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Expectancy and Pharmacology Influence the Subjective Effects of Nicotine in a Balanced-Placebo Design

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The expectancy and pharmacological effects of nicotine (0.60 mg) on memory and the subjective effects of cigarettes were examined by using a balanced-placebo design (i.e., expect either nicotine or no nicotine and receive either nicotine or no nicotine). A total of 120 college students who smoke were assigned to 1 of the 4 experimental groups, then rated the cigarettes on a number of dimensions and completed questionnaires on smoking urges, tension, and energy. Participants also completed tests of memory as well as predictions of memory. Pharmacology played a stronger role than expectancy in most ratings of the cigarettes, but significant effects of expectancy did emerge for feelings of increased wakefulness, concentration, calming, cigarette satisfaction, and hunger reduction. The presence of nicotine significantly reduced smoking urges, but expectancy alone reduced tension after smoking. Neither variable produced significant effects on memory or memory predictions. These findings demonstrate that nonpharmacological factors can play an important role in the self-reported effects of nicotine.

Keywords: balanced-placebo design, cigarette smoking, nicotine, stimulus expectancy

Many individuals who smoke may do so, at least in part, to induce cognitive changes in response to environmental demands. Consider college students who smoke while preparing for exams. Wesnes, Revell, and Warburton (1983) found that students smoked more cigarettes during exam weeks than during nonexam weeks. Moreover, 80% of students reported that smoking helped them concentrate, and 74% reported that smoking increased concentration. West and Lennox (1992) subsequently confirmed that college students smoked before exams to increase arousal during study, rather than to simply relieve stress or alleviate withdrawal. These studies suggest that nicotine's cognitive effects, or perhaps students' beliefs about nicotine's effects, may contribute to the maintenance of smoking behavior.

There is now increasing recognition in the field of nicotine and tobacco research that numerous factors, including nonpharmacological factors, can play important roles in maintaining smokers' addiction to cigarettes (Johnson, Bickel, & Kirshenbaum, 2004; Perkins, Sayette, Conklin, & Caggiula, 2003). Hundreds of articles have been published on the pharmacological effects of nicotine on human cognition (for reviews, see Heishman, Taylor, & Henningfield, 1994; Sherwood, 1993), and there is a substantial body of research pointing to cognitive improvements from cholinergic stimulation by specific nicotinic receptor agonists and cognitive impairments with nicotinic antagonists (Levin, 1992; Rezwani & Levin, 2001). In contrast, the role of nonpharmacological factors in participants' cognitive responses to smoking has been relatively understudied (Grunberg & Acri, 1991). The present research was designed to directly compare the effects of expectancy in smoking with the pharmacological changes induced by nicotine.

Stimulus expectancy (Kirsch, 1999; Perkins et al., 2004) can be manipulated through instructional sets, in which some participants are told to expect an active drug and others are told to expect an inactive drug. This type of expectancy is ignored in double-blind research, because in that research participants are not informed about which condition has been administered. Although double-blind research remains the standard protocol in clinical trials, it does have limitations (Kramer & Shapiro, 1984). Sutton (1991) has argued that continued reliance on double-blind designs is likely to create an overemphasis in the role of pharmacology and an underestimate of the role of stimulus expectancy in drug studies. He called for the increased use of a balanced-placebo design in nicotine and tobacco studies.

Two independent variables are included in a standard balanced-placebo design: type of substance expected (i.e., participants are told to expect either an active or an inactive substance) and type of substance received (i.e., participants receive either an active or an inactive substance). Thus, a 2 × 2 (Type of Instructional Set × Type of Substance Administered) factorial design is incorporated. Of the four conditions, two are deceptive in nature (some participants are told to expect an active substance but receive an inactive one, and other participants are told to expect an inactive substance but receive an active one). The major advantage

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of a balanced-placebo design is that the effects of stimulus expectancy can be directly compared with pharmacological effects. Despite calls by researchers to utilize the balanced-placebo design (Brandon, Juliano, & Copeland, 1999; Sutton, 1991), only two published studies have utilized it in research on cigarettes to date.

Juliano and Brandon (2002) examined whether the type of cigarette people expected and the type of cigarette they actually received influenced their levels of state anxiety, urge to smoke, and withdrawal symptoms. Participants abstained from smoking for 3 hrs before the study, and upon arrival they were placed in an anxiety-provoking situation. Not surprisingly, Juliano and Brandon found a main effect of nicotine: Cigarettes with nicotine reduced anxiety more than nicotine-free cigarettes. In addition, merely expecting to receive cigarettes with nicotine also reduced anxiety significantly, but only in smokers who believed nicotine would do so. Thus, response expectancy for anxiety seemed to moderate stimulus expectancy effects. A significant effect of stimulus expectancy also emerged for urge to smoke, though no significant effects were found for withdrawal measures.

In the Juliano and Brandon (2002) study, approximately one third of participants did not believe the deception. In general, it has been difficult to deceive people in the "told inactive substance but receive active substance" condition in balanced-placebo research, especially with alcohol (Martin & Sayette, 1993). Therefore, Perkins et al. (2004) conducted a smoking study using a modified balanced-placebo design. They told participants to expect either a regular dose or a low dose (instead of no dose) of nicotine in a cigarette, and they also manipulated the amount of nicotine actually administered. Instructional set did influence the perceived strength of the cigarette, as well as levels of liking and satisfaction. In contrast to Juliano and Brandon's findings, there was no reduction in cravings (although participants were not abstinent or in a high-stress situation as in the previous study). Unfortunately, Perkins et al. also found high levels of disbelief in their deceptive conditions, despite the modified instructions and the ingestion of only two puffs of the cigarette during smoking.

In the present research, we sought to extend the work of Juliano and Brandon (2002) and Perkins et al. (2004) using a standard balanced-placebo design with cigarette smokers. We tried to increase the effectiveness of the deception conditions in three ways. Following the suggestion of Juliano and Brandon, we used a lower dose of nicotine in the active drug condition (0.60 mg of nicotine compared with 1.10 mg in the Juliano & Brandon study and 0.90 mg in the Perkins et al. study) so that the pharmacological effects would be less likely to overshadow the stimulus expectancy effects. Second, we allowed participants to select their own cigarette from a package that contained a manufacturer's brand and labeling consistent with the instructional set (either nicotine or nicotine free) to increase the believability of the manipulation. Third, full debriefing of the participants as to the deceptive nature of the study was postponed until data were collected from all participants, in order to reduce the likelihood that smokers who completed the study would inform potential participants about the deception. We also sought to resolve previous inconsistencies on the effects of stimulus expectancy on cravings by administering the full Cigarette Evaluation Scale (CES; Westman, Levin, & Rose, 1992) immediately after participants smoked, along with additional measures of smoking urges, energy, and tension, on three separate occasions to track the time course of effects. Finally, we included measures of memory and memory predictions to assess whether expectancy versus pharmacology played a significant role in these areas.

We hypothesized main effects of instructional set (i.e., the type of cigarette participants were told they received) and nicotine (i.e., the presence or absence of nicotine in cigarettes) on several dependent measures. Consistent with past research, we expected to find a significant effect of instructional set on ratings of craving or urge reduction (Juliano & Brandon, 2002) and cigarette satisfaction (Perkins et al. 2004), as well as other dimensions of the CES. We sought to expand on these findings by assessing smoking urges, tension, and energy at three different points in the experiment. Next, we wanted to determine if the effects of instructional set and nicotine could be extended to more complex cognitive processes by including two distinct tests of memory and confidence. Finally, in cases where both variables produced statistically significant effects, we sought to compare the magnitude of effects in order to determine which variable produced the stronger effect.

Method

Participants

A total of 125 smokers were recruited from California State University, Long Beach, and were paid $30 each for their participation. Data from 5 participants were discarded due to errors during testing or failure to comply with instructions. Thus, 120 participants (30 women and 78 men, 12 missing gender data[1]) provided useable data for analyses. The age range of the participants was 18–57 years ($M = 22.2$, $SD = 6.3$). All participants completed a telephone screening interview to ensure their eligibility for participation: They all had smoked at least 10 cigarettes a day for at least 1 year, were not trying to quit smoking, and reported no major health concerns.

Participants were asked to abstain from using nicotine and caffeine products for 8 hr before the study. To ensure nicotine deprivation, we instructed all participants to complete an end tidal carbon monoxide (CO) breath analysis (Vitalograph, Lenexa, KS) upon arrival. Participants were not allowed to participate if their CO level exceeded 15 ppm.

[1] All participants responded to the demographic questionnaire, but these data were deleted inadvertently for 12 consecutive participants from the electronic handheld device.

Types of Cigarettes

Two types of cigarettes were used in this study: (a) Quest 1, which contains 0.60 mg of nicotine per cigarette by the Federal Trade Commission test method, and (b) Quest 3, which contains less than 0.05 mg nicotine per cigarette by the Federal Trade Commission test method. These nonmentholated cigarettes are matched for tar content (10 mg each) and size (85 mm each). Cigarettes were left in their packages until removed by a participant for smoking; in two of the four conditions, however, the types of cigarettes in each package had been switched before the experiment.

Questionnaires

Participants completed a total of 10 different questionnaires over the course of the experiment on an electronic handheld device (Palm Pilot Tungsten E; Palm, Sunnyvale, CA), including a demographic survey, a 6-item version of Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) and the 12-item Cigarette Dependence Scale (CDS; Etter, Le Houezec, & Perneger, 2003). They also completed a 20-item version of the Smoking Consequences Questionnaire–Adult (Copeland, Brandon, & Quinn, 1995) containing the most relevant subscales: (a) the Stimulation/State Enhancement subscale ($n = 7$ items), (b) the Boredom Reduction subscale ($n = 4$ items), and (c) the Negative Reinforcement/Negative Affect Reduction subscale ($n = 9$ items). The 10-item version of Questionnaire of Smoking Urges (QSU) developed by Cox, Tiffany, and Christen (2001) was included to measure cigarette cravings in participants three times during the course of the experiment. The 20-item version of Activation-Deactivation Adjective Checklist (AD-ACL; Thayer, 1986) also was used to measure participants' self-reported levels of arousal (i.e., tension and energy) three times during the course of the experiment. The 12-item Cigarette Evaluation Scale (CES; Westman et al., 1992) was administered immediately after participants smoked. One item was added to this scale as a manipulation check, which asked participants to indicate what type of cigarette they had just smoked (nicotine vs. nicotine free). Participants then answered two questions about how the cigarette they smoked would influence their performance on the upcoming memory tests (i.e., "Please rate the effect the cigarette will have on your ability to learn 40 pairs of unrelated nouns" and "Please rate the effect the cigarette will have on your ability to remember the answers to a series of trivia questions"). The same questions were asked again after the tasks (rephrased to reflect past performance), along with a second manipulation check, which asked participants to report the strength of the cigarette they smoked previously. Finally, the 33-item Social Desirability Scale (SDS; Crowne & Marlowe, 1960) was administered at the end of the study to assess the degree to which participants attempted to present themselves in a favorable manner.

Memory Tasks

Study and prediction task. Participants were asked to study 40 concrete, two-syllable, English nouns (e.g., market), presented on a computer monitor. The order of presentation was randomized for each participant, and all nouns appeared for two study trials of 3 s each. Immediately following the second trial, participants were asked to predict how likely they were to recall each noun (i.e., immediate prediction), on a scale of 0 (*definitely will not recall*) to 100 (*definitely will recall*). After studying and providing judgments for all 40 nouns, participants were asked to make a prediction of how many total words (0–40) they would recall (i.e., aggregate prediction).

Prospective remembering task. This task was used as a cognitive test as well as a distracter activity before the memory recall task. Participants were asked to answer 200 general knowledge questions (e.g., "What is the capital city of Norway?"), which appeared for 6 s on the monitor followed by a 3-s interval to select one of four alternatives ("Voss," "Oslo," "Trondheim," "Bergeb"). After each question, participants were asked to indicate their degree of confidence in their answer on a scale of 0–100. Within the same task, participants also were instructed to press the *a* key each time they saw the name of an animal in the question or the alternatives (i.e., prospective memory test). A total of six animal questions were presented, and *a* responses were scored as correct if they occurred during the animal question and response sequence or during the very next question and response sequence.

Memory recall task. Immediately after the prospective memory task, the participants were asked to write down as many of the English words as they could remember, with no time limitation. Misspellings were counted as correct if the first three letters of the word matched those of the actual word.

Design and Procedures

A 2 × 2 between-subjects factorial design was used. The two independent variables were type of instructions that participants received (told nicotine vs. told no nicotine) and type of cigarette that participants received (contained nicotine vs. contained no nicotine). We randomly assigned participants to one of four conditions based on their order of appearance: told nicotine–received nicotine ($n = 31$), told nicotine–received no nicotine ($n = 29$), told no nicotine–received nicotine ($n = 30$); told no nicotine–received no nicotine ($n = 30$). All participants completed the 2-hr experiment individually.

All procedures were reviewed and approved by the California State University Institutional Review Board. Participants signed an informed consent form upon arrival, which stated that they may or may not receive nicotine during the experiment, and completed a CO breath analysis to verify cigarette abstinence. Then, participants were asked to complete six questionnaires on the Palm Pilot, in the following order: demographics, FTND, CDS, Smoking Consequences Questionnaire, baseline QSU, and baseline AD-ACL. Next, participants were informed about which type of cigarette (nicotine vs. nicotine free) they would receive, although in two conditions the participants were deceived.

Several steps were taken to enhance the effectiveness of our deception. First, participants reviewed a small information leaflet provided by the manufacturer in each package of cigarettes explaining that cigarettes with different amounts of nicotine (including cigarettes free of nicotine) are now available commercially. Participants were then offered an open package of cigarettes from one of two cartons, both of which were labeled by the manufacturer, and asked to select a cigarette to smoke. We determined which of four conditions each participant received and arranged for the correct package of cigarettes (half of which had deceptive labels) to be presented. Participants were tested by one of three other experimenters who were not informed of the deceptive nature of the study. Thus, both the experimenter and the participant should have believed they received the type of cigarette shown on the package.

The experimenter accompanied participants to an open area outside the building to smoke the entire cigarette and to complete four questionnaires immediately afterward: the CES, two questions on the predicted effects of the cigarette on memory performance, and the QSU and AD-ACL questionnaires for the second time each. Upon returning to the lab, participants completed the study and prediction task as well as the prospective remembering task on the computer and then the memory recall test. After the memory recall phase, participants were asked to complete another questionnaire on the effects of the cigarette on the memory tasks, a final measure of QSU, and a final measure of AD-ACL. Lastly, participants were asked to complete the SDS. To control for the influence of caffeine, we asked participants to estimate the number of hours since they last consumed caffeine and the amount ingested. After all these procedures, participants were paid and partially debriefed, excluding the deceptive feature. After all testing was completed, letters explaining the four conditions and a summary of the main results were mailed to all participants.

Results

All tests of statistical significance were conducted with an alpha level set at .05 unless otherwise noted. Measures of effect size are reported for all statistically significant effects using eta squared (η^2), following Clark-Carter's (1997) criteria: η^2 of .010 is a small effect, η^2 of .059 is a medium effect, and η^2 of .138 or above is a large effect.

Instructional Set Manipulation Checks

In order to test whether participants believed the instructions about the type of cigarette they received, we performed two manipulation checks. Immediately after smoking, participants rated the cigarette on 12 dimensions of the CES. A 13th question was added: "What type of cigarette did you just smoke?" and participants chose either "Nicotine free" or "Nicotine." A total of 9 participants (7.5% of the sample) failed to select the type of cigarette that they were told they received: Five participants in the told nicotine–received no nicotine condition reported that they did not receive nicotine, 2 participants in the told no nicotine/received nicotine condition reported that they received nicotine, and 1 participant in each of the nondeceptive conditions reported that they received the opposite type of cigarette. Thus, a relatively small portion of the sample disbelieved the instructions based on the first manipulation check.

Near the end of the experiment, participants completed a second manipulation check. They were asked "How would you rate the amount of the nicotine that your cigarette contained?" and were given four alternatives: "nicotine free" (scored as –2), "moderately weak amount" (scored as –1), "moderately strong amount" (scored as + 1), and "very strong amount" (scored as + 2). The mean rating for all participants in the told no nicotine condition was -1.54 ($SD = 0.89$), and the mean in the told nicotine condition was -0.66 ($SD = 0.83$). A 2×2 analysis of variance (ANOVA) revealed a large, statistically significant effect of instructional set $F(1, 111) = 29.92$, $\eta^2 = .212$. Neither the presence or absence of nicotine nor the interaction between instructions and presence or absence of nicotine had a significant effect. To evaluate the influence of the 9 participants who disbelieved the instructions, we conducted the same ANOVA on cigarette strength omitting these individuals. The outcome of the three F tests did not change, but the effect size of instructional set increased by over 36% (i.e., η^2 increased from .212 to .290). Thus, including the 9 disbelievers in the analysis dampened the effect of instructional set considerably.

There has been some debate in the balanced-placebo literature as to how to treat data from participants whose behavior is inconsistent with the instructional set (e.g., Martin & Sayette, 1993). In our data, a relatively small number of participants produced a substantial reduction in effect size for cigarette strength, and so we decided to report all subsequent analyses excluding these participants. In most cases, this omission did not change the outcome of statistical significance testing. For completeness, we note the cases where tests of significance did differ in the Appendix.

Demographic Information

Participants' mean age, level of cigarette dependence (as assessed by the FTND and the CDS), and CO levels are shown in Table 1. A one-way ANOVA was conducted for each variable to test for significant differences across groups. None of the ANOVAs were significant.

Evaluation of Cigarettes

Immediately after smoking, participants rated their cigarette on the 12 dimensions of the CES (Westman et al., 1992). The mean ratings for each dimension across all four conditions are shown in Table 2, along with the outcome of inferential statistical tests and corresponding effect sizes. The expectancy of nicotine had a significant main effect in 5

Table 1
Mean Scores on the Demographic Variables Across Groups

	Condition (expected/received)							
	Nic/Nic		Nic/No nic		No nic/Nic		No nic/ No nic	
Dependent measure	*M*	*SEM*	*M*	*SEM*	*M*	*SEM*	*M*	*SEM*
Age (years)	23.12	1.68	22.78	1.53	22.30	1.17	20.96	0.55
Carbon monoxide level	5.37	0.48	6.37	0.63	6.21	0.61	6.76	0.46
Fagerström Test for Nicotine Dependence	10.10	0.42	9.29	0.38	9.00	0.32	8.86	0.27
Cigarette Dependence Scale	42.72	1.18	42.58	1.35	39.03	1.23	39.79	1.27
Smoking Consequences Questionnaire-Adult								
Negative Reinforcement/Negative Affect Reduction desirability	24.93	3.48	26.12	3.72	19.75	4.70	18.31	3.85
Negative Reinforcement/Negative Affect Reduction likelihood	56.07	3.62	58.58	4.15	53.25	3.37	49.25	3.33
State Enhancement/Stimulation desirability	6.10	3.38	11.50	3.49	2.41	3.56	2.44	3.02
State Enhancement/Stimulation likelihood	27.47	2.43	30.42	3.03	28.54	2.06	24.69	2.40
Boredom Reduction desirability	6.93	2.02	7.42	2.44	5.32	2.42	8.03	2.02
Boredom Reduction likelihood	22.87	1.91	26.38	1.93	23.81	1.67	22.38	1.74

Note. One-way analyses of variance confirmed that none of these dependent measures varied significantly across condition. Nic = nicotine.

of 12 cases (wakefulness, concentration, hunger reduction, satisfaction, and calming). The presence of nicotine had a significant main effect in 8 of 12 cases (satisfaction, calming, taste, dizziness, irritability reduction, craving reduction, nausea, and strength). Thus, the presence of nicotine produced a greater number of statistically significant findings with generally larger effect sizes. However, the effect sizes of instructional set were actually larger than pharmacological effect sizes for the dimensions of wakefulness, concentration, and hunger reduction.

Correlations between total scores on the SDS and each of the 12 dimensions were computed for each level of instructional set. If participants were responding untruthfully in order to appear more favorably, then significant correlations should have emerged. None of the correlations were reliably nonzero. In the told nicotine condition, which should have been most susceptible to social desirability, the correlations ranged from −.02 to +.15. Thus, none of the significant effects of instructional set can be accounted for by mere demand characteristics.

Table 2
Mean Ratings, F Ratios, and Effect Sizes by Condition for the Cigarette Evaluation Scale

	Condition (expected/received)								Effect					
	Nic/nic		Nic/No nic		No nic/Nic		No nic/ No nic		Expected		Received		Expected × Received	
Dimension	*M*	*SEM*	*M*	*SEM*	*M*	*SEM*	*M*	*SEM*	*F*	η^{2a}	*F*	η^{2a}	*F*	η^{2a}
Made me feel awake	3.77	0.36	3.71	0.33	2.89	0.37	2.55	0.28	8.98^{b**}	M				
Helped me concentrate	3.67	0.37	3.46	0.36	3.18	0.35	2.38	0.24	5.46^{b*}	S				
Reduced my hunger	3.50	0.36	3.54	0.43	3.14	0.31	2.45	0.30	4.28^{b*}	S				
Was satisfying	5.40	0.33	3.17	0.38	4.21	0.37	2.66	0.24	6.51^{b*}	S	32.53^{b***}	L		
Was calming	4.90	0.37	3.83	0.37	4.07	0.31	3.03	0.28	5.94^{b*}	S	9.91^{b**}	M		
Tasted good	4.57	0.31	2.50	0.36	4.07	0.38	2.34	0.25			33.16^{b***}	L		
Made me dizzy	3.10	0.42	1.63	0.24	2.36	0.27	1.62	0.16			13.67^{b***}	M		
Reduced my irritability	4.27	0.33	2.96	0.38	3.54	0.34	3.21	0.30			5.98^{b*}	S		
Reduced my cravings	4.07	0.40	3.50	0.36	3.64	0.31	2.76	0.28			4.49^{b*}	S		
Made me feel nauseous	1.33	0.14	1.71	0.30	1.32	0.14	1.86	0.26			4.57^{b*}	S		
Was very strong[c]	2.47	0.31	1.38	0.14	1.64	0.16	1.54	0.20			7.20^{d***}	M	4.86^{d*}	S
Gave me throat and chest sensations	2.53	0.31	2.13	0.31	2.96	0.37	2.24	0.28						

Note. *F* ratios reflect the outcomes of statistical comparisons using two-way (Expected × Received) analysis of variance; only significant *F* ratios are provided. Nic = nicotine.
[a] S = a small effect size; M = a medium effect size; L = a large effect size.
[b] $df = 1, 107$.
[c] Analyses of simple main effects were conducted to follow up on the significant interaction in this case: The expected nicotine-received nicotine group scores were significantly higher than the others, and no other significant differences emerged.
[d] $df = 1, 106$.
$^{*}p < .05$. $^{**}p < .01$. $^{***}p < .001$.

Smoking Urges, Tension, and Energy

Participants' levels of smoking urges were assessed with the QSU before smoking, immediately after smoking, and near the end of the experiment. A 3 × 2 × 2 (Time of Assessment × Instruction Set × Nicotine) mixed ANOVA revealed a statistically significant main effect of time and a statistically significant interaction between instructional set and time, $F(2, 212) = 63.87$, $\eta^2 = .376$, and $F(2, 212) = 6.32$, $\eta^2 = .056$, respectively. The pattern of means is illustrated in Figure 1A, collapsed across the effect of nicotine (which was not statistically significant). Participants who were told to expect nicotine began with slightly higher levels of smoking urges compared with participants who were told to expect no nicotine; immediately after smoking, however, this pattern was reversed. Both groups finished the experiment with equivalent levels of smoking urges. The simple main effects of time were significant for both levels of instruction set, Fs > 16.38, ps < .05. Post hoc paired t-tests showed that all comparisons over time were significant for the told nicotine group (ts > 5.47, ps < .05). For the group told no nicotine, the reduction in urges from before to immediately after smoking and after smoking to the end of the experiment (ts > 3.76, ps < .05) were statistically significant. These results were not due to demand characteristics, because correlations between SDS scores and QSU scores were nonsignificant for both levels of instructional set. Overall, being told that cigarettes contained nicotine did significantly reduce the participants' urge to smoke, but the effect was short lived.

Participants' levels of self-reported tension and energy over time were assessed with the two subscales of the AD-ACL. For the sum of the 10 items corresponding to tension, a three-way ANOVA revealed a statistically significant main effect of time and a statistically significant interaction between nicotine and time, $F(2, 214) = 10.67$, $\eta^2 = .091$, and $F(2, 214) = 4.30$, $\eta^2 = .039$, respectively (see Figure 1B); no other main effects or interactions were significant. Analysis of the simple main effects of time showed a significant effect when nicotine was administered $F(2, 114) = 15.35$, $\eta^2 = .212$, but no significant effect of time when no nicotine was administered. In the former case, post hoc paired t-tests showed a significant decrease in tension from before to after smoking, followed by a significant increase in tension comparing postsmoking scores with scores at the end of the experiment, (ts > 4.59, ps < .05). In regard to scores for the 10-item energy subscale, only the effect of time was significant, $F(2, 212) = 16.23$, $\eta^2 = .131$, and no follow-up analyses were conducted. Thus, cigarettes with nicotine did reduce participants' levels of tension immediately after smoking, but they did not influence self-reported levels of energy. These results contrast those reported for smoking urges, where instructional set (but not nicotine itself) played a significant role.

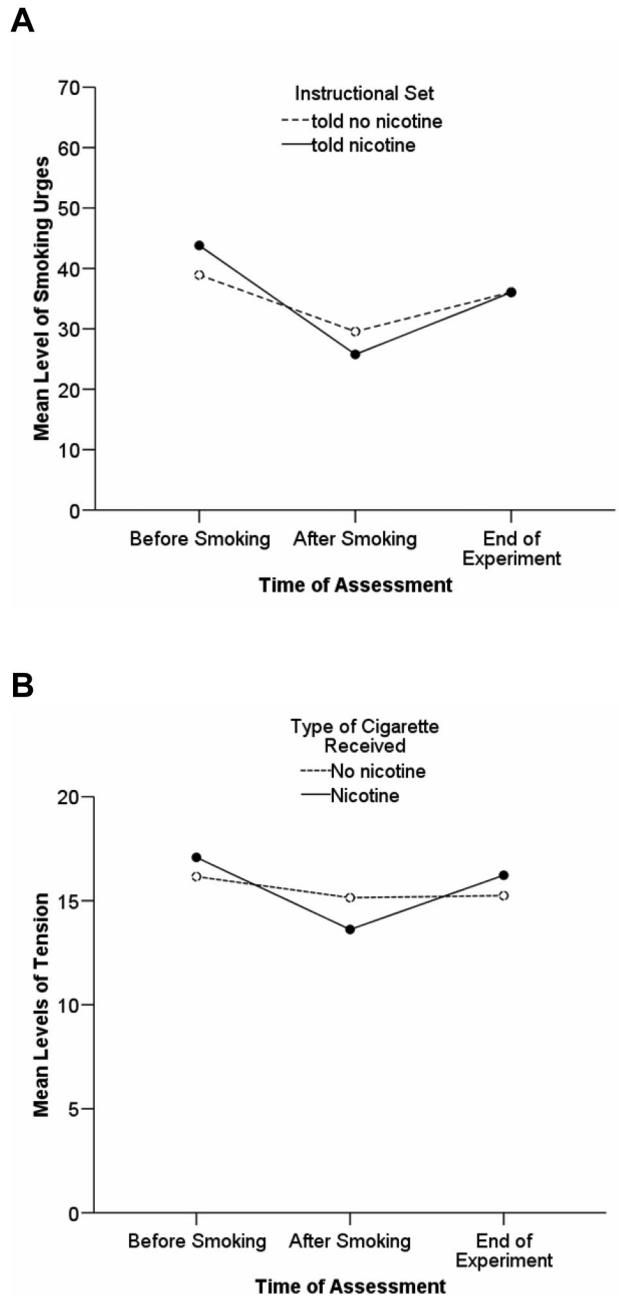

Figure 1. A: Mean responses on the Questionnaire of Smoking Urges over time collapsed across the presence or absence of nicotine. B: Mean responses on the Tension subscale of the Activation-Deactivation Adjective Checklist over time collapsed across instructional set.

Memory Performance

Study and prediction task. Participants provided two types of predictions regarding their future memory performance while studying the 40 English nouns: 40 item-by-item predictions (ranging from 0 to 100 each) and a single aggregate prediction ranging from 0 to 40 at the end of the task. Both types of judgments are shown as proportions in Table 3 for consistency. A 2 × 2 (Instruction Set × Nicotine Presence or Absence) ANOVA revealed no significant

Table 3
Mean Scores on the Computerized Tests of Memory and Confidence

Dependent measure	Nic/nic *M*	Nic/nic *SEM*	Nic/No nic *M*	Nic/No nic *SEM*	No nic/Nic *M*	No nic/Nic *SEM*	No nic/No nic *M*	No nic/No nic *SEM*
Noun-learning task								
Immediate prediction	.54	.04	.53	.04	.56	.04	.47	.03
Aggregate prediction	.50	.04	.49	.04	.51	.04	.46	.04
Actual memory score	.30	.02	.32	.04	.36	.04	.28	.03
Prospective remembering								
General knowledge accuracy	.59	.01	.61	.02	.59	.02	.59	.01
General knowledge confidence	.65	.03	.64	.02	.68	.02	.65	.02
Prospective remembering accuracy	.43	.06	.53	.06	.46	.06	.47	.06

Condition (expected/received).

Note. Nic = nicotine.

effects. Thus, neither the nicotine nor the expectancy of nicotine influenced participants' predictions of the memory performance.

Memory recall task. The third row of Table 3 lists mean recall performance across the four conditions. A 2 × 2 (Instruction Set × Nicotine Presence or Absence) ANOVA revealed no significant effects.

Prospective remembering task. Three aspects of the prospective remembering task were analyzed: general knowledge accuracy, confidence in the correctness of general knowledge answers, and prospective remembering accuracy. Mean scores are shown in the bottom half of Table 3. A 2 × 2 (Instruction Set × Nicotine Presence or Absence) ANOVA was conducted on each dependent measure, and no statistically significant effects emerged.

Discussion

We conducted this research to directly compare the pharmacological effects of nicotine in cigarettes with the effects of instructional sets on cigarette evaluation, smoking urges, tension, energy, and memory performance using a balanced-placebo design. The strongest effects were noted with the CES: 11 out of 12 dimensions were influenced by at least one variable, and two dimensions were influenced by both. Instructional set alone was sufficient to produce significant positive changes in response to the items "Made me feel awake," "Helped me concentrate," and "Reduced my hunger." Instructional set also produced significant effects along with nicotine for the items "Was calming" and "Was satisfying." These data provide strong evidence for the role of nonpharmacological factors such as stimulus expectancy in variables that may contribute to the maintenance of smoking behavior. Why only these particular items, and not the other seven dimensions, were influenced by expectancy is uncertain, especially because the factor structure of the CES has not been explored. It is tempting to speculate that cognitive factors (i.e., concentration, wakefulness, and calming) may be more susceptible to expectancy, but in contrast to this notion we found no statistically significant effects on our computerized memory and confidence measures.

The effects of instructional set and nicotine on craving reduction have been inconsistent in two previous studies using a balanced-placebo design. Juliano and Brandon (2002) used a 3-hr abstinence interval and found that both instructional set and nicotine reduced the urge to smoke. In contrast, Perkins et al. (2004) found no reduction in cravings in minimally abstinent smokers. We asked our participants to abstain for 8 hrs and found an effect of nicotine on the craving item of the CES as well as an effect of instructional set over time on the QSU. Thus, our findings of significant effects for both variables resemble those of Juliano and Brandon, which suggests that at least moderate deprivation may be necessary to uncover effects of these variables on participants' ratings of smoking urges.

Overall, the 12-item CES tended to show the greatest number of significant effects for both independent variables, even though some of the same constructs (e.g., smoking urges and tension) were assessed with reliable instruments that were administered several times during the experiment. One possible explanation is that the CES may be more susceptible to demand characteristics because each dimension is assessed with only one item. However, participants' responses to the SDS were not significantly correlated with any of the responses to the CES. Another possibility is that the CES showed the largest effects because it was the questionnaire administered immediately after smoking, when the influence of nicotine should be greatest. Mendelson, Sholar, Goletiani, Siegel, and Mello (2005) have shown that nicotine plasma levels can peak within 12–14 min after smoking, although lower nicotine cigarettes showed a longer time course. Most participants would have been just beginning the memory tasks about 15 min after smoking. Unfortunately, the plasma nicotine levels obtained after smoking were not measured in this study, although these data have been reported for low nicotine cigarettes in past research (Rose & Behm, 2004). The low dose of nicotine we used (0.60 mg, which would be considered a "light" or "ultralight" cigarette) combined with the short window available to detect changes due to nicotine may explain why we found no significant effects on our memory and confidence tasks. Lastly, the null findings on the memory tasks may have been affected by differences in baseline performance across groups, which was not assessed in this study.

A final consideration concerns the integrity of the balanced-placebo design. We observed only 9 participants out of 120 (i.e., 7.5%) who reported that they received a different type of cigarette than we instructed. This rate of disbelief is substantially lower than the rates reported by Juliano and Brandon (2002) and Perkins et al. (2004). The difference could be due to the modifications to our procedures noted earlier or perhaps to the lower dose of nicotine used, making it easier to convince participants in the told no nicotine–received nicotine condition. This antiplacebo condition has proven especially troublesome in past investigations using the balanced-placebo design (Perkins et al., 2004). In our study, however, only 2 participants disbelieved the antiplacebo condition. Thus, it may be possible to successfully execute a standard balanced-placebo design using commercially available cigarettes with varying levels of nicotine. The dosage may prove critical however, in that researchers can find themselves in a catch-22: Higher doses of nicotine would likely produce measurable changes in complex cognitive processes (such as memory), but using higher doses might challenge the validity of a standard balanced-placebo design.

We hope that researchers will continue to investigate factors related to the response expectancy and stimulus expectancy effects of nicotine. For example, Perkins et al. (2006) recently showed that dose instruction played a stronger role in nicotine reinforcement and reward in women compared with men. The present study has shown substantial effect sizes of stimulus expectancy for characteristics of cigarettes that may be important for maintaining smoking behavior, such as feelings of calmness, hunger reduction, wakefulness, improved concentration, and satisfaction. Increased use of the balanced-placebo design may continue to uncover expectancy effects that match, or even exceed, the pharmacological effects studied with more traditional designs.

References

Brandon, T. H., Juliano, L. M., & Copeland, A. L. (1999). Expectancies for tobacco smoking. In I. Kirsch (Ed.), *How expectancies shape experience* (pp. 263–299). Washington, DC: American Psychological Association.

Clark-Carter, D. (1997). *Doing quantitative psychological research: From design to report.* East Sussex, UK: Psychology Press.

Copeland, A. L., Brandon, T. H., & Quinn, E. P. (1995). The Smoking Consequences Questionnaire–Adult: Measurement of smoking outcome expectancies of experienced smokers. *Psychological Assessment, 7,* 484–494.

Cox, L. S., Tiffany, S. T., & Christen, A. G. (2001). Evaluation of the brief Questionnaire of Smoking Urges (QSU-brief) in laboratory and clinical settings. *Nicotine & Tobacco Research, 3,* 7–16.

Crowne, D. P., & Marlowe, D. (1960). A new scale of social desirability independent of psychopathology. *Journal of Consulting Psychology, 24,* 349–354.

Etter, J. F., Le Houezec, J., & Perneger, T. V. (2003). A self-administered questionnaire to measure addiction to cigarettes: The Cigarette Dependence Scale. *Neuropsychopharmacology, 28,* 359–370.

Grunberg, N. E., & Acri, J. B. (1991). Conceptual and methodological considerations for tobacco addiction. *British Journal of Addiction, 86,* 637–641.

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction, 86,* 1119–1127.

Heishman, S. J., Taylor, R. C., & Henningfield, J. E. (1994). Nicotine and smoking: Review of effects on human performance. *Experimental and Clinical Psychopharmacology, 2,* 345–395.

Johnson, M. W., Bickel, W. K., & Kirshenbaum, A. P. (2004). Substitutes for tobacco smoking: A behavioral economic analysis of nicotine gum, denicotinized cigarettes, and nicotine-containing cigarettes. *Drug and Alcohol Dependence, 74,* 253–264.

Juliano, L. M., & Brandon, T. H. (2002). Effects of nicotine dose, instructional set, and outcome expectancies on the subjective effects of smoking in the presence of a stressor. *Journal of Abnormal Psychology, 111,* 88–97.

Kirsch, I. (1999). Response expectancy: An introduction. In I. Kirsch (Ed.), *How expectancies shape experience* (pp. 3–13). Washington, DC: American Psychological Association.

Kramer, M. S., & Shapiro, S. H. (1984). Scientific challenges in the application of randomized trials. *Journal of the American Medical Association, 252,* 2739–2745.

Levin, E. D. (1992). Nicotinic systems and cognitive functions. *Psychopharmacology, 108,* 417–531.

Martin, C. S., & Sayette, M. A. (1993). Experimental designs in alcohol administration research: Limitations and alternatives in the manipulation of dosage-set. *Journal of Studies on Alcohol, 54,* 750–761.

Mendelson, J. H., Sholar, M. B., Goletiani, M. B., Siegel, A. J., & Mello, N. K. (2005). Effects of low- and high-nicotine cigarette smoking on mood states and the HPA axis in men. *Neuropsychopharmacology, 30,* 1751–1763.

Perkins, K. A., Doyle, T., Ciccocioppo, M., Conklin, C., Sayette, M., & Caggiula, A. (2006). Sex differences in the influence of nicotine dose instructions on the reinforcing and self-reported rewarding effects of smoking. *Psychopharmacology, 184,* 600–607.

Perkins, K. A., Jacobs, L., Ciccocioppo, M., Conklin, C., Sayette, M., & Caggiula, A. (2004). The influence of instructions and nicotine dose on the subjective and reinforcing effects of smoking. *Experimental and Clinical Psychopharmacology, 12,* 91–101.

Perkins, K., Sayette, M., Conklin, C., & Caggiula, A. (2003). Placebo effects of tobacco smoking and other nicotine intake. *Nicotine & Tobacco Research, 5,* 695–705.

Rezwani, A. H., & Levin, E. D. (2001). Cognitive effects of nicotine. *Biological Psychiatry, 49,* 258–267.

Rose, J. E., & Behm, F. M. (2004). Effects of low nicotine content cigarettes on smoke intake. *Nicotine & Tobacco Research, 6,* 309–319.

Sherwood, N. (1993). Effects of nicotine on human psychomotor performance. *Human Psychopharmacology: Clinical and Experimental, 8,* 155–184.

Sutton, S. R. (1991). Great expectations: Some suggestions for applying the balanced placebo design to nicotine and smoking. *British Journal of Addiction, 86,* 659–662.

Thayer, R. E. (1986). Activation-Deactivation Adjective Check List (AD ACL): Current overview and structural analysis. *Psychological Reports, 58,* 607–614.

Wesnes, K., Revell, A. D., & Warburton, D. M. (1983). Work and stress as motives for smoking. In G. Cimming & G. Bonsignore (Eds.), *Smoking and the lung* (pp. 233–248). New York: Plenum.

West, R., & Lennox, S. (1992). Function of cigarette smoking in relation to examinations. *Psychopharmacology, 108,* 456–459.

Westman, E., Levin, E., & Rose, J. (1992). Smoking while wearing the nicotine patch: Is smoking satisfying or harmful? *Clinical Research, 40,* 871A.

Appendix

Outcomes of Statistical Tests Including All Participants That Differed From Those Reported in the Main Text

Demographic Information

Including the 9 participants who disbelieved the instructions resulted in the one-way ANOVA for FTND total reaching statistical significance, $F(3, 116) = 3.29$, $p < .05$. Tukey's post hoc test revealed that the told nicotine–received nicotine group had significantly higher FTND scores compared with both groups that expected no nicotine.

Evaluation of Cigarettes

Including the 9 participants who disbelieved the instructions produced the following changes to tests of statistical significance: (a) for "Helped me concentrate," the main effect of instructional set became nonsignificant ($p = .06$); (b) for "Was satisfying," the main effect of instructional set became nonsignificant ($p = .06$); (c) for "Was calming," the main effect of instructional set became nonsignificant ($p = .10$); (d) for "Made me feel nauseous," the main effect of nicotine became nonsignificant ($p = .05$); and (e) for "Gave me throat and chest sensations," the main effect of nicotine became significant ($p < .05$).

Smoking Urges, Tension, and Energy

None of the tests of statistical significance differed from those reported in the main text.

Cognitive Performance

For the study prediction task, memory recall task, and prospective remembering task, none of the tests of statistical significance differed from those reported in the main text.

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