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Psychophysiological effects of nicotine abstinence and behavioral challenges in habitual smokers

Mustafa al'Absi*, Todd Amunrud, Lorentz E. Wittmers

Department of Behavioral Sciences, University of Minnesota School of Medicine, 10 University Avenue, Duluth, MN 55812-2487, USA

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Abstract

We tested the hypothesis that psychophysiological responses to behavioral challenges are enhanced by short-term abstinence from smoking. Blood pressure (BP), salivary cortisol levels, and withdrawal symptoms were measured after a period of smoking abstinence (18 h) or ad libitum smoking, during rest, and in response to acute behavioral challenges. Thirty habitual smokers (15 women and 15 men) participated in two laboratory sessions conducted on two separate days (after abstinence or ad libitum smoking). Cotinine concentrations in saliva and expired carbon monoxide were measured in both conditions. Abstinence produced significant withdrawal symptoms in all participants, with women reporting greater desire to smoke than men. Participants showed greater systolic BP responses to the behavioral challenges in the abstinence condition than the control condition. They also showed worse cognitive performance on the challenges in the abstinence than in the ad libitum condition. Men had greater salivary cortisol levels than women, and both men and women showed the expected decline in cortisol levels across time, but showed no difference between the abstinence and ad libitum smoking conditions in the laboratory or during ambulatory measurements. These results indicate that abstinence alters mood, performance, and BP responses to acute challenges but not adrenocortical responses. It is possible that these changes mediate stress-related vulnerability to smoking relapse.

Keywords: Behavioral stress; Cortisol; Gender differences; Nicotine addiction; Cognitive performance; Withdrawal; Mood

1. Introduction

This study was designed to determine effects of short-term abstinence from smoking on psychophysiological activity and mood changes both at rest and in response to acute behavioral challenges. Smokers report symptoms including anxiety, depression, restlessness, irritability, and physical symptoms, and may exhibit detriment in cognitive performance during abstinence (American Psychiatric Association, 1994; Hughes, 1992; Stitzer and Gross, 1988; Pritchard et al., 1992; Snyder et al., 1989). These symptoms begin within 4–24 h after smoking cessation and may contribute to risk for relapse (Stitzer and Gross, 1988; Gritz et al., 1991; Shiffman, 1982).

Smoking withdrawal symptoms after abstinence may be intensified by psychosocial stressors (Koval and Pederson, 1999; Perkins and Grobe, 1992) and may subsequently contribute to early relapse (Shiffman et al., 1996a; Carey et al., 1993). Data from laboratory experiments indicate an increase in the reported desire to smoke under acute stressful conditions (Perkins and Grobe, 1992; Perkins et al., 1994). Certain nicotine withdrawal symptoms may also resemble effect of stress (Hughes, 1992). It is, therefore, possible that abstinence from tobacco would result in a stress-like psychophysiological response profile that mediates or contributes to the stress-related enhancement of the desire to smoke (Parrott, 1995).

Acute stress produces significant sympathetic and adrenocortical changes, including rises in cortisol production and cardiovascular activation. An additive effect of nicotine and stress on these variables has been documented in several studies (Pomerleau and Pomerleau, 1990; Davis and Matthews, 1990; Dembroski et al., 1985; MacDougall et al., 1986). Effects of tobacco abstinence on response to stressful events are largely unknown (Kreek and Koob, 1998; Koob and Le Moal, 1997). Withdrawal from other classes of

* Corresponding author. Tel.: +1-218-726-7144; fax: +1-218-726-7559.
E-mail address: malabsi@umn.edu (M. al'Absi).

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drugs, such as opiates, cocaine, and alcohol, has been found to produce a stress-like physiological state (Cami et al., 1992; Mendelson et al., 1988; Wilkins and Gorelick, 1986). Early work suggests that smokers may exhibit lower blood pressure (BP) levels compared to nonsmokers, possibly due to temporary withdrawal during measurement (Mann et al., 1991), and one study found higher diastolic BP responses to a mental arithmetic challenge following overnight abstinence of smoking (Tsuda et al., 1996). Abstinence was also associated with enhanced cortisol levels in small samples of male smokers (Hughes et al., 1988; Pickworth et al., 1996), although one study did not support this association (Benowitz et al., 1984). These studies included a small number of subjects, did not address effects of behavioral challenge, and did not examine gender differences, leaving important questions about the presence and the significance of such changes open for future research.

Gender differences in smoking patterns have consistently been reported (King et al., 1990; Waldron, 1991; Wetter et al., 1999). Woman have more difficulties quitting (Wetter et al., 1999; Ward et al., 1997; Osler et al., 1999), and are more likely to use smoking to cope with negative affect than men (Dicken, 1978; Waldron, 1991). The heightened negative response to stress may predispose women to readily develop conditioned responses to smoking-related stimuli (Perkins et al., 2001). These responses may exacerbate withdrawal symptoms and predispose female smokers to relapse more often than men. Gender differences in psychobiological factors related to responses to stressful stimulation and to nicotine pharmacokinetics may also contribute to these effects (Grunberg et al., 1991). These differences, in turn, may be accentuated under stressful conditions and after abstinence.

The current study was conducted to examine effects of short-term abstinence from smoking on psychophysiological activity and responses to brief behavioral challenges and to evaluate withdrawal symptoms in male and female habitual smokers. This work should expand our understanding of multisystem changes during short-term abstinence, with the hope that subsequent work would determine the role of these changes in early relapse. We predicted that: (1) short-term abstinence would increase withdrawal symptoms and contribute to greater psychophysiological activity during brief laboratory stressors relative to ad libitum smoking; (2) women smokers would report more intense withdrawal symptoms than men, and these symptoms would be more pronounced during acute stress.

2. Method

2.1. Participants

Thirty healthy smokers, ages 18–47, primarily Caucasian (93%), were recruited by newspaper advertisements and by posters placed in the university community. A preliminary telephone screening interview was conducted. This interview included questions concerning any current or recent history of medical or psychiatric disorders, medication intake, and whether potential participants met smoking criteria (having smoked for an average of 15 cigarettes or more per day for a minimum of 2 years). If potential participants met the initial phone screening criteria, they were invited to a 30- to 45-min on-site screening session (see below for details). Participants were included if they had no history of a major illness or psychiatric disorder, weighed within ± 30% of Metropolitan Life Insurance norms, consumed fewer than two alcoholic drinks a day, and did not routinely use prescription medications (except contraceptives).

Participants signed a consent form approved by the Institutional Review Board of the University of Minnesota and were compensated for their participation. Thirty-six potential participants qualified for the study, and of those 30 were enrolled in the study. One female participant had two missing cortisol samples, but had complete cardiovascular, mood, and performance data. Another female participant completed only the abstinence condition. Complete ambulatory cortisol samples were available for 16 participants (eight women) due to the fact that this component was added later in the study.

3. Procedures

3.1. On-site screening

Upon arrival at the laboratory, the participant read and signed a consent form. The participant then provided a breath sample for assessment of expired carbon monoxide (CO), and completed forms related to medical history, smoking history, demographics, and other psychosocial variables described below. Weight and height were then measured, and this was followed by a brief interview conducted to explain the study, confirm eligibility, and address any questions or concerns the participant might have had. Female participants were asked about regularity of their menstrual cycle and use of contraceptive medications. The issue of whether phase of menstrual cycle or contraceptive use influences withdrawal symptoms has not been resolved and was not addressed in this study (Allen et al., 1996; Marks et al., 1999; Davis, 1999). Therefore, we did not restrict recruitment to a particular phase of the cycle, but did obtain self-report information on menstrual cycle phase and contraceptive use throughout the study.

3.2. Smoking abstinence assignment

All participants performed both conditions in a repeated-measure design. For the abstinence condition, participants were instructed not to smoke or use any tobacco products after 8:00 p.m. the evening prior to each laboratory session.

Laboratory sessions were conducted starting at around 2:00 p.m. the next day and continued until 5:00 p.m. For the ad libitum smoking condition, participants were instructed to continue to smoke at their normal rate. They were asked to smoke a cigarette of their preferred brand immediately prior to the experiment. Measurement of expired CO was performed prior to each session using MicroCO monitors (Micro Direct, Auburn, ME). CO readings on the abstinence condition did not exceed 12 parts per million (ppm).

Dietary restrictions included 24-h abstinence from alcohol and 48-h abstinence from medications (except contraceptives). To eliminate the possible effects of caffeine withdrawal in habitual coffee drinkers, we limited the caffeine restriction to 4 h prior to each laboratory session. Previous work suggests that effects of an acute dose of caffeine would be minimal or absent after 4 h (al'Absi et al., 1998).

3.3. Laboratory sessions

Two laboratory sessions (after abstinence and after ad libitum smoking) were conducted using a counterbalanced-order design. Participants reported to the laboratory between 1:30 and 2:00 p.m., at least 2 h after their last meal. Upon arrival to the laboratory, a breath sample was obtained for assessment of expired CO. Participants were asked to record the last time they smoked. Abstinent smokers must have abstained for at least 18 h prior to testing. Ad libitum smokers smoked one cigarette of their preferred brand immediately prior to the laboratory session. The participant was instrumented with a BP cuff and was seated in a semirecumbent position and observed from an adjacent control room through a one-way mirror. The protocol included a 90-min rest period, followed by two behavioral challenges (total of 16 min), and a recovery period (10 min). A saliva sample was collected every 30 min during the rest period and after performing the behavioral challenges (see Fig. 1 for outline of the protocol). After the recovery period, participants were scheduled for their second session or debriefed about the purpose of the experiment, compensated for their time, and thanked for participation. During rest periods, participants were allowed to read general interest materials or watch nature films or documentaries.

3.4. Behavioral challenges

Two behavioral challenges, the Paced Auditory Serial Addition Task (PASAT) and mental arithmetic task, were presented in a counterbalanced order. Participants performed the PASAT for 8 min (Gronwall, 1977). This task is a widely used neuropsychological measure used to assess attention, concentration, working memory, and information processing speed (Sherman et al., 1997; Lezak, 1995; Roman et al., 1991). It involves adding consecutive numbers as they are presented on an auditory tape and the participant responds with the accurate sum. The participant must sum each number

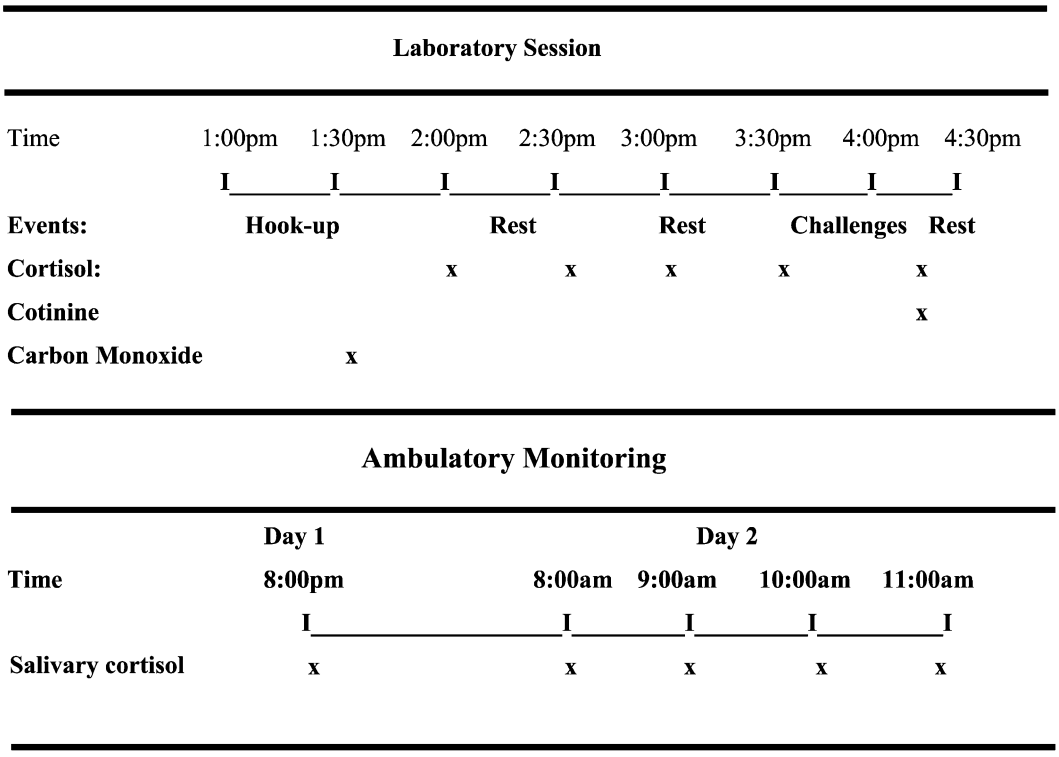

Fig. 1. Outline of the study protocol showing times when cortisol, cotinine, and CO samples were collected.

with the digit presented immediately before it. Four trials of the PASAT were used with different lengths of the interstimulus interval (Sherman et al., 1997). The version used in this experiment included 200 items and the interstimulus intervals of the four trials were 2.4, 2.0, 1.6, and 1.2 s. Measures obtained from the PASAT included the total number of correct responses, the total number of incorrect responses, and the omitted blank responses on each trial.

The mental arithmetic task required continuously adding the digits of a three-digit number and adding the sum to the original number (al'Absi et al., 1997). When a mistake was made, the participant was asked to go back to the previous correct number.

4. Dependent measures

4.1. Biochemical variables

Five saliva samples were collected during each laboratory session, before and after performing the behavioral challenges to assay for cortisol. A single saliva sample was also collected at the end of each session to assay for cotinine. In addition to the laboratory sessions, a subset of the sample (eight men and eight women) collected two sets of five saliva samples over 18 h of abstinence or ad libitum smoking. Samples were collected at approximately 8:00 p.m. the night before and at approximately 8:00, 9:00, 10:00, and 11:00 a.m. of the morning before each laboratory session (see Fig. 1). Sample collection was accomplished by providing 1–2 ml of saliva using cotton dental rolls held in the mouth until saturated and collected into a plastic tube (Salivette tubes; Sarstedt, Rommelsdorf, Germany). Samples were stored in −70 °C until they were assayed. The cortisol assay is a direct modification of commercially available kits using a time-resolved fluorescence immunoassay (Dressendorfer et al., 1992). Cotinine concentrations in saliva were measured by gas chromatography with nitrogen–phosphorus detection (Jacob et al., 1981).

4.2. Cardiovascular measures

Systolic and diastolic BP and heart rate (HR) were obtained using a Dinamap oscillometric monitor (Critikon, Tampa, FL). Data were obtained every 3 min during the rest period, and every 2 min during the behavioral challenges. Cardiovascular measures collected during baseline, the PASAT, the mental arithmetic task, and recovery were averaged to obtain respective values.

4.3. Subjective measures

Participants completed a self-report measure that included a list of symptoms derived from the DSM-IV list of withdrawal symptoms (American Psychiatric Association, 1994), from the Hughes–Hatsukami's Tobacco Withdrawal Symptom Checklist (WSC) (Hughes and Hatsukami, 1986), and from a subjective state scale we have used and found to be sensitive to effect of laboratory behavioral challenges (al'Absi et al., 1994). Items included the following: tension/anxiety, sadness/depression, irritability, anger, difficulty concentrating, restlessness, boredom, confusion, and impatience. Physical symptoms were headache, hunger, tremor, and drowsiness. Additional items measured how calm, content, in control, interested, and cheerful participants felt. Each item referenced a seven-point scale anchored by the end points *Not at All* and *Very Strong*. Participants marked the scale at the point that best described how they felt during the previous 30 min. This measure was administered at the beginning of each session and before and after performing the challenges. A similar rating scale was used to measure the desire to smoke.

During the screening session, participants completed the Fagerström Test of Nicotine Dependence (FTND) (Heatherton et al., 1991) that was used to assess nicotine dependence. Participants also completed the 10-item version of the Perceived Stress Scale (PSS) (Cohen et al., 1983), the Center for Epidemiologic Studies Depression (CES-D) Scale (Radloff, 1977), and the State–Trait Anxiety Inventory (Trait Form; STAI) (Spielberger et al., 1970) to assess perceived stress, depression, and anxiety, respectively.

5. Data analysis

Dependent variables were salivary cortisol, systolic and diastolic BP, HR, reported desire to smoke, withdrawal symptoms, salivary cotinine, and performance measures. Repeated multivariate analyses of variance (MANOVA) were conducted to evaluate cardiovascular, cortisol, and

Table 1
Participant characteristics

	Women ($n=15$)	Men ($n=15$)	P
Age (years)	26 (11.3)	23 (6.1)	n.s.
Height (in.)	66 (0.54)	71 (0.54)	.001
Weight (lb)	148 (6.5)	172 (6.5)	.02
Education (years)	14 (0.49)	14 (0.49)	n.s.
Physical activity (h/week)	2.8 (0.74)	3.4 (0.75)	n.s.
Caffeine (daily servings)	3.7 (0.85)	4.1 (0.85)	n.s.
CO at screening (ppm)	20 (3.9)	18 (2.6)	n.s.
Cigarettes/day	21 (2.3)	18 (2.3)	n.s.
Years smoking at current rate	5.0 (1.6)	3.0 (1.5)	n.s.
FTND	5.5 (0.46)	5.1 (0.46)	n.s.
PSS	14.3 (1.6)	13.0 (1.7)	n.s.
Depression (CES-D)	13.0 (2.5)	10.3 (2.6)	n.s.
Anxiety trait (STAI)	35 (2.3)	34 (2.4)	n.s.

Entries show mean (S.E.M.); CO, carbon monoxide (parts per million); FTND, Fagerström Test of Nicotine Dependence; CES-D, Center for Epidemiologic Studies Depression Scale; STAI, State–Trait Anxiety Inventory (Trait Form).

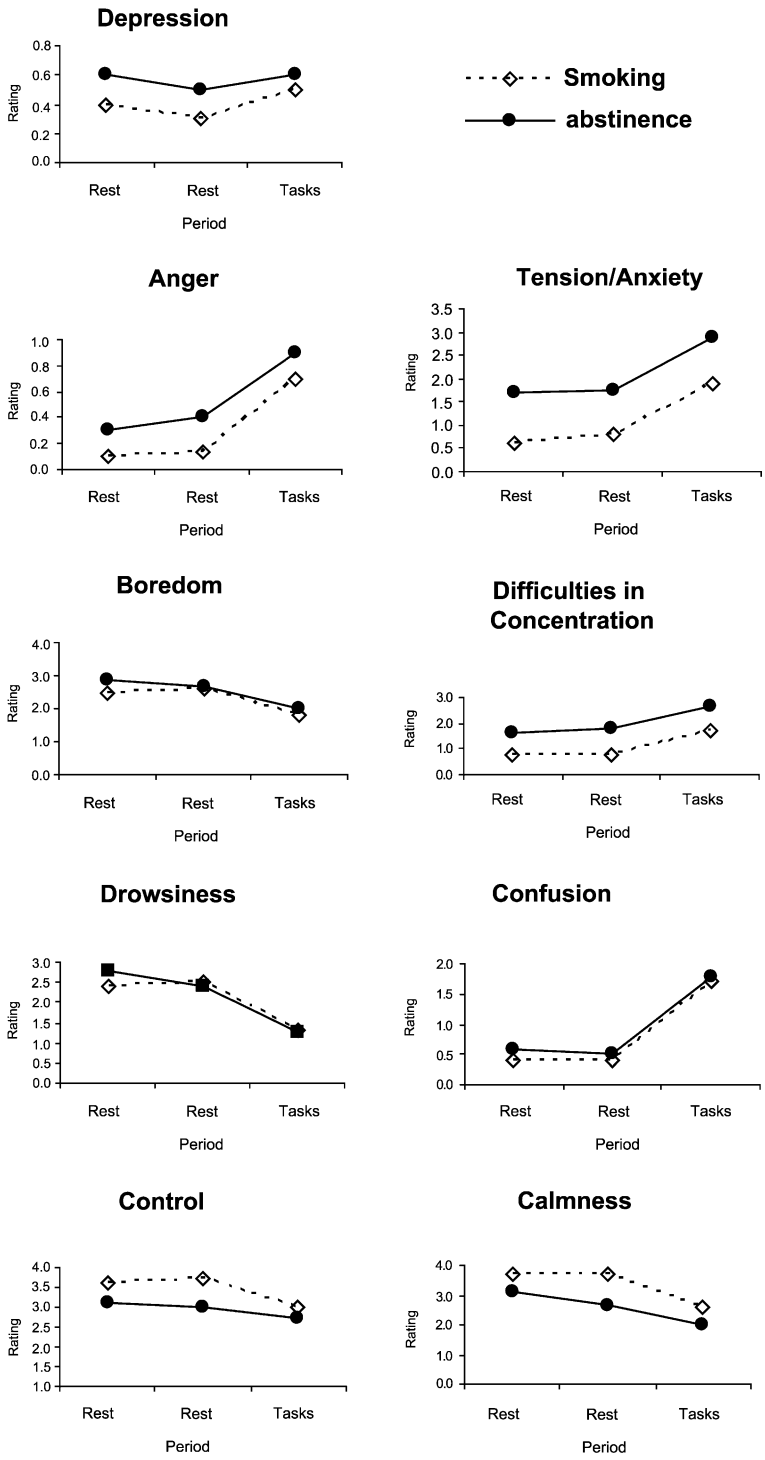

Fig. 2. Mean withdrawal and mood reports during baseline rest and following the behavioral challenges.

self-report data. These analyses included gender as a between-subject factor and two within-subject factors: Conditions (abstinence and ad libitum smoking) and Sampling Times. Salivary cotinine and performance measures were compared across conditions using ANOVA. All the analyses used Wilk's lambda correction to test sampling time effect and to correct for repeated measures.

6. Results

6.1. Participant characteristics

Table 1 shows demographic and smoking variables. Men and women were of comparable age, level of education, physical activity, number of hours of sleep, and had similar

CO levels (range = 5–43 ppm) during screening and on both days, F's(1,28) < 1.2, P's > .28). Scores on the FTND, PSS, CES-D, and STAI were comparable in men and women (P's > .20).

6.2. Withdrawal symptoms

During the abstinence session, participants reported greater anxiety, depression, anger, irritability, impatience, difficulties in concentrating, and drowsiness, and they reported being less calm and less content relative to the ad libitum smoking condition, [F's(1,27)>4.3, P's < .5]. Women reported being less calm and less in control than men on both days [F's(1,27)>4.1, P's < .05]. Repeated assessment of withdrawal before and after the challenges indicated that the behavioral challenges produced significant increases in reported anxiety, depression, anger, confusion, and difficulties in concentration, as depicted in Fig. 2 [F's(2,26)>5.8, P's < .01].

6.3. Desire to smoke

Participants reported stronger desire to smoke in the abstinence condition than in the ad libitum condition [$F(1,27) = 78.3$, $P < .0001$]. Women reported greater desire to smoke in both conditions than men [$F(1,27) = 4.4$, $P < .05$] (see Fig. 3). Analyses using the repeated measurement of the desire to smoke obtained before and after the challenges showed increases in the desire to smoke following the behavioral challenges [$F(2,26) = 35.2$, $P < .0001$]. Furthermore, the desire to smoke showed a progressive increase across time during the ad libitum condition but tended to be greater and more stable throughout the abstinence condition [$F(2,26) = 5.5$, $P < .01$]. This increase was also more pronounced in women, as indicated by a significant Gender × Period interaction [$F(2,26) = 3.83$, $P < .05$].

Fig. 3. Mean reported desire to smoke and standard error of the mean during baseline, rest, and the behavioral challenges. Women reported greater increases in their desire to smoke following the behavioral challenges in the smoking condition (P's < .05).

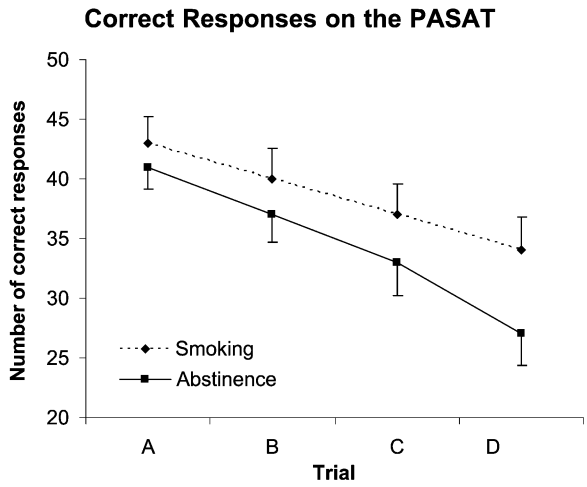

Fig. 4. Cognitive performance on the PASAT during ad libitum smoking and abstinence conditions. Significant deterioration in performance was noted in the abstinence condition ($P < .001$).

6.4. Performance measures

Participants exhibited worse performance on the PASAT task during the abstinence than during the ad libitum condition, as demonstrated by fewer correct responses and greater number of omitted blank responses [F's(1,27) >11.3, P's < .001] (see Fig. 4). On the mental arithmetic task, participants also produced fewer correct answers and had fewer total attempts completed in the abstinence than in the ad libitum condition [F's(1,27) > 4.6, P's < .05]. No gender differences were found in any of these performance parameters ($F < 1$).

6.5. Biochemical measures

6.5.1. Cotinine and CO

As expected, salivary cotinine was greater in the ad libitum than the abstinence condition [$F(1,22) = 51.2$, $P < .0001$] (see Fig. 5). Men had greater cotinine on both days than women [$F(1,22) = 6.4$, $P < .05$]. It should be noted that significant cotinine concentrations were present in the abstinence condition (90.8 and 152.9 ng/ml for women and men, respectively). These values were about 50% less than concentrations in the ad libitum condition, however. Considering that abstinence was for 18 h, the reduction is consistent with data on cotinine half-life (Curvall et al., 1990) and confirms compliance with the smoking abstinence restriction. Expired CO levels were smaller in the abstinence condition than in the ad libitum condition (6.7 and 27.3 ppm for abstinence and ad libitum smoking conditions, respectively) [$F(1,24) = 81.5$, $P < .0001$].

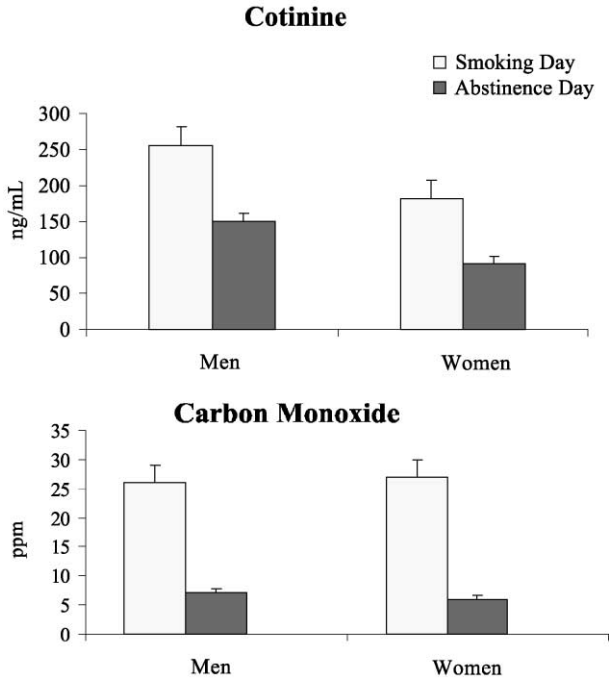

Fig. 5. Cotinine and CO measures obtained after ad libitum smoking or abstinence. All measures were greater in the ad libitum than the abstinence condition (P's < .001).

6.5.2. Cortisol concentrations

As shown in Table 2, participants showed the predicted declines over time in both conditions [$F(4,23) = 8.8$, $P < .0001$]. Men had greater cortisol concentrations than women across conditions [$F(1,26) = 4.8$, $P < .05$]. Salivary cortisol concentrations across the 18 h on both conditions showed the expected diurnal fluctuations [$F(4,11) = 6.6$, $P < .01$], but no differences between the ad libitum and abstinence conditions were found (F's < 1.1).

Table 2
Cortisol concentrations during ad libitum smoking and abstinence conditions

	Women		Men	
	Smoking	Abstinence	Smoking	Abstinence
Laboratory assessment				
Sample 1 (rest)	7.8 (1.5)	11.4 (2.3)	12.1 (1.4)	11.9 (2.2)
Sample 2 (rest)	6.0 (0.9)	8.2 (1.4)	9.4 (0.8)	9.5 (1.3)
Sample 3 (rest)	5.2 (0.8)	5.8 (0.8)	7.9 (0.7)	7.2 (0.8)
Sample 4 (rest)	4.2 (1.1)	5.2 (0.8)	7.4 (1.0)	6.8 (0.8)
Sample 5 (postchallenge)	4.4 (0.8)	4.9 (0.7)	6.6 (0.7)	7.4 (0.6)
Ambulatory assessment				
8:00 pm	9.6 (2.1)	8.0 (2.5)	6.4 (2.1)	8.1 (2.4)
8:00 am	23.6 (4.1)	16.3 (3.7)	21.4 (4.1)	18.3 (3.7)
9:00 am	20.9 (3.1)	18.0 (4.7)	12.7 (3.1)	20.9 (4.7)
10:00 am	11.8 (1.9)	14.4 (2.9)	12.6 (1.9)	13.8 (2.9)
11:00 am	11.2 (2.9)	9.6 (2.2)	15.7 (2.9)	13.6 (2.2)

Entries show means (S.E.M.) of cortisol concentrations. Laboratory assessment was conducted on two afternoons, after 18-h ad libitum smoking or abstinence (see Fig. 1 for details). Ambulatory assessment was completed in 16 participants during ad libitum or abstinence (see text for details).

To further evaluate cortisol concentrations in these smokers, we compared their resting cortisol levels from both conditions with data obtained from nonsmokers ($n = 24$ women and 18 men) enrolled in another ongoing protocol. Nonsmokers had completed two sessions (a stress session involving an extended public-speaking stressor and a control rest session). Data obtained from the rest sessions were used here. All sessions were completed at the same time of the day, and intervals among samples were comparable to the present study. We compared the prechallenge four cortisol samples obtained in each condition in the present study with the four cortisol samples obtained from nonsmokers. Each smoking condition was compared separately with the nonsmoking control group. During both conditions (ad libitum smoking and abstinence), smokers demonstrated significantly greater cortisol concentrations than nonsmokers [F's(1,66) > 13.2, P's < .001]. Cortisol concentrations declined across samples in both groups [F's(3,63) > 18.6, P's < .0001]. No significant Group × Sample interaction was found, indicating that the observed decline in cortisol concentrations was similar in both groups.

6.6. Cardiovascular responses

Table 3 shows BP and HR levels during baseline and during each of the behavioral challenges. Both systolic and diastolic BP showed significant increases in response to the behavioral challenges [F's(3,25) > 18, P's < .0001]. Furthermore, while baseline systolic BP levels were similar across days, a greater systolic BP response was observed in the abstinence condition, as shown by a significant Condition × Time interaction [$F(3,25) = 4.24$, $P < .01$]. Subsequent comparison of average response scores indicated greater systolic BP responses to the behavioral challenges in the abstinence than in the ad libitum condition [$F(1,27) =$

Table 3
Cardiovascular measures

	Women		Men	
	Smoking	Abstinence	Smoking	Abstinence
SBP (mm Hg)				
Baseline	107 (3.1)	106 (3.2)	113 (2.8)	111 (3.1)
PASAT	113 (3.0)	117 (3.6)	122 (2.9)	124 (3.5)
Mental arithmetic	111 (3.9)	115 (3.6)	122 (3.8)	125 (3.5)
DBP (mm Hg)				
Baseline	66 (2.1)	67 (1.9)	62 (2.0)	59 (1.8)
PASAT	74 (2.3)	74 (2.5)	71 (2.3)	70 (2.4)
Mental arithmetic	73 (2.4)	73 (2.8)	73 (2.4)	69 (2.6)
HR (beats/min)				
Baseline	74 (2.4)	68 (2.5)	65 (2.4)	61 (2.4)
PASAT	80 (2.0)	74 (2.5)	74 (1.9)	71 (2.4)
Mental arithmetic	78 (2.0)	72 (2.4)	71 (2.0)	69 (2.3)

Entries show mean (S.E.M.) of cardiovascular measures before (baseline) and during the PASAT and mental arithmetic. SBP, systolic blood pressure (mm Hg); DBP, diastolic blood pressure (mm Hg); and HR, heart rate (beats/min).

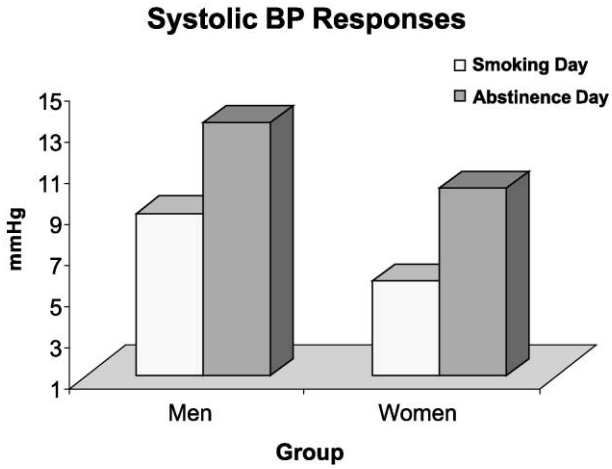

Fig. 6. Mean systolic BP responses to the behavioral challenges. Participants showed greater responses to the behavioral challenges in the abstinence than the ad libitum smoking conditions ($P < .01$).

8.9, $P < .005$] (Fig. 6). There was a trend towards greater overall diastolic BP levels in men during the ad libitum condition relative to abstinence but similar levels in both conditions in women, as indicated by a Gender × Condition interaction trend [$F(1,27) = 4.1$, $P = .054$].

Participants had higher HR in the ad libitum than in the abstinence condition [$F(1,27) = 17.1$, $P < .0001$] and women had higher HR than men [$F(1,27) = 4.7$, $P < .05$]. The challenges significantly increased HR [$F(3,25) = 16.7$, $P < .0001$], but no difference was obtained in HR responses to the behavioral challenges between ad libitum and abstinence conditions or between men and women (F's < 1.0).

7. Discussion

Short-term abstinence from smoking produced significant negative mood, led to deterioration in cognitive performance, and enhanced systolic BP responses to behavioral challenges. Although smoking history and levels of nicotine addiction were comparable, women reported more intense withdrawal symptoms than men. No changes were noted in cortisol concentrations during abstinence in response to the laboratory challenges or during the 18-h ambulatory measurement, although smokers in both conditions showed greater cortisol concentrations compared with a separate nonsmoking group. The behavioral challenges produced significant systolic and diastolic BP, HR, and mood changes, demonstrating the effectiveness of these challenges in producing significant psychophysiological changes. The decreased HR, in combination with the reduced cotinine concentrations and CO during the abstinence condition, corroborates the internal validity of the abstinence manipulation. As the sample in the study was comprised of mostly young adult smokers, further work will need to address this question with older smokers.

The present study confirms an enhanced desire to smoke under acute laboratory challenges, especially in women. These findings are consistent with earlier studies on effects of acute challenges (Perkins and Grobe, 1992) and effects of short-term abstinence (Perkins et al., 1994). It has been proposed that effects of abstinence and the stress-related increases in the desire to smoke may increase risk for smoking relapse (Carey et al., 1993; Shiffman et al., 1996b; Parrott, 1998; Hall et al., 1993; Glassman et al., 1988). Cohen and Lichtenstein (1990) found that smokers who failed to quit or relapsed after a short period reported high levels of stress prior to quitting and 1, 3, and 6 months after cessation. Persons who quit and maintained abstinence for the entire 6-month period reported a gradual decrease in stress levels. Decreased reported stress was associated with changes in status from smoking to abstinence, and increased reported stress was associated with changes from abstinence to smoking status (Cohen and Lichtenstein, 1990). Shiffman et al. (1996b) asked participants to record their first lapse within minutes of its occurrence. Participants whose lapses were precipitated by stress moved faster to a full relapse than those whose lapses were triggered by eating or drinking.

Biobehavioral mechanisms that mediate these effects of stress still need to be elucidated. It has been proposed that stress-induced physiological changes exacerbate nicotine withdrawal symptoms and enhance risk for relapse in abstinent smokers (Emmons et al., 1989; Swan et al., 1993). However, data supporting this hypothesis are not available (Gilbert, 1995). Our study partially supports this hypothesis and indicates that behavioral and performance variables might be influenced by abstinence more reliably than physiological responses to stress. For example, nicotine withdrawal seems to contribute to performance deterioration on attention and memory tasks as suggested by the present and previous studies (Ernst et al., 2001; West and Hack, 1991; Bell et al., 1999). Such deterioration during abstinence, combined with the greater reported distress, may contribute to perceived benefits from smoking (West, 1994), enhancing the reinforcing value of smoking after abstinence (Perkins et al., 1994).

The present study confirms gender differences in the reported desire to smoke, in spite of similar levels of nicotine addiction and smoking history. It is likely that this enhanced desire reflects greater negative affect experienced by women in this laboratory setting, due to uncertainty and tension. As indicated, women reported less control and less calmness than men in this setting. This finding agrees with a current line of research demonstrating that women use smoking as a method of coping with negative affect (Pomerleau et al., 1991; Perkins, 1999), and that predisposition for depression contributes to smoking in women more than in men (Frederick et al., 1988; Lee and Markides, 1991). Research has also suggested that women exhibited greater reactivity to smoking-related cues than men (Tiffany and Hakenewerth, 1991) and are less likely to maintain long-term abstinence (Ward et al., 1997).

Absence of effects of abstinence on salivary cortisol production during the ambulatory monitoring period and in response to the laboratory challenges does not support the hypothesis that abstinence is associated with enhanced adrenocortical activity. This finding is consistent with one earlier study (Benowitz et al., 1984), but in disagreement with another (Hughes et al., 1988). Hughes et al. (1988) assessed the effect of nicotine withdrawal on cortisol responses to the Dexamethasone Suppression Test (DST) in 10 smokers who were attempting to quit. They found greater cortisol levels during abstinence before the DST, compared with levels obtained during ad libitum smoking. Another study (Pickworth et al., 1996) found that changes in adrenocorticotropin (ACTH) and cortisol levels in individual participants correlated with reported withdrawal symptoms (Pickworth et al., 1996). These studies, however, were conducted on a small number of men, did not collect multiple samples for cortisol measurement, and did not assess effects of acute challenges.

In summary, this study demonstrates that smokers showed enhanced systolic BP responses to brief stressors, showed deterioration in performance and mood, and reported greater desire to smoke after short-term abstinence from smoking compared with ad libitum smoking. Women generally reported greater desire to smoke than men. It is possible that significant stress-like effects of abstinence would increase vulnerability to relapse when exposed to stressful events.

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