Does simulated alcohol exposure through virtual reality cue-exposure therapy decrease state levels of alcohol craving and anxiety in patients with alcohol use disorder?

Jula Pauline Bernhard   s1779346

Faculty of Behavioral, Management and Social Sciences, University of Twente

Positive Clinical Psychology & Technology

Supervisor: Dr. Alexandra Ghiţă

Second Supervisor: Prof. Dr. Gerben Westerhof

Date: 19-07-2021

Abstract

Background: Excessive alcohol consumption is widespread around the world. Regarding addiction, Alcohol Use Disorder (AUD) is a mental health concern that can have many implications. Craving and anxiety are two commonly experienced symptoms of people who have AUD. While cue-exposure therapy (CET) is a recognized concept to treat those symptoms, in regards to alcohol, findings of its effectiveness are not consistent. Here, the use of virtual reality (VR) can aid to enhance people's presence and immersion into several situations. This is called VR-CET. It was assumed that craving and anxiety levels of participants decreased over time. Moreover, a correlation between the variables was expected at both time points. Hence, the study tries to fill the literature gap by focusing on the effects on craving and anxiety after VR-CET treatment with the novel ALCO-VR application.

Methods: 21 patients from the Addictive Behavior Unit of the Hospital Clinic of Barcelona, Spain were recruited by the lead psychologist. Participants were attending an initial assessment, six VR-CET sessions, and an assessment three days after the last therapy session. Baseline and posttest measures of craving and anxiety were assessed.

Results: Analysis revealed a significant reduction in state anxiety and state-alcohol craving after treatment with the ALCO-VR application. Moreover, anxiety and craving were positively correlating at baseline and post-VR-CET sessions.

Conclusion: Overall, the current study contributes to the ongoing research on the effectiveness of the ALCO-VR software by showing a reduction in participant's craving and anxiety levels. Due to prolonged exposure to several alcohol-related contexts and beverages, participants were able to reduce their state-alcohol craving and state anxiety after the sessions. Therefore, symptoms of AUD were successfully targeted through the training. This indicates that participants may be able to remain abstinent.

Keywords: Alcohol Use Disorder, Virtual Reality, Cue-Exposure Therapy, Craving, Anxiety

Table of Contents

Introduction

Alcohol is one of the most commonly used substances around the world. In economically developed countries, alcohol is often easily accessible and used to socialize with others, resulting in high consumption of the beverage (Connor et al., 2015; Wackernah et al., 2014). Alcohol Use Disorder (AUD) is a public health concern (Connor et al., 2015; Rehm et al., 2015). According to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM–5; American Psychiatric Association, APA, 2013), AUD is divided into three categories: *mild*, *moderate*, and *severe* (Hasin et al., 2013). From 2012 to 2013, approximately 29% of Americans fell under the criteria of AUD at some time in their lives (Grant et al., 2015). The *DSM-5* AUD criteria are a combination of the former *DSM-IV* diagnoses of alcohol abuse and dependence. Moreover, craving, known as the strong desire to drink, was added as a criterion of AUD (Barrick & Connors, 2002; Yoon et al., 2021). Besides craving, the other ten criteria concern the hazardous use of alcohol, dependence, tolerance, withdrawal effects, and impaired control in regards to alcohol use patterns (Hasin et al., 2013). Furthermore, interpersonal problems are considered and a general adverse effect on the person's life is likely to occur (Barrick & Connors, 2002). An AUD diagnosis is given when at least two of the eleven criteria are met throughout one year (APA, 2013, as cited in Hasin et al., 2013). The presence of six or more criteria indicates severe AUD (Campbell et al., 2018).

Moreover, heavy drinking may affect one's overall health. Generally, people diagnosed with AUD have a higher mortality risk than the general population (Roerecke & Rehm, 2014). According to Shield et al. (2014), alcohol consumption is related to several chronic conditions and diseases, for example, pancreas or cardiovascular diseases. It can also affect the brain and result in severe cognitive impairments (Spindler et al., 2021). Furthermore, AUD is highly comorbid with other mental health disorders which disables the affected individual even more (Connor et al., 2015; Grant et al., 2015). Despite the prevalence and consequences of AUD in society, it often remains untreated or treatment has only short-term effects (Grant et al., 2015; Wackernah et al., 2014).

Abstinence maintenance or controlled drinking is regarded as one of the intended outcomes of AUD treatment. Nevertheless, after completion of treatment, 37% of people *relapse* (return to initial drinking patterns) after 3-months and 28% after 12-months (Andersson et al., 2019; Bottlender & Soyka, 2004). Charney et al. (2010) stress the importance of finding out who is likely to relapse as people often slip or relapse in the first

four weeks of abstinence. Several *protective factors* are significant to maintain abstinence such as employment, being of older age, and a stable marital relationship (Pareaud et al., 2021). Conversely, *risk factors* for facilitating relapse are unemployment, being of younger age, using other drugs besides alcohol, being diagnosed with another mental health disorder, and experiencing high levels of craving (Pareaud et al., 2021; Sliedrecht et al., 2019). Thus, investigating the various risk factors more in-depth is crucial to better understand the causes of relapse.

Mechanisms of Alcohol Use Disorder

Craving for alcohol is one of the essential factors in AUD and a predictor for relapse. Craving is the uncontrollable desire for alcohol, often called 'pathological appetite' (Addolorato et al., 2005). Studies have shown a causal relationship between alcohol craving and alcohol consumption (Bottlender & Soyka, 2004; Pareaud et al., 2021; Stohs et al., 2019). Therefore, focusing on identifying and treating craving early into the treatment of AUD is essential. Bernard and colleagues (2021) indicate that people's thoughts and their behaviors regarding alcohol are associated. Thereby, craving is linked to poor inhibition and thought suppression (Bernard et al., 2021; Naim-Feil et al., 2014). Further, a causal relationship between rumination and craving has been found for alcohol-dependent people which leads to the maintenance of the disorder (Caselli et al., 2013). Nevertheless, many factors are significant in terms of craving elicitation.

For instance, studies have shown that people with AUD often experience anxiety. Thereby, negative emotions are likely to be involved in craving (Pombo et al., 2016). As craving and negative affect are correlated, an emphasis must be put on the emotional aspects from the early start of therapy (Petit et al., 2017). Anker et al. (2019) demonstrated through a network modeling analysis that people who are drinking to cope with anxiety are likely to experience craving when being stressed. Over time craving elicits negative emotions that are handled with higher ingestion of alcohol (Anker et al., 2019; Sinha et al., 2009). Furthermore, heavy drinking individuals are often reporting high anxiety levels (Alati et al., 2004; Rodgers et al., 2000). Even though state anxiety has not been found to be a predictor of relapse in AUD, AUD is highly comorbid with anxiety disorders (AD) which may facilitate relapse (Connor et al., 2015; Gilpin et al., 2015; Oliva et al., 2018; Schellekens et al., 2015). Through therapeutic interventions tackling AUD, anxiety-related symptoms were shown to decrease after treatment (Gallagher et al., 2018; Rodgers et al., 2000).

Therefore, craving and anxiety evolve over time and are important mechanisms in the maintenance of AUD. Pavlovian learning processes can be applied to the development of AUD (Doñamayor et al., 2020). Meaning that a conditioned stimulus may elicit a conditioned response after being paired several times (Everitt & Robbins, 2005). Furthermore, King and colleagues (2016) stated that people who consider alcohol as a rewarding stimulus are likely to be in their early stage of addiction which may result in the development of AUD. Hence, alcohol use often starts as a goal-directed behavior and over the course of addiction, the conditioned response (craving) is likely to interfere with the maintenance and relapse of AUD (Doñamayor et al., 2020).

More specifically, craving can be involved in the decision-making process of acting on the urge to drink (Pombo et al., 2016). According to Incentive-Sensitization Theory of Addiction by Robinson and Berridge (1993), an unconditioned stimulus would result in subjective pleasure, here 'liking', while 'wanting' is an intense, incentive urge that is dependent on cues and is displayed through craving and attraction to the alcoholic beverage. Thus, 'liking' and 'wanting' belong to two separate neural pathways in the brain (Olney et al., 2018), whereby an incentive salience makes one 'wanting' the desired substance, here alcohol, because it is considered to be rewarding (Berridge & Robinson, 2016). As craving is cue- and context-dependent, abstaining from drinking is difficult for people suffering from AUD. Hereby, psychological therapy may be helpful to modify the individual learned response to drinking cues and contexts.

Psychosocial interventions

A variety of psychosocial interventions is offered for the treatment of AUD. Motivational interviewing (MI), self-help groups, or cognitive behavioral therapy (CBT) are examples of the most common therapeutic and community reinforcement approaches (Coriale et al., 2018). The differing approaches leave the clinicians the tasks to ensure that the chosen intervention suits the client. MI enhances motivation and is a brief and cost-effective intervention that is shown to be more effective to reduce alcohol consumption in individuals than no treatment (DiClemente et al., 2017; Vasilaki et al., 2006). Self-help groups are effective for people with AUD, who are looking for peer support during recovery or exchange of doubts and thoughts with other AUD individuals (Coriale et al., 2018). CBT is a popular talking therapy that integrates cognitive and behavioral principles (or methods; Bannink, 2012). Central to CBT is the identification of maladaptive thoughts and their

influence on the person's feelings and behavior. People with AUD may also take deterrent medication, as for example, disulfiram which makes alcohol consumption unpleasant because it changes the body's reaction to alcohol (Barrick & Connors, 2002).

Cue-exposure therapy in Alcohol Use Disorder

Another traditional approach to cope with craving and anxiety in AUD is cue-exposure therapy (CET; Mellentin et al., 2017). CET aims to extinguish the learned responses and behaviors and replace them with healthy ones (Craske et al., 2014; Heather & Bradley, 1990). During in vivo exposure in AUD, the client is exposed to an alcoholic beverage within a clinical setting (Conklin & Tiffany, 2002; Miranda et al., 2020; Monti et al., 2001). A desensitization hierarchy of relevant cues is established that the client is gradually exposed to (Lang & Lazovik, 1963). During the exposure, clients are not allowed to consume the beverage, while they learn to apply new skills or relaxation to replace the learned response (Lang & Lazovik, 1963; Monti et al., 2001; Rothbaum et al., 2000; Stasiewicz et al., 2007). Thus, participants are repeatedly exposed to alcohol-related cues which trigger alcohol-craving and anxiety but the effect lessens over time, called systematic desensitization (Bannink, 2012; MacKillop et al., 2010; Mellentin et al., 2017). After prolonged, graded exposure, it is expected that the client's motivation to drink has decreased and the habitual approach action tendency to alcohol is modified (Bannink, 2012; Mellentin et al., 2017; Stasiewicz et al., 2007). Habituation implies that craving is eliminated in daily-life situations (Craske et al., 2014; Drummond & Glautier, 1994). New inhibitory associations to the cues have been established.

Still, the effectiveness of CET is limited and has not been consistent (Mellentin et al., 2017). Individually tailored approaches are needed (Szegedi et al., 2000). For example, the context in which alcohol cues are present is important due to the context-dependency of triggers (Stasiewicz et al., 2007; Zironi et al., 2006). Therefore, the new associations may be context-dependent as well and results can not be generalized to real-life settings (Mellentin et al., 2017). This is supported by Conklin and Tiffany (2002) who reported in their meta-analytical review that a different context may lead to the execution of the original conditioned response. Thus, the newly learned associations may also be context-dependent and habituation may not have been reached (Craske et al., 2014; Stasiewicz et al., 2007). This so-called renewal effect highlights the importance of exposing individuals to alcohol-related cues in the suited environment because inhibitory learning is context-dependent (Bouton et

al., 2006). Over the years, novel technologies, such as virtual reality (VR), have emerged that may provide solutions for the limitations of current CET.

Concept of Virtual Reality

VR is a computer-generated simulation. In a constructed VR scenario that closely resembles reality, participants are able to explore and acquire the feeling of being 'there', called *sense of presence* (Bohil et al., 2011; Pan & Hamilton, 2018). Visual, auditory, and haptic inputs aid in making the scenario more realistic (Riva, 2009). Wearing a head-mounted display (HMD) during VR adds to the sense of presence and the sense of being part of a 'real' environment, termed *immersion*. Through VR, participants are able to explore different situations safely and under controlled conditions which gives them the chance to stop the simulation at any time (Maples-Keller et al., 2017). VR settings are easy to reproduce and give the client and therapist more freedom and possibilities (control of the therapist over the VR scenarios; Bohil et al., 2011). Moreover, through resembling reality and the possibility of individualizing the VR environment, VR is considered an ecologically valid instrument (Pan & Hamilton, 2018). Thereby, it is easier to generalize the learned behaviors during VR to the natural drinking environment (Ferrer-García & Gutiérrez-Maldonado, 2012; Mellentin et al., 2020). Yet, cybersickness or simulation sickness may be evoked through the conflict between sensory inputs (Pan & Hamilton, 2018; Segawa et al., 2020). When taking into account the concepts of presence, immersion, and individualization, VR-based interventions can facilitate traditional therapy.

Applying virtual reality cue-exposure therapy

More specifically, VR exposure therapy (VRET) or VR cue-exposure therapy (VR-CET) has been applied to several disorders. VR adds to CET through several sensual inputs that make the exposure more realistic (Lee et al., 2007; Riva, 2009). VR is adding the context-cues that make extinction of craving and anxiety more likely (Bouton et al., 2006). Ferrer-García et al. (2019) studied the effectiveness of VR-CET in bulimia nervosa and binge-eating disorder. Hereby, they stated that 70% of participants allocated to the VR-CET group remained abstinent in comparison to participants of the CBT group. Moreover, anxiety and craving responses were reduced through repeated exposure. In gambling, VR-CET evoked the urge to gamble but this craving decreased over time even for the strongest cue-related scenario (Park et al., 2015). Furthermore, Parsons & Rizzo (2008) concluded that

VRET yields benefits for people with anxiety disorders as distress and phobia symptoms were reduced after the VR-based therapy. The application of VR-CET to several disorders shows that it is a promising treatment in reducing craving but also anxiety.

VR-CET has also been used to treat substance use disorders. In their systematic review, Segawa et al. (2020) stated that VR-CET showed to be more effective than traditional CBT in reducing craving for drugs. During the exposure, drug-related cues are simulated to trigger interoceptive reactions of participants and to induce craving (Hone-Blanchet et al., 2014). Moreover, through personalized VR environments, VR-CET may be more effective and may enhance generalization of the therapy effects to the daily life of the participant (Ghiţă & Gutiérrez-Maldonado, 2018; Mostajeran et al., 2019). Specifically, regarding alcohol use, Cho et al. (2008) developed a VR system that induced alcohol craving through different contexts and the presentation of avatars in the VR environment. Indeed, participants experienced greater craving in an environment with an avatar to simulate social pressure and alcohol as a relevant cue present.

Current study

In this study, the newly created ALCO-VR software will be used to treat patients diagnosed with moderate and severe AUD who experienced relapse beforehand. Ghiţă, Teixidor, et al. (2019) identified scenarios in which people experience the greatest craving for alcohol use. Furthermore, they established environments in which their most triggering alcoholic beverages such as liquor, wine, or beer, were present. Time of the day and the presence of avatars were also taken into account. Thereby, four contexts, namely restaurant, bar, pub, and house with different alcohol-related stimuli resulted from the research. Based on the results of the initial study, a software was developed considering the factors that trigger craving in AUD patients, namely the "ALCO-VR" software.

Furthermore, the ALCO-VR software was tested to assess whether AUD patients felt more craving and anxiety when being exposed to the different environments compared to individuals who drink on social occasions. Indeed, people suffering from AUD reported more anxiety and craving after the cue-exposure VR scenarios than the control group (Ghiţă, Hernández-Serrano, Fernández-Ruiz, et al., 2019). The interplay of the environments and the five preferred alcoholic beverages added to the personalization of the VR environment. The conducted tests resulted in significantly higher responses towards the scenarios for people diagnosed with AUD. Therefore, confirming the validity of the ALCO-VR software in this

context. Hernández-Serrano et al. (2020) focused on individual variables that may predict the change in alcohol craving after treatment with the ALCO-VR software. Hereby, all participants showed changes in their level of craving at posttest measures, and participants in the VR-CET group were improving more than the control group. Moreover, individual changes were notable. Despite having experienced relapse after earlier treatment, VR-CET led to an improvement. Thus, in this study, the research questions can be formulated as follows:

What is the effect of VR-CET on alcohol craving and anxiety levels in AUD patients?

H1: A reduction in state-alcohol craving will be observed between baseline (pre-VR-CET) and after the VR-CET sessions (post-VR-CET).

H2: A reduction in state anxiety will be observed between baseline and posttest measures after treatment with the ALCO-VR software.

What is the relationship between state-alcohol craving and state anxiety in AUD patients before and after the VR-CET sessions?

H3: There is a positive relationship between state-alcohol craving and state anxiety at baseline time point.

H4: There is a positive correlation between scores of state-alcohol craving and state anxiety at post-VR-CET sessions in AUD patients.

Methods

Design

A within-subject design was employed. The dependent variables were change in 'state-alcohol craving' and 'state anxiety'. Time served as the independent variable. Further, a correlational design was employed to test the relationship between state-alcohol craving and state anxiety.

Participants

In total, 21 participants were recruited to participate in the study (10 female M_{age}= 50.10, SD_{age}= 5.95; 10 male M_{age}= 55.50, SD_{age}= 8.68). Yet, 1 person had to be excluded

from the analyses because he did not experience craving at baseline, which was required to answer the research questions.

Based on their clinical history, participants were enlisted by the lead psychologist of the Hospital Clinic of Barcelona to partake in the study. At time of recruitment, participants were under ambulatory treatment at the Addictive Behavior Unit of the Hospital Clinic of Barcelona, Spain, which served as an inclusion criterion. Moreover, participants were diagnosed with moderate or severe AUD classified according to the criteria of the *DSM-5* (APA, 2013). Selected participants were considered "resistant to treatment-as-usual (TAU)" as patients experienced relapse in the first six months after treatment discharge. TAU was a combination of psychosocial interventions and medication. Patients with severe psychopathology and cognitive impairment, using anti-craving medication, or who were pregnant were excluded from the study.

In table 1 the characteristics of participants before the assessment are presented. The mean age of participants was 52.80 years with a standard deviation (SD) of 7.76. Gender was, with 50%, equally distributed amongst the participants. Most participants held a bachelor's degree (40%) or had some sort of post-high school education (30%). 80% were considered to have a medium socioeconomic status and the majority of participants were in a relationship (45%) or divorced/ separated (35%). The mean abstinence rate was 77.10 days (SD = 93.45). 17.25 was the mean score on the AUDIT. This exceeds the cut-off score of 8 (Reinert & Allen, 2007; Saunders et al., 1993). 55.0% of participants were diagnosed with another psychiatric disorder. The majority of those suffered from a depressive disorder (20%). Moreover, most of the participants smoked (70.0%). 30% of participants received no medication. Yet, 30% of participants received disulfiram.

Table 1

Participants Characteristics at Baseline (n = 20)

	N (%) or Mean ± SD	Min	Max
Characteristics	**Total sample**		
Age	52.80 ± 7.76	36	67
Gender			
Female	10 (50.0%)		
Male	10 (50.0%)		
Education			
Secondary School	2 (10.0%)		
High School	3 (15.0%)		
Post-high school	6 (30.0%)		
Bachelor's degree	8 (40.0%)		
Master's degree	1 (5.0%)		
Socioeconomic status			
Low	3 (15.0%)		
Medium	16 (80.0%)		
High	1 (5.0%)		
Civil status			
Single	2 (10.0%)		
Married/ In a relationship	9 (45.0%)		
Separated/ divorced	7 (35.0%)		
Widower	2 (10.0%)		
AUDIT	17.25 ± 10.65	2	38
Abstinence duration /day	77.10 ± 93.45	3	360
Psychiatric comorbidity	11 (55.0%)		
Types of psychiatric comorbidity			
None	9 (45.0%)		
Depression	4 (20.0%)		
Depression + anxiety	2 (10.0%)		
Depression + anxiety + PD	1 (5.0%)		
PD	1 (5.0%)		
PTSD	1 (5.0%)		
PTSD + anxiety	1 (5.0%)		
Polydrug Use	1 (5.0%)		
Current smoker	14 (70.0%)		
Medication			
None	6 (30.0%)		
Antidepressants	4 (20.0%)		
Anxiolytics	4 (20.0%)		
Anxiolytics + antidepressants	6 (30.0%)		
Disulfiram	6 (30.0%)		

Note. SD = Standard deviation; AUDIT = Alcohol Use Disorder Identification Test;
PD = Personality Disorder; PTSD = Posttraumatic Stress Disorder

Materials

Hardware

An Oculus Rift S head-mounted display (Oculus VR, Irvine, CA, USA), touch controllers, and sensors were utilized as the VR equipment. Moreover, a computer suitable for VR technology was used.

Software

The ALCO-VR software was employed for the assessment sessions and the treatment of AUD patients. Based on the results of the study of Ghiţă, Teixidor, et al. (2019), the software was developed by the VR-Psy Lab of the University of Barcelona, Spain. The software entails four different VR environments, which are presented in Figure 1. The VR environments include a selection of several alcoholic beverages that are displayed in the background, social interactions through the presentation of human avatars, and different times of the day (day- and nighttime). To enhance the sense of presence, realistic movement of the wrist and respective visual feedback was set up. Thus, participants were able to approach objects and alcoholic beverages and interact with them by holding or observing them within the VR environment. All of which are features making the VR software an ecologically valid instrument (Ghiţă, Hernández-Serrano, Fernández-Ruiz, et al., 2019).

Intervention

The two parts of the intervention were the assessment and therapy sessions. During the assessment, a hierarchy of exposure was established by requesting the participants to rate the four environments and the alcoholic drinks on visual analog scales (VAS) from 0 (no alcohol craving/anxiety) to 100 (intense alcohol craving/anxiety). Thereby resulting in a hierarchical structure from the lowest-rated environment with the lowest-rated alcoholic drink to the highest-rated environment and the highest-rated alcoholic drink. From a selection of 220 alcoholic beverages, participants were able to choose their five favorite ones. Based on the assessment, the therapy sessions consisted of the selected cues and contexts. As the ALCO-VR software is part of an ongoing project and because of the nature of this study, the ratings on the VAS were not included in the present study.

Figure 1

Images of the four alcohol-related VR environments

Note. At-home environment is without avatars. At-home and pub is at night. Restaurant and bar is during the day.

Measures

Alcohol Use Disorders Identification Test

To indicate the severity of AUD, the Alcohol Use Disorder Identification Test (AUDIT) was used as a screening tool (see Appendix A; Donovan et al., 2006). Hereby, the Spanish version of the ten-item screening tool was chosen (Contel Guillamón et al., 1999). Out of the ten questions, three focused on the behavior concerning frequency and amount of drinking, other three items concerned alcohol dependence, and four questions concentrated on problems that were caused by alcohol use. The items were scored from 0 to 4. Only questions 9 and 10 were scored 0, 2, or 4. The maximum score was 40, whereas a score of 8 or higher suggested harmful drinking and indicated possible alcohol dependence (Reinert & Allen, 2007; Saunders et al., 1993). The test showed (very) good internal consistency with a Cronbach's alpha of α=.88 (Contel Guillamón et al., 1999).

Multidimensional Alcohol Craving Scale - Virtual Reality

State alcohol craving was assessed using the Multidimensional Alcohol Craving Scale - Virtual Reality (MACS-VR; Appendix B). The MACS-VR is a self-report scale to assess the intensity of alcohol craving during the VR exposure. It consisted of 12-items implemented on a five-point Likert scale (Guardia Serecigni et al., 2004). Further, the scale was divided into two sub-scales, "desire to drink" and "behavioral inhibition". To calculate the total score, the results of the two subscales were added. Craving then could be classified into four categories: *Non-existent* (0-12), *mild* (13-22), *moderate* (23-40), or *intense* (>40). The MACS-VR was a slightly modified version of the already verified MACS, which showed excellent internal consistency with a Cronbach's alpha of $\alpha=.94$ (Guardia Serecigni et al., 2004).

State-Trait Anxiety Inventory - State

State anxiety was examined using the Spanish version of the State-Trait Anxiety Inventory - State (STAI-State), a self-report questionnaire consisting of 20 items (see Appendix C; Spielberger et al., 1971). A three-point Likert scale ranging from "not at all" to "very much so" was administered to respond to the scale. Therefore, higher levels of state anxiety were indicated by higher scores on the scale. Spielberger et al. (1971) reported (very) good to excellent internal consistency ranging from $\alpha=.89$ to $\alpha=.91$.

Procedure

For an overview of the procedure, see figure 2. After obtaining ethical approval, AUD patients from the Addictive Behaviors Unit of the Hospital Clinic of Barcelona were invited to participate. Before the study was carried out, ethical approval was obtained by the Ethics Committees from the University of Barcelona and Hospital Clinic of Barcelona in September 2017. The ethical code number is 0377 (HCB/2017/0377). All AUD patients participated in this study based on their written informed consent. Afterwards, the researcher in charge of the study scheduled an assessment session with the participants lasting approximately one hour.

During the initial assessment, socio-demographic and clinical data of participants were collected. This included their age, gender, education, socioeconomic status, civil status, AUD history, abstinence, other mental health diagnoses, medication, and whether they currently smoked or not. One participant engaged in polydrug use, for example, cocaine and alcohol.

Before the assessment with the ALCO-VR software, participants were asked to fill in the AUDIT questionnaire. Afterwards, participants were able to familiarize themselves with the VR technology. A short tutorial was given involving a Head-Mounted Display (HMD) and controllers.

Figure 2

Flowchart of the procedure of the VR-CET treatment
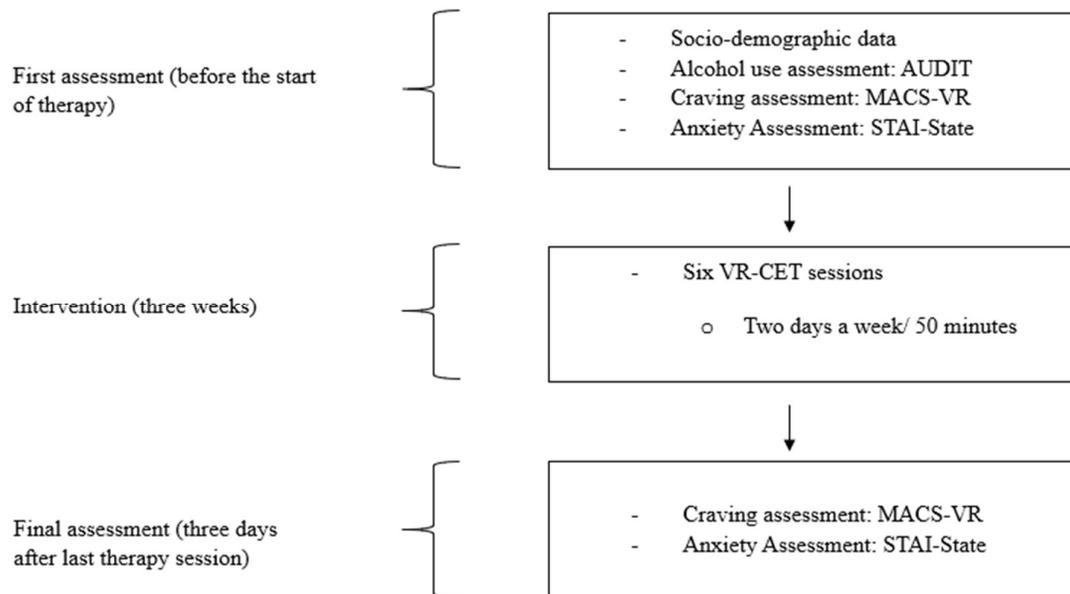
Following the tutorial, participants were exposed to each environment and each drink for 20 seconds. The hierarchy needed for the therapy part was created by the software. Olfactory stimuli in the form of samples of alcoholic beverages on cotton pads were used to increase immersion during the exposure. Thereby, the cotton pad was placed close to the participant while the alcoholic beverage was displayed in the VR environment. The VR-assessment took 10 to 15 minutes. Lastly, participants were asked to fill in the STAI - State, and MACS-VR. This study is part of a larger study and only data from state-alcohol craving and state anxiety will be presented in this thesis.

In the three subsequent weeks, participants were admitted to the therapeutic part of the ALCO-VR software in the form of VR-CET sessions. Every therapy session lasted around 50 minutes and patients were allocated to two sessions per week. The sessions included no additional psychotherapeutic methods besides CET. Thereby, the focus was

placed on systematic desensitization by exposing participants for a prolonged period to the same five alcohol-related stimuli in the four VR environments. Participants were instructed to grab the alcoholic beverage and observe it thoroughly without attempting to drink it. Thereby, patients were habituating to the drinks by preventing the initial response. Here, olfactory stimuli were used as well by applying small amounts of alcoholic drinks on cotton pads during the VR exposure.

The therapy sessions were based on the established hierarchy of the first assessment (which was an interplay between the preferred five beverages and the four VR environments: bar, pub, restaurant, and at-home). Participants underwent treatment through gradual exposure from the lowest rated to the highest-rated environment and alcoholic beverages.

Three days after completing the VR-CET intervention, a final assessment session took place. This session followed the same guideline as the first session. In contrast to the initial assessment, the AUDIT was not administered because it is used to assess problematic drinking behavior over the past year. For each patient, the therapeutic protocol lasted five weeks, including assessments and therapy. Experienced practitioners executed the intervention and participants were shortly debriefed after the sessions to prevent possible alcohol use. The experimenter counseled the patients until craving and anxiety (distress in this case) levels were minimal by disclosing any thoughts, emotions, or behaviors related to alcohol consumption.

Data Analysis

For the following analyses IBM SPSS Statistics version 27 (IBM Corp., 2020) was used. The scores of state-alcohol craving were calculated into a categorical variable to fit the categories of the MACS defined by Guardia Serecigni et al. (2004) as *non-existent* (0-12), *mild* (13-22), *moderate* (23-40), *intense* (>40). Normality testing for pre- and posttest state-alcohol craving and state anxiety was conducted. Skewness and kurtosis values, histograms, and Q-Q plots were taken into account. As normality assumptions for two scales (state-alcohol craving after VR-CET sessions and state anxiety at baseline) were violated ($W < .05$), nonparametric tests were performed to reject or accept the formulated hypotheses. The scores for state-alcohol craving and state anxiety pre-VR-CET and after VR-CET sessions were calculated and compared.

Regarding the first hypothesis, Friedman's ANOVA with the change in state-alcohol craving as the dependent variable was conducted. State-alcohol craving was measured at two

time points. Kendall's *W* was calculated. According to Tomczak and Tomczak (2014), Kendall's *W* is a suitable effect size estimate for Friedman's ANOVA. The relationship can vary from 0 (no relationship) to 1 (perfect relationship), whereby .1 to <.3 indicates a small effect, .3 to <.5 a moderate effect and ≥ .5 is considered a large effect. For the second hypothesis, Friedman's ANOVA with change in state anxiety as the dependent variable was performed and state anxiety was measured at two time points. Again, Kendall's *W* was calculated. For hypothesis three, a Spearman's correlation was conducted using the variables state-alcohol craving and state anxiety at baseline time point. A positive correlation was expected to be found. To test the fourth hypothesis, a Spearman's correlation was carried out. Here, the variables state-alcohol craving and state anxiety at post-VR CET sessions were used and a positive correlation was expected.

Afterwards, a Fisher's Z transformation was conducted to compare the two Spearman's rho correlation coefficients (Myers & Sirois, 2006). This was done to account for any significant relationship.

Results

Normality testing was executed with the Shapiro-Wilk test. The state-alcohol craving scores at baseline (pre VR-CET), $W(20) = .930$, $p = .151$ and the state anxiety scores post VR-CET sessions, $W(20) = .949$, $p = .355$, did not deviate significantly from normal. Yet, the state-alcohol craving scores post VR-CET, $W(20) = .872$, $p = .013$, and the state anxiety scores at baseline $W(20) = .893$, $p = .031$ did not meet the assumptions of normality. In Appendix D, the Q-Q plots and histograms supporting the Shapiro-Wilk test can be found. Non-parametric tests were applied to account for the deviations.

Hypotheses testing

For the first hypothesis, it was expected that a reduction in state-alcohol craving is observed between T_0 (baseline) and T_1 (post-intervention). At T_0, participants' mean score on state-alcohol craving was 31.65 with a SD of 11.79 (see Table 2). That is considered *moderate* craving. Most of the participants had *moderate* craving (40%, n = 8), followed by *mild* (30%, n = 6) and *intense* craving (30%, n = 6). Nobody showed non-existent craving levels. Overall the scores ranged from 16 to 53. At T_1, participants' mean score decreased to 19.80 (SD = 8.04). This mean score falls under the category *mild*, yet the range went from 12 to 40. After the VR-CET sessions, nobody indicated *intense* craving levels. Seven

participants (35%) showed *moderate* craving levels, eight (40%) *mild* ones, and five (25%) showed *non-existent* craving. Friedman's ANOVA showed that state-alcohol craving did significantly decrease after the VR-CET sessions, $\chi^2(1) = 12.250$, $p < .001$ with a Kendall's *W* of .613, confirming the first hypothesis.

Friedman's ANOVA was used to conduct analyses regarding the second hypothesis. It was expected that a reduction in state anxiety can be observed between T_0 (baseline) and T_1 (posttest). Before the intervention, participants' mean score on state anxiety was 20.25 (SD = 11.67; see Table 2). The scores ranged from 6 to 49. After the intervention, the overall score on state anxiety decreased to 7.90 with a SD of 5.78. At T_1, some participants experienced no anxiety at all (0), while the highest score was 19. A significant reduction in state anxiety after VR-CET sessions could be found, $\chi^2(1) = 16.200$, $p < .001$ with a Kendall's *W* of .810. Therefore, it could be concluded that state anxiety is reduced after the VR-CET sessions.

Table 2

Levels of Craving and Anxiety at Baseline and post-VR-CET (n = 20)

	Pre-VR-CET (T_0)		Post-VR-CET (T_1)	
	N (%) or Mean ± SD	**Median [Min, Max]**	**N (%) or Mean ± SD**	**Median [Min, Max]**
MACS-VR	31.65 ± 11.79	33.50 [16,53]	19.80 ± 8.04	17.00 [12,40]
Non-existent	0		5 (25.0%)	
Mild	6 (30.0%)		8 (40.0%)	
Moderate	8 (40.0%)		7 (35.0%)	
Intense	6 (30.0%)		0	
STAI-State	20.25 ± 11.67	17.00 [6,49]	7.90 ± 5.78	8.50 [0,19]

Note. MACS-VR = Multidimensional Alcohol Craving Scale-Virtual Reality; STAI = State-Trait Anxiety Inventory

To account for the third hypothesis, a Spearman's rank-order correlation was run to determine the relationship between state-alcohol craving and state anxiety at baseline measures. A positive correlation was found, which was statistically significant ($r_s = .564$, $p =.010$). Therefore, the findings were in line with the prediction.

Lastly, a Spearman's rank-order correlation was run to find out whether state-alcohol craving and state anxiety are positively correlated after the VR-CET sessions. There was a significant, positive relationship between state anxiety and state-alcohol craving at posttest, $r_s = .779$, $p < .001$.

The difference between state-alcohol craving and state anxiety at baseline and state-

alcohol craving and state anxiety after the VR-CET sessions was not statistically significant (z = -1.178, p = .119).

Discussion

This study was part of a larger project focusing on the novel ALCO-VR software's effectiveness to treat AUD patients who are prone to relapse. Heavy drinking individuals are often highly anxious and have an intense craving for alcohol. Reducing craving and anxiety can be accomplished together (Anker et al., 2019; Gallagher et al., 2018). VR opens the opportunity to control for the context-dependency and personalization of drinking cues, thereby adding ecological validity to traditional CET (Bohil et al., 2011; Campbell et al., 2018; Conklin & Tiffany, 2002; Ferrer-García & Gutiérrez-Maldonado, 2012; Ghiţă, Teixidor, et al., 2019; Pan & Hamilton, 2018). Applying this knowledge, the ALCO-VR software created by Ghiţă, Teixidor, et al. (2019) was used to investigate the effect of VR-CET on state-alcohol craving and state anxiety levels in patients with AUD. Moreover, the relationship between state-alcohol craving and state anxiety in AUD patients was assessed and interpreted.

Current findings

Regarding state-alcohol craving between baseline and after the VR-CET sessions (H1), a significant reduction could be found. In the end, some participants experienced no craving and none of the individuals experienced *intense* craving, while the highest score was just below the cut-off score. Previously, Ghiţă, Hernández-Serrano, Ruiz, et al. (2019) and Hernández-Serrano et al. (2020) demonstrated a reduction of alcohol craving after training with the ALCO-VR software. This is crucial as earlier studies have observed the fundamental influence of craving on alcohol abuse (Addolorato et al., 2005; Bottlender & Soyka, 2004; Caselli et al., 2013; Drummond, 2001; Pareaud et al., 2021; Stohs et al., 2019; Yoon et al., 2021).Therefore, the current findings add to the existing knowledge that the response to alcohol cues can be reduced after the sessions.

The process of systematic desensitization can account for that outcome (Bannink, 2012; Drummond & Glautier, 1994). After the six therapy sessions, participants seem to have habituated to the alcohol-cues (Craske et al., 2014; Drummond & Glautier, 1994; Lang & Lazovik, 1963; MacKillop et al., 2010; Mellentin et al., 2017; Stasiewicz et al., 2007). On a closer look, most participants still experienced craving. Possible explanations are that six

sessions may not be enough to extinguish state-alcohol craving for all individuals or that some participants did not fill in the self-report measures accurately (Haass-Koffler et al., 2014; Lee et al., 2007; Stasiewicz et al., 2007). However, the reduction in state-alcohol craving confirmed the prediction stated in H1.

State anxiety has also been found to significantly decrease after the training with the ALCO-VR software (H2). Hence, the findings conform to research on anxiety, showing that participants were able to reduce their anxiety (Gallagher et al., 2018; Rodgers et al., 2000). Overall, the mean score was reduced by 12.35 points. Interestingly, some people indicated to experience no anxiety after completion of the sessions. Even participants who still experienced higher state anxiety had a lower score than participants had on average before the intervention. During ALCO-VR training, participants were able to learn skills to refrain from drinking while being exposed to alcohol-cues. Eventually, this resulted in increased self-efficacy and higher motivation to change their drinking behavior (Lang & Lazovik, 1963; Monti et al., 2001; Spagnoli et al., 2014; Rothbaum et al., 2000). Therefore, indicating VR's clinical potential in decreasing anxiety responses after prolonged exposure.

A positive correlation between state-alcohol craving and state anxiety was shown (H3 and H4). The relationship was significant at both time points (at T_0 and T_1). Moreover, findings are in line with previous research that has shown that negative affect or anxiety and craving are often experienced together by individuals diagnosed with AUD (Anker et al., 2019; Fox et al., 2007; Rodgers et al., 2000; Sliedrecht et al., 2019). By displaying that state-alcohol craving and state anxiety are correlated over time, the importance of considering both symptoms during therapy is highlighted (McCaul et al.,2017). Even though state anxiety has not been found to be a predictor of relapse in AUD, AUD is highly comorbid with anxiety disorders (AD) and anxiety may facilitate relapse (Connor et al., 2015; Gilpin et al., 2015; Oliva et al., 2018; Schellekens et al., 2015). When comorbid, the disorders may maintain each other through a feed-forward cycle (Smith & Randall, 2012). Treatment focusing on craving may also have an effect on anxiety (Gallagher et al., 2018), yet personalized treatment to target both disorders is needed (Szegedi et al., 2000; Wolitzky-Taylor et al., 2018). This study indicated that the ALCO-VR software may be suitable to treat both symptoms. Importantly, a decrease in both craving and anxiety may help participants to refrain from further alcohol consumption.

The current study has shown that the implementation of VR in the treatment of AUD symptoms has led to a decrease in craving and anxiety. This is important as the current study focused on people who had relapsed. Participants presented high scores on the AUDIT,

indicating severe AUD (Reinert & Allen, 2007; Saunders et al., 1993). As classical CET has provided mixed small effects (Mellentin et al., 2017), the findings highlight the importance of providing individuals with tailored treatment. By exposing participants to four different contexts, VR enhanced the experience of CET by controlling for context cues which decreases the likelihood of the renewal effect (Bouton et al., 2006; Craske et al., 2014; Stasiewicz et al., 2007; Zironi et al., 2006). Additionally, VR can increase the client's motivation to participate and the treatment effects are easier integrated into real-life scenarios (Bohil et al., 2011; Mellentin et al., 2020; Pan & Hamilton, 2018; Szegedi et al., 2000).

Another strength is the focus on severe AUD patients. Previous research demonstrated that patients from AA groups and undergraduate students experienced a decrease in craving and that VR increased the effectiveness of CET (Choi & Lee, 2015; Kwon et al., 2006; Lee et al., 2007). Many studies researched the effect of VR-induced craving (Cho et al., 2008; Kim & Lee, 2015; Lee et al., 2009; Bordnick et al., 2008). However, those included social drinking individuals (Kim & Lee, 2015), people with no alcohol disorder (Cho et al., 2008), or people with AUD who sought no treatment (Bordnick et al., 2008). Lee et al. (2009) focused on inpatient alcohol-dependent individuals, yet they only included men and not women. Instead, the current study includes individuals with severe AUD who have individual differences, for example, comorbid mental health diagnoses and differences in severity of craving and anxiety. The current study is following former research and demonstrates a decrease in symptoms for patients with AUD after the VR-CET sessions. Therefore, the current findings provide implications for future clinical use.

Limitations and future research directions

Despite the promising findings of the study, some limitations have to be considered. First, follow-up measures are not yet available as they are currently collected. Therefore, until now, only short-term conclusions could be drawn on the effect of the ALCO-VR software on abstinence. Moreover, even though craving is a predictor for alcohol use, it is not the only symptom of AUD (Berridge & Robinson, 2016; Drummond, 2001; Grant et al., 2015). Future research should aim to establish whether a causal relationship between reduced craving and abstinence exists. This is important because 37% of patients relapse after three months of treatment (Andersson et al., 2019). During this study, self-report was used to measure craving, yet monitoring implicit physiological measures of participants may be recommendable to obtain more information for the assessment of craving measures (Choi &

Lee, 2015; Haass-Koffler et al., 2014).

Another consideration should be made regarding the sample size. Despite being adequate to represent AUD patients, with 20 sampled participants, the size of the sample is relatively small to generalize findings to a bigger population. Therefore, comparisons between subjects could not be made. Yet, it would have been interesting to investigate individual differences. In the present sample, participant's abstinence rates, AUD severity, medication, and other mental health diagnoses vary. Taking those variables into account might have given more insights into the individual needs to extinguish craving and anxiety (Alati et al., 2004; Connor et al., 2015). Furthermore, research shows the importance of personality traits on the development of AUD (Pombo et al., 2016). Impulsivity and poor inhibition are often associated with higher alcohol consumption and should be considered during treatment (Bernard et al., 2021; Stohs et al., 2019). Generally, the study's results show that sessions with the ALCO-VR software have helped AUD patients to reduce their craving and anxiety. However, no suggestions can be made on people's personality types that may aid or hinder successful training.

Further research should focus more on individual factors to investigate whether some people are benefiting more than others from the use of the software during treatment. Thereby, the target population could be specified. Additionally, other factors could be controlled to find out whether confounding variables interfere with the benefits. Moreover, it would be interesting to adapt the ALCO-VR software to other cultural contexts. Currently, the software is tailored to a Spanish sample. Therefore, it would be of great value to investigate the effectiveness of the software in other countries. For example, day bars are not a popular concept in the Netherlands, yet, this is one of the four scenarios in the current study.

Conclusion

All in all, the study demonstrated the change in craving and anxiety for patients with severe AUD after training with the ALCO-VR software. State-alcohol craving and state anxiety were reduced after the six VR-CET sessions. All of the participants with intense alcohol craving could reduce their craving levels. Furthermore, some participants did not experience anxiety after the training at all. The positive correlation of anxiety and craving demonstrated the need for specific training and interventions for people with AUD and AD.

In conclusion, the current research provides the next step for VR-CET and more

specific studies can be conducted. Hereby, a larger sample would be useful to specify the target population. Therein, a focus should lie on individual differences and in particular on traits that could hinder or enhance training with the ALCO-VR application. Different VR scenarios that represent alcohol-cues for other nationalities could also be implemented. Finally, follow-up measures could be presented to substantiate the current findings that state-alcohol craving and state anxiety is reduced after the treatment.

References

Addolorato, G., Leggio, L., Abenavoli, L., & Gasbarrini, G., (2005). Neurobiochemical and clinical aspects of craving in alcohol addiction: A review. *Addictive Behaviors*, *30*(6), 1209-1224. https://doi.org/10.1016/j.addbeh.2004.12.011

Alati, R., Kinner, S., Najman, J. M., Fowler, G., Watt, K., & Green, D. (2004). Gender differences in the relationships between alcohol, tobacco and mental health in patients attending an emergency department. *Alcohol and Alcoholism*, *39*(5), 463-469. https://doi.org/10.1093/alcalc/agh080

American Psychiatric Association (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5th edition). American Psychiatric Publishing. https://doi.org/10.1176/appi.books.9780890425596

Andersson, H. W., Wenaas, M., & Nordfjærn, T. (2019). Relapse after inpatient substance use treatment: A prospective cohort study among users of illicit substances. *Addictive Behaviors*, *90*, 222-228. https://doi.org/10.1016/j.addbeh.2018.11.008

Anker, J. J., Kummerfeld, E., Rix, A., Burwell, S. J., & Kushner, M. G. (2019). Causal network modeling of the determinants of drinking behavior in comorbid alcohol use and anxiety disorder. *Alcoholism: Clinical and Experimental Research*, *43*(1), 91-97. https://doi.org/10.1111/acer.13914

Bannink, F. (2012). What is CBT? In Bannink, F. (Eds.), *Practicing Positive CBT: From Reducing Distress to Building Success*. (pp.03-06). John Wiley & Sons.

Barrick, C., & Connors, G. J. (2002). Relapse prevention and maintaining abstinence in older adults with alcohol-use disorders. *Drugs & Aging*, *19*(8), 583-594. https://doi.org /10.2165/00002512-200219080-00004

Bernard, L., Cyr, L., Bonnet-Suard, A., Cutarella, C., & Bréjard, V. (2021). Drawing alcohol craving process: A systematic review of its association with thought suppression, inhibition and impulsivity. *Heliyon*, *7*(1), Article e05868. https://doi.org/10.1016/j.heliyon.2020.e05868

Berridge, K. C., & Robinson, T. E. (2016). Liking, wanting, and the incentive-sensitization theory of addiction. *American Psychologist*, *71*(8), 670-679. https://doi.org/10.1037/amp0000059

Bohil, C. J., Alicea, B., & Biocca, F. A. (2011). Virtual reality in neuroscience research and therapy. *Nature Reviews Neuroscience, 12*(12), 752–762. https://doi.org/10.1038/nrn3122

Bordnick, P. S., Traylor, A., Copp, H. L., Graap, K. M., Carter, B., Ferrer, M., & Walton, A. P. (2008). Assessing reactivity to virtual reality alcohol based cues. *Addictive Behaviors*, *33*(6), 743-756. https://doi.org/10.1016/j.addbeh.2007.12.010

Bottlender, M., & Soyka, M. (2004). Impact of craving on alcohol relapse during, and 12 months following, outpatient treatment. *Alcohol and Alcoholism*, *39*(4), 357-361. https://doi.org/10.1093/alcalc/agh073

Bouton, M. E., Westbrook, R. F., Corcoran, K. A., & Maren, S. (2006). Contextual and temporal modulation of extinction: Behavioral and biological mechanisms. *Biological Psychiatry*, *60*(4), 352-360. https://doi.org/10.1016/j.biopsych.2005.12.015

Campbell, E. J., Lawrence, A. J., & Perry, C. J. (2018). New steps for treating alcohol use disorder. *Psychopharmacology*, *235*(6), 1759-1773. https://doi.org/10.1007/s00213-018-4887-7

Caselli, G., Gemelli, A., Querci, S., Lugli, A. M., Canfora, F., Annovi, C., Rebecchi, D., Ruggiero, G. M., Sassaroli, S., Spada, M. M., & Watkins, E. R. (2013). The effect of rumination on craving across the continuum of drinking behaviour. *Addictive Behaviors*, *38*(12), 2879-2883. https://doi.org/10.1016/j.addbeh.2013.08.023

Charney, D. A., Zikos, E., & Gill, K. J. (2010). Early recovery from alcohol dependence: Factors that promote or impede abstinence. *Journal of Substance Abuse Treatment*, *38*(1), 42-50. https://doi.org/10.1016/j.jsat.2009.06.002

Cho, S., Ku, J., Park, J., Han, K., Lee, H., Choi, Y. K., Jung, Y.-C., Namkoong, K., Kim, J.-J., Kim, I. Y., Kim, S. I.,& Shen, D. F. (2008). Development and verification of an alcohol craving–induction tool using virtual reality: Craving characteristics in social

pressure situation. *CyberPsychology & Behavior*, *11*(3), 302-309. https://doi.org /10.1089/cpb.2007.0149

Choi, Y. J., & Lee, J. H. (2015). The effect of virtual covert sensitization on reducing alcohol craving in heavy social drinkers. *Virtual Reality*, *19*(2), 111-117. https://doi.org /10.1007/s10055-015-0264-6

Conklin, C. A., & Tiffany, S. T. (2002). Applying extinction research and theory to cue-exposure addiction treatments. *Addiction*, *97*(2), 155-167. https://doi.org /10.1046/j.1360-0443.2002.00014.x

Connor, J. P., Haber, P. S., & Hall, W. D. (2015). Alcohol use disorders. *The Lancet*, *387*(10022), 988-998. https://doi.org/10.1016/S0140-6736(15)00122-1

Contel Guillamón, M., Gual Solé, A., & Colom Farran, J. (1999). Test para la identificación de transtornos por uso de alcohol (AUDIT): Traducción y validación del AUDIT al catalán y castellano. *Adicciones*, *11*(4), 337-347.

Coriale, G., Fiorentino, D., De Rosa, F., Solombrino, S., Scalese, B., Ciccarelli, R., Attilia, F., Vitali, M., Musetti, A., Fiore, M., & Ceccanti, M. (2018). Treatment of alcohol use disorder from a psychological point of view. *Rivista di Psichiatria*, *53*(3), 141-148. http://dx.doi.org/10.1708/2925.29416

Craske, M. G., Treanor, M., Conway, C. C., Zbozinek, T., & Vervliet, B. (2014). Maximizing exposure therapy: An inhibitory learning approach. *Behaviour Research and Therapy*, *58*, 10-23. https://doi.org/10.1016/j.brat.2014.04.006

DiClemente, C. C., Corno, C. M., Graydon, M. M., Wiprovnick, A. E., & Knoblach, D. J. (2017). Motivational interviewing, enhancement, and brief interventions over the last decade: A review of reviews of efficacy and effectiveness. *Psychology of Addictive Behaviors*, *31*(8), 862-887. http://dx.doi.org/10.1037/adb0000318

Doñamayor, N., Ebrahimi, C., Garbusow, M., Wedemeyer, F., Schlagenhauf, F., & Heinz, A. (2020). Instrumental and pavlovian mechanisms in alcohol use disorder. *Current Addiction Reports*, *8*, 1-25. https://doi.org/10.1007/s40429-020-00333-9

Donovan, D. M., Kivlahan, D. R., Doyle, S. R., Longabaugh, R., & Greenfield, S. F. (2006). Concurrent validity of the alcohol use disorders identification test (AUDIT) and AUDIT zones in defining levels of severity among out-patients with alcohol dependence in the COMBINE study. *Addiction*, *101*(12), 1696-1704. https://doi.org./10.1111/j.1360-0443.2006.01606.x

Drummond, D. C. (2001). Theories of drug craving, ancient and modern. *Addiction*, *96*(1), 33-46. https://doi.org/10.1046/j.1360-0443.2001.961333.x

Drummond, D. C., & Glautier, S. (1994). A controlled trial of cue exposure treatment in alcohol dependence. *Journal of Consulting and Clinical Psychology*, *62*(4), 809-817. https://doi.org /10.1037/0022-006X.62.4.809

Everitt, B. J., & Robbins, T. W. (2005). Neural systems of reinforcement for drug addiction: From actions to habits to compulsion. *Nature Neuroscience*, *8*(11), 1481-1489. https://doi.org/10.1038/nn1579

Ferrer-García, M., & Gutiérrez-Maldonado, J. (2012). The use of virtual reality in the study, assessment, and treatment of body image in eating disorders and nonclinical samples: A review of the literature. *Body Image*, *9*(1), 1-11. https://doi.org/10.1016/j.bodyim.2011.10.001

Ferrer-García, M., Pla-Sanjuanelo, J., Dakanalis, A., Vilalta-Abella, F., Riva, G., Fernandez-Aranda, F., Forcano, L., Riesco, N., Sánchez, I., Clerici, M., Ribas-Sabaté, J., Andreu-Gracia, A., Escandón-Nagel, N., Gomez-Tricio, O., Tena, V., & Gutiérrez-Maldonado, J. (2019). A randomized trial of virtual reality-based cue exposure second-level therapy and cognitive behavior second-level therapy for bulimia nervosa and binge-eating disorder: Outcome at six-month followup. *Cyberpsychology, Behavior, and Social Networking*, *22*(1), 60-68. https://doi.org /10.1089/cyber.2017.0675

Fox, H. C., Bergquist, K. L., Hong, K. I., & Sinha, R. (2007). Stress-induced and alcohol cue-induced craving in recently abstinent alcohol-dependent individuals. *Alcoholism: Clinical and Experimental Research*, *31*(3), 395-403. https://doi.org /10.1111/j.1530-0277.2006.00320.x

Gallagher, C., Radmall, Z., O'Gara, C., & Burke, T. (2018). Anxiety and depression among patients with alcohol dependence: Co-morbid or substance-related problems?. *Irish Journal of Psychological Medicine*, *35*(2), 121-126. https://doi.org/10.1017/ipm.2017.25

Ghiţă, A., & Gutiérrez-Maldonado, J. (2018). Applications of virtual reality in individuals with alcohol misuse: A systematic review. *Addictive Behaviors*, *81*, 1-11. https://doi.org/10.1016/j.addbeh.2018.01.036

Ghiţă, A., Hernández-Serrano, O., Fernández-Ruiz, Y., Monras, M., Ortega, L., Mondon, S., Teixidor, L., Gual, A., Porras-García, B., Ferrer-García, M. & Gutiérrez-Maldonado, J. (2019). Cue-elicited anxiety and alcohol craving as indicators of the validity of ALCO-VR software: A virtual reality study. *Journal of Clinical Medicine*, *8*(8), Article 1153. https://doi.org/10.3390/jcm8081153

Ghiţă, A., Hernández-Serrano, O., Ruiz, J., Monras, M., Ortega, L., Mondon, S., Teixidor, L., Gual, A., Porras-García, B., Ferrer-García, M., & Gutiérrez Maldonado, J. (2019). Craving and anxiety responses as indicators of the efficacy of virtual reality-cue exposure therapy in patients diagnosed with alcohol use disorder. *Annual Review of Cybertherapy and Telemedicine, 17,* 77-82. https://doi.org/10.3390/jcm8081153

Ghiţă, A., Teixidor, L., Monras, M., Ortega, L., Mondon, S., Gual, A., Paredes, S. M., Urgell, L. V., Porras-García, B., Ferrer-García, M., & Gutiérrez-Maldonado, J. (2019). Identifying triggers of alcohol craving to develop effective virtual environments for cue exposure therapy. *Frontiers in Psychology*, *10*, Article 74. https://doi.org/10.3389/fpsyg.2019.00074

Gilpin, N. W., Herman, M. A., & Roberto, M. (2015). The central amygdala as an integrative hub for anxiety and alcohol use disorders. *Biological Psychiatry*, *77*(10), 859-869. https://doi.org/10.1016/j.biopsych.2014.09.008

Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, S. P., Jung, J., Zhang, H., Pickering, R. P., Ruan, J., Smith, S. M., Huang, B., & Hasin, D. S. (2015). Epidemiology of DSM-5 alcohol use disorder: Results from the national epidemiologic survey on alcohol and related conditions III. *JAMA psychiatry*, *72*(8), 757-766. https://doi.org/10.1001/jamapsychiatry.2015.0584

Guardia Serecigni, J. G., García, L. S., Cirac, B. G., Albet, J. T., Pociello, A. T., González, A. S., & Gil, A. M. (2004). Estudio de validación de la escala multidimensional de craving de Alcohol. *Medicina Clínica*, *123*(6), 211-216. https://doi.org/10.1016/S0025-7753(04)74463-2

Haass-Koffler, C. L., Leggio, L., & Kenna, G. A. (2014). Pharmacological approaches to reducing craving in patients with alcohol use disorders. *CNS Drugs*, *28*(4), 343-360. https://doi.org/10.1007/s40263-014-0149-3

Hasin, D. S., O'Brien, C. P., Auriacombe, M., Borges, G., Bucholz, K., Budney, A., Compton, W. M., Crowley, T., Ling, W., Petry, N. M., Schuckit, M., & Grant, B. F. (2013). DSM-5 criteria for substance use disorders: Recommendations and rationale. *American Journal of Psychiatry*, *170*(8), 834-851. https://doi.org/10.1176/appi.ajp.2013.12060782

Heather, N., & Bradley, B. P. (1990). Cue exposure as a practical treatment for addictive disorders: Why are we waiting? *Addictive Behaviors, 15*(4), 335-337. https://doi.org/10.1016/0306-4603(90)90043-W

Hernández-Serrano, O., Ghiţă, A., Figueras-Puigderrajols, N., Fernández-Ruiz, J., Monras, M., Ortega, L., Mondon, S., Teixidor, L., Gual, A., Ugas-Ballester, L., Fernández, M., Montserrat, R., Porras-García, B., Ferrer-García, M., & Gutiérrez-Maldonado, J. (2020). Predictors of changes in alcohol craving levels during a virtual reality cue exposure treatment among patients with alcohol use disorder. *Journal of Clinical Medicine*, *9*(9), Article 3018. https://doi.org/10.3390/jcm9093018

Higley, A. E., Crane, N. A., Spadoni, A. D., Quello, S. B., Goodell, V., & Mason, B. J. (2011). Craving in response to stress induction in a human laboratory paradigm predicts treatment outcome in alcohol-dependent individuals. *Psychopharmacology*, *218*(1), 121-129. https://doi.org/10.1007/s00213-011-2355-8

Hone-Blanchet, A., Wensing, T., & Fecteau, S. (2014). The use of virtual reality in craving assessment and cue-exposure therapy in substance use disorders. *Frontiers in Human Neuroscience*, *8*, Article 844. https://doi.org/10.3389/fnhum.2014.00844

IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp

Kim, D. Y., & Lee, J. H. (2015). Development of a virtual approach–avoidance task to assess alcohol cravings. *Cyberpsychology, Behavior, and Social Networking*, *18*(12), 763-766. https://doi.org/10.1089/cyber.2014.0490

King, A. C., Hasin, D., O'Connor, S. J., McNamara, P. J., & Cao, D. (2016). A prospective 5-year re-examination of alcohol response in heavy drinkers progressing in alcohol use disorder. *Biological Psychiatry*, *79*(6), 489-498. https://doi.org/10.1016/j.biopsych.2015.05.007

Kwon, H., Choi, J., Roh, S., Yang, B. H., & Lee, J. H. (2006). Application of virtual reality-cue exposure therapy for reducing alcohol craving. *Annual Review of CyberTherapy and Telemedicine*, *4*, 161-166.

Lang, P. J., & Lazovik, A. D. (1963). Experimental desensitization of phobia. *The Journal of Abnormal and Social Psychology, 66*(6), 519-525. https://doi.org/10.1037/h0039828

Lee, J. H., Kwon, H., Choi, J., & Yang, B. H. (2007). Cue-exposure therapy to decrease alcohol craving in virtual environment. *CyberPsychology & Behavior*, *10*(5), 617-623. https://doi.org/10.1089/cpb.2007.9978

Lee, S. H., Han, D. H., Oh, S., Lyoo, I. K., Lee, Y. S., Renshaw, P. F., & Lukas, S. E. (2009). Quantitative electroencephalographic (qEEG) correlates of craving during virtual reality therapy in alcohol-dependent patients. *Pharmacology Biochemistry and Behavior*, *91*(3), 393-397. https://doi.org/10.1016/j.pbb.2008.08.014

MacKillop, J., O'Hagen, S., Lisman, S. A., Murphy, J. G., Ray, L. A., Tidey, J. W., McGeary, J. E., & Monti, P. M. (2010). Behavioral economic analysis of cue-elicited craving for alcohol. *Addiction*, *105*(9), 1599-1607. https://doi.org10.1111/j.1360-0443.2010.03004.x

Maples-Keller, J. L., Bunnell, B. E., Kim, S. J., & Rothbaum, B. O. (2017). The use of virtual reality technology in the treatment of anxiety and other psychiatric disorders. *Harvard Review of Psychiatry*, *25*(3), 103-113. http://dx.doi.org/10.1097/HRP.0000000000000138

McCaul, M. E., Hutton, H. E., Stephens, M. A. C., Xu, X., & Wand, G. S. (2017). Anxiety, anxiety sensitivity, and perceived stress as predictors of recent drinking, alcohol craving, and social stress response in heavy drinkers. *Alcoholism: Clinical and Experimental Research*, *41*(4), 836-845. https://doi.org/10.1111/acer.13350

Mellentin, A. I., Nielsen, A. S., Ascone, L., Wirtz, J., Samochowiec, J., Kucharska-Mazur, J., Schadow, F., Lebiecka, Z., Skoneczny, T., Mistarz, N., Bremer, T., & Kühn, S. (2020). A randomized controlled trial of a virtual reality based, approach-avoidance training program for alcohol use disorder: A study protocol. *BMC psychiatry*, *20*(1), 1-12. https://doi.org/10.1186/s12888-020-02739-1

Mellentin, A. I., Skøt, L., Nielsen, B., Schippers, G. M., Nielsen, A. S., Stenager, E., & Juhl, C. (2017). Cue exposure therapy for the treatment of alcohol use disorders: A meta-analytic review. *Clinical Psychology Review*, *57*, 195-207. https://doi.org/10.1016/j.cpr.2017.07.006

Miranda Jr, R., O'Malley, S. S., Treloar Padovano, H., Wu, R., Falk, D. E., Ryan, M. L., Fertig, J. B., Chun, T. H., Muvvala, S. B. & Litten, R. Z. (2020). Effects of alcohol cue reactivity on subsequent treatment outcomes among treatment-seeking individuals with alcohol use disorder: A multisite randomized, double-blind, placebo-controlled clinical trial of varenicline. *Alcoholism: Clinical and Experimental Research*, *44*(7), 1431-1443. https://doi.org/10.1111/acer.14352

Monti, P. M., Rohsenow, D. J., Swift, R. M., Gulliver, S. B., Colby, S. M., Mueller, T. I., Brown, R. A., Gordon, A., Abrams, D. B., Niaura, R. S., Asher, M. K. (2001). Naltrexone and cue exposure with coping and communication skills training for alcoholics: Treatment process and 1-year outcomes. *Alcoholism: Clinical and Experimental Research*, *25*(11), 1634-1647. https://doi.org/10.1111/j.1530-0277.2001.tb02170.x

Mostajeran, F., Kirsten, A., Steinicke, F., Gallinat, J., & Kühn, S. (2019). *Towards gamified alcohol use disorder therapy in virtual reality: A preliminary usability study* [Paper presentation]. 2019 IEEE Conference on Virtual Reality and 3D User Interfaces, Osaka, Japan. https://doi.org/10.1109/VR.2019.8797817

Myers, L., & Sirois, M. J. (2006). Spearman correlation coefficients, differences between. In Kotz, C.B. Read, N. Balakrishnan, B. Vidakovic and N.L. Johnson (Eds.), *Encyclopedia of Statistical Sciences* (12th. Ed.). https://doi.org/10.1002/0471667196.ess5050.pub2

Naim-Feil, J., Fitzgerald, P. B., Bradshaw, J. L., Lubman, D. I., & Sheppard, D. (2014). Neurocognitive deficits, craving, and abstinence among alcohol-dependent individuals following detoxification. *Archives of Clinical Neuropsychology*, *29*(1), 26-37. https://doi.org/10.1093/arclin/act090

Oliva, F., Nibbio, G., Vizzuso, P., Sodano, A. J., Ostacoli, L., Carletto, S., & Picci, R. L. (2018). Gender differences in anxiety and depression before and after alcohol detoxification: Anxiety and depression as gender-related predictors of relapse. *European Addiction Research*, *24*, 163-172. https://doi.org/10.1159/000490046

Olney, J. J., Warlow, S. M., Naffziger, E. E., & Berridge, K. C. (2018). Current perspectives on incentive salience and applications to clinical disorders. *Current Opinion in Behavioral Sciences*, *22*, 59-69. https://doi.org/10.1016/j.cobeha.2018.01.007

Pan, X. & Hamilton, A. F. de C. (2018). Why and how to use virtual reality to study human social interaction: The challenges of exploring a new research landscape. *British Journal of Psychology, 109*, 395-417. https://doi.org/10.1111/bjop.12290

Pareaud, M., Girard, M., & Nubukpo, P. (2021). Factors for maintaining abstinence at 2 and 6 months after alcohol withdrawal. *Journal of Psychiatric Practice*, *27*(1), 2-13. https://doi.org/10.1097/PRA.0000000000000522

Park, C. B., Park, S. M., Gwak, A. R., Sohn, B. K., Lee, J. Y., Jung, H. Y., Choi, S.-W., Kim, D.-J., & Choi, J. S. (2015). The effect of repeated exposure to virtual gambling cues on the urge to gamble. *Addictive Behaviors*, *41*, 61-64. https://doi.org/10.1016/j.addbeh.2014.09.027

Parsons, T. D., & Rizzo, A. A. (2008). Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis. *Journal of Behavior Therapy and Experimental Psychiatry, 39*(3), 250-261. https://doi.org/10.1016/j.jbtep.2007.07.007

Petit, G., Luminet, O., Cordovil de Sousa Uva, M., Monhonval, P., Leclercq, S., Spilliaert, Q., Zammit, F., Maurage, P., & de Timary, P. (2017). Gender differences in affects and craving in alcohol-dependence: A study during alcohol detoxification. *Alcoholism: Clinical and Experimental Research*, *41*(2), 421-431. https://doi.org /10.1111/acer.13292

Pombo, S., Figueira, M. L., Walter, H., & Lesch, O. (2016). Motivational factors and negative affectivity as predictors of alcohol craving. *Psychiatry Research*, *243*, 53-60. https://doi.org/10.1016/j.psychres.2016.02.064

Rehm, J., Anderson, P., Barry, J., Dimitrov, P., Elekes, Z., Feijão, F., Frick, U., Gual, A., Gmel, G., Kraus, L., Marmet, S., Raninen, J., Rehm, M. X., Scafato, E., Shield, K. D., Trapencieris, M., & Gmel, G. (2015). Prevalence of and potential influencing factors for alcohol dependence in Europe. *European Addiction Research*, *21*(1), 6-18. https://doi.org/10.1159/000365284

Reinert, D. F., & Allen, J. P. (2007). The alcohol use disorders identification test: An update of research findings. *Alcoholism: Clinical and Experimental Research*, *31*(2), 185-199. https://doi.org/10.1111/j.1530-0277.2006.00295.x

Riva, G. (2009). Virtual reality: An experiential tool for clinical psychology. *British Journal of Guidance & Counselling*, *37*(3), 337-345. https://doi.org /10.1080/03069880902957056

Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: An incentive-sensitization theory of addiction. *Brain Research Reviews*, *18*(3), 247-291. https://doi.org/10.1016/0165-0173(93)90013-P

Rodgers, B., Korten, A. E., Jorm, A. F., Jacomb, P. A., Christensen, H., & Henderson, A. S. (2000). Non-linear relationships in associations of depression and anxiety with alcohol use. *Psychological Medicine*, *30*(2), 421-432. https://doi.org/10.1017/S0033291799001865

Roerecke, M., & Rehm, J. (2014). Cause-specific mortality risk in alcohol use disorder treatment patients: A systematic review and meta-analysis. *International Journal of Epidemiology*, *43*(3), 906-919. https://doi.org/10.1093/ije/dyu018

Rothbaum, B. O., Hodges, L., Smith, S., Lee, J. H., & Price, L. (2000). A controlled study of virtual reality exposure therapy for the fear of flying. *Journal of Consulting and Clinical Psychology, 68*(6), 1020-1026. https://doi.org/10.1037/0022-006X.68.6.1020

Saunders, J. B., Aasland, O. G., Babor, T. F., De La Fuente, J. R., & Grant, M. (1993). Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction*, *88*(6), 791-804. https://doi.org/10.1111/j.1360-0443.1993.tb02093.x

Schellekens, A. F. A., De Jong, C. A. J., Buitelaar, J. K., & Verkes, R. J. (2015). Co-morbid anxiety disorders predict early relapse after inpatient alcohol treatment. *European Psychiatry*, *30*(1), 128-136. https://doi.org/10.1016/j.eurpsy.2013.08.006

Segawa, T., Baudry, T., Bourla, A., Blanc, J. V., Peretti, C. S., Mouchabac, S., & Ferreri, F. (2020). Virtual reality (VR) in assessment and treatment of addictive disorders: A systematic review. *Frontiers in Neuroscience*, *13*, Article 1409. https://doi.org/10.3389/fnins.2019.01409

Shield, K. D., Parry, C., & Rehm, J. (2014). Chronic diseases and conditions related to alcohol use. *Alcohol Research: Current Reviews*, *35*(2), 155-171.

Sinha, R., Fox, H. C., Hong, K. A., Bergquist, K., Bhagwagar, Z., & Siedlarz, K. M. (2009). Enhanced negative emotion and alcohol craving, and altered physiological responses following stress and cue exposure in alcohol dependent individuals. *Neuropsychopharmacology*, *34*(5), 1198-1208. https://doi.org/10.1038/npp.2008.78

Sliedrecht, W., de Waart, R., Witkiewitz, K., & Roozen, H. G. (2019). Alcohol use disorder relapse factors: A systematic review. *Psychiatry Research*, *278*, 97-115. https://doi.org/10.1016/j.psychres.2019.05.038

Smith, J. P., & Randall, C. L. (2012). Anxiety and alcohol use disorders: Comorbidity and treatment considerations. *Alcohol research: Current Reviews*, *34*(4). 414-431.

Spagnoli, G., Gatti, E., Massari, R., Sacchelli, C., & Riva, G. (2014). Can virtual reality be useful to assess subjects with alcohol dependency? Development of a new assessment

protocol for patients with alcoholism. *European International Journal of Science and Technology*, *3*(1), 82-94.

Spielberger, C. D. (1971). Development of the spanish edition of the state-trait anxiety inventory. *Revista Interamericana de Psicologia*, *5*(3-4), 145–158.

Spindler, C., Trautmann, S., Alexander, N., Bröning, S., Bartscher, S., Stuppe, M., & Muehlhan, M. (2021). Meta-analysis of grey matter changes and their behavioral characterization in patients with alcohol use disorder. *Scientific Reports*, *11*(1), Article 5238. https://doi.org/10.1038/s41598-021-84804-7

Stasiewicz, P. R., Brandon, T. H., & Bradizza, C. M. (2007). Effects of extinction context and retrieval cues on renewal of alcohol-cue reactivity among alcohol-dependent outpatients. *Psychology of Addictive Behaviors*, *21*(2), 244-248. https://doi.org/10.1037/0893-164X.21.2.244

Stohs, M. E., Schneekloth, T. D., Geske, J. R., Biernacka, J. M., & Karpyak, V. M. (2019). Alcohol craving predicts relapse after residential addiction treatment. *Alcohol and Alcoholism*, *54*(2), 167-172. https://doi.org /10.1093/alcalc/agy093

Szegedi, A., Lörch, B., Scheurich, A., Ruppe, A., Hautzinger, M., & Wetzel, H. (2000). Cue exposure in alcohol dependent patients: preliminary evidence for different types of cue reactivity. *Journal of Neural Transmission*, *107*(6), 721-730. https://doi.org/10.1007/s007020070073

Tomczak, M., & Tomczak, E. (2014). The need to report effect size estimates revisited. An overview of some recommended measures of effect size. *Trends in Sport Sciences*, *1*(21), 19–25.

Valmaggia, L. R., Latif, L., Kempton, M. J., & Rus-Calafell, M. (2016). Virtual reality in the psychological treatment for mental health problems: An systematic review of recent evidence. *Psychiatry Research*, *236*, 189-195. https://doi.org/10.1016/j.psychres.2016.01.015

Vasilaki, E. I., Hosier, S. G., & Cox, W. M. (2006). The efficacy of motivational interviewing as a brief intervention for excessive drinking: A meta-analytic review. *Alcohol and Alcoholism*, *41*(3), 328-335. https://doi.org/10.1093/alcalc/agl016

Wackernah, R. C., Minnick, M. J., & Clapp, P. (2014). Alcohol use disorder: pathophysiology, effects, and pharmacologic options for treatment. *Substance Abuse and Rehabilitation, 5*, 1-12. http://dx.doi.org/10.2147/SAR.S37907

Wolitzky-Taylor, K., Niles, A. N., Ries, R., Krull, J. L., Rawson, R., Roy-Byrne, P., & Craske, M. (2018). Who needs more than standard care? Treatment moderators in a randomized clinical trial comparing addiction treatment alone to addiction treatment plus anxiety disorder treatment for comorbid anxiety and substance use disorders. *Behaviour Research and Therapy*, *107*, 1-9. https://doi.org/10.1016/j.brat.2018.05.005

Yoon, G., Thompson, K., Hakes, J. K., Westermeyer, J., Petrakis, I. L., & Kim, S. W. (2021). Alcohol craving and psychiatric disorders among current drinkers. *The American Journal on Addictions*, *30*(1), 34-42. https://doi.org/10.1111/ajad.13083

Zironi, I., Burattini, C., Aicardi, G., & Janak, P. H. (2006). Context is a trigger for relapse to alcohol. *Behavioural Brain Research*, *167*(1), 150-155. https://doi.org/10.1016/j.bbr.2005.09.007

Appendix A

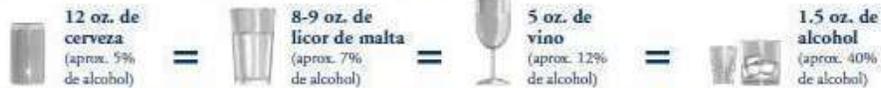**Alcohol Use Disorders Identification Test (AUDIT)**

AUDIT

PACIENTE: Debido a que el uso del alcohol puede afectar su salud e interferir con ciertos medicamentos y tratamientos, es importante que le hagamos algunas preguntas sobre su uso del alcohol. Sus respuestas serán confidenciales, así que le agradecemos su honestidad.

Para cada pregunta en la tabla siguiente, marque una X en el cuadro que mejor describa su respuesta.

NOTA: En los Estados Unidos *una bebida* se refiere a cualquier bebida que contiene aproximadamente 14 gramos de etanol o alcohol puro. Las bebidas que siguen a continuación son de diferentes tamaños sin embargo su contenido de alcohol es el mismo. Es por eso que todas son consideradas *una bebida*:

12 oz. de cerveza (aprox. 5% de alcohol) = **8-9 oz. de licor de malta** (aprox. 7% de alcohol) = **5 oz. de vino** (aprox. 12% de alcohol) = **1.5 oz. de alcohol** (aprox. 40% de alcohol)

Preguntas	0	1	2	3	4	
1. ¿Con qué frecuencia consume alguna bebida alcohólica?	Nunca	Una o menos veces al mes	De 2 a 4 veces al mes	De 2 a 3 más veces a la semana	4 o más veces a la semana	
2. ¿Cuantas consumiciones de bebidas alcohólicas suele realizar en un día de consumo normal?	1 o 2	3 o 4	5 o 6	De 7 a 9	10 o más	
3. ¿Con qué frecuencia toma 5 o más bebidas alcohólicas en un solo día?	Nunca	Menos de una vez al mes	Mensualmente	Semanalmente	A diario o casi a diario	
4. ¿Con qué frecuencia en el curso del último año ha sido incapaz de parar de beber una vez había empezado?	Nunca	Menos de una vez al mes	Mensualmente	Semanalmente	A diario o casi a diario	
5. ¿Con qué frecuencia en el curso del último año no pudo hacer lo que se esperaba de usted porque había bebido?	Nunca	Menos de una vez al mes	Mensualmente	Semanalmente	A diario o casi a diario	
6. ¿Con qué frecuencia en el curso del último año ha necesitado beber en ayunas para recuperarse después de haber bebido mucho el día anterior?	Nunca	Menos de una vez al mes	Mensualmente	Semanalmente	A diario o casi a diario	
7. ¿Con qué frecuencia en el curso del último año ha tenido remordimientos o sentimientos de culpa después de haber bebido?	Nunca	Menos de una vez al mes	Mensualmente	Semanalmente	A diario o casi a diario	
8. ¿Con qué frecuencia en el curso del último año no ha podido recordar lo que sucedió la noche anterior porque había estado bebiendo?	Nunca	Menos de una vez al mes	Mensualmente	Semanalmente	A diario o casi a diario	
9. ¿Usted o alguna otra persona ha resultado herido porque usted había bebido?	No		Sí, pero no en el curso del último año		Sí, el último año	
10. ¿Algún familiar, amigo, médico o profesional sanitario ha mostrado preocupación por un consumo de bebidas alcohólicas o le ha sugerido que deje de beber?	No		Sí, pero no en el curso del último año		Sí, el último año	
					Total	

Nota: Este cuestionario (el AUDIT) se reimprime con permiso de la Organización Mundial de la Salud y la Generalitat Valenciana Consellería de Benestar Social. Para reflejar las medidas de consumo en los Estados Unidos (14 gramos de alcohol puro), la cantidad de tragos en la pregunta 3 fue cambiada de 6 a 5. En el sitio *www.who.org* está disponible en forma gratuita un manual AUDIT con guías para su uso en la atención primaria.

Excerpted from NIH Publication No. 07-3769 **National Institute on Alcohol and Alcoholism** *www.niaaa.nih.gov/guide*

Appendix B

Multidimensional Alcohol Craving Scale - Virtual Reality (MACS-VR)

Escala Multidimensional de Craving de Alcohol (EMCA)

En los entornos de realidad virtual.	Muy de acuerdo	Bastante de acuerdo	Ni de acuerdo ni en desacuerdo	Bastante en desacuerdo	Muy en desacuerdo
1. He tenido ansia de beber	5	4	3	2	1
2. Habría hecho casi cualquier cosa por beber	5	4	3	2	1
3. He deseado beber	5	4	3	2	1
4. He podido controlar completamente mi deseo de beber	5	4	3	2	1
5. Tomar una copa habría sido ideal	5	4	3	2	1
6. He estado pensando la manera de ir a por una bebida	5	4	3	2	1
7. Beber hubiera sido maravilloso	5	4	3	2	1
8. He tenido muy a menudo la mente ocupada con imágenes relacionadas con la bebida	5	4	3	2	1
9. Las ganas de beber han sido muy intensas	5	4	3	2	1
10. Me hubiera sentido mejor si hubiera podido beber	5	4	3	2	1
11. He experimentado una vez o más un intenso deseo de beber	5	4	3	2	1
12. Aunque hubiese tenido la oportunidad no hubiera bebido	5	4	3	2	1

Appendix C

State-Trait Anxiety Inventory - State (STAI-State)

INVENTARIO DE ANSIEDAD ESTADO

(STATE-TRAIT ANXIETY INVENTORY-STAI)

Instrucciones: A continuación encontrará unas frases que se utilizan corrientemente para describirse uno a sí mismo. Lea cada frase y señale la puntuación de 0 a 3 que indique mejor como se siente *usted ahora mismo*, en este momento. No hay respuestas buenas ni malas. No emplee demasiado tiempo en cada frase y conteste señalando la respuesta que mejor describa su situación presente.

	Nada	Algo	Bastante	Mucho
1. Me siento calmado	0	1	2	3
2. Me siento seguro	0	1	2	3
3. Estoy tenso	0	1	2	3
4. Estoy contrariado	0	1	2	3
5. Me siento cómodo (estoy a gusto)	0	1	2	3
6. Me siento alterado	0	1	2	3
7. Estoy preocupado ahora pos posibles desgracias futuras	0	1	2	3
8. Me siento descansado	0	1	2	3
9. Me siento angustiado	0	1	2	3
10. Me siento confortable	0	1	2	3
11. Tengo confianza en mí mismo	0	1	2	3
12. Me siento nervioso	0	1	2	3
13. Estoy desasosegado	0	1	2	3
14. Me siento muy "atado" (como oprimido)	0	1	2	3
15. Estoy relajado	0	1	2	3
16. Me siento satisfecho	0	1	2	3
17. Estoy preocupado	0	1	2	3
18. Me siento aturdido y sobreexcitado	0	1	2	3
19. Me siento alegre	0	1	2	3
20. En este momento me siento bien	0	1	2	3

Appendix D

State-alcohol craving

Figure 3

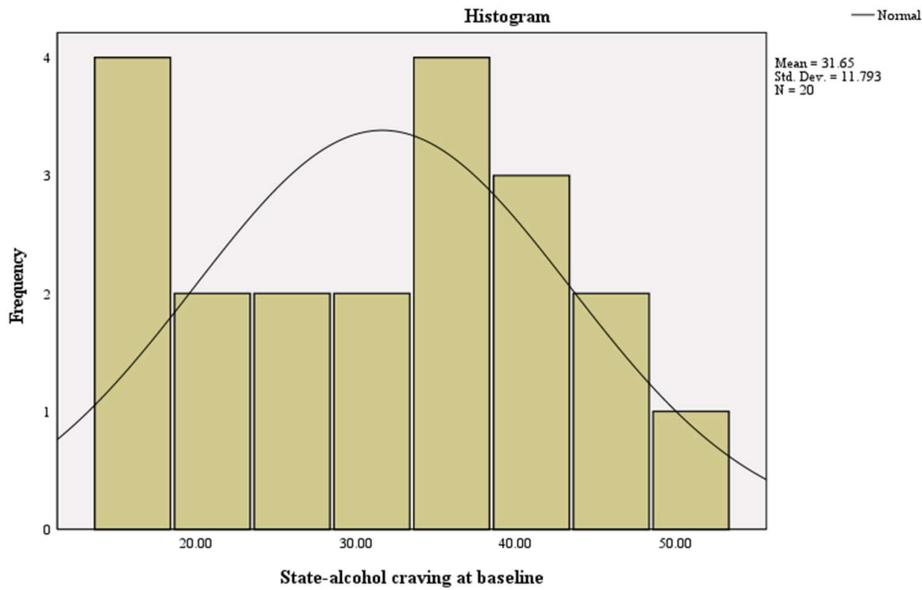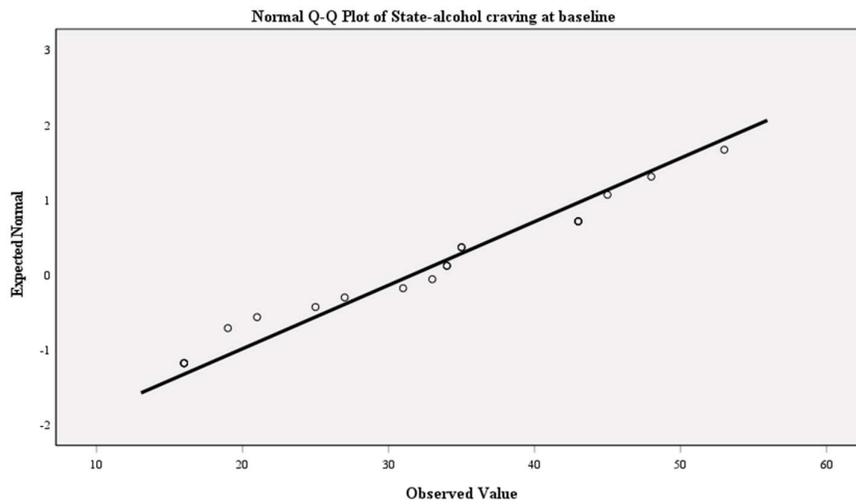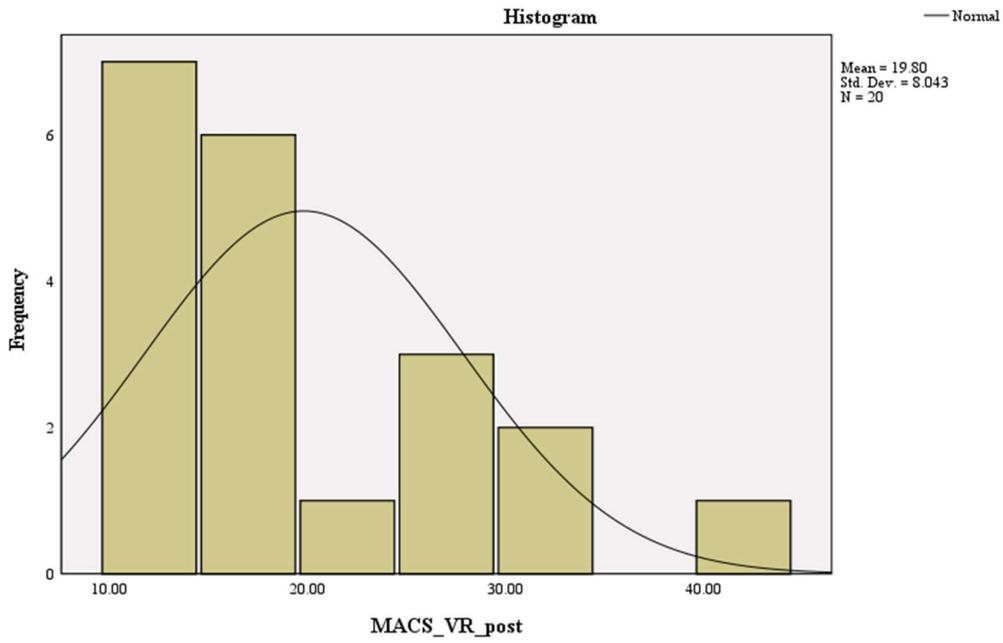*Histogram of State-alcohol craving at baseline*

Figure 4

Normal Q-Q Plot of State-alcohol craving at baseline
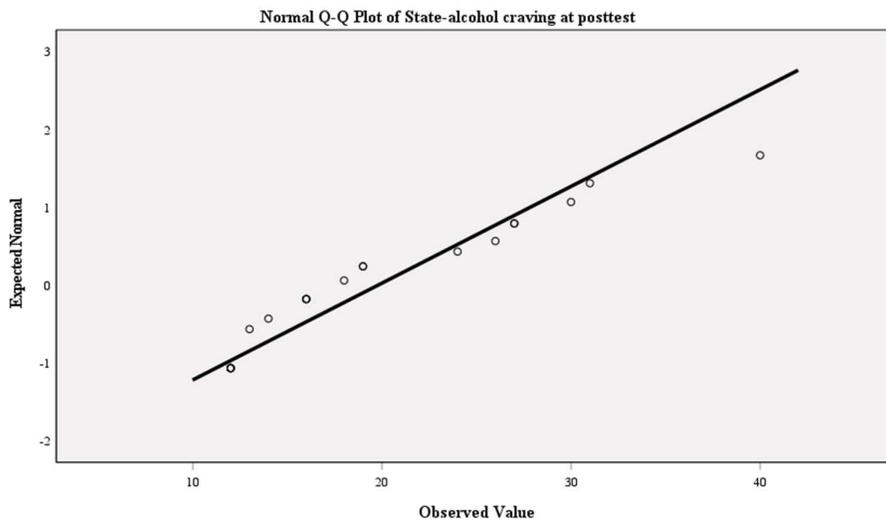
Figure 5

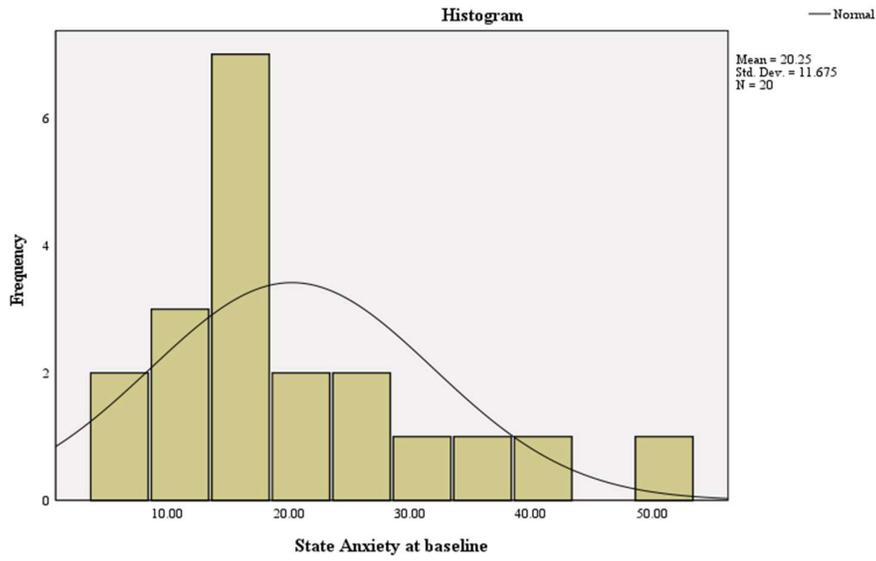*Histogram of State-alcohol craving at posttest*

Figure 6

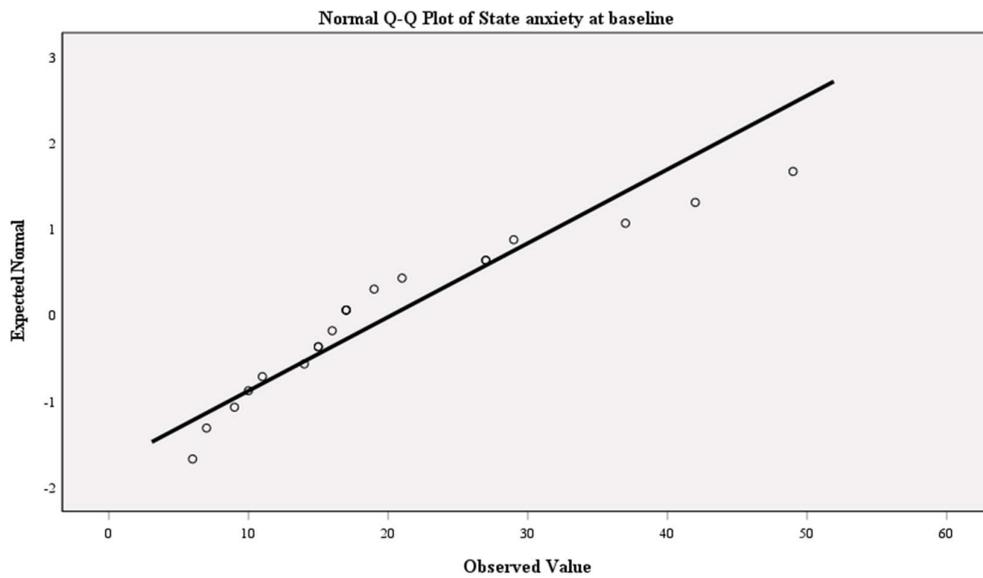*Normal Q-Q Plot of State-alcohol craving at posttest*

State anxiety

Figure 7

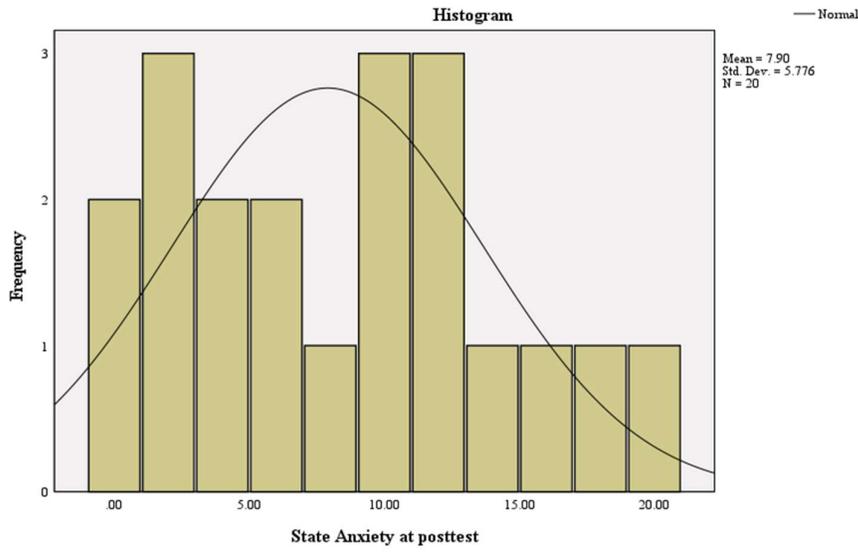*Histogram of State Anxiety at baseline*

Figure 8

Normal Q-Q Plot of State Anxiety at baseline

Figure 9

Histogram of State anxiety at posttest

Figure 10

Normal Q-Q Plot of State anxiety at posttest