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The effect of caffeine on high-intensity, intermittent exercise to exhaustion

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**THE EFFECT OF CAFFEINE ON HIGH-INTENSITY,
INTERMITTENT EXERCISE TO EXHAUSTION**

by

James A. Herman

**A thesis submitted in partial fulfillment
of the requirements for the degree of**

Master of Science

in

Kinesiology

**Department of Kinesiology
University of Nevada, Las Vegas
July 1997**

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ABSTRACT

Caffeine has been propoorted to increase endurance exercise time to exhaustion. However, the effects of caffeine on high-intensity, intermittent exercise to exhaustion have not been widely studied. Therefore, the purpose of this study was to examine the effect of caffeine on intermittent, high intensity exercise to exhaustion in individuals with minimal daily dietary caffeine consumption. Seven male participants, age 26 ± 2 years, body mass 77 ± 11 kg, and $VO_{2\max}$ 47 ± 7 ml/kg/min, performed a high-intensity exercise bout under both caffeine and placebo conditions administered in a counterbalanced, double blind fashion. Participants cycled at 120% of peak power output for 60 seconds followed by 120 seconds of recovery at 50 Watts. Work/rest cycles continued until voluntary exhaustion. Blood samples were taken immediately prior to administering caffeine or placebo beverages, one hour post absorption, and immediately following the conclusion of the exercise test. No significant difference in time to exhaustion was found between caffeine and placebo trials (12.5 ± 5.9 vs 12.3 ± 6.6 min), nor did peak blood lactate concentration differ between trials (11.3 ± 1.0 vs 11.6 ± 1.9 mM). These results suggest that caffeine treatment provides no significant improvement in performance time during intermittent, high-intensity exercise to exhaustion.

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CHAPTER I

INTRODUCTION

Caffeine is the most widely used psychoactive drug in the world (James, 1991).

The most common form of caffeine consumption is coffee, which accounts for approximately 54% of caffeine ingestion, with tea accounting for approximately 43%. The remaining 3% of caffeine ingestion is in the form of chocolate or cocoa products, soft drinks, and medications (Gilbert, 1984). Because caffeine is virtually free of barriers to diffusion, it produces many effects including restlessness, increased lipolysis resulting in a proported glycogen sparing effect, alterations in neuromuscular transmission and mental acuity. Physiological and psychological alterations in behavior derived from caffeine consumption, have led to its use by athletes in an attempt to enhance performance.

While some studies have reported ergogenic benefits from consuming caffeine (Costill, 1978; Jackman et al., 1996, Trice & Hymes, 1995), other studies fail to show caffeine related ergogenic benefits (Cadarette et al., 1983, Williams, 1988).

To date, much of the research concerned with the potential ergogenic benefits of caffeine has focused on endurance rather than short term exercise. Endurance athletes, such as triathletes and marathon runners, may find caffeine appealing because it is reported to alter substrate utilization (Costill et al., 1978; Spriet et al., 1992). Less clear

is the potential benefit for short term higher intensity activities where caffeine may act to modify neuromuscular transmission. Research findings in each of these areas have been inconsistent, with some studies reporting significant benefits while others show negligible differences between caffeine and control groups (Costill et al., 1992; Powers et al., 1983).

Currently, very little research has focused on the effects of caffeine on performance involving short, intense bouts of exercise, separated by brief periods of rest. It is possible that participants in sports such as hockey, tennis, and soccer may derive benefits from caffeine supplementation prior to competition. These benefits may include performing at a higher intensity for a longer period of time due to a decrease in the perception of fatigue, elevated catecholamine levels, or enhanced neuromuscular transmission. This study proposes to research the effects of caffeine on short term, high-intensity exercise in an effort to further define the role of caffeine in improving performance.

Limitations

1. Participants for this study were college age males of average physical characteristics and physical fitness level. Inference of data to the population should be done with caution.

Assumptions

1. Participants gave a maximal effort during the peak aerobic capacity pretest, and both exercise test protocols.
2. Participants abstained from all caffeine intake for a minimum of 4 days prior to the

beginning of the exercise test and maintained this behavior until the conclusion of the test.

3. Participants performed a 12 hour abstinence of food prior to performing the exercise tests.
4. Peak caffeine levels occur one hour post absorption on an empty stomach.

Statement of Hypotheses

Null Hypothesis:

H_0 : Caffeine will not enhance performance and extend the time to exhaustion during exercise that is intermittent and of high intensity.

Alternate Hypothesis:

H_1 : Caffeine will extend the time to exhaustion during intermittent, high-intensity exercise.

CHAPTER 2

LITERATURE REVIEW

Pharmacology

Caffeine is part of the family methylated xanthines whose structure is based on the purine ring. Caffeine's structure is represented by 1,3,7-trimethylxanthine and its most active isomers are theobromine (3,7-dimethylxanthine), theophylline (1,3-dimethylxanthine), and paraxanthine (1,7-dimethylxanthine). Caffeine, theobromine and theophylline are naturally occurring products while paraxanthine is not. Theophylline appears to convert reversibly between caffeine and theophylline isomers (Looser et al., 1974; Roberts & Waller, 1979) while theobromine and paraxanthine are products of caffeine metabolism (Arnaud, 1987). Xanthines are relatively insoluble in liquids. However, salt compound formation tends to improve xanthine solubility (Powers & Dodd, 1985).

The pharmacokinetics of caffeine are unique. Caffeine is virtually free of barriers to diffusion including the blood-brain barrier (Rall, 1985; Somani, Khana, & Bada, 1980). Plasma caffeine levels begin to increase within 15 minutes after an oral dose, with peak levels occurring within one to two hours depending on such factors as stomach contents and whether the caffeine was consumed during an activity or at rest (Axelrod & Reichenthal, 1953; Rall, 1980). The rate of caffeine excretion is a function of liver

metabolism. The half life of caffeine generally ranges from two to four hours, although infants and individuals with hepatic abnormalities or impairment tend to show an increased caffeine half life. Other factors affecting caffeine half life include age, gender, smoking, and oral contraceptive use (Blanchard & Sawers, 1983; Callahan, Robertson, Branfman, McComish, & Yesair, 1983; Yesair, Branfman, & Callahan, 1984; Parsons & Neims, 1978).

An integral component of the pharmacokinetics of caffeine is dose size. The effectiveness of caffeine as an ergogenic aid appears to be largely affected by the size of the caffeine dose administered. Graham and Spriet (1995) administered doses of 3, 6, and 9 mg per kilogram body weight to participants who ran at 85% $\dot{V}O_{2\max}$ until voluntary exhaustion. Endurance was significantly improved over the placebo trial with the 3 and 6 mg/kg doses but not with the 9 mg/kg dose, suggesting that athletes attempting to gain performance enhancement via caffeine supplementation need to avoid taking an excessively large dose. The International Olympic Committee has established a maximum acceptable urinary caffeine level of 12 $\mu\text{g/ml}$. Generally, a 9 mg/kg dose will not exceed this limit (Graham & Spriet, 1991; Van Soeren, Sathasivam, Spriet, & Graham, 1993). A lethal dose of caffeine ranges between 40 and 50 mg/kg but may be lower if other drugs are being taken concurrently. It appears that a dose between 3-6 mg/kg provides the optimal balance between performance enhancement and side effects which include jitters, gastrointestinal discomfort, and an inhibition in the ability to perform meticulous movements (Spriet, 1995).

While part of the effectiveness of caffeine as an ergogenic aide is based on caffeine dose size, a second factor is the relative amount of caffeine consumed daily. The question to be considered is whether minimal dietary caffeine supplementation is

ergogenically more effective than habitual caffeine use. Most studies agree that habitual caffeine use tends to impair the catecholamine response (Van Soeren et al., 1993; Robertson, Wade, Workman, Woosley, & Oates, 1981). Van Soeren et al. (1993) studied the effects of caffeine in naive and habitual caffeine users. Their results indicated that caffeine naive users showed a significant increase in epinephrine levels after consuming a 5 mg/kg caffeine dose and exercising on a cycle ergometer, while caffeine habituated participants showed no such increase in epinephrine levels. Robertson et al. (1981) controlled the diet of eighteen participants for fourteen days. Participants were randomly assigned to one of two groups. Group I received a placebo beverage with each meal while Group II received a placebo beverage with each meal during days one through three and ten through fourteen with caffeine beverages being consumed during days four through ten. Group II plasma epinephrine and norepinephrine levels were significantly elevated on day four but returned to baseline levels within four days, while the plasma catecholamine levels did not significantly change in the control group.

With respect to short term high intensity exercise, there are three main effector sites for caffeine in the human body, the central nervous system, the neuromuscular junction, and the muscle contractile process (Williams, 1991). Each has been implicated in the observed benefits of caffeine. Caffeine has pronounced effects on the central nervous system including reduced sleep, reduced reaction time, enhanced mental sharpness and neuromuscular transmission. The mechanism by which caffeine produces these results is unclear. Two hypotheses have been offered to explain the central nervous system effects. These are cyclic AMP accumulation through phosphodiesterase inhibition and competitive adenosine receptor blockade.

Indirectly, caffeine has been shown to promote cAMP accumulation (Sutherland

& Rall, 1958). Cyclic AMP mediates the actions of many neurotransmitters and hormones in the central nervous system (Sutherland, Robison, & Butcher, 1968), while the enzyme phosphodiesterase mediates cAMP breakdown (Choi, Shamim, Padgett, & Daly, 1988). Blocking phosphodiesterase will result in cAMP accumulation, prolonging cAMP function, thus promoting the actions of neurotransmitters and hormones in the central nervous system. However, the plasma caffeine levels required to initiate this response are estimated to be $300\mu\text{g/ml}$ which is well in excess of acceptable doses for humans (Fredholm 1985).

The second hypothesis proposed to explain the effects of caffeine on the central nervous system is a competitive adenosine receptor blockade. Adenosine is a nucleotide which inhibits neurotransmitter release. Caffeine appears to compete with adenosine for xanthine-sensitive adenosine receptors (Williams, 1987). There are two different adenosine receptor types, a high affinity receptor, A₁, and a low affinity receptor, A₂ (van Calker, Muller, & Hamprecht, 1979). The high affinity receptor has been shown to suppress physiological functions while the low affinity receptor has the opposite effect (Dunwiddie, 1985). As caffeine blocks both A₁ and A₂ adenosine receptors, neurotransmitter turnover is improved. The dosage required to achieve measurable changes in receptor binding is well within the limits of human consumption. Rall (1980) found that competitive adenosine receptor binding was possible with plasma caffeine concentrations ranging from 5 to $30\mu\text{M}$. Furthermore, caffeine's virtual lack of barriers makes it accessible to the unique xanthine-sensitive adenosine receptors located throughout the body. While adenosine receptor blockade accounts for the majority of caffeine's major effects, other mechanisms are suspected of playing important, but less remarkable, roles such as stimulation, calcium release and diminished calcium reuptake

by the sarcoplasmic reticulum. (Arnaud 1987).

Side Effects

While caffeine's primary physiological mode of action has not been established, several of side effects have been noted. These range from sleepless nights and heightened anxiety to quicker reflexes, heightened mental sharpness, and improved neuromuscular transmission.

Reduced Sleep

Caffeine, through central nervous system stimulation, has a dramatic effect on sleep and sleep deprivation. It has been suggested that caffeine's largest central nervous system effect in adults is on sleep (Dews, 1982). Numerous studies have found that caffeine produces a delay in sleep onset, a reduction in sleep time, increased body movements during sleep and an increase in the number of spontaneous awakenings (Muller-Limmroth cited in Battig, 1985; Mullin, 1933; Brezinova, 1975). People most susceptible to sleep disruption tend to be caffeine non-users or caffeine naive individuals. One study did not find an extended time to sleep onset (Nicholson & Stone, 1980). However, this was attributed to the dose being administered immediately prior to sleep which did not allow for adequate caffeine absorption to achieve peak plasma levels.

Reaction Time

Another aspect of central nervous system stimulation which has been extensively studied is reaction time. Faster reaction times have been reported (Rapoport, Jensvold, Elkins, Buchsbaum, Wiengartner, Ludlow, Zahn, Berg, & Neims, 1981; Jacobson & Edgley, 1987; Roache & Griffiths, 1987) with caffeine ingestion. Overall the results are

often contradictory and generally lacking in consistency. Much of the variability in results may be due to differences in the caffeine doses administered. Horst and Jenkins (1935) found that a 3 mg/kg dose resulted in consistently reduced reaction times while a 2 mg/kg dose resulted in inconsistent reductions in reaction time. Additionally, large doses of caffeine may provide no benefits at all. Jacobson and Edgley (1987) performed a study in which 300 mg caffeine, 600 mg caffeine or placebo were administered. Participants were situated in a chair with a bright light positioned directly in front of the chair. Additionally, participants placed the palm of their hand on a breaker switch located 60 degrees from horizontal on their right side. The reaction time test was initiated when the bright light was turned on and concluded when participants removed their hand off the breaker switch. A significant improvement in reaction time was found with the 300 mg dose while no improvements were found in the placebo or the 600 mg dose. Roache and Griffiths (1987) also tested reaction time with 200, 400, and 600 mg doses of caffeine. A computerized reaction time task required the participants to distinguish between randomly selected even and odd numbers ranging from 1 to 8. In response to the odd or even number, participants pressed a left or right telegraphing key, respectively. Trials began with the presentation of a randomly selected digit and terminated when either key was depressed. The time interval between trials varied from 0.5 seconds to 5 seconds apart. Test results indicated a significant reduction in reaction time with the 400 mg dose but no significant change in reaction time with the 200 or 600 mg dose. These results suggest that an optimal dose of caffeine for improving reaction time is between 300 and 400 mg depending on the body mass of the individual.

Mental Sharpness

Mental sharpness is defined as the ability to maintain focus on a task over a prolonged length of time. Caffeine has a distinct effect on this function of the central nervous system. It is believed that caffeine benefits mental sharpness by delaying the onset of mental fatigue, evidenced by a study performed by Fagen, Swift, and Tiplady (1988) in which participants were administered a 200 mg dose prior to performing prescribed tasks for one hour. The largest improvements in performance were found in the second half of the one hour test. However, the theory of delayed onset of mental fatigue has been contested by Battig and Buzzi (1986) who presented the task stimulus at a varied rate which participants could control, rather than at a fixed rate. For each correct response the interval between stimuli was decreased, and for each incorrect response the interval between stimuli was increased. The purpose of this study was to determine whether delayed onset of fatigue was truly responsible for improved mental sharpness. By adjusting the interval between task stimuli, processing rate rather than error rate, could be measured with respect to performance. Processing rate increased with increased caffeine doses of 150 and 450 mg over each ten minute segment of the testing session. These results provide evidence that improvements in mental performance are due to more than a delay in mental fatigue.

Neuromuscular Transmission

Caffeine has been shown to enhance neuromuscular transmission (Brekenridge, Burn, & Matshinsky, 1967; Hofmann, 1969; Wilson, 1973). Eke-Okoro (1982) studied reflex action in the lower leg in the presence of several variables including caffeine. The procedure was to electrically induce dorsiflexion and the subsequent plantar reflex was

measured in participants who had consumed an average of 125 milligrams of caffeine.

Results of this study showed that the stimulus threshold was reduced and the muscle afferent and efferent amplitudes were enlarged one hour after caffeine ingestion.

Breckenridge et al. (1967) proposed that increased muscular cyclic AMP is responsible for the enhanced rate of neuromuscular transmission. However, this theory was discounted when it was learned that caffeine's effects are directed toward the presynaptic neuron (Goldberg & Singer, 1969; Hofmann, 1969). In particular, elevated levels of neurotransmitter release were found. Apparently, caffeine increases the quantity of neurotransmitter released per stimulus, while the speed of the transmission is not affected by caffeine.

Free Fatty Acid Release

Recently, Graham and Spriet (1991) have shown that caffeine significantly increases catecholamine levels in the blood. Specifically, their results showed a rise in plasma epinephrine levels after consuming 6 mg/kg or more of caffeine. The effects of increased levels of epinephrine include increased free fatty acid release, increased heart rate, vasoconstriction, suppressed visceral muscle activity, and bronchiole dilation (Marieb, 1992). Each of these may be beneficial during exercise. However, the most notable of these effects is enhanced free fatty acid release because of a purported glycogen sparing effect (Chesley, Hultman, & Spriet, 1994; Graham & Spriet, 1991).

Increased plasma free fatty acid levels promote an accumulation of cAMP activating lipoprotein lipase and breaking down triglycerides into glycerol and free fatty acids. The advantage of an elevated free fatty acid level is a metabolic shift toward increased lipid oxidation which, in turn, reduces the demand for glucose and glycogen. Glycogen sparing in this manner, would allow the athlete to exercise at a higher

percentage of maximal capacity for a longer period of time. Glycogen sparing through lipid oxidation has been shown to occur during the first 15 to 20 minutes of exercise at 80% of maximal aerobic capacity ($\text{VO}_{2\text{max}}$) (Spriet, MacLean, Dyck, Hultman, Cederblad, & Graham, 1992). Spriet et al. (1992) performed a study with the dual purpose of examining the chronology of glycogen use during exercise in addition to identifying possible mechanisms for this glycogen sparing. Participants cycled to exhaustion at 80% $\text{VO}_{2\text{max}}$ one hour after ingesting 9mg/kg caffeine. Muscle biopsies were taken prior to the beginning of exercise, at the 15 minute mark, and at the completion of exercise. Results indicated a significant increase in the time to exhaustion between caffeine (96.2 ± 8.8 min) and placebo (75.8 ± 4.8 min). Furthermore, glycogen use was significantly reduced in the first 15 minutes of exercise during the caffeine vs. placebo trial (4.7 ± 1.5 vs. 10.6 ± 1.3 mmol·kg dry muscle⁻¹·minute⁻¹). The prolonged time to exhaustion during the caffeine exercise bout conformed with the length of time in which glycogen sparing occurred.

Several studies have shown a glycogen sparing effect of increasing free fatty acids (Essig, Costill, & VanHandel, 1980; Erickson, Schwarzkopf, & McKenzie, 1987; Spriet et al., 1992; Graham, Rush, & van Soeren, 1994), while others have not (Tarnopolsky, Atkinson, MacDougall, Sale, & Sutton, 1989; Toner, Kirkendall, Delio, Chase, Cleary, & Fox, 1982; Ravussin, Bogardus, Scheidegger, LaGrange, Horton, & Horton, 1986). Typically, the respiratory exchange ratio (RER) has been used to estimate the changes seen in fuel metabolism with caffeine consumption. However, two separate studies analyzed caffeine induced metabolic shifts directly via post-exercise muscle biopsy (Essig et al., 1980; Erickson et al., 1987). During 30 minutes of exercise at 69% $\text{VO}_{2\text{max}}$, Essig et al. (1980) found a 42% reduction in muscle glycogen use following ingestion of

5 mg/kg caffeine. Similarly, Erickson et al. (1987) found a 30% reduction in muscle glycogen use after 90 minutes of exercise at 65 to 70%VO₂max with a caffeine dose of 5 mg/kg body weight. The results of these studies suggest that increased uptake of free fatty acids in the muscle may suppress the need for glycolysis or glycogenolysis.

Increased lipid oxidation results in an increase in citrate concentration. Citrate inhibits phosphofructokinase (PFK) which limits the conversion of fructose-6-phosphate to fructose 1,6-bisphosphate, a rate limiting step in glycolysis. The result is a glycogen sparing effect through accumulation of glucose-6-phosphate.

The validity of glycogen sparing induced by elevated plasma epinephrine and the resultant increase in free fatty acid levels has been questioned in recent years. Two studies performed by Van Soeren (1993, 1996) have indicated that elevated epinephrine levels have no significant impact on RER or free fatty acid levels. In the first study, Van Soeren et al. (1993) examined the metabolic and catecholamine responses to caffeine in both caffeine users and non-users. Non-users performed two exercise bouts after consuming either 5mg/kg caffeine or placebo. Exercise bouts were completed on a cycle ergometer at 50% of maximal oxygen consumption and lasted for one hour. Caffeine users performed three exercise bouts designed to control for caffeine use. The first test, under placebo conditions, occurred after four days of voluntary caffeine abstinence. Over the next fourteen days, participants were given a 5mg/kg caffeine dose in two parts or a placebo. The second and third exercise tests occurred at seven day intervals and were similar to the exercise tests of the caffeine non-users. The results indicated that, despite significantly elevated epinephrine levels, non-users failed to show a decrease in RER or increase in free fatty acid concentration. Caffeine users were found to have elevated epinephrine levels during exercise under placebo conditions. However, caffeine users

also failed to show a change in free fatty acid concentration or RER. Because epinephrine stimulates glycogenolysis, it is possible that any benefits gained from glycogen sparing via elevated plasma free fatty acid levels would be neutralized. In the second study, Van Soeren, Mohr, Kjaer, and Graham (1996) tested six tetraplegics and two paraplegics to determine whether caffeine directly stimulated tissues or acted indirectly via increased epinephrine levels induced by caffeine. Subjects were given either a placebo or 6 mg/kg of caffeine. Epinephrine levels in the tetraplegic were not significantly elevated during the caffeine trial while plasma free fatty acid levels were elevated. Conversely, paraplegics showed a significant increase in epinephrine, similar to what would be expected from resting able-bodied individuals, and an increase in plasma free fatty acids. These results indicate that increased free fatty acid levels are not dependent on elevated epinephrine levels, and instead suggest that caffeine directly effects adipose tissues.

The concept that caffeine results in glycogen sparing has two potential limitations. First, glycogen sparing has only been shown to benefit endurance athletics engaging in aerobic exercise. High intensity exercise requires energy production which may exceed the oxidative capacity preventing the maximization of the potential advantages presented by elevated plasma free fatty acid levels. In fact, there may not even be a glycogen sparing effect in high intensity exercise. Jackman, Wendling, Friars, and Graham, (1996) studied the effects of caffeine on high intensity exercise. Fourteen participants ingested a 6mg/kg caffeine dose and cycled at 100% of maximal oxygen capacity three times, separated by six minutes of rest. The first two exercise bouts were two minutes in duration at a controlled power output. The third exercise bout continued to exhaustion. Jackman found that time to exhaustion was improved with caffeine compared with

placebo. Additionally, lactate production was higher during the caffeine trial. They concluded that the ergogenic benefit of caffeine was not the result of glycogen sparing.

A second limitation of glycogen sparing by caffeine is related to dietary constraints imposed on the subject. It has been reported that diets high in carbohydrate negate any caffeine-induced, glycogen sparing effects (Weir, Noakes, Myburgh, & Adams, 1987; Giles & McLaren, 1984). Weir et al. (1987) tested six trained runners under conditions of a high fat content meal alone, a high carbohydrate meal followed by caffeine ingestion, or a three day diet consisting of high fat or high carbohydrate meals in combination with caffeine. Following a dose of 6.5 mg/kg caffeine, participants exercised for 120 minutes at 75% of maximum oxygen uptake. The result was that free fatty acid levels did not rise as anticipated after a high carbohydrate diet and high carbohydrate meal followed by caffeine ingestion. Similarly, Giles and McLaren (1984) exercised participants for 120 minutes on a treadmill at 75% maximum oxygen uptake one hour after ingesting a 5 mg/kg caffeine dose alone or in combination with glucose ingestion. They found a significant decrease in peak plasma free fatty acid levels with glucose and caffeine ingestion compared to caffeine alone. These results have implications for athletes who carbohydrate-load prior to competitive events such as a marathon or triathlon. However, other studies contradict these results and show that caffeine-induced performances are not affected by high carbohydrate diets (Spriet et al., 1992). Spriet cycled eight subjects to exhaustion at 80% maximal oxygen uptake one hour after ingesting a 9 mg/kg caffeine dose or placebo. Each participant was instructed to consider the exercise as a hard workout in their weekly training program and to maintain diets similar to precompetition diets. Analysis of each subject's diet showed an average of 59.6% carbohydrate content prior to testing. Despite consuming a high

carbohydrate diet, participants cycled significantly longer in the caffeine trial than the placebo trial.

Although it is largely understood that elevated catecholamine levels promote elevated free fatty acid levels, the cause and effect relationship of caffeine and elevated catecholamine levels is less clear. The effects of caffeine on catecholamine secretion are confounded by studies (Graham & Spriet, 1991; Spriet et al., 1992) that failed to show an increase in norepinephrine despite an increase in epinephrine, suggesting that the effects of caffeine on catecholamine secretion are not affecting the sympathetic nervous system. Rather, caffeine appears to be acting on the adrenal medulla. A greater epinephrine response to caffeine has also been found during exercise (Kjaer, Bangsbo, Lortie, & Galbo, 1988), which was attributed to an increased rate of secretion rather than a decreased rate of epinephrine reabsorption.

While glycogen sparing may be the most significant ergogenic effect of caffeine, other ergogenic benefits have been reported. Several studies report that VO_2max is enhanced by caffeine consumption (Toner et al., 1982; Wiles, Bird, Hopkins, & Riley, 1992). Toner et al. (1982) found a statistically significant increase in VO_2max in subjects pedaling a cycle ergometer following caffeine ingestion relative to a control group. Wiles et al. found performance improvements in 1500 meter run and “finishing burst” sprint times following the consumption of caffeinated coffee. Additionally, eight of the ten participants in this study recorded higher VO_2 values during the caffeine trial. Wiles et al. (1992) observed that the higher VO_2 levels were probably due to faster running speeds during the caffeine trial. However, the faster running speeds could also be attributed to a general decrease in the perception of fatigue, which could cause participants to select a higher speed. Conversely, research exists which fails to show an

increase in $\text{VO}_{2\text{max}}$ with caffeine treatment (Powers, Byrd, Tulley, & Callender, 1983; Dodd, Brooks, Powers, and Tulley, 1991). Powers et al. (1983) studied, seven participants who performed a graded exercise test on a cycle ergometer one hour after consuming 5 mg/kg of caffeine or placebo. Initial resistance was 30 Watts and was increased by 30 Watts every three minutes. No difference in maximal oxygen uptake or time to exhaustion was found between caffeine and placebo trials. Dodd et al. (1991) used a similar test protocol in which initial resistance began at 50 Watts and increased by 30 Watts every two minutes. Nine caffeine habituated participants were compared with eight participants who abstained from caffeine consumption or were considered caffeine naive. Participants were given a placebo, 3 mg/kg, or 5 mg/kg caffeine one hour prior to beginning the test. While $\text{VO}_{2\text{max}}$ was significantly increased in caffeine naive participants, this only occurred after consuming 5 mg/kg caffeine. There was no significant difference in $\text{VO}_{2\text{max}}$ among caffeine habituated participants.

Caffeine and Skeletal Muscle

Skeletal muscle appears to be the target organ for many of caffeine's purported ergogenic effects. Because caffeine almost completely equilibrates with total body water, the highest concentration of caffeine can probably be found in skeletal muscle (Burg, 1975). It has been shown that type I and II skeletal muscle fibers have different levels of sensitivity to caffeine. Deuster, Bockman, & Muldoon, (1985) studied muscle contractures induced by caffeine. Isolated strips of cat soleus muscle (100% type I fibers) and gracilis muscle (95% type II fibers) were incubated with doses of caffeine ranging from 0.25 to 16 mM. The results showed that type I muscle fibers were significantly more sensitive to caffeine than type II muscle fibers. This difference in sensitivity to caffeine between type I and type II muscle fibers was also found in human skeletal

muscle by Mitsumoto, Deboer, Bunge, Andrish, Tetzlaff, and Cruse, (1990). Caffeine has been shown to stimulate calcium release from its storage site in the sarcoplasmic reticulum (Rall, 1985). This stored calcium can be subdivided into calcium-sensitive and inositol triphosphate-sensitive reservoirs. The action of caffeine on calcium stores in the sarcoplasmic reticulum may be inconsequential, however, because the dose of caffeine required to elicit a significant mobilization of calcium is toxic in vivo (Fredholm 1985). While a caffeine dose of 9 mg/kg body weight will produce an approximate plasma caffeine concentration of 15 $\mu\text{g/ml}$, it was determined that plasma caffeine concentrations of approximately 300 $\mu\text{g/ml}$ would have to be achieved to see any significant results on sarcoplasmic reticulum calcium release. Alternately, Poledna and Morad (1983) suggested that caffeine, rather than stimulating calcium release, suppressed calcium reuptake into the sarcoplasmic reticulum which would also facilitate muscle contraction. However, the caffeine dose required to achieve this effect is again prohibitive in vivo. In vitro studies performed on muscle tissue of individuals susceptible to malignant hyperthermia showed intensified muscle contractions after subjects consumed a caffeine load compared with muscle tissue from normal people (Britt, 1979; Britt, Endrenyi, Scott, & Frodis, 1980; Gronert, 1980). It was presumed that the intensified muscle contractions were due to an increased plasma calcium level in the malignant hyperthermia muscle.

The effects of caffeine on muscle tension and maximal voluntary force have also been studied to determine any beneficial effects from caffeine. Williams (1987) tested hand grip strength under caffeine and placebo conditions and found no difference in force production between the two conditions. Conversely, it has been shown that caffeine increases maximal tension production of the adductor pollicis when electrically stimulated (Lopes, Aubier, Jardin, Aranda, & Macklem, 1983). While improvements

were found at submaximal frequencies of stimulation (≤ 50 Hz), no improvements occurred at stimulation frequencies above 50 Hz. Additionally, maximal voluntary contraction have shown no improvement. Conversely, several studies have failed to show a significant effect of caffeine on tension or the maximal voluntary level of force produced during a muscle contraction (Bugyi, 1980; Lopes et al., 1983; Tarnopolsky et al., 1989; Williams, 1987). It was theorized that increased motor unit recruitment might occur during submaximal contractions as evidenced by an increase in tension produced at submaximal electrical stimulation (Lopes et al., 1983). However, Williams (1987) measured handgrip strength after caffeine ingestion and found no increase in motor unit activation as determined by an electromyogram. Additionally, caffeine did not improve the motor unit recruitment to force production ratio with submaximal handgrip contractions.

Caffeine and Performance

The effects of caffeine supplementation on performance have been investigated in several competitive situations, primarily endurance events. In general caffeine appears to have a positive ergogenic effect on endurance exercise. Costill, Dalsky, and Fink (1978) examined the exercise performance of nine competitive cyclists pedaling at 80% of VO_2max . Participants ingested either 330 mg of caffeinated coffee or decaffeinated coffee one hour prior to the onset of exercise. Average time to exhaustion improved from 75.5 minutes under placebo conditions to 90.2 minutes under caffeine conditions. Spriet et al. (1992) administered a 9 mg/kg caffeine dose to participants, one hour prior to cycling at 80% of VO_2max , and found a significant improvement in time to exhaustion during caffeine trials (96.2 ± 8.8 min) rather than placebo trials (75.8 ± 4.8 min).

The effects of caffeine on short term exercise are not as clear. Collomp, Caillaud,

Audran, Chanal, and Prefaut (1990) studied participants who cycled at 100% of their VO_2max until the required level of work could no longer be maintained. While participants work times were increased in the caffeine trial, the results were not significantly different from the placebo trial. Wiles, et al. (1992), on the other hand, showed a statistically significant improvement in performance with caffeine. Participants ran a 1500 meter time trial on a treadmill. Each participant also had to complete the run with a one minute finishing burst under either caffeine or placebo conditions. In the caffeine trials, there was a decrease in the amount of time needed to complete the 1500 meter run, and a faster one minute finishing burst, both of which were significantly different from the control trial.

It is possible that the ergogenic effects of caffeine may be related to the athletic level of the participants. The ergogenic effect appears to be more prevalent when competitive or highly trained athletes are used as participants. For example, Collomp, Ahmaidi, Chatard, Audran, and Prefaut (1992) studied freestyle sprint performance in two distinct groups. The first group consisted of seven swimmers who had been training an average of five times per week for at least four months, and had recently undergone sprint training in anticipation of a forthcoming swim meet. The second group consisted of seven subjects who were former competitive swimmers, but who had not practiced consistently, though they were occasionally swimming. All of the subjects were asked to abstain from any caffeinated drinks for one week prior to the test. Subjects were randomly given a gelatin capsule containing either 250 mg of caffeine or a placebo, and swam two 100-m sprints, separated by a twenty minute rest period. The time required to complete the 100-m sprint was significantly decreased in the trained subjects but not in the untrained subjects with caffeine. Collump also noted that while blood lactate

concentrations were significantly increased in both the trained and untrained swimmers, the trained swimmers had a higher relative blood lactate content after each 100-m sprint regardless of whether caffeine or placebo was being used, possibly due to a decline in the perception of fatigue with caffeine in trained athletes.

In summary, caffeine has been reported to have three main effector sites, the central nervous system, the neuromuscular junction, and the muscles contractile machinery. Two hypotheses proposed to explain central nervous system stimulation include phosphodiesterase inhibition and competitive adenosine receptor blockade through caffeine consumption. Through caffeine's effects on various physiological processes, a multitude of ergogenic benefits have been proposed, ranging from a glycogen sparing effect to sharper mental acuity and quicker reaction time. Most of the research has focused on endurance events which are aerobic by nature with very little research targeting high-intensity intermittent exercise. Therefore, the purpose of my study is to examine the effects of caffeine on high-intensity intermittent cycle ergometry to exhaustion.

CHAPTER 3

METHODOLOGY

Subjects

Seven apparently healthy male participants volunteered for this study.

Participants were selected based on their diet which consisted of minimal to negligible amounts of daily dietary caffeine. Daily caffeine intake was estimated to be less than 75 mg per day. The mean physical attributes (and standard deviation) of the participants were: age in years = 26.00 (± 1.83), body mass = 76.92 kg (± 10.56), and peak VO₂ = 46.99 ml/kg/min. (± 7.37).

Pretest

One week prior to the onset of the study, participants performed a peak oxygen uptake test on a Quinton cycle ergometer. Participants were connected to a Vista metabolic measurement system (Vacumed Inc., Ventura, CA) via a one way non-rebreathing mask. Participants were also fitted with a Vantage heart rate monitor. After a 5 minute warmup, participants began pedaling at 60 to 80 revolutions per minute, with initial resistance set at 50 Watts. Resistance was increased by 25 Watts every minute until peak oxygen consumption levels were determined. At the conclusion of the peak oxygen uptake test, a five minute warm down period followed. Following the pretest,

participants were instructed to abstain from caffeinated products for the next two weeks.

Test Protocol

Upon arrival on a test day, participants' body mass was determined, and a 50 μ l blood sample was drawn with two heparinized microtubules. Participants consumed a 300 ml cup of decaffeinated coffee containing either caffeine (6 mg/kg body weight) or placebo. After consuming the beverage, participants waited for one hour to allow for caffeine absorption. During this time, an explanation of the exercise protocol was given to participants with an opportunity to receive answers to any questions. Toward the end of the absorption period, participants were seated on the cycle ergometer and outfitted with a Vantage heart rate monitor. Immediately prior to the beginning of the exercise protocol, a second 50 μ l blood sample was drawn from each participant. The test protocol began with a five minute warmup at 50 Watts resistance followed by the test protocol sequence. Each sequence consisted of cycling for 60 seconds at 120% of the maximal power output achieved during the peak VO_2 pretest, with recovery periods of cycling at 50 Watts for 120 seconds. The sequence was computer programmed to generate accurate force load and interval duration. The exercise protocol was terminated when participants were unable to maintain a minimum of 60 revolutions per minute for 10 consecutive seconds. Immediately following the conclusion of the test, a third 50 μ l microtubule blood sample was drawn. A five minute warm down followed the end of the exercise test.

The participants were instructed to abstain from caffeine and report one week later for their second trial. Participants followed the same procedure as in the first trial, except participants received the opposite treatment to the first. The placebo and caffeine trials were administered to participants in a counterbalanced design. Following the second

trial, participants were asked whether they could distinguish between the two 300 milliliter beverages which they consumed, and which test protocol was more difficult.

Blood lactate levels were determined using a Yellow Springs Model 23L lactate analyzer (Yellow Springs Instruments, Yellow Springs, OH). Plasma caffeine levels were determined using a Gilford 260 spectrophotometer at a wavelength of 273 nanometers according to a modification of the procedure of Axelrod and Reichenthal (1953), and Routh, Shane, Arredondo, and Paul (1969) (see Appendix III). Further revisions were necessary to accommodate smaller blood samples than those required in the original procedure.

A double blind crossover design was implemented in this study to help control internal validity. Since this was a within subjects study, the statistical analysis used was a one way ANOVA with repeated measures for caffeine dose and paired t-Test for time to exhaustion, work stages completed, total power output, and lactate concentration.

CHAPTER 4

RESULTS

Plasma Caffeine Concentration

In the caffeine trial, plasma caffeine levels were significantly elevated over baseline levels one hour after consuming caffeine ($p < 0.001$) (Figure 1). Baseline caffeine levels were $1.66 \pm 0.21 \mu\text{g/ml}$ while post absorptive caffeine levels were $6.72 \pm 1.40 \mu\text{g/ml}$. Baseline and one hour post-absorption caffeine levels during the placebo trial were $1.51 \pm 0.22 \mu\text{g/ml}$ and $1.95 \pm 0.30 \mu\text{g/ml}$ respectively, and failed to reach significance (Figure 2).

Time to Exhaustion

Ingestion of 6 milligrams of caffeine per kilogram body weight one hour prior to intermittent cycling at 120% of peak power did not significantly increase exercise time over the placebo condition. The mean time to exhaustion during the caffeine trial was 12.54 ± 5.86 minutes while the placebo condition yielded a mean time to exhaustion of 12.31 ± 6.62 minutes (Figure 3). The difference in performance by work stages failed to reach significance. The mean number of work stages completed was 4.68 ± 1.94 and 4.59 ± 2.24 for caffeine and placebo trials respectively (Figure 4). The difference in total power output between caffeine and placebo trials was not significantly different (Figure

5). The mean total power output for caffeine and placebo trials was 1661.61 ± 701.75 Watts and 1630.38 ± 801.33 Watts respectively.

Blood Lactate Concentration

Figure 6 indicates blood lactate concentration achieved during caffeine and placebo trials. Blood lactate concentration averaged 11.33 ± 1.04 mM and 11.63 ± 1.89 mM during caffeine and placebo trials respectively and failed to reach significance.

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

CHAPTER 5

DISCUSSION

This study examined the effects of caffeine on healthy, active, college age males performing high-intensity, intermittent cycling. The primary finding of this study was that caffeine failed to significantly increase time to exhaustion over a placebo. Caffeine levels were significantly elevated during the caffeine trial compared with baseline levels. Additionally, plasma lactate levels were not significantly different between caffeine and placebo.

These findings differ from those of Trice and Haymes (1995). They investigated the effects of caffeine on high-intensity, intermittent exercise to exhaustion and found a significant increase in performance time of 16.25 minutes during the caffeine trial in addition to a 20 minute increase in the range of time to exhaustion. The exercise protocol used by Trice and Haymes and the protocol adopted for this study were based on two previous studies performed by Astrand, Astrand, Christensen, and Hedman (1960, 1960). Astrand et al. studied the effects of altering the length of work/rest periods while maintaining the work/rest ratio at 1 to 2 or 1 to 4. The total quantity of work to be performed within a 30 minute period was standardized to allow for direct comparisons between tests. Plasma lactic acid concentration was measured, while the same amount of work over a 30 minute period was maintained. Results indicated that a 60 second bout of

high-intensity exercise followed by a 120 second recovery period yielded lactic acid values of 142 mg per 100 ml, which was significantly higher than 60 seconds of work followed by 120 seconds of recovery which resulted in peak lactic acid values of 114 mg per 100 ml. Based on these results, it was decided to adopt the 60 second work and 120 second recovery work:rest ration for the current study. It was also decided that participants would cycle at 120% of their maximal power output.

Trice and Haymes exercise protocol, which consisted of three 30 minute repetitions of 60 second work and rest intervals at 85 to 90% of maximal power output resulted in plasma lactate levels of 4.00 ± 0.70 and 4.24 ± 0.86 for caffeine and placebo trials respectively. The exercise protocol for the current study attained plasma lactate levels of 11.33 ± 1.04 and 11.63 ± 1.89 for caffeine and placebo trials respectively. It is possible that Trice and Haymes found a significant improvement in time to exhaustion because participants reached a balance point between lactate production and removal. Additionally, if participants were cycling at 85% of $\text{VO}_{2\text{max}}$, recovery during the early stages of exercise might permit glycogen sparing through increased lipolysis. Previous studies have suggested that caffeine may inhibit lactate production via increased lipid oxidation resulting in a decrease in utilization of glucose and glycogen (Chesley, 1994; Graham & Spriet, 1991). Such benefits have been reported to occur within the first 15 to 20 minutes of exercise at 80% of maximal aerobic capacity (Spriet et al. 1992). This spared glycogen is then available for use in the later stages of exercise, extending the time to exhaustion. Trice and Haymes reported an increase in the time to exhaustion of 16.25 minutes. In the current study, an equilibrium between lactate production and elimination was unlikely because of the higher intensity of work load was prohibitive. At 120% of maximal aerobic capacity, participants were exercising well above the lactate threshold

making glycogen sparing unlikely.

It has been speculated that caffeine may be beneficial during anaerobic exercise. Collomp et al. (1992) compared a group of highly trained swimmers with occasional swimmers who were formerly highly trained. Each group performed two 100 meter freestyle sprints separated by 20 minutes, under both caffeine and placebo conditions. Blood lactate levels were similar for both groups regardless of the caffeine or placebo condition. However, only the highly trained swimmers improved their sprint speed during both sprints. Collomp et al. speculated that specificity of training may be necessary to obtain any ergogenic benefits from caffeine during supramaximal exercise. While participants for the current study were active, none had specifically trained on a cycle ergometer for any length of time under anaerobic conditions.

It is possible that the level of physical training may also be important in deriving ergogenic benefits from caffeine during short term, high intensity exercise. Highly trained athletes appear to draw greater benefits from caffeine than less well conditioned athletes (Collomp, Ahmaidi, Audran, Chanal, & Prefaut, 1991; Collomp et al., 1992; Wiles et al., 1992). Type I muscle fibers, which are highly oxidative, have been shown to be more sensitive to caffeine than type II fibers (Duester, 1985; Mitsumoto, et al., 1990). One of the adaptations to aerobic exercise is an increase in oxidative capacity of muscle as evidenced by an increase in both size and number of mitochondria (Essig and White, 1981). While the participants for this study were active, they were not considered highly trained. Whether caffeine would provide an advantage to highly trained endurance athletes during intermittent high-intensity exercise remains to be determined.

A recent study suggested that the manner in which caffeine is administered might have an impact on the ergogenic benefits associated with caffeine. Graham, Hibbert, and

Sathasivam (1995) reported that caffeine administered in tablet form may be more effective than regular coffee or caffeine dissolved in decaffeinated coffee. Participants performed 5 exercise tests in which they ran to exhaustion at 85% of their VO₂max one hour after consuming either a caffeine or placebo capsule with water, or regular coffee, decaffeinated coffee or decaffeinated coffee with a caffeine supplement. The caffeine dose and volume of liquid to be consumed were both standardized to eliminate any variability between tests. Graham et al. found no difference in time to exhaustion between the three beverages and placebo capsule. However, participants ran significantly longer after consuming caffeine in capsule form. Plasma epinephrine levels measured throughout the test indicated a significant increase between caffeine and placebo treatments, but no significant difference between caffeine treatments. It was postulated that caffeinated and decaffeinated coffee contain an additional element which negates the ergogenic benefits associated with caffeine.

In this study, caffeine was dissolved in a 300 mg cup of decaffeinated coffee. Following the conclusion of the last exercise test, six of seven participants correctly identified which exercise test contained caffeinated beverages. Five of the participants felt jittery prior to beginning the caffeine trial exercise protocol and one participant experienced post-exercise gastric discomfort associated with the caffeine beverage. Despite experiencing characteristics associated with consuming large quantities of caffeine, participants were unable to significantly improve time to exhaustion during the caffeine trial. This lends some validity to the belief that caffeine dissolved in decaffeinated coffee will increase levels of plasma epinephrine without providing any ergogenic benefits.

CHAPTER 6

CONCLUSIONS

Caffeine has been extensively studied in recent years in an attempt to capitalize on its potential ergogenic benefits. However, results are often inconsistent and contradictory, making an accurate assessment of caffeine's potential as an ergogenic aid a difficult task. This study focused on the effects of caffeine during high-intensity, intermittent exercise to exhaustion. The results of this study indicated that caffeine naive participants who consumed a large dose of caffeine one hour prior to undertaking a high-intensity, intermittent bout of exercise did not significantly improve the length of time to exhaustion. Though a caffeine dose of this magnitude will significantly elevate plasma caffeine levels, the level of exercise intensity appears to be too high to take advantage of the ergogenic benefits associated with caffeine during exercise of moderate intensity. Ergogenic benefits may be attainable at this level of work if the participants are highly trained and target their training toward anaerobic cycling sprints. Results of future caffeine studies in this realm are anticipated to be variable depending on individual differences in age, daily caffeine ingestion, and fitness level.

APPENDIX I

STATISTICAL RESULTS

Table 1: Plasma Caffeine Level - Caffeine Trial

Anova: Single Factor
 Pre/Post Plasma Caffeine Level (ug/ml)
 Caffeine Trial

SUMMARY

<i>Groups</i>	<i>Count</i>	<i>Sum</i>	<i>Average</i>	<i>Variance</i>
Pre-Treatment	7	11.653	1.665	0.045
Post Absorption	7	31.714	4.531	0.815

ANOVA

<i>Source of Variation</i>	<i>SS</i>	<i>df</i>	<i>MS</i>	<i>F</i>	<i>P-value</i>	<i>F crit</i>
Between Groups	28.747	1	28.747	66.805	3.02E-06	4.747
Within Groups	5.164	12	0.430			
Total	33.911	13				

Table 2: Plasma Caffeine Level - Placebo Trial

Anova: Single Factor
 Pre/Post Plasma Caffeine Level (ug/ml)
 Placebo Trial

SUMMARY

<i>Groups</i>	<i>Count</i>	<i>Sum</i>	<i>Average</i>	<i>Variance</i>
Pre-Treatment	7	10.571	1.510	0.047
Post Absorption	7	12.199	1.743	0.069

ANOVA

<i>Source of Variation</i>	<i>SS</i>	<i>df</i>	<i>MS</i>	<i>F</i>	<i>P-value</i>	<i>F crit</i>
Between Groups	0.189	1	0.189	3.267	0.096	4.747
Within Groups	0.696	12	0.058			
Total	0.885	13				

Table 3: Time to Exhaustion

t-Test: Paired Two Sample for Means
Time to Exhaustion (minutes)

	<i>Caffeine</i>	<i>Placebo</i>
Mean	12.54	12.31
Variance	34.39	43.78
Observations	7.00	7.00
Pearson Correlation	0.97	
Hypothesized Mean Difference	0.00	
df	6.00	
t Stat	0.36	
P(T<=t) one-tail	0.37	
t Critical one-tail	1.94	
P(T<=t) two-tail	0.73	
t Critical two-tail	2.45	

Table 4: Performance by Work Stages

t-Test: Paired Two Sample for Means
Work Stages

	<i>Caffeine</i>	<i>Placebo</i>
Mean	4.68	4.59
Variance	3.75	5.01
Observations	7.00	7.00
Pearson Correlation	0.98	
Hypothesized Mean Difference	0.00	
df	6.00	
t Stat	0.43	
P(T<=t) one-tail	0.34	
t Critical one-tail	1.94	
P(T<=t) two-tail	0.68	
t Critical two-tail	2.45	

Table 5: Total Power Output

t-Test: Paired Two Sample for Means
Power Output (Watts)

	<i>Caffeine</i>	<i>Placebo</i>
Mean	1661.61	1630.38
Variance	492447.53	642127.62
Observations	7.00	7.00
Pearson Correlation	0.98	
Hypothesized Mean Difference	0.00	
df	6.00	
t Stat	0.44	
P(T<=t) one-tail	0.34	
t Critical one-tail	1.94	
P(T<=t) two-tail	0.67	
t Critical two-tail	2.45	

Table 6: Plasma Lactate Concentration

t-Test: Paired Two Sample for Means
Plasma Lactate Concentration (mM)

	<i>Caffeine</i>	<i>Placebo</i>
Mean	11.33	11.63
Variance	1.08	3.55
Observations	6.00	6.00
Pearson Correlation	0.23	
Hypothesized Mean Difference	0.00	
df	5.00	
t Stat	-0.38	
P(T<=t) one-tail	0.36	
t Critical one-tail	2.02	
P(T<=t) two-tail	0.72	
t Critical two-tail	2.57	

APPENDIX II

**INSTITUTIONAL REVIEW COMMITTEE APPROVAL
INFORMED CONSENT**

UNLV

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DATE: October 9, 1996

TO: James a. Herman (KIN)
M/S: 3034

FROM: *Dr. Herman*
Dr. Lawrence Golding
Chairman, Biomedical Committee of the
Institutional Review Board

RE: Status of Human Subject Protocol entitled:
"Effects of Caffeine on High-Intensity, Intermittent
Exercise to Exhaustion"

OSP #504s1096-090

This memorandum is official notification that the protocol for the project referenced above has been approved by the Biomedical Committee of the Institutional Review Board. This approval is approved for a period of one year from the date of this notification and work on the project may proceed.

Should the use of human subjects described in this protocol continue beyond a year from the date of this notification, it will be necessary to request an extension.

If you have any questions or require any assistance, please give us a call at 895-1357.

cc: Dr. J. Young (KIN-3034)
OSP File

Office of Sponsored Programs
4505 Maryland Parkway • Box 451037 • Las Vegas, Nevada 89154-1037
(702) 895-1357 • FAX (702) 895-4242

**Consent Form for Participation in Research
Exercise Physiology Laboratory
University of Nevada, Las Vegas**

Title:

The Effects of Caffeine on High-Intensity, Intermittent Exercise to Exhaustion

Purpose:

Of all the central nervous system stimulants, caffeine is among the most widely used drugs in the world. Caffeine has been manipulated by athletes in an attempt to enhance their performance. Most of the research surrounding the purported effects of caffeine have focused on caffeine's influence during endurance exercise. To date, very little research has focused on high-intensity exercise to exhaustion. Therefore, the purpose of this study is to examine the effects of caffeine on high-intensity, intermittent exercise.

Procedures:

Participants will report to the exercise physiology lab at least one week prior to the beginning of the test protocol. At this time, peak oxygen uptake levels will be measured during an cycle ergometer exercise protocol. Prior to beginning the exercise protocol, a one way rebreathing valve will be fitted to the participant to measure respiratory gases. The warm up period of the exercise protocol will consist of the participant cycling for 5 minutes with minimal resistance. At the conclusion of the warm up period, the participant will pedal with a resistance of 50 watts for one minute. An additional 25 watts of resistance will be added at the end of each one minute segment. This will continue until the participant can not maintain an adequate level of work. Upon completion of the peak oxygen uptake test, participants will be asked to abstain from all caffeine during the following two weeks in an attempt to obtain the strongest possible effect from the caffeine sample. Caffeine abstinence spanning two weeks is necessary to allow participants to perform the exercise protocol under caffeine and placebo conditions.

Participants will report to the exercise lab at their assigned time, following a 12 hour overnight fast. At this time, a small blood sample will be drawn from the finger into a microtubule. Participants will be given a caffeine solution based on body mass or a placebo and asked to sit for one hour. At the end of the one hour absorption period, a second blood sample will be drawn from the finger into a microtubule. After a 5 minute warm up period with minimal resistance, the test protocol will begin. Based on results obtained from the peak oxygen uptake test, the participant will be asked to cycle 80 revolutions per minute for one minute at 120% of peak oxygen uptake. This period will be followed by a two minute rest period in which resistance will be reduced to 50 Watts. At the end of the two minute rest period, the same resistance will be placed on the cycle and the participant asked to cycle 80 revolutions per minute for one minute. These work/rest periods will continue until the participant is unable to maintain an adequate level of work consistent with the test parameters. At the end of the test, a third

micortubule blood sample will be drawn from the participant. A cool down period in which the participants cardiorespiratory condition will be closely monitored.

The following week will consist of the same procedure with the exception of the caffeine or placebo sample. Participants will receive the alternate supplement during the second week.

Risks:

Due to the intense level of exercise required for this experiment, participants may experience some muscle fatigue during the test protocol. Delayed onset muscle soreness may also develop within 48 hours following the exercise protocol. Abrupt cessation of caffeine consumption may result in some discomfort. Additionally, some gastrointestinal discomfort may result from consumption of caffeine or placebo solutions.

Benefits:

There are two benefits associated with this experiment. First, the participant will receive an accurate appraisal of their peak oxygen uptake capacity (VO₂ max) based on the current state of physical conditioning. Second, the results of this study will contribute to the knowledge and understanding of caffeine and its effect on athletic performance.

Confidentiality:

All information regarding this experiment will be held in the strictest of confidence. Only those people directly involved with this experiment will be permitted access to this information. If this study is published in a scientific journal or presented at a conference, names and identities will be altered to protect the confidentiality of the participants.

Right to refuse or withdraw:

Participation in this study is voluntary. Participants may refuse to sign the consent form or withdraw from the experiment at any time.

Questions:

Any questions or concerns that may arise can be addressed by Jim Herman at 735-4242 or John Young, Ph.D. at 895-4626. Questions regarding participant's rights during human subjects research can be answered by the UNLV Office of Sponsored Programs at 895-1357.

Please read the statement below, and sign and date this form if you agree with the conditions of the study.

I have read and understand this form and the content of the test procedure. Furthermore, I have volunteered for this study of my own volition. I understand the test protocol and all of my questions have been answered to my satisfaction. I acknowledge that I may withdraw from the study at any time without recrimination.

Participant Name (print)

Signature of Participant

Date

APPENDIX III

CAFFEINE ASSAY

CAFFEINE ASSAY

Principle:

The premise behind this method for caffeine extraction is based on caffeine's ability to absorb light at 273 nanometers. Below is a list of the reagents need to perform this assay. Also included is a list of instructions with values reduced for 25 microliter (μ l) blood samples.

Reagents:

NaCl
0.1 Normal (N) NaOH
Benzene
5 N HCl

Procedure:

1. Prepare each 2 ml capped ependorf tube with:

18.75 μ g NaCl
6.25 μ l NaOH
125 μ l Benzene

2. Add 25 μ l of serum to a prepared 1.5 ml ependorf tube.
3. Cap and mix by inversion and shake mechanically for 15 minutes.
4. Centrifuge tubes for 15 minutes (1000 x gravity).
5. Transfer 100 μ l aliquot of the upper phase to a tube containing 50 μ l of 5 N HCl.
6. Cap tubes and shake mechanically for 5 minutes.
7. Suction the benzene layer from the contents of the tube.
8. Transfer 37.5 to 40 μ l of the aqueous phase to a quartz micro cuvette and read in a spectrophotometer calibrated against a water blank at 273 nanometers.
9. Plot results on a regression line constructed from serial dilution samples of known concentration (5 μ g/ml to 20 μ g/ml).

Normal Values

Five milligrams of caffeine per kilogram body weight in 250 ml solution will result in plasma caffeine levels of 3.5 to 9.4 $\mu\text{g/ml}$ one hour later (Axelrod & Reichenenthal, 1953).

Reference:

Axelrod, J., & Reichenenthal, J. (1953). The fate of caffeine in man and a method for its estimation in biological material. Journal of Pharmacology and Experimental Therapeutics, 107, 519-523.

Routh, J., Shane, N., Aredondo, E., & Paul, W. (1969). Determination of caffeine in serum and urine. Clinical Chemistry, 15, 661-668.

APPENDIX IV

INDIVIDUAL DATA

Participant 1

Age (years)	27
Weight (kg)	89
VO ₂ (max·kg·BW)	43
Caffeine Trial	
Baseline Caffeine (μg/ml)	1.66
Peak Caffeine (μg/ml)	4.09
Placebo Trial	
Baseline Caffeine (μg/ml)	1.72
Peak Caffeine (μg/ml)	1.97
Lactate Concentration (mM/L)	
Caffeine Trial	12.00
Placebo Trial	-----
Time to Exhaustion (minutes)	
Caffeine Trial	12.85
Placebo Trial	12.60
Total Power Output (Watts)	
Caffeine Trial	1892
Placebo Trial	1794

Participant 2

Age (years)	25
Weight (kg)	65
VO ₂ (max·kg·BW)	60
Caffeine Trial	
Baseline Caffeine (μg/ml)	1.38
Peak Caffeine (μg/ml)	5.61
Placebo Trial	
Baseline Caffeine (μg/ml)	1.27
Peak Caffeine (μg/ml)	1.35
Lactate Concentration (mM/L)	
Caffeine Trial	10.30
Placebo Trial	11.70
Time to Exhaustion (minutes)	
Caffeine Trial	6.75
Placebo Trial	6.88
Total Power Output (Watts)	
Caffeine Trial	1073
Placebo Trial	1124

Participant 3

Age (years)	25
Weight (kg)	71
VO2 (max·kg·BW)	45
Caffeine Trial	
Baseline Caffeine ($\mu\text{g/ml}$)	1.52
Peak Caffeine ($\mu\text{g/ml}$)	5.79
Placebo Trial	
Baseline Caffeine ($\mu\text{g/ml}$)	1.54
Peak Caffeine ($\mu\text{g/ml}$)	1.79
Lactate Concentration (mM/L)	
Caffeine Trial	12.60
Placebo Trial	10.60
Time to Exhaustion (minutes)	
Caffeine Trial	8.45
Placebo Trial	6.77
Total Power Output (Watts)	
Caffeine Trial	1139
Placebo Trial	913

Participant 4

Age (years)	29
Weight (kg)	78
VO2 (max·kg·BW)	55
Caffeine Trial	
Baseline Caffeine ($\mu\text{g/ml}$)	1.69
Peak Caffeine ($\mu\text{g/ml}$)	4.25
Placebo Trial	
Baseline Caffeine ($\mu\text{g/ml}$)	1.47
Peak Caffeine ($\mu\text{g/ml}$)	1.59
Lactate Concentration (mM/L)	
Caffeine Trial	12.40
Placebo Trial	15.20
Time to Exhaustion (minutes)	
Caffeine Trial	24.63
Placebo Trial	24.98
Total Power Output (Watts)	
Caffeine Trial	3108
Placebo Trial	3234

Participant 5

Age (years)	23
Weight (kg)	72
VO ₂ (max·kg·BW)	46
Caffeine Trial	
Baseline Caffeine (μg/ml)	1.81
Peak Caffeine (μg/ml)	3.26
Placebo Trial	
Baseline Caffeine (μg/ml)	1.28
Peak Caffeine (μg/ml)	1.60
Lactate Concentration (mM/L)	
Caffeine Trial	10.30
Placebo Trial	11.40
Time to Exhaustion (minutes)	
Caffeine Trial	12.93
Placebo Trial	15.75
Total Power Output (Watts)	
Caffeine Trial	1628
Placebo Trial	1898

Participant 6

Age (years)	25
Weight (kg)	75
VO ₂ (max·kg·BW)	42
Caffeine Trial	
Baseline Caffeine (μg/ml)	1.56
Peak Caffeine (μg/ml)	4.69
Placebo Trial	
Baseline Caffeine (μg/ml)	1.85
Peak Caffeine (μg/ml)	2.15
Lactate Concentration (mM/L)	
Caffeine Trial	10.70
Placebo Trial	11.20
Time to Exhaustion (minutes)	
Caffeine Trial	12.70
Placebo Trial	12.33
Total Power Output (Watts)	
Caffeine Trial	1551
Placebo Trial	1430

Participant 7

Age (years)	27
Weight (kg)	94
VO ₂ (max·kg·BW)	40
Caffeine Trial	
Baseline Caffeine (μg/ml)	2.03
Peak Caffeine (μg/ml)	4.03
Placebo Trial	
Baseline Caffeine (μg/ml)	1.43
Peak Caffeine (μg/ml)	1.75
Lactate Concentration (mM/L)	
Caffeine Trial	11.70
Placebo Trial	9.70
Time to Exhaustion (minutes)	
Caffeine Trial	9.45
Placebo Trial	6.83
Total Power Output (Watts)	
Caffeine Trial	1242
Placebo Trial	1020

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