USING VIRTUAL REALITY TO INVESTIGATE CROSS-CUE REACTIVITY AND ENVIRONMENTAL CUES IN NICOTINE DEPENDENT PROBLEM DRINKERS

by

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(Under the Direction of Patrick S. Bordnick)

ABSTRACT

Traditional cue exposure has been limited by the inability to replicate realistic, complex, contextually based cues in a laboratory or clinic setting, and as a result limited generalization has occurred in the real world. VR cue exposure, which has been repeatedly demonstrated to elicit reactivity in drug- or alcohol-dependent individuals, represents an opportunity to expose participants to environmentally situated, complex, standardized cues without the expense or risks associated with a real-world drug or alcohol use situation. This study examined the effects of VR nicotine cues on nicotine and alcohol reactivity in non-treatment-seeking nicotine dependent problem drinkers. This study had two overarching goals: 1) to determine whether nicotine cues can elicit both nicotine and alcohol reactivity (cross-cue reactivity) in nicotine dependent problem drinkers, and 2) to determine whether the environmental context of cues affects nicotine and alcohol reactivity in this population. The VR cue environments utilized in this study contained visual, auditory, and olfactory nicotine cues such as cigarettes, lighters, other people smoking, coffee, soft drinks, and food, situated within a virtual office building courtyard and a virtual party setting. No overt alcohol cues were presented at any time during VR exposure. Participants were also exposed to 2 identical neutral rooms, containing no nicotine or alcohol

cues. Participants provided subjective ratings within VR of craving for nicotine and alcohol, attention paid to visual and olfactory nicotine and alcohol cues, and thoughts about smoking and drinking after exposure to each virtual room. Overall, participants reported increased reactivity in response to cue rooms vs. neutral rooms for both nicotine and alcohol, and for alcohol in the alcohol-appropriate party setting vs. the non-alcohol appropriate office setting. This study is the first to utilize VR cue environments in an investigation of cross-cue reactivity and environmental influence on polydrug users. In addition, this study contributes to the growing body of literature concerning the potential effects of continuing to smoke after achieving alcohol sobriety, particularly on the probability of relapse.

INDEX WORDS: Alcohol addiction, Nicotine dependence, Virtual reality, Cross-cue reactivity, Cue exposure, Cue reactivity

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DEDICATION

This dissertation is dedicated to my partner, who has tirelessly supported me throughout this degree program and all other aspects of our life together. Thank you, Rob, for your unwavering love and patience.

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CHAPTER ONE

INTRODUCTION

Alcohol addiction is a global problem. The World Health Organization (WHO, 2004) estimates that alcohol causes 1.8 million deaths per year worldwide, and is responsible for 9.2% of the total disease burden in the developed world. Worldwide, 76.3 million people have diagnosable alcohol disorders (WHO, 2004), and alcohol dependence is the fourth leading cause of disability in the world (Garbutt et al., 2005). In 2001-2002, 8.46% (17.6 million) of the adult population of the United States met criteria for alcohol abuse or dependence, up from 7.41% (13.8 million) a decade earlier (Grant et al., 2006). From 1991-1992 to 2001-2002, the rate of alcohol abuse in the US increased from 3.03% to 4.65%; during the same time period, the rate of alcohol dependence decreased from 4.38% to 3.81% (Grant et al., 2006). As of 1998 (most recent data available), alcohol abuse and dependence cost Americans $184.6 billion annually (Grant et al., 2006).

Alcohol use has been linked to increased risk of cancer, neuropsychiatric conditions, cardiovascular diseases, and digestive diseases (Rehm, Gmel, Sempos, & Trevisan, 2002), with an irregular heavy drinking pattern proving the most damaging (Rehm et al., 2002). In the year 2000, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2005), liver cirrhosis was the 12th leading cause of death in the United States, and the fourth leading cause of death in people age 45-54. Chronic alcohol abuse can result in permanent changes to the brain's reward systems and may cause shrinkage (a sign of brain damage) and problems with learning and memory (NIAAA, 2004a). Some studies have found that women are significantly

more susceptible to the damaging effects of chronic alcohol abuse than are men; others have not found this to be the case, but more research is needed on female alcoholics (NIAAA, 2004a). Women who drink alcohol during pregnancy may give birth to children with physical, learning, and behavioral problems, the most serious of which is fetal alcohol syndrome (NIAAA, 2004a). Fetal alcohol syndrome is the leading preventable birth defect in the U.S. (NIAAA, 2004a).

Until the early 1990s, nearly 90% of all alcoholics in treatment were regular smokers (Bobo & Husten, 2001). Currently it is estimated that approximately 80% of dependent drinkers are also smokers (Romberger & Grant, 2004). The combination of heavy drinking and smoking contributes to higher rates of cancer, pancreatitis, periodontal disease, and cardiovascular disease (Romberger & Grant, 2004), and some studies have found that smokers with alcoholic liver disease develop scarring of the liver more quickly than their non-smoker counterparts (NIAAA, 2005). In fact, 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). Alcoholism and smoking are both believed to have heritable components, and studies have demonstrated that genetic predisposition for one heightens the risk of the other as well (Drobes, 2002). Smoking may be higher in alcoholic individuals with concurrent mood disorders, as nicotine may be used as a mood regulator (Romberger & Grant, 2004; Trudeau, Isenhart, & Silversmith, 1995). Repeated pairing of drinking and smoking behaviors can lead to the formation of an association between the two, suggesting that continuation of one behavior (e.g., smoking) while attempting to abstain from another (e.g., alcohol) may trigger craving for both substances, thereby potentially increasing the risk of relapse in drinking behaviors (Bobo & Husten, 2001; Clements, Glautier, Stolerman, White, & Taylor, 1996; Conklin & Tiffany, 2002; Romberger & Grant, 2004).

Despite the overwhelming prevalence of nicotine addiction in problem drinkers, not enough is known about this population, which may differ from nonsmoking drinkers or smokers who do not abuse alcohol in important ways. For example, there is a gap in the literature concerning the ways that nicotine and alcohol addictions interact, and how exposure to each may stimulate craving for the other (cross-cue reactivity)—a crucial factor in attaining and maintaining abstinence from either substance. In addition, more research is needed into the ways that environmental factors (location, social interaction, mood, time of day, sights, smells, sounds, etc.) affect craving, and whether and how environmental context should be addressed in the development of more effective treatments of alcohol and nicotine addiction. Finally, most cue reactivity research to date has been hindered by the constraints of the research environment, wherein simple cues are often presented in an artificial context. This study, which examines nicotine dependent problem drinkers' responses to nicotine cues within complex and realistic virtual reality cue environments, has been developed in response to these knowledge gaps.

Theoretical Framework

This project was conceptually guided by a cue reactivity theoretical orientation. Cue reactivity is grounded in the principles of classical and operant conditioning (Pavlov, 1960, 1966; B. F. Skinner, 1969, 1974), which are discussed in detail in Chapter 2. Briefly, a cue reactivity approach involves exposing individuals to specific stimuli, including objects (e.g., alcohol, cigarettes, coffee) or environments (e.g., party, bar), which have been repeatedly paired with a particular behavior (e.g., smoking, drinking) or consequence (e.g., stress reduction, feeling intoxicated). Exposure to these stimuli is expected to elicit a reaction (e.g., craving, physiological responses, mood changes) based upon a previously established association between the stimuli and specific behaviors or consequences. Traditional cue exposure methods include the use of

photographs, videos, and/or actual paraphernalia as eliciting stimuli, as well as real-life exposure to cue environments (e.g., an airplane for treatment of fear of flying). These real-life exposures, however, are inherently limited by logistical and safety considerations, as many cue environments are either too difficult, inconvenient, and/or expensive to access (e.g., the airplane in the previous example, a party, a bar) or not safe for therapists or researchers to work (e.g., a drug use environment). This project employs the use of virtual reality environments in an attempt to expand and improve upon traditional cue exposure techniques by allowing for the creation of much more complex, immersive, realistic environments that incorporate a range of stimuli and more faithfully replicate actual smoking or drinking scenarios. In addition, this study applies the principles of cue reactivity in an examination of the ways in which substances can become triggers (cues) for other substances through repeated pairings (here, nicotine and alcohol).

Virtual Reality Cue Reactivity

Virtual reality has been used to construct realistic, convenient, and safe cue environments for assessment and treatment of phobias, such as fear of flying or fear of public speaking, and for addiction research. Phobias such as fear of flying, public speaking, and spiders have been successfully treated using VR cue environments (Cardenas, Munoz, Gonzalez, & Uribarren, 2006; Côté & Bouchard, 2005; Davidson & Smith, 2003; Garcia-Palacios, Hoffman, Carlin, Furness, & Botella, 2002; Krijn, Emmelkamp, Olafsson, & Biemond, 2004; Mühlberger, Weik, Pauli, & Wiedemann, 2006; Rothbaum et al., 2006; Thacker, 2003), which allow for repeated exposure to anxiety-provoking situations in a safe and controlled environment. This ability to realistically replicate environments which may not be easily accessed in a clinic or lab setting (e.g., airplane or large audience) has also proven useful in addiction research.

VR technology has also been employed in the development of drug- and alcohol-related virtual environments (e.g., party setting with people drinking alcohol, smoking cigarettes, and/or using marijuana), which have been used for studies of cue exposure and reactivity (Bordnick, Graap, Copp, Brooks et al., 2004; Bordnick, Graap, Copp, Brooks, & Ferrer, 2005; Bordnick et al., in review; Glanz, Rizzo, & Graap, 2003; Kuntze et al., 2001; Thacker, 2003). VR allows for the safe, reliable, standardized presentation of complex environments, incorporating sight, sound, smell, and realistic social interaction so as to create a sense of immersion (Bordnick, Graap, Copp, Brooks et al., 2004; Bordnick, Graap, Copp, Brooks, & Ferrer, 2005; Bordnick, Traylor, Graap, Copp, & Brooks, 2005; Cardenas et al., 2006; Davidson & Smith, 2003; Garcia-Palacios et al., 2002; Kuntze et al., 2001; Rothbaum et al., 2006; Thacker, 2003). Using virtual reality technology to embed alcohol and drug cues in more naturalistic settings will potentially increase the efficacy of cue-based coping skills training by orienting participants toward cues that more specifically replicate real-world drinking or smoking environments, thereby potentially exporting extinction effects outside of the laboratory or clinic environment (Bordnick, Graap, Copp, Brooks et al., 2004; Bordnick, Graap et al., 2005; Bordnick et al., in review). Please see Chapter 2 for a more comprehensive discussion of cue reactivity and its traditional limitations that may be addressed via virtual reality cue environments.

Purpose of the Study

This study examined the effects of VR nicotine cues on craving for nicotine and alcohol in 21 non-treatment-seeking nicotine dependent drinkers who met diagnostic criteria for nicotine and alcohol abuse or dependence. This study had two overarching goals: 1) to determine whether and to what degree nicotine cues stimulate craving for both nicotine and alcohol (cross-cue reactivity), and 2) to determine whether and to what degree the environmental context of these

cues affects levels of subjective craving for both nicotine and alcohol. While alcohol- and nicotine-focused VR cue exposure has been investigated several times in the past, this is the first known study to utilize VR cue environments in an investigation of cross-cue reactivity. In addition, this study contributes to the growing body of literature concerning the potential effects of continuing to smoke after achieving alcohol sobriety, particularly on the probability of relapse.

Significance of the Study

This study presents important potential implications for both research and practice by social workers and other helping professionals. Research implications include the fact that this is the first known study to employ the use of VR in examination of cross-cue reactivity. Further research into polysubstance use is necessary, and VR may be a tool for facilitation and standardization of such research. This study was also intended to contribute to the growing body of literature on the importance of context to cue reactivity, including craving. Practice implications of this latter point include contributing to development of best practices in treatment of alcohol addiction (as well as other substances and combinations thereof), as greater understanding of the role of environmental context in the development of coping skills and extinction of reactivity may help to develop more effective treatments used by social workers and other helping professionals. Specifically, this study was intended to help address whether and how nicotine cues affect alcohol craving, and hence whether and how recovery from alcohol addiction may be threatened by ongoing exposure to nicotine cues—including, of course, continuing to smoke.

Definition of Terms

Several significant concepts used in this project, including alcohol abuse and dependence, cue reactivity, craving, and virtual reality, are defined below.

DSM-IV Diagnostic Criteria for Alcohol Use Disorders

The fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV, American Psychiatric Association, 1994) identifies two alcohol use disorders, alcohol abuse and alcohol dependence, both of which are characterized as maladaptive patterns of alcohol use that leads to significant distress or impairment. In order to qualify for inclusion in this study, participants had to meet criteria for one of these diagnoses. Diagnostic criteria are drawn from the *DSM-IV* (APA, 1994) instead of the *DSM-IV-TR* (APA, 2000) because the diagnostic mental health screening instrument used in the study (see Chapter 3) is based on the *DSM-IV*. There are no substantial differences between the 1994 and 2000 APA criteria.

Alcohol abuse. A diagnosis of alcohol abuse requires the presence of one or more of the following criteria within a 12-month period: repeatedly failing to meet responsibilities at work, school, or home because of drinking; repeatedly drinking in situations that are physically hazardous; alcohol-related legal problems; and continuing to drink despite interpersonal consequences (APA, 1994).

Alcohol dependence. A diagnosis of alcohol dependence requires the presence of three or more of the following criteria within a 12-month period: tolerance; withdrawal; drinking more or for a longer period of time than intended; unsuccessfully attempting to reduce or stop drinking; spending a substantial amount of time obtaining, using, or recovering from alcohol; discontinuing or greatly reducing activities not associated with drinking; and continuing to drink despite psychological or physical consequences (APA, 1994).

Cue Reactivity

Cues, also known as triggers, are defined as objects, situations, social interactions, or environments that elicit a particular reaction due to repeated pairings of specific stimuli with specific behaviors and rewards (Conklin, 2006; Drummond, 2000; Pavlov, 1960; B. F. Skinner, 1969). In this study, the effect of repeated pairing of smoking with alcohol consumption was examined. The formation of these responses is known as conditioning, which is discussed in depth in Chapter 2. Cross-cue reactivity refers to the process by which behaviors (responses) may come to also function as cues in and of themselves; for example, the consumption of alcohol by someone who smokes when they drink can function as both a response to alcohol-related cues and a trigger for nicotine craving (Clements et al., 1996).

Cue reactivity may be exhibited physiologically, such as elevated heart rate, sweating, or salivation (Clements et al., 1996; Johnson, Chen, Schmitz, Bordnick, & Shafer, 1998; Rohsenow et al., 1994); behaviorally, such as initiation of drug use (Le Foll & Goldberg, 2005; Monti & Rohsenow, 1999); or subjectively, such as craving (Bordnick, Graap et al., 2005; Conklin, 2006; Cutler, 2005; Johnson et al., 1998; Schulze & Jones, 2000).

Craving

Craving is one of the most commonly studied aspects of reactivity. Despite decades of prolific research in the field of addiction, scientists have yet to agree upon a functionally operationalized definition of craving (Anton, 1999; Cutler, 2005; Drobes & Thomas, 1999; Tiffany, Carter, & Singleton, 2000). Jellinek and colleagues (1955) are generally credited with bringing the concept of craving to the forefront of alcohol dependence, naming it as the primary cause of addiction, excessive use, and relapse. More than 50 years later, however, the nature,

cause, and effect of craving remain fodder for scientific debate. Kozlowski and Wilkinson (1987) have eloquently summarized the difficulty at hand:

> Scientists sometimes spot a perfectly successful word in lively use outside the laboratory, grab it by the throat, drag it back to the laboratory, and put it on display as a 'technical term'. The word may need special training to behave itself in the halls of science and in the minds of scientists (who may have to unlearn the prior uses of the word). 'Craving' has continued to live in the common language, while being asked from time to time to do service in formal research on drug use. (p. 31)

While the specific characteristics and role of craving are still not fully understood, a number of theoretical models of craving have been proposed.

Some models of craving emphasize the behavioral aspects (grounded in the principles of classical and operant conditioning), while others focus more on the cognitive processes associated with the use of a substance (here, alcohol). Cue reactivity (discussed in depth in Chapter 2) is perhaps the most widely used behavioral methodology in research on craving and addiction. Within the cue reactivity model, drug- or alcohol-dependent participants are exposed to conditioned stimuli (paraphernalia or other cues associated with their substance of choice) via imaginal, video, audio, and in vivo methods, and reactivity to these cues is assessed via physiological, behavioral, and cognitive measures (Conklin, 2006; Conklin & Tiffany, 2002; Drummond, 2000; Litt & Cooney, 1999; Tiffany et al., 2000).

The behavioral aspects of craving are easier to objectively measure with experimental methods than are the cognitive aspects of craving, though the latter may be approximated via subjective self-report. A more detailed discussion of methods of measuring reactivity is presented in Chapter 2.

Virtual Reality

Virtual reality (VR) incorporates the use of computer graphics, film clips, sounds, smells, and/or sensations (e.g., vibrating platform) to create an immersive experience (Bordnick, Graap, Copp, Brooks et al., 2004; Rothbaum, Hodges, Ready, Graap, & Alarcon, 2001). The VR environments used in this study integrated visual, audio, and olfactory stimuli to simulate an outdoor courtyard and interior lobby of an office building, a party, and an art gallery. A head-mounted display equipped with a tracker was used to provide visual stimuli, and headphones were used to provide audio stimuli. When participants were immersed in the VR environments, they were able to look in any direction within the environment (up, down, and 360º laterally), and the tracker ensured that both visual and audio stimuli were congruent with the participant's movements.

Synopsis of Dissertation

In Chapter 2, a review of the literature of theoretical models of alcohol abuse, treatments of alcohol abuse, and the use of virtual reality in clinical research is presented. Chapter 3 outlines the study methods, assumptions, and limitations. In Chapter 4, the research findings are presented, and Chapter 5 contains a discussion of the implications of the findings and suggestions for future research.

CHAPTER TWO

REVIEW OF THE LITERATURE

In this chapter, a review of the literature concerning selected theoretical models of alcohol abuse, selected treatments of alcohol abuse, and the use of virtual reality in clinical research is presented.

Selected Theoretical Models of Alcohol Abuse

There are a number of theoretical models employed by alcohol abuse researchers. Cue reactivity, which is undergirded by classical and operant conditioning, forms the theoretical bedrock for the current study, are discussed below.

Cue Reactivity

Cue reactivity involves exposing an individual to objects or situations (cues) that are associated with a specific behavior in order to elicit a response (reactivity). Cue exposure, which may be used to reduce or extinguish reactivity to a particular cue through repeated exposure without the expected subsequent reinforcement, is used in addiction research. For example, an individual who regularly drinks beer may come to associate beer with a pleasant sensation of intoxication (or with a reduction of the unpleasant sensation of withdrawal). For this individual, the sight of beer may therefore elicit reactivity in the form of craving, thoughts about drinking, and/or physiological responses such as increased heart rate or sweating. If this individual wished to reduce or eliminate this reactivity, cue exposure methodology may be employed. In theory, if the individual were repeatedly exposed to beer without subsequently experiencing the pleasant effects of intoxication (or relief from the unpleasant effects of withdrawal), the association

between the object (beer) and the positive effects of drinking should diminish (classical conditioning), and the operant response should decay due to repeated lack of reinforcement (operant conditioning). In practice, however, this is not always the case, as individuals often experience spontaneous recovery (recurrence of the original conditioned response at full intensity) when they reenter the real world, due to the failure of the new conditioning to generalize to situations outside the treatment environment. A number of researchers have lamented traditional laboratory- or clinic-based cue exposure's inherent artificiality, and its inability to replicate complex environmental factors so as to more closely approximate the real world (Bordnick, Graap et al., 2005; Bordnick et al., in review; Conklin, 2006; Drummond, 2000; Havermans & Jansen, 2003; Le Foll & Goldberg, 2005).

Below is a discussion of classical and operant conditioning in relation to cue exposure and cue reactivity, specific and environmental cues related to drug and alcohol use, methods for measuring reactivity to cue exposure, and the use of virtual reality in cue exposure.

Classical Conditioning

Ivan Petrovich Pavlov (1849-1936) was a physiologist who was interested in studying behavior from a physiological perspective, as opposed to the psychological approach that was common in his day (1903/1966). In his research, Pavlov built upon historical scholarship of reflexes as the impetus for basic motor activities, categorizing reflexes as either positive (excitatory) or negative (inhibitory) (1927/1960). Pavlov chose salivation in dogs as the primary reflex for his studies, believing that this reflex provided tangible evidence of higher brain function as the organism reacted to external stimuli. Salivation was elicited in two ways: with food (alimentary reflex), and with an acid solution introduced to the mouth (defense reflex). Both of these are examples of what Pavlov called *unconditioned reflexes* (inborn or instinctive

reflexive reaction to direct stimuli; here, salivation in response to presentation of food or introduction of an acid solution to the mouth). Additional examples of unconditioned reflexes are an increased sense of well-being experienced by a nicotine dependent smoker after smoking a cigarette, or a sensation of intoxication after drinking alcohol.

In his research, Pavlov was interested in studying *conditioned reflexes* (reflexive reaction formed in response to environmental conditions rather than to a primary stimulus; here, salivation in response to a particular sound, sight, tactile sensation, or odor which has repeatedly preceded presentation of food or acid). Conditioned reflexes may be developed by consistently presenting a particular stimulus immediately prior to presenting an unconditioned stimulus (e.g., food or acid). Over time, the organism will begin to react to the conditioned stimulus (e.g., a particular sound or sensation) as they would to the unconditioned stimulus (e.g., when the sound of a horn has become a conditioned stimulus for presentation of food, the organism will salivate after hearing the sound even if the food has not yet been presented) (1927/1960). An alcohol dependent individual may develop a conditioned response, such as craving, in response to stimuli that have repeatedly been paired with drinking behavior, such as the sight of a particular brand of beer or the approach of the end of the work day. For people who regularly smoke when they drink, the sight or smell of a cigarette may become a conditioned stimulus for alcohol craving.

When a conditioned reflex is newly developed, it is generalized to the environment in which it was acquired, and simply being in that environment can elicit the conditioned response. Over time, however, the reflex becomes increasingly focused on the specific conditioned stimulus, and extraneous environmental stimuli are filtered out. Conditioned reflexes may be suppressed via external inhibition or internal inhibition. External inhibition is the overriding effect of additional, stronger stimuli in the environment. Pavlov (1927/1960) used as an example

the cessation of conditioned responses in a dog that has to urinate, and the immediate resumption of these responses after doing so. External inhibition is easier and faster to establish than internal inhibition, also known as *extinction*. Extinction is achieved through many unreinforced exposures to conditioned stimuli (Pavlov, 1927/1960). The extinction process can be affected by the strength of the reflex, the duration of the reflex in the life of the organism, changes in the environment, or simply the passage of time. The magnitude of the reflex corresponds to the magnitude of the extinction process necessary to inhibit the conditioned response (Pavlov, 1927/1960). One of the most significant difficulties with maintenance of experimental extinction is that extinction quickly reverses if a conditioned stimulus is again reinforced even once. A problem drinker who is trying to maintain abstinence might continue to spend time in drinking environments, such as a favorite bar. Over time, if the individual repeatedly goes to the bar but refrains from drinking alcohol, she/he may extinguish the conditioned response (experiencing craving) to being in the bar. According to the tenets of classical conditioning, however, if the individual drinks alcohol in that environment again—even once—she/he will experience an immediate reversal of the extinction (resumption of craving at full intensity). In addition, much as newly acquired conditioned reflexes are generalized to the environment, so too is newly acquired extinction of a conditioned reflex. Particularly when extinction is still relatively fresh, the conditioned response may be reinitiated in response to any change in the environment—including the organism's own internal state (Pavlov, 1927/1960).

Operant Conditioning

Burrhus Frederic Skinner (1904-1990) was a psychologist who, like Pavlov, objected to psychological, mentalistic, and conceptual theories, because none of these produced results that could be observed in the same way that the behavior they purport to explain could be observed

(1950/1982a). Unlike Pavlov, however, Skinner (1969) also objected to behavioral theories of simple cause and effect because he felt that they did not incorporate the entire cycle of human behavior. The crux of Skinner's theoretical argument was that behavior is not always controlled by overt stimuli; rather, he claimed that the more complex interactions between three "contingencies of reinforcement" (the situation where a response occurs, the response itself, and any reinforcing consequences) are the impetus for behavior (1969). Skinner (1982b) claimed that behavior is based upon the sum of an individual's prior experiences, which includes knowledge gained from observing and hearing about other people's experiences.

Skinner expanded further upon Pavlov's classical conditioning model by adding the concept of an *operant response*, which he distinguished from a reflex. Operant responses are emitted by an organism because of the interaction between the contingencies of reinforcement, not merely as a reaction to some immediate stimulus (1969; 1974). Operant responses are formed in response to reinforcement, and the experience of reinforcement increases the chances of the organism repeating the behavior. For example, an alcohol dependent individual who is experiencing unpleasant withdrawal symptoms may consume alcohol because she/he has learned that doing so will cause the withdrawal symptoms to lessen or cease. Drinking alcohol is the operant response which has been reinforced by prior positive outcomes (relief from withdrawal symptoms). Multiple contingencies may work in concert to strengthen a single behavior. In his famous article "'Superstition' in the Pigeon" (1948/1982c), Skinner described the formation of operant behaviors under a consistent reinforcement schedule. In eight separate experiments, he placed a hungry pigeon into a box with an automatic feeder programmed to dispense food at regular 15-second intervals, irrespective of any behavior emitted by the pigeon. By random chance, some behavior displayed by the pigeon would be immediately followed by the

presentation of food. As a result, in six of the eight cases, the pigeons began to repeat that specific behavior with greater frequency. As the behavior was repeatedly reinforced (through the regular presentation of food, which in actuality would have continued even had the pigeons done nothing at all), the pigeons continued to increase the frequency of the behavior, and in some cases the behavior became progressively more elaborate and intense. An alcohol dependent individual who has developed an operant response of drinking when confronted with stressful situations will repeat the behavior when exposed to stress if drinking has caused a reduction of stress in the past. Similarly, a smoker who has experienced a reduction of social anxiety after smoking will exhibit this operant response in future uncomfortable social situations.

As in the classical conditioning model, when response/reinforcement relationships are first established, responses are more generalized to a wide range of similar stimuli. As conditioning progresses, the organism becomes more discriminating and ultimately will respond only to very specific stimuli (1938; 1974). The process of discrimination is somewhat different in operant conditioning than in classical conditioning, however, as Skinner (1974) believed that straightforward behavioral contingencies (rather than mental processes, such as the recognition of signaling stimuli) determine the more specialized response. Like Pavlov, Skinner (1950/1982a) found that extinction is linked to environment; therefore, extinction in the original environment is most powerful, and transfer from the extinction environment to a different environment may reinitiate behavior. In addition, when an organism is returned to the extinction environment, “spontaneous recovery,” where the organism resumes the extinguished behavior for a brief time, is often observed (1950/1982a). This is often observed in addiction treatment, when patients resume drug or alcohol use after leaving treatment, despite having successfully

extinguished operant responses to drug or alcohol stimuli within the treatment environment, generally via a cue reactivity protocol.

Cue Reactivity and Addiction Research

Cue reactivity methodology is commonly used in addiction research. Below is a discussion of specific cues related to drug and alcohol use, specific cues vs. environmental context, and physiological, behavioral, and subjective methods for measuring reactivity to cues.

Cues Related to Drug and Alcohol Use

Cue reactivity methodology in addiction research centers upon the assumption that individuals come to associate certain objects, sounds, smells, moods, interpersonal interactions, and environmental contexts with drug or alcohol use. Encounters with these objects or circumstances therefore trigger an urge to use (craving) due to prior pleasant experiences subsequent to using. Figure 1 depicts a simple model of alcohol cue reactivity.

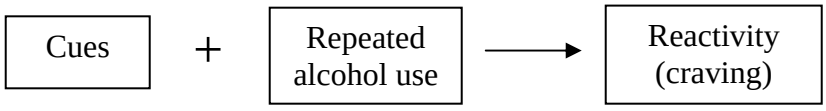


Figure 1. Simple model of alcohol cue reactivity.

In classical conditioning terms, conditioned stimuli (e.g., drugs or alcohol), through repeated pairings, become associated with unconditioned stimuli (e.g., a bar or cigarette pack). The conditioned stimuli then elicit the same reaction as the unconditioned stimuli (e.g., increased heart rate or craving). In operant conditioning terms, the pleasant experiences that follow drug or alcohol use reinforce future use, thereby establishing use as an operant behavior. An individual uses drugs or alcohol again because s/he hopes to replicate the pleasant experiences of prior use.

In addition, drug or alcohol use is reinforced by the negative consequences of not using, including withdrawal symptoms and craving.

Cues that are common to a range of addictions include the substance itself, paraphernalia used in consumption of the substance (e.g., crack pipe or heroin works), seeing the substance, smelling the substance, seeing others use the substance, the using environment, and mood states such as anxiety or depression (which many drugs of abuse can alleviate, at least in the short term). Cues specific to alcohol could include beer bottles or cans, liquor bottles, liquor stores, alcohol advertisements, cigarettes, bars, clubs, restaurants, social gatherings, televised sports, live sports, being at work, being at home, feeling stressed or anxious, feeling angry, and so on (Bordnick et al., in review; Litt & Cooney, 1999; Monti & Rohsenow, 1999; Schulze & Jones, 2000). Cues specific to cigarette smoking could include cigarettes, cigarette packaging, lighters, ash trays, cigarette advertisements, no smoking signs, anti-smoking public service announcements, coffee, alcohol, convenience stores, gas stations, entrances to buildings, social gatherings, bars, clubs, restaurants, being at home, being at work, feeling stressed or anxious, and so on (Bordnick, Graap, Copp, Logue et al., 2004; Bordnick, Graap et al., 2005; Colby et al., 2004; Conklin, 2006).

Some substance-specific cues may also elicit craving for a different substance in polydrug users. For example, many people cite alcohol as a strong factor in nicotine craving; the behaviors of drinking and smoking have been performed concurrently so many times that each has become a conditioned stimulus for the other (Bobo & Husten, 2001; Bowman & Walsh, 2003; Field, Mogg, & Bradley, 2005; Kohn, Tsoh, & Weisner, 2003; Lemon, Friedmann, & Stein, 2003; Romberger & Grant, 2004). Individuals who repeatedly pair drinking and smoking behaviors may develop cross-cue reactivity, wherein exposure to alcohol or alcohol-related

stimuli may elicit craving for nicotine (and vice versa). Figure 2 depicts a model of cross-cue reactivity between alcohol- and cigarette-related stimuli.

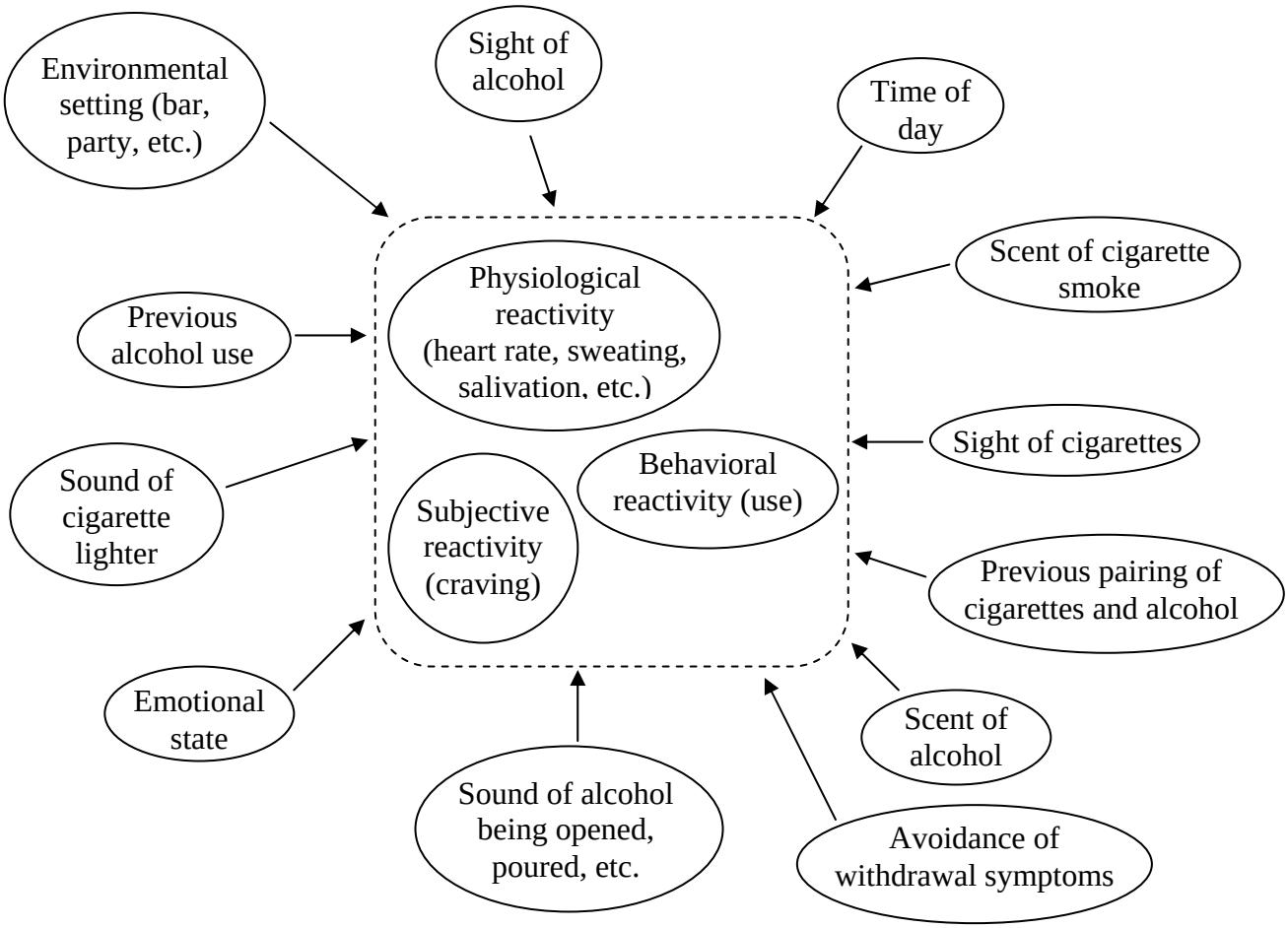


Figure 2. More complex model of cross-cue reactivity (alcohol and cigarettes).

As shown in Figure 2, an individual who has repeatedly paired drinking and smoking behaviors may experience reactivity to a wide range of stimuli, including specific cues (sight of cigarettes or alcohol, scent of cigarettes or alcohol, cigarette lighter) and environmental context (bar, party,

time of day). This reactivity may be physiological (increased heart rate, sweating), subjective (craving for cigarettes or alcohol), and/or behavioral (using cigarettes and/or alcohol). Furthermore, the repeated pairing of drinking and smoking behaviors may lead this individual to experience an increase in craving for alcohol after seeing, smelling, or smoking a cigarette. For recovering alcoholics who continue to smoke, this cross-cue reactivity can present difficulties (Bobo & Husten, 2001; Bowman & Walsh, 2003; Field et al., 2005; Romberger & Grant, 2004). Avoiding explicit alcohol cues may not be enough to prevent a relapse; they may also need to avoid explicit nicotine cues, as well as environmental contexts relevant to either alcohol or nicotine. Further complicating matters, they might not be aware of the presence of cross-cue reactivity, and therefore not realize the danger inherent in a particular situation that is identified with smoking and not drinking. In fact, the relative importance of environmental context may even increase after addicts have quit, since most aspiring quitters remove explicit cues such as the substance(s) and related paraphernalia from their immediate surroundings (Conklin, 2006). This phenomenon further suggests the importance of context in cue exposure treatment, and is discussed further below.

Both classical and operant conditioning models recognize the tendency of behavioral responses to generalize initially to a broad range of stimuli, and both incorporate the concept of extinction (achieved by repeatedly refraining from reinforcing behavior that had previously been associated/reinforced with a particular, often pleasant, experience). Establishing extinction via cue exposure for drug or alcohol use is a difficult prospect, because humans are complex beings operating under complex and sometimes conflicting contingencies of reinforcement in a complex environment. Skinner (1974) believed that mentalistic, unobservable perceptions can distract

from the specific steps one must take in order to change behavior. Specific reinforcements for specific behaviors must be removed if change is to be achieved.

Specific Cues and Environmental Context

In a review of craving literature, Drummond (2000) has identified four categories of cues utilized in cue-based research: exteroceptive (visual, olfactory, tactile); interoceptive (cognitive and mood state); temporal (time between cue and use, or time of day); and cue relationships (interaction of different cues in context). Traditional laboratory-based cue exposure has focused on the former two categories (exteroceptive and interoceptive), which are more proximal cues, rather than the latter two (temporal and cue relationships), which are more distal environmental cues (Conklin, 2006). This is largely due to the inherent difficulties of conjuring complex environmental contexts in a laboratory or treatment setting. As has been discussed above, however, environmental context can be a powerful determinant, dictating whether and to what extent an individual may experience reactivity to drug- or alcohol-related stimuli. For example, alcohol cues may be much more powerful in the evening than in the morning, or in a bar than in a laboratory (Drummond, 2000). Le Foll and Goldberg (2005) reviewed both animal (self-administration of nicotine and conditioned place-preference) and human research concerning the reinforcing influence of environmental context upon nicotine use, and found that environmental context, like specific cues, become associated with craving and use over repeated exposures. Bobo and Husten's (2001) review of smoking and drinking found that the two behaviors are mutually reinforcing, and that sociocultural influences tend to strengthen this association.

Given the importance of environmental context on drug craving and use, it follows that traditional cue exposure methodology should be expanded to include distal as well as proximal cues. Conklin (2006) has completed several preliminary studies exploring different ways in

which both levels of smoking cues could be made more realistic, comprehensive, and personalized within a laboratory environment. Participants were presented with photographs of smoking environments, which in one study were generic and in another were taken by the participants of their own smoking contexts, and found that the personalized distal cues were more effective than generic ones, and equally as effective as proximal cues, in terms of eliciting craving for alcohol (Conklin, 2006). Additional research is being conducted on the use of VR environments to increase effectiveness of cues and cue environments, and is discussed below.

Measuring Reactivity

Cue reactivity is typically assessed via physiological (blood pressure, heart rate, skin conductance, salivation), behavioral (drug seeking or use), or subjective (craving, mood, attention to cues) measures (Conklin, 2006; Tiffany et al., 2000). All three types of reactivity have been associated with drug use and relapse, as discussed below.

Physiological measures of reactivity. Researchers have found that blood pressure, heart rate, and skin conductance demonstrate reactions to drug- or alcohol-related cues as compared to neutral stimuli (Clements et al., 1996; Johnson et al., 1998). Salivation, generally measured via pre- and post-exposure weight of cotton dental rolls, is sometimes used as an additional physiological measure. Research has demonstrated that salivation increases in response to exposure to drug-related cue exposure (Colby et al., 2004; Cooney, Cooney, Pilkey, Kranzler, & Oncken, 2003; Rohsenow et al., 1994).

Behavioral measures of reactivity. Some studies have determined that drug use is often preceded by exposure to drug-related stimuli, including specific cues and environmental contexts (Le Foll & Goldberg, 2005; Monti & Rohsenow, 1999), and that higher levels of reactivity may correspond to higher levels of subsequent use (Monti & Rohsenow, 1999; Rohsenow et al.,

1994). Le Foll & Goldberg (2005) found that nicotine is self-administered at a higher level after exposure, as the drug itself comes to function as the reinforcement to the use response. Behavioral responses to drug- and alcohol-related cue exposure represent a potential risk of relapse for users in treatment.

Subjective measures of reactivity. Craving is the most widely studied subjective measure of cue reactivity, and a great many studies have demonstrated that craving increases in response to exposure to drug or alcohol cues (Bordnick, Graap et al., 2005; Bordnick et al., in review; Conklin, 2006; Cooney et al., 2003; Cutler, 2005; Field et al., 2005; Hutchison et al., 2001; Johnson et al., 1998; Rohsenow et al., 1994; Schulze & Jones, 2000; Tiffany et al., 2000). Researchers have also examined the relationship between drug or alcohol use and mood, and have suggested that people use in order to alleviate stress or other negative mood states such as depression, loneliness, or boredom (Bobo & Husten, 2001; Cutler, 2005). Some researchers have found evidence that exposure to drug or alcohol cues increases the amount of attention paid to subsequent drug or alcohol cues as compared to neutral cues (Field et al., 2005; Rohsenow et al., 1994).

Regardless of the specific method used, it is important to measure reactivity because it is one way to evaluate treatment efficacy. Different treatment methodologies target different types of reactivity, but all aim to alter the relationship between cues and responses.

Selected Treatments of Alcohol Abuse

Below is a discussion of factors contributing to alcohol abuse and dependence, prominent pharmacological and psychosocial treatment methodologies, and concurrent interventions for smoking and alcohol abuse.

Contributing Factors

Genetic, psychosocial, and environmental factors contribute to alcohol abuse and dependence (Kiefer & Mann, 2005; Pettinati & Rabinowitz, 2005). Research has shown that genetic factors influence both the subjective effects of alcohol (intoxication, sedation, and degree of pleasantness experienced) and susceptibility to developing alcoholism (NIAAA, 2004b). Some studies have estimated that alcoholism has a heritability rate of 50-60% (Heilig & Egli, 2006; NIAAA, 2000). Many researchers and practitioners subscribe to the disease model of alcoholism, wherein alcohol addiction is compared to other chronic diseases such as hypertension or diabetes (Garbutt et al., 2005; Heilig & Egli, 2006; Pettinati & Rabinowitz, 2005).

Female gender, marriage, and education are correlated with positive results in alcoholism treatment (Dawson et al., 2006; Moos & Moos, 2004), while substance-using friends, degree of dependence, level of consumption, early onset alcohol dependence, comorbid drug use, and comorbid psychiatric disorders contribute to poor treatment outcome (Dawson et al., 2006; Heilig & Egli, 2006). High levels of craving, the mistaken assumption that one can resume controlled drinking after an extended period of abstinence, high cue reactivity, and negative affect have all been specifically implicated in relapse (Heilig & Egli, 2006; Monti & Rohsenow, 1999).

Short-term and long-term treatment outcomes may vary, and there is some evidence that short-term outcomes (less than six months) are more heavily dependent on personal factors while long-term outcomes (more than six months) are more strongly linked to the treatment itself (Berglund, 2005). Hence, short-term success may not necessarily predict long-term success, as they may be based upon different mechanisms (Berglund, 2005).

Prominent Treatment Methodologies

Both pharmacological and psychosocial methods are used in treating alcohol addiction, though the latter approach remains far more prevalent than the former. Recently, however, an increasing number of studies are examining potential additive effects of combining the two approaches. Below is a discussion of some of the most commonly used pharmacological and psychosocial treatments for alcohol abuse and dependence.

Pharmacological Interventions

Treatment of alcoholism has long included the incorporation of a pharmacological component, albeit on a relatively limited scale. The goal of pharmacological intervention is to biologically disrupt the conditioned responses to alcohol-related stimuli by either inducing an aversive reaction to alcohol use or by blocking the positive effects of use. Currently, three different medications are approved for use in alcohol treatment: disulfiram, naltrexone, and acamprosate. Other medications are in preliminary stages of exploration but have not yet received approval for treatment of alcohol addiction. To date, no medications have demonstrated unambiguous effectiveness in either maintaining abstinence or preventing relapse, perhaps in part due to widespread problems with medication compliance. It is possible that pharmacological treatments of alcoholism have been restricted in part by the fact that outpatient substance abuse facilities are rarely equipped to monitor long-term medication regimens (Pettinati & Rabinowitz, 2005). In addition, McCarty, Edmundson, and Hartnett (2006) suggest that adoption of new intervention techniques is highly dependent upon agency culture and support of innovation in treatment, and that this can present a significant barrier to innovation in treatment.

Disulfiram. Discovered in 1939 and approved by the FDA for alcoholism treatment in 1954, disulfiram (Antabuse) was the first modern pharmacological treatment for alcoholism

(Kiefer & Mann, 2005; Pettinati & Rabinowitz, 2005). The object of disulfiram use is to establish an aversion to alcohol (vs. simply blocking its pleasurable effects). It blocks the metabolism of alcohol, resulting in a number of aversive symptoms after alcohol consumption such as tachycardia, flushing, nausea, and vomiting (Heilig & Egli, 2006; Kiefer & Mann, 2005; Pettinati & Rabinowitz, 2005). Disulfiram has not demonstrated reliable success in treating alcohol addiction, due in large part to extensive noncompliance—instead of avoiding alcohol, patients frequently avoid taking the medication when they wish to drink (Heilig & Egli, 2006; Pettinati & Rabinowitz, 2005). The physiological consequences of combining disulfiram are of substantial medical risk (Heilig & Egli, 2006; Kiefer & Mann, 2005), and for some patients dosages must be pushed very close to toxic levels before the desired reaction to alcohol is observed (Pettinati & Rabinowitz, 2005).

Naltrexone. Naltrexone (Revia), an opiate receptor agonist approved by the FDA for treatment of alcoholism in 1994 (ten years after being approved for treatment of opiate dependence), has been demonstrated in a number of studies to reduce craving and the reinforcing effects of alcohol (Kiefer & Mann, 2005; McCarty et al., 2006; NIAAA, 2004b; Pettinati & Rabinowitz, 2005; Verheul, van den Brink, & Geerlings, 1999), although a few studies disagree (Cutler, 2005; Morley et al., 2006). Naltrexone is somewhat more effective in preventing relapse than in maintaining abstinence (Kiefer & Mann, 2005), particularly in short-term treatment (Heilig & Egli, 2006) and in individuals with low dependence severity and mild baseline depression (Morley et al., 2006). Several studies have found naltrexone to be more effective in combination with cognitive behavioral coping skills training than in isolation (Berglund, 2005; Kiefer & Mann, 2005), particularly in medium-term treatment (Heilig & Egli, 2006). Other studies, however, have not found the combination to be significantly more beneficial than CBT

alone (Feeney, Connor, Young, Tucker, & McPherson, 2004). Some patients experience adverse gastrointestinal and/or neuropsychiatric side effects when taking naltrexone, leading to some problems with medication compliance (Pettinati & Rabinowitz, 2005). Efficacy of a monthly injection of long-acting naltrexone is being explored (Pettinati & Rabinowitz, 2005), with some preliminary positive results (Garbutt et al., 2005).

Acamprosate. Acamprosate (Campral) was approved for treatment of alcoholism by the FDA in 2004 (Pettinati & Rabinowitz, 2005). It acts as a glutamate antagonist in the brain, moderating the negative symptoms associated with alcohol withdrawal and thereby reducing craving (Heilig & Egli, 2006; Kiefer & Mann, 2005; Pettinati & Rabinowitz, 2005). Acamprosate has been shown in some studies to be approximately equivalent to naltrexone in improving abstinence rates vs. placebo in both the short- and long term (Heilig & Egli, 2006; Kiefer & Mann, 2005; Pettinati & Rabinowitz, 2005), though some other studies differ (Anton et al., 2006; Morley et al., 2006). In some studies, a combination of acamprosate and naltrexone has demonstrated effects beyond those of either medication alone (Berglund, 2005; Kiefer & Mann, 2005), though some other studies differ (Anton et al., 2006). In most studies, neither CBT (Berglund, 2005) nor a combined behavioral intervention (Anton et al., 2006) have demonstrated additive effects when combined with acamprosate.

Nalmefene. Nalmefene, an opiate receptor agonist similar to naltrexone, has demonstrated moderately encouraging effects on relapse and frequency of heavy drinking episodes in several studies (Kiefer & Mann, 2005), though results are not unanimous (Cutler, 2005). Nalmefene has not yet been approved as a treatment for alcohol dependence (Kiefer & Mann, 2005).

In addition to the medications discussed above, a number of dopaminergic, serotonergic, GABAergic, mood stabilizing, anticonvulsant, and sedating medications have been studied as

potential treatments for alcohol addiction, but are not yet approved for treatment of alcohol addiction. Results are largely preliminary and mixed (Kiefer & Mann, 2005; Pettinati & Rabinowitz, 2005).

Psychosocial Interventions

There are a number of psychosocial interventions for alcohol addiction treatment currently in use, including self-help groups, cognitive behavioral therapy, and motivational enhancement therapy. Additionally, brief interventions are often conducted by non-addiction specialists, such as primary care doctors and emergency room staff. Psychosocial interventions often emphasize reducing exposure to conditioned stimuli, encouraging avoidance of situations, environments, and people who are associated with drinking behavior. In addition, psychosocial interventions generally incorporate skills training and/or peer support, to be used when conditioned stimuli cannot be avoided.

Self-help groups. Self-help groups such as Alcoholics Anonymous (AA) remain the most widely used treatment for alcohol abuse and dependence, and regular attendance has been repeatedly linked to improved treatment outcomes (Connors, Tonigan, & Miller, 2001; Fiorentine, 1999; Miller, Ninoneuvo, Klamen, Hoffman, & Smith, 1997; Moos & Moos, 2004; Morgenstern, Labouvie, McCrady, Kahler, & Frey, 1997). Moos and Moos (2004) examined 1-year and 8-year outcomes for 473 individuals with alcohol use disorders who attended AA, and found that consistent participation, initiated early in the recovery process, was correlated with greater treatment success than sporadic attendance or delayed initiation. Kelly, Stout, Zywiak, and Schneider (2006) found that even low levels of participation in self-help groups may help promote abstinence, but that a higher level of participation may be important to relapse prevention.

Coping skills training. Coping skills training is conducted with a focus on relapse prevention, social or communication skills, urge-specific coping skills, and/or cognitive behavioral mood management (Monti & Rohsenow, 1999). Research has found a correlation between strong coping skills and more favorable treatment outcomes (Feeney et al., 2004; Monti & Rohsenow, 1999). In some studies, cue exposure is utilized as a way for patients to practice coping skills (Monti & Rohsenow, 1999; Rohsenow et al., 2001).

Brief interventions. Typically conducted with problem drinkers who do not meet criteria for alcohol dependence or abuse, brief interventions usually focus on reduction rather than cessation of alcohol consumption (Moyer & Finney, 2004/2005). Brief interventions usually include education, counseling, and nonjudgmental feedback (Moyer & Finney, 2004/2005). Some of the most common settings for brief interventions include primary care offices, hospitals, emergency rooms, police stations, and OB-GYN offices (Moyer & Finney, 2004/2005). Many doctors and nurses have expressed uncertainty about their qualifications to assess or treat problem drinking, but studies have shown that if staff is trained and encouraged to implement brief interventions, they can help a significant proportion of patients to avoid more severe future alcohol use disorders (Moyer & Finney, 2004/2005).

Concurrent Interventions for Smoking and Alcohol Abuse

Whether and how to treat nicotine addiction concurrently with alcohol addiction treatment has been an ongoing controversy in the addiction field for decades. In the addiction field, smoking is generally considered to be not as bad as other substances (Bobo & Husten, 2001; Cooney, Cooney, Pilkey, Kranzler, & Oncken, 2003), and fears that nicotine withdrawal could lead to alcohol relapse have led many to counsel smokers to continue smoking while their primary addiction is being addressed (Cooney et al., 2003; Romberger & Grant, 2004). Bowman

and Walsh (2003), in a call for smoking cessation programs to be integrated into alcohol and other drug treatment programs, cited the following common myths of addiction treatment:

- Substance abusers are intractable hard-core smokers, not interested in smoking cessation;
- Even should they be interested, substance abusers are not able to make changes to their smoking and other substance abuse behaviours concurrently;
- Attempting smoking cessation may impact the likelihood of successful intervention negatively for other substances of abuse; and
- That it is "unfair" to ask of someone that they reduce or cease multiple substances concurrently or within a short time period. (p. 74)

Conventional wisdom has maintained, "don't try to quit everything at once"; in AA parlance, "first things first" (Bobo & Husten, 2001). While historically AA discouraged its members to try to quit smoking simultaneously with drinking (Bobo & Husten, 2001), currently AA does not have an official position on smoking. Many (if not most) AA meetings remain smoker-friendly, however.

Contrary to these long-standing beliefs, a growing number of studies have found no evidence that smoking cessation increases risk of alcoholic relapse (Colby et al., 2004; Kohn et al., 2003; Lemon et al., 2003; Romberger & Grant, 2004). Cooney and colleagues (2003) exposed 40 alcohol-dependent smokers in treatment for alcoholism to neutral- and alcohol-related cues under both nicotine deprivation and non-deprivation conditions. They found that nicotine withdrawal does not increase urge to drink, which suggests that smoking cessation may not increase risk of relapse in dependent drinkers. Interestingly, however, they did find that exposure to alcohol cues resulted in increased urge to smoke, and concluded that "taken together,

the nicotine deprivation effects and the alcohol cue effects suggest that abstinent alcoholic smokers may smoke to cope with alcohol craving, but are not likely to drink to cope with tobacco craving" (p. 919). In fact, there is mounting evidence that quitting smoking *improves* treatment outcomes for alcoholics (Bobo & Husten, 2001; Drobes, 2002; Lemon et al., 2003). This may be partially due to shared neurobiological and psychosocial factors in smoking and drinking (Colby et al., 2004), which may heighten the risk of relapse for alcoholics in treatment if they do not avoid smoking situations as well as drinking situations. Additional research concerning the relationship between smoking and drinking, including investigations of cross-cue reactivity, are needed to further understand the substantial population of nicotine dependent problem drinkers. VR is one tool that may be used to enhance research into these and other issues affecting treatment, and is discussed below.

Virtual Reality and Clinical Research

Virtual reality has been used in a number of ways in clinical research, training, and practice during the previous three decades, including surgical training; motor rehabilitation (e.g. after stroke or traumatic brain injury); psychological treatments (e.g. phobias, eating disorders, or autistic spectrum disorders); and addiction research. These VR applications are discussed in some detail below.

Medical researchers have worked for decades to develop more sensitive tools with which to extend and refine their ability to operate within the smallest and safest possible boundaries (Dario & De Rossi, 1985; Jayawant, 1989; Nicholls & Lee, 1989; Pennywitt, 1986), and recent developments in this field of research have enhanced surgeons' ability to maintain a tactile connection with patients' organs and tissue during minimally invasive procedures which require the use of robotic surgical implements (Eltaib & Hewit, 2003; Heng et al., 2006; Wang et al.,

2007). In addition, VR has been widely used in surgical training, particularly for laproscopic procedures, providing an opportunity for novice surgeons to practice techniques in a safe and controlled environment (Champion & Gallagher, 2003; Eltaib & Hewit, 2003; Gallagher et al., 2005; Ganai, Donroe, St. Louis, Lewis, & Seymour, 2007; Kaufmann, 2001; Thacker, 2003). This ability of VR to create realistic, immersive scenarios which might otherwise be too dangerous, costly, or complex to replicate is a strength that is also appreciated by addiction researchers.

Three-dimensional, complex, controlled, interactive VR environments have also been used to augment assessment and rehabilitation for a number of physical and neurological disorders (Rizzo et al., 2001), including stroke (Gallichio & Kluding, 2004; Holden & Dyar, 2002; Jaffe, Brown, Pierson-Carey, Buckley, & Lew, 2004), acquired brain injury (Christiansen et al., 1998; Rose, Brooks, & Rizzo, 2005; Zhang et al., 2003), wheelchair training (Cooper et al., 2002; Harrison, Derwent, Enticknap, Rose, & Attree, 2002; Webster et al., 2001), functional activities of daily living (ADL) training (Gourlay, Lun, Lee, & Tay, 2000; Standen & Brown, 2005), and orthopedic disorders (Girone, Burdea, Bouzit, Popescu, & Deutsch, 2001). VR environments used in rehabilitation programs may motivate patients to work longer and harder on physical therapy tasks by providing concrete motivation and feedback (Holden, 2005). These characteristics are also valuable to addiction research, as the immersive experience allows for more comprehensive sources of motivation and feedback. For example, an individual who is using role-playing to learn refusal skills when offered a cigarette may find that doing so in VR provides a more realistic environment in which to practice, thereby increasing the chances of successful use of these skills in the real world.

Virtual reality has been used in the assessment and treatment of a range of anxiety disorders (Krijn et al., 2004). A number of specific phobias, both in adults (Choy, Fyer, & Lipsitz, 2007) and in youth and children (Ost, Svensson, Hellström, & Lindwall, 2001; Svensson, Larsson, & Ost, 2002), have been addressed with VR therapy, including fear of spiders (Antony et al., 2001; Garcia-Palacios et al., 2002; Teachman & Woody, 2003); other nature-related phobias (Davidson & Smith, 2003); fear of flying (Bornas et al., 2006; Mühlberger et al., 2006; Rothbaum et al., 2006; Wiederhold et al., 2002); agoraphobia (fear of crowds or open spaces) (Cardenas et al., 2006; Vincelli et al., 2003); and fear of heights (Choy et al., 2007; Emmelkamp et al., 2002). VR has also been used in the treatment of post-traumatic stress disorder (PTSD), particularly in Vietnam veterans (Rothbaum et al., 2001). Other researchers have employed VR to work with patients with autistic spectrum disorders, both in systematic desensitization programs (Koegel & Openden, 2004) and social skills training (Mitchell, Parsons, & Leonard, 2007). Rizzo and colleagues (2000) have constructed a virtual classroom to be used for assessment and treatment of attention deficit hyperactivity disorder. Others have evaluated the integration of VR into treatment of eating disorders (Myers, Swan-Kremeier, Wonderlich, Lancaster, & Mitchell, 2004; Riva, Bacchetta, Baruffi, Cirillo, & Molinari, 2000; Riva, Bacchetta, Baruffi, Rinaldi, & Molinari, 1999) and psychotherapy (Glanz, Rizzo, & Graap, 2003; Riva, 2005). Again, the ability of VR to create more realistic scenarios is a useful tool for researchers and practitioners alike, and addiction researchers are no exception.

Addiction researchers have incorporated VR cue reactivity into their studies of a number of substances, including nicotine (Baumann & Sayette, 2006; Bordnick, Graap, Copp, Brooks et al., 2004; Lee et al., 2003; Lee, Youngsik, Wiederhold, & Graham, 2005), alcohol (Bordnick et

al., in review), heroin and methadone (Kuntze et al., 2001), cocaine (Saladin, Brady, Graap, & Rothbaum, 2006) and other drugs of abuse (Thacker, 2003) (see Table 1).

Table 1

Addiction Research Incorporating VR

Authors	Year	Substance	Method	Findings
Kuntze, Stoermer, Mager, Roessler, Mueller-Spahn, & Bullinger	2001	Heroin and methadone	15 heroin users exposed to either VR cue environment (heroin; 5), heroin-related photographs (5), or neutral stimuli (5)	Incomplete report of findings (pilot study); participants in VR group experienced some increase in craving for heroin and physiological response
Lee, Ku, Kim, Kim, Kim, Yang, et al.	2003	Nicotine	30 smokers exposed to either VR cue environment (nicotine) or nicotine-related photographs	Participants in the VR group experienced significant increase in craving for nicotine; participants in non-VR group experienced no significant increase in craving
Bordnick, Graap, Copp, Brooks, Ferrer, & Logue	2004	Nicotine	13 smokers exposed to 2 VR neutral environments and 2 VR cue environments (nicotine)	Craving for nicotine was significantly higher in response to cue environments as compared to neutral

Table 1 continued

Authors	Year	Substance	Method	Findings
Lee, Youngsik, Wiederhold, & Graham	2005	Nicotine	8 adolescent smokers exposed to 2D & 3D VR neutral and cue environments (nicotine)	Craving for nicotine was significantly higher in response to cue environments as compared to neutral; fMRI indicated increased brain activity in response to cue environments (both 2D & 3D)
Bordnick, Graap, Copp, Brooks, & Ferrer	2005	Nicotine	10 smokers exposed to 2 VR neutral environments and 2 VR cue environments (nicotine)	Craving for nicotine was significantly higher in response to cue environments as compared to neutral; craving returned to baseline after second neutral; skin conductance was higher in response to cue environments as compared to neutral (nonsignificant due to sample size)
Baumann & Sayette	2006	Nicotine	20 smokers exposed to 1 VR neutral environment and 1 VR cue environment (nicotine)	Urge to smoke was significantly higher in response to cue environment as compared to neutral

Table 1 continued

Authors	Year	Substance	Method	Findings
Saladin, Brady, Graap, & Rothbaum	2006	Crack cocaine	11 crack cocaine users exposed to VR neutral environments and 7 VR cue environments (crack)	Craving for crack cocaine was significantly higher in response to cue environments as compared to neutral; heart rate was significantly elevated after 4 of the cue environments as compared to neutral; affect was significantly lower after cue environments as compared to neutral
Bordnick, Traylor, Copp, Graap, Brooks, Ferrer, Walton	in review	Alcohol	40 problem drinkers exposed to 2 VR neutral environments and 4 VR cue environments (alcohol)	Craving for alcohol was significantly higher in response to cue environments as compared to neutral; Attention paid to the sight of alcohol, smell of alcohol, and thoughts about drinking was significantly higher in response to cue environments as compared to neutral

The number of studies to date is relatively small because VR technology remains relatively novel, and there are a limited number of facilities worldwide equipped to conduct this research. As more researchers become acquainted with VR, and as VR technology is more widely employed, the number of studies is likely to increase dramatically, particularly concerning multiple substance use. As stated before, this study is the first known study to use VR in an examination of cross-cue reactivity in polysubstance users. It is expected that additional such studies will emerge with time, given VR's potential to create complex, realistic, cue-rich polydrug scenarios.

Virtual Reality Cue Reactivity

Traditional cue exposure has conventionally involved the presentation of tactile (e.g., paraphernalia or real or simulated drugs or alcohol), visual (e.g., photographs of drugs or alcohol), or audiovisual (e.g., film of drug or alcohol use) cues. In the case of using actual or simulated substances, additional olfactory and/or taste cues may be included. These cues, however, are inherently and artificially isolated from the context in which they would normally be encountered in real life. In many cases, extinction achieved in this artificial environment fails to generalize to the real world, leading to renewal of the behavior (relapse).

Given that the inherent artificiality and limited environmental context of laboratory- or clinic-bound cue exposure treatment may hinder generalization to real-world situations (Bordnick et al., in review; Conklin, 2006; Cooney et al., 2003), VR cue environments were developed with a goal of enabling researchers and clinicians to produce more realistic and complex coping skills training in a lab or clinic environment (Bordnick, Graap, Copp, Brooks et al., 2004; Bordnick, Graap et al., 2005). VR allows participants to become immersed in a cue environment without the distraction of role-playing with a known therapist or researcher. In

addition, VR allows participants to interact with complex cues that are situated within realistic settings. Ideally, if the VR environment successfully simulates a real world situation, coping skills and extinction acquired within VR should better translate into actual drug or alcohol cue settings.

In summary, VR is a tool that may potentially be used to create more realistic, immersive drug- and alcohol-related cue environments. These environments may prove to be a useful tool in the development and refining of theoretical models of addiction and treatment methodologies, particularly if it is found that using these more realistic and comprehensive environments in research and treatment leads to more authentic responses in research settings and/or better generalization from the lab or clinic to the "real world." This study is intended to advance this line of inquiry, exploring the potential for more complex environments to evoke cross-cue reactivity (here, the effect of exposure to nicotine cue environments on craving for both nicotine and alcohol in nicotine dependent problem drinkers).

CHAPTER THREE

RESEARCH METHODS

In this study, 21 male and female nicotine dependent problem drinkers were exposed to virtual cues, both nicotine-related and non-nicotine-related, in a specially designed virtual reality (VR) environment. The nicotine-related cues were presented in two contexts: an alcohol-appropriate setting and an alcohol-inappropriate setting. Participants rated subjective levels of craving for nicotine and alcohol in response to different types of cues and environmental contexts.

This chapter will outline the study hypotheses and rationale, and will describe study participant inclusion and exclusion criteria, financial compensation, measures, design and procedures, and data analysis plan.

Hypotheses

It has been demonstrated that VR nicotine cues elicit craving for nicotine in current smokers (Bordnick, Graap, Copp, Logue et al., 2004; Bordnick, Graap et al., 2005; Bordnick, Traylor et al., 2005), and it was expected that this finding would be replicated in the current study. In addition, according to the principles of classical and operant conditioning, when smoking and drinking behaviors are repeatedly conducted together, cross-cue reactivity is developed. In other words, if drinking is generally paired with smoking, then exposure to nicotine-related cues should elicit craving for alcohol as well as nicotine. This finding was also expected to be replicated in the current study.

The importance of environmental context to cue reactivity has also been discussed above. It was predicted that exposing participants to a setting in which smoking behavior is regularly paired with drinking behavior (here, a party scene) would elicit significant levels of craving for both cigarettes and alcohol because the environmental context is conducive to both smoking and drinking. Exposing participants to a setting in which smoking behavior has generally not been paired with drinking behavior (here, the exterior of an office building), however, was predicted to elicit significant levels of craving for cigarettes but not for alcohol. Craving for nicotine in both the party and the office building setting was predicted to be significantly higher than in response to neutral cues.

As discussed in previous chapters, one factor in craving is attention to cues. It was predicted that participants would report paying a higher degree of attention to nicotine cues in environments containing nicotine cues than in neutral environments. In addition, it was predicted that participants would report a higher degree of attention to nicotine cues in the alcohol-appropriate party setting than in the alcohol-inappropriate office building setting, as the additive effects of multiple cues (including anticipation of use) would elicit heightened levels of craving. Despite the fact that no overt alcohol cues were presented in any of the virtual settings, it was predicted that participants would report significant levels of attention to alcohol cues in the party setting, as the anticipation of drinking behavior serves as a sufficiently powerful cue in itself to inspire recall of more overt cues in similar alcohol-appropriate contexts.

Hence, this study was guided by the following eight hypotheses:

1. Virtual reality nicotine cues will elicit significantly higher self-reported levels of craving for *nicotine* than virtual reality neutral cues.

2. Virtual reality nicotine cues will elicit significantly higher self-reported levels of craving for *alcohol* than virtual reality neutral cues.
3. Self-reported levels of craving for *alcohol* will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).
4. Self-reported levels of craving for *nicotine* will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).
5. Self-reported degree of attention paid to *nicotine* cues will be significantly higher in virtual reality environments containing nicotine cues than in neutral cue environments.
6. Self-reported degree of attention paid to *alcohol* cues will be significantly higher in virtual reality environments containing nicotine cues than in neutral cue environments.
7. Self-reported degree of attention paid to *nicotine* cues will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).
8. Self-reported degree of attention paid to *alcohol* cues will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Participants

Participants were recruited via advertisements in *Creative Loafing* (a popular free arts and entertainment weekly paper for the Atlanta metro area). All participants were assigned an ID

number, which was used to label all study materials and instruments. Participants' identities were confidential, as only research personnel had access to study records containing identifying information.

Inclusion Criteria

Criteria for inclusion in the study included: provision of written informed consent; willingness to participate in a non-treatment research study; current drinker; current *DSM-IV* (APA, 1994) diagnosis of alcohol abuse or dependence; current smoker of at least 10 cigarettes (½ pack) per day; 21-65 years of age; in good physical health; literate in English and able to read at a 6th grade level; able to understand and complete the rating scales and questionnaires accurately; able to follow instructions; and able to wear a VR helmet for 40 minutes.

Exclusion Criteria

Criteria that was used to exclude potential participants included: *DSM-IV* (APA, 1994) psychiatric diagnosis of severe mental illness or substance abuse (other than nicotine dependence, alcohol abuse, or alcohol dependence) in the previous 30 days; pregnant; history of seizures or seizure disorders; fear of closed spaces or inability to wear a VR helmet; visual problems that prevent viewing of VR environments; currently taking any medications having a potential effect on craving, consumption, related behaviors, or mood; treated with any alcohol, smoking, or drug cessation medications, programs, or services in the previous 30 days; treatment seeking; participation in any other smoking- or alcohol-related studies or trials within the previous 30 days; self-reported use within the previous 30 days of opiates, cocaine, amphetamines, barbiturates, benzodiazepines, cannabis, or other prescription and non-prescription drugs that may affect participation in the study; pacemaker; history of serious health problems; breath alcohol level greater than 0.00.

Financial Compensation

Participants who completed only the telephone pre-screening were not financially compensated. Participants who completed the in-person screening were paid $10.00 as compensation for their time. Participants who were determined via the in-person screening process to be qualified for full participation in the study, and who completed all study protocols, were paid an additional $40.00 ($50.00 total). No participants were disqualified by the in-person screening process, and all completed the entire study and were paid $50.00.

Measures

Participants completed a variety of pen and paper measures before and after VR exposure, as well as subjective craving and attention ratings within the VR environment via an electronic game controller. All measures that were administered are discussed below.

Pre VR Exposure

Mini International Neuropsychiatric Interview

The Mini International Neuropsychiatric Interview (MINI, Sheehan et al., 2002) is based on the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV, APA, 1994). The MINI is a decision tree questionnaire, given in interview format, that screens for the following current *DSM-IV* (1994) diagnoses: major depressive episode, dysthymia, suicidality, (hypo)manic episode, panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder, alcohol abuse and dependence, non-alcohol psychoactive substance use disorders, psychotic disorders, anorexia nervosa, bulimia nervosa, generalized anxiety disorder, and antisocial personality disorder (Sheehan et al., 2002). The MINI has been used by the World Health Organization in a number of studies (e.g., Humeniuk & Ali, 2006; WHO, 2004). The MINI was used in this study to establish participant eligibility by

screening for a diagnosis of alcohol abuse or dependence (required for inclusion) as well as other mental health diagnoses (which would disqualify the individual from participation in the study). Please see Appendix A, which contains the initial overview questions and the alcohol abuse and dependence module.

Drinking History

Self-report of drinking behavior was collected regarding years drinking, number of quit attempts, current and past use levels, type of alcohol used, and brand preference. Please see Appendix B.

Smoking History

Self-report of smoking behavior was collected regarding years smoking, number of quit attempts, current and past use levels, and brand preference. Please see Appendix C.

Nicotine Dependence Questionnaire

The Nicotine Dependence Questionnaire (NDQ) is an 8-item questionnaire designed to measure the degree of nicotine dependence (heaviness of use). It is a modified version of the Fagerstrom Tolerance Questionnaire (Fagerstrom, 1978; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). Potential summed scores range from 0-15, with higher scores indicating higher levels of nicotine dependence. The FTND has demonstrated moderate internal consistency (.61) (Heatherton et al., 1991). Please see Appendix D.

Alcohol Dependence Scale

The Alcohol Dependence Scale (ADS, Skinner & Horn, 1984) is a 25-item instrument that was used to measure the severity of problem drinking behavior at intake. The ADS also provided a quantitative measure of alcohol dependence. Potential summed scores range from 0-47, with a score of 0 indicating no alcohol dependence; a score of 1-13 indicating a low level of

alcohol dependence; a score of 14-21 indicating an intermediate level of alcohol dependence; a score of 22-30 indicating a substantial level of alcohol dependence; and a score of 31-47 indicating a severe level of alcohol dependence (Skinner & Horn, 1984). The ADS has been demonstrated to have an 88% level of accuracy in diagnosing alcohol dependence (Ross, Gavin, & Skinner, 1990). Please see Appendix E.

Within VR Environment

Alcohol and Nicotine Craving Scales

Single item visual analog craving scales (VAS) for alcohol and nicotine were administered once pre-exposure (pen and paper) and four times during exposure (within the VR environment so as to avoid breaking immersion). Participants were asked to rate their current intensity of craving for alcohol or nicotine on a VAS ranging from 0 (not at all) to 100 (more than ever). The virtual scales were projected on a white background, and participants responded using a game controller. The craving VAS scale has been effectively used to measure craving in cue reactivity studies both in VR-based (Bordnick, Graap, Copp, Brooks et al., 2004; Bordnick, Traylor et al., 2005) and traditional methodologies (Cutler, 2005; Johnson et al., 1998; Preston & Jasinski, 1991). Please see Appendix F.

Alcohol and Nicotine Attention Scales

Modified versions of the Alcohol Attention Scale (Hutchison et al., 2001) were administered within the VR environment in much the same way as the craving scales (above). The modified Alcohol Attention Scale (AAS) and similar Nicotine Attention Scale (NAS) were used to measure attention to alcohol and nicotine cues. Participants were asked to rate the degree of attention they paid to alcohol or nicotine cues on an 11-point Likert scale ranging from 0 (didn't notice at all) to 10 (completely paid attention) for the following two pairs of questions:

"How much did you pay attention to the sight of alcohol [cigarettes] in the room?" and "How much did you pay attention to the smell of alcohol [cigarettes] in the room?". A third pair of questions, "How much did you think about drinking alcohol [smoking cigarettes] while you were in the room?", addressed thoughts about drinking/smoking, and was also answered on a Likert scale ranging from 0 (didn't think about drinking [smoking] at all) to 10 (thought about drinking [smoking] all the time). Please see Appendix G.

Post VR Exposure

Imagery Realism Presence Questionnaire-Revised

The Imagery Realism Presence Questionnaire-Revised (PQ, Witmer & Singer, 1998) consists of 15 items that assess aspects of presence in a virtual environment. Assessments include involvement/control, naturalness, and interface quality. Each item is rated on a Likert-type scale from 1-7. Potential summed scores range from 15-105, with higher scores indicating a greater degree of immersion in the VR environment. The PQ was used as a descriptive measure in this study. The PQ has good internal validity (.88), and it is the first measure developed to assess sense of presence in a virtual environment. Please see Appendix H.

Debriefing Form

All participants were debriefed post VR exposure. The debriefing form was used to collect qualitative data from each participant regarding the VR environments. In addition, participants were asked to describe additional environmental contexts that might also elicit craving for nicotine or alcohol. These qualitative data may then be useful in designing the next generation of VR environments. Please see Appendix I.

Design and Procedures

Participants who were found to meet study criteria (via telephone pre-screening and in-person screening) were exposed to a series of VR environments and asked to complete the measures and ratings described above before, during, and after exposure. Following is a description of the screening process and the VR environments.

Telephone Pre-Screening

Potential participants responding to study recruitment materials were, after providing verbal consent, pre-screened by telephone to ensure that they met preliminary study criteria (Appendix J). Callers who appeared to meet all study criteria were given an appointment at the Virtual Reality Clinical Research Center (VRCRC; Georgia Gwinnett College, Lawrenceville) for a more thorough in-person screening. Participants were asked not to consume any alcohol for at least 12 hours before their appointment, and told that if a breath alcohol sample taken upon arrival detected any alcohol present, then they would not be allowed to participate in the study and would be provided transportation home via taxi. Participants were also asked to bring at least one cigarette with them, to be smoked during a break midway through their appointment.

In-Person Appointment

When participants arrived at the VR lab for their scheduled appointment, they were assigned an ID code and asked to review and sign a written consent form (Appendix K). Then participants were given the breath alcohol test. All participants registered 0.00 for the breath alcohol test. If the test had registered alcohol in any participant's sample, s/he would not have been permitted to participate in the study and would have been provided transportation home via taxi. Next, participants completed the pre-exposure measures (described in the measures section

above), which included questions about demographic characteristics, alcohol and cigarette use, a brief mental health evaluation, and current levels of craving for nicotine and alcohol.

Participants were then given a brief orientation to VR, during which they had a chance to become accustomed to wearing the VR headset (which has screens that pull down in front of the eyes) and negotiating VR environments. The practice environments were devoid of nicotine or alcohol cues. Participants also practiced responding to questions within the VR environment using a game controller, using the same VAS and Likert scales that they would use to respond to the craving and attention questions in the course of the trial (described above). Participants were then asked to take a 10-15 minute break before the VR exposure portion of the study. Participants were asked to smoke one cigarette during this break in order to standardize the time since last nicotine administration across all participants.

VR Environment

After the break, participants put on the VR headset and noise-canceling headphones, and the VR portion of the study was initiated. For the first five minutes, participants sat quietly and listened to instrumental music. There was no visual component to this baseline period. At the end of this five-minute period, the VR exposure began.

The VR environment consisted of four different virtual rooms, and participants spent three minutes in each (for a total of 12 minutes of exposure, plus the 5-minute baseline and time to answer questions after each room; typically 22-24 minutes total). The rooms were as follows: neutral 1 (similar to an art gallery, with brief educational film clips on the buffalo and the flamingo); office building (the exterior courtyard and interior lobby of an office building); party (a home setting with people socializing); and neutral 2 (identical to neural 1). After each room, participants used the game controller to report craving for alcohol and nicotine (using the VAS

scales described above) and attention paid to alcohol and nicotine cues (using the Likert scales described above). No explicit alcohol cues, such as alcoholic drinks, were presented in any part of the VR environment.

Participants were randomly assigned to one of two paths through the rooms to control for potential order effects. Path 1 was neutral 1, office building, party, neutral 2. Path 2 was neutral 1, party, office building, neutral 2 (see Figure 3).

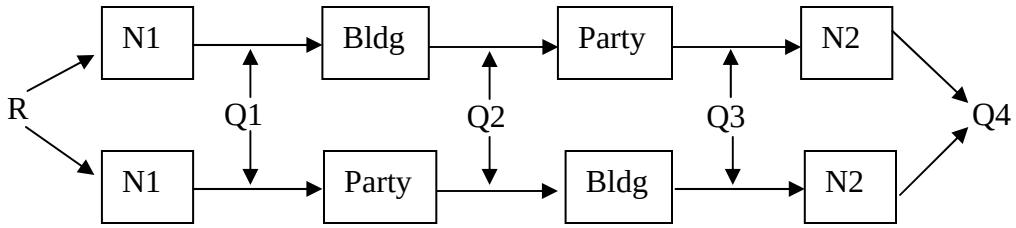


Figure 3. Paths through VR environment.

The two neutral rooms, which were identical, consisted of an empty room with video screens on two of the four walls. Participants were moved toward each video screen in turn, and were shown brief educational films on buffaloes and flamingoes. These films were not intended to elicit any associations with either nicotine or alcohol.

The two cue rooms, office building and party, both contained nicotine cues but no alcohol cues. The office building setting included an exterior courtyard and the interior lobby, including a convenience store selling cigarettes. In the courtyard, people were smoking, talking, and/or reading. The cigarettes they were smoking matched the participant's preferred brand, which the researcher preselected before initiating the VR environment. Inside the building there were

prominent “No Smoking” signs, and participants were taken through part of the lobby and past the convenience store. The party room consisted of a home setting, where people were talking, smoking, drinking soft drinks and coffee, eating, and listening to music. No alcohol was present, and no mention was made of alcohol. Again, all cigarettes matched the participant's preferred brand. In this room, the participant was approached, engaged in conversation, and offered a cigarette.

In addition to visual and audio stimuli, all four rooms incorporated olfactory cues, presented with The Scent Palette system (Envirodine Studios/Virtually Better, 2004). The Scent Palette system, a device connected via USB port to the computer running the VR environment, released specifically timed scents based upon pre-programmed triggers embedded in the VR environment. For example, when the participant passed by someone who was smoking, The Scent Palette system released the odor of cigarette smoke. Scents that were used in the VR environment included flowers (in neutral rooms 1 and 2, to control for the presence of scent in cue rooms), cigarette smoke, pine, pizza, and coffee. No alcohol scents were presented at any point in the VR environment.

Post VR exposure, participants completed the PQ (see Measures, above) and were debriefed by a master's-level clinician. All participants were offered referral information to smoking or alcohol treatment.

Data Analysis Plan

The following demographic and descriptive variables will be presented first: gender, age, ethnicity, diagnosis (alcohol abuse or dependence), alcohol dependency score, nicotine dependency score, number of drinks/cigarettes per day, age of initiation of regular

alcohol/cigarette use, and presence score. The remainder of the data analysis plan, organized by the eight study hypotheses, is presented below.

1. Virtual reality nicotine cues will elicit significantly higher self-reported levels of craving for *nicotine* than virtual reality neutral cues.

Results from the nicotine craving scales will be analyzed via one-way repeated measures analysis of variance (ANOVA) to determine whether craving for nicotine in rooms containing nicotine cues was significantly higher than craving in neutral rooms. If the data do not satisfy the assumption of sphericity (as they may not, given the relatively small sample size), the Huynh-Feldt correction will be used to ensure an appropriate *F*-value.

2. Virtual reality nicotine cues will elicit significantly higher self-reported levels of craving for *alcohol* than virtual reality neutral cues.

Results from the alcohol craving scales will be analyzed via one-way repeated measures ANOVA to determine whether craving for alcohol in rooms containing nicotine cues was significantly higher than craving in neutral rooms. If the data do not satisfy the assumption of sphericity, the Huynh-Feldt correction will be used.

3. Self-reported levels of craving for *alcohol* will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons will be utilized to determine whether craving for alcohol was significantly higher in the party environment than in the office building environment.

4. Self-reported levels of craving for *nicotine* will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons will be utilized to determine whether craving for nicotine significantly higher in the party environment than in the office building environment.

5. Self-reported degree of attention paid to *nicotine* cues will be significantly higher in virtual reality environments containing nicotine cues than in neutral cue environments.

Results from nicotine attention scales will be analyzed via one-way repeated measures ANOVAs (three total: one for sight, one for smell, and one for thoughts) to determine whether attention to nicotine cues in cue rooms was significantly higher than attention to nicotine cues in neutral rooms. Again, the Huynh-Feldt correction will be applied if the assumption of sphericity is not met.

6. Self-reported degree of attention paid to *alcohol* cues will be significantly higher in virtual reality environments containing nicotine cues than in neutral cue environments.

Results from alcohol attention scales will be analyzed via one-way repeated measures ANOVAs (three total: one for sight, one for smell, and one for thoughts) to determine whether attention to alcohol cues in nicotine cue rooms was significantly higher than attention to alcohol cues in neutral rooms. The Huynh-Feldt correction will be applied if necessary.

7. Self-reported degree of attention paid to *nicotine* cues will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons will be utilized to determine whether degree of attention paid to the sight, smell, and thoughts about nicotine was significantly higher in the party environment than in the office building environment.

8. Self-reported degree of attention paid to *alcohol* cues will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons will be utilized to determine whether degree of attention paid to the sight, smell, and thoughts about alcohol was significantly higher in the party environment than in the office building environment.

CHAPTER FOUR

RESEARCH FINDINGS

Following is a presentation of the research findings. Demographic and descriptive variables will be presented first, followed by the craving and attentional data, organized by the eight study hypotheses. Implications of these findings will be discussed in Chapter Five.

Demographic and Descriptive Variables

Participants were 61.9% (13) male and 38.1% (8) female. Ethnically, 66.7% (14) identified as African American, 28.6% (6) as White, and 4.8% (1) as Native American. Table 2 presents these demographic characteristics.

Table 2

Participant Gender and Ethnicity (n = 21)

Variable/Label	*n*	%
Gender		
Male	13	61.9%
Female	8	38.1%
Ethnicity		
African American	14	66.7%
White	6	28.6%
Native American	1	4.8%

Participants ranged in age from 25-58, with a mean age of 38.67 (*SD* = 9.87).

Of the 21 participants, 20 (95.2%) met *DSM-IV* (APA, 1994) criteria for alcohol dependence, and 1 (4.8%) met criteria for alcohol abuse. Scores on the Alcohol Dependence Scale ranged from 3-24, with a mean score of 12.95 (*SD* = 6.46; see Measures, Chapter 3). Baseline level of craving for alcohol ranged from 9-98 (out of 100), with a mean of 54.71 (*SD* = 24.26). Number of standard drinks per day ranged from 2-13, with a mean of 5.9 (*SD* = 3.22). Age of initiation of regular drinking ranged from 13-27, with a mean age of 17.76 (*SD* = 3.90). These alcohol use characteristics are depicted in Table 3.

Table 3

Alcohol and Nicotine Use Data (*n* = 21)

Variable/Label	M	SD
	Alcohol	
ADS score	12.95	6.46
Baseline craving	54.71	24.26
Drinks per day	5.90	3.22
Age of initiation	17.76	3.90
	Nicotine	
NDQ score	9.57	2.04
Baseline craving	51.38	24.39
Cigarettes per day	15.67	5.79
Age of initiation	19.67	5.22

All participants met criteria for nicotine dependence, according to scores on the Nicotine Dependence Questionnaire (NDQ; see Measures, Chapter 3) ranging from 7-12, with a mean score of 9.57 (*SD* = 2.04). This indicates that all participants had a high level of nicotine dependence. Baseline level of craving for nicotine ranged from 1-94 (out of 100), with a mean of 51.38 (*SD* = 24.39). Number of cigarettes smoked per day ranged from 10-30, with a mean of 15.67 (*SD* = 5.79). Age of initiation of regular smoking ranged from 12-30, with a mean age of 19.67 (*SD* = 5.22). These nicotine use characteristics are depicted in Table 2.

Scores on the presence questionnaire (PQ; see Measures, Chapter 3) ranged from 67-101, with a mean score of 82.05 (*SD* = 9.56). This indicates that participants were highly immersed in the VR environment.

Path 1 vs. Path 2

Twelve participants (57.1%) were randomly assigned to path 1 (office building first), and 9 (42.9%) were randomly assigned to path 2 (party first). The only significant difference between the participants assigned to path 1 and those assigned to path 2 was gender ($p < .05$). No significant difference between the groups was found for ethnicity ($p = .532$), age ($p = .897$), ADS score ($p = .368$), baseline alcohol craving ($p = .616$), number of drinks per day ($p = .807$), age of initiation of drinking behavior ($p = .370$), NDQ score ($p = .277$), baseline nicotine craving ($p = .952$), number of cigarettes per day ($p = .714$), age of initiation of smoking behavior ($p = .061$), or PQ score ($p = .248$). These characteristics of path 1 vs. path 2 are presented in Table 4.

Craving and Attentional Data

The craving and attentional data are presented below, organized by the eight study hypotheses.

Table 4

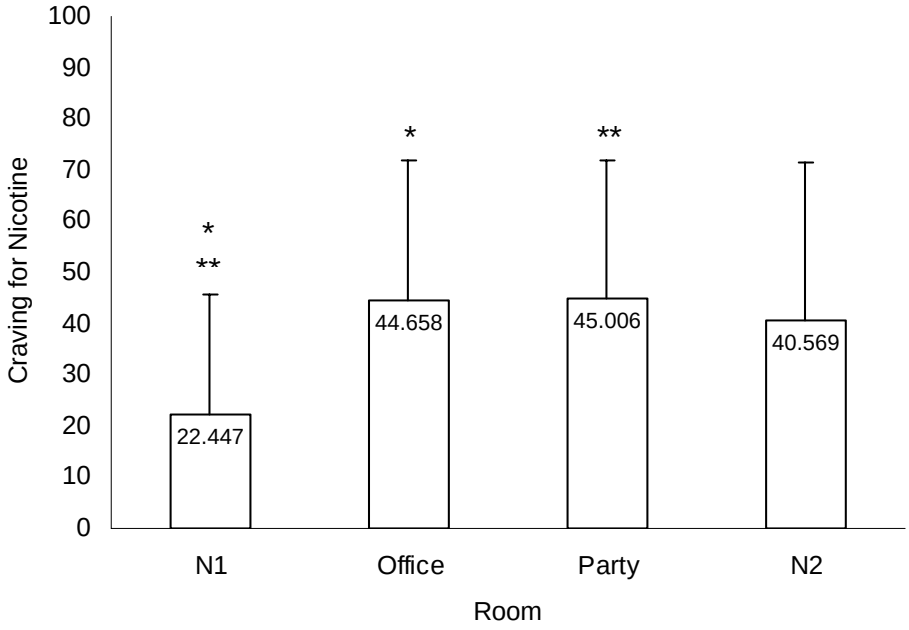
Participant Demographics and Descriptives by Path

Variable/Label	Path 1 (*n* = 12)	Path 2 (*n* = 9)	Sig.
Gender			.020*
Male	10	3	
Female	2	6	
Ethnicity			.532
African American	7	7	
White	4	2	
Native American	1	0	
Age	38.92	38.33	.897
ADS	14.08	11.44	.368
Baseline craving—Alcohol	52.33	57.89	.616
Drinks per day	5.75	6.11	.807
Age of initiation—Alcohol	17.08	18.67	.370
NDQ	10.00	9.00	.277
Baseline craving—Nicotine	51.67	51.00	.952
Cigarettes per day	16.08	15.11	.714
Age of initiation—Nicotine	17.83	22.11	.061
PQ	79.92	84.89	.248

Hypotheses 1

- Virtual reality nicotine cues will elicit significantly higher self-reported levels of craving for *nicotine* than virtual reality neutral cues.

A one-way repeated-measures ANOVA was conducted to determine whether craving for nicotine was higher in cue rooms (office building and party) than in neutral rooms. Figure 4 graphically depicts mean nicotine craving ratings for each room.



* $p < .001$ (Office vs. N1)
** $p < .01$ (Party vs. N1)

Figure 4. Mean craving for nicotine by room.

Overall, room was found to have a significant effect on nicotine craving: $F(3,60) = 5.756$, $p < .002$. Table 5 presents the ANOVA results.

Table 5

ANOVA Summary Table for Nicotine Craving

Source	df	SS	MS	F	p
Room	3	7177.441	2392.480	5.756	.002
Error	60	24938.980	415.650		

A significant overall linear trend was observed ($p < .02$). The assumption of sphericity was not violated ($p = .838$). It was found that craving for nicotine was significantly higher in both the office building ($p < .001$) and the party ($p < .01$) than in the first neutral room. Craving for nicotine was not found to be significantly higher in either the office building ($p = .500$) or the party ($p = .500$) than in the second neutral room, however. Hence, hypothesis 1 was partially supported. There was no significant interaction between room and path ($p = .240$), indicating that there was no order effect according to path (see Table 6).

Table 6

ANOVA Summary Table for Nicotine Craving by Path

Source	df	SS	MS	F	p
Room	3	7497.485	2499.162	6.146	.001
Room x Path	3	1760.409	586.803	1.443	.240
Error	57	23178.572	406.642		

Hypothesis 2

- Virtual reality nicotine cues will elicit significantly higher self-reported levels of craving for *alcohol* than virtual reality neutral cues.

A one-way repeated-measures ANOVA was conducted to determine whether craving for alcohol was higher in cue rooms (office building and party) than in neutral rooms. Figure 5 graphically depicts mean alcohol craving ratings for each room.

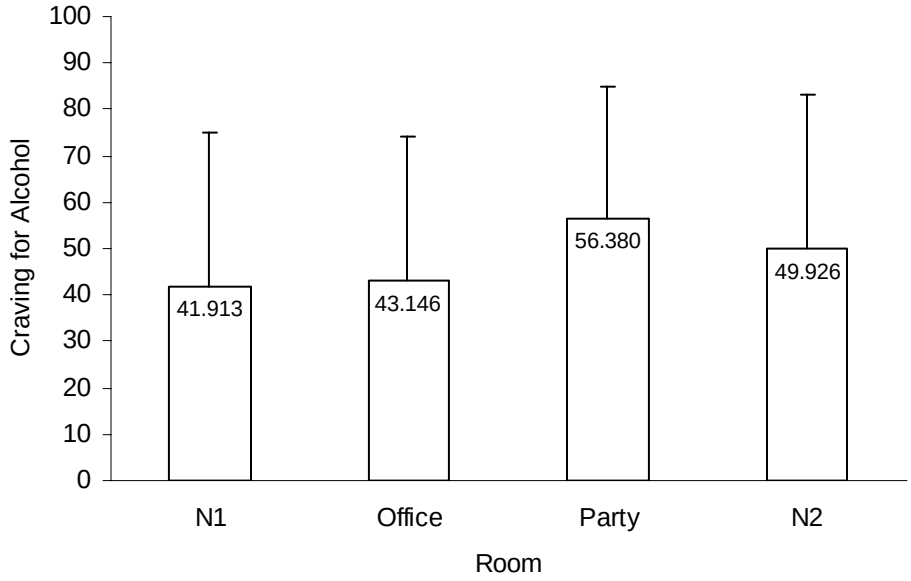


Figure 5. Mean craving for alcohol by room.

Overall, room was not found to have a significant effect on alcohol craving: $F(3,60) = 2.183$, $p = .099$. Table 7 presents the ANOVA results.

Table 7

ANOVA Summary Table for Alcohol Craving

Source	df	SS	MS	F	p
Room	3	2823.455	941.152	2.183	.099
Error	60	25873.454	431.224		

No significant overall linear trend was found (p = .099). The assumption of sphericity was not violated (p = .142). It was found that craving for alcohol was not significantly higher in either the office building setting (p = .500; p = .398) or the party (p = .239; p = .500) than in the first or second neutral rooms. Hence, hypothesis 2 was not supported. There was no significant interaction between room and path (p = .657), indicating that there was no order effect according to path (see Table 8).

Table 8

ANOVA Summary Table for Alcohol Craving by Path

Source	df	SS	MS	F	p
Room	3	2770.559	923.520	2.092	.111
Room x Path	3	713.769	237.923	.539	.657
Error	57	25159.685	441.398		

Hypothesis 3

- Self-reported levels of craving for *alcohol* will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons were made to determine whether craving for alcohol was higher in the alcohol-appropriate party setting than the non-alcohol-appropriate office building setting. To adjust for multiple comparisons, the Bonferroni correction was used. No significant difference in craving for alcohol was found between the two cue rooms ($p = .218$). Hence, hypothesis 3 was not supported.

Hypothesis 4

- Self-reported levels of craving for *nicotine* will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons were made to determine whether craving for nicotine was higher in the alcohol-appropriate party setting than the non-alcohol-appropriate office building setting. To adjust for multiple comparisons, the Bonferroni correction was used. No significant difference in craving for nicotine was found between the two cue rooms ($p = .500$). Hence, hypothesis 4 was not supported.

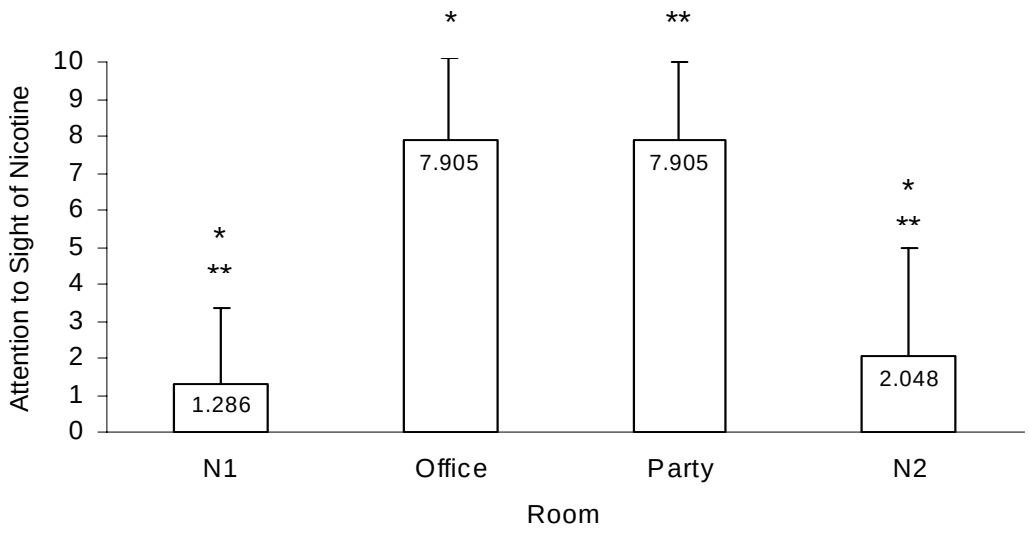
Hypothesis 5

- Self-reported degree of attention paid to *nicotine* cues will be significantly higher in virtual reality environments containing nicotine cues than in neutral cue environments.

Three one-way repeated measures ANOVAs were conducted (attention paid to the sight of cigarettes, attention paid to the smell of cigarettes, and thoughts about smoking) to determine whether attention to nicotine cues in cue rooms was significantly higher than attention to nicotine cues in neutral rooms.

Sight of Cigarettes

Figure 6 graphically depicts mean level of attention paid to the sight of nicotine for each room.



*p < .001 (Office vs. N1; Office vs. N2)
**p < .001 (Party vs. N1; Party vs. N2)

Figure 6. Mean level of attention to sight of nicotine by room.

Overall, room was found to have a significant effect on attention paid to the sight of cigarettes: $F(3,60) = 70.603$, $p < .001$. Table 9 presents the ANOVA results.

Table 9

ANOVA Summary Table for Attention to Sight of Nicotine

Source	df	SS	MS	F	p
Room	3	823.286	274.429	70.603	.000
Error	60	233.214	3.887		

No significant overall linear trend was found ($p = .258$). The assumption of sphericity was not violated ($p = .090$). It was found that attention to the sight of cigarettes was significantly higher in both the office building setting ($p < .001$) and the party setting ($p < .001$) than in either neutral room. Hence, this portion of hypothesis 5 was supported. There was no significant interaction between room and path ($p = .261$), indicating that there was no order effect according to path (see Table 10).

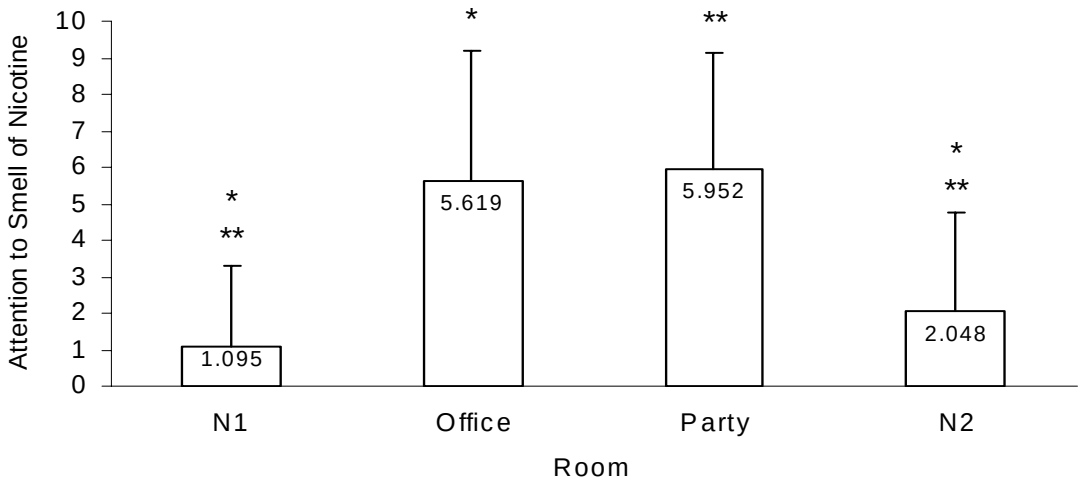
Table 10

ANOVA Summary Table for Attention to Sight of Nicotine by Path

Source	df	SS	MS	F	p
Room	2.736	793.675	290.097	69.350	.000
Room x Path	2.736	15.770	5.764	1.378	.261
Error	51.982	217.444	4.183		

Smell of Cigarettes

Figure 7 graphically depicts mean level of attention paid to the smell of nicotine for each room.



*p < .001 (Office vs. N1; Office vs. N2)
**p < .001 (Party vs. N1; Party vs. N2)

Figure 7. Mean level of attention to smell of nicotine by room.

Overall, room was found to have a significant effect on attention paid to the smell of cigarettes: $F(3,60) = 23.566$, $p < .001$. Table 11 presents the ANOVA results.

Table 11

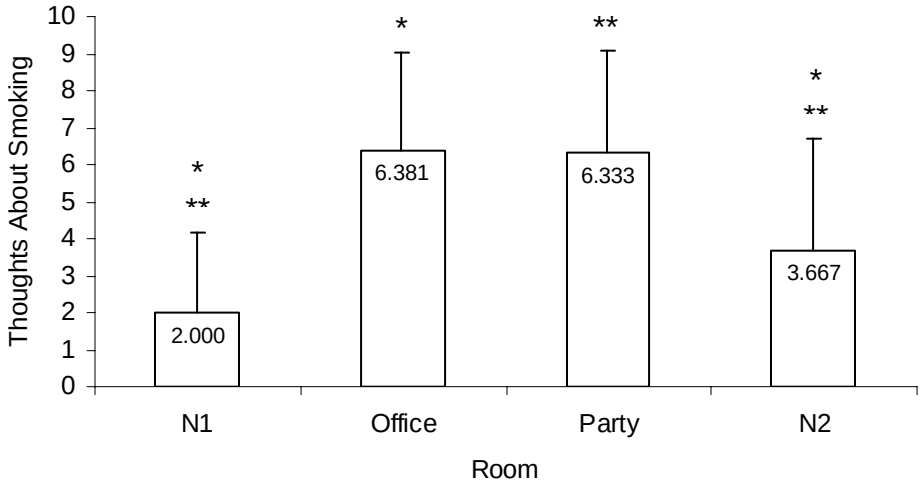
ANOVA Summary Table for Attention to Smell of Nicotine

Source	df	SS	MS	F	p
Room	3	383.655	127.885	23.566	.000
Error	60	325.595	5.427		

No significant overall linear trend was found ($p = .177$). The assumption of sphericity was not violated ($p = .437$). It was found that attention to the smell of cigarettes was significantly higher in both the office building setting ($p < .001$) and the party setting ($p < .001$) than in either neutral room. Hence, this portion of hypothesis 5 was supported. There was no significant interaction between room and path ($p = .367$), indicating that there was no order effect according to path (see Table 12).

Thoughts About Smoking

Figure 8 graphically depicts mean level of thoughts about smoking for each room.



*$p < .001$ (Office vs. N1; Office vs. N2)
**$p < .001$ (Party vs. N1; Party vs. N2)

Figure 8. Mean level of thoughts about smoking by room.

Overall, room was found to have a significant effect on thoughts about smoking: $F(3,60) = 22.004$, $p < .001$. Table 13 presents the ANOVA results.

Table 12

ANOVA Summary Table for Attention to Smell of Nicotine by Path

Source	df	SS	MS	F	p
Room	3	384.095	128.032	23.681	.000
Room x Path	3	17.429	5.810	1.075	.367
Error	57	308.167	5.406		

Table 13

ANOVA Summary Table for Thoughts About Smoking

Source	df	SS	MS	F	p
Room	3	289.952	96.651	22.004	.000
Error	60	263.548	4.392		

A significant overall linear trend was observed ($p < .03$). The assumption of sphericity was not violated ($p = .506$). It was found that thoughts about smoking were significantly higher in both the office building setting ($p < .001$) and the party setting ($p < .001$) than in either neutral room. Hence, this portion of hypothesis 5 was supported. There was no significant interaction between room and path ($p = .740$), indicating that there was no order effect according to path (see Table 14).

Table 14

ANOVA Summary Table for Thoughts About Smoking by Path

Source	df	SS	MS	F	p
Room	3	286.408	95.469	21.104	.000
Room x Path	3	5.693	1.898	.420	.740
Error	57	257.854	4.524		

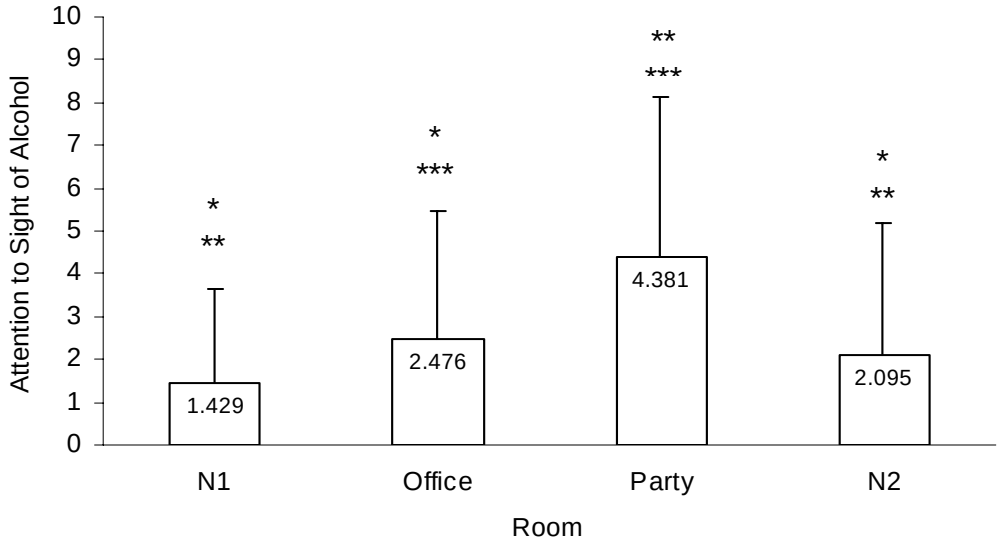
Hypothesis 6

- Self-reported degree of attention paid to *alcohol* cues will be significantly higher in virtual reality environments containing nicotine cues than in neutral cue environments.

Three one-way repeated measures ANOVAs were conducted (attention paid to the sight of alcohol, attention paid to the smell of alcohol, and thoughts about drinking) to determine whether attention to alcohol cues in cue rooms was significantly higher than attention to alcohol cues in neutral rooms.

Sight of Alcohol

Figure 9 graphically depicts mean level of attention paid to the sight of alcohol for each room.



*p < .001 (Office vs. N1; Office vs. N2)
**p < .001 (Party vs. N1; Party vs. N2)
***p < .03 (Office vs. Party)

Figure 9. Mean level of attention to sight of alcohol by room.

Overall, room was found to have a significant effect on attention paid to the sight of alcohol: $F(3,60) = 6.019$, $p < .001$. Table 15 presents the ANOVA results.

Table 15

ANOVA Summary Table for Attention to Sight of Alcohol

Source	df	SS	MS	F	p
Room	3	101.095	33.698	6.019	.001
Error	60	335.905	5.598		

No significant overall linear trend was found ($p = .182$). The assumption of sphericity was not violated ($p = .250$). It was found that attention to the sight of alcohol was significantly higher in the party room than in either neutral room ($p < .05$; $p < .01$). However, there was no significant difference between the office building setting and either neutral room ($p = .355$; $p = .500$). Hence, this portion of hypothesis 6 was partially supported. There was no significant interaction between room and path ($p = .496$), indicating that there was no order effect according to path (see Table 16).

Table 16

ANOVA Summary Table for Attention to Sight of Alcohol by Path

Source	df	SS	MS	F	p
Room	3	101.614	33.871	5.991	.001
Room x Path	3	13.662	4.554	.806	.496
Error	57	322.243	5.653		

Smell of Alcohol

Figure 10 graphically depicts mean level of attention paid to the smell of alcohol for each room.

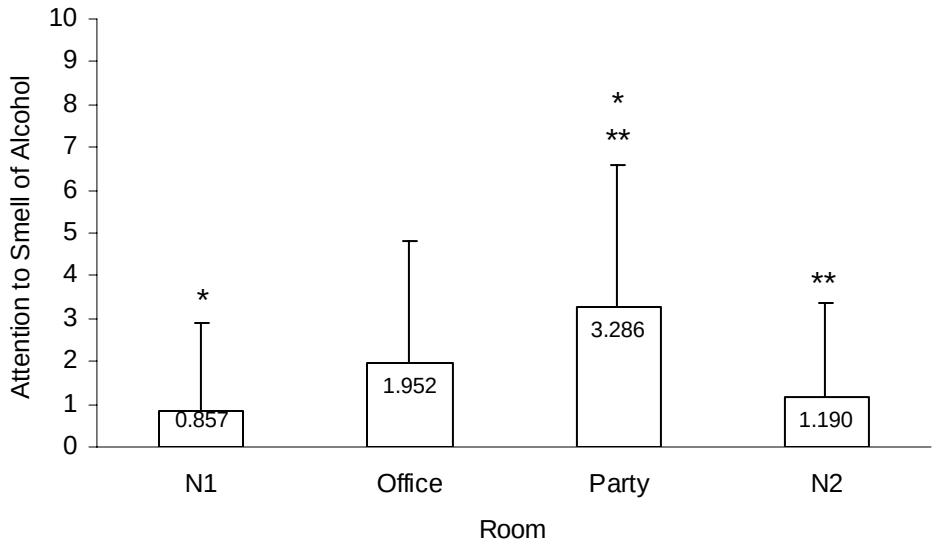


Figure 10. Mean level of attention to smell of alcohol by room.

Overall, room was found to have a significant effect on attention paid to the smell of alcohol: $F(3,60) = 5.339$, $p < .005$. Table 17 presents the ANOVA results.

Table 17

ANOVA Summary Table for Attention to Smell of Alcohol

Source	df	SS	MS	F	p
Room	3	73.274	24.425	5.339	.003
Error	60	274.476	4.575		

No significant overall linear trend was found ($p = .274$). The assumption of sphericity was not violated ($p = .923$). It was found that attention to the smell of alcohol was significantly higher in the party room than in either neutral room ($p < .005$; $p < .03$). However, there was no significant difference between the office building setting and either neutral room ($p = .340$; $p = .500$). Hence, this portion of hypothesis 6 was partially supported. There was no significant interaction between room and path ($p = .577$), indicating that there was no order effect according to path (see Table 18).

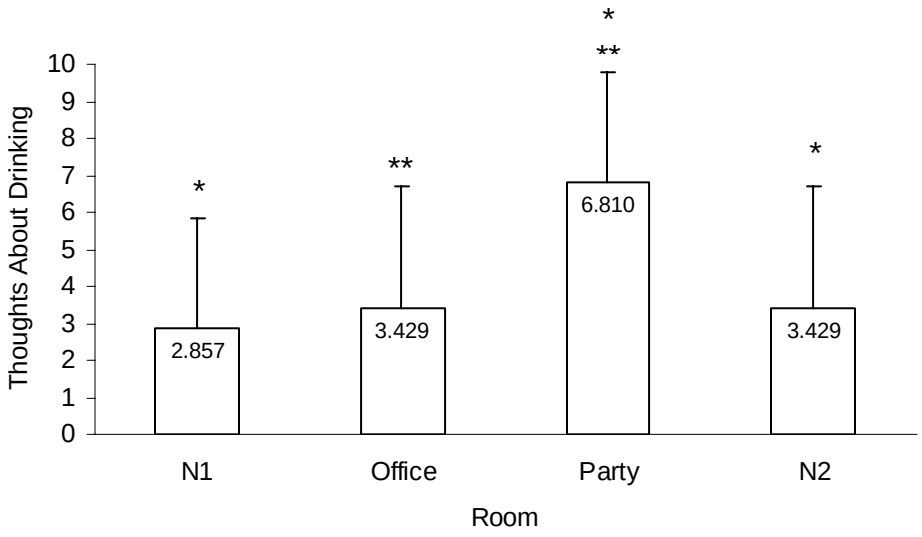
Table 18

ANOVA Summary Table for Attention to Smell of Alcohol by Path

Source	df	SS	MS	F	p
Room	3	67.003	22.334	4.801	.005
Room x Path	3	9.289	3.096	.666	.577
Error	57	265.188	4.652		

Thoughts About Drinking

Figure 11 graphically depicts mean level of thoughts about drinking for each room.



*p < .001 (Party vs. N1; Party vs. N2)
**p < .001 (Office vs. Party)

Figure 11. Mean level of thoughts about drinking by room.

Overall, room was found to have a significant effect on thoughts about drinking: $F(3,60) = 9.177$, $p < .001$. Table 19 presents the ANOVA results.

Table 19

ANOVA Summary Table for Thoughts About Drinking

Source	df	SS	MS	F	p
Room	3	205.464	68.488	9.177	.000
Error	60	447.786	7.463		

No overall linear trend was found (p = .066). The assumption of sphericity was not violated (p = .494). It was found that thoughts about drinking were significantly higher in the party room than in either neutral room (p < .001). However, there was no significant difference between the office building setting and either neutral room (p = .500). Hence, this portion of hypothesis 6 was partially supported. There was no significant interaction between room and path (p = .898), indicating that there was no order effect according to path (see Table 20).

Table 20

ANOVA Summary Table for Thoughts About Drinking by Path

Source	df	SS	MS	F	p
Room	3	204.217	68.072	8.755	.000
Room x Path	3	4.598	1.533	.197	.898
Error	57	443.187	7.775		

Hypothesis 7

- Self-reported degree of attention paid to *nicotine* cues will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons were made to determine whether attention paid to the sight of cigarettes, smell of cigarettes, and thoughts about smoking were higher in the alcohol-

appropriate party setting than the non-alcohol-appropriate office building setting. To adjust for multiple comparisons, the Bonferroni correction was used.

Sight of Cigarettes

No significant difference in attention paid to the sight of cigarettes was found between the two cue rooms ($p = .500$). Hence, this portion of hypothesis 7 was not supported.

Smell of Cigarettes

No significant difference in attention paid to the smell of cigarettes was found between the two cue rooms ($p = .500$). Hence, this portion of hypothesis 7 was not supported.

Thoughts About Smoking

No significant difference in thoughts about smoking was found between the two cue rooms ($p = .500$). Hence, this portion of hypothesis 7 was not supported.

Hypothesis 8

- Self-reported degree of attention paid to *alcohol* cues will be significantly higher in an alcohol-appropriate virtual reality context (party) than in one that is not alcohol-appropriate (exterior of office building).

Pairwise comparisons were made to determine whether attention paid to the sight of alcohol, smell of alcohol, and thoughts about drinking were higher in the alcohol-appropriate party setting than the non-alcohol-appropriate office building setting. To adjust for multiple comparisons, the Bonferroni correction was used.

Sight of Alcohol

Attention paid to the sight of alcohol was found to be significantly higher in the party than in the office building ($p > .03$). Hence, this portion of hypothesis 8 was supported.

Smell of Alcohol

No significant difference in attention paid to the smell of alcohol was found between the two cue rooms ($p = .145$). Hence, this portion of hypothesis 8 was not supported.

Thoughts About Drinking

Thoughts about drinking were found to be significantly higher in the party setting than the office building ($p < .001$). Hence, this portion of hypothesis 8 was supported.

CHAPTER FIVE

DISCUSSION

In this chapter, the study findings are summarized and discussed, as are some of the limitations of the study. Implications for both research and practice for social workers and other helping professionals are presented. Finally, suggestions for future research are offered.

Summary of Results

The major findings of the study are summarized below, organized by craving and attentional variables.

Craving

Four of the eight study hypotheses focused on craving for nicotine and alcohol in response to VR cue rooms. It was found that, as predicted in the first hypothesis, craving for nicotine was significantly elevated after exposure to both the party and the office building environments as compared to the first neutral room ($p < .01$). There was no significant difference between craving for nicotine after the cue rooms than after the second neutral room, however, indicating that craving did not return to baseline levels.

Craving for alcohol was not found to differ significantly by room ($p = .099$). This contradicts the second hypothesis, which predicted that craving for alcohol would be elicited by the presentation of nicotine cues.

The third and fourth study hypotheses predicted that craving for nicotine and alcohol would be higher following the party than the office building. This was not found to be the case

for nicotine craving, which was virtually identical between the two cue rooms (44.7 office vs. 46.0 party; $p = .500$).

In addition, no statistically significant difference was found in alcohol craving between the two cue rooms ($p = .218$). It is worth noting, however, that there is an observable difference in alcohol craving between the two rooms (43.1 office vs. 56.4 party), which may indicate a trend that with greater statistical power would reach statistical significance.

Attention to Cues

The remaining four study hypotheses addressed attention to visual and olfactory cues, and thoughts about smoking or drinking. The relevant findings are categorized below by sight, smell and thoughts.

Sight

Attention to the sight of nicotine was found to be significantly elevated in both cue rooms as compared to either neutral room ($p < .001$), as predicted in hypothesis 5.

Hypothesis 7 predicted that attention paid to the sight of nicotine would be higher in the party than in the office building; this was not found to be the case, as the ratings were identical for both (7.9).

Attention to the sight of alcohol was also found to be significantly elevated in both cue rooms as compared to either neutral room ($p < .001$), as predicted in hypothesis 6.

As predicted in hypothesis 8, attention to the sight of alcohol was found to be significantly higher in the party than the office building ($p < .03$).

Smell

Attention to the smell of nicotine was found to be significantly elevated for both cue rooms as compared to either neutral room ($p < .001$), as predicted in hypothesis 5.

Hypothesis 7's prediction that attention to the smell of nicotine would be higher in the party than in the office building, however, was not statistically demonstrated ($p = .500$).

Attention to the smell of alcohol was found to be significantly elevated in both cue rooms as compared to either neutral room ($p < .03$), as predicted in hypothesis 6.

Hypothesis 8's prediction that attention to the smell of alcohol would be greater in the party than the office building was not upheld, however, as no significant difference was observed between attention paid to the smell of alcohol in the two cue rooms ($p = .145$). It is worth noting that there is an observable difference between the two rooms (2.0 office vs. 3.3 party), which may indicate a trend that with greater statistical power would reach statistical significance.

Thoughts

Thoughts about smoking were found to be significantly elevated in both cue rooms as compared to either neutral room ($p < .001$), as predicted in hypothesis 5.

Hypothesis 7 predicted that thoughts about smoking would be higher in the party than in the office building; this was not found to be the case ($p = .500$).

Thoughts about drinking were found to be significantly elevated in both cue rooms as compared to either neutral room ($p < .001$), as predicted in hypothesis 6.

It was predicted in hypothesis 8 that thoughts about drinking would be higher in the party than in the office building, and this was found to be the case ($p < .001$).

Discussion of Results

This study examined the effect of exposure to virtual reality smoking cues on craving for nicotine and alcohol in a sample of 21 nicotine dependent problem drinkers. Two-thirds of the participants (14) identified as African American, and 13 were male. The mean age was approximately 39. Participants consumed an average of nearly 6 standard alcoholic drinks and

almost 16 cigarettes per day, and had, on average, a low to medium level of alcohol dependence and a high level of nicotine dependence. More than 95% (20) of participants met *DSM-IV* (APA, 1994) criteria for alcohol dependence; the remaining participant met criteria for alcohol abuse. These characteristics are in line with study inclusion/exclusion criteria, which required that participants smoke at least 10 cigarettes per day and meet *DSM-IV* (APA, 1994) criteria for alcohol abuse or dependence. Participants reported being highly immersed in the VR environment.

Participants were randomly assigned to one of two paths through the VR environment. The only difference between the paths was the order of presentation of the two cue rooms; all other aspects of the VR exposure were identical. Twelve participants were assigned to path 1 and 9 to path 2. There was a statistically significant difference between the groups in terms of gender, as the path 1 group consisted of 10 males and 2 females, and the path 2 group consisted of 3 males and 6 females. Pretrial, no statistically significant differences were found in ethnicity, age, level of alcohol or nicotine dependence, baseline craving for alcohol or nicotine, age of initiation of drinking or smoking behavior, number of cigarettes or drinks per day, or level of immersion in the VR environment. Path was also not found to have any effect on craving or attention to cues during VR exposure.

Participants were exposed to a series of four cue rooms, two neutral and two with nicotine cues. The neutral rooms were encountered at the beginning and the end of the exposure, with the two cue rooms being presented in between the neutral rooms. The neutral rooms, which were identical to each other, consisted of an empty room in which participants were shown two brief educational nature videos. The cue rooms consisted of an office building courtyard and a party setting. Nicotine cues were present in both cue environments, including cigarettes,

ashtrays, lighters, the smell of smoke, and people smoking. Neither cue environment contained overt alcohol cues, though one was an alcohol-appropriate setting (party) while the other was not (office building).

Nicotine Findings

The prediction that exposure to nicotine cues would elicit greater reactivity (in the form of nicotine craving, attention to visual and olfactory nicotine cues, and thoughts about smoking) as compared to neutral cues was largely upheld. The prediction that exposure to an alcohol-appropriate setting (party) would elicit greater nicotine reactivity than exposure to a non-alcohol appropriate setting (office building courtyard), however, was not upheld.

Cue Environments vs. Neutral Environments

A statistically significant increase in craving for nicotine after exposure to the cue rooms vs. the first neutral room was observed. This finding is in agreement with the majority of cue exposure literature (e.g., Bordnick, Graap, Copp, Logue et al., 2004; Bordnick, Graap et al., 2005; Colby et al., 2004; Conklin, 2006), which suggests that repeated pairing of nicotine-related stimuli and pleasurable smoking experiences leads to the creation of conditioned responses to nicotine-related stimuli, and the rewarding aspect of smoking leads to the creation of an operant response, wherein the smoker seeks to replicate the experience in hopes of achieving the same pleasant outcome. This, the first known study of reactivity to VR nicotine cues in polysubstance users, indicates that VR cue exposure is effective with individuals who use more than one type of substance. Additional research into different combinations of drugs and alcohol is indicated.

The observed increase in nicotine craving following exposure to nicotine cues is bolstered by the finding that attention to both the sight and smell of nicotine was higher in the cue rooms than in the neutral rooms. Given the presence of both visual and olfactory nicotine

cues in the cue rooms (and the absence thereof in the neutral rooms), this finding is also in line with the cue reactivity paradigm. In addition, the higher reported level of thoughts about smoking in the cue rooms vs. the neutral rooms also concurs with the cue reactivity paradigm.

The finding that nicotine craving failed to return to baseline levels after exposure to the second neutral room, however, does not initially appear to be in agreement with other similar VR cue reactivity studies (Bordnick, Graap, Copp, Brooks et al., 2004; Bordnick, Graap et al., 2005; Bordnick et al., in review), which found that craving levels in both smokers and drinkers returned to baseline levels after exposure to the second neutral room. This may indicate a potential difference between craving in monosubstance users (e.g., smokers only or drinkers only) and polysubstance users (here, nicotine dependent problem drinkers: craving in polysubstance users may persist longer, and may therefore increase the risk of relapse, or increase the difficulty of maintaining abstinence, for former polysubstance users in recovery. This difference, if observed in additional studies with larger sample sizes, would have significant implications for treatment of alcohol addiction, given the substantial portion of problem drinkers who are also smokers. It may be that drinkers who are also smokers need additional coping skills training and/or more rigorous extinction training than nonsmokers in order to achieve abstinence and prevent relapse, as their craving may be intensified by the interacting effects of alcohol and nicotine stimuli (cross-cue reactivity). Drinkers who smoke may also have formed more powerful conditioned responses to these stimuli due to the compounding effect of simultaneous nicotine and alcohol use. Additional research on different combinations of drug and alcohol use is indicated to determine how other combinations affect craving.

Alcohol-Appropriate Environment vs. Non-Alcohol Appropriate Environment

Several study hypotheses predicted that nicotine craving, attention to visual and olfactory nicotine cues, and thoughts about smoking would be higher in the party setting than in the office building setting. These predictions were made because it was thought that an alcohol-appropriate environment (party) might stimulate greater nicotine reactivity due to the compounding effect of a history of simultaneous use; however, this was not observed. This may indicate that nicotine craving is not affected by reactivity to alcohol cues. It may also indicate that for nicotine dependent drinkers, the primary contribution of environmental context to cue reactivity is simply the establishment of nicotine appropriateness. There may be a "ceiling effect" in these individuals, wherein the addition of alcohol appropriateness does not increase craving for, attention to, or thoughts about using nicotine any further. Future studies may wish to evaluate whether reactivity to nicotine cues is affected by actual *consumption* of alcohol, rather than simply exposure to the *potential* for consumption of alcohol.

Alcohol Findings

The prediction that exposure to alcohol cues would elicit reactivity (in the form of alcohol craving, attention to visual and olfactory alcohol cues, and thoughts about drinking) as compared to neutral cues was partially upheld, in that there was no significant difference between craving for alcohol in the cue rooms vs. either neutral room; however, a statistically significant increase in attention to the sight of alcohol, attention to the smell of alcohol, and thoughts about drinking after the cue rooms vs. both neutral rooms was observed. Further, the prediction that exposure to an alcohol-appropriate setting (party) would elicit greater alcohol reactivity than exposure to a non-alcohol appropriate setting (office building courtyard) was upheld.

Cue Environments vs. Neutral Environments

No significant difference in alcohol craving was observed following the cue rooms vs. either neutral room. It is possible that nicotine cues do not stimulate alcohol craving in nicotine dependent problem drinkers, indicating that cross-cue reactivity may not be a factor in assessment and treatment of this population. An alternate explanation for this finding, however, could be that participants were asked to abstain from alcohol use for 12 hours prior to their appointment. Hence, these participants, 95% of whom met DSM-IV (APA, 1994) criteria for alcohol dependence, may have had such a high baseline craving for alcohol due to the onset of withdrawal symptoms that exposure to cues failed to significantly increase their level of craving. In contrast, participants were asked to smoke one cigarette immediately prior to entering the VR environment, which may have led to lower initial levels of craving for nicotine (and, hence, allowed for demonstration of reactivity elicited by VR cues). Future studies incorporating pre-exposure priming with alcohol as well as nicotine are needed to determine whether nicotine cues can elicit alcohol craving in this population.

The findings concerning attention to alcohol cues and thoughts about drinking seem to support the suggestion that deprivation contributed to artificially high initial craving ratings, as increased reactivity, in the form of elevated attention to visual and olfactory alcohol cues and thoughts about drinking, was observed after exposure to the cue rooms vs. neutral rooms. These findings are particularly interesting because there were *no overt alcohol cues* at any point in the VR environments; yet, participants reported greater attention to both the sight and smell of alcohol in both cue rooms than in either neutral room. This may be the most compelling finding as pertains to cross-cue reactivity, as it appears that the presence of visual and olfactory nicotine

cues may have inspired participants to “fill in the blanks,” imagining that they had both seen and smelled alcohol where there was none.

A number of participants indicated that they thought they saw alcoholic drinks in the party setting, often stating that they assumed that the colorful plastic cups some partygoers were holding contained alcoholic beverages. The presence of these somewhat ambiguous cues could account for the increased attention to visual alcohol cues in the party setting. In the office building setting, however, it is more difficult to identify any objects or situations which could be identified as alcohol or alcohol-related, yet participants reported a greater degree of attention to the sight of alcohol in this setting than in the neutral rooms. Further, a significant increase in thoughts about drinking after both cues rooms as compared to either neutral room was observed. This seems to support the concept of cross-cue reactivity, as it appears that exposure to “pure” nicotine cues, even in a non-alcohol appropriate context, can affect alcohol reactivity. If these findings are replicated in future studies, this could have substantial implications for treatment of nicotine dependent problem drinkers, who may not be aware that exposure to nicotine cues, even in “safe” (non-alcohol appropriate) environments, may trigger reactivity, which may in turn increase the risk of relapse.

Alcohol-Appropriate Environment vs. Non-Alcohol Appropriate Environment

Several study hypotheses predicted that alcohol craving, attention to visual and olfactory nicotine cues, and thoughts about drinking would be higher in the party setting than in the office building setting. These predictions were made because it was thought that an alcohol-appropriate (party) setting might stimulate greater alcohol reactivity than a non-alcohol appropriate (office building) setting, due to conditioned reactivity developed after repeated exposure to other

drinking situations in alcohol-appropriate environments. Like the predictions concerning alcohol reactivity in cue rooms vs. neutral rooms, these predictions were partially upheld.

Attention to the sight of alcohol was found to be significantly higher in the party setting than in the office building setting, as were thoughts about drinking. These findings are likely due to the fact that drinking behavior is common in a party setting and less common in an office building setting, and therefore participants were exhibiting preestablished conditioned responses to the alcohol-appropriate party setting based upon their prior experiences. If so, this suggests that future research into environmental context of cues is needed in order to improve assessment and treatment of alcohol addiction, by determining whether and how environmental context should be incorporated into treatment settings.

While there was no statistically significant difference between alcohol craving ratings following exposure to the party and the office building, the mean party rating was higher than the mean office rating. Similarly, there was no statistically significant difference between attention to the smell of alcohol between the two cue rooms, yet again the mean party rating was higher than the mean office rating. These findings merit future investigation using larger samples, which would yield greater statistical power. If replicated, these findings would suggest that contextual factors and cross-cue reactivity may play an important role in alcohol craving and reactivity in nicotine dependent problem drinkers, and perhaps other polydrug users as well.

Limitations

This study has a number of limitations. Perhaps most prominent is that of sample size, which was appropriate for a pilot study such as this but poses obvious barriers to statistical power and generalizability. A larger sample would yield both greater statistical power, thereby

allowing for observation of more subtle effects, and would increase the representativeness of the sample group in relation to the greater population of nicotine dependent problem drinkers.

Another significant limitation is the fact that the research laboratory was located at Georgia Gwinnett College, which is not accessible via public transportation. Many potential participants were not able to participate because they did not have their own transportation. Georgia Gwinnett College's location, more than 30 miles from downtown Atlanta, also proved to be a barrier to many participants, including those with their own transportation. Heavy commuter traffic daily after approximately 3pm discouraged a number of participants from both making and keeping appointments.

Another geographic limitation is that all participants live in or around the Atlanta metro area. It is possible that nicotine dependent problem drinkers from other regions of the state or the country may differ in ways that would affect the findings of this study.

A substantial no-show rate (> 50%) may indicate systematic bias, as there is no way to determine whether those who failed to keep their appointments differed significantly in any way than those who came at their scheduled time. A conservative assumption would be that a no-show rate this high must be treated as suggestive of systematic bias.

Inclusion/exclusion criteria may also be seen as a limitation. Potential participants with any significant physical health issues were disqualified, yet the population of nicotine dependent problem drinkers may reasonably be expected to suffer from a higher level of health problems than those who do not engage in these behaviors. In addition, potential participants with any significant mental health issues were also disqualified, yet many people with mental health conditions use substances such as nicotine and alcohol to self-medicate. It is possible, therefore,

that the sample for this study was not representative of the greater population of nicotine dependent problem drinkers in terms of physical and mental health.

All study participants were required to be able to read and understand the English language, which systematically excluded those who do not communicate in English.

The study relied heavily on computer technology, which may mean that the results were affected by participants' baseline level of familiarity and comfort with computers. In addition, the equipment and software necessary to create VR environments would probably be prohibitively expensive for many research and treatment settings.

This study utilized exclusively self-report measures, which may raise questions about the reliability of the data provided. Participants could have provided misleading information on their demographic and descriptive measures, the mental health screening, and/or the craving and attention ratings taken in VR. While we attempted to screen all data provided and clarify any potentially contradictory or unclear responses, it is certainly possible that participants could have given false responses.

When asked for suggestions to improve the VR environments, participants provided the following critiques: the cigarette smoke scent was not realistic; there should be more people at the party; the music at the party should be louder; some people at the party should be dancing; the people in both the party and office building should interact more with participants; the people should act more natural and relaxed; there should be greater peer pressure; there should be opportunities to make choices; and there should be more things going on in the cue rooms. In addition, most participants indicated that a party without alcohol was not realistic—however, they still craved both nicotine and alcohol in response to the party cue environment.

Implications for Social Work and Other Helping Professions

Despite its limitations, the findings of this study have important implications for both research and practice for helping professionals, including social workers. First, this is the first known study of cross-cue reactivity using VR, and part of a growing body of research into the importance of environmental factors to craving and use. Cross-cue reactivity is an important area for addiction researchers because people use substances in environments which are very different from traditional laboratory settings. Use of a substance—here, alcohol—typically occurs in an environment that incorporates specifically substance-related cues (e.g., a beer bottle or mixed drink), more general environmental cues (e.g., a sporting event on television, a bar setting, or cigarette smoke), and social interaction. Each of these includes visual, auditory, olfactory, and tactile elements, all of which interact in complex ways that are not yet fully understood by addiction researchers. It is still unknown how important each of these constituent parts is in the cycle of craving and use (which, itself, remains relatively opaque). VR is uniquely suited to help determine the relative importance of different kinds of stimuli, given its ability to replicate realistic complex environments (and to add and remove particular elements of those environments at will) in a controlled setting.

While this study did not find a statistically significant increase in craving for alcohol after exposure to nicotine cues, there was an observable increase in craving for alcohol in the alcohol-appropriate party setting, despite the absence of any overt alcohol cues (bottles, cans, etc.). This study did find statistically significant increases in attention to visual and olfactory alcohol cues in response to the two cue environments, neither of which actually contained any alcohol-specific cues of any kind. In addition, thoughts about drinking were significantly elevated in response to the two cue rooms. These observed increases in craving, attention, and thoughts suggest that

environmental context may play a substantial role in alcohol addiction—and, potentially, abuse of other substances as well—and should therefore be incorporated into research protocols.

This study also presents implications for the field of addiction treatment. The findings concerning the impact of environmental context on alcohol craving, attention, and thoughts may suggest that incorporation of more environmental factors is required in order to increase treatment efficacy. In addition, clients in treatment may need to be educated about the potential impact of environment upon their risk of relapse. Many alcoholics in recovery may not be aware that exposure to a "dry" party has the potential to stimulate craving or thoughts about alcohol. Many more might be surprised to know that simple exposure to nicotine cues, even in an alcohol-inappropriate environment such as an office building, also has the potential to elicit thoughts about drinking due to cross-cue reactivity. Perhaps avoidance of nicotine cues, including quitting smoking (if applicable), can decrease the risk of relapse. Additional research is clearly needed to further explore the potential implications of this small pilot study.

Suggestions for Future Research

This study has broken important ground in the areas of cross-cue reactivity and the role of environmental context in substance addiction, and highlights a number of ways to improve the efficacy of future such research. First and foremost, larger studies are needed, with substantially higher numbers of participants. Efforts should be made to conduct studies in locations and facilities that are accessible via public transportation, as this was the single most prominent factor barring potential participants from participating in the study. Additional studies in different regions of the country, and in languages other than English, are also necessary.

In future studies it may be important to consider including some participants with mental health diagnoses (e.g., depression) and/or physical health conditions (e.g., COPD) that are

common to nicotine dependent problem drinkers. This could increase the representativeness of the participant pool, thereby increasing the validity of future findings.

Adding more objective measures, such as blood or urine tests, to self-report measures may improve the reliability of the data collected. In addition, this study was not able to measure the impact of exposure to cues on actual use; future studies involving measurement of consumption or other evaluation of actual use patterns during and/or post exposure may yield additional information.

In summary, this study is important because it utilized new technology to investigate two relatively new factors in addiction research: cross-cue reactivity and environmental impact on craving, attention to cues, and thoughts about using. VR provides researchers and practitioners the previously unattainable ability to present complex cue environments, and to manipulate the details of these environments, in a safe and controlled setting. This study examined cues relevant to nicotine dependent problem drinkers; future studies can and should incorporate additional polydrug scenarios, which ultimately could be customized according to each person's use patterns. More research, both with and without VR, on cross-cue reactivity and the impact of environmental context on craving, attention, thoughts, and actual use of a range of substances is clearly needed.

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APPENDICES

APPENDIX A

Mini International Neuropsychiatric Interview

Overview Questions

- Have you been consistently depressed or down, most of the day, nearly every day, for the past two weeks? NO YES
- In the past two weeks, have you been less interested in most things or less able to enjoy the things you used to enjoy most of the time? NO YES
- Have you felt sad, low or depressed most of the time for the last two years? NO YES
- In the past month did you think that you would be better off dead or wish you were dead? NO YES
- Have you ever had a period of time when you were feeling 'up' or 'high' or so full of energy or full of yourself that you got into trouble, or that other people thought you were not your usual self? (Do not consider times when you were intoxicated on drugs or alcohol.) NO YES
- Have you ever been persistently irritable, for several days, so that you had arguments or verbal or physical fights, or shouted at people outside your family? Have you or others noticed that you have been more irritable or over reacted, compared to other people, even in situations that you felt were justified? NO YES
- Have you, on more than one occasion, had spells or attacks when you suddenly felt anxious, frightened, uncomfortable or uneasy, even in situations where most people would not feel that way? Did the spells peak within 10 minutes? CODE YES ONLY IF THE SPELLS PEAK WITHIN 10 MINUTES. NO YES
- Do you feel anxious or uneasy in places or situations where you might have a panic attack or panic-like symptoms, or where help might not be available or escape might be difficult: like being in a crowd, standing in a line (queue), when you are away from home or alone at home, or when crossing a bridge, traveling in a bus, train or car? NO YES
- In the past month were you fearful or embarrassed being watched, being the focus of attention, or fearful of being humiliated? This includes things like speaking in public, eating in public or with others, writing while someone watches, or being in social situations. NO YES
- In the past month have you been bothered by recurrent thoughts, impulses, or images that were unwanted, distasteful, inappropriate, intrusive, or distressing? (e.g., the idea that you were dirty, contaminated or had germs, or fear of contaminating others, or fear of harming someone even though you didn't want to, or fearing you would act on some impulse, or fear or superstition that you would be responsible for things going wrong, or obsession with sexual thoughts, images or impulses, or hoarding, collecting, or religious obsessions.) NO YES
- In the past month, did you do something repeatedly without being able to resist doing it, like washing or cleaning excessively, counting or checking things over and over, or repeating, collecting, or arranging things, or other superstitious rituals? NO YES
- Have you ever experienced or witnessed or had to deal with an extremely traumatic event that included actual or threatened death or serious injury to you or someone else? EXAMPLES OF TRAUMATIC EVENTS INCLUDE SERIOUS ACCIDENTS, SEXUAL OR PHYSICAL ASSAULT, A TERRORIST ATTACK, BEING HELD HOSTAGE, KIDNAPPING, FIRE, DISCOVERING A BODY, SUDDEN DEATH OF SOMEONE CLOSE TO YOU, WAR, OR NATURAL DISASTER. NO YES

- Did you respond to the trauma with intense fear, helplessness, or horror? NO YES
- During the past month, have you re-experienced the even in a distressing way (such as, dreams, intense recollections, flashbacks or physical reactions)? NO YES
- In the past 12 months, have you had 3 or more alcoholic drinks within a 3 hour period on 3 or more occasions? NO YES
- Now I am going to show you / READ THE LIST BELOW of street drugs or medicines. In the past 12 months, did you take any of these drugs more than once, to get high, to feel better, or to change your mood? NO YES

Amphetamines	Speed	Crystal Meth	Dexedrine	Ritalin, Diet Pills
Cocaine	Crack	Freebase		
Heroin	Morphine, Methadone	Opium	Demerol	Codeine, Percondan, OxyContin
LSD	Mescaline	PCP	MDMA	Ecstasy
Inhalants	Glue	Ether	GHB	Steroids
THC, Marijuana	Cannabis, Hashish	Grass		Barbiturates, Valium, Xanax, Ativan

- How tall are you? ____ inches
- What was your lowest weight in the past 3 months? ____ lbs
- IS PATIENT'S WEIGHT LOWER THAN THE THRESHOLD CORRESPONDING TO HIS/HER HEIGHT? SEE TABLE BELOW NO YES

FEMALES	4'10	4'11	5'0	5'1	5'3	5'4	5'5	5'6	5'7	5'8	5'9
Weight (lbs)	85	86	87	89	94	97	99	102	104	107	110
MALES	5'3	5'4	5'5	5'6	5'7	5'8	5'9	5'10	5'11	6'	6'1
Weight (lbs)	108	110	111	113	115	115	118	120	122	125	127

- In the past three months, did you have eating binges or times when you ate a very large amount of food within a 2-hour period? NO YES
- In the last 3 months, did you have eating binges as often as twice a week? NO YES
- Have you worried excessively or been anxious about several things over the past 6 months? NO YES

Alcohol Abuse and Dependence Module

J2 In the past 12 months:

a	Did you need to drink more in order to get the same effect that you got when you first started drinking?	NO YES
b	When you cut down on drinking did your hands shake, did you sweat or feel agitated? Did you drink to avoid these symptoms or to avoid being hungover, for example, "the shakes," sweating or agitation? IF YES TO EITHER, CODE YES.	NO YES
c	During the times when you drank alcohol, did you end up drinking more than you planned when you started?	NO YES
d	Have you tried to reduce or stop drinking alcohol but failed?	NO YES
e	On the days that you drank, did you spend substantial time in obtaining alcohol, drinking, or in recovering from the effects of alcohol?	NO YES
f	Did you spend less time working, enjoying hobbies, or being with others because of your drinking?	NO YES
g	Have you continued to drink even though you knew that the drinking caused you health or mental problems?	NO YES

ARE 3 OR MORE J2 ANSWERS CODED YES?

NO YES

ALCOHOL DEPENDENCE
CURRENT

J3 In the past 12 months:

a	Have you been intoxicated, high, or hungover more than once when you had other responsibilities at school, at work, or at home? Did this cause any problems? (CODE YES ONLY IF THIS CAUSED PROBLEMS.)	NO YES
b	Were you intoxicated more than once in any situation where you were physically at risk, for example, driving a car, riding a motorbike, using machinery, boating, etc.?	NO YES
c	Did you have legal problems more than once because of your drinking, for example, an arrest or disorderly conduct?	NO YES
d	Did you continue to drink even though your drinking caused problems with your family or other people?	NO YES

ARE 3 OR MORE J3 ANSWERS CODED YES?

NO YES

ALCOHOL ABUSE
CURRENT

APPENDIX B

Drinking History

BAL: _____

How many alcohol beverages do you consume per day? _____

How long have you used at this rate? _____

What age did you first start drinking? _____

What type of alcohol do you consume? _____

What brand do you prefer? _____

Does the type or brand of alcohol influence your desire to drink? YES NO

Did you ever quit drinking for a period longer than a few days? _____

How many past quit attempts have you had? _____

What caused you to start again? _____

_____

_____

Describe some situations where you drink:

1. _____

2. _____

3. _____

4. _____

5. _____

Are there any situations that make you think about or crave alcohol?

1. _____

2. _____

3. _____

4. _____

5. _____

List any objects (food, drinks, ash trays) that make you crave or want to drink:

1. _____

2. _____

3. _____

4. _____

5. _____

List any social places where you drink or that make you think about drinking:

1. _____

2. _____

3. _____

4. _____

5. _____

Do you ever anticipate drinking? _____

If yes, when (describe): _____

APPENDIX C

Smoking History

How many cigarettes do you consume per day? _____

How long have you used at this rate? _____

What age did you first start smoking? _____

What age did you start smoking regularly? _____

What brand do you prefer? _____

Does the type or brand of cigarettes influence your desire to smoke? YES NO

Did you ever quit smoking for a period longer than a few days? _____

How many past quit attempts have you had? _____

What caused you to start again? _____

_____

_____

Describe some situations where you smoke:

1. _____

2. _____

3. _____

4. _____

5. _____

Are there any situations that make you think about or crave cigarettes?

1. _____

2. _____

3. _____

4. _____

5. _____

List any objects (food, drinks, ash trays) that make you crave or want to smoke:

1. _____

2. _____

3. _____

4. _____

5. _____

List any social places where you smoke or that make you think about smoking:

1. _____

2. _____

3. _____

4. _____

5. _____

Do you ever anticipate smoking? _____

If yes, when (describe): _____

APPENDIX D

Nicotine Dependence Questionnaire

1. How soon after you wake up do you smoke your first cigarette?
   [ ] Within 5 minutes (3)
   [ ] 6-30 minutes (2)
   [ ] 31-60 minutes (1)
   [ ] After 60 minutes (0)

2. Do you find it difficult to refrain from smoking in places where it is forbidden?
   [ ] Yes (1)
   [ ] No (0)

3. Which cigarette would you hate most to give up?
   [ ] The first one in the morning (1)
   [ ] All others (0)

4. How many cigarettes/day do you smoke?
   [ ] 10 or less (0)
   [ ] 11-20 (1)
   [ ] 21-30 (2)
   [ ] 31 or more (3)

5. Do you smoke more frequently during the first hours after waking than during the rest of the day?
   [ ] Yes (1)
   [ ] No (0)

6. Do you smoke if you are so ill that you are in bed most of the day?
   [ ] Yes (1)
   [ ] No (0)

7. How often do you inhale the smoke from your cigarette?
   [ ] Never (0)
   [ ] Sometimes (1)
   [ ] Always (2)

8. What type of cigarette do you smoke?
   [ ] Low nicotine (0.9 mg or less) (1)
   [ ] Medium nicotine (1.0-1.2 mg) (2)
   [ ] High nicotine (1.3 mg or more) (3)

APPENDIX E

Alcohol Dependence Scale

INSTRUCTIONS:

1. Carefully read each question and the possible answers provided. Answer each question by circling the ONE choice that is most true for you.

2. The word "drinking" in a question refers to "drinking of alcoholic beverages."

3. Take as much time as you need. Work carefully, and try to finish as soon as possible. Please answer ALL questions.

These questions refer to the past 12 months

1. How much did you drink the last time you drank?
   a. Enough to get high or less
   b. Enough to get drunk
   c. Enough to pass out

2. Do you often have hangovers on Sunday or Monday mornings?
   a. No
   b. Yes

3. Have you had the "shakes" when sobering up (hands tremble, shake inside)?
   a. No
   b. Sometimes
   c. Often

4. Do you get physically sick (e.g., vomit, stomach cramps) as a result of drinking?
   a. No
   b. Sometimes
   c. Almost every time I drink

5. Have you had the "DTs" (delirium tremens) – that is, seen, felt or heard things not really there; felt very anxious, restless, and over excited?
   a. No
   b. Sometimes
   c. Several times

6. When you drink, do you stumble about, stagger, and weave?
   a. No
   b. Sometimes
   c. Often

7. As a result of drinking, have you felt overly hot and sweaty (feverish)?
   a. No
   b. Once
   c. Several times

8. As a result of drinking, have you seen things that were not really there?
   a. No
   b. Once
   c. Several times

9. Do you panic because you fear you may not have a drink when you need it?
   a. No
   b. Yes

10. Have you had blackouts ("loss of memory" without passing out) as a result of drinking?
   a. No, never
   b. Sometimes
   c. Often
   d. Almost every time I drink

11. Do you carry a bottle with you or keep one close at hand?
    a. No
    b. Some of the time
    c. Most of the time

12. After a period of abstinence (not drinking), do you end up drinking heavily again?
    a. No
    b. Sometimes
    c. Almost every time I drink

13. In the past 12 months, have you passed out as a result of drinking?
    a. No
    b. Once
    c. More than once

14. Have you had a convulsion (fit) following a period of drinking?
    a. No
    b. Yes
    c. Several times

15. Do you drink throughout the day?
    a. No
    b. Yes

16. After drinking heavily, has your thinking been fuzzy or unclear?
    a. No
    b. Yes, but only for a few hours
    c. Yes, for one or two days
    d. Yes, for many days

17. As a result of drinking, have you felt your heart beating rapidly?
    a. No
    b. Yes
    c. Several times

18. Do you almost constantly think about drinking and alcohol?
    a. No
    b. Yes

19. As a result of drinking, have you heard “things” that were not really there?
    a. No
    b. Yes
    c. Several times

20. Have you had weird and frightening sensations when drinking?
    a. No
    b. Once or twice
    c. Often

21. As a result of drinking have you “felt things” crawling on you that were not really there (e.g., bugs, spiders)?
    a. No
    b. Yes
    c. Several times

22. With respect to blackouts (loss of memory):
    a. Have never had a blackout
    b. Have had blackouts that last less than an hour
    c. Have had blackouts that last for several hours
    d. Have had blackouts that last a day or more

23. Have you tried to cut down on your drinking but failed?
    a. No
    b. Once
    c. Several times

24. Do you gulp drinks (drink quickly)?
    a. No
    b. Yes

25. After taking one or two drinks, can you usually stop?
    a. Yes
    b. No

APPENDIX F

Alcohol and Nicotine Craving Scales

For each of the following questions, please make one slash mark through the line that best represents your level of craving AT THIS TIME.

1. What is your current level of craving for cigarettes?

_____

None More than ever ____ mm

2. What is your current level of craving for alcohol?

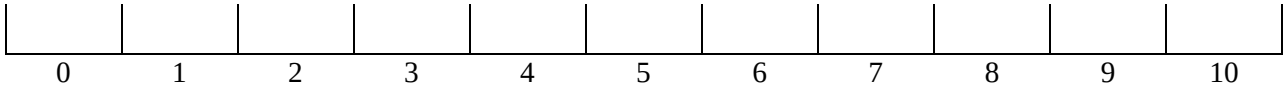
_____

None More than ever ____ mm

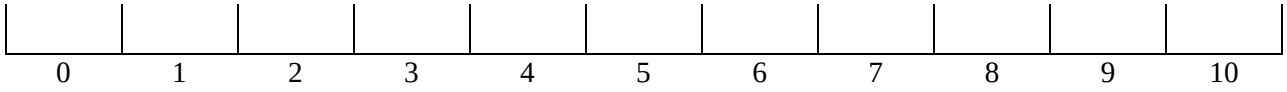
APPENDIX G

Alcohol and Nicotine Attention Scales

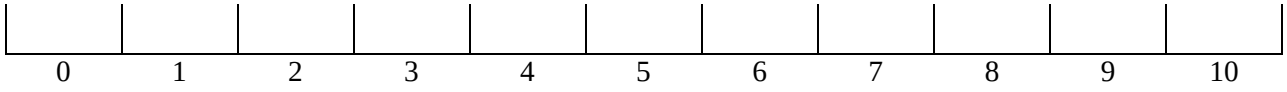
How much did you pay attention to the sight of alcohol in the room?



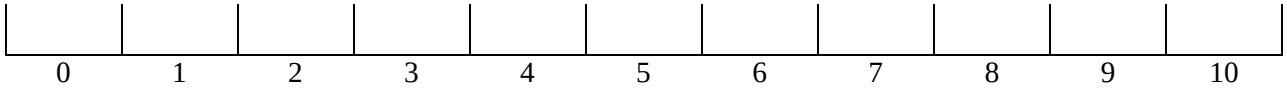
How much did you pay attention to the smell of alcohol in the room?



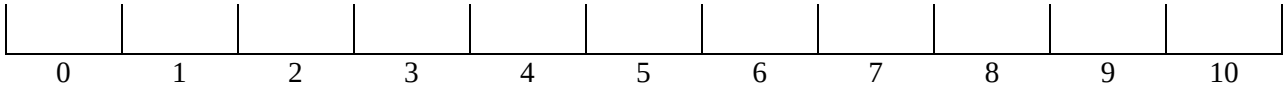
How much did you think about drinking alcohol while you were in the room?



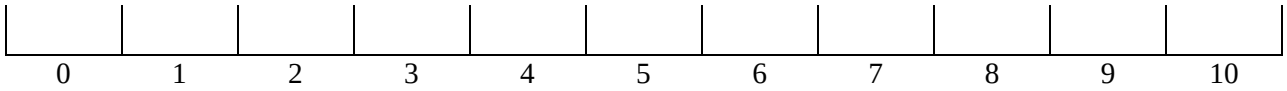
How much did you pay attention to the sight of cigarettes in the room?



How much did you pay attention to the smell of cigarettes in the room?



How much did you think about smoking cigarettes while you were in the room?



APPENDIX H

Imagery Realism Presence Questionnaire-Revised

Characterize your experience in the virtual environment by circling the appropriate number on this 7-point scale, in accordance with the question content and descriptive levels. Please consider the entire scale when making your responses, as the intermediate levels may apply. Answer the questions independently in the order that they appear. Do not skip questions or return to a previous question to change your answer.

With regard to the virtual environment…

1. How natural did your interactions with the environment seem?

1	2	3	4	5	6	7
Extremely artificial			Borderline			Completely natural

2. How much did the visual aspects of the environment involve you?

1	2	3	4	5	6	7
Not at all			Somewhat			Completely

3. How much did the auditory aspects of the environment involve you?

1	2	3	4	5	6	7
Not at all			Somewhat			Completely

4. How much did your experiences in the virtual environment seem consistent with your real world experiences?

1	2	3	4	5	6	7
Not consistent			Moderately consistent			Very consistent

5. How completely were you able to actively survey or search the environment using vision?

1	2	3	4	5	6	7
Not at all			Somewhat			Completely

6. How well could you identify sounds?

1	2	3	4	5	6	7
Not at all			Somewhat			Completely

7. How involved were you in the virtual environment experience?

1	2	3	4	5	6	7
Not involved			Mildly involved			Completely engrossed

8. How much delay did you experience between your actions and expected outcomes?

1	2	3	4	5	6	7
No delays			Moderate delays			Long delays

9. How quickly did you adjust to the virtual environment experience?

1	2	3	4	5	6	7
Not at all			Slowly			Less than one minute

10. How completely were your senses engaged in this experience?

1	2	3	4	5	6	7
Not engaged			Mildly engaged			Completely engaged

11. To what extent did events occurring outside the virtual environment distract from your experience in the virtual environment?

1	2	3	4	5	6	7
Not at all			Moderately			Very much

12. Overall, how much did you focus on using the display and control devices instead of the virtual experience and experimental tasks?

1	2	3	4	5	6	7
Not at all			Moderately			Very much

13. Were you involved in the experimental task to the extent that you lost track of time?

1	2	3	4	5	6	7
Not at all			Somewhat			Completely

14. Were there moments during the virtual environment experience when you felt completely focused on the task or environment?

1	2	3	4	5	6	7
None			Occasionally			Frequently

15. Was the information provided through different senses in the virtual environment (e.g., vision, hearing, touch) consistent?

1	2	3	4	5	6	7
Not consistent			Somewhat consistent			Very consistent

APPENDIX I

Debriefing Form

Describe your reactions to the VR rooms:

N1 _____

Building (1) _____

Party (2) _____

N2 _____

Which situation would cause the highest craving for nicotine?

B (1) _____ P (2) _____

Which situation would cause the highest craving for alcohol?

B (1) _____ P (2) _____

Do you have any suggestions to improve these VR rooms/situations?

_____

_____

_____

Are you interested in referrals for treatment?

_____

_____

APPENDIX J

Telephone Pre-Screening

DATE OF CONTACT:	APPOINTMENT DATE/TIME:

Date: _____

Male (1) _____ Female (2) _____

Height: _____ inches Weight: _____ lbs. Age: _____ years

Race: _____ (1 = White, 2 = African American, 3 = Hispanic, 4 = other)

Occupation: _____

Referred to Study via: _____

MEDICAL STATUS	YES	NO
1. Do you have any problems with your health? If yes: _____	☐	☐
1a. Are you pregnant?	☐	☐
2. Are you on any regular medication? If yes: _____	☐	☐
3. Do you have any current or past history of *seizures or seizure disorders*? If yes: _____	☐	☐
4. Do you have any problems viewing computers or television (ex. multimedia)?	☐	☐
5. Do you have a fear of closed spaces or would you be unable to wear a VR helmet?	☐	☐

CURRENT USE OF ALCOHOL ***Yes*** ***No***

6. Do you drink alcohol ? □ □

7. What is your usual brand name(s)? _____

8. What do you normally drink? (beer, liquor, wine, other) _____

9. What is your preferred drink? _____

DRINKING PATTERN

10. How many alcohol beverages, on average, do you drink each DAY? _____

11. How many alcohol beverages do you drink each WEEK? _____

12. Are you currently in alcohol treatment or attending AA? _____

CURRENT USE OF TOBACCO PRODUCTS ***Yes*** ***No***

13. Do you use tobacco products? □ □
14. Do you smoke cigarettes? □ □

15. If yes, what is your usual brand name(s)? _____

16. Lights or regular? _____ (Lights = 1, Regular = 2)

17. Non-filtered or filtered? _____ (Non-filtered = 1, Filtered = 2)

18. Menthol or non-menthol? _____ (Menthol = 1, Non-menthol = 2)

19. Regulars, Kings, 100s, or 120s? _____ (R = 1, K = 2, 100 = 3, 120 = 4)

20. How many cigarettes, on average, do you smoke each DAY? _____

21. How many cigarettes, on average, do you smoke each WEEK? _____

22. Are you currently in any type of stop smoking treatment? _____

PRESENT DRUG USAGE

23. Are you using or have you used any legal or illegal drugs like *(opiates, cocaine, amphetamines, barbiturates, benzodiazepines, marijuana, prescription drugs, or non-prescription drugs) in the past month?
Yes □ No □

PAST/PRESENT PSYCHIATRIC PROBLEMS

24. Have you ever been treated for psychiatric problems? Yes □ No □

25. Any current problems? If yes, _____

OTHER ENROLLMENT FACTORS

26. Can you read and write in the English language? Yes □ No □

27. Can you arrange transportation to Georgia Gwinnett College? Yes □ No □

28. Have you participated in a study trial in the past month? Yes □ No □

APPENDIX K

Informed Consent Form

Introduction

I agree to participate in a research study titled "Using Virtual Reality to Investigate Cross-Cue Reactivity and Environmental Cues in Nicotine Dependent Problem Drinkers" which is being conducted by Hilary Copp, University of Georgia, School of Social Work, 678-407-5517, under the direction of Dr. Patrick Bordnick. University of Georgia, School of Social Work, 678-407-5517. My participation is voluntary: I can refuse to participate or stop taking part at any time without giving any reason, and without penalty. I can ask to have information related to me returned to me, removed from research records, or destroyed.

Description/purpose of the study

The purpose of the study is to explore a new technology (virtual reality cue reactivity) for use in studying the effects of exposure to nicotine and alcohol cues on related craving, mood, and physiological body changes including heart rate and sweating. The relationship between craving for nicotine or alcohol and actual use has not been determined, and this study will focus on collection of information to further this knowledge.

Procedures:

If you are eligible to participate you will be enrolled in this research study.

Pre-Study Screening:

In order to determine if you qualify for this study, you will be asked to complete questionnaires and rating scales about your use of alcohol and other drugs. You will also be asked to complete rating scales about your craving, mood, and psychological well-being. You will also be asked questions about illegal drug use during the intake interview. If you qualify for this study and meet the eligibility criteria you will be asked to participate and enrolled. Upon enrollment, you will be asked to complete an initial 10-minute virtual reality (VR) session to familiarize yourself with the VR experience and the rating scales. Upon completion of the initial VR session, you will complete the virtual reality cue reactivity (VRCR-AD) session. You will be asked at all study visits (if more than one) to provide a breath sample that will be tested for alcohol use levels. You are expected not to drink alcohol or be intoxicated on any days that you have study appointments.

VRCR-AD Session:

You will have a scheduled appointment time between 9:00 am and 6:00 pm. Upon arrival you will be asked provide a breath sample to ensure that you are not currently drinking or intoxicated. If your breath sample has a reading over 0.00, you will be asked not to participate on that day, and provided transportation home (taxi). Upon completion of the breath sample

procedure, you will be asked to go outside and smoke one cigarette. When you return, you will enter the testing room and be seated in a comfortable, non-reclining chair. A member of the research staff will place monitoring pads on your skin for monitoring your heart rate and skin surface (sweating). You will be asked to put on the virtual reality (VR) head mounted display, which is like a hat/helmet with mini-television screens in front of your eyes and make adjustments for comfort. The VR helmet is equipped with two-way audio and with a monitored video display. You will be asked to relax until the VR session begins (approximately 5 minutes). You will hold a hand controller in your dominant hand. At the start of the VR session you will complete the baseline measures: nicotine craving scale, alcohol craving scale, nicotine attention scale, and alcohol attention scale. During the VR session, you will be exposed to 4 VR settings (2 neutral and 2 nicotine related), which will include visual, audio, and scent cues. The neutral settings consist of a room/hallway in which you can look around and move without the presence of nicotine cues. The 2 nicotine cue rooms include: the outside of a virtual office building, where people are talking and smoking, and a party setting, where people are smoking and will offer you a cigarette. There will be no actual nicotine offered in this study, only virtual cues. After each cue room you will complete self-report ratings using the hand controller. At the end of the VR session, sensors will be removed and you will complete questionnaires on VRAA task. You will be exposed to a virtual room that is divided into 4 sections. Two of the sections contain virtual smoking cues (i.e. virtual cigarettes, packs, ashtrays, etc.) and two sections contain virtual neutral cues (i.e. aquarium, flowers). You will be asked to explore the room freely using the hand controller for 5 minutes. Upon completion of the VR session you will de-brief (talk) with a Ph.D.- or masters-level clinician. The total time in VR will be approximately 30-45 minutes.

Possible benefits:

Your participation in this study may possibly lead to a more in-depth understanding of your drinking and alcohol craving, and may benefit others seeking treatment in the future. You may also learn about your own drinking behavior. You may also receive no direct benefit from your participation in this study.

Study participation and termination:

Your participation in this study is voluntary. You may refuse to participate. If you choose to participate, you can change your mind at any time and withdraw from the study. In either case, you will not be penalized nor lose any benefit to which you are otherwise entitled. You will be informed of any new findings that might lead you to reconsider whether or not you want to continue in this trial. If you arrive at the research center intoxicated, you will be asked not to participate, and transportation will be provided via taxi home.

Possible risks and discomforts:

There is the possibility of psychological effects from being asked and responding to sensitive questions during interviews. Some of these questions will be about drug use, legal problems, or your family. Exposure to VR nicotine-related scenarios/scenes may lead to increases in craving and urges, which may or may not lead to actual smoking post VR session. Data on the relationship between VR cue exposure, craving, and increases in actual use post exposure remain

unclear. You will be given a debriefing statement to take with you post VR session that further explains craving and alcohol use. You may experience mild anxiety or craving in the VRCR-AD session. You will be exposed to cues that you are familiar with and already experience in your daily life. Some participants in the past have reported slight nausea due to "simulator sickness." However, simulator sickness has not been a problem in any of the controlled studies now using VR for mental health. Since VR is a new medium for cue exposure, it is possible there are risks that are unknown at this time.

Time commitments:

This research study will last 1 day. You will be required to attend the clinic for the intake screening interview and a VR session. The screening interview and VR session (including debriefing) visit will last about 1-3 hours.

Financial considerations:

You will be paid $10.00 for the intake screening, and $40.00 for completing the VR session and assessment instruments (total for completing all requirements $50.00). You will also receive free parking during study participation visits.

In order to pay you for your participation, we need to collect your name, mailing address, and your social security number (per UGA Accounts Payable Honoraria and Fees Information Sheet, July 2005) on a separate payment form which will be provided to the School of Social Work business office and then forwarded to the UGA business office. We have been informed that these offices will keep your information private, but may have to release your name and the amount of compensation paid to you to the IRS, if ever asked. They will not, however, release any information regarding the particular study in which you participated. The VRCRC and researchers connected with this study have gone to great lengths to protect your information and will keep your name and information confidential in our locked files. However, we are not responsible once your name, mailing address, and social security number leave our center for payment, as required by the UGA business office.

I realize that if I do not provide this information, I will not be compensated. I also understand that if I decide not to provide the requested information and I waive my right to compensation, I can still take part in the research study.

_____ (Please put your initials.) *I do not want to provide my name, mailing address, and social security number for payment purposes. I understand that I will not be compensated for my participation.*

Compensation for injury:

No compensation is available for injury during this study. All research related injuries should be reported to Dr. Patrick Bordnick 678-407-5517.

Confidentiality:

Only the investigators in this study will have access to research records, which contain your identity. This information is kept strictly confidential (unless required by law) to protect your identity. Your identity will not be revealed in any publications based on this study.

Your Rights :

If you have any questions regarding the project or your participation, you may contact Hilary Copp at 678-407-5517. You agree that you have had the opportunity to ask questions about study-related procedures. You agree that you have spoken with research personnel, and that they have answered your questions to your satisfaction concerning this study. You agree that based on this information, your consent to participate in this study is voluntary.

I understand the procedures described above. My questions have been answered to my satisfaction, and I agree to participate in this study. I have been given a copy of this form.

_____	_____	_____
Name of researcher	Signature	Date

Telephone: _____

Email: _____

_____	_____	_____
Name of participant	Signature	Date

Please sign both copies, keep one and return one to the researcher.

Additional questions or problems regarding your rights as a research participant should be addressed to The Chairperson, Institutional Review Board, University of Georgia, 612 Boyd Graduate Studies Research Center, Athens, Georgia 30602-7411; Telephone (706) 542-3199; E-Mail Address IRB@uga.edu