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Emotional reactivity to emotional and smoking cues during smoking abstinence: Potentiated startle and P300 suppression

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Abstract

Negative affect is thought to be an important factor in the maintenance of cigarette smoking, and thus it is important to further develop objective measures of smoking-related emotional responses. Nonsmokers, nonabstinent smokers, and abstinent smokers participated in a cue reactivity task where eyeblink startle amplitude and startle probe P300 (P3) suppression were measured during the presentation of emotional pictures. During unpleasant pictures, the amplitude of both measures was smaller in nonabstinent smokers than in nonsmokers or abstinent smokers. P3 suppression, but not startle amplitude, was larger in abstinent smokers than in nonsmokers. Abstinence-induced increases in cigarette craving were associated with P3 suppression during tobacco-related pictures. Results suggest that tobacco abstinence increases emotional reactivity to unpleasant stimuli, which is consistent with negative reinforcement models of tobacco addiction.

Despite widespread awareness of the adverse health consequences of smoking and the benefits of quitting, it is estimated that 20 percent of the population continues to smoke cigarettes (Centers for Disease Control and Prevention, 2007). Most attempts to quit are unsuccessful, and in many cases relapse occurs during the first 2 days of abstinence (e.g., Gritz, Carr, & Marcus, 1991), which coincides with peak severity of withdrawal-induced affective changes such as increased anxiety and cigarette craving (e.g., Hughes, 1992). Smokers often report that anxiety, stress, or craving precipitate relapse (e.g., Shiffman et al., 2007) and that smoking a cigarette decreases anxiety (e.g., Juliano & Brandon, 2002). These effects provide support for negative reinforcement theories of tobacco addiction, which argue that dependent smokers continue smoking to escape or avoid negative affect (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Watkins, Koob, & Markou, 2000). Negative reinforcement theories predict that interventions that reduce the severity of aversive withdrawal symptoms or the anxiolytic consequences of smoking may be the most effective smoking cessation therapies, and assessment of smokers' emotional responses is becoming common in clinical investigations (e.g., West, Baker, Cappelleri, & Bushmakina, 2008).

Studies of withdrawal-induced affective changes have relied almost exclusively on self-report measures. This introduces several threats to reliability and validity, including variability in self-reported emotion and craving as a function of past withdrawal episodes (Tate, Pomerleau, & Pomerleau, 1993), smokers' expectancies about withdrawal symptoms

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(Gottlieb, Killen, Marlatt, & Taylor, 1987; Hughes, Pickens, Spring, & Keenan, 1985), and repeated administration of the same questionnaire (Gilbert et al., 1998). Many self-report measures may also lack sensitivity to subtle cognitive and emotional changes induced by nicotine administration (Tiffany, 1990). Furthermore, self-report measures cannot be used in animal models, increasing the difficulty of translating preclinical studies of potential smoking cessation treatments to clinical trials. It is therefore important to develop objective behavioral and physiological measures that can be used in conjunction with subjective measures (Lang, Bradley, & Cuthbert, 1990, 1998). This article focuses on the use of emotion-modulated startle as an objective, psychophysiological measure of smoking-related emotional responses.

Emotion-modulated startle refers to changes in the amplitude of the acoustically elicited startle reflex as a function of the emotional valence of stimuli that are present when the startle probe is delivered: startle amplitude increases in the presence of aversive stimuli (fear-potentiated startle) and decreases in the presence of pleasant stimuli (pleasure-attenuated startle). Fear-potentiated startle and pleasure-attenuated startle are reliable phenomena in humans (e.g., Grillon & Davis, 1997; Schupp et al., 2004) and in nonhuman animals (Davis & Astrachan, 1978; Schmid, Koch, & Schnitzler, 1995). The basic neural circuitry of fear-potentiated startle has been identified (e.g., Walker, Toufexis, & Davis, 2003) and suggests that the degree of startle potentiation or inhibition is reflective of the relative activation of appetitive or defensive motivational systems in the brain (Lang et al., 1990, 1998). The potential for detailed neurobiological analysis of affective startle modulation suggests that startle reflex measurement may be a useful model of affective changes induced by tobacco withdrawal.

Indeed, startle amplitude is potentiated in rats withdrawing from repeated daily nicotine injections (Engelmann, Radke, & Gewirtz, 2009) or continuously-infused nicotine (Helton, Modlin, Tizzano, & Rasmussen, 1993), consistent with the emergence of an anxiety-like state during tobacco withdrawal. In human smokers there is no evidence of such potentiation of “baseline” startle (Della Casa, Hofer, Weiner, & Feldon, 1998; Duncan et al., 2001; Grillon, Avenevoli, Daurignac, & Merikangas, 2007; Hogle & Curtin, 2006; Mueller, Mucha, & Pauli, 1998), likely due to large individual differences in startle amplitude. In some studies, however, abstinent smokers have shown greater potentiated startle to aversive cues (Cinciripini et al., 2006; Grillon et al., 2007; Hogle & Curtin, 2006), which suggests that drug deprivation alters the response of brain motivational systems to the presentation of negative emotional cues. However, this finding has not been consistently replicated in studies that used similar procedures (Geier, Mucha, & Pauli, 2000; Piper & Curtin, 2006). Thus, one goal of the current study was to provide an additional evaluation of whether increased startle responses to aversive cues reliably emerge during tobacco abstinence.

In contrast to negative affective pictures, previous studies have reported tobacco-related pictures to inhibit startle reactivity in abstinent and nonabstinent smokers (Cinciripini et al., 2006; Geier et al., 2000). These results might suggest that tobacco cues are generally appetitive for smokers, even in states of deprivation. On the other hand, the cues may only have been appetitive because the abstinent smokers were allowed to smoke immediately after the test session. Had the prospect of smoking a cigarette not been imminent, it is possible that smoking cues would have been aversive, eliciting responses associated with conditioned withdrawal (Poulos, Hinson, & Siegel, 1981; Wikler, 1973) or “frustrative nonreward” (cf. Drobos et al., 2001; Hull, 1943).

The current study was designed to answer several questions regarding startle modulation to pictorial stimuli during smoking cessation. First, in light of the issues raised above, we examined whether smoking cues would potentiate startle when presented 24 h into a 48-h

period of abstinence. Second, in addition to smoking-relevant pictures, we included standard neutral, pleasant, and unpleasant images as part of the picture set. The presence of both the latter two categories allowed more powerful inferences regarding the relative valence of the smoking pictures in abstinent and non-abstinent conditions (cf. Drobles et al., 2001). Specifically, we predicted that 24 h of abstinence would potentiate startle to unpleasant cues, but not pleasant cues (cf. Cinciripini et al., 2006; Grillon et al., 2007; Hogle & Curtin, 2006). Third, we included a control group of nonsmokers, which has not been consistently used in previous studies (e.g., Cinciripini et al., 2006; Hogle, Kaye, & Curtin, 2010) but is important in determining how smokers differ from nondependent individuals (Glautier & Tiffany, 1995). Finally, we selected smoking pictures on the basis of a preliminary ratings study to ensure that the smoking stimuli were viewed as highly pleasant and arousing by smokers.

This study also extended the cue reactivity literature by measuring the startle probe P300 (P3) in addition to startle blink amplitude. This ERP measure can be used to gauge the attention paid to a stimulus set (Isreal, Chesney, Wickens, & Donchin, 1980; Schupp, Cuthbert, Bradley, Birbaumer, & Lang, 1997). Hence, by measuring both startle blink amplitude and startle probe P3 suppression, it is possible to measure concurrently the effects of the emotional cue on relative activation of appetitive and defensive motivational systems and recruitment of cortical arousal systems (Schupp et al., 2004). Previous research has found evidence of startle probe P3 suppression during tobacco pictures in nonabstinent smokers (Versace et al., 2010). In the current study, we extended the measurement of startle probe P3 suppression to abstinent smokers and predicted that startle probe P3 suppression during tobacco pictures would be greater in abstinent smokers than in nonabstinent smokers (cf. Sayette & Hufford, 1994), and that smokers reporting the highest levels of craving would have the most P3 suppression.

Method

Design

This study was designed to measure psychophysiological responses during an emotional picture-viewing task 24 h into a 48-h period of tobacco abstinence. Participants came to the laboratory for three sessions (Fig. 1). During Visit 1, all participants completed several baseline measures and smokers were randomly assigned to the abstinent group or nonabstinent group. Visits 2 and 3 were scheduled 24 h apart, within 3 weeks of Visit 1. Psychophysiological recording during the picture viewing task took place during Visit 2. Smokers assigned to the abstinent group were instructed to stop smoking from 24 h before their scheduled time for Visit 2 through the end of Visit 3. Smokers assigned to the nonabstinent group were instructed to follow their normal smoking routine during the same 48-h period, and to smoke one additional cigarette at the start of Visits 2 and 3.

Participants

Participants were recruited via advertisements posted throughout the university campus and the surrounding community, and via campus-based websites. These advertisements solicited the participation of nonsmokers and daily smokers between the ages of 18 and 35 who were not currently seeking treatment for smoking cessation. Exclusion criteria included current diagnosis of major psychiatric illness, medical conditions or use of medications that would influence psychophysiological recording, and current use of over the counter or prescription stop-smoking remedies or current participation in stop-smoking counseling. Participants had a choice of \$50 or extra credit for their psychology course as compensation for completing all three visits. Smokers assigned to the abstinent group who met biochemical criteria for abstinence verification using expired air carbon monoxide (CO) received an additional cash

bonus of \$25 or additional course credit. Expired-air CO is a well-established, inexpensive, and noninvasive method of verifying short-term tobacco abstinence (Jarvis, Russell, & Saloojee, 1980; Jarvis, Tunstall-Pedoe, Feyerabend, Vesey, & Saloojee, 1987).

A total of 81 participants meeting these criteria gave written, informed consent to participate in the study: 24 nonsmokers (15 female), 28 smokers randomly assigned to the nonabstinent condition (14 female), and 29 smokers randomly assigned to the abstinent condition (16 female). The current analyses are limited to nonsmokers who reported never smoking a cigarette and smokers with expired-air CO levels greater than 6 parts per million (e.g., Marrone, Paulpillai, Evans, Singleton, & Heishman, 2010). Data from one nonsmoker were lost due to equipment failure, two smokers assigned to the abstinent condition withdrew from the study before the psychophysiological recording session, and one male smoker assigned to the abstinent condition failed to maintain abstinence for 24 h prior to the psychophysiological recording session and was excluded from further participation. This resulted in final sample sizes of 18 nonsmokers (10 female), 17 nonabstinent smokers (8 female) and 15 abstinent smokers (8 female). Data from 5 abstinent smokers (4 female) who were successfully abstinent at the start of Visit 2 but not at the start of Visit 3 were included in this analysis, as the primary interests of this study were the psychophysiological responses collected during Visit 2. The psychophysiological responses of this subgroup did not significantly differ from those of smokers who remained abstinent for the entire 48-h period.

Stimuli

Sixty full-color, 1024 × 768 pixel stimuli were presented via a 41 × 31 cm LCD video monitor (Model 2001FP, Dell, Round Rock, TX), subtending a horizontal viewing angle of 26 degrees. These stimuli were classified according to four categories, with 15 pictures in each category: low-arousal neutral, high-arousal pleasant, high-arousal unpleasant, and tobacco. The pleasant, neutral, and unpleasant stimuli were selected from the International Affective Picture System (Lang, Bradley, & Cuthbert, 1999). The specific IAPS pictures selected for this study were based on stimuli that have been found to be effective in previous studies (Cuthbert et al., 2007; Drobles et al., 2001).¹

Twelve of the tobacco pictures were obtained from a set of 48 collected by the authors from internet searches and print media (Engelmann & Cuthbert, 2008) and 3 were selected from a set provided by Paul Cinciripini (Carter et al., 2006). All tobacco pictures had been previously rated in our laboratory by smokers and nonsmokers on the same measures of affective valence, arousal, and dominance used to rate the IAPS pictures. The tobacco pictures used in this study were rated similarly to high-arousal pleasant IAPS pictures by smokers and similarly to low-arousal neutral IAPS pictures by nonsmokers (Engelmann & Cuthbert, 2008). These pictures contained scenes such as people preparing to smoke, people smoking alone or in social situations, and lit cigarettes with smoke clearly visible.²

Procedure

Participants who expressed interest in the study and met requirements for participation (as determined by phone and e-mail questionnaires) were invited to come to the laboratory for Visit 1. During this visit, each participant provided written informed consent, was further

¹The IAPS pictures used were: Pleasant: 4606, 4611, 4651, 4653, 4687, 4694, 7330, 7410, 7450, 7470, 7488, 8034, 8117, 8499, 8502; Neutral: 2383, 2516, 2880, 2980, 5531, 5740, 7050, 7080, 7095, 7170, 7175, 7179, 7205, 7550, 7705; Unpleasant: 1051, 1270, 1300, 1930, 2095, 6022, 6200, 6243, 6244, 6260, 8480, 9042, 9290, 8342, 9592.

²The tobacco stimuli from Carter et al. (2006) were: 402, 403, and 414. The remaining smoking stimuli were from Engelmann and Cuthbert (2008): S254, S359, S369, S377, S413, S435, S441, S454, S457, S460, S466, and S479. These stimuli are available upon request from the first author.

screened for the inclusion and exclusion criteria mentioned above, and was given an expired-air CO score (the average of two successive breath samples taken with a PiCo Smokerlyzer, Bedfont Scientific USA, Williamsburg, VA). All participants completed a series of questionnaires that addressed smoking history, fear and anxiety, personality traits, withdrawal symptoms experienced over the past 24 h, and cigarette craving (Tables 1 and 2). After completing the questionnaires, smokers were informed of their random assignment to the abstinent or nonabstinent condition, and Visits 2 and 3 were scheduled.

Upon arrival for Visit 2, smokers assigned to the nonabstinent group were asked to completely smoke one of their regular cigarettes. All participants provided expired-air CO samples, and completed questionnaires about their smoking over the past 24 h, withdrawal symptoms, and craving. Abstinent smokers were classified as successfully abstinent if their CO level was less than or equal to 6 ppm or half of their baseline level (whichever was lower) and if they reported smoking no cigarettes over the past 24 h. These CO criteria have been shown to reliably detect tobacco abstinence (e.g., Marrone et al., 2010).

Following the completion of questionnaires, electrodes to measure the startle response were placed over the *orbicularis oculi* muscle on the non-dominant side of the face according to published guidelines (Blumenthal et al., 2005) and electrodes for measuring the EEG were placed at the Fz, Cz, and Pz sites of the International 10–20 system (Jasper, 1958), and referenced to linked mastoids. The *orbicularis oculi* electromyogram (EMG) was bandpass-filtered (28–500 Hz), amplified, and digitized at a sampling rate of 1000 Hz from 100 ms before startle probe onset through 250 ms after startle probe offset. EEG traces were bandpass-filtered (0.1 – 40 Hz), amplified, and continuously sampled at a rate of 125 Hz. Vertical electrooculogram (vEOG) was measured for the purpose of correcting eye-blink artifacts in the EEG, and was obtained by splitting the signal from one of the *orbicularis oculi* electrodes and another electrode placed on the forehead directly above the pupil, and sampling the signal with the same parameters used for the EEG.

The picture-viewing task began immediately after electrode attachment. This task consisted of a 3-min relaxation baseline, followed by three picture viewing blocks. At the start of each block, participants were instructed to pay attention to the pictures and that the sensors were going to measure their “physiological reactions to the pictures.” The first block was a practice block, and consisted of four pictures (one from each category) and five startle probes. Each startle probe was a 50-ms, 95-dB white noise burst with instantaneous rise time, generated by a Coulbourn (Whitehall, PA) V85-05 noise generator and delivered binaurally via stereo headphones (Sennheiser PMX 100, Old Lyme, CT). Data from the practice block were not analyzed. The second and third blocks each consisted of 30 pictures and 30 startle probes, separated by a break of 3 min. On each trial, the picture was presented for 6 s, followed by an intertrial interval (ITI) ranging from 18–24 s during which a gray screen was presented. Pictures were presented in a random order with respect to content category, and four different orders were used across subjects to reduce the influence of order effects. During 12 of the 15 pictures from each category, a startle probe was presented 2.5 or 4.5 s after picture onset. Twelve additional startle probes were delivered during the ITIs (8, 10, or 12 s after picture offset). At the conclusion of the picture-viewing task, the electrodes were detached, and the participants completed a brief questionnaire and were dismissed until Visit 3.

The beginning of Visit 3 used the same procedure as that of Visit 2 (i.e., nonabstinent smokers smoke, CO measurement, and questionnaires). All participants then completed two picture memory tasks (free recall and recognition, the results of which are not reported here), followed by a subjective ratings task. During the subjective ratings task, participants rated the pictures on the dimensions of affective valence and arousal using the Self-

Assessment Mannequin, a computerized visual analog scale with five anchor points (Hodes, Cook, & Lang, 1985). Participants were then debriefed, compensated, and dismissed.

Physiological data reduction

For each startle probe, the EMG traces were digitally rectified and smoothed with a time-constant of 125 ms (Cook, 2003; Cook & Miller, 1992; Drobles et al., 2001). The filtered data were hand-scored with the assistance of software that provided onset latency, peak latency, and blink magnitude in μV for each trial (Balaban, Losito, Simons, & Grahm, 1986; Cook, 2003). Trials with excessive electrical artifact, spontaneous blinks, and blinks with an onset latency of < 20 ms or > 120 ms were rejected and not included in further analyses. Participants with $> 30\%$ of startle trials rejected due to artifact were not included in further analyses (an average of 1.9 trials per participant were rejected due to artifact). This criterion resulted in the exclusion of 1 nonabstinent smoker. Participants who did not blink on at least 60% of artifact-free trials were considered “non-blinkers” and were also excluded from further analyses. This criterion resulted in the exclusion of 4 nonsmokers, 2 nonabstinent smokers, and 3 abstinent smokers. Additionally, equipment failure resulted in the loss of all startle data for 1 nonsmoker and 1 nonabstinent smoker. Thus, final sample sizes for startle data were 13 nonsmokers, 13 nonabstinent smokers, and 12 abstinent smokers.

To correct for individual differences in the overall size of startle blinks, blink size was quantified as an amplitude T-score with each subject serving as his/her own reference distribution (Blumenthal et al., 2005). After eliminating all trials rejected due to artifact and all trials with 0 μV blink magnitude, the remaining trials were converted to standardized T-scores ($M = 50$, $SD = 10$). The T-scores were then averaged by picture category, giving each subject one startle amplitude score per category.

For each subject, raw EEG waveforms were digitally filtered using infinite impulse response filters with a high pass of 0.1 Hz and low pass of 30 Hz, followed by extraction of epochs from 300 ms before startle probe onset through 500 ms after startle probe offset. Epochs with off-scale or flat EEG or vEOG traces or with large ($> 300 \mu\text{V}$) deflections in the raw EEG were rejected. (An average of 2.6 out of 60 trials was rejected per participant, and no participant was excluded for exceeding the limit of 20 rejected trials). This was followed by eye movement correction using the algorithm of Gratton, Coles, and Donchin (1983) implemented in Fortran 77 (Miller, Gratton, & Yee, 1988). The epochs from individual trials were then averaged according to the category of picture that was on the screen when the startle probe was presented: tobacco, pleasant, neutral, or unpleasant. These average waveforms were baseline-corrected by subtracting the mean of the 120-ms window immediately preceding startle probe onset from all points in the waveform (Schupp et al., 1997). The P3 was quantified as the average value of the baseline-corrected waveform in a window lasting from 260–340 ms after startle probe onset (Keil et al., 2007). Equipment failure resulted in the loss of startle probe P3 data for 2 nonsmokers and 1 nonabstinent smoker, resulting in final sample sizes for P3 data of 16 nonsmokers, 16 nonabstinent smokers, and 15 abstinent smokers.³

Statistical analysis

Statistical analyses were conducted using SYSTAT 13 (SYSTAT Software, Chicago, IL). Participant characteristics and questionnaire scores that were only obtained during Visit 1

³A total of 50 participants provided data for at least one of the psychophysiological measures: $n = 35$ provided both startle and P3 data, $n = 3$ provided startle data only, and $n = 12$ provided P3 data only. Re-analysis of the data using the truncated sample of 35 participants who provided both startle and P3 data did not change the overall pattern of results or interpretation of the data. Statistical effects were unchanged, with three exceptions where effects that were significant in the full sample only approached significance in the truncated sample (see Results).

were analyzed using one-way ANOVA with group as a between-subjects factor, with significant results followed by comparison of individual group means using Tukey's Honestly Significant Difference (HSD) *post hoc* tests. Expired-air CO and questionnaire measures that were obtained during all three laboratory visits were analyzed using group X session mixed model ANOVAs, with significant interactions followed by simple effects tests for day or group using one-way ANOVA.

Psychophysiological responses to the pictures and SAM ratings were each analyzed using separate group (nonsmoker, nonabstinent, abstinent) X category ANOVAs (Drobes et al., 2001).⁴ The first ANOVA was used to assess the effect of smoking and abstinence on reactivity to standard emotional stimuli, with pleasant, neutral, and unpleasant as levels of the category factor. Following a significant group X category interaction, linear and quadratic components of the category factor were examined within groups. A significant linear trend was indicative of a difference in response between pleasant and unpleasant pictures (i.e., valence modulation) and a significant quadratic trend was indicative of a difference in response between neutral pictures and the linear combination of pleasant and unpleasant pictures (i.e., arousal modulation). Additional, follow-up ANOVAs contrasting responses to pleasant or unpleasant and neutral pictures were also examined within each group. The second ANOVA was used to assess smoking cue reactivity, with tobacco and neutral as levels of the category factor. In addition to these analyses, an *a priori* one-way ANOVA was used to test for significant between-groups differences in the [unpleasant - neutral] difference scores for startle amplitude as a measure of fear-potentiated startle (Vaidyanathan, Patrick, & Bernat, 2009). In all cases, the significance criterion was set at $p < .05$ and multivariate tests (Wilks' and its approximate F statistic) were used for effects involving repeated measures.

Results

Participant demographics and smoking history

Smokers were considered light to moderate according to the number of cigarettes smoked per day, CO levels produced during Visit 1, and scores on the FTND and HSI (Table 1). Nonabstinent and abstinent smokers did not differ significantly on the number of cigarettes smoked per day, maximum daily smoking rate, number of years they had been smoking, number of serious quit attempts, longest duration of abstinence during a quit attempt, FTND score, and HSI score (see Table 1 for group F tests).

Abstinence verification

Examination of expired-air CO readings revealed a pattern of results that was consistent with smoking throughout the day before all three laboratory sessions in smokers assigned to the nonabstinent condition, and with abstinence prior to Visits 2 and 3 in smokers assigned to the abstinent condition. Group X session ANOVA revealed a significant group X session interaction [$F(4,92) = 13.8, p < .001, \eta^2 = .39$], driven by main effects of group during each session (Table 1). As expected, both groups of smokers produced significantly greater CO levels than nonsmokers during Visit 1, but only nonabstinent smokers produced significantly greater CO levels than nonsmokers during Visits 2 and 3. The small increase in the mean CO level from Visit 2 to Visit 3 in the abstinent group was attributable to the 5 smokers who were abstinent at Visit 2 but not at Visit 3. For all participants, self-reported abstinence agreed with abstinence classification based on CO levels.

⁴To examine whether sex differences contributed to any of the effects observed here, we conducted a parallel set of group X sex X category ANOVAs. There were no significant effects of sex for any measure.

Self-report measures

Scores on questionnaires used to measure trait characteristics (FSS, EASI, and the STAI trait anxiety scale) indicated significant effects of group on two measures: the impulsivity subscale of the EASI and the trait anxiety scale of the STAI (Table 2). All three groups differed significantly on impulsivity scores, with abstinent smokers scoring the highest, followed by nonabstinent smokers and nonsmokers. For trait anxiety, abstinent smokers scored significantly higher than nonsmokers, but neither group scored significantly different from nonabstinent smokers.

Scores on questionnaires used to measure state characteristics (STAI state anxiety scale, MNWS, and QSU) indicated increased negative affect and cigarette craving during tobacco abstinence. There were statistically significant group X session interactions for MNWS withdrawal symptom scores [$F(2,29) = 3.91, p < .05, \eta^2 = .79$], QSU Factor 1 scores [$F(2,29) = 7.35, p < .01, \eta^2 = .66$], and QSU Factor 2 scores [$F(2,29) = 8.58, p < .01, \eta^2 = .63$]; the group X session interaction approached statistical significance for state anxiety scores [$F(4,92) = 2.30, p = .07, \eta^2 = .83$]. These interactions were the result of abstinent smokers scoring higher than nonabstinent smokers on the MNWS and QSU during Visits 2 and 3, but not during Visit 1. Abstinent smokers scored higher on the STAI-State scale than both nonsmokers and nonabstinent smokers during Visit 2 and higher than nonsmokers during Visit 3 (Table 2).

Subjective ratings of the pictures

Mean valence and arousal ratings of the pictures are presented in Table 2. Participants from all three groups rated the pleasant, neutral, and unpleasant pictures as expected, with pleasant pictures having the highest valence ratings and both pleasant and unpleasant pictures having the highest arousal ratings. This effect was evidenced in the ANOVA for pleasant, neutral, and unpleasant pictures by a significant main effect of category for valence and arousal [$F(2,46) > 193, ps < .001, \eta^2 < .11$] but non-significant main effects of group [$F(2,47) < 1.6, ps > .1$] and group X category interactions [$F(4,92) < 1.5, ps > .1, \eta^2 > .8$]. For valence, the linear trend of category [$F(1,49) = 377.38, p < .001$] was stronger than the quadratic trend [$F(1,49) = 23.10, p < .001$]. For arousal, the quadratic trend [$F(1,49) = 502.93, p < .001$] was stronger than the linear trend [$F(1,49) = 22.20, p < .001$].

Both groups of smokers rated the tobacco pictures more pleasant and arousing than neutral pictures, while the nonsmokers rated the tobacco pictures less pleasant but more arousing than neutral pictures. Thus, in the ANOVA for tobacco and neutral pictures, there were significant group X category interactions for valence [$F(2,47) = 20.62, p < .001$] and arousal [$F(2,47) = 3.35, p < .05$] and significant effects of category within all three groups [$F(2,47) > 10.2, ps < .01$]. Follow-up analysis using one-way ANOVA for the effect of group on the ratings of tobacco pictures found a significant effect of group for valence [$F(2,47) = 18.23, p < .001$] and arousal [$F(2,47) = 4.98, p < .05$]. For valence, Tukey's HSD *post hoc* tests indicated that both groups of smokers differed significantly from the nonsmokers ($ps < .001$). For arousal, the abstinent smokers differed significantly from the nonsmokers ($p < .05$).

Startle blink amplitude

Preliminary analyses found that raw startle amplitude (measured in μV) to probes delivered during the intertrial intervals or neutral pictures did not significantly differ between groups [$F(2,35) < 1.08, ps > .1$]. This is consistent with previous research that has found no evidence of withdrawal-potentiated startle in the absence of emotional stimuli (e.g., Hogle et al., 2010; Mueller et al., 1998). Startle amplitude T-scores are presented in Figure 2. While nonsmokers and abstinent smokers showed robust startle potentiation during unpleasant

pictures, relative to neutral pictures, nonabstinent smokers did not show this fear-potentiated startle effect. Although this was not reflected in the group X picture category interaction in the ANOVA for pleasant, neutral, and unpleasant pictures [$F(4,68) = 1.77, p > .1$], it was reflected in a significant effect in the *a priori* ANOVA for group on the [unpleasant - neutral] difference scores [$F(2,35) = 3.45, p < .05$].⁵ Tukey *post hoc* tests indicated that the difference between nonabstinent smokers and nonsmokers was statistically significant ($p = .05$) and that the difference between nonabstinent and abstinent smokers approached significance ($p = .1$). To document this effect more thoroughly, we conducted within-subject ANOVAs of unpleasant versus neutral startle values separately for each group; nonsmokers and abstinent smokers both showed robust effects [$F_s > 7.2, p_s < .05$], but not nonabstinent smokers [$F(1,12) < 1, p > .1$]. Comparison of effect sizes from these ANOVAs found that the degree of unpleasant versus neutral reactivity was similar for nonsmokers ($\eta^2 = .51$) and abstinent smokers ($\eta^2 = .40$).

Startle blink probabilities are presented in Table 3. The group X picture category ANOVAs found no significant group X category interactions [$F_s < 1, p_s > .1, \eta^2_s > .94$]. The main effect of group was statistically significant in the ANOVA for pleasant, neutral, and unpleasant pictures [$F(2,35) = 3.66, p < .05$] and approached significance in the ANOVA for tobacco and neutral pictures [$F(2,35) = 2.88, p = .07$]. Tukey *post hoc* tests indicated that this was the result of higher blink probability across all picture categories in nonabstinent smokers than in nonsmokers ($p < .05$). The main effect of picture category approached significance in the ANOVA for pleasant, neutral, and unpleasant pictures, suggestive of a trend toward greater blink probability during unpleasant pictures than during pleasant or neutral pictures [$F(2,34) = 2.64, p = .09, \eta^2 = .87$].

Startle probe P3

Inspection of grand average waveforms (Fig. 3) revealed a large P3 to the startle probe that was most pronounced at Pz, consistent with prior results (e.g., Cuthbert, Schupp, Bradley, McManis, & Lang, 1998; Keil et al., 2007). Because of this observation and of non-significant group X electrode site X category interactions [$F_s < 1, p_s > .1, \eta^2_s > .89$], further analyses were limited to data from Pz. The ANOVA for pleasant, neutral, and unpleasant pictures revealed a significant group X picture category interaction [$F(4,86) = 4.83, p < .01, \eta^2 = .67$], which appeared to be due to altered responses to unpleasant pictures in both groups of smokers as compared to nonsmokers. Specifically, nonabstinent smokers failed to show the usual suppression of P3 responses for unpleasant pictures (as compared to neutral), while abstinent smokers demonstrated an enhanced suppression of P3 (see Fig. 4). Analysis of [unpleasant - neutral] difference scores using one-way ANOVA for group [$F(2,44) = 8.70, p < .001$] revealed significantly more suppression to unpleasant pictures in the abstinent smokers than in the nonabstinent smokers or nonsmokers ($p_s < .01$ and $.05$, respectively).⁶ Consistent with this effect, within-subject ANOVAs of unpleasant versus neutral P3 values showed a non-significant effect for nonabstinent smokers [$F(1,15) < 1, p > .1$], and significant effects for both nonsmokers and abstinent smokers [$F_s > 8.2, p_s < .05$]. Comparison of effect sizes for these ANOVAs indicated that the abstinent smokers ($\eta^2 = .71$) had greater unpleasant versus neutral reactivity than nonsmokers ($\eta^2 = .35$). As another assessment of the P3 effects, linear trend tests (comparing pleasant versus unpleasant) were computed for each group. As is usually observed, the linear trend was non-significant for nonsmokers [$F(1,15) = 2.04, p > .1$]; however, P3 for nonabstinent smokers was smaller for

⁵In the truncated sample of 35 participants who provided both startle and P3 data, this effect only approached significance; $F(2,32) = 2.99, p = .06$.

⁶In the truncated sample of 35 participants who provided both startle and P3 data, the difference between nonsmokers and nonabstinent smokers only approached significance ($p < .15$).

pleasant than unpleasant content [$F(1,15) = 14.50, p < .01$], while the opposite effect was observed for abstinent smokers [$F(1,14) = 4.90, p < .05$].⁷

During tobacco pictures, all three groups showed suppressed P3 amplitude, as evidenced by a significant main effect of picture category [$F(1,44) = 28.91, p < .001, \eta^2 = .60$], but a non-significant group X picture category interaction [$F(2,44) < 1, p > .1, \eta^2 = .96$] in the ANOVA for tobacco and neutral pictures. Because the lack of a significant effect of abstinence on tobacco cue reactivity was unexpected, we conducted additional, individual differences analyses to determine whether factors such as cigarette craving had an influence on responses to tobacco cues.

Self-reported craving and psychophysiology

Smokers in the nonabstinent and abstinent groups were assigned to “low” vs. “high” craving subgroups based on median splits of their difference scores between Visits 1 and 2 on the Questionnaire of Smoking Urges (QSU). The scores from QSU Factor 1 (QSU1), a measure of cigarette craving, are presented in the upper panel of Figure 5. This shows the substantial increase in QSU1 scores at Visit 2 for the subgroup of abstinent smokers designated as “high” craving. Startle probe P3 amplitude was analyzed as a function of these subgroups using abstinence X subgroup X picture category ANOVAs. In the ANOVA for pleasant, neutral, and unpleasant pictures, there were no significant main effects or interactions involving craving subgroup [$F_s < 1.6, p_s > .1, \eta^2_s > .89$]. For tobacco and neutral pictures, the three-way group X craving subgroup X picture category interaction was statistically significant [$F(1,27) = 3.87, p = .05, \eta^2 = .87$]. The strongest P3 suppression to tobacco pictures was observed in the Abstinent-High craving subgroup [Fig. 5, *lower panel*; category $F(1,6) = 54.77, p < .001$]; P3 suppression only approached statistical significance in the Nonabstinent-Low craving group [$F(1,7) = 4.19, p = .08$] and was not significant in the Nonabstinent-High and Abstinent-Low groups [$F_s(1,7) < 2.6, p_s > .1$].

We also examined whether emotion-modulated startle varied as a function of the change in QSU1 scores from Visit 1 to Visit 2. No main effects or interactions involving QSU1 subgroup approached statistical significance [all $F_s < 2.7$, all $p_s > .1$]. Similarly, there were no significant main effects or interactions involving subgroup assignment based on median splits on any other self-report measure for both P3 suppression and emotion-modulated startle.

Discussion

This study examined startle blink amplitude and startle probe P3 suppression while nonsmokers, nonabstinent smokers, or smokers who had been abstinent for the past 24 h viewed pictures from four categories: tobacco, pleasant, neutral and unpleasant. Altered responses were observed in both groups of smokers, with three major patterns evident. First, nonabstinent smokers appeared to be less reactive to unpleasant pictures, relative to nonsmokers and abstinent smokers, both in fear-potentiated startle and P3 measures. Second, abstinent smokers were also more emotionally reactive to unpleasant pictures than nonsmokers, as indicated by P3 suppression. Third, abstinent smokers who reported the largest increases in cigarette craving during the first 24 h of abstinence showed greater P3 suppression during pictures of smoking-related cues than the other smokers in the study.

⁷In the truncated sample of 35 participants who provided both startle and P3 data, this effect only approached significance; $F(1,11) = 4.35, p = .06$.

Smoking, Abstinence, and Emotional Cue Reactivity

Fear-potentiated startle is thought to reflect increased activation of defensive motivational systems in the brain (Lang et al., 1990, 1998). In this study, nonsmokers and abstinent smokers showed robust fear-potentiated startle during unpleasant pictures, while nonabstinent smokers did not, suggesting that defensive motivational systems were less active in nonabstinent smokers than in nonsmokers or abstinent smokers. This suggests that nicotine may be anxiolytic for smokers, because the nonabstinent smokers – whose most recent cigarette was within 30 min of the start of the picture viewing task – differed from both 24-h-deprived smokers and from nonsmokers, and because the nonsmokers and 24-h-deprived smokers did not differ in fear-potentiated startle. This result is consistent with the findings of another study in which intranasal nicotine administration after 12 h of smoking abstinence reduced fear-potentiated startle (Cinciripini et al., 2006) and corrugator EMG (Robinson, Cinciripini, Carter, Lam, & Wetter, 2007) during unpleasant pictures and a recent study in which greater startle potentiation to a threatening context was observed in abstinent smokers than nonabstinent smokers (Hogle et al., 2010). Nicotine also has anxiolytic effects in animal models (Picciotto, Brunzell, & Caldarone, 2002), including potentiated startle (Engelmann et al., 2009; Vale & Green, 1996). Thus, although not all studies have found differences in fear-potentiated startle between nonabstinent and abstinent smokers (Geier et al., 2000; Piper & Curtin, 2006), there is a growing body of evidence in both the human and animal literature that nicotine administration reduces, and that withdrawal increases, fear-potentiated startle, as predicted by negative reinforcement theories of nicotine addiction (Baker et al., 2004).

Although a number of previous studies have assessed the effects of smoking and smoking cessation on startle reactivity, this study is the first, to our knowledge, to also assess the effects of smoking cessation on startle probe P3 suppression. The main finding in this data set was that smoking decreased and tobacco abstinence markedly increased startle probe P3 suppression during unpleasant pictures. This finding coheres with the results of other studies of smokers' attention to emotional pictures. For example, transdermal nicotine administration to 12-h abstinent smokers decreased P3 suppression to target stimuli in the presence of unpleasant distractors in a rapid visual information processing (RVIP) task (Gilbert et al., 2007), improved performance in the presence of unpleasant distractors in a similar RVIP task (Gilbert et al., 2005), decreased interference caused by unpleasant words in an emotional Stroop task (Rzetselny et al., 2008), and reduced eye-gaze at negative pictures in a two-choice viewing task (Gilbert et al., 2008). Thus, there is considerable evidence that tobacco abstinence increases, and nicotine replacement decreases, selective attention to unpleasant stimuli.

Considered together, the relatively low level of startle potentiation and P3 suppression during unpleasant stimuli in nonabstinent smokers and high level of P3 suppression during the same stimuli in abstinent smokers suggest that smoking decreases and abstinence increases emotional reactivity to unpleasant pictures. Interestingly, while the fear-potentiated startle effect was due to blunted responses to unpleasant cues in nonabstinent smokers, the startle probe P3 effect was driven by enhanced P3 suppression to unpleasant cues in abstinent smokers: analysis of [unpleasant - neutral] difference scores found that fear-potentiated startle did not differ between nonsmokers and abstinent smokers, whereas P3 suppression did not differ between nonsmokers and nonabstinent smokers. This difference between psychophysiological measures suggests that different aspects of smoking behavior (i.e., reduction of negative affect via smoking vs. increased negative affect during withdrawal) may be associated with different brain motivational systems (Watkins et al., 2000). It should be noted, however, that different subsets of participants were used for the startle and P3 analyses, which raises the possibility that differences between participants rather than between measures may have contributed to our results. This is unlikely, however,

as re-analysis of the data using 35 participants who provided data for both measures produced a highly similar pattern of results.

These comparisons also highlight a major advantage of including a group of nonsmokers in tobacco abstinence studies; without the nonsmoker group, it is not possible to make inferences about the conditions under which smokers produce abnormal responses (e.g., decreased fear-potentiated startle after smoking and increased P3 suppression during abstinence). These differences between nonsmokers and smokers may be an important factor in maintaining nicotine dependence, and may therefore be potential targets for smoking-cessation interventions (e.g., Watkins et al., 2000).

Craving modulates emotional responses to tobacco pictures

Contrary to our predictions, the stronger emotional reactivity of the abstinent group did not, as a whole, extend to their responses to tobacco-related pictures. A significant effect emerged, however, when the level of cigarette craving was included in the analysis. Specifically, those abstinent smokers who reported increases in cigarette craving (measured using the QSU1) between Visits 1 and 2 showed greater P3 suppression to the smoking-related cues. In fact, the Abstinent-High QSU1 group was the only group to show increased craving across sessions (Fig. 5, *upper panel*), suggesting that an overall effect of group on P3 suppression during tobacco pictures may have been obscured by the data of those smokers whose craving levels did not rise during abstinence. Interestingly, the differences in psychophysiological responses during unpleasant pictures were not dependent on QSU scores. This suggests that P3 suppression to unpleasant pictures and tobacco pictures may be under the control of different aspects of tobacco deprivation, and underscores the importance of including multiple psychophysiological measures to multiple categories of emotional stimuli in cue reactivity studies.

Potential limitations and future directions

The main conclusions drawn from our study are that smoking reduces and abstinence increases reactivity to unpleasant stimuli, and that smokers who show increased craving during abstinence are also more reactive to tobacco stimuli. These conclusions need to be interpreted, however, within the context of this study's limitation that the smokers we recruited were relatively young and light smokers and therefore perhaps not truly "dependent" on nicotine (cf. Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). Arguing against this, several of our findings agree with those from studies of heavy smokers. Heavy smokers have been shown to rate tobacco pictures similarly to other high-arousal pleasant stimuli (Carter et al., 2006; Orain-Pelissolo, Grillon, Perez-Diaz, & Jouvent, 2004) and to show reduced fear-potentiated startle during unpleasant pictures after acute nicotine administration (Cinciripini et al., 2006). Furthermore, nonabstinent, heavy smokers also exhibit suppressed startle probe P3 magnitude during tobacco pictures (Versace et al., 2010).

A further issue related to the use of light smokers is whether the abstinence effects can be attributed to a "true" nicotine withdrawal episode. Again, this concern is mitigated by the similarity of our findings to those in heavy smokers, and the results from several studies suggesting that signs and symptoms of tobacco withdrawal and difficulty quitting are evident in even the lightest (Davies, Willner, & Morgan, 2000; O'Loughlin et al., 2003; Sayette, Martin, Wertz, Shiffman, & Perrott, 2001) and most inexperienced (DiFranza et al., 2000; Kassel et al., 2007) smokers. Given the vulnerability of adolescent (Chassin, Presson, Rose, & Sherman, 1996) and college-age (Wetter et al., 2004) smokers to transition from light to heavy smoking, it is important to continue including participants from these groups in tobacco cue reactivity studies.

A final, potential concern is our adoption of a between-subjects abstinence manipulation, which prevents us from completely eliminating the possibility that abstinence effects reported here were due to differences in participant characteristics that were unrelated to abstinence. For example, abstinent smokers scored significantly higher than nonabstinent smokers on the impulsivity scale of the EASI and significantly higher than nonsmokers on trait anxiety, demonstrating that factors other than abstinence can differentiate between groups in a between-subjects design. However, no significant main effects or interactions involving median splits on EASI-I or STAI-Trait scores were found. The lack of significant differences among nonsmokers, nonabstinent smokers, and abstinent smokers on all other Visit 1 questionnaire scores is also encouraging, suggesting that smoking status was the largest and most important difference between groups. Furthermore, a between-subjects approach to smoking withdrawal studies is advantageous in that it avoids difficulties associated with between-sessions habituation to the pictures and the startle stimuli (Ornitz & Guthrie, 1989), participant fatigue and attrition, and the need to address order effects of the abstinent and nonabstinent condition.

Notwithstanding these potential concerns, the results of this study are supportive of several predictions of negative-affect reduction models of tobacco addiction. These models predict that smoking reduces negative affect (e.g., Koob & Le Moal, 2008; Solomon & Corbit, 1973; Watkins et al., 2000), which is supported by our finding of less fear-potentiated startle in nonabstinent smokers than in abstinent smokers or nonsmokers. A related prediction is that tobacco withdrawal increases emotional responses to unpleasant stimuli (Baker et al., 2004), which is supported by our finding of greater P3 suppression during unpleasant pictures in abstinent smokers than in nonabstinent smokers or nonsmokers. Affect-management models also predict that tobacco abstinence selectively increases attention to unpleasant and tobacco cues, but not pleasant or neutral cues (Gilbert, 1997), which is also supported by our P3 suppression results. Thus, the findings of this study highlight the need for further development of smoking-cessation therapies that target the negative affective consequences of tobacco use and abstinence. Moreover, the methods used in this study – measuring startle amplitude and P3 suppression to the startle stimulus – appear to be highly sensitive to these consequences and may therefore prove extremely useful tools in the development of new treatment strategies.

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Figure 1.

Timeline of laboratory visits. Visit 1 was an initial baseline and screening session. Visits 2 and 3 were scheduled 24 h apart, within 3 weeks of Visit 1. Smokers randomly assigned to the abstinent group were asked to stop smoking from 24 h before the start of Visit 2 through the end of Visit 3. Smokers randomly assigned to the nonabstinent condition continued their normal pattern of smoking throughout the study, and smoked one additional cigarette at the start of Visits 2 and 3.

Figure 2.

Mean standardized startle blink amplitude to auditory startle probes delivered during tobacco, pleasant, neutral and unpleasant pictures viewed by nonsmokers, nonabstinent smokers, and abstinent smokers. *Error bars* depict the mean $\pm$ 1 SEM. *Asterisks* indicate significant differences between responses to unpleasant and neutral pictures (*, $p < .05$; **, $p < .01$). n s = 13, 13, and 12 for nonsmokers, nonabstinent smokers, and abstinent smokers, respectively.

Figure 3.

Grand average waveforms for event-related potentials to startle probes delivered during tobacco, pleasant, neutral, and unpleasant pictures. The data plotted range from 120 ms before through 500 ms after startle probe onset. Startle probe onset occurred at the 0-ms time point and all waveforms were baseline corrected using the 120-ms pre-stimulus baseline. The EEG was measured in μV , where negative values are plotted above the x -axis and positive values are plotted below the x -axis. Electrode sites (Fz, Cz, and Pz) are plotted in rows and groups (nonsmokers, nonabstinent smokers, and abstinent smokers) are plotted in columns. n s = 16, 16, and 15 for nonsmokers, nonabstinent smokers, and abstinent smokers, respectively.

Figure 4.

Mean startle-probe P3 magnitude during tobacco, pleasant, neutral and unpleasant pictures at the Pz electrode site in nonsmokers, nonabstinent smokers, and abstinent smokers. P3 magnitude was quantified for each picture category for each subject using a window average lasting from 260–340 ms after startle probe onset. *Error bars* depict the mean $\pm$ 1 SEM. *Asterisks* indicate significant differences between responses to unpleasant and neutral pictures (*, $p < .05$; **, $p < .01$). $ns = 16, 16$, and 15 for nonsmokers, nonabstinent smokers, and abstinent smokers, respectively.

Figure 5.

Effect of change in self-reported cigarette craving on startle probe P3 magnitude during tobacco pictures. *Upper panel:* Mean change in QSU1 scores from Visit 1 to Visit 2 as a function of abstinence condition and median split on QSU1 change scores. *Lower panel:* Mean startle-probe P3 magnitude the Pz electrode site as a function of abstinence condition and median split on QSU1 change scores. *NA* = Nonabstinent, *A* = Abstinent, *LOW* = Low-QSU1 subgroup, *HIGH* = High-QSU1 subgroup. *Error bars* depict the mean $\pm$ 1 SEM. *** indicates a significant difference between tobacco and neutral pictures for the A-HIGH group, $p < .001$. $ns = 8, 8, 8,$ and 7 for NA-LOW, NA-HIGH, A-LOW, and A-HIGH, respectively.

Table 1Participant demographics and smoking history (Mean $\pm$ SEM)

	Nonsmokers	Nonabstinent Smokers	Abstinent Smokers	Group ANOVA
<i>N</i> (female)	18 (10)	17 (8)	15 (8)	
Percent minority	33.3	29.4	26.7	
Age (years)	20.8 $\pm$ 0.7	22.2 $\pm$ 1.2	21.7 $\pm$ 0.6	$F < 1$
Current CPD		10.9 $\pm$ 1.6	11.0 $\pm$ 1.5	$F < 1$
Maximum CPD		18.2 $\pm$ 3.2	15.0 $\pm$ 1.6	$F < 1$
Years smoked		7.3 $\pm$ 1.4	5.2 $\pm$ 0.7	$F = 1.57$
Quit attempts		4.0 $\pm$ 1.4	2.8 $\pm$ 1.3	$F < 1$
Maximum days abstinent		104.8 $\pm$ 54.5	98.4 $\pm$ 71.4	$F < 1$
FTND score		2.9 $\pm$ 0.4	3.3 $\pm$ 0.4	$F < 1$
HSI score		1.9 $\pm$ 0.3	2.1 $\pm$ 0.3	$F < 1$
Session 1 CO	2.4 $\pm$ 0.3 ^a	12.6 $\pm$ 1.5 ^b	13.5 $\pm$ 1.2 ^b	$F = 32.65^{***}$
Session 2 CO	2.0 $\pm$ 0.2 ^a	13.6 $\pm$ 1.8 ^b	2.4 $\pm$ 0.3 ^a	$F = 37.61^{***}$
Session 3 CO	1.8 $\pm$ 0.1 ^a	13.6 $\pm$ 2.2 ^b	4.5 $\pm$ 1.1 ^a	$F = 20.20^{***}$

Note: CPD = Cigarettes per day. FTND = Fagerström Test of Nicotine Dependence, measured on a 0–10 scale (Heatherton et al., 1991); HSI = Heavy Smoking Index, measured on a 0–6 scale (Chabrol, Niezborala, Chastan, & de Leon, 2005). Asterisks indicate statistically significant *F* tests in a one-way ANOVA for group ($*** p < .001$). On measures for which the ANOVA was statistically significant, means that do not share superscripts significantly differed in Tukey HSD *post hoc* tests.

Table 2

Self-report measures of personality traits, anxiety, withdrawal symptoms, craving, picture valence, and picture arousal (Mean $\pm$ SEM)

	Session	Nonsmokers	Nonabstinent Smokers	Abstinent Smokers	Group ANOVA
FSS	1	2.0 $\pm$ 0.1	1.8 $\pm$ 0.1	2.0 $\pm$ 0.1	$F < 1$
EASI-Sociability	1	3.7 $\pm$ 0.2	3.6 $\pm$ 0.2	3.5 $\pm$ 0.2	$F < 1$
EASI-Activity	1	2.9 $\pm$ 0.2	2.9 $\pm$ 0.2	2.8 $\pm$ 0.1	$F < 1$
EASI-Impulsivity	1	2.4 $\pm$ 0.1 ^a	3.0 $\pm$ 0.1 ^b	3.4 $\pm$ 0.1 ^c	$F = 16.00^{***}$
EASI-Fear	1	2.2 $\pm$ 0.1	2.5 $\pm$ 0.1	2.5 $\pm$ 0.2	$F = 1.41$
EASI-Anxiety	1	2.0 $\pm$ 0.1	2.3 $\pm$ 0.2	2.5 $\pm$ 0.2	$F = 1.54$
STAI-Trait	1	1.8 $\pm$ 0.1 ^a	2.0 $\pm$ 0.1 ^{ab}	2.3 $\pm$ 0.1 ^b	$F = 6.21^{**}$
STAI-State	1	1.6 $\pm$ 0.1	1.7 $\pm$ 0.1	1.9 $\pm$ 0.1	$F = 2.59$
	2	1.7 $\pm$ 0.1 ^a	1.9 $\pm$ 0.2 ^a	2.4 $\pm$ 0.1 ^b	$F = 8.34^{**}$
	3	1.5 $\pm$ 0.1 ^a	1.9 $\pm$ 0.2 ^{ab}	2.2 $\pm$ 0.2 ^b	$F = 8.16^{**}$
MNWS	1		1.4 $\pm$ 0.2	1.4 $\pm$ 0.2	$F < 1$
	2		1.3 $\pm$ 0.2	2.0 $\pm$ 0.2	$F = 9.02^{***}$
	3		1.0 $\pm$ 0.2	1.9 $\pm$ 0.2	$F = 8.84^{**}$
QSU Factor 1	1		4.8 $\pm$ 0.3	4.4 $\pm$ 0.3	$F < 1$
	2		3.8 $\pm$ 0.3	5.5 $\pm$ 0.3	$F = 14.14^{**}$
	3		4.0 $\pm$ 0.3	5.5 $\pm$ 0.4	$F = 9.35^{**}$
QSU Factor 2	1		2.9 $\pm$ 0.2	3.2 $\pm$ 0.4	$F < 1$
	2		2.5 $\pm$ 0.2	4.5 $\pm$ 0.4	$F = 20.98^{***}$
	3		2.6 $\pm$ 0.3	4.1 $\pm$ 0.5	$F = 8.07^{**}$
<i>Valence Ratings</i>					
Tobacco		286 $\pm$ 13	414 $\pm$ 18	413 $\pm$ 22	
Pleasant		434 $\pm$ 13	439 $\pm$ 20	444 $\pm$ 17	
Neutral		329 $\pm$ 5	346 $\pm$ 9	313 $\pm$ 7	
Unpleasant		137 $\pm$ 14	169 $\pm$ 16	163 $\pm$ 16	
<i>Arousal Ratings</i>					
Tobacco		137 $\pm$ 16	213 $\pm$ 21	240 $\pm$ 34	
Pleasant		324 $\pm$ 18	314 $\pm$ 25	313 $\pm$ 27	
Neutral		96 $\pm$ 11	134 $\pm$ 13	134 $\pm$ 20	

Session	Nonsmokers	Nonabstinent Smokers	Abstinent Smokers	Group ANOVA
Unpleasant	380 ± 21	373 ± 19	377 ± 25	

Note: FSS = Fear Survey Schedule, measured on a 1–5 scale (Wolpe & Lang, 1964); EASI = Emotionality, Activity, Sociability, and Impulsivity Inventory, measured on a 1–5 scale (Buss & Plomin, 1984); STAI = State-Trait Anxiety Inventory, measured on a 1–4 scale (Spielberger, 1979); MNWS = Minnesota Nicotine Withdrawal Scale, measured on a 0–4 scale (Hughes & Hatsukami, 1998); QSU = Questionnaire of Smoking Urges, measured on a 1–7 scale where Factor 1 measures cigarette craving and Factor 2 measures desire to avoid withdrawal (Tiffany & Drobes, 1991). Valence and Arousal ratings were obtained using a computerized visual-analog scale and quantified on a 0–640 scale. *Asterisks* indicate statistically significant *F* tests in a one-way ANOVA for group (***p* < .01, ****p* < .001). On measures for which the ANOVA was statistically significant, means that do not share superscripts significantly differed in Tukey HSD *post hoc* tests. *n*s = 18 nonsmokers, 17 nonabstinent smokers, and 15 abstinent smokers.

Table 3Startle blink probability by picture category (Mean $\pm$ SEM)

	Nonsmokers	Nonabstinent Smokers	Abstinent Smokers
Tobacco	0.88 $\pm$ 0.05	0.95 $\pm$ 0.03	0.85 $\pm$ 0.03
Pleasant	0.89 $\pm$ 0.04	0.92 $\pm$ 0.03	0.84 $\pm$ 0.03
Neutral	0.86 $\pm$ 0.42	0.94 $\pm$ 0.02	0.79 $\pm$ 0.06
Unpleasant	0.92 $\pm$ 0.03	0.97 $\pm$ 0.02	0.85 $\pm$ 0.04