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Alcohol-related attentional biases in recently detoxified inpatients with severe alcohol use disorder: an eye-tracking approach

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ABSTRACT

Background: Dominant theoretical models consider that attentional biases (AB) towards alcohol-related stimuli play a key role in the development and maintenance of alcohol use disorder (AUD). Their assessment has however showed high inconsistencies and has been mostly based on unreliable behavioral measures. This study evaluated the presence and extent of alcohol-related AB in recently detoxified inpatients with severe AUD by combining the visual probe task (VPT) paradigm with eye-tracking measures, known to improve the VPT reliability in subclinical populations.

Methods: We recruited 24 patients and 27 matched healthy controls. They performed the VPT (measuring reaction time when processing visual targets preceded by alcoholic and matched non-alcoholic pictures) combined with eye-tracking measures (dwell time, first fixation direction/duration, second fixation direction) during two sessions. Estimates of internal consistency, split-half reliability, and test-retest reliability were measured.

Results: Patients showed shorter dwell time for alcohol cues ($p = .004$, d=.853) and reduced number of fixations towards alcohol after a first fixation on non-alcohol cues ($p = .012$, d=.758) compared to controls. These findings suggest the presence of alcohol-related avoidance AB in detoxified patients with severe AUD. The VPT achieved excellent reliability for these eye-tracking measures. Reaction times and first fixation measures did not indicate any AB pattern and showed poor reliability.

Conclusions: The VPT, when combined with dwell time and second fixation direction, constitutes a reliable method for assessing AB in detoxified patients. It showed the presence of an alcohol-related avoidance bias in this clinical population, in contradiction with the approach bias predicted by theoretical models.

1. Introduction

Attentional biases (AB) are the tendency to orient one's attention towards salient or goal-directed stimuli. Prominent models (Bechara, 2005; Wiers et al., 2007) proposed that AB are present for alcohol-related stimuli in alcohol use disorder (AUD). The incentive-sensitization theory (Robinson and Berridge, 1993) suggests that repeated alcohol consumption sensitizes the reward system, enhancing the incentive properties of alcohol-related cues. By becoming more salient, these cues capture attention and generate AB. These AB would subsequently be related to higher craving and elevated relapse risk. Most influential models thus assume that AB play a key role in AUD onset and persistence (Volkow et al., 2019; Yücel et al., 2019).

Capitalizing on this background, behavioral paradigms have emerged to measure alcohol-related AB. The most commonly used tasks are the addiction Stroop task (Cox et al., 2006) and the visual probe task (VPT; Ehrman et al., 2002). In the addiction Stroop task, participants name the color of alcohol-related or neutral words. Detoxified patients

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with AUD are slower than healthy participants to name the color of alcohol-related words (Duka et al., 2002; Lusher et al., 2004). This is usually interpreted as alcohol-related AB, based on the rationale that the automatic capture of attention to process the semantic content of alcohol-related words slows down color naming. However, such interpretation is questionable, as this interference could also result from the mobilization of attention to inhibit alcohol-related words processing, then rather indexing avoidance AB of alcohol-related cues (Klein, 2007). Regarding the VPT (see Methods section for a full description), some previous studies suggested the presence of AB in AUD, detoxified patients responding faster to probes replacing alcohol-related stimuli (Loeber et al., 2009). However, other studies rather revealed an avoidance pattern in detoxified inpatients (Townshend and Duka, 2007), or did not show any difference with healthy participants (Field et al., 2013; Wiers et al., 2016). Similar inconsistencies exist across studies exploring AB in subclinical populations without AUD (e.g. heavy or binge college drinkers; for a review, see Field and Cox, 2008).

Such incoherence hampers the sound testing of theoretical assumptions and the emergence of empirically-based therapies. An underlying factor, which might explain such discrepancies, is that previous studies have inferred AB in detoxified patients with AUD exclusively from reaction time measures. The focus on behavioral data prevents the testing of the alternative proposal (i.e. the existence of avoidance AB) in the Stroop task. In the VPT, reaction times only inform about the location of attention at probe onset, not providing insight about the successive stages involved in attentional deployment over time (Field and Cox, 2008). A further weakness of VPTbased reaction times is their low internal reliability (Ataya et al., 2012) and high variability according to stimulus duration (Beraha et al., 2018): short durations (e.g. 50 ms) appear related to AB toward alcohol while longer ones (e.g. 500 ms) generate avoidance AB (Vollstadt-Klein et al., 2009). Despite these limitations, also underlined in other psychopathological states (Kruijt et al., 2019), the VPT paradigm is frequently implemented in clinical settings to improve AUD treatment by retraining AB (Heitmann et al., 2018). Its therapeutic efficacy nevertheless appears to be weak and its clinical relevance is debated (Christiansen et al., 2015a; Cristea et al., 2016).

A promising tool to overcome these mitigated findings is eye-tracking, providing an optimized measure of AB by detecting eye movements and gaze position with a high temporal resolution (Popa et al., 2015). Unlike behavioral measures, eye-tracking offers insights on the time course of AB and clarifies its core mechanisms by measuring the consecutive steps involved in attention (Armstrong and Olatunji, 2012): the direction and duration of the first fixation index early attentional capture, whereas dwell time (i.e. overall fixation time on a stimulus) reflects the latter and controlled maintenance of attention. Combining traditional paradigms with eye-tracking would thus clarify the spatial and temporal dynamics of AB, improving their measure's reliability (Christiansen et al., 2015b). Studies assessing AB in subclinical populations through combined VPT/eye-tracking (Maurage et al., 2020 for a review) showed that eye-tracking indexes are more reliable than reaction times (Christiansen et al., 2015b), and suggested the presence of alcohol-related AB in these populations (Fernie et al., 2012; Miller and Fillmore, 2010; Weafer and Fillmore, 2013), particularly under alcohol intoxication (Schoenmakers et al., 2008) or high craving (Bollen et al., 2020). These results were mostly observed at the late and controlled stages of attentional processing (i.e. longer dwell time for alcohol). Another eye-tracking study showed that hazardous drinkers with ambivalence (i.e., both positive and negative evaluations of alcohol) initially orient their attention towards alcohol, and then redirect it away from alcohol later during the trial, while those without ambivalence show alcohol-related AB throughout the trial (Lee et al., 2014). Novel theoretical predictions (Field et al., 2016) emerged regarding the role played by the perceived valence of alcohol cues on AB, suggesting that this approach-avoidance pattern of AB would appear in individuals with AUD experiencing motivational conflict (e.g. detoxified patients receiving treatment). This pattern can only be observed with eye-tracking (Field et al., 2016), through measures indexing attentional shift or disengagement. There is thus a need to test the reliability of a combined VPT/eye-tracking approach in patients with AUD to obtain the first reliable measure of AB in this population (Jones et al., 2018).

We explored the presence of alcohol-related AB among recently detoxified inpatients diagnosed with severe AUD by combining VPT with eye-tracking measures to disentangle two contradictory hypotheses: (1) eye-tracking findings in subclinical populations suggest that individuals with AUD might present AB towards alcohol, which is also predicted by theoretical models; (2) as AB are related to motivational states (e.g. craving, ambivalence) and as detoxified patients have motivational conflicts regarding alcohol cues (Field et al., 2016), they might present initial approach AB (i.e. early automatic attraction towards alcohol) followed by avoidance AB (i.e. reduced dwell time on alcohol), as suggested earlier (Vollstadt-Klein et al., 2009). At the methodological level, we postulated that eye-tracking will increase VPT reliability (Christiansen et al., 2015b).

2. Methods

2.1. Participants

Patients were recruited from an inpatient treatment unit during their second/third detoxification weeks (Psychiatric Hospital of Beau Vallon, Belgium) and screened using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998). Twenty-six detoxified inpatients (12 females) were selected as they met the DSM-V criteria for severe AUD, indicated by the presence of 6 or more symptoms. They had all abstained from alcohol for at least 7 days and were free of other psychiatric comorbidities (except nicotine dependence). It should be noted that none of the patients had followed a cognitive remediation therapy such as attentional bias modification during their treatment. Patients were matched for age and sex with a control group of 28 (13 females) healthy controls, free of any past or present psychiatric disorder or personal/family history of AUD. Control participants were recruited through social networks and emails and were selected if they did not usually consume more than ten alcohol units (i.e., one unit corresponding to 10 g of pure ethanol) per week and did not exceed three units per day. They were excluded if they scored higher than 8 at the Alcohol Use Disorders Identification Test (AUDIT; Babor and Robaina, 2016). Exclusion criteria for both groups included polysubstance use disorder and major past or present neurological disorder and/or trauma. They all had normal/corrected vision and were fluent French speakers. An a priori power computation (performed in G*Power v3.1.9.4) indicated that a sample size of 46 was required to detect a group x type of stimuli interaction (two measurements) in repeated-measures ANOVA, assuming a medium ($f = 0.25$) effect size with 0.90 power and $\alpha = 0.05$, as fulfilled by our sample size.

2.2. Apparatus

Participants were seated on an adjustable chair, facing an eye-tracker camera and an Asus Display Laptop PC equipped with a 17.3-inch FHD screen (resolution 1080 × 1920p; refresh rate 120 Hz). The presentation of the experimental task and its synchronization with eye-tracking were controlled using OpenSesame (Mathôt et al., 2012). Eye movements were recorded using an EyeLink Portable Duo remote mode eye-tracker (SR Research, Canada; sampling rate 1000 Hz; average accuracy range 0.25°-0.5°, gaze tracking range of 32° horizontally, 25° vertically).

2.3. Procedure

Participants attended a test-retest experimental design with two sessions separated by four days. They provided written informed consent to participate in the study and were not aware of the hypotheses

tested. They were seated 60 cm away from a laptop and were tested individually in a quiet room. At the first session, participants first filled in questionnaires assessing state anxiety (State Anxiety Inventory; Spielberger, 1993) and current alcohol craving [Obsessive-Compulsive Drinking Scale (OCDS; Anton et al., 1995) and Craving Visual Analogue Scale, C-VAS: "Indicate how much you want to drink alcohol right now (from 0 = not at all, to 100=strong desire)"], before performing the task. The procedure was repeated for the second session. The task was a computerized VPT lasting about 15 min. Prior to each block, the eye-tracker was calibrated to the screen using a built-in 9-point protocol. Between sessions, participants filled in questionnaires assessing depressive symptoms (Beck Depression Inventory-II; Beck et al., 1996), anxiety (Trait Anxiety Inventory; Spielberger, 1993), and impulsivity (UPPS-P Impulsive Behavior Scale; Billieux et al., 2012). The study protocol was performed in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Saint-Luc-UCLouvain Clinics and the local Ethics Committee of Beau Vallon Hospital. At the end of the two sessions, participants were debriefed and controls received financial compensation.

2.4. Stimuli

Twenty pairs of alcoholic beverage pictures (e.g. bottle of vodka) and matched non-alcoholic beverage pictures (e.g. bottle of water) without context, extracted from the validated Amsterdam Beverage Picture Set (ABPS; Pronk et al., 2015), were displayed on a black background. The picture sets were identical to those used in Bollen et al. (2020). Brands and writings were blurred to avoid reading and each picture pair was matched on color, size (444 × 444 pixels or 10.7 × 10.7° angle), brightness, and salience.

2.5. Visual probe task

The visual probe task procedure was identical to the one used in Bollen et al. (2020). Each trial started with a central fixation dot on a black background and participants had to fixate their gaze on it. The fixation dot was used as a drift check to confirm the reliability of the eye-gaze calibration. This instruction also ensured that participants initially focused their visual attention at the center of the screen in each trial. Two pictures (i.e. alcoholic and non-alcoholic beverage pictures) were then displayed in a counterbalanced order on the left and right side of the screen for a 2000 ms period, and then replaced by a probe (i.e. white arrow) appearing at the location previously occupied by one of the pictures (Fig. 1). Participants had to respond to the orientation of the probe by pressing the "up" or "down" key on the keyboard, as quickly and correctly as possible. Visual probes replaced the two types of pictures with equal frequency. Each trial was separated by an inter-trial interval of random duration (500−1500 ms). The task contained 84 trials, including four practice trials excluded from the analyses.

The performance was assessed through behavioral (reaction time) and eye-tracking measures (first fixation direction, first fixation duration, second fixation direction, dwell time). The reaction time for probes replacing alcohol pictures compared to those replacing non-alcohol pictures is the commonly used AB index. The first fixation direction indicates the stimulus that was first fixated during each trial (i.e. initial attentional capture). The first fixation duration indicates the duration of the first fixation made on a stimulus (i.e. persistence of attentional focus). The second fixation direction indicates how frequently the participant fixated a second stimulus after visiting the first one (i.e. attentional switch). The dwell time is the sum of fixation times on each stimulus during the whole trial (i.e. maintenance of attention). Gaze samples were qualified as fixations or saccades according to the standard Eyelink algorithms.

2.6. Data reduction and statistical analyses

We performed data reduction procedure for reaction times by removing trials with incorrect responses (3.58 % of trials), reaction times lower than 200 ms (0.56 % of trials) or higher than 2000 ms (0.07 % of trials). Starers (i.e. participants not making any eye movement towards stimuli in more than half of the trials; van Ens et al., 2019) were removed before performing the analyses (2 patients, 1 control), leading to a sample of 51 (24 patients, 27 controls) for the first session. Eleven participants dropped out during the testing period, leading to a sample size of 40 (19 patients, 21 controls) for the second session. To measure task reliability, we computed AB score for each measurement: reaction time (non-alcohol minus alcohol), first fixation direction (proportion of first fixation on alcohol compared to non-alcohol), first fixation duration (alcohol minus non-alcohol), second fixation direction for alcohol/non-alcohol (proportion of second fixation on alcohol/non-alcohol compared to no second fixation after a first fixation on non-alcohol/alcohol), and dwell time (alcohol minus non-alcohol). A positive/negative AB score for reaction time, first fixation duration, and dwell time indicated AB towards alcohol/non-alcohol.

We performed all statistical analyses using the SPSS software package (version 27.0). We performed between-group comparisons (i.e., independent t-tests) on demographic, psychopathological characteristics and alcohol consumption variables. We also performed Pearson's

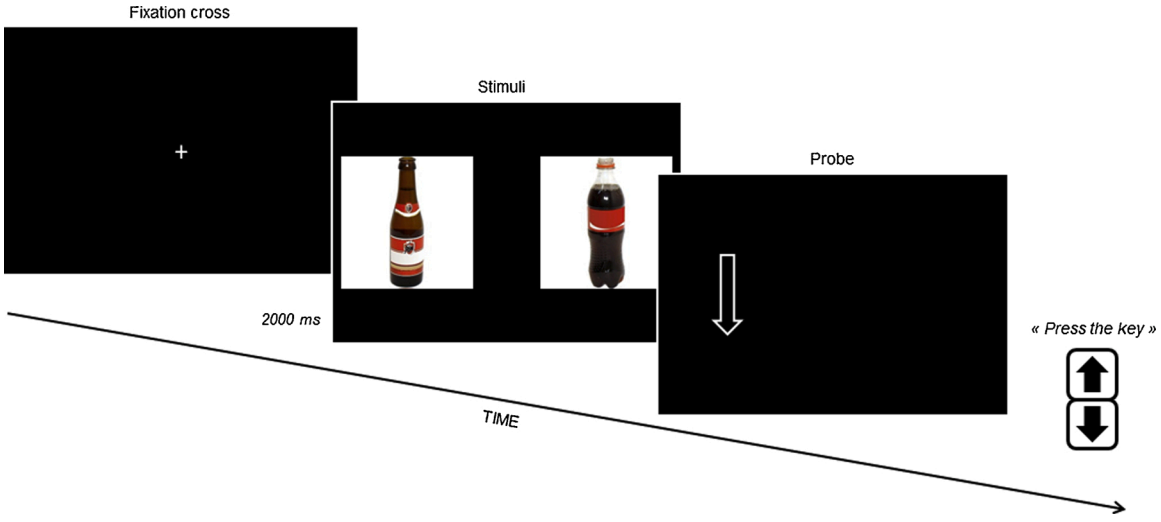

Fig. 1. Illustration of the visual probe task with alcohol-related and non-alcohol stimuli with example of matched pairs of stimuli.

correlations to explore the influence of psychopathological variables on the magnitude of alcohol-related AB (as indexed by dwell time) in the first session. These analyses were however conducted with an exploratory aim as the present study was not sufficiently powered to contrast correlations. We indexed the internal consistency of the task by (1) computing Cronbach's alpha for the 20 pairs of pictures; (2) computing bivariate Spearman-Brown correlations between AB score of the odd and even trials (split-half reliability). We indexed test-retest reliability by computing Pearson's correlations between AB score of the first and second sessions. For both sessions, we performed five 2 × 2 repeated-measures analyses of variance (ANOVAs) on behavioral (Reaction time) and eye-tracking (First fixation direction, First fixation duration, Second fixation direction and Dwell time) indices with Group (patients, controls) as between-subjects factor, Type (alcohol, non-alcohol) as within-subjects factor, and depression, anxiety and impulsivity scores as covariates (as they differed across groups and might influence AB). For reaction time, the Type factor encompassed, for each picture category, the trials in which the probe appeared at the same location as these pictures. We conducted Post Hoc tests (independent and paired samples t-tests) with a Bonferroni-corrected p-value of ($\alpha_{altered} = .05/2) = 0.025$. Note that we performed a complementary paired-samples t-test on first fixation laterality, which confirmed the left hemifield preference related to reading direction: more first fixations were directed leftwards (60 %; SD = 25) than rightwards [33 %; SD = 23; $t(50) = 4.004$, $p < .001$].

3. Results

3.1. Demographic, psychopathological, and alcohol-related measures (Table 1)

Patients and controls did not differ for age, sex, state anxiety and both assessments of subjective craving ($p > .050$). Patients showed higher depression [$t(29.38) = 6.524$, $p < .001$, d=1.955], trait anxiety [$t(49) = 5.564$, $p < .001$, d=1.619], impulsivity [$t(47.54) = 2.718$, $p = .009$, d=1.287], AUDIT scores [$t(24.68) = 14.040$, $p < .001$, d=4.277] and alcohol doses per day [$t(23.27) = 9.322$, $p < .001$, d=2.775] than controls. Regarding OCDS subscales, patients scored higher on obsessive thoughts (but not on compulsive desires) in the first session compared to controls [$t(24.21) = 3.661$, $p = .001$, d=1.087]. We found positive correlations between dwell time AB scores at first session and (1) depression ($r = .450$) and OCDS craving ($r = .407$) in patients; (2) impulsivity ($r = .410$) in controls.

Table 1
Demographic, psychopathological, alcohol consumption and craving measures [M (SD)] for detoxified patients with severe alcohol use disorder and healthy controls, and their correlations with dwell time attentional bias scores during the first session.

	Patients (n = 24) M (SD)	r	Controls (n = 27) M (SD)	r
Demographic measures				
Sex ratio (male/female) ns	12/12		14/13	
Age ns	49.88 (8.7)	−.177	49.52 (10.1)	.035
Psychopathological measures				
Beck Depression Inventory **	20.04 (10.2)	.450*	4.70 (4.6)	−.047
Trait Anxiety Inventory **	49.29 (8.6)	.336	35.48 (8.0)	−.141
State Anxiety Inventory ns	37.13 (13.8)	.118	31.11 (8.1)	−.110
UPPS-P *	43.90 (6.2)	−.224	38.30 (8.2)	.410*
Alcohol consumption measures				
Alcohol Use Disorder Identification Test **	27.00 (7.6)	.358	4.00 (2.0)	.156
Number of units per day **	14.08 (7.0)	−.339	0.74 (0.6)	.053
Craving measures				
VAS ns	4.42 (10.5)	.244	1.52 (6.0)	.235
OCDS ns	6.19 (6.7)	.407*	3.30 (2.8)	.316

Note: ns = Non-significant, * p < .05, ** p < .001.

3.2. Reliability estimates (Table 2)

Reaction time showed low and negative internal consistency, under the 0.70 cut-off score of acceptable internal reliability (Kline, 2000). It also presented low and negative split-half and test-retest reliabilities. First fixation direction and duration measures did not reach the cut-off score for acceptable reliability in terms of internal, split-half, or test-retest reliability. Conversely, dwell time and both indices of second fixation direction showed excellent internal consistency and split-half reliability. They also presented significant and positive correlations between test and retest sessions.

3.3. AB measures (Table 3)

Reaction Time. In both sessions, we found a Group effect [session 1: $F(1,46) = 5.741$, $p = .021$, $\eta_p^2 = .111$; session 2: $F(1,35) = 6.877$, $p = .013$, $\eta_p^2 = .164$], showing longer reaction times for patients compared to controls. Main effect of Type and its interaction with Group were inconclusive ($p > .050$).

First fixation direction. In both sessions, main effects of Type, Group and their interaction were inconclusive ($p > .050$).

First fixation duration. In both sessions, main effects of Type, Group and their interaction were inconclusive ($p > .050$).

Second fixation direction. In session 1, we found a marginal Type X Group interaction [$F(1,46) = 4.028$, $p = .051$, $\eta_p^2 = .081$] (Fig. 2). Patients (72 %; SD = 24) less frequently performed a second fixation towards alcohol after a first fixation on non-alcohol compared to controls [87 %; SD = 16; $t(39.00) = 2.640$, $p = .012$, d=.758], while groups did not differ regarding the second fixation on non-alcohol after a first fixation on alcohol ($p > .050$). Main effects of Type and Group were inconclusive ($p > .050$). In session 2, we found a Type effect [$F(1,35) = 6.333$, $p = .017$, $\eta_p^2 = .153$], showing a higher proportion of second fixations for non-alcohol (81 %; SD = 21) compared to alcohol (71 %; SD = 28). We found a Group effect [$F(1,35) = 4.119$, $p = .050$, $\eta_p^2 = .105$], showing that controls performed a second fixation more frequently than patients. We found a Type X Group interaction [$F(1,35) = 16.657$, $p < .001$, $\eta_p^2 = .322$]. Patients (59 %; SD = 28) less frequently performed a second fixation towards alcohol after a first fixation on non-alcohol compared to controls [82 %; SD = 23; $t(38) = 2.846$, $p = .007$, d=.901]. Groups did not differ regarding second fixation on non-alcohol after a first fixation on alcohol ($p > .050$).

Dwell Time. In session 1, we found a Type X Group interaction [$F(1,46) = 6.016$, $p = .018$, $\eta_p^2 = .116$]. Patients (393 ms; SD = 193) presented shorter dwell times on alcohol than controls [542 ms; SD = 158; $t(49) = 3.041$, $p = .004$, d=.853], while groups did not differ regarding dwell times on non-alcohol ($p > .050$). Main effects of Type and Group were inconclusive ($p > .050$). In session 2, a Type effect [$F(1,35) = 4.931$, $p = .033$, $\eta_p^2 = .123$] showed longer dwell times for non-alcohol (557 ms; SD = 311) than alcohol (409 ms; SD = 183). We also found a significant Type X Group interaction [$F(1,35) = 19.235$, $p < .001$, $\eta_p^2 = .355$]. Patients (319 ms; SD = 156) presented shorter dwell times on alcohol than controls [491 ms; SD = 169; $t(38) = 3.322$, $p = .002$, d=1.052] and compared to non-alcohol [579ms; SD=391; $t(18) = 2.466$, $p = .024$, d=.566]. Groups did not differ regarding dwell time on non-alcohol ($p > .050$). Main effect of Group was inconclusive ($p > .050$).

4. Discussion

The presence of AB towards alcohol in AUD is a core proposal of theoretical models. However, its experimental validation still faces issues as available data rely on unreliable reaction time-based measures. We investigated the presence and extent of AB in a population of detoxified inpatients diagnosed with severe AUD, by using a combined

Table 2
Internal consistency (Cronbach's alpha), split-half reliability (bivariate Spearman-Brown correlations) and test-retest reliability (bivariate Pearson correlations) for the first and second sessions of the VPT for reaction times and eye-tracking measures.

	Reaction Time	Dwell Time	First Fixation	First Fixation Duration	Second Fixation on alcohol	Second Fixation on non-alcohol
Internal consistency						
First session	−.156	.967	.027	.643	.870	.806
Second session	−.947	.980	.370	.437	.977	.811
Split-half reliability						
First session	.058	.804**	−.197	−.101	.830**	.840**
Second session	−.126	.763**	−.051	.326*	.875**	.762**
Test-retest reliability						
Both sessions	−.798**	.536**	.124	.304	.637**	.463**

Note: * p < .05, ** p < .001.

Table 3
Behavioral and eye-tracking indexes for the first and second sessions of the VPT (M [SD]) for detoxified patients with severe alcohol use disorder and healthy controls.

Variable	Type	First session		Second session	
		Patients (n = 24)	Controls (n = 27)	Patients (n = 19)	Controls (n = 21)
Reaction time (ms)	Alcohol	824 (439)	625 (145)	756 (214)	579 (147)
	Non-alcohol	795 (329)	634 (166)	789 (324)	588 (151)
First fixation direction (%)	Alcohol	37.33 (6.4)	37.59 (6.0)	36.00 (6.4)	37.95 (6.2)
	Non-alcohol	35.96 (5.8)	37.70 (5.9)	37.79 (8.0)	35.81 (6.2)
First fixation duration (ms)	Alcohol	227 (47)	253 (79)	220 (47)	259 (73)
	Non-alcohol	241 (95)	253 (81)	241 (72)	261 (75)
Second fixation direction (%)	Alcohol	71.70 (24.4)	87.17 (16.0)	58.87 (28.4)	82.10 (23.1)
	Non-alcohol	76.99 (22.9)	86.74 (18.5)	76.76 (21.2)	85.20 (19.7)
Dwell Time (ms)	Alcohol	393 (193)	543 (158)	319 (156)	491 (169)
	Non-alcohol	525 (337)	586 (214)	579 (391)	537 (223)

VPT/eye-tracking approach presenting higher reliability.

Regarding reaction time and first fixation indices, we did not observe any alcohol-related AB among patients. This null finding appears related to the poor reliability of reaction time (Ataya et al., 2012). Regarding the eye movements indices of initial attentional capture, neither first fixation direction nor duration reached acceptable reliability, in coherence with earlier results (Lazarov et al., 2018; Soleymani et al., 2020). The absence of early automatic attraction towards alcohol among patients could partly be caused by the classical dominance of the left visual field related to Western reading and writing habits (Foulsham et al., 2013). This left-gaze bias orients early attention towards the left hemifield, regardless of the stimuli (only 33 % of first fixations directed rightwards in the current study). We thus found no support for an automatic and early AB towards alcohol in severe AUD.

Researchers have suggested that, instead of being based on attention-grabbing properties of alcohol stimuli, AB may be characterized by a difficulty to disengage attention from them (Field et al., 2016; Soleymani et al., 2020). The second fixation direction indexes whether patients: (1) show difficulty to redirect attention away from alcohol cues, as indexed by a lower proportion of second fixation towards non-alcohol stimuli after a first fixation on alcohol stimuli, or (2) avoid processing alcohol-related stimuli after a first fixation on non-alcohol stimuli, as indexed by a lower proportion of second fixation towards alcohol. Our findings supported the latter proposal, revealing the presence of avoidance AB in detoxified patients with severe AUD. In the same vein, we showed shorter dwell times for alcohol-related stimuli among patients, which aligns with previous VPT studies reporting avoidance AB of alcohol in this population (Townshend and Duka, 2007). Both measures (second fixation direction, dwell time) provided excellent reliability (internal consistency, split-half reliability). Eye-tracking indexes thus highly increase VPT reliability (Bollen et al., 2020; Christiansen et al., 2015b), these sound results suggesting that detoxified inpatients present avoidance AB at later processing stages.

Such findings question theoretical assumptions regarding the role of AB in AUD (Bechara, 2005; Robinson and Berridge, 1993; Wiers et al., 2007). Based on the dominant models, our clinical sample was expected to present AB towards alcohol-related stimuli, since it was exclusively composed of patients diagnosed with the most severe pattern of AUD, usually characterized by massive cognitive dysfunctions (Stavro et al., 2013). AB towards alcohol might be observed in other AUD populations (e.g. untreated individuals) but the opposite pattern observed here among recently detoxified patients invalidates the proposal of consistent and stable AB in AUD. Previous findings in subclinical populations suggested that AB fluctuate alongside motivational states related to

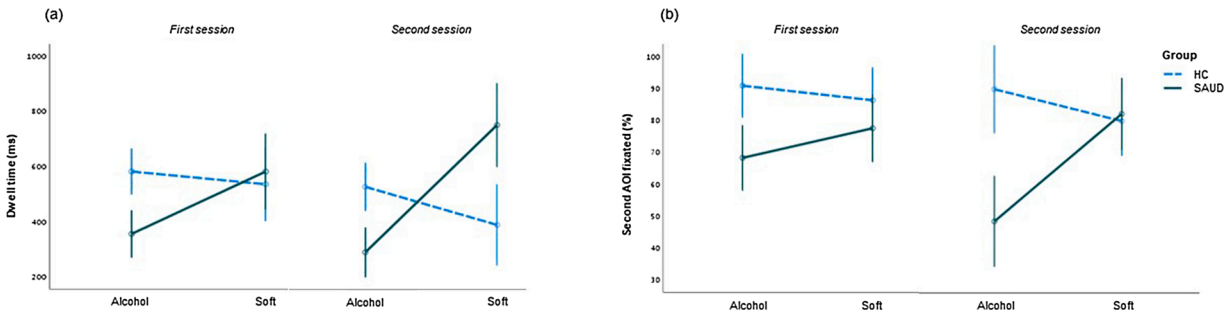

Fig. 2. (a) Dwell times and (b) proportion of second fixations for alcohol and non-alcohol stimuli observed in detoxified patients with severe alcohol use disorder and healthy controls during the first and second sessions when depression, anxiety and impulsivity are controlled for.

subjective craving (Bollen et al., 2020), stress (Field and Quigley, 2009) or ambivalence (Lee et al., 2014). Similarly, currently drinking patients with AUD presented reaction time-based AB towards alcohol, while abstinent patients rather showed avoidance AB (Sinclair et al., 2016). In the present study, the avoidance bias might be explained by patients' negative thoughts about alcohol, as they were involved in an abstinence process at testing time. Altogether, these findings suggest that AB vary with context and disease course. To experimentally test this assumption, further studies should evaluate alcohol-related AB in individuals with AUD not seeking treatment and/or not presenting motivational conflict regarding alcohol.

Our findings thus offer experimental support to the proposal of Field et al. (2016) that most models might have overstated the stability of AB in AUD: AB in addictive disorders might be driven by temporary changes in appetitive and/or aversive motivational states. The subjective valence [positive, negative, or both (i.e. ambivalence)] of the evaluation of substance cues might determine whether individuals maintain and/or override their gaze on them, resulting in different AB patterns. This provides a better explanation of the inconsistencies in the aforementioned VPT studies, where patients with AUD could either show approach or avoidance alcohol-related AB. In our sample, patients were all abstinent and most reported low craving and high abstinence motivation at testing time. These variables being related to negative evaluation and aversive state towards alcohol, they might explain why detoxified patients present avoidance AB. Moreover, our correlational analyses indicate that higher craving is associated with higher AB score, further supporting the impact of the motivational state on AB. Beyond the motivational state, the intensity of AUD presented by the experimental sample may vary between studies, both in terms of the number of diagnostic criteria encountered and the intensity/frequency of alcohol use, which could also influence the intensity of AB. Researchers and clinicians should thus reconsider the conditions in which attentional training should be conducted. Some patients might present genuine AB towards alcohol, and increasing the avoidance AB through attentional training might have a beneficial therapeutic impact, but the absence of AB towards alcohol in detoxified patients with severe AUD when using valid measures raises doubts regarding the usefulness of generalized attention training in this population.

The present study bares some limitations. First, our sample size was relatively small and statistical power was unsufficient for correlational analyses. Although these analyses were defined as exploratory, their results should be interpreted with caution. Second, we did not explicitly evaluate the patient's feelings and thoughts about alcohol use at testing time, preventing us from evaluating their impact on AB.

5. Conclusion

Capitalizing on reliable data combining VPT and eye-tracking, we showed that recently detoxified patients with severe AUD present avoidance AB of alcohol-related stimuli rather than approach AB, as suggested by most theoretical models. Avoidance AB appear at later and controlled processing stages (i.e. second fixation direction, dwell time) without influencing the initial capture of attention. These findings should lead to reconsider the interest of the therapeutic programs reducing AB in AUD, notably by reserving such intervention to patients presenting a genuine approach AB and/or high craving levels.

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Contributors

All authors contributed to draft the study design. ZB and PM created the study. ZB, PB and JD recruited the participants and collected the data. ZB, AP and PM conducted the statistical analyses. ZB drafted the manuscript and all authors provided critical revisions for important intellectual content. The final version of the manuscript was also approved by all authors.

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.

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