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Affective Reactivity During Smoking Cessation of Never-Quitters as Compared With That of Abstainers, Relapsers, and Continuing Smokers

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Abstract

Much effort has been devoted to examining the differences in postcessation affective experience between smoking abstainers and relapsers. However, little attention has been given to the affective changes of smokers who, despite their motivation to quit, fail to achieve even a brief period of abstinence. Using affect-modulated startle response and self-report questionnaires, we measured the postcessation affective changes of 115 smokers (60 men, 55 women) who participated in a laboratory investigation of affective reactivity during smoking cessation. Among our participants, 34 were abstainers (16 men, 18 women), 16 were never-quitters (8 men, 8 women), 19 were relapsers (8 men, 11 women), and 46 were controls (28 men, 18 women). We found a significant Stimulus Valence $\times$ Session $\times$ Group interaction effect on startle responses, which suggested that while abstainers, relapsers, and control exhibited the prototypical affect-modulated startle response across postcessation sessions, never-quitters displayed an atypical response pattern in which emotional pictures no longer modulated the startle response. Never-quitters also reported increasingly higher negative and lower positive affect across postcessation sessions. Using affect-modulated startle response and self-report questionnaires, this study found a significant difference in the affective reactivity between smokers who could and smokers who could not establish an initial abstinence of 24 hours.

Keywords

smoking; affect-modulated startle responses; nicotine withdrawal; negative affect; smoking relapse

Of the approximately 40% of current smokers in the United States who try to quit smoking every year (Centers for Disease Control & Prevention, 2008), only 5% quit successfully (Fiore et al., 2008; Hughes, Keely, & Naud, 2004). Smoking relapse remains a major challenge and a frequently studied phenomenon in the treatment of nicotine addiction. However, relatively little attention has been given to examine smokers who, despite their motivation to quit, fail to achieve even a brief period of abstinence.

By conventional definition, relapse occurs only after smokers fail to maintain an initial abstinence that lasts for at least 24 hours (Hughes et al., 2003). Previous studies have linked relapse with individual differences, including age (Ockene et al., 2000), education (Ockene et al., 2000), level of nicotine dependence (Killen, Fortmann, & Kraemer, 1992), and impulsivity (Doran, Spring, McChargue, Pergadia, & Richmond, 2004). In addition, smoking relapse has been linked to acute postcessation precipitants like negative affect (Borland, 1990; Brandon, Tiffany, Obremski, & Baker, 1990; Shiffman & Waters, 2004; Shiffman et al., 1996), craving (Killen & Fortmann, 1997; Shiffman, Perz, Gnys, Kassel, & Hickcox, 1997), and abstinence self-efficacy (Gwaltney, Shiffman, Balabanis, & Paty, 2005; Gulliver & Hughes, 1995), as well as situational determinants like exposure to smoking cues (Borland, 1990) and use of alcohol (Shiffman, 1982; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). Given that relapse is the primary obstacle that undermines a smoker's desire to quit, researchers have justifiably devoted extensive effort and will continue to give top priority to investigating smoking relapse.

In addition to smokers who successfully achieve long-term abstinence (abstainers) and smokers who relapse (relapsers), there exists a little-studied, third group of smokers who try to quit but cannot stop smoking for more than a few hours: These smokers can be described as "never-quitters." One study found that, as compared with abstainers, never-quitters reported a significant increase in perceived stress across a 6-month failed postcessation period (Cohen & Lichtenstein, 1990). However, most smoking cessation studies have focused on comparing abstainers with relapsers. Some researchers made the distinction between relapsers and never-quitters, but then excluded never-quitters from their data analyses (Borland, 1990). Other researchers considered never-quitters to be relapsers who relapsed early (i.e., within 24 hours) and merged both groups into a single category. Neither practice identifies the never-quitters as a separate subgroup of smokers who may be inherently different from smokers who are able to achieve an initial abstinence of 24 hours. Findings from two studies have shown that as many as 33% of smokers who enroll in smoking cessation programs are never-quitters (Borland, 1990; Mermelstein, Lichtenstein, & McIntyre, 1983). Excluding such a large group of smokers from analyses may not only prevent tobacco researchers from studying an important subgroup of smokers, but also diminish the representativeness of a study sample and compromise the generalizability of its findings. However, combining never-quitters with relapsers may mask the mechanisms that prevent the never-quitters from achieving initial abstinence.

Previous studies that sought to distinguish between subgroups of smokers have yielded findings that added significantly to our understanding of the smoking cessation and relapse processes. Using cluster analysis, Piasecki and colleagues identified several subgroups of smokers, each with a distinct postcessation withdrawal symptoms profile (Piasecki, Fiore, & Baker, 1998; Piasecki et al., 2000). They found that smokers who had atypical profiles (e.g.,

an extended course of unrelieved symptoms) were significantly less likely to maintain abstinence than those whose withdrawal symptoms improved steadily across the postcessation period (Piasecki et al., 1998; Piasecki et al., 2000). Another study examined smokers' depressive symptom profiles across both precessation and postcessation periods and found that a subgroup of smokers who reported a steep decline in depressive symptoms over time was significantly more likely to maintain abstinence from smoking than a subgroup who reported an increase in depressive symptoms and a subgroup with a steady decrease in depressive symptoms (Burgess et al., 2002). These findings revealed that different subgroups of smokers experience dissimilar nicotine withdrawal profiles, which may influence smokers' success in maintaining abstinence.

Of the possible symptoms of nicotine withdrawal, postcessation negative affect has been found to be one of the most powerful predictors of cessation failure (Kenford et al., 2002). However, while much effort has been devoted to examining the differences in postcessation affective experience between abstainers and relapsers, relatively little is known about the affective experience of never-quitters. Here, we reported the findings of a secondary analysis that used self-report questionnaires and affect-modulated startle response to examine possible affective differences among abstainers, relapsers, never-quitters, and control participants who continued to smoke.

Tobacco researchers have increasingly employed psychophysiological methods, like affect-modulated startle response, to characterize nicotine's effect on nonsubjective affective processes (Cinciripini et al., 2006; Geier, Mucha, & Pauli, 2000; Orain-Pelissolo, Grillon, Perez-Diaz, & Jouvent, 2004; Piper & Curtin, 2006). The affect-modulated startle response provides a reliable index of the nonsubjective processing of emotionally evocative stimuli. The startle response, typically measured by the strength of the eyeblink response at the orbicularis oculi muscle, is a defensive reflex elicited in response to an unexpected auditory probe (Vrana, Spence, & Lang, 1988). The response, which is systematically augmented by unpleasant cues that activate the defensive system but is inhibited by pleasant cues that activate the appetitive system (Cook, III, Hawk, Davis, & Stevenson, 1991; Cuthbert, Bradley, & Lang, 1996; Lang, 1995; Vrana et al., 1988), reflects the ebb and flow of the defensive and appetitive motivational systems (Lang, Bradley, & Cuthbert, 1990; Lang, 1995).

The affect-modulated startle response has been shown to be a sensitive measure of affective reactivity between subgroups of smokers. For example, in a study that examined the effects of sex, acute nicotine administration, and 12-hr nicotine deprivation on affect-modulated startle response, we found a significant three-way interaction among the three predictors (Robinson et al., 2007). The results showed that whereas nicotine suppressed negative reactivity in both male and female deprived smokers, relative to nondeprived male smokers, nicotine increased overall startle response among nondeprived female smokers, suggesting an increase in defensive or aversive motivation. Another study found that whereas nicotine lessened startle response to smoking cues in African American, but not in Caucasian American smokers, it attenuated Caucasian American, but not African American, smokers' startle response to negative and neutral stimuli (Lam et al., 2008). The findings from the second study suggested that motivational significance of nicotine may differ for African American and Caucasian American smokers. In both studies, affect-modulated startle response uncovered affective differences between subgroups of smokers that might otherwise be undetectable using subjective self reports of affect. As such, we use the startle eyeblink reflex to investigate affective differences among subgroups of smoking with varying success in achieving abstinence.

This paper is part of a larger study that examined the relationship between nicotine withdrawal and postcessation affective changes among smokers participating in a laboratory investigation. Findings on participants' corrugators electromyography has been published elsewhere (Robinson et al., 2011). We hypothesized that, as compared with smokers who abstained, those who failed to quit would exhibit greater negative affective reactivity, as measured by the affect-modulated startle response. We did not find support for our original hypothesis. Here, we report findings from exploratory analyses that showed smokers who were unable to achieve an initial abstinence of 24 hours exhibited a different pattern of affect-modulated startle response than smokers who successfully quit, smokers who relapsed, and smokers who continued to smoke.

Methods

Participants

We recruited 115 participants (60 men, 55 women) who were interested in quitting smoking from the Houston metropolitan area. Participants enrolled in the study were paid a total of \$125 for attending one enrollment session and four laboratory sessions. Individuals were eligible for the study if they were between the ages of 18 and 59 years, smoked 10 cigarettes per day, produced an expired carbon monoxide (CO) level >8 ppm, were fluent in English, and had no uncontrolled medical illness. Individuals were ineligible if they were taking psychotropic or narcotic medications, met the criteria for a current psychiatric disorder, reported hearing loss, or were involved in a current smoking-cessation activity. The University of Texas MD Anderson Cancer Center's institutional review board approved our protocol. We obtained written informed consent from the eligible participants.

Procedures

Telephone screening, enrollment session, laboratory sessions, and questionnaires—All potential participants were initially screened in a 40-min telephone interview to establish their eligibility for our study. The interview consisted of a telephone version of the PRIME-MD semistructured interview (Spitzer et al., 1994), which screens for major mental disorders and substance use. Participants who were deemed eligible after the telephone screening were invited to attend an initial enrollment session at MD Anderson Cancer Center, during which they answered questions regarding their demographic characteristics, health, and mood history. We obtained written informed consent during this enrollment session.

During the enrollment session, participants also completed the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977), the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988), the Wisconsin Smoking Withdrawal Scale (WSWS; Welsch et al., 1999), and the Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991). The CES-D is a 20-item self-report measure developed to assess depressive symptoms in community (nonclinical) populations. The PANAS is a 20-item scale that measures positive and negative affect over the past week. The WSWS is a self-report measure of nicotine withdrawal that consists of seven subscales: Anger, Anxiety, Concentration, Craving, Hunger, Sadness, and Sleep. The FTND is a six-item questionnaire that measures nicotine dependence by assessing various components of smoking behavior such as daily intake, difficulty in refraining from smoking, and time to first cigarette.

Except for the FTND, these questionnaires were also administered at the beginning of each of the four laboratory sessions. The first (baseline) laboratory session occurred 4 or 5 days before a participant's scheduled quit date. The second, third, and fourth laboratory sessions

occurred 1–2, 3–5, and 10–14 days postcessation, respectively. To ensure similar conditions of nondeprivation, we had participants smoke one cigarette before viewing the affective slides at their first laboratory session. All participants also were asked to limit their intake of caffeinated beverages to no more than 2 cups before 8 a.m. on the day of each laboratory session.

Behavioral smoking cessation therapy—Participants were informed of their group assignment (treatment vs. control) after their first laboratory (baseline) session. Participants who were randomly assigned to the treatment condition ($n = 69$) were required to set a quit date and received a guideline based standardized smoking cessation intervention, used in our previous studies (Cinciripini, McClure, Tsoh, Wetter, & Cinciripini, 2000), and met with a doctorate-level smoking cessation counselor for 30 min at the end of each laboratory session. Participants in the treatment group who were unable to achieve or maintain abstinence at the end of the study were offered a free 10-week supply of nicotine patches. Participants in the control group ($n = 46$) were offered self-help materials based on the counseling program described above and a free 10-week supply of nicotine patches at the end of the last laboratory session.

Smoking assessment—Smoking history variables that included years of smoking and typical smoking rate, defined as cigarettes smoked per day, were assessed at the orientation session. Smoking status was also evaluated at the beginning of each laboratory session using self-reported smoking in cigarettes per day since the previous session. Abstinence was biochemically verified using a CO level cut-off of >10 ppm.

Affective slide viewing—We used a PC loaded with Psychology Tools' E-Prime software (v 1.1; Pittsburgh, PA) to present $91.5 \text{ cm} \times 122 \text{ cm}$ slide images with a digital projector on a screen approximately 1.5 m from the participant. Forty-eight color slides were presented: Twelve each from the categories of pleasant, neutral, unpleasant, and cigarette using procedures similar to those of Cuthbert et al. (1996). The pleasant, neutral, and unpleasant slides were selected from the International Affective Picture System (IAPS;¹ Center for the Study of Emotion and Attention, 1999). The unpleasant slides were selected from the negatively valenced, high arousal dimensions, the pleasant slides from the positively valenced, high arousal dimensions, and the neutral slides from the neutrally valenced, low arousal dimensions. The cigarette slides, which consisted of smoking cues such as images of burning cigarettes and people smoking in a social context, were created for this type of experiment and were validated previously (Carter et al., 2006).

Each slide was presented for 6 s, followed by a randomly determined intertrial interval (ITI), when no slides were presented, that varied from 10 to 20 s. The order of slide presentation was counterbalanced so that participants saw each picture equally often in the first through 12th positions.

Startle probe trial—The acoustic startle stimuli were generated and amplified using a PC with Psychology Tools' E-Prime software. The noise burst was presented binaurally using Sennheiser HD500 (Wedemark, Germany) headphones. The acoustic startle stimulus consisted of a 50-ms 100-dB(A) presentation of white noise with instantaneous rise time. A startle probe was presented during 32 of the 48 slides, at a random time of 2.5–5 seconds after slide onset, such that a probe was presented during 8 of the 12 slides within each

¹The following IAPS slides were used: Pleasant, 4220, 4652, 4658, 4659, 4660, 4670, 5621, 5629, 8030, 8370, 8490, and 8500; Neutral, 7000, 7010, 7020, 7030, 7040, 7050, 7060, 7080, 7090, 7100, 7150, and 7170; Unpleasant, 3010, 3060, 3100, 3120, 3130, 3150, 3170, 3500, 6230, 6350, 6560, and 9410. The pleasant ($M = 6.54$, $SD = 0.59$) and unpleasant pictures ($M = 6.96$, $SD = 0.30$) did not differ on arousal but did differ from neutral ($M = 2.80$, $SD = 0.39$), $p < .05$.

valence condition. Counterbalancing for slide order was arranged so that, across subjects, each slide would be associated with a startle probe equally often. To enhance unpredictability of the startle presentation, we presented 16 startle probes during ITI, but these were not included in our analyses.

Startle response measurement—Electromyograph (EMG) electrodes (Ag-AgCl) filled with saline gel were attached to the participant's face on skin covering the orbicularis oculi muscle using a bipolar configuration (Fridlund & Cacioppo, 1986). The EMG signals were acquired and amplified with BIOPAC Systems (Goleta, CA) EMG100A Electromyogram Amplifier modules connected to a BIOPAC Systems MP100WSW bioamplifier. The data were recorded and displayed using BIOPAC Systems' AcqKnowledge III data acquisition software (version 3.5.3), with a sampling rate of 1,000 Hz. A 10- to 500-Hz bandpass filter (Tassinary & Cacioppo, 2000) and a 60-Hz notch filter were used online. We scored the orbicularis oculi facial EMG signal in microvolts (μV) after the results were rectified and smoothed using a five-sample boxcar filter. Trials with clear movement artifact or excessive baseline activity were marked as missing.

Data Reduction

Large individual differences exist in the absolute magnitude (μV) of the human startle response to an acoustic probe as measured by EMG activity in the orbicularis oculi muscle (Blumenthal et al., 2005). One way to minimize the variance due to individual differences and improve the probability of detecting the variance due to experimental conditions is to use standardized scores (Blumenthal et al., 2005). Prior to analyses, valence-related startle responses were standardized using each participant's own startle response elicited during the ITI, when no background cues were presented, as the reference distribution (Bonnet, Bradley, Lang, & Requin, 1995). First, we calculated the overall means and standard deviations of all ITI-related startle responses for each participant across all four sessions. We then applied the equation $T\text{score} = 50 + 10 * [(startle\ response\ to\ valence\ condition - overall\ mean\ of\ ITI-related\ startle\ response)/overall\ standard\ deviation\ of\ ITI-related\ startle\ response]$ to all valence-related responses to convert the absolute startle amplitudes to T scores. Outlying responses, defined as observations three standard deviations above the mean T score of 50, were identified and excluded from our analyses. Out of a total 14455 startle response, 17 outliers were identified and excluded from analyses. Once all individual trial responses were transformed to T scores, a mean valence T score was computed by averaging responses to all presentations of slides of the same valence within a session. As a result, four mean valence T scores were calculated for each session.

Statistical Analysis

The repeated design of our current study produced startle responses that were nested within a three-level structure of longitudinal data (i.e., stimulus valence nested within sessions nested within participants). Therefore, we used the PROC MIXED procedure in SAS (PROC MIXED, SAS Institute Inc, Cary, NC, version 9.1, Littell, Milliken, Stroup, Wolfinger, & Schabenberfer, 2006) to conduct linear multilevel modeling (LMM) to estimate the effects of Group, Session, and Stimulus Valence on startle responses. Analyses of an intercept-only model (i.e., a model with no predictors) found that an unstructured covariance structure provided the best fit with the correlation structure in the data set. A standard approach to model building was followed in which three-level LMMs that included stimulus valence as a level 1 predictor, session as a level 2 predictor, group as a level 3 predictor and cross-level interactions were conducted, in a step-wise fashion, to predict startle responses. All predictors were initially entered as fixed-effect predictors. To assess whether the slopes characterizing the relationship between lower-level predictors (e.g., stimulus valence and session) and startle responses varied among sessions and/or among

participants, we added the random slope coefficients for stimulus valence and session to the model one at a time. We used a log likelihood ratio test to evaluate whether adding a random slope coefficient significantly improved the goodness-of-fit of a model over one without the coefficient.

Unlike startle responses, participants' answers to self-report questionnaires (CES-D, PANAS, and WSWS) were nested within a two-level structure of longitudinal data (i.e., sessions nested within participants). Thus, two-level LMMs were conducted to evaluate the effects of session (level 1 predictor) and group (level 2 predictor) on these responses. Again, we used a log likelihood ratio test to assess model fit between one where session was entered as a fixed effect and another where the relationship between session and self-report measure responses was estimated to vary among participants.

Results

Our study focused on examining the affect-modulated startle response of 69 participants (32 men, 37 women) who were assigned to the behavioral smoking treatment condition and 46 participants (28 men, 18 women) who were assigned to the control condition. We hypothesized that smokers who failed to quit would exhibit significantly higher negative affective reactivity than smokers who abstained. However, we failed to find a significant main effect for abstinence status (i.e., control participants, abstaining participants, and nonabstaining participants) on startle response; nor did we find any significant interaction effect among abstinence status, stimulus valence (i.e., pleasant, neutral, unpleasant, and cigarette), and postcessation time points on startle response.

On subsequent, exploratory analyses, we further categorized the nonabstaining smokers into relapsers and never-quitters. At the orientation session, the four groups (i.e., controls, abstainers, never-quitters, and relapsers) did not differ from one another in their age, sex, race, education, typical smoking rate, years of smoking, FTND score, depression history, PANAS score, and CES-D score (see Table 1). All participants in the control condition continued to smoke at their usual level throughout the study (see Table 2). Of the 69 smokers who were assigned to the treatment condition, 34 (49%) continuously abstained throughout the postcessation time period (abstainers), 16 (23%) never abstained from smoking for at least 24 hours (never-quitters), and 19 (28%) achieved initial abstinence (abstained from smoking for 24 hours) but lapsed and returned to regular smoking (relapsers). One smoker who we categorized as abstainer reported smoking at the first postcessation session but reported complete abstinence on every day thereafter. Two of the abstainers lapsed and smoked a single cigarette during the study. Although the never-quitters were unable to stop smoking, they appeared to have tried to quit and had, on average, reduced their daily smoking rate significantly from baseline by 57% at 1–2 days postcessation. However, by 3–5 days postcessation, never-quitters have returned to smoking at a rate similar to that recorded at baseline. Among the relapsers, the majority of them (11 out of 19) relapsed and resumed regular smoking after they had attended their first postcessation laboratory session, typically scheduled between 1 and 2 days after their scheduled quit date (see Table 3). Another subgroups of relapsers (6 out of 19) did not resumed regular smoking until after they had attended their second postcessation laboratory session, typically scheduled between 3 and 5 days after their scheduled quit date. One relapser, who had not yet quit during the first postcessation visit, achieved smoking abstinence by the second visit but relapsed and reported to be smoking regularly at the third and final visit. One relapser who had quit on the scheduled quit date relapsed at the second session, but quit again and reported abstinence by the final visit.

Startle Response

We first conducted analyses to determine whether our physiological measures were sensitive to the valence of our slide stimuli and whether startle responses habituated across pre- and postcessation sessions as expected. We conducted LMM, including all subjects, regressing startle response on stimulus valence and session. We found significant main effects for stimulus valence, $F(3, 342) = 131.89, p < .0001$, and a significant main effect for session, $F(1, 1636) = 18.43, p < .0001$ (see Figure 1). To examine possible sex effect on startle response, a second LMM was conducted in which startle response was regressed on sex, stimulus valence, and session. Significant main effects were found for sex, $F(1, 113) = 4.93, p < .05$, stimulus valence, $F(3, 342) = 31.14, p < .0001$, and session, $F(1, 1626) = 5.94, p < .01$. However, no significant interaction among the three predictors was found.

We constructed LMMs to regress startle response on stimulus valence, session, and group. We found that the model with random slope effects for both stimulus valence and session significantly improved the model's fit over the model with a random slope effect for stimulus valence only ($\Delta\chi^2 = 32.9, p < .0001$) and the model in which all predictors were treated as fixed effects ($\Delta\chi^2 = 63.9, p < .0001$).

Using the best-fitting model, we found a significant Stimulus Valence $\times$ Session $\times$ Group interaction effect on startle responses, $F(9, 1612) = 1.89, p < .05$. Figure 2 shows that among controls, abstainers, and relapsers, stimulus valence exerted a significant and consistent modulating effect on startle amplitude (unpleasant slides > neutral slides > pleasant slides > cigarette slides) across all sessions of the study.

However, among never-quitters, the effect of stimulus valence on startle responses dissipated as the sessions progressed. The effect of stimulus valence on the startle response, while significant at baseline and at 1–2 days postcessation, became nonsignificant at sessions that occurred at 3–14 days postcessation, precessation baseline: $F(3, 333) = 15.48, p < .0001$; 1–2 days postcessation: $F(3, 333) = 16.21, p < .0001$; 3–5 days postcessation: $F(3, 333) = 1.92$, nonsignificant [*ns*]; 10–14 days postcessation: $F(3, 333) = 1.41, ns$. Furthermore, never-quitters exhibited a significantly larger reduction in startle potentiation, relative to ITI, to unpleasant stimuli (simple slope = -3.94) than to cigarette, simple slope = -1.81 ; $t(1612) = 3.16, p < .001$, pleasant, simple slope = -1.38 ; $t(1612) = 3.96, p < .001$, and neutral, simple slope = -1.63 ; $t(1612) = 3.52, p < .001$, stimuli across the preand postcessation sessions. Across groups, never-quitters' reduction in startle potentiation to unpleasant stimuli across session was significantly larger than that of controls, simple slope = -1.38 ; $t(1612) = 2.25, p < .05$, abstainers, simple slope = -1.36 ; $t(1612) = 2.15, p < .05$, and relapsers, simple slope = -1.35 ; $t(1612) = 2.00, p < .05$.

To examine if male and female never-quitters showed similar degradation in startle responses across the postcessation period, a LMM was conducted in which startle response was regressed on sex, group, stimulus valence, and session. A significant sex main effect, $F(1, 107) = 5.54, p < .05$, was found. However, sex did not interact significantly with any of the other predictors. We also repeated the final model and added age, race, depression history, typical smoking rate, years of smoking, baseline FTND score to the analysis. Adding these covariates to the model did not significantly alter the results.

Finally, analyses were conducted to determine if these findings reflected genuine group differences or if they simply reflected participants' smoking status (i.e., smoking or not smoking) at any given time. First, we included all participants (controls, abstainers, never-quitters, and relapsers) and conducted one analysis for each postcessation time point. For each analysis, we examined the effect of smoking status (i.e., smoking or not smoking) and stimulus valence on startle response. We found neither significant main effect for smoking

status nor significant interaction effect between smoking status and stimulus valence. Second, we included only participants in the treatment group (abstainers, never-quitters, and relapsers) and conducted one analysis for each postcessation time point. For each analysis, we examined the effect of smoking status (i.e., smoking or not smoking) and stimulus valence on startle response. We failed to find either significant main effect for smoking status or significant interaction effect between smoking status and stimulus valence.

Self-Report Measures

We constructed LMMs to examine the effects of Group and Session on CES-D, PANAS, and WSWs scores. We found no significant results when we compared postcessation depressive symptoms, as measured by CES-D, in controls, abstainers, never-quitters, and relapsers. However, we did find a significant Group $\times$ Session interaction effect on negative affect, as measured by the PANAS negative subscale, for controls, abstainers, never-quitters, and relapsers, $F(3, 323) = 2.74, p < .05$ (see Figure 3). The results indicated that adding a random slope effect to session did significantly improve the goodness-of-fit for a model that used group and session to predict self-report negative affect. Our results showed that abstainers, simple slope = 0.07; $t(323) = 2.04, p < .05$, and never-quitters, simple slope = 0.69; $t(323) = 2.35, p < .05$, reported a significant increase in negative affect across the precessation and postcessation periods compared with control participants who continued to smoke (simple slope = -1.04). No significant difference in negative affect changes was found among abstainers, never-quitters, and relapsers.

Using the best-fitting model, which included session as a random slope effect, we also found a significant Group $\times$ Session interaction effect on positive affect, as measured by the PANAS positive subscale, $F(3, 323) = 3.78, p < .05$ (see Figure 4). We found that abstainers (simple slope = 0.53) showed a significant increase in positive affect across the pre- and postcessation sessions as compared with relapsers, simple slope = -0.84 ; $t(323) = -2.13, p < .05$, and never-quitters, simple slope = -1.29 ; $t(323) = -3.13, p < .01$. No difference in positive affect changes was found between control participants and the other three groups of smokers.

We found a significant Group $\times$ Session interaction effect, $F(3, 323) = 4.58, p < .01$, on WSWs anxiety subscale scores when we applied the best-fitting model that included a random slope effect to session (see Figure 5). The results indicated that control participants, who continued to smoke, reported a significant decrease in self-reported anxiety withdrawal symptoms (simple slope = -0.64) than the changes reported by abstainers, simple slope = 0.11; $t(323) = 2.79, p < .01$, relapsers, simple slope = 0.37; $t(323) = 2.98, p < .01$, and never-quitters, simple slope = 0.20; $t(323) = 2.27, p < .05$. No differences were found among the three treatment subgroups. We did not find any significant differences in the smokers' responses to any other WSWs subscales (e.g., Anger, Concentration, Craving, Hunger, Sad, and Sleep).

These analyses were repeated with sex, age, race, depression history, typical smoking rate, years of smoking, baseline FTND score added to the models. No significant sex difference was found and including these covariates in the models did not significantly alter the results.

Discussion

Our study found that never-quitters, a little-studied subgroup of smokers who were unable to achieve initial abstinence, exhibited a pattern of affective reactivity as assessed by startle responses that was significantly different from those exhibited by smokers who were instructed to continue to smoke (controls), smokers who were able to abstain for 24 hours (abstainers), and smokers who achieved initial abstinence but relapsed (relapsers). Our

results showed that, starting at approximately three days after their scheduled quit date, never-quitters exhibited an atypical response pattern in which emotional pictures no longer modulated the startle response. In particular, the never-quitters exhibited, relative to ITI, blunted startle potentiation to unpleasant stimuli. These findings indicate that as never-quitters struggle to stop smoking, their affective reactions to unpleasant, neutral, pleasant, and cigarette stimuli become less distinct and eventually become a relatively flat, undifferentiated reactivity. Results from analyses that regressed startle response on smoking status and stimulus valence further suggested that this lack of startle modulation was unique to never-quitters and could not simply be explained by the effect of smoking status alone. Although female participants generally showed significantly larger startle responses, sex did not moderate any of the current findings and both male and female never-quitters displayed flat reactivity to emotional pictures starting shortly after their scheduled quit date.

This lack of affective modulation of the startle response has been documented previously in studies that investigated affective reactivity in both clinically and nonclinically depressed individuals (Allen, Trinder, & Brennan, 1999; Dichter, Tomarken, Shelton, & Sutton, 2004; Dichter & Tomarken, 2008; Forbes, Miller, Cohn, Fox, & Kovacs, 2005; Kaviani et al., 2004; Larson, Nitschke, & Davidson, 2007; Mneimne, McDermut, & Powers, 2008). Four studies found that while the startle responses of nondepressed individuals reflected the prototypical valence modulation, the startle responses of patients who were diagnosed with major depressive disorder were neither attenuated by pleasant stimuli nor potentiated by unpleasant stimuli (Allen et al., 1999; Dichter et al., 2004; Dichter & Tomarken, 2008; Forbes et al., 2005). Furthermore, there were some indications that the relationship between depression and affective modulation of the startle response might be moderated by the severity of the patients' depressive symptoms. That is, the lack of affective modulation of startle response was only found in highly depressed patients (Allen et al., 1999; Kaviani et al., 2004) and in patients who reported a high level of anhedonic symptoms (Kaviani et al., 2004).

In addition to clinically depressed patients, a lack of affective modulation of startle response was also evident in individuals with nonclinical depressive symptoms. Mneimne and colleagues (2008) examined college students and found that, compared with students who reported no depressive symptoms, defined as scoring <11 on the Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996), those who reported nonclinical depressive symptoms exhibited undifferentiated startle responses to pleasant, unpleasant, and neutral stimuli alike. Another study found that, relative to nondepressed college students, nonclinically depressed students showed reduced startle attenuation to pleasant stimuli but normal startle potentiation to unpleasant stimuli (Larson et al., 2007).

Previous studies have established a link between the lack of affective modulation of startle response and either clinical or nonclinical depression. Although we found no evidence that never-quitters had been diagnosed with major depressive disorder more often than had abstainers, relapsers, and control participants, never-quitters reported a significant increase in self-reported negative affect and a significant decrease in self-reported positive affect, as measured by the PANAS negative and positive affect subscales respectively, across the postcessation sessions. Both PANAS negative and positive affect subscales have been shown to be significantly correlated with the BDI, and they measure two dimensions of mood that are consistent with subjective depressive experiences of distress and anhedonia (Watson et al., 1988). Thus, while it is unlikely that a diagnosis of depression would account for the undifferentiated startle response in never-quitters, the post-cessation increase in negative affect and decrease in positive affect reported by never-quitters may explain the decomposition of their affect-modulated startle response.

Furthermore, it has been suggested (Dichter & Tomarken, 2008; Mneimne et al., 2008) that depressed individuals' startle hyporesponsivity to affective stimuli is consistent with emotion context insensitivity (ECI), a condition characterized by diminished reactivity to both pleasant and unpleasant stimuli (Rottenberg, Gross, & Gotlib, 2005). Rottenberg and colleagues (2005) hypothesized that ECI is detrimental to individuals' adjustment to the environment and have shown that, among depressed individuals, those who exhibited blunted reactivity to affective stimuli were significantly less likely to recover from depression than individuals who exhibited normal reactivity (Rottenberg, Kasch, Gross, & Gotlib, 2002). Given never-quitters' nonclinical depression and blunted responses to both appetitive and defensive stimuli, it is conceivable they would experience more difficulty adjusting to the many demands that were associated with quitting smoking and ultimately failed in establishing abstinence that was longer than 24 hours.

These findings are significant because they illustrated a phenomenon that had, heretofore, rarely been studied—a subgroup of smokers who were unable to abstain for even a brief amount of time and who reported depressive symptoms and exhibited a lack of startle modulation by valence. It is yet unclear whether the nonclinical depression and insensitivity to emotional context found in never-quitters was a preexisting trait that manifested itself more prominently when never-quitters were challenged by a quit attempt, or a by-product resulting from never-quitters becoming disillusion about their ability to attain success in smoking abstinence. Future studies should clarify the role depression and affective insensitivity play in smoking cessation.

In addition to depression, others have found a link between lack of affective modulation of startle response and low fearfulness (Cook, Davis, Hawk, Spence, & Gautier, 1992) and psychopathy (Patrick, Bradley, & Lang, 1993). However, there were no indications that never-quitters failed to show the prototypical affect modulated reactivity because there were more fearless or were more likely to meet criteria for psychopathy than abstainers, relapsers, and control participants.

A previous study have found that smokers who exhibited a higher overall startle response were more likely than those with lower level of startle response to quit smoking (Postma, Kumari, Sharma, Hines, & Gray, 2001), but we were unable to replicate that finding in our current study. Another study (Cinciripini et al., 2006) found that short-term (12 hours) nicotine deprivation attenuated startle responding to cigarette stimuli. However, the current results failed to show any group effects on startle modulation to cigarette slides. In fact, the current study did not find any difference in startle reactivity across the four laboratory sessions among abstainers, relapsers, and smokers who continued to smoke. Unlike Cinciripini et al. (2006), which investigated the acute effect of nicotine on startle responding among nontreatment seeking smokers, the current study examined affective reactivity among quitting smokers at time points when they had stopped smoking for a significantly longer period of time. The discrepancies in findings suggest that the startle paradigm may be sensitive to measuring the short-term nicotine deprivation, but not long-term smoking cessation effect on affect.

Regarding self-reported affective symptoms, we found that never-quitters experienced a significantly higher level of negative affect, as measured by PANAS negative subscale, than control participants; and a significantly lower level of positive affect, as measured by PANAS positive subscale, than abstainers across the postcessation period. These findings were consistent with our contention that never-quitters experienced nonclinical depressive symptomatology, which might explain their diminished sensitivity to both appetitive and defensive stimuli.

Abstainers reported significant increases in both positive and negative affect across the postcessation sessions. The findings suggest that while abstainers may feel positive and encouraged about their quitting progress, they were not immune to experiencing subjective negative affective symptoms. Compared with control participants, smokers assigned to the treatment group, regardless of their abstinence status, reported a significant increase in self-reported anxiety across the postcessation sessions. Anxiety is a symptom of nicotine withdrawal and previous studies (e.g., Hughes, Higgins, & Bickel, 1994) have found, as we did in the current study, that when smokers tried to quit, they experienced a transient increase in anxiety. However, it is unclear why the current study failed to find an increase in other withdrawal symptoms (e.g., sleep difficulties, lack of concentration) as measured by the WSWS.

Using self-report measures, we did not find that relapsers reported more postcessation negative affect than abstainers. Previous findings have established a strong link between postcessation negative affect and relapse (Borland, 1990; Brandon et al., 1990; Shiffman & Waters, 2004; Shiffman et al., 1996). However, these studies either asked smokers to recall their affect at the time of lapse or used ecological momentary assessment to record, in real time, smokers' negative affect at the time they lapsed. In contrast, we assessed smokers' negative affect at the time of attendance at laboratory sessions, which were temporally removed from when incidences of postcessation smoking occurred and might explain why we failed to find a higher level of postcessation negative affect among relapsers than among abstainers.

Our current study has several limitations. First, the findings reported here are borne out of secondary exploratory analyses, which were not informed by a priori hypotheses. The findings reported here need to be replicated in future studies that gear specifically toward the examination of never-quitters. Second, the term "never-quitter" describe smokers who were unable to abstain from smoking for >24 hours within the two weeks duration of the current study. Some of the never-quitters might have successfully quit, and relapsed, in the past; others might require multiple attempts and/or a longer time—beyond the current study's 2-week time span—in order to achieve abstinence. Thus, the current findings need to be replicated in future studies that 1) take into account never-quitters' history of cessation attempts and success and 2) use a prospective longitudinal design that examines the relation between affective reactivity and longer-term cessation success or failure among never-quitters. Third, participants were monitored only for 2 weeks after their scheduled quit date, and thus, the findings from the current study cannot be generalized to describe long-term affect reactivity among controls, abstainers, never-quitters, and relapsers. Fourth, our study examined a relatively small group of smokers, limiting its power to detect other potential subgroup differences. Our findings need to be replicated in future studies with a larger sample size. Finally, it was difficult to classify the consumption behaviors and withdrawal symptoms of smokers who relapsed into an interindividual category like "relapser." Depending on their quitting success at various times, relapsers' consumption behaviors and withdrawal symptoms may change from session to session, and they may behave more like abstainers at one session but mimic the struggles of never-quitters at another. Future studies should consider modeling the abstinence status as an intraindividual factor to account for these changes made by the relapsers.

Using affective modulated startle response and self-report questionnaires, this study found a significant difference in the affective reactivity between smokers who could and smokers who could not establish an initial abstinence of 24 hours. Never-quitters have received relatively little attention and were often excluded from analyses or counted as relapsers in previous studies. However, these findings caution researchers in either discounting never-quitters as unmotivated quitters or treating them simply as smokers who relapsed early. Our

results showed that although never-quitters were unsuccessful in abstaining from smoking, they often made obvious efforts to quit and reduced their daily cigarette consumption by as much as 50%. Furthermore, we found that unlike abstainers and relapsers, when never-quitters made an attempt to quit, they exhibited an atypical startle response profile that had previously been observed among depressed individuals. This particular finding highlights the need for future studies to consider never-quitters as a separate subgroup of smokers who experience a distinctive affective hyporeactivity profile and may require better understanding of their experience and a uniquely tailored intervention to assist them in quitting smoking.

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Figure 1.

Affect-modulated startle response (T score) across precessation and postcessation sessions. Session 1 = 4 or 5 days precessation, session 2 = 1–2 days postcessation, session 3 = 3–5 days postcessation, and session 4 = 10–14 days postcessation.

Figure 2. Affect-modulated startle response (T score) for a) never-quitters, b) abstainers, c) relapsers, and d) controls, across precessation and postcessation sessions. Session 1 = 4 or 5 days precessation, session 2 = 1–2 days postcessation, session 3 = 3–5 days postcessation, and session 4 = 10–14 days postcessation.

Figure 3.

Self-reported negative affect as measured by PANAS negative subscale for controls, abstainers, relapsers, and never-quitters, across precessation and postcessation sessions. Session 1 = 4 or 5 days precessation, session 2 = 1–2 days postcessation, session 3 = 3–5 days postcessation, and session 4 = 10–14 days postcessation.

Figure 4. Self-reported positive affect as measured by PANAS positive subscale for controls, abstainers, relapsers, and never-quitters, across precessation and postcessation sessions. Session 1 = 4 or 5 days precessation, session 2 = 1–2 days postcessation, session 3 = 3–5 days postcessation, and session 4 = 10–14 days postcessation.

Figure 5.

Self-reported anxiety symptoms as measured by WSWs anxiety subscale for controls, abstainers, relapsers, and never-quitters, across precessation and postcessation sessions. Session 1 = 4 or 5 days precessation, session 2 = 1–2 days postcessation, session 3 = 3–5 days postcessation, and session 4 = 10–14 days postcessation.

Table 1

Demographic Characteristics of Participants

Measure	Controls (<i>n</i> = 46)	Abstainers (<i>n</i> = 34)	Never-quitters (<i>n</i> = 16)	Relapsers (<i>n</i> = 19)	<i>F</i> value or χ^2
Age in years, mean (standard deviation [<i>SD</i>])	37.0 (11.35)	40.59 (9.92)	43.36 (8.56)	37.05 (11.92)	1.71
Sex: Female, <i>n</i> (%)	18 (39%)	18 (53%)	8 (50%)	11 (58%)	2.55
Ethnicity/race, <i>n</i> (%)					5.11
African American	14 (31%)	11 (32%)	7 (44%)	7 (36%)	
European American	24 (52%)	17 (50%)	8 (50%)	6 (32%)	
Hispanic or other	8 (17%)	6 (18%)	1 (6%)	6 (32%)	
Education, <i>n</i> (%)					4.08
High school	13 (28%)	11 (32%)	8 (50%)	5 (26%)	
Some college	23 (50%)	16 (47%)	7 (44%)	9 (48%)	
College graduate	10 (22%)	7 (21%)	1 (6%)	5 (27%)	
Body mass index, mean (<i>SD</i>)	26.95 (5.53)	27.27 (5.58)	28.74 (6.91)	25.36 (4.23)	1.04
Affect variables at baseline					
Depression history, <i>n</i> (%)	15 (33%)	10 (29%)	3 (19%)	8 (42%)	2.29
CES-D total score, mean (<i>SD</i>)	8.84 (7.09)	8.44 (6.05)	7.19 (5.26)	7.53 (10.35)	0.29
PANAS negative affect score, mean (<i>SD</i>)	15.24 (4.44)	14.97 (4.83)	14.88 (5.33)	13.89 (3.87)	0.39
PANAS positive affect score, mean (<i>SD</i>)	34.62 (7.76)	36.65 (8.02)	34.44 (9.52)	36.26 (5.18)	0.60
Smoking variables					
Typical smoking rate, mean (<i>SD</i>)	21.23 (7.87)	22.00 (9.24)	23.07 (8.53)	17.21 (3.94)	1.97
Years of smoking, mean (<i>SD</i>)	19.0 (11.04)	21.10 (10.37)	25.71 (10.19)	20.11 (12.48)	1.32
FTND score, mean (<i>SD</i>)	4.61 (2.17)	4.56 (2.32)	5.13 (2.39)	4.58 (1.77)	0.28

Table 2

Mean Daily Cigarette Consumption and Expired CO Across Sessions

	Baseline session	1-2 days postcessation	3-5 days postcessation	10-14 days postcessation	F value
Control (<i>n</i> = 46)					
Cigarette consumption, mean (<i>SD</i>)	16.24 (9.28)	20.52 (16.07)	20.14 (9.97)	20.57 (12.32)	1.35
Expired CO, mean (<i>SD</i>)	24.17 (12.15)	21.68 (12.98)	23.09 (12.18)	24.13 (13.52)	0.39
Abstainers (<i>n</i> = 34)					
Cigarette consumption, mean (<i>SD</i>)	14.05 (7.80)	0.51 [‡] (2.40)	0.93 [‡] (5.20)	0.02 [‡] (0.05)	67.11 ^{**}
Expired CO, mean (<i>SD</i>)	25.56 (9.60)	3.96 [‡] (5.40)	2.79 [‡] (1.30)	2.78 [‡] (1.45)	136.59 ^{**}
Never-quitters (<i>n</i> = 16)					
Cigarette consumption, mean (<i>SD</i>)	11.69 (7.68)	5.06 [‡] (5.85)	10.14 (7.68)	9.68 (5.17)	2.87 [*]
Expired CO, mean (<i>SD</i>)	26.13 (9.80)	17.69 (9.31)	18.38 (13.82)	24.31 (13.31)	2.01
Relapsers (<i>n</i> = 19)					
Cigarette consumption, mean (<i>SD</i>)	12.47 (7.58)	0.17 [‡] (0.42)	3.13 [‡] (4.01)	10.69 (7.74)	19.06 ^{**}
Expired CO, mean (<i>SD</i>)	25.68 (10.54)	3.14 [‡] (1.94)	12.37 [‡] (10.49)	23.78 (13.7)	19.72 ^{**}

[‡]Tukey's Studentized Range test indicated significant difference from baseline session.

^{*}*p* < .05.

^{**}*p* < .0001.

Table 3

Smoking Status of the Four Different Subgroups of Relapsers at Three Different Postcessation Time Points

	1–2 days postcessation	3–5 days postcessation	10–14 days postcessation
Subgroup 1 ($n = 11$)	Abstinent	Smoking	Smoking
Subgroup 2 ($n = 6$)	Abstinent	Abstinent	Smoking
Subgroup 3 ($n = 1$)	Smoking	Abstinent	Smoking
Subgroup 4 ($n = 1$)	Abstinent	Smoking	Abstinent