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Thermoregulatory effects of caffeine ingestion during rest and exercise in men

Nancy A. Dunagan
San Jose State University

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**Thermoregulatory effects of caffeine ingestion during rest and
exercise in men**

Dunagan, Nancy Elaine, M.A.

San Jose State University, 1993

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THERMOREGULATORY EFFECTS OF CAFFEINE INGESTION
DURING REST AND EXERCISE IN MEN

A Thesis

Presented to

The Faculty of the Department of Human Performance
San Jose State University

In Partial Fulfillment

Of the

Requirements for the Degree

Masters of Arts

By

Nancy A. Dunagan

May, 1993

APPROVED FOR THE DEPARTMENT OF HUMAN PERFORMANCE

A handwritten signature in cursive script, appearing to read "C. Cisar", written over a horizontal line.

Dr. Craig Cisar

A handwritten signature in cursive script, appearing to read "W. R. Holcomb", written over a horizontal line.

Dr. William Holcomb

A handwritten signature in cursive script, appearing to read "John E. Greenleaf", written over a horizontal line.

Dr. John Greenleaf

APPROVED BY THE UNIVERSITY

A handwritten signature in cursive script, appearing to read "Serena R. Stanford", written over a horizontal line.

THERMOREGULATORY EFFECTS OF CAFFEINE INGESTION
DURING REST AND EXERCISE IN MEN.

N. A. Dunagan

Thermoregulatory responses were measured at rest and during submaximal exercise in normal ambient conditions in 11 men with (CT) and without (NCT) the ingestion of 10 mg of caffeine/kg of body weight. After ingestion of caffeine or a placebo, data were collected throughout 30 minutes of rest and the following 70 minutes of leg ergometer exercise (~68% of $\text{VO}_{2\text{max}}$). There were no significant differences ($p < .05$) between NCT and CT in oxygen uptake, heart rate, rectal or skin temperatures, or skin heat conductance (2-way ANCOVA), or between NCT and CT in sweat rate (t -test). Thus, a high level of caffeine ingestion has no detrimental effects on body temperature responses during heavy exercise in normal ambient conditions.

I dedicate this thesis to my husband, Stephen E. Dunagan, who inspired me to greater achievement and supported me in my process toward that goal.

ACKNOWLEDGMENTS

This past Thanksgiving morning I awoke about 5:00 a. m. with the thoughts racing through my head of all the help I have received during the long journey of conceiving, doing, analyzing, and writing this study. Dr. Craig Cisar has always been available and helpful throughout this long process. During the long early hours of data collection Dr. Cisar was there. The assistance and direction Dr. Cisar gave was invaluable, and I sincerely appreciate the help he has given.

In the beginning, when the light went on, when the idea for this thesis was being formed, Dr. John Greenleaf at NASA AMES Research Center was willing to listen to this graduate student whom he had never seen or heard of before. During those discussions my ideas were molded and changed to form the ultimate plan. Dr Greenleaf has given much of his time and expertise to this research. Without his help I know this study would have been very different and may never have been accomplished.

Before data collection started I knew I would need large quantities of donated labor. Five technicians were needed for each trial, and each of the twelve volunteers went through three trials. I received a tremendous amount of help from friends, associates, and strangers willing to donate time and help as lab technicians. Al Christensen

was one of those friends. Al donated many hours of his time and assisted with every testing session. Not only did Al assist with about every type of data collection that occurred, but he was invaluable to me as a time keeper. He wrote a computer program that we used for keeping track of time and for data entry. The hours and genuine interest that Al gave to this project went far beyond what one expects from a friend, and I am deeply grateful to Al for the help he gave me.

As I mentioned earlier, this study could not have been done without the help of many friends, associates and strangers. By the end of data collection I considered all those who had helped out as friends. There were too many technicians to elaborate on each's contribution, but the following friends were of invaluable worth to me as lab technicians: Stephanie Adams, Leslie Bostick, Bonita Christensen, Mike Cole, Carlos Crownover, Jan Finger, Constance Honeychurch, Richard Devirt, JoAnne Gilleland, Tacy Hahn, Mindy Hansen, Susie Leary, Karen Marshall, Virginia Mendoza, Terri Oberg, Adrienne Robinson, Derek Tiefer, and Ken VanAalsburg. I am sure someone slipped through the cracks and I didn't get their name down, but these people monitored heart rates, temperatures, fans, workloads, and in general created a pleasant atmosphere within which to work.

Although I can't mention their names, the subjects in this study not only went through all kinds of discomforts, but they were fun to be around. This was quite an accomplishment in the early hours of the morning when a lot of this data collection was taking place.

While I was laying in bed those early hours on Thanksgiving many other people drifted in and out of my thoughts. People who had contributed to my whole educational and research experience. I had to share the physiology lab with Terri Wexted during those data collection months and Terri was very cooperative in working together with me. Minera Duke, a good friend and mentor, kept planting seeds of inspiration that enabled the idea of going back to school for a Masters degree to grow.

My children have lived through this experience with me. Meghan was three when I started, and is now in first grade. Christian was in kindergarten, and is now in third grade. Both have provided lots of hugs and pats on the back when I really needed those hugs and pats.

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CHAPTER I

Introduction

Chapter one presents the background information, statement of the purpose, null hypotheses, delimitations, limitations, operational definitions, significance of the problem, and the statistical analysis for this investigation.

Background Information

Caffeine has long been used for its alleged capability to uplift attitude, decrease fatigue, and increase work capacity (Rall, 1985). Only 50 milligrams of caffeine will evoke physiological responses involving the digestive system, the central nervous system, and the cardiovascular system (Somani & Gupta, 1988). Because of caffeine's possible ergogenic effects on athletic competition, the International Olympic Committee plasma caffeine concentrations to less than 15 ug/ml (Rosenbloom & Sutton, 1985).

Caffeine has been reported to either improve endurance capabilities (Chad & Quigley, 1989; Costill, Dalsky, & Fink, 1978; McNaughton, 1986; Sasaki, Maeda, Usui, & Ishiko, 1987) or to have no effect on aerobic performance (Aragyasami, Yang, & Winder, 1989; Bond, Adams, Balkisson, McRae, Knight, Ribbins, & Banks, 1987; Falk et al. 1989;

Tarnopolsky, Atkinson, MacDougall, Sale, & Sutton, 1989; Winder, 1986). Athletes continue to take caffeine before competition although data concerning caffeine's effectiveness as an ergogenic aid has been disparate. Because caffeine is so commonly ingested in situations which tax the thermoregulatory system, caffeine's effect on thermoregulation should be addressed.

There are several pharmacological effects of caffeine which could possibly cause shifts in temperature regulation. Caffeine increases urinary water and sodium secretion (O'Neil, Hynak-Hanbison, & Gordan, 1986). Thus caffeine may decrease the available fluid and electrolytes which are necessary for maintenance of body fluid volumes and evaporative and convective cooling. Caffeine also stimulates metabolic rate (Dullo & Miller, 1986; Dullo, Geissler, Horton, Collins, & Miller, 1989; Jequier, 1987; and LeBlanc, Jobin Cote, Samson, & Labrie, 1985). If the heat generated from the higher metabolic rate is not released through thermoregulatory avenues (convection, radiation, conduction, or evaporation), heat storage (and therefore body temperature) would ultimately be increased.

Caffeine's effect on the cutaneous vascular system is unclear. Several authors (Beckman, 1961; Govoni & Hayes, 1978; Kastrup, 1984) have attributed peripheral vasodilation to caffeine consumption. Cutaneous vasodilation would enhance internal heat dissipation via

conductance (Sawka, 1988). However, Robertson and Curatolo (1984) indicated that caffeine induces a pressor response by potentiating the effect of catecholamines on smooth muscle and actually increasing catecholamine release in most individuals. Epinephrine and norepinephrine constrict many arterioles, especially those in the skin (Schottelius & Schottelius, 1978), which would result in decreased heat dissipation by lowering conductance and evaporative heat loss. The stimulating effect of caffeine on the sympathetic nervous system and cardiovascular system may also play an important role in human temperature regulation: "Drugs that affect the cardiovascular and central nervous systems, either directly or via the autonomic nervous system, can have important implications for the maintenance of normal thermoregulation" (Rosenbloom & Sutton, 1985, p. 177).

Caffeine's effect on temperature regulation is beginning to receive scientific attention. Lin, Chandron, and Liu (1980) and Schlosberg (1983) found that caffeine produced hyperthermic responses in rats placed in normal and hot environments. Human subjects experienced less of a temperature decrease in a cold environment when given an ephedrine (1 mg/kg) and caffeine (2.5 mg/kg) mixture, but caffeine's exclusive effect on temperature regulation was unclear (Valerand, Jacob, & Kavanagh, 1989).

Research findings indicate caffeine may have a positive effect, negative effect, or no effect on temperature regulation. Starkenstein (1927) found a xanthine derivative (Diuretin) to increase extrarenal excretion in a steam environment. This additional water loss via perspiration could give short-term beneficial evaporative cooling to the body. But xanthines may produce dehydration under long-term heat exposures, ultimately putting stress of the thermoregulatory system. During sitting rest in heated conditions Biren, Al-Refaei, Finck, and Paolone (1992) found that skin temperatures and oxygen uptake increased with caffeine ingestion, which would normally result in heat storage (Pandolf, Sawka, & Gonzalez 1988). However, rectal temperature remained constant, most likely due to skin vasodilation, causing higher skin temperatures, thereby increasing heat conductance from the core to the skin.

Caffeine appears to have no effect on thermoregulation during exercise in cold environments (Doubt & Hsieh, 1991; Graham, Sathasivan, & MacNaughton, 1991). Graham et al. (1991) found a dose of 5 mg caffeine/kg body weight produced a significant increase in rectal temperature when subjects performed sub-maximal exercise during head-out water (28°C) immersion.

Falk et al. (1990) found ingested caffeine produced

tendencies toward greater sweat rate ($p < .07$) and higher final rectal temperature ($p < .068$) during treadmill running to exhaustion under normal ambient conditions. Five ml caffeine/kg caused no significant difference in rectal temperature at the completion of a two hour run (Gordon et al., 1982), but 2 of the 10 subjects reached rectal temperatures $>40^{\circ}\text{C}$.

Athletes often ingest caffeine prior to exercise, either inadvertently or specifically for its alleged ergogenic effects. Since many endurance competitions are performed in environments that tax the body's temperature regulating capabilities, the effect of caffeine on thermoregulation should be further addressed.

Statement of the Purpose

The purpose of this study was to determine if caffeine affects thermoregulatory factors such as rectal temperature, skin temperature, skin heat conductance, and sweat loss in active men at rest and when performing intensive sub-maximal aerobic exercise under normal ambient conditions.

Approach to the Problem

After pre-test measurements of height, weight, percentage body fat, and maximal oxygen uptake rate were

collected, 12 aerobically conditioned males (20 - 41 years of age) underwent a non-caffeine control trial (NCT) and a caffeine trial (CT) (10 mg caffeine per kg body weight) in normal ambient conditions. Rectal temperature, skin temperatures, oxygen uptake, and heart rate were recorded during 30 minutes of rest followed by 70 minutes of cycle ergometry exercise at approximately 68% of $\text{VO}_{2\text{max}}$. Total weight loss was determined from the subjects pre-drink weight (plus weight of ingested liquid) and their weight taken directly after the post-exercise cool-down period. Skin heat conductance, mean body temperature, mean skin temperature, and total sweat loss were calculated. Mean 10 minute values were analyzed using repeated measures two-way analyses of covariance. Weight loss and sweat loss were analyzed using dependent t -tests.

Null Hypotheses

There will be no significant differences found between the caffeine and non-caffeine trials in rectal temperature, mean skin temperature, skin heat conductance, or total sweat loss.

Delimitations

This study was limited to 12 healthy male volunteers ranging in age from 20 to 41 years. The subjects had less

than 18% body fat and all had been exercising aerobically at least three times per week for 30 minutes per session prior to testing.

Limitations

Factors in this study that could not be controlled included:

1. Variations in the genetic makeup of the subjects and their reaction to caffeine.
2. Slight temperature and humidity variations within the testing room.
3. Changes in the fitness level of the subjects during the testing period.

Assumptions

Assumptions made for this research included:

1. Subjects gave their best effort during the maximum oxygen uptake test and during the two test trials.
2. Subjects complied with dietary restrictions.
3. Subjects maintained their fitness level throughout the two-week experimental period.
4. Subject's heat acclimation status did not change during the study.

Definitions

The following definitions will be used in this study:

Catecholamines: The class of chemicals which includes epinephrine and norepinephrine (Astrand & Rodahl, 1986).

Conduction: Heat exchange between two solid surfaces that are in direct contact. The rate of conductance is directly related to the temperature differences between the two surfaces and the conductivity of the materials, and inversely related to the distance the heat must travel (Santee & Gonzalez, 1988).

Convection: Heat exchange that occurs between a surface and a fluid (Santee & Gonzales, 1988). Skin and air are involved in convection in normal human environmental conditions.

Diaphoretic: An adjective meaning "causing perspiration" (Stein, 1982).

Epinephrine: A hormonal substance released from the adrenal medulla when the body experiences pain, cold, hypotension, hypoglycemia, or hypoxia. Epinephrine causes constriction of many arterioles especially in the skin, mucous membranes, and kidneys; but causes dilation of the coronary system, skeletal muscles, and lungs (Schottelius & Schottelius, 1978).

Ergogenic: Inclined to increase work output (Astrand & Rodahl, 1986).

Evaporative heat loss: Moist heat exchange which requires evaporation of water. The physical determinant of evaporative heat loss is the water concentration gradient between the body surface and the environment. The physiological limits depend on sweating rate and the body hydration level (Santee & Gonzalez, 1988).

Mean body temperature: The average body temperature calculated as the sum of 80% of the rectal temperature and 20% of the mean skin temperature (Greenleaf & Reese, 1980).

Metabolic rate: Magnitude of heat production for living animals. Metabolic rate is calculated from oxygen uptake. One liter of oxygen consumed corresponds to approximately 20 kJ (4.8 kcal) (Astrand & Rodahl, 1986).

Norepinephrine: The principal chemical transmitter at peripheral sympathetic nerve terminals. Norepinephrine has a vasoconstrictive effect and raises both systolic and diastolic blood pressure (Schottelius & Schottelius, 1976).

Oxygen uptake rate: The volume of oxygen extracted by the body from the inspired air, and is usually expressed in liters of oxygen per minute (L/min) or milliliters of oxygen per kilogram of body weight per minute (mL/kg/min) (at 0°C, 760mm Hg, dry standard temperature and pressure). If the oxygen content of the body remains constant during the measurements, oxygen uptake rate is equivalent to the volume of oxygen utilized from the metabolic oxidation of

foodstuffs. One liter of oxygen corresponds to 4.7 to 5.05 kcal of energy liberated depending on the proportion of fat and carbohydrate metabolized (Astrand & Rodahl, 1986).

Pressor: Causing an increase in blood pressure via vasoconstriction (Stein, Hauck & Su, 1982).

Radiation: A process in which energy is released by one body, transmitted through an intervening medium, and absorbed by another body (Stein et al., 1982). The net radiation balance is determined by calculating the incoming radiation and subtracting the outgoing or emitted radiation (Pandolf et al., 1988).

Rectal temperature: The temperature recorded from the rectum (Pandolf et al., 1988). A probe depth of 16 centimeters was used in this study.

Skin heat conductance: The ratio between the average heat flow to the skin surface and the temperature gradient from the core to the skin surface (Greenleaf & Reese, 1980).

Skin temperature: In this study, mean skin temperature was calculated relative body surface area using coefficient and temperatures obtained from six skin sites: the upper arm, forearm, chest, back, thigh, and leg. Mean skin temperature (T_{sk}) was calculated as: $0.06 (T_{arm}) + 0.13 (T_{forearm}) + 0.19 (T_{chest}) + 0.20 (T_{back}) + 0.21 (T_{thigh}) + 0.21 (T_{leg})$ (Greenleaf & Castle, 1972).

Vasodilation: Dilation of the blood vessels (Stein et al., 1982).

Vasoconstriction: Constriction of the blood vessels (Stein et al., 1982).

Significance of the Problem

Athletes often ingest caffeine prior to exercise, either inadvertently or specifically for its ergogenic effects. Since many endurance competitions are performed in hot environments that tax an athlete's temperature regulating capabilities, the effect of caffeine on thermoregulation should be understood. The purpose for this study was to determine if caffeine affects thermoregulatory factors such as rectal temperature, skin surface temperature, skin heat conductance, and sweat rate in active men at rest and when performing intensive, sub-maximal aerobic exercise within normal ambient environmental conditions.

CHAPTER II

Review of Literature

Introduction

This chapter will discuss consumption of caffeine, physiological effects of ingested caffeine, general factors involved in thermoregulation, and findings concerning caffeine's effect on body temperature regulation.

Consumption of Caffeine

Caffeine is ingested freely in today's society. In an excellent review on caffeine Somani and Gupta (1988) identified many caffeine sources. Coffee contains approximately 100 to 150 mg of caffeine per eight ounce cup. Americans average 1.52 cups of caffeine containing beverages a day; however, up to 10% of America's adult population are believed to consume more than 1,000 mg of caffeine per day. Caffeine is also found in tea, cocoa, chocolate, cola drinks, approximately 2,000 nonprescription drugs, and over 1,000 prescription drugs.

Physiological Effects of Ingested Caffeine

Caffeine, one of three known methelated xanthine compounds (Power & Dodd, 1985), and is an alkaloid identified structurally as 1,3,7-trimethylxanthine (Jackobson & Kulling, 1989). Methylxanthines can be

absorbed via oral, rectal, or parenteral administration (Powers & Dodd, 1985). Only 50 milligrams of caffeine can evoke gastric secretion and activation of the central nervous and cardiovascular systems (Somani & Gupta, 1988). One gram of caffeine (about 6 - 7 cups of coffee) can increase respiration and cause insomnia, tachycardia, excitement, ringing in the ears, restlessness, and extra systoles (O'Neil et al., 1986). The acute lethal dose of caffeine for adults is 5 to 10 grams (Rall, 1985).

Orally ingested caffeine is rapidly absorbed through the gastrointestinal tract. Elevated 1,3,7-trimethylxanthine levels can be found in the blood 15 minutes after ingestion and are at peak concentrations 30 to 60 minutes later (Jackobson & Kulling, 1989). The liver metabolizes caffeine, leaving about 1% of the caffeine to be recovered in urine (Rall, 1985). The half life of caffeine has been determined to be 3.5 hours (Kastrup, 1984), 2 to 10 hours (Powers & Dodd, 1985), and 4 to 48 hours (Jackobson & Kulling, 1989). Varying metabolism with age may explain the large variation.

Caffeine crosses the blood-brain barrier freely and may act directly on the vagal, medullary, and vaso-motor centers (Jackobson & Kulling, 1989). Every system of the body controlled by the central nervous system may be affected by caffeine (Somani & Gupta, 1988). Acute pharmacological actions of caffeine include:

(1) stimulation of the sympathetic nervous system (Rosenbloom & Sutton, 1985); (2) stimulation of the resting metabolic rate (Jequier, 1987); (3) elevation of plasma epinephrine levels (Bangsbo, Jacobsen, Nordberg, Christensen, & Graham, 1992; Graham & Spriet, 1991); (4) increasing jejunal water and sodium secretion (O'Neil et al., 1986); (5) stimulation of cardiac and perhaps skeletal muscle (Powers & Dodd, 1985); (6) elevation of systolic (Robertson & Curatolo, 1984) and diastolic blood pressure (Pincomb, Wilson, Hee Sung, Passey, & Lovallo, 1991); (7) increasing gastric acid secretion (O'Neil et al., 1986); (8) relaxation of smooth muscle (Powers & Dodd, 1985); and (9) mobilization of free fatty acids (Powers & Dodd, 1985).

Three cellular mechanisms have been identified to explain caffeine's pharmacological effects. These mechanisms include: 1) the translocation of intracellular calcium, 2) the inhibition of the phosphodiesterase enzyme, and 3) the blocking of adenosine receptors (Powers & Dodd, 1985). Calcium permeability may be altered by caffeine at the muscle's sarcoplasmic reticulum, resulting in increased Ca^{2+} release. Phosphodiesterase is a catalyst for the conversion of cyclic AMP to 5'AMP. By decreasing phosphodiesterase, caffeine would indirectly elevate cyclic adenosine monophosphate (cyclic AMP) levels which would result in an increased release of glycerol and free fatty

acids from triglyceride stores. Adenosine, a component of ATP and nucleic acids, can affect organs via receptors on the cell's surface (Snyder, 1984). Peripherally administered adenosine will constrict bronchi, inhibit platelet aggregation, dilate blood vessels, reduce blood pressure, produce hypothermia, and inhibit the firing of most neurons (Borstel & Wurtman, 1984; Snyder, 1984). Suppressing adenosine caffeine often causes increases in blood pressure, renin release, catecholamines, and urine output, while simultaneously decreasing bronchial tone (Somani & Gupta, 1988). Because the concentration of caffeine required to inhibit phosphodiesterase is roughly 100 times that of normal caffeine ingestion, it is more likely that caffeine's molecular mechanism is related to the inhibition of adenosine receptors (Borstel & Wurtman, 1984; Fernstrom & Fernstrom, 1984; Snyder, 1984).

General Factors Involved in Thermoregulation

There are many factors that contribute to human thermoregulation. The First Law of Thermodynamics has been used by Santee and Gonzalez (1988) as a basis for measuring the thermal effects of the environment on living organisms. Heat storage (S) involves a balance between internal heat production from metabolism (M), heat exchange that occurs via evaporation (E), conductance (K), convection (C),

radiation (R), and work (W) either leaving the system (-) or by eccentric work (+) done on the system. The heat balance equation, according to Santee and Gonzalez (1988) is as follows:

$$S = M - (\pm W) \pm E \pm R \pm C \pm K \quad [W/m^2]$$

If the factors on the right side of the equation result in a positive sum for heat storage, the body temperature will increase. Alternatively, if the sum for heat storage is negative, body temperature will decrease. Insight into caffeine's effect on thermoregulation may be enhanced by indentifying its specific effect on any of the heat balance factors. For additional information concerning the mechanisms of thermoregulation, readings from Grayson and Kuehn (1977) or Santee and Gonzalez (1988) are recommended.

Effects of Caffeine on Thermoregulation

Until recently, little attention has been given to caffeine's effects on the thermoregulatory system. Starkenstein (1927) observed that a xanthine derivative (Diuretin) increased diuretic and diaphoretic (sweating) responses. At room temperature and in a steam bath total water loss (renal and extrarenal) were measured at the end of four hours under the following conditions: (1) without

water ingestion; (2) with 1 L tap water ingestion; (3) with 1 L of 0.9% NaCl solution ingestion; (4) with 2 g of Diuretin ingestion; and (5) with 1 L of 0.9% NaCl solution + 2 g Diuretin ingestion. Starkenstein concluded that Diuretin functioned as a weak diuretic at normal room temperature, but Diuretin acted as a diaphoretic in the steam bath.

Rectal temperature was monitored in resting rats during exposure to different ambient temperatures (Lin et al., 1980). Adult male rats were placed in either an 8, 22, or 30°C environment and given 20 minutes to attain thermal balance before being injected intraperitoneal or intraventricular with 10 to 20 mg caffeine/kg. Metabolic rate (calculated from oxygen uptake), respiratory evaporative heat loss (change in water vapor tension of the expired air), and body temperatures (rectal, back skin, foot skin, and tail skin temperatures) were measured each minute for 120 minutes after caffeine injection. In the second phase the rats were pre-treatment with either 6-hydroxydopamine (a central catecholaminergic nerve fiber destroyer), phentolamine (blocks alpha-adrenergic receptors), haloperidol (blocks dopaminergic receptors), or propranolol (a B-adrenergic blocker) before caffeine injections. In all environments, caffeine caused a dose-dependent increase in rectal temperature, which was

attributed solely to increased metabolic heat production. Caffeine injections also increased behavioral excitation, cutaneous vasodilation (estimated from higher foot and tail skin temperatures), and diuresis. The hyperthermia due to caffeine injections was attenuated when the rats were pretreated with 6-hydroxydopamine, phentolamine, and haloperidol. In addition to the blockade of alpha-adrenergic and dopaminergic receptors, destruction of central catecholaminergic nerve fibers, nullified caffeine's hyperthermic effect. Lin et al. (1980) suggested that "xanthines elicit a central activation of both adrenergic and dopaminergic receptors via release of endogenous noradrenaline and dopamine and lead to behavioral excitation and hyperthermia" (p. 207). The hyperthermic response to caffeine was therefore attributed to increased motor activity, which would result in increased metabolic heat production.

Schlosberg (1983) found that the thermoregulatory response of rats to caffeine was dose dependent and that tolerance to caffeine was rapidly developed. Adult male rats acclimated to an ambient temperature of 22°C were used in three experiments. Each protocol used injections of either water or caffeine (12.5, 25, 50, and 100 mg/kg). Experiments one and three were conducted in room temperatures of 21-23°C; experiment two was conducted in an environmental chamber with temperatures of either 4 or

32°C. In both experiment one and two the acute effects of caffeine on thermoregulation were measured, and in experiment three the effects of daily caffeine administration on thermoregulation over 28 days were measured. Results from experiment one indicated acute caffeine administration produced dose dependent changes in body temperature. The lower caffeine doses (12.5 and 25 mg/kg) were followed by hyperthermia. Peak significant temperature increases of ~1°C occurred 30 to 60 minutes after caffeine injection, and were no longer significantly different after 2 to 2.5 hours. Conversely, both higher caffeine doses (50 and 100 mg/kg) induced hypothermia. Maximal decreases in temperature between 1 to 1.5°C occurred two hours after caffeine injection. Three and a half hours after injection a 1°C deficit was still observed in the rats given 50 and 100 mg/kg of caffeine.

When the rats were put in different environmental conditions their body temperature response to caffeine was altered. In the 32°C environment there was no hypothermic response to 50 and 100 mg/kg of caffeine. Although the hyperthermic reactions to 12.5 and 25 mg/kg of caffeine were less pronounced, there were still significant temperature elevations found when compared to the control group 60 and 90 minutes after injection. When placed in the 4°C environment, the rats injected with 50 and 100 mg/kg

caffeine continued to have significantly lower body temperatures than the control group. While in the cold environment the 50 mg/kg dose produced a similar declining body temperature pattern as was observed in the normal ambient environment, the 100 mg/kg dose produced a drop of almost 4.5°C in body temperature after 3.5 hours. Neither of the lower doses of caffeine produced significant changes in body temperature when the rats were exposed to the cold environment. Caffeine dependent alterations in body temperature changed with duration of exposure to the drug. Tolerance to the hypothermic reaction to caffeine developed rapidly. By the 4th day the high caffeine groups displayed body temperatures no different from the control group. After seven days the 50 mg/kg group showed a hyperthermic effect which continued for the remaining 28 days. Rats receiving both of the lower caffeine doses continued to display a hyperthermic response throughout the duration of the experiment. These results were attributed to:

- (1) possible direct and/or indirect effects on the central and/or peripheral mechanisms involved in thermoregulation;
- or (2) a secondary effect of physiological and behavioral processes that is unrelated to temperature regulation.

This well designed study provided strong evidence that the thermoregulatory response of rats to caffeine is dose and tolerance dependent.

The effects of caffeine ingestion on thermoregulatory

response during endurance running was observed by Gordon, et al. (1982) in 10 male subjects who had trained together for 17 days. Caffeine consumption was prohibited for 24 hours before the test. The morning of the test all the subjects ingested the same breakfast three hours before the run and, later, 5 subjects were given 5 mg of caffeine/kg orally 1 hour before the run. Rectal temperature was taken before and within 2 minutes of completion of the 2 hour run. The environmental conditions, obtained from a near by weather station, included dry bulb temperatures ranging from 24.5-28.9°C, wind speed between 17-22 km/h, and relative humidity of 41-54%. All subjects were given 200 ml of cold water every 20 minutes during the run. Oral caffeine had no significant effect on rectal temperature, plasma volume, or electrolyte levels. Upon completion of the run 2 of the 10 subjects had reached rectal temperatures at the heat stroke threshold (40.6°C). The rate of temperature elevation was not available since rectal temperature was not monitored throughout the run. Environmental temperature, exercise intensity, fitness level, and caffeine tolerance were additional variables not closely monitored in this study.

At the other end of the temperature spectrum, the effect of an ephedrine-caffeine mixture on humans exposed to a cold environment was investigated by Valerand et al.

(1989). Nine adult male subjects underwent two cold exposure tests (10°C for three hours) directly after ingesting either a placebo or an ephedrine (1 mg/kg) plus caffeine (2.5 mg/kg) mixture. The subjects fasted 12 hours and refrained from alcohol use at least 48 hours prior to the test. Oxygen consumption and CO₂ production were measured during cold exposure in the last 10 minutes of each 30 minute interval. The decreases in core, mean skin, and mean body temperatures were significantly less ($p < .01$) during the ephedrine/caffeine trial when compared with those during the placebo trial. In addition, subjects who received ephedrine/caffeine exhibited greater energy expenditure (18.6%) and greater carbohydrate oxidation (41.5%) compared with placebo results. Heat loss during both trials was the same. Valerand et al. suggested the beneficial effects of the ephedrine/caffeine mixture were due exclusively to greater energy production via enhanced carbohydrate utilization. Because no investigators had established the individual effect of caffeine or ephedrine on cold responses, the separate responses of either drug has not been established.

Since 1990 several investigators have addressed caffeine's effect on thermoregulation. Falk et al. (1990) investigated caffeine's effect on body fluid balance and thermoregulation during treadmill exercise (70-75% VO₂max)

performed in a neutral environment (25°C, 50% RH). Seven male subjects underwent a placebo trial and a caffeine trial. A dosage of 5 mg caffeine/kg body weight was given 120 minutes prior to exercise, plus an additional 2 mg caffeine/kg body weight was given 30 minutes prior to exercise. Serum caffeine levels during the caffeine trial were 10.74 ± 0.98 ug/ml just prior to exercise, 13.07 ± 0.98 ug/ml after 15 minutes of exercise, and remained constant throughout the remainder of the test. Time to exhaustion was not significantly different between the placebo and caffeine trials (61.60 ± 9.99 and 63.91 ± 6.42 min, respectively). Mean total water loss ($1,376 \pm 154$ vs $1,141 \pm 158$ mL, respectively), sweat rate (12.4 ± 1.1 vs 10 ± 0.7 g/m²/min, respectively), rise in rectal temperature (2.1 ± 0.3 vs. 1.5 ± 0.4 °C, respectively), and calculated heat storage (134.4 ± 17.7 vs 93.5 ± 22.5 W, respectively) were not significantly different. Final rectal temperature, although not significantly different ($p = .068$), tended to be higher in the caffeine trial. Caffeine may hinder thermoregulation under higher dosages or more stressful conditions because of the observed tendency towards greater water loss with caffeine.

The influence of caffeine and exercise on catecholamines and metabolism was observed in 6 men during 2 hours of 5°C cold air exposure by Graham,

Sathasivam, and MacNaughton in 1991. Either a placebo or caffeine (5 mg/kg body weight) capsule was ingested 30 minutes before subjects were exposed to exercise (60 W) in the cold or exposed to sitting rest in the cold. Rectal temperature, skin temperatures, oxygen consumption, carbon dioxide production, and venous blood samples were taken prior to caffeine or placebo ingestion, and at 5, 30, 60, 90, 120 minutes into cold exposure. Caffeine caused a significantly (86%) greater increase in plasma epinephrine over the 2-hour period when compared to the placebo trials. Rectal and skin temperatures were not significantly affected by caffeine during any collection times. Because there was no decrease in resting core temperature, environmental conditions may not have been cold enough to produce observable temperature differences.

Another study concerning caffeine's effect on thermoregulation with a cold environment was carried out by Doubt and Hsieh in 1991. Four trials were completed using caffeine (5 mg/kg body weight) or a placebo in both cold water (18°C) and warmer water (28°C) to observe the possible additive physiological effects of caffeine and cold water during head out immersion ergometer exercise (1.5 W/kg body weight). Ten male subjects ingested either caffeine or the placebo 90 minutes prior to exercise and immersion conditions. Data were collected starting at immersion and continuing throughout 5 minutes of rest, 5

minutes of warm up, 55 minutes of exercise, and 15 minutes of recovery. Caffeine increased plasma free fatty acids ($52 \pm 18\%$), glycerol ($14 \pm 8\%$), lactate ($28 \pm 10\%$), as well as oxygen uptake ($9 \pm 3\%$), minute ventilation ($7 \pm 5\%$), heart rate ($4 \pm 1\%$), and rectal temperature ($2 \pm .4\%$), but had no effect on respiratory exchange ratio in the 28°C environment. The increase in rectal temperature was greater ($p < .01$) with caffeine ($\pm 0.78 \pm 0.09^{\circ}\text{C}$) than the placebo ($+0.55 \pm 0.15^{\circ}\text{C}$) trials during the 28°C exposure. Rectal temperature did not vary significantly during either the caffeine or placebo exposure during the 18°C exposure. Mean skin temperature tended to increase with caffeine by 0.1 to 0.2°C during both environmental conditions. Caffeine and cold did not have significant additive effects on thermoregulation; but, as stated earlier, caffeine stimulated a rectal temperature increase during the 28° exposure. The gradient for heat loss was low in the 28°C environment compared to the heat production, and vasodilation was insufficient to prevent the increase in core temperature.

Caffeine's effect on body temperature during exposure to a heated (40°C , 70% RH) and neutral (23°C , 40% RH) environment studied in 8 male volunteers who took either a placebo, a 4 mg/kg dose of caffeine, or a 8 mg/kg dose of caffeine 60 minutes prior to the experimental

period which consisted of 60 minutes sitting at rest in the neutral or hot air environments (Biren et al., 1992). Oxygen uptake was significantly higher ($p < .05$) for both caffeine trials when compared to the placebo trial with environment having no effect. Mean skin temperature was significantly higher for both the 4 mg/kg caffeine trial ($34.18 \pm 0.40^{\circ}\text{C}$) and the 8 mg/kg caffeine trial ($34.08 \pm 0.41^{\circ}\text{C}$) compared to the placebo trial ($33.84 \pm 0.28^{\circ}\text{C}$). Body core and mean body temperatures were unaffected by caffeine. It was concluded that "the caffeine induced increase in skin temperature reflected an increased conduction of heat from core to shell allowing rectal temperature to be maintained in spite of the drug induced metabolic increase" (p. S63).

Summary and Conclusion

A summary table of selected caffeine studies is found in Appendix H. Schlosberg (1983) found caffeine affected rat thermoregulatory responses during mild and extreme temperature conditions. Lower levels of caffeine produced a consistent hyperthermic effect throughout the 28 day experiment, whereas the high doses of caffeine initially produced hypothermic responses. After several days the high caffeine doses resulted in either a reduction or no change in temperatures. Thus, results indicated caffeine

may have positive, negative, or no effect on temperature regulation.

Starkenstein (1927) found a xanthine derivative (Diuretin) to increase extrarenal excretion in a steam bath. Additional water loss via sweat could give short term beneficial evaporative cooling to the body. But xanthines may produce dehydration under long term heated conditions, ultimately putting stress on the thermoregulatory system. During sitting rest Biren et al. (1992) found skin temperatures to increase with caffeine during heated conditions. Caffeine also increased oxygen uptake which would normally result in heat storage (Pandolf et al., 1988). Rectal temperature remained constant, most likely due to vasodilation in the skin (causing higher skin temperatures) thereby increasing heat conductance from the core to the surface of the body. Using an ephedrine-caffeine mixture on humans exposed to a cold environment for three hours, Valerand et al. (1989) found the drop in core, mean skin, and mean body temperatures were significantly less ($p < .01$) during the ephedrine/caffeine trial when compared with the placebo trial, but the exclusive effect of caffeine was not determined.

Two investigators found that caffeine had no effect on thermoregulation during exercise in the cold (Doubt et al., 1991; Graham et al., 1991). But Graham et al. (1991) did

find a significant increase in rectal temperature during sub-maximal exercise in 28°C with ingestion of 5 mg caffeine /kg body weight.

Falk et al. (1990) found that caffeine tended to produce greater sweat rate ($p < .07$) and higher final rectal temperature ($p < .068$) during treadmill running to exhaustion under normal ambient conditions. The only field study by Gordon et al. (1982) found that 5 ml caffeine/kg body had no significant differences on rectal temperature at the completion of a two-hour run. Two out of 10 subjects reached heat stroke level core temperatures ($>40^{\circ}\text{C}$).

There are several pharmacological effects of caffeine which could possibly cause shifts in temperature regulation; caffeine increases water and sodium excretion O'Neil et al. (1986) and may cause dehydration and compromise evaporative and convection cooling. Caffeine stimulates resting metabolic rate (Dullo & Miller, 1986; Dullo et al., 1989; Jequier, 1987; LeBlanc et al., 1985). If the heat generated from the higher metabolic rate is not released through either increased convection, radiation, conduction, or evaporation, heat storage (and therefore body temperature) would ultimately be increased. The stimulating effect of caffeine on the sympathetic nervous and cardiovascular systems may also play an important role in human temperature regulation (Rosenbloom

& Sutton, 1985).

Caffeine increases resting metabolic rate (Dulloo & Miller, 1986; Dulloo et al., 1989; LeBlanc et al., 1985) and produces dose dependent temperature changes in rats (Lin et al., 1980; Scholsberg, 1983). Research using human subjects found that xanthines: (1) increase sweating in steam bath conditions (Starkenstein, 1927); (2) increase skin temperature during heat exposure (Biren et al., 1992); (3) increase rectal temperature during immersion in 28°C water (Graham et al., (1991); (4) have no effect on thermoregulation during cold exposure (Doubt et al., 1991; Graham et al., (1991); (5) have no thermoregulatory effect in a normal ambient or hot ambient environments during rest (Biren et al., 1992); and (6) have no thermoregulatory effect during exercise (Falk et al., 1990; Gordon et al., 1982).

Studies on humans incorporating adequate controls in a normal environment, and when the thermoregulatory system is stressed (as during exercise), are necessary to determine the possible effect of caffeine on human temperature regulation.

CHAPTER III

Methods

Introduction

This chapter will present information on the subjects, and the measurements and methods to be used in the present investigation.

Subjects

The experimental protocol for this study was approved by the San Jose State University Human Subjects Institutional Review Board. Subjects were solicited verbally and through posted advertisement (Appendix C). Twelve male volunteers were tested, but data from one of the volunteers were not included due to difficulties with temperature measurements. Each subject was screened via questionnaire (Appendix A) for age, sex, medical history, family health history, addictive habits, and exercise-training routines. Only those considered "apparently healthy" by the standards found in the American College of Sports Medicine's (ACSM) Guidelines for Exercise Testing and Prescription (4th edition, 1991) were used in this study. Since fat provides thermal resistance (Toner & McArdle, 1988), subject's fat content was required to be below 18% fat (as measured by underwater weighing). All of subjects were non-smokers. Five of the subjects consumed

less than 100 mg caffeine per day; 3 subjects consumed 100-200 mg caffeine per day; and 2 subjects consumed 200-450 mg caffeine per day.

Additionally, only active volunteers (who exercised aerobically for a minimum of 30 minutes at least three times per week) were selected, since fitness level alters caffeine's effect on resting metabolic rate (LeBlanc et al., 1985). Volunteers were informed of the procedures and the possible risks of participating in this research, and subject consent (Appendix B) was obtained before initiation of testing.

Measurements and Methods

The 11 subjects completed three testing sessions. First, in the pre-test session the subject's weight, height, body fat percentage, and maximum oxygen uptake were measured. Using a single blinded method, the subjects then performed a caffeine and a non-caffeine exercise sessions. Both exercise sessions were completed within two weeks of the pre-test. The first exercise session took place at least 2 days after the pre-test. The second exercise session took place a minimum of 2 days after the non-caffeine exercise session or a minimum of 4 days after the caffeine exercise session.

Pre-test

Subjects were instructed not to eat, or drink 3 hours prior to testing (ACSM, 1991), and to not exercise for 12 hours before the pre-test. Data were recorded on a pre-test form (Appendix C) from measurements taken in the following order: height, weight, residual lung volume, body composition (relative fat, fat weight, and fat free weight), and maximum oxygen uptake.

Height

A stadiometer was used to measure the subjects height. The bare-footed subject stood (heels together) with his heel, buttocks, scapula, and cranium against a vertical pre-measured surface. With head held upright, arms to the side, and weight distributed evenly on both feet, the subject inhaled deeply and maintained an upright position as the technician brought the headboard to the most superior part of the subject's scalp. The subject then stepped away as the technician held the headboard in position and measured the subject's height to the nearest 0.1 cm (Christensen, 1990).

Weight

Subjects wore only shorts as they were weighed on a calibrated Accu-Weight Scale (San Francisco, CA). With weight evenly distributed on both feet the subject stood in the center of the platform and the technician added or

removed weights, and then moved the slide of the scale until the beam was centered. Weight was recorded to the nearest 0.05 kg (Christensen, 1990).

Maximal Oxygen Uptake

Maximal oxygen uptake was determined using a continuous progressive exercise method on a Monark 818 cycle ergometer at a pedal cadence of 60 revolutions per minutes (rpm). The ergometer seat was adjusted to allow the subject near full leg extension, and the handle bars was adjusted to a comfortable level. Before the test began the subject was informed about the testing procedure and given an opportunity to ask questions. During this pre-test a 10-second resting electrocardiogram strip was obtained. Throughout the test, respiratory parameters and heart rate were monitored continuously.

After a 5 minute warm-up at a power output of 180 kilopond meters per minute (kpm/min), the resistance was increased by 180 kpm/min each minute until the subject was unable to maintain the 60 rpm speed. The test would have been terminated if: (1) the subject did not elect to or could not continue; (2) the equipment failed; (3) the ECG showed abnormalities; and/or (4) signs of distress were indicated by loss of coordination (ACSM, 1991). Upon completion of the maximal test the subject was given a three to five minute exercise cool-down period in which the

heart rate declined to below 120 beats per minute. Before removing the electrodes, a final ECG strip was obtained.

The subject's heart rate was measured using a standard V5 electrode lead placement. Electrodes were connected to a type 410 physiological monitor (Tektronix Incorporated; Portland, OR) interfaced to a model 462 strip chart recorder (Thornton Associates Incorporated; Waltham, MA). An electrocardiogram (ECG) was printed (paper speed of 25 mm per minute) for the last 10 seconds of each minute during the test.

A headpiece attached to a Hans-Rudolph (Kansas City, MO) respiratory valve and mouthpiece was fitted to the subject. A nose clip was also attached to force breathing through the mouth. Inhaled air entered through a Parkinson-Cowan CD-4 dry test meter (New York, NY) and through the respiratory valve. A potentiometer, interfaced with an Apple II computer, recorded the volume of inspired air. Expired air passed through the Hans-Rudolph valve into a mixing chamber, then through a Wilmore-Costill spinner Valve System (WCVS) into two gas analyzers. The oxygen (FeO_2) and carbon dioxide (FeCO_2) concentrations of the expired air were measured with a Beckman LB-2 Medical Gas analyzer (Fullerton, CA) and an Applied Electrochemistry 5-3A analyzer (Sunnyvale, CA). Both analyzers were connected to an Apple II computer. To insure accurate gas analysis,

the gas analyzers were calibrated before and periodically during each test by the same technician. Data from inspired air and expired FeO_2 and FeCO_2 concentrations were calculated from one minute samples. Expired ventilation (V_E) was calculated from the inspired ventilation rate (V_I), oxygen uptake (VO_2), and carbon-dioxide production (VCO_2); respiratory exchange ration (R_E) was calculated from VCO_2 and VO_2 .

Body Composition

Body composition was determined by underwater weighing with correction for residual lung volume. Using the oxygen dilution method, residual lung volume was determined by averaging the two closest measurements (provided the measurements were within 2% of each other) collected from a model 505 Nitrayzer nitrogen gas meter (Med Science, St. Louis, MO). The same technician calibrated the Nitrayzer prior to each test.

To measure weight underwater (using a water filled tank), the subjects wore a weighted belt and sat in a webbed sling suspended from a Chatillon scale (New York, NY). Six to 10 trials were given where the subject exhaled as much air as possible when completely immersed. The average of three trials (that were within ± 0.05 kg) were used for the underwater weight (Cisar et al., 1987). Body composition was calculated using the equation developed by

Brozek, Grande, Anderson, and Keys (1963).

Caffeine/Non-Caffeine Sessions

The two exercise sessions were performed in an identical manner except the subjects were given either a non-caffeinated or a caffeinated drink. To control the possible effects of circadian rhythms on body temperature, both caffeine/non-caffeine sessions were conducted in the morning, at approximately the same time of the day (Stephenson & Kolka, 1988). Subjects wore brief shorts, shoes, and ankle socks. Back-up data were recorded on separate data collection sheets (Appendix F). The following paragraphs will present information on: pre-exercise test requirements; caffeine administration; environmental conditions; pre- and post-test weights; resting rectal temperature, mean skin temperatures, heart rate and oxygen uptake; exercise procedures; and exercise rectal temperature, mean skin temperatures, heart rate and oxygen uptake. Body surface area, average skin temperature, mean body temperature, respiratory water loss, sweat loss, and skin heat conductance formulas are included within the temperature sections.

Pre-Exercise Session Requirements

To eliminate any previously developed caffeine tolerance, before both exercise sessions the subjects were given a list of caffeine containing substances (Appendix D).

and asked not to eat or drink any caffeine containing substances for at least four days prior to their tests (Fisher, McMurray, Berry, Mar & Forsythe, 1986). To help normalize their hydration level, the subjects were asked to refrain from alcohol 24 hours prior to testing, and to not eat or drink eight hours prior to testing, and to abstain from strenuous exercise 24 hours before each exercise test.

Caffeine Administration

Both exercise tests were performed in an identical manner except subjects were given either a control mixture or a caffeine mixture. The control mixture contained Sugar Free Crystal Light (Kraft General Foods, Inc., White Plains, NY) dissolved in 237 ml (8 ounces) of water (37°C). The caffeine test used the same mixture with caffeine (Chemicals for Research and Industry, Martinez, CA) added at a dosage equivalent to 10 mg/kg body weight. To control psychosomatic effects related to learning or expectation the subjects were not told which session they were attempting. Several subjects did comment on the bitter taste of the caffeine drink. Five of the 11 subjects completed the caffeine session first.

Environmental Conditions

The environmental conditions, including dry bulb and wet bulb temperatures and barometric pressure, were recorded prior to and after the caffeine/non-caffeine

sessions. Rectal temperature levels during exercise are independent of ambient air temperatures between 5 and 30°C (41 and 86°F) (Gonzalez, Berglund & Gagge, 1978; Lind, 1963; Nielsen, 1970; Stolwijk, Saltin & Gagge, 1968). Ambient air temperatures during this study $20.72 \pm 0.80^{\circ}\text{C}$. A fan was turned on in front of the subjects during the exercise phase to enhance sweat evaporation and to keep sweat from dripping. Wind speed was measured via a hot wire anemometer and recorded three times during each session.

Pre and Post Session Weight

The same technician weighed the nude subject before he drank either mixture. The same equipment and procedures were used as in the pre-test session. The weight of the drink was added to the pre-exercise body weight. Then, immediately after the cool-down period, all equipment was removed from the subject and the remaining moisture wiped off before the final weight was measured and recorded.

Measurements Taken at Rest

Equipment required for data collection were attached to the subject after he had been initially weighed. Baseline measurements of heart rate were recorded prior to liquid ingestion. Electrode and thermistor placement are shown in Figures 1 and 2. The experimental set up is shown in Figure 3. Drinks were ingested within one minute, when

session time started. Rectal temperature and skin temperatures were recorded every minute, heart rate, VO_2 , and VCO_2 were recorded the 1st, 2nd and 3rd minutes, and every 8th, 9th, and 10th minute of each 10 minute cycle thereafter.

Rectal Temperature

After being weighed, the subject inserted a rectal probe (Yellow Springs Instrument Company; Yellow Springs, OH) 16 cm as indicated by a predetermined mark on the probe. The rectal probe was interfaced with a Squirrel Meter-Logger (Science Electronics Inc., Miamisburg, OH). Data collected on the Squirrel were downloaded and processed on a IBM compatible Leading Edge model "D" computer (Leading Edge Hardware Pro., Inc., Canton, MA). Rectal temperature (T_{re}) was recorded to the nearest 0.01°C every minute.

Thermistor
Placement

Electrode
Placement

FIGURE 1

Electrode and Thermistor Placement

FIGURE 2

Thermistor Placement

FIGURE 3

Experimental Set Up

Skin Surface Temperatures

Thermistors were attached to the skin with a prototype model of the YSI model PH09 probe holders which allowed for free air circulation around them. Thermistors were interfaced with a Squirrel Meter - Logger (Science Electronics Inc., Miamisburg, OH). Data collected on the Squirrel were down-loaded and processed on a IBM compatible Leading Edge model "D" computer (Leading Edge Hardware Pro., Inc., Canton, MA). Attachment sites for the thermistors were on the right side in the following positions: (1) arm - over the deltoid insertion on the humerus; (2) forearm - over the belly of the extensor carpi radialis longus; (3) chest - 3 cm over nipple; (4) back - directly posterior to the chest probe; (5) thigh - over the middle of the vastus lateralis; and (6) leg - on the lateral side and over the belly of the gastrocnemius muscle (J. E. Greenleaf, personal communication, February 27, 1991). Mean skin temperature (T_{sk}) was calculated as: 0.06 (arm) + 0.13 (forearm) + 0.19 (chest) + 0.20 (back) + 0.21 (thigh) + 0.21 (leg temperature) using the formula from Greenleaf and Castle (1972).

Oxygen Uptake

Oxygen uptake, carbon-dioxide production, expired ventilation, and respiratory exchange ratio were collected using the same technique and equipment as during the

maximal oxygen uptake rate. Oxygen uptake, carbon-dioxide production, expired ventilation, and respiratory exchange ratio were recorded the first, second and third minutes, and the eighth, ninth, and tenth minutes of each 10-minute cycle thereafter.

Body Surface Area

Body surface area was calculated with the DuBois formula cited by Greenleaf and Reese (1980) where body surface area (SA) in m² was:

$$71.84 [(wt)^{0.425} \times (ht)^{0.725}] \times 10^{-4} \quad (1)$$

Mean Body Temperature

Mean body temperature was calculated from Greenleaf and Reese (1980) where mean body temperature (T_{mb}) in °C was:

$$T_{mb} = 0.8 (T_{re}) + 0.2 (T_{sk}) \quad (2)$$

Total Water Loss

Total water loss was calculated with an equation from Ekblom, Greenleaf, Greenleaf, and Hermansen (1971), where total water loss in g/m²/hr was:

$$H_2O_{tot} = \{(total\ wt\ loss / SA)$$

$$- [118.614 (V_{CO_2}) - 85.742 (V_{O_2})] \times L/m^2 \quad (3)$$

Respiratory water loss

Respiratory water loss was calculated from an equation by Ekblom et al. (1971). Respiratory water loss in g/m²/hr was:

$$H_2O_{res} = V_{E_{BTPS}} [(H_2O_{do} - H_2O_{dar}) \times O_a] \times 60/m^2 \quad (4)$$

Where:

H_2O_{do} = water density at oral temperature (the mean oral temperature was determined using measurements taken prior to liquid consumption, and just after exercise completion).

H_2O_{dar} = water density at ambient room temperature.

O_a = relative humidity at ambient room temperature.

Sweat loss

Sweat loss was calculated using an equation from Ekblom et al. (1971). Sweat loss in g/m²/hr was:

$$\text{Sweat Loss} = (H_2O_{tl} - H_2O_{rl}) - H_2O_{il} \quad (5)$$

Where:

H_2O_{tl} = total water loss (weight lost in grams).

H_2O_{rl} = respiratory water loss.

H_2O_{il} = insensible water loss (equivalent to 18g/m²/hr).

Skin Heat Conductance

Mean skin heat conductance (Hsk) was calculated from the conductance equation of Greenleaf and Reese (1980) where mean skin heat conductance (Hsk) in kcal/m²/h/°C was:

$$Hsk = \frac{M_{gross} - E_{res} - C_{res} - W - (+S)}{SA (XT_{re60-70} - XT_{sk60-70})} \quad (6)$$

Where:

- M_{gross} = total heat production from oxygen uptake
(kcal/h)
- E_{res} = evaporative heat loss from the respiratory tract (kcal/h)
= 0.58 (respiratory water loss)
- C_{res} = conductive and convective heat loss from the respiratory tract (kcal/h), assumed to be zero
- W = heat loss due to external work (kcal/h)
= 0.86 x (work load in watts)
- $+S$ = change in body heat storage (kcal/h)
= 0.83 x wt [0.8 (T_{re 70-60}) + 0.2 (T_{sk 70-60})] x 6
weight (wt) in kilograms
- SA = body surface area (m²)
= 71.84 x [wt^(0.425) x ht^(0.725)] x 10⁻⁴
height (ht) in centimeters
- T_{re60} = rectal temperature after 60 minutes

$X_{T_{re} 60-70}$ = mean of T_{re} measured at 60, 65, and 70 minutes

$T_{re} 70-60$ = the difference between $T_{re} 70$ and $T_{re} 60$

Heart Rate

The subject's heart rate was measured using a standard V5 electrode lead placement connected to a model 410 physiological monitor (Tektronix Incorporated, Portland, OR) interfaced with a type 462 strip chart recorder (Thornton Associates Incorporated; Waltham, MA). An electrocardiogram (ECG) was printed (using a paper speed of 25 mm per minute) the last 10 seconds of the 1st, 2nd, and 3rd minutes, and the last 10 seconds of every 8th, 9th, and 10th minute of each 10 minute cycle thereafter for the duration of the test.

Exercise Procedures

After a 30 minute rest period the subject seated on the ergometer initiated cycling exercise and continued for 70 minutes. Caffeine blood level should have peaked during the exercise period since caffeine concentrations peak 30 to 60 minutes after ingestion (Jackobson & Kulling, 1989). Since the rise rectal temperature is dependent on the relative exercise load (Saltin & Hermanssen, 1966), the subject cycled using the same constant exercise load equivalent to approximately 65% of his previously determined VO_2 max. The exercise load was determined from

the following equation (Lang, Latin, Berg & Mellion, 1992) where exercise load in in kgm/min is:

$$\text{Load} = \{ \text{VO}_2 \text{ (ml/min)} - [(3.5 \text{ ml/kg/min} \times \text{kg body weight}) + 260 \text{ ml/min}] \} / 1.9 \text{ ml/min.}$$

A fan was turned on at the start of exercise to increase convective cooling and enhance evaporation sweat loss. To reduce sweat loss via dripping and enhance evaporative heat loss, sweat was wiped to drier areas of the body. Verbal encouragement was given throughout the exercise session.

The test protocol would be terminated if: (1) the subject did not want to (or could not) continue; (2) the equipment failed; (3) the ECG showed abnormalities indicating signs of distress; (4) signs of distress were indicated by loss of coordination (ACSM, 1991); or (5) if rectal temperature reached 40°C. Upon completion of the caffeine/non-caffeine sessions, the subject was given a 3 to 5 minute exercise cool-down period in which the heart rate declined to below 120 beats per minute. Before removing the electrodes a final ECG strip was obtained.

Physiological Parameters Monitored During Exercise

Exercise rectal temperature, mean skin temperatures, heart rate, VO₂, and CO₂ continued to be recorded during

exercise employing the same techniques and frequency periods as during the resting period. Body surface area, average skin temperature, mean body temperature, respiratory water loss, sweat rate, and skin heat conductance were calculated from the exercise data.

CHAPTER IV

DATA ANALYSIS

Introduction

This chapter will present information pertaining to: the level of significance, analysis of data, summary of findings, discussion of findings, conclusions, weaknesses, and recommendations for future research.

Level of Significance

A probability level (p) of .05 or less was selected as the level of statistical significance for all data analysis.

Analysis of data

Although 12 healthy men were tested, data from only 11 subjects were analyzed due to difficulties in collecting accurate temperature data for one subject. Mean, standard deviation, standard error of the mean, variance, standard error of the skew, range, minimum, maximum and sum were calculated for each variable to examine the descriptive nature of the data. Repeated measures two-way analysis of covariance were used to control for possible differences between the caffeine and control sessions at the average 9th minute. The repeated measures two-way analysis of

covariances was used to determine changes in the variables measured across time and to compare differences of effects of the two test treatments (control or caffeine) on the dependent variables. If significant interaction was present between the caffeine and control sessions, data were plotted to observe where the interaction occurred. Summary tables for each of the two-way analysis of covariance tests are presented in Appendix G. Repeated measures one-way analysis of variances (ANOVA) and Tukey post-hoc tests were used to determine if significant main effects were found across time in the caffeine or control sessions. Dependent t -tests were used to determine if significant differences existed between the two sessions in total weight loss, weight loss in grams per hour, total water loss, and total sweat loss.

Table 1 summarizes anthropometric and physiological data. Table 2 summarizes environmental conditions present during testing. Weight and sweat loss data collected during the caffeine and control sessions are summarized in Table 3, and physiological data collected during the caffeine and control sessions are summarized in Table 4.

Table 1

Anthropometric and Physiological Data

	Age	Surface Area (m ²)	Height (cm)	Fat%	Exercise Load kpm/min	VO ₂ max L/min	VO ₂ max mL/kg/min
Mean	29.18	1.961	180.14	12.3	1088.18	3.73	48.7
± SD	6.21	.116	4.43	3.7	153.02	.46	6.2

Table 2

Ambient Environmental Data

	Baro. Press.	Dry Bulb Temp.	Humidity	Wind m/min
Mean	760	20.72	64.2	156
± SD	1	.80	4.0	4

Table 3

Weight and Sweat Loss Data During Caffeine and Control Test

	Pre-Wt (kg)	Post-Wt (kg)	Wt loss (g)	Sweat loss (g/hr)
Caffeine Session				
Mean	76.76	75.69	1,072	378
± SE	2.53	2.50	84	36
Control Session				
Mean	76.85	75.79	1,062	393
SE	2.4	2.36	86	35

Table 4

Physiological Data During Caffeine and Control Test

	Exercise VO ₂ L/min	Exercise % of VO ₂ max	Resting VO ₂ L/m	Exercise Heart Rate	Resting Heart Rate
Caffeine Session					
Mean	2.55	68.7	.35	145	61
± SE	.09	1.7	.02	5	4
Control Session					
Mean	2.50	67.2	.34	145	64
± SE	.09	2.0	.01	7	4

There were no significant differences between the caffeine and control sessions in total weight loss ($p < .791$), weight loss in grams per hour ($p < .788$), total water loss ($p < .465$), or total sweat loss ($p < .465$).

Means and standard errors for oxygen uptake during the caffeine and control sessions are presented in Figure 4. Mean oxygen uptake for the 2nd minute was the average of minutes one, two, and three. There were no significant differences between sessions ($p < .16$), significant differences across time ($p < .001$) and significant interaction ($p < .032$) between caffeine and control sessions for oxygen uptake. Resting oxygen uptake was significantly lower than exercise oxygen uptake ($p < .05$). Interaction where oxygen uptake for both sessions was very

similar during rest and the first 10 minutes of exercise; then the caffeine curve rises slightly above the control session and remains higher until minute 100 where the control session rises slightly to become relatively equal to the caffeine session (Figure 4) .

Means and standard errors of the mean for heart rate during the caffeine and control sessions are presented in Figure 5. There were no significant differences between sessions ($p < .458$), significant differences across time ($p < .001$), or significant interaction ($p < .030$) between caffeine and control sessions for heart rate. Resting heart rates were significantly lower ($p < .05$) than exercise heart rates. Mean heart rate at minute 40 was also significantly lower than mean heart rate at minute 100. Interaction occurred where the caffeine session heart rates were below the control session heart rates up until minute 50 (Figure 5). At minutes 50, 60 and 70 both sessions have very similar heart rates, for minutes 80 and 90 the caffeine sessions have slightly greater non-significant heart rates, and at minute 100 both sessions are once again similar.

Means and standard errors of the mean for rectal temperature are presented in Figure 6. The differences between the caffeine and control rectal temperatures are presented in Figure 7. There were no significant

Figure 4. Oxygen Uptake ($\pm$ SE)

Figure 5. Mean Heart Rate ($\pm$ SE)

Figure 6. Mean Rectal Temperature ($\pm$ SE)

Figure 7. Mean Rectal Temperature Differences

differences between sessions ($p < .677$), significant differences across time ($p < .001$), or non-significant interaction ($p < .068$) between caffeine and control sessions for rectal temperature. Exercise rectal temperature to be significantly higher than resting rectal temperature. Rectal temperature was significantly lower during minutes 40 and 50 than minutes 60 through 100, and rectal temperature at minute 60 was significantly lower than minutes 70 through 100.

Means and standard errors of the mean for skin temperature are presented in Figure 8. Differences in mean skin temperatures for the caffeine and control sessions are presented in Figure 9. There were no significant differences between sessions ($p < .547$), non-significant differences across time ($p < .069$), or a non-significant interaction ($p < .886$) between caffeine and control sessions for mean skin temperatures.

Figure 10 presents means and standard errors of the mean for skin heat conductance. There were no significant differences between sessions ($p < .232$), significant differences across time ($p < .001$), or a non-significant interaction ($p < .085$) between caffeine and control sessions for skin heat conductance. Exercise skin heat conductance was significantly higher than resting skin heat conductance. During exercise, skin heat conductance at

Figure 8. Mean Skin Temperature ($\pm$ SE)

Figure 9. Mean Skin Temperature Differences ($\pm$ SE)

Figure 10. Mean Skin Heat Conductance ($\pm$ SE)

minute 40 was significantly greater than minutes at 50 and 60.

SUMMARY OF FINDINGS

Paired t -tests found no significant differences between the caffeine session and control session in total weight loss ($p < .791$), weight loss in grams per hour ($p < .788$), total water loss ($p < .465$), or total sweat loss ($p < .465$).

Summary tables for repeated measures two-way analysis of covariance applied to oxygen uptake, heart rate, rectal temperature, mean skin temperature, and skin heat conductance are found in Appendix G. Oxygen uptake had no significant differences between sessions ($p < .16$), significant differences across time ($p < .001$), and a significant interaction ($p < .032$) between caffeine and control sessions. Heart rate had no significant differences between sessions ($p < .458$), significant differences across time ($p < .001$), and a significant interaction ($p < .030$) for caffeine and control sessions. Rectal temperature had no significant differences between sessions ($p < .677$), significant differences across time ($p < .001$), and a non-significant interaction ($p < .068$) for caffeine and control sessions. Mean skin temperature had no significant differences between sessions ($p < .547$), no significant differences across time ($p < .069$), and non-significant interaction ($p < .886$) for caffeine and control sessions. Skin heat conductance had no significant

differences between sessions ($p < .232$), significant differences across time ($p < .001$), and non-significant interaction ($p < .085$) for caffeine and control sessions.

Repeated measures one-way analysis of variance (ANOVA) and Tukey post-hoc tests determined oxygen uptake, heart rate, rectal temperature, and skin heat conductance to be significantly lower during the resting phase than during the exercise phase. In addition to these differences across time produced by exercise, heart rates at minute 40 (10 minutes into exercise) were significantly lower than at minute 100 (70 minutes into exercise). Rectal temperatures were significantly lower at minutes 40 and 50 than minutes 60 through 100, and minute 60 was significantly lower than minutes 70 through 100. Skin heat conductance 10 minutes into the exercise phase (minute 40) was significantly greater than 20 and 30 minutes into the exercise phase (minutes 50 and 60).

Significant interaction, between caffeine and control sessions were found for oxygen uptake and heart rate. Oxygen uptake for both sessions were very similar during rest and the first 10 minutes of exercise; then the caffeine session rose slightly above the control session and remained higher until minute 100 where the control session rose slightly to become relatively equal to the caffeine session. Heart rates for the caffeine session

were below control session heart rates up until minute 50 of data collection. At minutes 50, 60 and 70, both sessions had very similar heart rates. During minutes 80 and 90 the caffeine session had slightly greater heart rates, and during minute 100 both sessions were once again very similar.

Discussion

The purpose of this study was to determine if caffeine affects rectal temperature, skin temperature, skin heat conductance, or sweat loss in aerobically trained men at rest and when performing sub-maximal aerobic exercise under normal ambient conditions. Rectal temperatures at rest and during sub-maximal exercise were not significantly affected by caffeine. This result is in agreement with results of Gorden et al. (1984), Falk et al. (1990), and Biren et al. (1992) who also found no significant effect of caffeine ingestion on rectal temperature. However, it should be noted that at minutes 80, 90, and 100 of the present study, caffeine rectal temperatures were 0.08 to 0.09°C higher than the control session. There are several possible causes for this trend toward higher rectal temperatures. Oxygen uptake in the caffeine session, although not significantly different, was consistently 0.06 to 0.1 L/min higher during exercise. Accompanying increases in

metabolic rate would increase rectal temperature unless the additional heat produced could be dissipated (Santee & Gonzalez, 1988). Skin temperatures were also consistently 0.38 to 0.50°C lower with caffeine. Although these differences were not significant, the lower temperatures during the caffeine session indicate that heat was not being released through increased vasodilation of the skin. Possible dehydration in the caffeine session due to increased urinary flow (O'Neil et al., 1986) may also have attributed to the slight increase in rectal temperature during the final stages of exercise. Our results do not agree with Doubt and Hsieh (1991), where exercise rectal temperature was significantly increased during head out immersion in 28°C water. The temperature gradient between the skin and water may not have been great enough to facilitate adequate heat transfer. The difference between evaporative heat loss in the present study and heat loss via convection to 28°C water is a likely explanation for the contradictory results between Doubt and Hsieh (1991) and the present study.

Mean skin temperatures tended to be lower in the caffeine session for all but the starting temperatures. This trend does not support the findings of Biren et al. (1992) where caffeine significantly increased resting skin temperatures in a normal environment. The reasons for this

discrepancy in skin temperature cannot be easily explained since caffeine dosage, environmental conditions, and exercise intensities, although not the same, were very similar for both investigations. Because caffeine ingestion acutely increases epinephrine levels (Bangsbo et al., 1992), a vasoconstrictive effect would be expected which could explain the small decrease in skin temperature in the present study.

Tendencies toward higher rectal temperatures during the last 30 minutes of the exercise period and lower skin temperatures observed in the caffeine session, should have produced lower skin heat conductance. Skin heat conductance tended to be lower for the caffeine session during exercise.

Sweat rate was not affected by caffeine, in agreement with Falk et al. (1990), who found that caffeine had a slightly greater sweat rate while the present investigation found a slightly lower sweat rate. The small decrease in sweat rate could be explained by possible vasoconstriction caused by elevated epinephrine levels.

The significant differences observed over time for oxygen uptake, heart rate, rectal temperature, and skin heat conductance were normal physiological responses that occur during exercise. Additional convective and evaporative cooling produced by the fan during exercise prevented skin temperatures from increasing significantly

during exercise.

Only slight non-significant differences in rectal temperature, skin temperature, heat skin conductance, and sweat rate were observed between and caffeine and control sessions, these differences were not significant.

Conclusion

Under the conditions of this study, a high dosage of caffeine has no detrimental effects on rectal temperature, mean skin temperature, skin heat conductance, or sweat rate during heavy exercise in normal ambient conditions.

Weaknesses

Blood samples were not drawn during this investigation so plasma caffeine levels, plasma volume, and epinephrine levels could not be established. Because plasma caffeine levels were not ascertained it is difficult to determine if an adequate amount of time elapsed for caffeine absorption to take place before exercise data collection occurred. Data derived from plasma volume would have produced information on hydration levels.

Rectal temperatures did not plateau in this study, indicating that a longer exercise period may have produced higher final rectal temperatures. It should be noted that most of the subjects in the present study probably would

not have been able to complete a much longer exercise session.

Recommendations for Future Research

Because of the trends toward higher rectal temperatures near the end of exercise in the caffeine session future studies should incorporate longer exercise periods. Stressing the thermoregulatory system via exercise in a hot environment would also be recommended. Biren et al. (1992) found that caffeine had no significant effect on rectal temperature during exercise in the heat, but the exercise lasted only 60 minutes. Research incorporating marathon conditions and durations in a hot environment could be conducted to establish the effects of caffeine on thermoregulation under these conditions that cause greater stress for the thermoregulatory system.

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APPENDIX A

HEALTH AND EXERCISE HISTORY QUESTIONNAIRE

Name _____

Date _____ Occupation _____

Work phone _____ Home phone _____

Work address _____

Home address _____

Physician name _____

Physician phone _____

Age _____ years Weight _____ lbs. Height _____ in.

Gender _____

Times you could be available for testing at SJSU.
(am) (pm)

Sunday	_____	_____
Monday	_____	_____
Tuesday	_____	_____
Wednesday	_____	_____
Thursday	_____	_____
Friday	_____	_____
Saturday	_____	_____

Medical History

Place a check next to any of the conditions that you have experienced.

☐ Heart attack	☐ Coronary angioplasty
☐ Cardiac surgery	☐ Chest discomfort
☐ Rapid heart beats	☐ Heart murmurs
☐ Unusual cardiac finding	☐ High blood pressure
☐ Stroke	☐ Ankle swelling
☐ Abnormal blood Lipids	☐ Diabetes
☐ Anemia	
☐ Limp	☐ Phlebitis (vein inflammation)
☐ Orthopedic problems, arthritis	
☐ Asthma, emphysema or bronchitis	
☐ Lightheadedness or fainting with exercise	
☐ Shortness of breath with exercise	

Please explain any of the above that you have experienced and give dates of occurrence. _____

- () Medications of any type
What kind of medications _____
- () Recent illness, hospitalization, or surgical procedure
Explain _____
- () Drug allergies
Explain _____

Family History:

- () Coronary disease
Relation, and age of death _____
- () Sudden death
Relation, and age of death _____
- () Lipid abnormalities
Relation, and age of death _____

Other Dietary Practices:

- () Caffeine consumption
- Coffee _____ cups/day _____ cups/week
- Colas _____ cups/day _____ cups/week
- Chocolate _____ bars/day _____ cups/week
- Other _____

- () Alcohol use
Approximately how much alcohol do you consume each day?

Smoking History:

- () Smoke less than 5 cigarettes/day
- () Smoke less than 1 pack/day
- () Smoke more than 1 pack/day
- () Have never smoked
- () Use to smoke but have quit
When did you quit? _____
- () Do you have any eating disorders?

Explain _____

Exercise History:

How often do you exercise?

- ☐ 0 to 1 times/week
- ☐ 2 times/week
- ☐ 3 to 5 times/week
- ☐ More than 5 times/week

How long are your exercise periods?

- ☐ 0 to 15 minutes ☐ 16 to 29 minutes ☐ 30 to 45 minutes
- ☐ 46 to 60 minutes ☐ more than sixty minutes

Place an X in the types of exercise you participate in regularly.

	Frequency/week	Duration (min),
☐ Cycling	_____	_____
☐ Walking	_____	_____
☐ Jogging	_____	_____
☐ Swimming	_____	_____
☐ Rowing	_____	_____
☐ Aerobics	_____	_____

Other (explain) _____

What do you consider your body type to be?

- ☐ lean
- ☐ average weight
- ☐ slightly over weight
- ☐ over weight

APPENDIX B

EFFECTS OF CAFFEINE ON THERMOREGULATION OF ACTIVE MEN
AT REST AND EXERCISE.

STATEMENT OF INFORMED CONSENT FOR OBTAINING
MEASUREMENTS OF: MAXIMUM OXYGEN UPTAKE, BODY COMPOSITION,
RECTAL, AND SKIN TEMPERATURES.

Purpose of the Study

The purpose of this study is to observe caffeine's effect on sweat loss, skin (surface) temperature, rectal temperature, mean body temperature, skin heat conductance, and heart rate during rest and exercise.

Invitation to Participate

You are being invited to participate in a thesis project. The purpose of this research is to determine if caffeine effects temperature regulation during rest and exercise. Your participation is voluntary, and you can choose not to participate at any time during the project. This experiment will require the completion of three trials within two weeks. The first trial (approximately one hour) will assess your maximum oxygen uptake, body composition (fat percentage), and height. The second and third trials (approximately two and a half hours) will be the same except one trial will have caffeine (in a dose equal to 10 milligrams of caffeine per kilogram of body weight) added to the drink that will be taken before the resting and bicycling period. All the experiments will be conducted at the San Jose State University campus.

Basis for Selection

You have been selected because you are: a healthy male, between the ages of 18 and 40 years old, relatively lean, and exercise aerobically at least three times per week for 30 minutes or more. If you decide to participate, your response to a health history questionnaire will be reviewed by an exercise physiologist and, if satisfactory, you will be asked to participated in the tests described below.

Explanation of Procedures

Body Composition (Fat Percentage)-(approximately 30 minutes)

Underwater weighing requires three measurements: residual lung volume (air left in the lungs after a maximal exhalation), body weight while under water, and normal body weight. Height will also be taken at this time. To measure residual lung volume you will be breathing room air through a mouthpiece. At the end of a normal expiration a valve will be turned so you will be breathing a mixture of helium and room air from a spirometer. Oxygen will be added to the spirometer when needed. After breathing this gas mixture for several minutes a maximal inhaled and exhale breath will be recorded. Several measurements may need to be taken.

To measure underwater weight you will be sitting on a sling so you are positioned neck deep in 820 to 850F water. After being completely submerged under the water you will need to exhale as much air as possible and remain under water for five to ten seconds as the measurement is taken. This underwater weight will be measured six to ten times with rest periods allow between measures.

Maximal Oxygen Uptake (approximately 30 minutes)

Maximal oxygen uptake will be determined using a cycle ergometer at a pedal cadence of 60 repetitions per minutes (rpm). After a five minute warm-up at a power output of 180 kilopond meters per minute (kpm/min), the resistance will be increased by 180 kpm/min every minute until you are unable to maintain the 60 rpm speed Throughout this maximal test, blood pressure will be measured every minute, where respiratory parameters and heart rate will be monitored continuously.

Caffeine/Non-Caffeine Trials (approximately two and a half hours each)

As mentioned previously these trials will be the same except one trial will have caffeine added (in a dose equal to 10 milligrams of caffeine per kilogram of body weight) to a diet drink mixture and the other trial will not have caffeine added. Before both of these trials you will be required to not eat or drink any caffeine for four days before the test. During these trials skin temperature will be measured using skin probes that will be held on with elastic bands; rectal temperature will be measured using a rectal probe; ventilation will be measured which will require you to breath into a mouth piece; and heart rate will be monitored which will require electrode application.

After drinking the liquid you will sit on a chair for 30 minutes while temperatures, respiration, and heart rate are recorded every ten minutes. These measurements will continue into the exercise phase, where you will pedal the ergometer

at a rate and resistance equal to 65% of your maximal work capacity. A fan will blow air on you as you complete 70 minutes of cycling.

Risks and Discomforts

Underwater Weighing

Although the water quality in the tank is maintained daily there is still a possible risk of infection from the water. This risk is small since the water is chemically treated and filtered daily. As with most pool underwater experiences there is a chance of chlorine irritation, swallowing water, and choking.

Residual Lung Volume

There may be some discomfort from the nose clip and from breathing through the mouthpiece. Some people experience dizziness and lightheadedness when performing breathing measurements.

Maximal Oxygen Uptake

There will be some discomfort that is common with high levels of exercise in this test: sweating, increased heart rate, increased breathing rate, elevated blood pressure, and fatigue. You may experience dryness in the mouth, throat, and chest. Toward the end of this maximal test you may incur abnormal blood pressure, fainting, dizziness, muscle cramps, muscle fatigue, and abnormalities in heart beat. You may feel lightheaded and slightly nauseous for a short while following the test. If abnormalities are detected in pulmonary function, electrocardiographic recordings, or if other abnormal physiological signs occur the test will be stopped and you will be asked not to continue the rest of the experiment.

Caffeine Effects / Caffeine Withdrawal

Adverse reactions to caffeine ingestion can include: restlessness, irritability, nervousness, insomnia, headache, nausea, vomiting, elevated blood glucose, tingling of the face, flushing, an increase or decrease in heart rate, and muscle twitching. At the dosage applied in this study caffeine may occasionally cause cardiac irregularities. Habitual caffeine consumers may experience headaches after being deprived of caffeine.

Sixty-Five Percent Bicycling Work Load

During this test you will experience the same types of discomfort as you would during heavy exercise: sweating,

increased heart rate, increased breathing rate, elevated blood pressure, and fatigue. You may experience lightheadedness and dryness in the mouth, throat, and chest.

Benefits from Participating in this Study

You will benefit from this study by receiving information about your body fat percentage and maximal oxygen consumption. If you are a caffeine user you may be interested in how caffeine effects your body temperature.

Assurance of Confidentiality

The information that will be obtained will be treated as privileged and confidential and will not be released or revealed without your expressed written consent. The data obtained, however, may be used for a statistical or scientific purpose with your right of privacy retained. Your right to confidentiality will be protected.

Withdrawal from the Study

Your participation in this research is voluntary. You may withdraw from this study at any time (including during a test) without prejudice. You may also decline to answer any question or item on the health history questionnaire. Maximal oxygen consumption testing will be supervised and conducted a Certified Exercise Test Technologist. Certified CPR personnel will also be present during all testing.

If you have any questions about this research feel free to ask them. If questions come up later or in case of an emergency please contact me (Nancy Dunagan) at (408) 248-7578 or Dr. Craig Cisar (408) 924-3018. In case there is a complaint you can contact Dr. Craig Cisar (408) 924-3018. If there are questions about research subject's rights, or in the event of research-related injury you may contact Dr. Serena Stanford, Associate Academic Vice President of Graduate Studies and Research at (408) 924-2480.

AGREEMENT TO PARTICIPATE IN RESEARCH

SAN JOSE STATE UNIVERSITY

RESPONSIBLE INVESTIGATOR: Nancy A. Dunagan

TITLE OF PROTOCOL: Effects of Caffeine on Thermoregulation of
Active Men at Rest and Exercise.

Consent

By signing this form, I agree that:

- (a) I have read the information provided above and
have decided to participate in this study;
- (b) I understand the discomforts and risks involved;
- (c) I understand that I can withdraw from this study
at any time without prejudice to my relations
with SJSU.
- (d) I understand that my identity will be kept
confidential.
- (e) I understand that I may ask questions about this
study at any time.

SIGNATURE OF SUBJECT _____

DATE _____

PRINTED NAME _____

SIGNATURE OF WITNESS _____

SIGNATURE OF INVESTIGATOR _____

APPENDIX C
RESIDUAL LUNG VOLUME
AND UNDERWATER WEIGHING DATA SHEET

Name _____

Vital Capacity (L) _____

Starting lung volume (VC + .5L) _____

Initial N2 reading after purging spirometer (%)			
trial 1	trial 2	trial 3	average

_____	_____	_____	_____
-------	-------	-------	-------

(ADD STARTING LUNG VOLUME)

N2 reading at end expiration of room air (%)

_____	_____	_____	_____
-------	-------	-------	-------

N2 reading at equilibrium during fast hard breathing (%)

_____	_____	_____	_____
-------	-------	-------	-------

N2 reading at end expiration after rebreathing technique (%)

_____	_____	_____	_____
-------	-------	-------	-------

Temperature of expired air (°C) _____ BTPS _____

Body Weight (KG) _____

Height cm _____

Under Water body weight (KG) _____

Average of three highest underwater weight scores within
.05kg of each other (KG) _____

Harness weight (KG) _____

Water temperature (F) _____ Water density (KG/L) _____

Min % fat 1 Max % fat 18%

APPENDIX D

List of Caffeine Sources

The following are caffeine containing foods and drinks that you should not have for four days prior to the test. If you accidentally do have some caffeine please contact Nancy Dunagan (408-248-7578) to re-schedule the test date. Please, read the content labels of the food and drink you ingest to double check and make sure caffeine does not go into your body. Your system needs to be clean from caffeine in order to obtain accurate results in this experiment.

Drinks

Coffee of any type (not even decaffeinated)
 Tea of any type
 Cola of any type
 Tab Dr. Pepper
 Mr. Pibb Aspen
 Mountain Dew Mellow Yellow
 Cocoa of any type Chocolate of any type

Food

Candies and Cookies containing chocolate and cocoa
 Check packages on frozen dairy products for caffeine
 Check gelatin and puddings for caffeine
 Drugs - Prescription
 APC's (Aspirin, Phenacetin, Caffeine)
 Cafergot Darvon
 Fiorinal Migral

Over the counter drugs

Vanguish, Excedrin	Ban-Drowz
Extra Strength Excedrin	Tirend
No-Doz	Kirkaffeine
Vivarin	Quick Pep
Appendirne	Dexatrim
Caffedrine	Dristan
Anacin, Aspirin compound, Bromoselter	
Cope, Emperin compound, Midol	

These lists were derived from Chung (1986), Kastrup (1989), and from Jacobson and Kulling (1989).

APPENDIX E ADVERTISEMENT TO SOLICIT SUBJECTS

EFFECTS OF CAFFEINE ON
THERMOREGULATION OF ACTIVE MEN
AT REST AND EXERCISE.

Are you interested in finding out your fat percentage and maximum oxygen consumption? You could have these measurements made free of charge and at the same time contribute to scientific research. To volunteer for this study you need to be:

MALE

BETWEEN 18 AND 40

AVERAGE TO LEAN BODY TYPE

EXERCISE AEROBICALLY AT LEAST 3 TIMES PER WEEK (CYCLE, JOG, ETC.) FOR AT LEAST 30 MINUTES EACH EXERCISE SESSION

TIME REQUIREMENT:

1 - 2 hour session and

2 - 2.5 hour sessions

If you are interested in helping with data collecting, or volunteering to be a subject call Nancy Dunagan at (408) 248-7578 to find out more about the study. There is no obligation. Participation in this research is on a voluntary basis.

APPENDIX F, DATA COLLECTION SHEETS

CAFFEINE/NON CAFFEINE TRIAL

1 OR 2

Name _____

ENVIRONMENTAL TEMPERATURE.

Wet bulb temp (sling psychrometer) two lowest agreeing temp

_____°C

Dry bulb temp _____°C

Relative humidity _____

Barometric pressure _____

STPD (standard temp & press dry) _____

STPD sat _____

BTPS (Body tem & press sat) _____

Pre-exercise weight _____

Oral Temperature 1 _____ pre-exercise

-Blindfold and put a nose clip on subject.

Drink mixture should be 37°C of 237 ml (8oz) lemonade.

-Drink temperature _____

Wind speed _____

Post-exercise weight _____

Oral Temperature 2 _____ post exercise

Name _____ Date _____

Test #1 or #2

Resting Time starts upon completion of drinking the beverage. Give volunteer one minute to drink liquid.

Time	Rect#1	Chest#3	Back#4	FArm#6	Calf#8	UArm#9	Thigh#10
1 m							
5 m							
10m							
20m							
29m							
Exercise Begins at 30m							
35m							
40m							
50m							
60							
70							
80							
90							
100							

cool down

GAS ANALYSIS AND HEART RATE DURING CAF/NON CAF TRIALS

NAME _____ DATE _____

TRIAL 1 OR 2

TIME	V_E	VO_2	VCO_2	HEART RATE
TAKE DRINK				
POST DRINK				
1 MIN				
2 MIN				
3 MIN				
8 MIN				
9 MIN				
10 MIN				
18 MIN				
19 MIN				
20 MIN				
28 MIN				
29 MIN				
30 MIN				

GAS ANALYSIS AND HEART RATE DURING CAF/NON CAF TRIALS

NAME _____ DATE _____
 TRIAL 1 OR 2

TIME	V_E	VO_2	VCO_2	HEART RATE
START EXER				
38 MIN				
39 MIN				
40 MIN				
48 MIN				
49 MIN				
50 MIN				
58 MIN				
59 MIN				
60 MIN				
68 MIN				
69 MIN				
70 MIN				
78 MIN				
79 MIN				
80 MIN				
88 MIN				
89 MIN				
90 MIN				
98 MIN				
99 MIN				
100 MIN				

APPENDIX G-1.

Repeated Measures Two Way Analysis of Covariance Summary
Table for Oxygen Uptake.

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	.34	9	.04		
Caffeine	.09	1	.09	2.35	.160

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	4.62	100	.05		
Time	266.48	10	26.65	577.03	.000

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	.51	100	.01		
Interaction	.11	10	.01	2.09	.032

APPENDIX G-2.

Repeated Measures Two Way Analysis of Covariance Summary
Table for Heart Rate.

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	1006.99	9	111.89		
Caffeine	67.37	1	67.37	.605	.458

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	10627.67	100	106.28		
Time	384786.79	10	38478.68	362.06	

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	1866.77	100	18.67		
Interaction	394.62	10	39.46	2.11	.030

APPENDIX G-3.

Repeated Measures Two Way Analysis of Covariance
Summary Table for Mean Rectal Temperature.

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	.74	9	.08		
Caffeine	.02	1	.02	.19	.677

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	6.27	90	.07		
Time	78.25	9	8.69	124.85	.000

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	1.06	90	.01		
Interaction	.20	9	.02	1.86	.068

APPENDIX G-4.

Repeated Measures Two Way Analysis of Covariance
Summary Table for Mean Skin Temperature.

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	7.63	9	.85		
Caffeine	.33	1	.33	.39	.547

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	42.41	90	.47		
Time	7.88	9	.88	1.86	.069

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	5.43	90	.06		
Interaction	.26	9	.03	.48	.886

APPENDIX G-5.

Repeated Measures Two Way Analysis of Covariance
Summary Table for Skin Heat Conductance.

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	707.31	9	78.26		
Caffeine	128.30	1	128.30	1.64	.232

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	2624.31	90	29.16		
Time	45701.29	9	5077.92	174.05	.000

SOURCE	SS	DF	MS	F	SIGNIFICANCE
Within Cells	597.65	90	9	6.64	
Interaction	105.72	9	11.75	1.77	.085

APPENDIX H1: Summary Table from Selected Caffeine Studies Using Animals

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
10-20 mg/kg	120 min	Rat	none	Increased rectal temperature in 8, 22, & 300 C environments	Lin Chandran & Liu (1980)
12.5 mg/kg 25 mg/kg 50 mg/kg 100mg/kg	up to 3.5 hrs	Rat	none	12.5 & 25 mg/kg produced increased body temperatures 50 & 100 mg/kg produced decreased body temperatures	Schlossberg (1983)
12.5 mg/kg 25 mg/kg 50 mg/kg 100 mg/kg	daily for 7 days	Rat		By the 4th day 50 & 100 mg/kg doses produced increased body temperatures that continued through the 7th day. Both 12.5 & 25 mg/kg doses increased body temperature all 7 days.	
10,20, 40mg/kg	30 min	Rat	none	10mg/kg, no effect. 20 & 40 mg/kg, higher interscapular temperatures	Wellman & Marmon (1985)

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
.8 mg/kg nicotine + 10 mg/kg caffeine	30 min	Rat	none	Increased inter-scapular temperature	Wellman Marmon Reich & Ruddle (1986)
5mg/kg, 25 mg/kg 50 mg/kg minutes	just prior to exercise	Rat	treadmill running 45 or 90	No effect on plasma FFA, or blood glycerol	Winder, (1986)
5 mg Caf. 25 mg Caf. or 9% sodium- chloride	immediate before exercise	Rats endurance trained	treadmill running 45 min, or 90 min, or exhaustion	Caf. did not enhance endurance time, or change liver glycogenolysis, liver cAMP, muscle glycogen plasma FFA, blood glucose, & blood lactate.	Aragy-or asami, Yang, & Winder, (1989)

APPENDIX H2: Summary Table from Selected Caffeine Studies Using Humans

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
~330 mg	60 min before exercise	Human cyclists	cycle at 80% V02 max until exhaustion	Caffeine increased exercise time, & decreased rate of perceived exertion	Costill, Dalsky, & Fink, (1978)
5mg/kg	1 hour & 3 hours	Human	2 hour run in hot/humid conditions	No significant differences in rectal temp., plasma volume & electrolyte level, but tendencies toward higher rectal temp. & lower plasma vol. for caffeine group	Gordon et al. (1982)
4 mg/kg	up to 2 hrs	Human trained/untrained	none	Trained subject had greater changes, but all increased resting metabolic rate, plasma epinephrine, & free fatty acid utiliz. decreased respiratory exchange ratio, & plasma norepinephrine	LeBlanc Jobin Cote Samson LaBrie (1985)
100-200mg	1 & 2 hrs	Human	none	Increase in metabolic stimulation, systolic & diastolic blood pressures	Ammaturo & Monti (1986)

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
ephedrine + 30 mg caffeine		lean/ post- obese		energy expenditure in post-obese	Miller (1986)
10 mg/kg & 15 mg/kg	60 min before exercise	Human female	treadmill running at 70-75% of V02max until exhaustion	15 mg dose increased maximal running time, lowered R, decreased FFA, and decreased rate of perceived exertion (RER)	Mc- Naughton (1986)
5 mg caf.	60 min before exercise	Human male	ergometer, graded work load	Caf. did not effect heart rate, minute ventilation R, glucose, or V02 at rest or during exercise.	Bond et al., (1987)
10 mg/kg & 15 mg/kg	60 min prior to exercise	Human female	ergometer increase work load 30kpm/min	Both doses of caf. increased time to exhaustion, and had lower blood lactate levels	Mc- Naughton (1987)

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
Sucrose (~81g) or Caffeine (~384mg) or Sucrose (~72g) + Caffeine (~396mg) or placebo	60 min before exercise & during exercise	Human male trained	treadmill running at ~80% of V02max until exhaustion	Caf. & Su + Caf increased time to exhaustion equally over control group	Sasaki, Maeda, Usui, & Ishiko, (1987)
5 mg/kg	60 min & 150 min	Human untrained female	90 min walk at 55% of V02 max	Caffeine increased V02, respiratory exchange ratio after 60 minutes rest and increased V02, free fatty acid and decreased R during 90 minutes of exercise	Chad & Quigley (1989)
100 mg every 2 hrs or 12hrs	up to 24 hrs	Human lean/post-obese	none	All increased resting metabolic rate during the 12 hours of caf. ingestion	Dullo et al. (1989)

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
5 mg/kg & 2.5 mg/kg	5 mg just prior to march, 2.5 mg. at 3rd & 5th hour of march	Human male	40 km march, followed by ergometer test until exhaustion	Caf had no effect on time to exhaustion, lactate levels were higher in caf. group	Falk et al., (1989)
6 mg/kg	60 min prior to exercise	Human male trained	treadmill running at 70% V02max for 90 min	Caf had no effect on V02, HR, R, RPE, plasma glucose, lactate, epinephrine, & norepinephrine.	Tarnopolsky, (1989)
5 mg/kg + 2.5 mg/kg	2 hours prior to exercise .5 hours prior to exercise	Human male	~70-75% V02max treadmill	No significant differences in rectal temp. or plasma volume. oxygen uptake was higher with caffeine	Falk et al. (1990)
5 mg/kg	90 minute before exercise	Human males	ergometer with work load ~1.5W/kg in 180 & 280C water	In 280C water caf. increased rectal temperature, FFA, glycerol, VE; In 180C water rectal temp. was not effected by caf.	Doubt & Hsieh, (1991)

Amount of caffeine	Time after ingestion	Subjects	Exercise	Results	Reference
5 mg/kg	.5 hours prior to exercise in cold or neutral temp.	Human male	60 W sitting ergometer	Caffeine increased plasma epinephrine but had no effect on rectal or skin temp.	Graham et al. (1991)
4 mg/kg and 8 mg/kg	60 minutes before exposed to hot or neutral temp.	Human	none	Skin temperature was higher in both caffeine trials, Rectal and mean body temperatures were not effected.	Biran et al. (1992)