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Effects of Nicotine on Emotional Distraction of Attentional Orienting: Evidence of Possible Moderation by Dopamine Type 2 Receptor Genotype

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Abstract

Introduction—Growing evidence suggests that attentional bias to, and distraction by, emotional stimuli may moderate affective states and motivation for nicotine and other drug use.

Methods—The present study assessed the effects of nicotine and dopamine receptor genotype on distraction by emotional pictures, during a modified spatial attention task, in 45 overnight-deprived habitual smokers.

Results—Relative to placebo, 14 mg nicotine patch produced shorter overall reaction times (RTs) and individuals with two dopamine type 2 receptor (DRD2) A2 alleles exhibited the greatest RT benefit from nicotine following emotionally negative pictures after the longest cue-target delay (800 ms), but benefitted least from nicotine following positive pictures after the shortest delay (400 ms). In contrast, at the shortest delay, A1 carriers did not benefit from nicotine following emotionally negative pictures but did following positive ones.

Conclusions—These genetic differences in the effects of nicotine on attention immediately following emotionally positive versus negative stimuli may reflect differential excitatory and inhibitory transmitter processes related to approach (reward) and avoidance (punishment) sensitivities of dopamine-related neural networks that support positive and negative affect.

Keywords

Nicotine; Smokers; Dopamine receptors; Genotype; Attentional orienting; Emotion; Distraction; Prime

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Declaration of conflict of interests

None of the authors has a potential conflict of interest with the proposed work.

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1. Introduction

Abstinent smokers frequently report negative mood states and increased distractibility by emotion-related stimuli (Kalman, 2002; Kassel et al., 2003; Spielberger, 1986). Recent studies suggest that attentional and affective responses to nicotine abstinence and nicotine replacement therapy (NRT) are moderated by dopamine-related genetic polymorphisms (Gilbert et al., 2005; Gilbert et al., 2009) and affect-related attentional and situational factors (Gilbert et al., 2008a, 2008b). Relatively little is known about when, how, and in whom nicotine withdrawal symptoms are most likely to occur (Gilbert et al., 2009; Kassel et al., 2003), though it is widely recognized that both nicotinic cholinergic and dopaminergic receptors are critical modulators of attentional processes and reinforcing effects of nicotine (Corrigall et al., 1992; Robinson and Berridge, 1993). Thus, characterizing genetically based individual differences in the effects of NRT on attentional orienting, in contexts that include emotional stimuli, could be useful in better understanding stress-related relapse in individuals attempting to remain smoking abstinent.

Placebo-controlled studies support the view that NRT in nicotine-deprived habitual smokers promotes attentional bias toward positive stimuli, but possibly not toward negative stimuli (Dawkins et al., 2006; Powell et al., 2004). These findings may largely reflect nicotine withdrawal in dependent individuals, though they could also in part reflect inherent effects of nicotine. Complementing these findings, others have found NRT in abstinent smokers to reduce distraction by emotionally negative stimuli (Gilbert et al., 2004, 2005, 2007; Rzetelny et al., 2008). However, none of these studies has assessed the effects of nicotine on emotional distraction during a spatial attention task using lateralized (left and right visual field) targets. Characterizing such effects of nicotine also allows testing of the hypothesis that the effects of nicotine, NRT, and nicotine withdrawal-related affective changes are based in part on changes in attentional bias to emotional stimuli. Such processes may reflect neural networks that include left-right brain differences in densities of receptors for dopamine, acetylcholine and other neurotransmitters (Gilbert et al., 2005) according to the the lateralized affective networks hypothesis of the Situation by Trait Adaptive Response (STAR) model (Gilbert 1995).

Consistent with this lateralized neural networks hypothesis, a number of studies support the view that nicotine and other cholinergic and dopaminergic receptor agonists and antagonists can alter responses to left versus right visual field stimuli (McClellon et al., 2003; reviewed by Gilbert et al., 2005 and by Tucker and Williamson, 1984). Thus, spatial attention tasks using lateralized targets could broaden understanding of brain mechanisms for nicotine replacement in nicotine-abstinent smokers. Examining how NRT alters attention to emotional stimuli could provide insight into the stressful effects of nicotine abstinence and into beneficial effects of NRT.

Dopamine is the neurotransmitter most frequently hypothesized to play an important role in the effects of nicotine and other drugs on attention, affect, and self-administration (Corrigall et al., 1992; Robinson and Berridge, 1993). The A1 genetic polymorphism of the dopamine type 2 receptor (DRD2) genotype has been found to be associated with a reduced number of DRD2 receptors (Thompson et al., 1997), with the attenuating effects of nicotine on

distraction (Gilbert et al., 2005), and with brain stress reactivity during smoking abstinence (Gilbert et al., 2004). Therefore, there is reason to believe that the DRD2 A1 allele may be associated with psychological benefits of NRT. The most widely analyzed DRD2-related genetic polymorphism, Taq1A, resides within the coding region of the ankyrin repeat and kinase domain containing 1 (ANKK1) gene and located near the 3' end of the DRD2 gene (Neville et al., 2004). This close proximity allows linkage of the Taq1A polymorphism to DRD2 expression.

Given genetic influences on broad factors including the disposition to smoke, smoking-related personality traits, the effects of nicotine, attention, and attentional bias and distraction (Gilbert et al., 2005; Gilbert and Gilbert, 1995; Heath et al., 1995), we chose to explore the possible moderating influences of dopamine receptor genotype on the ability of NRT to modulate attentional orienting in the context of emotional distractors. Though other genotypes may moderate the effects of NRT, only DRD2 polymorphisms were evaluated at present because of the modest sample size.

Current findings are from a larger study that found that the effects of NRT on distraction during a rapid visual information processing (RVIP) task were moderated by DRD2 genotype (Gilbert et al., 2005). Specifically, in the earlier report NRT was found to increase target detection accuracy and shorten RTs more in the presence of left-visual-field (LVF) than right-visual-field (RVF) emotional distractors, but shortened RTs more with RVF than LVF numeric distractors. Additionally, nicotine replacement therapy facilitated performance more in individuals with at least one A1 allele than in homozygous A2A2 individuals, especially with numeric distractors presented to the left hemisphere. NRT also tended to shorten RT to targets following negative stimuli more than other types of stimuli. The task described in the present report complements the earlier study by assessing the effects of NRT on spatial attention to lateralized target stimuli following centrally presented emotional distractors.

The present study used a modified version of Posner's (1980) cued target detection task (CTDT). The CTDT has been used in several studies to characterize nicotine's effects on cued attentional orienting (e.g., Thiel et al., 2005), though none of these studies assessed the influence of emotional stimuli as moderators. The CTDT requires the participant to fixate centrally while covertly directing attention to the side of a computer screen, cued by a central arrow. The individual then responds as quickly as possible to the appearance of the peripheral target, an asterisk. On different trials, the central arrow either directs attention to the side in which the target subsequently appears (valid cue) or to the side opposite of where the target appears (invalid cue). Reaction times (RTs) to targets are more rapid when the target is preceded by a valid central arrow cue, as attention has already been allocated to this location. The CTDT has advantages over other spatial and selective attention tasks, which include the ability to manipulate both the visual field of the targets and the time intervals between cues and the targets. The present study used central pictures differing in affective valence, rather than presenting central arrow cues, in order to better characterize the effects of emotion-related distraction by positive and negative valence pictures on subsequent lateralized targets.

Based on the above-reviewed evidence, it was hypothesized that DRD2 genotype, length of delay between the distractor and target stimulus, and the emotional valence (positive or negative) of the distractor would moderate the effects of nicotine replacement therapy on emotional distraction in overnight-abstinent smokers. The hypothesis that delay between the emotional distractor and target stimulus would be moderated by nicotine replacement therapy and genotype was based on the Situation by Trait Adaptive Response (STAR) model hypothesis (Gilbert, 1995, p. 213) that genotype moderates the effects of nicotine on the dissipation rate of attentional biasing to affective stimuli.

2. Methods

2.1. Participants

Forty-six smokers (24 female, 22 male) averaging 18.4 cigarettes per day (5.4 SD, 10–40 range) were used in the statistical analyses of nicotine's effects on attention. Mean age was 23.5 years (7.5 SD, 18–47 range). Because of the focus on genetics, only northern European Caucasians were used. Nicotine dependence was assessed with the Fagerström Test of Nicotine Dependence (FTND; Heatherton et al., 1991). The mean FTND score was 4.5 (1.6 SD, 1–8 range), indicating a moderate degree of dependence.

Participants were recruited by ads and community postings. Exclusion criteria included smoking fewer than 10 cigarettes/day on average for the past year, habitually using cigarettes with estimated nicotine deliveries of less than 0.6 mg, reported use of psychoactive drugs or medications other than caffeine, marijuana, and alcohol, excessive alcohol use (> 28 drinks/wk), non-English speaking, atypical sleep cycles, pregnancy, and visual problems.

Participants were instructed not to smoke for the 12 hours preceding each of the experimental sessions and only those who adhered to this 12-hour abstinence were included in the data analysis. Adherence was verified prior to each session with expired breath carbon monoxide (CO) concentration and self-report. Adherence was confirmed after sessions through nicotine and plasma cotinine levels. Sessions were rescheduled for those exceeding the maximum allowable CO ($N = 7$) and for those reporting 3 or more alcoholic drinks the night before session, fewer than 5 hours of sleep, illness, or drug use ($N = 8$). Marijuana use was prohibited for 72 hours prior to experimental sessions. Genotype was not significantly associated with age, FTND score, pre-session plasma cotinine level or patch-related plasma nicotine boost.

2.2 Design

During each of 4 experimental sessions, participants completed the emotional distractor target-detection (EDTD) task once, 4 hours after patch application. The study was double blind for the nicotine vs. placebo status of the patches. The active vs. placebo patch orders were counterbalanced across sessions in a within-participants design. Each participant received a nicotine patch on one of the first two experimental sessions and a second nicotine patch during one of the last 2 experimental sessions, while being on placebo patches during the other 2 sessions.

2.3. Procedures

Participants who completed 2 orientation sessions and 4 experimental sessions earned \$200. The study and consent form were approved by Southern Illinois University Human Subjects Committee. During the orientation, after an eligibility assessment, participants signed the IRB-approved consent form, and then completed questionnaires and practiced experimental tasks. Handedness was tested with the Edinburgh Handedness Inventory (Oldfield, 1971), and there were 43 right handed and 3 left handed individuals in the reported analyses. Participants were also screened for any visual deficits that would interfere with task performance. Participants were instructed to not consume alcohol or tobacco within 12 hours of the experimental session onset. Participants were provided no direct or suggestive information about the effects of nicotine.

2.3.1. Experimental sessions—Sessions began between noon and 2:00 p.m. and a minimum of 48 hours and a maximum of 7 days separated their onsets. Upon arrival, CO concentration was monitored and blood samples were taken prior to patch application. A Nicoderm® 14 mg transdermal patch or placebo patch (identical in appearance) was placed on the upper arm 4 hours prior to the onset of the EDTD task. A 14 mg patch was used because in pilot studies some smokers reported light headedness, nausea, and/or sickness with 21 mg patches.

Participants completed questionnaires or read other materials while waiting to begin experimental tasks. Nausea, sickness, dizziness, and mood states were assessed every 20 minutes with the Feeling State Questionnaire (Gilbert et al., 1992). The Patch Guess and Attribution Questionnaire (GAP; Gilbert et al., 2005) was completed at the conclusion of each experimental session to assess blindness to patch condition.

2.3.2 Assessment of nicotine and smoking abstinence—Pre-session CO concentrations of 10+ ppm resulted in rescheduling of the session (N=7). Plasma nicotine concentrations of greater than 2.0 ng/ml also resulted in elimination of 6 participants' data from analysis.

2.3.3. Genotyping dopamine (DRD2)—Dopamine type 2 receptor (DRD2) genotyping was performed on blood samples using TaqIA restriction-length polymorphisms assessed as described by Spitz et al. (1998) and Gilbert et al. (2004). Categorization for statistical purposes was as either Homozygous A2A2 allele or A1 allele carriers (A1A2 and A1A1 genotypes). Based on genotyping of DRD2 dopamine receptor alleles, 15 participants were classified as A1 allele carriers and 31 had a homozygous A2A2 genotype. The numbers of A1A1, A1A2, and A2A2 individuals were 2, 13, and 31, respectively. These proportions corresponded to the Hardy-Weinberg distribution, $\chi^2 (1, N = 46) = 0.18, p = 0.67$.

2.3.4 Picture stimuli—The picture distractors used in the emotional distractor target-detection (EDTD) were of three types: negative, positive, and neutral. Pictures were similar in terms of complexity, color, saturation, and brightness and were selected from the International Affective Picture System (Lang et al., 1995) and our laboratory (Gilbert et al., 2008a). The mean valence scores on the Lang et al. 9-point scale for these pictures were

(standard deviations in parentheses): negative 2.86 (.98), positive 6.93 (.99) and neutral 4.90 (.73), where “1” = extremely negative through “9” = “extremely positive”. Mean arousal ratings were negative 5.54 (1.8), positive 4.04 (1.8) and neutral 2.64 (1.2), where “1” = not at all arousing through “9” = “extremely” arousing. There were no significant differences between the mean scores of the IAPS and laboratory pictures. Details concerning the specific pictures used can be obtained from the authors.

2.4. Experimental Equipment, Software and Task

2.4.1. Equipment and software—The EDTD task was presented using SuperLab™ 2.0 stimulus presentation software and response pad (Cedrus Corp, San Pedro, CA).

2.4.2. Emotional distractor target detection (EDTD) task—The 20-minute EDTD task presented an emotional distractor picture prior to each target stimulus. Emotionally negative, neutral, and positive pictures were presented in blocks of 24 affectively similar picture trials (24 same valences consecutively). Order of blocks was counterbalanced so that each valence type occurred first, second, or third equally often.

Each trial consisted of the following sequence of events: a central fixation cross presented for 1500 ms; a distractor picture in the center of the computer monitor for 3000 ms; a delay with a fixation cross for either 400, 600, or 800 ms; a lateralized target asterisk presented peripherally to the left or right visual field for 100 ms; and a “blink” prompt for 1000 ms. Participants indicated their detection of the lateralized target asterisk by pushing either the left or right response pad button and were instructed to maintain fixation on the center of the screen and to respond as rapidly as possible to the asterisk target without making errors.

2.5. Analysis

The planned analyses were performed on correct responses measured in mean reaction times (RTs) that occurred between 100 and 1000 ms post target presentation. The number of response errors (incorrect button presses) was so small (less than 1%) that no meaningful analysis of errors by condition was possible. The initial statistical analysis used a mixed-design ANOVA involving Nicotine (nicotine vs. placebo) × Patch Exposure (first vs. second day of exposure to the nicotine and placebo patches) × Visual Field (left vs. right target location) × Valence (positive vs. negative vs. neutral picture) × Delay (400 ms vs. 600 ms vs. 800 ms delay between distractor picture offset and target onset) × Gender × Genotype. Probability values were based on Greenhouse and Geisser (1959) correction for sphericity of repeated measures. A nicotine main effect and higher-order interactions involving nicotine are described.

3. Results

3.1. Plasma Nicotine Concentration

The nicotine patch resulted in an increase in plasma nicotine concentration of approximately 14 ng/ml, compared to no change in the placebo condition (see Gilbert et al., 2005). Participant-reported abstinence time ranged from 12–16 hours.

3.2. Patch Blindness Assessment

The participants' certainty ratings of being on the nicotine patch were 57% for individuals on the nicotine patch and 47% for individuals on the placebo (statistically chance levels).

3.3. EDTD Task Results

As expected, nicotine reduced the mean RT, as evidenced by a significant main effect of of Nicotine, mean RT difference = 13.88 ms, (SE = 3.51), $F(1, 44) = 16.30$, $p < .001$, partial $\eta^2 = .270$. Most importantly, nicotine reduced RTs in a manner that depended on genotype, picture valence, and delay length, Nicotine $\times$ Valence $\times$ Delay $\times$ Genotype, $F(4, 176) = 3.00$, $p = .02$, partial $\eta^2 = .064$ (see Figure 1). Pairwise comparisons showed that in A1 carriers, after the shortest (400 ms) delay, nicotine reduced RTs to a greater extent after positive pictures than after negative pictures, $p = .011$.

In contrast, in homozygous A2 individuals, after the shortest delay, nicotine reduced RTs more following neutral than after positive pictures, $p = .007$. Also in A2 individuals, at the long delay (800 ms), nicotine reduced RTs to a greater extent following negative pictures compared to neutral, $p = .017$ and positive, $p = .014$, pictures.

Separate analyses of covariance (ANCOVAs), one with FTND dependence score and the other with age as covariates, revealed no significant moderation of the above-noted effects. There was no significant main effect for visual field or significant interaction of visual field with nicotine, valence, or genotype. The possibility of handedness influencing results was considered, and data was analyzed both including and excluding 3 left handed individuals. There was no overall difference in the pattern of results with and without the left handed participants, and thus they were included to increase power for other analyses. Interested readers can request these different analyses by contacting the first author.

Despite expected findings regarding lateralized effects of nicotine on emotional distraction of attentional processing, no significant interactions involving visual field and valence were observed.

4. Discussion

Nicotine's effects were moderated by type of emotional distractor, dopamine type 2 receptor (DRD2) genotype, and time between the emotional distractor and the target. While the following discussion refers to the effects of nicotine relative to placebo, the observed effects of nicotine versus placebo could also reflect effects of nicotine withdrawal alleviation in habitual smokers. For the sake of brevity, this is discussed as effects of nicotine because nicotine was the manipulated variable.

Nicotine reduced distraction (reduced RTs) following emotionally negative distractors (relative to positive and neutral distractors) only in homozygous A2 individuals; this effect of negative distractors was limited to the longest delay (800 ms). In contrast, at the shortest delay (400 ms), in homozygous A2 individuals, nicotine increased distraction by positive pictures relative to neutral pictures. Together, these two findings suggest that in A2 individuals, nicotine enhances distraction by (attention to) emotionally positive stimuli

relative to neutral stimuli after brief (400 ms) delays. However, at longer (800 ms) delays nicotine attenuates distraction by negative stimuli (relative to both positive cues and to neutral distractors, which do not differ from each other at this length of delay).

Thus, in homozygous A2 individuals, nicotine's ability to reduce distraction by negative picture stimuli, relative to positive and neutral pictures, appears to rely on processes that develop at some point between 600 and 800 ms after distractor offset. This finding in A2 individuals is consistent with other findings and theory (Gilbert, 1995; Gilbert et al., 2008a) suggesting that nicotine attenuates processing of negative affect when the negative stimulus is more temporally distal and less proximal. For example, Gilbert et al. (2008a) found greater reduction in negative affect by nicotine during the distal periods (shortly after stressors), than during actual stressor exposure, as well as reduced attentional bias (eye-gaze) toward negative pictures, relative to positive pictures, during the later but not earlier portions of picture presentations.

In contrast to homozygous A2 individuals, in A1 carriers nicotine did not differentially influence distraction by negative pictures relative to neutral distractors, but nicotine did decrease distraction by positive relative to negative distractors at the shortest (400 ms) post-distractor delay. This ability of nicotine to reduce distraction by positive stimuli in A1 carriers may be an exception to the more frequent finding (Dawkins et al., 2006; LeSage et al., 2006; Powell et al., 2004) that nicotine *generally increases* distraction by positive reinforcement-related cues in smokers. In contrast, the current finding that nicotine increased distraction by emotionally positive stimuli in homozygous A2 individuals at the shortest (400 ms) delay is consistent with the above-noted models by Powell et al. and others suggesting that nicotine enhances attentional and behavioral responses to (and distraction by) rewarding stimuli (reviewed by Chaudhri et al., 2006; Gilbert, 1995).

Nicotine may reduce distraction by positive stimuli relative to negative stimuli in A1 carriers at short delays because A1 carriers are highly sensitive to, and thereby distracted by, positive stimuli (relative to negative stimuli) when they are nicotine abstinent. Consistent with this possibility, during the placebo condition, the RTs of A1 carriers subsequent to positive stimuli were longer (slower) than in any of the other experimental conditions of either genotype.

Enhanced positive, relative to negative and neutral cue reactivity, in abstinent A1 carriers may also be related to the observation that A1 carriers tend to be impulsive in the presence of reward-related cues, have reduced sensitivity to negative stimuli/potential punishers, and are more likely to have attention-deficit-hyperactivity disorder and other impulse-related disorders (Blum et al., 2000; Noble et al., 1994). This differential reward vs. threat sensitivity in nicotine-deprived A1 carriers appeared in the present study only at the earliest (400 ms) delay. An ability of nicotine to reduce impulsivity associated with nicotine abstinence state-dependent (and possibly temperamentally-based) reward relative to punishment sensitivity could help explain the association of smoking with impulse-related disorders such as attention deficit hyperactivity disorder (Gilbert, 1995).

As a commonly reported motivation for smoking is to reduce negative affect (Gilbert et al., 1995), abstinent smokers often describe negative affect and affective distractibility (Kalman, 2002; Kassel et al., 2003), and NRT in the form of patches or gum can reduce such negative affect after smoking cessation (Piasecki et al., 2003), an important contribution of the current study is that effects of nicotine patches on negative emotional distractors were moderated by both genotype and time between emotional stimuli and targets. Thus, the ability of NRT to potentially mitigate emotional responses associated with smoking abstinence or withdrawal is better characterized.

4.1. Methodological Limitations and Future Directions

The present study was limited by a relatively modest sample size and was not a fully representative sample of smokers. Due to the effects found in this relatively modest sample, and under specific circumstances, spurious results are possible and of concern. Replication in larger, representative samples is clearly needed to test the reliability and generalizability of these findings and to assess additive and interactive effects of DRD2 genotype with other genes. The effects of nicotine were not assessed in non-Caucasians, or in very light, very heavy, older, or substance abusing smokers.

DRD2 Taq1A has not been reliably associated with smoking prevalence and the effects of NRT (David et al., 2008). Though Taq1A has been associated with the number of dopamine D2 receptor number (Thompson et al., 1997), attentional effects of NRT (Gilbert et al., 2005), and brain responses to smoking cessation (Gilbert et al., 2004), Taq1A is not actually located in the DRD2 gene, but rather the ANKK1 gene (Neville et al., 2004). Many neurotransmission-related genes are likely to play important roles in modulating the effects of nicotine on attention and affect, and vulnerability to nicotine dependence. For example, Munafò et al. (2005) found that the serotonin transporter gene modulated color-naming interference in ex-smokers, but not current smokers. Genetically based individual differences in cholinergic neurotransmission may be especially important in the case of certain types of attentional and other cognitive processing given that cholinergic neurotransmission has strong modulatory effects on attention and cognitive performance (Witte et al., 1997; reviewed by Levin et al., 2006; Levin and Simon, 1998).

As the current study used smokers, the effects cannot be generalized to ex-smokers and non-smokers and it cannot be determined whether these effects reflect amelioration of nicotine withdrawal or inherently beneficial effects of nicotine. Our findings are also limited by the use of only one dose of nicotine delivered by transdermal patch. Further systematic dose-response studies using several different nicotine doses and means of nicotine administration are therefore needed.

Since effects of nicotine on performance tasks can differ in nonsmokers compared to smokers (Newhouse et al., 2004), and attentional orienting in nonsmokers is not influenced by nicotine in some studies (Giessing et al., 2007), additional research which allows investigation of altered attentional processing of emotional stimuli by nicotine in both smokers and nonsmokers is clearly needed. Such insight into general emotional effects of nicotine versus withdrawal and nicotine abstinence is crucial. Other researchers have found that in nonsmokers, only certain performance domains, such as behavioral inhibition, are

improved by transdermal nicotine in nonsmokers, while attentional orienting was actually impaired by transdermal nicotine (Wignall and de Wit, 2011). Examining how nicotine can affect attention to emotional stimuli, using other attentional paradigms incorporating emotional stimuli, might provide additional insight into emotional cues and stressors associated with nicotine abstinence and smoking cessation as well.

5. Conclusions

Despite the above-noted limitations, the present study produced an interesting pattern of findings where the effects of nicotine on emotional distractors were moderated by DRD2 genotype and by the time between the emotional stimulus offset and the target.

Genetic differences in the effects of nicotine on attention directly following positive versus negative valence emotional stimuli may reflect differential excitatory and inhibitory neurotransmitter processes. These genetic differences might be related to approach (reward) and avoidance (punishment) sensitivities of dopamine-related neural networks that support positive and negative affect. Understanding and preventing stress-related or negative emotion-related relapse in individuals who might be genetically prone to have difficulty remaining smoking abstinent are potential implications.

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Highlights

- Attention bias to negative emotional stimuli may relate to nicotine and other drug use.
- We assess effects of nicotine and DRD2 genotype on emotional distraction during an attention task.
- Effects of nicotine were moderated by genotype and by time between emotional stimuli and targets.
- Such genetic differences may be associated with dopamine-related networks that support affect and with differential response to nicotine abstinence or withdrawal.

Figure 1.

Effects of nicotine RT benefits (placebo RT – nicotine RT) as a function of DRD2 genotype (A1 carriers [a] vs. homozygous A2s [b]), distractor offset-to-target delay, and valence of the emotional distractor picture during the emotional distractor target-detection task. In A1 carriers, RT benefit was greatest at the short (400 ms) delay with positive distractors. In contrast, in homozygous A2 individuals at the short delay RT shortening was greatest in the neutral condition, but at the long delay nicotine benefits were greater after emotionally

negative distractors than after both neutral and positive ones. Bars with the same letter differ significantly, $p < .02$, within the same distractor-to-target delay.