Virtual Reality Cue Reactivity Assessment in Cigarette Smokers

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ABSTRACT

Drug craving has purportedly been linked to relapse and to substance use. For over two decades, cue reactivity has been a viable method to assess craving and physiological reactions to drug stimuli. However, traditional cue reactivity has faced the following limitations: austere situations or stimuli, lack of complex cues, lack of standardization, and limited generalization outside of the lab setting. In order to improve cue methodologies, a virtual reality (VR) nicotine cue reactivity assessment system (VR-NCRAS) was developed and tested in a controlled experimental trial. Ten nicotine dependent smokers were exposed to VR smoking cues and VR neutral cues in a standardized, timed, computer controlled experiment. Subjective craving and physiological responses were recorded and compared across VR-NCRAS stimuli. Subjective cigarette craving increased significantly and corresponding physiological reactivity was observed in response to VR smoking cues. VR neutral cues did not result in subjective or physiological changes consistent with craving. Implications of these findings on substance abuse research and treatment are discussed.

INTRODUCTION

Cigarette smoking is legal for individuals 18 and older and occurs across a wide variety of daily life activities and social situations. Smokers may experience more conditioning of environmental cues than persons addicted to illegal substances. Environmental stimuli (i.e., waking up, eating, driving) are repeatedly paired with smoking and through classical conditioning become cues to initiate craving and lead to smoking.1 Studies of smokers in both the laboratory2-6 and in the natural environment7 have demonstrated a positive relationship between cue exposure and increases in subjective and physiological responses. In addition, situational cues involving social interactions, positive and negative affective experiences, physical smoking stimuli, and the presence of other smokers have been associated with craving and relapse.11,12 Assessing reactivity (craving and physiological responses) to drug cues has offered researchers and clinicians insight into potential relapse triggers and situations that lead to use.

Traditionally, laboratory cue-exposure (reactivity) studies involve exposure to cues via imaginal experiences (imagery scripts), multi-media (i.e., photos, video), or actual smoking materials (paraphernalia). Typically, participants are exposed to cues in a laboratory environment where physiology, self-reported mood state, and craving responses are recorded. These studies suggest that when smokers are exposed to visual, auditory, olfactory, and tactile (paraphernalia) smoking cues, increases in physiological arousal13-16 and in subjective urges and craving, compared to neutral (non-smoking related) cues1,3,6,13-16 are observed. Studies utilizing either
written or tape recorded scripts to enhance imagination of smoking urge situations have also been effective at eliciting both physiological arousal and subjective craving responses.\textsuperscript{13,19,20}

Recently, three groups have reported the use of virtual reality to elicit craving responses in smokers.\textsuperscript{21–23} While these studies varied significantly in design, population, VR stimuli and measures, each reported significant changes in subjective craving. Two of these studies were controlled trials\textsuperscript{21,22} that differed in whether subjects had just smoked or whether they were abstinent for 12 h.\textsuperscript{21} Results from these two trials both indicated that the relative magnitude of increases in subjective craving were similar.\textsuperscript{21,22} These differences in design with similar effects suggest that VR provides a robust method for assessing cue reactivity in smokers. Additionally, results provide clear evidence that using well-designed, immersive VR-NCRAS to present complex stimuli is a promising method for adding control and generalizability to future cue reactivity research.

In order to extend previous studies using VR cue reactivity, a controlled trial that included monitoring of both subjective craving and physiological reactivity (skin conductance response [SCR]) to smoking cues (inanimate and animate) and neutral cues in a sample of non-treatment seeking cigarette smokers was conducted. In the current investigation, it was hypothesized that smokers pre-loaded with nicotine would experience increases in subjective craving and in physiological reactivity in response to VR smoking cues compared to VR neutral cues.

**MATERIALS AND METHODS**

**Participants**

Ten non-treatment seeking, nicotine dependent smokers were recruited for participation in this trial. Participants met the following criteria: nicotine dependent; smoked at least 21 cigarettes per day; reported good physical health; and were able to wear a head-mounted display (HMD) for up to 40 min. Participants were excluded from participation if they had a diagnosis of severe mental illness; other substance dependence; used illicit drugs in the past month; or had other significant health issues.

**Design and procedures**

Participants responded to an advertisement in a local paper recruiting current smokers. After completing a telephone screening, pre-qualified participants were scheduled for a screening interview visit at the Virtual Reality Clinical Research Center–University of Georgia. Upon arrival, all study procedures were explained and informed consent was obtained from each participant. During the screening interview, all participants were assessed for study eligibility. Data on brand and cigarette preference were also collected as part of the interview process. All eligible participants then underwent a 20-min VR acclimation session in a VR environment unrelated to smoking cues to familiarize them with VR experience and with the built-in VAS rating scale.

After completion of the VR acclimation session, participants were instructed to take a 20–30-min break. Upon returning to the VR lab, disposable pre-gelled skin conductance electrodes (Multi Bio Sensors, El Paso, TX) were attached to the index and ring fingers of the non-dominant hand. To standardize the time since last cigarette use, participants were sent outside to smoke one cigarette ad libitum. After smoking, participants returned to the VR lab and were seated in a non-reclining chair. The SCR electrodes were hooked up to monitoring equipment (Coulbourn Instruments-LabLinc V) and monitoring of SCR was initiated. Participants donned the HMD (VFX-3D, Interactive Imaging Systems, Rochester, NY) and were provided with a game pad. Using a custom interface the researcher selected the experimental path, brand representation/type of cigarettes, presence of alcoholic beverages, and gender of person offering cigarettes (Fig. 1). The VR-NCRAS\textsuperscript{24} program was started, and participants entered a relaxation phase for 5 min in which they were immersed in a dark room while listening to music. After 5 min, participants were asked to stand and the VR-NCRAS moved each along a preprogrammed path to the next stimulus. Each participant then experienced a neutral cue room, two smoking cues rooms (one inanimate smoking cue room and the other a social interaction room involving smoking); ending on a final neutral cue room. Each room provided 3 minutes of exposure that included timed pauses in front of stimuli that allowed viewing of each relevant stimulus or social interaction. After each cue room, participants entered a questionnaire room (Fig. 2) and rated their craving intensity on a 100 point visual analog scale (VAS) by using the game pad to select a position along a line anchored on the left by “not at all” and on the right by “more than ever.” Integration of the VAS rating scale into VR was utilized to help maintain immersion in the VR experience. The entire VR-NCRAS session was computer...
guided and all participants experienced the same path and timing through the four cue rooms and questionnaire rooms. The experimental session was completed in 26 min.

VR-NCRAS cues

The VR-NCRAS neutral cues consisted of four animated underwater scenes designed to look like aquariums with accompanying audio arranged in a room. At pre-programmed intervals, participants were guided to each aquarium scene. Both neutral cue rooms were identical. The VR-NCRAS smoking cues included a room that contained smoking paraphernalia (i.e., burning cigarettes, cigarette packs, a bar, and a percolating coffee pot) and a separate room that consisted of a party setting, in which participants interacted with people in VR who were smoking, drinking, and who offered a cigarette to the participant. The experimenter controlled the VR social interactions using a keyboard interface. Each social interaction occurred between participants and video of people inserted into the three dimensional world. The video people are images of actors and actresses filmed using blue screen techniques which allow them to appear more realistic in the VR environment.

RESULTS

Ten nicotine dependent cigarette smokers (five female and five male) who met study criteria participated in this trial. The participants were 50% Caucasian, 40% African American, and 10% other and ranged in age from 19 to 53 (mean 27.1, SD = 11.3) years. On average, participants started smoking at age 15.9 (3.4), smoked 25.9 (7.8) cigarettes per
day, smoked at that rate for 7.8 (9.8) years, and reported 2.3 (1.4) quit attempts, when they quit smoking for at least a few days.

**Subjective craving**

A repeated measures ANOVA was used to compare craving ratings across VR-NCRAS cue rooms (Neutral cue room 1, Smoking paraphernalia cue room, Smoking social party cue room, Neutral cue room 2) and a significant main effect was found ($F(3,9) = 14.3, p < 0.000$). Post hoc analysis indicated VR-NCRAS smoking cue rooms led to significantly increased craving compared to VR-NCRAS neutral cue rooms (Fig. 3). Pair wise comparisons are noted in figure 3. Average craving ratings across cue rooms were 26.2, 65.6, 68.2, and 46.8 for neutral cue room 1; smoking paraphernalia cue room, smoking social party cue room and neutral cue room 2, respectively. Note that craving ratings in neutral cue room 2 trended downward, were lower than smoking cue room ratings, but neutral cue room 1 craving levels were not re-achieved. Craving ratings between smoking cue inanimate and animate rooms were not significantly different within this small sample. However subjective reports from participants indicated that the social interactions containing more complex cues more closely resembled their real world experiences. Overall, craving ratings increased approximately 110% from neutral to smoking cue rooms.

**Physiological reactivity**

SCR data were recorded in real time across all cue rooms. SCR data were averaged at 15-sec intervals across the 3 min of exposure time in each room (baseline, neutral cue room 1, smoking paraphernalia cue room, smoking social party cue room, and neutral cue room 2). Average SCR data for all participants across VR cue rooms are presented in Figure 4. SCR increased during VR smoking cue rooms compared to neutral cues and baseline. The small sample size limits our ability to detect the clinically meaningful changes on the SCR data. Based upon other cue studies and power calculations estimating a medium sized effect, sample sizes of 50 subjects or larger would be preferred to detect significant changes in SCR. The addition of repeated measures would lower the number of subjects needed, though larger samples are needed in future studies to provide adequate power to detect significant changes on SCR.

**DISCUSSION**

This second, controlled trial using VR-NCRAS confirmed and extended our original findings demonstrating that VR-NCRAS smoking cues effectively increase subjective craving. In addition, the current study also extends our original work by demonstrating that VR-NCRAS also leads to observable changes in SCR in non-deprived nicotine dependent smokers. The VR technology utilized in this trial allowed experimental manipulation of cues in a systematic, standardized, and repeatable methodology. VR-NCRAS smoking cues incorporated both smoking paraphernalia and social interactions. These data support the idea that craving and nicotine cue reactivity can be studied using complex VR cues. The addition of controlled social interactions, computer timing, and a shared experience between the researcher and the participant may provide ad-
vantages over imaginal, multimedia, and paraphernalia presentations in a lab setting.

As demonstrated in our previous trial,22 and in the current trial the second neutral cue served to decrease subjective craving. In addition to craving, observed changes in SCR suggested that these VR based methodologies warrant further investigation in larger samples. Overall, data in this VR trial are similar to results using traditional cue reactivity methodologies. Specifically, our results are in agreement with these traditional cue studies that demonstrate increased reactivity to smoking cues compared to neutral cues in smokers.5,6,13,16–18

The results of this investigation, although promising, should be viewed with caution due to the small sample size. In addition to increases in sample size, incorporation of objective measures (functional–magnetic resonance imaging [fMRI], heart rate/blood pressure) would improve the assessment of reactivity and will aid in the validation of VR-NCRAS. These findings replicate earlier findings and suggest that well designed VR simulations can be utilized to assess craving in nicotine dependent persons. Future research incorporating larger samples, diverse age groups, brain imaging, different smoking use levels (deprived vs. pre-loaded), and drug manipulation will help create VR environments that are robust enough to start treatment trials using VR to augment current treatment procedures. Cue reactivity trials currently are underway for cannabis, alcohol, and cocaine dependent persons. These studies will build upon the success of this trial and will add olfactory cues as well.

In summary, results from our previous trial22 and current data indicate that VR-NCRAS is a viable medium to elicit and assess drug craving and reactions. VR systems incorporating complex cue and social interactions may serve to provide researchers and clinicians new tools for understanding and treating drug abuse in smoking and across other drugs of abuse that have similar conditioned reactions to cues in the environment.

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REFERENCES


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