The effect of caffeine ingestion on

cardiovascular and thermoregulatory function

during maximal and submaximal exercise

by

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GENERAL INTRODUCTION

The concept of exercise performance has commonly challenged the highest abilities of the athlete as the performer, and of the exercise physiologist as the evaluator of the athlete's performance. In addition, researchers have investigated the use of various ergogenic aids that may alter the physiological processes. The results and conclusions of such investigations have added greatly to the body of knowledge as it relates to physical performance.

Caffeine is classified as a mild stimulant and euphoriant. It is through these characteristics that caffeine exerts its effects on various systems of the human body. Direct stimulation of the cerebral cortex and enhanced secretion of the catecholamine epinephrine results from caffeine administration (18). Stimulation of cardiac muscle by caffeine has been shown to influence heart rate as well as changes in electro-cardiographic activity. The myocardial stimulation and various influences on vasomotor tone due to caffeine ingestion have been shown to alter resting blood pressures (20). Caffeine administration decreases vital tubular reabsorption of sodium (Na^+) and increases the glomerular filtration rate, leading to a diuretic effect (18). Caffeine may also cause an increase in metabolic heat production through a stimulation of the thermoregulatory functions of the hypothalamus (26).

While the general stimulatory effect of caffeine taken in smaller dosages (less than 200 mg) is known to overcome fatigue and drowsiness and improve mental concentration for extended periods, larger caffeine

dosages (more than 500 mg) may cause such side effects as the impairment of motor function, nervousness, irritability, insomnia, tachycardia, and cardiac arrhythmias (18). The diuretic effect of caffeine administration may promote a state of hypohydration (2).

The use of caffeine and its effect on exercise performance has presented an element of physiological interest in which controversy has often been the result. Administration of caffeine is known to increase plasma free fatty acid levels through the activation of cyclic AMP (cAMP). Cyclic AMP activates triglyceride lipases, which hydrolise triglycerides in adipose tissue and increase the levels of free fatty acids circulating in blood plasma (18). It has been suggested that an elevation in plasma free fatty acids is associated with an increase in the utilization of fats and a diminished use of carbohydrates as an energy source for muscular work during prolonged exercise (8). Since the depletion of carbohydrate stores, in the form of muscle and liver glycogen, and a decrease in blood glucose levels are associated with muscular fatigue, a "sparing" of carbohydrates through an increase in fatty acid metabolism may prolong exercise duration (8, 17). Although improvement in exercise performance with the ingestion of caffeine has been demonstrated, it has, as yet, to be universally accepted.

Caffeine has known effects on the nervous, respiratory, cardiovascular, and thermoregulatory systems. However, little research is available on the specific effects of these systems to caffeine administration with exercise. It is common knowledge that as the human body progresses from a resting state to an active state specific physiological changes

must take place in order to meet the increased metabolic demands of the body. Such changes are largely mediated through neural responses. Heart rate, blood pressure, ventilation, and the regulation of heat production are all physiological processes that generally parallel changes in human activity levels. Whether or not the ingestion of caffeine, with the intent of improving exercise performance, simultaneously influences hemodynamic, respiratory, or thermoregulatory responses to exercise so as to beneficially or adversely affect performance is a question that is yet to be answered.

Statement of the Problem

It was the purpose of this investigation to: 1) observe changes in the cardiovascular response pattern (heart rate, blood pressure, electrocardiographic activity) during maximal and submaximal exercise resulting from caffeine ingestion and 2) to determine the effects of caffeine ingestion on heat stress during submaximal exercise as determined by blood constituents (hemoglobin, hematocrit, serum sodium (Na^+) and potassium (K^+) and body temperatures) on healthy untrained males ages 21-28.

Hypotheses

With the administration of caffeine serving as the experimental trial and the administration of the placebo as the control trial, the following hypotheses were tested by appropriate statistical procedures:

1. No significant differences will be found between control and experimental trials in heart rate and blood pressure responses during

maximal or submaximal exercise.

2. There will be no change in electrocardiographic activity between control and experimental trials during maximal or submaximal exercise.

3. Body temperature will exhibit no significant difference between control and experimental trials during submaximal exercise.

4. Serum electrolyte levels (Na^+, K^+) and hematological constituents (hemoglobin, hematocrit) will not change significantly between control and experimental trials during submaximal exercise.

5. There will be no significant differences between control and experimental trials in urinary output before and after exercise in the submaximal work bouts.

6. Respiratory or metabolic parameters (minute ventilation, oxygen consumption, respiratory exchange ratio) will not change significantly between control and experimental trials during maximal or submaximal exercise.

Limitations

Each subject was instructed to keep caffeine consumption and dietary habits consistent throughout the course of the investigation. However, because the dietary control was voluntary and conducted outside of the laboratory setting, it may only be assumed that such control was rigidly followed.

Assays were not conducted in this study to determine caffeine concentrations in blood. According to previous research, peak blood

caffeine concentration occurs approximately one hour post-ingestion. It was assumed that the subjects in the present investigation exhibited peak caffeine concentration levels at this same time period.

Delineations

The subjects used in this investigation were all volunteers responding to advertised notices. All subjects were either students at Iowa State University or residents of the Ames, Iowa community.

Justification

Caffeine has been widely used by individuals competing in endurance activities, such as running and cycling, with the belief that this substance may benefit performance. However, the known effects of caffeine on such physiological processes as heart rate, blood pressure, electrocardiographic responses, and thermoregulation may be such during prolonged activity that performance may actually be impaired. In addition, the effects of caffeine on cardiovascular responses may also prove detrimental to maximal exercise performance. Due to a lack of available information focusing on the specifics of cardiovascular and thermoregulatory adaptations to exercise as influenced by caffeine ingestion, as well as the possible adverse effects of caffeine and exercise to an individual's physical health, this investigation was designed and conducted with the belief that the data gathered may provide insight into questions concerning the use of a popular substance on exercise performance that have yet to be addressed.

Explanation of Thesis Format

This thesis follows the optional or alternate thesis format which
includes two papers intended for submission to the Journal of Applied
Physiology and as such, utilized the style of manuscript required by
that publication. A general introduction, review of pertinent litera-
ture, and general summary were included to meet graduation requirements
at Iowa State University. The additional review of literature, in ex-
panded form, necessitated an additional list of literature citations
which should not be confused with citations within the individual pa-
pers.

Human Subjects Statement

The Iowa State University Committee on the Use of Human Subjects
in Research reviewed this project and concluded that the rights and wel-
fare of the human subjects were adequately protected, that risks were
outweighed by the potential benefits and expected value of the knowledge
sought, that confidentiality of data was assured and that informed con-
sent was obtained by appropriate procedures.

REVIEW OF LITERATURE

The use of caffeine and its effect on physiological functions during exercise has been widely studied due to a possible role in promoting the mobilization and utilization of free fatty acids as an energy source during prolonged exercise. Although the effects of caffeine on the cardiovascular, thermoregulatory, nervous, and other systems have been documented under resting conditions, the purpose of this review was to summarize information on the effects of caffeine on the forementioned systems during exercise.

Van Handel et al. (26) examined the effects of various caffeine dosages (0, 22.5, 35, and 150 mg) administered in a 10 oz. decaffeinated cola solution on heart rate and blood pressure responses in six men and six women volunteers (20-42 years) during a six-hour resting state. Blood pressure values were reported as pulse pressure (PP=systolic blood pressure - diastolic blood pressure) and mean arterial pressure (MAP = 1/3 pulse pressure + diastolic pressure). Pulse pressure exhibited a significant (p < .05) decrease of 4 to 5 mm Hg (no actual values reported) during the first 15 minutes following ingestion of each of the assigned solutions and then remained relatively stable throughout the rest of the trial. No significant differences were observed due to differences in caffeine concentration levels. Mean arterial pressure increased significantly (p < .05) during the first 30 minutes after ingestion of the 150 mg solution only, and remained elevated throughout the end of the trial (no values reported). Nonsignificant increases

of MAP of lesser magnitude were observed for the 22.5 and 35 mg solutions, as compared to the 150 mg solution 30 minutes post-ingestion. Throughout the six hour period, mean arterial pressure remained at pre-ingestion levels for the 0 mg solution.

Heart rate decreased significantly ($p < .05$) by approximately six beats/minute during the first 30 minutes from pre-ingestion values (mean of 62 to 56 beats/min.) for all solutions and remained stable until the end of the trial. No significant differences ($p > .05$) for the heart rate were reported between solutions at any point during the experiment.

Heart rate response as an indicator of tolerance to caffeine-mediated cardiovascular effects was examined by Cotton (8). A total of 149 subjects (138 males, 11 females; no ages reported) were used and each was assigned to one of two categories (coffee drinker or non-coffee drinker). The noncoffee drinkers were classified as those consuming not more than one serving of a caffeinated beverage per day, while all others were classified as coffee drinkers. The caffeine solution consisted of 150 mg of powdered caffeine added to decaffeinated coffee. The placebo solution consisted of decaffeinated coffee with 150 mg of powdered lactose added. Subjects were instructed to record heart rate measurements at their normal bedtime in the following manner: 3 times at 5 minute intervals before and 30 to 40 minutes after ingestion of the assigned solution. Caffeine-induced bradycardia (a decrease in resting heart rate > 5 beats/min.) was experienced in a significantly ($p < .05$) larger percentage of the noncoffee drinkers (41%) as compared to the coffee drinkers (23%). No significant

differences in the occurrence of bradycardia were experienced between groups following administration of the placebo solution. The occurrence of tachycardia (increase in resting heart rate > 5 beats/min.) was not significant for either group or between groups following ingestion of either solution. No actual heart rate values were reported. Individual acquired tolerance to the effects of a mild dosage of caffeine was offered as an explanation for the lower incidence of bradycardia experienced by the coffee group as compared to the noncoffee group. No specific time period was suggested as necessary to acquire such a tolerance.

Robertson et al. (24) studied heart rate, blood pressure, and respiratory rate during rest to determine the influence of caffeine ingestion. Nine subjects (6 males, 3 females, 21-30 years) ingested either a caffeine (250 mg) or a placebo (1 gm Pero rye-barley extract) solution and were then instructed to rest in a supine position for three hours. Heart rate and blood pressure were recorded at 15 minute intervals during the trial periods, and respiratory rate was measured for a 10 minute period one hour after ingestion of each solution. Blood pressure exhibited a significant ($p < 0.05$) increase in the caffeine trial compared to the placebo trial, with maximum mean increases of 14 mm Hg systolic pressure and 10 mm Hg diastolic pressure (no actual values were reported for blood pressure readings) occurring one hour post-ingestion. Both systolic and diastolic blood pressures for the caffeine trial remained significantly ($p < 0.05$) elevated above placebo trial blood pressure values throughout the three-hour period. A significant ($p < 0.05$)

decrease in heart rate (5 beats/minute) was observed 45 minutes follow-
ing the ingestion of caffeine. This decrease in heart rate lasted for
approximately one hour. Thereafter, heart rate increased significantly
($p < 0.05$) from 60 beats/minute to 70 beats/minute in the caffeine trial
and remained elevated for the duration of the experimental period. No
significant changes in heart rate were observed in the placebo trial.
The authors noted that the period of maximum decline in heart rate corre-
sponded with the period of greatest blood pressure elevation. Respira-
tory rate measured one hour post- ingestion was significantly ($p < 0.05$)
greater in the caffeine trial (16.1±2.3 breaths/min.) compared to the
placebo trial (13.4±1.6 breaths/min.). No further respiratory measures
were reported.

Bertrand et al. (5) reported data from a 10-year longitudinal study
(1968-1978) conducted by the International Business Machines Corporation
(IBM) in which no specific relation between daily caffeine consumption
and blood pressure elevation was observed. Data were gathered from
72,101 IBM employees. Physiological variables recorded were resting
heart rate, blood pressure, electrocardiogram, and caffeine consumption
habits during this 10-year period. A large majority of the subjects
(95%) exhibited resting systolic blood pressure <140 mm Hg and resting
diastolic blood pressure <90 mm Hg regardless of caffeine consumption
habits. Data in this investigation were published in response to the
forementioned study by Robertson et al. in which clinical concerns for
hypertensive patients who were also heavy caffeine consumers were pro-
posed. The authors in the present study suggested that caffeine

consumption habits did not appear to correlate highly with the incidence
of hypertension. However, the authors recommended further longitudinal
studies be conducted on caffeine consumption habits of individuals de-
fined as clinically hypertensive.

Gould et al. (15) examined the effects of caffeine on resting heart
rate and blood pressure in 15 subjects with normal or abnormal cardiac
function. Five of the subjects were classified as having normal cardiac
function and 10 subjects had identifiable heart disease. Each subject
drank 6 oz. of hot water containing 158 mg of caffeine. Heart rate
and blood pressure measurements were recorded 20 minutes following in-
gestion of the caffeine. No significant (p < 0.05) changes in resting
heart rate or blood pressure were observed in either group. Actual
values for heart rate and blood pressures for either group were not
reported. The authors concluded that caffeine ingested in small amounts
(at least not in excess of the dosage in this study) appears to be safe
for cardiac patients.

In addition to its influence on heart rate and blood pressure,
caffeine has been indicated as a possible cause of cardiac arrhythmias,
most notably pre-ventricular contractions. The onset of arrhythmic
activity has traditionally led many investigators to link the use of
caffeine to an increase in the risks of sudden heart attacks.

In the forementioned study by Gould et al., subjects were monitored
for changes in electrocardiographic activity following ingestion of
the caffeine solution (158 mg). A standard 12 lead resting electro-
cardiogram was used. The occurrence of arrhythmias produced by caffeine

were not found in any of the subjects with either normal or abnormal cardiac function.

Dobmeyer et al. (11) performed a recent investigation to determine the effects of caffeine administration on cardiac electrical activity. Seven volunteers (20-31 years) with normal cardiac function and 12 cardiac patients (17-61 years) were monitored for the occurrence of arrhythmic activity after oral ingestion of caffeinated coffee (200 mg caffeine) or intravenous caffeine (200 mg) administration. Catheters were positioned into the heart at the mid left atrium, the coronary sinus, the His bundle, and the right ventricular apex to monitor all electrical activity. In addition, arrhythmic promotion was performed and measured by application of an electrical stimulus to the myocardium. No significant changes were noted in impulse conduction intervals or recovery time periods in either group regardless of the method of caffeine administration. Effective refractory periods for impulse conduction were, however, significantly ($p < 0.05$) shortened or lengthened, depending on the respective recording site, in both groups. Changes in refractory periods were not significant regardless of the method of caffeine administration. Specific length of the observed refractory period time intervals were not reported. Application of the extra stimuli produced ventricular tachycardia following caffeine ingestion in two of the cardiac patients and in none of the normal subjects. Supraventricular arrhythmias (atrial flutter-fibrilation, supraventricular tachycardia) following extrastimulus and caffeine ingestion were reported in three of the normal subjects and in six of the cardiac patients. Observed

ventricular and supraventricular arrhythmias were apparently the same regardless of the method of caffeine administration. Atrial flutter-fibrilation was recorded in two normal subjects and one cardiac patient when the extrastimulus was applied without ingesting caffeine. The conclusion was drawn from this investigation that the incidence of arrhythmic activity observed, primarily in the cardiac patients, should pose questions and further research on the use of caffeine by those individuals known to be most susceptible to possible adverse effects of caffeine.

Mathieu et al. (20) conducted a study on the association of arrhythmogenic occurrence and caffeine consumption habits. Subjects were 113 volunteers (no age or sex distributions were reported) who were classified as heavy caffeine consumers (>5 cups coffee/day). Each subject ingested 300 mg of caffeine and was monitored for changes in resting electrocardiogram one hour post-ingestion. Tachycardia (increase in heart rate > 5 beats/min.) occurred in 24 subjects, while 7 subjects experienced bradycardia (decrease in heart rate < 5 beats/min.). No other arrhythmias were reported. Further research comparing the effects of various caffeine dosages and caffeine consumption habits was suggested.

The effect of caffeine on the renal system has been well documented. The decrease in renal tubular reabsorption of sodium (Na^+) and water, and increase in the glomerular filtration rate produced by caffeine administration has been shown to lead to a pronounced diuretic effect. An increased body fluid loss through induced diuresis is known

to have a marked effect on hypohydration. In addition to its ability to enhance fluid losses, caffeine is known to influence heat production through stimulation of thermoregulatory centers within the hypothalamus. The following section of this review will examine possible effects on human thermoregulatory processes as determined by caffeine administration, as both a diuretic and heat-producing substance.

Bellet et al. (3) measured total urine production following caffeine ingestion in a resting data study. Eighteen males (18-22 years) ingested either a caffeine solution (220 mg caffeine in 500 ml water) or a control solution (500 ml water) and then sat for three hours. Urine samples were collected during the test period to determine total urine production. The ingestion of the caffeine solution produced a mean urine volume of 496.5 ml. Mean urine volume for the caffeine trial was significantly ($p < 0.01$) greater than mean urine volume for the control trial (325.8 ml).

Robertson et al. (24) examined urinary electrolyte concentrations (Na^+, K^+) in three female and six male subjects (21-30 years) following the ingestion of either 250 mg caffeine in 300 ml water or a placebo of 300 ml water. Subjects were maintained in a resting state for 3 hours. Urine excretion volume for the caffeine trial was significantly ($p < 0.05$) greater than urine volume for the placebo trial (469 ± 43 ml to 366 ± 30 ml, respectively). In addition, urinary Na^+ excretion was greater ($p < 0.05$) following caffeine ingestion (16.4 ± 2.4 m Eq) than following ingestion of the placebo (14.4 ± 2.5 m Eq). No significant differences, however, were found between solutions for urinary K^+

excretion.

The diuretic effect of caffeine was also investigated by Dorfman and Jarvik (12). Forty-one medical students (20-30 years) received 300 mg of caffeine mixed in 2.5 gm of decaffeinated coffee. Each subject was instructed to collect all urine excreted during an eight hour period following the ingestion of caffeine. Total urine volume was determined and total urine Na^+ and K^+ concentration were measured. Total mean volume (386 ml) for the caffeine trial did not differ from the placebo trial (337 ml). There was a significant ($p < 0.01$) difference in Na^+ excretion between the caffeine and placebo trials (54.9 m Eq to 34.8 m Eq, respectively).

Wager-Srdar et al. (27) studied the thermoregulation effects of caffeine ingestion in eight male rats by measuring colonic temperatures. Caffeine was administered subcutaneously in a dose of 50 mg/kg body weight. A saline solution was administered as the placebo. Colonic temperature was recorded 5, 10, 15, 20, 25, 30, 45, 60, 75, 90 and 120 minutes after the respective solution was given. The saline placebo produced a slight decrease in baseline temperature that began 20 minutes post-administration and continued throughout the experimental period. However, the mean change in temperature for the placebo trial was not found to differ significantly from baseline. Caffeine ingestion produced an increase in temperature above baseline that began five minutes post-administration and persisted throughout the experiment. Contrary to the changes observed in the placebo trial, mean caffeine temperature changes were found to be significantly ($p < 0.05$) different from

baseline. The authors did not report actual temperature values.

In a forementioned study by Van Handel et al., urine production was measured following the ingestion of various caffeine dosages. Only the 150 mg solution produced a urine volume that was significantly (p < 0.05) greater than the control (0 mg) solution (430 ml to 300 ml, respectively). Total urine volume increased above the control volume for the 22.5 and 35 mg solutions, but these increases were not statistically significant. In addition to total urine volume, core temperature was measured in an attempt to determine the effects of caffeine on heat production. Temperatures for each subject were measured every 30 minutes during the six hour period. No significant changes were noted in core temperatures above pre-ingestion values for any of the caffeine solutions. The authors indicated that a larger dose of caffeine may have been required to elicit a significant increase in body core temperature.

In a study by Costill et al. (7) in which metabolic responses due to caffeine ingestion and its effects on exercise performance were investigated, heart rates were not found to differ significantly between caffeine and placebo trials. Nine competitive cyclists (7 males, 2 females) were given 330 mg of caffeine mixed with 5 gm of decaffeinated coffee or a placebo solution of 5 gm of decaffeinated coffee one hour prior to the exercise bout. All subjects were instructed to exercise at approximately 80% $\dot{V}O_2$max until exhaustion. Heart rates for the caffeine trial were higher at 30 minutes (158±3 to 167±4 beats/min.), 50 minutes (171±3 to 170±4 beats/min.) and the final collection period

(176 ± 5 to 173 ± 4 beats/min) during exercise, although none of the dif-
ferences were found to be significant.

Ivy et al. (17) performed a similar investigation (7 male, 2 female
trained cyclists) on the metabolic effects of caffeine and carbohydrate
feedings during endurance exercise. Exercise consisted of two hours
of bicycle ergometry conducted at approximately 80% of the subjects
$\dot{V}O_2$max. Three trials were assigned, with one trial serving as the con-
trol trial, one trial serving as the caffeine trial, and one trial serv-
ing as the carbohydrate trial. Two hundred and fifty mg of caffeine
were ingested one hour prior to exercising in the caffeine trial, with
an additional 250 mg of caffeine ingested at 15 minute intervals during
the exercise bout. An aqueous glucose polymer solution, equivalent
to 25% of the estimated total carbohydrate content utilized by each
subject during a pre-experiment practice trial, served as the carbo-
hydrate solution. The control solution consisted of an artificially
sweetened lemonade drink. Carbohydrate and control solutions were ad-
ministered immediately prior to and at 15 minute intervals during the
first 90 minutes of exercise. Heart rate was measured at 10 minute
intervals throughout the exercise bout. Mean heart rate for the
caffeine trial was higher than mean heart rate values reported for the
control and carbohydrate trials (173 ± 1.55 to 170 ± 1.13 and 169 ± 1.08
beats/min., respectively). However, the differences in heart rates
between treatments were not found to be statistically ($p < 0.05$) sig-
nificant.

Caffeine mediated effects on exercise performance and cardiovascular function were studied by Perkins and Williams (21). Fourteen female subjects (22.1 years) performed a standardized progressive workload exercise bout on a bicycle ergometer until exhaustion was reached. The initial workload was 300 kgm for one minute, and was increased 100 kgm/min. until a pedalling rate of 40 RPM could no longer be maintained. Three different caffeine trials were used, with a caffeine dosage of 4 mg/kg body weight, 7 mg/kg body weight, and 10 mg/kg body weight assigned to each subject. Caffeine was dissolved in 3 oz. of orange juice. The placebo contained 3.5 mg/kg body weight sodium citrate also dissolved in 3 oz. of orange juice. Solutions were ingested 30 minutes prior to exercise. Heart rate measurements were taken prior to exercise (resting heart rate), during the last 15 seconds of workloads 300, 400 and 500 kgm (submaximal heart rate), and the last 15 seconds prior to the cessation of exercise (maximal heart rate). No significant differences were noted in resting, submaximal, or maximal heart rates between placebo and any of the caffeine treatments. Differences between the caffeine dosages were also not significant.

Toner et al. (25) examined the effects of caffeine on both maximal and submaximal heart rate response during a discontinuous maximal exercise bout. Eight males (28±4 years) volunteered as subjects. Both the placebo solution (3 gm of 97% decaffeinated coffee in 230 ml of water) and the caffeinated solution (350 mg caffeine anhydrous in 230 ml of water) were ingested 30 minutes before the exercise bout. The exercise protocol consisted of two separate trials (caffeine and

placebo) using a bicycle ergometer with the exercise intensity progressively increased until the subject reached the exhausted state. Each workload lasted 5 minutes with a 10 minute rest interval. Heart rates were recorded during the last 15 seconds of each workload and at the cessation of exercise. Submaximal heart rate was determined as the heart rate value observed at the end of the first and second workload. Maximal heart rate was determined as the heart rate value recorded at the immediate cessation of exercise. Ingestion of the caffeine solution significantly ($p < 0.01$) increased maximal heart rate by 5 beats/min. compared to ingestion of the placebo solution (185 beats/min. to 180 beats/min., respectively). However, no significant differences were found between trials for submaximal heart rate at either workload intensity.

Heart rates were observed by Powers et al. (22) in an investigation to assess the effects of caffeine on metabolism and performance during graded exercise. Seven male subjects volunteered to participate in two separate graded exercise trials on a bicycle ergometer. Workload intensity was initially set at 30 W and progressively increased by 30 W every 3 minutes until each subject reached a state of exhaustion. A gelatin capsule containing caffeine in a 5 mg/kg body weight dose was ingested for the caffeine trial. A gelatin capsule without added caffeine was ingested for the placebo trial. All subjects were blindfolded prior to the administration of each capsule. Heart rates were recorded during the last 30 seconds of each workload. No significant differences were found for heart rate values between treatments at any

point during exercise.

Gordon et al. (14) examined the effects of caffeine ingestion on submaximal cardiovascular function during a prolonged exercise bout. Ten males (19.4±1.5 years) participating in a physical instructors training course served as subjects. Subjects were randomly assigned to a caffeine group or a control group, with five subjects per group. Exercise consisted of one hour and 40 minutes of continuous running on a motorized treadmill at an intensity equal to 70% of the subject's $\dot{V}O_2$max. Caffeine (5 mg/kg body weight dissolved in 250 ml of an artificially sweetened orange drink) was ingested one hour prior to the exercise bout. The placebo solution was the same as the caffeine solution, except that no caffeine was added. Heart rates were recorded at the cessation of exercise only. Mean heart rate for the caffeine group was 171±9 beats/min. The control group exhibited a mean heart rate of 165±4 beats/min. The differences in mean heart rates between the groups were not statistically significant. In addition, electrocardiographic activity for each subject was monitored in order to determine the presence of arrhythmias during prolonged exercise as affected by caffeine. The procedure used involved six standard leads (I, II, III, AVR, AVL, AVF) and two precordial leads (V_1 and V_5). Although no arrhythmias were observed, the authors concluded that the age and physical fitness levels of the subjects used in this investigation may not be completely indicative of normal exercise ECG responses as influenced by caffeine in other subjects. Further research was specified on ECG responses following caffeine ingestion in individuals

suffering from ischemic heart disease, hypertension, and other cardio-vascular abnormalities.

Evidence has been presented and documented that an increase in body core temperature coupled with excessive loss of fluid during pro-longed exercise may act as a detriment to peak performance. Core tem-peratures in excess of 40°C and fluid losses exceeding 6-10% total body weight have been reported following exercise longer than 1-2 hours dura-tion (1). Although these are generally extreme cases, core temperature readings of 40°C and fluid losses equivalent to 3-5% of total body weight are commonly found in endurance exercise participants. The re-sultant dehydration and thermal stress·may not only impair exercise performance, but may also endanger physical health through a reduction in sweat rate, reduction in total circulatory function, and disturbances in cardiac function and electrolyte balance. In addition, the induce-ment of diuresis before and/or during exercise may contribute to de-hydration during exercise, so that normal thermoregulatory functions are further disrupted (6, 13).

As a known diuretic agent and thermoregulatory stimulant, it is possible that the use of a caffeinated substance during prolonged exer-cise may actually impair rather than enhance exercise performance. However, few data are presently available to provide evidence of the effects of caffeine on thermoregulation and exercise performance.

In a previously mentioned investigation by Van Handel et al. in which various physiological functions were monitored in subjects at rest following caffeine ingestion, it was stated that possible

caffeine-mediated effects on changes in body fluids and core temperature may significantly compromise thermoregulatory functions during prolonged exercise. The ingestion of a 150 mg caffeine solution in this study produced a significant diuresis, but no change in core temperature as compared to lesser caffeine dosages. These results prompted the authors to recommend further study with a specific focus on thermoregulation as influenced by caffeine ingestion during prolonged exercise.

In a forementioned article, Gordon et al. examined the effects of caffeine ingestion on thermoregulation in 10 male subjects during a one hour 40 minute run on a treadmill. A blood sample was drawn prior to the exercise bout and two minutes before the end of the exercise bout to determine changes in electrolytes (Na^+, K^+, Cl^-, Ca^{++}, Mg^{++}). Hemoglobin and hematocrit were calculated from the samples to determine percentage changes in plasma volume. Subjects were weighed prior to and following exercise, and a water deficit value (based on change in weight) was calculated. No significant differences existed for water deficit, percent change in plasma volume, or rectal temperatures (measured during exercise) between the caffeine and control groups. However, the authors indicated the need for further research on caffeine and exercise thermoregulation by using greater caffeine dosages.

In summary, the following statements may be drawn: an array of conflicting data exists on the issue of changes in cardiac function as influenced by caffeine during both resting and exercising conditions; observed caffeine effects on the cardiovascular system appear to be

largely dose-related; the effects of caffeine on thermoregulation during exercise have not been thoroughly investigated. Although it is beyond the scope of the present investigative endeavor to review all literature on the problem as stated, each source was chosen with the belief that it provided valid representation of the currently available data.

SECTION I. THE EFFECT OF CAFFEINE INGESTION ON
CARDIOVASCULAR FUNCTION DURING MAXIMAL AND SUBMAXIMAL EXERCISE

INTRODUCTION

The effect of caffeine on the physiological responses to exercise has been widely studied from its possible influential role on metabolic substrate utilization during a prolonged exercise bout (9, 21, 26, 30). Caffeine has been shown to increase plasma free fatty acid levels in resting man (3, 18, 31) as well as increase fat metabolism during submaximal exercise (9, 21, 26). It has been demonstrated that an increase in fat metabolism has a sparing effect on the use of muscle glycogen for substrate during prolonged exercise and may, therefore, enhance exercise performance (9, 21). In contrast, other investigations have not found improvement in exercise performance with caffeine ingestion (25, 30).

Limited data are available as to the effects of caffeine on cardiovascular function during maximal and submaximal exercise. Resting heart rate and electrocardiographic activity may be altered through the direct stimulation of cardiac tissue by caffeine (3, 4, 5, 13, 18, 22, 28). Cardiac muscle stimulation and various influences on vasomotor tone due to caffeine ingestion have been shown to alter resting blood pressure (18, 22, 27).

Heart rate has generally been the only cardiovascular parameter studied during prolonged exercise. Costill et al. (9), Gordon et al. (17), and Perkins and Williams (25) found no change in heart rate during exercise following the ingestion of caffeine. Maximal heart rate has been shown to either increase (26, 30) or not change (25) with the use

of caffeine. Blood pressure response during maximal and submaximal exercise due to caffeine ingestion have not been reported. In addition, Gordon et al. (17) found no electrocardiographic abnormalities during submaximal exercise following the ingestion of caffeine.

The purpose of this study was to assess the effect of caffeine ingestion on cardiorespiratory function during maximal and submaximal exercise.

METHODS

Subjects

Six untrained males (21-28 years) volunteered as subjects for this experiment. All subjects were either students at Iowa State University or nonstudent members of the Ames, Iowa community. Each subject was informed of the risks and stresses associated with this study and gave their written consent. Subjects were asked to report to each exercise trial in a 12-hour fasted state. In addition, a 48-hour abstinence from any caffeine-containing product and a consistent dietary pattern 24 hours prior to all exercise trials were required of each subject.

Exercise Regimens

Exercise regimens used in this investigation consisted of both a maximal and submaximal protocol. Two separate trials were conducted for each protocol, with one trial designated as the control treatment (decaffeinated) and one trial designated as the experimental treatment (caffeine). The order of treatments was randomly assigned in a double-blind design. Maximal exercise bouts were performed on a Monark bicycle ergometer with the workload increasing in a progressive step-wise manner. RPM was set at 60. The initial pedal resistance was set at 0 kp for 4 minutes, increased to 1 kp for two minutes, and increased by .5 kp every two minutes thereafter until exhuastion. Exhaustion was determined as the point at which the pedalling rate could no longer be maintained. Submaximal exercise bouts were also conducted on a Monark bicycle ergometer. The protocol consisted of 90 minutes of continuous

exercise at 60% of the subject's maximal oxygen consumption. Cycling speed was also set at 60 RPM.

One hour prior to the caffeine treatment for both the submaximal and maximal work bouts, each subject ingested 390 mg of caffeine citrate dissolved in 18 oz. of decaffeinated cola. An additional 65 mg of caffeine dissolved in 6 oz. of decaffeinated cola was administered immediately prior to exercise for both .the submaximal and maximal bouts. During the 90-minute submaximal exercise bout, an additional 65 mg caffeine in 6 oz. decaffeinated cola was ingested at 15 minute intervals. Total caffeine dosage ingested was 455 mg for the maximal exercise bout and 780 mg for the submaximal exercise bout. The solution for the decaffeinated control treatment for both maximal and submaximal exercise was administered by repeating the same protocol used for the caffeine treatment minus the caffeine.

Analytical Methods

Oxygen consumption was determined by using an automated open circuit method. Expired oxygen and carbon dioxide concentrations were measured with an Applied Electrochemistry S-3A analyzer and a Beckman LB-2 analyzer, respectively. Both analyzers were calibrated with known gas concentrations prior to each exercise treatment. Inspired air volume was measured with a calibrated Pneumoscan S-301 spirometer. Room temperature for each treatment was maintained at 21°C and relative humidity ranged from 35-50%. Maximal values for minute ventilation ($\dot{V}_E$), oxygen consumption ($\dot{V}O_2$), and respiratory rate (RR) for the maximal exercise bouts were

recorded as the highest value observed for each measure during exercise. Respiratory values in the submaximal bouts were recorded for $\dot{V}e$, $\dot{V}O_2$, and respiratory exchange ratio (RER) immediately prior to exercise and at 10, 30, 60, and 90 minutes of exercise. Heart rate (HR), blood pressure (BP), and a standard 12-lead electrocardiogram (ECG) were recorded prior to fluid ingestion, immediately prior to exercise, at the end of each workload, and immediately following the cessation of exercise in the maximal exercise bouts. During the submaximal bouts, HR, BP, and ECG were recorded prior to fluid ingestion, immediately prior to exercise, and at 10, 30, 60, and 90 minutes of exercise. Heart rate and ECG were monitored using an International Medical Corp. Viagraph.

Statistical Analysis

Maximal values for $\dot{V}O_2$, $\dot{V}e$, and RER were analyzed by a t-test procedure applied to differences between treatments for each variable. Data for rate pressure product (RPP=[HRmax XSBPmax]÷100) were also analyzed by a t-test procedure. Data for HR, BP, $\dot{V}e$, $\dot{V}O_2$, and RER recorded in the submaximal exercise bouts were analyzed with a split-plot analysis of variance procedure to determine significant interaction between treatment and time. If significant interaction was found, further clarification of the interaction was determined by performing t-tests of the time period means between treatments. The .05 level of probability was chosen to determine significant results.

RESULTS

Data for heart rate (HR) and blood pressure (BP) response (mean ± S.E.) during maximal exercise for both treatments are summarized in Table 1. Pre-fluid heart rate for the caffeine treatment (75.3 ± 3.5 beats/ min) was 6.7% higher (p > 0.05) than the decaffeinated pre-fluid heart rate (70.3 ± 3.5 beats/min). Heart rate measurements taken one hour post-fluid ingestion exhibited a decrease for both treatments from pre- fluid values, with a mean caffeine heart rate of 69.2 ± 3.5 beats/min, which was 7.6% higher (p > 0.05) than the decaffeinated mean of 64.0 ± 3.50 beats/min. Mean maximal heart rate for the caffeine treatment was 4.1% higher (p > 0.05) than the decaffeinated treatment (196.3 ± 3.5 beats/min to 188.3 ± 3.5 beats/min, respectively).

Blood pressure values (systolic/diastolic, mean ± S.E.) prior to fluid ingestion were 117.0 ± 4.8/77.3 ± 2.2 mmHg for the decaffeinated treatment and 116.7 ± 4.8/78.6 ± 2.2 mmHg for the caffeine treatment. Post-fluid blood pressures showed little change from pre-fluid measure- ments for the decaffeinated treatment (117.3 ± 4.8/75.7 ± 2.2 mmHg), but revealed a slight increase from pre-fluid values for the caffeine treatment (121.3 ± 4.8/80.0 ± 2.2 mmHg). However, this difference was not significant. Systolic blood pressure taken at maximal exercise was 3.0% higher for the caffeine treatment (217.0 ± 4.8 mmHg) than the decaf- feinated treatment (210.3 ± 4.8 mmHg). However, maximal diastolic pres- sure was slightly higher for the decaffeinated treatment compared to the caffeine treatment.

Table 1. Mean (±SEM) for heart rate (HR) and blood pressure (SBP, DBP) values at rest- pre-fluid, rest- post-fluid and maximal exercise for caffeine (C) and decaffeinated (D) treatments

Variable	Treatment	Pre-fluid	Post-fluid	Max Exercise
HR (b/min)	D	70.3 (±3.5)	64.0 (±3.5)	188.3 (±3.5)
	C	75.3 (±3.5)	69.3 (±3.5)	196.3 (±3.5)
SBP (mmHg)	D	117.0 (±4.8)	117.0 (±4.8)	210.3 (±4.8)
	C	116.7 (±4.8)	121.3 (±4.8)	217.0 (±4.8)
DBP (mmHg)	D	77.3 (±2.3)	75.7 (±2.3)	83.0 (±2.3)
	C	78.6 (±2.3)	80.0 (±2.3)	82.4 (±2.3)

As in the heart rate measurements, differences between treatments in blood pressure values were not found to be statistically (p > 0.05) significant at any of the observation periods. Rate pressure product (RPP=[HRmax X SBPmax]÷100) was also calculated as an indicator of cardiac work at maximal exercise. RPP was 7.0% higher (p > 0.05) for the caffeine treatment (426) as compared to the decaffeinated treatment (396).

Data for oxygen consumption ($\dot{V}O_2$max), minute ventilation ($\dot{V}$emax), and respiratory rate (RRmax) at maximal exercise for both treatments are summarized in Table 2. Maximal $\dot{V}O_2$ was slightly higher for the caffeine treatment (49.1 ± 1.5 ml·kg^{-1}·min^{-1}) when compared to the decaffeinated treatment (48.6 ± 1.5 ml·kg^{-1}·min^{-1}) although the difference was not significant (p > 0.05). No statistical (p > 0.05) difference was found between treatments for $\dot{V}$emax, although the mean value for the caffeine treatment (131.0 ± 6.9 L/min) was slightly higher than the decaffeinated treatment (129.9 ± 6.9 L/min). Maximal RR for the caffeine treatment (51.6 ± 1.4 breaths/min) was 9.0% higher (p > 0.05) than the decaffeinated treatment (47.0 ± 1.4 breaths/min).

Data for cardiovascular and respiratory function during submaximal exercise are summarized in Tables 3-4 and Figures 1-5. Pre-fluid HR values were similar between caffeine (68.7 ± 5.2 beats/min) and decaffeinated (68.8 ± 5.2 beats/min) treatments. Similar HR values for both treatments were also observed immediately prior to exercise. Throughout the 90 minute exercise bout, HR values were slightly higher at all measurement periods for the caffeine treatment when compared to the decaffeinated treatment (Table 3, Figure 1). Mean exercise HR was 4.3%

Table 2. Mean (±SEM) for oxygen consumption ($\dot{V}O_2$) and minute ventilation ($\dot{V}e$) value at maximal exercise for the caffeine (C) and the decaffeinated treatment

Variable	Treatment	Max Exercise
$\dot{V}O_2$ (ml$\cdot$Kg$^{-1}\cdot$min^{-1})	D	48.8 (±1.5)
	C	49.1 (±1.5)
$\dot{V}e$ (L/min)	D	129.9 (±6.9)
	C	131.0 (±6.9)

Table 3. Mean (±SEM) heart rate (HR) and blood pressure (SBP, DBP) values at rest pre-fluid, rest post-fluid, and during exercise for the caffeine (C) and decaffeinated (D) treatments

Variable	Treatment	Pre-fluid	Post-fluid	10 ex	30 ex	60 ex	90 ex
HR (b/min)	D	68.8 (±5.2)	70.0 (±5.2)	148.5 (±5.2)	156.0 (±5.2)	155.3 (±5.2)	165.6 (±5.2)
	C	68.7 (±5.2)	70.3 (±5.2)	154.7 (±5.2)	162.5 (±5.2)	164.5 (±5.2)	171.5 (±5.2)
SBP (mmHg)	D	115.0 (±4.2)	112.7 (±4.2)	148.7 (±4.2)	154.0 (±4.2)	158.3 (±4.2)	162.0 (±4.2)
	C	117.0 (±4.2)	118.0 (±4.2)	164.0 (±4.2)	168.0 (±4.2)	170.0 (±4.2)	171.0 (±4.2)
DBP (mmHg)	D	74.3 (±1.4)	72.3 (±1.4)	76.3 (±1.4)	76.3 (±1.4)	75.7 (±1.4)	74.6 (±1.4)
	C	74.0 (±1.4)	74.3 (±1.4)	78.3 (±1.4)	78.7 (±1.4)	79.7 (±1.4)	79.3 (±1.4)
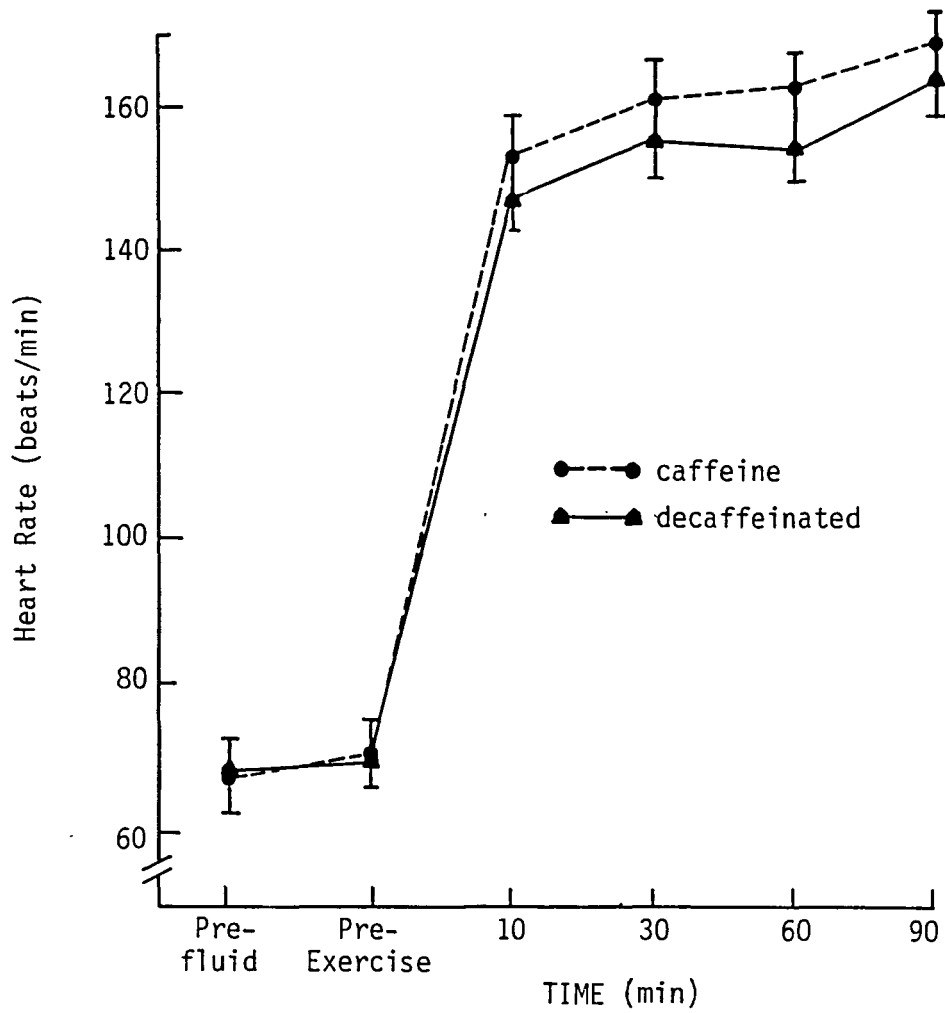
Figure 1. Mean (±SEM) values for heart rate at rest pre-fluid, rest
pre-exercise and at 10, 30, 60 and 90 minutes during exercise
for the caffeine and decaffeinated trials

higher for the caffeine treatment (163.3 ± 5.2 beats/min) when compared to the decaffeinated treatment mean (156.3 ± 5.2 beats/min). Results similar to HR response were observed for both systolic and diastolic BP during exercise, with BP values higher in the caffeine treatment. Both systolic and diastolic BP decreased slightly from pre-fluid to pre-exercise values in the decaffeinated treatment while BP remained relatively stable during the same period in the caffeine treatment (Table 3, Figure 2). Mean exercise systolic and diastolic BP were 7.4% and 4.1% higher, respectively, for the caffeine treatment when compared to the decaffeinated treatment. Differences between treatment means for HR and BP were not significant (p > 0.05).

Oxygen consumption values were higher for the caffeine trial at all measurement periods (Table 4, Figure 3). Mean exercise $\dot{V}O_2$ was 8.0% higher for the caffeine treatment (32.6 ± 0.9 ml·kg^{-1}·min^{-1}) when compared to the decaffeinated treatment (30.4 ± 0.9 ml·kg^{-1}·min^{-1}). Similar results were observed for minute ventilation ($\dot{V}_E$) Table 4, Figure 4). A 9.0% increase in mean exercise $\dot{V}_E$ was seen in the caffeine treatment (46.6 ± 1.8 L/min) when compared to the decaffeinated treatment (42.4 ± 1.8 L/min). Neither of the above differences were statistically significant (p > 0.05). In addition, no significant (p > 0.05) differences were observed between treatments for mean exercise respiratory exchange ratio (RER). Evaluation of electrocardiogram (ECG) tracings during both maximal and submaximal exercise bouts did not reveal the presence of any abnormal ECG recordings for either treatment.
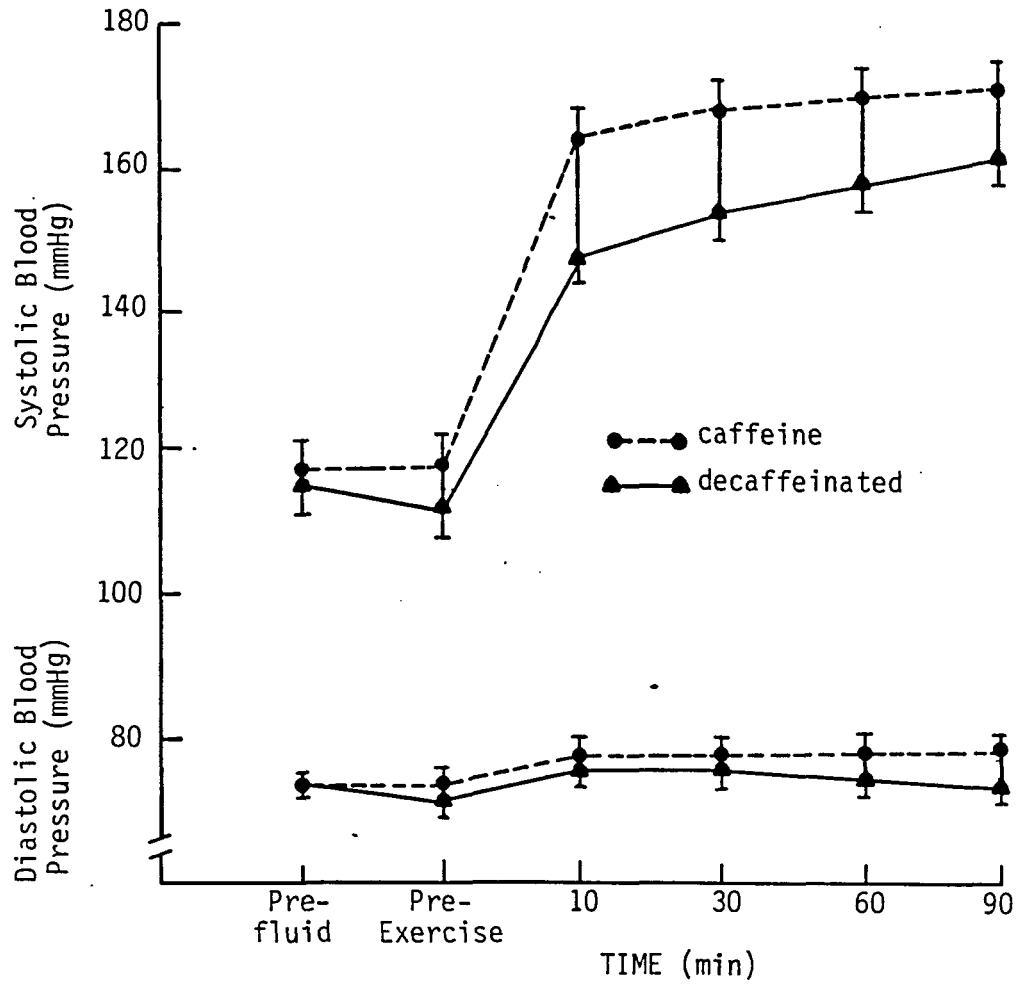
Figure 2. Mean (±SEM) values for systolic and diastolic blood
pressure at rest pre-fluid, rest pre-exercise, and at 10,
30, 60 and 90 minutes during exercise for the caffeine and
decaffeinated trials

Table 4. Mean (±SEM) oxygen consumption (VO_2) minutes ventilation (Ve), and respiratory exchange ratio (RER) at rest pre-exercise and during exercise for the caffeine (C) and decaffeinated (D) treatments

Variable	Treatment	Pre-exercise	10 ex	30 ex	60 ex	90 ex
$\dot{V}O_2$ (ml·kg⁻¹·min⁻¹)	D	4.8 (±0.9)	26.5 (±0.9)	30.1 (±0.9)	30.4 (±0.9)	33.1 (±0.9)
	C	5.4 (±0.9)	29.8 (±0.9)	33.0 (±0.9)	33.3 (±0.9)	34.5 (±0.9)
$\dot{V}e$ (L/min)	D	9.2 (±1.9)	47.0 (±1.9)	51.6 (±1.9)	49.7 (±1.9)	54.5 (±1.9)
	C	10.3 (±1.9)	51.9 (±1.9)	56.9 (±1.9)	55.7 (±1.9)	58.2 (±1.9)
RER	D	0.80 (±0.01)	0.94 (±0.01)	0.82 (±0.01)	0.80 (±0.01)	0.80 (±0.01)
	C	0.82 (±0.01)	0.91 (±0.01)	0.83 (±0.01)	0.82 (±0.01)	0.82 (±0.01)
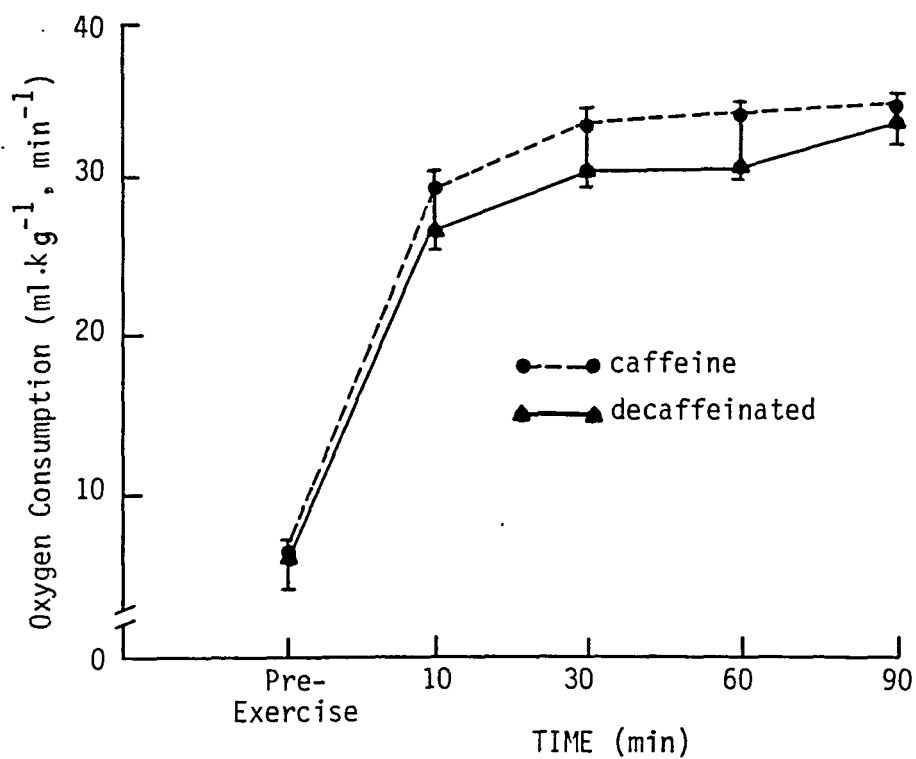
Figure 3. Mean (±SEM) values for oxygen consumption at rest
pre-exercise and at 10, 30, 60 and 90 minutes during
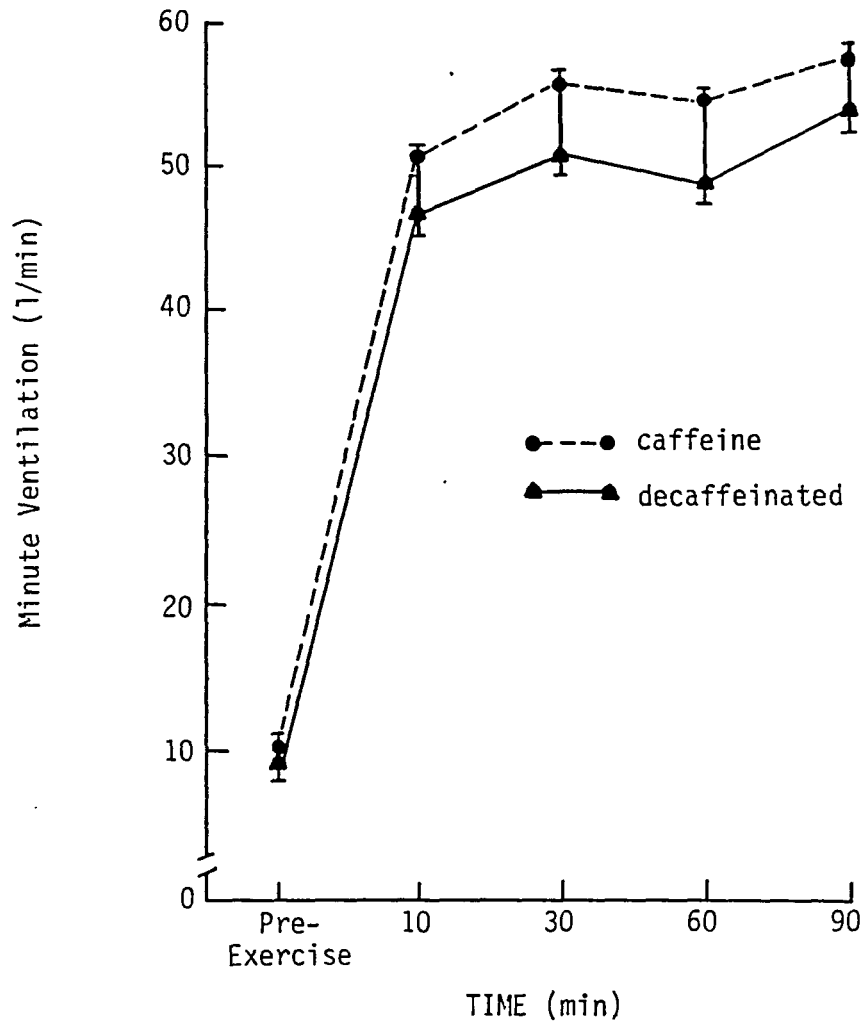exercise for the caffeine and decaffeinated trials

Figure 4. Mean (±SEM) values for minute ventilation at rest
pre-exercise and at 10, 30, 60, and 90 minutes during
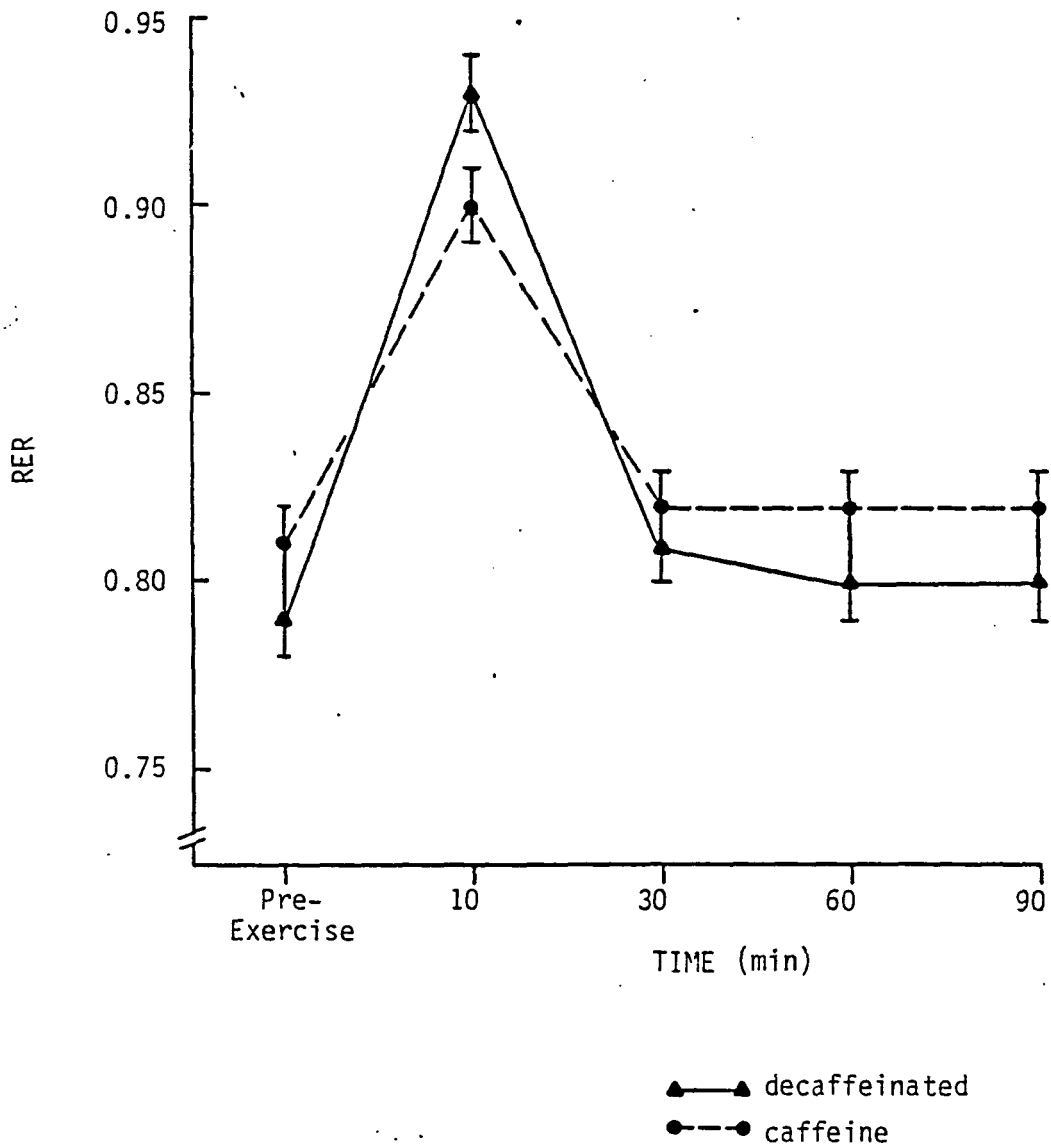exercise for the caffeine and decaffeinated trials

Figure 5. Mean (±SEM) values for respiratory exchange ratio (RER) at rest pre-exercise, and at 10, 30, 60 and 90 minutes during exercise for the caffeine and decaffeinated treatments

DISCUSSION

The results of this investigation did not reveal any statistically significant effects of caffeine ingestion on selected cardiovascular and respiratory functions during maximal and submaximal exercise. However, there was a definite trend across all subjects. Findings on maximal HR are in agreement with the work of Perkins and Williams (25), who, using a similar protocol, found no difference in maximal HR between caffeine and placebo trials. However, Toner et al. (30) demonstrated a significant elevation in maximal HR when 350 mg caffeine was ingested. It has been shown that ingestion of caffeine will cause an elevation in resting HR through direct stimulation of the myocardium and through the effects of norepinephrine on cardiac muscle as a result of enhanced sympathetic discharge (20,21). Tachycardia is especially present when the caffeine dose is in excess of 200 mg (22). Robinson et al. (29) indicated that the sympathetic system is the only nervous input regulating the heart during maximal intensity. Therefore, the 4.1% elevation in HR during maximal exercise following caffeine ingestion in the present study seems to be mediated through an enhanced sympathetic discharge. Considering the caffeine dosage used in the present investigation for the maximal exercise trial (455 mg) an elevation in maximal HR above decaffeinated control values would be expected.

Toner et al. (30) reported no significant difference in HR during submaximal workloads following caffeine ingestion. However, three out of eight subjects did exhibit an increased HR with caffeine. In the

present study, a 4.3% increase in mean exercise HR was observed with
the ingestion of caffeine. Although this increase was not statistically
significant, all subjects showed a similar HR response. Since Toner
et al. did not observe a significant elevation in HR during submaximal
exercise following caffeine ingestion, it was suggested that during sub-
maximal exercise caffeine may enhance both parasympathetic and sympa-
thetic discharge. Due to the fact that all subjects in the present in-
vestigation exhibited an elevated HR following caffeine ingestion, it
would appear that sympathetic activity overrides parasympathetic activity
during submaximal exercise.

Data for both maximal and submaximal BP revealed no significant
difference between caffeine and decaffeinated treatments. Little in-
formation is available on the specific effects of caffeine on BP during
exercise. However, it has been shown that caffeine ingestion produces
antagonistic effects on the vascular system. Dilation of coronary, pul-
monary, and systemic blood vessels by direct action on the vascular mus-
culature favor a decrease in BP, whereas, constriction of blood vessels
through stimulation of the medullary vasomotor center and direct myo-
cardial stimulation favor an increase in BP (27). Based upon the results
of this study, it appears that the effects of caffeine on BP responses
during exercise parallel heart rate responses to caffeine ingestion as
previously explained. Although it has been shown that caffeine may act
to reduce vasoconstriction and increase muscle blood flow since both
caffeine and epinephrine, which is elevated by caffeine, act to reduce
peripheral resistance (3, 4, 15, 20, 30), the slight increases in BP

observed in the present study may be due to increased cardiac output as a result of elevated HR.

The effect of caffeine on $\dot{V}O_2$max is not well documented. Toner et al. (30) found a small but significant increase in $\dot{V}O_2$max following the ingestion of 350 mg of caffeine. In contrast, Ganslen et al. (16) have shown that 200 mg of caffeine did not increase $\dot{V}O_2$max in one subject during treadmill running. Margaria et al. (23) showed that $\dot{V}O_2$max during treadmill running was not altered after 100 or 250 mg in three subjects. Results of the present study agree with the findings of Ganslen et al. and Margaria et al. Submaximal $\dot{V}O_2$ did not differ significantly between the caffeine and the decaffeinated trials. This also is in agreement with the findings of Costill et al. (9), Ivy et al. (21), and Toner et al. (30). Although the difference in $\dot{V}O_2$ between treatments was not statistically significant for the submaximal exercise, all subjects showed a consistently higher (mean 8.0%) $\dot{V}O_2$ during the caffeine trial. Two possible reasons for an increase in oxygen consumption may be related to the elevated HR observed during the caffeine trial and the possibility of an increase in stroke volume as reported by Grollman (19) which would have an effect on increasing cardiac output.

Minute ventilation ($\dot{V}e$) during maximal and submaximal exercise and

respiratory rate (RR) during maximal exercise are not in agreement with previous research. Ganslen et al. (16) found a significant increase in $\dot{V}e$ and RR both at rest and during maximal exercise following caffeine ingestion. Caffeine is known as having the strongest effect of all xan-

xanthines as a respiratory stimulant (27). In the present study, caffeine did, in fact, appear to have some effect on respiratory stimulation as $\dot{V}e$ and RR values were consistently higher (though not significant) during the caffeine trial.

Respiratory exchange ratio (RER) did not respond as expected when caffeine was ingested before and during the submaximal exercise bout. The use of caffeine has been shown to increase fat oxidation for energy utilization by stimulating free fatty acid release (9, 21). An increase in fat utilization is usually characterized by a lower RER value, as compared to an increase in carbohydrate utilization, due to the greater volume of CO_2 produced relative to the volume of O_2 consumed when fatty acid is oxidized (20). Based on the respiratory exchange ratio observed in this study, an increase in fat oxidation due to the ingestion of caffeine was not demonstrated as RER did not differ between trials. In fact, RER values were slightly higher over the course of the 90-minute exercise bout for the caffeine treatment. Fox and Mathews (15) reported that an increase in ventilation during exercise will result in an excess of CO_2 in expired air. It was previously mentioned that the ingestion of caffeine elevated both RR and $\dot{V}e$ values as compared to the decaffeinated treatment. The increased ventilatory drive along with the increase in $\dot{V}CO_2$ when caffeine was ingested may have masked any change in RER

as an indicator of substrate utilization during exercise. It should be noted that plasma concentrations of free fatty acids or glucose were not measured.

In summary, these data indicate that 445 mg of caffeine ingested prior to a maximal exercise bout and 780 mg of caffeine ingested prior to and during a submaximal exercise bout does not have a statistically significant effect on heart rate, systolic and diastolic blood pressure, minute ventilation, or oxygen consumption. However, there appears to be a consistent trend across all measures that warrants further investigation.

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SECTION II. THE EFFECT OF CAFFEINE INGESTION ON
THERMOREGULATORY FUNCTION DURING SUBMAXIMAL EXERCISE

INTRODUCTION

Caffeine has been widely studied as a possible ergogenic aid to exercise performance through its sparing effect on muscle glycogen. During prolonged exercise, caffeine has been shown to enhance fat metabolism and retard the depletion of muscle glycogen stores (3, 8, 11). The depletion of glycogen has been indicated as a detriment to exercise performance (1, 3, 8). However, data on the physiological effects of caffeine during exercise have been somewhat limited, focusing primarily on its role in substrate utilization and its influence on selected cardiorespiratory parameters (heart rate, oxygen consumption, ventilatory rate). Though not widely investigated, caffeine may play a role in thermoregulatory processes at rest by stimulating metabolic heat production (7, 9, 16), inducing diuresis (15), and affecting gastric fluid emptying time (10). It has been speculated that some combination of these caffeine-influenced thermoregulatory effects could possibly reduce endurance exercise performance (hyperthermia, etc.), especially when exposed to a hot humid environment (5, 15).

Various studies have investigated physiological responses during exercise with regard to altered thermoregulatory function. Claremont et al. (2) found a significant reduction in both submaximal exercise performance and heat tolerance following a drug-induced diuresis. Decreased cardiac output during submaximal exercise and decreased work time during maximal exercise following thermal stress-induced dehydration were reported by Saltin (13). A state of dehydration induced by withholding fluids during exercise significantly elevated rectal and mean

body temperatures and reduced sweat loss in an investigation by Ekblom et al. (4). However, few data are available on the subject of caffeine-mediated thermoregulatory control during exercise. In one of the few such investigations reported to date, Gordon et al. (5) found no significant changes with the ingestion of caffeine in rectal temperature, plasma volume, or plasma-electrolytes (Na^+, K^+, Cl^-, Ca^{2+}, Mg^{2+}) following a two hour run. The purpose of this study was to assess the effect of caffeine ingestion on thermoregulatory function during a submaximal exercise bout.

METHODS

Subjects

Six untrained males (21-28 years) volunteered as subjects for this experiment. All subjects were either students at Iowa State University or nonstudent members of the Ames, Iowa, community. Each subject was informed of the risks and stresses associated with this study and gave their written consent. Subjects were asked to report to each exercise trial in a 12-hour fasted state. In addition, a 48-hour abstinence from any caffeine-containing products and a consistent dietary pattern, 24 hours prior to each exercise trial, were required of each subject.

Exercise Regimen

The exercise regimen used in this investigation was a submaximal protocol consisting of 90 minutes of continuous exercise on a Monark bicycle ergometer. Cycling speed was set at 60 RPM. Exercise intensity was set at 60% of the subject's measured maximal oxygen consumption. Two exercise trials were performed, with one trial designated as the caffeine experimental treatment and one trial as the decaffeinated control treatment.

One hour prior to the caffeine treatment, each subject ingested 390 mg caffeine citrate dissolved in 18 oz. decaffeinated cola. Additional caffeine dosages of 65 mg caffeine citrate dissolved in 6 oz. decaffeinated cola were ingested immediately prior to exercise and at 15 minute intervals during the exercise bout. Total caffeine dosage ingested by each subject was 780 mg. The solution for the decaffeinated

treatment was administered by repeating the same protocol used for the caffeine treatment minus the caffeine.

Analytical Methods

Oxygen consumption ($\dot{V}O_2$) was determined by using an automated open circuit method. Expired oxygen and carbon dioxide concentrations were measured with an Applied Electrochemistry S-3A analyzer and a Beckman LB-2 analyzer, respectively. Both analyzers were calibrated with known concentrations prior to each exercise trial. Room temperature for each trial was maintained at 21°C and relative humidity ranged from 35-50%. Oxygen consumption values were recorded immediately prior to exercise, and at 10, 30, 60, and 90 minutes of exercise. Heart rate (HR) was monitored using an International Medical Corp. Viagraph at rest- pre-fluid ingestion, rest- pre-exercise, and at 10, 30, 60, and 90 minutes of exercise.

Skin temperature was monitored with surface electrodes placed on the thigh, forearm, forehead, and trunk. Core temperature (T_{REC}) was monitored with a rectal probe inserted prior to testing. All temperatures were recorded at rest pre-fluid, rest- pre-exercise, and 10, 30, 60, and 90 minutes of exercise. Mean skin temperature ($\overline{T}_{SKIN}$) and mean body temperature ($\overline{T}_{BODY}$) were calculated using the following formulas as reported by Saltin (13):

$$\overline{T}_{SKIN} = T_{THIGH} (.39) + T_{TRUNK} (.35) + T_{ARM} (.19) + T_{HEAD} (.07)$$
$$\overline{T}_{BODY} = \overline{T}_{SKIN} (.33) + T_{REC} (.67)$$

A 5cc blood sample was taken at rest pre-fluid, rest pre-exercise, and 10, 30, 60, and 90 minutes of exercise. Blood samples were analyzed for hemoglobin (Hb), hematocrit (Hct), and serum electrolytes (Na^+ and K^+). Electrolytes were determined with a Unicam Atomic SP-90 Absorption Spectrophotometer. Pre- and post-exercise urine (UR) samples were collected and measured for total urine volume for each subject. Pre-exercise urine samples were collected for a period following the initial resting fluid ingestion to immediately preceding exercise. Post-exercise urine samples were collected for a 20-minute period following the cessation of exercise. Each subject was instructed to void all urine immediately prior to the initial fluid ingestion. Body weight was determined prior to the initial fluid ingestion after voiding, and immediately following post-exercise urine collection.

Statistical Analysis

Urine volume was analyzed by a t-test procedure applied to differences between treatments. Data for body weight (BW) taken at pre- and post-exercise, and for $\dot{V}O_2$, HR, $\overline{T}_{BODY}$, T_{REC}, HEMO, HCT, Na^+, and K^+ taken prior to and during exercise were analyzed with a split-plot analysis of variance procedure to determine significant interactions between treatment and time. If significant interaction was found, further clarification of the interaction was determined by performing t-tests of the individual time period means between treatments. The .05 level of probability was chosen to determine significant results.

RESULTS

Table 1 and Figures 1 and 2 depict mean (±SE) values for $\overline{T}_{BODY}$ and T_{REC} for the caffeine and decaffeinated treatments. No significant (p > 0.05) differences were observed between treatments at rest or during exercise for either variable. Mean exercise values for $\overline{T}_{BODY}$ were 36.3 ± 0.1°C for the caffeine treatment and 36.1 ± 0.1°C for the decaffeinated treatment. Mean T_{REC} values during exercise were 37.6 ± 0.1°C for the caffeine treatment and 37.4 ± 0.1°C for the decaffeinated treatment.

Serum electrolyte levels of Na^+ and K^+ (Table 2, Figures 3 and 4) increased slightly above resting values during exercise in both the caffeine and decaffeinated treatment, though the changes were not statistically significant (p > 0.05). Differences between treatments for both Na^+ and K^+ were not significant (p > 0.05) at any point, with mean exercise Na^+ values of 144.7 ± 1.2 meq/l and 145.3 ± 1.2 meq/l for the caffeine and decaffeinated treatments, respectively. Mean exercise values for K^+ were identical for both treatments at 5.0 ± 0.5 meq/l. It did appear that serum levels of K^+ increased at a slightly greater rate in the caffeine treatment as exercise progressed from the 10 minute to the 90 minute period.

Data for Hb (Table 3, Figure 5) exhibited a mean (±SE) exercise value 2.3% higher in the caffeine treatment (17.2 ± 0.3 gm) when compared to the decaffeinated treatment (16.8 ± 0.3 gm). However, the difference was not statistically significant (p > 0.05). Mean (±SE) Hct (Table 3, Figure 6) showed a similar response to Hb, with Hct 1.3% higher during exercise in the caffeine treatment when compared to the decaffeinated

Table 1. Mean (±SEM) body temperature (T_{BODY}) and rectal temperature (T_{REC}) values at rest and during exercise in the caffeine (C) and decaffeinated (D) treatments

| Measure	Treatment	Pre-fluid	Pre-exercise	Exercise Time			
				10	30	60	90
$\overline{T}_{BODY}$ (°C)	C	35.5 (±0.1)	35.4 (±0.1)	35.8 (±0.1)	36.2 (±0.1)	36.6 (±0.1)	36.7 (±0.1)
	D	35.8 (±0.1)	35.6 (±0.1)	35.7 (±0.1)	36.2 (±0.1)	36.2 (±0.1)	36.4 (±0.1)
T_{REC} (°C)	C	36.9 (±0.1)	36.7 (±0.1)	37.1 (±0.1)	37.5 (±0.1)	38.0 (±0.1)	38.0 (±0.1)
	D	37.0 (±0.1)	36.9 (±0.1)	36.9 (±0.1)	37.5 (±0.1)	37.7 (±0.1)	37.7 (±0.1)
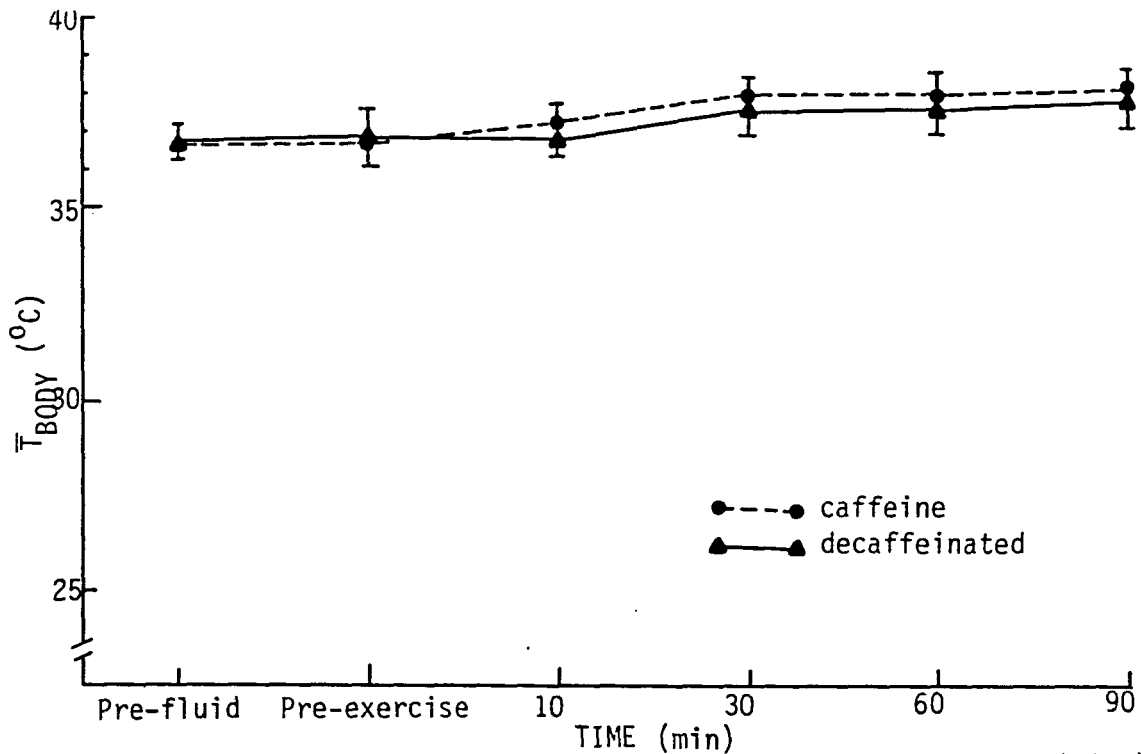
Figure 1. Mean (±SEM) values for mean body temperature at rest and during exercise in the caffeine and decaffeinated treatments
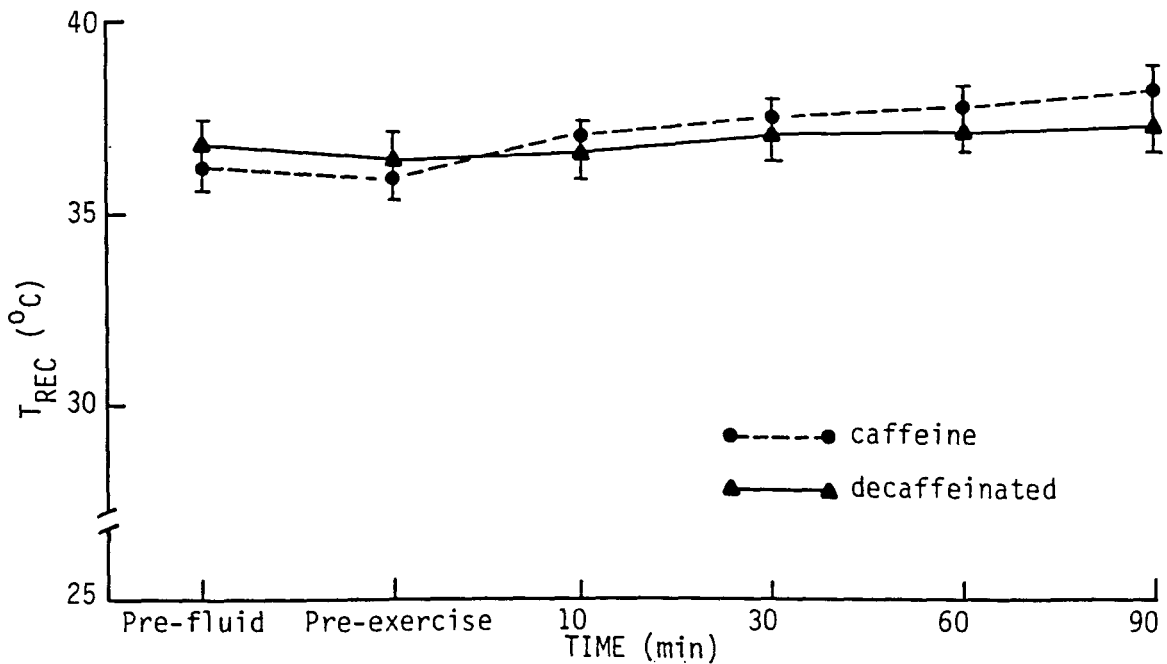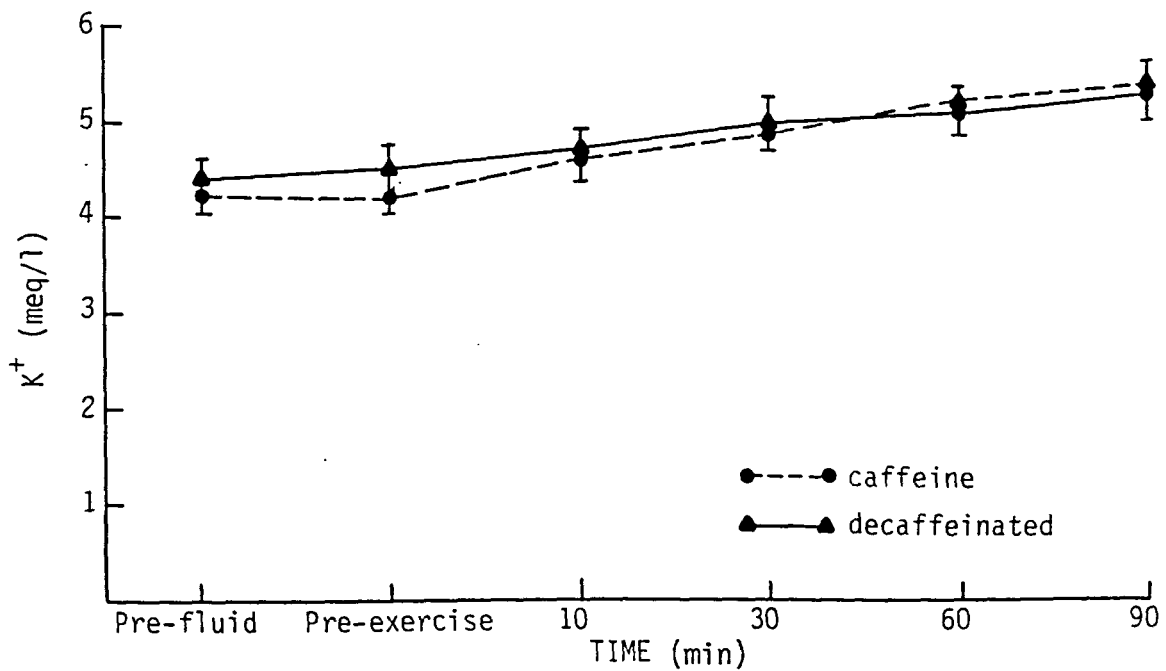

Figure 2. Mean (±SEM) values for rectal temperature at rest and during exercise in the caffeine and decaffeinated treatments

Table 2. Mean (±SEM) values for serum sodium (Na^+) and potassium (K^+) levels before and during exercise in the caffeine (C) and decaffeinated (D) treatments

| Measure	Treatment	Pre-fluid	Pre-exercise	Exercise Time			
				10	30	60	90
Na^+ (meq/l)	C	143.4 (±1.2)	142.9 (±1.2)	143.5 (±1.2)	144.6 (±1.2)	145.1 (±1.2)	145.8 (±1.2)
	D	144.6 (±1.2)	144.7 (±1.2)	145.0 (±1.2)	145.3 (±1.2)	145.2 (±1.2)	145.7 (±1.2)
K^+ (meq/l)	C	4.2 (±0.5)	4.2 (±0.5)	4.6 (±0.5)	4.9 (±0.5)	5.2 (±0.5)	5.4 (±0.5)
	D	4.4 (±0.5)	4.5 (±0.5)	4.7 (±0.5)	5.0 (±0.5)	5.1 (±0.5)	5.3 (±0.5)
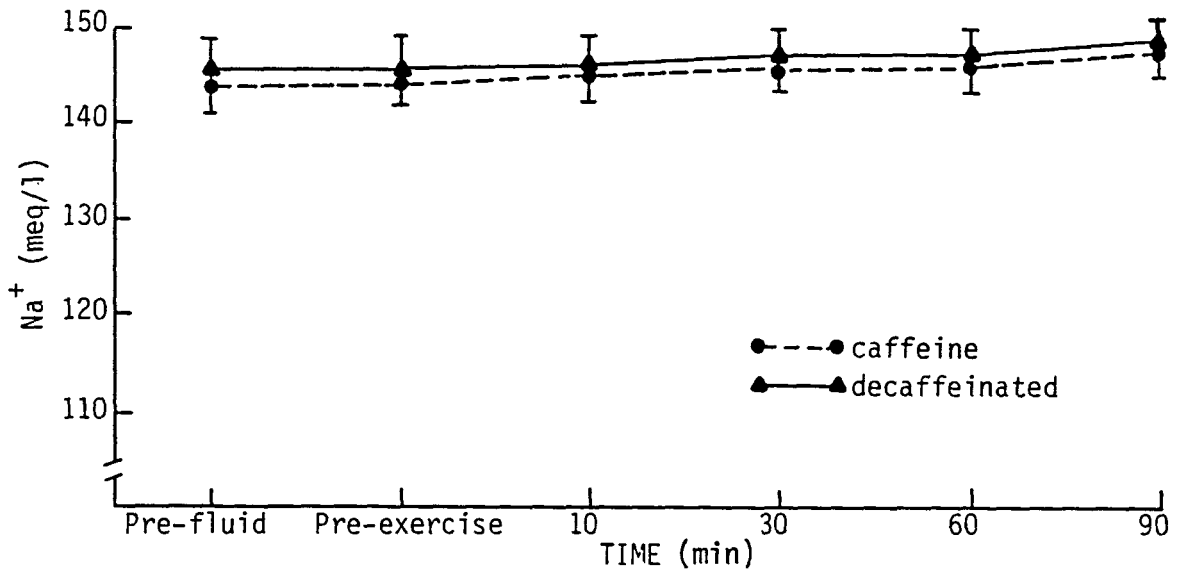
Figure 3. Mean (±SEM) values for serum Na$^+$ at rest and during exercise in the caffeine and decaffeinated treatments

Figure 4. Mean (±SEM) values for serum K$^+$ at rest and during exercise in the caffeine and decaffeinated treatments

Table 3. Mean (±SEM) hemoglobin (Hb) and hematocrit (HCT) values at rest and during exercise in the caffeine (C) and decaffeinated (D) treatments

Measure	Treatment	Pre-fluid	Pre-exercise	Exercise Time			
				10	30	60	90
Hemo (gm)	D	15.7 (±0.3)	16.2 (±0.3)	16.9 (±0.3)	16.9 (±0.3)	16.8 (±0.3)	16.9 (±0.3)
	C	15.9 (±0.3)	16.4 (±0.3)	17.2 (±0.3)	17.4 (±0.3)	17.1 (±0.3)	17.4 (±0.3)
HCT (%)	D	45.0 (±0.8)	47.0 (±0.8)	48.3 (±0.8)	47.8 (±0.8)	48.6 (±0.8)	48.2 (±0.8)
	C	45.1 (±0.8)	47.4 (±0.8)	48.6 (±0.8)	49.3 (±0.8)	48.0 (±0.8)	49.5 (±0.8)
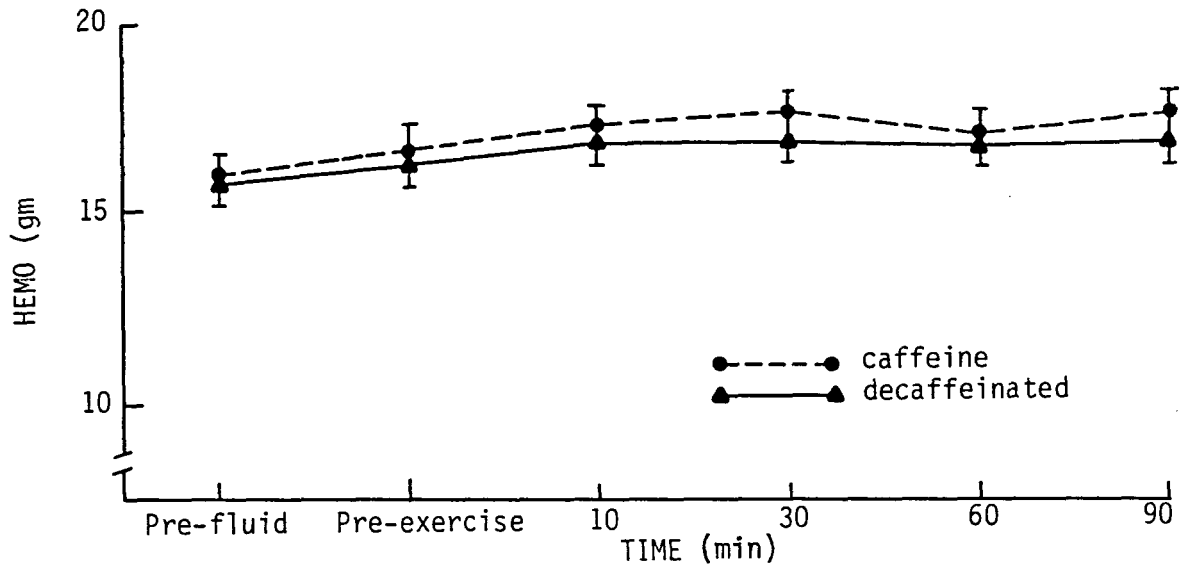
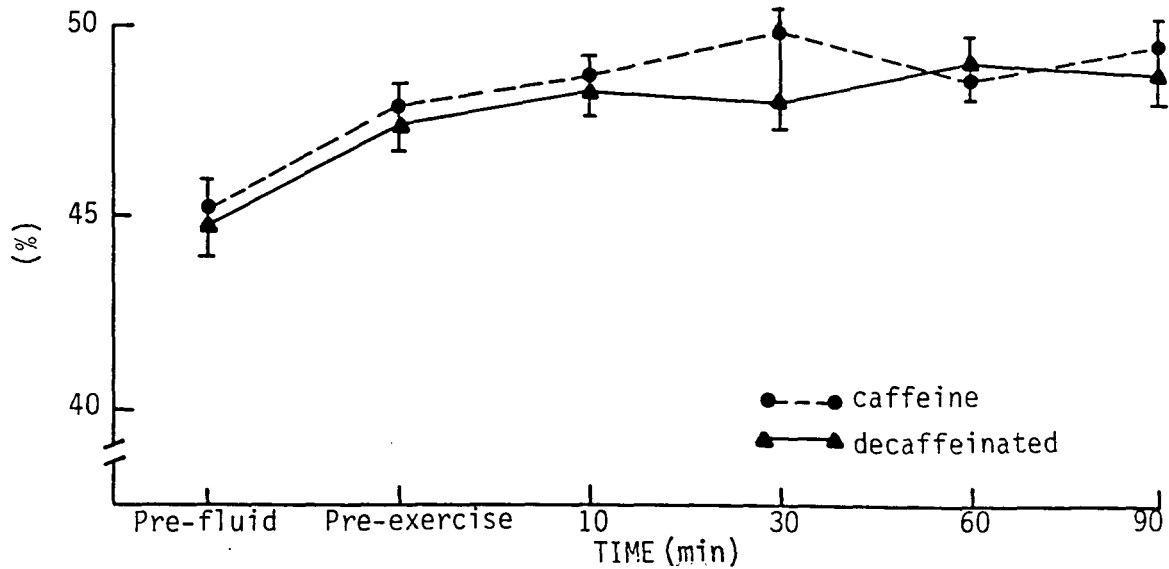Figure 5. Mean (±SEM) values for hemoglobin at rest and during exercise in the caffeine and decaffeinated treatments

Figure 6. Mean (±SEM) values for hematocrit at rest and during exercise in the caffeine and decaffeinated treatments

treatment. However, no significance ($p > 0.05$) was found between treatments.

Heart rates (Figure 7) did not differ significantly ($p > 0.05$) between treatments although the mean exercise value was 4.2% higher for the caffeine treatment. Changes in body weight (Figure 8) did not differ ($p > 0.05$) from pre-exercise to post-exercise for either treatment nor were they significant at any measurement period between treatments.

Despite the lack of statistical support for a caffeine-induced fluid volume change as evidenced by hemodynamic and body weight data, urine volume was 21.2% higher in the caffeine treatment (264.1 ml) as compared to the decaffeinated treatment (208.6 ml). However, the difference between treatments was not significant ($p > 0.05$).
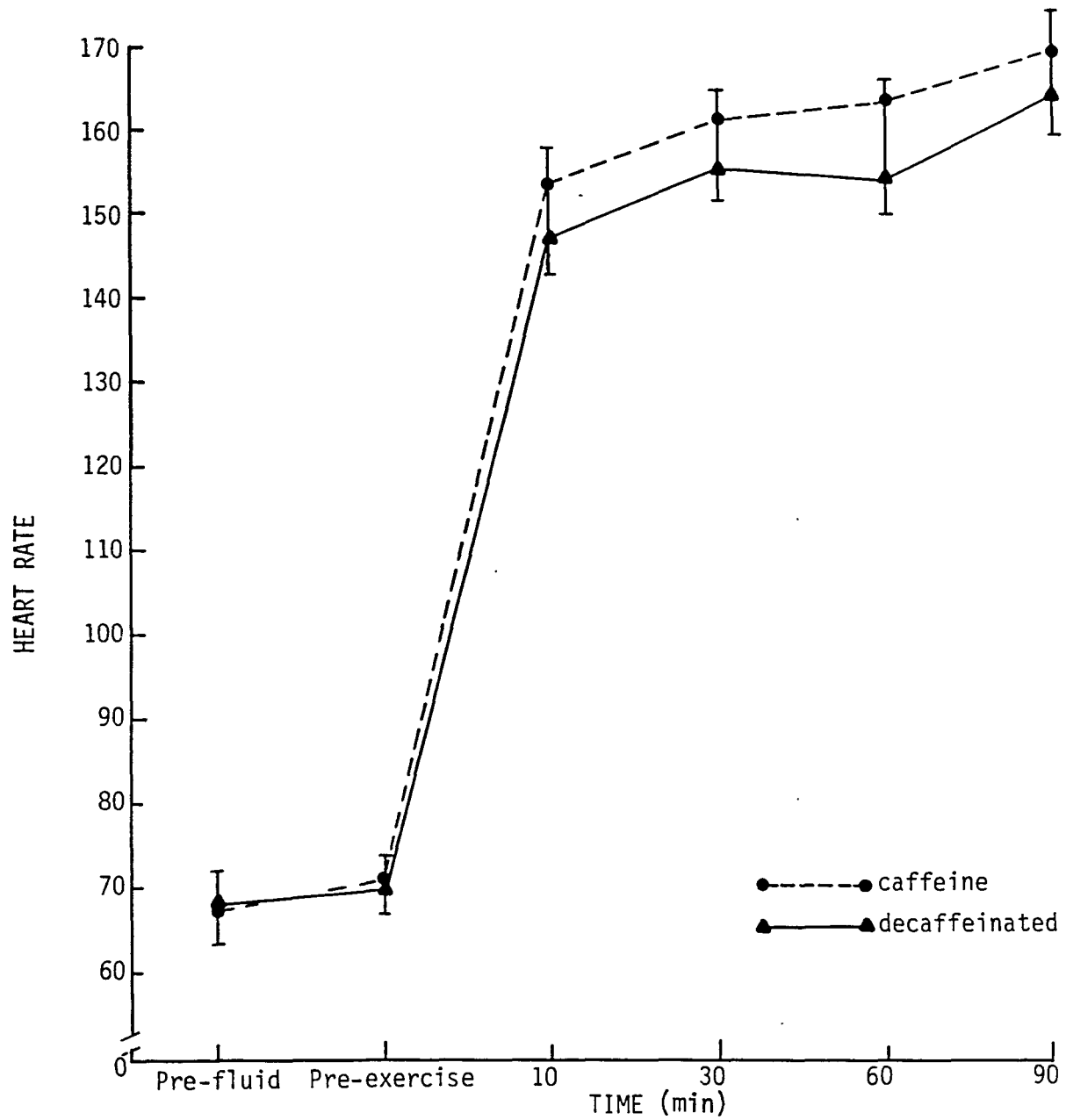
Figure 7. Mean (±SEM) values for heart rate at rest and during exercise
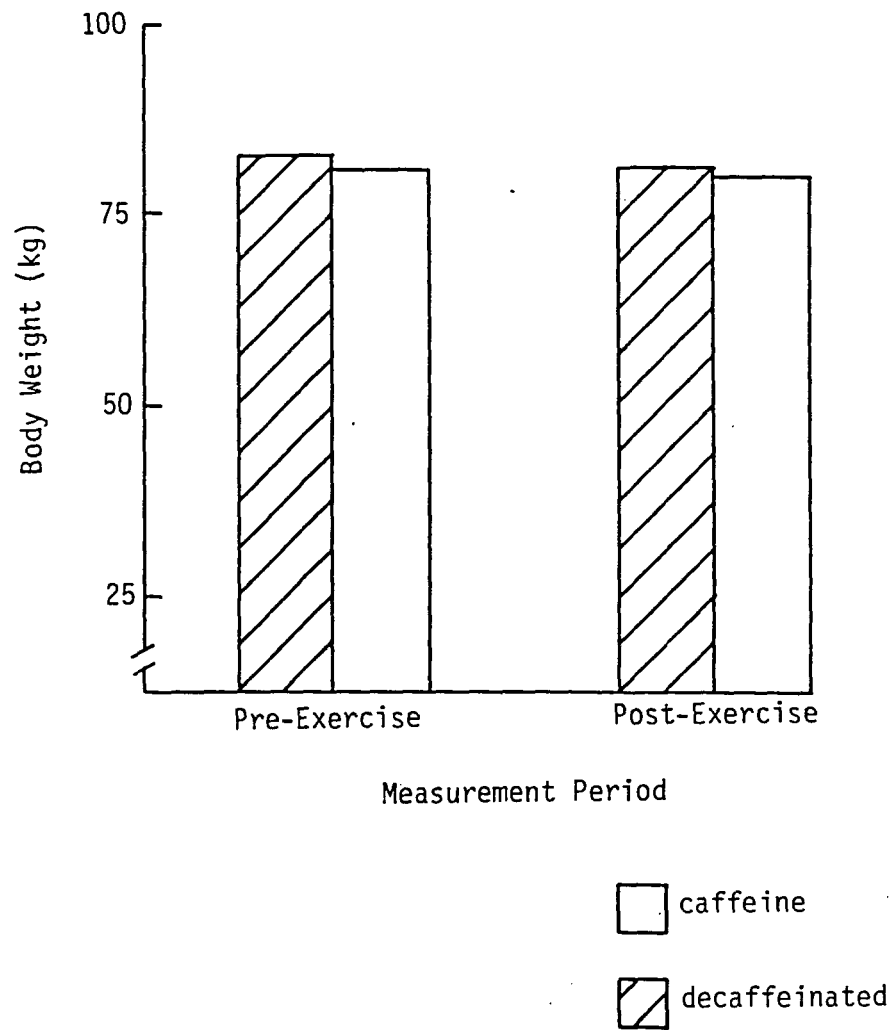   in the caffeine and decaffeinated treatments

Figure 8. Changes in body weight at pre- and post-exercise periods for the caffeine and decaffeinated treatments

DISCUSSION

Based on the results of this investigation, the ingestion of caffeine had no statistically significant effect on thermoregulatory control during submaximal exercise. However, a definite trend existed across all subjects. As previously indicated, little information is available on the specific effects of caffeine on thermoregulation during exercise. It has been shown that caffeine ingestion at rest is capable of stimulating increases in metabolic heat production and core temperature (7, 9, 16), and inducing diuresis (15). Increases in heat production occur in part due to the stimulatory effects of enhanced epinephrine release by caffeine on the thermoregulatory centers of the hypothalamus (12). In addition, caffeine has a direct affect on the renal tubular system so that glomerular filtration rate is increased and Na^+ reabsorption is decreased, leading to a diuretic effect (6).

Results for core temperature and changes in hemodynamic constituents (HEMO and HCT) are in agreement with the work of Gordon et al. (5), who found no differences in rectal temperature, percent change in plasma volume, or water deficit between caffeine and control trials following two hours of running at approximately 75% HR max. The authors suggested that the failure of caffeine to affect cardiac output (as evidenced by no change in HR between trials; stroke volume (SV) was not measured) would have a similar effect on renal blood flow before and during exercise and would partially account for the lack of observed differences in water loss. It was also suggested that the known dilating effects of caffeine on peripheral vasculature should compensate for an increase

in metabolic heat production, in terms of blood flow distribution to the skin, therefore, helping to maintain core temperature. Finally, the authors indicated that the caffeine dosage required to elicit the above effects may be in excess of that used in their study (5 mg/kg body weight). In the present investigation, a caffeine dosage of 780 mg was ingested by each subject. An increase in exercise HR of 4.3% was observed in the caffeine treatment, and UR volume was 21% higher with caffeine. In addition, core, skin, and body temperature, and HEMO and HCT values were consistently higher during exercise in the caffeine treatment. Although these differences were not significant, it would appear that the caffeine dosage used in this study may have affected cardiac output and metabolic heat production sufficiently to evoke the observed results.

It has also been demonstrated that a reduction in body fluids through either drug-induced diuresis or thermal dehydration will significantly affect thermoregulation by reducing the circulatory response needed for metabolic heat dissipation and, therefore, augmenting the increase in core temperature normally observed during prolonged exercise when using a variety of protocols (2, 4, 13). Although the results were not significant, a 21% mean increase in UR volume in the present investigation with the ingestion of caffeine may cause one to expect a diuretic-influenced effect on core and body temperatures. Although not statistically significant, all subjects did exhibit an increase in all temperature readings in the caffeine treatment. However, it should be noted that none of the subjects suffered from symptoms

of heat illness.

There were no significant differences in serum electrolytes Na^+ and K^+ concentrations between treatments. This is in agreement with the forementioned study by Gordon et al. (5). These results are also similar to the work of Wilkerson (17) who, in a noncaffeine related study, found no change in plasma Na^+ or K^+ concentrations above control during different exercise durations (9 min, 14 min, 19 min), each conducted at 60% $\dot{V}O_2$ max. Caffeine is known to directly affect the renal tubules so that Na^+ reabsorption is decreased. An excessive loss of electrolytes during prolonged exercise, especially when associated with high rates of fluid loss, is known to disturb normal homeostatic circulatory and nervous function (14). The Na^+ and K^+ help regulate the function of neuromuscular control. The trend observed in the present investigation regarding the loss of fluid between treatments might lead to a change in serum electrolyte concentrations. However, this did not appear to be true. It should be reported that UR volume samples were not assayed for Na^+ or K^+ content. Also, the problem exists that the measurement of electrolyte concentrations relative to blood fluid volume may not be indicative of actual serum electrolyte content when change in blood fluid volume is not considered (17). Blood fluid volume changes were not measured in this investigation.

In summary, these data indicate that 780 mg of caffeine ingested prior to and during a submaximal exercise bout does not have a statistically significant effect on thermoregulatory control, as determined by core and body temperatures, urine loss, hemodynamic constituents (Hb

and Hct), and serum electrolytes (Na^+ and K^+). However, there appears to be a consistent trend across most of the parameters measured that warrants further investigation.

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GENERAL SUMMARY

This investigation was intended to assess the effects of caffeine ingestion on cardiovascular function (heart rate, blood pressure, electrocardiographic activity) during maximal and submaximal exercise and to determine the caffeine-mediated effects of thermoregulatory control during submaximal exercise as determined by hemodynamic variables (hemoglobin, hematocrit, serum electrolytes), fluid loss, and body temperatures. Subjects used were six healthy untrained males ages 21-28. Maximal exercise was conducted using a step-wise protocol to $\dot{V}O_2max$ on a cycle ergometer. Submaximal exercise consisted of 90 minutes continuous work on a cycle ergometer at 60% $\dot{V}O_2max$. All variables were monitored at regular intervals both prior to and during exercise.

The results indicated that the ingestion of 455 mg caffeine in the maximal exercise trial and 780 mg caffeine in the submaximal trial failed to produce statistically significant changes in any of the cardiovascular or thermoregulatory parameters observed when compared to a control trial. However, a definite trend did appear to exist across a majority of the measures for all subjects. The observed trend, combined with a general lack of available data on the effects of caffeine on cardiovascular or thermoregulatory function during exercise, should warrant further investigation.

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