

Intermittent and daily smokers' subjective responses to smoking

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Abstract

Rationale One third of US smokers are intermittent smokers (ITS) who do not smoke daily. Unlike daily smokers (DS), whose smoking is negatively reinforced by withdrawal relief, ITS may be motivated by immediate positive reinforcement. In contrast, incentive salience theory posits hypothesis that “liking” of drug effects fades in established users, such as DS. **Objective** This study aims to compare ITS' and DS' hedonic responses to smoking.

Methods Participants were 109 ITS (smoking 4–27 days/month) and 52 DS (smoking daily 5–25 cigarettes/day), aged ≥ 21 , smoking ≥ 3 years, and not quitting smoking. For 3 weeks, participants engaged in ecological momentary assessment, carrying an electronic diary that asked them to rate their most recent smoking experience on 0–100 visual analog scales (satisfaction, enjoyment [averaged as “pleasure”], feeling sick, feeling a “rush,” enjoying upper respiratory sensations, and immediate craving relief). Hierarchical random effect regression analyzed 4476 ratings.

Results ITS found smoking pleasurable (mean = 69.7 ± 1.7 [SE]) but significantly less so than DS did (77.6 ± 2.3 ; $p < 0.006$). ITS also reported more aversive response (ITS 18.2 ± 1.4 , DS 11.6 ± 2.0 ; $p < 0.007$). Even though ITS are more likely to smoke at bars/restaurants, when drinking

alcohol, or when others were present, they did not report more pleasure in these settings (compared to DS). More extensive smoking experience was unrelated to craving or smoking effects among DS, but predicted greater craving, greater pleasure, and less aversion among ITS.

Conclusions The findings were largely inconsistent with incentive-salience models of drug use.

Keywords Smoking · Daily smoking · Non-daily smoking · Hedonic response · Liking · Tobacco dependence

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Cigarette smoking is persistent and resistant to change. This has been explained primarily by tobacco dependence, which is considered to drive continued smoking through negative reinforcement; as nicotine levels drop, smokers begin to develop craving and withdrawal, motivating them to smoke, and reinforcing smoking via symptom relief or avoidance (Benowitz 2010). This dynamic readily applies to most daily smokers (DS), who maintain steady-state nicotine levels over the course of a day. Yet, population surveys indicate that 25–33% of adult smokers in the USA do not smoke daily (Centers for Disease Control and Prevention 2012; Substance Abuse and Mental Health Services Administration 2013). It is clear that the smoking of these intermittent smokers (ITS) is not driven by this negative-reinforcement dynamic, as ITS do not develop increased withdrawal or even increased craving when they abstain, even for days at a time (Shiffman et al. 2015). We have suggested that ITS may be motivated by more immediate and positive reinforcement from smoking (Shiffman et al. 2012a), i.e., that ITS smoke for immediate reward, rather than for the negative

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reinforcement of withdrawal or craving relief. This suggests that ITS would enjoy smoking more than DS.

This conceptualization fits well into Robinson and Berridge's (2003) posited contrast and dissociation between drug "wanting" and drug "liking." Robinson and Berridge (2003) have posited that drug users initially experience liking when using drugs, but, as episodes of use accumulate and as dependence develops, liking fades, and wanting—which is likely expressed as craving—comes to dominate the motivation for drug use. If Robinson and Berridge's (2003) conceptualization of the process is accurate, it suggests that ITS would "like" smoking more than DS do, experiencing smoking as more pleasurable and hedonically satisfying. In these analyses, we analyze and compare DS' and ITS' ratings of hedonic satisfaction after smoking cigarettes in real-world contexts.

Although, as Berridge et al. (2009) point out, positive reinforcement is not completely equivalent to subjectively experienced pleasure, the literature does suggest that subjective hedonic effects of smoking may be useful readouts of reinforcement, and are subject to individual differences. People who experience more positive responses to their first smoking experience are more likely to progress to regular smoking (Sartor et al. 2010), and those who report more positive immediate responses to smoking, whether in real-life environments (Shiffman et al. 2006; Shiffman and Kirchner 2009) or in the lab (Strong et al. 2011), are more likely to relapse when they quit. A number of studies suggest that hedonic response demonstrates a dose-response relationship with nicotine dose in an acute administration paradigm (Kalman 2002), is correlated with dopamine response in the brain upon acute nicotine administration (Barrett et al. 2004), and is associated with genetic individual differences (Agrawal et al. 2014). Conversely, aversive responses of feeling sick after smoking or nicotine administration have also shown genetic linkages and acute dose-response effects (Agrawal et al. 2014; Kalman 2002), and could play a role in deterring smoking, perhaps limiting ITS smoking.

Studies have also examined upper airway sensations of smoking as potentially important to smoking reinforcement (Perkins et al. 2008; Rose et al. 2000), possibly due to conditioning. Finally, some studies have examined smoker reports of experiencing a "head rush" from smoking. Although such effects are somewhat ill-defined, and are not commonly reported (Piasecki et al. 2011), studies report that individuals who experience a "rush" when first smoking are more likely to progress to smoking and dependence (Agrawal et al. 2014; DiFranza et al. 2004; Sartor et al. 2010), and Dar et al. (2007) reports that such responses are considered pleasurable, so potentially reinforcing. Accordingly, we evaluate ITS' and DS' responses to smoking cigarettes in their natural environment, including pleasurable responses, aversive responses, upper airway sensations, and subjective rush effects.

While our major focus is on the subjective response to smoking, we also examine craving in relation to individuals' smoking history. Incentive sensitization theory predicts (Berridge et al. 2009) that wanting or craving would increase with increased drug use, even more so than liking or pleasure decreases. Previous analyses of Ecological Momentary Assessment (EMA) data from DS and ITS established that DS, who have often smoked hundreds of thousands of cigarettes (Berridge et al. 2009), do indeed report more craving than ITS, even between cigarettes during unrestrained ad lib smoking (Shiffman et al. 2014a). Conversely, ITS show more modest levels of craving, even when abstaining for days at a time (Shiffman et al. 2015). In these analyses, we examine whether a more extensive prior smoking history—i.e., having smoked more cigarettes—is associated with increased craving, as predicted by the theory.

Methods

Subjects

The sample consisted on 109 ITS (defined as smoking 4–27 days per month) and 52 DS (defined as smoking daily, at least 5 cigarettes per day). All subjects had to be 21 or older, to have smoked for at least 3 years, and to not be trying to quit smoking. Some ITS ($n = 72$, 66%) had a history of past daily smoking for at least 6 months (see Shiffman et al. (2014b) for detailed data on recruiting and screening). This is a subsample of participants in a previously reported study of EMA observations of smoking (Shiffman et al. 2014b) and laboratory-based cue reactivity (Shiffman et al. 2013). Table 1 shows the demographic and smoking profiles of the two samples. As previously documented (Shiffman et al. 2012c), ITS were about 4 years younger than DS, but did not differ on other demographic dimensions.

Table 1 Demographics and smoking history of ITS and DS

	DS (%)		ITS (%)	
	Mean	SD	Mean	SD
% female	46		48	
% white	69		72	
Age*	39.12	11.19	34.79	11.66
Education (years)	13.85	2.34	14.91	2.29
Income (\$1000)	29.23	20.84	33.39	26.87
Cigarettes/day	15.26	5.70	2.83	2.40
FTND	5.12	1.77	1.34	1.64
Lifetime cigarettes (thousands)	128.04	91.34	40.50	56.76
Time since last cigarette ^a (min)	195.23	294.91	757.53	1330.98

* $p < 0.05$

^a When smoking cigarettes that were later rated; from EMA data

Procedures

EMA The primary data were collected by EMA (Stone and Shiffman 1994; Shiffman et al. 2008), using electronic diaries over 3 weeks of ad lib smoking. Subjects carried a palmtop-computer-based Electronic Diary (Palm Tungsten E2) programmed to administer an EMA protocol that has been described elsewhere (Shiffman et al. 2014b). Briefly, subjects were instructed to record each cigarette smoked on ED, as they started smoking it. Data about craving and about the circumstances surrounding the smoking occasion were collected on a subset of those smoking occasions, selected at random, especially among DS, whose smoking occasions were too numerous to all be assessed (Shiffman et al. 2014b). Data on responses to smoking were not collected at that time, since the EMA report was to be completed when subjects first started smoking, and subjects would not be able to report its effects. Reports of the subjective responses to smoking were collected at a later time, when subjects were “beeped” at random, at times when they were not smoking (primarily to collect comparative data on non-smoking occasion). On those occasions, if the subject had recorded smoking a cigarette since the last non-smoking assessment, the ED administered an assessment of the subject’s response to the most recent cigarette smoked. (Due to a programming error that was discovered when the study was already under way, this contingency was not in effect for the first part of the study; thus, these data are only available for a subset of the subjects who participated in the EMA study.) A total of 4476 (2373 from DS, 2103 from ITS) assessments of subjective responses were available for analysis. The median lag between smoking and reporting subjective response was 62 min (IQR 67) for DS and 82 (IQR 84) for ITS; lag time had no effect on the ratings in terms of level, variability, intercorrelations, or covariance structure.

The time-tagged EMA records of smoking allowed for computation of the inter-cigarette interval, i.e., the time, in minutes, between cigarettes. This was analyzed as a potential moderator of response to smoking. We also analyzed as a moderator the context in which the cigarette being rated had been smoked, by linking the reports of context to the later reports of response to smoking. These analyses were limited to the subset of cases where the rated smoking occasion had been randomly selected for assessment (2397 smoking occasions: 830 DS, 1567 ITS).

Analyses of craving used ratings made on assessed smoking occasions, as well as craving ratings made when subjects were beeped at random when not smoking. As these analyses did not involve the ratings of response to smoking, which were limited to a subsample, as described above, they used a larger sample of subjects and occasions: 163 DS and 195 ITS who provided EMA data (DS 21,684 assessment occasions; ITS 21,424 assessment occasions) and also completed the lifetime smoking history.

Assessment On the randomly scheduled non-smoking occasion most immediately following recording of a cigarette, subjects were asked to rate their response to it on questions, loosely derived from the Cigarette Evaluation Questionnaire (Cappelleri et al. 2007). Specifically, they responded to the following questions using 0–100 VAS scales, and referring to the most recent cigarette: Was the cigarette satisfying? Was the cigarette enjoyable/pleasing? (highly correlated, 0.79, combined as ratings of pleasurable, $\alpha = 0.88$) Did smoking make you feel sick or ill? (aversive response) Did you enjoy the feelings in your throat and chest? Did smoking give you a rush? Did smoking immediately relieve your craving for a cigarette? These last four questions were not highly correlated with others, so were analyzed separately. On smoking occasions selected at random (Shiffman et al. 2014b), participants were asked where they were, whom they were with, and whether they had been drinking in the past 15 min. These contextual variables were linked to the subsequent ratings of response to the index smoking episode. On all assessment occasions, subjects rated craving on a 0–100 point scale.

Other data Subjects completed questionnaires that assessed demographics, dependence, and smoking history; analyses have been reported in Shiffman et al. (2012b, 2012c). Subjects also were interviewed to construct a detailed lifetime history of their smoking, by identifying sequential periods marked by stable smoking patterns, and characterizing smoking patterns in each (Brigham et al. 2008; Shiffman et al. 1994). This allowed estimation of total lifetime cigarette consumption, but was available only for 161 subjects. It also allowed for identification of ITS who had previously smoked daily for at least 6 months, whom we dubbed “converted ITS” or CITS, in contrast to native ITS (NITS), who had never smoked daily.

Analysis

Ratings were compared between DS and ITS. Hierarchical mixed linear models (SAS PROC MIXED), using a compound symmetry covariance structure, were used to account for multiple ratings from each subject. An analysis within the ITS group compared the subjective ratings of CITS versus NITS.

As Piasecki et al. (2008) reported that subjective response to smoking was moderated by recent alcohol consumption, and situational contexts of smoking—particularly the presence of others, being in a bar or restaurant, and drinking alcohol—differ between DS and ITS (Shiffman et al. 2014b), the analyses were repeated while controlling for these situational factors in the observations where such situational data had been obtained. A further analysis also examined whether the ITS-DS differences in hedonic ratings differed by these situational

settings, i.e., whether there was a group-by-context interaction effect on rated smoking pleasure.

Additional analyses were conducted separately for DS and ITS, because the predictors (time since last cigarette and lifetime cigarette consumption) covered such different, non-overlapping, ranges of values in the two groups. An analysis assessed the relationship between subjective ratings and the time (log-transformed minutes) since the previous smoking occasion. Additional analyses assessed the relationship between ratings of pleasurable and log-transformed lifetime cigarette consumption, and between craving and lifetime consumption; the analyses of craving included an indicator variable distinguishing smoking and non-smoking occasions.

Results

DS-ITS differences in responses to smoking

Figure 1 shows the mean ratings for DS and ITS. Both ITS and DS rated smoking as pleasurable—i.e., well above the mid-point of the 100-point scale. However, DS rated smoking as significantly more pleasurable than ITS did ($p < 0.006$). Both DS and ITS rated aversiveness as low, well below the mid-point of the 100-point scale, but ITS rated aversiveness significantly higher ($p < 0.007$).

Both groups also rated as low or modest the sensation of a rush, but ITS' ratings of this experience were significantly higher ($p < 0.03$). There were no DS-ITS differences in rated relief of craving—both groups reported substantial immediate craving relief. There were also no differences in ratings of enjoying upper airway sensations, with both groups rating it as modest.

Influence of situational context of smoking

Controlling for situation contexts (see “Methods” section) did not affect group differences in ratings; ITS reported

significantly less pleasurable, more aversion, and more rush after smoking (details not shown). We also examined whether contexts in which ITS were especially likely to smoke—when with others, in bars or restaurants, and when drinking alcohol—were associated with greater pleasure from smoking among ITS, compared to DS. This was not the case; there was no context \times group interaction for bar/restaurant settings, or for alcohol (Table 2). Further, the data for pleasure when others were present ran in the direction opposite to the hypothesis, with a significant interaction ($p < 0.03$) such that, among DS, there was no difference in pleasure whether being alone or with others ($p > 0.18$); among ITS, pleasure was almost significantly ($p < 0.06$) higher when ITS were smoking when alone.

Moderators of responses to smoking

Within DS and ITS, respectively, analyses examined whether response to smoking was related to the time since the previous cigarette. There were no associations among DS, where the variation in time since last cigarette was limited (Table 1). Among ITS, where time since last cigarette was much more variable (Table 1), the only effect was that reported head rush was significantly increased ($p < 0.0001$) when more time had passed since the previous cigarette; the rating was increased by about half a point for every hour that passed since the previous cigarette.

Among ITS, we tested whether response to smoking differed between NITS and CITS. They did not (details not shown).

Analyses also examined, within each group, whether cumulative experience with smoking—the estimated total number of cigarettes smoked to date—was associated with changes in responses to smoking. Among DS, there were no associations; a greater number of self-administrations did not result in significantly less pleasure or in any other changes in response. Among ITS, those with greater smoking experience reported more pleasure from smoking ($p < 0.003$), while

Fig. 1 Mean responses to individual cigarettes, by DS and ITS. Error bars represent the standard errors. ** $p < 0.01$, * $p < 0.05$

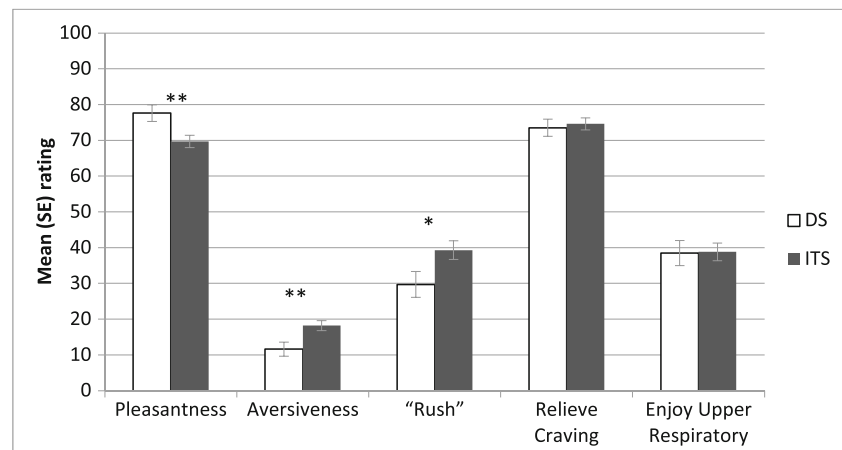


Table 2 Pleasure in response to smoking, by group and situational context of smoking

Context	Group	Group		Interaction test <i>p</i> value
		DS mean (SE)	ITS mean (SE)	
With others	No	76.73 (2.4)	71.79 ^a (1.8)	<0.025
	Yes	78.26 (2.4)	70.01 ^a (1.7)	
In bar/restaurant	No	77.53 (2.3)	70.86 (1.7)	0.169
	Yes	79.59 (3.5)	68.35 (2.5)	
Drinking alcohol	No	77.75 (2.4)	70.57 (1.7)	0.237
	Yes	75.14 (3.3)	71.41 (2.2)	

^a Simple main effects contrast within ITS, after interaction, $p < 0.051$. No significant difference among DS

experiencing less head rush ($p < 0.03$) and less aversion ($p < 0.002$).

Craving (wanting) and cigarette consumption history

Analyses examined the relationship between lifetime cigarette consumption and craving. Among DS, there was no relationship ($B = 1.08$, ± 2.03 , $p > 0.50$, person-level $r = 0.06$, $p > 0.40$). Among ITS, those with a history of more extensive smoking reported greater craving ($B = 3.21$, ± 0.79 , $p < 0.0001$, $r = 0.40$, $p < 0.0001$).

Discussion

It had been hypothesized that ITS would find smoking more enjoyable, displaying the liking that is thought to characterize early drug use (Robinson and Berridge 2003), while DS would show little liking. This analysis, based on rated response to many hundreds of real-world smoking occasions, contradicts the hypothesis. DS in fact rated their cigarettes as highly satisfying and enjoyable (78 on a 0–100 scale), and ITS rated smoking as slightly but significantly less satisfying and enjoyable than this. Further, among DS, those who had more episodes of use (i.e., lifetime cigarettes) did not find their cigarettes significantly less pleasurable, nor did they report greater craving. Conversely, among ITS, the more cigarettes an individual had smoked up to that time, the more pleasurable they found their cigarette smoking experiences, and the stronger their craving. These findings largely contradict the assertion of Robinson and Berridge (2003) that liking diminishes or disappears, while craving increases as drug use progresses and dependence is established. Together with data showing that DS display strong craving—both when they reach for a cigarette and even between cigarettes (Shiffman et al. 2002)—the data indicate that long-time, established daily smokers show *both* wanting and liking,

regardless of the extent of their prior smoking. These findings are consistent with those we reported on a sample of heavier smokers seeking smoking-cessation treatment (Shiffman and Kirchner 2009).

Contrary to hypothesis, ITS did not find smoking more pleasurable than DS, but in fact reported less pleasure. ITS may simply find nicotine self-administration less rewarding, which could play a role in limiting their smoking and progression to heavier smoking and dependence. While their ratings of pleasure were lower than those of DS, ITS did rate smoking as quite pleasurable—70 on a 100-point scale—so direct, immediate positive reinforcement from smoking may help explain their persistent smoking. Thus, ITS, too, like smoking, if less so than DS. Other data show that they also experience craving, though they do so primarily in the presence of cues that trigger their smoking (Shiffman et al. 2014a). Unlike DS, they experience little craving between bouts of smoking (Shiffman et al. 2014a), even when they abstain for days at a time (Shiffman et al. 2015). However, the ITS with more extensive smoking histories showed increased craving, which is consistent with Robinson and Berridge's (2003) account of the relationship between cumulative drug use experience and wanting.

Other EMA evidence (Shiffman et al. 2014b) suggests that situational cues play a dominant role in triggering ITS smoking. Based on the EMA findings that ITS are particularly likely to smoke when drinking alcohol, being at a bar or restaurant, and being with others (Shiffman et al. 2014b), we expected that ITS would report finding smoking more pleasurable (i.e., positively reinforcing) in those settings. That was not the case; in fact, ITS tended to report slightly greater pleasure when smoking alone, whereas DS reported the opposite. This finding undermines the idea that the contexts that trigger smoking among ITS act as discriminative stimuli indicating when smoking will be more reinforcing, and creates a paradox in which ITS differentially smoke in settings where smoking is not necessarily more rewarding. In some respects, this finding is consistent with incentive sensitization theory; in that, it shows that certain stimuli can trigger drug use even if the stimulus setting is not associated with greater reinforcement from smoking.

ITS showed limited signs of acute tolerance. They reported less of a head rush from smoking if they had previously smoked more recently. However, such acute tolerance effects were not evident either for pleasure or for aversive responses. The meaning of head rush experiences and their motivational relevance is not clear, but the experience seems to be reinforcing (Agrawal et al. 2014; DiFranza et al. 2004; Sartor et al. 2010; Dar et al. 2007), suggesting that, for ITS, smoking after a long period of abstinence, with attendant loss of acute tolerance, may be more rewarding, much as the first cigarette of the day is thought to be for DS (though see Shiffman and Kirchner 2009).

Notably, ITS rated smoking as more aversive than DS did, though both groups generally reported low aversiveness ratings. It is possible that ITS' aversive reactions to smoking may help limit their progression to heavier smoking. However, we also found that ITS' aversive reactions to smoking diminished with greater smoking experience, suggesting that continued smoking can lead to tolerance to these effects, perhaps permitting progression to heavier smoking, especially in light of the finding that ITS' craving increased with growing smoking experience.

It is important to consider that these cross-sectional observations capture subjects' behavior at a particular point in the developmental history of nicotine use, making inferences about effects over time tenuous. For example, although DS with more smoking experiences did not experience significantly more craving or less pleasure in smoking than those with less experience, it is possible that DS in general experienced less craving and greater pleasure from smoking early in their careers, and that those effects have diminished, as proposed by incentive sensitization theory. It is possible that the DS in this study are, collectively, at a plateau in the trajectory of liking and wanting, having already experienced the changes posited by incentive sensitization theory. Similarly, CITS, who used to smoke daily, may have experienced less pleasure from smoking at that time, even though that effect is not evident in these data, which were collected after they had converted to non-daily smoking.

At the same time, the data may give some insight into the development of craving and response to smoking over time. We have previously suggested that ITS behavior may represent an arrested state of development of smoking (Shiffman 1989)—i.e., that their behavior may resemble that seen early in smoking careers, before further escalation of smoking and progression to full dependence. From that perspective, the finding that ITS with more smoking experience find smoking more pleasurable and less aversive, and that they experience greater craving, suggests that early in smokers' careers, smoking may become increasingly "liked," as positive responses are enhanced and aversive, punishing, responses fade, and increasingly "wanted." Perhaps this promotes increasing consumption to the point that physical dependence develops, and withdrawal avoidance and withdrawal relief become more prominent negative reinforcers of smoking.

Why certain individuals are able to avoid that progression to daily smoking is not known. There is evidence that genetic factors play a role. Korhonen et al. (2009) have demonstrated that genetic factors distinguish daily and non-daily smokers, and other studies (Madden et al. 1999) have shown that there are independent genetic contributions to onset of smoking (in which ITS participate) and progression to heavy smoking or dependence (which do not characterize ITS). It is unlikely that genetic

variations are the sole explanation, however, as US rates of non-daily smoking have changed substantially over time, in a manner that seems correlated with the advent of increasing costs of smoking and restrictions on smoking (Shiffman 2009). Genetic factors and the policy environment may interact, in that, people may engage in heavy smoking, whether genetically predisposed or not, when there are few impediments to that behavior. However, when policy pressures impede smoking, only those with particular genetic (or other) vulnerabilities may persist in daily or heavy smoking.

One limitation of these data is that they rely on self-reported subjective ratings of pleasure, which may not fully capture liking or positive reinforcement. Indeed, Robinson and Berridge (2003) specifically caution that conscious subjective experience may not be a good indicator of positive reinforcement. However, in past studies, such self-reports of pleasure have been shown to be related to smoking behavior (Agrawal et al. 2014; Sartor et al. 2010; Urban and Sutfin 2010) as well as to mechanistically relevant brain changes (Rose 2008), and to predict important outcomes such as relapse (Shiffman et al. 2006; Strong et al. 2011). Another limitation is that the ratings of response to smoking were not obtained immediately after smoking. Analysis indicated that the length of this time lag did not affect the ratings, but it is not known whether ratings that were truly immediate might have produced a different result. Also, the samples of DS and ITS were not necessarily representative, and were relatively small, limiting statistical power. A strength of the data, in contrast to laboratory-based assessments of response to smoking, was the use of EMA methods to collect data about real-world smoking episodes, which should better represent smokers' experiences (Shiffman et al. 2008). The ability to quantify, even if only approximately and retrospectively, the extent smokers' prior smoking, also allowed us to address, albeit imperfectly, how craving and responses to smoking change with accumulating tobacco use.

In summary, we found that DS find smoking quite pleasurable, thus displaying liking as well as wanting. There was no indication that DS' positive responses to smoking diminished with increased smoking experience, or that their craving increased. Both findings contradict the Robinson and Berridge (2003). ITS rated smoking as pleasurable, but less so than DS did, while finding smoking more aversive than DS did, which may explain their failure to accelerate their smoking. ITS' reports of aversiveness decreased with more extensive smoking history, suggesting development of tolerance to such reactions over time. Conversely, ITS' pleasure at smoking and their craving for smoking increased with increasing smoking experience, suggesting the potential for an accelerating trajectory of smoking. How ITS are able to avoid the typical escalation into heavier and daily smoking deserves further exploration.

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Compliance with ethical standards

Conflict of interest Dr. Shiffman consults to eRT, which provides electronic diary services for clinical research. In the past 3 years, Shiffman has provided services for GlaxoSmithKline Consumer Healthcare on stop-smoking medications, for NJOY, Inc., on electronic nicotine delivery systems, and since February 2015, for Reynolds American, Inc. (RAI), on stop-smoking medications and non-combusted harm-minimization tobacco/nicotine products.

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