

# Acute Effects of Alcohol on Intrusive Memory Development and Viewpoint Dependence in Spatial Memory Support a Dual Representation Model

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**Background:** A dual representation model of intrusive memory proposes that personally experienced events give rise to two types of representation: an image-based, egocentric representation based on sensory-perceptual features; and a more abstract, allocentric representation that incorporates spatiotemporal context. The model proposes that intrusions reflect involuntary reactivation of egocentric representations in the absence of a corresponding allocentric representation. We tested the model by investigating the effect of alcohol on intrusive memories and, concurrently, on egocentric and allocentric spatial memory.

**Methods:** With a double-blind independent group design participants were administered alcohol (.4 or .8 g/kg) or placebo. A virtual environment was used to present objects and test recognition memory from the same viewpoint as presentation (tapping egocentric memory) or a shifted viewpoint (tapping allocentric memory). Participants were also exposed to a trauma video and required to detail intrusive memories for 7 days, after which explicit memory was assessed.

**Results:** There was a selective impairment of shifted-view recognition after the low dose of alcohol, whereas the high dose induced a global impairment in same-view and shifted-view conditions. Alcohol showed a dose-dependent inverted "U"-shaped effect on intrusions, with only the low dose increasing the number of intrusions, replicating previous work. When same-view recognition was intact, decrements in shifted-view recognition were associated with increases in intrusions.

**Conclusions:** The differential effect of alcohol on intrusive memories and on same/shifted-view recognition support a dual representation model in which intrusions might reflect an imbalance between two types of memory representation. These findings highlight important clinical implications, given alcohol's involvement in real-life trauma.

**Key Words:** Alcohol, allocentric, hippocampus, intrusions, post-traumatic stress disorder (PTSD)

A primary symptom of posttraumatic stress disorder (PTSD) is the presence of highly distressing intrusive memories, consisting of vivid sensory recollections of the original event (1–3). An analogue trauma paradigm, using a distressing video, provides a prospective way to investigate factors affecting the development of intrusive images within a laboratory environment (4). Such prospective studies are important, because they provide a controlled setting where specific cognitive processes can be directly measured and manipulated. Previously, we showed that alcohol intoxication while viewing a trauma video resulted in a dose-dependent inverted "U"-shaped curve of intrusive images (5). A lower dose of alcohol (.4 g/kg) increased the number of intrusions reported in the week after exposure, whereas a higher dose (.8 g/kg) induced no increase compared with placebo. The use of alcohol with its differential effect on intrusions therefore provides a pharmacological tool to directly dissociate memory processes that might function in intrusive memory development. Furthermore, because many real-life traumas such as being a victim of aggressive behaviors or road traffic accidents often involve alcohol intoxication, it is clinically important to delineate these effects. In the present study we

investigated whether the dose-dependent effect of alcohol on intrusive memories could be explained in terms of different brain systems for encoding viewpoint-dependent and viewpoint-independent representations of an event and their relationship with the encoding of traumatic material.

It has been suggested that the intrusion of trauma memories occurs due to strong perceptual priming during the original event (3), but the dose-dependent effect of alcohol on intrusions (5) is difficult to conceptualize within this account. Although alcohol induces a robust impairment in episodic memory with specific decreases in recollection (6–8), perceptual priming is left intact (9). An alternative theoretical account is offered by dual representation theory (10,11) and its recent revision in light of a model of the neuronal mechanisms of healthy memory (12–14).

Healthy memory of an event comprises two closely linked representations in this account (12,13,15). One is an image-based egocentric representation of the event, reliant on the perceiver's viewpoint, supported by early sensory areas, and modulated by representations of its affective characteristics in the insula and amygdala. The other type of representation is allocentric and independent of viewpoint, providing a spatiotemporal context that is both flexible and explicitly accessible, supported by the hippocampus and medial temporal lobe (16–18). When working normally, the two types of representation of an event are closely linked via visuospatial working memory representations in medial parietal cortex. Retrieval of egocentric representations, consisting of sensory/perceptual imagery, is controlled via its corresponding allocentric representation and is subject to conscious manipulation and top-down control from prefrontal areas (13,14).

A number of functional magnetic resonance imaging studies have reported both diminished hippocampal activation and reduced hippocampal volume in PTSD patients, along with a

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range of related memory disruptions (19–22). More specifically, Gilbertson *et al.* (23) found allocentric memory impairments in twins discordant for combat-related PTSD, suggesting underlying reductions in hippocampal function. Prolonged stress is proposed to downregulate hippocampal function (24) through associated glucocorticoid release (25–27). Such stress-induced changes have been proposed to differentially affect different components of memory, particularly reducing spatiotemporal context of an event (28,29).

Hippocampal-dependent memory might also be specifically susceptible to the effects of alcohol, given that alcohol is known to impair episodic memory (6,7) and reduce hippocampal function (8). In animal models, alcohol specifically impairs hippocampal-dependent spatial memory, whereas nonspatial reference memory is preserved (30). Thus, if alcohol selectively impairs hippocampal-dependent allocentric memory, subsequent intrusive imagery should increase, provided that egocentric memory is relatively unimpaired. However, if a more global impairment of encoding occurs, consistent with effects of higher doses of alcohol on the functional magnetic resonance imaging response to simple visual stimulation (approximately .7–.8 g/l) (31,32), there should be no corresponding increase in intrusive imagery.

Under the aforementioned model of healthy memory, downregulation or damage to the hippocampal system should be revealed as a specific impairment in memory tasks requiring an allocentric representation of space compared with tasks solvable with egocentric representations (15). King *et al.* (33) designed a task to probe allocentric memory and tested a patient (34) with focal bilateral hippocampal damage. In this paradigm, participants are given a viewpoint from the rooftops of a virtual courtyard in which objects, sequentially presented in different locations within the courtyard, must be encoded. Between presentation and test, the participant's viewpoint might be changed to a different location overlooking the courtyard. Although object location recognition from the same-viewpoint can be solved with egocentric or allocentric memory, shifted-view recognition relies solely on allocentric memory. King *et al.* (33,35) found that hippocampal damage led to a selective impairment of shifted-view object location recognition, whereas same-view object location memory was intact.

In this study we aimed to replicate our previous finding that alcohol induces a dose-dependent “U”-shaped effect on intrusive memory but a linear decrease in deliberate recall and recognition, suggesting that intrusions and explicit memory are processed in different ways. We also hypothesized that the lower dose of alcohol would be associated with a selective impairment of shifted-view recognition, whereas the higher dose would be associated with impairment in both same- and shifted-view recognition.

## Methods and Materials

### Participants

Forty-eight 18–35-year-old healthy volunteers (24 men) were recruited from the University College London student population. Participants were right-handed and social drinkers (weekly consumption of 2–14 units for women and 2–21 units for men). Participants were screened for a history of mental health treatment (psychologically/pharmacologically), previous experience of trauma, and problematic drinking (36). The study was carried out in accordance with the Declaration of Helsinki and approved by the University College London ethics committee.

### Design

An independent-group double-blind design was used with participants randomly assigned to one of three groups ( $n = 16$ ; eight men): a placebo beverage, a low dose of alcohol, or a high dose of alcohol. Participants were tested on two separate occasions 7 days apart, receiving alcohol on the first test session.

### Alcohol Administration

Participants were administered either alcohol (.4 or .8 g/kg) or matched placebo. The alcohol beverage consisted of 90% vol/wt diluted with tonic water (Schweppes, Uxbridge, United Kingdom) and was divided equally into  $10 \times 50$  mL portions. Each beverage was mixed with two drops of Tabasco sauce (McIlhenny, Avery Island, Louisiana) to mask the taste. The placebo beverage consisted of  $10 \times 50$  mL portions of tonic water and Tabasco sauce. Beverages were consumed at 3-min intervals.

### Procedure

Participants were screened before testing. On the first day of testing, participants filled out the alcohol usage questionnaire and a baseline mood visual analogue scale (VAS) and were instructed on the use of the online diary to record intrusive memories. They then consumed the drinks over the 30 min followed by 10 min to allow alcohol to be absorbed. The post-drink VAS was next completed, and individuals performed the viewpoint-dependent memory task. Finally, the trauma video was shown to individuals, followed by a post-film VAS. Participants returned a week later and received a surprise memory test for the trauma video. All participants were debriefed and paid.

### Assessments

**Alcohol Usage.** The alcohol usage questionnaire (37) is a 12-item questionnaire designed to provide a measure of habitual alcohol consumption. The items cover drinking-related behaviors of wine, spirits, and beer as well as assessing the speed of consumption. The final three items provide a separate measure of binge drinking (38).

**Viewpoint-Dependent Memory.** Viewpoint-dependent memory was assessed through the use of a virtual environment (VE) observed on a desktop computer, consisting of a courtyard surrounded by visually distinct buildings (33). Participants were able to navigate along two of the VE perimeter walls at rooftop level. Within the courtyard, 21 placeholders were randomly distributed and used for the presentation of test stimuli. Presentation and test took place at two locations in opposite corners of the courtyard, involving a rotation of  $140^\circ$  in viewing orientation when moving from one view to the other. Participants were required to navigate toward one of the presentation locations, identified by a marker, and on contact their view was automatically adjusted to a standard view of the courtyard with all placeholders visible.

At presentation, images of everyday objects appeared one at a time over placeholders within the VE for 3 sec each, with a 1-sec interstimulus interval. The number of objects presented in each trial was counterbalanced between three list lengths ( $n = 3$ ,  $n = 6$ , or  $n = 9$ ) to reduce predictability and any strategy that participants might develop. Participants were instructed to remember the specific location of each object. After each trial, memory was tested either from the same viewpoint as presentation or from the shifted-viewpoint. Viewpoint at test was counterbalanced, and presentation order of viewpoint and list length were randomized. Object recognition at test for object locations was tested in a random order with each object presented at the

**Table 1.** Means  $\pm$  SDs for Demographic Data Across the Three Treatment Groups

	Placebo	Low Dose	High Dose
Age, yrs	22.56 $\pm$ 3.56	22.68 $\pm$ 4.61	23.18 $\pm$ 3.66
Number of Yrs in Education	16.06 $\pm$ 1.12	16.50 $\pm$ 1.63	16.37 $\pm$ 1.02
Alcohol Usage	27.43 $\pm$ 16.99	31.77 $\pm$ 24.11	27.44 $\pm$ 21.63
Alcohol Binge	17.28 $\pm$ 10.30	22.40 $\pm$ 17.27	19.85 $\pm$ 19.18

original placeholder and three foils of the same object at other placeholders. Each object image included a colored square superimposed on it and participants were required to press the corresponding colored key on the keyboard to identify their chosen response to an object location. Small-scale pilots (35) showed that performance between conditions can be approximately matched by restricting the foils in the same-view condition to the nearest five locations to the target while spreading them evenly over all other locations in the shifted-view condition.

**Trauma Video.** The trauma video paradigm was administered with the same procedure as our previous study (5). Participants were shown a video consisting of road traffic accidents (39) involving horrific imagery. This video has been used successfully to induce memory intrusions in a number of previous studies (40–42). Participants recorded spontaneous intrusions over the following week via an online diary. Participants were required to record all intrusions consisting of visual imagery and thoughts and report whether they had consumed any alcohol when the intrusions occurred. Because images are the primary symptom of PTSD, self-generated thoughts were omitted from analysis. To check that intrusions were of the viewed footage, descriptions of intrusions were matched to scenes of the video. After Day 7, participants returned to the laboratory and completed a surprise cued recall and recognition test of the footage they had viewed. The cued recall test consisted of four questions for each of the five scenes. The recognition test involved 35 forced choice questions (four choices/question) and was equally divided into 6 questions/scene.

**Subjective Ratings.** A 16-item VAS (43) was used to measure subjective feelings of mood “at the moment” and used as a manipulation check and to observe whether any participants showed adverse effects after beverage consumption. Items are presented with 100-mm lines anchored at the end of each scale with antonyms, providing scores of sedation, discontentedness, and anxiety.

### Statistical Analysis

All statistical analyses were performed with SPSS version 13 (SPSS, Chicago, Illinois). Viewpoint-dependent memory for object locations was analyzed with a mixed factorial analysis of variance (ANOVA), with group as a between-participant factor (placebo vs. low-dose vs. high-dose) and list length (3 vs. 6 vs. 9) and view (same-view vs. shifted-view) as within-participant factors. Results from the trauma film paradigm were analyzed with polynomial trend analyses to examine whether previous findings had been replicated. A quadratic trend analysis tested whether increases in alcohol dose showed an inverted “U”-shaped relationship to the number of intrusions. To rule out possible confounding effects, intrusions that occurred under the influence of alcohol were omitted from analyses. A linear trend analysis tested whether explicit memory for video footage after the 7 days decreased as alcohol dose increased. Subjective

ratings were analyzed with a mixed factorial ANOVA, with group as a between-participant factor and time as a within-participant factor (baseline vs. post-drink vs. post-film). Post hoc comparisons and simple effects were Bonferroni-corrected.

## Results

### Demographic Data

There were no significant differences between groups on age [ $F(2,45) = .11, p = .90$ ], years in education [ $F(2,45) = .49, p = .62$ ], alcohol usage [ $F(2,45) = .23, p = .80$ ], and alcohol binge [ $F(2,45) = .41, p = .67$ ] (Table 1).

### Blood Alcohol Concentration

A  $2 \times 2$  mixed factor analysis showed a significant group  $\times$  time interaction [ $F(1,30) = 4.43, p = .046$ ] and a main effect of group [ $F(1,30) = 30.58, p < .001$ ] but no main effect of time [ $F(1,30) = .06, p = .80$ ]. The high-dose group showed higher blood alcohol concentration levels than the low-dose group after consumption ( $p < .001$ ) and at the end of testing ( $p < .001$ ). The low-dose group showed a tendency of lower blood alcohol concentration levels at the end of testing ( $p = .08$ ) compared with after consumption (Table 2).

### Subjective Measures

Analysis of sedation ratings showed a significant group  $\times$  time interaction [ $F(4,90) = 2.76, p < .04$ ], a main effect of time [ $F(2,90) = 36.80, p < .001$ ], and no main effect of group [ $F(2,45) = 2.64, p = .08$ ]. Post hoc analysis revealed a significant group difference post-drink [ $F(2,45) = 4.24, p = .02$ ], with the low dose group giving higher ratings of sedation than the placebo group ( $p = .02$ ). Analysis of discontentedness ratings showed a significant main effect of time [ $F(2,90) = 15.53, p < .001$ ] and no main effect of group [ $F(2,45) = .34, p = .71$ ] or group  $\times$  time interaction [ $F(4,90) = .34, p = .71$ ]. Post hoc analysis showed that ratings of discontentedness significantly increased from baseline to post-film ( $p < .001$ ) and post-drink to post-film ( $p < .001$ ). Anxiety ratings showed no significant main effect of group [ $F(2,45) = 1.08, p = .35$ ] or time [ $F(2,90) = 2.23, p = .11$ ] and no group  $\times$  time interaction [ $F(4,90) = 1.32, p = .27$ ] (Table 3).

### Effects of Alcohol on Same- Versus Shifted-View Recognition

A mixed factorial ANOVA of the mean percentage of correctly recognized items showed significant interactions of group  $\times$  view [ $F(2,45) = 5.08, p = .01$ ] and list length  $\times$  view [ $F(2,90) = 26.94, p < .001$ ] and main effects of group [ $F(2,45) = 8.07, p < .001$ ], list length [ $F(2,90) = 102.90, p < .001$ ], and view [ $F(2,45) = 106.40, p < .001$ ] (Figure 1). Post hoc analysis showed a greater number of items correctly recognized in the same-view condition compared with the shifted-view condition for the placebo group [ $F(1,15) = 24.08, p < .001$ ], low-dose group [ $F(1,15) = 48.78, p < .001$ ], and high-dose group [ $F(1,15) = 37.90, p < .001$ ]. Analyses

**Table 2.** Means  $\pm$  SDs and Ranges for blood alcohol concentration (BAC) Across the Two Alcohol Groups

	Low Dose		High Dose	
	Mean	Range	Mean	Range
BAC1	.22 $\pm$ .11	.02–.48	.48 $\pm$ .25	.16–.92
BAC2	.16 $\pm$ .07	.05–.28	.55 $\pm$ .25	.18–1.04

BAC measurements (g/l) were taken 40 min after the start of the beverage consumption period (BAC1) and after the trauma video at the end of the session (BAC2).

**Table 3.** Means  $\pm$  SDs for Mood Ratings as a Function of Group Over the Test Session

	Baseline			Post-Drink			Post-Film		
	Placebo	Low Dose	High Dose	Placebo	Low Dose	High Dose	Placebo	Low Dose	High Dose
Sedation	25.36 $\pm$ 15.61	30.09 $\pm$ 11.90	24.22 $\pm$ 14.21	28.22 $\pm$ 16.10	45.10 $\pm$ 17.46	39.11 $\pm$ 16.27	37.07 $\pm$ 17.45	47.47 $\pm$ 19.68	49.39 $\pm$ 12.96
Discontent	30.10 $\pm$ 18.64	26.15 $\pm$ 12.19	21.86 $\pm$ 12.60	25.43 $\pm$ 17.84	24.26 $\pm$ 12.59	23.56 $\pm$ 14.98	32.84 $\pm$ 16.74	38.34 $\pm$ 18.82	32.05 $\pm$ 21.30
Anxiety	29.75 $\pm$ 21.00	27.84 $\pm$ 8.57	28.34 $\pm$ 17.70	20.88 $\pm$ 14.90	30.25 $\pm$ 15.65	35.53 $\pm$ 16.75	31.91 $\pm$ 22.14	37.50 $\pm$ 17.43	34.40 $\pm$ 12.40

also showed that the effect of viewpoint on placebo performance was driven by a significant difference between same and shifted-view at list length 3 [ $F(1,15) = 58.31, p < .001$ ], whereas no significant differences were found at list lengths 6 and 9 ( $F$  values  $< .30$ ). Separate analyses of each view showed a significant difference between groups on correctly recognized items on the same-view condition [ $F(2,45) = 3.77, p = .03$ ] and the shifted-view condition [ $F(2,45) = 10.30, p < .001$ ]. For same-view, the high-dose group had significantly poorer recognition accuracy than the placebo group ( $p = .03$ ), whereas the low-dose group was unimpaired ( $p = 1$ ). The difference between high- and low-dose groups did not reach significance ( $p = .18$ ). For shifted-view, both the low- and high-dose groups recognized significantly fewer items than the placebo group ( $p = .04$  and  $p < .001$ , respectively), and there was no difference between low- and high-dose groups ( $p = .17$ ).

A critical aspect of these results concerns whether there is a differential effect of alcohol level on same- and shifted-view performance. Figure 1 and the aforementioned analyses suggest that low levels of alcohol specifically impair shifted-view performance, whereas high levels impair performance on both same view and shifted view. However, one complicating factor is that overall performance varies between the same view and shifted view. To avoid this concern separate analyses were carried out on the two list lengths for which the placebo group showed a similar performance for same-view and shifted-view conditions (list lengths 6 and 9). The aforementioned group  $\times$  view interaction is still significant [ $F(2,45) = 6.15, p < .01$ ], in addition to the view  $\times$  list interaction [ $F(2,45) = .21, p = .02$ ] and with main effects of view [ $F(1,45) = 33.02, p < .001$ ], list [ $F(1,45) = 9.82, p < .01$ ], and group [ $F(2,45) = 10.45, p < .001$ ]. Further analysis showed a significant difference on same-view recognition between placebo and high-dose groups ( $p = .03$ ) but no difference between placebo and low-dose groups ( $p = 1$ ). The difference between low- and high-dose groups on the same-view performance approached significance ( $p = .08$ ). Shifted-view

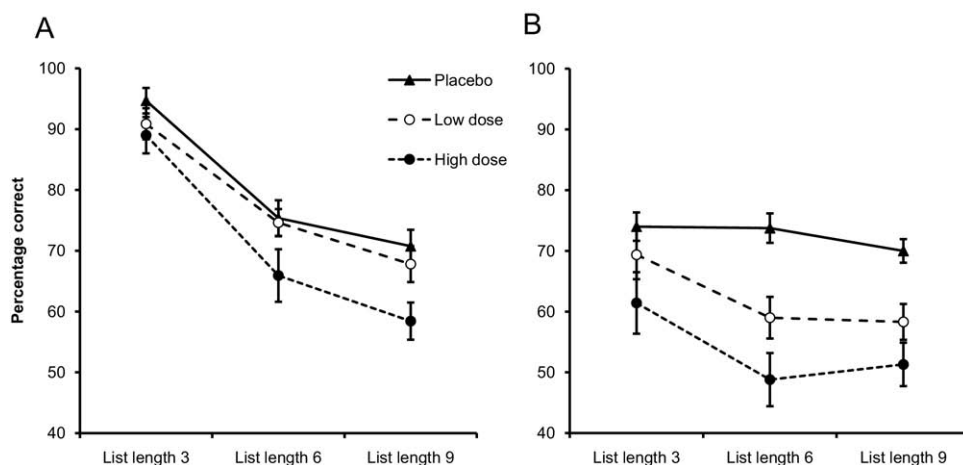
recognition showed significant differences between the placebo and low-dose groups ( $p < .01$ ) and between placebo and high-dose groups ( $p < .001$ ) and no difference between the low- and high-dose groups ( $p = .12$ ).

### Effects of Alcohol on Intrusions

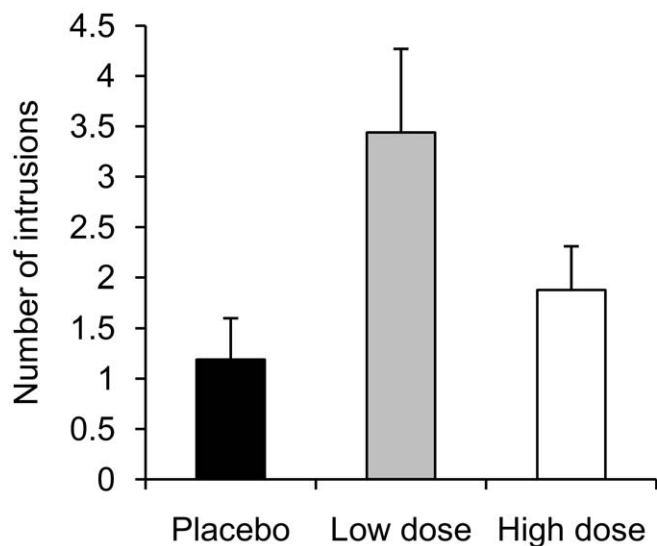
Analysis of intrusive memories showed the predicted dose-dependent inverted “U”-shaped curve on the number of intrusions reported, confirmed by the significant quadratic trend across groups [ $F(1,45) = 6.62, p = .01$ ] with an increase after the low dose of alcohol (Figure 2). Explicit memory for the footage showed the expected decrease in performance as alcohol dose increased (Figure 3), revealed by the significant linear trend across groups on both cued recall [ $F(1,45) = 6.88, p = .01$ ] and recognition [ $F(1,45) = 7.09, p = .01$ ].

### Same- Versus Shifted-View Recognition and Intrusions

A correlation was performed on each group to examine the relationship between same-view and shifted-view recognition and the number of intrusions. Bivariate outliers were determined with the residuals and a Tukey 1.5 hinged spread analysis. The placebo group showed a negative relationship between intrusions and decreases in shifted-view recognition, controlling for same-view performance [ $r(11) = -.66, p = .01$ ]. To further assess contributions of the observed alterations in memory performance and intrusions, and given the small sample size of the previous correlations, group data were analyzed together. Because the intrusion data had a U-shaped distribution, it was only appropriate to test for a linear effect within a subset of the data. The subset of most relevance to understanding normal intrusive memory involved the performance of the no-alcohol and low-dose groups. Due to outliers, three participants were removed, and the analysis was run controlling for same-view scores and group assignment (placebo vs. low dose). A negative relationship between intrusions and decreases in shifted-view recognition was observed [ $r(25) = -.43, p = .03$ ], confirming that the



**Figure 1.** Mean percentage of correctly recognized items as a function of group and list length for (A) same-view and (B) shifted-view conditions. Bars represent SEM.



**Figure 2.** Mean (SEM) number of intrusive memories reported in the 7 days after exposure to the trauma video.

greater the impairment in recognition, the more intrusions were reported by participants. No other significant correlations were found.

## Discussion

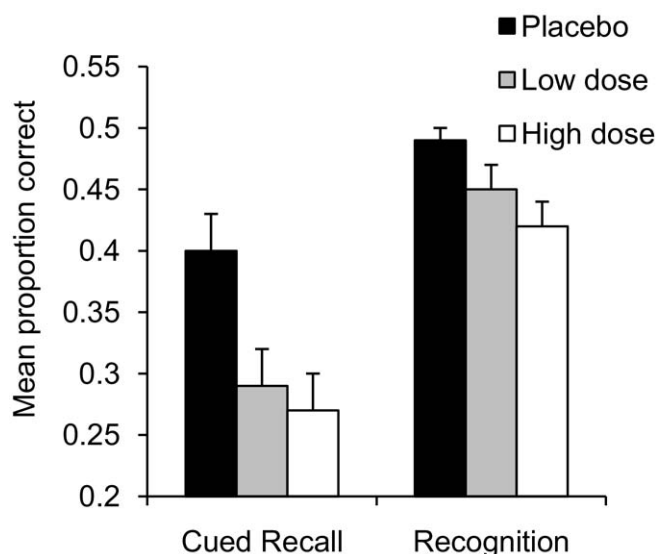
In the present study, we examined the acute effects of alcohol on same-view and shifted-view recognition for object locations to explore the mechanisms underpinning the inverted-U dose-response effect on intrusion memories we found previously. We observed, as predicted by a neurobiologically based dual representation model (14), a selective impairment of shifted-view object location recognition after a low dose of alcohol, whereas same-view recognition was left intact. In contrast and also as predicted, the high dose of alcohol induced a more global effect on object location recognition, with impairments on both same-view and shifted-view conditions. We also replicated our previous findings (5) that intoxication with alcohol during exposure to a trauma video induces a dose-dependent inverted “U”-shaped curve on intrusive memories but a linear decrease in explicit memory performance, supporting a dissociation between intrusive memories and memory measured through typical explicit memory measures. In line with our hypothesis, greater decrements in shifted-view recognition were associated with an increase in intrusions in the placebo and low-dose groups who had preserved same-view recognition.

To our knowledge, this is the first study to assess egocentric versus allocentric memory after acute alcohol intoxication. The two doses of alcohol were successful in attaining the study objectives of dissociating key memory processes. The low-dose and placebo groups did not differ on the same-view condition, suggesting that the egocentric memory system was intact. However, the low-dose group only showed a tendency to differ from the high-dose group on same-view recognition after controlling for task difficulty, raising the question of what would be an optimal dose before same-view recognition becomes impaired after alcohol. The observed reduction in allocentric memory after the low dose is in accordance with previous studies reporting acute deficits in the encoding of spatiotemporal context within episodic memory (6–8).

Accounts of intrusive memories proposing dissociable memory systems posit that successful storage of spatiotemporal context is essential to the suppression of involuntary re-experiencing (11,14,29). Sensory and perceptual features are thought to be encoded to form an egocentric representation that underpins such re-experiencing. In the absence of contextual information encoded within allocentric memory, egocentric image-based representations are free to involuntarily enter consciousness. The increase in intrusive memories after the low dose is consistent with such a model.

The high dose of alcohol impaired performance in both the shifted- and same-view conditions. The decrease in shifted-view recognition was similar to that produced by the low dose, reflecting reduced encoding within allocentric memory. The basis for the decreased accuracy in the same-view condition is not entirely clear. Items in the same-view condition can be solved through allocentric or egocentric memory, and thus the global decrease might reflect impairment of egocentric memory at the high dose. Importantly, alcohol is known to affect multiple cognitive abilities, including attentional functions (44–46) and working memory (47,48). Presumably these impairments become more pronounced as alcohol dosage increases although few studies have specifically addressed acute dose-response curves in cognitive function (49). Thus, the reduction in same-view performance might reflect a direct effect on egocentric memory or an indirect effect on component cognitive processes that contribute to egocentric memory.

The global decrease in both egocentric and allocentric memory at the high dose of alcohol might help to explain why there was no increase in intrusions relative to placebo. The same impairments that decreased same-view performance might have affected encoding of the trauma footage to reduce the number of intrusions. Of particular relevance here is the evidence that concurrent tasks that compete for visuospatial processing are able to decrease intrusions (41,50), highlighting a possible target for the effect of the high dose of alcohol. However, the precise mechanism underlying the effect of the high dose on intrusions is not entirely clear, and a direct effect on egocentric memory



**Figure 3.** Explicit memory for trauma video. Mean (SEM) number of items correct responses for cued recall and recognition for each group 7 days after viewing the trauma video.

and/or an indirect result of disruptions to contributory cognitive processes needs to be ruled out in future studies.

A possible explanation for the effect of alcohol on allocentric memory might be related to neurochemical changes in hippocampal function. An allocentric representation requires the successful encoding of spatial information and is impaired after hippocampal damage (33,35). Alcohol-induced decrements in memory are proposed to occur via alterations in hippocampal neuronal activity (8,30,51) via its actions both as an N-methyl d-aspartate antagonist and as a potentiator of  $\gamma$ -aminobutyric acid (GABA)-mediated inhibition, known mechanisms of blocking long-term potentiation.

Speculatively, one mediator of the decrease in same-view recognition induced by the high dose might involve the effect of alcohol on parietal regions, specifically important in the role of attention and egocentric memory. Alcohol potentiates the action of endogenous GABA through increasing GABA<sub>A</sub> receptor subunit sensitivity (52,53). Drugs that stimulate the release of endogenous GABA, such as clonidine, have been found to show regional specific increases in frontal and parietal cortex (54). It has thus been proposed that alcohol might share a similar action and increase GABA-receptor sensitivity in the parietal cortex, particularly disrupting spatial attentional processing (46). It is possible that increases in alcohol dose differ in their functional specificity, with more global effects at higher doses.

A variety of findings have suggested a role for the hippocampus in the development of intrusive memories (11,28,29). The hippocampus plays an important role in regulating the hypothalamic-pituitary-adrenal axis and is particularly susceptible to prolonged stress (24). Marked increases in cortisol during high levels of stress can impair functioning of the hippocampus (27,55) and thus lead to a decrease in hippocampal-dependent memory. The disruption of the memory processes detailed in the present study could theoretically occur via stress-induced alterations in hippocampal function and highlight a common mechanism in intrusive memory development during a traumatic event. The current findings also further emphasize the way in which alcohol interacts with information processing during real-life trauma. Alcohol-induced neurochemical alterations in memory during trauma could be a risk factor for the later development of PTSD.

One potential limitation of our study concerns the extent to which the trauma video paradigm resembles real life trauma. Although the two situations clearly differ, there are also reasons for optimism. The trauma video did induce small albeit nonsignificant increases in anxiety, although significant increases in discontentedness were observed. The use of a trauma video does fulfill DSM-IV (56) criterion A1, in that participants witnessed death and serious injury, and has been successfully used in a wide range of studies (4). Findings using such methods have been influential in the progression of clinical theory, and detailed assessments of acute dose-response effects are clearly not possible in real-life trauma.

In conclusion, the present findings offer important insights into both the interaction between alcohol and intrusions and the mechanisms underpinning intrusive memory. The dose-response alcohol-induced impairment of same-view and shifted-view recognition and the inverted “U”-shaped curve shown by intrusions support theories that propose a dual representation system underlying intrusive memory phenomena. Given the involvement of alcohol intoxication in real-life trauma such as a road traffic accidents and violence, these findings have important clinical implications.

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1. Brewin CR (2003): *Posttraumatic Stress Disorder: Malady or Myth?* New Haven, Connecticut: Yale University Press.
2. Ehlers A, Clark DM (2000): A cognitive model of posttraumatic stress disorder. *Behav Res Ther* 38:319–345.
3. Ehlers A, Hackmann A, Michael T (2004): Intrusive re-experiencing in post-traumatic stress disorder: Phenomenology, theory, and therapy. *Memory* 12:403–415.
4. Holmes EA, Bourne C (2008): Inducing and modulating intrusive emotional memories: A review of the trauma film paradigm. *Acta Psychol* 127:553–566.
5. Bisby JA, Brewin CR, Leitz JR, Curran HV (2009): Acute effects of alcohol on the development of intrusive memories. *Psychopharmacology* 204: 655–666.
6. Curran HV, Hildebrandt M (1999): Dissociative effects of alcohol on recollective experience. *Conscious Cogn* 8:497–509.
7. Leitz JR, Morgan CJ, Bisby JA, Rendell PG, Curran HV (2009): Global impairment of prospective memory following acute alcohol. *Psychopharmacology* 205:379–387.
8. Soderlund H, Grady CL, Easdon C, Tulving E (2007): Acute effects of alcohol on neural correlates of episodic memory encoding. *NeuroImage* 35:928–939.
9. Hashtroudi S, Parker ES, DeLisi LE, Wyatt RJ, Mutter SA (1984): Intact retention in acute alcohol amnesia. *J Exp Psychol Learn Mem Cogn* 10: 156–163.
10. Brewin CR, Dalgleish T, Joseph S (1996): A dual representation theory of posttraumatic stress disorder. *Psychol Rev* 103:670–686.
11. Brewin CR (2001): A cognitive neuroscience account of posttraumatic stress disorder and its treatment. *Behav Res Ther* 39:373–393.
12. Burgess N, Becker S, King JA, O’Keefe J (2001): Memory for events and their spatial context: Models and experiments. *Philos Trans R Soc Lond B Biol Sci* 356:1493–1503.
13. Byrne P, Becker S, Burgess N (2007): Remembering the past and imagining the future: A neural model of spatial memory and imagery. *Psychol Rev* 114:340–375.
14. Brewin CR, Gregory JD, Lipton M, Burgess N (2010): Intrusive images in psychological disorders: Characteristics, neural mechanisms, and treatment implications. *Psychol Rev* 117:210–232.
15. O’Keefe J, Nadel L (1978): *The Hippocampus as a Cognitive Map*. Oxford: Oxford University Press.
16. Burgess N, Maguire EA, O’Keefe J (2002): The human hippocampus and spatial and episodic memory. *Neuron* 35:625–641.
17. Eichenbaum H, Cohen NJ (2004): *From Conditioning to Conscious Recollection: Memory Systems and the Brain*. New York: Oxford University Press.
18. Squire LR (1992): Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychol Rev* 99:195–231.
19. Bremner JD, Randall P, Scott TM, Bronen RA, Seibyl JP, Southwick SM, *et al.* (1995): MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. *Am J Psychiatry* 152: 973–981.
20. Bremner JD, Randall P, Vermetten E, Staib L, Bronen RA, Mazure C, *et al.* (1997): Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse—a preliminary report. *Biol Psychiatry* 41: 23–32.
21. Gilbertson MW, Shenton ME, Ciszewski A, Kasai K, Lasko NB, Orr SP, Pitman RK (2002): Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. *Nat Neurosci* 5:1242–1247.
22. Shin LM, Shin PS, Heckers S, Krangel TS, Macklin ML, Orr SP, *et al.* (2004): Hippocampal function in posttraumatic stress disorder. *Hippocampus* 14:292–300.
23. Gilbertson MW, Williston SK, Paulus LA, Lasko NB, Gurvits TV, Shenton ME, *et al.* (2007): Configural cue performance in identical twins discordant for posttraumatic stress disorder: Theoretical implications for the role of hippocampal function. *Biol Psychiatry* 62:513–520.

24. Kim JJ, Diamond DM (2002): The stressed hippocampus, synaptic plasticity and lost memories. *Nat Rev Neurosci* 3:453–462.
25. Kirschbaum C, Wolf OT, May M, Wippich W, Hellhammer DH (1996): Stress- and treatment-induced elevations of cortisol levels associated with impaired declarative memory in healthy adults. *Life Sci* 58:1475–1483.
26. de Kloet ER, Oitzl MS, Joels M (1999): Stress and cognition: Are corticosteroids good or bad guys? *Trends Neurosci* 22:422–426.
27. Sapolsky RM (1992): *Stress, the Aging Brain, and the Mechanisms of Neuron Death*. Cambridge, Massachusetts: MIT Press.
28. Elzinga BM, Bremner JD (2002): Are the neural substrates of memory the final common pathway in posttraumatic stress disorder (PTSD)? *J Affect Disord* 70:1–17.
29. Jacobs WJ, Nadel L (1998): Neurobiology of reconstructed memory. *Psychol Public Policy Law* 4:1110–1134.
30. Matthews DB, Silvers JR (2004): The use of acute ethanol administration as a tool to investigate multiple memory systems. *Neurobiol Learn Mem* 82:299–308.
31. Gundersen H, Specht K, Gruner R, Erslund L, Hugdahl K (2008): Separating the effects of alcohol and expectancy on brain activation: An fMRI working memory study. *NeuroImage* 42:1587–1596.
32. Levin JM, Ross MH, Mendelson JH, Kaufman MJ, Lange N, Maas LC, *et al.* (1998): Reduction in BOLD fMRI response to primary visual stimulation following alcohol ingestion. *Psychiatry Res* 82:135–146.
33. King JA, Burgess N, Hartley T, Vargha-Khadem F, O'Keefe J (2002): Human hippocampus and viewpoint dependence in spatial memory. *Hippocampus* 12:811–820.
34. Vargha-Khadem F, Gadian DG, Watkins KE, Connelly A, Van Paesschen W, Mishkin M (1997): Differential effects of early hippocampal pathology on episodic and semantic memory. *Science* 277:376–380.
35. King JA, Trinkler I, Hartley T, Vargha-Khadem F, Burgess N (2004): The hippocampal role in spatial memory and the familiarity—recollection distinction: A case study. *Neuropsychology* 18:405–417.
36. Ewing JA (1984): Detecting alcoholism. The CAGE questionnaire. *JAMA* 252:1905–1907.
37. Mehrabian A, Russell JA (1978): A questionnaire measure of habitual alcohol use. *Psychol Rep* 43:803–806.
38. Townshend JM, Duka T (2001): Patterns of alcohol drinking in a population of young social drinkers: A comparison of questionnaire and diary measures. *Alcohol Alcohol* 37:182–192.
39. Steil RI (1996): *Posttraumatische intrusionen nach verkehrsunfallen [Post-traumatic Intrusions After Road Traffic Accidents]*. Frankfurt, Germany: Peter Lang.
40. Brewin CR, Saunders J (2001): The effect of dissociation at encoding on intrusive memories for a stressful film. *Br J Med Psychol* 74:467–472.
41. Holmes EA, Brewin CR, Hennessey RG (2004): Trauma films, information processing, and intrusive memory development. *J Exp Psychol Gen* 133: 3–22.
42. Murray J, Ehlers A, Mayou RA (2002): Dissociation and post-traumatic stress disorder: Two prospective studies of road traffic accident survivors. *Br J Psychiatry* 180:363–368.
43. Bond A, Lader M (1974): The use of analogue scales in rating subjective feelings. *Br J Med Psychol* 47:211–214.
44. Abroms BD, Gottlob LR, Fillmore MT (2006): Alcohol effects on inhibitory control of attention: Distinguishing between intentional and automatic mechanisms. *Psychopharmacology* 188:324–334.
45. Koelega HS (1995): Alcohol and vigilance performance: A review. *Psychopharmacology* 118:233–249.
46. Schulte T, Muller-Oehring EM, Strasburger H, Warzel H, Sabel BA (2001): Acute effects of alcohol on divided and covert attention in men. *Psychopharmacology* 154:61–69.
47. Grattan-Miscio KE, Vogel-Sprott M (2005): Effects of alcohol and performance incentives on immediate working memory. *Psychopharmacology* 181:188–196.
48. Schweizer TA, Vogel-Sprott M, Danckert J, Roy EA, Skakum A, Broderick CE (2006): Neuropsychological profile of acute alcohol intoxication during ascending and descending blood alcohol concentrations. *Neuropsychopharmacology* 31:1301–1309.
49. Bisby JA, Leitz JR, Morgan CJA, Curran HV (2010): Decreases in recollective experience following acute alcohol: A dose–response study. *Psychopharmacology* 208:67–74.
50. Holmes EA, James EL, Coode-Bate T, Deerprouse C (2009): Can playing the computer game “Tetris” reduce the build-up of flashbacks for trauma? A proposal from cognitive science. *PLoS ONE* 4:e4153.
51. White AM, Matthews DB, Best PJ (2000): Ethanol, memory, and hippocampal function: A review of recent findings. *Hippocampus* 10:88–93.
52. Criswell HE, Simson PE, Duncan GE, McCown TJ, Herbert JS, Morrow AL, Breese GR (1993): Molecular basis for regionally specific action of ethanol on gamma-aminobutyric acidA receptors: Generalization to other ligand-gated ion channels. *J Pharmacol Exp Ther* 267:522–537.
53. Soldo BL, Proctor WR, Dunwiddie TV (1994): Ethanol differentially modulates GABAA receptor-mediated chloride currents in hippocampal, cortical, and septal neurons in rat brain slices. *Synapse* 18:94–103.
54. Pittaluga A, Raiteri M (1988): Clonidine enhances the release of endogenous gamma-aminobutyric acid through alpha-2 and alpha-1 presynaptic adrenoceptors differentially located in rat cerebral cortex subregions. *J Pharmacol Exp Ther* 245:682–686.
55. McEwen BS (1999): Stress and hippocampal plasticity. *Annu Rev Neurosci* 22:105–122.
56. American Psychiatric Association (2000): *Diagnostic and Statistical Manual of Mental Health. Text Revision, 4th ed.* Washington, DC: American Psychiatric Association.