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ORIGINAL INVESTIGATION

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Effects of caffeine on cognition and mood without caffeine abstinence

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Abstract The objective of this study was to evaluate the effects of low doses (75 mg and 150 mg) of caffeine on mood and cognition in healthy people, with minimal abstinence of 1 h from caffeine. Improvements were obtained in cognition for attention, problem solving and delayed recall, but not immediate recall or working memory, but performance in the placebo condition was close to the maximum, giving little margin for improvement. For mood, there were statistically significant increase in clearheadedness, happiness and calmness and decreases in tenseness. These mood and performance-enhancing effects of caffeine cannot be seen as representing an alleviation of deficits induced by caffeine abstinence, because there was only minimal deprivation from caffeine.

Key words Caffeine · Attention · Memory · Problem solving · Mood

Introduction

Caffeine users reported feelings of increased alertness and wakefulness and enhanced ability to work and concentrate (Goldstein and Kaizer 1969; Goldstein et al. 1969; Zwyghuizen-Doorenbos et al. 1990). These experiences of users have been confirmed in placebo-controlled laboratory studies. Caffeine decreases reaction time, (Lieberman et al. 1987; Clubley et al. 1979; Kerr et al. 1991), enhances cognition (Bättig et al. 1984; Bättig and Buzzi 1986; Smith et al. 1990; Smith et al. 1993a, b; Frewer and Lader 1991). More recently studies have shown that, in placebo-controlled laboratory studies, relatively low doses of caffeine enhance cognition after the participants have abstained for 12 h (Lieberman et al. 1987) and 16 h (e.g. Bättig et al. 1984; Bättig and Buzzi 1986). In addition, 200 mg caffeine produced faster and intensified stimulus encoding (Lorist et al. 1994).

However, these effects have not always been reported (Svensson et al. 1980). Consequently, it has been suggested that the behavioral effects of caffeine are capricious (Dews et al. 1984). In the same vein, James (1991) concluded that "Considering largely negative, or at best, equivocal nature of the evidence, it is disconcerting to observe how serious commentators continue to succumb to the myth of caffeine's enhancing behavioural effects." (p. 271).

In addition, interpretation of these performance-enhancing effects of caffeine has been suggested as representing alleviation of deficits induced by caffeine abstinence, rather than an absolute improvement in performance (James 1994). Rall (1990), writing in the most recent edition of Goodman and Gilman, comments: "Since the long term ingestion of caffeine can produce tolerance and evidence of physical dependence (Griffiths and Woodson 1988), the history of exposure to methylxanthines will influence the effect of a given dose. Hence enhanced alertness, energy and ability to concentrate could reflect alleviation of withdrawal symptoms in some instances" (p. 621).

The aim of our study was to examine whether low doses of caffeine could improve performance in users who were NOT deprived of caffeine. Our studies used a comprehensive set of test procedures which we had developed for studying the effects of drugs on human cognitive efficiency and mood.

Materials and methods

Participants

Eighteen healthy, non-smoking, male volunteers were used, aged between 18–30 years old and all were regular coffee drinkers, more

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than three cups per day. They gave an end-tidal alveolar carbon monoxide sample to confirm smoking status. They normally had coffee soon after awakening. Those who had participated in a drug study within the previous 3 months were excluded, as were all those who had received a regular course of CNS medication during the 4 weeks prior to the start of the study. Volunteers with a history of alcohol or drug abuse and anyone whose weight was less than 60 kg or greater than 80 kg (142–175 lb) were also excluded. The study was carried out according to the Declaration of Helsinki on Human Rights; all participants gave written informed consent to participate.

Dose manipulation

The study was a randomised, double-blind, two-way cross-over study, comparing oral doses of 75 mg caffeine and 150 mg caffeine with placebo, in the range of Lieberman and his team (Lieberman et al. 1987) and corresponding to the amount of caffeine obtained from one and two average cups of coffee.

In order to ensure that the participants were only minimally deprived of caffeine, they were given a dose of caffeine mixed with decaffeinated instant coffee to give a total dose of 75 mg caffeine. This dose was drunk 1 h prior to coming to the laboratory. This was explained to the volunteers as a method of ensuring that everyone was in exactly the same state before testing.

At the laboratory, the caffeine was administered in the form of anhydrous caffeine tablets, crushed and dissolved in drip-brewed, decaffeinated coffee. Testing was begun 45 min after ingestion, just prior to the peak plasma level of caffeine at 1 h.

The volunteers received the three doses on 3 separate weeks. The interval between treatment periods was 1 week.

Psychological testing

Computers in individual experimental rooms presented each of the four tests described below and collected the data generated by each volunteer. Each testing session lasted approximately 45 min.

The attentional testing was carried using Rapid Visual Information Processing, in which monitored digits were presented sequentially on video screens at a rate of 100 per minute. They were instructed to detect and respond to targets of three consecutive odd or even digits as quickly as possible. Independent measures were made of both the speed and accuracy of decision making. This test has proven sensitivity to improvements, as shown by studies with the cholinergic agonist, nicotine (Wesnes and Warburton 1983, 1984a, b; Parrott and Winder 1989).

The verbal memory testing used parallel lists of 20 words with each list matched for frequency (Kucera and Francis 1967), concreteness (Colorado Concreteness Norms 1973) and number of syllables (Battig and Montague 1969). Participants were presented with the word list at a rate of one word every 2 s, over headphones. At the end of each list, each volunteer completed a written recall of as many items as they could remember. Two lists were completed in each experimental trial period, and delayed recall was also monitored.

The non-verbal working memory testing was based on a subset of the CANTAB computerised non-verbal test battery (Morris et al. 1987), which had been modified for use with young volunteers. Touch sensitive screens were used, with participants indicating their selection by touching the appropriate item or position on the screen. The tests were spatial recognition and a test of visuo-spatial memory.

For the spatial recognition task, the program presented a five-item sequence of boxes, each in a different location on the screen. This was followed by a five-trial recognition phase in which volunteers selected the correctly located box from a choice of two locations. There was a total of five novel sequences in this task.

In the test of visuo-spatial memory, participants were asked to remember of locations of abstract visual stimuli hidden in a set of eight boxes. Each box opened in turn to reveal the shape inside. The shapes then appeared in turn in the centre of the screen and participants indicated the box in which each appeared. The sequence of presentation in the test was repeated until the subject remembered the correct location of all eight items on a single trial. All test items were in the same colour in order to assess memory for location of each shape in the absence of colour cues.

Problem solving skills were examined using the Baddeley Semantic Verification Task (Baddeley 1968). In this task, a sentence describing the order of two letters (e.g. A follows B) is presented on the screen together with the two letters (e.g. AB or BA). The volunteers were required to evaluate the veracity of the sentence as a description of the order of the letters and to indicate their decision by pressing the appropriate response key (YES for correct order, NO for incorrect). "YES" and "NO" responses and reaction times to make those responses were recorded for each sentence. The response to the sentence, or an interval of 10 s, initiated the presentation of the next problem in the series. There were 64 sentences involving four different grammatical constructions; four different letter pairs were randomly used in the test sessions.

Mood assessment was made at the beginning of each test period to evaluate effective changes (attention, happiness and calmness) in the volunteers, using Bond-Lader Visual Analogue Scales (Bond and Lader 1974). Research has shown that people can precisely assess their mood state and the strength of their subjective experience on a selected dimension (Bond and Lader 1974; Warburton 1989; Warburton et al. 1989).

Adverse events

We did not anticipate any adverse effects with our procedures, but adverse events occurring during the study period were recorded. All volunteers were obliged to notify the investigator if they suffered any adverse event. In addition, enquiries made as to whether the volunteer had experienced any adverse event was limited to a general question, e.g. "Have you felt unusual in any way, since you took the drink?"

Procedures

Prior to the start of the study, volunteers were trained on the experimental tasks. This training familiarised them with the experimental procedures and minimised the possibility that practice effects will interfere with the assessment of the effects of caffeine.

Participants came to the laboratory at 9 a.m., having fasted and abstained from drinking alcohol for 24 h prior to starting each treatment period, including the baseline testing session. The use of other "substances" was prohibited for 3 days prior to the study. In addition, they were instructed not to vary their alcohol and caffeine coffee consumption during the "substance" abstinence days. The volunteers were allowed to use caffeine containing products until bedtime before testing. A urine sample was obtained at the laboratory to ensure compliance with the abstinence restrictions.

Volunteers were tested on Friday to avoid the "week-end effect" of disrupted sleeping patterns. Each testing session began at 45 min after ingestion of caffeine in the laboratory, in order to be certain of testing within the maximum peak plasma levels of caffeine. In each case, parallel unrepeated forms of the tasks were used. The mood test was given at the beginning and at the end of the session, i.e. at 45 min and 90 min after ingesting the caffeine.

Results

The results were analyzed using the Analysis of Variance and General Linear Models procedures of the SAS statistics package.

Attention

An analysis of the data revealed improvements in rapid visual information processing. For correct detections in the attentional test, the overall analysis of variance analysis showed a significant dose effect of caffeine improving performance [$F(2,233) = 4.86$, $P < 0.01$], with a significant interaction between caffeine and time on the test, with more detections with time on the task relative to placebo, and the effect was dose related [$F(18,233) = 2.16$, $P < 0.01$]. For reaction times on the same test, there was a significant reduction [$F(2,233) = 3.51$, $P < 0.05$] by caffeine and a significant interaction between caffeine and time on the test, with faster responses with time on the task relative to placebo; the effect was dose related [$F(18,233) = 1.78$, $P < 0.05$].

Verbal memory

There was no effect of caffeine on the number of words correctly recalled on the immediate recall test [$F(2,34) = 2.14$, $P > 0.05$]. There was a significant dose effect on delayed recall, with more words remembered with caffeine relative to placebo and the effect was dose related [$F(2,34) = 5.99$, $P < 0.01$].

Non-verbal working memory

There was no evidence of improved working memory with the spatial recognition task [$F(2,34) = 2.44$, $P > 0.1$] or the visuo-spatial memory [$F(2,34) = 2.89$, $P > 0.05$], but performance in the placebo condition was close to the maximum in both cases.

Problem solving

The semantic verification task showed a significant improvement in the number of correct verifications [$F(2,34) = 5.23$, $P < 0.01$], but no effect on reaction times [$F(2,34) = 2.41$, $P > 0.1$].

Mood

On the Mood Scales, there were statistically significant increases on the Happiness scales: friendliness [$F(2,34) = 3.68$, $P < 0.05$], contentedness [$F(2,34) = 3.52$, $P < 0.05$] and happiness [$F(2,34) = 4.59$, $P < 0.025$] and also the subjects were calmer [$F(2,34) = 5.36$, $P < 0.01$] and less tense [$F(2,34) = 4.43$, $P < 0.025$]. They also felt more clearheaded [$F(2,34) = 6.43$, $P < 0.005$].

Adverse effects

None of the participants reported any adverse effects.

Discussion

The objective of our study was to evaluate the effects of low doses of caffeine on cognition and mood. The studies were performed without caffeine abstinence, in order to examine the additional question of caffeine tolerance and withdrawal relief.

First, the analysis of the data revealed improvements in cognition on the attentional test, both for correct detections and reaction times. There was an absolute improvement of performance and a prevention of the vigilance decrement. Second, there was improved problem solving on the semantic verification task. Third, there was an improvement in delayed recall, but not immediate recall. Fourth, there was no evidence of improved working memory with the spatial recognition task or the visuo-spatial memory task, but performance in the placebo condition was close to the maximum in both cases giving little margin for improvement. Fifth, there were statistically significant increases in clearheadedness, happiness and calmness and decreases in tenseness.

The improved performance on attentional performance with these doses is consistent with the findings of Lieberman and his co-workers (Lieberman et al. 1987), who found that doses as little as 32 mg caffeine produced enhanced auditory vigilance and decreased visual reaction time. Our doses were somewhat higher at 75 mg caffeine and 150 mg caffeine plus the residual amount of caffeine from ingesting 75 mg caffeine 1 h earlier. Clubley et al. (1979) found improvements in attention with 75 mg caffeine and Bättig and his co-workers (Bättig et al. 1984; Bättig and Buzzi 1986) obtained attentional improvements with 150 mg caffeine and 450 mg caffeine, as did Swift and Tiplady (1988) with 150 mg caffeine on choice reaction time. In addition, 200 mg caffeine produced increased perceptual sensitivity and arousal (Lorist et al. 1994).

Our maximum dose was about half the 3 mg caffeine per kg (or 225 mg for a 75 kg person) used by Smith and colleagues to improve attention (Smith et al. 1990, 1993a, b). In addition, Stroop performance, a perceptual intrusion measure of attention, was improved by 250 mg caffeine (Hasenfratz and Bättig 1992) and attentional improvements were found

with 450 mg caffeine (Bättig et al. 1984; Bättig and Buzzi 1986).

From these data, it is clear that attention can be improved with the caffeine equivalent of one or two cups of coffee, two to four cups of tea and three to six cola drinks and the larger doses are not required for improvement. The magnitude of the improvements was comparable to those produced by nicotine (Wesnes and Warburton 1984a) and cigarette smoking (Wesnes and Warburton 1983, 1984b). For correct detections, they were 13.1% for 75 mg caffeine and 16.5% for 150 mg caffeine and the percent reductions in reaction time were 2.3% (75 mg) and 6.7% (150 mg).

It has been argued in a review of the effects of "stimulant" drugs and vigilance that there must be several mechanisms underlying performance changes with nicotine and caffeine, since nicotine acts on cholinergic pathways while caffeine blocks adenosine receptors (Koelega 1993). Since that review, it has emerged that mesopontine cholinergic neurons are under the inhibitory control of endogenous adenosine (Rainnie et al. 1994). As caffeine blocks the adenosine receptors, it would release the cholinergic neurons from inhibitory control and so increase electrocortical arousal – the same effect as nicotine (Warburton and Rusted, 1993). Thus, there is no incompatibility between the qualitative similarity in effects of caffeine and nicotine or, indeed, the quantitative equivalence which has been found in this study and those with nicotine (Wesnes and Warburton 1983, 1984a, b).

There were improvements in delayed recall on the verbal memory task and no effect on immediate verbal memory, spatial recognition and visuo-spatial working memory. These findings are not in accord with the finding that as little as 100 mg caffeine impairs short term memory (Terry and Anthony 1986), nor the general model of caffeine's effects on cognition which argues that caffeine facilitates performance of tasks with low memory load, i.e. attentional tasks and disrupts performance on tasks with high memory load, such as word list recall (Humphreys and Revelle 1984).

An important aspect of our study was the fact that participants had been minimally deprived of caffeine, receiving 75 mg caffeine 1 h prior or taking the experimental dose of 75 mg or 150 mg or placebo. A similar study by Smith and his colleagues (Smith et al. 1994) showed improved psychomotor performance after only 1 h deprivation from caffeine. These are supported by the study of Jarvis (1993) which examined the relation between habitual tea and coffee consumption and cognitive performance using data from the Health and Lifestyle Survey (Cox et al. 1987). Jarvis (1993) found that there was a dose-related improvement in cognitive performance as a function of daily caffeine consumption.

These findings and ours suggest that tolerance to the performance-enhancing effects of caffeine, if it occurs at all, is incomplete and contradicts the claim of James (1994) that caffeine only produces improvements because it is reversing the effects of caffeine withdrawal.

Mood

The effects of a drug on mood state depend on the questions which are asked of the participants and whether the scales allow for positive and negative effects. In our study, we found increases using visual analogue scales representing happiness, calmness and alertness (Bond and Lader 1974) both doses of 75 mg caffeine and 150 mg caffeine given 1 h after a dose of 75 mg caffeine. These results are consistent with several studies which have used similar doses, but with 10–12 h of caffeine deprivation.

With equivalent doses and using a visual analogue scale, no mood changes were found by Lieberman and his co-workers (Lieberman et al. 1987), but Swift and Tiplady (1988) found mood improvement in young people with a dose of 200 mg caffeine, 50 mg larger than our highest dose. Of particular interest, the participants in the latter study were more alert and calmer with caffeine ingestion than they were in our study. Increased alertness is commonly reported (Goldstein and Kaizer 1969; Goldstein et al. 1969; Zwyghuizen-Doorenbos et al. 1990) in similar studies.

Another scale which measures subjective effects is an adjective check list, such as the Profile of Mood States (McNair et al. 1971). Using the Profile of Mood States, Roache and Griffiths (1987) found doses of caffeine ranging from 200 to 600 mg made their volunteers feel friendlier, more vigourous and less fatigued and more aroused, but also angrier. Their 200 mg dose of caffeine would have produced plasma levels which would be similar to those of our participants. Increased alertness was reported by Griffiths (Silverman et al. 1992) with doses between 18 mg and 100 mg caffeine in five out of eight volunteers, but greater anxiety/nervousness in three out of eight participants with similar doses to ours.

It has been found that the liking for coffee could be predicted from the production of a feeling of well-being, its calming and relaxing effects and its energising effects (Cines and Rozin 1982). Thus, it seems that the pleasures of caffeinated beverages are derived in part from their mild mood enhancing effects. Our study shows that the people need not abstain prior to use for the mood enhancing effects to be seen.

In summary, this study has shown that performance and mood effects can be obtained with doses as low as 75 mg and 150 mg when the participants had only been minimally deprived of caffeine and had received 75 mg caffeine 1 h before the laboratory testing. Thus, the mood and performance-enhancing effects of caffeine cannot be seen as representing alleviation of deficits induced by caffeine abstinence, but rather as absolute improvements.

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