COFFEE VERSUS CAFFEINE: EFFECTS ON SUBJECTIVE AND BEHAVIORAL MEASURES OF ALERTNESS

1991

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Abstract

Title of Dissertation: Coffee versus caffeine: Effects on subjective and behavioral measures of alertness.

Mary Kathleen O'Keeffe, Doctor of Philosophy, 1991

Dissertation directed by: Andrew S. Baum, Ph.D., Professor, Department of Medical Psychology

This research was designed to address two main hypotheses. First, that coffee ingested by regular coffee drinkers has subjective and behavioral effects beyond those attributable to caffeine. And second, that caffeine presented in coffee produces different subjective and behavioral effects than caffeine presented in a novel beverage.

Examination of the hypotheses was accomplished by crossing beverage (coffee versus non-caffeinated herbal tea) with caffeine content (0 versus 200 mg), thus exposing subjects to coffee with and without caffeine, and caffeine with and without coffee. Forty-eight coffee drinkers and 10 non-coffee drinkers participated in the study. Non-coffee drinkers were exposed only to the non-caffeinated herbal tea, and served as control subjects.

Subjects participated in a single morning session, following overnight abstinence. Blood pressure, heart rate, mood and caffeine withdrawal-related symptoms, as well as performance on an auditory vigilance task, were measured before and after beverage administration. Subjects and

experimenter were blind to the caffeine content of the beverage.

Caffeine was associated with an increase in diastolic and systolic blood pressure, and a decrease in heart rate. Caffeine was also associated with more positive affect, fewer withdrawal related symptoms, and enhanced performance over time. Coffee, with or without caffeine, was found to ameliorate withdrawal-related headache and desire for a stimulant. Both coffee and caffeine were associated with better performance over time compared to the non-caffeinated herbal tea. Caffeine presented in a novel beverage was not found to affect subjective or behavioral measures differently than caffeine presented in coffee.

Comparisons between the coffee drinking experimental and non-coffee drinking control subjects suggested that coffee drinkers were experiencing caffeine withdrawal-related discomfort at the beginning of the session, and that caffeine's subjective effects in coffee drinkers were primarily the result of the amelioration of withdrawal. Control subjects remained more relaxed throughout the session than experimental subjects.

The results of this study provide evidence that coffee has measurable effects beyond those directly attributable to caffeine. Additionally, the findings do not suggest that caffeine presented in coffee is associated with effects that differ from caffeine presented in a novel beverage.

Coffee versus caffeine: Effects on subjective and behavioral measures of alertness.

by

Mary K. O'Keeffe

Dissertation submitted to the Faculty of the Department of Medical Psychology of the Uniformed Services University of the Health Sciences in partial fulfillment of the requirements for the degree of Doctor of Philosophy 1991

Dedication

To my parents, Ret T. O'Keeffe and John E. O'Keeffe Jr., for the tremendous love, support and encouragement they have continuously provided me throughout my life. And with special thanks for their most precious gifts to me: Larry, Terese, Turner and Patrick.

Acknowledgement

The successful completion of the requirements for a Doctor of Philosophy degree does not occur without the support and assistance of family, friends and colleagues. I offer my sincere thanks to those who have helped me throughout this endeavor.

I would like to thank Michele Cruikshank, who acted as experimental assistant for this project, for her superb technical assistance. In addition, I thank my father, John E. O'Keeffe Jr., for helping me to program the auditory vigilance task on the Zenith portable computer.

Thanks also goes to the members of my dissertation committee, Dr. John Sarvey, Dr. James Barrett, Dr. Jerome Singer, and my faculty advisor and mentor Dr. Andrew Baum. Dr. Sarvey served as the "picky" (his words) pharmacologist on the committee, and encouraged the thorough section on the pharmacology of caffeine which adds valuable depth to the introduction section of this thesis. Dr. Barrett helped tremendously with the research design, and gave a great deal of his time to serve as the second reader for both the dissertation proposal and the final thesis. The wit and expertise that accompanied his generous assistance will be long remembered and appreciated. Dr. Singer served as chair to the dissertation committee, and recommended the inclusion of the non-coffee drinking control group which provided interesting and important information. And finally, a heartfelt thanks goes to Dr. Baum for his invaluable

assistance in every phase of this project. As my faculty advisor and mentor over the past six years, Andy Baum has provided my with unending support and guidance, and I appreciate his patience and friendship more than I can express.

As the dedication of this dissertation indicates, I owe my success in graduate school to the love and support of my parents, and to them I am immensely grateful. I also wish to thank my sister Terese Domenech, her husband Juan Domenech, and my beautiful and brilliant nieces Marisa, Sarah and Caitlin - my retreats to their home over the course of my graduate career were certainly responsible for the maintenance of my mental health.

In conclusion, I thank my best friend and partner in life, Joseph Allen Hemler, for many, many things including his unending love and encouragement. But most of all, I thank him for his unfaltering confidence in my ability to achieve any goal that I set for myself.

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Introduction

Overview

The purpose of this dissertation research was to investigate the hypothesis that coffee ingested by regular coffee drinkers has measurable subjective and behavioral effects beyond those directly attributable to caffeine. That is, due to the history of repeated association between coffee and caffeine, the cultural values ascribed to coffee drinking, and possibly even active components other than caffeine in coffee, coffee drinkers may report positive affect and subjective alertness and display evidence of enhanced concentration and vigilance following coffee consumption regardless of the coffee's caffeine content. Additionally, the hypothesis that caffeine presented in coffee produces subjective and behavioral effects in regular coffee consumers that are less pronounced than the effects of caffeine presented in a novel beverage was tested.

Drawing from recent evidence that some degree of tolerance develops to caffeine's alerting effects (Zwyghuizen-Doorenbos, Roehrs, Lipschutz, Timms, & Roth, 1990) it was anticipated that separating caffeine intake from the visual, olfactory and taste stimuli previously associated with its consumption might restore its full alerting effect in coffee drinkers, as drug tolerance has been shown to be situationally specific (see Goudie & Demellweek, 1986). Evaluation of these hypotheses was accomplished by crossing caffeine content (0

versus 200 mg) with beverage (decaffeinated coffee versus non-caffeinated herbal tea), thus exposing subjects to caffeine with and without coffee, and coffee with and without caffeine. Subjects given coffee were told that they were receiving regular, caffeinated coffee and those receiving the non-caffeinated herbal tea were told that their beverage contained no caffeine. The design employed was similar to the "balanced placebo" design advocated by Marlatt and colleagues for alcohol research (Marlatt, Demming & Reid, 1973; Marlatt & Rosenow, 1980; Rosenow & Marlatt, 1981). These researchers have argued that a "balanced placebo" design is necessary for separating the pharmacological effects of alcohol from subject's expectations of how they will be affected by alcohol.

While there is scattered evidence suggesting that decaffeinated coffee and caffeinated coffee may affect mood and task performance similarly, research has generally used decaffeinated coffee as the control beverage, thus precluding comparison of coffee beverages with non-coffee beverages. The research presented in this dissertation represents the only work to date that has examined independent effects of coffee and caffeine on subjective response and task performance in a sample of average coffee drinkers (3-4 cups per day, based on U.S. survey, International Coffee Organization, 1982). The only previous study to use a 2 x 2 design (crossing caffeine with beverage) with coffee drinkers examined salivation rate as the primary dependent measure, and did not evaluate task

performance (Rozin, Reef, Mark & Schull, 1984).

Research presented in the introduction of this thesis will demonstrate that coffee drinking is a pervasive behavior that deserves experimental attention because of its enormous popularity and possible link with negative health outcomes. Also, coffee and caffeine are associated with cultural values and possess reinforcing properties similar to the two other most frequently used licit drugs in the United States, alcohol and nicotine.

Coffee and caffeine consumption.

A majority of people over 10 years of age in the United States regularly consume coffee (Gilbert, 1984). Caffeine, the primary psychoactive component of coffee, is probably the most popular drug in the world. It is found in a variety of beverages and foods, and it has been estimated that nearly 100 percent of the population in North America ingests caffeine in some form (Morgan, Stults & Zabik, 1982).

Coffee accounts for approximately 54 percent of caffeine intake world wide, and though national rates of coffee drinking have been decreasing rather steadily since the 1950's, 56.3 percent of North American adults drink coffee regularly (Gilbert, 1984). What is the allure of coffee? Why is caffeine so popular?

It is a commonly held notion that the reason coffee and caffeine are so popular is because they simply make people feel good. When coffee drinkers are asked why they drink

coffee, the most common answers are "because I enjoy it" and "because I like the taste" (Goldstein & Kaizer, 1969). Yet anecdotal evidence suggests that while most people like the smell of coffee brewing, many coffee drinkers did not initially like its taste. Anyone can do an informal survey of coffee drinkers and find that many can remember the circumstances under which they developed a taste for coffee (e.g. late night study sessions in college, cross country "road" trips, working evenings or midnight shifts, morning gatherings with friends or coworkers where everyone else was drinking coffee, etc.). Thus coffee drinking, like alcohol consumption and cigarette smoking, is more than just a method of administering a primary psychoactive constituent. Indeed, it is a very complex social custom, and like alcohol and cigarettes, it is one symbol of being an adult in the United States. By understanding the factors that contribute to the initiation and maintenance of coffee drinking, we may also gain insight into the processes of licit drug self-administration that contribute significantly to the compromised health and well-being of literally millions of people in the United States and around the world.

Coffee and caffeine are readily available and no legal restrictions or sanctions govern their use - their sale is not regulated in the same manner as alcohol or cigarettes. Common sources of caffeine are noted in Table 1. Caffeine occurs naturally in coffee, tea and cocoa. Though it is also naturally present in the kola nut, cola soft drinks are

caffeine fortified, and other soft drinks, such as Mountain Dew and Sunkist Orange, simply add caffeine that is sold as a by-product of the decaffeination process by coffee companies (Gilbert, 1984).

While coffee and caffeine are considered relatively benign by the general public, their intake has been associated with coronary heart disease, cancer and other health outcomes that will be discussed below. Through the reviews on coffee and caffeine's effects on subjective response, task performance, and their ability to function as reinforcers, it will become evident that the properties of both coffee and caffeine may contribute to the maintenance of coffee drinking. The purpose of this dissertation research was to separate these two components of coffee drinking (i.e. coffee and caffeine) and examine their independent effects on subjective response and task performance, in addition to observing their combined effects. It is unlikely that coffee drinking can ever be examined totally independent from caffeine's influence, not because of the trace amounts of caffeine that are present in decaffeinated coffee, but because of the history of association between coffee and caffeine. Coffee may acquire some of caffeine's stimulating or performance enhancing properties as a result of its repeated pairing with caffeine. By providing regular coffee drinkers with coffee both with and without caffeine, and caffeine both with and without coffee, it was possible to examine whether or not coffee influences mood and performance in the relative absence

of caffeine. The reverse question, the extent to which caffeine influences these measures in the absence of coffee, has been considered by a number of investigators whose research will be discussed below. But the research to date has generally failed to use both decaffeinated coffee and non-coffee control beverages, thus the effects of caffeine in coffee cannot be compared to the effects of caffeine in a vehicle that does not have a history enmeshed in social custom and repeated association with caffeine.

The extent and prevalence of coffee and caffeine use is not the only reason why the self-administration of these substances warrants research attention. Several studies have suggested that coffee drinking may have negative health consequences. Given the potential link between coffee and health, and coffee's similarity to other licit drugs that contribute to the morbidity and mortality of many Americans, the pursuit of a more thorough understanding of factors related to its use is worthwhile and important.

Coffee and health

A large body of research has accumulated on the potential health consequences of coffee and caffeine consumption. Coffee and caffeine have been considered as risk factors in the development of coronary heart disease, a number of cancers (including bladder and kidney cancer, breast cancer and benign breast disease, pancreatic cancer, and ovarian cancer), and pregnancy complications (see Curatolo &

Robertson, 1983; Dews, 1984; Ernster, 1984; and Wolfrom & Welsch, 1990, for reviews). More recently, coffee's effect on fertility, immune response, and the development of diabetes mellitus has also been considered (Cramer, 1990; Melamed, Kark & Spirer, 1990; Tuomilehto, Tuomilehto-Wolf, Virtala & LaPorte, 1990; Weinberg & Wilcox, 1990; Wilcox, Weinberg & Baird, 1988). Additionally, the recognition of an array of side-effects associated with heavy coffee consumption, including restlessness, anxiety, irritability, agitation, insomnia and gastrointestinal complaints, have led to the inclusion of "caffeine intoxication/ caffeinism" as a classification in the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition- Revised (DSM-III-R)(American Psychiatric Association, 1987).

It should be noted that most of the research examining coffee's impact on different health measures or outcomes fails to differentiate between coffee and caffeine. As a suggestion by Cramer (1990) in the infertility discussion below indicates, there are many components of coffee, and future research will need to determine which of these are responsible for any established associations between coffee and health. Also, with the exception of some of the research on heart disease, the studies linking coffee consumption with negative health outcomes generally do not differentiate between coffee's direct effects on health and its effects on possible mediators of specific disease or illness states.

Coronary heart disease.

Much of the attention to coffee's disruptive effects on health has focused on its possible link with coronary heart disease (CHD). Heavy coffee drinking has been associated with increased total serum cholesterol levels, an established risk factor for CHD (Forde, Knutson, Arneson & Thelle, 1985; Klatsky, Petitti, Armstrong, & Friedman, 1985; Thelle, Arneson & Forde, 1983). Coffee intake has been reported to have arrhythmagenic effects (Graboys, 1983; Flynn, 1970), though recent evidence does not support a link between coffee and cardiac arrhythmias (Chelsky et al., 1990; Myers, 1991). Also, it has been suggested that coffee, particularly in combination with stress, may lead to essential hypertension via an autoregulatory mechanism - repeated exposure to blood flow in excess of regulatory demand may lead to permanent increases in vascular resistance (Coleman, Granger & Guyton, 1971; Lane & Williams, 1987). Due to a large number of contradictory findings reported, reviews of the literature have led to conclusions that "there is little evidence to implicate caffeine in the etiology of myocardial infarction or fatal coronary heart disease"(Ernster, 1984, pg 386), and "failure of numerous retrospective and prospective studies to show any association between coffee consumption and myocardial infarction appears to justify the conclusion that coffee intake is not a risk factor for this disease"(Curatolo & Robertson, 1983, pg. 647). Studies published since the time of these reviews, however, have continued to provide evidence

for a coffee-CHD link (Forde et al., 1985; Klatsky et al., 1985; Klatsky, Friedman & Armstrong, 1990; LaCroix, Mead, Liang, Thomas & Pearson, 1986; LeGrady et al., 1987; Tverdal et al., 1990).

LaCroix and colleagues (1986) followed a sample of 1130 men over a 19 to 35 year period. Questionnaire data assessing habits of daily living (including cigarette smoking and coffee drinking) were obtained every five years as part of a long-term prospective investigation of risk factors for chronic diseases. Measurement of blood pressure and serum cholesterol at the time of entry into the study was measured in a subsample of 864 men. Incidence of disease and mortality were measured annually. A dose-dependent relationship was found for coffee consumption and incidence of CHD (acute myocardial infarction, angina pectoris & sudden cardiac death) during the 19 to 35 years of follow-up. When base-line age, serum cholesterol, current smoking and current hypertension were taken into account, both average (over the years studied) and most recent level of coffee intake were significantly related to CHD. When average daily coffee intake over the years studied was examined, the relative risk of CHD for those drinking 1-2, 3-4, and $\geq$5 was 1.36, 2.04, and 2.77 times that of those who didn't drink coffee, respectively. Coffee drinking was not found to significantly predict CHD after controlling for other risk factors when the measure of coffee intake was consumption at study onset. The authors note that previous prospective studies have used only a single measure

of coffee consumption which was distant in time from the measurements of CHD, and suggest that the temporal separation of the measurements of coffee drinking and CHD may be responsible for failures to find positive associations.

A recently published study of coffee drinking and CHD-related mortality in Norway followed approximately 38,000 men and women over an average of 6 years (Tverdal et al., 1990). Daily coffee intake, height, weight, blood pressure, serum cholesterol, smoking history and physical activity level were measured at the initial screening. When age, smoking and serum cholesterol levels were controlled for, males drinking two or more cups of coffee per day were found to have a significantly greater risk of CHD related death compared to men drinking fewer than two cups per day. Coffee consumption was also related to CHD-deaths in women, but this relationship did not remain significant after other risk factors were taken into account. They conclude that coffee may affect CHD related mortality independently of its effects on cholesterol.

Consistent with the equivocal body of evidence on the coffee and CHD link, two recently published studies conducted in the United States have reported conflicting results. Klatsky and colleagues (1990) examined 101,774 hospital admissions over an eight year period. After controlling for other known risk factors, drinking more than 4 cups of coffee per day was associated with a significant increase (1.41 relative risk) in myocardial infarction. The authors advise that people at risk for heart attacks should restrict coffee

intake.

In contrast, Grobbee et al.(1990) followed a sample of 45,589 men over a two year period and found no association between caffeinated coffee consumption and cardiovascular disease. In this study, heavy consumption of decaffeinated coffee was associated with an increase (1.63 relative risk) in CHD. Grobbee and associates conclude that "there seems to be little merit in switching from caffeinated to decaffeinated coffee as a means of reducing the risks of cardiovascular disease"(p. 1031) and "caffeinated coffee as it is currently consumed by men in the United States causes no substantial increase in the risk of coronary heart disease or stroke"(p. 1031).

It is important to note that few of the studies mentioned above examine caffeine intake separately from coffee intake. Thus while the effects of coffee on CHD are inconclusive, the role of caffeine in the development of CHD is relatively unknown. The question of whether or not coffee drinking leads to increased incidence of coronary heart disease, and if so, whether the effect is mediated via effects on serum cholesterol or blood pressure, or is independent of these established risk factors, remains open to further investigation. The conclusions drawn by previous reviewers (Curatolo & Robertson, 1983; Ernster, 1984) appear to have been premature. Given the high incidence of coffee consumption in the United States (56.3 % in U.S., Gilbert, 1984), its relationship with our nation's number one cause of

death warrants further study.

Cancer.

Coffee consumption has been reported to be related to renal cancer, cancer of the bladder or lower urinary tract, breast cancer and benign breast disease, cancer of the pancreas, and ovarian cancer (See Curatolo & Robertson, 1983; Grice, 1984 ; Ernster, 1984; and Wolfrom & Welsch, 1990, for reviews). However, data supporting a relationship between coffee and caffeine consumption and these types of cancer are also equivocal. With regard to bladder cancer, a number of authors have reported significant relationships with coffee intake (Clavel & Cordier, 1991; Cole, 1971; Hartge, Hoover, West & Lyon, 1983; Howe et al., 1980; Marrett, Walter & Meigs, 1983; Shennan, 1973; Simon, Yen & Cole, 1975; Wynder & Goldsmith, 1977), but many of these did not account for other risk factors or find dose-response relationships, and a number of studies have reported no association between coffee intake and bladder cancer (Morgan & Jain, 1974; Morrison et al., 1982; Najem et al., 1982). A recently published study found that coffee was associated with a dose dependent increase in risk for bladder cancer in smoking and non-smoking men, but not women (Clavel & Cordier, 1991). Evidence for a link between coffee consumption and renal cancer is even weaker. Though two studies have reported associations between national rates of kidney cancer and per capita coffee intake (Armstrong & Doll, 1975; Shennon, 1973), clinical studies have failed to

confirm this relationship (Armstrong, Garrod & Doll, 1976; McLaughlin et al., 1981; Wynder, Mabuchi & Whitmore, 1974).

Similarly, results from research examining the possible link between coffee drinking and cancer of the pancreas have not been consistently positive. Research which has found a significant positive relationship (MacMahon, Yen, Trichopoulos, Warren & Nardi, 1981) has been criticized for selection of a control population whose coffee intake may have been restricted. Nomura, Stemmerman & Heilbrun (1981) also reported a relationship between coffee intake and pancreatic cancer, but other potential risk factors were not taken into account. Other researchers have failed to find any association between coffee consumption and cancer of the pancreas (Goldstein, 1982; Jick & Dinan, 1981: Whittemore, Paffenbarger, Anderson & Halpern, 1983). Research investigating the link between coffee and breast cancer and/or benign breast disease has also yielded inconclusive results (Boyle et al., 1984; Mansel, Webster, Burr & St. Leger, 1982; Schairer, Brinton & Hoover, 1987; Wolfrom & Welsch, 1990).

Stocks (1970) reported a significant correlation between national per capita consumption of caffeine and ovarian cancer, and Trichopoulos et al. (Trichopoulos, Papapostolou & Polychronopoulou, 1981) reported finding a significant dose response relationship between coffee intake and cancer of the ovaries. A subsequent study (Hartge, Lesher, McGowan & Hoover, 1982) has also reported a link between coffee intake and ovarian cancer. Thus, coffee drinking may

contribute to the etiology of ovarian cancer, though further research is necessary to confirm this connection.

Complications in pregnancy.

In 1980, the Food and Drug administration advised pregnant women to avoid or limit caffeine intake. Results of an FDA study, finding congenital defects in offspring of rats given caffeine during pregnancy, were considered the primary force behind the 1980 press release (Ernster, 1984). Another study reported alarming findings from a study of 16 pregnant women whose caffeine intake was greater than 600 mg per day (Weathersbee, Olsen & Lodge, 1977). The pregnancy outcomes of these heavy caffeine consumers were compared to those of 356 women with little or no caffeine intake. Only one of the heavy caffeine consuming women was reported to have an uncomplicated delivery, while nearly 80 percent of the caffeine abstainers had uncomplicated deliveries. This study did not evaluate or consider other risk factors, however, and the small number of women in the heavy consumption category makes comparisons between the two groups less meaningful. More recently, larger and more well controlled studies have failed to find any consistent relationship between caffeine consumption and undesirable pregnancy outcomes (Linn et al, 1982, Rosenberg, Mitchell, Shapiro & Slone, 1982). While moderating caffeine intake during pregnancy may be advisable given any chance of risk to the developing fetus (caffeine readily crosses the placenta; Somani, Khanna & Bada, 1980) the evidence to date

does not support a clear connection between caffeine intake and complications in pregnancy.

Caffeine Intoxication/ Caffeinism.

As mentioned in the introduction to this section, caffeine intoxication, also called caffeinism, has been included as a separate classification in the DSM-III-R. The diagnostic criteria for caffeine intoxication includes:

> "A. Recent consumption of caffeine, usually in excess of 250 mg.
>
> B. At least five of the following signs: restlessness, nervousness, excitement, insomnia, flushed face, diuresis, gastrointestinal disorder, muscle twitching, rambling flow of thought or speech, tachycardia or cardiac arrhythmia, periods of inexhaustibility, or psychomotor agitation.
>
> C. Not due to any physical or other mental disorder, such as an Anxiety disorder"(p.139, American Psychiatric Association, 1987).

Caffeinism is reportedly a particular risk in people who consume more that 500 mg caffeine per day, and thus ten percent of coffee drinkers in the United States may be susceptible (Greden, Fontaine, Lobetsky & Chamberlin, 1978). Symptoms of caffeinism have been reported to be indistinguishable from symptoms of anxiety neurosis, complicating diagnosis of psychiatric patients with heavy caffeine intakes (Greden, 1974).

Unfortunately, most of the studies discussing caffeinism have involved psychiatric patients (Greden, 1974; Greden et al., 1978; Winstead, 1976), and little attempt has been made to understand the prevalence or relevance of this phenomenon in the general population. Gilliland & Andress (1981) have examined caffeine intake and symptoms of caffeinism in a sample of undergraduates. Consumption of the caffeine equivalent of 5 or more cups of coffee per day (n = 39 out of 159) was associated with significantly more reports of somatic symptoms, anxiety and depression relative to caffeine abstinence. Additionally, as noted below in the performance section, the academic performance of the heavy consumers appeared to suffer as well, with this group having significantly lower GPA's and earning lower marks in the introductory psychology class. It is not possible to determine from this study whether or not a high level of caffeine consumption led to academic difficulties and symptoms of psychological and somatic distress. Alternatively, students experiencing academic problems may suffer from anxiety and depression as a result, and consume more caffeine in an attempt to prolong study time. Despite an inability to establish causality, the results of the study are intriguing. Individuals with anxiety problems should probably be advised to limit intake of caffeine, and future research must be directed at determining the causative role of caffeine in caffeinism.

Other health issues

Coffee has been examined in a number of health related areas in addition to those mentioned above. For example, coffee has been implicated as a risk factor in the development of diabetes mellitus in susceptible individuals (Tuomilehto et al., 1990). These authors speculate that coffee consumption during pregnancy may adversely affect the development of pancreatic cells in genetically vulnerable fetuses, thus compromising their ability to produce insulin. A comparison of annual per capita coffee intake plotted against annual incidence of diabetes mellitus revealed a correlation of 0.74. While no firm association has yet been identified, research examining this link will undoubtedly be pursued.

Recent research of coffee's effect on immune function has shown that response to mitogen (concanavalin A, phytohemagglutinin) stimulation was significantly higher after five weeks of abstinence from caffeine than following five weeks of regular coffee drinking (approximately 3 to 4 cups per day)(Melamed et al., 1990). Chemotaxis of mononuclear leukocytes was significantly lower during the abstinence period than during the coffee period. T-lymphocytes, T-helper cells and B cell counts were not significantly affected by abstinence, but T-suppressor cells and natural killer cell counts were significantly lower during the no coffee period. While the report discusses these results in terms of the effects of coffee on immune response, it appears that the

abstinence from coffee was responsible for the changes observed - examination of baseline measures obtained at the onset of the study (baseline was pre-intervention in regular coffee drinkers) reveals values similar to those found during the coffee period. Whether the changes reflect response to coffee or response to abstinence cannot be determined from this study. The authors note that the clinical significance of these findings are unclear.

Finally, coffee has recently been implicated in infertility (Cramer, 1990; Weinberg & Wilcox, 1990; Wilcox et al., 1988). Wilcox et al. (1988) found that women who were actively trying to conceive and consumed more than one cup of coffee per day were significantly less likely to become pregnant than women comsuming less than one cup per day. This relationship remained significant after age, frequency of intercourse, age of menarche onset, and cigarette smoking were controlled for. Cramer (1990) has suggested that tannic acid, found in both caffeinated and decaffeinated coffee and in tea, may be responsible for coffee's effect on fertility. Future research, employing prospective methods, will be necessary to confirm the association between coffee (or tannic acid) and infertility.

Pharmacology of Caffeine.

It is probably safe to assume that the primary psychoactive or behaviorally active substance in coffee is caffeine. It should be noted, however, that coffee's chemical

composition is complex, and includes other substances with potential actions of their own. In addition to small amounts of theobromine and theophylline, coffee contains many other compounds including amino acids, carbohydrates, lipids, proteins and vitamins (Spiller, 1984). A study by Boublik and colleagues (Boublik et al., 1983) revealed that caffeinated and decaffeinated instant coffee powder solutions and brewed coffee competed with naloxone, an opiate antagonist, for binding to opiate receptors in rat brain membranes. While there is currently no evidence that the opiate receptor binding activity of coffee is either behaviorally or physiologically meaningful in terms of its effects on coffee drinkers, it is important to recognize that coffee contains ingredients other than caffeine. The degree to which these ingredients contribute to the maintenance of coffee self-administration remains to be determined.

Pharmacological actions of caffeine.

Caffeine (1,3,7 trimethylxanthine), with theophylline and theobromine, belongs to a class of naturally occurring alkaloids known as the methylxanthines. While caffeine is the most prevalent of these substances, theophylline and theobromine are also common. They are found in black and green teas (caffeine, theophylline and theobromine) and in cocoa and chocolate (caffeine and theobromine). The methylxanthines are considered central nervous system stimulants (though theobromine has little effect on the CNS), and have known

effects on the cardiovascular system, smooth muscle, respiratory activity, and gastric secretion (Rall, 1985, Truitt, 1971). Circulatory system effects of caffeine include decreased peripheral resistance, increased cerebral vasoconstriction, increased arterial blood pressure and cardiac stimulation. Theophylline is the most potent of the methylxanthines, and is used therapeutically for the treatment of bronchial asthma, chronic obstructive lung disease, and apnea in premature infants (Rall, 1985). Caffeine's therapeutic use is primarily in combination with analgesics for the treatment of headache - the increased cerebral vasoconstriction following caffeine intake leads to decreased cerebral blood flow and oxygen tension (Rall, 1985). It has also been suggested that caffeine may be of therapeutic value in the treatment of hyperkinetic behavior in children (Schnackenberg, 1973), though its use for hyperactivity has not been widely adopted.

Caffeine is readily absorbed, and after oral ingestion reaches peak plasma levels in 30 to 60 minutes (Rall, 1985; Robertson et al., 1978; Smits, Thien & van't Laar, 1985). It is metabolized primarily in the liver, and only about one percent is excreted unchanged in the urine. The primary metabolites of caffeine include paraxanthine (1,7 dimethylxanthine), theophylline (1,3 dimethylxanthine), and theobromine (3,7 dimethylxanthine); paraxanthine has been identified as the main plasma metabolite of caffeine and the primary pathway of caffeine metabolism in humans (Bonati et

al., 1982). Following caffeine administration, caffeine concentrations in plasma remain significantly and substantially higher than metabolite concentrations (Kaplan, Tai, Greenblatt & Shader, 1990). Rats trained to discriminate caffeine from placebo respond to theophylline and paraxanthine in a caffeine appropriate manner, but fail to respond to theobromine (Carney, Holloway & Modrow, 1985).

Caffeine readily crosses the placenta and the blood brain barrier (Somani et al., 1980). Its plasma half-life is about three and a half hours, but this is variable (1.5 to 9.5 hours), and a number of factors are known to affect elimination rate (Bonati et al., 1982). Pregnancy and liver disease have been found to prolong caffeine metabolism (Parsons, Pelletier, & Neims, 1976; Statland & Demas, 1980), and oral contraceptive use has been reported to nearly double caffeine half-life (Patwardhan, Desmond, Johnson & Schencker, 1980). Cigarette smoking has been found to substantially reduce the clearance rate of caffeine (Parsons & Neims, 1978). Plasma concentrations of caffeine have been shown to accurately reflect brain caffeine concentrations in mice (Kaplan et al., 1990).

At doses of 35 mg to 250 mg, caffeine has been reported to enhance performance on vigilance and reaction time tasks, increase mental alertness, and decrease drowsiness and fatigue in humans (Leiberman, Wurtman, Emde, Roberts & Lovella, 1987a; Rall, 1985; Truitt, 1971; Weiss & Laties, 1962). Its effects on task performance will be considered in

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more detail in a later section.

Moderate doses of caffeine (1.5 to 32 mg/kg) have been reported to stimulate locomotor activity and operant responding in rodents and monkeys (Buckholtz & Middaugh, 1987; Choi, Shahim, Padgett & Daly, 1988; File, Baldwin, Johnston & Wilks, 1988; Kaplan, et al., 1989, 1990; Katz & Goldberg, 1987; Katz, Prada & Goldberg, 1988; Logan, Carney, Holloway & Seale, 1989; Spealman, 1988). Higher doses of caffeine (32 to 40 mg/kg) have been associated with suppressed motor activity decreased operant responding (File et al., 1988; Kaplan, et al., 1990; Katz & Goldberg, 1987; Logan et al., 1989). Caffeine has also been found to reduce social interaction and aggressive behavior in rats, and these actions have been related to caffeine's anxiogenic properties in humans (Baldwin & File, 1989; File et al., 1988).

Contrary to popular conceptions, caffeine has not been found to meaningfully restore performance impaired by alcohol consumption (Fudin & Nicastro, 1988; Nuotto, Matilla, Seppala & Konno, 1982). At higher doses, caffeine can produce nervousness, anxiety, tremors, restlessness and insomnia (Greden, 1974; Rall, 1985; Truitt, 1972). Similarly, people who do not regularly consume caffeine report that it produces nervousness, anxiety and insomnia (Goldstein & Kaizer, 1969). Reports of fatal caffeine overdose are rare, but sensory disturbances and mild delirium have been reported at doses of 1 gram or more (Rall, 1985).

Caffeine relaxes smooth muscle, though theophylline

is regarded as more potent in this regard and is preferred over caffeine for the treatment of asthma and obstructive pulmonary disease. Diuresis and increased secretion of gastric acid and pepsin are also associated with caffeine intake (Rall, 1985; Truitt, 1971). It should be noted, however, that increased gastric acid secretion is associated with ingestion of roasted grain beverages (irritating oils are released during the roasting process) regardless of caffeine content, and both caffeinated and decaffeinated coffee stimulate a much stronger gastric acid response than caffeine alone (Cohen & Booth, 1975).

In addition to direct actions on the central nervous system, caffeine also stimulates adrenal medullary hormone release. Robertson and colleagues (1978) have reported that caffeine produces substantial increases in plasma epinephrine and norepinephrine in addition to increasing plasma renin, blood pressure and respiration rate. In this well controlled study nine subjects (six male, three female) who had abstained from all sources of caffeine for 21 days prior to the research trials were brought to the laboratory for two experimental sessions. Sessions were separated by at least five days. The subjects were admitted to the research ward on the evening before each session, and given nothing by mouth after midnight. At 7:00am a heparin lock IV was inserted for blood collection, and 90 minutes later subjects were given 300ml of a barley flavored beverage to which 250 mg caffeine (experimental beverage) or nothing (placebo) was added. Blood

pressure, heart rate and respiration rate were monitored throughout the session (from 8:00am until noon), and blood samples were taken 30 minutes after beverage consumption and every hour thereafter until noon.

Plasma caffeine was found to peak at 30 minutes for five of the subjects, 60 minutes for three of the subjects, and 120 minutes for the remaining subject (mean = 60 minutes). Plasma epinephrine and norepinephrine were dramatically increased (75% and 207% respectively) following caffeine but not placebo. Plasma dopamine was not significantly different following caffeine and placebo. Renin activity (angiotensin I) was also found to increase following caffeine (57%), and was unchanged following placebo. Blood pressure was significantly elevated following caffeine consumption as compared to placebo at 30 minutes post beverage, and had not returned to baseline by the end of the session (three hours post beverage). Subsequently, Robertson has reported that the pressor effects of caffeine are not due solely to increases in catecholamines, as this response is seen in subjects with autonomic dysfunctions that prevent sympathetic responsiveness (Curatolo & Robertson, 1983). Heart rate showed a biphasic effect, with an initial drop through the first 60 minutes and then a rise to above baseline levels throughout the rest of the session (Robertson et al., 1978). The authors suggest that the heart rate response may be a baroreceptor-mediated compensation for the increased blood pressure, though they note that pulse rate began to rise before blood pressure

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returned to baseline. Other studies have also shown that caffeine leads to increases in blood pressure and catecholamines; effects on heart rate are more variable, but at least initial decreases following caffeine are usually reported (Freestone & Ramsey, 1982; Smits, Thien & van't Larr, 1985a, 1985b).

Potential mechanisms of action.

A number of theories have been proposed to explain caffeine's effects on the central nervous system. It has been speculated that the stimulant properties of caffeine are due to its inhibition of phosphodiesterase and the resulting increase in cyclic AMP. Caffeine has been found to inhibit phosphodiesterase, which is an enzyme that degrades cyclic AMP. If caffeine intake raised levels of cyclic AMP (the second messenger of the catecholamines), this could account for its stimulant effect (Sutherland & Rall, 1958; Butcher & Sutherland, 1962). It has more recently been discovered, however, that the brain levels of caffeine necessary to inhibit phosphodiesterase are much higher (about 100 times) than those reached after doses normally consumed by humans (Fredholm, Fuxe & Agnati, 1976; Smellie, Davis, Daly & Wells, 1979). Also, phosphodiesterase inhibitors are not consistently found to have stimulant properties (Beer, Chasin, Clody, Voge & Horovitz, 1972).

A theory that has received the most attention and empirical support recently involves caffeine's actions on

adenosine receptors (Daly, Bruns & Snyder, 1981; Snyder, 1985; Snyder, Katims, Annau, Bruns & Daly, 1981; Snyder & Sklar, 1984; Zhang & Wells, 1990). Adenosine is a purine that is involved in a number of neural metabolic pathways including the formation of ATP. It has marked sedative properties, thought to be partially related to its ability to block potassium-stimulated release of norepinephrine from the cortex (Harms, Wardeh & Mulder, 1978). There is also evidence that adenosine inhibits the release of a number of neurotransmitters including acetylcholine, norepinephrine, dopamine, and GABA (Daly et al., 1981; Snyder & Sklar, 1984). Methylxanthines have been found to block adenosine receptors in rats at dose levels comparable to a few cups of coffee, and the stimulant properties of a number of methylxanthines have been found to be associated with their affinity for adenosine receptors (Snyder et al., 1981).

Caffeine's action as a central nervous system stimulant may primarily be the result of its blockade of adenosine receptors. It has also been shown that chronic caffeine administration elevates brain adenosine receptors (Boulenger, Patel, Post, Parma & Marangos, 1983; Chou, Khan, Forde & Hirsh, 1985) and peripheral adenosine receptors (Zhang & Wells, 1990). Both tolerance to caffeine's stimulant properties and the withdrawal syndrome that is associated with cessation in heavy coffee drinkers will be discussed in later sections. The increase in adenosine receptors that has been seen with chronic administration in rats may account for

tolerance, as more drug would be necessary following chronic intake to block the same proportion of receptors. Likewise, the sudden cessation of caffeine intake in the chronic user may expose a larger number of adenosine receptors, accounting for some of the symptoms associated with caffeine withdrawal (Snyder & Sklar, 1984). It should be noted, however, that the up-regulation of adenosine receptors has not been universally accepted as the mechanism of caffeine tolerance, and a recent study found no evidence to support this mechanism (Holtzman, Mante & Minneman, 1991).

Two adenosine receptor subtypes (A_1 and A_2) have been identified. A_1 receptors are associated with the inhibition of adenylate cylase and decreased formation of cyclic AMP; A_2 receptors are associated with stimulation of adenylate cylase and an increase in cyclic AMP (Rall, 1990). Recent research has been directed at targeting the specific adenosine receptor subtypes that may regulate response to methylxanthines. Several groups have administered adenosine agonists that have differential sensitivities to these receptor subtypes in combination with caffeine or other methylxanthines and measured behavioral response (Buckholtz & Middaugh, 1987; Katz et al., 1988; Spealman, 1988; Spealman & Coffin, 1986). Caffeine has been found to antagonize the sedating effects of adenosine agonists L-Phenylisopropyladenosine (L-PIA) and N-ethylcarboxamidoadenosine (NECA) (Buckholtz & Middaugh, 1987; Spealman, 1988). Adenosine agonists of the PIA variety (e.g. L-PIA, R-PIA) are reportedly more potent at A_1 receptor

subtypes, while the agonist NECA is more potent at A_2 receptor sites (Willaims, 1987).

The existence of two types of A_2 receptors (A_{2a} and A_{2b}) has also been recently reported, with A_{2a} subtypes being associated with a greater affinity for adenosine than A_{2b} subtypes (Rall, 1990). One of the most recent reports has called into question the role of adenosine receptors (A_1 and A_2) not only in the development of tolerance to caffeine but additionally in mediating caffeine's behavioral stimulant effects (Holtzman et al., 1991). Thus the mechanism by which caffeine exerts its stimulant effects has not been conclusively established, and future studies will certainly continue to focus on this question.

Tolerance.

The degree to which regular consumers of caffeine become tolerant to its effects is an issue that is open to debate. A number of animal studies have demonstrated that tolerance develops to caffeine's effects on locomotor activity and operant responding with chronic administration (File et al., 1988; Finn & Holtzman, 1986; Holtzman & Finn, 1988; Meliska, Landrum & Landrum, 1990). In addition, several empirical studies have supported the assertion that tolerance develops to caffeine's stimulating properties in humans (Colton, Gosselin & Smith, 1968; Robertson, Wade, Workman, Woolsey & Oates, 1981; Zwyghuizen-Doorenbos, et al., 1990).

Perhaps the most frequently cited of the human studies

is the research done by Robertson and colleagues (1981), which examined tolerance to caffeine's cardiovascular and endocrine effects. Subsequent to the Robertson et al. (1978) study that found substantial increases in blood pressure, heart rate, plasma catecholamines and plasma renin activity with caffeine, these researchers set out to determine whether or not these effects would persist with chronic administration.

Subjects who had abstained from all sources of caffeine for 21 days prior to the study's onset participated in a 14 day experiment. Eighteen subjects were randomly assigned to one of two groups. Group I received a placebo beverage with every meal throughout the study; group II received placebo with every meal on days 1-3 and 10-14, and 250 mg caffeine with each meal on days 4-9. Thus, during caffeine administration, subjects in group II were receiving a total of 750 mg caffeine per day. Sampling of blood pressure, heart rate, plasma renin and catecholamines, and plasma caffeine was performed throughout the study.

Both systolic and diastolic blood pressure were found to increase significantly following 250 mg caffeine on the first and second days of caffeine administration (study days 4 and 5), but by the fourth day of caffeine administration blood pressure returned to baseline levels and did not vary from baseline for the remainder of the study. Blood pressure did not decrease below baseline on day 10 following discontinuation of caffeine and return to placebo beverage administration with meals. Plasma renin activity was

significantly elevated from baseline following 250 mg caffeine on the first day of caffeine administration, but not on the last day of caffeine. Similarly, for plasma epinephrine and norepinephrine, while significant increases were seen following the first caffeine administration, no increases were seen following caffeine on the final day of caffeine ingestion. Thus, these subjects developed tolerance to caffeine's effects on blood pressure, catecholamine, and plasma renin activity following six days of chronic caffeine administration. It is interesting to note that the plasma half-life of caffeine in these subjects following 250 mg did not change significantly with chronic administration. The authors note that blood levels increased slightly but consistently over the six days of caffeine administration, and that prior to the morning caffeine on the final day of caffeine administration, subjects had low but detectable levels of caffeine in their bloodstream.

In their 1981 report, Robertson et al. also mention an "ancillary" study which examined the effects of an acute dose of 250 mg caffeine in 16 regular coffee drinkers (3 cups/day) who had abstained from caffeine for 24 hours. Only blood pressure and heart rate were assessed in this group. Subjects whose pre-session blood levels of caffeine were 1 μg per ml or less showed significant blood pressure increases in response to caffeine, but those whose pre-session blood levels of caffeine were greater than 1 μg per ml did not show significant blood pressure responses to caffeine. This also

provides evidence for tolerance with chronic caffeine consumption, and suggests that certain blood levels of caffeine may need to be maintained for tolerance to occur. Smits, Thien and van't Laar (1985a) have also found evidence that the cardiovascular effects of a single dose of caffeine depend upon circulating blood levels of caffeine at the time of drug administration.

The Robertson et al. (1981) research has drawn some criticism from researchers who view their discussion as attempting to "close the book" on the caffeine tolerance question. The primary criticisms have revolved around the schedule of caffeine administration and the amount of caffeine used in the main study. Regular coffee drinkers tend to drink the majority of their coffee in the morning or early afternoon (Gilbert, 1984; Griffiths et al., 1986). By giving subjects three doses of coffee, one with each meal, Robertson et al. (1981) did not mimic caffeine consumption as it naturally occurs. Also, Lane and Manus (1989) have noted that the daily dose of caffeine administered (750 mg) reflects a level of consumption that is reached by less than 10% of adult caffeine users in the United States. Therefore, the tolerance that was observed following Robertson and colleagues' (1981) chronic caffeine administration may not be meaningful in terms of its generalizability to the typical caffeine consumer. A number of subsequent studies have found acute doses of caffeine to increase blood pressure in regular coffee drinkers (Goldstein, Shapiro, Hui & Yu, 1990; Lane, Adcock, Williams & Kuhn, 1990;

Lane & Manus, 1989; Lane & Williams, 1987; Ratliff-Crain et al., 1989, Sung, Lovallo, Pincomb & Wilson, 1990). In a study designed to directly test whether or not tolerance to caffeine develops at doses typically consumed by humans, Lane and Manus (1989) exposed 10 regular coffee drinkers to a pretreatment dose of 125 mg caffeine followed 2 hours later by either a placebo administration, or placebo plus 125 mg caffeine. Subjects abstained from all sources of caffeine from dinner the evening before the sessions. Compared to the placebo administration, the second dose of caffeine was found to significantly increase mean arterial and diastolic blood pressure, but not systolic blood pressure. Similarly, Goldstein and colleagues (1990) recently reported that a second cup of coffee (decaffeinated plus 150 mg caffeine) given to regular coffee drinkers at 11:00am (with the first cup given at 8:00am) produced a significant increase in blood pressure relative to placebo. Thus, while it appears that tolerance may develop to caffeine's blood pressure effects following chronic administration of high doses, tolerance to caffeine's pressor effect does not appear to occur with patterns of use typical of the average American coffee drinker (Gilbert, 1984; Goldstein et al., 1990; Lane et al., 1990; Lane & Manus, 1989; Robertson et al., 1981).

In addition to the cardiovascular effects of caffeine, tolerance has been reported to develop to a number of caffeine's other effects. For example, regular coffee drinkers have been shown to develop tolerance to caffeine's salivation

inducing properties (Rozin et al., 1984; Winsor & Strongin, 1933). Recently, Zwyghuizen-Doorenbos et al. (1990) have reported finding evidence for tolerance to caffeine's augmentation of sleep latency. Caffeine was found to significantly increase latency to unambiguous stage 1 sleep or stage 2 sleep in moderately sleepy subjects. However, sleep latency was found to significantly decrease over four caffeine administrations (250 mg). Latency following the final caffeine presentation was still significantly longer than that of a placebo group, however, suggesting that complete tolerance did not occur.

Examination of a recently published animal study may shed some light on the tolerance controversy (Meliska, Landrum & Landrum, 1990). Caffeine was administered to rats in drinking water on either a chronic (continuous) or subchronic (every other day) basis, and its effect on running behavior on a free access activity wheel was observed. A control group that received only water was used for comparison. Rats in the three groups consumed equivalent volumes of fluid throughout the study. Behavior on the activity wheel was examined over two baseline and 15 experimental days. Rats given chronic access to caffeinated drinking water did not exhibit activity that differed significantly from the control animals. Alternatively, those given caffeine on an every other day basis showed significantly more wheel running on the fifth, sixth, seventh and eighth caffeine exposure days (experimental days 9, 11, 13 and 15) than either the control animals or the

animals receiving chronic caffeine. Wheelrunning in the subchronic caffeine group did not differ from that of either the control or chronic caffeine group on the water exposure days (experimental days 2, 4, 6, 8, 10, 12, and 14).

It thus appears that while chronic caffeine intake may lead to the development of complete tolerance to its behavioral effects, subchronic caffeine consumption may actually lead to a sensitization of caffeine's effects. Typical human self-administration patterns may more closely reflect the subchronic administration in the Meliska et al. (1990) study than either the chronic administration in this rat study or the chronic, high dose administration in the Robertson et. al (1982) research.

To summarize, it appears that the extent to which tolerance develops appears to be at least partially dependent upon the blood levels of caffeine that are maintained. As mentioned previously, Smits et al. (1985a) found a significant negative correlation between blood pressure response to caffeine and basal plasma caffeine levels. These authors suggest that people with short plasma caffeine half-life may be the most resistant to tolerance. Thus factors which are known to decrease caffeine half-life, such as cigarette smoking (Parsons & Neims, 1978), may influence the persistence of caffeine's effects with chronic intake. Consumption patterns may also influence the degree to which an individual caffeine consumer develops tolerance. The Meliska et al. (1990) research revealed that while chronic exposure was not

associated with increase activity in rats, subchronic exposure was associated with marked behavioral stimulation.

Coffee drinking typically occurs in the morning and early afternoon (Gilbert, 1984). The coffee drinker who consumes two to four cups of coffee early in the day may have completely eliminated caffeine in the 16 to 20 hours between their last coffee of the day, and the first cup the next morning (Smits et al. 1985a). On the other hand, with the per capita intake of caffeinated soft drinks on the rise (Gilbert, 1984), and the pattern of caffeinated soda consumption appearing to be more evenly spaced throughout the day, the length of time between the last caffeine of one day and the first caffeine of the next may be getting smaller. This may particularly apply to individuals who consume caffeine from a number of sources. Research evaluating the effects of caffeine on any number of variables should consider factors known to influence caffeine metabolism, as well as determine all dietary sources of caffeine and time since last intake, in order to control individual variability in sensitivity to caffeine as much as possible. Additionally, the possibility that coffee drinkers develop tolerance to some of caffeine's effects while remaining sensitive to others is an empirical question that deserves research attention.

Withdrawal.

Omission of morning coffee in regular coffee consumers

can lead to a caffeine withdrawal syndrome that is characterized by headache, lethargy and fatigue, and irritability (Golstein & Kaizer, 1969; Greden, Victor, Fontaine & Lubetsky, 1980; Griffiths, Bigelow & Liebson, 1986; Griffiths et al., 1990a; Griffiths & Woodson, 1988a; Shorofsky & Lamm, 1977). Goldstein & Kaizer questioned 239 women about their coffee drinking behavior. When asked "How do you think you would be affected if you did not have any coffee at all in the morning" (pg. 485, question #8 of 9 total questions), respondents who drank three or more cups of coffee a day reported that they would experience headache, irritability, inability to work effectively, nervousness, restlessness and lethargy. In a discussion of the problems that the caffeine withdrawal headache presents to Jewish people observing the Yom Kippur 25 hour fast, Shorofsky and Lamm (1977) suggest that coffee drinking be gradually reduced so that no coffee is consumed for one to two days before the fast. Alternatively, they suggest that caffeine suppositories can be used on the morning of the fast to prevent the onset of headache.

Griffiths and colleagues (1986) examined the coffee drinking behavior of heavy coffee drinkers (mean 12 cups/day) in an inpatient laboratory. Caffeine dose of decaffeinated coffee was manipulated in a double blind fashion, and when the coffee drinkers were switched abruptly from 100 mg of caffeine per cup to no added caffeine, a number of symptoms were reported by subjects and staff. On the first two days

following the switch to decaffeinated coffee, subjects reported significantly more headache, fatigue, less vigor, less liking of coffee, and less stimulant effect (subjective) for the coffee. Also, on a caffeine withdrawal scale (identified only as a mood questionnaire) both subjects and staffs' rating of subjects were significantly elevated on the first two days of decaffeinated coffee. The average onset latency for withdrawal symptoms was 19 hours post caffeinated coffee.

The Griffiths et al. (1986) work makes an important contribution to the understanding of the caffeine withdrawal syndrome, as neither subjects nor ward staff were aware of the caffeine dose present in the subjects' coffee. The fact that withdrawal symptoms reliably appeared following discontinuation of added caffeine, and that these symptoms were pronounced enough to change the ward staffs' ratings of the subjects' mood, demonstrates that awareness of the restriction of caffeine is not a necessary component of the syndrome. It should be mentioned, however, that subjects in this study were very heavy coffee drinkers, most of whom also had histories of drug or alcohol abuse. While this restriction of the subject sample limits the generalizability of the results, the fact that a number of other studies have reported similar caffeine withdrawal related symptoms suggests that this phenomenon is not exclusively associated with unusually heavy caffeine intake.

Griffiths & Woodson (1988a) have reviewed research

relating to caffeine's physical dependence properties in animals and humans. These authors reported finding only six animal studies that examined the effects of caffeine withdrawal in animals. Decreased locomotor activity following cessation of chronic caffeine administration was the most consistently reported withdrawal-related observation in animals. Additionally, one study not mentioned by Griffiths and Woodson has also identified hypoactivity in rats following termination of chronic caffeine administration (Herz & Beninger, 1987).

Human studies that were reviewed included case reports, clinical observations, surveys and experimental studies. Headache and lethargy were the two most consistently reported withdrawal symptoms in humans. Other symptoms, including anxiousness, irritability, nausea, confusion, tremor and "craving" for coffee have been reported less frequently. They report that the onset of caffeine withdrawal is typically 12 to 24 hours following caffeine termination - it is worth noting that much of the research that has examined caffeine's effects on mood and performance has required a 12 hour abstinence from caffeine prior to the onset of experimental sessions. Symptoms typically peak at 20 to 48 hours post caffeine, and the duration of withdrawal is approximately one week. The reviewed research suggests that severity of withdrawal may be a function of dose, but the authors note that this has not been established experimentally. Several of the studies examined reported withdrawal symptoms following

relatively low daily intake (2-4cups coffee/day). Finally, caffeine withdrawal was reported following caffeine administration via both capsules and beverages, and caffeine administered in capsules or beverages suppresses headache induced by caffeine abstinence. Indeed, caffeine is reportedly more effective than aspirin at suppressing withdrawal-related headache.

Subsequent to their review on caffeine's physical dependence properties, Griffiths and collegues (1990a) conducted a study that demonstrated measurable caffeine withdrawal-related symptoms in subjects with a low daily caffeine intake (100 mg of caffeine per day). All subjects had been maintained on 100 mg of caffeine per day (ten 10mg capsules administered on the hour from 8am to 5pm daily) for over 100 days, and all dietary sources of caffeine were forbidden. Placebo capsules were substituted in a double-blind procedure for a 12 day period, following which the caffeine capsules were reinstated. Subjective response was measured at 8am, 12 noon, 4pm and 8pm daily, using a variety of adjective checklists. Withdrawal symptoms were reported by four of the seven subjects, including increased headaches and lethargy and decreased energy and ability to concentrate.

A second phase of the study followed, during which placebo was randomly substituted for caffeine on five occassions over a six week period. Comparisons of subjective ratings between placebo and caffeine days revealed significant increases in withdrawal-related symptoms on placebo days for

all seven subjects. Symptoms including headache, lethargy, decreased energy and inability to concentrate appeared around 4 hours following the placebo substitution (19 hours since last caffeine capsule), and peaked approximately 12 hours after the substitution (27 hours post caffeine).

This study demonstrates that a reliable withdrawal syndrome may follow caffeine cessation in individuals with relatively low caffeine intakes (i.e. 100 mg/day). The sample used in the study consisted of the behavioral pharmacologists who were the authors of the report. Given the double-blind administration procedure employed, it is unlikely that the findings were influenced by the unusual characteristics of the sample. However, future research should be directed at replicating these findings in a sample more representative of the general population.

Ratliff-Crain et al. (1989) found that some of the feelings associated with caffeine withdrawal were ameliorated by decaffeinated coffee. In this study, regular coffee drinkers who consumed 4 or more cups of coffee a day participated in two laboratory sessions. Prior to one of the sessions subjects were asked to refrain from their usual morning coffee; prior to the other session subject were asked to follow their normal morning routine which included drinking coffee. The subjects were randomly assigned to either a caffeinated coffee, decaffeinated coffee, or caffeine free herbal tea condition - the same beverage was consumed during both the deprived and non-deprived sessions. During the

session subjects were exposed to an experimental challenge. As would be expected, coffee deprivation was associated with greater subjective desire for coffee. Desire for coffee increased significantly over the two and a half hour session for subjects given herbal tea. In contrast, desire for coffee did not change significantly over time in subjects receiving either decaffeinated or caffeinated coffee. Thus, coffee ingestion, regardless of caffeine content, tempered desire for coffee in subjects deprived of their morning coffee. Also, caffeine deprived subjects receiving coffee reported feeling significantly less lethargic following the experimental challenge than those receiving herbal tea. Not all of the effects of caffeine withdrawal were eased with decaffeinated coffee however. Only caffeinated coffee eliminated reports of headache or "need aspirin" on deprivation days, and receiving caffeine during the session was associated with subjective reports of less trouble concentrating, and less discomfort during the task. It therefore appears that decaffeinated coffee may ease but not eliminate caffeine withdrawal syndrome.

There is some evidence that caffeine withdrawal may compromise task performance. Griffiths et al. (1986) report that performance on a circular lights psychomotor task decreased following change from caffeinated to decaffeinated coffee, though this decline did not reach statistical significance. In a study designed to look at the effects of caffeine withdrawal on performance, Rizzo, Stamps & Fehr

(1988) compared 20 non-users of caffeine with 20 regular users (200-600 mg/day) on a signalled reaction time task and heart rate on two experimental sessions. For the first session regular users were asked to abstain from caffeine for four hours prior to arrival at the lab; for the second they were asked to abstain from all sources of caffeine for the two days preceding the session. The experimental sessions were separated by seven days, and caffeine intake was monitored via self-monitoring forms from 24 hours before the first session through completion of the second session. No differences were found on performance on the reaction time task or heart rate responses to the task between the regular caffeine users and the non-users on the first session. On the second session, however, when the regular caffeine consumers had been deprived of caffeine for 48 hours, the non-users had significantly shorter reaction times than the users. Also, the non-users showed greater heart rate decelerations in response to the signal accompanying the task, which the authors interpret as an index of attention (heart rate deceleration during task signaling represents an increase in attention). Unfortunately, these authors did not measure symptom reporting or subjective response to the caffeine deprivation. The study suggests, however, that caffeine withdrawal in regular users may not only lead to physical and emotional discomfort, but also to

Psychophysiological and behavioral effects of caffeine and coffee.

As mentioned in the introduction, it is widely held that the reason that caffeine containing beverages are so

popular is that caffeine makes people feel good. In the following sections, research that has examined caffeine's effects on mood and subjective response, its function as a reinforcer, and its effect on task performance will be examined. Evaluation of the way that caffeine affects mood and behavior can be more difficult that one might initially assume. Not only is dose level likely to moderate caffeine's effects, but also prior experience with caffeine containing beverages. If the research subjects have a limited history of caffeine consumption, they may be more sensitive to its effects. Indeed, initial sensitivity to caffeine's dysphoric effects may have contributed to the avoidance of dietary caffeine. On the other hand, employing research subjects with more extensive caffeine use histories presents other problems. Many studies ask participants to refrain from caffeine intake for 12 to 24 hours prior to the experimental procedure. Caffeine withdrawal has an onset time of 12 to 24 hours (Griffiths & Woodson, 1988a), and thus the appearance of more positive subjective states or enhanced performance in caffeine using subjects may not only be due to the stimulating properties of caffeine, but perhaps also to caffeine's amelioration of withdrawal symptoms. Few studies consider the potentially confounding effects of caffeine withdrawal when they use regular coffee drinkers or caffeine consumers as subjects. These limitations will be acknowledged where appropriate.

Mood and subjective response.

Goldstein & Kaizer (1969) and Graham (1988) have conducted questionnaire surveys to attempt to examine the subjective effects of coffee or caffeine. Goldstein & Kaizer (1969) examined a group of 229 women, and divided respondents into four groups based on their usual coffee drinking patterns. Abstainers were defined as those drinking less than a cup per day (n=23); light users drank one to two cups per day (n=20); moderate users three to four cups per day (n=27); and heavy users drank more than five cups of coffee a day (n=26). Of those who did not drink coffee, 25% reported religious reasons, 37% reported that they did not like the taste, and fewer that 10% reported physical symptoms such as nervousness or shakiness as reasons for avoiding coffee.

When those who drank coffee were asked "Why do you drink coffee?", the five main reasons reported were: "I enjoy it" (72%), "I like the taste" (72%), "helps me wake up" (46%), "it is a habit" (45%), and "gets me going in the morning" (42%). These reasons remain the most frequently cited within each of the coffee drinking groups. When asked about behavioral changes associated with drinking morning coffee, the heavy (≥5cups/day) and moderate (3-4cups/day) groups reported (in order of frequency) as the five most common changes: "I perk up", "am more alert", "am more active", "work more efficiently", and "am less irritable". Those drinking one to two cups per day also noted the first four changes, but instead of "am less irritable", the fifth change cited by

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these drinkers was "become nervous". Thus, it appears that in this sample of coffee drinkers, both reasons for consuming coffee and subjective behavioral effects attributed to coffee are similar among groups with different daily consumption patterns. It is worth noting that those drinking more coffee mentioned a reduction in irritability, which may be an amelioration of withdrawal, as one of their top five behavioral responses in contrast to those drinking less coffee, a greater proportion of whom mentioned nervousness. Once again, it seems that baseline caffeine intake is an important variable to consider when predicting response to caffeine.

Graham (1988) asked a sample of 246 college students "How frequently would you consume coffee under the following circumstances or for the following reasons?" followed by 18 reasons which subjects were to rate on a four point scale from "never" to "nearly always/always". Reasons receiving the five highest scores from all coffee drinkers in the sample were: "like the taste", "feeling tired", "with friends who are drinking coffee", "to pep up" and "time of day". Component analysis was conducted on responses to this question, and four factors were found to account for 56% of the variance in coffee drinking. Consumption patterns of the students were best predicted by what Graham calls "beverage motives" ($r = .46$) for drinking coffee, including "like the taste", "habit", "time of day", "thirsty" and "to relax", and "relief motives" ($r = .44$), including "to help concentrate", "feeling

depressed", "to celebrate", "upset", "under pressure or tense" and "to relieve pain". "Stimulant motives" such as "feeling tired", "to pep up", and "to keep from slowing down" and "sociability motives" such as "to be sociable", "with friends who are drinking coffee", "to be polite" and "part of a social activity" showed more modest (r=.22 and .20 respectively), but statistically significant, correlations with consumption.

From these two questionnaire studies, it appears that subjective reports of simply enjoying coffee and liking its taste are among the most frequently cited reasons for drinking coffee in these samples. Coffee's stimulant properties are also often mentioned as reasons for consumption. It is possible that coffee drinkers are reluctant to report drinking coffee merely for its stimulating effects because of the social undesirability associated with this response. Saying that one drinks coffee because it is stimulating may seem too much like "drug use".

A number of investigations have examined the subjective effects of one or several doses of caffeine compared to placebo. Bruce and colleagues (Bruce, Scott, Lader & Marks, 1986) examined the effects of single doses of 0, 250 and 500 mg caffeine in nine regular coffee drinkers (mean intake 428 mg/day). Subjects were instructed to abstain from caffeine for 24 hours before each session. They reported to the laboratory at noon on three occasions, approximately one week apart. Capsules containing one of the three test doses were given orally in random order. Measures were taken

at 1, 3, and 5 hours post capsule administration. Subjective measures included a mood scale with three factors: the first representing alertness, the second contentedness, and the third calmness. Somatic symptoms were assessed using a bodily symptom scale, and anxiety was measured using the state form of the Spielberger State Trait Anxiety Inventory (Spielberger, 1970). In addition to subjective reports, blood levels of caffeine along with urinary metabolites were examined, as well as physiological response to caffeine. Task performance was also evaluated, and will be discussed in the following section.

Both 250 and 500 mg caffeine significantly increased subjective alertness in these subjects compared to placebo. For the 250 mg dose, this effect peaked at 1 hour post drug, while for 500 mg the rise in alertness was maintained throughout the 5 hour measurement period. Neither dose of caffeine significantly affected the contentedness or calmness factors of the mood scale. Both doses of caffeine were also found to lead to significant increases in the bodily symptom rating of "shaking or trembling", peaking at 1 hour post drug. The authors also report significantly fewer symptoms of tiredness and headache after caffeine administration, though neither the separate effects for dose nor time course of response are described for these symptoms. Unfortunately, the 24 hour abstinence apparently resulted in the occurrence of withdrawal symptoms, which might be anticipated in a group of subjects whose mean intake is 428 mg caffeine per day. This

makes the finding of apparent increased alertness with caffeine less clear, as caffeine may have genuinely acted to enhance subjective alertness, or may have merely restored alertness that was compromised due to caffeine withdrawal. By examining the pattern of subjective alertness from pre-drug to 3 hours post-drug on the placebo trial, alertness appears to substantially decrease over time, thus suggesting that alertness decreased with continued caffeine deprivation.

Studies by Chait and colleagues (Chait & Griffiths, 1983; Chait & Johanson, 1988) have examined caffeine's effects on subjective response without inducing withdrawal; subjects were not instructed to refrain from caffeine use pre-session. The research by Chait & Johanson (1988) examined response to caffeine in 18 human subjects who been trained to discriminate between amphetamine and placebo. The caffeine use histories of these subjects were not described in the report, but they were drawn from a sample of 36 initial subjects who reported little or no caffeine use. Compared to placebo, administration of 100 mg caffeine (in capsules) was related to significant increases in subjective ratings of stimulation, and significant decreases in subjective fatigue. When given 300 mg caffeine, significant increases in subjective anxiety, vigor, arousal, stimulation and positive mood, and significant decreases in ratings of fatigue and sedation relative to placebo were reported.

Chait & Griffiths (1983) administered a wider range of doses of caffeine (50 to 800 mg - in capsules) to six

subjects (mean coffee intake 2 cups/day) in a study of the effects of caffeine on cigarette smoking and subjective response. While 200 mg caffeine was found to significantly decrease anxiety relative to placebo, both 400 and 800 mg caffeine were associated with significantly higher levels of anxiety than placebo. An overall dysphoric mood was also associated with 400 and 800 mg caffeine. Caffeine was not found to have a meaningful influence on ad lib cigarette smoking in these subjects.

Recently, Griffiths and colleagues (1990b) conducted a study aimed at determining the extent to which low doses of caffeine produce reliable subjective effects. Subjects in this study, who had an average pre-study caffeine intake of 384 mg per day (range 223-791), were given progressively decreasing doses of caffeine (i.e. 170, 100, 56, 32, 18, 10 & 5.6 mg) in order to determine the lowest dose of caffeine that could be discriminated from placebo at greater than chance levels. The doses were introduced in descending order, with at least 20 exposures per dose. Once it was determined that the subject would be unable to make an accurate discrimination at a certain dose, they were re-exposed to 100 mg caffeine for approximately 20 trials in order to re-establish the discrimination and evaluate subjective response to the 100mg dose. Subjective response to the 100 mg dose was examined with a 19 item questionnaire that represented symptoms characteristic of caffeine ingestion or caffeine withdrawal. Also the 49 item Addiction Research Center

Inventory (ARCI, Haertzen, 1974) was given, which has five subscales that are designed to be sensitive to euphoria, sedation, dysphoria, intellectual efficiency and amphetamine-like stimulation.

Of the seven subjects, four could discriminate the 18 mg dose of caffeine from placebo at significantly better than chance levels. One of the subjects reliably discriminated 10 mg caffeine from placebo. The 100 mg caffeine dose was associated with increases in subjective reports of alertness, well-being, concentration, energy, self-confidence and euphoria, and decreases in reports of headache and sleepiness. The fact that low doses of caffeine could be reliable differentiated from placebo suggests that caffeine may have psychoactive properties at doses much lower than previously thought. As in the Griffiths et al., 1990a research, the subjects in this study were all professional behavioral pharmacologists, and thus their familiarity with the psychopharmacological properties of caffeine may have facilitated discrimination at low doses. Replication with a sample more representative of the typical caffeine consumer will be necessary to determine the generalizability of these findings.

In a study that used decaffeinated coffee rather than capsules as the vehicle for caffeine administration, Goldstein, Kaizer & Warren (1965) looked at the effects of 0 mg, 150 mg and 300 mg caffeine on subjective mood and performance on an alertness and a coordination task. The mood

questionnaire assessed subjective mental alertness, well-being, nervousness, and physical stimulation. Twenty medical students (caffeine use history not reported) served as subjects in this study. Participation involved attending experimental sessions on nine consecutive days, with three random exposures to each of the caffeine doses. Sessions began at 7pm, and subjects were instructed not to consume any caffeine from breakfast on the morning of the session. In this study, neither 150 mg nor 300 mg produced changes in task performance that differed from placebo. Mood was only affected significantly by 300 mg caffeine, following which subjects reported more nervousness and more mental alertness than after placebo. The fact that decaffeinated coffee was used as placebo in this study may be partially responsible for the fact that few caffeine versus placebo differences were observed. As mentioned previously, a history of coffee drinking could lead to conditioned caffeine-like responses to decaffeinated coffee. If the decaffeinated coffee had an effect on mood and performance similar to what had previously been experienced with caffeinated coffee, responses to the caffeine in the experimental conditions may have been masked.

Several researchers have compared the response of regular caffeine consumers with subjects who are relatively caffeine naive (Goldstein, Kaizer & Whitby, 1969; Kuznicki & Turner, 1986; Leiberman, Wurtman, Emde, Roberts & Loviella, 1987). In a procedure similar to the one described above, Goldstein and colleagues (1969) compared subjective response

to 0 mg, 150 mg and 300 mg caffeine in a decaffeinated coffee vehicle between 18 non-coffee drinking and 38 heavy coffee drinking (≥5 cups/day) women. In contrast to Goldstein, et al. (1965), subjects in this study were given nine dated vials containing decaffeinated coffee plus either lactose or caffeine. Subjects were exposed to each of the caffeine doses three times, in random order. Following overnight abstinence (from dinner the previous evening), subjects were instructed to prepare the beverage with hot water, sugar and cream to taste following breakfast. Subjective mood was assessed before beverage consumption, and at 30 minute intervals for 2 hours post beverage. Caffeine was found to have differential effects on subjects depending upon their history of consumption. One hour after either 150 or 300 mg caffeine, subjects with a history of heavy coffee drinking felt significantly more content than the subjects who were not regular coffee drinkers. Heavy coffee drinkers felt significantly more alert than non-drinkers one hour after 300 mg caffeine. On the other hand, those who did not regularly drink coffee reported significantly more upset stomach and irritability one hour after 150 mg or 300 mg caffeine than regular drinkers, and significantly more nervous after 300 mg. Some significant differences emerged between the two groups following placebo that are suggestive of a conditioned response to coffee in the heavy drinkers. Following decaffeinated coffee, regular users reported significantly less sleepiness and significantly more alertness than non-

users. Thus, there may have been a conditioned response to the coffee beverage that made those with a history of caffeinated coffee use feel more stimulated following decaffeinated coffee.

Differential effects of caffeine on mood have not been reported in other studies that have examined caffeine's effects on users versus non-users (Kuznicki & Turner, 1986; Liebermann et al., 1987a). Neither of these studies report any direct mood effects for caffeine on either type of subject. The studies both used vehicles for caffeine administration other than coffee (Kuznicki & Turner, 1986, used an orange flavored beverage, Leiberman et al., 1987a, used capsules), but coffee has not been a necessary prerequisite to finding that caffeine affects mood (e.g. Chait & Griffiths,1983; Chait & Johanson, 1988). Both required a 12 hour caffeine abstinence prior to the experimental sessions, and both used doses (Kuznicki & Turner, 1986-0 mg to 160 mg, Liebermann et al. 1987a-0 mg to 256 mg) that have produced mood effects in other studies. Finally, the instruments used to assess mood were also similar to those used in other studies. With no obvious difference that might account for the lack of a caffeine-mood relationship in these two studies, the reliability of caffeine's effect on mood is somewhat questionable.

One other study worth mentioning examined the influence of age on caffeine's effects (Swift & Tiplady, 1988). Young (18 to 37 years old) and old (65 to 75 years old) subjects with a history of "normal"(not defined) caffeine

intake were given a capsule containing either 200 mg caffeine or placebo. Sessions took place in the morning, and no instructions to abstain prior to the experimental session are mentioned in the report. Following caffeine, young subjects reported increases in subjective alertness, calmness, steadiness and degree of interest relative to placebo. With older subjects caffeine was found to enhance task performance, but no significant changes in subjective state were found relative to placebo. Thus, it appears that young coffee drinkers may enjoy caffeine's subjective effects to a greater extent than older coffee drinkers, or, as suggested by the authors, that older individuals have more difficulty with accurately reporting subjective state.

Existing evidence generally supports the conclusion that caffeine ingestion in moderate doses (100 mg to 250 mg) is associated with increases in subjective alertness and decreases in fatigue or sleepiness (Bruce et al., 1986; Chait & Johanson, 1988; Goldstein et al., 1969; Griffiths et al., 1990b; Swift & Tiplady; 1988). At higher doses, or in caffeine naive subjects, caffeine may be related to dysphoric effects such as nervousness and anxiety (Chait & Griffiths, 1983; Chait & Johanson, 1988; Goldstein et al., 1969). Decaffeinated coffee may also have acquired properties that enhance subjective alertness (Goldstein et al., 1969). Research examining response to coffee or caffeine must recognize that while a decaffeinated coffee placebo condition may provide valuable information, it may not be the optimal control

condition.

Caffeine as a reinforcer.

Related to a discussion of caffeine's effects on mood and subjective response is the examination of whether or not caffeine acts as a reinforcer in humans. This question has been the focus of a recent review (Griffiths & Woodson, 1988b), and a number of empirical studies (Griffiths, Bigelow & Liebson, 1986, 1989; Griffiths et al., 1986; Griffiths & Woodson, 1988c; Kozlowski, 1976; Stern, Chait & Johanson, 1989). Griffiths and colleagues (1985) have stated that the ability of a drug to act as a reinforcer is one of two criteria needed for classification as a drug of abuse. The other feature is that the drug produces harmful effects for either the individual user or society. Given the fact that caffeine does appear to be associated with adverse health outcomes, analysis of its ability to function as a reinforcer may reveal whether or not it has the defining characteristics of a drug of abuse.

In their review of the evidence concerning caffeine's reinforcing properties, Griffiths and Woodson (1988b) briefly examined the findings of animal research in this area before evaluating the human work. Of the 11 studies examined, only four provided evidence of self-administration in rats or primates. They concluded that while caffeine has been found to maintain drug self-administration in animals under certain conditions and doses, it does not do so as reliably as other

drugs of abuse such as cocaine or d-amphetamine. The conclusions they draw from the evaluation of human research are similar - that under certain conditions and doses humans will self-administer caffeine and report positive subjective effects associated with caffeine intake. As with animals, however, they note that these patterns are not as strong or consistent as with classic drugs of abuse.

Some of the first studies that examined the role of caffeine in human coffee drinking behavior were conducted by Kozlowski (1976). In a series of three experiments, caffeine content of coffee was manipulated and self-administration assessed. Lower doses of caffeine (25 mg and 50 mg) were associated with significantly more coffee intake than 100 mg caffeine doses. Kozlowski interpreted these findings as evidence that caffeine content determines coffee intake, suggesting that subjects were attempting to regulate their caffeine intake by drinking more of the low caffeine coffee. Griffiths & Woodson (1988b) argue that the 100 mg caffeine may have suppressed coffee drinking by producing unpleasant levels of arousal, thus explaining the significantly lower intake of this dose of caffeinated coffee. Consumption of the 50 mg caffeine was reported to be associated with significantly greater subjective well-being than the 100 mg caffeine, making the Griffiths and Woodson (1988b) interpretation feasible. Griffiths and colleagues have done a number of studies evaluating caffeine's reinforcing effects in humans (Griffiths, Bigelow & Liebson, 1986, 1989; Griffiths et al.,

1986; Griffiths & Woodson, 1988c). Results from a series of studies conducted with very heavy coffee drinkers (9 to 25 cups/day, n=9), most of whom had a history of alcohol or drug abuse, on a residential research ward revealed that coffee intake and subjective liking were an inverted U-shaped function of caffeine dose (Griffiths et al., 1986). The subjects resided on the research ward for the duration of the protocol, and all sources of caffeine, other than that provided via experimental procedures, were restricted. Caffeine content of coffee was manipulated, and self-administration of (as well as subjective response to) the freely available experimental coffee was monitored. Intake and subjective liking were found to increase slightly from 0 mg to 25 mg and 50 mg, and then to decrease in a dose dependent fashion with 100 mg, 200 mg, and 400 mg caffeine per cup of coffee. Statistical analyses of these data are unfortunately not reported.

In a related group of experiments, Griffiths, Bigelow and Liebson (1986) used a choice paradigm to examine whether or not caffeinated coffee would be consistently chosen over decaffeinated coffee when provided under double-blind conditions. Subjects (again, very heavy coffee drinkers with histories of alcoholism and/or drug abuse, n=9) were maintained on a background coffee containing either 0 mg or 100 mg caffeine for at least 10 days. After intake on the background coffee beverage stabilized, they were exposed to a standard choice procedure: subjects were given a supply of

one of two distinctly coded vials on two consecutive days (e.g. coffee "A" on day 11, coffee "B" on day 12). One of the coded supply of vials contained decaffeinated coffee plus 100 mg caffeine, the other had decaffeinated coffee with lactose added to make it visibly similar to the caffeinated coffee. A "choice" day followed, where subjects chose from the two coded coffees which one they would like to drink for the day. When subjects had been maintained on a background of caffeinated coffee, they consistently chose the coffee containing 100 mg caffeine. When maintained on decaffeinated, subjects were equally likely to choose either the caffeinated or the decaffeinated coffee. Once again, baseline consumption is an important factor to consider when evaluating response to caffeine.

In a study using subjects with caffeine intake levels more representative of the general population (mean 361 mg/day; approximately 3 to 5 cups of coffee per day, no addiction histories, n=12), a choice procedure was again employed, only this time using capsules rather than coffee (Griffiths & Woodson, 1988c). Subjects were to abstain from caffeine from bedtime the evening before experimental sessions. They were told that the study involved evaluating different chemicals found in coffee, tea, cocoa and cola, and that in addition to caffeine and other methylxanthines, other agents that were potentially just as potent might be given. Placebo or caffeine (100, 200, 400 & 600 mg) was given in color coded capsules on two consecutive days (order of

exposure was randomized), and on the following day subjects were to choose the colored capsule they preferred. This three day sequence was repeated until subjects had been exposed to a choice between placebo and each active dose 10 times. Subjective assessments of drug liking, mood (Profile of Mood States, McNair, Lorr & Droppleman, 1971) and symptoms (a caffeine/caffeine withdrawal sensitive questionnaire) were made at 3.5 and 8 hours following drug administration: subjects were given the questionnaires to take with them and asked to fill them out at these times.

The 100 mg caffeine capsule produced significant increases in subjective liking, vigor, stimulation and nervousness and decreases in tiredness, sluggishness, fatigue, headache and desire for caffeinated beverages compared to placebo. Subjects disliked the effects of 400 and 600 mg caffeine significantly more than placebo or 100 mg caffeine. With regard to choice behavior, 100 mg and 200 mg were chosen over placebo at rates significantly greater than chance, though the authors note that there was substantial inter-subject variability. Preference for caffeine was found to decrease as a function of dose, and choice of the 400 and 600 mg did not differ from chance levels. Four of the 12 subjects consistently avoided the highest dose of caffeine. This is the first study to show that caffeine, apart from coffee, can serve as a reinforcer. It is notable that this research was conducted with subjects whose regular caffeine intake was within a normal range. Previous research by Griffiths and

colleagues (Griffiths et al., 1986; Griffiths, Bigelow & Liebson 1986) has been done with subjects whose caffeine intake placed them in the top one percent of caffeine consumers in the United States (International Coffee Organization, 1981). This study showed that caffeine can function as a reinforcer in a subject sample with more representative daily caffeine intakes.

In a report of caffeine self-administration research, Griffiths et al. (1989) describe a series of in-patient studies, again using very heavy coffee drinkers (range 7 to 20 cups per day, n=10) with histories of drug or alcohol abuse. In the first reported experiment, subjects were found to prefer 100 mg caffeine to placebo in a choice procedure, even following extended caffeine abstinence. In the second study, subjects were required to work (ride an exercise bike) to get either caffeinated coffee, decaffeinated coffee, caffeine capsules or placebo capsules. The work requirement was raised in increments until self administration was suppressed, and then dropped back to a more moderate level. Subjects resumed work for the caffeinated coffee, the caffeine capsules, and the decaffeinated coffee, but not for the placebo capsules. Thus, both caffeine and coffee appeared to have reinforcing properties in this group of subjects. Subjective ratings revealed that decaffeinated coffee was liked significantly more than the placebo pills, but significantly less than the caffeinated coffee or caffeine capsules. The authors note that "the extent to which drinking

of decaffeinated coffee is maintained by conditioned reinforcers established by past pairing with caffeine or, alternatively, by pharmacologically active substances in coffee other than caffeine cannot be determined" (pg 138).

Another recent study examined the reinforcing properties of caffeine in subjects with no history of drug abuse and a mean daily intake of 155 mg caffeine per day (Stern et al., 1989). Eighteen subjects were exposed to a choice procedure similar to that described above. Participants did not reside on a residential research ward, and regular caffeine intake was monitored but not restricted throughout the study. Preference for doses of 100 and 300 mg caffeine capsules versus placebo capsules was examined, as well as subjective response to the different capsules. The 100 mg dose of caffeine was not chosen over placebo at a level significantly different from chance. The 300 mg dose was chosen significantly less than chance, suggesting that this dose had aversive properties for these subjects. Subjective drug liking did not differ among the three conditions, however the 300 mg dose was associated with significant increases in self reported anxiety and stimulation, and a decrease in sedation. When subjects were divided into those who chose caffeine versus those who chose placebo, caffeine choosers were found to report positive and stimulant effects of both 100 and 300 mg caffeine while non-choosers reported no effects from the 100 mg dose, and negative effects such as increased anxiety with the 300 mg dose.

Stern and colleagues (1989) suggest that the findings of Griffiths & Woodson (1988c) may have differed from their own as a consequence of the overnight abstinence employed in the Griffiths & Woodson study. The abstinence may have induced withdrawal symptoms that were alleviated by caffeine, thus caffeine was chosen more often than chance among caffeine deprived subjects. Another potentially important difference between the two studies is the regular caffeine consumption of the research participants. Subjects in the Griffiths and Woodson (1988c) study consumed an average of 361 mg caffeine per day, while the Stern et al. (1989) subjects consumed and average of 155 mg per day. If these subjects were assigned to groups in the fashion of Goldstein & Kaizer (1969), the Griffiths and Woodson subjects would be considered "moderate" users, while the Stern et al. subjects would fall into the "light" user category. As mentioned previously, Goldstein and Kaizer (1969) found that "light" users were more likely than "moderate" or "heavy" users to associate morning coffee intake with nervousness. Evidence from many of the studies reviewed suggests that baseline caffeine intake is an important factor in evaluating response to caffeine.

As Griffiths & Woodson (1988b) conclude in their review of the literature, caffeine does not maintain self-administration as reliably as other drugs of abuse such as cocaine or d-amphetamine. It does appear to be reinforcing in moderate doses with subjects who have a history of moderate or heavy caffeine use. This places caffeine in a category

similar to the other most widely used drugs in the world, namely nicotine and alcohol. Nicotine, for example, is not as consistently self-administered in either humans or animals as cocaine or d-amphetamine (Griffiths, Brady & Bradford, 1979). Alcohol has also been found to serve as a reinforcer only under a limited range of conditions (Mello, 1973; Meisch, 1977). Nicotine can serve as either a reinforcer or a noxious stimulus, and its function is dependent upon a number of factors including prior nicotine use history and dose (Koop, 1988; Goldberg & Henningfield, 1988). The preceding review of the human caffeine literature suggests that this is also be the case with caffeine.

Task performance.

Over the past 100 years, many studies have evaluated the effects of caffeine on a wide range of tasks. Results of these studies have been reviewed (Gilliland & Bullock, 1984; Sawyer, Julia & Turin, 1982; Weiss & Laties, 1962), and the conclusions generally state that caffeine can enhance performance of certain tasks under certain conditions. The Weiss & Laties review (1962) is the most thorough conducted to date.

Weiss and Laties set out to address two questions. First, does caffeine actually enhance performance or simply restore performance that is compromised due to fatigue or boredom; and second, are the performance enhancing effects counterbalanced by caffeine's negative effects. In response

to the first of these questions, it was concluded that caffeine's performance enhancing effects are not limited to situations where subjects are tired or bored. Boredom and fatigue lower overall performance, however, and thus caffeine's effects are more pronounced under these circumstances. In response to the second question, it was suggested that while caffeine appears to be a relatively benign drug, the tremor and dysphoric subjective effects associated with higher doses (240 mg and above) may be problematic. The following review will consider more recent research that has examined caffeine's general effects on a variety of performance tasks, and also a few investigations which have considered how factors such as age, previous caffeine history, and personality variables may influence caffeine's effect on performance.

Liebermann and colleagues (1987a) have examined the effects of a range of caffeine doses on performance. Twenty non-smoking male subjects with a baseline caffeine intake of less than 400 mg per day participated in the study. Subjects were each exposed to a no-drug pre-session during which they became familiar with the experimental procedures, and five drug sessions that involved ingesting capsules containing 0, 32, 64, 128 or 256 mg caffeine. Exposure to each of the doses was counterbalanced. Abstinence from all sources of caffeine for 12 hours was required prior to all of the sessions except the no drug pre-session.

All of the sessions were conducted in the morning,

with the capsules being given at 8:00 am and the onset of testing 40 minutes later. A series of eight performance measures were administered which included (in order of administration) a four-choice reaction time task, a continuous performance task, an auditory vigilance task, three motor performance tasks, a digit symbol substitution task, and a simple auditory reaction time task. Subjective mood measures were also administered. For the purpose of brevity, only measures which were sensitive to the caffeine manipulation will be described.

The auditory vigilance task is perhaps the most consistently caffeine sensitive task reported in the literature. In this study the 60 minute version of the auditory vigilance task (referred to as a Wilkinson auditory vigilance task, Wilkinson, 1970) involved presentation of a 400ms tone once every two seconds. Forty times throughout the one hour task, a signal tone was presented that was approximately 330ms. Subjects were to respond to the shorter tone by pressing a key. Correct responses and false positives were recorded. The four-choice reaction time task was ten minutes in duration, and involved the presentation of a visual stimulus in one of four places on a video screen. Subjects were to respond to stimulus presentation by striking one of four keys that corresponded to the stimulus location. Response latency, incorrect responses, and errors of omission were recorded. The task involved 500 stimulus presentations.

The investigators divided subjects into two groups,

those consuming an average of less than 100 mg caffeine per day versus those consuming 100 to 400 mg caffeine per day. Since no between group differences were found, the subjects' data was pooled for analysis. All doses of caffeine significantly improved detection of the shorter signal tones on the auditory vigilance task relative to placebo. False positive responses (responses when the signal tone had not actually been presented) were unaffected by caffeine. All doses of caffeine also significantly decreased reaction time on the four-choice reaction time task compared to placebo. Errors and omissions on the four-choice reaction time task were unaffected by caffeine. It should be noted that improvements in performance did not follow a dose response pattern, and generally all doses affected responses similarly.

Liebermann and colleagues (1987b) followed this study with an examination of the effects of caffeine alone (64 mg) and in combination with 800 mg aspirin. The authors proposed that since this aspirin-caffeine combination is available in pain preparations, it would be of value to examine its effects on mood and performance. Procedures were similar to those used in the initial caffeine study (e.g. n = 20; presentation of drug in capsules following 12 hour caffeine abstinence). Once again 64 mg caffeine, both alone and in combination with aspirin, significantly enhanced performance of the auditory vigilance task compared to placebo. Caffeine did not significantly affect performance of the four-choice reaction time task. It did, however, significantly decrease reaction

time on a simple auditory vigilance task that involved simply pressing a key as quickly as possible after a tone presentation.

Roache and Griffiths (1987) examined the effects of caffeine alone and in combination with diazepam, reasoning that the prevalence of usage for both of these substances was high enough to expect that they would often be used in combination. Nine male subjects, seven of whom were non-smokers, participated in the study. All of the subjects reported drinking the caffeine equivalent of two cups of coffee per day or less. Subjects were exposed to 0, 200, 400 and 600 mg caffeine (via capsules) alone and in combination with 0, 10, or 20 mg diazepam, making a total of 12 drug conditions (4 caffeine x 3 diazepam doses). Abstinence from caffeine was required from 8:00am on the morning of the sessions, and sessions lasted from 9:30am to 3:00pm. Drug administration was double blind and counter-balanced. Performance tasks were administered pre-drug, and at 1, 2, 3, and 4 hours post-drug. Included in the performance battery were a circular lights task, digit symbol substitution, choice reaction time, number recall, serial subtraction, and a delayed recognition task. Staff and subjective assessments of mood and symptoms were also made.

Caffeine enhanced performance on the choice reaction time task and the circular lights task. The choice reaction time task lasts about ten minutes, and involves pressing one of two keys (left or right) in response to whether numbers

presented on a video screen were even or odd. Significant decreases in reaction time on this task were seen with caffeine relative to placebo, though post hoc analyses of differences with each dose level were not reported. The circular lights task requires subjects to press a series of buttons corresponding to the illumination of a series of stimulus lights arranged in a circle. The number of lights correctly responded to in 60 seconds is recorded. Caffeine significantly enhanced performance on the circular lights task compared to placebo, though once again post hoc comparisons of the effects of the different doses were not made. When given with diazepam, caffeine was found to antagonize the sedation and performance disruption that was observed with diazepam alone.

Recent studies from the Sleep Disorders and Research Center of the Henry Ford Hospital have reported significant enhancement of auditory vigilance with caffeine, independent of sleep/alertness manipulations (Rosenthal, Roehrs, Zwyghuizen-Doorenbos, Plath & Roth, in press; Zwyghuizen-Doorenbos et al., 1990). Zwyghuizen-Doorenbos et al. (1990) looked at caffeine's effects on sleep latency and performance in 24 non-smokers who consumed 250 mg caffeine per day or less. Subjects slept in a sleep laboratory on evenings prior to the three consecutive study days to insure that all were getting no more or less than 8 hours of sleep per night for the duration of the study. All were instructed to avoid caffeine from the evening prior to the first experimental

session through the third session.

Subjects were divided into a caffeine group and a placebo group. At 9:00am and again at 1:00pm, following breakfast and lunch, subjects were given decaffeinated coffee. For the placebo group, the decaffeinated beverage never contained added caffeine; for the caffeine group 250 mg caffeine was added to the decaffeinated coffee on days one and two, but not on day three. Latency to sleep was measured one and three hours following both morning and afternoon coffee administration in a quiet, darkened room. Ninety minutes following the morning coffee, subjects worked on a divided attention task for 15 minutes. This task involved tracking a moving target across a video screen with a joystick, and simultaneously pressing a button when a stimulus appeared on the periphery of the screen. At 2:30pm, 90 minutes after the afternoon coffee, subjects performed an auditory vigilance task. This version of the auditory vigilance task required subjects to detect 400ms signal tones appearing randomly within a series of 270ms tones and respond to the signal tones by pressing a key. The task lasts for 40 minutes, and is divided into four 10 minute intervals for scoring purposes. Latency to response, in addition to number of correct responses, omitted responses, and false positives were measured.

Sleep latency and auditory vigilance were significantly affected by caffeine. Subjects given 250 mg caffeine had significantly longer sleep latencies than those

given placebo. The caffeine group also had significantly faster reaction times and significantly fewer errors on the auditory vigilance task than the placebo group. Divided attention was not affected by caffeine.

A particularly interesting result of this study was that on the third session, when both groups received placebo (decaffeinated coffee), subjects who had received caffeine on days one and two did significantly better on the auditory vigilance task and had significantly longer sleep latencies than subjects receiving placebo on days one and two. Pre-session evaluation revealed no differences between groups on any measures, thus it appears that there was a conditioned response to the decaffeinated coffee in the caffeine group. This is the first study to demonstrate a possible conditioned response to caffeine on an objective measure of alertness. Problems with this conclusion lie in the fact that the placebo group received decaffeinated coffee throughout the three day study. Previous UCS-CS pairings of caffeine with the coffee vehicle would lead one to predict a conditioned response to decaffeinated coffee in any individual with a history of regular coffee consumption.

Unfortunately, the authors do not describe the coffee intake histories of their subjects beyond noting that all consumed no more than 250 mg caffeine per day. It is therefore impossible to determine whether or not conditioned alerting effects would be expected with the first day's exposure to decaffeinated coffee. Examination of the performance data from

the first to the third day for the placebo does reveal a slight drop in performance as would be expected with the extinction of a conditioned enhancement. Both reaction time and number of errors on the auditory vigilance task tended to increase from day one to day three (Placebo group: mean(SD) # errors: 1.8(2.4), 2.8(2.7), 4.3(5.4); mean(SD) reaction time: 583(287), 567(266), 631(313), for days 1 to 3 respectively-admittedly, the large standard deviations suggest that these differences would not be significant) which is contrary to the practice effect that might be expected on this type of task. This drop may also have been a manifestation of caffeine withdrawal in these subjects. Without any subjective measures of mood or withdrawal-type symptoms, along with a lack of more specific information about the regular caffeine intake of these subjects, the presence or absence of a conditioned response in the placebo group cannot be determined.

With a procedure similar to that described for Zwyghuizen-Doorenbos et al. (1990), Rosenthal et al. (in press) have recently looked at the effect of 0, 75 and 150 mg caffeine on performance and sleepiness following 5 hours versus 8 hours of sleep. This study examined 36 non-smoking males, with baseline caffeine consumption levels of 250 mg per day or less. With the same timeline and tasks employed in Zwyghuizen-Doorenbos et al. (1990) research, subjects were assigned to either a placebo, 75 mg or 150 mg caffeine condition, and once again caffeine was administered via

decaffeinated coffee following breakfast and lunch. Subjects spent evenings prior to the experimental session in the sleep laboratory. Prior to the sessions subjects were allowed either five or eight hours of sleep. Order of presentation of the sleep manipulation was counterbalanced across subjects. Both the 75 mg and the 150 mg caffeine groups did significantly better than the placebo group on the auditory vigilance task, and no interactions between caffeine dose and sleep time were observed. The 75 mg and the 150 mg caffeine groups did not differ from one another. Errors on the auditory vigilance task were infrequent, and thus caffeine did not affect vigilance errors. Once again, caffeine did not have a significant effect on the divided attention task.

Foreman and colleagues (Foreman, Barraclough, Moore, Mehta & Maddon, 1989) have suggested that caffeine may impair processing of confusing stimuli. In a study of 32 undergraduate males (mean caffeine intake 262 mg/day, smoking status not indicated), subjects receiving 250 mg caffeine in decaffeinated coffee performed significantly more slowly than those given decaffeinated coffee with no added caffeine on a numerical version of the Stroop task. Following overnight abstinence, subjects reported to the laboratory and were randomly assigned to either the 0, 125 or 250 mg caffeine condition. Thirty minutes after beverage administration, subjects were exposed to a word recall task, a response time task (subjects had to point to missing parts of concentric circles-latency to response and errors were measured), and a

numerical version of the Stroop task. Though recall and response time on the pointing task were unaffected by the caffeine manipulation, subjects who received 250 mg caffeine were significantly slower than the decaffeinated group on the Stroop. The 125 mg caffeine group did not differ from either of the other groups, and 250 mg did not result in more errors on the Stroop task, only slower performance. As mentioned earlier, the use of decaffeinated coffee as the only control beverage may make it difficult to find between group differences, as decaffeinated coffee may acquire some of the performance and subjective effects of caffeinated coffee through classical conditioning (Goldstein et al., 1969; Zwyghuizen-Doorenbos et al., 1990).

These studies have shown that caffeine, in doses from 35 mg to 256 mg, has a consistently enhancing effect on performance of an auditory vigilance task (Leiberman et al, 1987a, 1987b; Rosenthal et al., in press; Zwyghuizen-Doorenbos et al., 1990). Caffeine's effects on other reaction time tasks, both simple and complex, are inconsistent, with some studies showing a performance enhancing effects while others fail to find improved performance with caffeine (Foreman et al., 1989; Liebermann et al., 1987a, 1987b; Nuotto et al., 1982; Roache & Griffiths, 1987; Rosenthal et al., in press; Zwyghuizen-Doorenbos, 1990). A number of factors such as caffeine dose, subject's prior experience with caffeine, and task complexity or difficulty may interact in undetermined ways thus leading to the variable results reported with non-

auditory reaction time tasks. Caffeine does not appear to affect proofreading performance (Ratliff-Crain et al, 1989), hand-eye coordination (Goldstein et al., 1965a; Nuotto et al, 1982), visual discrimination and recall (Foreman et al., 1989; Goldstein et al., 1965a), symbol substitution, (Bruce et al., 1986; Roache & Griffiths, 1987) or serial subtraction (Roache & Griffiths, 1987). Finally, caffeine has been reported to disrupt the speed at which subjects can complete the confusing, conflicting cue Stroop task (Foreman et al., 1989). A number of factors may influence whether or not an individual will experience changes in performance levels with caffeine. Among the factors that have been addressed in the literature have been caffeine history, personality type, and age. Some of this research will now be considered.

Potential mediators of caffeine's influence on task performance. One study mentioned in the discussion of caffeinism examined the caffeine - performance - mood relationship in a different way, by evaluating the effects of chronic caffeine consumption on subjective well being and academic performance (Gilliland & Andress, 1981). Following a questionnaire survey of 1,500 college freshman, subsamples were randomly selected that represented four categories of caffeine consumers: thus the sample of interest consisted of 40 caffeine abstainers, 40 light consumers (< equivalent 1 cup coffee/day), 40 moderate consumers (caffeine equivalent to 1-5 cups of coffee/day), and 39 heavy consumers (> equivalent 5 cups coffee/day). Daily caffeine consumption was then

correlated with responses to several questionnaires including the Spielberger State-trait Anxiety Inventory (Spielberger, 1970), the Beck Depression Inventory (Beck, 1978), a questionnaire assessing caffeine side effects, and a somatic complaint instrument. When compared to abstainers, the moderate and heavy users reported significantly more trait anxiety and depression. The high users also reported significantly more negative side effects of caffeine and more somatic complaints than abstainers. Finally, grade point averages for the semester and course grades were found to be significantly lower in the high caffeine consumers as compared with the caffeine abstainers.

The authors also reported examining cigarette smoking's relationship to these factors, and found that heavy caffeine use was associated with heavy smoking. However, with the exception of course grade and grade point average, the relationship that held for heavy caffeine and the variables assessed (i.e. higher trait anxiety, higher depression scores, more somatic complaints) was not found for heavy smokers. It is suggested that moderate to heavy caffeine use may result in a disruptive pattern of symptoms similar to caffeinism. This study is interesting in that it suggests a link between heavy chronic caffeine consumption and compromised academic performance, yet its assumption of the direction of causality seems inappropriate. It appears equally likely that students who are experiencing academic difficulty, and perhaps anxiety and depression relating to academic status (observed levels

of these variables were not outside a "normal" range), would use a legal, freely available substance with known stimulant properties as a means of extending study time and wakefulness.

In support of the conclusion that chronic caffeine administration may lead to compromised performance are results of another study which was designed to evaluate the acute effects of caffeine on task performance in heavy users versus light users. Loke & Meliska (1984) examined extended visual vigilance performance in 12 low (mean intake 44 mg/day) and 12 high (mean intake 204 mg/day) caffeine users after two hours of caffeine deprivation. Subjects were randomly assigned to receive capsules containing either placebo, 195 or 325 mg caffeine. Immediately after receiving the capsules, subjects were exposed to the visual vigilance task for 90 minutes, which involved detecting speed changes in stimuli presented on a screen in front of the subject. False responses, correct responses, missed signals and reaction times were measured. This procedure varied from that typically used in research examining caffeine's effects on reaction time, in that subjects were exposed to the task immediately following caffeine/placebo ingestion.

Caffeine had no effect on performance of the visual vigilance task. However, subjects who regularly consumed 204 mg/day of caffeine did significantly worse (made fewer correct responses, and had more false responses) than the subjects who regularly drank 44 mg/day of caffeine. The lack of a main effect for caffeine on the performance task is addressed by

the authors, who note that subjective reports of boredom did not increase from the beginning to the end of the task. It has been suggested that caffeine's effects on task performance are most pronounced when subjects are impaired due to boredom or fatigue (Barmack, 1940), and the authors speculate that perhaps their subject were not sufficiently bored with the task for caffeine enhancement to occur.

An alternative explanation of their failure to find an effect for experimentally administered caffeine could be that the procedures for task administration masked any caffeine effect. By the time caffeine had reached peak plasma levels in these subjects (45 to 60 minutes post capsule administration), they had been engaged in the visual vigilance task for more than 30 minutes. It is possible that the amount of practice that the subjects had received in this 30 minute period raised performance to a level difficult to improve further. The more standard procedure in this type of experiment is to allow caffeine to approach peak levels prior to onset of the task.

The fact that regular use was associated with significantly poorer performance is somewhat similar to the finding of Gilliland and Andress (1981) that heavy to moderate caffeine consumers had poorer academic performance. Though these two studies differ dramatically in the method of assessing performance, they are similar in the fact that in each of these studies those who regularly consumed more coffee did more poorly. Unfortunately, the Loke and Meliska (1984)

research did not measure other background factors such as cigarette smoking or alcohol consumption that may have contributed to the results. There is some evidence that cigarette and caffeine use are related (Istvan & Matarazzo, 1984). It may even be the case that the heavy caffeine consumer group had more smokers in it, and that the experimental task (lasting 90 minutes) inducing nicotine withdrawal related discomfort in smoking subjects.

Another study compared the performance of subjects drinking 3 to 5 cups of coffee per day (n=50) with subjects drinking 1 or fewer cups per day (n=20), all of whom were non-smokers (Kuznicki & Turner, 1985). This research did not find differences between these two groups independent of acute caffeine administration. Caffeine was found to have differential effects on these groups, with 160 mg having little effect on performance of a rotary pursuit task (task onset 30 to 45 minutes post drug) in the heavy coffee drinkers, but significantly impairing performance in the light users. No effects for caffeine or average daily coffee consumption were found on performance of a choice reaction time task or a reverse tracing task. Finally, Liebermann et al. (1987a) failed to find any differences between subjects consuming less than 100 mg caffeine per day compared to those consuming between 100-400 mg per day on the auditory vigilance or choice reaction time tasks described above.

The data supporting a negative relationship between regular, heavy caffeine intake and performance is

inconclusive. Those who regularly ingest large quantities of caffeine have been found to do more poorly in terms of academic performance and visual vigilance when compared to subjects with lower daily caffeine intake (Gilliland & Andress, 1981; Loke & Meliska, 1984), but the procedures employed in these studies have not allowed for definitive conclusions. Also, other work comparing heavy and light caffeine consumers has failed to find any group performance differences independent of caffeine administered during the session (Kuznicki & Turner, 1985; Liebermann et al., 1987a). It may be that regular intake of caffeine has to exceed a certain amount before chronic intake impairs performance (though the Loke & Meliska heavy users consumed only an average of 204 mg per day). Alternatively, other unidentified factors related to attention or information processing may be associated with heavy, chronic caffeine intake and affect performance independently of regular caffeine consumption.

Revelle and colleagues (Anderson & Revelle, 1982; Revelle, Amaral & Turriff, 1976; Revelle, Humphreys, Simon & Kirby, 1980) have proposed that individuals may respond differentially to caffeine depending upon certain personality characteristics. Drawing from H. J. Eysenck's (1976) theory on introversion and extroversion, and tied to the Yerkes-Dodson law (1908), these authors have suggested that caffeine will bring extroverted individuals to a more optimal level of arousal (as they are chronically under-aroused) thereby enhancing performance. On the other hand, caffeine will place

introverts, who are supposedly chronically aroused, on the descending arm of the inverted-U shaped function of arousal and performance, thus impairing their performance. Revelle has paid particular attention to the impulsivity subscale of the Eysenck Personality Inventory (Eysenck & Eysenck, 1964). Impulsivity is a construct related to extroversion, and is characterized by positive responses to questions about longing for excitement, often doing things on the spur of the moment, and acting or speaking without stopping to think.

In a series of five experiments, Revelle et al. (1980) had subjects participate in one or two experimental sessions. All were instructed to abstain from dietary caffeine for six hours prior to the session, and the personality assessment took place after being given the experimental beverage during the 30 minute period prior to task administration. For the first, third & fifth experiments, subjects participated in two experimental sessions, receiving a caffeinated (experiments 1 & 3, 200 mg caffeine; experiment 5, 4 mg/kg, probably about 200-400 mg caffeine total) orange flavored beverage in one and an orange drink with quinidine added for the other. The second and fourth experiments were one session. During the second all received 200 mg caffeine and for the fourth half received caffeine and half placebo. Experiments 1 and 2 were conducted in the morning; 3 had both a morning and an evening session; 4 was either morning or evening depending on the subject's preference; and 5 was conducted in the evening. The average regular caffeine intake

of the subjects in each experiment was not noted.

The tasks administered were basically similar to the verbal section of the Graduate Record Examination, with duration ranging from 10 to 30 minutes. The general pattern of results confirmed the hypothesis that the performance of the high impulsive scoring subjects (above the median) was better with caffeine than placebo, but this held only when subjects were run in the morning, and only on the first day of the two day sessions - practice and evening sessions appeared to attenuate the effect for caffeine in these subjects. The low scoring impulsives generally did worse following caffeine, but again only in the morning of the first day. The authors suggest that the pattern reverses when sessions were conducted in the evening, though this trend is slight, and only significant in one of the experiments (Exp.3).

In a similar study, Anderson & Revelle (1982) again gave subjects the Eysenck Personality Inventory (Eysenck & Eysenck, 1964) and divided them into high and low impulsive groups based on a median split. Baseline caffeine intake of subjects is not mentioned, though all were instructed to avoid caffeine for six hours prior to the experimental session. Subjects were randomly assigned to receive placebo (again, orange flavored breakfast drink) or caffeine (4 mg/kg) plus placebo, with approximately equal numbers of high and low impulsives in each condition. An 18 minute proofreading task was administered 30 minutes after beverage consumption. Once

again, those scoring low on impulsivity did significantly worse in terms of errors identified and lines read with caffeine than with placebo. Subjects who had scored above the median on impulsivity did not differ with regard to errors detected following placebo versus caffeine, though they did read significantly more lines after caffeine than after placebo.

These two studies allege to support the theory that the personality differences of extroversion versus introversion, and more specifically high impulsiveness versus low impulsiveness, reflect differences in resting levels of arousal, and that these baseline arousal differences will result in a differential response to caffeine. Caffeine is said to increase arousal of highly impulsive subjects, bringing them towards a level necessary for optimal performance. However, for subjects low in impulsivity, who already have a high baseline level of arousal, caffeine puts them over the top, so to speak, thus compromising performance. It must be noted, however, that these studies rarely mention the baseline caffeine intake of their subjects. In Revelle et al. (1980), baseline intake is mentioned briefly as a possible confound, but only in relation to caffeine withdrawal. The influence of baseline influence is dismissed since the caffeine levels of most subjects were below that previously identified as leading to a withdrawal syndrome. It is mentioned that regular intake of caffeine was not measured in every experiment, but the number of experiments

that did assess baseline consumption is not clear. They note that there was no noticeable relationship between caffeine intake and personality variables except in experiment 5 (the reader does not know when else it was measured), where the high impulsives were found to consume significantly more coffee than the low impulsives. In the Anderson & Revelle (1982) experiment, regular caffeine intake is not even mentioned.

It appears that a more parsimonious explanation of the link between measured impulsivity and response to caffeine may emerge if one examines the caffeine history of the subjects in this research. Subjects scoring high on impulsivity may be subjects with a higher regular caffeine intake, as was found in Revelle et al's (1980) experiment 5. Research discussed previously by Kuznicki & Turner (1985) found that caffeine disrupted the performance of subjects with a low usual intake but did not affect subjects who regularly consumed three to five cups per day. Also mentioned previously was the finding that light users of caffeine are more likely to associate its ingestion with nervousness than moderate or heavy users (Goldstein & Kaiser, 1969). The possibility that findings of compromised task performance in subjects scoring low on impulsivity are the result of a restricted history of caffeine exposure must be addressed before the independent influence of this personality construct can be seriously considered.

Swift and Tiplady (1988), examined the role of age in

response to caffeine. While the young (18 to 37 years old) subjects were sensitive to caffeine's subjective arousal effect, the older (65 to 75 years old) subjects showed a greater sensitivity to its performance enhancing effects. In this two-session experiment subjects were given either 200 mg caffeine in capsules, or placebo capsules, in counter-balanced presentation. Subjects were exposed to a test battery including a continuous attention task, during which the subjects had to monitor a screen for stimulus changes; a choice reaction time task that involved pressing a series of buttons that corresponded to the lighting of stimulus lights; and a decision making task during which the subject had to respond (yes or no) as to whether or not each of a series of line drawings represented an animal. While caffeine was not found to affect performance in the younger subjects, older subjects were found to do significantly better on the continuous attention task and the choice reaction time task after caffeine administration than after placebo. Thus it appears that age, or perhaps some unidentified factor associated with age such as history of previous caffeine consumption (baseline levels are not reported other than saying that they represented "normal" intake), may influence response to caffeine in a meaningful way.

The literature on caffeine and task performance is large and diverse and it is difficult to draw strong conclusions. Caffeine consistently appears to enhance performance of an auditory vigilance task at doses from 35 to

256 mg (Leiberman et al, 1987a, 1987b; Rosenthal et al., in press; Zwyghuizen-Doorenbos et al., 1990). Other performance-enhancing effects are equivocal (Foreman et al., 1989; Liebermann et al., 1987a, 1987b; Nuotto et al., 1982; Roache & Griffiths, 1987; Rosenthal et al., in press; Zwyghuizen-Doorenbos, 1990). Caffeine has been reported to disrupt the speed at which subjects can complete a confusing task (Foreman et al., 1989).

Chronic consumption of caffeine has been associated with poorer academic performance and poorer performance of a visual vigilance task (Gilliland & Andress, 1981; Loke & Meliska, 1974). The relationship between consumption and performance disruption may reflect caffeinism in those with heavy intakes (>500 mg/day), or alternatively, may reflect the influence of another factor such a cigarette smoking, depression or anxiety that is compromising performance. Other researchers have not found chronic intake to be associated with impaired performance, but instead have provided evidence that caffeine disrupts performance in those with a limited history of exposure (Kuznicki & Turner, 1986).

Personality factors and age have both been suggested as mediators of the relationship between caffeine and performance (Anderson & Revelle, 1982; Revelle et al., 1976; Revelle et al., 1980; Swift & Triplady, 1988). Future research examining these relationships may reveal that caffeine use history is responsible for apparent associations between personality and/or age and the performance effects of

caffeine.

Summary and justification of research.

The purpose of the above review has been to highlight some of what is known about coffee drinking and the actions of its most pharmacologically active ingredient, caffeine. A number of authors have referred to caffeine as a drug of abuse (Austin, 1979; Gilbert, 1976; Gilliland and Bullock, 1984; Greden, 1981; Griffiths and Woodson, 1988a). Griffiths and Woodson (1988a) argue that caffeine has the defining characteristics of a drug of abuse: reinforcing properties and adverse effects that have the capacity to harm the individual and/or society. Yet coffee is more than just caffeine - it is a legally sanctioned, social beverage consumed by a majority of Americans. The research conducted for this dissertation was designed to permit the evaluation of the subjective and behavioral effects of coffee both with and without caffeine.

It has been estimated that 56.3 percent of individuals over 10 years of age in the United States regularly drink coffee, and that those coffee drinkers consume approximately 3.37 cups per day (Gilbert, 1984). Per capita coffee consumption (over 10 years of age) for the U.S. is estimated at 1.92 cups per day. Total caffeine consumption from all sources, including coffee, tea, soft-drinks, and other sources (noted in Table 1) has been estimated at 211 mg per day (Gilbert, 1984). With this high prevalence of consumption,

it is important to understand not only the potential consequences of coffee and caffeine intake, but also the reasons for its popularity.

The analysis above has shown that caffeine is a potent central nervous system stimulant. Caffeine intake is associated with increased cardiac stimulation and arterial blood pressure, as well as increased locomotor activity in animals and enhanced alertness in humans (File et al., 1988; Rall, 1985; Spealman, 1988; Weiss & Laties, 1962). In addition to its central actions, it activates catecholamine release and thus its effects are a reflection of both direct and indirect stimulation of the CNS (Rall, 1985; Robertson et al., 1978). Tolerance has been reported to its stimulant effects, but it is doubtful that complete tolerance occurs under patterns of regular use (Lane & Manus, 1989; Meliska et al., 1990; Robertson et al., 1981; Zwyghuizen-Doorenbos et al., 1990). A withdrawal syndrome has been reported following abrupt discontinuation of use, and is characterized by headache and lethargy (Greden et al., 1980; Griffiths & Woodson, 1988a; Griffiths et al., 1990a). Coffee and caffeine consumption has been associated with heart disease, cancer, infertility, diabetes mellitus and a psychiatric diagnosis called caffeinism (Cramer, 1990; Curatolo & Robertson, 1983; Dews, 1984; and Ernster, 1984; Tuomilehto et al., 1990; Weinberg & Wilcox, 1990; Wilcox et al., 1988). Though a direct cause and effect link has not been established for any of these conditions, the combined research does provide evidence

suggesting that caffeine or coffee intake may have adverse health outcomes.

Coffee drinkers report "because I enjoy it" and "I like the taste" as the main reasons for drinking coffee (Goldstein & Kaizer, 1969). Studies of caffeine's subjective effects have shown that moderate doses (100 mg to 250 mg) are associated with increases in subjective alertness and decreases in fatigue or sleepiness (Bruce et al., 1986; Chait & Johanson, 1986; Goldstein et al., 1969; Griffiths et al., 1990; Swift & Tiplady, 1988). Decaffeinated coffee may acquire properties resulting in subjective alertness (Goldstein et al., 1969; Ratliff-Crain et al., 1989). The circumstances under which caffeine acts as a reinforcer appear to be more limited than classic drugs of abuse such as d-amphetamine or cocaine, but under certain conditions caffeine has found to function as a reinforcer (Griffiths, Bigelow & Liebson, 1986, 1989; Griffiths & Woodson, 1988a, 1988b; Stern et al., 1989). Evidence also suggests that decaffeinated coffee may acquire some reinforcing properties, as subjects "like" decaffeinated coffee more and will work harder to self-administer it than non-caffeinated placebo pills (Griffiths et al. 1989). Similarly, regular coffee drinkers who had been deprived of their morning coffee reported significantly less "desire" for coffee following decaffeinated coffee or caffeinated coffee than after non-caffeinated herbal tea (Ratliff-Crain et al., 1989)

Caffeine's effects on task performance are equivocal,

though it does appear to consistently improve performance of auditory vigilance tasks (Leiberman et al., 1987a, 1987b; Rosenthal et al., in press; Zwyghuizen-Doorenbos et al.,1990). In addition to evidence that decaffeinated coffee may have acquired subjective and reinforcing properties, it also appears that it may develop conditioned performance enhancing effects (Zwyghuizen-Doorenbos et al., 1990).

Problems with research to date.

Three major problems have emerged from the review of caffeine's and coffee's effects. First, the caffeine intake history (average caffeine consumed per day, years consuming caffeine) of subjects in these experiments is frequently not mentioned. It has been shown that response to caffeine in terms of subjective mood state and task performance may differ as a function of regular intake (Goldstein & Kaizer, 1969; Kuznicki & Turner, 1986). Some researchers refer to their subjects as "normal" caffeine consumer without any further information about typical daily intake (e.g. Swift & Triplady, 1988), while others fail to report any information about the regular caffeine consumption of subjects (e.g. Anderson & Revelle, 1982). Still others report vague ranges such as $\leq$250 mg per day, without providing details about how many subjects were essentially caffeine naive (e.g. Zwyghuizen-Doorenbos et al., 1990). The research conducted for this dissertation addressed this problem by recruiting a sample that represented the average coffee drinker (consuming 3-4 cups of coffee per

day), and by collecting individual information about patterns of coffee and caffeine use.

Second is the complicated problem of pre-session deprivation. Subjects in many of the described studies are instructed to abstain from all dietary sources of caffeine from one week to six hours prior to the experimental session (e.g. Revelle et al., 1980; Zwyghuizen-Doorenbos et al., 1990). As mentioned previously, onset of withdrawal symptoms generally emerge following 12 to 24 hours of abstinence in heavy users. In some cases, it is impossible to determine whether changes with caffeine are the result of the stimulating properties of caffeine, or its amelioration of withdrawal. One study that exemplifies this problem was conducted by Bruce and colleagues (1986). Subjects with a regular caffeine intake of 428 mg per day were deprived of all sources of caffeine for 24 hours prior to session onset. Caffeine was reported to decrease subjective tiredness and headache, and increase alertness in these subjects as compared to placebo, though these results were almost certainly due to a relief from withdrawal symptoms.

On the other hand, if subjects are not restricted from caffeine prior to the experimental session, it is difficult to determine what influence morning coffee consumption may have had on experimental findings (e.g. Stern et al., 1989; Swift & Tiplady, 1988). Short of evaluating subjects in both the non-deprived and deprived state, as done by Ratliff-Crain and colleagues (1989), the optimal procedure requires

evaluating regular intake of subjects, measuring potential withdrawal symptoms, and restricting caffeine for a minimum amount of time pre-session. This study recruited coffee drinkers who regularly consumed 3 to 4 cups of coffee per day, and caffeine intake was restricted from midnight on the evening prior to the session. Incidence of headache, negative affect and lethargy was evaluated to examine potential withdrawal symptoms. In addition, a non-coffee drinking control group was included, and comparisons between this group and the coffee drinkers on the subjective and behavioral measures allowed for an examination of the influence of caffeine deprivation.

Finally, a number of researchers use decaffeinated coffee as the vehicle for caffeine administration without the use of other, non-coffee controls (e.g. Goldstein et al., 1965; Griffiths et al., 1986; Rosenthal et al., in press; Zwyghuizen-Doorenbos et al.,1990). Some of the research presented in this thesis has suggested that coffee may have the capacity to influence psychological and behavioral outcomes independently of caffeine (Goldstein, et al., 1969; Griffiths et al., 1989; Ratliff-Crain et al., 1989; Rozin et al., 1984; Zwyghuizen-Doorenbos et al., 1990). Marlatt and colleagues (Donovan & Marlatt, 1980; Marlatt, Demming & Reid, 1973; Marlatt & Rosenow, 1980; Rosenow & Marlatt, 1981) have discussed the importance of separating subject's expectations about drug effects from the actual pharmacological effects of a drug by employing a "balanced placebo" design. These

researchers have used this design in alcohol research, crossing subject's beliefs about the alcohol content of the experimental beverage with actual alcohol content of the beverage. In a study of alcohol self-administration using both alcoholics and social drinkers, the instructional set accompanying the beverage (whether subjects were led to believe that the beverage did or did not contain alcohol) predicted amount of beverage consumed, while actual alcohol content of beverage did not (Marlatt, et al., 1973). Both alcoholics and social drinkers drank about twice as much of the experimental beverage when they believed it contained alcohol regardless of the actual alcohol content of the beverage. In a review of the alcohol literature using "balanced placebo" designs, Marlatt and Rosenow (1980) concluded that belief that alcohol had been consumed had a more powerful influence than actual alcohol intake on measures of aggressiveness, social anxiety, sexual arousal and craving for alcohol.

Like consumers of alcohol, coffee drinkers may come to expect that coffee will affect them in a particular way. Only two studies have been published that have directly examined the influence of caffeine related expectancies, and neither of these actually administered caffeine (Christensen, White, Krietsch & Steele, 1990; Kirsch & Weixel, 1988). In the Christensen et al. (1990) study, undergraduates (regular caffeine intake not reported) were given a pill and told that it was caffeine. Half were told that caffeine produces

alertness, euphoria, clearer flow of thought, nervousness, internal trembling and sleeplessness. The other half were not given any information regarding caffeine's effects. Forty-five minutes after receiving the placebo, subjects were given a 12 item questionnaire assessing symptoms related to caffeine ingestion.

Not surprisingly, the subjects given the information regarding the pill's effects were significantly more likely to report these effects than subjects not given the information. Unfortunately, the potent demand characteristics of the procedure used in this study preclude meaningful interpretation of the results. Subjects simply reported what they were told, and it is equally likely that the undergraduates involved in the study would have reported itchy feet and hot flashes had they been told that the pill would produce these effects. No attempt was made to check whether or not subjects actually believed that the pills contained caffeine. Regretfully, the methodological problems of the Christensen et al. (1990) research limit its contribution to the understanding of the role of expectancy in response to caffeine.

Another study examined response to decaffeinated coffee with differing instructional sets (Kirsch & Weixel, 1988). Undergraduates with a mean intake of 3.2 cups of coffee per day (range not reported) served as subjects in this study. Half of the subjects were told that the coffee was either caffeinated or decaffeinated, and half were told that

the coffee was caffeinated. Response to the decaffeinated coffee varied depending upon the information provided. Those told that the coffee was caffeinated showed some evidence of increased alertness, tension and systolic blood pressure relative to baseline, while those who were "blind" to the caffeine content did not show meaningful changes from baseline. A number of performance measures, including digit span, symbol substitution, reaction time and rotor pursuit, failed to show any differences between the groups. The authors argue that instructions given with the administration of a placebo may influence response, and use their results to advocate the use of the Marlatt and Rosenow (1980) balanced placebo design in psychopharmacological research.

Expectations or conditioned responses may lead some studies to fail to find caffeine-placebo differences because the placebo (decaffeinated coffee) is producing effects in the same direction as the caffeinated coffee (e.g. Goldstein et al., 1965b). In order to separate the effects of caffeine from the effects of coffee, the research conducted for this dissertation involved the administration of coffee with and without caffeine, and alternatively, caffeine with and without coffee. This procedure is different from the "crossed placebo" design suggested by Marlatt (see Rosenow & Marlatt, 1981), as they suggest an identical vehicle for all four conditions (believe alcohol/alcohol; believe alcohol/no alcohol; believe no alcohol/alcohol; and believe no alcohol/no alcohol). While this procedure allows for the examination of

expectations independent of drug intake, it does not allow for the separate examination of vehicle effects that are not the result of expectancy. Specifically, the examination of non-cognitively mediated conditioned effects cannot be examined using the "balanced placebo" design as proposed by Marlatt (Donovan & Marlatt, 1980; Marlatt et al., 1973; Marlatt & Rosenow, 1980; Rosenow & Marlatt, 1981).

Does coffee have actions beyond those of caffeine?

As is mentioned above, there is some evidence that coffee may acquire some of caffeine's subjective and behavioral effects - i.e. through a repeated association with caffeine, coffee may come to act as a conditioned stimulus, eliciting a conditioned response similar to the unconditioned response seen following caffeine administration. Briefly, as Pavlov (1927) suggested more than 60 years ago, when a neutral stimulus is repeatedly paired with an unconditioned stimulus (UCS -a stimulus capable of eliciting a characteristic [unconditioned] response, the UCR), the neutral stimulus may come to elicit responses similar to those elicited by the unconditioned stimulus. The neutral stimulus is then referred to as the conditioned stimulus (CS), and the response it elicits is called the conditioned response (CR). This process is referred to as stimulus substitution, as the previously neutral CS comes to substitute for the UCS.

In addition to direct, stimulus substitution type conditioning, evidence has also emerged suggesting that

conditioned stimuli may elicit responses in the opposite direction of the UCS termed opponent processes or conditioned compensatory responses (Siegel, 1979; Solomon, 1980). This opponent process/ compensatory conditioning has been used as a model for explaining drug tolerance, proposing that the CR gradually comes to counteract the UCR and thus observable drug effects are diminished with chronic administration (Goudie & Demellweek, 1986; Siegel, 1975). For example, Siegel (1975) has reported that animals that have developed tolerance to morphine's analgesic effect (as measured by paw-lick latency following hot plate exposure) are hypersensitive when exposed to drug-predictive conditions but injected with placebo. It is beyond the scope of this dissertation to provide a detailed review of conditioning factors in drug use, dependence and tolerance (see Barrett & Witkin, 1986; Childress, McClelland & O'Brien, 1986; Eikelboom & Stewert, 1982; Goudie & Demellweek, 1986; and Stewert, deWit & Eikelboom, 1984 for reviews). Examples will, however, be noted as necessary to support the hypothesis that coffee may develop some of the properties of caffeine.

Research has shown that some opiate addicts will report a "high" following self-administration of saline in a naturalistic setting with the regular injection rituals (e.g. tourniquet, music) (Levine, 1974; O'Brien, Chaddock, Woody & Greenstein, 1974). Physiological response, in the form of pupillary constriction, has also been reported following the self-injection by opiate addicts of saline, though the author

notes that this response was never to the degree as that seen with opiate injection (O'Brien, 1975).

Direct conditioning effects have been reported less frequently for stimulants. Eikelboom and Stewart (1981) reported that rats given a saline injection in an environment previously paired with amphetamine injection showed conditioned hyperthermia compared to rats given saline in other non-drug related environments. Barr and colleagues (1983) have shown that the hyperactivity associated with cocaine injection can be classically conditioned in rats.

Several studies have directly examined the conditioning properties of caffeine in animals (Herz & Beninger, 1987; Steigerwald, Rusiniak, Eckel & O'Regan, 1989). Herz and Beninger (1987) examined environment-specific conditioning in rats with various doses of caffeine or amphetamine. During the conditioning part of the study, animals were given an injection of either caffeine (0.1, 1.0, 10.0 or 30.0 mg/kg), amphetamine (0.1, 0.5, 1.0, 5.0 mg/kg) or saline and placed in an activity monitor for 60 minutes. Animals receiving drug were given saline injections when returned to the home cage, and animals receiving saline prior to the activity monitor were injected with drug when returned to the home cage (all doses were represented). This home cage injection insured that activity examined on test (no-drug) days would not simply be the result of previous drug exposure, but instead the result of the previous association between drug and the activity environment.

Activity on test (no-drug) days revealed a dose response conditioned effect for amphetamine: subjects with a history of association between amphetamine and the activity monitor showed increased activity when placed in the monitor without amphetamine relative to saline controls and animals that had received amphetamine in the home cage. This activity was higher in animals that had previously received the higher doses of amphetamine (0.5, 1.0, 5.0) preceding the activity environment. The results for caffeine were less straightforward, due to a pronounced hypoactivity that occurred 23 hours post caffeine (suggested to be caffeine withdrawal). Subjects that had previous experience with caffeine in the test environment showed significantly less hypoactivity than those previously given caffeine in the home cage, and the authors conclude that conditioning was able to partially counteract effects of the 23 hour post caffeine hypoactivity.

Steigerwald and colleagues (1989) examined the aversive conditioning properties of caffeine in rats. In a series of experiments, varying doses of caffeine (1.25, 5.0 or 20.0 mg/kg) were given in association with either taste or place cues. Conditioned taste and place aversions developed when the stimulus had been paired with the highest dose of caffeine.

Findings from the Herz and Beninger (1987) and Steigerwald et al. (1989) suggest that a stimulus previously associated with caffeine may come to elicit responses similar to those produced by caffeine. Some recent animal research

has focused on caffeine's ability to influence to acquisition or extinction of conditioned responding to shock or apomorphine related cues (Carey, 1990a, 1990b; Winsky & Harvey, 1987). Caffeine alone was not found to influence the acquisition of conditioned response to a shock related cue, though it did antagonize the disruptive effects that an adenosine antagonist (L-PIA) had on acquisition (Winsky & Harvey, 1987). Caffeine has also been found to reinstate an extinguished response to an apomorphine related cue (Carey, 1990a, 1990b). While these studies do not bear direct relevance to the conditioning properties of caffeine, they may offer some clues to the mechanisms involved in conditioned drug responding.

Only one study has been reported that exclusively examines conditioning factors associated with caffeine in humans (Rozin et al. 1984). Rozin and colleagues (1984) claim that caffeine's salivation-inducing effects show conditioned opposition following administration of decaffeinated coffee, while the subjective alerting effects of caffeine show evidence of direct conditioning following decaffeinated coffee. Twenty-four regular coffee drinkers (range 2 to 11 cups per day) participated in four experimental sessions. Subjects were deprived from all food and beverages for two hours prior to the sessions. Caffeine content (placebo versus 200 mg) was crossed with beverage (coffee versus apple juice), and all subjects were exposed to the resulting four conditions. Salivation was measured during a 10 minute

baseline, and then once every 5 minutes post-beverage. Subjective alertness was measured via an adjective checklist, administered pre-beverage and 30 minutes after beverage consumption.

Apple juice turned out to be an unfortunate choice as a control beverage in a study using salivation as a dependent measure - both the caffeinated and non-caffeinated apple juice dramatically increased salivation rate. Tolerance to the saliva-eliciting properties of caffeinated coffee is reported. A significant decrease in salivation was seen following administration of the decaffeinated coffee, and the authors suggest conditioned opposition to caffeine's salivary enhancement. Subjective mood assessment revealed that caffeine produced significantly more wakefulness than placebo (lactose), and that coffee produced significantly more wakefulness than apple-juice (caffeine by beverage interaction term not reported). Post hoc analyses or planned comparisons, necessary to determine whether the decaffeinated coffee produced wakefulness that was significantly different from the caffeinated or non-caffeinated apple juice, are not reported.

A number of other studies discussed in this dissertation have suggested that coffee may elicit caffeine-like responses in the absence of caffeine in humans (Goldstein, et al., 1969; Griffiths et al., 1989; Kirsch & Weixel, 1988; Ratliff-Crain et al., 1989; Zwyghuizen-Doorenbos et al., 1990). The most recent of these found that following two days of exposure to caffeinated coffee, subjects given

decaffeinated coffee did significantly better on an auditory vigilance task, and showed significantly longer sleep latencies (objectively measured) than subjects who had been maintained on decaffeinated coffee for the duration of the experiment (Zwyghuizen-Doorenbos et al., 1990).

Smits et al., (1985a, 1985b) reported a direct cardiovascular response to decaffeinated coffee, i.e. regular coffee drinkers showed significant increases in diastolic blood pressure after decaffeinated coffee. Kirsch and Weixel (1988) found that decaffeinated coffee was associated with an increase in systolic blood pressure, but only when subjects were told that the coffee was caffeinated. Ratliff-Crain et al. (1989) found no evidence for conditioned blood pressure or heart rate responses following decaffeinated coffee. Coffee may serve as a conditioned stimuli to caffeine, producing conditioned responses in subjective alertness, task performance, and/or cardiovascular response. In order to determine the conditioned effects of coffee, repeated pairing of caffeine and coffee would need to be presented in a controlled setting, followed by the presentation of coffee alone. Ideally, conditioned responses to the coffee would be observed and recorded, followed by an eventual decline with extinction. Without the demonstration of extinction in the absence of continued CS-UCS pairing, it is impossible to determine whether or not the effects of coffee are due to conditioning, expectancy, or alternatively to some other undetermined ingredient in coffee (e.g. Boublik et al., 1983).

Thus, this research was not designed to establish whether or not coffee serves as a conditioned stimulus. Instead, its goal was to examine the broader question of whether or not coffee has actions independent of its caffeine content, and additionally, whether caffeine in coffee acts differently than caffeine provided in a novel beverage.

Research objectives and overview

The primary objectives of this study were to determine 1) if decaffeinated coffee has effects on task performance and/or subjective reports of mood and somatic symptoms in regular coffee drinkers and 2) if caffeine administered in coffee affects task performance and subjective response differently than caffeine administered in a novel, non-coffee beverage. Caffeine content (0 vs. 200mg) was crossed with beverage (decaffeinated coffee vs. non-caffeinated herbal tea), yielding a 2 X 2 factorial design. For the purpose of this study, regular coffee drinkers were those who reported an average daily intake of 15 to 25 ounces of coffee per day (based on national average of 3-4 five ounce cups per day, International Coffee Organization, 1982), and had been drinking coffee for at least one year. In addition, a non-coffee drinking control group was examined to determine whether or not individuals who refrain from regular caffeine intake differed from regular coffee drinkers with regard to task performance, mood or symptom reporting.

Subjects participated in a single two and a half hour

session. All sessions were conducted in the morning, starting between 6 and 10 a.m. Prior to the session subjects were asked to abstain from a number of food items, including but not limited to all common dietary sources of caffeine, from midnight on the night before the session. This was done to insure that normal dietary caffeine would not influence the experimental procedures. Coffee drinking subjects were randomly assigned to one of the four experimental conditions: 1) decaffeinated coffee with 200mg added caffeine, 2) decaffeinated coffee with added lactose (placebo), 3) non-caffeinated herbal tea with 200mg added caffeine and 4) non-caffeinated herbal tea with added lactose. The purpose of the lactose was to enable the experimenter to remain blind to the caffeine manipulation. All of the non-coffee drinking control subjects were assigned to the non-caffeinated tea condition with no added caffeine.

Participants given coffee were informed that they were receiving regular caffeinated coffee, and those given herbal tea were told that they were receiving non-caffeinated herbal tea. Vials of caffeine or lactose were coded in advance by an experimental assistant to insure that all parties to the experimental session were blind to the caffeine content of the experimental beverages. The primary dependent measures were the assessments of subjective mood and symptoms, and task performance. Blood pressure and heart rate were monitored throughout the session, and the resulting physiological data was used to confirm the caffeine manipulation. Responses to

items asking subjects to estimate the caffeine content of the experimental beverage were examined to confirm that subjects believed the information given regarding the beverage's caffeine content.

Hypotheses.

As previously noted, the history of repeated association between coffee and caffeine in regular coffee drinkers, along with the cultural or social value awarded coffee and the possibility of other active ingredients contained therein, suggest that coffee may have subjective and behavioral effects even in the absence of pharmacologically active doses of caffeine. Marlatt and Rosenow (1980) have reported that with alcoholics and social drinkers, the belief or expectation that a drink contains alcohol is a more powerful predictor of mood and behavioral response to the beverage than the actual alcohol content of the drink. Likewise, coffee drinkers may expect certain sensations when they drink coffee, and these expectations may have a significant influence on affect and behavior.

Also, caffeine administered in coffee may elicit a different pattern of responses than caffeine administered independently of coffee. While research has suggested that people respond differently to caffeinated coffee verses decaffeinated coffee, and has referred to those differences as the effects of caffeine (Foreman et al., 1989; Goldstein et al., 1965a, 1965b, Goldstein et al., 1969; Rosenthal et al., in press; Smits et al., 1985a, 1985b; Zwyghuizen-

Doorenbos et al., 1990) no research to date has compared subjective and behavioral response to caffeine presented in coffee versus caffeine presented in a non-coffee control beverage.

By administering decaffeinated coffee with and without added caffeine, and caffeine with and without coffee, the research presented in this dissertation permits the examination of the individual subjective and behavioral effects of coffee and caffeine. Based on evidence presented in the preceding literature review, the following outcomes were predicted:

1. Subjects receiving a beverage with caffeine would exhibit better task performance (faster reaction times and fewer errors on an auditory vigilance task), more positive mood states and more subjective alertness (as measured by the Profile of Mood States, McNair et al., 1971), and fewer signs of withdrawal related somatic complaints (as measured by the caffeine withdrawal sensitive Feelings and Mood questionnaire adapted from Ratliff-Crain et al., 1989) than subjects receiving a beverage without added caffeine. Support for a predicted main effect for caffeine on the primary dependent measures comes from the research presented above that caffeine consistently enhances performance on auditory vigilance tasks (Leiberman et al., 1987a, 1987b, Rosenthal et al., in press; and Zwyghuizen-

Doorenbos et al., 1990), that it tends to be related to subjective alertness and positive affect (Bruce et al., 1986; Chait & Johanson, 1986; Goldstein et al., 1969; Griffiths et al., 1990; Swift & Tiplady, 1988), and that it alleviates withdrawal symptoms that may be seen with caffeine abstinence (Griffiths & Woodson, 1988a).

2. It was predicted that performance on the auditory vigilance task, subjective alertness and positive mood would be enhanced by the decaffeinated coffee with no added caffeine relative to the non-caffeinated herbal tea with no added caffeine. Evidence supporting this hypothesis comes from the findings of Zwyghuizen-Doorenbos et al. (1990) that suggest that coffee may acquire some of caffeine's performance enhancing effects, and various other research findings that suggest that coffee may elicit caffeine-like subjective responses regardless of caffeine content (Goldstein et al., 1969; Griffiths et al., 1989; Ratliff-Crain et al., 1989)

3. It was hypothesized that caffeine presented in a non-coffee beverage would have a more potent effect on task performance and subjective response than caffeine presented in coffee. This prediction was based on evidence that some degree of tolerance develops to caffeine's performance enhancing effect (Zwyghuizen-Doorenbos et al., 1990). Thus

separating caffeine ingestion from the taste and smell of stimuli previously associated with caffeine intake may restore its full effects in regular coffee drinkers. Research has shown that drug tolerance shows contextual or situational specificity - without stimuli previously paired with drug administration tolerance will not be observed (Dafters & Anderson, 1982, Goudie & Demellweek, 1986). For example, human subjects have been shown to develop tolerance to the tachycardia produced by alcohol ingestion, yet when alcohol is administered to tolerant subjects in an environment previously associated with placebo the alcohol induced tachycardia effect is fully restored (Dafters & Anderson, 1982).

Predictions involving the non-coffee drinking control group were not as direct. Justification for the inclusion of this non-coffee drinking group was based primarily on results from a study that examined relaxation in smokers and non-smokers (Silverstein, 1982). Thirty smokers and 10 non-smokers completed the study. Subjects were exposed to a number of shocks that increased in intensity, and they were told to inform the experimenter of 1) when they could first feel the shocks, 2) when the shocks became painful and, 3) when the shocks became unbearable. Immediately prior to shock onset, one third of the smokers were offered a high nicotine yield cigarette, one third were offered a low nicotine yield

cigarette, and one third were not permitted to smoke. Smokers in the smoking conditions were permitted to smoke prior to and in-between shock administrations. Non-smokers were not provided with the opportunity to smoke.

Silverstein hypothesized that if nicotine had a relaxing effect, smokers in the high yield nicotine condition would be able to endure greater intensities of shock than the three other groups. The smoking subjects in the high nicotine yield smoking group were able to endure greater shock intensities than either the low nicotine yield smokers or the deprived smokers. Their shock endurance threshold did not differ, however, from that of the non-smokers. The results suggest that nicotine does not calm or relax the smoker, but instead brings them to the level of relaxation that they would have maintained had they never started smoking.

In the present research, it was possible that caffeine provided to regular coffee drinkers may not actually enhance subjective mood and task performance, but instead bring mood and performance to a level that it would have been had coffee drinking never been initiated. Inclusion of the non-coffee drinking control subjects allowed for the evaluation of this possibility.

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Main Dependent Measures

1. Task Performance: Response Latency

False Positives

Errors of Omission

2. Subjective Response: Profile of Mood States (POMS)
(McNair, Lorr & Droppelman, 1971)
scales: Tension, Depression, Anger, Vigor, Fatigue, Confusion.

Feelings and Mood Questionnaire
(adapted from Ratliff-Crain, O'Keeffe & Baum, 1989)
scales: Relaxed, Lethargic, Headache, Need a stimulant.

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Health consequences of coffee/caffeine

Coronary heart disease

Cancer: renal, bladder, pancreatic, ovarian, breast.

Complications in pregnancy

Caffeine intoxication/ caffeinism

Other: Diabetes mellitus, immune function, infertility, G.I .disturbances, benign breast disease.

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Coffee and CHD

Klatsky and collegues studied 101,774 men and women over an eight year period. After controlling for other risk factors, coffee intake of >4 cups/day was associated with a significant increase in myocardial infarction.

CONCLUSION

" Persons at risk of myocardial infarction should consider limitation of coffee intake" (Klatsky, Freidman & Armstrong, 1990)

Grobbee and collegues studied 45,589 men over a two year period, and found no association between caffeinated coffee intake and CHD. Heavy consumption of decaffeinated coffee was related to CHD.

CONCLUSION

"Caffeinated coffee as it is currently consumed by men in the United States causes no substantial increase in the risk of coronary heart disease or stroke" (Grobbee et al., 1990)

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Conclusions:

1. Caffeine was associated with more positive mood and more subjective alertness than no caffeine. Caffeine was also associated with better task performance over time than no caffeine.

2. Coffee had some measurable effects independent of caffeine. Decaffeinated coffee was associated with better task performance over time relative to non-caffeinated herbal tea. Decaffeinated coffee was also associated with less headache and desire for a stimulant than non-caffeinated herbal tea.

3. Caffeine presented in a non-coffee beverage did not have more potent effects than caffeine presented in coffee.

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Title

Coffee versus Caffeine: Effects on subjective and behavioral measures of alertness.

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Manipulation Checks

1. Caffeine Estimates
2. Physiological Response
3. Beverage Questionnaires

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Subject Characteristics

Age	34 years (20 - 48)
Years drinking coffee	16.8 (3 - 37)
Average daily consumption (oz. / day)	17.4 ounces (9 - 30)
Education	16 years (12 - 17+)

Methods

Subjects

Subjects for this study were 48 coffee drinkers (29 women, 19 men) and 10 non-coffee drinkers (5 women, 5 men). Subjects were recruited through local newspaper advertisements and bulletin board notices. These advertisements recruited healthy non smokers between the ages of 18 and 45 for participation in a study of the effects of common foods and beverages on mood and performance. Telephone screening was conducted on all respondents, soliciting information on age, health status, smoking history, prescription, over the counter and illicit drug use, coffee (caffeinated and decaffeinated), tea and soft drink use, and alcohol use. For the coffee drinkers, individuals who reported drinking between 15 and 25 ounces of coffee per day, and who had been drinking caffeinated coffee regularly for at least 1 year were eligible for participation. Eligibility for the coffee drinking experimental groups also required no extensive history of decaffeinated coffee use, and consumption of no more than 100mg of caffeine per day from other sources (noted in Table 1). No regular caffeinated coffee use and intake of no more than 100 mg caffeine per day from all sources was required for eligibility in the non-coffee drinking group.

Cigarette smokers, those with a history of alcohol abuse or liver disease, and women who were pregnant or taking oral contraceptives were ineligible as these factors have been

shown to have significant effects on caffeine metabolism (Parsons & Neims, 1978; Parsons et al., 1979; Patwardhan et al., 1980; Statland & Demas, 1980). Recruitment did not require equal numbers of men and women, as there is no evidence that caffeine or coffee affect men or women differently beyond the influence of the above mentioned factors. Subjects had to be in good health, with no regular drug use (either prescription, over the counter, or illicit) and no known hearing disabilities (due to the auditory nature of the task) to be considered for participation. Characteristics of the resulting subject sample are described in the results section. Subjects were paid $25 for participation in the study.

Measures

Questionnaires were administered to assess mood, subjective alertness, somatic symptoms indicative of caffeine withdrawal, caffeine history, food and beverage consumption pre-session, subjective response to the task and response to the experimental beverage. Also, since scores on the Jenkins Activity Survey for Health Prediction (JAS) (Jenkins, Rosenman & Zyzanski, 1972) have been found to be related to performance on reaction time tasks of long duration (Glass, 1977), this instrument was given during the session.

Mood

The Profile of Mood States (POMS, McNair et al., 1971) was used to evaluate mood as it has previously been found to

be sensitive to the effects of caffeine and caffeine withdrawal (Chait & Griffiths, 1983; Griffiths, Bigelow & Liebson, 1986; Griffiths & Woodson, 1988c). The POMS is a standardized, 65-item questionnaire with six empirically derived scales: Tension; Depression; Anger; Vigor; Fatigue; and Confusion. Subjects rated on a Likert-type scale the degree to which they were experiencing the moods and feelings expressed by the 65 adjectives.

Mood and somatic symptoms were also examined using a modified version of the Feelings and Mood questionnaire developed by Ratliff-Crain et al. (1989). This 18-item questionnaire asks subjects to report on a 7-point scale ("not at all" to "extremely") how much they are experiencing certain moods, physical discomforts, desire for coffee or something to "jazz" them up, and desire for aspirin.

Task performance

The auditory vigilance task used in this study was the same as that used by Rosenthal et al., (in press) and Zwyghuizen-Doorenbos et al.,(1990), except that it has been modified for use from a Zenith portable personal computer. As noted previously, caffeine has consistently been found to enhance performance on auditory vigilance tasks (Leiberman et al., 1987a, 1987b; Rosenthal et al., in press; Zwyghuizen-Doorenbos et al.,1990). Following a brief, three minute practice version of the task, subjects performed an initial 10 minute version of the task that served as the baseline

performance measure. Following beverage administration, the full 40 minute task was administered, with scoring broken down into four 10 minute blocks. Throughout the task, 900hz "background" tones were presented for 250 milliseconds once every three seconds. "Signal" tones of 450 milliseconds (also 900hz) occured quasi-randomly, with 12 "signal" tones presented every ten minutes. Order of "signal" presentations within the "background" tones was randomized from the random number generator within the computer, so that each 10 minute block and each 40 minute task has a different random sequence of "background" to "signal" tones.

Subjects were provided with standard, written instructions that were read aloud by the experimenter. They were instructed to rest their index finger of their right hand lightly on a key marked with a smiley face (☺), and to depress the key as quickly as possible after they believed they had heard one of the longer "signal" tones. Subject's key presses were confirmed by a different toned "beep" of the computer. Latency to key press, false positives (presses in the absence of a "signal" tone), and errors of omission were recorded for each 10 minute block.

Extraneous sources of variance

A "food today" questionnaire was given at the beginning of the session, and subjects were asked to list all foods, beverages and drugs consumed in the 12 hour period preceding the session. Caffeine history was assessed using

the "diet inventory", a questionnaire soliciting information about diet and exercise. Included on the "diet inventory" are items assessing years drinking coffee, regular daily coffee intake, and regular daily caffeine intake from a variety of sources including coffee, tea, soft drinks, chocolate, and over the counter medications.

The Jenkins Activity Survey (Jenkins, Rosenman & Zyzanski, 1972), a 54 item scale used in the assessment of the Type A behavior pattern, was administered. Though this questionnaire is no longer the preferred instrument for measurement of the Type A behavior pattern (more objective assessments are now favored), previous research has shown that individuals scoring high on the Pattern A dimension of this scale tend to become impatient, restless and distracted with tasks similar to the auditory vigilance task that was used in this experiment (Glass, 1977). It was therefore important to identify this potentially confounding characteristic in advance so that the variance it contributed to the task performance measures could be measured and statistically controlled if necessary.

Following task presentation a task questionnaire was given that required subjects to rate separately how difficult, challenging, boring, frustrating and enjoyable they found the task on a 7-point scale of "not at all" to "extremely". Subjects were also be asked how much experience they have had with similar tasks. Two versions of a beverage questionnaire were delivered, one immediately following beverage consumption

and one at the end of the experimental session. The first asked subjects to list what beverage they consumed during the session, and to rate (again on a 7-point scale) how much they liked the beverage, how good the beverage tasted, how bitter is tasted, how hot it was, how strong it was, and how difficult it was to drink the beverage in the time allowed. At the end of this questionnaire subjects were asked to recall what the experimenter had told them about the caffeine content of the beverage (was it caffeinated or non-caffeinated?), and asked to give their personal estimate of the caffeine content of the beverage consumed during the session by marking a visual analog line. The caffeine content of different popular beverages (herb tea, instant decaffeinated coffee, cola, brewed coffee, strong brewed coffee) was noted at the appropriate corresponding places on the line to serve as standards for comparison. The second beverage questionnaire was given at the end of the session, and subjects were again asked to recall what the experimenter told them about the caffeine content of the beverage. They were also asked once again to give their personal estimate of the caffeine content of the beverage by marking the visual analog line (described above). This version of the beverage questionnaire also asked subjects to rate separately the degree to which information from the experimenter and feelings produced by the beverage contributed to their estimate of caffeine content.

Experimental beverages.

The coffee beverage was Maxwell House brand French Roast decaffeinated coffee prepared to manufacturer's specifications using 2 tablespoons of ground coffee and 12 fluid ounces of water. Ground coffee brewed with an automatic drip coffee maker was used in order to approximate the visual and aromatic stimuli generally associated with coffee drinking. Pre-session taste testing with pilot subjects revealed that the decaffeinated coffee with 200 mg added caffeine could not be reliably discriminated from the decaffeinated coffee with added lactose when the coffee was prepared in the above mentioned fashion.

The non-coffee beverage was Lipton cinnamon-apple herbal tea, containing no caffeine, brewed stronger than manufacturer's specifications using three tea bags for 12 fluid ounces of water. Pre-session taste testing with this beverage revealed that subjects could discriminate the tea with 200 mg added caffeine from the tea with added lactose at better than chance levels. When one gram of non-nutritive sweetener (i.e. Sweet-n-low) was added to this preparation, reliable discrimination was no longer possible. Thus, the herbal tea was always prepared using one gram on non-nutritive sweetener. This beverage was poured from an opaque "hot pot" type vessel in order to separate it from the visual stimuli associated with coffee intake.

Twenty-four vials containing 200mg caffeine were prepared in advance and coded with subject numbers by an

experimental assistant. Similarly, 24 vials containing powdered lactose of a quantity visually similar to the 200mg caffeine were also prepared in advance and coded. This coding procedure enabled the experimenter (as well as the subject) to remain blind to the caffeine manipulation. Contents of the vial were poured into a coffee cup prior to the session and thus without the subjects' knowledge. Non-dairy creamer (Cremora) and non-nutritive sweetener (Sweet-n-low) were available for the subjects to add to their beverage if they wished.

Procedures

Subjects who meet the criteria outlined in the "subjects" section above were scheduled for the experimental session, and mailed an instruction sheet listing foods and beverages that were to be avoided from midnight on the night before the session. The list of substances to be avoided included alcohol of any type, coffee, tea and soft drinks (regular or decaffeinated), chocolate, and ice cream. Ice cream was included to minimize the salience of the caffeine containing beverages on the list. Directions to the laboratory, and scheduled date and time were also noted on the instruction sheet. The evening before the session subjects were telephoned to confirm the appointment and reminded to follow the guidelines presented on the instruction sheet.

Experimental sessions were conducted in a comfortable, sound attenuated room. Upon arrival to the laboratory (always

between the hours of 6 and 10 a.m.) subjects were given a brief description of the study, and informed consent was obtained. The description of the study read:

> "As you were told over the phone, the purpose of this study is to examine the effects of common foods and beverages on mood and performance. The food or beverage that you receive may contain substances such as proteins, amino acids, vitamins, caffeine or sweeteners. These substances will not exceed what is normally found in common dietary items. You will be asked to complete some questionnaires that will let us know how you are feeling and provide us with some general background information. You will also be asked to perform some tasks that you may find challenging, but not unpleasant or stressful. Finally, your blood pressure and heart rate will be monitored occasionally. I will place a cuff around your arm and inflate it every couple of minutes - the procedure is like having your blood pressure taken in a doctor's office. Do you have any questions?"

After signing the informed consent, subjects were asked to list all foods, beverages, and medications taken from midnight the previous night on the "food today" questionnaire. Responses were checked for caffeine abstinence: all subjects complied with the pre-experimental instructions. A blood pressure cuff was then placed around their non-preferred arm, and blood pressure and pulse were measured once every three minutes. Blood pressure was measured on a standard mercury

column, with the blood pressure cuff being initially inflated to 180 mmHg to occlude blood flow in the brachial artery. A stethoscope was placed over the artery and Korotkoff sounds were monitored as pressure in the cuff was deflated. For subsequent blood pressure measurements the cuff was inflated to 20 mmHg higher that the last systolic blood pressure to allow for minimal subject discomfort. Heart rate was also measured on the non-preferred arm at the wrist. Beats were counted for a measured fifteen second interval, and then multiplied by four to approximate a measure of beats per minute.

Fifteen minutes of resting blood pressure were monitored, with the last two measurements recorded as baseline. Following the 15 minute rest period, the POMS, Feelings and Mood questionnaire, JAS, and Diet Inventory were given. Instructions for the POMS and Feelings and Mood questionnaire asked subjects to let their responses reflect how they were feeling at that moment. Subjects were then given instructions for the auditory vigilance task, and following a short, three minute demonstration/practice test the 10 minute version of the task was started. Following the task subjects were given the task response questionnaire.

The beverage was prepared prior to the 10 minute task, in order to let it cool to a temperature that permitted comfortable consumption. Following the baseline task, the beverage was provided with standard written instructions that were read aloud by the experimenter. Subjects were told that

they would have ten minutes to drink beverage, and that because it was important that everyone drink the same amount they needed to finish the entire contents of the cup. Subjects given coffee were told that the coffee was regular, caffeinated coffee and subjects given the herbal tea were told that their beverage was non-caffeinated, herbal tea. They were also told to pay attention to how they liked the beverage and how it tasted, because they would be asked to answer some questions about the beverage after they had finished it. Subjects were free to add non-dairy creamer and non-nutritive sweetener as they wished, and use of these substances was recorded. If subjects had not finished the beverage in the 10 minutes allowed, the experimenter informed them that the 10 minutes was up and stood beside them in a way that non-verbally encouraged them to finish up quickly. Beverage Questionnaire A was given immediately following beverage consumption.

A thirty minute post beverage "rest" period followed to allow caffeine to approach peak plasma levels, during which subjects were required to work on a proofreading task. The proofreading task was administered with standard written instructions to focus attention away from physiological symptoms that may have provided information about the actual caffeine content of the beverage. Blood pressure and heart rate were measured once every three minutes during this 30 minute period.

Following the 30 minute proofreading task, subjects

were again given the POMS and Feelings and Mood questionnaire and instructed to fill them out for how they were feeling at that moment. Subjects were then given a mandatory restroom break to allow them to stretch and empty their bladders.

The 40 minute auditory vigilance task was then given. Following the task, subjects were asked to complete the task response questionnaire and Beverage Questionnaire B. After experimental procedures were completed the subject was asked verbally what they thought the caffeine content of their beverage was, and their response to this question was recorded. The experimenter then opened a sealed envelope prepared in advance by the experimental assistant. Inside the envelope was a well-folded slip of paper that revealed the actual caffeine content of the beverage. Debriefing included informing the subject of the actual caffeine content of the beverage. Subjects were then paid and thanked for participation. Sessions lasted approximately two and one half hours. An outline of the experimental procedure is presented in Table 2.

Results

Data Analyses

The hypotheses explored in this research focused on the effects of coffee and caffeine on various response outcomes. Baseline response levels were not of critical interest except as a basis for comparison and to assure comparability of groups before experimental treatment. For most of the analyses to be described, scores representing change from baseline were the data of primary importance. Baseline differences among groups were considered for background variables (e.g. age, education level, years drinking coffee, amount of coffee consumed per day), and for individual difference variables (e.g. sex, coffee drinking status, Type A behavior pattern scores).

Data from the physiological assessments and task performance were analyzed using a repeated measures multivariate analysis of covariance (MANCOVA). Baseline measures were entered as covariates, to statistically for variance contributed by baseline differences among subjects. Jennings (1987) has argued that multivariate analyses should be used with repeated measures designs when the measurements are taken near to one another in time, as such measurements are often highly correlated and thus may violate assumptions of sphericity that are made with univariate analyses. Beverage (herbal tea versus coffee) and caffeine content (0 versus 200mg caffeine) were entered as between subject factors, and time was entered as a within subjects factor.

For analyses of physiological response, change from baseline was assessed over time using a 2x2x5 design, with baseline entered as a covariate. The last two readings of the five baseline measurements were averaged to constitute the baseline reading. Thus the baseline measure represented an average of two resting blood pressures or heart rates after the subjects has been seated for over 10 minutes and had acclimated to the experimental setting and measurement procedure. The five post-beverage readings were obtained by collapsing the first and second, third and fourth, and so on through the ninth and tenth post-beverage measurements. The procedure of collapsing two blood pressure or heart rate measurements was used to reduce the variability that subtle changes in arm positioning or posture may have contributed to the individual measurements (Webster, Newham, Petrie & Lowell, 1984).

For analysis of task performance, change from baseline over time was examined using a 2x2x4 design, again with baseline entered as a covariate. Performance on the 40 minute post-beverage task was examined in four 10 minute intervals. Previous research has shown that performance on this type of vigilance task declines over time, therefore the task is typically analyzed in 10 minute intervals to allow for the examination of average performance over time (Rosenthal et al., in press; Zwyghuizen-Doorenbos et al, 1990).

Subjective response, measured by the POMS, the Feelings and Mood questionnaire, and the task questionnaire was also evaluated using change scores, using a 2x2 ANCOVA,

with baseline scores entered as covariates. Univariate analyses of variance (ANOVAs) were performed on baseline measures to determine whether or not there were baseline differences for sex on the primary dependent measures. Sex was also entered as a between subjects factor with experimental condition, and MANCOVAs were performed on change from baseline scores to evaluate possible sex x time and/or sex x condition x time interactions. A similar procedure for performance measures was used for Type A behavior pattern scores (using a median split to group subjects on the basis of scores on the Jenkins Activity Survey). Univariate ANOVAs were conducted on background variables such as age, years drinking coffee and amount of coffee consumed per day in order to examine the comparability of these variables among conditions. Differences among groups on responses to the beverage questionnaires were also evaluated using ANOVAs.

Planned comparisons were performed to evaluate Hypothesis 2; that those given decaffeinated coffee with no added caffeine would respond with more subjective alertness, better performance and fewer withdrawal related symptoms than those given non-caffeinated herbal tea with no added caffeine; and Hypothesis 3; that those given caffeine in a novel beverage (i.e. non-caffeinated herbal tea) would exhibit more alertness and better performance than those given caffeine presented in coffee. The MANCOVAs, ANCOVAs and ANOVAs, as well at the planned comparisons, were conducted using the Statistical Package for the Social Sciences - X (SPSS-X) data

analytic package (SPSS Inc., 1988).

Dunnett's (1955, 1964) method of comparing multiple treatments with a single control group, as described in Howell's Statistical Methods for Psychology (1982), was used to compare subjects in the caffeine naive control group with experimental subjects receiving the herbal tea, both with and without the added 200mg of caffeine. These comparisons were made to determine whether or not individuals who refrain from regular caffeine use were different from regular coffee drinkers with respect to the primary dependent measures. The non-coffee drinking controls were compared only with the coffee drinkers given herbal tea so that beverage consumed during the session was similar across these three groups. Baseline differences and differences over time were evaluated. In addition, since absolute values were of particular interest in the comparisons between non-coffee drinking controls and experimental subjects in the tea conditions (in order to evaluate whether or not caffeine actually enhances measurements relative to the controls), post-beverage measures for these groups were examined.

Finally, Multiple Regression/Correlation (MRC) analyses, as described by Cohen and Cohen (1983), were conducted on the primary dependent measures. Baseline, beverage (coffee versus herbal tea), caffeine (0 versus 200 mg), beverage x caffeine interaction, Type A status, and sex were entered hierarchically (in the above order) into the regression equations to evaluate the proportion of variance

(change in R^2) that each of these factors contributed to the total variance of the primary dependent variables. The beverage x caffeine interaction was coded as recommended by Cohen and Cohen (1983), in their discussion of interaction coding for factorial designs. Additionally, the contributions that Type A status and sex made to the variance in baseline measures of the primary dependent variables was examined, with hierarchical entry of Type A and sex, in that order. Hierarchical multiple regressions were conducted using the SPSS-X data analytic package (SPSS Inc., 1988).

Comparability of experimental groups.

No significant differences were found between groups for age, education, weight, height, amount of coffee consumed per day, years drinking coffee or food consumed pre-session. Subjects were an average of 34 years old (range 20-48), and most were college graduates (range 12 - 17+ years of education). Average weight was 150 pounds (range 110 to 230) and average height was 67.3 inches (range 60 to 74). The experimental subjects drank an average of 17.4 ounces of coffee per day (range 9-30), and had been drinking coffee for an average of 16.8 years (range 3-37). Of the 58 subjects, 34 were female and 24 were male. An attempt was made to evenly distribute sex across groups, and the following ratios resulted: the non-caffeinated herbal tea, caffeinated herbal tea, and decaffeinated coffee groups were each composed of 5 males and 7 females, the caffeinated coffee group of 4 males

and 8 females, and the non-coffee drinking controls were evenly split with 5 males and 5 females.

Manipulation checks

Both subjective and physiological manipulation checks were performed. Subject's beliefs about the caffeine content of their beverage were examined to insure that those receiving the herb tea really believed that the beverage was not caffeinated and that those receiving coffee actually thought that their beverage was caffeinated. Subjects were asked twice during the experimental session to estimate the caffeine content of their beverage. Beverage questionnaire A (BQA) was given to subjects immediately following the 10 minute beverage consumption period. At the bottom of BQA, subjects were asked to rate "how much caffeine your beverage contained" on a visual analog scale that provided examples of the caffeine content of common beverages. Beverage questionnaire B (BQB) was given at the end on the experimental session, and it asked subjects to rate "how much caffeine YOU THINK your beverage contained" on a visual analog scale, again with examples of the caffeine content of common beverages. Responses to these two items constituted the primary subjective manipulation checks, though responses to other items on the beverage questionnaires will also be considered in this section.

Blood pressure and heart rate were also examined to insure that subjects receiving caffeine were experiencing the increase in blood pressure and decrease in heart rate that are

characteristic of caffeine response by the time they began the post-beverage task (approximately 40 minutes post beverage). All analyses involving blood pressure and heart rate will be discussed in this section.

Caffeine estimates.

A significant main effect for beverage indicated that subjects receiving coffee during the session reported that their beverage contained significantly more caffeine than those receiving herbal tea. This difference was apparent when asked immediately after receiving the beverage on BQA, and, more importantly, when asked at the end of the session with emphasis placed on their own perception on BQB, $F(1,44)$ = 318.70 and 74.01 respectively, $ps<.001$ (See Table 3). No effects were seen for caffeine or the caffeine x beverage interaction. Estimates did not change significantly from BQA to BQB.

Analysis using hierarchical multiple regression, with entry of beverage, caffeine, and the beverage x caffeine interaction, in that order, revealed that beverage was responsible for 88 percent of the variance in caffeine estimates on BQA (change in R^2=.88), and 76 percent of the variance in estimates on BQB (change in R^2 = .76), $ps<.001$. Changes in R^2 for caffeine and the caffeine x beverage interaction were insignificant for both BQA and BQB. Comparisons between the non-coffee drinking control subjects with the experimental subjects receiving herbal tea showed no

significant differences among these groups for caffeine estimates on either BQA or BQB (see Table 3). Subjects in all three of the herbal tea conditions reported receiving comparable amounts of caffeine in their beverage.

Physiological Response

Significant main effects for caffeine were seen for heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), with MANCOVAs yielding a multivariate $F(1,43)= 6.02, p <.05$ for HR, $F(1,43)=31.01$, $p < .001$ for DBP, and $F(1,43)=36.96$, $p <.001$ for SBP (see Figure 1). Caffeine presented in either the coffee or the herbal tea significantly increased DBP and SBP and significantly decreased HR in this sample of regular coffee drinkers.

A caffeine x time interaction was found for SBP, $F(4,76) =3.55$, $p < .01$, with SBP differences between the caffeine and non-caffeine groups increasing substantially over time. No main effects on HR, SBP or DBP were found for beverage, nor were there any caffeine x beverage, beverage x time, or caffeine x beverage x time interactions.

These results show that consumption of the caffeinated beverages produced significant increases in SBP and DBP and significant decreases in HR relative to the non-caffeinated beverages. By the time subjects were to begin the post-beverage POMS, Feelings and Mood questionnaire, and auditory vigilance task, caffeine had produced marked hemodynamic changes.

Exploration of sex differences at baseline for HR, SBP and DBP by ANOVA showed significantly higher SBP and DBP for women at baseline as compared to men (*M* SBP for females = 110.21 mmHg, for males = 99.95 mmHg, $F(1,40)=67.46$, $p < .01$; *M* DBP for females = 75.05 mmHg, for males = 67.53 mmHg, $F(1,40)=8.04$, $p<.01$). There were no significant differences between males and females for baseline HR. With baseline entered as a covariate, analysis of change scores by way of MANCOVA showed no significant effects for sex, sex x condition or sex x condition x time interactions for SBP, DBP or HR.

Dunnett's test showed no baseline differences between the experimental (i.e. coffee drinking) subjects in the herb tea conditions compared to the non-coffee drinking control subjects for SBP or DBP. Control subjects showed significantly lower HR at baseline compared to the tea drinking experimental subjects (*M* for control subjects = 63.0 bpm, for experimental subjects 73.17 bpm, $p < .05$)(see Figure 2). Comparison of change scores revealed no significant differences over time for HR, SBP or DBP between the non-coffee drinking control group and either the experimental group given non-caffeinated herbal tea or the experimental group given caffeinated herbal tea.

No differences for HR, DBP or SBP for the non-caffeinated tea versus decaffeinated coffee comparison, or the caffeinated herbal tea versus caffeinated coffee comparison were revealed using orthogonal contrasts.

Beverage questionnaires

In addition to evaluating caffeine estimates, BQA required subjects to rate how much they liked the beverage; how good the beverage tasted; how bitter the beverage was; how hot the beverage was; how strong the beverage was; and how difficult was it to drink the beverage in the time allowed. On BQB, subjects were asked the degree to which "information the experimenter gave you" and "physical feelings" influenced their caffeine ratings.

No significant effects were found for caffeine, beverage, or the caffeine x beverage interaction on BQA items asking how subjects liked the beverage, how good it tasted, how hot it was, or how difficult it was to drink in the time allowed. A significant main effect for beverage was found for items asking "how bitter was the beverage" and "how strong was the beverage", $F(1,44) = 16.80$ and 8.80 respectively, $ps < .01$. Subjects reported the coffee beverages to be significantly stronger and more bitter than the herbal tea beverages regardless of caffeine content. A main effect for beverage was also revealed for the BQB item "how much did information the experimenter gave you influence your rating of the caffeine content". Subjects receiving herbal tea reported that the information from the experimenter influenced them more than subjects given coffee, $F(1,44)=5.71$, $p<.05$. No effects for caffeine or the beverage x caffeine interaction were seen for this item, and there were no significant differences with regard to caffeine, beverage, or caffeine x

beverage interaction for the BQB item asking "how much did physical feelings experienced after drinking the beverage influence your rating of the caffeine content".

Coffee was perceived to be stronger and more bitter than tea, but the addition of 200 mg of caffeine did not influence the taste ratings. The lack of an effect for beverage on the taste ratings corroborates the pilot study taste test results that added caffeine could not be perceived in the experimental beverages on the basis of taste. Subjects receiving the herbal tea reported that their caffeine estimates were influenced by the experimenter's instructions to a significantly greater degree than subjects receiving coffee. This relationship was also unrelated to actual caffeine content. Subjects were undoubtedly much more familiar with coffee than the apple-cinnamon herbal tea. It therefore makes sense that they would rely more heavily on the experimenter's instructions for information, since previous exposure to the beverage was limited. Neither caffeine nor beverage were related to the degree to which subjects reported that "physical feelings" influenced their caffeine estimates.

In summary, manipulation checks showed that subjects receiving coffee believed that their beverage contained substantially more caffeine than subjects receiving herbal tea regardless of actual caffeine content, and that by the time subjects began the post-beverage measurements, those receiving 200 mg of caffeine showed significant increases in blood pressure and decreases in heart rate relative to subjects

receiving no added caffeine. Thus, the manipulation of beverage and caffeine appear to have been successful. The unexpected sex differences for blood pressure did not interact with experimental condition, and did not influence measurements of change from baseline. Non-coffee drinking controls showed lower baseline heart rates than coffee drinkers, but no baseline differences were seen with blood pressure. The only differences between non-coffee drinkers and coffee drinkers for change scores were a function of caffeine, with the caffeinated herbal tea resulting in higher blood pressures in the coffee drinkers.

Subjective Response

POMS and Feelings and Mood questionnaire.

The primary subjective measures of interest were responses from the Profile of Moods States (POMS, McNair et al., 1971) and the Feelings and Mood questionnaire. As described previously, the POMS has six empirically derived scales representing tension, depression, vigor, anger, fatigue and confusion. Post-beverage responses to the 18-item Feelings and Mood questionnaire were subjected to a Factor Analysis using SPSS-X, and five factors were identified with Eigenvalues > 1. Results of the Factor Analysis are presented in Table 4. Upon reliability testing, four of the five factors yielded a Cronbach's α >.80, and were thus considered in subsequent analyses. They will be referred to as the "relaxed", "lethargic", "need a stimulant" and "headache"

factors of the Feelings and Mood questionnaire.

No significant effects for caffeine, beverage, or the caffeine x beverage interaction were revealed with ANCOVA for the tension, depression, fatigue or confusion scales of the POMS. Beverage, caffeine and the beverage x caffeine interaction were examined using MRC, and were found to contribute insignificantly to the variance in these four POMS scales. A significant main effect for caffeine was found for the POMS anger scale using ANCOVA, $F(1,43)=3.91$, $p=.05$ (see Figure 3A). Anger scores for those receiving caffeine decreased slightly from baseline, while scores for those not receiving caffeine increased. Caffeine accounted for 7.7 percent of the variance in change from baseline for anger (change in $R^2=.077$), $p<.05$. An effect for caffeine approached significance when the POMS vigor score was examined, $F(1,43)=3.09$, $p=.086$; vigor scores increased for those receiving caffeine, accounting for 4.8 percent of the variance (change in $R^2 = .048$) , $p=.09$ (see Figure 3B). There was no effect for beverage, nor was there a caffeine x beverage interaction for either the anger or the vigor scales of the POMS.

The relaxed factor of the Feelings and Mood questionnaire did not vary systematically as a function of caffeine, beverage, or the caffeine x beverage interaction, and MRC did not show that caffeine or beverage contributed meaningfully to the variance in relaxed scores. Significant main effects for caffeine were found for the lethargy and

headache factors using ANCOVAs, $F(1,43)=6.98$ and 7.28 respectively, $ps = .01$) (see Figure 4). Scores for both of these factors increased for subjects not receiving caffeine, and decreased for subjects who did receive caffeine. Caffeine accounted for 11 percent of the variance in lethargy scores (change in $R^2 = .11$), $p=.01$, and 13 percent of the variance in headache scores (change in $R^2 = .13$), $p=.01$. No effects for beverage were seen for headache, and no significant effects for beverage or the caffeine x beverage interaction were found for lethargy.

A significant main effect for beverage was seen using for the need a stimulant factor, $F(1,43)=8.71$, $p<.01$ (see Figure 5) and MRC showed that beverage accounted for 14 percent of the variance in the need a stimulant scores (change in $R^2=.14$) $p < .01$. Scores for this factor decreased substantially more for those given coffee during the session as compared to those given the herbal tea. No effects for caffeine were found in need a stimulant scores.

In summary, subjects receiving caffeine showed significant decreases in anger, lethargy, and headache scores and marginal increases in vigor scores compared with subjects not receiving caffeine. In addition, subjects receiving coffee (regardless of caffeine content) showed significant decreases in the need a stimulant factor compared with those receiving herbal tea.

Baseline differences for sex were found for the POMS fatigue scale and the need a stimulant factor of the Feelings

and Mood Questionnaire, with ANOVAs yielding $F(1,56) = 5.15$ and 4.98 respectively, $ps < .05$(see Figure 6A & 6B). Women scored significantly higher at baseline on both the fatigue and the need a stimulant measures than did men. Sex contributed 11 percent of the variance in need a stimulant scores (change in $R^2 = .11$), $p < .05$, and only 8 percent of the variance in fatigue scores (change in $R^2 = .08$) $p = .06$. No other baseline differences for sex were seen with regard to the POMS or Feelings and Mood Questionnaire. When change from baseline was examined using ANCOVAs, only POMS vigor scores differed significantly by sex, $F(1,56) = 4.91$, $p < .05$ (see Figure 6C). Men's vigor scores increased substantially from baseline, while women's vigor scores remained about the same. Sex contributed 7 percent of the variance in the change from baseline scores for vigor (change in $R^2 = .07$), $p < .05$. No other differences emerged when change from baseline was examined with regard to sex, and no interactions of sex x condition were seen for any of the POMS or Feelings and Mood questionnaire scales.

Dunnett's tests comparing the non-coffee drinking control subjects with the experimental subjects receiving herbal tea were conducted to determine whether or not the control subjects were different from the regular coffee drinkers either at baseline or over the session. Some baseline differences in subjective report were found. Non-coffee drinkers reported higher vigor and relaxed scores and lower depression, confusion, lethargy and need a stimulant scores at baseline than the coffee drinkers (see Figure 7).

Baseline relaxed and need a stimulant scores for the non-coffee drinking controls were significantly different from either of the experimental tea conditions (ps<.05), while baseline differences on vigor, depression, confusion and lethargy only reached significance for the control versus caffeinated tea condition comparison (ps<.05). No baseline differences were seen for the tension, anger, or fatigue scales of the POMS, or the headache factor of the Feelings and Mood questionnaire. The observed baseline differences suggest either that coffee drinkers chronically experience more negative affect and need for a stimulant than non-coffee drinkers, or alternatively, that the pre-session abstinence instructions led to the onset of caffeine withdrawal-related symptoms in the coffee drinkers.

Examination of post-beverage scores allowed for the evaluation of these two possibilities. The experimental group receiving non-caffeinated herbal tea reported significantly more fatigue, confusion, lethargy, headache and need a stimulant, and significantly less relaxation, than the non-coffee drinking control group following exposure to the experimental beverage (ps < .05)(See Figures 8). In contrast, the experimental group receiving caffeinated tea differed from the control group on only two measures, relaxation and need a stimulant (ps < .05). The continued deprivation of the experimental non-caffeinated herbal tea group was associated with continued reports of negative affect and lethargy, as well as the onset of headache, suggesting that caffeine

withdrawal was responsible for many of the observed differences. The experimental group receiving caffeinated tea continued to report less relaxation and more need for a stimulant than the control group. The continued need for a stimulant in both of the experimental groups is probably the result of the coffee deprivation experienced in these groups: main effects revealed that beverage, but not caffeine, predicted need a stimulant scores. The fact that relaxed factor scores were higher for the control group throughout the session implies that some of the differences between the coffee drinkers and non-coffee drinkers were not the result of either coffee or caffeine deprivation.

When change from baseline was examined in these groups, caffeine was associated with significant increases in vigor, with the experimental group receiving caffeinated tea showing significant increases relative to the non-coffee drinking controls and the coffee drinkers receiving non-caffeinated tea ($p<.05$), (See Figure 9). This significant increase in vigor with caffeine suggests that coffee drinkers do not develop tolerance to caffeine's alerting effects. It should be noted, however, that the caffeine-related increase in vigor did not translate into higher overall vigor scores for the caffeinated tea group post beverage; post beverage vigor scores of the experimental group receiving caffeinated tea did not differ significantly from those of the non-coffee drinking controls.

Planned comparisons revealed significant differences

between the decaffeinated coffee group and the non-caffeinated herbal tea group for change from baseline on the need a stimulant and headache factors of the Feelings and Mood questionnaire (ps <.05) (see Figure 10). The non-caffeinated herbal tea group showed greater increases in need a stimulant and headache factor scores than the decaffeinated coffee group. Decaffeinated coffee without added caffeine was associated with less need for a stimulant and headache than herbal tea without added caffeine. No significant differences were seen between the decaffeinated coffee and non-caffeinated herbal tea group for change from baseline on any of the POMS scales, or the relaxed or lethargy factors of the Feelings and Mood questionnaire.

No differences were found with planned comparisons for any of the POMS scales or the Feelings and Mood questionnaire factors between the caffeinated coffee and caffeinated herbal tea groups. Thus the vehicle of caffeine administration did not meaningfully influence subjective response to caffeine.

Task questionnaire

After both the 10 minute baseline task and the 40 minute post-beverage task subjects were asked to rate the task on six items: difficult, challenging, boring, frustrating, enjoyable, and practice with similar tasks. When either the post-beverage ratings or the change from baseline ratings were examined using ANCOVA, no significant main effects were found for either caffeine or beverage, and there were no significant

interactions for caffeine x beverage for any of these items.

Summary: Anger, lethargy and vigor appear to have varied as a function of the caffeine content of the beverage, regardless of whether the beverage was coffee or herbal tea. Planned comparisons revealed that without added caffeine, subjects receiving coffee had lower headache and need a stimulant scores than subjects receiving herbal tea.

Baseline differences were found for sex, with women reporting more fatigue and need for a stimulant that men. Men's vigor scores increased more over the session than did women's. Baseline differences also emerged for coffee drinking status, with the non-coffee drinking controls reporting less confusion, depression, lethargy and need a stimulant, and more vigor and relaxation than the coffee drinkers. When post-beverage scores were examined, the non-coffee drinking controls were comparable to the coffee drinkers who had received caffeinated herbal tea on confusion, fatigue, lethargy and headache, but differed on these measures from the coffee drinkers who had not received caffeine in their herbal tea. The non-coffee drinkers remained more relaxed over the session than the coffee drinkers in the herbal tea groups.

Task Performance

No main effects for caffeine or beverage were seen for response latency (RL), false positive responses (FP), or errors of omission (EO) using MANCOVAs. Neither caffeine nor

beverage were found to account for significant proportions of the variance in RL, FP or EO during the fourth 10 minute period of the post-beverage task. When change from baseline over time was examined with MANCOVA, a caffeine x time interaction approached, but did not reach, statistical significance for RL, $F(3,132)= 2.18$, $p=.093$, (see Figure 11). Response latencies appeared to remain lower over time for subjects receiving caffeine. A significant caffeine x beverage x time interaction for RL was found, $F(3,132)=2.71$, $p<.05$) using MANCOVA. Post hoc examination of this interaction was accomplished using the Tukey (1977) method as described by Hays (1981)(pp.434-436). During the last 10 minute interval of the post-beverage test the caffeinated coffee group performed significantly better (ie. had lower RLs relative to baseline) than the non-caffeinated tea group ($p<.05$), but did not differ significantly from either the decaffeinated coffee or the caffeinated tea group (see Table 5). In other words, task performance, as measured by response latency, was better in subjects receiving caffeine in coffee compared to subjects receiving non-caffeinated herbal tea. Performance in groups receiving either the caffeinated herbal tea or the decaffeinated coffee did not differ from one another. No significant interactions were found for FP responses or EOs using MANCOVA or MRC.

No differences were found on baseline performance measures (RL, FP, or EO) with regard to sex, nor were there any sex x time or sex x condition x time interactions for any

of the performance measures. Sex was not found to contribute significantly to the variance of any of the performance measures.

Type A scores from the Jenkins Activity Survey were examined with respect to task performance by performing a median split on the distribution of Type A scores (range 118 to 379, median 222). Those scoring below and above the median were compared for baseline performance. Also, Type A x condition interactions, Type A x time interactions, and Type A x condition x time interactions were examined. No significant baseline differences between those scoring above versus below the median on Type A for RL, FP or EO were revealed with MANCOVA. A significant contribution to variance in baseline performance was found using MRC only for EO's, $R^2 = .10$, $p<.05$, with higher Type A scores being associated with more errors of omission. No significant interactions were found for Type A x condition , Type A x time, or Type A x condition x time analyses for any of the performance measures. Similarly, MRC revealed no significant proportions of variance accounted for by Type A with regard to performance during the last 10 minute period of the task.

Dunnett's tests revealed no baseline performance differences between the non-coffee drinking control group versus either of the experimental groups that received the herbal tea. Likewise, no differences emerged for change from baseline over time for any of the performance measures when comparing the control group with either the caffeinated tea

group or the non-caffeinated tea group.

Comparison of the decaffeinated coffee and the non-caffeinated herbal tea groups by orthogonal contrasts revealed an interaction with time for RL, with the decaffeinated coffee group showing significantly less decline in performance than the non-caffeinated tea group during the last 10-minute post-beverage period ($p<.05$) (see Table 6). Coffee, independent of caffeine, was associated with better task performance over time than was herbal tea. Performance measures of FP and EO did not differ significantly between the decaffeinated coffee and non-caffeinated herbal tea groups.

The caffeinated coffee and caffeinated herbal tea groups were found to differ on EO, with the caffeinated tea group showing fewer omission errors than the caffeinated coffee group relative to baseline ($p <.05$) (see Table 7). Subjects receiving caffeine in the novel beverage, herbal tea, made fewer errors of omission than those receiving caffeine in coffee. It should be noted, however, that all of the groups made very few EOs, and the mean scores representing change from baseline were all less than 1.

Summary: No main effects for caffeine or beverage were seen for task performance. When change in performance was examined over time, a caffeine x time interaction approached significance, suggesting that subjects receiving caffeine has less decline in performance over time. A significant caffeine x beverage x time interaction was found,

and post hoc examination of this interaction revealed that during the last 10 minutes of the task subjects in the caffeinated coffee group maintained significantly shorter response latencies than those in the non-caffeinated tea group. Performance in the decaffeinated coffee group and the caffeinated herbal tea group fell between the caffeinated coffee group and non-caffeinated herbal tea group.

No effects were found for sex when either baseline or change from baseline over time was examined. Type A behavior pattern was positively associated with errors of omission at baseline, but no other effects were found for Type A when either baseline or change from baseline over time was evaluated. Non-coffee drinking control subjects did not differ from coffee drinkers at baseline or over time on any of the performance measures. Fewer errors of omission were made over time when coffee drinkers received caffeine in herbal tea than when the caffeine was provided in coffee. Finally, coffee drinkers who were not given caffeine did significantly better with regard to response latency over time following coffee than following herbal tea.

Table 8A-F presents the changes in R^2 for each independent variable (baseline, beverage, caffeine, beverage x caffeine interaction, Type A and sex) listed in order of hierarchical multiple regression entry for the POMS sub-scales[1]. Table 9A-D presents the changes in R^2 for each independent variable listed in order of hierarchical multiple

regression entry for the Feelings and Mood factors. Changes in R^2 for each independent variable, again listed in order of hierarchical entry, for the task performance measures are listed in Table 10A-C.

Discussion

This research was designed and conducted to address two main questions. First, does coffee have subjective and behavioral effects beyond those directly attributable to caffeine? And second, does caffeine presented in coffee produce different subjective and behavioral effects than caffeine presented in a novel, non-coffee beverage? The results of this study provide evidence that coffee does have measurable effects beyond those directly attributable to caffeine. Additionally, the findings of this research do not suggest that caffeine presented in coffee is associated with effects that differ from caffeine presented in a novel beverage.

In addition to evaluating coffee drinkers' subjective and behavioral responses to coffee and caffeine, the responses of coffee drinkers were compared with a non-coffee drinking control group. This control group was included to examine whether caffeine actually enhances alertness and performance in coffee drinkers, or alternatively, simply brings them to a level similar to those who never initiated regular caffeine use? Caffeine was required to bring the coffee drinkers to a degree of subjective well-being comparable to the non-coffee drinkers, and in the case of relaxation, coffee drinkers never reached the level of the controls. Thus, coffee drinkers deprived of caffeine may experience more negative affect than non-coffee drinkers, and caffeine may lead to only a partial improvement of subjective well-being.

In discussing these results, each hypothesis will be addressed in turn, in conjunction with the supporting and/or refuting data generated by this research.

Effects of caffeine.

Hypothesis 1 does not correspond directly with either of the questions mentioned above, but instead predicted a replication of previous research findings that caffeine enhances task performance and mood. Results from this study correspond with previous research that has shown that caffeine ingestion is associated with increases in subjective alertness and positive affect, performance enhancement, and decreases in headache and lethargy (Bruce et al., 1986; Chait & Johanson, 1986; Goldstein et al., 1969; Griffiths et al., 1990; Griffiths & Woodson, 1988a; Leiberman et al., 1987a, 1987b, Rosenthal et al., in press; Swift & Tiplady, 1988; Zwyghuizen-Doorenbos et al., 1990).

Subjects receiving 200 mg of caffeine in their experimental beverage reported significantly less anger, headache and lethargy than subjects receiving lactose in their beverage. Subjects receiving caffeine also reported increases in vigor that approaced significance relative to those receiving lactose. The finding that caffeine was associated with decreases in headache and lethargy suggests that the experimental subjects may have been experiencing some withdrawal-related symptoms at session onset. Subjects that did not receive caffeine during the session increased reports

of headache and lethargy, suggesting that they continued to experience withdrawal-related symptoms, and that these symptoms increased in severity over time.

All subjects had been instructed to avoid dietary caffeine from midnight on the evening before the session until arrival at the laboratory, and this caffeine deprivation may have resulted in the onset of withdrawal symptoms for some subjects. Griffiths and Woodson (1988a) have reported that the withdrawal symptoms begin to appear in coffee drinkers following anywhere from 12 to 24 hours of caffeine abstinence. Coffee drinkers in this study had probably been abstinent for at least 12 hours at session onset, as they were moderate coffee drinkers and typically confined their intake to morning and early afternoon hours. Both the evidence of caffeine withdrawal-related symptoms following deprivation, and the evidence of amelioration of these symptoms with subsequent caffeine intake, are consistent with previous research findings (Greden et al., 1980; Griffiths et al.,1986, 1990a; Griffiths & Woodson, 1988a). For example a recent study by Griffiths et al. (1990a) showed that caffeine deprivation following even low levels of chronic administration (i.e. 100 mg caffeine/day) resulted in increased reporting of headaches and lethargy, and decreases in energy and ability to concentrate. Reinstatement of 100 mg of caffeine per day alleviated these withdrawal-related symptoms.

Results from this study correspond with previous findings of performance enhancement with caffeine with some

qualification (Leiberman et al, 1987a, 1987b, Rosenthal et al., in press; Zwyghuizen-Doorenbos et al, 1990). Researchers who have found enhancement of auditory vigilance performance as a function of caffeine typically report differences that emerge in the last 30-40 minutes of the task: caffeine ingestion results in a lessening of the time related performance deterioration (T. Roehrs, personal communication, July 1990). The caffeine x time interaction approached significance for response latency, suggesting that those receiving caffeine did better over time. The significant caffeine x beverage x time interaction and subsequent post hoc analysis revealed that subjects receiving caffeinated coffee had lower response latencies (i.e. reaction times) during the last 10 minutes of the task than subjects receiving the non-caffeinated herbal tea. A number of studies have reported using decaffeinated coffee as the vehicle for caffeine versus placebo administration, without the inclusion of a non-coffee control beverage (Goldstein et al., 1965; Griffiths et al.,1986; Rosenthal et al., in press; Zwyghuizen-Doorenbos et al., 1990). If decaffeinated coffee had been the only vehicle used in this study, no significant difference in task performance for caffeine would have been seen; the decaffeinated and caffeinated coffee groups did not differ.

While physiological responses were not mentioned in Hypothesis 1, it was expected that a main effect for Caffeine would be seen for systolic and diastolic blood pressure and heart rate. Contrary to findings by Robertson et al. (1981),

and consistent with findings from more recent research (Goldstein et al., 1990; Lane et al., 1990; Lane & Manus, 1989; Ratliff-Crain et al., 1989), these regular coffee drinkers did not show evidence of tolerance. Caffeine was associated with a significant increase in systolic and diastolic blood pressure, and a significant decrease in heart rate.

Support for a main effect for caffeine, consistent with Hypothesis 1, was therefore generally positive. Subjects receiving caffeine showed evidence of increased alertness, decreased negative affect, and decreased lethargy and headache when compared to subjects receiving lactose. Evidence for behavioral enhancement with caffeine was not as clear. The borderline interaction of caffeine x time, and the post hoc finding that the caffeinated coffee group performed significantly better than the non-caffeinated tea group during the last 10 minutes of the task, suggest that caffeine contributed to lower response latencies. Finally, caffeine produced a significant increase in blood pressure (systolic and diastolic) and decrease in heart rate.

Effects of coffee independent of caffeine.

The results of this study provided some support for the hypothesis that coffee affects subjective and behavioral response independently of caffeine. Expectations or conditioned effects of coffee appear to have influenced several of the dependent measures. First, a main effect for

beverage was found for the need a stimulant factor of the Feelings and Mood questionnaire. The need a stimulant factor includes negative loadings on "alert" and "mentally sharp", along with positive loadings on "would like a cup of coffee" and "would like something to jazz you up". Coffee was associated with a significant decrease in need a stimulant relative to the herbal tea, regardless of caffeine content. Comparisons between experimental groups not receiving added caffeine in their beverage revealed that decaffeinated coffee subjects reported less need for a stimulant and less headache than non-caffeinated herbal tea subjects. While decaffeinated coffee and caffeinated coffee were not examined by planned comparison (a priori contrasts must be guided by explicitly stated hypotheses), the headache and need a stimulant responses of the decaffeinated coffee group resembled those of the caffeinated coffee group.

The finding that decaffeinated coffee was associated with lower need a stimulant scores corresponds with the Ratliff-Crain et al. (1989) report that decaffeinated coffee ameliorated desire for coffee relative to herbal tea. In that study, desire for coffee reflected response to a single item, while the need a stimulant factor in the present research represents responses to several inter-correlated items that reflect low alertness and mental clarity and high desire for coffee and something to "jazz" one up. Thus the finding that decaffeinated coffee was associated with lower scores on this factor not only replicates the work of Ratliff-Crain et al.,

but broadens it; consumption of decaffeinated coffee appears to be associated with less "need" for a cup of coffee as well as less "desire" for coffee.

Ratliff-Crain et al. (1989) did not find that decaffeinated coffee ameliorated headache relative to herbal tea. The fact that decaffeinated coffee consumption was associated with lower scores on the headache factor than non-caffeinated herbal tea in this research, but not in the Ratliff-Crain et al. study, could be due to the differences between the subject samples in average daily coffee consumption. Subjects in the present study drank an average of 17.4 ounces per day in contrast to the heavier coffee drinkers in the Ratliff-Crain et al. study, who consumed an average of 28.5 ounces per day. If intensity of withdrawal-related symptoms are a function of average daily caffeine intake, as is suggested by Griffiths and Woodson (1988a), decaffeinated coffee may useful in combatting withdrawal symptoms in coffee drinkers with moderate to low intake.

Decaffeinated coffee was not associated with more positive (or less negative) mood when compared with non-caffeinated herbal tea. No differences were found between these two groups on the depression, anger or confusion scales of the POMS or the relaxed factor of the Feelings and Mood questionnaire.

Interestingly, planned comparison did reveal a difference between the decaffeinated coffee group and the non-caffeinated tea group for response latency on the auditory

vigilance task. During the last 10 minute period of the task, subjects receiving decaffeinated coffee had response latency change scores less than half the size of the non-caffeinated herbal tea group. Thus, decaffeinated coffee appears to have tempered the decline in auditory vigilance task performance that occurs over time relative to non-caffeinated herbal tea. Inspection of Table 5 suggests that response latency during the last 10 minutes of the task was smallest for the group receiving caffeinated coffee, followed by the decaffeinated coffee and caffeinated tea groups whose responses were very similar. The non-caffeinated tea group clearly showed the slowest response latencies during the last 10 minutes of the task.

The results of this study provide some support for the second hypothesis: coffee appears to have subjective and behavioral effects independent of caffeine in caffeine experienced subjects. Decaffeinated coffee ameliorated symptoms of withdrawal in this sample of moderate coffee drinkers. This finding suggests that decaffeinated coffee may be useful in helping coffee drinkers make the transition to caffeine abstinence should they need to do so for health reasons. While decaffeinated coffee has been associated with coronary heart disease (Grobbee et al., 1990), and is as likely as caffeinated coffee to increase gastric acid secretions (Rall, 1985), it may be useful in dealing with the acute phase of caffeine withdrawal.

Anecdotal evidence from television commercials and

restaurant, supermarket, and gourmet shop coffee selections suggests that decaffeinated coffee is a much more popular beverage now than it was 10 years ago. Certainly the major impetus for its increasing popularity is the 1980's increase in health consciousness that brought with it an increase in the advertising and availability of foods with less fat and no preservatives, artificial colors or artificial flavors. However, the findings in this and the Ratliff-Crain et al. (1989) suggest that some of its popularity may also be the result of its amelioration of caffeine withdrawal-related symptoms, particularly in moderate (2-4 cups per day) coffee drinkers. Future research should be directed at examining the effects of decaffeinated coffee (with appropriate controls, of course) in a sample with a wider range of daily coffee intake.

Decaffeinated coffee was also associated with better task performance than the non-caffeinated herbal tea. While it is not possible to determine the contributions that expectation, conditioning, or other potentially active substances in decaffeinated coffee make to the differences observed, it is interesting that the effects reflect both withdrawal-related symptoms and performance, but not positive affect. It should be noted that there were no differences between the decaffeinated coffee and the non-caffeinated herbal tea groups on any of the physiological measures, and thus no evidence was found for either a direct or an opponent process-type conditioned physiological response.

Caffeine in coffee versus caffeine in a novel beverage.

Hypothesis 3 predicted that caffeine presented in a novel beverage (i.e. herbal tea) would produce more potent effects on mood, alertness and performance than caffeine presented in coffee. This hypothesis was based on two assumptions. First, that some degree of tolerance develops to caffeine's effects on mood, alertness and performance; and second, that separating caffeine intake from the stimuli previously paired with ingestion (i.e. the sight, smell and taste of coffee) would restore its full subjective and behavioral effects. Research by Zwyghuizen-Doorenbos et al. (1990) has shown that some degree of tolerance develops to caffeine's stimulating effects. In addition, it has been shown that effects of alcohol that fade over time as a result of tolerance reappear when alcohol is presented in a novel environment (Dafters & Anderson, 1982).

This hypothesis stands in direct contrast to what would be predicted based on the expectancy effects reported by Marlatt and colleagues (1973, 1980, 1981). Marlatt and Rosenow (1980) have reported that expectations regarding whether or not a beverage contained alcohol were more potent predictors of response to an experimental beverage than the actual alcohol content of the beverage. Based on this work, it would be anticipated that caffeine presented in coffee would have more potent effects on mood and behavior than caffeine presented in herbal tea.

Planned comparison of the caffeinated coffee group

with the caffeinated herbal tea group provided a test of these two theories (situational specificity of tolerance versus expectancy). Neither of the theories received strong empirical support. There were no significant differences between the decaffeinated coffee with caffeine added and the non-caffeinated herbal tea with caffeine added for any of the POMS scales or any of the factors from the Feelings and Mood questionnaire.

With regard to task performance, no differences were seen on the measure previously found to be most sensitive to caffeine's effects - response latency. However, when errors of omission were examined, subjects receiving the caffeine in herbal tea made significantly fewer errors than subjects receiving caffeine in coffee. It should be noted that errors of omission showed little variation (changes from baseline fell between 1 and -1).

Thus, Hypothesis 3 received very little support. Subjective report showed no differences between the caffeinated coffee and caffeinated herbal tea group. Performance measures revealed that subjects in the caffeinated tea group made significantly fewer errors during the last 10 minutes of the task than the caffeinated coffee group, though this finding cannot be interpreted as unqualified support for Hypothesis 3. The contrasting expectancy hypothesis received no direct support; subjects in the caffeinated coffee condition, who expected to experience caffeine effects, showed no more alertness, enhanced mood or enhanced performance than

the caffeinated herbal tea groups, who did not expect to experience caffeine effects. It should be noted, however, that the findings for Hypothesis 2, namely that decaffeinated coffee produced measurable effects, do provide indirect support for the expectancy hypothesis. Nevertheless, the expectancy findings from alcohol research (e.g. Rosenow & Marlatt, 1981), that expectations concerning the alcohol content of a beverage are stronger predictors of response than actual alcohol content, cannot be extended to caffeine and coffee on the basis of the findings of this study.

Comparisons with the non-coffee drinking control subjects.

Comparisons were made between the non-coffee drinking control group and the two coffee drinking groups that were given herbal tea to determine whether or not caffeine enhanced mood, alertness and performance in coffee drinkers beyond levels observed in a sample that never initiated regular coffee drinking. Based on previous research with nicotine and smokers (Silverstien, 1982), it was possible that the mood, alertness and performance enhancement that coffee drinkers experience with caffeine may be the result of caffeine's amelioration of withdrawal rather than actual caffeine-related enhancement. Silverstien (1982) found that cigarette smokers who were deprived of nicotine behaved more anxiously than non-smokers or smokers given nicotine. Nicotine did not result in less anxious behavior in the smokers as compared to the non-smokers, however, but instead produced behavior that was

similar to that of the non-smokers.

Griffiths and Woodson (1988a) have argued that caffeine, like nicotine, has the two main characteristics of a drug of abuse; namely that possesses reinforcing properties, and has the potential to harm the individual user and/or society. Given caffeine's suspected abuse liability, and the well documented syndrome of caffeine withdrawal, it seemed reasonable to suspect that caffeine may not actually enhance mood, alertness and performance, but instead merely attenuate withdrawal-related disruption.

Non-coffee drinkers were compared with the coffee drinkers in the herbal tea conditions only, as these three groups were exposed to identical experimental procedures (with the exception of the 200 mg of caffeine that was presented to the caffeinated tea group). Examination of baseline differences revealed that, upon arrival at the laboratory, non-coffee drinkers had higher vigor and relaxed scores, and lower confusion, depression, lethargy and need a stimulant scores than the coffee drinkers. The findings that coffee drinkers were significantly more depressed, lethargic and confused, and less vigorous and relaxed, suggest that these subjects were demonstrating some subjective signs of withdrawal at the beginning of the session. Following beverage administration, the coffee drinkers who had received non-caffeinated herbal tea reported more confusion, fatigue, lethargy and headache post beverage than either the non-coffee drinkers or the coffee drinkers receiving 200 mg of caffeine

in their herbal tea. The non-coffee drinkers and the coffee drinkers who received caffeinated tea were comparable on these measures post beverage. Thus, the subjects who did not receive caffeine continued to experience withdrawal-related symptoms.

The non-coffee drinking group remained significantly more relaxed than either of the coffee drinking groups following beverage consumption, suggesting that some of the baseline differences between these groups were not attenuated with caffeine. Caffeine did appear to produce evidence of enhanced alertness, as significant increases in vigor were seen in the caffeinated tea group relative to the non-caffeinated tea group and the non-coffee drinking controls. This increase did not result in the caffeinated tea group having significantly higher post-beverage vigor scores, however.

These results are somewhat similar to those reported by Silverstein (1981), with regard to the relaxing effects of nicotine. As mentioned previously, Silverstein measured shock tolerance in smokers and non-smokers. Smokers deprived of nicotine had significantly lower tolerance for shock than smokers given the opportunity to smoke a high nicotine yield cigarette or nonsmokers, who were comparable with regard to shock tolerance. Silverstein interpreted these results as support for the hypothesis that "the calming effect attributed to smoking a cigarette is due to the action of nicotine in ending withdrawal symptoms in addicted smokers rather than to

a sedative property of cigarette smoking" (p. 946).

While these two experiments do share some conceptual similarities, they have some important differences. This study measured caffeine's effects on mood, alertness and behavioral performance directly, while Silverstein's measure of nicotine's relaxing effect (shock tolerance) was indirect. Additionally, caffeine's stimulating effects are well established. Caffeine increases locomotor activity in animals (Snyder & Sklar, 1984) and enhances performance in human subjects, both with and without extensive histories of caffeine use (Weiss & Laties, 1962; Lieberman et al., 1987a, 1987b). In contrast, support for the calming effects of nicotine, which were the focus of the Silverstein research, is equivocal (Gilbert, 1979).

The Silverstein research reported that evidence for a paradoxical effect of nicotine was not found when smokers receiving nicotine were compared with nonsmokers. This research, in contrast, reports that evidence for an established effect for caffeine was not found when coffee drinkers receiving caffeine were compared with non-coffee drinkers. Nevertheless, the results of this study do suggest that the alerting and mood enhancing effects associated with caffeine in regular coffee drinkers may be due, in part, to the action of caffeine in ending withdrawal symptoms rather than the its stimulating properties.

Type A and Gender

It was anticipated that Type A scores, as measured by the Jenkins Activity Survey, might act alone or in interaction with caffeine to influence performance measures. Previous research has suggested that Type As become impatient, restless, and distracted while performing vigilance tasks (Glass, 1977). Type A scores were not found to influence response latency or false positive responses, nor did they interact with caffeine to influence these measures. Type A scores accounted for a small but significant portion of the variance in baseline Errors of Omission, with Type A's making more errors. Change from baseline on this measure was not influenced by Type A status. Therefore, little evidence was found to suggest that scores on the Type A behavior scale of the Jenkins Activity Survey influenced performance on the auditory vigilance task.

Sex of subject was found to influence blood pressure and subjective reports in unexpected ways. Females had significantly higher systolic and diastolic blood pressure than males at baseline. Sex did not influence post beverage measures of change from baseline for blood pressure. Baseline differences also emerged for fatigue and need a stimulant, with females reporting significantly more fatigue and need for a stimulant than males. When change from baseline was examined, no sex differences for blood pressure, fatigue and need a stimulant were seen. Only vigor showed a significant effect for sex, with males reporting an increase in vigor over

the session relative to females.

The finding that women had higher baseline blood pressures, higher baseline fatigue and need a stimulant scores, and smaller increases from baseline in vigor scores were not expected and cannot be explained. Perhaps the deprivation instructions were more stressful for women, leading to increases in baseline blood pressure, fatigue and need for a stimulant. Baseline differences for sex were not seen on relaxation or tension measures, however, arguing against the mediation of stress-related changes. The fact that distribution of males and females was relatively equal among the experimental groups, and that sex did not interact with experimental condition, supports a conclusion that these differences did not meaningfully influence the experimental procedures.

Summary and Conclusions

In this research, caffeine content of beverage (0 vs. 200 mg of caffeine) was crossed with beverage (coffee versus herbal tea), in order to evaluate the separate contributions that coffee and caffeine make to subjective and behavioral measures of alertness. In addition, non-coffee drinkers were compared with coffee drinkers to determine whether or not caffeine enhances mood and performance in coffee drinkers beyond the level that is regularly seen in non-coffee drinkers. It was hypothesized that caffeine would enhance subjective mood and alertness and performance relative to placebo (lactose) in coffee drinkers. Results confirmed this hypothesis. Coffee drinkers who received caffeine showed less negative affect and more alertness following caffeine. Caffeine was also associated with less performance decline over time, though this effect did not reach statistical significance.

Caffeine increased blood pressure and decreased heart rate relative to placebo. Tolerance to caffeine's hemodynamic effects apparently does not occur in the regular coffee drinker. It was also hypothesized that coffee would have measurable subjective and behavioral effects independent of the effects of caffeine. This hypothesis also received support. Subjects given decaffeinated coffee reported less headache and need for a stimulant than subjects given non-caffeinated herbal tea. Decaffeinated coffee was also associated with a smaller decline in performance over time

compared to herbal tea. Decaffeinated coffee did not demonstrate measurable mood enhancement relative to herbal tea.

Decaffeinated coffee attenuated withdrawal-related headache and need for a stimulant in this sample. Previous research from this laboratory (i.e. Ratliff-Crain et al. 1989) also found that decaffeinated coffee ameliorated desire for coffee, though the heavy coffee drinkers used in the previous study did not report that decaffeinated coffee relieved headache. Differences in sample characteristics may account for this discrepancy. Severity of caffeine withdrawal symptoms may be dose dependent (Griffiths & Woodson, 1988a), and thus decaffeinated coffee may ameliorate withdrawal headache in light to moderate, but not heavy coffee drinkers. Thus the possibility that decaffeinated coffee may reduce caffeine withdrawal symptoms, and that this reduction may be influenced by the caffeine dose maintained pre-withdrawal, warrants further research attention.

Decaffeinated coffee was also associated with better task performance than herbal tea suggesting that the "decaffeinated coffee as placebo" procedure used by some caffeine researchers may mask experimental differences. Whether the effects of decaffeinated coffee are due to expectancy effects or conditioned effects cannot be determined from this study. Caffeine presented in coffee did not produce effects that were significantly more powerful than caffeine presented in herbal tea, suggesting that caffeine expectancies

do not influence outcomes as profoundly as alcohol expectancies (Rosenow & Marlatt, 1981). Future research should be designed to test the conditioning hypothesis and determine whether a non-coffee stimulus associated with caffeine ingestion acquires caffeine-like properties following repeated exposure in humans, and whether these acquired effects extinguish over time.

Comparisons between non-coffee drinking control subjects and coffee drinkers given either caffeinated or non-caffeinated herbal tea suggest that the alerting and mood enhancing effects associated with caffeine in regular coffee drinkers may be due, in part, to the amelioration of withdrawal-related symptoms. Following beverage administration, coffee drinkers receiving caffeinated tea were comparable to non-coffee drinkers on measures of headache, confusion, fatigue and lethargy, while coffee drinkers receiving non-caffeinated tea scored significantly higher than the non-coffee drinkers on each of these measures.

Increases in vigor scores for coffee drinkers receiving caffeinated tea suggest that regular coffee drinkers do not develop tolerance to caffeine's alerting effects. Coffee drinking in the general public may represent a subchronic level of administration similar to the subchronic presentation of caffeine to rats in the recent report by Meliska and colleagues (1990). In this study, rats that were given caffeine in their drinking water chronically became tolerant to its effects on behavior (i.e. wheelrunning), while

rats that were given caffeine in their drinking water every other day became sensitized to its behavioral effects (i.e. spent more time wheelrunning with repeated exposures). Perhaps the one of the reasons that caffeine and coffee are so popular is that regular patterns of self-administration do not result in the development of tolerance to their alerting effects.

In conclusion, this is the only reported research to date to use a balanced placebo design to examine the effects of caffeine and coffee on subjective and behavioral measures of alertness. In addition to confirming previous reports that caffeine enhances alertness, strong evidence was found to suggest that coffee produces subjective and behavioral effects independent of caffeine. Coffee was also found to ameliorate caffeine withdrawal symptoms independently of caffeine.

Findings support the advocacy of balanced placebo designs in psychopharmacological research. First, because main effects of a drug may be masked when placebo is potentially active due psychological factors such as conditioning and expectancy. Second, because a full understanding of a drug related behavior requires the evaluation of both the primary pharmacologically active component of a drug and the acquired properties of popular vehicles of administration, both alone and in combination.

Table 1

Caffeine content in common sources.

Source	caffeine content(mg.)	
Ground coffee-drip	112-142	per 5 oz. cup (a,b).
Ground coffee-percolated	64-124	per 5 oz. cup (a,b).
Ground coffee-decaff.	2-5	per 5 oz. cup (a).
Instant coffee	40-108	per 5 oz. cup (a,b).
Instant coffee-decaff.	2-8	per 5 oz. cup (a).
Black tea- 1 min. brew	28	per 5 oz. cup (b).
Black tea- 5 min. brew	47	per 5 oz. cup (b).
Green tea- 1 min. brew	15	per 5 oz. cup (b).
Green tea- 5 min. brew	32	per 5 oz. cup (b).
Instant tea	24-31	per 5 oz. cup (a)
Cocoa	5-42	per 5 oz. cup (a,b)
Coca-Cola	65	per 12 oz. can (b).
Pepsi-Cola	43	per 12 oz. can (b).
Dr. Pepper	61	per 12 oz. can (b).
Jolt Cola	71	per 12 oz. can (c).
Mountain Dew	55	per 12 oz. can (b).
Sunkist Orange	20	per 12 oz. can (d).
Chocolate candy bar	5-6	per 1 oz. bar (a,b).
Baking chocolate	18-118	per 1 oz. block (a).
Anacin, Midol, Vanquish	32	per tablet (e).
Excedrin	60	per tablet (e).
No Doz	100	per tablet (e).
Vivarin	200	per tablet (e).

(a = from Barone & Roberts, 1984
b = from Bunker & McWilliams, 1979
c = from The caffeine kick, U.S. News and World Report, 1988
d = from Canada Dry Corp., personal communication- consumer info.
e = from Greden, 1974)

Table 2

	Outline of experimental procedure.	Time example for 6am study onset time:
1.	Arrival at laboratory - between 6am and 10am.	6:00am
2.	Study description and informed consent.	6:00-6:10
3.	Food today questionnaire - checked for compliance with deprivation instructions.	6:10-6:12
4.	Fifteen minutes of baseline blood pressure and heart rate.	6:12-6:27
5.	Baseline POMS, Feelings and Mood Questionnaire.	6:27-6:32
6.	Jenkins Activity Survey and Diet Inventory.	6:32-6:40
7.	Three minute practice on Auditory Vigilance Task.	6:40-6:43
8.	Ten minute baseline on Auditory Vigilance Task.	6:43-6:53
9.	Task Questionnaire A.	6:53-6:54
10.	Ten minute beverage administration period.	6:54-7:04
11.	Beverage Questionnaire A.	7:04-7:06
12.	Thirty minute post beverage rest. Proofreading task administered. BP and HR measured.	7:06-7:36
13.	Post-beverage POMS, Feelings and Mood Questionnaire.	7:36-7:41
14.	Forty minute post-beverage Auditory Vigilance Task.	7:41-8:21
15.	Task Questionnaire B.	8:21-8:22
16.	Beverage Questionnaire B.	8:22-8:24
17.	Pay and Debrief.	8:24-8:30

Table 3

	Tea -	Tea +	Coffee -	Coffee +	Non-coffee drinking Tea control
BQA	11.62[a] (5.28)	5.56[a] (1.44)	145.70[b] (3.25)	152.14[b] (3.25)	0.45[a] (0.19)
BQB	12.00[a] (5.46)	7.70[a] (1.68)	129.27[b] (7.22)	146.83[b] (2.74)	0.45[a] (0.19)

Mean caffeine estimates in milligrams, with standard errors indicated in parentheses. Estimates were recorded immediately after the 10 minute beverage consumption period (BQA) and at the end of the session (BQB).
Numbers with non-shared suprascripts are significantly different at $p < .05$.

Table 4

Factor Analysis results for Feeling and Mood questionnaire. Factors identified with Eigenvalues > 1, with corresponding Cronbach's alpha.

Factor 1: Relaxed alpha=.86	
"relaxed"	.83
"calm"	.82
"restless"	-.74
"comfortable"	.74
"irritable"	-.68
"nervous"	-.54

Factor 2: Lethargy alpha=.90	
"sleepy"	.82
"sluggish"	.81
"lethargic"	.75
"having trouble concentrating"	.64

Factor 3: Need a Stimulant alpha=.85	
"would like a cup of coffee"	.80
"need something to jazz you up"	.75
"mentally sharp"	-.70
"alert"	-.68

Factor 4: Headache alpha=.97	
"headache"	.91
"need an aspirin"	.91

Factor 5: Overstimulated alpha=.34	
"need something to calm you down"	.80
"stomach upset"	.65

Table 5

	Tea-	Tea+	Coffee-	Coffee+
Response Latency	a 1117.8 (160.3)	ab 533.4 (220.0)	ab 506.5 (159.0)	b 272.7 (177.7)

Mean change from baseline scores for response latency in milliseconds, with standard errors indicated in parentheses. Times represent change scores for the last 10 minute period of the 40 minute post beverage task.

Numbers with non-shared suprascripts are significantly different at $p < .05$.

Table 6

	Tea-	Coffee-
Response Latency, milliseconds	1117.83 (160.3)	506.54 (159.0)

Mean change from baseline for last 10 minute period of 40 minute post-beverage task, with standard errors indicated in parentheses. Orthogonal contrast revealed significant difference at $p<.05$.

Table 7

	Tea+	Coffee+
Errors of Omission	-0.42 (0.14)	0.73 (0.21)

Mean change from baseline averaged over the four 10 minute periods of 40 minute post-beverage task, with standard errors indicated in parentheses. Orthogonal contrast revealed significant difference at $p<.05$.

Table 8a

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: POMS Tension (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level $p=$
Baseline Tension	<.001	.99
Beverage	.005	.65
Caffeine	<.001	.89
Bev. x Caff. interaction	.045	.16
Type A	<.001	.87
Sex	<.001	.87

Dependent Variable: POMS Tension, Baseline

I.V.	Change in R^2	Significance level $p=$
Type A	.010	.49
Sex	.002	.78

Table 8b

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: POMS Depression (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Depression	.090	.03
Beverage	.005	.63
Caffeine	.017	.36
Bev. x Caff. interaction	.003	.72
Type A	.011	.47
Sex	.017	.37

Dependent Variable: POMS Depression, Baseline

I.V.	Change in R^2	Significance level p=
Type A	.003	.71
Sex	.004	.69

Table 8c

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: POMS Vigor (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Vigor	.220	<.01
Beverage	.013	.38
Caffeine	.048	.09
Bev. x Caff. interaction	.019	.29
Type A	.014	.37
Sex	.066	.04

Dependent Variable: POMS Vigor, Baseline

I.V.	Change in R^2	Significance level p=
Type A	.002	.75
Sex	.007	.58

Table 8d

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: POMS Anger (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Anger	.075	.06
Beverage	<.001	.97
Caffeine	.077	.05
Bev. x Caff. interaction	<.001	.94
Type A	.027	.25
Sex	<.001	.96

Dependent Variable: POMS Tension, Baseline

I.V.	Change in R^2	Significance level p=
Type A	<.001	.85
Sex	.003	.72

Table 8e

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: POMS Fatigue (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Fatigue	.230	<.01
Beverage	.022	.26
Caffeine	.020	.28
Bev. x Caff. interaction	.028	.19
Type A	.022	.25
Sex	.005	.57

Dependent Variable: POMS Fatigue, Baseline

I.V.	Change in R^2	Significance level p=
Type A	.004	.68
Sex	.077	.06

Table 8f

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: POMS Confusion (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Confusion	.096	.03
Beverage	.006	.59
Caffeine	.038	.17
Bev. x Caff. interaction	.037	.17
Type A	.012	.44
Sex	.002	.74

Dependent Variable: POMS Tension, Baseline

I.V.	Change in R^2	Significance level p=
Type A	.004	.65
Sex	.012	.46

Table 9a

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Feelings and Mood Relaxed (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Relaxed	.037	.19
Beverage	.003	.69
Caffeine	.008	.54
Bev. x Caff. interaction	>.001	.98
Type A	.013	.45
Sex	.011	.49

Dependent Variable: Feelings and Mood Relaxed, Baseline

I.V.	Change in R^2	Significance level p=
Type A	<.001	.90
Sex	<.001	.86

Table 9b

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Feelings and Mood Lethargy (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Lethargy	.174	<.01
Beverage	.012	.42
Caffeine	.112	.01
Bev. x Caff. interaction	.011	.42
Type A	.025	.22
Sex	.009	.45

Dependent Variable: Feelings and Mood Lethargy, Baseline

I.V.	Change in R^2	Significance level p=
Type A	.005	.62
Sex	.067	.08

Table 9c

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Feelings and Mood Need a Stimulant (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Need a Stim.	.172	<.01
Beverage	.139	<.01
Caffeine	<.001	.89
Bev. x Caff. interaction	.016	.32
Type A	.009	.45
Sex	<.001	.87

Dependent Variable: Feelings and Mood Need a Stim., Baseline.

I.V.	Change in R^2	Significance level p=
Type A	.009	.52
Sex	.112	.02

Table 9d

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Feelings and Mood Headache (change from baseline- see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Headache	<.001	.99
Beverage	.046	.15
Caffeine	.132	.01
Bev. x Caff. interaction	.035	.17
Type A	.005	.60
Sex	.020	.31

Dependent Variable: Feelings and Mood Headache, Baseline

I.V.	Change in R^2	Significance level p=
Type A	.027	.27
Sex	.029	.25

Table 10a

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Auditory Vigilance Task, Response Latency (change from baseline for last 10 minutes of post-beverage task - see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Response Latency	.029	.25
Beverage	.043	.15
Caffeine	.017	.37
Bev. x Caff. interaction	.010	.49
Type A	.021	.33
Sex	.051	.12

Dependent Variable: Auditory Vigilance Task, Response Latency, Baseline.

I.V.	Change in R^2	Significance level p=
Type A	.024	.30
Sex	.056	.11

Table 10b

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Auditory Vigilance Task, False Positives (change from baseline for last 10 minutes of post-beverage task - see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline False Positives	.129	.01
Beverage	.006	.57
Caffeine	<.001	.98
Bev. x Caff. interaction	.006	.60
Type A	.004	.67
Sex	.004	.67

Dependent Variable: Auditory Vigilance Task, False Positives, Baseline.

I.V.	Change in R^2	Significance level p=
Type A	.031	.23
Sex	.041	.16

Table 10c

Proportion of variance for each independent variable (IV), listed in order of multiple regression entry.

Dependent Variable: Auditory Vigilance Task, Errors of Omission (change from baseline for last 10 minutes of post-beverage task - see footnote 1).

I.V.	Change in R^2	Significance level p=
Baseline Errors of Omission	.041	.17
Beverage	.032	.22
Caffeine	.006	.61
Bev. x Caff. interaction	.026	.27
Type A	.022	.31
Sex	.023	.30

Dependent Variable: Auditory Vigilance Task, Errors of Omission, Baseline.

I.V.	Change in R^2	Significance level p=
Type A	.102	.03
Sex	.002	.73

Figure Caption: **1A**: Mean heart rate (beats per minute), represented as change from baseline over the 30 minute post-beverage period, for the four experimental groups (Tea- = herbal tea with no added caffeine; Tea+ = herbal tea with 200 mg of added caffeine; Coffee- = decaffeinated coffee with no added caffeine; Coffee+ = decaffeinated coffee with 200 mg of added caffeine). MANCOVA revealed a significant main effect for caffeine, $p < .05$. Overall means and standard errors for the caffeine (Tea+ and Coffee+) and no caffeine (Tea- and Coffee-) groups, collapsed over the five post-beverage measurements, were -5.49 (0.68) and -2.28 (0.60) respectively.

1B: Mean systolic blood pressure, represented as change from baseline over the 30 minute post-beverage period, for the four experimental groups. MANCOVA revealed a significant main effect for caffeine, $p < .001$. Overall means and standard errors for the caffeine (Tea+ and Coffee+) and no caffeine (Tea- and Coffee-) groups, collapsed over the five post-beverage measurements, were 4.01 (0.73) and -2.52 (0.65) respectively.

1C Mean diastolic blood pressure, represented as change from baseline over the 30 minute post-beverage period, for the four experimental groups MANCOVA revealed a significant main effect for caffeine, $p < .001$. Overall means and standard errors for the caffeine (Tea+ and Coffee+) and no caffeine (Tea- and Coffee-) groups, collapsed over the five post-beverage measurements, were 4.75 (0.65) and -0.06 (0.58) respectively.

Figure 1

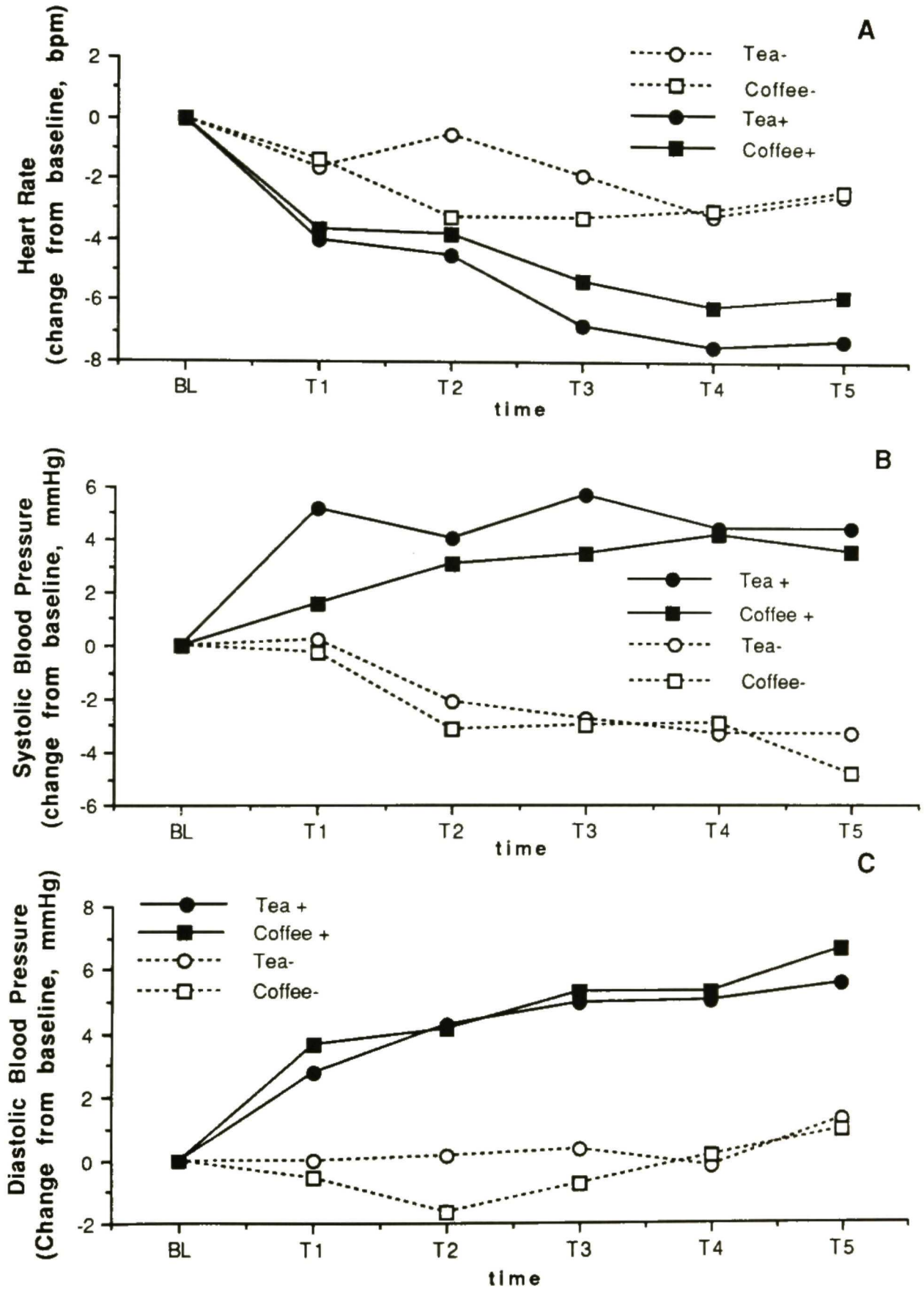

A
Heart Rate
(change from baseline, bpm)
2
0
-2
-4
-6
-8
Tea-
Coffee-
Tea+
Coffee+
BL
T1
T2
T3
T4
T5
time
B
Systolic Blood Pressure
(change from baseline, mmHg)
6
4
2
0
-2
-4
-6
Tea +
Coffee +
Tea-
Coffee-
BL
T1
T2
T3
T4
T5
time
C
Diastolic Blood Pressure
(Change from baseline, mmHg)
8
6
4
2
0
-2
Tea +
Coffee +
Tea-
Coffee-
BL
T1
T2
T3
T4
T5
time

Figure Caption: **2:** Mean heart rates (beats per minute), at baseline and over the 30 minute post-beverage period, for the experimental groups receiving herbal tea (Tea- = herbal tea with no added caffeine; Tea+ = herbal tea with 200 mg of added caffeine) and the non-coffee drinking control group (Control). Dunnett's test revealed differences between the control group and both the Tea- and Tea+ group at baseline and post beverage, ps <.05. Means and standard errors for the Control, Tea- and Tea+ groups at baseline were 63.0 (1.40), 72.17 (1.26) and 74.17 (1.73) respectively.

Figure 2

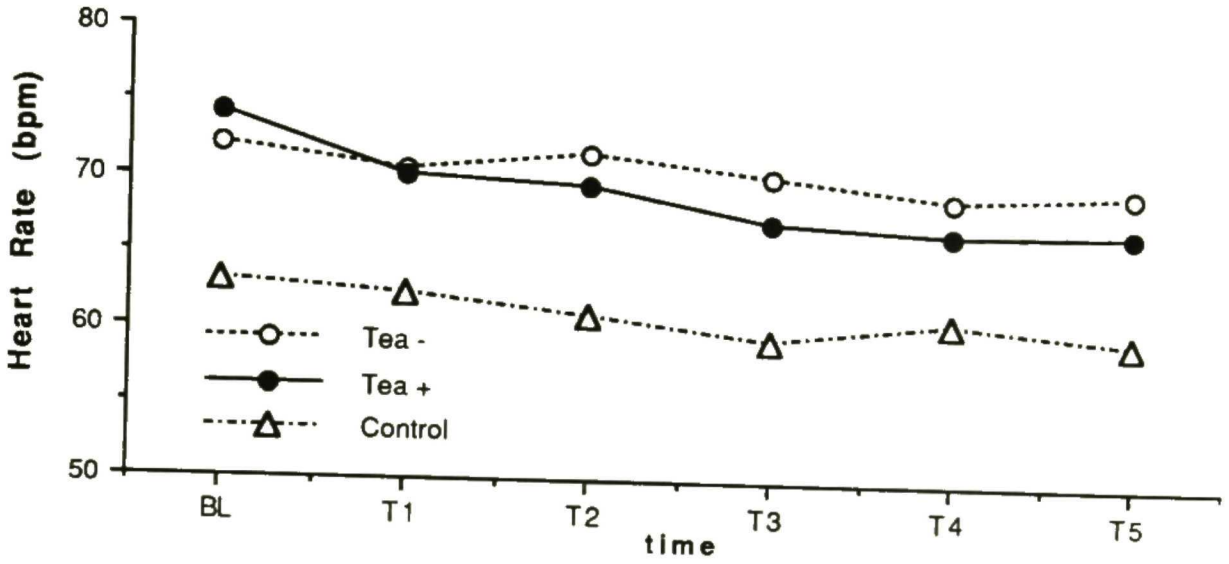


Figure Caption: **3A:** Mean scores from the POMS Anger scale representing change from baseline for the caffeine (herbal tea with 200 mg of added caffeine and decaffeinated coffee with 200 mg of added caffeine, collapsed) and no caffeine (herbal tea with no added caffeine and decaffeinated coffee with no added caffeine, collapsed) groups. Standard errors are indicated with vertical bars. ANCOVA revealed a significant main effect for caffeine, $p = .05$.

3B: Mean scores from the POMS Vigor scale representing change from baseline for the caffeine (herbal tea with 200 mg of added caffeine and decaffeinated coffee with 200 mg of added caffeine, collapsed) and no caffeine (herbal tea with no added caffeine and decaffeinated coffee with no added caffeine, collapsed) groups. Standard errors are indicated with vertical bars. ANCOVA revealed a near significant main effect for caffeine, $p = .09$.

Figure 3

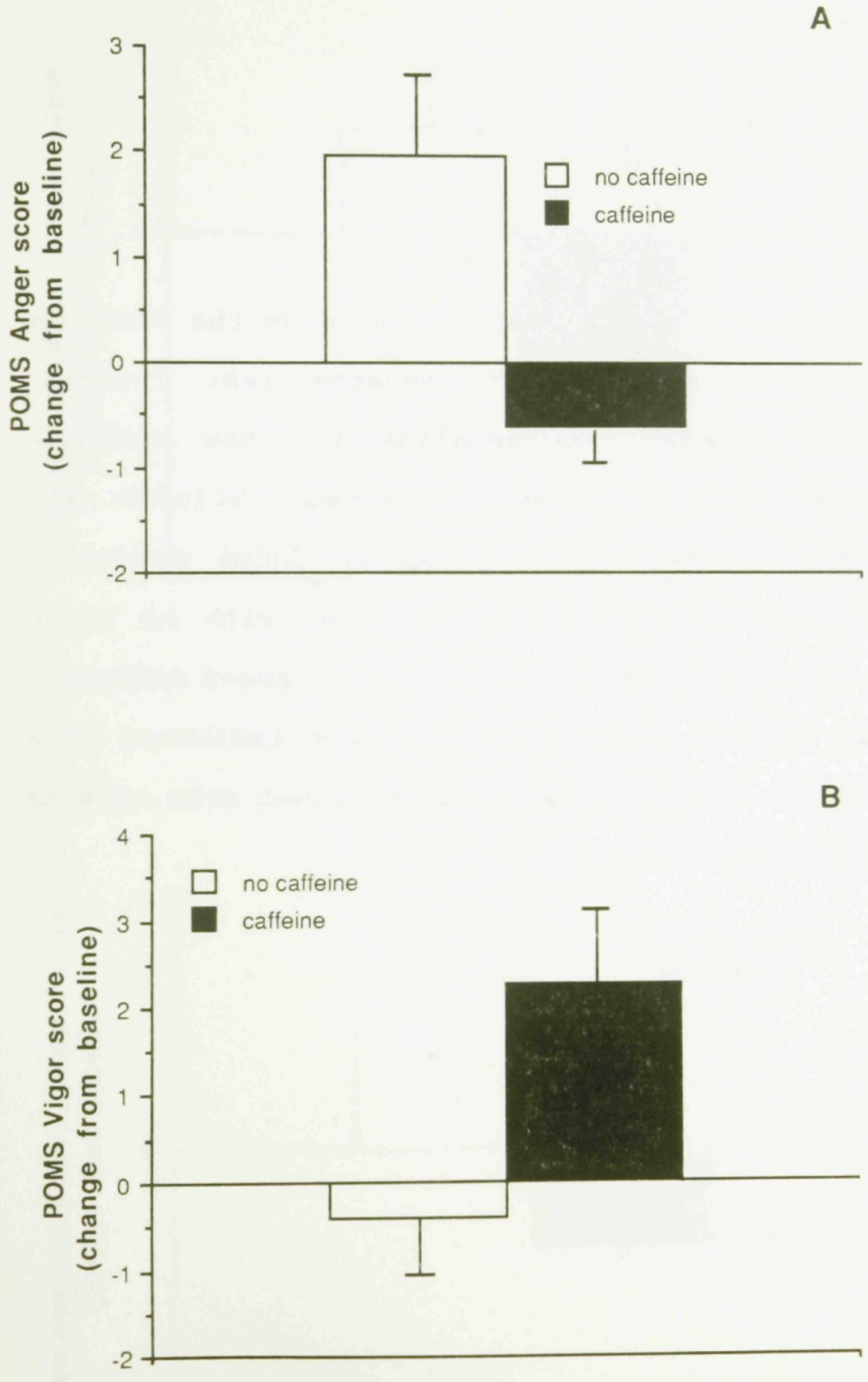

A
POMS Anger score
(change from baseline)
3
2
1
0
-1
-2
no caffeine
caffeine
B
POMS Vigor score
(change from baseline)
4
3
2
1
0
-1
-2
no caffeine
caffeine

Figure Caption: **4A & B** : Mean scores from the Feelings and Mood Lethargy (4A) and Headache (4B) factors, representing change from baseline for the caffeine (herbal tea with 200 mg of added caffeine and decaffeinated coffee with 200 mg of added caffeine, collapsed) and no caffeine (herbal tea with no added caffeine and decaffeinated coffee with no added caffeine, collapsed) groups. Standard errors are indicated with vertical bars. ANCOVA revealed significant main effects for caffeine, ps <.01.

Figure 4

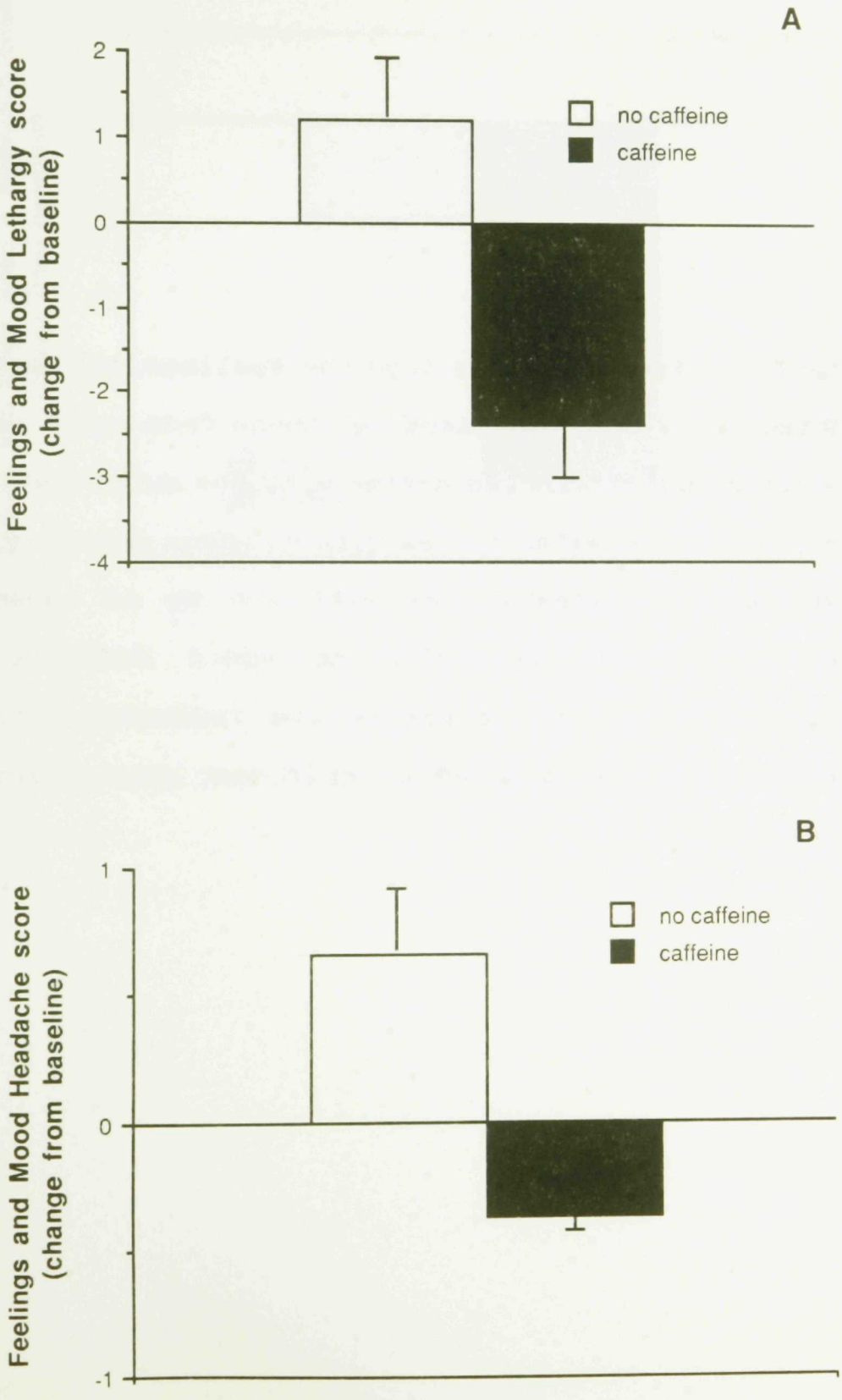

A
Feelings and Mood Lethargy score
(change from baseline)
2
1
0
-1
-2
-3
-4
no caffeine
caffeine
B
Feelings and Mood Headache score
(change from baseline)
1
0
-1
no caffeine
caffeine

Figure Caption: 5: Mean scores from the Feelings and Mood Need a Stimulant factor representing change from baseline for the coffee (decaffeinated coffee with 200 mg of added caffeine and decaffeinated coffee with no added caffeine, collapsed) and tea (herbal tea with 200 mg of added caffeine, and herbal tea with no added caffeine, collapsed) groups. Standard errors are indicated with vertical bars. ANCOVA revealed a significant main effect for beverage, $p < .01$.

Figure 5

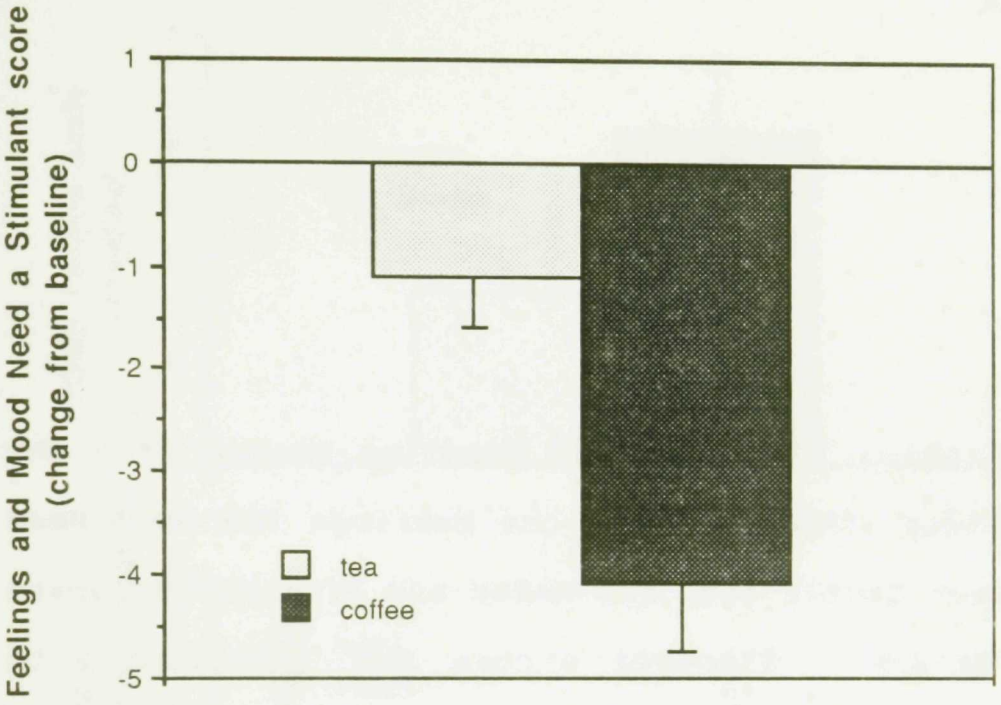

Feelings and Mood Need a Stimulant score
(change from baseline)
1
0
-1
-2
-3
-4
-5
tea
coffee

Figure Caption: **6A & B:** Mean baseline scores from the POMS Fatigue (6A) scale and the Feelings and Mood Need a Stimulant factor (6B) for males and females collapsed across groups. Standard errors are indicated with vertical bars. ANOVA revealed significant effects for sex, ps <.05.

6C: Mean scores from the POMS Vigor scale representing change from baseline for males and females collapsed across groups. Standard errors are indicated with vertical bars. ANCOVA revealed a significant effect for sex, p <.05.

Figure 6

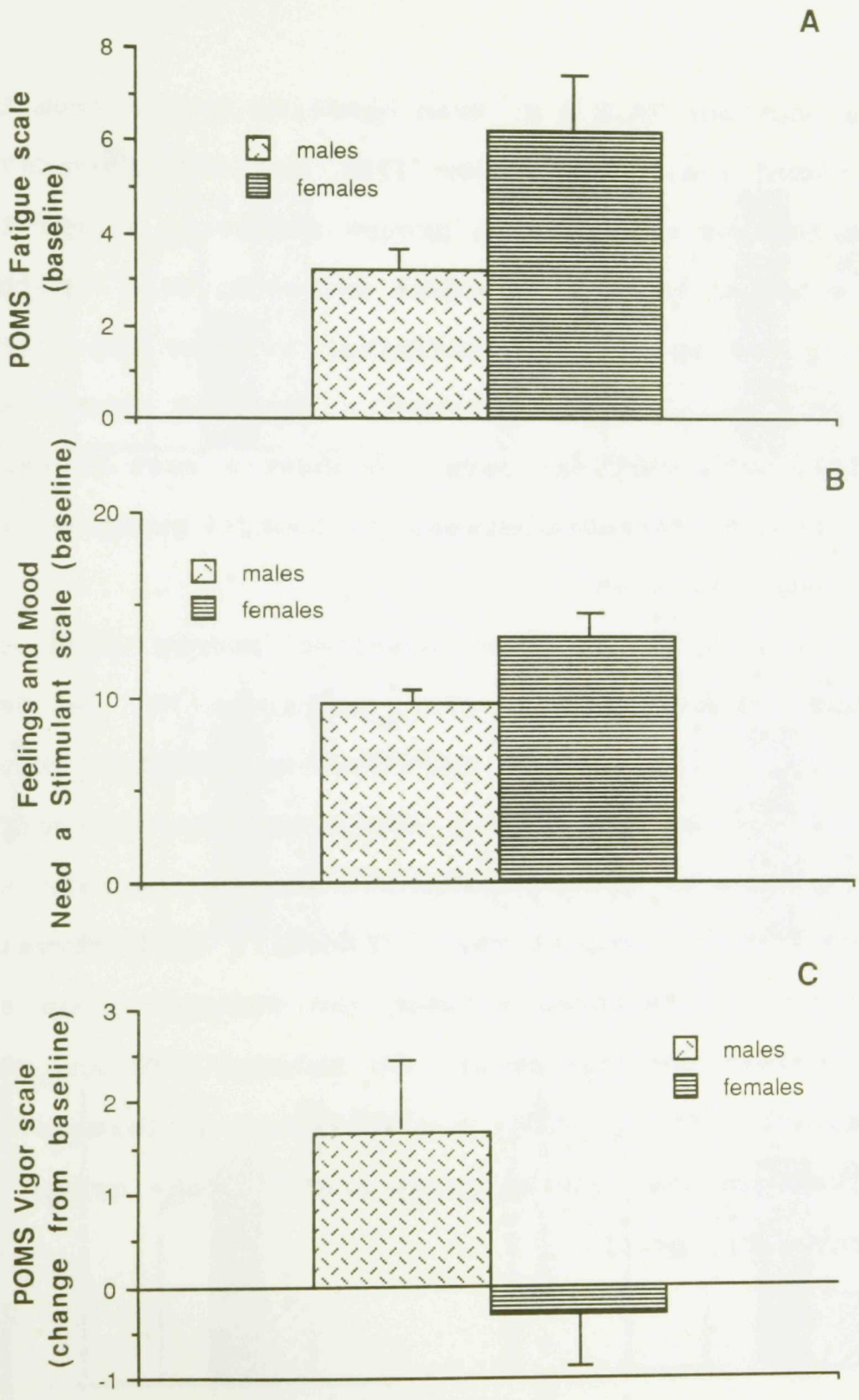

A
POMS Fatigue scale
(baseline)
8
6
4
2
0
males
females
B
Feelings and Mood
Need a Stimulant scale (baseline)
20
10
0
males
females
C
POMS Vigor scale
(change from baseliine)
3
2
1
0
-1
males
females

Figure Caption: **7A,B & C:** Mean baseline scores from the POMS Vigor (7A), Depression (7B) and Confusion (7C) scales for the experimental groups receiving herbal tea (Tea- = herbal tea with no added caffeine; Tea+ = herbal tea with 200 mg of added caffeine) and the non-coffee drinking control group (Control). Standard errors are indicated with vertical bars. Dunnett's test revealed significant differences between the Control group and the Tea+ groups, ps <.05.

7D, E, & F: Mean baseline scores from the Feelings and Mood Relaxed (7D), Lethargy (7E) and Need a Stimulant (7F) factors for the experimental groups receiving herbal tea (Tea-& Tea+) and the non-coffee drinking control group (Control). Standard errors are indicated with vertical bars. Dunnett's test revealed significant differences between the Control group and both the Tea- and Tea+ group, for Relaxed (7D) and Need a Stimulant (7F), ps <.05. A significant difference was found between the Control group and the Tea+ group for Lethargy (7E), p<.05.

Figure 7

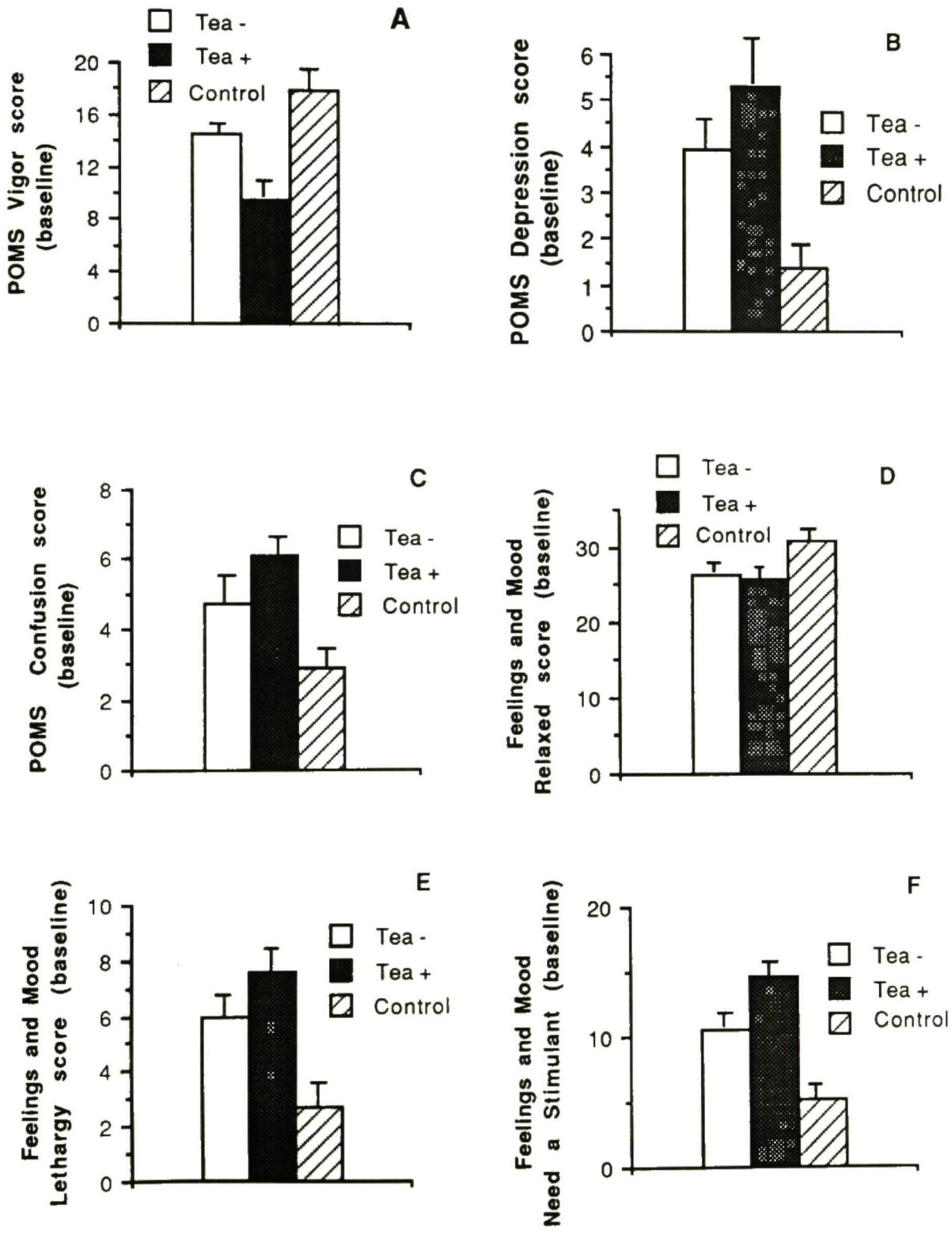

A
Tea -
Tea +
Control
POMS Vigor score (baseline)
20
16
12
8
4
0
B
POMS Depression score (baseline)
6
5
4
3
2
1
0
Tea -
Tea +
Control
C
POMS Confusion score (baseline)
8
6
4
2
0
Tea -
Tea +
Control
D
Feelings and Mood Relaxed score (baseline)
30
20
10
0
Tea -
Tea +
Control
E
Feelings and Mood Lethargy score (baseline)
10
8
6
4
2
0
Tea -
Tea +
Control
F
Feelings and Mood Need a Stimulant (baseline)
20
10
0
Tea -
Tea +
Control

Figure Caption: **8A,B,C & D**: Mean post beverage scores from the POMS Fatigue (8A) and Confused (8B) scales and the Feelings and Mood Lethargy (8C) and Headache (8D) factors for the experimental groups receiving herbal tea (Tea- = herbal tea with no added caffeine; Tea+ = herbal tea with 200 mg of added caffeine) and the non-coffee drinking control group (Control). Standard errors are indicated with vertical bars. Dunnett's test revealed significant differences between the Control group and the Tea- group, ps <.05.

8E & F: Mean baseline scores from the Feelings and Mood Relaxed and Need a Stimulant Factors scale for the experimental groups receiving herbal tea (Tea- & Tea+) and the non-coffee drinking control group (Control). Standard errors are indicated with vertical bars. Dunnett's test revealed significant differences between the Control group and both the Tea- and Tea+ group, ps <.05.

Figure 8

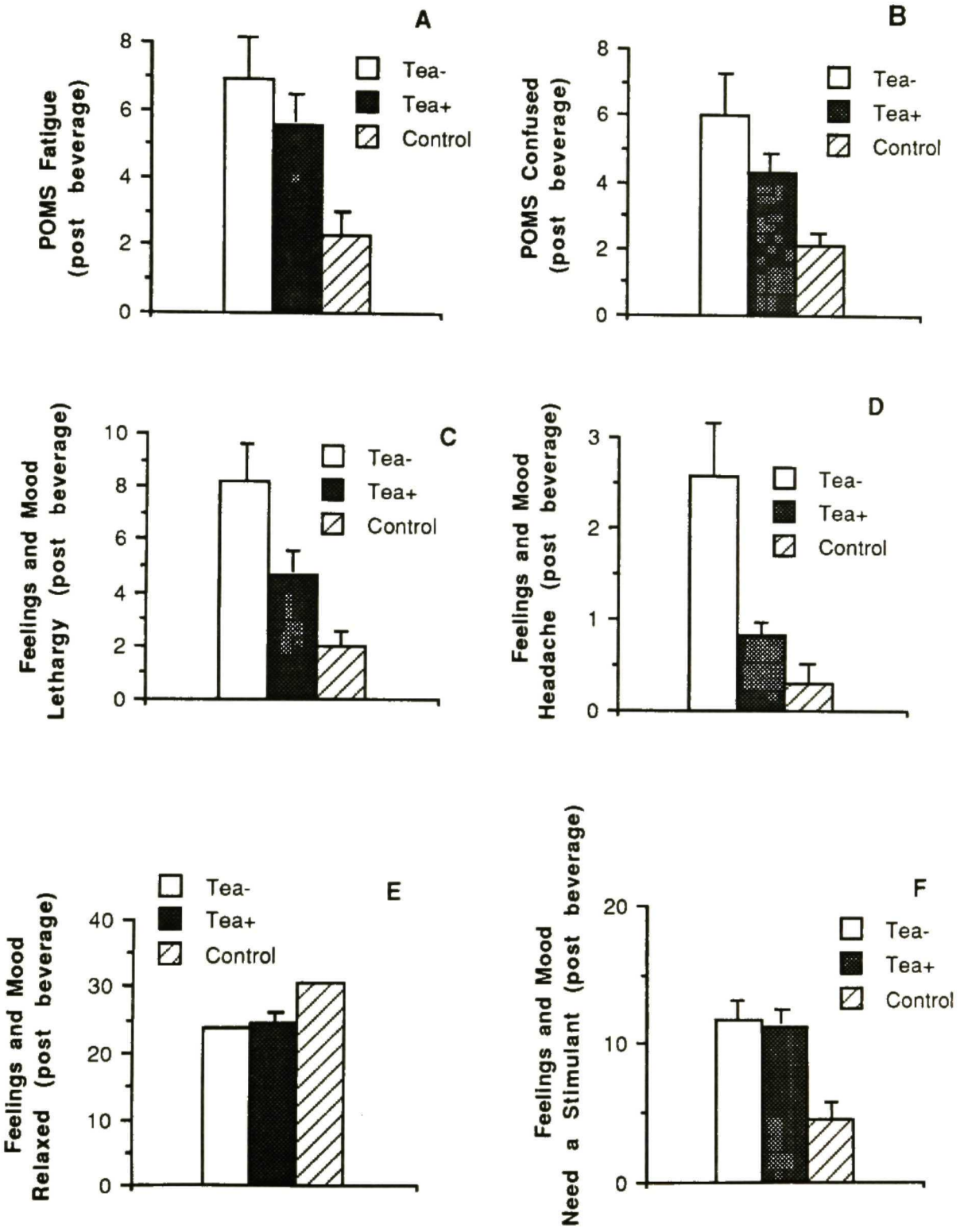

A
POMS Fatigue (post beverage)
8
6
4
2
0
Tea-
Tea+
Control
B
POMS Confused (post beverage)
8
6
4
2
0
Tea-
Tea+
Control
C
Feelings and Mood Lethargy (post beverage)
10
8
6
4
2
0
Tea-
Tea+
Control
D
Feelings and Mood Headache (post beverage)
3
2
1
0
Tea-
Tea+
Control
E
Feelings and Mood Relaxed (post beverage)
40
30
20
10
0
Tea-
Tea+
Control
F
Feelings and Mood Need a Stimulant (post beverage)
20
10
0
Tea-
Tea+
Control

Figure Caption: **9**: Mean scores from the POMS Vigor scale representing change from baseline for the experimental groups receiving herbal tea (Tea- = herbal tea with no added caffeine; Tea+ = herbal tea with 200 mg of added caffeine) and the non-coffee drinking control group (Control). Standard errors are indicated with vertical bars. Dunnett's test revealed a significant difference between the Control group and the Tea+ group, $p < .05$.

Figure 9

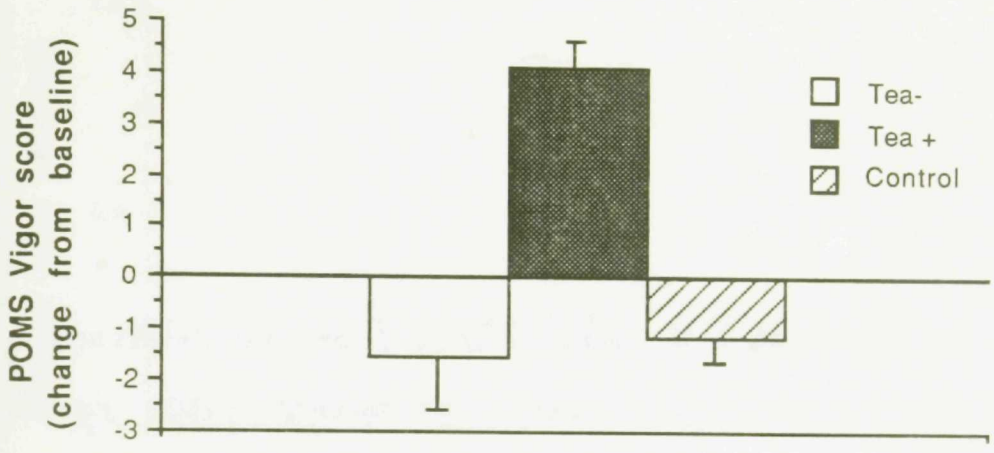

POMS Vigor score
(change from baseline)
5
4
3
2
1
0
-1
-2
-3
Tea-
Tea +
Control

Figure Caption **10A & B**: Mean scores from the Feelings and Mood Headache (10A) and Need a Stimulant (10B) factors representing change from baseline for the experimental groups receiving herbal tea with no added caffeine (Tea-) and decaffeinated coffee with no added caffeine (Coffee-). Standard errors are indicated with vertical bars. Planned comparisons revealed significant differences between the Tea- and Coffee- groups, ps <.05.

Figure 10

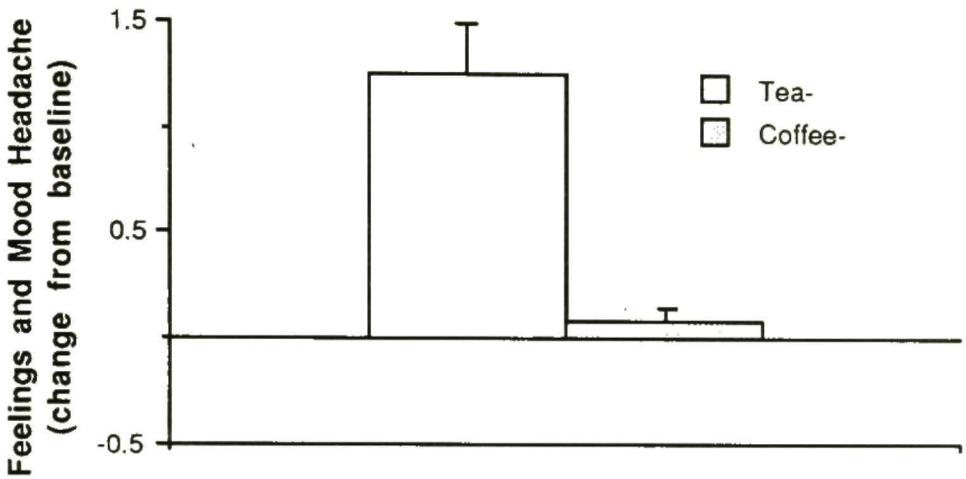
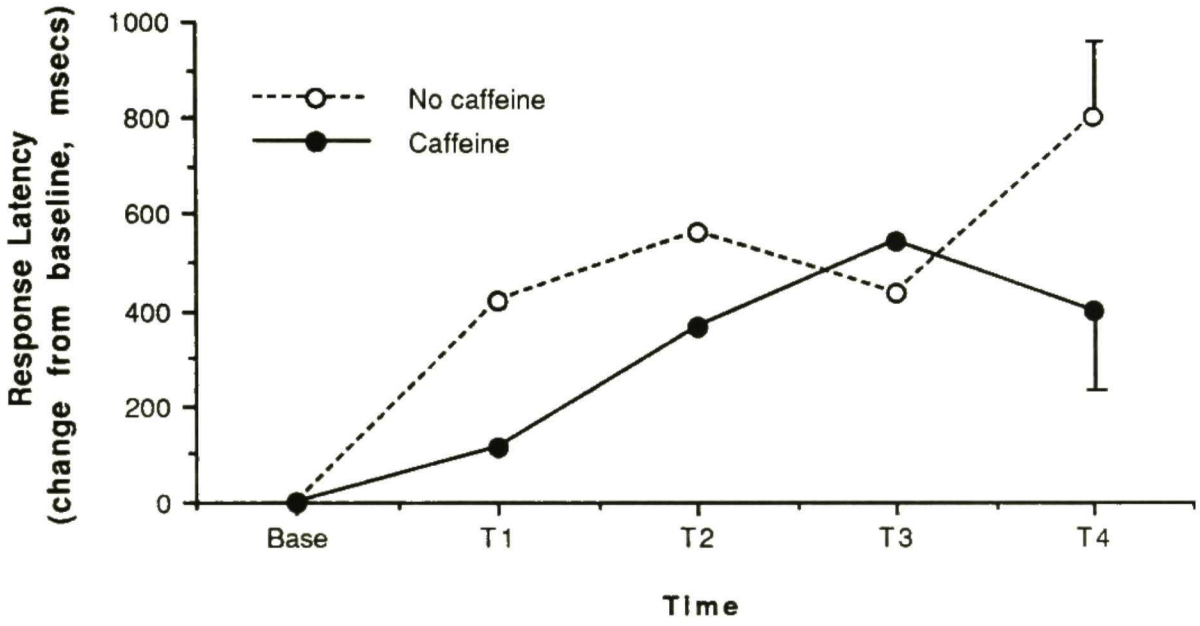

Feelings and Mood Headache
(change from baseline)
1.5
0.5
-0.5
Tea-
Coffee-

Figure Caption: **11:** Mean Response Latency (milliseconds) from the auditory vigilance task, represented as change from baseline over the 40 minute post-beverage task for the caffeine (herbal tea with 200 mg of added caffeine and decaffeinated coffee with 200 mg of added caffeine, collapsed) and no caffeine (herbal tea with no added caffeine and decaffeinated coffee with no added caffeine, collapsed) groups. Standard errors are indicated for the forth 10 minute period with vertical bars. MANCOVA revealed a near significant interaction for caffeine x time, $p = .09$.

Figure 11


Response Latency
(change from baseline, msecs)
1000
800
600
400
200
0
No caffeine
Caffeine
Base
T1
T2
T3
T4
Time

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Footnote

[1] Note that what is being predicted is change from baseline scores. The contribution that baseline values of the dependent measures make to the variance in change from baseline for the dependent measures may be lower than would be expected if post-beverage measures been predicted. Baseline was associated with significant changes in R^2 for 7 of the 13 primary dependent variables reflecting change from baseline in Tables 8a through 10c ($p < .05$).