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EFFECTS OF CAFFEINE AND CAFFEINE WITHDRAWAL ON SUSTAINED ATTENTION, ENCODING OF NEW INFORMATION AND SEMANTIC MEMORY

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ABSTRACT

Background: The behavioural effects of caffeine are well established, but there has been a debate about the underlying mechanisms. It has been suggested that caffeine withdrawal may impair cognitive performance and that the beneficial effects of caffeine might represent the removal of the deleterious effects of caffeine deprivation rather than an actual net benefit due to caffeine use. This view was tested here using a washout methodology. **Method:** The study had three parts. The first examined the effects of two doses of caffeine (1.5 mg/Kg and 3mg/Kg) and placebo on sustained attention, encoding new information and retrieval from semantic memory. The participants were 144 university students. Following this, half of the participants were given caffeinated coffee and tea to drink for a week, whereas the others were given decaffeinated products. Performance was tested each day. At the end of the week, the acute caffeine challenge was repeated. **Results:** The results showed that in part one of the study, administration of caffeine improved performance. In contrast, there was no evidence of impairment when participants were deprived of caffeine. It has been argued that participants should be deprived of caffeine for about a week to remove the adverse effects of deprivation before studies of the acute effects of caffeine are carried out. This was done here, and the beneficial effects of caffeine were still observed after a week of caffeine deprivation. **Conclusions:** These results support the view that caffeine consumption benefits performance, whereas caffeine withdrawal produces no impairments. Indeed, the effects of acute caffeine ingestion did not reflect the reversal of the effects of caffeine withdrawal.

KEYWORDS: Caffeine; Caffeine withdrawal; Sustained attention; Semantic memory; Encoding of new information.

INTRODUCTION

The extensive research on the behavioural effects of caffeine has been reviewed several times.[1-7] Tasks sensitive to caffeine's effects have been identified, and these involve sustained attention and the encoding of new information.[8] Recent research[9-11] has also shown that information retrieval from semantic memory is faster and more accurate after caffeine. All of these tasks are influenced by other factors that increase alertness, and explanations of the effects often relate to adenosine[12,13] and subsequent effects on neurotransmitters such as noradrenaline[14] and acetylcholine.[15]

An alternative explanation is based on the view that caffeine withdrawal impairs performance and that these adverse effects are removed by subsequent ingestion of caffeine.[16-25] James[16] questioned whether the superior performance in caffeine conditions is due to actual enhancement or merely reflects performance impaired in caffeine-free conditions. Smith[26,27] argued that the evidence for the adverse effects of caffeine withdrawal is not strong, and this has been confirmed in a study of caffeine withdrawal and headaches[28] and an alternative view was proposed.[29] Similarly, Rogers et al.[17] concluded that "... in a review of recent studies, we find no unequivocal evidence of impaired psychomotor performance associated with caffeine withdrawal".

Another problem with the caffeine withdrawal explanation is that it cannot account for effects in naive users or animals. Indeed, Rogers et al.[17] have shown that the beneficial effects of caffeine on performance can be demonstrated in non-users and users who had caffeine withdrawn for varying periods (1.5 hr, 13 h and seven days). More recently, four lines of research have addressed the reversal of the withdrawal view and shown it to be untenable. The first has shown that the effects of caffeine can be demonstrated soon after (within 3 hours) withdrawal starts.[30] Similarly, research has given caffeine within the experimental setting and then shown that subsequent doses produce changes in performance.[31-33] Another paradigm has involved comparing groups with different levels of regular consumption (e.g. consumers v non-consumers of caffeinated drinks).[34-36] The results from these studies have shown that caffeine changes the performance of non-consumers, who, by definition, cannot be caffeine-deprived. The last approach used a washout technique where one group is given caffeinated beverages for a week and another decaffeinated. Such studies show that caffeine

withdrawal did not affect performance, and acute effects of caffeinated ingestion can be demonstrated in those who have undergone a seven-day washout.[37]

The most important aspect of the caffeine withdrawal approach is not the emphasis on withdrawal per se but the identification of the need to use a range of experimental paradigms to examine the effects of caffeine and its withdrawal.[25] One of the problems in comparing studies of caffeine and caffeine withdrawal is that they have used different paradigms, had different designs and varied in experimental power. The present study aimed to test the withdrawal hypothesis using one of the recommended methods. The first part of the research involved a standard caffeine challenge using tests known to be sensitive to the effects of caffeine. Dose-response was also examined to get a better interpretation of causality. Those arguing for withdrawal reversal would suggest that any positive effects of caffeine reflect the reversal of withdrawal's adverse effects in the caffeine-free condition. Half the participants in the present study continued using caffeinated products for a week to directly examine withdrawal effects, whereas the others were provided with caffeine-free drinks. If there are adverse effects of caffeine withdrawal, these should appear at this study stage. It has been suggested that the adverse effects of caffeine withdrawal should have gone after seven days. If a caffeine challenge is repeated with these participants given decaffeinated products for a week, there should now be no beneficial effects of caffeine because the adverse effects of caffeine withdrawal have gone. An alternative view is that caffeine will improve performance following short-term and seven days of withdrawal and that it will be difficult to demonstrate the effects of caffeine withdrawal during the washout period.

The following experiment tested these views and had the following methodological features. First, two doses of caffeine were compared with placebo in a double-blind study. The fact that larger doses of caffeine produce more significant effects than smaller doses also leads to problems for the withdrawal explanation. If a person is given a dose equivalent to their regular intake, they have not had caffeine withdrawn. However, the literature shows that additional caffeine may lead to beneficial effects. Secondly, tests known to be sensitive to the effects of caffeine were used. Finally, caffeine abstinence is difficult to assess unless saliva samples are taken, and that was done here.

METHOD

The present research was approved by the School of Psychology Ethics Committee, and was carried out with the informed consent of the participants. The experiment consisted of three

parts. The effects of a single caffeine challenge were examined in the first and third parts. Participants were allocated to one of the following conditions: placebo, 1.5 mg/kg caffeine, and 3 mg/kg caffeine. They remained in the same condition for parts 1 and 3 of the study. Following the first challenge study, they were assigned to the caffeine consumption condition or the decaffeinated condition. All participants were supplied with coffee and tea bags to last them a week. For this week, they were required to only consume coffee and tea made from these supplies and abstain from consuming any other caffeinated products. Both the acute caffeine challenges and the withdrawal part of the study were double-blind.

Participants

One hundred and forty-four volunteers (72 female; 72 male; mean age = 21.3 years) were recruited from the Health Psychology Research Unit Panel. There were equal numbers of males and females in each condition. Similarly, the conditions did not differ in terms of age, weight, regular caffeine consumption, smoking, alcohol consumption, use of milk and sugar in drinks, and the personality dimensions of trait anxiety, impulsivity, sociability, morningness and obsessionality.

Those who drank coffee or tea less frequently than once a week were not eligible for the study. Similarly, those who smoked more than five cigarettes in the daytime were excluded. They were paid £50 for participating in the study.

Procedure

All participants were weighed and familiarised with the computerised performance tests in one session prior to the test day. They then completed a caffeine diary for the 24 hours prior to the start of the experiment. The evening before their test day, participants were required to limit their alcohol consumption to a maximum of four units. On the test day, they abstained from drinking any alcohol, doing any strenuous physical exercise and drinking caffeinated beverages for two hours before the test session.

Saliva samples were taken to determine caffeine levels at baseline and over the test session. During the test session, they completed a questionnaire about their previous night's sleep, food consumed and alcohol consumption.

Groups of participants started their tests at 8.00, 11.00, 14.00 or 18.00. Equal numbers of volunteers in the different caffeine conditions were tested at these times. They completed a

baseline session and then provided a saliva sample, followed by the consumption of a cup of coffee. One hour later, a second saliva sample was taken, and the next performance session started. At the end of the tests, another saliva sample was taken, and this part of the experiment then ended.

Nature of the drink

All drinks were made with one rounded teaspoon of decaffeinated coffee in a 150ml mug of boiling water. To this, either the placebo or caffeine solution was added in accordance with the condition code. The placebo solution consisted of preserved water, while the caffeine solutions contained 15% w/v caffeine (equivalent to 1.5mg/kg) or 30% w/v caffeine (equivalent to 3mg/kg) accordingly. Milk and sugar were added in accordance with their usual preference, and this was recorded.

Performance tasks

These tasks were selected because previous studies have shown that they are sensitive to the effects of caffeine.

Five choices serial reaction time task

Five boxes were displayed on the screen, and a light appeared in one of the boxes. The participant pressed the corresponding key, and the light then appeared in another box, and the volunteer was required to press the next key. This task lasted for 3 minutes. The number of correct trials was the primary outcome of this task.

Focused attention choice reaction time

Target letters were upper case A's and B's. Before presentation of the letters, three warning crosses were presented on the screen. Volunteers had to respond to the A or B presented in the centre of the screen and ignore distracters presented either side. The warning crosses were on the screen for 500 msec and were then followed by the letter. The central letter was either accompanied by nothing, asterisks either side, letters which were the same as the target or different letters. The targets and distracting letters were always A or B. The letter A was responded to with the fore-finger of the left hand, and the letter B with the fore-finger of the right hand. Participants were given ten practice trials which were then followed by three blocks consisting of sixty four trials. Each block contained equal numbers of near/far distracter conditions, A and B responses and equal numbers of the distracter conditions. The

nature of the previous trial was controlled. The speed of encoding new information (response time to targets which differed from the previous trial) was the primary outcome of this task.

Repeated digits detection task

Participants were shown three-digit numbers on the screen at the rate of 100 per minute. Each digit was normally different from the preceding one, but occasionally (8 times a minute), the same number was presented on successive trials. Volunteers had to detect these repetitions and respond as quickly as possible. The task lasted for 3 minutes. The percentage of targets detected was the primary outcome of this task.

Semantic processing task

This test measured 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. The primary outcome for this task was the number of sentences attempted.

Regular caffeine consumption phase

Following the challenge, study participants were given their supplies for the next week. During the course of the week, they kept a log of coffee and tea consumption. Saliva samples were also taken each day to assess whether they were complying with instructions. Performance was also assessed on these days, and the procedures were as in the previous part of the experiment.

Second acute caffeine challenge

After seven days of controlled consumption, the participants carried out a second acute challenge condition. The methods and procedures were identical to the first acute phase.

RESULTS

First acute condition

Analyses of covariance, with the baseline data as covariates and the post-drink data as dependents, were carried out. The between factors were caffeine dose, time of day, regular caffeine consumption (categorised as high or low on a median split, median = 195 mg) and gender. The encoding of new information in the focused attention task, five-choice task,

repeated digits task and semantic processing task all showed significant benefits following caffeine consumption.

These results are shown in Table 1. The five-choice and repeated digits tasks showed a clear dose-response effect, with the best performance occurring in those who were given 3 mg/kg caffeine. Comparable effects were seen in the 1.5 mg and 3 mg groups for the encoding of new information. In the semantic processing task, only the 3mg/kg caffeine group differed from the placebo. These results demonstrate quite clearly that caffeine consumption is related to performance, often in a dose-response fashion. None of these effects was modified by the regular level of caffeine usage, time of day or personality. In other words, the present methodology has demonstrated significant and robust effects of caffeine. If these results reflect the removal of the negative effects of caffeine withdrawal, then such effects should be apparent when subjects consume caffeine-free beverages over a longer time period. This was examined in the next part of the study.

Table 1: Acute effects of different doses of caffeine (Scores are the adjusted means from the analyses of covariance).

	0 mg	1.5 mg/kg	3.0mg/kg	p value
Repeated digits task hits (%)	57.0	62.5	67.5	p <0.05
Number correct five-choice serial response task	439.6	445.4	453.2	p <-0.05
Focused attention reaction time to different stimuli (msec)	395	384	382	p <0.05
Semantic processing task number completed	131.6	131.9	135.4	p < 0.05

Weekly consumption of caffeinated and decaffeinated drinks

The results from the controlled consumption part of the study are shown in Table 2. Analyses of covariance revealed no effect of caffeine withdrawal on the performance tasks, which were sensitive to the acute effects of the caffeine challenge. It is possible that these negative results reflected poor compliance by the subjects. However, analyses of the saliva levels of the decaffeinated group showed that the mean level was not significantly different from zero, whereas the caffeine group had levels which showed that caffeinated beverages had been consumed. Another possibility is caffeine withdrawal effects depend on other factors such as regular level of usage, time of day or personality. This suggestion seems unlikely, given the lack of interactions in the analyses.

Table 2: Effects of controlled consumption of caffeine (scores are the adjusted means from the analysis of covariance).

	Day 1 caff	Day 1 decaff	Day 2 caff	Day 2 decaff	Day 3 caff	Day 3 decaff	p-value
Repeated digits hits (%)	61.0	59.3	61.1	60.0	61.8	60.8	p >0.05
Five-choice serial response task number correct	454	453	462	460	466	469	p >0.05
Focused attention reaction time to different stimuli (msec)	364	367	366	363	362	366	p >0.05
Semantic processing task number completed	137.3	140.0	141.3	133.0	138.3	139.2	p >0.05

Acute effects of caffeine after seven days of caffeine withdrawal

These analyses examined the effects of caffeine on participants who had caffeine withdrawn for seven days. The descriptive statistics are shown in Table 3. Results from the five-choice and repeated digits tasks revealed an identical dose-response pattern to that seen in the first part of the study. Similarly, the effect of caffeine on alternations in the focused attention task and the semantic processing task were also significant. Acute effects of ingestion of caffeine were clearly present even after withdrawal, which argues against the withdrawal-reversal view. Indeed, rather than removing the effects of caffeine, withdrawal appeared to make the acute effects of caffeine slightly bigger.

Table 3: Acute effects of caffeine challenge in those who had caffeine withdrawn for a week (Scores are the adjusted means from the analysis of covariance).

	0 mg	1.5 mg/kg	3.0mg/kg	p value
Repeated digits task hits (%)	55.4	62.0	64.6	p <0.05
Number correct five-choice serial response task	469	501	512	p <-0.05
Focused attention reaction time to different stimuli (msec)	383	371	365	p <0.05
Semantic processing task number completed	145.3	149.8	150.2	p < 0.05

DISCUSSION

The results from this study confirm that the performance of cognitive tasks is improved following the consumption of caffeinated coffee. The improvement was usually in the form of dose-response, with 3 mg/kg caffeine being associated with the best performance. These results were apparent both before and after a one-week withdrawal period, which suggests

that the beneficial effects of caffeine cannot be accounted for by impairments in the caffeine-free condition. The view is further supported by the absence of negative effects during the period when caffeine was withdrawn. A direct test of the withdrawal-reversal explanation of the effects of caffeine on cognitive performance shows, therefore, that there is little support for this view. It should also be noted that in the initial part of the study, the participants were not allowed to consume caffeine for two hours before the start of the study, and the positive effects of caffeine at this time cannot be attributed to withdrawal reversal.

The present findings do not show that caffeine withdrawal effects do not occur at all but suggest that they are restricted to certain contexts. Indeed, Rogers et al.[17] argue that caffeine withdrawal influences mood but not performance. Smith has suggested that the effects of caffeine withdrawal on subjective reports do not necessarily reflect a pharmacological effect but may, at least in part, be due to expectancy effects. This issue needs to be examined in further studies, but it now appears that in moderate caffeine users, it is unlikely that caffeine withdrawal will produce impairments that show up in the objective measures that are sensitive to the acute effects of caffeine. The present results replicated the effects of caffeine on psychomotor performance and semantic processing. These sensitive tasks can now be used to clarify which of the many CNS mechanisms influenced by caffeine[38] underlie the present findings. Research should also continue to evaluate the practical benefits of caffeine consumption when operational efficiency and safety are endangered by reduced alertness.

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