WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 13, 2166-2190. Research Article ISSN 2277– 7105

CAFFEINE, MOOD, VERBAL REASONING, SEMANTIC PROCESSING AND LEVELS OF PROCESSING: AN INVESTIGATION OF STATE-DEPENDENT MEMORY

Dominic P. Nguyen-Van-Tam PhD and Andrew P. Smith PhD*

Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, 63 Park Place, Cardiff CF10 3AS, UK.

Article Received on
20 August 2022,
Revised on 09 Sept. 2022,
Accepted on 30 Sept. 2022
DOI: 10.20959/wjpr202213-25780

***Corresponding Author**
Andrew P. Smith PhD
Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, 63 Park Place, Cardiff CF10 3AS, UK.

ABSTRACT

Background: The effects of caffeine on cognition have been widely studied, but there are still gaps in the literature, especially in the area of memory. The present study aimed to confirm the positive effects of caffeine on semantic processing and executive function. It also investigated whether caffeine consumption can lead to state-dependent learning. In addition, the study examined whether caffeine interacted with the level of the processing carried out at encoding and subsequently influenced delayed recall. **Methods:** Participants (N=98) completed two laboratory sessions on consecutive days. Separate groups either received caffeine or placebo on each day or had a different condition on each day. The caffeine dose was 4mg/kg and was carried out double-blind. Each day the participants rated their mood before and after the memory tests. On the first day, the memory tests investigated semantic processing, logical reasoning and immediate recall following different levels of processing. On the second day, delayed recall of the words shown in the levels of processing test was also examined. **Results**: Caffeine led to greater reported alertness, sociability and anxiety. The performance of the semantic processing and logical reasoning tasks was significantly better in the caffeine condition. Caffeine did not interact with the level of encoding and had no significant effect on immediate recall. The delayed recall was significantly worse in the caffeine condition. There was no evidence of state-dependent memory in this study. **Conclusion:** The results from this study confirm the effects of caffeine on mood, semantic processing, and executive function. There was no evidence that caffeine leads to state-dependent memory. Although the level of processing influenced immediate recall, caffeine did not modify this effect. The delayed

recall was found to be impaired in the caffeine condition. These results extend our knowledge of caffeine and memory and show that semantic processing and logical reasoning tasks can be used as positive controls in future research on this topic.

KEYWORDS: Caffeine; State-dependent memory; Semantic processing; Executive function; Levels of processing; Delayed recall; Mood.

INTRODUCTION

The effects of caffeine on cognition have been extensively reviewed.[1-8] and much of the literature has been concerned with sustained attention and psychomotor speed.[9] One literature review[10] has identified a number of relatively well-established findings regarding caffeine and memory and a number of areas where evidence is more limited but where replication may be warranted. This review has also identified areas of memory research where the effects of caffeine have yet to be studied. The present study attempted to address issues in all of these potential areas of study. Specifically, it aimed to reproduce the relatively well-established positive effects of caffeine on semantic memory and provide further data regarding the effects of caffeine on executive function and caffeine interactions with levels of processing. The phenomena of state-dependency, which has been studied with regard to other psychoactive drugs but not, to date, with regard to caffeine, was also investigated.

The effect of caffeine on semantic memory has been studied extensively in a series of experiments by Smith et al.[11-15], and in 4 out of the five studies, caffeine was found to improve performance on a computerised version of Baddeley's semantic memory task.[16] In all of the studies where caffeine effects were recorded, caffeine increased the number of trials attempted or else improved the mean reaction time for correctly answered trials and in one of the studies also improved the accuracy of retrieval.[11] The effect has been reported using relatively low doses of caffeine: 40mg[15] and 1.5 mg/kg[14] and it was concluded that the effects of caffeine on semantic memory appear to be fairly robust. The present study attempted to replicate the effects of caffeine on both speed and accuracy of retrieval from semantic memory that have been described by Smith et al.[11-15] again using Baddeley's semantic memory test.[16]

Seven studies have looked specifically at the effects of caffeine on central executive function, and of these three,[11-13] have found positive effects of using Baddeley's logical reasoning task.[17] The present study aimed to replicate the effects of caffeine on the executive function

that have been described in the literature and optimised conditions for the detection of a caffeine effect by using a relatively simple design and a moderately large dose of caffeine (4 mg/kg).

The numerous studies which have attempted to investigate the effects of caffeine on recall tasks, whether attempting to measure 'short-term memory' or the phonological loop, have largely failed to demonstrate significant effects of caffeine.[12,18-22] Two studies have found significant main effects of caffeine on free recall tasks, with Terry and Phifer[23] finding a negative effect and Smith et al. (1994b)[13] a positive effect, and it is frequently concluded that caffeine does not have any robust effect on free recall. Gupta[24] has produced strong evidence however that the effects of caffeine on free recall may actually interact with the level of processing. The finding of caffeine effects on free recall after incidental encoding makes intuitive sense as it would be expected that in explicit recall tasks, participants would, quite reasonably, attempt to encode words as deeply as possible to optimise recall which might leave little scope for modification of performance by caffeine. If encoding was incidental, however, and the level of processing was manipulated by the experimenter to be sub-optimal for recall, it might leave more opportunity for caffeine effects to be detected. The present experiment also used an incidental encoding task and controlled levels of processing before free recall in order to identify any possible interactions between caffeine and the level of processing.

The phenomenon of state-dependent memory has been demonstrated for a variety of centrally acting drugs such as alcohol[25] and diazepam[26] but has never been demonstrated convincingly with caffeine. The study, therefore, investigated the possibility of state-dependent memory following the ingestion of caffeine.

The rationale behind the present methodology is now described. A moderately high dose of caffeine (4mg/kg) was used in the experiment because previous research has only reported a main effect of caffeine on semantic processing with larger doses such as 4mg/kg[11, 13] and 3mg/Kg.[12] Although positive results have also been obtained using 1.5mg/kg by Smith et al.[12], another study using 1.5mg/kg[14] has failed to find an effect. Similarly, where effects of caffeine have been reported on executive function, studies have also used moderately high doses of caffeine in the order of 3-4mg/kg.[11-13] The experimental design was manipulated so that it could be determined whether there were any state-dependent effects by using the four groups formed by the combination of caffeine and placebo conditions on day one and day

two of testing. Potentially these effects may take the form of state-dependent learning effects, where performance is better if the task is performed in the same condition in which it was previously performed or state-dependent memory effects, where recall is superior if retrieval takes place in the same state as encoding. This design also had the advantage of producing experimental groups, which allowed investigation of whether caffeine produced its effects on delayed recall at the encoding of stimuli or at retrieval.

As the effects of caffeine on memory appear to be relatively difficult to detect compared to the other psychotropic effects of caffeine, a measure of subjective mood was built into the test battery. This measure is known to be sensitive to caffeine[11,13] and was used as a positive control to ensure that the experimental procedure was sufficiently rigorous to produce caffeine effects. It would be expected that caffeine would have more effect on mood in conditions of fatigue,[12,15] so the positive control task was carried out both before and after the memory tasks in order that the effects of caffeine on mood in non-fatigued and fatigued conditions could be determined.

The following hypotheses about the main effects of caffeine were tested.

A) Caffeine (4mg/kg) will significantly improve semantic memory performance; the number of trials attempted will be increased, the accuracy of responses will be increased, and the mean reaction time for correct responses will be decreased.
B) Caffeine (4mg/kg) will significantly improve central executive function; the number of trials attempted will be increased, the accuracy of responses will be increased, and the mean reaction time for correct responses will be decreased.
C) Caffeine (4mg/kg) will significantly improve self-rated alertness and self-rated sociability and significantly increase self-rated anxiety. Increases in self-rated alertness will be greatest under conditions of fatigue, namely at the end of the test battery, post-memory test.

The following hypotheses about the interaction between exposure to caffeine on day one and exposure to caffeine on day two were tested.

A) For participants given caffeine (4mg/kg) on both days or placebo on both days, recall on day two will be superior to that of participants given caffeine on one day of testing and placebo on the other.

B) For participants in the same condition on both days, there will not be a significant difference between cognitive performance on day one and cognitive performance on day two.

METHOD

The study was carried out with the approval of the ethics committee School of Psychology and the informed consent of the participants.

Design

The experiment employed a mixed design with caffeine condition as the between-subject factor and performance on day one and day two as a within-subject factor. The administration of caffeine was double-blind to eliminate potential demand characteristics.

Participants

Ninety-six participants were used in the experiment (mean age of 21.40 years; 48 males and 48 females). All were non-smokers and regular daily consumers of caffeinated coffee or tea. Participants were paid £20 on completion of the study.

Procedure

Participants were briefly familiarised with the test battery no more than one week prior to their first test session. The familiarisation session presented the tests in identical order to those used in the test sessions but used short versions of the tasks that lasted for approximately 1 minute each. During the familiarisation session participants were allowed to ask questions as necessary in order to clarify instructions and objectives. After the demonstration of the computer tasks, participants were weighed without shoes or coats so that the amount of caffeine they were to receive could be calculated. At familiarisation, participants were also given a sheet of written instructions which advised them that during testing, normal sleeping patterns and meal times should be adhered to as much as possible and that there were prescribed periods during which they should not consume alcohol or caffeine.

Participants were either tested in the morning or evening, and the procedures for these two times are shown below.

Morning testing

2200 Begin abstinence from alcohol until the end of the experiment.

Test day 1: 0030 Begin abstinence from self-administered caffeine

0830 Present for testing after normal breakfast

0850 Test battery (baseline)

0915 Expectancy effects questionnaire, administration of caffeine or placebo, eating and sleeping questionnaire, caffeine discrimination questionnaire

1015 Test battery (post-drink)

1045 Participants were allowed to resume normal caffeine intake

Test day 2: 0030 Begin abstinence from self-administered caffeine

0915 Present for testing after normal breakfast, administration of caffeine or placebo, eating and sleeping questionnaire, caffeine discrimination questionnaire

1015 Test battery (post-drink)

1115 Debriefing and participants were allowed to resume normal caffeine and alcohol intake.

Evening testing

Where participants were tested in the evening, the same procedure was used with baseline testing on day 1 starting at 1850 and the post-drink test battery on days 1 and 2 starting at 1945. Participants were again expected to refrain from alcohol from 12 hours prior to the beginning of the experiment until the end of the experiment and also to abstain from self-administered caffeine for 8 hours prior to each test session.

Experimental beverages

All drinks were made with one rounded teaspoonful of decaffeinated coffee in 150ml of boiling water with milk and sugar added to each participant's taste. To this was added the appropriate amount of either solution A or solution B (each potentially carrying 20mg/ml of caffeine) such that in the active condition, participants would consume 4mg/kg of caffeine dissolved or, in the placebo condition, sterile water only. The code for the solutions was held by a third party and was not revealed until after all the data analysis had been carried out.

Measures

Subjective mood

The subjective mood was measured using 18 computerised visual analogue mood rating scales.[27] Each bipolar scale was comprised of a pair of adjectives, e.g. happy - sad, at either end of a horizontal line. Participants were then required, using buttons on the external control box, to move a cursor from an initial central position on the line to a position which was

representative of their present mood state. Participants then pressed another key to enter the data and bring up another mood scale. Previous research has derived three main factors from these 18 initial scales: alertness, sociability and anxiety and these were extracted and used as indices of subjective mood.

The exclusion criteria for this data was a score exactly equidistant from each extreme on more than 9 out of 18 bipolar scales at any test session, which was taken to be indicative that a participant was attempting to simply finish the test as quickly as possible and was not actually recording their subjective mood.

Performance tasks

All tasks were presented on a microcomputer. For the recall test, encoding was carried out using a computer to present the stimuli, but when asked to recall the stimuli, participants were asked to write down the words on a response sheet.

Semantic memory

This test measures the speed and accuracy of retrieval from semantic memory. Participants were shown a sentence (e.g. dogs have wings or canaries have wings) and asked to make a decision as to whether the sentence was true or not. Another sentence was shown immediately after a decision had been made about the first, and the task continued in this way for a total of 3 min. Indices of performance were the number of sentences attempted, the percentage of judgements made correctly and the mean reaction time for correct verifications.

The exclusion criteria for this test were failure to attempt at least 50 trials at baseline and/or failure to get at least 80% of the trials correct.

Logical reasoning task

This task is a test of the executive function component of the working memory model. In this task, participants were shown a sentence describing the order of a letter pair (e.g. A follows B) and a letter pair such as B.A. Participants were then required to judge whether the statement was true or false by pressing the appropriate response key. The task went on for 3 min, and the number of statements attempted, the percentage correct, and the mean reaction time for correct responses were recorded. The exclusion criteria for the task were failure to provide correct verifications for at least 50% of the simple active statements in the baseline condition.

Recall- 2 levels of processing

Intentional learning was used to encode a list of 40 words, half acoustically and the other half semantically. The encoding tasks consisted of a series of 2-second presentations of stimuli consisting of a word and a question relating to the word. Two types of questions were used; one relating to whether the word rhymed with another given word and one asking whether the word described a member of a specified category taken from Battig and Montagu's norms.[28] Participants were required to carry out two tasks; first, to respond to the question as quickly as possible by pressing the appropriate buttons on the computer keyboard and secondly, to try to remember the word. Word lists were counterbalanced for order across the baseline and post-drug conditions and presented in a fixed random order within each list. Word lists were counterbalanced for order, and each word list was matched exactly for length and frequency according to Kuçera and Francis' norms.[29] Within each list, there were an equal number of words within each encoding category, and within coding categories, there were an equal number of positive and negative correct answers. Indices of performance were the total number of words recalled, the percentage of the stimuli list recalled correctly and the number of intrusions. The exclusion criteria for the recall task were failure to correctly recall at least two words correctly in the baseline condition.

Delayed recall (day two)

To test delayed free recall, participants were asked to attempt to recall, in any order, the words that were presented in the levels of processing task on the previous day. Participants were not informed beforehand that delayed recall would be tested.

Order of tests

Familiarisation / baseline /post-drug day 1:

1. Subjective mood
2. Semantic memory
3. Logical reasoning
4. Recall (2 levels of processing, immediate recall)
5. Subjective mood

Post-drink day 2

On test day two, the recall task was substituted with a delayed recall test in which participants were required to recall the stimuli presented in the recall task on day 1.

Analysis

To control for individual differences in performance, all the performance and mood measures were generally analysed using ANCOVA using the relevant index of performance from the baseline condition as a covariate.

Analysis of the data proceeded in five distinct stages.

1. Determination of the main effects of caffeine on day one so that a direct and straightforward comparison with other similar studies could be made.
2. Investigation of reliability of the effects of caffeine across day one and day 2 using a fully between-subject design to test the effect of repeat exposure to caffeine and a placebo-controlled design to investigate order effects.
3. Investigation of possible state-dependent learning effects on the semantic memory and logical reasoning tasks.
4. Investigation of the effect of caffeine on day two on recall of stimuli encoded on day one as part of the recall task and investigation of possible state-dependent memory effects.
5. Further investigation of the effects of caffeine on semantic memory and executive function, including the potential mediation of the effects of subjective alertness and the independence of caffeine effects on the two tasks.

RESULTS

Main effects of caffeine on day 1

Subjective mood: No participants were excluded, and 96 complete data sets were used. A series of ANCOVAs were performed, with mood at baseline as a covariate. It was found that pre-memory test numerical values indicated that subjective alertness, sociability and anxiety were all increased by caffeine. In the tests of subjective mood after the memory battery consumption of caffeine significantly increased self-rated alertness, $F(1, 93) = 5.52$, $MSe = 1255.65$, $p < 0.05$, sociability, $F(1, 93) = 4.44$, $MSe = 457.01$, $p < 0.05$, and anxiety level, $F(1, 93) = 6.44$, $MSe = 157.91$, $p < 0.05$ (see table 1). This finding is entirely consistent with the literature, which suggests that caffeine increases subjective alertness and hedonic tone (particularly where participants are in states of low arousal) and that moderate doses of caffeine also increase anxiety.

Table 1: Subjective mood, day 1: Adjusted means pre-memory test, post-memory test in caffeine (4mg/kg) and placebo conditions (S.E.s in parentheses)

Test	Index of performance	Caffeine (4mg/kg)	Placebo	Significant main effect of caffeine
Mood (pre-memory tests)	Alertness 0 (low)-400 (high)	238.41 (4.70)	227.10 (4.70)	Yes*
	Sociability 0 (negative)-300 (positive)	190.47 (3.34)	182.15 (3.34)	Yes*
	Anxiety 0 (high)-150 (low)	82. 64 (2.00)	85.11 (2.00)	No
Mood (post-memory tests)	Alertness 0 (low)-400 (high)	225.83 (5.12)	208.84 (5.12)	Yes**
	Sociability 0 (negative) - 300 (positive)	184.54 (3.10)	175.32 (3.10)	Yes**
	Anxiety 0 (high)-150 (low)	80.48 (1.82)	87.00 (1.82)	Yes***

* $p < 0.05$, one-tailed
** $p < 0.05$
*** $p < 0.025$

Semantic memory: Analysis was carried out on 95 complete data sets as one participant met the exclusion criteria. ANCOVAs performed on all three indices of performance using the relevant indices of performance from the baseline condition as covariates revealed main effects of caffeine on number of trials attempted, $F(1,92) = 8.68$, $MSe = 91.37$, $p < 0.005$, percentage of trials correct, $F(1, 92) = 5.43$, $MSe = 8.4$, $p < 0.05$ and MRT for correct trials, $F(1, 92) = 6.75$, $MSe = 18430.54$, $p < 0.05$ (see Tables 2, 3 and 4). It should also be noted that for the semantic memory task, caffeine appeared to have a consistent effect in reducing variance. For the number of trials attempted, the non-adjusted S.E. was 3.63 in the caffeine condition and 4.54 in the placebo condition; for the percentage of trials correct, it was 0.54 in the caffeine condition and 0.86 in the placebo condition, and for MRT for correct trials, it was 45.94 in the caffeine condition and 52.28 in the placebo condition.

Table 2: Semantic memory, day 1: number of trials attempted in caffeine (4mg/kg) and placebo conditions (scores are the adjusted means, S.E.s in parentheses)

Mean	*Caffeine (4mg/kg)*	*Placebo*
Adjusted (S.E.)	134.81 (1.39)	128.96 (1.40)

Table 3: Semantic memory, day 1: percentage of trials correct in caffeine (4mg/kg) and placebo conditions (scores are the adjusted means, S.E.s in parentheses).

Mean	*Caffeine (4mg/kg)*	*Placebo*
Adjusted (S.E.)	95.58 (0.42)	93.20 (0.42)

Table 4: Semantic memory, day 1: MRT (msec) for correctly answered trials in caffeine (4mg/kg) and placebo conditions (scores are the adjusted means, S.E.s in parentheses)

Mean	*Caffeine (4mg/kg)*	*Placebo*
Adjusted (S.E.)	1263.20 (19.95)	1336.55 (19.74)

Logical reasoning: One participant met the exclusion criteria, and analysis was therefore carried out on 95 complete data sets.

Effects at baseline: It would be expected that at baseline, performance on the logical reasoning task would be mediated by the syntactic difficulty of the statements. To investigate whether this was the case, ANOVAs were carried out on the percentage of statements correct and MRT for correct statements with simple-negative and active-passive statement types as within-subject factors. It was found that simple statements were answered significantly more accurately and more quickly than negative statements and that active statements were answered significantly more accurately and more quickly than passive ones. For the percentage of statements answered correctly, it was found that there was an interaction between simple-negative and active-passive statement types, which indicated that simple-active statements were responded to most accurately.

Caffeine effects: A series of ANCOVAs, using the relevant index of performance from baseline as covariate revealed significant main effects of caffeine for the number of statements answered, $F(1, 92) = 4.02$, $MSe = 48.38$, $p < 0.05$ and for the percentage of statements correct, $F(1, 92) = 4.42$, $MSe = 18.49$, $p < 0.05$ (Tables 5 and 6). For MRT for correctly answered trials, there were no statistically significant effects, $F(1, 92) = 0.97$, $MSe = 386174.42$, $p > 0.05$, but the means indicated that, as might be expected, MRT was faster in the caffeine condition. The adjusted MRT was 3173.21 (S.E. 91.57) msec in the caffeine condition and 3301.42 (S.E. 90.59) msec in the placebo condition. Non-adjusted means were 3372.10 (S.E. 171.67) msec and 3106.67 (S.E. 166.65) msec, respectively. When the MRT for correctly as well as incorrectly verified trials was analysed (i.e. MRT for all trials completed), it was found that the main effect of caffeine reached one-tailed statistical significance and was very near to two-tailed significance, $F(1, 84) = 3.70$, $MSe = 983.869.19$,

p = 0.057. The adjusted mean was 3088.54 in the caffeine condition compared to 3334.12 in the placebo condition. Non-adjusted means were 3218.15 (S.E. 148.66) in the caffeine condition and 3185.50 (S.E. 172.82) in the placebo condition.

There was no statistically significant difference in the MRT for correctly or incorrectly answered trials and no interactions between MRT for correctly or incorrectly answered trials and caffeine conditions. Further analysis was carried out to determine whether there was any differential effect of caffeine on the different types of statement (described above). The analyses used a mixed ANCOVA with simple or negative and active or passive statement types as within-subject factors with the four relevant indices of performance from the baseline condition as covariates. It was found that there were no statistically significant interactions between statement type and caffeine for any parameter of performance.

Table 5: Logical reasoning, day 1: number of trials attempted in caffeine (4mg/kg) and placebo conditions (scores are the adjusted means, S.E.s in parentheses).

Mean	***Caffeine (4mg/kg)***	***Placebo***
Adjusted (S.E.)	61.28 (1.03)	58.35 (1.01)

Table 6: Logical reasoning, day 1: percentage of trials correct in caffeine (4mg/kg) and placebo conditions (scores are the adjusted means, S.E.s in parentheses).

Mean	***Caffeine (4mg/kg)***	***Placebo***
Adjusted (S.E.)	92.94 (0.63)	91.07 (0.62)

Recall

Ninety-three complete sets of recall data were analysed; 3 participants were excluded.

Effects at baseline: A repeated-measures ANOVA was used to analyse the effect of the level of processing at baseline for words recalled correctly. It was found that, as expected and in line with the level of processing paradigm, significantly more words were recalled correctly after deep encoding than after shallow encoding.

Caffeine effects

A series of ANCOVAs, each using the relevant index of performance at baseline as a covariate, failed to reveal any significant effects for total words recalled, percentage of words recalled correctly or the number of intrusions. In the caffeine condition, 18.14 (S.E. 1.13) % of words were recalled correctly as opposed to 17.90 (S.E. 1.12) in the placebo condition. In

the caffeine condition, there were 2.41 (S.E. 0.34) intrusions compared to 2.43 (S.E. 0.34) in the placebo condition.

To determine whether there was a level of processing effect for correctly recalled words, a further mixed ANCOVA was carried out with caffeine as the between-subject factor, level of processing as the within-subjects factor and the number of correctly recalled words after deep or shallow processing at baseline as the covariates. It was found that as expected there was a level of processing effect, $F(1, 90) = 17.82$, $MSe = 57.49$, $p < 0.00025$. After deep encoding, 19.89 words were recalled correctly compared to 15.44 after shallow encoding (S.E.s cannot be calculated as there was more than one covariate per level of factor). The non-adjusted means were 20.43 (S.E. 1.03) after deep encoding and 14.89 (S.E. 1.06) after shallow encoding. There was no interaction between the level of processing and caffeine.

Summary of results from day 1

- The usual profile of caffeine effects on mood was demonstrated.
- Caffeine improved executive function and retrieval from semantic memory but did not affect immediate recall.
- For executive function and semantic memory, caffeine increased the accuracy of response and speed retrieval, suggesting that improvements in performance are not mediated solely by processing speed.
- Caffeine improved self-rated alertness and sociability and increased anxiety, particularly post-memory tests.
- On the logical reasoning task, caffeine did not interact in any way with the level of syntactic difficulty of the trial.

Reliability of the effects of caffeine

Significant main effects of caffeine were found on day one for semantic memory and executive function, which is consistent with the literature. It is not known, however, how reliable these results are. For example, can they be demonstrated on the second day of testing with the second dose of caffeine? The reliability of the effect of caffeine over day one and day two was tested by analysing the performance data for a subset of participants who were given caffeine on both days or placebo on both days. The analysis used a mixed ANCOVA with performance on day one and day two as a within-subject factor, caffeine as a between-subject factor and performance at baseline as a covariate.

Semantic memory: For all parameters of performance, there were overall trends for caffeine to increase performance compared to placebo, with the trend reaching significance in the case of the number of trials attempted, $F(1, 44) = 4.87$, $MSe = 129.54$, $p < 0.05$ (table 7). No interactions between caffeine and the day of testing were found. Significant effects of day of testing were found for percentage of trials correct and for MRT for correct trials, $F(1, 44) = 5.70$, $MSe = 4.13$, $p < 0.05$ and $F(1, 44) = 7.79$, $MSe = 3479.68$, $p < 0.01$ (Table 7). Inspection of the adjusted means indicated that on day two, MRT was improved at the expense of a lower percentage of trials correct.

Logical reasoning: There was no effect of caffeine on the number of trials attempted over days 1 and 2 however caffeine significantly increased the percentage of trials correct (table 8), $F(1, 44) = 3.65$, $MSe = 23.24$, $p < 0.05$ (one-tailed) and significantly decreased MRT for correct trials, $F(1, 44) = 3.02$, $MSe = 1282833.18$, $p < 0.05$ (one-tailed). No significant interactions between caffeine condition and day of testing were found. For the percentage of trials correct, there appeared to be a practice effect with a highly significant difference in performance between day one and day 2, $F(1, 44) = 248.69$, $MSe = 11.87$, $p < 0.0001$ (table 8). No other practice effects approached significance.

Table 7: Semantic memory performance, day 1 and day 2: Adjusted means in caffeine (4mg/kg) or placebo conditions (S.E.s in parentheses)

Outcome	Caffeine Condition	Day 1	Day 2	Significant main effect of day of testing	Significant interaction between caffeine and day of testing	Days 1 and 2: significant main effect of caffeine
Number of trials	Caffeine	133.27 (1.97)	134.42 (1.81)	No	No	Yes*
	Placebo	129.71 (1.93)	128.10 (1.77)			
% trials correct	Caffeine	94.27 (0.59)	92.70 (0.69)	Yes*	No	No
	Placebo	92.69 (0.57)	92.30 (0.675)			
MRT correct trials (msec)	Caffeine	1263 (28)	1257 (28)	Yes**	No	No
	Placebo	1319 (27)	1318 (27)			

* $p < 0.05$

** $p < 0.01$

Table 8: Logical reasoning, day 1 and day 2: Adjusted means in caffeine (4mg/kg) or placebo conditions (S.E.s in parentheses)

Outcome	Caffeine Placebo	Day 1	Day 2	Significant main effect of day of testing	Significant interaction between caffeine and day of testing	Days 1 and 2: significant main effect of caffeine
Number of trials	Caffeine	61.22 (1.63)	64.01 (1.47)	No	No	No
	Placebo	59.33 (1.60)	64.66 (1.44)			
% of trials correct	Caffeine	92.31(0.95)	93.93 (0.82)	Yes**	No	Yes*
	Placebo	90.62 (0.93)	91.70 (0.80)			
MRT correct trials (msec)	Caffeine	2985 (153)	2797 (122)	No	No	Yes*
	Placebo	3264 (149)	3017 (119)			

* $p < 0.05$, one-tailed

** $p < 0.0001$

State-dependent learning and semantic memory and logical reasoning

State-dependent effects can be demonstrated when behaviour or stimuli learnt in one context are best performed or recalled in the same context. Usually, the phenomenon is applied to memory, but it can also be applied to other aspects of performance. It is unknown whether any such phenomena can be demonstrated for performance under caffeine. Further analysis examined the effects of performing the semantic memory and logical reasoning tasks under the influence of caffeine on day one on performance in caffeine or placebo conditions on day 2. The analysis used a between-subjects ANCOVA with caffeine conditions on day one and day two as between-subject factors and the relevant index of performance at baseline as a covariate.

Semantic memory: There was no evidence of any state-dependent effects (indicated by an interaction between the effects of caffeine on day one and day two on performance on day 2) or of any effects of caffeine on day one on performance on day 2 (table 9). Acute ingestion of caffeine, i.e. consumption of caffeine on day 2 did however lead to a significant increase in the number of trials attempted, $F(1, 90) = 3.63$, $MSe = 92.18$, $p < 0.05$ (one-tailed). In the caffeine condition, 133.44 (S.E. 1.40) trials were attempted as opposed to 129.68 (S.E. 1.39) in the placebo condition.

Table 9: Semantic memory on day two: Adjusted means in caffeine (4mg/kg) and placebo conditions on day one and day 2 (S.E.s in parentheses).

Index of performance	Condition on day 1	Condition on day 2	Adjusted mean
Number of trials attempted	Caffeine	Caffeine	135.59 (2.02)
	Caffeine	Placebo	129.80 (1.96)
	Placebo	Caffeine	131.28 (1.97)
	Placebo	Placebo	129.56 (1.97)
Percentage of trials correct	Caffeine	Caffeine	93.47 (0.71)
	Caffeine	Placebo	94.49 (0.70)
	Placebo	Caffeine	94.02 (0.70)
	Placebo	Placebo	92.73 (0.70)
MRT correct trials (msec)	Caffeine	Caffeine	1257.54 (28.14)
	Caffeine	Placebo	1299.38 (27.42)
	Placebo	Caffeine	1300.32 (27.40)
	Placebo	Placebo	1323.02 (27.57)

Logical reasoning: For all parameters of the logical reasoning task, there was no evidence of state-dependency denoted by an interaction between caffeine conditions on day one and day two and no significant effects of caffeine (table 10).

Table 10: Logical reasoning on day two: Adjusted means in caffeine (4mg/kg) and placebo conditions on day one and day 2 (S.E.s in parentheses)

Index of performance	Condition on day 1	Condition on day 2	Adjusted mean
Number of trials attempted	Caffeine	Caffeine	63.83 (1.43)
	Caffeine	Placebo	62.98 (1.39)
	Placebo	Caffeine	66.05 (1.39)
	Placebo	Placebo	64.55 (1.40)
Percentage of trials correct	Caffeine	Caffeine	94.39 (0.85)
	Caffeine	Placebo	93.74 (0.81)
	Placebo	Caffeine	92.81 (0.81)
	Placebo	Placebo	92.14 (0.82)
MRT correct trials (msec)	Caffeine	Caffeine	3007.95 (109.97)
	Caffeine	Placebo	2959.58 (108.79)
	Placebo	Caffeine	2854.51 9107.52)
	Placebo	Placebo	3068.48 (109.64)

Effects of caffeine on delayed recall and state-dependent recall

To investigate the possibility of caffeine effects on delayed recall and to investigate state-dependent recall, a series of between-subject ANOVAs were carried out with caffeine condition on day one and caffeine condition on day two as between-subject factors and performance on day two as the dependent variable. It was found that there was no evidence of

state-dependency effect, which would be indicated by an interaction between caffeine condition on day one and day 2, nor were there any effects of caffeine condition on day one on performance on day 2.

Two main effects of caffeine condition on day two were found. Caffeine on day two significantly reduced the total number of words recalled, $F(1, 89) = 5.02$, $MSe = 10.60$, $p < 0.05$ with 4.73 (S.E 0.48) per cent of words recalled correctly in the caffeine condition and 6.24 (S.E. 0.48) in the placebo condition. Caffeine also significantly reduced the number of words recalled correctly, $F(1, 89) = 5.13$, $MSe = 5.13$, $p < 0.05$ (table 11).

Table 11: Delayed recall, day 2: mean words recalled in caffeine (4mg/kg) or placebo conditions (S.E.s in parentheses)

Outcome	Condition on day 1	Condition on day 2	Mean words recalled	Significant main effect of caffeine on day 1	Significant main effect of caffeine on day 2	Evidence for state-dependent recall
Total words recalled	Caffeine	Caffeine	4.83 (0.68)	No	Yes*	No
		Placebo	7.04 (0.68)			
	Placebo	Caffeine	4.63 (0.67)			
		Placebo	5.44 (0.68)			
Percentage of words recalled correctly	Caffeine	Caffeine	4.89 (1.18)	No	Yes*	No
		Placebo	9.13 (1.18)			
	Placebo	Caffeine	4.90 (1.16)			
		Placebo	5.98 (1.18)			
Number of words recalled incorrectly	Caffeine	Caffeine	2.87 (0.48)	No	No	No
		Placebo	3.30 (0.48)			
	Placebo	Caffeine	2.63 (0.47)			
		Placebo	3.00 (0.48)			

* $p < 0.05$

Effects of caffeine on retrieval and interactions with the level of processing

A further repeated measures ANOVA was performed to ascertain whether caffeine on day 2 interacted with the level of processing at encoding on day 1, i.e. if there was a caffeine effect confined to retrieval and interacting with the level of encoding. The interaction between the level of encoding and caffeine condition did not reach significance. After deep encoding, 5.96 (S.E. 0.99) per cent of words were recalled correctly after caffeine as opposed to 9.13 (S.E. 1.00) per cent in the placebo condition. After shallow encoding, 3.83 (S.E. 0.97) per cent of words were recalled correctly in the caffeine condition, and 5.98 (0.98) per cent were recalled correctly in the placebo condition. As expected, there was a highly significant main effect of

the level of processing, $F(1, 91) = 13.09$, $MSe = 25.75$, $p < 0.0001$, with 4.90 (S.E. 0.69) words recalled correctly after shallow processing and 7.54 (S.E. 7.00) recalled after deep processing. The main effect of caffeine also reached significance at the 5% level, $F(1, 91) = 5.05$, $MSe = 65.23$, $p < 0.05$, with 4.89 (S.E 0.83) per cent of words recalled correctly in the caffeine condition as opposed to 7.55 (S.E. 0.84) in the placebo condition.

Further investigation of the effects of caffeine on semantic memory and executive function

Reliable effects of caffeine have been found on measures of semantic memory and executive function, but it is unknown how these effects are produced. Using the present data, two possibilities can be explored. The first of these is that the caffeine effects on the two tasks are mediated by subjective alertness, such that caffeine effects on memory are secondary to changes in alertness. The second possibility is that both tasks measure a common cognitive construct such that corresponding measures of performance on both tasks will be highly correlated.

The association between memory performance and alertness

It has been suggested that the effects of caffeine on memory may be mediated to a large extent by the effect of caffeine on alertness. To test whether this was the case, a series of ANCOVAs were carried out using performance at baseline as a covariate to control for individual differences but using an additional covariate to control for alertness in the post-drink test session. As the effects of caffeine on alertness had only been found after the memory tests, it was considered that the appropriate covariate to employ was the change in alertness from the beginning to the end of the battery. The effect of the covariate change in alertness was found to be statistically significant for the number of trials attempted on the semantic memory task ($F[1, 91] = 8.65$, $MSe = 84.36$, $p < 0.005$) and for number of trials attempted ($F[1, 91] = 7.99$, $MSe = 44.96$, $p < 0.01$) and MRT for correct trials on the logical reasoning task ($F[1, 91] = 8.07$, $MSe = 358621.71$, $p < 0.01$). It was found, however, that after controlling for alertness and baseline performance, the profile of caffeine effects for both the semantic memory and logical reasoning tasks was unchanged.

For semantic memory there was a main effect of caffeine on number of trials attempted, ($F1, 91) = 7.49$, $MSe = 84.36$, $p < 0.01$, percentage of trials correct $F(1, 91) = 5.01$, $MSe = 8.42$, $p < 0.05$ and MRT for correct trials, $F(1, 91) = 18160.82$, $p < 0.05$. This reflected faster and more accurate performance in the caffeine condition. For the logical reasoning task there were main effects of caffeine for number of trials attempted, $F(1, 91) = 3.18$, $MSe = 44.96$, p

< 0.05 (one-tailed) and percentage of trials correct, $F(1, 91) = 4.11$, MSe = 18.64, $p < 0.05$. Again, this reflected faster and more accurate performance in the caffeine condition.

The independence of caffeine effects on semantic memory and logical reasoning tasks

If the effects of caffeine on the semantic memory task and the executive function task were found to be highly correlated, the possibility would exist that the effects were the result of a caffeine effect on a common cognitive mechanism(s) rather than independent effects on semantic memory and executive function. To test this hypothesis, Pearson's product-moment correlation coefficients were calculated between all parameters of semantic memory and logical reasoning performance for the group who were given caffeine. Change scores from baseline were used as the indices of performance to control for individual differences in performance. It was found that there were no significant correlations between any corresponding parameters of performance (e.g. number of trials attempted on the semantic task and number of trials attempted on the logical reasoning task). The only significant correlations between parameters of semantic memory and logical reasoning were for trials correct on the semantic memory task, the number of trials attempted on the logical reasoning task ($r = 0.308$, $df = 47$, $p < 0.05$) and the percentage of trials correct on the semantic memory task and MRT on the logical reasoning task ($r = -0.392$, $df = 47$, $p < 0.01$).

DISCUSSION

The primary objective of the present study was to replicate previous studies which have found the effects of caffeine on semantic memory and executive function. The other objective of the study was to investigate the phenomena of state-dependent learning and recall, as these have been studied extensively for other centrally acting drugs but only once to date in relation to caffeine.

In order to confirm that the methodology of the study was rigorous enough to produce caffeine effects, the study used subjective mood as a positive control task as this task is known to be sensitive to caffeine. On measures of subjective mood, it was found that there was the usual profile of caffeine effects. On day 1 of testing, the pre-memory test, there were trends toward improvements in self-rated alertness and sociability, and post-memory test, caffeine significantly improved self-rated alertness and sociability and significantly increased anxiety. These findings are compatible with the existing literature, which suggests that caffeine increases alertness[13] and, at high doses, such as 4mg/kg, increases anxiety.[19] The effects of caffeine on sociability are not as well documented, but Warburton[30] has reported

an increase in self-rated happiness following exposure to caffeine and Roache and Griffiths[31] have reported an association between caffeine and self-rated friendliness. Both factors are components of sociability, and the present results are taken to be fully consistent with the existing literature.

It was found that there were positive caffeine effects on the semantic memory task both on day one and using the repeated exposure fully between-subject design for day one and day two. Specifically, it was found that there was a significant main effect of caffeine on the speed of processing, as indicated by an increase in the number of trials correctly completed and a decrease in MRT for correct trials. This result is consistent with previous studies[11-15] that have found that caffeine increases the speed of processing. Importantly, however, it was also found here that, as Smith et al.[11] have described, there was also a significant improvement in the accuracy of retrieval from semantic memory. This finding is important as it suggests that the effects of caffeine on semantic memory are not mediated solely by processing speed. Furthermore, there was no apparent trade-off between speed and accuracy, as exposure to caffeine appears to have a concurrent positive effect on both parameters. The profile of caffeine effects on semantic memory is fully consistent with the effects described in previous studies, and the semantic memory task can be used as a positive control task in future caffeine studies.

There were also main effects of caffeine on the logical reasoning task on day one, and using the repeated exposure fully between subjects design showed caffeine to increase both the speed and accuracy of performance. This result is consistent with the literature, where four out of six studies have also described significant improvements in executive function performance after caffeine.[11-13, 30] Again, as well as increases in parameters of performance related to the speed of cognitive processing, there were also concurrent increases in the accuracy of performance, suggesting that the effects of caffeine on memory are not purely due to cognitive processing speed. At baseline, there were effects of syntactic difficulty on the percentage of statements correct and MRT for correct statements. Simple statements were found to be answered more accurately and more quickly than negative statements, and active statements were answered more accurately and more quickly than passive ones indicating that performance on this task was a function of the complexity of the memory load. This effect of memory load was present in the post-drink test session on day one but did not interact with caffeine. This suggests that the effects of caffeine on logical reasoning are independent of

memory load and that the increases in performance observed after caffeine do not result from increased performance on trials of a particular syntactic type. The profile of caffeine effects on the logical reasoning task has replicated the findings of several previous studies, and along with the semantic memory task, logical reasoning can be used as a positive control in future studies.

For the immediate recall task on day 1, there was no main effect of caffeine on the total words recalled, the number of correct words recalled or the number of intrusions. This result is consistent with previous findings, where the majority of studies have also reported that there are no effects of caffeine on recall.[11,13-15,18-23,30,32] The expected main effect of the level of processing was found with acoustic processing leading to significantly poorer recall than semantic processing, but there was no interaction with caffeine.

When recall of the encoded stimuli was attempted 24 hours later, acute ingestion of caffeine prior to retrieval led to a significant decrease in total words recalled and total words recalled correctly, suggesting that the largest effects of caffeine are at retrieval, not encoding. Previous studies have failed to make this differentiation between encoding and retrieval, and the few studies that have looked at delayed recall have usually asked participants to both encode and retrieve stimuli under the influence of caffeine. Using such a method, Terry and Phifer (1986) found a detrimental effect of caffeine on STM, but it is impossible to tell whether caffeine was affecting encoding, retrieval or both.

Apart from replicating some of the established effects of caffeine on human memory, one of the other major aims of the study was to establish whether there are any state-dependent effects associated with caffeine (i.e. state-dependent learning or state-dependent memory phenomena). The analysis failed to show any evidence of an effect of caffeine on either state-dependent learning for the semantic memory and logical reasoning tasks or state-dependent memory phenomena on the recall tasks. Regarding state-dependent memory, Eich (1980), in a review of the literature, states that the most centrally acting drug should, in theory, be capable of eliciting state-dependency at the correct dose but suggested that the phenomena occur most reliably when there is a main effect of the drug at encoding, storage or recall. In the case of caffeine, these main effects do not appear to be present, and it is surmised that the effects of caffeine at this dose are too subtle in comparison with other changes of state (e.g. those produced by alcohol) to produce state-dependent learning or state-dependent memory phenomena.

Analyses of the data also investigated the relationship between the effects of caffeine on memory and the effects of caffeine on mood and, specifically, the extent to which the effects of caffeine on semantic memory and executive function might reflect changes in alertness. A series of ANCOVAs were carried out with an alertness measure as an additional covariate. The analyses revealed that when alertness was controlled for, semantic memory and logical reasoning still showed the same profile of caffeine effects that had been observed without the additional covariate (though for both tasks, the number of trials attempted was now marginally less significant). The present data do not support the suggestion that subjective alertness contributes greatly to the effects of caffeine on semantic memory or executive function.

The final part of the analysis attempted to ascertain whether there was a relationship between the effects of caffeine on semantic memory and logical reasoning tasks or whether the effects on the tasks were mediated by a common mechanism(s). It was found that there was little evidence of a strong relationship between the effects of caffeine on the two tasks as no statistically significant correlations were found between corresponding measures of speed or accuracy. The only statistically significant correlations were between the percentage of trials correct on the semantic memory task and measures of speed of performance on the logical reasoning task. As these correlations were between dissimilar parameters, they do not provide any evidence that a common cognitive mechanism is affected by caffeine.

CONCLUSIONS

In summary, the study has successfully replicated known caffeine effects on semantic memory and executive function, including improvements in accuracy on both tasks, which suggests that caffeine does not simply increase cognitive processing speed. The study failed to find any evidence of state-dependent effects, and no effects of caffeine were found on immediate free recall for acoustically or semantically processed stimuli through acute consumption of caffeine significantly decreased recall of stimuli encoded 24 hours earlier. No evidence was found that caffeine effects interact with the parameter of subjective alertness. Importantly it has been shown that caffeine effects on memory are not mediated solely through subjective alertness and that when alertness is controlled for, the effects of caffeine on speed and accuracy of semantic memory performance and executive function are still statistically significant. It has also been shown that there is no evidence that caffeine effects

on semantic memory and executive function are highly related and, therefore, possibly mediated by a common mechanism.

ACKNOWLEDGEMENT

The research described here was supported by an ESRC PhD studentship.

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