

Greater Sensitivity to Subjective Effects of Nicotine in Nonsmokers High in Sensation Seeking

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The personality characteristic of sensation seeking is associated with risk of smoking, perhaps because of greater initial sensitivity to nicotine. Young healthy nonsmokers ($N = 37$) were administered 0, 10, and 20 $\mu\text{g}/\text{kg}$ nicotine by nasal spray in 3 separate sessions, and subjective responses were assessed. Sensation-Seeking Scale (SSS) scores were then correlated with these responses. A comparison group of smokers ($N = 55$) was included to determine whether sensation seeking was associated specifically with initial sensitivity to nicotine or with general sensitivity regardless of past nicotine exposure. SSS subscales, particularly Experience Seeking and Disinhibition, were correlated with subjective responses to nicotine in nonsmokers but generally not in smokers. These findings indicate that sensation seeking is associated with greater initial sensitivity to nicotine's subjective effects and may provide directions for further study of individual-differences characteristics that predispose people to the risk of becoming smokers.

Theories of individual differences that predispose people to smoking or other substance abuse generally indicate that stable background factors, such as personality, are largely responsible (e.g., Gilbert & Gilbert, 1995; Tarter, 1988). Implicit in this conceptualization is the notion that drugs of abuse, including nicotine, may produce quantitatively, or even qualitatively, different acute effects on initial exposure in individuals who are predisposed to drug abuse as compared with drug effects in nonpredisposed individuals. For example, the "sensitivity" model of O. F. Pomerleau (1995) hypothesizes that individuals who are likely to become nicotine-dependent experience greater positive, as well as aversive, effects of nicotine on initial exposure to smoking (i.e., greater "initial sensitivity") as compared with individuals who are likely to remain nonsmokers. With repeated exposure, however, the predisposed individuals become highly tolerant to the aversive effects while maintaining large positive responses, thus increasing the likelihood of continued smoking and onset of dependence (O. F. Pomerleau, 1995). Because variability in initial sensitivity to drugs is the foundation of most views of individual differences in

predisposition to drug abuse, a key to identifying individuals predisposed to nicotine dependence may be improving our understanding of individual variation in initial sensitivity to nicotine's effects.

Research has explored factors associated with individual variability in sensitivity to drugs in humans (e.g., Davidson & Schenk, 1994; Hutchison, Wood, & Swift, 1999; McCaul, Turkkan, Svikis, & Bigelow, 1991; Pollock, 1992). A chief focus has been linking personality factors to risk of drug use. For example, impulsivity–disinhibition and its overlapping characteristics of sensation seeking and novelty seeking are widely related to drug abuse, including smoking (e.g., Bickel, Odum, & Madden, 1999; Mitchell, 1999). Sensation seeking, as measured most commonly by the Sensation-Seeking Scale (SSS; Zuckerman, 1994), purportedly assesses the tendency to seek "varied, novel, complex, and intense sensations and experiences" (p. 27). Scores on the SSS and on a measure of a similar characteristic, novelty seeking (Tridimensional Personality Questionnaire; Cloninger, Svrakic, & Przybeck, 1993), are associated with greater risk of drug use (Howard, Kivlahan, & Walker, 1997), including initiation or persistence of smoking (e.g., Heath, Madden, Slutske, & Martin, 1995; C. S. Pomerleau, Pomerleau, Flessland, & Basson, 1992). In a recent study, higher scores on several SSS subscales were associated with greater subjective mood responses to amphetamine (20 mg orally) in healthy, non-drug-abusing young adults (Hutchinson et al., 1999). This observation suggests that sensation seeking may be related to greater initial sensitivity (i.e., in drug-naïve individuals) to some drugs of abuse, which could provide a strong link in explaining the association between the personality characteristic and predisposition to drug abuse.

Novelty seeking in animals has also been shown to be related to greater sensitivity to various drugs, such as morphine (Deroche, Piazza, LeMoal, & Simon, 1993) and am-

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phetamine (Klebaur & Bardo, 1999). Commonalities between nicotine and other drugs in the likely sites of action in the brain (e.g., Pich et al., 1997) suggest that similar factors should be associated with nicotine sensitivity, and other animal research is consistent with this notion. Mice exhibiting greater nicotine-induced locomotor activity also show greater conditioned place preference to nicotine (Schechter, Meehan, & Schechter, 1995), which may relate to nicotine's pleasurable effects. Moreover, genetic control of initial sensitivity to nicotine (Marks, Campbell, Romm, & Collins, 1991) and to nicotine self-administration (Shoab, Schindler, & Goldberg, 1997) has been clearly shown in rodents.

Nevertheless, virtually no research has explored the factors that relate to individual differences in initial nicotine sensitivity in humans, perhaps in part because of methodological difficulties. Initial sensitivity to a drug must be examined by using drug-naïve individuals because long-term adaptation to drug effects occurs with chronic exposure, such as onset of chronic tolerance to nicotine in smokers (Arcavi, Jacob, Hellerstein, & Benowitz, 1994; Perkins et al., 1993; Perkins, Grobe, et al., 1994). Alteration in drug sensitivity due to chronic tolerance is particularly relevant to examinations of individual differences in initial sensitivity. Animals that are initially more sensitive to nicotine (Collins, Miner, & Marks, 1988) or other drugs (Cools & Gingras, 1998) typically develop the greatest chronic tolerance after long-term drug exposure and become equally as sensitive as, or less sensitive than, initially insensitive animals. If humans who are initially more sensitive to nicotine also develop the greatest chronic tolerance from long-term smoking, as suggested by O. F. Pomerleau (1995), the relationship between personality factors and nicotine sensitivity should be weak or nonexistent among smokers. The extent and the time course of any reversal of adaptation to chronic nicotine following cessation of smoking are unknown, leaving uncertain the possible appropriateness of using ex-smokers to examine initial sensitivity to nicotine. Thus, the clearest examination of personality factors and initial nicotine sensitivity probably requires the study of nicotine effects in nonsmokers.

However, administration of nicotine via tobacco smoking to human volunteers naïve to nicotine is difficult because of their inability to inhale and absorb nicotine from smoking and because of the imprecise dosing and absorption of thousands of other compounds besides nicotine (e.g., Perkins et al., 1986; O. F. Pomerleau, Pomerleau, & Rose, 1989). Novel methods such as transdermal nicotine are safe and provide more precise dosing but nevertheless produce much slower uptake of nicotine than from smoking. Rapid uptake of nicotine may be a key to its reinforcing or rewarding effects (Russell, 1990). Intravenous administration of nicotine is precise and can be rapid but involves significant safety risks as well as participant preparation and monitoring (e.g., lying prone with indwelling catheters), which could interfere with valid assessment of subjective mood effects due to the drug per se. For these reasons, a better method for assessing acute mood effects due to rapidly administered nicotine may be the use of nasal spray nicotine dosing (e.g., Perkins et al., 1986).

In the present study, we examined the relationship between the personality characteristic of sensation seeking and subjective and cardiovascular responses to nasal spray nicotine in nonsmokers. Nonsmokers were examined so that responses would better reflect initial sensitivity to nicotine unconfounded by onset of chronic tolerance through long-term exposure to nicotine from smoking. We hypothesized that higher sensation-seeking scores would be associated with greater magnitude of increases in positive, as well as aversive, mood effects. Cardiovascular responses were not expected to be related to sensation seeking but were examined to determine possible specificity of the relationship between this personality characteristic and responses to nicotine. The relationship between sensation seeking and responses to nicotine was also examined in smokers for comparison. On the basis of the animal research discussed previously, we expected few significant effects of sensation seeking on nicotine responses of smokers, indicating that sensation seeking was specifically related to initial, and not general, sensitivity to nicotine.

Method

Participants

Participants were 37 nonsmokers (19 men and 18 women) and 55 smokers (25 men and 30 women) originally recruited for two studies of nicotine tolerance that generally involved very similar methods. The data reported here are from measures and procedures that were identical between the studies. Nonsmokers denied any past or current regular use of tobacco or any nicotine-containing product and were excluded if they reported a lifetime exposure of more than 100 cigarettes or other uses of tobacco. All but 1 had a lifetime exposure of no more than 30 cigarettes. The mean number of lifetime uses of tobacco (number of times cigarettes, cigars, smokeless tobacco, etc., had been used) for nonsmokers was 8.3 ($SD = \pm 17.4$). Among those who had ever used tobacco, the mean duration since their last use of tobacco was 9.6 years ($SD = \pm 7.8$ years). Thus, it is very unlikely that significant adaptation to nicotine effects, notably chronic tolerance, had developed after such modest and distant prior exposure to tobacco. Their responses to nicotine therefore likely reflected initial sensitivity to the drug. All nonsmokers and smokers were examined by a physician to rule out current or past medical or psychiatric problems, and urine drug screens were obtained to exclude participants with substance abuse problems. Mean characteristics of nonsmokers and smokers are presented in Table 1.

Measures

Personality measure. The SSS (Zuckerman, 1994) contains 40 true-false items. Four subscales of the SSS contain 10 items each and are termed Thrill and Adventure Seeking (TAS), Experience Seeking (ES), Disinhibition (DIS), and Boredom Susceptibility (BS). The range of scores for each subscale is from 0 to 10, and the total SSS score can range from 0 to 40. Mean SSS total and subscale scores for nonsmokers and smokers are also presented in Table 1. The scores for these participants were comparable to norms for U.S. young adults, except for the somewhat lower total and DIS scores (norms: total = 21, DIS = 5.8; Zuckerman, 1994). Nonsmokers had lower scores than smokers on the ES and DIS subscales and on the total SSS.

Table 1
Age, Smoking History Characteristics, and Sensation-Seeking Scale Scores
of Nonsmokers and Smokers

Characteristic	Nonsmokers (<i>N</i> = 37)	Smokers (<i>N</i> = 55)
	<i>M</i> ± <i>SD</i>	<i>M</i> ± <i>SD</i>
Male (%)	51	45
Age (in years)	28.8 ± 6.2	32.7 ± 11.1
FTND score (0–10)		5.4 ± 1.7
Cigarettes/day		21.4 ± 6.4
Years smoking		15.5 ± 10.5
Sensation-Seeking Scale scores		
Total	16.6 ± 6.4*	19.3 ± 6.4*
Thrill and Adventure Seeking	6.5 ± 2.8	6.2 ± 3.0
Experience Seeking	4.6 ± 2.1**	5.7 ± 1.8**
Disinhibition	3.2 ± 2.4***	4.8 ± 2.0***
Boredom Susceptibility	2.2 ± 1.9	2.6 ± 1.8

Note. FTND = Fagerstrom Test of Nicotine Dependence (see Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991).

* $p \leq .05$. ** $p \leq .01$. *** $p \leq .001$ for differences between nonsmokers and smokers.

Subjective responses to nicotine. The subjective measures were (a) the Profile of Mood States shortened form (POMS; McNair, Lorr, & Droppleman, 1971) scales of Tension, Confusion, Vigor, and Fatigue and the composite scale of Arousal (determined by subtracting Confusion and Fatigue from Tension plus Vigor) and (b) the Visual Analog Scale (VAS; ranging from 0 = *not at all* to 100 = *very much*) items of "head rush," "relaxed," "pleasant," and "jittery." POMS scale scores were normalized by converting each to 0–100 scales to simplify comparisons between these scales and with VAS items. These and similar scales have been used in numerous studies of the subjective effects of nicotine and other drugs (e.g., Fischman & Foltin, 1991; Perkins, Grobe, & Caggiula, 1997; Perkins, Grobe, Weiss, Fonte, & Caggiula, 1996). These scales provided a mix of presumably pleasurable (e.g., VAS—pleasant, POMS—Vigor) and aversive (e.g., VAS—jittery, POMS—Confusion) effects of nicotine to determine whether personality may be associated with only some subjective mood effects. Responses to several of these measures (VAS items of pleasant and relaxed, POMS scales of Vigor and Arousal) have been associated with greater reinforcement from nicotine by nasal spray in smokers (Perkins, Grobe, & Caggiula, 1997; Perkins et al., 1996). Thus, these measures may relate to nicotine's rewarding or reinforcing effects. In addition, responses to other measures (VAS—jittery, VAS—head rush) have been associated with behavioral discrimination of nicotine in smokers and nonsmokers (Perkins, DiMarco, Grobe, Scierka, & Stiller, 1994; Perkins, Sanders, D'Amico, & Wilson, 1997).

Cardiovascular assessment. Heart rate (HR; in beats per minute), systolic blood pressure (BP), and diastolic BP were obtained automatically by a Dinamap BP recorder (Critikon, Inc., Tampa, FL).

Procedure

All procedures complied with American Psychological Association ethical standards in the treatment of human participants. The participants took part in three experimental sessions, one for each nicotine dose (0, 10, and 20 $\mu\text{g}/\text{kg}$). Each session was scheduled at approximately the same time of day (± 1 hr) for each participant. Smokers abstained overnight from smoking prior to each session (confirmed by expired-air carbon monoxide < 13 ppm).

During the three experimental sessions, participants initially rested quietly after placement and testing of the BP cuff. A baseline assessment of subjective measures was then obtained, along with baseline measures of BP and HR. Participants were then administered 0, 10, or 20 $\mu\text{g}/\text{kg}$ nicotine via measured-dose nasal spray once every 30 min for 90 min (total of three presentations of assigned dose per session). These doses are at the lower half of the range of nicotine absorbed by smokers after smoking cigarettes (e.g., Benowitz & Jacob, 1984) and are amounts that naive individuals are likely to absorb in initial experimentation with smoking (McNeill, Jarvis, Stapleton, West, & Bryant, 1989). Thus, differences in sensitivity to these doses may generalize to variability in responses to initial smoking exposure in naive teens experimenting with cigarettes. This dosing method has been shown to produce reliable boosts in plasma nicotine and has been described previously (Perkins et al., 1986; Perkins, Grobe, et al., 1994). Doses were presented on separate days, and the order of doses across days was counterbalanced. Dosing took approximately 2 min, followed by 1 min of quiet rest prior to subjective and cardiovascular assessments during Minutes 3–7 postdosing. Participants remained at quiet rest during testing and during intervals between trials. This procedure was repeated for each trial of exposure to the same dose of nicotine or placebo. Three trials at the same dose within a session were used to increase the reliability of responses to that dose. Responses to nicotine or placebo were averaged across the three trials.

Data Analyses

The relationships of SSS total and subscale scores with responses to nicotine were initially determined by Pearson correlations of these scores with response to each nicotine dose (10 or 20 $\mu\text{g}/\text{kg}$) for each measure. The degrees of freedom for these correlations were 36 for nonsmokers and 54 for smokers (i.e., one less than n of samples). Response to each spray was first assessed as the change from prespray baseline to postspray response and averaged across the three trials. For the correlations, response to each of the two nicotine doses was determined by taking the difference in change score between each dose versus placebo. Thus, this value isolated the influence of nicotine per se by eliminating influences due to nonspecific aspects of the dosing

procedure (e.g., responding to the sensory effects of the placebo nasal spray procedure). Correlations were done separately for responses to 10 $\mu\text{g}/\text{kg}$ and to 20 $\mu\text{g}/\text{kg}$ doses because of the possibility of nonlinear dose-response effects of nicotine on subjective responses in nonsmokers (Perkins et al., 1993; Perkins, Grobe, et al., 1994). To determine whether sensation seeking was more closely associated with initial nicotine sensitivity (i.e., only in nonsmokers) than with general sensitivity (i.e., in smokers), we compared the number of significant correlations for nonsmokers versus smokers by using chi-square. To determine whether sensation seeking moderated these responses, we performed analyses of variance (ANOVAs) for each response that was significantly correlated with SSS score, using nicotine dose (0, 10, or 20 $\mu\text{g}/\text{kg}$) as a within-subjects variable and high versus low SSS score as a between-subjects variable. Dichotomous assignment of nonsmokers to high or low SSS subgroups was determined by median split of scores on each subscale. Presence of a significant interaction of high versus low SSS subgroup by dose would indicate that SSS moderates responses to nicotine. A similar approach for determining moderation of personality on acute response to amphetamine was performed by Hutchison et al. (1999). Similar analyses (correlations, followed by ANOVAs for responses significantly correlated with SSS score) were performed with smokers, for comparison with nonsmokers' results.

Results

The dose-response relationships between nicotine and subjective and cardiovascular responses are presented separately in Figure 1 for nonsmokers and the comparison group of smokers. The flattening of the dose-response curves for subjective responses in smokers, relative to nonsmokers, provides evidence for chronic tolerance (Kalant, 1989). Chronic tolerance was not observed for cardiovascular responses.

Correlations Between SSS Subscales and Nicotine Responses

The SSS subscales of ES and DIS were significantly correlated with several subjective responses of nonsmokers to nicotine (particularly the 10 $\mu\text{g}/\text{kg}$ dose), as shown in Table 2. ES and DIS scores were significantly correlated with VAS—head rush and the POMS scales of Vigor, Confusion, and Arousal, and DIS was also correlated with VAS—pleasant response (to the 10 $\mu\text{g}/\text{kg}$ dose) and POMS—Tension. The SSS subscale of TAS was correlated with VAS—jittery, VAS—relaxed (inversely), and POMS—Tension, whereas the total SSS score was significantly correlated only with VAS—head rush. However, no SSS subscales were correlated with any of the cardiovascular responses to nicotine in nonsmokers, except ES with diastolic BP response to the 20 $\mu\text{g}/\text{kg}$ dose ($r = .40, p < .01$; not shown in Table 2).

By contrast, only 6 of 90 correlations, about what one would expect by chance (4 or 5), were significant between SSS subscales and subjective responses of smokers to nicotine (not shown in Table 2). The DIS subscale was correlated inversely with VAS—relaxed response to the 10 $\mu\text{g}/\text{kg}$ dose ($r = -.32, p < .01$) and the 20 $\mu\text{g}/\text{kg}$ dose ($r = -.27, p < .05$). The BS subscale was correlated with

POMS—Vigor response to 10 $\mu\text{g}/\text{kg}$ nicotine ($r = .25, p < .05$) and with POMS—Arousal response to 20 $\mu\text{g}/\text{kg}$ nicotine ($r = .36, p < .01$). Finally, the ES subscale was inversely correlated with POMS—Vigor ($r = -.22, p < .05$) and POMS—Arousal ($r = -.26, p < .05$) responses to 10 $\mu\text{g}/\text{kg}$ nicotine (rather than directly correlated with each, as in nonsmokers; see Table 2). These 6 significant correlations for smokers were significantly fewer than the number of significant correlations for nonsmokers (18 of 90), $\chi^2(1, N = 91) = 6.92, p < .01$.

Also in contrast to the results for nonsmokers, SSS scores were correlated with HR responses in smokers. Total SSS score ($r = .39, p < .01$) and three of the four SSS subscales (TAS, $r = .35, p < .01$; ES, $r = .25, p < .05$; and BS, $r = .33, p < .01$) were significantly correlated with HR response to 20 $\mu\text{g}/\text{kg}$ nicotine. However, the SSS subscales were not significantly correlated with BP responses to nicotine, except ES with systolic BP response to 10 $\mu\text{g}/\text{kg}$ nicotine ($r = .24, p < .05$).

SSS Moderation of Nicotine Responses

ANOVAs performed on responses to nicotine that were significantly correlated with personality in nonsmokers indicated significant main effects of dose for all the subjective responses (as suggested in Figure 1). No main effects of SSS subscale scores were significant for any of these responses. Significant or marginally significant interactions of Nicotine Dose \times SSS Score, suggesting moderation, were observed for ES and VAS—head rush response to nicotine, $F(2, 70) = 3.16, p < .05$; ES and POMS—Confusion response, $F(2, 70) = 2.63, p < .10$; and DIS and POMS—Tension response, $F(2, 70) = 2.82, p < .10$. Responses to these measures as a function of high versus low SSS subscale scores are presented in Figure 2. Thus, although SSS subscale scores were correlated with many of the subjective responses to nicotine in nonsmokers, few of these responses seemed to be moderated in a significant fashion by sensation seeking. In the ANOVA for diastolic BP response, only the main effect of nicotine dose was significant. No main or interaction effect involving ES score was significant, suggesting no moderation of ES on BP response to nicotine in nonsmokers.

ANOVAs of SSS Subscale \times Nicotine Dose for smokers revealed a significant main effect of dose only for VAS—relaxed and POMS—Arousal. Lack of dose effects in smokers indicates flattened dose-response curves and chronic tolerance for most responses (as suggested in Figure 1). The interaction of SSS Subscale \times Nicotine Dose was significant only for the effect of BS on POMS—Arousal response to nicotine, $F(2, 106) = 3.26, p < .05$, as shown in Figure 2. In the ANOVAs of HR response to nicotine by SSS subscales, BS interacted with dose, $F(2, 106) = 4.68, p = .01$, as did total SSS score, $F(2, 106) = 4.15, p < .05$ (see Figure 2), suggesting that BS and total sensation-seeking score moderated HR response to nicotine in smokers.

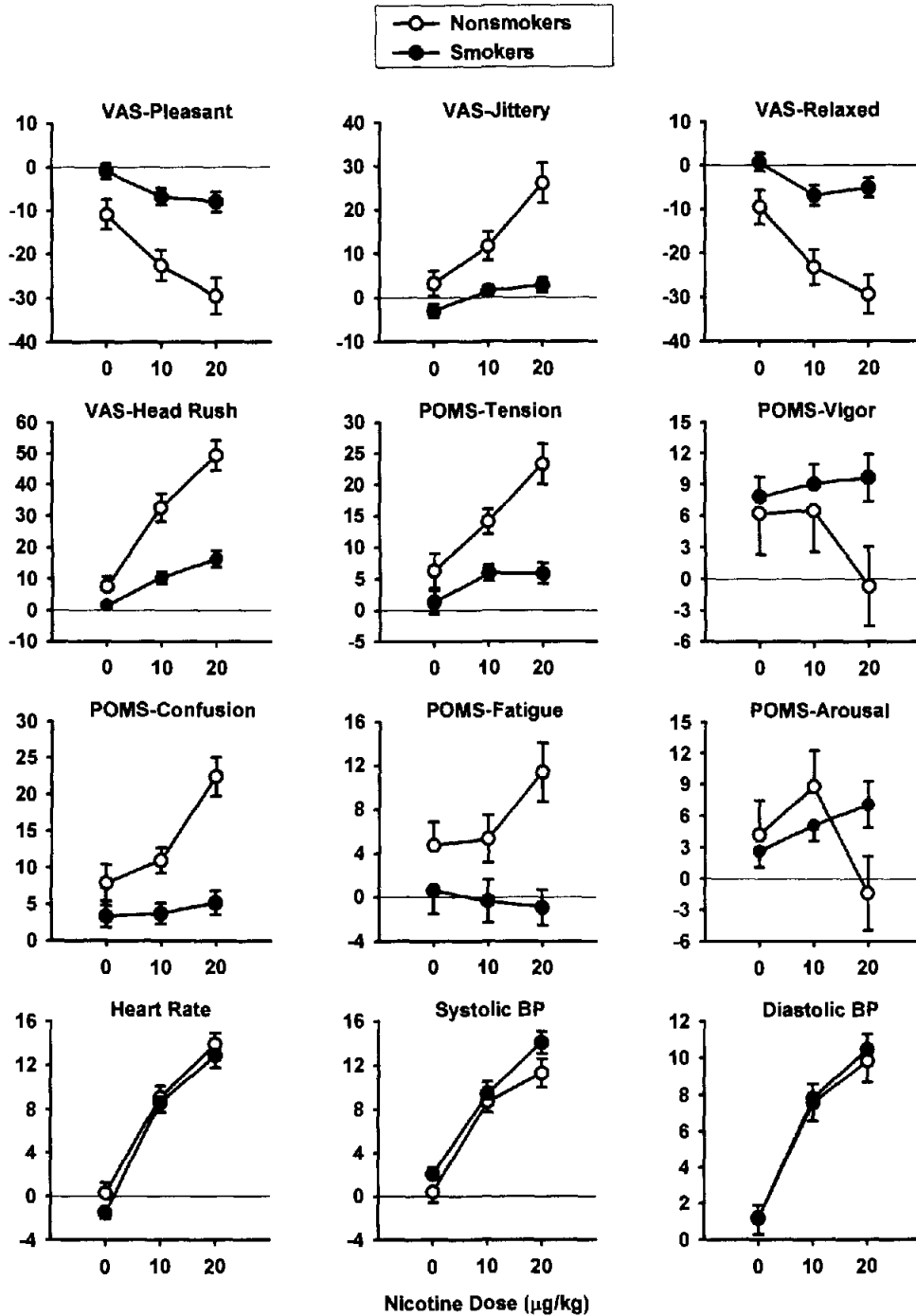


Figure 1. Dose-response relationships between nasal spray nicotine (0, 10, and 20 µg/kg) and subjective and cardiovascular responses in nonsmokers and smokers. Values are mean (±SEM) changes from resting baseline level (before dosing) to responses after dosing, averaged across three dosing trials. VAS = Visual Analog Scale; POMS = Profile of Mood States; BP = blood pressure.

Discussion

Subscales of Zuckerman's (1994) SSS, particularly the ES and DIS subscales, were significantly correlated with

several subjective responses to 10 µg/kg, and to a lesser extent 20 µg/kg, nicotine in nonsmokers. To our knowledge, this study is the first to relate any stable individual-differences variable, other than participant's sex (Perkins,

Table 2
Correlations Between Sensation-Seeking Scale (SSS) Scores and Subjective Responses to Nicotine (10 and 20 µg/kg) in Nonsmokers

Subjective response	Dose (µg/kg)	SSS total	Thrill and Adventure Seeking	Experience Seeking	Disinhibition	Boredom Susceptibility
VAS						
Pleasant	10	—	—	—	.44**	—
	20	—	—	—	—	—
Jittery	10	—	.35*	—	—	—
	20	—	—	—	—	—
Relaxed	10	—	-.31*	—	—	—
	20	—	—	—	—	—
Head rush	10	.33*	—	.36*	.27*	—
	20	.33*	—	.53***	—	—
POMS						
Tension	10	—	.31*	—	.30*	—
	20	—	—	—	.33*	—
Vigor	10	—	—	.34*	.35*	—
	20	—	—	—	—	-.30*
Confusion	10	—	—	—	—	—
	20	—	—	.33*	.27*	—
Fatigue	10	—	—	—	—	—
	20	—	—	—	—	—
Arousal	10	—	—	.42**	.44**	—
	20	—	—	—	—	—

Note. Dashes indicate nonsignificant correlations, which were omitted to reduce clutter and to highlight the significant correlations. VAS = Visual Analog Scale; POMS = Profile of Mood States.
 * $p < .05$. ** $p < .01$. *** $p < .001$.

Sanders, et al., 1997), to initial sensitivity to nicotine (i.e., in nonsmokers). Because nonsmokers are, by definition, virtually naive to nicotine, greater responses to nicotine in nonsmokers with higher SSS scores are consistent with the notion that the personality characteristic of sensation seeking is associated with greater initial sensitivity to nicotine. These results are also very similar to previous findings of greater sensitivity to d-amphetamine in nondependent individuals as a function of sensation seeking and novelty seeking (Hutchison et al., 1999), including the specific SSS subscales (i.e., ES and DIS) that were associated with drug sensitivity. The comparability of findings between these studies suggests that the increase in sensitivity to drugs due to sensation seeking may be broad and not specific to nicotine.

These results may provide direction for the study of possible mechanisms by which to explain the greater predisposition to smoking in teens high in sensation seeking and its associated characteristics (Heath et al., 1995; C. S. Pomerleau et al., 1992). Significant correlations among nonsmokers were more common for responses to 10 µg/kg nicotine, a dose closer to that likely obtained by teens experimenting with smoking (McNeill et al., 1989), compared with 20 µg/kg nicotine. In addition, ES and DIS subscale scores in nonsmokers were each associated with responses on several subjective measures that have been linked to greater nicotine spray self-administration in smokers: VAS—pleasant, POMS—Vigor, and POMS—Arousal (Perkins, Grobe, & Caggiula, 1997; Perkins et al., 1996). Both personality subscales were also associated with VAS—head rush, an effect that has been related to behavioral discrimination of nicotine in smokers and nonsmokers

(Perkins, Sanders, et al., 1997). These measures may generally be seen to reflect "pleasurable stimulation," which also describes the responses that were elevated to a greater extent after amphetamine administration among non-drug abusers with higher ES and DIS subscale scores in Hutchison et al.'s (1999) study. Thus, the pattern of subjective measures on which those with higher ES and DIS scores responded with greater effects is consistent with sensation seeking increasing the predisposition to reinforcing effects of nicotine and, perhaps, other drugs. However, in the present study, DIS scores were also associated with greater POMS—Tension and POMS—Confusion responses, which likely reflect aversive mood effects of nicotine. Greater aversive as well as pleasurable responses to nicotine in those with high DIS scores are consistent with the notion that those with greater initial sensitivity to nicotine are more responsive to aversive as well as positive mood effects (O. F. Pomerleau, 1995). In any case, if similar relationships between personality and subjective effects of nicotine are seen among teens during early tobacco experimentation, interventions focused on teens with elevated scores on the SSS subscales of ES and DIS may prove to be a useful direction for smoking prevention efforts. This possibility is further supported by the observation in this study (see Table 1) and others (e.g., Mitchell, 1999) that ES and DIS are the particular SSS subscales that tend to be higher in smokers than nonsmokers.

The general lack of association between sensation seeking and cardiovascular responses to nicotine in nonsmokers suggests that this personality characteristic is not related to all nicotine responses but may be specifically associated with subjective mood effects and other effects that may be

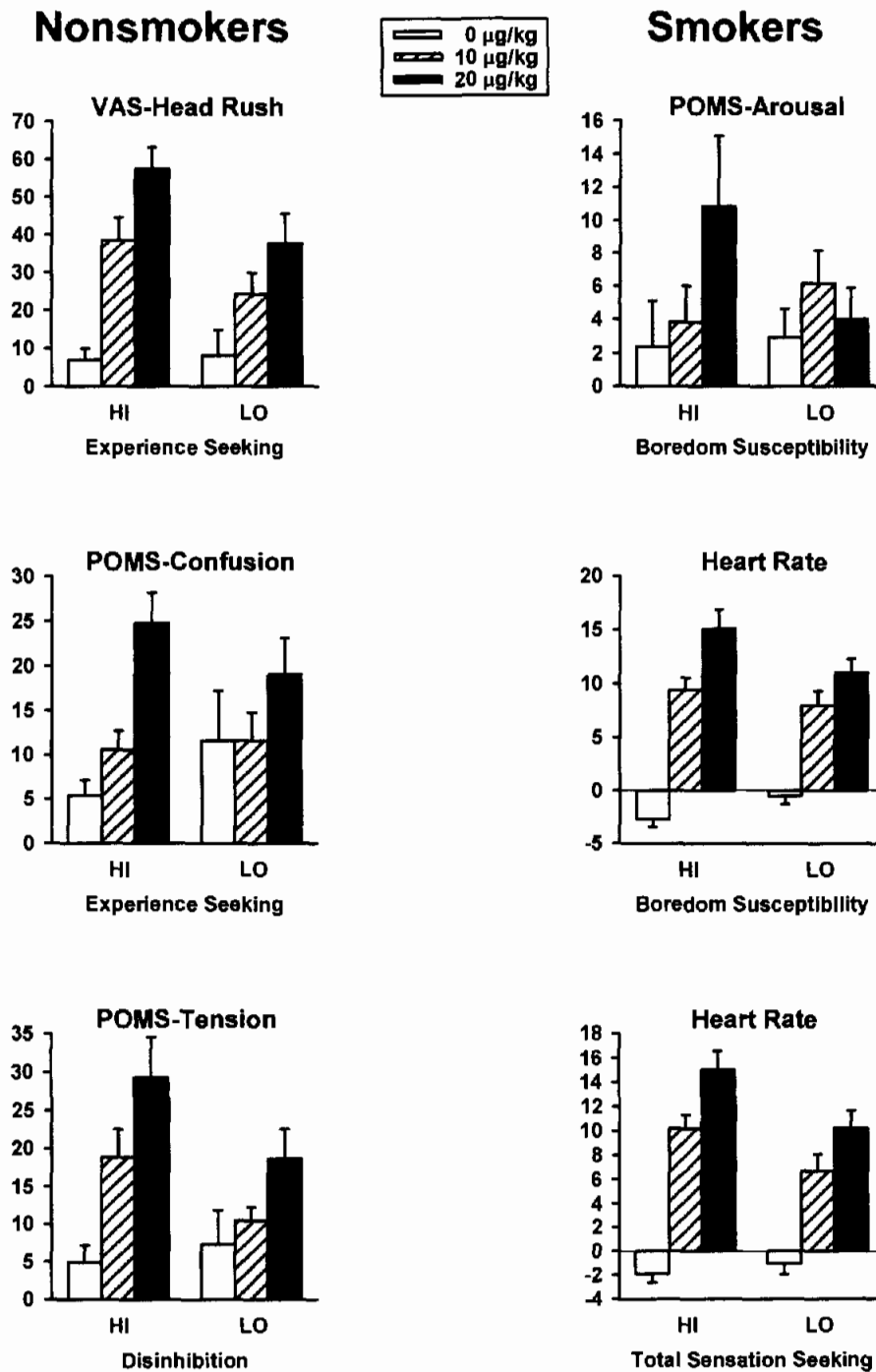


Figure 2. Mean (\pm SEM) responses to nicotine (0, 10, and 20 μ g/kg) as a function of high (HI) versus low (LO) scores on Sensation-Seeking Scale (SSS) subscales in nonsmokers and smokers. Analyses of variance indicated significant or marginally significant interactions of Subscale \times Dose for each response shown (see the *SSS Moderation of Nicotine Responses* section of the text). VAS = Visual Analog Scale; POMS = Profile of Mood States.

relevant to nicotine reinforcement. As noted, the subjective responses linked to sensation seeking in this study have also been related to nicotine reinforcement and discrimination in prior studies. However, more direct measures of reinforce-

ment (e.g., nicotine self-administration) are needed to provide a clearer test of this possibility. Moreover, other effects of nicotine, such as behavioral performance and cognitive-processing tasks (Perkins, Grobe, et al., 1994) and psycho-

physiological responses (e.g., Hutchison et al., 1999), should be examined to further determine the generalizability of the association of sensation-seeking personality with nicotine sensitivity.

Very few relationships between sensation seeking and subjective responses to nicotine were seen in smokers, despite greater statistical power to detect significant correlations due to the larger sample size of smokers ($N = 55$) versus nonsmokers ($N = 37$). Because smokers are more chronically tolerant than nonsmokers to these subjective responses to nicotine (Perkins et al., 1993; Perkins, Grobe, et al., 1994; see also Figure 1), the lack of a relationship between SSS score and response in smokers is consistent with the possibility that onset of chronic tolerance from long-term nicotine exposure dampens variability in responding because of individual differences (Collins et al., 1988; O. F. Pomerleau, 1995), including personality. In fact, ES subscale scores were directly correlated with POMS—Vigor and POMS—Arousal responses to 10 $\mu\text{g}/\text{kg}$ nicotine in nonsmokers but were inversely correlated with these same responses in smokers (i.e., higher ES scores were associated with attenuated responses in smokers). These particular results are very consistent with animal research showing that differences in initial sensitivity to nicotine and other drugs across certain rodent strains are lost, and even reversed, following chronic exposure to nicotine or other drugs (Collins et al., 1988; Cools & Gingras, 1998). Notably, however, SSS scores of smokers were consistently associated with effects of nicotine on HR, a response to which smokers do not seem to develop chronic tolerance (Figure 1). In general, therefore, individual differences in "initial" sensitivity to the subjective, if not HR, effects of the low and moderate nicotine doses used in this study likely cannot be assessed in smokers but require examination of nicotine responses in nicotine-naïve participants. However, it is still possible that responses of smokers to nicotine doses larger than 20 $\mu\text{g}/\text{kg}$, which could produce greater variability in subjective effects among smokers (Perkins et al., 1993), may yet be associated with individual-differences characteristics such as personality.

The relationship between nicotine sensitivity and other personality factors, such as novelty seeking (Cloninger et al., 1993; Heath et al., 1995), as well as other individual-differences characteristics of nonsmokers should be examined to determine what other factors may be associated with greater initial sensitivity to nicotine. Similar to sensation seeking, novelty seeking in humans is characterized by impulsivity, stimulation seeking, and sensitivity to reward or reinforcement, and it is believed to be influenced by dopaminergic mechanisms (Cloninger et al., 1993). Nicotine stimulates dopamine release and inhibits dopamine reuptake (Pontieri, Tanda, Orzi, & Di Chiara, 1996). Differences in dopaminergic activity have been associated with novelty-seeking and drug-seeking behaviors in animals, suggesting a common biological, and possibly genetic, origin (Dellu, Mayo, Piazza, LeMoal, & Simon, 1993). Moreover, genetic factors that may relate to dopamine function in humans are associated with smoking status and may influence initial sensitivity to nicotine, perhaps mediated through

the personality characteristics of novelty seeking and sensation seeking (e.g., Lerman et al., 1999; Noble et al., 1994; Sabol et al., 1999).

In contrast, finding significant correlations per se between sensation seeking and subjective responses to nicotine in nonsmokers does not indicate a causal relationship. Sensation seeking could simply covary with other factors that are actually directly responsible for this variability in sensitivity to nicotine. Moreover, few of these subscales appeared to significantly moderate sensitivity to subjective effects of nicotine, given the few ANOVA interactions involving SSS subscale and nicotine dose. The relatively small sample size (37 nonsmokers) and somewhat arbitrary median-split division of participants into high and low subgroups may have limited our chances of observing significant interactions.

This study has several strengths, such as the use of multiple doses of nicotine to determine possible nonlinear dose-response effects in nonsmokers (Figure 1), inclusion of a comparison group of similar-aged smokers, administration of nicotine using a measured dosing procedure, and assessment of subjective and cardiovascular responses (for comparison) using a variety of measures. Nevertheless, this study also has several limitations that restrict its conclusions. First, we examined nicotine responses in adult nonsmokers, rather than nicotine-naïve teens (for ethical and practical reasons). These young adults were already past the age of greatest risk for onset of smoking, and nonsmoking adults high in sensation seeking may differ from typical teens high in sensation seeking in ways that are protective from smoking risk (i.e., they may also have other factors that counteract the influence of sensation seeking on smoking risk). Second, nicotine was administered by nasal spray, and responses to nicotine via other routes of administration may produce different relationships with personality. Careful assessment of plasma nicotine exposure is also needed to clearly determine that greater sensitivity to nicotine in nonsmokers higher in sensation seeking is functional in nature and not due to dispositional factors. Dispositional differences are unlikely here, given past research showing reliable dosing with this nasal spray method (Perkins et al., 1986; Perkins, Grobe, et al., 1994). Dispositional differences are also unlikely given the general lack of relationship of sensation seeking with cardiovascular responses in nonsmokers, because systematically higher plasma nicotine levels in nonsmokers high in sensation seeking would lead to greater responses on all measures, not just subjective effects. Finally, personality characteristics may influence responses to other aspects of tobacco smoke exposure besides nicotine intake per se (such as sensitivity to smell of smoke; e.g., Perkins, Sexton, et al., 1994). Relationships between personality and response to nicotine in isolation may not necessarily predict relationships between personality and response to smoke exposure, limiting the relevance of this research to understanding the influence of personality on risk of tobacco dependence.

In conclusion, results of this study indicate that sensation seeking and particularly the characteristics of experience seeking and disinhibition are associated with greater initial sensitivity to several of nicotine's subjective effects but not

its cardiovascular effects. By contrast, sensation seeking generally was not related to subjective responses to nicotine in smokers, suggesting that its influence is on initial, and not general, sensitivity to nicotine. These findings may provide direction for further study of individual-differences characteristics that increase the risk of becoming a smoker.

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The Publications and Communications Board has opened nominations for the editorships of *Journal of Applied Psychology*, *Journal of Consulting and Clinical Psychology*, *Journal of Educational Psychology*, *Psychological Bulletin*, and *Journal of Personality and Social Psychology: Interpersonal Relations and Group Processes* for the years 2003–2008. Kevin R. Murphy, PhD, Philip C. Kendall, PhD, Michael Pressley, PhD, Nancy Eisenberg, PhD, and Chester A. Insko, PhD, respectively, are the incumbent editors.

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