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Effects of Nicotine and Emotional Priming on Ability to Inhibit Eye-Gaze Toward Emotional

Stimuli in an Antisaccade Task in Nonsmokers

Thesis

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Thesis Sponsor: David G. Gilbert, Ph.D.

Abstract

Saccadic eye movement tasks like the antisaccade task (AST) have been used to assess impulsivity and response inhibition in a variety of populations, including tobacco-abstinent smokers. Previous studies using ASTs have shown nicotine to reduce reaction times (RTs) compared to nicotine abstinence possibly reinforcing the habit of smoking. Previous research has also shown nicotine to reduce attention to and distraction by emotionally negative stimuli, which may account for some of the ability of nicotine to reduce negative affect. The present study was the first to assess the interactive effects of nicotine, emotional priming and emotional target stimuli on AST performance in nonsmokers. Ten male and 14 female college student nonsmokers wore a nicotine and placebo patch on separate, counterbalanced, days during which they performed ASTs. The ASTs consisted of sequences with a prosaccade or antisaccade cue followed by an emotional priming picture and emotional target face. Findings revealed an expected main effect of Saccade Type such that reaction times (RTs) were longer (slower) in antisaccade trials compared to prosaccade trials and an overall RT shortening (speeding) effect of nicotine compared to placebo. The effects of Drug interacted with Saccade type, such that nicotine speeded RTs on antisaccade trials more than on prosaccade trials. However, most importantly, both Prime Valence and Target Valence moderated the effects of nicotine in poor baseline-performing individuals, but not others, such that nicotine decreased RTs most during negative prime with the negative target condition, relative to other prime-target combinations. These findings support the view that emotional primes and targets can be important modulators of an inherent ability of nicotine to modulate cognitive and/or affective processes in poor baseline performing nonsmokers.

Introduction

Nicotine dependence and related smoking behavior is the most important cause of preventable disease (Mokdad, et al., 2004); however, it is not clear why some individuals who experiment with smoking progress to nicotine dependence while others do not. One possibility suggested by the literature is that nicotine may enhance attentional performance during demanding tasks and that this may be experienced as reinforcing by some individuals. Another possibility is that nicotine may reduce attentional bias to emotionally negative stimuli and thereby reduce negative affect (Asgaard, Gilbert, Malpass, Sugai, & Dillon, 2010; Gilbert, Rabinovich et al., 2008). The proposed study tested these two possibilities by using a novel, emotional picture version of the antisaccade task.

The antisaccade task measures response inhibition by requiring subjects to inhibit looking at a novel stimulus (Pierrot-Deseilligny, Muri, Ploner, Gaymard, & Rivaud-Pechoux, 2003). The study is also based on the recent findings by Asgaard et al. (in press) that nicotine can reduce emotionally negatively primed attentional bias to (eye-gaze toward) emotionally negative picture stimuli. Thus, the goal of this study was to assess the effects of an acute dose of nicotine on the ability to inhibit automatic attention to (eye-movement towards) emotionally negative pictures, relative to emotionally neutral and emotionally positive pictures. In addition the study assessed whether the effects of nicotine are moderated by emotional priming with emotionally negative, positive, or neutral picture stimuli. The present study, also sought to better understand the mechanisms that may reinforce nicotine self-administration. Smokers report believing that their primary reason for smoking is to enhance cognitive performance and to regulate mood (Gilbert, 1995; Spielberger, 1986). Thus, this study was designed to better characterize nicotine's effects

on cognitive performance with reaction time latency and mood regulation with emotional prime and target valences in a computerized AST.

Nicotine, relative to deprivation, has been found to enhance cognitive performance in tobacco smokers and a small but growing number of studies have assessed the effects of nicotine in nonsmokers in order to determine whether the cognitive and affective effects of this drug are in part inherent or alternatively are simply due to the alleviation of nicotine withdrawal symptoms. Consistent with the view that nicotine can enhance attention, studies have found nicotine to decrease Reaction times (RTs), while RTs increase when tobacco smokers are deprived of nicotine in antisaccade task (AST) (Dawkins et al. 2006).

In smokers, nicotine, relative to placebo, reduces attention to and distraction by negative stimuli as assessed by eye-gaze (Gilbert et al., 2008), brain activation (Gilbert et al., 2007), and RT (Gilbert, 2005), and thereby may reduce negative affect (Gilbert, 1995). Nicotine has been found to be especially effective in reducing distraction during tasks that involve executive functions (Gilbert et al., 2005; Warburton, 1998). Nicotine has been found to enhance executive functioning in the AST, a task that involves the inhibition of automatic processing and via the imposition of executive functions. The antisaccade task measures response inhibition by requiring subjects to inhibit looking at a novel stimulus (Pierrot-Deseilligny, Muri, Ploner, Gaymard, & Rivaud-Pechoux, 2003). The study is also based on the recent findings by Asgaard et al. (in press) that nicotine can reduce emotionally negatively primed attentional bias to (eye-gaze toward) emotionally negative picture stimuli. Thus, the goal of this study is to assess the effects of an acute dose of nicotine on the ability to inhibit automatic attention to (eye-movement towards) emotionally negative pictures, relative to emotionally neutral and emotionally positive

pictures. In addition the study would assess whether the effects of nicotine are moderated by emotional priming with emotionally negative, positive, or neutral picture stimuli.

This study assessed the effects of nicotine on distraction by emotional stimuli in nonsmokers using an (AST), as well as the effects of emotional priming and target images in nonsmoking individuals that differ in terms of their baseline (nicotine-free mean RTs). The AST is a challenging novel task that combines the inhibition of automatic processing with distraction by emotional stimuli into one task that has never been tested on smokers or nonsmokers. Work by Pettiford et al. (2007) showed that in dependent smokers, overnight abstinence significantly increased antisaccade errors with simple, non-emotional, target stimuli, while having no effect on prosaccade performance. Nonsmokers have also been shown to increase reaction time on an acute does of nicotine, while performing a simple antisaccade task (Rycroft et al., 2007). However, once again this was using a non-emotional antisaccade task. Nicotine has also shown that it affects higher voluntary control and not just simple motor and visual control (Larrison et al., 2004). The proposed study will use nonsmokers, rather than smokers because there is a lack of information about the effects of nicotine in individuals who are not nicotine dependent. Previous research has found that individuals with lower baseline task performance benefit more from nicotine (Perkins et al. 1992). Thus, the effects of baseline RT performance on AST performance were also evaluated with the expectation the individuals with relatively poorer performance during the placebo condition would benefit more from nicotine than those who performed relatively better during the placebo condition.

Hypotheses

It was predicted that, relative to placebo, nicotine patch would reduce antisaccade reaction times (RT), and that nicotine would have its greatest beneficial effects in the condition

where an emotionally negative prime picture precedes the presentation of an emotionally negative picture in the antisaccade condition.

Methods

Participants

10 male and 14 female college student nonsmokers (no smoking in past year and fewer than 100 cigarettes in life), aged 18 to 30 completed the study. Participants wore nicotine patch one day and placebo patch another day beginning 6 hours before task onset.

Materials

Eye-tracking system. An Arrington Research Inc. computerized system using ViewPoint Software (Scottsdale, AZ) was used to collect eye-gaze direction (toward or away from target) using a 60 Hz sampling rate. A Dell stimulus-presentation computer communicated with the Arrington computer via SuperLab (Cedrus Corporation, San Pedro, CA) serial output connection that time-marked the onset of visual stimuli with eye-gaze direction in real time. The SuperLab computer presented the AST task through the eyetracking goggles.

Patches. Seven mg Walgreen brand (manufactured by Novartis) slow release nicotine patches were obtained from a local Walgreen pharmacy. The placebo patches consisted of placebo patch was a 5cm × 5cm bandage.

Antisaccade Task (AST) Each AST consisted of 36 prosaccade and 36 antisaccade targets randomly intermixed. The task format was as follows a fixation cross centered in the middle of the screen for 200 ms. A red or green circle followed for 1000 ms (red indicated look away from the target face, while green indicated look toward the target face that appeared later). An emotional priming picture (positive, negative, or neutral) presented for

2000 ms. A mask presented for 50 ms. Another fixation cross presented for 1000 ms. A blank gap or black screen presented for 200 ms. An emotional target Ekman face (positive, negative, or neutral target) was finally presented for 1000 ms randomly on the right or left part of the screen (all other images presented in the middle of the screen). The red or green circle indicated whether the participant should look in the opposite visual field (away from) the position of the emotional target face or in the same visual field (toward the) emotional target face respectively.

Stimuli. Priming pictures were taken from the International Affective Picture System (Lang et al., 1995). Target pictures were smiling, angry, and neutral faces from the Ekman Picture Series (Ekman & Friesen, 1977).

Procedure

Recruitment of participants was accomplished through flyers posted around a large Midwestern University and in the surrounding community. Participants were screened through an initial phone screener and through a more comprehensive screening at the beginning of their practice session to determine qualified applicants. Criteria included age between 18-35, no mental or serious physical disorders, no smoking in the last year, and fewer than 100 cigarettes in their lifetime. Each participant completed one orientation day, two morning patch placement days, and two afternoon experimental sessions that were 6 hours after the morning patch placement. The practice session consisted of practicing the AST twice. The afternoon experimental sessions both consisted of the participant completing the AST four times. The AST was presented on 18-inch LCD color computer monitors that use Super Lab software in conjunction with Arrington eye tracking system and software. Saccades were recorded for all trials, but reaction times were calculated only for

correct targets. In order to count as a saccade the participant's eyes had to move more than 3 degrees from the midline in the correct direction and maintain that direction consistently for 150 ms. Reaction times meeting these criteria faster than 80 ms were thrown out.

Results

The overall analysis used was a mixed-design multivariate ANOVA with one between subjects factor, Placebo Performance (PP) Group (three groups [top, middle, bottom] RT on placebo day) and 5 within subjects factors (Drug [nicotine vs. placebo], Prime Valence [positive, negative, boring], Target Valence [positive, negative, boring], Visual Field [right vs. left], and Saccade Type [antisaccade vs. prosaccade]). This MANOVA revealed a significant main effect of Drug, such that nicotine was associated with shorter (faster) RTs overall across AST conditions, F(1,20) = 6.83, p = .017. There was also a Drug × PP Group interaction, F(2,20) = 5.46, p = .013, such that those in the slow PP group benefitted more from nicotine, relative to placebo, than the other two groups. A Drug × Saccade Type, F(1,20) = 10.22, p = .005, reflected the fact that nicotine shortened RTs relative to placebo more in the antisaccade than prosaccade condition. A Drug × Saccade Type × PP Group interaction, F(2,20) = 6.35, p = .007, indicated that those in the slow PP group benefitted more from nicotine, relative to placebo, in the antisaccade condition, but not the prosaccade condition. Finally, a Drug × Saccade Type × PP Group × Prime Valence × Target Valence interaction, F(8,32) = 2.66, p = .023, such that those in the slow PP group benefitted more from nicotine, relative to placebo, in the antisaccade condition, but not the prosaccade condition and in the negative prime with negative target condition, but not in the positive prime with positive target condition. In addition, the slow PP group had significant nicotine benefits in the negative prime with neutral and positive target, the neutral prime with boring

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and positive target, and the positive prime with negative target. Individuals in the middle PP group benefitted from nicotine relative to placebo in the neutral prime with negative target, as well as, the neutral target with a negative or positive prime.

As expected, independent of patch type, antisaccade RTs were much slower than prosaccade, F(1, 20) = 122.15, p < .001,(Fig. 2.). There was an effect of prime across patch types such that relative to neutral primes, negative primes had an overall longer RT (p=.001). Negative primes also tended to have lengthier RTs relative to positive primes (p=.071). Thus consistent with previous research negative pictures have a greater distracting (RT slowing) effect.

Discussion

The present study looked to determine the effects of nicotine not only on an AST, but on an AST that had emotional prime and target images. Findings showed multiple interactions between drug type, saccade type, prime type, target type, and placebo performance group with no interaction of visual field. As expected, a significant interaction showed nicotine to reduce RT in all AST conditions. This nicotine performance improvement (faster RT) in nonsmokers shows similar benefits seen in previous studies on smoking abstinent individuals (Rycroft et al., 2007; Larrison et al., 2004). The benefits of nicotine (faster RT), however were significantly improved for Antisaccade trials, but not on Prosaccade trials. This could possibly be due to the greater difficulty of the inhibition process of an Antisaccade. The Antisaccade may need to utilize higher cognitive centers that are unnecessary for the simpler more habitual Prosaccade.

The lowest placebo performance group showed the greatest benefit from nicotine compared to the other two performance groups. This supports the view of previous research

that nicotine shows the greatest benefits in lower baseline performing individuals (Perkins et al. 1992). Consistent with our hypotheses, long RTs during the placebo condition predicted greater benefits (reduced RTs) from nicotine, and Prime and Target valence moderated these effects of nicotine on RT. These greater benefits of nicotine in individuals who were poorperforming (long-RT) during the baseline (placebo) condition are consistent with the selfmedication hypothesis of nicotine use (Gilbert, 1995) and the associated growing literature indicating that the benefits of nicotine are greater in individuals with low baseline performance and in those with cognitive impairments (e.g., ADHD, schizophrenics, Alzheimer's disease, depressive symptoms).

Both Prime Valence and Target Valence moderated the effects of nicotine in poor baseline-performing individuals. In this group in the placebo condition a negative prime with a negative target was associated with a very long (slow) RT (408 ms) while in the nicotine condition RT was 338 ms, 70 ms less. In contrast, in the positive prime with positive target condition PP individuals did not significantly benefit from nicotine (RT for nicotine only 38 ms shorter than for placebo). In addition, the slow PP group had significant nicotine benefits in the negative prime with neutral and positive target, the neutral prime with boring and positive target, and the positive prime with negative target. This clearly shows a complex emotional prime and target valence interaction occurring. Interestingly the middle PP group benefitted from nicotine relative to placebo in the neutral prime with negative target, as well as, the neutral target with a negative or positive prime. There is not a clear interaction of all of a certain prime or target having a significant effect, but interactions of specific primetarget combinations are having a significant effect on RT. A larger pool of participants could help flush out a more consistent pattern to further analyze the combinations that nicotine

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helps modulate the most. The nicotine benefits mediated by emotional primes and targets are significantly seen only in the slow (bottom) two-thirds of the placebo performance group. The upper one-third showed no significant improvement from nicotine across all combination types of emotional primes and targets.

The overall pattern of findings supports the view that emotional primes and targets can be important modulators of an inherent ability of nicotine to modulate cognitive and/or affective processes in poor baseline performing nonsmokers.

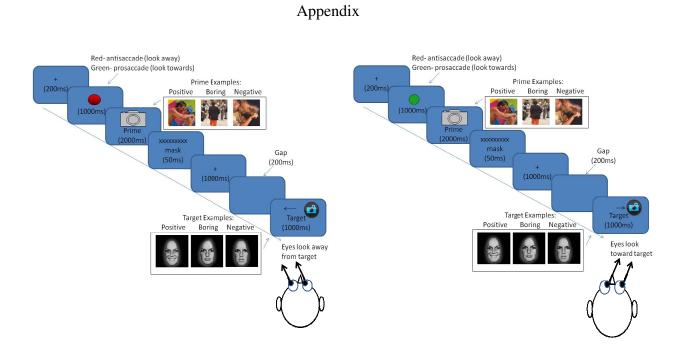


Figure 1. Diagram showing the sequence of stimuli during the anti-saccade and pro-saccade tasks.

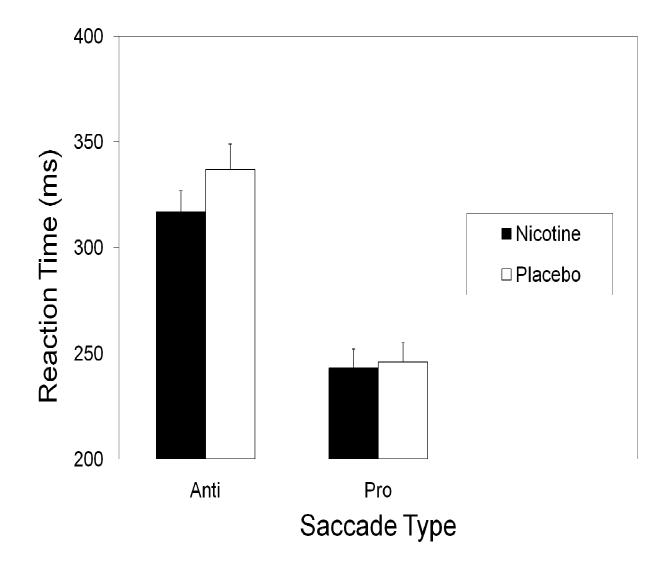


Figure 2. Effects of nicotine on RT as a function of saccade type (anti vs. pro). Nicotine reduced RT in the antisaccade, but not prosaccade during the AST.

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