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Effect of High-Dose Nicotine Patch on the Characteristics of Lapse Episodes

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Objective: Nicotine patch improves treatment outcomes, but lapses are still common. To understand the process of relapse on patch, we investigated differences in the antecedents (withdrawal, setting, triggers) of lapse episodes experienced on high-dose (35 mg) nicotine patches versus placebo. ***Design:*** Participants were smokers who lapsed during a randomized, double-blind trial of active patches ($n = 100$) versus placebo ($n = 85$). Participants used electronic diaries to monitor their smoking, affect, and activities in real time for 5 weeks during their cessation attempt. ***Results:*** We analyzed 490 lapse episodes (active: 266; placebo: 224). Lapses on nicotine patch were characterized by significantly lower positive affect and higher negative affect than placebo lapses. Participants treated with high-dose patch were also significantly more likely to lapse in situations involving little or no craving. Situational antecedents of lapses on patch resembled those on placebo. ***Conclusion:*** The results suggest that treatment with patch may set a higher threshold for affective stimuli to provoke lapses, but does not change the proximal cues that trigger lapses. This suggests that behavioral relapse-prevention strategies developed for unmedicated smokers should also apply to those treated with nicotine patch.

Keywords: transdermal nicotine replacement, withdrawal, relapse, smoking cessation, lapse

Nicotine dependence remains notoriously difficult to overcome: Even with pharmacotherapy combined with behavioral support, approximately 70% of cessation attempts end in relapse (Fiore et al., 2008). The process of relapsing necessarily involves repeated lapses (i.e., individual instances of smoking). Unfortunately, once a single lapse occurs, complete relapse seems almost unavoidable: One estimate puts the likelihood of failure following a lapse at 95% (Kenford et al., 1994). Understanding how and why smokers lapse is the first step in developing more effective relapse-prevention treatment strategies.

Nicotine replacement therapy (NRT) decreases the risk of lapsing (Stead, Perera, Bullen, Mant, & Lancaster, 2008; Shiffman, Scharf, et al., 2006; Tønnesen et al., 1999). NRT is typically posited to work by reducing withdrawal symptoms and craving (Hughes, 1993), but analyses by Ferguson, Shiffman, and Gwaltney (2006) suggested that this mechanism does not fully account for NRT's effects. Another mechanism by which nicotine patches might prevent lapses is by reducing smokers' reactions to smoking cues, such as negative affect, alcohol, and exposure to others smoking, which seem to trigger lapses (Shiffman, 1982). However, five studies (Havermans, Debaere, Smulders, Wiers, & Jansen, 2003; Morissette, Palfai, Gulliver, Spiegel, & Barlow, 2005; Rohsenow et al., 2007; Tiffany, Cox, & Elash, 2000; Waters et al., 2004) confirm that nicotine patch does not buffer smokers against provocation by these cues. Consistently, nicotine patch significantly reduced the level of background craving (i.e., craving outside of highly tempting situations; Ferguson & Shiffman, 2009), but did not protect against the spike in craving that resulted from exposure to a smoking-related cue. Furthermore, unlike nicotine gum (Niaura et al., 2005; Shiffman et al., 2003), patch treatment also fails to accelerate recovery from provoked cravings (Waters et al., 2004). These findings suggest that the efficacy of nicotine patch may not be driven by reduced reactions to smoking cues.

Conversely, nicotine patch is effective at reducing background levels of nicotine craving (Shiffman, Ferguson, Gwaltney, Balabanis, & Shadel, 2006; Transdermal Nicotine Study Group [TNSG], 1991; Teneggi et al., 2002) and withdrawal symptoms (Rose, Levin, Behm, Adivi, & Schur, 1990; Shiffman, Ferguson, et al., 2006; TNSG, 1991). Because of this blunted underlying tonic drive to smoke, immediate cues may actually play a more important role during patch treatment. Consistent with this, less dependent smokers, who suffer less craving and withdrawal, are more likely to lapse in the presence of a particular cue—alcohol (Shiffman et al., 1997). This finding suggests that environmental cues could play a greater role in relapse in patients treated with patch. It is as if endogenously driven nicotine-seeking on the one hand and external environmental cues on the other are in competition to provoke lapses: When withdrawal severity is strong, tonic symptoms dominate, and lapses happen even absent environmental

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cues; however, when background craving and withdrawal are reduced (e.g., by patch treatment), external environment cues may become more prominent factors in lapses.

However, it is also possible that treatment with patch would reduce the effect of cues because the noncontingent nicotine supplied by nicotine patches should, over time, extinguish conditioned associations with such cues (Hughes, 1993). If patch affects the impact of cues in either direction, we would expect to see differences between treated and untreated smokers in the immediate antecedents of smoking lapses.

It is clinically relevant to understand whether the characteristics of lapse situations vary across treatments. Behavioral relapse-prevention strategies focus on understanding stimuli associated with lapsing (e.g., drinking alcohol) and either learning to avoid these situations or preparing coping strategies for dealing with them when they occur. But increasing proportions of smokers are using NRT to assist their quits; indeed, 70% of smokers using behavioral treatment were also using pharmacotherapy—mostly NRT (Shiffman, Brockwell, Pillitteri, & Gitchell, 2008). If lapse situations vary when smokers are using NRT, it may be necessary to tailor behavioral relapse-prevention strategies accordingly.

Contrasting lapses that occur during active treatment with those that occur while untreated will also help clarify the role of abstinence-induced withdrawal effects in lapses. Previous studies of untreated quit attempts have found that smoking lapses occur more frequently in moments of emotional distress (Shiffman et al., 1996). However, because this finding is based on studies of nicotine-deprived smokers (without NRT), it is not clear whether the emotional distress reported is the result of withdrawal effects, reactivity to situational stressors (see Shiffman & Waters, 2004), or some combination of the two. If the elevated emotional distress observed during lapses is due to withdrawal, participants on patch should show lower levels of negative affect, with other smoking-related stimuli becoming more prominent in lapse episodes. Conversely, if negative affect at lapse is driven by situational factors, then active patches may have little effect on negative affect levels in lapses. Indeed, smokers treated with patches might report greater negative affect because, in the absence of nicotine withdrawal, a greater emotional shock may be needed to trigger smoking in the patch group than in the placebo group.

Patch treatment could also affect the level of craving observed in lapses. Lapses generally occur in the presence of intense craving, but this is not always the case: Some lapses occur when patients are experiencing little or no craving (Catley, O'Connell, & Shiffman, 2000; Shiffman et al., 1996). Such absent-minded lapses are consistent with Tiffany's (1990) proposition that automatic action schemata—learned patterns of responses—maintain drug use and cause lapses, with craving being epiphenomenal. If patch treatment reduces the prominence of craving in driving relapse, we would expect to see an increase in automatic lapses. If patch users were found to be more susceptible to low-craving lapses, it may be necessary to particularly address this during relapse-prevention training.

In this study, to help understand the process of lapsing on nicotine patches, we compared lapses occurring on patch treatment with those on placebo, evaluating three primary hypotheses. We hypothesized that lapses on patch would be more likely to occur in the absence (or near absence) of craving. We predicted that lapses on patch would be more likely to involve alcohol (by analogy to lapses among low-dependent smokers). And, we considered that negative affect might be either higher or lower among participants treated with patch. In addition to these, we also explored a variety of other differences in lapse antecedents (e.g., situational settings, smoking triggers) between treatment groups.

We evaluated these associations in the context of a randomized trial in which smokers (stratified by baseline smoking and craving) were randomized to either high-dose (35 mg) nicotine patch or placebo. We used ecological momentary assessment (EMA; Stone & Shiffman, 1994) to collect near real-time data immediately following individual lapse episodes, at which time participants reported on the severity of withdrawal and craving immediately before the lapse and on the social and environmental setting where the lapse occurred.

Method

Participants

Participants were 185 smokers who had volunteered to take part in a smoking cessation program at the University of Pittsburgh. These participants were a subset of a large sample ($N = 324$; Shiffman, Scharf, et al., 2006). Participants were recruited using media advertising and fliers. To be eligible, smokers had to be 21–65 years of age, to have smoked 15 or more cigarettes per day for at least 5 years, to be in good health, and to express motivation and confidence to quit. Smokers were excluded if they reported regular use of noncigarette tobacco products, a weight of less than 110 pounds, specific medical counterindications for patch use, recent alcohol or drug abuse, or mental illness. Smokers were also excluded if they reported participating in a smoking cessation trial within the past 30 days or use of bupropion within the past 2 months. Women who were pregnant or breast-feeding were excluded.

Figure 1 shows the flow and disposition of participants (see also Ferguson et al., 2006; Shiffman, Scharf, et al., 2006). The present analysis focuses on those participants who suffered at least one lapse while under observation after achieving initial abstinence. Accordingly, the analysis excluded 19 (5.9% of the original 324) participants who failed to achieve initial abstinence (24 consecutive hr of abstinence), 99 (30.6%) participants who did not report lapsing during the treatment period, and 21 (6.5%) participants whose lapses did not meet our selection criteria for analysis (explained below).

Overall, 56% of the 185 participants were women and 85% were Caucasian. Participants had a mean age of 38.9 years ($SD = 8.97$), had been smoking for a mean of 21.9 years ($SD = 9.12$), and smoked a mean of 25.0 cigarettes per day ($SD = 9.15$). Participants reported previously having made a mean of 3.7 attempts to quit smoking ($SD = 4.0$) and had a mean score on the Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991) of 6.1 ($SD = 1.9$). Participants' average motivation to quit was 92.0 (0–100 scale, $SD = 8.3$), and their self-efficacy to quit was 86.7 ($SD = 12.6$). In this sample, 100 (54.1%) participants were on active patches and 85 (45.9%) on placebo patches. The treatment groups did not differ on any of the baseline characteristics. The study was approved by the University of Pittsburgh Institutional Review Board, and written informed consent was obtained from all participants.

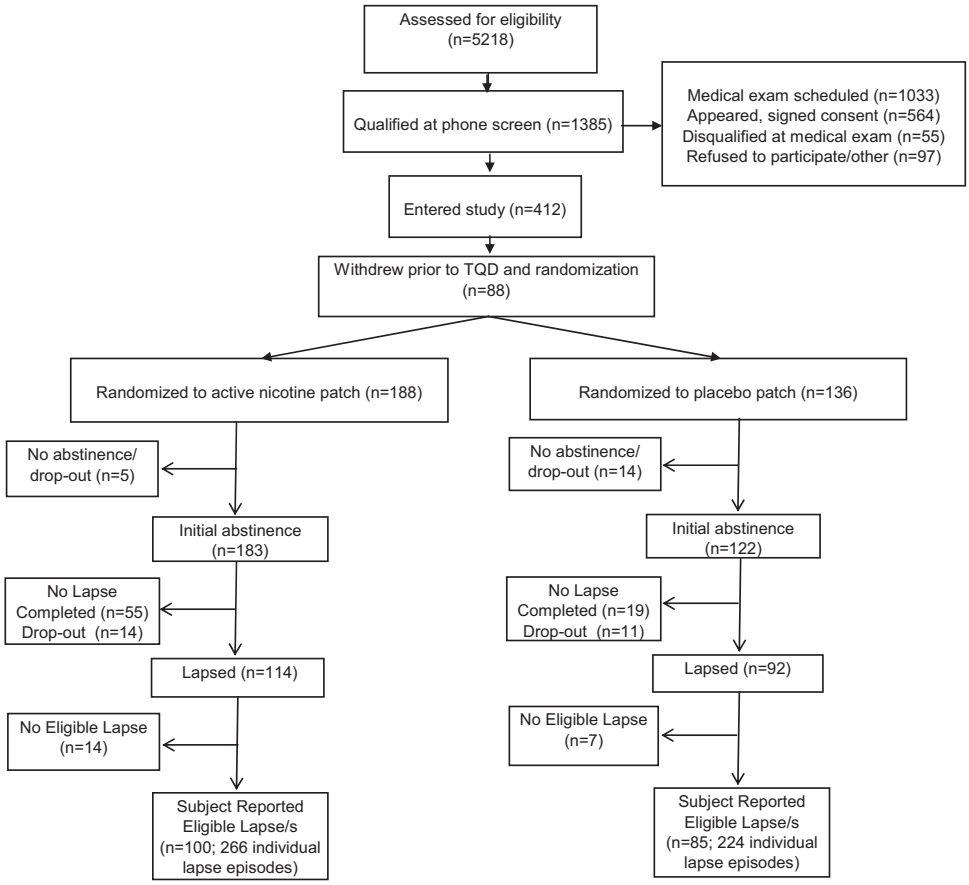

Figure 1. Disposition of candidates and participating subjects. TQD = target quit day.

Materials and Procedure

Study overview. Detailed information regarding the procedures and measures has been reported elsewhere (Ferguson et al., 2006; Shiffman, Ferguson, et al., 2006; Shiffman, Scharf, et al., 2006). Briefly, participants used electronic diaries (EDs; Shiffman et al., 1996; Stone & Shiffman, 1994) to monitor their ad-lib smoking, affect, and activities in real time for 16 days prior to a clinic-mandated target quit date on Day 17 of the study. On Day 17, participants were randomized to active or placebo patches (with stratification by baseline smoking rate and baseline craving) and instructed to quit smoking completely. Assessments via EDs continued for 5 weeks following treatment randomization. During this time, participants were randomly prompted to provide information about their affect and activities, and any instances of smoking (i.e., lapses) were to be reported in real-time using the EDs.

Treatment. Smokers were randomized to high-dose patch (35 mg) or placebo. High-dose patch was used to address the concern that currently approved doses (21 mg) may not provide adequate nicotine replacement for many smokers (e.g., Dale et al., 1995; Killen, Fortmann, Davis, Strausberg, & Varady, 1999). In this study, the 35-mg patch achieved complete nicotine replacement (averaging 125% of baseline levels; Shiffman, Scharf, et al., 2006), and nearly eliminated background craving and withdrawal symptoms (Shiffman, Ferguson, et al., 2006), allowing one to assess the circumstances of lapses occurring under complete nicotine replacement. As described previously (Ferguson et al., 2006; Shiffman, Scharf, et al., 2006), at a designated target quit day, participants were randomized (double-blind), in a 3:2 ratio, to receive either nicotine or placebo patches. (Given that nicotine patch decreases the odds of lapsing [e.g., Fiore et al., 2008], 30% more participants were randomized to nicotine patch than placebo to allow for approximately equal numbers of lapse events in the two groups.) Individuals randomized to nicotine patches wore one 21- and one 14-mg patch (NicoDerm CQ, GlaxoSmithKline, Pittsburgh, PA) for the first 3 weeks of treatment, one 21-mg and one placebo patch for the following 2 weeks, and two placebo patches for 1 final week (data excluded from analyses), making a total of 5 weeks of active treatment. (Like the dose, the length of treatment used in this study was nonstandard—5 weeks rather than the recommended 10. This length of treatment was chosen as the study was primarily designed to study smoking lapses, which are most common within the early stages of a quit attempt.) Individuals randomized to placebo patch treatment always wore inactive patches, which were otherwise identical to the active patches. In additional to patch treatment, participants attended up to six sessions of group cognitive–behavioral therapy, delivered by clinicians who were blind to patch treatment status. Two of the therapy

sessions occurred prior to quitting, one on the designated target quit day, and the remaining sessions during patch treatment. Each therapy session lasted approximately 90 min. Treatment content included the use of coping to avoid lapsing, but avoided discussion of lapse antecedents and abstinence violation effects (Marlatt & Gordon, 1985). Groups mixed participants on active and placebo patches.

Lapse assessments. The approach used in this study was similar to that used in previous EMA smoking and relapse studies (Shiffman et al., 1996). Participants were instructed to carry an ED with them throughout the waking day. Following treatment randomization, EDs automatically determined (and logged) the time and date when participants achieved initial abstinence—defined as a continuous 24-hr period during which no cigarettes were reported. Once initial abstinence had been achieved, all instances of smoking that occurred—even just a single puff—were treated as smoking lapses.

When participants lapsed, they were required to record the event on their ED immediately following the episode. During these lapse assessments, affect and withdrawal were assessed using a series of mood adjectives derived from the circumplex model of affect (Russell, 1980); the circumplex model posits that affective state can be described by two dimensions of emotion: positive/negative valence and arousal. Participants were presented with an adjective (e.g., "Happy?") and asked to record their response on a 0- to 10-point scale. Based on a factor analysis, these responses were used to form five standardized factor scores ($M = 0$, $SD = 1$): Positive Affect (items: *happy*, *content*, *calm*), Negative Affect (*frustrated*, *irritable*, *miserable*, *sad*, *worried*), Arousal (*sleepy*, *tired*), Attention Disturbance (*spacey*, *hard to concentrate*), and Restlessness (*restless*, *jittery*, *fidgety*). Urge to smoke (both before and during the event) was assessed using a single item (0- to 10-point scale). More detail on the affect and withdrawal assessments used can be found in Shiffman, Ferguson, et al. (2006). In addition to affect and withdrawal measures, participants reported the primary trigger (only a single response was accepted) of the lapse (see list in Table 1) and also designated all triggers that played a role (multiple responses accepted). Participants were also asked to report their location immediately before the lapse event (see list in Table 1), whether they were with other people at the time of the lapse (responses: no, yes, others in view), whether others people were smoking, and the activity they were doing immediately before the lapse occurred (see list in Table 1). Each lapse was time- and date-stamped by the ED when it was reported.

In addition to real-time reports, participants completed a confessional at the end of each study day, in which they were able to report any lapses that had occurred during the day that they had failed to report in real time. These confessed lapses were not assessed in detail because doing so would introduce errors associated with retrospective recall (Hammersley, 1994), but were used to identify lapses that were not preceded by at least a day of abstinence.

In addition to recording lapses, participants were to record instances of strong temptation to smoke. Furthermore, the ED beeped participants 4 to 6 times each day at random times for assessments, with the limitation that no random prompts were scheduled within 10 min of a recorded lapse or self-reported temptation. The assessments at these moments were largely similar to those administered after smoking lapses (data not analyzed in this article).

To be eligible for inclusion in the following analyses, a lapse event must have (a) been recorded in real time and (b) followed at least 1 calendar day of abstinence (that is, the participant must again have met the original criterion for quitting before a new smoking episode would be counted as a lapse). If more than one lapse occurred on a given day, only the first lapse for that day was eligible for analysis. Finally, we truncated all lapses that occurred after 20 recorded lapses because data became increasing sparse.[1] (Once participants met criteria for relapse—namely smoking five cigarettes a day for 3 consecutive days—the ED no longer solicited reports for each lapse occasion as participants were considered to be engaging in ad-lib smoking. Some participants also dropped out when they were repeatedly lapsing.)

Analytic Plan

To test our hypotheses, we analyzed three primary variables—self-reported craving, affect, and alcohol consumption at the time of lapsing. To test for differences in affect immediately prior to lapse, we compared self-reported affect across treatment groups. To test the effect of patch on the likelihood of "automatic" lapses, we compared the patch groups on the frequency of lapses that were preceded by very low levels of craving (defined as 0 or 1 on our 0- to 10-point craving scale). (A craving cutoff of 1 [as opposed to zero] was used because ratings of zero are rare, even during periods of ad-lib smoking.) Finally, we hypothesized that lapses on nicotine patch would be more likely to involve alcohol consumption; as such, we compared frequency of lapses in which participants reported drinking alcohol across the patch groups.

To further examine the characteristics of lapsing on active patch versus placebo, we compared the antecedents (withdrawal, setting, smoking triggers) associated with lapses across treatment groups using a series of exploratory analysis. Given the exploratory nature of these comparisons, we did not adjust for multiple comparisons, instead using an alpha of .05.

As each participant could contribute multiple observations, all treatment comparisons were conducted using generalized estimation equations (Zeger, Liang, & Albert, 1988), which are designed to account for the autocorrelation of data in repeated measures designs. To analyze categorical variables that contained multiple

[1] We also conducted our analysis including only first lapse episodes that were reported in real time ($n = 169$; nicotine patch lapses = 91, placebo lapses = 78), a sample that can be considered a more "pure" sample of smoking lapses. We conducted analyses on this restricted sample to check whether our decision to allow for the inclusion of multiple lapse episodes per participant may have somehow skewed the results. The results from this more restrictive sample were largely the same as those presented in this article. Specifically, contrasting first lapse on nicotine patch with those that occurred on placebo patch, we found no group differences in the context (situations or activities), craving, or withdrawal under which these events occurred, nor did we see differences in the lapse triggers. However, as in the larger main sample, first lapses on nicotine patch occurred in the presence of higher levels of negative affect and lower levels of positive affect (compared with those that occurred on placebo patches). Finally, a greater proportion of first lapses on nicotine patch occurred in the presence of low levels of craving, but the difference between groups was not statistically significant (10% vs. 8%).

levels (e.g., smoking triggers, location prior to lapse, and activity prior to lapse), we converted each level of the variable to a binary (no, yes) variable and then analyzed separately.

For presentation, continuous variables (craving and withdrawal severity) are shown as least-squares means (which take into account the clustering of the data), and categorical variables are shown as column percentages with corresponding 95% confidence intervals. As baseline characteristics did not differ between the two groups, which had been randomized within strata of smoking rate and craving, no covariates were used in the analyses. Odds ratios were used as a measure of effect sizes for categorical variables, and Cohen's *d* scores (based on raw means and standard deviations) were used for continuous variables.

After adjusting the estimate of the standard deviation based on the observed intraclass correlation among episodes (Hintze, 2004), a between-subjects power analysis indicated that this study's sample size would provide 80% power to detect small differences in the means of continuous variables ($d = 0.3$, or a "small" effect size; Cohen, 1992), as well as differences in proportion for binary variables ($d = 0.1–0.2$, "small" effect sizes).

Results

Lapse Selection

A total of 490 lapse episodes (active: 266; placebo: 224) recorded by the 185 participants met the criteria for inclusion in our analysis. On average, each participant reported 2.6 ($SD = 1.7$, maximum = 9) eligible lapses during monitoring; this was similar across the two treatment groups (active: $M = 2.7$, $SD = 1.7$, maximum = 9; placebo: $M = 2.6$, $SD = 1.7$, maximum = 8).

Craving

On average, participants reported relatively high levels of craving both immediately before ($M = 6.9$ on a 0–10 scale, $SD = 2.8$) and during smoking lapses ($M = 7.5$, $SD = 2.5$). The average level of craving reported by participants treated with active patches did not differ from that reported by participants on placebo patches (see Table 1). Only 6.9% of the lapse events analyzed met our criteria for very low prelapse craving levels, but, as hypothesized, these were more likely to occur on active patches (effect size = 3.5; see Table 1).

Affect

The levels of negative and positive affect reported by the two treatment groups during lapses are shown in Table 1. Participants on active patches reported significantly more emotional distress—lower levels of positive affect (effect size = 0.2) and higher levels of negative affect (effect size = 0.2)—immediately before smoking lapses (see Table 1). No group differences were observed in levels of attention disturbance, arousal, or restlessness.

Alcohol

Across treatment groups, participants reported drinking alcohol immediately before 8.7% of lapse episodes. Participants treated with active or placebo patches were equally likely to report drinking alcohol in association with lapse episodes (see Table 1).

Antecedents of Lapses, by Treatment Group

Table 1 shows the other characteristics of lapse episodes by treatment group. Exploratory analyses found that the groups did not differ in the activities they reported engaging in prior to a lapse (see Table 1). When asked about the activities they were engaged in immediately prior to their lapse, participants most frequently reported that they were working (27.9% of lapses). Interacting with other people (27.4%), drinking (24.2), and leisure (20.6%) were other activities frequently endorsed prior to a lapse.

Similar results were found when the time of the lapse and self-reported smoking triggers were examined. On average, lapses occurred at 4:32 p.m., with lapses on active patches occurring about 1 hr later in the day than those on placebo (see Table 1), but the difference was not significant. The majority of lapses on both active and placebo patches occurred during the p.m. hours (active: 68.0%; placebo: 69.2%), with almost half occurring in the late afternoon or later (between 4:01 p.m. and midnight; active: 46.6%; placebo: 45.5%; see Table 1). In terms of smoking triggers, again, no significant differences were seen between the two treatment groups (see Table 1). Stress was reported as the primary lapse trigger for approximately a third of all lapses (32.0%). Similarly, when participants were asked to list any triggers that contributed to lapse, stress was noted as having played a role in almost half (42.2%) of all the lapse episodes analyzed. Other commonly endorsed triggers were bad mood (24.9% of lapses), smoking cues (21.8%), eating or drinking (18.8%), and other triggers (27.4%).

Finally, no significant differences in setting were found between treatment groups (see Table 1). Across the groups, lapses were most likely to occur at home (43.7% of lapses) or at the workplace (19.8%). The majority of lapses occurred when participants were either with other people or could see other people (64.1% of lapses) and, in such cases, the other people were often also smoking (59.6%).

Discussion

Comparisons of lapse situations among smokers on high-dose patch and placebo showed the settings of smoking lapses to be surprisingly similar. Within that broad context, we did find two meaningful differences that confirmed hypotheses about how NRT would affect lapse episodes.

First, participants treated with nicotine patches reported significantly more emotional distress immediately prior to lapses—lower levels of positive affect and higher levels of negative affect. These differences were relatively substantial: 0.15 and 0.17 standard deviations for positive and negative affect, respectively (see Table 1), equivalent to approximately half the effect of high-dose patch treatment on affect (Shiffman, Ferguson, et al., 2006). The higher level of distress in nicotine patch lapsers must be interpreted in light of the fact that outside of lapses, high-dose NRT reduced negative affect and increased positive affect, on average eliminating the increase in distress due to quitting smoking (Shiffman, Ferguson, et al., 2006). This addresses one of our research questions by suggesting that the distress associated with lapses is not withdrawal-driven, but likely environmentally and situation-

Table 1
Characteristics of Lapse Episodes, by Treatment Group

Variable	Lapse		Effect size[f]	*p*
	Nicotine patch (n = 266)	Placebo (n = 224)		
Lapses at each time of day, % [95% CI]				
12:01 a.m.–4:00 a.m.	9.4 [6.2, 13.6]	3.6 [1.6, 6.9]	2.8	*ns*
4:01 a.m.–8:00 a.m.	5.3 [2.9, 8.7]	8.5 [5.2, 12.9]	0.6	
8:01 a.m.–noon	17.3 [12.9, 22.4]	18.8 [13.9, 24.5]	0.9	
12:01 a.m.–4:00 p.m.	21.4 [16.7, 26.9]	23.7 [18.3, 29.8]	0.9	
4:01 p.m.–8:00 p.m.	23.7 [18.7, 29.3]	25.0 [19.5, 31.2]	0.9	
8:01 p.m.–midnight	22.9 [18.0, 28.5]	20.5 [15.4, 26.4]	1.2	
Mean (*SE*) time of lapse	4:52 p.m. (26.65)	3:55 p.m. (27.17)	0.2	*ns*
Mean (*SE*) urge to smoke				
Urge before[a]	6.77 (0.28)	7.09 (0.25)	0.1	*ns*
Urge during[a]	7.33 (0.25)	7.45 (0.23)	0.1	*ns*
Difference	0.58 (0.12)	0.41 (0.14)	0.1	*ns*
Low craving lapses, % [95% CI]	10.2 [6.5, 13.8]	3.1 [0.9, 5.4]	3.5	.03
Mean (*SE*) affect/withdrawal symptoms				
Positive affect[b]	−0.07 (0.06)	0.08 (0.05)	0.2	.04
Negative affect[b]	0.08 (0.06)	−0.09 (0.05)	0.2	.03
Attention disturbance[a]	2.13 (0.17)	2.53 (0.25)	0.2	*ns*
Arousal[a]	6.54 (0.26)	7.06 (0.23)	0.3	*ns*
Restlessness[a]	3.54 (0.24)	3.35 (0.24)	0.1	*ns*
Social setting, % [95% CI]				
With others? No	34.5 [28.7, 40.6]	37.6 [31.1, 44.4]	0.9	*ns*
With others? Yes	60.2 [53.9, 66.1]	56.4 [49.8, 63.0]	1.2	*ns*
Others in view? Yes	5.4 [3.0, 8.8]	6.0 [2.8, 9.1]	0.9	*ns*
Others smoking? Yes[c]	60.8 [53.1, 68.2]	58.1 [49.3, 66.5]	0.9	*ns*
Activity immediately prior to lapse, % [95% CI][d]				
Working	25.2 [20.1, 30.9]	31.3 [25.2, 37.8]	1.4	*ns*
Chores	12.6 [8.9, 17.3]	12.8 [8.7, 18.0]	1.0	*ns*
Leisure	19.5 [15.0, 24.8]	21.9 [16.6, 27.9]	1.2	*ns*
Inactive	6.4 [3.8, 10.0]	7.1 [4.1, 11.3]	1.1	*ns*
Interacting with others	30.8 [25.3, 36.8]	23.2 [17.9, 29.3]	0.7	*ns*
Eating (within 15 min)	7.6 [4.7, 11.5]	11.4 [7.5, 16.4]	1.6	*ns*
Any drinking (within 15 min)	25.7 [20.5, 31.4]	22.5 [17.1, 28.6]	0.8	*ns*
Alcohol (within 15 min)[e]	9.9 [6.3, 13.5]	7.3 [3.9, 10.8]	0.7	*ns*
On telephone	4.5 [2.4, 7.8]	5.8 [3.1, 9.7]	1.3	*ns*
Other activity	24.8 [19.7, 30.5]	23.2 [17.9, 29.3]	0.9	*ns*
Primary trigger attributed to lapse, % [95% CI]				
Bad mood	10.5 [7.1, 14.9]	12.5 [8.5, 17.6]	0.8	*ns*
Stress	32.3 [26.7, 38.3]	31.7 [25.7, 38.2]	1.0	*ns*
Good mood	4.1 [2.1, 7.3]	2.7 [1.0, 5.7]	1.6	*ns*
Eating or drinking	11.3 [7.7, 15.7]	9.4 [5.9, 14.0]	1.2	*ns*
Smoking cues	12.8 [9.0, 17.4]	16.1 [11.5, 21.5]	0.8	*ns*
Relaxing	3.4 [1.6, 6.3]	4.5 [2.2, 8.1]	0.7	*ns*
Boredom	3.0 [1.3, 5.8]	5.4 [2.8, 9.2]	0.5	*ns*
In transition	4.5 [2.4, 7.7]	2.2 [0.7, 5.1]	2.1	*ns*
Other trigger	18.0 [13.6, 23.2]	15.6 [11.1, 21.1]	1.2	*ns*
Any trigger attributed to lapse, % [95% CI][d]				
Bad mood	23.7 [18.7, 29.3]	26.3 [20.7, 32.6]	1.2	*ns*
Stress	43.6 [37.6, 49.8]	40.6 [34.1, 47.4]	0.9	*ns*
Good mood	10.9 [7.4, 15.3]	7.6 [4.5, 11.9]	0.7	*ns*
Eating or drinking	19.2 [14.6, 24.4]	18.3 [13.5, 24.0]	0.9	*ns*
Smoking cues	21.4 [16.7, 26.9]	22.3 [17.0, 28.3]	1.1	*ns*
Relaxing	10.5 [7.1, 14.9]	8.9 [5.5, 13.5]	0.8	*ns*
Boredom	10.2 [6.8, 14.4]	11.2 [7.4, 16.0]	1.1	*ns*
In transition	8.3 [5.3, 12.3]	5.4 [2.8, 9.2]	0.6	*ns*
Other trigger	28.2 [22.9, 34.0]	26.3 [20.7, 32.6]	0.9	*ns*

(*table continues*)

Table 1 (*continued*)

Variable	Lapse		Effect size[f]	*p*
	Nicotine patch (n = 266)	Placebo (n = 224)		
Location immediately prior to lapse, % [95% CI]				
Home	45.1 [39.0, 51.3]	42.0 [35.4, 48.7]	1.1	*ns*
Workplace	17.7 [13.3, 22.8]	22.3 [17.0, 28.4]	0.7	*ns*
Others home	6.4 [3.8, 10.0]	2.7 [1.0, 5.7]	2.5	*ns*
Bar/restaurant	8.6 [5.6, 12.7]	10.7 [7.0, 15.5]	0.8	*ns*
Vehicle	10.9 [7.4, 15.3]	12.5 [8.5, 17.6]	0.9	*ns*
Outside	7.9 [5.0, 11.8]	6.3 [3.5, 10.3]	1.3	*ns*
Other	3.4 [1.6, 6.3]	3.6 [1.6, 6.9]	0.9	*ns*

Note. Percentages are column percentages; *ns* = not significant ($p > .05$).
[a] Scores could range from 0 to 10, with a higher value indicating a higher level of the variable. [b] Factor scores with a mean of 0 and a standard deviation of 1. [c] Excludes lapse episodes that occurred when participant reported being alone. [d] Columns do not add to 100 as participants could endorse multiple triggers. [e] The proportion of participants drinking alcohol is a subset of those who reported any drinking. [f] Effect sizes are odds ratios for the categorical variables and Cohen's *d* scores for the continuous variables.

ally driven. This is also suggested by the fact that the groups did not differ on other withdrawal-related measures, such as attention disturbance or restlessness. Furthermore, the fact that smokers on nicotine patch actually reported more distress prior to lapsing suggests that a higher level of distress may have been needed to precipitate a lapse, given the protection apparently afforded by nicotine patch. In other words, nicotine patch treatment protects against lapses, but this protection can be overcome by sufficiently powerful situational affective triggers. Thus, smokers on NRT may be protected from withdrawal-related stress, and may be rendered more tolerant of emotional distress, but they still need to be alert to the potential impact of significant distress. This suggests that smokers treated with NRT may need to avoid particularly stressful or distressing situations, where possible, or to develop effective coping to minimize distress.

The data also confirmed the hypothesis that participants treated with nicotine patches would be more likely to report lapses associated with a near absence of craving. Roughly 7% of all the lapses we analyzed occurred when participants were experiencing little or no craving, and these lapses were more common among participants on nicotine patches. Such low-craving lapses have been described as reflecting automatic behavior or action schemata triggered by smoking cues in the absence of any craving (Catley et al., 2000; Tiffany, 1990). Thus, the excess of such lapses on nicotine patch suggests that nicotine treatment suppresses craving, but may not completely suppress these behavioral triggers, thus making low-craving lapses relatively more common. This finding suggests that people treated with patch need especially to be cautioned to watch for such automatically triggered behavior and keep very conscious of their behavior, lest they lapse absentmindedly. However, it should be noted that the vast majority of lapses in both groups still occurred in the presence of relatively high levels of conscious craving.

Indeed, the excess incidence of low-craving lapse episodes aside, the average levels of craving reported by the two groups during lapse episodes were strikingly similar. Despite findings from this study (Shiffman, Ferguson, et al., 2006) and others (Shiffman & Ferguson, 2008; Teneggi et al., 2002; TNSG, 1991) confirming that nicotine patch significantly reduces background craving, we found that during and just before a lapse, smokers on NRT experienced equal levels of craving. If smokers on nicotine patch had lower background craving but equal situational craving, this implies that these smokers' craving had to increase more steeply in the moments before a lapse. Close examination of craving leading up to lapse episodes will be necessary to understand what smokers experience immediately before a lapse, and whether action can be taken to intervene, perhaps heading off a lapse before it can occur.

We had also hypothesized that smokers treated with high-dose patch would be more likely to lapse when drinking, by analogy to the greater role of alcohol in lapses among less dependent smokers (Shiffman et al., 1997). However, we did not find a difference in the role of alcohol in lapses while on nicotine patch. Indeed, more generally, the immediate settings of lapses were similar for those on NRT and those on placebo. That is, although patch treatment reduces the risk of suffering a lapse (Shiffman, Gorsline, & Gorodetzky, 2002; Tønnesen et al., 1999), even in this very sample (Shiffman, Scharf, et al., 2006), when NRT-treated smokers do lapse, the immediate situational antecedents are similar to those seen in untreated smokers. This finding is somewhat perplexing given the reasons to expect differences. However, one needs to remember that our data only address the presence, and not the strength, of most of the triggers assessed; for example, although smoking cues were equally endorsed as the trigger of lapses by both groups, the cues that nicotine patch participants cited may have been more potent than those cited in placebo lapses. NRT may help participants survive situations of milder provocation in which they would otherwise have lapsed (had they been untreated), while still leaving them susceptible to lapse when they encounter particularly potent provocations. Further research will be needed to determine the merit of this hypothesis, however.

This is only the second study in the literature reporting the details of lapse episodes as assessed by EMA. The details of lapse situations seen in this study are almost identical to those reported in the prior study (Shiffman et al., 1996). Lapses frequently occurred in the presence of other people and when others were smoking nearby. Stress was reported as being the primary trigger for lapse episodes in both treatment groups and playing a role in almost half of lapses. Bad mood, smoking cues, and eating or drinking were other frequently endorsed lapse triggers. The majority of lapses occurred in the afternoon or evening (see Brandon,

Tiffany, & Baker, 1986; Shiffman et al., 1996; Tønnesen et al., 1999), perhaps because craving is highest during this period (Shiffman, 1979; Shiffman & Ferguson, 2008; Teneggi et al., 2002), when participants may be free from work-related smoking restrictions and may encounter important cues such as alcohol. This detailed description of lapse episodes should be useful in treatment to inform smokers regarding what situations they need to avoid or be prepared to cope with. Clinically, our findings suggest that smokers using NRT, like untreated smokers, are susceptible to environmental triggers and cannot rely on pharmacotherapy alone; instead, smokers using NRT may also need to implement coping strategies (Shiffman, 1984) to maintain abstinence.

It is important to note that our findings should be regarded as applying to lapses on nicotine patch, but not necessarily on other medications. By virtue of its mode of application, patch provides steady-state treatment that does not vary with situational demands. In contrast, acute forms of NRT (gum, lozenge, inhaler, nasal spray) may provide opportunities to respond to situational demands by self-administering a rescue dose to relieve craving, which could substantially change the dynamics of lapse situations. This has been demonstrated in laboratory studies with nicotine gum (Niaura et al., 2005; Shiffman et al., 2003). It is hard to know how the present results might apply to nonnicotine medications such as bupropion or varenicline, which likely share some mechanisms with patch, including chronic, steady-state administration and relief of background craving (Durcan et al., 2002; Gonzales et al., 2006) but not provoked craving (Hussain, Zawertailo, Zack, Busto, & Selby, 2007; Niaura, Hitsman, Shadel, DiBernedetti, & Price, 2007). Further studies will be needed to address such questions.

A strength of this study was the use of EMA (Shiffman, Stone, & Hufford, 2008), with detailed reports of lapse episodes collected in near real time, limiting the opportunity for bias due to retrospective recall (Hammersley, 1994). Furthermore, the study was well powered to detect even small differences, strengthening the case that the absence of significant differences is indicative of a true absence of group differences. Nevertheless, it still has a number of limitations. Although the use of high-dose nicotine patches provided the high degree of relief from background craving and withdrawal severity needed for the analyses conducted, the use of a non–FDA-approved dose and duration limits our ability to generalize the results, as does our sample of heavy, dependent smokers; we cannot be sure our findings will generalize to standard doses of patch and or to the overall population of patch users. However, as the higher dose provided in this study would tend to strengthen the patch–placebo contrast, differences that were not observed here are unlikely to be found for lower, approved doses, making high-dose patches a powerful test for our hypotheses. In addition, we performed multiple tests on exploratory analyses; however, our analysis was focused on a few primary hypotheses, some of which were upheld. Finally, it is possible that some lapses were not reported by participants (either in real time or during end-of-day reports).

In this study, we directly compared the characteristics of lapse episodes that occurred during nicotine patch treatment with those that occurred during placebo treatment. NRT-treated smokers lapsed under greater affective distress, perhaps because it took more psychological force to drive them to smoke when their craving was suppressed by patch treatment. NRT-treated smokers were also more likely to lapse under very low craving, perhaps when automatic action schemata were activated by situational cues. Otherwise, NRT did not seem to affect the immediate antecedents of lapses, contrary to the theoretical cases that can be made to suggest that it should. Clinically, our findings are supportive of the current practice of providing the same types of counseling to patients irrespective of whether they are using pharmacotherapy; our findings suggest that behavioral relapse-prevention strategies developed on the basis of studies of unmedicated smokers—for example, avoiding smoking cues—should apply to smokers treated with NRT. Studies have shown that behavioral treatment adds incrementally to the efficacy of nicotine patches. Our findings suggest why this is so: Smokers on nicotine patches face the same situational challenges that untreated smokers face and need behavioral strategies to counter them.

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