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Original Investigation

Effects of acute nicotine administration on ratings of attractiveness of facial cues

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Abstract

Introduction: It has been suggested that one mechanism by which nicotine may exert an influence over behavior is by enhancing the reinforcing properties of other stimuli. We therefore sought to test the hypothesis that nicotine enhances the hedonic impact of behaviors performed in the presence of nicotine, using ratings of facial attractiveness, as we considered these to have considerable ecological validity in the context of the social environment within which cigarette smoking takes place.

Methods: Male and female participants attended a single testing session and were randomized to smoke either a nicotine-containing or a denicotinized cigarette, after which they completed ratings of attractiveness of 20 male and 20 female faces. Participants were required to have abstained from smoking for 24 hr prior to testing, and the nicotine manipulation was conducted double blind.

Results: A 2 × 2 × 2 mixed-model repeated measures analysis of variance indicated a significant main effect of cigarette, reflecting higher attractiveness ratings in the nicotinized compared with the denicotinized condition.

Discussion: Our data indicate that nicotine increases ratings of attractiveness of facial cues. We did not observe any evidence that these effects differed between males and females. We also did not observe effects on subjective ratings of mood, suggesting that the effects we observed on ratings of attractiveness may not simply reflect global hedonic effects, or a positivity bias in questionnaire responding, in the nicotine condition.

Introduction

Despite the widely acknowledged addiction potential of tobacco, due primarily to the actions of nicotine, the psychoactive and hedonic effects of nicotine are modest (Balfour, 2004). For example, nicotine presented intravenously in doses comparable with those obtained from a single cigarette puff produces only modest ratings of liking and satisfaction (Rose, Behm, Westman, & Johnson, 2000). While dependent smokers experience considerable negative reinforcement through the relief of withdrawal symptoms, in particular after overnight abstinence, the role of positive reinforcement, in particular among young, non-dependent smokers at an early stage in the progression to regular smoking and dependence, is unclear.

One mechanism by which nicotine may exert an influence over behavior is by enhancing the reinforcing properties of other stimuli (Donny et al., 2003). For example, nicotine appears to increase responding for a concurrently available, reinforcing, nonpharmacological stimulus in animal models, even when the nicotine is neither temporally nor causally associated with the behavior (Donny et al., 2003). In other words, in addition to its action as a primary reinforcer, nicotine may serve to potentiate the reward value of other stimuli (Balfour, 2004). Other evidence from animal models indicates increased responding for food, alcohol, and cocaine (Bechtholt & Mark, 2002; Clark, Lindgren, Brooks, Watson, & Little, 2001; Popke, Mayorga, Fogle, & Paule, 2000) and decreased thresholds for brain reward stimulation (Kenny & Markou, 2006) following the administration of nicotine.

The mechanism proposed to account for this effect (Balfour, 2004) is the increase in extracellular dopamine evoked in the medial shell of the nucleus accumbens by the administration of nicotine (e.g., by smoking a cigarette). In particular, any activity or stimulus experienced while dopamine overflow remains elevated will have increased hedonic impact (Balfour, 2004). As a result, an increase in dopamine overflow resulting from nicotine administration could exert a more general positive influence on other behaviors performed concurrently. This, in turn, might contribute to the pleasure associated with the habit and, therefore, to the addiction potential of nicotine, independently of any direct hedonic effects of nicotine administration (Balfour, 2004). To date, the majority of evidence for these effects comes from animal models of nicotine administration and self-administration.

While negative reinforcement processes are important in maintaining tobacco use and strengthening dependence, they cannot explain why people begin to use tobacco or continue to

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do so until dependence has developed. Therefore, positive reinforcement models are likely of particular importance in the early stages of tobacco use and in the development of dependence (Glautier, 2004). The potentiation by nicotine of the reward value of other stimuli may comprise part of the process whereby tobacco use is initiated and maintained prior to the development of dependence. Furthermore, as tolerance to the effects of nicotine develops with increasing dependence, negative reinforcement processes may come to dominate over positive reinforcement processes, so that this potentiating effect of nicotine may decline in relative (or absolute) strength as dependence develops.

We sought to test the hypothesis that nicotine enhances the hedonic impact of behaviors performed in the presence of nicotine compared with the same behaviors performed in the absence of nicotine. We used ratings of facial attractiveness, as we considered these to have considerable ecological validity in the context of the social environment within which cigarette smoking takes place. Also, evidence suggests that facial attractiveness is correlated with activity in the reward pathways such as the orbitofrontal cortex and striatum (Aharon et al., 2001; Kampe, Frith, Dolan, & Frith, 2001; O'Doherty et al., 2003). We recruited young, nondependent adults at a relatively early stage in their smoking career since we would expect the effects of nicotine on the hedonic aspects of other behaviors to be greatest prior to or during the development of dependence. Moreover, we tested participants when they were nicotine free (i.e., after at least overnight abstinence) to maximize the effects of nicotine administration and because we expected withdrawal effects to be negligible in nondependent smokers. Finally, we included male and female participants to explore possible sex differences, given a broad literature that suggests differential effects of nicotine in men and women (Perkins, Donny, & Caggiula, 1999).

Methods

Design and overview

Male and female participants attended a single testing session and were randomized to smoke either a nicotine-containing or a denicotinized cigarette, after which they completed ratings of attractiveness of 20 male and 20 female faces. The experimental design therefore consisted of two between-subjects factors of cigarette (nicotinized, denicotinized) and sex (male, female) and one within-subjects factor of target sex (male, female). Participants were required to have abstained from smoking for 24 hr prior to testing, and the nicotine manipulation was conducted double blind.

Participants

Male and female (n = 48, 50% male) nondependent smokers (with a score of less than 3 on the Fagerström Test for Nicotine Dependence [FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991]) were recruited from the staff and students at the University of Bristol and the general population. Participants received either £5 or course credit for participation, as appropriate. The study was approved by the Faculty of Science Research Ethics Committee.

After providing informed consent, participants completed a screening process, consisting of an interview conducted by a trained researcher, to ensure good physical and psychiatric health. Exclusion criteria included drug dependence (excluding caffeine) and significant current or past medical or psychotic illness. Participants also were required to be free from medication and illicit substances, indicated by self-report, and were required to abstain from smoking for 24 hr prior to the study, with recent abstinence confirmed by exhaled carbon monoxide (CO) breath test (<5 ppm).

Materials

Cues for the attractiveness task comprised 40 photographic facial stimuli (20 male and 20 female, mean age 21 years). 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 2,048 × 3,072 pixels in full color. All images had a constant background consisting of a gray cloth. The photographic subjects wore no overt facial jewelry, and cues to clothing were masked with a neutral smock. Participants were asked to pose, standing, with a neutral expression and photographed at a distance of approximately 150 cm. The camera lens was at the same horizontal plane as the eyes for each photograph. This procedure provides replicable images of the same individual and provides images that are equivalent to experience of faces in day-to-day interaction (Stephan, Clement, Owen, Dobrostanski, & Owen, 2004). All the photographic subjects were University of Bristol undergraduate students of European ancestry in 2005, and each individual was the current heterosexual partner of one other individual in the opposite-sex face set.

The questionnaire measures used included the FTND, the Spielberger State-Trait Anxiety Inventory (STAI state anxiety subscale only; Spielberger, Gorusch, Lushene, Vagg, & Jacobs, 1983), and Visual Analog Scales (VAS) of mood, anxiety, and craving, comprising the items "happy," "drowsy," "depressed," "anxious," "energetic," "irritable," and "craving a cigarette" rated on a 100-mm scale from "not at all" to "extremely."

Procedures

On test days, participants were randomized to receive either a nicotinized (0.6 mg nicotine) or a denicotinized (0.005 mg nicotine) cigarette. Cigarettes were administered between subjects, as previous studies in our laboratory have demonstrated that the use of a within-subjects design can lead to an unblinding of the cigarette condition among participants. Cigarettes were commercially available reduced-nicotine Quest cigarettes (Vector Tobacco Ltd., Durham, NC) that had been labeled independently by a third party so that the procedure was conducted double blind.

Baseline ratings included self-report measures of mood and craving (FTND, STAI state anxiety, VAS). Participants were then given their cigarettes to smoke and completed the ratings of facial attractiveness. After smoking the entire cigarette, participants completed self-report measures of mood and craving (STAI state anxiety, VAS).

For the ratings of facial attractiveness, facial stimuli were presented in a blocked format (male and female), with the order of blocks randomized across participants. The testing was self-paced, and participants were required to rate each face for

attractiveness, using a 7-point Likert scale anchored at "very unattractive" and "very attractive." Responses were entered using numeric keys on the testing computer. The presentation of facial stimuli was controlled by the E-Prime (version 1.2) software package.

After completing the attractiveness rating task, participants completed an awareness check to test whether they were aware of whether their cigarettes contained nicotine. Participants were then briefed as to the purpose of the study.

Data analyses

Data were analyzed within a 2 × 2 × 2 mixed-model repeated measures analysis of variance (ANOVA) framework, with cigarette (nicotinized, denicotinized) and sex (male, female) as between-subjects factors. For the analysis of attractiveness rating data, target sex (male, female) was included as a within-subject factor, and for the analysis of questionnaire data, time (pre-cigarette and post-cigarette) was included as a within-subjects factor.

An alpha level of .05 was maintained throughout. All analyses were performed using SPSS version 12.0.

Results

Characteristics of participants

Four participants were excluded based on high exhaled CO readings, so that the final sample for analysis consisted of 44 participants (52% male). Participants were aged on average 23 years ($SD = 5$), began testing at 14:01 ($SD = 89$ min), smoked 33 cigarettes/week ($SD = 18$), had smoked for 7 years ($SD = 4$), and had an average FTND score of 0 ($SD = 0.5$), indicating that they were nondependent.

A series of 2 × 2 ANOVAs, with cigarette (nicotinized, denicotinized) and sex (male, female) as between-subjects factors, were conducted to assess the matching of participants in the four cells of the experimental design on a number of variables. We found no significant differences in cigarettes per week, years smoking, FTND score, or baseline STAI state anxiety ($p > .20$), but significant differences in age ($p = .012$) and start time ($p = .032$) were observed. We therefore included age and start time as supplementary covariates in subsequent analyses.

Questionnaire measures

A series of 2 × 2 × 2 mixed-model repeated measures ANOVAs, with cigarette (nicotinized, denicotinized) and sex (male, female) as between-subjects factors and time (pre-cigarette, post-cigarette) as a within-subjects factor, were used to examine STAI state anxiety and VAS data.

State anxiety

For STAI state anxiety data, we found marginal main effects of sex, $F(1, 40) = 2.88$, $p = .097$, and cigarette, $F(1, 40) = 3.05$, $p = .088$. No other main effects or interactions approached statistical significance ($p > .20$).

Visual Analog Scales

For VAS data, we found that there was a significant main effect of time for ratings of "irritable," $F(1, 40) = 10.39$, $p = .003$, reflecting a decrease from pre-cigarette to post-cigarette. In addition, we found significant time × cigarette, $F(1, 40) = 5.43$, $p = .025$, and time × sex, $F(1, 40) = 4.22$, $p = .047$, interactions, the former reflecting a greater decrease in the nicotinized compared with the denicotinized condition and among females compared with males on ratings of "irritable." We also found a significant main effect of time for ratings of "craving a cigarette," $F(1, 40) = 24.57$, $p < .001$, reflecting a decrease from pre-cigarette to post-cigarette, but this was not qualified by a significant time × cigarette interaction ($p = .47$). No other main effects or interactions were significant ($p > .05$). In particular, no time × cigarette interactions, which would reflect a differential effect of cigarette over time, were significant ($p > .17$).

Attractiveness rating task

A 2 × 2 × 2 mixed-model repeated measures ANOVA, with cigarette (nicotinized, denicotinized) and sex (male, female) as between-subjects factors and target sex (male, female) as a within-subjects factor, was used to examine attractiveness rating data. We found a significant main effect of cigarette, $F(1, 40) = 5.37$, $p = .026$, reflecting higher attractiveness ratings in the nicotinized condition compared with the denicotinized condition, and a significant main effect of target sex, $F(1, 40) = 12.23$, $p < .001$, reflecting higher attractiveness ratings for female faces compared with male faces, as typically observed in studies of facial attractiveness (Bashour, 2006).

No other main effects or interactions were significant ($p > .12$). Removing three participants of non-European ancestry did not alter these results nor did including as covariates age, start time, or VAS ratings of "irritable" and "craving a cigarette" post-cigarette. In all cases, the main effect of cigarette remained significant ($p = .018$–$.047$).

Awareness check

At the end of testing, participants were asked whether they thought their cigarettes contained nicotine. Participants were accurate in 57% of cases, which was not significantly different from chance, $t(43) = 0.90$, $p = .37$.

Discussion

Our data indicate that, among nondependent smokers who have not smoked recently, nicotine increases ratings of attractiveness of facial cues. This finding is consistent with current theories of nicotine addiction, which suggest that part of the addiction potential of nicotine stems from its ability to noncontingently enhance the positively reinforcing properties of other stimuli. We did not observe any evidence that these effects differed between males and females. Also, we did not observe any effects of nicotine on subjective ratings of mood, indicating that the effects we observed on ratings of attractiveness may not have simply been a consequence of global hedonic effects, or a positivity bias in questionnaire responding, in the nicotine condition. We did observe effects on ratings of "irritable," reflecting a greater decrease in the nicotinized compared with the denicotinized condition, but when measure was included as a covariate in the analyses of ratings of attractiveness, our results were not altered substantially. Moreover, although we observed a decrease of ratings of "craving a cigarette" over time, this did not differ between cigarette conditions, suggesting that it was not a result of withdrawal relief.

These data are important because they complement and extend evidence from the animal literature that suggests that nicotine exerts both direct and indirect effects that may act synergistically to produce nicotine dependence with repeated exposure. In particular, in addition to increasing the incentive salience of cues explicitly paired contingently with nicotine presentation, it may also potentiate the impact of moderately pleasurable or reinforcing cues to which the individual is exposed when nicotine is noncontingently present. In particular, the prolonged hypersensitivity to reward that persists after acute nicotine intake has terminated may serve as a powerful interoceptive discriminative stimulus (Donny et al., 2003; Kenny & Markou, 2006) and may contribute to relapse even after long periods of abstinence.

Several limitations of the present study should be considered when interpreting these results. First, we did not include a set of control stimuli to ascertain whether the observed effects of nicotine were specific to facial cues or were more general. Although the general lack of effects on self-reported mood ratings suggests that our results do not simply arise from global hedonic effects or reporting biases, future studies should include a range of categories of stimuli as control conditions. In particular, careful delineation of stimuli that might be considered to be broadly positively reinforcing or to encourage approach behavior (such as facial cues) and those that might not (such as household objects) would be valuable. Investigation of the effects of nicotine on facial cues projecting positive and negative emotional expressions also would be informative.

Second, we restricted our recruitment to light, nondependent smokers to maximize the acute effects of nicotine and model their impact in the development of dependence. We further required participants to be nicotine free to maximize the effects of nicotine administration. Although we expected negligible withdrawal effects in nondependent smokers, the effects of nicotine administration on ratings of "irritability" over time suggest that this was not entirely the case. Future studies should include dependent smokers, both satiated and in withdrawal, to explore whether the effects we report here are likely to be of greatest importance in the development of dependence or are a consequence of withdrawal relief. In addition, the use of more detailed and sensitive measures of withdrawal symptoms and positive and negative affect should be included in future studies. It also might be valuable to test differing doses of nicotine, across both nondependent and dependent smokers.

Third, our sample size was relatively small due to practical constraints on data collection and may have lacked power to detect sex differences in the effects we observed. Although our current data suggest that any sex differences are likely to be negligible, these results should be regarded as preliminary and require replication (in larger samples) and extension (by the inclusion, e.g., of a control condition).

Fourth, we did not control for familiarity effects (whereby study participants may have known the photographic subjects) or the ancestry of participants and target faces. However, all photographic subjects were no longer at the University of Bristol, so we consider it unlikely that study participants, who were primarily current undergraduate students, would have been familiar with them, and removing participants of non-European ancestry did not alter our results.

In conclusion, our data suggest that nicotine increases ratings of attractiveness of facial cues, consistent with evidence that nicotine potentiates the reinforcing properties of rewarding stimuli. These effects do not appear to be due to global hedonic effects or reporting bias following nicotine administration, although further research, including the use of more sensitive measures of withdrawal symptoms and positive and negative affect, as well as appropriate control conditions, is needed to exclude this possibility. If these findings prove robust, they provide support in humans for evidence of the effects of nicotine on brain reward systems that has, to date, been drawn largely from research using animal models.

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Declaration of Interests

None declared.

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