Original Investigation

Effects of Abstinence in Adolescent Tobacco Smokers: Withdrawal Symptoms, Urge, Affect, and Cue Reactivity

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Abstract

Introduction: The aim of this study was to evaluate abstinence effects in adolescent daily smokers by examining the effects of experimentally manipulated acute smoking abstinence on measures including: (a) withdrawal symptoms, (b) reactive irritability, (c) smoking urges, (d) affect, and (e) responses to smoking cues.

Methods: Participants (ages 13–19, 74 daily smokers, and 22 nonsmokers) completed baseline questionnaires and laboratory assessments (Session 1) and returned 1–4 days later to repeat the laboratory assessments (Session 2); half of the smokers were randomly assigned to overnight tobacco abstinence preceding Session 2.

Results: During Session 2, abstinent smokers reported significantly greater increases in withdrawal symptoms, smoking urges, and negative affect compared with smokers who did not abstain and compared with nonsmokers. Although there was not a significant effect of abstinence on differential reactivity to smoking versus neutral cues, abstinence did result in significantly increased peak provoked urges and negative effect. There was not a significant effect of abstinence on positive affect or reactive irritability.

Conclusions: Our results suggest that adolescents experience increases in withdrawal symptoms, smoking urges (un-cued and peak provoked), and negative affect (un-cued and peak provoked) after acute smoking abstinence, but do not experience the increases in reactive irritability or decreases in positive affect that have been shown in adult smokers. Overall findings support the withdrawal relief and negative reinforcement models of smoking maintenance in adolescents and point to

withdrawal, urge, and negative affect as important targets for treatment.

Introduction

Negative reinforcement models, such as withdrawal-relief, show promise for understanding the maintenance of smoking behavior in adult dependent smokers (Baker, Brandon, & Chassin, 2004; Watkins, Koob, & Markou, 2000). These approaches contend that smoking abstinence produces aversive withdrawal effects, which lead to reuptake of smoking to alleviate these symptoms. In this context, determining the nature of specific tobacco abstinence effects is informative and can provide intervention targets. Although smoking abstinence effects have been widely studied in adult smokers (Hughes, 2007), similar research in adolescents is relatively limited. Abstinence effects in adolescent smokers may differ from those measured in adults based on characteristic differences in smoking intensity, chronicity, neurodevelopment, and dependence severity.

Recent studies on adolescent smoking abstinence effects provide support for negative reinforcement models of smoking maintenance and progression. Experimental studies by Colby et al. (2010) and Jacobsen et al. (2005), Jacobsen, Pugh, Constable, Westerveld, and Mencl (2007), and Jacobsen, Slotkin, Westerveld, Mencl, and Pugh (2006) found that adolescent daily smokers experience robust increases in negative affect, withdrawal symptoms, and smoking urges after acute (12–24 hr) smoking abstinence. Further support is provided by studies that have demonstrated dramatic reductions in aversive symptoms

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during smoking reinstatement among adolescent daily smokers (Colby et al., 2010; Corrigan, Zack, Eissenberg, Belsito, & Scher, 2001; Zack, Belsito, Scher, Eissenberg, & Corrigan, 2001).

Studies on the effects of abstinence on positive affect in adolescent smokers have been more limited. The only study to evaluate the effects of smoking abstinence and reinstatement on positive affect in adolescent smokers (Colby et al., 2010) found no significant effects, in contrast to studies with adult smokers which found that abstinence reduces positive affect (al'Absi, Hatsukami, & Davis, 2005; al'Absi, Hatsukami, Davis, & Wittmers, 2004; Leventhal, Waters, Moolchan, Heishman, & Pickworth, 2010). These results with adolescents require replication, but may point to differences in smoking determinants between adolescent and adult smokers.

Although these findings show that adolescent smokers experience abstinence effects on key measures, they also tentatively suggest that the phenomenology of smoking abstinence may differ in adolescent versus adult smokers. In this context, examining a broader range of abstinence effects in adolescent smokers may improve understanding of these potential differences. For example, studies in adult smokers have found that overnight abstinence increases reactivity to irritable stimuli (i.e., reactive irritability; Acri & Grunberg, 1992) and smoking-related cues (i.e., cue reactivity; Sayette, Martin, Wertz, Shiffman, & Perrott, 2001; Watson, Carpenter, Saladin, Gray, & Upadhyaya, 2010), yet, the influence of abstinence on these measures in adolescent smokers has not been tested. In addition, the question of how individual differences in baseline smoking characteristics predict the severity of abstinence effects is an important issue that has received little prior attention in adolescents.

The aim of this study was further delineate the nature of abstinence effects in adolescent daily smokers by examining the effects of experimentally manipulated acute smoking abstinence on a broad array of measures including: (a) self-reported withdrawal symptoms, (b) reactive irritability, (c) smoking urges, (d) positive and negative affect, and (e) urge reactivity to in vivo presentation of smoking cues. We hypothesized that overnight abstinence in adolescent daily smokers would increase smokers' withdrawal symptoms, reactive irritability, smoking urges, negative affect, and smoking cue reactivity and decrease smokers' positive affect. This study also tested the hypothesis that the magnitude of abstinence effects on these measures would be positively predicted by baseline smoking severity, including daily smoking rate, biological markers of exposure to smoking, number of consecutive days abstinent, and dependence.

Methods

Participants

Participants were recruited by advertisements and flyers in area schools and the surrounding community. Adolescents interested in the study completed a telephone screen to establish eligibility. Adolescents had to be 13–19 years old and able to read and speak English to be eligible. "Daily smokers" were defined as those who reported smoking more than 100 cigarettes lifetime and who described their current smoking as "daily" (vs. "weekly" or "less than weekly"). "Nonsmokers" were defined as those who reported having smoked fewer than 100 cigarettes in their lifetime and none in the past 6 months. Participants

were ineligible if they reported daily use of alcohol or any other drug other than tobacco (assessed at baseline assessment). Adolescents were excluded if they were pregnant or nursing.

Informed consent was obtained for participants aged 18–19; for minors, informed assent and parental consent were both obtained. All participants received \$50 for completing the study, and smokers additionally received brief smoking intervention and educational handouts related to quitting smoking. All procedures were approved by the Brown University Institutional Review Board.

Design and Test Procedures

The study used a mixed between- and within-subjects experimental design. Participants were measured twice: at Session 1 (S1) when assessments were taken under normal baseline conditions and at Session 2 (S2) when assessments were repeated to evaluate abstinence effects. Changes in responses from S1 to S2 were compared in the following groups: (a) nonsmokers (NONSMT; $n = 22$), (b) abstainers: smokers randomly assigned to abstain from smoking after 10 p.m. before S2 (ABST; $n = 47$), and (c) *ad lib* smokers: smokers randomly assigned to continue smoking according to their usual pattern before S2 (ADLIB; $n = 27$). Randomization of smokers was stratified by age and gender to ensure that the ABST and ADLIB groups did not differ on these characteristics. Eligible NONSMK participants were selected from a pool of interested candidates based on their age and gender, to ensure that smokers and nonsmokers were comparable on these characteristics.

Standard *presession instructions* included: no use of alcohol, illicit drugs, or nonprescription drugs for 24 hr and (for the accuracy of cotinine assays) no dairy products or large meals within 1 hr of each session. Smokers were instructed to bring their cigarettes to each session and to smoke normally before S1. All sessions started between 2 and 6 p.m., resulting in 16–20 hr smoking abstinence at S2 for the ABST group.

Session 1. During S1 (approximately 2 hr), participants first provided breath and saliva samples for expired carbon monoxide (CO) and cotinine levels and completed demographic and smoking questionnaires. Smokers were then instructed to smoke a cigarette and nonsmokers took a 5-min break. Smokers then provided another sample of breath CO, completed past-24 hr withdrawal symptom ratings, and completed the reactive irritability and cue reactivity protocols (all measures described below).

Session 2. Before S2, ABST smokers were told to refrain from smoking cigarettes after 10 p.m., and ADLIB smokers were instructed to smoke at their usual rate. S2 (approximately 1 hr) occurred within 4 days of S1. ABST participants were required to exhibit $CO \leq 10$ ppm on arrival, otherwise they were rescheduled. ADLIB smokers were instructed to smoke a cigarette on arrival (5 min); nonsmokers and ABST smokers took a 5-min break. Participants then completed the *Minnesota Nicotine Withdrawal Scale* (MNWS) and the reactive irritability and cue reactivity protocols.

Smoking and Demographic Measures

Expired CO levels were obtained using a Bedfont Smokerlyzer.

Saliva samples were collected for *cotinine* analysis by gas chromatography (Salimetrics, LLC, State College, PA).

Demographic variables included age, gender, race/ethnicity, and years of education.

Tobacco Use History queried age of various tobacco use milestones and history of abstinence and quit attempts.

The 30-day *Timeline Followback for Smoking* (Lewis-Esquerre et al., 2005), a calendar-assisted retrospective recall of cigarettes per day, was used to measure daily smoking rate.

Nicotine dependence. The modified Fagerström Tolerance Questionnaire (mFTQ; Prokhorov et al., 2000), a 7-item assessment that has been validated with adolescents, was used to measure nicotine dependence.

Measures of Abstinence Effects

Withdrawal symptoms were measured using the MNWS (Hughes, 1992; Hughes & Hatsukami, 1986), which includes seven symptoms rated from 0 (not present) to 4 (severe); the scale score is the sum of these items. "Desire to smoke" was rated but not included in the scale score to measure desire/urge to smoke and withdrawal separately (Hughes & Hatsukami, 1998).

Reactive irritability. The Reactive Irritability Scale (RIS) is a reliable and valid measure of irritability during smoking withdrawal; among adults, the RIS distinguishes abstaining smokers from *ad lib* smokers better than self-reported irritability (Acri & Grunberg, 1992). The RIS uses magnitude estimation of self-reported irritability with audio-taped environmental sounds. Each of eight common sounds (sirens, dog barking, telephone, bowling, horse trotting, bugle, diving, and fire engine) were played from an audio tape which the participant heard through headphones while seated alone in the laboratory. A reference sound was also played. The participant was instructed to first rate the level of irritability experienced on hearing the reference sound by marking an X on a continuous line from "not at all irritating" to "extremely irritating." This level was assigned a value of 500. After this, the participant heard the reference sound repeated before each target sound. The participant then rated the relative irritability of each target sound by assigning a numerical value relative to the target sound.

Smoking urge was measured using the *Questionnaire on Smoking Urges (QSU)s Brief Form*, (Tiffany & Drobes, 1991), a 10-item abbreviated version of the 32-item QSU ($\alpha = .98$). The QSU has a total score plus two empirically derived factors; Factor 1 reflects the intention and desire to smoke as well as desire to smoke for reward ($\alpha = .98$), and Factor 2 reflects intense desire to smoke as well as desire to smoke to relieve withdrawal ($\alpha = .96$). Items were rated from 1 (strongly disagree) to 7 (strongly agree).

The Positive/Negative Affect Scale (PANAS; Watson, Clark, & Tellegen, 1988), a widely used 20-item measure with reliable subscales, was used to measure positive (PANAS-PA; $\alpha = .96$) and negative (PANAS-NA; $\alpha = .93$) affect. Participants rated adjectives describing their affect "right now" from 1 (very slightly or not at all) to 5 (extremely).

Cue reactivity protocol. In the cue reactivity laboratory protocol (Shiffman et al., 2003), participants were presented a tray containing a set of neutral cues then a tray containing a set of smoking cues. Smoking cues consisted of a pack of the

participant's usual brand of cigarettes, an ashtray, a lighter, and a cigarette; neutral cues consisted of a small pad of paper, a pencil, and an eraser. During each presentation of cues, the participant was instructed via recorded instructions to manipulate individual items for 2 min. During the smoking cue presentation, participants were also instructed to light the cigarette (without putting in their mouth) by holding the lighter at the end of the cigarette while holding the cigarette at a downward angle. The dependent variables were QSU and the PANAS, administered at three points during the cue reactivity protocol, to measure cue-elicited changes in urge and affect responses. The first administration followed a 5-min relaxation period before any cues (neutral or smoking) being presented, the second followed the presentation of neutral cues and the final administration followed the set of smoking cues. Responses to the QSU and the PANAS following relaxation were used to evaluate abstinence effects on urge and affect generally, whereas QSU and PANAS ratings in response to neutral cues were subtracted from ratings in response to smoking cues to measure urge reactivity to cues in each session.

Data Analysis

To examine group equivalence at baseline, one-way between-groups analyses of variance (ANOVAs) and Chi-square tests were used on key baseline demographic and smoking variables. To analyze smoking abstinence effects on the dependent variables (CO level, MNWS, QSU, PANAS-PA, and PANAS-NA scores) before cue presentation, and cue-induced changes in urges and affect (responses after smoking cue – responses after neutral cue), we conducted separate 3×2 mixed ANOVAs, with group (ABST vs. ADLIB vs. NONSMK) as a between-subjects variable and session (S1 vs. S2) as a within-subjects variable. Because responses on the RIS-II are not normally distributed, Kruskal–Wallis tests of the difference score (RIS-II S2 rating – RIS-II S1 rating) were used to analyze smoking abstinence effects on reactive irritability. Next, planned interaction contrasts were used to compare the changes from S1 to S2 in the ABST group with each control condition (ADLIB and NONSMK) separately. Finally, relationships between baseline smoking variables (cigarettes per day, longest consecutive abstinence from smoking, mFTQ score, CO, and cotinine) were measured in the subsample of ABST participants using zero-order correlations between S2–S1 changes score and the baseline smoking characteristic.

ANOVAs were tested in SAS using PROC GLM for unbalanced cell sizes (SAS Institute Inc., 2003). All other analyses were completed using SPSS statistical software (version 19.0).

Results

Participant Characteristics

Of the 177 individuals who completed the screening interview, 112 were eligible, agreed to participate, and attended S1. Percentages of enrolled participants in the ABST, ADLIB, and NONSMK conditions who completed the study were 82%, 84%, and 96%, respectively. A 3 (Group) $\times$ 2 (Study completion) Chi-square test ($df = 2$) indicated no significant differences in completion rate between groups ($\chi^2 = .23$ and $p = .89$). The final sample ($N = 96$) is described in Table 1. There were no demographic differences between the three groups, and the

Table 1. Baseline Sample Characteristics: Demographic and Smoking Variables by Group

	ABST (<i>n</i> = 47)	ADLIB (<i>n</i> = 27)	NONSMK (<i>n</i> = 22)	<i>F</i> / <i>X</i> ²	<i>p</i> value
Demographic characteristics					
Female, <i>n</i> (%)	29 (61%)	16 (59%)	14 (63%)	.10	.95
Age, <i>M</i> (<i>SD</i>)	16.4 (1.8)	16.2 (1.8)	15.9 (1.6)	.05	.91
Race/ethnicity, <i>n</i> (%)					
Native American	9 (19%)	4 (15%)	1 (4.5%)		
Asian/Pacific Islander	3 (6%)	1 (4%)	0 (0%)		
Black/African American	3 (6%)	4 (15%)	5 (23%)		
Hispanic	4 (9%)	2 (7%)	7 (32%)		
Non-Hispanic White	38 (81%)	19 (70%)	10 (46%)		
Other	3 (6%)	2 (7%)	8 (36%)		
Total years education, <i>M</i> (<i>SD</i>)	10.9 (2.0)	10.5 (1.9)	10.6 (1.4)	.42	.66
Smoking characteristics, <i>M</i> (<i>SD</i>)					
Cig/day in past 30 days	9.3 (5.3)	9.5 (5.9)	–	.03	.87
Years regular smoking	2.1 (2.1)	1.9 (1.6)	–	.21	.65
mFTQ	4.5 (1.7)	4.5 (1.6)	–	.00	.99
Expired CO (ppm)	10.9 (7.1)	11.3 (6.4)	–	.83	.37
Salivary cotinine (ng/ml)	98.2 (62.6)	110.5 (42.7)	–	.05	.82

Note. ABST = abstinent smokers; ADLIB = nonabstinent smokers; Cig = cigarettes; CO = carbon monoxide; mFTQ = modified Fagerström Tolerance Questionnaire; NONSMK = nonsmokers.

two smoking groups also did not differ on any of the baseline smoking characteristics.

Smoking Abstinence Effects

Manipulation check. Compliance with the smoking abstinence manipulation was confirmed with a Group (ABST vs. ADLIB) $\times$ Time (S1 vs. S2) mixed factorial ANOVA of CO levels, which yielded a significant Group $\times$ Time interaction effect, $F(1, 71) = 58.00, p < .0001$, and partial $\eta^2 = .26$. In the ABST group, mean CO levels decreased significantly from S1 to S2 (from 14.9 ± 7.1 ppm to 3.8 ± 1.9 ppm), whereas CO in the ADLIB smokers did not decrease (16.9 ± 6.4 ppm to 18.5 ± 7.0 ppm).

Withdrawal symptoms. A Group (ABST vs. ADLIB vs. NONSMK) $\times$ Time (S1 vs. S2) mixed factorial ANOVA of MNWS scores showed a significant Group $\times$ Time interaction effect, $F(2, 92) = 23.31, p < .0001$, and partial $\eta^2 = .19$. Interaction contrasts showed that MNWS scores increased significantly from S1 to S2 in the ABST group (from 10.8 ± 6.5 to 16.1 ± 2.5) but did not change in either the ADLIB (11.2 ± 6.2 vs. 9.8 ± 6.7) or the NONSMK (3.8 ± 3.6 vs. 3.0 ± 2.5) groups.

Reactive irritability. The median rating for the overall sample and each group at S1 and S2 are reported in [Supplementary Table 1](#). As in previous research ([Acri & Grunberg, 1992](#), Studies 2 and 3), linear regressions were fit using the 8 median ratings as observations, which regressed the median ratings from the present sample on the median ratings in [Acri and Grunberg \(1992\)](#) Study 1. Consistent with past data, the overall median values for each stimulus generally fit a linear model ($R^2 \geq .72$). However, when evaluating whether slope parameters could be used in primary analyses, individual participant ratings tended to fit poorly with the linear model both at S1, M (*SD*) of $R^2 = .36$ (.27), and S2, M (*SD*) of

$R^2 = .33$ (.27), suggesting that slope estimates for each participant were not reliable. Therefore, the primary analyses were based on the average rating of the eight stimuli for each participant.

We then used a Kruskal–Wallis test to test whether the changes in RIS-II ratings from S1 to S2 differed across groups. Results showed that difference scores (S2 rating – S1 rating) for average RIS-II ratings among the three groups did not significantly differ, Kruskal–Wallis $X^2(2) = 3.31$ and $p = .19$.

Smoking urges. A Group (ABST vs. ADLIB vs. NONSMK) $\times$ Time (S1 vs. S2) mixed factorial ANOVA of QSU-Total scores after relaxation tested the effect of abstinence on overall (unelicited) smoking urges (Mean [*SD*] presented in [Table 2](#)). Results showed a significant Group $\times$ Time interaction effect, $F(2, 93) = 44.9, p < .0001$, and partial $\eta^2 = .23$. Interaction contrasts showed that QSU-Total scores increased significantly from S1 to S2 in the ABST group but did not change from S1 to S2 in either the ADLIB or NONSMK groups. This pattern of significant results was the same for the ANOVAs testing the effects of abstinence on QSU-F1 and F2 scores ([Table 2](#)).

Positive and negative affect. Means (*SD*) for this measure are presented in [Table 2](#). A Group (ABST vs. ADLIB vs. NONSMK) $\times$ Time (S1 vs. S2) mixed factorial ANOVA of PANAS-NA scores after relaxation tested the effect of abstinence on negative affect. Results showed a significant Group $\times$ Time interaction effect, $F(2, 91) = 8.1, p < .001$, and partial $\eta^2 = .17$. Interaction contrasts showed that PANAS-NA scores increased significantly from S1 to S2 in the ABST group (from 16.0 to 19.8) but did not change from S1 to S2 in the ADLIB (14.8 vs. 13.9) or the NONSMK (12.4 vs. 12.8) groups. The corresponding ANOVA of PANAS-PA was not significant ($F(2, 91) = 0.8, p = .45$, and partial $\eta^2 = .001$), reflecting no change in positive affect from S1 to S2 in any of the groups.

Table 2. Questionnaire on Smoking Urges (QSUs), Positive/Negative Affect Scale (PANAS), and Cue Reactivity Means (SD) by condition

		S1						S2					
		Relax		Neutral		Smoking		Relax		Neutral		Smoking	
		<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
PANAS-NA	<i>n</i>												
ABST	45	16.0	5.6	15.5	5.5	17.4	6.2	19.8	6.2	19.8	6.8	20.8	8.0
ADLIB	26	14.8	4.2	14.9	5.4	16.7	6.1	13.9	4.7	14.3	4.9	16.4	5.8
NONSMK	21	12.4	3.0	12.7	4.4	13.9	6.0	12.8	3.9	12.2	3.3	13.2	4.2
PANAS-PA													
ABST	46	25.6	7.4	24.5	8.7	25.2	9.5	23.1	9.4	22.4	9.7	23.5	10.8
ADLIB	25	22.0	6.3	23.0	8.5	23.8	8.6	21.7	8.2	20.9	8.6	21.9	9.0
NONSMK	21	27.5	9.9	26.8	11.2	26.0	11.3	24.9	11.4	24.5	11.2	23.8	10.8
QSU-Total													
ABST	47	3.1	1.5	3.2	1.7	4.3	2.0	5.2	1.7	5.3	1.7	5.6	2.0
ADLIB	27	2.9	1.7	3.2	1.9	4.1	2.2	2.3	1.3	2.6	1.5	3.7	2.2
NONSMK	22	1.0	0.0	1.0	0.0	1.0	0.4	1.1	0.2	1.1	0.2	1.0	0.2
QSU-Factor 1													
ABST	47	3.7	1.7	3.8	2.0	4.9	2.0	6.0	1.6	5.9	1.7	4.9	2.0
ADLIB	27	3.3	2.0	3.7	2.2	4.7	2.3	2.6	1.5	3.0	1.7	4.7	2.3
NONSMK	22	1.0	0.0	1.0	0.0	1.1	0.4	1.1	0.2	1.1	0.2	1.1	0.4
QSU-Factor 2													
ABST	47	2.5	1.5	2.7	1.8	3.6	2.2	4.5	2.0	4.6	2.0	5.0	2.1
ADLIB	27	2.5	1.4	2.8	1.7	3.6	2.3	2.0	1.2	2.2	1.3	3.1	1.9
NONSMK	22	1.0	0.0	1.0	0.0	1.0	0.0	1.0	0.2	1.0	0.2	1.0	0.0

Note. *Ns* vary slightly across measures due to missing data. ADLIB = nonabstinent smokers; ABST = abstainers; NA = Negative Affect subscale; NONSMK = nonsmokers; PA = Positive Affect subscale; PANAS = Positive and Negative Affect Scale; QSU = Questionnaire on Smoking Urges—Brief; S1 = session 1; S2 = session 2; SD = reactivity means.

Cue-induced urge and affect reactivity. The *M* (*SD*) of each measure by cue condition is reported in Table 2.

Smoking urge reactivity. The ANOVA of QSU-Total scores yielded a significant Group effect, $F(2, 93) = 13.78, p < .0001$, and $\eta^2 = .23$. Pairwise contrasts showed cue-induced changes in urge across the two sessions were greater in the ABST and ADLIB groups than the NONSMK group (ABST and ADLIB did not differ). There was also a significant Group $\times$ Time interaction, $F(2, 93) = 7.74, p = .0008$, and partial $\eta^2 = .07$. Simple effect analyses showed that urge reactivity to smoking cues (using change scores; smoking cue ratings – neutral cue ratings) declined significantly from S1 to S2 among ABST participants, whereas cue-induced change scores did not differ across sessions for ADLIB or NONSMK participants. This pattern of significant results was the same for QSU-F1 and F2 scores. This pattern of results appeared to be a function of greater urge ratings in response to neutral cues at S2 in the ABST group, leaving little room for cue-induced urge reactivity to be expressed when smoking cues were introduced (Sayette et al., 2001). To further examine this possibility, we subsequently analyzed abstinence effects on “peak provoked craving” (PPC; Sayette, Griffin, & Sayers, 2010), that is, QSU-Total urge score in response to smoking cues without adjusting for ratings in response to neutral cues (Niaura et al., 2005; Waters et al., 2004). That 3×2 ANOVA yielded a significant Group $\times$ Time interaction effect, $F(2, 93) = 13.9, p < .0001$, and partial $\eta^2 = .23$. Interaction contrasts showed that QSU-Total urge scores after smoking cues increased

significantly from S1 to S2 in the ABST group but did not change from S1 to S2 in either the ADLIB or NONSMK groups.

Positive and negative affect reactivity. There were no significant effects of Group, Time, or interactions between these measures on PANAS-NA and PANAS-PA cue-induced change scores. After the PPC model, we subsequently analyzed abstinence effects on “peak provoked negative affect” (i.e., PANAS-NA in response to smoking cues without adjusting for ratings in response to neutral cues). That 3×2 ANOVA yielded a significant Group $\times$ Time interaction effect, $F(2, 91) = 6.9, p = .002$, and partial $\eta^2 = .23$. Interaction contrasts showed that PANAS-NA scores following smoking cues increased significantly from S1 to S2 in the ABST group but did not change from S1 to S2 in either the ADLIB or NONSMK groups.

Relationship of Baseline Smoking Measures With Abstinence Effects

Within the ABST group, correlation analyses showed that greater baseline CO levels predicted abstinence-induced increases in MNWS ($r = .29$ and $p = .04$); greater baseline cotinine levels predicted abstinence-induced increases in PANAS-NA ($r = .32$ and $p = .03$); greater baseline nicotine dependence and fewer consecutive nonsmoking days at baseline both predicted abstinence-induced increases in peaked provoked urges (greater S2–S1 change in QSU to smoking cues; $r = .32, p = .03$ and $r = -.41, p = .004$, for nicotine dependence and consecutive

nonsmoking days, respectively). Finally, fewer consecutive non-smoking days at baseline predicted greater abstinence-induced increases in un-cued smoking urges (S1–S2 changes in QSU during relaxation; $r = -.24$, $p = .08$) at trend-level significance. Correlations with all other measures were nonsignificant.

Conclusions

Summary of Findings

This study demonstrated robust effects of abstinence on withdrawal symptoms, smoking urge, and negative affect in a sample of adolescent smokers. However, abstinence did not significantly influence positive affect, or reactive irritability. Although abstinence did not increase urge reactivity to smoking cues, it did increase PPC and affect, that is, urge and affect ratings in the presence of smoking cues, unadjusted for responses to neutral cues. These findings extend prior research by testing a broad array of outcome measures within one study, including indices of reactive irritability and cue reactivity that have not been examined in prior controlled studies of adolescent tobacco abstinence. This multimeasure approach is useful in characterizing the phenomenology of adolescent smoking abstinence by showing that responses of adolescent smokers to abstinence overlap those of adult smokers in some (i.e., increases in negative affect, withdrawal symptoms, and overall smoking urges; Colby et al., 2010; Corrigan et al., 2001; Zack et al., 2001) but not other aspects (i.e., no increase in reactive irritability or reduction in positive affect; al'Absi et al., 2005, 2004; Leventhal et al., 2010).

Contrary to our hypotheses, we did not find that acute abstinence led to increases in urge or affective reactivity to smoking cues. Inspection of mean values of QSU scores after neutral cue exposure indicated that ABST participants scored close to the upper limit of the range of possible values on this measure in S2, leaving limited range to demonstrate increases in urge following the smoking cue exposure, resulting in a ceiling effect for cue-induced change scores. This likely accounted for ABST participants showing a reduction in urge reactivity from S1 to S2. Similar findings have frequently been reported in adult smokers (Drobes & Tiffany, 1997; Sayette & Hufford, 1994; Sayette et al., 2001; Tidey, Rohsenow, Kaplan, Swift, & Adolfo, 2008), leading researchers to additionally examine effects on PPC, focusing on urge ratings during exposure to smoking cues without adjusting for urges during neutral cues (e.g., Donny, Griffin, Shiffman, & Sayette, 2008; Sayette et al., 2000). Studies support the clinical relevance of PPC and show that peak provoked urge ratings are reduced by nicotine patch (Morissette, Palfai, Gulliver, Spiegel, & Barlow, 2005; Tiffany, Cox, & Elash, 2000; Waters et al., 2004) and nicotine gum (Niaura et al., 2005; Shiffman et al., 2003). Indeed, our study found a significant effect of abstinence on peak provoked urges and negative affect, but did not find a significant effect of abstinence on urge or affective reactivity when accounting for ratings to neutral cue exposure. These findings suggest that abstinence paired with exposure to smoking cues may present a greater vulnerability to relapse in these adolescent smokers.

Greater levels of baseline nicotine dependence and shorter periods of abstinence from smoking were associated with greater abstinence-induced increases in peaked provoked urges.

In addition, higher biochemical smoking markers were associated with greater increases in withdrawal and negative affect during abstinence. Taken together, these findings suggest that increased baseline smoking severity is associated with increased abstinence effects on key measures and support conceptualizations of adolescent smoking that include withdrawal-type effects as a part of the adolescent dependence process. Our results are in contrast to those of Smith et al. (2008), who found no relationship between baseline smoking measures and withdrawal symptoms in adolescent smokers at 3.5 hr postabstinence in an inpatient setting. It is possible that this difference can be ascribed to the longer period of smoking abstinence in this study and the fact that participants underwent abstinence in their natural environments, as perceived opportunity to smoke influences withdrawal symptom levels (Droungas, Ehrman, Childress, & O'Brien, 1995).

Taken together, these findings provide critical evidence to broaden our understanding of withdrawal in adolescent smokers by suggesting that adolescent withdrawal is characterized by negative subjective experiences that may be augmented by smoking-related environmental cues. In addition, our findings point to withdrawal, urge (both un-cued and peak provoked), and negative affect (both un-cued and peak provoked) as candidate mediators of treatment efficacy in adolescents and suggest that future treatment trials should be designed to test mediation through these mechanisms. Such designs may improve on our current studies, which provide only mixed evidence for pharmacotherapy and nicotine replacement therapy in adolescent smokers. Pharmacotherapy trials in this population have been limited in other ways that inhibit their ability to definitively evaluate treatment efficacy (Breland, Colby, Dino, Smith, & Taylor, 2009). As such, it remains unclear whether the lack of efficacy emerges because these treatments do not effectively reduce abstinence effects or, alternatively, because the theoretical approach is incorrect (i.e., these treatments are effective at reducing abstinence effects, but reducing the negative effects of abstinence does not improve cessation outcomes). Mediation tests focused on key mechanisms are still required to answer this question and our findings point to withdrawal, urge, and negative affect as strong candidate measures for this pathway. Regardless of any implications for cessation trials, this study's finding that adolescent smokers experience sizeable withdrawal effects potentially has broader treatment implications and suggests that the abstinence syndrome may be worthy of therapeutic intervention among adolescents attempting to quit smoking.

Limitations and Future Directions

These findings should be interpreted in the context of the study's limitations. First, this is a laboratory study with adolescents who are not necessarily interested in quitting. Although findings demonstrate the acute effects of smoking abstinence, these laboratory assessments may not directly translate to the real-world experience of motivated quitters making a quit attempt. More naturalistic designs (i.e., the use of ecological momentary assessment of withdrawal effects) will be important for future research. In addition, the current design cannot disentangle the effects of abstinence from nicotine specifically versus withdrawal from the behavioral and psychological effects of smoking abstinence more generally. Our findings should be followed up with studies that include additional comparison

groups that decouple the effects of smoking and nicotine. For example, we recently found that sensorimotor replacement for smoking was more effective than nicotine replacement at reversing abstinence-induced craving, nicotine withdrawal symptoms, and usual-brand smoking among adult smokers with and without serious mental illness (Tidey, Rohsenow, Kaplan, Swift, & AhnAllen, 2012). Similar studies in adolescents could indicate whether temporary substitution of very low nicotine cigarettes for nicotine-containing cigarettes may provide a pathway toward reducing nicotine dependence in this population.

Supplementary Material

Supplementary Table 1 can be found online at <http://www.ntr.oxfordjournals.org>

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Declaration of Interests

None declared.

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