Exploring trait anxiety and alcohol craving in patients diagnosed with alcohol use disorder

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Abstract

Background: The treatment of Alcohol Use Disorder (AUD) is a high point of interest for health departments and research. Alcohol craving and anxiety are two decisive factors in the maintenance of AUD. Many AUD patients are diagnosed with a dual diagnosis of anxiety or report high levels of anxiety and alcohol craving. Despite, a variety of treatment approaches (e.g., cue-exposure therapy (CET)) high rates of relapse are common in AUD individuals. Virtual Reality (VR) enriches CET by enhancing the individual's interaction with contexts, cues, and realistic environments. The combination of both approaches is called VR-CET and was applied in this study through the ALCO-VR software. The focus of this study lies on the effects of VR-CET treatment on trait-craving and trait anxiety levels of AUD individuals who are at high risk of relapse.

Methods: A within-subjects design was conducted to look at the effects of VR-CET treatment sessions on participant's trait anxiety and alcohol trait craving levels. Further, their reports on drinking patterns and the relationship towards anxiety and craving were studied. Participants (N = 21) were patients from the Addictive Behaviour Unit of the Hospital Clinic of Barcelona. A repeated measures ANOVA and Friedmann Test were conducted as well as a Pearson's-Correlation and a Spearman's Correlation.

Results: The results showed a significant reduction in trait anxiety and trait craving after VR-CET treatment. Trait anxiety was positively correlating with drinking patterns, while trait craving was not.

Conclusion: Finally, the current study contributes to the current research on the efficacy of the ALCO-VR software, by showing the reduction of anxiety and craving in AUD individuals. Future research could focus on sociodemographic individual differences of participants and include longitudinal data to investigate long-term efficacy and benefits after using VR-CET in AUD individuals.

Keywords: Alcohol use disorder, cue-exposure therapy, virtual reality, anxiety, craving

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Introduction

Alcohol use disorder (AUD) is a transnational health issue. Worldwide around three million deaths per year (5.3% of all deaths) are the consequence of heavy alcohol consumption (Bernard, Cyr, Bonnet-Suard, Cutarella, & Bréjard, 2021). Unfortunately, AUD is one of the most common undertreated disorders in the developed countries and contributes to the global burden of disease (Rehm et al., 2015). It is prevalent in young adults (aged 18 to 29), where less than 15% receive adequate treatment (Cohen, Feinn, Arias, & Kranzler, 2007). For the majority of patients, the first treatment is postponed after reaching their thirties (Hall & Teesson, 1999). Individuals with such a diagnosis have lost control of their drinking behaviour and continue to consume alcoholic beverages, despite the consequences for their health and social environment. Consuming high amounts of alcohol while being at risk of developing physical or mental health damage, refers to as *hazardous drinking* (Grossi et al., 2021). Individuals with these patterns seem to use alcohol in order to cope with difficult emotions (Dawson et al., 2005). *Harmful drinking* refers to a drinking pattern where physical and mental health are damaged and might have additional consequences in other life areas (Frone, 2016).

Among the most common symptoms of AUD are tolerance development, withdrawal symptoms, loss of control over alcohol use, difficulties at work, at school or at home because of alcohol consumption (Snelleman, 2017; de Bruijn, van den Brink, de Graaf, & Vollebergh (2006). Further, individuals with an alcohol dependence continue to drink although experiencing physical and psychological problems (Barrick & Connors, 2002). Four main categories for alcohol dependence can be formulated: *impaired control* (being unable to stop alcohol consumption on any given occasion), *craving* (strong urge to consume alcohol), *physical dependence* (body symptoms as nausea, sweating, shakiness, and anxiety, when not drinking) and *tolerance* (the amount of alcohol intake needs to increase in order to have an effect for the individual). Since alcohol has rewarding and socially facilitating effects at low doses, it provides an explanation for the persistence of alcohol consumption. Expectations regarding the pleasurable effects of alcohol (e.g., tension reduction and increased confidence) as well as an individual's capability to stay abstinent (self-efficacy), contribute to the development of AUD (Connor, George, Gullo, Kelly, & Young, 2011).

The urge to consume alcohol, *alcohol craving*, can be described as one of the core mechanisms in the development and maintenance of AUD. According to the literature, craving is the strong desire to consume alcohol, which then results in psychological as well as physiological changes in individuals with AUD (Yoon, Thompson, Hakes, Westermeyer,

Petrakis & Kim, 2020; Ghiţă & Gutiérrez-Maldonado, 2018). When craving for alcohol, a cognitive effort is needed to inhibit an automatic response to alcohol and occur when an AUD patient tries to stay abstinent (Bernard et al., 2021). Kavanagh, Andrade and May (2005) and May, Andrade, Panabokke and Kavanagh (2004) introduced the Elaborated Intrusion Theory of Desire (EITD), which provides insights into the processes of cravings and their impact on addictive behaviours. The theory describes craving as a cycle of mental elaboration of an initial intrusive thought. A distinction between associative processes that provoke *intrusive thoughts* about an appealing objective and controlled processes of cognitive *elaboration* that focus on thoughts with stronger affective links was outlined. This prioritization leads to an intrusion with other cognitive demands. EIDT proposes that craving consists of intrusive thoughts of drinking followed by verbal or image fragments, the elaborated thoughts. Especially under tension or cognitive demands suppressing thoughts often results in the opposite, the repressed thought becomes more retrievable by the mind (Wegner & Erber, 1992).

Transferring the EITD processes to alcohol craving it can be associated with an inhibition mechanism. This implies that an AUD patient who tries to restrain alcohol-related thoughts is faced with even more upcoming thoughts related to alcohol. These thoughts and memories about cues (e.g., people, places, things, emotions) associated with alcohol use can promote alcohol craving and alcohol consumption further which may facilitate relapse (Soravia, Moggi, & Quervain, 2021). As craving is a dynamic mechanism, another study indicated that some AUD individuals may not experience alcohol craving at all, whereas social drinkers without AUD may experience high levels of alcohol craving (Yoon et al., 2020). Since there can be observed a variance in the levels of craving, one might consider other possible factors that could include use of other substances or a psychiatric co-morbidity that promote relapses in AUD individuals (Durazzo & Meyerhoff, 2017).

The most common co-morbidity in AUD patients is *anxiety* (Stewart & Conrod, 2008). Anxiety is another facilitator for alcohol consumption in individuals with AUD that can range from mild distress to an anxiety disorder (Blanco, Flórez-Salamanca, Secades-Villa, Wang, & Hasin, 2018). Anxiety may be developed before the onset of compulsive drinking habits, but it can also be involved in the process of abstinence maintenance (Gilpin, Herman, & Roberto, 2015). Interestingly, individuals with a dual diagnosis of anxiety disorders and AUD have become a growing point of interest in research, since recovery and maintaining abstinence is a greater problematic in these individuals (Anker, Kummerfeld, Rix, Burwell, & Kushner, 2018). Further, a network modelling analysis showed that social anxiety and stress can cause

alcohol craving in AUD patients, which promotes alcohol consumption and therefore accelerate relapse (Anker et al., 2018). Despite of a variety of effective psychological and pharmacological treatment possibilities, high rates of relapse are common in AUD patients, especially in the first three months (McKay & Hiller-Sturmhofel, 2011). Bottlender and Soyka (2005) found that 45 percent of alcohol dependent individuals experience relapse at 3-year follow-up. Examples of non-pharmacological treatments are the Cognitive Behavioural Therapy (CBT), Motivational Enhancement Therapy or behavioural therapies based on conditioning (Connor, Haber, & Hall, 2016). Despite these promising therapy approaches in short term there are several theories that explain high relapse rates in the long term. One explanation emerged from the neuroscientific community, which states that individuals with long-term alcohol consumption developed certain cognitive and emotional processes that endorse negligent drinking behaviour (Koob, 2013). Due to altered reward pathways, increased alcohol craving and relapses are the consequence (Robinson & Berridge, 2008). These consequences can arise even if the individuals have been abstinent for years.

Other studies have explored explanations how different cues facilitate alcohol craving followed by a relapse (Pericot-Valverde, Garcia-Rodriguez, Guiterrez-Maldonado, & Secades-Villa, 2015). The *situational specificity* hypothesis states that alcohol craving is determined by real life drinking cues and contexts (Wall, McKee, Hinson, & Goldstein, 2001; Monk & Heim, 2013). This contextual reliance in alcohol craving is emulated by the cue-reactivity paradigm, where alcohol related stimuli are risk factors that promote heavy drinking episodes and AUD (Stein, Fey, Koenig, Oehy & Moggi, 2018). The cue-reactivity paradigm led to the development of the cue-exposure therapy (CET) (Mellentin, Nielsen, Nilsen, Yu, & Stenager, 2016). CET is a behavioural approach to treat substance use disorders (SUD). Individuals are exposed to relevant cues (e.g., drugs, alcohol) to change conditioned responses (Conklin & Tiffany, 2002). This therapy is based on the Pavlovian conditioning model (Pavlov, 1927). Transferred to alcohol, alcohol-related stimuli would represent the unconditioned stimulus (US) and the effect of alcohol, positive and rewarding properties, would be the unconditioned response (UR). A neutral stimulus such as the colour of the drink or the sound of a bar can be associated with the US and therefore become a conditioned stimulus (CS). The CS provokes a conditioned response (CR) when being paired with the UR. This process can lead to cue-induced cravings which might cause alcohol addiction (Drummond, 2001).

Classical conditioning states that addiction is learned via reinforcement and that a conditioned response can be changed by core mechanisms of systematic desensitization

(Ferrer-García et al., 2017). Systematic desensitization is derived from experimental psychology (Rachman, 1967). Traditionally it is used to effectively treat phobias, where an individual would gradually be exposed to its fears in order to become less vulnerable. Regarding CET, AUD individuals will be exposed to alcohol-related stimuli, without consuming any beverages, to elicit craving. There is the assumption that being continuously exposed to a certain type of alcohol-related stimuli will reduce psychophysiological responses and therefore diminish conditioned responses like alcohol craving (Mellentin et al., 2016). The main aim of the CET is to prevent future relapses and it does that by building coping skills that increase self-efficacy (Giovancarly et al., 2016; Barlow et al., 2016). However, it was found that most CET therapy treatments were inconsistent considering that many were conducted by showing only one cue to the participants, an auditory, visual, photographic, or in vivo cue (e.g., one glass of an alcoholic drink), within a controlled setting (Conklin & Tiffany, 2002). These settings made it difficult to generalize the effects of CET therapy into real-life situations of AUD patients, as addiction is a complex condition that involves multiple variables (Wiederhold & Rizzo, 2005).

Considering the limitations of CET approach, there has been a growing interest in applying technological advances. An emerging technology explored as a complementation towards existing methods is virtual reality (VR). This technology has become more and more popular over the past two decades and has developed to one of the more ecologically valid assessment and treatment instruments regarding alcohol craving in AUD (Ghiţă & Gutiérrez-Maldonado, 2018). VR enriches the classical CET therapy by adding a broad range of sensory perceptions like visual, auditory, olfactory, or tactile stimuli, thus recreates a realistic real-life environment for the users, instead of a controlled clinical setting (Riva, 2009). The VR systems offers a high degree of interaction, which has a positive effect on the personal perception of the individuals while being in the VR environment (Ferrer-García et al., 2010). This technique brings the advantage that an increased subjective and physiological craving can be targeted more effectively and thus offers more realistic results. Nevertheless, there is still the need for more in-depth research regarding the effectiveness of virtual reality cue-exposure therapy (VR-CET) as there is not yet enough evidence of VR in diminishing alcohol craving and the often-followed relapses (Ghiţă et al., 2021).

The current study is part of a larger project “ALCO-VR: Virtual Reality-based protocol for the treatment of patients with severe alcohol use disorder” with aims to test the efficacy of VR-CET in patients diagnosed with severe AUD. The first of these studies was aimed at identifying alcohol-related cues and contexts that provoke craving in AUD patients

to develop realistic virtual environments with a clinical significance (Ghiţă et al., 2019a). A bar, a restaurant, a pub and at-home environments were the cues and contexts that elicited alcohol-craving the most. The second study was based on these results and was focused on the development and validation of the "ALCO-VR" platform (Ghiţă et al., 2019b). The last study of the whole project is currently collecting all the outcomes of the previous studies in order to test the efficacy of VR-CET in AUD patients (Hernández-Serrano et al., 2020).

This study focuses on trait anxiety and craving levels of AUD patients. The main objective is to explore the efficacy of VR-CET with emphasis on trait anxiety and alcohol craving in AUD patients. Further, there is the aim to get an improved understanding of individuals with AUD considering their drinking patterns and the relationship towards anxiety and alcohol craving. Anxiety and craving are strong core mechanisms in the maintenance of alcohol consumption. Therefore, this study is interested in exploring these relationships before the planned treatment with VR-CET and find out whether these mechanisms follow a similar direction.

Research Questions

This study aims at answering the following questions:

1. What effect does VR-CET treatment have on the levels of trait anxiety and alcohol craving of AUD individuals?

Additionally, two hypotheses are formulated regarding the research question:

H_{1a}: There will be a significant decrease in trait anxiety levels at pre- and post- VR-CET sessions in AUD individuals.

H_{1b}: There will be a significant decrease in trait-alcohol craving between pre-VR-CET session compared to post-VR-CET sessions in AUD individuals.

2. What is the relationship between drinking patterns, trait anxiety and craving in AUD individuals?

H_{2a}: There is a significant relationship between drinking patterns and trait anxiety levels of AUD patients.

H_{2b}: There is a significant relationship between drinking patterns and craving of AUD patients.

Method

Design

Ethical approval was obtained from the Ethics Committees at the University of Barcelona and Hospital Clinic of Barcelona. The ethical code number is 0377 (HCB/2017/0377) and the approval date was 09/2017. The collected data was part of a larger study; however, this study investigates the levels of trait anxiety and alcohol craving of AUD individuals before and after VR-CET treatment sessions. A within-subject design was employed.

Participants

A total of 21 participants N (= 21) were recruited from the Hospital Clinic of Barcelona and participated in this study after providing written informed consent. Included were individuals that have been diagnosed with AUD according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (5th Ed.) (American Psychiatric Association, 2013). Further, focus lied on patients who showed resistance towards treatment-as-usual (TAU), meaning that these patients experienced relapse in the first six months after treatment discharge from the Addictive Behaviours Unit of the Hospital Clinic of Barcelona. The patients were selected by the lead clinical psychologist from the hospital based on their clinical history while they were under ambulatory treatment (receiving TAU). This treatment included pharmacotherapy and psychosocial care. Exclusion criteria were severe psychopathology (e.g., psychosis), severe cognitive impairment, use of anti-craving medication (e.g., naltrexone) and pregnancy. The clinical anamnesis included dual pathology, the specific type of the pathology (depression, anxiety etc.), smoking patterns, medication (anxiolytics, antidepressants etc), and abstinence period before their inclusion in the study.

The characteristics of the participants at baseline are described in Table 1. The mean age of the participants was 52.80 with a standard deviation (SD) of 7.76. Gender was almost equally represented with 11 male and 10 female participants. The majority of participants had

a bachelor's degree as an educational level (38.1%) or a post-high school graduation (33.3%). Further, most participants had a medium socioeconomic status (76.2%) and were in a relationship (42.9%) or separated (33.3%). More than half of the participants had an additional diagnosis to AUD (57.1%), where 42.9% participants had depression and 19% depression and anxiety. Over 70% were currently smoking. While nearly one third of the participants received no medication, 33.3% got disulfiram prescribed. The mean abstinence rate was 74.19 with an SD of 92.06.

Table 1

Characteristics of Participants at Baseline (n=21)

	N(%) or Mean ± SD	**Min**	**Max**
Characteristics	**Total Sample**		
Age	52.80 ± 7.56	36	67
Gender			
Male	11 (52.4%)		
Female	10 (47.6%)		
Education			
Secondary school	2 (9.5%)		
High School	3 (14.3%)		
Post-high school	7 (33.3%)		
Bachelor's degree	8 (38.1%)		
Master's degree	1 (4.8%)		
Socioeconomic status			
Low	3 (14.3%)		
Medium	16 (76.2%)		
High	1 (4.8%)		
Civil Status			
Single	3 (14.3%)		
In a relationship	9 (42.9%)		
Divorced/ Separated	7 (33.3%)		
Widower	2 (9.5%)		
Psychiatric Comorbidity	12 (57.1%)		
Types of psychiatric comorbidity			
None			
Depression	9 (42.9%)		
Depression + Anxiety	4 (19.0%)		
Depression + Anxiety + PD	3 (14.3%)		
PD	1 (4.8%)		
PTSD	1 (4.8%)		
PTSD + anxiety	1 (4.8%)		
Polydrug Use	1 (4.8%)		
Current Smoker			
Yes	15 (71.4%)		
No	6 (28.6%)		
Medication			
No	6 (28.6%)		
Antidepressants	5 (23.8%)		
Anxiolytics	4 (19.0%)		
Anxiolytics + Antidepressants	6 (28.6%)		
Disulfiram			
Yes	7 (33.3%)		
No	14 (66.7%)		

Abstinence Days	74.19 ± 92.06	3	360

SD = Standard deviation; PD = Personality Disorder; PTSD = Posttraumatic Stress Disorder

Materials

The VR equipment

Hardware. The VR equipment consisted of an Oculus Rift S head-mounted display (HMD) (Oculus VR, Irvine, CA, USA), sensors, touch controllers and a computer compatible with VR technology (INTEL(R) Core (TM) i7 – 2600 CPU, 16.0 GB RAM, Operating System 64bits, processor x64, graphic card NVIDIA GeForce GTX 1080 Ti).

Software. For the assessment and treatment of the AUD patients the "ALCO-VR" software (developed by the VR-Psy Lab, University of Barcelona, Spain) was used. In previous studies factors that trigger alcohol craving in AUD patients were explored. It was found that restaurants, bars, pubs, and home environments were cues and contexts were some of the main causes for alcohol craving. Therefore, four realistic VR environments were designed which included social interactions (human avatars), alcoholic drinks and different time settings (daytime or night-time) (Ghiţă, 2019a). A hierarchy of exposure from the lowest-rated environment with the lowest-rated alcoholic drink to the highest-rated environment and the highest-rated alcoholic drink was established. Figure 1 displays a screenshot of the four different VR environments. A special focus laid on the interaction authenticity between the participants and the simulation. Participants were able to access alcoholic drinks and other things in the environments due to realistic movements of the wrists and real-time feedback.

Measurements

Alcohol consumption, *drinking behaviours* and a*lcohol-related problems* were explored with the Alcohol Use Disorders Identification Test (AUDIT) (Guillamón, Solé, & Farran, 1999). The Spanish version of AUDIT was used and consists of a 10-item self-report scale that helps to expose excessive alcohol consumption. AUDIT contains three questions regarding the consumption of alcoholic beverages (amount and frequency), four questions with focus on dependence, and three questions on the consequences of alcohol consumption. The scores per question range from 0 to 4, excluding the questions 9 and 10, which are scored as 0, 2 or 4. In total one could score from 0 to 40 points, where a score of 8 or higher displays precarious drinking behaviour and additionally a possible alcohol dependence. The AUDIT has good test-retest reliability and internal consistency (López et al., 2019; Alvarado et al.,

2009). In this study the AUDIT was used to indicate the severity of AUD in the participants (Donovan, Kivlahan Doyle, Longabaugh, & Greenfield, 2006).

Trait anxiety was examined with the Spanish version of the State-Trait Anxiety Inventory (STAI – only the trait subscale) to investigate *trait anxiety* of the participants (Spielberger, Gonzalez-Reigosa, Martinez-Urrutia, Natalicio, & Natalicio, 1971). The STAI was developed to assess trait and state anxiety in research and clinical settings. It includes two 20-item scales that measure the intensity of anxiety as an emotional state (state anxiety) and individual differences in anxiety proneness as a personality trait (trait anxiety). This study focuses on trait anxiety, therefore only the results of the trait scale will be included. Participants rated how often they experienced anxiety-related feelings and cognitions with a 4-point scale from 1 (“almost never”) to 4 (“almost always”). The STAI has a high internal consistency with a Cronbach’s alpha of .86 (Quek et al., 2004). The test-retest reliability of .84 and .83 appears to be well established (Spielberger et al., 1971).

Alcohol craving was measured with the Multidimensional Alcohol Craving Scale (MACS), to investigate alcohol craving in the previous week of the participant (Guardia et al., 2004). The MACS is a self-report scale used to explore the “intensity of alcohol craving experienced by the participant in his/her previous week”. It consists of two sub-scales “desire to drink” and “behavioural disinhibition”. Participants responded to a 5-point Likert scale from 1 (“strongly disagree”) to 5 (“strongly agree”). The total craving score was calculated by the sum of 12 items that classify craving as non-existent when a participant scores 0 to 12, as mild with a score of 13 to 22, as moderate with a range of 23 to 40 or as intense when the total score is above 40 as in the literature of Guardia et al. (2004). The MACS presents good psychometric properties, the internal consistency Cronbach’s alpha .94 (Guardia et al., 2004).

Figure 1

Images of the four different VR environments

Procedure

AUD patients from the Addictive Behaviours Unit of the Hospital Clinic of Barcelona were invited to participate. All participants reported their sociodemographic data including the information described in the design section. In the initial assessment participants were asked complete the three different questionnaires and socio-demographical and clinical data were collected. The AUDIT to detect problematic drinking in the past year. The STAI to explore the participants trait anxiety and the MACS to assess levels of craving during the past week. Then the researchers provided the participants with a short tutorial in order become familiar with the VR technology to explore the four VR environments and the alcoholic drinks. The ALCO-VR software started by assessing how much craving and anxiety was triggered by images of the four VR environments (Figure 1) and alcoholic beverages. Based on the individual's responses an exposure hierarchy was established that consisted of an interplay between the first five chosen alcoholic drinks and the environments. The first ALCO-VR session (in total six VR-CET sessions) started with the lowest rated alcoholic drink (from the five preferred beverages) within the lowest rated VR environment. This was

followed by a gradual exposure from the lowest rated to the highest rated beverages and environments. After this part the Oculus Rift Head Mounted Displays (HMD) were attached to the heads of the participants. Then the 3D virtual reality experience (approximately 10-15 min) started and were first exposed to a neutral environment with a glass of water in a white room to familiarize the participants with the technology. Then the participants were exposed to the different environments followed by their individual hierarchy. In total the assessment lasted approximately 50 minutes. In the post assessment participants completed the MACS and STAI again to explore possible changes in their trait anxiety and trait-craving.

Data Analysis

To analyse the data IBM SPSS Statistics version 26 was used. Descriptive statistics were calculated to characterize the participants at baseline. Including participants demographics and a clinical anamnesis. Further, scores of trait craving were transformed into a categorical variable “non-existent” (0-12), mild (13-22), moderate (23-40), intense (>40). Normality was assessed for pre- and post-tests of trait anxiety and trait craving. Q-Q plots were included in the assessment of normality. Normality assumptions were violated in one case, therefore parametric and non-parametric tests were performed to investigate the hypotheses. A repeated measures ANOVA and a Friedman Test were conducted to explore whether significant differences can be found in the pre- and post-scores of trait anxiety (H1a) and trait craving (H1b). A Pearson’s-Correlation and a Spearman’s Correlation were used to analyse whether there is a significant relationship between trait anxiety and drinking patterns of AUD patients (H2a) and trait craving and drinking patterns of AUD patients (H2b).

Results

The total scores of the questionnaires are shown in Table 2. The mean score of AUDIT was 16.95. The pre-test mean score on trait anxiety was 29.71 and 24.67 on trait craving. The post-test mean score was 22.81 on trait anxiety and 19.86 on trait-craving. Most participants had mild trait craving (47.6%) or moderate trait craving (38.1%) in the initial assessment. While 9.5% experienced intense trait craving. In the post assessment over the half of patients reported mild trait craving (52.4%) or moderate trait craving (28.6%). 19% had non-existent trait-craving levels and no intense trait craving was reported.

Table 2

Questionnaire scores N = 21

Questionnaire	Mean	SD	Min	Max
AUDIT (drinking pattern)	16.95	10.47	2	38
STAI Pre (Trait Anxiety)	29.71	11.90	10	51
STAI Post (Trait Anxiety)	22.81	13.65	1	53
MACS Pre (Trait Craving)	24.67	11.90	12	49
Non-existent	1 (4.8%)			
Mild	10 (47,6%)			
Moderate	8 (38.1%)			
Intense	2 (9.5%)			
MACS Post (Trait Craving)	19.86	8.61	12	40
Non-existent	4 (19%)			
Mild	11 (52.4%)			
Moderate	6 (28.6%)			
Intense	0 (0%)			

SD = Standard deviation; AUDIT = Alcohol Use Disorder Identification Test; STAI = Trait-Anxiety Inventory; MACS = Multidimensional Alcohol Craving

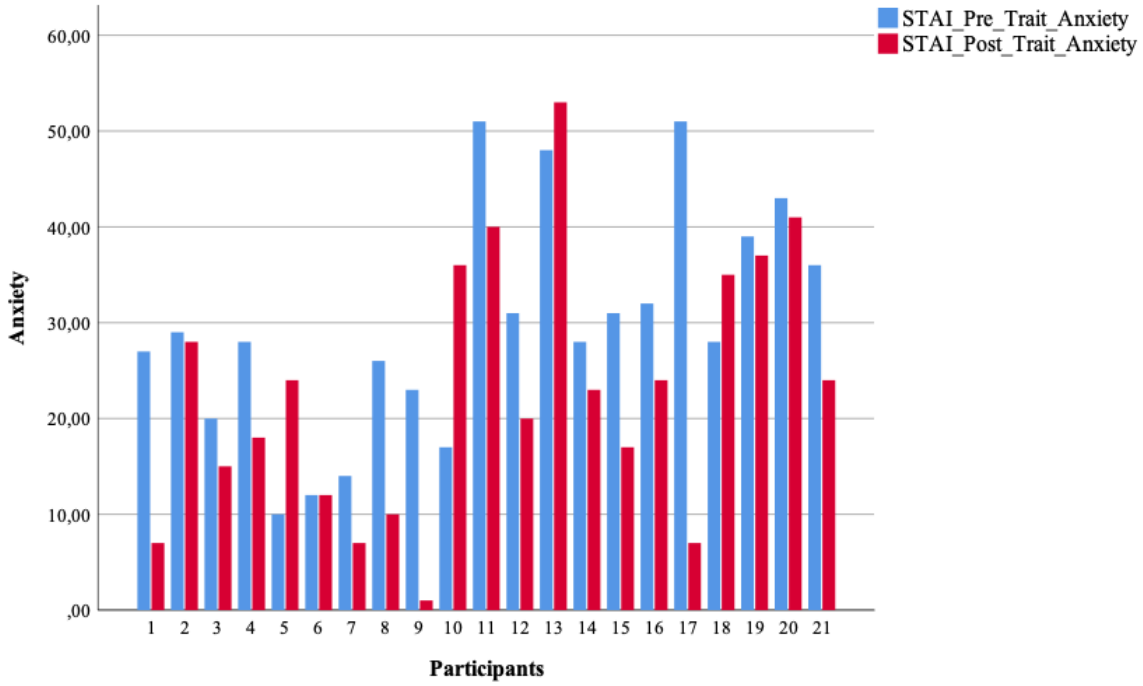
Normality testing was conducted with the Shapiro-Wilk test. Pre- and post-scores of trait-anxiety did not deviate significantly from normality, $W(21) = 0.954$, $p = .410$ and $W(21) = 0.964$, $p = .610$. The pre-scores of trait-craving did not deviate from a normal distribution, $W(21) = .913$, $p = .063$, while the post-scores of trait-craving significantly deviate from normality, $W(21) = 0.841$, $p = .003$. Considering the Q-Q plots of trait-craving it was determined that the data points from the pre- and post-scores stray from the line in a non-linear fashion, therefore the data was not normally distributed, although the Shapiro-Wilk test implied that the pre-scores of trait craving were normally distributed. The Q-Q plots can be found in Appendix A.

Hypothesis testing

A repeated measures ANOVA with a Greenhouse-Geisser correction determined that mean trait anxiety levels differed statistically significantly between time points $F(1.000, 20.000) = 5.625$, $p < 0.028$. Therefore, we can conclude that the therapy program might elicit a statistically significant reduction in trait-anxiety. In Figure 2 pre- and post-scores of all participants were compared. It showed an overall reduction of trait anxiety levels except for four cases, where participants showed higher levels of trait anxiety in the post-assessment. The effect size Cohen's *d* for trait anxiety was 0.54.

Figure 2

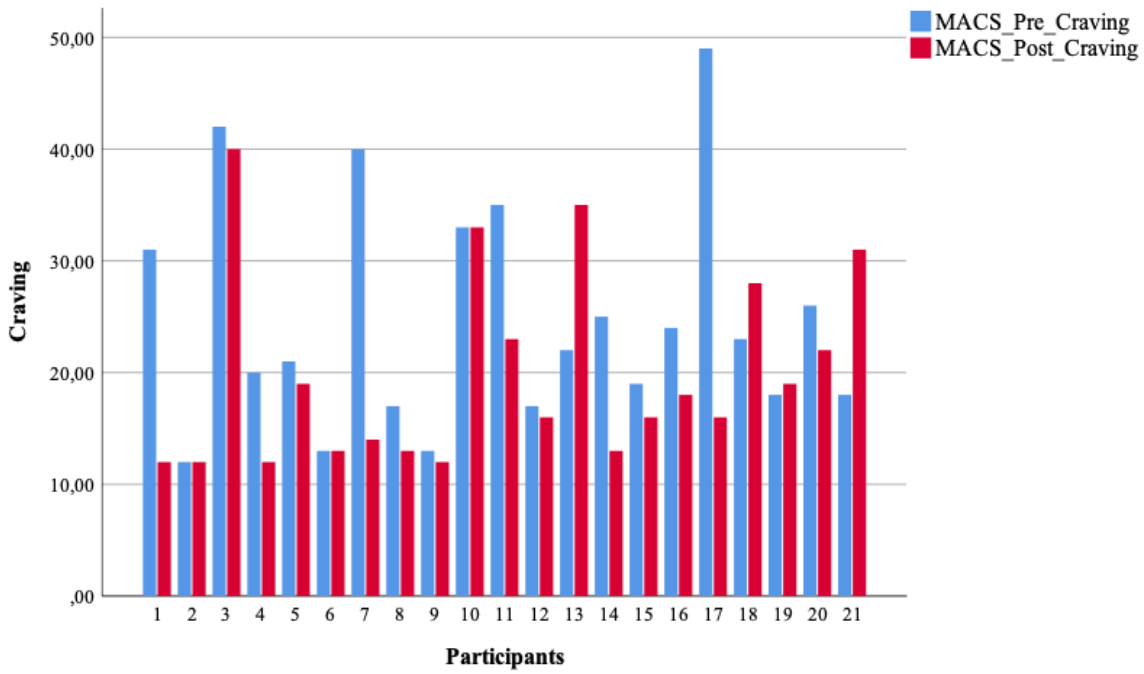
Pre and Post Trait Anxiety Levels (STAI) of participants



Due to deviations from normality the non-parametric Friedman test was used to investigate the differences between pre- and post-scores of trait craving. There was a statistically significant difference in trait craving before and after the treatment, $\chi 2(1) = 4.455$, $p = .035$. In Figure 3 pre- and post-scores of all participants were compared for trait craving. The majority of participants showed lower levels of trait craving yet there were four participants who displayed higher craving levels and in three cases the trait craving levels remained the same. The effect size Cohen's *d* for trait craving was 0.51.

Figure 3

Pre and Post Craving Levels (MACS) of participants



A Pearson product-moment correlation was run to determine the relationship between trait-anxiety and drinking patterns of AUD patients. There was a strong, positive correlation between trait-anxiety and drinking patterns, which was statistically significant (r = .619, n = 21, p = 0.003). A Spearman's rank-order correlation was run to determine the relationship between trait-craving and drinking patterns (as reflected by AUDIT) of AUD patients. There was no significant correlation between trait craving and drinking patterns $r_s(21)$ = .007, p = .976.

Discussion

The current study was part of a larger project that aims to investigate the effectiveness of ALCO-VR software as an assessment and treatment tool for AUD individuals who are at risk of relapse. Alcohol is one of the main causes for the high burden of diseases worldwide (Bernard et al., 2021). Due to the complex nature of AUD many patients experience relapse after treatment. Alcohol craving and anxiety are two important factors that are responsible for the maintenance of AUD (Soravia et al., 2021; Blanco et al., 2018). This study focused on the effects of VR-CET to decrease trait anxiety and alcohol trait craving of AUD individuals. Its second objective was to assess whether there was an existing relationship between drinking patterns, trait anxiety and craving in AUD individuals. The results indicated that the levels of trait anxiety (H1a) and alcohol craving (H1b) of the participants were reduced after VR-CET treatment. A positive relationship was found between trait-anxiety and drinking patterns, while a relationship of trait-craving and drinking patterns could not be confirmed.

Current Findings

In line with previous studies alcohol trait craving was reduced (H_{1b}) after VR-CET treatment sessions for most participants (Hernández-Serrano et al., 2020; Ghiţă, et al., 2019c). Some participants reported no craving and none of the participants experienced intense craving. The first possible explanation for the results could be the successful implementation of the ALCO-VR sessions. The technology of VR brings the advantage to create realistic environments that are typical settings for alcohol consumption which incorporates contextual reliance that is one of the main factors promoting high alcohol craving levels (Ghiţă & Gutiérrez-Maldonado, 2018). A reduction of these levels can be explained by the process of systematic desensitization which reduces psychophysiological responses and therefore diminishes the conditioned responses like alcohol craving (Mellentin et al., 2016; Rachman, 1967). This process might have been even more successful in an VR environment, which allows for high interaction with the stimuli (Ferrer-García et al., 2010). The human sense of boundary between the real world and the VR environment helps to attain immersion in an illusion (Murray, 2020). Even though participants are aware of wearing VR equipment they experience a double consciousness which displays the virtual world surprisingly real. Meaning, that the psychophysiological processes which would occur in a real-life situation can be activated. Participants in this study were exposed to alcoholic beverages in typical Spanish bars, pubs, restaurant, and home environments (Ghiţă et al., 2019a). The impression

of experiencing a familiar situation in an alcohol related setting could have accelerate psychophysiological processes and therefore alcohol craving. The systematic exposure using VR-CET might have led to a habituation of participants towards alcohol cues and to the desired reduction of alcohol craving (Ferrer-García et al., 2010). Habituation is referred to as a "decrease in responsiveness to a repeated stimulus" (Grissom & Bhatnagar, 2009). Despite the decreased levels of alcohol craving, there were four participants who showed higher levels of alcohol-craving. One explanation might be that individuals with severe AUD interfere with acknowledging the negative consequences of drinking during cue-exposure of alcohol-related stimuli (Suzuki et al., 2020). Without learned cognitive strategies participants might have experienced difficulties in regulating their alcohol-craving. This negative affect was also found to predict relapse in individuals who smoke but correlated with drinking problems. Healthy adults can apply cognitive strategies to regulate affective responses to alcohol-related stimuli in everyday life, while AUD individuals are able to use these strategies in a traditional laboratory setting but might not be able to use them properly in a realistic VR environment (Suzuki et al., 2020). Another explanation might be the medium effect size of trait anxiety. Cohen (1988) described an effect size of 0.5 as a medium effect, which can be used as an orientation that might indicate that the effects of the treatment sessions were not as large as expected.

The findings were similar regarding trait-anxiety (H_{1a}), most participants showed a reduction in their anxiety levels. Prior research found that anxiety is associated with relapse in AUD patients, regardless starting before alcohol consumption or during a period of abstinence (Gilpin et al., 2015). The application of the self-medication model could be considered as an explanation for the results of this study (Smith & Randall, 2012). It proposes that individuals with anxiety disorders consume alcohol to cope with their symptoms of anxiety. This assumption is shared by several models for example self-medication, (Khantzian, 1985; Quitkin et al., 1972) and tension reduction (Conger et al., 1999). Stewart and Conrod (2008) introduced the "vicious cycle of comorbidity" where biopsychosocial outcomes of anxiety sustain alcohol consumption or the other way around. Through the VR-CET treatment and abstinence the cycle's maintenance could have been hindered as participants displayed decreased alcohol-craving levels and were not consuming any alcohol which could have let to the reduced anxiety levels. Interestingly, four participants showed higher rates of trait-anxiety in the assessment after treatment. AUD is because of its complex nature difficult associated with poor treatment outcomes to and especially individuals who suffer from comorbid anxiety (Anker et al., 2018; Kessler, 2004). Ghiţă et al. (2019c) found a response pattern of AUD

patients during VR-CET. These patterns showed greater levels of craving and anxiety during exposure to alcohol-related contexts. This pattern could have been an influencing factor in these four cases after the treatment as well. The exposure towards alcoholic cues might have elicited related emotions like mental distress and experiences and therefore the participants could have felt more anxious in general (Bakken, Landheim, & Vaglum, 2007). Further, the effect size for trait anxiety were 0.54 which can also be interpreted as a medium effect.

The second objective of this study was to assess the relationship between drinking patterns and alcohol trait craving or trait-anxiety. A positive relationship of trait-anxiety and drinking patterns was found (H_{2a}). This finding adds to previous research that showed how anxiety induces alcohol consumption (Smith & Randall, 2012). In the study of Kessler (1997) 35.8 percent of alcohol dependent men and 60.7 percent of women had a comorbid anxiety disorder. Individuals then often consume alcohol in order to self-medicate these mood problems (Brady & Randall, 1999). Moreover, when experiencing alcohol withdrawal anxiety is increased which contributes to relapse (Gilpin et al., 2015; Hershon, 1973). This again supports precisely the "vicious cycle of comorbidity" with is responsible for the maintenance of anxiety and alcohol consumption (Stewart & Conrod, 2008).

Surprisingly, alcohol craving and drinking patterns did not correlate positively (H_{2b}). Alcohol craving is described as the urge to consume alcohol, which makes it less comprehensive why no relationship was found (Yoon et al., 2020; Ghiţă & Gutiérrez-Maldonado, 2018). An explanation might be that most of the participants were abstinent for at least a month and therefore alcohol craving might have been less present during the first and only assessment of drinking patterns and the first assessment of alcohol craving. Alcohol related environmental cues and contexts elicit relapse and induce craving (Shi et al., 2009). Participants might have been in less contact with these cues during the time of abstinence and might therefore experience less craving. These assumptions would need more research in order to be confirmed.

Strengths and Limitations

VR has been an upcoming technology over the past years, with an immense variety of applications that include games, art pieces, educational explorations, and research. Next to these general advantages it enriches traditional CET by adding ecological validity to this study due to the application of various cues and a realistic environment in contrast to a traditional laboratory setting without additional sensory perceptions (Ghiţă & Gutiérrez-Maldonado, 2018). Participants were exposed to four different VR environments (bar, pub,

restaurant, at home environment) adding to the realistic perception of the alcohol related context, which is needed for a complex condition as addiction (Wiederhold & Rizzo, 2005). In previous studies of Ghiţă et al. (2019a) alcohol-related cues and contexts were identified that provoke craving in AUD patients and represent another strength of this study. They thoroughly designed the environments for the ALCO-VR platform, including specific alcoholic beverages and original cues and contexts that elicited alcohol-craving the most. This preparation and an additional validation of ALCO-VR platform makes it more likely to support the participants with their needs and to develop a functional and effective treatment instrument (Ghiţă et al., 2019b). Another strength of this study was that even though all participants were at high risk for relapse and were familiar with several treatment approaches the results showed improvements in anxiety and craving levels of the participants. Therefore, the findings in this study can be interpreted as important and worth to investigate further.

Despite the promising findings this study had several limitations that require consideration. First, the sample of this study consisted of 20 participants. Although, this is an adequate sample for a small-scale study the small sample size makes it difficult to generalize the results to other AUD patients. Additionally, an investigation of individual differences (i.e., medication intake, psychiatric co-morbidities) was not applicable due to the small sample size. However, this might have given additional information regarding the effectiveness of ALCO-VR in treating AUD individuals. Further, no differentiation between personality traits could be made which was a practical decision due to the small sample size. Bernard et al. (2021) found that there is an association between alcohol craving, impulsivity, and inhibition. Impulsivity is a personality trait which leads to impulsive behaviour and when individuals are exposed to alcohol-related stimuli a poorer inhibition ability and increased craving is present (Papachristou et al., 2013). Considering personality traits in a study with AUD individuals might bring deeper insights in the efficacy of ALCO-VR and therefore a successful treatment. Second, the current study is part of an ongoing project, therefore no long-term follow-up data is available. Lacking this information, it is difficult to draw solid conclusions regarding long-term effects of VR-CET treatment. Third, the ALCO-VR software was designed based on typical establishments of Spanish bars, pubs, restaurant, and home environments. The high contextual dependency of alcohol-craving could be a limitation in the application of ALCO-VR software in abroad populations.

Future Research

Future research could focus on individual differences and personality traits. Moreover, there is the possibility to investigate user accessibility as the ALCO-VR software is used and suited for a clinical setting, but there might be ways to expand the software and more individuals could benefit from it. The study is part of a larger project aiming to develop VR therapy tools on the attempt to find a promising treatment for AUD. This project was conducted in Spain with typical VR environments in a Spanish context (i.e., typical bar, pub, restaurant, at home environment). Further research could examine and design environments that are suitable for other countries and evaluate the benefits for these settings and another target population. The benefits would be valuable for the whole health care system as AUD is responsible for millions of deaths. Moreover, it would be interesting to explore if not only alcohol craving and anxiety levels would have positively changed but additionally alcohol consumption and the individual's well-being.

Conclusion

This study demonstrated the efficacy of VR-CET by reducing the trait anxiety and trait-craving levels of AUD individuals. The assumption that a combination of VR and CET therapy is a valid assessment and treatment instrument regarding treating AUD was therefore confirmed (Ghită & Gutiérrez-Maldonado, 2018; Riva, 2009). First, the assessment showed that alcohol trait craving, and trait anxiety were significantly reduced after the treatment. Second, this study supported findings that drinking behaviour is related to anxiety. Follow up studies could focus on sociodemographic individual differences of participants and include longitudinal data to investigate long-term efficacy and benefits after using VR-CET in AUD individuals. Further, it should be explored whether this treatment decreases the possibility of relapse in the real world and a larger sample would help to draw conclusions on future studies.

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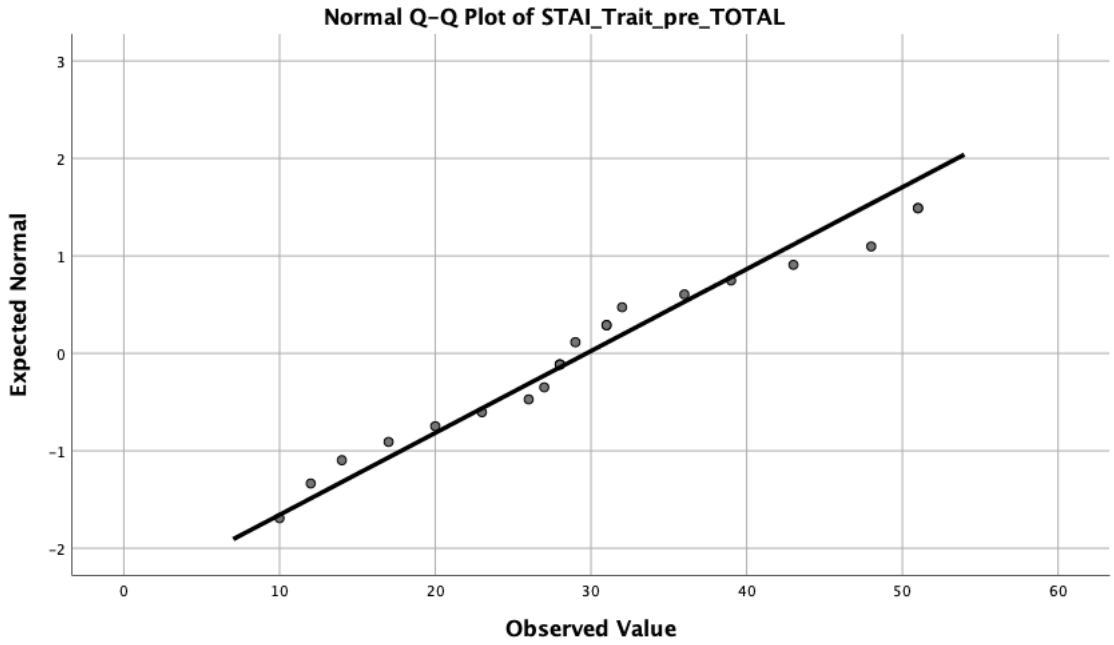
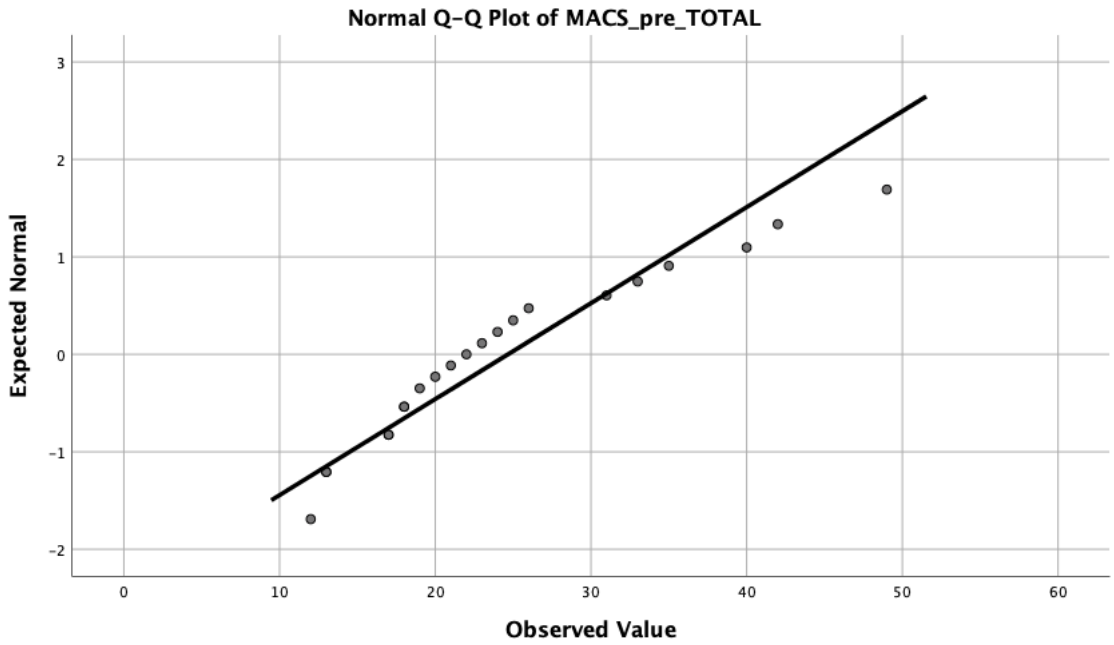
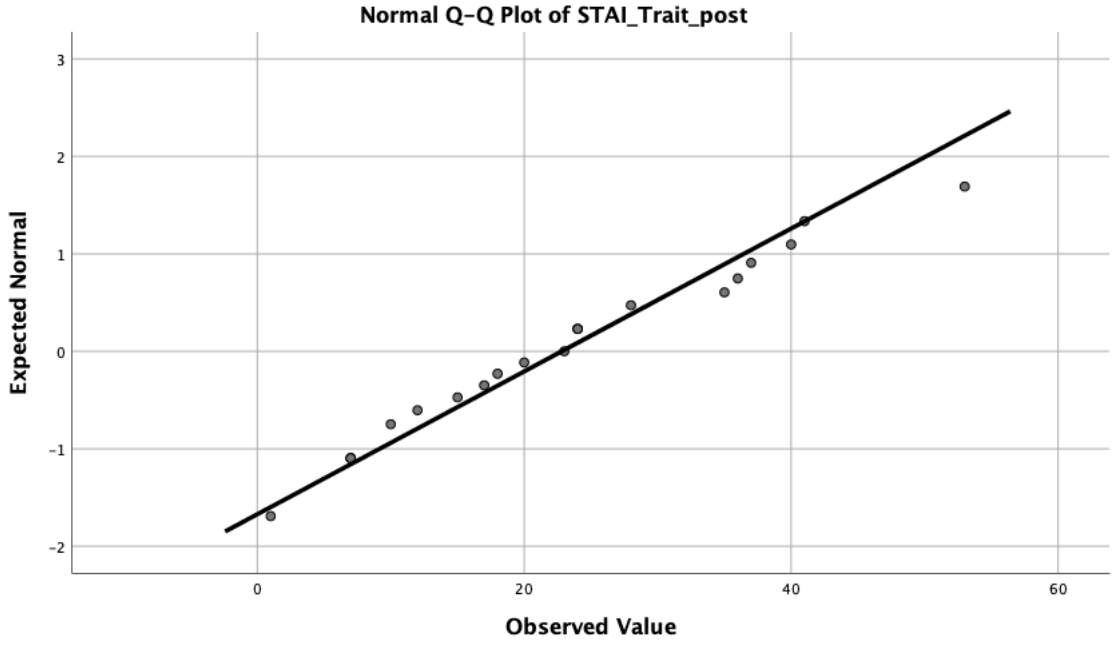
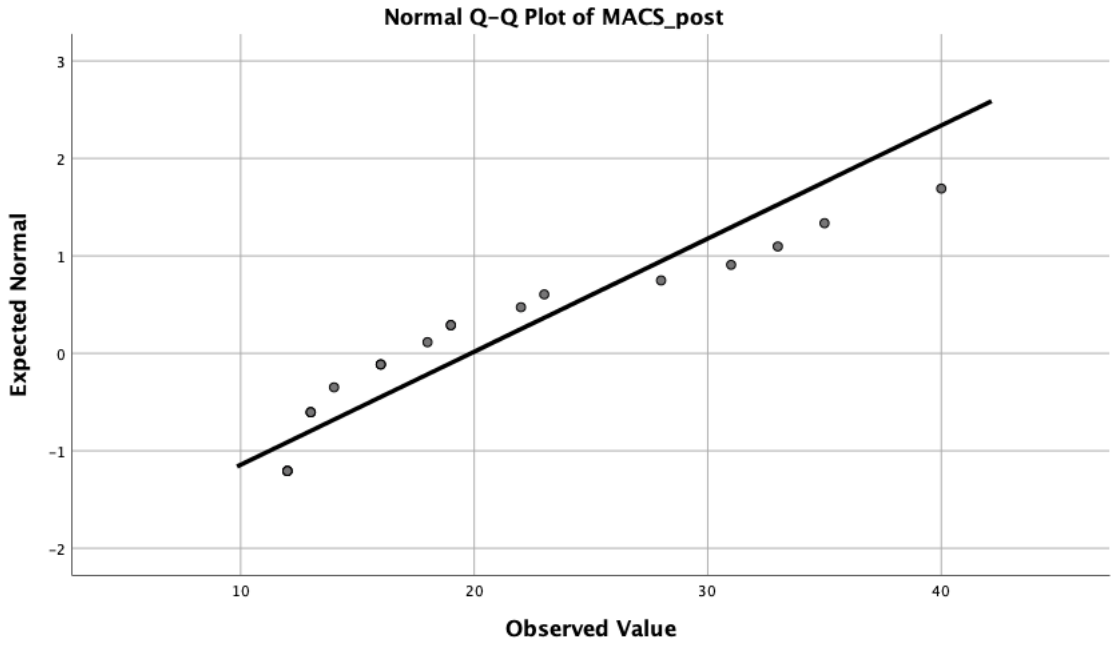
APPENDIX

APPENDIX A






Normal Q-Q Plot of STAI_Trait_post
Expected Normal
Observed Value
3
2
1
0
-1
-2
0
20
40
60


Normal Q-Q Plot of MACS_post
Expected Normal
Observed Value
3
2
1
0
-1
-2
10
20
30
40

APPENDIX B

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*:

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 Conselleria 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 C

Trait Anxiety Inventory (STAI)

INVENTARIO DE ANSIEDAD RASGO

(STATE-TRAIT ANXIETY INVENTORY-STAI)

Instrucciones: A continuación encontrara 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 en general***, en la mayoría de las ocasiones. No hay respuestas buenas ni malas. No emplee demasiado tiempo en cada frase y conteste señalando la respuesta que mejor describa como se siente usted generalmente.

	Casi nunca	A veces	A menudo	Casi siempre
21. Me siento bien	0	1	2	3
22. Me canso rápidamente	0	1	2	3
23. Siento ganas de llorar	0	1	2	3
24. Me gustaría ser tan feliz como otros	0	1	2	3
25. Pierdo oportunidades por no decidirme pronto	0	1	2	3
26. Me siento descansado	0	1	2	3
27. Soy una persona tranquila, serena y sosegada	0	1	2	3
28. Veo que las dificultades de amontonan y no puedo con ellas	0	1	2	3
29. Me preocupo demasiado por cosas sin importancia	0	1	2	3
30. Soy feliz	0	1	2	3
31. Suelo tomar las cosas demasiado seriamente	0	1	2	3
32. Me falta confianza en mí mismo	0	1	2	3
33. Me siento seguro	0	1	2	3
34. No suelo afrontar las crisis o dificultades	0	1	2	3
35. Me siento triste (melancólico)	0	1	2	3
36. Estoy satisfecho	0	1	2	3
37. Me rondan y molestan pensamientos sin importancia	0	1	2	3
38. Me afectan tanto los desengaños que no puedo olvidarlos	0	1	2	3
39. Soy una persona estable	0	1	2	3
40. Cuando pienso sobre asuntos y preocupaciones actuales me pongo tenso y agitado	0	1	2	3

APPENDIX D

Multidimensional Alcohol Craving Scale (MACS)

Escala Multidimensional de Craving de Alcohol (EMCA)

Durante la última semana.	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