

Acute Effects of Alcohol on Trauma Memories

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Submitted for the degree of Doctor of Philosophy

University College London

December 2010

I, James A. Bisby confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Abstract

Memory disturbances following a trauma are a characteristic feature of posttraumatic stress disorder. Despite alcohol's frequent involvement in real-life traumatic events, our understanding of its contribution to trauma-related symptoms is unclear. The research in this thesis aimed to determine the way in which alcohol intoxication during a traumatic experience might influence memory for the event. Experiment 1 showed that alcohol impaired recognition associated with recollection with greater reductions as dose increased (0, 0.4, 0.6, 0.8g/kg); in contrast, recognition associated with familiarity was preserved. Experiments 2 and 3 utilised an analogue trauma film to examine how low (0.4g/kg) and high (0.8g/kg) doses of alcohol affected intrusive imagery and explicit memory for the footage. Alcohol during encoding resulted in a dose-dependent inverted U-shaped curve on intrusive imagery, with increased intrusions only following a low dose. Explicit memory for the footage was reduced in a dose-dependent linear manner. In addition, experiment 3 concurrently assessed same- and shifted-view object location recognition to determine the mechanisms that might underpin alcohol's effects on trauma memory. Results showed that a low dose of alcohol selectively impaired shifted-view recognition, thought to rely on an allocentric representation. However, same-view recognition was preserved, suggesting a spared egocentric representational system. In contrast, the high dose disrupted both same- and shifted-view recognition, suggesting a global disruption in both memory systems. Experiment 4 examined the effects of alcohol (0.4/kg) on contextual fear acquisition and extinction and both same- and shifted-view recognition. Fear acquisition was unaffected by alcohol, whilst extinction learning was impaired with persistent conditioned responses throughout extinction. Alcohol-induced reductions in extinction learning were highly correlated with decreases in shifted-view recognition, supporting the role of contextual encoding in extinction. The findings of these studies suggest that alcohol dose-dependently influences trauma memories and this could result in a distinct set of trauma-related symptoms.

Acknowledgements

First and foremost I would like to thank my supervisor Professor Val Curran. Her constant support, encouragement and advice have been amazing throughout the whole of this thesis. Without her I would not have been able to achieve everything I have done over the past three years. I will forever be indebted for her guidance, and especially for the day she made the decision to take a chance on an unknown Northerner as a PhD student! Val, you are an inspiration to us all and I feel lucky to have been a research student under your supervision.

I would like to thank my parents for being especially supportive of me throughout this thesis and for never questioning my decisions. A very special thank you to Julie for her constant support over the past three years. This journey represents so much more than just a thesis: without it our life together would have never been known.

I also want to thank all the people who have been an integral part of helping me to get through this PhD; Lorna Stewart, Ravi Das, Tom Freeman, Dr. Celia Morgan, Nathalie Mentzelopoulos, Leslie and Ian Muetzelfeldt and Matt Robinson. You have all made everything much more worthwhile!

I have been lucky enough to work with many great people over the past three years and I would particularly like to thank Professor Chris Brewin, Dr John King, Professor Neil Burgess and Professor Morris Moscovitch for their advice and valuable discussions throughout.

Finally, I would like to say a special thank you to Dr. Sandra Sunram-Lea, not only for her advice and support before I started this thesis but also for her persistence, as without it this journey would have never begun.

The work presented in this thesis has also been published as the following journal articles:

Bisby JA, Brewin CR, Leitz JR & Curran HV (2009). Acute effects of alcohol on intrusive memory development. *Psychopharmacology* 204: 655-666.

Bisby JA, Leitz JR, Morgan CJA & Curran HV (2010). Decreases in recollective experience following acute alcohol; a dose-response study. *Psychopharmacology* 208: 67-74.

Bisby JA, King JA, Brewin CR, Burgess N & Curran HV (2010). Acute effects of alcohol on intrusive memory development and viewpoint dependence in spatial memory support a dual representation model. *Biological Psychiatry* 68: 280-286.

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Chapter 1: Introduction

This chapter is structured into three main sections. The first section presents some of the background information on the development of posttraumatic stress disorder (PTSD) and its associated memory disruptions and symptomatology. I will briefly outline the way in which potential external factors could influence memory and therefore the development of trauma-related symptoms, including alcohol. As one of the main aspects of this research relates to memory processes, the section is brought to a close with the presentation of a model of healthy human memory, which will be referred to throughout this thesis. The second and third sections of this chapter present reviews of the current literature. Firstly, research concerning PTSD and its related memory disruptions is reviewed. Secondly, the literature relating to way in which alcohol has been shown to affect memory is discussed. The chapter concludes by defining the specific research questions.

1.1 Posttraumatic stress disorder

Traumatic events are a regular occurrence in the world in which we live. A trauma can involve many different types of event ranging from a serious assault on a single individual to a natural disaster that is experienced by a nation. The actual likelihood that an individual will at some time in their life experience such an event is extremely high. Epidemiological studies suggest that the lifetime probability rate of a personal traumatic experience can be as high as 95% (Kessler et al., 2005). In the aftermath of a trauma, many individuals do not show any subsequent mental health problems, however, some will go on to develop psychological, trauma-related symptoms. In the majority of people, these symptoms will diminish in the weeks that follow. A small proportion of these individuals may experience persistent symptoms and go on to develop PTSD, a debilitating condition in response to the life-threatening event. Lifetime prevalence of the disorder is estimated to be between 4% and 10% (Fear et al., 2010; Kessler et al., 1995; 2005).

As a condition, PTSD is characterised by a wide range of psychological symptoms. The DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders-IV-*Text*

Revision; American Psychiatric Association, 2000) defines three main symptom clusters of i) re-experiencing, ii) avoidance and numbing, and iii) hyper-arousal. Patients are often plagued with re-experiencing of the original event in the form of vivid and distressing imagery that enters consciousness involuntarily in response to trauma reminders. These persistent re-experiencing episodes and accompanying distress lead the individual to purposefully avoid reminders of the event including people, situations and circumstances resembling or associated with the trauma. Individuals also show a general elevated level of arousal with exaggerated startle response, hyper-vigilance, increased irritability and difficulties in sleeping.

For a diagnosis of PTSD, an individual must meet a number of set criteria defined by the DSM-IV-TR. In brief, the individual must have experienced, or witnessed actual or threatened death or injury, and their response should have involved intense fear, horror or helplessness. The traumatic event must also be persistently re-experienced in some form, such as intrusive recollection, distressing dreams, or intense psychological reactions to internal or external cues that symbolise the event in some way. The individual must show some level of avoidance of trauma-related stimuli, and a numbing of general responsiveness. Persistent symptoms of increased arousal and the duration of the associated symptoms should have been present for over 1 month.

Although the majority of individuals who develop trauma-related symptoms do so shortly after the event, some may not experience any related issues until a long period of time has lapsed. The DSM-IV-TR describes delayed-onset if a period of at least 6 months has passed between the trauma and the onset of symptoms. Despite its inclusion in DSM criteria for PTSD, some authors have expressed scepticism on whether the condition exists (North et al., 2004). In a recent systematic review, Andrews et al. (2007) found that the literature did support the existence of delayed-onset PTSD in the absence of prior symptoms, although it was rare. However, a larger number of delayed-onset reports were explained by exacerbated prior symptoms or the reactivation of diminished symptoms.

Although there is a wide range of symptoms associated with PTSD that can be severely debilitating and long lasting, many clinical theories agree that the central component to the disorder is a disturbance in memory (e.g., Brewin et al., 2010; Ehlers and Clark, 2000). These specific trauma-related disruptions comprise two primary deficits (for reviews, see Brewin and Holmes, 2003; Brewin et al., 2007). Firstly, the ability to voluntarily retrieve the trauma memory is significantly reduced with amnesia for specific details of the event rendering memories typically disorganised and fragmentary (Harvey & Bryant, 2001; Conway & Pleydell-Pearce, 2000). Secondly, individuals show enhanced involuntary retrieval of the trauma memory in the form of intrusive imagery. These images are accompanied by intense revisualizations of a traumatic scene containing prominent sensory information and are experienced as a reliving or ‘flashback’ of the incident. For example, Ehlers and Clark (2000) describe a patient who continually experienced the face of a driver as they had seen it seconds before a car crash. These experiences are triggered involuntarily through specific reminders that in some way relate to the trauma, such as a sound or smell, which was present during the original event.

Following the development of PTSD the associated symptoms can persist for many years. Treatment methods typically consist of psychological and/or pharmacological methods although their efficacy is often limited. Treatment guidelines and empirical evidence suggest that trauma focussed psychotherapy should be considered a first line treatment (Forbes et al., 2010; NICE; 2005). A number of meta-analyses have been carried out to examine treatment efficacy in PTSD, highlighting moderate effect sizes following psychotherapy in the form of cognitive behavioural therapy (CBT), eye movement desensitisation reprocessing (EMDR) and dynamic therapy (Bradley et al., 2005; Seidler and Wagner, 2006; Sherman, 1998). A range of pharmacological treatments currently exists for PTSD patients. The most common pharmacological agents offered to PTSD patients are selective serotonin reuptake inhibitors (SSRI). In a randomised, double-blind trial, Tucker et al. (2003) did not find any differences between citalopram, sertraline, and placebo on PTSD symptoms, although all groups showed general improvements over the 10 week period. However, typical response rates to pharmacotherapy range from 53-60% and 32-38% for active medication and placebo, respectively (Rothbaum et al., 2006).

Therefore, the search for active agents that can generate high response rates in PTSD continues (for a review, see Ravindran and Stein, 2009).

1.2 Influencing Trauma Memory

Understanding the way in which memory for a traumatic event can be altered and the specific factors that can lead to these changes is a key question. There are many external and internal factors that could potentially influence the processing and psychological outcome, both during and in the aftermath, of a traumatic event. These can include a wide range of pre-existing individual differences, changes that occur during the actual event, and the processes involved in the aftermath of the experience. In a recent meta-analysis, Brewin et al. (2000) identified a number of risk factors that can increase an individual's vulnerability to the development of PTSD. In some populations, specific factors such as gender, age, education, race and the experience of previous trauma were found to be influential. In addition, the most uniform predictive factors were observed in an individual's psychiatric history and psychiatric family history. These findings were further supported by Ozer et al. (2003) whom, through a meta-analysis, found that previous experience of trauma, family history of psychopathology, prior psychological adjustment and the level of threat experienced during the trauma were all predictive of the development of PTSD. However, they found that the strongest predictors were based on peritraumatic psychological processes, suggesting that the distinct changes that occur *during* the event are more predictive than any prior individual characteristic.

Peritraumatic processes involve the specific processes that occur during the experience of the actual traumatic event. It is of particular interest that peritraumatic processes have such a high impact on the psychological outcome following trauma suggesting that a range of independent factors could potentially impinge on these processes. For example, changes in information processing (Brewin, 2001; Ehlers and Clark, 2000), changes in subjective emotional state (Davis and Clark, 1998) as well as pre-existing individual differences (e.g., Lapsa and Alden, 2008; see below for a comprehensive review of these processes and related findings). One factor that could play a fundamental role in the processing of a traumatic event is the use of

licit and/or illicit substances consumed by an individual prior to the event occurring. It is well established that the many substances can have disruptive effects on memory (Curran and Weingartner, 2002; Morgan and Curran, 2006; Ranganathan and D'Souza, 2006; White, 2003). During the experience of trauma, changes in brain neurochemistry through substance use could alter the way in which an individual experiences and stores the event into memory.

Alcohol is one of the most popular recreational drugs used in the western world. It has been shown to induce a wide range of effects on cognitive function in humans (e.g., Abrams et al., 2006; Curran and Hildebrandt, 1999; Fillmore et al., 2005; Rose and Duka, 2008; Scaife and Duka, 2009). In relation to trauma and PTSD, alcohol is often implicated. For instance, there is high co-morbidity between PTSD rates and alcohol abuse (approximately 36-52%; Breslau and Davis, 1992; Kessler et al., 1995). To explain such rates of co-morbidity, two common pathways have been identified (Jacobsen et al., 2001). In one pathway, alcohol abuse precedes the development of PTSD with abusers repeatedly placing themselves in dangerous situations and, as a result, more likely to experience physical and psychological trauma (e.g., Cottler et al., 1992). In the second pathway, PTSD precedes the development of a substance use disorder with alcohol used to self-medicate against trauma-related symptoms. A self-medication hypothesis of alcohol use in PTSD patients is strongly supported in the literature (e.g., Epstein et al., 1998; Leeies et al., 2010). Patients often use alcohol as a way to reduce ongoing symptoms including anxiety (Bremner et al., 1996) and are more likely to use alcohol in response to negative emotions (Waldrop et al., 2007). Furthermore, cues resembling the traumatic experience can trigger alcohol craving in PTSD patients (Coffey et al., 2002). However, the consequences of self-medication of alcohol use or abuse on PTSD remain unclear.

In addition to the relationship between PTSD and alcohol use post-trauma, it is also of particular interest to understand the way in which alcohol consumed prior to the event could affect subsequent symptoms. Alcohol is frequently associated with the occurrence of real-life traumatic events, including rape, serious physical assault, and road traffic accidents (Abbey et al., 2004; Roy-Byrne et al., 2004). Limited research

has been conducted to investigate the way in which acute alcohol intoxication could interact with processes during a traumatic experience. However, of these few studies there have been inconsistent results. Maes et al. (2001) examined PTSD rates and symptoms in a large group of survivors from a boat accident. They found that those who had consumed alcohol at the time of the event showed lower PTSD rates. In another studies, assessment of rape victims revealed no difference in PTSD rates between individuals who had consumed alcohol and those who were sober at the time (Littleton and Henderson, 2009). However, these studies were heavily reliant on retrospective reports with some individuals asked to report on event related information over 6 months in the past. We therefore have little, if any, understanding of the way in which acute alcohol intoxication at the time of a trauma may affect an individual's subsequent psychological wellbeing.

1.3 A Model of Healthy Human memory

Given the primary focus on the way in which memory is disrupted during the development and persistence of PTSD, it is first important to set out a framework of healthy human memory. The specific terminology and role of these memory components will be referred to throughout this thesis. It is well established that memory is not a unitary concept but involves multiple interacting systems (e.g., Cohen and Squire, 1980; Squire and Zola-Morgan, 1991; Schacter and Tulving, 1994; Tulving, 1985). Over the past decades, a large body of evidence from cognitive, neuropsychological and cognitive neuroscience research has provided evidence for a multiple memory systems view (e.g., Graf et al., 1984; Maguire et al., 2010; Scoville and Milner, 1957; Yonelinas et al., 2002; Warrington and Weiskrantz, 1982). Although many agree on the existence of multiple memory systems, the specific details captured by each component are intensely debated (e.g., Burgess et al., 2001; Byrne et al., 2007; O'Keefe and Nadel, 1978; Nadel and Moscovitch, 1997; Squire and Zola-Morgan, 1991; Schacter et al., 2008; Tulving, 1985; 2002; Tulving and Schacter 1990). Furthermore, the specific terminology used by different theorists often clouds the debate. Figure 1.1 illustrates a contemporary taxonomy of human memory comprising declarative/non-declarative memory and working memory systems, each with a range of dissociable

components (see Baddeley, 2003; Squire and Zola-Morgan, 1991; Schacter and Tulving, 1994). This section will now describe each of these components and the particular neural mechanism(s) thought to play a role in their functioning. For clarity throughout this thesis, the specific terminology outlined in Figure 1.1 will be used or, where this is not possible, new specific terminology that is introduced will be defined by where it would be expected to fit within the illustrated model.

The long-term memory system defined within the model comprises two principle subsystems, declarative/explicit memory and non-declarative/implicit memory. Declarative or explicit memory forms the basis of an individual’s conscious memory for events that have occurred, so called as the individual is able to freely ‘declare’ the information at will (Cohen and Squire, 1980). In contrast, non-declarative or implicit memory involves a collection of non-conscious learning and memory abilities that are expressed through performance and in the absence of explicit knowledge (Schacter and Tulving, 1994; Squire and Zola-Morgan, 1991).

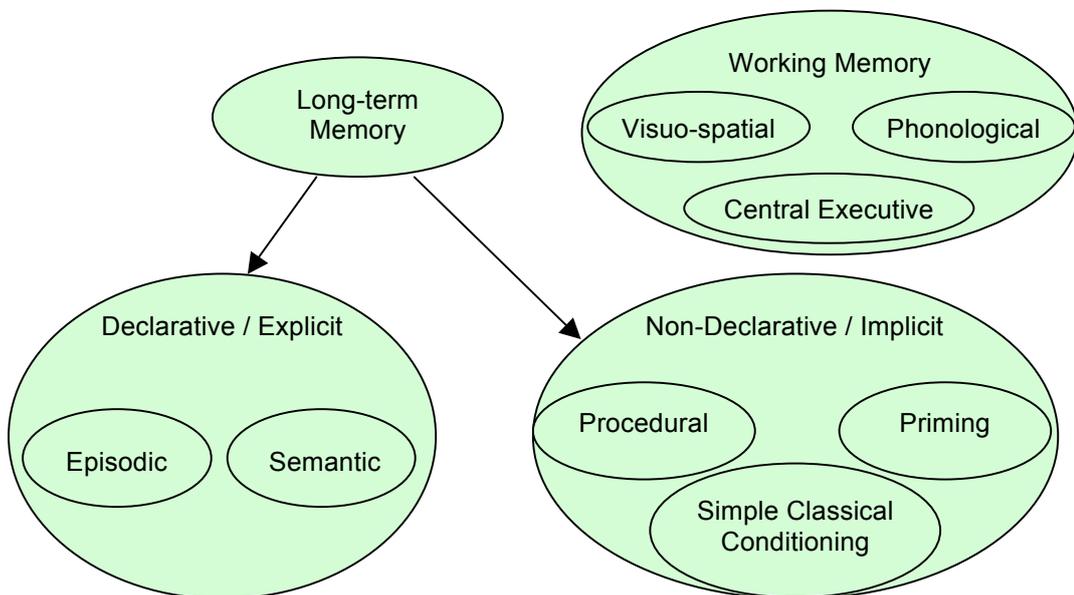


Figure 1.1. A taxonomy of human memory. The illustration shows the different components thought to be principally attributed to each subsystem.

Declarative memory can be divided into two components of episodic memory and semantic memory. Episodic memory involves memory for personally experienced events that can be re-experienced in the context of which the memory originally occurred (Tulving, 1983; 1985). This form of memory is proposed to provide a clear spatio-temporal context during encoding that enhances retrieval of the memory at a later time. The encoding of episodic memory relies on activity in the hippocampus and surrounding medial temporal lobe, and in the prefrontal cortex (PFC). Retrieval of episodic memory is supported by the hippocampus, PFC, precuneus and thalamus (Squire and Zola-Morgan, 1991; Tulving, 2001; Wagner et al., 2005). Semantic memory involves our long established memory about objects, facts and general knowledge about the world (Eichenbaum and Cohen, 2001; Squire, 1992; Tulving, 1983). The anatomical locus of semantic knowledge is difficult to relate to a single brain region (e.g., Thompson-Schill, 2003). However, it has been proposed that the encoding of semantic knowledge relies on the temporal lobe (Squire, 1992), whereas its retrieval is primarily associated with activations in the left PFC and temporal regions (for a review, see Cabeza and Nyberg, 2000).

Non-declarative memory comprises a number of dissociable subsystems. Procedural memory involves habit-based learning where the individual learns a set of associations that are not necessarily obvious or explicitly definable. Over a repeated set of learning phases, an individual's performance improves, typically assessed through enhanced speed or accuracy on a task. Performance on such tasks is thought to rely on integrity of the basal ganglia (Packard et al., 1989; Squire and Zola-Morgan, 1996). Another form of non-declarative memory is classical conditioning. Tasks investigating classical conditioning often utilise a fear conditioning paradigm where the repeated presentation of stimuli is paired with an aversive outcome. Over time, the individual acquires an association between the conditioned stimulus and unconditioned stimulus and generates a conditioned response. The neural system primarily associated with performance on these tasks involves activity in the amygdala (Ledoux, 2000). However, despite its categorisation within a non-declarative memory system, some have argued that more explicit memory processes play a functional role in conditioning (Lovibond and Shanks, 2002; Hogarth and Duka, 2006). Perceptual priming involves the enhanced performance or

identification of previously object/items without explicit knowledge of the item (Schacter and Tulving, 1994). Word stem completion tasks are often utilised to assess perceptual priming where an individual must complete a stem with the first word that comes to mind. Priming is thought to rely on activity in the neocortex and is associated with increased activation in extrastriate visual regions (for a review, see Schacter, 1999).

A working memory system is also illustrated in the model, referring to the maintenance and manipulation of information in short-term memory. Working memory comprises the central executive, supported by two storage systems. The central executive provides a time-limited attentional capacity. This is supported by two extra storage systems: the phonological loop, which is based on sound and language, and the visual-spatial sketchpad (for a review, see Baddeley, 2003). Working memory is often associated with activation in the prefrontal cortex, anterior cingulate, parietal and occipital regions (D'Esposito, 2000).

1.4 Trauma memory

As described in section 1.1, memory disturbances following a traumatic event typically involve decrements in *voluntary* recall of the event and the enhancement of *involuntary* memories in the form of trauma-related imagery. These involuntary, distressing memories are considered a primary symptom of individuals diagnosed with PTSD (DSM-IV; APA, 2000). A defining characteristic of intrusions is their associated sensory qualities including visual, olfactory, gustatory, touch and movement related experiences (Horowitz, 1970). In response to trauma-related cues, intrusive memories can spontaneously enter consciousness, lacking any top down control and being experienced in the present.

Given these defining attributes, it is not surprising that research concerning trauma memory has a long history (e.g., Janet, 1904). Early work was pioneered by Horowitz (1976; 1986) who proposed that PTSD occurred due to an inability to assimilate the traumatic experience with prior knowledge and beliefs. Providing a psychodynamic interpretation, Horowitz suggested that because the new trauma

information could not be reconciled with old information, trauma memories would thus break into consciousness in the form of intrusions and nightmares. The trauma therefore promotes two opposing mechanisms. One involves the suppression of unwanted thoughts and memories relating to the trauma, whereas the other attempts to bring the traumatic material in to mind to be integrated with previous knowledge. Early theories of PTSD have been particularly influential in the proposal of more recent accounts of the way in which memory is affected following extreme stress.

A number of further accounts have provided theoretical based assumptions of trauma memory, including conditioning and information processing accounts. Keane et al. (1985) proposed that the intense reaction to the traumatic event resulted in a form of fear conditioning with trauma related stimuli becoming associated with the intense fear experienced at the time of the event. Although these responses could normally be extinguished through repeated exposure to trauma-related stimuli, the avoidance of such stimuli by individuals would lead to the inability to integrate the memory successfully. The persistent avoidance strategies in individuals associated with the suppression of symptoms would reinforce the ongoing PTSD and contribute to its maintenance. Although theories of fear conditioning can successfully explain many of the psychophysiological features observed in PTSD (e.g., Milad et al., 2009; Orr et al., 2000; Pitman et al., 1999), they cannot provide a complete account of the visual imagery often re-experienced by individuals, and the reduction in declarative memory.

Recent theories have significantly progressed in their accounts of the way in which neurobiological and cognitive mechanisms may play a functional role in the development of trauma-related symptoms and PTSD. This section will now review the literature on trauma memory and PTSD. I will first discuss some of the current clinical theories of trauma memory with particular emphasis on the way in which intrusive memories develop following a trauma. I will then review the empirical research from both clinical and non-clinical populations and what they show in reaction to trauma memory and PTSD. Finally, I will discuss the neurobiological mechanisms that have been proposed to play a fundamental role in processing

stressful situations and the way in which these mechanisms may be implicated in PTSD.

1.4.1 Emotional processing theory

Foa et al. (1989) initially proposed a fear network theory suggesting that trauma memories are disrupted by the extreme distress experienced during encoding, forming a network of strong negative associations between distinct nodes. This network forms a memory representation of the traumatic event and each node incorporates independent attributes such as the traumatic event, fear, and the behavioural and physiological response experienced by the individual. They argued that future cues, similar to ones during the event, are able to activate the fear network in memory causing arousal with information from the network breaking into consciousness in the form of flashbacks.

Elaborating on the early fear network theory, Foa and colleagues (Foa and Riggs, 1993; Foa and Rothbaum, 1998) proposed an emotional processing account of PTSD. In an attempt to incorporate the growing knowledge about PTSD, they identified pre-existing vulnerabilities as a risk factor. That is, individuals with more rigid views prior to the trauma will be more susceptible to developing PTSD because the extreme nature of the event would disrupt the individual's ability to successfully integrate the information into memory. Individuals with more rigid positive views would see the trauma as a contradiction of their beliefs, whereas negative views would be confirmed. Negative appraisals of behaviours and responses formed during and after the event could increase perceptions of incompetence. Negative appraisals may interact with prior beliefs, reinforcing negative schemas involving danger and impotence, which they suggest underlies PTSD.

1.4.2 A cognitive model of trauma memory

Ehlers and Clark (2000) proposed a cognitive model of PTSD (see Figure 1.2), suggesting that persistent PTSD occurs when individuals process the trauma as a

continuing current threat, whether it is an external threat of injury or an internal threat to the self. Two primary mechanisms underlie this cognitive model: 1) the negative appraisals of the trauma and 2) the integration of the trauma into memory.

Ehlers and Clark identified several types of appraisal that might contribute to a sense of current threat. For example, individuals may over generalise from the event and as a consequence start to perceive normal activities as highly dangerous. Further, the way in which an individual behaved during the event may affect their long-term psychological wellbeing, interpreting their behaviour as a causal factor in the event. Other appraisals include those of one’s initial PTSD development, interpreting their own and other people’s reactions following the event that might therefore exacerbate symptoms. The persistence of negative appraisals for the event and its sequelae then maintain PTSD by directly generating negative emotions and negative coping strategies.

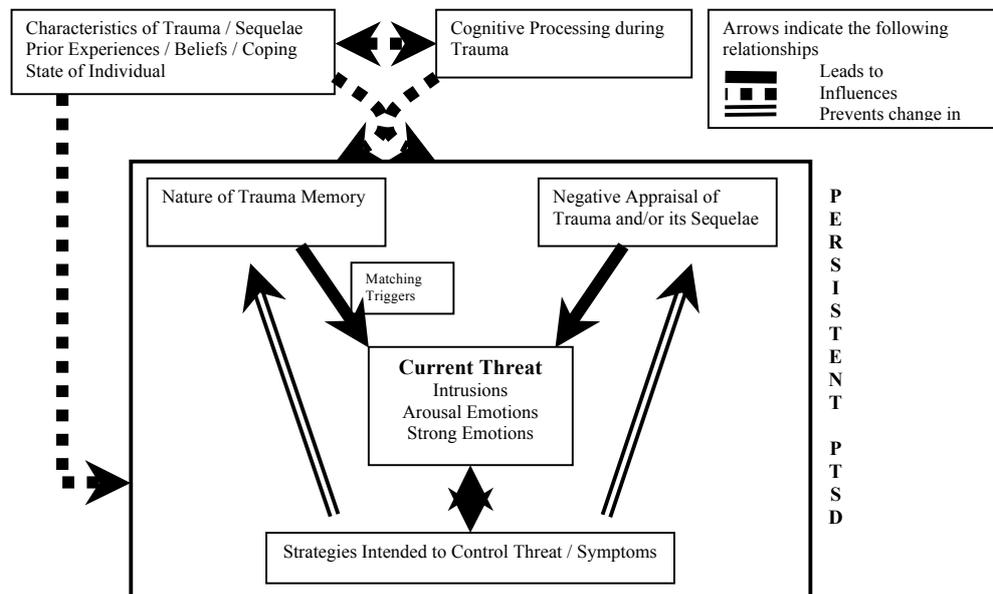


Figure 1.2. The specific components and their interactions proposed by Ehlers and Clark (2000) in their cognitive model of PTSD.

Ehlers and Clark also proposed that the specific thought processes that occur during the trauma would subsequently influence appraisals; through a process they termed ‘mental defeat’. They suggest that through mental defeat an individual experiences the loss of all psychological autonomy and the sense of not being human any more. Through this process, victims are therefore more likely to see the trauma as support for a negative view of oneself in a way that promotes thoughts that the individual may be permanently damaged by the trauma.

Another primary component in the development of PTSD involves the nature of the trauma memory. Ehlers and Clark suggest that during a traumatic event, the memory is poorly elaborated and thus poorly integrated within its spatial-temporal context alongside previous autobiographical memories. The trauma also results in strong Stimulus – Stimulus (S-S) and Stimulus – Response (S-R) associations for the traumatic material causing the memory and/or emotional response more likely to be triggered via matching cues. Finally, the trauma leads to strong perceptual priming of trauma-related stimuli with the consequence that discrete stimuli are more likely to be noticed in the future and therefore will trigger intrusions. Overall, emphasis is placed on the distinction between conceptual versus data-driven processing. Conceptual processing refers to the processing of meaning from a situation, storing the information in an organised way and providing a spatio-temporal context within declarative memory. Data-driven processing refers to processing of the sensory and perceptual characteristics of an event without integration of any conceptual meaning (see Roediger, 1990), strongly associated with perceptual priming within a non-declarative memory system. Ehlers and Clark (2000) propose that the level of conceptual processing during a traumatic event is central to both the nature of the memory and the individual’s ability to purposely retrieve information. If the individual engages less in conceptual processing and more data-driven processing then the trauma will be difficult to retrieve and the memories will be accompanied by strong perceptual priming for stimuli present at the time.

In light of the above memory deficits observed in individuals diagnosed with PTSD, Ehlers and Clark (2000) propose that, to reduce related symptoms, the trauma memory needs to be integrated into its correct context. Through the use of cognitive

behavioural interventions (e.g. Foa and Rothbaum, 1998), the memory can be elaborated on and contextualised within a safe environment, reducing the associated distress and providing an updated coherent memory that can be communicated. In integrating the trauma within autobiographical memory, the event can be established as a memory in the past and not one that generates ongoing fear and distress to related cues experienced in the future. In addition, Conway and Pleydell-Pearce (2000) suggest that through integration of the trauma memory into autobiographical memory, the emotional aspects of the trauma become associated with verbal labels that are stored in memory. During recall of the trauma memory, these verbal labels are retrieved to communicate the trauma and, consequently, no or little affect occurs.

1.4.3 Dual representation theory

The dual representation account of intrusive memory development (Brewin, 2001; Brewin et al., 2010) is based on the proposal that memory for an event is processed via two closely linked interacting memory systems, each forming a distinct representation of an event (Burgess et al., 2001; Byrne et al., 2007; O’Keefe and Nadel, 1978). One type of representation, termed a contextual-representation (C-rep) is abstract and contextually bound and forms the basis of an individual’s deliberate retrieval of experienced events. The other type of representation refers to lower-level sensation-based memory, termed S-reps, and provides an image-based, egocentric representation, which stores the spatial layout of an experience in relation to the perceiver’s own viewpoint.

During the encoding of an event, C-reps provide a spatial layout of the scene that is independent of the perceiver’s viewpoint, storing the information as an allocentric representation, which is supported by hippocampal and parahippocampal regions. This information can be retrieved to construct short-term, image-based egocentric representations to aid immediate behaviour. Encoding of normal episodic memories involves the activation of lower level sensory processes, driven by perception that aids the formation of higher-level representations. Egocentric representations supported by the precuneus and surrounding parietal lobe can thus be translated into

allocentric representation during encoding. The same mechanism also supports the retrieval of information from an allocentric representation to form image-based, egocentric representations during deliberate retrieval of memory. For normal encoding, these S-reps quickly decay and become inaccessible. S-reps also store the sensory processes experienced such as fear or disgust and are associated with activity in the amygdala. Healthy memory for an event therefore comprises an S-rep and its corresponding C-rep. The association between both representations allows the successful integration of information into autobiographical memory and provides increased top down control over its retrieval via connections from the PFC to the medial temporal lobe.

During a traumatic event, intrusive memories arise through the encoding of an S-rep without its corresponding C-rep. The extreme nature of the event enhances the encoding of the S-rep through associated amygdala activity whilst the increase in glucocorticoid release renders the hippocampus inactive and thus unable to successfully store a corresponding C-rep. This therefore results in the inability to integrate the memory within autobiographical memory. During retrieval, cues in the environment matching the traumatic event trigger the S-rep, involving egocentric imagery and the emotional response associated with the event. Due to the impoverished corresponding C-rep, top down control over its retrieval is reduced and thus unable to suppress the intrusive imagery experience.

1.4.4 Peritraumatic dissociation

There is evidence that peritraumatic dissociation may be an important factor in PTSD. Dissociation is defined by DSM-IV-TR as a “disruption of the usually integrated functions of consciousness, identity or perception of the environment” (APA, 2000). In the context of trauma, it can be common for individuals to show dissociative reactions when in a stressful situation, with one study showing that 96% of soldiers undergoing survival training reported such symptoms (Morgan et al., 2001). Dissociative reactions are characterised by a reduced awareness of one’s surroundings, de-realisation, emotional numbing and de-personalisation often resulting in perceptual alterations, impairments in memory or a detachment from

one's environment (Cardena and Spiegel, 1993). Such mental states are thought to arise during a traumatic incident as a way to restrict the adverse emotional consequences of the event by reducing awareness of the experience (Putman, 1989; van der Kolk and van der Hart, 1989). Elzinga and Bremner (2002) suggest that such dissociative reactions impair memory encoding, causing trauma information to be stored inefficiently. As a result, traumatic memories cannot be accessed and their emotional processing is impaired (Marmar et al., 1994). Further, research has shown that increases in dissociation during a traumatic event are predictive of the future development of PTSD (Ehlers et al., 1998; Murray et al., 2002). However, testing this hypothesis is hampered because it is difficult to experimentally induce dissociation in the laboratory (e.g., Holmes et al., 2004).

1.4.5 Studies investigating trauma memories in PTSD patients

Research concerning trauma-related memories in a clinical population most often involves the examination of patients' retrospective reports. These studies have been influential in determining some of the key characteristics that are common to PTSD symptomatology. One common factor that has been identified from such studies is the disorganisation and fragmentary content associated with patients' verbal recall of the traumatic experience. For example, van der Kolk and Fisler (1995) instructed PTSD patients to provide a detailed written narrative of their trauma. They found that patients often reported that, during a period of time after the trauma, they were unable to give a complete narrative of the event. Information provided within the narratives was also found to consist of sensory, dissociative and affective elements. Halligan et al. (2003) examined the narratives of current, past and non-PTSD assault victims. One of the main characteristics to emerge from PTSD patients' narratives was the disorganisation of the memories. Furthermore, they found that the degree of disorganisation was predictive of later PTSD symptoms.

In a recent study, Jones et al. (2007) examined the organisation and content of trauma memories by assessing a large sample of road traffic accident survivors. Individuals' narratives of related trauma memories were assessed 1-week, 3-week, and 3 month post-trauma. Results showed that narratives in individuals later

diagnosed with PTSD were less coherent and more repetitive in comparison to those individuals not later diagnosed with PTSD. Narratives in the PTSD sample were also found to contain more sensory words and temporally non-consecutive chunks. A regression analysis also revealed that global coherence, fragmentation, and repetition components of the trauma memory were highly predictive of later PTSD at 3 months.

In addition to examining the organisation and content of patients' free recall of the traumatic experience, other studies have explored the distinct characteristics of intrusive memories in PTSD. Hellowell and Brewin (2004) examined the possible differences in the content and language of flashbacks compared to voluntary memories of the trauma. Patients were required to give written narratives of their trauma memory and then later reported which parts of the narrative had been written during a 'flashback' and which parts during autobiographical memory retrieval. Examination of the narratives showed that more sensory perceptual words were used to describe moments when a 'flashback' was being experienced. Interestingly, narratives provided during 'flashback' were associated with primary emotions such as fear, horror or helplessness, whereas secondary emotions such as guilt, shame and anger were associated with autobiographical memory recall.

Hackmann et al. (2004) examined the phenomenological aspects of intrusive memories in PTSD patients. They found that intrusive re-experiences only consisted of a small number of instances of memory for the traumatic event. These intrusions were often described as short sensory 'snapshots' of the experience, involving high perceptual content in a range of modalities. However, visual imagery was found to be the most common intrusive re-experience reported, often associated with a sense of 'now-ness'. The majority of patients also reported that intrusive memories represented stimuli during the experience that predicted the onset of events that became more traumatic. For example, a trauma victim may repeatedly re-experience the face of an oncoming driver or the headlights of an oncoming car seconds before a crash. This key focus on stimuli that indicates impending danger has been termed a 'warning signal hypothesis' (Ehlers et al., 2002).

In another study examining the characteristics of intrusive memories, Speckens et al. (2007) found that patients' intrusions predominantly consisted of sensory experiences of short duration. Their study also provided further evidence that feelings of fear, anxiety, helplessness and numbness were reported to be stronger *at the time* of the trauma, whereas secondary emotions of anger, shame or guilt were more intense post-trauma. Reynolds and Brewin (1999) also found that the emotions associated with the event in PTSD were feelings of fear, helplessness and horror, consistent with DSM-IV categorisation (APA, 2000). Intrusions were reported as being vivid and often accompanied by physical sensations. Intrusions were also found to involve a strong dissociative element with individuals reporting out-of-body experiences.

Holmes et al. (2005) examined the emotional and cognitive themes within trauma memory 'hotspots'. The term 'hotspot' refers to the specific part of a trauma memory that causes the highest emotional distress (e.g., Ehlers and Clark, 2000; Foa and Rothbaum, 1998). They examined the verbal reports of the specific intrusive memories patients were re-experiencing on a frequent basis and compared them with reports of the 'worse moment' of the traumatic event. They found that the majority of intrusive memories in patients could be matched to an associated trauma memory 'hotspot'. Interestingly, the emotions associated with trauma-related 'hotspots' were not always the typical PTSD diagnostic emotions of fear, helplessness or horror, but included other associated emotions such as shame, sadness, guilt and disgust. In addition, the cognitive themes identified in patients' verbal reports often involved a severe threat to the self, whether physical or not (e.g., Ehlers and Clark, 2000). The identification of specific trauma-related 'hotspots' and their relationship with intrusive memories was later replicated in a larger sample (Grey and Holmes, 2008). They identified a number of distressing moments ('hotspots') from the trauma that were likely to be re-experienced as intrusions. However, they also found that the number of 'hotspots' was fewer than their previous study (3.7 vs 6.1) and they also observed higher reports of fear as the primary emotion. Feelings of anger or sadness were found to be more highly associated with post-trauma emotions.

Overall, a common theme is observed from studies examining the narratives of PTSD patients in relation to their trauma memories. That is, declarative memory of the traumatic event is typically fragmentary and disorganised with individuals demonstrating difficulties in retrieving complete details from the event. On the other hand, intrusive memories are often described as consisting of sensory perceptual qualities from a small number of instances from the original trauma. The emotions often associated with the trauma are fear, helplessness and horror, whereas secondary emotions associated with after the event includes anger, shame and guilt.

1.4.6 Experimental studies with PTSD patients

Experimental studies in PTSD patients provide a unique opportunity to assess specific deficits in individuals that might be related to the development and maintenance of the disorder. Typical assessment measures involve assessing trauma victims with or without PTSD on tasks to examine cognitive function. For instance, several studies have shown consistent impairments of those with PTSD in tasks assessing immediate and delayed memory recall (Bremner et al., 1993; Jenkins et al., 1998; Vasterling et al. 2002; Yehuda et al., 1995). It has also been suggested that such declarative memory-related deficits may hinder the success of treatment for patients (Wild and Gur, 2008). However, it is inherently problematic to determine whether the observed deficits in PTSD were pre-existing or a related consequence of the traumatic experience.

In an attempt to bridge the gap between memory-related deficits and processes that may underlie the cognitive mechanisms of intrusive imagery, Michael et al. (2005) assessed perceptual priming in PTSD. They proposed that intrusive memories in PTSD might occur due to strong perceptual priming of trauma-related stimuli (e.g., Ehlers and Clark, 2000). They employed a widely used word stem completion task (e.g., Graf et al., 1984). The task used to examine if trauma victims demonstrated enhanced priming of trauma-related information consisted of trauma-related, general threat, and neutral words. Assault victims with or without PTSD encoded words from each category, as well as neutral match words for each category (e.g., *for* ____, *forced* or *formal*). Participants were then presented with word stems and required to

complete the stem with the first word that came into mind. Assault survivors with PTSD showed a greater priming effect for trauma-related words than those individuals without PTSD. However, no differences were observed between groups on general threat or neutral words. The authors suggest that word stems from trauma-related words acted as a cue to trigger trauma-related information, paralleling the way in which trauma-related cues would trigger intrusive imagery.

Hellawell and Brewin (2002) investigated the specific cognitive processes that might be involved during episodes of ‘flashback’ and autobiographical memory of a trauma in PTSD patients. To achieve this, they instructed PTSD patients to provide written narratives of their traumatic experience and then, during episodes of normal autobiographical memory retrieval or a flashback, they were stopped and asked to perform a secondary task. The secondary task was either verbal or visual-spatial. The verbal task involved counting backwards in threes from a given number, whereas the visual spatial task was the trail-making test (TMT; Reitan and Wolfson, 1985). Results showed that when the visual-spatial task was administered during a flashback phase of the narrative, performance on the task was *impaired* compared to periods of ordinary memory retrieval during the narrative. When participants were given the concurrent tasks during ordinary memory retrieval, performance was *enhanced* compared to baseline. The authors argue that flashbacks interfere with performance on the TMT due to placing greater demands on visual-spatial processing, thus competing for the same cognitive resources (e.g., Brewin et al., 1996; Brewin, 2001; Brewin et al., 2010).

In an innovative study, McIsaac and Eich (2004) examined the content of trauma-related memories in PTSD when retrieved from either a field perspective or an observer perspective. An observer perspective involves retrieving the past memory as a detached spectator, whereas a field perspective involves an individual recollecting the event as if they were seeing it through their own eyes. Patients were instructed to recall their traumatic memory and provide details of the way in which they were observing the event unfold. Patients’ accounts revealed that when recalling a trauma memory from a field perspective, they associated significantly more emotional and physical reactions to the memory. In contrast, memories

recalled from an observer perspective contained more information about the spatial relations and peripheral details of the scene and were associated with less anxiety. McIsaac and Eich suggest that patients may use an observer perspective as a cognitive device to mentally distance themselves from the emotional aspects of the event, watching the event as a detached spectator rather than being involved in the traumatic episode. They also propose that utilising this perspective during therapy may impair emotional processing of the event and hinder the ability for exposure-based approaches to diminish related fear (e.g., Foa and Rothbaum, 1998).

To summarise, observational and experimental studies in a clinical population have demonstrated a variety of memory-related deficits in PTSD. To clarify the specific aspects of memory that are key in these symptoms / deficits, Figure 1.2 illustrates a model of memory with the specific subsystems thought to be involved.

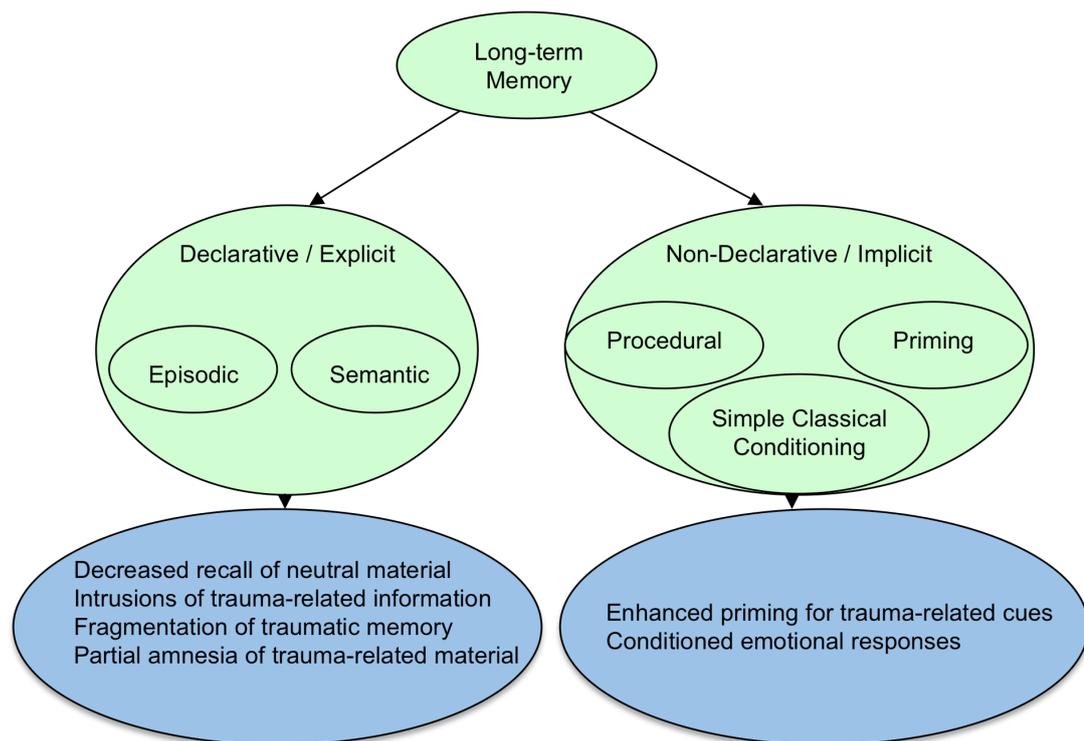


Figure 1.3. A model of human memory and the way in which the specific memory related deficits observed in PTSD patients are thought to affect each subsystem.

As highlighted, it is difficult to ascertain whether observed memory impairments in patients are pre-existing and therefore a potential vulnerability factor, or whether they are a consequence of the traumatic event. It is reassuring to note that some prospective studies in PTSD patients have provided valuable insights into the cognitive processes involved in trauma-related memory. Firstly, whilst the ability to provide accurate detailed recall of any traumatic episode is compromised, it would seem that the characteristics associated with intrusive memories involve some level of visual-spatial or perceptual processing (e.g., Hellowell and Brewin. 2002; Michael et al., 2005). Furthermore, in light of the specific emotional qualities attached to memories recalled from a field perspective, it may be that individuals show difficulties in the ability to generate emotionally controlled memories from an observer perspective

1.4.7 Experimental studies in healthy volunteers

As described above, investigating intrusive memories typically involves the examination of retrospective reports from individuals following a traumatic experience. Factors that alter processing during the event (peritraumatic processes) are (i) important in understanding the way in which a trauma is stored within memory, and (ii) predictive of later PTSD symptoms (Brewin et al., 2001; Ozer et al., 2003). Retrospective experimental studies in patients are therefore limited in the conclusions that can be drawn in elucidating factors that might play a part in intrusive memory development.

As a way to overcome these issues, several authors have developed creative paradigms to assess the occurrence of intrusive memories. For example, Bryant and Guthrie (2005; 2006; 2007) carried out a series of studies to assess factors in trainee fire fighters prior to exposure to a real fire. Another method that has received increasing attention is an analogue trauma paradigm.

A trauma film paradigm involves showing a short film depicting severe, and horrific scenes of death and/or serious injury to a group of healthy volunteers. The trauma film paradigm has a long history with its first reported use carried out by Lazarus

and colleagues (e.g., Lazarus and Alfert, 1964; Lazarus and Opton, 1964; Lazarus et al., 1965). These initial studies involved the assessment of physiological reactions to the aversive nature of the film rather than examining memory-related processes. Horowitz and colleagues (Horowitz, 1975; Horowitz and Becker, 1971a; 1971b; Horowitz et al., 1972) further developed the trauma film paradigm by instructing participants to record the number of intrusive thoughts of the footage immediately after viewing. In this series of studies, they examined a range of factors and their involvement with the number of intrusions experienced by individuals (e.g., cognitive processing, attention, and the content of the films).

Recently, studies have utilised the trauma film to examine a wide range of factors that may play a role in intrusive memory development. The paradigm most often used is illustrated in Figure 1.3. The method typically consists of a range of pre-film assessments using various mood state measurements. Individuals are then required to watch a short film of scenes depicting horrific imagery, injury and death. During exposure to the film footage participants may watch the film under normal conditions, or they may be asked to perform a secondary concurrent task. Measurements during the film may include physiological recordings to assess responses to the content. After the film has ended, further state measures are repeated to examine the impact of the footage on the viewer. Participants are then required to keep a diary over the next 7 days in which they must record any intrusive memories of the footage. They are then required to return at which point follow up measures may be administered, such as an explicit memory recall or recognition test of the traumatic material.

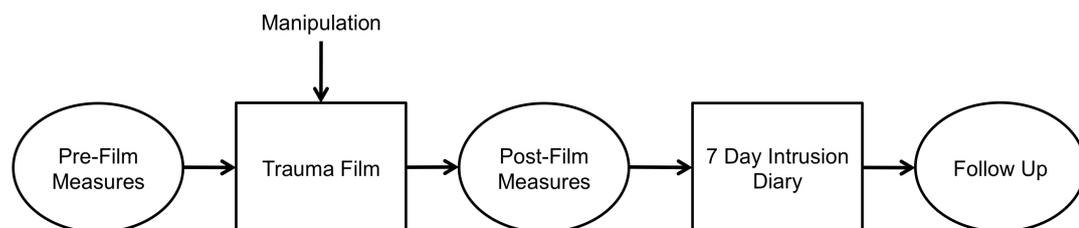


Figure 1.4. An illustration of a typical trauma film paradigm including each of the aspects in which different manipulations and measurements might take place.

A number of studies have used a correlational approach with the trauma film paradigm to examine how trait and/or state measures relate to intrusion frequency. Davies and Clark (1998) examined a range of predictor measures to assess their association with film-induced intrusions, including neuroticism, trait anxiety, depression, tendency to suppress unpleasant thoughts, self-rated proneness to intrusions and changes in negative mood. They found that intrusion frequency was predicted by changes in negative mood induced by the film, thought suppression tendencies, and self-rated proneness to intrusions. Using a similar methodology, Laposa and Alden (2008) assessed trait anxiety, intelligence, depression, trait dissociation and changes in state anxiety and their relationship to intrusive memories following exposure to a trauma film paradigm. Their results suggested that trait anxiety, trait dissociation and depression were predictive of later intrusive memory reports. Furthermore, increases in anxiety induced by the film correlated with the number of intrusions experienced.

The trauma film paradigm thus offers a valuable tool to investigate peritraumatic processes and associated intrusive memories. Brewin and Saunders (2001) attempted to manipulate dissociative processes during a trauma film by instructing participants to perform a concurrent visuo-spatial tapping task as a way to divide their attention. They predicted that divided attention would increase the number of intrusions experienced through increasing dissociative reactions during encoding of the footage. Interestingly, they found that the number of intrusions reported in the tapping task group was reduced compared to a no task control group. They proposed that the visuo-spatial tapping task might have interfered with the same cognitive resources required to form image-based representation needed for intrusions to occur. To further examine this idea, Holmes et al. (2004) carried out a series of experiments to assess different cognitive concurrent tasks with increasing demands and their effect on intrusive memory frequency. Firstly, they examined three visual-spatial tapping tasks during encoding of the traumatic film; a single tapping task where one key was pressed continually, a regular tapping task (as used by Brewin and Saunders, 2001), and an over-practiced tapping task, compared with a no-task

control. Their results revealed no effect of a single tapping task on intrusions although both other visuo-spatial tasks increased intrusions compared to the control group. There was also a linear increase in intrusion frequency as the cognitive demands of the visuo-spatial tapping task increased.

To further examine dual task processing during trauma film encoding, Holmes et al. (2004) also carried out a further experiment to investigate the way in which a verbal concurrent task might influence intrusive re-experiences. Intrusive memories were assessed in three groups; given (i) a verbal interference task (counting backwards in threes), (ii) a verbal enhancement task (verbalising the scenes from the footage as they occurred), and (iii) a no task control. They found that the group who performed the verbal interference task reported significantly more intrusive memories than the control group. However, the verbal enhancement task did not affect the number of intrusive memories reported compared to the control group. The authors explain these findings in terms of a dual representation account of intrusive memory. They propose that a visuo-spatial tapping task may compete for cognitive resources shared by the generation of image-based representations that would normally form the basis of intrusions. Therefore intrusions were decreased using a visuo-spatial concurrent task. However, the authors suggest that the verbal inference task impaired the ability to integrate conceptual aspects of the experience that would contribute to a spatio-temporal context of the event thus resulting in the inability to suppress intrusive memories.

An intriguing aspect of the Holmes et al. (2004) study concerns the physiological data recorded during the trauma film experience in participants. When comparing the specific scenes of the film that were reported as intrusions by individuals, heart rate during those scenes was found to be significantly *reduced* compared to other parts of the film that were not reported as intrusions. The authors explain this finding as a possible dissociative reaction with participants demonstrating a ‘freeze or surrender’ response to threat (e.g., Nijenhuis et al., 1998). However, a criticism of this aspect of the study involves the length of time that heart rate was recorded and averaged across each scene of the trauma film (approximately 3 minutes). For example, a number of traumatic images may have induced increases or decreases in

heart rate throughout the length of a traumatic scene. However, interpretation of fine changes in physiology that might have occurred at specific time points would be lost in this assessment due to averaging across the complete episode. Furthermore, the ability to support this finding during a real-life traumatic experience is limited for obvious practical reasons.

Rather than using a between participants design, Stuart et al. (2006) modified the trauma film paradigm to employ a within participants design. Participants were instructed to perform a visuo-spatial grounding task (modelling clay shapes) whilst watching half of the trauma film. The other half of the film was watched without instruction and served as a control. Scenes of the film viewed under instruction to model shapes were found to be associated with fewer intrusive memories than those watched without instruction, further supporting the role of visual-spatial processing in intrusive memory development. To rule out the possibility that the results of the previous findings might be due to distraction, Holmes and colleagues carried out a further study using a larger sample to investigate a verbal interference and visuo-spatial concurrent task (Bourne et al., 2010). Previous findings were replicated with a reduction in intrusive memories following a concurrent visuo-spatial task, whereas intrusions were increased following a verbal interference task. However, participants in the verbal interference task were also found to show inferior explicit memory recall for the footage. These studies (Brewin and Saunders, 2001; Holmes et al., 2004; Bourne et al., 2010) are consistent with the view that changes in intrusive memory reports following a trauma film cannot be interpreted in terms of a distraction hypothesis. As shown, a visuo-spatial task performed during encoding of a traumatic film resulted in increases in intrusive memory reports rather than decreases as predicted by a distraction hypothesis, therefore supporting a dual processing model.

In an attempt to examine the role of cognitive processing style and intrusive memories, Halligan et al. (2002) instructed participants to take on a particular processing style while watching the trauma film. They instructed participants to either become absorbed in the images and sounds of the film or to concentrate on the story and think about the meaning of the film, eliciting data-driven processing

associated with perceptual priming or conceptual processing that would provide a spatio-temporal context, respectively. Results showed that the data-driven processing group demonstrated reduced explicit memory recall of the footage compared to the conceptual processing group. However, the two groups did not differ in the number of intrusive memories experiences in the week following the film. The authors suggest that the processing style instructions may have been confounded by the natural processing style used by participants. Despite this, a positive correlation was observed with increases in perceptual/data-driven processing associated with increases in intrusions, whereas increases in conceptual processing were negatively correlated with intrusion increases.

Kindt et al. (2008) examined the specific cognitive processing style both during and immediately after a traumatic film. In one experiment, participants watched a trauma film and then immediately afterwards they were administered a task to elicit either a conceptual or perceptual cognitive processing style. They found that individuals in the perceptual processing group reported more intrusions than the conceptual processing group. In a second experiment, participants were given the processing style instruction prior to watching the trauma film and required to take on that style throughout. They found that the conceptual processing style group reported fewer intrusions than both the perceptual processing group and the neutral group. However, a criticism of this study involves the way in which intrusive memory data were collected. Participants were instructed to give a rating of intrusion frequency using a simple visual analogue scale (0 = no intrusions – 100 = frequent intrusions), which was completed one week after viewing the film rather using a diary method (e.g., Holmes et al., 2004).

To examine the hypothesis that intrusive memories occur due to strong perceptual priming (see Ehlers and Clark, 2000), Michael and Ehlers (2007) carried out two experiments to investigate priming for items immediately preceding a short traumatic story. Participants watched a number of traumatic and neutral stories presented as slides. Each story consisted of three slides; the first slide involved the main character in a neutral setting and contained two neutral objects in the background used as test stimuli. The second slide depicted the plot of the story with

something neutral or traumatic happening and included a central object important to the theme of the story (e.g., a knife). The final slide continued the story with either a neutral or traumatic picture. Immediately after the encoding phase, participants performed a blurred object recognition test to assess perceptual priming of the test stimuli, and a recognition test to assess explicit memory. Their results revealed greater perceptual priming for objects that immediately preceded traumatic slides compared to neutral. In their second experiment, similar methodology was used and, in addition, the frequency of intrusive memories was assessed. The previously reported enhanced perceptual priming effect was replicated. They also found that individuals required to elaborate on the slides immediately after viewing showed an attenuation of the enhanced perceptual priming effect and reduced intrusive memory reports. However, a criticism of this study involves the way in which intrusive memories were recorded from participants. Rather than using a diary method, as utilised by Holmes et al. (2004), Michael and Ehlers assessed intrusive memory reports using questionnaires that were sent to participants approximately one month after the initial study had occurred. Therefore, results on intrusive memories within this study were based heavily on retrospective reports and some of the accuracy in these measurements may have been greatly reduced.

Dissociation is difficult to manipulate within a laboratory setting although several authors have attempted to induce dissociative states in participants whilst viewing a trauma film. Holmes et al. (2004) tried to increase dissociation by instructing participants to continually stare at a dot prior to a trauma film but no effect was observed. Kindt and van den Hout (2003) examined changes in dissociative state induced by a trauma film and its relationship with memory fragmentation. Although increases in dissociation during the film were associated with reduction in ‘perceived memory fragmentation’ by participants, an objective memory test of memory recall showed no effect.

An interesting method to manipulate dissociation can be seen in studies using hypnosis. Holmes et al. (2006) examined the detachment component of dissociation by instructing participants, whilst under hypnosis, to view one part of the trauma film normally and another part as a detached observer, disconnected from their own

body. Although the trauma film was found to induce increases in state dissociation, no differences were observed in the number of intrusions experienced from the parts of the film under the two different viewing conditions. Further difficulties to manipulate dissociation through hypnotic suggestion were reported by Hagenaaers et al. (2007). Using the trauma film, they were also unable to show dissociation-related changes in intrusive memories with no apparent differences compared to controls. Overall, laboratory based manipulations of dissociation have had little success.

A number of recent studies have examined the possible manipulation of intrusive memory experiences by administering cognitive tasks *immediately after* viewing a trauma film. For instance, Krans et al. (2009) administered a recognition memory test immediately after participants viewed the trauma film. However, questions on the test only related to half of the scenes that they had observed. Participants were found to experience fewer intrusions for scenes that were followed by the memory test. Furthermore, participants demonstrated greater voluntary memory 7 days after exposure to the trauma film. Holmes et al. (2009) provided evidence that administering a computer game after watching a trauma film can reduce intrusions. In this study participants watched the trauma film and then, 30 mins later, were instructed to play the computer game ‘Tetris’ or read a magazine. Participants who played Tetris were found to report significantly fewer intrusive memories than those who read a magazine. They argue that the game placed demands on the cognitive resources required for intrusive imagery within the consolidation window, thus reducing the ability to successfully consolidate aspects of the traumatic material that would form the basis of intrusions.

In summary, the findings presented here provide strong evidence that an analogue trauma film can be used to successfully manipulate and assess many factors that might play a role in the development of intrusive memories. It is clear that individual differences and changes in mood state induced by the film, such as anxiety, dissociation and distress, are associated with the development of intrusive memories, similar to those factors that have been implicated in PTSD. It is interesting to note that a large body of research has provided significant evidence in trying to generate theoretical accounts to explain what factors might play a part in

trauma experiences and related intrusive memories. That is, cognitive processes that contribute to a verbal and contextual representation of the original traumatic material seem to be impaired during encoding of the traumatic material, possibly due to direct disruptions in memory or through indirectly affecting memory through the described changes in affective state. In contrast, cognitive processes that contribute to the intrusive imagery that is re-experienced may involve lower level visuo-spatial processes that are associated with sensory/perceptual aspects of the event. By providing tasks that compete for cognitive resources of these visuo-spatial processes intrusive memories can be reduced, whether administered during or after the event.

1.4.8 Neurobiological factors in PTSD

The experience of an extremely stressful event can produce a range of neurobiological changes that could potentially interact with an individual's memory. Research has identified multiple neurobiological systems that may be implicated in the development of PTSD. The two particular systems that have received considerable attention are the noradrenergic system and the hypothalamic-pituitary adrenal axis (HPA; e.g., de Boer et al., 1990; Yehuda et al., 1996; 1998). Further, stress-induced changes in noradrenaline and HPA axis functionality have been shown to have disruptive effects on the hippocampus, PFC and amygdala, essential structures in human memory (Elzinga and Bremner 2002; Kim and Diamond, 2002; LeDoux, 2000; Vermetten and Bremner, 2002). The way in which these systems interact during prolonged stress has been particularly influential in proposals of the neurobiological substrates thought to underlie PTSD. The next section will describe the systems thought to play a role during the stress response and their interaction with memory.

1.4.9 The noradrenergic system and the amygdala

The noradrenergic system plays an influential role during stress by preparing the body for a fight or flight response. In addition, the release of noradrenaline in the brain in response to stress regulates memory consolidation, enhancing the storage of

emotion related information (Cahill and McGaugh, 1998; McGaugh and Roozendaal, 2002). Extensive research has shown that post-training injections of adrenaline enhance memory in a dose-dependent way (for a review, see McGaugh, 2004). This enhancement of memory seems to be, in part, mediated by the activation of β -adrenergic receptors (Introini-Collison et al., 1992). This has also been confirmed through the use of β -adrenergic antagonists. For instance, the administration of propranolol has been shown to attenuate the enhancement of memory for an emotionally arousing story but not for a neutral one (Cahill et al., 1994).

The role of the noradrenergic system in the emotional enhancement of memory is thought to involve the amygdaloid complex (Cahill and McGaugh, 1998). Early studies in rodents showed that electrical stimulation of the amygdala immediately after an aversive learning paradigm disrupted memory retention (Goddard, 1964). Further, lesions to the amygdala have been shown to block the memory enhancing effects of adrenaline (McGaugh et al., 1996). Intra-amygdala injection of the β -adrenergic antagonist propranolol was also found to block the memory enhancing effects of adrenaline (Liang et al., 1986).

In humans, Cahill et al. (1995) showed that damage to the amygdala resulted in an attenuation of enhanced emotional declarative memory. In this study, a short slide show depicting a story was shown to participants. Key slides involved emotional information, whereas the rest of the slides were considered neutral. They found that, whilst the control participants showed an enhancement of memory for emotional slides compared to the neutral ones, a patient with bilateral lesions to the amygdaloid complex showed no such effect despite normal memory for the neutral slides. The authors propose that these findings, taken together with the same blockade of emotional memory enhancement following a β -adrenergic antagonist support the view that the enhancement of emotional memory in humans involves activation of β -adrenergic receptors and is mediated by activity in the amygdala.

A large body of evidence has highlighted the role of noradrenaline in PTSD. For example, Lemieux and Cole (1995) examined 24-hour catecholamine excretion in a

group of females with a history of sexual abuse, both with and without PTSD, and compared them to non-abused females without PTSD. They found that the group with a history of abuse and PTSD had significantly greater noradrenaline levels than the controls. However, noradrenaline levels in the group with a history of abuse without PTSD were in between the two groups. Geraciotti et al. (2001) examined cerebrospinal fluid concentrations of noradrenaline in combat veterans with PTSD compared to healthy controls. Veterans with PTSD showed elevated noradrenaline levels, which were strongly positively correlated with PTSD symptoms. In light of the suggestion that PTSD sufferers demonstrate increased baseline noradrenergic activity, Southwick et al. (1993) administered an acute dose of yohimbine in a double-blind fashion to combat veterans diagnosed with PTSD. Yohimbine is a competitive antagonist at both pre- and post-synaptic α_2 -adrenoreceptors, thus blocking auto-receptor inhibition of noradrenaline release (Khoshbouei et al., 2002). Southwick et al. found that acute administration of yohimbine induced panic attacks and flashbacks in the PTSD patients, whereas healthy controls showed none of these symptoms.

Considerable evidence also highlights the role of the amygdala in fear conditioning (LeDoux, 2000). During a typical fear-conditioning paradigm, a neutral conditioned stimulus (CS) is continually co-presented with an aversive unconditioned stimulus (US). Over time, the animal acquires an association between the CS and US resulting in a conditioned fear response, typically demonstrated by freezing in response to the previous neutral CS. It is proposed that the amygdala plays a functional role in associating the conditioned and unconditioned stimulus (LeDoux, 2000). Lesions to the amygdala have been found to block fear acquisition in rodents (Phillips and LeDoux, 1992) and humans (LeBar et al., 1995). Bechara et al. (1995) assessed fear acquisition and declarative knowledge for the CS-US pairing in a patient with bilateral amygdala damage. Whilst the patient demonstrated impaired fear acquisition, declarative knowledge of the association was intact. Several studies have shown preserved fear acquisition in PTSD patients through the use of a fear-conditioning paradigm (Blechert et al., 2007; Orr et al., 2000; Peri et al., 2000). Furthermore, studies using fMRI have shown that patients diagnosed with PTSD show exaggerated amygdala activity compared to controls using a range of

behavioural measures (Bremner et al., 2003; Rauch et al., 2000; Shin et al., 1997; Shin et al., 2004).

In summary, an increase in noradrenaline during elevated stress is a fundamental component of the stress response. During a traumatic event, the rapid secretion of noradrenaline may strengthen emotional aspects of the memory trace and enhance fear conditioning due to its effect on the amygdala. The observed alterations in noradrenaline and associated amygdala activity in PTSD might therefore partially underlie both an individual's vulnerability to PTSD development and the persistence of associated symptoms.

1.4.10 Prefrontal cortex

The prefrontal cortex (PFC) plays an essential role in guiding behaviour and is fundamental in providing inhibitory control over the amygdala. The PFC uses 'online' representations to guide behaviour effectively, allowing inhibition of inappropriate responses and facilitating planning and the execution of organised behaviour (Arnsten, 1998). Exposure to stress has been shown to induce catecholamine release in the PFC (Goldstein et al., 1996). Noradrenaline can impair the PFC through its actions at α -1 adrenergic receptors although it has an opposite enhancing effect at α -2 adrenergic receptors (e.g., Arnsten et al., 1988; 1999). Noradrenaline has a higher affinity for α -2 than α -1 receptors. Low levels of noradrenaline release may engage α -2 receptors, while higher concentrations may engage α -1 receptors impairing the PFC (Arnsten, 1998). Research has shown that dopamine may also impair PFC function via D1-receptor stimulation. Exogenous application of dopamine D1 agonists have been shown to impair working memory performance in primates (Cai & Arnsten, 1997). Infusion of a D1 agonist directly into the PFC in rats also produced working memory deficits (Zahrt et al., 1997).

A wide body of research has provided evidence that the PFC is essential in inhibiting the amygdala. For example, electrical stimulation of the infralimbic subregion of the mPFC has been shown to reduce freezing in rodents (Milad and Quirk, 2002). Furthermore, Quirk et al. (2003) found that, through the use of

extracellular recording, responsivity of the amygdala was significantly reduced by electrical stimulation to the amygdala. Rats with lesions to the mPFC also display an inability to extinguish fear responses following fear conditioning compared to rats without lesions (Morgan et al., 1993). In humans, lesions to the PFC are associated with impairments in emotion regulation and the ability to correctly interpret emotional expressions from others during social situation (Damasio et al., 1994).

Several authors have shown decreased activation or even a failure to activate the mPFC in PTSD patients during traumatic script driven imagery (Bremner et al., 1999a; Lanius et al., 2001; Shin et al., 2004) and the presentation of trauma-related stimuli (Bremner et al., 1999b; Hou et al., 2007). Further studies have also revealed diminished mPFC activity in PTSD patients on tasks investigating extinction learning (Bremner et al., 2005), the retrieval of an extinction memory (Milad et al., 2008), emotional stroop interference (Shin et al., 2001), and emotional word recall (Bremner et al., 2003). In addition, increased activation in the mPFC seems to be inversely correlated with increased levels of symptom severity in PTSD (Hopper et al., 2007; Shin et al., 2004; Williams et al., 2006).

Overall, the role of the PFC is vital in the ability to exert top-down inhibitory control over the amygdala. Trauma-related increases in noradrenaline may implicate the PFC and thus the responsivity of the amygdala during a traumatic experience. A generalised reduction in PFC activity following the traumatic event in PTSD patients may also underlie, in part, the inability to extinguish fear resulting in the ongoing exaggerated reaction in response to trauma-related cues in the environment.

1.4.11 Cortisol and the hippocampus

The hypothalamic-pituitary-adrenal (HPA) axis regulates the body's physiological response during stress. Prolonged stress causes the release of corticotropin releasing factor (CRF) from the hypothalamus, which stimulates the secretion of adrenocorticotropic releasing hormone (ACTH) from the pituitary. This results in a marked increase in the production of glucocorticoids (e.g., cortisol) from the adrenal glands. The subsequent elevation in cortisol levels results in a negative feedback

loop, terminating the physiological stress response via cessation of ACTH and CRF release. The hippocampus is a medial temporal lobe structure that is vital in the formation of stable declarative/explicit memory (Squire & Zola-Morgan, 1991). It is also a target for stress hormones and has a high concentration of corticosteroids receptors. The hippocampus serves as an essential component in the termination of stress responses through providing glucocorticoid-mediated negative feedback to support inhibition of the HPA (Kim & Diamond, 2002). Due to its high concentration of glucocorticoid receptors, the hippocampus is particularly sensitive to stress. Findings from animal studies have shown that high levels of glucocorticoid release may impair the hippocampal function (McEwen, 1999).

Basal levels of corticosteroids are associated with the effective induction of long-term potentiation (LTP) in the hippocampus (Diamond et al., 1992). In contrast, exposure to stress or elevated levels of corticosteroid has been found to impair LTP and enhance long-term depression (LTD) in the hippocampus (Krugers et al., 2005). Thus, high levels of stress may lead to impairments in the ability to form new memory traces. Little is known about the relationship between stress and its effects on LTP and LTD although it has been suggested that *N*-methyl-D-aspartate (NMDA) receptors may be involved. Kim et al., (1996) found that during stress, NMDA receptor-dependent changes occur in the CA1 area of the hippocampus leading to changes in LTP and LTD. However, the administration of an NMDA antagonist before stress was found to block hippocampal plasticity. Wiegert et al. (2005) also found that corticosterone, via glucocorticoid receptor activation, selectively impairs NMDA receptor-dependent synaptic plasticity in the hippocampus.

Kirschbaum et al., (1996) examined the association between both stress and treatment induced cortisol levels and memory in humans. Participants exposed to a brief stress test revealed a significant negative relationship between cortisol levels and declarative memory performance. In a randomised double blind design, participants receiving 10mg cortisol displayed impaired performance on a declarative memory and spatial thinking task compared to those given placebo. Groups showed no significant differences on tests of procedural memory.

Newcomer et al. (1999) found that administration of cortisol in humans produced transient impairments in verbal declarative memory. However, these memory impairments were only observed in an increased cortisol level reflecting a moderate stress response.

Research has identified a number of neuroendocrinological differences in PTSD patients compared to controls although findings have been far from consistent. Given the association between increases in stress and glucocorticoid release, one might predict elevated cortisol levels in an individual's response to a trauma. Surprisingly, evidence suggests unexpectedly low cortisol levels in individuals who have experienced a traumatic event. In a series of studies, Yehuda et al., (1990; 1991; 1992) found lower levels of basal cortisol in urine, saliva and plasma in PTSD patients compared to controls. However, Pitman and Orr (1990) found no evidence of lower basal urinary cortisol excretion in PTSD patients compared to controls. Further, following an interview where participants were instructed to describe a stressful event, PTSD patients and controls showed significant increases in cortisol excretion but no group differences were found. To elucidate the relationship between stress-mediated changes in cortisol release and later PTSD development, McFarlane et al. (1997) examined plasma cortisol in a sample of road traffic accident survivors immediately after the event. They found that those who developed PTSD at a 6-month follow up interview were found to demonstrate significantly *lower* levels of cortisol immediately after the event.

Although lower cortisol release in some PTSD patients might be difficult to conceptualise within the view that a traumatic event should produce an elevated stress response, one explanation might involve enhanced negative feedback sensitivity of the HPA axis in PTSD. Using low dose dexamethasone suppression tests, Yehuda et al. (1995) found that combat veterans with PTSD showed greater cortisol suppression compared to veterans without PTSD or controls. In a further study, MacFarlane et al. (2011) assessed cortisol suppression in individuals within 24 hours of experiencing a traumatic accident. Using dexamethasone suppression tests, they found that greater cortisol suppression after the event was correlated with increased PTSD symptoms at 6 months. As mentioned, increases in glucocorticoid

release during stress plays a functional role in the encoding and consolidation of emotional memories (e.g., Roozendaal et al., 2006). Therefore, a blunted stress response following a traumatic experience may paradoxically disrupt consolidation processes and thus impair memory of the event (Yehuda et al., 2004).

In terms of hippocampal alterations, neuroimaging studies have consistently shown diminished hippocampal volume in PTSD patients (Bremner et al., 1997; 2003; Gilbertson et al., 2002; Smith, 2005; Stein et al., 1997; Winter and Irlé, 2004). However, Bonne et al. (2001) did not find any differences in hippocampal volume between trauma survivors with and without PTSD. They suggest that the smaller hippocampal volume observed in other studies might precede the traumatic event thereby increasing the likelihood of developing PTSD. Bremner et al. (1995) found that verbal declarative memory deficits in PTSD were inversely correlated with hippocampal volume, whilst other studies have shown an inverse relationship between hippocampal volume and PTSD symptom severity (Bremner et al., 2003). Gilbertson et al. (2002) assessed hippocampal volume in monozygotic twins discordant for trauma exposure. Twin-pairs, where the trauma-exposed individual had developed PTSD, had significantly smaller hippocampi than twin-pairs where the trauma-exposed individual did not develop PTSD. Further, disorder severity of the PTSD patients was negatively associated with hippocampal volume of the patients and patients' unexposed twin. Functional neuroimaging studies have also shown decreases in hippocampal activation during the encoding of neutral or emotional stimuli (Astor e al., 2006; Shin et al., 2004).

In summary, some studies have identified neuroendocrinological alterations in PTSD patients, particularly demonstrating low cortisol levels. However, these findings seem to be inconsistent and it is difficult to conclude from these studies if these changes in cortisol levels were apparent before the trauma or were caused by the event. Evidence seems to support both diminished hippocampal volume and decreases in hippocampal activation in PTSD. The findings also highlight the possibility that such deficits may increase an individual's vulnerability to the later development of PTSD following trauma exposure. Reduced hippocampal function may therefore impair an individual's ability to successfully encode the event into

memory, thus resulting in maladaptive processing of the traumatic experience. Such deficits may contribute to the impairments in voluntary recall of the event and the fragmentary nature of the trauma memory. It should be noted that the PFC also comprises a large number of glucocorticoid receptors, which suggests that this area may also play an important role in response to increases in cortisol (Lupien and Lepage, 2001). Stress and cortisol treatments have been shown to impair PFC function and related cognitive processes (Elzinga and Roelofs, 2005; Wolf et al., 2001). As mentioned above, the PFC plays an important role to inhibit the amygdala and regulate the HPA axis in response to stress (Amat et al., 2005). Therefore, increases in cortisol and the related effects on PFC function during a traumatic event may contribute to a further exaggerated fear response from a lack of inhibition over amygdala activity (e.g., Milad et al., 2008).

1.5 Acute Alcohol and Human Memory

1.5.1 Alcohol and human memory

Alcohol's ability to cloud memory has been recognised for many years (e.g., Goodwin et al., 1970; Ryback, 1971). Many individuals who are familiar with alcohol's intoxicating effects are likely to have experienced alcohol-induced memory impairments. These memory-related disruptions can range from very mild 'gaps' in memory such as forgetting a name of someone you met, to complete 'blackouts' for events that occurred whilst intoxicated. The term 'blackout' refers to amnesia for specific events that occurred during a drinking episode without the loss of consciousness and should not be confused with 'passing out' (e.g., Jennison and Johnson, 1994). During a 'blackout', it has been suggested that individuals are able to perform a wide range of other tasks whilst heavily intoxicated (Goodwin, 1995). Alcohol-induced blackouts were originally thought to be a hallmark symptom of progressive alcoholism (Jellinek, 1952). However, recent research has identified that these memory-related disruptions are a frequent occurrence in social drinkers (White et al., 2004).

Research concerning alcohol-induced ‘blackouts’ highlights a general disruption in memory for events. However, ‘blackouts’ only capture an extreme aspect of a spectrum in relation to the way in which alcohol can affect one’s memory. Memory research over the past decades has significantly advanced our understanding and led to a clearer picture of alcohol’s effects on memory. Intriguingly, numerous reports have shown alcohol to affect memory in unique ways with certain aspects being disrupted, whilst others are spared (e.g., Hashtroudi et al., 1984; Lister et al., 1991). This section will now describe the current literature on alcohol’s effects on memory in relation to the specific memory systems outlined previously in section 1.2. In addition, the primary brain mechanisms and neurochemical alterations that are thought to underlie alcohol-induced memory deficits will be detailed.

1.5.2 Episodic memory

Episodic memory refers to our memory for personally experienced events, allowing one to perform mental time travel when retrieving an event from the past (Tulving, 1985). When alcohol is administered prior to the experience of new information, memory for that information is reduced. For example, Jones and Jones (1977) administered alcohol (low or high dose; 0.52 g/kg or 1.04 g/kg) or a matched placebo beverage to participants and had them learn word lists. Individuals in the alcohol groups showed decreases in the number of words they could recall both immediately and following a delay compared to the placebo group. However, only delayed recall was affected in a dose-dependent way with greater impairments as the alcohol dose increased. Acute alcohol-induced reductions in free and cued recall have been consistently shown in many further studies (e.g., Hashtoudi et al., 1984; Jones, 1973; Leitz et al., 2009; Lister et al., 1991; Soderlund et al., 2007).

Studies investigating the way in which alcohol affects recognition memory have provided inconsistent results. Some studies have shown impaired word and picture recognition following alcohol intoxication (Maylor et al., 1987; Parker et al., 1975; Ray and Bates, 2006), whereas a number of others studies have not (Goodwin et al., 1969; Hashtroudi et al., 1984). These contrasting results can be explained in terms of the type of recognition task used and in relation to proposals made by dual

processing theories of recognition memory. Dual processing theories argue that recognition of a previous item can be solved via two distinct processes, namely recollection and familiarity (for a review, see Yonelinas, 2002). Recollection involves consciously remembering the specific details of an experience, such as when and where an item was encountered (Mandler, 1980) and is considered a defining characteristic of episodic memory (Tulving, 1983; 1985). In contrast, familiarity reflects the recognition of an item based on a feeling of ‘knowing’ alone, thus lacking the distinct qualitative richness experienced during recollection.

In an attempt to investigate recollection and familiarity components of recognition memory, Curran and Hildebrandt (1999) utilised a remember-know paradigm. In this study, participants were administered either alcohol or a matched placebo and then presented with word pairs of opposites (e.g., winter-SUMMER). Individuals were instructed to read aloud the second word of each pair and try to remember the word for a later memory test. Half of the word pairs were presented with only the first letter of the second word and required participants to generate the second word. (e.g., north-S___). During the recognition test, participants were instructed to identify words from a list, which they recognised as a previously seen item. However, for each word recognised they were required to give a further ‘remember’ or ‘know’ response. Individuals were instructed to give a remember response if, on recognition, they recollect specific contextual details of the encoding experience, or to give a ‘know’ responses if recognition is solely based on a feeling of familiarity. They found that alcohol impaired recognition with conscious awareness compared to placebo, while leaving recognition without conscious recollection unaffected. They also revealed that alcohol reduced the mnemonic advantage of a generation versus read condition of the task, which was found to enhance recollective experience in the placebo group. A criticism of this study involves the amount of alcohol and administration technique utilised within the design. A typical procedure for acute alcohol studies involves the administration of alcohol adjusted for the weight of each participant, aimed to attain a specific blood alcohol concentration level. However, Curran and Hildebrandt administered a set amount of alcohol to individuals, increasing the confounding effects of individual differences in the absorption and elimination of alcohol (Eckardt et al, 1998). Further, blood alcohol

concentration levels were not measured during testing and, therefore, this is problematic in assessing the contribution of the level of intoxication on memory performance. However, similar findings have also been found in further studies assessing alcohol's affects on distinct recognition processes. Ray and Bates (2006) also found that alcohol intoxication during encoding impaired recognition associated with recollection, whereas recognition based on priming was unaffected.

The ability to store conscious associations between presented stimuli is considered an important process underlying the generation of false memories. False memories are typically observed within research when a new 'lure' item that is associated to a number of previous studied items, is identified as a previously observed item. A popular procedure utilised within false memory research is the DRM paradigm (Deese, 1959; Roediger & McDermott, 1995) where individuals study a number of related items and then at test are presented with a number of veridical and critical words that they must recognise as 'old' or 'new'. An important factor within false memory findings is the ability for participants to form conscious associations between veridical items with research suggesting that factors that may impair such associations may decrease false memories (Libby & Neisser, 2001; Roediger et al., 2001). In terms of alcohol's ability to impair the formation of conscious associations between study words, alcohol may therefore decrease the number of false memories during testing. However, studies examining this have produced contrasting findings.

Utilising the DRM paradigm, Milani and Curran (2000) assessed false recognition and recollective experience following a small dose of alcohol (0.26 – 0.28 g/kg) to gauge the effects of social drinking. After hearing items at study, participants were required to recall as many as they items they could. Following a week, participants were assessed on a standard recognition test and were required to acknowledge each item recognised with either a 'remember' or 'know' response. Results revealed no difference between the alcohol and placebo group on overall measures of recall and recognition of studied words, as well as no effect on false memory. However, alcohol was found to increase the number of 'remember' responses for critical items compared to the placebo group. However, Mintzer and Griffiths (2001) were unable to replicate this finding from a similar dose of alcohol (0.27 g/kg) as well as a larger

dose (0.6 g/kg). After finding no effects of alcohol on false recognition and recollective experience, they argue that the differences demonstrated by Milani and Curran (2000) might be due to use of a free recall task following encoding. Therefore, alcohol may impair the ability to differentiate between studied items and self-generated critical items at recall resulting in both types of items recognised with a remember response at test. Mixed findings for measures using recognition following alcohol have led to the suggestion that tasks using free recall may show a greater impairment following acute intoxication (Mintzer & Griffiths, 2001).

Garfinkel et al. (2006) examined false memories following acute alcohol intoxication compared to placebo using tests of free recall and stem completion. Consistent with previous findings in relation to alcohol's amnesic effects on episodic memory, alcohol was found to decrease recall of veridical items compared to the placebo group. In addition, the alcohol group showed fewer false memories than the placebo group when required to freely recall items, although there no group differences were observed using stem completion. Through examining participants' awareness judgments of recalled items they revealed that in the alcohol group, awareness of veridical items increased with repetition at encoding although awareness judgments for critical items also increased with repetition with individuals more likely to accept critical lure words as original study words. The opposite was seen in the placebo group with more rejections of critical lures demonstrated as a function of repetition at encoding. These findings further support an alcohol-induced disruption in the ability to form explicit associations at encoding leading to a decrease in the recall of critical words and a reduction in false memories through blocking associative processes between lure words.

Alcohol's ability to affect emotional memory has received little attention. Emotional material has been shown to typically enhance memory in sober participants (Cahill and McGaugh, 1998). It has been suggested that alcohol may dampen the stress response during emotional events by reducing the initial appraisals of the emotional information (Sayette, 1993). Knowles and Duka (2003) found that individuals given a placebo displayed enhanced memory recall of emotional items compared to non-emotional stimuli. However, this enhancement was not observed in intoxicated

individuals. Participants in the alcohol group were found to show a less pronounced difference between recall of emotional and neutral stimuli. The authors stipulated that these findings further support alcohol's ability to hinder deep processing of information and override the mnemonic advantage of emotional stimuli. In a recent study, Brown et al. (2010) found that alcohol administered prior to the encoding of an emotional story impaired memory during the emotional parts of the story disproportionately during the primacy phase of the task. However, research on emotional memory under alcohol intoxication to date remains limited.

An interesting aspect of alcohol's ability to affect memory relates to the distinct differences between encoding and retrieval processes. Whilst alcohol has consistently been shown to impair encoding of new information, the retrieval of past memories is preserved (Parker et al., 1976; Petros et al., 1985). Intriguingly, research suggests that when alcohol is administered immediately after learning, memory for the previous items can be facilitated (Lamberty et al., 1990; Mueller et al., 1983; Parker et al., 1980). Recently, Moulton et al. (2005) presented a prose recall task to participants and then administered alcohol or a matched placebo drink. Participants' memory was tested only when all individuals were again sober. In support of an alcohol facilitation effect, they found that post-learning administration of alcohol enhanced memory for the prose compared to placebo. It has been proposed that this facilitation effect may occur due to alcohol's ability to impair the acquisition of new information and thus reduce interference from further information experienced after the learning episode (Mueller et al., 1983).

Several authors have attempted to elucidate the memory impairing effects of alcohol through the investigation of memory performance at different limbs of the blood alcohol concentration curve (BAC). The ascending and descending limbs of the blood alcohol concentration curve are well documented, with stimulatory effects associated with rising BAC levels and sedation during falling BACs (e.g., Earleywine and Martin, 1993; Martin et al., 1993). In an early study, Jones and Vegas (1973) found that long-term verbal declarative memory was more impaired during the ascending limb, whereas visual-spatial memory showed a greater reduction during the descending limb. In a recent study, Soderlund et al. (2005)

examined a range of episodic memory tasks at different points of the BAC curve. They found that alcohol impaired encoding processes irrespective of limb. However, memory retrieval was also impaired during the rising limb. However, Schweizer et al. (2006) found no differences in memory performance on ascending and descending limbs of the BAC curve.

Some researchers have suggested that alcohol may act to create a drug-induced state that could provide an internal context during memory storage and its retrieval (Goodwin, 1995). State dependent learning refers to the internal or external context that may influence both encoding and retrieval processes (Baddeley, 1982). When returning to the same emotional or physiological state that was experienced during encoding, memory recall can be facilitated (e.g., Godden and Baddeley, 1975). Anecdotal evidence has long suggested that alcoholics occasionally hide money or alcohol while intoxicated, have no recollection of where they placed the items while sober, but seem to remember the information when again intoxicated (Goodwin, 1971). However, empirical studies have been unable to provide compelling evidence. Weissenbourn and Duka (2000) investigated the effects of an acute dose of alcohol on the encoding and retrieval of low and high associated word pairs. No state-dependency effect was observed. Individuals who consumed alcohol prior to encoding and retrieval were found to remember fewer items than controls irrespective of whether the items were emotional or neutral, suggesting an overall impairment of memory.

In summary, episodic memory is consistently impaired during alcohol intoxication with specific decrements during encoding, whereas retrieval seems less affected. Although a large body of evidence exists concerning alcohol-induced memory deficits, there is a range of apparent areas that require further research. For example, little is understood about the way in which alcohol might affect emotional processing in memory and its related mechanism. Given the observed facilitation of memory when alcohol is consumed immediately following a learning phase, the specific basis for this effect needs further study to elucidate the way in which consolidation processes are implicated following alcohol.

1.5.3 Semantic memory

Semantic memory refers to our general knowledge about the world. Tulving (1972; 2002) contrasted this form of memory with episodic memory in that semantic memory contains knowledge and facts in absence of the context it was learned in. Very few experimental investigations have assessed alcohol's acute effects on semantic memory. Using a semantic memory task that requires individuals to answer general knowledge questions, participants showed fewer correct answers after receiving a high dose of alcohol (0.8g/kg) compared to placebo, but not after a lower dose (0.4g/kg; Kleykamp et al., 2010; Nelson et al., 1986). Wendt and Risberg (2001) examined alcohol's effects on a verbal fluency task, which requires individuals to generate as many words as possible beginning with a specified letter. In this study, alcohol was found to impair verbal fluency resulting in fewer words produced compared to a placebo group.

A popular approach for examining semantic memory processes is through the use of a semantic priming task. During this task, priming is evidenced by a response to a target word (e.g., lion) being facilitated when it is preceded by a semantically related word (e.g., tiger). Using this paradigm, Lister et al. (1991) found that neither a low (0.3g/kg) nor moderate (0.6g/kg) dose of alcohol impaired priming compared to a placebo group although the study was substantially underpowered ($n=9$). In a more recent study, Ray et al. (2004) utilised a similar semantic priming task and tested participants under both alcohol and placebo conditions. They found no difference in priming between alcohol and placebo conditions, providing further evidence that semantic processing is not affected following acute intoxication. However, Sayette et al. (2001) examined alcohol's effects on semantic priming through the use of an indirect priming task that requires more complex priming associations. Indirect priming refers to the ability of a prime (e.g., lion) to facilitate responding to a target (e.g., stripes; a relationship mediated by tiger). Utilising this task, Sayette et al. (2001) found that alcohol disrupted indirect priming, resulting in slower response latencies to primed words and a smaller difference between unprimed and primed words compared to placebo. Overall, under certain circumstances, alcohol does show some level of disruption in semantic memory processes. However, given the

lack of consistency and limited experimental support it is difficult to infer whether such deficits are directly attributable to acute alcohol intoxication. Furthermore, although indirect priming tasks have been suggested as being a more sensitive measure than direct priming (Sayette, 1996), it is difficult to conclude the precise processes involved during such a task.

1.5.4 Attention and executive function

Attention and executive processes play a fundamental part in any memory task. Divided attention is significantly impaired by alcohol, evidenced by a decrease in performance when two tasks are carried together compared to when performed independently (Landauer and Howat, 1993; Roehrs et al., 1994). Alcohol is proposed to spare vigilance, described as a readiness to detect and respond to unpredictable and rare events (Fagan et al., 1987; Linnoila, 1974). In addition to assessing divided attention following alcohol intoxication, Schulte et al. (2001) examined covert attention, the ability to shift attentional focus according to a central cue. As in previous studies, divided attention was impaired by alcohol, and covert attention was impaired with increased reaction times but only for stimuli appearing in the left visual field. The authors suggest this is due to a more prominent disruption to the right hemisphere by alcohol (also see Volkow et al., 2008). Performance on sustained attention tasks, attending to one source of for a prolonged period is unaffected (Rohrbaugh et al., 1988).

Executive processes are thought to monitor, direct, and regulate behaviour to achieve a desired goal and minimise the possibility of a negative outcome (Barkley, 1997). As previously mentioned, executive function is thought to comprise higher order processes including associative learning, memory, problem solving, and planning. Research findings suggest that executive functioning is disrupted during intoxication only at higher doses. For instance, Weissenborn and Duka (2003) assessed performance on a Tower of London task (Shallice, 1982) following a high dose of alcohol (0.8 g/kg). Deficits were observed on the planning time and the number of trials completed in the minimum number of moves. In contrast, Leitz et al. (2009) found that performance on the Tower of London was preserved by a

moderate dose of alcohol (0.6 g/kg). Interestingly, Paraskevaides et al. (2010) found enhanced performance on the Tower of London task following a moderate dose of alcohol (0.6 g/kg). Lyvers and Maltzman (1991) administered a moderated dose of alcohol to participants and examined performance on Wisconsin card-sorting task. They found that alcohol produced increased perseveration errors suggesting set-switching deficits.

Response inhibition also forms a significant part of executive processes. Performance on the Go/No-Go task has been shown to be impaired under the influence of alcohol with increased false alarm rates (Finn et al., 1999; Marinkovic et al., 2000; Rose and Duka, 2008; de Wit et al., 2000). Rose and Duka (2008) also assessed acute alcohol intoxication (0.6 g/kg) on interference inhibition through the use of Stroop task (Stroop, 1935). Performance on the colour Stroop task was impaired by alcohol with increased error rates. Using a modified version of the Stroop task, which involved the use of alcohol-related words, individuals in the alcohol group again showed increased error rates suggesting impaired interference inhibition, consistent with previous reports (e.g., Duka and Townshend, 2004). Participants performed two Go/No-Go tasks, one involving neutral pictures, whereas the other consisted of alcohol-related pictures. Results revealed that during intoxication, responses to the alcohol-related pictures were slower than the neutral pictures. To summarise, alcohol seems to consistently impair executive processes at higher doses while lower doses seem to affect specific components. For example, inhibitory control is affected at lower doses whilst planning processes are preserved.

1.5.5 Working memory

Working memory refers to a limited capacity system that temporarily stores information to support human thought processes, providing an interface between perception, long-term memory and action (for a review, see Baddeley, 2003). The components that make up this system include two slave systems that act as modality specific storage buffers and a central executive that comprises a control system of limited attentional capacity. One buffer is specialised for verbal input, forming the phonological loop that supports rehearsal of incoming stimuli, while the second

buffer store processes visuo-spatial information. Baddeley (2000) later added an episodic buffer to the system that is proposed to act as an interface between components and incorporate conscious awareness of information that needs to be processed and maintained.

Research investigating alcohol's acute effects on an individual's ability to maintain and process information within working memory has generated mixed findings from a range of behavioural tasks. One task that has often been utilised to examine working memory following alcohol consumption is the Sternberg Memory Scanning task, a task devised to provide a measure of temporary active memory or 'working memory' (Sternberg, 1969). In this task, participants are presented with sets of stimuli (e.g., letters), which they must quickly scan and store in memory. After a short delay, a single item is presented and participants are required to indicate if the item was in the original set. Performance on this task is assessed by speed and accuracy. A series of studies have shown that acute alcohol intoxication does not affect performance on this task (Hindmarch et al., 1991; Kennedy et al., 1993; Wilkinson, 1995). However, Grattan-Miscio and Vogel-Sprott (2005) examined alcohol's effects on the Sternberg Memory Scanning task and varied the number of stimuli presented in each set. They found that alcohol intoxication (approximately 0.7g/kg) resulted in slower reaction times and increased error rates compared to placebo. This impairment was only apparent during trials when 6 items needed to be held in memory, although not during trials with 2 or 4 items. They also found that when participants were given a monetary incentive for correct performance, the alcohol group no longer differed from the placebo group on reaction times but still demonstrated increased error rates.

Schweizer et al. (2006) examined alcohol's effects on both verbal and visuo-spatial working memory. Visuo-spatial working memory was assessed using a task where participants are presented with a matrix of X's and O's on a screen for 1.5 seconds and are required to remember the location of three randomly highlighted X's or O's whilst performing a secondary task for 30 seconds. Results showed that individuals administered alcohol performed significantly worse than those in the placebo condition, evidenced by a reduction in the total percentage correct. However, a

problem with this study was that the alcohol group also showed poor performance prior to drug administration. In the verbal working memory task, individuals were required to hold three consonants in memory for 18 seconds whilst engaged in a backward counting task; alcohol did not affect performance. In another study, Weissenborn and Duka (2003) also assessed performance on a spatial working memory task, which required individuals to search boxes presented as spatial arrays in order to collect tokens. Participants were instructed that once a token was found in a box, that box would not be used again. Results revealed that alcohol (0.8g/kg) did not affect the number of errors compared to placebo.

In addition to the number of behavioural studies assessing alcohol-induced impairments in working memory, several studies have used fMRI to examine alcohol related changes in neural activity during working memory task performance. Paulus et al. (2006) compared individuals who showed a low and high response to alcohol during fMRI on a measure of visual working memory. Participants were presented with an array of 2, 4 or 6 coloured dots at random locations on the screen. Following a short delay, an array of coloured dots was presented with the colours being either the same as originally viewed or a single dot differed in colour. Participants were required to respond if the array was the same or different from the original array. They found that alcohol (approximately 0.7g/kg) did not affect error rates or response times. However, alcohol intoxication was found to attenuate working memory load-dependent increases in neural activation patterns in dorsolateral prefrontal cortex and posterior parietal cortex. Trim et al. (2010) used the same visual working memory task to assess alcohol intoxication during fMRI. They found that alcohol impaired performance resulting in a decrease in response accuracy and an increase in misses, although no effect on reaction time was observed. However, the reduction in performance following alcohol was only seen when cognitive demand was higher.

In two studies, Gundersen et al. (2008a; 2008b) assessed working memory performance during fMRI following alcohol (approximately 0.8g/kg) or placebo during an n-back working memory task. Both studies showed no differences between groups, neither in response accuracy nor response latency. However, fMRI

data from one study (2008a) revealed that alcohol reduced neural activity in dorsal anterior cingulate cortex (dACC) and parietal cortex, while a second study (2008b) revealed reductions in dACC following alcohol but only when cognitive load was increased during the task.

Overall, the literature highlights mixed findings of alcohol's effects on working memory. Although studies using fMRI have consistently shown alcohol-induced reductions in brain areas thought to be involved during working memory task performance, these findings do not translate to behavioural results. This may suggest that alcohol-induced impairments in working memory may only become apparent on more sensitive tasks or, as some behavioural evidence suggests, when cognitive demands of the task are higher. Furthermore, it may also be that individuals with lower cognitive resources might demonstrate greater cognitive impairments following alcohol (e.g., Finn et al., 1999).

1.5.6 Non-declarative memory

To date, research investigating the way in which alcohol can affect non-declarative memory is limited. Perceptual priming has received the most attention with a small number of studies exploring alcohol's effects on performance. Priming refers to the facilitation of detecting or processing a perceptual object based on recent experience (Shimamura, 1986; Tulving and Schacter, 1990). Studies investigating alcohol's acute effects on tasks assessing perceptual priming have generally shown that performance seems to be spared. To investigate alcohol's effects on priming, Hashtroudi et al. (1984) presented a list of words to intoxicated and sober individuals. Participants were then shown partially degraded words, which included previously seen words mixed with new words. They found that the alcohol group (0.8g/kg) identified fewer words than the placebo group, irrespective of whether the word to be identified was new or old. However, both groups showed a similar facilitation effect when analysing the difference between old and new words identified suggesting that priming might be spared following alcohol intoxication.

Lister et al. (1991) assessed both a low (0.4g/kg) and moderate dose (0.6g/kg) of alcohol on a word completion task. Participants were presented with a number of words and later received words with three letters missing. Individuals were required to complete the word with the first solution that came to mind. Results revealed that both alcohol groups showed intact priming with no differences in performance compared to placebo. Thus, the intact performance on tasks assessing perceptual priming seems to be consistent throughout the limited literature (e.g., Soderlund et al., 2005).

1.5.7 Neurobiological factors in alcohol-induced amnesia

Alcohol was initially hypothesised to exert its effects on cognition via a global depression of brain function (Wallace, 1932). However, the last few decades have provided evidence that alcohol actually generates selective effects on neural activity, disrupting specific brain structures and related behaviour. Alcohol's primary site(s) of action are thought involve functional alterations to a number of ligand-gated ion channels. In relation to alcohol's ability to disrupt memory, its primary mechanism is thought to involve alterations to GABAergic and glutamatergic neurotransmitter systems. Furthermore, through its neurochemical action, alcohol is thought to suppress hippocampal activity to disrupt memory (White et al., 2000).

1.5.8 Alcohol and the hippocampus

Goodwin et al. (1969) and Ryback (1970) originally proposed that alcohol might affect memory in humans by disrupting the hippocampal formation. This assumption was based on the observation that the acute impairments in memory during alcohol intoxication were similar to those demonstrated by individuals with hippocampal damage. Recently, further research has provided some support for this hypothesis although the specific mechanisms are far from being completely understood (for reviews, see Matthews and Silvers, 2004; White et al., 2000).

A large body of evidence now suggests that the functioning of neurons in the hippocampus is acutely disrupted following alcohol administration (for reviews, see

Matthews and Morrow, 2000; Matthews and Silvers, 2004; White et al., 2000). For instance, acute alcohol intoxication attenuates stress-induced c-fos expression in the rat hippocampus (Ryabinin et al., 1995; 1997). It has recently been shown that alcohol disrupts hippocampal neurophysiology by suppression of pyramidal cells in sub region CA1 (White and Best, 2000). Damage to region CA1 of the hippocampus can elicit severe reductions in explicit forms of memory (Zola-Morgan et al., 1986). Degradation in hippocampal function by alcohol as a mechanism for observed reductions in memory was recently supported in humans through the use of fMRI. Soderlund et al. (2007) found that reductions in episodic memory following alcohol were associated with decreased activity in the hippocampus.

Region CA1 of the hippocampus also plays a crucial role in spatial memory. Hippocampal CA1 neurons have been shown to have preferential firing fields (place fields) for specific locations of an experienced environment (McNaughton et al., 1983; O'Keefe and Dostrovosky, 1971). These hippocampal place cells have been proposed to underlie spatial information processing in memory (O'Keefe and Nadel, 1978). Interestingly, acute administration of alcohol in rodents has been shown to alter the spatial specificity of hippocampal place cells (Alexandrov et al., 1993; Matthews et al., 1996; Matthews et al., 1999).

1.5.9 Alcohol alterations in GABA and memory disruptions

The neurotransmitter GABA acts as the brain's major inhibitory system. Many of alcohol's behavioural effects are generated via its action on the GABAergic neurotransmitter system with anxiolytic, sedative-hypnotic, cognitive-impairing, and anticonvulsant properties (Frye et al., 1982; Givens and McMahon, 1997). Alcohol enhances GABA mediated inhibition at some subtypes of GABA_A receptors at low doses, whereas other subtypes are modulated at higher doses (for reviews, see Grobin et al., 1998; Kumar et al., 2009). Alcohol's GABA-enhancing action is found at low doses (<0.1 g/l), although at higher doses (>0.25 g/l) it has a direct action on the receptor and can cause prolonged opening of the ion channel that is independent of GABA (Ticku et al., 1992).

Several studies have shown that acute alcohol administration enhances GABA mediated inhibition in the hippocampus (e.g., Wan et al., 1996; Weiner et al., 1994). Furthermore, acute alcohol intoxication increases brain concentration of the neuroactive steroid alloprenanolone (a potent GABA_A receptor agonist) in a dose-dependent manner and its blockade has been shown to prevent many of alcohol's debilitating effects (van Doren et al., 2000). Acute administration of alloprenanolone has been shown to inhibit hippocampal pyramidal cells supporting the role of GABA alterations on hippocampal function by alcohol (Silvers et al., 2003). Further evidence of the role of GABA as a mechanism for alcohol induced memory deficits is provided by studies investigating memory function following administration of other GABA agonists. In humans, acute administration of a benzodiazepine has been shown to induce similar impairments in memory function (for a review, see Curran, 1991).

Several authors have focussed on alcohol's ability to alter GABA mediated inhibition as a potential mechanism to attenuate alcohol-induced deficits. For instance, Cook et al. (2005) found that administration of a selective GABA α 5-subtype inverse agonist attenuated some of alcohol's effects on reward and sedation in rats. Nutt et al. (2007) examined the effects of a pre-treatment of a GABA α 5-subtype inverse agonist prior to receiving alcohol on memory function in humans. Pre-treatment with the inverse agonist was found to significantly reduce alcohol's disruptive effect on memory for a word list. The hippocampus contains a high density of α 5-subtype-containing receptors (Fritschy and Mohler, 1995; Lingford-Hughes et al., 2002) and therefore highlights the role of GABA related alterations that may underlie at least part of alcohol's ability to disrupt memory.

1.5.10 Alcohol alterations in glutamate/NMDA and memory disruptions

Glutamate forms part of the brain's major excitatory neurotransmitter system. Acute alcohol acts to antagonise activity at the NMDA receptor at concentration above 0.1 g/l, thus opposing the effects of glutamate (Lovinger et al., 1989). The hippocampus contains a high density of NMDA receptors, which play an essential role in long-term potentiation LTP and the formation of new memories (Collingridge and Bliss,

1995). Alcohol has been shown to inhibit the induction of LTP (Blitzer et al., 1990; Givens and McMahon, 1995), disrupt hippocampal theta rhythm activity (Givens, 1995), and generate memory deficits similar to those following hippocampal lesions (see Matthews and Silvers, 2004). In addition to antagonising NMDA receptor activity, alcohol also reduces the overall level of glutamate released at synapses within the hippocampus (Reynolds and Brien, 2003; Shimizu et al., 1998).

NMDA receptor activity is crucial in allowing calcium into the cell, which triggers long lasting changes in both the structure and function of the cell. Alcohol is proposed to disrupt LTP induction through antagonism of NMDA2 receptor activation therefore preventing an influx of calcium into the cell that would potentiate cell-related changes (Kalluri et al., 1998). It has also been demonstrated that, in addition to the observation that alcohol readily blocks the induction of NMDA-dependent LTP, it does not block its expression (Blitzer et al., 1990). Furthermore, acute alcohol has been shown to enhance long-term depression (LTD; Hendrierson et al., 2002). In humans, drugs that block NMDA receptor activity such as ketamine have been shown to disrupt memory in a similar way to alcohol (for a review, see Morgan and Curran, 2007).

1.6 Acute effects of alcohol on trauma memories

Having reviewed the literature firstly on PTSD and trauma memory and secondly on the acute effects of alcohol upon human memory, I hope the stage is now set for the main focus of this thesis. The research reviewed in this chapter outlines a distinct set of memory-related deficits in individuals diagnosed with PTSD with reductions in voluntary / declarative memory for the traumatic event. Further, a hallmark symptom of PTSD involves the repeated involuntary memories, or intrusions, that are triggered by cues matching those experienced at the time of the traumatic event. Theoretical accounts and empirical evidence have been particularly influential in attempts to try and elucidate the specific mechanisms that might underpin these distressing and fear provoking memory intrusions. Although the precise terminology and systems proposed by such accounts are heavily debated, most clinical theories agree that as a result of the traumatic event, declarative memory for the event is

impaired, whereas image-based sensory / perceptual features are preserved although not under conscious control.

It is extraordinary given that alcohol is so often implicated in road traffic accidents, rape and violent assaults that virtually no research has yet investigated the way in which acute alcohol intoxication may impact upon trauma memory. The literature reviewed in this chapter has outlined the way in which an acute dose can affect memory processes. That is, declarative memory is robustly impaired, with observed decreases in episodic memory encoding following an acute dose. However, other memory processes, including recognition based on perceptual features and non-declarative memory, are unaffected. Given that reductions in declarative memory and enhanced encoding of perceptual characteristics of a traumatic episode are thought to contribute to the development of intrusive memories, it is expected that alcohol intoxication during a traumatic experience might result in an increase in intrusive imagery. This is the major purpose of the studies which comprise this thesis.

In the next chapter, an empirical study is reported in which the effects of three doses of alcohol (0.4, 0.6, 0.8 g/kg) on recollective experience are examined. This informed the choice of doses which were used in the two subsequent studies of the acute effects of alcohol on trauma memory (Chapter 3) and on trauma memory and viewpoint dependence in spatial memory (Chapter 4). A fourth empirical study (Chapter 5) focussed on viewpoint dependence in spatial memory and contextual fear memory. Finally the General Discussion (Chapter 6) integrates this thesis' findings and draws out their implications both clinically and for future research.

Chapter 2: Acute Effects of Alcohol on Recollection: A Dose-response Study

2.1 Overview

Alcohol can have a wide range of debilitating effects on cognition (e.g., Abrams et al., 2006; George et al., 2005; Hernandez et al., 2006; Schweizer and Vogel-Sprott, 2008; Schweizer et al., 2006; Weissenborn and Duka, 2003). In particular, memory processes following acute intoxication are of key interest because some aspects of memory performance are impaired while others are unaffected. Episodic memory deficits following acute alcohol have robustly been demonstrated (Curran and Hildebrandt, 1999; Leitz et al., 2009; Soderlund et al., 2007), whereas perceptual priming, the enhanced identification of perceptual objects due to prior experience (Tulving and Schacter, 1990), is typically left intact (Hashtroudi et al., 1984; Lister et al., 1991). The aim of the present study was to further elucidate alcohol's impairing effects on memory through contrasting three different doses of alcohol on recognition memory performance. Through addressing this research question, a specific dose(s) would be identified to examine alcohol's effects on trauma memory in the experiments to follow.

2.2 Introduction

Converging evidence shows that recognition of a previously experienced item reflects two distinct memory processes, namely recollection and familiarity (for a review, see Yonelinas, 2002). Recollection involves consciously remembering the specific details of an experience, such as when and where an item was encountered (Mandler, 1980) and is considered a defining characteristic of episodic memory (Tulving, 1983; 1985). In contrast, familiarity reflects the recognition of an item based on a feeling of 'knowing' alone, thus lacking the distinct qualitative richness experienced during recollection. It has also been suggested that if recollection and familiarity involve separate aspects of memory, they should be anatomically dissociable, with each process reliant on different brain regions and neural

mechanisms (for a review, see Rugg and Yonelinas, 2003). On one hand, the hippocampus is proposed as a critical structure in the storage and retrieval of the distinct recollective aspects that contribute to recognition memory, whereas, on the other hand, the adjacent medial temporal cortex, specifically the perirhinal cortex, supports recognition based on familiarity (see Aggleton and Brown, 1999; Brown and Aggleton, 2001; but see Manns et al., 2003 and Wixted and Squire, 2004 for an opposing view).

According to Tulving (1985), recollection and familiarity can be behaviourally dissociated by indexing an individual's subjective experience during recognition. Specifically, individuals are required to give a 'remember' response if, on recognition, they recollect specific contextual details of the encoding experience, or to give a 'know' response if recognition is solely based on a feeling of familiarity (also see Jacoby, 1991; Yonelinas, 2002; Yonelinas and Jacoby, 1995; Yonelinas et al., 1998 for a series of extended methods to dissociate recollection and familiarity). Despite proposals that 'remember' and 'know' responses reflect differences in memory strength and confidence ratings rather than two dissociable processes (Donaldson, 1996), studies using the remember-know procedure have yielded considerable empirical support (for a review, see Gardiner, 2009). In addition to the proposal that recollection and familiarity involve distinct neural processes, specific evidence has shown that 'remember' and 'know' responses can be dissociated in terms of neural activity (e.g., Henson et al., 1999; Rugg et al., 1998). Furthermore, patients with hippocampal pathology show selective deficits in 'remember' but not 'know' responses compared to healthy controls (Turriziani et al., 2008).

Research investigating alcohol's acute effects on memory has shown a range of effects of impaired recall in both laboratory (Leitz et al., 2009) and naturalistic (Moore et al., 2007) environments. A slight facilitation effect on memory has even been shown when alcohol is consumed following the encoding of to-be-remembered information (Parker et al., 1981). In relation to recognition memory, research has generated a number of contrasting findings. Some studies have shown alcohol-induced impairments in recognition memory while others have not (see Chapter 1.5 for a review). Importantly, studies that have not shown any impairment in

recognition memory have typically used word recognition tasks that require individuals to acknowledge whether a word at test is new or old. Recognition judgments within these tasks can be solved based solely on familiarity in the absence of recollection. However, studies that have used a procedure that requires participants to recollect the experience at test have consistently demonstrated a reduction in recognition memory following alcohol. In particular relevance to the remember-know procedure, Curran and Hildebrandt (1999) showed that alcohol selectively impaired recognition associated with recollection, whereas recognition based on familiarity was left intact.

Although cognitive deficits are regularly observed following acute alcohol intoxication, few studies have purposely examined the way in which alterations in dose might contribute to its detrimental effects (cf. Kano et al., 2003). In relation to assessing alcohol's dose-dependent effects on recognition memory, a number of parallels can be drawn from drugs that share alcohol's neurochemical action. Lorazepam is a benzodiazepine, which, like alcohol, facilitates gamma-aminobutyric acid (GABA) neurotransmission in the brain. Recognition memory performance following lorazepam shows a similar pattern of results to the one observed in alcohol, with selective impairments in recollection but intact recognition based on familiarity (Bishop and Curran, 1995; Curran et al., 1993). Huron et al. (2002) investigated the dose-dependent effects of lorazepam on recognition memory through use of the remember-know procedure. They found that lorazepam decreased recognition associated with recollection in a linear fashion, as measured by 'remember' responses, with further decrements as dose increased, whilst recognition based on familiarity, as measured by 'know' responses, showed no reductions compared to a placebo group. Alcohol's effect on memory also relies on its capacity to block *N*-methyl-D-aspartate (NMDA) receptors. Hetem et al. (2000) found that the NMDA antagonist ketamine produced a more global impairment of recognition memory with reductions in both 'remember' and 'know' responses.

The present study aimed to further investigate alcohol's ability to impair aspects of recognition memory across three increasing doses of alcohol: a low dose (0.4 g/kg), a moderate dose (0.6 g/kg), and a high dose (0.8 g/kg). Recognition memory was

indexed through use of the remember-know procedure. It was expected that alcohol would selectively impair recognition memory associated with recollection while recognition based on familiarity would show no difference from the placebo condition. In relation to dose-dependent effects, we predicted that, like lorazepam, increasing doses of alcohol would decrease recognition memory associated with recollection in a linear fashion, and recognition based on familiarity would show no dose-response relationship. In addition, it was also important to examine the dose-related responses of alcohol on dissociable components of memory that may relate to the storage of traumatic material to be assessed in the forthcoming Chapters. For example, the dual processing accounts of memory described above on recollection and familiarity (Yonelinas and Rugg, 2003) bear distinct similarities to dual processing theories of intrusive memory highlighting contextual and perceptual memory systems (e.g., Brewin, 2001; Brewin et al., 2010). Assessing these particular memory characteristics may provide further insight into the way in which alcohol may affect trauma memory and the specific cognitive mechanisms involved.

2.3 Method

2.3.1 Participants

Sample size was determined in advance. A power calculation indicated that for a significance level of $p < 0.05$ and a power of 80%, a sample size of 18 in each group was required. The current study recruited a total of sixty-eight volunteers (34 males and 34 females). Participants were recruited via advertisement from the undergraduate and postgraduate population at University College London. The study was carried out in accordance with the Declaration of Helsinki and was approved by the UCL ethics committee (see appendices). Participants gave written, informed consent prior to taking part. Inclusion criteria included that participants were aged 18 – 35 and were moderate social drinkers (average weekly consumption of 2-14 units for females and 2-21 units for males). The CAGE (Ewing, 1984) alcohol screening questionnaire was administered to assess individuals for problematic drinking and participants who scored 2 or more (out of 4) were excluded from taking

part. Participants were also administered an initial breathalyser to check they had not consumed any alcohol prior to taking part in the experiment.

2.3.2 Design

An independent group design was used whereby male and female participants were randomly assigned to one of four conditions; a placebo beverage, a low, moderate or high dose of alcohol.

2.3.4 Alcohol administration

Participants were administered either alcohol (0.4 g/kg, 0.6 g/kg or 0.8 g/kg) or a matched placebo beverage. Participants were aware they would receive one dose of alcohol or placebo. The alcohol beverage consisted of 90% v/w alcohol diluted with tonic water (Schweppes Ltd., Uxbridge, UK), equally divided into 10 x 50ml portions and then mixed with two drops of Tabasco sauce (McIlhenny Co., Avery Island, Louisiana, USA) to mask the taste of alcohol. The placebo beverage consisted of 10 x 50ml portions of tonic water and Tabasco sauce only. All participants were requested to consume the 10 beverages at 3 minute intervals, giving a total 30 minute consumption period.

2.3.5 Procedure

On arrival at the laboratory, participants filled out the alcohol usage questionnaire and mood rating scale. They then received the beverages, which were consumed over the 30-min period. An extra 10 mins passed after consuming the last beverage to allow alcohol to be readily absorbed into the blood. Participants next filled out another post drink mood rating scale and a breathalyser was administered. They were then given the encoding phase of the remember-know. The time taken to complete the encoding phase of the experiment was approximately 10mins, within the ‘alcohol window’ for testing (see Rose and Duka, 2006). Participants performed a recognition task on the words they had encoded and were required to acknowledge each answer with a ‘remember’, ‘know’ or guess response in accordance with the

remember-know procedure. Finally, participant and experimenter were asked to guess on which treatment they thought had been consumed during the session.

2.3.6 Alcohol usage

The Alcohol Usage Questionnaire (Mehrabian and Russell, 1978) is a 12-item questionnaire designed to provide an accurate measure of individuals' habitual alcohol drinking habits (see appendix). Factors include the amount of wine, beer and spirits consumed in a typical week and the speed of drinking. The final 3-items were taken as a separate total to give a score for binge drinking (Townshend and Duka, 2001).

2.3.7 Subjective measures

Two visual analogue scales were used to record subjective feelings of mood 'at the moment' and to assess any adverse effects from alcohol administration. The two scales were presented with 100mm lines anchored with antonyms at each end of the scales (attentive-dreamy and drowsy-alert).

2.3.8 Remember-Know

Ninety-six word pairs were used in the study, which were opposites and the same word pairs as used by Curran and Hildebrandt (1999). In the read condition word pairs were presented in full (e.g., NORTH – SOUTH) and in the generate condition the first letter of the second word was presented (e.g., NORTH – S_____). All pairs were randomly divided into four study lists with half of each list designated to a generate condition and the other half to the read condition. All four lists were then reversed so all word pairs in the generate condition were changed to a read condition and read word pairs became generate word pairs. Therefore, eight study lists were produced with four different sets of word pairs and each response word appeared once in a generate condition and once in a read condition.

Participants were instructed that the rule for the word pairs was ‘opposites’ and that they were required to say the second word of each pair aloud. They were informed that some of the pairs would be written in full and that some of the pairs would be presented with only the first letter of the second word. They were told to try and remember each word they said out loud as their memory for these words would be tested. Each word pair was presented one at a time on a computer screen and participants were given 5 seconds to study the word after saying it. The recognition task consisted of 24 studied response words randomly mixed with another 24 lure words taken from the 96 word pairs. Target words and lure words were yoked across groups and within each group target words for half the participants and lure words for the other half. Word lists were counterbalanced across groups. During test, participants were instructed to indicate, from the list of 48 words, which words they had previously seen by circling each one. For each item recognised, they were asked to indicate whether they remembered (R), Knew (K) or guessed that the word was from the study list.

Participants were fully instructed on the distinction between the ‘remember’, ‘know’ and ‘guess’ responses prior to the start of the experimental procedure. They were told that a ‘remember’ response should be given if on recognition they became aware of some aspect of what happened or what they experienced when they originally saw the word. A ‘know’ response should be given if they were able to recognise the word but were not consciously able to recollect any specific details about the original encoding episode. The distinction was further illustrated through the use of an example and it was made clear that remember-know judgments were not a rating of confidence. Finally, participants were instructed to give a ‘guess’ response if they were uncertain of whether they had seen the word. After the recognition test was completed, participants were asked to explain the reason for which they had marked one of the words as ‘remember’ and one as ‘know’ to confirm that they used the appropriate reasoning behind their answers.

2.3.9 Statistical analysis

Data were checked for univariate outliers and as none were beyond 2.5 standard deviations, the original dataset was used. All statistical analyses were performed using SPSS version 14. One participant was omitted from analyses as when asked to define their use of ‘remember’ and ‘know’ responses they were unable to show a complete understanding of the distinction. Where data violated assumptions of normality, Kruskal-Wallis tests were used. Groups were first assessed on the total number of items correctly recognised using a 4 x 2 repeated measures ANOVA with group as a between participant factor (placebo, low, moderate, high dose) and processing (generate and read) as a within participants factor. To establish specific treatment effects on each aspect of recollective experience, separate 4 x 2 ANOVAs were performed on ‘remember’ and ‘know’ responses with group as a between factor and processing as a within participant factor. As we expected impairments in memory performance to decrease in a dose-dependent fashion, polynomial trend analyses to test for proportionate changes in the group means as dose increased were carried on both ‘remember’ and ‘know’ responses. Post hoc analyses were corrected using Bonferroni correction with adjusted p-values where applicable or, in the case of analyses using the Kruskal-Wallis test, individual planned comparisons were performed using Mann-Whitney *U* tests. Data were also analysed using a signal detection method, however, due to the low distribution of false alarm rates across groups results were confounded and thus are not reported.

2.4 Results

2.4.1 Demographics

There were no group differences in the number of years spent in education [$F(3,67) = .73, p = .54$], alcohol usage score [$F(3,67) = 0.25, p = .86$] or alcohol usage binge score [$F(3,67) = .44, p = .73$]. Age showed a group difference approaching significance [$F(3,67) = 2.33, p = .08$] although any observable age differences were small (Table 2.1).

Table 2.1. Means \pm standard deviations of demographic data across the four treatment groups.

	Placebo (N=15)	Low dose 0.4 g/kg alcohol (N=16)	Moderate dose 0.6 g/kg alcohol (N=20)	High dose 0.8 g/kg alcohol (N=16)
Age (years)	24.88 \pm 3.98	25.06 \pm 3.42	25.30 \pm 3.44	22.56 \pm 2.53
Years in education	16.31 \pm 1.99	16.25 \pm 1.84	16.00 \pm 1.59	15.50 \pm 1.46
AUQ score	34.19 \pm 14.89	33.71 \pm 18.80	36.51 \pm 24.53	39.31 \pm 21.30
AUQ binge score	21.69 \pm 9.96	22.71 \pm 16.33	24.51 \pm 18.89	27.75 \pm 16.79

2.4.2 Blood alcohol concentration

Blood alcohol concentration (BAC) levels after the alcohol consumption period are shown for the three alcohol groups in Table 2.2. Analysis of BAC levels revealed a significant difference between alcohol groups on BAC levels [$\chi^2(2) = 24.82, p < .001$]. Independent group comparisons (Bonferroni correct alpha of .017) revealed significant differences between low dose and moderate dose groups [$U = 81.50, p = .012$], low dose and high dose groups [$U = 1.50, p < .001$] and moderate dose and high dose [$U = 65.50, p = .003$].

Table 2.2. Means \pm standard deviations and ranges of blood alcohol concentration (BAC; g/l) levels across three alcohol groups following beverage consumption.

	Low dose 0.4 g/kg (N=16)		Moderate dose 0.6 g/kg (N=20)		High dose 0.8 g/kg (N=16)	
	Mean	Range	Mean	Range	Mean	Range
BAC	0.33 \pm 0.09	0.14 – 0.48	0.59 \pm 0.21	0.12 – 0.92	0.74 \pm 0.17	0.46 – 0.99

2.4.3 Manipulation check

As participants had no measure to compare their guess on different doses of alcohol, data were analysed on whether participant and experimenter guessed placebo or

alcohol. Analysis of participants' guess on which treatment they had received showed no significant difference between correct and incorrect guesses for the placebo group [$\chi^2 = .07, p = .80$] with participants guessing correctly 53.30 percent of the time, confirming that the double-blind procedure was effective. Analysis of alcohol groups showed that participants in the low dose [$\chi^2 = 9.00, p = .003$], moderate dose [$\chi^2 = 7.20, p = .007$] and high dose [$\chi^2 = 22.25, p < .001$] guessed correctly the majority of the time. Analysis of experimenter's guess on treatment showed no significant difference between correct / incorrect guesses for placebo [$\chi^2 = 1.67, p = .20$] with the experimenter guessing correctly 66.30 percent of the time. Experimenter guesses on alcohol groups showed significant differences between correct / incorrect guesses for low dose [$\chi^2 = 9.00, p = .003$], moderate dose [$\chi^2 = 9.80, p = .003$] and high dose [$\chi^2 = 9.00, p = .003$] with the experimenter guessing correctly the majority of the time.

2.4.4 Overall recognition memory

See Table 2.3. Analysis of the overall proportion of correctly recognised items showed a significant main effect of group [$F(3,63) = 6.16, p = .001, \eta^2 = 0.20$] and processing [$F(1,63) = 68.93, p < .001, \eta^2 = 0.51$] but no group x processing interaction [$F(3,63) = .46, p = .71$]. Both the moderate and high doses of alcohol were found to impair the recognition memory compared to the placebo group ($p = .03$, with Cohen's $d = 0.88$ and $p < .001, d = 1.6$, respectively; Cohen (1988) defines effect sizes of 0.2 as small, 0.5 as medium and 0.8 as large). A generate effect was observed in processing with individuals correctly recognising a higher proportion of words in the generate condition than in the read condition. Linear effects across treatment groups with further reductions as alcohol dose increased were confirmed following trend analyses for overall recognition [$F(1,63) = 16.45, p < .001$] and both generate [$F(1,63) = 10.97, p = .002$] and read conditions [$F(1,63) = 11.63, p = .001$]. The number of false alarms was low and analysis showed no significant difference between treatment groups ($F(3,63) = 1.89, p = .14$).

Table 2.3. Means \pm standard deviations of the proportion of items correctly recognised and the number of false alarms across treatment groups.

	Placebo (N=15)	Low dose 0.4 g/kg alcohol (N=16)	Moderate dose 0.6 g/kg alcohol (N=20)	High dose 0.8 g/kg alcohol (N=16)
Generate	0.82 \pm 0.16	0.75 \pm 0.21	0.66 \pm 0.21	0.59 \pm 0.24
Read	0.62 \pm 0.24	0.46 \pm 0.22	0.44 \pm 0.29	0.32 \pm 0.16
Guess	0.09 \pm 0.09	0.04 \pm 0.05	0.09 \pm 0.14	0.07 \pm 0.09
False alarms	0.67 \pm 0.89	1.44 \pm 2.22	0.55 \pm 0.89	1.75 \pm 2.49

2.4.5 Remember – Know

See Figure 2.1. Guess responses during the recognition task were at floor level and thus were omitted from the analysis. Analysis of ‘remember’ responses showed significant main effects of group [$F(3,63) = 2.78, p = .048, \eta^2 = 0.12$] and processing [$F(1,63) = 66.77, p < .001, \eta^2 = 0.52$] but no group x process interaction [$F(3,63) = .25, p = .87$]. Trend analysis confirmed a linear reduction across treatment groups [$F(1,63) = 9.31, p = .03$] with the proportion of ‘remember’ responses decreasing as alcohol dose increased. Participants were also found to correctly recognise more items encoded in the generate condition compared to the read condition.

Analysis of ‘know’ responses showed no significant main effects of group [$F(3,63) = .94, p = .47$], processing [$F(1,63) = .35, p = .56$] or interaction of group x processing [$F(3,63) = .85, p = .42$]. Polynomial trend analysis also showed no linear effects of recognition associated with ‘know’ responses across treatment group [$F(1,63) = 2.43, p = .12$].

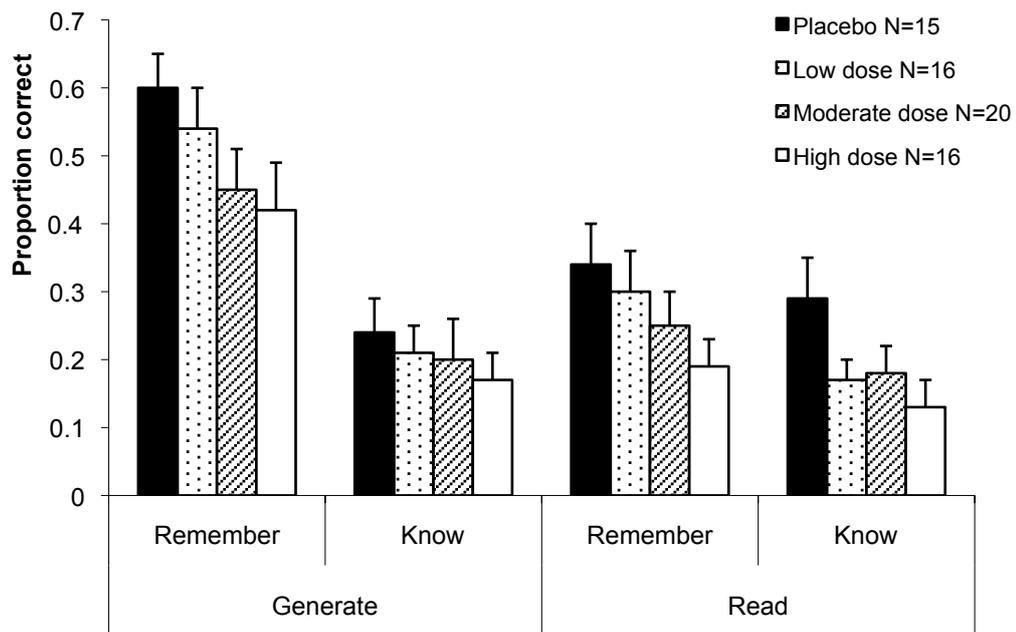


Figure 2.1. Means (SEM) proportion of correct responses as a function of generate/read and remember/know conditions across all treatment groups.

2.4.6 Relationship between BAC levels and memory measures

To investigate effects BAC levels on memory, all alcohol groups were correlated with memory measures. Increases in BAC levels were found to inversely correlate with the total number of items correctly recognised [$r(52) = -.36, p = .01$]. ‘Know’ responses to correctly recognised items and BAC levels were also found to be negatively correlated [$r(52) = -.32, p = .02$], while no relationship was observed between BAC levels and ‘remember’ responses [$r(52) = -.14, p = .33$]. Analyses of both generate and read conditions showed a negative relationship between read items and BAC levels [$r(52) = -.36, p = .01$], while BAC levels and generate items showed a tendency to be correlated [$r(52) = -.24, p = .08$] with increases in BAC levels associated with decreases in performance.

2.4.7 Subjective measures

A repeated measures ANOVA of drowsiness ratings showed a significant main effect of time [$F(1,64) = 52.79, p < .001$] but no main effect of group [$F(3,64) =$

1.73, $p = .17$] or group x time interaction [$F(3,64) = .74$, $p = .74$]. Results showed that drowsiness ratings increased from pre (23.03 \pm 18.49) to post drink (42.59 \pm 21.55) administration. Analysis of attentive-dreamy ratings revealed a significant main effect of time [$F(1,64) = 29.83$, $p < .001$] and a trend of a group main effect [$F(3,64) = 2.60$, $p = .06$] but no group x time [$F(3,64) = 1.15$, $p = .34$]. Dreamy ratings increased from pre (25.56 \pm 20.68) to post drink (42.20 \pm 24.26) administration.

2.5 Discussion

The present study aimed to investigate the acute effects of alcohol on recognition memory and the way in which increases in dosage may further contribute to reductions in memory performance. With increasing alcohol dose, there was a linear reduction in recollection associated with recognition memory, evidenced by ‘remember’ responses. In contrast, no dose-dependent pattern of impairment was evident on recognition associated with familiarity with ‘know’ responses unaffected by alcohol.

2.5.1 Alcohol-induced impairments in Memory

This is the first demonstration of a dose-dependent reduction in episodic memory following alcohol administration across three increasing doses. Indeed, studies with humans comparing three doses of any drug are surprisingly rare. The alcohol-induced impairment in recollection, with familiarity left intact, is in accordance with previous studies utilising a similar paradigm to the one used here (e.g., Curran and Hildebrandt, 1999). Given that recollection is a defining characteristic of episodic memory, encapsulating ‘autonoetic consciousness’ (Tulving, 1983; 1985), the observed reduction in recollection is consistent with a large body of evidence showing episodic memory deficits following acute alcohol intoxication (Leitz et al., 2009; Ray and Bates, 2006; Soderlund et al., 2007). The observed reduction in recollection following increases in alcohol dose suggests that episodic memory impairments are dose-dependently sensitive to alcohol-induced impairments. The

observed pattern of results on episodic memory is reminiscent of the effects of drugs like lorazepam (Huron et al., 2002), which shares alcohol's GABAergic effects.

Regarding overall recognition memory irrespective of the conscious awareness during retrieval, the moderate and high doses of alcohol decreased the number of items correctly recognised compared to the placebo group. A linear trend was also observed across treatment groups although it may be, in part, driven by the specific effect on 'remember' responses. Despite this overall recognition memory deficit, the selective linear decrease in recollection following alcohol provides further clarity to studies showing contrasting effects on recognition memory (e.g., Curran and Hildebrandt, 1999; Goodwin et al., 1969; Hashtroudi et al., 1984; Ray and Bates, 2006). Specifically, these findings suggest that alcohol may not impair the ability to recognise previously encoded items per se: the decision of whether an item is 'new' or 'old' can indeed be successfully achieved by familiarity (know responses) alone. In contrast, it would seem that alcohol preferentially reduces the encoding of the qualitative aspects of an event that contribute to the recollective experience during recognition. The results presented here, along with previously reported contrasting findings on recognition memory deficits following alcohol (e.g., Goodwin et al., 1969; Hashtroudi et al., 1984; Maylor et al., 1987; Ray and Bates, 2006), highlight the importance of examining the subjective awareness associated with recognition memory in alcohol studies.

The results concerning the correlation analysis performed on alcohol intoxication levels and associated reductions in memory are of particular interest. While reductions in recollection were found to be a function of the alcohol dose consumed, recognition based on familiarity showed an inverse relationship with intoxication levels, measured through BAC. Although such decreases in familiarity were small, it might be that such impairments might become more apparent at higher doses. This proposal would be consistent with a more prominent NMDA antagonistic effect at high alcohol doses (e.g., Krystal et al., 2003) and similar global decreases in recognition memory as observed following other NMDA antagonists, such as ketamine (Hetem et al., 2000).

Irrespective of treatment group, our results replicate previous findings that recognition with conscious recollection can be affected by manipulations in the levels of processing at encoding (Gardiner et al., 1998). Individuals were found to recognise more items associated with conscious recollection when they were encoded during a generate condition compared to a read condition. This increase in recollection was not evident in recognition based on familiarity. This generation effect, through a deeper level of processing, is associated with the generation of a more elaborate, longer lasting, stronger memory trace (Craik and Lockhart, 1972). Our results also further support the literature that recollection and familiarity can be experimentally dissociated (see Gardiner, 2009; Gardiner et al., 1998; Rajaram and Roediger, 1994). Our findings further highlight the relevance of the use of pharmacological manipulation in the investigation and dissociation of memory processes (e.g., Bishop et al., 1995; Curran et al., 1993; Sunram-Lea et al., 2008).

2.5.2 Mechanisms for alcohol-induced impairments

The finding that alcohol decreases recollection provides support to the proposal that alcohol may induce its amnesic qualities through specific alterations in hippocampal function (e.g., Matthews and Silvers, 2004; Soderlund et al., 2007; White et al., 2000). Given the specific role of the hippocampus in recollection (e.g., Aggleton and Brown, 1999; Brown and Aggleton, 2001), alcohol may down-regulate hippocampal function through a range of neurochemical interactions. These include alterations in GABA-mediated inhibition and acute blockade of NMDA activity, thus leading to a decrease in long-term potentiation. Interestingly, alcohol may primarily engage different neurotransmitter systems as the level of intoxication increases. Low doses may principally act on GABA_A receptors, whereas high levels of intoxication lead to a more prominent antagonism of NMDA receptors (Krystal et al., 2003). At higher doses, alcohol might produce more global effects on recognition similar to those observed following ketamine (e.g., Hetem et al., 2000). It is therefore possible that the neurochemical mechanisms following alcohol intoxication differentially contribute to alcohol's amnesic qualities at different levels of intoxication.

2.4.3 Limitations

Although the current findings provide strong results in relation to alcohol's ability to affect memory processes, there are also limitations to consider. One methodological criticism concerns the distinct categorisation of memory processes and the reliance placed on an individual's interpretation of the characteristics relating to 'remember' and 'know' responses. For example, changing the specific instructions given to participants as part of the 'remember-know' procedure has been shown to influence related responses (Geraci et al., 2009). Furthermore, some have argued that, rather than two dissociable systems, 'remember' and 'know' responses actually reflect different levels of confidence attributed to the remembered item on the task of recognition, termed a signal detection approach (e.g., Donaldson, 1996; Dunn, 2004). However, to perform the specific statistical tests required to assess signal detection theory, false alarm rates of recognition must be included (see Green and Swets, 1966). Unfortunately, false alarm rates in the current study were at floor level and, therefore, this analysis could not be carried out.

2.5.4 Conclusion

In conclusion, this is the first study to purposefully plot alcohol-induced impairments in human memory over a range of doses and within the parameters of the same task. The findings show that recognition memory is impaired following intoxication through alcohol and that specific effects on recollection are driving such decrements. Our findings also highlight the fact that alcohol-induced reductions in memory occur in a dose-dependent manner. Interestingly, the correlation between blood alcohol concentration and recognition based on familiarity suggests that alcohol may exert more global effects on memory as dose the level of intoxication increases. Such global reductions in memory may only be detectable at higher doses than those reported here. On the basis of the dose-dependent effects of alcohol on recollection found in this study, doses of 0, 0.4 and 0.8 g/k were selected to provide maximum contrast for the studies of trauma memories reported in the following two chapters.

Chapter 3: Acute Effects of Alcohol on Intrusive Memories

3.1 Overview

Alcohol is a frequent factor in real life trauma including rape, violent assault and road traffic accidents. However, to date no research has examined how alcohol may interact with processes during a traumatic event and specifically how alcohol may contribute to both the development and maintenance of PTSD following a traumatic event. As discussed in Chapter 1, PTSD is a condition that may occur following an event that is both overwhelming to the individual and typically involves actual or threatened death or injury. Following a traumatic event, a hallmark symptom of PTSD is the repeated involuntary intrusive memories of the event itself (Brewin, 2001; Brewin & Holmes, 2003). Despite these ongoing disruptions in memory following trauma, not all individuals go on to develop PTSD. Prominent theories have identified a number of risk factors that may be involved in both the development and maintenance of PTSD. These include background factors that may increase an individual's vulnerability, changes in peritraumatic processing that may cause alterations in how the event is processed and represented within memory, and a number of post trauma processes that may contribute to the continuation of the disorder. Although these broad ranges of risk factors all play an important role, recent accounts have focused on the cognitive processes involved during the event (e.g., Brewin, 2001; Brewin et al., 1996; Ehlers & Clark, 2000). Particularly, these theories have identified how changes in cognitive processing may disrupt representation of the event within memory and thus increase the ongoing memory intrusions that are a primary symptom of PTSD.

The main aim of the present experiment was to investigate how alcohol may influence both peritraumatic processing during the encoding of a stressful event and the subsequent development of intrusive memories in the following week. A stressful film paradigm provides an analogue method to examine intrusive memories within a laboratory-based environment. This method requires participants to watch a

stressful film and keep a diary for the following week, detailing any times that they experience memory intrusions. A number of studies have employed this methodology, using both correlational and experimental designs, to investigate intrusive memory development (for a review, see Holmes & Bourne, 2008). Manipulations in processing during the encoding of the stressful film have been successful in both increasing and decreasing memory intrusions. Holmes et al. (2004) carried out an influential study on intrusive memories by manipulating visuo-spatial processing during encoding of a stressful film. They found that individuals who carried out a secondary visuo-spatial task while viewing a stressful film showed a decrease in the number of memory intrusions in the following week compared to controls. In a second manipulation, a verbal interference task was found to increase the number of intrusions compared to a no task control. As described in detail (Chapter 1.4.7), Holmes et al. proposed that these findings support a dual processing account of intrusive memory development rather than a distraction hypothesis that would predict a reduction in intrusive memories following a secondary concurrent task during trauma encoding. They argued that the visuo-spatial tapping task might compete for similar cognitive resources that would be required to generate image-based representations of the event. Therefore, intrusive memories were decreased using a visuo-spatial concurrent task due to reduction in available cognitive resources needed to produce visual imagery. In contrast, the verbal inference task impaired the ability to encode conceptual characteristics of the experience that would form an individual's verbal reports of the event. These conceptual aspects are proposed to inhibit involuntary retrieval of trauma memories (e.g., Brewin, 2001; Brewin et al., 2010; Ehlers and Clark, 2000). Therefore, the selective impairment in these processes resulted in an over-representation of related imagery and a reduction in the ability to suppress involuntary retrieval of the traumatic footage.

3.2 Introduction

Theoretical accounts of the way in which these manipulations contribute to changes in intrusive memory development have highlighted the amount of conscious processing that the event receives and how it is represented within memory. These accounts have been described in detail in Chapter 1.4. The dual-representation

theory (Brewin et al., 1996; Brewin, 2001; Brewin et al., 2010) emphasises a multiple component memory system whereby two separate systems work in parallel, processing different aspects of the event. Information that is consciously processed is stored as a contextual memory representation (C-rep), which integrates information within an individual's autobiographical memory. These memories form the basis of individuals' verbal reports of the event, which can be easily recalled and communicated to others. Information that does not receive high levels of conscious processing is processed as a sensory memory representation (S-rep), primarily consisting of sensory information, especially visuo-spatial information, in the form of images.

A neuropsychological basis for the differences in memory representations proposed in relation to the dual representation theory emphasises how changes in stress-hormones may alter processing via the hippocampus (Brewin, 2001; Brewin et al., 2010). In addition to playing an essential function in the initial storage of declarative memory (Squire & Zola-Morgan, 1991), the hippocampus is thought to be particularly sensitive to increases in stress due to its high concentration of glucocorticoid receptors and role in providing glucocorticoid-mediated negative feedback to support inhibition of the HPA (Kim & Diamond, 2002). Increases in cortisol release following extreme or prolonged stress is proposed to down regulate hippocampal function (McEwen, 1999) and has been shown to reduce declarative memory for an experience in humans (Kirschbaum et al., 1996). Brewin et al. (2010) suggest that, during a traumatic event, hippocampally based C-reps are disrupted, decreasing the amount of information consciously processed. This results in an over representation of information processed as an S-rep. The neurobiological changes that occur during the stressful event also impair prefrontal pathways and the ability to inhibit the responsivity of the amygdala. This leads to an inability of the impoverished C-reps to block the lower level S-reps, resulting in an increase in involuntary re-experiencing of the event.

Alcohol (the world's most popular recreational drug) has been shown to exert a number of effects on cognitive processes. Acutely consumed, alcohol's effects are complex with research highlighting differential effects on separate components of

memory. As discussed in Chapter 1, in relation to contemporary models of memory (e.g., Squire & Zola-Morgan, 1991), alcohol acutely impairs aspects of declarative memory while leaving non-declarative memory intact. Previous studies have shown that episodic memory is particularly impaired during acute alcohol intoxication (Curran & Hildebrandt, 1999; Duka et al., 2001; Weissenborn & Duka, 2001).

Although no research to date has investigated the way in which alcohol may affect memory for a traumatic event, a few studies have examined its effect on memory for emotional stimuli through use of typical tasks of recall and recognition. As emotional events are typically remembered better than neutral events in sober individuals it has been proposed that emotional information enhances in-depth processing (Craik & Lockhart, 1992). Recent accounts of this memory advantage for emotional information have suggested that such an enhancement depends on stress-hormone and noradrenergic modulation of the amygdala (for a review, see Chamberlain et al., 2006). While alcohol impairs the mnemonic advantage of emotional stimuli (Knowles & Duka, 2004), recent accounts of emotional memory have highlighted a contrast between memory for central gist and peripheral detail of emotional stimuli. It is suggested that the amygdala focuses attention on key aspects of emotional stimuli or central gist, while memory for peripheral detail is reduced or suppressed (Adolphs et al., 2001). No study to date has examined alcohol's effect on gist and detail aspects of an emotional event although parallels can be drawn from studies on other GABA-ergic modulators of episodic emotional memory. Buchanan et al. (2003) found that the benzodiazepine triazolam selectively impaired memory for gist information while information for detail was left intact due to a preferential effect on the amygdala. However, Kamboj and Curran (2006) found that the benzodiazepine lorazepam produced a global impairment of both gist and detail information due to a possible effect on both the amygdala and other associated emotional memory pathways. The present experiment aimed to examine memory for gist and detail for a stressful film following alcohol intoxication.

As described (Chapter 1.4.4), dissociation is a highly influential factor during the experiencing of a traumatic event, which may influence intrusive memory development. Dissociation is characterised as a “disruption of the usually integrated

functions of consciousness, identity or perception of the environment” (APA, 2000). It is common during the experience of a traumatic event for individuals to show dissociative reactions, including a reduced awareness of one’s surroundings, de-realisation, emotional numbing and de-personalisation (Cardena and Spiegel, 1993; Morgan et al., 2001). It is proposed that individuals may attempt to reduce the adverse emotional consequences of a traumatic incident by restricting awareness of the experience, resulting in a dissociative mental state (Putman, 1989; van der Kolk and van der Hart, 1989). Increases in peritraumatic dissociation during the experience of a traumatic event are strong predictors of PTSD (Ozer et al., 2003). A number of studies have elicited (non-pharmacological) increases in dissociation in a laboratory environment (e.g., Leonard et al., 2003), although only a few have examined the relationship between peritraumatic dissociation and intrusive memory development. Findings are inconsistent with some studies showing a positive relationship between peritraumatic dissociation and intrusive memory development (Kindt et al., 2005; Holmes et al., 2004) while others do not (Kindt & van der Hout, 2003; Holmes et al., 2006; Stuart et al., 2006).

It has been proposed that increases in peritraumatic dissociation may alter mental processes during an event and therefore lead to a disruption in the way in which information is encoded (Ehlers & Clark, 2000). To date, no study has examined pharmacological manipulations of state dissociation and its relation to intrusive memory development. However, some drugs like ketamine, that shares alcohol’s neuro-chemical action on glutamatergic transmission, have been found to induce marked increases in state dissociation (e.g., Morgan et al., 2006). The present experiment aimed to measure changes in state dissociation both following consumption of placebo or alcohol and during the trauma film. This was the first study to assess state dissociation following stressful stimuli following acute alcohol. Although it was expected that participants would show increased dissociation during the trauma film, it was not known whether alcohol would interact to affect peritraumatic dissociation.

Physiological measures during a stressful event have shown that physical hyperactivity is characteristic of PTSD (Giesbrecht et al., 2008; Orr et al., 1995;

Pitman et al., 1990). Despite this, recent proposals have suggested that dissociative responses during a traumatic event may result in a physiological suppression (Griffin et al., 1997). Holmes et al. (2004) found that a reduction in heart rate during the experience of a trauma film was related to an increase in the number of intrusive memories individuals reported in the following week. They also found that heart rate during those episodes of the film that subsequently intruded was lower than non-intruding episodes of the film. It has been proposed that this heart rate reduction reflects a ‘freeze’ or ‘surrender’ reaction in response to trauma (Nijenhuis et al., 1998). Alcohol intoxication during aversive stimuli has only been shown to affect physiological responsivity in individuals who have a family history of alcoholism due to an increased sensitivity to the negative reinforcing effects of alcohol (Finn et al., 1990). However, alcohol is recognised as an anxiolytic and therefore may decrease arousal during a stressful event which may in turn affect memory for the event. The present study therefore incorporated state measures of mood and physiological indices throughout the test session in which the beverage was consumed and the trauma film viewed.

Predictions for alcohol’s effect on intrusive memory development were based on the premises of the dual-representation theory. Due to alcohol’s ability to impair episodic memory, it was predicted that alcohol might disrupt memories encoded as C-reps. This would result in an over-representation of the events encoded as S-reps. As a consequence of this, the impoverished C-rep would be unable to block involuntary re-experiencing of the event and intrusions would therefore be more frequent in participants given alcohol compared to those given placebo. However, it is difficult to determine the way in which these differences in memory intrusions may influence typical encoding and consequent recall of events at follow up. Based on some evidence of alcohol’s ability to impair the mnemonic advantage for emotional stimuli (Knowles & Duka, 2004), it was expected that memory for the events as assessed through explicit memory measures may demonstrate a dose dependent alcohol impairment on both recall and recognition.

3.3 Method

3.3.1 Participants

A power calculation was used to determine the sample size, which indicated that for a significance level of $p < 0.05$ and a power of 80%, a minimum sample size of 14 participants in each group was required. Forty-eight paid volunteers (24 males and 24 females) were recruited via advertisement from the undergraduate and postgraduate population at University College London. The study was carried out in accordance with the Declaration of Helsinki and was approved by the UCL ethics committee (see appendices). Participants gave written, informed consent prior to taking part in the study. The inclusion criteria were that participants were aged 18 – 35, had not previously experienced or witnessed any traumatic event, and had not received any mental health treatment in the form of therapy or medication. Participants could only take part in the study if they were moderate social drinkers (average weekly consumption of 2-14 units for females and 2-21 units for males). The CAGE (Ewing, 1984) alcohol screening questionnaire was administered to assess individuals for problematic drinking and participants who scored 2 or more (out of 4) were excluded from taking part. Participants were also administered an initial breathalyser to check they had not consumed any alcohol prior to taking part in the experiment.

3.3.2 Design

An independent group design was used whereby male and female participants were randomly assigned to one of three conditions ($n = 16$; 8 females); a placebo beverage, a low dose of alcohol, or a high dose of alcohol. Volunteers participated in two testing sessions one week apart, receiving a beverage only on the first day of testing.

3.3.3 Alcohol administration

Participants were administered either alcohol (0.4 g/kg or 0.8 g/kg) or a matched placebo beverage. The alcohol beverage consisted of 90% v/w alcohol diluted with tonic water (Schweppes Ltd., Uxbridge, UK), equally divided into 10 x 50ml portions and then mixed with two drops of Tabasco sauce (McIlhenny Co., Avery Island, Louisiana, USA) to mask the taste of alcohol. The placebo beverage consisted of 10 x 50ml portions of tonic water and Tabasco sauce only. All participants were requested to consume the 10 beverages at 3 minute intervals, giving a total 30 minute consumption period. This procedure has been used in a number of studies examining alcohol's effects on cognitive function (e.g., Duka et al., 2001; Knowles & Duka, 2004).

3.3.4 Procedure

Participants were firstly screened prior to the test day. On arrival to the laboratory, participants were instructed on the use of the 7 day diary they were required to be keep following the testing session. Participants were first administered a breathalyser and required to fill out measures of alcohol usage (AUQ) and trait dissociation (DES). Participants were then connected to the heart rate and skin conductance monitors, and a 3 minute baseline recording was taken. The first baseline state dissociation (DSS) and mood visual analogue scale (VAS) were then administered. Participants then continued with the beverage consumption period of 30 minutes, followed by a further 10 minutes to allow the alcohol to be absorbed. The second breathalyser, DSS and mood VAS was then administered (post drink) after the beverage consumption period. Participants next viewed the trauma film alone in the laboratory. Following the film, the third breathalyser, DSS and mood VAS were administered and ratings of attention and distress were taken in relation to the trauma film. The time taken to complete the trauma film paradigm and mood rating scales was approximately 20mins, within the 'alcohol window' for testing (see Rose and Duka, 2006). Participants returned for the follow up session 1 week later. Participants carried out the cued recall and recognition memory tests, and diary

information was checked and the most frequent intrusion was identified. Participants were then debriefed and paid.

3.3.5 Trauma film

The trauma video includes 12.5 minutes of real life footage (compiled by Steil, 1996) viewed on a large screen with the participant seated directly in front. The film consisted of five scenes of road traffic accidents involving horrific imagery showing various emergency service personnel attending to victims, dead bodies being moved, injured individuals screaming and body parts among the wreckage. Each clip was preceded by a short narrative to set the scene for the footage about to be viewed (Figure 3.2). In respect of ethical considerations, a number of previous studies have used the same trauma film (e.g., Brewin & Saunders, 2001; Holmes et al., 2004; Murray, 1997) and have found no continued distress following the end of the experiment. Although the film involves a number of horrific graphic scenes, the content is similar to that witnessed in television coverage of road traffic accidents and emergency service work.

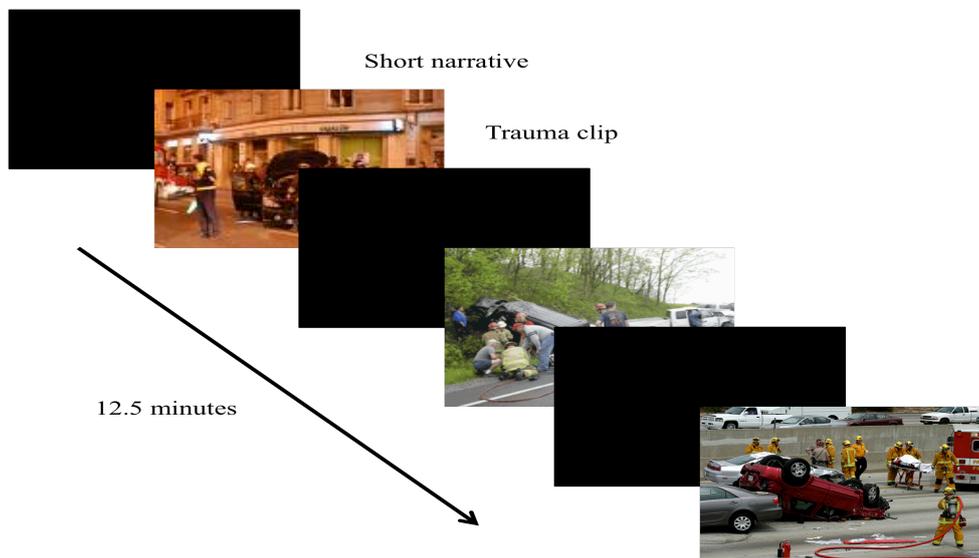


Figure 3.1. Images showing examples of footage taken from the trauma film. The overall film consisted of five short clips each preceded by a short descriptive narrative

Intrusions. Previous studies using a diary method have required participants to keep a written diary over 7 days and return with the completed diary at follow up. The present study used an improved methodology. Participants were instructed to keep an online diary of any memory intrusions during the 7 days following viewing the trauma film and were required to record whether they had consumed alcohol when the intrusion occurred. They were informed that a memory intrusion was ‘spontaneously occurring’ and asked to fill in the online diary each day, even if zero intrusions occurred. They received alerts via both email and text message each day to remind them to fill in the online diary. When the diary was submitted each day, an email was sent to the experimenter to record if participants had kept an up-to-date diary. Clear written instructions were provided on how to fill in the diary information. Participants were required to give detail of the number of memory intrusions they had experienced each day and, for each intrusion, state whether the intrusion was an image, thought or combination and provide a brief description of what the intrusion involved.

3.3.6 Trait measures

Dissociation Experience Scale (DES-II; Carlson & Putnam, 1993). The DES-II is a 28-item dissociative trait questionnaire designed to examine personal dissociative experiences (see appendix). Participants are required to indicate for each item the percentage of time they have a given experience in their daily life. The measure shows good reliability with test-retest correlation coefficients between 0.79 and 0.84 (Carlson and Putnam, 1993). The measure also shows good internal consistency with split-half coefficients from 0.83 to 0.93 (Bernstein et al., 1986).

Alcohol Usage Questionnaire (AUQ; Mehrabian & Russell, 1978): The AUQ is a 12-item questionnaire designed to provide an accurate measure of individuals’ habitual alcohol drinking habits. Factors include the amount of wine, beer and spirits consumed in a typical week and also the speed of drinking (see appendix). The final 3-items were also taken as a separate total to give a score for binge drinking (Townsend & Duka, 2002). The AUQ has been used in a number of studies to

examine participants' habitual alcohol consumption (Duka et al., 2001; Weissenborn & Duka, 2003; Knowles & Duka, 2004).

3.3.7 Subjective ratings

Dissociative State Scale (DSS; adapted from Bremner et al., 1998): The DSS is a 19-item measure designed to tap subjective state dissociative symptoms (see appendix). The measure has been shown to have high internal consistency (Cronbach's alpha = 0.94). Each item is rated on a 5 point scale anchored from 0 (not at all) to 4 (extremely). The measure consists of 3 subscales: amnesia, derealisation and depersonalisation. Coefficient alpha values for the subscales are reported as 0.74 for amnesia, .82 for depersonalization, and .90 for derealisation.

Mood rating scale (Bond & Lader, 1974): A 16-item visual analogue scale was used to record subjective feelings of mood 'at the moment' (see appendix). The 16-items as presented with 100mm lines anchored with antonyms at each end of the scales (e.g., calm – excited). Principal components analysis yields three main factors of sedation, discontentedness and anxiety. High reliability and validity have been demonstrated in the use of visual analogue scales to assess current mood (Ahearn, 1997). Two extra items were added to the scale to measure tipsiness and depression.

Attention and distress. Participants were requested to rate how distressing they found the trauma film on a 100mm scale anchored from 'not at all' to 'extremely' distressing. Participants also rated the amount of attention they felt they had paid to the film on a 100mm scale anchored from 'none at all' to 'total attention'.

Guess on treatment. Participants and the experimenter were required to make a guess on which treatment condition the participant had been assigned to; placebo, low dose or high dose.

3.3.8 Physiological measures

Heart rate. Heart rate was recorded via a blood flow optical sensor attached to the participant's index finger on the non-dominant hand. The sensor was attached to a peripheral pulse amplifier (Contact Precision Instruments, Psylab, London) and continuous recordings were carried out online throughout the experiment.

Skin conductance. Skin conductance responses were measured via silver / silver chloride (Ag/AgCl) electrodes attached to the palm of the non-dominant hand. KY jelly was used as a conductive gel. Responses were transformed through a SC5 24 bit digital skin conductance amplifier (Contact Precision Instruments, Psylab, London). A minimum criterion for skin conductance response detection of 0.02 microsiemens was used.

Mean heart rate and skin conductance were calculated offline following the experiment for the 3 minute baseline period, the 3 minute post drink period, the duration of the trauma film, and the 3 minute post film period. Timings of the trauma film and physiological measures were synchronised. In addition, specific episodes of the trauma film that subsequently intruded in the 7 days following encoding were compared to episodes of the film that did not intrude.

3.3.9 Assessment at day 7

Cued recall (see appendix). A 20-item cued recall test assessed memory for the five scenes of the trauma film. Items included questions in regard to the different scenes, e.g., what was the colour of the car in scene 1 and were equally split into 4 questions for each scene.

Recognition (see appendix). Recognition memory was assessed on the five scenes of the trauma film following the procedure of Cahill et al. (1994). Testing involved 35 forced choice questions (four options per question) equally divided into 6 questions per slide. Each set of 6 questions was equally divided into 3 questions tapping gist and 3 tapping detail.

3.3.10 Statistical Analysis

All data were checked for univariate outliers. One participant was omitted from the intrusive memory analysis due to poor compliance with keeping the online diary over the 7 days. It has been suggested that impairments in memory during alcohol intoxication might be due to state-dependent learning, with increased memory performance when individuals are returned to a intoxicated state (Weissenborn and Duka, 2000; 2001). To rule out these possible confounding effects, intrusions that occurred under the influence of alcohol were omitted from analyses. Skin conductance data for one participant was not recorded due to a technical error. All statistical analyses were performed using SPSS version 16. Group differences were analysed with one way analysis of variance (ANOVA). Where data violated assumptions of normality Kruskal-Wallis tests were used. Mood scales, state dissociation, heart rate and skin conductance were analysed as 3 x 3 repeated measures analysis of variance (RMANOVA) with group (placebo versus low dose versus high dose) as a between participants measure and time (baseline versus post drink versus post film) as a within participants factor. Heart rate and skin conductance during episodes of the film that subsequently intruded was compared to recordings for the rest of the stressful film. As the focus of this analysis included specifically examining intrusion data and its associated physiological response, participants who recorded zero memory intrusions over the 7 days were omitted from this analysis (all other analyses were performed including participants with zero intrusions). Post hoc comparisons and simple effects were Bonferroni corrected with adjusted p-values or, in the case of analyses using the Kruskal-Wallis test, individual planned comparisons using Mann-Whitney *U* tests were carried out. All analyses were initially carried out with gender as a between participants factor. As no significant effects of gender emerged on any measure, these analyses are not reported.

3.4 Results

3.4.1 Demographics and trait scores

There were no group differences in age [$F(2,47) = 2.75, p = 0.75$], number of years in education [$F(2,47) = 1.03, p = 0.36$], trait dissociation [$F(2,47) = 0.45, p = 0.64$], alcohol usage [$F(2,47) = 0.45, p = 0.64$] or alcohol binge scores [$F(2,47) = 0.78, p = 0.46$] (Table 3.1).

Table 3.1. Means \pm standard deviations of demographic data across the three treatment groups.

	Placebo (N=16)	Low dose 0.4 g/kg alcohol (N=16)	High dose 0.8 g/kg alcohol (N=16)
Age	24.88 \pm 3.98	25.06 \pm 3.42	22.56 \pm 2.53
Years in education	16.31 \pm 1.99	16.25 \pm 1.84	15.50 \pm 1.46
DES-II score	19.31 \pm 14.38	18.22 \pm 12.29	22.79 \pm 16.05
AUQ score	34.19 \pm 14.89	33.71 \pm 18.80	39.31 \pm 21.30
AUQ binge score	21.69 \pm 9.96	22.71 \pm 16.33	27.75 \pm 16.79

3.4.2 Blood alcohol concentration

Blood alcohol concentration (BAC) following beverage consumption (BAC 1) and following the trauma film (BAC 2) are shown in table 3.2.

Table 3.2. Means \pm standard deviations and ranges of BAC levels (g/l) at two time points for alcohol groups; 40 mins following start of beverage consumption (post drink; BAC 1), and 70 mins following start of beverage consumption (post film; BAC 2).

	Low dose 0.4 g/kg alcohol (N=16)		High dose 0.8 g/kg alcohol (N=16)	
	mean	range	mean	Range
BAC 1	0.33 \pm 0.09	0.14 to 0.48	0.74 \pm 0.17	0.46 to 0.99
BAC 2	0.22 \pm 0.09	0.12 to 0.41	0.68 \pm 0.25	0.37 to 1.33

3.4.3 Memory intrusions

Analysis of the number of intrusive images over the 7 days post film (Figure 3.2) revealed a significant difference between the groups [χ^2 (2) = 8.19, $p < 0.05$]. Planned comparisons revealed that the low dose group reported more intrusive images than both the placebo ($U = 71.50$, $p = 0.05$, $r = 0.35$) and the high dose group ($U = 51.50$, $p < 0.01$, $r = 0.50$). The high dose group was also found to report significantly fewer intrusive images than placebo ($U = 76.50$, $p = 0.05$, $r = 0.35$). The number of intrusive thoughts participants reported over the 7 days following the film only showed a group difference approaching significance (χ^2 (2) = 5.58, $p = 0.06$). The total number of intrusive images and thoughts demonstrated a significant difference between groups (χ^2 (2) = 12.42, $p < 0.01$). Individual comparisons revealed that the low dose group reported more intrusions than both the placebo group ($U = 69.50$, $p < 0.05$, $r = 0.36$) and the high dose group ($U = 36.50$, $p < 0.001$, $r = 0.60$) and a trend between the placebo and high dose group [$U = 79.00$, $p = 0.07$].

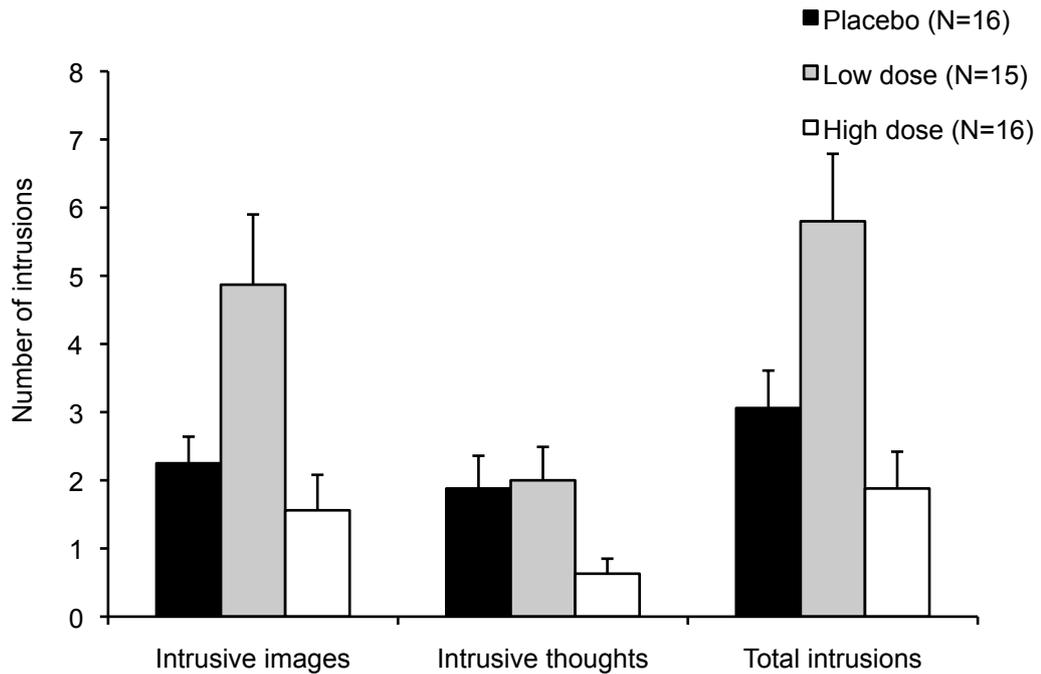


Figure 3.2. Means (SE) number of intrusive memories recorded over 7 days following the stressful film as a function of group.

3.4.4 Explicit memory assessments after 7 days

Cued recall. A one way ANOVA of total cued recall scores showed a significant difference between the groups [$F(2,46) = 11.99, p < 0.001, \eta^2 = 0.34$]. Post hoc analysis showed that the placebo group scored significantly more correct than the high dose group ($p < 0.001, d = 1.90$), and the low dose group scored more correct than the high dose group ($p < 0.01, d = 1.02$). There was no significant difference between placebo and low dose groups on cued recall scores ($p = 0.48$; Figure 3.3).

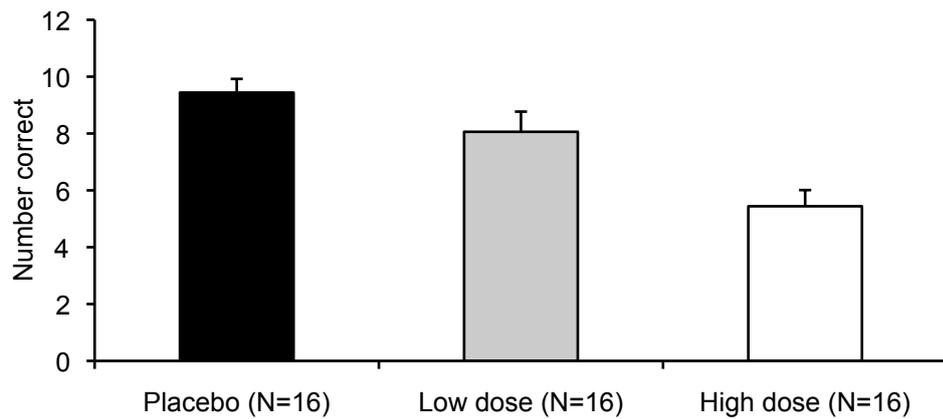


Figure 3.3. Cued-recall performance: means (SE) of correctly recalled information in the cued-recall test as a function of group

Recognition. A one way ANOVA on the total number of correct answers (gist + detail) for the recognition test showed a significant group effect [$F(2,46) = 7.67, p < 0.01, \eta^2 = 0.25$; Figure 3.4]. Post hoc analysis revealed that the placebo group (18.75 ± 3.98) produced more correct answers than the high dose group ($14.13 \pm 3.03; p < 0.001, d = 1.26$). A trend was demonstrated with the placebo group producing somewhat more correct answers than the low dose group ($15.87 \pm 3.00; p = 0.07$). No difference was found between the low and high dose groups in the total number of correct answers ($p = 0.47$).

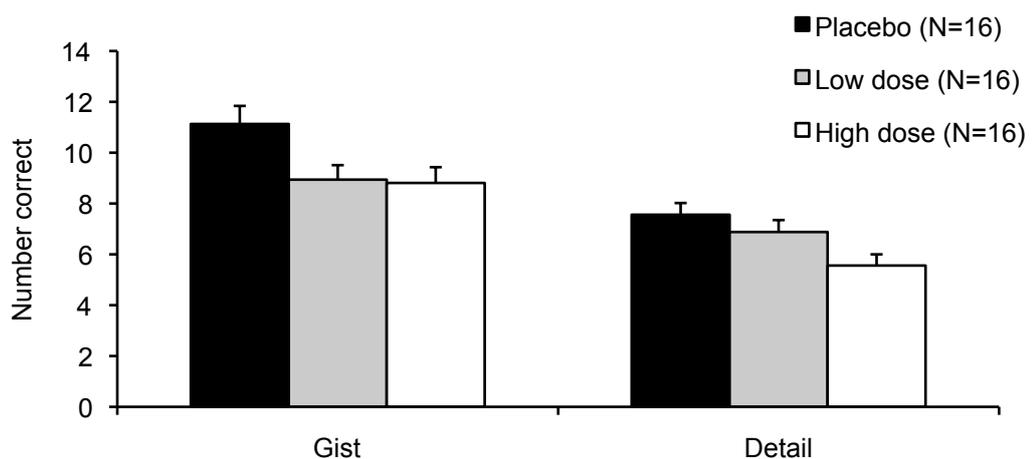


Figure 3.4. Recognition memory performance: means (SE) of correctly recognised information in the recognition test split by gist and detail.

Recognition for gist and detail (Figure 3.4). Analysis of recognition scores split for gist and detail revealed a significant difference between groups for both gist [$F(2,46) = 4.03, p < 0.05, \eta^2 = 0.19$] and detail [$F(2,46) = 6.21, p < 0.01, \eta^2 = 0.15$]. Post hoc analysis showed that the placebo group recognised more gist information than the high dose group ($p < 0.05, d = 0.91$) although the difference between placebo and low dose groups on gist scores only approached significance ($p = 0.07$). No difference emerged between low dose and high dose on gist recognition. Analysis of detail information showed that the placebo group correctly recognised more information than high dose ($p < 0.01, d = 1.13$), while there were no differences between the placebo group and low dose group scores. Differences between low dose and high dose approached significance ($p = 0.06$).

3.4.5 Subjective ratings

Tipsy ratings. RMANOVA of tipsy ratings displayed a significant interaction of group x time [$F(4,90) = 8.69, p < 0.001$] and main effects of both group [$F(2,45) = 12.85, p < 0.001$] and time [$F(2,90) = 107.49, p < 0.001$]. As seen in Fig. 2.6, groups' ratings increased over the test session. This increase was confirmed through post hoc analysis showing that all three groups' ratings increased significantly from baseline to post drink ($p < 0.001$). Both low ($p < 0.05$) and high doses ($p < 0.001$) of alcohol showed a significantly higher increase compared to placebo from baseline to post drink although there was no significant dose response with the difference between low and high dose only approaching significance ($p = 0.07$). All groups showed a significant decrease from post drink to post film ($p < 0.05$) although both low ($p < 0.05$) and high dose ($p < 0.001$) groups showed significantly higher ratings post film than placebo. There was no difference between low and high dose groups at post film ($p = 0.27$).

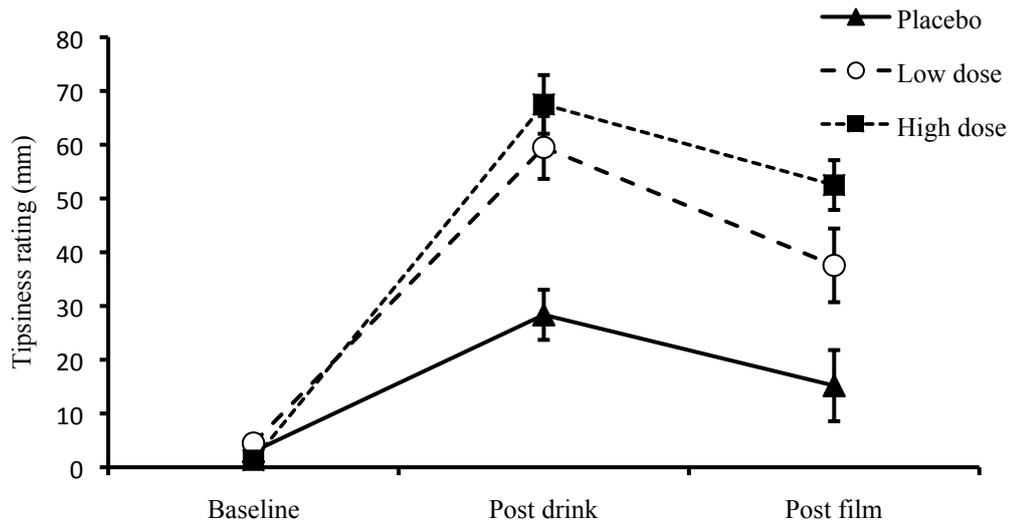


Figure 3.5. Mean (SE) ratings of tipsiness as a function of group and time.

Mood VAS. (Table 3.3) RMANOVA of sedation ratings demonstrated a significant main effect of group [$F(2,45) = 3.50, p < 0.05$] and time [$F(2,90) = 21.93, p < 0.001$] and a trend towards an interaction of group x time [$F(4,90) = 2.10, p = 0.09$]. Post hoc analysis of main effects showed a significant increase in sedation ratings from baseline to both post drink ($p < 0.001$) and post film ($p < 0.001$). No significant change was found between post drink and post film ($p = 0.63$). The high dose group displayed a significant higher rating of sedation than placebo ($p < 0.05$) but there were no differences between placebo and low dose ($p = 0.44$), and low dose and high dose ($p = 0.76$).

Analysis of anxiety ratings through a RMANOVA demonstrated a main effect of time [$F(2,90) = 7.24, p < 0.001$] but not of group [$F(2,45) = 0.35, p = 0.71$] and no group x time interaction [$F(4,40) = 1.87, p = 0.12$]. Post hoc analysis revealed that anxiety significantly increased from baseline to post film ($p < 0.001$). No significant changes in anxiety ratings were displayed between baseline and post drink ($p = 0.12$) and post drink to post film ($p = 0.29$).

RMANOVA of discontentedness ratings revealed a significant group x time interaction [$F(4,90) = 3.36, p < 0.05$] and main effect of time [$F(2,90) = 20.33, p <$

0.001] but not of group [$F(2,45) = 0.32, p = 0.73$]. As seen in figure 3.6, the high dose group differed from both placebo and low dose groups. Post hoc analysis showed that the high dose group displayed a significantly higher rating at baseline compared to placebo ($p = 0.05$) and a trend to higher ratings than the low dose group ($p = 0.08$). No group showed any significant change in discontentedness between baseline and post drink ratings ($p > 0.9$). Both the placebo ($p < 0.01$) and low dose ($p < 0.01$) groups' ratings significantly increased from post drink to post film but the high dose group showed no change ($p = 0.72$).

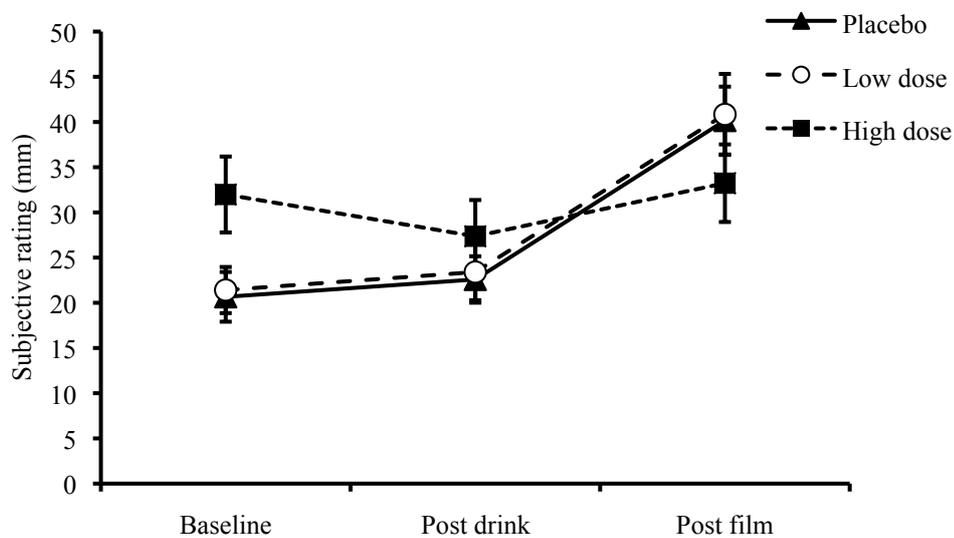


Figure 3.6. Mean (SE) ratings of discontentedness as a function of group by time.

Analysis of depression ratings using a RMANOVA showed a main effect of time [$F(2,90) = 14.40, p < 0.001$] but not of group [$F(2,45) = 0.50, p = 0.61$] or group x time interaction [$F(4,90) = 0.74, p = 0.57$]. Post hoc analysis showed that depression significantly increased from baseline to post film ($p < 0.01$) and post drink to post film ($p < 0.001$). There was no significant change in depression from baseline to post drink ($p = 0.50$).

Dissociative state scale (DSS). RMANOVA of overall DSS score (Table 3.3) showed only a significant main effect of time [$F(2,90) = 14.52, p < 0.001$] but not of group [$F(2,45) = 0.60, p = 0.55$] and no group x time interaction [$F(4,90) = 0.70, p =$

0.53] (table 2). Post hoc analysis revealed a reliable difference between baseline (3.38 ± 5.43) and post drink (6.60 ± 9.78 ; $p < 0.01$), baseline and post film (9.52 ± 11.58 ; $p < 0.001$), and post drink to post film ($p < 0.05$).

RMANOVA of the DSS amnesia subscale revealed only a significant main effect of time [$F(2,90) = 3.41$, $p < 0.05$] but not of group [$F(2,45) = 1.82$, $p = 0.17$] or group x time interaction [$F(4,90) = 0.42$, $p = 0.79$]. Post hoc analysis showed a significant difference between baseline and post drink ($p = 0.05$), a trend between baseline and post film ($p = 0.09$), but not between post drink and post film ($p = 0.90$).

Table 3.3. Means \pm standard deviations for state dissociation and mood ratings as a function of group over the three time points of the test session: baseline, post drink, and post film.

	Baseline			Post drink			Post film		
	Placebo (N=16)	Low dose (N=16)	High dose (N=16)	Placebo (N=16)	Low dose (N=16)	High dose (N=16)	Placebo (N=16)	Low dose (N=16)	High dose (N=16)
Sedation	21.53 \pm 9.18	22.53 \pm 11.38	24.20 \pm 8.90	30.14 \pm 13.65	33.85 \pm 11.22	41.08 \pm 11.84	24.03 \pm 13.30	35.14 \pm 15.33	38.61 \pm 15.85
Discontentedness	20.66 \pm 11.01	21.41 \pm 10.21	31.98 \pm 16.81	22.59 \pm 10.27	23.40 \pm 12.45	27.35 \pm 16.05	40.16 \pm 15.02	40.84 \pm 21.09	33.23 \pm 17.15
Anxiety	21.75 \pm 13.80	23.03 \pm 16.33	26.94 \pm 16.23	23.69 \pm 17.86	28.69 \pm 17.27	34.81 \pm 15.52	39.06 \pm 14.74	33.06 \pm 16.83	31.78 \pm 16.90
Depression	11.88 \pm 16.01	19.38 \pm 22.88	21.75 \pm 22.27	10.63 \pm 14.36	13.50 \pm 11.68	17.75 \pm 18.72	27.63 \pm 20.16	31.44 \pm 26.28	27.19 \pm 25.25
Dissociation	2.38 \pm 3.38	3.69 \pm 6.20	4.06 \pm 6.39	3.69 \pm 5.95	6.75 \pm 8.04	9.38 \pm 13.51	8.75 \pm 10.55	8.94 \pm 9.06	10.88 \pm 14.97
Amnesia	0.25 \pm 0.58	0.50 \pm 1.03	0.75 \pm 1.18	0.50 \pm 1.03	0.88 \pm 0.96	1.56 \pm 2.63	0.95 \pm 1.24	1.00 \pm 2.03	2.25 \pm 4.40
Depersonalisation	0.31 \pm 0.70	0.94 \pm 1.88	0.81 \pm 2.23	0.81 \pm 1.38	1.44 \pm 3.56	2.31 \pm 4.81	1.88 \pm 2.73	2.31 \pm 2.36	2.94 \pm 4.33
Derealisation	1.81 \pm 2.61	2.25 \pm 3.61	2.50 \pm 3.71	2.38 \pm 4.03	4.38 \pm 4.27	5.50 \pm 6.51	5.94 \pm 7.16	5.63 \pm 5.19	5.69 \pm 8.64

A RMANOVA of the DSS depersonalisation subscale demonstrated a main effect of time [$F(2,90) = 7.41, p < 0.01$] but not of group [$F(2,45) = 0.66, p = 0.53$] or interaction of group x time [$F(4,90) = 0.31, p = 0.87$]. Post hoc analysis showed a significant change from baseline to post drink ($p < 0.05$), and baseline to post film ($p < 0.01$). There was no significant change from post drink to post film ($p = 0.33$) on ratings of depersonalisation.

RMANOVA of the derealisation subscale of the ADSS revealed a time main effect [$F(2,45) = 13.79, p < 0.001$], but no main effect of group [$F(2,45) = 0.26, p = 0.77$] or group x time interaction [$F(4,90) = 1.15, p = 0.34$]. Post hoc analysis revealed that derealisation ratings increased significantly from baseline to post drink ($p < 0.001$). A significant change was also found from baseline to post film ($p < 0.001$) and a change from post drink to post film approached significance ($p = 0.08$).

Post film ratings (Table 3.4). One way ANOVAs revealed no group differences in ratings of how distressing individuals found the film [$F(2,47) = 0.73, p = 0.486$] or how much attention was paid to the film [$F(2,46) = 2.09, p = 0.135$].

Table 3.4. Means \pm standard deviations of subjective ratings (mm) of distress and attention given by participants following encoding of the trauma film.

	Placebo (N=16)	Low dose 0.4 g/kg alcohol (N=16)	High dose 0.8 g/kg alcohol (N=16)
Distress	40.00 \pm 25.30	51.19 \pm 26.25	44.38 \pm 27.44
Attention	77.31 \pm 13.82	83.50 \pm 11.62	73.63 \pm 15.65

3.3.6 Physiological measurements

Table 3.5. Means \pm standard deviations of heart rate for: different times throughout the test session.

	Placebo (N=16)	Low dose 0.4 g/kg alcohol (N=16)	High dose 0.8 g/kg alcohol (N=16)
Baseline	73.20 \pm 6.44	73.82 \pm 15.26	79.16 \pm 13.10
Post drink	69.71 \pm 7.59	76.08 \pm 13.71	78.72 \pm 10.16
During the trauma film	70.04 \pm 7.82	74.74 \pm 9.85	78.40 \pm 9.79
Post film	69.97 \pm 9.06	74.69 \pm 11.90	80.62 \pm 11.47

Heart rate (Table 3.5). A 3 x 4 RMANOVA revealed a trend towards a main effect of group [$F(2,44) = 2.72, p = 0.07$] but no main effect of time [$F(1,44) = 0.15, p = 0.70$] or interaction of group x time [$F(6,132) = 0.42, p = 0.74$]. A RMANOVA of heart rate during the episode of the film was the most frequent intrusive memory compared to heart rate for the rest of the film showed no significant main effect of group [$F(2,36) = 2.32, p = 0.11$] and change in heart rate [$F(1,36) = 1.04, p = 0.75$]. No significant interaction was displayed [$F(2,36) = 1.23, p = 0.31$]. Similarly, a RMANOVA of heart rate for episodes of the film that intruded compared to episodes of the film that did not intrude showed no significant main effect of group [$F(2,36) = 2.08, p = 0.14$], heart rate change [$F(1,36) = 0.32, p = 0.58$] and group x heart rate change interaction [$F(2,36) = 0.61, p = 0.55$].

Table 3.6. Means \pm standard deviations of heart rate for the most frequent intrusive episodes and the remainder of the film, and average of intrusive and non-intrusive episodes.

	Placebo (N=12)	Low dose 0.4 g/kg alcohol (N=13)	High dose 0.8 g/kg alcohol (N=13)
Most frequent intrusion	71.01 \pm 7.53	76.52 \pm 9.29	78.75 \pm 11.65
Remainder of film	70.97 \pm 7.32	75.80 \pm 10.13	80.03 \pm 12.37
Intrusions	70.21 \pm 8.21	76.77 \pm 9.75	78.84 \pm 11.68
Non-intrusions	71.25 \pm 7.15	75.67 \pm 10.34	77.12 \pm 10.56

Skin conductance. RMANOVA for skin conductance demonstrated a significant main effect of time [$F(1,45) = 15.92, p < 0.001, \eta^2 = 0.27$] but not of group [$F(2,45) = 0.48, p = 0.62$] or group x time interaction [$F(2,45) = 1.01, p = 0.42$]. As seen in Figure 3.7, skin conductance increased particularly during the trauma film. Post hoc analysis showed that skin conductance significantly increased from baseline to during the film ($p < 0.001, d = 1.14$), and then decreased post film ($p < 0.05, d = 0.69$). There was also a significant change from post drink to during the film footage ($p < 0.001, d = 0.20$) and from during the film to post film ($p < 0.01, d = 0.69$).

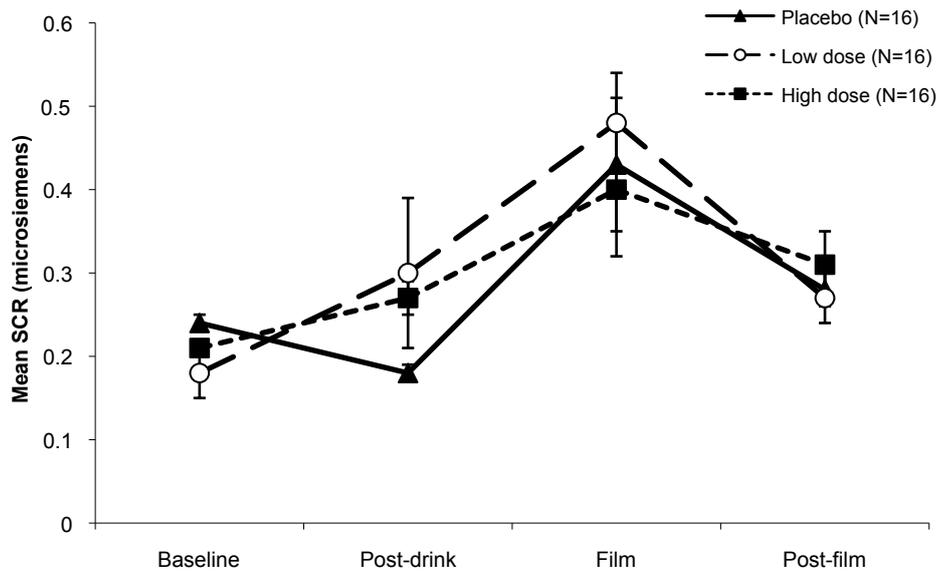


Figure 3.7. Average skin conductance readings as a function of group by time. Bars represent SE.

Skin conductance for the episode of the film that was the most frequent memory intrusion compared to the rest of the film (Table 3.7) revealed a significant main effect of episode [$F(1,35) = 4.88, p < 0.05, \eta^2 = 0.13$] but no main effect of group [$F(2,35) = 0.86, p = 0.43$] or group x heart rate change interaction [$F(2,35) = 1.01, p = 0.37$]. Further analysis showed a significant increase in skin conductance during the episode of the film that was the most frequent intrusion compared to average skin conductance for the rest of the film. A RMANOVA of skin conductance for episodes of the film that intruded compared to episodes of the film that did not intrude showed no significant main effect of group [$F(2,35) = 0.73, p = 0.49$], skin conductance change [$F(1,35) = 1.76, p = 0.19$] or group x skin conductance change interaction [$F(2,35) = 0.55, p = 0.58$].

Table 3.7. Means \pm standard deviations of skin conductance for most frequent memory intrusion versus the remainder of the trauma film, and episodes of the film that intruded versus episodes that did not intrude.

	Placebo (N=12)	Low dose 0.4 g/kg alcohol (N=13)	High dose 0.8 g/kg alcohol (N=13)
Most frequent intrusion	0.52 \pm 0.40	0.59 \pm 0.32	0.38 \pm 0.24
Remainder of film	0.44 \pm 0.32	0.41 \pm 0.27	0.36 \pm 0.19
Intrusions	0.47 \pm 0.38	0.55 \pm 0.38	0.38 \pm 0.26
Non-intrusions	0.43 \pm 0.26	0.44 \pm 0.26	0.36 \pm 0.18

3.4.7 Correlations

Data were first checked for bivariate outliers using the residuals and a Tukey 1.5 hinged spread analysis. No outliers were identified and therefore all data were used for the correlational analyses. Combined low and high dose alcohol group scores on cued recall scores showed a significant negative correlation with BAC levels both post drink [$r(32) = -0.44, p < 0.05$] and post film [$r(32) = -0.43, p < 0.05$] with the number of correct items recalled decreasing as BAC levels increased. Participants' scores on the dissociation experience scale (DES-II) tended to positively correlate with the number of intrusive images for the low dose group [$r(15) = 0.50, p = 0.06$]. A trend towards a positive correlation between the number of intrusive images and attention ratings for the stressful film also emerged [$r(47) = 0.26, p = 0.08$]. No other significant correlations emerged.

3.4.8 Manipulation check

Chi square analysis (Table 3.8) of participants' guess on which treatment they had received showed no significant difference between groups in correct / incorrect responses ($\chi^2 (2) = 3.73, p = 0.16$). Analysis of the experimenter's guess on treatment also showed no significant difference between group and correct / incorrect response ($\chi^2 (2) = 0.58, p = 0.75$).

Table 3.8. Frequencies for the number correct and incorrect guesses on treatment by participants and experimenter.

	Placebo (N=16)	Low dose 0.4 g/kg alcohol (N=16)	High dose 0.8 g/kg alcohol (N=16)
<i>Participant</i>			
Correct guess	9	13	8
Incorrect guess	7	3	8
<i>Experimenter</i>			
Correct guess	11	12	10
Incorrect guess	5	4	6

3.5 Discussion

The present study aimed to examine the effects of an acute dose of alcohol on intrusive memories and explicit memory following the encoding of a trauma film. The number of memory intrusions in the week following the film showed clear group differences following alcohol at encoding compared to placebo. Explicit memory for the trauma film was assessed through tests of cued recall and recognition and again clear alcohol induced impairments were observed. Changes in peritraumatic processing were reflected in both subjective and physiological

measures following the trauma film. However, alcohol did not contribute to these effects and no relationship was observed between these changes and memory intrusions.

A major finding to emerge from the present study was the differential effects of alcohol on memory for the trauma film observed in both memory intrusions and explicit memory. Intriguingly, alcohol dosage showed an inverted ‘U’ shape curve on the number of intrusive memories. Compared to placebo, a low dose of alcohol increased the number of intrusions whereas a high dose of alcohol resulted in a marginal decrease. In contrast, explicit memory for the trauma film showed a clear linear effect of alcohol with memory performance decreasing as alcohol dosage increased. It is important to note that the changes in the number of memory intrusions cannot simply be due to differences in distress caused by the film or by the amount of attention participants paid to the film as no group differences were evident on either measure. Importantly, these findings on intrusive memories do not mirror the typical effects of alcohol on explicit measures of cued recall and recognition. The distinct qualitative difference in the pattern of alcohol’s effect highlights a possible involvement of different memory systems in intrusive memory and explicit memory.

3.5.1 Intrusive memory

Observed group differences in the number of intrusive memories reported can be interpreted in terms of a dual-representation account of memory for trauma (Brewin et al., 1996; Brewin 2001). It was hypothesised that alcohol would impair the C-rep system through impairments in conscious memory for the event. It was predicted that this impairment would lead to an over-representation of information as a S-rep. This would result in the inability of C-reps to suppress involuntary memory intrusions via the S-memory system and in turn, increase in the number of reported intrusions in the following week. This prediction was supported by the findings observed in the low dose of alcohol group showing an increase in reported memory intrusions compared to the placebo group. The decrease in conscious memory for

the event was further supported through the reduced explicit memory performance following alcohol at encoding.

Several authors have highlighted the relationship between decreases in conscious memory for a traumatic event and an increase in intrusive memory development (Conway & Pleydell-Pearce, 2000; Ehlers & Clark, 2000; Foa & Hearst-Ikeda, 1996). Factors that disrupt encoding during encoding of a traumatic event are proposed as leading to a more fragmented representation of the event and more frequent intrusions. This was supported by an alcohol-induced impairment in explicit memory for the event and increase in memory intrusions. The reduction in explicit memory highlights particular relevance within a PTSD framework. A persistence of PTSD is characterised by poor elaboration of the trauma memory, resulting in an inadequate integration within autobiographical memory (Ehlers & Clark, 2000). However, this selective impairment of C-reps and increased experience of memory intrusions was not found following a high dose of alcohol. In contrast, the high dose of alcohol showed a reduction in memory intrusions compared to both the placebo and low dose groups.

The observed decrease in memory intrusions following the high dose of alcohol is difficult to explain through current accounts of intrusive memory development. (e.g., Brewin et al., 1997; Ehlers & Clark, 2000). Interpretations of memory disruptions in individuals, following a traumatic event, have been linked to multiple memory systems (e.g., Squire & Zola-Morgan, 1991). During a traumatic event declarative (explicit) and non-declarative (implicit) memory processes may be affected in different ways (Elzinga & Bremner, 2002). Parallels can be drawn between the C-rep and S-rep systems and declarative and non-declarative memory systems, respectively; although a precise overlap may not be definitive (Brewin, 2001). Alcohol's effects on memory are typically observed through impairment of declarative memory, specifically episodic memory (Curran & Hilderbrandt, & 1999; Duka et al., 2001; Weissenborn & Duka, 2001), whilst non-declarative memory is left intact (Hashtroudi et al., 1983; Lister et al., 1991). In line with this distinction, alcohol should impair C-reps while leaving memories processed via the S-memory system unaffected. While the impaired C-reps were supported through results on

explicit memory performance, a reduction of information processed via the S-memory system cannot be supported by the current literature.

The contrasting finding of alcohol's effect on intrusive memory development and explicit memory following the trauma film are of particular interest. It might be speculated that the high dose of alcohol impaired both conscious and non-conscious aspects of memory, leading to a decrease of information processed via both C-reps and S-reps. This was reflected by a general decrease in both explicit memory and intrusive memories. As discussed, within the dual representation theory, parallels can be drawn between the S-memory system and non-declarative memory system. Although non-declarative memory processes are typically left in tact following acute alcohol, research is limited (Hashtroudi et al., 1983; Lister et al., 1991). It might be speculated that some aspects of non-declarative memory may be more sensitive to a high dose of alcohol (e.g., Chun & Phelps, 1999).

Another explanation for alcohol's differential effect on intrusive memory may concern the way in which visuo-spatial aspects of an experience are encoded into memory. Some have proposed that the spatial components of an event that contribute to visual imagery may be processed in a different way than the type of information assessed through typical tests of recall and recognition (e.g., Bryne et al., 2007). In this account (Burgess et al., 2001; Bryne et al., 2007; O'Keefe and Nadel, 1978), spatial and temporal aspects of an event are processed and encoded via two dissociable systems, comprising distinct cognitive and neural mechanisms. One system is dependent on the individual's viewpoint, forming an egocentric representation of the event driven by perception that serves to contribute to immediate action. The second system integrates the spatio-temporal context of a scene to form an allocentric representation, which is world-centred and independent of the perceiver's viewpoint, contributing to an individual's long-term memory for an event that can be freely retrieved. In light of the current findings reported here, alcohol may dose dependently affect these systems in different ways, a finding that has been demonstrated in rodents assessing similar memory processes following alcohol (for a review, see Matthews and Silvers, 2004). Speculatively, a low dose of alcohol might selectively impair an episodic based allocentric representation of a

visual event. The result would be a decrease in conscious memory for the event due to a reduction of encoding within autobiographical memory. In contrast, a high dose of alcohol may induce a more global impairment on both representations in memory resulting in a more prominent general reduction in memory.

The present findings demonstrated that, whilst intrusive imagery was clearly affected by alcohol, intrusive thoughts of the trauma showed no differences between any of the groups. The DSM-IV (APA, 1998) states that intrusive recollections of a traumatic event can take the form of images or thoughts. However, some studies have proposed that, whilst intrusive images are a common occurrence after a traumatic event, intrusive thoughts are rare (Ehlers et al., 2002). Assessing the occurrence of intrusive thoughts is complex because they may involve post-event processes associated with rumination and worry, rather than specific intrusive memories (Brewin and Holmes, 2003). Deliberate evaluation and appraisal of the traumatic event should be distinguished from intrusive imagery. In relation to the described models of intrusive memory development, self-generated might be considered retrieval of more explicit types of memory in verbal forms that would not necessarily contribute to spontaneously experienced images (e.g., Brewin et al., 2010; Ehlers and Clark, 2000). Previous studies have also shown that peritraumatic emotions triggered by traumatic material can impact on intrusive imagery but not intrusive thoughts (Hagenaars et al., 2010). The current findings relating to alcohol provide further support to this distinction between intrusive images and thoughts.

3.5.2 Explicit memory

Explicit memory assessed 7 days after initial encoding showed an alcohol dose response on cued recall with decreases in memory as dose increased. This finding was further supported with a negative relationship between increasing BAC levels and decreasing cued recall scores. Alcohol's ability to impair episodic memory is robust in the literature (e.g., Curran & Hildebrandt, 1999; Duka et al., 2001). This is also apparent within emotional episodic memory where alcohol blocks enhanced memory for emotional salient stimuli, as observed in healthy controls (Knowles & Duka, 2002). The current findings therefore provide further support of alcohol's

impairing effect on emotional episodic memory with both alcohol groups showing a decrease in performance compared to placebo.

Assessment of recognition memory after seven days also showed that alcohol impaired performance on the number of correctly recognised items. Both the high and low dose of alcohol impaired recognition memory compared to the placebo. No difference was found between the two alcohol groups on recognition memory although the impairment was more pronounced in the high dose group than the low dose group compared to placebo. Numerous methodologically diverse studies have assessed the effects of alcohol on recognition memory and findings have been mixed with some studies demonstrating impairments (Parker et al., 1976; Ryback et al., 1970), whereas others have not (Goodwin et al., 1969; Parker & Tulving, 1983; Hashtroudi et al., 1983). The current findings suggest that alcohol at moderate doses can impair recognition memory when assessed a week after encoding.

When recognition items were examined independently for gist and detail, the placebo group correctly recognised more gist items than both alcohol groups. Recognition for detail information showed that the high dose group recognised less detail information than both low dose and placebo groups. Emotional stimuli have been shown to typically enhance gist recognition while suppressing memory for detail (Adolphs et al., 2001). The current study supports this finding through a general increase in gist recognition compared to detail. Unlike the placebo, neither alcohol group benefited from the emotional aspects of the film on gist recognition. This finding is consistent with previous studies that have shown that alcohol blocks the usual enhancement of memory for emotional salient information (Knowles & Duka, 2004). However, as the film did not involve neutral stimuli it is difficult to conclude if these effects were due to alcohol's ability to block enhancement of emotional stimuli or general alcohol impairment in memory. The present findings also mirror those of recent studies examining benzodiazepines' effects on emotional episodic memory (Buchanan et al., 2003; Kamboj and Curran, 2006). The present study showed that the low dose of alcohol displayed a selective effect on gist memory recognition while the high dose revealed a more global effect on both gist

and detail. These findings may suggest a role of GABAergic modulation of emotional episodic memory.

3.5.3 Peritraumatic processing

There was a clear increase in state dissociation during the test session, particularly following the stressful film, and this was unaffected by alcohol. Increases in peritraumatic dissociation are thought to be a strong predictor of memory intrusions through disruptions in conscious processing. In terms of dual-representation theory (Brewin et al., 1996; Brewin 2001), it is proposed that changes in dissociation restrict encoding via the C-memory system and thus increase the likelihood of intrusive memories. Attempts have been made to increase dissociative experiences within a laboratory and measure the consequential intrusive memory development. While some have found a positive relationship between increases in dissociation and the number of reported intrusions (Holmes et al., 2004), others have found no association between these factors (Holmes et al., 2006). Despite a general increase in state dissociation, the present study did not find that this was related to the number of reported intrusive memories. Interestingly as no differences were found between the groups in state dissociation, the group differences in the number of memory intrusions were clearly not due to observed increases in dissociative symptoms. Therefore, group differences in the number of intrusive memories can be attributed to alcohol's effect on memory and not due to other implicating factors such as dissociative changes. In relation to the specific measures used to assess dissociative reactions, particularly during an analogue trauma study, one must be cautious in interpreting the results. The DES-II (Carlson and Putman, 1993) and DSS (adapted from Bremner et al., 1998) are both questionnaire-based measures that involve the completion of numerous check boxes in response to defined 'dissociative experiences'. It has been argued that positive responses on such check boxes cannot fully capture the distinct changes in awareness that may occur during an extremely traumatic event or dissociative experience (Bryant, 2007).

Changes in mood across the testing session showed a similar effect to dissociation with a general increase for all groups in sedation, anxiety and depression ratings

over the course of the test session. However, while both the placebo and low dose groups showed an increase in discontentedness following the film, the high dose group showed no change throughout the test session. The high dose of alcohol may thus have decreased arousal for the emotional aspects of the stressful film. This may have contributed to the decrease of intrusive memory development following the trauma film. Individuals' tipsiness ratings showed that all groups reported an increase following the beverage consumption period. Both low and high dose groups showed similar increases in tipsiness ratings following beverage consumption while the placebo group showed an increase but much lower than the alcohol groups. This placebo effect provides support for the double blind procedure utilised, as does the effectiveness of blinding showed by participants' and experimenter's guesses on treatment.

Physiological measures did not show changes in heart rate between any of the time points taken during the experimental phase. Heart rate during those episodes of the film which subsequently intruded in the following week showed no difference to heart rate during the rest of the film. This lack of change was evident across all groups. The fact that alcohol consumption did not produce any effect on heart rate is consistent with previous findings. Finn et al. (1990) found an increase in heart rate following alcohol consumption but only in individuals with multigenerational family histories of alcoholism. Whilst none of the groups showed any changes in heart rate during the stressful film, alcohol may have reduced or dampened individuals' responses to the stressful stimuli (e.g., Curtin et al., 1998) although this does not explain why participants in the placebo group also showed no change.

Attempts to generalise these findings are difficult due to the obvious constraints in obtaining heart rate recordings at the time of an actual traumatic event. Laboratory based experiments examining heart rate during aversive events have revealed unclear findings. Holmes et al. (2004) found that heart rate in healthy volunteers demonstrated a reduction during a stressful film. A further decrease was also observed in heart rate during episodes of the film that subsequently intruded in the following week compared to heart rate for the rest of the film. They proposed that a reduction in heart rate during these episodes may be due to a dissociative response.

Suggestions have however been made that changes in heart rate may be confounded by to the participants' expectation of a stressful task (e.g., Prins et al., 1995). It is possible that, during testing, participants become accustomed to the setting and heart rate results may be due to relaxation and a realisation that they are not in a threatening environment.

Skin conductance data showed that individuals displayed an increased responsivity throughout the duration of the trauma film compared to other periods of the experimental phase. However, no differences were observed between the three groups. Alcohol's effect on skin conductance response is consistent with previous studies. Finn et al. (1990) found that acute alcohol did not produce significant changes in skin conductance compared to placebo when presented with an aversive stimulus. This was supported in the present study with both alcohol groups showing a similar skin conductance response to the placebo group. The present study is the first to measure skin conductance throughout a stressful film paradigm. It is clear that the stressful film generally increased skin conductance across all groups. This increase parallels trauma research and a highlighted increase in skin conductance in response to aversive auditory probes (Giesbrecht et al., 2008). Further examination of skin conductance data showed that there was a higher increase during episodes of the film that subsequently intruded compared to the remainder of the film. This suggests an increase in autonomic arousal during these periods is consistent with suggestions that amygdala responses to fear are sustained by feedback from autonomic arousal (Le Doux, 1998).

3.5.4 Limitations

An inevitable limitation of the present study is the use of a stressful film to induce intrusive memories in participants. The film itself does show a number of unpleasant and horrific scenes although it must be highlighted that viewing such events on a video rather than in real life is highly likely to change their impact on the individual. However, the film does fulfil DSM-IV (American Psychiatric Association, 1994) criterion A1 for a traumatic event with participants witnessing death and suffering. The trauma film paradigm has also been used to great success in the development of

clinical theories (e.g., Horowitz, 1969; Lazarus et al., 1965). Changes in mood and dissociation following the film in the present study provide further evidence that the use of such a paradigm has ecological validity.

A further issue with the present methodology may involve the use of diaries to record intrusions. However, past studies have used a procedure where participants are required to keep a written diary over the 7 days and then return with the completed diary for a follow up session (e.g., Brewin & Saunders, 2001; Davies & Clark, 1999). This provides no control over participants simply filling in the diary all on a single day. The present study used an improved innovative diary procedure through use of an online website for participants to fill in each day. Through the use of this novel method, participants' diary compliance was observed each day. Through the use of email and text messages as reminders, compliance was high. In this respect, the current study has made a positive development in methodology.

Another limitation of the current study involves the examination of memory for emotional information without providing a neutral comparison. Research highlights the dissociable cognitive and neural mechanisms thought to underpin memory for emotional and neutral material with emotional information found to facilitate memory recall (e.g., Cahill and McGaugh, 1998). However, Knowles and Duka (2004) found that acute alcohol administration prior to a learning episode of neutral and emotional words resulted in a general impairment of memory compared to a placebo group. Free recall of emotional and neutral items was reduced in the alcohol group suggesting that alcohol may not generate differential effects on memory for emotional and neutral information. Therefore, it might be expected that such processes would not be differentially affected within the current paradigm. However, given that the results of the current study do not parallel a typical linear disruption of memory it would be of interest, and theoretically relevant, to investigate alcohol's ability to affect emotional and neutral aspects of a traumatic experience to examine if these processes are disrupted in a similar ways.

3.5.5 Conclusions

In conclusion, alcohol dose-dependently impaired explicit memory for the trauma film whereas only the low dose of alcohol increased intrusive memories, while the high dose decreased memory intrusions. The effects of the low dose can be conceptualised within dual representation theory as impaired declarative memory for the event and therefore decreased information processed via the C-memory system, resulting in an over-representation of information via the S-memory system and a subsequent increase in memory intrusions. Findings relating to the higher dose of alcohol are more difficult to conceptualise in this framework. Speculatively, they may involve impairments to either visual processing of an event or non-declarative aspects of memory. However, it must be noted that changes in arousal induced by alcohol intoxication might also contribute to the observed differential effect on memory. Alcohol is well known for its action as a potent anxiolytic and has been shown to reduce stress in a number of situations (e.g., Levenson et al., 1980; Sayette, 1999; Sher, 1987; Sher et al., 2007). Therefore, at lower doses, some of the emotional aspects of the traumatic material might be maintained, thus, contributing to the intrusive imagery experienced by individuals, whereas general declarative memory for the event is reduced. However, at higher doses, these emotional aspects of the material may be further diminished due to a greater alcohol-induced reduction in arousal, resulting in an overall deficit in memory. Further investigation into alcohol-induced reductions in arousal and its potential role in the specific deficits in trauma memory would be needed.

Chapter 4: Acute Effects of Alcohol on Viewpoint Dependence in Spatial Memory and Intrusive Memory Development

4.1 Overview

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 (Brewin, 2003; Ehlers and Clark, 2000; Ehlers et al., 2003). As observed in Chapter 3, an analogue trauma paradigm, utilising a distressing video, provides a prospective way to investigate factors affecting the development of intrusive images within a laboratory environment (for a review, also see Holmes and Bourne, 2008). Utilising this prospective approach provides a controlled setting where specific cognitive processes can be directly measured and manipulated. In the previous chapter, alcohol intoxication while viewing a trauma video resulted in a dose-dependent inverted ‘U’ shaped curve of intrusive images. A lower dose of alcohol (0.4g/kg) increased the number of intrusions reported in the week following exposure, while a higher dose (0.8g/kg) induced no increase compared to 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, as many real-life traumas such as being a victim of aggressive behaviours or experiencing a road traffic accident often involve alcohol intoxication, it is clinically important to delineate these effects. As proposed above (Chapter 3.5.1), one potential explanation for the differential effect displayed following a low and high dose of alcohol might involve the way in which different aspects of an event are stored within memory. That is, memory for an event may comprise two representations, one involving the spatio-temporal context of the event and the other involving sensory/perceptual imagery, encoded relative to the perceiver. Therefore, the present study aimed to further the findings of alcohol’s inverted U shaped curve on intrusive memories through investigating whether the dose-dependent effect 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.

4.2 Introduction

Some theoretical accounts of intrusive memory development propose that the intrusion of trauma memories occurs due to strong perceptual priming during the original event (Ehlers and Clark, 2000; Ehlers et al., 2003). However, the finding that alcohol dose-dependently affects intrusive memories in different ways is difficult to conceptualise within this account. Although alcohol induces a robust impairment in episodic memory with specific decreases in recollection (Curran and Hildebrandt, 1998; Soderlund et al., 2007), perceptual priming is left intact following high doses (Hashtroudi et al., 1984). An alternative theoretical account for the development of intrusive memories following a traumatic event is offered by dual representation theory (Brewin et al., 1996; Brewin et al., 2010) and its close link with the neuronal mechanisms of healthy memory (Burgess et al., 2001; Byrne et al., 2007).

Healthy memory of an event comprises two closely linked representations in this account (Burgess et al., 2001; Byrne et al., 2007; O’Keefe and Nadel, 1978). One is an image-based egocentric representation of the event, reliant on the perceiver’s viewpoint and 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 spatio-temporal context that is both flexible and explicitly accessible, supported by the hippocampus and medial temporal lobe (Burgess et al., 2002; Eichenbaum and Cohen, 2004; Squire, 1992). 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 (Byrne et al., 2007; Brewin et al., 2010).

A number of functional magnetic resonance imaging (fMRI) studies have reported both diminished hippocampal activation and reduced hippocampal volume in PTSD

patients, along with a range of related memory disruptions (Bremner et al., 1995; Bremner et al., 1997; Gilbertson et al., 2002; Shin et al., 2004). More specifically, Gilbertson et al. (2007) found allocentric memory impairments in twins discordant for combat-related PTSD, suggesting underlying reductions in hippocampal function. Prolonged stress is proposed to down-regulate hippocampal function (Kim and Diamond, 2002) through associated glucocorticoid release (Kirschbaum et al., 1996; de Kloet et al., 1999; Sapolsky, 1992). Such stress-induced changes have been proposed to differentially affect different components of memory, particularly reducing spatio-temporal context of an event (Elzinga and Bremner, 2002; Jacobs and Nadel, 1998).

Hippocampal-dependent memory may also be specifically susceptible to the effects of alcohol, given that alcohol is known to impair episodic memory (Curran and Hildebrandt, 1999) and reduce hippocampal function (Soderlund et al., 2007). In animal models, alcohol specifically impairs hippocampal-dependent spatial memory, while non-spatial reference memory is preserved (for a review, see Matthews and Silver, 2004). 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 fMRI response to simple visual stimulation (approx. 0.7-0.8g/l; Gundersen et al., 2008; Levin et al., 1998), there should be no corresponding increase in intrusive imagery.

Under the above model of healthy memory, down-regulation or damage to the hippocampal system should be revealed as a specific impairment in memory tasks requiring an allocentric representation of space compared to tasks solvable with egocentric representations (O'Keefe and Nadel, 1978). King and colleagues (2002) designed a task to probe allocentric memory and tested a patient (Vargha-Khadem et al., 1997) 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 using egocentric or allocentric memory, shifted-view recognition relies solely on allocentric memory. King et al. (2002; 2004) found that hippocampal damage led to a selective impairment of shifted-view object location recognition while same-view object location memory was intact.

This study aimed to replicate the 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. It was also hypothesised 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.

4.3 Methods

4.3.1 Participants

A power calculation indicated that for a significance level of $p < 0.05$ and a power of 80%, a minimum sample size of 14 participants in each group was required. Forty-eight 18-35 year old healthy volunteers (24 males, 24 females) were recruited from the University College London student population. Participants were right handed and social drinkers (average weekly consumption of 2-14 units for females and 2-21 units for males). Participants were screened for a history of mental health treatment (psychologically or pharmacologically), previous experience of trauma and problematic drinking (CAGE; Ewing, 1984). The study was carried out in accordance with the Declaration of Helsinki and approved by the University College London ethics committee (see appendices).

4.3.2 Design

An independent-group double-blind design was used with participants randomly assigned to one of three groups ($n=16$; eight males): 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.

4.3.3 Alcohol Administration

Participants were administered either alcohol (0.4 or 0.8g/kg) or matched placebo. The alcohol beverage consisted of 90% v/w diluted with tonic water (Schweppes Ltd., Uxbridge, UK) and was divided equally into 10x50ml portions. Each beverage was mixed with two drops of Tabasco sauce (McIlhenny Co., Avery Island, LA, USA) to mask the taste. The placebo beverage consisted of 10x50ml portions of tonic water and Tabasco sauce. Beverages were consumed at 3-min intervals.

4.3.4 Procedure

Participants were screened prior to arrival on the initial test day. 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 next 30mins followed by a 10mins resting period to allow for 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. The time taken to complete both the viewpoint-dependent task and film trauma paradigm was approximately 30mins, within the ‘alcohol window’ for testing (see Rose and Duka, 2006). Participants returned a week later and received a surprise cued recall and recognition memory test for the trauma footage viewed on day 1. All participants were finally debriefed and paid.

4.3.5 Alcohol usage

The alcohol usage questionnaire (Mehrabian and Russell, 1978) is a 12-item questionnaire designed to provide a measure of habitual alcohol consumption. The items cover drinking related behaviours of wine, spirits, and beer, as well as

assessing the speed of consumption. The final three items provide a separate measure of binge drinking (Townshend and Duka, 2001).

4.3.6 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 (King et al., 2002). 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° in viewing orientation when moving from one view to the other. Participants were required to navigate towards 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 seconds each, with a 1 second inter-stimulus interval. The number of objects presented in each trial was counterbalanced between three list lengths ($n=3, 6$ or 9) to reduce predictability and any strategy 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 randomized. Object recognition at test for object locations was tested in a random order with each object presented at the original placeholder and three foils of the same object at other placeholders. Each object image included a coloured square superimposed on it and participants were required to press the corresponding coloured key on the keyboard to identify their chosen response to an object location. Small-scale pilots (King et al., 2004) 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.

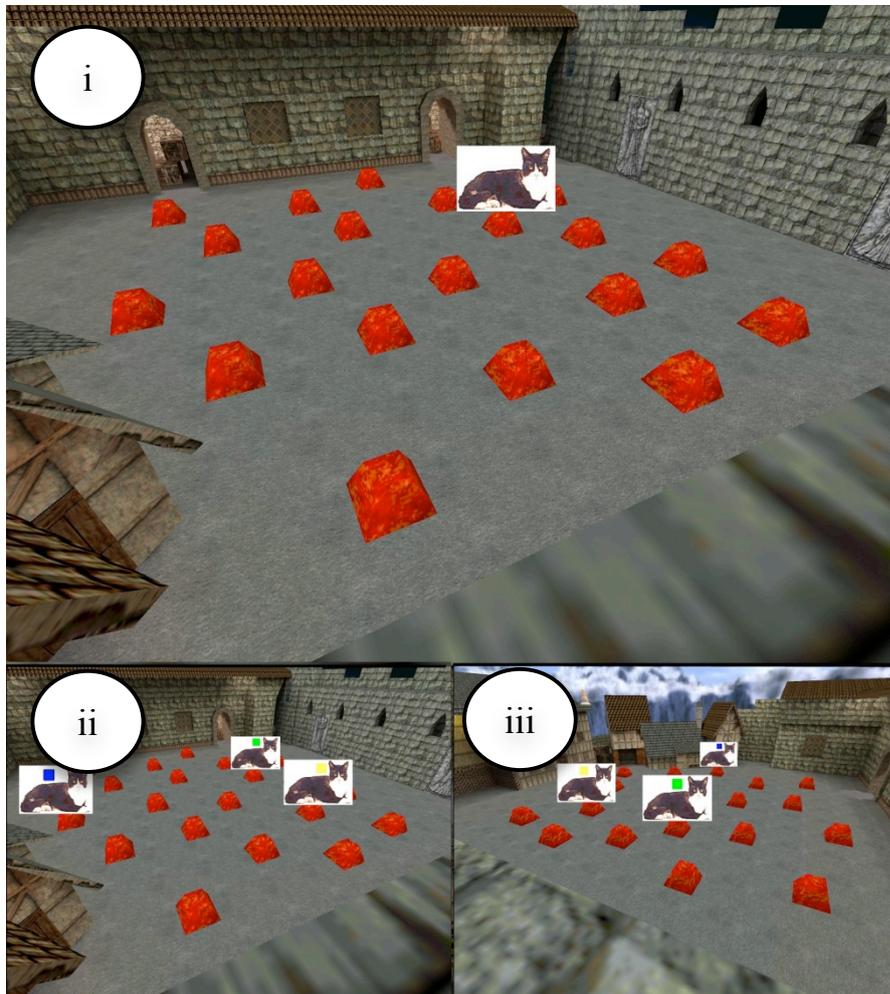


Figure 4.1. Views of the virtual environment showing the (i) presentation of a typical item from one location and testing from (ii) same-view and (iii) shifted-view.

4.3.7 Trauma film

The trauma video paradigm was administered using the same procedure as in the previous chapter. Participants were shown a video consisting of road traffic accidents (Steil, 1996) involving horrific imagery. This video has been used successfully to induce memory intrusions in a number of previous studies (Brewin and Saunders, 2001; Holmes et al., 2004; Murray et al., 2002). 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. As 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 per question) and was equally divided into six questions per scene.

4.3.8 Subjective ratings

A 16-item visual analogue scale (Bond and Lader, 1974) was used to measure subjective feelings of mood ‘at the moment’ and used as a manipulation check and to observe if any participants showed adverse effects following beverage consumption. Items are presented with 100mm lines anchored at the end of each scale with antonyms, providing scores of sedation, discontentedness and anxiety.

4.3.9 Statistical analysis

All statistical analyses were performed using SPSS version 13. All data were checked for assumptions of normality and univariate outliers and as none were beyond 2.5 standard deviations, the original dataset was used. Viewpoint dependent memory for object locations was analysed using a mixed factorial ANOVA with group as a between participant factor (placebo versus low dose versus high dose) and list length (3 versus 6 versus 9) and view (same-view versus shifted-view) as within participant factors. Results from the trauma film paradigm were analysed using polynomial trend analyses to examine if previous findings had been replicated. A quadratic trend analysis tested if increases in alcohol dose showed an inverted ‘U’ shaped relationship to the number of intrusions. It has been argued that some of the memory deficits observed during alcohol intoxication might be due to state-dependent learning, with increases in memory retrieval when individuals are again intoxicated at test (Weissenborn and Duka, 2000). To rule out these possible

confounding effects, intrusions that occurred under the influence of alcohol were omitted from analyses. A linear trend analysis tested if explicit memory for video footage after the 7 days decreased as alcohol dose increased. Subjective ratings were analysed using a mixed factorial ANOVA with group as a between participant factor and time as a within participant factor (baseline versus post-drink versus post-film). Post hoc comparisons and simple effects were corrected for multiple comparisons using Bonferroni- correction and, where used, p-values were adjusted accordingly. All analyses were initially carried out with gender as a between participants factor. As no significant effects of gender emerged on any measure, these analyses are not reported.

4.4 Results

4.4.1 Demographics

See Table 4.1. There were no significant differences between groups on age [$F(2,45) = 0.11, p = 0.90$], years in education [$F(2,45) = 0.49, p = 0.62$], alcohol usage [$F(2,45) = 0.23, p = 0.80$], and alcohol binge [$F(2,45) = 0.41, p = 0.67$].

Table 4.1. Means \pm standard deviations for demographic data across the three treatment groups.

	Placebo (N=16)	Low dose (N=16)	High dose (N=16)
Age	22.56 \pm 3.56	22.68 \pm 4.61	23.18 \pm 3.66
Number of years 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

4.4.2 Blood alcohol concentration

See Table 4.2. A 2x2 mixed factor analysis showed a significant group x time interaction [$F(1,30) = 4.43, p = 0.046$] and a main effect of group [$F(1,30) = 30.58, p < 0.001$] but no main effect of time [$F(1,30) = 0.06, p = 0.80$]. The high dose

group showed higher BAC levels than the low dose group following consumption ($p < 0.001$) and at the end of testing ($p < 0.001$). The low dose group showed a tendency of lower BAC levels at the end of testing ($p = 0.08$) compared to following consumption.

Table 4.2. Means \pm standard deviations and ranges for blood alcohol concentration (BAC; g/l) across the two alcohol groups. Measurements were taken 40mins following the start of the beverage consumption period (BAC1) and following the trauma video at the end of the session (BAC2).

	Low dose (N=16)		High dose (N=16)	
	mean	range	mean	range
BAC1	0.22 \pm 0.11	0.02 – 0.48	0.48 \pm 0.25	0.16 – 0.92
BAC2	0.16 \pm 0.07	0.05 – 0.28	0.55 \pm 0.25	0.18 – 1.04

4.4.3 Subjective ratings

See Table 4.3. Analysis of sedation ratings showed a significant group x time interaction [$F(4,90) = 2.76, p < 0.04$], a main effect of time [$F(2,90) = 36.80, p < 0.001$] and no main effect of group [$F(2,45) = 2.64, p = 0.08$]. Post hoc analysis revealed a significant group difference post-drink [$F(2,45) = 4.24, p = 0.02$] with the low dose group giving higher ratings of sedation than the placebo group ($p = 0.02$; corrected p -value). Analysis of discontentedness ratings showed a significant main effect of time [$F(2,90) = 15.53, p < 0.001$] and no main effect of group [$F(2,45) = 0.34, p = 0.71$] or group x time interaction [$F(4,90) = 0.34, p = 0.71$]. Post hoc analysis showed that ratings of discontentedness significantly increased from baseline to post-film ($p < 0.001$; corrected p -value) and post-drink to post-film ($p < 0.001$). Anxiety ratings showed no significant main effect of group [$F(2,45) = 1.08, p = 0.35$] or time [$F(2,90) = 2.23, p = 0.11$] and no group x time interaction [$F(4,90) = 1.32, p = 0.27$].

Table 4.3. Means \pm standard deviations for state dissociation and mood ratings as a function of group over the three time points of the test session: baseline, post drink, and post film.

	Baseline			Post drink			Post film		
	Placebo (N=16)	Low dose (N=16)	High dose (N=16)	Placebo (N=16)	Low dose (N=16)	High dose (N=16)	Placebo (N=16)	Low dose (N=16)	High dose (N=16)
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 ^a	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

4.4.4 Same- versus shifted-view recognition

See Figure 4.2. A mixed factorial ANOVA of the mean percentage of correctly recognized items showed significant interactions of group x view [$F(2,45)=5.08, p=.01, \eta^2 = 0.19$] and list length x view [$F(2,90)=26.94, p<.001, \eta^2 = 0.39$], and main effects of group [$F(2,45)=8.07, p<.001, \eta^2 = 0.27$], list length [$F(2,90)=102.90, p<.001, \eta^2 = 0.69$] and view [$F(2,45)=106.40, p<.001, \eta^2 = 0.71$]. Post hoc analysis using paired samples t-tests (Bonferonni corrected alpha of 0.017) showed a greater number of items correctly recognized in the same-view condition compared to the shifted-view condition for the placebo group [$t(15) = 4.91, p < .001, d = 1.06$], low dose group [$t(15) = 6.98, p < .001, d = 1.74$] and high dose group [$t(15) = 6.16, p < .001, d = 1.19$]. Analyses 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 [$t(15) = 7.64, p < .001, d = 2.33$], while no significant differences were found at list lengths 6 and 9 (p 's $> .50$). Separate analyses of each view showed a significant difference between groups on correctly recognized items on the same-view condition [$F(2,45) = 3.77, p = .03, \eta^2 = 0.14$] and the shifted-view condition [$F(2,45) = 10.30, p < .001, \eta^2 = 0.31$]. For same-view, the high dose group had significantly poorer recognition accuracy than the placebo group ($p=.03, d = 0.87$), while the low dose was unimpaired ($p > 0.9$). The difference between high and low dose groups did not reach significance ($p=.18$). For shifted-view, both the low dose and high dose groups recognized significantly fewer items than the placebo group ($p=.04, d = 1.21$ and $p<.001, d = 1.50$, 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 above analyses suggest that low levels of alcohol specifically impair shifted-view performance while high levels impair performance on both same- and shifted-views. However, one complicating factor is that overall performance varies between the same- and shifted-views. 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 above group x

view interaction is still significant [$F(2,45)=6.15, p<.01, \eta^2 = 0.22$], in addition to the view x list interaction [$F(2,45)=.21, p=.02, \eta^2 = 0.13$] and with main effects of view [$F(1,45)=33.02, p<.001, \eta^2 = 0.42$], list [$F(1,45)=9.82, p<.01, \eta^2 = 0.18$] and group [$F(2,45)=10.45, p<.001, \eta^2 = 0.32$].

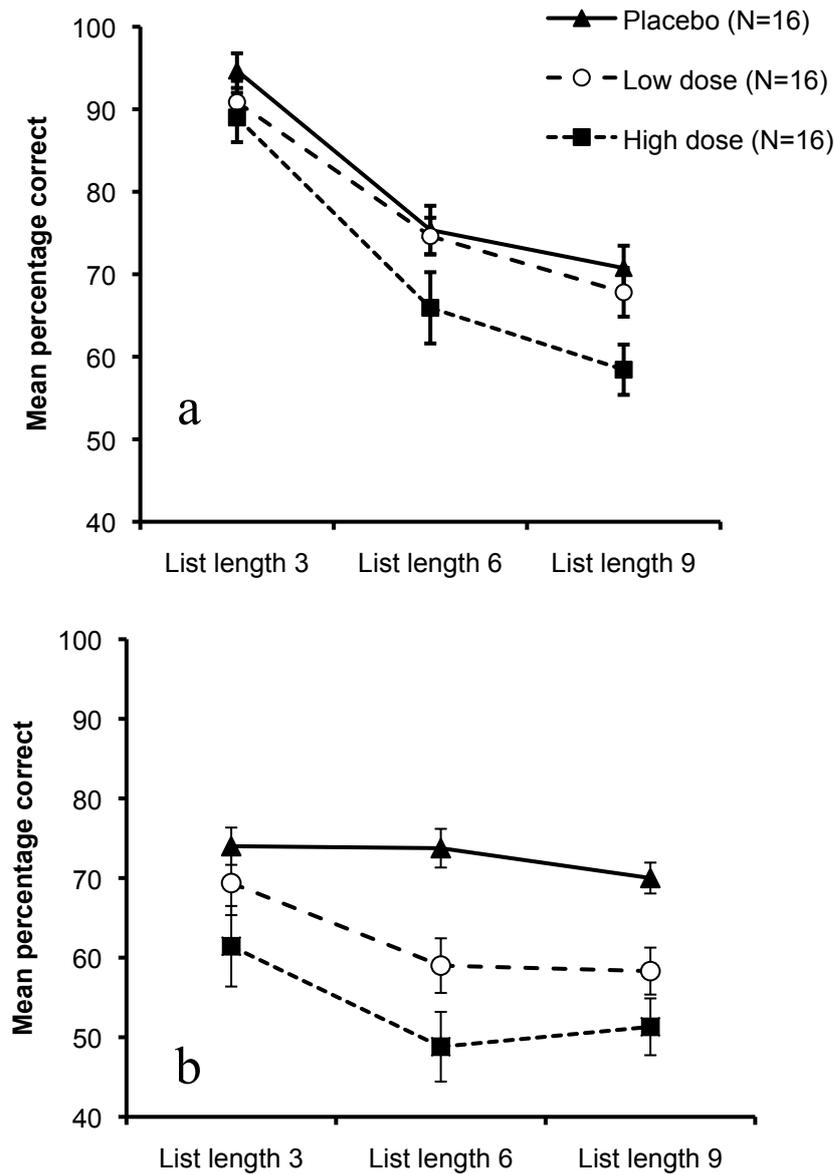


Figure 4.2. Mean percentage of correctly recognised items as a function group and list length for (a) same-view and (b) shifted-view conditions. Bars represent SEM.

Further analysis showed a significant difference on same-view recognition between placebo and high dose groups ($p=.03$, $d = 0.90$), but no difference between placebo and low dose groups ($p > .9$). The difference between low and high dose groups on the same-view performance approached significance ($p=.08$, $d = 0.75$). Shifted-view recognition showed significant differences between the placebo and low dose groups ($p<.01$, $d = 1.39$), and between placebo and high dose groups ($p<.001$, $d = 1.87$), and no difference between the low and high dose groups ($p=.12$).

4.4.5 Intrusive and explicit memory

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 [$F(1,45) = 6.62$, $p = 0.01$] with an increase following the low dose of alcohol (Figure 4.3).

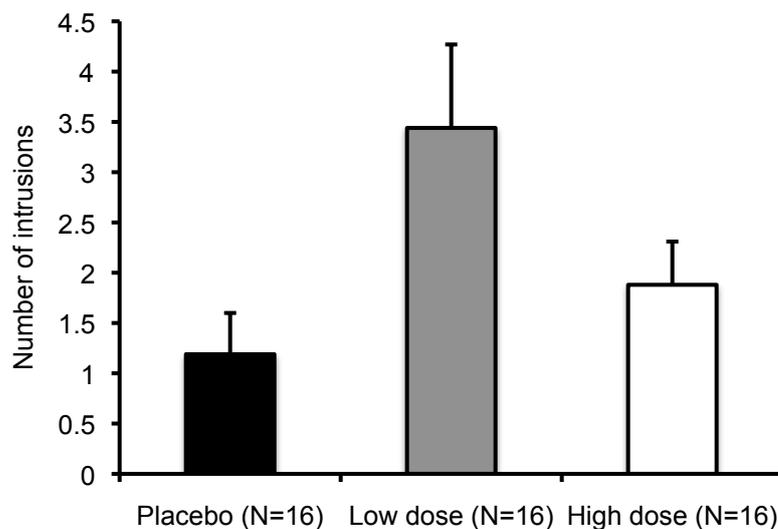


Figure 4.3. Mean (SEM) number of intrusive memories reported in the 7 days after exposure to the trauma video.

Explicit memory for the footage showed the expected decrease in performance as alcohol dose increased (Figure 4.4.), revealed by the significant linear trend across

groups on both cued recall [$F(1,45) = 6.88, p = 0.01$] and recognition [$F(1,45) = 7.09, p = 0.01$].

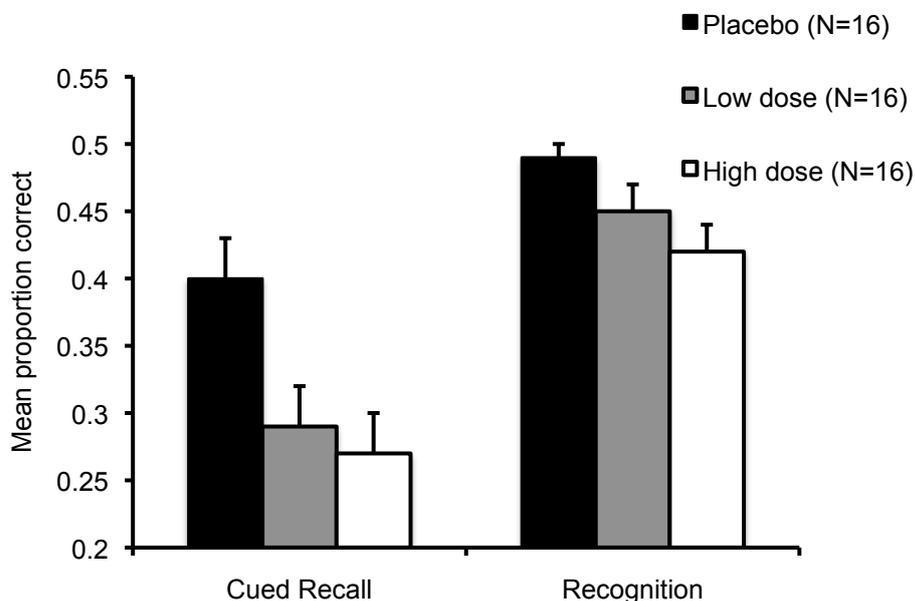


Figure 4.4. Explicit memory performance for trauma video. Mean (SEM) number of memories reported in the 7 days after exposure to the trauma video.

4.4.6 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 using 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 ($r(11) = -0.66, p = 0.01$). 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. As 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 from this correlation and the analysis was run controlling for same-view scores and group assignment (placebo versus low dose).

A negative relationship between intrusions and decreases in shifted-view recognition was observed ($r(25) = -0.43, p = 0.03$) confirming that the greater the impairment in recognition, the more intrusions were reported by participants. No other significant correlations were found.

4.5 Discussion

The present study 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 found previously. As predicted by a neurobiologically based dual representation model (Brewin et al., 2010), a selective impairment of shifted-view object location recognition following a low dose of alcohol was observed while 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. The results also replicated the previous findings from chapter 3 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 the 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.

4.5.1 Alcohol on intrusions and viewpoint dependence in spatial memory

To our knowledge, this is the first study to assess egocentric versus allocentric memory following 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 following alcohol. The observed reduction in allocentric memory following the low dose is in accordance with previous studies reporting acute deficits in the encoding of spatio-temporal context within episodic memory (Curran and Hildebrandt, 1998; Soderlund et al., 2007).

Accounts of intrusive memories proposing dissociable memory systems posit that successful storage of spatio-temporal context is essential to the suppression of involuntary re-experiencing (Brewin, 2001; Brewin et al., 2010; Jacobs and Nadel, 1998). 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 following 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 may reflect impairment of egocentric memory at the high dose. Importantly, alcohol is known to affect multiple cognitive abilities, including attentional functions (Abroms et al., 2006; Koelega, 1995; Schulte et al., 2001) and working memory (Grattan-Miscio and Vogel-Sprott, 2005; Schweizer et al., 2006). Presumably these impairments become more pronounced as alcohol dosage increases although few studies have specifically addressed acute dose-response curves in cognitive function. (although see chapter 2). 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 may help to explain why there was no increase in intrusions relative to placebo. The same impairments that decreased same-view performance may have

affected encoding of the trauma footage so as to reduce the number of intrusions. Of particular relevance here is the evidence that concurrent tasks that compete for visuo-spatial processing are able to decrease intrusions (Holmes et al., 2004; Holmes et al., 2009), 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 and/or an indirect result of disruptions to contributory cognitive processes needs to be ruled out in future studies.

It is interesting to note that no gender differences were observed on any of the tasks used within this study. Some research has shown that a male advantage exists for some forms of spatial processing. For example, males have been found to perform better than females at remembering distances and routes along explored routes (Montello et al., 1999; Postma et al., 2004). In relation to the specific spatial processes examined in the current study, mental rotation and spatial navigation tasks typically reveal an advantage for males over females (Astur et al., 1998). This is particularly significant in the current line of research as females are at higher risk of developing PTSD following a traumatic experience (Ozer et al., 2003). However, it has been proposed that gender differences in spatial memory may be due to males and females utilising different strategies and it is not clear if the observed reductions by females are a direct effect of spatial memory deficits (Burgess et al., 2004). It is therefore assumed that the equal gender split of participants did not affect the results although future studies specifically examining gender affects might require a larger sample size.

4.5.2 A mechanism for alcohol-induced effects on memory

A possible explanation for the effect of alcohol on allocentric memory may be related to neurochemical changes in hippocampal function. An allocentric representation requires the successful encoding of spatial information and is impaired following hippocampal damage (King et al., 2002; 2004). Alcohol induced decrements in memory are proposed to occur via alterations in hippocampal neuronal activity (Gundersen et al., 2008; Soderlund et al., 2007; White et al., 2000)

via its actions both as an NMDA antagonist and as a potentiator of GABA-mediated inhibition, known mechanisms of blocking LTP.

Speculatively, one mediator of the decrease in same-view recognition induced by the high dose may 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_A receptor subunit sensitivity (Soldo et al., 1994; Criswell et al., 1993). Drugs that stimulate the release of endogenous GABA, such as clonidine, have been found to show regional specific increases in frontal and parietal cortex (Pittaluga and Raiteri, 1988). It has thus been proposed that alcohol may share a similar action and increase GABA-receptor sensitivity in the parietal cortex, particularly disrupting spatial attentional processing (Schulre et al., 2001). 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 (Brewin, 2001; Jacobs and Nadel, 1998; Matthews and Silver, 2004). The hippocampus plays an important role in regulating the hypothalamic-pituitary-adrenal axis and is particularly susceptible to prolonged stress (Kim and Diamond, 2002). Marked increases in cortisol during high levels of stress can impair functioning of the hippocampus (McEwen, 1999; Salpolsky, 1992) 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.

4.5.3 Limitations

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 non-significant, increases in anxiety, although significant increases in discontentedness were observed. The use of a trauma video does fulfill DSM-IV (APA, 2000) criterion A1 in that participants witnessed death and serious injury, and has been successfully used in a wide range of studies (Holmes and Bourne, 2008). 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.

A further issue in regard to the specific methodology used here involves the task demands of same- and shifted-view object location recognition conditions. It could be argued that the two conditions involve general differences in difficulty, with alcohol-induced impairments representative of increased difficulty during shifted-view recognition. However, in an attempt to match the two conditions, it has been found that 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, performance in sober participants can be matched (see King et al., 2004). Further, examination of the results showed that the placebo group performed at a similar level on both same- and shifted- conditions for list lengths 6 and 9. Therefore, these findings provide some evidence in supporting the use of a direct comparison between same- and shifted-view performance.

4.5.4 Conclusions

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 which 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.

Chapter 5: Acute Effects of Alcohol on Viewpoint Dependence in Spatial Memory and Contextual Fear Memory

5.1 Overview

The ability to learn from experiences that elicit fear is an essential adaptive function. Information about cues and contexts that might predict danger must be integrated into memory so that, when similar information is experienced again in the future, the appropriate response can be made. Posttraumatic stress disorder (PTSD) is a severe reaction to a fearful traumatic event in which individuals develop trauma-related symptoms (APA, 2000). A primary symptom of PTSD is the intrusive imagery and reactivation of fear in response to trauma-related cues (Brewin, 2003; Ehlers and Clark, 2000; Pitman, 2000). Alcohol is frequently associated with the occurrence of real-life traumatic events and is often used by individuals as a way of self-medicating against related symptoms. From a clinical perspective, it is therefore essential to delineate the way in which alcohol might interact with trauma memory. The previous chapters have provided evidence that alcohol can dose-dependently affect intrusive memories in different ways. A low dose of alcohol was found to increase intrusive imagery, associated with selective reductions in shifted-view recognition that relies on the ability to encode spatial-temporal context. In contrast, egocentric memory supported by sensory/perceptual input was spared, possibly underpinning the increase in intrusive imagery. The present study aimed to further explore the selective reduction in shifted-view object location recognition following a low dose of alcohol by investigating the ways in which these processes may be associated with contextual fear memory.

5.2 Introduction

A contextual fear-conditioning paradigm offers a valuable method to further investigate alcohol-induced impairments in memory related to the processing of an aversive event. Fear conditioning has often been utilised as way of developing and testing hypothesis driven models of the psychophysiology and neural correlates of fear processing in PTSD (e.g., Milad et al., 2008; 2009; Orr and Pitman, 1993;

Rauch et al., 1999). Some researchers have proposed that the initial traumatic experience and the related symptoms in PTSD could be considered a complex form of fear conditioning (Grillon et al., 1996; Pitman, 1988). In a typical fear-conditioning paradigm (see Figure 5.1), a neutral conditioned stimulus (CS) is paired with an aversive unconditioned stimulus (US) such as a mild electric shock. After acquiring the association between the CS and US, the CS alone induces a conditioned fear response, such as freezing in rodents (LeDoux, 1998) or skin conductance responses (SCR) in humans (Craig, 2002). Following repeated presentation of the CS in the absence of the US, the CR gradually diminishes, a phenomenon termed extinction (for a review, see Myers and Davis, 2002). Importantly, the reduction in responding to the CS does not reflect ‘unlearning’ of the association between the CS and US but instead represents the formation of an inhibitory memory (for a review, see Delamater, 1996), modulated by its specific context (Bouton, 2004). Evidence for the existence of both the conditioning and extinction memories in parallel has been observed by the return of the CR under certain conditions, including the passage of time (spontaneous recovery; Pavlov, 1927; Rescorla, 2004), a change in context after extinction (renewal; Bouton and Ricker, 1994), or the post-extinction presentation of US-only trials (reinstatement; Rescorla and Heth, 1975).

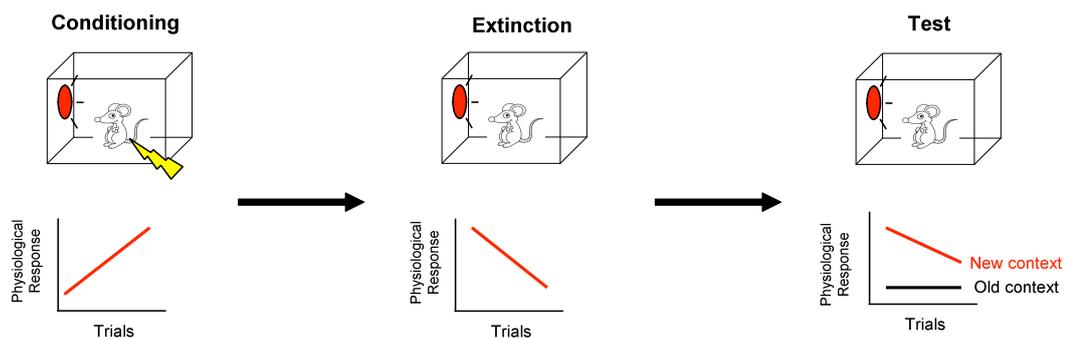


Figure 5.1. A simple illustration of a typical fear-conditioning paradigm showing each phase of the protocol and the physiological responding during each phase.

The role of context is particularly influential in the acquisition and extinction of fear with storage of contextual information thought to rely on integrity of the hippocampus (Corcoran and Maren, 2004; Bouton, 2004; LaBar and Phelps, 2005).

When an aversive US is administered during acquisition, the fear response not only becomes associated to discrete cues but also to the context in which the experience occurred. Several researchers have reported that damage to the hippocampus impairs contextual but not auditory fear conditioning in rodents (Kim and Fanselow, 1992; Kim et al., 1993; Phillips and LeDoux, 1992). The hippocampus is widely regarded as being essential in the storage of spatial relations between elements in the environment (Eichenbaum and Cohen, 2004; Fanselow, 2009; Nadel and Moscovitch, 1997), providing a spatial-temporal context within an allocentric representation (Burgess et al., 2001; Byrne et al., 2007; O'Keefe and Nadel, 1978). In this view, the hippocampus is not required to form direct associations between specific stimuli and unconditioned responses, a process which is predominantly mediated by the lateral amygdala (Maren, 2003; Phelps and LeDoux, 2005). However, the successful storage of contextual information during acquisition is proposed to provide a unitary representation that can enhance fear responses when retrieval occurs in the same context (e.g., Fanselow et al., 1993; Rudy and O'Reilly, 1999; 2001).

During extinction, context plays an important modulatory role and involves a new learning of an association between the CS and *no* aversive outcome within the new environment (for a review, Bouton, 2004). Hippocampal lesions have been shown to impair extinction learning in a number of paradigms (Becker and Olton, 1980; Fischer et al., 2007; Schmaltz and Theios, 1972). Following extinction, the hippocampus has also been shown to be important in the context modulation of extinction recall in animals (Corcoran and Maren, 2004) and in humans (LaBar and Phelps, 2005; Milad et al., 2009). Extinction recall (sometimes referred to as extinction retention) refers to the ability for an animal or person to exhibit the extinction memory thus inhibiting the fear reaction in response to the CS.

Although intrusive memory and fear memory consist of different paradigms to measure related memory systems, recent accounts have identified common psychological and neural mechanisms in the distinct psychopathology observed in the development and persistence of PTSD (e.g., Brewin, 2001; Brewin et al., 2010; Rauch et al., 1999; 2006). In particular, the successful encoding of spatial-temporal

context, supported by the hippocampus is thought to be critical in exerting top-down control over involuntary memory retrieval (Brewin et al., 2010; Byrne et al., 2007). During a traumatic event, prolonged stress may down regulate hippocampal function through associated glucocorticoid release (Kim and Diamond, 2002; Salpolsky, 1992). In contrast, sensory/perceptual bound characteristics associated with lower-level processing are stored, associated with their affective modulation via the amygdala (LeDoux, 1998). In the absence of a corresponding context, trauma-related cues in the environment can trigger involuntary retrieval of lower-level sensation-based representations and the re-activation of fear (Brewin et al., 2010; Jacobs and Nadel, 1998; Rauch et al., 1999).

Decreases in hippocampal activity and reduced hippocampal volume in PTSD patients have consistently been shown (Bremner et al., 1995; 1997; 2003; Shin et al., 2002). A number of studies have also reported specific impairments in fear *extinction* learning, whereas fear *acquisition* seems to be intact (Bleichert et al., 2007; Orr et al., 2000; Peri et al., 2000). In addition, Milad and colleagues (2008; 2009) have shown that the recall of an extinction memory is impaired in PTSD patients and that extinction recall is correlated with increased hippocampal and ventral/medial prefrontal cortex activation supporting the view of the contextual modulation of extinction recall.

Hippocampal-dependent memory may be particularly sensitive to an acute dose of alcohol due to ethanol's neurochemical action on glutamatergic and GABAergic systems (for reviews, see Matthews and Silvers, 2004; White et al., 2003). Alcohol is known to block NMDA receptor activity and potentiate GABA mediated inhibition, both processes required for LTP and LTD that are thought to underlie synaptic plasticity in memory. Episodic memory is robustly impaired following acute alcohol (Curran and Hildebrandt, 1998; Leitz et al., 2009) with reductions in performance associated with decreases in hippocampal activity (Soderlund et al., 2007). Furthermore, findings from the previous chapter indicate that allocentric memory, which is supported by the hippocampus (King et al., 2002; 2004), is selectively impaired following a low dose of alcohol. However, image-based

egocentric memory, which relies on sensory/perceptual input, supported by early sensory areas, seems to be spared.

NMDA and GABA receptor activity is a critical component of fear acquisition (Harris and Westbrook, 1999; 2001) and its extinction (Akirav et al., 2006; Harris and Westbrook, 1998; Ledgerwood et al., 2005; Walker et al., 2002). Alcohol might therefore be expected to disrupt fear acquisition and extinction. Research into alcohol's effect on the storage and expression of fear memory to date has been restricted to animal studies, with disruptions in the acquisition of fear only evident at higher doses (e.g., Gulick and Gould, 2007; Pautassi et al., 2007). Alcohol also impairs context-dependent learning but not cue-dependent learning in fear conditioning paradigms (e.g., Gould, 2003; Melia et al., 1996). Extinction learning has also been found to be impaired following alcohol in rodents (Lattal, 2007), but not during a discriminative learning paradigm in humans (Loeber and Duka, 2009).

The present study aimed to examine the effects of a low dose of alcohol (0.4 g/kg) on contextual fear memory and, concurrently, on same- and shifted-view object location recognition. It was expected that the low dose of alcohol would impair the encoding of contextual information, as evidenced by a selective reduction in shifted-view recognition as observed previously (Chapter 4). In contrast, sensory/perceptual associations would be spared as evidenced by intact performance on same-view recognition. It was predicted that this selective reduction in shifted-view recognition would translate to the fear memory paradigm through alcohol-induced reduction in the contextual characteristics associated with the acquisition and extinction of fear. However, in light of the spared same-view recognition supported by sensory/perceptual input, it was also predicted that learning the association between the conditioned and unconditioned stimulus would be preserved. It was not known if impairments to contextual encoding would be seen during extinction learning itself or later (on day 2) during a test of extinction recall.

5.3 Method

5.3.1 Participants

Sample size was determined in advance using a power estimation, which indicated that for a significance level of $p < 0.05$ and a power of 80%, a sample size of 17 participants in each group was required. Due to time restriction, a total of thirty-two healthy volunteers (20 females) were recruited from the University College London undergraduate and postgraduate population. The study was carried out in accordance with the Declaration of Helsinki and was approved by the University College London Ethics Committee (see appendices). Participants gave written, informed consent prior to taking part in the study. The inclusion criteria were that participants were aged 18 – 35 and had not received any mental health treatment in the form of therapy or medication. Participants could only take part in the study if they were moderate social drinkers (average weekly consumption of 2-14 units for females and 2-21 units for males). The CAGE (Ewing, 1984) alcohol screening questionnaire was administered to assess individuals for problematic drinking and participants who scored 2 or more (out of 4) were excluded from taking part. Participants were also administered an initial breathalyser to check they had not consumed any alcohol prior to taking part in the experiment.

5.3.2 Design

An independent-group double-blind design was used with participants randomly assigned to one of two treatments ($n=16$ per group): a placebo beverage or a low dose of alcohol. Participants were tested on two separate occasions on consecutive days, receiving alcohol or placebo only on the first test session.

5.3.3 Drug administration

Participants were administered either alcohol (0.4g/kg) or a matched placebo beverage. The alcohol beverage consisted of 90% v/w diluted with tonic water (Schweppes Ltd., Uxbridge, UK) and was divided equally into 10x50ml portions.

Each beverage was mixed with two drops of Tabasco sauce (McIlhenny Co., Avery Island, LA, USA) to mask the taste. The placebo beverage consisted of 10x50ml portions of tonic water and Tabasco sauce. Beverages were consumed at 3-min intervals.

4.3.4 Procedure

Participants were screened prior to arrival on the initial test day. On the first day of testing, participants filled out the alcohol usage questionnaire and baseline mood visual analogue scales (VAS). They then consumed the drinks over the next 30-min followed by a 10-min resting period to allow for alcohol to be absorbed. The post-drink VAS was next completed and individuals performed the viewpoint-dependent memory task. Finally, acquisition and extinction phases of the contextual fear memory paradigm were carried out followed by a final VAS. The time taken to complete the viewpoint-dependent task and fear acquisition and extinction paradigm was approximately 30mins, within the ‘alcohol window’ for testing (see Rose and Duka, 2006). Participants returned the next day and performed the fear memory recall task. All participants were finally debriefed and paid.

5.3.5 Alcohol usage

The alcohol usage questionnaire (Mehrabian and Russell, 1978) was used to provide a score of participants’ habitual alcohol use (see appendix). The 12-item covers drinking related behaviours of wine, spirits, and beer, as well as assessing the speed of consumption. The final three items were taken to provide a separate measure of binge drinking (Townshend and Duka, 2001).

5.3.6 Viewpoint dependent memory

Viewpoint-dependent memory was assessed through the use of a virtual environment (VE) and is described in detail in the previous Chapter. In brief, the VE comprised a virtual courtyard in which participants could navigate along two of the 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. During each trial, participants navigated towards 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. The number of objects presented in each trial was counterbalanced between two list lengths ($n=6$ or 9). 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 a shifted-viewpoint. Viewpoint at test was counterbalanced and presentation order of viewpoint and list length randomized. Object recognition at test for object locations was tested in a random order with each object presented at the original placeholder and three foils of the same object at other placeholders. Each object image included a coloured square superimposed on it and participants were required to press the corresponding coloured key on the keyboard to identify their chosen response to an object location.

5.3.7 Fear memory acquisition, extinction and recall

Fear memory was assessed through the use of an adapted 2-day fear-conditioning protocol that occurred within the same virtual environment used to assess viewpoint-dependent memory. As in the previous task, participants could navigate along two of the perimeter walls at rooftop level. The specific procedure is depicted in Figure 5.2. During the task, participants first chose a level of shock intensity that was significantly annoying yet not too uncomfortable for use in the experiment. A black box was placed in the centre of the virtual courtyard, which served as the stimuli for which the conditioned stimulus (CS) could be manipulated. Each trial began from a neutral location on the perimeter wall and a traffic cone appeared at one of the two far corners of the VE at rooftop level. Participants navigated towards the cone and on contact their view was shifted to a standard one of the black box. For each trial the box remained black for 3-sec and then changed to the CS (red or yellow), which remained on screen for a further 6-sec. During the habituation phase on day 1, the CS+ and CS- were presented from each of the two viewpoints (four of each).

Acquisition took place from one of the two corners of the courtyard, which included 16 trials of 8 CS+ and 8 CS- presented in random order. Acquisition and extinction was counterbalanced across the two viewpoints of the VE. CS+ was paired with shock with a 60% partial reinforcement rate. When shock occurred it did so 250ms before CS+ offset and therefore both CS+ and shock co-terminated. For all phases except the habituation phase participants were informed that they may or may not receive a shock.

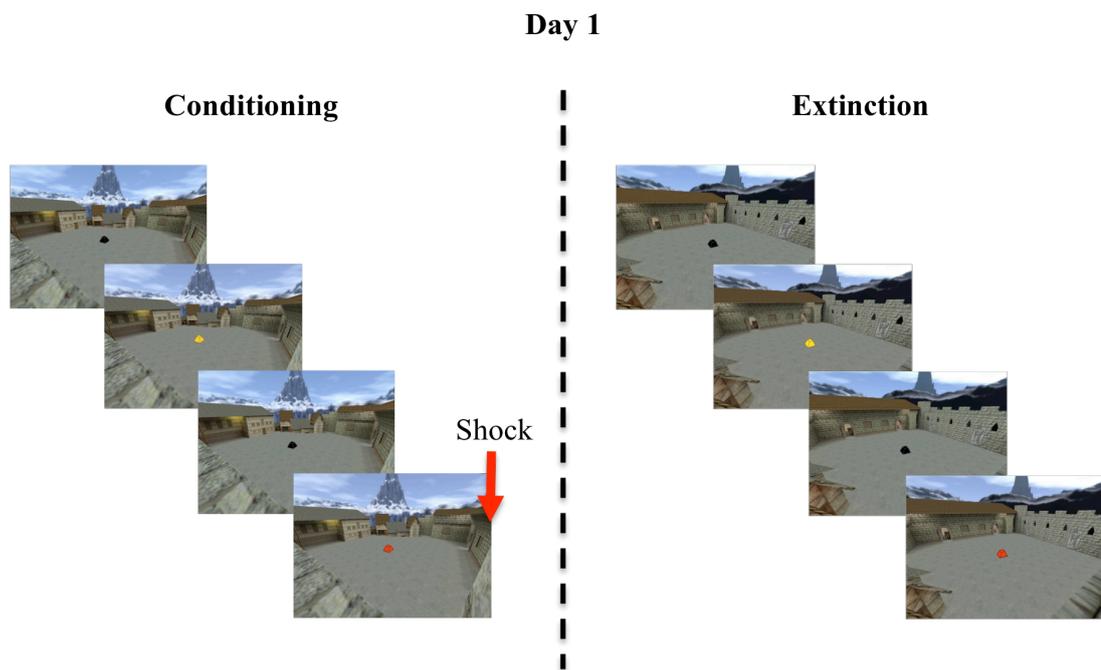


Figure 5.2. Illustration of the fear memory acquisition and extinction phases. During each phase, participants' view was changed to a standard one of the black box that, after a short delay, changed to the CS. CS+ was paired with shock only during acquisition.

Recall on day 2 occurred in the same VE as day 1 (see Figure 5.3). Participants again started from the same neutral location and navigated to a cone that appeared in one of the two corners of the VE. Presentation of the first three CS was counterbalanced between the acquisition and extinction viewpoint (half participants received three CS+ from acquisition and extinction viewpoint first), followed by a randomised order of further CS presentations.

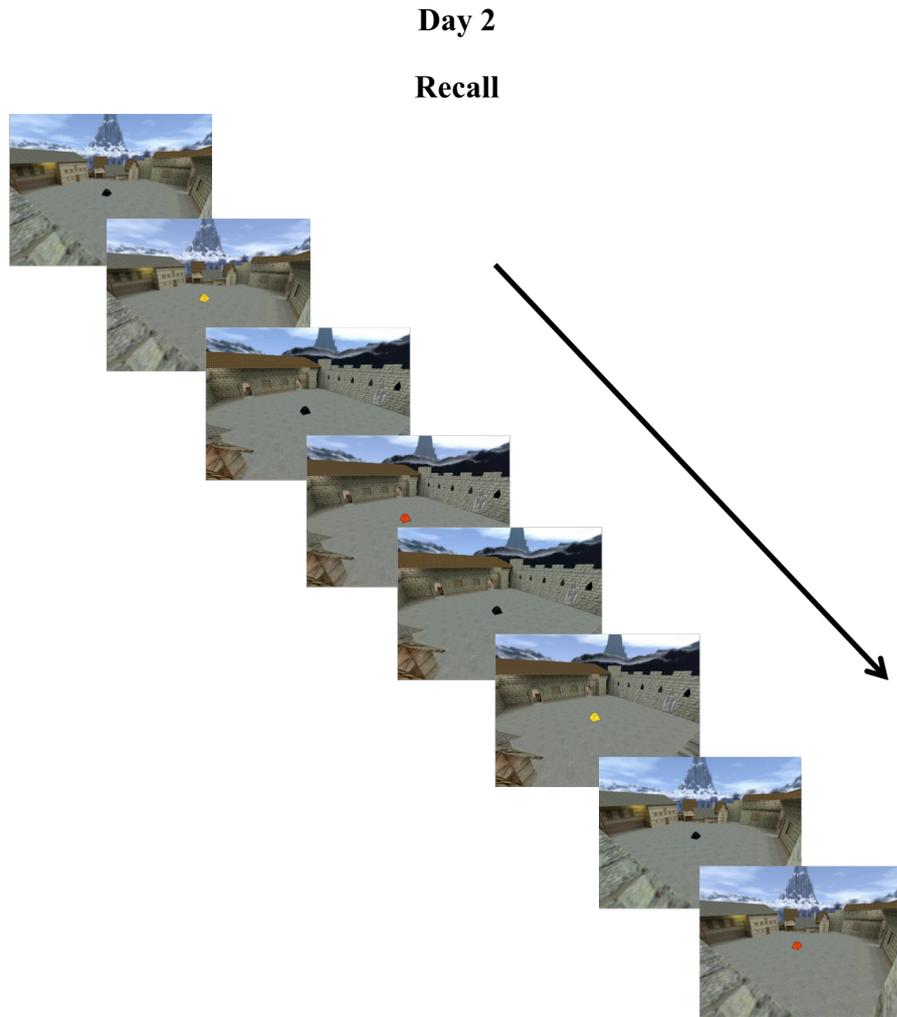


Figure 5.3. Illustration of the fear memory recall phases that occurred on day 2. Participants experienced the CS+ and CS- from both viewpoints 1 and 2, which were presented in a randomised order.

5.3.8 Physiological measures

Physiological reactions were measured online during each phase through skin conductance responses (SCR) via silver / silver chloride (Ag/AgCl) electrodes attached to the index and middle finger of the non-dominant hand. Responses were

transformed through a SC5 24 bit digital skin conductance amplifier (Contact Precision Instruments, Psylab, London).

5.3.9 Subjective ratings

A 16-item visual analogue scale (Bond and Lader, 1979) was used to measure subjective feelings of mood 'at the moment' and used as a manipulation check and to observe if any participants showed adverse effects following beverage consumption. Items are presented as 100mm lines anchored at the end of each scale with antonyms, providing scores of sedation, discontentedness and anxiety.

5.5.10 Statistical analysis

All statistical analyses were performed using SPSS version 13. Data were checked for assumptions of normality and univariate outliers. No outliers were determined and therefore the original data set was used. Viewpoint-dependent memory for object locations was analysed using a mixed factorial ANOVA with group as a between participant factor (placebo versus alcohol) and list length (6 versus 9) and view (same-view versus shifted-view) as within participant factors. SCR data were analysed by subtracting the mean SCR of the CS- from the mean of the CS+ to calculate the difference in responses. The acquisition phase was analysed between groups using an independent samples t-test on the late phase (last 4 presentations; e.g., Schiller et al., 2009). Extinction was assessed using a 2x2 mixed factor analysis with group as a between factor (placebo versus alcohol) and phase as a within factor (early versus late). Recall of fear was also analysed using a 2x2 mixed factor ANOVA with group as a between factor and condition as a within factor (conditioning viewpoint versus extinction viewpoint). Subjective ratings were analysed using a mixed factorial ANOVA with group as a between participant factor and time as a within participant factor (baseline versus post-drink versus post-tasks). Post hoc comparisons and simple effects were corrected for multiple comparisons using Bonferroni correction through adjusted *p*-values.

5.4 Results

5.4.1 Demographics

Independent samples t-tests showed no differences between groups on age [$t(30) = 0.76, p = 0.45$], years in education [$t(30) = 0.86, p = 0.39$], alcohol usage [$t(30) = 0.06, p = 0.95$], and alcohol binge [$t(30) = 0.23, p = 0.82$].

Table 5.1. Means \pm SDs for demographics across treatment groups.

	Placebo (N=16)	Alcohol (N=16)
Age (years)	22.88 \pm 3.79	23.94 \pm 4.07
Education (years)	16.56 \pm 1.41	17.00 \pm 1.41
Alcohol usage (AUQ)	28.68 \pm 13.23	29.07 \pm 22.58
Alcohol binge (AUQ)	18.53 \pm 10.39	19.98 \pm 22.73

5.4.2 Blood alcohol concentration

Analysis of blood alcohol concentration (BAC) for the alcohol group showed a significant decrease from post-beverage consumption to the end of the test session on day 1 [$t(15) = 3.10, p = 0.007$].

Table 5.2. Means \pm SDs and ranges for blood alcohol concentration (BAC) following beverage consumption (BAC1) and at the end of the test session (BAC2).

	Mean	Range
BAC 1 (g/l)	0.32 \pm 0.19	0.14 – 0.88
BAC 2 (g/l)	0.24 \pm 0.12	0.02 – 0.51

5.4.3 Subjective ratings

Repeated measures ANOVA on sedation ratings showed a trend of a group x time interaction [$F(2, 60) = 2.74, p = 0.07$] and no main effects of group [$F(1, 30) = 0.50, p = 0.47$] or time [$F(2, 60) = 1.84, p = 0.17$]. Further analysis of simple main effects revealed a significant change in sedation over time in the alcohol group [$F(2, 30) = 8.19, p = 0.001$] with a significant increase from baseline to post beverage [$p = 0.003$]. Analysis of discontentedness ratings showed no significant main effects of group [$F(1, 30) = 0.33, p = 0.57$] or time [$F(2, 60) = 0.75, p = 0.48$], and no group x time interaction [$F(2, 60) = 0.83, p = 0.44$]. Analysis of anxiety ratings showed a tendency towards a main effect of group [$F(1, 30) = 3.66, p = 0.06$] with reduced anxiety ratings in the alcohol group. There was no main effect of time [$F(2, 60) = 1.80, p = 0.16$] or group x time interaction [$F(2, 60) = 0.48, p = 0.62$].

Table 5.3. Means \pm SDs (mm) for subjective ratings as a function of treatment groups across the test session.

	Placebo (N=16)			Alcohol (N=16)		
	Baseline	Post drink	Session end	Baseline	Post drink	Session end
Sedation	25.14 \pm 26.77	23.84 \pm 16.06	26.04 \pm 18.76	14.97 \pm 10.76	28.04 \pm 16.00	21.31 \pm 11.91
Discontentedness	22.15 \pm 16.85	19.70 \pm 16.07	24.94 \pm 19.47	18.43 \pm 12.03	19.90 \pm 16.57	19.70 \pm 14.55
Anxiety	27.00 \pm 21.59	20.97 \pm 17.67	26.69 \pm 20.47	13.53 \pm 15.16	12.66 \pm 13.59	17.59 \pm 18.88

5.4.4 Viewpoint dependent memory

See figure 5.3. Analysis of correct object location recognition showed significant interactions of group x view [$F(1,30) = 11.37, p = 0.002, \eta^2 = 0.28$] and view x list length [$F(1, 30) = 6.77, p = 0.014, \eta^2 = 0.18$]. Significant main effects of view [$F(1, 30) = 11.37, p = 0.002, \eta^2 = 0.26$] and list length [$F(1, 30) = 6.65, p = 0.015, \eta^2 = 0.18$] were also found. Further analysis revealed that the groups did not differ on

same-view recognition ($p = 0.90$) but on shifted-view recognition the alcohol group recognised significantly fewer object locations correctly compared to placebo ($p = 0.018$, $d = 0.76$). The alcohol group also showed a significant decrease in shifted-view performance compared to same-view ($p < 0.001$, $d = 1.34$) whilst the placebo group showed no difference between conditions ($p = 0.58$).

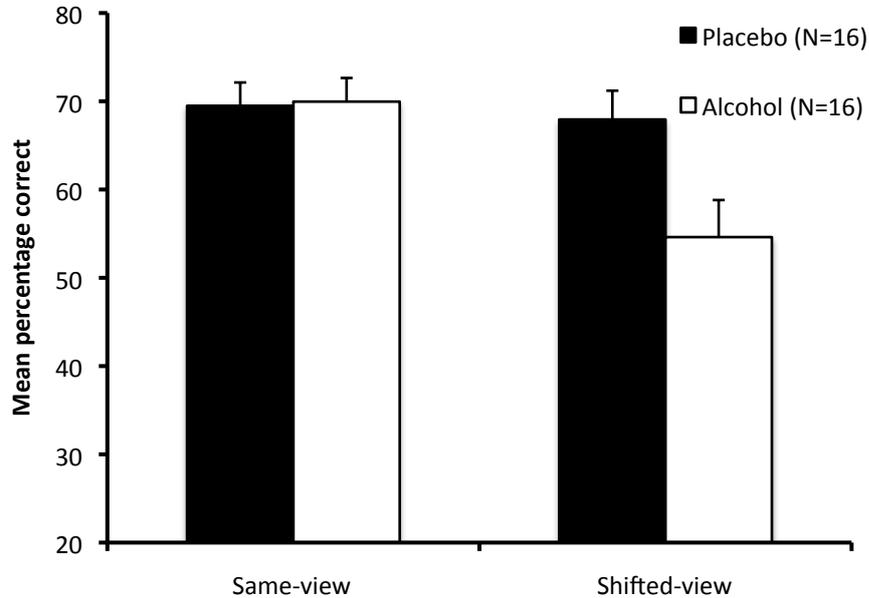


Figure 5.3. Mean (SE) percentage of correctly recognised object locations as a function of condition and group.

5.4.5 Fear acquisition and extinction

Due to technical issues two participants were omitted from the fear memory analysis, as their data could not be retrieved. SCR data from each phase were analysed by comparing the mean increase in amplitude (CS+ minus CS-) during the 6-sec prior to shock. Both groups were found to demonstrate comparable levels of fear (see Figure 5.4) during the late phase (last 4 presentations) of acquisition [$t(28) = 1.00$, $p = 0.33$,].

Analysis of mean SCRs during early and late phases of extinction (first 4 presentations versus last 4 presentations) showed a significant group x phase interaction [$F(2,28) = 9.13$, $p = 0.005$, $\eta^2 = 0.22$] and main effects of both group

[$F(1,28) = 6.95$, $p = 0.014$, $\eta^2 = 0.11$] and phase [$F(1,28) = 5.76$, $p = 0.023$, $\eta^2 = 0.27$]. Further analysis showed a clear decrease in responses from the early to late phase of extinction for the placebo group [$t(14) = 4.29$, $p = 0.001$, $d = 1.00$]. In the alcohol group, no change from early to late phase of extinction was observed [$t(14) = 0.40$, $p = 0.69$]. Mean conditioned responses during the early phase of extinction did not differ between groups [$t(28) = 0.61$, $p = 0.56$] although the alcohol group showed greater responses during the late phase of extinction compared to placebo [$t(28) = 3.43$, $p = 0.002$, $d = 0.97$].

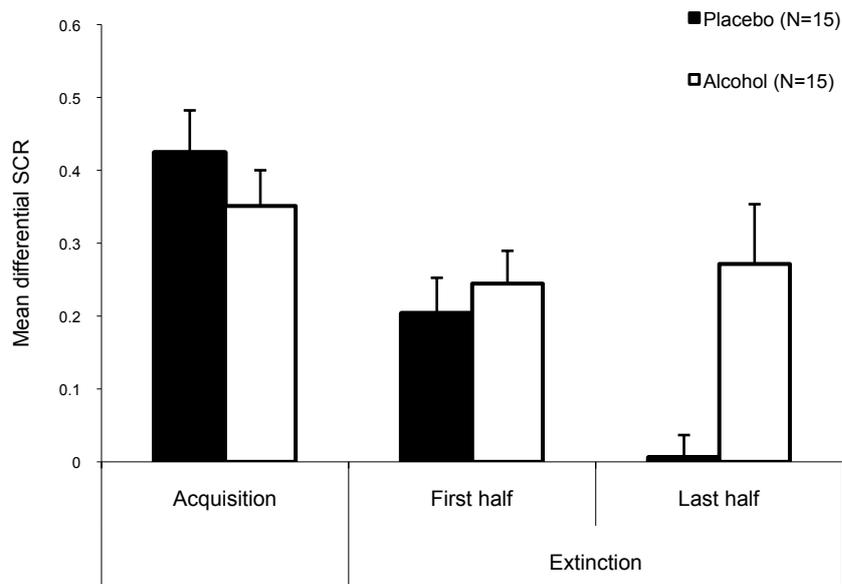


Figure 5.4. Means (SE) skin conductance responses (CS+ minus CS-) during the late phase of acquisition (last 4 presentations) and the early (first half) and late phase (last half) of the extinction phase.

5.4.6 Fear recall

Recall involved a further extinction phase on day 2 from each of the two viewpoints. Analysis of SCR data revealed a significant interaction of group x condition [$F(28) = 6.29$, $p = 0.018$, $\eta^2 = 0.18$] and a main effect condition [$F(1, 28) = 11.65$, $p = 0.002$, $\eta^2 = 0.29$] but not of group [$F(1, 28) = 0.84$, $p = 0.37$]. Post hoc analysis showed intact extinction retention in the placebo group with greater SCRs from the

acquisition viewpoint compared to the extinction viewpoint [$t(28) = 3.31, p = 0.005, d = 2.21$]. However, impaired extinction learning in the alcohol group was confirmed with a continuation of fear responding from both viewpoints. That is, the alcohol and placebo groups demonstrated similar SCRs from the acquisition viewpoint [$t(28) = 0.70, p = 0.49$], whilst the alcohol group showed greater SCRs than placebo from the extinction viewpoint [$t(28) = 2.84, p = 0.008, d = 1.77$]. Mean responses from each viewpoint did not differ in the alcohol group [$t(28) = 1.08, p = 0.33$].

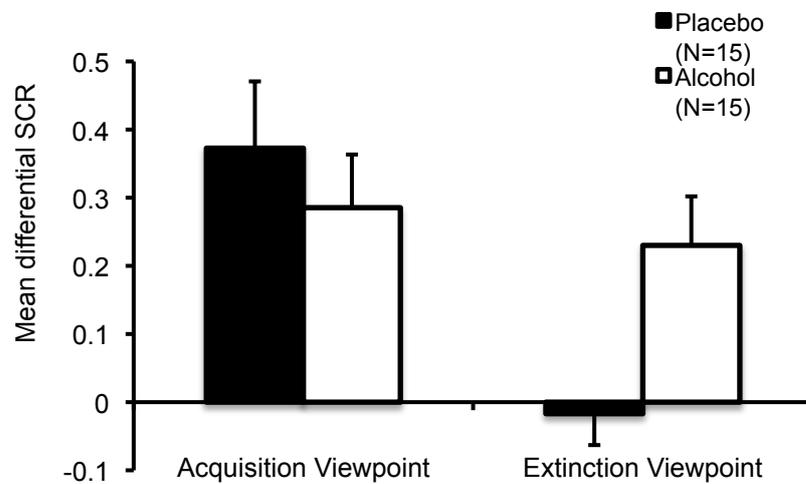


Figure 5.5. Means (SE) of SCR data from day 2 during recall from both acquisition and extinction viewpoints across treatment groups.

5.4.7 Fear memory recall and shifted-view performance

A correlation was performed within each group to examine the relationship between shifted-view recognition and fear extinction and recall while controlling for same-view recognition. Data were checked for bivariate outliers using the residuals and a Tukey 1.5 hinged spread analysis. No outliers were identified and therefore all data were included in the correlation analyses. The alcohol group showed a negative relationship between reductions in shifted-view recognition and conditioned responses during the last half of extinction learning [$r(12) = -0.56, p = 0.039$]. A

negative relationship was also observed between shift-view performance and fear recall (SCR) from the extinction viewpoint on day 2 [$r(12) = -0.81, p < 0.001$].

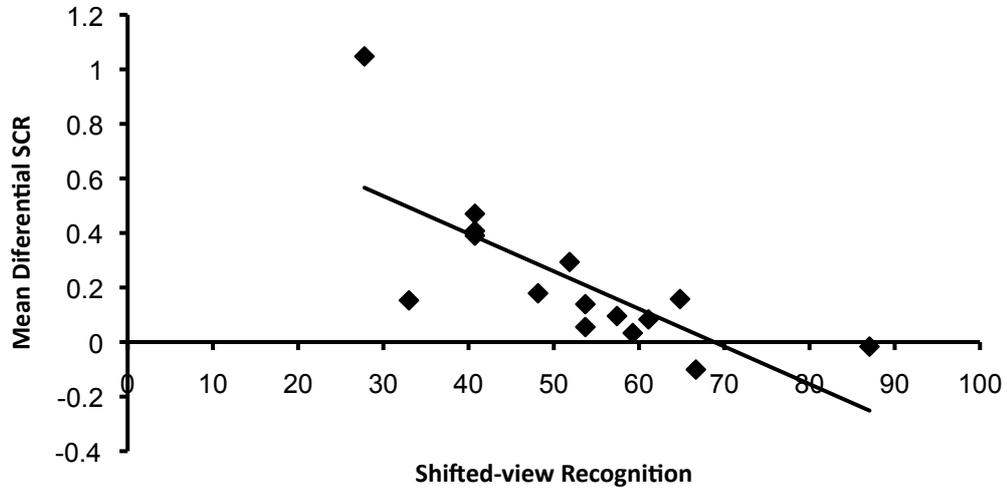


Figure 5.6. Scatter plot showing the observed negative relationship in the alcohol group (N=15) between shifted-view recognition and fear extinction recall on day 2.

5.5 Discussion

The present study aimed to further examine the previous finding of alcohol-induced alterations in the integration of an aversive event and the associated disruptions in viewpoint-dependent spatial memory. To approach the study objectives, a virtual reality environment was used in which contextual fear memory and, concurrently, same- and shifted-view object location recognition could be assessed. The fear memory paradigm was performed overlooking a virtual courtyard with fear acquisition carried out from a specific viewpoint of the environment. Intact fear acquisition was observed from both groups, evidenced by similar levels of conditioned responses at the end of the acquisition block. Extinction, performed from a novel viewpoint of the virtual courtyard, was clearly impaired following alcohol with conditioned responses continuing throughout extinction training. The present study also replicated the previous finding of a selective reduction in shifted-view object location recognition following alcohol, whereas same-view recognition was spared. Alcohol-induced reductions in shifted-view recognition were found to

be associated both with impaired extinction learning and also with the impaired extinction recall on day 2.

5.5.1 Alcohol and fear memory

Fear conditioning was seemingly unaffected following alcohol. The placebo and alcohol group demonstrated comparable conditioned responses during the acquisition phase of learning. This suggests that individuals who were administered alcohol were able to form the required association between the conditioned and unconditioned stimuli for fear conditioning to occur. Intact fear acquisition was also confirmed on day 2 with both groups demonstrating conditioned responses from the same viewpoint in which acquisition occurred. Surprisingly, to the author's knowledge this is the first study to assess fear acquisition and extinction following alcohol in humans (although see Loeber and Duka, 2009). However, the intact fear acquisition found following alcohol is consistent with previous rodent data showing that alcohol impairs context-dependent learning but not cue-dependent learning in fear conditioning paradigms (e.g., Gould, 2003; Melia et al., 1996).

Extinction learning was performed from a second location of the virtual environment providing a novel viewpoint of the conditioned stimulus. The placebo group showed the expected reduction in conditioned responses between early and late phases of the extinction block showing that fear was successfully extinguished from the new location. In contrast, extinction learning was clearly impaired following alcohol with increased conditioned responses under alcohol persisting throughout the extinction phase of learning. The observed impairment in extinction learning is in accordance with other reports of impaired fear extinction in rodents (Lattal, 2007). In addition, the inability to extinguish fear under alcohol was further supported during the test of recall on day 2 with continued conditioned responses to the conditioned stimulus from the extinction viewpoint. In contrast, the placebo group showed intact extinction retention during recall with a decrease in conditioned responses from the extinction viewpoint. However, the impairment in extinction learning following alcohol is in contrast with the findings reported by Loeber and Duka (2009). In their study, alcohol did not affect extinction learning during a

discriminative instrumental learning task. One explanation for these differing results may involve differences in methodology. Loeber and Duka administered alcohol following the discriminative training phase, whereas the study reported here administered alcohol prior to the acquisition phase. This may suggest that alcohol disrupted the formation of a complete contextual representation of the experience during fear acquisition, which may have further implicated processes during extinction learning.

5.5.2 Alcohol's effects on same- and shifted-view recognition

Whereas both groups demonstrated similar levels of performance on same-view recognition, a selective reduction in shifted-view object location recognition under alcohol was observed. This selective impairment following alcohol replicates the previous findings highlighting the sensitivity of allocentric memory to disruption by a low dose of alcohol, whilst egocentric memory seems to be disrupted only at higher doses (see Chapter 4). These findings are also consistent with alcohol-induced deficits in the encoding of spatial-temporal context within episodic memory (Curran and Hildebrandt, 1998; Leitz et al., 2009) and hippocampal-dependent spatial memory performance in rodents (Matthews and Silvers, 2004; White et al., 2003).

The observed alcohol-induced reduction in allocentric memory may help to elucidate the fear memory deficits observed here. Indeed, any reduction in the ability to store contextual information required for an allocentric representation would be expected to produce impairments on all aspects of the fear memory paradigm. The placebo group showed marginal, albeit non-significant, increases in conditioned responses from the acquisition viewpoint during fear acquisition and recall, suggesting enhanced conditioning in the associated context (e.g., Rudy and O'Reilly, 1999; 2001). However, following the reductions in contextual encoding, alcohol intoxication may have resulted in a context-independent representation during acquisition. The term context-independent refers to a representation associated with its sensory/perceptual characteristics (e.g., Winocur et al., 2007). The subtle reductions in conditioned responses under alcohol may reflect decreased

contextual encoding that would be expected to facilitate retrieval of the conditioned response.

Reductions in extinction learning following alcohol were found to be associated with shifted-view recognition performance, highlighting a possible role of allocentric memory in the ability to extinguish fear. Context plays an influential role in extinction learning with individuals forming a new association between the conditioned stimulus and no aversive outcome within a new context (Bouton, 2004; Myers and Davies, 2002). Observed decreases in allocentric memory may have contributed to an inability to encode the change in context resulting in the continued response to the conditioned stimulus throughout extinction training. Furthermore, context contributes to the expression of the extinction memory, with a change from the extinction context resulting in the renewal of fear (Bouton and Ricker, 1994). Alcohol-induced increases in conditioned responses from the extinction viewpoint were highly associated with decreases in shifted-view recognition. This further supports the important role of contextual information in the successful encoding and expression of extinction learning (Bouton, 2004; Milad et al., 2009; Vansteenwegen et al., 2005).

Given the important role of context within the current paradigm and fear memory generally (e.g., Bouton, 1988), it is essential to consider other factors that might contribute to the specific context in which fear is acquired and extinguished. One potential issue in attempting to delineate contextual influences on fear acquisition and extinction is that contexts are ill defined, often comprising many features and modalities. (see Rudy and O'Reilly, 1999; 2004). Alcohol might be considered to provide its own internal context during intoxication, resulting in state-dependent learning and retrieval (e.g., Weissenborn and Duka, 2000; 2003). As described, the new association between the conditioned stimulus and no aversive outcome is highly modulated by a change in context during extinction learning (Bouton, 2002; Phillips and LeDoux, 1996). Throughout the current paradigm, alcohol-induced changes in state would be consistent during acquisition and extinction, despite a change in the spatial context. This could lead to the alcohol group demonstrating persistent conditioned responses to the conditioned stimulus in the new spatial context because

of no change to the individual's internal context. However, the observation that the alcohol group showed continued fear responding at recall despite being sober might suggest otherwise. One possible explanation for this result may be due to the finding that extinction learning was clearly impaired. Therefore, individuals would have not acquired an extinction memory that could be retrieved during the recall test of fear on day 2. As alcohol did not disrupt the ability to encode perceptual features of the experience and, importantly, the stimulus-response associations, conditioned responding would persist to discrete stimuli irrespective of changes in context.

If alcohol intoxication generates a change in an individual's internal context during the acquisition and extinction of fear, it is plausible that intoxication at a later day could contribute to a re-instatement of fear. For example, research has shown that when a conditioned response is extinguished, if the fear-eliciting stimulus is presented in the original context, the conditioned response can be re-instated (Bouton, 1984). Therefore, if individuals whom acquired fear under the influence of alcohol performed extinction learning sober, the future presentation of the unconditioned stimulus during alcohol intoxication could again generate a re-instatement effect and the recall of fear.

5.5.3 Alcohol's effects on brain neurochemistry

The reduction in allocentric memory and impairments in the contextual modulation of fear memory are consistent with proposals that alcohol exerts its debilitating effects on memory via degradation of hippocampal neurophysiology (for a review, see Matthews and Silvers, 2004). The human hippocampus is particularly important in the encoding of spatial information to form an allocentric representation (Burgess et al., 2001; 2002; O'Keefe and Nadel, 1978) and is impaired in patients with hippocampal damage (King et al., 2002; 2004). Furthermore, the hippocampus is critical in the contextual modulation of fear acquisition, extinction and extinction expression during retrieval (Bouton, 2004; Quirk and Mueller, 2008). Acute alcohol administration inhibits NMDA-dependent and NMDA-independent LTP as well as enhancing NMDA-dependent LTD (Blitzer et al., 1990; Givens and McMahon, 1995; Hendricson et al., 2002). In addition, alcohol is known to potentiate GABA

mediated inhibition (Kumar et al., 2009). Alcohol may therefore alter hippocampal function through interacting with glutamate and GABAergic neurotransmitter systems resulting in the observed reductions in contextual encoding.

5.5.4 Limitations

A limitation of the present study is in trying to ascertain whether the low dose of alcohol generated a specific effect on acquisition that carried over into extinction, or if the impairment was selectively caused through a direct impairment in extinction learning. The acute dose of alcohol may have impaired contextual encoding during acquisition that would be required for top-down control during extinction learning. However, alcohol may have selectively contributed to extinction learning deficits through the inability to associate a change in contextual information. Further studies will be required to tease these two distinct processes apart.

5.5.5 Conclusions

In conclusion, the present study provides further insight into alcohol's ability to affect memory processes during an aversive event. The findings are in line with those of previous Chapters in this thesis that show that a low dose of alcohol can disrupt the encoding of contextual information during an event, while sensory/perceptual processes seem to be spared. From a clinical approach, these results provide new data on the use of alcohol in individuals diagnosed with PTSD. Indeed, if alcohol does disrupt both the extinction of fear expression and how the information is represented within memory, this could have important clinical implications for PTSD sufferers with co-morbid alcohol abuse and their successful progression in therapy.

Chapter 6: General Discussion

The principal aim of this research was to investigate the way in which acute alcohol intoxication during a traumatic experience could affect an individual's memory for the event. In addressing this research question, this research also intended to further examine the underlying cognitive mechanisms involved in the development of intrusive memories, a primary symptom of individuals diagnosed with PTSD.

This final Chapter will first summarise the main findings of reported studies and discuss them in relation to current accounts of trauma memory and intrusive imagery. This will be followed by a discussion the specific mechanisms thought to play a role in trauma-related disturbances in memory and the way in which alcohol has been shown to affect each aspect.

In an attempt to integrate the present findings and incorporate the previous literature highlighted within this thesis, a basic framework to explain the way in which increases in alcohol dose can interact with specific components of memory to generate the observed alterations in trauma memory will be proposed.

Given the clear clinical relevance of investigating the effects of alcohol on memory for a traumatic event, the present findings will be discussed in relation to the wider body of literature on alcohol and trauma, focusing on the clinical implications generated from the results presented in this thesis.

Finally, an outline including proposals for future research in the investigation of alcohol use and its association with the persistence of PTSD symptoms will be proposed.

6.1 Alcohol-induced effects on trauma memories

6.1.1 Contrasting findings

A major finding that emerged from this research was alcohol's ability to affect memory for a traumatic event in different ways. Chapters 3 and 4 described a prospective design in which individuals were required to watch a trauma film following administration of alcohol (low or high dose) or a matched placebo. Participants were instructed to record any intrusive memories of the film over the following week and then returned on day 7 for a surprise explicit memory test of the film footage. Intriguingly, alcohol administration prior to viewing the film resulted in a dose-dependent inverted 'U' shaped curve on the number of intrusions reported. That is, individuals administered a low dose (0.4 g/kg) of alcohol showed an increase in the number of intrusive memories reported, whereas individuals administered a high dose (0.8 g/kg) of alcohol did not show any increase compared to the placebo group. In contrast to this dose-dependent 'U' shaped curve on intrusions, explicit memory of the footage was affected in a linear manner, evidenced by greater reductions as the alcohol dose increased. These contrasting findings of intrusive memory reports and explicit memory of the same aversive stimuli are unique. Indeed, this differential effect on memory highlights the possible involvement of different memory systems in the development of intrusive imagery and the explicit recall of trauma related information.

6.1.2 Limitations for a single memory system approach

The observed increase in intrusive imagery combined with a reduction in explicit memory following administration of a low dose of alcohol parallels proposals that the extreme nature of a traumatic experience can exert differential effects on specific components of memory. It has been suggested that prolonged stress during a traumatic event results in distinct decrements in voluntary recall of the experience, whilst involuntary memory in the form of intrusive imagery is enhanced (e.g., Brewin et al., 2010; Ehlers and Clark, 2000; Elzinga and Bremner, 2002). The differential effect on voluntary and involuntary memory following a low dose of

alcohol is difficult to explain within recent cognitive theories proposing a single memory system view. Rubin and colleagues (2008; 2009) argue that the stress and arousal experienced during a traumatic event will result in the enhancement of both voluntary and involuntary forms of memory. They suggest that the increase in emotional arousal would be expected to enhance encoding of the event, in line with accounts of an emotional enhancement of memory (e.g., Cahill and McGaugh, 1998; McGaugh, 2003). In this view, intrusions would therefore occur through different retrieval mechanisms from the same memory system, one triggered via cues in the environment and the other through deliberate recall. Within this model, alcohol would be expected to influence both voluntary and involuntary forms of memory in similar ways. Yet the observed increases in intrusive imagery and decreases in explicit memory following a low dose of alcohol suggest that these disruptions in trauma memory cannot be explained by a single memory system approach.

6.1.3 Perceptual priming cannot explain alcohol-induced alterations

Administration of a high dose of alcohol resulted in further reductions in voluntary, explicit memory of the traumatic footage. However, the high dose did not generate an increase in intrusive memories, as observed following a low dose of alcohol. The finding of reduced voluntary memory and the absence of an increase in the number of intrusions is difficult to conceptualise within some clinical accounts of intrusive memory development that argue that intrusions occur due to strong perceptual priming (e.g., Ehlers and Clark, 2000; Ehlers et al., 2004). Previous research has indeed shown that perceptual priming is unaffected following acute alcohol intoxication, even at higher doses (Hashtroudi et al., 1984; Lister et al., 1991). However, it must be noted that no study to date has directly assessed the acute effects of alcohol on perceptual priming within an aversive paradigm and therefore empirical evidence is needed to test this assumption. In relevance to the observed effect following the high dose, the two studies in Chapters 3 and 4 reported marginally different results. While in Chapter 3, the number of intrusions reported by individuals administered a high dose (0.8 g/kg) was decreased compared to the placebo group, in Chapter 4, it was similar to the number recorded by the placebo group. This subtle difference between the two studies may be due to the level of

intoxication achieved following alcohol administration. The blood alcohol concentration recorded within Chapter 3 was marginally higher for the high dose compared to that observed in Chapter 4. Therefore, greater increases in intoxication in Chapter 3 may explain the further reduction in the number of intrusive memories experienced following the traumatic material.

6.1.4 Support for a dual representation model

The findings following both the low and high doses of alcohol are particularly supportive of a dual representation model of intrusive memory development (Brewin, 2001; Brewin et al., 2010). As described in some detail (Chapter 1.4), this account is based on the assumption that memory for an event is encoded via two closely linked representations (e.g., Burgess et al., 2001; Byrne et al., 2007; O’Keefe and Nadel, 1978). One type is egocentric and image based, dependent on the perceiver’s own viewpoint. The other type is contextual, allocentric and viewpoint independent, and is flexible and consciously accessible. During the traumatic event, this account proposes that the increase in stress will disrupt the storage of a contextual representation resulting in decreased voluntary recall, whereas egocentric imagery is intact. Trauma-related cues in the environment thus trigger egocentric imagery and the associated emotional response in absence of conscious top-down control that would inhibit involuntary retrieval.

Within the present findings, a low dose of alcohol was found to selectively impair allocentric memory, whereas egocentric memory was seemingly spared. Intrusive imagery was also increased following the low dose and, when egocentric memory was intact, greater decreases in allocentric memory were found to be associated with the increases in intrusive imagery. The selective decrease in contextual memory following a low dose of alcohol may parallel the expected reduction in contextual forms of memory generated following an acute reaction to prolonged stress (e.g., Kim and Diamond, 2002; Kirschbaum et al., 1996; Newcomer et al., 1999). This would support the idea that stress disrupts voluntary recall while imagery is free to spontaneously enter consciousness. The dual representation model was further supported by the global impairment of allocentric and egocentric memory following

administration of a high dose of alcohol. Intrusive imagery was not increased following the high dose supporting the idea that both voluntary and image-based memory representations were disrupted. The precise mechanisms within this model and alcohol-induced effects are discussed in greater detail below.

6.2 How does alcohol generate its effects on trauma memory?

6.2.1 Encoding of spatial-temporal context is critical

Throughout this thesis, alcohol has been shown to induce acute decrements in the encoding of various forms of memory, including explicit recall, allocentric memory, recollection and contextual fear memory. A common factor shared by these ‘kinds’ of memory is that they all rely on the formation of a spatial-temporal context during an experienced event. The encoding of such contextual information refers to the ability to form a unitary representation of an event, associating the independent elements experienced by an individual with the specific time and place at which the event occurred. These attributes can later be deliberately retrieved from memory and contribute to one’s conscious reports of an event. The ability to provide an intact spatial-temporal context during an event underlies a number of traditional accounts of human memory, whether it is considered to be declarative, episodic, associative, recollective or allocentric (e.g., Burgess et al., 2001; Eichenbaum and Cohen, 2004; O’Keefe and Nadel, 1978; Squire and Zola-Morgan, 1991; Schacter and Tulving, 1994; Tulving, 1983). Crucial to the storage of these specific forms of memory are the hippocampus and medial temporal lobe (Burgess et al., 2001; Eichenbaum and Cohen, 2004; Squire, 1992), a proposal supported by a vast array of studies providing evidence that damage to the hippocampal formation results in clear impairments in the ability to encode contextual information that would support the above forms of memory (e.g., King et al., 2002; 2004; Scoville and Milner, 1957; Maguire et al., 1998; Spiers et al., 2001; Vargha-Khadem et al., 1978).

6.2.2 Spatial-temporal context is necessary for conscious memory

A disruption in the ability to encode contextual information resulting in specific memory systems deficits may shed light on the precise memory impairments observed following an acute dose of alcohol. In line with previous studies (reviewed in Chapter 1), and using a set of methodologically diverse tasks, the results reported throughout this thesis showed clear disruptions in the storage of information that would provide a spatial-temporal context to support conscious forms of memory. The ability to provide a spatial-temporal context is indeed considered a defining characteristic of recollection during episodic memory retrieval (Tulving, 1983). The remember-know procedure utilised (Chapter 2) provided evidence that alcohol impairs recognition memory associated with recollection, whereas recognition based on familiarity alone was found to be preserved. Furthermore, recollection was reduced in a greater manner as the doses of alcohol (0, 0.4, 0.6, 0.8 g/kg) administered to individuals increased.

6.2.3 Acute alcohol intoxication results in decreases in the storage of contextual information

Alcohol was also found to disrupt the storage of contextual information required to solve shifted-view object location recognition (Chapter 4 & 5). Shifted-view recognition is thought to require an allocentric representation of an event, providing a cognitive map and the spatial-temporal context that can be deliberately and flexibly accessed (Burgess et al., 2001; Byrne et al., 2007; O'Keefe and Nadel, 1978). The observed reduction in allocentric memory further supports the suggestion that alcohol impairs the ability to encode contextual information. Disrupted contextual encoding was further confirmed through the use of a contextual fear memory paradigm (Chapter 5). Participants were able to form the association between the conditioned stimulus and the aversive shock, demonstrating anticipatory fear similar to that of the placebo group. However, extinction learning was clearly impaired following alcohol administration. These, the first findings in humans, are consistent with previous animal studies (e.g., Lattal, 2007). This observed impairment may be due to the inability to store new contextual information with a

change in the conditioned stimulus/response association, a process that is fundamental to the acquisition of an extinction memory and its modulation (Boulton, 2004). This was supported by the significant positive correlation between reductions in shifted-view recognition and impaired extinction learning. Interestingly, Loeber and Duka (2009) did not find any alcohol-induced impairment in extinction learning during a discriminative instrumental learning task. One potential reason contributing to these differing results may involve differences in methodology. Loeber and Duka administered alcohol following the discriminative training phase, whereas in the study reported in Chapter 5, alcohol was administered prior to the acquisition phase. This may suggest that alcohol disrupted the formation of a complete contextual representation of the experience during fear acquisition, which may have further implicated processes during extinction learning. Overall, the results support a model in which acute alcohol intoxication decreases the storage of contextual information.

6.2.4 Alcohol impairs hippocampal function

It was beyond the remit of this research to study the effects of alcohol on trauma memory within a functional brain-imaging context. However, the impairments in contextual encoding are particularly supportive of proposals that alcohol generates its effect on memory through impairing hippocampal function (e.g., Matthews and Silvers, 2004; Ryabinin, 1998; White and Best, 2003; White et al., 2000). The hippocampus is a crucial structure in the storage and modulation of contextual information within memory. Alcohol is thought to degrade hippocampal neurophysiology through its interactions with GABAergic and glutamatergic neurotransmitter systems. Alcohol's enhancement of GABA mediated inhibition and blockade of NMDA receptor activity might therefore down regulate hippocampal function resulting in specific impairments in the encoding of contextual information. Further evidence for this assumption has been provided through the use of fMRI with alcohol-induced impairments in episodic memory associated with reduction in hippocampal function (Soderlund et al., 2007). As outlined previously, other drugs that share part of alcohol's neurochemical action on GABA and NMDA receptor activity have also been shown to generate similar effects on encoding, including

benzodiazepines (for a review, see Curran and Weingartner, 2002) and ketamine (for a review, see Morgan and Curran, 2006).

6.2.5 How does this affect trauma memory?

How do the observed impairments in the encoding of contextual information translate to the distinct alterations in memory for a traumatic event? In accordance with previous studies detailing alcohol-induced decreases in explicit memory (e.g., Curran and Hildebrandt, 1999; Leitz et al., 2009; Lister et al., 1991), reductions in the storage of contextual information following alcohol provide an explanatory framework for the observed impairments in voluntary memory for an aversive event. Here, the successful storage of contextual information during a traumatic event is suggested to be a fundamental process in the ability to inhibit persistent involuntary imagery (Brewin, 2001; Brewin et al., 2010; Elzinga and Bremner, 2002; Jacobs and Nadel, 1998). In turn, in the absence of contextual modulation, intrusive imagery triggered by trauma-related cues in the environment is re-experienced. In light of this, a disruption to the storage of contextual information during an aversive event following a low dose of alcohol would suggest that the increase in intrusive imagery is driven via some form of memory or image-based representation that must remain intact during intoxication.

In addition to the direct memory related deficits associated during alcohol intoxication, it is important to acknowledge alcohol's role as an anxiolytic and the way in which increases in sedation might influence the results reported here. Decreases in arousal following alcohol have consistently been shown with a number of proposals that alcohol should reduce stress and anxiety-based responding in some situations (e.g., Levenson et al., 1980; Sayette, 1999; Sher, 1987; Sher et al., 2007). In the current set of studies, alcohol groups demonstrated increases in anxiety and sedation during the traumatic footage similar to the placebo group. However, it is plausible that alcohol might generate some of its effects on memory by increasing sedation as alcohol dose increases. As discussed in Chapter 3, at a lower dose of alcohol some of the emotional aspects of the traumatic material might be maintained although it is difficult to conclude this as most studies investigating emotional

memory following alcohol have administered high doses (e.g., Knowles and Duka, 2004; Brown et al., 2010). This could become associated with the spared visual imagery or egocentric representation reported within this thesis, resulting in emotionally bound intrusive recollections of the traumatic event. However, at higher doses, these emotional aspects of the material may be further diminished due to a greater alcohol-induced reduction in arousal, resulting in an overall deficit in memory (e.g., Knowles and Duka, 2004). Further investigation into alcohol-induced reductions in arousal and its potential role in the specific deficits in trauma memory would be needed.

6.2.6 Support for an image-based memory system

The existence of an image-based memory system supported by sensory/perceptual input is not a new idea (e.g., Janet, 1904; Brown and Kulik, 1977; Johnson, 1983). Recently, it has been proposed that short-term spatial memory and imagery can be driven by perception to form egocentric representations of an event, supported by the precuneus (Burgess et al., 2001; Byrne et al., 2007). These egocentric representations are modulated by directed attention, storing spatial locations of objects relative to the perceiver's head direction to form a viewpoint-dependent representation. The results presented in Chapter 4 provided support for proposals that intrusive imagery may involve the reactivation of egocentric representations in the absence of contextual support (e.g., Brewin et al., 2010). A low dose of alcohol was found to increase intrusive imagery, and disrupt contextual encoding, while egocentric memory was seemingly spared. However, the high dose of alcohol did not increase intrusions, but caused a global reduction in egocentric and contextual memory. Furthermore, a correlation was performed on those individuals who showed intact same-view recognition performance (placebo and low dose), examining the relationship between shifted-view recognition and the number of intrusive memories. There was a negative correlation between the two measures with greater reductions in shifted-view recognition associated with increases in intrusive memories.

6.2.7 What we learned from fear-conditioning

Interestingly, the use of a fear-conditioning paradigm in Chapter 5 revealed that individuals administered a low dose of alcohol were able to form an association between the conditioned stimulus and aversive shock, consistent with previous animal data showing intact cue-dependent learning in rodents following alcohol (Gould, 2003; Melia et al., 1996). This supports the idea that individuals administered a low dose of alcohol are able to form lower level associations that could contribute to the generation of trauma-related fear associated with intrusive imagery. The formation of the conditioned stimulus and unconditioned stimulus association in a fear memory paradigm is thought to rely on integrity of the amygdala (LeDoux, 2000). The ability for the alcohol group to acquire fear to a cue during fear conditioning suggests that amygdala function may have been unaffected. Although context-dependent learning is selectively disrupted at lower doses of alcohol (Melia et al., 1996), higher doses have been shown to impair cue-dependent learning during fear conditioning in rodents (Sonner et al., 1998). Consistent with the global reduction in memory observed following a high dose of alcohol, this would suggest a general increase in alcohol's intoxicating effects on memory providing a further contributing mechanism for no increase in intrusive imagery following higher doses. However, there is also a possibility that the higher dose of alcohol could have indirectly affected egocentric memory. Alcohol is known to impair other cognitive processes including attention (Abroms et al., 2006; Koelega, 1995; Schulte et al., 2001) and working memory (Grattan-Miscio and Vogel-Sprott, 2005; Schweizer et al., 2006) that may have indirectly contributed to the ability to form an egocentric representation during an event. Further research would be required to investigate the way in which these cognitive processes interact following acute alcohol intoxication to further elucidate this issue.

Skin conductance was used as an objective measure of anticipatory fear during fear conditioning. Despite alcohol's known anxiolytic properties that are thought to dampen stress responses (e.g., Sayette, 1999), skin conductance was unaffected by a low dose of alcohol. This was also supported by the results reported in Chapter 3 where both low and high dose alcohol groups demonstrated similar increases in skin

conductance response during the trauma film. Research assessing skin conductance responses following acute alcohol administration has produced inconsistent results (e.g., Sher, 1987; Maltzman & Marinkovic, 1996). However, it has been proposed that such inconsistencies may be due to differences in methodology and under certain circumstances, skin conductance levels may only be reduced at higher doses of alcohol (Sher et al., 2007). Although skin conductance was not impaired by a high dose of alcohol during exposure to a trauma film (Chapter 3), anticipatory fear responses during a fear-conditioning paradigm remain unknown.

In addition to the proposed disruption in hippocampal function detailed above, alcohol intoxication also results in impairments in behaviours that are ascribed to the prefrontal cortex (e.g., Weissenborn and Duka, 2003). As described (Chapter 1), the PFC is thought to be important in suppressing amygdala-mediated responses (Hariri et al., 2000). In the context of a fear-conditioning paradigm, a disruption to the PFC may result in an exaggerated response to fear provoking stimuli. As observed from the results in Chapter 5, alcohol intoxication may not affect the ability to acquire the association between the conditioned stimuli and conditioned response but may prevent the suppression of fear reactions during extinction learning and therefore the ability to learn the new association and extinction learning. Speculatively, during a traumatic event a low dose of alcohol might diminish explicit memory for the event through disruption to the hippocampus. However, impairment in prefrontal cortex might lead to an exaggerated amygdala response and learned association of fear to the trauma-related stimuli. This would be complementary to the results reported within this thesis that a low dose of alcohol disrupts explicit recall for the event, whereas the fear-related intrusions are preserved and re-experienced.

6.3 A framework for alcohol-induced alterations in trauma memory

As observed throughout this thesis, alcohol has intriguingly distinct effects on trauma memory, particularly in relation to the dose-dependent inverted ‘U’ shaped curve on intrusive imagery. Some of the mechanisms that may be acutely implicated by alcohol intoxication and thus responsible for alterations in voluntary and involuntary memory following a traumatic experience have been outlined. To briefly

summarise the current findings, Table 6.1 illustrates each of the measures assessed throughout this thesis and the way in which a low and high dose of alcohol has been shown to affect each one. The memory processing that is thought to be principally involved during each measure is also detailed.

Table 6.1. Specific measures of memory used throughout the experimental chapters of this thesis. The arrows represent the way in which low and high doses of alcohol were found to effect each of the measures (↓ decreases, ↑ increases, ↔ no effect). The table also shows the specific memory system thought to be primarily involved during each measure and outlines the proposed memory system of the model described.

Task	Processing	Low dose	High dose	Proposed system
Intrusive memories	Allocentric / Egocentric	↑	↔	CMS/visuo-spatial imagery
Recollection	Episodic	↓	↓	CMS
Familiarity	Perceptual recognition	↔	↔	Sensory/perceptual
Explicit memory	Declarative	↓	↓	CMS
Same-view recognition	Egocentric	↔	↓	Visuo-spatial imagery
Shifted-view recognition	Allocentric	↓	↓	CMS
Context-dependent fear	Contextual	↓	↓	CMS
Cue-dependent fear	Emotional	↔	?	Emotional processing

To integrate the related dose-dependent effects on each task and the way in which they may be involved in trauma memory, the next section will detail a basic framework in an attempt to conceptualise alcohol's acute effects. The model is based on the present findings and incorporates the wider literature on alcohol and memory. Although the model is somewhat speculative, it is aimed to generate hypotheses and discussion concerning the observations and evidence base on alcohol-induced disruptions in trauma memory. The overall model is illustrated in

Figure 6.1 and comprises four major components, including (1) sensory/perceptual processing, (2) a contextual memory system (CMS) and further modules for (3) visual-spatial imagery and (4) emotional processing. All the components are interconnected, postulating distinct circuits that interact and contribute to the encoding and retrieval of a trauma memory. The current findings of this thesis provided strong support for a dual representation account of intrusive memories (Brewin et al., 2010). It is therefore acknowledged that the components of the proposed model share some similarities in the information each module is thought to process and the way in which they interact. However, a distinguishing feature of the model here is that it only comprises the specific cognitive processes and memory systems that would be required to explain alcohol's dose-dependent effects on trauma memory. I will now outline each of the components and the way in which alcohol is thought to affect them.

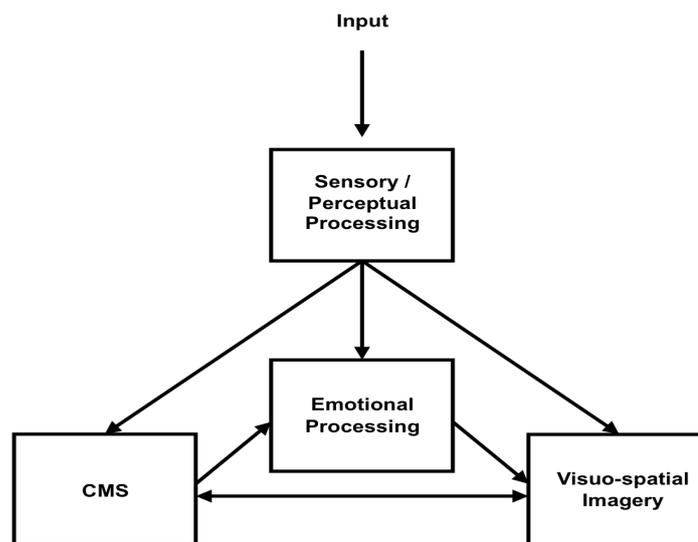


Figure 6.1. An illustration of the specific components included in the model of the way in which alcohol affects trauma memory. The model comprises four major components, affected in different ways following increasing doses of alcohol during the encoding of a traumatic event.

6.3.1 Sensory/Perceptual processing

Sensory/perceptual processing forms the initial gateway during the encoding of a specific experience. Early sensory areas in the brain involved in visual perception

capture perceptual qualities of stimuli from a scene as the information is processed (Suzuki and Amaral, 2003). In line with established theories of memory, these sensory/perceptual details contribute to non-declarative forms of memory including procedural and perceptual learning (Squire and Zola-Morgan, 1991; Eichenbaum and Cohen, 2004) and visuo-spatial working memory (Baddeley, 2003). The ability to identify objects based on their perceptual features parallels the perceptual representation system (PRS) outlined by Tulving and Schacter (1990) in that the prior experience of perceptual objects can enhance identification without explicit knowledge. Research has shown that implicit forms of memory are typically preserved by alcohol, even at high doses (Hashtroudi et al., 1984; Lister et al., 1991; Soderlund et al., 2007).

As described in Chapter 2, recognition of previously experienced items/objects can be solved through perceptual identification alone, resulting in correct recognition associated with a feeling of familiarity (Mandler, 1980; Tulving, 1983; Yonelinas, 2002). The findings within this thesis (Chapter 2) suggest that even following a high dose of alcohol, recognition associated with familiarity is spared (also see Curran and Hildebrandt, 1999). These findings suggest that sensory/perceptual processing within the proposed model is preserved following increasing doses of alcohol.

6.3.2 Contextual memory system

The storage of contextual information is an integral part of the ability to form stable memories that can be freely and consciously accessed. The CMS within the model is parallel to a declarative/episodic memory system in the storage of conscious forms memory, supported by the hippocampus and medial temporal lobe (e.g., Squire, 1992; Squire and Zola-Morgan, 1991). Encoding of spatial relations between features and boundaries are also mapped out in the CMS to form an allocentric representation of a scene and can be used to perform shifted-view recognition (e.g., Burgess et al., 2001; Byrne et al., 2007). Retrieval from the CMS memory system would be expected to provide the spatial-temporal context that contributes to the recollective experience within episodic memory (Tulving, 1983). The storage of contextual information would also support top down control via prefrontal areas

resulting in deliberate and flexible retrieval of memories (e.g., Burgess and Shallice, 1996).

As evidenced from the previous literature and the findings throughout this thesis, the storage of information within the CMS is particularly disrupted by acute doses of alcohol on a range of measures (e.g., Leitz et al., 2009; Lister et al., 1992). Encoding within the CMS would be expected to be further reduced as the amount of alcohol consumed increased. This greater reduction in context-dependent aspects of memory by increasing alcohol dosage is supported by the findings of the current thesis (see Chapters 2, 3 & 4). Alcohol is hypothesised to impair the storage of contextual memory through its direct effects on the hippocampus via associated alterations in GABAergic and glutamatergic neurotransmission (Hoffman and Matthews, 2001; Matthews and Silvers, 2004; Ryabinin, 1998; White and Best, 2003; White et al., 2000). However, low dose effects on memory may be due to more dominant interactions with GABA_A receptor activity. Alcohol enhances GABA-mediated inhibition at low concentrations (< 0.10 g/l; Ticku et al., 1992), whilst antagonism of NMDA receptor activity occurs at higher concentrations (> 0.10 g/l; Lovinger et al., 1989). Therefore some level of NMDA receptor disruption would be expected at the low doses of alcohol used in this thesis (~0.20 – 0.40 g/l), although more prominent effects on NMDA receptor function at higher doses are proposed (Krystal et al., 2003).

6.4.3 Visual-spatial imagery

Perceptual information during the event can be held in mind to form visual imagery of a scene irrespective of associated contextual information. These image-based memories involve the storage of stimuli and their locations relative to the perceiver's viewpoint in the form of an egocentric representation (Burgess et al., 2001; Byrne et al., 2007; O'Keefe and Nadel, 1978) and can be used to perform same-view recognition (e.g., King et al., 2002; 2004). It has been proposed that the ability to form egocentric representation and visual imagery of an experience relies on the precuneus and surrounding medial parietal cortex (Burgess et al., 2001; Byrne et al., 2007; Hassabis et al., 2007; Schacter et al., 2007). The current findings showed that

performance on same-view object location recognition that requires an egocentric representation was differentially affected by low and high doses of alcohol (Chapter 4). Individuals administered a low dose of alcohol were able to perform same-view recognition, whereas individuals administered a high dose showed impaired recognition. Thus, egocentric memory only becomes impaired at higher doses of alcohol.

Disruptions in the ability to store egocentric representations of an event may be due to a relationship between increases in intoxication and the related increases in cognitive processing required for encoding of visual-spatial imagery. For instance, individuals administered a high dose of alcohol can perform some short-term spatial memory tasks when the cognitive load is low (e.g., Wiessenborn and Duka, 2003). However, high doses of alcohol have been found to reduce neuronal activity in prefrontal and parietal areas during working memory tasks only when cognitive load is high (Gundersen et al., 2008a: 2008b). Interestingly, it has been proposed that the retrieval of information from past experience can be reconstructed in the form of visual imagery to support remembering the past and imagining future events (e.g., Addis et al., 2009; Schacter et al., 2007). Recently, it has been shown that during intoxication by a moderate dose of alcohol, the ability to imagine future events is attenuated, resulting in prospective memory impairments (Leitz et al., 2009; Parakaveidas et al., 2010). It has also been suggested that imagining future events requires the construction of egocentric representations (Byrne et al., 2007). The impairment in same-view recognition might therefore also suggest that higher doses of alcohol may impair the ability to reconstruct mental imagery.

6.4.4 Emotional Processing

Sensory/perceptual features of a traumatic experience are strongly linked with the specific emotional reactions elicited at the time (e.g., Ehlers and Steil, 1995; Grey et al., 2000; Holmes et al., 2005). As discussed previously, the association between cues in the environment and the emotional response elicited at the time of an experience is thought to be supported by the amygdala as evidenced in numerous fear conditioning studies (LeDoux, 2000). The generation of event related imagery

is also proposed to be associated with associated fear reactions via the amygdala. For example, the retrieval of information when taking a first person perspective can involve more emotional reactions and physiological sensations than when generating an observer perspective of a memory (McIsacc and Eich, 2002; 2004).

Emotional processing via the amygdala may be preserved following low doses of alcohol. Previous studies have shown impaired context-dependent learning but intact cue-dependent learning following alcohol (Melia et al., 1996). This was further supported by the findings in Chapter 5, with individuals administered a low dose of alcohol still able to learn the conditioned and unconditioned association resulting in similar fear acquisition levels. However, cue-dependent learning in fear conditioning may be reduced following higher alcohol doses as observed in rodents (Sonner et al., 1998). Further enhanced GABA activity would contribute to a disruption in the ability to acquire cue-dependent fear associations (for a review, see Makkar et al., 2010). The enhancement of GABA would also be expected to generate larger anxiolytic effects, along with sedation that could interact with the processing of the emotional aspects of an experience. The more prominent antagonism of NMDA receptor activity would also be expected to contribute to reduced amygdala function, given their importance in the acquisition of fear (e.g., Goosens and Maren, 2004).

6.4.5 Alcohol intoxication and trauma memory within the model

As described in detail, acute alcohol intoxication affected trauma memory in different ways. The next section will outline the way in which each dose of alcohol is expected to contribute to the observed alterations in trauma memory (see Figure 6.2). Following a low dose of alcohol, it is expected that the storage of contextual information within the CMS would be selectively reduced. This would result in the observed disruption in explicit forms of memory, namely recollection (e.g., Tulving, 1985). Further, this would also contribute to the selective impairment of allocentric memory detailed within this thesis. In specific relation to trauma memory, this deficit would result in a reduction in voluntary recall of the event. It is hypothesised that the neurobiological mechanisms thought to underpin this effect would involve alcohol-induced changes in NMDA receptor function and GABA-mediated

inhibition, resulting in impairment of LTP and generating a down regulation of hippocampal function (e.g., Matthews and Silvers, 2004; Ryabinin, 1998; White and Best, 2003).

The ability to form associations between discrete stimuli and the emotional response during the experience would be preserved during a low dose of alcohol, supported by the amygdala. These lower level associations would also be linked to visual-spatial imagery, contributing to the intact formation of egocentric representations and the ability to acquire fear as observed throughout this thesis. Visual-spatial imagery would therefore support the mechanism for intrusive imagery, closely associated with visuo-spatial working memory and supported by parietal regions (e.g. Byrne et al., 2007). Therefore, the preservation of visual-spatial imagery combined with emotional processing would contribute to the formation of the intrusive imagery re-experienced by individuals in response to cues.

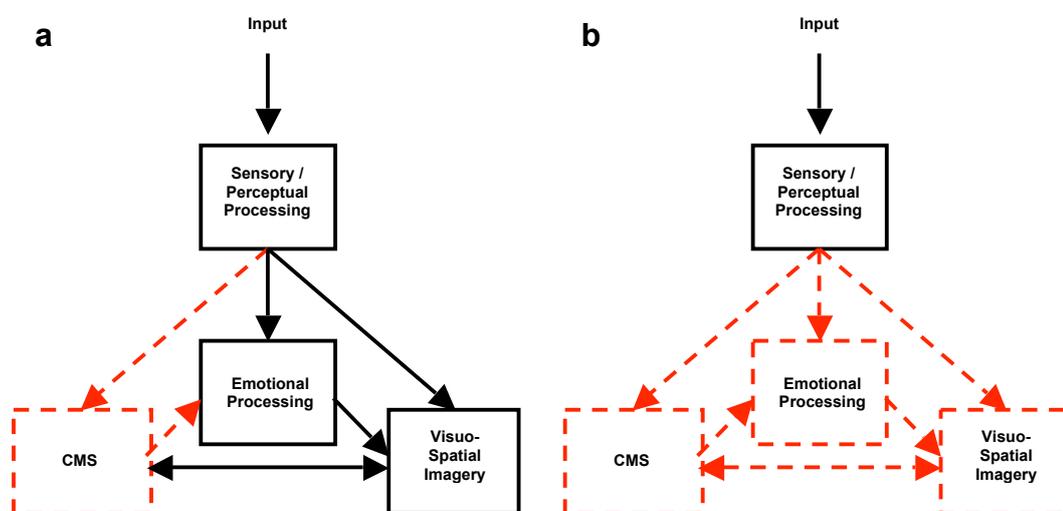


Figure 6.2. An illustration of the framework showing the specific components predicted to be disrupted following a (a) low dose of alcohol and a (b) high dose of alcohol. The dashed lines represent the parts of the model that are thought to be impaired following the given alcohol dose.

The increases in alcohol intoxication would be expected to generate more significant neurochemical alteration to NMDA and GABA receptor function, resulting in

greater reductions in the storage of information within the CMS. This would lead to a greater decrease in voluntary, explicit recall for the traumatic experience. The higher dose of alcohol would contribute to a more global disruption of memory, thus decreasing the ability to store visual-spatial imagery in the form of egocentric representations. It is also speculated that emotional associations between cues and the fear response are also reduced due to a direct decrease in amygdala function. However, as observed in Chapter 2, perceptual recognition would still be spared, aiding the ability to store information within non-declarative memory and supporting recognition associated with familiarity (e.g., Hashtroudi et al., 1984).

6.4 Limitations of the research

As with most research, the studies reported throughout this thesis are not without limitations. One inevitable limitation involves the use of an analogue trauma film to prospectively investigate intrusive memories in relation to the symptoms observed in PTSD. Although the trauma film does contain a number of horrific scenes, it is both ethically and methodologically difficult to replicate the extreme nature of an actual traumatic event within a laboratory environment. However, it must be emphasised that the use of such analogue methods has provided great success in the development of clinical theories (e.g., Horowitz, 1969; Lazarus et al., 1965). In addition, the paradigm has been shown to induce mood-related changes in individuals, which therefore suggests some level of ecological validity.

Another limitation of the current research involves the ability of alcohol to generate more general disruptive effects on cognition. It is well established that alcohol not only affects memory but also impairs a number of other cognitive processes. For instance, alcohol has been shown to impair divided attention (Billings et al., 1991; Schreckenberger et al., 2004; Schulte et al., 2001), resulting in a deterioration of performance on two tasks when performed together, compared with when performed individually. However, sustained attention only seems to be impaired on some continuous performance tasks (Dougherty et al., 2000). Increases in the attentional capacity demanded by a task or experience could therefore play an important factor in dictating alcohol's effects on memory. It is therefore possible that alcohol-

induced effects on attentional processing could have indirectly contributed to some of the memory impairments reported here. However, it is clear that further investigation would be required to elucidate the precise contribution of an attentional deficit by alcohol.

6.5 What are the clinical implications of this research?

Given the frequent involvement of alcohol before, during and/or after traumatic events, it is clinically important to understand the way in which intoxication during a traumatic experience contributes to subsequent trauma-related symptoms. Elucidating the specific disruptions in memory following alcohol not only advances our knowledge of the cognitive and neural mechanisms thought to be involved, but also complements clinical strategies in an attempt to support a patient's successful progression in therapy. The findings from the studies reported throughout this thesis highlight a range of clinical implications in relation to alcohol consumption and exposure to a traumatic experience. In consideration of the findings it is also of particular relevance to emphasise that different amounts of alcohol led to different effects and could therefore potentially each result in a distinct set of trauma-related symptoms.

6.5.1 Moderate alcohol consumption prior to a traumatic experience might increase vulnerability to PTSD

The observed increase in intrusive imagery following a low dose suggests that prior consumption of a moderate dose of alcohol may increase an individual's risk for later PTSD development. That is, alcohol may interact with specific components of memory, resulting in an over-representation of lower-level sensory information in the absence of contextual information. This would lead to the automatic reactivation of imagery in response to related environmental cues. Therefore, moderate alcohol consumption prior to a traumatic experience could potentially increase an individual's vulnerability to PTSD. A number of other pre-exposure risk factors (e.g., gender, prior trauma, socioeconomic disadvantage and prior psychopathology) are thought to increase a person's vulnerability to the development of trauma-related

symptoms and the future development of PTSD (as discussed in Chapter 1). It may be that moderate levels of alcohol could exacerbate these pre-existing vulnerabilities and increase an individual's risk of traumatic problems.

6.5.2 Global disruptions in memory following a high dose of alcohol may lead to the construction of 'worse case scenarios'

At higher doses, alcohol was observed to generate a global reduction in memory although recognition associated with familiarity was preserved. Therefore, one could hypothesize that, if alcohol disrupts the encoding of information resulting in a decrease in intrusive memories, trauma-related symptoms might be less frequent. This may however not be the case: global disruptions in memory might result in a different set of symptoms. While many patients often claim that their memories and related intrusions of a trauma are exact representations of the incident that occurred (van der Kolk and Fisler, 1995), it has been suggested that patients' reports of the trauma are not accurate and often include an exaggerated perception of what really happened (Frankel, 1994; 1996; Grunert et al., 1988). Furthermore, Bryant and Harvey (1998) found that many trauma victims attributed high levels of accuracy to their version of the traumatic event but that this version was not consistent with third person accounts of the event. In turn, one might suggest that global amnesia following a large amount of alcohol could in turn lead an individual to imagine the 'worse case scenario' (e.g., Merckelbach et al., 1998).

Exposure-based therapies often utilise the fragmentary components of what a patient can remember from the trauma as a way of diminishing related-fear and distress in a safe environment (Foa and Rothbaum, 1998). However, with a global reduction in memory following a large amount of alcohol, individuals may not be able to bring the traumatic imagery to mind and therefore related symptoms might become more resistant to clinical interventions. This proposal has some support from the recent literature. Kaysen et al. (2010) assessed female sexual assault victims who had or had not consumed alcohol prior to the traumatic experience. The average amount of alcohol reported by individuals was approximately 6 drinks. Victims' symptoms were assessed over a 6-month period. Individuals who had consumed alcohol

reported fewer intrusive memories than individuals who had not consumed alcohol. However, trauma-related symptoms were more resilient in those who consumed alcohol and symptoms did not diminish over time compared to the non-alcohol group whose symptoms progressively improved. These findings support the global reduction in trauma memory observed following a high dose of alcohol and the idea that trauma-related symptoms in these individuals may be more persistent and more resistant to treatment.

6.5.3 Impaired extinction learning

The observed impairment in extinction learning has a wide range of clinical implications for individuals consuming alcohol during and possibly following the trauma. In relevance to PTSD, patients have been shown to demonstrate impaired extinction learning (Orr et al., 2000) and the impaired ability to later retrieve an extinction memory (Milad et al., 2009). In light of the observed impairment in extinction learning following alcohol, if patients were to consume alcohol following a traumatic event this could potentially exacerbate reductions in extinction learning and their ability to later retrieve an extinction memory. Extinction learning is a major mechanism in exposure-based therapy in the attempt to diminish symptoms in anxiety disorders (e.g., Foa and Rothbaum, 1998). Therefore, continued alcohol use long after the traumatic event has occurred, and following the diagnosis of PTSD could result in the persistence of trauma-related symptoms (for further discussion, see section 6.6).

6.5.4 Other implications

The occurrence of a traumatic event may lead to a criminal investigation and the case appearing in a court of law. Individuals who were present during the event would therefore be required to give eyewitness testimony. A victim, suspect and/or eyewitness may have consumed alcohol at the time of the event and therefore their ability to provide an accurate report of the incident could be called into question. As observed in the findings throughout this thesis, and the previous related literature, alcohol can have severely disruptive effects on memory. When a judge and jury hear

witness testimony from an individual, alcohol intoxication at the time of the event can be a determining factor in appraising the reported accuracy and ‘version’ of events (for a review, see Curran, 2006). Further, the findings of this thesis suggest that the ability to recognise related information might depend on the specific viewpoint that information was experienced and the dose of alcohol consumed during a witnessed event. The inability to purposefully recall information under alcohol intoxication could also potentially make a witness more suggestive.

6.6 Future Directions

Future studies aiming to replicate and further the findings of the research detailed within this thesis could potentially improve and strengthen the present methodology. For example, the current set of studies utilised a sample population that was predominately undergraduate university students. It would be expected that such a sample of participants would be of a similar cohort and would therefore demonstrate a similar standard of performance on cognitive tasks and possible trauma processing. Research has shown that individual differences play an influential role in the development of trauma-related symptoms (e.g., Ozer et al., 2003). Furthermore, individual differences play a crucial role in the way an individual responds to an acute dose of alcohol (e.g., Weafer and Fillmore, 2008). Therefore, future studies could assess a wide range of individual differences across individuals and explore their contribution to alcohol-induced alterations in trauma-memory.

One specific factor that could potentially influence results involves working memory capacity. Lower working memory capacity is associated with increased intrusive and avoidance thinking (Brewin and Smart, 2005; Klein and Boals, 2001). Individuals with lower working memory capacity have also been shown to exhibit greater impairments on executive function tasks compared to individuals with higher working memory capacity following an acute dose of alcohol (Finn et al., 1999; Peterson et al., 1992). Further studies may therefore attempt to either control or assess this factor by measuring baseline working memory capacity and examining its role in alcohol-induced changes in intrusive memory development. However, despite these restrictions in relation to the current set of studies and given the

obvious difficulties in attempting to investigate processes that occur during the experience of an acute trauma, it must be acknowledged that the current methodology has provided strong findings that are consistent with present theoretical accounts of intrusive memory development.

In addition to examining the ways in which alcohol may affect trauma memories when consumed prior to an event, individuals may drink in the aftermath of the incident or even on a more long-term basis as a way of self-medicating against trauma-related symptoms. As pointed out in Chapter 1, many individuals diagnosed with PTSD also regularly consume alcohol as a way of diminishing related anxiety (Bonin et al., 2000; Chilcoat et al., 1998; Kushner et al., 2000). It is therefore clinically relevant to further investigate the way in which alcohol use could affect the processing of trauma memory during these time periods in relation to the consolidation and/or reconsolidation of related memories. Analogue paradigms could be used such as the trauma film or fear conditioning where alcohol is administered at different time points during re-exposure to the film or conditioned stimuli. Furthermore, research within PTSD patients could naturalistically investigate the relationship between their alcohol consumption and exposure therapy and how this might affect their response to psychological therapy. Such investigations will advance our understanding of the way in which alcohol use might further affect symptom development and persistence in anxiety-related disorders, such as PTSD.

6.6.1 Alcohol and memory consolidation

It has been long acknowledged that the transformation of transient short-term memories into stable, consolidated long-term memories is a time-dependent process (e.g., Hebb, 1949). From a neurobiological perspective, two forms of memory consolidation have been proposed: (1) the initial process of cellular and synaptic reorganisation that occurs over short time periods during encoding (minutes to hours), and (2) the more prolonged alterations to distributed neural networks that can extend to days, months, or even years (Dudai, 2004). It is of particular interest that administration of specific pharmacological agents in the time period

immediately following encoding of a task can have detrimental effects on the formation of a stable memory representation (e.g., Birioni et al., 1989; Carbo Tano et al., 2009; Parwani et al., 2005).

In relation to trauma memory, information processing and memory consolidation in the immediate aftermath of the event offers a transient time period in which secondary processes may be able to influence the development of related symptoms. Recent experimental evidence suggests that such manipulation can reduce the occurrence of intrusive imagery. For instance, Holmes et al., (2009) showed that when participants performed a computer task, proposed to load visual-spatial processing, following exposure to a trauma film intrusive imagery in the following week was significantly reduced compared to those participants who did not perform the computer task. Furthermore, the administration of propranolol within 6 hours following the experience of a traumatic event has been suggested to reduce trauma-related symptoms (Brunet et al., 2008) and PTSD rates (Vaiva et al., 2003; although see Sharp et al., 2010; Pitman et al., 2002 for opposing results).

Anecdotal evidence suggests that many individuals are likely to consume alcohol in the aftermath of a trauma as a way to reduce emotional arousal and anxiety. As post-event administration of drugs has been shown to disrupt memory formation, it is theoretically conceivable that alcohol consumption could affect consolidation processes. Alcohol's ability to affect consolidation processes is currently unclear. Animal evidence suggests that post-learning administration of alcohol can impair memory consolidation (Castellano and Populin, 1990; Lattal, 2007). Furthermore, post-training administration of drugs that enhance GABA mediated inhibition or antagonise NMDA receptor activity have been found to reduce fear responding at a later test (Makkar et al., 2010; Parwani et al., 2005). However, several human studies have shown that post-learning administration of alcohol can facilitate memory recall and recognition (Parker et al., 1980; 1981). It has been suggested that this effect may be due to early excitatory effects by alcohol resulting in enhancement of consolidation, or through a reduction in retroactive interference (Mueller et al., 1983). Furthermore, alcohol has been found to facilitate memory for emotional stimuli over neutral (Knowles and Duka, 2007). However, the way in

which alcohol may affect consolidation processes following an aversive traumatic event is presently unknown.

6.6.2 Alcohol and re-consolidation

A high proportion of patients diagnosed with PTSD also have co-morbid substance abuse and symptoms in these individuals may be more severe and more resistant to treatment (Saladin et al., 1995). As discussed in Chapter 1, the most widely used substance amongst PTSD patients is alcohol, with between 36% and 52% of patients reporting co-morbid alcohol abuse (Breslau and Davis, 1992; Kessler et al., 1995). Surprisingly, little is known of the way in which alcohol use might contribute to the maintenance of PTSD.

Alcohol's anxiolytic action may potentially alleviate individuals' distress and anxiety related to symptoms. Consistent with this, a self-medication hypothesis is widely supported within the PTSD literature (e.g., Kushner et al., 2000; Robinson et al., 2009). Patients often report the use of alcohol and/or other central nervous system (CNS) depressants as a way of reducing hyper-arousal symptoms (Bremner et al., 1996). Despite alcohol's ability to acutely reduce arousal-based symptoms, we do not yet understand the way in which it affects these or other PTSD symptoms on a long-term basis.

Recent findings on reconsolidation processes suggest a potential mechanism by which alcohol to lead to more persistent trauma-related symptoms. The previously accepted notion that once a memory has been consolidated, it is impenetrable to further manipulation has been challenged. Although a consolidation hypothesis following an event is widely accepted, it has been proposed that when the memory is later retrieved, it returns to a transient labile state (Nader and Schafe, 2000). During this period, the memory becomes amenable to internal or external influences and can be enhanced or disrupted. Reconsolidation processes provide clear advantages over typical extinction mechanisms. Extinction relies on the formation of a novel association between the trauma reminder and its outcome, providing a new memory aimed to inhibit the original acquired fear memory. However, the properties of

extinction are open to *renewal* (the recovery of fear when the cue is experienced outside of the extinction context), *reinstatement* (the recovery of fear when an unconditioned stimulus is presented alone) and *spontaneous recovery* over time. In relation to reconsolidation, when extinction occurs after reactivation of a memory into its labile state, there is a greater reduction in fear response, which is long lasting (> 1 year) in humans (Schiller et al., 2010).

Although most of the literature has focused on the reconsolidation of conditioned fear, procedural learning and explicit memory have also been shown to be disrupted through similar processes. When a previously formed memory is reactivated prior to the presentation of new to-be-learned information, the new information becomes integrated within the original memory, and interferes with the original memory at its retrieval (Hupbach et al., 2007; Walker et al., 2003). It has been proposed that for an explicit memory to become unstable, the memory must be reactivated in the same spatial context in which the original encoding took place (Hupbach et al., 2009). This in turn means that a range of physiological, environmental and psychological boundary conditions must be met before certain forms of memory can become unstable and sensitive to manipulation following reactivation (Nader and Hardt, 2009). Given that the primary symptom of PTSD is the re-experiencing of intrusive imagery, it is not known how such imagery in the context of trauma may be manipulated through reconsolidation processes.

A reconsolidation hypothesis offers an attractive potential mechanism for the updating of memories in relation to the symptoms observed in PTSD. Reactivation of a previously encoded trauma memory can occur under a range of different circumstances, including involuntary retrieval in the form of a distressing ‘flashback’ or within a clinical setting during psychological therapy. However, the use of pharmacological agents, such as alcohol, following reactivation may disrupt reconsolidation processes, thus exacerbating symptoms and reductions in treatment efficacy. NMDA receptor activation plays an influential role in both extinction and reconsolidation. Pre-clinical findings show that the extinction of conditioned fear is blocked following administration of NMDA antagonists prior to extinction learning (Baker and Azorlosa, 1996; Lee and Kim, 1998). Similarly, impairments in

reconsolidation processes following NMDA antagonists have been shown in contextual fear, and spatial and odour-reward memories when administered following the reactivation of a previous memory (Lee et al., 2006; Przybylski and Sara, 1997; Suzuki et al., 2004; Torras-Garcia et al., 2005). Interestingly, it has been shown that administration of the NMDA antagonist ketamine shortly after a traumatic incident is associated with sustained PTSD symptomatology in humans (Schonenberg et al., 2005; Winter and Irle, 2004; although see McGhee et al., 2008 for an opposing view).

Other drugs that share part of alcohol's neurochemical action have also been shown to disrupt reconsolidation processes. Midazolam, a short acting benzodiazepine that increases GABA-mediated inhibition, was found to decrease the conditioned fear response when administered to rats following the reactivation of a previously acquired fear memory (Bustos et al., 2010). However, in the only study to assess alcohol's effects on reconsolidation, Nomura and Matsuki (2008) found that rats administered alcohol following a reactivation procedure demonstrated enhanced fear. If alcohol administration following the reactivation of a previous trauma memory can disrupt reconsolidation and lead to the persistence of PTSD related symptoms, this would highlight major issues in the treatment of patients who consume alcohol. To date, alcohol's effect on reconsolidation processes in humans remains unknown.

6.7 Journey to the bottom of a PhD pint glass

It is easy to look back over the past 3 years and wonder where the time has gone. Luckily, the experiences during my PhD have allowed me to always view the glass as '*half full*'. It has been a long journey but each new finding along the way has stimulated a new curiosity for the next scientific question to be addressed. Reflecting upon the results, this research has produced novel findings in an area that was relatively unknown at the beginning of the studies. It is of particular interest that some of these findings were reported by the national and international media (see Figure 6.3). The Telegraph, for example, focused on the idea of 'drinking to forget'; even though the press release made it clear the alcohol was consumed prior to

individuals watching the ‘painful’ scenarios. Daily India.com led with the idea that moderate drinking can make memories more ‘painful’.



Figure 6.3. A selection of media reports on the findings from Chapter 4 in relation to alcohol’s effects on memory for a traumatic event.

In summary, this research has generated important findings, which enhance our understanding of the way in which alcohol may disrupt memory during a traumatic event. The findings also advance our understanding of the cognitive mechanisms thought to play a functional role in trauma memory. Due to its disruptive effects on memory, alcohol use during a traumatic event may, depending on the actual dose consumed, increase an individual’s vulnerability to the later development of PTSD.

Chapter 6 – General discussion

Although the findings from this thesis are both novel and informative, the way in which alcohol can affect an individual's memory both during and after a traumatic event needs to be further investigated to provide a more complete understanding of this interaction.

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Professor Valerie Curran
Sub-department of Clinical Health Psychology
UCL

29 January 2008

Dear Professor Curran

Notification of Ethical Approval

Project ID/Title: 1338/001: The Acute Effects of Alcohol on Spontaneous Memories

I am pleased to confirm that the Vice-Chair of the UCL Research Ethics Committee has approved your research proposal for the duration of the study i.e. until 1st February 2009.

Approval is subject to the following conditions:

1. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form'.

The form identified above can be accessed by logging on to the ethics website homepage:
<http://www.grad.ucl.ac.uk/ethics/> and clicking on the button marked 'Responsibilities Following Approval'.

2. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. Both non-serious and serious adverse events must be reported.

Reporting Non-Serious Adverse Events.

For non-serious adverse events you will need to inform Ms Helen Dougal, Ethics Committee Administrator (h.dougal@ucl.ac.uk), within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair of the Ethics Committee will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Reporting Serious Adverse Events

The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

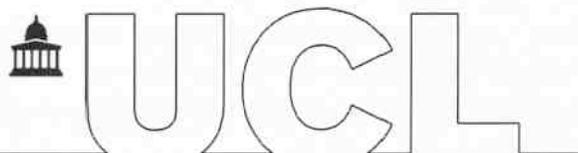
On completion of the research you must submit a brief report (a maximum of two sides of A4) of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

Yours sincerely



Sir John Birch
Chair of the UCL Research Ethics Committee

Cc: James Bisby and Professor Chris Brewin, Sub-department of Clinical Health Psychology



Professor Valerie Curran
Clinical Psychopharmacology Unit
Department of Clinical, Education and Health Psychology
UCL
Gower Street

26 November 2008

Dear Professor Curran

Notification of Ethical Approval

Ethics Application: 1338/003: Acute effects of alcohol on spatial memory for visual events

In my capacity as Chair of the UCL Research Ethics Committee, I am pleased to confirm that your application has been approved for the duration of the project, i.e. until 1st December 2009. However, the researchers must be certain that the participants are moderate social drinkers, since 6-7 units could badly upset an inexperienced drinker.

Approval is subject to the following conditions:

1. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form'.

The form identified above can be accessed by logging on to the ethics website homepage: <http://www.grad.ucl.ac.uk/ethics/> and clicking on the button marked 'Key Responsibilities of the Researcher Following Approval'.

2. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. Both non-serious and serious adverse events must be reported.

Reporting Non-Serious Adverse Events.

For non-serious adverse events you will need to inform Ms Helen Dougal, Ethics Committee Administrator (h.dougal@ucl.ac.uk), within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair of the Ethics Committee will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Reporting Serious Adverse Events

The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

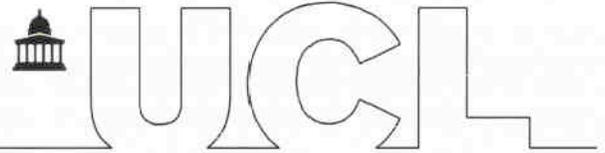
On completion of the research you must submit a brief report (a maximum of two sides of A4) of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

Yours sincerely



Sir John Birch
Chair of the UCL Research Ethics Committee

Cc: James Bisby, Clinical Psychopharmacology Unit, Dept of Clinical, Education and Health Psychology, UCL



Professor H. Valerie Curran
Clinical Psychopharmacology Unit
UCL Research Department of Clinical, Education
and Health Psychology
1-19 Torrington Place
London
WC1E 7HB

19 April 2010

Dear Professor Curran

Notification of Ethical Approval:

Ethics Application: 1338/004: Acute effects of alcohol on contextual memory

I am pleased to confirm that in my capacity as Chair of the UCL Research Ethics Committee I have approved your project for the duration of the study (i.e. until March 2011).

Approval is subject to the following conditions:

1. You must seek Chair's approval for proposed amendments to the research for which this approval has been given. Ethical approval is specific to this project and must not be treated as applicable to research of a similar nature. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing the 'Amendment Approval Request Form'.

The form identified above can be accessed by logging on to the ethics website homepage: <http://www.grad.ucl.ac.uk/ethics/> and clicking on the button marked 'Key Responsibilities of the Researcher Following Approval'.

2. It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. Both non-serious and serious adverse events must be reported.

Reporting Non-Serious Adverse Events.

For non-serious adverse events you will need to inform Dr Angela Poulter, Ethics Committee Administrator (ethics@ucl.ac.uk), within ten days of an adverse incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Chair or Vice-Chair of the Ethics Committee will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Reporting Serious Adverse Events

The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator immediately the incident occurs. Where the adverse incident is unexpected and serious, the Chair or Vice-Chair will decide whether the study should be terminated pending the opinion of an

independent expert. The adverse event will be considered at the next Committee meeting and a decision will be made on the need to change the information leaflet and/or study protocol.

On completion of the research you must submit a brief report (a maximum of two sides of A4) of your findings/concluding comments to the Committee, which includes in particular issues relating to the ethical implications of the research.

Yours sincerely

p.p. Angela Parker

Sir John Birch
Chair of the UCL Research Ethics Committee

Cc. Mr James Bisby, UCL Department of Clinical, Education and Health Psychology

14	Some people have the experience of sometimes remembering a past event so vividly that they feel as if they were reliving that event.	0%	10	20	30	40	50	60	70	80	90	100%
15	Some people have the experience of not being sure whether things that they remember happening really did happen or whether they just dreamed them.	0%	10	20	30	40	50	60	70	80	90	100%
16	Some people have the experience of being in a familiar place but finding it strange and unfamiliar.	0%	10	20	30	40	50	60	70	80	90	100%
17	Some people find that when they are watching television or a movie they become so absorbed in the story that they are unaware of other events happening around them.	0%	10	20	30	40	50	60	70	80	90	100%
18	Some people find that they become so involved in a fantasy or daydream that it feels as though it were really happening to them.	0%	10	20	30	40	50	60	70	80	90	100%
19	Some people find that they sometimes are able to ignore pain.	0%	10	20	30	40	50	60	70	80	90	100%
20	Some people find that they sometimes sit staring off into space, thinking of nothing, and are not aware of the passage of time.	0%	10	20	30	40	50	60	70	80	90	100%
21	Some people find that when they are alone they talk out loud to themselves.	0%	10	20	30	40	50	60	70	80	90	100%
22	Some people find that in one situation they may act so differently compared with another situation that they feel almost as if they were two different people.	0%	10	20	30	40	50	60	70	80	90	100%
23	Some people sometimes find that in certain situations they are able to do things with amazing ease and spontaneity that they would usually be difficult for them (for example, sports, work, social situations, etc.).	0%	10	20	30	40	50	60	70	80	90	100%
24	Some people sometimes find that they cannot remember whether they have done something or have just thought about doing that thing (for example, not knowing whether they have just mailed a letter or have just thought about mailing it).	0%	10	20	30	40	50	60	70	80	90	100%
25	Some people find evidence that they have done things that they do not remember doing.	0%	10	20	30	40	50	60	70	80	90	100%
26	Some people sometimes find writings, drawings, or notes among their belongings that they must have done but cannot remember doing.	0%	10	20	30	40	50	60	70	80	90	100%
27	Some people sometimes find that they hear voices inside their head that tell them to do things or comment on things that they are doing.	0%	10	20	30	40	50	60	70	80	90	100%
28	Some people sometimes feel as if they are looking at the world through a fog so that people and objects appear far away or unclear.	0%	10	20	30	40	50	60	70	80	90	100%

Participant ID

Date

Alcohol Usage Questionnaire (AUQ)

The following questions ask you about your habitual use of various types of alcoholic drinks. Please consider your drinking for the last six months in answering the questions and take your time to give an accurate answer to each question.

1. On how many days per week do you drink wine, or any wine type product eg sherry, port, martini (at least one small glass)? _____ Please state your usual brand(s) _____

2. On those days you do drink wine (or similar), about how many glasses (pub measure) do you drink? _____ If you are unsure, please estimate the number of bottles or parts of a bottle _____

3. How many glasses (pub measure) of wine do you have in a week, in total?

4. On how many days per week do you drink beer or cider (at least half a pint)? _____ Please state your usual brand (eg Carlsberg Special, White Lightening, etc) _____

5. On those days you drink beer/cider, about how many pints do you typically have?

6. How many pints of beer/cider do you drink in a week, in total? _____

7. On how many days per week do you drink spirits (whiskey, vodka, rum, etc., but not wine or beer)? _____ Please state your usual brand (eg Smirnoff Blue Label) _____

8. On those days you do drink spirits, about how many shorts (pub measure) do you typically have? _____ If unsure please estimate number of bottles or part bottles _____

9. How many drinks of spirits do you have in a week, in total? _____

10. When you drink, how fast do you drink? (Here, a drink is a glass of wine, a pint of beer or a shot of spirit, straight or mixed) Please circle the correct response:

Drinks per hour:

7+ 6 5 4 3 2 1 1 in 2 hours 1 in 3 or more hours

11. How many times have you been drunk in the last 6 months? By 'drunk' we mean loss of co-ordination, and/or inability to speak clearly _____

12. What percentage of the times that you drink do you get drunk? _____

CONFIDENTIAL - DDS

Please answer the following questions by circling a number from 0 to 4 indicating how you feel **AT THIS MOMENT IN TIME**, in this room:

1. At this moment in time: Do things seem to be moving in slow motion?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

2. At this moment in time: Do things seem unreal to you as if you are in a dream?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

3. At this moment in time: Do you have some experience that separates you from what is happening; for instance, do you feel as if you are in a movie or play, or as if you are a robot?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

4. At this moment in time: Do you feel as if you are looking at things from outside your body?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

5. At this moment in time: Do you feel as if you are watching the situation as an observer or spectator?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

6. At this moment in time: Do you feel disconnected from your own body?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

7. At this moment in time: Does your sense of your own body feel changed: for instance, does your own body feel unusually large or unusually small?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

8. At this moment in time: Do people seem motionless, dead or mechanical?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

9. At this moment in time: Do objects look different than you would expect?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

10. At this moment in time: Do colours seem diminished in intensity?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

11. At this moment in time: Do you see things as if you were in a tunnel, or looking through a wide angle photographic lens?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

12. At this moment in time: Does this experience seem to take much longer than you would have expected?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

13. At this moment in time: Do things seem to be happening very quickly, as if there is a lifetime in each moment?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

14. At this moment in time: Do things happen that you cannot account for?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

15. At this moment in time: Do you space out or in some other way lose track of what is going on?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

16. At this moment in time: Do sounds almost disappear or become much stronger than you would have expected?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

17. At this moment in time: Do things seem to be very real, as if there is a special sense of clarity?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

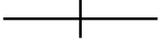
18. At this moment in time: Does it seem as if you are looking at the world through a fog, so that people or objects seem far away or unclear?

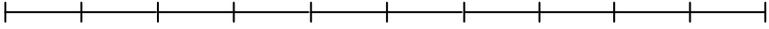
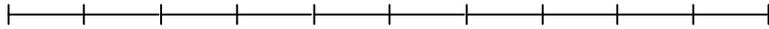
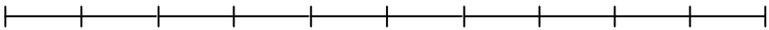
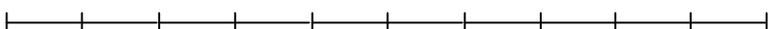
not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

19. At this moment in time: Do colours seem much brighter than you would have expected?

not at all	slightly	moderately	considerably	extremely
0	1	2	3	4

MRS Participant ID Date Occasion: Baseline / Pre / Post

- a. Please rate the way you feel in terms of the dimensions given below.
- b. Regard the line as representing the full range of each dimension.
- c. Mark clearly and perpendicularly across each line, ie. 
- d. Rate your feelings as they are **AT THE MOMENT**.

Sober		Drunk
Alert		Drowsy
Calm		Excited
Strong		Feeble
Muzzy		Clear-headed
Well coordinated		Clumsy
Lethargic		Energetic
Contented		Discontented
Troubled		Tranquil
Mentally slow		Quick witted
Tense		Relaxed
Attentive		Dreamy
Incompetent		Proficient
Happy		Sad
Antagonistic		Amicable
Interested		Bored
Withdrawn		Gregarious
Not at all Depressed		Depressed

Cued Recall Memory Test

Please the following questions in relation to the video you viewed 7 days ago:

1. At the beginning of the first scene, the camera shows a vehicle in flames. What was the colour of the vehicle?
2. In the first scene, a paramedic is seen helping an injured person in a vehicle. What part of the victim's body was seen sticking out of the wreckage?
3. In the first scene, one of the vehicles involved in the accident is a Volkswagen Beetle. What was the colour of this car?
4. What was in the blanket that the man was wearing a cap and long coat was carrying at the end of the first scene?
5. What was the type of vehicle that the female was trapped in during scene two?
A sedan
6. When the female was finally cut from the vehicle, which part/s of her body were cut and bleeding?
7. What was the age group of the female trapped in the vehicle in the second scene?
8. During the second scene, what was the female placed on when she was finally freed from the wreckage?
9. How many dead bodies were there in the third scene?

10. At the beginning of the third scene, how many fire engines are there at the scene of the accident?
11. In scene three, a body was laid partially in a car covered by a blanket. What body part did you see hanging out from under the blanket?
12. What kind of vehicle is shown at the end of the third scene?
13. In scene four, who were the two men lifting bodies into the coffins?
14. How many doctors in white coats were shown at the scene of the accident in scene four?
15. How many bodies were lifted into coffins during the fourth scene?
16. In scene four, what was the colour of the helmets worn by the rescue crew?
17. In the final scene, what was the female student receiving medical attention wearing?
18. In the final scene, what medical procedure does the paramedic perform on the injured individual?
19. Can you remember any other medical procedures that were performed on the injured student?
20. During the final scene, what is the colour of the blanket under the injured girl's head?

Trauma Film Recognition Memory Test

Please choose the correct answer from each of the statements below that relate to the film you watched:

Scene 1

- 1) At the start of the scene, fire fighters hurry to extinguish the flames on a:
 - a) Motorbike
 - b) Sports car
 - c) School bus
 - d) Lorry

- 2) The accident had occurred due to:
 - a) An oil spillage
 - b) A drunk driver
 - c) A sudden rain storm
 - d) A police chase

- 3) The several collisions have occurred:
 - a) On a local housing estate
 - b) On a motorway
 - c) In a busy town centre
 - d) In a car park

- 4) A man who has a bandaged head and is badly cut is helped away from the wreckage by two men. The man is:
 - a) In a wheelchair
 - b) Walking
 - c) On a stretcher
 - d) On crutches

- 5) Due to the accident:
 - a) A single person later died in hospital
 - b) A number of people lost their lives
 - c) There were some injuries but no deaths
 - d) There were no serious injuries or deaths

- 6) A man opens a blanket to reveal an injured child. The child is wearing:
 - a) A black jacket
 - b) A blue jacket
 - c) An orange Jacket
 - d) A red jacket

Scene 2

- 1) A woman screams in agony and seems to lose consciousness. She is wearing:
 - a) A black t-shirt
 - b) A white t-shirt
 - c) A red t-shirt
 - d) A green t-shirt

- 2) A man lies on a stretcher as paramedics cut away his clothes to reveal:
 - a) Cuts to his arms
 - b) Cuts his legs
 - c) Cuts to his back
 - d) Cuts to his chest

- 3) Due to the remote location, it took the ambulance and fire crew a long time to reach the accident. This resulted in:
 - a) The woman being permanently disabled
 - b) A child losing its life
 - c) No one was injured
 - d) A family drowned

- 4) The accident has taken place in:
 - a) England
 - b) Germany
 - c) America
 - d) France

- 5) The man involved in the accident is:
 - a) A middle aged Asian man
 - b) A young white man
 - c) A middle aged white man
 - d) A young Asian man

- 6) The man crashed into the vehicle because:
 - a) He had swerved to miss a pedestrian
 - b) He was drunk
 - c) He suffered a heart attack
 - d) He was driving too fast

Scene 3

- 1) The accident has involved a
 - a) Head on collision on a bridge
 - b) Car that swerved to miss a pedestrian
 - c) Multiple pile up on the motorway
 - d) School bus that lost control

- 2) A body that lies at the side of the wreckage is covered by
 - a) A striped blanket
 - b) A bright red blanket
 - c) A plain blue blanket
 - d) A transparent plastic sheet

- 3) Fire fighters lift the dead body from the wreckage. The body is a :
 - a) Young woman
 - b) Middle aged white man
 - c) A young Asian man
 - d) A middle aged woman

- 4) The crowd that has gathered
 - a) Help the injured from the wreckage
 - b) Observer the accident from the side of the road
 - c) Help push the smashed vehicle to the side of the road
 - d) Are pushed away from the scene by armed police

- 5) A dead body is revealed outside a car as emergency workers lift the body. The body is wearing a blood soaked:
 - a) Blue jacket
 - b) White t-shirt
 - c) Green sweatshirt
 - d) The body has no top on

- 6) As the body is pulled away from the wreckage, the rescue crew:
 - a) Drag away the smashed vehicle
 - b) Extinguish the flames that have engulfed the vehicle
 - c) Lay the body on the road and cover it with blankets
 - d) Make way for the emergency helicopter to land

Scene 4

- 1) A woman lies motionless in a vehicle with no roof as emergency workers surround the vehicle. The vehicle is:
 - a) Blue
 - b) Red
 - c) White
 - d) Brown

- 2) Due to the accident:
 - a) A number of people died
 - b) No one was seriously injured
 - c) A man was permanently disabled
 - d) A cyclist was killed

- 3) As the emergency crew work around the vehicle, one emergency worker holds the motionless woman by her:
 - a) Arms
 - b) Legs
 - c) Collar
 - d) Hand

- 4) The accident involved:
 - a) Two cars that had collided on a road
 - b) A school bus that had hit a tree
 - c) A car and a pedestrian
 - d) A good vehicle that had hit a building

- 5) One of the dead bodies that is placed in a coffin is wearing a:
 - a) Blue dress
 - b) Pink jumper
 - c) Orange jacket
 - d) Yellow jacket

- 6) The accident had taken place:
 - a) In the snow
 - b) On a clear mild day
 - c) On a rainy night
 - d) On a clear night

Scene 5

- 1) The accident had involved:
 - a) A family
 - b) A single male
 - c) A mother and child
 - d) Two female students

- 2) Paramedics work frantically to:
 - a) Gain access to the injured
 - b) Attend to the injured girl in the ambulance
 - c) Drive the ambulance to the scene of the accident
 - d) Move the injured man from the wreckage

- 3) The paramedic bandages the individual's injured:
 - a) Leg
 - b) Head
 - c) Arm
 - d) Shoulder

- 4) The injured individual is worked on in:
 - a) An emergency helicopter
 - b) An ambulance
 - c) The hospital emergency room
 - d) The middle of the road

- 5) The paramedic attending to the injured person is wearing a:
 - a) Blue uniform
 - b) Green uniform
 - c) Brown uniform
 - d) Orange uniform

- 6) The injured individual was wearing:
 - a) A torn t-shirt
 - b) A dark jacket
 - c) No top
 - d) A blue sweatshirt