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Using virtual reality to investigate complex and contextual cue reactivity in nicotine dependent problem drinkers

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ABSTRACT

Alcohol and cigarette smoking frequently co-occur among adults in the U.S., resulting in a myriad of deleterious health outcomes. Cue reactivity has been posited as one factor that precludes individuals from overcoming alcohol and nicotine dependency. While cue reactivity studies have focused on the impact of proximal cues on cue reactivity, much less is known about the unique impact of complex and contextual cues. This pilot study compares nicotine and alcohol cue reactivity among a sample of nicotine dependent, daily drinkers ($N=21$) across neutral, party, and office courtyard virtual reality (VR) contexts embedded with proximal smoking cues to: 1) explore and compare the effects of complex nicotine cues on alcohol cross-cue reactivity between nicotine/alcohol dependent drinkers and nicotine dependent/non-alcohol dependent daily drinkers, and 2) assess the effectiveness of VR for eliciting cue-induced nicotine craving responses using complex nicotine cues. Nicotine dependent/non-alcohol dependent drinkers had significantly lower craving for alcohol in the non-alcohol congruent office courtyard VR scene and there was no difference in the alcohol-congruent party scene when compared to the alcohol dependent group, suggesting that the non-alcohol dependent daily drinking group was more likely to react to contextual cues. Consistent with prior cue reactivity studies, dependent smokers experienced significantly higher craving for nicotine in the VR smoking congruent contexts compared to the neutral contexts; however, nicotine/alcohol dependent participants did not return to baseline craving after exposure to smoking cues. These results suggest substantive differences in the ways that nicotine-dependent, daily alcohol drinkers and nicotine/alcohol dependent drinkers experience craving, whether cross-cue or traditional.

Alcohol consumption and cigarette smoking frequently co-occur with approximately 46.2 million adults in the United States reporting use of both alcohol and tobacco products, and 6.2 million of those reporting both alcohol use disorder and nicotine dependence (Falk, Yi, & Hiller-Sturmhöfel, 2006). The combination of drinking, particularly heavy drinking, and smoking is a major public health concern. Co-morbid alcohol and nicotine dependence has been shown to have a multiplicative impact on health outcomes including higher rates of cancer, pancreatitis, periodontal disease, and cardiovascular disease, and it is estimated that smoking-related health conditions are the leading cause of death in people who have been previously treated for alcohol dependence (Romberger & Grant, 2004). Despite the overwhelming prevalence of nicotine dependence in regular, heavy drinkers and the serious public health implications of co-morbid smoking and drinking behaviors, there is still much to learn about individuals who are both nicotine and alcohol dependent, including a better understanding of the processes that contribute to their continued substance use.

Cue reactivity centers upon the assumption that certain visual, auditory, olfactory, social, and contextual stimuli related to drug or alcohol use may have powerful properties that play an important role in maintaining substance use behaviors and precipitating relapse (Carter & Tiffany, 1999; Tiffany, 1995). It is thought to be based in part on classical conditioning theory (Pavlov, 1927; Tiffany, 1995) and involves conditioned responses, such as craving, triggered by cues related to past drug or alcohol consumption (Childress et al., 1993; O'Brien, Childress, McLellan, & Ehrman, 1993). Cues have been conceptualized on several levels given the complexity with which such cues occur in the real-world. In order to establish clear definitions of cue types we proposed the following classifications:

Proximal cues. Proximal cues are specific objects, such as a package of cigarettes or a bottle of beer, that typically accompany substance

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use. They are referred to as such because of their relative proximity to actual drug or alcohol use (Conklin, 2006). Proximal cues are the most commonly used cue type in traditional cue reactivity studies.

Contextual cues. Contextual cues refer to the physical environment or setting where substance use occurs, such as a bar, party, or drug shoot house. Contextual cues may be further subdivided into places with or without social interactions. An example of a contextual cue with social interaction would be a party setting where people are socializing. An example of a contextual cue without social interactions would be the same party context without people present. Exposure to contextual cues can elicit reactivity without proximal cues present, based on previous paired associations with proximal cues. Thus, the context itself can serve as a stimulus capable of eliciting reactivity (Paris et al., 2010). Because they are difficult to produce using traditional cue exposure methods, contextual cues are not used as often in cue reactivity studies as proximal cues.

Complex cues. Complex cues represent the combination of proximal cues and contextual cues. Complex cues are the closest to real world use environments due to the presentation of proximal cues in the context where use occurs, such as people drinking alcoholic beverages in a bar or smokers congregating outside of a building where an individual typically smokes during breaks. Over time it is assumed that these complex cues, by virtue of their pairing with the unconditioned drug or alcohol stimuli, become conditioned cues capable of eliciting conditioned responses in the form of reactions such as increased craving and autonomic reactivity. Presumably, these cue-specific reactions reflect motivational processes that are responsible for both continued substance use, as well as relapse. Indeed, it has been suggested that the most powerful predictor of continued abstinence is loss of craving (Bordnick & Schmitz, 1998; Smith & Frawley, 1993). While many cue reactivity studies have focused on the impact of proximal cues and, to a lesser extent, complex cues on cue reactivity, much less is known about the unique impact of contextual cues.

Because smoking and drinking behaviors often occur together, cues more directly associated with the activity of one (e.g., smoking) can sometimes serve as an implicit cue for the other (e.g., drinking alcohol), a phenomenon known as cross-cue reactivity (Bobo & Husten, 2001; Drobes, 2002; Erblich, Montgomery, & Bovbjerg, 2009; Gulliver, Kamholz, & Helstrom, 2006). Studies examining smokers in various stages of treatment (pretreatment, during treatment, or posttreatment) have demonstrated both alcohol and smoking cross-cue reactivity (Cooney et al., 2007; Cooney, Cooney, Pilkey, Kranzler, & Oncken, 2003; Drobes, 2002; Gulliver et al., 1995; Rohsenow et al., 1997). Currently, research on cross cue reactivity in non-treatment seeking nicotine and alcohol dependent individuals, as well as individuals who are not alcohol dependent, is lacking. Erblich et al. (2009) reported significantly elevated levels of cross-cue reactivity in a sample of non-treatment seeking nicotine dependent social drinkers, but alcohol dependent individuals were not included for comparison. These studies provide evidence that cross-cue reactivity occurs in individuals who both drink and smoke, but further research is needed to better understand the specific influence of complex cues on cross-cue reactivity within non-treatment seeking and non-alcohol dependent populations. This study intends to enhance understanding of cross-cue reactivity in these populations by exploring differences in alcohol cross-cue reactivity to complex smoking cues between two groups of non-treatment seeking individuals: 1) those that are both nicotine and alcohol dependent, and 2) those who are nicotine dependent non-alcohol dependent daily drinkers.

Limitations of investigating cross-cue reactivity may lie in the methods used in typical cue-reactivity studies. Most studies utilize a similar research methodology in which in vivo proximal cues or pictures of proximal, contextual, or complex cues are presented in a laboratory setting, followed by an assessment of craving. Even when pictures of contextual or complex cues are presented, these cues are artificially isolated from the context in which they would normally be encountered in the real world. For example, even though a participant is looking at a picture of people drinking in a bar, that participant is still very aware of the reality of sitting in a laboratory looking at a picture of people drinking in a bar. The laboratory context in which the picture is presented is incongruent with most substance use contexts. Thus, there is little opportunity to examine the true impact of contextual and complex cues and the ecological validity of findings is limited.

Virtual reality (VR) cue exposure systems have the capacity to provide complex cues through an immersive human–computer interaction that provides active participation within a three dimensional virtual environment. For this reason, VR has the potential to expand cue reactivity methodology by allowing the manipulation of proximal, contextual, and complex cues to provide a degree of ecological validity that in vivo cue presentations and still photographs have yet to achieve. VR has been used to study cue reactivity across a variety of substances and samples (Bordnick et al., 2009, 2004, 2008; Carter, Bordnick, Traylor, Day, & Paris, 2008; Traylor, Bordnick, & Carter, 2008). Results from these studies have repeatedly found that exposure to VR cues elicited significantly greater craving than exposure to VR neutral cues, demonstrating that VR cue exposure was effective in manipulating craving in substance dependent individuals. However, VR has not been yet been used to examine cross-cue reactivity.

This pilot study utilizes VR to both explore the effects of complex nicotine cues on alcohol cross-cue reactivity and assesses whether this study will replicate prior studies, which have identified VR as an effective medium in eliciting typical cue-induced reactivity responses using complex cues. As such, the primary aims of this study are to: 1) compare alcohol cross-cue reactivity between non-treatment seeking samples of nicotine/alcohol dependent drinkers and nicotine dependent/non-alcohol dependent daily drinkers who are exposed only to nicotine (smoking) cues, and 2) replicate nicotine cue reactivity findings from previous VR studies in this sample of nicotine dependent drinkers.

1. Materials and methods

1.1. Participants

Twenty-one non-treatment seeking nicotine dependent participants who consumed alcohol daily were recruited via advertisements in a local weekly free arts and entertainment paper. A total of 51 individuals responded to the advertisements, but 30 people were screened out of the study because they either did not meet the full inclusionary criteria or they answered in the affirmative to questions regarding the exclusionary criteria. Inclusion criteria included meeting the DSM-IV diagnosis of nicotine dependence; consuming an average of two or more drinks per day; smoking an average of ten or more cigarettes per day; being between the ages of 21–65; being in good physical health; and having the ability to wear a VR helmet for 40 min. Exclusion criteria included having a current or past diagnosis of a DSM-IV severe mental illness or current DSM-IV diagnosis of dependence or abuse of any substance other than alcohol and nicotine; being pregnant; having a history of seizures or seizure disorders; fearing closed spaces; having visual problems that prevented viewing of VR environments; seeking or engaging in treatment with any alcohol, smoking, or drug cessation medications, programs, or services in the previous 30 days; participating in any