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RESEARCH REPORT

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Craving modulates attentional bias towards alcohol in severe alcohol use disorder: An eye-tracking study

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Abstract

Background and aims: Competing models disagree on three theoretical questions regarding alcohol-related attentional bias (AB), a key process in severe alcohol use disorder (SAUD): (1) is AB more of a trait (fixed, associated with alcohol use severity) or state (fluid, associated with momentary craving states) characteristic of SAUD; (2) does AB purely reflect the over-activation of the reflexive/reward system or is it also influenced by the activity of the reflective/control system and (3) does AB rely upon early or later processing stages? We addressed these issues by investigating the time-course of AB and its modulation by subjective craving and cognitive load in SAUD.

Design: A free-viewing eye-tracking task, presenting pictures of alcoholic and non-alcoholic beverages, combined with a concurrent cognitive task with three difficulty levels.

Setting: A laboratory setting in the detoxification units of three Belgian hospitals.

Participants: We included 30 patients with SAUD self-reporting craving at testing time, 30 patients with SAUD reporting a total absence of craving and 30 controls matched on sex and age. All participants from SAUD groups met the DSM-5 criteria for SAUD.

Measurements: We assessed AB through early and late eye-tracking indices. We evaluated the modulation of AB by craving (comparison between patients with/without craving) and cognitive load (variation of AB with the difficulty level of the concurrent task).

Findings: Dwell time measure indicated that SAUD patients with craving allocated more attention towards alcohol-related stimuli than patients without craving ($P < 0.001$, $d = 1.093$), resulting in opposite approach/avoidance AB according to craving presence/absence. SAUD patients without craving showed a stronger avoidance AB than controls ($P = 0.003$, $d = 0.806$). AB did not vary according to cognitive load ($P = 0.962$, $\eta^2_p = 0.004$).

Conclusions: The direction of alcohol-related attentional bias (approach/avoidance) appears to be determined by patients' subjective craving at testing time and does not function as a stable trait of severe alcohol use disorder. Alcohol-related attentional bias appears to rely on later/controlled attentional stages but is not modulated by the saturation of the reflective/control system.

KEYWORDS
Alcohol, alcohol use disorder, attentional bias, avoidance bias, cognitive load, eye-tracking

INTRODUCTION

Alcohol-related attentional bias (AB) is the preferential allocation of attention towards alcohol-related stimuli. Prominent theoretical models assume that AB plays a causal role in the onset and persistence of severe alcohol use disorder (SAUD) [1–3]. The incentive–sensitization theory [4] postulates that repeated alcohol exposures sensitize the reflexive/reward system, enhancing the incentive properties of alcohol-related cues through conditioning. Becoming more salient, these cues capture attention (i.e. generate AB) and guide individuals towards alcohol consumption. Hence, interventions targeting AB have emerged, postulating that reducing AB through attentional retraining would reduce consumption and relapse risk. These interventions, while increasingly implemented in clinical settings with some promising effect on clinical outcomes, led to inconsistent results regarding their impact on AB [5, 6]. Such discrepancies might result from the fact that several theoretical questions remain to be clarified in this research field, namely: (1) is AB mainly a trait (fixed, associated with SAUD severity) or state (fluid, associated with momentary motivational states) characteristic of SAUD; (2) does AB purely reflect the over-activation of the reflexive/reward brain system or is it also influenced by the activity of the reflective/control system; and (3) is AB characterized by an early/automatic hijacking of attention by alcohol-related stimuli or rather relies on later and more controlled processing stages?

Regarding the first question, traditional models assume that AB progressively develops through associative learning and reflexive/reward system over-sensitization, finally constituting an enduring and potentially permanent SAUD characteristic [4, 7]. These models thus understated the sensitivity of AB to momentary states (e.g. motivational component of current craving) compared to the influence of stable factors related to SAUD (e.g. duration, severity). In the last decade, there has been more emphasis [8] on how fluctuating factors would moderate the behavioural expression of the reflexive/reward system (i.e. AB). Taking a step further, Field and colleagues suggested that AB is partly driven by temporary changes in appetitive and/or aversive states [9]. According to their theoretical account, AB would result from momentary motivational evaluations of alcohol-related stimuli, hence constituting a state rather than trait marker of SAUD. The subjective evaluation (positive, negative, ambivalent) of alcohol-related cues would lead individuals to maintain their attention on it or conversely ignore it, resulting in different AB patterns [9]. The reported [10, 11] intra-individual AB fluctuations according to current motivational value of alcohol (e.g. motivational component of current craving [12], drinking status [13]) support this proposal. Patients with SAUD might present an AB strongly affected by their current states, which would hence not constitute a key causal factor for SAUD persistence, raising doubt on the rationale of AB retraining. However, the very few studies exploring AB in SAUD used unreliable measures [14] applied on recently detoxified patients (known to frequently present aversive/ambivalent alcohol evaluation and low craving), which might explain the inconsistent results [15]. The only study [16] using reliable eye-tracking measures showed both an avoidance bias in recently-detoxified patients with SAUD and a positive correlation between AB and craving. These results call for directly addressing the inconsistent theoretical assumptions regarding AB fluctuations [4, 9].

The second question relates to the dual-process models [1, 17], postulating that SAUD emerges from (1) the under-activation of the 'reflective/control system', responsible for deliberative and controlled responses, and (2) the overactivation of the 'reflexive/reward system', initiating automatic and appetitive behaviours. In this view, AB results from the overactivation of the reflexive/reward system, but the role played by the reflective/control system in its occurrence remains unclear. Indeed, dual-process models stated that situational factors such as cognitive load could selectively impair the reflective/control system, leading the reflexive/reward system to take the lead (therefore assuming a continuous interaction between systems). Nevertheless, they simultaneously stated that reflexive/reward processes operate in an effortless manner, independently from the availability of cognitive resources [8, 18]. Previous studies also suggested that AB is not an artefact of patients' impaired cognitive/executive functioning [19], but rather a genuine consequence of the reflexive/reward system's overactivation [20]. However, studies in other psychopathological states showed that AB might be increased by executive dysfunction [21–23], suggesting that AB is affected by the activity of the reflective/control system. In line with this proposal, the paradigms classically used to measure AB cannot rule out the possibility that participants use their executive functions to voluntarily modify their AB; for example, by using oculomotor inhibition to actively avoid saccades towards alcohol-related stimuli. An experimental way to assess this role of the reflective/control system in AB would be to saturate this system through a concurrent cognitive task that places high demands on cognitive resources, thus hampering their ability to modulate AB. In other words, the temporary reduction of available cognitive resources would reduce the ability of the reflective/control system to modulate AB. Conversely, if AB is independent of the reflective/control system, saturating this system should have no influence on AB.

The third question is whether AB relies upon early and automatic attentional processes (generating an uncontrolled capture of attention towards alcohol [1, 17]), or on later and more controlled ones (being related to a longer processing time for alcohol-related cues and/or to a difficulty to disengage attention from them [24]). When simultaneously presenting alcohol-related and non-alcohol-related stimuli, eye-tracking allows the dissociation, with high temporal/spatial resolution, between (1) the initial attentional capture quickly following the appearance of alcohol-related cues, by measuring early indices such as first area of interest (AOI) visited (i.e. percentage of trials in which alcohol versus non-alcohol AOIs were fixated first) from (2) the controlled maintenance of attention towards alcohol, by measuring late indices such as dwell time (i.e. sum of fixation times on alcohol versus non-alcohol AOIs during the whole trial). An early/automatic AB is thus inferred by the modification of early indices (e.g. higher percentage of first fixations towards alcohol-related stimuli), while a late/controlled AB is inferred by the modification of late indices (e.g. higher dwell time for alcohol-related stimuli). Eye-tracking studies showed that AB mainly appears at late processing stages in subclinical and clinical populations [25–27], thus questioning its early/automatic nature.

Here, we directly address these three conceptual questions, as (1) we clarify whether AB is stable or affected by motivational states by comparing recently detoxified SAUD patients with or without craving in a free-viewing eye-tracking task assessing AB. If AB is modulated by temporary appetitive states, such as the motivational component of craving, patients reporting craving at testing time (defined here as the intense and irrepressible desire to consume alcohol right now) will tend to show an AB towards alcohol-related stimuli (i.e. approach bias), while patients without craving will tend to avoid these stimuli (i.e. avoidance AB); (2) we investigate whether reducing the capacity of the reflective/control system (by placing a temporary load on cognitive resources) would increase AB. If the reflective/control system plays a role in AB modulation, its saturation in the high cognitive load condition of the concurrent task (i.e. the reduction of cognitive resources available to inhibit AB) will lead to a higher AB towards alcohol-related stimuli compared to the low cognitive load conditions (where cognitive resources are available to voluntarily modulate AB); (3) we determine the temporal dynamics of AB by distinguishing early/automatic and late/controlled processing steps. If AB is related to late processing stages rather than early/automatic ones, it will only be observed for the indices of controlled attentional maintenance (i.e. dwell time, namely higher total time spent on alcohol-related stimuli than on non-alcohol-related stimuli) and not for the indices related to the early attentional capture (i.e. first AOI visited, namely higher number of first fixations towards alcohol-related stimuli than towards non-alcohol-related stimuli).

METHODS

Participants

Before starting data acquisition, we recruited and allocated 30 patients (15 women) who self-reported craving at testing time (i.e. scored higher than zero at the baseline craving visual analogue scale (VAS): 0 = no desire at all to consume alcohol right now, to 100 = terrible desire to consume alcohol right now) to the experimental craving group, and 30 patients (10 women) who did not report craving at baseline (i.e. scored zero at the VAS) to the non-craving group. All patients fulfilled DSM-5 criteria for SAUD and were tested during their detoxification treatment in three Belgian hospitals. They had all been abstinent for at least 7 days and were free of psychiatric comorbidities (except tobacco use disorder). We recruited 30 healthy controls (15 women) through social networks and e-mails. Controls were free of any past/present psychiatric disorder and personal/parental SAUD history. They consumed fewer than 10 standard alcohol units (10 g of pure ethanol per unit) per week and never exceeded 3 units per day. They scored lower than 8 at the AUDIT [28] (score from 0 to 40; $\alpha = 0.960$) and had to refrain from consuming alcohol the day before testing. Exclusion criteria for all groups included polysubstance use disorder and major past/present neurological trauma and/or disorder. All participants had normal or lens-corrected vision and were fluent in French.

Procedure

Participants provided written informed consent and were tested individually. Before starting data acquisition, they completed questionnaires assessing state anxiety (STAI-S; score from 20 to 80; $\alpha = 0.960$) and current alcohol craving. We used the Alcohol Craving Questionnaire–Short Form Revised (ACQ-SF-R [29]; score from 12 to 84; $\alpha = 0.874$) for a multi-dimensional assessment of craving and the VAS single-item (score from 0 to 100) to obtain a quick and specific measure of the motivational component of craving. The computerized experimental task comprised three parts and lasted 20–30 minutes. We re-assessed craving through the VAS after each part.

We performed a standard nine-point eye-gaze calibration at the beginning of each experimental phase. Between them, participants completed questionnaires measuring psychopathological variables; namely, depression (BDI-II [30]; score from 0 to 39; $\alpha = 0.914$), trait anxiety (STAI-T [31]; score from 20 to 80; $\alpha = 0.949$) and impulsivity (UPPS-P [32]; score from 20 to 80; $\alpha = 0.898$). The study protocol followed the Declaration of Helsinki and was approved by the Ethics Committee of Saint-Luc-UCLouvain Clinics (reference number: 2019/26MAR/141). After the experiment, we debriefed participants and controls received financial compensation. As this study was not pre-registered, its results should be considered as exploratory. The data that support the findings of this study are available on request from the corresponding author.

Apparatus

Participants were seated at a desk, facing an eye-tracker camera and an Asus Display Laptop PC with a 17.3-inch FHD screen (resolution = 1080 × 1920; refresh rate = 120 Hz, placed 60 cm away from the eyes). We controlled the presentation of the task and its synchronization with eye-tracking using OpenSesame [33]. We recorded eye movements using an EyeLink Portable Duo (SR Research, Ottawa, ON, Canada; sampling rate = 1000 Hz; average accuracy range = 0.25°–0.5°, gaze tracking range = 32° horizontally, 25° vertically).

Free-viewing eye-tracking task

The AB task was replicated from Soleymani *et al.* [34]. In each trial, participants had to first fixate a central fixation dot appearing on the background screen for at least 100 ms. We used this dot as a drift check for eye-gaze calibration, and to ensure that participants focused their attention at the centre of the screen. Once the eye-tracking device detected the eyes at the centre of the screen, a 4 × 4 matrix replaced the dot for 6000 ms. The matrix presented 16 full-colour 250 × 250 images of eight alcoholic and eight non-alcoholic beverages without context. The four inner pictures always consisted of two alcohol and two non-alcohol pictures, while we randomized the 12 outer pictures. Participants were asked to look freely at the pictures. To support the participants' task engagement, we presented three types of stimuli: bottle, bottle with empty glass or bottle with filled glass. A total of 218 pictures were extracted from the ABPS battery [35], the selected stimuli being culturally relevant for the Belgian population.

Participants completed three experimental conditions, each containing 54 trials: one presenting solely the free-viewing task (i.e. baseline) without any concurrent task, and two presenting the free-viewing task alongside a concurrent cognitive task of increasing difficulty (i.e. low cognitive load, level 1 and high cognitive load, level 2, see Fig. 1). Levels 1 and 2 were used to saturate the reflective/control system and explore the impact of depleting cognitive resources on AB, always measured through the free-viewing task performed simultaneously. The baseline free-viewing task was always performed first to ensure a valid measure of AB (i.e. uncontaminated by the concurrent cognitive task). Then, we presented levels 1 and 2 in a counterbalanced order between participants to control for potential learning or fatigue effects between these two conditions.

Concurrent auditory cognitive task

In level 1, we presented a series of digits orally through headphones and participants had to detect the appearance of a target digit ('5') by mouse-clicking (low cognitive load, as participants only had to pay attention to the presented digit without further cognitive processing). In level 2, we presented another series of digits orally, and participants had to mouse-click each time the sum of the two last digits was equal to 10 (high cognitive load, as participants had to store digits in their working memory and perform additions throughout the task). A male French voice [36] pronounced each digit at the same pace. We used Audacity® software to mark the onset/offset of each digit and then compressed the sampled period in an OGG file. The duration of enunciation and silent periods for each digit was set to 2000 ms. In both levels, we presented the series of digits in a continuous manner to keep the difficulty level constant. The dependent variables for this concurrent cognitive task were correct responses (i.e. percentage of target digits for which the participant correctly mouse-clicked), false alarms (i.e. number of non-target digits for which the participant mouse-clicked) and delayed responses (i.e. number of target digits for which the participant mouse-clicked after the onset of the following digit).

Data analysis

No data-reduction procedure was performed, as the free-viewing task did not measure any behavioural performance. Seven individuals (two patients with craving, three patients without craving, two control participants) were not able to participate in our experiment due to poor eye-tracking calibration. We set our sample size to 30 participants per group, based on previous work exploring AB in SAUD [12, 16, 37–39]. We performed a simulation-approach power analysis for exploratory three-way analysis of variance (ANOVA) designs [40] assuming an alpha of 0.05, a sample size of 30 per group and a Bonferroni adjustment for multiple comparisons, which indicated a power of 0.65 and 0.95 for detecting a small- to medium-effect size (η^2_p = 0.022) in our 3 × 2 and 3 × 2 × 3 within–between interactions, respectively. We defined AOI for the free-viewing task as the zone in pixels covered by each image, leading to 16 AOIs per trial (corresponding to the number of stimuli shown per trial in the free viewing task). We assessed early

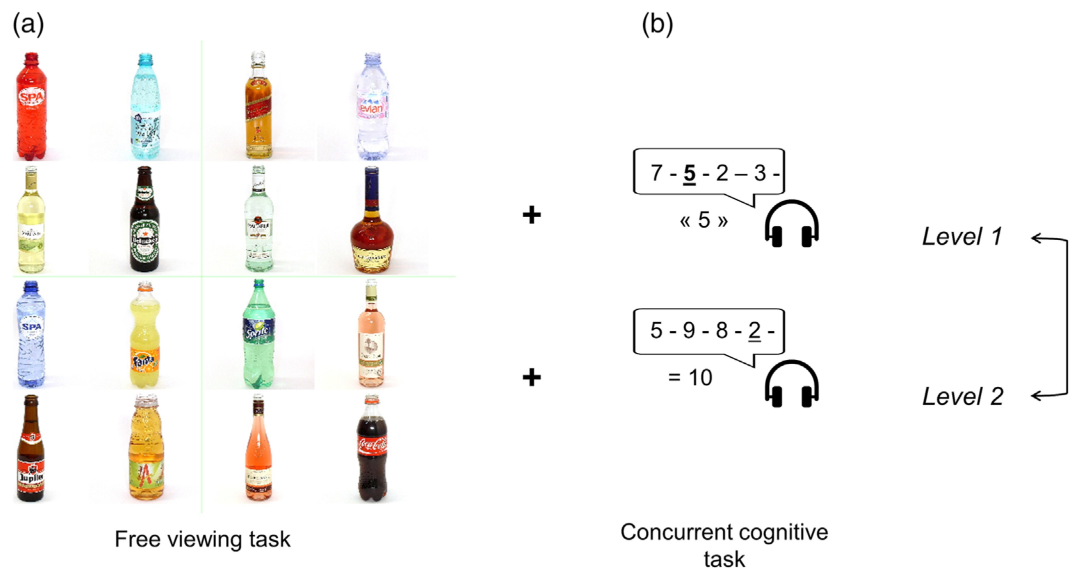

FIGURE 1 Illustration of a trial from the eye-tracking free-viewing task (a) and of the concurrent cognitive task with low (level 1) and high (level 2) cognitive load (b).

AB processes through the first AOI visited index and late AB processes through dwell time index. EyeLink algorithms qualified gaze samples as fixations or saccades. For the concurrent task, we performed a manipulation check to verify that the level of difficulty was higher in level 2 than in level 1 by contrasting the percentage of correct responses, and the number of false alarms and delayed responses in both levels.

We performed all statistical analyses using SPSS version 27.0. We performed between-group comparisons (independent *t*-tests; χ^2 tests) on demographic, psychopathological and alcohol-related variables. As an estimate of reliability, we computed Cronbach's alpha for the first AOI visited and dwell time measures at baseline.* Following a well-established procedure [41, 42], we calculated AB scores (difference scores or percentages for alcohol versus non-alcohol stimuli) separately for each matrix, leading to 54 AB scores for each AB measure. Considering the established left-gaze bias effect on the first AOI visited (i.e. left hemifield preference related to reading direction [43]), we also estimated the reliability of this measure when comparing AOIs on the left versus right part of the screen. We performed a manipulation check of the cognitive load and increased difficulty from level 1 to level 2 by conducting 3 × 2 ANOVAs on data from the concurrent task (correct responses, false alarms, delayed responses) with Group (craving/non-craving/controls) as between-subjects factor and Level (1/2) as within-subject factor. We performed 3 × 3 × 2 ANOVAs on AB indices (first AOI visited/dwell time, to test our third hypothesis) with Group (craving/non-craving/controls, to test our first hypothesis) as between-subjects factor, Level (baseline/1/2, to test our second hypothesis) and Stimuli (alcohol/non-alcohol) as within-subject factors. We reran these analyses by adding education level, age at first consumption, state and trait anxiety, depression and impulsivity as covariates (as at least two groups differed on these potentially confounding variables, see Results section) and reported the results in the Supporting information, Table S1. We conducted *post-hoc* tests with a Bonferroni-corrected *P*-value of $\alpha_{altered} = 0.05/3 = 0.017$. Finally, we performed Pearson's correlations to explore the influence of all demographic, psychological and alcohol-related variables on AB magnitude (indexed by dwell time) and on craving at baseline.

RESULTS

Demographic, psychopathological and alcohol-related measures

Both groups of SAUD patients had fewer years of education, earlier age at first consumption (for craving SAUD patients only) and higher state anxiety, trait anxiety, depression and impulsivity than controls (Table 1). Craving and non-craving SAUD patients did not differ except for trait anxiety.

As expected, both groups of SAUD patients reported consuming more alcohol per week and had higher AUDIT score than controls, and non-craving SAUD patients reported lower craving than craving SAUD patients (for all VAS and ACQ-SF-R) and controls (for all VAS).

Manipulation check: concurrent cognitive task

Correct responses, false alarms and delayed responses

We found Level effects showing lower percentages of correct responses ($F_{(1,73)} = 38.380$, $P < 0.001$, $\eta^2_p = 0.345$), more false alarms ($F_{(1,73)} = 9.880$, $P = 0.002$, $\eta^2_p = 0.119$) and more delayed responses ($F_{(1,73)} = 9.175$, $P = 0.003$, $\eta^2_p = 0.112$) in level 2 than level 1. Other main effects and interactions were inconclusive (all *P*-values ≥ 0.078).

These results show that the concurrent cognitive task successfully intensified the saturation of the reflective/control system by increasingly recruiting cognitive resources between levels 1 and 2.

Free-viewing AB task

AB reliability

Internal consistency of AB scores was high for dwell time ($\alpha = 0.976$). It was low for the first AOI visited when comparing alcohol versus non-alcohol AOIs (regardless of the position of those AOIs; $\alpha = 0.047$) but conversely, high when comparing AOIs on the left versus right (regardless of their alcohol/non-alcohol content; $\alpha = 0.908$).

This latter result suggests that the low reliability of the first fixation towards alcohol/non-alcohol AOIs is mainly due to left-gaze bias predominance (participants more frequently directed their first fixation on the left AOI compared to the right AOI; $t_{(89)} = 11.412$, $P < 0.001$, $d = 1.203$) rather than to the poor psychometric quality of the first AOI visited index *per se*.

Early AB processing stages

First AOI visited

We found a stimuli effect showing that participants performed first fixations more frequently towards non-alcohol than alcohol stimuli. Other main effects and interactions were inconclusive (Table 2).

Late AB processing stages

Dwell time

We found a Stimuli effect showing longer dwell time for non-alcohol than alcohol stimuli. We also found a Stimuli × Group interaction (Fig. 2): SAUD patients with craving presented longer dwell time on alcohol ($t_{(58)} = 4.234$, $P < 0.001$, $d = 1.093$) and shorter dwell time on non-alcohol ($t_{(58)} = 3.586$, $P < 0.001$, $d = 0.926$) than SAUD patients

*We dismissed the inclusion of two supplementary eye-tracking measures from our analyses (i.e. first saccade latency, number of AOIs visited) because of their redundancy with the main measures of early and late AB processes, but also in view of the poor reliability for the latter ($\alpha = 0.385$) and inability to test the reliability of the former (as the number of observations was too small when separated by type of stimuli, trial and participant).

TABLE 1 Demographic, psychopathological and alcohol consumption measures (mean, standard deviation) and independent-sample *t*-test or χ^2 test comparing SAUD patients with craving (Craving), SAUD patients without craving (Non-craving) and control participants (Controls).

	Craving (*n* = 30)	Non-craving (*n* = 30)	Controls (*n* = 30)	Craving versus Non-craving		Craving versus controls		Non-craving versus controls	
				t or χ^2	*P*	*t* or χ^2	*P*	*t* or χ^2	*P*
Demographic measures									
Sex ratio (M/F)	20/10	15/15	15/15	1.714	0.190	1.714	0.190	0.000	1
Age	42.90 (10.66)	48.07 (9.35)	47.87 (10.39)	1.996	0.051	1.827	0.073	0.078	0.938
Years of education	12.47 (2.85)	13.07 (4.23)	16.07 (2.83)	0.644	0.522	4.873	< 0.001	3.192	0.002
Psychopathological measures									
BDI-II	11.56 (7.03)	8.68 (8.29)	2.93 (3.69)	1.324	0.192	5.778	< 0.001	3.449	0.001
STAI-S	40.47 (15.28)	36.12 (16.76)	28.83 (7.56)	1.050	0.298	3.737	< 0.001	2.170	0.034
STAI-T	52.24 (9.18)	45.52 (12.5)	32.30 (11.99)	2.145	0.037	6.617	< 0.001	4.109	< 0.001
UPPS-P	48.79 (8.28)	44.39 (9.33)	37.43 (7.51)	1.773	0.082	5.274	< 0.001	3.114	0.003
Alcohol consumption measures									
AUDIT	33.50 (5.43)	30.75 (6.68)	3.30 (1.70)	1.516	0.136	28.532	< 0.001	21.769	< 0.001
First consumption (age)	13.85 (3.16)	15.72 (4.89)	15.28 (1.89)	1.756	0.084	2.092	0.041	0.454	0.652
Doses per week	32.12 (24.22)	21.90 (13.15)	0.47 (0.43)	1.802	0.077	6.833	< 0.001	8.919	< 0.001
Years of SAUD	13.40 (9.70)	9.67 (8.58)	NA	1.580	0.119	NA	NA	NA	NA
Previous detoxification	2.28 (2.88)	3.00 (4.21)	NA	0.770	0.445	NA	NA	NA	NA
Days of abstinence	35.50 (39.51)	39.07 (43.86)	NA	0.331	0.742	NA	NA	NA	NA
Baseline craving (VAS)	22.73 (23.40)	0.00 (0.00)	2.30 (4.84)	5.322	< 0.001	4.684	< 0.001	2.601	0.012
Post-level 0 craving (VAS)	29.27 (25.98)	0.00 (0.00)	4.53 (11.20)	6.171	< 0.001	4.789	< 0.001	2.217	0.031
Post-level 1 craving (VAS)	28.03 (26.32)	0.00 (0.00)	4.67 (11.28)	5.833	< 0.001	4.469	< 0.001	2.266	0.027
Post-level 2 craving (VAS)	28.20 (27.00)	0.00 (0.00)	4.70 (11.36)	5.721	< 0.001	4.394	< 0.001	2.266	0.027
Baseline craving (ACQ-SF-R)	35.70 (14.13)	17.97 (7.78)	18.17 (5.07)	6.019	< 0.001	6.396	< 0.001	0.118	0.907

Abbreviations: ACQ-SF-R = Alcohol Craving Questionnaire–Short Form Revised; AUDIT = Alcohol Use Disorder Identification Test; BDI-II = Beck Depression Inventory-II; NA = not applicable to this group; STAI-S = State–Trait Anxiety Inventory–State; STAI-T = State–Trait Anxiety Inventory–Trait; SAUD = severe alcohol use disorder; UPPS-P = Urgency-Premeditation-Perseverance-Sensation Seeking-Positive Urgency Impulsive Behavior Scale; VAS = Visual Analogue Scale.

TABLE 2 ANOVA results for eye-tracking measures of early and late AB processing stages.

	First AOI visited				Dwell time			
	d.f.	*F*	*P*	η^2_p	d.f.	*F*	*P*	η^2_p
Between-subjects effects								
Group	2	1.521	0.224	0.035	2	0.416	0.661	0.010
Error (Group)	85				85			
Within-subjects effects								
Stimuli	1	13.467	< 0.001	0.137	1	18.279	< 0.001	0.177
Stimuli × Group	2	1.029	0.362	0.024	2	9.688	< 0.001	0.186
Error (Stimuli)	85				85			
Level	2	0.716	0.490	0.008	2	2.237	0.110	0.026
Level × Group	4	1.885	0.115	0.042	4	0.243	0.913	0.006
Error (Level)	170				170			
Stimuli × Level	2	0.717	0.490	0.008	2	0.630	0.534	0.007
Stimuli × Level × Group	4	1.359	0.250	0.031	4	0.153	0.962	0.004
Error (Stimuli × Level)	170				170			

Abbreviations: ANOVA = analysis of variance; AB = attentional bias; AOI = area of interest; d.f. = degrees of freedom; η^2_p, = partial eta-squared.

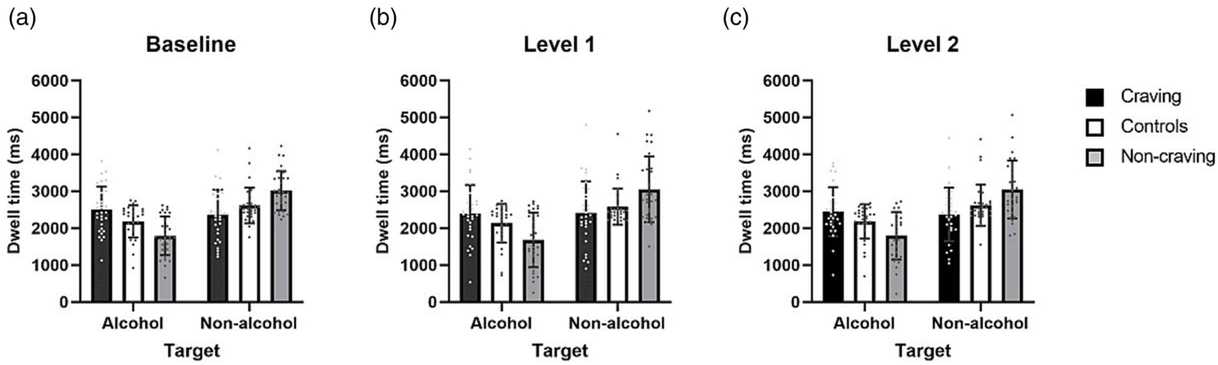

FIGURE 2 Dwell time observed in patients with severe alcohol use disorder reporting craving (Craving), patients reporting no craving (Non-craving) and control participants (Controls) in the free-viewing task at baseline (a), level 1 (b) and level 2 (c) for alcohol and non-alcohol stimuli.

TABLE 3 AB eye-tracking measures for the three levels of cognitive load (mean, standard deviation) comparing SAUD patients with craving (Craving), SAUD patients without craving (Non-craving) and control participants (Controls).

	First AOI visited (in %)		Dwell time (in ms)	
	Alcohol	Non-alcohol	Alcohol	Non-alcohol
Craving (*n* = 30)				
Baseline	25.73 (4.76)	27.27 (4.58)	2495 (631)	2355 (688)
Level 1	26.73 (3.22)	27.03 (3.28)	2387 (784)	2406 (865)
Level 2	26.14 (3.06)	27.59 (3.12)	2447 (665)	2375 (723)
Non-craving (*n* = 30)				
Baseline	27.03 (3.37)	26.87 (3.42)	1794 (523)	3018 (531)
Level 1	25.07 (3.50)	28.87 (3.57)	1681 (735)	3054 (864)
Level 2	25.14 (3.55)	28.76 (3.52)	1796 (641)	3048 (785)
Controls (*n* = 30)				
Baseline	25.93 (3.80)	27.93 (3.73)	2184 (437)	2617 (480)
Level 1	24.57 (4.65)	27.80 (4.83)	2137 (522)	2582 (489)
Level 2	26.07 (4.13)	27.63 (4.13)	2184 (463)	2622 (561)

Abbreviations: AB = attentional bias; AOI = area of interest; ms = milliseconds; SAUD = severe alcohol use disorder.

without craving (Table 3). Moreover, both SAUD patients without craving and controls showed longer dwell time on non-alcohol than alcohol stimuli (non-craving: $t_{(29)} = 5.635$, $P < 0.001$, $d = 1.029$; controls: $t_{(29)} = 2.775$, $P = 0.010$, $d = 0.507$), but this difference was higher in non-craving SAUD patients than controls (alcohol: $t_{(58)} = 3.122$, $P = 0.003$, $d = 0.806$; non-alcohol: $t_{(58)} = 2.826$, $P = 0.007$, $d = 0.730$). Other main effects and interactions were inconclusive (Table 2).[†]

Note that the level effect did not lead to any significant main effect or interaction on indices of AB, suggesting that the results of the free-viewing task and the related AB were not modulated by the intensity of the cognitive load generated by the concurrent task.

[†]The stimuli × group interaction for dwell time remained significant in the supplementary analyses that added as covariates all the demographic, psychological and alcohol-related variables differing between groups. Other main effects and interactions were inconclusive for both AB indices (see Supporting information, Table S1 for detailed results).

Correlations

Dwell time

In SAUD patients, we found positive correlations between dwell time at baseline and craving before (VAS: $r = 0.443$, $P < 0.001$; ACQ: $r = 0.546$, $P < 0.001$) and after (VAS: $r = 0.486$, $P < 0.001$) the task. All other correlations in SAUD patients and controls between AB and demographic, psychological or alcohol-related variables were inconclusive (all *P*-values ≥ 0.060).

Craving

In SAUD patients, we found a negative correlation between craving VAS score at baseline and age ($r = -0.289$, $P = 0.025$). All other correlations in SAUD patients and controls were inconclusive (all *P*-values ≥ 0.197).

DISCUSSION

Addiction models postulate that AB is a major index of the overactivation of the reflexive/reward system [4, 17], causally implicated in SAUD persistence. In the last decade, concurrent models placed greater emphasis on the moderating role of situational factors (e.g. craving, cognitive load) on the links between alcohol use severity and AB [8, 9]. Nevertheless, a theoretical blur persists on the nature and role played by AB in SAUD. We thus experimentally addressed three remaining questions on AB; namely, how is it affected by current motivational state and cognitive load, and what is its time-course?

First, we showed the main role played by craving in the magnitude and direction of AB, offering experimental support to the theoretical proposals that AB is affected by current motivational state rather than stable. Indeed, craving SAUD patients spent more time looking at alcohol stimuli than patients without craving, while the reverse was found for non-alcohol stimuli. Moreover, both controls and non-craving SAUD patients showed an avoidance bias for alcohol-related stimuli (i.e. shorter dwell times for alcohol-related stimuli), this bias being even stronger in the latter group. These results are in line with recent findings showing an avoidance bias in SAUD patients reporting very low craving and high abstinence motivation [16]. Altogether, our findings question the proposal of a long-lasting and potentially permanent AB in SAUD, as we could not find any AB among recently-detoxified patients when using reliable eye-tracking measures (i.e. dwell time). The opposite AB patterns between the two groups of patients support the theoretical account that AB is driven by temporary changes in appetitive/aversive motivational states regarding alcohol, and that its stability along the disorder might have been overstated [9]. The subjective momentary evaluation of alcohol-related cues (indexed here by the motivational component of craving and assessed through VAS) constitutes an important predictor of whether individuals maintain and/or override their gaze on them, resulting in avoidance/approach AB. In line with our hypothesis [15] we showed that, during the detoxification process, non-craving patients present an avoidance bias towards alcohol. This result makes sense as these patients, being abstinent in clinical settings and motivated to avoid alcohol outside the clinic, present a negative evaluation and aversive state towards alcohol. Such avoidance bias is also identified, although to a lesser extent, among control participants, which was expected, as this group comprised low drinkers presenting reduced attraction towards alcohol. Conversely, craving patients show motivational conflict (i.e. craving associated with abstinence motivation), thus not leading to a strong AB towards alcohol (i.e. no significant difference with control participants) and confirming that AB is not a strong and stable characteristic of patients presenting SAUD. Correlational analyses further support this proposal that AB is influenced by current motivational states rather than by stable consumption characteristics (e.g. SAUD duration, consumption frequency or intensity), as AB was not associated with any index of SAUD severity, except VAS craving scores (specifically assessing the motivational component of craving). Future research should investigate whether AB might also fluctuate with other components of this multi-dimensional construct (e.g. bodily sensations) and/or momentary aversive states (as postulated by [9]).

The concurrent cognitive task supported the proposal that AB relies on the overactivation of the reflexive/reward system and might be quite independent from the reflective/control system, as AB patterns were not influenced by the extent of cognitive resources available. However, this null result cannot be interpreted as definitive proof that the reflective/control system does not influence AB. Indeed, while our manipulation check demonstrated that we efficiently increased cognitive load across conditions (i.e. worse performance in level 2 than level 1), the cognitive resources of the reflective/control system might have been insufficiently saturated to impact the reflexive/reward system and AB, and our sample size might have been too low to detect a subtle impact of cognitive load on AB. This independence of AB towards the reflective/control system should be confirmed in future studies that more strictly manipulate the saturation of cognitive resources.

Finally, we suggest that AB, regardless of its direction (approach/avoidance), is significantly underpinned by late attentional stages (assessed through dwell time measures) and is mainly characterized by a preferential maintenance of attention towards alcohol/non-alcohol stimuli. In contrast, the facilitated capture of attention could not be reliably assessed in the present study (similarly to previous ones [16, 33, 44]), as the measure of first AOI visited was contaminated by the classical dominance of the left side of the visual field related to reading/writing habits [43]. Nevertheless, we observed that the presumably strong attention-grabbing properties of alcohol-related stimuli (as postulated by dominant models [4]) did not overcome the left-gaze bias, even in participants showing stronger AB towards alcohol at later processing stages (i.e. SAUD patients with craving), and were actually contradicted by the higher percentage of first fixations towards non-alcohol-related stimuli in all our participants. This casts doubt upon the postulated automatic/early nature of AB in SAUD [17], already questioned by heterogeneous findings when manipulating stimuli duration in behavioural experiments [45, 46]. In contrast, our results regarding the late component are in line with eye-tracking studies in subclinical [47] and clinical [16] populations, as well as with earlier studies targeting such malleable late components in attentional retraining [6, 24]. We thus highlighted the relevance of dwell time measures to investigate the preferential maintenance of attention throughout the trial, and we encourage future studies to increase the reliability of early eye-tracking indices by presenting stimuli vertically to override the predominant left-gaze bias and/or by developing AB tasks specifically exploring the early attentional capture by alcohol-related cues [48].

As our study was not pre-registered, its results should be considered exploratory. Although none of the assessed demographic and psychopathological variables correlated with AB (including the educational level for which groups were not matched), it should also be acknowledged that other unmeasured biasing variables might have modulated AB (e.g. alcohol-related motivations, subclinical psychiatric comorbidities). Finally, while we followed the current guidelines to reliably explore AB in alcohol use disorders, notably by using eye-tracking measures and the recommended free-viewing task [49], other paradigms that require more active engagement of participants could be adapted to reliably measure AB (e.g. visual search task [50]). Despite these limits, our findings should lead researchers and clinicians to reconsider the role of AB in SAUD and the conditions in which AB modification programmes should be conducted. Some patients with high craving and/or low abstinence motivation might present genuine AB and could thus benefit from attentional training [6]. Indeed, as AB is more easily triggered by specific motivational states (i.e. high craving, positive alcohol evaluation), interventions could have stronger effects by administering attentional training when patients are currently in this state, or by using other interventions directly modifying this state (e.g. mindfulness or visual cognitive interference [51]). However, most recently-detoxified patients already avoid alcohol-related cues, raising doubts on the usefulness of generalized attention training in this population. Importantly, the increasing accessibility of reliable AB measures by using low-cost eye-tracker or newly developed AB paradigms [52] helps clinicians to identify patients who will benefit most from attention training. Finally, the strong relationship between AB and craving observed here and previously [53] highlights the need to identify and target psychological factors triggering craving in SAUD to break the vicious circle between craving, AB and alcohol-seeking behaviour, traditionally described as the three pathways to relapse [54].

CONCLUSION

We used eye-tracking measures to clarify three major theoretical questions on AB in SAUD, namely whether AB is stable, independent of the reflective/control system and early/automatic. We showed that AB is not stable in detoxified patients with SAUD, but is rather determined by the presence of craving, patients with/without craving presenting opposite AB patterns. The absence of craving is associated with a strong avoidance AB for alcohol-related cues, thus questioning most theoretical frameworks proposing that AB constitutes a central and long-lasting SAUD feature [4]. We thus argue, in line with alternative theoretical proposals, that AB rather expresses momentary changes in appetitive/aversive evaluation of alcohol-related cues [9]. We also offer preliminary data to suggest that AB might not be influenced by increased cognitive load (and might thus be quite independent from the activity of the reflective/control system) and is mainly related to later and more controlled stages of attentional processing, thus not being related to early/automatic attentional capture.

AUTHOR CONTRIBUTIONS

Zoé Bollen: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); project administration (lead); software (lead); visualization (equal); writing—original draft (lead). **Arthur Pabst:** Formal analysis (supporting); visualization (equal); writing—review and editing (equal). **Nicolas Masson:** Conceptualization (supporting); methodology (supporting); writing—review and editing (equal). **Reinout W. Wiers:** Methodology (supporting); visualization (supporting); writing—review and editing (equal). **Matt Field:** Methodology (supporting); visualization (supporting); writing—review and editing (equal). **Pierre Maurage:** Conceptualization (supporting); methodology (supporting); project administration (supporting); supervision (lead); writing—original draft (supporting); writing—review and editing (equal).

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DECLARATION OF INTERESTS

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 STATEMENT

Data will be made available upon request to the authors.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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