A Direct Test of the Influence of Nicotine Response Expectancies on the Subjective and Cognitive Effects of Smoking

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Regardless of actual nicotine content, expectations about the nicotine content of a cigarette influence the rewarding subjective effects of smoking, and may even affect cognitive performance. These effects are theorized to be mediated by beliefs about effects of cigarette smoking, or response expectancies. However, few studies have directly manipulated response expectancies. Understanding the effects of such manipulations could improve effectiveness of nicotine-dependence treatments and medications. Using a 2×2 between-subjects factorial design, cigarette smokers ($N = 80$) smoked either a nicotine or a placebo (denicotinized) cigarette crossed with instructions that the cigarette would either enhance or impair cognitive and motor performance. As predicted, participants in the "told enhance" condition reported significantly greater beliefs that nicotine had beneficial effects on performance than those in the "told impair" condition. Compared to those "told impair," those "told enhance" reported more psychological reward, enjoyable physical sensations, and craving reduction from the cigarette, as well as greater motivation to perform well on a cognitive task. Relative to placebo cigarettes, nicotine cigarettes produced greater reports of satisfaction, craving reduction, and dizziness. Smoking a nicotine cigarette produced better performance on the Rapid Visual Information Processing Task, a test of sustained attention; but the expectancy manipulation had no effect. These data suggest that response expectancies can be experimentally manipulated and can influence perceived rewarding effects of cigarette smoking, but do not appear to affect cognitive performance. These findings add to our understanding of the benefits and limitations of expectancy manipulations, both experimentally and as a treatment technique.

Keywords: expectancies, nicotine, cognitive, Rapid Visual Information Processing Task, placebo effects

It has been suggested that placebo or nocebo effects result from expectations individuals have about a drug or treatment. The knowledge that one has been administered a drug or treatment is referred to as a *stimulus expectancy*, whereas idiosyncratic beliefs about the effects that the drug or treatment will have on one's feelings, cognitions, or behaviors are referred to as *response expectancies* (Kirsch, 1985; Perkins, Sayette, Conklin, & Cagguila, 2003). According to expectancy-based conceptualizations of placebo effects, the belief that one has consumed a drug activates response expectancies, which directly produce responses or symptoms consistent with the expected effects of the drug (Kirsch, 1999). It is believed that response expectancies not only affect reactions to placebos, but also influence the pharmacological effects of drugs (Kirsch, 1999; Perkins et al., 2003). Investigating the mechanisms of placebo effects provides an opportunity to learn more about mind−body interactions and may uncover ways to control placebo effects to improve the effectiveness of treatments and medications (Copeland & Brandon, 2000; Finniss, Kaptchuk, Miller, & Bennedetti, 2010; Fucito & Juliano, 2007).

There is growing evidence that the rewarding and reinforcing effects of cigarette smoking may be due in part to placebo effects. Studies using the balanced placebo design, which crosses actual drug exposure (nicotine vs. placebo cigarettes) with expected drug exposure (told nicotine vs. placebo), have demonstrated that expecting nicotine influences responding to placebo (denicotinized) and nicotine cigarettes. In general, expecting nicotine in a cigarette, regardless of actual drug content, produces increased smoking behavior (Perkins et al., 2008), reduced urges and cravings to smoke (Kelemen & Kaighobadi, 2007; Perkins et al., 2008), improved mood (Juliano, Fucito, & Harrell, 2011), greater smoking satisfaction (Juliano et al., 2011; Kelemen & Kaighobadi, 2007; Perkins et al., 2004; Perkins et al., 2008), and a variety of other self-reported positive responses (e.g., greater wakefulness, concentration) compared to expecting placebo. Furthermore, a recent study demonstrated that expecting nicotine resulted in fewer errors on the Rapid Visual Information Processing (RVIP) task, a computerized cognitive task assessing sustained attention (Juliano et al., 2011). Thus, there is mounting evidence that subjective, affec-

tive, behavioral, and perhaps even cognitive effects of smoking may be in part due to expectancy effects. At present, it is unclear how stimulus expectancies exert these effects. It may be related to response expectancies. However, smoking research, like most research investigating drug-related placebo responding, has focused primarily on manipulating stimulus expectancies, with less emphasis on manipulating or evaluating response expectancies. *Self-report* measures of smoking response expectancies have been included in some placebo research. For example, Juliano and Brandon (2002) found that expecting nicotine during smoking produced greater anxiety reduction than expecting placebo, but only among smokers who reported greater expectancies that smoking alleviates negative affect. Another investigation found that self-reported response expectancies for the performance-enhancing effects of cigarette smoking assessed after smoking and completing a cognitive performance task (i.e., RVIP) were associated with actual performance in some cases (Kelemen, 2008). Studies involving caffeine have shown that participants' beliefs about the effects of caffeine can predict subjective or performance-enhancing effects of decaffeinated coffee (e.g., Fillmore & Vogel-Sprott, 1992; Flaten, Aasli, & Blumenthal, 2003; Kirsch & Wiexel, 1988). However, because response expectancies were not manipulated in any of these studies, their causal role in placebo responding cannot be determined.

There is a fairly limited body of research involving direct manipulations of the expected effects of a drug to determine the resulting effects on drug and placebo responding. Two prior studies involving nicotine replacement therapy (NRT) found that manipulations designed to alter expectancies for nicotine replacement resulted in differential reactions to placebo NRT (Fucito & Juliano, 2007; Tate, Stanton, Green, & Schmitz, 1994). Participants given information about NRT benefits reported greater overall vigor when on placebo NRT (Fucito & Juliano, 2007). Similarly, participants who drank coffee and were told that caffeine enhances cognitive performance reported greater performance motivation and fewer negative somatic effects than those told caffeine impairs performance (Harrell & Juliano, 2009). Furthermore, manipulating the expected effects of caffeine or alcohol (i.e., participants told that the drug would either enhance or impair performance) has been shown to influence cognitive and motor performance, resulting in effects consistent with the manipulation for adults given decaffeinated coffee (Fillmore, Mulvihill, & Vogel-Sprott, 1994; Fillmore & Vogel-Sprott, 1994) and in the opposite direction of the manipulation for participants in caffeine withdrawal (Harrell & Juliano, 2009) or receiving alcohol (Fillmore et al., 1994; Fillmore, Roach, & Rice, 2002). The present study was designed to evaluate the influence that expectancies for the effects of cigarette smoking have on reactions to smoking. We were particularly interested in expectancies for the cognitive-enhancing effects of cigarette smoking. Various aspects of cognitive performance, including attention and memory, are enhanced after the administration of nicotine compared to placebo, especially after a period of nicotine deprivation (Heishman, Kleykamp, & Singleton, 2010). Furthermore, smoking for cognitive enhancement is rated as one of the most common motives for smoking (Gilbert, Sharpe, Ramanaiah, Detwiler, & Anderson, 2000). Smoking levels increase during times of high cognitive load, such as before an exam (Patterson, Lerman, Kaufmann, Neuner, & Audrain-McGovern, 2004), and the cognitive and affective effects of nicotine are likely connected in systematic ways (Waters & Sutton, 2000), so that smoking for affective regulation may be related to beliefs about cognitive enhancement, for example, decreasing feelings of anxiety by enhancing perceived coping ability (Kassel & Shiffman, 1997). Given that cigarette smokers often smoke as a means of enhancing or maintaining consistent levels of performance, challenging performance response expectancies may be an effective treatment tool.

The goal of the present study was to determine whether response expectancies for cigarette smoking could be manipulated and if such expectancies directly influenced the rewarding effects of cigarette smoking. In this 2×2 factorial study, we manipulated smokers' expectancies for the performance effects of nicotine by informing some participants that smoking enhances cognitive performance and others that it impairs cognitive performance. We also controlled actual nicotine exposure with some participants smoking cigarettes with nicotine and others smoking placebo (denicotinized) cigarettes. As such, participants were randomly assigned to one of the following four conditions: (a) told enhance/given nicotine; (b) told enhance/given placebo; (c) told impair/given nicotine; and (d) told impair/given placebo. Performance expectancies, cognitive performance, cigarette ratings, smoking urge, performance motivation, and resistance to drug effects were assessed. The RVIP task, a commonly used test of sustained attention, was used to assess cognitive performance because this task has been shown to be sensitive to the effects of nicotine (Heishman et al., 2010; Prichard & Robinson, 1998) and, in a prior study, was sensitive to the effects of a stimulus expectancy manipulation (Juliano et al., 2011). Smokers who were told that smoking enhances performance were expected to report more positive nicotine performance expectancies, demonstrate greater cognitive performance, and report more positive reactions to the cigarette (e.g., satisfaction), lower urges to smoke, more motivation to perform well, and less resistance to drug effects, relative to those *told impair*. Smokers *given nicotine* were expected to perform better on the test of sustained attention than those *given placebo*. We were also interested in potential interactions between the expectancy manipulation and cigarette type, including the possibility of a replication of prior findings that participants *told impair* performed better than those *told enhance*, but only for those *given placebo* (Harrell & Juliano, 2009).

Method

Participants

Participants were recruited from the university community (37%) and the Washington, DC, metropolitan area (63%). Participants were required to be at least 18 years old and to smoke between 6 and 40 cigarettes per day. Individuals with chronic smoking-related diseases (e.g., emphysema) were excluded from participation. Participants ($N = 80$, 30.0% women, $M_{age} = 32.8$ years, $SD = 13.5$) smoked a mean of 14.2 ($SD = 7.0$) cigarettes per day. The mean Fagerström Test of Nicotine Dependence (FTND) score was 4.1 ($SD = 2.3$). Most of the participants identified themselves as either African American or Black (44%) or White (43%). Table 1 shows demographic and other characteristics of the sample.

Table 1

Premanipulation Values by Condition

	Conditions (told/given)			
	Enhance/nicotine	Enhance/placebo	Impair/nicotine	Impair/placebo
Values	n (%) or M (SEM)	n (%) or M (SEM)	n (%) or M (SEM)	n (%) or M (SEM)
Female	3 (15.8%)	8 (40.0%)	7 (38.9%)	6 (26.1%)
Age (years)*	34.21 (2.96)	26.17 (3.04)	39.30 (2.88)	31.30 (2.69)
Cigarettes per day	14.37 (1.62)	13.06 (1.67)	15.73 (1.58)	13.50 (1.48)
Expectancy	4.87 (0.22)	5.40 (0.22)	5.04 (0.21)	5.23 (0.20)
Withdrawal (MNWS)	1.06 (0.14)	0.80 (0.14)	0.69 (0.14)	0.78 (0.13)
FTND	4.16 (0.52)	3.39 (0.54)	4.35 (0.51)	4.22 (0.47)
Urge	5.40 (0.38)	5.41 (0.39)	5.40 (0.37)	5.51 (0.35)

Note. MNWS = Minnesota Nicotine Withdrawal Scale; FTND = Fagerström Test of Nicotine Dependence.
* Those given nicotine cigarettes were significantly older ($M = 36.82$ years, $SD = 14.21$) than those given placebo cigarettes ($M = 29.05$ years, $SD = 11.70$), $F(1, 79) = 7.68$, $p = .007$, $\eta^2 = 0.09$.

Materials

Experimental cigarettes. The experimental cigarettes were marketed under the trade name Quest (Vector Tobacco, Timberlake, NC). The nicotine cigarette contained a yield of 0.6 mg of nicotine and 10 mg of tar (Quest 1) and the placebo cigarette contained a yield of no more than 0.05 mg nicotine and 10 mg of tar (Quest 3). Nicotine yield refers to measurements of nicotine yield in mainstream smoke by the U.S. Federal Trade Commission method (Hatsukami et al., 2010). It is important to note that nicotine delivery was not directly measured (Donny, Houtsmuller, & Stitzer, 2007). The actual tobacco rods of Quest 1 cigarettes contain a total of 8.9 mg of nicotine, whereas Quest 3 cigarettes contain 0.48 mg of nicotine (Becker, Rose, & Albino, 2008). The dose absorbed from Quest 3 or similar denicotinized cigarettes produces pharmacological effects that are arguably insignificant (Pickworth, Fant, Nelson, Rohrer, & Henningfield, 1999; but see Barrett, 2010; Brody et al., 2009; Gross, Lee, & Stitzer, 1997). Participants were given either a menthol cigarette (47%) or nonmenthol cigarette (53%), depending on their usual smoking preferences. All cigarettes were blinded and coded by an experimenter who had no contact with participants. Prior research has shown than participants can be convinced they are smoking nicotine cigarettes when denicotinized cigarettes are administered (Juliano et al., 2011).

Carbon monoxide. Carbon monoxide (CO) levels were measured in parts per million (ppm) using a Micro III Smokerlyzer (Bedfront Scientific, Kent, England). Breath CO samples were taken to encourage compliance with instructions to abstain from smoking for 12 hr 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.

Performance Measures

RVIP task. The RVIP is a widely used test of sustained attention (or vigilance) that has been shown to be sensitive to the effects of nicotine (Heishman et al., 2010; Juliano et al., 2011). Participants viewed a series of single digits presented on the computer screen at a rate of 100 digits per min for 12 min. Participants were told to press a mouse button as quickly as possible whenever they detected three consecutive odd or three consecutive even numbers. To increase motivation for the RVIP task on the experimental day and to improve sensitivity, participants were informed that they would earn 3 cents for each correct detection (hit) and lose 3 cents for each false alarm. Response targets appeared eight times per min with 8−36 digits appearing between each target. Reaction time and responses were recorded by the computer. Responses that occurred 100−1,500 ms after the target were scored as hits. Sensitivity, which takes into account the number of both hits and false alarms was computed as $A' = 0.5 + [(hr − far) + (hr − far)^2]/4*hr*(1 − far)]$ (Sahgal, 1987), where hr is hit rate and far is false alarm rate. The RVIP task was administered using DirectRT software (Empirisoft, New York).

Finger tapping. Tapping, a measure of psychomotor speed described previously (Harrell & Juliano, 2009), was originally included. However, software problems led to large amounts of missing data and thus the data were not interpretable.

Self-Report Measures

Demographics and smoking history questionnaire. A 15-item questionnaire was developed for this study to assess demographic information (e.g., sex, age, race) and smoking history. It also included the FTND (Heatherton, Kozlowski, Frecker, & Fagerström, 1991), a widely used and validated 6-item measure of nicotine dependence.

Minnesota Nicotine Withdrawal Scale. The Minnesota Nicotine Withdrawal Scale (MNWS), a standardized 8-item measurement of nicotine withdrawal symptomatology as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (Hughes & Hatsukami, 1986; Toll, O'Malley, McKee, Salovey, & Krishnan-Sarin, 2007), was modified to expand contracted items (i.e., one item: "irritability, frustration, or anger" was expanded to three separate items), yielding 13 items (average Cronbach's alpha = .83). Items were rated on a 5-point rating scale from 0 (*none*) to 4 (*severe*). The mean of all 13 items is used to measure withdrawal.

Cigarette Evaluation Scale. The Cigarette Evaluation Scale (Rose, Behm, & Westman, 2001) assessed participants' immediate reactions to smoking. A total of 10 items were rated using a 7-point scale, ranging from 1 (*not at all*) to 7 (*extremely*). Based on Rose

et al. (2001), two items were combined as a measure of satisfaction ("Was it satisfying?"; "Was there a good taste?"; Cronbach's alpha = .78) and four items were combined as a measure of psychological reward ("Did it calm you down?", "Did it make you feel more awake?", "Did it reduce your hunger for food?", "Did it make you feel less irritable?"; Cronbach's alpha = .78). A third factor noted in Rose et al. (2001), consisting of the items nausea and dizziness, had low internal consistency (0.41), so these two items were analyzed separately. In addition to the eight items above, the questionnaire included two additional items measuring craving relief and enjoyment of airway sensations.

Expectancy measurement. Based on prior similar research on caffeine and alcohol (Fillmore & Vogel-Sprott, 1994; Harrell & Juliano, 2009), participants were asked about their expectancies for the general effects of nicotine on hand−eye coordination as well as their expectancies for specific aspects of task performance (e.g., improve accuracy on the RVIP task). For general expectancies, participants were asked to rate the statement, "I believe nicotine has the following effect on hand−eye coordination and speed." For task-specific expectancies, participants were asked to rate a number of expectancy statements about specific aspects of the tasks (RVIP and tapping). For example, "I expect that nicotine [would/did] have the following effect on my [measure] performance on the RVIP (or tapping) task." Response options ranged from 1 (*largely impair*) to 9 (*largely enhance*). These items were administered both before and after the expectancy manipulation. Measures included "speed" (RVIP and tapping), "accuracy" (RVIP), and "avoid slowing down" (tapping). The mean rating on all five items was used as the measure of expectancy for nicotine effects on task performance. Cronbach's alpha averaged .77.

Urge rating. Three items (Kozlowski, Pillitteri, Sweeney, Whitfield, & Graham, 1996) from the Questionnaire of Smoking Urges (Tiffany & Drobes, 1991) were used to assess participants' cravings, wants, and desires to smoke on a 7-point Likert scale, ranging from 1 (*not at all*) to 7 (*extremely*). The Cronbach's alpha in this study averaged .93.

Task motivation and drug resistance. Immediately after finishing the RVIP task for the final time, participants were asked to compare how motivated they were after the manipulation with their motivation level before the manipulation. They rated their motivation on a 5-point scale, ranging from 1 (*much less than earlier today*) to 5 (*much more than earlier today*). Previous research on caffeine, using a similar manipulation, found an increase in participants' task motivation after "told enhance" instructions relative to "told impair" instructions (Harrell & Juliano, 2009). Drug resistance was also assessed based on prior expectancy research (Fillmore et al., 1994; Harrell & Juliano, 2009; also see Fillmore et al., 2002). Participants were asked, "How much did you try to resist any effects of the nicotine?" and answered on a scale ranging from 0 (*not at all*) to 10 (*extremely*).

Procedure

Interested volunteers were screened by telephone. Eligible participants attended a baseline visit prior to the experimental day to collect baseline information and practice the RVIP to ensure sufficient task comprehension and to reduce the influence of practice effects during the experimental session. Participants were told to smoke as they normally would before their first visit. On arrival, participants gave informed consent, provided a CO sample, and completed self-report and performance measures. To maximize power, a CO cutoff was not used. Participants also smoked one of their own cigarettes ad libitum and rated the cigarette.

The experimental session was scheduled within the next 2 days. Because research has shown that cognitive effects of nicotine are more robust after periods of nicotine withdrawal (Heishman et al., 2010), participants were instructed to abstain from nicotine for 12 hr prior to the second visit. On arrival, participants provided a CO sample and were asked to report the time of their last cigarette. Next they completed premanipulation self-report and performance measures. The participant was then given either a nicotine or a placebo (denicotinized) cigarette to smoke ad libitum, crossed with one of two types of instructions designed to manipulate the expected effects of smoking (performance enhancement vs. performance impairment), resulting in four conditions: (a) *told enhance/given nicotine*; (b) *told enhance/given placebo*; (c) *told impair/given nicotine*; and (d) *told impair/given placebo.*

Instructions appeared on the computer screen and were also read aloud to the participants by the experimenter. Instructions, based on prior research with caffeine (Fillmore & Vogel-Sprott, 1992; Harrell & Juliano, 2009), were as follows:

> This cigarette contains a fairly strong dose of nicotine so that we can observe sizable effects in the shortest period of time. As mentioned earlier, the purpose of this experiment is to assess the effects of nicotine on motor performance.
>
> **Told enhance group.** A number of recent studies have reported that cigarettes improve performance in tasks that involve quick responses to visual stimuli, like video games or data entry. Our tasks involve all of the same skills. Because the effects obtained before were with small doses, we expected to see much stronger enhancing effects of nicotine in the laboratory with this large dose of nicotine. Administering large amounts of nicotine to produce enhancement of performance allows us to understand how nicotine causes this improvement.
>
> **Told impair group.** Recent research has found that nicotine has a negative effect on hand−eye coordination and speed. A number of studies have reported that cigarettes impair performance in tasks that involve quick responses to visual stimuli, like video games or data entry. Our tasks involve all of the same skills. Many people report these impairing effects. They seem to still learn the task, but learning is less efficient. Because the effects obtained before were with small doses, we expected to see much stronger disruptive effects of nicotine in the laboratory with this large dose of nicotine. Administering large amounts of nicotine to produce impairment of performance allows us to understand how nicotine causes this disruption.

After smoking, participants again completed self-report and performance measures. Then they rated how motivated they were to perform the task, relative to both earlier that day and on the prior visit. Finally, participants were asked to rate their experience in the study using a standard experimental evaluation form. Another CO sample was obtained and participants were compensated $30 plus additional compensation based on their performance on the RVIP tasks (up to $5.76). This was the first time any feedback about task performance was provided. Participants were then debriefed about the purpose of the study.

Results

Baseline Data

A series of 2 × 2 (Told Enhance vs. Told Impair × Given Nicotine vs. Given Placebo) analyses of variance and chi squares, when relevant, were conducted to check for baseline equivalence. Alpha was set at $p < .05$. There were no significant differences on any baseline or premanipulation measures with the exception of age. Baseline values are presented in Table 1. Despite random assignment, those given nicotine cigarettes were significantly older ($M = 36.82$ years, $SD = 14.21$) than those given placebo cigarettes ($M = 29.05$ years, $SD = 11.70$), $F(1, 79) = 7.68$, $p = .007$, $\eta^2 = .09$. To control for this baseline difference, age was entered as a covariate in all statistical analyses. It is notable that there were no baseline differences in expectancies for the performance-enhancing effects of nicotine ($p = .986$). In fact, prior to the manipulation, the mean expectancy ratings were nearly identical in the told enhance ($M = 5.14$) and told impair ($M = 5.13$) conditions. Sex was initially included in the analyses, but no significant effects of sex were found. Thus, the results reported do not include sex.

Main Outcomes

RVIP performance. A series of 2 × 2 (Enhance vs. Impair × Nicotine vs. Placebo) analyses of covariance (ANCOVAs) were conducted on RVIP task indices, controlling for premanipulation performance and age. Contrary to predictions, there were no effects of the expectancy manipulation on RVIP performance. However, as shown in Figure 1a, participants who smoked a nicotine cigarette had a significantly greater number of hits on the RVIP, $F(1, 78) = 4.63$, $p = .04$, $\eta^2 = .032$, and showed greater sensitivity, $F(1, 78) = 6.14$, $p = .02$, $\eta^2 = .027$, as compared to those who smoked a placebo cigarette. There were no effects of nicotine on RVIP reaction time.

Cigarette ratings. A series of 2 × 2 (Enhance vs. Impair × Nicotine vs. Placebo) ANCOVAs were conducted on cigarette ratings, controlling for baseline ratings of the participant's own cigarette at the initial visit as well as age. Findings are summarized in Table 2. Compared to the told impair condition, those told enhance reported greater psychological reward ($p = .047$), enjoyable sensations in throat and chest ($p = .045$), and less craving ($p = .020$). Relative to placebo cigarettes, those who smoked nicotine cigarettes reported greater satisfaction ($p = .002$), dizziness ($p = .010$), and less craving ($p = .039$). There were no interactions between drug and expectancy factors.

Urge rating. A 2 × 2 (Enhance vs. Impair × Nicotine vs. Placebo) ANCOVA, controlling for baseline urge and age, found no significant effects for nicotine or expectancy on urge ratings, or any interactions.

Motivation and drug resistance. Based on prior published research findings (Fillmore et al., 1994; Harrell & Juliano, 2009), a series of 2 × 2 (Enhance vs. Impair × Nicotine vs. Placebo) ANCOVAs, adjusted for baseline differences in age, were conducted on ratings of motivation and resistance. As shown in Figure 1b, there was a main effect of expectancy with those told enhance reporting significantly more motivation for performance on the postmanipulation RVIP ($M = 3.50$, $SE = 0.18$) than those told impair ($M = 2.90$, $SE = 0.17$), $F(1, 79) = 6.10$, $p = .02$, $\eta^2 = .07$. There was neither an effect of nicotine nor a significant expectancy by nicotine interaction effect on reported motivation. There were no effects of the manipulations on ratings of drug resistance.

Manipulation Checks

Expectancy manipulation. A 2 × 2 (Enhance vs. Impair × Nicotine vs. Placebo) ANCOVA was conducted on postmanipulation expectancies for the performance-enhancing effects of nicotine, controlling for age premanipulation expectancies for the performance-enhancing effects of nicotine and baseline differ-
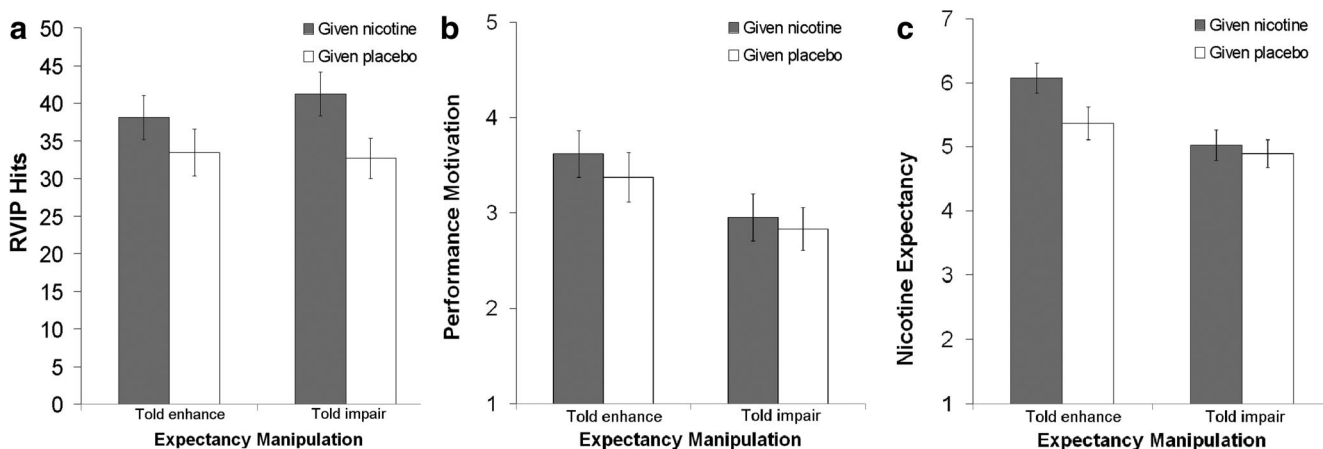

Figure 1. Postmanipulation Rapid Visual Information Processing (RVIP) task hits by condition adjusted for age and premanipulation RVIP hits (a). Postmanipulation RVIP performance motivation by condition adjusted for age. Motivation rated on a 5-point scale, ranging from 1 (*much less than earlier today*) to 5 (*much more than earlier today*) (b). Postmanipulation nicotine performance response expectancy by condition adjusted for age and premanipulation nicotine performance response expectancy (c).

Table 2

Covariate Adjusted Cigarette Ratings Across the Experimental Conditions

| | Conditions (told/given) | | | | Effects | |
| | Enhance/nicotine | Enhance/placebo | Impair/nicotine | Impair/placebo | Main effect nicotine | Main effect expectancy |
Conditions	M^a (SEM)	M^a (SEM)	M^a (SEM)	M^a (SEM)	F, η^2	F, η^2
Satisfaction	3.82 (0.29)	3.12 (0.31)	3.89 (0.30)	2.66 (0.27)	$F = 10.15,$*** 0.102	ns
Psychological reward	3.00 (0.21)	2.82 (0.23)	2.54 (0.22)	2.41 (0.20)	ns	$F = 4.07,$* 0.032
Dizziness	3.25 (0.32)	2.13 (0.34)	2.80 (0.33)	2.16 (0.29)	$F = 7.00,$** 0.075	ns
Nauseous	1.53 (0.22)	1.22 (0.24)	1.49 (0.23)	1.51 (0.20)	ns	ns
Reduced craving	4.79 (0.40)	4.21 (0.42)	4.12 (0.41)	2.95 (0.37)	$F = 4.43,$* 0.039	$F = 5.67,$* 0.050
Enjoyable sensations in throat and chest	3.41 (0.30)	3.28 (0.32)	3.12 (0.31)	2.34 (0.27)	ns	$F = 4.17,$* 0.033

Note. There were no significant interaction effects.
[a] Adjusted for baseline ratings and group differences in age.
* $p < .05$. ** $p < .01$. *** $p < .001$.

ences in age. As shown in Figure 1c, participants in the told enhance condition reported significantly greater postmanipulation expectancies for the performance-enhancing effects of nicotine ($M = 5.72$, $SE = .17$) than those in the told impair condition ($M = 4.96$, $SE = .16$), $F(1, 79) = 10.26$, $p = .002$, $\eta^2 = .09$. In terms of absolute change, paired-sample t tests showed that participants in the told enhance condition showed a significant increase in expectancies for the performance-enhancing effects of nicotine ($+0.65$), $t(36) = 3.18$, $p = .003$, and participants in the told impair condition showed a decrease (-0.23), $t(42) = -1.47$, $p = .148$, that was not significant.

Withdrawal. To determine the effects of cigarette abstinence on the participants, paired t tests were conducted comparing reports on the practice session to reports at the beginning of the experimental session, prior to cigarette smoking. Participants reported significantly more hours of abstinence on the experimental session, with instructions to abstain for 12 hr ($M = 13.57$, $SE = 0.29$) than on the practice session, under ad lib smoking instructions ($M = 2.54$, $SE = 0.91$), $t(79) = 12.18$, $p < .001$. CO readings were significantly lower in the experimental session ($M = 9.18$, $SE = 0.96$) than in the practice session ($M = 17.10$, $SE = 1.25$), $t(79) = -8.04$, $p < .001$. Urge ratings were significantly higher in the experimental session ($M = 5.43$, $SE = 0.18$) compared to the practice session ($M = 4.30$, $SE = 0.23$), $t(79) = 4.77$, $p < .001$. No effects were found for the MNWS. Because the lack of a finding for the MNWS was unexpected, a paired t test comparing the MNWS pre- and postcigarette was conducted. The results indicated a significant drop postcigarette, $t(75) = 7.83$, $p < .001$. This effect was found for both the given nicotine group, $t(38) = 5.73$, $p < .001$, and the given placebo group, $t(36) = 5.47$, $p < .001$.

Smoking behavior. A $2 \times 2 \times 2$ mixed-factor ANCOVA was performed with breath CO (pre- and postsmoking) as the within-subjects factor, dose expectancy (enhance vs. impair) and nicotine dose (nicotine vs. placebo) as between-groups factors, and age included as a covariate. As expected, CO levels increased significantly from an average of 9.09 ppm ($SE = 1.04$) prior to smoking the cigarette to 13.24 ppm ($SE = 0.98$), approximately 30 min after smoking the cigarette, $F(1, 69) = 19.09$, $p < .001$. There were no other main effects or interactions indicating differences in smoking exposure based on the experimental manipulations.

Discussion

This study used a 2×2 between-subjects factorial design to evaluate changes in the subjective and performance-enhancing effects of cigarette smoking resulting from manipulations of nicotine response expectancies and actual nicotine exposure. As hypothesized, daily cigarette smokers reported changes in their expectancies for nicotine's effects on performance consistent with response expectancy manipulations. Smokers told that nicotine enhances performance reported that the experimental cigarette, irrespective of its nicotine content, was more psychologically rewarding, more effective at reducing cravings, and caused more enjoyable physical sensations. Furthermore, participants expecting enhancement reported greater motivation than participants told that performance would be impaired, but there was no difference between the two groups in reported efforts to resist drug effects. Contrary to predictions, there was no effect of the expectancy manipulation on sustained attention performance, as measured by the RVIP task, or on smoking urge. Regardless of expectancy, nicotine administration produced greater ratings of smoking satisfaction and dizziness, less smoking craving, and improved performance on the RVIP. No interactions between the expectancy and drug manipulations were observed.

Our brief laboratory manipulation was effective in altering the expectancies of daily cigarette smokers, resulting in two groups that differed significantly in their expectancies for the effect of nicotine on performance, despite having similar expectancies before the manipulation. In terms of absolute change, those told that nicotine enhances performance reported a significant increase in nicotine performance expectancy, while those told nicotine impairs performance reported a decrease in nicotine performance expectancy that was not significant. Nicotine has been shown to enhance cognitive performance, and smokers appear to hold expectancies consistent with this effect. Thus, it is not too surprising that the expectancy manipulation had a stronger effect among individuals who were told that nicotine enhances performance compared to those who were told that nicotine impairs performance. This is consistent with the idea that expectancy change occurs most easily when instructions match participants' experience (Bolles, 1972; Christiansen, Goldman, & Inn, 1982; Kirsch & Lynn, 1999). This study, along with others, demonstrates that expectancy change

for smokers is possible in the laboratory and should be investigated further (Copeland & Brandon, 2000). If treatments and prevention campaigns incorporate expectancy challenges, further research is needed to determine how these challenges can be most effective.

Relative to those expecting impairment, participants expecting performance enhancement reported that the experimental cigarette, irrespective of its nicotine content, produced more psychological reward, more enjoyable physical sensations, and less craving. This is consistent with prior research showing that expectancy manipulations for one particular response (in this case, performance) may generalize to other responses (Harrell & Juliano, 2009). This may represent support for the memory network model in expectancy theory (Collins & Loftus, 1975; Goldman, Del Boca, & Darkes, 1999). This theory suggests that information is stored in "nodes" in memory and that a network of pathways links the information. Activation of one "node" leads to spreading activation of other information. Recent alcohol and tobacco research supports this theory (Linkovich-Kyle, Schreiner, & Dunn, 2012; O'Connor & Colder, 2009). However, it is important to note that there were no effects of the expectancy or nicotine manipulations on ratings of smoking urge. It is possible that the instructions to all participants that the cigarette contained nicotine, combined with the act of smoking itself, may have had a strong effect on urge, thereby overshadowing any potential effect of the response expectancy manipulation. Denicotinized cigarettes have been found to reduce deprivation-induced craving, at times similar to regular cigarettes (Barrett, 2010; Gross et al., 1997).

Motivation, broadly construed, has been suggested as a potential mechanism of placebo effects (Geers, Weiland, Kosbab, Landry, & Helfer, 2005; Hyland & Whalley, 2008). Consistent with prior research (Harrell & Juliano, 2009), we found that instructions that the drug enhances performance produced greater self-reported motivation for the RVIP task, but did not affect performance, potentially due to performance-based payment. Although not suggested by the authors, some published data has suggested that increases in motivation may be related to performance enhancement after placebo administration (Attwood, Terry, & Higgs, 2010). Further research is needed to explore the role of motivation in placebo effects to better understand how placebos affect health behaviors and other reactions, in both the short and the long term (Hyland, 2011).

We did not find the expected effect of the expectancy manipulation on actual cognitive performance. Two prior studies with caffeine found changes in motor performance consistent with the instructions, with those told enhance showing greater performance on the task (Fillmore et al., 1994; Fillmore & Vogel-Sprott, 1992). Of note, two other studies, one involving alcohol (Fillmore et al., 1994) and another involving caffeine users in withdrawal (Harrell & Juliano, 2009), found effects of the expectancy manipulation in the opposite direction, with those told impair actually performing better than those told enhance. Given the unique pharmacological properties of smoking and nicotine and the fact that there are no prior published studies that have assessed immediate reactions to smoking after directly manipulating smoking performance expectancies, it is difficult to explain the null findings in the present study. It appears that the expectancy manipulation was powerful enough to alter subjective outcomes but not the performance outcome. Although objective changes have been observed in re-

sponse to placebo manipulations, most placebo research has focused on subjective effects. Future placebo research that includes both subjective and objective measures will improve our understanding of the full range of drug outcomes that are influenced by placebo processes.

Prior research has suggested that attempts to resist the impairing effects of the drug may account for improved performance among individuals led to expect that the drug will impair performance (Fillmore et al., 1994; Harrell & Juliano, 2009). There are a number of prior studies that have shown that resistance to drug effects, particularly alcohol, is associated with improved performance (Fillmore & Vogel-Sprott, 1995a, 1995b; Sdao-Jarvie & Vogel-Sprott, 1992) and, further, that instructions that interfere with resistance to drug effects can lead to impaired performance (Fillmore et al., 2002; Fillmore & Vogel-Sprott, 1994). This phenomenon is sometimes referred to as behavioral tolerance (Vogel-Sprott, 1997). It is possible that behavioral tolerance develops to withdrawal, similarly to how it develops to alcohol.

It is important to note that, due to nicotine abstinence instructions, the current study cannot discriminate nicotine withdrawal relief from nicotine performance enhancement. Nonetheless, consistent with prior research, nicotine administration led to greater smoking satisfaction and dizziness, and less craving (Juliano et al., 2011; Kelemen & Kaighobadi, 2007; Perkins et al., 2004). Furthermore, nicotine increased RVIP sensitivity (see Heishman et al., 2010, for a review). These findings are useful not only in providing additional data on the effects of nicotine in the context of smoking but also as a positive control by which to compare the magnitude of effects of the expectancy manipulation. Including pharmacological and psychosocial manipulations within the same study allows for a deeper understanding of both manipulations.

Study Limitations

The expectancy manipulation overall led to groups that had significantly different performance expectancies, but it was more effective in promoting nicotine performance enhancement expectancies. This may be due to participants' preexisting beliefs. Future research should explore ways of producing more powerful expectancy manipulations, especially when the information contradicts smokers' preexisting expectancies. Some research has noted sex differences with respect to the effects of nicotine instructions on cigarette smoking outcomes (Perkins et al., 2006). The disproportionate recruitment of men (70%) in the present study prohibits a powerful analysis of sex effects. All participants were led to believe that the cigarette contained nicotine, even though only 50% of participants actually received nicotine. Because additional control groups were not included, we do not know what impact stimulus expectancy or the simple act of smoking had on outcomes (Perkins et al., 2008; Perkins, Karelitz, Conklin, Sayette, & Giedgowd, 2010). Nevertheless, we were able to demonstrate that our expectancy manipulation had an effect beyond these factors on some of the measures.

Implications

A growing body of research supports the idea that drug effects are directly influenced by the expected outcomes of drug taking. This study demonstrated that performance expectancies of nicotine

could be experimentally manipulated and that expectancies influenced subjective reactions to smoking and task motivation. Clinically, this study provides further evidence that expectancy manipulations are possible and thus may be useful for treatment of nicotine dependence. These manipulations could take the form of expectancy challenges (Copeland & Brandon, 2000), advertisements, or hypnosis (Kirsch & Lynn, 1999). An important caveat to this advice is that expectancy manipulations appear to be most effective when they match a participant's experience. Thus, it may be more useful to point out the negative effects of cigarette smoking than to attempt to counter accurate beliefs about positive nicotine effects, such as cognitive enhancement. Rather than attempting to convince patients that nicotine impairs performance, treatment providers may want to challenge beliefs that nicotine is essential for adequate performance. Another strategy may be to note that nicotine withdrawal, which could be avoided with prolonged nicotine abstinence, is responsible for cognitive decrements. Future research should examine these possibilities. A greater understanding of the mechanisms underlying placebo effects, including response expectancy, will allow us to harness such effects to improve the overall effectiveness of pharmacological and psychological treatments.

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