Journal of Adolescent Health 40 (2007) 54–60

JOURNAL OF
ADOLESCENT
HEALTH

Original article

Smoking Topography in Response to Denicotinized and High-Yield Nicotine Cigarettes in Adolescent Smokers

Jon D. Kassel, Ph.D.[a,*], Justin E. Greenstein, M.A.[a], Daniel P. Evatt, M.A.[a], Margaret C. Wardle, M.A.[a], Marisa C. Yates, M.A.[a], Jennifer C. Veilleux, B.A.[a], and Thomas Eissenberg, Ph.D.[b]

[a]*Department of Psychology, University of Illinois at Chicago, Chicago, Illinois*
[b]*Department of Psychology, Virginia Commonwealth University, Richmond, Virginia*

Manuscript received April 6, 2006; manuscript accepted August 14, 2006

Abstract

Purpose: The objective of this study was to explore the smoking topography of adolescent smokers. It is well established that the majority of adult nicotine-dependent smokers began smoking as adolescents. Whereas recent advances have been made with respect to identification of factors that predispose to nicotine dependence, very little is known about the actual smoking behavior (e.g., topography) of adolescent smokers, or its relationship to nicotine dependence. Correspondingly, the extent to which adolescent smokers smoke to obtain nicotine is also unknown.

Methods: In the present study, we assessed several topographical indices of smoking (e.g., puff volume, puff number) in a sample of 35 light, adolescent smokers. Moreover, we examined whether smoking behavior is different in response to smoking a denicotinized relative to a high-yield, nicotine cigarette.

Results: All participants evidenced a significant increase in expired air carbon monoxide after the smoking of a cigarette. Results of independent-sample *t*-tests revealed that adolescents who smoked a low-yield nicotine cigarette took significantly more puffs per cigarette than did those who smoked a high-yield cigarette.

Conclusions: These findings suggest that adolescent smokers do titrate their nicotine intake in response to smoking denicotinized cigarettes, but do so not by taking larger puffs or smoking more quickly, but by simply taking more puffs per cigarette. Implications of the findings and future directions for this type of research with adolescents are discussed.

Keywords: Adolescence; Smoking; Dependence; Topography

The pathways leading to smoking initiation, maintenance, and nicotine dependence are, no doubt, complex, comprised of numerous psychological, biological, and contextual influences [1]. It has become increasingly clear, however, that the vast majority of adult smokers, most of whom meet criteria for nicotine dependence, began smoking as adolescents. Indeed, whereas small comfort can be derived from the observation that adolescent smoking in the United States appears to have peaked in the mid-1990s [2], more recent data indicate that the rate of decline in adolescents' use of cigarettes has been decelerating over the past several years [3]. In fact, among eighth graders, smoking rates have plateaued, a potentially bad omen for smoking trends among the current generation of young adults.

In response to the multiple challenges posed by adolescent smoking, dubbed a "pediatric disease" by Kessler and colleagues [4], a burgeoning research movement has attempted to better understand the determinants, correlates, and consequences of smoking behavior in young people

*Address correspondence to: Dr. Jon D. Kassel, Department of Psychology, University of Illinois at Chicago, 1007 W. Harrison St., Behavioral Sciences Building, Room 1009, Chicago, IL, 60607.
E-mail address: jkassel@uic.edu

1054-139X/07/$ – see front matter
doi:10.1016/j.jadohealth.2006.08.006

(see reviews in [1,5–8]). As a result, significant progress has been made on numerous fronts. Yet, one question that remains unanswered is precisely how and/or when nicotine dependence emerges among young smokers. Whereas many have assumed that the majority of adolescent smokers are, or will inevitably become, nicotine dependent, the fact is that we know very little about the actual smoking behavior of adolescents and the extent to which such behavior is related to the emergence of nicotine dependence in adolescence [6,9]. There is strong reason to believe, however, that adolescent smoking differs in several important respects from smoking behavior most often seen in adults. Relative to adults, who frequently manifest highly entrenched smoking patterns, the smoking of young people tends to be far more variable with respect to rate, frequency, and topography [8]. To be clear, however, regardless of one's age, to become dependent on tobacco, the smoker must be repeatedly exposed to active doses of nicotine.

Whereas a fairly large literature addresses the smoking topography of daily—often nicotine-dependent—smokers, a host of ethical, legal, and pragmatic obstacles renders investigation of smoking topography in adolescent smokers a most difficult undertaking [10]. Only within the past several years have studies examining the smoking topography of adolescent smokers begun to emerge [11–16]. Taken together, these investigations suggest that young smokers appear to take smaller and more puffs than adult smokers. At the same time, there is reason to believe that adolescent smokers *do* self-administer physiologically active doses of nicotine [12,15], and that some topographical indices (puff volume) are actually predictive of smoking cessation outcome [13]. As such, these observations are critically important as they begin to shed light on the manner in which adolescents actually smoke cigarettes, and the potential relationship between these behaviors and the emergence of nicotine dependence.

The objective of the present study was to further explore the smoking topography of adolescent smokers. More specifically, we were interested in determining whether young smokers exhibit differential topographical responses when smoking denicotinized, as compared with high-yield nicotine cigarettes. Although we use a between-subjects design, in which each participant is exposed to only one nicotine condition, such an approach can still provide indirect, yet potentially important, evidence for nicotine titration [17,18]. Titration could be discernible in a number of ways, including decreased inter-puff intervals, increased puff volume, and/or increased number of puffs per cigarette. Indeed, such topographical indices have a rich history within the realm of studying adult nicotine dependence (see [17]) and can, in part, serve as a read-out of nicotine seeking. Put simply, although inconsistencies in the literature are to be found, there is ample evidence suggesting that most smokers—at least heavier, regular smokers—partially compensate in response to smoking a cigarette of a different smoke yield (see Scherer, 1999 for an extensive review [17]). Moreover, such compensatory smoking behavior is likely driven by attempts to regulate nicotine intake (e.g., up-regulation in response to a lower nicotine yield cigarette [19]). Again, however, the extent to which adolescent smoking behavior is motivated by attempts to self-regulate nicotine intake is as yet unknown.

Methods

Participants

This study was approved by the Institutional Review Board at the University of Illinois at Chicago. Given that most of the study participants were under 18 years of age, such individuals also provided signed parental consent forms, in addition to the participant's own signed assent. (Participants who were 18 years old needed to provide only their own signed consent form.) Because of the potentially sensitive nature of the study (i.e., administration of nicotine via cigarettes to minors), great care was taken in ensuring that all participants and their parents understood the objectives of the study and the requests being made of the participants. To be clear, no participant was mandated to smoke as a part of their study participation. Rather, adolescents were given the opportunity to smoke "as much or as little" of the cigarette as they so desired.

Thirty-five adolescent smokers were recruited from the Chicago greater metropolitan area as part of their participation in a larger IRB-approved study assessing the acute effects of nicotine on emotional response in adolescent smokers (Kassel JD et al, unpublished manuscript, University of Illinois at Chicago, Chicago, IL, 2006). Participants received either monetary compensation or, if they were university students, course credit for their participation in this one visit, 90-minute study. Participants were between 15 and 18 years of age and were required to have smoked for at least 4 weeks, and smoke a minimum of one cigarette a week, but no more than five cigarettes a day on average. (Although establishing a maximum cut-off of five cigarettes per day ultimately represents an arbitrary decision, there is reason to believe that smoking at this level or less is frequently indicative of nondependent smoking. Moreover, the same criteria have been used to define tobacco chippers—individuals who, although though they smoke with some degree of regularity, do not appear to progress to nicotine dependence [20]). Thus, our intention was to assess nicotine-seeking in a relatively young, novice group of smokers. Participants were then randomly assigned to one of two experimental groups: a high-yield nicotine (HY) or denicotinized (DN) cigarette condition.

Cigarettes

To ensure standardization in nicotine and tar yields within the DN and HY nicotine conditions, research cigarettes (Ultratech/Lifetech, Inc., Lafayette Hill, PA) containing .06 mg nicotine/17.9 mg tar and 1.14 mg nicotine/15.9 mg tar nicotine levels were used, respectively. The DN cigarettes were designed to have the appearance, draw and taste of standard cigarettes but to contain and deliver virtually no nicotine (<.06 mg), while at the same time delivering tar and carbon monoxide (CO). (For a detailed description of the pharmacokinetic and pharmacodynamic characteristics of both the DN and HY cigarettes, the reader is referred to Pickworth et al, 1999 [21].) Importantly, these same research cigarettes have been used in numerous experimental studies of smoking behavior (e.g., [22–24]), thereby establishing their overall utility, particularly with respect to the effectiveness of the placebo (DN) cigarette. In the present study, all participants were led to believe that they would be receiving and smoking a "regular" nicotine-yield cigarette.

Measures

Smoking topography. Smoking topography was assessed using the Clinical Research Support System (CreSS; Plowshare Technologies, Baltimore, MD). Indices included number of puffs per cigarette, puff volume, puff duration, interpuff interval, and maximum flow rate (velocity) per puff. Previous research supports the reliability and validity of this assessment method of smoking topography in older, dependent smokers [25], as well as in adolescents [12].

Nicotine dependence. Nicotine dependence was assessed using a modified version of The Fagerström Tolerance Questionnaire (mFTQ) [26], specifically designed to measure dependence in adolescent smokers [27]. Previous findings indicate that this measure is valid and applicable to adolescent smokers [27].

Craving. Cigarette craving—construed as an integral component of the tobacco withdrawal syndrome—was assessed at the study's outset with the craving subscale of the Shiffman-Jarvik Withdrawal Questionnaire [28]. This six-item measure has been widely used and proven valid and reliable (alpha coefficient of .86 in the present sample).

Cigarette ratings. At the study's end, all participants completed a brief questionnaire querying them about the "harshness," "strength," and "pleasantness" of the research cigarette they smoked. Response options ranged from 1 (not at all) to 4 (very much so) [29].

Other smoking behavior. With respect to the actual day of testing, all participants were asked both how recently they had smoked and how many cigarettes they had smoked before their participation in the study.

Procedure

Upon their arrival at the laboratory, all participants completed either informed consent or assent, and the details of the procedure were reiterated verbally. All sessions were scheduled between 1:00 PM and 4:00 PM. Participants were then given the opportunity to smoke a research cigarette provided by the experimenter, and were blind to the nicotine content of the cigarette. After being instructed to smoke, in an ad libitum manner, as much or as little of the cigarette as they wanted, participants lit the cigarette and then inserted it into the CreSS mouthpiece. (To enhance the ecological [external] validity of the study, we believed it important to not mandate that participants smoke their entire cigarette. Indeed, given the nature of this sample—young, relatively light smokers—it was imperative that they be allowed to smoke in an ad libitum style, for ethical reasons as well as to best capture smoking topography in as unrestrained a manner as possible.) At the study's end, participants were debriefed, compensated, and given referrals to smoking cessation programs. All participants provided expired air breath samples—both immediately before and after smoking the research cigarette—that were assessed for alveolar carbon monoxide (CO) levels by using a Vitalograph EC 50 carbon monoxide monitor.

Results

Sample characteristics

Participants were randomized into either the DN (n = 19) or HY (n = 16) experimental groups. (Using the G-power program [30] with which to conduct power analyses, we found that we had reasonable power [.63] to detect large effect sizes and only modest power [.30] to detect medium size between-group effects.) Sample characteristics can be found in Table 1. The sample was ethnically diverse, comprised of 43% Caucasians, 25% Asian/Pacific Islanders, 17% Hispanics, 6% African Americans, and 9% Others. Independent sample *t*-tests revealed that the two experimental groups were comparable in terms of: age, gender, ethnicity, proportion of community to student participants, amount smoked, years smoked, recency of smoking, number of cigarettes smoked on the study day, baseline craving, and levels of nicotine dependence. Whereas independent sample *t*-tests revealed that the groups also rated their respective research cigarettes comparably with respect to perceived harshness ($p > .10$) and strength ($p > .90$), the HY cigarettes were rated as significantly more pleasant (3.67 vs. 3.06) than the DN cigarettes, $p < .02$. Taken together, participants smoked an average of 20 cigarettes a week, and had started smoking just over 2 years ago. Their scores on the mFTQ were indicative of very low levels of nicotine dependence (M = 2.2, SD = 1.33). Thus, as intended, the study sample was comprised of young, relatively light smokers.

Importantly, correlational analyses revealed that neither time since last cigarette ($r = -.27$, $p > .10$) nor number of cigarettes smoked on the day before the experimental session ($r = .24$, $p > .10$) was significantly associated with

Table 1
Smoking and demographic characteristics of the sample

	Full sample (n = 35)	HY nicotine group (n = 16)	LY nicotine group (n = 19)	t(33)
Age (years)	17.5 (1.1)	17.5 (1.1)	17.5 (1.1)	−.071
Gender (# female)	18	8	10	—
mFTQ	2.2 (1.4)	2.2 (1.4)	2.1 (1.4)	.67
Baseline craving	25.26 (6.07)	25.75 (5.84)	24.84 (6.39)	.44
Time since last cig (hours)[a]	11.14 (18.72)	15.35 (25.90)	7.63 (8.86)	1.19
Cigs smoked today	1.68 (1.89)	1.93 (1.87)	1.48 (1.93)	.70
Days a week smoke	5.6 (1.7)	5.8 (1.6)	5.5 (1.8)	.53
Cigs a day smoke	3.6 (1.7)	3.4 (1.2)	3.8 (2.0)	−.65
Years smoked	2.3 (1.4)	2.7 (1.3)	2.0 (1.4)	1.57
Cig harshness	2.6 (1.0)	2.4 (1.1)	2.9 (.9)	1.67
Cig strength	2.6 (1.0)	2.6 (1.2)	2.6 (.7)	.02
Cig pleasantness	3.4 (.7)	3.7 (.6)	3.1 (.8)	−2.57*

HY = high yield; LY = low yield; mFTQ = modified Fagerstrom Tolerance Questionnaire; cig = cigarette. Numbers in parentheses are standard deviations.

* $p < .05$.

[a] Because of the highly skewed nature of this variable, all analyses were conducted using a logarithmic transformation. The data presented here, though, are based on raw scores.

baseline craving or with any of the smoking topography indices (all *p*s > .30).

Smoking topography measures

All smoking topography data were first processed through the software program, Puff Clean Up (Plowshare Technologies, Baltimore, MD), to remove any artifacts from raw data recorded from the CreSS unit. Initial zero-order correlational analyses revealed no significant associations between the topography measures and the measure of nicotine dependence, except for the following: Average puff volume was significantly correlated with nicotine dependence ($r = .35$, $p < .05$).

Next, we assessed pre- to postsmoking boosts in exhaled carbon monoxide across the two nicotine conditions by conducting a mixed model, repeated measures (pre- and postcigarette CO breath readings) analysis of variance. Results revealed a significant main effect for time, such that on average, CO increased by 8 ppm in response to smoking, $F(1,33) = 111.16$, $p < .001$. Whereas the interaction effect between time and nicotine condition was not significant, $F(1,33) = 2.36$, $p = .10$, a trend emerged such that those who smoked the DN cigarette showed higher CO boosts (M = 9.05) than did those in the HY condition (M = 6.75).

Independent sample *t*-tests were then conducted to determine if any differences in smoking topography emerged as a result of cigarette condition (HY vs. DN). As can be seen in Table 2, these analyses indicated that the DN smokers took significantly more puffs than the HY smokers, $t(33) = 3.02$, $p < .005$. Group differences (DN > HY) also emerged for interpuff interval total $t(33) = 3.76$, $p < .0001$, and flow total, $t(33) = -2.10$, $p < .05$. Because these latter

Table 2
Smoking topography indices

	Full sample (n = 35)	HY nicotine group (n = 16)	DN nicotine group (n = 19)	t(33)
Puff number	17.51 (8.7)	15.10 (6.3)	23.20 (8.9)	−3.02**
Average volume (mL)	43.07 (20.2)	45.42 (22.2)	40.10 (18.7)	.67
Average duration (s)	1.18 (.4)	1.12 (.4)	1.00 (.4)	.15
Average IPI (s)	23.54 (12.9)	24.23 (12.9)	23.00 (13.2)	.27
Average flow (mL/s)	55.23 (18.8)	57.24 (18.9)	53.40 (19.0)	.60
Total volume (mL)	862.92 (521.5)	713.05 (461.8)	988.80 (547.2)	−1.60
Total duration (s)	20.65 (10.6)	16.70 (9.7)	23.98 (11.5)	−2.00
Total IPI (s)	368.60 (113.7)	289.50 (90.6)	435.2 (130.5)	−3.76***
Total flow[a]	1117.33 (623.8)	877.53 (490.4)	1319.26 (744.2)	−2.03*

HY = high yield cigarette; DN = denicotinized cigarette; IPI = inter-puff interval; CO = expired air carbon monoxide. Numbers in parentheses are standard deviations.

* $p < .05$; ** $p < .005$; *** $p < .001$.

[a] Total flow is calculated by summing the flow (velocities) for each puff and, as such, is determined in great part by total puff number.

two measures are derived, in part, from puff number, the resulting group differences are likely attributable to the significant difference in puff number observed between the two nicotine conditions. Group differences in total puff volume and total duration approached significance, with *p* values equaling .10 and .052, respectively.

Last, we calculated a compensation index (CI; Thurau and von Hees, 1990, as cited in [17]), which determines, in relative units, the degree to which a smoker responds to a change in smoking (nicotine) yields with a change in some aspect of smoke uptake (e.g., number of puffs). This algorithm can be expressed as the following, whereby a CI of 0 is reflective of no compensation, a CI of 1 reflects complete compensation, and a CI falling between 0 and 1 indicates partial compensation:

$$\mathrm{CI} = 1 - \frac{\%\ \text{Change of uptake marker for A}}{\%\ \text{Change of cigarette smoke yield of A}}$$

where A is a tobacco smoke constituent (in the present case, nicotine). Hence, we used the CI algorithm to compare change across the two nicotine conditions (DN and HY) with respect to puff number and total puff volume.

As applied to the significant group difference found with puff number, the index was .63, indicative of partial compensation. Although as noted earlier, the difference in total puff volume between the two nicotine conditions was not statistically significant, the resultant CI index was .30, also reflecting partial compensation.

Discussion

As adolescent cigarette smoking remains a profound public health concern, research addressing the actual smoking behavior of adolescents is sorely needed. Assessment of smoking topography provides one such valuable tool through which the manner in which young smokers smoke their cigarettes can be determined. Hence, assessment of smoking topography in adolescent smokers represents an important step in characterizing differences in smoke exposure, and provides the opportunity to examine whether adolescents manifest differential smoking behavior in response to self-administration of a denicotinized cigarette.

Several interesting findings emerged from the present study. First, consistent with the findings of previous research (e.g., [11,12,14,15]), we found that adolescent smokers appear to self-administer physiologically active doses of nicotine. This deduction is supported by the significant boost in expired air CO (~8 ppm) seen in all study participants, regardless of whether they smoked the HY or DN nicotine cigarette. And, although the differences in CO boost between the two nicotine conditions were not significant, a marginal trend emerged, suggesting that those who smoked the DN cigarette may have taken in more CO, perhaps as a result of titrating their smoking. Clearly, more research will be needed to see if this is, indeed, a reliable or meaningful finding.

Second, and perhaps more importantly, indirect evidence of nicotine titration was seen in the number of puffs taken per cigarette; those in the DN nicotine condition took significantly more puffs per cigarette than did the HY smokers. Whereas compensatory smoking is more typically evidenced by increases in puff volume (which was not observed in this study), the finding of increased puffs per cigarette nonetheless represents a potentially important and novel manifestation of titration in young, light smokers. Indeed, as Benowitz [31] points out, "Of course, smokers are not limited in the number of puffs they may take from a cigarette . . . If smokers receive less tar and nicotine per puff from lower yield products, they can easily compensate by taking more puffs" (p. 18). Moreover, significant nicotine effects were also observed for total flow rate, or velocity of inhalation, and marginal nicotine effects were seen for total puff volume and duration. As noted earlier, although such findings are driven by the fact that the DN smokers took more puffs relative to HY smokers, they are nonetheless important, as they reflect (particularly total puff volume) increased smoke exposure by the DN group. Finally, findings derived from the compensation index—indicative of partial compensatory responses in total puff number and total puff volume—are both novel and intriguing in terms of better understanding adolescent smoking behavior.

The actual number of puffs per cigarette observed in the HY condition (15.1) was similar to that observed in other studies [11,12,15] of adolescent smokers, where number of puffs have typically ranged from 14 to 16. Of note, however, is that the sample of adolescent smokers in the present study smoked considerably less (in terms of days a week and cigarettes per day) relative to adolescent smokers assessed in previous investigations. Furthermore, the number of puffs per cigarette more typically seen in adult smokers ranges from 10 to 12. Thus, it appears that, relative to their adult counterparts, adolescent smokers take more puffs per cigarette and also tend to exhibit lower puff volumes. Again by way of comparison, the average puff volume observed in the current study (43 mL) is slightly higher than those reported in earlier investigations of adolescent smokers (e.g., 35–38 mL [11]; 34.5 mL [12]; 39 mL [14]). Indeed, somewhat surprisingly, the puff volumes detected in the present study of very light smokers approximates volumes typically observed in adult, dependent smokers [15,31]. Of course, cross-study comparisons of the kind described herein must be interpreted with great caution, as certain aspects of the study design and/or measurement techniques may have differentially affected puffing parameters across investigations.

Several limitations of the study need to be acknowledged. We used a between-subjects design, such that each participant was exposed to only one of the two cigarette conditions. Ideally, studies of nicotine compensation should use a repeated measures, within-subjects design [17], which ultimately affords greater statistical power and allows the participant to act as their own control. Nonetheless, it could be argued that the between-subjects approach taken in the current study provided a most conservative test of assessing compensatory-like behavior (i.e., titration) for these same reasons. Correspondingly, it is conceivable that some potentially significant effects (e.g., total puff volume, CO intake) went undetected due to inadequate statistical power. Also, participants were asked to smoke a research cigarette provided to them by the experimenter, in lieu of smoking their own typical brand. (In fact, anecdotal reports from many of the participants indicated they did not have a "usual" cigarette brand, as they often simply borrowed their cigarettes from others.) In concert with the artificiality of the laboratory environment, this approach may have weakened the ecological (external) validity of our findings. Moreover, given that we studied the smoking of a single cigarette, we cannot ultimately know how representative these findings are at the level of any given smoker, nor can the findings of this study speak to how smoking topography may vary across the course of a day when multiple cigarettes are smoked.

Finally, it is important to note that those in the HY condition rated their cigarettes as more pleasant relative to those who smoked the DN cigarettes. The extent, if any, to which this differential subjective preference affected puff parameters, is not known, although it is conceivable that those in the HY took fewer puffs simply because these cigarettes were more satisfying (a notion not too dissimilar from the very premise of compensatory smoking, i.e., titration). However, results from an analysis of covariance, in which we controlled for pleasantness ratings, still revealed a significant difference in puff number between the two nicotine conditions ($p = .006$), suggesting that such a difference cannot be attributable to perceived differences in pleasantness across the two nicotine conditions.

In summary, expanding our knowledge base of smoking behavior among adolescents is imperative to scientific and tobacco control research agendas. Because the majority of nicotine-dependent adult smokers began smoking as adolescents, it is clear that the factors governing smoking initiation and subsequent trajectories toward dependence need to be identified. The results of the present study add to this growing database, showing that nicotine titration does occur, even in relatively young and light adolescent smokers. Interestingly, and perhaps importantly, the nature of this compensatory behavior is somewhat unusual. In response to smoking a denicotinized cigarette, adolescents appeared to titrate not by puffing harder or more quickly, but rather by simply taking more puffs per cigarette. Future research is certainly needed to assess the reliability and validity of these findings. Finally, the extent to which nicotine compensation itself may be a marker of nicotine dependence (e.g., [32]) needs further empirical scrutiny. In the present study, we observed a significant (positive) correlation between puff volume and a measure of nicotine dependence (mFTQ). Acknowledging that laboratory studies with adolescent smokers present daunting challenges, more research of this nature is sorely needed to advance our understanding of smoking behavior in this most vulnerable age group.

Acknowledgments

This study was supported by the Ferno Award for Innovative Research from the Society for Research on Nicotine and Tobacco, and Pharmacia and Upjohn. Preparation of this article was also made possible, in part, by Grant 1PO1CA98262 from the National Cancer Institute, and by Grant 5RO1AA12240-04 from the National Institute on Alcohol Abuse and Alcoholism. Portions of this paper were presented at the 10th Annual Meeting of the Society for Research on Nicotine and Tobacco, February 18–21, 2004.

References

[1] Jamner LD, Whalen CK, Loughlin SE, et al. Tobacco use across the formative years: a road map to developmental vulnerabilities. Nicotine Tob Res 2003;5:S71–87.
[2] Johnston LD, O'Malley PM, Bach JG, Schulenberg JE. Monitoring the Future National Survey Results on Drug Use, 1975–2004, Volume I: Secondary School sStudents (NIH Publication No. 05-5727). Bethesda, MD: National Institute on Drug Abuse, 2005.
[3] Johnston LD, O'Malley PM, Bach JG, Schulenberg JE. Decline in teen smoking appears to be nearing its end. University of Michigan News and Information Services, Vol. 2005. Ann Arbor, MI; 2005. Available from: www.monitoringthefuture.org
[4] Kessler DA, Natanblut SL, Wilkenfeld JP, et al. Nicotine addition: a pediatric disease. J Pediatr 1997;130(4):518–24.
[5] Eissenberg T, Balster RL. Initial tobacco use episodes in children and adolescents: current knowledge, future directions. Drug Alcohol Depend 2000;59:S41–60 (suppl 1).
[6] Kassel JD. Are adolescent smokers addicted to nicotine? The suitability of the nicotine dependence construct as applied to adolescents. J Child Adolesc Subst Abuse 2000;9:27–49.
[7] Kassel JD, Stroud LR, Paronis CA. Smoking, stress, and negative affect: correlation, causation, and context across stages of smoking. Psychol Bull 2003;129:270–304.
[8] Mermelstein R, Colby SM, Patten C, et al. Methodological issues in measuring treatment outcome in adolescent smoking cessation studies. Nicotine Tob Res 2002;4:395–403.
[9] Colby SM, Tiffany ST, Shiffman S, Niaura RS. Are adolescent smokers dependent on nicotine? A review of the evidence. Drug Alcohol Depend 2000;59:S83–95.
[10] Moolchan ET, Mermelstein R. Research on tobacco use among teenagers: ethical challenges. J Adolesc Health 2002;30:409–17.
[11] Aung AT, Pickworth WB, Moolchan ET. History of marijuana use and tobacco smoking topography in tobacco-dependent adolescents. Addict Behav 2004;29:699–706.
[12] Corrigall WA, Zack M, Eissenberg T, et al. Acute subjective and physiological responses to smoking in adolescents. Addiction 2001; 96:1409–17.
[13] Franken FH, Pickworth WB, Epstein DH, Moolchan ET. Smoking rates and topography predict adolesent smoking cessation following treatment with nicotine replacement therapy. Cancer Epidemiol Biomarkers Prev 2006;15:154–7.

[14] Moolchan ET, Hudson DL, Schroeder JR, Sehnert SS. Heart rate and blood pressure responses to tobacco smoking among African-American adolescents. J Natl Med Assoc 2004;96:767–71.
[15] Wood T, Wewers ME, Groner J, Ahijevych K. Smoke constituent exposure and smoking topography of adolesent daily cigarette smokers. Nicotine Tob Res 2004;5:853–62.
[16] Zimmerman DM, Sehnert SS, Epstein DH, et al. Smoking topography and trajectory of asthmatic adolescents requesting cessation treatment. Prev Med 2004;39:940–2.
[17] Scherer G. Smoking behaviour and compensation: a review of the literature. Psychopharmacology 1999;145:1–20.
[18] Battig K. Nicotinic and non-nicotinic aspects of smoking: motivation and behavioural effects. In: Snel J, Lorist MM, eds. Nicotine, Caffeine and Social Drinking: Behaviour and Brain Function. Amsterdam, Netherlands: Harwood Academic Publications, 1998:83–113.
[19] Russell MAH. Nicotine and the self-regulation of smoke intake. In: Wald N, Froggatt P, eds. Nicotine, Smoking and the Low Tar Programme. New York, NY: Oxford University Press, 1989.
[20] Shiffman S, Paty JA, Kassel JD, et al. Smoking behavior and smoking history of tobacco chippers. Exp Clin Psychopharmacol 1994;2:126–42.
[21] Pickworth WB, Fant RV, Nelson RA, et al. Pharmacodynamic effects of new denicotinized cigarettes. Nicotine Tob Res 1999;1:357–64.
[22] Juliano LM, Brandon TH. Effects of nicotine dose, instructional set, and outcome expectancies on the subjective effects of smoking in the presence of a stressor. J Abnorm Psychol 2002;111:88–97.
[23] Eid NC, Fant RV, Moolchan ET, Pickworth WB. Placebo cigarettes in a spaced smoking paradigm. Pharmacol Biochem Behav 2005;81:158–64.
[24] Pickworth WB, O'Hare ED, Fant RV, Moolchan ET. EEG effects of conventional and denicotinized cigarettes in a spaced smoking paradigm. Brain Cog 2003;53:75–81.
[25] Lee EM, Malson JL, Waters AJ, et al. Smoking topography: reliability and validity in dependent smokers. Nicotine Tob Res 2003;5:673–9.
[26] Fagerstroem K-O. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict Behav 1978;3(suppl 4):235–41.
[27] Prokhorov AV, De Moor C, Pallonen UE, et al. Validation of the modified Fagerstrom tolerance questionnaire with salivary cotinine among adolescents. Addict Behav 2000;25:429–33.
[28] Shiffman SM, Jarvik ME. Smoking withdrawal symptoms in two weeks of abstinence. Psychopharmacology 1976;50:35–9.
[29] Kassel JD, Unrod M. Smoking, anxiety, and attention: support for the role of nicotine in attentionally mediated anxiolysis. J Abnormal Psychol 2000;109:161–6.
[30] Faul F, Erdfelder E. GPOWER: A Priori, Post-hoc, and Compromise Power Analyses for MS-DOS (Computer program). Bonn, FRG: Bonn University, 1992.
[31] Benowitz NL. Compensatory smoking of low-yield cigarettes. Risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine. Vol. Smoking and Tobacco Control Monograph No. 13: NIH Pub. No. 02-5047; 2001:39–64.
[32] Fagerstrom KO, Bates S. Compensation and effective smoking by different nicotine dependent smokers. Addict Behav 1981;6:331–6.