Elicit nicotine craving with virtual smoking cues

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Abstract

Craving is a strong desire to consume that emerges in every case of substance addiction. Previous studies have shown that eliciting craving with an exposure cues protocol can be a useful option for the treatment of nicotine dependence. Thus, the main goal of this study was to develop a virtual platform in order to induce craving in smokers. Fifty five undergraduate students were randomly assigned to two different virtual environments: high-arousal contextual cues and low-arousal contextual cues scenarios (seventeen smokers with low nicotine dependency were excluded). An eye-tracker system was used to evaluate attention towards these cues. Eye fixation on smoking-related cues differed between smokers and nonsmokers, indicating that smokers focused more often on smoking-related cues than nonsmokers. Self-reports of craving are in agreement with these results and suggest a significant increase in craving after exposure to smoking cues. In sum, these data support the use of virtual environments for eliciting craving.

Keywords: Nicotine Craving; Virtual Reality Cues; Eye Tracking; Smokers
Introduction

Smoking is a major cause of premature death, and it is responsible for several types of cancer, including lung, pancreatic and oral cancer.\(^1\) Smoking is the major cause of preventable death in the US, and the second worldwide.\(^2\) Tobacco dependence is responsible for approximately 440000 premature deaths per year in the United States, 2004.\(^3\) In Europe also, according to the WHO, smoking is one of the most important risk factors for premature mortality and is directly or indirectly linked to 1.6 million deaths per year. By 2020, the WHO expects a worldwide toll of c. 10 million deaths from smoking.\(^4\)

One cause acts as a main factor of this tragic scenario: the common denominator of any smoker is the experience of repeated episodes of intense craving for cigarettes. This urge to consume forms a pattern of compulsive behavior and is associated to stimuli that may be responsible for triggering the need for consumption.\(^5\) Some authors suggest that the persistence of inappropriate behaviors and social dysfunction in drug addicts are due to an unbalance between the bottom-up and top-down cognitive systems that control decision making.\(^6\) The output of the reward system in short or long-term reward depends on the balance between the bottom-up reactive and the top-down reflective systems. The reactive system is based on the automatic responses from the amygdala circuits, whereas the prefrontal structures underlie a more cognitive decision from the reflective system. Although temptation and loss of control over drug intake is bottom-up, the willpower to resist to drugs is top-down dependent, blocking decisions in favor of short-term
gain. However, the neural circuits become addicted after repeated exposure to the drug and the system learns to fire a seeking behavior in the presence of internal (craving) and external cues (people, places, etc.).

The classical conditioning theories help explain the association between external or internal cues, smoking-related cues, and addictive behavior. Acute craving behavior is usually triggered when smokers are exposed to situational or environmental cues that are associated with smoking, such as emotional distress or alcohol consumption. However, this association between the urge for smoking and external stimuli can be, paradoxically, the gateway to the treatment of smoking habits.

Psychotherapy, and more specifically cognitive-behavioral therapy, has a long history of using exposure-based therapies (ET) to challenge patients with distressful events. Psychotherapeutic intervention in substance abuse relies on human learning models. Research on this topic has shown that exposure to cues of the substance while the substance is absent will lead to an unlinking of the relationship between conditioned and unconditioned stimuli. ET seeks to produce an emotional detachment between stimuli, event, or the memory of both, on the one hand, and the uncontrolled reactive behavior that follows, on the other. After completing ET, it is supposed that the patient is able to deal with the former distressful stimuli, event or memory, in a controlled and rational manner.

In a cognitive and behavioral rationale, ET was first developed for the treatment of anxiety disorders. Typically, visual and auditory cues,
which are related with the anxiogenic stimuli, are displayed to elicit anxiety levels and help patients in the deconstruction of maladaptive behaviors. In smoking addictive behaviors, cues follow the same principle, but they are displayed in order to elicit craving. Exposure to tobacco related pictures or movies can help elicit craving in smoking dependent individuals.\textsuperscript{9,10}

Nevertheless, exposing individuals to such media may be less effective than to virtual reality (VR) contextual cues. The option for VR resides on its ability to drawn (immersion) the participants into a setting that was specifically designed for a certain purpose, allowing a free interaction with virtual worlds. This means, that contrary to picture and video, participants are free to move their avatar around. On the other hand, and due to the realism and the meaningfulness of the VR scenarios (particularly the ones designed to deal with emotional disorders), patients perceive their experience as if it were real, or at least, very close to real. Even if participant claims that the scenario is not real, in the majority of the cases, VR is able to trick participant’s perception, especially if an emotional content is present. This feature of VR is of paramount relevance for treating addictions, as craving is reported to be more intense when the individual is inserted in a natural setting.\textsuperscript{11,12}

There is an extensive literature on the efficacy of VR cues and contextual settings for the elicitation of craving.\textsuperscript{13,14,15,16,17} Even with non-clinical samples, craving can be easily elicited with VR, allowing health promotion interventions in earlier stages of nicotine dependence.\textsuperscript{18} Also, some studies have illustrated the advantage of
eliciting craving through VR over traditional exposure techniques. For example, smokers that had been immersed in a virtual bar with five type of cues (an alcoholic drink, a pack of cigarettes, a lighter, an ashtray and a glass of beer) reported significantly higher nicotine craving after being exposed to cues than did smokers who looked at pictures with the exact same content. Although no studies are available comparing video and VR cues, it was reported that in vivo cues produce higher craving rates than active video cues. Other authors found no effect of smoking cues that were displayed during a movie presentation on craving.

There is also some initial evidence suggesting that cognitive dimensions such as attention may be involved in the VR experience. One study has suggested that only smokers show enhanced attention to smoking-related cues. Attention to those cues increases when participants gaze longer at smoking-related pictures, or when they initially fixate on those cues rather than on neutral stimuli. These mechanisms occur when the stimulus is to be processed in detail, which might be a propeller of the smoking behavior. Therefore, eye movement measurements can add relevant information about smokers’ behavior towards smoking-related cues while immersed in VR scenarios.

The current study was carried out to assess the effectiveness of a VR environment designed to elicit craving in smokers. Craving elicited by exposure to smoking-related cues was assessed by both self-reports and eye gazing towards relevant stimuli to assess attentional processing during exposure. We expected that smokers exposed to a VR scenario
with smoking cues would produce a higher number of eye fixations on those cues than nonsmokers. In this case, we also expected that smokers report an increase in subjective craving after being exposed to a high arousal condition.

Method

Participants

72 undergraduate students from a university campus in Lisbon where (38 smokers), with an average age of 21.65 years (SD = 4.20). Seventeen smokers with low nicotine dependence (11%), according to the Fagerstrom Test for Nicotine Dependence\textsuperscript{27} were excluded from the analysis. The final sample consisted of 21 (38.2%) smokers and 34 (61.8%) nonsmokers. The average of amount of smoking of smokers’ participants per day was of 12, and the average nicotine addiction test score was of 4 points. No association was found between gender and smoking vs. not smoking ($\chi^2(1) = .116, p > .05$). The same result was obtained for the association between gender and control (low arousal) vs. experimental (high arousal) condition ($\chi^2(1) = .437, p > .05$). None of the participants reported brain injuries, cognitive impairments or other psychiatric disorders. All participants had computer and videogame experience.

Measures

VR-related variables such as presence and cybersickness were assessed with self-report measures, namely the Presence Questionnaire (PQ)\textsuperscript{28} for presence, and the Simulator Sickness Questionnaire (SSQ)\textsuperscript{29} for cybersickness symptoms.
Craving was assessed by a brief 10-item form of the Questionnaire of Smoking Urges (QSU), whereas nicotine severity dependency was estimated by the Fagerstrom Test for Nicotine Dependence (FTND).

Stimuli presentation were displayed on a Tobii-T60 Eye Tracking System (Tobii Technology AB, Sweden), with an embedded infrared camera that recorded eye movements at a sampling rate of 60 Hz. The eye tracker was plugged to an Intel Core2 6550 Desktop computer with a 4 GB ATI Radeon 4870 X2 graphic board.

**Virtual environments**

Two different VR environments (high-arousal cues and low-arousal cues) were developed. The 3D modeling was performed using 3D Max (Autodesk®), while world interaction and animation was carried out through Unity v.2.6 (Unity Technologies®). The main difference between the two conditions was related to presence of smoking activation cues. Both environments were based on a three-room apartment with a bathroom, kitchen, bedroom and a living room with pop music playing and virtual characters interacting within a social event. However, in the high-arousal condition there were also smoking cues like cigarettes and tobacco packages, video clips with smoking cues playing in a LCD, whereas in the low-arousal condition, all smoking-related cues were absent (Figure 1).

**Procedure**

The study was carried out in a soundproof room. The 21 smokers had to smoke a cigarette, outside the laboratory, 5 minutes before the beginning of the experiment. Each participant was informed of the purpose of the
study and consented to participate. After agreement, the participants fill out the nicotine-related self-reports (QSU, FTND) and were engaged in the VR session. After concluding the session, QSU was again filled, as well as, presence (PQ) and cybersickness (SSQ) scales.

The experimental session started off with written instructions on the computer screen, followed by the calibration and a training trial (which were not part of the stimulus material). Following practice, each participant (smoker and nonsmoker) was randomly assigned to high-arousal (with smoking and smoking related cues) or low-arousal (with no smoking and no smoking related cues) conditions. Participants were seated at 60 cm from the eye tracker screen and were instructed to explore the virtual apartment during 5 minutes and to pay attention to all the details in the environment.

Participants were free to move around the scenario. An experimenter sitting in a different room but watching through an LCD screen participants’ actions within the VR environment ensured that the full roaming actually took place.

During the VR session, gaze data of both eyes were recorded by the eye tracker with an average accuracy of 0.5° of visual angle. Eye fixations were only registered in the high arousal condition (when smoking-related cues were displayed in the VR setup). Each trial began with the calibration of the eye tracker. The gaze data were analyzed with Tobii Studio v.2.13 (Tobii Technology AB, Sweden). The number of ocular fixations and duration time were measure through dynamic Areas Of Interest (dAOI). The Tobii Studio 3.0 tool was used in order to create
AOIs around the smoking cues that had appeared in each participant's visual field and were interpolated through key frames that corresponded to certain points on the media timeline. These dAOI allowed us to measure the allocation of attention while moving stimuli (cues) were displayed, independently of participant's point of view. The eye tracking data was used to compare the number of fixations between two groups (smokers and nonsmokers) that had the same probability of gazing, or not gazing, at the smoking cues displayed in the virtual world. All participants that were enrolled in these two groups were asked to roam the entire scenario but with no specific instructions to look at smoking cues. We expected that smokers would gaze more often than nonsmokers at smoking cues. No accurate measures were intended to be taken.

Results
In order to investigate whether smoking participants in the high arousal exposure met the same conditions of those of low arousal cues environment, comparisons between these two conditions were performed for nicotine dependency severity (FTND) and subjective craving (QSU).

An independent samples t test showed no statistically significant differences for subjective craving and for nicotine dependency severity between smokers engaged in the high arousal and smokers in the low arousal VR conditions. These data suggest that the initial levels of craving and the severity of nicotine dependency were similar amongst all smokers, independently of the scenario they were exposed to.

Differences in fixations between smokers and nonsmokers to smoking cues during the VR session
Fixations were only assessed during the exposure to high arousal cues. Due to a non-normal distribution of ocular fixations (that persisted after log transformations being performed), the Mann-Whitney non-parametric was selected conducted for this analysis. According to some authors\textsuperscript{31,32,33} non-parametric tests are still the best option for non-normal distributions. A measure of effect size, $r$, was calculated from the probability value of the test-statistic ($r = Z/\sqrt{n}$).\textsuperscript{34} The results revealed a significant difference between groups (smokers and non-smokers) in eye-fixations to smoking-related cues ($U = 20.000$, $Z = -2.47$, $p = .013$, $r = .52$). The number of eye-fixations on relevant cues was higher in smokers ($MR = 16.00$) than in nonsmokers ($MR = 8.93$) (Figure 2).

**Effects of smoking and VR cues on VR-related variables**

The dependent variables were presence (PQ) and cybersickness (SSQ) total scores. Data that was not normally distributed was rank transformed and globally ranked.\textsuperscript{35} All transformed data was analyzed using two-way univariate ANOVAs. The results showed a significant interaction effect of smoking and VR on cybersickness ($F(1,47) = 5.41$, $p = .025$, $\eta^2_p = .026$). The interaction effect was decomposed using simple effects with *Bonferroni* adjustment for multiple comparisons. Simple effect analyses showed higher levels of cybersickness for smokers compared to non-smokers when exposed to high-arousal cues VR condition ($t(21) = 2.55$, $p = .019$, $d_s = 1.16$). Figure 3 depicts the interaction effects between these factors. However, no significant differences were found on cybersickness levels between smokers and non-smokers in low-arousal
Elicit nicotine craving... 12

VR condition. For presence, no significant main or interaction effects were found (all $ps > .05$).

**Effects of smoking and VR cues on subjective craving levels**

In order to examine a possible effect of smoking and VR cues on QSU after the exposure to different scenarios, the computation of $\Delta$QSU (QSU after - QSU before) was performed. *Kolmogorov-Smirnov* test was significant for $\Delta$QSU, showing that the data was not normally distributed. All data were globally ranked from smallest to largest score and average ranks were assigned in case of ties. All transformed data was then analyzed using a factorial ANOVA on a 2X2 factorial design. The ANOVA was performed with two between-subjects factors of two levels each, namely smoking (smoker vs. non-smoker) and scenario (low-arousal vs. high-arousal). Results show an interaction effect of smoking and scenario on $\Delta$QSU ($F(1, 50) = 4.83$, $p = .033$, $\eta^2_p = .11$). The interaction effect was decomposed with simple effects with a *Bonferroni* adjustment for multiple comparisons. These analyses showed a significant larger $\Delta$QSU for smokers compared to non-smokers when they were exposed to high-arousal cues scenario condition ($t(21) = 11.02$, $p < .001$, $d = 4.31$). However, no significant differences were found on $\Delta$QSU between smokers and non-smokers in low-arousal VR condition (Figure 4).

**Discussion**

In line with previous studies, our results indicate that nicotine craving may increase with the display of cues in virtual reality environments. However, this was true only when smokers were exposed to smoking
cues, which are in agreement with our initial purpose suggesting that the exposure to tobacco or smoking-related cues in a virtual environment can elicit nicotine craving in smokers. These data concur with results from other studies.\textsuperscript{14,17,18,19} The exposure to smoking cues would promote stimulus control in several ways.\textsuperscript{37} One approach is based on classical and operant conditioning theories, where extinction may occur when a conditioned stimulus lose its capacity to elicit a response in the absence of unconditioned stimulus. During exposure it is possible to systematically desensitize those participants and simultaneously provide coping skills that will help dealing with these situations.

Regarding presence, our results showed that no significant differences were observed between smokers and non-smokers and also between high-arousal and low-arousal conditions. It would be interesting in future studies to assess whether these differences between our data and data from prior studies with alcohol and cocaine addicts are due solely to the type of substances under study or they are related to other endogenous or exogenous factors.\textsuperscript{38,39} One possible explanation for this discrepancy may derive from the fact that cocaine and alcoholic addicts may react more vividly to the presence of cues than smokers do, being, in this way more engage in the virtual experience.

Such trend was not observable on the other VR-related dimension under study. In fact, when it comes to cybersickness, the smoking participants reported higher scores when engaged in the activating smoking setup than non-smokers. Being a measure of physical discomfort, the cybersickness scale may have captured the distress state
associated with the craving behavior of the smokers when they were interacting with smoking-related cues.

The severity of nicotine dependence and the time period since the last cigarette were also controlled in order to ensure similar study conditions among smokers that were exposed to high and low arousal environments. Because no significant differences were found between the exposure of smokers to these two scenarios, it is reasonable to assume that the distinction between smokers that were exposed to high-arousal and low-arousal cues are not related to differences in the baseline condition.

Although no significant effects were found on presence, the higher number of fixations during the exposure of smokers to smoking cues may suggests a differentiate response of the central nervous towards the activating cues. This result may support the hypothesis that smoking craving make smoking related-cues more salient to the smokers’ participants that were exposed to these cues and context. These data may also suggest eye-tracking as an alternative measure to other indicators based on arousal to study addictive behaviors in the presence of relevant cues.

These results, however, need to be complemented with data from neurophysiological methods. The relationship between craving and the activity of the peripheral nervous system (PNS) have been also explored. Findings from other studies have suggested that exposure to smoking-related cues in a VR setup induce an increased autonomic reactivity through skin conductance level (SCL) and heart rate (HR).
Psychophysiological indexes have been used because they are a reliable reflex of autonomic activation of the PNS. Such techniques are indirect measures of emotion and sensitive indicators of arousal. Skin conductance is completely innervated by sympathetic division of the peripheral nervous system and it is capable of differentiating physiological outcomes due to a relaxing state from others resulting from more exciting states. On the other hand, HR has also been related to emotional processing as an index for cue reactivity. Greater HR acceleration may reflect activation of the autonomic nervous system to fear, anger or sadness emotional states.

The event-related potentials (ERP) may be another option. The P300, or other late potentials, could provide a more comprehensive insight on the neural responses that underlie the processing of these cues in smokers. For example, some studies suggest that smokers show enhanced frontal activity during the presentation of smoking related pictures, specifically through the late positive component (LPP). Our data shows the engagement of frontal activity during the processing of smoking stimuli, providing evidence for greater cortical processing in smokers, when exposed to smoking cues, suggesting that smokers may look more often for smoking cues than other environmental stimuli.

In summary, the use of virtual reality environments as an exposure technique is of major interest since these environments gather all ecological aspects and naturalness of real world situations. The use of virtual environments as an exposure technique should be included in the toolbox of existing smoking cessation programs, where self-control,
stimulus control and improvement of strategies for coping with smoking-related stimulus or situations may occur.
References


Figure 1. Virtual reality cues in high-arousal (LEFT) and low-arousal (RIGHT) conditions
Figure 2. Differences in fixations between smokers and nonsmokers to smoking cues
Figure 3. Effects of smoking and VR cues on cybersickness (ranked scores)
Figure 4. Effects of smoking and VR cues on subjective craving levels (ranked ΔQSU scores)