Pergamon

Pharmacology Biochemistry and Behavior, Vol. 47, No. 4, pp. 919–926, 1994

0091-3057/94 $6.00 + .00

Caffeine Antagonizes EEG Effects of Tobacco Withdrawal

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Received 10 May 1993

COHEN, C., W. B. PICKWORTH, E. B. BUNKER AND J. E. HENNINGFIELD. *Caffeine antagonizes EEG effects of tobacco withdrawal.* PHARMACOL BIOCHEM BEHAV 47(4) 919–926, 1994.—Six current cigarette smokers and coffee drinkers were given combinations of 0, 150, or 300 mg caffeine and 0, 2, or 4 mg nicotine polacrilex following 12-h nicotine and caffeine abstinence. On one study day, subjects were allowed to smoke cigarettes and to drink caffeinated beverages and no drugs were given. Tobacco and caffeine abstinence impaired performance on the serial addition/subtraction and digit recall tasks; decreased scores on the MBG scale and ratings of "clear-headed" and "quick-witted"; and increased ratings of "irritability," "muscular tension," "headache," "drowsy," "clumsy," "feeble," and "dreamy." The deprivation caused characteristic EEG signs of nicotine withdrawal including increased theta power and decreased alpha frequency. These EEG effects were reversed by cigarette smoking and caffeine administration, but nicotine polacrilex was less effective. Deprivation-induced performance and subjective measures were not changed by administration of nicotine and caffeine combinations.

Nicotine Caffeine Withdrawal EEG

IT is now well documented that tobacco deprivation is accompanied by changes in mood, performance, and physiological measures including the electroencephalogram (EEG). These signs and symptoms appear after periods of deprivation as short as 4 h and persist for several days or months. Some of the signs and symptoms return progressively to preabstinence levels, reflecting a rebound phenomenon characteristic of opioid and sedative withdrawal syndromes (12,17,29,35,38).

Because the probability of relapse to tobacco may be related to the intensity of withdrawal symptoms, it would be of clinical importance to identify factors that affect the magnitude of the syndrome. The possibility that caffeine intake might modulate the intensity of tobacco withdrawal symptoms is suggested by several observations from clinical and epidemiological studies. Caffeine produces some effects opposite to those of nicotine deprivation. For example, caffeine can increase measures of arousal, vigilance, and performance on cognitive tests, produce EEG activation, and increase heart rate and blood pressure (13). On the other hand, caffeine can also produce certain effects in common with those of nicotine deprivation such as anxiety, tension, and impairment of certain types of psychomotor performance (1,3,7,11,13). These observations have led to the hypothesis that caffeine intake during nicotine deprivation might exacerbate symptoms of withdrawal (33). Together, this information indicates that the effect of caffeine on the signs and symptoms of nicotine deprivation is unclear and could either mitigate or exacerbate the tobacco withdrawal syndrome.

The present study was designed to determine whether nicotine, caffeine, or their combination diminish or increase signs and symptoms of 12-h nicotine abstinence on measures previously demonstrated to be sensitive indices of nicotine deprivation. The effects of two doses of caffeine on cigarette smoking, mood, heart rate, blood pressure, and EEG were compared to those of two doses of nicotine administered via polacrilex gum. Furthermore, the possible interactive effects of caffeine and nicotine were evaluated by combinations of caffeine and nicotine polacrilex. A session where subjects were not deprived of tobacco or caffeine served as a control condition.

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METHOD

Subjects

Participants were six healthy, paid, male volunteers ranging in age from 25 to 32 years (mean: 28.2 years) and weighing 67 to 80 kg (mean: 74.5 kg). They resided on the residential research unit of the Addiction Research Center for the approximately 3-week duration of the study. They had histories of regular cigarette smoking for 7 to 19 years (mean: 13.0) and their scores on the Fagerstrom Tolerance Questionnaire (6), a measure of nicotine dependence where scores above 6 indicate severe dependence, were 7 to 9 (mean: 8.0). Their coffee consumption ranged from 3 to 10 cups per day (mean: 5.1). No subject reported regular use of illicit drugs or levels of alcohol consumption indicative of dependence.

Procedure

Before beginning the study, subjects practiced on the tasks until stable performance was obtained. Following the 3-day training phase, they participated in the study 4 days per week (0800–1300 h) for a total of ten experimental sessions. The tests and recordings were conducted in electrically shielded and sound-attenuated test chambers with a one-way observation window. Subjects were informed that they might receive placebo or caffeine or nicotine alone and in combination. They were prohibited from using caffeine-containing substances and tobacco products for 12 h prior to and during an experimental session but were allowed to smoke and consume coffee immediately following sessions. This deprivation period was monitored by research staff; exhaled carbon monoxide (CO) levels ranged from 6 to 16 ppm (mean: 11 ppm) at the start of the sessions. At the beginning of an experimental session, after baseline EEG and vital sign recordings were obtained, subjects answered a battery of questionnaires and completed performance tasks. Tasks were always presented in the same order: circular lights task, PAB, questionnaires, tracking task, hole-and-stylus steadiness test (described below).

Study measures were collected five times over the experimental session: before drugs (baseline), after caffeine or placebo capsule, after nicotine or placebo gum, and before and after cigarette smoking (Table 1). Chewing of the gum was monitored by the staff and the pace of chewing was governed by a tone presented every 3 s for 15 min; subjects were instructed to bite the gum once at each sounding of the tone. Subjects were then allowed to drink decaffeinated coffee ad lib for 20 min during the time between gum administration and cigarette smoking. It was emphasized to subjects that they were free to drink as much or as little coffee as they desired. Subjects served themselves the coffee and added milk and/or sugar if they desired. At the end of the ad lib drinking period, subjects were asked to smoke one cigarette of their usual brand using a cigarette holder. They were instructed to smoke as much of the cigarette as they desired.

On one experimental day (nondeprived condition), the subjects were not required to abstain from the use of caffeine-containing substances and tobacco products prior to and during an experimental session. However, they were not allowed to smoke while performing the test battery. On this one day, subjects were not given capsules or gum. When two subjects participated in the experiment on the same day, the times of drug administration and test battery completion were staggered by 30 min. As an incentive, subjects were paid $5 per session contingent upon how well they did on the performance tasks.

TABLE 1

EXPERIMENTAL TIME LINE

Experimental Time (min)	Clock Time*	Activity†
	0800	Baseline: CO, EEG, performance, questionnaires
0	0900	Capsules administration
25	0925	EEG, coffee questionnaire
30–45	0930–0945	Gum administration
50	0950	EEG, performance, questionnaires
90–110	1030–1050	Decaffeinated coffee available
125	1105	EEG, questionnaire, performance
135	1115	Smoke cigarette #1
150	1130	EEG
170	1150	Smoke cigarette #2
180	1200	CO

*When two subjects ran concurrently, time for second subject was advanced by 30 min.

†CO = exhaled carbon monoxide; EEG = cortical electroencephalogram; performance = PAB tasks, steadiness, circular lights, and tracking tasks; questionnaires = ARCI, POMS, caffeine and nicotine effect, desire to smoke, cigarette and coffee questionnaire, mood and bodily symptoms questionnaire.

Drug Administration

Anhydrous caffeine (150 or 300 mg) or placebo (lactose) was contained in three gelatin capsules that were administered orally with approximately 240 ml of water. The nicotine gum and the placebo gum were supplied by Marion Merrell Dow (Kansas City, MO). Various combinations of two pieces of gum containing either 0 or 2 mg of nicotine were used to produce doses of 0, 2, and 4 mg nicotine. Three doses of caffeine (0, 150, 300 mg) and three doses of nicotine (0, 2, 4 mg nicotine gum) were administered in combination (under double-blind conditions) such that all nine possible dose combinations and the nondeprived condition were balanced among subjects. During ad lib coffee drinking periods, commercially available decaffeinated coffee was used. Coffee was prepared with 5 g (approximately 1 tablespoon) of decaffeinated coffee per 400 ml of water.

Subject Ratings

Several psychometric instruments were administered during daily tests to assess the possible effects of nicotine and caffeine abstinence, as well as the effects of drug administration. These are described below.

Profile of Mood States (POMS) Questionnaire (23). From the 65 items of the POMS questionnaire, seven standard factor scores (tension/anxiety, depression/dejection, anger/hostility, vigor, fatigue/inertia, confusion/bewilderment, friendliness) and one composite factor (positive mood) were calculated.

The Addiction Research Center Inventory (ARCI). The version of the ARCI (10) used consisted of five scales: MBG, a general measure of drug-induced euphoria; A, a scale specific for dose-related effects of *d*-amphetamine; BG, a scale consisting mainly of items relating to intellectual efficiency and energy; PCAG, a measure of sedation; and LSD, a measure of dysphoria and somatic symptoms.

Caffeine and Nicotine Effect Questionnaire. The strength, acceptability, and liking for the drugs (caffeine or placebo capsules, and nicotine or placebo gum) were rated on five-point scales. Strength: 1, it was definitely a blank; 2, it might have been a blank but not sure; 3, it was probably a weak dose; 4, it was a medium-strong dose; 5, it was an extremely strong dose. Acceptability: 1, I would strongly resist another dose; 2, I would mildly resist another dose; 3, I would neither resist nor seek one; 4, I would mildly desire another dose; 5, I would strongly desire another dose. Liking: 1, not at all; 2, slight; 3, moderate; 4, a lot; 5, an awful lot.

Desire to smoke. Subjects rated their desire to smoke on a five-point scale (15): 1, I would strongly resist a cigarette; 2, I would mildly resist a cigarette; 3, I would neither resist nor seek one; 4, I would mildly desire a cigarette; 5, I would strongly desire a cigarette.

Cigarette and Decaffeinated Coffee Questionnaires. The questionnaires consisted of 100-mm visual line analog scales on which subjects rated each of the following characteristics: strength (very weak to very strong); harshness (not harsh to very harsh); taste (very bad to very good); satisfaction (very unsatisfying to very satisfying).

Mood and Bodily Symptoms Questionnaire (3). This questionnaire contained 16 different 100-mm lines, each labeled at the extremes with opposing adjectives: alert–drowsy, strong–feeble, fuzzy–clearheaded, well coordinated–clumsy, lethargic–energetic, mentally slow–quick-witted, attentive–dreamy, incompetent–proficient, interested–bored, contented–discontented, troubled–tranquil, happy–sad, antagonistic–amicable, withdrawn–gregarious, calm–excited, tense–relaxed. The questionnaire also contained 13 items: anxiety, sweating, shaking or trembling, palpitations, nausea or sickness, dizziness, irritability, loss of appetite, muscular tension, indigestion or stomach trouble, physical tiredness, headache, and concentration. The subjects rated each symptom on a 100-mm line in which the poles were labeled absent (left end) and severe (right end).

Performance Tasks

Performance Assessment Battery (PAB). Subjects performed six computer-delivered tasks from the Walter Reed Army Institute for Research Performance Assessment Battery (PAB) (36): two-letter search, column addition task, logical reasoning, pattern recognition, serial addition/subtraction, and digit recall. The tasks from the Performance Assessment Battery are briefly described below; detailed descriptions and information appear elsewhere (35,36). In the two-letter search task, two letters appear concomitantly above a string of 20 letters. Subjects must determine if the two letters are contained in the string. The column addition task required the subjects to mentally add a column of five two-digit numbers. In the logical reasoning task, each trial presented the letter pair "AB" or "BA" and a statement that described the order of the letters (e.g., A precedes B); subjects indicated whether the statement was true or false. The pattern recognition task is a test of visual memory in which a referent pattern of X's are displayed for a brief time (1.5 s), the screen goes blank for 3.5 s, and a second pattern of X's is displayed. The subjects must indicate whether the pattern is the same or different from the referent pattern. In the serial addition/subtraction task, each trial involved the sequential rapid presentation of two random digits followed by a plus or minus sign and a "?" prompt. Subjects rapidly performed the indicated operation. Each trial of the digit recall task began with the simultaneous presentation of nine random digits for 1 s, a blank screen for 3 s, followed by a display of eight of the original digits in a different order. Subjects were required to select the missing digit. For each of the tasks, dependent variables were response time and accuracy.

Circular lights and tracking task. The circular lights task of hand–eye coordination has been described elsewhere (14); it involves rapidly pushing lighted buttons on a wall-mounted panel. The score is the number of hits in 1 min. The tracking task required the subject to keep pointers on the center of two targets moving across a computer screen. One target moved in a horizontal direction only and was tracked with arrow keys on the keyboard, and the other target moved in two dimensions and was tracked with a computer "mouse." The percentage of time on each target and the average difference from the center of each target were recorded.

Hole-and-Stylus Steadiness Test. Hand tremor was measured by the hole-and-stylus steadiness test. The subjects successively inserted a metal stylus (2 mm in diameter) into nine different holes of diminishing size in a metal plate. The metal plate was mounted on a rack, facing the subject, at about shoulder level. The subject was instructed to rest his elbow on the table, to insert the stylus in the first hole and to hold it for 5 s as steadily as possible without touching the sides of the hole. The duration of contacts was automatically recorded. This task was performed with the stylus held in the right hand and in the left hand successively. The duration of contacts and the critical hole at which subjects touched the sides were analyzed.

Physiological Measures

Vital signs. Recordings of heart rate, systolic and diastolic blood pressure, and oral temperature were collected.

EEG recordings. One-minute periods of spontaneous EEG (eyes closed) were recorded from gold cup electrodes placed at Fz, Pz, C3, C4 (reference: linked ears) while the subject was comfortably seated in an armchair (29). The EEG was collected and analyzed with the Nicolet Pathfinder II. Samples with artifacts were automatically rejected. For each 1-min sample, the computer calculated the power (amplitude, μV^2) and peak frequency in the following frequency bands; delta, 0.25–3.75 Hz; theta, 4–7 Hz; alpha, 7.25–14 Hz; and beta, 14.25–25 Hz.

Smoking Behavior

Cigarette smoking and caffeine drinking. At the end of the test sessions subjects smoked two cigarettes of their own brand through a plastic cigarette holder connected via flexible tubing to a pressure-sensitive switch, interfaced to a computer. The number of puffs, the total puffing time, and the total smoking time were recorded. The cigarette butts were weighed. Carbon monoxide (CO) in samples of expired air was measured using an Ecolyzer (National Draeger, Pittsburgh, PA) according to procedures described by Henningfield et al. (16). Following the 20-min ad lib coffee drinking period, residual coffee was measured to enable calculations of the total volume of decaffeinated coffee drunk by the subjects.

Statistical Analyses

Tobacco and caffeine abstinence effects. The tobacco and caffeine abstinence effects were assessed by comparing data from the nondeprived day with those from the day when drugs were placebos. Repeated measure ANOVAs were performed (34). Analyses included the factors of condition (i.e., nondeprived day, placebo day), time, and electrode for EEG measures. *t*-Tests were employed in the analysis of the ratings on the Decaffeinated Coffee and Cigarette Effects Questionnaires and the volume of decaffeinated coffee drunk because these measures did not have a predrug observation. Expired air CO was analyzed as change scores by subtracting presmoking from postsmoking values.

Nicotine and caffeine substitution effects. The effects of caffeine and/or nicotine were analyzed only on those variables where tobacco and caffeine abstinence effects were found. Separate two-factor (i.e., nicotine at 0, 2, 4 mg and caffeine at 0, 150, 300 mg), repeated measure ANOVAs were performed; when time course was examined, the third factor of time was also included.

Cigarette smoking effects. The effects of cigarette smoking were analyzed only on those variables where tobacco and caffeine abstinence effects were found, by comparing data from the placebo day obtained before and after smoking by means of paired, two-tailed *t*-tests (34).

RESULTS

EEG Recordings

Twelve-hour tobacco and caffeine abstinence produced significant effects on alpha frequency [condition: $F(1, 5) = 8.00, p < 0.05$] and theta power [condition: $F(1, 5) = 16.53, p < 0.01$; condition × electrode: $F(3, 15) = 3.77, p < 0.05$; condition × time: $F(3, 15) = 3.46, p < 0.05$]. As illustrated in Figs. 1 and 2, the deprivation increased theta power and decreased alpha frequency. These EEG effects persisted for the duration of the 3-h test session. The most pronounced EEG effects of tobacco abstinence on alpha frequency occurred at the posterior (Pz) electrode, and changes in theta power were strongest at the frontal (Fz) electrode (29). Therefore, for clarity of presentation, only Fz- and Pz-specific effects of tobacco and caffeine deprivation and/or substitution were illustrated.

Compared to placebo treatment, caffeine produced several significant effects on EEG. Specifically, theta power at Fz was decreased by caffeine, $F(2, 10) = 8.21, p < 0.01$; both 150 and 300 mg caffeine fully suppressed the increase in theta power induced by caffeine and tobacco deprivation (Fig. 1, upper panel). The caffeine effect was maximal 50 min after administration of the capsules and was still evident at 125 min.

A main caffeine effect was observed on alpha frequency at Pz, $F(2, 10) = 4.23, p < 0.05$; the persistent decrease in alpha frequency induced by caffeine and tobacco deprivation that continued over the course of the session was not observed when 300 mg caffeine was administered (Fig. 2, upper panel). The caffeine effect was still present at 125 min after capsule administration.

Nicotine gum did not produce statistically significant effects; however, the 4 mg nicotine gum tended to decrease theta power at Fz (Fig. 2, lower panel) and increase alpha frequency (Fig. 1, lower panel). The nicotine effect was maximal immediately after gum chewing and was gone at 75 min after the gum chewing.

There was no significant caffeine interaction with nicotine on any of these measures [theta power: $F(4, 20) = 0.38$, NS; alpha frequency: $F(4, 20) = 1.91$, NS[].

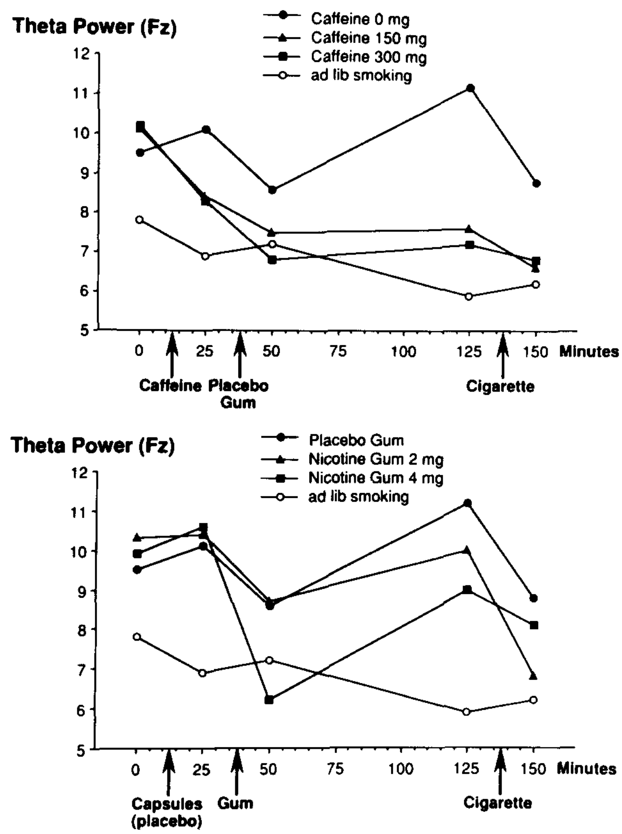

FIG. 1. Mean EEG theta power in relaxed subjects with eyes closed during ad lib smoking, nicotine and caffeine deprivation, and caffeine substitution (upper panel) or nicotine substitution (lower panel). A 1-min period of spontaneous EEG was recorded at the beginning of the sessions, 25 min after caffeine or placebo capsules, following nicotine or placebo gum, and before and after smoking a cigarette.

Smoking a cigarette decreased theta power at Fz ($p < 0.01$) and increased alpha frequency at Pz ($p < 0.05$) in the deprived condition. Postsmoking values from the deprived day were not statistically different from those obtained in the nondeprived condition. Cigarette smoking had the greatest effect on reducing theta power and increasing alpha frequency in the placebo caffeine–placebo gum (deprivation) condition and after placebo caffeine–active gum conditions (Figs. 1 and 2, lower panels). Cigarette smoking had the smallest EEG effects in the conditions in which the subjects were given active caffeine doses (Figs. 1 and 2, upper panels).

Subject Ratings

The 12-h tobacco and caffeine abstinence produced significant effects on the MBG scale of the ARCI and on nine items of the Mood and Bodily Symptoms Questionnaire (Fig. 3). The deprivation decreased scores on the MBG scale, $F(1, 5) = 6.62, p < 0.05$; increased ratings of irritability, $F(1, 5) = 8.60, p < 0.05$, muscular tension, $F(1, 5) = 8.62, p < 0.05$, headache, $F(1, 5) = 7.15, p < 0.05$, drowsy, $F(1, 5) = 6.64, p < 0.05$, feeble, $F(1, 5) = 15.90, p < 0.05$, clumsy, $F(1, 5) = 7.19, p < 0.05$, and dreamy, $F(1, 5) = 13.23, p < 0.05$; and decreased ratings of clear-headed, $F(1, 5) = 7.39, p < 0.05$, and quick-witted, $F(1, 5) = 6.24, p < 0.05$. The magnitude of the difference on these scales between

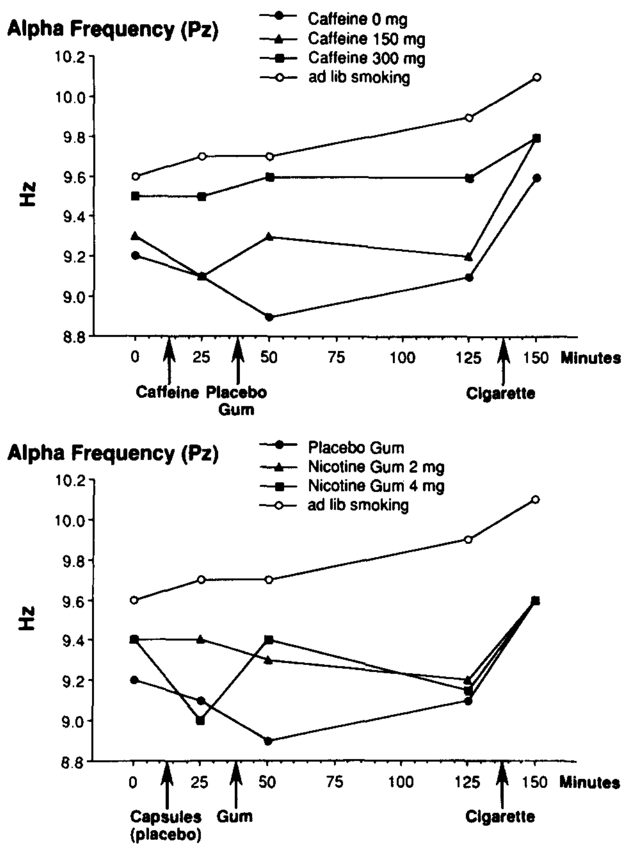

FIG. 2. Mean EEG alpha frequency in relaxed subjects with eyes closed during ad lib smoking, nicotine and caffeine deprivation, and caffeine substitution (upper panel) or nicotine substitution (lower panel). A 1-min period of spontaneous EEG was recorded at the beginning of the sessions, 25 min after caffeine or placebo capsules, following nicotine or placebo gum, and before and after smoking a cigarette.

the deprived and nondeprived conditions did not significantly change over the course of the experimental session.

A significant interaction of nicotine by caffeine by time occurred on subject ratings of attentive–dreamy, $F(4, 20) = 5.18$, $p < 0.01$. On this measure the 2 mg, but not the 0 or 4 mg, nicotine gum increased ratings of dreamy; however, both doses of caffeine prevented the increase.

Decaffeinated Coffee Consumption

One subject did not drink decaffeinated coffee during the nondeprived condition; the decaffeinated coffee consumption for the other five subjects was analyzed. Subjects in the deprived condition drank a larger volume of decaffeinated coffee than they did in the nondeprived condition: 246 vs. 142 ml ($p < 0.05$). The effects of caffeine and nicotine on consumption were not statistically significant; however, caffeine, and to a lesser extent nicotine, tended to decrease coffee consumption (Fig. 4).

Performance Tasks

The 12-h tobacco and caffeine abstinence produced significant impairment on two of the PAB tasks. Overnight deprivation significantly increased the response time on the column addition task, $F(1, 5) = 32.00$, $p < 0.01$, and decreased the accuracy (percent of correct responses) on the digit recall task, $F(1, 5) = 15.43$, $p < 0.05$. A significant interaction between nicotine, caffeine, and time was obtained on the percent of correct responses on the digit recall task, $F(4, 20) = 3.43$, $p < 0.05$. The combination of 150 mg caffeine with the two doses of nicotine showed opposite effects; 2 mg nicotine increased performance accuracy, whereas the 4 mg nicotine decreased the percent of correct responses. Performance on the psychomotor tasks was not significantly affected by the deprivation.

Other Measures

Physiological measures and topographical measures of cigarette smoking were not significantly affected by the deprivation, or by any combination of drug, or drug and placebo conditions.

DISCUSSION

Twelve-hour deprivation from tobacco products and caffeinated beverages and food was accompanied by:

1. EEG changes, including an increase in theta power and a decrease in alpha frequency,
2. mood changes and appearance of bodily symptoms as reflected by increased scores on ratings of irritable, drowsy, dreamy, headache, muscular tension, feeble, clumsy, and decreased scores on ratings of clear-headed, quick-witted, and on the MBG scale of the ARCI, a general measure of drug-induced euphoria (10),
3. cognitive impairment observed on two out of six tasks of the Performance Assessment Battery: the digit recall and the arithmetical calculation tasks.

These effects are typical of those after tobacco deprivation in heavy smokers (38) and represent subjective, physiological, and performance constituents of nicotine withdrawal. On the other hand, the time course of caffeine deprivation on EEG and performance measures is not known. Subjective complaints of headache and fatigue begin 12 to 19 h after caffeine cessation and peak at 24 to 48 h (9), and the onset of these symptoms is variable among subjects (8). Although it is possible that some of the effects recorded in the study were due to caffeine deprivation, the time course of action and the pattern of effects suggest that the EEG changes on the morning of the study were primarily due to nicotine deprivation. This claim is bolstered by the observation that smoking the cigarettes at the end of the session rapidly and completely reversed the EEG signs of withdrawal.

Other studies have reported EEG changes following nicotine deprivation (18,37). In a study of the time course of the tobacco withdrawal syndrome, it was observed that the EEG returned to preabstinence levels on day 10, reflecting a rebound phenomenon of a withdrawal syndrome rather than the disappearance of the effects of nicotine (29). In the present study, smoking a single cigarette reversed the EEG changes induced by tobacco deprivation. Our results on the rapid EEG change induced by a single cigarette agree with a puff-by-puff dynamic analysis of EEG changes (19). In both studies, smoking increased alpha frequency and decreased theta power, and these effects were evident by the fourth puff in the paced puffing procedure. Furthermore, Revell (31) demonstrated changes in human performance by cigarette smoking on a puff-by-puff basis. These results and those of the present

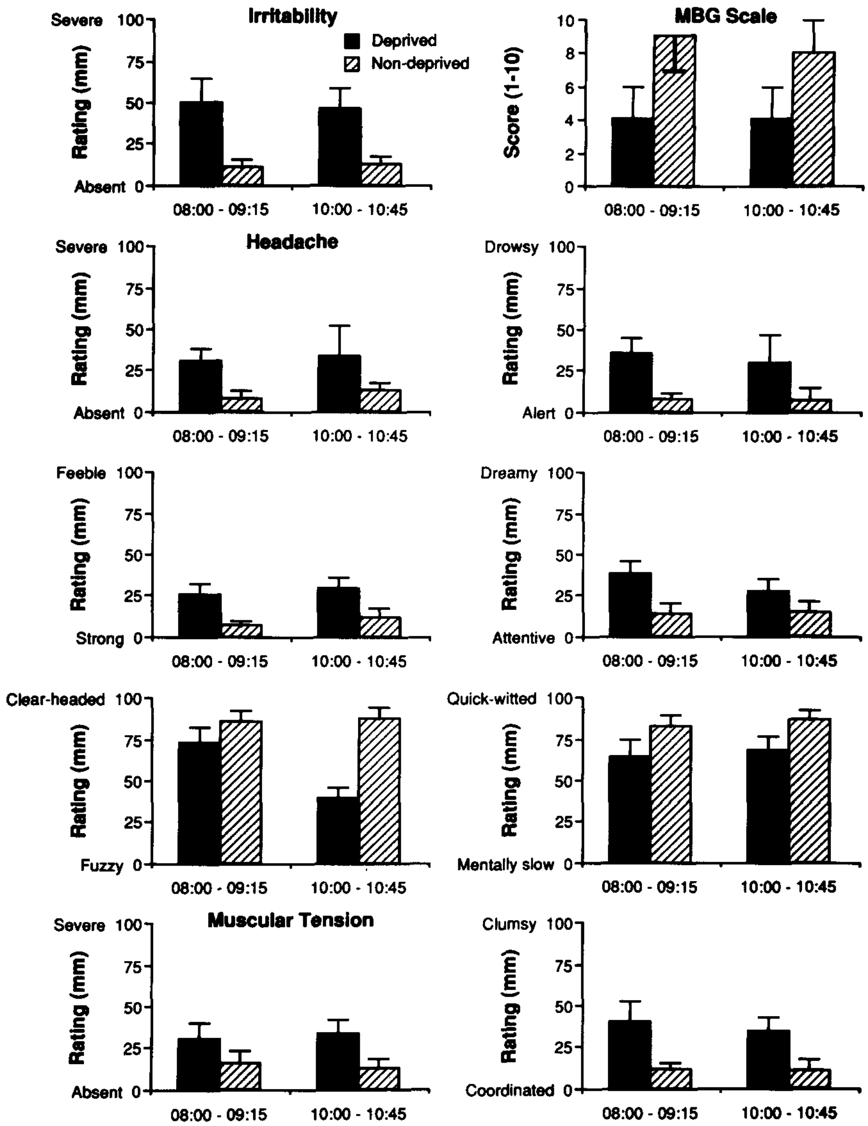

FIG. 3. Mean ± SEM scores on the MBG scale of the ARCI, mood and bodily symptom ratings at the beginning of the sessions (0800–0915) and following placebo capsules and gum during nicotine and caffeine deprivation (closed bars) and during ad lib smoking (cross hatched bars).

study emphasize the remarkable sensitivity of the EEG and performance to a single cigarette in the abstinent smoker.

In a previous study, 4 mg, but not 2 mg, nicotine gum reversed the EEG effects of tobacco abstinence by increasing alpha and beta frequency and decreasing theta power (28). In the present study the results were similar. The 2 mg dose was also ineffective at changing the EEG signs and the 4 mg nicotine gum increased alpha frequency and decreased theta power, but the effects were short-lived and did not reach statistical significance. On the other hand, cigarette smoking did reverse the EEG effects of overnight tobacco deprivation. It is possible that the delivery of nicotine from gum chewing in the present study was not fast enough or the amount of nicotine absorbed was insufficient to significantly reverse the EEG effects. Extraction of nicotine from the polacrilex is incomplete (28) and variable between subjects regardless of the chewing paradigm (24).

Caffeine reversed the EEG changes induced by tobacco deprivation. The dose of 150 mg blocked the decrease in theta power; the 300 mg dose blocked the decrease in theta power and the increase in alpha frequency. The EEG effects of caffeine were maximal at 55 min and were still present at 125 min. Compared to the effects of nicotine, caffeine effects were slower to develop, had a greater intensity, and were more persistent.

EEG alpha slowing and increased theta power after nicotine deprivation have been previously associated with diminished arousal and impairment on attentional processes (5,19,29,30). In the present study, although there were EEG changes and subjects complained of drowsiness, performance

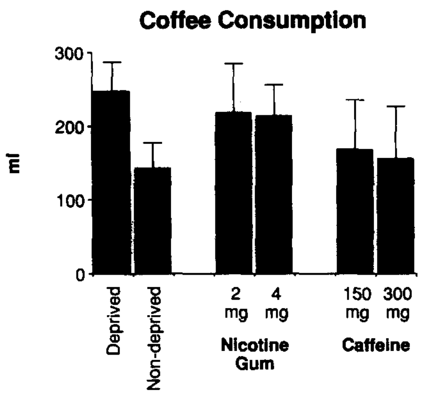

FIG. 4. Mean volume of coffee drunk during nicotine and caffeine deprivation (deprived), during ad lib smoking (nondeprived), and during nicotine or caffeine substitution.

(accuracy and response speed) on cognitive tasks was only slightly impaired by tobacco withdrawal. It is possible that 12-h abstinence from tobacco might have not been sufficient to affect performance. Measures of cognitive impairment are generally maximal between 24 and 48 h after cessation of smoking. Furthermore, some cognitive tests appear to be more sensitive measures of the tobacco withdrawal syndrome than others. For example, the digit recall task was a sensitive measure of tobacco withdrawal in the present experiment and impairment in performing this task has been observed as early as 4 h after tobacco deprivation (35).

Subjects consumed more coffee during the tobacco-deprived condition than during the nondeprived condition. This observation may be interpreted as showing that tobacco-deprived smokers substitute caffeine for nicotine. Several studies have investigated the effects of caffeine on ad lib cigarette smoking. In some studies, caffeine increased smoking (2,21,22,27); in others caffeine decreased smoking behavior (4,20,24). In the present study and in the study by Rose (32), caffeine did not significantly affect smoking topography of the test cigarettes. It would probably be best to investigate such regulation over several days and as a function of the type of activities subjects have to perform.

In experiments designed for the study of the tobacco withdrawal syndrome, it is usual to ask subjects to refrain not only from nicotine but also from caffeine and from other drugs several hours before the beginning of a test session, to avoid any actions of these agents on the tested responses. In light of the results of the present study that caffeine blocked EEG signs and one symptom (attentive–dreamy) of nicotine withdrawal, this precaution appears justified. The inability of caffeine and nicotine combinations to reverse subjective effects in the present study extends previous research by Rose (32), who reported that smoking prevented the subjective arousal induced by caffeine. By choosing a short period of abstinence in the present study, it was possible to observe a specific nicotine abstinence syndrome. However, in protracted studies, subjects may experience caffeine withdrawal symptoms. A comparative study of the nicotine withdrawal effects between caffeine users and nonusers may highlight the specificity of each syndrome.

The present findings support the hypothesis that caffeine can suppress some symptoms of tobacco deprivation. The results are relevant to the question of whether caffeine should be consumed while quitting smoking. The results of the present study suggest that caffeine may have a beneficial effect. In another study (26), there were few significant interactions between caffeine and nicotine, suggesting that administration of caffeine does not exacerbate the nicotine withdrawal syndrome. The conclusion that caffeine may be used to alleviate tobacco withdrawal symptoms is thus tendered with caution. The present work does not predict the effects of caffeine on the success to quit. It should also be emphasized that the present study assessed the effects of caffeine and not those of coffee. Coffee is often consumed while smoking a cigarette, and in some smokers, coffee can serve as a stimulus that might precipitate cigarette seeking.

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