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The Influence of Nicotine Dose and Nicotine Dose Expectancy on the Cognitive and Subjective Effects of Cigarette Smoking

Laura M. Juliano, Lisa M. Fucito, and Paul T. Harrell
American University

This study investigated the independent and interactive effects of nicotine dose and nicotine dose expectancy on smoking outcomes using a 2 (given nicotine vs. placebo) × 2 (told nicotine vs. placebo) Balanced Placebo Design (BPD). Smokers ($N = 148$) completed the Rapid Visual Information Processing Task (RVIP) and measures of smoking urge, mood, and cigarette ratings (e.g., satisfying) after smoking a nicotine or placebo cigarette crossed with instructions that the cigarette contained either nicotine or no nicotine. Nicotine cigarettes (0.6 mg nicotine) produced better sustained attention performance than placebos as indicated by RVIP reaction time, hits, and sensitivity (A′). Nicotine cigarettes also produced better mood and greater rewarding subjective effects of the cigarettes on 11 of 11 dimensions compared to placebos. Nicotine instructions resulted in fewer RVIP false alarms, better mood, and greater rewarding subjective effects of the cigarettes on 9 of 11 dimensions compared to placebo instructions. Nicotine dose by nicotine dose expectancy interactions were also observed for urge and tension-anxiety, such that the dose expectancy manipulation produced differential effects only among those who smoked placebo cigarettes. In contrast a significant interaction for self-reported vigor-activity demonstrated that the dose expectancy manipulation produced effects only among those who smoked nicotine cigarettes. This study provides additional evidence that nicotine improves cognitive performance, and provides initial evidence that denicotinized cigarettes smoked under the guise that they contain nicotine influence cognitive performance, albeit with less robust effects than nicotine. These data may inform the development of expectancy-based interventions for tobacco dependence.

Keywords: smoking, expectancies, placebo, nicotine, cognitive performance

In addition to nicotine, there is evidence that nonpharmacological factors such as expectancy play a role in the immediate rewarding effects of cigarette smoking. According to expectancy theory, a smoker will experience urge reduction in response to smoking a placebo cigarette, if the smoker has the *stimulus (or dose) expectancy* that he or she is smoking an active nicotine cigarette and has the *response expectancy* that nicotine reduces urges to smoke (Kirsch & Lynn, 1999; Perkins, Sayette, Conklin, & Caggiula, 2003). Expectancy theory proposes that response expectancies produce direct self-confirming automatic responses (e.g., negative affect reduction) to a situation (e.g., treatment, drug, or placebo) and can explain placebo and nocebo effects (Kirsch & Lynn, 1999). Conditioning processes have also been offered as an explanation for placebo effects.[1] For example, several studies have demonstrated that denicotinized cigarettes smoked under double-blind conditions alleviate smoking craving and withdrawal symptoms (e.g., Buchhalter, Acosta, Evans, Breland, & Eissenberg, 2005; Donny, Houtsmuller, & Stitzer, 2007) and function as a reinforcer (Shahan, Bickel, Madden, Badger, 1999). The sensorimotor aspects of smoking (e.g., sensations of smoke in one's throat) presumably become conditioned stimuli due to their previous associations with nicotine, thereby producing rewarding effects in the absence of nicotine (Rose, 2006). However, research has shown that denicotinized cigarettes smoked under different dose expectancy sets produce different effects, suggesting an important role of expectancy.

Controlled research studies across a range of drugs, including cigarette smoking and nicotine replacement products provide evidence that directly manipulating dose ex-

Laura M. Juliano, Lisa M. Fucito, and Paul T. Harrell, Department of Psychology, American University.

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Lisa M. Fucito is now at the Yale University School of Medicine, Department of Psychiatry. Paul T. Harrell is now at the Johns Hopkins University School of Public Health, Department of Mental Health.

Correspondence concerning this article should be addressed to Laura M. Juliano, PhD, Department of Psychology, American University, 4400 Massachusetts Avenue, NW, Washington, DC 20016. E-mail: juliano@american.edu

[1] The empirical evidence for expectancy theory and conditioning as mechanisms of placebo effects is reviewed by Stewart-Williams and Podd (2004).

pectancies and/or response expectancies (i.e., manipulating the expected effects of the drug) can influence the magnitude of responses to placebos and active drugs (e.g., Fillmore & Vogel-Sprott, 1996; Fillmore, Mulvihill & Vogel-Sprott, 1994; Fucito & Juliano, 2007; Harrell & Juliano, 2009; Metrik et al., 2009; Perkins et al., 2006; Perkins et al., 2009). Understanding the direct role that nonpharmacological factors such as expectancy play in the full range of effects of cigarette smoking may help us to better understand the persistence of smoking behavior and develop innovative expectancy-based treatment strategies (Copeland & Brandon, 2000).

An important motivation for smoking that has yet to be adequately addressed in smoking expectancy research is the enhancement of cognitive performance. It has been suggested that the effects of smoking on cognition, mood and arousal are likely connected in systematic ways and are all outcomes that smokers are seeking from nicotine (Waters & Sutton, 2000). Smoking for cognitive enhancement is reported as a common motive for smoking (Gilbert et al., 2000), and a large body of experimental research has confirmed that smoking and/or nicotine improves performance on cognitive processes including but not limited to sustained attention, alerting attention, orienting attention, episodic memory, and working memory (Heishman, Kleykamp, & Singleton, 2010; Koelega, 1993; Prichard & Robinson, 1998). Improvements in sustained attention (or vigilance) observed after smoking appear to be particularly robust (Koelega, 1993).

A recent study evaluated vigilance performance, memory, and subjective effects in 5-hr abstinent smokers before and after smoking a nicotine or denicotinized cigarette under double-blind conditions (Kelemen, 2008). After smoking participants were asked to guess which type of cigarette they smoked (resulting in a post hoc quasi independent variable to assess *dose expectancy*) and rate the effect that the cigarette has (or had) on his or her performance on the cognitive tasks (*response expectancy*). The authors concluded that dose expectancy partially mediated the relationship between nicotine and subjective effects, and that response expectancies assessed after participants completed the cognitive tasks, but not before, were associated with actual performance in some cases. However, this retrospective design prohibits making causal interpretations about the role of expectancies in smoking outcomes. It is quite possible that participants who had the most salient pharmacological effects of nicotine simply were more likely to guess correctly that they smoked a nicotine cigarette as well as report that nicotine had a greater effect on their performance.

The present study utilized the Balanced Placebo Design (BPD) to examine the causal roles of nicotine dose expectancies and nicotine dose in the cognitive and subjective effects of cigarette smoking. The BPD is a 2×2 factorial design (Rohsenow & Marlatt, 1981) in which the experimenter manipulates both the content of the drug (e.g., nicotine vs. placebo cigarette) and the information provided to participants about drug content, or *dose expectancy* (e.g., told nicotine or placebo cigarette). In the case of smoking the four conditions are: (a) Given Nicotine/Told Nicotine, (b) Given Nicotine/Told Placebo, (c) Given Placebo/Told Nicotine, and (d) Given Placebo/Told Placebo (Perkins et al., 2003). Less than a handful of published studies to date have used the BPD with cigarette smoking, with denicotinized cigarettes functioning as placebos (Juliano & Brandon, 2002; Kelemen & Kaighobadi, 2007; Perkins et al., 2008; Perkins et al., 2004). As a whole these studies provide evidence that the belief that one is smoking a nicotine cigarette, independent of actual nicotine ingestion, leads to greater reports of smoking liking and/or satisfaction (Kelemen & Kaighobadi, 2007; Perkins et al., 2004; Perkins et al., 2008), reduced smoking urges and/or cravings (Kelemen & Kaighobadi, 2007; Perkins et al., 2008), greater rewarding subjective effects of smoking (Kelemen & Kaighobadi, 2007), and decreased latency to smoke (Perkins et al., 2008). Not surprisingly, smoking BPD studies have also shown that relative to placebos, nicotine cigarettes better alleviate smoking urges or cravings (Juliano & Brandon, 2002), withdrawal symptoms (Juliano & Brandon, 2002; Perkins et al., 2008), and negative affect (Juliano & Brandon, 2008; Kelemen & Kaighobadi, 2007) as well as produce greater reports of smoking satisfaction (Juliano & Brandon, 2002: Perkins et al., 2004; Perkins et al., 2008) and other rewarding effects of smoking (Juliano & Brandon, 2002; Kelemen & Kaighobadi, 2007; Perkins et al., 2008). At times smoking BPD studies have revealed significant interactions between nicotine pharmacology and nicotine dose expectancies such that nicotine dose expectancy manipulations have had greater effects on subjective (e.g., urge) or behavioral responses (i.e., work for cigarette puffs) when placebo or low nicotine cigarettes are smoked compared to nicotine cigarettes (Juliano & Brandon, 2002; Perkins et al., 2004). Nicotine dose and nicotine dose expectancy usually show additive effects with the magnitude of positive responses typically largest in the given nicotine/told nicotine condition and smallest in the given placebo/told placebo conditions. Some BPD studies have also identified moderators of reactions to the dose expectancy manipulations including baseline smoking outcome expectancies (Juliano & Brandon, 2002), mood state (Perkins et al., 2008), and gender (Perkins et al., 2004).

To expand upon this prior work, the present study used the BPD to evaluate the independent and interactive effects of nicotine pharmacology and nicotine dose expectancy on smokers' responses to the Rapid Visual Information Processing (RVIP) task, a commonly used test of sustained attention. In addition, subjective effects were assessed with measures of smoking urge, mood, and rewarding effects of the cigarette (e.g., satisfaction); each of which has been shown to play a role in smoking behavior. Main effects for both nicotine and nicotine dose expectancy were hypothesized such that participants who were either told nicotine or given nicotine would show greater sustained attention performance and positive subjective effects in response to smoking compared to those told placebo or given placebo. We were also interested in identifying possible interactions between nicotine dose and nicotine dose expectancies.

Method

Participants

One hundred and fifty-three smokers (87 males and 66 females) were recruited from American University and the local Washington, D.C. community and 148 participants (82 males and 66 females) completed the two day protocol. Inclusion criteria were as follows: at least 18 years of age, a smoking history of at least 10 cigarettes per day for a minimum of one year, and no chronic smoking-related medical condition or psychiatric condition that would interfere with study participation. Participants (mean age = 29.65, *SD* = 12.24) smoked a mean of 13.56 (*SD* = 5.60) cigarettes per day for a mean of 10.59 years (*SD* = 10.30). The mean Fagerström Test of Nicotine Dependence score was 3.76 (*SD* = 2.11). Most of the participants identified themselves as either Caucasian (55%) or African American (34%). Fewer than half of the participants were full-time students. Participant characteristics across the four conditions are shown in Table 1.

Measures and Materials

Breath carbon monoxide (CO). Carbon monoxide levels were measured in parts per million from breath samples using a Bedfont Micro III Smokerlyzer (Kent, U.K.). Breath CO samples were taken to encourage compliance with instructions to abstain from smoking for three hours prior to arrival. Presmoking to postsmoking changes in CO level also provided a rough measure of the amount of smoke inhaled during the experimental manipulation.

Demographics/smoking history questionnaire. A 15-item questionnaire was developed for this study to assess demographic information and smoking history. It included the Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991), which is a widely used six item measure of nicotine dependence.

Smoking consequences questionnaire-adult. This 55-item questionnaire (SCQ-A; Copeland, Brandon, & Quinn, 1995) assesses smoking outcome expectancies a scale from *0 = Completely unlikely* to *9 = Completely likely*. The items cluster into the following 10 factors: (a) negative affect reduction, (b) stimulation/state enhancement, (c) health risk, (d) taste/sensorimotor stimulation, (e) social facilitation, (f) weight control, (g) craving/addiction, (h) negative physical feelings, (i) boredom reduction, and (j) negative social impression. It is reliable (alpha coefficients ranged from 0.83 to 0.96) and associated with smoking status, level of dependence, and smoking treatment outcome.

Urge rating scale. This three item self-report measure assessed participants' cravings, wants, and desires to smoke on scale from *1 = strongly disagree* to *7 = strongly agree*. These three items have demonstrated adequate reliability and validity in assessing smoking urge (Kozlowski, Pillitteri, Sweeney, Whitfield & Graham, 1996). Cronbach's alpha in the present study averaged 0.95.

Profile of mood states-short form (POMS-SF). The short form of the POMS (McNair, Lorr, & Droppelman, 1971) is a 30-item adjective checklist that assessed total mood disturbance and mood specific problems using six subscales: (a) tension-anxiety, (b) depression-dejection, (c) anger-hostility, (d) vigor-activity, (e) fatigue-inertia, and (f) confusion-bewilderment. Participants rated the items on a 5-point scale ranging from *0 = not at all* to *4 = extremely*. The short form has good psychometric properties and is highly correlated with the full 65 item scale. Cronbach's alpha for the individual factors was good (>.80) on all factors except for confusion-bewilderment (not analyzed), and for total mood disturbance (including confusion-bewilderment items) was excellent (*M* = 0.92).

Cigarette evaluation scale. This 14-item questionnaire (Rose, Behm, & Westman, 2001) assessed participants' immediate reactions to the experimental cigarettes using a 7-point scale from *1 = not at all* to *7 = extremely*. In reference to the cigarette that participants had just smoked, they were asked questions such as: Was it satisfying?, Did it taste good?, Did you enjoy the sensations of smoke in your throat and chest? In addition to the 10 items described by Rose et al. (2001) the following four items were also included: (a) Did it immediately reduce your cravings for cigarettes?, (b) Did it taste different than your usual brand?, (c) Did it make you feel more alert? and (d) Did it make you feel less anxious?

Rapid visual information processing (RVIP). The RVIP is a test of sustained attention or vigilance. This task has been used in many studies of drug effects, and has been shown to be especially sensitive to the effects of smoking and nicotine (Koelega, 1993; Prichard & Robinson, 1998). Participants viewed a series of single digits presented on the computer screen at a rate of 100 digits per minute for 12 minutes. Participants were told to press a mouse button as quickly as possible whenever they detected three consecu-

Table 1
Baseline Values for Demographic Variables and Dependent Measures

Variable[1]	Mean (*SD*)
Age (years)	29.65 (12.23)
Cigarettes per Day	13.56 (5.60)
Years Smoked	10.59 (10.30)
FTND	3.76 (2.11)
Carbon Monoxide	7.72 (4.58)
Self Reported Urge	5.49 (1.71)
POMS Depression	2.18 (3.33)
POMS Anger	2.86 (4.20)
POMS Tension	3.94 (3.72)
POMS Fatigue	4.96 (4.67)
POMS Vigor	6.91 (4.67)
POMS Total Mood Disturbance	31.32 (17.28)
RVIP Reaction Time	516.17 (124.62)
RVIP Hits	35.33 (16.45)
RVIP False Alarms	17.99 (35.55)
RVIP Sensitivity	0.79 (0.19)

Note. [1] A series of 2 × 2 ANOVAS indicated that there were no significant differences between groups at baseline on any variables (all *p*'s > .1). FTND = Fagerström Test of Nicotine Dependence; POMS = Profile of Mood States-Short Form; RVIP = Rapid Visual Information Processing Task.

tive odd or three consecutive even numbers (96 potential hits). To increase motivation to perform well on the RVIP task and improve sensitivity, on the experimental day participants were informed that they would earn 2.5 cents for each correct detection (hit) and lose 2.5 cents for each false alarm. Response targets appeared eight times per minute with 8 to 36 digits appearing between each target. Reaction time and responses (hits and false alarms) were recorded by the computer. Responses that occurred 100 ms to 1,500 ms after the target were scored as hits. Sensitivity, which takes into account both the number of hits and false alarms was computed as $A' = .5 + [(hr\text{-}far)+(hr\text{-}far)^2]/4^*hr^*(1\text{-}far)]$. Response bias was computed as $B'[(h\text{-}h)^2\text{-}(f\text{-}f)^2]/[(h\text{-}h)^2 + (f\text{-}f)^2]$ (Saghal, 1987). The RVIP was administered using DirectRT software (Empirisoft Research Software, New York. Available from http://www.empirisoft.com/). The RVIP was administered during a practice session, and then on the experimental day both before and after smoking the experimental cigarette as has been done in previous smoking studies (see Prichard & Robinson, 1998).

Experiment evaluation form. This measure was developed primarily to evaluate the credibility of the dose expectancy manipulation. Because of the deception involved in the BPD methodology, it is important to assess if participants believe what they are told about the nicotine dose of the cigarette. At the end of the study, participants were asked to indicate the type of cigarette they smoked by endorsing one of five choices: (a) definitely placebo, (b) probably placebo, (c) I don't know, (d) probably nicotine, or (e) definitely nicotine. Those who were told nicotine but who endorsed either of the placebo choices and those who were told placebo but endorsed either of the nicotine choices were coded as "nonbelievers" for later analyses.

Experimental cigarettes. The experimental cigarettes were marketed under the trade name *Quest* (Vector Tobacco, Timberlake, NC). The nicotine cigarette contained 0.6 mg of nicotine and 10 mg of tar (*Quest* 1) and the placebo cigarette contained no more than 0.05 mg nicotine and 10 mg of tar (*Quest* 3). Although the placebo cigarettes contain a small amount of nicotine, the dose absorbed is unlikely to produce pharmacological effects (Pickworth, Fant, Nelson, Rohrer, & Henningfield, 1999). Participants were given either a menthol cigarette (36%) or nonmenthol cigarette (64%) depending on their usual smoking preferences.

Procedure

Participants who responded to the advertisements were informed that this was a study investigating "immediate reactions to smoking a brand of commercially available cigarettes." Those who met eligibility requirements were scheduled to attend a baseline visit during which participants gave informed consent, provided a CO breath sample, completed baseline measures (Demographics, SCQ-A, POMS-SF, and Urge[2]) and completed a 12-min practice trial of the RVIP. No smoking took place during the baseline session.

A second laboratory visit was scheduled within the next two days and participants were instructed to abstain from smoking for three hours prior to their appointment time. Upon arrival participants were taken to an experimental room where they provided a CO breath sample and were queried about compliance with the abstinence requirement. Those who reported smoking within the past three hours were rescheduled to complete the experiment on another day ($n = 5$). After this point all measures, tasks, and instructions were delivered via computer. First, participants completed measures of smoking urge, mood (POMS-SF), and the 12 minute RVIP task. Next, participants were instructed by the computer to remove a cigarette from a box that was located on the desk. The cigarette contained either 0.6 mg nicotine or 0.05 mg nicotine depending on participant assignment and was placed in the box before the participant arrived. The computer screen presented one of two scripts with corresponding voiceover depending on whether the participant was assigned to the told nicotine or told placebo condition. Thus, there were four experimental conditions: (a) Given Nicotine/Told Nicotine ($n = 37$), (b) Given Nicotine/Told Placebo ($n = 40$); (c) Given Placebo/Told Nicotine ($n = 36$), and (d) Given Placebo/Told Placebo ($n = 35$).

> **Told nicotine instructions.** In this portion of the experiment, you are asked to smoke a cigarette and then rate the cigarette. The cigarette you will smoke is a normal tobacco cigarette than contains a standard amount of nicotine. Please remove the cigarette, lighter, and ashtray from the box that is located next to the computer. Please light and smoke the cigarette as you would normally smoke.
>
> **Told placebo instructions.** In this portion of the experiment, you are asked to smoke a cigarette and then rate the cigarette. The cigarette you will smoke is a normal tobacco cigarette except that it is a placebo; it contains no nicotine. Please remove the cigarette, lighter, and ashtray from the box that is located next to the computer. Please light and smoke the cigarette as you would normally smoke.

Having the dose expectancy manipulation delivered via computer allowed experimenters to be blind to both the nicotine content of the cigarette and the dose expectancy manipulation. Participants were observed smoking through a one-way mirror and experimenters recorded the smoking duration and number of puffs taken. Participants were instructed to press the left mouse button key when they were finished smoking, which began the computerized administration of postsmoking measures including cigarette ratings (CES), urge, mood (POMS-SF) and the 12 minute RVIP task.

The experimenter then returned to the room to inform participants that the experiment was over and to administer the experiment evaluation form. Another CO sample was taken and then participants were debriefed about the purpose of the experiment (to evaluate reactions to smoking

[2] Participants also completed a measure of expectancies for nicotine that was not used in the present analyses as it has not yet been validated.

cigarettes with different levels of nicotine), but not about the nicotine content of the experimental cigarette. Information about the experimental cigarette was provided to participants at a later date by the primary investigator. Participants were paid $20 plus any additional compensation they earned based on their RVIP performance (up to $4.80). After the participant left the laboratory, the experimenter weighed the cigarette remains.

Results

Data Analytic Strategy

A series of 2 (nicotine dose) × 2 (dose expectancy) analyses of variance (ANOVAs) were conducted on measures that were collected at only one time point (i.e., CES, measures of smoking behavior) and to evaluate baseline equivalence on all measures collected on the practice day. A series of 2 (nicotine dose) × 2 (dose expectancy) analyses of covariance (ANCOVA's) were conducted on measures that were collected before and after smoking (e.g., CO, urge, mood, and RVIP indices) with the presmoking score entered as the covariate and postsmoking score entered as the dependent variable. Significant interactions were followed up with simple comparisons of the dose expectancy manipulation in the given nicotine groups (Given Nicotine/Told Nicotine vs. Given Nicotine/Told Placebo) and the given placebo groups (Given Placebo/Told Nicotine vs. Given Placebo/Told Placebo). All analyses were conducted at first without regard to gender and then repeated including gender as an independent variable (see Perkins et al., 2006). There were no effects of gender on any of the dependent measures so all analyses are reported with men and women combined.

Baseline Data

There were no differences between groups at baseline on expired air CO, age, race, smoking rate, years smoked, nicotine dependence (FTND), smoking outcome expectancies (SCQ-A), or any of the dependent measures (all p's $>.10$). Table 1 shows the means and standard deviations for the entire sample.

Manipulation Checks

Dose expectancy manipulation. To test the credibility of the dose expectancy manipulation participants were asked to respond to a question that asked what type of cigarette they smoked. Eighty-two percent of participants ($n = 122$) reported smoking a cigarette consistent with what they were told. Not surprisingly, the highest rates of disbelief were in the conditions in which participants were deceived with 15% (6/40) of those in the given nicotine/told placebo group and 36.11% (13 of 36) of those in the given placebo/told nicotine group not believing the manipulation. In contrast 10.81% (4/37) of those in the given and told nicotine group and 8.57% (3/35) in the given and told placebo group reported smoking a cigarette type different from what they were told. All analyses were conducted using both the subsample of 122 participants who provided reports consistent with the nicotine dose expectancy manipulation and the full sample of 148 participants. There were no differences in findings among the two types of analyses. Thus, we present data using the full sample of participants to maintain roughly equivalent sample sizes and utilize all collected data.

Cigarette manipulation. The next set of analyses was performed to examine how participants smoked the experimental cigarettes. As shown in Table 2, there was a main effect of nicotine dose on smoking duration with participants in the given nicotine groups smoking longer than those in the given placebo groups, $M = 216.37$s versus $M = 180.77$s, $F(1, 143) = 13.36$, $p < .001$, $\eta^2 = 0.09$. There was a significant dose expectancy by nicotine dose interaction for total number of cigarette puffs, $F(1, 143) = 13.34$, $p < .001$, $\eta^2 = 0.09$. Simple comparisons revealed that among participants given nicotine those told nicotine took a greater number of puffs than those told placebo $F(1, 75) = 8.45$, $p = .005$, but among those given placebo, those told nicotine took fewer puffs than those told placebo, $F(1, 68) = 5.20$, $p = .026$. There were no significant group differences on the weights of postsmoking cigarette remains ($M = .49$, $SD = .09$) or CO boost ($M = 3.52$, $SD = 2.41$).

Dependent Variables

Cognitive performance. As shown in Figure 1, there was a main effect of nicotine on RVIP reaction time with those given nicotine exhibiting shorter reaction times to targets than those given placebo, $F(1, 141) = 4.28$, $p = .04$, $\eta 2 = 0.030$. Participants given nicotine also had a greater number of hits ($M = 39.40$, SE 1.50) than those given placebo ($M = 34.63$, SE 1.58), $F(1, 141) = 9.53$, $p = .002$, $\eta^{2\ =}$ 0.067, and showed greater sensitivity on the task, $F(1, 141) = 4.26$, $p = .041$, $\eta^2 = 0.030$. As shown in Figure 2, there was a main effect of dose expectancy on the number of false alarms such that those told nicotine had fewer false alarms than those told placebo, $F(1, 141) = 6.94$, $p = .009$, $\eta^2 = 0.049$. There were no effects of dose expectancy or nicotine dose on response bias, and no dose expectancy by nicotine dose interactions.

Smoking urge. For smoking urge, there was a significant nicotine dose by dose expectancy interaction, $F(1, 143) = 5.47$, $p = .020$, $\eta^2 = 0.04$. As depicted in Figure 3, simple effects tests revealed no dose expectancy effect among participants given nicotine, $F(1, 74) = 2.22$, $p = .141$, but a significant dose expectancy effect among participants given placebo, $F(1, 68) = 32.31$, $p < .0001$, with those told nicotine reporting lower smoking urge than those told placebo.

Mood. There were main effects for nicotine, $F(1, 143) = 16.35$, $p < .01$, $\eta^2 = 0.12$ and dose expectancy, $F(1, 143) = 7.18$, $p < .01$, $\eta^2 = 0.05$ for total mood disturbance, with those given nicotine showing less mood disturbance than those given placebo and those told nicotine showing less mood disturbance than those told placebo. Similarly, main effects for nicotine dose and dose expectancy were found for the depression-dejection and anger-hostility fac-

Table 2
Measures of Smoking Exposure

	Condition (Given/Told)				Effect			
	Nicotine/ Nicotine	Nicotine/ Placebo	Placebo/ Nicotine	Placebo/ Placebo	Main effect nicotine	Main effect dose expectancy	Nicotine X dose expectancy
	Mean[a] *(SEM)*	Mean *(SEM)*	Mean *(SEM)*	Mean *(SEM)*	F η^2	F η^2	F η^2
Smoking duration (s)	214.81 (9.69)	217.93 (9.32)	182.44 (9.83)	179.09 (10.11)	$F = 13.36^{***}$, 0.09	*ns*	*ns*
Number of puffs	13.76 (0.56)	11.28 (0.54)	9.94 (0.57)	11.56 (0.58)	$F = 9.90^{**}$, 0.07	*ns*	$F = 13.34^{***}$, 0.09
CO boost	3.43 (0.40)	3.22 (0.40)	3.41 (0.42)	4.03 (0.42)	*ns*	*ns*	*ns*
Cigarette weight (g)	0.48 (0.01)	0.48 (0.01)	0.50 (0.01)	0.49 (0.01)	*ns*	*ns*	*ns*

Note. CO = Carbon Monoxide.
† $p < .08$. * $p < .05$. ** $p < .01$. *** $p < .001$.

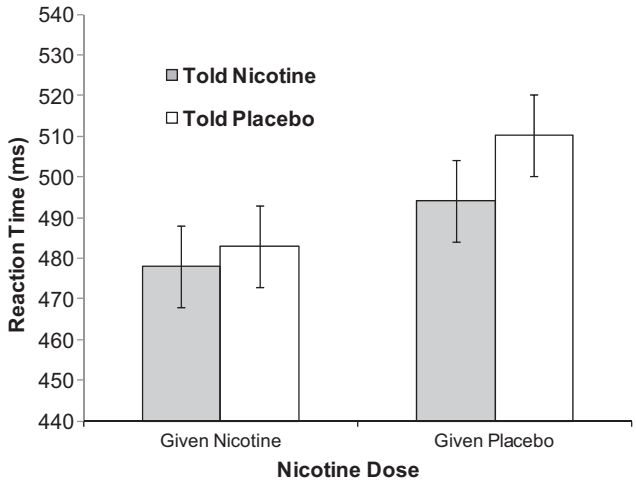

Figure 1. Reaction time (ms) to RVIP targets across the four experimental conditions showing a main effect of nicotine dose.

tors (see Table 3), and only nicotine dose on the fatigue-inertia factor. Significant interactions were observed for the tension-anxiety and vigor-activity factors with simple comparisons revealing differences between the told nicotine and told placebo conditions only in the context of placebo for tension-anxiety, $F(1, 68) = 7.29$, $p = .009$ and only in the context of nicotine for vigor-activity, $F(1, 74) = 5.32$, $p = .024$.

Subjective ratings of the cigarettes. As shown in Table 4, main effects of nicotine dose were observed for all 11 rewarding subjective ratings of the cigarette and main effects of dose expectancy were observed for 9 of 11 rewarding subjective cigarette ratings. Main effects of nicotine dose were also observed for ratings of dizzy and tastes different than usual brand. There were no interactions.

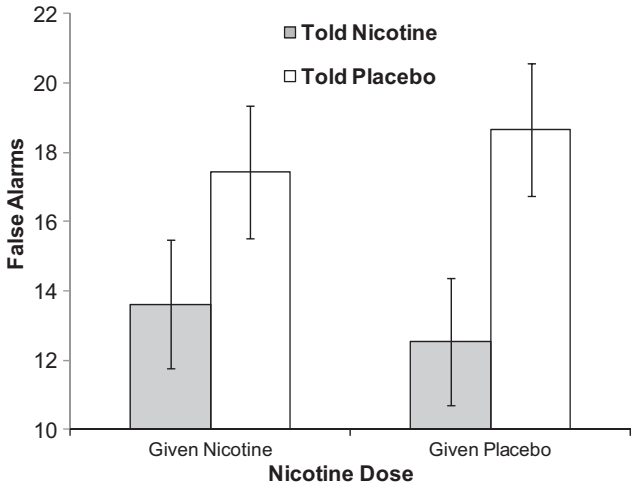

Figure 2. Number of RVIP false alarms across the four experimental conditions showing a main effect of nicotine dose expectancy.

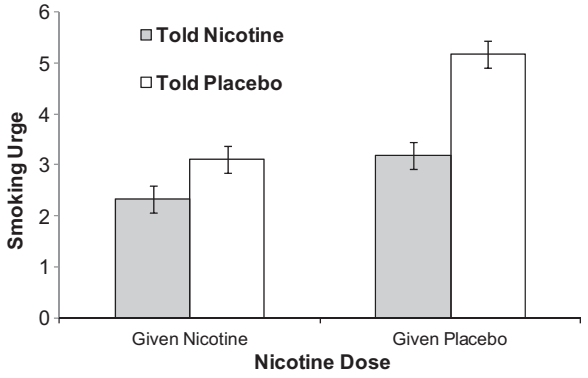

Figure 3. Mean self-reported smoking urge across the four experimental conditions. Simple effects tests following a significant nicotine dose by dose expectancy interaction revealed an effect of the nicotine dose expectancy manipulation in the context of placebo administration but not nicotine administration.

Discussion

This study is the first to evaluate the independent and interactive effects of nicotine dose and nicotine dose expectancy on cognitive performance improvements after cigarette smoking. Consistent with many previous studies, nicotine cigarettes led to better performance on a test of sustained attention (RVIP) than placebo cigarettes. Three-hour abstinent smokers who smoked nicotine cigarettes demonstrated faster reaction time, greater accuracy (hits), and greater sensitivity on the RVIP. There was no effect of nicotine on response bias. Participants who were told that the cigarette was a placebo produced a greater number of false alarms than those told nicotine, regardless of actual dose. Interestingly, the rate of false alarms is typically not influenced by nicotine administration (Koelega, 1993; Prichard & Robinson, 1998), but in this case appeared to be influenced by dose expectancy. However, the size of this effect was small and this preliminary finding should be followed up with additional research.

As far as urge to smoke, there was a nicotine dose by dose expectancy interaction. As has been found in other smoking BPD studies (Juliano & Brandon, 2002; Kelemen & Kaighobodi, 2007), being told nicotine produced significantly lower urge than being told placebo, but only in the context of smoking a placebo cigarette. The dose expectancy manipulation had little effect in the context of actual nicotine administration. This suggests that either nicotine or the belief that one is smoking a nicotine cigarette is sufficient to attenuate smoking urges, but that dose expectancies are not adding to the effect of nicotine. Perkins and colleagues (2008) found that those who were told nicotine reported lower smoking urges relative to those told placebo, but only in the context of positive mood not a negative mood. It has been suggested that stressful cognitive situations may moderate the relative contributions of nicotine and smoking somatosensory stimulation to smoking craving (Baldinger, Hasenfratz, & Battig, 1995). Thus it is possible that our findings may not generalize across different mood states.

Table 3
Covariate Adjusted Profile of Mood States Ratings Across the Experimental Conditions

	Condition (Given/Told)				Effect		
	Nicotine/ Nicotine	Nicotine/ Placebo	Placebo/ Nicotine	Placebo/ Placebo	Main effect nicotine	Main effect dose expectancy	Nicotine X dose expectancy
	Mean[a] (*SEM*)	Mean (*SEM*)	Mean (*SEM*)	Mean (*SEM*)	F η^2	F η^2	F η^2
POMS Depression-Dejection	1.17 (0.29)	1.49 (0.28)	1.74 (0.29)	*2.70 (0.30)*	$F^{b} = 9.51^{**}$ 0.066	$F = 4.95^{*}$ 0.035	*ns*
POMS Anger-Hostility	1.32 (0.49)	2.51 (0.48)	3.01 (0.50)	4.35 (0.51)	$F = 12.75^{***}$ 0.089	$F = 6.60^{*}$ 0.046	*ns*
POMS Tension-Anxiety	2.24 (0.43)	2.40 (0.42)	2.97 (0.44)	4.84 (0.44)	$F = 13.47^{***}$ 0.094	$F = 5.50^{*}$ 0.039	$F = 3.93^{c*}$ 0.027
POMS Fatigue	3.87 (0.46)	4.35 (0.44)	4.68 (0.47)	5.21 (0.47)	$F = 3.28^{\dagger}$ 0.023	*ns*	*ns*
POMS Vigor	7.70 (0.65)	5.14 (0.62)	5.50 (0.65)	5.58 (0.66)	*ns*	$F = 3.56^{\dagger}$ 0.025	$F = 4.22^{d*}$ 0.030
POMS Total mood disturbance	24.81 (1.66)	29.41 (1.60)	31.68 (1.69)	36.06 (1.74)	$F = 16.35^{***}$ 0.115	$F = 7.18^{**}$ 0.051	*ns*

Note. SEM = Standard Error of the Mean. η^2 = effect size.
[a] covariate adjusted means, baseline score as covariate. [b] *df* (1,143) for all analyses. [c] Effect of dose expectancy in the context of placebo administration with those told placebo reporting greater tension than those told nicotine. $F(1, 68) = 7.29$, $p = .009$. No effect of dose expectancy in the context of nicotine administration. [d] Effect of dose expectancy in the context of nicotine administration with those told placebo reporting less vigor than those told nicotine, $F(1, 74) = 5.32$, $p = .024$. No effect of dose expectancy in the context of placebo administration.
† $p < .08$. * $p < .05$. ** $p < .01$. *** $p < .001$.

Table 4
Cigarette Ratings Across the Experimental Conditions

	Conditions (Given/Told)				Effects			
	Nicotine/ Nicotine	Nicotine/ Placebo	Placebo/ Nicotine	Placebo/ Placebo	Main effect nicotine	Main effect instructions	Nicotine X instructions
	Mean (*SEM*)	Mean (*SEM*)	Mean (*SEM*)	Mean (*SEM*)	F η^2	F η^2	F η^2
Satisfying	5.40 (0.24)	4.30 (0.23)	3.17 (0.24)	2.29 (0.25)	$F^a = 78.68^{***}$ 0.546	$F = 17.16^{***}$ 0.119	*ns*
Tastes good	4.41 (0.25)	3.70 (0.24)	2.53 (0.25)	1.94 (0.26)	$F = 52.85^{***}$ 0.367	$F = 6.66^{*}$ 0.046	*ns*
Enjoyable sensations in throat and chest	3.86 (0.26)	3.48 (0.25)	3.17 (0.26)	2.29 (0.27)	$F = 13.36^{***}$ 0.093	$F = 6.05^{*}$ 0.042	*ns*
Calming	4.46 (0.22)	3.43 (0.22)	2.89 (0.23)	1.86 (0.23)	$F = 49.05^{***}$ 0.341	$F = 21.26^{***}$ 0.148	*ns*
Less irritable	3.68 (0.25)	2.58 (0.24)	2.50 (0.25)	1.77 (0.26)	$F = 15.54^{***}$ 0.108	$F = 13.27^{***}$ 0.092	*ns*
Helped Concentrate	3.43 (0.24)	2.88 (0.23)	2.28 (0.25)	1.80 (0.25)	$F = 20.88^{***}$ 0.145	$F = 4.50^{*}$ 0.031	*ns*
Reduced craving	4.86 (0.27)	4.00 (0.26)	3.81 (0.27)	2.11 (0.28)	$F = 29.74^{***}$ 0.207	$F = 22.40^{***}$ 0.156	*ns*
Less anxious	3.78 (0.23)	2.65 (0.23)	2.75 (0.23)	1.69 (0.24)	$F = 18.97^{***}$ 0.132	$F = 22.95^{***}$ 0.159	*ns*
More alert	3.10 (0.21)	2.48 (0.20)	2.19 (0.21)	1.97 (0.21)	$F = 11.80^{***}$ 0.082	$F = 4.31^{*}$ 0.030	*ns*
More awake	3.38 (0.24)	2.75 (0.23)	2.25 (0.24)	2.00 (0.24)	$F = 15.79^{***}$ 0.110	$F = 3.45^{\dagger}$ 0.024	*ns*
Reduced hunger	2.30 (0.22)	2.45 (0.21)	1.94 (0.22)	1.34 (0.22)	$F = 11.26^{**}$ 0.078	*ns*	*ns*
Different from usual brand	4.59 (0.23)	4.85 (0.22)	6.31 (0.23)	6.49 (0.23)	$F = 54.63^{***}$ 0.379	*ns*	*ns*
Dizzy	2.73 (0.27)	2.83 (0.26)	1.83 (0.27)	1.57 (0.28)	$F = 15.72^{***}$ 0.109	*ns*	*ns*
Nauseous	1.38 (0.17)	1.58 (0.16)	1.64 (0.17)	1.94 (0.17)	$F = 3.49^{\dagger}$ 0.023	*ns*	*ns*

Note. SEM = Standard Error.
[a] *df* (1,144) for all analyses.
† $p < .08$. * $p < .05$. ** $p < .01$. *** $p < .001$.

One prior smoking BPD study (Perkins et al., 2004) did not find any effects on smoking urge. However, that study differed from the others in that presmoking abstinence was very brief (only one hr) and participants took only two puffs on the experimental cigarette prior to rating urge. It is possible that greater abstinence and more smoking exposure leads to more robust BPD effects on urge, although these factors have not been directly tested.

As far as mood, there were main effects of nicotine dose such that participants who smoked nicotine cigarettes had lower ratings of depression-dejection, anger-hostility, fatigue-inertia, and total mood disturbance compared to those who smoked placebo cigarettes. Furthermore, main effects of dose expectancy were observed such that those who were told nicotine reported lower ratings of depression-dejection, anger-hostility, and total mood disturbance than those told placebo. For the tension-anxiety and vigor-activity factors there were nicotine dose by dose expectancy interactions. Similar to urge, dose expectancy had an effect on tension-anxiety in the context of placebo administration but not nicotine administration. However, dose expectancy effects were observed for vigor-activity only among those given nicotine, such that being told nicotine produced much greater vigor than being told placebo. In this case, one could conclude that smoking a nicotine cigarette under the guise that it was a placebo lessened the pharmacological effects of nicotine, resulting in an "antiplacebo" effect (see Perkins et al., 2003). Other BPD studies to date have not used the POMS or other comprehensive measures of mood, but rather have assessed one or two mood dimensions. In general, prior research has shown that denicotinized cigarettes smoked under double-blind conditions have more robust effects on craving reduction than negative affect reduction (Buchhalter et al., 2005; Rose, 2006). Our findings suggest that, in addition to nicotine, dose expectancy has important effects on mood. Given that mood states may influence motivation to smoke (Conklin & Perkins, 2005), and many smokers believe that smoking improves mood (Copeland et al., 1995), this should be further explored.

A number of main effects were observed for both the nicotine factor and dose expectancy factor on subjective ratings of the experimental cigarettes. Compared to placebo cigarettes, nicotine cigarettes led to greater rewarding effects on all 11 dimensions. Nicotine cigarettes were also rated higher on similarity to one's usual brand and dizziness. Relative to those told placebo, participants who were told nicotine reported greater rewarding effects of the cigarette on 9 of 11 dimensions. Interestingly, there were no nicotine dose by dose expectancy interactions on subjective ratings of the cigarettes, which was also the case in the Kelemen and Kaighobadi (2007) study (with the exception of cigarette strength, which was not measured in this study). The effect sizes for nicotine effects were generally larger than the effect sizes for dose expectancy effects, also similar to Kelemen and Kaighobadi (2007). Other studies have also shown effects of nicotine dose and dose expectancy on smoking satisfaction and/or liking (Perkins et al., 2008; Perkins et al., 2004). The present study adds to the data by demonstrating that the perceived rewarding effects of ciga-

rette smoking are highly influenced by both nicotine dose and dose expectancy and have additive but not interactive effects. This could have implications for the use of denicotinized cigarettes as a treatment tool, or a component of expectancy challenge interventions.

Smoking behavior was also affected by both nicotine dose and dose expectancy. Participants who smoked a nicotine cigarette spent significantly more time smoking than those who smoked a placebo cigarette. For the total number of puffs an interaction was observed. Among participants given nicotine, those who were told nicotine took more puffs than those told placebo, but among those given placebo, those told nicotine took fewer puffs than those told placebo. Although the effects of the manipulations on smoking behavior is interesting in its own right, smoking behavior could have confounded the effects of the experimental manipulations on the other dependent measures. To investigate this possibility, we reran all analyses including the number of puffs and/or smoking duration as covariates in the ANCOVA models for all dependent measures. Doing so did not have any effects on the subjective outcomes (urge, POMS, ratings of the cigarettes), the dose expectancy effect on false alarm RVIP outcomes, or the nicotine dose effects on RVIP hits. However, for RVIP reaction time and RVIP sensitivity adding these covariates reduced the significant main effects of nicotine dose to statistical trends. Studies that control smoking exposure across the conditions of the BPD would eliminate systematic differences in smoking exposure that could confound the manipulations, but this would likely result in less naturalistic smoking conditions.

The findings in this study and others suggest that the expected dose of the cigarette influences responses to smoking, but this does not shed light on the influence of smokers' underlying beliefs about the effects of smoking on smoking outcomes (i.e., response expectancies). Future studies could attempt to directly manipulate the expected effects of smoking to evaluate their causal role in smoking outcomes. Furthermore, future studies could assess baseline self-reported response expectancies to test theoretical propositions regarding the mechanisms underlying dose expectancy effects. This is especially important given data that suggests that smokers may have misperceptions about the effects of nicotine obtained via nicotine replacement products (e.g., Bansal, Cummings, Hyland & Giovino, 2004). Little is known about smokers' beliefs about the contributions of nicotine to the effects of smoking and measures that assess these beliefs need to be developed and validated.

It is important to note that 18% of participants reported smoking a type of cigarette different from the intended dose expectancy manipulation. The highest rates of disbelief were in the given placebo and told nicotine condition (i.e., 36%), followed by the given nicotine and told placebo condition (15%). These rates are different than the Juliano and Brandon (2002) study, in which the highest rates of disbelief were in the given nicotine and told placebo condition. There are important differences between the present study and this prior BPD study. Central to the issue of the credibility of the dose expectancy manipulation is that the present study used cigarettes with about half as much nicotine as those used Juliano and Brandon (2002). Furthermore, in the present study the dose expectancy manipulation was delivered by computer. Moreover, in the present study we assessed the believability of the dose expectancy manipulation with an item that had an equal number of options for nicotine and placebo. This is an improvement over the 6-point scale used in Juliano and Brandon (2002) that had only one placebo option (0 mg nicotine) and five nicotine options (.06 to 1.7 mg). Perkins et al. (2008) also found higher rates of disbelief in the in the conditions involving deception (27.5–32.5%) than the conditions not involving deception (12.5%–20%). Kelemen and Kaighobadi (2007) reported overall lower rates of disbelief and also used *Quest* cigarettes with 0.6 mg nicotine, but placed the experimental cigarettes in commercially labeled packs that were consistent with the dose expectancy manipulation, and used a delayed debriefing procedure. We also used a delayed debriefing procedure to reduce the possibility that participants would have been tipped off about the deception in the study. It is also important to note that the question about cigarette type was not asked until the end of the experiment, and thus may not reflect what participants believed at the time they smoked the cigarette. Future work in this area should continue to improve the credibility of the dose expectancy manipulation as well as its assessment.

This study did not have a nonsmoking control group and thus the absolute effects of smoking exposure independent of nicotine dose or dose expectancy cannot be evaluated. Perkins and colleagues (2008) included a no-smoking control group along with the BPD conditions and compared participants who did not smoke to those who were told and given a placebo cigarette. They concluded that the smoking ritual regardless of dose expectancy or nicotine dose attenuated negative affect relative to a no smoking condition in the context of a negative mood induction but not a positive mood induction. An evaluation of pre- to postsmoking change scores on the POMS-SF in the present study showed that for four out of five factors and total mood disturbance, mood worsened after smoking in the told and given placebo condition (vigor-activity was unchanged). Our urge data revealed substantial urge reduction in groups that were either given nicotine or told nicotine (anywhere from 2.21 to 3.46 unit reduction on a 7-point scale). However, urge in the told and given placebo condition was nearly unchanged after smoking (.19 unit decrease). Thus, it does not appear that individuals in this study who knowingly smoked a placebo cigarette experienced any absolute benefit from it; albeit it is possible that they could have been worse off if no smoking took place. Given the suggestion that denicotinized cigarettes may be a useful quitting tool (Rose, 2006), more research is needed to determine the contextual factors that determine how smokers respond when they knowingly smoke denicotinized cigarettes.

It should be noted that we relied on self-report to assess recent smoking exposure on the day of the experimental manipulation. Participants were instructed to abstain from smoking for 3 hours prior to the appointment time. Upon arrival they were asked when they last smoked, and five

participants who reported smoking in the prior 3 hours were rescheduled. We informed participants that we would assess recent smoke exposure with a CO test to encourage them to comply, but we did not use the CO results to exclude participants. Thus one potential limitation of the study is that participants could have misreported recent smoking. Future studies should better control for recent smoking exposure. Another potential limitation is that reactions to the unfamiliar cigarettes used in this study may not generalize to conditions in which participants are smoking their usual brand of cigarette.

This study provides additional evidence that nicotine plays an important role in the cognitive and rewarding subjective effects of cigarette smoking. This study also provides preliminary evidence that dose expectancy influences the cognitive performance enhancement experienced from smoking, and additional evidence that it influences smoking urge, mood and other subjective rewarding effects of cigarettes (e.g., improved concentration). Future studies should continue to evaluate the role of nonnicotine factors such as expectancy in the persistence of cigarette smoking and its effective treatment. There is preliminary evidence that smokers' expectancies for smoking (Copeland & Brandon, 2000) are modifiable and that challenging the validity of these beliefs may affect smoking motivation (Copeland & Brandon, 2000). Future research is needed to better characterize the expectancies that smokers have about nicotine, especially in the context of smoking. Furthermore, studies that attempt to directly manipulate nicotine dose and/or response expectancies could shed light on their causal role in both the effects of cigarette smoking and the effectiveness of nicotine replacement products (Fucito & Juliano, 2007; Perkins et al., 2009). Research should also continue to evaluate the effects of dose expectancies and response expectancies on other types of cognitive performance. A greater understanding of expectancy effects will guide the development of expectancy based interventions and will no doubt improve our overall understanding of clinical outcomes.

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