0.65</td>
</tr>
</tbody>
</table>

| **Cycling (n = 6)** |
| Lactate |
| PL      | 0.82±0.06 | 0.89±0.08 | 3.13±0.60 | 3.22±0.76 | 2.95±0.85 |
| CAF     | 1.01±0.08 | 1.14±0.08 | 4.26±0.83 | 4.91±1.07 | 4.10±1.15 |
| Glucose |
| PL      | 3.42±0.31 | 3.48±0.16 | 3.74±0.36 | 3.93±0.48 | 3.96±0.58 |
| CAF     | 4.00±0.37 | 3.85±0.23 | 3.71±0.34 | 4.48±0.34 | 4.08±0.38 |

Values are means ± SE; n, no. of subjs. * Significantly different from PL. † Significantly different from -60 min.
into the importance of metabolic responses in explaining the improved performance after caffeine ingestion. In summary, this study demonstrated that consuming 9 mg/kg of caffeine produced a powerful ergogenic effect during running and cycling to exhaustion in trained competitive runners. Caffeine ingestion also dramatically increased plasma epinephrine concentration above control responses at rest and during exercise but had no effect on norepinephrine responses. The high dose of caffeine and elevated epinephrine concentrations were associated with elevated plasma glycerol concentrations but no significant changes in plasma FFA or RER during exercise.

Future studies that measure exogenous FFA and muscle triacylglycerol and glycogen utilization throughout exercise to exhaustion are required to conclusively determine whether the ergogenic effects of caffeine ingestion are due to a shift toward greater fat utilization and a sparing of carbohydrate utilization. This study also demonstrated that ingestion of caffeine in amounts that produce acceptable urinary caffeine levels (as indicated by the IOC) was associated with dramatic ergogenic effects.

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