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Effects of Nicotine and Nicotine Expectancy on Attentional Bias for Emotional Stimuli

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Abstract

Introduction—Nicotine's effects on mood are thought to enhance its addictive potential.

However, the mechanisms underlying the effects of nicotine on affect regulation have not been reliably demonstrated in human laboratory studies. We investigated the effects of abstinence (experiment one), and nicotine challenge and expectancy (experiment two) on attentional bias towards facial emotional stimuli differing in emotional valence.

Methods—In experiment one, 46 nicotine-deprived smokers were randomized to either continue to abstain from smoking or to smoke immediately before testing. In experiment two, 96 nicotine deprived smokers were randomized to smoke a nicotine or denicotinized cigarette and to be told that the cigarette did or did not contain nicotine. In both experiments participants completed a visual probe task, where positively valenced (happy) and negatively valenced (sad) facial expressions were presented, together with neutral facial expressions.

Results—In experiment one, there was evidence of an interaction between probe location and abstinence on reaction time, indicating that abstinent smokers showed an attentional bias for neutral stimuli. In experiment two, there was evidence of an interaction between probe location, nicotine challenge and expectation on reaction time, indicating that smokers receiving nicotine, but told that they did not receive nicotine, showed an attentional bias for emotional stimuli.

Conclusions—Our data suggest that nicotine abstinence appears to disrupt attentional bias towards emotional facial stimuli. These data provide support for nicotine's modulation of attentional bias as a central mechanism for maintaining affect regulation in cigarette smoking.

Keywords

Abstinence; Nicotine; Emotion; Attentional Bias; Visual Probe Task

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Declaration of Interests

All authors declare that they have no conflicts of interest.

Introduction

Nicotine's effects on mood are thought to enhance its addictive potential. The mood-enhancing effects of nicotine may promote self-administration in smokers (1,2), while reduction of negative affect may play a role in maintaining smoking behaviour (3). Negative affect following a quit attempt has been associated with increased likelihood of treatment failure and may account for 50% of all abstinence relapses (4). These findings suggest that affect may critically impact smoking behavior and relapse.

The mechanisms underlying the effects of nicotine on affect regulation have not been reliably demonstrated in human laboratory studies (5). However, one line of evidence has shown that nicotine non-contingently enhances the positive value of non-nicotine related stimuli. Nicotine has been shown to potentiate the reinforcing value of environmental stimuli in rats (6). Attwood and colleagues (7) recently showed a similar effect in humans, where participants were randomized to smoke a nicotine or denicotinized cigarette and rate the attractiveness of faces presented on a computer screen. Those in the nicotine condition rated faces as more attractive than those in the denicotinized condition. The detection and processing of emotional stimuli may be influenced via nicotine's direct effects on attentional processes. Specifically, nicotine has been suggested to modulate attentional bias to emotional stimuli (8,9). It is generally agreed that nicotine enhances attention towards positive affective stimuli; however, nicotine's influence over attention towards negative affective stimuli is still unclear.

Two theories have been proposed: the incentive sensitization theory (10,11) posits that prolonged drug use may lead to neuroadaptations that drive "hypersensitivity" or sensitization to drugs and drug-related stimuli, where drugs such as nicotine promote attentional bias to aversive stimuli (10,11). However, the Situation by Trait Adaptive Responses (STAR) model (8) hypothesizes that addictive drugs reduce negative affect to a greater degree when negative stimuli are presented alongside competing stimuli. This model suggests that nicotine reduces attentional bias to negative stimuli when equally salient attentional alternatives are available (12). Nicotine may therefore function in a similar manner to a positive emotional prime, enhancing the reinforcing value of positive or neutral stimuli, while attenuating the value of negative stimuli competing for attention. Previous studies have shown that nicotine biases attentional processing to increase positive affect and attentional bias towards positive stimuli, whilst reducing attentional bias towards negative stimuli (13,14). These studies use a range of measures for examining attentional biases for emotional stimuli. However, to date, no study has examined the effect of nicotine on attentional bias towards negative and positive affective facial stimuli using a visual probe task measure of attentional bias.

The visual probe task has been used to assess attentional biases in drug use (15,16) and mood disorders (17,18). It requires participants to respond to a probe that is presented immediately following a stimulus pair (an affective stimulus and a matched neutral stimulus). In half of the trials the probe is presented behind the affective stimulus and in the other half behind the neutral stimulus. The assumption is that faster responses to probes replacing affective stimuli reflect attentional bias towards affective stimuli, since the focus of

attention is already in the location of the salient stimulus. Therefore, in experiment one, we investigated the effects of nicotine abstinence on attentional bias, task, to positive and negative facial stimuli and hypothesized that nicotine abstinence would decrease attentional bias towards positive stimuli whilst increasing attentional bias towards negative stimuli.

Non-pharmacological factors (e.g., expectancy) may also play a role in the affect regulation of cigarette smoking. Expectancy theory argues that the effects of a substance are mediated by consciously held expectancies (19,20). For example, a smoker may experience a reduction in self-reported withdrawal-related symptoms such as affect and craving after smoking a denicotinized cigarette, if the smoker has the *stimulus* expectancy that they are smoking an active, nicotine cigarette and the *response* expectancy that nicotine reduces negative mood (19). Double-blind studies of denicotinized versus nicotine cigarettes have demonstrated that denicotinized cigarettes reduce cigarette cravings and alleviate withdrawal symptoms (21–23).

Stimulus expectancy can be manipulated using a balanced placebo design (24), where participants are randomized to one of four combinations comprising actual drug challenge (drug vs. placebo) and expectancy condition (told drug vs. told placebo). Using this methodology, following double-blind administration of denicotinized versus nicotine cigarettes, only smokers receiving denicotinized cigarette who also expected to receive nicotine reported a decreased in smoking urge, consistent with expectancy theory (25). These findings suggest that the expectation of having received nicotine will produce desirable effects may maintain smoking behavior and undermine successful cessation. To date, no studies have specifically focused on the role of both acute nicotine administration and nicotine expectancy on responses to affective stimuli. In experiment two, we hypothesized that both nicotine challenge and nicotine expectancy; would increase attentional bias towards positive stimuli whilst decreasing attentional bias towards negative stimuli.

Experiment One: Methods

Design

A double-blind between-subjects design, with nicotine abstinence (abstinent, non-abstinent) as a between-subjects factor, and stimulus type (positive, negative) and validity (valid, invalid) as within-subject factors.

Participants

Smokers were recruited from students and staff at the University of Bristol and members of the general public. Smokers were required to smoke a minimum of 5 cigarettes (or 7 roll-ups) a day, and smoke within 1 hr of waking. Prior to the test session all participants were asked to abstain from smoking for 12 hr (overnight abstinence, verified by exhaled CO test). On the test day participants were randomized to either continue to abstain from smoking or were asked to smoke just before coming to the laboratory. Participants received £7 each for participation. The study was approved by the University Of Bristol Faculty Of Science Research Ethics Committee.

Materials

Questionnaire measures used included measures of nicotine dependence (Fagerström Test for Nicotine Dependence; FTND), (26) cigarette craving (Questionnaire of Smoking Urges; QSU), (27) nicotine withdrawal (Minnesota Nicotine Withdrawal Scale; MNWS), (28) mood (Positive and Negative Affect Schedule; PANAS), (29) Visual Analogue Scales (VAS) of “happy,” “drowsy,” “depressed,” “anxious,” “energetic,” “irritable,” and “craving a cigarette” (each item rated on a 100 mm scale from “Not at all” to “Extremely”). The FTND was completed once at baseline. The QSU, MNWS, VAS, and PANAS were administered once at baseline and once after the visual probe task.

Visual probe task stimuli consisted of 28 photographic images of facial expressions. Stimuli were created using eight individuals photographed with each expression (happy, sad, and neutral). Four additional neutral facial expression images from four other individuals were used for baseline practice trials. Images were generated using prototypical composite images of the six basic facial expressions of emotion (angry, disgusted, fearful, happy, sad, and surprised) from 12 male and 12 female faces showing each of the six expressions. Original images were collected from photographing individuals in Bristol. To construct these images, the 12 original images were each delineated with 172 feature points, which allows both shape and color information to be averaged across the faces to generate ‘average’ angry, disgusted, fearful, happy, sad, and surprised expressions, using established techniques (30). We then created sequences of 15 equally spaced images for both men and women for each emotion for use as experimental stimulus sets. The facial photographic images were collected using a Canon EOS300D at a focal length of 50 mm under standardized lighting conditions provided by two lateral diffuse portaflash DL1000 studio lights. Images were captured at a resolution of 2048 by 3072 pixels, in full color. There was a constant background for all images and clothing was masked with a neutral smock. Individuals were asked to pose, standing, with neutral, happy, and sad expressions and photographed at a distance of approximately 150 cm.

Procedure

All participants were tested between 9 am and 12 pm in a laboratory in the School of Experimental Psychology at the University of Bristol. Prior to the test session all participants were asked to abstain from smoking for 12 hr. On the test day participants were randomized to either continue to abstain from smoking or asked to smoke one of their own cigarettes under supervision just before entering the laboratory. After providing informed consent, all participants completed a screening process to confirm good physical and psychiatric health, absence of current use of psychiatric medication and illicit drugs (except cannabis), and normal or corrected to normal vision. Participants were required to avoid drinking alcohol for 24 hr prior to the test session (verified by exhaled breath alcohol using an AlcoDigital 3000, AlcoDigital Ltd) and to abstain from smoking for 12 hr (verified by exhaled CO using a Bedfont Micro Smokerlyzer Breath CO Monitor, Bedfont Scientific Ltd). Abstinence was verified by exhaled CO, with a cut-off of <8 ppm for study inclusion. Participants in non-abstinent group were then asked to smoke one of their own cigarettes (supervised by a researcher) and participants allocated to the abstinent group remained abstinent. Baseline

questionnaire measures were completed (FTND, PANAS, MNWS, QSU, VAS) and participants completed the visual probe task.

In the visual probe task, participants were required to identify characteristics of a probe that replaced the emotional stimulus on 50% of trials (valid condition) and neutral stimulus on 50% of trials (invalid condition). Valid trials refer to trials in which the probe replaces the “relevant” or emotional stimulus and invalid trials refer to those in which the probe replaces the “competing” or neutral stimulus. Each trial began with a central fixation cross, presented for 1000 ms, replaced with a stimulus pair, displayed side by side for 500 ms. Following the picture pair, a probe was presented in the location of one of the stimuli, until a response was made. Probes replacing emotional stimuli were valid trials, while probes replacing neutral stimuli were invalid trials. Each trial had an inter-trial interval of 1000 ms. Participants were instructed to focus on the fixation cross in each trial, and then respond to a probe, which could either be a circle or a square, by pressing the up or down arrows on the keyboard respectively. Practice stimuli were presented in a single block of 8 trials each consisting of two picture pairs of neutral images. Experimental stimuli were presented in random sequence in four blocks of 36 trials, with each block consisting of four baseline trials (neutral/neutral) and 32 experimental trials (positive/neutral or negative/neutral). Each picture type and each probe type was presented with equal frequency on both the left and right side of the screen in each of the eight possible presentations. On completion of the task, participants completed questionnaire measures (QSU, MNWS, PANAS, VAS) and were reimbursed for their time and received a full debrief.

Data Analysis

For visual probe data, mean correct reaction times were analysed within a $2 \times 2 \times 2$ design, with abstinence (abstinent, non-abstinent) as a between-subjects factor, and stimulus type (positive, negative) and validity (valid, invalid) as within-subject factors. Outlier response times of less than 200 ms and greater than 2000 ms (31) were removed for each subject before data analysis. Skewness tests indicated that visual probe data were normally distributed. Mixed-model ANOVAs were conducted of mean QSU, MNWS, PANAS, VAS scores with a within-subjects factor of time (baseline, post-task) and abstinence as between-subjects factor.

Results

Characteristics of Participants

Participants ($n = 46$; 59% male) were, on average, aged 23 years ($SD = 6$, range 18–51) and had a FTND score of 3.59 ($SD = 1.48$, range 1–7). Descriptive data were analyzed using a series of univariate ANOVAs to compare abstinent and non-abstinent groups. As expected the abstinent group had higher levels of tobacco withdrawal ($p < .001$, $\eta^2 = 0.31$) and cigarette craving ($p < .001$, $\eta^2 = 0.50$), and had decreased positive mood ($p = .001$, $\eta^2 = 0.21$) and lower exhaled CO ($p < .001$, $\eta^2 = 0.37$) compared with the non-abstinent group. Abstinent smokers were more anxious, depressed and irritable and less happy and energetic (p s < 0.05) than non-abstinent smokers. Group did not differ substantially with respect to

any other demographic or baseline variables ($ps > 0.12$). Table 1 shows the characteristics of abstinent and non-abstinent participants.

Cigarette craving and withdrawal

A mixed-model ANOVA of mean QSU scores indicated a main effect of time ($F[1, 44] = 22.96, p < .001, \eta^2 = 0.34$), such that craving increased from baseline to post-task for all participants, and a main effect of group ($F[1, 44] = 34.16, p < .001, \eta^2 = 0.44$), such that abstinent smokers had greater craving compared with non-abstinent smokers. There was no evidence for any other main effects or interactions ($ps > 0.13$). A mixed-model ANOVA of mean MNWS scores indicated a main effect of group ($F[1, 43] = 16.20, p < .001, \eta^2 = 0.27$), such that abstinent smokers had higher tobacco withdrawal compared with non-abstinent smokers. There was no evidence for all other main effects or interactions ($ps > 0.20$).

Mood

A mixed-model ANOVA of PANAS positive affect scores indicated a main effect of time ($F[1, 44] = 30.68, p < .001, \eta^2 = 0.41$), such that positive mood increased from baseline to post-task for all participants, and a main effect of group ($F[1, 44] = 11.68, p = .001, \eta^2 = 0.21$), such that non-abstinent smokers had greater positive mood compared with abstinent smokers. There was no evidence for any other main effects or interactions ($ps > 0.84$). A mixed-model ANOVA of mean PANAS negative affect scores indicated no evidence for any main effects or interactions ($ps > 0.15$). Mixed-model ANOVAs of mean VAS scores revealed a similar pattern of results.

Visual probe task

All error trials were removed from the data analysis. The overall percentage of errors was 5%, there were no differences by group. A mixed-model ANOVA of reaction time data indicated evidence of an interaction between validity and abstinence ($F[1, 43] = 6.29, p = .016, \eta^2 = 0.13$). There was no evidence for any other main effects or interactions ($ps > 0.25$). For the interaction between validity and abstinence, simple effects analyses were conducted for abstinent and non-abstinent participants separately. There was no evidence for a main effect of validity in non-abstinent participants ($F[1, 22] = 0.81, p = .38, \eta^2 = 0.04$), but evidence of a main effect of validity in abstinent participants ($F[1, 21] = 7.65, p = .012, \eta^2 = 0.27$). Further posthoc analyses indicated that participants in the abstinent condition were faster to respond to probes replacing neutral stimuli ($M = 662, SD = 89$) compared to those replacing emotional stimuli ($M = 678, SD = 106$). These data are shown in Figure 1.

Discussion

Our data did not support the first hypothesis that nicotine abstinence would decrease attentional bias towards positive emotional stimuli whilst increasing attentional bias towards negative emotional stimuli. However, our data did indicate that nicotine abstinence increased attentional bias to neutral stimuli, compared with emotional stimuli. This effect was not specific to emotion (i.e., positive vs. negative). This finding adds to a growing body of research (32,33), indicating a role for nicotine abstinence in the affect regulation of cigarette

smoking. However, our data are the first to suggest that nicotine abstinence may modify affect regulation by reducing attentional bias for emotional facial expression stimuli.

Studies of healthy adults demonstrate attentional bias towards emotional stimuli in favor of neutral stimuli, as an established feature of human emotional processing (34–36). Our data suggest that smoking abstinence may disrupt these emotional processing correlates of affect regulation, by favoring neutral stimuli over emotion stimuli. However, these data are in contrast to previous evidence of nicotine's specific effect on attentional bias, with a bias towards positive stimuli and a bias away from negative stimuli (13, 37, 38). This discrepancy may reflect differences in study stimuli and/or nicotine administration, where previous studies have used affective word stimuli and nicotine patches (38). Additionally, our findings should be interpreted with caution since our findings did not support our hypotheses and findings from previous studies.

Experiment Two: Methods

Design

A double-blind between-subjects placebo-controlled design, with nicotine challenge (nicotinized, denicotinized) and expectancy (told nicotinized, told denicotinized) as between-subject factors, and stimulus type (positive, negative) and validity (valid, invalid) as within-subject factors.

Participants

Non-dependent social smokers (defined as smoking a maximum of two cigarettes per day, or 14 per week; with a score of less than 3 on the FTND) were recruited from students and staff at the University of Bristol and members of the general public. Prior to the test session all participants were asked to abstain from smoking on the morning of testing and to abstain from drinking alcohol for 12 hr (overnight) prior to testing. On the test day participants were randomized to smoke a nicotinized or denicotinized cigarette and were additionally randomized to be told that the cigarette did or did not contain nicotine. Participants received £5 each for participation. The study was approved by the University of Bristol Faculty of Science Research Ethics Committee.

Materials

Questionnaire measures used were; FTND, QSU, PANAS, and VAS. The FTND was completed once at baseline. The QSU, VAS, and PANAS were administered once at baseline and once after the visual probe task. Visual probe task stimuli were identical to those used in experiment one.

Procedures

All participants were tested between 12 p.m. and 6 p.m. in a laboratory in the School of Experimental Psychology at the University of Bristol. After providing informed consent, all participants completed a screening process identical to the one reported in experiment one. Prior to the test session, all participants were asked to abstain from smoking for the morning of testing (verified by exhaled CO) and to abstain from drinking alcohol for 12 hr (verified

by exhaled breath alcohol). Following screening procedures baseline questionnaire measures were completed (FTND, PANAS, QSU, and VAS). Participants were next randomized to receive either a nicotine or denicotinized cigarette and were additionally randomized to be told that the cigarette either did or did not contain nicotine. Cigarettes were prepared, labeled, and placed in a blinding envelope by an experimental collaborator with no participant contact to maintain blinding. Cigarettes were Quest, denicotinized cigarettes (Quest 1; contains no more than 0.05 mg nicotine) or nicotine cigarettes (Quest 3; 0.6 mg nicotine). Participants smoked the cigarette and completed the visual probe task, which was identical to that used in experiment one. On completion of the task, participants completed questionnaire measures (QSU, PANAS, VAS) and were reimbursed for their time, unblinded and received a full debrief.

Data analysis

For visual probe data, mean correct response reaction times were analyzed within a $2 \times 2 \times 2 \times 2$ design, two between-subjects factor of challenge (nicotine, denicotinized) and expectancy (told nicotine, told denicotinized) and stimulus type (positive, negative), and validity (valid, invalid) as within-subject factors. Outlier response times of less than 200 ms and greater than 2000 ms (31) were removed for each subject before data analysis. Skewness tests indicated that visual probe data were not normally distributed, but could be normalized using a log10 transformation. Mixed-model ANOVAs were conducted of mean QSU, PANAS, and VAS scores with a within-subjects factor of time (baseline, post-task) and challenge and expectancy as between-subjects factors.

Results

Characteristics of Participants

Participants ($n = 96$; 50% male) were on average aged 21 years ($SD = 1$, range 18–28) and had a FTND score of 0.1 ($SD = 0.4$, range 0–2). Descriptive data were analyzed using a series of univariate ANOVAs to compare challenge and expectancy groups. Groups did not differ according to any descriptive variables ($ps > 0.09$). Table 2 shows characteristics of nicotine versus denicotinized challenge by expectancy group participants.

Cigarette Craving

A mixed-model ANOVA of mean QSU scores indicated a main effect of time ($F[1, 91] = 15.79$, $p < .001$, $\eta^2 = 0.15$), such that craving decreased from baseline to post-task for all participants. There was no evidence for any other main effects or interactions ($ps > 0.21$).

Mood

A mixed-model ANOVA of mean PANAS positive mood scores indicated a main effect of time ($F[1, 92] = 44.41$, $p < .001$, $\eta^2 = 0.33$), such that positive mood decreased from baseline to post-task for all participants. There was no evidence for other main effects or interactions ($ps > 0.21$). A mixed-model ANOVA of mean PANAS negative mood scores indicated was no evidence for all main effects and interactions ($ps > 0.23$). Mixed-model ANOVAs of mean VAS scores revealed a similar pattern of results.

Visual Probe Task

All error trials were removed from the data analysis. The overall percentage of errors was 4%, there were no differences by group. A mixed-model ANOVA indicated evidence of a main effect of validity ($F[1, 92] = 4.03, p = 0.048, \eta^2 = 0.04$), such that all participants were faster to respond to probes replacing emotional stimuli ($M = 2.79, SD = 0.1$) compared to those replacing neutral stimuli ($M = 2.80, SD = 0.1$). This main effect was qualified by evidence of a validity $\times$ challenge interaction ($F[1, 92] = 3.55, p = .063, \eta^2 = 0.04$) and a validity $\times$ challenge $\times$ expectancy interaction ($F[1, 92] = 5.31, p = 0.023, \eta^2 = 0.06$). There was no evidence for any other main effects or interactions ($ps > 0.13$). For the validity $\times$ challenge interaction, simple effects analyses were conducted for participants receiving nicotine and denicotinized cigarettes separately. There was evidence for a main effect of validity in the nicotine condition only ($F[1, 46] = 5.69, p = .021, \eta^2 = 0.11$). Further post-hoc analyses revealed that participants in the nicotine condition were faster to respond to probes replacing emotional stimuli ($M = 2.78, SD = 0.08$) compared to those replacing neutral stimuli ($M = 2.79, SD = 0.08$). For the validity $\times$ challenge $\times$ expectancy interaction, simple effects analyses were conducted for challenge and expectancy groups separately. There was evidence for a main effect of validity for participants in the nicotine condition who were told that their cigarette did not contain nicotine only ($F[1, 23] = 7.97, p = .010, \eta^2 = 0.26$). Further post-hoc analyses revealed that participants were faster to respond to probes replacing emotional stimuli ($M = 2.78, SD = 0.09$) compared to those replacing neutral stimuli ($M = 2.79, SD = 0.09$). There was no evidence for a main effect of validity in any other condition ($ps > 0.37$). These data are shown in Figure 2.

Discussion

Data did not support our second hypothesis that nicotine challenge and nicotine expectancy; would increase attentional bias towards positive stimuli whilst decreasing attentional bias towards negative stimuli. Our data suggest that nicotine, irrespective of expectancy increased attentional bias to emotional stimuli compared with neutral stimuli, this effect was not specific to emotion. Consistent with the STAR model of affect regulation (8) these data suggest that nicotine serves decrease attention towards irrelevant “neutral” stimuli and directs attention towards the most salient and relevant “emotional” stimuli. This finding should be treated with caution as our hypothesis was not supported and this effect was not observed in our first experiment, where nicotine did not increase attentional bias for emotional stimuli. These incongruent findings may reflect a difference in smoking behaviors of participants in the two experiments or that the effect observed here in experiment two reflects rejection of our null hypothesis.

Additionally, findings indicate that nicotine increases attentional bias for emotional stimuli, but only when smokers hold the expectancy that they are smoking a denicotinized cigarette. These data indicate that nicotine, increased attentional bias for emotional stimuli, even when nicotine delivery was not expected. In line with previous evidence (19,20,22,24), our data suggest that the expectation of nicotine reduced cigarette craving in the denicotinized challenge group only.

Data also indicated that expectation of nicotine reduced anxiety, but only for smokers in the nicotine challenge. These data are consistent with the suggestion that smokers hold expectations that nicotine delivery will produce desirable effects on mood that together with nicotine's direct effects may maintain smoking behaviour (19).

Limitations

The finding of the two experiments should be interpreted with consideration of the following limitations. One limitation of this experiment is the potential of denicotinized cigarettes to deliver a low dose of nicotine (39). However, this dose is sustainably less than that of smoking a nicotine cigarette. Additionally, the between-subject design of our experiments is a potential limitation, where we have reduced statistical power to observe differences in nicotine's effects. This limitation is reflected in the partial support for our study hypotheses and the inconsistent findings between experiments. However, a within-subjects design was used to limit potential practice effects on the visual probe task (40).

Conclusions

Our data suggest that nicotine abstinence disrupts attentional bias towards emotional facial stimuli and that nicotine increases bias towards emotional stimuli. These data provide support for nicotine's modulation of attentional bias as a central mechanism for maintaining affect regulation in cigarette smoking. Our data also suggest a role for nicotine expectancy in affect regulation, where expectation of nicotine appears to reduce cigarette craving and anxiety.

Together, these data suggest that pharmacological (nicotine) and non-pharmacological (expectancy) factors may operate at different levels of affect regulation. Whilst, our mood data suggest a role for nicotine expectancy at an explicit level (e.g., self-reported mood and craving) our attentional bias data indicate that nicotine delivery may exert its effects on affect regulation at an implicit, early processing stage. Beliefs about the expectation of nicotine on affect may occur at a conscious level of awareness, where an individual can access expectations about nicotine (e.g., "Nicotine will improve withdrawal symptoms"). In contrast, nicotine may directly influence attentional processing, outside of an individual's awareness. This evidence is important in our understanding of the role affect regulation plays in maintaining smoking, but also for understanding how negative affect may contribute to unsuccessful quit attempts and relapse. Our data suggest that low mood and deficits in emotional processing are important characteristics of nicotine abstinence that could be potentially targeted in novel cessation programs.

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A.S.A. and M.M. designed the study and wrote the protocol. S.A. undertook the statistical analysis and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript. We thank Sophie Parker, Matt Brandon and Anna Johnson for collecting the data.

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References

1. Stein EA, Pankiewicz J, Harsch HH, et al. Nicotine-induced limbic cortical activation in the human brain: a functional MRI study. *Am J Psychiatry*. 1998; 155:1009–1015. [PubMed: 9699686]
2. Warburton DM, Mancuso G. Evaluation of the information processing and mood effects of a transdermal nicotine patch. *Psychopharmacology (Berl)*. 1998; 135:305–310. [PubMed: 9498735]
3. Baker TB, Piper ME, McCarthy DE, Majeskie MR, Fiore MC. Addiction motivation reformulated: an affective processing model of negative reinforcement. *Psychol Rev*. 2004; 111:33–51. [PubMed: 14756584]
4. Shiffman S, Paty JA, Gnys M, Kassel JA, Hickcox M. First lapses to smoking: within-subjects analysis of real-time reports. *J Consult Clin Psychol*. 1996; 64:366–379. [PubMed: 8871421]
5. Kassel JD, Stroud LR, Paronis CA. Smoking, stress, and negative affect: correlation, causation, and context across stages of smoking. *Psychol Bull*. 2003; 129:270–304. [PubMed: 12696841]
6. Donny EC, Chaudhri N, Caggiula AR, et al. Operant responding for a visual reinforcer in rats is enhanced by noncontingent nicotine: implications for nicotine self-administration and reinforcement. *Psychopharmacology (Berl)*. 2003; 169:68–76. [PubMed: 12774186]
7. Attwood AS, Penton-Voak IS, Munafò MR. Effects of acute nicotine administration on ratings of attractiveness of facial cues. *Nicotine Tob Res*. 2009; 11:44–48. [PubMed: 19246440]
8. Gilbert DG. The situation x trait adaptive response (STAR) model of drug use, effects, and craving. *Hum Psychopharmacol Clin Exp*. 1997; 12:S89–S102.
9. Kassel JD, Shiffman S. Attentional mediation of cigarette smoking's effect on anxiety. *Health Psychol*. 1997; 16:359–368. [PubMed: 9237088]
10. Robinson TE, Berridge KC. The neural basis of drug craving: an incentive sensitization theory of addiction. *Brain Res Rev*. 1993; 18:247–291. [PubMed: 8401595]
11. Robinson TE, Berridge KC. The psychology and neurobiology of addiction: an incentive-sensitization view. *Addiction*. 2000; 95(suppl 2):S91–117. [PubMed: 11002906]
12. Gilbert, DG. Smoking: Individual differences, psychopathology and emotion: The Series in Health Psychology and Behavioral Medicine. Philadelphia, PA: Taylor and Francis; 1995.
13. Asgaard GL, Gilbert DG, Malpass D, Sugai C, Dillon A. Nicotine primes attention to competing affective stimuli in the context of salient alternatives. *Experimental and Clinical Psychopharmacology*. 2010; 18(1):51–60. [PubMed: 20158294]
14. Gilbert DG, Rabinovich NE, Malpass D, et al. Effects of nicotine on affect are moderated by stressor proximity and frequency, positive alternatives, and smoker status. *Nicotine Tob Res*. 2008; 10:1171–1183. [PubMed: 18629727]
15. Field M, Mogg K, Zetteler J, Bradley BP. Attentional biases for alcohol cues in heavy and light social drinkers: the roles of initial orienting and maintained attention. *Psychopharmacology (Berl)*. 2004; 176:88–93. [PubMed: 15071718]
16. Adams S, Ataya AF, Attwood AS, Munafò MR. Effects of acute alcohol consumption on alcohol-related cognitive biases in light and heavy drinkers are task-dependent. *J Psychopharmacol*. 2012; 26:245–253. [PubMed: 21708838]
17. Bradley BP, Hogg K, White J, Groom C, de Bono J. Attentional bias for emotional faces in generalized anxiety disorder. *Br J Clin Psychol*. 1999; 38:267–278. [PubMed: 10532148]
18. Mogg K, Bradley BP. Attentional bias in generalized anxiety disorder versus depressive disorder. *Cogn Therapy Res*. 2005; 29:29–45.
19. Kirsch I, Lynn SJ. Automaticity in clinical psychology. *Am Psychol*. 1999; 54:504–515. [PubMed: 10424156]
20. Perkins K, Sayette M, Conklin C, Caggiula A. Placebo effects of tobacco smoking and other nicotine intake. *Nicotine Tob Res*. 2003; 5:695–709. [PubMed: 14577986]
21. Shahan TA, Bickel WK, Madden GJ, Badger GJ. Comparing the reinforcing efficacy of nicotine containing and de-nicotized cigarettes: a behavioral economic analysis. *Psychopharmacology (Berl)*. 1999; 147:210–216. [PubMed: 10591889]

22. Donny EC, Houtsmuller E, Stitzer ML. Smoking in the absence of nicotine: behavioral, subjective and physiological effects over 11 days. *Addiction*. 2007; 102:324–334. [PubMed: 1722288]
23. Perkins KA, Grottenthaler A, Ciccocioppo MM, Conklin CA, Sayette MA, Wilson AS. Mood, nicotine, and dose expectancy effects on acute responses to nicotine spray. *Nicotine Tob Res*. 2009; 11:540–546. [PubMed: 19351782]
24. Marlatt, GA.; Rohsenow, DJ. Cognitive processes in alcohol use: Expectancy and the balanced placebo design. *Advances in Substance Abuse: Behavioral and Biological Research*. Mello, NK., editor. Vol. 1. Greenwich: CT JAI Press; 1980. p. 159-199.
25. Juliano LM, Brandon TH. Effects of nicotine dose, instructional set, and outcome expectancies on the subjective effects of smoking in the presence of a stressor. *J Abnorm Psychol*. 2002; 111:88–97. [PubMed: 11866182]
26. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict*. 1991; 86:1119–1127. [PubMed: 1932883]
27. Tiffany ST, Drobes DJ. The development and initial validation of a questionnaire on smoking urges. *Br J Addict*. 1991; 86:1467–1476. [PubMed: 1777741]
28. Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. *Arch Gen Psychiatry*. 1986; 43:289–294. [PubMed: 3954551]
29. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*. 1988; 54:1063–1070. [PubMed: 3397865]
30. Tiddeman B, Burt M, Perrett D. Prototyping and transforming facial textures for perception research. *IEEE Comput Graphics Appl*. 2001; 21:42–50.
31. Ratcliff R. Methods for dealing with reaction time outliers. *Psychol Bull*. 1993; 114:510–532. [PubMed: 8272468]
32. Carmody TP. Affect regulation, nicotine addiction, and smoking cessation. *J Psychoactive Drugs*. 1992; 24:111–122. [PubMed: 1506996]
33. Benowitz NL. Neurobiology of nicotine addiction: implications for smoking cessation treatment. *Am J Med*. 2008; 121:S3–10. [PubMed: 18342164]
34. García-Ogueta MI. Attention processes and neuropsychological syndromes. *Rev Neurol*. 2001; 32:463–467. [PubMed: 11426410]
35. Rees G. Attention, adaptation, and the motion aftereffect. *Neuron*. 2001; 32:6–8. [PubMed: 11604133]
36. Berman R, Colby C. Attention and active vision. *Vision Res*. 2009; 49:1233–1248. [PubMed: 18627774]
37. Gilbert DG, Riise H, Dillon A, Huber J, Rabinovich NE, Sugai C. Emotional stimuli and context moderate effects of nicotine on specific but not global affects. *Exp Clin Psychopharmacol*. 2008; 16:33–42. [PubMed: 18266550]
38. Rzetelny A, Gilbert DG, Hammersley J, Radtke R, Rabinovich NE, Small SL. Nicotine decreases attentional bias to negative-affect-related Stroop words among smokers. *Nicotine Tob Res*. 2008; 10:1029–1036. [PubMed: 18584466]
39. Brody AL, Mandelkern MA, Costello MR, et al. Brain nicotinic acetylcholine receptor occupancy: effect of smoking a denicotinized cigarette. *Int J Neuropsychopharmacol*. 2009; 12:305–316. [PubMed: 18706128]
40. Henson R, Hartley T, Burgess N, Hitch G, Flude B. Selective interference with verbal short-term memory for serial order information: a new paradigm and tests of a timing-signal hypothesis. *Q J Exp Psychol A*. 2003; 56:1307–1334. [PubMed: 14578087]

Figure 1.
Mean visual probe reaction times (ms) by abstinence group.
Values are expressed as mean $\pm$ SEM.

Figure 2.

Mean visual probe reaction times (ms) by nicotine challenge and nicotine expectancy.

Values are expressed as mean $\pm$ SEM.

Table 1

Participant Demographic Characteristics Including Age, Exhaled CO, FTND, PANAS, QSU, VAS Mood, and MNWS Total Scores for Abstinent and Non-abstinent Smokers.

	Abstinent (n = 22)	Non-abstinent (n = 24)	p value
Age (years)	23±7	24±5	<i>p</i> = .642
Exhaled CO2	6±2	11±5	<i>p</i> < .001
FTND	3±1	3±2	<i>p</i> = .161
PANAS (+ve)	24±6	30±6	<i>p</i> = .001
PANAS (–ve)	16±7	13±4	<i>p</i> = .124
QSU	43±10	23±10	<i>p</i> < .001
VAS (Happy)	52±18	62±15	<i>p</i> = .047
VAS (Drowsy)	51±26	41±23	<i>p</i> = .185
VAS (Depressed)	27±25	13±12	<i>p</i> = .018
VAS (Anxious)	38±28	18±18	<i>p</i> = .005
VAS (Energetic)	43±22	56±16	<i>p</i> = .026
VAS (Irritable)	33±30	16±22	<i>p</i> = .033
MSNW	20±9	9±7	<i>p</i> < .001

Values are expressed as mean ± SD.

Table 2

Participant Demographic Characteristics Including Age, Exhaled CO, FTND, PANAS, QSU and VAS Mood Total Scores by Challenge Condition (Nicotinised, Denicotinised) and Expectancy (Told Nicotine, Told Placebo).

	Nicotinised		Denicotinised		<i>p</i> value
	Told nicotine (n = 24)	Told placebo (n = 24)	Told nicotine (n = 24)	Told placebo (n = 24)	
Age (years)	21±2	20±1	21±2	21±1	<i>p</i> = .662
Exhaled CO2	1±0.8	0.9±0.8	0.8±0.6	0.9±0.9	<i>p</i> = .103
FTND	0.1±0.2	0.2±0.5	0.2±0.4	0.04±0.2	<i>p</i> = .094
PANAS (+ve)	27±6	27±7	30±7	29±8	<i>p</i> = .827
PANAS (−ve)	13±2	13±2	13±3	14±6	<i>p</i> = .665
QSU	20±7	24±9	24±12	25±10	<i>p</i> = .542
VAS (Happy)	70±10	64±13	67±12	68±18	<i>p</i> = .197
VAS (Drowsy)	40±28	40±24	31±20	37±21	<i>p</i> = .498
VAS (Depressed)	11±13	16±11	16±18	14±17	<i>p</i> = .210
VAS (Anxious)	22±21	19±16	21±15	35±23	<i>p</i> = .310
VAS (Energetic)	48±22	51±19	52±17	54±18	<i>p</i> = .983
VAS (Irritable)	14±14	20±19	20±17	21±21	<i>p</i> = .516

Values are expressed as mean ± SD.