THE INTERACTION BETWEEN CAFFEINE AND ANXIETY LEVEL DURING STRESS

A thesis
submitted in partial fulfilment
of the requirements for the Degree
of
Master of Science in Psychology
in the
University of Canterbury

by

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University of Canterbury
1985

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ABSTRACT

An experiment was conducted to examine the potential interaction of caffeine and psychological stress in human subjects. More specifically, subjects comprised of those who showed 'high' and 'low' trait anxiety levels as determined by administration of the Spielberger Trait - Anxiety Inventory. Each student consumed caffeine on a regular basis (2 or more cups of coffee and/or tea per day).

Subjects were run in a single-blind, randomized cross-over design with caffeine (400mg) and placebo. Each subject participated in two, one and a half hour experimental sessions held one week apart.

The cardiovascular effects of a high (400mg) dose of caffeine, equivalent to 4 or 5 cups of coffee, were measured during periods of rest and psychological stress. The stressor involved the administration of a mental arithmetic task (serial subtraction) with a set time limit. Subjects were required to perform as well as they could under challenging conditions. In addition, subjects reported subjective "alertness" and "tension" after each part of each session, using 10cm visual analogue scales representing each of these two dimensions.

Previous investigations have documented correlations between caffeine intake and variables of heart rate, blood

pressure, alertness, tension, and performance, but there has been no experimental work comparing the response of high and low trait anxiety subjects with respect to these variables.

Since caffeine is a central nervous system stimulant it is reasonable to suggest that the drug could be used as a means for low anxiety people to reach an optimal level of arousal, and hence perform optimally in a stressful situation (eg. exams or public speaking). Likewise, it is equally reasonable to suggest that caffeine usage may well be avoided by those people who have high anxiety levels if they are to perform well.

The experimental results showed that the order of drug presentation proved more than caffeine administration to be the most recurrent and important variable involved in interaction. Caffeine did not appear to have a potential additive effect on the cardiovascular measurements and subjective self reports, with that produced by psychological stress. High anxiety female subjects showed the greatest elevation in resting systolic and diastolic blood pressure with caffeine consumption. Low anxiety males showed the greatest elevation in diastolic blood pressure with caffeine consumption during the stressful situation. High anxiety males and low anxiety females showed the greatest elevations in heart rate during rest. Males showed greater reported levels of tension with caffeine consumption both at rest and during stress, than did females. High anxiety subjects showed greater elevations in alertness both at rest and during stress following caffeine consumption than low anxiety subjects. Finally, caffeine

consumption was found to have no effect on performance in a mental arithmetic task, in both high and low anxiety groups.

It is concluded from the results that caffeine administration (400mg) cannot be used as a means for a low anxiety person to reach an optimal drive or stress level to perform optimally during a stressful situation. Likewise, there was no evidence to suggest that those who have high anxiety levels should avoid caffeine consumption to achieve such a goal.

CHAPTER ONE

INTRODUCTION

SOURCE AND HISTORY

Nonmedically, caffeine is the most widely used central nervous system stimulant. Found in a number of plants it is contained in beverages and/or flavourings being popular in the form of coffee, tea, cocoa and "cola" drinks.

Caffeine is found in various prescription medications and over-the-counter preparations.

Table 1 illustrates the common sources of caffeine and its approximate concentrations.

Caffeine is also found in certain noncola softdrinks, such as Mellow Yellow, Mountain Dew, and Sunkist Orange, as well as in teas containing mate', guarena, and youpon.

Man discovered caffeine in many forms:

- Coffee was found in Arabia and Turkey; after spreading to these and other near Eastern and African regions from Ethiopia.
- Tea was found in China.

- The kola nut was found in common use in west Africa, and was later introduced into cola drinks as a source of caffeine.
- The cocoa tree was discovered in Mexico, the West Indies, and much of central and south Africa. Chocolate from this tree was the favourite beverage of the Emperor Montezuma; it was said that 50 pitcherfuls a day were prepared for his use. Throughout the world this drink soon became popular.
- The ilex plant, source of the caffeine drink known as mate' or Paraguayan tea, was found in Brazil and elsewhere in the American tropics. In the United States this tea is still drunk as yerba mate', and it rivals coffee and tea in popularity in parts of South America.
- Cassina - also known as youpon, the Christmas berry tree, and the North American tea plant, was found in common use as the source of a caffeine beverage among Indians from Virginia to Florida and west along the Gulf coast to the Rio Grande. Cheney (1925), reported at the time that "none of the Indians but their great Exploits of War and Noble Actions, are admitted to the use of this noble beveridge."

White settlers in these regions prepared a tea known as the "Black Drink", "Black Drought", or dohoon, from the same plant.

They also produced a drink containing both alcohol and caffeine by letting the leaves ferment.

Table 1

Common Sources of Caffeine

Source	Concentration
Beverages	
Brewed coffee	85 mg/150 ml
Instant coffee	60 mg/150 ml
Brewed black tea	50 mg/150 ml
Brewed green tea	30 mg/150 ml
Instant tea	30 mg/150 ml
Decaffeinated coffee	3 mg/150 ml
Cola drinks	32-65 mg/12 oz
Cocoa	6-142 mg/150 ml
Prescription medications	
APGs (asprin, phenacetin, and caffeine)	32 mg/tablet
Cafergot	100 mg/tablet
Darvon compound	32 mg/tablet
Fiorinal	40 mg/tablet
Migrol	50 mg/tablet
Over-the-counter preparations	
Anacin, asprin compound, Bromo-Seltzer	32 mg/tablet
Cope, Easy-Mens, Empirin compound,	
Midol	32 mg/tablet
Vanquish	32 mg/tablet
Excedrin	60 mg/tablet
Pre Mens	66 mg/tablet
Bromoquinine	15 mg/tablet
Sinarest	30 mg/tablet
Dristan	30 mg/tablet
No Doz	100 mg/tablet
Vi Varin	100-220 mg/tablet

Source: Sawyer et al. (1981) (Taken from Stephenson (1977) and Graham (1978).

When newly introduced, coffee was considered to be an intoxicating brew, dangerous to health. However, coffee became a welcome and socially acceptable drink despite medical warnings and efforts to suppress it (Stephenson, 1977).

The controversey over the health aspects of coffee continues. Increasingly the debate has focused on caffeine. Heavy users of caffeine containing beverages report tolerance (including cross-tolerance among the Xanthine (Theophylline, Caffeine, and Theobromine) beverages), physical dependence with withdrawal symptons and craving (Brecher et al., 1972).

The basis for the popularity of all the caffeine containing beverages has been the ancient belief that these beverages had stimulant and antisoporific actions that elevated mood, decreased fatigue, and increased capacity for work (Roll, 1980).

For example, legend credits the discovery of coffee to a prior of an Arabian convent. Shepherds reported that goats that had eaten the berries of the coffee plant gamboled and frisked about all through the night instead of sleeping. Mindful of the long nights of prayer that he had to endure, the prior instructed the shepherds to pick the berries so that he might make a beverage from them.

Classical pharmacological studies, principally of caffeine during the first half of this century have confirmed these beliefs, and have revealed that Xanthines possess other important pharmacological properties as well.

Pharmacological Properties

Caffeine pharmacologically impacts most physiological systems. With regard to the central nervous system (CNS), caffeine is a power stimulant. Such stimulation undoubtedly accounts for the popularity of caffeinated beverages. It is claimed (Ritchie, 1975; Graham, 1978), that coffee and tea promote rapid, clear thinking, improved intellectual effort, enhanced mental activity, and decreased drowsiness, fatigue, and reaction time - all valued commodities in an achievement oriented society. Most of these stimulating actions are accounted for by the fact that caffeine affects all parts of the cortex. Caffeine also affects the respiratory, vasomotor, and vagal centres of the medulla, as well as all parts of the spinal cord at high doses.

Caffeine's action on the cardiovascular system can be detected in systemic, coronary, and cerebral circulation patterns. The coronary arteries and the pulmonary and general systemic vessels become dilated following caffeine ingestion. Heart rate and force of contraction also increase. Many of these peripheral effects cannot be observed directly, however, because they tend to be masked by central stimulating effects upon the medulla. Therefore, at moderate doses a person may notice no change in heart rate, no tachycardia (rapid beating), or even a slight bradycardia (slow beating).

Caffeine significantly affects gastric secretion within the gastrointestinal system which results in prolonged enlargement of both volume and acidity.

The commonly experienced "coffee diuresis" is a result of caffeine's effect on the renal system.

Finally, caffeine relaxes smooth muscles (especially of the bronchi), strengthens the contraction of skeletal muscles, and increases basal metabolic rate an average of 10 per cent among regular coffee drinkers (Brecher at al., 1972).

Table 2 illustrates the Biological effects of caffeine.

Table 2

Biological Effects of Caffeine

- Diuretic
- Cardiac Muscle stimulant
- Central Nervous System stimulant
- Smooth Muscle Relaxant
- Stimulates Fastric Acid Secretion
- Elevates Plasma Free Fatty Acids and Glucose
- Pharmacologically Active Dose 200 mg
- Probably not Mutagenic for Man

Source: Graham (1978)

Caffeine and related Xanthines serve a number of specific medicinal purposes as listed in Table 3.

Table 3

Pharmacological Uses of Caffeine
and Related Compounds

Desired Action	Preferred Compound
Cerebral Stimulation	Caffeine (Coffee)
Coronary Dilation	Theophylline (Tea)
Diuresis	Theobromine (Cocoa)
Respiratory Stimulant for Premature Infants	Caffeine

Source: Graham (1978)

Note that caffeine is preferred as a stimulant, theophylline from tea is preferred as a coronary dilator, and theobromine from cocoa is preferred as a diuretic (Krontz, 1954).

The annual world consumption of coffee exceeds four million tons (Robertson et al., 1978). In some countries this amount translates into a per capita ingestion of 100g of pure caffeine each year.

Dosage is a relevant consideration in the study of caffeine pharmacology. Fifty to 200mg of caffeine is typically required to produce expected pharmacological actions (Greden, 1974). Truitt (1971) refers to doses of over 250mg as being "large".

Of clinical significance, this dosage is frequently exceeded in everyday life. As indicated in Table 1, caffeine is widely available in a multiplicity of beverages and medications. When cumulatively considered, an individual can ingest doses much higher than 250mg - often without being aware of it. For example, three cups of coffee, two over-the-counter headache tablets, and one cola drink consumed in one morning approximates an intake of 500mg caffeine.

It is easy to see that among heavy coffee or tea drinkers dosages would frequently exceed this by gross amounts.

Definitive tests have shown that caffeine is not adaptive, ie. regular consumption does not diminish its stimulant effects. However, caffeine-withdrawal headache is well documented.

The consumption of high levels of caffeine clearly becomes a toxic condition. The LD_{50} of orally administered caffeine for the mouse, rat, guinea pig, rabbit, cat, dog and hamster has ranged from 100 to 1050mg per kg (Graham, 1978).

Within recent years, the chronic effects of caffeine have been of much interest. No growth retardation, reproductive impairment, nor any other pathological problems have been found at levels of 35 to 60mg per kg of body weight daily for 26 weeks administered to rats in drinking water. No adverse effects on fertility or mortality of rats were produced after daily injection with 100mg caffeine per kilogram of body weight for four generations.

However, higher levels of caffeine near the LD_{50}, ie. 150mg per kilogram, produced a variety of pathological effects over periods of 100 days; the effects included loss of hair, dermotitis, thymic atrophy and congestion of many organs (Select Committee on GRAS Substances, 1976).

Whether any relationship exists between caffeine and the pathogenesis of peptic ulcers has long been debated. Several experimental animals as well as human subjects in single dose experiments have shown stimulation of gastric secretion by caffeine. However, a variety of feeding studies

have failed to establish a clear-cut cause and effect relationship between caffeine ingestion and induction or exacerbation of peptic ulcer (Select Committee on GRAS Substance, 1976).

Several studies have indicated that caffeine may exhibit genetic activity in vitro, but in vivo investigations failed to demonstrate mutagenic effects of caffeine (Kreybig and van Czok, 1975; Furmanova, 1976; Weathersbee et al., 1977; Timson, 1977).

The transfer of caffeine across the placental barrier occurs readily and the developing foetus as well as the gonads are subject to the same levels of caffeine present in body water of other tissues. In a variety of studies teratogenic effects have been shown with laboratory animals when caffeine was administered other than by the oral route. However, teratogenic effects were generally absent at oral doses of 50mg per kilogram of body weight and lower (Graham, 1978).

Major interest has recently been focused on the cardiovascular effects of caffeine after the suggestion that coffee drinking might be associated with an increased risk of myocardial infarction; caffeine ingestion has long been known to predispose to extrasystoles.

In spite of the widespread consumption of caffeine and its broad spectrum of pharmacologic activity, substantial gaps in the understanding of its cardiovascular and endocrine

pharmacology remain. For example, it has been reported to increase respiration slightly at high doses (Scott and Chem, 1944), but it has variably been said both to raise (Salla Torre et al, 1952), and to lower, (Cotton et al., 1968), the heart rate, both to increase (Grollman et al., 1930), and to decrease (Starr et al., 1937), the arteriovenous oxygen difference, to raise blood pressure and cardiac output (Stepp et al., 1938; Ritchie, 1975; Robertson et al., 1978; Lane, 1983), and to elevate oxygen consumption (Haldi et al., 1944). Thus contradictions exist in the literature concerning the hemodynamic and humoral effects of the drug in man.

Questions have been raised recently about the possible role of caffeine as a cause of cancer. Japanese newspaper reports mentioned recent studies indicating that caffeine may cause endocrine tumors in female rats (Food Chemicals, 1977). Graham (1978) reports that no published scientific studies have been found on the influence of caffeine per se on carcinogenesis. Studies of coffee drinking in humans and feeding of coffee solids to rats show no causal relationship between caffeine and cancer (Select Committee on GRAS Substances, 1976).

Performance Effects

Considering the general availability and widespread use of caffeine as a mild stimulant in coffee, tea, and cola drinks, few contemporary studies of its effects on human performance have been reported.

As Regina, Smith, Keiper and McKelvy (1974) have indicated, there is a conspicuous lack of contemporary literature concerning the drug.

Graham (1978) characterized caffeine as a 'cortical stimulant which relieves fatigue, increases awareness, decreases appetite, and often becomes moderately addictive'.

Caffeine has been described as an almost ideal stimulant in that it enhances cognition and motor activity and produces few or no side effects for most people (Thompson, 1975). Grollman (1951) pointed out that although ideas become clearer, thought flows more freely, and fatigue and drowsiness disappear, caffeine ingestion often leads to inhibition of logical, connected thought, and much effort is required to focus attention on a single object.

Behavioural effects are partially dependent upon the tolerance level of the user, which is increased by chronic usage. Doses that increase tolerance result in indigestion, nervousness, and insomnia (Leukel, 1972), and these disturbances often are antecedents for more serious pathologies.

Caffeine has been reported to enhance human performance in some situations (Baker and Theologus, 1972; Franks et al., 1975; Hauty and Payne, 1955; Hollingworth, 1912; Regina et al., 1974), but not in others (Catell, 1930; Cheney, 1935, 1936; Weiss and Laties, 1962).

This variability in outcomes suggests that caffeine effects may be highly 'task-specific' and raises the question of the circumstances under which caffeine produces a facilitatory effect.

The consumption of caffeine in large amounts, is a common practice used to overcome drowsiness and forestall sleep. Ritchie (1975) has contended that dosages of 1000mg of caffeine are capable of producing untoward reactions referrable in large part to the central nervous system. Restlessness and excitement which may progress to mild delerium with sensory disturbances are said to entail such responses.

In a 1936 case report McManny and Schube describe a 'caffeine-induced psychotic state'. Greden (1974) directed attention to caffeine as an etiologic factor in certain anxiety states.

A case report by Stillner (1978) supported Ritchie's contentions about toxic effects of excessive amounts of caffeine, and indicates that the common practice of using caffeine to stay awake may give rise to a hazardous sequelae. As little as five 200mg tablets of readily available over-the-counter preparations of caffeine appears to be sufficient to generate a delerium (ie. experiencing tremor, impaired memory, altered levels of consciousness, vertigo, pronounced anxiety, and sensory disturbances, including visual illusions and hallucinations).

Even small amounts may lead to sufficient sensory and motor disturbances to prove dangerous in situations such as long-distance driving.

Indeed, such effects of caffeine on behaviour and performance merit closer attention.

Mood Effects

The perspective gained from previous literature regarding the effects of caffeine on anxiety and mood is not a clear one. Reports concerning caffeine are mostly based on clinical impression. In two of the correlational studies (Greden et al., 1978; Winstead, 1976) a positive relationship was found between the consumption of caffeine and anxiety. However, in two other correlational studies (Hire, 1978; Lynn, 1973) the relationship was negative.

Two experimental studies (De Freitas and Schwartz, 1979; Goldstein et al., 1965) did not control for usual consumption and body weight.

Only two studies have related caffeine consumption to mood. A correlational study by Greden et al (1978) with psychiatric patients, showed an inverse relationship, while Goldstein et al. (1965), in an experimental study, demonstrated no effects, although did not control for usual consumption or body weight.

Furthermore, there is evidence to suggest that the effect of caffeine in psychiatric patients could be an indirect one through the interference with antipsychotic drug effect (Kulhanek et al., 1979).

Examining the potential interaction of caffeine and psychologic stress in human subjects, Lane (1983) found that moderate doses of caffeine (two or three cups of coffee), elevated blood pressure in healthy young males during periods of rest and stress. Blood pressure during stress was also significantly higher after caffeine had been consumed. More importantly, the author concludes that the elevation of blood pressure due to caffeine adds to that elicited by stress.

Recently a study by Veleber and Templer (1984) using normal subjects, involved a double blind procedure and controlled for body weight and usual consumption. They found that consumption of moderate (250mg) doses of caffeine increased anxiety, depression, and hostility.

Although all the studies mentioned do provide us with some insight into possible relationships between caffeine consumption and mood effects they have also served to lay a foundation upon which future research should be built.

The general public has been reluctant to classify caffeine as a drug, even though heavy use of caffeine produces dependence, tolerance, and withdrawal symptoms. This reflects the drug's "domestication", that is, its incorporation into our daily life in such rituals as the coffee break and the coffee club.

There is little doubt that the popularity of caffeine containing beverages depends on their stimulant action, although most people are unaware of any stimulation. The degree to which an individual is stimulated by a given amount of caffeine varies. For example, some persons boast of their ability to drink several cups of coffee in the evening and yet "sleep like a log". On the other hand, there are rare persons who are so sensitive to caffeine that even a single cup of coffee will cause a response bordering on toxic.

Very little is known about the effects of caffeine in the general population. Is there a normal pattern of usage? Are the effects of caffeine consistent in a given population or do they vary? Research indicates that there are individual differences in tolerance to caffeine and that there are interactive effects between caffeine and other drugs (Robertson et al., 1978; Jung et al., 1981; Childs, 1978; Gilliland, 1980; Keisler and McLaughlin, 1972; Revelle et al., 1976, 1980).

Some of the differences in response to caffeine may be due to individual differences in the metabolic half-life of caffeine (Horning et al., 1977) and differing rates of absorption (Robertson et al., 1978).

Factors such as age, sex, mental state, personality type, and degree of physical fitness may effect the way in which people differ in response to caffeine. There could be differences between racial and ethnic groups, particularly those groups where caffeine consumption has been high for

centuries as opposed to groups for whom it is a relatively new substance.

Individual differences in response to caffeine may well be further understood with information of this kind.

There is no doubt that a certain degree of tolerance (Cotton et al., 1968) and of psychic dependence (ie. habituation) develops to caffeine containing beverages.

This is probably true even in those individuals who do not partake to excess. However, the morning cup of coffee is so much part of the European and American dietary habit that one seldom looks upon its consumption as a drug habit. The feeling of well-being and the increased performance it affords, although possibly obtained at the expense of decreased efficiency later in the day, are experiences that few individuals would care to give up.

CHAPTER TWO

REVIEW OF THE LITERATURE

Chemistry of Caffeine

Caffeine is an alkaloid structurally identied as 1,3, 7-trimethylxanthine. It is one of several xanthine derivatives which occur naturally in coffee beans, tea leaves, kola nuts and cocoa beans. Theophylline (1,3-dimethylxanthine) and theobromine (3,7-dimethylxanthine) are also well known. There is close similarity chemically between these alkaloids and metabolically important compounds such as the purines, xanthine and uric acid.

Coffee (Coffee arabica), Tea (Thea sinensis), Chocolate (Theobroma cocoa) and kola (Cola nitidia), are the most common plants in which caffeine occurs. It is readily extracted from these plants and is very soluble in boiling water, from which it crystallizes as a monohydrate with one molecule of water; from organic solvents it crystallizes as an anhydrous material, melting at 235 to 237^{o}C; it sublimes at 176^{o}C at atmospheric pressure without decomposition.

Pure caffeine is adourless, has a distinctly bitter taste and is stable at temperature, pH and salt concentrations normally encountered in food processing (Graham, 1978).

PHARMACOLOGICAL PROPERTIES AND PHYSIOLOGICAL EFFECTS OF CAFFEINE

Caffeine is characterized as a central nervous system stimulant. Furthermore, it affects metabolic and cardiovascular functions. Caffeine also stimulates the adrenal medulla to secrete hormones which themselves are known to affect these just mentioned variables and which are also closely associated with emotion, stress, and arousal.

Caffeine acts on the kidney to produce diuresis, stimulates cardiac muscle, and relaxes smooth muscle, notably bronchial muscle.

To follow is a brief review of the literature of studies concerning caffeine and:

a) Adrenal Medullary Activity
b) Respiratory and Cardiovascular effects
c) Central Nervous System
d) Smooth Muscle
e) Skeletal Muscle
f) Gastric Secretion
g) Metabolism
h) Toxicology
i) Mutagenic effects
j) Other Illnesses.

Adrenal Medullary Activity

The consumption of caffeine leads to increases in the amount of epinephrine and norepinephrine secreted by the adrenal medulla (Levi, 1967; Bellet et al., 1969; Lentinietat, 1974). Robertson et al. (1978) recorded increases in plasma epinehrine (207%), plasma norepinephrine (75%), urinary metanephrine (100%), and urinary normetanephrine (52%) in nine healthy non-coffee drinkers who had fasted overnight and abstained from any caffeine consumption in the previous week, one hour after ingesting 250mg of caffeine.

While such increases were substantial and significant, Tepperman (1965) pointed out that the adrenal medulla is capable of producing increases of up to 1000% during the full-blown panic reaction known as the "flight or fight" response.

A number of effects throughout the body occur as a result of increases in catecholamine levels. Being a neurotransmitter, norepinephrine increases activity at peripheral autonomic synapses. It is also found at high concentrations in brain structures that have their influence primarily on the autonomic nervous system and in some of those involved in the motivational and emotional aspects of behaviour (Thompson, 1975).

Responses to epinephrine resemble those produced by stimulation of the sympathetic nervous system. Epinephrine

has also been associated with emotion. Schacter and Singer (1962) found that subjects injected with an epinephrine solution explained their resulting physiological arousal on the basis of cognitive and social determinants. In the presence of someone acting euphorically, subjects interpreted their own arousal as euphoria; in the presence of someone acting out anger, they interpreted their own arousal as anger. Therefore, if the consumption of caffeine increases epinephrine levels sufficiently, these increases may aggravate whatever the emotional tone of the individual is at the time.

The pattern of epinephrine and norepinephrine levels that occur with regular daily ingestion of caffeine also needs to be determined. Jung et al. (1981), found that among regular coffee drinkers only 3 of 22 subjects after oral caffeine ingestion, and in 3 of 14 subjects following intravenous caffeine, recorded catecholamine increases of the magnitude found in the Robertson et al. (1978) study.

One could infer from this that the majority of these subjects either never showed increases in catecholamines, or, had become tolerant and ceased to respond in this way. Since there were no significant differences in the coffee-drinking behaviour between subjects showing increases in catecholamines and other subjects in the study, then elevated catecholamine levels and increases arousal states may come to be interpreted by such individuals as 'normal'.

Increases in epinephrine and norepinephrine would be expected to have both physical and emotional consequences in the form of increased stress and anxiety. A number of the effects of caffeine in humans are consistent with the effects of increased levels of epinephrine and/or norepinephrine.

Caffeine may act as a sympathomimetic drug in some people (Sawyer et al., 1981). Sympathomimetic drugs are those which cause changes in the body usually associated with sympathetic arousal. Through the release of norepinephrine, many sympathomimetic drugs act indirectly on the sympathetic nervous system. Innes and Nickerson (1975) regarded the release of epinephrine from the adrenal glands, as the prototype of the sympathomimetic agents.

Caffeine causes increases in both of these hormones and on this basis, Sawyer et al. (1981) hypothesized that it is a sympathomimetic agent in some, if not all, individuals. Further complications exist as, like caffeine, epinephrine is also a central nerous system stimulant.

Sawyer et al. (1981) argued that a differentiation of the effects of caffeine from those of norepinephrine and epinephrine as well as determining the manner in which they may interact is necessary if we are to understand the real effects of caffeine.

Table 4 summarizes the similarities and differences between the reported activity of caffeine and that of epinephrine and norepinephrine on various physiological variables.

Table 4

A Comparison of the Effects of Caffeine, Epinephrine, and Norepinephrine on Human Physiology

Physciological variable	Effects reported for: Caffeine	Epinephrine	Norepinephrine
	Ritchie (1975)	Innes and Nickerson (1975)	Innes and Nickerson (1975)
Respiration			
Respiratory rate	+	+	?
O_2 consumption	+	+	?
CO_2 consumption	+	+	?
Cardiovascular effects			
Heart function			
Rate	+,-	+	0,-
Cardiac output	+,-	+	0,-
Force of contractions	+,-	?	?
Cardiac rhythm	+,-,0	+,-,0	+,-,0
Compensatory vagal activity	Present	May be present	Present
Circulation			
Coronary	+,-	+	+
Pulmonary	+,-	-	?
Skeletal muscle	+,-	+	0,-
Hepatic	+,-	+	-
Cutaneous	+,-	-	-
Renal	+,-	-	-
Cerebral	-	+	0,-
Peripheral resistance	+,-	+	+
Blood pressure	+	+	+
CNS stimulation	+	+	0
Anxiety reaction			
Anxiety	+	+	+
Restlessness	+	+	+
Periods of depression	+	?	?
Tremors	+	+	+
Flushing	+	-	-
Diuresis	+	?	?
Insomnia	+	?	?
Sensory distrubances	+	?	?
Skeletal muscle			
Neuromuscular transmission	Facil-itated	Facilitated	?
Power of contractions	+	+	?
Fatigue	-	-	?

From Sawyer et al., 1981.

+, increase; -, decrease; 0, no change; ?, information not given.

Sawyer et al. (1981) question whether caffeine is a sympathomimetic agent, in which case some of its effects would be due to increases in catecholamines and not to the direct action of caffeine itself.

Respiratory and Cardiovascular Effects

Consumption of caffeine leads to increases in respiratory rate, oxygen consumption, and carbon dioxide elimination as a result of stimulation of the medullary respiratory centre (Table 4).

In a study by Robertson et al. (1978), the respiratory rate was determined during a 10 minute interval of quiet breathing, of nine healthy non-coffee drinkers following the ingestion of 250mg caffeine. Where as the respiratory rate 60 minutes after placebo averaged 13.4 1.6 (mean ±S.D), the comparable value after caffeine was 16.1 2.3 per minute (mean ±S.D). This value was significant at $P<0.05$ by a paired t-test. The degree of respiratory acceleration appeared to correlate with plasma caffeine levels over the range observed in their subjects ($r=0.73$, $P<0.02$).

All parts of the circulatory system are directly effected by caffeine and these actions may be antagonized by caffine's stimulation of compensatory vagal centres in the medulla. Cardiac muscle is strongly stimulated by caffeine, which increases force of contraction, heart rate, and cardiac output (Table 4).

The effect is masked because the drug also stimulates the medullary vagal nuclei, which in turn, decrease heart rate. The result of these two opposing actions may be bradycardia, tachycardia, or no change (Truitt, 1971; Stephenson, 1977).

There also may be variations over time. Caffeine has an antagonistic action on the circulation of the blood (Table 4). Caffeine dilates the coronary, pulmonary, and general systemic blood vessels by causing a relaxation of the smooth muscle in the vessel walls, it may also constrict blood vessels by stimulating the medullary vasomotor centre. No compensatory activity on the part of the medulla takes place in the brain itself, where caffeine causes a constriction of the blood vessels with a decrease in cerebral blood flow (Truitt, 1971; Ritchie, 1975).

The response of blood pressure to caffeine is thought to depend on the balance between central vasomotor and myocardial stimulation, which tends to increase it, and central vagal stimulation and peripheral blood vessel dilation, which tend to decrease it (Ritchie, 1975). Significant elevations in blood pressure were found in Robertson's et al. (1978) study, 30 minutes after nine healthy male subjects ingested 250mg caffine (Table 4).

The hyperglycemic action of caffeine has been documented. Wachman et al. (1970), demonstrated that a large dose of caffeine will diminish glucose tolerance and reduce pancreatic insulin release in normal subjects. A similar

effect was found by Studlar (1973), particularly in insulin-dependent diabetic patients. Naismith et al. (1970), noted that blood glucose dropped slightly when caffeine was withdrawn and did not return to pretest levels. The work of Sandberg and Bellet (1969) did not support the hyperglycerine action of caffeine; in their studies, normal subjects had lower glucose levels when receiving glucose and caffeine than when receiving glucose alone. However, in diabetic patients, higher blood sugar levels were found at 30, 60, and 90 minutes than when receiving glucose alone.

Free fatty acids may rise after a dose of caffeine (Lentini et al., 1974; Naismith et al., 1970; Wachman et al., 1970). Because they can also fluctuate in response to emotional changes, caution is suggested in attaching significance to this finding (Naismith et al., 1970).

Heart rate, blood pressure levels, glucose and fatty acid blood concentrations were observed by Handel et al. (1977) in six men and six women aged 20-42 years, before and within 360 minutes after oral administration of coca cola with caffeine (22.5, 35 and 150mg) but without sugar. Clinically significant effects (an increase in mean blood pressure level, glucose and free fatty acid levels and urinary catecholamine excretion) were induced only by 150mg of caffeine.

The results of a study on 50,000 subjects reported by Bertrand et al. (1977) demonstrated the absence of a relationship between coffee intake and blood pressure

elevation. Williamson (1978) has criticized this conclusion and enumerated the methodological errors. He has pointed out for example, that the authors took the half-life period as 12 hours though it had not in fact been determined.

Much interest has developed concerning a possible deleterious effect of caffeine in the etiology of acute myocardial infarction. An association between myocardial infarction and coffee usage has been shown in a U.S. surveillance study, and some of these patients are now restricted as to caffeine use (Bowan and Rand, 1980). Jick and coworkers (1973) reported that individuals drinking more than 5 to 6 cups of coffee per day are about twice as liable to suffer myocrdial infarction. However, in an equally careful study Klatsky and associates (1973) found no independent association between coffee drinking and a subsequent first myocardial infarction: they suggested that the discrepancy in the findings of the two groups may be related to factors such as cigarette smoking or the selection of control subjects. Further studies have confirmed that coffee drinking is associated with little, if any, increased incidence of coronary heart disease (Dowber et al., 1974; Hennekens et al., 1976).

The effect of coffee intake on the conductive system of the heart has recently been studied for the first time in 12 patients with organic heart disease in an attempt to resolve contradictory data on the cardiovascular effect of coffee. ECG was recorded before and 20 minutes after the intake of coffee with 150mg of caffeine. It was noted that

coffee intake lowered the effective and functional refractory period of the a/v node, the effect probably being mediated by catecholamine release (Gould et al., 1979).

Multiple measurements of multiple variables should be included in the study of caffeine and its effects on the circulatory system and the medullary centres. As Ritchie (1975) stated, "The observation of a single function, for example, blood pressure, is deceiving because the drug may act on a variety of circulatory factors in such a way that blood pressure may remain essentially unchanged." Sawyer et al. (1981) added that although caffeine has not been associated with an increased frequency of respiratory, cardiac, circulatory, or hypertensive disorders (except for myocardial infarction (Bowan and Rand, 1980), neither have the effects of caffeine on these abnormal populations been studied in an experimental setting. Until this is done, the assumption that caffeine is not contraindicated for these populations will remain an open question.

Central Nervous System

Caffeine can stimulate all parts of the central nervous system when high enough concentrations are attained (Table 4). It is not only the vagal centres in the medulla which are affected, but also the cortex and the spinal cord.

Caffeine stimulates all portions of the cortex. Doses of 50 to 200mg can result in increased alertness, decreased drowsiness, and lessened fatigue. Doses in the range of 200

to 500mg may produce headache, tremors, nervousness, and irritability. Hypersethesia, pleasant or unpleasant, may occur after excessive coffee intake (Ritchie, 1970; Truitt, 1971).

In the course of a series of studies on caffeine's psychotropic effects Goldstein et al. (1965, 1969) found that the drug had no demonstrable effect on objectively measured performance, although it made the subjects feel more alert and physically active. In some subjects, caffeine caused a feeling of "nervousness" rather than alertness.

There were both qualitative and quantitative differences in responses to caffeine that were related to the degree of habitual caffeine consumption. Heavy users became less jittery and nervous and had fewer headaches with increasing doses of caffeine. In the abstainers, caffeine produced jitteryness, nervousness, and gastrointestinal complaints (Goldstein, 1969).

The effectiveness of caffeine in preventing attention lapses was studied in a visual monitoring test analogous to night driving. Caffeine was effective in preventing attention lapses after the first hour, and the effect persisted over the remaining 2 to 3 hours of the experiment (Mitchell et al., 1974).

Ritchie (1975), summarized the then current attitudes about, and research on, the action of caffeine in the following terms:

> "Caffeine results in a more rapid and clearer flow of thought, and allaying of drowsiness and fatigue. After taking caffeine one is capable of a greater sustained intellectual effort and a more perfect association of ideas. There is also a keener appreciation of sensory stimuli, and reaction time is appreciably diminished. In addition, motor activity is increased: typists, for example, work faster and with few errors."

Recent studies show large variations in these effects depending on such variables as dosage of caffeine and personality type. For example, Revelle et al. (1976) found that under 200mg of caffeine and time stress, accuracy of extraverts increased while accuracy of introverts decreased in a verbal ability test.

A number of EEG studies concerning caffeine's stimulating effect on the cortex show inconsistencies.

For example, contingent negative variation is a slow surface-negative electrical potential of the human brain, and its amplitude is related to attention and arousal. Both increases (Ashton et al., 1974) and decreases (Jenssen et al., 1978) in contingent negative variation amplitudes have been reported at comparable time periods (about 30 minutes) after the ingestion of 300mg caffeine.

Looking at other aspects of EEG activity, Klein and Salzman (1975), reported reductions in auditory event-related potentials, 2 hours following the ingestion of 300mg caffeine. Walpow and Penny (1978), found that the decreases in temporal N_1P_2 amplitudes to auditory evoked responses usually caused by habituation and fatigue did not occur

following caffeine. Thus these results indicate both increases and decreases in functions.

Only after massive doses (probably between 2 and 5gms) is the spinal cord stimulated by caffeine (Julien, 1981). Increased excitability of spinal reflexes might be observed and, at even higher doses, convulsions and death may ensue (Ritchie, 1975). The convulsive dose, however, is so high (over 10gms, the equivalent of 100 cups of coffee) that death from caffeine is highly unlikely. Very few people would consume such high amounts of caffeine in the space of a day even if they were regular heavy consumers.

Smooth Muscle

Caffeine relaxes various muscles other than those of blood vessels. The most important action in this respect is their ability to relax the smooth muscles of the bronchi, especially if the bronchi have been constricted either experimentally by histamine or clinically in asthma (Roll, 1980).

Skeletal Muscle

Caffeine has been shown by objective measurements to increase the capacity for musclar work in man. Foltz et al. (1942), first worked their four subjects to exhaustion on a bicycle ergometer. Then, after a 10-minute rest, the subjects worked to exhaustion again. The administration of 500mg caffeine during the rest period significantly increased

output during the second work period when compared to control injections.

Huidibro and Amenbar (1945), found that doses of 3.5mg/kg caffeine increases twitch tension of the indirectly stimulated quadriceps muscle of cats.

Caffeine causes marked increases in tension of frequencies slightly below those producing tetanus and is accompanied by fusion of individual contractions, perhaps owing to a prolonged contraction time (Goffart and Ritchie, 1952).

Such observations may be explained in part by the ability of caffeine to increase the release of acetylcholine, as judged by augmentation of the amplitude and rate of rise of end-plate potentials in curarized rat diaphragm (Goldberg and Singer, 1969). Caffeine can also increase the resting tension of denervated muscle (Huidibro, 1945).

The site of action of caffeine in the excitation-contraction coupling process in skeletal muscle has been a controversial subject for some time. Axelsson and Thesleff (1958) did not observe contraction when caffeine was injected intracellularly and they therefore suggested that caffeine acted on the plasma membrane. Caldwell and Walstar (1963) found, however, that intracellular injection of caffeine did elicit contraction. It was later shown that caffeine released bound calcium from sarcoplasmic reticulum isolated from skeletal muscle (Weber and Herz, 1968; Ogawa, 1970). As

suggested by Luttgow and Oetliker (1968), and by Thorpe and Seeman (1971), caffeine nevertheless could exert its effect by displacing calcium from the plasma membrane and its invaginations, the T tubules.

Thorpe and Seeman's (1971) results indicated that caffeine acts at only one site in the excitation-contraction coupling system, the sarcoplasmic reticulum. Caffeine did not displace calcium from the sarcolemma, but it did release a significant portion of the calcium bound to sarcoplasmic reticulum. As reported previously (Weber and Herz, 1968) this effect on the reticulum was inhibited by procaine.

Gastric Secretion

The ability of caffeine to stimulate gastric secretion in man is well documented (Roth et al., 1944; Czok, G. 1972; Volkheimer et al., 1972; Meiderer et al., 1973; Cohen and Booth, 1975).

Man is relatively sensitive, and moderate oral or parental doses of caffeine cause secretion of both acid and pepsin (Debas et al., 1971). Patients with active ulcer disease can be identified by a sustained elevation of acid secretion in response to high doses of caffeine. Normal patients show only a transitory rise (Roth et al., 1944).

Such studies have encouraged the hypothesis that excessive use of caffeine-containing beverages, by promoting gastric acid secretion, contributes to the pathogenesis of

peptic ulcer in the ulcer-prone individual and renders the management of the condition more difficult.

The primary effect probably results from stimulation of the gastric myenteric and submucous nerve networks by caffeine. A secondary effect is believed to come from the central nervous system stimulation via the cholinergic nerve fibres. Caffeine has been shown to cause an increase in cyclic 3',5' adenosine monophosphate, which appears to be involved in the stimulation of hydrogen ion secretion by the gastric mucosa (Harris et al., 1965, 1969).

It has long been known that beverages made from roasted grain containing no caffeine stimulate acid secretion in man as much as does coffee (Cohnell and Berg, 1931). Similarly, Cohen and Booth (1975) demonstrated that both decaffeinated coffee and coffee were equally potent in stimulating gastric acid secretion. Their results indicated that coffee in either form may contain stimulants for acid secretion other than caffeine, or possibly a compound which potentiates the action of caffeine or a secretagogue which acts independently. Czok (1972) attributed these effects to caffeine and "le sostanze di torrefazione del caffe," the compounds resulting from roasting and brewing of coffee.

In view of the responsiveness of the human gastric mucosa to caffeine and other substances in various beverages, there should be awareness of the ubiquitous use of coffee and colas in the pathogenesis of peptic ulcer and in the management of the patient with an ulcer.

Metabolism

After ingestion caffeine is rapidly and essentially completely absorbed from the gastrointestinal tract. It passes quickly into the central nervous system and into various tissues in approximate proportion to their water content; tissue response is proportional to caffeine content (Axelrod and Reichenthal, 1953).

Caffeine reaches maximum levels in the blood between 30 and 120 minutes after ingestion, the mean time being 60 minutes (Robertson et al., 1978). Among different individuals, the metabolic half-life of caffeine varies between 4 and 10 hours (Horning et al., 1977) ie. 4 hours after ingesting one cup of brewed coffee (85mg caffeine), a person with a rapid rate of biotransformation will still have a minimum of 42.5mg of caffeine in his/her system. Ingesting two more cups of coffee at this time would add 170mg caffeine, for a total of 212.5mg - a figure above the pharmacologically active dose given by Graham (1978) as 200mg and by Truitt (1971) as between 50 and 200mg. Individuals with lower rates of biotransformation would have higher levels and would accumulate caffeine more rapidly. This difference in turnover rate may be helpful in explaining individual differences in response to caffeine.

Excretion is primarily renal, being almost equally divided between single methyl group xanthines and methyluric acids. Only 1 per cent remains unchanged (Axelrod and Reichenthal, 1953). While Cornish and Christman (1957)

reported that 48 hours are needed to clear 66 per cent of 100mg caffeine dose, Axelrod and Reichenthal stated that there was no day-to-day accumulation of the drug after a 500mg dose. The drug is fatal at doses of 3,000 to 10,000mg, if taken in a brief time span (Dimaio and Garriott, 1974).

Cellular metabolic effects of caffeine include increases of muscle lactic acid, stimulation of oxygen consumption, and muscle twitches and contractures in high concentrations (Ritchie, 1970; Truitt, 1971). Miller et al. (1974) investigated the ability of caffeine to potentiate normal thermic responses and found that it caused a marked increase in oxygen consumption. These authors suggested that caffeine, by virtue of its negligible energy values and thermogenic properties, could be of value in weight-reducing regimes.

Sutherland et al. (1968) provided a biochemical explanation for some of the metabolic and physiologic effects of the methylxanthines. The enzyme, phosphodiesterase, is necessary to convert cyclic 3',5' adenosine monophosphate to 5' adenosine monophospate. Methylxanthines inhibit phosphodresterase breakdown of cyclic 3',5' adenosine monophosphate, which then prolongs its metabolic stimulating action in the cells.

Toxicology

Caffeine is considered a relatively safe drug; however, both accidental and intentional poisonings have

occurred. A five-year-old girl died after ingesting 5,000mg caffeine alkaloid from her mother's bottle of over-the-counter diuretic. In other cases, patients have unintentionally been given caffeine rather than their correct medications with fatal results (Dimaio and Garriott, 1974). Suicide has been reported due to caffeine ingestion. The individual intending to misuse it, however, is usually thwarted by another of its pharmocologic properties, that of potent gastric irritation, which causes vomiting (Alsott et al., 1973).

The concentration of caffeine in postmortem blood has ranged from 80 g/ml to over 1mg/ml. Untoward reaction, however, may be observed following the ingestion of 1g (15mg/kg) or more of caffeine, leading to plasma concentrations above 30 µg/ml. These are mainly referable to the CNS and circulatory systems. Insomnia, restlessness, and excitement are the early symptoms, which may progress to mild delerium. Sensory disturbances such as ringing in the ears and flashes of light are common. The muscles become tense and tremulous. Tachycardia and extrasystoles are frequent, and respiration is quickened (Dimaio and Garriott, 1974).

Mutagenic Effects

Caffeine induces chromosomal abnormalities both in plant cells and in mammalian cells in culture and has potent mutagenic effects on microorganisms either alone or in combination with other mutagens (Timson, 1977). These effects seem to be associated with inhibition of DNA repair

processes. The doses required to induce such inhibition, however, are significantly higher than those usually consumed by humans. Furthermore, available evidence suggests that caffeine is neither mutagenic by itself nor in combination with known mutagens in mammals.

At very high doses, caffeine appears to have some teratogenic activity in mammals. One retrospective study (Weathersbee et al., 1977) indicated that pregnant women who ingest more than 600mg of caffeine per day in beverages may have an increased incidence of spontaneous abortion, still birth, or premature delivery.

Kreybig and von Czok (1975) have analyzed other authors' data and the results of their own study of mutagenic and teratogenic effects of caffeine and soluble coffee in pregnant rats. Such effects were indeed observed after administration of high doses of caffeine - 240mg/kg (intraperitoneally) and 264mg/kg (orally) in rats, and 304 and 410kg/mg respectively in mice. These doses greatly exceeded those usually taken by man, even in cases of coffee dependence. Taking this into account, normal coffee intake by pregnant women may be considered harmless unless it is proved injurous on other grounds.

All the same, there are experimental data showing an effect of caffeine on cellular mitotic activity. Furmanova et al. (1976) have demonstrated that a caffeine concentration of 0.05336% suppresses the division of cells in Allium cepa L. root by 50%.

In the light of these data, the depressive action of caffeine on the division of cells requires further investigation (Furmanova et al., 1976).

Other Illnesses

Caffeine in combination with an analgesic, such as aspirin, is widely employed in the ordinary types of headache. There are few data to substantiate this use. Caffeine is also used in combination with an ergot alkaloid in the treatment of migraine. The ability of caffeine to produce constriction of cerebral blood vessels may improve the therapeutic response (Rall, 1980).

Because caffeine stimulates brain motor centres, it may be contraindicated for some epileptic patients. However, in some cases, the patient learns that drinking coffee relieves attacks. As an adjunct to diphenylhydantion, caffeine may be used to allay the drowsiness induced by the former; children and adults may be directed to drink a prescribed number of cups of coffee. Caffeine and herbs were the only treatment for narcolepsy until ephedrine sulphate was introduced in 1930 and amphetamine in 1935 (Lennox et al., 1960).

After the claim that coffee could substitute for amphetamine or methylphenidate in the treatment of hyperkinetic behaviour in children (Schnockenberg, 1973), there have been a number of reports both confirming and denying the original observations (Reichard and Elder, 1977; Firestone et

al., 1978). However, these studies involved the use of single doses of caffeine unadjusted for body weight.

A number of studies concerning caffeine, coffee, and cancer were reviewed in the British Medical Journal (1976). In animals, laboratory tests of caffeine for carcinogenicity gave essentially negative results.

Caffeine, ascorbic acid, and sodium salicylate increase circulating serum levels of interferon in response to viral infection. Caffeine was the least active in elevating interferon levels (Geber et al., 1975).

Caffeine has been withheld from patients with gout, due to the possibility that it could be converted into additional uric acid. Since the development of the uricase method of determining uric acid, all reported studies have indicated there is no increase in true uric acid secretion (Cornish and Christman, 1957).

Statland et al. (1976) reported on a male patient with diabetes, seizure disorder, a history of alcohol abuse, and liver disease who was hospitalized after complaints of severe abdominal pain for three days. His status deteriorated from alert to combative and finally to hepatic coma. Laboratory testing of his serum by gas-liquid chromatography revealed caffeine. A decrease in diphenylhydantion and witholding of caffeine and diazepam resolved the coma in 48 hours. The authors suggested the monitoring of caffeine levels in patients with comprised hepatic function who are also heavy coffee drinkers.

CAFFEINE EFFECTS ON PERFORMANCE

The belief that caffeine enhances mental and physical performance is widespread and deeply embedded in our folklore, but experimental support for this belief is neither extensive nor unequivocal.

One of the most comprehensive literature reviews of performance effects of caffeine was carried out by Weiss and Laties (1962). These investigators reviewed numerous early studies which had reorted performance enhancement with caffeine. Among them were improved ergonomic output on a bicycling task (Foltz, Ivy and Barborka, 1942), decreased reaction time (Cheney, 1935, 1936; Horst and Jenkins, 1935), increased tapping rate (Hollingworth, 1912; Lehman and Csank, 1957), more accurate compensatory tracking (Seashore and Ivy, 1953), greater galvanic skin response conditioned amplitudes (Switzer, 1935), and a slight increase in typing speed (Hollingworth, 1912). However, caffeine has been found to disrupt or to produce no effect upon many of these variables (Adler, Burkhardt, Ivy and Arkinson, 1950; Hawk, 1929; Hollingworth, 1912; Hull, 1935).

Thus, specific effects of the drug are not known. Weiss and Laties (1962) indicated some general conclusions without the benefit of analyses of treatment interactions:

1. caffeine has little or no effect on reaction time
2. caffeine impairs hand steadiness
3. caffeine produces equivocal effects on motor co-ordination
4. caffeine is capable of counteracting motor performance decrements produced by alcohol ingestion.

Fleishman and Bartlett (1969), who reviewed research on the effects of drugs on human performance, pointed out the need for experimental studies evaluating the effects of specific drugs and dosage on specific classes of human performance.

Caffeine has mixed effects with those in the workplace. Stimulation, increasing arousal, and anxiety do not necessarily result in improved performance. A summary of work in this area compiled by Truitt in 1971 includes:

1. a prolonged and slightly increased ability to perform exhausting work,
2. an unpredictable effect on simple and complex tasks involving choice and descrimination,
3. tremor interference with hand steadiness,
4. possible influences on eye-hand co-ordination, and
5. improved mental activity in simple arithmetic, typing and uncoding.

More recently caffeine has been shown to affect such variables as vigilance, accuracy, and reaction time. Sawyer et al. (1981) produced a summary of recent findings on caffeine and performance. This is illustrated in Table 5. Some endurance components are also included in Table 4 to compare caffeine's effects to those of epinephrine and norepinephrine on muscular contraction.

One can extrapolate these simple tasks to more complex tasks in such situations as experimental work, industry, and daily living. As well as subject and work accuracy and efficiency being affected, individual differences occur and

Table 5

Summary of Recent Findings: Effects of Caffeine on Performance

Performance Variable	Effect of Caffeine
Physical endurance	
Bicycle ergometer	
Fixed load	+ (Costill et al., 1978)
Progressive load	0 (Perkins and Williams, 1975)
Motor Skills	
Rapidity and accuracy	- higher doses, + lower doses (Paroli, 1972)
Eye-hand co-ordinate	- (Putz-Anderson et al., 1981)
Vigilance	
Visual	
Night-driving analogue	+ (Baker and Theologus, 1972)
Target scanning	
Low coffee users	-
High coffee users	0 (Childs, 1978)
Auditory	+,0 (Clubley et al., 1974)
Auditory	
Extroverts	+
Introverts	0 (Keister and McLaughlin, 1972)
Reaction Time	
Regular reaction time	- (Paroli, 1972)
Choice reaction time	
Decision time	+
Motor time	- (Smith et al., 1977)
Verbal tests	
GRE practice test	
Speed and accuracy	
Extroverts	+ with increasing dosage
Introverts	First +, then -, with increasing dosage (Gilliland, 1977)
Verbal test, time stress	
Accuracy	
Extroverts	+
Introverts	- (Revelle et al., 1976)
Verbal test	
Accuracy	
Low impulsives	+, AM: - PM
High impulsives	-, AM: + PM (Revelle et al., 1980)

From Sawyer et al., 1981.

+, increases; -, decreases; 0, no change.

of caffeine are the results of direct stimulation, action through epinephrine, or indeed both, remains an unanswered question.

Vigilance, Reaction Time, and Motor Skills

The results of early investigations on caffeine effects on performance are conflicting. Payne and Hauty (1954) found the onset of fatigue slower after caffeine 20mg in a vigilance test. As early as 1912 Hollingworth reported that caffeine 300mg reduced reaction times.

Gilliland and Nelson (1939) also found reaction times were reduced after one to two cups of coffee. Later in more controlled studies, Knowles (1963) and Franks et al. (1975) recorded reaction times after caffeine 250 and 300mg/70kg, which were shortened but not significantly different from placebo.

Clubley et al. (1978) obtained significant decrements in reaction time after caffeine 75-300mg but the observed decrement after caffeine 100mg did not differ significantly from that following the placebo.

Since only the subjects varied between the two trials these results are probably indicative of considerable subject variation in sensitivity to caffeine, an observation previously made by Goldstein, Warren and Kaiser (1965).

there are interactive effects with personality variables. Changes which make work easier or more difficult may interact with arousal and anxiety levels to reduce or increase stress levels on the job.

Caffeine has been reported to increase the capacity for muscular work (Ritchie, 1975). It has been argued that this is due to central nervous system stimulation, although peripheral effects cannot be discounted. Evidence for this effect comes from measurements and studies with the bicycle ergograph.

However, both significant effects (Costell et al., 1978) at a fixed workload, and non significant effects (Perkins and Williams, 1975) using a progressive workload, in muscular work capacity have been reported. Factors such as the use of constant versus increasing workloads and/or the degree of physical fitness of subjects may be helpful in explaining the differing results of these two studies.

Sawyer et al. (1981) argued that one could hypothesize that these effects of caffeine on endurance are a combination of action of the central nervous system and action through sympathetic arousal. Furthermore, Inner and Nickerson (1970) reported that epinephrine facilitates neuromuscular transmission (ie. muscles contract for a weaker stimulus), increases the power of the contractions, and temporarily abolishes fatigue due to prolonged rapid stimulation of motor nerves. Ritchie (1975) reported that caffeine affects muscles in a similar manner. Therefore, whether the effects

Increased tapping rates after 324mg caffeine have been reported by Gilliland and Nelson (1939) Holck and Smith (1939), Lehman and Csonk (1957), but Flory and Gilbert (1943) found no effect after the same dose. Clubley et al. (1978) found tapping rates to be increased by caffeine doses of 150 and 300mg, but not 75 or 100mg. Tapping requires muscular work and since caffeine is known to strengthen and prolong the concentration of isolated skeletal muscle (Huidibro, 1945; Goffart and Ritchie, 1952) its effects on tapping may be due to a peripheral action. However, since these effects occur with doses also producing subjective arousal, peripheral effects and central stimulation cannot be separated.

Subjective arousal after caffeine (150-300mg) has been reported (Barmack, 1940; Goldstein et al., 1965) although Knowles (1963) claimed no subjective effects occurred after 250mg caffeine.

Past research suggests that caffeine enhances performance in tasks requiring visual vigilance and seems to be especially effective in situations where vigilance normally becomes degraded due to boredom and fatigue (Baker and Theologus, 1972; Hauty and Payne, 1955; Regina et al., 1974). Holland (1958) defines a vigilance task as a monotonous perceptual task which involves the monitoring of some infrequent but critical signs. Consequently, long-term performance of such monotonous tasks produces visual or task-induced fatigue.

Regina et al. (1974) required subjects to drive an automobile for 90 minutes after consuming either 200mg of caffeine or a placebo. Following the initial drive, subjects ingested a supplemental dose (200mg) of either caffeine or placebo and continued the driving task for an additional 90 minutes. Caffeine ingestion significantly decreased response times for acceleration, decelerations, and high beam signals.

In an earlier study on a task analogous to night driving, Baker and Theologus (1972) found that, 1 hour after ingesting 200-400mg caffeine, alertness increased, ie. there were significantly fewer attention lapses.

Lake and Meliska (1984) tested the effect of caffeine on a simple visual vigilance task under conditions designed to produce boredom and fatigue. Contrary to expectation, no improvement was found in vigilance as a result of caffeine ingestion compared to control. Thus, caffeine did not reverse a progressively deteriorating performance relative to control.

Increases in motor performance were reported (Smith et al., 1977) in eight male university students on a choice reaction time task divided into two components: a decision component, ie. the time required to make a decision; and a motor component, ie. the time required to implement that decision. Following 200mg caffeine, decision scores were increased and motor scores were decreased. This illustrates how careful definition of the elements of a performance task is necessary to separate the specific effects of caffeine.

The regularity of caffeine consumption may also effect performance. Childs (1978) reported that 'high coffee users' responded significantly faster and more accurately in a visual scanning task than 'lower coffee users' when they ingested 400mg caffeine, but not when placebo or 200mg caffeine was ingested.

Mental Tasks and Personality Variables

Caffeine has been reported to show improvements in simple arithmetic and uncoding (Truitt, 1971), faster solving of maths problems (Paroli, 1972), and adverse effects on the recall of a series of nonsense syllables (Hull, 1935).

Studies involving more complicated mental tasks have shown an association between caffeine's effects and personality types. Eysenck's (1962) extraversion-intraversion model, predicted that the effects of a stimulant drug would be in an intraverting direction. In contrast, extraversion was associated with increased speed and decreased accuracy. Subjects in the caffeine studies have been divided into personality groups on the basis of Eysenck's theories.

Table 6 shows some findings of studies involving caffeine effects and personality types.

Sawyer et al. (1981) point out that, while the division of subjects into extraverts and intraverts allows for the use of more sophisticated statistical tests, intraversion and extraversion are not manipulated and the

Table 6

Caffeine Effects and Personality Types

Task	Condition (mg Caffeine)	Personality Group Performance		Researchers
		Extroverts	Introverts	
Recording of digits	0 mg	Decrease	No change	Keister and McLaughlin, 1972
	200 mg	No decline	No decline	Extroverts performed like introverts through increased persistence and accuracy, in acord with Eysenck's theory of the interaction of stimulants and personality types.
GRE practice test	Increasing dosages	Increase	Increase then decrease	Gilliland, 1980 This suggests a limit to the beneficial introverting effects obtained through caffeine.
Verbal ability test under stress	200mg caffeine plus time stress	Increase	Decrease	Revelle et al., 1976 This suggests that while caffeine may help extroverts perform on this task, the performance of introverts is impaired under high levels of caffeine or added stress.

results show an association among personality variables, caffeine, and performance, but not causality. However, one wonders if manipulation of intraversion and extraversion would ever be possible.

CAFFEINISM

Caffeinism, a diagnosis recently included in the third edition of the American Psychiatric Associations Diagnostic and Statistical Manual of Mental Disorders (DSM-III), is characterized by a constellation of affective, sleep, and psychophysiological manifestations. Caffeinism can be pharmacologically defined as the ingestion and consequent actions of high doses of caffeine, whether from tea, coffee, cola drinks, over the counter substances, or prescription medications.

Symptoms of caffeinism are best understood as dose-related extensions of caffeine's expected pharmacological actions (Greden, 1974). The main symptomatic areas involve, 1. anxiety manifestions, 2. depression, 3. tolerance, 4. withdrawal symptoms, 5. Restless Legs syndrome.

Anxiety Manifestations

Several clinical reports have suggested a link between caffeine consumption and anxiety in psychiatric patients (Greden, 1974; Furlong, 1975; Winstead, 1976; Greden et al., 1978; Stillner et al., 1978; Mikkelsen, 1978).

Greden et al. (1978) found that psychiatric inpatients estimates of prehospitalization caffeine consumption were correlated with anxiety, depression, and the use of sedative hypnotics and minor tranquilizers. In another report Greden (1974) concluded that for three patients, excessive caffeine consumption produced anxiety symptoms indistinguishable from anxiety neurosis. Greden (1974) and Furlong (1975) reported the symptoms of caffeinism to be nervousness, tremulousness, muscle twitching, insomnia, sensory disturbances, palpitations, flushing, arrythmias, diuresis, and periods of anxiety, agitation and depression.

Anxiety and some of the other symptoms of caffeinism were listed by Innes and Nickerson (1975) as side effects of both epinephrine and norepinephrine injections (see Table 4). Sawyer et al. (1981) pointed out that since caffeine increases the levels of these hormones it is not clear whether one or all of these agents is the precipitating factor in the resulting anxiety. Furthermore, they added that these may interact with situational variables so that subclinical levels of anxiety increase to clinical levels. In two of the three case studies given by Greden (1974), situational sources of anxiety were clearly present.

Significantly higher trait anxiety and depression scores were obtained for moderate (one to five cups per day) to high (five or more cups per day) coffee consumers in a study to determine the relationship between regular coffee consumption and the incidence of caffeinism in a non-clinical population (Gilliland and Andress, 1981). These anxiety

levels were subclinical, but the authors suggest that they may indicate significant and stressful differences in such factors as sleep patterns and nervousness. The high consumers also reported significantly higher levels of caffeinism symptoms, higher frequencies of psychophysiological disorders and lower academic performances.

Depression

Periods of depression and agitation were listed by Greden (1974) among the symptoms of caffeinism. Ritchie (1975) states, "There is no doubt that excitation of the central nervous system produced by large amounts of caffeine is followed by depression."

A number of psychiatric studies (Furlong, 1975; Greden et al., 1978; Neil et al., 1978) and non clinical studies (Gilliland and Andress, 1981), reported a higher incidence of depression among high caffeine consumers, than with low users and abstainers. These suthors suggested that self-medication with caffeine could be an attempt to alleviate the anergia and hypersomnia experienced during certain types of depression. Neil et al. (1978) warned that excessive use of caffeine in this manner can "lead to diagnostic confusion and complicate pharmacotherapy". Although Bowen et al. (1981) found that caffeine does not precipitate or otherwise lower the amounts of circulating antipsychotic drugs, the possibility of competitive interactions between caffeine and these drugs still remains.

More recently research by Veleber and Templer (1984) involved a double blind experiment which controlled for body weight and usual consumption using three dosage levels, 0mg, 150mg or 300mg caffeine, with normal subjects. The subjects were twice administered the Multiple Affect Adjective checklist (MAAC; Zuckermin, Lubin, Vogel and Valerious, 1964) which has three scales assessing current anxiety, depression and hostility. Caffeine was found to increase anxiety, depression and hostility.

Finding a positive relationship between postanxiety scores and caffeine dosage was expected because of the previous literature and caffeine's known pharmacological actions. However, the positive relationship between post depression scores and caffeine dosage was less predictable. Although popular belief holds that caffeine raises mood, it is widely recognized that other central nervous stimulants, such as amphetamines and cocaine, produce depression following an initial mood elevation. Veleber and Templer (1984) believe that the positive relationship in depression found in their study may be due to time-after-consumption parameters. That is, if the posttest MAAC had been administered sooner, a positive relationship may not have been found.

The authors suggested that future research that delineates for whom caffeine is harmful should explore such time-after-consumption parameters.

Tolerance

An acquired tolerance to two actions of caffeine has been demonstrated unequivocally in man, namely diuresis (Eddy and Downs, 1928) and parotid gland secretion (Winsor and Strongin, 1933). These examples of tolerance were recognized by the responses to the ingestion of caffeine in coffee or water before and during the chronic consumption of caffeinated beverages.

The sleep-disturbing properties of caffeine are clearly more marked among non-users than among habitual users of coffee (Goldstein, 1964a). Differences were also noted in the extent to which caffeine disturbed the soundness of sleep. Subjects who were heavy coffee drinkers tended to report sleeping more soundly on placebo nights. In another investigation, Goldstein (1964b) established that 150 to 200mg caffeine taken shortly before bedtime prolonged the time required to fall asleep, although the effect was less pronounced in heavy caffeine drinkers.

Colton et al. (1968) also reported that sensitivity to caffeine was greater in non-coffee drinkers who reported disturbed sleep patterns, particularly delayed onset of sleep. Coffee drinkers were relatively insensitive to the actions of caffeine.

It has been suggested that tolerance may develop to the mood-altering properties of caffeine, such as nervousness and anxiety. However, extensive reviews of the pharmacologic

actions of this alkaloid (Eichler, 1938) and the psycholgical and behavioural effects of caffeine (Weiss and Laties, 1962), made little mention of tolerance. Indeed, Greden (1974) reported that individuals with caffeinism can be recognized by their chronic anxiety.

Studies have indicated that as little as 500mg (about five cups of coffee) ingested daily can result in the development of tolerance and of habituation, leading to a gradual increase of daily consumption (Goldstein, 1964; Colton et al., 1968; Goldstein and Kaizer, 1969; Greden, 1980). As one can imagine, chronic ingestion of caffeine, with daily intakes of ten or more cups of coffee per day, may develop into a routine ritual. However, if such a dose was ingested by a non coffee drinker, then one would expect the clinical and pharmacological consequences to be readily apparent.

Caffeine Withdrawal Symptoms

The development of caffeine-withdrawl headache is well documented (Dreisbach and Pfeiffer, 1943; Miller, 1960; Goldsteon and Kaizer, 1969). Dreisbach and Pfeiffer (1943) described the typical reaction. Headaches as extreme in severity as the subjects had ever experienced were produced by the sudden withdrawal of caffeine. The subjects were unaware that the capsules had been switched to placebos. The headache which developed was slow in onset, central in origin, became generalized after 4 to 6 hours, and was sometimes accompanied by nausea and vomiting. Blood chemistry

studies indicated serum calcium fell and serum phosphorus rose. Goldstein and Kaizer (1969), reported on caffeine withdrawal in a group of housewives in the natural setting of their homes. Moderate to heavy coffee drinkers described a special set of reactions in additions to headache; irritability, inability to work effectively, nervousness, restlessness, and lethargy. Three elements associated with caffeine withdrawal headache by Greden et al. (1978) are regular consumption of 500mg caffeine per day, development of tolerance, and sudden abrogation of caffeine intake.

Headache may occur simply from excessive use of caffeine. Some patients with recurring headaches resort to caffeine-containing analgesics. As the time from the last intake increases, the likelihood of headache also increases. Taking caffeine relieves the headache only temporarily and thus sets up a vicious cycle of recurring headaches (Selbach, 1973; Miller, 1960).

Hypertensive headache has been relieved by intravenous administration of caffeine. Selbach (1973) suggests that constriction of cerebral arteries decreases the brain swelling caused by hypertension. Caffeine administration during the first or prodromal phase of the four phases of migraine headache blocked further headache development in some individuals (Selbach, 1973).

In an ongoing investigation of caffeinism, Greden et al. (1980) used a questionnaire to determine whether there is a constellation of psychiatric characteristics associated

with this type of headache. They found that persons who are susceptible to the syndrome generally report more symptoms of anxiety and depression and rate higher in tests evaluating those parameters; consume more antianxiety agents; feel they are less healthy; and have a significantly higher caffeine intake that persons without caffeine-withdrawal headaches.

Coupling these findings with those reported by Dreisbach (1943) and Goldstein (1969), Greden et al. (1980) concluded that the caffeine-withdrawl headache does exist as a clinical psychiatric syndrome.

In a subjective evaluation of the symptoms of caffeine withdrawl (Roller, 1981), a 40-year-old healthy male (90kg) who regularly drank 900-1100mg caffeine daily, abstained from coffee for 72 hours. Headache started 6 hours later, followed by tiredness and lassitude, rhinnorrhea, leg pains, and diaphoresis and, later still, general muscle pains as with influenza. When the subject resumed coffee drinking, all symptoms were alleviated within 3 hours. Roller urged further studies to confirm the presence of these symptoms in others, to quantify these effects, and to determine the role of these effects in caffeine usage.

Caffeine withdrawal programs will precipitate withdrawal symptoms including anxiety. White et al. (1980), found that regular consumers of caffeine had higher muscle tension after three or more hours of abstinence than low caffeine consumers. This difference was absent after double-blind administration of caffeine citrate or placebo. Among

subjects receiving placebo, anxiety was highly correlated with prior caffeine use, suggesting that even a brief withdrawal may produce anxiety in the regular user.

Restless Legs Syndrome

Lutz (1978) on the basis of therapeutic experience with 62 patients over an 11 year period, concluded that caffeine is the major factor in the causation of the 'restless legs syndrome'. Other clinical, constitutional-hereditary (ie. "neurotic") and environmental (eg. sedentary occupation, exercise deprivation) factors, including seasonally heightened or stress-related autonomic arousal may enter the clinical picture in varying degrees and modify the individual sensitivity to caffeine.

The main symptom of restless legs consists of unpleasant creeping sensations in the lower legs, between the knee and ankle. Many patients experience simultaneous restlessness in their arms, shoulders, nuchal and pectoral muscles although the flexor muscles of legs, arms and sometimes thighs with their greater muscle bulk are preferred sites. The creeping sensations are usually localized deep in the extremities into the muscles or bones, but most patients have difficulty in precisely localizing their discomfort. The discomfort appears only at rest and elicits on irresistable need to move their limbs. It generally appears in the evening and early night and may be associated with severe insomnia. The unpleasant sensation is usually described as having a crawling, restless or aching quality.

Caffeine is responsible for the increased nervous system arousal (cortex, medulla, spinal cord) as well as for the direct peripheral contractile effect on the striated muscle. Lutz (1978) believes that the increased striated muscle contractility interfers with the microcirculation to sensory nerve endings, leading to increased irritability of these structures, responsible for the dysphoric sensation of muscular restlessness. This sensation could also be viewed as a toxic sensory disturbance. Toxic sensory manifestations (eg. hypersthesias) are known to occur with caffeinism.

The nocturnal preference of restless legs can be explained on the basis of increasing central nervous system excitation as the day goes on and relative sensory isolation at night which leads to increased proprioceptive awareness.

Treatment consists of the elimination of caffeine-containing beverages, food and medications (often used to counteract the restless leg syndrome) and the temporary administration of diazepam with its central sedative and peripheral muscle relaxing effect.

PROBLEMS INVOLVED WITH RESEARCH INTO THE EFFECTS OF CAFFEINE

1. Most of the reported effects have been clinically observed or inferred from survey data, and there has been very little experimental research. As a result, there is little evidence for a causal link between the wide range of reported effects and caffeine intake.

2. The small subject samples evident in the experimental, survey and clinical data, tend to reduce reliability of the reports of caffeine effects.

3. Caffeine has a number of physiological effects. These effects are considered to be transient, returning to base-line levels as caffeine is depleted from the system. Studies in this area have been done using healthy subjects who have typically abstained from caffeine for a period of time prior to the experiments. In fact, the systems of people who drink coffee regularly during the day and evening may never be completely clear of caffeine.

   The effects of this kind of constant stimulation have not been studied at all (Sawyer et al., 1981). Nor have experiments been done on chronically ill persons whose physiological levels are already abnormal, so it is not certain what kinds of changes caffeine will induce in these areas.

4. The literature on the cardiovascular and autonomic effects of caffeine in man includes few double-blind studies, and even these reports have generally failed to separate adequately the truly caffeine-naive subjects from the population of coffee drinkers. Even some double-blind studies that include "coffee drinker" and "non-coffee drinker" categorizations define the non-coffee drinker in such a way that a person ingesting 85mg of caffeine (1 cup of coffee) daily would qualify as a "non-coffee drinker" (Colton et al., 1968).

   The identification of truly caffeine-naive subjects for study may be important, since tolerance clearly develops to such effects of caffeine as diuresis (Eddy and Downs, 1928), parotoid-gland secretion (Winsor and Strongin, 1933), bradycardia and sleep disturbance (Colton et al., 1968).

   It seems likely that the physiological effects of single doses of caffeine could be underestimated if subjects had not totally abstained from caffeine in the period before study. Furthermore, in studies on catecholamine output after caffeine, the dietary intake of sodium has rarely been controlled, though dietary sodium has a definite effect on urinary and plasma catecholamine levels (Robertson et al., 1977).

5. Many researchers have failed to note and take account of their subjects' histories of caffeine intake. This is very important when considering that tolerance to caffeine

does exist and there is variability to some effects of caffeine and not to others.

6. A basic problem in gathering information is that many people are unaware of the amount of caffeine that they actually ingest. Beyond their coffee and tea consumption they are not aware that caffeine is present in many other common substances.

7. Laboratory findings are often limited by their questionable transfer to events outside the laboratory setting. On the other hand, attempts to study phenomena in natural settings often sacrifice manipulative control and precision of measurement.

CHAPTER THREE

THE EXPERIMENT

INTRODUCTION

Caffeine has physiological effects which are similar to those observed in association with psychological or psychosocial "stress". Both caffeine and acute psychological stress will produce elevations in plasma epinephrine and norepinephrine paralleled by elevations in blood pressure and heart rate, in addition to their other effects (Kanzett, 1975; Rose, 1980; Mason, 1975; Ritchie, 1975; Robertson et al., 1978).

The similarity of these two patterns of cardiovascular and hormonal responses suggests the possibility that stress and caffeine could interact or, more specifically, that caffeine may intensify the cardiovascular and hormonal effects produced by stress. The pathogenesis of both coronary artery disease and hypertension are currently thought to be significantly influenced by the physiological effects of psychological stress (Taggart and Carruthers, 1981).

Because caffeine consumption and stress are both common features of contemporary life, a caffeine-related potentiation of these harmful effects of stress could have

especially important implications for the development of cardiovascular disease. Psychologically, the potential additive effect of caffeine on stress could have an effect on one's performance when encountering a stressful situation, eg. exams or public speaking.

The hypothesis that caffeine can intensify responses to stress is supported by the work of three main studies in this area (Cobb, 1974; Henry and Stephens, 1980; Lane, 1983).

Cobb (1974) carried out a long term study of automobile factory workers. The subjects studied came from two companies that closed at the end of 1965 and 1966, respectively, and from four companies for which there was no threat of termination. The terminees were visited during the phase of anticipation, shortly after the closing, and 6, 12 and 24 months later. At each visit to the subject's home, a standardized set of physiological, psychological, social and economic data were collected by public health nurses. The controls were visited at similar intervals except that very few were followed beyond 12 months. The two groups of 100 terminess and 74 controls were virtually homogenous over 43 variables including, academic level, wages, age, and marital status.

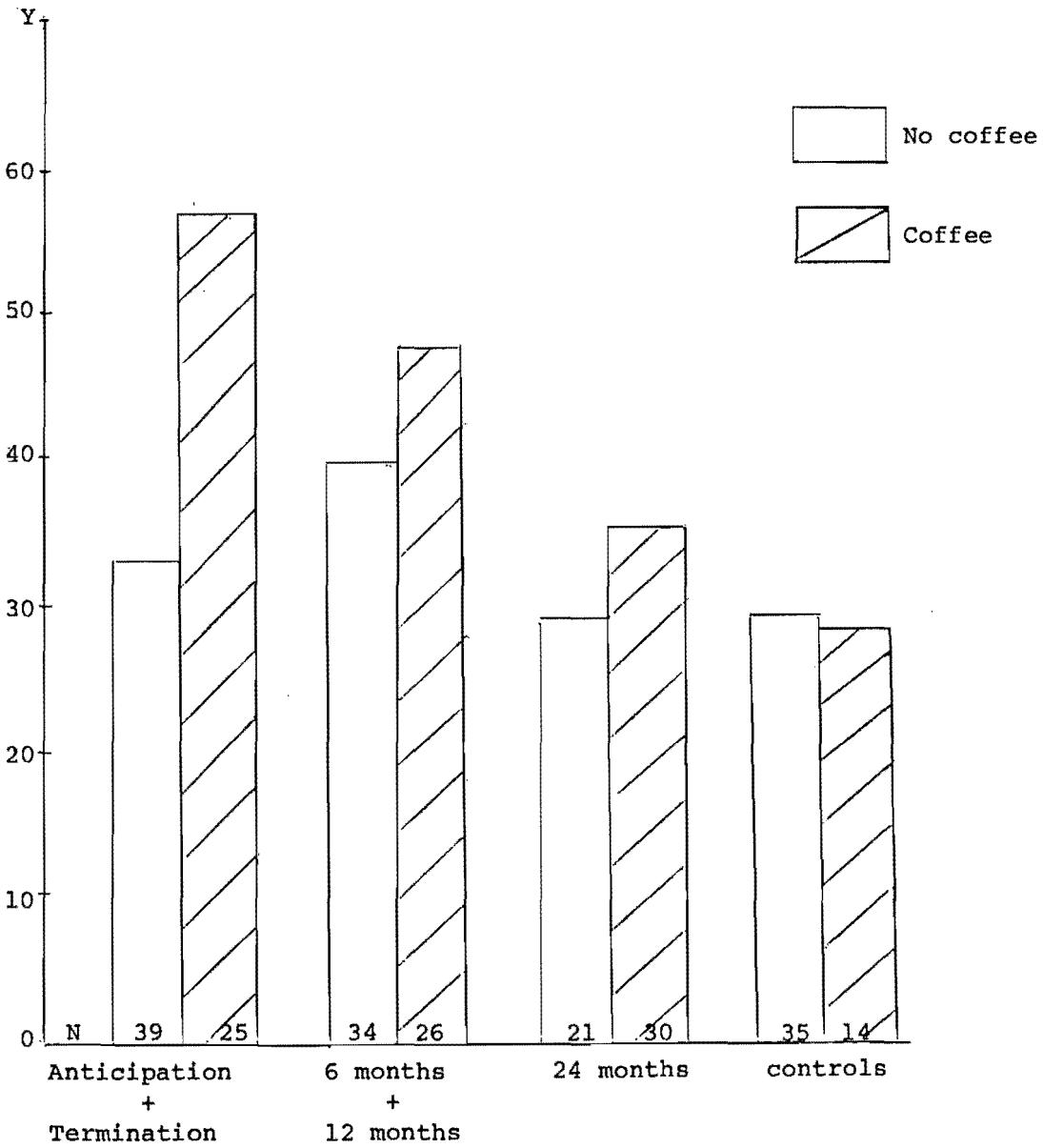
Cobb found that the mean rate of norepinephrine excretion was significantly elevated for those whose jobs ended, before termination and for twelve months afterwards. Of particular interest however, was the finding that when automobile workers consumed coffee during the time of

anticipation and of termination, their increase in norepinephrine output was significantly greater than that of non-coffee-drinking workers who lost their jobs.

Figure 1 illustrates the physiological changes in men whose jobs were termninated. The effect of coffee consumption is also shown.

Figure 1

Physiological changes in men whose jobs were terminated



Norepinephrine excretion rate by phase and by whether or not coffee was taken. From Cobb (1974).

There was no coffee effect at all among those who were in no danger of losing their jobs and for all of the terminees at 24 months, but for the stressful period of anticipation plus termination there was a highly significant difference and for 6 and 12 months later, there was a slight, non-significant difference.

Cobb's research demonstrates the importance of considering interactions with the environment when looking at physiological processes. He explains his findings by suggesting the possibility that caffeine intake at stressful times, could accentuate, perhaps to a critical point, a neurotransmitter response cycle that enhances already-developing clinical symptoms.

Henry and Stephens (1980) investigated caffeine as an intensifier of stress-induced hormonal and pathophysiologic changes in mice. They demonstrated that the substitution of coffee for drinking water produced greatly increased rates of disease and mortality in mice living in large community cages, where stressful, competitive interaction typically led to cardiovascular and renal pathology. Caffeine-related enhancements of these effects of competitive social stimulation included increases in blood pressure, adrenal weight, and plasma renin and corticosterone. Caffeine produced similar results, although to a lesser degree, in mice whose environment was less stressful. The authors concluded from the study that caffeine can indeed intensify responses to stress.

This finding is reminiscent of Henry's (1969, 1970) observation of hypertension in mice. Isolated mice had little or no rise in blood pressure when given coffee rather than water; while those mice boxed in groups of eight so they had the opportunity to fight, had significantly greater rises if they were on coffee.

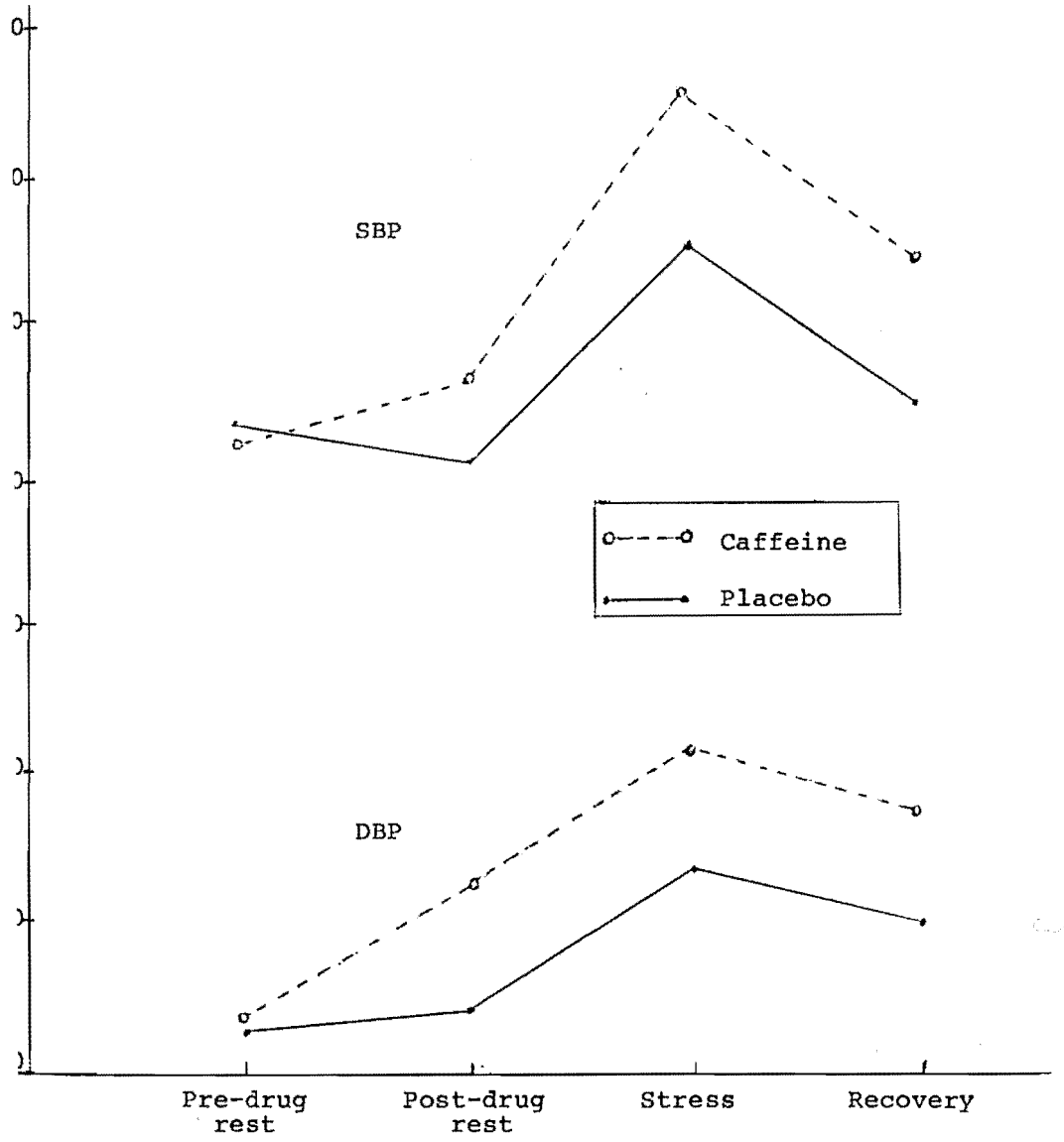
More recently Lane (1983), examined the potential interaction of caffeine and psychological stress in 10 "caffeine-naive" human subjects. The cardiovascular effects of a moderate dose of caffeine (250mg), equivalent to two or three cups of coffee, were measured during periods of rest and psychological stress. Comparisons of caffeine and placebo were made with regard to levels of cardiovascular activity during rest and stress and to the magnitude of cardiovascular response elicited by the psychological stressor. Moderate doses of caffeine were found to show elevations in blood pressure (both systolic and diastolic) during periods of rest and stress. Blood pressure during stress was also significantly higher after caffeine had been consumed.

Figure 2 shows the effects of caffeine on systolic and diastolic blood pressure at rest and during psychological stress.

Lane (1983) concluded from his findings that the elevation of blood pressure due to caffeine appeared to add to that elicited by stress.

Figure 2

Effect of caffeine on blood pressure at rest and during psychological stress



From Lane (1983)

The elevation in systolic and diastolic blood pressure produced by caffeine was significant ($p<0.05$) for the Post-drug rest, Stress, and Recovery periods. The effect of caffeine was equivalent at each of these three points.

NATURE AND SCOPE OF THE EXPERIMENT

The present study examined the potential interaction of caffeine and psychological stress in human subjects who regularly consumed caffeine. More specifically subjects comprised of those who showed 'high' and 'low' anxiety levels as determined by administration of the Spielberger Trait - Anxiety Inventory, and consumed 2 or more cups of coffee and/or tea per day.

The cardiovascular effects of a high (400mg) dose of caffeine, equivalent to 4 or 5 cups of coffee were measured during periods of rest and psychological stress. The magnitude of the effect of caffeine on blood pressure and heart rate before (resting) and during stress was made. Subjective ratings of alertness and tension were recorded respectively after each part of the experiment and scored from the visual analogue scales yielding numbers from 0 to 100. Comparisons of performance in a mental arthimetic task (stressor) between caffeine and a placebo were made, as well as a determination of any significant effects between subjects with high anxiety levels and those with low anxiety levels.

Aims of the Experiment

1. To measure any subsequent changes in physiological responses to caffeine in blood pressure (systolic and diastolic), during rest and stressful situations.

2. To measure the effects of caffeine upon psychological performance during a stressful situation, ie. does caffeine impair of enhance performance?

3. To measure self reported "alertness" and "tension" following caffeine consumption, ie. is caffeine associated with greater or less reported alertness and tension during a stressful task than during a resting period?

4. To determine whether caffeine shows any additive effect on the cardiovascular measurements and subjective self reports, with that produced by psychological stress.

5. To determine whether any significant differences in 1, 2, 3, and 4 exist between subjects with high trait anxiety levels and those with low trait anxiety levels.

Rationale and Hypotheses of the Experiment

Previous investigations have highlighted the importance of the inverted-U relationship between the amount of stress induced by the task and performance efficiency (Yerkes and Dodson, 1908). According to the inverted-U hypothesis, task performance is optimal at intermediate levels of task difficulty or stress (drive level) and poor when drive level is either low enough to cause boredom or too high causing task interference (Broadhurst, 1959; Hebb, 1955; Malmo, 1959).

Anxiety levels then, can increase or decrease performance. If one is too anxious one tends not to do so

well, as is the case if one were not at all anxious. However, at intermediate levels of anxiety optimal performance may be obtained.

Although past research has looked at the effects of caffeine on anxiety and stress among regular and non-regular consumers, I am unaware of any studies regarding comparisons of the effects of caffeine on those in the population who have generally high trait anxiety levels and those who have generally low anxiety levels.

Caffeine consumption has been shown to increase arousal and awareness levels due to its central nervous system stimulant properties (Thompson, 1975; Ritchie, 1975; Graham, 1978).

I have addressed the relationship between caffeine consumption, level of anxiety (Trait - High vs Low), and performance efficiency in a study of mental arithmetic (Stressor), to test the hypothesis that:

> Caffeine consumption might be used as a means for a low anxiety person to reach an optimal level of anxiety in order to perform well in a stressful situation eg. exams or speech. Likewise, caffeine consumption may well be avoided by those who have high anxiety levels if they are to perform well under psychological stress.

PROCEDURE

Subjects

Thirty-eight volunteer stage one Psychology students comprising 23 females and 15 males participated in the experiment. The ages ranged from 17 to 40 years with a mean age of 22.

The subjects were screened for testing in the experiment according to the following criteria:

- They regularly consumed caffeine, ie. drinking at least 2 or more cups of coffee and/or tea per day.

- They obtained scores which were at the extremes of the Spielberger Trait - Anxiety Inventory, ie. High anxiety subjects and Low anxiety subjects.

Apparatus

The experiment was carried out in a controlled laboratory setting. Noise was kept to a minimum, and the subject sat on a chair beside a desk for the entire session.

a) Physiological measurements

Blood pressure. An electronic 3005 blood pressure meter was used to record subject's systolic and diastolic blood pressure in mm Hg.

Heart rate. The digital heart rate monitor (Model 77065), electronically measured heart rate in beats per minute (BPM) to within an accuracy of ±1 BPM.

b) Performance measurements

A set of 2 figure and 3 figure subtraction problems (devised by the author) was used in the serial subtraction mental arithmetic task which provided the stressor in the experiment, eg. (14-9, 219-102, 911-712). The same set was administered to all subjects, on both testing sessions.

A standard tape recorder was used to record the student's responses to the mental arithmetic task. Results were later audited to determine performance.

c) Subjective reports

Reports of subjective "Tension" and "Alertness" were taken at certain intervals during the experiment, using Visual Analogue Scales (VAS). Each of these involved a horizontal line 10cm long with a statement at one end that the symptom, feeling or attitude could not be stronger and at the other that it was completely absent. After being made to understand what it was meant to signify, subjects made a mark somewhere along its length to indicate their impression of the strength of that feeling. Measurement to the nearest mm provided a sufficiently large number of categories to allow considering it as a continuum, and so the scores met assumptions necessary for parametric analyses.

A digital stopwatch was used for timing throughout the experiment.

d) Trait Anxiety Inventory

To assign subjects to either the High anxiety group or the Low anxiety group the Spielberger Trait Anxiey Inventory (Spielberger, 1970) was administered. Instructions to the subject indicated that the given scale ("Trait") anxiety referred to the subject's habitual mode or feeling.

The "A-trait scale" comprises 20 statements which refer to how the subject generally feels. Each statement (eg. "I lack self-confidence") is rated on a 4 point scale from "almost never" to "almost always".

e) Drugs

Caffeine. The caffeinated drinks contained caffeine BP (white powder form). The drink consisted of 400mg caffeine mixed in 48mls of water and 2mls of "Thriftee" diabetic drink concentrate to lower the bitterness and make more palatable.

Placebo. Placebo drinks contained quinine sulphate as it provided sufficient bitterness to mimick the taste of caffeine. As this component is pharmacologically inactive at doses of or below 5mg/50ml, the drink consisted of 5mg quinine sulphate mixed in 48mls of water and 2mls of "Thriftee" diabetic drink concentrate.

Method

Two hundred stage one Psychology students who regularly consumed caffeine (2 or more cups of coffee and/or tea per day) completed a self-evaluation questionnaire (Spielberger Trait Anxiety Inventory). The sample population

in the experiment comprised those who obtained scores at either extreme of the scale, ie. High and Low anxiety scores.

Criterion for assignment to High and Low Anxiety groups

As about 40 subjects were required for any valid and reliable representation, the following criterion was used as a means of assigning roughly equal numbers to the experimental groups.

High Anxiety group. Comprised subjects who scored 51 and above on the Trait Anxiety Inventory. N=22. (ie. top 11% of scores)

Low Anxiety group. Comprised subjects who scored 36 and below on the Trait Anxiety Inventory. N=20. (ie. bottom 10% of scores)

Subjects who scored between 36 and 51 were excluded from the experiment.

Although initially 42 subjects agreed to participate in the experiment only 38 completed both sessions.

The subjects who failed to complete the experiment (all females) were not able to cope with the stressor (mental arithmetic task), becoming very anxious, agitated, nervous, noticably shaking - 3 even to the point of crying. The other female subject who failed to complete both sessions, had a history of epilepsy. During the mental arithmetic task she began to show symptoms of the initial stages of an epileptic seizure, ie. shaking, crying, involuntary spasms in her arms.

Although perhaps being an unfortunate consequence of the experiment, the behaviour of these four subjects did serve an indirectly useful purpose, indicating that the mental arithmetic task was indeed a potent stressor.

Subjects were briefed prior to the experiment about location, time etc. and were asked to refrain from drinking any caffeine (coffee, tea, cocoa, cola, chocolate) on the day of the experiment).

Each subject was individually dealt with. An initial 15 minute Predrug resting baseline was taken while the subject sat quietly. Both heart rate (HR) and blood pressure (systolic, SBP, and Diastolic, DBP) measurements were taken at 3 minute intervals. This provided a measure of cardio-vascular activity for later comparisons. At the end of this Predrug resting period, the subject was administered two visual analogue scales - a "Tension" scale and an "Alertness" scale for completion.

Caffeine or the placebo was then administered using a single-blind procedure. The subject drank either 50ml of cordial containing 400mg of caffeine, or the 50ml of cordial containing the placebo quinine sulphate. The order of administration was random for each subject, but counter-balanced such that half of the subjects received caffeine first and the other half placebo first. Each subject then relaxed for 30 minutes and read magazines. This allowed sufficient time for plasma caffeine levels to reach near maximum (Robertson et al., 1978).

Following this, measurements of heart rate and blood pressure were taken every 3 minutes during a 15 minute Post-drug resting baseline interval while the subject sat quietly. At the end of this Postdrug resting period, subjects completed the "Tension" and "Alertness" visual analogue scales.

After this second resting baseline, instructions were given for the psychological stressor, namely performance on a serial subtraction mental arithmetic task under challenging conditions. Instructions read;

> "You are now going to be given a mental arithmetic task. You have exactly two six minute periods to subtract as quickly as possible without making errors.
>
> Being at the stage one level you should be able to answer everyone correctly with no mistakes.
>
> Your answers will be tape recorded for later analysis, as a comparison with other stage one students, and results will be posted on the stage one noticeboard next term.
>
> Give one answer only even if you think you've made a mistake and do not work out aloud. You must have an answer for each question.
>
> Remember to go as quickly and as well as you can in a loud clear voice.
>
> Any Questions?"

Tasks of this type are known to produce elevations in heart rate and blood pressure, as well as elevations in plasma epinephrine, norepinephrine, prolactin and cortisol (Lane, 1983).

Subjects performed this task continuously for two six minute periods with a 15 minute "stress" interval while heart

rate and blood pressure were measured every 3 minutes. At the end of this "stress" period subjects completed "Tension" and "Alertness" visual analogue scales.

The final 15 minute Recovery period involved the subject again sitting quietly while cardiovascular activity (heart rate and blood pressure) was assessed every 3 minutes. "Tension" and "Alertness" scales were also administered.

The second session for each subject was identical to the first with the exception of the drug condition. Heart rate, systolic blood pressure, and diastolic blood pressure were averaged separately for each of the four periods in each experimental session. The tape recordings of the mental arithmetic task performances were audited and the total number attempted and percentage correct determined. The subjective ratings of "alertness" and "tension", recorded retrospectively after each part of both sessions were scored from visual analogue scales yielding numbers from 0 to 100.

CHAPTER FOUR

RESULTS

The effects of caffeine were analysed with respect to the following experimental variables:

A: Trait anxiety level (high or low)

B: Sex (male or female)

C: Order of drug condition presentation

ie. caffeine (1st) → placebo (2nd)

or

placebo (1st) → caffeine (2nd)

D: Drug condition (caffeine or placebo)

Results were reported under three main headings;

1. Physiological measures
   - systolic blood pressure (SBP)
   - diastolic blood pressure (DBP)
   - heart rate (HR)

2. Subjective report measures
   - tension
   - alertness

3. Performance measures

- total attempted in mental arithmetic task
- percentage correct in mental arithmetic task

Calculations

Calculations involved four way ANOVA's (A, B, C, D repeated on D, unequal groups). In view of the large number of analyses, the null hypothesis was only rejected at $p<.01$. Three groups of ANOVA's were performed, ie.

1. Predrug ANOVA's

ANOVAs were performed at the predrug level of each of the physiological and subjective report measures to determine if any significant differences existed before drug administration.

2. ANOVA's on three difference scores

As the main emphasis of the experiment focused on the significant changes each measure (SBP, DBP, HR, tension and alertness) could undergo between the four periods of the experiment, results were reported as:

$$x = \frac{\text{postdrug value - predrug value}}{\text{postdrug value + predrug value}}$$

$$y = \frac{\text{stressor value - postdrug value}}{\text{stressor value + postdrug value}}$$

$$z = \frac{\text{recovery value - stressor value}}{\text{recovery value + stressor value}}$$

Example: Predrug - Postdrug SBP (x):

Predrug SBP value = 115 mm Hg, Postdrug SBP value = 127 mm Hg

$$x = \frac{\text{postdrug value-predrug value}}{\text{postdrug value+predrug value}} = \frac{127-115}{127+115} = \frac{12}{242} = .05 \text{ mm Hg}$$

3. Performance ANOVA's

Separate ANOVA's were carried out on the performance scores calculated as:

a) Total attempted

b) Percent correct

PREDRUG DATA

The following tables represent the mean values obtained for each measure in each group at the predrug level of the experiment.

Physiological Measures

Table 7

Predrug systolic blood pressure (SBP) mmHg

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	121.5	126.3
	Low	Caffeine 1st → Placebo 2nd	119.3	120.8
	High	Placebo 1st → Caffeine 2nd	125.2	135.5
	Low	Placebo 1st → Caffeine 2nd	125.4	126.9
Female	High	Caffeine 1st → Placebo 2nd	112.7	116.8
	Low	Caffeine 1st → Placebo 2nd	127.7	124.9
	High	Placebo 1st → Caffeine 2nd	116.2	119.8
	Low	Placebo 1st → Caffeine 2nd	121.1	128.3

Table 8

Predrug diastolic blood pressure (DBP) mmHg

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	73.6	67.4
	Low	Caffeine 1st → Placebo 2nd	70.4	65.9
	High	Placebo 1st → Caffeine 2nd	75.8	77.4
	Low	Placebo 1st → Caffeine 2nd	69.3	78.0
Female	High	Caffeine 1st → Placebo 2nd	75.6	76.7
	Low	Caffeine 1st → Placebo 2nd	83.2	74.7
	High	Placebo 1st → Caffeine 2nd	67.3	74.8
	Low	Placebo 1st → Caffeine 2nd	73.7	82.0

Table 9

Predrug heart rate (HR) bpm

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	74.5	81.6
	Low	Caffeine 1st → Placebo 2nd	80.7	72.5
	High	Placebo 1st → Caffeine 2nd	71.0	71.8
	Low	Placebo 1st → Caffeine 2nd	75.6	70.7
Female	High	Caffeine 1st → Placebo 2nd	88.5	88.5
	Low	Caffeine 1st → Placebo 2nd	79.8	80.7
	High	Placebo 1st → Caffeine 2nd	89.7	78.0
	Low	Placebo 1st → Caffeine 2nd	79.8	89.2

Subjective Measures

Table 10

Predrug tension - mm

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	31.0	31.2
	Low	Caffeine 1st → Placebo 2nd	25.0	18.5
	High	Placebo 1st → Caffeine 2nd	29.0	52.6
	Low	Placebo 1st → Caffeine 2nd	22.7	27.7
Female	High	Caffeine 1st → Placebo 2nd	38.0	25.2
	Low	Caffeine 1st → Placebo 2nd	27.6	30.1
	High	Placebo 1st → Caffeine 2nd	24.2	41.7
	Low	Placebo 1st → Caffeine 2nd	26.8	32.5

Table 11

Predrug alertness - mm

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	42.7	43.2
	Low	Caffeine 1st → Placebo 2nd	54.2	47.7
	High	Placebo 1st → Caffeine 2nd	49.0	59.3
	Low	Placebo 1st → Caffeine 2nd	57.7	63.0
Female	High	Caffeine 1st → Placebo 2nd	47.5	46.2
	Low	Caffeine 1st → Placebo 2nd	58.6	50.0
	High	Placebo 1st → Caffeine 2nd	53.7	70.5
	Low	Placebo 1st → Caffeine 2nd	51.8	56.1

The ANOVA analyses of each predrug measure revealed no significant main effects or interactions ($F(1,30)<7.56$, $p<.01$)

ANOVA's ON THREE DIFFERENCE SCORES

The order of drug presentation proved more than any other main effect (ie. anxiety trait, sex, or drug condition) to be the most recurrent variable involved in interactions. No attempts were made to interpret any significant four-way interactions on the grounds that they occurred so infrequently as to be psychologically insignificant.

PHYSIOLOGICAL MEASURES

Systolic blood pressure (SBP) Predrug-Postdrug period (x)

Table 12 shows the mean difference values obtained for SBP in each group for the predrug-postdrug period (x).

Table 12

Mean differences in SBP for x

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.004	-.028
	Low	Caffeine 1st → Placebo 2nd	.024	-.024
	High	Placebo 1st → Caffeine 2nd	.015	-.038
	Low	Placebo 1st → Caffeine 2nd	.042	-.018
Female	High	Caffeine 1st → Placebo 2nd	.030	-.027
	Low	Caffeine 1st → Placebo 2nd	.030	-.040
	High	Placebo 1st → Caffeine 2nd	.023	-.058
	Low	Placebo 1st → Caffeine 2nd	.005	-.021

Analysis of variance, revealed no significant main effects in SBP for the predrug-postdrug period ($F(1,30)<7.56$, $p<.01$). However an interaction effect between sex, anxiety level, and order of drug presentation (ABC) did occur ($F(1, 30)=96.5$, $p<.001$). Table 13 gives the mean differences for the interaction of ABC.

Between the predrug and postdrug periods, high anxiety males who received caffeine on the first test showed smaller SBP differences than low anxiety males who received caffeine on the first test. High anxiety males who received caffeine on the second test also showed a smaller difference in SBP between the predrug and postdrug periods than low anxiety males who received caffeine on the second test.

However, the high anxiety females showed a greater SBP difference between the predrug and postdrug periods on receiving caffeine on the first test than did low anxiety females who received caffeine on the first test. But, on receiving caffeine on the second test, high anxiety females showed smaller SBP differences between the predrug and postdrug periods than the low anxiety females who received caffeine second.

Table 13

Mean differences for ABC

		Caffeine 1st→Placebo 2nd	Placebo 1st→Caffeine 2nd
Male	High Anxiety	-.024	-.023
	Low Anxiety	0	0
Female	High Anxiety	.003	-.035
	Low Anxiety	-.010	.016

Note: Values obtained as the result of the mean values of caffeine minus the mean values of placebo. 0 = no difference in means.

Systolic blood pressure (SBP) Postdrug-Stressor period (y)

Table 14 shows the mean difference values obtained for SBP in each group for the postdrug-stressor period (y).

Table 14

Mean differences in SBP for y

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.035	.044
	Low	Caffeine 1st → Placebo 2nd	.042	.015
	High	Placebo 1st → Caffeine 2nd	.054	.060
	Low	Placebo 1st → Caffeine 2nd	.008	.006
Female	High	Caffeine 1st → Placebo 2nd	.035	.033
	Low	Caffeine 1st → Placebo 2nd	.026	.060
	High	Placebo 1st → Caffeine 2nd	.014	.040
	Low	Placebo 1st → Caffeine 2nd	.038	.043

Analysis of variance showed the order of drug presentation to be a significant main effect on SBP between the postdrug and stressor periods ($F(1,30)=16.6$, $p<.01$). That is, it was the order of drug presentation which determined the resulting SBP, rather than any other factor(s), eg. caffeine administration. If it was due to the drug then the resulting SBP would be the same regardless of the order in which the drug was administered.

No significant interaction effects occurred for SBP between the postdrug and stressor periods ($F(1,30)<7.56$, $p<.01$).

Systolic blood pressure (SBP) Stressor-Recovery period (z)

Table 15 shows the mean difference values obtained for SBP in each group for the stressor-recovery period (z).

Table 15

Mean differences in SBP for z

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	-.016	-.023
	Low	Caffeine 1st → Placebo 2nd	-.018	-.019
	High	Placebo 1st → Caffeine 2nd	-.007	-.036
	Low	Placebo 1st → Caffeine 2nd	-.017	-.037
Female	High	Caffeine 1st → Placebo 2nd	-.074	-.034
	Low	Caffeine 1st → Placebo 2nd	-.024	-.020
	High	Placebo 1st → Caffeine 2nd	-.022	-.030
	Low	Placebo 1st → Caffeine 2nd	-.029	-.040

Analysis of variance revealed no significant main effects or interactions in SBP between the stressor and recovery periods ($F(1,30)<7.56$, $p<.01$).

Diastolic blood pressure (DBP) Predrug-Postdrug period (x)

Table 16 shows the mean difference values obtained for DBP in each group for the predrug-postdrug period (x).

Analysis of variance revealed no significant main effects in DBP between the predrug and postdrug periods ($F(1,30)<7.56$, $p<.01$). However an interaction effect between the anxiety level and drug condition (BD) existed ($F(1,30) = 9.41$, $p<.01$). Table 17 gives the mean differences for the interaction of BD.

Table 16

Mean differences in DBP for x

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	-.016	-.002
	Low	Caffeine 1st → Placebo 2nd	.030	.006
	High	Placebo 1st → Caffeine 2nd	.049	-.083
	Low	Placebo 1st → Caffeine 2nd	.203	.008
Female	High	Caffeine 1st → Placebo 2nd	.061	.012
	Low	Caffeine 1st → Placebo 2nd	.023	.008
	High	Placebo 1st → Caffeine 2nd	.073	-.027
	Low	Placebo 1st → Caffeine 2nd	.023	.061

Table 17

Mean differences for BD

	Caffeine	Placebo
High anxiety	.167	-.1
Low anxiety	.279	.362

Following the administration of caffeine, high anxiety subjects showed a greater difference in DBP than was the case after administration of placebo. Low anxiety subjects had the reverse trend, showing a smaller difference in DBP in the caffeine condition compared to the placebo condition between the predrug and postdrug periods.

Caffeine administration tended to show greater DBP differences during the resting periods than placebo with low anxiety subjects but not with high anxiety subjects.

Diastolic blood pressure (DBP) Postdrug-Stressor period (y)

Table 18 shows the mean difference values obtained for DBP in each group for the postdrug-stressor period (y).

Table 18

Mean differences in DBP for y

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.051	.044
	Low	Caffeine 1st → Placebo 2nd	.047	.037
	High	Placebo 1st → Caffeine 2nd	.011	.058
	Low	Placebo 1st → Caffeine 2nd	.040	.090
Female	High	Caffeine 1st → Placebo 2nd	.046	.049
	Low	Caffeine 1st → Placebo 2nd	.044	.046
	High	Placebo 1st → Caffeine 2nd	.028	.048
	Low	Placebo 1st → Caffeine 2nd	.028	.083

Analysis of variance revealed no significant main effects in DBP between the postdrug and stressor periods ($F(1,30)<7.56$, $p<.01$). Two interaction effects however, did occur. Table 19 gives the mean differences for the interaction of sex and anxiety level (AB). Table 20 gives the mean differences for the interaction of anxiety level and order of drug presentation (AC).

Firstly, a sex and anxiety level interaction (AB), ($F(1,30)=65.3$, $p<.01$) revealed that low anxiety males showed greater DBP differences between the postdrug and stressor periods than high anxiety males. The same was true for females. Low anxiety females showed greater DBP differences between the postdrug and stressor periods than high anxiety females. Sex differences were reversed in the high and low anxiety groups. That is, females showed greater DBP

differences than males in the high anxiety group, while males showed greater DBP differences than females in the low anxiety group.

Secondly, an anxiety level and order of drug presentation interaction (AC), ($F(1,30)=65.3$, $p<.01$) revealed that high anxiety subjects who received caffeine on the first test showed greater DBP differences between the postdrug and stressor periods than low anxiety subjects who received caffeine on the first test. However, low anxiety subjects who receive caffeine on the second test showed greater DBP differences between the postdrug and stressor periods than high anxiety subjects who received caffeine on the second test.

Therefore, regardless of the order of drug presentation, caffeine administration showed greater difference effects than did placebo for both high and low anxiety subjects with DBP, between the postdrug and stressor periods.

Table 19

Mean differences for AB

	High anxiety	Low anxiety
Male	.164	.214
Female	.171	.201

Table 20

Mean differences for AC

	Caffeine 1st → Placebo 2nd	Placebo 1st → Caffeine 2nd
High anxiety	.19	.145
Low anxiety	.174	.241

Diastolic blood pressure (DBP) Stressor-Recovery period (z)

Table 21 shows the mean difference values obtained for DBP in each group for the stressor-recovery period (z).

Table 21

Mean differences in DBP for z

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.015	.005
	Low	Caffeine 1st → Placebo 2nd	.006	.026
	High	Placebo 1st → Caffeine 2nd	.009	.027
	Low	Placebo 1st → Caffeine 2nd	.022	.005
Female	High	Caffeine 1st → Placebo 2nd	-.008	.033
	Low	Caffeine 1st → Placebo 2nd	.018	0
	High	Placebo 1st → Caffeine 2nd	-.23	.022
	Low	Placebo 1st → Caffeine 2nd	.170	-.036

Analysis of variance revealed no significant main effects or interactions in DBP between the stressor and recovery periods ($F(1,30)<7.56$, $p<.01$).

Heart rate (HR) Predrug-Postdrug period (x)

Table 22 shows the mean difference values obtained for HR in each group for the predrug-postdrug period (x).

Table 22

Mean differences in HR for x

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	-.023	-.048
	Low	Caffeine 1st → Placebo 2nd	-.115	-.012
	High	Placebo 1st → Caffeine 2nd	.024	.038
	Low	Placebo 1st → Caffeine 2nd	-.090	.033
Female	High	Caffeine 1st → Placebo 2nd	-.038	.006
	Low	Caffeine 1st → Placebo 2nd	.026	.003
	High	Placebo 1st → Caffeine 2nd	-.044	-.022
	Low	Placebo 1st → Caffeine 2nd	-.035	.005

Analysis of variance revealed no significant main effects or interactions in HR between the predrug and postdrug periods ($F(1,30)<7.56$, $p<.01$).

Heart rate (HR) Postdrug-Stressor period (y)

Table 23 shows the mean difference values obtained for HR in each group for the postdrug-stressor period (y).

Table 23

Mean differences in HR for y

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.022	.036
	Low	Caffeine 1st → Placebo 2nd	.021	.012
	High	Placebo 1st → Caffeine 2nd	.032	.026
	Low	Placebo 1st → Caffeine 2nd	.015	.025
Female	High	Caffeine 1st → Placebo 2nd	.033	.021
	Low	Caffeine 1st → Placebo 2nd	.055	.05
	High	Placebo 1st → Caffeine 2nd	.004	.014
	Low	Placebo 1st → Caffeine 2nd	.024	.031

Analysis of variance revealed no significant main effects or interactions in HR between the postdrug and stressor periods ($F(1,30)<7.56$, $p<.01$).

Heart rate (HR) Stressor-Recovery period (z)

Table 24 shows the mean difference values obtained for HR in each group for the stressor-recovery period (z).

Table 24

Mean differences in HR for z

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	-.017	-.056
	Low	Caffeine 1st → Placebo 2nd	-.055	-.03
	High	Placebo 1st → Caffeine 2nd	-.02	-.028
	Low	Placebo 1st → Caffeine 2nd	-.018	-.005
Female	High	Caffeine 1st → Placebo 2nd	-.026	-.035
	Low	Caffeine 1st → Placebo 2nd	-.014	-.02
	High	Placebo 1st → Caffeine 2nd	-.01	-.009
	Low	Placebo 1st → Caffeine 2nd	.011	-.03

Analysis of variance revealed no significant main effects in HR between the stressor and recovery periods ($F(1,30)<7.56$, $p<.01$). However, a significant interaction effect between anxiety level and order of drug presentation (BC) did occur ($F(1,30)=11.1$, $p<.01$). Table 25 gives the mean differences for the interaction of BC.

Both high and low anxiety subjects showed smaller differes in HR's when they received caffeine on the first test session, compared to placebo on the first test session between the stressor and recovery periods.

Table 25

Mean Differences for BC

	Caffeine 1st → Placebo 2nd	Placebo 1st → Caffeine 2nd
High anxiety	-.134	-.05
Low anxiety	-.20	-.024

SUBJECTIVE REPORT MEASURES

Tension Predrug-Postdrug period (x)

Table 26 shows the mean difference values obtained for tension in each group for the predrug-postdrug period (x).

Table 26

Mean differences in tension for x

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.153	.024
	Low	Caffeine 1st → Placebo 2nd	.096	.233
	High	Placebo 1st → Caffeine 2nd	.217	-.037
	Low	Placebo 1st → Caffeine 2nd	.177	.094
Female	High	Caffeine 1st → Placebo 2nd	-.099	.008
	Low	Caffeine 1st → Placebo 2nd	.260	.093
	High	Placebo 1st → Caffeine 2nd	.233	.025
	Low	Placebo 1st → Caffeine 2nd	.097	-.187

Analysis of variance revealed no significant main effects in tension between the predrug and postdrug periods ($F(1,30)<7.56$, $p<.01$). However, two significant interaction effects did occur. Table 27 gives the mean differences for the interaction of anxiety level and order of drug presentation (BC). Table 28 gives the mean differences for the interaction of order of drug presentation and drug condition (CD).

Firstly, an interaction between anxiety level and order of drug presentation (BC), $F(1,30)=8.8$, $p<.01$, outlined in Table 27, showed that low anxiety subjects who received caffeine on the first text showed greater differences in reported subjective tension than high anxiety subjects who received caffeine on the first test, between the predrug and postdrug periods.

However, the reverse occurred when caffeine was experienced on the second test. That is, high anxiety subjects who received caffeine on the second test showed greater differences in reported tension between the predrug and postdrug periods than low anxiety subjects who experienced caffeine on the second test.

Secondly, a significant interaction between order of drug presentation and drug condition (CD), $F(1,30)=16.2$, $p<.01$) revealed that subjects who received caffeine on the first test showed greater tension differences between the predrug and postdrug periods in the caffeine condition than the placebo condition.

However, those subjects who received caffeine on the second test showed smaller tension differences between the predrug and postdrug periods in the caffeine condition than the placebo condition.

Table 27

Mean differences for BC

	Caffeine 1st → Placebo 2nd	Placebo 1st → Caffeine 2nd
High anxiety	.086	.437
Low anxiety	.682	.181

Table 28

Mean differences for CD

	Caffeine 1st → Placebo 2nd	Placebo 1st → Caffeine 2nd
High anxiety	.41	.722
Low anxiety	.358	1.12

Tension Postdrug-Stressor period (y)

Table 29 shows the mean difference values obtained for tension in each group for the predrug-postdrug period (y).

Table 29

Mean differences in tension for y

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.36	.07
	Low	Caffeine 1st → Placebo 2nd	.19	.40
	High	Placebo 1st → Caffeine 2nd	.3	.27
	Low	Placebo 1st → Caffeine 2nd	.25	.40
Female	High	Caffeine 1st → Placebo 2nd	.4	.38
	Low	Caffeine 1st → Placebo 2nd	.36	.3
	High	Placebo 1st → Caffeine 2nd	.22	.5
	Low	Placebo 1st → Caffeine 2nd	.073	.21

Analysis of variance revealed no significant main effects in tension between the postdrug and stressor periods ($F(1,30)<7.56$, $p<.01$). However, an interaction effect between order of drug presentation and drug condition (CD) occurred ($F(1,30)=15.24$, $p<.01$). Table 30 gives the mean differences for the interaction of CD.

Subjects who received caffeine on the first test showed greater differences in tension with the caffeine condition, than with the placebo condition, between the postdrug and stressor periods. In contrast, subjects who received caffeine on the second test showed smaller differences in tension with the caffeine condition than with the placebo condition between the postdrug and stressor periods.

Hence, we have an order of drug presentation effect. It is not the caffeine which is accountable for tension differences, but whether the subject received it on the first or second test. If caffeine administration did in fact result in these tension differences, then the order of its presentation would have no effect.

Table 30

Mean differences for CD

	Caffeine 1st → Placebo 2nd	Placebo 1st → Caffeine 2nd
Caffeine	1.31	.843
Placebo	1.15	1.4

Tension Stressor-Recovery period (z)

Table 31 shows the mean difference values obtained for tension in each group for the stressor-recovery period (z).

Table 31

Mean differences in tension for z

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.163	-.29
	Low	Caffeine 1st → Placebo 2nd	.033	.07
	High	Placebo 1st → Caffeine 2nd	-.336	-.64
	Low	Placebo 1st → Caffeine 2nd	-.12	-.34
Female	High	Caffeine 1st → Placebo 2nd	-.26	-.23
	Low	Caffeine 1st → Placebo 2nd	-.34	-.27
	High	Placebo 1st → Caffeine 2nd	-.17	-.24
	Low	Placebo 1st → Caffeine 2nd	.053	-.24

Analysis of variance revealed no significant main effects in tension between the stressor and recovery periods ($F(1,30)<7.56$, $p<.01$). However, an interaction effect between sex and order of drug presentation (AC), ($F(1,30)= 9.24$, $p<.01$) showed that opposite trends in tension had occurred for the two sexes between the stressor and recovery periods. Table 32 gives the mean differences for the interaction of AC.

Male subjects who received caffeine on the first test showed a greater difference in tension than those males who received caffeine on the second test. On the other hand, female subjects who received caffeine on the first test showed a smaller difference in tension than those females who received caffeine on the second test.

Table 32

Mean differences for AC

	Caffeine 1st → Placebo 2nd	Placebo 1st → Caffeine 2nd
Male	- .024	-1.43
Female	-1.11	- .6

Alertness Predrug-Postdrug period (x)

Table 33 shows the mean difference values obtained for alertness in each group for the predrug-postdrug period (x).

Table 33

Mean differences in alertness for x

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	-.009	-.017
	Low	Caffeine 1st → Placebo 2nd	.017	.028
	High	Placebo 1st → Caffeine 2nd	.039	.005
	Low	Placebo 1st → Caffeine 2nd	-.019	.049
Female	High	Caffeine 1st → Placebo 2nd	-.073	.114
	Low	Caffeine 1st → Placebo 2nd	.003	.035
	High	Placebo 1st → Caffeine 2nd	-.082	-.331
	Low	Placebo 1st → Caffeine 2nd	.031	-.021

Analysis of variance revealed no significant main effects or interactions between the predrug and postdrug periods ($F(1,30)<7.56$, $p<.01$).

Alertness Postdrug-Stressor period (y)

Table 34 shows the mean difference values obtained for alterness in each group for the postdrug-stressor period (y).

Table 34

Mean differences in alertness for y

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.05	.22
	Low	Caffeine 1st → Placebo 2nd	.06	.08
	High	Placebo 1st → Caffeine 2nd	.55	.21
	Low	Placebo 1st → Caffeine 2nd	.16	.12
Female	High	Caffeine 1st → Placebo 2nd	.19	-.03
	Low	Caffeine 1st → Placebo 2nd	.23	.05
	High	Placebo 1st → Caffeine 2nd	.27	.11
	Low	Placebo 1st → Caffeine 2nd	.08	.02

Analysis of variance revealed a significant order of drug presentation effect in alertness between the postdrug and stressor periods ($F(1,30)=16.3$, $p<.01$). However, the significant interaction of order of drug presentation with anxiety level and drug condition (BCD) ($F(1,30)=8.3$, $p<.01$) makes a detailed consideration of order of drug presentation effects inapprorpaite. Table 35 gives the mean differences for the interaction of BCD.

High anxiety subjects who received either caffeine in the first test or placebo in the first test showed greater differences in alertness under the caffeine condition than the placebo condition between the postdrug and stressor periods. Low anxiety subjects under the same conditions also showed this trend.

Table 35

Mean differences for BCD

		Caffeine	Placebo
High anxiety	Caffeine 1st → Placebo 2nd	.24	.197
	Placebo 1st → Caffeine 2nd	.82	.32
Low anxiety	Caffeine 1st → Placebo 2nd	.29	.132
	Placebo 1st → Caffeine 2nd	.25	.14

Alertness Stressor-Recovery period (z)

Table 36 shows the mean difference values obtained for alertness in each group for the stressor-recovery period (z).

Table 36

Mean differences in alertness for z

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	.17	.096
	Low	Caffeine 1st → Placebo 2nd	.034	-.021
	High	Placebo 1st → Caffeine 2nd	-.022	.014
	Low	Placebo 1st → Caffeine 2nd	-.038	-.002
Female	High	Caffeine 1st → Placebo 2nd	-.006	-.076
	Low	Caffeine 1st → Placebo 2nd	.124	.016
	High	Placebo 1st → Caffeine 2nd	.18	.175
	Low	Placebo 1st → Caffeine 2nd	.065	.089

Analysis of variance revealed no significant main effects in alertness between the stressor and recovery periods ($F(1,30)<7.56$, $p<.01$). However, a significant interaction effect between sex, order of drug presentation and drug condition (ACD) ($F(1,30)=13.2$, $p<.01$) did exist. Table 37 gives the mean differences for the interaction of ACD.

Male subjects who received caffeine on the first test showed a greater difference in alertness under the caffeine condition than the placebo condition between the stressor and recovery periods. This trend was also illustrated by the females who complimented the same group under the same conditions.

In contrast, both males and females who received caffeine on the second test showed smaller differences in alertness under the caffeine condition than the placebo condition between the stressor and recovery periods.

Overall, differences were greater for male and female subjects who received caffeine on the first test.

Table 37

Mean differences for ACD

		Caffeine	Placebo
Male	Caffeine 1st → Placebo 2nd	.204	.075
	Placebo 1st → Caffeine 2nd	-.04	.012
Female	Caffeine 1st → Placebo 2nd	.118	-.06
	Placebo 1st → Caffeine 2nd	.245	.26

PERFORMANCE MEASURES

Total attempted

Table 38 shows the mean number obtained for the total number of subtraction problems attempted for each group in the mental arithmetic task.

Table 38

Mean number of total attempted

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	95.2	103.2
	Low	Caffeine 1st → Placebo 2nd	104.7	107.7
	High	Placebo 1st → Caffeine 2nd	104	93.3
	Low	Placebo 1st → Caffeine 2nd	85.2	87.7
Female	High	Caffeine 1st → Placebo 2nd	85.3	89
	Low	Caffeine 1st → Placebo 2nd	66	70.1
	High	Placebo 1st → Caffeine 2nd	100.5	89.2
	Low	Placebo 1st → Caffeine 2nd	112.1	104.1

Analysis of variance revealed no significant main effects in the total number attempted in the mental arithmetic task ($F(1,30)<7.56$, $p<.01$). However analysis revealed two significant interaction effects.

There was a significant interaction between order of drug presentation and drug effects (CD) (($F(1,30,=12$, $p<.01$), which is more appropriately considered in the light of a significant anxiety level x order of drug presentation x drug condition (BCD), ($F(1,30)=49.7$, $p<.01$) interaction. Table 39 gives the mean values for the interaction of BCD. This showed that high and low anxiety subjects who received caffeine on the first test showed a lower performance in the

total number attempted when under the caffeine condition as compared to the placebo condition. In contrast, high and low anxiety subjects who received caffeine on the second test showed a greater performance in the total number attempted when under the caffeine condition as compared to the placebo condition.

Both high and low anxiety subjects performed better in the total number attempted on the second test regardless of the drug condition.

Table 39

Mean values for BCD

		Caffeine	Placebo
High anxiety	Caffeine 1st → Placebo 2nd	180.5	192.2
	Placebo 1st → Caffeine 2nd	240.5	185.2
Low anxiety	Caffeine 1st → Placebo 2nd	170.7	177.8
	Placebo 1st → Caffeine 2nd	197.3	191.8

Percentage correct

Table 40 shows the mean number obtained for the percentage correct for each group in the mental arithmetic task.

Table 40

Mean number of percentage correct

Sex	Anxiety level	Order of drug presentation	Caffeine condition	Placebo condition
Male	High	Caffeine 1st → Placebo 2nd	64.6	66.8
	Low	Caffeine 1st → Placebo 2nd	59.9	71.6
	High	Placebo 1st → Caffeine 2nd	78.3	72.9
	Low	Placebo 1st → Caffeine 2nd	74.3	59.3
Female	High	Caffeine 1st → Placebo 2nd	58.8	65.2
	Low	Caffeine 1st → Placebo 2nd	60.5	70.7
	High	Placebo 1st → Caffeine 2nd	58	58
	Low	Placebo 1st → Caffeine 2nd	70.2	64

Analysis of variance revealed no significant main effects in performance with respect to the percentage correct in the mental arithmetic task ($F(1,30)<7.56$, $p<.01$). However a number of interactive effects occurred, especially those involving order of drug presentation. Table 41 gives the mean values for the interaction between sex, anxiety level, and order of drug presentation ABC. Table 42 gives the mean values for the interaction between anxiety level, order of drug presentation and drug condition BCD.

Finally, an interaction between sex, anxiety level, and order of drug presentation (ABC), ($F(1,30)=187$, $p<.01$) showed that high and low anxiety male subjects who received caffeine on the first test attained very similar percentage correct performances in the mental arithmetic task.

High anxiety female subjects who received caffeine on the first test showed lower percentage correct performances than the low anxiety females. High anxiety males who received caffeine on the second test showed greater percentage correct performances than the low anxiety males who received caffeine on the second test. However, high anxiety females who received caffeine on the second test showed lower percentage correct performances than the low anxiety group.

Thus, high anxiety male subjects showed a higher percentage correct performance than low anxiety males when caffeine was administered on the second test, while high anxiety female subjects showed a lower percentage correct

performance than low anxiety females when caffeine was administered on the first test.

Finally, the two significant interactions of anxiety level with drug condition (BD) and order of drug presentation with drug condition (CD), are more appropriately considered in the light of a significant interaction between anxiety level, order of drug presentation and drug condition (BCD), ($F(1,30)=1839$, $p<.01$). Table 42 gives the mean values for the interaction of BCD. This showed that both high and low anxiety subjects who received caffeine on the first test showed lower percentage correct performances when under the caffeine condition as compared to the placebo condition. In contrast, high and low anxiety subjects who received caffeine on the second test showed higher percentage correct performances when under the caffeine condition as compared to the placebo condition.

Table 41

Mean values for ABC

		Caffeine 1st→Placebo 2nd	Placebo 1st→Caffeine 2nd
Male	High anxiety	131.4	151.2
	Low anxiety	131.5	133.6
Female	High anxiety	124	116
	Low anxiety	131.2	134.2

Table 42

Mean values for BCD

		Caffeine	Placebo
High anxiety	Caffeine 1st → Placebo 2nd	123.4	132
	Placebo 1st → Caffeine 2nd	136.3	130.9
Low anxiety	Caffeine 1st → Placebo 2nd	120.4	142.3
	Placebo 1st → Caffeine 2nd	144.5	123.3

CHAPTER FIVE

DISCUSSION

An unfortunate consequence of the present experimental design was the fact that the order of drug presentation proved more than any other factor, (ie. high or low anxiety trait, sex, or drug condition) to be the most recurrent variable involved in significant interactions. The order of drug presentation was the only significant main effect within the experiment, which made detailed consideration of certain interaction effects difficult if not inappropriate.

PHYSIOLOGICAL MEASURES

Blood Pressure

Earlier studies demonstrated that caffeine (in amounts roughly equivalent to several cups of coffee) can significantly elevate resting blood pressure in subjects who do not regularly consume caffeinated products (Ritchie, 1975; Innes and Nickerson, 1975; Robertson et al., 1978; Lane, 1983).

The results of the present experiment involving regular consumers of caffeine who scored at the extremes of the Trait - Anxiety Inventory, however, did not support these findings. That is, caffeine (in amounts roughly equivalent to about five cups of coffee) did not significantly elevate resting blood pressure in subjects who drink two or more cups

of coffee and/or tea per day in both high and low anxiety subjects.

More importantly the present study demonstrated that caffeine did not appear to have any additive effect on blood pressure measurements with that provided by psychological stress.

The results of the present study of the effects of acute administration in human subjects did not support Cobb's (1974) report on physiological changes in men whose jobs were abolished, the chronic effects in mice reported by Henry and Stephens (1980), and Lane's (1983) study of the potential interaction of caffeine and stress in caffeine naive subjects. It suggested that among high and low anxiety subjects who regularly consumed caffeine, the combination of caffeine and stress in daily life may not produce significantly greater elevations in blood pressure than would occur with either caffeine or stress alone.

Caffeine consumption has been implicated by epidemiologic research as a risk factor for heart disease, although the results have been mixed and conclusions remain controversial. Two reports (Paul et al., 1963; Yudkin and Roddy, 1964) indicated positive associations that were subsequently explained, at least in part, by the effects of other variables, specificially cigarette smoking (Paul, 1967) and sucrose intake (Paul, 1968; Yudkin and Morland, 1967).

The results of two prospective studies showed no association between coffee drinking and coronary heart disease (Dawber et al., 1975; Klotsky et al., 1973), but the results of two case control studies of survivors of myocardial infarction showed positive asociations (Jick et al., 1973; Bowan and Rand, 1980).

The results of the present study demonstrated that caffeine may not be associated with increased risk of heart disease in subjects whose anxiety levels are at the extremes of the continuum, that is, both high and low anxiety subjects. However, the experiment did reveal some interesting interaction effects.

Firstly, a significant interaction effect between sex, anxiety level, and order of drug presentation revealed that low anxiety males and high anxiety females showed greater elevations in systolic blood pressure on receiving caffeine on the first testing session, than high anxiety males and low anxiety females for the predrug and postdrug resting periods. That is, caffeine tended to show greatest elevation in systolic blood pressure during the resting periods for low anxiety males and high anxiety females upon receiving caffeine as a first test experience.

Secondly, a significant interaction between anxiety level and drug condition showed that high anxiety subjects appeared to be more at risk with respect to elevations in diastolic blood pressure than low anxiety subjects between the predrug and postdrug resting periods when caffeine was

administered. That is, high anxiety subjects were more susceptable to elevations in resting diastolic blood pressure than low anxiety subjects following caffeine consumption during the resting periods. This coupled with the finding that high anxiety female subjects showed the greatest elevations in systolic blood pressure during rest, suggests that this group (female subjects with high anxiety levels) are most at risk to such changes in resting blood pressure and should, therefore, more than any other group studied, avoid caffeine consumption because of the possible consequences of hypertension and cardiovascular disorders.

Thirdly, a significant interaction effect between sex and anxiety level revealed that the low anxiety groups for both males and females showed greater elevations in diastolic blood pressure, than the high anxiety males and females during stress. Low anxiety males showed the greatest elevation in diastolic blood pressure for this period. Also, regardless of the order of drug presentation, ie. whether caffeine was presented on the first or second test, caffeine administration produced greater elevations than did the placebo for both high and low anxiety subjects for diastolic blood pressure during the stressor (mental arithmetic task).

Therefore low anxiety males showed the greatest elevation in diastolic blood pressure upon caffeine consumption during stress and could therefore also be at risk of hypertension and cardiovascular problems especially if their lifestyle and workplace proved highly stressful.

Heart Rate

The effect of caffeine on heart rate has been particularly controversial with elevation (Scott et al., 1944), depression (Fleisch and Wenner, 1954) and no change (Ritchie, 1975; Stephenson, 1977) being reported. In patients with complete heart block, intravenous administration of caffeine slowed the arterial rate whereas the ventricular rate was accelerated (Semerov, 1923). Furthermore, since caffeine administration did not lead to bradycardia in the vagotomized dog (Sallmon and Pilcher, 1912), the slowing of heart rate may be a baroreceptor-mediated effect in compensation for the raised blood pressure, or a direct effect at the level of the brainstem.

Lane (1983) found that administration of caffeine (250 mg) resulted in no significant change in heart rate among subjects who did not consume caffeine regularly, for both periods of rest and stress. The results of the present experiment confirm that Lane's findings are also applicable to high and low anxiety subjects who regularly consume caffeine. That is, administration of caffeine (400mg) resulted in no significant change in heart rate among high and low anxiety subjects during periods of both rest and stress, for subjects who regularly consume caffeine.

A significant interaction effect between sex and anxiety level for the predrug and postdrug resting periods existed. The finding that high anxiety males and low anxiety females showed the greatest elevations in heart rate during rest could imply that these two groups are the most

susceptable to possible cardiovascular disorders following caffeine consumption. However, the present experiment revealed that administration of caffeine (equivalent to doses of about 5 cups of coffee) did not appear to significantly effect heart rate, in either high or low anxiety subjects during rest or during a stressful situation. Therefore, it would be incorrect to single out high anxiety males and low anxiety females as prime candidates for possible cardiovascular disorders with such caffeine consumption.

One could say then, that, caffeine consumption (400mg) did not potentiate or add to any changes in heart rate to the elevation produced by psychological stress, and would therefore in such doses pose no real threat to cardiac function during a stressful situation.

SUBJECTIVE REPORTS

Alertness

Goldstein (1965, 1969) reports that subjects vary greatly with respect to the subjective feelings of alertness induced by caffeine. The finding in the present study that caffeine administration (400mg) had no real significant effects on reported levels of alertness during both rest and stress did not support earlier reports of increased subjective alertness (Barmack, 1940; Goldstein et al., 1969; Clubley et al., 1978; Lane, 1983).

However, the present study specifically involved subjects who scored at the extremes of the Trait - Anxiety

Inventory (high and low anxiety subjects) compared with a more general cross section of anxiety levels in the earlier studies. One could suggest from this that high and low anxiety subjects rather than moderately anxious subjects, may least expect their alertness levels to be effected by caffeine consumption, in doses of about five cups of coffee.

A significant interaction between anxiety level, order of drug presentation, and drug condition for reported levels of alertness existed between the postdrug and stressor phases. Administration of caffeine to both high and low anxiety subjects regardless of order of drug presentation, showed greater differences in reported alertness under the caffeine condition than the placebo condition. This implied that administration of caffeine increased subjective alertness at this period. Overall, high anxiety subjects showed a greater difference than low anxiety subjects. This could perhaps suggest that both high and low anxiety subjects should consume caffeine before a stressful situation to increase alertness levels, particularly in high anxiety subjects.

A significant interaction between sex, order of drug presentation, and drug condition revealed an order of drug presentation effect, rather than a drug effect for reported levels of alertness. If caffeine did produce these difference effects, then results would be the same regardless of whether caffeine was administered on the first test or on the second test. This was not the case.

Tension

A significant interaction between order of drug presentation and drug condition in the experiment, revealed that it was the order in which caffeine was presented rather than the drug itself which determined the level of reported subjective tension. If tension differences between the experimental periods was due to caffeine then the order of presentation (receiving caffeine on the 1st or 2nd test), would have no effect on the reported tension. That is, subjects who received caffeine on the second test would also show greater tension differences in the caffeine condition than the placebo condition for the resting periods. This, however, was not the case. The order of drug presentation effect was also accountable for reported tension levels during stress.

Opposite trends in reported levels of tension for the two sexes were shown in the interaction between sex and order of drug presentation following the stressful task. From the results one could imply that administration of caffeine to males results in greater reported levels of tension than females following a stressful situation. That is, males may well be wise to avoid consumption of caffeine before a stressful task. The added tension experienced may well impair one's performance, making the individual unable to fully relax, think clearly, or carry out the task as efficiently in a stressful situation, eg. exams or making a public speech. This would probably increase other 'negative' emotions and feelings such as nervousness, dry throat, stage fright etc., as well as compounding any physiological effects

such as increased blood pressure, perspiration, or heart rate. As was the case with the cardiovascular measurements, caffeine administration did not show any additive effect on either tension or alertness with that produced by psychological stress.

PERFORMANCE IN THE MENTAL ARITHMETIC TEST

As mentioned earlier, reports on caffeine's effects on mental tasks are limited and tend towards isolated studies, for example, improvements in simple arithmetic and uncoding (Truitt, 1971), faster solving of maths problems (Paroli, 1972) and adverse effects of the recall of a series of nonsense syllables (Hull, 1935).

The results of the present study indicated that, although high anxiety subjects attempted slightly more problems in the mental arithmetic task with the consumption of caffine, and low anxiety subjects attempted slightly fewer problems under the same condition, the difference between the two groups was insignificant.

However, significant interactions between order of drug presentation, anxiety level, and drug condition existed. Again, the order of drug presentation, appeared to be the most prominent factor in the relationship. That is, both high and low anxiety subjects performed better in the total number attempted on the second test, regardless of the drug condition. Caffeine proved neither to enhance nor impair the total number of maths problems attempted.

Overall, both high and low anxiety subjects showed lower percentage correct performances when under the caffeine condition as compared to the placebo condition. However, as was the case in the total number attempted, an order of drug presentation effect occurred. That is, both high and low anxiety subjects showed higher percentage correct performances in the second test regardless of the drug condition. In this respect caffeine could be said to neither enhance nor impair the percentage correct in the mental arithmetic task.

From the experimental results then, one can conclude that if a high or low anxiety person who regularly consumes caffeine is going to perform a stressful mental task, for example an exam, and consumes caffeine in doses equivalent to about 5 cups of coffee prior to the exam, then that person should not expect his/her performance to be enhanced or impaired by the drug.

Thus the results of the present study do not support the hypothesis that caffeine administration be used as a means for low anxiety subjects to reach an optimal drive or stress level to perform optimally during a stressful situation. Likewise, there was no evidence to suggest that those who have high anxiety levels should avoid caffeine consumption to achieve such a goal.

SUMMARY OF CAFFEINE EFFECTS

- The order of drug presentation proved more than caffeine administration to be the most recurrent variable involved in interaction.

- Caffeine did not appear to have a potential additive effect on the cardiovascular measurements and subjective self reports, with that produced by psychological stress.

- High anxiety female subjects showed the greatest elevation in resting systolic and diastolic blood pessure with caffeine consumption.

- Low anxiety males showed the greatest elevation in diastolic blood pressure with caffeine consumption during the stressful situation.

- High anxiety males and low anxiety females showed the greatest elevations in heart rate during rest.

- Males showed greater reported levels of tension with caffeine consumption both at rest and during stress, than did females.

- High anxiety subjects showed greater elevations in alertness both at rest and during stress following caffeine consumption than low anxiety subjects.

- Caffeine consumption had no effect on performance in a mental arithmetic task, in both high and low anxiety subjects.

Although the present study failed to find any major significant differences between high and low anxiety subjects response to caffeine, this failure is in itself a finding. However, most, if not all studies on caffeine have involved a general cross section of anxiety levels, and future research which specifically investigates caffeine's effects on high and low trait anxiety subjects is clearly warranted.

SUGGESTIONS FOR FUTURE RESEARCH

1. Future research should avoid having an order of drug presentation effect. This could be overcome by having a between groups experimental design which involves a single session whereby some subjects consume caffeine only, and other subjects consume placebo only. By having a single session one would avoid any problems of familiarity and expectation.

2. It must be remembered that when discussing the physiological, subjective, and performance effects of 400mg caffeine (equivalent in dosage to about 5 cups of coffee) used in the experiment, this was administered in a single dose. When extrapolating the effects to daily life, one must be careful as caffeine consumption is usually spread over the day. The effects of 400mg of caffeine 'loaded' into the system at a single sitting would almost certainly

be greater than if consumed over 3 or 4 sittings in the period of a day. Future research should take this factor into account when looking at daily levels of caffeine and their effects.

3. A study of caffeine and its effects on the circulatory system and the medullary centres should include multiple measurements of multiple variables. The present study limited the physiological measurements to cardiovascular measurements in blood pressure and heart rate. As Ritchie (1975) pointed out, "The observation of a single function, for example, blood pressure, is deceiving because the drug may act on a variety of circulatory factors in such a way that blood pressure may remain essentially unchanged". Future research should include multiple measurements of such things as catecholomine release and blood plasma levels of caffeine for more accurate and valid results.

4. If one is to study the differences between high and low trait anxiety subjects in response to caffeine, then a standard definition or categorization of what constitutes high and low trait anxiety is required. For example, the present study categorized high anxiety subjects as those who scored 51 and above (top 10%) and low anxiety subjects as those who scored 36 and below (bottom 10%) on the Spielberger Trait Anxiety Inventory. There is a need for future research to deliniate just what constitutes high and low trait anxiety.

5. The hormonal variation in females during menstruation was not taken into account in the present study. Cycle response to caffeine may have very important implications not only because of the effect this could have on females behaviour (tiredness, inability to concentrate, more emotional etc.), but also the way in which caffeine may interact with or effect the hormonal inbalance. For example, it may be that caffeine exaggerates existing behaviour during the cycle leading to such things as greater tension levels, and interference with performance, than in a female who is not menstruating. Future research should also consider what effect(s) caffeine has on women who use the contraceptive pill.

6. The search for explanations of the individual differences and interactions of caffeine with other variables should involve subject characteristics being recorded with great care. As Sawyer et al. (1981) point out, people may differ in response to caffeine according to age, sex, mental state, personality type, and degree of physical fitness. There could be differences between racial and ethnic groups, particularly those groups where caffeine consumption has been high for centuries as opposed to groups for whom it is a relatively new substance. Information of this kind may lead to new insights in understanding individual differences in response to caffeine.

7. More experimental replication of existing findings with larger subject samples is important, along with more information regarding subjects ingestion of a variety of psychoactive substances and their histories of caffeine intake. It is important that experimental replications use the same levels of caffeine and assess the same effects using the same testing and measuring methods.

ACKNOWLEDGEMENTS

I would like to thank Dr Robert Hughes for his supervision and guidance, and Rebecca Cox for her kind assistance in this study.

Thanks to Ijan Beveridge for his co-operation.

Many thanks also to the students of the University of Canterbury who participated in the experiment, whom without, this study would not have been possible.

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APPENDICES

APPENDIX 1

SELF-EVALUATION QUESTIONNAIRE

SELF-EVALUATION QUESTIONNAIRE

STAI FORM X-2

ME _____ DATE _____

ECTIONS: A number of statements which people have l to describe themselves are given below. Read each state- t and then blacken in the appropriate circle to the right of statement to indicate how you *generally* feel. There are no t or wrong answers. Do not spend too much time on any statement but give the answer which seems to describe you generally feel.

	ALMOST NEVER	SOMETIMES	OFTEN	ALMOST ALWAYS
I feel pleasant	①	②	③	④
I tire quickly	①	②	③	④
I feel like crying	①	②	③	④
I wish I could be as happy as others seem to be	①	②	③	④
I am losing out on things because I can't make up my mind soon enough	①	②	③	④
I feel rested	①	②	③	④
I am "calm, cool, and collected"	①	②	③	④
I feel that difficulties are piling up so that I cannot overcome them	①	②	③	④
I worry too much over something that really doesn't matter	①	②	③	④
I am happy	①	②	③	④
I am inclined to take things hard	①	②	③	④
I lack self-confidence	①	②	③	④
I feel secure	①	②	③	④
I try to avoid facing a crisis or difficulty	①	②	③	④
I feel blue	①	②	③	④
I am content	①	②	③	④
Some unimportant thought runs through my mind and bothers me	①	②	③	④
I take disappointments so keenly that I can't put them out of my mind	①	②	③	④
I am a steady person	①	②	③	④
I get in a state of tension or turmoil as I think over my recent concerns and interests	①	②	③	④

APPENDIX 2

TENSION AND ALERTNESS SCALES

VERSITY OF CANTERBURY DEPARTMENT OF PSYCHOLOGY

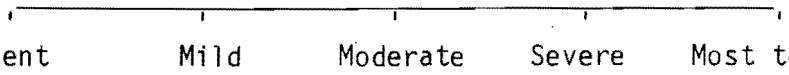
Tension and Alertness Scales

ow are two visual analogue scales, a Tension scale, and an Alertness
ıle.

: statements "Most tense" and "Most alert" at one end of the scales
ɲnifies that this symptom, feeling or attitude could not be stronger,
ɨ at the other that it is completely "absent".

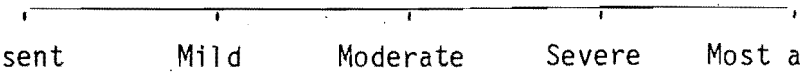
· each of the two scales make a mark, | , somewhere along its length
indicate your impression of the strength of that feeling now.

Tension Scale



Absent Mild Moderate Severe Most tense

Alertness Scale



Absent Mild Moderate Severe Most alert

APPENDIX 3

PREDRUG ANOVA TABLES

PHYSIOLOGICAL MEASURES

Predrug systolic blood pressure (SBP)

Source	df	F
Between Ss		
A (sex)	1	1.37
B (anxiety)	1	<1
C (order)	1	<1
AB	1	3.39
AC	1	<1
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	<1
ABCD	1	<1
Error	30	

Predrug diastolic blood pressure (DBP)

Source	df	F
Between Ss		
A (sex)	1	1.37
B (anxiety)	1	<1
C (order)	1	<1
AB	1	1.34
AC	1	1.91
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	<1
ABCD	1	<1
Error	30	

Predrug heart rate (HR)

Source	df	F
Between Ss		
A (sex)	1	1.07
B (anxiety)	1	<1
C (order)	1	<1
AB	1	<1
AC	1	<1
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	4.56
BCD	1	7.5
ABD	1	<1
ABCD	1	<1
Error	30	

SUBJECTIVE MEASURES

Predrug tension

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	2.99
C (order)	1	<1
AB	1	1.09
AC	1	<1
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	2.49
ACD	1	<1
BCD	1	<1
ABD	1	<1
ABCD	1	<1
Error	30	

Predrug alertness

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	5.56
AB	1	<1
AC	1	<1
BC	1	1.34
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	<1
ABCD	1	<1
Error	30	

APPENDIX 4

ANOVA TABLES ON THREE DIFFERENCE SCORES FOR THE PHYSIOLOGICAL MEASUREMENTS AND SUBJECTIVE SELF REPORTS

PHYSIOLOGICAL MEASURES

Systolic blood pressure (SBP) x: Predrug-Postdrug period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	1.26
C (order)	1	<1
AB	1	2.37
AC	1	2.47
BC	1	<1
ABC	1	96.5 (p<.001)
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	<1
ABCD	1	<1
Error	30	

Systolic blood pressure (SBP) y: Postdrug-Stressor period

Source	df	F
Between Ss		
A (sex)	1	1.26
B (anxiety)	1	4.05
C (order)	1	16.6 (p<.001)
AB	1	<1
AC	1	<1
BC	1	<1
ABC	1	4.7
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	1.07
ABCD	1	1.6
Error	30	

Systolic blood pressure (SBP) z: Stressor-Recovery period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	4.97
C (order)	1	1.38
AB	1	<1
AC	1	4.5
BC	1	<1
ABC	1	3.8
Error	30	
Within Ss		
D (drug)	1	6.3
AD	1	1.5
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	1.6
ABD	1	4.5
ABCD	1	<1
Error	30	

Diastolic blood pressure (DBP) x: Predrug-Postdrug period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	<1
AB	1	<1
AC	1	<1
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	2.4
AD	1	1.86
BD	1	9.41 ($p<.01$)
CD	1	2.76
ACD	1	<1
BCD	1	<1
ABD	1	<1
ABCD	1	9.6
Error	30	

Diastolic blood pressure (DBP) y: Postdrug-Stressor period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	-
AB	1	65.3 (p<.01)
AC	1	-
BC	1	65.3 (p<.01)
ABC	1	-
Error	30	
Within Ss		
D (drug)	1	4.76
AD	1	-
BD	1	-
CD	1	4.76
ACD	1	-
BCD	1	<1
ABD	1	<1
ABCD	1	54
Error	30	

Diastolic blood pressure (DBP) z: Stressor-Recovery period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	1.57
C (order)	1	<1
AB	1	<1
AC	1	<1
BC	1	1.3
ABC	1	2.9
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	2.7
CD	1	<1
ACD	1	<1
BCD	1	2.5
ABD	1	3.2
ABCD	1	<1
Error	30	

Heart rate (HR) x: Predrug-Postdrug period

Source	df	F
Between Ss		
A (sex)	1	1.00
B (anxiety)	1	<1
C (order)	1	<1
AB	1	6.17
AC	1	4.74
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	5.62
AD	1	<1
BD	1	1.97
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	5.02
ABCD	1	2.65
Error	30	

Heart rate (HR) y: Postdrug-Stressor period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	1.5
AB	1	<1
AC	1	<1
BC	1	<1
ABC	1	1.1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	1.03
BD	1	<1
CD	1	1.85
ACD	1	<1
BCD	1	<1
ABD	1	3.48
ABCD	1	<1
Error	30	

Heart rate (HR) z: Stressor-Recovery period

Source	df	F
Between Ss		
A (sex)	1	1
B (anxiety)	1	<1
C (order)	1	2.4
AB	1	<1
AC	1	<1
BC	1	11.1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	<1
ABD	1	1.3
ABCD	1	73.9
Error	30	

SUBJECTIVE REPORT MEASURES

Tension x: Predrug-Postdrug period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	<1
AB	1	<1
AC	1	<1
BC	1	8.8
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	2.26
AD	1	<1
BD	1	<1
CD	1	16.22
ACD	1	<1
BCD	1	<1
ABD	1	1.9
ABCD	1	23.5
Error	30	

Tension y: Postdrug-Stressor period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	<1
AB	1	1.68
AC	1	2.11
BC	1	3.35
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	2.16
BD	1	2.86
CD	1	15.24
ACD	1	<1
BCD	1	<1
ABD	1	4.78
ABCD	1	8.27
Error	30	

Tension z: Stressor-Recovery period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	1.75
C (order)	1	1.9
AB	1	1.0
AC	1	9.24 ($p<.01$)
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	5.05
AD	1	1.5
BD	1	<1
CD	1	1.14
ACD	1	<1
BCD	1	2.2
ABD	1	2.3
ABCD	1	<1
Error	30	

Alertness x: Predrug-Postdrug period

Source	df	F
Between Ss		
A (sex)	1	1.28
B (anxiety)	1	1.9
C (order)	1	2.16
AB	1	<1
AC	1	1.48
BC	1	<1
ABC	1	2.8
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	1.2
ACD	1	3.06
BCD	1	2.4
ABD	1	<1
ABCD	1	16.3
Error	30	

Alertness y: Postdrug-Stressor period

Source	df	F
Between Ss		
A (sex)	1	1.7
B (anxiety)	1	5.94
C (order)	1	16.3
AB	1	1.2
AC	1	7
BC	1	<1
ABC	1	<1
Error	30	
Within Ss		
D (drug)	1	3.1
AD	1	1.2
BD	1	<1
CD	1	<1
ACD	1	<1
BCD	1	8.3 ($p<.01$)
ABD	1	<1
ABCD	1	2.0
Error	30	

Alertness z: Stressor-Recovery period

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	<1
AB	1	<1
AC	1	3.1
BC	1	<1
ABC	1	1.03
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	<1
BD	1	<1
CD	1	1.3
ACD	1	13.2 ($p<.01$)
BCD	1	<1
ABD	1	<1
ABCD	1	11.09
Error	30	

APPENDIX 5

ANOVA TABLES FOR TOTALS ATTEMPTED AND PERCENTAGE CORRECT SCORED BY SUBJECTS IN MENTAL ARITHMETIC TASK

Total attempted

Source	df	F
Between Ss		
A (sex)	1	<1
B (anxiety)	1	<1
C (order)	1	<1
AB	1	<1
AC	1	3.0
BC	1	<1
ABC	1	1.7
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	1.2
BD	1	<1
CD	1	12.0
ACD	1	<1
BCD	1	47.1
ABD	1	<1
ABCD	1	<1
Error	30	

Percentage correct

Source	df	F
Between Ss		
A (sex)	1	1.9
B (anxiety)	1	<1
C (order)	1	<1
AB	1	2.0
AC	1	<1
BC	1	<1
ABC	1	18.7
Error	30	
Within Ss		
D (drug)	1	<1
AD	1	3.6
BD	1	9.1
CD	1	4.4
ACD	1	<1
BCD	1	183.9
ABD	1	<1
ABCD	1	<1
Error	30	