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Moderation of nicotine effects on covert orienting of attention tasks by poor placebo performance and cue validity

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ABSTRACT

Introduction and rationale: Given baseline-dependent effects of nicotine on other forms of attention, there is reason to believe that inconsistent findings for the effects of nicotine on attentional orienting may be partly due to individual differences in baseline (abstinence state) functioning. Individuals with low baseline attention may benefit more from nicotine replacement.
Method: The effects of nicotine as a function of baseline performance (bottom, middle, and top third of mean reaction times during placebo) were assessed in 52 habitual abstinent smokers (26 females/26 males) utilizing an arrow-cued covert orienting of attention task.
Results: Compared to a placebo patch, a 14 mg nicotine patch produced faster overall reaction times (RTs). In addition, individuals with slower RTs during the placebo condition benefitted more from nicotine on cued trials than did those who had shorter (faster) RTs during placebo. Nicotine also enhanced the validity effect (shorter RTs to validly vs. invalidly cued targets), but this nicotine benefit did not differ as a function of overall placebo-baseline performance.
Conclusions: These findings support the view that nicotine enhances cued spatial attentional orienting in individuals who have slower RTs during placebo (nicotine-free) conditions; however, baseline-dependent effects may not generalize to all aspects of spatial attention. These findings are consistent with findings indicating that nicotine's effects vary as a function of task parameters rather than simple RT speeding or cognitive enhancement.

1. Introduction

Nicotine and other cholinergic drugs can enhance a variety of attentional systems (see Levin and Simon, 1998; Newhouse et al., 2004; Rezvani and Levin, 2001 for reviews). For example, nicotine results in robust vigilance-enhancing and alerting effects (Gilbert et al., 2005). In a recent meta-analysis, Heishman et al. (2010) found significant beneficial effects of nicotine in both habitual smokers and nonsmokers on six components of cognitive functioning: fine motor, alerting attention-accuracy and response time (RT), orienting attention-RT, short-term episodic memory-accuracy, and working memory-RT, with effect sizes from 0.30 to 0.86. These findings support enhancement of cognitive functioning as a motive for smoking (Spielberger, 1986).

However, there are less consistent findings of nicotine's effects on attentional orienting, the multi-stage process of selectively allocating attention to discrete areas of the visual field (Posner, 1980). Attentional orienting is a critical neurocognitive activity for attending to important environmental events during activities such as driving, monitoring children, or even playing sports. Covert orienting of attention tasks (COAT; Posner, 1980) require participants to fixate centrally while covertly directing attention, without foveal eye movement, when cued laterally by a central arrow. Then, as quickly as possible, they respond to a peripheral target. On different trials, the central arrow either directs attention to the side at which the target subsequently appears (valid cue) or to the side opposite of the target (invalid cue). Reaction times (RTs) to targets are typically more rapid when preceded by valid relative to invalid cues (the validity effect), as attention has already been allocated to this target location. In contrast, RTs are typically slower in invalidly cued trials, where attention must be reoriented to unexpected target locations (Posner, 1980; Petersen and Posner, 2012).

The COAT has been used to characterize nicotine's enhancement of cued spatial attention (e.g., Thiel et al., 2005), which may have relevance to reinforcing effects of nicotine and motives for smoking. Research indicates that nicotine and cholinergic agonists can enhance visuospatial reorienting during the COAT and related tasks (Thiel et al., 2005; Thiel and Fink, 2008; Vossel et al., 2008). Such evidence points to nicotine speeding RTs for invalid cued targets and thereby reducing the validity effect, but other studies of the effects of nicotine on cued attentional orienting have been inconsistent.

One possible reason for inconsistent findings is that the effects of nicotine in nonsmokers may differ from the effects in smokers

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(Heishman et al., 2002; Newhouse et al., 2004). In nonsmokers, Griesar et al. (2002) reported that transdermal nicotine, relative to placebo, reduced RTs to targets during a covert attention task, and nicotine was associated with a trend for increased validity effects; this validity effect improvement by nicotine only approached statistical significance, perhaps due to the small sample size ($N = 12$). Alternately, nicotine may have a general arousal effect, but no effect specifically associated with attentional orienting (Hahn et al., 2007). Other studies suggest that nicotine may have no effects on cued attentional orienting tasks in nonsmokers (Giessing et al., 2007) or that nicotine reduces reaction times (RTs) in both smokers and nonsmokers for invalid trials without influencing valid trials (Vossel et al., 2008; Witte et al., 1997).

The aforementioned inconsistent findings could also reflect that nicotine's effects on attentional reorienting relative to orienting depend upon the proportion of valid cues (e.g., 90% vs. 60% valid cues), as nicotine's effects on reorienting may not occur (and validity effects may actually improve with nicotine) under lower cueing reliability (i.e., 60%; Vossel et al., 2008).

Another important factor that may account for the inconsistent pattern of findings across studies is individual differences in baseline (nicotine-free) task performance. The present investigation examined the possibility that the effects of nicotine on visuospatial attention may depend, in part, on individual differences in baseline (placebo or abstinent state) attentional functioning. More specifically, individuals with poorer baseline attentional performance might differentially respond to nicotine versus those with better baseline performance. Perkins (1999) and Newhouse et al. (2004) review evidence supporting the view that poor baseline attentional/cognitive performance is associated with greater benefits from nicotine. Consistent with baseline-dependency, Patterson et al. (2010) recently found that poorer working memory on a rapid information processing task (the N-Back) during nicotine abstinence predicted more rapid resumption of smoking in individuals attempting smoking cessation. Baseline-dependent effects of nicotine have also been observed for P3 event-related potential amplitudes during involuntary novel auditory processing in nonsmokers, demonstrating increased attentional enhancement by nicotine only in individuals with relatively poor attentional capacity (Knott et al., 2014). We are not aware of studies assessing the influence of existing placebo-baseline deficits on covert spatial attention enhancement by nicotine in smokers.

Both theory and a large body of evidence also suggest that individual differences in neurobiological states and traits may mediate situational variability in the effects of nicotine on cognition and affect (Eysenck, 1980; Gilbert et al., 1989; Perkins, 1999). Eysenck (1980, 1997) proposed that nicotine's effects are moderated by pre-drug baseline brain activation that in turn is influenced by genetically influenced dispositional traits, situational arousal, and fatigue potential of the environment. It is therefore critical that the moderation of nicotine's effects by situational and individual difference factors be better characterized by systematic and well-controlled investigations, to investigate when and in whom nicotine influences visuospatial attention and to seek resolution of mixed findings. Current findings are from a larger study examining effects of nicotine replacement therapy (NRT), in the form of transdermal patches, and the moderation by DRD2 genotype, on selective attention and distraction. Specifically, in earlier reports, NRT was found to improve target detection accuracy and shorten RTs during rapid visual information processing (RVIP), depending on distractor visual field and DRD2 genotype (Gilbert et al., 2005). Also, DRD2 genotype and cue-target delays predicted differential nicotine benefit following emotionally positive and negative images (Hammersley et al., 2013).

The present study also examined gender because accumulating evidence suggests that NRT may be less effective in women and that women may be less sensitive to nicotine's reinforcing effects and more influenced by smoking cues (Perkins et al., 1999; Perkins, 2001). More recent research also indicates that acute effects of nicotine may be differentially influenced by impulsivity-related factors (i.e., novelty seeking and disinhibition) in men versus women (Perkins et al., 2008), and that nicotine dose sensitivity can be influenced by whether a cognitive task tends to show sex-specific performance differences (i.e., gender-preferred tasks; Poltavski et al., 2012). However, gender differences in the effects of nicotine on visuospatial attention have not been characterized well in published studies. Nicotine patch may be an excellent manner to assess gender differences because the minimal sensory impact associated with this means of nicotine administration minimizes alternative explanations of these differences.

Primary aims of the present study were to assess cognitive/attentional individual differences in response to nicotine as a function of baseline performance levels during visual-spatial attention performance given previous theory (Eysenck, 1980; Perkins, 1999), and to further clarify inconsistent findings of the effects of nicotine on attentional orienting. Based on the above evidence, we expected that poorer placebo-baseline attention would predict greater effects of nicotine replacement therapy, and also that cue validity and gender would moderate nicotine's effects on COAT performance in overnight-deprived, moderately nicotine-dependent smokers.

2. Material and methods

2.1. Participants

The present study was approved by the Human Subjects Committee, the Institutional Review Board for the university, in accordance with ethical standards for human research. Participants used in the statistical analyses were 26 female and 26 male smokers with a mean age of 23.2 years (6.8 SD, 18–47 range) who smoked an average of 18.38 (5.4 SD, 10–40 range) cigarettes per day. Nicotine dependence was assessed with the Fagerström Test of Nicotine Dependence (FTND; Heatherton et al., 1991). The mean FTND score was 4.36 (1.5 SD, 1–8 range), indicating a moderate degree of dependence for the typical participant. Two males and two females were African Americans and the remaining participants were Caucasian.

Participants were recruited by newspaper ads and postings at the university and in the community. They were screened for both psychiatric and neurological history, by phone and during a face-to-face interviews, prior to consent for participation in the study. These interviews included screening for head injury history, current and former psychoactive drug or medication use, prescription and over-the-counter medications in the past two months, antihistamine use, allergies and possible allergic reactions, acute stressors, current and former psychological problems/diagnoses, prior exposure to nicotine patch, medical conditions in the past year, sleep patterns and duration, vision problems such as such as limited movement, limited vision, or lazy eye in either or both eyes or color blindness, and blood donation history. We further screened for medical conditions, including blood disorders, high blood pressure and heart disease, seizures or epilepsy, blood clotting disorders or deficiency, liver disease, bulimia or anorexia, and currently pregnant or trying to become pregnant. Exclusion criteria included smoking fewer than 10 cigarettes per day for the past year, habitual cigarette estimated nicotine deliveries of <0.6 mg, use of psychoactive drugs or medications other than caffeine, marijuana, and alcohol, excessive alcohol use (more than 28 drinks/week), age <18 or more than 48 years, non-English speaking, atypical sleep cycles, pregnancy, serious medical illness, and uncorrected visual problems. Age was restricted because of slower reaction times (Langan et al., 2010; Seidler et al., 2010) and poorer sight (Owsley, 2011; Faubert, 2002) with increasing age.

Participants were instructed not to smoke for the 12 h preceding each of the experimental sessions and only those who adhered to this 12-hour abstinence were included in the data analysis. Adherence was checked prior to each session with expired breath carbon monoxide concentrations (see procedure section).