ORIGINAL INVESTIGATION

Motivation to quit smoking and startle modulation in female smokers: context specificity of smoking cue reactivity

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Abstract

Rationale Cue reactivity and startle reflex modulation paradigms have been used in addiction research to determine the affective motivational state of craving induced by viewing drug-related cues. However, recent studies suggest that cue reactivity and startle reflex modulation in people with addictions can be suppressed, or even reversed, depending on context.

Objective The present study looked at the contextual specificity of smoking cue startle modulation by examining individuals with low and high motivation to quit smoking. *Materials and methods* Emotional modulation of the startle reflex was examined in 32 female smokers exposed to affective stimuli and tobacco cues. The sample was divided into high and low motivation to quit smoking groups using the Processes of Change Questionnaire.

Results The tobacco cues produced a greater startle magnitude in the group with high motivation to quit smoking than the group with low motivation, which was independent of craving level.

Conclusion Motivation to be abstinent is a relevant contextual factor accounting for variance in cue reactivity in individual smokers.

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Introduction

The startle blink reflex modulation paradigm (Bradley and Lang 2007) has been the methodology most frequently used in recent years to investigate the underlying mechanism of craving induced by viewing tobacco cues. It is assumed that the presence of augmentation or inhibition of the startle reflex while drug-related images are presented provides an objective indicator of the affective motivational state (whether appetitive or aversive) induced by the images (Mucha et al. 2006). This opposite effect has been interpreted, according to the motivational priming hypothesis, as due to the congruence versus incongruence between the motivational system engaged by the perceptual stimuli and the type of reflex being elicited: unpleasant stimuli that engage the aversive motivational system potentiate defensive reflexes whereas pleasant stimuli that engage the appetitive motivational system inhibit them (Lang and Davis 2006).

Results in the area of tobacco smoking have been controversial. While some studies have found an increase in startle magnitude (Elash et al. 1995), others have found a reduction (Geier et al. 2000; Cinciripini et al. 2006) or no differences between smokers and nonsmokers (Orain-Pettissolo et al. 2004). These discrepancies suggest that tobacco stimuli are not homogenous with regard to their control of addictive behavior (Mucha et al. 2008). Different contextual factors, such as whether the tobacco stimulus depicts cigarettes from the beginning or the end of smoking (Mucha et al. 2008; Winkler et al. 2010), or whether smokers are at that moment motivated to quit smoking or not (Dempsey et al. 2007), may modulate reactivity to smoking cues suppressing or even reversing the physiological response. Evidence of context effects in nonhuman animals is relatively extensive (Moses et al. 2007; Walker and Davis 2002; Siegel and Ramos 2002). However, research on context effects in humans is still in its infancy (Grillon 2008). Evidence in support of such effects in humans is particularly relevant given recent arguments that addiction research needs to move beyond biology to recognize situational and psychosocial factors that underlie addictive behavior (Kalant 2010).

According to the transtheoretical model of behavioral change, people who are ready to change their smoking behavior and become abstinent perceive smoking cues as being more negative and dangerous than people who are not contemplating such a change (Janis and Mann 1977; Prochaska and Velicer 1997). Several studies have investigated whether the motivation to quit smoking affects the reactivity to smoking cues (McDermut and Haaga 1998; Andersen and Keller 2002). Highly motivated individuals report greater feelings of guilt, negative affect in response to smoking cues, and more perceived risks than less-motivated individuals (McCoy et al. 1992; McKee et al. 2005). Given these affective differences, motivation to quit smoking may be a relevant factor influencing the startle reflex modulation. To our knowledge, only one study has examined this effect. Dempsey et al. (2007) reported that male smokers with a low motivation to quit smoking showed robust startle inhibition to smoking pictures in comparison to highly motivated individuals. However, the level of craving was not evaluated in this study, so it was not possible to conclude whether the startle blink modulation was due to differences in craving state or differences in motivation to quit smoking.

The aim of the present study was to investigate in female smokers the influence of motivation to quit smoking on startle reflex modulation controlling differences in craving state. Female participants were selected because the only study that has examined motivation to quit smoking and startle modulation was conducted in men (Dempsey et al. 2007). Gender differences may be relevant, given reports of differences between men and women in reactivity to smoking cues (Field and Duka 2004; Perkins et al. 2001; Heishman et al. 2010) and startling noises (Vila et al. 1992). We hypothesize that female smokers who were motivated to quit smoking would report more negative affect and show a higher startle reflex magnitude while viewing tobacco-related stimuli than smokers who were not motivated to quit, independent of self-reported craving level.

Method

Participants

The study was in accordance with the Declaration of Helsinki (1991) and was approved by the local ethic committee of the University of Granada. The sample was comprised of 32 female university students, between 18 and 30 years old (mean of 22.93 years; standard deviation [SD]=3.35). Participant exclusion criteria included hearing difficulties, ongoing illicit substance use, reporting mental health problems, or being under medical or psychological treatment. The mean number of years that participants smoked was 7.18 (SD=3.55), with a mean current consumption of 14.8 cigarettes daily (SD=5.04). The mean time since the participant's last cigarette was 3.3 h (SD=2.8) and the mean Fagerström Test for Nicotine Dependence (FTND; Spanish adaptation: Becoña and Vázquez 1998) score was 2.46 (SD=1.6).

Startle reflex modulation test

Affective and tobacco-related stimuli were still photographs and 3D computer-generated 20-s video clips. The affective photographs were selected from the International Affective Picture System (IAPS, Lang et al. 2008). The photographs consisted of pleasant, unpleasant, and neutral images (codes: 4659, 4664, 4672, 3053, 3102, 9405, 2200, 7035, 7140, 7130, and 7705; Center for the Study of Emotion and Attention 1995). Tobacco-related photographs depicted typical smoking situations and were rated with high desirability levels by smokers in previous studies (Muñoz et al. 2009; codes: 34, 36, and 37). The 3D video clips were elaborated for the present study using Blender 3D design software (Blender Foundation, http://www.blender.org/). They showed similar situations to those depicted in the IAPS and tobacco photographs, but with characters in motion (people smoking, landscapes, road accidents). Specific details on these 3D stimuli are reported separately (Muñoz et al., manuscript in preparation).

Participants underwent a startle reflex modulation test that was divided into two blocks: one block with still photographs (block A) and one block with 3D video clips (block B). Half of the participants underwent block A first and block B second, and the other half underwent block B first and block A second. Each block consisted of 28 trials, 24 with startle and 4 without it. Startle was evoked by a white noise burst of 105 dB intensity, 50 ms duration, and instantaneous rise time. Within each block, stimuli were divided into four affective categories with three exemplars from each category: pleasant, neutral, unpleasant, and tobacco-related, all with evocation of the startle reflex. In addition, two neutral stimuli were presented in each block with no evocation of startle. These 14 stimuli were presented twice within the block in counterbalanced order using a Latin square design that yielded four different orders of presentation of each stimulus. Participants were randomly assigned to these orders.

The sequence of the psychophysiological test was as follows: (a) initial 5-min rest period with no stimulation, (b) the 28 trials of block A (or B), (c) a 2-min rest period indicated by an asterisk in the center of the screen, (d) the 28 trials of block B (or A), and (e) a 4-min rest period without stimulation. The protocol for each trial was as follows: (a) a 3-s baseline recording period, (b) projection of visual stimulus (6 s for photographs and 20 s for 3D videos), (c) startle noise (in startle trials) at 1,050, 2,050, or 3,050 ms before the end of the visual stimulus, and (d) 6 s of post-stimulus recording. The inter-trial interval ranged between 2 and 4 s.

Apparatus

The following equipment was used: (a) a Powerlab 4/25T Polygraph (AdInstruments ETC) to record the startle reflex by electromyography of the orbicular muscle of the left eye, (b) a Visionstation VS1024-XL20 immersion system (Elumens ETC) for presenting photographs and 3D video clips on a concave hemispherical screen, and (c) a PC to digitally generate the white sound heard through Telephonics TDH49P earphones and present the visual stimuli.

Measures

Startle reflex

Electromyographic (EMG) activity of the orbicular muscle was recorded using a sampling rate of 1,000 Hz and a frequency band filter of 30–500 Hz. Data were analyzed off-line using a Matlab program that rectified and integrated the signal in an interval from 50 ms (baseline) before to 250 ms after the startle sound. Reflex magnitude was defined as the amplitude of the integrated EMG response, starting between 21 and 110 ms after initiation of the stimulus. Trials with a maximum peak in the window that did not reach more than two standard deviations above the mean of the baseline were computed as zero. Finally, scores were converted into standard scores with a mean of 50 and standard deviation of 10 (Blumenthal et al. 2005).

Questionnaires and self-reports

The Questionnaire on Smoking Urges (QSU; Tiffany and Drobes 1990; Spanish adaptation: Cepeda-Benito, Henry, Glaves and Fernández, 2004) was used to assess the baseline level of craving when the participants arrived at the experimental session. This questionnaire was used to ensure that differences in startle reflex and affective evaluation between groups were independent of differences in craving state. The QSU consists of 26 items divided in two factors. The first factor consists of 15 items reflecting intention and desire to smoke, as well as anticipation of pleasure from smoking. The second factor contains 11 items reflecting anticipation of abstinence-syndrome alleviation and of positive consequences from smoking.

The Processes of Change Inventory (PCI; Prochaska et al. 1988) identifies 10 cognitive and behavioral changes performed by smokers who want to quit smoking: consciousness raising, dramatic relief, environmental reevaluation, social liberation, self-reevaluation, stimulus control, helping relationship, counter conditioning, reinforcement management, and self-liberation (DiClemente and Prochaska 1998). The PCI is particularly interesting because it was designed to measure behaviors that are executed by smokers to quit smoking, thereby determining the level of motivation to quit. The inventory consists of 40 items (4 items for each change process) with responses on a four-point Likert scale (0=not at all; 3=often) and assesses the frequency with which different cognitivebehavioral strategies are activated by smokers. We used a Spanish adaptation of the questionnaire that has shown reliable psychometric properties in consumers of different addictive substances (Tejero and Trujols 1994).

The Self-Assessment Manikin (SAM; Bradley and Lang 2000; Lang 1980) is an easily and rapidly applied nonverbal pictographic scale designed, in the context of Lang's dimensional theory of emotion (Lang 1995), to assess participant's feelings while viewing IAPS images in three general emotional dimensions: valence, arousal, and dominance. Each dimension is represented by five humanoid figures that indicate different levels of intensity from 1 (lower end) to 9 (upper end) with the possibility of marking intermediate scores between figures. The valence dimension (pleasant versus unpleasant) reflects the direction of two primary motivational systems: the appetitive (related to consummatory, breeding, or approach behavior) and the defensive (related to protective, escape, or avoidance behavior). This dimension is represented by five figures ranging from a smiling to a frowning face. The arousal dimension (calm versus activated) reflects response intensity, i.e., the level of energy required to carry out the behavior irrespective of its direction. This dimension represents the activation of either motivational system (appetitive or defensive) or the co-activation of both. It is represented by five figures ranging from an apparently agitated to a sleepy-looking figure. Finally, the dominance dimension (feeling dominant versus feeling dominated) is related to the degree of power or sense of control over the emotion (Osgood et al. 1957) and helps to distinguish

emotions under the control of the subject from those under the control of the environment. It is represented by five figures ranging from a very large to a very small one.

The Pictographic Assessment of Desire (PAD; Muñoz et al. 2009; Muñoz et al. 2010) was used to assess the strength of craving produced by the images. Similar to the SAM, it consists of a scale made of five humanoid figures representing different degrees of craving. The figure on the extreme left depicts a salivating face, representing maximum desire to consume the substance, whereas the figure on the opposite extreme depicts a relaxed face, representing no desire to consume the substance.

Procedure

Participants were recruited from flyers posted around various campus locations at the University of Granada. The volunteers who smoked more than 10 cigarettes per day were screened by phone to determine if they fulfilled the inclusion criteria. Upon their arrival at the laboratory, participants were informed about the study and their written informed consent was obtained. Then they answered a questionnaire to confirm the inclusion criteria. This questionnaire included items based on the ADIS-IV (Brown et al. 1994) in order to screen out mental health problems such as anxiety and mood disorders. Next, they completed the QSU and the PCI and sat in front of the hemispheric screen. EMG electrodes were applied, and a preprogrammed experimental session was administered. Upon completion of the physiological test, the participants rated the photographs and 3D video clips on the three SAM scales and the PAD scale.

Statistical analysis

Participants were divided into two groups (high and low motivation) by median splitting the sample according to their PCI score. One-way ANOVAs were used to analyze age, number of years of smoking, daily cigarette use, time elapsed since last cigarette, nicotine dependence (FTND), and craving scores (QSU factors 1 and 2) to examine whether differences between low and high motivation groups could be due to differences in severity of addiction or craving levels. The hypothesis regarding the greater enhancement of the startle reflex and more negative assessment of tobacco-related stimuli in smokers with high motivation to quit was tested applying $2\times(4)$ ANOVAs, with group as a between-group factor and category (pleasant, neutral, unpleasant, and tobacco) as a repeated measures factor. No group differences in the effects of presentation type (still photographs versus 3D video clips) were found; a comparison of the two methods will be reported elsewhere (Muñoz et al., manuscript in preparation). In all analyses involving repeated measures, the Greenhouse–Geisser epsilon correction was applied to control for violation of the sphericity assumption. Results are reported with the original degrees of freedom and the corrected p values. When significant effects were found, post-hoc analyses were performed using Holm test. As regards the startle data, post-hoc analyses examined, first, whether both groups showed the expected startle modulation by pleasant, neutral, and unpleasant images and, second, whether both groups differed in the startle responses while viewing the tobacco images. The level of significance was set at 0.05.

Results

Age and smoking characteristics Table 1 shows the means (and standard deviations) of smoking characteristics in the high and low-motivation groups, as well as the one-way ANOVA results. No significant group differences were found in age, number of years of smoking, daily cigarette use, time elapsed since last cigarette, nicotine dependence, intention and desire to smoke (QSU factor 1), anticipation of positive consequences from smoking (QSU factor 2), and general craving level (QSU total score).

Startle magnitude Initial assessment of the startle raw data revealed mean and ±SD overall startle scores (collapsed over the different stimulus test conditions) of 142.87 μ V (±72.76 μ V) and 167.67 μ V (±77.50 μ V) and 118.06 μV (±60.17 μV) in the participants with high and low motivation to quit smoking, respectively. Figure 1 depicts the magnitude of the startle reflex (in standard scores) corresponding to each stimulus category as a function of the motivation to quit smoking. As can be seen, both groups showed a progressive increase in startle magnitude from pleasant to unpleasant images, with neutral images occupying an intermediate position. In these three categories, the low-motivated group showed somewhat larger magnitudes than the highmotivated one. Responses to tobacco images showed a further increase for the high-motivated group but a decrease for the low-motivated one, the difference in startle magnitude between the two groups being reversed. The $2(\times 4)$ ANOVA results revealed significant effects of group ($F[1, 30]=4.20, p<0.05; \eta p^2=0.123$) and category $(F[3, 90]=6.94, p<0.001; \eta p^2=0.188)$. Moreover, a significant group×category interaction was found in the linear trend (F[1, 30]=5.71, p < 0.03; $\eta p^2 = 0.147$). While the high-motivated group showed a progressive linear increase along the four picture categories (pleasant,

	Low motivation	High motivation	F	p value	ηp^2
Age	22.56 (3.1)	23.00 (4.21)	<i>F</i> (1, 30)=0.112	0.741	0.004
Years smoking	7.31 (3.6)	7.06 (3.5)	F(1, 31) = 0.038	0.846	0.001
Daily cigarettes	15.9 (4.4)	14.0 (5.3)	F(1, 31) = 1.27	0.271	0.040
Last cigarette (hours)	3.21 (4.1)	3.25 (3.7)	F(1, 31) = 0.000	0.984	0.000
FTND score	2.4 (1.7)	2.5 (1.7)	F(1, 31) = 0.011	0.918	0.000
Craving (QSU-1)	4.27 (1.1)	4.45 (0.8)	F(1, 30) = 0.229	0.636	0.007
Craving (QSU-2)	2.40 (0.9)	2.86 (0.8)	F(1, 30)=2.19	0.149	0.067
Craving (total)	3.48 (1.0)	3.78 (0.7)	F(1, 31) = 0.876	0.357	0.028
Valence (across the four categories)	5.12 (3.3)	4.76 (2.2)	F(1, 30) = 5.56	0.025^{a}	0.156
Arousal (across the four categories)	4.77 (1.7)	5.80 (1.9)	F(1, 30) = 11.49	0.002^{a}	0.277
Dominance (across the four categories)	5.08 (1.9)	4.91 (1.8)	F(1, 30) = 0.327	0.572	0.011
Desire (across the four categories)	4.26 (2.2)	5.51 (2.2)	F(1, 30) = 7.44	0.011 ^a	0.199
Valence (tobacco stimuli)	6.64 (1.0)	5.54 (1.3)	F(1, 30) = 6.34	0.017^{a}	0.175
Arousal (tobacco stimuli)	4.36 (1.1)	6.04 (1.5)	F(1, 30) = 12.21	0.001^{a}	0.289
Dominance (tobacco stimuli)	6.01 (1.1)	4.86 (1.8)	F(1, 30) = 4.51	0.042^{a}	0.131
Desire (tobacco stimuli)	6.65 (1.7)	7.64 (1.2)	F(1, 30)=3.43	0.074	0.103

 Table 1
 Means (standard deviation) of age, smoking characteristics, and subjective ratings of images in groups with high and low motivation to quit smoking together with ANOVA results

^a Significant differences

neutral, unpleasant, and tobacco), the low-motivated group showed a decrease after the unpleasant category. The Holm tests comparing the three affective categories (pleasant, neutral, and unpleasant) showed significant differences in both groups between pleasant and neutral (p<0.05), and pleasant and unpleasant (p<0.01) images. No significant differences were found between neutral and unpleasant images. The Holm tests comparing tobacco image with the three affective categories showed significant differences between tobacco and pleasant, and neutral in the high motivation group (p<0.01). No differences were found in the low-motivation group. Finally, comparison between high and low-motivation

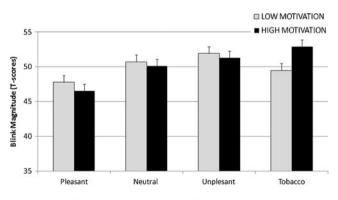


Fig. 1 Eye-blink startle magnitude while viewing pleasant, neutral, unpleasant, and tobacco-related stimuli as a function of motivation to quit smoking (*bars* are standard error for the means)

groups in each stimulus category revealed significant group differences only in tobacco images (p < 0.05).

Emotional ratings of images The $2\times(4)$ ANOVAs for valence, arousal, dominance, and desire ratings across the four categories yielded the following significant results: (a) main effect of group in valence (p < 0.025), arousal (p < 0.002), and desire (p < 0.011); (b) main effect of category in the four scales (all p < 0.0001); and (c) group × category interaction effect in dominance (p < 0.037). As can be seen in Table 1, high-motivated participants rated the images (across the four categories) significantly less pleasant, more arousing, and inducing greater desire than low-motivated participants (main effect of group). As also seen in Table 1, these differences were maintained when the contrasts were limited to tobacco images (valence, p < 0.017; arousal, p < 0.001), except for the desire scale (p>0.07). High-motivated participants also rated the tobacco images causing a lowered sense of dominance (control) than low-motivated participants $(p < 0.042, \text{ group} \times \text{category interaction})$. Finally, the Holm tests comparing tobacco images with pleasant, neutral, and unpleasant images revealed that tobacco images were rated significantly (a) more positive than neutral (p < 0.001) and unpleasant (p < 0.0001) images but less positive than pleasant ones (p < 0.0001); (b) more arousing than neutral images (p < 0.0001) but less arousing than unpleasant ones (p < 0.0001); (c) more dominant than unpleasant images (p < 0.0001) but less dominant than pleasant ones (p < 0.027);

and (d) inducing more desire than pleasant (p < 0.0001), neutral (p < 0.0001), and unpleasant (p < 0.0001) images.

Discussion

As anticipated, the motivation to quit smoking significantly affected startle reflex modulation and subjective ratings of tobacco-related stimuli. Female smokers with high motivation to quit smoking showed a greater eye-blink startle magnitude when viewing the tobacco-related images than low-motivated smokers. They also rated their feelings while viewing tobacco-related stimuli as more negative, more activating, and as more controlled by cues than low-motivated smokers. There were no significant differences between the two groups in age, number of years of smoking, daily cigarette use, time elapsed since last cigarette, severity of addiction, and craving measures (QSU).

In general, stimulus presentation revealed the expected startle modulation (Bradley et al. 2001b; Vrana et al. 1988; Cuthbert et al. 1998; Bradley and Sabatinelli 2002) reduced magnitude with pleasant images and increased magnitude with unpleasant ones. However, the magnitude of the eye blink did not significantly differentiate neutral from unpleasant stimuli. This pattern of affective modulation concerning neutral images is not uncommon (Bradley et al. 2001b). In our study, it may be explained by the fact that the stimuli were presented twice, producing a familiarity effect that could have disrupted the stability of startle reflex modulation (Larson et al. 2000).

The greater startle magnitude to tobacco-related images in high-motivated smokers is consistent with previous findings (Elash et al. 1995) showing that startle blink reflex to smoking cues is potentiated among nicotine-dependent individuals. Such potentiation has been interpreted, in line with the motivational priming hypothesis (Lang 1995), in terms of activation of the aversive motivational system and the desire to relieve the discomfort produced by the tobacco cues (Glautier and Tiffany 1995; Laberg 1990; Ludwig and Wikler 1974; Stewart et al. 1984; Wikler 1948; Elash et al. 1995). The opposite effect that was found in smokers with low motivation to quit smoking is also consistent with previous findings (Geier et al. 2000; Cinciripini et al. 2006) showing startle reflex inhibition when nicotine-dependent individuals view tobacco cues. This finding has been interpreted, also in line with the motivational priming hypothesis (Lang 1995), in terms of activation of the appetitive motivational system and the desire to experience the positive effects of the substance (Geier et al. 2000; Cinciripini et al. 2006). Thus, motivation to quit smoking is a relevant contextual factor helping to clarify contradictory reports concerning startle modulation by tobacco cues. This finding also adds to only a small handful of systematic data revealing context specificity of reactivity evoked by smoking and alcohol stimuli (Artiges et al. 2009; Mucha et al. 2000, 2006).

The reversed effects of tobacco cues depending on motivation to quit smoking cannot be explained in terms of differences between the two groups in craving state or addictive behavior. Participants with high and low motivation to quit smoking reported equal levels of craving upon arrival at the laboratory. No significant differences were found between the two groups in age, number of years smoking, daily cigarette use, time elapsed since last cigarette, and severity of addiction. Desire evoked by smoking cues after the test tended to be higher in the high motivation group, but the difference did not reach statistical significance. Significant differences did appear in affective assessment of the tobacco cues, which is a finding consistent with previous reports of greater negative affect in response to smoking cues in people ready to change their smoking behavior and become abstinent (McDermut and Haaga 1998; Dempsey et al. 2007). Thus, the reversed effect found in our study concerning startle reflex modulation depending on motivation to quit smoking may be explained by the more negative evaluation of tobaccorelated cues by smokers highly motivated to quit smoking, a factor not contemplated in previous studies.

The relevance of our findings should be evaluated taking into consideration two methodological limitations. The current study only included female participants. Previous studies on startle reflex modulation that included male and females smokers (Geier et al. 2000, Orain-Pelissolo et al. 2004) have not reported results on gender differences. However, gender differences have been found with regard to reactivity to tobacco cues, affective pictures, and startling noises (Field and Duka 2004; Perkins et al. 2001; Heishman et al. 2010; Bradley et al. 2001a; Moltó et al. 1999; Vila et al. 1992, 2001). Moreover, although our results-in female smokers-are consistent with those of Dempsey et al. (2007)-in male smokers-concerning startle potentiation in people motivated to quit smoking, there are apparent differences between both studies concerning other aspects. Such differences include responses to non-smoking cues or to smoking cues in nonmotivated smokers that may reflect important gender differences. Unfortunately, this type of comparison is impossible unless males and females are examined simultaneously in the same study. A second limitation concerns the division of our participants into high and low motivation to quit smoking using the median split, a method that does not guarantee a clinical meaningful cut point (Maxwell and Delaney 1993). Both limitations will have to be corrected in future studies by examining male and female smokers specifically recruited on the basis of their high and low motivation to quit smoking.

In summary, we confirmed that the acoustic startle magnitude is modulated in a predictable way by smoking cues and by standardized, nondrug emotional stimuli. Moreover, the effect of the smoking cues is further modulated by motivation to quit smoking. This feature of the test participants is suggested to be an additional context, which modulates the reactivity to smoking cues.

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