Published in final edited form as:

J Adolesc Health. 2008 July ; 43(1): 46–54. doi:10.1016/j.jadohealth.2007.12.004.

Effects of acute tobacco abstinence in adolescent smokers as compared with nonsmokers

Anne E. Smith, Dana A. Cavallo, Tricia Dahl, Ran Wu, Tony P. George, and Suchitra Krishnan-Sarin

Yale University School of Medicine

Abstract

Purpose—Abstinence effects such as nicotine withdrawal and mood changes contribute to the maintenance of cigarette smoking in adult smokers and emerging reports on adolescent smokers suggest they may experience similar subjective effects when deprived. This study aimed to prospectively document tobacco abstinence induced changes during the first 48 hours of abstinence in adolescent smokers compared with nonsmokers, to distinguish effects distinct from typical adolescent lability.

Methods—57 adolescent smokers and 44 adolescent nonsmokers were assessed during a 48 hour inpatient session. Characteristic nicotine withdrawal symptoms, cravings for cigarettes, and mood symptoms were measured at 13 time points following initiation of abstinence.

Results—The only abstinence related effects observed were changes in craving for tobacco and feelings of anger. Tobacco craving increased and peaked quickly following initiation of abstinence and displayed a slight decrease towards the end of the 48 hour abstinence period, while anger symptoms peaked after more prolonged abstinence. Overall, smokers' symptoms and cravings were positively associated with amount of daily smoking but not with reports of dependence or biological measures of extent of use.

Conclusions—We observed that among adolescent smokers, the primary effects associated with abstinence from cigarettes are relatively minimal and include a heightened and persistent craving to smoke and increases in anger. Although smokers had greater negative mood symptoms compared with nonsmokers, the presence and severity of most of these symptoms appear to be minimally altered by abstinence and not associated with dependency or biological indicators of amount of tobacco use.

Research in adult smokers has shown that experiencing such abstinence effects as nicotine withdrawal and mood changes are important in the maintenance of cigarette smoking [1], and recent evidence indicates that the pattern, duration, and severity of withdrawal symptoms including negative affect, are particularly significant predictors of relapse in adult smokers [2,3,4]. However, the experience of tobacco withdrawal has not been as thoroughly evaluated in adolescent smokers.

Retrospective evaluations from adolescent smokers indicate withdrawal experiences similar to those of adults when not smoking; including reported increases in cravings, nervousness,

Please address correspondence to Suchitra Krishnan-Sarin, Ph.D., Yale University School of Medicine, Department of Psychiatry, CHMC, S 208, 34 Park Street, New Haven, CT 06519. Address e-mail correspondence to suchitra.krishnan-sarin@yale.edu. Phone: 203-794-7595, Fax: 203-974-7606.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

restlessness, irritability, hunger, difficulty concentrating, sadness, and sleep disturbances [5, 6]. Prospective studies of tobacco abstinence in adolescent smokers which suggest that these young smokers experience increases in subjective withdrawal symptoms and changes in objective physiological responses associated with tobacco deprivation (i.e. increases in craving, anxiety, and restlessness, and decrease in heart rate) [7]. Adolescents trying to quit smoking frequently report urges to smoke, irritability, and difficulty concentrating [8]. However, it is unclear whether these reported symptoms are distinct from the daily lability experienced by adolescents in general; indeed in one retrospective report on adolescent smokers, reports of withdrawal symptoms (in the last 30 days for nonsmokers and at the time of most recent quit effort for smokers), did not distinguish light smokers from non-smokers [9].

Emerging evidence, from adolescent response to pharmacological treatments and preclinical examinations suggests significant differences characterizing tobacco dependence of adult and adolescent smokers. For example, cravings may be the single most salient symptom associated with the abstinence experience in adolescence. Retrospective reports of cravings are able to distinguish both light and heavy smokers from non-smokers [9] and extent of cravings have been associated with lapse during cessation for adolescents [11]. The efficacy of nicotine patch treatment, which is known to be effective for smoking cessation in adult smokers, has been less conclusively established with adolescent smokers [12,13,14]. Moreover, Killen et al. have demonstrated that administration of the nicotine patch did not prevent development of all nicotine withdrawal symptoms in adolescents [7]. Preclinical studies indicate that nicotine use resulted in differential patterns of changes in both behavioral and brain development/synaptic function outcomes in adolescent compared with adult rats [15] and that these differences extend to the evaluation of nicotine withdrawal [16]. More specifically, although adult rats evidence symptoms of withdrawal, these symptoms are absent in adolescent rats. As a result, we cannot assume that adolescent smokers are similar to adult smokers in the nature of tobacco dependence and in the experience of withdrawal symptoms, and further systematic evaluation of the presence, characterization, and influence of withdrawal and dependence is necessary.

A well-developed picture of tobacco withdrawal in adolescents is necessary to further our understanding of the potential influences of dependence and withdrawal on tobacco cessation. Recent data illustrates the difficulty adolescents experience when trying to quit smoking: nearly 73% of adolescents who had reported smoking daily at some point had tried to quit smoking but only 13.5% were former smokers [17]. Furthermore, adolescent smokers may also go through significant periods of abstinence from tobacco on a daily basis since they spend a majority of their time in non-smoking environments like schools. It is therefore important to identify any significant cognitive and mood changes these adolescent smokers experience on a daily basis that may compromise their productivity and learning abilities in addition to contributing to difficulty with tobacco cessation.

We analyzed the effects of acute tobacco abstinence in adolescent male and female smokers by conducting a prospective evaluation of commonly identified behavioral abstinence symptoms during a 48 hour inpatient tobacco abstinence period. This duration was determined based on evidence in the literature that nicotine withdrawal-related cognitive decrements can appear as early as 4 hours, and peak within 48 hours, of abstinence initiation [18,19], symptoms are greatest at the earliest points of abstinence [20] and timing and severity of symptoms may be particularly salient to the establishment of long term abstinence [21,22]. The intent of this study was to characterize tobacco abstinence effects in adolescent smokers in a controlled environment and to differentiate these effects from normal variations related to typical adolescent lability. Hence we also included nonsmoking control participants. We hypothesized that adolescent smokers would experience alterations in abstinence symptoms over time when

compared with nonsmokers. We also explored associations between symptoms and self report measures of dependence and objective measures of use.

Method

Participants

47 adolescent nonsmokers (20 males, 27 females) and 55 adolescent smokers (28 males, 27 females) participated in this study. All smokers were self-reported daily smokers and nonsmokers were self-reported never daily smokers who reported no tobacco use in the past 6 months and no history of regular use of any tobacco products. These categories were confirmed biochemically with cotinine levels assessed at 2 outpatient visits prior to the inpatient session. Cotinine levels below 10 ng/ml were required for the nonsmoker group; cotinine levels above 10 ng/ml were required for the smoker group. Participants were 69% Caucasian, 14% African American, 7% Hispanic, 1% Asian, and 9% Other/Multiracial and ranged in age from 14 to 18 years old. Participants were recruited from area high schools and via newspaper advertisements in local newspapers

Procedures

Procedures for this study were approved by the Institutional Review Board of Yale University School of Medicine. Adolescents were initially screened over the phone and if initial requirements were met a first interview was scheduled. Adolescents were accompanied by a parent to an intake session where permission from the parent and assent from the child were obtained. Adolescents who had other co-existing psychopathology (as determined by DISC-IV directed interview to establish current and past DSM-IV criteria for substance abuse and psychiatric disorders conducted by a Ph.D. level psychologist) or self-reported regular daily use of other substances including marijuana and alcohol were excluded from the study. A brief physical exam included urine drug screens to confirm non-user status, and pregnancy screens were conducted to ensure that the females were not pregnant. (Parents were not provided with any information about the adolescent's tobacco/drug use or pregnancy status.) Following the screening appointment, if the adolescent was eligible he or she was scheduled to participate in an outpatient orientation and intake session. During the outpatient session, smokers and nonsmokers were familiarized with the inpatient rooms at the Children's Clinical Research Center at Yale-New Haven Hospital (CCRC), and were asked to complete a battery of assessments similar to those that would be completed during the abstinence period. These appointments were conducted 5–7 days before the inpatient abstinence period. Sessions for female subjects were not scheduled during the late luteal phase of the menstrual cycle to avoid premenstrual syndrome symptoms which may be confused for or exacerbate withdrawal symptoms [23].

In order to ensure that all participants were not missing school in order to participate, and so that the smokers were most likely to have had opportunity to maintain normal smoking behavior prior to the inpatient abstinent period, these sessions were scheduled to be held on weekends or holidays. Urine drug screens were repeated prior to the inpatient and outpatient sessions to confirm that the subjects had not used any other substances; if the drug screens were positive the sessions were rescheduled. Prior to the inpatient tobacco abstinent period, smokers were asked to smoke normally and were not asked to be abstinent from cigarettes. They were instructed to not smoke after 5 pm and breath carbon monoxide levels were obtained upon arrival at the CCRC. The inpatient sessions started at 6 pm on the first day (Day 1) and continued until 4 pm, 46 hrs later on the third day (Day 3). During this period, all participants stayed in private rooms at the CCRC. Smokers were required to be abstinent and abstinence was verified periodically using breath CO (< 10 ppm) and urine cotinine (decreasing) measurements. When they were not completing assessments participants were allowed to watch TV, read and play

computer games in their rooms. They were allowed to have family visitors only between 4–5:45 pm on Day 2; no assessments were conducted during this period.

Measures

All assessments were obtained repeatedly during the 48 hour abstinence period approximately every 2 hours following the initiation of abstinence (at 5 pm the day of admission), with the exception of the overnight time period which resulted in a span of 11 hours between assessments the first night and 9 hours between assessments the second night. This resulted in 13 assessment points between 6 pm at time of admission and 4 pm at time of discharge 46 hours later. Smokers and non-smokers completed all of the assessments with the exception of the craving measure which was administered only to smokers as it specifically refers to cigarette use and cigarette cravings.

Nicotine withdrawal symptoms—All participants rated the extent of their experience on each of seven¹ items assessing subjective experience of tobacco withdrawal on a 0 (none) to 4 (severe) scale using the Minnesota Nicotine Withdrawal Scale [24]. As the purpose of including nonsmokers in this study was to obtain control assessments this scale was presented to participants as “Symptom Rating scale” and all participants (smokers and nonsmokers) were informed that “The following is a list of symptoms some people may experience. Please rate the severity of symptoms at the present time”. Analyses were conducted on individual items (range = 0 – 4) and for a summed overall “withdrawal discomfort score” with a range of 0 to 28 [26].

Nicotine craving—Smokers completed the Shiffman-Jarvik Questionnaire. This is a seven-item subscale of the Shiffman-Jarvik Withdrawal Questionnaire, which was developed through factor analyses of ex-smokers symptom reports and has been reliably used to assess changes in craving during nicotine withdrawal [25].

Mood symptoms—All participants were assessed using the Profile of Mood States (POMS) [26]. The POMS is a self-report scale consisting of 72 adjectives that can be further classified into 8 primary domains of anxiety, depression, anger, vigor, fatigue, confusion, friendliness and elation. The POMS has been successfully used in adolescents to document changes in mood [27]. The anger, tension and confusion scales in particular have been shown to be sensitive to nicotine withdrawal [28]. The anxiety, depression, anger, vigor, fatigue, and confusion subscales were examined in the present analyses.

Dependence—Smokers completed the Fagerstrom Test for Nicotine Dependence (FTND), which consists of six items, and provides a measure of an individual's nicotine dependence which has been closely related to biochemical indices of smoking in adolescent smokers [10].

Statistical Analyses

Withdrawal symptom variables were analyzed using repeated measures ANOVA's with smoking status (smoker, nonsmoker) as between subjects factors and time of assessment as a within subjects factor. The interaction of smoking status and time is indicative of the presence of abstinence related effects, with smokers expected to experience changes in negative mood symptoms and typical withdrawal symptoms beyond those observed in the control group. These analyses included gender as a covariate. As only smokers completed the Shiffman-Jarvik Craving measure, the repeated measures ANOVA was run with time of assessment as the within

¹As we asked participants to rate symptoms they were experiencing in the moment, we did not ask them to repeatedly rate insomnia/sleep problems which are typically part of the scale.

subjects factor. Again, gender was included as a covariate. Further correlational analyses were conducted to explore the associations between peak withdrawal symptoms and measurements of nicotine dependence, including the FTND, CO and cotinine levels at admission, and self reports of amount of daily smoking.

Results

Demographics and baseline tobacco use

Table 1 presents descriptive statistics for the sample, categorized by smokers and non-smokers. Smokers were older than nonsmokers but male and female smokers were similar in age. Smokers also reported greater number of total drinks consumed and greater rates of total marijuana use in the past 30 days as compared with nonsmokers. As seen in Table 1, male smokers reported smoking more cigarettes daily, using more marijuana, had higher tobacco dependence (FTND) scores, and higher admission CO levels when compared with female smokers, but were not significantly different from female smokers in number of years of daily smoking or urine cotinine levels at admission.

Nicotine Withdrawal Scale

The interaction between time and smoking status for reports of cravings ($F(12,948)=3.49, p<.01$), reflected a peak at 3.5 hours post abstinence ($M=2.57, SD=1.28$) and a subsequent slight decline over time in cravings for smokers with lowest reports at 29 hours post abstinence ($M=1.73, SD=1.46$; *paired t-test between peak and lowest point* $t(47)=3.25, p=.002$) and lower cravings at the end of the 48 hours compared to the first time point (*paired t-test* $t(47)=2.16, p<.05$). Nonsmokers continuously reported cravings to be absent. There were no other differences between smokers and non smokers for course of symptoms over time. The course for each individual symptom and overall withdrawal ratings by smokers and nonsmokers is presented in Table 2 and Figure 1.

There were significant overall group differences between smokers and nonsmokers on total withdrawal ($F(1,74)=36.09, p<.001$), reports of cravings ($F(1,79)=102.63, p<.01$), ratings of difficulty concentrating ($F(1,79)=6.232, p<.05$), and irritability ($F(1,76)=4.14, p<.05$), with smokers reporting greater levels of all symptoms.

Profile of Mood States

Smokers and nonsmokers differed in their ratings of anger over time ($F(12,780)=1.917, p<.05$); smokers were observed to experience slight increases in anger over the 48 hour period, while nonsmokers reported consistent and low levels of anger throughout. These results are presented in Table 2 and Figure 3. In addition to changes observed over time, significant group differences were noted between smokers and nonsmokers on ratings of vigor ($F(1,69)=5.69, p<.05$) and confusion ($F(1,49)=5.32, p<.05$). Smokers reported lower levels overall of vigor ($M=5.22, SD=5.59$) and higher levels overall of confusion ($M=5.05, SD=2.92$) compared with nonsmokers' ratings of vigor ($M=8.38, SD=5.42$) and confusion ($M=3.55, SD=1.17$).

Shiffman-Jarvik Craving Scale

Analyses of changes in tobacco craving over the 48 hour abstinence period in smokers revealed a significant change over time ($F(12,504)=2.896, p<0.001$), with no effect for gender. Craving scores peaked at 3.5 hours of abstinence and had decreased slightly but significantly by the end of the 48 hours (*paired t-test* $t(47)=3.24, p<.001$) – see Figure 2.

Correlations with Nicotine Dependence Measures

Exploratory analyses assessed the relationship between peak withdrawal symptoms, reports of withdrawal and cravings at 1.5 hours (the initial assessment point) following abstinence, with measures of dependence (FTND) and tobacco use. Pearson correlations indicated no relationship between peak withdrawal symptoms and dependence scores, CO levels, cotinine levels, or amount of daily smoking. Reports of withdrawal symptoms and cravings at the first time point following admission (ie. 1.5 hours following imposed abstinence) were positively associated with reported number of daily cigarettes. These results are presented in Table 3.

Discussion

This study aimed to document the presence of tobacco abstinence effects beyond the existence of typical adolescent lability. The results suggest that adolescent smokers, in comparison with nonsmokers, experience few symptoms characteristic of tobacco-withdrawal while abstinent. Notably, changes in craving and anger appear to be the only predominant changes associated with tobacco abstinence.

Cravings and anger may be of particular relevance in understanding tobacco dependence in adolescents. Extent of cravings may play a role in failure to sustain tobacco abstinence in adolescent [11] and is considered to be an inherent aspect of adult smoking behavior [30]. Overall ratings of cravings across the 48 hours were of moderate severity and similar to that reported by adult populations [19]. Smokers' cravings peaked at 3.5 hours following admission and followed a steady and moderate decline (Cohen's d calculated on change between peak cravings and final cravings = .67). In fact, almost 50% of the smokers reported their peak level of cravings at that time point, and despite residing in an environment lacking in such cues as smoking friends or access to cigarettes, adolescents' cravings never totally subsided. Anger has been found to be not only a significant withdrawal symptom in adults [4], but also a potential precedent for smoking behavior [31]. Similarly, externalized negative affect has been found to be associated with increased risk for smoking among adolescents [32], and our findings suggest that smoking adolescents experience an increase in angry feelings in response to tobacco abstinence. Although, laboratory examinations of adult smokers have also observed generally mild symptoms overall in response to abstinence [24], the absence of emergence of significant negative mood symptoms, and the overall minimal discomfort (with the exception of reports of cravings) related to tobacco abstinence that we [33] and others [7] have observed in adolescent smokers are generally in contrast with literature describing adult abstinence effects [4]. Perhaps more reflective of the preclinical literature, which has found reduced nicotine withdrawal in adolescent compared with adult animals [16], our findings suggest that basic physiologically induced nicotine withdrawal and mood changes may not be a highly influential force in smoking maintenance in adolescent smokers.

Heightened overall negative symptoms, including greater irritability, difficulty concentrating, lower levels of vigor, and higher levels of confusion were observed in smokers compared with nonsmoking counterparts. However, these symptoms appear to reflect overall trait differences or characteristics that may predispose some adolescents to smoke rather than a result of the establishment of abstinence. These symptoms were positively correlated with the amount of reported daily smoking but not with biological measures of use, possibly suggesting that perception of amount of use could influence a teenager's experience of withdrawal. Regardless, these heightened symptoms in adolescent smokers as compared with nonsmoking controls may have relevance for treatment planning and implementation as mood states that could impact cessation. Furthermore, these are symptoms which may be misinterpreted by adolescents and others interacting with the adolescents during times of attempted cessation, as indicative of withdrawal. Discussing evidence that these symptoms are potentially present in similar

intensity prior to abstinence could be a useful cognitive tool in restructuring attributions made during a quit attempt.

Smokers' reported symptoms of withdrawal and cravings were not related to biological measures of use or self-report ratings of dependence and were only modestly related to the number of daily cigarettes smoked. Although dependence was associated with biological measures of extent of smoking and self reports of amount of smoking, more dependent smokers were not necessarily reporting higher levels of cravings or withdrawal. These results also support preclinical evidence of minimal nicotine withdrawal symptoms in adolescent animals [16], and raise questions regarding the significance of withdrawal to smoking maintenance in adolescents. Certainly the minimal withdrawal symptoms lessen the aversive nature of smoking thereby increasing the reward and reinforcement aspect of use. Smoking related cues have been shown to increase urges to smoke and withdrawal symptoms in adolescent smokers [34]. It is possible that the absence of tobacco and social cues in the hospital setting resulted in lower reported symptoms than these smokers experience in their life settings – a point that has been made in the adult literature [35,36]. If this were the case, it would appear to indicate that adolescent smoking is heavily directed by contextual cues and less directed by purely physiological or emotional reactivity to abstinence. Another possibility is that adolescent smokers, accustomed to regular periods during which their smoking is externally restricted, have developed coping strategies to effectively minimize withdrawal symptoms for some period of time. In fact, the later emergence of angry feelings experienced by smokers may have been due to experiencing cravings while also confined and unable to smoke, receive any social support, or distraction from their cravings; basically a symptom of diminishing coping resources. Despite the possibility that smokers may be able to minimize withdrawal symptoms for some amount of time, the observed differences in mood states, particularly difficulty concentrating and irritability, may contribute to less optimal functioning in school. Moreover, the consistent and moderately severe cravings may result in behaviors with serious consequences for the adolescent, such as smoking in school or missing class to smoke. Additional research is required to assess the relative contributions of nicotine withdrawal and cravings to daily school performance and functioning.

A significant strength of this study is the comparison with non-smoking controls, as withdrawal effects may be misidentified as either expected adolescent lability [9], or symptoms of more serious affective disturbance [37]. Additionally, the experimental inpatient setting reduced potential for the relative influence of tobacco related cues, increasing the strength of the observed findings as specifically related to tobacco abstinence. The prospective nature of the study allows for greater confidence in the accurate reporting of symptoms, in contrast with previous retrospective reports which have been found to be unreliable, particularly for adult male smokers [38].

A limitation to this study is the lack of control over possible variation of time of last cigarette prior to admission, and as such these results may underestimate the severity and/or time of initiation of withdrawal effects. Smoking participants were instructed to smoke normally before attending the session which began in the early evening, but to not smoke after 5pm. All sessions were conducted on a weekend or holiday so that potential restrictions on smoking would be minimized and participants would be more likely to be smoking freely. The initial assessment of symptoms occurred approximately 1.5 hours after the establishment of abstinence as participants were asked to not smoke after 5 pm and procedural necessities related to admission (such as admission paperwork and facility orientation) occurred at 6pm. This may account for elevated symptoms at the first rating point, and subsequently the course of symptoms described here does not include an increase from a baseline collected immediately following smoking. However, CO levels at time of admission were indicative of recent smoking ($M=15.97$, $SD=8.4$) and the average peak of cravings was at the 3.5 hour point following

abstinence suggesting that most participants had smoked at a time close to admission and the establishment of abstinence. Nevertheless, this delay in assessment limits the interpretation of changes in reports of symptoms. A second limitation is the considerable heterogeneity of the number of cigarettes smoked on a daily basis. This range, while associated with dependence and use measures, did not appear to be related to peak withdrawal but was moderately associated with reports of withdrawal and cravings at the first time point. Future investigations should consider examination of symptoms reported by heavier and lighter smokers, with clear distinctions between categories. Further, while we have described the course of symptoms over a 48 hour period, given other research suggesting that adult symptoms may increase and decrease over longer periods of time [2], and the findings themselves that cravings did not decline considerably, a lengthier period of observation may better describe the course of symptoms following abstinence. Additionally, as mentioned earlier, this study was conducted in an inpatient setting which was devoid of environmental cues related to cigarette smoking; it is possible that greater withdrawal effects would have been observed in a more naturalistic setting as a result of tobacco related cues [35,36] in the environment. Similarly, adolescent participants who were smokers were not seeking treatment for their smoking and were not trying to attain long term abstinence from cigarettes. Withdrawal effects may be different for adolescents who are attempting to quit smoking more permanently. Finally, due to institutional concerns regarding the provision of tobacco products to minor participants, we were not able to include an inpatient *smoking* comparison group, which would have enabled clearer distinctions between trait and state differences observed between the smokers and nonsmokers to be attributed to abstinence effects.

In summary, this paper presents a preliminary prospective examination of tobacco withdrawal during an acute abstinence period in adolescent smokers. Only differences in reports of cravings and angry mood over time were noted as abstinent effects experienced by smokers. Smokers differed from nonsmokers on overall mood states during the inpatient session, including reporting greater irritability, difficulty concentrating, confusion, and less vigor, but these did not change over time during the abstinence period. Although symptoms and cravings were positively associated with amount of daily smoking, they were not associated with reports of dependence or biological measures of extent of use. The notable absence of emergence of withdrawal symptoms possibly indicates only minimal discomfort associated with the establishment of abstinence from tobacco smoking. However, the presence of heightened negative mood states in adolescent smokers compared with nonsmokers may still have implications for treatment development and refinement.

Acknowledgements

Preparation of this manuscript was supported by National Institute of Child Health and Human Development Grant, R01HD31688 to S. Krishnan-Sarin.

References

1. Centers for Disease Control and Prevention. Tobacco Use Among Adults—United States, 2005. Morbidity and Mortality Weekly Report [serial online] 2006;55:1145–1148.
2. Piasecki TM, Fiore MC, Baker TB. Profiles in discouragement: Two studies of variability in the time course of smoking withdrawal symptoms. *J of Abnorm Psychol* 1998;107:238–251. [PubMed: 9604553]
3. Piasecki TM, Niaura R, Shadel WG, Abrams DB, Goldstein MG, Fiore MC, et al. Smoking withdrawal dynamics in unaided quitters. *J Abnorm Psychol* 2000;109:74–86. [PubMed: 10740938]
4. Hughes JR. Effects of abstinence from tobacco: Etiology, animal models, epidemiology, and significance: A subjective review. *Nicotine Tob Res* 2007;9:329–339. [PubMed: 17365765]
5. McNeill AD, West RJ, Jarvis M, Jackson P, Bryant A. Cigarette withdrawal symptoms in adolescent smokers. *Psychopharmacology* 1986;90:533–536. [PubMed: 3101108]

6. Rojas NL, Killen JD, Haydel KF, Robinson TN. Nicotine dependence among adolescent smokers. *Arch Pediatr Adolesc Med* 1998;152:151–156. [PubMed: 9491041]
7. Killen JD, Ammerman S, Rojas N, Varady J, Haydel F, Robinson TN. Do adolescent smokers experience withdrawal effects when deprived of nicotine? *Exp Clin Psychopharmacol* 2001;9:176–182. [PubMed: 11518093]
8. Riedel BW, Robinson LA, Klesges RC, McLain-Allen B. Ethnic differences in smoking withdrawal effects among adolescents. *Addict Behav* 2003;28:129–140. [PubMed: 12507532]
9. Prokhorov AV, Hudman KS, Cinciripini PM, Marani S. “Withdrawal symptoms” in adolescents: A comparison of former smokers and never smokers. *Nicotine Tob Res* 2005;7:909–913. [PubMed: 16298726]
10. Prokhorov AV, de Moor C, Pallonen UE, Hudmon KS, Koehly L, Hu S. Validation of the modified Fagerström Tolerance Questionnaire with salivary cotinine in adolescents. *Addict Behav* 2000;25:429–433. [PubMed: 10890296]
11. Bagot KS, Heishman SJ, Moolchan ET. Tobacco craving predicts lapse to smoking among adolescent smokers in cessation treatment. *Nicotine Tob Res* 2007;9:647–652. [PubMed: 17558821]
12. Hurt RD, Croghan GA, Beede SD, Wolter TD, Croghan IT, Patten CA. Nicotine patch therapy in 101 adolescent smokers. *Arch Pediatr Adolesc Med* 2000;154:31–36. [PubMed: 10632247]
13. Moolchan ET, Robinson ML, Ernst M, Cadet JL, Pickworth WB, Heishman SJ, Schroeder JR. Safety and efficacy of the nicotine patch and gum for the treatment of adolescent tobacco addiction. *Pediatrics* 2005;115:e407–e414. [PubMed: 15805342]
14. Hanson K, Allen S, Jensen S, Hatsukami D. Treatment of adolescent smokers with the nicotine patch. *Nicotine Tob Res* 2003;5:515–526. [PubMed: 12959789]
15. Slotkin TA. Nicotine and the adolescent brain: Insights from an animal model. *Neurotoxicol Teratol* 2002;24:369–384. [PubMed: 12009492]
16. O'Dell LE, Bruijnzeel AW, Ghosland S, Markou A, Koob GF. Nicotine withdrawal in adolescent and adult rats. *Ann N Y Acad Sci* 2004;1021:167–174. [PubMed: 15251887]
17. MMWR. Youth Tobacco Surveillance – United States, 2000. *Morbidity and Mortality Weekly Report* 2001;50:1–84. [PubMed: 11215787]
18. Snyder FR, Davis FC, Henningfield JE. The tobacco withdrawal syndrome: Performance decrements assessed on a computerized test battery. *Drug Alcohol Depend* 1989;23:259–266. [PubMed: 2752917]
19. Hatsukami DK, Hughes JR, Pickens RW, Sviki D. Tobacco withdrawal symptoms: An experimental analysis. *Psychopharmacology* 1984;84:231–236. [PubMed: 6438682]
20. Cummings KM, Giovino G, Jaen CR, Emrich LJ. Reports of smoking withdrawal symptoms over a 21 day period of abstinence. *Addict Behav* 1985;10:373–381. [PubMed: 4091070]
21. Kenford SL, Smith SS, Wetter DW, Jorenby DE, Fiore MC, Baker TB. Predicting relapse back to smoking: Contrasting affective and physical models of dependence. *J Consul Clin Psychol* 2002;70:216–227.
22. West RJ, Hajek P, Belcher M. Severity of withdrawal symptoms as a predictor of outcome of an attempt to quit smoking. *Psychol Med* 1989;19:981–985. [PubMed: 2594893]
23. Carpenter MJ, Upadhyaya HP, LaRowe SD, Saladin ME, Brady KT. Menstrual cycle phase effects on nicotine withdrawal and cigarette craving: a review. *Nicotine Tob Res* 2006;8:627–638. [PubMed: 17008190]
24. Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry* 1986;43:289–294. [PubMed: 3954551]
25. Shiffman S, West RJ, Gilbert DG. Recommendation for the assessment of tobacco craving and withdrawal in smoking cessation trials. *Nicotine and Tobacco Research* 2004;6:599–614. [PubMed: 15370156]
26. McNair, DM.; Lorr, M.; Droppleman, LF. *Edits Manual: Profile of Mood States*. San Diego: Educational and Industrial Testing Service; 1981.
27. Burnett K, Kleiman ME. Psychological characteristics of adolescent steroid users. *Adolescence* 1994;29:81–89. [PubMed: 8036984]

28. Hughes JR, Hatsukami DK, Pickens RW, Svikis DS. Consistency of the tobacco withdrawal syndrome. *Addict Behav* 1984;9:409–412. [PubMed: 6532150]
29. Gilbert DG, McClernon FJ, Rabinovich NE, Plath LC, Jensen RA, Meliska CJ. Effects of smoking abstinence on mood and craving in men: influences of negative-affect-related personality traits, habitual nicotine intake and repeated measurements. *Pers Individ Differ* 1998;25:399–423.
30. Piasecki TM. Relapse to smoking. *Clinical Psychology Review* 2006;26:196–215. [PubMed: 16352382]
31. Delfino RJ, Jamner LD, Whalen CK. Temporal analysis of the relationship of smoking behavior and urges to mood states in men versus women. *Nicotine Tob Res* 2001;3:235–248. [PubMed: 11506767]
32. Whalen CK, Jamner LD, Henker B, Delfino RJ. Smoking and moods in adolescents with depressive and aggressive dispositions: Evidence from surveys and electronic diaries. *Health Psychology* 2001;20:99–111. [PubMed: 11315734]
33. Smith AE, McFetridge A, Cavallo D, Liss T, Krishnan-Sarin S. Preliminary examination of tobacco withdrawal in adolescent smokers during smoking cessation treatment. *Nicotine Tob Research*. (in press)
34. Upadhyaya HP, Drobles DJ, Thomas SE. Reactivity to smoking cues in adolescent cigarette smokers. *Addict Behav* 2004;29:849–856. [PubMed: 15219329]
35. Heil SH, Tidey JW, Holmes HW, Badger GJ, Higgins ST. A contingent payment model of smoking cessation: Effects on abstinence and withdrawal. *Nicotine Tob Research* 2003;5:205–213.
36. Pickworth WB, Fant RV, Butschky MF, Henningfield JE. Effects of transdermal nicotine delivery on measures of acute nicotine withdrawal. *J Pharmacol Exper Ther* 1996;279:450–456. [PubMed: 8930145]
37. Strong DR, Kahler CW, Ramsey SE, Abrantes A, Brown RA. Nicotine withdrawal among adolescents with acute psychopathology: An item response analysis. *Nicotine Tob Res* 2004;6:547–557. [PubMed: 15203788]
38. Pomerleau CS, Tate JC, Lumley MA, Pomerleau OF. Gender differences in prospectively versus retrospectively assessed smoking withdrawal symptoms. *J Subst Abuse* 1994;6:433–440. [PubMed: 7780301]
39. DiFranza JR, Savageau JA, Fletcher K, Ockene JK, Rigotti NA, McNeill AD, Coleman M, Wood C. The development of symptoms of tobacco dependence in youths: 30-month follow-up data from the DANDY study. *Tobacco Control* 2002;11:228–235. [PubMed: 12198274]

Nicotine Withdrawal Symptoms in Adolescents

Figure 1.
Mean standard errors illustrating withdrawal symptoms between smokers and nonsmokers.

Figure 2.
Mean craving symptoms in adolescent smokers across 46 hour abstinent period.

Figure 3.
Mean standard errors illustrating POMS between smokers and nonsmokers.

Table 1

Demographics

Variable		Smokers N (%) or M (SD)	Non-Smokers N (%) or M (SD)	F
Female		27 (49%)	27 (57%)	
Ethnicity				
	Caucasian	38 (69%)	35 (74%)	
	African American	9 (16%)	7 (15%)	
	Hispanic	6 (11%)	5 (11%)	
	Asian	1 (2%)	0	
	Other/Multiracial	1 (2%)	0	
Age		16.4 (1.25)	15.5 (1.31)	10.53*
Alcohol use: # of drinks in last 30 days		4.81(10.80)	0.85 (1.77)	5.13*
Marijuana use: # of joints in last 30 days		1.97 (3.66)	0.18 (0.89)	8.63*
Variable		Male Smokers M (SD)	Female Smokers M (SD)	
FTND at Baseline		4.61 (2.17)	3.41 (2.06)	4.42*
Number of Daily Cigarettes		15.38 (8.45)	10.52 (5.23)	6.09*
Number of Years Daily Smoking		2.93 (2.26)	2.11 (1.34)	2.64
Cotinine at Inpatient Admission		1135.96 (721.31)	1081.58 (951.23)	.057
CO at Inpatient Admission		15.67 (9.02)	10.29 (6.95)	6.01*
Alcohol use: # of drinks in last 30 days		6.27 (14.02)	3.54 (6.24)	.831
Marijuana use: # of joints in last 30 days		3.23 (4.78)	0.65 (1.06)	7.19*

*
p <.05

Table 2
Statistical comparisons between smokers and non-smokers for Nicotine Withdrawal and POMS scales.

	Group		Time		Group × Time		p
	df	F	p	df	F	df	
Nicotine Withdrawal Scale							
Total	1, 75	34.89	<.001	12, 900	1.56	12, 900	.31
Craving	1, 80	103.72	<.001	12, 960	1.64	12, 960	.08
Irritability	1, 77	4.08	.05	12, 924	1.92	12, 924	.03
Difficulty Concentrating	1, 80	8.33	<.01	12, 960	2.54	12, 960	.01
Depressed Mood	1, 80	.151	.69	12, 960	.655	12, 960	.79
Restlessness	1, 78	.385	.54	12, 936	1.93	12, 936	.03
Excessive Hunger	1, 80	1.061	.31	12, 960	5.49	12, 960	<.001
POMS							
Anger	1, 66	2.97	.09	12, 792	1.69	12, 792	.07
Depression	1, 69	3.25	.08	12, 828	1.07	12, 828	.39
Vigor	1, 67	5.56	.02	12, 804	3.34	12, 804	<.001
Confusion	1, 50	5.44	.03	12, 600	.83	12, 600	.62
Tension	1, 69	2.90	.09	12, 828	1.54	12, 828	.10
Fatigue	1, 67	1.33	.25	12, 804	3.15	12, 804	<.001
							.03

Table 3
Correlations between withdrawal symptoms, cravings, and dependence and use measures for smokers.

	Withdrawal at 1.5 hrs	Craving at 1.5 hrs	FTND	# daily cigarettes	Co Level at 1.5hrs	Cotinine at 1.5hrs
Peak Withdrawal rating ^a	.528**					
Withdrawal at 1.5 hrs ^a		.460**	.179	.202	.152	.020
Craving at 1.5 hrs ^b			.102	.313*	.099	.145
FTND		.412		.353*	.197	-.008
# daily cigarettes			.145	.652**	.323*	.371**
CO Level at 1.5 hrs					.320*	.318*
Cotinine at 1.5 hrs						.531**

* Note: p<.05

** p<.01

^aTotal withdrawal score includes single item rating of craving

^bCravings measured by Shiffman-Jarvik scale.