THE EFFECTS OF CAFFEINE ON COGNITIVE PERFORMANCE

Caffeine is the most widely used psychoactive substance in the world. According to Spiller (1998), 82% of people that are over the age of 18 years use caffeine on a daily basis. Since caffeine is a stimulant (Spiller, 1998), it is consistent that caffeine does increase arousal (Loke, 1998). However, results regarding its effects on cognitive tasks have been mixed. In this introduction we will consider some of the different tasks in which caffeine's effects have been tested.

Many studies of caffeine's effects have failed to control for a number of obvious critical procedural variables. These variables include caffeine dose, subject's weight, subject's caffeine use frequency, subject's drug use history, time of day effects, the influence that food consumption may have on caffeine, gender effects, withdrawal effects and temporal factors. Few if any studies have tried to control for all or even most of these variables at one time. Most studies have taken only one or two of these factors into consideration during testing. So, it is likely that the influence of these subject and procedural variables may be the reason that results have been conflicting.

The following presents a brief review of the results from studies of caffeine on various cognitive functions:

THE EFFECTS OF CAFFEINE ON CRITICAL FLICKER FUSION

Kerr, Sherwood and Hindmarch (1991), tested the effects of caffeine on a critical flicker fusion task. The CFF task provides an index of state of arousal of the central nervous system (Hindmarch, Quinlan, Moore, and Parkin, 1998). The subjects see a set of lights blinking and they are to indicate when the light's frequency that they see is perceived as one continuous light source, that is, when the blinking lights that are being

observed by the subject are perceived as one light that is constantly glowing. Ten females were given a dose of either 300mg of caffeine (which is relatively high) or a placebo. Subjects were tested at the same times on Monday, Wednesday, and Friday. Kerr et al. (1991) showed that caffeine did not have significant effects in the critical flicker fusion task.

In contrast Hindmarch, Quinlan, Moore, and Parkin (1998), asked subjects to abstain from caffeine on the evening prior to testing. They took 10 female and 9 male subjects and administered either 0mg of caffeine or 100mg of caffeine to them. The subjects were tested at 900am, 200pm, and 700pm. Before being given caffeine the subjects were given a critical flicker fusion task. Then 20-minutes after dosing the subjects were given the same task again. The results showed that the caffeine improved performance on the critical flicker fusion task. Caffeinated beverage consumption resulted in a higher CFF level than decaffeinated beverages. This means that the subjects were able to see the light blinking for a longer period of time before reporting it as a continuous light source. One explanation for the mixed results between the CFF studies may be that different caffeine doses were administered across these studies. The conflicting results suggest that cortical arousal is decreased by higher doses of caffeine while low/moderate doses of caffeine help to improve cortical arousal.

THE EFFECTS OF CAFFEINE ON REACTION TIME

Foreman, Barraclough, Moore, Metha, & Madon (1989) showed that high doses of caffeine had no effect on a choice reaction time task in males. Thirty males were asked to abstain from caffeine containing products between 9pm the night before the study until testing. On the test day the subjects were randomly assigned to one of three conditions:

0mg caffeine, 125mg caffeine, or 250mg of caffeine (moderate/high doses). Thirty minutes after caffeine ingestion the testing began. The choice reaction task involved one; three, or five, circles presented on a screen, the subjects were to touch the screen as quickly as possible wherever they observed the "circle was broken". There were no significant effects of the caffeine condition found on response time in this task.

Likewise, Hindmarch, Quinlan, Moore, and Parkin (1998), also studied the effects of caffeine on reaction time. They used 10 female and 9 male subjects and administered either 0mg of caffeine or 100mg of caffeine (moderate dose). Before being given caffeine the subjects were given a choice reaction time task. This choice reaction time task required subjects to place their dominant hands in the center of a touch sensitive pad. When one of six surrounding lights randomly lit up the subject was to touch it as quickly as possible. Then 20-minutes after dosing the subjects were given the same task again. These results are consistent with Foreman et al. (1989) showing that caffeine did not significantly improve performance on a choice reaction time task.

In contrast, Kerr, Sherwood and Hindmarch (1991), used 10 females and administered a dose of either 300mg of caffeine (high dose) or a placebo. The subjects were tested on a choice reaction time task (see Hindmarch et al., 1998). Caffeine ingestion significantly improved performance on the choice reaction time task.

Kerr et al. (1991) used the same choice reaction time task as Hindmarch et al. (1998). But Kerr et al. (1991) administered a 300mg dose and this significantly improved performance on the choice reaction time task while the 100mg dose given by Hindmarch et al. (1998) did not. These results suggest a higher dose of caffeine may be required to have any effects on this particular task, which is contrasting to the effects that caffeine

might have on the critical flicker fusion. However, Kerr et al. (1991) tested their subjects 20 minutes after ingestion. This may have resulted in caffeine not being distributed throughout the subject. Subjects may have been tested before caffeine was "on board". For caffeine to reach peak plasma levels it takes about 30 minutes (Kamimori et. al. 2002, Maisto, Galizio, & Conners, 1999, Spiller 1998, Warburton, 1995).

Durlach (1998) looked at the effects of low doses of caffeine on reaction times. The subjects were 8 males that did not smoke who were asked to abstain from caffeine and alcohol from 930pm the evening before each weekly test session until testing. The subjects were given either 60mg (low dose) of caffeine or 0mg of caffeine. 42 minutes after ingestion of caffeine a simple (SRT) and choice (CRT) reaction time task was conducted. In the simple reaction time task, a white circle remained constantly on the screen. A yellow spot appeared inside it. The subject, who had their hand on a response pad, was to touch the yellow dot on the screen as quickly as possible. Reaction times were recorded. The choice reaction time task was identical except that the yellow dot could appear in any one of five circles on the screen. No significant effect was found on the simple and choice reaction time tasks.

THE EFFECTS OF CAFFEINE ON ATTENTION AND SUSTAINED ATTENTION

Durlach (1998) administered a rapid visual information-processing task, which is a test of attention. The subjects were given either 60mg (low dose) of caffeine or placebo. Subjects were required to watch a stream of digits and to depress a response pad whenever they saw the sequences 3-5-7, 5-7-9, 2-4-6, of 4-6-8. There were no significant affects of caffeine on the rapid visual information-processing task.

In a study conducted by Mitchell and Redman (1992), results were mixed. The subjects' caffeine use habits were assessed by a survey and then subjects (based on their reported use of caffeine) were designated as: low caffeine users, (less than 120mg a day), moderate caffeine users, (between 120mg and 300mg a day), or high users, (300mg or more of caffeine in a day). The subjects were given 4mg/kg of caffeine, (which is a very high dose compared to other studies) or a placebo. Mitchell and Redman (1992) also controlled for time of day effects by testing the subjects at 1am, 7am, 1pm, and 7pm. Subjects were asked to abstain from caffeine and any other psychoactive substance use for 24 hours prior to testing. They were also asked not to eat or smoke during the hour between dosing and testing. The subjects were first given a mental arithmetic (MA) task. This task required subjects to add as many successive pairs of single digit numbers as possible in 1 minute. A serial search (SS) task required subjects to search through 36 lines of 30 randomly generated capital letters, to test their sustained attention. Subjects were asked to indicate whether a particular line contained the letter "E". The last test was a verbal reasoning (VR) task that contained 32 items. Each item consisted of a sentence describing the relationship between two letters (for example, "W is not proceeded by B"), followed by the letter pair in either order ("WB" or "BW"). Subjects were asked to circle "yes or no" according to whether they thought the sentence accurately agreed with the rule. There were no significant effects of caffeine on the mental arithmetic. The moderate and low users did significantly better than the high users on the mental arithmetic and verbal reasoning and caffeine improved performance on the serial search. Moreover, the time to complete the tasks under the influence of caffeine was faster than placebo.

Warburton (1995), looked at the effects of moderate doses of caffeine on attention. Warburton tested subjects at 9am after the subjects had not eaten or consumed any alcohol for 24 hours before testing. Though subjects were given no instructions for their caffeine use before testing, subjects were to abstain from any other substances for three days prior to testing. 18 male subjects rated as "regular" coffee drinkers (more than 3 cups per day) were tested. The subjects were randomly assigned to one of three caffeine groups on three separate occasions (a placebo group, a 75mg dose group, or a 150mg dose group of caffeine). One hour before entering the study all subjects were administered a 75mg dose of caffeine to ensure that none of them were caffeine deprived, and that the participants were at approximately the same plasma levels of caffeine. Upon entering the study the subjects were given their assigned dose of caffeine. Testing began 45 minutes after ingestion, just prior to the peak plasma levels of caffeine at 1 hour (Warburton, 1995).

An attention task using a rapid visual information processing procedure consisted of 100 digits being presented across a screen in one minute. The subjects were to press a button whenever three odd or even numbers came up in a row. Warburton's (1995) results showed that there was a significant dose-dependent increase in accuracy of performance on this task. Problem solving skills were also examined; this task involved a sentence describing the order of two letters (e.g. A follows B). The subjects then decided if the sentence describing the letters was correct and pressed (Y) for "YES" and (N) for "NO". This task is very similar to Mitchell and Redman's (1992) verbal reasoning task. Caffeine significantly improved performance on this task; which agrees with Mitchell

and Redman's (1992) results showing moderate doses of caffeine increased performance on problem solving skills.

Smith, Rusted, Eaton-Williams, Savory, and Leathwood (1990) found results that agreed with the results Warburton (1995) found on sustained attention. Smith et al. (1990) used 32 subjects (16 male and 16 female) and asked them to consume what they considered a "normal lunch". All subjects were tested at two different times. Subjects were run in caffeine and no-caffeine conditions before and after lunch. The two sessions were run a week apart. The subjects abstained from caffeine for 3 hours prior to testing. Subjects were given doses of either 3mg/kg caffeine or a placebo. The Bakan vigilance task was administered. This task involved the presentation of digits across a screen at a rate of 100 digits per minute. The subjects pressed a response button as quickly as possible when they detected a sequence of either 3 consecutive odd or even numbers (see Warburton, 1995). The results showed that caffeine significantly improved performance on the Bakan vigilance task, which suggests that caffeine aids in sustained attention.

Ruijter, Lorist, Snel & Ruijter (2000), also examined caffeine's effects on sustained attention. In this study they took twelve healthy subjects (4 male and 8 female) and administered 250mg (high dose) of caffeine or placebo. Then the subjects were given a concentration task. The task consisted of a slide with 3, 4, or 5 dots on it. Half of the participants were instructed to press a button with their right index finger when 4 dots were shown and press another button with the left when 3 or 5 dots were present. To eliminate the advantages/disadvantages of handedness the other half of participants did the opposite, pressing a button with the right index finger when 3 or 5 dots were shown on the slide and pressing another button with their left index finger when 4 dots were

shown. Caffeine did not affect this concentration task, which is in contrast to Smith et al. (1990).

Moreover, Foreman, Barraclough, Moore, Metha, & Madon (1989), showed that high doses of caffeine actually impaired performance, in males, on a numerical version of the Stroop task. In this study they took 32 males and asked them to abstain from caffeine containing products between 9pm the night before the study until testing. On the testing day the subjects were assigned to one of three conditions: 0mg caffeine, 125mg caffeine, or 250mg of caffeine. Thirty minutes after ingestion they began a test of sustained attention, a numerical Stroop task. This task consisted of a line of 1, 2, 3, or 4 digits appearing at the center of a screen. (e.g. three "2"s, four "3"s). The control condition involved 1-4 geometric symbols in a row on a screen (e.g. ***). The subject was required to place the fore and middle fingers of their left hand on the keys numbered 1 and 2 and the fore and middle fingers of their right hand on the numbers 3 and 4. Each time a series of numbers was displayed the subject had to respond by pressing the number on the keyboard that was the same as the number of digits on the screen, ignoring the value of the numbers being shown. For example, if "3333" appeared on the screen the subject would respond by pressing the number four with their right middle finger. On this Stroop-Like task the high dose caffeine group made slower responses than did the no-caffeine group. However, the low caffeine group did not differ significantly from control performance. These results suggest caffeine may produce dose-dependent effects that impair performance at higher doses.

THE EFFECTS OF CAFFEINE ON SHORT TERM MEMORY

Durlach (1998) used a low dose (60 mg of caffeine) to study short-term memory. Subjects took a delayed match to sample task (DMS). The subjects were shown a complex visual pattern (the sample) and had to decide which of the four patterns that appeared below it was identical. On the simultaneous trials, the sample remained on the screen while the subjects made their choice. On the delayed trials the sample disappeared and the choices appeared with a delay of 0, 4, or 12 seconds. Results showed that caffeine increased performance on the delayed match to sample task.

A paired associates learning task (PAL) was also administered. The subject was required to learn where different patterns appeared on the computer screen. Different patterns were shown on different locations on the computer screen. After all patterns were displayed, each pattern appeared in the center of the screen and the subject had to touch the location of where that pattern had previously occurred. Caffeine increased performance on delayed match to sample. But caffeine did not affect performance on the paired associates learning task.

Kerr, Sherwood and Hindmarch (1991) also tested the effects of caffeine on short-term memory. Three hundred milligrams of caffeine (high dose) or a placebo was administered. Ten female participants were tested at the same times on Monday, Wednesday, and Friday. The participants were given a short-term memory task that required them to determine whether a test digit was contained within a short sequence of 4 digits that were presented on a screen for 1.2 seconds. The test digit was shown 1 second later and the time taken for the subject to react was recorded. Caffeine ingestion significantly improved performance on this short-term memory task.

Hindmarch, Quinlan, Moore, and Parkin (1998), before being administrated a (100mg) dose of caffeine subjects were given a short-term memory task. Then 20-minutes after dosing the subjects were given the same short-term memory task again. In this task subjects were shown a sequence of random numbers. This subject was to try to remember the numbers in this sequence. After being shown the sequence the subjects were then shown a target digit and they were to indicate if that target digit was in the sequence previously shown. The subjects responded by pressing the buttons on the computer's mouse and the reaction time was recorded. Hindmarch et al. (1998) found that caffeine (100mg) did not have a significant effect on a short-term memory task similar to Kerr, Sherwood and Hindmarch (1991) who found that caffeine (300mg) did significantly improve reaction times over the no-caffeine group. The conflict here may have been due to Hindmarch et al. (1998) testing only 20-minutes after caffeine ingestion. According to Spiller (1998), Kamimori et. al. (2002), Maisto, Galizio, & Conners (1999), and Warburton (1995), 20-minutes is not ample time for caffeine to take effect on a person.

THE EFFECTS OF CAFFEINE ON VERBAL MEMORY

Foreman, Barraclough, Moore, Metha, & Madon (1989) used 32 males and administered 0mg caffeine, 125mg caffeine, or 250mg of caffeine. Thirty minutes after ingestion, testing began. A free recall "supraspan" word list, which is a task of verbal memory, was administered. This task consisted of 15 lists of 15 words each. The words were listed vertically on two separate sheets of paper. The subjects were given 20 seconds to look at the word list and then 45 seconds to write down as many words as they could recall. There was no significant effect of caffeine on the supraspan task.

Warburton (1995), looked at the effects of moderate doses of caffeine on verbal memory using procedures described for Warburton's study on sustained attention. Testing began 45 minutes after ingestion, just prior to the peak plasma levels of caffeine at 1 hour (Warburton, 1995). An auditory task of verbal memory was administered. This task had parallel lists of 20 words that were played in each ear of the subjects. The words were presented over headphones at a rate of one word every 2 seconds. At the end of each list the volunteers tried to recall as many words as possible. Later a delayed recall test for the words was given. The results showed that there was no effect of caffeine on immediate recall for verbal memory but there was significant increase in accuracy of delayed recall of the words.

Mitchell and Redman (1992) used a survey to assess the participants' caffeine use habits. Then designated participants as (based on their reported use of caffeine): low caffeine users (less than 120mg a day) moderate caffeine users (between 120mg and 300mg a day) and high users (300mg or more of caffeine in a day). The volunteers were given 4mg/kg of caffeine, (a very high dose compared to other studies) or a placebo. These researchers controlled for time of day effects by testing the subjects at 1am, 7am, 1pm, and 7pm. Participants were asked to abstain from caffeine and any other psychoactive substance use for 24 hours prior to testing and not to eat or smoke during the hour between dosing and testing.

The subjects were given a short-term memory test (STM), which consisted of 20 five- or six-letter nouns that were presented on a computer screen for 2 seconds each. At the end of the session the subjects were asked to recall as many words as possible in a 2 minute time period. There were no significant effects of caffeine on the verbal memory.

In contrast, Terry and Phifer, (1986) found that a small dose of caffeine significantly impaired performance on the auditory and verbal learning test (AVLT). The AVLT is a test of verbal memory that provides measures of memory span, learning over trials, interference, and delayed recall. The subjects consisted of 19 females and 13 males. The subjects were either given 0mg of caffeine or 100mg of caffeine (an average dose). The subjects were asked to abstain from caffeine between 930am on the testing day until the test times (1230pm or 2pm). Forty-minutes after caffeine ingestion the subjects were given trials with different word lists to test their verbal recall. Analysis showed that the control group performed better on several dimensions of verbal recall than did the caffeine group.

In contrast, Walker et al. (2002) at UNC-Wilmington found that caffeine improved performance on a paired word associates (PWA) task. In this study 15 females were required to drink at least one cup of coffee (approximately 153.4mg of caffeine) in 10 minutes.

The paired word associates task consisted of 40 pairs of words. Each pair was shown to the subjects one at a time. After all the pairs were shown the subjects were given a sheet of paper with only one of the words from the pair on it and were asked to recall as many matches as they could. This task tests the subject's ability to store and recall words from their verbal short-term memory. The results showed that caffeine significantly improved performance on the paired word associates task.

THE EFFECTS OF CAFFEINE ON MENTAL ROTATION

The mental rotation task is a test of a person's ability to rotate objects in their mind. For example, two-dimensional Necker cubes may be shown in different views. The

subjects then could be asked to pick images that are identical to the target object. The other objects may be mirror images of the target object.

The effects of caffeine on mental rotation have also been conflicting. Smith, Rusted, Eaton-Williams, Savory, and Leathwood, (1990), took 32 subjects (16 male and 16 female) and asked them to consume what they considered a "normal lunch". All subjects were tested at two different times. Before lunch at 1030am and after lunch at 130pm. Subjects were run in caffeine and no-caffeine conditions before and after lunch. The two sessions were run a week apart. The subjects abstained from caffeine for 3 hours prior to testing. Subjects were given either 3mg/kg caffeine (high dose) or a placebo. A mental rotation task was also administered, where a given letter (e.g. R) was presented in different rotated positions. The subject was to determine if the letter in an upright position would be the same or if it would be a mirror image of that letter.

Performance on the MRT was not significantly different before lunch, but caffeine significantly improved performance on the MRT after lunch. These results agree with Walker et al. (2002) who found that caffeine improved performance on the mental rotation task (MRT).

Loke (1990), used 32 healthy subjects, (16 male and 16 female) and administered 0mg, 200mg, 400mg, and 600mg of caffeine on three separate dosing days. The subjects were either assigned to a Monday, Wednesday, Friday dosing period or a Tuesday, Thursday, Saturday dosing period. The subjects were tested from 9am-11am on their assigned days for 2 weeks. So, each subject had 6 experimental sessions. A survey was used to screen out any unhealthy subjects, subjects on medication, or subjects who had a history of drug use. A card rotation task, which was used to measure visual-spatial

ability, required the subjects to determine if each of eight test shapes following a standard shape were the 'same' as or 'different' from the standard. 'Same' items were identical to the standard when rotated on the page. 'Different' items were those shapes that were mirror images of the standard. A dose-dependent caffeine effect did occur on the card rotation task. Performance increased on this task with the 200mg and 400mg dose but a deficit in performance was observed with the 600mg dose.

HYPOTHESIS

The goal of this study was to examine the affects of caffeine on performance on the mental rotation task and the paired word associates task. Loke (1990) found a dose-dependent effect of caffeine on performance on the mental rotation task. Therefore, it was predicted that at lower doses caffeine would improve performance on these tasks, while performance would decline with higher doses. Additionally rigorous attempts have been made in this study to control for factors that may have played a role in the mixed results of previous studies. In addition to caffeine dose and body weight (placebo 0mg/kg, 1mg/kg, 2mg/kg, or 3mg/kg), time of day effects were controlled for by all subjects being tested at 6pm on weekdays. Requiring the subjects to abstain from caffeine for 3 hours before the study helped control for withdrawal and over-dose effects. A screening survey was used to eliminate subjects that used other psychoactive substances. Potential influences of tolerance/over sensitivity to caffeine were also controlled. Only subjects that fell into the definition of an "average" caffeine user were used. Because a preliminary study on mental rotation and verbal memory showed caffeine significantly improved performance on these tasks, these two tasks were used in this present study.

METHOD

Participants

Participants were selected through a survey screening process. The IRB approved survey allowed a look at past drug use and caffeine use. The survey used a Likert type scale in reference to different substance use and the frequency of use. Participants responded to questions about caffeine use on a scale from (0=none to 4=several times a day). Caffeine use throughout the week was also assessed.

Subjects were not recruited for further testing if they reported current non-caffeine stimulant use or were on birth control medications due to birth control medication's effects on caffeine's metabolism (Spiller 1998). All subjects were over the age 18 years old. The survey was given to University of North Carolina at Wilmington psychology students (Appendix A). Subjects were selected if they qualified as "average" caffeine users as determined by the experimenter. Caffeine use was assessed across reported consumption of caffeinated coffee; tea, soft drink and chocolate. The scores from these four categories of caffeine were summed. If their score was between 5-11 then the subjects qualified as an average caffeine user. "Low" caffeine users were not allowed to participate to rule out the possibility of an over sensitivity to the effects of caffeine. Also, "high" users of caffeine were not allowed to participate to control for tolerance to the effects of moderate doses of caffeine. In essence, the operational definition of an "average" user was someone that consumed approximately 2.06 cups of coffee a day or approximately 170mg of caffeine a day. This definition of level of caffeine intake is based on Loke (1988) and Mitchell and Redman (1992) who classified low users as people consuming less than 120mg of caffeine a day, moderate users as those who

consume 120mg-300mg of caffeine a day, and high users as anyone consuming more than 300mg of caffeine in a day.

The subjects were randomly assigned in a double-blind procedure to one of four caffeine conditions: control (0mg/kg caffeine), low dose (1.0mg/kg caffeine), moderate dose (2.0mg/kg), or high dose (3.0mg/kg). Subjects were asked to abstain from caffeine use for 3 hours prior to the experiment so that any caffeine that had been taken throughout the day would be a minimal factor (Spiller, 1998). Nicotine may interfere with caffeine effects on cognition (Spiller, 1998). They were also asked to abstain from nicotine use for 30 minutes prior to the experiment session. Testing was conducted at 6pm on weekdays. It was found that between the times of 3pm-7pm coffee, tea, and cola are consumed the least by undergraduate students (Loke, 1988). Therefore compliance with abstinence should have been easier.

Materials

Surveys were used to assess the potential subjects' caffeine use and SAT scores. Informed consent forms (Appendix B) were administered upon entering the study. A weight scale was used to weigh subjects before dosing. Preparation of caffeine capsules was done while the subjects were taking a "substance use" validity check survey. Subjects were administered capsules with water (8 ounces) containing caffeine at 1mg/kg dose, 2mg/kg dose, 3mg/kg dose or 0mg/kg dose. A video that was neither too stimulating nor excessively boring, called "Secret of the Psychics" was shown for 30 minutes. This allowed time for onset of caffeine effects (Spiller (1998), Kamimori et. al. (2002), Maisto, Galizio, & Conners (1999), and Warburton (1995)). At the end of the 30-minute period the subjects were administered the first test. The subjects were

administered the Mental Rotation Task (MRT) (Vandenberg, 1978) as a timed slide show via "Power Point". The mental rotation task is a test of a person's ability to rotate objects in their mind. Two-dimensional Necker cubes were shown in different views. The subjects were asked to pick out the two of four images that were identical to a target object. The other two objects were mirror images of the target object. Each slide was shown for 30 seconds. Next, a Paired Word Associates Task (PWA) (Pavio 1971) was given to the subjects via a Power Point presentation. Each pair of words was shown for 10 seconds. At the end of the presentation volunteers were asked to recall one of the matching words that were shown before. Participants recorded their answers on an answer sheet that was provided to them with their specified subject number on the sheet. The answer sheet contained one of the words from the pairs that were shown to them before. The participants were asked to write down the matching word that was shown next to the word that is on the paper given to them.

Procedure

Classroom screening surveys were administered to assess the subject's caffeine use for this study. The screening survey was administered to psychology students attending UNC-Wilmington. The survey consisted of a list of substances that may have an effect on the way caffeine works or substances that may have similar effects as caffeine, such as cocaine or amphetamines. Other questions assessed the subject's caffeine consumption on a week or a typical day. This survey provided the opportunity to select of subjects that were operationally define as "moderate caffeine users", and to screen out people that used other psychoactive drugs that may have similar effects as caffeine.

When the surveys were distributed in the classrooms the potential subjects were instructed that if they might be interested in volunteering for a follow up study to provide their phone number in the designated place on the survey. The potential subjects were also instructed to use a code name because the surveys asked for some potentially confidential information about the persons past drug use. If selected the potential participant were called by an experimenter and a standardized phone conversation (Appendix C) was used to inform the volunteer about participating in the caffeine study.

Volunteers (maximum 4 in any session) were greeted by an experimenter at the subject pool sign-up board and escorted to the room where the experiment was to take place. Upon entering the study the subjects were asked to fill out an informed consent form that was read to them by the experimenter. The subjects were then weighed. An abbreviated screening survey was re-administered as a validity check. At this time the subjects were randomly assigned to their caffeine condition (a placebo, 0mg/kg caffeine, low dose, 1mg/kg caffeine, a moderated dose, 2mg/kg caffeine, or high dose, 3mg/kg caffeine in capsule form (Sigma)). Drug administration procedures were blind. Capsules were prepared, based on body weight, by one experimenter while the subjects were filling out their validity surveys. That experimenter then recorded which subject would be receiving which dose of caffeine in a logbook. The capsules were placed in labeled dosing trays and given to the subjects with an 8-ounce cup of water.

After consuming the capsules and finishing the surveys the subjects watched a neutral video entitled “Secret of the Psychics” and were asked to refrain from talking or having any other interaction with each other. This was to allow the caffeine to be absorbed (Spiller, 1998). After 30 minutes had elapsed the video was turned off and the

first test began. The first test was a computerized version of the Vandenberg (1978) Mental Rotation Task (MRT). The subjects were allowed 3 practice trials to be sure that they were familiar with the task. This test consisted of two parts, each with 10 problems. Subjects were given 30 seconds for each problem. After the MRT was completed the subjects went directly into a computerized version of the Paired Word Association Task (PWA), (Pavio, 1971). Each pair of 40 words was projected onto a computer screen for 10 seconds. The participants were instructed to memorize as many words as possible. After all the paired words were displayed the subjects were given a PWA Response Form. Subjects were instructed that they would be shown a single word from each of the word pairs that were previously viewed. Subjects were asked to recall the other word of the pair to the best of their ability. The first 5 and last 5 were eliminated from testing to reduce primacy and recency effects. Thirty single test words were shown. Subjects were not penalized for guessing. The purpose of the PWA Task was to assess the subjects' ability to store and recall words from the subjects' short-term memory (Pavio, 1971).

RESULTS

One hundred and thirteen subjects were tested. There were 100 SAT scores reported (mean score = 1125.45, standard deviation = 110.378). The lowest SAT score reported was 850 and the highest SAT score reported was 1500. The drug screening survey consisted of a scale that rated caffeine use for the past week. The scales assessed coffee, tea, caffeinated soft drinks and chocolate consumption. The response scale ranged from 0-4 where 0 = none at all, 1 = once a week, 2 = 2-3 times a week, 3 = almost everyday and 4 = several times a day. For purposes of post-hoc analysis of coffee use history as it may relate to MRT and PWA performance in the current study potential

subjects that had scored below a 5 or above a 12 were excluded. “High” caffeine users were excluded to prevent the possibility of tolerance to caffeine having an affect on performance and “low” caffeine users were excluded to eliminate the possibility that they might be oversensitive to the effects of the caffeine dosing. Eighty participants who were included in the present study were classified in the “low” range of caffeine use after filling out the drug screening survey, achieving a score 5-8 on a 16-point scale. In this study 33 participants were classified as “high” caffeine consumers, scoring between 8-12 on a 16-point scale (see fig. 1) (See methods section for definition of participant classification).

Ten males and 11 females were randomly assigned to the placebo capsule group N=21 (mean age= 19.76) and ten males and 10 females were randomly assigned to the 1mg/kg capsule group (mean age=20.95). Ten males and 11 females were randomly assigned to the 2mg/kg capsule group (mean age=20.57) and 6 males and 6 females were randomly assigned to the 3mg/kg group (mean age=19.25). A second experiment was conducted with a coffee beverage condition and will be discussed in more detail later. There were 10 males and 10 females randomly assigned to a placebo coffee beverage group (mean age= 19.35), and 9 males and 10 females assigned to the 2mg/kg coffee beverage group (mean age= 19.53). The 3mg/kg group was discontinued after 12 subjects had been tested because some of the subjects reported feeling nausea.

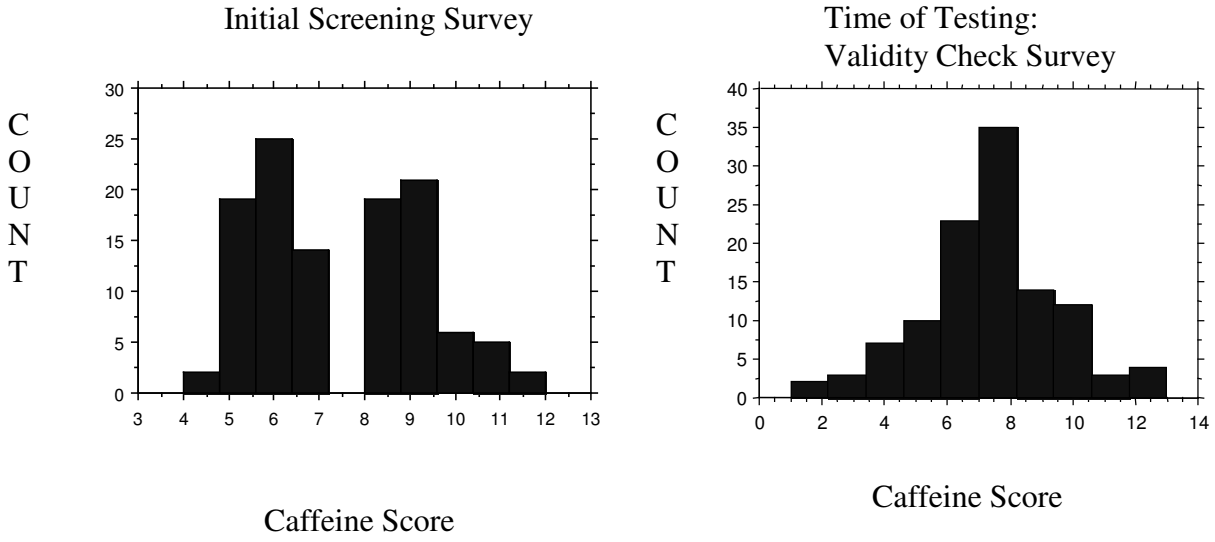

FIGURE 1: Drug Screening Survey Scores for Reported Caffeine Use. “Low” caffeine users were defined as participants that scored between 4-7 and “high” caffeine users were defined as participants that scored between 8-12. In the second week the scores approached a more normal distribution. Count: Number of participants in that score range. Caffeine Score: Score on screening survey and validity check survey.

EXPERIMENT 1

The percent correct on the mental rotation and paired word associates task was calculated and the effects of the 4 caffeine doses (0mg/kg, 1mg/kg, 2mg/kg, and 3mg/kg) were assessed with a between group ANOVA. After primary ANOVA results post-hoc analysis was done to determine differences. An ANOVA for the effects of caffeine dose on Mental Rotation showed that the results were not significant for caffeine in capsule form (see fig.5). However, an ANOVA did show a significant difference across gender for the MRT (see figs. 3 & 4). Analysis of gender effects in the MRT produced results consistent with past research (Parsons 2004 & Vecchi & Girelli 1998) (see fig. 3) [$F(1,101) = 16.601$, $p < .0001$, power= .991]. Males performed better on the MRT task. Also, the effects of caffeine in beverage form had a greater effect on males than it did on females (see figs. 3 & 6), [$F(5,101) = .792$, $p = .5580$, power= .269].

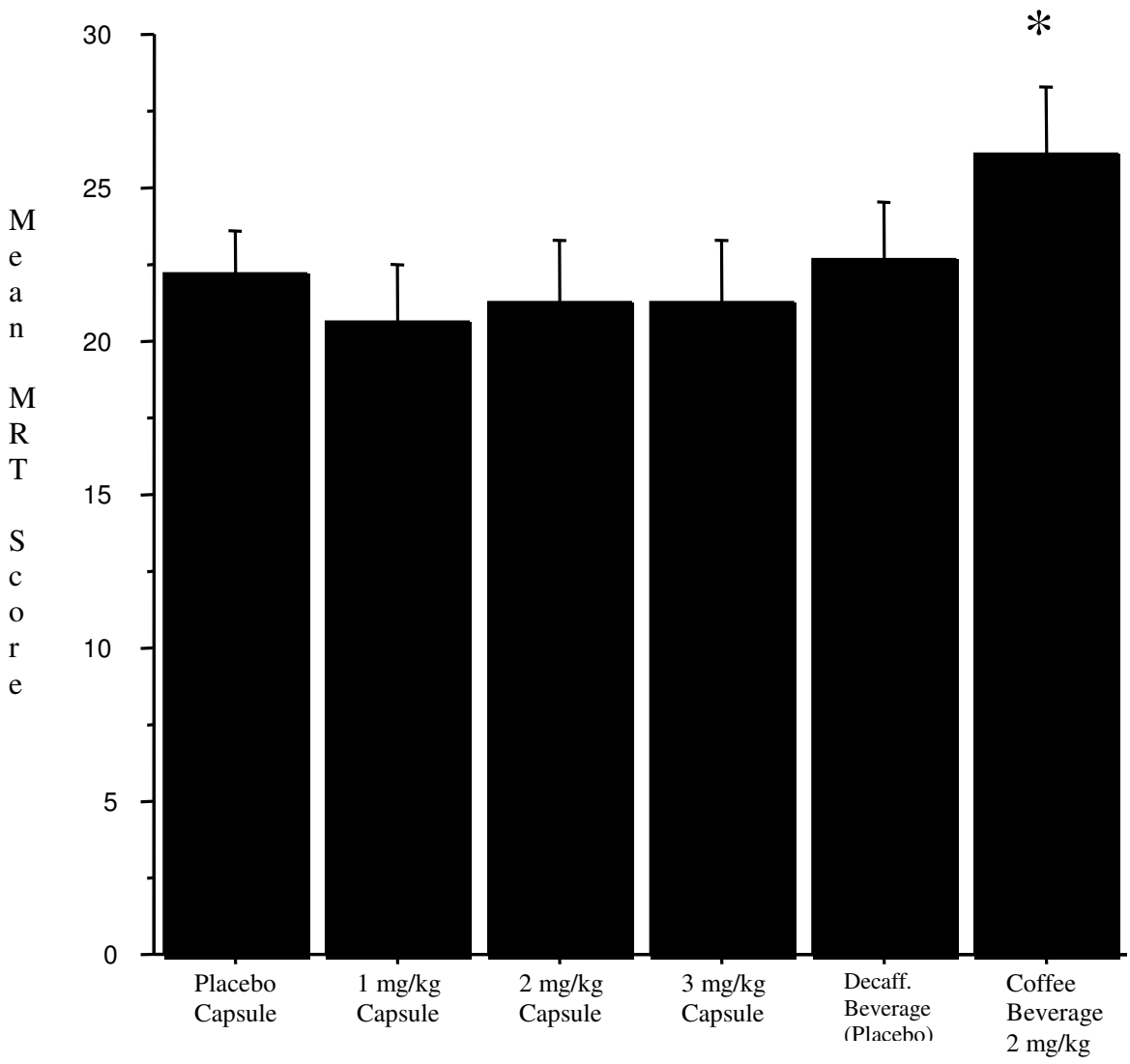

FIGURE 2: The figure above shows that subjects in coffee beverage condition (2mg/kg) performed significantly better than other caffeine conditions on the Mental Rotation Test of visuo-spatial ability. However, administration of caffeine in capsule form failed to affect MRT performance versus controls. [$F(5,107) = 1.078$, $\underline{p} = .37$,] The histograms reflect mean scores for each condition with SEM error bars.

When caffeine consumption scores the week before testing were analyzed as a covariate for MRT performance there was no significant effect for the covariate [F (5,101)= .832, *p*= .5301, power= .282]. Also, there was not a significant interaction between reported caffeine use for the week prior to entering the study and caffeine condition [F (5,101) = 1.097, *p*= .3667, power= .370] (see fig. 4).

When SAT scores were analyzed as a covariate for MRT performance there was no significant effects for the covariate [F (5,88)= .975, *p*= .4375, power= .327]. There was no significant interaction between SAT (mean = 64.423) score and MRT score (mean = 74.175) [F (5,88)= 1.123, *p*= .3543, power= .375].

Although not significant, analysis of the effects of caffeine performance the Paired Word Task did approach significance [F (5,107) = 2.107, *p*= .0673, power= .675] (fig. 5) in the direction of the hypothesis. This trend was explained mostly between the 0mg/kg (mean = 10.667) capsule group and the 1mg/kg capsule group (mean = 13.95, *p*= .0673). Consistent with past results (Jorm, Anstey, Christensen, & Rodgers (2004), Weiss, Kemmler, Deisenhammer, Fleischhacker, & Delazer (2003)) females performed better on the PWA than males [F (1,101)= 6.854, *p*= .01012, power= .744] (see fig. 6 & 7). Again there was no significant interaction between gender and condition [F (5,101) = .946, p= .4549, power= .320]. A covariate analysis for the PWA between caffeine consumption the week before and caffeine condition did not significantly explain the results [F (1,101)= 1.695, *p*= .1514, power= .549], and there was no significant interaction between caffeine use the week before testing and PWA score [F (5,101)= 1.365, *p*= .2438, power= .457].

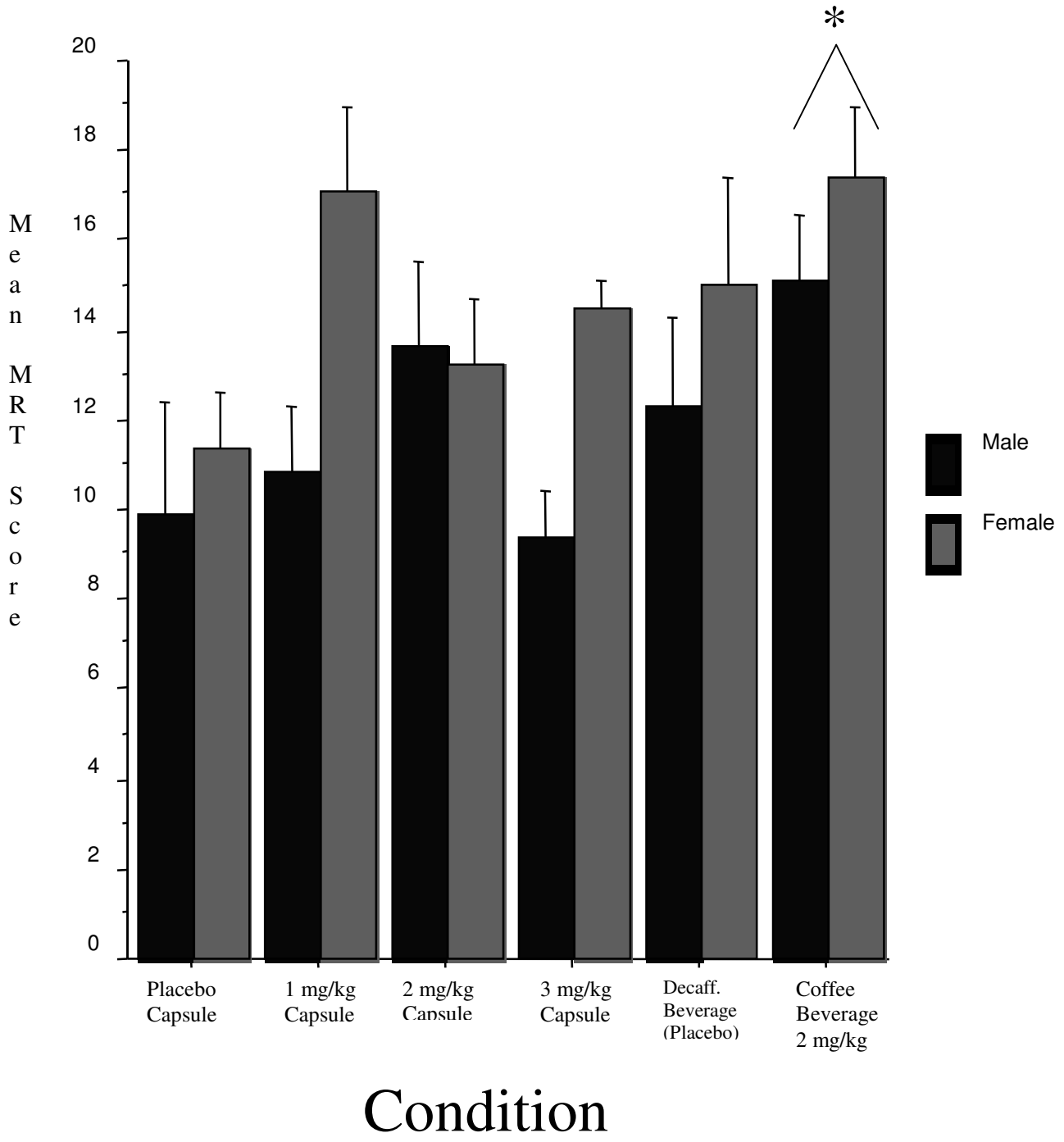

FIGURE 3: The results here agree with past research where males perform significantly better than females on spatial MRT (means +/- SEMS). Females were mot affected to the same degree. However, caffeine had an overall significant effect on male performance in the current MRT task [$F(1,101) = 17.04$, $\underline{p} < .01$], for male performance in the coffee beverage condition versus other conditions as well as for female coffee beverage (2mg/condition performance versus female performance in other conditions).

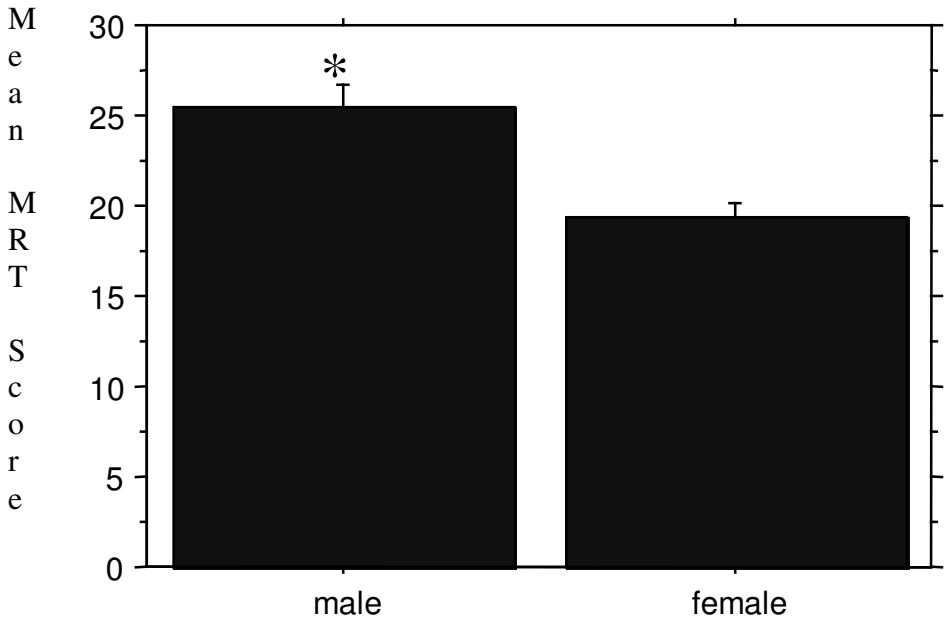

Figure 4: MRT Results by Gender. The figure above shows that males performed significantly better than females on the MRT task.

Interaction Bar Plot for MRT by gender
Effect: gender
Error Bars: ± 1 Standard Error(s)

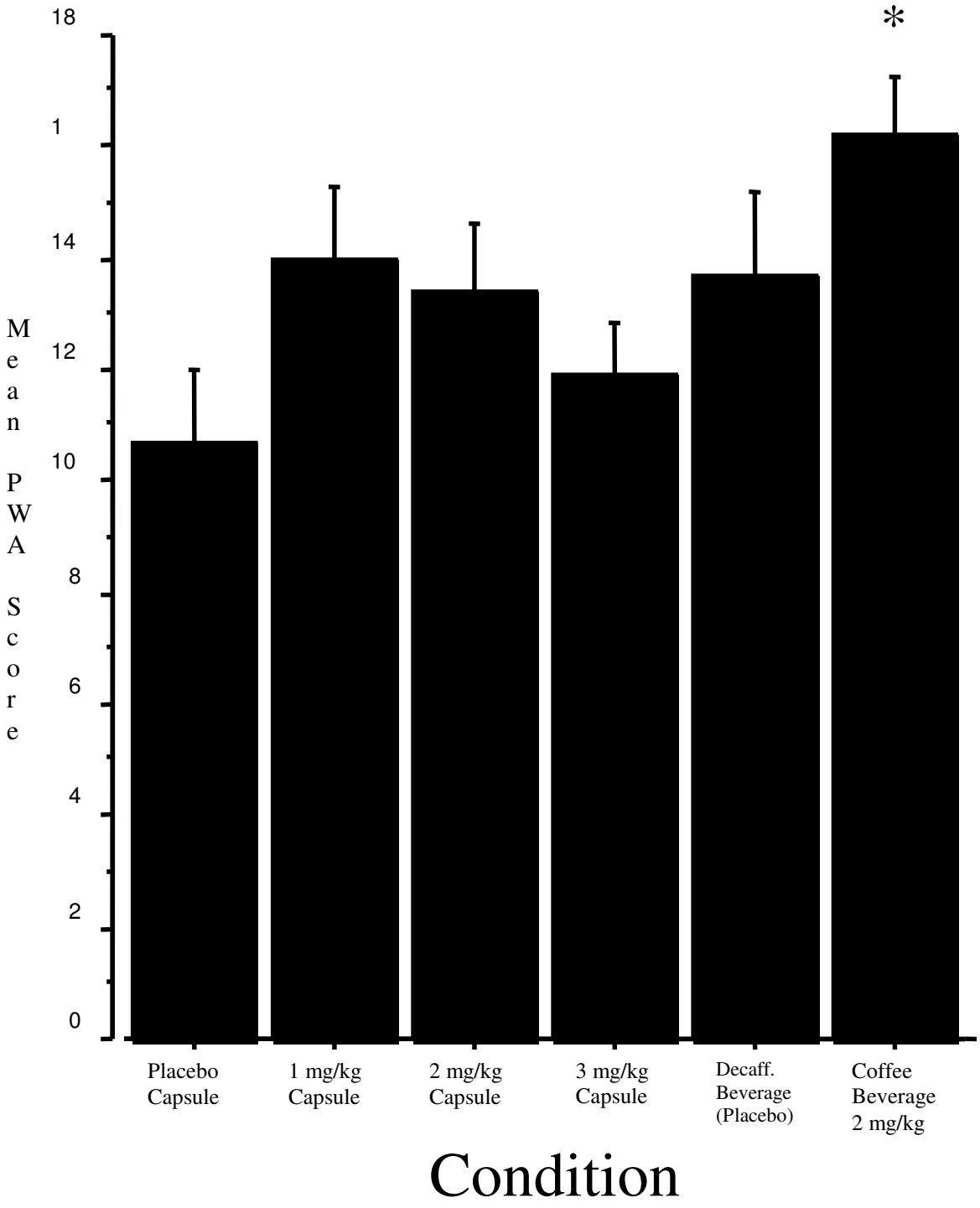

FIGURE 5: The figure above shows that subjects in coffee beverage condition (2mg/kg) performed significantly better than other caffeine conditions on the PWA test of verbal memory. [$F(5,107) = 2.107$, $\underline{p} = .07$] The histograms reflect mean scores for each condition with SEM error bars.

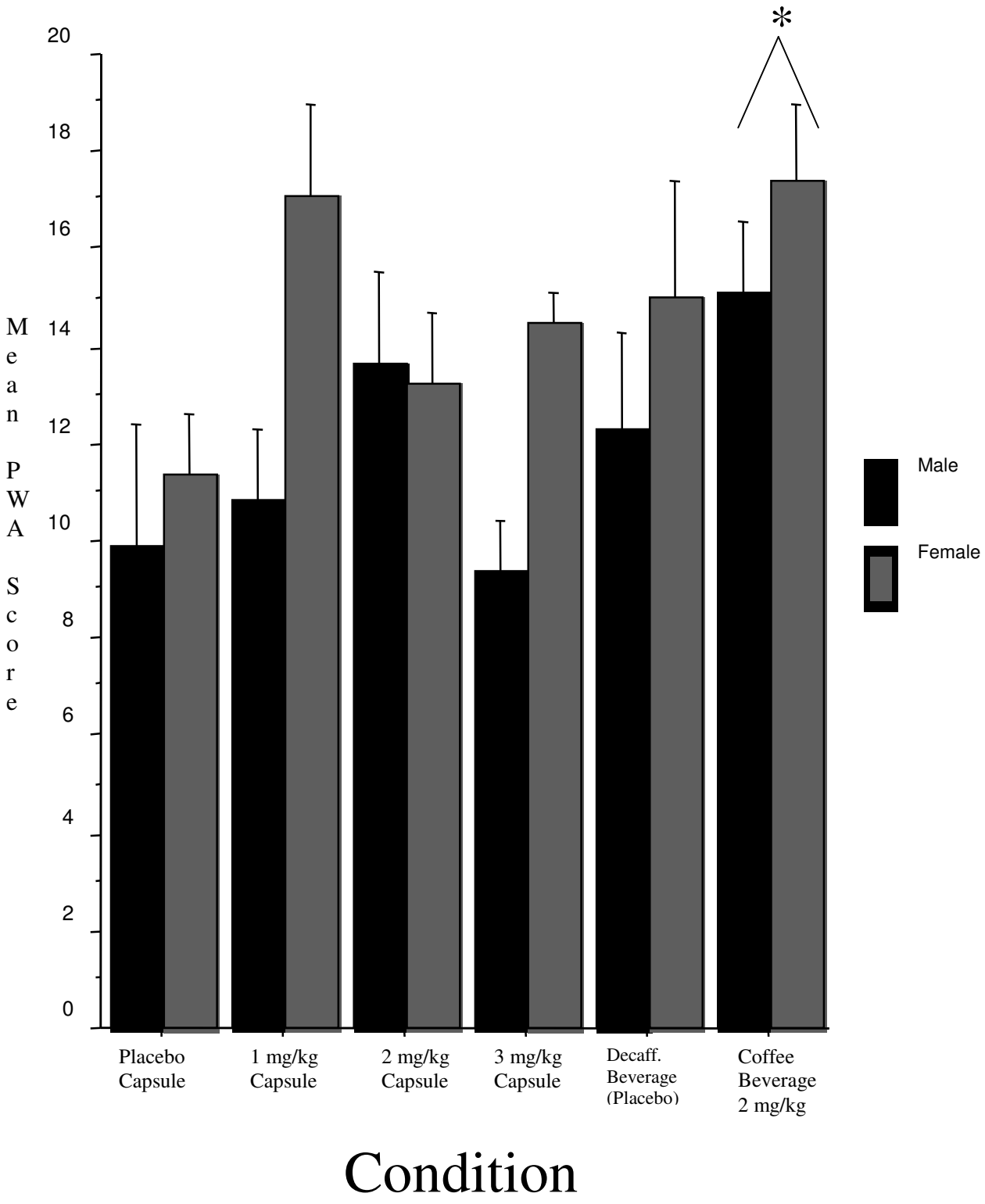

FIGURE 6: The results above (means +/- SEMS) agree with past research where overall females [$F(1,101) = 17.04$, $\underline{p} < .06$], performed significantly better than males on this verbal memory task. The results show mean performance for males and females on PWA recall.

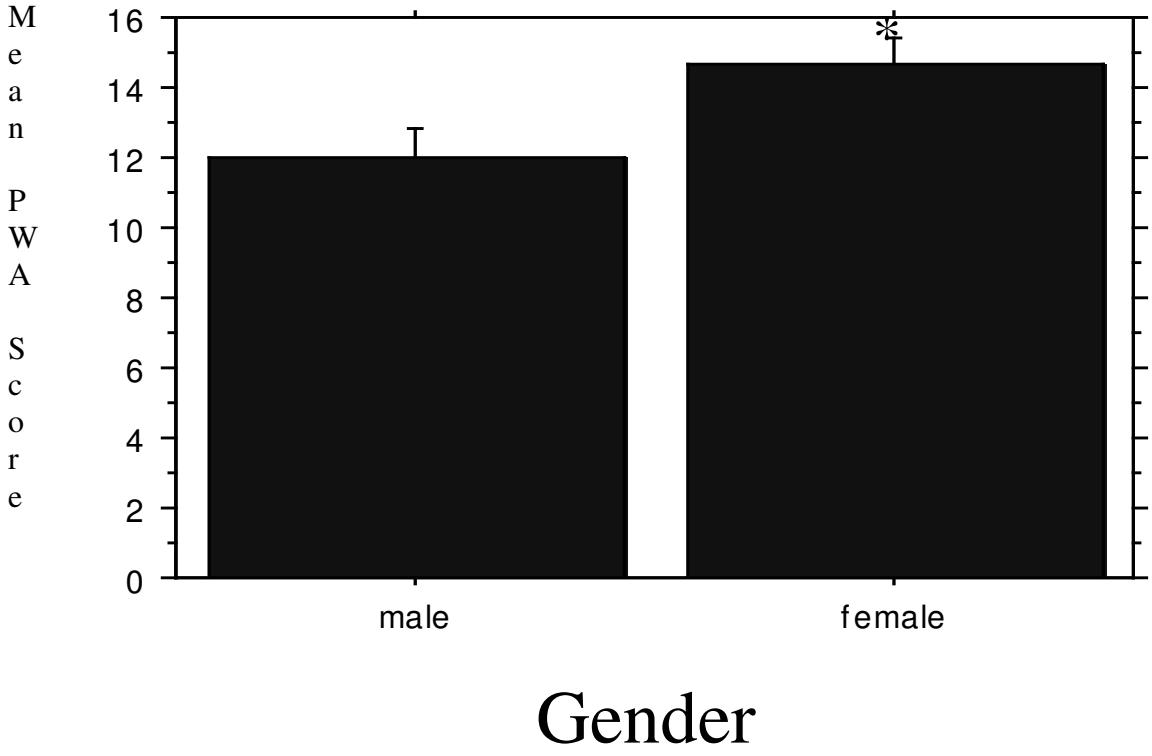

Figure 7: MRT Results by Gender. The figure above shows that females performed significantly better than males on the PWA task.

Error Bars: ± 1 Standard Error(s)

A covariate analysis between SAT score and PWA score did not significantly change from the ANOVA scores on with condition alone [F (5,88)= .381, *p*= .8605, power= .143]. There was no significant interaction between SAT score and PWA score [F (5,88)= .479, *p*= .7912, power= .171]. So, preexisting group differences in caffeine use are not likely to account for the results.

DISCUSSION

Past research has shown that caffeine can either increase performance (Mitchell and Redman 1992, Kerr, Sherwood and Hindmarch 1991, Hindmarch 1998, Smith et al. 1990, Warburton 1995, Durlach 1998, Terry and Phifer 1986 & Walker 2001), or decrease performance (Foreman 1999) or both (e.g. an inverted U shape in performance (Loke 1990)). However, no significant effect of caffeine in capsule form was found on MRT or PWA performance at any dose in the current study.

There are several possible factors that may have influenced these results. First, subjects may not have been compliant in abstaining from caffeine or food before entering the study. For example, some subjects may have consumed caffeine containing products and come into the experiment already saturated with caffeine. If so then our dose may have actually pushed them over the top of their performance curve. Another possible factor includes the possibility that some of the subjects may have participated with a full stomach, while others complied and refrained from eating for 3 hours prior to coming into the study. Clearly stomach contents could affect absorption rates of caffeine (Maisto, Galizio, & Conners, 1999).

Yet, another factor in the results may be that the caffeine administration in capsules may have different absorption rates than that of a cup of coffee. Liguori, Hughes

& Grass (1997) examined the absorption rates of caffeine when administered in capsules, coffee and a soft drink. The results showed that the mean peak increases in salivary caffeine with coffee (9.7 ± 1.2μg/ml) and cola (9.8 ± 0.9μg/ml) were similar. Although the mean peak increase in salivary caffeine appeared lower with capsules (7.9 ± 0.6μg/ml). They also found that the time to peak effect differed across vehicles. They found that the time to peak for coffee (mean ± SD = 42 ± 5 min) and cola (mean ± SD = 39 ± 5 min) was similar, but was longer with capsules (mean ± SD = 67 ± 7 min). Kamimori (2002) found that absorption rates for caffeine administered in capsules to peak in the bloodstream was between 84-120 minutes. Since subjects watched the distracter movie for only 30 min (see procedure) this may not have been long enough for the caffeine absorption to reach maximum levels. However, anecdotal observations suggested that caffeine capsules were clearly having effects within the testing time frame and in some cases appeared to produce clear behavioral effects within a short time span.

Expectancy is another factor that may have influenced our results. Since people usually do not consume caffeine in a capsule their expectancies of what will happen to them may have been influenced. Caffeine is typically consumed in the beverage form (a cup of coffee or a soft drink). Mikalsen, Bertelsen & Flated (2001), found that subjects that were told that they were receiving caffeine in a beverage reported increased arousal. They also found that information about the content of the drink altered arousal in the direction indicated by the information. Christensen, White, Krietsch, & Steele (1990) and Christensen, Miller & Johnson (1990) also found a significant expectancy effect of caffeine on ratings of alertness, headache, rapidity of heartbeat, sleepiness, and clearness of thought flow.

Since caffeine form may have had at least 2 potential influences in this study a second experiment was conducted in order to compare the results of caffeine given in a capsule form to the effects potentially associated with caffeine in coffee. In this second study the effects of a 0mg/kg cup of coffee and a 2mg/kg cup of coffee were compared to the results of the first study where caffeine was given in a capsule form.

EXPERIMENT 2

PROCEDURE

The procedures used in experiment 2 was identical to those described for experiment 1 with the following exceptions:

Once subjects were recruited to the study they were randomly assigned to receive a decaffeinated cup of coffee or a 2mg/kg cup of coffee. The coffee was prepared, based on body weight, by another experimenter while the subjects filled out validity check surveys. That experimenter preparing the coffee recorded, in a logbook, which subject received which dose of caffeine. The "coffee" cups were numbered by the experimenter that prepared the coffee and then given to the subjects with an 8-ounce cup of water, so that the testing experimenters were blind as to which subject was receiving which dose of caffeine. While consuming the coffee the subjects watched a neutral video entitled "Secret of the Psychics" for 15 minutes and were asked to refrain from talking or having any other interaction with each other. Then the video was watched for another 30 minutes. After 45 minutes elapsed the video was turned off and the first test began. This was to allow the caffeine to be absorbed (Spiller (1998), Kamimori et. al. (2002), Maisto, Galizio, & Conners (1999), and Warburton (1995)). As for experiment 1 a computerized version of the Vandenberg, (1978) Mental Rotation Task (MRT) task was administered.

Following the MRT task a computerized version of the Paired Word Association Task (PWA) was administered, Pavio (1983).

RESULTS (STUDY 2)

Again, the results were consistent with past research showing that males scored better than females on the MRT [$F(1,101) = 16.601$, $p<.0001$, power = .992] (Fig. 3 & 4).

An ANOVA for performance on the Mental Rotation showed that in experiment 2 there was a trend for the coffee 2mg/kg group to perform better than the caffeine capsule groups. The coffee 2mg/kg group (mean score = 26.105) scored significantly better (Fig.1) on the MRT than the 1mg/kg capsule group (mean score = 22.214) [$F(5,107) = 1.078$, $p = .0399$,] and the coffee 2mg/kg group (mean score = 26.105) and approached significance over the 2mg/kg capsule group (mean score = 21.310) [$F(5,107) = 1.078$, ($p = .0708$)] the 3mg/kg capsule group (mean score = 21.250) [$F(5,107) = 1.078$, ($p = .1156$)] and the placebo capsule group (mean score = 22.214) [$F(5,107) = 1.078$, ($p = .1416$)] with a power of 0.364. There was no significant difference between the placebo capsule group and any of the caffeine capsule groups. There was no significant difference between the 2mg/kg coffee group and the decaffeinated coffee group.

Females performed better on the PWA than males [$F(1,101)= 7.693$, $p=.0068$, power = .793] (Fig. 6 & 7).

An ANOVA for the affects of caffeine on the PWA showed that the 2mg/kg coffee group (mean score = 16.211) did significantly better than the placebo capsule caffeine group (mean score = 10.667) [$F(5,107) = 2.107$, $p = .0026$], and the 3mg/kg capsule condition (mean score = 11.917) [$F(5,107) = 2.107$, $p = .0430$]. The 2mg/kg coffee condition (mean score = 16.211) did better that than the 2mg/kg capsule condition

(mean score = 13.429) [F(5,107) = 2.107, $\underline{p}$ = .1251], the coffee placebo condition (mean score = 13.650) [F(5,107) = 2.107, $\underline{p}$ = .1626], and the 1mg/kg capsule condition (mean score = 13.950) [F(5,107) = 2,107, $\underline{p}$ = .2172], but did not achieve significance (power = 0.675).

Although it is likely that caffeine in beverage form did have time to reach a peak levels of absorption and might be an explanation for why the 2mg/kg caffeine coffee group scored higher than the caffeinated capsule groups, it still does not help to explain why the decaffeinated coffee group also scored better than most of the capsule groups. Nor does it explain why performance on the second task in this study did not produce significant effects since better caffeine absorption should have occurred.

DISCUSSION

This study has attempted to control for a number of variables that other studies have neglected and attempted to set a standard protocol for future caffeine research. Clearly some variables that need to be controlled in a standardized way in any drug study are body weight, sex, time of day effects, medications that subjects are on, drug/caffeine use history, withdrawal issues, caffeine saturation issues, dose curve effects, and expectancy effects. Yet many past studies have failed to adequately control these variables. Only through appropriately standardized controlled studies can we start to compare results from one study to the next.

The larger purpose of this study was to examine caffeine's effects on verbal short-term memory and visuo-spatial memory. The results showed that caffeine when administered in a capsule produces mixed results (see figs. 2 & 5). However, caffeine administered to subjects in coffee produced significant improvements in these tasks

compared to caffeine in capsules (see figs. 2 & 5). This clearly suggests that conditional drug effects, i.e. expectancies are also critical to control in future caffeine studies.

A Brief History Of Caffeine

Caffeine is the world's most widely used psychoactive substance even surpassing the use of nicotine and alcohol. Caffeine is also the only psychoactive substance that has managed to overcome the resistance and disproval of cultures around the world. Someone can acquire caffeine just about anywhere (Weinberg & Bealer, 2001). Caffeine is unregulated, sold without license, offered over the counter in tablet and capsule form and even added to products intended for children. Over 85% of Americans use caffeine on a daily basis. It can be assumed that the use of caffeine is partially based on its effects on cognition. Yet little reliable evidence exists regarding its effects on cognition (Weinberg & Bealer, 2001).

Coffee, tea, and caffeinated soft drinks are the three most popular beverages in the world today and anthropologists believe that early Stone Age man was ingesting caffeine as early as 700,000 B.C. They believe that the leaves, seeds and bark of caffeine containing plants were either chewed or ground up to make a paste for ingestion. But, the scientific discovery of caffeine did not occur until 1819 when Friedlieb Ferdinand Runge first isolated the chemical from coffee.

Pharmacology of Caffeine

Because caffeine is water-soluble it easily passes through cell membranes, including the blood-brain barrier. It is classified as a central nervous system stimulant and an analeptic (a drug that restores strength and vigor). After caffeine ingestion, caffeine quickly makes its way into the blood stream. Typically 30-90 minutes after consuming a

cup of coffee with a typical 100-mg dose of caffeine, a 200-pound man would attain a concentration of about 1mg/kg of body weight. A 100-pound woman would attain about 2mg/kg (Weinberg & Bealer, 2001). Other drugs can affect caffeine metabolism, i.e. smoking can increase the rate at which caffeine is metabolized by half, but alcohol reduces this rate, and oral contraceptives can decrease it by two-thirds. (Weinberg & Bealer, 2001). Consequently caffeine is absorbed throughout the body within minutes of ingestion.

Caffeine is thought to act as an adenosine antagonist. Adenosine is a neurotransmitter with mood depressing, sleep inducing, and anticonvulsant properties. Adenosine also decreases urination and gastric secretion. Adenosine decreases the rate of spontaneous nerve cell firing and depresses evoked nerve cells potentials in the brain by inhibiting the release of other neurotransmitters that control the excitability of the central neurons. The most widely held theory about caffeine's mechanism of action is that it acts as a competitive antagonist of adenosine, i.e. caffeine accomplishes its effects by blocking the binding of adenosine to its receptor. Simply put, caffeine acts as a key that fits into the receptors where adenosine would fit and blocks adenosines entry into the receptor site. By doing this, caffeine blocks many of adenosine's effects. The result is that when caffeine is ingested we are less sleepy or tired, as we might otherwise have been. (Weinberg & Bealer, 2001). Furthermore, it is possible that adenosine is involved in certain mental processes. These processes may include verbal short-term memory, mental rotation, arousal (both physical and mental), and mood. (Liguori, Hughes, & Grass, 1997, Fillmore, 1994, Milkalsen, 2001, Smith, Sturgess & Gallagher, 1999, Kamimori et al. 2002, Warburton, 1995, Loke, 1990, Durlach, 1998).

Studies of Caffeine on Cognition

Many studies of caffeine effects on cognition have been conducted. However, these studies have produced mixed results. One potential reason for these conflicting results is because mixed procedural standards have been used, and in some cases they lack control over critically relevant variables.

For example, Loke (1990) did not control for subject body weight and did not take into consideration caffeine withdrawal issues; they had subjects abstain from caffeine for the whole 2 weeks of testing. Loke (1990) also failed to control for potential expectancy effects (they administered caffeine in capsules).

Likewise, Mitchell and Redman (1982) failed to control for withdrawal effects, (they had subjects abstain from caffeine for 24 hours prior to testing), and they failed to assess other drug use history. They also failed to look at a dose-response relationship in their caffeine study and they failed to assess expectancy effects (administered caffeine in capsules).

Kerr, Sherwood and Hindmarch (1991) did not control for body weight, (they either administered 0mg or 300mg of caffeine in a capsule), nor did they examine a dose response curve. They also had a 24-hour caffeine abstinence period, which may have resulted in caffeine withdrawal.

Smith et al. (1990) did control for a quite a few variables including body weight (0mg/kg or 300mg/kg administered in coffee), gender, and time of day. They also had subjects refrain from alcohol for 24 hours prior to testing and had subjects abstain from caffeine consumption for 3 hours before testing. However, they did not examine a dose-response curve, or look at user history for other drugs or for caffeine.

Ruijter et al. (2000) administered either a 0mg or 200mg dose of caffeine in a cup of coffee. Ruijter et al. (2000) controlled for sex, time of day and caffeine intake. However, they failed to assess body weight, and user history of other substances. They also did not have subjects abstain from caffeine. Therefore, subjects may have potentially come in with caffeine "on board".

Warburton (1995) controlled for sex and time of day. They had subjects refrain from food or alcohol intake for 24 hours prior to testing. They told subjects to practice normal caffeine use habits. They also had subjects refrain from other drug use for 3 days before testing. However, they did not control for body weight (they gave either doses of 0mg, 75mg or 150mg of caffeine in a cup of coffee).

Foreman et al. (1999) controlled for gender by testing only males. They controlled for time of day, caffeine and alcohol use. They examined a dose-response curve by administering either a 0mg, 125mg, or 250mg dose of caffeine in a cup of coffee. However, Forman (1999) failed to control for body weight and drug use history. They also failed to control for withdrawal effects (subjects abstained from caffeine for 12 hours prior to testing).

Walker et al. (2002) studied the effects of caffeine on mental rotation and a paired-word task after subjects were given a cup of coffee. They found that caffeine improved performance on both tasks in females. They controlled for gender, user history and had subjects abstain from any drugs for 8 hours prior to testing. However, they did not control for tolerance, withdrawal effects, and body weight.

Hindmarch (1998) examined the differences of a 0mg dose versus a 100mg dose of caffeine in a cup of tea on a critical flicker fusion task, a choice reaction time task, and

a short-term memory task. They found that caffeine improved performance on the critical flicker fusion task. Hindmarch controlled for sex, smoking history, time of day (9am, 2pm and 7pm), and had subjects abstain from caffeine the evening prior to testing. They did not control for withdrawal effects, body weight, drug use history, and they did not say if the subjects abstained from caffeine between all 3 dosing sessions.

Durlach (1998) looked at a small dose of caffeine 60mg versus 0mg in a cup of tea on 8 non-smoking males. They also had subjects abstain from caffeine from 9pm the night prior to testing until the testing time. However, they did not control for withdrawal effects, weight or examine drug use history.

Terry and Phifer (1986) looked at a 0mg or 100mg dose (in Gatorade) of caffeine's effects on an auditory verbal learning task. They found that caffeine improved performance. They controlled for gender, time of day (1230pm or 2pm), and had subjects abstain from caffeine from 930 pm the night before testing. However, Terry and Phifer (1986) did not look at a dose-dependent response curve, did not control for body weight, withdrawal effects, and failed to examine drug and caffeine use history.

In the current study, body weight was controlled for, a dose-response curve was examined, and expectancy effects were examined (administered 0mg/kg, 1mg/kg, 2mg/kg or 3mg/kg in capsule versus 0mg/kg or 2mg/kg of caffeine in a cup of coffee). Also subjects abstained from caffeine 3 hours prior to participation to assure that they were neither saturated with caffeine nor in caffeine withdrawal. Subjects were instructed not to eat 1 hour prior to testing to reduce the competition for absorption in the stomach. Subjects were instructed to refrain from use of nicotine 1 hour prior to entering the study to minimize drug interactions, (but without producing nicotine withdrawal). Screening

was conducted for caffeine use and drug use history to screen out "high" and "low" caffeine users. "Low" caffeine users were not allowed to participate to rule out the possibility of an over sensitivity to the effects of caffeine. Also "high" caffeine users were not allowed to participate to reduce the possibility of a tolerance to the caffeine doses used in this study. Potential subjects who reported current use of illicit drugs were not recruited. Subjects on birth control were also screened out due to birth control medications effects on caffeine absorption (Spiller, 1998).

PWA, MRT, and Gender Differences

Differences in gender performances on MRT and PWA found in our study are congruent with past research (Jorm, Anstey, Christensen & Rodgers 2004, Voyer, Voyer and Bryden 1995, & Weiss et al. 2003). Males typically performed significantly better than females on MRT type spatial tasks. While, females typically performed better than males on verbal memory tasks. Voyer, Voyer and Bryden (1995) conducted a meta-analysis of 286 studies of visuo-spatial ability and found that males out-performed females by 0.6 standard deviations on such tasks. Weiss et al. (2003) conducted a study of visuo-spatial ability and verbal tests on 51 women and 46 men. Their results agreed with the findings from this study that men perform better on visuo-spatial ability and females perform better on verbal memory.

The Effects of Caffeine on Cognitive Performance in the Present Study

The lack of significant effects of caffeine administered in capsule form in the present study on MRT and PWA (Fig. 2) are not consistent with Loke (1990), Smith et al. (1990), & Walker et al. (2002) but are consistent with Warburton (1995) who did not find a significant effect of caffeine on visuo-spatial ability. A significant difference across any

caffeine capsule condition was not found. However, when the caffeine was administered in a "beverage", MRT performance improved. The 2mg/kg caffeine coffee group did significantly better on the MRT than the 1mg/kg capsule group (p= .0399) and showed a trend for better performance compared to the placebo (p= .1416), 2mg/kg (p= .0708) and 3mg/kg (p= .1156) capsule groups. PWA results showed that the 2mg/kg coffee group (mean score = 16.211) did significantly better than the placebo capsule caffeine group (mean score = 10.667) [$F(5,107) = 2.107$, $\underline{p} = .0026$], and the 3mg/kg capsule condition (mean score = 11.917) [$F(5,107) = 2.107$, $\underline{p} = .0430$]. The 2mg/kg coffee condition (mean score = 16.211) did better that than the 2mg/kg capsule condition (mean score = 13.429) [$F(5,107) = 2.107$, $\underline{p} = .1251$], the coffee placebo condition (mean score = 13.650) [$F(5,107) = 2.107$, $\underline{p} = .1626$], and the 1mg/kg capsule condition (mean score = 13.950) [$F(5,107) = 2,107$, $\underline{p} = .2172$], but did not achieve significance (power = 0.675).

There may be a number of reasons why results across different caffeine studies are discrepant. One possible factor is "compliance". Subjects may come into a study already partially saturated with caffeine so a low or moderate dose may boost their performance while a higher dose may cause the performance to decline as it pushes subjects over the performance curve. Another explanation of the incongruent results found between different studies of caffeine could be that caffeine may be influenced by stress and/or anxiety. Subjects are likely to experience stress/anxiety while being tested and this may have a synergistic effect with the arousal effects of caffeine. Many participants may experience anxiety when tested particularly if they are receiving a drug capsule (especially when they are not sure what is in the capsule). The combination of this anxiety with caffeine effects may have pushed them over the peak of the dose-effect

curve for caffeine on performance (Loke, 1990). The difficultly with these "over the peak" arguments in our results is that if people were coming in partially saturated with caffeine then the 0mg/kg, 1mg/kg and the 2mg/kg capsule dose condition should have shown an increase in performance versus the 3mg/kg capsule group. This did not occur. The same logic would be expected for the coffee groups. Yet, the high dose (2mg/kg dose) of coffee actually showed the best performance of all the groups on the MRT task.

Food consumption is another issue of compliance that needs to be considered. Since in this study testing on subjects was conducted at 6 pm some of the subjects may have come in on a full stomach. This would have an effect on the bioavailability of caffeine (Maisto, Stephen, Galizio, Mark, & Conners, Gerard 1990).

Caffeine is usually not consumed in a capsule. Usually the transport method for caffeine involves a food substance (i.e. chocolate) or a beverage transport (i.e. soft drink, or coffee). Participants in this study did better, on the MRT, when they received a 2mg/kg caffeine dose in coffee compared to the caffeine in capsule administration. Likewise, on the verbal short-term memory task the 2mg/kg coffee group did better than subjects receiving caffeine in a capsule form. Since, people typically consume caffeine in a beverage form this raises the issue of conditioned drug cues and expectancies in drug studies. Ross and Olson (1981) described 5 factors to consider in placebo expectancy effects in pharmacological research: (1) the direction of the placebo effect seems to be related to the drug under study (2) the strength of the placebo effect is proportional to the strength of the drug (3) the "side effects" of placebos are often similar to the side effects of the drugs which they are being compared (4) short-term time-effect curves have been found to be similar in drug and placebo treatments and (5) drug and placebo treatments

show similar dose effect. When given a coffee beverage, many conditioned cues may signal the "oncoming caffeine effects". These cues then are likely to produce the expectation of the stimulating effects of caffeine and they expect that the beverage is going to help performance. This logic is consistent with the results where subjects' performance for both the placebo coffee and the caffeinated coffee groups was better than performances for the caffeine capsule group.

Fillmore, & Vogel-Sprott (1994) also found that the expectancies about caffeine effects could influence behavioral responses to a drug. Fillmore, & Vogel-Sprott (1994) examined individual differences in subjects' expectations about the effect of caffeine on psychomotor performance. Their results showed that when subjects received caffeine they performed significantly better than placebo and no-treatment groups. But, that subjects who expected the most improvement displayed the best performance under caffeine. They found the same pattern when subjects expected to get caffeine and received a placebo. In the no treatment group when subjects did not believe that caffeine had been administered, their expectations about its effects did not predict their performance. Fillmore, & Vogel-Sprott's (1994) findings suggest that participants should exhibit an observable performance change if they expect certain effects. This agrees with the results of this study where both the 2mg/kg and the 0mg/kg caffeine coffee groups did significantly better or showed a trend for better performance than most of the caffeine capsule groups.

Alternatively differences across capsule and coffee performance may be related to differences in pharmako-kinetics. Previous studies have shown that caffeine administration in capsules may take longer to completely enter the system than we

allowed for in this study (Kamimori et al. 2002, & Liguori, Hughes & Grass 1997). However, anecdotal reports from our subjects indicated that the caffeine in capsule form could be "felt" by the subjects shortly after caffeine administration occured.

Summary

Many procedural difficulties may be responsible for the mixed results that have been seen between caffeine studies. To be able to accurately compare results across studies we need to establish a standardized way to study caffeine's effects. Many critical factors may influence the effects of caffeine on task performance. Some of these factors include, caffeine use history, drug use history, and contents in stomach. Other factors include chemicals that may alter caffeine's absorption rate (i.e. birth control), body weight, withdrawal effects, time of day, and a performance curve. Expectancy effects for caffeine also need to be taken into consideration when conducting studies on caffeine's performance. This study has attempted to control for as many as these variables as possible and we hope that this study will help set the standard for controlled and accurate caffeine research.

This study does have a low power for MRT and PWA collapsed. However, it is possible that our results may underestimate the effects. Also, within this study, when the results were separated and examined by gender (see fig 5, 3, 6 & 4) the results are stronger and generally consistent with an inverted U-shape function. (Yerkes-Dodson, 1908), the mildly stimulated group (1mg/kg) and the heavily stimulated group (3mg/kg) did not perform as well as the moderately stimulated group (2mg/kg) (see figs. 5 & 6). Results showed that there were no significant differences in performance between the dose groups. But when a cup of coffee was added, performance for subjects given

decaffeinated coffee and caffeine coffee was significantly better, or showed a trend for better performance, on the MRT and the PWA task than did the capsule conditions. The results agreed with past research that males performed better than females on the mental rotation and that females performed better on verbal memory. Moreover, the results suggest a gender interaction with caffeine and cognitive task in that the effect of caffeine on MRT performance was mostly accounted for by male subjects while the effects of caffeine on PWA performance was mostly accounted for by female subjects.

The results of this study raise the questions for future research not only on expectancy but also on gender differences that may occur with caffeine or with caffeine expectancy (see figs. 3 & 6).

One possible study that could be conducted to measure the strength of the expectancy would be to administer no caffeine to subjects while telling them that a beverage that they are about to consume contains or does not contain caffeine. Also, to further study the expectancy effects. The subjects could be instructed that caffeine has either a hindering or helping effect on the task they are about to perform.