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Differential cigarette-related startle cue reactivity among light, moderate, and heavy smokers

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ABSTRACT

In this study, we examined the relationship between the level of daily cigarette consumption and the startle response to affective and cigarette-related cues among treatment-seeking smokers. Before receiving any behavioral or pharmacological treatment, 136 smokers attended a baseline laboratory session, during which we recorded their reflexive eyeblink responses to acoustic startle probes while they were viewing pleasant, unpleasant, neutral, and cigarette-related pictures. We found that 1) cigarette-related and pleasant pictures similarly reduced the startle magnitude compared to neutral pictures; 2) the magnitude of startle modulation rendered by pleasant or unpleasant pictures did not differ among light, moderate, and heavy smokers; and 3) startle attenuation by cigarette-related pictures was greater in heavy smokers than in light smokers. These results suggest that similar to pleasant stimuli, cigarette-related cues are motivationally salient for smokers, and that this salience increases with nicotine dependence.

1. Introduction

Unfortunately, relapse is the most frequent outcome of a smoking cessation attempt. Many smokers have reported that their smoking relapses were associated with situations in which cigarette-related cues were present (Shiffman et al., 2007). Given the prevalence of environmental smoking-related cues, it is important to better understand smokers' reactivity to these cues in order to prevent relapse more effectively. Consistent with this reported association between relapse and the presence of smoking cues, many laboratory studies have demonstrated that smokers have greater reactivity to cigarette-related cues than non-cigarette-related cues by measuring self-reported craving (Payne, Smith, Sturges, & Holleran, 1996; Sayette, Martin, Wertz, Shiffman, & Perrott, 2001; Tidey, Rohsenow, Kaplan, & Swift, 2005), attentional bias (Ehrman et al., 2002; Hogarth, Mogg, Bradley, Duka, & Dickinson, 2003; Waters, Shiffman, Bradley, & Mogg, 2003), event-related potentials (Parker & Gilbert, 2008; Versace, Minnix, et al., 2011; Versace et al., 2010) and hemodynamic response (David et al., 2005; Due, Huettel, Hall, & Rubin, 2002; Smolka et al., 2006).

In addition to these various measures, a psychophysiological methodology called the affectively modulated startle response has been frequently used to evaluate the motivational salience of cigarette-related cues in smokers. The startle eyeblink response, the magnitude of which is usually measured by voltage changes in the orbicularis oculi electromyography (EMG) in response to an abrupt and loud acoustic probe, is sensitive to foreground motivationally relevant cues. The startle response is enhanced to unpleasant pictures and attenuated to pleasant pictures (Vrana, Spence, & Lang, 1988). By including cigarette-related pictures in this paradigm, researchers can compare the salience of these smoking cues in relation to other motivationally significant stimuli. Several studies have demonstrated that in smokers, cigarette-related pictures and pleasant pictures led to comparable reductions in startle magnitude, suggesting the appetitive salience of the smoking cues (Cinciripini et al., 2006; Dempsey, Cohen, Hobson, & Randall, 2007; Geier, Mucha, & Pauli, 2000; Rehme et al., 2009), although one study reported the opposite finding using this method (Munoz et al., 2010).

Although cigarette-related cues have generally been found to be appetitive for smokers, findings concerning the relationship between cigarette-related cue reactivity and the severity of nicotine dependence have been equivocal. Several studies have found that smokers

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who were more dependent on nicotine were more reactive (e.g., greater self-reported craving) to cigarette-related cues than less dependent smokers (Payne et al., 1996; Sayette et al., 2001; Smolka et al., 2006). Other studies have found the opposite: less-dependent smokers were more reactive (e.g., larger attentional bias) to cigarette-related cues than more-dependent smokers (Hogarth et al., 2003; Mogg, Field, & Bradley, 2005; Rehme et al., 2009; Vollstädt-Klein et al., 2011). It is unclear what factors may account for these discrepant findings. For example, there are considerable methodological differences across these studies, ranging from self-report (Sayette et al., 2001) to various psychophysiological assessments (e.g., blood flow level in Vollstädt-Klein et al., 2011 and attentional bias in Hogarth et al., 2003). Although they were used to assess cue reactivity in general terms, these methods may have measured distinct aspects of cue reactivity, such as the subjective evaluation of craving and attentional allocation. In addition, sample characteristics, such as smoking deprivation and its duration as well as basic demographics (e.g., sex and race), may have interacted with the above-mentioned methodological differences to make the relationship between nicotine dependence and cue reactivity more complicated.

Nevertheless, no reports so far have studied the relationship between cigarette-related cue reactivity and nicotine dependence exclusively in an adequately sized clinical sample of smokers. In general, these smokers wish to quit, but are subject to potential smoking cue-related relapse once they start to quit. Therefore, a better understanding of their reactivity to cigarette-related cues may improve intervention outcomes among these treatment-seeking smokers by preventing cue-related relapse. In the current study, we enrolled smokers who were participating in a clinical cessation program and evaluated the impact of daily cigarette consumption levels on cigarette-related and affective cue reactivity among these smokers. Given the role of smoking cues in relapse (Shiffman et al., 2007) and higher relapse probability among heavier smokers (Dale et al., 2001), we hypothesized that heavier smokers would have higher reactivity (i.e., greater startle attenuation) to cigarette-related cues than lighter smokers and that responses to pleasant and unpleasant cues would not differ between the groups.

2. Material and methods

2.1. Participants

Participants from the Houston metropolitan area were recruited into a smoking cessation clinical study using newspaper, radio, and Internet advertisements. Only smokers, who wished to quit smoking, were aged 18–65 years, were fluent in English, smoked ≥5 cigarettes per day (CPD), had an expired carbon monoxide (CO) level ≥6 ppm, and reported no uncontrolled medical illnesses were included in the treatment study. Individuals were excluded from the program if they were taking psychotropic medications, had psychiatric disorders or were abusing substances other than nicotine, were involved in any other smoking cessation treatment, or had contraindications for bupropion or varenicline (these two drugs were administered randomly after the laboratory session assessments reported herein). A total of 182 treatment-seeking smokers met these inclusion and exclusion criteria and attended the initial laboratory session, before which they were asked to smoke ad libitum. Because of unsatisfactory data quality (see details in Section 2.3 Data acquisition and reduction), 46 participants were excluded, resulting in 136 participants being included in the current report. Using criteria established by the Centers for Disease Control and Prevention (Maurice et al., 2006), we divided these participants into three groups based on their CPD: heavy smokers (N = 30, CPD: ≥25); moderate smokers (N = 61, CPD: 15–24); and light smokers (N = 45, CPD: 5–14). The smoking group distribution of the participants who were excluded (N = 46) and included (N = 136) in the data analysis was similar to that in the Centers for Disease Control and Prevention report ($p = 0.17$ for both) (Maurice et al., 2006). This study was approved by The University of Texas MD Anderson Cancer Center Institutional Review Board. All participants provided written informed consent.

2.2. Experimental design and stimuli

E-Prime software (v1.2; Psychology Software Tools, Sharpsburg, PA, USA) running on a Pentium 4 computer was used to deliver the experimental stimuli (i.e., pictures and acoustic startle probes). The picture set was created from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2005) and cigarette-related picture collections previously used by our laboratory (Carter et al., 2006; Cinciripini et al., 2006; Versace et al., 2010) and others (Gilbert et al., 2005). Each set included equal numbers (N = 24) of pictures in the following four categories: pleasant, unpleasant, neutral, and cigarette-related. Pleasant and unpleasant pictures were matched according to arousal level on the normative data (e.g., erotica and mutilations as high arousing pictures for pleasant and unpleasant categories, respectively) from the International Affective Picture System (Lang et al., 2005). The content of the neutral and cigarette-related pictures was perceptually and conceptually matched (e.g., similar scenarios). The acoustic stimulus consisted of a 50-ms 100 dB(A) burst of white noise with instantaneous rise time binaurally delivered through insert earphones (model 3A, 10 Ω; E-A-R Auditory Systems, Indianapolis, IN, USA).

We presented the entire picture set twice in two blocks, and each block contained two segments. Each picture was presented for 4 s followed by a random inter-trial interval of 3–5 s. For each category of 48 pictures, 12 of them were randomly probed between 2.5 and 3.5 s after picture onset by acoustic stimuli, yielding 48 startle probes for each participant. No consecutive pictures were probed by the acoustic stimulus, and the minimum and average time between startle probes was about 9 and 21 s, respectively. The orders of both pictures and startle probes were counter-balanced, and no two pictures of the same category were presented in two consecutive trials.

Besides the startle reflex assessment, high-density electroencephalography and corrugator EMG activity were recorded, and some of these results have been the subject of other reports (Versace, Lam, et al., 2011; Versace, Minnix, et al., 2011).

2.3. Data acquisition and reduction

Two recording electrodes (Ag-AgCl) were placed on the orbicularis oculi muscle under the right eye, and the EMG activity was acquired and amplified with an EMG100C module connected to an MP150WSW bioamplifier (BIOPAC Systems, Goleta, CA, USA) sampled at 1000 Hz. AcqKnowledge III data acquisition software (v3.8.2; BIOPAC Systems) was used to record data that had been filtered (28–500 Hz), rectified and smoothed by a five-sample boxcar filter (Blumenthal et al., 2005). Before starting the experiment, we checked sensor impedance (<30 kΩ) and visually examined data quality to ensure proper data collection.

Startle responses were first examined offline on a trial-by-trial basis using AcqKnowledge software. Trials with excessive noise or no scoreable startle response were considered missing, and 46 of 182 participants who had over 33% missing trials were considered startle nonresponders and excluded from subsequent analysis. The relatively high loss of data may have been due to the age of our sample, as older subjects tend to respond less to startle probes (Ellwanger, Geyer, & Braff, 2003; Ford et al., 1995; Ludewig et al., 2003), and relatively high sensor impedance, which may have attenuated the EMG signal and permitted electromagnetic interference intrusion that reduced the data quality (Blumenthal et al., 2005). The former hypothesis is supported by the age difference ($t_{(180)} = 2.76$, $p < 0.01$) between nonresponders (mean [M] = 48.39 years, standard deviation [SD] = 10.15 years) and responders (M = 43.44 years,