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Miguel Ángel Muñoz, Sofía Idrissi, María Blasa Sánchez-Barrera, MaCarmen Fernández-Santaella, and Jaime Vila

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BRIEF REPORT

Tobacco Craving and Eyeblink Startle Modulation Using 3D Immersive Environments: A Pilot Study

Miguel Ángel Muñoz

University of Granada and University of the Balearic Islands

Sofía Idrissi, María Blasa Sánchez-Barrera,
M^aCarmen Fernández-Santaella, and Jaime Vila
University of Granada

Both the cue reactivity and startle reflex modulation paradigms have been used in addiction research to investigate the motivational mechanism of craving. However, while there is a growing body of literature that indicates the utility of 3D technology in addiction-relevant cue reactivity research, no study has been reported on its utility using the startle reflex modulation paradigm. The aim of the present study was to extend the 3D technology to research on tobacco craving using the startle reflex methodology. Participants were 32 university students who smoked more than 10 cigarettes daily. They participated in a psychophysiological testing to assess the modulation of the startle reflex induced by viewing pleasant, unpleasant, and tobacco-related 3D immersive environment stimuli (3D-IEs). Results confirmed that 3D-IEs were effective in inducing emotional states to modulate the startle response. Pleasant and unpleasant 3D-IEs modulated the startle response, as expected: The reflex was increased while viewing unpleasant stimuli and decreased while viewing pleasant ones. Tobacco-related 3D-IEs were similar to unpleasant stimuli in increasing the startle response. However, they were subjectively evaluated as positive, which suggests that the mechanism underlying craving coactivates both aversive and appetitive motivational tendencies.

Keywords: immersive environments, tobacco craving, startle reflex, cue reactivity

Craving has been conceptualized as a subjective, emotional, and motivational state of intense desire to consume a given substance (Tiffany, 1999). The construct of craving has been found to be prominent in the maintenance of many addictive behaviors, including cigarette smoking. The overwhelming desire to consume plays such an important role in addiction that most treatment programs include strategies for managing craving (O'Brien, 2005). The cue-reactivity or cue-exposure paradigm (Glautier & Tiffany, 1995; Laberg, 1990) has been used by different investigators to examine the motivational mechanisms of evoked craving (Anton, 1999; Drummond, 2001). The procedure consists of assessing drug users' subjective and/or physiological reactivity to substance-related stimuli that are presented either as pictures, videos, or

sentences (Drobes, 2002; Drummond, 2001; Tiffany, Carter, & Singleton, 2000; Tong, Bovbjerg, & Erblich, 2007).

In recent years, the startle reflex modulation paradigm (Bradley & Lang, 2007), in addition to the cue reactivity paradigm, has been used to investigate the mechanisms underlying craving. It is assumed that augmentation or attenuation of the startle reflex, when drug-related images are presented, provides an objective index of the affective motivational state (appetitive or aversive) induced by the images. Thus, unpleasant stimuli that engage the aversive motivational system potentiate defensive reflexes, whereas pleasant stimuli that engage the appetitive motivational system diminish them. Research in the area of tobacco craving has been controversial. Some studies suggest activation of the appetitive motivational system (Cinciripini et al., 2006; Geier, Pauli, & Mucha, 2000), while others found that smoking-cue pictures had no effect on the startle reflex (Orain-Pelissolo, Grillon, Perez-Diaz, & Jouvent, 2004). Elash, Tiffany, and Vrana (1995), using imagery scripts with smoking cues, found an augmented startle response in coherence with activation of aversive motivational system. Recently, Muñoz, Viedma-del-Jesus, et al. (2010) confirmed these results using smoking-cue pictures. These discrepancies suggest that tobacco-related cues are not homogeneous with regard to their influence over addictive behavior.

Previous research has demonstrated the utility of simulation technology in the assessment of smoking-related cue reactivity (Culbertson et al., 2010; Kuntze et al., 2001; Saladin, Brady, Graap, & Rothbaum, 2006). For example, several studies have

Miguel Ángel Muñoz, Department of Psychology, University of Granada, Granada, Spain, and Department of Psychology, University of the Balearic Islands, Illes Balears, Spain; Sofia Idrissi, María Blasa Sánchez-Barrera, M^aCarmen Fernández-Santaella, and Jaime Vila, Department of Psychology, University of Granada, Granada, Spain.

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Correspondence concerning this article should be addressed to Miguel Ángel Muñoz, Departamento de Psicología, University of Islas Baleares, Cra. de Valldemossa, km 7.5. C.p.18011, Palma de Mallorca (Illes Balears, Spain). E-mail: miguelamuoz@yahoo.es

shown that smoking cues, when presented in 3D immersive environments (3D-IE), reliably elicit greater self-reported tobacco craving (Bordnick et al., 2004; Bordnick, Graap, Copp, Brooks, & Ferrer, 2005; Bordnick et al., 2008; Bordnick, Traylor, Graap, Copp, & Brooks, 2005; Carter, Bordnick, Traylor, Day, & Paris, 2008; Moon & Lee, 2009; Traylor, Bordnick, & Carter, 2008). There is also new evidence that skin conductance may be modulated by 3D-IE smoking cues (Choi et al., 2011) and that proximal 3D-IE smoking cues may elicit greater cue-induced craving than distal 3D-IE smoking cues (Paris et al., 2011). These studies document that immersive technology can increase the experimental control and generalizability of cue reactivity research, allowing to handle simultaneously proximal tobacco stimuli and distal smoking-related environments (Bordnick, Graap, et al., 2005; Bordnick et al., 2008; Saladin et al., 2006).

The aim of the present study was to extend the 3D technology to research on tobacco craving using the startle reflex modulation methodology and compare the effects on the eyeblink startle magnitude of viewing 3D-IEs smoking and affective cues. We hypothesized that the virtual stimuli would be effective in inducing emotional states and in producing the startle reflex modulation phenomenon of response enhancement to unpleasant stimuli and response attenuation to pleasant stimuli. Based on the results of previous research (Muñoz, Viedma-del-Jesus, et al., 2010), we further hypothesized that the startle reflex would be enhanced for smokers viewing tobacco 3D virtual stimuli.

Method

Participants

The study procedures were consistent with the Declaration of Helsinki (1991) principles and were approved by the local ethics committee of the University of Granada. The data presented here were obtained as part of a larger study on the role of contextual factors in tobacco craving. The sample consisted of 32 female university students between the ages of 18 and 30 years (mean age 22.93 years; standard deviation [*SD*] = 3.35). Prospective participants who reported hearing difficulties, ongoing illicit substance use, psychiatric problems, or ongoing medical or psychological treatment were excluded from the study. Participants smoked for an average of 7.18 years (*SD* = 3.55), with a mean daily consumption of 14.8 cigarettes (*SD* = 5.04). The mean time since the participant's last cigarette was 3.3 hours (*SD* = 2.8), and the mean Fagerstöm test score was 2.46 (*SD* = 1.6). The mean level of craving, evaluated with the Questionnaire on Smoking Urges (QSU) when participants arrived at the experimental session, was 3.63 (*SD* = .89; range 1 to 7).

Immersive Environments

3D immersive environment stimuli (3D-IEs) were computer-generated for the present study using Blender 3D design software (Blender Foundation, <http://www.blender.org/>). The 3D-IEs portrayed pleasant, neutral, and unpleasant situations (e.g., people, landscapes, road accidents) similar to those depicted by the static photographs of the International Affective Picture System (IAPS; commonly used in startle reflex modulation research) but also included moving characters. The tobacco-related 3D-IEs, based on

pictures used in previous studies (Muñoz, Viedma-del-Jesus, et al., 2010) that depicted typical smoking situations, also incorporated moving characters. Thus, tobacco-related 3D-IEs contained cigarette packets, ashtrays, and smoking people in smoking-related environments (parties, pubs, and people offering tobacco). To increase experimental control, each 3D-IE stimulus was recorded as a 20-s video clip adapted to fit to a semispherical screen with a 180° field of view. The wider field of view available on the display, and the improved peripheral vision provided by the semispherical screen, afforded situational and contextual awareness of the surroundings, thereby creating a feeling of immersion or "being there" (Macedonio, Parsons, Diguseppe, Weiderhold, & Rizzo, 2007; Slater, 2009).

Psychophysiological Test

Following an initial 5-min rest period with no stimulation, the psychophysiological test consisted of a sequence of 22 trials. In each trial, a 3D-IE stimulus was presented. In 18 out of the 22 trials, a startle reflex was elicited by a burst of white noise of 105-dB intensity, 50-ms duration, and instantaneous rise time. The 3D-IE stimuli paired with the startle evocation belonged to three affective categories, with three exemplars per category: pleasant (happy individual, landscape sunset, and water skiing), unpleasant (gun, morgue, and car accident), and tobacco-related (invitation to smoke, social celebration, and leisure time). In order to avoid the possibility that participants might predict the presentation of the startle noise, two neutral stimuli were presented with no evocation of startle. These 11 stimuli were presented twice in a counterbalanced order using a Latin-square design that yielded four different orders of presentation of each stimulus. Participants were randomly assigned to one of these presentation orders.

The protocol for each trial was as follows: (a) a 3-s baseline recording period; (b) projection of the 3D-IE stimulus; (c) the white noise burst (in startle trials) presented either 1050, 2050, or 3050 ms before the end of the visual stimulus; and (d) 6 s of poststimulus recording. The intertrial interval ranged from 2 to 4 s (see Figure 1).

Apparatus

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

Measures

Startle reflex. Electromyographic (EMG) activity of the orbicular muscle was recorded using a sampling rate of 1000 Hz and a frequency band filter of 30 to 500 Hz. Data were analyzed off-line using a Matlab program that rectified and integrated the signal in an interval from a baseline of 50 ms before the onset of the white noise burst to 200 ms after the offset of the white noise

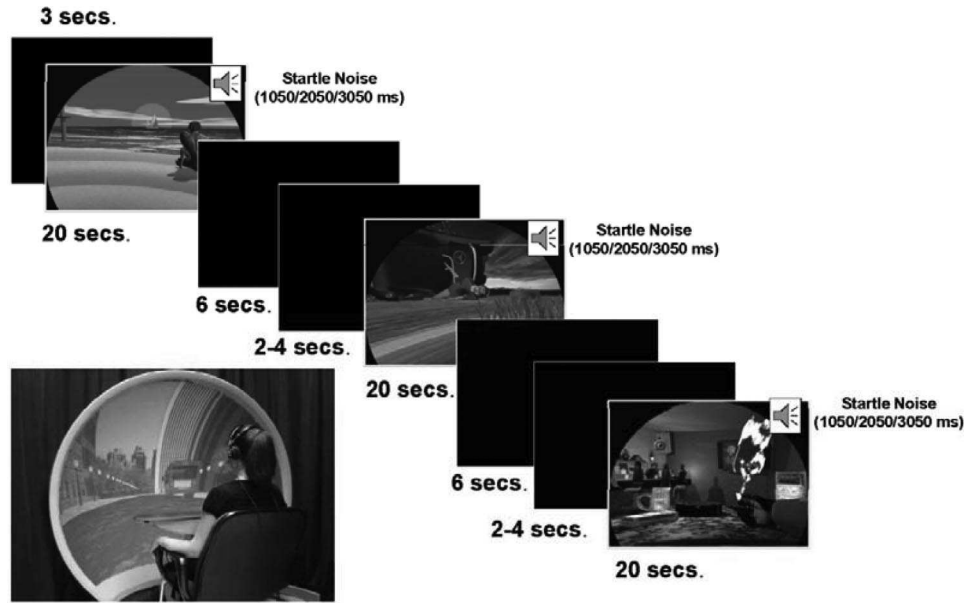


Figure 1. Startle reflex paradigm as it appeared on Visionstation VS1024-XL20 immersion system (3D-IEs pleasant, unpleasant, and tobacco).

burst. The magnitude of the reflex was defined as the amplitude of the integrated EMG response occurring between 21 and 110 ms after initiation of the stimulus. Trials with a maximum peak in that time window (21 to 110 ms) 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 Self-Assessment Manikin (SAM) (Bradley & Lang, 1994; Bradley & Lang, 2000) is a nonverbal pictographic scale designed to assess a participant's feelings in three general emotional dimensions: valence (pleasant vs. unpleasant), arousal (relaxed vs. activated), and dominance (feeling in control vs. feeling controlled). Each dimension is represented by five humanoid figures that indicate different levels of intensity, ranging from 1 (the lower end) to 9 (the upper end), with markings between the figures indicating intermediate scores.

The Pictographic Assessment of Desire (PAD) (Muñoz, Martínez, Fernandez-Santaella, Vila, & Cepeda-Benito, 2010) was used to assess the strength of the craving produced by the 3D-IEs. Similar to the SAM, it consists of a scale of five humanoid figures that represent different degrees of craving.

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 met the inclusion criteria for the study. Upon arriving at the laboratory, the study was described to the participants, and their written informed consent obtained. They then responded to a questionnaire to confirm that they met the study inclusion criteria and completed the QSU. Next, they

sat in front of the hemispheric screen, the EMG electrodes were applied, and the preprogrammed experimental session was administered. Upon completion of the psychophysiological testing, the participants rated the 3D-IEs on the three SAM scales and the PAD scale.

Statistical Analysis

Analysis of the magnitude of the startle response consisted of a $3 \times 3 \times 2$ repeated measures analysis of variance (ANOVA) with the following factors: Stimulus Category (pleasant, unpleasant, and tobacco-related), Stimuli (the three different 3D-IE stimuli per category), and Repetition (the first and second exposure of each 3D-IE stimulus). Analysis of the self-reported data (Valence, Arousal, Dominance, and Desire) consisted of one-way repeated measures ANOVA with Stimulus Category (pleasant, unpleasant, and tobacco-related) as the single repeated measures factor. 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 corrected p values. Post hoc tests were performed using the Bonferroni correction. The level of significance was set at 0.05.

Results

Affective Modulation of Startle

Figure 2 depicts the magnitude of the startle response for each Stimulus Category. The $3 \times 3 \times 2$ repeated measures ANOVA revealed significant main effects of Stimulus Category ($F[2, 62] = 7.918, p < .01; \eta_p^2 = 0.203$) and Repetition ($F[1, 31] = 16.854,$

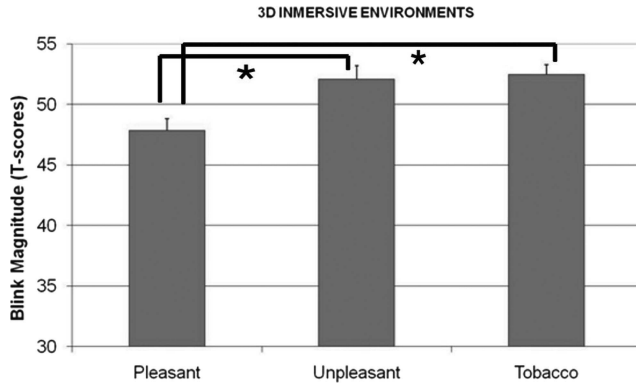


Figure 2. Eyeblink startle magnitude during visualization of pleasant, unpleasant, and tobacco 3D-IEs (bars are standard error of the mean, $p < 0.01$).

$p < .001$; $\eta_p^2 = 0.352$).¹ No other significant main or interaction effects were found. The startle response magnitude was greater for the unpleasant and tobacco-related categories than for the pleasant category. Post hoc Bonferroni comparisons of the three stimulus categories revealed significant differences between the pleasant and unpleasant categories ($p < .01$), and between the pleasant and tobacco-related categories ($p < .01$) but no significant difference between the unpleasant and tobacco-related categories. On the other hand, all stimulus categories showed a greater startle response during the first presentation compared to the second presentation.

Self-Report Measures

Table 1 presents the means and standard deviations of the subjective reactions to the three categories of 3D-IE stimuli (pleasant, unpleasant, and tobacco-related). In general, emotional reactions to the pleasant and unpleasant 3D-IEs were consistent with their a priori classification: Pleasant stimuli produced feelings rated as more positive and more dominant, but less arousing, than unpleasant stimuli. Valence, Arousal, and Dominance ratings of the tobacco-related 3D-IE stimuli were more similar to the pleasant than the unpleasant stimuli. However, with regard to desire, ratings of craving were higher for the tobacco-related stimuli than for either the pleasant or unpleasant stimuli.

The one-way repeated measures ANOVAs for Valence, Arousal, Dominance, and Desire yielded significant effects for the four scales: Valence ($F[2, 62] = 198.57, p < .0001; \eta_p^2 = 0.865$), Arousal ($F[2, 62] = 22.37, p < .0001; \eta_p^2 = 0.419$), Dominance ($F[2, 62] = 42.85, p < .001; \eta_p^2 = 0.580$), and Desire ($F[2, 62] = 36.28, p < .0001; \eta_p^2 = 0.539$). Post hoc pairwise comparisons between the three stimulus categories yielded the following results: (a) for Valence, significant differences were found between the three categories (all p values $< .001$), with tobacco-related stimuli being judged as more similar to the pleasant stimuli than to the unpleasant stimuli; (b) for Arousal, significant differences were found between the pleasant and unpleasant categories ($p < .0001$), and between the tobacco-related and unpleasant categories ($p < .0001$), with unpleasant stimuli being judged as more arousing than either the pleasant or tobacco-related stimuli; (c) for Dominance, significant differences were found between the three categories (all

p values $< .004$), with pleasant stimuli being judged as more dominant than either the unpleasant or tobacco-related stimuli; and (d) for Desire, significant differences were found between the tobacco-related and pleasant categories ($p < .0001$), and between the tobacco-related and unpleasant categories ($p < .0001$), with tobacco-related stimuli being judged as eliciting greater feelings of craving than either of the other two stimulus categories.

Discussion

The goal of the present study was to extend the traditional startle reflex modulation paradigm to incorporate 3D immersive technology in the investigation of the motivational mechanism of tobacco craving in humans. The results show that 3D-IEs were effective in both inducing emotional states and showing affective modulation of the startle reflex in the expected direction (Bradley, Codispoti, Cuthbert, & Lang, 2001; Codispoti, Bradley, & Lang, 2001): augmentation in response to unpleasant stimuli and attenuation in response to pleasant stimuli. Moreover, the study replicated previous findings that smoking cues potentiate the startle reflex, suggesting that the underlying motivational mechanism of tobacco craving is aversive rather than appetitive. However, also consistent with previous findings (Muñoz, Viedma-del-Jesus, et al., 2010), tobacco-related 3D-IEs were subjectively evaluated as pleasant rather than unpleasant, although they produced lower levels of positive valence and dominance and higher levels of desire than pleasant stimuli.

The smoking cues used in this study were 3D-IE stimuli generated to depict pleasant and unpleasant circumstances as well as typical smoking situations. Our results support the view that virtual immersive environments can evoke physiological and subjective responses. However, our 3D immersive environment stimuli were specifically generated for the present study, and several methodological limitations should be acknowledged. First, there are no normative data for the ratings of valence, arousal, and dominance of 3D-IE stimuli to provide the necessary basis for comparison with traditional IAPS stimuli used in startle reflex modulation research. Second, our study did not include a neutral condition, which would have provided a reference to illustrate relative differences across pleasant, unpleasant, and tobacco-related stimuli. This would help to show that the greater startle responses related to the smoking stimuli are not idiosyncratic and due to the particular 3D-IE stimuli created for this study. Third, our assessment of nicotine dependence was based only on subjective reports. No blood nicotine or breath carbon monoxide levels were assessed.

¹ In order to test level of dependence and level of craving as potential moderators, we calculated the $3 \times 3 \times 2$ repeated measures ANOVA with FTND and QSU scores as covariates. Likewise, ANOVA analysis of the self-reported data (Valence, Arousal, Dominance, and Desire) were conducted with FTND and QSU scores as covariates. The analysis yielded no significant main or interaction effects of FTND and QSU scores. The correlations between startle blink amplitudes, self-reported data, and level of dependence and level of craving showed significant positive correlations between QSU scores with desire scale for all categories of 3D-IEs ($p < .05$) and with Arousal scores for tobacco-related 3D-IEs. Finally, FTND correlated positively with Desire scores in pleasant environments and with Arousal in tobacco-related environments. To simplify description of the results, these factors are not included in the present analysis.

Table 1
Mean (Standard Deviation) of SAM and Desire Scale Scores for 3D-IE

	Valence <i>M (SD)</i>	Arousal <i>M (SD)</i>	Dominance <i>M (SD)</i>	Desire <i>M (SD)</i>
Pleasant	6.83 (1.0)	4.25 (1.6)	6.28 (1.3)	3.88 (1.7)
Unpleasant	1.70 (.7)	6.81 (1.9)	2.95 (1.6)	4.35 (2.5)
Tobacco-related	5.28 (1.5)	4.84 (1.8)	5.11 (1.7)	7.07 (1.7)

Note. Significant differences were found between the three categories for Valence and Dominance ($ps < 0.001$); unpleasant category showed significant differences with pleasant and tobacco-related categories for Arousal ($ps < 0.0001$); tobacco-related category showed significant differences with pleasant and unpleasant categories for Desire ($ps < 0.001$). 3D-IE = 3D immersive environment stimuli; SAM = Self-Assessment Manikin.

And fourth, only female smokers participated in the study. Firm conclusions would require examining similarities and differences between smokers and nonsmokers, as well as between males and females. Further studies are needed to replicate the present results overcoming these limitations.

Keeping the limitations in mind, the demonstration that 3D-IE technology is an effective method of stimulus presentation in cue reactivity studies has relevant theoretical and methodological implications. Theoretically, the finding that tobacco-related stimuli augmented the startle response, but were subjectively assessed as positive, suggests coactivation of aversive and appetitive motivational tendencies, as already reported (Muñoz, Viedma-del-Jesus, et al., 2010). This dissociation has been explained in terms of an approach–avoidance motivational conflict triggered by the tobacco cues (Breiner, Stritzke, & Lang, 1999; Stritzke, Breiner, Curtin, & Lang, 2004). Methodologically, our results suggest that 3D immersive technology could be an efficient method for investigating context effects in addictive behavior (Alvarez, Johnson, & Grillon, 2007; Rizzo, Schultheis, Kerns, & Mateer, 2004). Recent studies have shown that cue reactivity can be suppressed, or even reversed, depending on context. For instance, physiological reactivity to tobacco-related cues has been found to vary depending on whether the tobacco-related stimulus depicts cigarettes at the beginning or the end of smoking (Mucha, Pauli, Weber, & Winkler, 2008; Winkler et al., 2010). Research on context effects in humans is difficult to conduct using traditional static photographs, due to the difficulty in varying the contextual factors while keeping the cue and the subject constant. Thus, contextual effects on addictive behaviors, such as situational tolerance or context conditioning, which has previously been demonstrated only in nonhuman subjects (Siegel & Ramos, 2002; Walker & Davis, 2002), might be effectively investigated in humans using virtual reality technology.

In summary, the present study reveals that 3D immersive technology is an effective method for inducing emotional states and craving in cue-exposure paradigms. Moreover, the finding that the startle response was enhanced when smokers viewed tobacco-related 3D-IE stimuli, although participants judged the elicited feelings as pleasant, reveals dissociation between the subjective and the physiological aspects of emotion that must be explained by future research.

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