Craving and Anxiety Responses as Indicators of the Efficacy of Virtual Reality-Cue Exposure Therapy in Patients Diagnosed with Alcohol use Disorder

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Abstract. *Introduction*: Virtual Reality (VR) technology has shown promising results as an assessment and treatment instrument in substance use disorders, particularly in attempts to reduce craving. A common application of the VR technology in treatment is based on cue-exposure therapy (CET). Following from previous results, the present case series is part of a larger project aiming to test the efficacy of the Virtual Reality-Cue Exposure Therapy (VR-CET) versus Cognitive-Behavioral Therapy (CBT). *Method*: Eight patients between ages 40 and 55 (M_{age} = 49, *SD* = 5.54) from the Addictive Behaviors Unit at the Hospital Clinic of Barcelona participated in this study after providing written informed consent. Patients were randomly assigned to the VR-CET group (three patients) or the CBT group (five patients). The protocol of the clinical trial consisted of a pre-treatment session (the initial assessment session), six sessions of CBT or VR-CET, and a post-treatment session (post-assessment session). The VR-CET sessions consisted of exposure to alcohol-related cues and environments aiming to reduce anxiety and craving responses to alcohol-related stimuli. The CBT sessions consisted of classical standardized therapy for the treatment of addictions, as previously applied in other clinical trials. In the pre- and post-treatment sessions, patients completed several measures of alcohol craving and anxiety and visual analog scales (VAS) during VR exposure. *Results*: Our data indicated a significant reduction in both groups in all scores of craving and anxiety responses, as assessed by the different instruments. In addition, the VR-CET group obtained lower scores on anxiety and craving responses than the CBT group. *Conclusions*: In this ongoing project, the first phase of the clinical trial showed significant improvements in terms of craving and anxiety reduction in both groups, emphasizing that VR-CET can be as efficient as CBT. In addition, patients in the VR-CET group obtained slightly better scores than patients in the CBT group, suggesting the clinical potential of the VR technology in the treatment of substance use disorders. We propose that VR-based CET can be a useful complement to existing treatment methods for AUD patients.

Keywords. Alcohol use disorder, anxiety, craving, virtual reality, assessment, cue-exposure therapy, cognitive-behavioral therapy

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1. Introduction

Empirical studies have suggested that alcohol craving and the related anxiety interfere with treatment outcomes in alcohol use disorder (AUD) patients. Targeting alcohol cravings, a commonly used psychological treatment method is cue-exposure therapy (CET). CET relies particularly on ideals of Pavlovian conditioning, indicating that repeated unreinforced exposure to alcohol-related cues may disrupt and extinguish the urge to consume alcohol (craving) [1]. Although this technique has been widely used, the outcomes of different studies are inconsistent, mainly because the exposure involves limited alcohol-related cues in a safe and secure environment, a circumstance that restricted the later generalization of the effects of the therapy to daily-life activities of the patients. Based on the principles of cue-exposure, Virtual Reality (VR) technology has shown promising results as an assessment and treatment instrument in substance use disorders, particularly in attempts to reduce craving. The outcomes of studies implementing VR in the treatment of AUD patients [2] have emphasized its clinical potential as a complementary instrument in substance use disorders. VR facilitates the responses of individuals within a safe, secure environment that ensures high ecological validity. The current study is part of a larger project aiming to test the efficacy of Virtual Reality-Cue Exposure Therapy (VR-CET) versus Cognitive-Behavioral Therapy (CBT) in a multi-site clinical trial in patients diagnosed with AUD considered resistant to treatment as usual (TAU). The case series included in the present study represent the first phase of the clinical trial, targeting responses of alcohol craving and anxiety as indicators of the efficacy of VR- CET versus CBT.

2. Method

2.1 Participants

Eight patients between ages 40 and 55 (M_{age} = 49, *SD* = 5.54) from the Addictive Behavior Unit of the Hospital Clinic, Barcelona participated in this study after providing written informed consent. Ethical approval was obtained from the Institutional Review Board of the University of Barcelona and the Hospital Clinic of Barcelona. Dual diagnoses consisted of anxiety, depression and borderline personality disorders. In addition, patients self-reported their use of tobacco, cannabis and cocaine in the last month prior to the experiment. Pharmacotherapy of the patients included disulfiram, anxiolytics, antidepressants and antipsychotics. The inclusion criteria were an AUD diagnosis, with particular emphasis on resistance to TAU (i.e., patients with at least one failed attempt to cease alcohol consumption within six months after completion of treatment), ambulatory treatment for at least two years, and a minimum of three-day abstinence prior to the first assessment session. Exclusion criteria were severe cognitive impairment, severe co- morbid psychopathology (e.g., schizophrenia), opioid addiction, epilepsy or pregnancy.

2.2 Instruments

- *Alcohol Use Disorder Identification Test* (AUDIT) [3]: a ten-item scale used to assess alcohol consumption severity.
- *Multidimensional Alcohol Craving Scale* (MACS) [4]: a self-report scale exploring the intensity of alcohol craving experienced by the participant in the previous week.
- *Multidimensional Alcohol Craving Scale – Virtual Reality. (MACS-VR)*: an ad-hoc modified version of the MACS used to assess the intensity of alcohol craving experienced during VR exposure.
- *State-Trait Anxiety Inventory* (STAI) [5]: a questionnaire assessing the individual's level of anxiety at a particular moment (state) and in general (trait).
- *Visual Analog Scales* (VAS): self-report scales during VR exposure, used to indicate cue-induced craving levels (VAS-C) and cue-induced anxiety responses VAS-A) on a scale from 1 to 100.

- *Hardware*: the VR equipment consisted of an Oculus Rift head-mounted display (HMD), sensors, Touch controllers and a computer compatible with the 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*: The "ALCO-VR" software (Figure 1) was created considering multiple variables for triggering alcohol craving (sounds, social interaction, moment of the day etc.), based on a previous study [6]. The ALCO-VR platform consisted of two parts: assessment and therapy. Both stages started with a hierarchy of exposure from the lowest-rated environment with the lowest- rated alcoholic drink to the highest-rated environment and highest-rated drink. The ALCO-VR consisted of four VR alcohol-related environments: restaurant, bar, pub, and at-home, and a menu of 22 alcoholic beverages. All the environments were specifically created to simulate real-life scenarios base on patients' experiences.

Figure 1. Images of the ALCO-VR environments.

2.3. Procedure

Patients were randomly assigned to the VR-CET group (three patients) or the CBT group (five). The protocol of the clinical trial consisted of eight sessions: a pre-treatment session (the initial assessment), six one-hour sessions of CBT or VR-CET and a post-treatment session (post-assessment). The VR-CET sessions consisted of cue-exposure to alcohol-related cues and environments of the ALCO-VR software aiming to reduce anxiety and craving responses to alcohol-related stimuli. The CBT sessions consisted of classical standardized therapy for the treatment of addictions. In the pre-treatment session, significant data of the anamnesis were recorded such as dual diagnoses, medication, abstinence data (supported by urine analyses), other substance use (illicit or licit) during the month prior to the experiment and any alcohol consumption (Table 1). Patients were then asked to complete several self-report scales of alcohol craving and anxiety, such as the AUDIT, STAI (the trait part), and MACS questionnaires. Subsequently, patients were exposed to the assessment part of the ALCO-VR software, in which they could choose their preferred alcoholic beverages and approach them from all angles. During VR exposure, every 20 seconds, patients were asked to report their cue-induced anxiety and craving on the VAS-A and VAS-C. After this stage, patients completed the MACS-VR and the state part of the STAI.

Olfactory stimuli corresponding to each drink were introduced during the exposure. Previously prepared alcoholic beverages were transferred on cotton pads and placed on the table close to the participant every time a new alcoholic drink appeared during the exposure. The post-treatment session repeated the procedure of the pre-treatment session almost identically, except for the anamnesis and the completion of AUDIT. After each session ofassessment or therapy, patients received a short debriefing aiming to reduce their craving and anxiety levels and to minimize any later alcohol consumption.

3. Results

Table 1 presents descriptive data of the patients randomly assigned to the VR-CET or CBT groups. The AUDIT scores may change depending on the abstinence period of each patient because it was designed specifically to depict hazardous drinking patterns in the individual in the last year. Therefore, total scores above 20 indicated a severe AUD. The total scores of patients 7 and 8 suggested a moderate AUD or harmful drinking patterns, while patient 4's score might suggest a mild drinking pattern, but it was interpreted as a disorder in remission mainly because of the patient's long-term abstinence.

Table 1. Descriptive data of the patients assigned to the VR-CET/CBT groups.

Patient	Age	Gender	Group	Dual diagnosis	Medication	Abstine-nce (days)	Other substances	AUDIT
1	49	Male	VR-CET	None	Anxiolytics,	42	Tobacco, cannabis,	28
2	49	Female	CBT	BPD, anxiety, depression	Anxiolytics, antidepressants	38	Tobacco, cannabis, cocaine	36
3	55	Female	CBT	None	Anxiolytics, antidepressants	245	Tobacco	33
4	54	Female	VR-CET	None	Antidepressants	360	Tobacco	2
5	44	Female	VR-CET	BPD	Anxiolytics, antipsychotics	5	Tobacco, cannabis, cocaine	38
6	51	Male	CBT	BPD, anxiety, depression	Anxiolytics, antipsychotics	28	Tobacco, cannabis,	36
7	40	Female	CBT	BPD	Anxiolytics, antidepressants, antipsychotics,	42	Tobacco	14
8	55	Male	CBT	BPD	Disulfiram	15	Tobacco	16

*BPD, Borderline Personality Disorder; Other substances (referring to substances other than alcohol consumed in the month prior to therapy).

Table 2 shows the results of the STAI, MACS and MACS-VR questionnaires in the pre and post VR-CET/CBT. In the pre-treatment session, all patients obtained higher scores of craving and anxiety. Higher STAI scores indicated higher levels of anxiety. The STAI results suggested moderate levels of anxiety in the VR-CET group (in both subtests) and in the CBT group on the state subtest, while the trait part of STAI indicated clinically significant anxiety in the CBT group; however, groups obtained lower scores on STAI (on both subtests), indicating the efficacy of the treatments. We emphasize the low scores obtained by the patients in the VR-CET group on the state subtest of the STAI, which suggest mild state-anxiety after the treatment. Regarding alcohol craving, the MACS scores in the pre-treatment session in both groups suggested a moderate level of craving in the week prior to the experiment. In the post-treatment assessment session, both groups obtained mild alcohol craving scores. In addition, the MACS-VR scores indicated a severe craving level in the pre-treatment session. These scores were lower in the post-treatment assessment session, with a mild level of craving in the VR-CET group and a moderate level in the CBT group

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Table 2. Assessment of anxiety and craving responses in the pre-post treatment (VR-CET versus CBT).

	VR-CET		**CBT**	
	Pre VR-CET *M(SD)*	**Post VR -CET M*(SD)***	**Pre CBT M*(SD)***	**Post CBT M*(SD)***
STAI-trait	21 (13)	18.33 (9.81)	43 (7.31)	21.8 (14.82)
STAI-state	16 (14.17)	7.67 (10)	20 (16.41)	16.2 (8.61)
MACS	23 (6.8)	20.67 (9.6)	35.6 (10)	18.8 (5.4)
MACS-VR	36.33 (13.86)	18.67 (9.86)	42.2 (10.8)	25.4 (11.67)

The data for anxiety and craving levels reported on the STAI, MACS and MACS-RV questionnaires were consistent with those for cue-induced anxiety and craving responses reported on the two VASs (Figures 2 and 3). Our data indicated a significant reduction in both groups in cue-induced anxiety and craving responses. As both figures indicate, scores of cue-induced anxiety and craving responses were lower in the VR-CET group than in the CBT group. In addition, patient 3, in the CBT group, presented similar scores for craving in the pre- and post-CBT assessment sessions, and higher scores for anxiety in the post-CBT assessment.

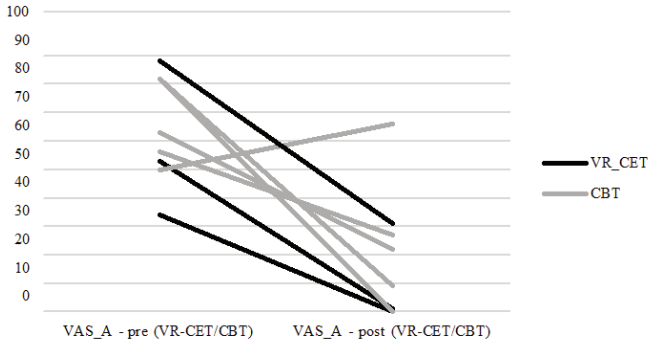

Figure 2. Cue-induced anxiety responses reported on VAS-A.

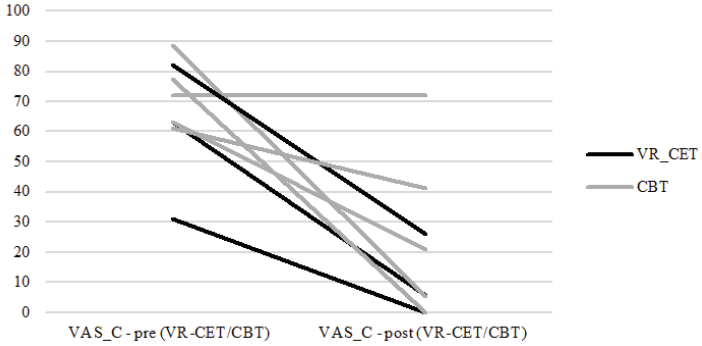

Figure 3. Cue-induced alcohol craving responses reported on the VAS-C.

4. Conclusions

Our data indicated improvements in various measurements of anxiety and craving in both groups and suggest that the VR-CET approach was as efficient as the CBT approach in this study. We highlight the craving and anxiety responses in the VR-CET group, which obtained better scores on the VAS-C and VAS-A than the patients in the CBT group. We interpret these data at post-treatment as a result of a desensitization process regarding alcohol content, and an indication of the clinical potential of VR technology in AUD treatment. As this study emphasized the first phase of a clinical trial, there are important limitations to be mentioned such as gender imbalance, dual diagnosis, medication and abstinence period, that may potentially influence our data.

The present study is an ongoing project and these data indicate promising results in terms of craving and anxiety reduction. We propose that CET based on VR can be a useful complement to existing treatment methods for AUD patients.

5. Acknowledgments

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6. References

[1] M. M. Pina and R. A. Williams, Alcohol cues, craving, and relapse: Insights from animal models, *Recent Advances in Drug Addiction Research and Clinical Applications* (2016), 47–79.
[2] A. Ghiţă and J. Gutiérrez-Maldonado, Applications of virtual reality in individuals with alcohol misuse: A systematic review, *Addictive Behaviors* **81** (2018), 1–11.
[3] M. Contel Guillamón, A. Gual Solé, and J. Colom Farran, Test para la identificación de trastornos por uso de alcohol (AUDIT): Traducción y validación del AUDIT al catalán y castellano, *Adicciones* **11** (1999), 337–347.
[4] J. Guardia Serecigni *et al.*, Estudio de validación de la Escala Multidimensional de Craving de Alcohol, *Medicina Clinica* **123** (2004), 211–216.
[5] C. D. Spielberger, F. Gonzalez-Reigosa, A. Martinez-Urrutia, L. F. S. Natalicio, and D. S. Natalicio, Development of the Spanish Edition of the State-Trait Anxiety Inventory, *Interamerican Journal of Psychology* **5** (1971), 3–4.
[6] A. Ghiţă *et al.*, Identifying triggers of alcohol craving to develop effective virtual environments. for cue exposure therapy, *Frontiers in Psychology* **10** (2019), 1–11.