THE EFFECT LICIT AND ILLICIT DRUGS HAVE ON TRAUMA PROCESSING AND MEMORY

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Submitted as a requirement of the degree of Doctor of Clinical Psychology

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DECLARATION

I declare that this thesis contains no material which has been accepted for the award to the candidate of any other degree or diploma, except where due reference is made in the text of the examinable outcome. To the best of my knowledge this thesis contains no material previously published or written by another person except where due reference is made in the text of the examinable outcome.

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Signed:
ACKNOWLEDGEMENT

I would first like to thank my primary supervisor Grant Devilly. He always had such confidence in my ability as a researcher. I would also like to thank my additional supervisor Greg Murray for all his assistance and support during the process of preparing the final report. Thank-you also to Katherine Owens for all knowledge and guidance during the research testing phase. I would also like to thank Rebecca King for all her help and support during the course of testing and writing up. Thank-you to the two research nurses, Jenny Lloyd and Sue Redden without whom the research would not have been possible. Thank-you also to the other staff of the BSI for always offering their help and assistance. Thank-you to my father for reading and contributing feedback to all the initial drafts of my thesis, and for the rest of my family for pretending to understand what the thesis was about! Thank-you to Rob for putting up with my continual complaints and cries for help with the computer! Finally, thank-you to all my friends who were always there to offer support and remind me that this thesis would end eventually!
ABSTRACT

Preliminary research suggests that depressant drugs such as alcohol may represent a protective factor against developing Post-traumatic Stress Disorder (PTSD), and stimulant drugs such as methamphetamine and methylenedioxyamphetamine (MDMA) a risk factor for the development of PTSD. Based on this preliminary research, the current study explored the effect alcohol, methamphetamine and MDMA had on trauma processing and memory. Sixty-one healthy adults participated in a double-blind, placebo controlled crossover design containing three conditions that involved the consumption of either 0.42mg/kg of d-methamphetamine, 100mg of MDMA, 1.3 grams/kg of alcohol or placebo in a randomised order. The procedure used to measure affective processing and memory was the immediate and delayed recall and recognition performance following completion of the Lexical Decision Task (LDT) and International Affective Picture System (IAPS) Task. The results supported some of the hypotheses formulated with regards to the effect alcohol and methamphetamine would have on emotional processing and storage of traumatic stimuli. The results did not support the hypotheses formulated with regards to the effect MDMA would have on emotional processing and storage of traumatic stimuli. Alcohol alters affective reactions to traumatic stimuli, reducing arousal levels and impairing threat estimation. Alcohol also has an inhibiting effect on the memory systems responsible for the storage and retrieval of such stimuli. Methamphetamine consumption appears to increase visual memory for emotional stimuli in general, but may impair short-term memory for verbally stored trauma-related stimuli, while enhancing long-term memory for such stimuli. MDMA consumption may temporarily improve short-term memory for trauma-related stimuli, but appears to reduce long-term visual and verbal memory. The effect
appears specific to threat-related visual stimuli with memory for emotional stimuli in general remaining intact. The methodology implemented in the study was unable to truly simulate the presentation of traumatic stimuli, and the dose of stimulants used was probably lower than is consumed in recreational use. The study indicates that alcohol is a significant protective factor against later developing PTSD after exposure to a trauma. Whilst the trends in the data indicate that methamphetamine may pose a risk for later developing PTSD, the low power levels of the sample were unable to confirm if these effects were significant. The effect MDMA has on the risk of later developing PTSD is mixed and appears to have a minimal impact. The results of the current study should prompt continued research into the role trauma processing and memory play in the pathogenesis of PTSD.
CHAPTER 1: INTRODUCTION

1.1 Post-traumatic Stress Disorder

Most people who experience a traumatic event will develop transient symptoms of stress such as fear and anxiety (Foa, Stekette, & Rothbaum, 1989; Morgan, Krystal, & Southwick, 2003). For the majority, these symptoms may serve an adaptive role and subside within a relatively short period of time. For a minority of people, however, the symptoms persist and may evolve into Post-traumatic Stress Disorder (PTSD) (refer to glossary). PTSD is a condition that results from exposure to a traumatic stressor that involves the actual or threatened death or serious injury of the individual, or the threat to one’s physical integrity (American Psychiatric Association, 2000). PTSD can also result from witnessing an event that involves the death, injury or threat to the physical integrity of another person, or learning of an unexpected or violent death, serious harm or threat of injury experienced by a family member or close associate. The individual’s response to the trauma must involve intense fear, helplessness or horror and result in impairment of functioning.

PTSD has been the subject of considerable empirical research, since it was first included in the Diagnostic and Statistical Manual of Mental Disorders (DSM) in 1980. An important goal of research in the trauma area is to determine factors that may increase or decrease a person’s chance of developing the disorder. A large body of research exists evaluating the influence psychological, social and biological factors have on PTSD prevalence (see for example Brewin & Holmes, 2003; Buckley, Blanchard, & Neill, 2000; Vermetten & Bremner, 2002a; Vermetten & Bremner, 2002b; Williams & Yule, 1995). In contrast only two uncontrolled studies have evaluated the impact
intoxication with alcohol or stimulants at the time of the trauma has on the risk of later developing PTSD.

The present study investigated the acute effects of alcohol, methamphetamine and Methyleneoxyamphetamine (MDMA) on affective processing and memory for trauma and non-trauma related information in healthy individuals. In order to understand the predictions made, the introduction will discuss two studies that have examined the effects of various drugs on PTSD prevalence. The first of these studies examined the effects of alcohol and will be discussed below, the second examined the effects of amphetamines and will be discussed later in the thesis. In order to understand the model of PTSD discussed by the authors of both studies, a biological model of PTSD based on maladaptive emotional memory storage will be reviewed in addition to the relevant pharmacological, animal and psychological evidence supporting the model. The rationale behind the hypothesised role alcohol, Methamphetamine and MDMA may play in emotional processing will then be reviewed, and the aims and hypotheses of the current study described. Important terms and concepts will be defined and operationalised in each relevant section of the thesis.

1.2 Alcohol as a protective factor against PTSD

In the first study, researcher attempted to determine factors that predicted the development of PTSD in a sample of 127 adults following a ballroom fire (Maes, Delmeine, Mylle, & Altanura, 2001). PTSD symptoms were evaluated using the Composite International Diagnostic Interview (CIDI), administered seven to nine months after the traumatic event. Results revealed that a sense of control during the trauma in addition to the consumption of alcohol and actual alcohol intoxication acted as a significant protective factor against the development of PTSD. These variables
appear to represent genuine preventative factors, with statistical analyses indicating a moderate effect size.

The authors proposed two possible explanations for their results, the first being that the anxiolytic effects of alcohol may have reduced the overall level of arousal and anxiety experienced during the traumatic event (Maes et al., 2001). Anxiolytic refers to drugs used in the treatment of anxiety (refer to glossary) (Kandel, Schwartz, & Jessel, 2000). However, as alcohol did not have any significant associations with the other peri-traumatic variables identified in the study, the researchers suggested an alternative explanation which they viewed as more plausible (Maes et al.).

They suggest that alcohol intoxication reduced the encoding, consolidation or retrieval of the traumatic memories and fear responses conditioned to them (Maes et al., 2001). Emotional memory storage is believed to be dependent upon the activation of central noradrenergic systems and N-methyl-D-aspartate (NMDA) related mechanisms in amygdala structures. According to the researchers alcohol may inhibit the NMDA-mediated synaptic pathways usually activated in these amygdala structures, by attenuating the effects stress has on Noradrenergic turnover in the amygdala and locus coeruleus.

1.3 A biological model of PTSD as a disorder of memory

Based on current research knowledge a biological model of dysfunctional emotional memory storage, involving the release of catecholamines and adrenergic activation, is proposed to explain the development and subsequent symptoms of PTSD (Vaiva et al., 2003). Catecholamine is the term used to describe a group of neurotransmitters including dopamine, noradrenaline and adrenaline (refer to glossary)
Adrenergic is the term used to describe a neuron that responds to the neurotransmitters Noradrenaline or Adrenaline (refer to glossary).

At the time trauma is experienced victims are believed to experience a surge of catecholamines such as adrenaline and noradrenaline both peripherally and centrally (Vaiva et al., 2003). The peripheral release of these catecholamines is designed to facilitate the ‘fight or flight’ response and often produces symptoms such as trembling, hyperventilation, sweating and tachycardia (Bryant, Harvey, Guthrie, & Moulds, 2000; Shalev et al., 1998; Turnbull, 2006). Research has found these symptoms are a precursor to increased physiological reactivity in patients who later develop PTSD (e.g., Blanchard, Kolb, Gerardi, Ryan, & Pallmeyer, 1986; Orr, 1994; Orr, Pitman, Lasko, & Herz, 1993; Pitman, Orr, Forgue, De Jong, & Claiborn, 1987). Research indicates this increased physiological reactivity may be a consequence of the trauma, rather than an individual susceptibility (Orr et al., 2000; Pitman et al.). In PTSD patients, the peripheral release of catecholamines is then triggered by reminders of the trauma (Turnbull, 2006). This persistent release of the catecholamines can cause changes in the receptor functioning leading to down regulation and depletion of adrenaline and noradrenaline. Down-regulation refers to the decrease in the ability of a neurotransmitter to bind to a receptor due to a reduction in the number or sensitivity of receptors following flooding of a pharmacological or physiological substance (refer to glossary).

Centrally, increased levels of catecholamines are believed to cause abnormally prolonged adrenergic activation in structures such as the amygdala and locus coeruleus, the key components of the fear circuit (Vaiva et al., 2003). The locus coeruleus is a site that contains a large number of noradrenergic neurones and has projections to several
brain regions including the amygdala, hippocampus, cingulate, entorhinal and orbitofrontal cortex (refer to glossary) (Vermetten & Bremner, 2002a). The locus coeruleus is the first site to receive sensory inputs from brainstem regions, and plays a critical role in perceiving, evaluating and responding to threatening stimuli (Ferry, Roozendaal, & McGaugh, 1999; Vermetten & Bremner). Increased firing of noradrenaline neurones in the locus coeruleus produces increased attention and alertness, while decreased firing induces drowsiness and sleep (O’Donnell, Hegadoren, & Coupland, 2004). The hippocampus is responsible for new learning and sorting and storing memories (refer to glossary) (Turnbull, 2006).

The amygdala is a collection of neural structures in the temporal lobe of the limbic brain that controls many aspects of emotional and social behaviour (refer to glossary) (Shin et al., 1997). The amygdala has been implicated in fear conditioning and the storage of memory in other brain regions such as the hippocampus, striatum and neocortex (Vermetten & Bremner, 2002a). Evidence from both human and animal studies provides support for the central role the amygdala plays in emotional memory formation (for a review see Pelletier & Pare’, 2004; Richter-Levin & Akirav, 2003; Tomaz, Frank, & Conde, 2003).

Some research suggests increased activation of the noradrenergic dependent amygdala pathways leads to a critical period of increased synaptic plasticity in the hippocampus, enhancing the consolidation of an emotional event into long term memory (Richter-Levin & Akirav, 2003; Vaiva et al., 2003; Ferry, Roozendaal, & McGaugh, 1999). Synaptic plasticity refers to any short or long term changes in a neuron’s excitability and morphology, frequently changing behavioural, physiological or cognitive outcomes (refer to glossary) (Kandel, Schwartz, & Jessel, 2000).
Recent research suggests synchronised oscillatory activity in the basolateral nucleus of the amygdala is responsible for the memory enhancement (Pelletier & Pare’, 2004; Tomaz, Frank, & Conde, 2003). The basolateral nucleus is the main site where all sensory modalities converge (Tomaz, Frank, & Conde). The basolateral nucleus is thought to be involved in the formation of aversive associations by coordinating inputs from the thalamus and hippocampus as well as areas of the cerebral cortex (O’Donnell, Hegadoren, & Coupland, 2004). Research suggests oscillatory activity in this complex promotes synaptic plasticity by facilitating interactions between neocortical and temporal lobe regions (Pelletier & Pare’, 2004).

This enhanced synaptic plasticity is thought to result in the storage of an overly strong emotional memory and fear conditioning that subsequently manifest as symptoms of PTSD (Vaiva et al., 2003). Since the retrieval of the traumatic memories is often accompanied by increased catecholamine levels, this may further enhance the encoding of the traumatic event in PTSD patients (Elzinga & Bremner, 2002). The enhanced encoding following retrieval, may also account for the sharpness and strong conditioning responses associated with the retrieved memory. Noradrenergic hyperactivity in the prefrontal cortex is also suggested to result in a failure of the individual to contain intrusive thoughts and trauma memories (O’Donnell, Hegadoren, & Coupland, 2004).

1.4 The nature of the traumatic memory

The brain is responsible for storing both explicit and implicit memory (Turnbull, 2006). Explicit (or declarative memory) refers to memory that is stored in a verbal and logical form. Implicit (or non-declarative) memory refers to memory that is stored in the form of sensations such as sight, sounds, tastes and feelings. The hippocampus is
responsible for managing the storage of explicit memories, while the amygdala is responsible for managing the storage of implicit memories. When large amounts of noradrenaline, adrenaline and endogenous opioids are released, storage of explicit memory is impaired. Traumatic memories are, therefore, more likely to be stored in implicit form as emotions and sensations. Because the verbal and logical form of the memory was impaired, survivors may only be able to recall fragmented parts of the event and experience feeling and sensations without a clear source or verbal template to explain the feelings and sensations.

The dual representation theory suggests that traumatic memories can be of two types (Brewin, Dalgeish, & Joseph, 1996). Verbally accessible memory (VAM), which is similar to explicit memory, is believed to be stored mainly in the left cerebral hemisphere. Situationally accessible memory (SAM), which is similar to implicit memory is believed to be stored mainly in the right cerebral hemisphere and contains sensory and emotional information. The situationally accessible memory is thought to be involved in the major symptoms of PTSD such as traumatic dreams and flashbacks. Evidence in support of this theory is the finding that individuals with lesions to their right hemisphere limbic systems following a head injury are at lower risk for later developing PTSD (Turnbull, 2006).

A recent Functional Magnetic Resonance Imaging (fMRI) study has found significant differences between left and right hemisphere activity in individuals with and without PTSD when recalling traumatic information (Hull, 2002). Participants who did not have PTSD showed a greater activation in their left hemisphere regions when recalling traumatic information, while participants with PTSD showed greater activation in right hemisphere regions. This suggests that the traumatic memories recalled in
PTSD patients contains more non-verbal information such as sensations and feelings, while the memories recalled for non-PTSD individuals are more verbal in nature. This finding will be discussed in further detail below.

1.5 Glucocorticoids and storage of emotional events

Although multiple other stress induced neuromodulators such as adrenaline and glucocorticoids are involved in the storage of emotional events, they appear to do so through activation or inhibition of the noradrenergic pathway (Morgan et al., 2003). A neuromodulator is a compound that influences either the release of a neurotransmitter or a neurone’s response to the neurotransmitter (refer to glossary) (Kandel, Schwartz, & Jesssell, 2000). A glucocorticoid describes any steroid produced by the adrenal gland that is primarily involved in protein, fat and carbohydrate metabolism and glucose regulation (refer to glossary). Activation of catecholamines and glucocorticoids facilities the appropriate acute coping behaviours in times of stress (Turnbull, 2006).

Some researchers suggest the excessive glucocorticoid activity involved in an individual’s response to a traumatic event and subsequent reminders of the trauma might lead to atrophy and cell death in the hippocampus (Turnbull, 2006). As the hippocampus is responsible for managing the explicit memories of the traumatic event, the damage to this region is believed to impair the appropriate recall and processing of the memories. This disables the spatial and temporal framework attached to the memories of the trauma, leading to the symptoms characteristic of a flashback. In order to achieve hippocampal atrophy however, excessive and prolonged or repeated bursts of very high levels of glucocorticoids would have to be present (Hull, 2002). Research suggests that the basal levels of glucocorticoids in PTSD patients are in fact lower than normal. Additionally, hippocampal atrophy has been associated with several other
disorders such as schizophrenia, bipolar disorder, alcohol abuse and dementia. These contrasting reports make it difficult to accurately determine the contribution of glucocorticoid deregulation in PTSD. As discussed above, many of the behavioural symptoms of PTSD are better attributed to deregulation in the noradrenergic system (O’Donnell, Hegadoren, & Coupland, 2004). Deregulation of the glucocorticoid system might result in the failure to inhibit the stress response activated in the amygdala, locus coeruleus and other limbic structures that results in the subsequent maintenance and progression of PTSD symptoms.

1.6 Evidence supporting a dysfunctional emotional memory circuit in PTSD:

Noradrenaline levels

Preclinical studies have shown that an extended period of alarm and arousal facilitates the onset of sensitisation in the stress system and long-term potentiation, the most accepted model of long term memory storage (refer to glossary) (Blank, Nijolt, Eckart, & Spiess, 2002). Furthermore, evidence of noradrenergic hyperactivity has been found in a large proportion of traumatised individuals who later develop PTSD in most studies (O’Donnell, Hegadoren, & Coupland, 2004). Evidence of noradrenergic hyperactivity has included heightened physiological responses to trauma-related cues, elevated urine levels of noradrenaline and adrenaline excretion and increased cerebrospinal noradrenaline levels (Morgan et al., 2003; Southwick et al., 1999).

A total reduced number of peripheral alpha-adrenergic receptors, a subtype of adrenergic receptors (refer to glossary), have also been found in PTSD patients compared to controls (Morgan et al., 2003; Southwick et al., 1999). This is suggested to result from down-regulation of these receptors due to the chronic elevated levels of circulating noradrenaline in PTSD patients. Research has also documented exaggerated
behavioural and psychological responses following administration of Yohimbine (Morgan et al., 2003; Southwick et al., 1999). Yohimbine is an antagonist that binds to the alpha auto-receptors in the noradrenergic system (refer to glossary) (Kandel, Schwartz, & Jessell, 2000). The binding of Yohimbine to these receptors blocks their inhibiting function and causes increased activity in the noradrenergic system. All of these studies have used a control group of other psychiatric conditions in addition to healthy controls (O’Donnell, Hegadoren, & Coupland, 2004).

Most of these studies have used peripheral measures to examine the role noradrenaline plays in PTSD. This makes the results of these studies dependent on evidence that demonstrates an interaction between peripheral and central levels of noradrenaline. In a study conducted by Geracioti and colleagues (2001), cerebral spinal fluid (CSF) levels of noradrenaline levels were compared at baseline to plasma levels in a sample of PTSD patients and controls. They found significantly higher CSF levels of noradrenaline in PTSD patients compared to controls but no significant differences in plasma levels. The CSF noradrenaline levels were also positively correlated with PTSD severity scores. This suggests that the abnormally elevated levels of noradrenaline in PTSD patients may occur following stressful stimuli only (O’Donnell, Hegadoren, & Coupland, 2004). While the studies examining the noradrenergic systems in PTSD patients have found higher than normal levels of noradrenaline, it is not yet know whether these changes precede the trauma or result from the trauma.

Further evidence supporting the dysfunctional emotional memory circuit, is the finding that patients with quadriplegic rather than paraplegic spinal cord injuries are less likely to develop PTSD (Radinitz et al., 1998). In quadriplegic injury the connection between the brain and the adrenal glands is severed, meaning the peripheral
physiological arousal associated with the symptoms of PTSD would not occur. Theoretically, this loss of physiological arousal would result in a reduction in the strength of the traumatic memory and conditioned fear response consolidated into memory in quadriplegic patients. The physiological arousal that occurs during re-experiencing of traumatic events, a condition postulated to increase the severity of PTSD symptoms, would also not occur in these patients.

1.7 Neuro-imaging research

Neuro-imaging studies have also consolidated the view that an abnormal memory circuit is implicated in PTSD (Richter-Levin & Aikirav, 2003). These studies have shown that biological changes following trauma exposure involve alterations in brain function and structure as well as neurochemical systems (Hull, 2002). Results of these studies indicate that abnormal memory storage results from a hyper-responsive amygdala, rather than a failure of inhibitory control by the anterior cingulate cortex usually involved in modulating responses to stress (Gilboa et al., 2004; Vermetten & Bremner, 2002a). It is suggested the absence of increased activity in the anterior cingulate cortex may be associated with the inability of people with PTSD to extinguish fear (refer to glossary) (Hull, 2002). Several studies have reported increased cerebral blood flow in limbic regions and decreased flow in prefrontal, parietal, hippocampal and temporal regions in PTSD patients during a trauma-related condition relative to a control condition. (Bremner, Krystal, Southwick, & Charney, 1996; Rauch et al., 1996; 1996 Shin et al., 1997). These studies have controlled for depression in their analyses, with the brain activation results remaining significant (Rabe, Beauducel, Zollner, Maercker, & Karl, 2006).
Increased amygdala responsiveness to the presentation of traumatic stimuli is accompanied by decreased activity in the prefrontal cortex, which is believed to play a role in the retrieval of verbal memory (Hull, 2002). Early studies also documented decreased blood flow in Broca’s area while patients were being exposed to trauma related memories. Broca’s area is involved in speech production and may explain why patients with PTSD are unable to label the emotions they experience during a symptom provocation procedure.

The failure of some studies to find amygdala activation in patients presented with generalised trauma pictures or combat sounds is most likely due to the nature of the stimuli presented, with greater emotional responsiveness more likely with personal narratives of traumatic events (Hull, 2002). Furthermore, while the amygdala is responsible for encoding the emotional significance of the traumatic event, it may not be involved in subsequent recall of the event. In support of this hypothesis, Bremner and colleagues (2005) used a fear-conditioning and extinction learning paradigm to investigate the integrity of the amygdala involvement in PTSD patients. They found that compared to controls, PTSD patients showed greater amygdala activation during acquisition of the conditioned response. Decreased activation in the anterior cingulate cortex was the only significant change in brain activation sites during extinction of the conditioned response for PTSD patients compared to controls. These findings suggest that while increased activity in the amygdala is involved in initial acquisition of a conditioned response, it is decreased activity in the anterior cingulate that is responsible for extinguishing the response. Past studies that have not found significant activation in the amygdala during a symptom provocation procedure have been inducing a condition that is separate or different to the initial acquisition of conditioned fear responses.
Using a word stem completion task, Shin and colleagues (2004) found a diminished involvement of the hippocampus in firefighters with PTSD compared to firefighters without PTSD. Of interest was the finding that the baseline hippocampal activity was higher in firefighters with PTSD compared to those without PTSD. The hippocampus is known to play a role in contextual fear conditioning, and the researchers therefore speculated that the elevated baseline hippocampal activity in PTSD patients might impair extinction of fear conditioning to novel contexts.

More recent studies have used script-driven symptom provocation to activate a PTSD symptomatic state. This technique involves the preparation of a script describing each participant’s traumatic experience that is then read to him or her, while they are instructed to imagine the events the script portrays (Rauch et al., 1996). Although these studies have documented a pattern of changes associated with a PTSD symptomatic state, it has been argued that the majority failed to include an appropriate control group of trauma survivors without PTSD. This meant the observed changes in brain activation may have been due to trauma exposure and not PTSD (Hull, 2002). In the symptom provocation studies using Vietnam veterans with PTSD, individuals with combat exposure without PTSD, and controls with no combat exposure or PTSD, evidence of amygdala hyperactivity in PTSD patients was shown to be symptom related and specific to PTSD (Liberzon et al., 1999; Pissota et al., 2002; Shin et al., 1997).

Imaging studies have also examined the metabolic response in brain regions during a noradrenaline challenge in PTSD and control participants (Bremner et al., 1996). Noradrenaline has a U-shaped curve of effect on the brain, with low doses producing an increase in blood flow, and high doses producing a decrease. A pattern of decreased metabolism in cerebral, anterior cingulate gyrus and hippocampal regions
was obtained for PTSD participants, with increased metabolism in these regions for the control group. This pattern of results is consistent with a potentiation of central noradrenergic responsiveness in PTSD.

A study conducted by Bremner and colleagues (2003) assessed the memory circuit involved in women with and without PTSD by examining their retrieval of emotionally valenced word pairs. The women with PTSD displayed a pattern of brain activation similar to that obtained when patients were exposed to trauma cues designed to activate a PTSD symptomatic state. The results provide convergent evidence that a specific brain circuit involved in the processing of emotional information in general is dysfunctional and contributes to the symptoms of PTSD.

Recent research also suggests that loss of consciousness following a trauma may play a protective role against PTSD (Glaesser, Neuner, Lutgehetmann, Schmidt, & Elbert, 2004; Gil, Caspi, Ben-Ari, Koren, & Klein, 2005). Furthermore, memory for the traumatic event is positively associated with a risk for later developing PTSD. Taken together, these imaging findings provide evidence in support of the dysfunctional emotional processing model of PTSD and the role memory plays in the development and maintenance of PTSD symptoms.

1.8 The mechanisms involved in emotional memory

Research has indicated that emotional arousal including increased attention, rehearsal and increased elaboration plays a role in the encoding and consolidation of explicit and consciously accessible emotional memory (Hamann, 2001). However, recent research has also identified specific neural and hormonal mechanisms involved in emotional memory. The most currently accepted model postulates that enhanced memory for emotional stimuli results from effects both at the time of encoding and
processes that occur after encoding. Encoding involves creating the initial representation of the emotional event. This process involves the amygdala, which modulates and enhances the activity of other brain regions involved in memory. The post-encoding process involve consolidation, the process whereby the new memory is made more permanent. Emotional arousal causes the release of stress hormones which interact with the amygdala to enhance the consolidation of emotional stimuli in memory regions including the hippocampus. Research suggests the amygdala is involved in the storage of negative and positive emotional stimuli. The amygdala has also been implicated in the process of retrieval, with the temporal pole involved in the psychological process of retrieving emotional memories.

1.9 Drug influences on emotional processing and memory

Two important terms must first be defined. An agonist is a drug that binds to a receptor and activates it (refer to glossary) (Kandel, Schwartz, & Jessell, 2000). Antagonists are drugs that bind to a receptor and inhibit it (refer to glossary). Extensive animal pharmacology research has shown that post-training drug infusion of the amygdala modulates memory formation across tasks and brain regions (Debiec & Ledoux, 2004; Richter-Levin & Akirav, 2003). Furthermore, these drug-modulation effects are both dose and time dependent.

Although a substantial amount of animal research has documented the involvement of the β-adrenergic hormonal stress system in emotional memory storage, until recently research using human subjects had not been conducted. A β-adrenergic is a subtype of adrenergic receptors (refer to glossary) (Kandel, Schwartz, & Jessel, 2000). In order to determine the relationship between stress hormones and emotional memory in humans, Cahill and colleagues (1994) examined the effect a β-adrenergic receptor
antagonist (propranolol hydrochloride) had on long-term memory for an emotionally arousing story. Propranolol binds to peripheral and central β-adrenergic receptors causing decreased activity in the noradrenergic system (refer to glossary) (Vaiva et al., 2003). Researchers theorised that if emotional memory required the activation of β-adrenergic receptors, administering the Propranolol would impair memory for the emotional story, leaving the memory for a matched neutral story intact (Cahill et al., 1994).

Supporting expectations, propranolol produced significant and selective memory impairment for the emotional story for both recall and recognition (Cahill et al., 1994). Furthermore, participants in the placebo condition showed superior memory performance for those elements of the story associated with emotional arousal. Importantly the Propranolol treatment selectively impaired memory for the more emotional story only, indicating the impaired memory was not due to the effects of sedation or impaired attention. The subjective emotional reactions immediately after viewing the story were also not impaired, meaning the effects of propranolol cannot be attributed to a reduced subjective emotional responsiveness.

Cahill and colleagues (1995) also examined memory for an emotional story in a patient with impaired amygdala functioning. Consistent with the results obtained with a Propanol treatment, the patient failed to show enhanced memory for the emotional phase of the story, despite experiencing increased emotional arousal and normal memory for the neutral phase of the story. More recently, in another case study, Taylor and Cahill (2002) described the successful treatment of a 44-year-old woman who had experienced five motor vehicle accidents, with the last three causing severe PTSD episodes of over 6 months duration. Following a sixth accident the PTSD symptoms re-
emerged and she began treatment, taking 60mg of propranolol twice a day commencing 48 hours after the incident. Rating scores on the Clinician-Administered PTSD Rating Scale dropped from an initial 86 to 56 points eleven days after treatment and continued to drop to 25 points after nine months of treatment. These results are the first of their kind and suggest propranolol may be effective in treating and preventing initial and re-emergent PTSD symptoms by disrupting the consolidation of the traumatic memory.

Because propranolol blocks both peripheral and central beta-receptors, it was not known whether the memory effects obtained in the above trials were due to action at peripheral or central receptors (Van Stegan, Everaerd, Cahill, McGaugh, & Gooren, 1998). In order to examine this issue, the effects of propanol, a placebo, and nadolol, (a beta-blocker incapable of crossing the blood brain barrier) were compared for their memory impairing effects. A beta-blocker is a drug that binds to β-adrenergic receptors and inhibits the receptors’ action. Administered to participants between 1-3 hours before viewing an emotional and neutral story, propranolol but neither nadolol nor placebo impaired memory for the emotional story. Together these results support the assumption that central beta-receptor activation is involved in enhanced memory for emotional events.

Recent research suggests this enhanced emotional memory may be the result of adrenergic activation during memory consolidation rather than encoding. In a study conducted by Southwick and colleagues (2002) intravenous injections of Yohimbine, a noradrenaline stimulant, or a placebo, were administered to participants 5 minutes after viewing an emotionally arousing story. Because the Yohimbine was administered after the learning had occurred, the improvements obtained in memory could not have
resulted from increased attention or motivation during encoding, but instead appears to have enhanced post-learning memory consolidation.

1.10 Therapeutic use of anti-adrenergic agents

Despite evidence for adrenergic abnormalities in PTSD, the use of anti-adrenergic agents in clinical trials has received little attention. Anti-adrenergic agents describe an agonist with a site of action that results in the inhibition of adrenergic receptor activity (refer to glossary) (Kandel, Schwartz, & Jessell, 2000). Some preliminary trials have used clonidine and propranolol with combat survivors, abused children and women with PTSD as treatment interventions for the symptoms of hyperarousal and nightmares (Famularo, Kinscherff, & Fenton, 1990; Morgan, Krystal, & Southwick, 2003; Southwick et al., 1999). Clonidine, like propranolol, is an agonist that binds to auto-receptors in the noradrenergic system causing decreased activity in the noradrenergic system (refer to glossary) (Kandel, Schwartz, & Jessell). However, the results of these studies should be interpreted with caution, as none of them were double blind or placebo controlled (Southwick et al., 1999). Within these limitations, results suggested that adrenergic agonists such as clonidine or anti-adrenergic blocking agents such as propranolol may have therapeutic benefits. Administered immediately after a trauma, these agents may have a preventative effect, impairing the consolidation of the emotional memory and reducing the likelihood of PTSD symptoms.

This hypothesis was recently tested in a double blind pilot study conducted by Pitman and colleagues (2002). A sample of 18 participants was administered propranolol within 6 hours of experiencing a traumatic event, and continued to take the medication for 10 days followed by a 9-day taper period. Results showed that a greater number of the placebo participants met the criteria for PTSD after one month and
displayed heightened physiological responses to a script driven trauma cue at the three-month follow-up. Although the authors suggested these results further confirmed the role β-adrenergic activation plays in emotional memory storage, there were problems in the research that limits the reliability of these conclusions. Small unequal sample sizes and a high attrition rate led to a low experimental power level, and although some statistically significant differences were identified, these lack reliability. Furthermore, the propranolol should have been administered earlier than 6 hours post-trauma, for an effective impairment in the memory storage process to occur. After six hours, the memory for the traumatic event may have already consolidated into memory. However, recent PET imaging studies suggest that it can take up to six hours for a memory of a newly learned skill to be stored (Schadmehr & Holocomb, 1997). These findings may also be true for memories that are autobiographical in nature, in which case the protocol of propranolol administration within 6 hours may still have been capable of inducing some change in memory storage.

In a replication of the above study, Vaiva and colleagues (2003) administered propranolol to 11 participants between 2 to 20 hours after a trauma, with a control group of 8 participants. Results revealed significant differences in PTSD symptom severity in favour of those receiving the Propranolol. However, limitations in sample size and methodology again make conclusions from the study unreliable, with independent analysis of their results revealing only a moderate effect size when controlling for the small sample size. Furthermore, the resulting 95% confidence intervals are far too wide to have trust in the size of the effect, ranging from –0.41 to 1.44 (Devilly, 2004). Although, disadvantaged by the small effect size, the two studies add weight to the suggestion that Post-trauma memory consolidation is regulated by adrenergic activation.
More recent animal research has suggested that Propranolol may be an effective treatment for PTSD patients some time after the original traumatic event had been experienced. Debiec and Ledoux (2004) examined the impact of reconsolidation of traumatic memories using a rat sample. Reconsolidation refers to the dynamic process of retrieving and storing events in memory (refer to glossary). They found that post-training administration of propranolol did interfere with the reconsolidation of memory but not the initial consolidation of auditory fear conditioning. These results were obtained in rats two days and two months after the initial learning and suggest propranolol may effectively influence old as well as recent memories. These results are only preliminary and not necessarily generalisable to humans. However, the results suggest propranolol could be given as a treatment for PTSD if given within the context of traumatic memory reactivation.

1.11 Amphetamines as a risk factor for PTSD

In the second study exploring peri-traumatic intoxication on PTSD prevalence, the effects of alcohol, amphetamines and cocaine were explored (Zatzick et al., 2002). A sample of 101 injured trauma survivors being held in a hospital ward were assessed for alcohol and drug intoxication in addition to PTSD, depressive and dissociative symptoms prior to the trauma. PTSD symptom severity was then assessed during interviews conducted 1, 4 and 12 months after the trauma. Random coefficient regression models were constructed using variables present at the time of initial hospitalisation to predict PTSD symptom levels in the year following the trauma. The toxicology screen revealed that 37% of the survivors returned a positive result for alcohol and 16% for stimulants such as amphetamine and cocaine.
The positive alcohol screen did not add any significant power to the model derived by the researchers (Zatzick, et al., 2002). A possible explanation for this result may be the lack of a stipulated minimum to return a positive result (such as 0.05 blood alcohol concentration). However, the results did reveal that stimulant intoxication with either cocaine or amphetamines at the time of the trauma was associated with an increased risk and severity of later PTSD symptomatology. A positive screen for stimulants showed a moderate effect size when added to the model. This result appears consistent with the hypothesis that excitation of amygdalic functioning through the presence of central stimulants would produce results opposite those obtained after ingesting NMDA inhibitors such as alcohol or the β-adrenergic antagonist Propranolol. Although this assumption has yet to be directly tested, increased noradrenergic hyperactivity and subsequent reactions to psychological stress has been linked to the increased release of dopamine in chronic methamphetamine users (Kunio, Kimihiko, Shigenori, Takeo, & Yoshimori, 2000).

1.12 Emotional processing of trauma related stimuli in PTSD patients

The core symptoms of PTSD, such as involuntary intrusive flashbacks and recurrent nightmares suggest abnormalities in the brain circuits responsible for processing and storing memory (Liberzon et al., 1999). Neuropsychological studies exploring cognitive deficits in emotional processing and recall in PTSD patients support the evidence accumulated by neuroimaging studies that have attempted to identify neuroanatomical regions activated during induced PTSD symptomatic states.

Neuropsychological studies of delinquent youth, combat veterans, rape victims, childhood sexual abuse and Holocaust survivors diagnosed with PTSD have yielded evidence of memory and attention deficits when compared to controls (see for example
Bremner et al., 2003; Danforth, Gansler, & McMackin, 1999; Golier et al., 2002; Yehuda, Golier, Halligan, & Harvey, 2004). Research also suggests patients with PTSD show a deficit in verbal declarative memory, and a preference for remembering trauma related information (see for example Bremner et al.; McNally, Kaspi, Riemann, & Zeitlin, 1990; Semple et al., 1996; Vrana, Roodman, & Beckham, 1995;). These findings are consistent with both deficits in encoding and retrieval and enhanced encoding or retrieval of trauma-related stimuli.

Further research has also suggested PTSD patients have difficulty inhibiting irrelevant information (Cottencin, et al., 2006). The memory systems in PTSD patients are believed to become saturated with traumatic memories, with patients no longer able to use their inhibition processes. Dissociation was also believed to play a protective role in this memory retrieval process, by inhibiting retrieval of traumatic stimuli (DePrince & Freyd, 1999). This deficit has been investigated using the directed forgetting paradigm. The task involves presenting a series of stimuli in which some are to be forgotten and some remembered. Although research initially supported the above theory, more recent studies have found no association between a tendency to dissociate and poorer recall for trauma over neutral stimuli (Devilly et al., 2007). Research did find that individuals with a tendency to dissociate remembered fewer words overall, and showed a tendency to favour recall of trauma over neutral words. This research suggests that false recall is particularly likely for traumatic stimuli, and that dissociation in individuals is likely to lead to poorer memory recall or memory errors in general.

1.13 Theories explaining the cognitive impairments evident in PTSD patients.

Information-processing theories suggest the cognitive impairments associated with PTSD may reflect a cognitive bias, with patients selectively allocating more
resources to the processing of information congruent with their traumatic memories or emotion in general (Foa & Kozak, 1986; Foa, Steketee, & Rothbaum, 1989; Martin, Williams, & Clark, 1991; McNally et al., 1990). Furthermore, research has consistently indicated that these cognitive biases exist specifically for clinical patient groups, and are not evident in non-clinical populations with equivalent anxiety levels (Martin et al., 1991).

The increased responsiveness and attending to negative and threat-related stimuli in PTSD patients has also been supported by electrophysiological studies. In a recent review of PTSD and event-related potentiation studies, it was revealed that PTSD patients consistently show increased P300 amplitudes to trauma related cues compared to non-PTSD trauma controls (Karl, Malta, & Maercker, 2005). The increased amplitude was interpreted as reflecting a selective and higher attention and sensitivity to trauma-related cues.

It has also been shown that the increased attending and processing of such information was unrelated to past exposure to the feared situations and specific for threat stimuli that is idiosyncratic to the anxiety disorder (Cassiday, McNally & Zeitlin, 1992; Foa, Feske, Murdock, Kozak, & McCarthy, 1991; Kaspi, McNally, & Amir, 1995; McNally et al., 1990). The preferential recall pattern identified in PTSD patients lends further support to the suggested involvement of specific brain areas such as the amygdala and hippocampus in the disorder.

The following sections will discuss the three drugs chosen for examination in the current project. Each section will describe the structure and action of each drug, current research knowledge concerning the subjective and objective effects of each drug and the impact each drug has on cognitive and emotional processing. Further sections
will discuss the impact each drug is predicted to have on emotional processing and memory, in addition to providing a rationale for the selection of each drug for examination.

1.14 Current research knowledge of the effects licit and illicit drugs have on emotional processing and memory

1.15 Alcohol

Alcohol, (ethanol), is a central nervous system depressant, with the degree of depression proportional to its concentration in the blood (Jaffe, 1995). Alcohol is readily absorbed from the gastrointestinal tract, and quickly travels to all fluids and tissues in the body. The onset of action is related in part to how quickly alcohol passes through the stomach, therefore drinking on an empty stomach produces almost instant intoxication. The relationship between blood alcohol levels and the degree of central depression is most accurate immediately after consuming alcohol when the levels are rising, rather than 3 to 4 hours later when levels are the same but the alcohol levels are falling. Maximum blood alcohol levels are obtained about 30 to 90 minutes after consumption, with blood levels providing a good estimate of brain levels.

Ethanol has a very simple chemical structure, yet its exact mechanism of action in the central nervous system is still not fully understood (Jaffe, 1995). The reticular activating system of the brain stem, responsible for maintaining arousal and integrative control of higher order functions is most sensitive to the effects of alcohol (refer to glossary). After consuming a moderate amount of alcohol, humans initially experience a stimulating feeling of excitement and an increased level of confidence and mood swings. Memory, insight and the ability to concentrate are affected next, with higher doses producing impairment in neuromuscular coordination. Despite still being able to
move around, humans become significantly impaired in both judgement and reaction
time, with increased feelings of sleepiness. Higher doses of alcohol can cause
respiratory depression, sleep or unconsciousness.

Several different mechanisms have been proposed to explain how alcohol
depresses the central nervous system (Jaffe, 1995). One of these mechanisms is thought
to be alcohol’s ability to alter the ion channels in the neurone cell membrane, increasing
the movement of chloride across the membrane causing a reduction in neuronal
transmission. Alcohol ingestion causes an increase in receptor functioning and the
inhibition of Glutamate receptor functioning (Kandel, Schwartz, & Jessel, 2000).
GABA receptors are the main inhibitory neurotransmitters in the central nervous system
controlling the arousal state and motor and sensory activity (refer to glossary).
Glutamate receptors are the major excitatory neurotransmitters of the central nervous
system (refer to glossary). Inhibition of these neurones produces cognitive impairments,
memory disturbances and an inability to process and learn new information. GABA and
Glutamate are believed to play a role in the encoding of factual and emotional memories
(Vaiva et al., 2004). One of GABA’s main functions is to regulate the intensity and
duration of the central hyperadrenergic response activated in a stressful situation.
alcohol also produces increased dopamine and serotonin and stimulates the release of
endorphins and enkephalines, the brain’s opiate neuropeptides (refer to glossary).

It has been hypothesised that abnormalities in GABA inhibition may increase
the awareness and response to acute stress (Vaiva et al., 2004). Specifically, decreased
GABA activity in the amygdala may increase an individual’s vulnerability to stress.
This hypothesis was tested by measuring plasma GABA levels during the first few
hours after a trauma exposure in a sample of 108 traffic accident victims. The study
found victims who went on to develop PTSD after six weeks had significantly lower GABA levels than the victims with no PTSD. This finding seems consistent with other research suggesting alcohol consumption and intoxication prior to a traumatic event reduces the risk of later developing PTSD by increasing GABA activity in the CNS. Additionally, although a coma and unconsciousness is still not well understood, it is theorised to be partly induced by disruptions in the glutamate pathway (Friedman, 2002). Dissociation is also believed to result from a disruption of glutamate functioning. The effect alcohol has on glutamate and GABA activity may therefore explain why consumption can protect against PTSD.

1.16 Research exploring the effect alcohol has on cognition and emotional memory

Research exploring cognitive functioning following alcohol consumption has consistently found impairments in information processing ability. Research indicates that even at low doses, simple visual and auditory reaction times are increased (Lemon, Chesher, Fox, Greely, & Nabke, 1993). Interestingly, research examining free recall following alcohol consumption found impaired ability to explicitly remember words, with implicit memory remaining intact, suggesting selective memory impairment (Lister, Gorenstain, Fisher-Flowers, Weingarther, & Eckardt, 1991). Research also suggests that as the demands of the task increase, for example under dual-task conditions, the alcohol-induced impairments also increase (Maylor, Rabbit, James, & Kerr, 1990).

A preliminary double-blind, electro-encephalographic (EEG) study examined the effect a moderate amount of alcohol had on brain function, cognition and performance in a sample of eight participants (Ilan & Gevins, 2001). The results found that alcohol impaired performance on psychomotor and memory tasks with a
widespread increase in background EEG power. These neuro-physiological changes were still evident several hours after chemical and behavioural indicators of intoxication had diminished. These results appear to indicate that neural populations required for accurate stimulus processing were less available for use following alcohol consumption and remained unavailable for several hours after consumption.

Initially, it was not clear whether impairment in the early stages of information processing was responsible for the observed impairment in total information processing following alcohol consumption. A study conducted by Tzambazis and Stough (2000) explored inspection time (IT), simple reaction time, choice reaction time and cognitive ability with the WAIS-R following the consumption of 40ml of alcohol. Alcohol had a significant impact on inspection time, simple and choice reaction time suggesting an alcohol induced slowing of early information processing, in addition to an observed impairment in higher-order complex tasks. These results suggest alcohol significantly impairs total information processing independently of the early stages.

In research conducted by Grattan-Miscio and Vogel-Sprott (2005) the effect alcohol had on immediate working memory was systematically examined using the Sternberg Memory Scanning task, a task designed to measure working memory as distinct from the other three stages of memory. Significantly slower reaction times and increased errors were evident following alcohol ingestion. Furthermore, these impairments increased as the task demands increased and working memory was functioning at near maximum level. Interestingly, when a reward for performance on the task was introduced, reaction time and rate of scanning improved in those participants who had ingested alcohol and did not differ to the placebo group. The study
also found that as alcohol concentrations were lowered, reaction time and scanning time improved, however accuracy remained impaired.

1.17 The impact alcohol has on post-trauma cognitive functioning.

Previous research examining cognitive functioning following alcohol consumption and a traumatic event has been inconclusive as a result of the various methods used to assess both alcohol consumption and cognitive functioning. In a recent study, the relationship between pre-injury alcohol consumption and post-injury cognitive functioning following a traumatic brain injury was examined (Turner, Kivlahan, Rimmele, & Bombardier, 2006). This study prospectively examined the relationship between alcohol-related variables and cognitive performance in a group of 124 patients admitted to the inpatient rehabilitation ward of a major hospital. Blood alcohol levels were obtained through blood tests and standardised self-report measures used to obtain information from the participants about alcohol consumption and alcohol-related problems prior to the traumatic brain injury. No independent report from relatives or friends was used to validate this self-report data. In contrast to the research previously discussed, the results of this study suggested alcohol use prior to a traumatic brain injury was not related to post-injury cognitive functioning. More specifically, both a history of alcohol consumption and the BAC level on admittance to hospital was not related to cognitive functioning during or following recovery. A significant limitation to these conclusions, however, is the failure to test patients after a fixed interval of time or to use standardised inclusion criteria. A baseline measure of cognitive functioning prior to the trauma was also not possible, making it difficult to accurately compare functioning following the trauma and alcohol intoxication.
Research is only beginning to examine the effect alcohol use prior to traumatic events has on the cognitive, emotional and physiological reactions of victims (Clum, Nishith, & Coulhoun, 2002). One study investigated the association between reported alcohol use prior to a sexual assault and self-reported peritraumatic reactions in a sample of 57 female college students. Participants completed questionnaires assessing perceptions of assault severity and physical and emotional peritraumatic symptoms experienced after the event. Alcohol use at the time of the trauma was associated with perceptions of the assault as less severe. These findings may suggest an alcohol-induced memory disruption, resulting in an impaired ability to remember one’s responses during the sexual assault or the sexual assault itself. However, as the relationship between self-reported memories for the event was not significantly related to the amount of alcohol use reported, an alternative explanation for these results may be possible, such as a dampening of the emotional response activated by the traumatic event. Supporting this hypothesis is research that found alcohol consumption decreased the negative impact of an emotional film on mood (Van Tilburg & Vingerhoets, 2002). Similarly, recent research has found that alcohol impairs memory for emotional and neutral stimuli shown after drug administration (Knowles & Duka, 2004). Because of the limited number of recalled events, the research was unable to compare the effects of alcohol on positive and negative stimuli separately but a trend was found towards the level of arousal predicting better recall of the stimuli. Taken together, the results of this research are consistent with a hypothesis that alcohol intoxication at the time a traumatic event is experienced reduces the likelihood of later developing PTSD by impairing the traumatic memory and reducing emotional responsiveness.

1.18 Why examine the effect alcohol has on emotional memory?
Of all licit and illicit drugs consumed during the occurrence of traumatic events, alcohol is one of the most common. Excessive alcohol consumption is the most common cause of both intentional and unintentional traumatic injury (Tjipto, Taylor, & Liew, 2006). In Australia it has been estimated that 44% of fire injuries, 34% of falls and drowning, 30% of car accidents, 47% of assaults, 16% of child abuse, 10% of suicides and 7% of industrial accidents are associated with alcohol use (National Health and Medical Research Council, 2001). It is estimated that 34% of offenders and 31% of victims of violence and homicide are also under the influence of alcohol at the time of the event. Injuries caused by road accidents or violence are the most common consequence of alcohol intoxication for young adults. Between 1990 and 1997, 52% of people injured during alcohol-related road accidents were aged between 15-24 years and 23% were aged between 25-34 years.

A recent study conducted at the Royal Melbourne Hospital in Australia found that 39% of young emergency department patients were classified as at risk from their hazardous drinking (Tjipto, Taylor, & Liew, 2006). Furthermore, many of these patients had not received any previous advice to decrease their alcohol consumption. Research also suggests those individuals who report drinking above low-risk levels or who drank beer in the six hour period prior to their injury were significantly more likely to sustain a serious rather than mild injury (Watt, Purdies, Roche, & McClure, 2006). This research suggests alcohol has a significant impact on an individual’s risk for engaging in an activity that could result in the occurrence of a trauma. The potential cost to the community of alcohol-related traumatic responses is high. Emerging research also suggests alcohol might modify the sympathetic nervous system response activated following a trauma (Woolf, Cox, Kelly, McDonald, & Hamill, 1990). While alcohol
appears to reduce the noradrenaline and adrenaline catecholamine levels in patients after a severe head injury, in patients with only mild head injuries alcohol causes an increase in these catecholamine levels. This research raises the question of whether alcohol intoxication at the time of the trauma might have a significant impact of the resulting patient outcome and emotional response to a trauma. Depending on the amount consumed, alcohol may actually increase or decrease the emotional response to trauma.

1.19 Methamphetamine

Methamphetamine (d-N, a-dimethylphenylethylamine), is an addictive psychostimulant, chemically similar to amphetamines, but producing a more pronounced effect on the central nervous system and less peripheral effects (Bustamante et al., 2002; Jaffe, 1995; Parfitt, 1999). Methamphetamine is believed to be particularly potent given its quick absorption and release into the blood stream and slow process of elimination (Cook et al., 1992). Methamphetamine is used to maintain wakefulness, increase general mood, improve cognitive and sensory performance, to suppress appetite, increase physical endurance, and in high doses, to produce intense euphoria (Moszczynska et al., 2004; Oyler et al., 2002). Amphetamines cause increased heart rate, respiration, systolic and diastolic blood pressure and in high doses may cause cardiac arrhythmias (Jaffe, 1995).

Methamphetamine increases dopamine and noradrenaline levels, by augmenting the release from neurones and blocking re-uptake. This produces increased nerve cell activity mainly in the dopaminergic systems (Jaffe, 1995; Nordahl, Salmon, & Leamon, 2003; Sekine et al., 2001). Methamphetamine also influences serotonergic, noradrenergic and glutamatergic systems, through interactions with 5-HT transporters,
monoamine transporters and N-methyl-D-aspartate (NMDA) receptors (Adams, Hanson, & Keefe, 2000; Nordahl, Salo, & Leamon).

In humans methamphetamine is readily absorbed from the gastrointestinal tract after consumption (Schepers et al., 2003). The average elimination half-life is 10.1 hours with a range of 6.4 – 15.1 hours (Cook et al., 1992). Amphetamines have a long duration of action, between 8-13 hours, and rapidly and efficiently cross the blood-brain barrier (Nordahl, Salo, & Leamon, 2003). Methamphetamine influences both behaviour and cognition in humans, with studies reporting alterations in memory, attention, impulsivity and decision-making (Mewaldt & Ghoneim, 1979; Nordahl, Salo, & Leamon, 2003). Any improvements in performance are often subtle and are most obvious following periods of sleep deprivation or when participants are made to perform mundane tasks (Comer, Haney, Foltin, & Fischman, 1996; Jaffe, 1995). These improvements also appear more pronounced on tasks requiring improvements in vigilance and reaction times rather than memory and learning (Comer et al., 1996).

1.20 Research exploring the effect amphetamines have on cognition and emotional memory.

The amygdala receives a rich supply of neurones from the mesencephalic dopaminergic system, with specific activation of this pathway reported to have occurred following exposure to a conditioned fear arousal stimulus (Coco, Kuhn, Ely, & Kilts, 1992). These findings suggest that dopamine release in the amygdala may be involved in the expression or acquisition of conditioned fear responses stored in memory (Vermetten & Bremner, 2002b). Research also suggests that dopamine function plays a central role in frontal cortical mediation of working memory (Tops et al., 2004). Furthermore, it has been shown that the presence of stress induced glucocorticoids such
as cortisol can alter the mesocorticolimbic dopaminergic system involved in the modulation of memory consolidation, suggesting stress-induced changes in memory storage (Roozendaal, De Quervain, Ferry, Setlow, & McGaugh, 2001).

Amphetamines are known to stimulate the release of catecholamines (Ferry, Roozendaal, & McGaugh, 1999). Experiments using amphetamine provided some of the first evidence that catecholamines played a role in memory consolidation. Several studies have documented enhanced memory following the administration of amphetamines either before or after learning (Ferry et al; Packard, Cahill & McGaugh, 1994). These memory-enhancing effects have been obtained for several different animal training paradigms including inhibitory avoidance, active avoidance and appetitive discrimination. For example, in a conditioned place preference task, that involves the association between environmental stimuli and the rewarding treatment, extinction (which is considered new learning), was facilitated following peripheral and intra-amygdala injections of amphetamines (Schroeder & Packard, 2003). These results support the view that amphetamine enhances memory retention by influencing memory storage processes (Ferry et al., 1999).

If research is correct in suggesting stimulants such as amphetamines increase fear sensitivity and facilitate the encoding and storage of emotionally laden stimuli through limbic stimulation, one would expect such activation when intoxicated with the drugs. At the very least, stimulant drugs would have an influence on attention, which in turn affects perception (Driver & Mattingly, 1995).

1.21 Why examine the effect methamphetamine has on emotional memory?

In Australia, exposure to trauma is a common experience among the general adult population, with PTSD a possible outcome of such exposure. Data obtained in the
Australian National Morbidity Study, provided an estimated 12-month prevalence rate of 1.33% for a sample of 1061 participants (Creamer, Burgess, & McFarlane, 2000). Amphetamine is the second most popular drug among Australians, with an estimated 8% of the population having used it (Makkai & McAlister, 1993). Amphetamine use is particularly widespread among young Australians with an estimated 17% of 14-24 year old males having used the drug.

Recent research indicates that amphetamine use is very much a social activity (Darke, Ross, Cohen, Hando, & Halt, 1995). Evidence from experimental studies has also found increased levels of aggression and an increased sensitivity to stress following chronic amphetamine use (Kunio, Kimihiko, Shigenori, Takeo, & Yoshinori, 2000; Sokolov, Schindler, & Cadet, 2004; Szuster, 1990). The social nature of amphetamine use combined with evidence of increased aggression means users may be placing themselves in high-risk situations, exposing themselves to potential traumatic scenarios in a state of increased sensitivity (Darke et al.; Kunio et al.).

1.22 Methylenedioxymethamphetamine (MDMA, Ecstasy)

Methylenedioxymethamphetamine, (MDMA), is a synthesised drug and member of the hallucinogen family (Parfitt, 1999). MDMA has stimulant properties similar to amphetamine in addition to hallucinogen properties similar to Lysergic Acid Diethylamide (LSD). For this reason MDMA is often referred to as a stimulant-hallucinogen. The vast majority of users consume MDMA orally, with its effects lasting approximately 4 to 6 hours (Baggot, Jerome, & Stuart, 2001). The typical dose of MDMA is between one to two tablets with each tablet usually containing 60 to 120 milligrams of MDMA. Pharmacokinetic studies have indicated that MDMA is rapidly absorbed into the blood stream, with a peak concentration of between 1 to 3 hours.
Once in the body the MDMA metabolites inhibit MDMA metabolism. This means any subsequent dose of the drug results in unusually high blood levels.

The majority of previous MDMA research has administered doses equivalent to 1.5 to 1.7 mg/kg of MDMA and has been proven safe even at doses of 2.5mg/kg (Baggot, Jerome, & Stuart, 2001). Within these clinical trials, MDMA has generally been well tolerated with hypertensive episodes the most common negative side effect. A hyperkinetic episode refers to a period of excessive involuntary motor activity. In surveys of MDMA users, the commonly reported effects are generally consistent with those reported during clinical trials. Users of MDMA report experiencing a state of extreme positive feelings and relaxation, and increased sociability and empathy towards others. MDMA eliminates feelings of anxiety and suppresses eating, drinking and sleep. MDMA does not produce hallucinations, but users report experiencing distorted perception and time, moderate thought disturbances such as accelerated thinking, thought blocking or impaired decision making and moderate feelings of derealization.

Users also experience nausea, jaw clenching and teeth grinding, increased motor tension, panic attacks and blurred vision (Parfitt, 1999). These effects last for approximately six hours after drug administration (Baggot, Jerome, & Stuart, 2001). Effects that persist beyond six hours include impaired immune functioning, lasting about two days, and altered cerebral blood flow that can last for up to several weeks. MDMA use also results in an increased heart rate, blood pressure and core body temperature. Many MDMA users describe experiencing a hangover in the days following their MDMA use, with symptoms of fatigue, drowsiness, sore jaw muscles, loss of balance and headaches.
The mechanism of action of MDMA is still not fully understood. MDMA increases the activity levels of three main neurotransmitters: serotonin, dopamine and noradrenaline (Baggot, Jerome, & Stuart, 2001). Similar to amphetamine, the drug causes these three neurotransmitters to be released from their storage sites in the neurones, producing an increase in brain activity. Compared to methamphetamine, MDMA causes larger amounts of serotonin to be released, with only small amounts of dopamine and noradrenaline released. Serotonin is believed to be involved in the regulation of mood states, including depression and anxiety (refer to glossary). Serotonin is also thought to be involved in food intake, emotion, pain, sleep and impulsive violence (Kandel, Schwartz, & Jessell, 2000). Acute doses of MDMA produces marked changes in the brain’s dopamine and serotonin system. While the changes to the dopamine systems appear transient, some research suggests the changes and depletions in the serotonin systems may be longer lasting (Lyles & Cadet, 2003).

1.23 Serotonin

Serotonin plays an important role in an individual’s response to trauma, helping the person to monitor their environment and respond to the changing stimuli or environment appropriately (Turnbull, 2006). The serotonin system appears to modulate the brain’s responsiveness to noradrenaline, and in low or depleted levels interferes with the arousal of the individual. Animals with depleted levels of serotonin, have been shown to display behaviours consistent with the symptoms of hyperarousal often seen in PTSD patients. Stress-induced deregulation of serotonin also interferes with behavioural inhibition that can lead to aggression and impulsively or a compulsive re-enactment of the trauma in PTSD patients. The serotonergic system has important reciprocal relationships with the key limbic structures involved in the brain’s response to stress.
Excessive activity of the hypothalamic-pituitary adrenocortical system in chronic PTSD patients can produce changes in serotonin receptor regulation and abnormal levels of the neurotransmitters released. Clinical studies have associated depression, rage, aggression, panic and obsessional thoughts and addictions with low serotonin levels in PTSD patients.

1.2.4 Research exploring the effect MDMA has on cognition

The consequences of MDMA use in recreational users remains relatively unclear. There has been some evidence of permanent damage to serotonergic neurones in regions such as the prefrontal cortex and hippocampus following MDMA use in animals (Lyvers, 2006; Parfitt, 1999). In these studies, the degree of damage appeared to depend on the dose taken and the number of times the drug was consumed. In some of these studies neurochemical markers for the serotonin system did return to normal after some time had passed following cessation of drug use. It is not known whether this was due to regeneration of cells or simply compensatory changes in the remaining undamaged neurones (Lyles & Cadet, 2003).

The impact of MDMA on serotonergic systems and cognitive functioning in humans remains controversial (Lyvers, 2006). There is some evidence of permanent damage to memory function following heavy MDMA use (Curran & Verheyden, 2003; Kalechstein, DeLaGarza, Mahoney, Fantegrossi, & Newton, 2007). In some studies, MDMA users produce results consistent with significant deficits in verbal and prospective or everyday memory function (Bhattachary & Powell, 2001; Lyvers, 2006). In contrast a number of studies examining working memory function, and performance on facial processing, encoding and retrieval have found no significant differences between MDMA users and controls (Daumann et al., 2003a, 2003b, 2005).
A recent meta-analysis examined eleven studies that had investigated the impact of MDMA use on neuro-cognitive functioning (Kalechstein, DeLaGarza, Mahoney, Fantegrossi, & Newton, 2007). The analysis found a medium effect size for the association between MDMA use and decreased performance on measures of verbal and nonverbal learning, memory and executive functioning. Effects sizes approaching medium levels were obtained for the association between MDMA use and decreased performance on measures of attention, concentration and psychomotor speed. The analysis also found that the results did not vary as a function of the methodology employed in the 11 studies.

In contrast a similar review that also examined the neuro-imaging research and associated changes in cognitive functioning in abstinent MDMA users was unable to come to any conclusions regarding long-term effects following exposure (Cowan, 2007). According to Cowan, the varied experimental designs and few replications across research groups has produced conflicting findings. The author argues that only with replications of study results and assessments conducted in drug naive participants will a conclusion regarding the safety of MDMA use be obtained.

Research has consistently found that heavy users of MDMA score significantly higher than matched controls on measures of obsessive traits, paranoid thoughts, and disturbed mood and sleep patterns. They also show increased levels of impulsivity (Baggot, Jerome & Stuart, 2001; Lyvers, 2006; Thomasius et al., 2002). Research also suggests that as MDMA users age, the damage to their serotonergic systems can lead to the onset of depressive and anxiety disorders (Lamers, Bechana, Rizzo, & Ramaekers, 2006).

1.25 Limitations in the MDMA research reviewed.
Serious methodological limitations are present in all of the research that has examined the long-term consequences of MDMA use (Lyvers, 2006). These include sample size and failures to adequately match MDMA users to controls; confounding drug use, particularly cannabis; and lack of a clear association between changes in brain imaging measures and cognitive functioning. Inconsistent evidence regarding the existence and reversibility of changes in brain neurochemistry and the relevance of animal models of MDMA neurotoxicity to humans also make conclusions regarding MDMA induced brain changes speculative. The majority of studies are retrospective and have only investigated individuals who have stopped taking MDMA for several weeks or months, with no real long-term follow-up. Some authors also argue that many of the participants used in these studies might have had pre-drug deficits in their serotingergic systems and on cognitive measures. Studies investigating the long-term consequences of MDMA use are also complicated by the fact that what is sold as ecstasy in non-regulated contexts may or may not actually contain MDMA (Baggot, Jerome, & Stuart, 2001).

1.26 Research exploring the effect MDMA has on emotional memory

Recently, research has begun to investigate the interaction between environmental stress and the effect MDMA has on brain neurochemistry. One study found that when rats were administered MDMA prior to being exposed to an environmental stressor, the normal stress-induced release of serotonin in the prefrontal cortex and hippocampus was blunted (Baggot, Jerome, & Stuart, 2001). The MDMA also blunted the release of dopamine and glutamate in the hippocampus. The pre-treatment with MDMA did not, however, blunt the release of the major stress hormones
associated with the body’s stress response. This suggests that MDMA may have a very specific effect on the biological stress response in humans.

Another research group investigated MDMA’s influence on dopaminergic neurones in the presence of acute and chronic stress (Johnson et al., 2001). This research found that acute stress was protective against the MDMA induced neurotoxicity to dopamine neurones. However, chronic stress was either not protective against this dopaminergic damage or enhanced the damage. Taken together, these preliminary results suggest that MDMA administration in humans prior to a trauma may increase the behavioural stress responses associated with the peripheral and central release of catecholamines, yet may impair the memory for the traumatic event by blunting neurotransmitter release in the amygdala and hippocampus. The resulting effect this would have on the risk of later developing PTSD remains unclear.

1.27 Why examine the effect MDMA has on emotional memory?

Based on responses from the ‘2001 National Drug Strategy Household Survey’, 20% of Australians aged between 20 to 29 years have used ecstasy, a significant increase from the previous 1998 survey. For responses based on drug use over the last 12 months, ecstasy use increased from 1.1% in 1991 to 2.9% in 2001. Reports also suggest the drug is often combined with other drugs such as methamphetamine, LSD, Viagra and marijuana (Baggot, Jerome, & Stuart, 2001).

In the 1970’s despite the lack of any real evidence to support its usefulness, MDMA was used by many psychotherapists as a regular part of therapy (Baggot, Jerome, & Stuart, 2001). Anecdotal evidence suggested the drug assisted patients in their discussion of emotional issues, reducing defences and fear of painful feelings and allowing them to achieve a greater insight into their thoughts and feelings. These
therapists also claimed that MDMA enhanced retrieval of previously suppressed memories, leading to a reduction in emotional symptoms. Currently, there has been no clear therapeutic benefits demonstrated (Pham & Puzantian, 2001; Turner & Parrott, 2000).

Recently, the Food and Drug Administration, (FDA), in the United States of America, (USA), have given final clearance for a series of trials to be conducted into the usefulness of MDMA in treating PTSD (Doblin, 2002). A study is currently being conducted in Madrid, Spain with PTSD patients. This is the world’s first trial into the efficacy of MDMA-assisted psychotherapy. The rationale behind these trials is that MDMA is a relatively safe drug, with effects lasting only about 4 hours and a gradual return to baseline levels after 2 hours. Additionally it is argued that because the drug impacts on emotion more than cognition, the resulting state is very close to normal and can be easily remembered after the drug has worn off. When used therapeutically, MDMA would be used as an adjunct to psychotherapy, with the drug administered no more than four times. The assumption underpinning this approach is that MDMA reduces the fear associated with traumatic memories. However it is widely believed that the central therapeutic mechanism in exposure treatment for PTSD is confronting of the fear associated with the traumatic memories (Hembree, Rauch, & Foa, 2003).

1.28 The current study

Based on the preliminary results of studies exploring the effect alcohol or central stimulants have on individuals who have experienced a traumatic event, it is suggested healthy individuals administered either a depressant drug or stimulant drug would demonstrate either a suppression or excitation in their emotional processing and memory systems. When administered a central depressant such as alcohol, individuals
would show decreased scores on valency and arousal ratings for emotional stimuli and poorer recall for such stimuli. When administered a stimulant such as methamphetamine or MDMA individuals would show increased scores on valency and arousal ratings for emotional stimuli and show enhanced recall for such stimuli.

Only two preliminary and uncontrolled studies have evaluated the role of peri-traumatic intoxication on the prevalence of PTSD. The present study investigated the acute effects of alcohol, methamphetamine and MDMA on affective reactions, processing and memory for trauma and non-trauma related information in healthy individuals. Verbal and visual stimuli were used as simulation for the experience of trauma events. Verbal and visual stimuli were chosen in order to allow for any differences between the emotional response and memory for language versus visual based information.

The study was a repeated-measures, counter-balanced, double-blind, placebo controlled experimental design. Participants were selected for the alcohol, methamphetamine and MDMA comparisons based on specific inclusion and exclusion criteria. Different participants were selected for each comparison to ensure they had no previous exposure to the test stimuli. Methamphetamine and MDMA were chosen for comparisons due to their large consumption in recreational settings, past research suggesting drug induced memory and affective changes and good tolerability in past research studies. Additionally, there is limited research examining the effect MDMA has on affective reactions and memory, despite a trial currently being conducted to investigate the usefulness of the drug as a treatment for PTSD.

The procedure used to measure affective processing and immediate and delayed recall of traumatic stimuli was the performance on the Lexical Decision Task (LDT).
The procedure used to measure affective reactions and delayed recognition of traumatic stimuli was the performance on the International Affective Picture System (IAPS) Task. The LDT task required individuals to view a set of words and non-words displayed on a computer. The real words presented to individuals possessed either a positive, neutral, negative or threat-related emotional valency. The task was designed to induce an emotional response in participants after reading an emotionally valenced word. The threat-related words were designed to simulate the experience of a traumatic event. Individuals reaction time to the words presented in the LDT provided a measure of processing speed as participants were required to read the word and then indicate whether the word presented was a real or non-word.

The IAPS paradigm requires individuals to view and rate on valence and arousal scales a selection of positive, neutral, negative and threat-related pictures (Lang, Bradley, & Cuthbert, 1999). The task was designed to induce arousal and fear following the presentation of the threat-related pictures (threat-related will hereafter be referred to as threat). The threat pictures were designed to simulate the experience of a traumatic event. The valence and arousal ratings provided a measure of affective reactions. Using threat pictures had several advantages over the use of other techniques for simulating a traumatic experience. Pictures can be presented in an identical fashion to all participants and have a greater resemblance to the type of traumatic triggers that PTSD patients are exposed to in their environment (Canli et al., 2000; Canli et al., 1999).

After completing the LDT, short-term memory for the words was assessed by an immediate free recall test. Repeating the recall test two weeks after the initial testing session assessed long-term memory for the words. Long-term recognition of the pictures from the IAPS Task was obtained two weeks after the initial testing session.
using a recognition test with matched distracter items. Immediate short-term memory for the pictures was not assessed, as presenting the pictures for recognition a second time would have interfered with the long-term memory results. Short-term recall of the LDT words was not considered to interfere with the long-term results as recall does not involve presenting the words a second time.

The study included a measure of both immediate recall and long term recall for the LDT, in order to assess whether the effect alcohol, methamphetamine and MDMA has on memory was due to reduced or enhanced encoding or storage. It was assumed immediate recall would measure drug effects on encoding, while long-term recall would measure drug effects on storage.

1.29 Aims and hypotheses

1.30 Affective reactions

The current study examined the difference between drug and placebo conditions for valence and arousal ratings to threat pictures in the IAPS Task.

Specifically, the current study tested the hypothesis that compared to the placebo condition, the alcohol condition participants would rate the threat pictures presented in the IAPS Task as having a lower negative valence and lower arousal rating. Compared to the placebo condition, in the methamphetamine and MDMA condition participants would rate the threat pictures presented in the IAPS Task as having a greater negative valence and higher arousal rating.

1.31 Memory

The current study examined the difference between drug and placebo conditions for recognition rates for threat pictures from the IAPS Task and immediate and delayed recall for the threat words from the LDT.
Specifically, the current study tested the hypothesis that compared to the placebo condition, the alcohol condition would produce decreased long-term recognition for threat pictures from the IAPS Task. Compared to the placebo condition, the methamphetamine and MDMA conditions would produce increased long-term recognition of the threat pictures from the IAPS Task.

The current study also tested the hypothesis that compared to the placebo condition, the alcohol condition would produce decreased short and long-term recall of the threat words presented in the LDT. Compared to the placebo condition, methamphetamine and MDMA conditions would produce increased short and long-term recall of the threat words presented in the LDT.

As part of an exploration of memory performance on the IAPS Task the current study measured the degree of confidence participants had for their recognition of threat pictures from the IAPS Task. This measure was included in the study in order to explore any drug related increases in confidence irrespective of memory accuracy. As part of an exploration of memory performance on the LDT the immediate recall test was measured in two epochs to allow for an exploration of primacy and recency effects on recall.

1.32 Processing

The current study examined the difference between drug and placebo conditions for reaction times to threat words from the LDT. This variable was examined as a possible mediator on memory performance.

Specifically, the current study tested the hypothesis that compared to the placebo condition, the alcohol condition would produce increased reaction times to the threat words in the LDT. Compared to the placebo condition, the methamphetamine and
MDMA conditions would produce decreased reaction times to the threat words in the LDT.

1.33 General and neutral emotional processing

The current paradigm adopted in the study allows for the hypothesis generating exploration of general and neutral emotional processing. The main aim of the current study is to explore responses specific to threat words and pictures. General emotional processing and responses to neutral stimuli will be used as a reference when discussing results in order to determine if results are specific to threat stimuli or evident across all emotive and non-emotive stimuli. This was conducted in order to remain consistent with past methodologies that used primary processing as a reference when investigating secondary processing (see for example DePrice & Freyd, 2001; Devilly et al., 2007). If it is determined that significant results exist for both general or neutral processing and processing of threat stimuli, further analysis will be conducted in order to control for threat stimuli.

1.34 Covariates

Literature suggests that factors such as gender, anxiety sensitivity and exposure to trauma may increase an individual’s response to depressant and stimulant drugs or influence their performance on measures of affective reactivity and memory. Research suggests that females and males tend to respond differently to alcohol consumption with differing behavioural and emotional consequences (Van Tilburg & Vingerhoets, 2002). Anxiety sensitivity refers to the tendency to fear physical and cognitive symptoms of anxiety and could increase affective reactions to trauma information (Reiss, Peterson, Gursky, & McNally, 1986). Past trauma exposure may increase attention and arousal to threat-related stimuli (Foa & Kozak, 1986; Foa, Steketee, &
Rothbaum, 1989; Martin, Williams, & Clark, 1991; McNally et al., 1990). These variables were systematically measured in the study and included as covariates in the analyses.

The research was expected to indicate whether licit or illicit drug use could decrease or increase a person’s chance of later developing PTSD by attenuating or enhancing the processing and storage of emotional stimuli. Results from the research were expected to contribute to a larger knowledge base relating to the effect central nervous system depressant drugs and stimulant drugs have on cognitive processes in humans, with specific relevance to post traumatic stress reactions.

CHAPTER 2: METHOD

2.1 Experimental design

The study employed a repeated-measures, counter-balanced, double-blind, placebo controlled experimental design. Participants were selected for the alcohol, methamphetamine or MDMA comparison based on specific inclusion and exclusion criteria. All three comparisons were conducted in parallel studies conducted at the Brain Sciences Institute at Swinburne University of Technology. The testing procedure was the same for all comparisons. Participants were randomly allocated to undergo drug or placebo in the first of their two conditions. The matched word and picture sets were randomly paired, and participants randomly allocated a pair across their two testing sessions. Both the participants and the experimenter were blinded for all testing sessions, and both were asked to make a forced choice guess as to whether they had consumed the drug or placebo at the end of each session.

2.2 Participants

2.3 Inclusion criteria
The participants in the methamphetamine and MDMA comparisons also participated in a larger study on the effects of methamphetamine and MDMA on driving and cognition. Participants in all three comparisons were recruited from the university and surrounding community through advertisements and word-of-mouth referrals. Persons responding were screened with a short interview over the phone and examined by a registered medical practitioner to determine their suitability for inclusion in the study. All participants were put through a routine intake interview, which assessed their drug taking history, current medication and recreational drug use. No participant took part in more than one comparison, as several exposures to the testing stimuli would have an impact on the memory performance.

Exclusion criteria for all comparisons included a current or past history of substance abuse, current use of prescription medication (with the exception of the contraceptive pill) or a pre-existing physical or neurological condition. Individuals with a current psychiatric condition, a significant health problem such as gastrointestinal or bleeding disorder, or who were pregnant or lactating were also excluded. There were no restrictions set on caffeine or tobacco consumption. However participants were required to abstain from consuming either substance on all testing days.

All participants in the methamphetamine and MDMA comparisons were required to have experimented with amphetamines but be irregular users, having previously consumed the drug no more than once a month. This was needed in order to ensure that all participants had experienced prior exposure to the drug, with no negative side effects. Irregular use was required to ensure no substance abuse or dependence issues existed. Participants in the alcohol comparison were required to be moderate drinkers, with a weekly average of about half to one drink per day for females and one
to three drinks per day for males. They were also required to have experience with drinking vodka and with drinking 5 or more standard alcoholic drinks on a single occasion. This was to ensure the participants had past experience with the drinking protocol. All participants were required to be aware of the general effects of alcohol, methamphetamine or MDMA. Participants in the alcohol comparison were required to have a body weight within 20% of the normal range according to gender, height and stature, and a body mass index below 28kg/m², as excess or insufficient weight can impact on alcohol absorption and side effects. The participants in all comparisons were required to abstain from taking any psycho-active recreational drugs for two weeks before testing and not at all during the actual testing phase. Participants were also instructed not to drink caffeinated beverages or engage in heavy exercise on the day they arrived at the laboratory. Those participants with sessions in the afternoon were asked to eat a light breakfast and lunch. Participants in the methamphetamine and MDMA comparisons were paid a sum of $500 for their involvement in the study. Participants in the alcohol comparison were not paid for their involvement in the study.

2.4 Demographics

2.4.1 Alcohol versus Placebo

Data included in the alcohol comparison was from a sample of 11 females and 9 male adults between the ages of 21 and 35 years. The mean age of female participants in the alcohol comparison was 24.27 years (SD = 3.93). The mean age of male participants was 25 years (SD = 2.87). All participants had obtained a tertiary education, and all but three participants had obtained further education. Most participants were right-handed, with only five participants using their left hand. Twelve participants were smokers and eight non-smokers. On average, all participants reported consuming 3 to
10 standard alcoholic drinks per week. All but six individuals had consumed cannabis in the past, with most participants currently consuming the drug on a monthly or yearly basis. All but six participants had consumed amphetamines in the past, with most participants currently consuming the drug every six months or longer. All but five participants had consumed MDMA in the past, with most currently consuming the drug every six months or longer. Only ten participants had consumed cocaine in the past, with most currently consuming the drug every six months or longer. Only two participants had consumed heroin in the past, with only one participant currently consuming the drug every six months. One participant had used inhalants in the past, but was not currently inhaling. For further information on the demographic information collected for participants in the alcohol comparison refer to Table 1 attached in Appendix 1.

2.4.2 Methamphetamine versus Placebo

Data included in the methamphetamine comparison was from a sample of 11 females and 10 males between 18 and 45 years of age. The mean age of female participants in the methamphetamine comparison was 25.90 years (SD = 2.92). The mean age of male participants was 26.91 years (SD = 3.70). All participants had obtained a tertiary education, and all but eight participants had obtained further education. Most participants were right-handed, with only three participants using their left hand and one using both. Fourteen participants were smokers and seven non-smokers. On average, all participants reported consuming 2 to 10 standard alcoholic drinks per week or every month. All but two participants had consumed cannabis in the past, with most participants currently consuming the drug on a monthly or yearly basis. All participants had consumed amphetamines in the past, with most participants
currently consuming the drug on a monthly or yearly basis. All but one participant had consumed MDMA in the past, with most currently consuming the drug on a monthly or yearly basis. All but three participants had consumed cocaine in the past, with most currently consuming the drug every 18 months or longer. Only six participants had consumed heroin in the past, with only one participant currently consuming the drug every two months. Two participants had used inhalants in the past, with only one currently inhaling once a month. For further information on the demographic information collected for participants in the methamphetamine comparison refer to Table 2 attached in Appendix 1.

2.4.3 MDMA versus Placebo

Data included in the MDMA comparison was from a sample of 11 females and 9 males between 18 and 45 years of age. The mean age of the female participants in the MDMA comparison was 25 years (SD = 2.55). The mean age of the male participants was 24.55 years (SD = 2.911). All participants had obtained a tertiary education, and all but eight participants had obtained further education. Most participants were right-handed, with only three participants using their left hand. Twelve participants were smokers and eight non-smokers. On average, all participants reported consuming 1 to 10 standard alcoholic drinks per week or every month. All participants had consumed cannabis in the past, with most participants currently consuming the drug on a monthly or yearly basis. All participants had consumed amphetamines in the past, with most participants currently consuming the drug on a monthly or yearly basis. All participants had consumed MDMA in the past, with most currently consuming the drug on a monthly or yearly basis. All but five participants had consumed cocaine in the past, with most currently consuming the drug every 6 months or longer. Only two
participants had consumed heroin in the past but were not currently consuming the drug. No participants had used inhalants in the past. For further information on the demographic information collected for participants in the MDMA comparison refer to Table 3 attached in Appendix 1.

2.5 Procedure

Previous drug research has indicated that as blood alcohol levels increase, impairment in performance increases (Kim, Yoon, Choi, & Go, 2003). Research has found that a blood alcohol concentration (BAC) level of >.05%, with a target of 0.1% is associated with significant cognitive impairments. The BAC level used in this study was 0.1%, following the ingestion of vodka and orange juice with a dash of peppermint essence. The necessity of this amount of alcohol has been well established by a number of studies that have investigated the effects alcohol has on cognitive functioning (Wiese, Shlipak, & Browner, 2000; Kim et al., 2003; Verster, Duin, Volkerts, Schreuder, & Verbaten, 2003). Participants were required to drink 1.3 grams of alcohol per kg of body weight, approximately 6-8 standard drinks over a three hour period until they reached a BAC level of 0.1%. Water, orange juice and peppermint essence was used as the placebo. Peppermint essence was added to the alcoholic and placebo drinks in order to control for the taste of the liquids as much as possible. The added peppermint essence meant participants were unable to smell if their drink contained the placebo or alcohol. This was confirmed by an initial test trial. The amount of orange juice used meant participants were unable to taste when alcohol was added. Repeated BAC tests were undertaken to ensure each participant had reached the level of 0.1%.

Street amphetamine tablets have been reported to contain between 75 to 125 mg of amphetamine (Cami et al., 2000). Previous drug research has typically used doses of
between 0.10 to 0.40mg/kg of amphetamines, with amphetamine-related effects dose dependant and higher doses producing more significant results (De Wit, Crean, & Richards, 2000; Martinez et al., 1997; Wiegmann, Stanny, McKay, Neri, & McCardie, 1996). The dose of d-methamphetamine used in the current study was 0.42mg/kg, and was selected because this dose is within safe limits. This dose has also been used in other trials that have found a moderate to strong effect on behavioural inhibition (De Wit, Crean, & Richards). Research also suggests a dose at this level is required in order to obtain significant effects for memory in humans (Martinez et al.). Furthermore in pre-pilot trials, a smaller dose led all participants to ‘guess’ that they had not received the drug. The drug was purchased from the pharmaceutical company Lipomed, in Arlesheim, Switzerland and called Desoxyn.

Typical recreational amounts of MDMA have been reported to contain between 50 to 150 mg of MDMA (Cami et al., 2000). Previous drug research has used single doses ranging from 75 to 150 mg (Cami et al.; De La Torre et al., 2000; Farre et al., 2004; Samyn et al., 2002). The dose of MDMA used in the current study was a single dose of 100mg, and was selected because it is within safe limits and is considered to be the typical recreational dose for most individuals (Farre et al.; De La Torre et al.). The drug was also purchased from the pharmaceutical company Lipomed, in Arlesheim, Switzerland.

The Desoxyn or MDMA was encapsulated in a gelatine coating. Flour encapsulated in a gelatine coating was used as the placebo and rendered the tablets visually indistinguishable to the placebo. The Victorian Department of Health Services approved the purchase, store and administration of the substances on schedule eight and nine of the Drug, Poisons and Controlled Substances Act (1981).
2.6 Drug administration procedure

The drug administration procedure varied for the alcohol comparison due to the nature of the drug being administered. For each experimental session in the alcohol comparison a research nurse administered either 30ml of vodka and 230ml of orange juice or 30ml of water and 230ml of orange juice in a different room to the experimenter over a dosing period of three hours. Each participant drank approximately two drinks each hour, with each drink containing about 2 standard drinks. The research nurse monitored participants throughout the experimental session for any adverse effects. Participants were also required to remain at the centre under the supervision of the research nurse for approximately two hours after testing, or until their BAC level was down to 0.05%. A breathalyser was used to monitor the BAC levels at hourly intervals by the research nurse. If after the three hours period, participants had not reached a BAC level of 0.1%, additional alcohol was administered. The breathalyser used was the Lion Alcometer® SD-400 PA, on loan from the Victorian Police, Brunswick office. The instrument was calibrated at the Brunswick office prior to use.

For the methamphetamine and MDMA comparison, a research nurse administered either 0.42mg/kg of Desoxyn, 100mg of MDMA or the placebo to all participants in a different room to the experimenter and remained on-site throughout the entire testing session. A medical doctor was on-call during all sessions to stabilise any participants who experienced adverse effects.

In the alcohol comparison, testing began immediately after the participant had reached a BAC level of 0.1%, as levels of alcohol in the blood begin to decline rapidly at higher doses. Participants were monitored for their BAC level every hour until reaching the 0.1% level and prior to beginning the first experimental tasks. A final
measure was also taken after completing the final task and before arranging transportation home. Participants were required to remain at the research unit for an average of two hours after reaching a BAC level of 0.1%. Previous research has indicated that two hours is the average period of time needed for BAC levels to drop from 0.1% to 0.05% (Verster, Duin, Volkerts, Schreuder, & Verbaten, 2003). Over this period of time the participants’ BAC level dropped significantly and the effects of intoxication were reduced.

Preliminary kinetic studies suggest methamphetamine and MDMA have peak plasma concentrations between 2 to 4 hours and a long range of action between 8 to 13 hours (Angrist, Corwin, Bartlik, & Cooper, 1987; Cook et al., 1992; Kalant, 2001; Nordahl, Salo & Leamon, 2003), therefore testing in the methamphetamine and MDMA comparison began 3 hours post-administration. Blood samples were taken at two separate intervals during the methamphetamine and MDMA testing sessions. All blood samples were collected using a 10ml syringe, by venipuncture from the antecubital vein. The first blood test was taken prior to receiving the drug to provide a baseline level. The second blood test was then taken after 180 minutes had elapsed and prior to the experimental tasks. Blood sampling is a safe method of predicting current methamphetamine and MDMA plasma levels (Cook et al., 1992; Schepers et al., 2003).

Blood samples were first screened for the 7 major drug classes (opiates, amphetamines, benzodiazapines, cannabinoids, barbiturates, cocaine and methadone) and if a drug was detected they were further analysed using the Gas Chromatograph-Mass Spectrometer (GC/MS) method. This determined which drug and the specific level that was present in the sample. GC/MS is considered to be the most accurate means of testing for the presence of drugs in blood (Clarkson, Lesser, & Paul, 1998). If
a baseline blood sample contained drugs, data from that experimental session was excluded from analysis. If levels were detected but were inactive it was not considered a violation of the inclusion criteria.

Participants were not allowed to drive after any of the experimental sessions. Transport was provided in the form of cab vouchers. The investigators informed the taxi company that the customer would be mildly intoxicated with a substance and if required accompanied some of the participants’ home to ensure their safety.

To avoid the subjective effects of expectancy in all comparisons, participants were informed they would be receiving a single oral dose of a stimulant, depressant or placebo during each of the experimental sessions, with both participants and the experimenter blinded. For each session both experimenter and participant were required to make a forced choice guess as to whether the participant had been given the drug or placebo.

During the initial screening and medical checks, all participants in all comparisons completed the NART-R (Revised version, NART-R, Nelson & Willison, 1991), Posttraumatic Stress Diagnostic Scale (PDS; Foa, 1995), Anxiety Sensitivity Index (Reiss, Peterson, Gursky, & McNally, 1986) and the Symptom Checklist-90-R (SCL-90-R; Derogatis, 1994). Attention was paid to any person's indicating they had experienced a trauma, to ensure there were no clinical signs of PTSD. Attention was also paid to any high scores on the SCL-90-R to ensure there was no clinically significant psychological condition that might be worsened by involvement in the study. Participants in the alcohol comparison also completed the Alcohol Use Disorders Identification Test (AUDIT) to ensure they were not currently experiencing an alcohol abuse or dependence disorder (Saunders, Aasland, Babor, De Le Fuente, & Grant,
Demographic information and informed consent forms were also completed during this initial screening session.

2.7 Testing procedure

During the first experimental session after consuming either the placebo or drug, participants were asked to complete the Lexical Decision Task (LDT) in which they indicated whether letter sequences presented on a computer screen formed real or non words. At the end of the task, participants were tested for their immediate memory of the words with a free recall test. Participants were then presented with, and asked to rate on valency and arousal, a selection of pictures from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 1999).

Two weeks later during the second experimental session, immediately after again consuming the placebo or drug, the participants were asked for free-recall of the words they were shown in the original LDT. Participants were then tested on their long-term recognition of the pictures they were shown in the original IAPS Task. Due to the design of the larger drugs and driving study the participants in the methamphetamine and MDMA comparisons were also completing, the drugs were administered prior to the LDT and IAPS memory tasks. The potential confounding effects of this were deemed minimal, because the memory tasks took only 5 minutes to the complete and the drugs would most likely not have been absorbed and producing an effects in such a short amount of time. However, administering the alcoholic drinks prior to conducting the memory tasks was considered to be a more significant confounding effect, with alcohol having a faster rate of action. For this reason the memory tasks were conducted prior to administering any drinks in the alcohol comparison.
After three hours had elapsed, participants were then taken again through the LDT, short-term recall tests and IAPS Task, with new words and pictures, matched for affect valency to those presented in the first session. The word list sets and picture sets were counterbalanced independently of the testing condition both within and between subjects across the two presentation time periods to ensure there were no carry-over effects.

Two weeks later the participants returned a third time to complete the free recall and recognition tasks as in the second session. After all testing had been completed the participants were asked to complete a de-briefing questionnaire and discuss the study with the experimenter. For all comparisons the research nurse did frequent checks of vitals and orientation during the experimental conditions, and prior to sending each participant home. Participants were advised to abstain from driving, operating any machinery or consuming any alcohol or medication for at least twenty-four hours after each of the two experimental sessions. Each session was conducted two weeks apart to ensure that the drug had been completely eliminated from the body prior to the next experimental session. The human research ethics committee of Swinburne University of Technology had approved the procedure. All testing was conducted by a researcher, with experience in drug research and a probationary psychologist. A research assistant with a background in psychology and psychophysiology also assisted in data collection. In addition the supervisor of the study was a registered clinical psychologist who was available to assess and de-brief any participants who experienced an adverse reaction to any of the testing stimuli. Please refer to Figure 2.1 for an overview of the experimental design.
Immediate Recall of LDT words IAPS valence and arousal Ratings.

Two weeks

Long-term Recall of LDT words Recognition of IAPS pictures

Two weeks

Long-term Recall of LDT words Recognition of IAPS pictures

Drug or Placebo
Drug or Placebo (Methamphetamine/MDMA comparison)

Drug or Placebo (Alcohol comparison)

LDT
Immediate Recall of LDT words IAPS valence and arousal Ratings.

Three hours

Condition 1

Condition 2

Figure 2.1 Testing procedure diagram for all three comparisons
2.8 Measures

2.9 The Lexical Decision Task (LDT).

Word lists are a familiar paradigm for assessing learning and several memory studies have found the LDT to be a valid method of inducing an affective state (eg. Hopko et al., 2003; Wikström, Lundh, Westerlund, & Högman, 2004). The word lists used in the current study were taken from the Affective Lexicon of English words, and were approximately matched for word length and frequency of usage in the English language (Bradley & Lang, 1999). Two separate word lists were constructed and randomly presented to participants during either the first or second session in order to account for ordering effects. Each list consisted of 40 real words and 20 non-words. Of the 40 real words presented, ten words were used from four emotional categories: positive, negative, neutral and threat. Examples of the positive words include “laughter” and “champion”. Neutral words included “item” and “basket”. Negative words included “unhappy” and “upset” and threat words included “killer” and “massacre”. The non-words were formed by randomly selecting ten words from each emotion category and changing one vowel in each, this method was adapted in previous research conducted by Foa and colleagues (1991). Examples of the non-words include “koller” and “champium”. Only the real words were used in analyses.

The LDT was presented on a Neuroscan computer using the GENTASK software program (1994). The words and non-words from each emotional category were presented on the computer screen in a random sequence order for a presentation time of three seconds. The words were presented in a white Arial font, size 48 against a black background. The stated objective of the participant’s task was to determine if the
participant could correctly recognise a real word from a non-word. If the letters on the screen formed a real word the participants were instructed to press the left keypad button, labeled “Yes”. If the letters on the screen formed a non-word, the participants were instructed to press the right keypad button, labeled “No”. The participants used both hands to hold the keypad and made responses by pressing alternating buttons with either thumb.

Participants were instructed to respond as quickly as possible. The task took approximately 9 minutes to complete. Time taken to respond to each word type was computed and used as a measure of processing speed. At the end of the task the participants were asked to repeat as many of the real words they had just seen within 60 seconds. The number of words for each words type (positive, negative, neutral and threat) was recorded in two 30 second periods in order to measure the degree of accessibility. Two weeks later and again in the third session participants were again asked to recall the real words they had seen in the initial testing session within 60 seconds. A copy of the word lists is attached in Appendix 2.

2.10 The International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999).

The IAPS is a set of 700 pictures depicting positive, neutral, negative and threat pictures. For each slide a measure of valence and arousal has been normed on the general population (Lang, Bradley, & Cuthbert, 1999). The picture system is the most commonly accepted method for presenting emotionally laden stimuli in order to induce an affective state, and has excellent psychometric properties (Valence $\alpha = 0.94$; Arousal $\alpha = 0.93$). Participants viewed a total of 20 colour pictures containing five pictures from four emotional categories to reflect positive, negative, neutral and threat emotional
stimuli. Two separate picture sets were devised and randomly presented to participants during either the first or second session in order to account for ordering effects (For details of all the pictures chosen for the IAPS Task see Appendix 2).

Examples of the positive pictures include “a sunset” and “ice cream”. Neutral pictures include “towel” and “basket”, negative pictures include “garbage” and “injection”. The threat pictures include “knife” and “a dead body”. Based on the classification systems adopted in previous research, a classification system according to the normative valence and arousal ratings was adopted in order to select pictures from the four emotional categories. Positive pictures were classified as any slides with a normative valence rating between 6.5 and 9 and arousal rating between 4.5 and 5.5. Negative pictures were classified according to a valence rating between 1.5 and 3 and arousal rating between 4 and 5. Neutral pictures were classified according to a valence rating between 4 and 5 and an arousal rating between 1.5 and 3. Threat pictures were classified according to a valence rating between 1.5 and 3 and arousal rating between 5.5 and 8.

In order to ensure picture sets were as similar as possible in the two conditions per subject, the mean and standard deviation valence and arousal ratings for all the pictures included in both sets were tested prior to conducting the research to ensure there were no significant differences between any of the ratings for all the pictures in each set. Furthermore, the content of each of the picture groups were matched to be as similar as possible. The 20 pictures for each list were presented on a computer screen in a random sequence order for a presentation time of 7 seconds. Before each picture was displayed a fixation cross appeared on the screen. This was the signal for participants to look at the screen. Once the picture disappeared from the screen the participants were
then instructed to rate the picture on a nine-point scale for both valence and arousal on a visual rating sheet (See Appendix 2. for a copy of the response sheet). The valence scale is located on the left of the response sheet and the arousal scale on the right. Participants were instructed to put a cross through their chosen ratings for both scales for each picture. High scores on the valence scale indicated a rating of pleasant, while low scores indicated a rating of unpleasant. High scores on the arousal scale indicated the picture induced strong arousal either positive or negative, while low scores indicated no induced arousal. After making their ratings, participants then pressed any button to progress to the next picture. The task took approximately 5 minutes to complete.

In the second and third session, participants were presented with and asked to complete a recognition test for the IAPS images they had seen in the previous session. The test contained two pictures from each emotional category that had been presented in the task completed in the first and second sessions. Equal numbers of distracter pictures from each emotional category, which had not been present in any of the previous sessions, were also included in the recognition test. These distracter items were matched for valence and arousal to the pictures that had been presented in the task. Participants were required to indicate with a “yes” if they recalled the picture or a “no” if they could not remember the picture being presented. Recognition accuracy was determined by calculating the number of pictures correctly recognised for each emotional category. Participants were also required to provide an estimate of their degree of confidence in their decision, providing a percentage estimate.

The recognition test was presented in serial order with pages in a random order. Participants were instructed to complete each page independent of the others. The participants were also instructed that they were not permitted to look forward in the test.
or look back over the test once a page had been completed. This procedure was implemented due to recent research that has found the accuracy and degree of confidence a person has in their recognition of a stimulus is heavily influenced by the presence of several alternative stimuli (Wells & Olsen, 2003). A copy of the instructions presented to participants is attached in Appendix 2.

2.11 Questionnaires

2.11.1 The Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986).

The Anxiety Sensitivity Index, (ASI), is a 16-item self-report questionnaire designed to measure anxiety sensitivity, a tendency to fear the physical and cognitive symptoms of anxiety, due to the belief that such symptoms may be dangerous or harmful (Reiss, Peterson, Gursky, & McNally, 1986). The questionnaire was included due to the possible need to measure and control for the level of anxiety sensitivity in the participants. High levels of anxiety sensitivity in the participants should increase alertness to any stimuli signalling the possibility of becoming anxious, and increase ratings of negative valence for such stimuli (Reiss, Peterson, Gursky, & McNally, 1986). Thus any significant results obtained could be explained both in terms of stimulant induced amygdalic excitation or high levels of anxiety sensitivity (Stewart & Pihl, 1994).

Examples of items included in the questionnaire include “It scares me when I feel faint”. Respondents rated on a five-point Likert scale the extent to which they agreed with each item, ranging from “very little” (coded 0) to “very much” (coded 4). Total scores range from 0 to 64. The ASI has been subject to extensive research and is widely accepted as the most accurate measure of anxiety sensitivity (e.g. Asmundson,
Bonin, Frombach, & Norton, 2000; Nixon & Bryant, 2003; Rodriguez, Bruce, Pagano, Spencer, & Keller, 2004; Sandin, Chorot, & McNally, 2001).

The instrument’s psychometric properties and predictive validity have been well established (α = 0.71 – 0.75; Reiss, Peterson, Gursky, & McNally, 1986). Several exploratory factor analyses of the ASI have been conducted using clinical and non-clinical samples (Taylor, 1995). Three of these studies have obtained a single factor solution, while three obtained four factor solutions. The inconsistencies across these studies may indicate that the ASI factor structure is inherently unstable, or varies across populations. A copy of the questionnaire is attached in Appendix 2.

2.11.2 The National Adult Reading Test (Revised version, NART-R; Nelson & Willison, 1991).

The National Adult reading Test, Revised, (NART-R), is currently the most widely recommended measure of premorbid intelligence (Cerawford, Nelson, Blackmore, Cochrane, & Allan, 1990; Nelson & Willison, 1991). This questionnaire was included in the study for demographic purposes, in addition to IQ possibly being a covariate with outcome. Research has shown that the NART is capable of predicting a substantial proportion of the variance within the normal population; and is largely resistant to neurological or psychiatric disorders and insensitive to age or social status (e.g. Cerawford et al., 1990; Nelson & O’Connell, 1978; O’Carroll et al., 1992; Willshire, Kinsella, & Prior, 1991). Research conducted in Australia, using a modified version of the NART, found high correlations (r = .51**) between NART scores and WAIS-R IQ scores in a large Australian sample (Willshire, Kinsella, & Prior).

Test administration requires the participant to read aloud a list of 50 irregular words such as “chord”, whose correct pronunciation cannot be obtained by applying the
normal grapheme-phoneme rules (Nelson, & O’Connell, 1978; Willshire, Kinsella, & Prior, 1991). The ability to read these irregular words is assumed to measure premorbid intelligence, since they are likely to be read correctly only if the participant is familiar with the word and recognises it in its written form (Nelson, & O’Connell; Willshire, Kinsella, & Prior). The responses given by participants are scored separately as correct or incorrect according to their pronunciation. The WAIS Full scale, Verbal and Performance IQ’s are estimated from the number of errors made by the respondent (Nelson & Willison).

The NART-R is quickly and easily administered and research supports its validity in estimating IQ across time (Berry et al., 1994; Bright, Jaldow, & Kopelman, 2002). The NART has demonstrated excellent reliability ($\alpha = 0.90-0.93$) with a high degree of inter-rater reliability on scoring (eg. Crawford et al., 1989; Crawford, Parker, Stewart, Besson, & De Lacey, 1989; O’Carroll, 1987; Nelson & Willison, 1991). Test-retest reliability across a 10-day period has also demonstrated excellent reliability ($\alpha = 0.98$; Crawford et al.). A copy of the NART-R is attached in Appendix 2.

2.11.3 The Posttraumatic Stress Diagnostic Scale (PDS; Foa, 1995).

The Posttraumatic Stress Diagnostic Scale, (PDS), is a 49-item self-report measure, designed to provide a PTSD diagnosis and information on the frequency and severity of PTSD symptoms (Foa, 1995). The diagnosis derived from the PDS was used for screening purposes to ensure no participant was currently experiencing clinically significant symptoms of PTSD. The measure was also used as a covariate to control for participants who had experienced a trauma in the past.

The structure and content of the questionnaire mirrors the DSM-IV diagnostic criteria for PTSD and is suitable for respondents aged 18 to 65 years. The PDS has
demonstrated good psychometric properties with a high level of internal consistency (.92 Total symptom severity, .78 Re-experiencing, .84 Avoidance, .84 Arousal). The PDS has good test-retest reliability, with a kappa of .74 obtained using a retest sample of 110 participants, with an 87% agreement between diagnoses at two time points. Satisfactory test-retest reliabilities for the four cluster scores have also been obtained (.83 Total symptom severity, .77 Re-experiencing, .81 Avoidance, .85 Arousal). The PDS has shown a high level of diagnostic agreement, sensitivity and specificity with the Structured Clinical Interview for the DSM-III-R (SCID), with a kappa of .65 and 82% agreement between the two measures (Foa, Cashman, Jaycox, & Perry, 1997).

The questionnaire requires participants to first indicate the type of traumatic event experienced, then describe when it occurred and answer questions regarding injuries and emotional difficulties experienced (Foa, 1995). The participant then rates items assessing post-traumatic difficulties such as intrusive thoughts and pictures on a scale from 0 (not at all or only one time) to 3 (5 or more times a week/almost always). The symptom severity scores range from 0 to 51, with higher scores indicating a greater degree of symptomatology. Finally participants answer in a yes/no format whether the trauma has interfered with various activities such as work and relationships. A copy is attached in Appendix 2.

2.11.4 The Symptom Checklist – 90-Revised (SCL-90-R; Derogatis, 1992).

The SCL-90-R is a 90 item, multi-dimensional, self-report measure of psychiatric symptoms. The checklist is used to assess for the presence of psychiatric symptoms, and provides a summary of the respondent’s current psychological functioning. The measure was used for screening purposes to ensure no participants were currently experiencing any significant psychiatric disturbance. The Global Scale of
Distress was used for the primary measure due to the nature and stability of the construct. The measure provides scores on nine primary symptom dimensions in addition to three global indices of distress. The measure was designed to reflect psychological symptom patterns from community, medical and psychiatric populations. The measure has been widely used in research investigating emotional reactions to traumatic events, and can be used for an initial assessment of clinical status or as an outcome measure following therapeutic treatments (Baum, Gatchel, & Schaeffer, 1983).

The nine primary symptom dimensions include Somatisation, Obsessive-compulsive, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. The three global index measures include a Global Severity Index, Positive Symptom Distress Index and Positive Symptom Total Index. Respondents are asked to rate how much distress a particular symptom or problem has caused them over the past week, for example “awakening at night.” Respondents rate their level of distress on a scale of 1 to 4 ranging from “Not At All” to “Extremely”. Scores are calculated according to the nine dimensions and three indices.

All symptom dimensions on the SCL-90-R have demonstrated good internal consistency (Horowitz, Rosenberg, Baer, Ureno, & Villasenor, 1988). Using a data set of 209 symptomatic volunteers and 103 psychiatric outpatients, one study found internal consistency coefficients ranging from .77 for the Psychoticism dimension to .90 for the Depression dimension. The SCL-90-R has also demonstrated good test-retest reliability across the nine symptom dimensions. In a population of 94 psychiatric outpatients, test-retest coefficients ranged from .80 to .90.

The SCL-90-R has good criterion and construct validity, with analyses indicating the empirical results match the theoretical structure on most dimensions, with
slight overlaps between the Anxiety and Anxiety Phobic dimensions, and splitting between items on the Psychoticism dimensions (Derogatis & Cleary, 1977). The SCL-90-R has been moderately correlated (.42) with scores on the MMPI, and has also demonstrated good convergent and discrimination validity when compared to other measures such as The Middle Hospital Questionnaire (Crown & Crisp, 1979; Derogatis, Rickels, & Rock, 1979). The Depression scale of the SCL-90-R has been shown to correlate strongly with the Beck Depression Inventory and the Asberg Rating Scale (Peveler & Fairburn, 1990). A copy is attached in Appendix 2.

2.11.5 Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, De Le Fuente, & Grant, 1993).

The Alcohol Use Disorders Identification Test (AUDIT) is a brief screening questionnaire developed for the World Health Organisation (WHO) for the early detection of hazardous and harmful alcohol consumption in health care settings (Saunders, Aasland, Babor, De Le Fuente, & Grant, 1993). This questionnaire was used for screening purposes in the current study, to ensure the participants had experience in drinking 5 or more standard alcoholic drinks on a single occasion and to ensure no participant was suffering from alcohol dependence. These requirements meant that participants were not necessarily excluded if they reached the cut-off score of 8. However the answers to items 4 to 10 were examined to ensure there was no evidence of alcohol dependence.

The AUDIT has been employed across a wide range of countries, including Australia and New Zealand and in various community and clinical populations (see for example; Banwell, O’Brien, Hamilton, & Attewell, 1999; Cherpitel & Clark, 1995; Hulse, Saunders, Roydhouse, Stockwell, & Basso, 2000; Lennings et al., 1997; Seppa,
Makela, & Sillanaukee, 1995). The questionnaire has been used in age groups ranging from university students to the elderly (see for example; Aertgeerts et al., 2000; Powell & McInness, 1994). The questionnaire is reported to be the most accurate screening questionnaire for detecting alcohol abuse and dependence and has been employed in more than 100 research papers (Degenhardt, Conigrave, Wutzke, & Saunders, 2001).

There are 10 items in the AUDIT (Saunders, Aasland, Babor, De Le Fuente, & Grant, 1993). Questions 1 to 3 inquire about the quality and frequency of alcohol consumption, for example “How often do you have a drink containing alcohol?” Questions 4 to 6 inquire about possible symptoms of dependence, for example “How often during the last six months have you needed a first drink in the morning to get yourself going after a heavy drinking session?” Questions 7 to 10 inquire about the presence of alcohol-related problems, for example “Have you or someone else been injured as a result of your drinking?” Each item response is scored from 0 to 4, from left to right across the page. The last two items with only three responses are scored 0, 2, or 4. Possible scores range from 0 to 40, with the cumulative cut-off score $\geq 8$ for men and women.

The sensitivity of the AUDIT has been reported to range from 85% to 92% in most studies, using the recommended cut-off of 8 and the current version of the ICD and DSM Substance use disorders criteria (Cherpiel & Clark, 1995; Saunders, Aasland, Babor, De Le Fuente, & Grant, 1993; Steppa, Makela, & Sillanaukee, 1995). The questionnaire has demonstrated an overall specificity of 94%. There is some research that suggests the AUDIT may be less sensitive in women than men, however this finding has not yet been replicated (Cherpitel, 1995). All items on the questionnaire
have shown high intra-scale reliability ranging from 0.93 to 0.81, with relatively little variability across countries (Saunders et al.).

A copy of the questionnaire is attached in Appendix 2.

2.11.6 Demographics and Medical Questionnaires

Demographic information including age, gender, and education level, employment status, handedness, height and weight and current health status was obtained with two brief questionnaires (see Appendix 2).

2.11.7 Drug Use History and De-briefing Questionnaires

The drug use questionnaire was a self-administered questionnaire that collected information regarding past and current drug use patterns across various drug types. The drug types included tobacco, caffeine, alcohol, cannabis, MDMA (ecstasy), cocaine, amphetamines, heroin and inhalants (See Appendix 2). The de-briefing questionnaire was administered at the end of the study (See Appendix 2).

2.12 Data Analysis

For the purposes of the current thesis, specific analyses were conducted to examine the effect the drug condition had upon threat stimuli. Overall results across all stimuli types and for neutral stimuli was also examined to use as reference to determine if the effect was specific for threat stimuli. If significant results were obtained for general or neutral processing and threat stimuli, the analyses were repeated controlling for threat. Positive, negative and neutral stimuli were not examined in the current thesis. These variables were included in all tasks in order to remain consistent with past methodologies and to address hypotheses outside the current thesis, such as reward processing.
Hypothesis testing involved a series of repeated measure ANOVA’s. In order to examine the possible confounding effect of covariates, difference scores were calculated and scatter plots conducted with all covariates. If initial examination determined a relationship between the difference scores and the covariates, then analyses were repeated while controlling for the covariate. It was decided not to transform any of the skewed variables as ANOVA is relatively robust to violations of normality when sample sizes are equal and skewness rather than outliers cause the non-normality (Tabachnick & Fidell, 2007). All the variables with skewed data were transformed, with all the analyses reported repeated. However, analyses of the transformed data did not differ to the results reported and it was decided not to transform the data.

The multivariate statistic Wilk’s Lambda was reported. An alpha level of 0.05 was decided upon and when reporting significant results, estimated power level ($P$), in addition to Hedge’s $\hat{g}$ effect size were included. Hedge’s $\hat{g}$ was used as it accounts for unequal and small sample sizes (Devilly, 2004). Effect sizes have been reported for significant and non-significant results in order to account for the small sample sizes and to allow for inspection of power. Power was also reported separately to facilitate interpretation of results. A Bonferroni correction was not applied to the data for multiple reasons. First, the study used single measures within each domain, e.g. short-term recall for short-term memory, rather than multiple measures within each domain. Secondly, this was an exploratory study and the first of its kind. Therefore there were no hypotheses to replicate but rather hypotheses to test. If a Bonferroni correction had been applied to the data, it is highly likely that Type II error would have been sacrificed for Type I error. This was the first time a controlled trial had attempted to administer CNS stimulants and depressants to determine the effect they have on emotional processing.
and memory. All non-controlled research studies have found at least a moderate effect for suppressants and stimulants on later trauma processing (Zatzick et al., 2002). Therefore, we estimated that in a controlled environment with regulated doses of drugs, we would obtain a moderate to large effect between the experimental and placebo conditions for each of the three drug types. With a sample size of 20 participants for each drug condition and alpha set at 0.05, and assuming an effect size of 0.65, we would derive a power of 0.8. The within subjects power would be much higher.

CHAPTER 3: RESULTS

3.1 Alcohol versus placebo comparison

3.2 Data screening

There were 20 cases included in the analysis. Data was analysed using the Statistical Package for the Social Sciences (SPSS) version 16.0. Data screening revealed two missing values in the IAPS delayed recognition test results. It was decided that these missing values would be replaced with the group mean for that picture for participants in the same condition. Ten implausible values were identified in the LDT reaction time results and were the result of mechanical error in the button recognition feature of the LDT. All implausible values were replaced with the group mean for that word for participants in the same condition. Table 1 contains the means and standard deviations for all tasks across all picture and word types in the alcohol versus placebo comparison. The results for all stimuli were presented for completeness and so the reader could compare responses for emotive versus non-emotive stimuli. This was also consistent with past methodologies (see for example DePrice & Freyd, 2001; Devilly et al., 2007).
<table>
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<th>Independent Variable</th>
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<th>M</th>
<th>SD</th>
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</table>

Note: For Affective Picture Task Valence, 9 = Positive, 1 = Negative, Arousal, 1 = Low, 9 =High.
For IAPS Recognition Accuracy, 1 = Correct, 2 = Incorrect.
3.3 Testing of assumptions

Prior to hypothesis testing the assumptions underlying analysis of variance (ANOVA) were examined. All observations were independent of each other and tests of normality were conducted for all variables. Results of normality tests are presented below. Histograms and Q-Q plots for all variables are contained in Appendix 3.

3.4 Affective Reactions

All variables derived from the IAPS Task were normally distributed, except for arousal of neutral pictures in the alcohol condition, which was negatively skewed (Skewness = -0.04, Standard Error = 0.51). Valence of neutral pictures in the alcohol condition was negatively skewed (Skewness = -1.02, Standard Error = 0.51) and positively skewed in the placebo condition (Skewness = 2.35, Standard Error = 0.51).

3.5 Memory

Overall accuracy and confidence ratings for their responses to all items for the IAPS delayed recognition test were normally distributed. Recognition accuracy for threat pictures was positively skewed in the alcohol (Skewness = 0.33, Standard Error = 0.51) and placebo condition (Skewness = 0.59, Standard Error = 0.51). Recognition confidence ratings for threat pictures was normally distributed in the alcohol condition, but negatively skewed in the placebo condition (Skewness = -1.67, Standard Error = 0.51). Recognition accuracy for neutral pictures was positively skewed for the alcohol (Skewness = 0.40, Standard Error = 0.51), and placebo condition (Skewness = 0.50, Standard Error = 0.51). Recognition confidence ratings for the neutral pictures were normally distributed.
Overall Short-term recall in the alcohol and placebo condition was normally distributed. Short-term recall for threat words in the alcohol condition was normally distributed, and positively skewed in the placebo condition (Skewness = 0.25, Standard Error = 0.51). Short-term recall for neutral words was positively skewed in the alcohol condition (Skewness = 1.67, Standard Error = 0.51), and the placebo condition (Skewness = 0.21, Standard Error = 0.51).

Overall Short-term recall for the first 30-second epoch in the alcohol and placebo condition was normally distributed. Overall Short-term recall for the second 30-second epoch was positively skewed in the alcohol (Skewness = 1.20, Standard Error = 0.51) and the placebo condition (Skewness = 0.55, Standard Error = 0.51). Short-term recall for the first 30-second epoch for threat words in the alcohol and placebo condition was normally distributed. Short-term recall for the second 30-second epoch for threat words was positively skewed in the alcohol (Skewness = 2.12, Standard Error = 0.51) and placebo condition (Skewness = 1.62, Standard Error = 0.51). Short-term recall for the first 30-second epoch for neutral words was positively skewed for the alcohol (Skewness = 1.82, Standard Error = 0.51) and placebo condition (Skewness = 0.51, Standard Error = 0.51). Short-term recall for the second 30-second epoch for neutral words was positively skewed for the alcohol (Skewness = 4.47, Standard Error = 0.51) and placebo condition (Skewness = 1.62, Standard Error = 0.51).

Overall long-term recall was normally distributed in the placebo condition, but positively skewed in the alcohol condition (Skewness = 2.39, Standard Error = 0.51). Long-term recall for threat words in the placebo condition was normally distributed, but positively skewed in the alcohol condition (Skewness = 1.93, Standard Error = 0.51). Long-term recall for neutral words was positively skewed in the alcohol condition
(Skewness = 4.47, Standard Error = 0.51) and the placebo condition (Skewness = 3.44, Standard Error = 0.51).

3.6 Processing

All variables in the LDT were normally distributed.

3.7 Covariates

Seventeen of the participants had never experienced a trauma, with two of the individuals who had experienced a trauma currently experiencing mild distress and one individual currently experiencing moderate distress. Based on the diagnosis and symptom description obtained from the PTDS, no participant was currently experiencing a level of distress that would exclude them from the analysis. Due to the unequal numbers of individuals who had experienced a trauma, this variable was not included in analyses. Scores on the Symptom Checklist 90-R indicated no psychiatric symptoms in any of the participants, with a very low or absent level of global distress. This variable was therefore not included in the analysis. Anxiety sensitivity index scores and estimated IQ scores remained in the analysis and normality testing indicated they were both normally distributed.

3.8 Hypothesis testing

3.9 Affective reactions

A one-way repeated measures ANOVA, with condition (alcohol or placebo) as the within subjects variable was conducted to examine the effect alcohol had on valence and arousal ratings to threat pictures. Means and 95% confidence intervals for the IAPS Task valence and arousal ratings for the alcohol and placebo conditions are displayed in Figures 3.2 and 3.3.
Figure 3.2. IAPS Task mean valence ratings for threat pictures. Error bars indicate upper bounds of the 95% confidence intervals above the means.

Figure 3.3. IAPS Task mean arousal ratings for threat pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was no significant difference between alcohol and placebo conditions for overall valence ratings to the IAPS Task ($F(1, 19) = 1.09, p = 0.31, P = 0.17, \text{Hedge's } \hat{g} = -0.29, 95\% \text{ confidence: -0.91, 0.33}$). There was also no significant difference between alcohol and placebo conditions for overall arousal ratings to the IAPS Task ($F(1, 19) = 1.02, p = 0.33, P = 0.16, \text{Hedge's } \hat{g} = -0.26, 95\% \text{ confidence: -0.88, 0.36}$).
In contrast to expectations, there was no significant difference between alcohol and placebo conditions for valence ratings to threat pictures \((F(1, 19) = 0.54, p = 0.47, P = 0.11, \text{Hedge’s } \hat{g} = -1.20, 95\% \text{ confidence: } -0.83, 0.42)\). As hypothesised, there was a significant difference between alcohol and placebo conditions for arousal rating to threat pictures \((F(1, 19) = 6.51, p < .05, P = 0.68, \text{Hedge’s } \hat{g} = -0.63, 95\% \text{ confidence: } -1.26, 0.01)\). As expected, participants made lower arousal ratings of threat pictures in the alcohol condition (See Figure 3). Confirming that these findings occurred exclusively for threat pictures, there was no significant difference between alcohol and placebo conditions for arousal rating to neutral pictures \((F(1, 19) = 0.01, p = 0.93, P = 0.05, \text{Hedge’s } \hat{g} = 1.50, 95\% \text{ confidence: } 0.79, 2.20)\). See Figure 3.4 for a comparison of mean arousal ratings to threat and neutral pictures for the alcohol and placebo condition.

![Figure 3.4. IAPS Task mean Arousal ratings for threat and neutral pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.](image-url)
3.10 Memory

3.11 IAPS Task recognition performance

A one-way repeated measures ANOVA with condition (alcohol and placebo) as the within subjects variable was conducted to examine the effect alcohol had on accuracy and confidence ratings on the recognition test for threat pictures. Means and 95% confidence intervals for recognition accuracy and confidence ratings for the alcohol and placebo conditions are displayed in Figures 3.5 and 3.6.

Figure 3.5. Mean recognition accuracy for threat pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.
Figure 3.6. Mean recognition ratings of confidence for threat picture. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was no significant difference between alcohol and placebo conditions for overall recognition accuracy ($F(1, 19) = 0.07, p = 0.80, P = 0.06, \text{Hedge’s } \hat{g} = 0.13, 95\% \text{ confidence: } -0.49, 0.75$). There was also no significant difference between alcohol and placebo conditions for overall confidence ratings ($F(1, 19) = 0.01, p = 0.94, P = 0.05, \text{Hedge’s } \hat{g} = -0.02, 95\% \text{ confidence: } -0.63, 0.60$). Contrary to predictions, there were no significant differences between alcohol and placebo conditions for recognition accuracy to threat pictures ($F(1, 19) = 0.11, p = 0.75, P = 0.06, \text{Hedge’s } \hat{g} = -0.15, 95\% \text{ confidence: } -0.77, 0.47$)(See Figure 3.5). There were also no significant differences between alcohol and placebo conditions for ratings of confidence to threat pictures ($F(1, 19) = 0.57, p = 0.46, P = 0.11, \text{Hedge’s } \hat{g} = -0.21, 95\% \text{ confidence: } -0.83, 0.41$) (See Figure 3.6).

3.12 LDT recall performance

A one-way repeated measures ANOVA, with condition (alcohol and placebo) as the within subjects variable was conducted to examine the effect alcohol had on short-term and long-term recall rates for the threat words in the LDT. Means and 95%
confidence intervals for short-term rates for the alcohol and placebo conditions are presented in Figure 3.7.

![Figure 3.7](image_url)

*Figure 3.7. LDT mean short-term recall for threat words. Error bars indicate the upper bounds of the 95% confidence intervals above the means.*

There was a significant difference between the alcohol and placebo conditions for overall short-term recall ($F(1, 19) = 12.93, p < .05, P = 0.93, \text{Hedge's } \hat{g} = -1.02, 95\% \text{ confidence: } -1.68, -0.36$). As would be expected participants recalled significantly more words overall in the placebo condition (see Table 3.1). Contrary to expectations, there was no significant difference between alcohol and placebo conditions in short-term recall rates for threat words ($F(1, 19) = 4.22, p = 0.54, P = .50, \text{Hedge’s } \hat{g} = -0.72, 95\% \text{ confidence: } -1.36, -0.08$).

Data collection for short-term recall involved recording the number of words recalled for each 30-second epoch in order to measure the degree of accessibility. A one-way repeated measures ANOVA, with condition (alcohol and placebo) as the within subjects variable was conducted to examine the effect alcohol had on short-term recall rates for the threat words in the first 30-second epoch. Means and 95% confidence
intervals for short-term recall rates for threat words in the alcohol and placebo conditions in the first 30-second epoch are presented in Figure 3.8.

![Figure 3.8](image)

Figure 3.8. LDT mean short-term recall for threat words in the first 30-second epoch. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was a significant difference between alcohol and placebo conditions for overall short-term recall for the first 30-second epoch \((F(1, 19) = 14.50, p < .05, \eta^2 = 0.95, \text{Hedge's } \hat{g} = -1.07, \text{95% confidence: -1.74, -0.41})\). Participants recalled significantly more words overall in the placebo condition for the first 30-second epoch (see Table 3.1). There was also a significant difference between alcohol and placebo conditions for short-term recall of the threat words in the first 30-second epoch \((F(1, 19) = 4.97, p < .05, \eta^2 = 0.56, \text{Hedge's } \hat{g} = -0.76, \text{95% confidence: -1.41, 0.12})\). Participants recalled significantly more threat words in the placebo condition for the first 30-second epoch (See Figure 3.8). This is in contrast to the recall of neutral words, where no significant difference was evident between conditions for the first 30-second epoch \((F(1, 19) = 2.95, p = 0.10, \eta^2 = 0.37, \text{Hedge's } \hat{g} = -0.52, \text{95% confidence: -1.15, 0.11})\). For a comparison of mean short-term recall rates in the first 30-second epoch for the threat and neutral words in the alcohol and placebo condition see Figure 3.9.
A one-way repeated measures ANOVA, with condition (alcohol and placebo) as the within subjects variable was conducted to examine the effect alcohol had on short-term recall rates for the threat words in the second 30-second epoch. Means and 95% confidence intervals for short-term recall rates for threat words in the alcohol and placebo conditions in the second 30-second epoch are presented in Figure 3.10.

There was no significant difference between alcohol and placebo conditions for overall short-term recall for the second 30-second epoch ($F(1, 19) = 0.79, p = 0.39, P =$
0.14, Hedge’s $\hat{g} = -0.26$, 95% confidence: -0.89, 0.36). There was also no significant
difference between alcohol and placebo conditions for the short-term recall of threat
words in the second 30-second epoch ($F(1, 19) = 0.19$, $p = 0.67$, $P = 0.07$, Hedge’s $\hat{g} =$
-0.13, 95% confidence: -0.75, 0.49).

A one-way repeated measures ANOVA, with condition (alcohol and placebo) as
the within subjects variable was conducted to examine the effect alcohol had on long-
term recall rates for the threat words in the LDT. Means and 95% confidence intervals
for long-term recall rates for the alcohol and placebo conditions are presented in Figure
3.11.

![Figure 3.11](image.png)

**Figure 3.11.** LDT mean long-term recall for threat words. Error bars indicate the upper bounds of the 95% confidence intervals
above the means.

There was a significant difference between alcohol and placebo conditions for
overall long-term recall ($F(1, 19) = 14.41$, $p < .05$, $P = 0.95$, Hedges $\hat{g} = -0.91$, 95%
confidence: -1.57 , -0.26). As would be expected participants recalled more words
overall from the placebo condition (See Table 3.1). As predicted, there was also a
significant difference between alcohol and placebo condition for long-term recall of
threat stimuli \((F(1, 19) = 7.60, p < .05, P = 0.74, \text{Hedge's } \hat{g} = -0.91, 95\% \text{ confidence: -1.56, -0.26})\). As expected, participants recalled more threat words from the placebo condition (See Figure 3.11). This is in contrast to the recall of neutral words, where no significant difference was evident between conditions \((F(1, 19) = 2.22, p = 0.16, P = 0.28, \text{Hedge's } \hat{g} = -0.26, 95\% \text{ confidence: -0.88, 0.36})\). For a comparison of long-term recall rates for threat and neutral words in the alcohol and placebo condition see Figure 3.12.

![Figure 3.12. LDT mean long-term recall for threat and neutral words. Error bars indicate the upper bounds of the 95% confidence intervals above the means.](image)

### 3.13 Processing

A one-way repeated measures ANOVA, with condition (alcohol and placebo) as the within subjects variable was conducted to examine the effect alcohol had on reaction times to the threat words presented in the LDT. Means and 95% confidence intervals for reaction times in the alcohol and placebo conditions are presented in Figure 3.13.
There was no significant difference between alcohol and placebo conditions for overall reaction times \((F(1, 19) = 1.05, p = 0.32, P = 0.16, \text{Hedge’s } \hat{g} = -0.24, 95\% \text{ confidence: -0.86, 0.38})\). There was also no significant difference between alcohol and placebo conditions for reaction times to threat words \((F(1, 19) = 0.88, p = 0.36, P = 0.15, \text{Hedge’s } \hat{g} = -0.24, 95\% \text{ confidence: -0.87, 0.38})\).

3.14 Covariates

3.15 Estimated IQ and anxiety sensitivity

In order to determine whether estimated IQ and anxiety sensitivity co-varied with condition for any of the results, difference scores from placebo to the alcohol condition for each variable were calculated for each participant. Difference scores were calculated in order to determine if the differences between conditions were due to the experimental condition or the covariates. Scores on the Symptom Checklist 90-R indicated no psychiatric symptoms in any of the participants, with a very low or absent level of global distress. This variable was therefore not included in the analysis. Additionally only three participants had experienced a trauma and were currently
experiencing mild post-trauma symptoms. Therefore because of the unequal numbers this variable was also excluded from the analysis. The mean and standard deviation difference scores from placebo to alcohol for all participants in the IAPS Task, Recognition Task and LDT are summarised in Table 3.2.

Table 3.2
*Means and standard deviation difference scores from placebo to alcohol for threat words and pictures*

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAPS Task Valence ratings</td>
<td>0.19</td>
<td>1.16</td>
</tr>
<tr>
<td>IAPS Task Arousal ratings</td>
<td>1.08</td>
<td>1.89</td>
</tr>
<tr>
<td>Recognition Accuracy</td>
<td>0.02</td>
<td>0.27</td>
</tr>
<tr>
<td>Recognition Ratings of Confidence</td>
<td>3.46</td>
<td>20.47</td>
</tr>
<tr>
<td>LDT Short-term recall</td>
<td>1.00</td>
<td>2.18</td>
</tr>
<tr>
<td>First 30-second epoch</td>
<td>0.95</td>
<td>1.91</td>
</tr>
<tr>
<td>Second 30-second epoch</td>
<td>-0.05</td>
<td>0.51</td>
</tr>
<tr>
<td>LDT Long-term recall</td>
<td>1.00</td>
<td>1.62</td>
</tr>
<tr>
<td>LDT Reaction times</td>
<td>0.07</td>
<td>0.32</td>
</tr>
</tbody>
</table>

N = 20

Note: For IAPS Task Valence, 9 = Positive, 1 = Negative, Arousal, 1 = Low, 9 =High. For IAPS Task Accuracy, 1 = Correct, 2 = Incorrect. A negative number means the participant’s score increased in the alcohol condition. A positive number means the participant’s score decreased in the alcohol condition.

The average estimated IQ score was 115.75 (SD = 3.70), with a range from 109 to 124. The average anxiety sensitivity score was 11.75 (SD = 6.74), with a range from 1 to 27. In order to identify possible covariates, correlations were conducted between the
difference scores and estimated IQ and anxiety sensitivity. For each correlation, scatterplots for each dependent variable and covariate were conducted for males and females separately. This was conducted because research suggests alcohol influences males and females differently (Van Tilburg & Vingerhoets, 2002). For an examination of correlations for all relevant variables please refer to Appendix 4. For the purposes of the current thesis, a significant correlation was needed to be included in further analyses. There were no significant correlations between any of the dependent variables or covariates.

3.16 Methamphetamine versus placebo comparison

3.17 Data screening

Analysis in the methamphetamine comparison employed the same statistical procedure as for the alcohol comparison. Details will not be repeated in this section. There were 21 cases included in the analysis. Data screening revealed nine missing values in the IAPS delayed recognition test results. It was decided that these missing values would be replaced with the group mean for that picture for participants in the same condition. Four implausible values were identified in the LDT reaction time results. All implausible values were replaced with the group mean for that word for participants in the same condition. Table 3.3 contains the results for all tasks across all picture and word types in the methamphetamine versus placebo comparison.
<table>
<thead>
<tr>
<th>Test</th>
<th>Independent Variable</th>
<th>Condition</th>
<th>Positive</th>
<th>Negative</th>
<th>Neutral</th>
<th>Threat</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAPS Valence ratings</td>
<td>Methamphetamine</td>
<td>7.19</td>
<td>2.96</td>
<td>5.12</td>
<td>2.59</td>
<td>4.47</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>7.15</td>
<td>3.05</td>
<td>5.00</td>
<td>2.49</td>
<td>4.42</td>
</tr>
<tr>
<td>Arousal ratings</td>
<td>Methamphetamine</td>
<td>3.53</td>
<td>4.50</td>
<td>2.35</td>
<td>6.09</td>
<td>4.12</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>4.10</td>
<td>4.78</td>
<td>2.50</td>
<td>6.06</td>
<td>4.36</td>
</tr>
<tr>
<td>Delayed Recognition Accuracy</td>
<td>Methamphetamine</td>
<td>1.18</td>
<td>1.11</td>
<td>1.24</td>
<td>1.07</td>
<td>1.15</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>1.19</td>
<td>1.26</td>
<td>1.36</td>
<td>1.10</td>
<td>1.23</td>
</tr>
<tr>
<td>Delayed Recognition Ratings of Confidence</td>
<td>Methamphetamine</td>
<td>81.37</td>
<td>81.29</td>
<td>75.21</td>
<td>83.98</td>
<td>80.46</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>72.37</td>
<td>73.73</td>
<td>66.19</td>
<td>82.54</td>
<td>73.71</td>
</tr>
<tr>
<td>LDT Immediate recall</td>
<td>Methamphetamine</td>
<td>1.67</td>
<td>1.33</td>
<td>1.00</td>
<td>2.57</td>
<td>1.64</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>3.00</td>
<td>2.00</td>
<td>2.00</td>
<td>2.90</td>
<td>2.48</td>
</tr>
<tr>
<td>First 30-second epoch</td>
<td>Methamphetamine</td>
<td>1.57</td>
<td>0.71</td>
<td>0.86</td>
<td>2.14</td>
<td>1.32</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>2.38</td>
<td>1.71</td>
<td>1.76</td>
<td>2.57</td>
<td>2.11</td>
</tr>
<tr>
<td>Second 30-second epoch</td>
<td>Methamphetamine</td>
<td>0.10</td>
<td>0.62</td>
<td>0.14</td>
<td>0.43</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>0.62</td>
<td>0.29</td>
<td>0.24</td>
<td>0.43</td>
<td>0.32</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>Methamphetamine</td>
<td>0.29</td>
<td>0.24</td>
<td>0.29</td>
<td>1.38</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>0.62</td>
<td>0.14</td>
<td>0.67</td>
<td>0.93</td>
<td>0.48</td>
</tr>
<tr>
<td>Reaction times</td>
<td>Methamphetamine</td>
<td>1.02</td>
<td>0.31</td>
<td>0.89</td>
<td>0.94</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>0.92</td>
<td>0.21</td>
<td>0.95</td>
<td>0.23</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Note: For Affective Picture Task Valence, 9 = Positive, 1 = Negative, Arousal, 1 = Low, 9 = High.
For IAPS Recognition Accuracy, 1 = Correct, 2 = Incorrect.
3.18 Testing of assumptions

Prior to hypothesis testing the assumptions underlying analysis of variance (ANOVA) were examined. All observations were independent of each other and tests of normality were conducted for all variables. Results of normality tests are presented below. Histograms and Q-Q plots for all variables are contained in Appendix 3.

3.19 Affective reactions

Valence of neutral pictures in the methamphetamine condition was positively skewed (Skewness = 0.37, Standard Error = 0.50) and negatively skewed in the placebo condition (Skewness = -0.23, Standard Error = 0.50). Arousal of neutral pictures was positively skewed in the methamphetamine (Skewness = 0.46, Standard Error = 0.50) and placebo condition (Skewness = 0.86, Standard Error = 0.50). All remaining variables were normally distributed.

3.20 Memory

Overall accuracy in the methamphetamine condition was positively skewed (Skewness = 0.72, Standard Error = 0.50) and normally distributed in the placebo condition. Overall confidence ratings were negatively skewed in the methamphetamine (Standard Error = -1.35, Standard Error = 0.50) and placebo condition (Standard Error = -1.20, Standard Error = 0.50). Recognition accuracy for threat pictures was positively skewed in the methamphetamine (Skewness = 1.92, Standard Error = 0.50) and placebo condition (Skewness = 1.69, Standard Error = 0.50). Recognition confidence ratings for threat pictures was negatively skewed in the methamphetamine (Skewness = -1.18, Standard Error = 0.50), and placebo condition (Skewness = -1.83, Standard Error = 0.50). Recognition accuracy for neutral pictures was positively skewed in the
methamphetamine condition (Skewness = 0.61, Standard Error = 0.50), and negatively skewed in the placebo condition (Skewness = -0.93, Standard Error = 0.50). Recognition confidence ratings for the neutral pictures were normally distributed.

Overall Short-term recall was normally distributed. Short-term recall for threat words in the methamphetamine condition was positively skewed (Skewness = 0.31, Standard Error = 0.50), and negatively skewed in the placebo condition (Skewness = -0.50, Standard Error = 0.50). Short-term recall for neutral words was positively skewed in the methamphetamine condition (Skewness = 1.80, Standard Error = 0.51), and normally distributed in the placebo condition.

Overall Short-term recall for the first 30-second epoch in the methamphetamine and placebo condition was normally distributed. Overall Short-term recall for the second 30-second epoch was positively skewed in the methamphetamine (Skewness = 0.53, Standard Error = 0.50) and the placebo condition (Skewness = 0.24, Standard Error = 0.50). Short-term recall for the first 30-second epoch for threat words was negatively skewed in the methamphetamine (Skewness = -0.16, Standard Error = 0.50) and placebo condition (Skewness = -0.17, Standard Error = 0.50). Short-term recall for the second 30-second epoch for threat words was positively skewed in the methamphetamine (Skewness = 1.46, Standard Error = 0.50) and placebo condition (Skewness =1.85, Standard Error = 0.50). Short-term recall for the first 30-second epoch for neutral words was positively skewed for the methamphetamine condition (Skewness = 1.53, Standard Error = 0.50) and normally distributed in the placebo condition. Short-term recall for the second 30-second epoch for neutral words was positively skewed for the methamphetamine (Skewness = 3.53, Standard Error = 0.50) and placebo condition (Skewness = 2.32, Standard Error = 0.50).
Overall Long-term recall was positively skewed in the methamphetamine (Skewness = 0.69, Standard Error = 0.50) and placebo condition (Skewness = 1.03, Standard Error = 0.50). Long-term recall for threat words was positively skewed in the methamphetamine (Skewness = 0.14, Standard Error = 0.50) and placebo condition (Skewness = 2.98, Standard Error = 0.50). Long-term recall for neutral words was positively skewed in the methamphetamine (Skewness = 2.16, Standard Error = 0.50) and placebo condition (Skewness = 1.27, Standard Error = 0.50).

3.21 Processing

All variables in the LDT were normally distributed except for mean reaction time to threat words in the placebo condition which was positively skewed (Skewness = 1.29, Standard Error = 0.50).

3.22 Covariates

Twelve of the participants had experienced a trauma, with only one of the individuals meeting criteria for mild post-trauma symptoms. Based on the diagnosis and symptom description obtained from the PTDS, no participant was currently experiencing a level of distress that would exclude them from the analysis. Due to the unequal numbers of individuals who had experienced a trauma, this variable was not included in analyses. Scores on the Symptom Checklist 90-R indicated no psychiatric symptoms in any of the participants with a very low or absent level of global distress. This variable was therefore not included in the analysis. Estimated IQ scores and Anxiety sensitivity remained in the analysis. Estimated IQ scores were normally distributed and Anxiety Sensitivity scores positively skewed (Skewness = 1.93, Standard Error = 0.50). Blood plasma levels of methamphetamine after three hours was also included in the analysis and normality testing indicated it was normally distributed.
It was decided not to transform any of the skewed variables as ANOVA is relatively robust to violations of normality when sample sizes are equal and skewness rather than outliers cause the non-normality (Tabachnick & Fidell, 2007). All the variables with skewed data were transformed, with all the analyses reported below repeated. However, analyses of the transformed data did not differ to the results reported below.

3.23 Hypothesis testing

3.24 Affective reactions

A one-way repeated measures ANOVA, with condition (methamphetamine or placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on valence and arousal ratings to threat pictures. Means and 95% confidence intervals for the IAPS Task valence and arousal ratings for methamphetamine and placebo conditions are displayed in Figures 3.14 and 3.15.
Figure 3.14. IAPS Task mean valence ratings for threat pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was no significant difference between methamphetamine and placebo conditions for overall valence ratings to the IAPS Task ($F(1, 20) = .352, p = 0.66, P = 0.09, \text{Hedge’s} \, \hat{g} = 0.15, 95\% \text{ confidence: -0.46, 0.76}$). Contrary to expectations, there was also no significant difference between methamphetamine and placebo conditions.
for valence ratings to threat pictures ($F(1, 20) = 0.20, p = 0.66, P = 0.07, \text{Hedge's } \hat{g} = 0.12$, 95% confidence: -0.49, 0.73).

There was no significant difference between methamphetamine and placebo conditions for overall arousal ratings to the IAPS Task ($F(1, 20) = 0.92, p = 0.35, P = 0.15, \text{Hedge's } \hat{g} = -0.17$, 95% confidence: -0.78, 0.43). Contrary to expectations, there was also no significant difference between methamphetamine and placebo conditions for arousal ratings to threat pictures ($F(1, 20) = 0.01, p = 0.93, P = 0.05, \text{Hedge's } \hat{g} = 1.69$, 95% confidence: -0.59, 0.62).

3.25 Memory

3.26 IAPS Task recognition performance

A one-way repeated measures ANOVA with condition (methamphetamine and placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on accuracy and confidence ratings to the recognition test for threat pictures. Means and 95% confidence intervals for recognition accuracy and confidence ratings for methamphetamine and placebo conditions are displayed in Figures 3.16 and 3.17.
There was a significant difference between methamphetamine and placebo conditions for overall recognition accuracy ($F (1, 20) = 8.97, p < .05, P = 0.81, \text{Hedge’s } \hat{g} = -0.62, 95\% \text{ confidence: } -1.23, 0.00$). Participants were more accurate in their recognition of pictures from the methamphetamine condition (See Table 3.3). There was
also a significant difference between methamphetamine and placebo conditions for overall confidence ratings ($F(1, 20) = 6.31, p < .05, P = 0.67, \text{Hedge's } \hat{g} = 0.40, 95\% \text{ confidence: } -0.21, 1.01$). Participants were more confident in their recognition performance from the methamphetamine condition (See Table 3.3). In contrast to predictions, there were no significant differences between methamphetamine and placebo conditions in recognition accuracy for threat pictures ($F(1, 20) = 0.49, p = 0.49, P = 0.10, \text{Hedge's } \hat{g} = -0.15, 95\% \text{ confidence: } -0.76, 0.45$). There were also no significant difference between methamphetamine and placebo conditions for ratings of confidence to threat pictures ($F(1, 20) = 0.14, p = 0.71, P = 0.06, \text{Hedge's } \hat{g} = 0.08, 95\% \text{ confidence: } -0.52, 0.69$).

3.27 LDT recall performance

A one-way repeated measures ANOVA, with condition (methamphetamine and placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on short-term and long-term recall rates for the threat words in the LDT. Means and 95% confidence intervals for short-term recall rates for the methamphetamine and placebo conditions are presented in Figure 3.18.
There was a significant difference between the methamphetamine and placebo condition for overall short-term recall ($F(1, 20) = 15.42, p < .05, P = 0.96, \text{Hedge’s } \hat{g} = -1.04, 95\% \text{ confidence: } -1.69, -0.40$). In contrast to expectations, participants recalled significantly more words overall in the placebo condition (See Table 3.3). Contrary to expectations, there was no significant differences between methamphetamine and placebo conditions in short-term recall rates for threat words ($F(1, 20) = 0.52, p = 0.48, P = 0.11, \text{Hedge’s } \hat{g} = -0.21, 95\% \text{ confidence: } -0.81, 0.40$).

A one-way repeated measures ANOVA, with condition (methamphetamine and placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on short-term recall rates for the threat words in the first 30-second epoch. Means and 95% confidence intervals for short-term recall rates in the first 30-second epoch for the methamphetamine and placebo conditions are presented in Figure 3.19.
There was a significant difference between methamphetamine and placebo conditions for overall short-term recall for the first 30-second epoch ($F(1, 20) = 18.81, p < .05, P = 0.99, \hat{g} = -1.11, 95\% \text{ confidence: } -1.75, -0.46$). Participants recalled significantly more words overall in the placebo condition for the first 30-second epoch (See Table 3.3). There was no significant difference between methamphetamine and placebo conditions for short-term recall of the threat words in the first 30-second epoch ($F(1, 20) = 1.22, p = 0.28, P = 0.18, \hat{g} = -0.31, 95\% \text{ confidence: } -0.91, 0.30$).

A one-way repeated measures ANOVA, with condition (methamphetamine and placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on short-term recall rates for the threat words in the second 30-second epoch. Means and 95% confidence intervals for short-term recall rates for the methamphetamine and placebo conditions in the second 30-second epoch are presented in Figure 3.20.
Figure 3.20. LDT mean short-term recall for threat words in the second 30-second epoch. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was no significant difference between methamphetamine and placebo conditions for overall short-term recall for the second 30-second epoch ($F(1, 20) = 0.35, p = 0.56, P = 0.09, \text{Hedge's } \hat{g} = -0.14, 95\% \text{ confidence: } -0.75, 0.47$). There was also no significant difference between methamphetamine and placebo conditions for the short-term recall of threat words in the second 30-second epoch ($F(1, 20) = 0.19, p = 0.67, P = 0.07, \text{Hedge's } \hat{g} = 0.13, 95\% \text{ confidence: } -0.47, 0.74$).

A one-way repeated measures ANOVA, with condition (methamphetamine and placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on long-term recall rates for the threat words in the LDT. Means and 95\% confidence intervals for long-term recall rates for the methamphetamine and placebo conditions are presented in Figure 3.21.
Figure 3.21. LDT mean long-term recall for threat words. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was no significant difference between methamphetamine and placebo conditions for overall long-term recall ($F(1, 20) = 0.28, p = 0.61, P = 0.08, \text{Hedges } \hat{g} = 0.14, 95\% \text{ confidence: } -0.46, 0.75$). In support of predictions, there was a significant difference between methamphetamine and placebo conditions for long-term recall of threat stimuli ($F(1, 20) = 8.64, p < .05, P = 0.80, \text{Hedge’s } \hat{g} = -0.79, 95\% \text{ confidence: } 0.16, 1.42$). As expected, participants recalled more threat words from the methamphetamine condition (refer to Figure 3.21). This is in contrast to the recall of neutral words, where no significant difference was evident between conditions ($F(1, 20) = 2.12, p = 0.16, P = 0.28, \text{Hedge’s } \hat{g} = -0.49, 95\% \text{ confidence: } -1.11, 0.12$). For a comparison of long-term recall rates for threat and neutral words in the methamphetamine and placebo condition see Figure 3.22.
3.28 Processing

A one-way repeated measures ANOVA, with condition (methamphetamine and placebo) as the within subjects variable was conducted to examine the effect methamphetamine had on reaction times to the threat words presented in the LDT. Means and 95% confidence intervals for reaction times in the methamphetamine and placebo conditions are presented in Figure 3.23.

There was no significant difference between methamphetamine and placebo conditions for overall reaction times ($F(1, 20) = 0.02, p = 0.88, P = 0.05$, Hedge’s $\hat{g}$...
There was also no significant difference between methamphetamine and placebo conditions for reaction times to threat words ($F(1, 20) = 0.86, \ p = 0.36, \ P = 0.14, \ \text{Hedge's} \ \hat{g} = -0.22, \ 95\% \ \text{confidence:} \ -0.83, \ 0.38$).

### 3.29 Covariates

#### 3.30 Estimated IQ, anxiety sensitivity and blood plasma levels.

In order to determine whether estimated IQ, anxiety sensitivity and blood plasma levels of methamphetamine co-varied with condition for any of the results, difference scores from placebo to the methamphetamine condition for each variable were calculated for each participant. Scores on the Symptom Checklist 90-R indicated no psychiatric symptoms in any of the participants with a very low or absent level of global distress. This variable was therefore not included in the analysis. Additionally although twelve participants had experienced a trauma, only one was currently experiencing mild post-trauma symptoms. Therefore this variable was also excluded from the analysis. The mean and standard deviation difference scores from placebo to methamphetamine for all participants in the IAPS Task, Recognition Task and LDT are summarized in Table 3.4.
Table 3.4
*Means and standard deviation difference scores from methamphetamine to placebo for threat words and pictures*

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAPS Task Valence ratings</td>
<td>-0.10</td>
<td>1.07</td>
</tr>
<tr>
<td>IAPS Task Arousal ratings</td>
<td>-0.03</td>
<td>1.46</td>
</tr>
<tr>
<td>Recognition Accuracy</td>
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<td>0.16</td>
</tr>
<tr>
<td>Recognition Ratings of Confidence</td>
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<td>17.77</td>
</tr>
<tr>
<td>LDT Short-term recall</td>
<td>0.33</td>
<td>2.13</td>
</tr>
<tr>
<td>First 30-second epoch</td>
<td>0.43</td>
<td>1.78</td>
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<tr>
<td>Second 30-second epoch</td>
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<td>1.00</td>
</tr>
<tr>
<td>LDT Long-term recall</td>
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</tr>
<tr>
<td>LDT Reaction times</td>
<td>0.06</td>
<td>0.30</td>
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</tbody>
</table>

*N = 21*

Note: For IAPS Task Valence, 9 = Positive, 1 = Negative, Arousal, 1 = Low, 9 =High.
For IAPS Task Accuracy, 1 = Correct, 2 = Incorrect.
A negative number means the participant's score increased in the methamphetamine condition.
A positive number means the participant’s score decreased in the methamphetamine condition.

The average estimated IQ score was 114.14 (SD = 1.31), with a range from 100 to 122. The average anxiety sensitivity score was 10.71 (SD =1.84), with a range from 0 to 38. The average blood plasma levels of methamphetamine after 3 hours were 71.05ug/L (SD = 42.35), with a range from 17 to 138ug/L (See Table 4 in Appendix 4). One sample was unable to be taken and two samples contained levels below 10ug/L and were therefore classified as “Not detected.” Additionally, three participants tested
positive for Cannabinoid metabolites, but the levels were inactive and therefore not considered to be having any effect on functioning. In order to identify possible covariates, correlations were conducted between the difference scores and estimated IQ, anxiety sensitivity and blood plasma levels. For an examination of correlations for all relevant variables please refer to Appendix 4. There were no significant correlations between any of the dependent variables or covariates.

3.31 MDMA versus placebo comparison

3.32 Data screening

Analysis in the MDMA comparison employed the same statistical procedure as for the Alcohol comparison. Details will not be repeated in this section. There were 20 cases included in the analysis. Data screening revealed eleven missing values in the IAPS delayed recognition test results. It was decided that these missing values would be replaced with the group mean for that picture for participants in the same condition. Four implausible values were identified in the LDT reaction time results. All implausible values were replaced with the group mean for that word for participants in the same condition. Table 3.5 contains the results for all tasks across all picture and word types in the MDMA versus placebo comparison.
Table 3.5
Means and standard deviations for all tasks across all word and picture types for the MDMA versus placebo comparison

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<tr>
<th>Test</th>
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<th>SD</th>
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<td>0.64</td>
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</tr>
<tr>
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<td>MDMA</td>
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<tr>
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<td>0.83</td>
<td>0.21</td>
<td>0.93</td>
<td>0.30</td>
</tr>
</tbody>
</table>

N = 20
Note: For Affective Picture Task Valence, 9 = Positive, 1 = Negative, Arousal, 1 = Low, 9 = High.
For IAPS Recognition Accuracy, 1 = Correct, 2 = Incorrect.
3.33 Testing of assumptions

Prior to hypothesis testing the assumptions underlying analysis of variance (ANOVA) were examined. All observations were independent of each other and tests of normality were conducted for all variables. Results of normality tests are presented below. Histograms and Q-Q plots for all variables are contained in Appendix 3.

3.34 Affective reactions

Overall valence ratings in the MDMA condition were positively skewed (Skewness = 1.72, Standard Error = 0.51) and normally distributed in the placebo condition. Valence of threat pictures was positively skewed in the MDMA condition (Skewness = 0.82, Standard Error = 0.51) and normally distributed in the placebo condition. Valence of neutral pictures was negatively skewed in the MDMA condition (Skewness = -0.04, Standard Error = 0.51) and positively skewed in the placebo condition (Skewness = 2.46, Standard Error = 0.51). Arousal of neutral pictures was positively skewed in the MDMA (Skewness = 0.63, Standard Error = 0.51) and placebo condition (Skewness = 0.41, Standard Error = 0.51). All remaining variables were normally distributed.

3.35 Memory

Overall recognition accuracy was positively skewed in the MDMA (Skewness = 0.50, Standard Error = 0.51) and the placebo condition (Skewness = 0.06, Standard Error = 0.51). Overall confidence ratings were normally distributed. Recognition accuracy for threat pictures was positively skewed in the MDMA (Skewness 1.52, Standard Error = 0.51) and placebo condition (Skewness = 4.47, Standard Error = 0.51). Confidence ratings for threat pictures was normally distributed. Recognition accuracy for neutral pictures was positively skewed in the MDMA (Skewness = 0.04, Standard Error = 0.51).
Confidence ratings for the neutral pictures were normally distributed.

Overall Short-term recall was positively skewed in the MDMA condition (Skewness = 1.31, Standard Error = 0.51) and normally distributed in the placebo condition. Short-term recall for threat words was normally distributed in the MDMA condition and positively skewed in the placebo condition (Skewness = 0.46, Standard Error = 0.51). Short-term recall for neutral words was positively skewed in the MDMA (Skewness = 1.37, Standard Error = 0.51), and placebo condition (Skewness = 0.89, Standard Error = 0.51).

Overall Short-term recall for the first 30-second epoch was normally distributed in the MDMA and placebo condition. Overall Short-term recall for the second 30-second epoch was positively skewed in the MDMA (Skewness = 2.20, Standard Error = 0.51) and the placebo condition (Skewness = 0.69, Standard Error = 0.51). Short-term recall for the first 30-second epoch for threat words was normally distributed in the MDMA condition and negatively skewed in the placebo condition (Skewness = -0.04, Standard Error = 0.51). Short-term recall for the second 30-second epoch for threat words was positively skewed in the MDMA (Skewness = 2.63, Standard Error = 0.51) and placebo condition (Skewness = 2.42, Standard Error = 0.51). Short-term recall for the first 30-second epoch for neutral words was positively skewed for the MDMA (Skewness = 1.34, Standard Error = 0.51) and placebo condition (Skewness = 0.10, Standard Error = 0.51). Short-term recall for the second 30-second epoch for neutral words was positively skewed for the MDMA (Skewness = 3.51, Standard Error = 0.51) and placebo condition (Skewness = 0.95, Standard Error = 0.51).
Overall Long-term recall was positively skewed in the MDMA (Skewness = 1.96, Standard Error = 0.51) and placebo condition (Skewness = 0.88, Standard Error = 0.51). Long-term recall for threat words was positively skewed in the MDMA (Skewness = 1.78, Standard Error = 0.51) and placebo condition (Skewness = 0.49, Standard Error = 0.50). Long-term recall for neutral words was positively skewed in the MDMA (Skewness = 1.86, Standard Error = 0.51) and placebo condition (Skewness = 2.70, Standard Error = 0.51).

3.36 Processing

All variables in the LDT were normally distributed.

3.37 Covariates

Six of the participants had experienced a trauma, with only one of the individuals meeting criteria for moderate post-trauma symptoms. Based on the diagnosis and symptom description obtained from the PTDS, no participant was currently experiencing a level of distress that would exclude them from the analysis. Due to the unequal numbers of individuals who had experienced a trauma, this variable was not included in analysis. Scores on the Symptom Checklist 90-R indicated no psychiatric symptoms in any of the participants with a very low or absent level of global distress. This variable was therefore not included in the analysis. Estimated IQ and Anxiety sensitivity remained in the analysis. Estimated IQ and Anxiety Sensitivity scores were both normally distributed. Blood plasma levels of MDMA after three hours was also included in the analysis and normality testing indicated it was normally distributed.

It was decided not to transform any of the skewed variables as ANOVA is relatively robust to violations of normality when sample sizes are equal and skewness
rather than outliers cause the non-normality (Tabachnick & Fidell, 2007). All the variables with skewed data were transformed, with all the analyses reported below repeated. However, analyses of the transformed data did not differ to the results reported below (See Appendix 3. for an examination of all histograms and normality curves for each variable).

3.38 Hypothesis testing

3.39 Affective reactions

A one-way repeated measures ANOVA, with condition (MDMA or placebo) as the within subjects variable was conducted to examine the effect MDMA had on valence and arousal ratings to threat pictures. Means and 95% confidence intervals for the IAPS Task valence and arousal rating for MDMA and placebo conditions are displayed in Figures 3.24 and 3.25.

Figure 3.24. IAPS Task mean valence ratings for threat pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.
There was no significant difference between MDMA and placebo conditions for overall valence ratings to the IAPS Task ($F(1, 19) = .137, p = 0.72, P = 0.06$, Hedge’s $\hat{g} = 0.10$, 95% confidence: -0.722, 0.52). Contrary to expectations, there was also no significant difference between MDMA and placebo conditions for valence ratings to threat pictures ($F(1, 19) = 0.51, p = 0.48, P = 0.10$, Hedge’s $\hat{g} = -0.19$, 95% confidence: -0.81, 0.43).

There was no significant difference between MDMA and placebo conditions for overall arousal ratings to the IAPS Task ($F(1, 19) = 0.85, p = 0.37, P = 0.14$, Hedge’s $\hat{g} = 0.24$, 95% confidence: -0.38, 0.86). In contrast to expectations, there was also no significant difference between MDMA and placebo conditions for arousal ratings to threat pictures ($F(1, 19) = 0.84, p = 0.37, P = 0.14$, Hedge’s $\hat{g} = 0.28$, 95% confidence: -0.34, 0.91).

3.40 Memory

3.41 IAPS Task recognition performance

A one-way repeated measures ANOVA with condition (MDMA and placebo) as the within subjects variable was conducted to examine the effect MDMA had on
accuracy and confidence ratings for the picture recognition test for threat pictures.

Means and 95% confidence intervals for recognition accuracy and confidence ratings for MDMA and placebo conditions are displayed in Figures 3.26 and 3.27.

![Figure 3.26. Mean recognition accuracy for threat pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.](image1)

![Figure 3.27. Mean recognition ratings of confidence for threat pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.](image2)

There was a significant difference between MDMA and placebo conditions for overall recognition accuracy ($F (1, 19) = 7.04, p < .05, P = 0.71, \text{Hedge }'s \hat{g} = 0.88, 95\% \text{ confidence: } 0.233, 1.53$). Participants were more accurate in their recognition of pictures from the MDMA condition (see Table 3.5). There was no significant difference
between MDMA and placebo conditions for overall confidence ratings \( F(1, 19) = 1.26, p = 0.28, P = 0.19, \) Hedge’s \( \hat{g} = -0.21, 95\% \) confidence: -0.83, 0.41). There was a significant difference between MDMA and placebo conditions in recognition accuracy for threat pictures \( F(1, 19) = 8.14, p < .05, P = 0.77, \) Hedge’s \( \hat{g} = 0.66, 95\% \) confidence: 0.03, 1.30). In contrast to expectations, participants were more accurate in their recognition of pictures from the placebo condition (see Figure 3.26). In contrast, there was no significant difference between MDMA and placebo conditions in recognition accuracy for neutral pictures \( F(1, 19) = 0.96, p = 0.34, P = 0.15, \) Hedge’s \( \hat{g} = 0.30, 95\% \) confidence: -0.32, 0.93). For a comparison of recognition accuracy for threat and neutral pictures in the MDMA and placebo conditions see Figure 3.28. There was no significant difference between MDMA and placebo conditions for ratings of confidence to threat pictures \( F(1, 19) = 2.07, p = 0.17, P = 0.28, \) Hedge’s \( \hat{g} = -0.32, 95\% \) confidence: -0.94, 0.31).

![Figure 3.28](image)

*Figure 3.28.* Mean recognition accuracy for threat and neutral pictures. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

### 3.42 LDT recall performance

A one-way repeated measures ANOVA, with condition (MDMA and placebo) as the within subjects variable was conducted to examine the effect MDMA had on
short-term and long-term recall rates for the threat words in the LDT. Means and 95% confidence intervals for short-term recall rates for the MDMA and placebo conditions are presented in Figure 3.29.

![Figure 3.29. LDT means short-term recall for threat words. Error bars indicate the upper bounds of the 95% confidence intervals above the means.](image)

There was a significant difference between the MDMA and placebo conditions for overall short-term recall ($F(1, 19) = 4.56, p = 0.05, P = 0.53, \text{Hedge's } \hat{g} = 0.68, 95\% \text{ confidence: } 0.04, 1.32$). Participants recalled more words overall in the MDMA condition (See Table 3.5). Contrary to expectations, there were no significant differences between MDMA and placebo conditions for short-term recall of threat words ($F(1, 19) = 1.12, p = 0.30, P = 0.17, \text{Hedge's } \hat{g} = 0.34, 95\% \text{ confidence: } -0.28, 0.97$).

A one-way repeated measures ANOVA, with condition (MDMA and placebo) as the within subjects variable was conducted to examine the effect MDMA had on short-term recall rates for the threat words in the first 30-second epoch. Means and 95%
confidence intervals for short-term recall rates for the MDMA and placebo conditions in
the first 30-second epoch are presented in Figure 3.30.

![Bar chart showing short-term recall for threat words in the first 30-second epoch]

*Figure 3.30. LDT mean short-term recall for threat words in the first 30-second epoch. Error bars indicate the upper bounds of the 95% confidence intervals above the means.*

There was no significant difference between MDMA and placebo conditions for
overall short-term recall for the first 30-second epoch \( F(1, 19) = 5.84, p = 0.03, P = 0.63, \) Hedge’s \( \hat{g} = 0.78, \) 95% confidence: 0.13, 1.42). There was also no significant
difference between MDMA and placebo conditions for short-term recall of the threat words in the first 30-second epoch \( F (1, 19) = 0.95, p = 0.34, P = 0.15, \) Hedge’s \( \hat{g} = 0.35, \) 95% confidence: -0.28, 0.97).

A one-way repeated measures ANOVA, with condition (MDMA and placebo) as the within subjects variable was conducted to examine the effect MDMA had on short-term recall rates for the threat words in the second 30-second epoch. Means and 95% confidence intervals for short-term recall rates for the MDMA and placebo conditions in the second 30-second epoch are presented in Figure 3.31.
There was no significant difference between MDMA and placebo conditions for overall short-term recall for the second 30-second epoch ($F(1, 19) = 0.39, p = 0.54, P = 0.09, \text{Hedge’s } \hat{g} = 0.21, 95\% \text{ confidence: } -0.41, 0.83$). There was also no significant difference between MDMA and placebo conditions for the short-term recall of threat words in the second 30-second epoch ($F(1, 19) = 0.11, p = 0.74, P = 0.06, \text{Hedge’s } \hat{g} = 0.11, 95\% \text{ confidence: } -0.51, 0.73$).

A one-way repeated measures ANOVA, with condition (MDMA and placebo) as the within subjects variable was conducted to examine the effect MDMA had on long-term recall rates for the threat words in the LDT. Means and 95\% confidence intervals for long-term recall rates for the methamphetamine and placebo conditions are presented in Figure 3.32.
There was no significant difference between MDMA and placebo conditions for overall long-term recall ($F(1, 19) = 0.02, p = 0.89, P = 0.05, Hedges' g = 0.05, 95\% confidence: -0.57, 0.67$). Contrary to expectations, there was also no significant difference between MDMA and placebo conditions for long-term recall of threat stimuli. ($F(1, 19) = 1.57, p = 0.23, P = 0.22, Hedges' g = -0.41, 95\% confidence: -1.03, 0.22$).

3.43 Processing

A one-way repeated measures ANOVA, with condition (MDMA and placebo) as the within subjects variable was conducted to examine the effect MDMA had on reaction times to the threat words presented in the LDT. Means and 95\% confidence intervals for reaction times in the MDMA and placebo conditions are presented in Figure 3.33.
Figure 3.33. LDT mean reaction time for threat words. Error bars indicate the upper bounds of the 95% confidence intervals above the means.

There was no significant difference between MDMA and placebo conditions for overall reaction times ($F (1, 19) = 0.76, p = 0.39, P = 0.13$, Hedge’s $\hat{g} = -0.13$, 95% confidence: -0.75, 0.49). There was also no significant difference between MDMA and placebo conditions for reaction times to threat words ($F (1, 19) = 0.53, p = 0.47, P = 0.11$, Hedge’s $\hat{g} = 0.11$, 95% confidence: -0.51, 0.73).

3.44 Covariates

3.45 Estimated IQ, anxiety sensitivity and blood plasma levels.

In order to determine whether estimated IQ, anxiety sensitivity and blood plasma levels of MDMA co-varied with condition for any of the results, difference scores from placebo to the MDMA condition for each variable were calculated for each participant. Scores on the Symptom Checklist 90-R indicated no psychiatric symptoms in any of the participants with a very low or absent level of global distress. This variable was therefore not included in the analysis. Additionally although six participants had experienced a trauma, only one was currently experiencing moderate post-trauma symptoms. Therefore this variable was also excluded from the analysis. The mean and
standard deviation difference scores from placebo to MDMA for all participants in the
IAPS Task, recognition task and LDT are summarized in Table 3.6.

Table 3.6
Means and standard deviation difference scores from placebo to MDMA for
threat words and pictures

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAPS Task Valence ratings</td>
<td>0.20</td>
<td>1.25</td>
</tr>
<tr>
<td>IAPS Task Arousal ratings</td>
<td>-0.38</td>
<td>1.85</td>
</tr>
<tr>
<td>Recognition Accuracy</td>
<td>-0.08</td>
<td>0.12</td>
</tr>
<tr>
<td>Recognition Ratings of Confidence</td>
<td>3.71</td>
<td>11.55</td>
</tr>
<tr>
<td>LDT Short-term recall</td>
<td>-0.55</td>
<td>2.33</td>
</tr>
<tr>
<td>First 30-second epoch</td>
<td>-0.45</td>
<td>2.06</td>
</tr>
<tr>
<td>Second 30-second epoch</td>
<td>-0.10</td>
<td>1.33</td>
</tr>
<tr>
<td>LDT Long-term recall</td>
<td>0.45</td>
<td>1.61</td>
</tr>
<tr>
<td>LDT Reaction times</td>
<td>-0.07</td>
<td>0.23</td>
</tr>
</tbody>
</table>

N = 20
Note: For IAPS Task Valence, 9 = Positive, 1 = Negative, Arousal, 1 = Low, 9 = High.
For IAPS Task Accuracy, 1 = Correct, 2 = Incorrect.
A negative number means the participant's score increased in the MDMA condition.
A positive number means the participant's score decreased in the MDMA condition.

The average estimated IQ score was 113.80 (SD = 6.18), with a range from 100
to 123. The average anxiety sensitivity score was 11.80 (SD = 7.68), with a range from 4
to 33. The average blood plasma levels of MDMA after 3 hours was 197.05ug/L (SD = 69.00), with a range from 104 to 299ug/L (see Table 5 in Appendix 4). One sample was
unable to be collected and one person tested positive for inactive cannabinoid metabolites and another for Codeine metabolites. In order to identify possible covariates correlations were conducted between the difference scores and estimated IQ, anxiety sensitivity and blood plasma levels. For an examination of correlations for all relevant variables please refer to Appendix 4. There were no significant correlations between any of the dependent variables or covariates.

3.46 Summary of hypotheses for all drug comparisons.

Table 3.7 presents a summary of the hypotheses for the threat stimuli for all the drug comparisons.

Table 3.7

<table>
<thead>
<tr>
<th>Test</th>
<th>Hypothesis</th>
<th>Drug comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAPS</td>
<td>Valence</td>
<td>Alcohol Methamphetamine MDMA</td>
</tr>
<tr>
<td></td>
<td>Arousal</td>
<td>No Yes No No-no-opposite direction</td>
</tr>
<tr>
<td></td>
<td>Recognition Accuracy</td>
<td>No No No-opposite direction</td>
</tr>
<tr>
<td></td>
<td>Recognition Confidence</td>
<td>No No No</td>
</tr>
<tr>
<td>LDT</td>
<td>Immediate recall</td>
<td>No No No</td>
</tr>
<tr>
<td></td>
<td>Delayed recall</td>
<td>Yes Yes No</td>
</tr>
<tr>
<td></td>
<td>Processing Speed</td>
<td>No No No</td>
</tr>
</tbody>
</table>
CHAPTER 4: DISCUSSION

Given that most people who experience a trauma recover with no intervention, a great deal of research has attempted to identify factors that best predict the minority of individuals likely to develop PTSD. Preliminary research suggests that depressant drugs may represent a protective factor against developing PTSD and stimulant drugs a risk factor for the development of PTSD. Based on this preliminary research, the current study explored the effect alcohol, methamphetamine and MDMA had on trauma processing and memory. The study aimed to explore whether alcohol intoxication would reduce processing and memory of threat stimuli, while methamphetamine and MDMA would enhance processing and memory of such stimuli. The results of this thesis were expected to provide some insight into the primed memory effects noted in PTSD patients and the biological memory system implicated in PTSD symptomatology.

The results of the experiment supported some of the hypotheses formulated with regards to the effect of alcohol and methamphetamine on trauma processing and memory. The results did not support the hypotheses formulated with regards to the effect MDMA would have on emotional processing and storage of traumatic stimuli. The discussion begins by discussing the results obtained for each of the three drugs and how they may relate to previous research and the biological model proposed to be involved in the aetiology of PTSD. The discussion then provides several explanations that may explain the failure to support the hypotheses formulated. Finally, a number of limitations inherent in the study are addressed and directions for future research provided in the concluding statements.
4.1 Affective reactions to trauma-related stimuli in the alcohol comparison

The prediction that alcohol would decrease ratings of valence and arousal to threat stimuli was partially supported. No significant differences were obtained between conditions for the valence ratings across all picture types or threat pictures presented in the IAPS Task. Across all pictures types, valence ratings remained relatively similar from placebo to alcohol conditions. In support of the hypotheses, results revealed a significant difference in arousal ratings between alcohol and placebo conditions for the threat pictures. As expected, participants made lower arousal ratings to the threat pictures in the alcohol condition. This is in contrast to the results across all picture types or neutral pictures, in which no significant results were obtained. This suggests the changes in arousal were specific to threat pictures and were not simply the result of sedation or poor attention.

The results suggest that individuals who were intoxicated judged the threat pictures as less threatening and less negatively arousing than when in the placebo condition. These results appear consistent with research that suggests alcohol may increase GABA actively and disrupt an individual’s evaluation and response to threatening or stress-inducing stimuli (Vaiva et al., 2004). These results have important implications, as they suggest that when an individual is intoxicated they may be more likely to under-estimate the level of danger in a given situation. This is based on the assumption that the level of arousal associated with an event has a greater impact on threat estimation than valency (Knowles & Duka, 2004; Moshe & Neta, 2007). This inference is also consistent with Australian data that indicates intoxicated individuals admitted to hospital were more likely to sustain a serious rather than minor injury, possibly as a result of impaired threat estimation (Tjipto, Taylor, & Liew, 2006). This
would also mean the conditioned stress response attached to the memory of the event may be weaker. This inference is consistent with research that found individuals intoxicated at the time a trauma occurred rated the event as less severe and suffered fewer PTSD symptoms (Clum, Nishith, & Coulhoun, 2002).

4.2 Memory for trauma-related stimuli in the alcohol comparison

Contrary to the hypotheses, recognition accuracy did not differ significantly between alcohol and placebo conditions for all pictures types or specifically for threat pictures. Although no significant differences were obtained between conditions, it is clear from the pattern of results that recognition accuracy was the highest for the threat pictures. However, there was very little difference between conditions. The degree of confidence participants had in their responses to the recognition test also failed to differ significantly between alcohol and placebo conditions for all picture types and specifically for threat pictures. Consistent with the recognition accuracy, participants appear to have provided higher confidence ratings for the threat pictures, although again the difference between conditions was minimal.

There were no significant differences between conditions for short-term recall of the threat words. The pattern of results obtained suggests that recall was higher in the placebo rather than alcohol condition for threat words. The result across all word types suggests that alcohol impaired encoding and immediate retrieval for verbal information across all emotional valences. This may indicate that the memory reducing effect is not necessarily specific to threat and stress-inducing stimuli, and is more likely related to the sedative effects of alcohol ingestion.

In support of hypotheses, there was a significant difference between alcohol and placebo conditions for short-term recall of threat words in the first 30-second epoch. As
expected, participants recalled more threat words when in the placebo condition. This suggests the alcohol reducing effects on memory may be evident during the early processes involved in encoding the information. This effect was also evident across all words types, with the exception of neutral words. This result may indicate that words with an emotional valency are affected to a greater extent by the alcohol, or it may simply indicate that recall of neutral words is poor regardless of the alcohol reducing effects. There were no significant differences between conditions for recall of the threat words in the second 30-second epoch.

The first 30-seconds of free recall was most likely influenced by the primacy effect, with the later 30-seconds influenced by the recency effect. Participants were not instructed that they would be tested on their memory after the performance, and they were also required to indicate if the word was a real or non-word. This was done in order to make the memory recall as naturalistic as possible. The primacy effect occurs when individuals recall more information from the start of a list of words, with the words rehearsed enough to have entered short or long-term memory (Zhang et al., 2003). The recency effect occurs when individuals recall more information from the end of a list of words, with these words located in the maintenance rehearsal loop of working memory. The results obtained suggests that the alcohol reducing effects may be more evident during the encoding process of moving words from working memory to short and long-term memory.

Research has explored the impact the recency and primacy effect have on an individual’s recall of negative and pleasurable emotional experiences. Interestingly, for negative affect experiences, the recency effect has a greater impact on the memory recall, while for pleasurable events the primacy effect has a greater impact (Rode,
Rozin, & Durlach, 2007). The results obtained are not consistent with this research, although the threat words may not have been negative enough to have truly represented a negative emotional event. This limitation will be discussed further later in the thesis. Given the differing results obtained for recall in the first and second epochs, further research would benefit from a more specific examination of serial position memory effects with regards to trauma memory.

In support of the hypotheses formulated with regards to long-term recall of trauma-related stimuli, participants recalled significantly more threat words from the placebo condition. The long-term memory results for threat words are consistent with the short-term recall results and suggest that the alcohol impairing effect on memory may occur at the encoding, storage and retrieval stages of memory. These results are consistent with research that found alcohol intoxication represented a protective factor against developing PTSD, hypothetically achieved through reducing the encoding and storage of trauma-related stimuli (Maes, Delmeine, Mylle, & Altanura, 2001). The results of the IAPS Task also suggest alcohol may protect against PTSD by reducing the level of arousal to such stimuli. The failure of some research (e.g., Turner, Kivlahan, Rimmelé, & Bombardier, 2006) to find similar results is most likely due to differing levels of intoxication in participants and failure to use adequate controls or a placebo condition.

The impact that alcohol has on memory may also help to explain the high rates of alcohol abuse among individuals with PTSD (Ouimette, Brown, & Najavits, 1998). Research now suggests that drug induced changes in memory can occur both during encoding and initial storage of the stimuli into memory and during retrieval and further consolidation of the stimuli (Debiec & Ledoux, 2004). The dampening effect alcohol
has on reactions to threat stimuli and memory for such stimuli, may help to explain why alcohol is used by many sufferers to reduce the strength and impact of Post-traumatic symptoms. This may occur by weakening the fear associated with the event recalled or by impairing the reconsolidation of the event.

Research has demonstrated that an important motivator for alcohol abuse among trauma victims is to reduce the impact of negative emotions (Grayson & Nolen-Hoeksema, 2005, Wilkie & Stewart, 2005). Research has also concluded that PTSD rather than trauma exposure is a risk factor for developing a drug disorder after controlling for early life events (Reed, Anthony, & Breslau, 2007). Furthermore, research is beginning to find associations between particular PTSD symptoms and alcohol addiction. For example, research has linked a flooding of endorphins within the central nervous system to the dissociative reactions common to PTSD (Turnbull, 2006). The release of endogenous opioids (endorphin) during a traumatic event is proposed to have an action on the frontal lobes of the brain, reducing attention and awareness of the perceptual field. This is believed to cause the feeling of emotive numbing and stress-induced analgesia that immediately follows the trauma. Chronic endorphin depletion, possibly as a result of persistent endorphin flooding following exposure to triggers of the trauma, has also been linked to the development of alcohol dependency (Turnbull, 2006).

4.3 Processing speed in the alcohol comparison.

In contrast to the hypotheses formulated, there were no significant differences between the alcohol and placebo conditions for reaction times to the threat words in the LDT. Participants attended and responded to the threat words in a similar amount of
time when intoxicated and sober. This suggests that the memory results obtained were not the result of faster orientating and responding to the stimuli.

4.4 Affective reactions to trauma-related stimuli in the methamphetamine comparison

The prediction that methamphetamine would increase ratings of valence and arousal to threat pictures presented in the IAPS Task was not supported. There were no significant differences obtained between conditions for all pictures types- specifically for the threat pictures. Valence and arousal ratings remained relatively similar from the placebo to methamphetamine conditions. These results are in contrast to preliminary research that suggested that when intoxicated with a stimulant, individuals were at a greater risk of developing PTSD due to an increased sensitivity and response to threatening stimuli (Zatick et al., 2002). The results obtained suggest that methamphetamine does not significantly alter an individual’s perception and evaluation of threatening stimuli.

4.5 Memory for trauma-related stimuli in the methamphetamine comparison

There was a significant difference between conditions for overall recognition accuracy and confidence ratings to the pictures in the recognition test. Participants were more accurate and had greater confidence in their responses for all picture types when in the methamphetamine condition. In contrast to the hypotheses, there were no significant differences obtained between conditions for accuracy or confidence ratings to the threat pictures. The pattern of results suggests that participants were more confident in their responses from the methamphetamine condition. This suggests that methamphetamine may have a memory enhancing effect for emotional stimuli overall, but not specifically for threatening stimuli. This would seem consistent with the earlier results for affective reactions that suggest emotional responses to the
stimuli did not differ significantly for the threat stimuli. The results are consistent with other memory research that found methamphetamine improved overall memory (Ferry, Roozendaal, & McGaugh, 1999; Packard, Cahill, & McGaugh, 1994).

Analysis of the short-term recall performance following the LDT provided unexpected results. Participants recalled significantly more words overall when in the placebo condition. There was no significant difference between conditions for recall of the threat words. When examining recall in the first and second 30-second epoch, results again proved unexpected. Participants again recalled significantly more words overall in the placebo condition during the first 30-seconds. Again these differences did not occur for recall of the threat words. There were no significant results for recall during the second 30-second epoch for overall or threat words.

Consistent with hypotheses a significant difference was evident between conditions for long-term recall of threat words. Participants recalled more threat words when in the methamphetamine condition. This effect appears specific to the threat words and was not evident across all word types or neutral words. Combined with the affective reaction findings from the IAPS, these results suggest that while methamphetamine may not enhance affective responses to threat stimuli, it does enhance long-term memory for such stimuli. These results are consistent with the enhanced recognition performance for emotional stimuli from the methamphetamine condition. The current theory underlying the development of PTSD requires that a strong conditioned fear response is stored with the memory of the traumatic event. The current results suggest that within our sample, long-term memory for the traumatic event may be stored to a greater degree following methamphetamine consumption but a significantly stronger affective response to the stimuli does not occur.
The poorer short-term recall performance for emotional stimuli in general after consuming methamphetamine is in contrast to the results for the picture recognition test in which recognition was better when in the methamphetamine condition. There are several factors that may explain the discrepancy in results. The stimulant enhancing effects may have had differing impacts on visual rather than verbal memory. Methamphetamine may have enhanced recall of overall visual information, but somehow reduced memory for verbal information. Participants were also required to perform a simple verbal task while viewing the words in the LDT and this may have reduced the encoding processes needed to store the emotional stimuli in memory. Research has examined the impact a visual-spatial and verbal task has on memory when conducted at the same time a traumatic event such as a film is encoded (Holmes, Brewin, & Hennessy, 2004). The study conducted by Holmes, Brewin and Hennessy, examined the rate of memory intrusions in participants after viewing the film and was based on the dual-representation theory of memory. This theory suggests intrusions, as seen in individuals with PTSD, is the result of information being stored in situationally accessible memory (SAM) rather than verbally accessible memory (VAM) due to limited attention. The memory is then automatically retrieved by exposure to relevant cues and experienced as an intrusion. The research found that when individuals were made to complete a visual-spatial pattern tapping task that reduced the capacity of the SAM system, the rate of memory intrusions was reduced. When participants completed a verbal task that reduced the capacity of the VAM system, the rate of intrusions increased. Based on the results of this research, it may have been interesting to examine implicit memory or visual memory of the words presented in the LDT in order to
determine if completing the verbal task during encoding had differing effects on the verbal versus visual memory for the words. Alternatively, because visual memory was assessed using a recognition test as a prompt, this may have inadvertently increased visual memory performance. This would most likely explain why no result was obtained for the recognition performance when participants were in the alcohol condition. Additionally, both the recognition test and long-term memory tests suggest that methamphetamine had a memory enhancing effect while the short-term results suggest a memory impairing effect. The short-term memory test was administered while participants were still intoxicated with methamphetamine, while the recognition tests and long-term recall tests were administered two weeks later. Methamphetamine may inhibit initial explicit recall of stimuli due to intoxication, but once metabolised memory may improve, suggesting no failure to encode but, rather, a failure of recall while intoxicated.

4.6 Processing speed in the methamphetamine comparison.

Consistent with the results in the alcohol comparison, there were no significant differences evident between the methamphetamine and placebo conditions for reaction times to the threat words in the LDT. Participants attended and responded to the threat words in a similar amount of time when intoxicated with methamphetamine and when in the placebo condition. This suggests that the memory results obtained are not the result of faster orientating and responding to the stimuli.

4.7 Affective reactions to trauma-related stimuli in the MDMA comparison

Similarly to the methamphetamine results, there were no significant differences obtained between conditions for all picture types or specifically for the threat pictures for the valence and arousal ratings to the IAPS Task. Valence and arousal
ratings remained relatively similar from the placebo to methamphetamine conditions. These results are in contrast to preliminary research that suggested that when intoxicated with a stimulant, individuals were at a greater risk of developing PTSD due to an increased sensitivity and response to threatening stimuli (Zatzick et al., 2002). The results obtained suggest that MDMA, like methamphetamine, does not significantly alter an individual’s perception and evaluation of threatening stimuli. The results are also in contrast to anecdotal research that suggest MDMA consumption increases emotional responsiveness (Baggot, Jerome, & Stuart, 2001). These results would suggest that MDMA does not have any significant impact on emotional expression or regulation and would, therefore, be unlikely to improve patient outcome in individuals with PTSD by increasing their expression of negative emotion (Doblin, 2002).

4.8 Memory for trauma-related stimuli in the MDMA comparison

There was a significant difference between conditions for overall accuracy to the picture recognition test. Participants were more accurate in their responses from the MDMA condition. There was also a significant difference between conditions for accuracy ratings to the threat pictures. In contrast to the hypotheses, participants were more accurate in their recognition of threat pictures when previously in the placebo condition. These results suggest that while MDMA may improve memory for emotional stimuli overall, MDMA may have a dampening effect on memory for threatening information. This effect appears to be specific to the threat information, with no significant differences between conditions for accuracy of neutral pictures. In contrast to hypotheses, there was no significant difference between conditions for confidence ratings across all picture types or specifically to threat pictures.
The pattern of results suggests participants had greater confidence in their responses to the threat pictures when in the placebo condition. The results of the recognition test are in contrast to past research that suggested amphetamines would enhance memory for traumatic stimuli (Zatzick et al., 2002). However the results are consistent with some of the MDMA research that has documented memory impairments following MDMA consumption (Kalechstein, DeLaGarza, Mahoney, Fantegrossi, & Newton, 2007). This generalisation should be interpreted with caution as much of the MDMA research has been conducted on regular MDMA users and often had serious methodological limitations. The reason for the memory improvement across all picture types in the MDMA condition remains unclear, but may be that while MDMA improves memory for positive information, it reduces memory for negative information. The results for the positive pictures would therefore have influenced the results overall.

In contrast to the hypotheses, there were no significant differences between conditions for short-term recall across all word types or threat words. The pattern of results suggests participants recalled more threat words when in the MDMA condition. There were also no significant differences between conditions for short-term recall across all word types or specifically threat words in the first or second 30-second epoch. The pattern of results obtained for the first 30-second epoch suggests participants tended to recall more threat words when in the MDMA condition. The recall of threat words in the second 30-second epoch was similar between conditions. In contrast to hypotheses, there were no significant differences between conditions for long-term recall across all word types or threat words. The pattern of results obtained is in contrast to those obtained for the short-term recall of words. Participants tended to recall more threat words when previously in the placebo condition.
The contrasting results for the MDMA memory tests are similar in differences to those obtained for the methamphetamine comparison and may be due to the times when memory was tested or the chemical purity of the drug. This will be discussed later in the thesis. The different rates of drug metabolism and various individual differences in term of susceptibility to the drug effects may explain some the discrepancy in the results. The pattern of results would suggest that MDMA consumption reduces long-term visual and verbal memory performance, but may improve short-term memory performance.

The results obtained in the MDMA comparison may be the result of the higher levels of serotonin, dopamine and noradrenaline released following MDMA consumption. The action of these three neurotransmitters may have resulted in initial improvements in short-term memory of the threatening stimuli by increasing activity in the emotional processing circuit, while a sharp decrease and depletions in these neurotransmitters in the hours following consumption resulted in decreased long-term memory performance. The sharp increase in serotonin in particular would have been expected to have had a more significant impact on emotional responsiveness to the threatening stimuli, but due to the induced positive mood state, significant changes may only be evident for the positive pictures. The implications of these results are in direct opposition to those obtained for the methamphetamine comparison and suggest that MDMA has no effect on affective reactions to trauma-related information but may inhibit memory for visual trauma-related information. These implications should be interpreted with caution as they are based on trends observed in the data and need to be repeated with a larger sample size to confirm if any significant differences exist.
4.9 Processing speed in the MDMA comparison.

There were no significant differences evident between the MDMA and placebo conditions for reaction times to the threat words in the LDT. Participants attended and responded to the threat words in a similar amount of time when intoxicated with MDMA and when in the placebo condition. This suggests that the memory results obtained are not the result of faster orientating and responding to the stimuli.

4.10 Gender, anxiety sensitivity, estimated IQ, trauma experience and blood plasma levels.

Results failed to reveal any significant covariance between any of the results obtained and Anxiety Sensitivity or estimated IQ. There was also no covariance between gender and the obtained results, despite research suggesting alcohol had differing effects on males and females (Van Tilburg & Vingerhoets, 2002). Although no predictions were forwarded regarding these factors, the failure to obtain any significant covariance may indicate these variables were unlikely to have influenced the results obtained in this research.

The current study excluded individuals from participating if they were showing severe symptoms of PTSD. These individuals were excluded as it was predicted to have an impact on the results obtained. Individuals who had experienced a trauma in the past but were not showing any post-traumatic symptoms were included in the analyses. The experience of trauma was then investigated as a covariate to determine if a past trauma history had a relation to the results obtained. However as relatively few individuals in the sample had ever experienced a trauma the measure was unable to be included in the analyses. Further research could benefit from including a sample of participants with a
trauma history to determine the impact this variable may have on trauma processing and memory.

The blood plasma levels for the methamphetamine comparison varied significantly between participants. Furthermore, two participants had levels so low they were classified as not detected. This was despite several repeated tests of the blood samples and a calculation of doses based on height and weight. The blood plasma levels did not co-vary with any obtained results, but the variability in the blood plasma levels and the low levels of the drug after three hours may help to explain why no significant differences were obtained. It is possible that the dose of methamphetamine administered to participants was not large enough to induce significant changes in cognitive functioning. This will be discussed later in this section.

The blood plasma levels for the MDMA comparison were more consistent and produced blood plasma levels within the expected range. This suggests that the single dose of 100mg had similar absorption and distribution rates between participants. The limitation of using a single dose for all participants meant variability between absorption and metabolism of the drug was evident between participants and may have impacted on the results obtained. However, this does not appear to be supported by the blood data, with no covariance evident between the blood levels of MDMA and any of the results obtained.

4.11 The biological model of PTSD

One of the most currently accepted models of PTSD, describe it as a disorder of memory (Vaiva et al., 2003). According to this model, a traumatic event stimulates the release of central catecholamines that cause an over-consolidation of memory for the event. The result is a deeply engraved and primed traumatic memory that is then
clinically expressed in the form of PTSD symptoms (Foa, Steketee, & Rothbaum, 1989; Vaiva et al., 2004). Based on this model, the current study predicted that alcohol intoxication would decrease trauma processing and memory due to depressant induced inhibition in this memory circuit. This was believed to indicate that individuals who were exposed to a trauma when they were intoxicated were at a lowered risk of developing PTSD. Methamphetamine and MDMA was expected to increase trauma processing and memory due to the stimulant induced excitation in this memory circuit. This was believed to indicate that individuals who had consumed stimulants and were exposed to a trauma were at an increased risk of developing PTSD.

The current findings suggest alcohol alters affective reactions to traumatic stimuli, reducing the arousal level and impairing threat estimation. Alcohol also has an inhibiting effect on the memory systems responsible for the storage and retrieval of such stimuli. The current findings do not appear to support recent research that suggested stimulant induced adrenergic activation in the emotional memory circuit would enhance trauma processing and memory. Methamphetamine consumption appears to increase visual memory for emotional stimuli in general, but may impair short-term memory for verbally stored trauma-related stimuli, while enhancing long-term memory for such stimuli. MDMA consumption may temporarily improve short-term memory for trauma-related stimuli, but appears to reduce long-term visual and verbal memory. This effect appears specific to threat visual stimuli with memory for emotional stimuli in general remaining intact. Research is still yet to determine the specific action of MDMA, and it is unclear what effects the stimulant and hallucinogenic properties of the drug would have on cognitive functions.
4.12 Contrasting theories of PTSD development

The current study is based upon the assumption that the dysfunctional memory storage model is correct (Pitman, 1989). According to this model, PTSD results from a side-effect of naturally occurring and adaptive processes of memory storage. In contrast there are several opposing theories to the one proposed by Pitman, with alternative drug agents suggested as possible therapeutic interventions. For example, the neurophysiological kindling model of PTSD suggests anti-kindling agents such as antiepileptics may have preventative and therapeutic value (Iancu, Rosen, & Moshe, 2002). The stress-induced neurotoxicity model suggests drugs that block hippocampal neuron damage, such as selective serotonin re-uptake inhibitors, may be useful in preventing PTSD (Conrad et al., 1996). No controlled trials have taken place with any of the drugs mentioned so the correct model for PTSD remains unresolved.

4.13 Variables explaining the obtained results

In explaining the failure of the current study to support the hypotheses for affective reactions and long-term memory for the threat stimuli, several explanations are possible. First, the experimental tasks used in the study were most likely incapable of inducing the level of trauma and emotional processing required to accurately determine whether alcohol, methamphetamine and MDMA would pose a significant protection against, or risk for, later developing PTSD. During the final testing session, when asked how distressing they found the experimental stimuli, the majority of participants felt the experience did not significantly differ from everyday experiences such as watching a movie or news report. The definition of a traumatic event, however, involves an event that departs from everyday life and involves an intense level of stress (American Psychiatric Association, 2000). Therefore, it can be argued that the current study was
unable to truly test the hypotheses formulated, because the stress induced by the experimental tasks was not high enough. The IAPS and LDT paradigms are commonly used measures for generating emotional reactions in individuals, however other methods used in research include the stressful film paradigm, in which participants are asked to watch a traumatic film (Devilly & Varker, 2008; Lazarus, Opton, Nomikos, & Rankin, 1965). These alternative methods of simulating a traumatic experience may be useful to include in further research.

The method for assessing emotional reactions to the trauma-related pictures in the IAPS Task was based on the empirically supported approach of including valence and arousal bipolar dimensions (Russell & Carroll, 1999). However, recent research suggests that these two bipolar dimensions may not fully account for all emotional reactions and responses (Watson & Tellegen, 1999; Yik, Russell, & Barett, 1999). Research has found that the correlations between positive and negative feelings can vary substantially based upon the descriptions used in the measures, as well as measurement error. These variables were controlled for as much as possible by using a standardised measurement tool to assess affective reactions in the current study.

This was the first time a randomised controlled trial had attempted to administer a CNS depressant drug or stimulant drug in order to determine the effect on emotional processing and memory. Therefore, there was no previous research upon which to base our power analysis. However, all non-controlled research studies had found at least a moderate effect for stimulants on later trauma processing (Zatzick et al., 2002). Controlled research examining the effect of alcohol on information processing had found a moderate to large effect size (Grattan-Miscio & Vogel-Sprott, 2005). Therefore, we estimated that in a controlled environment with regulated doses of drugs, we would
obtain a moderate to large effect between the experimental and placebo conditions for each of the three drug types. With a sample size of 20 participants for each drug condition and alpha set at 0.05, and assuming an effect size of 0.65, we would derive a power of 0.8. The within subjects power would be much higher. However the results of the research suggest that if significant differences do exist between drug and placebo conditions, they are likely to be minimal. Therefore in order to determine if true differences do in fact occur, a much large sample size will be needed in future replications of the current research design.

An additional variable that may explain the results obtained is the dose and type of methamphetamine and MDMA administered to participants. Research suggests that the cognitive changes produced as a result of methamphetamine and MDMA intoxication are dose dependent (Wiegmann et al., 1996). The doses used in the current study were most likely less than is usually consumed during recreational use. For example, research indicates doses of methamphetamine consumed for recreational purposes can range from 75 to 125mg (Cami et al., 2000). The dose used in the current study was only about 40 to 45mg, having been limited by ethical concerns. Consistent with this explanation, the participants frequently commented that they were unsure whether they had been administered the placebo or methamphetamine and the blood results varied significantly, with some levels so low they were classified as not detected. Additionally, in the methamphetamine and MDMA comparisons, the drugs were administered immediately before participants were tested for their delayed recall and recognition in the second experimental condition. Although it was assumed the drugs would not have been absorbed and impacting on cognition in such a short period of
time, there is also a possibility that for some participants the drug may have influenced memory recall.

The chemical purity of the drugs used in the current research was of a high standard, however the chemical purity of drugs taken within a recreational setting are often of a lower chemical purity and contain other chemical compounds that may significantly alter cognitive functioning. This may explain the failure of the current research to replicate past research in which recreational doses of methamphetamine and MDMA were examined. It would be beneficial to compare the amphetamines used in the current study with samples obtained in recreational settings to compare the chemical compounds in each. Furthermore, in recreational settings a cocktail of drugs is often consumed, for example methamphetamine and alcohol together. Further research should also endeavour to directly compare the different drugs and examine the results following consumption of a combination of drugs. The current research did directly compare the effects of MDMA and methamphetamine, however these results were beyond the scope of the current thesis.

An additional variable that may explain the failure to support the hypotheses is the timing of the cognitive tests. It was decided that testing would occur after 180 minutes had elapsed as methamphetamine and MDMA both reach peak plasma levels between 2-3 hours after consumption. However, methamphetamine has a longer range of action than MDMA and it may have been beneficial to test participants in the Methamphetamine comparison after a longer period of time, with participants in the MDMA tested at an earlier time. Many participants in the MDMA comparison reported to the experiment in the de-briefing session that they felt they reached the peak period after only 2 hours and by the end of the 3 hour testing time felt the drug was no longer
having a significant impact. Although the research conducted by Zatzick and colleagues (2002) was unable to examine the amount of drug consumed by the participants, because it involved recreational use, it was most likely higher than the dose given in the current study. Furthermore, participants in the current study spent the testing sessions seated in their chairs, which may have had an unknown effect on the drug effects. Future research may need to administer a dose typical of normal recreational use and have participants engage in more physical activity in order to obtain a more realistic drug effect.

The IAPS Task and LDT were designed to induce a sense of stress or arousal following the presentation of the threat stimuli. However, some research has suggested that stress, such as that induced in the current study, may reduce rather than enhance the effects of drugs in both animals and humans (Söderpalm, Nikolayev & De Wit, 2003; Stone et al., 2002). Studies have found that acute pain, disturbing films and social stress can decrease the subjective responses to alcohol or methamphetamine (Breslin, Hayward, & Baum, 1994; Garlind et al., 1960; Söderpalm & De Wit, 2002; Söderpalm et al.). These reports, although preliminary and based on subjective self-reports, may explain the results obtained. It is possible that some as yet unknown factor, such as a hormonal or neurochemical mechanism triggered by the stressful words or images presented in the study, may have dampened the effects of the drugs for stressful stimuli only.

Finally, it must be noted that the research conducted by Zatzik and colleagues (2002), was the first of its kind and was only able to examine the effect amphetamine had on PTSD symptoms in 16 individuals. Furthermore, the dose, time of consumption, and type of trauma experienced were all un-controlled. The preliminary research
examining the effects alcohol has on affective reaction and memory had better sample sizes and a larger knowledge base of similar research. Therefore, despite theoretical models and additional drug research supporting the hypothesised role stimulants may play in emotional processing and memory, the current results add weight against the preliminary results of Zatzick et al. (2002). Numerous psychological and physical characteristics have been identified as risk factors for developing PTSD (see for example Brewin & Holmes, 2003). It may have been one of these factors or several individual factors together, such as personality type and drug use that caused the increased PTSD symptoms noted in the research conducted by Zatzick and colleagues.

It is clear from the results obtained, and from that of past research that alcohol has direct inhibiting effects on memory for trauma-related information and may help to explain why individuals who were drunk when they experienced a trauma were at a lowered risk of later developing PTSD. The results may also help to explain why there is a high rate of alcohol abuse among PTSD patients, not just for the sedating effects of the drug, but because the drug may inhibit memory retrieval and re-consolidation. Although it is tempting to conclude that stimulants would therefore enhance processing and memory of trauma-related stimuli, the mechanisms by which stimulants influence cognitive processes are most likely far more complex and variable than was suggested by preliminary research. For example several studies have found that the effects of consuming a stimulant such as methamphetamine vary between individuals with varying degrees of anxiety sensitivity (Stewart & Kushner, 2001). Although measured in the current study, this variable was not addressed in the research conducted by Zatzick and colleagues (2002).
A number of limitations should be noted. First, as discussed above, cell sizes were small and many of the comparisons had less than $50\%$ chance of detecting a significant difference. It is possible that with a larger sample size, a significant difference between the drug and placebo conditions would have been evident. It is suggested future research should attempt to test a sample size of at least 50 or more in order to ensure greater confidence in any results obtained.

The counterbalancing and randomisation of the experimental stimuli was a strength of this study. However, it meant that due to the nature of the randomisation process there was an equal balance between the word and picture types participants completed in each condition. For example, when randomised to Word Set 1, they were also randomised to Picture Set 2. Although precautions were taken to ensure the word and picture sets were as similar as possible, it is still possible that the results obtained were influenced somewhat by the type of list or picture set completed. Future research should endeavour to ensure there is an equal division between the numbers of participants that receive each list type in each condition.

The recognition test used to test the long-term memory for the pictures shown in the IAPS task was administered on pieces of paper rather than a computer screen. Because the participants had originally viewed the pictures on a computer screen it is possible that the recognition was poorer when the pictures were presented on paper rather than the computer screen. In future, the recognition test should be presented on the computer screen in order to ensure the medium of presentation remains consistent.

Although the current study attempted to control for the level of anxiety sensitivity in the participants, this was only assessed with a self-report measure. It may have been necessary to use a different measure in order to ensure that the level of anxiety sensitivity was accurately controlled.
have been beneficial to include physiological measures such as the galvanic skin response or heart rate during the experimental sessions, in order to obtain an objective measure of induced anxiety in the participants while they were completing the experimental tasks. Furthermore, although the ASI is a reliable tool for assessing anxiety sensitivity, it may also have been beneficial to administer a state/trait anxiety measure, as the participant’s anxiety state at each testing session may have varied.

There is strong evidence that attention affects both early and late stages of perception, influencing processing and memory (Driver & Mattingley, 1995). Because the drugs in the current study were administered before the learning, the analysis of memory was complicated by the fact that the drugs may have indirectly influenced learning and memory by affecting attention, motivation and arousal levels (Ferry et al., 1999). Future research could benefit from administering the drugs believed to enhance or inhibit memory both before and after learning has taken place. This would allow the experimenter to determine whether any enhanced or reduced memory for trauma-related information was due to the drug effects at consolidation or encoding.

The current study was based on the assumption that memory and arousal mechanisms active during the acute stress response are directly related to the maintenance of chronic PTSD. However some research exists that suggests that the mechanisms active during the acute stress response are not related to the development of chronic PTSD. Research conducted by McFarlane, Weber and Clark (1993) found a diminished P300 Evoked Response Potential in PTSD patients following the presentation of a three tone auditory discrimination task. This finding suggested that a noradrenergic mechanism underpins PTSD patients’ difficulty evaluating the significance or relevance of information presented. It may be the case that some other
mechanism activated at the time of the acute stress response is related to the later
development and maintenance of chronic PTSD (Difede & Barocas, 1999).

Finally, it is also important to note that although the testing paradigms were
based on empirically supported measures, the ecological validity of the measures used
to induce a trauma response in participants was low. The stimuli used were highly
unlikely to induce the same sort of stress response seen in individuals who are exposed
to a traumatic event and experience a physiological and psychological traumatic stress
response. For this reason, the results of the current study should be interpreted with
cautions.

4.15 Conclusions and future research directions

In conclusion, the results obtained supported some of the hypotheses
that predicted alcohol intoxication would reduce trauma processing and memory. The
results failed to support all the hypotheses that predicted stimulants would excite the
brain circuit responsible for responding and storing traumatic memories. The failure to
support the stimulant hypotheses may be due to the low power of the design and it is
possible that with a larger sample the expected results would be significant. The
methodology implemented in the study was unable to truly simulate the presentation of
traumatic stimuli, and the dose of stimulants used was probably lower than is consumed
in recreational use. Furthermore, some research suggests a stressful experience such as
that implemented in the current study can dampen subjective responses to drugs and the
timing of the testing may have meant the drug effects had worn off or not reached peak
levels when participants were tested. Yet despite these possible explanations, it may be
that stimulants such as methamphetamine and MDMA are unlikely to have a large
impact on an individuals’ risk of later developing PTSD. Future research may benefit
from an examination of other forms of stimulants such as cocaine, as was also examined in the research conducted by Zatzick and colleagues (2002).

Future research should also examine the effect all three drugs have on processing and memory for positive emotional stimuli. A preliminary examination of the results obtained in the current study suggests that the drugs tended to improve memory for positive words and pictures. Several reasons for these improvements could be possible. A positivity bias with selective attention and memory for positive information may have occurred (Tops et al., 2004). Alternatively participants may have recalled a greater number of positive words and pictures because it was congruent with the positive mood induced by consumption of the drugs.

The results of the current study should prompt continued research into the role trauma processing and memory may play in the pathogenesis of PTSD. Future research should also endeavour to examine the effect medications used in the treatment of PTSD have on trauma processing and memory. Many PTSD patients are routinely prescribed anti-depressants and anti-anxiety drugs to help reduce PTSD symptoms and associated depression (Foa, Davidson, & Frances, 1999). The results of such an investigation would also contribute to the research knowledge regarding the biological memory circuit believed to be involved in the manifestation of PTSD symptomatology.

Research would suggest that the neurobiological changes believed to contribute to the symptoms of PTSD may permanently sensitise the emotional processing system, with treatment and recovery made more difficult (Morgan, Krystal, & Southwick, 2003). For this reason identifying factors that influence a person’s chance of developing PTSD means early interventions and preventative measures may be implemented
with the hope of improving the outcomes following potentially traumatic events.
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**GLOSSARY**

*Adrenergic*. The term used to describe a neuron that responds to the neurotransmitters Noradrenaline or Adrenaline.

*Agonists*. A drug that binds to a receptor and activates it.

*Alpha-adrenergic receptor*. A receptor in the Noradrenergic system.

*Amygdala*. A collection of neural structures in the temporal lobe of the limbic brain that controls many aspects of emotional and social behaviour.

*Antagonists*. A drug that binds to a receptor and inhibits it.

*Anterior cingulate cortex*. Provides an inhibiting function and is involved in a wide range of autonomic functions including modulating the response to stress.
Anti-adrenergic agents. An agonist with a site of action that results in the inhibition of adrenergic receptor activity.

Anxiolytic. A treatment for anxiety.

Beta-adrenergic (β-adrenergic). A receptor in the Noradrenergic system.

Beta-blocker. A drug that binds to Beta-adrenergic receptors and inhibits its action.

Catecholamines. The term used to describe a group of neurotransmitters including Dopamine, Noradrenaline and Adrenaline.

Clonidine. An agonist that binds to auto-receptors in the Noradrenergic system, causing decreased activity.

Down-regulation. The decrease in the ability of a neurotransmitter to bind to a receptor due to a reduction in the number or sensitivity of receptors following flooding of a pharmacological or physiological substance.

Enkephalines. The brain’s opiate neuropeptides involved in regulating pain.

GABA receptors. The main inhibitory neurotransmitters in the central nervous system.
Glucocorticoid. Any steroid produced by the adrenal gland that is primarily involved in protein, fat and carbohydrate metabolism and glucose regulation.

Glutamate receptors. The main excitatory neurotransmitters of the central nervous system.

Hippocampus. Responsible for learning, sorting and storing memories.

Locus Coeruleus. Site that contains a large number of noradrenergic neurones and has projections to several brain regions including the amygdala, hippocampus, cingulate, entorhinal and orbitofrontal cortex.

Long-term potentiation. The most accepted model of long-term memory storage.

Nadolol. A beta-blocker incapable for crossing the blood brain barrier.

Neuromodulator. A compound that influences either the release of a neurotransmitter from a neuron or a neuron’s response to a neurotransmitter.

Post-traumatic Stress Disorder (PTSD). PTSD is a condition that results from exposure to a traumatic stressor that involves the actual or threatened death or injury of the individual. The response to the stressor must involve intense fear, horror or helplessness, with symptoms present for at least one month. The
disturbances caused by the condition must cause significant distress or clinically impair normal functioning of the individual.

*Propranolol.* An agonist that binds to the auto-receptors in the Noradreneric system, causing decreased activity in the Noradrenergic system. Also referred to as an Anti-adrenergic agonist.

*Reconsolidation.* The dynamic process of retrieving and storing events in memory.

*Reticular activating system.* System of the brain stem responsible for maintaining arousal and integrative control of higher order functions.

*Serotonin.* Involved in the regulation of mood states, including depression and anxiety. It is also thought to be involved in food intake, emotion, pain, sleep and impulsive behaviours.

*Synaptic plasticity.* The term used to describe short and long term changes in a neuron’s excitability and morphology.

*Yohimbine.* An antagonist that binds to Alpha-receptors in the Noradrenergic system that function as inhibiting auto-receptors, resulting in increased activity in the Noradrenergic system.
APPENDIX 1

Demographic and drug use information for participants in the alcohol, methamphetamine and MDMA comparison.
Table 1
Demographic information for participants in the alcohol comparison

<table>
<thead>
<tr>
<th>Participant Number</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Education level</th>
<th>Handedness</th>
<th>Smoker</th>
<th>Alcohol (drinks/week)</th>
</tr>
</thead>
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<tr>
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<td>Female</td>
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<td>10</td>
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<tr>
<td>2</td>
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<td>5-10</td>
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<td>Undergraduate degree</td>
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<td>Yes</td>
<td>2-3</td>
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<tr>
<td>4</td>
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<td>Both</td>
<td>Yes</td>
<td>4-8</td>
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<tr>
<td>5</td>
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<td>TAFE Diploma</td>
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<td>Yes</td>
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<tr>
<td>6</td>
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<td>Private Pilot licence</td>
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<td>Yes</td>
<td>10</td>
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<td>7</td>
<td>26</td>
<td>Female</td>
<td>Undergraduate degree</td>
<td>Left</td>
<td>Yes</td>
<td>8</td>
</tr>
<tr>
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<td>Male</td>
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<td>Right</td>
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<td>&gt; 3</td>
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<td>Year 12</td>
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<td>17</td>
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<td>Female</td>
<td>Postgraduate degree</td>
<td>Left</td>
<td>No</td>
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*Note. NA, Not Applicable, NR, No Response*
<table>
<thead>
<tr>
<th>Cannabis (these days)</th>
<th>Cannabis (most)</th>
<th>Cannabis time use</th>
<th>Ecstacy (these days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rarely (shared joint)</td>
<td>Rarely (shared joint)</td>
<td>No answer</td>
<td>Less than monthly (1-3)</td>
</tr>
<tr>
<td>Rarely (THC study)</td>
<td>Monthly (1 joint)</td>
<td>No answer</td>
<td>Bi-monthly</td>
</tr>
<tr>
<td>1-2 times yearly</td>
<td>1-2 times yearly</td>
<td>No answer</td>
<td>Monthly</td>
</tr>
<tr>
<td>Monthly (1/2 cookie)</td>
<td>Daily (2 bongs)</td>
<td>1.5 years</td>
<td>6-monthly (1/2-1 tablet)</td>
</tr>
<tr>
<td>Less than weekly (one joint)</td>
<td>Daily (4 bongs)</td>
<td>12 years</td>
<td>6-monthly</td>
</tr>
<tr>
<td>Never</td>
<td>Weekly (2 bongs)</td>
<td>4 years</td>
<td>Monthly (every1-2 months, one tablet)</td>
</tr>
<tr>
<td>Monthly (one joint monthly)</td>
<td>Daily (1/2 gram - 6-8 bongs)</td>
<td>2 years</td>
<td>3-monthly (one tablet)</td>
</tr>
<tr>
<td>Other</td>
<td>Daily (8 bongs)</td>
<td>2 years regularly, 6 years ago</td>
<td>6-monthly</td>
</tr>
<tr>
<td>Yearly, if at all</td>
<td>Weekly (2 grams over weekend)</td>
<td>Occasionally-4 years, Often-8 months</td>
<td>Yearly (one tablet)</td>
</tr>
<tr>
<td>Monthly (one joint)</td>
<td>Less than weekly (1-2 joints)</td>
<td>7 years</td>
<td>6-monthly (one tablet)</td>
</tr>
<tr>
<td>Other</td>
<td>Monthly</td>
<td>10 years</td>
<td>6-monthly (1-2 tablets)</td>
</tr>
<tr>
<td>Other (one joint)</td>
<td>Weekly</td>
<td>4 years</td>
<td>Other (none in last year)</td>
</tr>
<tr>
<td>Monthly (one joint)</td>
<td>Daily (10 bongs)</td>
<td>6 months</td>
<td>Other (every couple of months, 1/2 tablets)</td>
</tr>
<tr>
<td>Never</td>
<td>Months ago (not sure)</td>
<td>once</td>
<td>Never</td>
</tr>
<tr>
<td>few times a year (few bongs)</td>
<td>Months ago</td>
<td>1 year</td>
<td>Never</td>
</tr>
<tr>
<td>Never</td>
<td>NA</td>
<td>NA</td>
<td>Never</td>
</tr>
<tr>
<td>Never</td>
<td>years ago(1/2 joint)</td>
<td>rarely, once or twice.</td>
<td>Never</td>
</tr>
<tr>
<td>Never</td>
<td>NA</td>
<td>NA</td>
<td>Never</td>
</tr>
<tr>
<td>Never</td>
<td>Twice (one puff)</td>
<td>1 week</td>
<td>once every 2-3 months</td>
</tr>
<tr>
<td>2 months ago</td>
<td>3-4 times a year (1/2 joint)</td>
<td>7 years</td>
<td>2 years ago</td>
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</tbody>
</table>

*Note.* NA, Not Applicable, NR, No Response
<table>
<thead>
<tr>
<th>Ecstasy (most)</th>
<th>Ecstasy time use</th>
<th>Cocaine (these days)</th>
<th>Cocaine (most)</th>
</tr>
</thead>
<tbody>
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<td>Weekly (2-3)</td>
<td>Approx. 3 yrs</td>
<td>Only 4 times</td>
<td>No answer</td>
</tr>
<tr>
<td>Monthly (1 tablet)</td>
<td>5 yrs</td>
<td>Once</td>
<td>Once</td>
</tr>
<tr>
<td>Weekly</td>
<td>3 yrs</td>
<td>6-monthly</td>
<td>Monthly</td>
</tr>
<tr>
<td>Weekly (2 tablets)</td>
<td>2 years</td>
<td>Yearly (one line)</td>
<td>Monthly (3 lines)</td>
</tr>
<tr>
<td>6-monthly</td>
<td>2 years</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Weekly (every 1-2 weeks, one tablet)</td>
<td>4.5 years</td>
<td>Other (Never)</td>
<td>Twice</td>
</tr>
<tr>
<td>Weekly (3 tablets)</td>
<td>4 years</td>
<td>Other (Never)</td>
<td>6-monthly (one point)</td>
</tr>
<tr>
<td>Weekly</td>
<td>3 years</td>
<td>6-monthly (one line)</td>
<td>Monthly (2 lines)</td>
</tr>
<tr>
<td>Monthly (3-4 tablets)</td>
<td>2 years</td>
<td>Not in last 12 months</td>
<td>3 occasions (1-3 lines each time)</td>
</tr>
<tr>
<td>Monthly (one tablet)</td>
<td>2 years</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Monthly and Weekly (2-4 tablets)</td>
<td>No answer</td>
<td>Other (1/4 line)</td>
<td>Other (1/4 line)</td>
</tr>
<tr>
<td>Monthly (2-3 tablets)</td>
<td>3 years</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Weekly (6 tablets)</td>
<td>6 months</td>
<td>6-monthly (one line)</td>
<td>6-monthly (one line)</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>Never</td>
<td>NA</td>
</tr>
<tr>
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<td>Never</td>
<td>NA</td>
</tr>
<tr>
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<td>NA</td>
<td>Never</td>
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</tr>
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<td>NA</td>
<td>Never</td>
<td>NA</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>Never</td>
<td>NA</td>
</tr>
<tr>
<td>Monthly (2 tablets)</td>
<td>3 years</td>
<td>Never</td>
<td>Once(3 points)</td>
</tr>
<tr>
<td>twice ever(1/2 tablet)</td>
<td>1 years</td>
<td>Never</td>
<td>NA</td>
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*Note.* NA, Not Applicable, NR, No Response
<table>
<thead>
<tr>
<th>Cocaine time use</th>
<th>Amphetamine (these days)</th>
<th>Amphetamine (most)</th>
<th>Amphetamine time use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-regular user</td>
<td>6-monthly ( 1-2 lines)</td>
<td>Weekly (1- 2 points)</td>
<td>5 months</td>
</tr>
<tr>
<td>Once</td>
<td>Nil</td>
<td>6-monthly ( 1 line)</td>
<td>5 years</td>
</tr>
<tr>
<td>2 yrs</td>
<td>Yearly</td>
<td>Yearly</td>
<td>1 year</td>
</tr>
<tr>
<td>one year</td>
<td>Yearly (one line)</td>
<td>6-monthly (2 lines)</td>
<td>1 yr</td>
</tr>
<tr>
<td>N/A</td>
<td>Monthly</td>
<td>Monthly</td>
<td>7 years</td>
</tr>
<tr>
<td>Didn't really use it</td>
<td>Monthly (every 2 months, 1/2 point)</td>
<td>Monthly (every 1-2 months, 1 point)</td>
<td>4 years</td>
</tr>
<tr>
<td>Unsure</td>
<td>6-monthly (one point, 2-3 lines)</td>
<td>Weekly (1 point)</td>
<td>4 years</td>
</tr>
<tr>
<td>In 1996-first time-never regular</td>
<td>Never</td>
<td>Monthly (2 lines)</td>
<td>3 years</td>
</tr>
<tr>
<td>2 years</td>
<td>6-monthly (3 points)</td>
<td>6-monthly (1-3 points)</td>
<td>4 years</td>
</tr>
<tr>
<td>N/A</td>
<td>6-monthly (one line)</td>
<td>6-monthly (1-2 lines)</td>
<td>3 years</td>
</tr>
<tr>
<td>Only taken once- 3 years ago</td>
<td>6-monthly (one line)</td>
<td>6-monthly (1 line)</td>
<td>3 years</td>
</tr>
<tr>
<td>N/A</td>
<td>Other</td>
<td>Yearly (1 line)</td>
<td>Only one time</td>
</tr>
<tr>
<td>Very rare - when it's offered</td>
<td>Other (fortnightly, 3 points)</td>
<td>Weekly (1 gram)</td>
<td>One year</td>
</tr>
<tr>
<td>NA</td>
<td>Never</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
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<td>Never</td>
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</tr>
<tr>
<td>NA</td>
<td>Never</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>1 week</td>
<td>once every 2-3 months</td>
<td>monthly(3 points)</td>
<td>3 years</td>
</tr>
<tr>
<td>NA</td>
<td>Never</td>
<td>NA</td>
<td>NA</td>
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</table>

Note. NA, Not Applicable, NR, No Response
Table 1

**Demographic information for participants in the alcohol comparison**

<table>
<thead>
<tr>
<th>Heroin use (these days)</th>
<th>Heroin use (most)</th>
<th>Heroin time use</th>
<th>Inhalants (these days)</th>
<th>Inhalants (most)</th>
<th>Inhalants time use</th>
</tr>
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<tbody>
<tr>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Once</td>
<td>Once (1 hit)</td>
<td>only once</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Monthly (3 inhale)</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>One year</td>
</tr>
<tr>
<td>6-monthly (few pipes of smack)</td>
<td>Monthly (few pipes of smack)</td>
<td>Had it six times</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Not at all</td>
<td>Weekly (2 boxes of bulbs)</td>
<td>4 years</td>
</tr>
<tr>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<td>Never</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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</table>
| Note. NA, Not Applicable, NR, No Response
Table 2

Demographic information for participants in the methamphetamine comparison

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Education level</th>
<th>Handedness</th>
<th>Smoker</th>
<th>Amount (cigarettes/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>Female</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Left</td>
<td>Yes</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Left</td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Both</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>22</td>
<td>Female</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>24</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>23</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>6</td>
</tr>
<tr>
<td>9</td>
<td>28</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>25</td>
</tr>
<tr>
<td>10</td>
<td>24</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>5-10</td>
</tr>
<tr>
<td>12</td>
<td>27</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>6-8</td>
</tr>
<tr>
<td>13</td>
<td>24</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>30</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>15</td>
<td>25</td>
<td>Male</td>
<td>Post-graduate</td>
<td>Right</td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>16</td>
<td>34</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>17</td>
<td>24</td>
<td>Female</td>
<td>Post-graduate</td>
<td>Left</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>18</td>
<td>21</td>
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<td>Secondary</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
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<td>19</td>
<td>22</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
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<td>NA</td>
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<td>20</td>
<td>23</td>
<td>Female</td>
<td>Secondary</td>
<td>Right</td>
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</tr>
<tr>
<td>21</td>
<td>23</td>
<td>Female</td>
<td>Post Graduate</td>
<td>Right</td>
<td>Yes</td>
<td>when drinking alcohol</td>
</tr>
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</table>

Note. NA, Not Applicable, NR, No Response
<table>
<thead>
<tr>
<th>Coffee</th>
<th>Amount (cups/day)</th>
<th>Frequency (Alcohol)</th>
<th>Alcohol (drinks/week)</th>
<th>How often needed drink in morning</th>
<th>How long drinking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times week</td>
<td>2-3</td>
<td>Never</td>
<td>13 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times week</td>
<td>6</td>
<td>Never</td>
<td>14 years</td>
</tr>
<tr>
<td>Yes</td>
<td>12</td>
<td>2-3 times a month</td>
<td>6</td>
<td>Never</td>
<td>Since age 14</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times week</td>
<td>8</td>
<td>Never</td>
<td>10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times week</td>
<td>8-10</td>
<td>Never</td>
<td>10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>2-3 times a month</td>
<td>6</td>
<td>Never</td>
<td>6 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times week</td>
<td>6-8</td>
<td>Never</td>
<td>9-10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1-2</td>
<td>Daily</td>
<td>6</td>
<td>Never</td>
<td>8 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>1-2 times week</td>
<td>3</td>
<td>Once a year</td>
<td>12 years</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>1-2 times week</td>
<td>1-2</td>
<td>Never</td>
<td>Since age 18</td>
</tr>
<tr>
<td>Yes</td>
<td>2-3</td>
<td>Daily</td>
<td>2-3</td>
<td>Never</td>
<td>12 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times week</td>
<td>4-6</td>
<td>Never</td>
<td>13 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times week</td>
<td>1-2</td>
<td>Never</td>
<td>7 years</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>1-2 times a week</td>
<td>2-4</td>
<td>Never</td>
<td>14 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>1-2 times a week</td>
<td>10</td>
<td>Never</td>
<td>10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>3-5 times a week</td>
<td>1-2</td>
<td>Never</td>
<td>17 years</td>
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<td>2</td>
<td>1-2 times a week</td>
<td>2</td>
<td>Never</td>
<td>8 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2 week</td>
<td>1-2 times a week</td>
<td>10</td>
<td>Never</td>
<td>5 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times week</td>
<td>3-4</td>
<td>Never</td>
<td>6 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>daily</td>
<td>1-3</td>
<td>Never</td>
<td>3 years</td>
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<tr>
<td>Yes</td>
<td>NR</td>
<td>1-2 times a week</td>
<td>6</td>
<td>twice</td>
<td>8 years</td>
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Note. NA, Not Applicable, NR, No Response
<table>
<thead>
<tr>
<th>Consume Cannabis</th>
<th>Last time consumed Cannabis</th>
<th>Frequency (Cannabis)</th>
<th>Amount (Cannabis)</th>
<th>How long (Cannabis)</th>
<th>Consume Amphetamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once-twice a year</td>
<td>One joint</td>
<td>2-3 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>One day ago</td>
<td>Once-twice a week</td>
<td>2 pipes</td>
<td>14 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>1-2 times a week</td>
<td>6-8 bongs</td>
<td>Since 14 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>2 joints</td>
<td>6 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 week ago</td>
<td>1st time in 6 years</td>
<td>1 joint</td>
<td>3 years</td>
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</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>Once a month</td>
<td>1 joint</td>
<td>4 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>Once a month</td>
<td>2 joints</td>
<td>6 years</td>
<td>Yes</td>
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<tr>
<td>Yes</td>
<td>Years ago</td>
<td>Once a year</td>
<td>1 joint</td>
<td>8 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>3 years ago</td>
<td>Once a year</td>
<td>1 joint</td>
<td>Couple of years</td>
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<tr>
<td>Yes</td>
<td>3 weeks ago</td>
<td>2-3 times a year</td>
<td>¼ joint</td>
<td>Since age 17</td>
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</tr>
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<td>More 1 week ago</td>
<td>2-3 times a month</td>
<td>1 joint</td>
<td>12 years</td>
<td>Yes</td>
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<tr>
<td>Yes</td>
<td>Days ago</td>
<td>Once a month</td>
<td>1 joint</td>
<td>10 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>1-2 times a week</td>
<td>2-3</td>
<td>Since age 10</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>occasionally</td>
<td>couple of joints</td>
<td>6 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>1-2 times a week</td>
<td>3 joints</td>
<td>10 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Five years ago</td>
<td>Never</td>
<td>Part of a joint</td>
<td>5-7 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>Daily almost daily</td>
<td>1 joint</td>
<td>8 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>2 years ago</td>
<td>never since 2006</td>
<td>NR</td>
<td>2 months</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>more than a month ago</td>
<td>3-4 times a year</td>
<td>1 joint</td>
<td>5-6 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>more than a week ago</td>
<td>2-3 times a month</td>
<td>1/2 - 1 joint</td>
<td>2-3 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>days ago</td>
<td>3-4 times a year</td>
<td>one joint</td>
<td>2 years</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Note.* NA, Not Applicable, NR, No Response
Table 2

Demographic information for participants in the methamphetamine comparison

<table>
<thead>
<tr>
<th>Last time used consumed Amphetamines</th>
<th>Frequency</th>
<th>Amount</th>
<th>How long</th>
<th>Consumed MDMA</th>
<th>Last time consumed MDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>More 1 month ago</td>
<td>Every 2 months</td>
<td>2-3 lines</td>
<td>Every now and again</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Once-twice a year</td>
<td>5 points</td>
<td>12 years</td>
<td>Yes</td>
<td>One year ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Special occasion</td>
<td>1 point</td>
<td>Since age 17</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Once a month</td>
<td>2 lines</td>
<td>6 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Once a month</td>
<td>½ gram</td>
<td>8 years</td>
<td>Yes</td>
<td>2 months</td>
</tr>
<tr>
<td>2.5 years ago</td>
<td>Twice ever</td>
<td>1-2 lines</td>
<td>Twice in 2 years</td>
<td>Yes</td>
<td>4 months ago</td>
</tr>
<tr>
<td>2 years ago</td>
<td>Not very</td>
<td>1 point</td>
<td>2 months</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>6 times in 3 years</td>
<td>1 line</td>
<td>3 years</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>2 points</td>
<td>5 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
</tr>
<tr>
<td>More 1 year ago</td>
<td>Rarely, 3 times in life</td>
<td>1 line</td>
<td>Since age 18</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>Days ago</td>
<td>1-2 times a month</td>
<td>2 lines</td>
<td>12 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>1 point</td>
<td>8 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 2 years ago</td>
<td>Never</td>
<td>as much as available</td>
<td>5-6 years</td>
<td>Yes</td>
<td>more 2 years ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>NR</td>
<td>1-2 grams</td>
<td>3 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>3 points</td>
<td>7 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
</tr>
<tr>
<td>Three years ago</td>
<td>Twice a year</td>
<td>1/2 to one line</td>
<td>2 years</td>
<td>Yes</td>
<td>Six months ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Infrequently</td>
<td>1 line</td>
<td>5 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>6 months ago</td>
<td>Not any more</td>
<td>1 line</td>
<td>only tried once</td>
<td>Yes</td>
<td>10 months ago</td>
</tr>
<tr>
<td>more than a month ago</td>
<td>3-4 times a year</td>
<td>1+ lines</td>
<td>3-4 years</td>
<td>Yes</td>
<td>more than 1 month ago</td>
</tr>
<tr>
<td>3 years ago</td>
<td>hardly ever</td>
<td>NR</td>
<td>only once</td>
<td>Yes</td>
<td>more than a month ago</td>
</tr>
<tr>
<td>18 months ago</td>
<td>once a year</td>
<td>3 lines</td>
<td>2 years</td>
<td>Yes</td>
<td>7 months ago</td>
</tr>
</tbody>
</table>

*Note.* NA, Not Applicable, NR, No Response
Table 2

Demographic information for participants in the methamphetamine comparison

<table>
<thead>
<tr>
<th>How often</th>
<th>Amount (MDMA)</th>
<th>How long (MDMA)</th>
<th>Consume (MDMA)</th>
<th>Last time (Cocaine)</th>
<th>Frequency (Cocaine)</th>
<th>Amount (Cocaine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 2 months</td>
<td>1 tablet</td>
<td>Since age 19</td>
<td>Yes</td>
<td>More 1 year ago</td>
<td>Hardly ever</td>
<td>Five lines per night</td>
</tr>
<tr>
<td>Once a year</td>
<td>1-2 tablets</td>
<td>10 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once every 18 months</td>
<td>2 lines</td>
</tr>
<tr>
<td>Special occasion</td>
<td>1-2 tablets</td>
<td>Since age 21</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>When can afford it</td>
<td>1 point</td>
</tr>
<tr>
<td>Once a month</td>
<td>1-2 tablets</td>
<td>6 years</td>
<td>Yes</td>
<td>Ages ago</td>
<td>Very infrequent</td>
<td>1 point</td>
</tr>
<tr>
<td>Every 6 months</td>
<td>1/2-1 tablet</td>
<td>8 years</td>
<td>Yes</td>
<td>3 months</td>
<td>2-3 times a year</td>
<td>3 points</td>
</tr>
<tr>
<td>Once every 6 months</td>
<td>1 tablet</td>
<td>4 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Twice in 3 years</td>
<td>1 point</td>
</tr>
<tr>
<td>Not very</td>
<td>2 tablets</td>
<td>6 months</td>
<td>Yes</td>
<td>2 years ago</td>
<td>Not very</td>
<td>2 lines</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Once a month</td>
<td>1 tablet</td>
<td>10 years</td>
<td>Yes</td>
<td>2 years ago</td>
<td>Very rarely</td>
<td>2 lines</td>
</tr>
<tr>
<td>Other</td>
<td>1/4-1 tablet</td>
<td>Since age 18</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Once a month</td>
<td>1/2-2 tablets</td>
<td>13 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once every 2 months</td>
<td>2 lines</td>
</tr>
<tr>
<td>3-4 times per year</td>
<td>1-2 tablets</td>
<td>8 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>one rare occasions</td>
<td>1 line</td>
</tr>
<tr>
<td>never</td>
<td>2-26</td>
<td>5-6</td>
<td>Yes</td>
<td>more 5 years ago</td>
<td>never</td>
<td>1 gram</td>
</tr>
<tr>
<td>Randomly</td>
<td>lots</td>
<td>6 years</td>
<td>Yes</td>
<td>8 years ago</td>
<td>8 years ago</td>
<td>grams</td>
</tr>
<tr>
<td>Once a month</td>
<td>1-2 tablets</td>
<td>7 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Infrequently</td>
<td>2 grams</td>
</tr>
<tr>
<td>3-4 times per year</td>
<td>1/2 to 1 tablet</td>
<td>15 years</td>
<td>Yes</td>
<td>6 years ago</td>
<td>Rarely</td>
<td>1 gram</td>
</tr>
<tr>
<td>Infrequently</td>
<td>1 tablet</td>
<td>5 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Infrequently</td>
<td>1 gram</td>
</tr>
<tr>
<td>never now</td>
<td>2 tabs</td>
<td>18 months</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>4-5 months</td>
<td>1-2 tablets</td>
<td>3-4 years</td>
<td>Yes</td>
<td>more than a month ago</td>
<td>once a year</td>
<td>1 line</td>
</tr>
<tr>
<td>every few months</td>
<td>NR</td>
<td>4 years</td>
<td>Yes</td>
<td>3 years ago</td>
<td>used twice</td>
<td>NR</td>
</tr>
<tr>
<td>3 times a year</td>
<td>11/2 tabs</td>
<td>3 years</td>
<td>Yes</td>
<td>over a year ago</td>
<td>once every few months</td>
<td>2 lines</td>
</tr>
</tbody>
</table>

*Note. NA, Not Applicable, NR, No Response*
Table 2

*Demographic information for participants in the methamphetamine comparison*

<table>
<thead>
<tr>
<th>How long Consume (Cocaine)</th>
<th>Last time Consume (Heroin)</th>
<th>Frequency Consume (Heroin)</th>
<th>Amount Consume (Heroin)</th>
<th>How long Consume (Heroin)</th>
<th>Consume Inhalants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Five times in life</td>
<td>Yes</td>
<td>More 1 year ago</td>
<td>Twice</td>
<td>One pipe</td>
<td>Twice</td>
</tr>
<tr>
<td>10 years</td>
<td>Yes</td>
<td>More one month ago</td>
<td>Never-once</td>
<td>One hit</td>
<td>Once</td>
</tr>
<tr>
<td>Since age 24</td>
<td>Yes</td>
<td>Over one year</td>
<td>Hardly ever</td>
<td>One hit</td>
<td>Since age 30</td>
</tr>
<tr>
<td>4 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>5 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Twice in 3 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3 months</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>NA</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>5 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>NA</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>8 years</td>
<td>Yes</td>
<td>2-3 weeks ago</td>
<td>Once every 2 months</td>
<td>1 hit</td>
<td>6 years</td>
</tr>
<tr>
<td>can't calculate</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>not long</td>
<td>Yes</td>
<td>only once</td>
<td>never</td>
<td>1 point</td>
<td>only once</td>
</tr>
<tr>
<td>1 year</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>6 months</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3 months</td>
<td>No</td>
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<td>NA</td>
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<td>No</td>
<td>NA</td>
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<td>NA</td>
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<td>NA</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3-4 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>NR</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Note:* NA, Not Applicable, NR, No Response
Table 2
Demographic information for participants in the methamphetamine comparison

<table>
<thead>
<tr>
<th>Last time consumed (Inhalants)</th>
<th>Frequency (Inhalants)</th>
<th>Amount (Inhalants)</th>
<th>How long (Inhalants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Teenager</td>
<td>Once a month</td>
<td>Can between 5 people</td>
<td>Last time at age 16</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
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<td>NA</td>
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</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>4 years ago</td>
<td>Once or twice</td>
<td>Enough to feel dizzy</td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
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</tr>
<tr>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Note. NA, Not Applicable, NR, No Response</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3
Demographic information for participants in the MDMA comparison

<table>
<thead>
<tr>
<th>Participant number</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Education level</th>
<th>Handedness</th>
<th>Smoker</th>
<th>Amount (cigarettes/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>28</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>1-2</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>Female</td>
<td>Secondary</td>
<td>Left</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>22</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Left</td>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>24</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>1-2</td>
</tr>
<tr>
<td>8</td>
<td>28</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>15+</td>
</tr>
<tr>
<td>9</td>
<td>25</td>
<td>Female</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>22</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>26</td>
<td>Male</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>7-10</td>
</tr>
<tr>
<td>12</td>
<td>22</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>8</td>
</tr>
<tr>
<td>13</td>
<td>25</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Right</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>24</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>15</td>
<td>23</td>
<td>Female</td>
<td>Post-graduate</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>16</td>
<td>22</td>
<td>Female</td>
<td>Undergraduate</td>
<td>Left</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>17</td>
<td>27</td>
<td>Female</td>
<td>Post-graduate</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>18</td>
<td>28</td>
<td>Female</td>
<td>Honours</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>19</td>
<td>21</td>
<td>Male</td>
<td>Secondary</td>
<td>Right</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>20</td>
<td>23</td>
<td>Female</td>
<td>Post Graduate</td>
<td>Right</td>
<td>Yes</td>
<td>when drinking alcohol</td>
</tr>
</tbody>
</table>

*Note. NA, Not Applicable, NR, No Response*
Table 3
Demographic information for participants in the MDMA comparison

<table>
<thead>
<tr>
<th>Coffee</th>
<th>Amount (cups/day)</th>
<th>Frequency (Alcohol)</th>
<th>Alcohol (drinks/week)</th>
<th>How often needed drink in morning</th>
<th>How long drinking</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times week</td>
<td>1-4</td>
<td>Once every 6 months</td>
<td>6 years</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>2-3 times a month</td>
<td>2-5</td>
<td>Never</td>
<td>12 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2-3</td>
<td>1-2 times week</td>
<td>1-2</td>
<td>Never</td>
<td>15 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>1-2 times week</td>
<td>1-8</td>
<td>Never</td>
<td>9 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>2-3 times a month</td>
<td>10</td>
<td>Never</td>
<td>8 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>Once a month</td>
<td>5-6</td>
<td>Never</td>
<td>13 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>2-3 times a month</td>
<td>5-6</td>
<td>Never</td>
<td>8 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1 Daily</td>
<td>2-4</td>
<td></td>
<td>Once a month</td>
<td>10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1 Daily</td>
<td>4</td>
<td></td>
<td>Never</td>
<td>10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>2-3 times a month</td>
<td>4-5</td>
<td>Once every 2-3 months</td>
<td>6 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>2-3 times a month</td>
<td>5-6</td>
<td>Never</td>
<td>9-10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times week</td>
<td>4-10</td>
<td>Never</td>
<td>6 years</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
<td>1-2 times a week</td>
<td>5</td>
<td>Never</td>
<td>13 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times a week</td>
<td>4</td>
<td>Never</td>
<td>Since age 16 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>Daily or almost daily</td>
<td>3</td>
<td>Never</td>
<td>10 years</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times week</td>
<td>8-10</td>
<td>Never</td>
<td>6 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times a week</td>
<td>2-3</td>
<td>Never</td>
<td>9</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
<td>1-2 times a week</td>
<td>3</td>
<td>Never</td>
<td>12 years</td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1-2 times a week</td>
<td>6-10</td>
<td>2-3 times a year</td>
<td>4 years</td>
</tr>
<tr>
<td>Yes</td>
<td>NR</td>
<td>1-2 times a week</td>
<td>6</td>
<td>twice</td>
<td>8 years</td>
</tr>
</tbody>
</table>

*Note. NA, Not Applicable, NR, No Response*
Table 3

Demographic information for participants in the MDMA comparison

<table>
<thead>
<tr>
<th>Consume Cannabis</th>
<th>Last time consumed Cannabis</th>
<th>Frequency (Cannabis)</th>
<th>Amount (Cannabis)</th>
<th>How long (Cannabis)</th>
<th>Consume Amphetamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>1-2 times week</td>
<td>One-two joints</td>
<td>10 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>2-3 times a month</td>
<td>One joint</td>
<td>12 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 year ago</td>
<td>Once</td>
<td>2-3 pipes</td>
<td>7 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Hours ago</td>
<td>1-2 times a week</td>
<td>2-3 joints</td>
<td>6 months</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Year ago</td>
<td>Rarely</td>
<td>1 joint</td>
<td>Infrequently 2 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>1 joint</td>
<td>13 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once</td>
<td>1 joint</td>
<td>Once</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Years ago</td>
<td>Years ago</td>
<td>NR</td>
<td>8 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once every 6 months</td>
<td>1 joint</td>
<td>5 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once a month</td>
<td>1-2 joints</td>
<td>3 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>3 years ago</td>
<td>Every 3-4 months</td>
<td>1/2 joint</td>
<td>5 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>1-2 times a week</td>
<td>1-6 bongs</td>
<td>5 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Monthly</td>
<td>NR</td>
<td>10 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>Days ago</td>
<td>Daily or almost daily</td>
<td>2 joints</td>
<td>Since age 17</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 week ago</td>
<td>2-3 times a month</td>
<td>few joints</td>
<td>8 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>More 1 week ago</td>
<td>depends on supply</td>
<td>couple of joints</td>
<td>5 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>8 years ago</td>
<td>Never</td>
<td>Once</td>
<td>Once</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>more than a month ago</td>
<td>once a year</td>
<td>1 joint</td>
<td>12 years</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>more than a week ago</td>
<td>once a month</td>
<td>‘ew joints b/w friend</td>
<td>1 year</td>
<td>Yes</td>
</tr>
<tr>
<td>Yes</td>
<td>days ago</td>
<td>3-4 times a year</td>
<td>one joint</td>
<td>2 years</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Note. NA, Not Applicable, NR, No Response
### Table 3

*Demographic information for participants in the MDMA comparison*

<table>
<thead>
<tr>
<th>Last time used consumed</th>
<th>Frequency (Amphetamines)</th>
<th>Amount (Amphetamines)</th>
<th>How long (Amphetamines)</th>
<th>Consumed MDMA</th>
<th>Last time (MDMA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>One line</td>
<td>8 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Once every second month</td>
<td>1-2 lines</td>
<td>7 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>2-3 times a month</td>
<td>2-3 points</td>
<td>5 years</td>
<td>Yes</td>
<td>More 1 year ago</td>
</tr>
<tr>
<td>More 1 year ago</td>
<td>Rarely</td>
<td>1 point</td>
<td>Unsure</td>
<td>Yes</td>
<td>More 1 year ago</td>
</tr>
<tr>
<td>Over a year</td>
<td>Infrequently</td>
<td>1 line</td>
<td>Infrequently 6 months</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>Over a year</td>
<td>No longer</td>
<td>2 lines</td>
<td>2 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Twice a year</td>
<td>1/2-3 points</td>
<td>3-4 years</td>
<td>Yes</td>
<td>8 months</td>
</tr>
<tr>
<td>More 1 week ago</td>
<td>2-3 times a month</td>
<td>Few points</td>
<td>6 years</td>
<td>Yes</td>
<td>Days ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Every couple of months</td>
<td>1 line</td>
<td>7 years</td>
<td>Yes</td>
<td>Days ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>Twice a year</td>
<td>2-3 lines</td>
<td>2 months</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>5-6 points</td>
<td>5 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
</tr>
<tr>
<td>6 months ago</td>
<td>Few times a year</td>
<td>half a gram</td>
<td>3 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
</tr>
<tr>
<td>Once</td>
<td>Once</td>
<td>One bomb</td>
<td>Once</td>
<td>Yes</td>
<td>2 years ago</td>
</tr>
<tr>
<td>More 1 month</td>
<td>Almost never</td>
<td>2 lines</td>
<td>A few times</td>
<td>Yes</td>
<td>More 1 month ago</td>
</tr>
<tr>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>10 lines</td>
<td>6 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
</tr>
<tr>
<td>More 1 month ago</td>
<td>once or twice ever</td>
<td>couple of lines</td>
<td>NA</td>
<td>Yes</td>
<td>More 1 week ago</td>
</tr>
<tr>
<td>7 years ago</td>
<td>Not any more</td>
<td>1 line</td>
<td>Only occasionally</td>
<td>Yes</td>
<td>7 years ago</td>
</tr>
<tr>
<td>more than month ago</td>
<td>once a month</td>
<td>2 lines</td>
<td>4 years</td>
<td>Yes</td>
<td>more than a month ago</td>
</tr>
<tr>
<td>more than a month ago</td>
<td>3-4 times a year</td>
<td>up to 4 lines</td>
<td>2 years</td>
<td>Yes</td>
<td>more than a month ago</td>
</tr>
<tr>
<td>18 months ago</td>
<td>once a year</td>
<td>3 lines</td>
<td>2 years</td>
<td>Yes</td>
<td>7 months ago</td>
</tr>
</tbody>
</table>

*Note.* NA, Not Applicable, NR, No Response
Table 3
Demographic information for participants in the MDMA comparison

<table>
<thead>
<tr>
<th>How often (MDMA)</th>
<th>Amount (MDMA)</th>
<th>How long (MDMA)</th>
<th>Consume Cocaine</th>
<th>Last time Cocaine</th>
<th>Frequency Cocaine</th>
<th>Amount Cocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once a month</td>
<td>1 tablet</td>
<td>8 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once every 6 months</td>
<td>1-3 lines</td>
</tr>
<tr>
<td>Every second month</td>
<td>1 tablet</td>
<td>7 years</td>
<td>Yes</td>
<td>Six months ago</td>
<td>Once a year</td>
<td>2-3 lines</td>
</tr>
<tr>
<td>Special occasion</td>
<td>1-2 tablets</td>
<td>5 years</td>
<td>Yes</td>
<td>More 1 year ago</td>
<td>Infrequently</td>
<td>1 line</td>
</tr>
<tr>
<td>Rarely</td>
<td>1 tablet</td>
<td>6 months</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Infrequently</td>
<td>1 tablet</td>
<td>6 months</td>
<td>Yes</td>
<td>Over a year</td>
<td>Rarely</td>
<td>1 line</td>
</tr>
<tr>
<td>Once every 3-4 months</td>
<td>1-2 tablets</td>
<td>5-6 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Once every 8 weeks</td>
<td>1 tablet</td>
<td>4 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>1 year</td>
<td>½ gram</td>
</tr>
<tr>
<td>Once a month</td>
<td>1 tablet</td>
<td>6 years</td>
<td>Yes</td>
<td>Months ago</td>
<td>Once a month</td>
<td>1 gram</td>
</tr>
<tr>
<td>Every couple of months</td>
<td>1 tablet</td>
<td>7 years</td>
<td>Yes</td>
<td>More 1 month ago</td>
<td>Once a year</td>
<td>1 line</td>
</tr>
<tr>
<td>Twice every 2 years</td>
<td>2-3 tablets</td>
<td>2 months</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Once every 2 months</td>
<td>2 tablets</td>
<td>5 years</td>
<td>Yes</td>
<td>7 months ago</td>
<td>once per year</td>
<td>1 gram</td>
</tr>
<tr>
<td>every 4-5 months</td>
<td>1-3 tablets</td>
<td>3 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
<td>Rarely</td>
<td>1 line</td>
</tr>
<tr>
<td>Not often</td>
<td>1-2 tablets</td>
<td>4 years</td>
<td>Yes</td>
<td>2 years ago</td>
<td>Not often</td>
<td>1 line</td>
</tr>
<tr>
<td>Once every 3 months</td>
<td>2 tablets</td>
<td>Since age 18</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2-3 times a month</td>
<td>1 tablet</td>
<td>6 years</td>
<td>Yes</td>
<td>More 1 week ago</td>
<td>Once a month</td>
<td>10 lines</td>
</tr>
<tr>
<td>2-3 times a month</td>
<td>1-2 tablets</td>
<td>1.5 years</td>
<td>Yes</td>
<td>Ages ago</td>
<td>once or twice</td>
<td>couple of lines</td>
</tr>
<tr>
<td>every now and then</td>
<td>1 tablet</td>
<td>3 years</td>
<td>Yes</td>
<td>7 years ago</td>
<td>once</td>
<td>2 lines</td>
</tr>
<tr>
<td>once a month</td>
<td>1 tablet</td>
<td>4 years</td>
<td>Yes</td>
<td>more than a month ago</td>
<td>once a month</td>
<td>2-3 lines</td>
</tr>
<tr>
<td>once a month</td>
<td>2</td>
<td>2 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3 times a year</td>
<td>11/2 tabs</td>
<td>3 years</td>
<td>Yes</td>
<td>over a year ago</td>
<td>once every few months</td>
<td>2 lines</td>
</tr>
</tbody>
</table>

*Note.* NA, Not Applicable, NR, No Response
Table 3
Demographic information for participants in the MDMA comparison

<table>
<thead>
<tr>
<th>How long (Cocaine)</th>
<th>Consume (Heroin)</th>
<th>Last time (Heroin)</th>
<th>Frequency (Heroin)</th>
<th>Amount (Heroin)</th>
<th>How long (Heroin)</th>
<th>Consume Inhalants</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 years</td>
<td>Yes</td>
<td>8 years ago</td>
<td>Never</td>
<td>One hit</td>
<td>8 years ago</td>
<td>No</td>
</tr>
<tr>
<td>Once</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>1 year</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>18 months</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>2-3 years</td>
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<td>NA</td>
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<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>NA</td>
<td>Yes</td>
<td>2 years ago</td>
<td>Once</td>
<td>4 hits</td>
<td>Once</td>
<td>No</td>
</tr>
<tr>
<td>5 years</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>1 year</td>
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<td>NA</td>
<td>NA</td>
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<td>No</td>
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<tr>
<td>1 year</td>
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<td>No</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
</tr>
<tr>
<td>4 years</td>
<td>No</td>
<td>NA</td>
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*Note. NA, Not Applicable, NR, No Response*
Table 3

Demographic information for participants in the MDMA comparison

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<th>Last time consumed (Inhalants)</th>
<th>Frequency (Inhalants)</th>
<th>Amount (Inhalants)</th>
<th>How long (Inhalants)</th>
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APPENDIX 2.

Word list sets, IAPS picture selection, questionnaires and ethics application.

**LDT Wordlist One**

<table>
<thead>
<tr>
<th>Real words</th>
<th>Positive</th>
<th>General threat</th>
<th>Neutral</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>passion</td>
<td>killer</td>
<td>basket</td>
<td>misery</td>
<td></td>
</tr>
<tr>
<td>laughter</td>
<td>terrorist</td>
<td>barrel</td>
<td>alchoholic</td>
<td></td>
</tr>
<tr>
<td>pleasure</td>
<td>bomb</td>
<td>bathroom</td>
<td>disloyal</td>
<td></td>
</tr>
<tr>
<td>affection</td>
<td>mutilate</td>
<td>butter</td>
<td>jealous</td>
<td></td>
</tr>
<tr>
<td>delight</td>
<td>murderer</td>
<td>contents</td>
<td>terrible</td>
<td></td>
</tr>
<tr>
<td>humour</td>
<td>hostage</td>
<td>column</td>
<td>unhappy</td>
<td></td>
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<tr>
<td>miracle</td>
<td>suffocate</td>
<td>context</td>
<td>depressed</td>
<td></td>
</tr>
<tr>
<td>paradise</td>
<td>brutal</td>
<td>detail</td>
<td>neglect</td>
<td></td>
</tr>
<tr>
<td>romantic</td>
<td>assassin</td>
<td>errand</td>
<td>grief</td>
<td></td>
</tr>
<tr>
<td>sunset</td>
<td>gun</td>
<td>fabric</td>
<td>shamed</td>
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<table>
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<td>koller</td>
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<td>mosery</td>
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<td>marderer</td>
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<td>sunsat</td>
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LDT Wordlist Two

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<td>rainbow</td>
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<td>item</td>
<td>gloom</td>
<td></td>
</tr>
<tr>
<td>champion</td>
<td>lethal</td>
<td>locker</td>
<td>upset</td>
<td></td>
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<tr>
<td>cheer</td>
<td>threat</td>
<td>patent</td>
<td>unfaithful</td>
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<tr>
<td>comedy</td>
<td>war</td>
<td>pencil</td>
<td>guilty</td>
<td></td>
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<tr>
<td>joyful</td>
<td>aggressive</td>
<td>pamphlet</td>
<td>insult</td>
<td></td>
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<tr>
<td>lucky</td>
<td>slaughter</td>
<td>rattle</td>
<td>trouble</td>
<td></td>
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<td>massacre</td>
<td>reserved</td>
<td>funeral</td>
<td></td>
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<td>triumph</td>
<td>explosion</td>
<td>statue</td>
<td>lonely</td>
<td></td>
</tr>
<tr>
<td>loved</td>
<td>danger</td>
<td>sphere</td>
<td>unwell</td>
<td></td>
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<td>adorable</td>
<td>pistol</td>
<td>tower</td>
<td>distressed</td>
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<table>
<thead>
<tr>
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</thead>
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<tr>
<td>humir</td>
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<tr>
<td>triumph</td>
</tr>
<tr>
<td>champium</td>
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<tr>
<td>joyful</td>
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</tbody>
</table>
IAPS picture selection

Positive pictures

<table>
<thead>
<tr>
<th>Set One</th>
<th>Mean Valance (SD)</th>
<th>Mean Arousal (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kitten</td>
<td>8.21 (1.21)</td>
<td>4.31 (2.63)</td>
</tr>
<tr>
<td>Waterfalls</td>
<td>7.34 (1.74)</td>
<td>5.71 (2.53)</td>
</tr>
<tr>
<td>Sunset</td>
<td>8.00 (1.48)</td>
<td>4.92 (2.49)</td>
</tr>
<tr>
<td>Brownie</td>
<td>7.63 (1.74)</td>
<td>4.87 (2.59)</td>
</tr>
<tr>
<td>Gold</td>
<td>6.96 (1.64)</td>
<td>5.60 (2.40)</td>
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<td><strong>7.63</strong></td>
<td><strong>5.08</strong></td>
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<table>
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<th>Mean Valance (SD)</th>
<th>Mean Arousal (SD)</th>
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</thead>
<tbody>
<tr>
<td>Seal</td>
<td>8.19 (1.53)</td>
<td>4.61 (2.54)</td>
</tr>
<tr>
<td>Mountains</td>
<td>7.33 (1.73)</td>
<td>4.61 (2.59)</td>
</tr>
<tr>
<td>Sky</td>
<td>7.61 (1.48)</td>
<td>4.51 (2.85)</td>
</tr>
<tr>
<td>Ice cream</td>
<td>7.53 (1.73)</td>
<td>5.76 (2.21)</td>
</tr>
<tr>
<td>Money</td>
<td>7.51 (1.72)</td>
<td>5.78 (2.49)</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>7.63</strong></td>
<td><strong>5.05</strong></td>
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Neutral pictures

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<th>Mean Arousal (SD)</th>
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</thead>
<tbody>
<tr>
<td>Duck in oil</td>
<td>2.12 (1.93)</td>
<td>5.50 (2.52)</td>
</tr>
<tr>
<td>Burn</td>
<td>2.56 (1.32)</td>
<td>4.31 (1.81)</td>
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<tr>
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<td>2.49 (1.29)</td>
<td>5.52 (1.86)</td>
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<tr>
<td>Injection</td>
<td>3.34 (1.75)</td>
<td>5.23 (2.09)</td>
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<tr>
<td>Smoke</td>
<td>2.80 (1.54)</td>
<td>4.26 (2.44)</td>
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<td><strong>2.66</strong></td>
<td><strong>4.96</strong></td>
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</tbody>
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<table>
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<th>Set Two</th>
<th>Mean Valance (SD)</th>
<th>Mean Arousal (SD)</th>
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</thead>
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<tr>
<td>Sick kitty</td>
<td>2.68 (1.92)</td>
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<td>Crying boy</td>
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<td>5.09 (2.15)</td>
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<tr>
<td>Cemetery</td>
<td>2.06 (1.54)</td>
<td>4.00 (2.09)</td>
</tr>
<tr>
<td>Dental exam</td>
<td>3.72 (1.89)</td>
<td>5.39 (2.26)</td>
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<tr>
<td>Gargbage</td>
<td>2.88 (1.52)</td>
<td>4.40 (2.11)</td>
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<td><strong>4.73</strong></td>
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Negative pictures

<table>
<thead>
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<th>MEAN AROUSAL (SD)</th>
</tr>
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<tbody>
<tr>
<td>Towel 7002</td>
<td>4.97 (0.97)</td>
<td>3.16 (2.00)</td>
</tr>
<tr>
<td>spoon 7004</td>
<td>5.04 (0.60)</td>
<td>2.00 (1.66)</td>
</tr>
<tr>
<td>Iron 7030</td>
<td>4.69 (1.04)</td>
<td>2.99 (2.09)</td>
</tr>
<tr>
<td>Shoes 7031</td>
<td>4.52 (1.11)</td>
<td>2.03 (1.51)</td>
</tr>
<tr>
<td>building 7491</td>
<td>4.82 (1.03)</td>
<td>2.39 (1.90)</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>4.81</strong></td>
<td><strong>2.51</strong></td>
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<table>
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<th>SET TWO</th>
<th>MEAN VALANCE (SD)</th>
<th>MEAN AROUSAL (SD)</th>
</tr>
</thead>
<tbody>
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<td>basket 7010</td>
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<td>fork 7080</td>
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<td>2.32 (1.84)</td>
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<td>hair dryer 7050</td>
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<td>2.75 (1.80)</td>
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<td>umbrella 7150</td>
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<td>2.61 (1.76)</td>
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<td>Office 7700</td>
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<td>2.95 (2.17)</td>
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Threat pictures

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<td>Bomb 9630</td>
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<td>6.91 (2.57)</td>
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<td>Knife 6300</td>
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<td>6.61 (1.97)</td>
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<td>suicide 6570</td>
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<td>6.24 (2.16)</td>
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<tr>
<td>Starving child 9040</td>
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<td>5.82 (2.15)</td>
</tr>
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<th>MEAN AROUSAL (SD)</th>
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<td>dead body 3120</td>
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<td>6.84 (2.36)</td>
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<tr>
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<td>5.77 (2.21)</td>
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<td><strong>6.54</strong></td>
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</tbody>
</table>
IAPS Task response sheet

The valence scale is located on the left and the arousal scale is located on the right. Participants indicated their responses with a cross through the chosen rating.
## IAPS Task Recognition Test One distracter pictures

### Positive

<table>
<thead>
<tr>
<th></th>
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<th>Arousal</th>
<th>Arousal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bunnies</td>
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<td>4.10</td>
</tr>
<tr>
<td>Torte</td>
<td>7260</td>
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<td>5.11</td>
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<tr>
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### Neutral

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<th>Arousal</th>
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<tbody>
<tr>
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<td>Fabric</td>
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### Negative

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<th>Arousal</th>
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<tr>
<td>Eye disease</td>
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<td>5.35</td>
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<td><strong>4.95</strong></td>
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### Threat

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</thead>
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<td>Gang</td>
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<tr>
<td>Tumor</td>
<td>3261</td>
<td>1.82</td>
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<tr>
<td><strong>Average:</strong></td>
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<td><strong>6.02</strong></td>
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### IAPS Task Recognition Test Two distracter pictures

**Positive**

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<tbody>
<tr>
<td>Horse</td>
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<tr>
<td>Pizza</td>
<td>7350</td>
<td>7.10</td>
</tr>
<tr>
<td><strong>Average:</strong></td>
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<td><strong>4.51</strong></td>
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</tbody>
</table>

**Neutral**

<table>
<thead>
<tr>
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<th>Arousal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamp</td>
<td>7175</td>
<td>4.87</td>
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<td>Dust Pan</td>
<td>7040</td>
<td>4.69</td>
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</tr>
<tr>
<td></td>
<td>Valence</td>
<td>Arousal</td>
</tr>
<tr>
<td>----------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
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<tr>
<td>Jail</td>
<td>2722</td>
<td>3.47</td>
</tr>
<tr>
<td><strong>Average:</strong></td>
<td>3.23</td>
<td>4.08</td>
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<tr>
<td><strong>Threat</strong></td>
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<td></td>
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<td>Injury</td>
<td>3350</td>
<td>2.54</td>
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<td>2.70</td>
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<tr>
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<td>6.05</td>
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Instructions to Participants

SESSION ONE

General greeting

Hello, my name is Tamara and I am one of the research assistants carrying out the experiment, I am going to be taking you through some cognitive and memory tasks.

Lexical Decision Task Instructions (LDT)

The first task you are going to complete is called a Lexical Decision task. The task involves the presentation of a series of words that are displayed on the computer screen one at a time. The objective of this task is to see if you can identify whether the words presented are real or non-words. If the word displayed on the screen is a real word, such as the word “today” press the LEFT response button here on the keypad like this. If the word displayed is not a real word such as “todid” press the RIGHT button here, like this.

Each time a word is presented it will stay on the screen for a few seconds and you should make your response as quickly as possible. If you have not made your response by the time the word disappears from the screen you must still make your response in order for the next word to appear. After you have pressed the button, the word might stay on the screen for a few seconds before the next word comes up, just ignore this. If you press the button again, don’t worry about it, it won’t stuff up the task and will wait for your next answer to the next word on the screen.

Do you have any questions?

This task will take about 12 minutes to complete. When you are ready you can press the spacebar on the keyboard to start the task.
Recall Test Instructions

Now I want you to recall as many real words as you can from the Lexical Decision task I just got you to complete. You will have 60 seconds from the time I say start, and please stop when I say to. But I only want you to try to recall the real words you saw not any of the non-words ok. I’ll tell you when 30 seconds have passed.

Any questions?

Alright, we are starting now.

That was great, thanks.

The Affective Picture task instructions (IAPS)

Now I want you to complete an affective picture task, in this task you will see a series of pictures displayed on the computer screen one at a time, and I want you to rate them on this sheet according to how happy or sad and stimulated or unaroused they make you feel. The task starts with a fixation cross in the centre of the screen, when you see this you need to look at it because that is where the picture will be displayed. A picture will then appear on the screen for a few seconds, then it will disappear. When it disappears I want you to rate the picture on this page like this. This scale is related to your feelings about the picture. If you felt completely happy, pleased, satisfied, contented or hopeful ect. during the presentation, you would put an X here, or if after viewing the picture you felt completely unhappy, annoyed, unsatisfied, sad, despaired or bored, I want you to put an X here. In terms of this scale to the right, it described more of your physical state. If you felt stimulated, excited, frenzied, jittery, wide awake or aroused during the presentation, you would put an X here, or if after viewing the picture
you felt relaxed, calm, sluggish, dull, sleepy or unaroused, you would put an X here.

Make sure participants understands ratings scales, discuss what middle values would represent and repeat examples if necessary.

Please make all your responses without thinking too much, and try to make sure you do not skip any.

Once you have made each of your ratings for the picture, you need to press any button on the keypad and the next fixation and picture will come up.

The task will take about 10 minutes to complete.

Do you have any questions?

When you are ready press the spacebar on the keyboard to start the task.

End of session

Thank-you very much, please come with me and I will direct you to the nurse.

And please do not tell any of the other participants about what you did in here.

SESSION TWO

General greeting

Hi, nice to see you again, I will be taking you through the memory and cognitive tasks like the ones you did in the first session. Before we begin though, I am going to test your memory for the words and pictures that you saw during the first session.

Long-term recall test

First I would like you to complete a free recall test, by recalling as many real words as you can from the Lexical Decision task you completed two weeks ago. (You remember how I asked you to recall as many real words as you could after completing the Lexical Decision task last time you were here – well it’s the same thing, just a long
term test of your memory). You will have 60 seconds from the time I say start, and please stop when I say to. I’ll tell you when 30 seconds has passed, I have to wait for the full 60 seconds even if you can’t remember any more words.

Any questions?

Please begin.

That was great- thank you.

Recognition test

Now I would like you to complete this recognition test. The test contains a total of 16 pictures some of which you saw in the affective picture task you did two weeks ago, and some that you didn’t see. On each page, one picture is presented, below each picture I want you to tick either yes or no depending on whether you remember the picture being presented or not. After answering either yes or no, please provide a percentage estimate of the degree of confidence you have in your Decision, for example if you were absolutely certain you remember the picture you would write 100%, if you were slightly less confident you might put 70% and so on. Please complete every page independently and do not look back at the previous pages and ratings you made, or look forward at the other pictures in the test. This task will only take about 5 minutes to complete.

Any questions?

You may begin now.

LDT Instructions

Ok now I want you to complete the Lexical Decision task again. As you might remember the task involves the presentation of a series of words that are displayed on
the computer screen one at a time. The objective of this task is to see if you can identify whether the words are real or non-words. If the word displayed on the screen is a real word, such as the word “today” press the LEFT response button here on the keypad like this. If the word displayed is not a real word such as “todid” press the RIGHT button here, like this.

Each time a word is presented it will stay on the screen for a few seconds and you should make your response as quickly as possible. If you have not made your response by the time the word disappears from the screen you must still make your response in order for the next word to appear. You only need to press the button once. After you have pressed the button, the word might stay on the screen for a few seconds before the next word comes up, just ignore this. And if you press the button again, don’t worry about it, it won’t stuff up the task and will wait for your answer to the next word.

Do you have any questions?

This task will take about 10 minutes to complete. When you are ready press the spacebar on the keyboard to start the task.

Recall Test Instructions

Now I want you to recall as many real words as you can from the Lexical Decision task I just got you to complete. You will have 60 seconds from the time I say start, and please stop when I say to. But I only want you to try to recall the real words you saw not any of the non-words ok. I will tell you when 30 seconds has passed.

Any questions?

Alright, we are starting now.

That was great, thanks.
The IAPS instructions

Great now I want you to complete an affective picture task again. Like the previous times in this task you will see a series of pictures displayed on the computer screen one at a time, and I want you to rate them on this sheet according to how happy or sad and stimulated or unaroused they make you feel. The task starts with a fixation cross in the centre of the screen, when you see this you need to look at it because that is where the picture will be displayed. A picture will then appear on the screen for a few seconds, then it will disappear. When it disappears I want you to rate the picture on this page like this. This scale is related to your feelings about the picture. If you felt completely happy, pleased, satisfied, contented or hopeful etc. during the presentation, you would put an X here, or if after viewing the picture you felt completely unhappy, annoyed, unsatisfied, sad, despaired or bored, I want you to put an X here. In terms of this scale to the right, it described more of your physical state. If you felt stimulated, excited, frenzied, jittery, wide awake or aroused during the presentation, you would put an X here, or if after viewing the picture you felt relaxed, calm, sluggish, dull, sleepy or unaroused, you would put an X here. Make sure participants understands ratings scales, discuss what middle values would represent and repeat examples if necessary.

Please make all your responses without thinking too much, and try to make sure you do not skip any.

Once you have made each of your ratings for the picture, you need to press any button on the keypad and the next fixation and picture will come up.

The task will take about 10 minutes to complete.

Do you have any questions?

When you are ready press the spacebar on the keyboard to start the task.
Thank-you very much, please come with me and I will direct you to the nurse.
And please do not tell any of the other participants about what you did in here

SESSION THREE

Complete the recall and recognition tests as per second session.

End of session

Thank-you very much, that was your final task for this session, please complete this de-briefing questionnaire and feel free to ask me any questions about the study.
<table>
<thead>
<tr>
<th>Item</th>
<th>Very Little</th>
<th>A Little</th>
<th>Some</th>
<th>Much</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>It scares me when I feel faint.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is important to me to stay in control of my emotions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It scares me when my heart beats rapidly.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It embarrasses me when my stomach growls.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is important to me not to appear nervous.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>When I cannot keep my mind on a task, I worry that I might be going crazy.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It scares me when I feel &quot;shaky&quot; (trembling)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Today's Date: 

If any of the items concern something that is not part of your experience (e.g., "It scares me when I feel shaky" for someone who has never trembled or had the "shakes"), answer on the basis of how you think you might feel if you had such an experience. Otherwise answer all items on the basis of your own experience.

Circle the one phrase that best represents the extent to which you agree with...
8. It scares me when I am nauseous.
   Very Little  A Little  Some  Much  Very Much

9. When I notice that my heart is beating rapidly, I worry that I might have a heart attack.
   Very Little  A Little  Some  Much  Very Much

10. It scares me when I become short of breath.
    Very Little  A Little  Some  Much  Very Much

11. When my stomach is upset, I worry that I might be seriously ill.
    Very Little  A Little  Some  Much  Very Much

12. It scares me when I am unable to keep my mind on a task.
    Very Little  A Little  Some  Much  Very Much

13. Other people notice when I feel shaky.
    Very Little  A Little  Some  Much  Very Much

14. Unusual body sensations scare me.
    Very Little  A Little  Some  Much  Very Much

15. When I am nervous, I worry that I might be mentally ill.
    Very Little  A Little  Some  Much  Very Much

16. It scares me when I am nervous
    Very Little  A Little  Some  Much  Very Much
National Adult Reading Test-Revised

Place the NART word sheet in front of the participant. I want you to read slowly down this list of words, starting here. (Point to ACHE) After each word please wait until I say “next” before reading the next word. I must warn you that there are many words that you probably won’t recognise, in fact most people don’t know them all just have a guess at these, OK? Go ahead.

Reinforce all responses – That’s fine/ good.
<table>
<thead>
<tr>
<th></th>
<th>Word</th>
<th></th>
<th>Word</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CHORD</td>
<td>26</td>
<td>SUPERFLUOUS</td>
</tr>
<tr>
<td>2</td>
<td>ACHEN</td>
<td>27</td>
<td>SIMILE</td>
</tr>
<tr>
<td>3</td>
<td>DEPOT</td>
<td>28</td>
<td>BANAL</td>
</tr>
<tr>
<td>4</td>
<td>AISLE</td>
<td>29</td>
<td>QUADRUPED</td>
</tr>
<tr>
<td>5</td>
<td>BOUQUET</td>
<td>30</td>
<td>CELLIST</td>
</tr>
<tr>
<td>6</td>
<td>PSALM</td>
<td>31</td>
<td>FACADE</td>
</tr>
<tr>
<td>7</td>
<td>CAPON</td>
<td>32</td>
<td>ZEALOT</td>
</tr>
<tr>
<td>8</td>
<td>DENY</td>
<td>33</td>
<td>DRACHM</td>
</tr>
<tr>
<td>9</td>
<td>NAUSEA</td>
<td>34</td>
<td>AENON</td>
</tr>
<tr>
<td>10</td>
<td>DEBT</td>
<td>35</td>
<td>PLACEBO</td>
</tr>
<tr>
<td>11</td>
<td>COURTEOUS</td>
<td>36</td>
<td>ABSTEMIOUS</td>
</tr>
<tr>
<td>12</td>
<td>RAREFY</td>
<td>37</td>
<td>DETENTE</td>
</tr>
<tr>
<td>13</td>
<td>EQUIVOCAL</td>
<td>38</td>
<td>IDYLL</td>
</tr>
<tr>
<td>14</td>
<td>NAIVE</td>
<td>39</td>
<td>PUERPERAL</td>
</tr>
<tr>
<td>15</td>
<td>CATACOMB</td>
<td>40</td>
<td>AVER</td>
</tr>
<tr>
<td>16</td>
<td>GAOLED</td>
<td>41</td>
<td>GAUCHE</td>
</tr>
<tr>
<td>17</td>
<td>THYME</td>
<td>42</td>
<td>TOPIARY</td>
</tr>
<tr>
<td>18</td>
<td>HEIR</td>
<td>43</td>
<td>LEVIATHAN</td>
</tr>
<tr>
<td>19</td>
<td>RADIX</td>
<td>44</td>
<td>BEATIFY</td>
</tr>
<tr>
<td>20</td>
<td>ASSIGNATE</td>
<td>45</td>
<td>PRELATE</td>
</tr>
<tr>
<td>21</td>
<td>HIATUS</td>
<td>46</td>
<td>SIDEREAL</td>
</tr>
<tr>
<td>22</td>
<td>SUBTLE</td>
<td>47</td>
<td>DEMESNE</td>
</tr>
<tr>
<td>23</td>
<td>PROCREATE</td>
<td>48</td>
<td>SYNCOPE</td>
</tr>
<tr>
<td>24</td>
<td>GIST</td>
<td>49</td>
<td>LABILE</td>
</tr>
<tr>
<td>25</td>
<td>GOUGE</td>
<td>50</td>
<td>CAMPANILE</td>
</tr>
</tbody>
</table>
**Posttraumatic Stress Diagnostic Scale**

1a. Have you ever experienced any event(s) (such as those below) that have significantly distressed you (an event during which you experienced an intense sense of fear, helplessness or / and horror)?

Yes [ ] (go to question 1b, directly below) No [ ] (finish)

1b. If yes, please record the number of times (N^4) you have experienced the event (use C if the event was experienced continuously over a period of more than 3 months). Also, if any of the events occurred within the last 3 months please put the approximate date next to the event. Please record how distressing all experiences were at the time or immediately after the event, and how much distress you currently experience over the event, by circling a number (1-5) under each column. However, should you not wish to specify the actual event but did experience a traumatic event like those below please just complete item 14.

<table>
<thead>
<tr>
<th>Type of Event (and Date)</th>
<th>Level of Distress Experienced at the Time</th>
<th>Level of Distress Experienced Currently</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Serious accident, fire or explosion</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td>2. Natural disaster (e.g., flood, earthquake, hurricane)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3. Non-sexual assault by someone you know (e.g., being mugged, shot, stabbed, attacked)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4. Non-sexual assault by a stranger (e.g., being mugged, shot, stabbed, attacked)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5. Sexual assault by someone you know (e.g., rape, attempted rape)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6. Sexual assault by a stranger (e.g., rape, attempted rape)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>7. Military combat or war zone</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>8. Imprisonment (e.g., hostage, prison inmate, prisoner of war)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>9. Torture</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>10. Life-threatening illness</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>11. Witnessed any of the above</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>12. Other: Please specify</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>13. Other: Please specify</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>14. I do not wish to specify the event, but one has occurred</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
2a. These questions looks at how the event from above (1c) affects you now. Please answer the following questions according to what has happened during the past month using the 0-3 scale below. Do not spend too much time on any statement.

0 = Not at all or only one time  
1 = Once per week or less/a little bit/once in a while  
2 = 2 to 4 times per week/somewhat/half the time  
3 = 5 or more times per week/very much/almost always

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Have you had upsetting thoughts or images about the event that came into your head when you didn’t want them to?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Have you been having bad dreams or nightmares about the event?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Have you had the experience of reliving the event, acting or feeling as if it were happening again?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Have you been very EMOTIONALLY upset when you were reminded of the event (includes becoming scared, angry, sad, guilty, etc.)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Have you been experiencing PHYSICAL reactions when you were reminded of the event (e.g. break out in a sweat, heart beats fast)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Have you been trying not to think about, talk about or have feelings associated with the event?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Have you been trying to avoid activities, people or places that you associate with the event?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Are there any important parts about the event that you still cannot remember?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Have you found that you are much less interested or participate much less often in important activities?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Have you felt distant or cut off from others around?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Have you felt emotionally numb (e.g. feel sad but can’t cry, unable to have loving feelings)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Have you felt that your future plans or hopes will not come true (e.g. will have no career, marriage, children, or long life)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Have you been having problems falling or staying asleep?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Have you been irritable or having fits of anger?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Have you been having trouble concentrating (e.g. drifting in and out of conversations, lose track of storey on TV, forgetting what you read, etc.)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Have you been overly alert (e.g. checking to see who is around you, uncomfortable with your back to a door, etc.)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Have you been jumpy or easily startled (e.g. when someone walks up behind you)?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2b. How long have you experienced the problems that you have reported above?

- [ ] Less than 1 month
- [ ] 1 to 3 months
- [ ] 3 to 6 months
- [ ] More than 6 months

2c. How long after the event did these problems begin?

- [ ] Less than 1 month
- [ ] 1 to 3 months
- [ ] 3 to 6 months
- [ ] More than 6 months
2d. Have these problems interfered with any of the following areas of your life during the past month? Please rate (circle) for each event...

<table>
<thead>
<tr>
<th>Life Area</th>
<th>Not applicable</th>
<th>Not at all</th>
<th>A little bit / sometimes</th>
<th>Definitely / often</th>
<th>Markedly / very often</th>
<th>Very severely / continuously</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Household chores and duties</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Relationships with friends</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Fun and leisure activities</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Schoolwork</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Relationships with family</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Sex life</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>General satisfaction with life</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Overall level of functioning in all areas of your life</td>
<td>na</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
SCL-90-R
Symptom Checklist-90-R

Leonard R. Derogatis, PhD

Last Name  First  MI

ID Number

Age  Gender  Test Date

DIRECTIONS:
1. Print your name, identification number, age, gender, and testing date in the area on the left side of this page.
2. Use a lead pencil only and make a dark mark when responding to the items on pages 2 and 3.
3. If you want to change an answer, erase it carefully and then fill in your new choice.
4. Do not make any marks outside the circles.

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DO NOT SEND TO NATIONAL COMPUTER SYSTEMS
USE ONLY FOR HAND SCORING

Product Number
06618
**INSTRUCTIONS:**
Below is a list of problems people sometimes have. Please read each one carefully, and blacken the circle that best describes HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU DURING THE PAST 7 DAYS INCLUDING TODAY. Blacken the circle for only one number for each problem and do not skip any items. If you change your mind, erase your first mark carefully. Read the example before beginning, and if you have any questions please ask them now.

<table>
<thead>
<tr>
<th>NOT AT ALL</th>
<th>A LITTLE BIT</th>
<th>MODERATELY</th>
<th>QUITE A BIT</th>
<th>EXTREMELY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
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</tbody>
</table>

**EXAMPLE**
HOW MUCH WERE YOU DISTRESSED BY:

1. Bodyaches

<table>
<thead>
<tr>
<th>NOT AT ALL</th>
<th>A LITTLE BIT</th>
<th>MODERATELY</th>
<th>QUITE A BIT</th>
<th>EXTREMELY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

1. Headaches
2. Nervousness or shakiness inside
3. Repeated unpleasant thoughts that won’t leave your mind
4. Faintness or dizziness
5. Loss of sexual interest or pleasure
6. Feeling critical of others
7. The idea that someone else can control your thoughts
8. Feeling others are to blame for most of your troubles
9. Trouble remembering things
10. Worried about being alone or unwanted
11. Feeling easily annoyed or irritated
12. Feeling afraid in open spaces or on the streets
13. Feeling low in energy or slowed down
14. Thoughts of ending your life
15. Hearing voices that other people do not hear
16. Trembling
17. Feeling that most people cannot be trusted
18. Poor appetite
19. Crying easily
20. Feeling shy or uneasy with the opposite sex
21. Feelings of being trapped or caught
22. Suddenly scared for no reason
23. Tempers outbursts that you could not control
24. Feeling afraid to go out of your house alone
25. Blaming yourself for things
26. Pains in lower back
27. Feeling blocked in getting things done
28. Feeling lonely
29. Feeling blue
30. Worrying too much about things
31. Feeling no interest in things
32. Feeling fearful
33. Your feelings being easily hurt
34. Other people being aware of your private thoughts
35. Feeling others do not understand you or are unsympathetic
36. Feeling that people are unfriendly or dislike you
37. Feeling that people are unfriendly or dislike you
<table>
<thead>
<tr>
<th>NOT AT ALL</th>
<th>A LITTLE BIT</th>
<th>MORE EXTREMELY</th>
<th>QUITE A BIT</th>
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</tr>
</tbody>
</table>

**HOW MUCH WERE YOU DISTRESSED BY:**

- Having to do things very slowly to ensure correctness
- Heart pounding or racing
- Nausea or upset stomach
- Feeling inferior to others
- Soreness of your muscles
- Feeling that you are watched or talked about by others
- Trouble falling asleep
- Having to check and double-check what you do
- Difficulty making decisions
- Feeling afraid to travel on buses, subways, or trains
- Trouble getting your breath
- Hot or cold spells
- Having to avoid certain things, places, or activities because they frighten you
- Your mind going blank
- Numbness or tingling in parts of your body
- A lump in your throat
- Feeling hopeless about the future
- Trouble concentrating
- Feeling weak in parts of your body
- Feeling tense or keyed up
- Heavy feelings in your arms or legs
- Thoughts of death or dying
- Overeating
- Feeling uneasy when people are watching or talking about you
- Having thoughts that are not your own
- Having urges to beat, injure, or harm someone
- Awakening in the early morning
- Having to repeat the same actions such as touching, counting, or washing
- Sleep that is restless or disturbed
- Having urges to break or smash things
- Having ideas or beliefs that others do not share
- Feeling very self-conscious with others
- Feeling uneasy in crowds, such as shopping or at a movie
- Feeling everything is an effort
- Spells of terror or panic
- Feeling uncomfortable about eating or drinking in public
- Getting into frequent arguments
- Feeling nervous when you are left alone
- Others not giving you proper credit for your achievements
- Feeling lonely even when you are with people
- Feeling so restless you couldn’t sit still
- Feelings of worthlessness
- The feeling that something bad is going to happen to you
- Shouting or throwing things
- Feeling afraid you will faint in public
- Feeling that people will take advantage of you if you let them
- Having thoughts about sex that bother you a lot
- The idea that you should be punished for your sins
- Thoughts and images of a frightening nature
- The idea that something serious is wrong with your body
- Never feeling close to another person
- Feelings of guilt
- The idea that something is wrong with your mind
This questionnaire looks at alcohol intake and its effects. There are no right or wrong answers, just circle the answer that is correct for you.

1. How often do you have a drink containing alcohol?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Monthly</th>
<th>2-4 Times</th>
<th>2-3 Times</th>
<th>4 Or More</th>
</tr>
</thead>
<tbody>
<tr>
<td>Or Less</td>
<td></td>
<td>A Month</td>
<td>A Week</td>
<td>Times A Week</td>
<td></td>
</tr>
</tbody>
</table>

2. How many drinks containing alcohol do you have on a particular day when you are drinking?

<table>
<thead>
<tr>
<th>Option</th>
<th>1 Or 2</th>
<th>3 Or 4</th>
<th>5 Or 6</th>
<th>7 To 9</th>
<th>10 Or More</th>
</tr>
</thead>
</table>

3. How often do you have six or more drinks on one occasion?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Less Than Monthly</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily Or Almost Daily</th>
</tr>
</thead>
</table>

4. How often during the last six months have you found that you were not able to stop drinking once you had started?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Less Than Monthly</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily Or Almost Daily</th>
</tr>
</thead>
</table>

5. How often during the last year have you failed to do what was normally expected from you because of drinking?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Less Than Monthly</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily Or Almost Daily</th>
</tr>
</thead>
</table>

6. How often during the last six months have you needed a first drink in the morning to get yourself going after a heavy drinking session?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Less Than Monthly</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily Or Almost Daily</th>
</tr>
</thead>
</table>

7. How often during the last six months have you had a feeling of guilt or remorse after drinking?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Less Than Monthly</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily Or Almost Daily</th>
</tr>
</thead>
</table>

8. How often during the last six months have you been unable to remember what happened the night before because you had been drinking?

<table>
<thead>
<tr>
<th>Option</th>
<th>Never</th>
<th>Less Than Monthly</th>
<th>Monthly</th>
<th>Weekly</th>
<th>Daily Or Almost Daily</th>
</tr>
</thead>
</table>

9. Have you or someone else been injured as a result of your drinking?

<table>
<thead>
<tr>
<th>Option</th>
<th>No</th>
<th>Yes, But Not In The Last 6 Months</th>
<th>Yes, During The Last 6 Months</th>
</tr>
</thead>
</table>

10. Has a relative or friend or a doctor or other health worker, been concerned about your drinking or suggested you cut down.

<table>
<thead>
<tr>
<th>Option</th>
<th>No</th>
<th>Yes, But Not In The Last 6 Months</th>
<th>Yes, During The Last 6 Months</th>
</tr>
</thead>
</table>
Demographics Questionnaire

Please provide the following information:

Name:

Email address:

Phone No. (mob) _____________ (b) _____________

Age: ___________ Years __________ Months __________

Gender (circle): Female / Male

Highest Educational Level: (e.g. Year 12 / B.App.Sc, etc.): ______________________________

Handedness (circle): Left / Right / Both

Have you ever suffered any serious head injuries or periods of unconsciousness? Yes / No

If yes, please specify: ______________________________

Do you have any hearing problems? Yes / No

If yes, please specify: ______________________________

Is English your first language? Yes / No
**PATIENT MEDICAL QUESTIONNAIRE**

Name:  
D.O.B:  
Phone:  
Sex:  

Instructions: These questions are designed to help us understand any medical problems that you may have. All information given will be treated in the strictest confidence. The research nurse will go through these questions with you.

Height (cm):  
Weight (kg):  

Medical History:
Are you allergic to anything that you know of?

- Medications?  □ Yes  □ No  
- Foods?  □ Yes  □ No  
- Surgical Tape?  □ Yes  □ No  
- Any other substance?  □ Yes  □ No  
If yes, please give details:

---

Do you take any medications (prescription or over-the-counter)?

□ Yes  □ No  

Background and concurrent disease:

Medications:

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
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<tbody>
<tr>
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<td>Respiratory</td>
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<td>Metabolic/Endocrine</td>
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<tr>
<td>Neurologic</td>
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</tbody>
</table>

If yes, give details below:
<table>
<thead>
<tr>
<th>Condition</th>
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<th>No</th>
</tr>
</thead>
<tbody>
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<td>Dermatological</td>
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<td>Hematological</td>
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<tr>
<td>Neoplastic</td>
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<tr>
<td>Other (specify)</td>
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</tbody>
</table>

Do you have any of the following problems?
- Heart problems?
- High or low blood pressure?
- Respiratory problems?
- Stomach or intestinal problems?
- Liver problems?
- Kidney or urinary problems?
- Diabetics?
- Anemia or blood disorders?
- Epilepsy or fitting?
- Eyesight problems or colour blindness?
- Cancer?
- Skin disorders?
- Anxiety or depression?
- Any other psychological problem?

If you answered YES to any of the above questions, please give details:

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**FEMALES ONLY**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you or could you be pregnant?</td>
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<tr>
<td>Are you breastfeeding?</td>
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<tr>
<td>On contraceptive pill?</td>
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</table>

Signature of Research Nurse:
Date:
Drug Use History Questionnaire

Please fill out the following information about your use of the following substances.

Note: If the questions are not applicable to you please write N/A.

1. Have you ever consumed alcohol?
   - [ ] Yes / [ ] No

1.1 When was the last time you consumed alcohol? Please tick a box
   - [ ] Hours ago
   - [ ] Days ago
   - [ ] More than 1 week ago
   - [ ] More than a month ago
   - [ ] Other. Please specify ____________________________

1.2 How frequently do you consume alcohol? Please tick a box
   - [ ] Daily or almost daily
   - [ ] One or two times a Week
   - [ ] Two or three times a Month
   - [ ] Once a month
   - [ ] Other. Please specify ____________________________

1.3 How many standard drinks do you typically consume in a drinking session?

1.4 How often during the last year have you needed a drink in the morning to get yourself going after a heavy drinking session? Please tick a box
   - [ ] Daily or almost daily
   - [ ] Once or twice a Week
   - [ ] Two or three times a Month
   - [ ] Once a month
   - [ ] Other. Please specify ____________________________

1.5 How long have you been drinking alcohol for? ____________________________
2. Have you ever consumed cannabis (marijuana)?
   Yes / No

   2.1 When was the last time you consumed cannabis? Please tick a box
   □ Hours ago
   □ Days ago
   □ More than 1 week ago
   □ More than a month ago
   □ Other. Please specify:

   2.2 How frequently do you consume cannabis? Please tick a box
   □ Daily or almost daily
   □ One or two times a Week
   □ Two or three times a Month
   □ Once a month
   □ Other. Please specify:

   2.3 When you consume cannabis, how much do you typically have? (i.e. One joint, 3 bongs)

   2.4 How long have you or did you use cannabis for?

3. Have you ever consumed amphetamines (speed)?
   Yes / No

   3.1 When was the last time you consumed amphetamines? Please tick a box
   □ Hours ago
   □ Days ago
   □ More than 1 week ago
   □ More than a month ago
   □ Other. Please specify:

   3.2 How frequently do you consume amphetamines? Please tick a box
   □ Daily or almost daily
   □ One or two times a Week
   □ Two or three times a Month
   □ Once a month
   □ Other Please specify:

   3.3 When you consume amphetamines, how much do you typically have? (i.e. One line, 1 point)

   3.4 How long have you or did you use amphetamines for?
4. Have you ever consumed MDMA (Ecstasy)?
   Yes / No

4.1 When was the last time you consumed ecstasy? Please tick a box
   - Hours ago
   - Days ago
   - More than 1 week ago
   - More than a month ago
   - Other. Please specify

4.2 How often do you consume ecstasy? Please tick a box
   - Daily or almost daily
   - One or two times a week
   - Two or three times a month
   - Once a month
   - Other. Please specify

4.3 When you consume ecstasy, how many tablets do you typically have?

4.4 How long have you or did you use ecstasy for?

5. Have you ever consumed cocaine?
   Yes / No

5.1 When was the last time you consumed cocaine? Please tick a box
   - Hours ago
   - Days ago
   - More than 1 week ago
   - More than a month ago
   - Other. Please specify

5.2 How frequently do you consume cocaine? Please tick a box
   - Daily or almost daily
   - One or two times a week
   - Two or three times a month
   - Once a month
   - Other. Please specify

5.3 When you consume cocaine, how much do you typically have? (e.g. One line, 1 point)

5.4 How long have you or did you use cocaine for?
6. Have you ever consumed heroin? Yes/No

6.1 When was the last time you consumed heroin? Please tick a box.

☐ Hours ago
☐ Days ago
☐ More than 1 week ago
☐ More than a month ago
☐ Other. Please specify __________

6.2 How frequently do you consume heroin? Please tick a box.

☐ Daily or almost daily
☐ One or two times a Week
☐ Two or three times a Month
☐ Once a month
☐ Other Please specify __________

6.3 When you consume heroin, how much do you typically have? (i.e. one hit)

6.4 How long have you or did you use heroin for?

7. Have you ever used inhalants (urethol, glue, etc.)? Yes/No

7.1 When was the last time you consumed inhalants? Please tick a box.

☐ Hours ago
☐ Days ago
☐ More than 1 week ago
☐ More than a month ago
☐ Other. Please specify __________

7.2 How frequently do you consume inhalants? Please tick a box.

☐ Daily or almost daily
☐ One or two times a Week
☐ Two or three times a Month
☐ Once a month
☐ Other Please specify __________

7.3 When you consume inhalants, how much do you typically have?

7.4 How long have you or did you use inhalants for?
DEBRIEFING QUESTIONNAIRE

Subject No:  
Date:  
Time:  

1. Were you comfortable?
   - Hungry/Thirsty
   - Caffeine cravings
   - Physical comfort
   - Fatigue
   - Nausea

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2. Were you unsure of any instructions?
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3. Do you think you received alcohol or the placebo? Do you think there was a difference in your performance?
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4. Did any of the words or pictures significantly distress you?
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5. Can you think of anything else that may have affected the data?
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6. Any concerns/comments/queries?
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Thank-you for your participation.
Copies of the Ethics Forms and Consent forms for the alcohol, methamphetamine and MDMA comparisons were included in order to provide the reader with additional information about the procedures in place to ensure participant and experimenter safety during the experimental sessions. Please note that the methamphetamine and MDMA ethics form is for the larger study conducted examining the effect the drugs had on driving performance. Participants in the methamphetamine and MDMA study received more specific information about the current study procedures during their first interview.
### APPLICATION FOR ETHICS APPROVAL

**SECTION A: GENERAL INFORMATION**

**PROJECT FULL TITLE:** The effect of alcohol on psychological processing and memory of trauma and non trauma related information.

**SHORT TITLE:** (If applicable)  

**APPLICANT/DETAILS**
- **Principal Investigator/SUPervisor:** Professor Grant Dovill
  - Tel No(s): 5221 5020
  - Email: g.dovill@swin.edu.au
  - Fax: 5221 5277
- **Swinburne Staff Reference No.:** 023
- **Swinburne Staff Name:** Adjunct Staff Member
- **Address for correspondence:**

**Main Student Investigator(s):** Tamara Wulan
- Tel No(s): 0412 321 802
- Email: 2147@svu.edu.au
- Student ID Number: 2147401
- Degree Being Undertaken: BA(Hons) Clinical

List below the names of other Undergraduate, Associate Investigators and Research Assistants (including those with access to identifiable data). If no copies are required for additional investigators/assistants, Appendix D should be used.

<table>
<thead>
<tr>
<th>Name &amp; Title</th>
<th>Position</th>
<th>Email</th>
<th>Tel No(s)</th>
<th>Student ID Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Redouc Hesta</td>
<td>Research Assistant</td>
<td><a href="mailto:mesta@group.swin.edu.au">mesta@group.swin.edu.au</a></td>
<td>9214 5007</td>
<td></td>
</tr>
<tr>
<td>Jenny Lloyd</td>
<td>Research Nurse</td>
<td><a href="mailto:jolly@swin.edu.au">jolly@swin.edu.au</a></td>
<td>9214 4444</td>
<td></td>
</tr>
</tbody>
</table>

**Proposed Period During Which Human Research Activity Requiring Ethics Approval is Needed:**
- **From:** 01 01 2008
- **To:** 01 12 2008

**TYPE OF ACTIVITY**
- [X] Research by Staff Member
- [ ] Supervised Postgraduate Research
- [ ] Supervised Undergraduate Research
- [X] List of students involved

**BROAD CATEGORY OF RESEARCH**
- [ ] Social/Cultural
- [ ] Psychological
- [ ] Other (please specify)

**FOR RESEARCH INVOLVING CLINICAL TRIALS OR IONISING RADIATION, please contact the Research Ethics Officer.**

Human Research Ethics Committee

Page 1
Human Research Risk/Review Classification (NB: Checking 2 is inconsistent with published risk criteria.):

- [ ] Minimal Risk
- [x] Low Impact Research Only
- [ ] SUHREC
- [ ] OIEC (HGS - A/D)
- [ ] OIEC (GDT A/B)
- [ ] Other
- [ ] Notification Only

To enable a determination as to whether prima facie your research activity is Minimal Risk or Low Impact, please classify by selecting (X) any one or more boxes below as to whether your research activity involves:

- [ ] National or International participants, including those dependent on care
- [ ] Indigenous or Kaplan or城镇化 groups
- [ ] Other types of research requiring HRREC level clearance
- [ ] Multi-center/Other site requiring HRREC level approval
- [ ] Research conducted overseas
- [ ] Data access/without at individual's prior consent
- [ ] Multi-center/Other site requiring HRREC level approval
- [ ] Data access/without at individual's prior consent
- [ ] Data access/without at individual's prior consent
- [ ] Data access/subject to statutory guidelines for reporting
- [ ] Identification of participants: individual/group in research outcomes with full consent or without consent for that research
- [ ] Sensitivity information released outside research environment: (e.g., requiring consent; commercial, professional, cultural, etc.)
- [ ] Personally identifiable containing information about an activity or other activity
- [ ] Physically identifying/relocating techniques or significant physical contact/behavior (e.g., CT scan, MRI, other imaging etc.
- [ ] Working in hazardous environments (e.g., asbestos, dangerous goods, etc.)
- [ ] Handling hazardous substances (e.g., radioactive, chemical, etc.)
- [ ] Administration of medications/substance treatments
- [ ] Administration of other non-medical substances
- [ ] Psychological/behavioral interventions, including counseling
- [ ] Assessment of an individual using treatment of privacy
- [ ] Withdrawal: withdrawal of treatment or professional advice in the absence of any procedures or exercises
- [ ] Notification of consent
- [ ] Limited or non-disclosure of research information
- [ ] Participants recruitment/redemption via third party
- [ ] Human research activity accompanied by withdrawal
- [ ] Participation in research, places or significant payments
- [ ] Research participant researchers/research assistants at risk

PLEASE NOTE: If you have selected any one or more of the above boxes, your project will automatically be put for SUHREC ethical review. If the ethical review is granted, then your project will be reviewed by the SUHREC ethical review committee. If in doubt, you may wish to seek legal advice for unanswerable or unanswerable ethical review by the SUHREC ethical review committee. If your project is selected, you will be notified of the relevant SHREC. However, the relevant SHREC may still consider the relevant risks for SUHREC approval or SUHREC may review or override the SHREC decision.

Human Research Ethics Committee
(Aug 2004 - Amended August 2006)
Post Traumatic Stress Disorder (PTSD), has been the subject of considerable empirical research, since it was first included in the Diagnostic and Statistical Manual of Mental Disorders (DSM-I) in 1980. An important goal of research in the trauma area is to determine factors that may increase or decrease a person’s chance of developing the disorder. A large body of research exists evaluating the influence of psychological, social and biological factors on PTSD prevalence (see for example Brown & Huhner, 2001; Buckley, Blanchard & Noll, 2000; Vermetten & Kramar, 2002a; Vermetten & Bremner, 2002b; Williams & Yule, 1985). In contrast only two uncontrolled studies have evaluated the impact of alcohol on individuals at the time of the trauma has on the risk of later developing PTSD. The aim of this study is to investigate the acute effects of alcohol on information processing and memory for trauma and non-trauma related information in healthy individuals. This would be the first controlled investigation into the area and would lead to new insights into the cognitive processing of trauma related information with implications for the brain functioning and prevention of PTSD specifically, and anxiety reactions generally.

The Effects Alcohol has on Cognition and Memory

Research exploring cognitive processing following alcohol consumption has consistently found impairments in information processing ability. Research indicates that even at low doses visual and auditory reaction times are increased following alcohol consumption (Lemon et al., 1990). Research examining free recall following alcohol consumption found impaired ability to explicitly remember words, with implicit memory remaining intact, suggesting selective memory impairment (Lister et al., 1991). Research also suggests that the demands of the task increase, for example under dual-task conditions, the alcohol-induced impairments increase (Maylor et al., 1990).

A recent, double-blind, Electroencephalographic (EEG) study examined the effect of moderate amounts of alcohol on brain function, cognition and performance in a sample of eight participants (Iton & Govino, 2001). Alcohol impaired performance on psychomotor and memory tasks with a widespread increase in background EEG power. These physiological changes were still evident several hours after the chemical and behavioral indicators of intoxication had diminished. These results appear to indicate that brain regions required for accurate stimulus processing were less available for use following alcohol consumption and remain unavailable for several hours after consumption.

Initially, it was not clear whether impairment in the early stages of information processing was responsible for the observed impairment in total information processing following alcohol consumption. A study conducted by Tramontana and Slough (2000) explored inspection time (IT), alliance reaction time, reaction time and cognitive ability with the WAIS-R following the consumption of 40ml of alcohol. Alcohol significantly affected inspection time suggesting an alcohol induced slowing of early information processing, in addition to an observed impairment in simple and choice reaction times as well as higher order complex tasks on the WAIS-R. These results together suggested alcohol significantly impaired total information processing independently of the early stages.

Similarly, in research conducted by Miccio and Vogel-Sprott (2005), the effect alcohol had on immediate working memory was systematically examined using the Standard Memory Scanning task, a task designed to measure working memory as distinct from the other three stages of memory. Significantly slower reaction times and increased errors were evident following alcohol ingestion. Furthermore, these impairments increased as the task demands increased and working memory was functioning at near maximum level. Interestingly, when a reward for performance on the task was introduced, reaction time and rate of scanning improved in those participants who had ingested alcohol and did not differ to the placebo group. The study also found that as alcohol concentrations...
were lowered, reaction time and scanning time improved, however accuracy remained impaired.

In a more recent study, the relationship between pre-injury alcohol consumption and post-injury cognitive functioning following a traumatic brain injury was examined (Tumur, Kivlani, Rimmler & Horremmeier, 2009). Previous research in this area has been inconclusive as a result of the various methods used to assess both alcohol consumption and cognitive functioning. This study prospectively quantified the relationship between alcohol-related variables and cognitive performance in a group of 124 patients admitted to the inpatient rehabilitation ward of a major hospital. Blood alcohol levels were obtained through blood tests and standardized self-report measures used to obtain information about alcohol consumption and alcohol-related problems. No independent report from relatives or friends was used to validate these self-report data.

In contrast to previous research findings, the results of the study suggested alcohol use prior to a traumatic brain injury was not related to post-injury cognitive functioning. More specifically, both a history of alcohol consumption and the Blood Alcohol Concentration (BAC) on admission to hospital was not related to cognitive functioning during or following recovery. A significant limitation to these conclusions however, is the failure to test patients after a fixed interval of time or to use standardized inclusion criteria.

Alcohol as a protective factor against PTSD

Although research has examined alcohol use following a traumatic event, very little research has examined the effect alcohol use prior to the traumatic event has on the cognitive, emotional and physiological reactions of victims. In a study conducted by Maas and colleagues, researchers attempted to determine factors that predicted the development of PTSD in a sample of 127 adults following a barroom fight (Maas et al., 2000). PTSD symptoms were evaluated using the Composite International Diagnostic Interview (CIDI), administered seven to nine months after the traumatic event. Results revealed that a sense of control during the trauma in addition to the consumption of alcohol and actual alcohol intoxication acted as a significant protective factor against the development of PTSD. These variables appear to represent genuine preventative factors, with statistical analyses indicating a moderate effect size.

The authors proposed two possible explanations for their results, the first of which suggests that the anxiolytic effects of the alcohol may have reduced the overall level of arousal and anxiety experienced by victims during the traumatic event (Maas et al., 2001). Anxiolytic refers to drugs used in the treatment of anxiety (Kandel, Schwartz & Jaffe, 2000). However, as alcohol did not have any significant associations with the other peri-traumatic variables identified in the study, the researchers suggested an additional reason they viewed as more plausible (Maas et al., 2000).

They suggest that the alcohol intoxication reduced the encoding, consolidation or retrieval of the traumatic memory and fear responses conditioned to them (Maas et al., 2001). Emotional memory is believed to be dependent upon the activation of central Noradrenergic systems and N-methyl-D-aspartate (NMDA)-related mechanisms in amygdala structures. According to the researchers, alcohol may inhibit the NMDA-mediated synaptic pathways usually activated in these amygdala structures, by attenuating the stress response on Norepinephrine turnover in the amygdala and locus coeruleus.

A more recent study investigated the association between reported alcohol use prior to a sexual assault and self-reported post-traumatic reactions in a sample of 67 college students (Chu, Neush & Cullum, 2002). The women were required to complete questionnaires assessing the perception of the assault severity and the physical and emotional post-traumatic symptoms experienced after the event. Alcohol use at the time of the assault was associated with perceptions of the assault as less severe. These findings may suggest an alcohol-induced memory distortion, resulting in an impaired ability to remember one's response during the sexual assault. However, as the relationship between self-reported...
memories for the event was not significantly related to the amount of alcohol use reported, an alternative explanation for these results may be possible, such as the alcohol numbing the anxiety response cultivated during and following the traumatic event.

Why Examine the Effect Alcohol Has on Emotional Memory

Of all illicit and illegal drugs consumed during the occurrence of traumatic events, alcohol is one of the most common. Excessive alcohol consumption is the most common cause of both intentional and unintentional traumatic injury (Tippett, Taylor & Law, 2000). In Australia it has been estimated that 44% of all injuries, 74% of deaths, and drowning, 30% of car accidents, 47% of assaults, 10% of child abuse, 10% of suicides and 7% of industrial accidents are associated with alcohol use (NHMRC, 2001). It is estimated that 34% of offenders and 31% of victims of violence and homicide are also under the influence of alcohol at the time of the event. Injuries caused by road accidents or violence are the usual common consequence of alcohol intoxication for young adults. Between 1990 and 1997, 63% of people injured during alcohol-related road accidents were aged between 15-34 years and 29% were aged between 25-34 years.

A recent study conducted at the Royal Melbourne Hospital in Australia, found that 39% of the young emergency department patients were classified as at risk from their hazardous drinking (Tippett, Taylor & Law, 2000). Furthermore, many of these patients had not received any previous advice to cut down their alcohol consumption. Research also suggests those individuals who report drinking above the low-risk levels or who drank more than six hours before their injury were significantly more likely to sustain a serious rather than mild injury (Watt et al., 2003). This research suggests alcohol has a significant impact on an individual's risk for engaging in an activity that could result in the occurrence of a trauma when intoxicated. The potential cost to the community of alcohol-related traumatic injury is significantly high. Emerging research also suggests alcohol might modify the sympathetic nervous system response activated following a trauma (Wooll et al., 1998). While alcohol appears to reduce the norepinephrine and adrenaline levels in patients after a severe head injury, in patients with only mild head injuries, alcohol causes an increase in these catecholamine levels. This research raises the question of whether alcohol intoxication at the time an individual experiences a trauma might significantly impact the resulting patient outcome and emotional response to a trauma.

Summary

In summary, the primary aim of the current study is to examine the effect alcohol has on affective reactions and processing of trauma and non-trauma related material in healthy individuals. The study also aims to examine the effect alcohol has on memory for trauma and non-trauma related material. It is hypothesised that alcohol intoxication will impair the memory for the traumatic material more than the non-trauma related material and similarly impair the memory for the traumatic material. It is hoped the current research will contribute to a greater knowledge base relating to the effect central nervous system stimulants and depressants have on cognitive functioning.
A2 WHAT - BRIEF DESCRIPTION OF PROJECT

In plain English

Twenty healthy volunteers of both sexes, aged between 21 and 36 years, will take part in the study. All participants will undergo a screening process to ensure that they are fit to participate (Appendix A1). All participants will be screened to ensure they are physically and mentally healthy, free from prescription medications (with the exception of the contraceptive pill and drugs of abuse). Participants will be required to be moderate drinkers, weekly averaging between 0.5-1 drink per day for females, and 1-3 drinks per day for males. They will also need to be experienced in binge drinking (drinking 5 or more standard alcohol drinks on a single occasion). Participants will also be required to have a body weight within 20% of the normal range according to gender, height and stature, and their body mass index to be below 25kg/m².

Participants will initially contact the researcher and discuss the study and a time will be set up for an interview. The information sheet and consent form will then be sent out and completed in the interview. Participants will be asked to read the information sheet outlining the details of the study (Appendix A1). All questionnaires will be answered and subsequently participants will be asked to complete a consent form (Appendix A4).

The study will involve a double-blind (the experimenter and the participant will not know whether the drug administered is active, placebo-controlled (active drug effects will be compared to placebo effects) study design and will comprise two main experimental sessions (Alcohol and Placebo). The research nurse, who will be administering the alcohol and placebo conditions, will allocate each participant to their experimental condition (alcohol or placebo). Only she will have a copy of the condition allocation for each participant. This sheet will contain only the participant number (U1) and will be locked securely in a filing cabinet at the BSI. There will be a two-week wash-out period between the two testing sessions. In total, participants will come in three times. On one of these occasions they will receive alcohol. On the other occasions they will receive the placebo. The third occasion only involves the follow-up memory test. They will not receive anything on this third occasion. Participants receive the alcohol condition once and the placebo condition once.

The dose of alcohol to be administered will be comprised of 30ml of vodka, mixed with 200ml of water and 200ml of orange juice, with a dash of peppermint essence. The participants will be required to consume 1.3 grams of alcohol per kg of body weight over a 3-hour period. The peppermint essence is used to control for the taste of the vodka to assist in the blinding of experimental conditions. The research nurse will be administering the alcohol and monitoring all participants throughout the session. Participants will be sufficiently intoxicated to reach a Blood Alcohol Concentration (BAC) level at 0.1.

In the first experimental occasion, after reaching a BAC of 0.1, participants will be asked to undertake the Lexical Decision Task, followed by a one-minute verbal short-term recall test. Participants will then be asked to undertake the Affectional Picture Task. These tasks take about 20 minutes to complete. Blood alcohol level readings will be made both before and at completion of the experimental tasks with a Breath tester. At the completion of the first experimental session, participants will be required to remain at the Brain Sciences Institute (BSI) for a minimum of at least 2 hours or more until they reach a BAC level of 0.06. Participants will then be provided with a taxi voucher for their transportation home.

For those participants who may require additional assistance during their transportation home (females in particular and participants still displaying signs of intoxication), they will be accompanied by one of the experimenters.

Two weeks later, before administering the drug condition, participants will be asked to complete a one-minute free recall test, followed by a picture recognition test. They will then be given the drug condition over a period of 3 hours. Participants will then be asked to complete the Lexical Decision Task, short-term recall test and Affectional Picture Task. Participants will remain at the BSI for a minimum period of 2 hours until reaching a BAC of 0.05 before being transported home by taxi. All testing presentations will be randomised and counterbalanced. Two weeks later participants will return a third time to...
A. HOW PROCEDURES

Please detail clearly and sufficiently the proposed research methods and procedures and instruments to be used in the project, including all screening and measurement techniques and in whom the participant will be subjected, and estimate those which may have adverse consequences.

Please include any special procedures, techniques, instruments, equipment, etc. (be specific in detail if not indicated).

Individuals will be recruited through local advertisements (Appendix A2). Individuals interested in participating in the current protocol will initially be informed about the details of the study and have requirements over the phone by one the study's investigators. The investigators will also use this opportunity to make an initial determination as to whether the individual violates any of the exclusion criteria* (Appendix A2). Before beginning the phone screen the possible participant will be told that the phone screen may include revealing some personal information about medical issues and possible criminal behaviour such as illegal drug use. Permission will be asked to discuss these topics before proceeding. Possible participants will be told the information is required for screening purposes only and will remain confidential unless issues of harm are revealed. If they subsequently do not choose to take part in the study this information will be destroyed. Participants will be told that the information obtained in the phone screen will be stored securely in the BSI in a locked filing cabinet. The individual will then be invited to meet the investigators at the BSI and told that an information sheet will be sent out for them to read before attending the interview (Appendix A3).

This interview will take place in a private room with no other students or participants present. At this meeting the investigator will ask the participant about their understanding of the study requirements and all participants will be given the opportunity to raise any questions or concerns. The researcher will take this opportunity to ensure the participant has understood what is required of them and will discuss all the possible risks and measures taken to reduce these risks. Participants will also be told that if, during the course of the screening interview information is revealed that seems unlikely to participate they will not be selected for the project and their details destroyed. They will be assured of anonymity, and that if certain criteria make it unsafe to include certain information it will be told that during the screening process certain questionnaires ask for information such as illegal drug use. They will be told that this information will remain highly confidential and stored safely at the BSI. They will also be told that apart from the consent form only numbers and no names will appear on the documents and all other documents used in the study. The consent form will be stored separately to the other documents used in the study. Participants will then be asked to sign the consent form (Appendix A4). An individual not involved in the study will witness this. The participants will then be told that for screening purposes some questionnaires need to be filled out and that all information will remain confidential and stored securely (Appendix A5). They will be told that this questionnaires cover the relevant medical and psychiatric history, alcohol drinking habits and experiences, illicit and licit drug use, anxiety sensitivity, premorbid intelligence and any post-traumatic stress symptoms. Participants will be informed that the main researcher is a probationary psychologist who has been trained and is experienced in accessing for sensitive information such as those included in the questionnaires. She will be supervised by the Director of Research, Professor Coen Devilly, who is a registered psychologist with clinical and forensic specialties.

After completing these, the participants will have a brief interview with the Institute's Registered Nurse where they will discuss the details of the study in detail and their responses to the questionnaires. The Nurse will use this opportunity to determine whether the potential participants have understood what will be required from them and whether they are suitable candidates for entry into the study. Potential participants will also have their height and weight measured by the Nurse. The Nurse will also take vital signs such as blood pressure for a baseline measure to use during the study.

Each participant will be booked in to participate in three sessions that will be conducted 2 weeks apart. The project will involve a repeated measures, double blind, placebo controlled methodology. Each of the two experimental sessions will involve more than 6 hours. The third follow-up session will involve only 20-30 minutes. In one of the experimental sessions, participants will receive the placebo, in the other experimental session they will receive the placebo, in the third condition, they receive nothing. This...
research nurse, who will be administering the alcohol and placebo conditions, will allocate each participant to their experimental condition (alcohol or placebo). Only she will have a copy of the condition allocation for each participant. This sheet will contain only the participant number (01) and will be locked securely in a filing cabinet at the BSI.

For each experimental condition participants will be instructed to abstain from drinking alcohol for a period of 24 hours and no other prescription medications or drugs for at least 7 days prior to the sessions. Participants will be asked to have a standard meal before catching a taxi to the BSI. Participants will then be instructed to drink 13 grams of alcohol per kg of body weight over a 3-hour period (an average of 0.8 standard drinks) until they reach a BAC level of 0.1. The necessity for this amount of alcohol has been established by a number of studies that have examined the effects of alcohol on cognitive functioning (Wiese, Shiffrick & Bronner, 2000; Kim et al., 2003; Versler et al., 2003). The standard drink will be comprised of 30ml of vodka mixed with 320ml of orange juice and peppermint essence in disposable clear plastic cups. The placebo will comprise of water, orange juice and peppermint essence to control for the taste as much as possible. Vodka was chosen as this is associated with less of a hangover effect the next morning (Wiese, Shiffrick & Bronner, 2000). Over the 3-hour drinking period the participant will be seated in a relaxed and controlled environment and will be closely monitored by the study's investigators at all times. At hourly intervals the Registered Nurse will take the participant's BAC with a Breathalyser and monitor for any negative side effects. The study will be conducted in the BSI during working hours with other colleagues and supervisors in surrounding areas who will be notified that participants will be drinking alcohol. The university security will also be notified of the study. The participants will cease drinking once they have reached a BAC of 0.1.

Participants will then be asked to undertake a Lexical Decision Task. Words and non-words will be displayed via an IBM computer, and the participants' task will be to indicate whether the letters on the screen form a real word or a non-word (list attached as appendix B1). The real words will possess either a neutral, positive, negative or threat-related emotional valency. At the end of the task, participants will be asked for free recall of the real words, which they had just seen within sixty seconds. These tasks will take about 15 minutes to complete. Participants will then be presented with, and asked to rate, six sets of images, a selection of neutral, positive or threat-related pictures from the International Affective Picture System (Lang & Olmon, 1998; see appendix C).

This task will take 10 minutes to complete. All testing presentations will be randomised and counterbalanced. The researcher or research assistant trained in psychophysiology and psychology will administer the tests.

Two weeks later before being administered the drug condition; the participants will be asked for free recall of the words they were shown in the original lexical decision task (two weeks earlier followed by a recognition recall task of the pictures presented during the Affective Picture system task). They will then be given the drug condition and taken through the lexical decision task and International Affective Picture System task again, with new words and pictures, matched for affect valency to those in the first session. The word list sets and the International Affective Picture presentation sets will be presented in random order across the two presentation time periods. Two weeks later when the participants return for their third follow-up they will be asked to complete the free-recall and recognition tasks as in the second session and asked to complete a deception questionnaire about their involvement in the study.

For each of the two experimental conditions, upon completing the cognitive tasks, the participants will be required to remain at the BSI with the experimenter in a sedate environment for a minimum of two hours. This will occur despite one occasion involving placebo to ensure consistency in the research design. Past research in addition to the previous experiences of researchers within the Drugs and Driving Research Unit have indicated that 3 hours is the average amount of time required for individual RAC levels to drop significantly and for the effects of intoxication to become greatly reduced (Versler et al., 2003). Participants will not be allowed to leave the BSI until their RAC levels have dropped to 0.05. Although this is the legal limit to drive the participants will not be allowed to transport themselves home. The study's investigators will arrange transportation home for participants from the BSI via taxi vouchers. Prior to booking this transportation the investigators will inform the taxi company that the intended customer had been drinking alcohol up until 2 hours previously. For certain participants the investigators will accompany the participants during their transportation home following the drinking
session, rather than let them travel unaccompanied by taxi. Females in particular and any
participants still displaying signs of intoxication (i.e. speech impairment, physically unwell,
motor difficulties) will be accompanied home by a police officer. Participants will be
instructed not to drink or consume any drugs or prescription medication for at least 24 hours
after the experimental session and to abstain from driving for at least 24 hours.
Participants will have the numbers of the researchers and registered nurse at the BSI and
be instructed to call if they experience any adverse reactions the following day.

A4 DESCRIBE ANY RISK THAT MAY ARISE TO THE PARTICIPANT / DONOR?

Risk to participants (and to researchers) can be real but does not need to be physical. Risk includes such as: self-harm, sexual harassment, and external
liability, disease, physical harm, loss of employment or professional standing. etc. Please consider each possibility carefully.

Some research institutions may put the participant at risk through what is being done or simply through their participation.

Please describe the risk you perceive and the precaution measures to be taken.

There is the possibility of legal risk as a result of participants disclosing sensitive
information about illegal drug use to the researcher. The participant will be told that this
information is required for screening purposes and is not the main aim of the study.
Participants will be told that the information will remain confidential unless information is
revealed that involves a possible risk of harm to themselves or others. Permission will be
sought before asking for this information. The individual who will obtain the information is
a working probationary psychologist and research nurse who both have their own ethical
and legal obligations to report criminal behaviour. This information obtained will be
recorded on documents that only have a number as the identifier and will be stored
securely and separately to the consent forms and names of all participants.

It is likely that individuals will experience increased attention and concentration. Impaired
motor control, elevated mood and decreased anxiety following the consumption of the
active drug alcohol. At high BAC levels individuals might also experience dizziness,
nausea, a dry mouth and muscle aches. Participants might also experience a hangover
the following day involving a headache and some nausea. The research nurse will
administer the alcohol and continue to monitor the participants throughout the
experimental sessions. The likelihood of participants experiencing these negative
reactions has been controlled for as much as possible by making sure participants are
regular drinkers with experience drinking vodka and 6% standard drinks on one occasion,
and ensuring they receive the amount appropriate to their height and weight. The risk of a
hangover the next day has been reduced as much as possible by using vodka, a clear
spirit which is associated with less of a hangover than the coloured alcohols.

The registered nurse will monitor the participants throughout the session for any negative
reactions and participants will cease drinking if they feel ill. Participants will be told that
they can stop drinking and withdraw from the study at any time, if participants do withdraw
they will still be asked to take the taxi home and not to consume any prescription
medication, illicit drugs or alcohol for at least 24 hours after the testing session.
Participants will also be told they can contact the researchers or research nurse at the
BSI the next day if they are experiencing any adverse reactions.

There is a possible risk that participants could injure themselves when intoxicated during
to their impaired motor control. For this reason participants will be seated in the waiting
room while drinking and asked to watch tv or read a book or magazine. They will be
administered in plastic cups, so if these are dropped there is no risk of cutting. All these
cups will be disposed of after use with new ones used for each participant. Participants
will be told that they will not be allowed to leave the BSI at any time during the
experimental session or that if they choose to withdraw they will still be asked to take the
taxi home. Participants selected for involvement in this study will also be required to have a
mature attitude with a genuine desire to contribute to research. Previous experience with
similar research has indicated that participants rarely become agitated or over-sensitive
and in danger of harming themselves during their drinking session. Many past
participants have commented that the environment of the BSI is quite sobering.

Alcohol impairs driving ability and for this reason the study will be providing participants
with taxi vouchers for their transportation to and from all of the experimental sessions.
Participants will remain at the BSI after their testing session for at least two hours. During
this time they will be asked to sit in the waiting room and watch tv or read a book or
magazines. Participants will be required to have a BAC of 0.05 the legal limit and to have
a residual check with the registered nurse before leaving the BSI. If the research nurse
believes that the participants need to remain at the centre longer before leaving.
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A5. ANY RISK THAT MAY ARISE TO THE RESEARCHER / ADMINISTRATOR?

There is a possible risk of injury to the researchers and research nurse during the experimental sessions, if an intoxicated participant becomes agitated or violent. This risk is very low and past research in the drugs and driving field has never had any incident of participants becoming agitated or violent. To control for this possibility the research will be conducted at the RC5 during working hours, with surrounding colleagues and students who will be informed that participants will be drinking alcohol. The university security will also be informed about the study and will be notified in the event of a participant becoming agitated or argumentative.

A6. WHAT BENEFITS ARE ANTICIPATED FROM THE PROJECT?

Clinical principles would require that benefits flowed from the activities that pleased a skilled researcher.

A7. POTENTIAL PROBLEMS

This would be the first controlled investigation into the area and would lead to new insights into the cognitive processing of trauma related information with implications for the pathophysiology and prevention of PTSD specificity, and anxiety reactions generally. It is hoped that the current research would indicate whether alcohol could increase or decrease a person’s chance of later developing PTSD by enhancing or attenuating the processing and storage of emotional memories. Results from the current study will also contribute to a larger knowledge base relating to the effect central nervous system depressants have on cognitive functioning.

A8. PROFESSIONAL ETHICAL ABILITY & TRAINING (Researchers/Students/Assistants)

(a) Sufficiently detail what investigations/assessments will be done in this project and their empirical appropriateness to the research... using (appropriate) techniques... (and with appropriate skills and experience in dealing with any contingencies...)

Human Research Ethics Committee
The researcher who will be running this project with the assistance of a research assistant has previously conducted similar research under the supervision of Dr. Keithstone Pascoalino as part of the drug and driving unit. She has been involved in the methamphetamine study conducted in 2004, the alcohol hangover study conducted in 2005, and is currently involved in the methamphetamine and MDMA study being conducted over 2007 and 2008. The researcher will be involved in the recruitment of participants and the administration of the cognitive tasks. The researcher is also a probationary psychologist with ethical and legal obligations as part of the profession and experience in discussing issues of confidentiality. The research assistant will assist the researcher in the recruitment of participants and the administration of the cognitive tasks. The research assistant is currently running the methamphetamine and MDMA drug and driving study. The research nurse will administer the alcohol and placebos and measure the BAC levels of participants. The research nurse will also monitor participants throughout the experimental sequence and complete medical check before participants leave after the testing occasion. The research nurse is also a probationary psychologist and has had extensive experience working on research protocols over the past couple of years.

(b) Sufficient detail, any other transcriptions reported to investigators is carried out the project.

N/A

A9 FUTURE USE OF DATA
Will any of the data be used by yourself, your students or others for any purpose other than for this project as described in the protocol? If so please describe.

N/A

A10 EXTERNAL INVOLVEMENT
Is a body external to the sponsors involved in the initiation or support of the project? 

☑  Yes. Name of body/organisation:

If an external body is associated with the project you must provide the IREC with detail of the arrangements, including details of any funding or other resources being provided. A copy of relevant papers from the external arrangement should also be attached.

☑  No.

A11 EXTERNAL APPROVALS
Projects involving other organisations in the community may require approval from other organisations or their ethical committees, etc. for such things as access to prospective participants, contact lists, data files, etc. A copy of such approvals may be required to be provided to the IREC at the time of application or be made available as soon as possible. In which case the project may not commence, until such evidence is provided.

☑  Yes. At least one approval has been obtained to sought.

☑  No. (please explain)

A12 RESEARCHER / SPONSOR RELATIONSHIP
Is there any relationship or association between the sponsor and any of the researchers listed in Section A of this form, for example are any of the researchers directors, officers, employees, shareholders or promoters of the sponsor or do they receive any personal benefits from the sponsor under any other contracts or arrangements?

☑  No.

☑  Yes (please explain the relationship(s), including how a conflict of interest situation does not arise.)
SECTION B: ETHICAL ISSUES OVERVIEW

B ETHICAL ISSUES

(a) Non-Limited Disclosure or Notification In any detail in relation to research outcomes, methods or questions being utilized from participants? Or clearly defined at any level disclosing?

(b) Intent the data collection process involve access to confidential personal data (including access to data without the prior consent of the participants)?

(c) Will participants have pictures taken of them, e.g., photographs, video recordings?

(d) Will interviews or in-home conducted, will they be recorded by electronic device?

(e) Will participants be asked to perform any acts or make statements which might compromise them, diminish self-esteem or cause them embarrassment or regret (minimal risk or significant)?

(f) Might any aspect of your study reasonably be expected to place the participant at risk of bodily injury or death?

(g) Might any aspect of your study reasonably be expected to place the participant at risk of bodily injury or death?

(h) Will the research involve access to data and/or subject to data privacy legislation?

(i) Will participants be asked to perform any tests or make statements which might compromise them, diminish self-esteem or cause them embarrassment or regret (minimal risk or significant)?

(j) Will interviews or in-home conducted, will they be recorded by electronic device?

(k) Will any treatment be used with potentially unpleasant or harmful side effects?

(l) Does the research involve any stimuli, tasks, investigations or procedures which may be experienced by participants as stressful, innocent, aversive or unpleasant during or after the research procedures?

(m) Will the research involve the use of invasive procedures or the administration/inhalation of medication, programs or services (health, educational, commercial, of other)?

(n) Will any samples of body fluid or body tissue be required specifically for the research which would not be required in the case of ordinary treatment?

(o) Will participants be fingerprinted or DNA fingerprinted?

(p) Are there in your opinion any other ethical issues involved in the research?

NOTE: If the answer to any of the above questions is "yes", please explain and justify fully in sufficient detail. (The box below will expand to fit your response.)

(e) A minimal risk due to the disclosure of private medical information. The information is necessary to ensure that participants who are involved in the study are fully informed and without any medical conditions that might be compromised by alcohol intoxication. The information is also needed to minimise the likelihood of adverse reactions following the alcohol intoxication. Private medical information about psychiatric symptoms is needed to ensure none of the participants are experiencing any clinical symptoms that might put them at a higher risk of experiencing adverse reactions to the testing material in addition to compromising the results of the study.

(f) Alcohol has a moderate risk of inducing negative symptoms such as dizziness, nausea and muscle aches. This risk will be minimised as much as possible as discussed elsewhere. It is necessary to get individuals intoxicated to a level of 0.1 or previous research has documented the most significant results at these levels and has previously been used in other research at Swinburne. Previous research has also found this level of be safe and well tolerated BAC level for experimental testing. This is also the level that is more commonly associated with the increased risk of engaging in dangerous behaviour that might lead to a traumatic event.

(g) A placebo is one of the compounds that will be orally administered, which does not contain the active treatment (alcohol). It is an important component of the experimental design as the condition allows the...
experimenter to ascertain that the observed results are due to the administration of the alcohol. The placebo will contain peppermint essence to control for the taste of the alcohol.

(em) Breath Alcohol Concentrations will be measured with the use of a Breathalyser. This is the most commonly used method for measuring the level of alcohol in the body and is minimally intrusive. It is necessary to measure the participant’s Breath Alcohol concentrations to measure when they are at the target level for testing and to ensure they are at the legal limit when leaving the BC.
SECTION C: PARTICIPANT DETAILS

C1 PARTICIPANT DETAILS

The composition of the participant group may, in some circumstances, disturb and invalidate an outcome, and data may arise through the composition of the participant group.

How many individual participants will be involved? (Number/number ranges for which approval is sought)

Males: 10

Females: 10

Total participants: 20

Over what range of ages?

From (youngest): 18

To (oldest): 35

If there is a gender or age imbalance in the number of participants please explain why.

N/A

C2 RECRUITMENT

How will participants be recruited/selected?

Please outline the process in sufficient detail how this is to occur.

Note: Where participants are obtained from or through schools, hospitals, prisons or other institutions, separate institutional or other authority will probably be needed. If existing for participants by advertisement or poster places attach proposed topic or text.

See also Request Information (Patient Statements and Signed Consent Form) at this part of this approval form.

Participants will be recruited through advertisement on community and university notice boards, and by word of mouth (Appendix A3). All participants will be screened to ensure they are physically and mentally healthy, free from prescription medications (with the exception of the contraceptive pill) and drugs of abuse. Participants will have no history of current or past substance abuse, no pre-existing physical or neurological conditions, no history of cardiac, endocrine, gastrointestinal, or bleeding disorders and not pregnant or lactating. Participants will not have any serious psychiatric disorder that would put them at a higher risk of adverse reactions to the testing material. Participants will be required to be moderate drinkers, weekly averaging between 0.5-1 drink per day for females, and 1-3 drinks per day for males. They will also need to be experienced in binge drinking (drinking 3 or more standard alcoholic drinks on a single occasion). Participants will also be required to have a body weight within 20% of the normal range according to gender, height and stature, and their body mass index to be below 35 kg/m². In addition, any participants with a mature attitude and a genuine willingness to contribute to research will be selected for involvement in the study.

Participants will initially be briefly screened over the telephone, and the information sheet sent for them to read before attending an interview (see section A3 for more details). At this interview (the details of the study will be explained and the consent form signed). The participants will then fill out a set of questionnaires (Appendix A6) that gather information about demographics, medical history, drug use, anxiety sensitivity, psychiatric symptoms, pre-morbid IQ and traumatic stress reactions. These screening questionnaires will be used to ensure none of the participants are suffering from any serious medical or psychological conditions that might put them at an increased risk of adverse reactions as a result of alcohol intoxication. While the AUDIT is the specific measure used to determine the amount of alcohol each participant consumes, information will be sought about all other illicit drugs is also assessed. There is a need to assess for all possible drugs of abuse to ensure the participants are not currently suffering from another substance abuse or dependence problem that would exclude their involvement in the study. This information is also needed to ensure it has no impact on the results of the study. Anxiety sensitivity, pre-morbid IQ and history of trauma will be used as covariates in the research analysis. Some of the demographic information will be used to describe the sample. After completing the questionnaires, the participants will have an interview with the research nurses who will again discuss the study requirements with them and their answers to the medical questionnaires. At this meeting the research nurse will measure the participants' weight and height to ensure that they meet the criteria for entry into the study. The nurse will also take some baseline data of pulse and blood pressure to use for comparison in the medical check during the study. If during the course of these interviews and questionnaires, information is revealed that renders an individual unable to participate, they will be told they are unable to participate and if appropriate the reasons for this given. Their consent form and details will be destroyed. Participants who meet all the criteria and successfully complete the screening process will be asked to participate and their testing session booked.
C3 PRE-EXISTING CONDITIONS

In some situations, an underlying medical or other significant condition of a participant may result in an otherwise relatively
immediate adverse effect caused by excessive stress and exacerbates the condition. Researchers must, therefore, be aware of such
situations and be able to address the resulting issues.

Unparticipants have any medical or other significant conditions of which you are aware, e.g., diabetes, asthma, depression, epilepsy? What
steps was in place to handle any existing problems (you may need to collaborate with A3. A4. A5 of the form)

Participants will be screened prior to involvement in the study to ensure they are healthy
and without any pre-existing medical conditions that may cause danger to the participant
or violate any of the study criteria (case section A1).

C4 DISCLOSURE AND INFORMED CONSENT

How will participants be informed about the project in order to give valid consent?

☐ Consent Information Statement(s) is/are (are) included
☐ Consent Form(s) is/are (are) included
☐ A copy must be attached to your application. A guide to consent instruments is given at the end of this form
☐ Consent information statement(s) is/are (are) and consent implied by return of anonymous questionnaire
☐ Oral advice (please explain how and why)
☐ Other (please explain how and why)

Copy attached as Appendix A3 and A4

Copies of appropriate consent instruments must be attached to your application. Please consult the Guide to Human Research Informed
Consent Instruments when preparing informed consent instruments.

C5 COMPENSATION

Consent to participate must be freely given and not obtained through the use of reward, coercion, or power relationships.

Provide details of any financial or other reward or inducement being offered to subjects for participation. Indicate the cost of the funds

Participation in this study will be entirely voluntary

C6 RELATIONSHIP TO INVESTIGATOR(S)

Please advise if the investigators are related to the investigator for employment, marriage, etc.

Some investigators linked with the investigator through some particular relationship - e.g., employees ultimately responsible for some aspects of the

C7 INVOLVEMENT OF SPECIAL GROUPS

Particular issues of consent may arise when special groups of participants are to be involved. There may be, for example, a need to obtain informed

A special group of people - e.g., Indigenous Australians, children, and young persons (Guideline 4.7) group with special circumstances - e.g.,

Please identify and describe the nature of the group and procedures used to obtain permission.

Note: Persons proposing research projects involving Indigenous Australians should consult with the relevant University manager of Indigenous programs prior to

C8 PRIVACY

The University is subject to the Victorian Information Privacy and Health Records Act as well as the Commonwealth Privacy Act and, in particular, the

Data the research involves access to data which was collected by an organisation for its own purposes to not specifically collected for this project;

if yes, please indicate what details are or are not disclosed and how will be obtained. If yes, please indicate what details are or are not disclosed and how will be obtained. If yes, please indicate what details are or are not disclosed and how will be obtained.

C9 LOCATION OF STUDY

Please indicate where the research will be conducted.

Yes

No

I Human Research Ethics Committee

SECTION D: DATA & PUBLICATION ARRANGEMENTS

Please consult carefully your responses to this section. You need to be clear as to what is occurring within respect to data collection, retention and disposal.

D1 DATA COLLECTION/RECORDING

Please note that, with any information or data collected/retrieved, if any individual can reasonably be identified, the information can be deemed "personal information" or "health information" under National Health Information Privacy Principles (NHPPP).

(a) What is the form that will be used to collect/record?

Data will be collected through questionnaires, consent forms, and e-consent forms.

(b) In relation to any data collection or subsequent use, you need to acknowledge either or both of the following:

- An individual can be identified U&I as potentially identifiable / Non-identifiable.
- An individual is Non-identifiable. Data will be retained/collected anonymously with no reasonable possibility of being identified.

The study is a repeated measures design and informed consent is obtained. Therefore, participant names and contact details are not used. These details will be on the consent form. Participants will be allocated a number and this number will appear on all other measures, including the questionnaires and all data collection methods such as the laboratory task and memory tasks. The researchers will retain copies of the questionnaires, consent forms, and all data collection methods in a locked filing cabinet in the Brain Sciences Institute, separate to the testing materials. The consent forms will be stored with these details, also separate to the testing materials. The study has been completed and the data entered the names of the participants corresponding to the numbers will be destroyed and the consent forms will be destroyed. The data collected in the study will remain at the BSI for at least 5 years. If after this time the data is no longer being used or published, the data will be destroyed. The research nurse, who will be administering the alcohol and placebo conditions, will allocate each participant to their experimental condition (alcoholic or placebo). Only the research nurse will have a copy of the condition allocation for each participant. This sheet contains only the participant number (01) and will be locked securely in a filing cabinet at the BSI.

D2 DATA SECURITY

Please note that data must be held for sufficient time to allow for retrieval. For data that is published this may be for as long as interest and discussion periods follow publication. It is recommended that the minimum period for retention is at least 5 years from the date of publication but for specific types of research, such as clinical research, 15 years (or more) may be more appropriate. (Section 4.5 of Swinburne's Policy on Data Protection).

Please indicate how data (all types of data, including, e.g., signed consent forms) will be securely retained (e.g., electronic form in password-protected disk drive, locked filing cabinet, etc.) and where? With more than one type of data, will the types be separately stored? If your explanation, you will need to make clear how the confidentiality and/or anonymity will be maintained.

Human Research Ethics Committee

(Aug 2007; Amended August 2007)
Copies of the computer data will be stored on a password-protected computer at the Brain Sciences Institute. Only participant numbers will be recorded on the data collected (with the exception of the consent form). Following completion of each recording session, the data will be stored securely in a locked filing cabinet in the Brain Sciences Institute.

(b) Following completion of study,

All computer data will be written in a (3), which will be password protected. Data on computers will be deleted as they are archived to CD-ROM. Written materials and the CDs will be securely stored at the Brain Sciences Institute. This material will be stored separately to the consent forms.

D3 PUBLICATION/OUTPUT (as Section 3.2 Revised Aug 2007)

Please explain in sufficient detail:

(a) What, if any, publication (conference, news media, academic journal, other journal, etc.) is envisaged following on or in relation to this project, both in terms of data proper and/or analysis of data?

(b) Will participants be informed about any envisaged research publication/outcome? (this information is normally to be included in the information given prior to obtaining informed consent.)

(c) Would any participants be able to be identified through the publication of data proper or research findings? If so, explain why this is necessary.

(a) Data recorded and analysed will comprise a clinical research study and may also be included in scientific publications and presentations.

(b) All participants will be informed that the data will be used for a research study and may also be included in a scientific publication or presentations. Participants will be informed that their confidentiality will be respected with no subject referred to by name, or numbers will be used for all data collected and this data presented in group format.

(c) No participant will be referred to by name, if individual data is presented only a number will be used for the identifier. The results will be presented as group data.

D4 INDIGENOUS ISSUES

Storage arrangements for data relating to research into Indigenous matters must be determined in accordance with the Policy on the Conduct of Research about Aboriginal and Torres Strait Islander People (Section 4.5 Revised Aug 2007).

What consultation has taken place and what arrangements have been made?

N/A

D5 OTHER ISSUES (as Section 5.5 Revised Aug 2007)

Are there any other issues relating to data collection, retention, use or disclosure which the ethics committee should be made aware of, if so, please explain how you are to deal with this.

(N/A, Research involves solely impacting on any individual or group for directly pertaining, etc.)

N/A
**SECTION E: SUBSTANCES & CLINICAL ISSUES**

**E1 ADMINISTRATION OF SUBSTANCES/AGENTS**

<table>
<thead>
<tr>
<th>Name or Substance</th>
<th>Dose or Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td></td>
</tr>
<tr>
<td>1-2 Standard drinks (1 standard drink = 15ml + 125ml orange juice)</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td></td>
</tr>
<tr>
<td>Orna</td>
<td></td>
</tr>
<tr>
<td>Oracell</td>
<td></td>
</tr>
</tbody>
</table>

**Anticipated effects**

Alcohol: The initial effects of alcohol intoxication will be decreased attention and concentration, impaired memory and slowed reaction times and motor control. This will be combined with an elevated mood, decreased anxiety and mild nausea at high BAC levels. Twenty-four hours after the drug administration some participants might experience a hangover. This might include some nausea, fatigue, dry mouth, muscle aches or tight, headache, with a possible impairment in attention and memory. The possibility of a hangover has been reduced as much as possible by using vodka as a clear alcoholic liquid.

**NOTE:**

If the research involves administration of foreign substances or invasive procedures, please attach a statement specifying responsibility for those procedures by a medical or paramedical practitioner with indemnity insurance.

*STATEMENT ATTACHED*

We are not administering a controlled or foreign substance, so this is not required. Professor Grant currently, the supervisor of the current study does have professional indemnity insurance but this is also considered necessary.

**E2 BODY FLUIDS OR TISSUE**

**What fluids or tissue? How will these be collected?**

Blood alcohol concentrations will be obtained with a Breathalyser, a new tube for each participant will be provided, or the tube sterilised after each use.

**Frequency and volume**

N/A

**How are samples to be stored?**

N/A

**How will samples be disposed of?**

N/A

**Who will take the samples?**

Registered Nurse

**What are their qualifications for doing this?**

Registered Nurse: With experience in several research projects including all the drugs and driving projects.

**Do participants sign, or are we made aware, of the Hepatitis B or HIV risks? If so, how will these risks be handled?**

N/A

**Do participants carry, as far as we know, any other contagious diseases or viruses? If so, how will these risks be handled?**

N/A
SECTION F  DECLARATIONS

With respect to this project, I/We, the undersigned Investigator(s)/Assistant(s) agree:

- To undertake human research activity or handle data confidentially in accordance with Swinburne requirements, including any standard or special ethics clearance conditions, under the proper direction of the responsible Swinburne manager and/or principal Swinburne (or other) researcher/supervisor.

<table>
<thead>
<tr>
<th>NAME</th>
<th>(block letters)</th>
<th>SIGNATURE</th>
<th>DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professor Grant Devilly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamara Wolan</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All listed applicants must sign. The Chief Investigator/Supervisor is also responsible for personnel subsequently joining the project. Expand this table or duplicate this page as required. NB: This information is subject to Swinburne or external audit.

**Please note that**

PROJECTS MUST NOT COMMENCE WITHOUT PRIOR WRITTEN APPROVAL from the Human Research Ethics Committee (SUHREC) or its appropriate Subcommittee (SHESC)

Declaration of Compliance by Chief Investigator(s)/Student Supervisor(s).

I declare that the above project has been developed and will be conducted in accordance with relevant Swinburne standards, policies and codes of practice, including any standard or special conditions for on-going ethics clearance. I further declare that all listed and subsequently appointed researchers or assistants involved in this project will be made aware of the conditions of ethics approval as communicated to me, including approved documentation and procedures.

Signature & Date: ..............................................................

Name of Signatory & Position: ..............................................................

Form checked by a Research & Ethics Advisor (REA)? Yes ☐ No ☐ REA initial & Date: ..............................................................

Endorsement of Head of Academic Unit (or Delegate) or Above.

I declare that this project has been developed and will be conducted in accordance with relevant Swinburne standards, policies and codes of practice, and has research merit, adequate resourcing and appropriate leadership/supervision.

Signature & Date: ..............................................................

Name of Signatory & Position: ..............................................................

(Please note: This endorsement must be given by an authorised official who is not also a chief or co-investigator of the project and who is not also the supervisor of a student investigator with an interest in the project.)

Human Research Ethics Committee
(Aug 2004, Form amended August 2007)
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Appendix A
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A2 Phone Screen and Advertising
A3 Information Statement
A4 Informed Consent Declaration
A5 Participant Questionnaires

Appendix B
B1 Lexical decision task word selection
B2 International Affective Picture task picture selection
B3 Debriefing questionnaire about the study
APPENDIX A1

INCLUSION AND EXCLUSION CRITERIA

To be included in this study each participant is required to be between the ages of 21 and 35 years. Each participant is required to have no history of current or past substance abuse, not taking any prescription medication (with the exception of contraceptive pills for females) and have no pre-existing physical or neurological conditions. Individuals with a current psychotic disorder or psychiatric symptoms that are likely to be worsened by alcohol or exposure to negative pictures will be excluded. Individuals with a significant health problem such as gastrointestinal or bleeding disorders, or who are pregnant or lactating will also be excluded.

Additionally, all participants are required to be moderate drinkers, with a weekly average of about half to one drink per day for females and one to three drinks per day for males. All participants are required to be aware of the general effects of alcohol. They will also need to be experienced in binge drinking (drinking 5 or more standard alcoholic drinks on a single occasion). Participants also need to be experienced in drinking vodka. Participants will be required to have mature attitude with a genuine interest in contributing to research. The reasons for their involvement will be specifically asked to ensure they will take the study seriously.

Participants are required to have a body weight within 20% of the normal range according to gender, height and stature, and a body mass index below 28kg/m². The participants’ caffeine consumption needs to be less than five cups per day, and their nicotine use less than ten cigarettes per day. The participants will be required to abstain from taking any psycho-active recreational drugs for two weeks before testing and not at all during the actual testing phase. Participants will be instructed not to drink caffeinated beverages or engage in heavy exercise on the day they arrive at the laboratory. They will be asked to have a standard meal before attending.
APPENDIX 2

Alcohol Study Telephone Screening

TODAY'S DATE ...................................................... (code: ____)
NAME ........................................................................
MAILING ADDRESS: ................................................. postbox

TELEPHONE NUMBERS  (mobile) ........................................
(home) ................................................................. (work)

WHAT IS THE BEST TIME TO CALL ................................
EMAIL ...........................................................................
Is it checked daily?  □ Yes □ No

Discuss need to ask about sensitive information about drug use and medical issues.
Report on confidentiality and privacy of phone call.
Permission given verbally to continue phone screen  Yes/No

Inclusion Criteria

☐ Age 21-35

☐ Available for testing in work hrs (10-5pm)

☐ No history of liver or kidney disease, heart conditions, brain injury or neurological disorder, uncontrolled asthma, eyesight or inner ear problems, arm or leg injuries, current mental health problems (especially psychosis) or more than 25 kg overweight.
(Participants should consider themselves in general good health.)

☐ If applicant is female, explain that she cannot be pregnant or breastfeeding.

☐ Not taking the following medications or other drugs?

- Anti-psychotics
- Anti-depressants & mood stabiliser
- Antiepileptic medications
- Anticoagulant
- Anti-Parkinson's medication
- Anti-cholinergic drugs
- Antibiotics
- Drug treatments for alcoholism
- Sedatives
- Recreational drug use more than once weekly.

☐ Are you taking any other medications? If so, which dose and purpose?

☐ Are you prepared to drink about 5-8 standard drinks on one occasion? □ Yes □ No

☐ Are you experienced in drinking vodka? YES/NO

☐ We can only recruit participants who HAVE experience in binge drinking but do not have a substance abuse problem.

Do you fit this category?  □ Yes □ No
How often do you drink alcohol? ........................................

Human Research Ethics Committee
[Aug 2004, Form amended August 2007]
☐ Are you available to complete a testing session once a fortnight, each session consisting of approximately 3.5 hours the first day, over a 6 week period (i.e., no exams or holidays coming up during testing)  □ Yes □ No

☐ Have you participated in a study at the Brain Science Institute before? □ Yes □ No
If yes, which study? ........................................................................................................

☐ Applicant booked in for information session and meeting with nurse?  □ Yes □ No
When .................................................................................................................................
Participants Information during phone screen

0. Before we can recruit you into this study, you will need to complete some questionnaires and a brief interview with the research nurse and myself. We will also need to measure your height and weight to determine the amount of alcohol to be given. At the initial interview we will need to get you to complete a series of questionnaires to ensure you meet all the criteria for involvement in the study. This might mean that you do not end up participating if information is revealed that means you are not able to participate, is that alright with you?

6. There are three testing sessions, two weeks apart, when you will be required to come into Swinburne. At each of the two first sessions you will consume one of two conditions; Alcohol or placebo. The amount of alcohol is 1.3g per kg, which is about 5-8 standard drinks, over three hours, you need to have experience in this, do you? Have you drunk vodka before? What is your experience of vodka like? This will mean your BAC will be 0.1. You will then be asked to complete a lexical decision task, which is a computer task involving responses to words, and an affective picture system task, that required you to rate a series of pictures. We will also get you to complete some memory tasks. There are only two experimental sessions that will take about 5.5 hours to complete.

9. Participation will be confidential and taxi vouchers will be provided to get to the Brain Sciences Institute and to go home after the two main testing sessions. You will have to remain at the centre with the researchers for about 2 hours after each of the two main experiential sessions before you are allowed to leave, this is to ensure your safety. The third session will only take about 30 minutes and involves some follow-up memory tests, you will be able to transport yourself to this session and back.
The Effect Alcohol has on affective processing and memory for trauma and non-trauma related information

The Brain Sciences Institute at Swinburne University of Technology will soon be running a research trial examining the effect alcohol has on emotional memory for words and pictures. This study will also examine the impact mood and history of life events has on memory for words and pictures. The words and pictures will range from positive (e.g. a sunset) to negative (e.g. a dead person) in order to cover the full range of emotional memory.

This study will require participants to come to the Brain Sciences Institute on three occasions. On one of these occasions you will be required to drink alcohol (5-8 standard drinks over 3 hrs). The type of alcohol to be consumed will be vodka and orange juice. On the other occasion you will be required to drink a placebo drink (water and orange juice). One each of these occasions, after initially administering the alcohol or placebo over a three hour period, we will then test your responses and memory for a series of words and pictures. These two occasions will take no more than six hours in total. The third occasion involves a quick memory test only, and takes about 20 minutes. You will receive the alcohol once and the placebo once.

Potential participants must be between the ages of 21 and 35 years and be regular drinkers who have experience with drinking more than 5 standard drinks on a single occasion. They must not be taking any form of prescription medication (exception the contraceptive pill), have any history of alcohol or substance abuse, and generally be in good health.

To ensure your safety throughout the study transportation to and from the centre will be provided in the form of taxi vouchers.

If you are interested in participating please contact:
Tamara Wolan or Rebecca Neate
Ph: 9214 4444
Email: 2147904@student.swin.edu.au or rneate@swin.edu.au
**SWINBURNE UNIVERSITY OF TECHNOLOGY**

**INFORMATION STATEMENT**

The Effect Alcohol has on affective processing and memory of trauma and non-trauma related information

Research Investigators: Professor Grant Devilly and Tamara Wolan
Brain Sciences Institute
Swinburne University of Technology

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This is an information sheet with specific details about the study, please read it carefully before attending the meeting with the Researcher, at which time you are free to ask any questions. If after reading the information you decide not to participate we completely understand and will remove all your details from our records.

**Introduction**

This study will be examining the effect alcohol has on emotional memory for words and pictures. This study will also be examining the impact mood and history of life events has on emotional memory for words and pictures. In this study we will be showing you positive pictures (e.g. a sunset), neutral pictures (e.g. a fan), and negative pictures (e.g. a dead person). This is in order to cover the full range of emotional memory.

**Aims**

This study is part of a clinical research project that I am completing as part of my doctorate in clinical psychology. The results of the study may also be published in a paper later down the track. The primary aims of the current study are to examine the effect alcohol has on processing and memory for emotional words and pictures.

**Study Details**

You are invited to take part in this study. However please note, in order to be involved in the study we must check that you are in good health with no possible factors that could put you at risk during the study. For this reason we will ask you to initially go through a screening process, involving an interview with the Researcher and Research Nurse to discuss the specifics of the study and for you to fill in some questionnaires. After this screening process we will confirm if you are still able to take part in the study.

At this screening interview we will ask you to fill in some questionnaires that ask about some general demographic information, some medical history and if applicable, your drug use history. We will also ask you to fill in some
questionnaires that ask about your tendency to experience anxiety, details about clinical symptoms such as depression, and any history of traumatic events. In addition we will ask you to complete a quick reading test to get an estimate of your IQ. All these questionnaire measures are used for screening purposes or for additional factors to include in the analysis of results. The researcher who will be administering these questionnaires is a probationary psychologist and has experience in these activities. She will be supervised by the director of research, Professor Grant Devilly, who is a registered psychologist with clinical and forensic specialties.

The study consists of three sessions, with two main experimental sessions. This means on one of the occasions you will receive the alcohol and on the other, the placebo. The third session is a quick follow-up memory test and does not involve the administration of any substance. This means you only receive the alcohol one time and the placebo the other. On arrival on the first testing day, a baseline Blood Alcohol Concentration (BAC) measure will be taken with the Breathalyser. Following this, the alcohol or placebo will be administered. Both the alcohol and placebo will be mixed with orange juice. You will be asked to consume the alcohol or placebo over a period of three hours, with your BAC monitored at hourly intervals. The research nurse will be administering the alcohol and the placebo condition and will remain throughout the experimental sessions to monitor for any negative reactions. We will ask you to sit in our waiting room over the three-hour period, it is private with a TV and DVD player, lots of movies and books or magazines for your entertainment. The researcher and nurse will check you regularly and we will take your BAC level every hour.

The type of alcohol to be consumed will be vodka, this was chosen because it is usually well tolerated and is not commonly associated with hangovers the following day. The amount of alcohol to be consumed will be 1.3 grams measured according to your height and weight. This is about 6-8 standard drinks over the three hours, with every plastic cup containing 30ml of vodka and 230ml of orange juice. We will ask you to have a standard meal before attending the session. The placebo will be water and orange juice. A dash of peppermint essence will be added to the alcohol and placebo drink to try to control for the taste as much as possible. This is a double-blind study; therefore, neither you nor the researcher will know what condition (alcohol or placebo) has been taken until the completion of the trial. It is still likely that you will be able to tell which condition you are in, despite trying to control for the taste as much as possible. However please do not tell the researcher, as this will interfere with the study design.

Once you have reached a BAC level of 0.1 you will be asked to complete a lexical decision task, which involves the presentation of a series of words on a computer screen. You will be asked to indicate whether the words on the screen form a real or non-word. You will also be asked to complete some simple memory tasks. These tasks involve a free recall test and a recognition test. You will then be asked to complete an affective picture system task. This involves the presentation of a series of pictures that we then ask you to rate your emotional responses to. This will conclude the first experimental testing session. You will then be required to remain at the centre in the waiting room.
for about two hours or more until your BAC level has dropped to 0.05. After a medical check with the centre’s research nurse we will provide you with a taxi voucher for transport home and call the taxi for you. If the investigators feel it is necessary, one will accompany you home to assure your safety.

The medical check will involve the research nurse checking your orientation, blood pressure and pulse and assessing for any negative reactions, e.g. disorientation or agitation. If the research nurse concludes that for your own safety you should remain at the testing site longer until negative effects have diminished, we will ask you to remain in the waiting room for a longer period. If during the administration of the alcohol you start to feel unwell at any time we will ask you to stop consuming the alcohol and monitor you. Your safety will always be the first priority.

The second time you come to the centre you will initially be asked to complete some memory tasks, then again consume either alcohol or placebo and complete the computer tasks. You will again be required to remain at the centre for two hours, and then be given a taxi voucher for transportation home. The third session does not involve the administration of alcohol or placebo, but involves some follow-up memory tasks. This third session will only take about 20-30 minutes. The two main experimental sessions will take about 5.5 hours each.

During those sessions where you will be administered the alcohol it is likely you will feel the following effects: decreased attention and memory, slowed reaction time, impairment of motor-co-ordination, elevated mood, decreased anxiety and possibly some mild nausea at high BAC levels.

If you consent to participating in the trial, you must agree not to consume alcohol for at least 24 hours prior to each session, and no other drugs for at least 7 days prior to each session. Alcohol can seriously impair driving ability, therefore taxi vouchers will be provided for transportation to and from both experimental sessions. In addition, you must agree not to drive, operate any heavy machinery, nor consume any alcohol, drugs or prescription medications, for at least 24 hours after the experimental sessions.

Additionally, applicants must fulfill the following criteria: Participants must have no history of current or past substance abuse (persistent compulsive use of a substance), have no pre-existing physical or neurological conditions, no history of cardiac, endocrine, gastrointestinal, or bleeding disorders, not pregnant or lactating, and not taking any prescription medication. Participants must not have any current psychotic disorder (Schizophrenia) or any psychiatric symptoms that may be worsened by participation in the study. Participants are required to have experience with drinking 6-8 standard drinks over a period of three hours and also have experience in drinking vodka. We will also require that you have a mature attitude and have a genuine interest in contributing to the research aims.

Your safety, rights and privacy
Your participation in this study is voluntary and you are free to withdraw from the study at any time, even in the middle of drinking the alcohol. If you decide
to withdraw, you are still required to abide by the safety restrictions advising you not to drive after the administration of the alcohol, and not to consume alcohol, drugs or any other prescription medications for at least 24 hours after each session. We will also still ask you to use the taxi vouchers to get home from the centre. If you withdraw all your details will be destroyed and your data will not be used.

The screening process we ask you to go through prior to your involvement in the study is to ensure there are no factors that could put you at risk during the study. Part of this screening process requires some information about any illegal drug use. This information will be collected in a private room, with the documents stored securely in a locked filing cabinet in the centre. This information will not be disclosed to anyone else unless you disclose information that puts you or another person at risk. Additionally, your name will not appear on any documents except the consent form. On all forms you fill out and all the data recording sheets, a number will be used (e.g., SD1). There will be one document with the names and matching numbers. This sheet of names and number details and the consent forms will be stored securely in a locked filing cabinet and separate to the other materials used in the study. At the conclusion of the study, the details of names and matching numbers will be destroyed making your data de-identified.

To ensure your safety during the experimental sessions, as previously discussed the research nurse will administer the alcohol and monitor you and complete a medical check before you can leave. Asking you to remain at the centre until your BAC level drops is also for your safety. The taxi voucher to and from the centre is used to ensure your safety and make sure you do not drive when intoxicated. You will be able to transport yourself to the third session that only requires a quick memory test. As part of this need to ensure your safety it will also not be possible for you to leave the Centre at any time during the experimental sessions. Finally, please note that the Breathalyser we will be using will be sterilised after each use, so there will be no risk of cross contamination of breath.

Your consent to participate in this study will be obtained by asking you to read and then sign an informed consent form. This signing will be witnessed by an affiliate at the BSI who is not directly involved in the study. This will be stored separately to the other research data in a locked filing cabinet.

Any questions regarding the project entitled 'The Effects Alcohol has on effective processing and memory for trauma and non-trauma related information' can be directed to the Investigator Tamara Wolan, of the Brain Sciences Institute, Swinburne University (ph: 9214444, email: 2147904@student.swin.edu.au, Tamara.Wolan@easternhealth.org.au) Or the Supervising Investigator, Professor Grant Devilly (ph: 9214 5277, email: gdevilly@swin.edu.au).

Thank you for taking the time to read this information sheet. You will retain a copy of this information and the signed consent form for your own records.
This project has been approved by Swinburne’s Human Research Ethics Committee (SUHREC) in line with the National Statement on Ethical Conduct in Research Involving Humans. If you have any concerns or complaints about the conduct of this project, you can contact: Research Ethics Officer, Swinburne Research (H88), Swinburne University of Technology, P O Box 218, HAWTHORN VIC 3122. Tel (03) 9214 5218 or +61 3 9214 5218 or resethics@swin.edu.au

Swinburne University of Technology
Informed Consent Form

The Effect Alcohol has on affective processing and memory for trauma and non-trauma related information

Research Investigators: Prof. Grant Devilly and Tamara Wolan

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Please read the Information Statement and this consent form carefully before signing.

I (the participant) have read and understood the information statement and understand the general purposes, methods and demands of the study. Any questions I have asked have been answered to my satisfaction.

I agree to be interviewed by the researcher and research nurse before being able to take part in the study. I am aware that after the screening process I may not be able to participate. I give consent for sensitive information to be collected and I am assured that my confidentiality will be protected.

I have no history of current or past substance abuse, have no pre-existing physical or neurological conditions, no history of cardiac, endocrine, gastrointestinal, or bleeding disorders, not pregnant or lactating, not taking any prescription medication, and I have previously engaged in binge drinking and have experience drinking vodka. I do not have a current psychotic disorder or psychiatric symptoms that may be worsened by participation in this study.

I agree that for the two main experimental sessions I will be administered either 1.3 grams of alcohol or a placebo drink containing water and orange
juice over a three-hour period. I am aware that the amount of alcohol to be consumed is 6-8 standard drinks. I am aware I will only receive alcohol once and the placebo once. The third time involves only a follow-up memory test.

Since alcohol is known to influence mood and motor functioning, I acknowledge that I may experience elevated mood, decreased attention and concentration and impaired motor functioning. I agree to remain at the centre after the experimental testing for at least 2 hours or until my BAC level is at 0.05. I agree to be assessed by the research nurse, and if the research nurse concludes that for my own safety, I should remain at the testing site until negative symptoms diminish, I agree to remain at the testing site.

I agree that in the experimental sessions in which I may possibly be administered alcohol, I will not drive or ride to or from the session. I agree that I will utilise the transport to and from home provided for me by the researchers.

I agree to follow all the other safety procedures that are in place to assure my safety throughout the testing session. I am assured that my anonymity will be preserved and I will not be identifiable.

I agree that I should not consume alcohol for at least 24 hours or any prescription medications or other drugs for at least 7 days prior to my sessions.

I agree that I should not drive or ride, operate any machinery, nor consume alcohol or any prescription medication for at least 24 hours after my sessions.

I agree to participate in this activity, and understand that I am free to withdraw from the study at any time with no explanation required and my details will be destroyed.

I agree that research data collected for the study will be presented in a research project and may also be published.

Do you agree to all these conditions and volunteer to take part?

(please write Yes or No).

NAME OF PARTICIPANT

SIGNATURE.......................................................... DATE............

NAME OF PRINCIPLAN INVESTIGATOR

SIGNATURE.......................................................... DATE............

WITNESS NAME.......................................................... DATE............

SIGNATURE.......................................................... DATE............
Dear Grant and Tamara

SUHREC Project 0708/152 The effect Alcohol has on affective processing and memory of trauma and non-trauma related information
Prof G Devilly FLSS MS Tamara Wolan
Approved Duration: 18/03/2008 To 01/12/2008

I refer to the ethical review of the above project protocols undertaken by Swinburne's Human Research Ethics Committee (SUHREC). Your responses to the review, as emailed on 3 March 2008 with attachments and further clarification by email on 5 March 2008, were put to a delegate of SUHREC for consideration.

I am pleased to advise that approval for the project to proceed has been given as submitted to date in line with standard on-going ethics clearance conditions here outlined.

- All human research activity undertaken under Swinburne auspices must conform to Swinburne and external regulatory standards, including the National Statement on Ethical Conduct in Human Research and with respect to secure data use, retention and disposal.

- The named Swinburne Chief Investigator/Supervisor remains responsible for any personnel appointed to or associated with the project being made aware of ethics clearance conditions, including research and consent procedures or instruments approved. Any change in chief investigator/Supervisor requires timely notification and SUHREC endorsement.

- The above project has been approved as submitted for ethical review by or on behalf of SUHREC. Amendments to approved procedures or instruments ordinarily require prior ethical appraisal/clearance. SUHREC must be notified immediately or as soon as possible thereafter of (a) any serious or unexpected adverse effects on participants and any redress measures; (b) proposed changes in protocols; and (c) unforeseen events which might affect continued ethical acceptability of the project.

- At a minimum, an annual report on the progress of the project is required as well as at the conclusion (or abandonment) of the project.

- A duly authorised external or internal audit of the project may be undertaken at any time.

Please contact me if you have any queries about on-going ethics clearance. The SUHREC project number should be quoted in communication.

Best wishes for the project.

Yours sincerely

Keith Wilkins
Secretary, SUHREC
**HUMAN RESEARCH ETHICS COMMITTEE**

**APPLICATION FOR ETHICS APPROVAL**

of a

**RESEARCH PROTOCOL**

---

**SECTION A: GENERAL INFORMATION**

<table>
<thead>
<tr>
<th>PROJECT TITLE</th>
<th>The Effects of MDMA and Methylphenidate on Driving and Sobriety Test Performance.</th>
</tr>
</thead>
<tbody>
<tr>
<td>APPLICANT DETAILS</td>
<td>Show names and contact details (When project is part of student research Coordinating Supervisor must list name RV)</td>
</tr>
<tr>
<td>Name</td>
<td>Professor Con Stough</td>
</tr>
<tr>
<td>Qualifications</td>
<td>BSc (Hons) PhD (Adel) MAPS</td>
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<tr>
<td>Tel No</td>
<td>9214 8167</td>
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<td>Email</td>
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</tr>
<tr>
<td>Fax</td>
<td>9214 6230</td>
</tr>
<tr>
<td>School / Research Centre / Institute</td>
<td>Centre for Neuropsychology</td>
</tr>
<tr>
<td>Address for correspondence</td>
<td>Swinburne University, P.O. Box 218, Hawthorn 3122</td>
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<tr>
<td>Name &amp; contact details: Dr Katherine Papafotiou Qualifications</td>
<td>BSc (Hons), PhD (Swinburne University)</td>
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<tr>
<td>Tel No</td>
<td>9214 5757</td>
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Names of other Senior and Associate Investigators:

| Name | Dr Edward Ogden PSM Qualifications | M.A., M.B., B.Med.Sc., B.S., Dip.Crim |
| Tel No | 9247 6187 |

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**PERIOD DURING WHICH ACTIVITIES REQUIRING ETHICS APPROVAL WILL OCCUR**

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<th>01 12 2007</th>
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**TYPE OF ACTIVITY**

- [ ] Research by Academic Staff Member
- [ ] Supervised Postgraduate Research
- [ ] Supervised Undergraduate Research
- [ ] Contract Research (Contract has not yet been drawn. Copy of contract will be forwarded once ethical approval has been given)
- [ ] Supervisor Data Practice

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Subject code: Subject the Number of students involved
The current protocol has four main aims:
1. To assess the effects of methamphetamine and MDMA on driving behaviour.
2. To assess the efficiency of sobriety tests, currently being used by Victoria Police, to test for the presence of methamphetamine and MDMA.
3. To assess the relationship between driving impairment and the level of methamphetamine and MDMA detected in blood and saliva.
4. To assess the sensitivity and specificity of several saliva drug detection devices for use on the roadside by law enforcement.

The relevant statistics, literature and changes in Victorian drug legislation are discussed.

Introduction
Recent surveys indicate a dramatic increase in the incidence of drug use within the community. Australia has the highest reported prevalence of methamphetamine and MDMA use compared to the rest of the world (UNODC, 2004; NZ second highest, USA third highest). In addition, road statistics indicate that drug-related road accidents and deaths have increased dramatically over the past 15 years. The most recent data shows that in 2003, 31% of road crashes involved drugs other than alcohol, and 28% involved alcohol levels of 0.5% BAC and above (The Age, 2004). Methamphetamine and MDMA belong to the amphetamine/stimulant family of drugs. Methamphetamine is used in the form of methamphetamine hydrochloride as a stimulant of the central nervous system, and as an appetite suppressant. Methamphetamine is commonly prescribed in the form of Dexydone for treatment of weight loss, Attention Deficit Hyperactivity Disorder, and Narcolepsy. Methamphetamine is widely abused in the community for its ability to increase behavioural alertness and excitement and is commonly referred to on the street as 'speed'. In contrast, MDMA resembles the chemical structure of amphetamine and hallucinogenic material like mescaline; thus, the pharmacological effects are a combination of these (The Complete Drug Reference, Appendix A). MDMA was used legally in psychotherapy in the USA prior to 1985; however, it is currently being used illicitly for its euphoric and hallucinogenic effects, and it's ability to allow party-goers to remain active for long periods of time. As opposed to methamphetamine, MDMA has less of an effect on dopamine and noradrenaline, with its primary action being to stimulate the release of serotonin that is known to promote positive mood and euphoria. MDMA is commonly referred to on the street as 'Ecstasy'.

Driving, Methamphetamine and MDMA
The increase in amphetamine use and amphetamine-related road crash statistics, encouraged the Inquiry into Amphetamine and 'Party Drug' use in Victoria by the Drugs and Crimes Prevention Committee, Parliament of Victoria, in 2004. The inquiry highlights that the incidence of amphetamine/stimulant use is increasing, particularly amongst young adults and truck drivers. In addition, the inquiry reports a concern over false perceptions that unlike depressants such as alcohol, amphetamines enhance driving and motor skills. The lack of conclusive research on the effects of amphetamines on driving skills, in particular methamphetamine and MDMA, and a lack of police roadside drug testing across the board, has contributed to a false sense of security about amphetamine users being able to safely drive a motor vehicle. Research into the effects of cannabis on driving ability has helped dispel the myth that since cannabis smoking has been associated with driving more slowly, that driving is not impaired. Projects conducted at the Driving and Driving Research Unit (CDRU) at Swinburne University have helped clarify that although smoking cannabis may be associated with driving more slowly, it is also associated with an increase in lane weaving and impaired braking ability (Papadopoulos et al., 2004). To date, research on the effects of amphetamines on performance is inconsistent. The reports suggest that amphetamine can either impair (Ward et al., 1987; Mills et al., 2001; Hunt, 1992, 1997; Green, 1995; de Waard et al., 2002; Logue et al., 1992; Eysden & Ryan, 1998) or improve performance on tasks that assess driving related skills (de Wilt et al., 2002; Wagg and de Wilt, 1999; Curmi, et al., 2003; Halliday et al., 1994; Fleming et al., 1995). Literature examining whether amphetamine and MDMA impair cognitive performance is also inconsistent. MDMA given in a 125mg dose has been associated with mild decrease in responses on the Digit Symbol Substitution Test, while a tendency towards improvement was observed with 40mg of amphetamine. Preliminary data from amphetamine research...
conducted at the DCRU suggests that the consumption of dextroamphetamine is associated with inappropriate vehicle indicator use, driving through red traffic lights and a decrease in reaction time to emergency situations. However, continued research is required to support these conclusions. In addition, the effects of MDMA should be investigated and compared. Inconsistent results between amphetamines and MDMA may be due to MDMA having greater impairing effects on performance when compared to other amphetamine-type drugs (dextroamphetamine and methamphetamine); since unlike most amphetamines, that predominantly increase levels of dopamine and noradrenaline, MDMA predominantly stimulates the release of serotonin. This distinction is important when generalising the effects of amphetamines on performance and research comparing the effects of typical amphetamines (e.g., methamphetamine) and MDMA is critical to the interpretation of impairment in driving behaviours. It is vital that further research into the effects of methamphetamine and MDMA be conducted in order to contribute to the discussion on whether amphetamines/stimulants impair driving behaviours. The current protocol aims to do this.

Drugs and Sobriety Testing Procedures

As a result of the growing number of drug-related road deaths, the Victorian Government and Police bodies have acknowledged that a means of detecting drug-impaired drivers is essential. In December 2000, the Victorian Government passed legislation authorising Victoria Police officers to administer sobriety tests to drivers suspected of being impaired by a drug/s other than alcohol. The sobriety tests being used were originally designed to test for the presence of impairment associated with alcohol intoxication. However, since each drug class will alter neural processes differently, it is likely that performance on the SFSTs for different drug classes will also differ. It is, therefore, problematic that law enforcement agencies depend only on reports describing the effects of alcohol on SFSTs performance in order to determine impairment, especially since each Victorian SFST case alcohol is not the cause (in Victoria SFSTs are only performed if BAC readings are below 0.05% legal limit). This potential problem is highlighted by the findings of a DCRU study on the effects of cannabis on SFSTs performance (Papafotious, et al., 2001). The study revealed that cannabis affected performance on SFSTs differently to alcohol. A study conducted by Burns & Moskowitz (1977) revealed that the Horizontal Gaze Nystagmus test was the most sensitive test of impairment in the case of alcohol. In contrast, the study by Papafotious, et al. (2004) found that in the case of cannabis, the best test (from the SFST battery) of impairment was the One Leg Stand test. Preliminary results from a project conducted at the DCRU, on the effects of dextroamphetamine on performance, reveal that sobriety tests are effective in identifying only 5% of participants who had consumed dextroamphetamine. It is not clear whether the same results would be obtained in the case of the most common amphetamines: methamphetamine and MDMA; since no investigations have cytologically examined whether these sobriety tests efficiently detect impairment. The current protocol aims to do this.

Drugs and Saliva Drug Testing

In December 2003, the Victorian Government approved the trial of random roadside saliva testing to identify the presence of drugs in drivers, with positive drug saliva tests resulting in prosecution and fines. Several saliva drug-testing devices have been developed and manufactured, however, many have not yet been systematically tested for their reliability and validity in detecting the presence of methamphetamine and MDMA. Several devices are currently available to test saliva: Drager, OralAid, oral Drug, Crib Screen and Cortisal Rapiscan (to name a few). Apart from one recent study using the Rapiscan device (which showed that the device needed further work to improve its accuracy) there are no evaluation data available to indicate the reliability or validity of these devices (Buxton, et al., 2001) to test for the presence of drugs in human saliva. This is a major limitation for the usefulness of these devices. There are currently no standard analytical cut-off values available to determine when a test is positive or negative as there are for urine tests. However, unlike urine that contains the metabolites of a drug (drugs can be detected up to 30 days after drug consumption), saliva contains the parent drug, similar to blood (Samyn, et al., 1999). The prospect of using saliva to test for drug presence, therefore, is more appealing than using urine, as saliva has been shown to indicate recent drug use and would therefore be a better indicator of current impairment (Buxton, et al., 2001). In addition, saliva sampling is virtually non-invasive, fast, and easy to execute by non-scientists (police officers) (Gremmell, et al., 1999) compared to urine and blood sampling. For these reasons law enforcement and government agencies prefer to invest resources in the validation of saliva testing devices to ensure that they are sensitive to detect drugs after recent drug use, as well as to detect a specific level of a drug that is known to cause impairment. Since the introduction of these drug detection procedures, the DCRU has lead the research that reports the sensitivity and accuracy of sobriety testing and saliva drug detection devices, with reference to the recent consumption of cannabis and amphetamines and driving impairment. The current application will examine the sensitivity of several hand-held saliva drug screening devices to test for the presence of methamphetamine and MDMA, and determine which saliva tests would be most...
appropriate for use in a roadside setting (user-friendliness, speed of information output, accuracy, etc.). In addition, the project will evaluate the relationship between the level of methamphetamine and MDMA in blood and saliva, and performance on a driving simulator, to determine whether it is likely that a drug cut-off level can be applied to drivers as in the case with 0.05% BAC. The effects of the drug 24 hours after consumption will also be examined. This part of the project is exploratory and has never before been investigated, however, the results will contribute significantly to the establishment of an appropriate safe cut-off drug level for amphetamines (if no driving impairment is observed at a particular mean level of the drug in blood/saliva). The data will also help establish which saliva drug-testing device is most accurate in testing for recent drug consumption (as opposed to 24 hours post drug administration). An evaluation of doped-driver detection methods, currently being used by law enforcement or being considered for use, to test drivers for the presence of drugs, is essential to the successful implementation, and community acceptance, of drug detection procedure. This will also help educate the community on the harmful effects of driving while under the influence of drugs. The current protocol aims to do this.

Summary

In summary, the aim of the present study is to investigate whether methamphetamine and MDMA impair driving ability, and if so, in what way. In addition, the project will evaluate the efficiency of Victoria Police sobriety tests to detect impairment associated with methamphetamine and MDMA. The project will examine the sensitivity of several hand held saliva drug screening devices, and determine which saliva tests would be most appropriate in a roadside setting, to screen drivers for recent methamphetamine and MDMA use. In addition, the project will evaluate the relationship between the level of each drug in blood and saliva, and performance on driving, to determine whether it is likely that a safe drug cut-off level can be applied to drivers - the effects of the drug 24 hours after consumption will be examined. This part of the project is exploratory and has never before been investigated, however, the results will contribute significantly to the establishment of an appropriate cut-off drug level for amphetamines (if no driving impairment is observed). The project will also establish which saliva drug testing device is most likely to test for recent drug consumption, as opposed to 24 hours post drug consumption. For these reasons the National Drug Law Enforcement Research Fund and VicRoads have agreed to support the current protocol and will provide over $500,000 in funding to conduct the research.

Note: This protocol includes the same dose of Methamphetamine previously approved by the Swinburne University Human Research Ethics Committee, 0.42mg/kg of d-methamphetamine (HREC Register Number 02/49). The dose of MDMA to be administered is slightly higher than the dose previously approved by the HREC: 100mg of d-MDMA compared to 75mg of d-MDMA (HREC Register Number 04/05). However, it should be noted that the dose proposed in the current application is still below those administered in other human clinical trials (up to 150mg MDMA by Cami, et al., 2000). The previously HREC approved projects also included the SFSTs, driving simulator task and saliva tests/kits to be administered in the present protocol (HREC Register Numbers 02/49 and 04/05).

A2 WHAT - BRIEF DESCRIPTION OF PROJECT

In plain English

Fifty healthy adult participants aged between 21 and 35 years will take part in the study. All participants will undergo a screening process and medical examination to ensure that they are fit to participate (see section C2 of this application). Participants will read an information sheet outlining the details of the study (Appendix B1). All questions will be answered and subsequently participants will be asked to complete a consent form1 (Appendix B2).

The study will involve a double-blind (the experimenter and the participant will not know whether the drug administered is active), placebo-controlled (active drug effects will be compared to placebo effects) study design and will comprise three experimental sessions (Methamphetamine, MDMA, and placebo). In each session, initially one blood and saliva sample will be taken. These samples will be later analysed for the 7 major drug classes to ensure that participants were drug free prior to testing.

In each session, Methamphetamine2, MDMA3, or placebo4 will be administered. The dose of Methamphetamine administered will be 42mg/kg of d-methamphetamine, the dose of MDMA administered will be 100mg of MDMA and the placebo dose will contain only four (all doses will be masked using the same gelatin capsule) (the administration of 42mg/kg of methamphetamine and 75mg of MDMA has been previously approved by the HREC 02/49 and 04/05). Once the drug has been administered, participants will be asked to wait 3 hours for drug blood
levels to peak (methamphetamine and MDMA has been reported to peak in the blood 2 to 4 hours after consumption). At 3 hours post drug administration, the driving simulator will be administered, followed by the Standardized Field Sobriety Test (SFSTs see Appendix D). These tests will take 30 minutes to complete. A second blood and saliva sample will be taken at 3.5 hours, and this will complete the first phase of testing. Participants will be provided with a taxi voucher for transport home, as well as an additional taxi voucher for transport back to the laboratory, for further testing at 24 hours post drug administration. At 24 hours post drug administration a third (final) blood and saliva sample will be taken and the driving simulator tasks and SFSTs will be administered for a second (final) time. At this time, if amphetamine is still detected in the participant’s saliva (the saliva device reports whether any drug is present in the saliva within 10 mins of saliva collection), a taxi voucher will be provided to the participant for transport home. This completes phase one and two of the session. This process will occur on three occasions so as to gather performance and sensitivity data relating to methamphetamine, MDMA and placebo. Results from each session will be compared to investigate whether methamphetamine and/or MDMA impair performance. Additionally, at each time point where a saliva sample is taken, a hand held saliva drug test will be administered (devices being implemented for use on the road side by law enforcement). This part of the project will examine the specificity’s ability to test for a specific drug class; methamphetamine and MDMA and sensitivity’s ability to accurately produce a valid positive and negative drug test result based on manufacturer cut-off values; e.g. where a cut-off value of 250ng/ml methamphetamine is applied to a device, the presence of 100ng/ml methamphetamine in saliva should result in a negative drug test result, and the presence of 250ng/ml of methamphetamine in saliva should result in a positive drug test result.

Note: The administration of the driving simulator and SFSTs has been previously approved by the HREC (02/49 and 04/05). The HREC has previously approved the collection of blood and saliva at the post drug administration time points specified in the current application, and up to 27 hours after drug consumption (HREC 02/49 amendment dated 04/07/04). The dose of methamphetamine to be administered, and the slightly lower dose of MDMA than that to be administered, has been previously approved by the HREC (02/49 and 04/05). The difference between the current protocol and the previously approved protocols is that this study involves the administration of methamphetamine and MDMA in the same study (three sessions including placebo), as opposed to two separate studies, (HREC 02/49: Methamphetamine and placebo, HREC 04/09: MDMA and placebo). The current protocol also excludes EEG testing. Although the dose of MDMA to be administered in the current protocol is slightly greater than previously approved, the original 75mg MDMA has been cited in previous studies to be on the low end of MDMA administration. The requested dose of 100mg of MDMA has been previously administered to human participants in several experimental studies, and the present protocol aims to replicate those dose and subjective effects. Some researchers have previously administered doses of up to 150mg of MDMA, and the largest lethal dose of MDMA has been reported to be 45 mg/kg in animals (over 3400mg for a 70kg individual) (Gudat-Quent, et al. 1996). A dose ranging between 75 and 125mg has been reported as the effective dose for most individuals.

Footnotes:
1. Informed Consent will be obtained from all individuals participating in the study and those who do not satisfy the requirements (for safety reasons) will be excluded from the study.
2. The form of Methamphetamine to be administered in this study will be 42 mg/kg encapsulated in a gelatin coating, rendering them visually indistinguishable in accordance with the double-blind design of the investigation.
3. The form of MDMA that will be administered in this study will be 100mg MDMA or placebo encapsulated in a gelatin coating, rendering them visually indistinguishable in accordance with the double-blind design of the investigation.
4. Placebo capsules will contain only flour.
5. The CyberCAR Life Driving Simulator includes measures such as basic steering ability and speed control. The driving simulator will be located at Swinburne University, specifically at the Centre of Neuropsychology, where all testing sessions will take place.
6. Standardized Field Sobriety Tests (SFSTs) include the Horizontal Gaze Nystagmus, Walk and Turn, and the One Leg Stand, the same tests currently being used by Victoria Police to test drivers for impairment associated with drugs other than alcohol.

A3 HOW - PROCEDURES
Please describe all procedures to which the participants will be subjected, and asterisk those which may have adverse consequences.

If you feel that it is necessary to include further material, please append.

Individuals interested in participating in the current protocol will initially be informed about the details of the study (Appendix D). Once participants agree to participate they will be screened using a short interview and a medical examination which will be conducted by a medical doctor, Dr. Edward O’Don (M.A., M.B., B.Med.Sc., Dip.Ophm).
Each participant will be booked to participate in three sessions that will be conducted 2 weeks apart. The project will involve repeated measures, double blind, placebo controlled methodology. Each session will involve 3.5 hours of testing on a first day followed by 30 minutes of testing 24 hours after drug consumption. Therefore, one entire session will be complete after approximately 24.5 hours.

The following will occur in each experimental session (three in total):

- On arrival, a blood and saliva sample will be taken from the participant. All blood samples will be collected using a 10ml syringe, by venipuncture from the antecubital vein. All saliva samples will be collected using a 1ml collection swab placed in the mouth. The first sample collected will be labelled the baseline sample and be later analysed for the presence of any of the seven major drug classes ( opiates, amphetamines, benzodiazepines, cannabinoids, barbiturates, cocaine and methadone). Any baseline samples that have any drug detected in them, will mean that results from that particular session, will not be used in the analysis, as it will be unclear which drug was causing any impairment observed. Once the baseline blood and saliva sample has been taken, the methamphetamine, MDMA or placebo tablet will be administered. Methamphetamine and MDMA will be placed in a gelatin capsule mixed with flour. The placebo capsule will contain only flour. The methamphetamine, MDMA and placebo capsule will therefore appear identical and ensure that the project remains double blind. The participants will be observed during drug taking, by the nurse, to ensure that they have consumed the drug capsule in each of the 3 experimental sessions. This will ensure that participants do not take the capsule away from them.

- Participants will be asked to wait for 3 hours after the administration of the drug to allow the level of that drug to peak in blood. Amphetamine blood levels have been reported to peak in blood approximately 3.5 hours after ingestion (Kahn, 2001). This information will be shared with the simulator task to be administered first (approximately 30 minutes to complete), followed by the SFSTs (approximately 10 minutes to complete). A second blood and saliva sample will be obtained, immediately after the performance tests are complete, to allow us to determine whether impairment (if observed) is related to the levels of amphetamine found in the blood and saliva. This phase one of the session and participants will be provided with a taxi voucher for transport home. Participants will be reminded they should not drive or consume any alcohol, drugs, or medications for at least 24 hours (also specified in signed consent form). Participants will also be provided with a second taxi voucher for transport back to the Centre for Neuropsychology the next morning, 24 hours after the administration of the drug.

- On arrival, 24 hours post drug a third (final) blood and saliva sample will be obtained from the participant. The driving simulator task will be administered for a second time (approximately 25 minutes to complete), followed by the SFSTs for a second time (approximately 10 minutes to complete). At this time, if amphetamine is still detected in the participant's saliva (the saliva device reports whether any drug is present in the saliva within 10 minutes of saliva collection), a third taxi voucher will be provided to the participant for transport home. This completes one session.

Additionally, at each time point where a saliva sample is taken, a hand held saliva drug test will be administered (devices being implemented for use on the road side by law enforcement). This part of the project will examine the specificity (ability to test for a specific drug class: methamphetamine and MDMA) and sensitivity (ability to accurately produce a valid positive and negative drug test results based on manufacturer cut-off values: e.g. where a cut-off value of 50ng/ml methamphetamine is applied to a device, the presence of 40ng/ml methamphetamine in saliva should result in a negative drug test result, and the presence of 80ng/ml of methamphetamine in saliva should result in a positive drug test result).

Note: The methods employed in this methamphetamine and MDMA project are identical to previously approved projects, specifically, dexamphetamine, methamphetamine and MDMA studies (HREC Register Number 02/30, 02/49 and 04/05 respectively).
A4 DESCRIBE ANY RISK THAT MAY ARISE TO THE PARTICIPANT / DONOR?

Risks to participants (e.g. research participants) can be real but do not need to be physical. Risk includes such things as psychological, economic or social implications of being a participant.

Some research activities may put the participant at risk through what is being done or simply through their participation. Please describe the risk you perceive and the protective measures to be taken.

The present study poses minimal risk to participants as doses of 10mg/100kg of MDMA, separately. However, methamphetamine and MDMA can impair driving ability, hence participants will be advised not to drive for at least 24 hours after any of the sessions. Taxi vouchers will be provided for participants who are unable to arrange transport home. Participants will be instructed not to consume any medication or alcohol for at least 24 hours after methamphetamine and MDMA administration in order to eliminate any adverse effects. Information pertaining to possible side effects of the medication can be found in Section E.1 below. A research nurse will be on-site when the methamphetamine and MDMA is administered, and throughout the entire experimental sessions. A medical doctor, Dr Edward Ogden, will be on-call throughout all experimental sessions to stabilise participants who experience any adverse effects. The doctor will be located at Doncaster, Melbourne Inner-City or Mulgrave during sessions, no more than 20 minutes from testing location. In case of an emergency situation the nurse will attend to the participant until the medical arrives. This protocol has been used in all drug and driving research projects approved by the HREC.

A5 DESCRIBE ANY RISK THAT MAY ARISE TO THE RESEARCHER / ADMINISTRATOR?

Some research activities may put the researcher at risk through what is being done or simply through their participation. Please describe the risk you perceive and the protective measures to be taken.

Any risks associated with blood and saliva sampling will be minimised by aseptic techniques (e.g. gloves) (see Appendix E.3).

A6 WHAT BENEFITS ARE ANTICIPATED FROM THE PROJECT?
(a) To the Participant

(b) More generally

The proposed project, for the first time, will provide essential information regarding the efficiency of the probity tests and saliva drug detection devices, currently being used by Victoria Police, in identifying driving impairment associated with recent methamphetamine and MDMA consumption. The research will contribute to the recommendations set out in the Premiers Drug Advisory Council and the Inquiry into Amphetamine and 'Party Drug' use in Victoria, and provide Victoria Police with essential information on driving performance, speed performance, and blood and saliva drug levels, associated with the recent consumption of methamphetamine and MDMA.

Finally, for the first time, the project will identify whether methamphetamine and MDMA impair driving behaviours 24 hours post drug administration. Additionally, the project will identify the sensitivity and specificity of currently available saliva drug testing devices to test for methamphetamine and MDMA. This information will help law enforcement agencies identify the most appropriate roadside drug screening tools. The results of the study will also contribute to educating the community on the potential harm that drug use may have on road safety.

A7 POTENTIAL PROBLEMS

From time to time in the course of a research project important information, such as individuals or risk, or entire environment events may come to pass.

What procedures are in place to handle unexpected or particularly significant personal information that may come to light through the project? Such as identification of unknown, medical or psychiatric condition, a previously depressed person, etc.

A medical doctor, Dr Edward Ogden, will be on-call throughout all experimental sessions to stabilise participants who experience any adverse events until the medical doctor arrives. The research nurse will administer the methamphetamine and MDMA and will be located on-site during all testing sessions. This protocol has been used in all drug and driving research projects approved by the HREC.

A8 ETHICAL TRAINING - CLASS BASED PROJECTS & EXERCISES

Class based projects can be memorable or can, through experience, lack of training, etc. lead to unexpected problems and so must be considered in that different light.

Where the project is a class based exercise, please describe briefly the training your students have or will have received in ethical conduct of research.

N/A

Please describe briefly the measures taken to ensure that your students are competent to carry out the project.

N/A
### A9 FUTURE USE OF DATA
Will any of these data be used by yourself, your students or others for any purpose other than for this project as described in the protocol? If so please describe.

| N/A |

### A10 EXTERNAL INVOLVEMENT
Is a body external to Swinburne involved in initiation or support of the project?

- [x] Yes Name of body/organisation: NDLERF and VioReads (Contact will be forwarded once ethical approval has been granted)

If an external body is associated with the project, you must provide the HREC with details of the arrangements, including details of any funding being provided. A copy of the contractual arrangements should be attached.

| No |

### A11 EXTERNAL APPROVALS
Projects involving other bodies may require approval from other institutions or ethics committees, next of kin, etc. for such things as access to prospective participant lists, data, facilities, etc. A copy of such approvals must be provided to the HREC at the time of application or be made available as soon as possible. No project may commence, until such approvals are provided.

<table>
<thead>
<tr>
<th>Please indicate, as appropriate, if formal clearance/permission has been obtained or sought</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institution</td>
</tr>
<tr>
<td>Next of Kin (for special groups)</td>
</tr>
</tbody>
</table>

| N/A |

| No (please explain) |
SECTION B: ETHICAL ISSUES OVERVIEW

B1 ETHICAL ISSUES

(please indicate (by X as appropriate) what is in your view are the ethical issues involved in this research. The following is a checklist of possible ethical issues.)

Double click on 'check box' to select

YES NO

(a) Is description of any kind to be used? (Refer National Statement 17?)

(b) Does the data collection process involve access to confidential personal data (including access to data provided for a purpose other than this particular research)?

(c) Will participants have pictures taken of them, e.g. photographs, video recording?

   If "YES", please explain below how you intend to retain confidentiality and ultimately dispose of the material.

(d) If interviews are to be conducted, will they be tape recorded?

(e) Will participants be asked to perform any acts or make statements which might be expected to compromise them, diminish self-esteem or cause them to experience embarrassment or regret?

(f) Might any aspect of your study reasonably be expected to place the participant at risk of criminal or civil liability?

(g) Might any aspect of your study reasonably be expected to place the participant at risk of damage to their financial standing or social standing or employability?

(h) Will the research involve access to data banks subject to privacy legislation?

   [Note: annual reporting to DoH, required in the Act. Must be reported to HREC (settlement)]

(i) Will participants come into contact with any equipment, which uses an electrical supply in any form e.g. audiometer, biofeedback, electrical stimulation, etc.? If "YES", please outline below what safety precautions will be used.

(j) Will any treatment be used with potentially unpleasant or harmful side effects?

(k) Does the research involve any stimuli, tasks, investigations or procedures which may be experienced by participants as stressful, aversive or unpleasant during or after the research procedures?

(l) Will the research involve the use of no-treatment or placebo control conditions?

(m) Will any samples of body fluid or body tissue be required specifically for the research, which would not be required in the case of ordinary treatment?

(n) Will participants be fingerprinted or DNA "fingerprinted"?

(o) Are there in your opinion any other ethical issues involved in the research?

NOTE: If the answer to any of the above questions is "yes", please explain and justify below. (The box below will expand to fit your response.)

1) A placebo is one of the compounds that will be orally administered, which does not contain the active treatment, i.e. methamphetamine or MDMA. It is an important component of the experimental design as the condition allows the experimenter to ascertain that the observed results are due to the administration of the drug methamphetamine or MDMA or due to normal responses. The placebo will contain only flour.

m) Blood and saliva samples will be taken before, during and after behavioural tasks to examine the relationship between methamphetamine and MDMA, and performance on driving and subjective tests. This relationship will be used to establish the efficiency of sobriety testing and saliva drug detection devices to predict the presence of methamphetamine and MDMA in impaired drivers.

o) Methamphetamine and MDMA is thought to influence driving ability, therefore, all participants will be provided with a taxi voucher to get home. They will also be advised to not drive, operate machinery, or consume any medications or alcohol for at least 24 hours after each experimental session.

SECTION C: PARTICIPANT DETAILS
C1 PARTICIPANT DETAILS

The composition of the participant group may, in some circumstances, disturb and invalidate an outcome, and risks may arise through the composition of the participant group.

How many individual participants will be involved? (Number for which approval is sought)

- Males: 25
- Females: 25
- Total participants: 50

If there is a gender imbalance in the number of participants please explain why

Over what range of ages?

From (youngest): 21
To (oldest): 32

If there is an age imbalance in the number of participants please explain why

C2 RECRUITMENT

How will participants be recruited?

- Indicate how names of potential participants will be obtained.

NOTE: where participants are obtained from sources other than schools, hospitals, prisons or other institutions, permission/approval from the relevant or appropriate authority must be sought. If by advertisement or poster please attach a copy of the proposed advertisement or poster.

Participants will be recruited through advertisements on community and university notice boards, media releases and by word of mouth. Individuals will be screened to ensure they are deemed suitable to participate in the study. Participants will have no history of current or past substance abuse, have no pre-existing physical or neurological conditions, no history of psychiatric, cardiac, endocrine, gastrointestinal, or bleeding disorders, not pregnant or lactating, and not taking any medication. Participants will also be required to have experimented with amphetamines previously. All participants must have a full drivers license (no probationary drivers).

C3 PRE-EXISTING CONDITIONS

In some situations an underlying medical condition of a participant may result in an otherwise relatively innocuous situation causing excessive stress and exacerbate the condition. Participants must therefore be aware of such conditions and have addressed the resulting issues.

Do participants have any medical condition of which you are aware, e.g. diabetes, asthma, depression, epilepsy? What steps are in place to handle any resulting problems?

- Participants will be screened by a registered medical practitioner, Dr. Edward Ogden, before they participate in the study to ensure that they are healthy and without any pre-existing medical conditions that may cause danger to the participant or violation of the studies criteria (see Section C2).

C4 DISCLOSURE AND INFORMED CONSENT

How will participants be informed about the project?

- Individual Forms of Disclosure and Signed Informed Consent will be used.

A copy must be attached to your application.

- Individual Forms of Disclosure and consent implied by return of anonymous questionnaire.

- Verbal advice (please explain how and why).

- Other (Please explain how and why).

Copy attached as Appendix 1, to be completed by the HREC.

C5 COMPENSATION

Participants will be paid $600 for their entire participation in the investigation. Each session involves one visit to the laboratory: one visit on initial day of testing, and one visit 24 hours post drug administration, as reimbursement for time and out of pocket expenses. This amount is essential because of the nature of the study. The study involves three 3.5 hour attendance, including participants coming back to the laboratory 24 hours after drug administration for 24 hours later testing. If a participant does not attend one of the sessions, or the day after (24 hours later) testing session, this will render the data from a potential 12 hours of testing void. In addition, the effects of the drugs are likely to extend over some level beyond the testing session.

C6 RELATIONSHIP TO INVESTIGATOR(S)

Free consent may be difficult to ensure if the participant is dependent upon the investigator for employment, assistance etc.

Some relationships could be considered either lower or higher in terms of the investigator's knowledge, authority, responsibility, or position of the investigator, family members, friends etc.
C7 INVOLVEMENT OF SPECIAL GROUPS

Particular issues of consent may arise where special groups of participants are to be involved. There may be, for example, a need to obtain informed consent from persons other than the direct participant. Examples of such special groups include:

- special cultural groups (e.g., Indigenous Australians);
- children and young persons (Guidelines section 4.2);
- groups with special circumstances (e.g., persons with an intellectual or mental impairment (Guidelines s. 5)).

Describe the nature of the groups and procedures used to obtain permission.

Note: Persons proposing research projects involving Indigenous Australians should consult with the relevant University manager of Indigenous projects prior to finalising definition of the project.

N/A

C8 PRIVACY

The University is subject to the Privacy Act and, in particular, the Privacy principles set out therein and is required to report annually on projects which collect or utilise particular records.

Does the research involve access to data which was collected by an organisation for its own purposes (i.e., not specifically collected for this project) such as student records, other data banks, human pathology or diagnostic specimens obtained by an institution(s)?

No

C9 LOCATION OF STUDY

Please indicate where the research will be carried out. If the research will not be on University premises permission of owner/occupier will be required. Indicate how permission will be obtained. NB: Please provide the Secretary, HREC with a copy of the permission when obtained.

Swinburne Centre for Neuropsychology, Applied Science Building, Swinburne University of Technology.
SECTION D: RECORDING, STORAGE & PUBLICATION DATA

D1 RECORDING OF DATA
Data must be retained for a period of at least five years from the date of any publication which is based upon it. See Swelltrack’s Policy on the Conduct of Research.

(a) How will data be recorded?
(Data must be recorded in a durable form with appropriate references.)

- Driving performance data will be automatically recorded on a floppy disk. Performance on the spatial tests administered will be recorded on paper and subsequently transferred to disk. Following the completion of each recording session the data will be archived on to CD-ROM. Blood and saliva samples will be stored in a -20 degrees freezer and then analysed. Data will then be transferred to disk. All data will be stored securely.

(b) Will confidentiality of results be maintained?

- NO (explain)
- YES

The investigation is a repeated measures design and informed consent is obtained. Therefore, each participant will provide names and contact details for tracing. However, these details will be accessible only to the investigators throughout the study. Once the data has been recorded and organised, names will be replaced with subject codes.

(c) Will participants be:

- Identified: data that allow the identification of a specific individual are referred to as identified data.
- Potentially identifiable: data may have identifiers removed and replaced by a code. In such cases it is possible to re-identify the person by whom the data relates so the process of de-identification is reversible.
- De-identified: not re-identifiable, anonymous (the process of de-identification is irreversible).

Explain how anonymity will be assessed through the study.

Those categories are more fully defined in the National Statement.

See section D1 (b) repeated measures and informed consent.

D2 SECURITY OF DATA

Please indicate how security will be maintained

(a) During the study

- All data will be stored on a computer in the Centre for Neuropsychology within a password-protected database. Data will be deleted as it is archived to CD-ROM or disk. CD-ROMs and disks will be stored in a secured cabinet.

(b) Following completion of study

- All data will be written to CD, which will be password protected and printed copies will be disposed of. All blood and saliva samples will be disposed of.

D3 PUBLICATION

The policy on the Conduct of Research requires, inter alia, that no individual persons or community group may be identified in any publication without their specific and informed consent.

Please explain:

What publication, if any, is envisaged following the project?

Will participants be informed that results from this study may appear in publications? (This information is normally to be included in the information given prior to obtaining informed consent.)

Would any participants be able to be identified through the publication? Explain why this is necessary.

It is anticipated that the results of this investigation will be published in a peer-reviewed journal. The results may also be presented at a conference or journal club. All participants will be informed that the results from the proposed study may be published and presented at the end of the study. Participants will be informed that their confidentiality will be respected; no subject will be referred to by name, and data will be presented as group data. This information will be included in the “Information for Participants” and consent form.

D4 INDIGENOUS ISSUES

Storage arrangements for data relating to research into Indigenous matters must be determined in compliance with the Policy on the Conduct of Research after consultation with the communities involved. What consultation has taken place and what arrangements have been made.

N/A
D5 ANY OTHER INFORMATION OF WHICH THE COMMITTEE SHOULD BE AWARE

The Centre for Neuropsychology holds a Permit to Purchase and Obtain Possess or Controlled Substances. This permit allows the Centre to purchase, obtain and administer amphetamines in clinical trials and for research and educational purposes. Holding this permit exempts Swinburne University of Technology and the participants recruited by Swinburne University of Technology from any legal prosecution. (See Appendix C)
SECTION E: SUBSTANCES & CLINICAL ISSUES

E1 ADMINISTRATION OF SUBSTANCES/AGENTS

<table>
<thead>
<tr>
<th>Name of substance(s)</th>
<th>Methamphetamine</th>
<th>MDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosage per administration</td>
<td>40mg/kg</td>
<td>100mg</td>
</tr>
<tr>
<td>Frequency of administration</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total amounts to be administered</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Anticipated effects:

Methamphetamine: Impairment of motor-coordination, loss of appetite, increased heart rate, rapid pulse rate, over stimulation, restlessness, and insomnia, shortness, and increased energy. MDMA: Impairment of motor-coordination, loss of appetite, increased heart rate, rapid pulse rate, over stimulation, restlessness, and insomnia, shortness, increased energy, positive mood, empathy, and euphoria.

Considering that participants will only receive one dose of methamphetamine or MDMA per session, adverse side effects are not anticipated.

The dose of methamphetamine to be administered in the current protocol has been previously approved by the HREC (Register Number 02/049). The methamphetamine project was previously conducted at Swinburne University using the same dose of methamphetamine. The project did not result in any adverse effects on participants. Participants did, however, report a wakefulness lasting beyond 24 hours post-drug administration.

The dose of MDMA to be administered is slightly higher than the dose previously approved by the HREC: 100mg d- or l-MDMA compared to 75mg d- or l-MDMA (Register Number 04/05). Although the dose of MDMA to be administered in the current protocol is slightly greater than previously approved, the original 75mg MDMA has been cited in previous studies to be on the low end of MDMA administration. The reported dose of 100mg of MDMA has been previously administered to human participants in several experimental studies, and the present protocol aims to replicate those doses and subjective effects. Typical recreational setting doses of MDMA have been reported to range between 50-150 mg (Cani et al., 2000). The 100 mg dose to be administered in this study is considered to be the typical recreational dose for most individuals and is equal to the dose administered in previous research (de la Torre et al., 1996; Farno et al., 2000). The dose to be administered is also less than some doses administered in previous MDMA research, where 200mg over two days, 125mg single dose and 150mg single dose of MDMA have been previously administered (Samyn et al., 2002; Cani et al., 2000). It should also be noted that researchers who have administered 75mg and 125mg doses of MDMA to participants (Cani et al., 2000; Samyn et al., 2002) purchased the MDMA from the same company as we have, Lipomed, Aesch, Switzerland. Finally, the lowest lethal dose of MDMA has been reported to be 49 mg/kg in animals (over 3400mg for a 40kg individual) (Budavari, et al. 1996).

NOTE: If the research involves administration of known substances or invasive procedures, please attach a statement accepting responsibility for those procedures by a medical or paramedical practitioner with indemnity insurance.

E2 DRUG TRIALS

CTN: Phase I
CTN Phase II
CTN Phase III
CTX
Routine / Other

CTN: Notification Schemes – Safety of the drugs has not been reviewed or approved by the Therapeutic Goods Administration (TGA), Canberra, and responsibility for the evaluation rests with the Ethics Committee.

CTX: The safety of the drug has been reviewed or approved by the TGA, Canberra. Routine: drugs are marketed in Australia and, in that formulation, are being used for an approved indication and in an approved dosage regimen.

E3 BODY FLUIDS OR TISSUE

What fluids or tissues? How will samples be obtained?
Blood samples will be taken using a syringe. Saliva will be obtained using Cusan’s saliva kit (see Appendix H).

**Frequency and timing:**

Blood samples will be taken at three different time points during each experimental session. 10mLs of blood will be taken per sample. Therefore, 30mLs of blood will be taken in these two sessions. Saliva will be taken at the same time points; 1mL of saliva will be taken per sample, therefore 3mLs in total.

**How are samples to be stored?**

Blood and saliva samples will be stored in a -20 degrees Celsius freezer.

**How will samples be disposed of?**

All samples will be placed in biological waste bags and disposed of by the health services.

**Who will take the samples?**

A registered nurse or phlebotomist will collect samples.

**What are their qualifications for doing so?**

Registered Nurse or phlebotomy qualifications.

**Do participants carry, as far as you know, the Hepatitis B or HIV virus?**

No.

**Do participants carry, as far as you know, any other contagious diseases or viruses?**

No.
## SECTION F  DECLARATIONS

We, the undersigned, are familiar with, and have access to copies of the University’s Policy on the Conduct of Research, the Privacy Act’s Privacy Principles and the National Statement on Ethical Conduct in Research Involving Humans (refer http://www.health.gov.au/public/policy/nar.htm). We accept responsibility for the conduct of this research in accordance with the principles contained in the National Statement and any other conditions specified by the Human Research Ethics Committee of the University.

All listed applicants must sign

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<td>Professor Con Slough</td>
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<td>Dr. Katherine Papaioiou</td>
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<td>Dr. Edward Ogden</td>
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All listed applicants must sign

APPLICATIONS SHOULD NORMALLY BE PROCESSED FIRST BY THE SCHOOL ETHICS SUB-COMMITTEE WHICH HAS THE POWER TO APPROVE APPLICATIONS WHERE THERE IS NO RISK TO THE PARTICIPANTS, RESEARCHERS OR UNIVERSITY BEYOND THE EVERYDAY NORM.

SCIENTIFIC MERIT

Research / Scientific Merit is a key element in consideration of the ethics of a protocol (refer National Statement at f.13, 1.14 & 1.15). The Human Research Ethics Committee may seek expert advice and assistance group in the evaluation of the scientific merit where appropriate.

YOU ARE REMINDED THAT PROJECTS MUST NOT COMMENCE WITHOUT PRIOR WRITTEN APPROVAL FROM THE HUMAN RESEARCH ETHICS COMMITTEE OR ITS APPROPRIATE SUB-COMMITTEE. APPLICATIONS SHOULD BE DIRECTED THROUGH THE SCHOOL ETHICS SUB-COMMITTEE IN THE FIRST INSTANCE.

HAVE YOU INCLUDED ALL NECESSARY ATTACHMENTS – COPIES OF QUESTIONNAIRES, INTERVIEW PROTOCOLS, CONTRACTS ETC. REFER GUIDELINES
12 March, 2007

Keith Wilkins
Research Ethics Officer
Office of Research and Graduate Studies

Dear Keith Wilkins,

Re:
HREC Register Number: 05/10
Chief Investigators: Prof C Scough, Dr K Papafotiou, Dr E Ogdin
Project Title: The Effects of MDMA and Methamphetamine on Driving and Sobriety Test Performance

Proposed Duration of Project: 01/09/02 - 01/09/03

The above protocol has been approved by the HREC. The chief investigators would like to submit the following updates and amendments for consideration by the HREC.

Attached you will find a request, for approval by the HREC, some minor amendment to the study 05/10, and also three amendments regarding the inclusion of additional tasks. Please note the requests to include the specified tasks have been previously approved by the HREC for our previous studies that have involved the administration of similar amphetamines (dexamphetamine 02/30 and methamphetamine 02/49) No problems were encountered in previous studies.

Minor Amendments:

1. Request to extend project to the end date
Due to delays in grant application approvals, the study is now due to end 01 Dec 2009. The project was approved for funding by the Australian Research Council in late 2006.

2. Change to funding arrangement
Although the application was submitted for funding to the National Law Enforcement Research Fund, it was not successful due to factors extending beyond the merit of the project. The project was resubmitted for funding to the Australian Research Council Discovery program and was successful. The funding source should therefore be amended to ARC.

3. Update on currency of insurance
Contact with Carol Balm, Swinburne University Insurance Officer, has indicated that the Swinburne University Insurance Policy has been extended to cover this study. There is therefore no issue with the study commencing.

4. Updated Information Sheet and Consent Form
The Information Sheet has been amended to include reference to ARC funding and the Consent Form has been updated to include the following complaints information:
"If you have any concerns or complaints about the conduct of this project, please contact: Research Ethics Officer, Office of Research & Graduate Studies (H68), Swinburne University of Technology, P O Box 218, HAWTHORN VIC 3122. Tel (03) 9214 5218 or reece@swin.edu.au"

Task Amendments

5. Inclusion of Cognitive Drug Research Cognitive Tests
The research team would like to add to the task an additional cognitive test battery. The proposed task to be administered will assess the effect of methamphetamine and MDMA on cognitive performance, such as reaction time, working memory, tracking and visual processing (see Appendix A for protocol and task description). Cognitive tasks have been administered in previous drug trials conducted at the Drugs and Driving Research Unit, Brain Sciences Institute, Project 02/49, and will allow for a significant comparison of cognitive effects across our drug studies.

6. Inclusion of Lexical Task Cognitive Tests
The research team would like to add to the task list an additional cognitive performance task. The proposed task to be administered will assess the effect of methamphetamine and MDMA on the processing of trauma and non-trauma related information (see Appendix B for protocol and task description). These tasks have been administered in previous drug trials conducted at the Drugs and Driving Research Unit, Brain Sciences Institute,
Project 02/49 amendment, and will allow for a significant comparison of
cognitive effects across our drug studies.

7. Inclusion of Mood Questionnaire
The research team would like to add to the task list a mood questionnaire.
This part of the study hopes to identify the changes in mood associated with
the consumption of methamphetamine and MDMA. This part of the study
will identify when negative moods effects dissipate after the consumption
of methamphetamine and MDMA. In addition, the administration of the mood
questionnaire is in line with previous suggestions by the HREC, where it was
suggested that mood be monitored once performance testing is complete, in
order to ascertain the extent of negative mood effects. The current
amendment extends this suggestion even further, to include the assessment
of mood not only at 3 hours and 4 hours after administration of each drug,
but also at 24 hours, 48 hours (2 days) and 120 hours (5 days) and 240 hours
(10 days) (see Appendix C for protocol and task description).

Please advise if there is any further information you require to approve the
above amendments.

Yours sincerely,

[Signature]
Professor Con Steagall
The Effects of Methamphetamine (Speed) and MDMA (Ecstasy) on Driving and Sobriety Test Performance

Research Investigators: Professor Con Stough and Dr. Katherine Papadotis
Swinburne Centre for Neuropsychology
Swinburne University of Technology
This study is being funded by the Australian Research Council (ARC).
Part of the study involving the collection and analysis of saliva samples, and the administration of the Court Rapidan saliva drug test, is being funded by Siemens Medical Solutions Diagnostics Pty Ltd.

PARTICIPANT’S NAME:

SUBJECT CODE | CODE

The present study has four major aims:
1. To investigate the effects of methamphetamine (Speed) and MDMA (Ecstasy) on driving behaviours;
2. To assess the efficiency of sobriety tests, currently being used by Victoria Police, to test for the presence of methamphetamine and MDMA;
3. To assess the relationship between driving impairment and the level of methamphetamine and MDMA detected in blood and saliva;
4. To assess the sensitivity and specificity of several drug detection devices for use on the roadside by law enforcement.

The study consists of three sessions, each with two phases. On arrival, a baseline blood and saliva sample will be taken. Following this, the methamphetamine, MDMA or placebo tablet will be administered. Each saliva sample will involve the administration of 4 or less saliva drug detection kits.

The methamphetamine (speed) and MDMA (ecstasy) to be administered will be purchased from Lipomed, Aarlesheim, Switzerland. Other researchers who have previously investigated the effects of amphetamines on performance have purchased the drug from this company (Cami, et al., 2000; Samyn et al., 2002).

The dose of Methamphetamine administered will be 0.42mg/kg of d-methamphetamine, the dose of MDMA administered will be 100mg of MDMA and the placebo dose will contain only flour (all doses will be masked using the same gelamine capsules). Once the drug has been administered, you will be asked to wait 3 hours for drug blood levels to peak. At 3 hours post drug administration, a second blood and saliva sample will be taken followed by the driving simulator and the Standardised Field Sobriety Tests (SFSTs). You will then be asked to complete a number of computerised and pen and paper tasks. These tasks will assess the effect that Methamphetamine and MDMA have on cognitive performance, such as; reaction time, working memory, tracking and visual processing as well as the effect on the
processing and memory of trauma and non-trauma related information. These tests will take approximately two hours to complete. This will conclude the first phase of testing. You will be provided with a taxi voucher for transport home, as well as an additional taxi voucher for transport back to the laboratory for further testing at 24 hours post drug administration. At 24 hours post drug administration a third (final) blood and saliva sample will be taken and the driving simulator task and SFSTs and the computerised cognitive tasks will be administered for a second (final) time. At this time, if amphetamine is still detected in your saliva, a taxi voucher will be provided for transport home.

In addition to the tests described above, you will also be asked to complete a number of mood questionnaires throughout the test sessions. These will be administered on the day of testing at: baseline, 3 hours post drug administration, 5 hours post drug administration and 24 hours post drug administration. You will also be contacted by telephone to complete the questionnaires at 48 hours, 5 days and 10 days post drug administration. These questionnaires will take 5 minutes to complete and will help identify the changes in mood associated with the consumption of Methamphetamine and MDMA.

This completes phase one and two of the session. This process will occur on three occasions so as to gather performance and specimen data relating to methamphetamine, MDMA and placebo. Results from each session will be compared to investigate whether methamphetamine and/or MDMA impair performance.

This is a double-blind study; therefore, neither you nor the researcher will know what dose has been taken until the completion of the trial. During those sessions where you will be administered the active methamphetamine and MDMA it is likely you will feel the following effects: impairment of motor-co-ordination, loss of appetite, increased heart rate, rapid pulse rate, over stimulation, restlessness, and insomnia.

The consumption of methamphetamine and MDMA is likely to have the following effects on humans:

**Methamphetamine (Speed):** Impairment of motor-co-ordination, loss of appetite, increased heart rate, rapid pulse rate, over stimulation, restlessness, and insomnia, alertness, and increased energy. Anxiety and possibly panic attacks may be experienced at higher doses.

**MDMA (Ecstasy):** Impairment of motor-co-ordination, loss of appetite, increased heart rate, rapid pulse rate, over stimulation, restlessness, insomnia, alertness, increased energy, positive mood, empathy, and euphoria. Anxiety and possibly panic attacks may be experienced at higher doses.

Following the administration of the drug, and prior to the administration of performance tests (3 hour waiting period), participants will be asked to sit in a waiting room, where video, books and magazines will be available for entertainment. In addition, at the completion of each session, each participant will be assessed by the research nurse for the presence of negative mood effects induced by the drugs, eg. Agitation. If the research nurse concludes that for the participants own safety, that the participant should remain at the testing site until negative mood effects have diminished, the participant will be asked to remain in the waiting room where video, books and magazines will be available for entertainment.
If you consent to participating in the trial, you must agree not to consume alcohol for at least 24 hours prior to each session, and no other drugs for at least 7 days prior to each session. Amphetamines are known to influence driving ability, therefore taxi vouchers will be provided for those who cannot make alternative transport arrangements home from the first phase and back to the laboratory for the second phase in each session. In addition, you must agree not to drive or ride, operate any machinery, nor consume any alcohol, drugs or medications, for at least 24 hours after each experimental session.

Additionally, applicants must fulfill the following criteria: Participants must have no history of current or past substance abuse (persistent compulsive use of a substance), have no pre-existing physical or neurological conditions, no history of psychiatric, cardiac, endocrine, gastrointestinal, or bleeding disorders, nor pregnant or lactating, and not taking any medication. Participants are required to have experimented with amphetamines previously. All participants must have a full driver’s license (no probationary drivers).

Your participation in this study is voluntary and you are free to withdraw from the study at any time. If you decide to withdraw, you are still required to abide by the safety restrictions advising you not to drive for at least 24 hours after the administration of methamphetamine and MDMA, and not to consume alcohol, drugs or any other medications for at least 24 hours after each session.

It is expected that the results of this study will be published in a peer-reviewed journal and will be presented at national conferences. The identity of participants will not be disclosed and all data will be presented as group data.

Any questions regarding the project entitled ‘The Effects of Methamphetamine (speed and) MDMA (ecstasy) on Driving Ability and Sobriety Test Performance’ can be directed to the Chief Investigator Dr Katherine Papafotou of the Brain Sciences Institute, Swinburne University (ph: 9214 5757 email: kpapa@swin.edu.au).

If you have any concerns or complaints about the conduct of this project, please contact: Research Ethics Officer, Office of Research & Graduate Studies (H68), Swinburne University of Technology, P O Box 218, HAWTHORN VIC 3122. Tel (03) 9214 5218 or resethics@swin.edu.au
SWINBURNE UNIVERSITY OF TECHNOLOGY

Informed Consent Form

The Effect of Methamphetamine (Speed) and MDMA (Ecstasy) on Driving and Sobriety Test Performance

Research Investigators: Prof. Con Stough and Dr. Katherine Papadotou
This study is being funded by the Australian Research Council (ARC).
Part of the study involving the collection and analysis of saliva samples, and the administration of the
CovaPepweed saliva drug test, is being funded by Siemens Medical Solutions Diagnostics Pty Ltd.

PARTICIPANT'S NAME: _____________________________

SUBJECT CODE: ____________

I (the participant) have read and understood the information above and understand the general
purposes, methods and demands of the study. Any questions I have asked have been answered to my
satisfaction.

I have no history of current or past substance abuse, have no pre-existing physical or neurological
conditions, no history of psychiatric, cardiac, endocrine, gastrointestinal, or bleeding disorders, am not
pregnant or breastfeeding, not taking any medication, and I have previously experimented with
amphetamine.

I agree that for the experimental sessions I will be administered a capsule that may contain either no
methamphetamine or MDMA, or 420μg of methamphetamine, or 100μg of MDMA.

Since amphetamines are known to influence mood. I acknowledge that I may possibly experience
negative mood effects such as agitation. I agree to be assessed by the research nurse, and if the
research nurse concludes, that for my own safety, I should remain at the testing site until negative
mood symptoms diminish, I agree to remain at the testing site.

I agree that in the experimental sessions in which my possibly be administered methamphetamine or
MDMA, I will not drive or ride to or from the session. I agree that I will utilize the transport home
provided for me by the researchers, if I have not arranged my own transport.

I agree that I should not consume alcohol for at least 24 hours or any medications or other drugs for at
least 7 days prior to my sessions.

Methamphetamine is known to influence driving ability; therefore, I agree to utilise the transport/taxi
services arranged to get home.

I agree that I should not drive or ride, operate any machinery, nor consume alcohol or any medication
for at least 24 hours after my sessions.

I am satisfied with the explanation given in relation to the project, and my consent is freely given.

I agree to participate in this activity, and understand that I am free to withdraw from the study at any
time.

I agree that research data collected for the study may be published or provided to other researchers on
the condition that anonymity is maintained and that I cannot be identified.

NAME OF PARTICIPANT: _____________________________
SIGNATURE: ________________________________________ DATE: ____________

NAME OF PRINCIPAL INVESTIGATOR: _____________________________
SIGNATURE: ________________________________________ DATE: ____________
SIGNATURE: ________________________________________ DATE: ____________
Dear Con,

SUHREC Project 05/10 The Effects of MDMA and Methamphetamine on Driving and Sobriety Test Performance
Prof Con Stough et al Lab HTS8

Approved Duration Extended to 01/12/2009 [Project Modified/Expanded February/March 2009]

I refer to your request to extend clearance to 01 December 2009 for a modified and expanded project as submitted by hardcopy on 13 February 2009 and subsequent emails on 19 February and 4 March 2009, the latter with updated consent instruments following consideration of the recent modified protocols by a delegate of Swinburne’s Human Research Ethics Committee (SUHREC). In summary, the request included trialling additional testing devices, additional funding, a wider number of participants and new researcher contact details.

I am pleased to advise that approval for the extended and modified project has been given as submitted to date in line with current standard on-going ethics clearance conditions here outlined.

- All human research activity undertaken under Swinburne auspices must confirm to Swinburne and external regulatory standards, including the National Statement on Ethical Conduct in Human Research and with respect to secure data use, retention and disposal.

- The named Swinburne Chief Investigator/Supervisor remains responsible for any personnel appointed to or associated with the project being made aware of all clearance conditions, including research and consent procedures or instruments approved. Any change in chief investigator/Supervisor requires timely notification and SUHREC endorsement.

- The above project has been approved as submitted for ethical review by or on behalf of SUHREC. Amendments to approved procedures or instruments ordinarily require prior ethical approval/clearance. SUHREC must be notified immediately or as soon as possible thereafter of (a) any serious or unexpected adverse effects on participants and any redress measures; (b) proposed changes in protocols; and (c) unforeseen events which might affect continued ethical acceptability of the project.

- At a minimum, an annual report on the progress of the project is required as well as at the conclusion (or abandonment) of the project.

- A duly authorised external or internal audit of the project may be undertaken at any time.

Please contact me if you have any queries about on-going ethics clearance or if you need a signed ethics clearance certificate. The SUHREC project number should be quoted in communication.

Best wishes for the continuing project.

Yours sincerely,
Keith Wilkins
Secretary, SUHREC

*************************************************************************
Keith Wilkins
Research Ethics Officer
Swinburne Research (H68)
Swinburne University of Technology
P O Box 218
HAWTORN VIC 3122
Tel: 9214 3218
APPENDIX 3.

Histograms and Q-Q plots for all variables in the alcohol, methamphetamine and MDMA comparison.

Histograms and normality plots for all variables in the Alcohol comparison

**IAPS Task**

*Figure 1.* Histogram of mean valence ratings to all pictures in the alcohol condition.
Figure 2. Normal Q-Q plot of mean valence ratings to all pictures in the alcohol condition.

Figure 3. Histogram of mean valence ratings to all pictures in the placebo condition.

Figure 4. Normal Q-Q plot of mean valence ratings to all pictures in the placebo condition.
Figure 5. Histogram of mean arousal ratings to all pictures in the alcohol condition.

Figure 6. Normal Q-Q plot of mean arousal ratings to all pictures in the alcohol condition.
Figure 7. Histogram of mean arousal ratings to all pictures in the placebo condition.

Figure 8. Normal Q-Q plot of mean arousal ratings to all pictures in the placebo condition.
**Figure 9.** Histogram of mean valence ratings to threat pictures in the alcohol condition.

**Figure 10.** Normal Q-Q plot of mean valence ratings to threat pictures in the alcohol condition.
Figure 11. Histogram of mean valence ratings to threat pictures in the placebo condition.

Figure 12. Normal Q-Q plot of mean valence ratings to threat pictures in the placebo condition.
Figure 13. Histogram of mean arousal ratings to threat pictures in the alcohol condition.

Figure 14. Normal Q-Q plot of mean arousal ratings to threat pictures in the alcohol condition.
Figure 15. Histogram of mean arousal ratings to threat pictures in the placebo condition.

Figure 16. Normal Q-Q plot of mean arousal ratings to threat pictures in the placebo condition.
Figure 17. Histogram of mean valence ratings to neutral pictures in the alcohol condition.

Figure 18. Normal Q-Q plot of mean valence ratings to neutral pictures in the alcohol condition.
Figure 19. Histogram of mean valence ratings to neutral pictures in the placebo condition.

Figure 20. Normal Q-Q plot of mean valence ratings to neutral pictures in the placebo condition.
Figure 21. Histogram of mean arousal ratings to neutral pictures in the alcohol condition.

Figure 22. Normal Q-Q plot of mean arousal ratings to neutral pictures in the alcohol condition.
**Figure 23.** Histogram of mean arousal ratings to neutral pictures in the placebo condition.

**Figure 24.** Normal Q-Q plot of mean arousal ratings to neutral pictures in the placebo condition.
Recognition test results

Figure 25. Histogram of mean accuracy ratings to all pictures previously in the alcohol condition.

Figure 26. Normal Q-Q plot of mean accuracy ratings to all pictures previously in the alcohol condition.
Figure 27. Histogram of mean accuracy ratings to all pictures previously in the placebo condition.

Figure 28. Normal Q-Q plot of mean accuracy ratings to all pictures previously in the placebo condition.
Figure 29. Histogram of mean confidence ratings to all pictures previously in the alcohol condition.

Figure 30. Normal Q-Q plot of mean confidence ratings to all pictures previously in the alcohol condition.
Figure 31. Histogram of mean confidence ratings to all pictures previously in the placebo condition.

Figure 32. Normal Q-Q plot of mean confidence ratings to all pictures previously in the placebo condition.
Figure 33. Histogram of mean accuracy ratings to threat pictures previously in the alcohol condition.

Figure 34. Normal Q-Q plot of mean accuracy ratings to threat pictures previously in the alcohol condition.
Figure 35. Histogram of mean accuracy ratings to threat pictures previously in the placebo condition.

Figure 36. Normal Q-Q plot of mean accuracy ratings to threat pictures previously in the placebo condition.
Figure 37. Histogram of mean confidence ratings to threat pictures previously in the alcohol condition.

Figure 38. Normal Q-Q plot of mean confidence ratings to threat pictures previously in the alcohol condition.
**Figure 39.** Histogram of mean confidence ratings to threat pictures previously in the placebo condition.

**Figure 40.** Normal Q-Q plot of mean confidence ratings to threat pictures previously in the placebo condition.
Figure 41. Histogram of mean accuracy ratings to neutral pictures previously in the alcohol condition.

Figure 42. Normal Q-Q plot of mean accuracy ratings to neutral pictures previously in the alcohol condition.
Figure 43. Histogram of mean accuracy ratings to neutral pictures previously in the placebo condition.

Figure 44. Normal Q-Q plot of mean accuracy ratings to neutral pictures previously in the placebo condition.
Figure 45. Histogram of mean confidence ratings to neutral pictures previously in the alcohol condition.

Figure 46. Normal Q-Q plot of mean confidence ratings to neutral pictures previously in the alcohol condition.
Figure 47. Histogram of mean confidence ratings to neutral pictures previously in the placebo condition.

Figure 48. Normal Q-Q plot of mean confidence ratings to neutral pictures previously in the placebo condition.
LDT performance

Figure 49. Histogram of mean short-term recall for all words in the alcohol condition.

Figure 50. Normal Q-Q plot of mean short-term recall for all words in the alcohol condition.
Figure 51. Histogram of mean short-term recall for all words in the placebo condition.

Figure 52. Normal Q-Q plot of mean short-term recall for all words in the placebo condition.
Figure 53. Histogram of mean short-term recall for threat words in the alcohol condition.

Figure 54. Normal Q-Q plot of mean short-term recall for threat words in the alcohol condition.
Figure 55. Histogram of mean short-term recall for threat words in the placebo condition.

Figure 56. Normal Q-Q plot of mean short-term recall for threat words in the placebo condition.
**Figure 57.** Histogram of mean short-term recall for neutral words in the alcohol condition.

**Figure 58.** Normal Q-Q plot of mean short-term recall for neutral words in the alcohol condition.
Figure 59. Histogram of mean short-term recall for neutral words in the placebo condition.

Figure 60. Normal Q-Q plot of mean short-term recall for neutral words in the placebo condition.
Figure 61. Histogram of mean short-term recall in the first epoch for all words in the alcohol condition.

Figure 62. Normal Q-Q plot of mean short-term recall in the first epoch for all words in the alcohol condition.
Figure 63. Histogram of mean short-term recall in the first epoch for all words in the placebo condition.

Figure 64. Normal Q-Q plot of mean short-term recall in the first epoch for all words in the placebo condition.
Figure 65. Histogram of mean short-term recall in the second epoch for all words in the alcohol condition.

Figure 66. Normal Q-Q plot of mean short-term recall in the second epoch for all words in the alcohol condition.
Figure 67. Histogram of mean short-term recall in the second epoch for all words in the placebo condition.

Figure 68. Normal Q-Q plot of mean short-term recall in the second epoch for all words in the placebo condition.
Figure 69. Histogram of mean short-term recall in the first epoch for threat words in the alcohol condition.

Figure 70. Normal Q-Q plot of mean short-term recall in the first epoch for threat words in the alcohol condition.
Figure 71. Histogram of mean short-term recall in the first epoch for threat words in the placebo condition.

Figure 72. Normal Q-Q plot of mean short-term recall in the first epoch for threat words in the placebo condition.
**Figure 73.** Histogram of mean short-term recall in the second epoch for threat words in the alcohol condition.

**Figure 74.** Normal Q-Q plot of mean short-term recall in the second epoch for threat words in the alcohol condition.
Figure 75. Histogram of mean short-term recall in the second epoch for threat words in the placebo condition.

Figure 76. Normal Q-Q plot of mean short-term recall in the second epoch for threat words in the placebo condition.
Figure 77. Histogram of mean short-term recall in the first epoch for neutral words in the alcohol condition.

Figure 78. Normal Q-Q plot of mean short-term recall in the first epoch for neutral words in the alcohol condition.
Figure 79. Histogram of mean short-term recall in the first epoch for neutral words in the placebo condition.

Figure 80. Normal Q-Q plot of mean short-term recall in the first epoch for neutral words in the placebo condition.
Figure 81. Histogram of mean short-term recall in the second epoch for neutral words in the alcohol condition.

Figure 82. Normal Q-Q plot of mean short-term recall in the second epoch for neutral words in the alcohol condition.
Figure 83. Histogram of mean short-term recall in the second epoch for neutral words in the placebo condition.

Figure 84. Normal Q-Q plot of mean short-term recall in the second epoch for neutral words in the placebo condition.
Figure 85. Histogram of mean long-term recall for all words in the alcohol condition.

Figure 86. Normal Q-Q plot of mean long-term recall for all words in the alcohol condition.
**Figure 87.** Histogram of mean long-term recall for all words in the placebo condition.

**Figure 89.** Normal Q-Q plot of mean long-term recall for all words in the placebo condition.
Figure 90. Histogram of mean long-term recall for threat words in the alcohol condition.

Figure 91. Normal Q-Q plot of mean long-term recall for threat words in the alcohol condition.
Figure 92. Histogram of mean long-term recall for threat words in the placebo condition.

Figure 93. Normal Q-Q plot of mean long-term recall for threat words in the placebo condition.
Figure 94. Histogram of mean long-term recall for neutral words in the alcohol condition.

Figure 95. Normal Q-Q plot of mean long-term recall for neutral words in the alcohol condition.
**Figure 96.** Histogram of mean long-term recall for neutral words in the placebo condition.

**Figure 97.** Normal Q-Q plot of mean long-term recall for neutral words in the placebo condition.
Processing

Figure 98. Histogram of mean reaction times for all words in the alcohol condition.

Figure 99. Normal Q-Q plot of mean reaction times for all words in the alcohol condition.
Figure 100. Histogram of mean reaction times for all words in the placebo condition.

Figure 101. Normal Q-Q plot of mean reaction times for all words in the placebo condition.
Figure 102. Histogram of mean reaction times for threat words in the alcohol condition.

Figure 103. Normal Q-Q plot of mean reaction times for threat words in the alcohol condition.
Figure 104. Histogram of mean reaction times for threat words in the placebo condition.

Figure 105. Normal Q-Q plot of mean reaction times for threat words in the placebo condition.
Figure 106. Histogram of mean reaction times for neutral words in the alcohol condition.

Figure 107. Normal Q-Q plot of mean reaction times for neutral words in the alcohol condition.
**Figure 108.** Histogram of mean reaction times for neutral words in the placebo condition.

**Figure 109.** Normal Q-Q plot of mean reaction times for neutral words in the placebo condition.
Figure 110. Histogram of estimated IQ scores for participants in the alcohol condition.

Figure 111. Normal Q-Q plot of estimated IQ scores for participants in the alcohol condition.
Figure 112. Histogram of Anxiety Sensitivity scores for participants in the alcohol condition.

Figure 113. Normal Q-Q plot of Anxiety Sensitivity scores for participants in the alcohol condition.
Histograms and normality plots for all variables in the methamphetamine comparison

**IAPS Task**

*Figure 1.* Histogram of mean valence ratings to all pictures in the methamphetamine condition.

*Figure 2.* Normal Q-Q plot of mean valence ratings to all pictures in the methamphetamine condition.
Figure 3. Histogram of mean valence ratings to all pictures in the placebo condition.

Figure 4. Normal Q-Q plot of mean valence ratings to all pictures in the placebo condition.
Figure 5. Histogram of mean arousal ratings to all pictures in the methamphetamine condition.

Figure 6. Normal Q-Q plot of mean arousal ratings to all pictures in the methamphetamine condition.
Figure 7. Histogram of mean arousal ratings to all pictures in the placebo condition.

Figure 8. Normal Q-Q plot of mean arousal ratings to all pictures in the placebo condition.
Figure 9. Histogram of mean valence ratings to threat pictures in the methamphetamine condition.

Figure 10. Normal Q-Q plot of mean valence ratings to threat pictures in the methamphetamine condition.
Figure 11. Histogram of mean valence ratings to threat pictures in the placebo condition.

Figure 12. Normal Q-Q plot of mean valence ratings to threat pictures in the placebo condition.
Figure 13. Histogram of mean arousal ratings to threat pictures in the methamphetamine condition.

Figure 14. Normal Q-Q plot of mean arousal ratings to threat pictures in the methamphetamine condition.
Figure 15. Histogram of mean arousal ratings to threat pictures in the placebo condition.

Figure 16. Normal Q-Q plot of mean arousal ratings to threat pictures in the placebo condition.
Figure 17. Histogram of mean valence ratings to neutral pictures in the methamphetamine condition.

Figure 18. Normal Q-Q plot of mean valence ratings to neutral pictures in the methamphetamine condition.
Figure 19. Histogram of mean valence ratings to neutral pictures in the placebo condition.

Figure 20. Normal Q-Q plot of mean valence ratings to neutral pictures in the placebo condition.
Figure 21. Histogram of mean arousal ratings to neutral pictures in the methamphetamine condition.

Figure 22. Normal Q-Q plot of mean arousal ratings to neutral pictures in the methamphetamine condition.
Figure 23. Histogram of mean arousal ratings to neutral pictures in the placebo condition.

Figure 24. Normal Q-Q plot of mean arousal ratings to neutral pictures in the placebo condition.
Recognition test results

Figure 25. Histogram of mean accuracy ratings to all pictures previously in the methamphetamine condition.

Figure 26. Normal Q-Q plot of mean accuracy ratings to all pictures previously in the methamphetamine condition.
Figure 27. Histogram of mean accuracy ratings to all pictures previously in the placebo condition.

Figure 28. Normal Q-Q plot of mean accuracy ratings to all pictures previously in the placebo condition.
Figure 29. Histogram of mean confidence ratings to all pictures previously in the methamphetamine condition.

Figure 30. Normal Q-Q plot of mean confidence ratings to all pictures previously in the methamphetamine condition.
Figure 31. Histogram of mean confidence ratings to all pictures previously in the placebo condition.

Figure 32. Normal Q-Q plot of mean confidence ratings to all pictures previously in the placebo condition.
Figure 33. Histogram of mean accuracy ratings to threat pictures previously in the methamphetamine condition.

Figure 34. Normal Q-Q plot of mean accuracy ratings to threat pictures previously in the methamphetamine condition.
Figure 35. Histogram of mean accuracy ratings to threat pictures previously in the placebo condition.

Figure 36. Normal Q-Q plot of mean accuracy ratings to threat pictures previously in the placebo condition.
Figure 37. Histogram of mean confidence ratings to threat pictures previously in the methamphetamine condition.

Figure 38. Normal Q-Q plot of mean confidence ratings to threat pictures previously in the methamphetamine condition.
Figure 39. Histogram of mean confidence ratings to threat pictures previously in the placebo condition.

Figure 40. Normal Q-Q plot of mean confidence ratings to threat pictures previously in the placebo condition.
Figure 41. Histogram of mean accuracy ratings to neutral pictures previously in the methamphetamine condition.

Figure 42. Normal Q-Q plot of mean accuracy ratings to neutral pictures previously in the methamphetamine condition.
Figure 43. Histogram of mean accuracy ratings to neutral pictures previously in the placebo condition.

Figure 44. Normal Q-Q plot of mean accuracy ratings to neutral pictures previously in the placebo condition.
Figure 45. Histogram of mean confidence ratings to neutral pictures previously in the methamphetamine condition.

Figure 46. Normal Q-Q plot of mean confidence ratings to neutral pictures previously in the methamphetamine condition.
Figure 47. Histogram of mean confidence ratings to neutral pictures previously in the placebo condition.

Figure 48. Normal Q-Q plot of mean confidence ratings to neutral pictures previously in the placebo condition.
**LDT performance**

*Figure 49.* Histogram of mean short-term recall for all words in the methamphetamine condition.

*Figure 50.* Normal Q-Q plot of mean short-term recall for all words in the methamphetamine condition.
**Figure 51.** Histogram of mean short-term recall for all words in the placebo condition.

**Figure 52.** Normal Q-Q plot of mean short-term recall for all words in the placebo condition.
Figure 53. Histogram of mean short-term recall for threat words in the methamphetamine condition.

Figure 54. Normal Q-Q plot of mean short-term recall for threat words in the methamphetamine condition.
Figure 55. Histogram of mean short-term recall for threat words in the placebo condition.

Figure 56. Normal Q-Q plot of mean short-term recall for threat words in the placebo condition.
Figure 57. Histogram of mean short-term recall for neutral words in the methamphetamine condition.

Figure 58. Normal Q-Q plot of mean short-term recall for neutral words in the methamphetamine condition.
**Figure 59.** Histogram of mean short-term recall for neutral words in the placebo condition.

**Figure 60.** Normal Q-Q plot of mean short-term recall for neutral words in the placebo condition.
Figure 61. Histogram of mean short-term recall in the first epoch for all words in the methamphetamine condition.

Figure 62. Normal Q-Q plot of mean short-term recall in the first epoch for all words in the methamphetamine condition.
Figure 63. Histogram of mean short-term recall in the first epoch for all words in the placebo condition.

Figure 64. Normal Q-Q plot of mean short-term recall in the first epoch for all words in the placebo condition.
Figure 65. Histogram of mean short-term recall in the second epoch for all words in the methamphetamine condition.

Figure 66. Normal Q-Q plot of mean short-term recall in the second epoch for all words in the methamphetamine condition.
Figure 67. Histogram of mean short-term recall in the second epoch for all words in the placebo condition.

Figure 68. Normal Q-Q plot of mean short-term recall in the second epoch for all words in the placebo condition.
Figure 69. Histogram of mean short-term recall in the first epoch for threat words in the methamphetamine condition.

Figure 70. Normal Q-Q plot of mean short-term recall in the first epoch for threat words in the methamphetamine condition.
Figure 71. Histogram of mean short-term recall in the first epoch for threat words in the placebo condition.

Figure 72. Normal Q-Q plot of mean short-term recall in the first epoch for threat words in the placebo condition.
Figure 73. Histogram of mean short-term recall in the second epoch for threat words in the methamphetamine condition.

Figure 74. Normal Q-Q plot of mean short-term recall in the second epoch for threat words in the methamphetamine condition.
Figure 75. Histogram of mean short-term recall in the second epoch for threat words in the placebo condition.

Figure 76. Normal Q-Q plot of mean short-term recall in the second epoch for threat words in the placebo condition.
Figure 77. Histogram of mean short-term recall in the first epoch for neutral words in the methamphetamine condition.

Figure 78. Normal Q-Q plot of mean short-term recall in the first epoch for neutral words in the methamphetamine condition.
Figure 79. Histogram of mean short-term recall in the first epoch for neutral words in the placebo condition.

Figure 80. Normal Q-Q plot of mean short-term recall in the first epoch for neutral words in the placebo condition.
**Figure 81.** Histogram of mean short-term recall in the second epoch for neutral words in the methamphetamine condition.

**Figure 82.** Normal Q-Q plot of mean short-term recall in the second epoch for neutral words in the methamphetamine condition.
Figure 83. Histogram of mean short-term recall in the second epoch for neutral words in the placebo condition.

Figure 84. Normal Q-Q plot of mean short-term recall in the second epoch for neutral words in the placebo condition.
Figure 85. Histogram of mean long-term recall for all words in the methamphetamine condition.

Figure 86. Normal Q-Q plot of mean long-term recall for all words in the methamphetamine condition.
Figure 87. Histogram of mean long-term recall for all words in the placebo condition.

Figure 89. Normal Q-Q plot of mean long-term recall for all words in the placebo condition.
Figure 90. Histogram of mean long-term recall for threat words in the methamphetamine condition.

Figure 91. Normal Q-Q plot of mean long-term recall for threat words in the methamphetamine condition.
Figure 92. Histogram of mean long-term recall for threat words in the placebo condition.

Figure 93. Normal Q-Q plot of mean long-term recall for threat words in the placebo condition.
**Figure 94.** Histogram of mean long-term recall for neutral words in the methamphetamine condition.

**Figure 95.** Normal Q-Q plot of mean long-term recall for neutral words in the methamphetamine condition.
Figure 96. Histogram of mean long-term recall for neutral words in the placebo condition.

Figure 97. Normal Q-Q plot of mean long-term recall for neutral words in the placebo condition.
Processing

Figure 98. Histogram of mean reaction times for all words in the methamphetamine condition.

Figure 99. Normal Q-Q plot of mean reaction times for all words in the methamphetamine condition.
Figure 100. Histogram of mean reaction times for all words in the placebo condition.

Figure 101. Normal Q-Q plot of mean reaction times for all words in the placebo condition.
**Figure 102.** Histogram of mean reaction times for threat words in the methamphetamine condition.

**Figure 103.** Normal Q-Q plot of mean reaction times for threat words in the methamphetamine condition.
Figure 104. Histogram of mean reaction times for threat words in the placebo condition.

Figure 105. Normal Q-Q plot of mean reaction times for threat words in the placebo condition.
Figure 106. Histogram of mean reaction times for neutral words in the methamphetamine condition.

Figure 107. Normal Q-Q plot of mean reaction times for neutral words in the methamphetamine condition.
Figure 108. Histogram of mean reaction times for neutral words in the placebo condition.

Figure 109. Normal Q-Q plot of mean reaction times for neutral words in the placebo condition.
Figure 110. Histogram of estimated IQ scores for participants in the methamphetamine condition.

Figure 111. Normal Q-Q plot of estimated IQ scores for participants in the methamphetamine condition.
Figure 112. Histogram of Anxiety Sensitivity scores for participants in the methamphetamine condition.

Figure 113. Normal Q-Q plot of Anxiety Sensitivity scores for participants in the methamphetamine condition.
**Figure 114.** Histogram of blood plasma levels (ug/L) for participants in the methamphetamine condition.

**Figure 115.** Normal Q-Q plot of blood plasma levels (ug/L) for participants in the methamphetamine condition.
Histograms and normality plots for all variables in the MDMA comparison

IAPS Task

Figure 1. Histogram of mean valence ratings to all pictures in the MDMA condition.

Figure 2. Normal Q-Q plot of mean valence ratings to all pictures in the MDMA condition.
**Figure 3.** Histogram of mean valence ratings to all pictures in the placebo condition.

**Figure 4.** Normal Q-Q plot of mean valence ratings to all pictures in the placebo condition.
Figure 5. Histogram of mean arousal ratings to all pictures in the MDMA condition.

Figure 6. Normal Q-Q plot of mean arousal ratings to all pictures in the MDMA condition.
Figure 7. Histogram of mean arousal ratings to all pictures in the placebo condition.

Figure 8. Normal Q-Q plot of mean arousal ratings to all pictures in the placebo condition.
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**Figure 11.** Histogram of mean valence ratings to threat pictures in the placebo condition.

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Figure 23. Histogram of mean arousal ratings to neutral pictures in the placebo condition.

Figure 24. Normal Q-Q plot of mean arousal ratings to neutral pictures in the placebo condition.
Recognition test results

Figure 25. Histogram of mean accuracy ratings to all pictures previously in the MDMA condition.

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Figure 43. Histogram of mean accuracy ratings to neutral pictures previously in the placebo condition.

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Figure 47. Histogram of mean confidence ratings to neutral pictures previously in the placebo condition.

Figure 48. Normal Q-Q plot of mean confidence ratings to neutral pictures previously in the placebo condition.
LDT performance

Figure 49. Histogram of mean short-term recall for all words in the MDMA condition.

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Figure 60. Normal Q-Q plot of mean short-term recall for neutral words in the placebo condition.
Figure 61. Histogram of mean short-term recall in the first epoch for all words in the MDMA condition.

Figure 62. Normal Q-Q plot of mean short-term recall in the first epoch for all words in the MDMA condition.
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Figure 64. Normal Q-Q plot of mean short-term recall in the first epoch for all words in the placebo condition.
Figure 65. Histogram of mean short-term recall in the second epoch for all words in the MDMA condition.

Figure 66. Normal Q-Q plot of mean short-term recall in the second epoch for all words in the MDMA condition.
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Figure 72. Normal Q-Q plot of mean short-term recall in the first epoch for threat words in the placebo condition.
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Figure 74. Normal Q-Q plot of mean short-term recall in the second epoch for threat words in the MDMA condition.
Figure 75. Histogram of mean short-term recall in the second epoch for threat words in the placebo condition.

Figure 76. Normal Q-Q plot of mean short-term recall in the second epoch for threat words in the placebo condition.
Figure 77. Histogram of mean short-term recall in the first epoch for neutral words in the MDMA condition.

Figure 78. Normal Q-Q plot of mean short-term recall in the first epoch for neutral words in the MDMA condition.
**Figure 79.** Histogram of mean short-term recall in the first epoch for neutral words in the placebo condition.

**Figure 80.** Normal Q-Q plot of mean short-term recall in the first epoch for neutral words in the placebo condition.
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Figure 86. Normal Q-Q plot of mean long-term recall for all words in the MDMA condition.
Figure 87. Histogram of mean long-term recall for all words in the placebo condition.

Figure 89. Normal Q-Q plot of mean long-term recall for all words in the placebo condition.
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Figure 91. Normal Q-Q plot of mean long-term recall for threat words in the MDMA condition.
Figure 92. Histogram of mean long-term recall for threat words in the placebo condition.

Figure 93. Normal Q-Q plot of mean long-term recall for threat words in the placebo condition.
Figure 94. Histogram of mean long-term recall for neutral words in the MDMA condition.

Figure 95. Normal Q-Q plot of mean long-term recall for neutral words in the MDMA condition.
Figure 96. Histogram of mean long-term recall for neutral words in the placebo condition.

Figure 97. Normal Q-Q plot of mean long-term recall for neutral words in the placebo condition.
Figure 98. Histogram of mean reaction times for all words in the MDMA condition.

Figure 99. Normal Q-Q plot of mean reaction times for all words in the MDMA condition.
Figure 100. Histogram of mean reaction times for all words in the placebo condition.

Figure 101. Normal Q-Q plot of mean reaction times for all words in the placebo condition.
Figure 102. Histogram of mean reaction times for threat words in the MDMA condition.

Figure 103. Normal Q-Q plot of mean reaction times for threat words in the MDMA condition.
Figure 104. Histogram of mean reaction times for threat words in the placebo condition.

Figure 105. Normal Q-Q plot of mean reaction times for threat words in the placebo condition.
Figure 106. Histogram of mean reaction times for neutral words in the MDMA condition.

Figure 107. Normal Q-Q plot of mean reaction times for neutral words in the MDMA condition.
Figure 108. Histogram of mean reaction times for neutral words in the placebo condition.

Figure 109. Normal Q-Q plot of mean reaction times for neutral words in the placebo condition.
Figure 110. Histogram of estimated IQ for participants in the MDMA comparison.

Figure 111. Normal Q-Q plot for estimated IQ for participants in the MDMA comparison.
Figure 112. Histogram of Anxiety Sensitivity scores for participants in the MDMA condition.

Figure 113. Normal Q-Q plot for Anxiety Sensitivity scores for participants in the MDMA condition.
**Figure 114.** Histogram of blood plasma levels (ug/L) for participants in the MDMA comparison.

**Figure 115.** Normal Q-Q plot for blood plasma levels (ug/L) for participants in the MDMA comparison.
APPENDIX 4.

Blood Plasma levels for the Methamphetamine and MDMA comparisons and covariate correlations for all drug conditions.
Table 4
*Blood plasma levels of Methamphetamine after three hours*

<table>
<thead>
<tr>
<th>Participant No.</th>
<th>Screening Result</th>
<th>GC/MS Meth ug/L</th>
<th>Additional Drug detected</th>
<th>ug/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not Detected</td>
<td>&lt; 10ug/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Positive</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Positive for Cannabinoids</td>
<td>25</td>
<td>delta 9-THC-COOH</td>
<td>162</td>
</tr>
<tr>
<td>4</td>
<td>Not Detected</td>
<td>&lt; 10ug/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Positive</td>
<td>67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Positive for Cannabinoids</td>
<td>73</td>
<td>delta 9-THC-COOH</td>
<td>27</td>
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<tr>
<td>7</td>
<td>Positive</td>
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<td>Positive</td>
<td>58</td>
<td></td>
<td></td>
</tr>
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<td>Positive</td>
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<td>Positive</td>
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<td>13</td>
<td>Positive for Cannabinoids</td>
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<td>delta 9-THC-COOH</td>
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<tr>
<td>21</td>
<td>Positive</td>
<td>138</td>
<td></td>
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</tbody>
</table>
Table 5

*Blood plasma levels of MDMA after three hours*

<table>
<thead>
<tr>
<th>Participant No.</th>
<th>Screening Result</th>
<th>GC/MS MDMA ug/L</th>
<th>Additonal Drug detected</th>
<th>ug/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Positive</td>
<td>154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Positive</td>
<td>183</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Positive for opiates</td>
<td>157</td>
<td>codine</td>
<td>44</td>
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<td>4</td>
<td>Positive</td>
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<td>Positive</td>
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<tr>
<td>8</td>
<td>Positive</td>
<td>176</td>
<td></td>
<td></td>
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<tr>
<td>9</td>
<td>No Sample</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Positive</td>
<td>220</td>
<td>delta 9-THC-COOH</td>
<td>9</td>
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<tr>
<td>20</td>
<td>Positive</td>
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<td></td>
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</tr>
</tbody>
</table>
Scatter-plots of difference scores for all variables and covariates in the alcohol comparison

*IAPS Task valence and arousal ratings*

**Figure 1.** Difference scores for IAPS valence for threat pictures and estimated IQ for males and females.

**Figure 2.** Difference scores for IAPS valence for threat pictures and anxiety sensitivity for males and females.
Figure 3. Difference scores for IAPS arousal for threat pictures and estimated IQ for males and females.

Figure 4. Difference scores for IAPS arousal for threat pictures and anxiety sensitivity for males and females.
**IAPS Task Recognition test**

**Figure 5.** Difference scores for recognition accuracy for threat pictures and estimated IQ for males and females.

**Figure 6.** Difference scores for recognition accuracy for threat pictures and anxiety sensitivity for males and females.
Figure 7. Difference scores for recognition confidence for threat pictures and estimated IQ for males and females.

Figure 8. Difference scores for recognition confidence for threat pictures and anxiety sensitivity for males and females.
**LDT Short-term recall**

*Figure 9.* Difference scores for short-term recall of threat words and estimated IQ for males and females.

*Figure 10.* Difference scores for short-term recall for threat words and anxiety sensitivity for males and females.
Figure 11. Difference scores for short-term recall in the first epoch for threat words and estimated IQ for males and females.

Figure 12. Difference scores for short-term recall in the first epoch for threat words and anxiety sensitivity for males and females.
Figure 13. Difference scores for short-term recall in the second epoch for threat words and estimated IQ for males and females.

Figure 14. Difference scores for short-term recall in the second epoch for threat words and anxiety sensitivity for males and females.
**LDT Long-term recall**

![Graph](image)

**Figure 13.** Difference scores for long-term recall of threat words and estimated IQ for males and females.

![Graph](image)

**Figure 14.** Difference scores for long-term recall for threat words and anxiety sensitivity for males and females.
**LDT Reaction time**

*Figure 15.* Difference scores for reaction times to threat words and estimated IQ for males and females.

*Figure 16.* Difference scores for reaction times to threat words and anxiety sensitivity scores for males and females.
Scatter-plots of Difference scores for all variables and covariates in the Methamphetamine comparison

IAPS Task valence and arousal ratings

**Figure 1.** Difference scores for IAPS valence for threat pictures and estimated IQ.

**Figure 2.** Difference scores for IAPS valence for threat pictures and anxiety sensitivity.
Figure 3. Difference scores for IAPS valence for threat pictures and blood levels of Methamphetamine.

Figure 4. Difference scores for IAPS arousal for threat pictures and estimated IQ.
Figure 5. Difference scores for IAPS arousal for threat pictures and anxiety sensitivity.

Figure 6. Difference scores for IAPS arousal for threat pictures and blood levels of Methamphetamine.
IAPS Task Recognition test

Figure 7. Difference scores for recognition accuracy for threat pictures and estimated IQ.

Figure 8. Difference scores for recognition accuracy for threat pictures and anxiety sensitivity.
Figure 9. Difference scores for recognition accuracy for threat pictures and blood levels of Methamphetamine.

Figure 10. Difference scores for recognition confidence for threat pictures and estimated IQ.
Figure 11. Difference scores for recognition confidence for threat pictures and anxiety sensitivity.

Figure 12. Difference scores for recognition confidence for threat pictures and blood levels of Methamphetamine.
LDT Short-term recall

Figure 13. Difference scores for short-term recall of threat words and estimated IQ.

Figure 14. Difference scores for short-term recall for threat words and anxiety sensitivity.
Figure 15. Difference scores for short-term recall for threat words and blood levels of Methamphetamine.

Figure 16. Difference scores for short-term recall in the first epoch for threat words and estimated IQ.
Figure 17. Difference scores for short-term recall in the first epoch for threat words and anxiety sensitivity.

Figure 18. Difference scores for short-term recall in the first epoch for threat words and blood levels of methamphetamine.
Figure 19. Difference scores for short-term recall in the second epoch for threat words and estimated IQ.

Figure 20. Difference scores for short-term recall in the second epoch for threat words and anxiety sensitivity
Figure 21. Difference scores for short-term recall in the second epoch for threat words and blood levels of methamphetamine.

LDT Long-term recall

Figure 22. Difference scores for long-term recall of threat words and estimated IQ.
Figure 23. Difference scores for long-term recall for threat words and anxiety sensitivity.

Figure 24. Difference scores for long-term recall for threat words and blood levels of methamphetamine.
**LDT Reaction time**

![Graph](image)

**Figure 25.** Difference scores for reaction times to threat words and estimated IQ.

![Graph](image)

**Figure 26.** Difference scores for reaction times to threat words and anxiety sensitivity scores.
Figure 27. Difference scores for reaction times to threat words and blood levels of methamphetamine.

Scatter-plots of difference scores for all variables and covariates in the MDMA comparison

IAPS Task valence and arousal ratings

Figure 1. Difference scores for IAPS valence for threat pictures and estimated IQ.
Figure 2. Difference scores for IAPS valence for threat pictures and anxiety sensitivity.

Figure 3. Difference scores for IAPS valence for threat pictures and blood levels of MDMA.
Figure 4. Difference scores for IAPS arousal for threat pictures and estimated IQ.

Figure 5. Difference scores for IAPS arousal for threat pictures and anxiety sensitivity.
Figure 6. Difference scores for IAPS arousal for threat pictures and blood levels of MDMA.

IAPS Task Recognition test

Figure 7. Difference scores for recognition accuracy for threat pictures and estimated IQ.
Figure 8. Difference scores for recognition accuracy for threat pictures and anxiety sensitivity.

Figure 9. Difference scores for recognition accuracy for threat pictures and blood levels of MDMA.
Figure 10. Difference scores for recognition confidence for threat pictures and estimated IQ.

Figure 11. Difference scores for recognition confidence for threat pictures and anxiety sensitivity.
Figure 12. Difference scores for recognition confidence for threat pictures and blood levels of MDMA.

LDT Short-term recall

Figure 13. Difference scores for short-term recall of threat words and estimated IQ.
Figure 14. Difference scores for short-term recall for threat words and anxiety sensitivity.

Figure 15. Difference scores for short-term recall for threat words and blood levels of MDMA.
Figure 16. Difference scores for short-term recall in the first epoch for threat words and estimated IQ.

Figure 17. Difference scores for short-term recall in the first epoch for threat words and anxiety sensitivity.
Figure 18. Difference scores for short-term recall in the first epoch for threat words and blood levels of MDMA.

Figure 19. Difference scores for short-term recall in the second epoch for threat words and estimated IQ.
Figure 20. Difference scores for short-term recall in the second epoch for threat words and anxiety sensitivity.

Figure 21. Difference scores for short-term recall in the second epoch for threat words and blood levels of MDMA.
LDT Long-term recall

Figure 22. Difference scores for long-term recall of threat words and estimated IQ.

Figure 23. Difference scores for long-term recall for threat words and anxiety sensitivity.
Figure 24. Difference scores for long-term recall for the threat words and blood levels of MDMA.

LDT Reaction time

Figure 25. Difference scores for reaction times to threat words and estimated IQ.
Figure 26. Difference scores for reaction times to threat words and anxiety sensitivity scores.

Figure 27. Difference scores for reaction times to threat words and blood levels of MDMA.