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Nicotine Craving and Cue Exposure Therapy by Using Virtual Environments

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ABSTRACT

Smokers who are exposed to cues associated with smoking show cardiovascular reactivity and an increase in smoking urges as compared to when they are presented with neutral cues. Cue exposure therapy (CET), which refers to the repeated exposure to drug-related cues in order to extinguish this learned association, has increasingly been proposed as a potential treatment of addictive behaviors, including tobacco smoking. The result of our pilot study suggests that a cue elicited using a virtual environment (VE) is more effective than other cue exposure devices. The VE was composed of craving environments (virtual bar) and objects (an alcoholic drink, a packet of cigarettes, a lighter, an ashtray, a glass of beer, and advertising posters) that are likely to trigger craving, a smoking avatar, and an audio environment that included the noisy sound and music of a restaurant. Sixteen late-adolescent males who smoked at least 10 cigarettes a day were recruited to participate in the VE-CET study. The CET virtual bar program consisted of six sessions, and the participants were exposed repeatedly to each session using different questions and procedures. Although the effects of CET did not yield significant reductions in all of the dependent variables, the craving for cigarettes was gradually decreased during the course of the sessions. This tendency was closely related to the reduction in the smoking count between the morning before the experiment and the start of the experiment. Based on these preliminary results, it appears that VE-CET maybe a useful tool to use in treatment programs to help reduce craving in those who are nicotine dependent.

INTRODUCTION

CUE EXPOSURE has been advocated as a potentially effective method of treating addictive behaviors.[1] It is widely recognized, both clinically and empirically, that drug use and relapse are often strongly cue and context specific. When addicts encounter cues previously paired with drug use—for example, drug paraphernalia or contexts in which drugs were taken—they evoke responses such as drug-seeking behavior and withdrawal-like symptoms that are presumed to motivate or mediate drug use.[2]

Typically, cue exposure therapy (CET) refers to the manualized and repeated exposure to drug-related cues, aimed at reducing the cue reactivity by extinction. In addition, CET involves repeated unreinforced exposure to stimuli that have previously been associated with drug use in an attempt

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to extinguish an addict's conditioned responses to such cues. This technique has been utilized in treatments across most drugs of abuse, including opiates,[3] alcohol,[4] and nicotine.[5]

Tobacco smoking is the greatest preventable cause of death in developed countries and is a significant health problem in developing countries. Although the prevalence of smoking has gradually declined among adults in developed countries, worldwide consumption of tobacco is still rising. It is predicted that about three million smokers worldwide die annually from smoking, and that the rapid increase in smoking in developing countries will cause this toll to rise to about 10 million annually by the year 2030.[6] Several hundred million adults who are current smokers are expected to die from smoking.[6] Although the harmful health effects from smoking are widely known, it has been estimated that each year fewer than 10% of smokers attempt to quit, and that only 3% of smokers successfully do so.[7]

Cue reactivity is widely studied among addictive behaviors, particularly in smoking.[8,9] Smokers show heart-rate and blood-pressure reactivity, report greater urges to smoke, and report lower self-efficacy not to smoke in response to a wide variety of cues, including interpersonal interaction cues,[10,11] standardized positive and negative affect scripts,[12] cognitive stress,[13] in vivo visual and olfactory cues,[14] and contexts associated with a high risk of relapse.[15]

Smokers who are exposed in the laboratory to cues associated with smoking show cardiovascular reactivity and an increase in smoking urges compared to when they are presented with neutral cues.[11,12] This increased cue reactivity predicts a decreased likelihood of successful cessation.[15,16] Despite some debate as to the precise mechanisms contributing to cue reactivity,[17] there is an emerging consensus that such mediating mechanisms involve multiple cognitive, behavioral, and physiological response systems.[1,9] The incremental use of cue exposure treatment along with established pharmacological and cognitive-behavioral skills training treatments may provide a stronger relapse-prevention strategy for smoking than currently available treatments.

Research has shown that many smokers experience an increase in the desire to smoke when exposed to smoking-related cues.[18] A strong desire or craving to smoke seems to play an important role in the maintenance of cigarette smoking.[19] According to learning-based theories, cue-induced craving might partly reflect a conditioned response established by a learned association between that cue (conditioned stimulus) and nicotine intake (unconditioned stimulus).[9] CET, which tries to extinguish this learned association, has increasingly been proposed as a potential treatment of addictive behaviors, including tobacco smoking.[20] Results from a pilot study examining the effect of CET in nicotine addiction showed, however, that repeated exposure to smoking-related cues without subsequent nicotine intake did not extinguish craving.[21]

A virtual environment (VE) can make a person look, feel, hear, and interact in a computer-generated situation. Nemire et al.[22] used this approach to investigate its potential for preventing teen smoking. In this study, 22 secondary school students were randomly assigned to three conditions (daily life training, VE training, and non-VE training) for eight sessions. The VE condition was constructed so that the participants, navigating in a virtual park, were tempted to smoke by an avatar. Nemire et al.[22] reported that the participants in the VE successfully learned information about smoking and acquired superior skills in coping with and rejecting smoking opportunities than the other groups. Participants in this group also preferred the experience of the VE as a method of education. Gonzalez,[23] in a study of cocaine addiction, showed that participants' arousal and craving increased when exposed to cocaine-related cues (an instrument and a crack dealer) in a virtual crack house. A study of heroin addiction reported that a 3D object in a virtual bar is at least as good or better at eliciting subjective and physiological craving than pictures or neutral cues in VE.[24] CET and the other therapeutic methods that are effective in reducing craving are mainly used in cognitive behavioral therapy (CBT). Although CBT can be effective in treating dependence on nicotine, combining it with VR exposure therapy may be more effective. These results all seem to suggest that smoking-related cues presented three-dimensionally in an interactive VR world are more effective at eliciting arousal than two-dimensional cues presented via non-interactive, still photographs. In particular, the VE can provide various stimuli simultaneously, can provide both individual and emotional stimuli, and can give participants a sense of presence or immersion in the stimulus environment.

In a previous pilot study,[25] we designed a VE system to create a desire for nicotine, which was based on the responses from a survey on nicotine craving. The VE was composed of locations and objects that were likely to trigger craving, and avatars which were smoking cigarettes. We compared this VE system with a classical device (2D picture), and measured the degree of self-reporting of craving for nicotine. The results from our pilot study suggested that the VE was more immersive and evoked nicotine craving more effectively than traditionally used methods. This greater effectiveness appears to arise

FIG. 1. Representative stimuli in the three-dimensional (virtual bar) condition.

from the fact that VEs can present a context-specific stimulus with a high degree of ecological validity. However, our pilot study has been the study that confirmed the power of VE to reduce nicotine craving. In the present paper, we applied the VE-CET repeatedly to nicotine addicts, to confirm whether this method reduces the degree of craving for the drug over the course of the treatment sessions.

MATERIALS AND METHODS

Participants

Sixteen late-adolescent males who smoked at least 10 cigarettes a day were recruited and offered $US70 to participate in the VE-CET study (mean age = 17.13 years, SD = 0.83; mean cigarettes/day = 15.33, SD = 4.98). Participants completed a brief medical screening form and reported no concurrent neurological disorders or current use of psychoactive medications. Participants were instructed to abstain from alcohol for 24 h prior to treatment, but allowed to smoke ad libitum prior to treatment. One participant did not take part in the experiment for personal reasons.

The virtual reality instrument and CET scenarios

The virtual reality system consisted of a Pentium IV PC, OpenGL Accelerator VGA card, a head-mounted display (i-visor DH-4400VPD), and a 3DOF position sensor (Intertrax2). The PC generated real-time 3D virtual images for the participant to navigate. The position sensor (tracker) relayed the participant's head orientation into the computer.

The design of the VE was based on our preliminary study of nicotine craving. The background environment was a public bar with various objects displayed, such as an alcoholic drink, a pack of cigarettes, a lighter, an ashtray, a glass of beer, advertising posters (alcohol and cigarettes), and an avatar offering a cigarette (Fig. 1). The audio environment included the noisy sounds and music of a restaurant.

Procedures

Before the experiment, participants were asked for their demographic data, medical history, and a survey of their smoking behavior (a daily smoking count and where they typically smoked). They were also asked to complete a modified Fagerstrom Tolerance Questionnaire (FTQ) and a self-rating scale to record their level of nicotine craving at that moment (0–10). Before and after the experiment, participants were instructed to complete the Simulator Sickness Questionnaire (SSQ) and the Presence Questionnaire (PQ).[26–28] After each CET session, participants also answered six questions related to their craving at that moment (Table 1). Their answers to each ques-

TABLE 1. QUESTIONS FOR CRAVING

Q1: "How much do you want to smoke a cigarette right now?"
Q2: "Are you tempted to have a smoke right now?"
Q3: "Do you have a plan to act on that temptation right now?"
Q4: "When the avatar tried to persuade you to have a cigarette, how much did you want to smoke?"
Q5: "To what degree did you feel that this virtual reality was similar to the actual world?"
Q6: "Did you feel more desire in the virtual situation when you saw objects such as a lighter, an ashtray, and a glass of beer?"

TABLE 2. CONTENTS OF THE CET PROGRAM IN EACH OF THE SESSIONS

Session	*Theme*	*CET Program Content (each session = 20 min)*
1	**Initial navigation**	The participant was free to navigate during the initial session. 1. Have you navigated VR sufficiently? 2. Tell us about what you felt and thought after the VR. 3. How do you feel and think about the objects and situations in the VR, and then what would you do?
2	**The person eliciting craving**	Interview with the participant about the person eliciting craving (open-ended) 1. Did you want to smoke when the avatar offered you a cigarette in the bar? 2. Whose offering a cigarette made you strongly want to smoke? Think about the location and person who offered you your first ever cigarette. 3. Whose offer of a cigarette is hardest for you to refuse (e.g., a schoolmate, a buddy, a girlfriend, an adult, etc.)?
3	**The object eliciting craving**	Interview with the participant about the object eliciting craving (open-ended) 1. What object made you most strongly want to smoke (e.g., the cigarette, the alcoholic drink)? 2. Did you want to smoke the cigarette that was on the table when you were drinking with your friend? If you did want to smoke it, why? 3. Who did you think was going to offer you your first cigarette in the bar?
4	**The situation eliciting craving**	Interview with the participant about the situation that elicits craving (open-ended) 1. What situation in the virtual bar made you want to smoke the most? 2. Did you want to smoke when you saw a smoker near your table in the bar? 3. Did you still want to smoke when your cigarette was finished while you were having an alcoholic drink? Yes/No If so, what method would you use in this situation to obtain a cigarette?
5	**Comprehensive review**	Interview with the participant about the stimuli as a whole. 1. Whose offer of a cigarette made you crave for a smoke? 2. What object made you crave for a cigarette? 3. What situation made you crave for a cigarette?
6	**Final navigation**	The participant was free to navigate during the final session. 1. How do you feel and think now after you've navigated the VR for several sessions? (Compare with the first session.) 2. How do you feel and think now about the objects and situations that you saw in the VR, and what do they make you feel like doing? 3. If the VR experience happened to you in real life, what would you do?

FIG. 2. The experimental procedure for one session.

tion were given as a rating on an 11-point scale, ranging from "not at all" to "extremely." The participants then practiced with a VE exercise until they became familiar with the interfaces and navigation in the virtual public bar. The CET virtual bar program consisted of six sessions, each session including different questions and procedures (Table 2). The experimental procedure is presented in Figure 2.

RESULTS

The demographic data—age and daily smoking count—and the mean score of the questionnaire data—the FTQ, SSQ, and PQ—are presented in Table 3.

The differences in the scores of the pre-experiment and post-experiment questionnaires were not significant (repeated measures ANOVA). The participants reported moderate levels of nicotine dependency, presence, and ability to control the VR device; and low to moderate levels of cybersickness.

As shown in Table 4, a trend was observed that the daily smoking count of smokers (11.00–14.47) was reduced, except in the third session, compared with the pre-experiment count (15.33). However,

TABLE 3. THE DEMOGRAPHIC DATA AND THE RESULTS OF REPEATED MEASURES ANOVA FOR THE DEMOGRAPHIC DATA AND THE QUESTIONNAIRES

Questionnaires	*Preexperiment*	*Postexperiment*	*F*
FTQ	3.60 ± 2.06	3.40 ± 2.06	0.677
SSQ	2.13 ± 0.95	2.28 ± 0.96	0.479
PQ	5.53 ± 0.92	5.47 ± 0.95	0.083

Age, 17.00 ± 0.76 years; smoking count/day, 15.33 ± 7.98.

the morning smoking count decreased significantly through the sessions (from 2.93 to 1.29; F[1,14] = 7.374, $p < 0.05$).

In slightly greater detail, Figure 3 shows the change in the smoking count between the morning and the daily total across sessions. For each measure, although there is no significant difference in the count between successive pairs of sessions (i.e., during a period of almost 24 h), the decrease was significant over longer time intervals. The morning smoking count significantly decreases from session one to six, whereas the daily smoking count shows a slightly decrease from sessions three to six.

Figure 4 illustrates the results obtained from rating craving according to the six questions (Q1-Q6) that were posed after each CET session. The questions were divided into two categories (Craving and VR-craving). The changes in either category were not significantly different through the sessions, although the Craving category showed a tendency to decrease gradually. In particular, Figure 4b shows that craving was reduced in the items for current craving (Q1) compared with the "thinking about" (Q2) and "planning" (Q3) of smoking be-

TABLE 4. THE RESULTS OF REPEATED MEASURES ANOVA WITH RESPECT TO THE SMOKING COUNT AND THE LEVEL OF CRAVING IN EACH SESSION

Variables	*Session 1*	*Session 2*	*Session 3*	*Session 4*	*Session 5*	*Session 6*	*F*
Morning smoking count	2.93 ± 1.98	2.80 ± 1.86	2.27 ± 1.33	2.00 ± 1.25	2.00 ± 1.36	1.29 ± 1.27	7.374[a]
Daily smoking count		11.00 ± 6.93	16.07 ± 6.94	14.47 ± 8.75	13.27 ± 9.97	14.33 ± 9.74	3.699
Planning (min)		15.67 ± 17.61	23.67 ± 22.16	22.67 ± 21.12	19.33 ± 20.08	20.67 ± 19.17	0.217
Craving (items 1–3)	5.74 ± 1.75	6.72 ± 1.62	5.24 ± 2.59	5.69 ± 2.11	6.02 ± 2.21	5.26 ± 2.33	0.119
VR craving (items 4 and 6)	5.14 ± 2.63	4.79 ± 2.30	5.00 ± 2.47	5.61 ± 2.18	5.36 ± 2.11	4.93 ± 2.35	0.193

[a]$p < .05$.

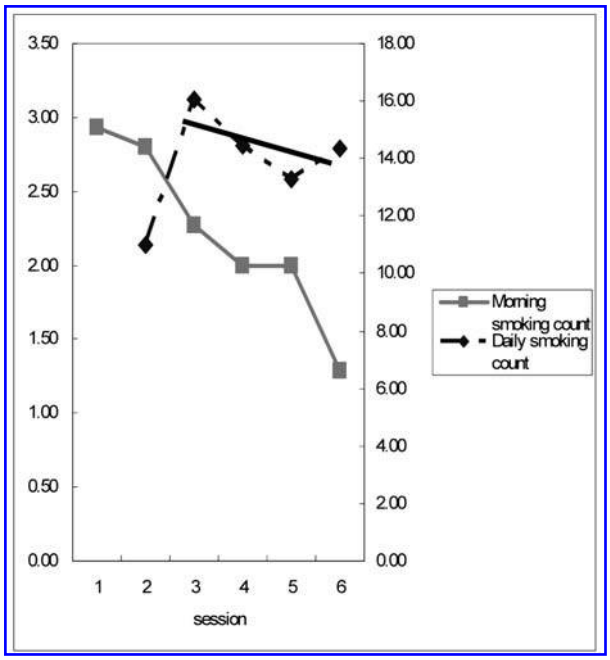

FIG. 3. Morning and daily smoking count as a function of session number.

havior. Figure 4c shows that the VR context or situation (Q6) caused more craving than the smoking avatar and objects (Q4; liquor bottle, wineglass, cigarette, lighter, and ashtray).

DISCUSSION

This study investigated the possibility that CET is an effective treatment technique for a smoker. Although the effects of CET did not yield significant reductions in all of the dependent variables, because of the brief sessions, the craving for cigarettes was gradually decreased during the course of the sessions. This tendency was closely related to the reduction in the morning smoking count between the morning before and the start of the experiment. Although the reduction should be considered to the effect of the observer because of the daily treatment (participants' demand characteristics to the experiment), still the total quantity of smoking and craving was gradually decreased during the course of the sessions.

There was a relatively higher response level for the 'thinking about' and 'planning of smoking behavior' items than for items related to current craving. This suggests that adolescents express their greater craving in the first two items when asked about their craving.

Most CET studies have suggested that effective therapy requires in vivo cues rather than picture or photo cues. In particular, Donny et al.[29,30] and others[31,32] have suggested that environmental cues associated with nicotine delivery are capable of maintaining nicotine-seeking behavior. This suggestion is consistent with the belief that conditioning to environmental stimuli may play a significant role in the process of drug dependence and relapse in humans.[33,34] Therefore, the environmental cues of VE have more application to CET than do non-environmental cues. While animal studies are precisely controlled, addictive behavior in humans is highly variable across individuals, and therefore more difficult to study and to cure. Because human addicts use drugs in numerous environments under various circumstances, a VE may be more effective in human participants because it is capable of presenting many circumstances.

In this study, only male students were selected to control the effects of gender. Frankenhauser[35] suggested that gender differences in cardiovascular reactivity were relatively related to same-gender stimuli. Moreover, cardiovascular reactivity in response to standardized stressful laboratory challenges can differ between men and women[36,37] and can differentially predict smoking outcomes.[13] It is therefore possible that different types of smoking-cue manipulation produce different levels of reactivity in male and female smokers. A comparative study is therefore necessary to identify gender differences with respect to CET cues, including cardiovascular reactivity.

This study has several limitations. In future studies, longer therapy sessions should be used, with a multimodal approach that includes olfactory and tactile stimuli in addition to the visual and auditory stimuli that we were used. Some studies[38,39] have reported that olfactory stimuli can improve participants' memory; VE-CET therapy may thus be more effective with the addition of such stimuli.

The cues for craving depend on such variables as personal experience, age, and stimuli of various kinds. Niaura et al.[40] proposed that it is inappropriate to apply the same treatment methods across different drugs. Schenk and Partridge[41] reported on the importance of environmental stimuli in drug dependence and relapse. Brauer et al.[42] determined that craving cues for tobacco smoking are more important in the maintenance of smoking behavior than its onset. We recommend that these results be taken into account in the design of future studies into VE-CET therapy.

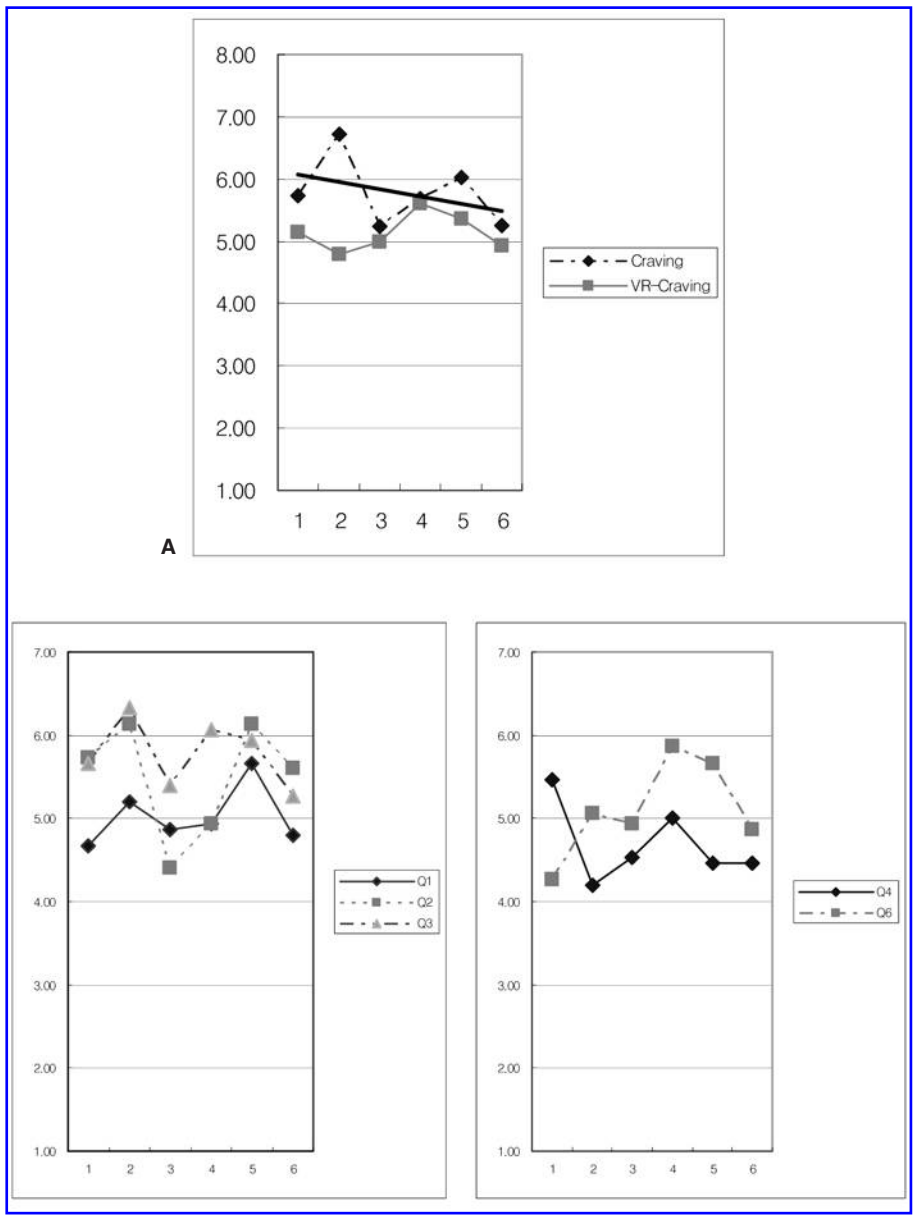

FIG. 4. The change in craving after each session: Craving = (Items 1 + 2 + 3)/3. VR craving = (Items 4 + 6)/2.

In many studies, although cue reactivity is assumed to be a reliable and valid phenomenon, results vary according to the types of stimulus, the parameters of the responses, the psychological and physical situation, for example, gender, pre-existing coping strategies, the emotional state of the participants,[43] their nicotine blood levels, and their levels of fatigue and of nicotine dependency. Payne et al.[43] showed that the craving for nicotine was more strongly related to negative than positive emotional states, so it will be necessary in future studies to control the various variables of psychological and physical situations related to the craving cues of smoking. Because exposure to craving cues affects the psychophysiological response differently,[44] our study was limited in that it was restricted to measuring participants' subjective responses. In studies that are based on the measurement of craving, we recommend that objective physical indices such as psychophysiological measures be employed to objectively confirm the effects of VE treatment. In particular, it may be valuable to investigate brain activity using fMRI to corroborate other measurements of the effectiveness of CET therapy.

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