Pharmacology Biochemistry and Behavior, Vol. 58, No. 1, pp. 203–208, 1997

0091-3057/97 $17.00 + .00

ELSEVIER

PII S0091-3057(97)00007-5

Effects of Brief Caffeinated-Beverage Deprivation on Mood, Symptoms, and Psychomotor Performance

JAMES D. LANE

Department of Psychiatry and Behavioral Science, Duke University Medical Center
Durham, NC 27710

Received 11 December 1995; Accepted 21 October 1996

LANE, J. D. *Effects of brief caffeinated-beverage deprivation on mood, symptoms, and psychomotor performance.* PHARMACOL BIOCHEM BEHAV **58**(1) 203–208, 1997.—The effects of short-term deprivation of caffeinated beverages on mood, withdrawal symptoms, and psychomotor performance were studied in habitual coffee drinkers. Twenty-four male and female coffee drinkers were tested at midday (1130–1330 h) under two conditions. On one day they consumed caffeinated beverages ad lib prior to testing, and on the other they remained caffeine abstinent. The order of treatments was counterbalanced. Mood and withdrawal symptom reports were collected by questionnaires. Psychomotor performance was tested with a computerized test battery. Caffeinated-beverage deprivation was associated with decreased vigor and increased fatigue and with symptoms including headache. No changes in psychomotor performance were observed. Even short periods of caffeinated-beverage deprivation, equivalent in length to missing regular morning coffee, can produce noticeable unpleasant caffeine-withdrawal symptoms by the middle of the day. These symptoms may be a common side effect of habitual caffeinated beverage consumption. © 1997 Elsevier Science Inc.

Caffeine Drug withdrawal Affect Cognitive performance Blood pressure

CAFFEINE is one of the most commonly used drugs, but it is not without side effects. Perhaps the most frequent is the pattern of physiological withdrawal symptoms that occur when habitual consumers abruptly stop. The characteristics and time course of the withdrawal syndrome appear to be consistent [reviewed in (9)] and are characterized by headache and arousal deficits that develop in a day or two and last up to a week with continued abstinence. The syndrome occurs even in people who consume as little as 100 mg of caffeine daily, equivalent to a single cup of coffee (8). One recent study of caffeine withdrawal in low to moderate consumers (20) found that caffeine deprivation for 2 days produced increases in symptoms of depression and anxiety, decreases in vigor and friendliness, and increases in fatigue and confusion. Deprivation also elicited a variety of specific symptoms related to irritability, sleepiness and fatigue, difficulty with thinking and working, headache, and feeling generally unwell. These effects can be clinically important because the symptoms associated with caffeine withdrawal overlap with medical complaints commonly reported to physicians.

Most experimental investigations of caffeine withdrawal symptomatology have involved several days of caffeine deprivation [e.g., (2,10,20)]. Although long periods of caffeine deprivation provide the opportunity to observe the full range and intensity of symptoms as they develop and resolve over time, such extended deprivation is relatively uncommon under normal circumstances, except for the rare individuals who attempt to quit caffeine consumption "cold turkey." Shorter periods of deprivation, for example, when a regular coffee drinker misses his or her normal morning coffee, would be much more common in everyday life. Studies suggest that these short deprivation periods too can lead to clinically significant withdrawal symptoms, such as headache and fatigue (2,7,16,21).

In an earlier study of caffeine's effects on neuroendocrine stress reactivity in the work environment (13), I assessed mood and withdrawal symptoms in people who were deprived of caffeine overnight and then received either 300 mg of caffeine or placebo at the start of the workday. Participants performed their normal work activities for 4 h and then rated their experience of the morning. When given placebo, partici-

Requests for reprints should be addressed to James D. Lane, Department of Psychiatry and Behavioral Sciences, Box 3830, Duke University Medical Center, Durham, NC 27710. E-mail: jdlane@acpub.duke.edu

pants reported higher levels of sleepiness, lethargy, and headache and a reduced desire to socialize. They also reported casually that it was much harder to work and to pay attention to what they were doing. Simply being deprived of normal morning coffee appeared to have clinically significant effects on these regular coffee drinkers, even after a few hours of deprivation.

The current study was designed to pursue this observation and to investigate the effects of such short-term caffeine deprivation on withdrawal symptoms and psychomotor performance. I sought to explore how regular coffee drinkers would feel during a normal workday morning if deprived of their regular morning coffee and whether such deprivation produced cognitive performance deficits that could affect their work. Regular coffee drinkers were tested at midday after mornings when they either consumed coffee and other caffeinated drinks ad lib or abstained completely from caffeine. Self-report questionnaires assessed mood and caffeine withdrawal symptoms, and a battery of computerized psychomotor tasks assessed psychomotor performance. Based on earlier observations, it was expected that even this brief period of deprivation would be associated with detectable withdrawal symptoms and performance decrements.

METHODS

Participants

Ten male and 14 female volunteers participated in the study, which was approved by the Duke University Medical Center Institutional Review Board for protection of human subjects. All were healthy nonsmokers recruited from the Duke University community who reported during telephone screening that they drank two to five cups of coffee daily, or consumed the equivalent amount of caffeine in a combination of coffee, tea, and soft drinks. Mean age was 32 years (SD = 8, range = 22–49 years). Each person's daily caffeine intake was estimated from self-reported beverage consumption by conversion with standard values for the caffeine content of beverages (11). Mean estimated daily caffeine intake from all beverage sources was estimated to be 547 mg (SD = 275, range = 127–1,245 mg). At the completion of the study, each participant was paid for taking part.

Materials

Mood and symptoms. Subjective mood was assessed using the Profile of Mood States (POMS; EdITS, San Diego, CA, USA), which contains 65 adjective rating items (4-point scale) that describe feelings (e.g., friendly, tense, grouchy, etc.). Standard scales measured six general moods: Tension–Anxiety, Depression–Dejection, Anger–Hostility, Vigor–Activity, Fatigue–Inertia, and Confusion–Bewilderment. This questionnaire has adequate internal consistency and reliability and has been sensitive to the mood effects of a variety of drugs (15). Moreover, the POMS detected mood changes during 2 days of caffeine deprivation in a study by Silverman and colleagues (20). Caffeine withdrawal symptoms were assessed with an inventory similar to that used earlier by Griffiths and colleagues (8,20). The inventory contains 32 items in which specific physical, mental, and affective symptoms of caffeine withdrawal are rated on a 0 to 3 scale.

Psychomotor performance. Psychomotor performance was assessed using a computerized battery of five brief tests selected from the Delta Human Performance Measurement System (Essex Corp., Columbia, MD, USA) presented on a personal computer (386SX). Stimuli for each task were presented on a color monitor and responses were made using the computer keyboard. Specific tests were selected to assess a variety of psychomotor performance functions, including motor response speed, response selection speed, short-term memory, symbol manipulation, and complex reasoning. All tests had a fixed duration and, with the exception of reaction time, performance was scored as the number of correct responses. Tasks were presented in the following fixed order, with instructions to perform each task as quickly and accurately as possible. *Tapping* (20 s): Participants pressed the S and D keys alternately with the index and middle fingers of the dominant hand as quickly as possible. This was a test of simple motor speed. *Continuous recall, numbers* (120 s): Pairs of single-digit numbers were presented on the color monitor, one number above the other and separated by a line. The subject determined whether the top number of each pair was the same as the bottom number of the previous pair and responded by pressing the S (same) or D (different) key on the keyboard. The keypress triggered the immediate presentation of the next pair of numbers, and the determination and response were repeated until the task ended. This task assessed the ability to encode and store information in working memory. *Choice reaction time* (120 s): The monitor displayed three outlined boxes with corresponding numbers underneath. On each trial one box was filled, and the participant pressed the corresponding number on the numeric keypad. The intertrial interval was random, between 1 and 5 s. Feedback was provided for incorrect responses, and the score was the average response time for all trials. This choice reaction time task assessed response selection and motor speeds. *Code substitution* (120 s): This test was based on that developed by Wechsler (23). Nine characters were displayed in a row across the top of the monitor, with the numbers 1 through 9 beneath them in parentheses. Beneath this display were two rows of 10 characters with empty parentheses beneath them. The subject responded by pressing the digit associated with each character in order from left to right. As each row was completed, a new row appeared until the task ended. This task assessed associative memory, symbol manipulation, and response speeds. *Grammatical reasoning* (120 s): This test was a modification of that described by Baddeley (1). The monitor displayed a series of stimulus items, which were sentences of different structures that described the positional relationship between two accompanying letters (i.e., AB). The task combined active vs. passive wording, positive vs. negative wording, and the key words "follows" vs. "precedes" to form a variety of sentences (e.g., "A is not preceded by B"). Subjects determined whether each sentence correctly described the sequence of the two letters and responded by pressing the T (true) or F (false) key. Each response triggered immediate presentation of the next item. This task assessed complex logical reasoning.

Design and Procedures

Design. The study used a within-subject (crossover) design to compare two experimental conditions, ad lib caffeinated-beverage consumption and deprivation. Conditions were presented on two different days, with order counterbalanced across participants. Mood, symptoms, and performance were evaluated in both conditions as repeated measures.

Orientation session. Prior to testing, participants completed an orientation and training session. The experiment was explained in detail, and participants gave informed consent. They then completed background questionnaires and a brief

inventory of normal daily caffeinated-beverage consumption. The technician gave instructions for performance of the battery of psychomotor tests. He went through the battery once with the participant, explaining each test and answering questions. Then the participant practiced the tests, completing the entire battery five times. If the participant needed more practice to reach stable performance, an additional training session was scheduled. After training, the two test sessions were scheduled and the participant was instructed regarding the experimental conditions planned for each day.

Experimental days. Test sessions were scheduled between 1130 and 1330 h. Both sessions for a participant were scheduled at the same time of day within a period of less than 2 weeks. In the ad lib consumption condition, participants were instructed to consume coffee, tea, etc. as they normally would during the morning prior to testing at midday. Each received a preprinted diary card to record each beverage serving, including type of drink and approximate serving size. In the deprivation condition, participants were instructed to abstain from any caffeinated beverages prior to testing at midday. This deprivation state was intended to model the effects of missing normal morning caffeine, thus the total length of deprivation varied depending on when the person last consumed caffeine on the day prior to testing. Including the overnight period, deprivation could range from 12 to 28 h.

When participants arrived at midday for testing, they turned in their diary cards for the morning and provided oral confirmation of their compliance with the instructions for the day. They sat quietly for approximately 10 min while completing the POMS and caffeine withdrawal symptoms questionnaires. Participants were instructed to base their answers on how they had felt that morning up to arrival at the laboratory. Three measurements of seated blood pressure and heart rate were collected at 1–2-min intervals using an automated monitor (Dinamap Vital Signs Monitor; Critikon, Tampa, FL, USA). Then participants moved to an adjacent room to perform the battery of psychomotor tests. The entire session lasted approximately 30 min and ended with instructions for the second day of testing if necessary.

RESULTS

Diary records revealed that 8 of the 24 participants consumed no caffeinated beverages prior to testing on the ad lib consumption day. Although they had followed instructions to consume as much as they wanted, they were dropped from analysis because their data were irrelevant to the comparison of ad lib consumption vs. deprivation conditions. The remaining 16 included 5 males and 11 females. In these participants, average age was 34 years (SD = 9, range = 22–49 years), and self-reported daily caffeine consumption averaged 612 mg (SD = 291 mg, range = 152–1,245 mg). Estimated caffeine intake during the morning prior to testing on the ad lib day averaged 336 mg (SD = 214, range = 125–782 mg), equivalent to two or three 8-ounce cups of brewed coffee.

The ad lib and deprivation conditions were compared by paired *t*-test, using a two-tailed criterion of $\alpha \leqslant 0.05$ for declaring statistical significance. Statistically significant differences are summarized in Table 1, which includes calculated values for effect size [$d = \text{mean}_{diff}/SD_{diff}$; (4)] to facilitate comparisons among different variables.

During caffeinated-beverage deprivation, mean arterial blood pressure was lower (mean = −5.5 mmHg, SE = 1.9), with trends for lower systolic and diastolic blood pressures as well (mean = −4.0/−3.0 mmHg). Heart rate differences were not observed. Differences in mood were detected by scores on the POMS scales for Vigor–Activity, which were lower by a mean −8.1 points (SE = 2.0), and Fatigue–Inertia, which were higher by a mean 6.3 points (SE = 2.2). These differences represent about one-third of the total range of these POMS scales.

Caffeinated-beverage deprivation was also associated with the presence of a number of caffeine withdrawal symptoms (Table 1). Effects were generally apparent more for cognitive than for emotional or physical symptoms on this list. The largest deficits appeared for energy/active, desire to socialize/talkativeness, and ability to concentrate, and the greatest increases were observed in drowsy/sleepy, lethargy/fatigued/tired/sluggish, and yawning. Among the physical symptoms, deprivation was associated with increases in headache and flu-like feelings.

Caffeinated-beverage deprivation did not affect psychomotor task performance. Performance on the serial memory task was slightly worse in the deprivation condition, with a 6% decrease in the number of correct responses (mean = −5.2, SE = 2.4, $p < 0.05$). However, this effect was confounded by an interaction with treatment order, and the deficit was observed only in subjects who were deprived in their first test session. Because the interaction suggests that practice effects may have contributed to the difference between conditions, this effect must be viewed cautiously.

Potential differences between heavy and light consumers in the size of caffeine-withdrawal effects were explored by Pearson product-moment correlations. Difference scores contrasting the ad lib and deprived conditions were calculated to represent withdrawal effects for each of the mood, symptom, and performance variables and correlated with reported daily caffeine intake. Significant ($p < 0.05$) correlations were found for three relevant symptoms: urge to do task/work-related activities ($r = 0.76$), ability to concentrate ($r = 0.63$), and muzzy/foggy/not clear-headed ($r = -0.54$). For these three similar cognitive symptoms, heavier habitual daily consumption was associated with stronger short-term withdrawal effects.

DISCUSSION

Periods of experimental caffeinated-beverage deprivation equivalent to people skipping their normal morning coffee produced detectable symptoms of caffeine withdrawal at midday. These effects were observed both in the POMS measures of self-rated mood and in the appearance of specific symptoms that have been associated with caffeine withdrawal. The pattern of results is similar to that observed for longer periods of deprivation (9) and in my earlier ambulatory study (13).

The POMS factor for Vigor–Activity represents a mood of vigorousness, ebullience, and high energy associated with feeling cheerful, alert, active, and full of pep (15). The POMS factor for Fatigue–Inertia represents a mood of weariness, inertia, and low energy. The combination of reduced vigor and increased fatigue reported on the POMS was consistent with the pattern of reported withdrawal symptoms, which emphasized decreased levels of arousal associated with difficulty in concentrating. However, the shorter period of deprivation in our study was not associated with increases in anxiety or depression, as noted in longer periods of caffeine deprivation (20).

It is noteworthy that even this short period of deprivation produced significant ratings of headache and flu-like symptoms. On average, these differences may appear small in magnitude, but examination of the number of participants who experienced these particular symptoms suggests a different

TABLE 1

CARDIOVASCULAR, MOOD, SYMPTOM, AND PERFORMANCE EFFECTS OF SHORT-TERM CAFFEINE DEPRIVATION

Measurement	Ad Lib Consumption	Deprivation	Effect Size
Cardiovascular			
SBP (mmHg)	118.9	114.9	−0.44
DBP (mmHg)	71.2	67.3	−0.52
MAP (mmHg)	85.7	80.2*	−0.71
HR (bpm)	71.0	68.3	−0.28
Profile of Mood States			
Tension–Anxiety	7.5	7.6	0.01
Depression–Dejection	3.6	5.5	0.26
Anger–Hostility	3.6	6.0	0.32
Vigor–Activity	20.1	12.0*	−1.00
Fatigue–Inertia	4.1	10.4*	0.71
Confusion–Bewilderment	4.6	10.4	0.25
Caffeine withdrawal symptoms			
Irritable/gross/grumpy	0.3	0.7	0.41
Alert/attentive/observant	2.3	1.9	−0.28
Lightheaded/dizzy	0.1	0.4*	0.58
Upset stomach	0.3	0.4	0.18
Well-being	2.2	1.6*	−0.57
Blurred vision	0.1	0.1	0.15
Desire to socialize/talkativeness	1.9	1.1*	−1.08
Anxious/nervous	0.4	0.4	0.00
Urge to do task/work-related activities	2.1	1.4	−0.53
Drowsy/sleepy	0.5	1.7*	1.01
Ability to concentrate	2.3	1.7*	−0.83
Difficulties sleeping	0.4	0.7	0.33
Muscle pain or stiffness	0.3	0.4	0.00
Yawning	0.4	1.4*	0.93
Energy/active	2.3	1.3*	−1.17
Runny nose	0.1	0.3	0.36
Jittery/shaky	0.30	0.2	−0.15
Depressed	0.3	0.5	0.26
Lethargy/fatigued/tired/sluggish	0.5	1.6*	0.93
Muzzy/foggy/not clear headed	0.3	0.8*	0.58
Content/satisfied	2.2	1.7*	−0.68
Headache	0.1	0.7*	0.73
Flu-like feelings	0.0	0.3*	0.65
Sweating	0.3	0.4	0.16
Self-confidence	2.4	2.2	−0.37
Limb tremor	0.3	0.1	−0.25
Heavy feelings in arms and legs	0.2	0.8*	0.58
Muscle cramps	0.1	0.1	−0.25
Need to pass water frequently	0.7	0.6	−0.13
Loss of sex drive	0.1	0.3	0.34
Hot or cold spells	0.2	0.3	0.20
Heart pounding	0.3	0.3	0.00
Psychomotor tasks			
Tapping	158.8	157.2	−0.13
Serial memory	83.3	78.1	−0.54
Choice reaction time	449	461	0.08
Digit symbol	62.3	58.4	−0.39
Logical reasoning	31.7	31.2	−0.10

Ratings or values under ad lib consumption and deprivation conditions are listed. Effect size (d) is defined as $\text{mean}_{\text{diff}}/\text{SD}_{\text{diff}}$ for within-subject differences between ad lib and deprivation conditions. This calculation permits comparison of the relative sizes of treatment effects in different variables, as suggested by Cohen (4). SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial blood pressure; HR, heart rate.

*Two-tailed $p < 0.05$ for paired t-test comparing ad lib consumption and deprivation conditions.

interpretation. Only one person reported headache on the ad lib consumption day, and the headache was given a rating of 1 on the 0 to 3 scale. In contrast, 10 people reported headache during the morning of deprivation, including 4 who gave their headache the maximum rating available. No one reported any flu-like symptoms during ad lib consumption, but five people did during deprivation, rating the magnitude as a 1. Thus, even short periods of caffeinated-beverage deprivation may produce clinically significant physical symptoms in regular coffee drinkers. In many respects, these observations are similar to reports of headache symptoms during short-term caffeine abstinence associated with religious fasting (17) and surgical procedures (3,6,18,22).

The observed differences in casual blood pressure (lower when caffeine-deprived) are consistent with laboratory findings that caffeine administration is associated with increases in blood pressure (11). Our own laboratory studies have found that a single 250 mg dose of caffeine raises resting systolic and diastolic blood pressure by 7–10 mmHg 60 min after administration [e.g., (14)]. The effects seen here are consistent with these earlier observations, given the variability in caffeine dose and timing in the present ad lib study. They confirm that ad lib caffeine consumption is associated with elevated blood pressure compared with caffeine abstinence, even in habitual coffee drinkers who should have developed tolerance to the drug's effects. This finding has implications for epidemiological studies of caffeine and cardiovascular disease risk, which have often collected blood pressure data under fasting (thus, caffeine-deprived) conditions. Casual blood pressure in heavy coffee drinkers is probably underestimated under such conditions, which could lead to false negative results regarding the association of coffee drinking and elevated blood pressure and misleading conclusions about the coronary disease risks associated with coffee or caffeine. Coffee's potential as a hypertension and coronary disease risk factor may need to be reevaluated.

Although anecdotal reports from participants and subjective measures of mood and symptoms suggested the presence of diminished cognitive capacity and functional impairment during caffeinated beverage deprivation, no deficits in psychomotor task performance were found. Similar negative results are common in the decades of research into caffeine's effects on performance, where comparisons of caffeinated and caffeine-deprived conditions yield performance differences that are typically small and capricious [reviewed in (5,11,12, 19)]. The battery of tasks covered a variety of psychomotor functions from simple to complex. Only the serial memory task yielded possible evidence of impairment, and this was compromised by an order interaction. Given the changes in mood and symptoms, performance deficits caused by functional impairment or decreased motivation would be expected. It is possible that the specific tasks of the present study do not tap the dimensions of cognitive performance affected by caffeine deprivation. Furthermore, these tasks were all of relatively short duration, and participants may have been able to push themselves to overcome any withdrawal-related deficits. Recently Streufert and colleagues reported that caffeine deprivation produced significant deficits in managerial performance measures collected during long, complex work simulations (21). Perhaps longer periods of more naturalistic cognitive and work-related tasks will provide a clearer demonstration of performance deficits in future studies.

The attempt to investigate whether heavier consumers experienced stronger withdrawal symptoms yielded some supporting evidence of correlation. This effort was hindered by the relatively small sample size, but relationships were observed for at least some of the symptoms. Other studies have demonstrated that deprivation can produce symptoms of withdrawal even in people who consume light to moderate amounts of caffeine, even as low as 100 mg (one cup of coffee) per day (8,20). Although this may be true, our preliminary evidence suggests that the experience of withdrawal symptoms may be more intense in people who habitually consume larger amounts of caffeine.

Compliance with instructions for caffeine abstinence was not confirmed objectively by measures of caffeine level in plasma or saliva. However, the possibility that some participants failed to maintain abstinence in the deprivation condition is not a serious limitation. Participants were asked directly about their compliance with instructions for abstinence or diary record-keeping, and we have no reason to suspect their reports. Moreover, scattered noncompliance with the abstinence condition would not likely yield the significant differences between ad lib and deprived conditions observed here. Rather, it would tend to increase the variability of scores in the deprived condition, making it even more difficult to detect differences between the two.

The present study was intended to simulate natural conditions of caffeinated beverage consumption and deprivation in the real world. This decision had several implications for the outcome. Because participants were asked to consume ad lib, caffeinated beverages, and presumably caffeine dose, varied both in amount and timing. Variations in caffeine dose probably contributed to variability among participants in scores for mood, symptoms, and performance on the ad lib day, which may have prevented detection of differences in some variables. In contrast, expectations about the effects of caffeine deprivation may have contributed to the observed differences in mood and symptoms, which were based on retrospective self-reports. Participants were not blind to treatment condition, because they maintained their own ad lib or abstinent status, and beliefs about caffeine withdrawal symptoms could have colored their reports. Moreover, the disruption of other normal routines that was caused by the experimental demands for caffeinated beverage deprivation may have had a negative effect on mood during the morning. A naturalistic study such as this cannot control these extraneous factors. As a result, observed differences reflect more than the presence or absence of caffeine. However, they do represent the broader experience of caffeinated-beverage deprivation, which naturally includes the expectations and the changes in routine, and which was the subject of the investigation.

In many respects, the present study confirms what most regular coffee drinkers would probably admit: they suffer when they don't get their regular morning coffee. However, investigation of the clinically significant effects of even brief periods of deprivation is worthwhile because these symptoms (e.g., headache, fatigue, etc.) are such common complaints presented to physicians and may be otherwise difficult to explain. Moreover, given the widespread use and increasing popularity of coffee, it is worth noting that habitual caffeine consumption is not without a potential cost to well-being. At the very least, habitual coffee drinkers run the risk of misery when they cannot get their regular cup.

ACKNOWLEDGEMENTS

This research was supported by grants from the National Institute on Drug Abuse (R01 DA 06957) and the National Heart, Lung, and Blood Institute (R01 HL 51634). I thank Robert Holeman for his invaluable assistance in the collection of data.

REFERENCES

1. Baddeley, A. D.: A three-minute reasoning test based on grammatical transformation. Psychon. Sci. 10:342; 1968.
2. Bruce, M.; Scott, N.; Shine, P.; Lader, M.: Caffeine withdrawal: A contrast of withdrawal symptoms in normal subjects who have abstained from caffeine for 24 hours and for 7 days. J. Psychopharmacol. 5:129–134; 1991.
3. Camann, W. R.; Murray, R. S.; Mushlin, P. S.; Lambert, D. H.: Effects of oral caffeine on postdural puncture headache. A double-blind, placebo-controlled trial. Anesth. Analg. 70:181–184; 1990.
4. Cohen, J.: Statistical power analysis for the behavioral sciences. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
5. Dews, P. B.: Behavioral effects of caffeine. In: Dews, P. B., ed. Caffeine: Perspectives from recent research. Berlin: Springer-Verlag; 1984:86–103.
6. Fennelly, M.; Galletly, D. C.; Purdie, G. I.: Is caffeine withdrawal the mechanism of postoperative headache? Anesth. Analg. 72: 449–453; 1991.
7. Goldstein, A.; Kaizer, S.; Whitby, O.: Psychotropic effects of caffeine in man. IV. Quantitative and qualitative differences associated with habituation to coffee. Clin. Pharmacol. Ther. 10:489–497; 1969.
8. Griffiths, R. R.; Evans, S. M.; Heishman, S. J.; Preston, K. L.; Sannerud, C. A.; Wolf, B.; Woodson, P. P.: Low-dose caffeine physical dependence in humans. J. Pharmacol. Exp. Ther. 255: 1123–1132; 1990.
9. Griffiths, R. R.; Woodson, P. P.: Caffeine physical dependence: A review of human and laboratory animal studies. Psychopharmacology (Berl.) 94:437–451; 1988.
10. Hofer, I.; Battig, K.: Cardiovascular, behavioral, and subjective effects of caffeine under field conditions. Pharmacol. Biochem. Behav. 48:899–908; 1994.
11. James, J. E.: Caffeine and health. New York: Academic Press; 1991.
12. James, J. E.: Does caffeine enhance or merely restore degraded psychomotor performance? Neuropsychobiology 30:124–125; 1994.
13. Lane, J. D.: Neuroendocrine responses to caffeine in the work environment. Psychosom. Med. 56:267–270; 1994.
14. Lane, J. D.; Adcock, R. A.; Williams, R. B.; Kuhn, C. M.: Caffeine effects on cardiovascular and neuroendocrine responses to acute psychosocial stress and their relationship to level of habitual caffeine consumption. Psychosom. Med. 52:320–336; 1990.
15. McNair, D. M.; Lorr, M.; Droppleman, L. F.: EdITS manual for the Profile of Mood States. San Diego, CA: EdITS; 1992.
16. Mitchell, S. H.; de Wit, H.; Zacny, J. P.: Caffeine withdrawal symptoms and self-administration following caffeine deprivation. Pharmacol. Biochem. Behav. 51:941–945; 1995.
17. Mosek, A.; Korczyn, A. D.: Yom Kippur headache. Neurology 45:1953–1955; 1995.
18. Nikolajsen, L.; Larsen, K. M.; Kierkegaard, O.: Effect of previous frequency of headache, duration of fasting and caffeine abstinence on perioperative headache. Br. J. Anaesth. 72:295–297; 1994.
19. Rogers, P. J.; Richardson, N. J.; Dernoncourt, C.: Caffeine use: Is there a net benefit for mood and psychomotor performance? Neuropsychobiology 31:195–199; 1995.
20. Silverman, K.; Evans, S. M.; Strain, E. C.; Griffiths, R. R.: Withdrawal syndrome after the double-blind cessation of caffeine consumption. N. Engl. J. Med. 327:1109–1114; 1992.
21. Streufert, S.; Pogash, R.; Miller, J.; Gingrich, D.; Landis, R.; Lonardi, L.; Severs, W.; Roache, J. D.: Effects of caffeine deprivation on complex human functioning. Psychopharmacology (Berl.) 118:377–384; 1995.
22. Weber, J. G.; Ereth, M. H.; Danielson, D. R.: Perioperative ingestion of caffeine and postoperative headache. Mayo Clin. Proc. 68:842–845; 1993.
23. Wechsler, D.: Measurement and appraisal of adult intelligence. Baltimore, MD: Williams and Wilkins Co.; 1958.