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"Paradoxical" Effects of Smoking on Subjective Stress Versus Cardiovascular Arousal in Males and Females

KENNETH A. PERKINS,[1] JAMES E. GROBE, CAROLYN FONTE AND MICHAEL BREUS

Western Psychiatric Institute & Clinic, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213

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PERKINS, K. A., J. E. GROBE, C. FONTE AND M. BREUS. *"Paradoxical" effects of smoking on subjective stress versus cardiovascular arousal in males and females.* PHARMACOL BIOCHEM BEHAV 42(2) 301-311, 1992.—Cigarette smoking has sometimes been found to decrease subjective stress while simultaneously increasing cardiovascular arousal, contrasting effects referred to as the "nicotine paradox." The present study assessed acute effects of cigarette smoking on subjective stress vs. cardiovascular arousal in minimally deprived male and female smokers who smoked (n = 16) or sham smoked (unlit cigarette, n = 15) and a comparison group of male and female nonsmokers (n = 12) who sham smoked only. All subjects participated in two sessions (high- or low-challenge computer task) in which they smoked or sham smoked prior to each of two 20-min task trials. Results showed reduced subjective stress in smoking smokers compared with sham-smoking smokers during the high- but not low-challenge task. However, this stress reduction occurred only immediately after smoking and dissipated midway through each trial. In males, smoking appeared to reduce stress below that of nonsmokers, while smoking in females attenuated stress only partially to the level of nonsmokers. In contrast with the attenuated stress effects, cardiovascular arousal (especially heart rate) was increased immediately after smoking during both tasks and did not appear to be directly related to subjective changes. These findings suggest that the stress-reducing effects of smoking may be transient, situationally specific, partly gender dependent, and dissociated from the effects of smoking on cardiovascular arousal.

Subjective stress Cardiovascular arousal Behavioral challenge Smoking Gender

TOBACCO smoking is anecdotally reported to reduce subjective stress and increase feelings of calm, effects that may be important in reinforcing tobacco use. Yet, empirical support for the stress-reducing effects of smoking is surprisingly mixed. Although several studies have shown reduced subjective stress due to smoking during a psychological challenge [e.g., (7,13,23,31)], almost as many have found no such effect [e.g., (4,8,27)]. Methodological differences among these studies, such as temporal proximity of smoking to subjective assessment, could potentially explain their different findings. For example, Jarvik et al. (13) found anxiety relief, as measured by the "state" version of the State-Trait Anxiety Inventory (STAI), due to smoking during anticipation of a stressful anagram task and a cold pressor task, but this pretask smoking had no effect on subsequent STAI values obtained after each task. Smoking also had no effect on the STAI before or after the other two tasks used in this study (uncontrollable white noise and an auditory vigilance task), further demonstrating equivocal evidence of stress reduction due to smoking.

One intriguing aspect of the relationship between smoking and stress is that, while smoking may attenuate subjective indices of stress, it simultaneously increases physiological responses usually associated with heightened stress, such as cardiovascular arousal. This contrast between subjective vs. physiological responses to smoking during stress has been called the "nicotine paradox" (5,17). Nesbitt (17) found that smoking prolonged endurance to electric shock pain, implying decreased "emotional responding" to the stressor, while simultaneously increasing heart rate, a physiological effect often associated with increased "emotional responding." Furthermore, the significant correlation observed between pain endurance and heart rate was offered as an indication that the cardiovascular effects of smoking may actually mediate the subjective stress reduction (17). The interpretation of these specific results is clearly open to debate (5). Nevertheless, in addition to providing an interesting research question concerning mechanisms responsible for the calming effects of smoking the disparity between acute subjective and cardiovas-

[1] Requests for reprints should be addressed to Kenneth A. Perkins, Ph.D., Western Psychiatric Institute & Clinic, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213.

cular effects of smoking and nicotine during stress may have implications for the relationship between smoking and coronary heart disease (2).

In addition to the mixed empirical support for stress reduction by smoking, relatively little research has examined possible gender differences in subjective effects of smoking during stress. Indeed, we are aware of *no* controlled lab study that has specifically compared male and female smokers on subjective responses to smoking during stress, an omission common to most basic research on smoking and nicotine (24). This absence of studies on possible gender differences is surprising since there is some evidence that males and females may tend to smoke for different "reasons" [e.g., negative affect reduction in females vs. subjective stimulation for males, (12)]. It has also been suggested that female smokers may have greater cardiovascular responses to smoking during stress (1) relative to male smokers (15).

Moreover, there has been little consideration of the notion that the subjective stress-reducing effect of smoking is not a ubiquitous "property" of smoking but may be specific to the ongoing level of subjective arousal or environmental challenge (10). For example, it has recently been shown that magnitude of subjective effects of smoking and nicotine may depend on a predrug baseline subjective state (21), suggesting that smoking may have different subjective effects depending on the momentary subjective state of the smoker. Manipulation of intensity of environmental stressor may reveal differential subjective effects of smoking depending on the degree of arousal or challenge elicited (6). However, it is not clear that the cardiovascular effects of smoking are similarly situationally dependent [e.g., (20,23)], suggesting a dissociation between the subjective and cardiovascular effects of smoking rather than the causal inverse relationship indicated by the nicotine paradox (17).

The present study explored the apparently paradoxical relationship between the subjective and cardiovascular effects of smoking in briefly deprived male and female smokers under conditions of high vs. low behavioral challenge. This was designed as an initial study manipulating smoking exposure to obtain subjective stress reduction vs. cardiovascular arousal under somewhat naturalistic conditions (i.e., cigarette smoking) as a prelude to subsequent research on the possible mechanisms involved (i.e., nicotine per se vs. nonnicotine constituents of tobacco smoke). Although it has commonly been assumed that nicotine intake explains the subjective effects of smoking, this has not been conclusively demonstrated and there is increasing evidence that nonnicotine influences may be important [e.g., (14)]. The goals of this study were to demonstrate the nicotine paradox in female as well as male smokers and determine whether it may be present under conditions of high but not low challenge. Notably, inclusion of the low-challenge condition also provided for determination of whether the subjective effects of smoking were specifically stress reducing, in which case effects should be observed only during high and not low challenge, or were instead the result of a less situationally specific influence such as tobacco withdrawal relief, in which case similar effects should be observed between conditions regardless of behavioral challenge. Furthermore, a comparison group of nonsmokers was included to ascertain whether smoking provides enhanced subjective relief in smokers (i.e., reduction in stress *below* that of nonsmokers) or whether smoking merely "normalizes" subjective state in smokers briefly deprived of tobacco [i.e., reduction in stress equal to that of nonsmokers (9)].

METHOD

Subjects

Potential subjects were interviewed by phone concerning smoking history, as well as use of illegal drugs. Smokers were defined as those smoking at least 15 cigarettes per day for at least 1 year, while nonsmokers were those with a lifetime exposure of less than 20 cigarettes. Subjects with other smoking histories or who admitted to drug use were excluded. Informed consent was obtained from all subjects after the nature and consequences of their participation were explained. Thirty-two smokers were randomly assigned to smoke or sham-smoke groups while all 12 nonsmokers sham smoked. However, one female smoker in the sham-smoke group was discarded after admitting to recent drug abuse during a screening interview for a subsequent study, leaving seven females in that group. See Table 1 for subject demographic and smoking history characteristics, including a measure of tobacco dependence [Fagerstrom Tolerance Questionnaire, (3)]. There were no significant differences across groups or gender on any of these characteristics, although number of years smoking was marginally longer in males vs. females, $F(1, 27) = 3.23, p < 0.10$.

Tasks

High challenge. The high-challenge task consisted of a computerized memory recall task running concurrently with a secondary reaction time task. Subjects were presented with a sequence of digits (1–4) in random order on a monitor and were required to immediately repeat the sequence in either the same or reverse order by responding on the four keys of a computer keypad using their preferred hand (similar to "Simon Says"). Subjects were informed by computer instructions if sequences were to be repeated in the same or reverse order, and orders were presented randomly but with equal frequency during each trial. Difficulty of the task (i.e., number of digits in each sequence) was manipulated by the computer to ensure approximately 40% success for all subjects regardless of ability to do the task. Subjects received $.50 for each correct response and had $.25 deducted for each incorrect response. Superimposed on this task was a reaction time task in which subjects had to respond quickly on one of the keys whenever any of the four digits (1–4) briefly appeared in a different location on the monitor (approx. once per min). The time criterion for this secondary task was determined by the computer to ensure approximately 50% success for all subjects regardless of ability. Subjects received $1.00 for a correct response to the secondary task and were penalized $1.00 for an incorrect or slow response, in addition to the monetary reward provided for the primary task. The mean ± SE amount of money received from this task was $8.52 ± 0.39. Task success was made equal across subjects to rule out smoking-induced improvement in task performance as a means to explain attenuation of subjective stress by smoking (30). Thus, the objective was to examine direct rather than indirect effects of smoking on subjective stress.

Low challenge. The low-challenge task consisted of simply detecting target numbers (1–4) from among nonnumerical symbols presented singly very slowly on the monitor (one every 4 s). Numbers occurred approximately once/min. Subjects received $.05 for each correct response and were penalized $.05 for each incorrect response, but there was no incentive for speed of responding. The mean amount of money received

TABLE 1

MEAN (± SE) CHARACTERISTICS OF SUBJECT SAMPLES

Group	n	Age (yrs)	Fagerstrom Score	Cigarettes per Day (No.)	Years Smoking	Brand Nicotine Content (mg)
Smokers—smoking						
Males	8	22.4	5.4	21.6	7.1	0.75
		(1.6)	(0.7)	(1.6)	(1.2)	(0.05)
Females	8	21.0	4.1	19.8	5.6	0.69
		(1.2)	(0.6)	(1.9)	(0.9)	(0.08)
Smokers—sham						
Males	8	21.1	5.6	20.5	4.6	0.92
		(0.6)	(0.8)	(2.0)	(0.8)	(0.09)
Females	7	20.0	6.0	21.4	4.8	0.86
		(0.9)	(0.5)	(2.6)	(0.5)	(0.12)
Nonsmokers						
Males	6	21.8	–	–	–	–
		(1.4)	–	–	–	–
Females	6	21.3	–	–	–	–
		(1.8)	–	–	–	–

from this task was $1.80 ± 0.02. Only two subjects made a total of two incorrect responses of over 1,000 responses by all 43 subjects during the course of this study,confirming the ease of this task.

Subjective and Cardiovascular Measures

Subjective measures consisted of both the "Stress" and "Arousal" subscales of the Stress–Arousal Checklist [SACL, (16)], the "state" version of the STAI (28), and 100-mm visual analog scales (VAS) of "Relaxed" and "Annoyed." The less familiar SACL has been used in various psychophysiological studies of stress and arousal (16). The Stress subscale consists of 19 adjectives directly or inversely related to stress (e.g. "tense," "calm"), each with four response choices (definitely feel, feel slightly, cannot decide, definitely do not feel). The Arousal subscale consists of 14 adjectives similarly related to subjective arousal (e.g., "alert," "tired"). Each response was scored 0–3, with 3 being in the direction of maximal stress or arousal (potential maximum scores = 57 and 42, respectively).

Heart rate (HR) and systolic (SBP) and diastolic blood pressure (DBP) were obtained automatically by a Dynamap blood pressure recorder (Critikon Inc., Tampa, FL). HR is assessed by the Dynamap by the counting of the pulse rate at the brachial artery during the period of blood pressure measurement (approx. 30 s).

Standardized Smoking/Sham-Smoking Exposure

The smoking/sham-smoking procedure involved computerized instructions presented on a video monitor in which subjects puffed on cue using a lit or unlit cigarette of their preferred brand once every 20 s for 2.5 min (total of 8 puffs). Nonsmokers puffed on an unlit Marlboro Light cigarette. This procedure was designed to standardize smoke exposure among smoking smokers and control for potential subjective effects of repeated deep breathing with or without smoke intake (i.e., puffing). Use of smokers' preferred brand was included to increase generalizability of results to the natural environment (e.g., include potential subjective influences cued by specific taste of brand). Expired-air carbon monoxide (CO) was employed to verify consistency of smoke intake among smoking smokers, as well as differential smoke exposure between smoking smokers and the sham-smoking groups.

Procedure

Subjects participated in two sessions, one involving the high- and the other the low-challenge task, with the order of sessions counterbalanced between subjects. Subjects were instructed to maintain their usual pattern of smoking and eating prior to the afternoon session on both days. Upon arriving at the lab, smokers in either group immediately smoked a cigarette ad lib. Then, all subjects read quietly for 1 h prior to the beginning of the session to induce minimal deprivation in the smokers (approx. 1.5 h prior to task trials). At the beginning of each session, the blood pressure cuff was placed on the upper portion of their nonpreferred arm. Subjects then rested quietly for 10 min and completed each subjective measure (resting baseline). Cardiovascular measures were obtained just before the subjective measures. After being introduced to the task assigned for that day (high vs. low challenge), subjects engaged in a 5-min baseline trial with the task under incentive conditions and completed the task baseline subjective measures. Cardiovascular measures were obtained 2 and 4 min into the 5-min trial.

Subjects subsequently engaged in two task trials, each 20 min in length. Depending on group assignment, each trial began with smoking or sham smoking according to the procedure described above. Then, subjects completed subjective measures and engaged in the task for two 5-min blocks, separated by an additional subjective assessment at the midpoint of the trial to determine the persistence of the subjective effects of smoking. Cardiovascular measures were obtained 2 and 4 min into each of the two 5-min task blocks for each trial. Expired-air CO was obtained from all subjects at the beginning of each session and after the initial subjective assessment following each exposure to smoking or sham smoking. Thus, the 20-min sequence for each of the two trials was:

smoke/sham (2.5 min), subjective assessment (3 min), CO assessment (0.5 min), task performance plus cardiovascular assessments (5 min), subjective assessment (3 min), task plus cardiovascular assessments (5 min), and preparation for next trial (1 min).

Data Analyses

Resting and task baseline values were analyzed by analyses of variance (ANOVAs) with gender and group (smokers/smoke, smokers/sham, nonsmokers) as between-subjects factors and task (high vs. low challenge) as the within-subjects factor to determine the success of randomization of subjects. The ANOVA of task baseline values was also designed to determine significant differences between tasks to confirm the manipulation of high vs. low challenge (i.e., stress). Analyses of subjective measures first involved an overall multivariate analysis of covariance (MANCOVA) using task baseline trial values as covariates, with gender and group as between-subjects factors and task (high vs. low challenge), trial (2), and period (i.e., 5-min block, two per trial) as within-subjects factors. This significant MANCOVA was followed by similar ANCOVAs for each subjective measure. Cardiovascular responses were each analyzed by ANCOVA. Follow-up comparisons for significant ANCOVAs were performed using Fisher's LSD test (11). To reduce the likelihood of Type I errors due to the number of follow-up comparisons to the higher-order interactions involving trials and periods, those comparisons were considered significant only if $p < 0.01$. Data are presented as mean ± SE.

RESULTS

There was no significant effect of session (day 1 vs. day 2) on each resting and task baseline value. Analyses of expired-air CO confirmed equal smoke exposure between the groups of smokers during the task baseline trials, prior to smoking/sham smoking [24.1 ± 1.4 ppm for smoking smokers vs. 22.9 ± 1.1 ppm for sham-smoking smokers, $F(1, 27) < 1$; CO for nonsmokers was 3.8 ± 0.2 ppm]. Following smoking/sham smoking, CO of smoking smokers was significantly higher than that of sham-smoking smokers, as expected, $F(1, 27) = 25.46$, $p < 0.001$, but CO was similar between the high- and low-challenge tasks for smoking smokers (27.4 ± 1.6 vs. 27.7 ± 1.7 ppm, respectively) and for sham-smoking smokers (18.9 ± 1.1 vs. 17.0 ± 0.9 ppm). There were no differences in CO between male and female smokers [$F(1, 27) < 1$]. Thus, the standardized puffing procedure provided equal smoking exposure between tasks in the smoking smokers, as well as a distinct difference in exposure between the smoking smokers and sham-smoking smokers. In addition, there were no significant differences among groups in the high-challenge task performance, verifying the standardization of task difficulty across subjects.

Subjective Measures

There were no significant differences among groups on subjective measures during resting and task baselines. During the baseline trial with the high-challenge task, subjects reported greater stress [16.5 ± 1.4 vs. 9.2 ± 1.2; $F(1, 37) = 23.44$, $p < 0.001$] and arousal [27.1 ± 1.3 vs. 20.4 ± 1.3; $F(1, 37) = 28.63$, $p < 0.001$], more anxiety [18.5 ± 0.7 vs. 15.1 ± 0.6; $F(1, 37) = 23.84$, $p < 0.001$], being more "annoyed" [24.3 ± 3.5 vs. 11.4 ± 2.8; $F(1, 37) = 15.88$, $p < 0.001$], and being less "relaxed" [49.1 ± 4.0 vs. 67.8 ± 3.6; $F(1, 37) = 25.95$, $p < 0.001$] than during the low-challenge task. Subjective distress was therefore successfully manipulated by use of these different tasks.

Results of the overall MANCOVA of subjective responses revealed no significant main effects of gender or group, but marginally significant effects were observed for task, $F(4, 30) = 2.21$, $p < 0.10$, and group × task, $F(8, 60) = 1.93$, $p < 0.08$. Notably, there were significant effects of trials, $F(4, 34) = 3,29$, $p < 0.03$, and periods, $F(4, 34) = 6.10$, $p < 0.001$, as well as significant interactions of group × period, $F(8, 68) = 2.09$, $p < 0.05$, and task × period, $F(4, 34) = 4.31$, $p < 0.01$. Thus, it was apparent that the temporal proximity of assessment to smoking/sham smoking during one of the tasks was important in determining smoking's effects. The results of subsequent ANCOVAs for each subjective measure are presented below. Data presented in the figures are for males and females combined unless a significant effect of gender was found.

SACL Stress and Arousal. For SACL Stress, there were no significant main effects of group or gender, and no significant interactions of group × gender, group × task, or task × gender. However, the interaction of group × task × gender was significant, $F(2, 36) = 4.00$, $p < 0.05$. As shown in Fig. 1 (top), among females overall stress during the high-challenge task was significantly greater for sham-smoking smokers than for smoking smokers, while stress for nonsmokers was marginally less than that for smoking smokers. There were no significant differences among male groups or among any groups during the low-challenge task.

In terms of the pattern of acute changes within trials, there was a significant effect of period [i.e., 5-min block; $F(1, 37) = 13.84$, $p < 0.001$] and significant interactions of period × group, $F(2, 37) = 4.22$, $p < 0.05$, and of period × task, $F(1, 37) = 14.76$, $p < 0.001$. These effects were due to sharp reductions in stress in smoking smokers immediately after smoking during the high- but not low-challenge task. However, this stress reduction during the high-challenge task largely disappeared by the midpoint of each trial, nearly 10 min after smoking (see Fig. 1, bottom). Among males, stress immediately after smoking/sham smoking was nonsignificantly greater in nonsmokers compared with smoking smokers, while among females stress at these points was significantly less for non smokers compared with smoking smokers.

Interestingly, the main effect of group on SACL Arousal was significant, $F(2, 36) = 6.89$, $p < 0.005$, as smoking smokers reported *greater* subjective arousal compared with sham-smoking smokers and nonsmokers, especially during the low-challenge task, as shown in Fig. 2. The group × task × gender interaction did not reach significance, $F(2, 36) = 2.18$, $p > 0.10$, and there were no other significant main or interaction effects involving gender or group.

STAI anxiety. The main effect of group on STAI Anxiety was only marginally significant, $F(2, 36) = 2.67$, $p < 0.10$, as nonsmokers tended to be less anxious during either task compared with either group of smokers (Fig. 2). There were no other significant main or interaction effects involving gender or group.

VAS annoyed and relaxed. There were no significant main effects of group or gender for either Annoyed or Relaxed (Fig. 2). However, similar to results for SACL Stress (see Fig. 1), smoking acutely influenced Annoyed during high-challenge task trials, depending on temporal proximity of subjective assessment to smoking/sham smoking. These acute effects were demonstrated by a significant main effect of period, F(1,

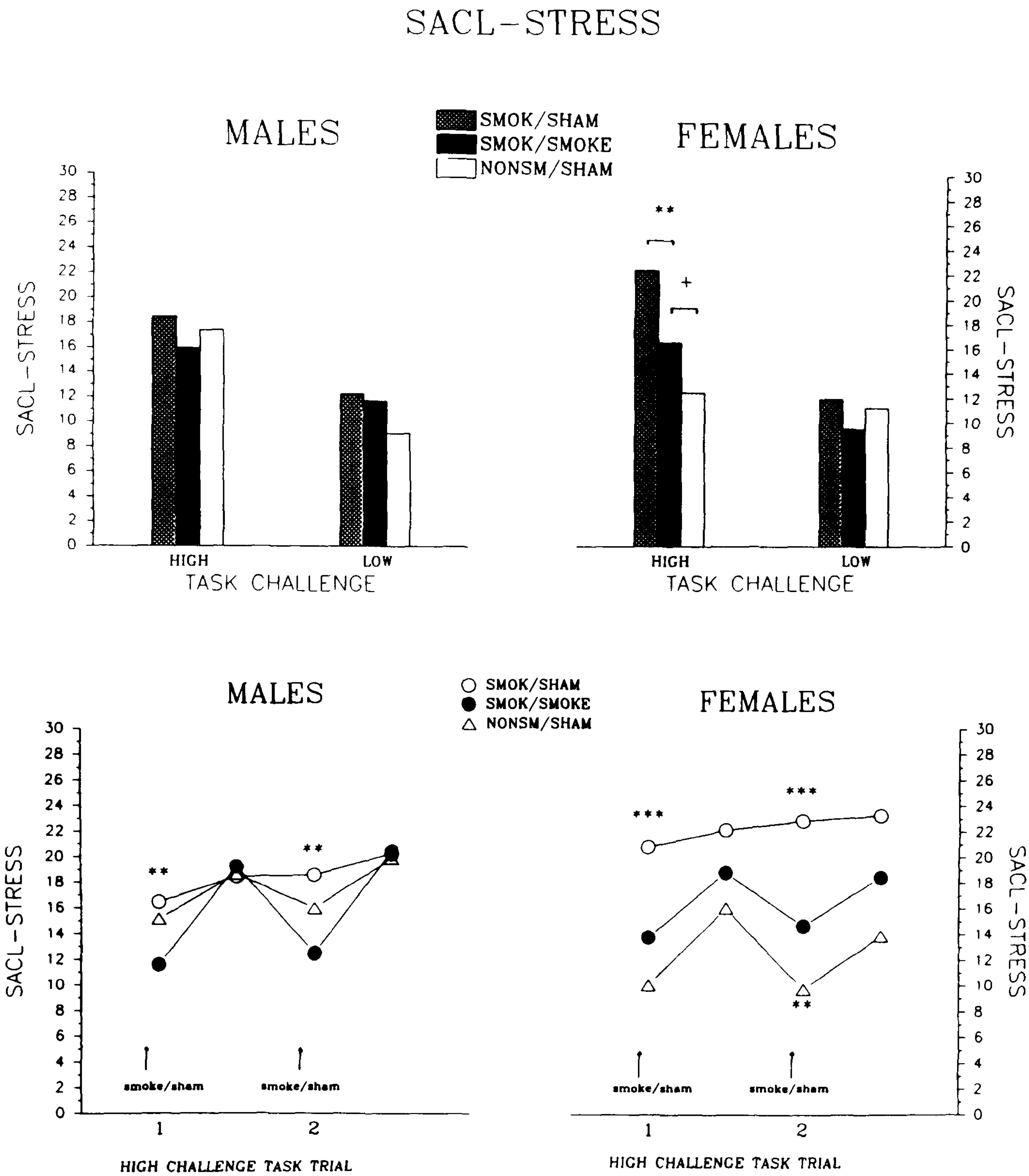

FIG. 1. Overall covariate-adjusted mean subjective stress during the high- and low-challenge tasks (top) and at each assessment point immediately after smoking/sham smoking and midway through each trial of the high-challenge task (bottom) in males and females of each group. $+p < 0.10$, $**p < 0.01$, $***p < 0.001$ for differences from smoking smokers.

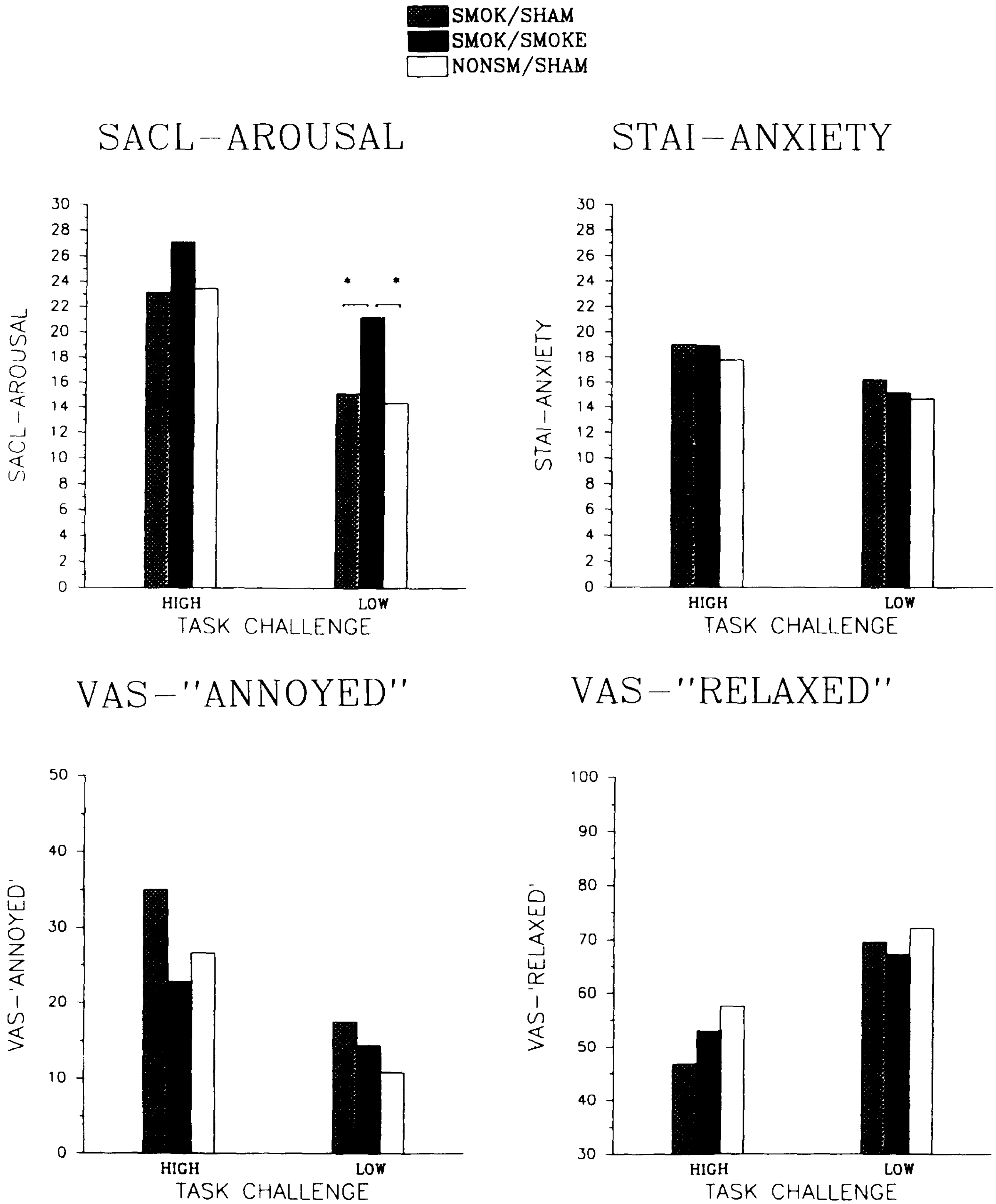

FIG. 2. Overall covariate-adjusted mean subjective responses during the high- and low-challenge tasks for each group. $*p < 0.05$ for differences from smoking smokers.

37) = 14.32, $p < 0.001$, and interactions of period × group, $F(2, 37) = 6.07$, $p < 0.01$, and of period × task, $F(1, 37) = 12.32$, $p < 0.005$. As shown in Fig. 3, smoking smokers were less annoyed than sham-smoking smokers immediately after smoking during the high-challenge task, but this effect was minimal by the midpoint of each trial. There were no differences between smoking smokers and nonsmokers, and there was no such effect of smoking during the low-challenge task.

Similar transient effects of smoking during the high-challenge task were observed for Relaxed, helping to explain the significant interactions of period × task, $F(1, 37) = 6.50$, $p < 0.02$, and of period × task × group × gender, $F(2, 37) = 3.39$, $p < 0.05$. Among males, smoking smokers were more relaxed immediately after smoking during the high-challenge task, compared with sham-smoking smokers (Fig. 3). Among females, however, nonsmokers were more relaxed at the beginning of each trial of this task compared with sham-smoking smokers and smoking smokers. There were no effects of smoking during the low-challenge task.

Cardiovascular Responses

There were no significant differences among groups in resting and task baseline HR, SBP, and DBP. As with the subjective measures, the high-challenge task elicited significantly greater HR [73.4 ± 1.8 vs. 69.8 ± 1.8 BPM; $F(1, 37) = 9.42$, $p < 0.005$], SBP [115.7 ± 1.5 vs. 110.1 ± 1.4 mmHg; $F(1, 37) = 24.36$, $p < 0.001$], and DBP [66.4 ± 1.1 vs. 60.6 ± 1.0 mmHg; $F(1, 37) = 29.89$, $p < 0.001$] during the task baseline trial compared with the low-challenge task.

For HR, there were significant main effects of group, $F(2, 36) = 31.29$, $p < 0.001$, and gender, $F(1, 36) = 4.42$, $p < 0.05$, as smoking smokers showed greater HR compared with other groups, as expected, and females showed smaller HR compared with males (Fig. 4, top). Furthermore, similar to SACL Stress and VAS Relaxed, there were significant main and interaction effects of period, $F(1, 37) = 6.72$, $p < 0.02$, period × group, $F(2, 37) = 4.76$, $p < 0.02$, and period × task, $F(1, 37) = 4.61$, $p < 0.05$. However, in contrast with the immediate reductions in subjective stress due to smoking during the high-challenge task (Fig. 1), noted above, HR was acutely increased immediately following smoking (Fig. 4, bottom). This differential direction of change in subjective stress vs. HR responses following smoking, consistent with the nicotine paradox, was observed for both males and females.

Similar but less pronounced effects of smoking were found for SBP and DBP (not shown). For SBP, significant main effects of group, $F(2, 36) = 10.18$, $p < 0.001$, gender, $F(1, 36) = 5.46$, $p < 0.03$, and period, $F(1, 37) = 5.07$, $p < 0.05$, were observed, as well as a significant interaction of period × task × gender, $F(1, 37) = 6.14$, $p < 0.02$. For DBP, only the main effects of group, $F(2, 36) = 11.70$, $p < 0.001$, and period, $F(1, 37) = 4.90$, $p < 0.05$, were significant. Interestingly, the effects of smoking on DBP observed during the low-challenge task appeared to be absent during the high-challenge task for both males and females, suggesting that smoking and stress may have less than additive influences on DBP.

Notably, there were no significant correlations between changes in subjective vs. cardiovascular responses from task baseline to task trials 1 and 2 for the 16 smoking smokers. A significant negative correlation would have been expected if the opposing ("paradoxical") actions of smoking on subjective vs. cardiovascular responses were somehow directly related or tied to a common mechanism, as indicated by the nicotine paradox (17).

DISCUSSION

On the surface, these results tend to support the notion of simultaneous effects of tobacco smoking on reducing subjective stress while increasing cardiovascular arousal in both males and females, consistent with the nicotine paradox. However, careful evaluation of these results indicates that these seemingly paradoxical effects appear to be unrelated, or dissociated. In contrast with subjective stress reduction due to smoking, which was observed only during the high-challenge task, the HR and SBP arousing effects of smoking were similar during either task, suggesting that these particular effects of smoking are not influenced by situational demands. (The DBP arousing effects of smoking were observed only during the low- and not the high-challenge task, the opposite of the subjective effects.) This observation is consistent with previous research showing similar cardiovascular effects of nicotine during stress vs. quiet rest (20). Further evidence from this study that smoking's subjective and cardiovascular effects are unrelated was the lack of correlation between them, as well as the observation that the subjective effects were very transient after smoking while the cardiovascular effects tended to be more sustained.

The lack of direct relationship between subjective vs. cardiovascular responses would indicate that cardiovascular increases due to smoking do not influence a smoker's appraisal of his/her subjective state of stress of relaxation, at least not in the same manner as cardiovascular increases due solely to behavioral challenges. This is consistent with recent results showing no relationship between nicotine's effects on cardiovascular arousal vs. ratings of perceived exertion during physical stress [i.e., bicycle exercise (22)]. Subjective stress reduction may therefore result from other physiological effects of smoking, such as decreased perception of muscle tension or other CNS effects (5,7,26), but not from cardiovascular effects. Thus, it would seem that the nicotine paradox is a paradox only if it is assumed that increased cardiovascular arousal uniformly reflects heightened subjective stress or that subjective relief from stress is not possible in the presence of increased cardiovascular arousal, neither of which appears tenable. On the other hand, subjective arousal (SACL Arousal) was increased by smoking during both tasks and thus may not be a situationally dependent subjective effect of smoking. It is also possible that subjective arousal may be influenced by cardiovascular changes to a greater degree than is subjective stress (SACL Stress, VAS items), although there were no significant correlations between SACL Arousal and cardiovascular responses.

As noted above, the results of this study provide evidence that smoking does alleviate subjective stress. Importantly, however, this stress-reducing effect was very transient and had generally dissipated by the midpoint of each task trial (10 min after smoking), especially for males. Furthermore, smoking had no effect on the STAI, a common measure of acute change in anxiety. Such short duration and selectivity of smoking's effects could explain the failure of many past studies to find a stress-reducing effect of smoking if subjective assessment was not done soon after smoking (13) and several measures were not used. Nevertheless, this brief mood-modulating effect may be sufficient to provide substantial re-

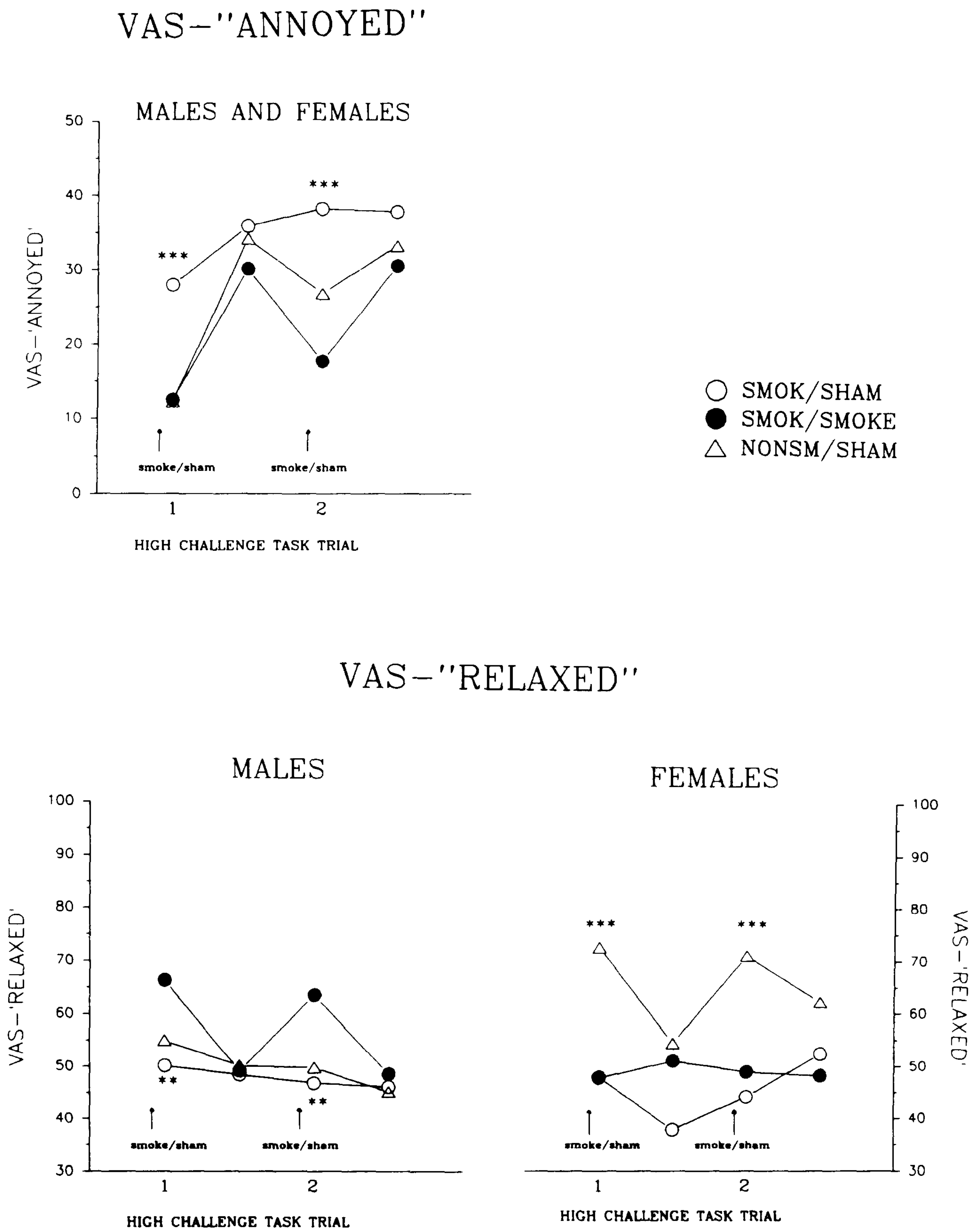

FIG. 3. Covariate-adjusted mean VAS scale scores at each assessment point immediately after smoking/sham smoking and midway through each trial of the high-challenge task for each group. $^{**}p < 0.01$, $^{***}p < 0.001$ for differences from smoking smokers.

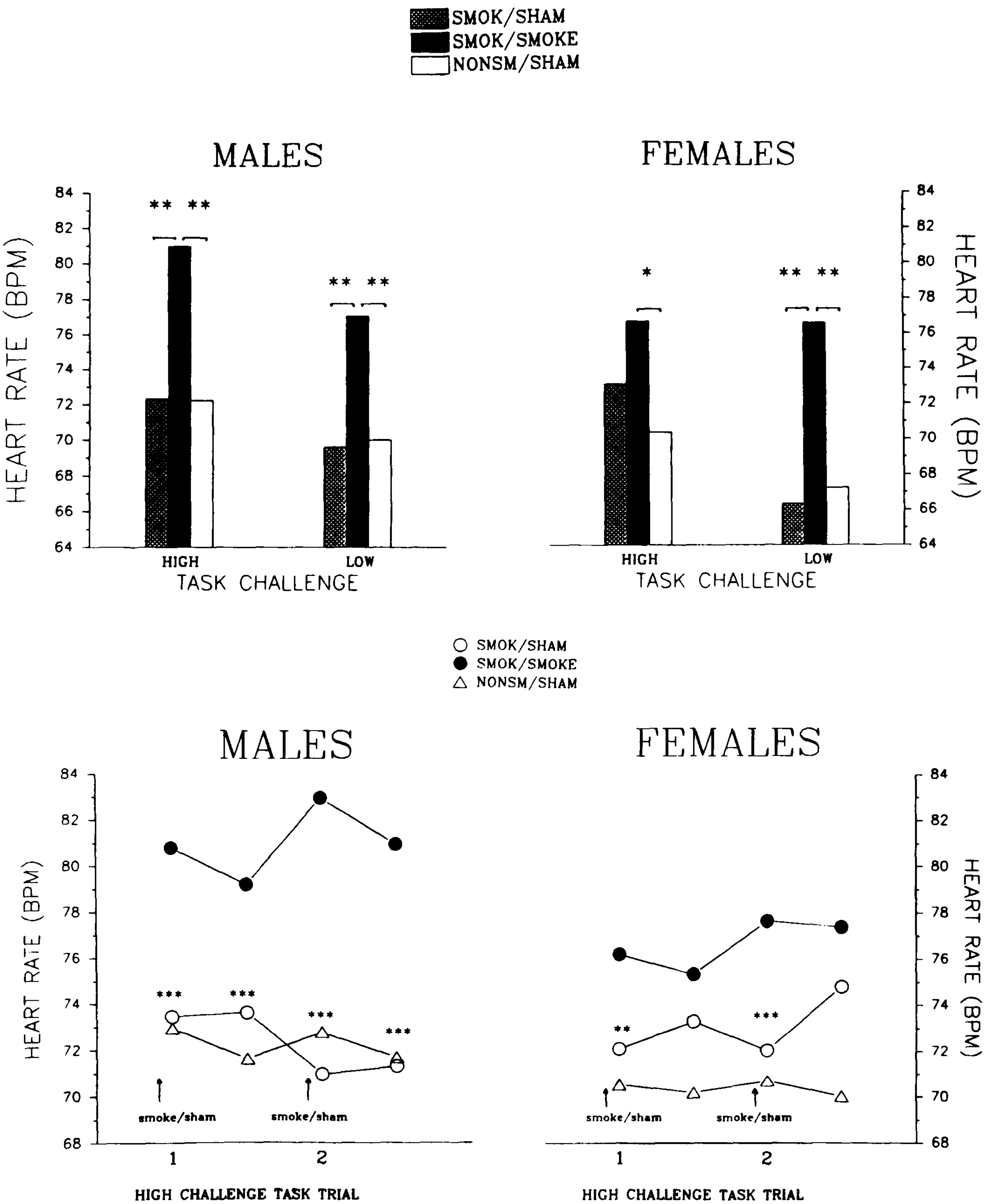

FIG. 4. Overall covariate-adjusted mean heart rate responses during the high- and low-challenge tasks (top) and at each assessment point immediately after smoking/sham smoking and midway through each trial of the high-challenge task (bottom) in males and females of each group. $+p < 0.10$, $*p < 0.05$, $**p < 0.01$, $***p < 0.001$ for differences from smoking smokers.

inforcement for smoking under stress conditions observed in some studies (23,25), as well as the tendency of many smokers to chain-smoke in certain situations. On the other hand, smoking may still have more prolonged, if indirect, stress-reducing effects via nicotine-induced improvement in task performance (30). Task performance success was standardized in this study to avoid this possibility since we were interested in direct effects of smoking on subjective stress.

It may be argued that tobacco withdrawal could have produced the elevated subjective stress in the smokers who sham smoked during the high-challenge task. However, tobacco deprivation was minimal (approx. 1.5 h during the task) and would be unlikely to have induced substantial withdrawal. In any case, if the subjective stress of sham-smoking smokers had been solely a function of time since last smoked (i.e., tobacco withdrawal) similar results should have been (but were not) observed during the low-challenge task. Another alternative is that subjective stress was heightened by the sham-smoking procedure for smokers in that group, compared with their potential responses in the absence of sham smoking. This also seems unlikely since some research has found *decreased* subjective stress following sham smoking (18) and, again, there was no heightened stress following sham smoking during the low-challenge task.

The results of this study also suggest that gender differences in the subjective stress effects of smoking may be important. Although there were few such gender differences, results for SACL Stress and VAS Relaxed (Figs. 1 and 3) tend to suggest that the transient effect of smoking "moved" subjective responses of males further in the direction of calm, beyond that of nonsmokers [i.e. "true" stress reduction effect (9)], while it only partially "normalized" subjective state for females (i.e., brought subjective state closer to that of nonsmokers). However, some of this gender difference may be due to the particular stressor employed here, a solitary computer task. Previous research suggested that certain laboratory stress tasks may be less stressful for females physiologically (29) and perhaps subjectively. It would be useful to determine the degree to which the results from the present study generalize to other types of stressors, as well as more naturalistic stress situations.

Finally, future research should focus on whether these stress-reducing effects of smoking may be due specifically to nicotine intake or to nonnicotine aspects of smoking, such as nonnicotine sensory stimuli or its discriminative stimulus effects. It is conceivable both are involved since subjective stress has been shown to be attenuated by chewing nicotine gum (26), by nonnicotine smoking stimulation (14), and by selective pairing of a smoking (and nicotine) cue with stress (19).

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REFERENCES

1. Dembroski, T. M.; MacDougall, J. M.; Cardozo, S. R.; Ireland, S. K.; Krug-Fite, J. Selective cardiovascular effects of stress and cigarette smoking in young women. Health Psychol. 4:153–167; 1983.
2. Epstein, L. H.; Perkins, K. A. Smoking, stress, and coronary heart disease. J. Consult. Clin. Psychol. 56:342–349; 1988.
3. Fagerstrom, K.-O. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict. Behav. 3:235–241; 1978.
4. Fleming, S. E.; Lombardo, T. W. Effects of cigarette smoking on phobic anxiety. Addict. Behav. 12:195–198; 1987.
5. Gilbert, D. G. Paradoxical tranquilizing and emotion-reducing effects of nicotine. Psychol. Bull. 86:643–661; 1979.
6. Gilbert, D. G.; Robinson, J. H.; Chamberlin, C. L.; Spielberger, C. D. Effects of smoking/nicotine on anxiety, heart rate, and lateralization of EEG during a stressful movie. Psychophysiology 26:311–320; 1989.
7. Gilbert, D. G.; Welser, R. Emotion, anxiety, and smoking. In: Ney, T.; Gale, A., eds. Smoking and human behavior. New York: John Wiley & Sons; 1989:171–196.
8. Hatch, J. P.; Bierner, S. M.; Fisher, J. G. The effects of smoking and cigarette nicotine content on smokers' preparation and performance of a psychosocially stressful task. J. Behav. Med. 6: 207–216; 1983.
9. Hughes, J. R. Distinguishing withdrawal relief and direct effects of smoking. Psychopharmacology (Berl.) 104:409–410; 1991.
10. Hughes, J. R.; Higgins, S. T.; Bickel, W. Behavioral "properties" of drugs. Psychopharmacology (Berl.) 96:557; 1988.
11. Huitema, B. E. The analysis of covariance and alternatives. New York: John Wiley & Sons; 1988.
12. Ikard, F. F.; Tomkins, S. The experience of affect as a determinant of smoking: A series of validity studies. J. Abnormal Psychol. 81:172–181; 1973.
13. Jarvik, M. E.; Caskey, N. H.; Rose, J. E.; Herskovic, J.; Sadeghpour, M. Anxiolytic effects of smoking associated with four stressors. Addict. Behav. 14:379–386; 1989.
14. Levin, E. D.; Rose, J. E.; Behm, F.; Caskey, N. H. The effects of smoking-related sensory cues on psychological stress. Pharmacol. Biochem. Behav. 39:265–268; 1991.
15. MacDougall, J. M.; Dembroski, T. M.; Slaats, S.; Herd, J. A.; Eliot, R. S. Cardiovascular effects of stress and cigarette smoking. J. Human Stress 9:13–21; 1983.
16. Mackey, C. J. The measurement of mood and psychophysiological activity using self-report techniques. In: Martin, I.; Venables, P. H., eds. Techniques in psychophysiology. New York: Wiley; 1980:501–562.
17. Nesbitt, P. Smoking, physiological arousal and emotional response. J. Personal Social Psychol. 25:137–144; 1973.
18. O'Connor, K. Individual differences and motor systems in smoker motivation. In: Ney, T.; Gale, A., eds. Smoking and human behavior. New York: John Wiley & Sons; 1989:141–170.
19. Perkins, K. A.; Epstein, L. H.; Jennings, J. R. Smoking as a cue for subjective and behavioral responses to a stressor. J. Subst. Abuse 3:29–38; 1991.
20. Perkins, K. A.; Epstein, L. H.; Jennings, J. R.; Stiller, R. The cardiovascular effects of nicotine during stress. Psychopharmacology (Berl.) 90:373–378; 1986.
21. Perkins, K. A.; Grobe, J. E.; Epstein, L. H.; Caggiula, A. R.; Stiller, R. L. Effect of nicotine on subjective arousal may be dependent on baseline subjective state. J. Subst. Abuse (in press).
22. Perkins, K. A.; Sexton, J. E.; Solberg-Kassel, R. D.; Epstein, L. H. Effects of nicotine on perceived exertion during low-intensity activity. Med. Sci. Sports Exercise 23: 1283–1288; 1991.
23. Pomerleau, C. S.; Pomerleau, O. F. The effects of a psychological stressor on cigarette smoking and on subsequent behavioral and physiological responses. Psychophysiology 24:278–285; 1987.
24. Pomerleau, C. S.; Pomerleau, O. F.; Garcia, A. W. Biobehav-

ioral research on nicotine use in women. Br. J. Addict. 86:527–531; 1991.
25. Rose, J. E.; Ananda, S.; Jarvik, M. E. Cigarette smoking during anxiety-provoking and monotonous tasks. Addict. Behav. 8:353–359; 1983.
26. Russell, P. O.; Epstein, L. H.; Sittenfield, S.; Block, D. R. The effects of nicotine chewing gum on the sensitivity to muscle tension. Psychopharmacology (Berl.) 89:230–233; 1986.
27. Shiffman, S.; Jarvik, M. E. Cigarette smoking, physiological arousal, and emotional response: Nesbitt's paradox re-examined. Addict. Behav. 9:95–98; 1984.
28. Spielberger, C.; Gorsuch, R.; Lushene, N. Manual for the state-trait anxiety inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.
29. Stoney, C. M.; Davis, M. C.; Matthews, K. A. Sex differences in physiological responses to stress and in coronary heart disease: A causal link? Psychophysiology 24:127–131; 1987.
30. Warburton, D. M. Psychopharmacological aspects of nicotine. In: Wonnacott, S.; Russell, M. A. H.; Stolerman, I. P., eds. Nicotine psychopharmacology. New York: Oxford University Press; 1990:77–111.
31. Woodson, P. P.; Buzzi, R.; Nil, R.; Battig, K. Effects of smoking on vegetative reactivity to noise in women. Psychophysiology 23:272–282; 1986.