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Changes of attentional bias in patients with alcohol use disorder during abstinence: A longitudinal study

Berta Escudero [a,b], Francisco Arias Horcajadas [b,c], Laura Orio [a,b,c,*]

[a] *Department of Psychobiology and Behavioral Sciences Methods, Faculty of Psychology, Complutense University of Madrid, Pozuelo de Alarcón 28223, Spain*
[b] *Instituto de investigación Sanitaria Hospital Universitario, 12 de Octubre (imas12), Madrid 28041, Spain*
[c] *Riapad: Research Network in Primary Care in Addictions, Spain*

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ABSTRACT

Background: Alcohol Use Disorder (AUD) is linked to an attentional bias towards alcohol-related cues (e.g. images, smells), which acquire incentive properties and promote continued consumption.

Method: We investigated how the general and alcohol attentional bias evolved longitudinally in AUD patients along two periods of abstinence: $t = 0$ (baseline, 1–3 months of abstinence) and $t = 1$ (follow-up; 6 months of abstinence), as well as their relationship with alcohol-related variables. General and alcohol-specific attentional bias were evaluated by the Classic and the Alcohol Stroop tests (neutral and alcohol conditions) in abstinent AUD patients and controls.

Results: At $t = 0$, the AUD group exhibited both general and alcohol-specific attentional biases, with greater effect in the general bias. At $t = 1$, alcohol-specific attentional bias decreased specifically in the AUD group and reached control levels (with interference index levels increasing from 1-3 months to 6 months). However, general attentional bias showed a trend toward improvement but it did not significantly change through abstinence process (linear mixed models, controlling for age, BMI, sex and education).

Conclusions: In AUD patients, general and alcohol attentional biases exhibit different trajectories during abstinence, with the attentional bias toward alcohol improving significantly throughout this process whereas general attentional bias is maintained.

1. Introduction

Attentional bias (AB) refers to the orientation toward certain stimuli or aspects of the environment, often to the detriment of other stimuli. AB has been proposed as a transdiagnostic cognitive process (Garland & Howard, 2014) of various psychological disorders such as anxiety (MacLeod, 2019; Bar-Haim et al., 2007), depression (Mennen et al., 2019; Peckham et al., 2010) or addictive disorders (Field & Cox, 2008; George & Koob, 2010). It involves three components: facilitation (towards non-target stimuli), difficulty disengaging (from threatening stimuli) and attentional avoidance (away from the threat) (Cisler et al., 2009; Cisler & Koster, 2010).

AB plays a crucial role in maintaining drug addiction behavior (reviewed in George & Koob, 2010). Regarding alcohol abuse, alcohol AB refers to the preferential allocation of attentional resources toward alcohol-related cues. Alcohol AB has been observed in heavy drinkers and patients with alcohol dependence (reviewed by Bollen et al., 2022; Wiers et al., 2017) and abstinent patients for 2 to 4 weeks in alcohol detoxification (Sanchez-López et al., 2015), although research predominantly involves non-clinical populations (cited in Sinclair et al., 2015). General AB refers to the preferential allocation of attentional resources toward non-alcohol related stimuli, suggesting a broader difficulty in managing attention across various contexts (not just those directly related to alcohol cues).

AB to drug cues has been conceived as an automatic mode in response to a stimulus (stimulus–response, S-R/reinforcement learning). In the context of alcohol addiction, one fundamental mechanism for the development and maintenance of addictive behaviors is classical conditioning (CC) learning, and extensive studies have shown the influence of alcohol cue-reactivity (e.g., images and smells) on craving for alcohol intake (reviewed in Vujanovic et al., 2019; Field et al., 2013). Drinking cues become conditioned stimulus for alcohol consumption and a

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* Corresponding author at: Department of Psychobiology and Behavioral Sciences Methods, Faculty of Psychology, Complutense University of Madrid, Pozuelo de Alarcón 28223, Spain.

E-mail address: lorio@psi.ucm.es (L. Orio).

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discriminative stimulus for compulsivity to alcohol-seeking behavior due to operant conditioning (S-R). Thus, alcohol-related stimuli may lead to conditioned responses of craving and arousal to alcohol (CC), and act as discriminators for repeated alcohol self-administration behavior (S-R). Repeated alcohol self-administration makes a substance more attractive to the consumer, with strong incentive-motivational properties, making the stimuli more salient based on reward ('Incentive-Sensitization Theory') (Robinson & Berridge, 1993). Therefore, alcohol-related stimuli are highly salient to the consumer and act as cues (discriminators) for drinking behavior, resulting in AB (Field & Cox, 2008). However, a different theoretical perspective considers AB as an effect of a goal-directed decision-making process, so that it fluctuates depending on motivational state (context, craving, desire, etc.) (Bollen et al., 2022; Rose et al., 2013; 2018; Watson et al.,2021; 2022).

Understanding the dynamics of AB in the context of alcohol addiction is crucial for designing effective interventions. Whereas some theories expose that learned associations to alcohol cues do not extinguish during abstinence (Collins & Brandon, 2002; Hermans & Van Gucht, 2006), others argue that AB may vary during abstinence (Gladwin et al., 2015; Wiers et al., 2011; Eberl et al., 2013). However, the stability of AB is not yet established.

Attentional bias can be measured by eye-tracking (i.e. Skinner IW et al., 2018). reaction times (i.e. Buodo et al., 2002), dot probe tasks (MacLeod et al., 1986), interference tasks, etc. The Emotional Stroop Task (EST) has become an accepted paradigm for studying AB although there is ongoing debate about whether the EST can distinguish between its three previously mentioned components (facilitation, difficulty disengaging and attentional avoidance) (Cisler et al., 2009; Cisler & Koster, 2010). Therefore, the concept of 'interference inhibition' (measured by the interference index) is widely used to comprehensively assess AB (reviewed in Rogers et al., 2020).

The present study explored two types of attentional bias (general non-alcohol AB and alcohol AB) in AUD patients in outpatient treatment using the interference index derived from the Stroop tests. We analyzed AB changes during alcohol abstinence: baseline (t = 0; 1–3 months of abstinence) and follow-up (t = 1; 6 months of abstinence) in these AUD patients. Additionally, we investigated associations with alcohol behavior variables, such as age at which drinking begins, alcohol consumption (in standard drinking units or SDU) (Griffith et al., 2003), and length of abstinence. We hypothesize that: (1) AUD patients exhibit greater AB than controls; (2) AB (interference index) for alcohol AB vary as a function of the length of abstinence, so longer abstinence periods in AUD subjects result in improved bias. We compared alcohol AB with general non-alcohol AB to understand the specific nature of alcohol-related cues in a clinic population.

2. Materials and methods

2.1. *Study Participants*

A total of 33 detoxified AUD patients (24 men and 9 women) (AUD group) and 43 controls (21 men and 22 women) (control group) were included, all white Caucasian. Patients were recruited (Fig. 1) from the outpatient structured 'Alcohol Program' at the 'Addictive Behaviors and Dual Pathology' Unit of the 'Hospital Universitario 12 de Octubre' in Madrid (Spain) while controls were randomly sampled from the general population with similar sociodemographic characteristics. The AUD participants received pharmacological and psychological interventions as part of the 'Alcohol Program' (Supporting Methodology 1 for details).

Patients were initially recruited with 1–3 months of abstinence and followed-up after 6 months of abstinence. A recruitment diagram (t = 0) is provided in Fig. 1. In this longitudinal study, the drop-out rate (relapses) between t = 0 and t = 1 was 4 patients, with no loss of control subjects.

2.2. *Participant Inclusion and Exclusion criteria*

Inclusion criteria. Age between 18 and 65 years old. In patients, AUD

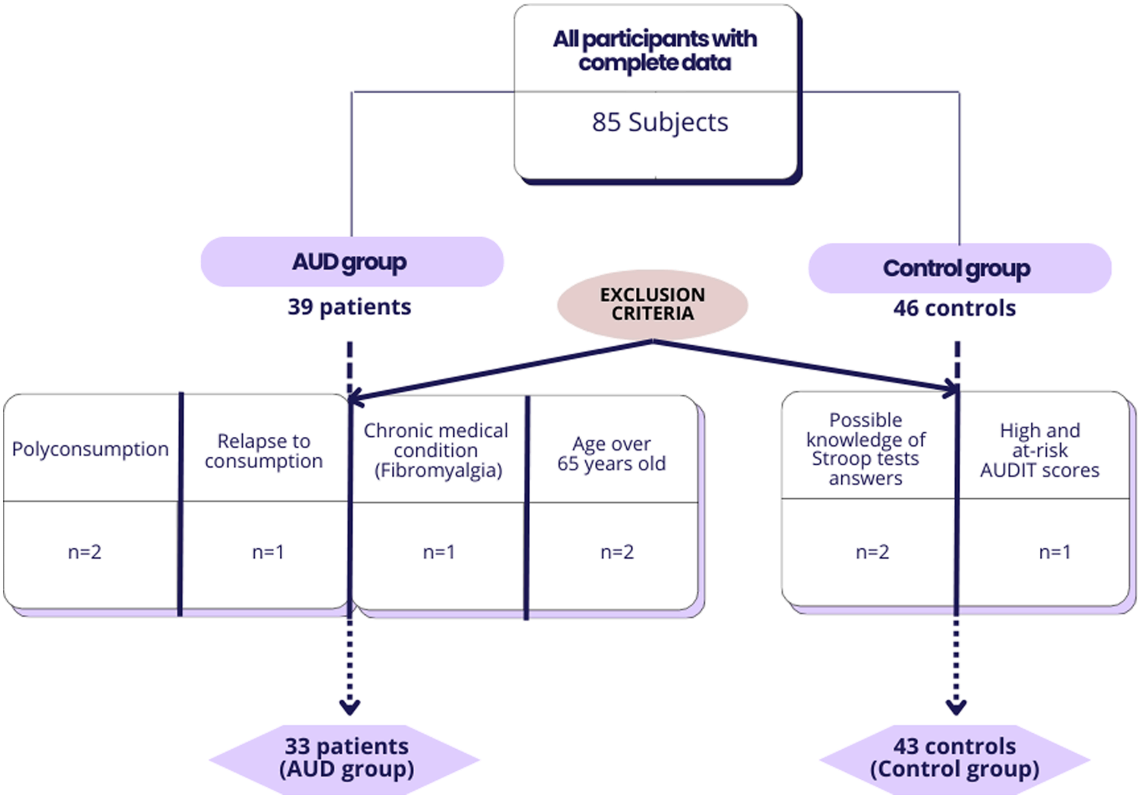

Fig. 1. Recruitment diagram at t = 0. Abbreviations: AUD = alcohol use disorder; AUDIT = Alcohol Use Disorders Identification Test.

diagnosis (DSM-5 criteria; APA, 2013) and alcohol abstinence for at least 4 weeks before testing. Abstinence was assessed via exhaled breath analysis using the Dräger alcotest 6810 (AlcoDigital, UK) during hospital visits, complemented with some hepatic biomarkers (Supporting Methodology 2). Self-reports were also considered when assessing alcohol abstinence.

Exclusion criteria. History of abuse or dependence on other drugs (including alcohol in the control group) (except for tobacco), infectious diseases (such as HIV), liver disease (chronic hepatitis, cirrhosis or liver cancer), chronic medical conditions, comorbid psychiatric disorders, and chronic use of anti-inflammatory medications. To ensure compliance, consult Supporting Methodology 2.

2.3. *Ethics*

This study was approved by the Research Ethics Committee of Hospital 12 de Octubre, Madrid (N°CEIm: 19/002) and adhered to World Medical Association Declaration of Helsinki. Participants provided written informed consent, and data were coded for anonymity and confidentiality.

2.4. *Cognitive and clinical assessment*

The Classic Stroop test measures general (non-alcohol) AB (Stroop, 1935; Golden, 1975, 1978). The Alcohol Stroop test (Sánchez-López et al., 2015) measures alcohol-specific attentional bias. Alcohol Stroop test features two conditions: neutral (emotionally neutral) and alcohol (emotionally relevant). It is a version of the Stroop (1935) color-naming task and a pivotal instrument in clinical practice (Cox et al., 2003; Field & Cox, 2008).

Both tests (Classic and Alcohol) include a third sheet that measures AB or the ability to suppress reading response by presenting colored words printed in a different color than the written word. The third sheet assesses AB (naming colors vs. words), as the automatic verbal response to the color word could interfere with the task (Golden, 1978), and it is measured by the interference index. The interference index, equivalent to 'interference resistance', measures AB and it was obtained using the formula initially detailed in Golden et al. (1978) (Supporting Methodology 3). A higher interference index indicates lower susceptibility to interference and greater selective attention (lower attentional bias). Interference index scores below 14.76 on the Alcohol Stroop test (Sánchez-López et al., 2015) and below zero on the Classic Stroop test (Golden et al., 1978) signify an AB deficit. Both groups underwent Classic and Alcohol Stroop tests at t = 0, repeated at t = 1.

During the clinical assessment, sociodemographic, pharmacological, alcohol-related data were (including length of abstinence and Standard Drinking Units (SDU)) (Griffith et al., 2003) and possible relapses were collected through a semi-structured interview.

2.5. *Data analysis*

Sociodemographic, pharmacological, and alcohol-related variables were compared between the AUD and control groups or between men and women within the AUD group using Student's *t*-test, Fisher's exact test or Chi-square test, based on normality assumptions (Kolmogorov-Smirnov test).

AB in each Stroop condition (*Classic, Neutral, Alcohol)* was analyzed at t = 0 and t = 1 [Mean (SD); N (%)]. Differences between the AUD and control groups were observed using Student's *t*-test and Fisher's exact test. Coefficients (r) were used to study the relationship between AB and alcohol-related variables at t = 0 in the AUD group.

A repeated measures 2-way ANCOVA (*Group*: AUD, control) x (*Conditions*: Classic, Neutral, Alcohol) was used to determine AB at t = 0, controlling for age, BMI, sex and education. Huyn-Feldt statistic and partial eta squared (η^2) are reported, with Bonferroni *post hoc* test performed. Linear mixed models were applied to assess AB changes over time in two groups (control-AUD) for each Stroop condition, controlling for age, BMI, sex and education. Time of abstinence was used as a level 1 predictor, and sex, age, BMI and education were used as level 2 covariates. Therefore, the model incorporated the following predictor variables: time of abstinence (level 1), group (0 = control, 1 = AUD); age, BMI, sex (0 = female, 1 = male), and education (coded as 1 = college, 2 = no high school, 3 = high school). Restricted maximum likelihood (REML) was used as the estimation method.

To determine alcohol AB in the AUD group, interference effects were compared against a criterion derived from previous research (Koster et al., 2005). By subtracting the interference index of the neutral Stroop from that of the alcohol Stroop condition, scores significantly different from zero indicated attentional bias.

Statistical analyses were performed using IBM SPSS Statistical version 25.0 software (IBM, Armonk, NY, USA) with a significance level of $p < 0.05$.

3. Results

3.1. *Sociodemographic, pharmacological and alcohol-related data*

Table 1 compares sociodemographic variables at t = 0 between AUD and control groups. The AUD group had a significantly higher average age (Table 1), with no other differences observed ($p > 0.05$, n.s.).

Pharmacological and alcohol-related variables in the AUD group at t = 0 are presented in Table 2. Disulfiram was the most used medication (87.9 %), followed by antidepressants (48.5 %) and anticonvulsants (42.4 %). Mixed drinks were the preferred choice, with no sex differences. Other variables, including age at onset of problematic drinking, time of abstinence since last consumption, and SDU, showed no differences (Table 2).

Table 1

Sociodemographic, physiological and alcohol variables in the AUD and control groups.

Variables at t = 0		**AUD (N = 33)**	**Control (N = 43)**	***p*-Value**
Age *[mean (SD)]*	Years old	49.36 (7.41)	37.30 (12.25)	**0.00** ^{a}
BMI *[mean (SD)]*	kg/m^2	26.44 (4.84)	24.85 (3.82)	0.07 ^{a}
Sex *[N (%)]*	Women	9 (27.3)	22 (51.2)	0.06^{b}
	Men	24 (72.7)	21 (48.8)	
Education *[N (%)]*	No high school	3 (9.1)	1 (2.3)	0.12^{c}
	High school	9 (27.3)	6 (14.0)	
	College	21 (63.6)	36 (83.7)	
Current work status *[N (%)]*	Employed	26 (78.8)	40 (93.0)	0.09^{b}
	Unemployed	7 (21.2)	3 (7.0)	
Age of first alcohol consumption *[mean (SD)]*	Years old	15.36 (1.85)	14.47 (2.15)	0.06 ^{a}
Time of abstinence since last consumption at t = 0 *[mean (SD)]*	Days	44.94 (16.45)	4.08 (4.47)	**0.00** ^{a}
Time of abstinence since last consumption at t = 1 *[mean (SD)]*	Days	160.52 (27,46)	5.37 (9.13)	**0.00** ^{a}
Current smoking status *[N (%)]*	Yes	20 (60.6)	17 (39.5)	0.06^{c}
	Former	5 (15.2)	4 (9.3)	
	No	8 (24.2)	22 (51.2)	

Note. SD = standard deviation; N = total of cases; AUD = alcohol use disorder; BMI = body mass index; No high school, high school and college = no high school degree, high school degree, and college degree, respectively.. The significant values ($p < 0.01$) are denoted by bold entries in the table: ^{a} p Value from Student's *t*-test; ^{b} Value from Fisher's exact test; ^{c}p Value from Chi-square test.

Table 2
Pharmacological and alcohol-related variables in the AUD group at t = 0.

Variables in AUD-diagnosed patients		Total Sample (N = 33)	Women (N = 9)	Men (N = 24)	p-Value
Psychiatric medication use *[N (%)]*	Antidepressants	16 (48.5)	6 (66.7)	10 (41.7)	0.26 [a]
	Anxiolytics	7 (21.2)	3 (33.3)	4 (16.7)	0.36 [a]
	Anticonvulsants	14 (42.4)	5 (55.6)	9 (37.5)	0.44 [a]
	Antipsychotics	4 (12.1)	0 (0)	4 (16.7)	0.55 [a]
	Disulfiram	29 (87.9)	8 (88.9)	21 (87.5)	1.00 [a]
Preferred type of alcoholic beverage *[N (%)]*	Beer	10 (30.3)	3 (33.3)	7 (29.2)	0.87[b]
	Wine	0	0 (0)	0 (0)	
	Distillate	6 (18.2)	2 (22.2)	4 (16.7)	
	Mixed	17 (51.5)	4 (44.4)	13 (54.2)	
Age of problematic drink. *[mean (SD)]*	Years old	29.39 (11.22)	36.11 (12.93)	27.58 (9.81)	0.16[c]
Time of abs. last consumption *[mean (SD)]*	Days	44.94 (16.45)	46.56 (16.63)	44.33 (16.70)	0.74[c]
SDU *[mean (SD)]*	Per days	24.88 (13.02)	26.11 (9.37)	24.42 (14.29)	0.74[c]

Note. SD = standard deviation; N = total of cases; AUD = alcohol use disorder; Age of problematic drink. = Age of problematic drinking; time of abs. last consumption: time of abstinence since last consumption; SDU = standard drinking units. [a] p Value from Fisher's exact test; [b] Value from Chi-square test; [c] p Value from Student's *t*-test.

3.2. Comparison of time reactions and AB deficit

Table 3 presents performance disparities between the AUD and control groups in each Stroop test (and conditions) at both time points (t = 0 and t = 1). AUD group exhibited poorer performance in all three Stroop conditions (classic, neutral, alcohol) at both time points, with longer response latency and fewer words named (in W, C and WC) compared to controls (p = 0.00).

At t = 0, there was a significant AB deficit difference between AUD and control group for both Classic and Alcohol tests, with a higher prevalence of AB deficit in the AUD group (p = 0.000). However, at t = 1, while the AUD group retained the bias deficit in the classic condition, differences in the alcohol condition disappeared, resulting in the deficit's absence (p > 0.05, n.s.). Control group scores exceeded specified cut off points for both tests, as expected (Table 3).

3.3. AB (Interference Index) at t = 0

We performed a repeated two-way ANCOVA on AB (interference index scores) at t = 0, with *Stroop conditions* (classic, neutral, alcohol) and *group* (AUD and control) as factors, controlling for age, BMI, sex and education. Results are represented in Fig. 2. We found a *group* effect [F (1,68) = 7.49, p = 0.008, $\eta^2 = 0.10$], with a greater AB in the AUD group, with no effect of Stroop conditions on bias scores (p = 0.46). An interaction *group*tests* [F(1,68) = 4.86, p = 0.03, $\eta^2 = 0.07$] was found, and Bonferroni *post hoc* test showed differences between AUD and control groups in the Classic (p = 0.0005) and Alcohol Stroop (p = 0.0004), with higher AUD bias, but not in the neutral Stroop (p = 0.99, n.s.).

The Classic Stroop test had the lowest interference index for both groups, suggesting greatest AB towards non-alcohol content compared to neutral or alcohol content (see Fig. 2).

We assessed alcohol AB using criteria established by Koster et al. (2005) (review method section, data analysis). Results are presented in Fig. 3: while the control group lacked statistically significant AB [t(41) = 1.87, p = 0.07], the AUD group had a significant negative AB [t(31) = -3.03, p = 0.005], indicating difficulty in focusing on alcohol-associated words.

Table 3
Differences between AUD and control groups in the Classic and Alcohol Stroop tests at two time points (t = 0 and t = 1).

Variables			t = 0			t = 1		
			AUD (*n* = 33)	Control (*n* = 43)	*p-Value*	AUD (*n* = 29)	Control (*n* = 43)	*p-Value*
Classic Stroop Test		**W** *[Mean (SD)]*	97.61 (18.82)	116.72 (12.96)	**0.00** [a]	94.90 (20.49)	114.49 (13.65)	**0.00** [a]
		C *[Mean (SD)]*	61.61 (13.92)	83.05 (13.13)	**0.00** [a]	63.34 (13.99)	83.81 (12.69)	**0.00** [a]
		WC *[Mean (SD)]*	37.15 (10.16)	55.56 (14.23)	**0.00** [a]	37.83 (10.81)	57.63 (12.32)	**0.00** [a]
		Deficit of Attentional bias*[N (%)]*	18 (54.5)	6 (14.0)	**0.00**[b]	15 (51.7)	6 (14.0)	**0.00**[b]
Alcohol Stroop Test	***Neutral Condition***	**W** *[Mean (SD)]*	89.24 (25.44)	113.21 (15.05)	**0.00** [a]	90.76 (20.40)	112.3 (12.15)	**0.00** [a]
		C *[Mean (SD)]*	61.09 (14.53)	83.26 (15.84)	**0.00** [a]	62.28 (14.82)	83.16 (14.41)	**0.00** [a]
		WC *[Mean (SD)]*	54.85 (14.20)	68.67 (12.25)	**0.00** [a]	53.86 (12.71)	66.70 (11.77)	**0.00** [a]
	Alcohol Condition	**W** *[Mean (SD)]*	89.09 (22.91)	110.14 (15.13)	**0.00** [a]	89.14 (20.37)	110.91 (12.63)	**0.00** [a]
		C *[Mean (SD)]*	62.82 (14.87)	82.33 (13.56)	**0.00** [a]	61.93 (14.92)	83.16 (14.96)	**0.00** [a]
		WC *[Mean (SD)]*	51.09 (12.93)	69.67 (11.73)	**0.00** [a]	55.31 (12.25)	68.63 (11.96)	**0.00** [a]
		Deficit of Attentional bias *[N (%)]*	13 (40.6)	2 (4.8)	**0.00**[b]	4 (14.3 %)	8 (18.6)	0.75[b]

Note. SD = standard deviation; N = total of cases; W = words read on the first slide; C = colors named on the second slide; WC = colors named on the third slide; Deficit of attentional bias *[N (%)]* based on the cut-off point 14.76 (alcohol Stroop interference index) and zero (classic Stroop interference index). The significant values between the AUD and the control group in each period of abstinence are denoted by bold entries in the table: [a] p Value from Student's *t*-test; [b] Value from Fisher's exact test.

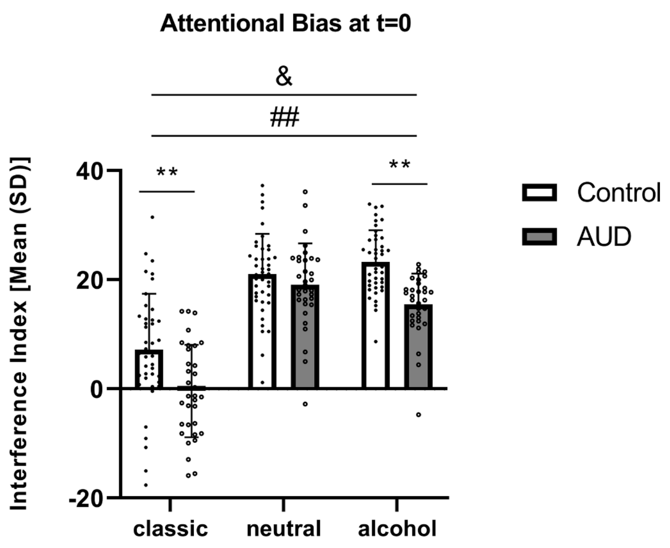

Fig. 2. Attentional bias (interference index) at t = 0. Two-way repeated-measures ANCOVA with *Group* (AUD, control) and *Stroop Tests (*classic, neutral, alcohol) as factors. Results expressed as mean (SD). ## means effect of *Group*, p < 0.01; & means effect of interaction *Group*Tests,* p < 0.05. ** means difference between the AUD and control groups in the Classic and Alcohol Stroop tests (Bonferroni *post hoc* test, p < 0.01). Abbreviations: AUD = alcohol use disorder; SD = standard deviation; classic, neutral and alcohol = classic, neutral and alcohol Stroop conditions, respectively.

3.4. *Correlations between Sociodemographic/Alcohol-related variables and AB at t = 0*

We examined the relationship between AB and sociodemographic/alcohol-related variables at t = 0 (Table 4). Results showed a positive correlation between length of abstinence since the last consumption and alcohol AB (r = 0.70, p < 0.01). In essence, longer abstinence periods (1 to 3 months) were associated with lower alcohol AB at baseline. Additionally, a negative relationship was found between SDU and alcohol AB (r = -0.58, p < 0.01), suggesting that higher SDU intake was linked to increased alcohol attentional bias. Other variables did not reach significance (p > 0.05, n.s.).

3.5. *Changes of AB (Interference Index)*

Fig. 4 illustrates AB progression (classic, neutral, alcohol) in the AUD group. To assess progression of general and alcohol AB (interference index) during alcohol abstinence from t = 0 to t = 1, linear mixed models were employed, controlling for age, BMI, sex and education.

General non-alcohol AB (classic condition) showed no significant change during abstinence (from t = 0 to t = 1), according to the mixed model analysis [*time of abstinence* effect: F(1,70) = 2.56, p = 0.11, n.s.]. This suggests that the AUD group maintained differences with controls at t = 1. No significant *group* effect was observed [F(1,109) = 2.94, p = 0.09, n.s.], although it marginally approaches significance. The *age* covariate showed a significant effect [F(1,68) = 12.93, p = 0.001], indicating that interference index in the classic condition declines with increasing age, with a decrease of 0.29 for each year [Estimate standard error (Est (s.e.)) = -0.29 (0.08)].

In contrast, alcohol AB decreased during abstinence (alcohol condition) in the AUD group, with interference index levels increasing from t

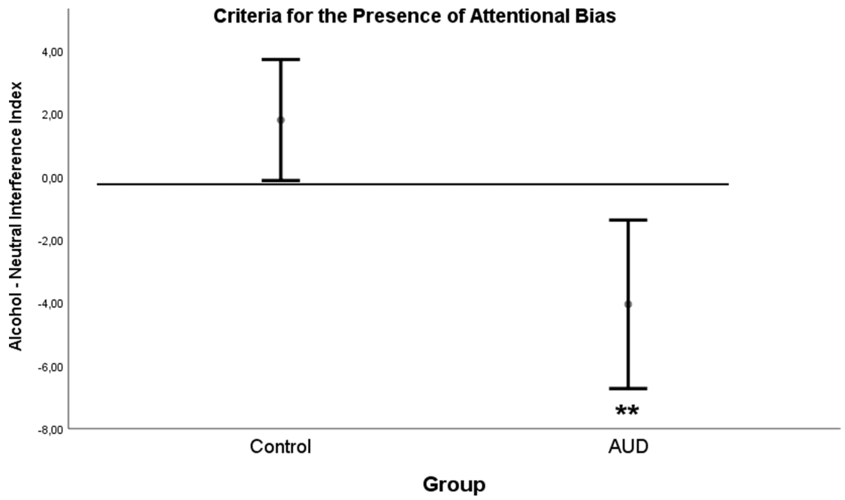

Fig. 3. Attentional bias against the criteria established by Koster et al. (2005) analysed for alcohol Stroop test. Significant difference for the AUD group, indicating the existence of alcohol attentional bias. **: means a statistically significant difference compared to the criterion of 0 (p < 0.01). Negative scores indicate a lower capacity for resisting interference from alcohol-related stimuli compared to neutral stimuli, indicative of attentional bias toward alcohol-related stimuli. Abbreviations: AUD = alcohol use disorder.

Table 4
Correlations of atentional bias with sociodemographic/physiological /alcohol-related variables in the AUD group at t = 0.

Interference index in Stroop conditions. AUD group (n = 33)	Age	BMI	Age of first alcohol consumption	Age probl.drink	Time of abstinence since last consumption	SDU
Classic	0.13	−0.11	−0.21	−0.26	0.12	−0.09
Neutral	−0.02	−0.03	−0.15	0.14	0.18	−0.27
Alcohol	−0.27	−0.01	0.01	−0.09	**0.70****	**−0.58****

Note. Abbreviations: AUD = alcohol use disorder; N = total of cases; BMI = body mass index. SDU = Standard Drinking Units. Spearman's rank correlation coefficient (r). **: *p* < 0.01.

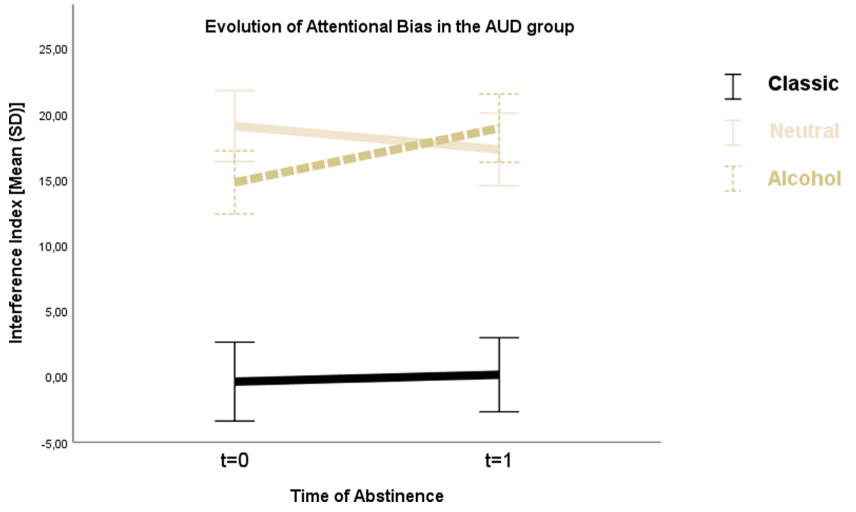

Fig. 4. Changes of attentional bias as time of abstinence progresses in the AUD group. Abbreviations: AUD = alcohol use disorder; classic, neutral and alcohol = classic, neutral and alcohol Stroop condition.

= 0 to t = 1. Specifically, mixed model analysis revealed: (1) a *group* effect [F(1,89) = 13.81, p = 0.00], with higher AB in the AUD group (compared to controls). At t = 0, the AUD group showed 6.22 points less interference index (higher attentional bias) than the control group [Est (s.e.) = -6.22 (1.67)]; (2) a *time of abstinence* effect [F(1,60) = 4.28, p = 0.04)], which means that there is a significant decrease in the interference index in control group of 1.77 [Est (s.e.) = -1.77 (0.85)]; (3) a *group*time of abstinence* interaction effect [F(1,64) = 23.11, p = 0.00], indicating that the difference of 6.22 points in the interference index at t = 0 between the AUD group and the control group disappears at t = 1 by 6.54 points [Est (s.e.) = 6.54 (1.36)]. Consequently, alcohol AB improved over abstinence in the AUD group, reaching control levels (unpaired Student's *t*-test, p = 0.35, n.s.). The effect of this interaction is visually depicted in Figure S1 of Supporting Results ; (4) *Age* covariate showed a significant effect [F(1,64) = 6.33, p = 0.01], indicating that interference index in the alcohol condition declines with increasing age, with a decrease of 0.16 for each year [Est (s.e.) = -0.16 (0.06)].

No changes were observed in the neutral condition (not significant effects) controlling for other effects (covariates) [*Group:* F(1,98) = 0.06, p = 0.80, n.s.; *time of abstinence:* F(1,71) = 2.72, p = 0.10, n.s.; *group*time of abstinence:* F(1,73) = 0.01, p = 0.93, n.s.)], consistent throughout abstinence for both groups.

4. Discussion

This study aimed to assess if alcohol AB change by long-term abstinence in AUD patients compared with general AB and with controls. We found that AUD subjects showed a greater AB for general and alcohol-related cues during early abstinence (1–3 months) compared to controls. Alcohol AB correlated with alcohol-related variables during this abstinence period in the AUD group. However, while the alcohol AB improved over time (from t = 0 to t = 1), non-alcohol AB remained stable. The possible implications of these findings are discussed below.

At t = 0, we found general and alcoholic AB in the AUD group compared to controls. AB in AUD subjects displayed slower reaction times when color-naming alcohol-related words are presented in individuals with alcohol dependence (Fadardi & Cox, 2006; Lusher et al., 2004; Manchery et al., 2017; Müller-Oehring et al., 2019), according to our results in alcohol attentional bias. However, we observed that the AUD group showed stronger general AB (non-related to alcohol). This is an interesting finding as AUD patients may have a broader difficulty in managing general attentional across various contexts and towards stimuli unrelated to alcohol. This general attentional difficulty is crucial for understanding that patients with AUD may have a broader challenge in selecting stimuli from the environment for further processing, which in turn determines subsequent behavioral choices. However, the reduction of alcohol AB may be also aligned with other variables, such as motivation to drink. For example, some studies found that heavy drinkers (Duka & Townshend, 2004; Weafer & Fillmore, 2013) and those in early stages of drinking (Roberts & Fillmore, 2015) (as our AUD cohort at t = 0) showed a reduction in alcohol AB, possibly due to the temporary rewarding effects of alcohol consumption satisfying the motivation to drink (Monem, 2019). Moreover, as Weafer & Filmore suggested (2013), finding less alcohol AB in these patients may be linked to a reduction in the incentive-motivational properties of alcohol-related stimuli. In this sense, aligning with the theoretical perspective that consider AB as an effect of a value-based decision process, once AB for alcohol has been established during the addiction process, it could be changed even in early stages of abstinence (t = 0) (compared to non-alcohol attentional bias) when the alcohol substance may be less desirable.

To further understand general and alcohol AB, we explored their relationship with alcohol-related variables at t = 0 in the AUD group. Factors such as AUD severity or individual differences may influence attentional bias. Our results showed a positive correlation between previous SDU (indicating disorder severity) and alcohol AB, consistent with prior studies (Hallgren & McCrady, 2013; Waters et al., 2009). This suggests that alcohol AB may increase with heavier drinking or dependence indexes (cited by Loeber et al., 2009), although Lusher et al. (2004) found no association. Our results highlight the importance of considering drinking-related variables in modulating AB (Loeber et al., 2009). Furthermore, early abstinence may play a crucial role in reducing alcohol AB (higher interference index), as indicated by a positive correlation between time of abstinence since last consumption at t = 0 and interference index in the alcohol condition.

There are few studies that assess AB in AUD patients following extended periods of abstinence. It is not clear if AB remain stable (Franken, 2003; Hermans & Gucht, 2006) or fluctuate over time (Christiansen et al., 2015; Field et al., 2014). Some studies indicate a reduction (Gladwin et al., 2015; Eberl et al., 2013), while others show no change in AB (Cox et al., 2002). Based on models of Robinson & Berridge (1993; 2001), AB was proposed to be stable and permanent. However, according to the theories of the value-based decision process, AB fluctuates based on environmental and internal factors (stress, craving, desire, alcohol cue exposure, etc.) (revised in Bollen et al., 2022). In this sense, after a period of abstinence and treatment, the value of alcohol may decrease, leading to the normalization of alcohol AB (Watson et al., 2022). Our findings reveal an improvement in alcohol AB from t = 0 to t

= 1 in the AUD group, reaching control levels at t = 1. Similarly, Christensen (2009) found that long-term abstinent former problem drinkers had less alcohol AB than current problem drinkers. Therefore, alcohol AB may be malleable according to cognition and motivation and the meaning of alcohol cues could be altered in long-term abstainers. On the other hand, non-alcohol AB was more resistant to change, showing not significant improvement over time of abstinence. Therefore, general non-alcohol AB may be a stable cognitive condition of alcohol addiction, signaling a broader bias in attention within the AUD context.

Maintaining initial abstinence is clinically crucial to mitigate alcohol AB, as long-term abstainers may develop the capacity to resist or divert their attention from alcohol cues. Therefore, the ability to disengage should be trained during treatment as alcohol AB apparently may reverse its nature during abstinence. This study has several limitations to consider. (1) The reliance of a single task (Stroop test) for AB assessment may yield unclear interpretations, as noted in other research (Pennington et al., 2021). Other methods to assess attentional bias such as the eye-tracking paradigm or reaction times by dot-probe task may be used to provide more robust results. Also, there are different manifestations of attentional bias, such as initial orienting, maintenance, engagement or disengagement, threat avoidance, etc. (reviewed in Mogg & Bradley, 2016), which evaluation may provide useful insights into these results. (2) Caution is warranted when interpreting alcohol AB due to the relatively small sample size, limiting generalizability. Further research with larger sample sizes is necessary for validation. (3) Participants were required to maintain abstinence a minimum of four weeks to ensure both adherence to the Alcohol Program and minimize subject loss. Other AUD subjects entering the program without achieving this duration of abstinence were not included, and this may unintentionally bias the sample since, on one hand, the majority of relapses might take place during the first month and, on the other hand, attentional bias are thought to be present also in newly abstinent patients. In this regard, the small number of relapses (12 %) in this study precluded us from exploring the potential association between alcohol AB and relapse rates.

5. Conclusion

In conclusion, alcohol AB may evolve differently compared to general AB throughout prolonged abstinence in AUD patients. While alcohol AB might decrease during abstinence, non-alcohol AB may remain consistent in AUD patients. Our results highlight the importance of considering these biases during the abstinence period in clinical programs in order to promote patientś recovery.

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CRediT authorship contribution statement

Escudero Berta: Conceptualization, Investigation, Formal analysis, Writing – original draft. **Arias Horcajadas Francisco:** Methodology, Resources. **Orio Laura:** Supervision, Project administration, Funding acquisition, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Personal data of subjects are maintained private according to the law. Other data in the manuscript are freely available upon request to the corresponding author (lorio@psi.ucm.es).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2024.108098.

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