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The effect of cannabis use on prospective memory processes in young adults

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PhD

2011

The effect of cannabis use on prospective memory processes in young adults

Janice Bartholomew

A thesis submitted in partial fulfilment of the requirements of Northumbria University for the degree of Doctor of Philosophy.

This research project was carried out in the Department of Psychology, School of Life Sciences, Northumbria University.

November 2011

Abstract

Remembering to perform an intended task at the appropriate time (prospective memory) is an important aspect of memory functioning in the real world. Previous research has suggested that recreational drug use has a detrimental effect upon this ability. To date relatively few studies have investigated the effect of cannabis use on prospective memory performance. In addressing this hiatus, the present thesis extended this initial research to encompass three aims. Firstly, the thesis evaluated the psychometric properties of an objective prospective memory video procedure in order to mitigate criticisms associated with the use of self-report assessment of memory failures in many of these initial studies. Secondly, the thesis documents a series of quasi-experimental studies comparing cannabis users and non-users in order to examine the effect of cannabis use on prospective memory. Finally, the thesis explored the nature of the deficits observed in an attempt to better understand the neurobiological vulnerability of the cognitive processes underpinning prospective memory to the psychopharmacological effects of cannabis.

The findings across all of the studies documented suggested that cannabis use, even in relatively light users with short duration of use, has a detrimental effect on prospective memory in young adults. In addition, the findings presented suggested that the deficits observed in current cannabis users recover on cessation of cannabis use and that time-based prospective memory was more vulnerable to the effects of cannabis use than event-based prospective memory. Furthermore, the findings presented suggested that these deficits arise as a consequence of problems in retrieval of the intentions rather than problems in their encoding and that these

retrieval problems arise as a consequence of failures in cue identification rather than problems retrieving the task to be performed. The findings presented found no evidence that the prospective memory deficits observed were related to the number of joints smoked per week, duration of use, estimated lifetime consumption or to the age at which cannabis use commenced. Although the scale of the deficits appeared trivial with cannabis users recalling, on average, only two items fewer than non-users, the magnitude of the effect was moderate suggesting practical significance, particularly as the deficits were observed in independent cohorts comprising cannabis users with light use and relatively short duration of use.

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Author's Declaration

I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work.

Name: Janice Bartholomew

Signature:

Date:

Acknowledgements

I would like to express my sincere thanks to Steve Holroyd who has been a true friend and mentor. I will be forever indebted of his support and encouragement, of constructive feedback on draft versions of this thesis and manuscripts prepared for publication, and especially for allowing me access to his students in the recruitment of participants for my studies. Without his support this thesis would not have reached fruition. A mere thank you will never be enough.

I would also like to thank my supervisors Dr Tom Heffernan and Dr Colin Hamilton and to extend my thanks to Dr Lynn McInnes for her impartial advice.

Chapter 1
Introduction

1.1 History and prevalence of cannabis use

The hemp plant botanically classified by Linnaeus in 1735 as *Cannabis sativa* has a long history of use for industrial, medicinal and recreational purposes (Iversen, 2008). For example, clay pots decorated with strands of hemp fibre discovered by archaeologists in Taiwan date to circa 8000 B.C. (Earleywine, 2002) while the first use of cannabis for medicinal purposes was documented circa 2737 B.C. when the Chinese emperor Shen Neng advocated its use for a wide variety of ailments (Ben Amar, 2006; Earleywine, 2002; Parrott, Morinan, Moss and Scholey, 2004; Zuardi, 2006). Hemp fibres were used in the manufacture of rope circa 600 B.C. due to their strength and durability and were used in cloth from circa 450 B.C. and paper circa 1 A.D. until eventually being replaced by cotton and synthetic fibres and forestry-derived paper while more reliable synthetic medicines replaced cannabis preparations for medicinal purposes (Earleywine, 2002; Iversen, 2008; Zuardi, 2006). The first recreational use of cannabis is less clear although its use in shamanistic religious ceremonies by nomadic tribes of northeast Asia during the Neolithic period seems likely (Iversen, 2008).

Recreational use of cannabis became widespread reaching peak levels of use during the 1960s and 1970s (Parrott *et al*., 2004). In 1971 the United Kingdom government declared cannabis to be a drug of misuse, making its possession and use illegal. Under the original terms of the Act, cannabinol and its derivatives were classified as Class A drugs while cannabis and cannabis resin were classified as Class B drugs

(Misuse of Drugs Act, 1971). This classification has undergone several revisions in recent years. Initially, following advice from the Advisory Council on the Misuse of Drugs (2002), the classification was relaxed with all four products being reclassified as Class C drugs (Misuse of Drugs Act Amendment, 2003) making penalties for its possession and use less severe. Despite arguments from the Advisory Council on the Misuse of Drugs (2008), however, this decision was subsequently repealed by the Home Office and all four products were reclassified as Class B drugs (Misuse of Drugs Act Amendment, 2008).

Today, cannabis remains the most commonly used illicit recreational drug in the United Kingdom across all age groups and particularly among teenagers (16 to 19 years) and young adults (20 to 24 years) (MacLeod and Page, 2011; Smith and Flatley, 2011; Toner and Freel, 2010). For example, in a recent survey in England and Wales, 20% of teenage and 15% of young adult respondents declared use of cannabis within the twelve months preceding the survey (Smith and Flatley, 2011).

1.2 Cannabis Psychopharmacology

Cannabis has a complex chemical nature comprising 489 compounds of which 70 are cannabinoids specific to the plant *Cannabis sativa* (ElSohly and Slade, 2005). These cannabinoids are most highly concentrated in the leaves and flowers and in the resin secreted by the bracts of the female plant and are responsible for the psychoactive effects associated with cannabis use (Ameri, 1999; Ashton, 2001; Iversen, 2008). The principal psychoactive cannabinoid within this complex chemical cocktail is δ^9-tetrahydrocannabinol (Gaoni and Mechoulam, 1964) and the pharmacokinetics and pharmacodynamics of this cannabinoid are therefore subsequently described.

1.2.1 Pharmacokinetics

The amount of the unaltered drug entering the systemic circulation (bioavailability) differs depending on the route of administration. When smoke from cannabis is inhaled, it enters the lungs which are lined with alveolar sacs that increase the surface area of the lungs for gaseous exchange and have an extensive capillary network enabling δ^9-tetrahydrocannabinol to readily enter the bloodstream. By this route, depending on smoking practices in terms of depth and duration of inhalation and the level of experience of the user, 10-25% of unaltered δ^9-tetrahydrocannabinol enters the systemic circulation and peak plasma concentration is experienced within minutes (Benson and Bentley, 1995; Grotenhermen, 2003; Parrott *et al*., 2004). By comparison, when cannabis is administered orally within food and/or drinks, some δ^9-tetrahydrocannabinol is lost as a result of degradation by stomach acids and δ^9-tetrahydrocannabinol absorbed into the circulation from the gastrointestinal tract must first pass through the liver via the hepatic portal vein. In the liver, some of the δ^9-tetrahydrocannabinol is metabolised such that only 6% of the initial unaltered δ^9-tetrahydrocannabinol enters the systemic circulation and peak plasma concentrations are not experienced for 1-3 hours (Benson and Bentley, 1995; Grotenhermen, 2003; Parrott *et al*., 2004).

As δ^9-tetrahydrocannabinol is highly lipid-soluble and readily accumulates in various adipose (fatty) tissues throughout the body (Ashton, 2001; Iversen, 2008; Parrott *et al*., 2004), plasma concentrations of δ^9-tetrahydrocannabinol rapidly decline. Any remaining plasma δ^9-tetrahydrocannabinol undergoes metabolism in the liver. Metabolism of δ^9-tetrahydrocannabinol leads to the production of the psychoactive metabolite 11-hydroxy-tetrahydrocannabinol which contributes to the effects of δ^9-

tetrahydrocannabinol. As δ^9-tetrahydrocannabinol and its metabolites are eliminated from the body in urine and faeces, however, the δ^9-tetrahydrocannabinol stored in adipose tissues leaks back into the bloodstream to be eliminated (Ashton, 2001; Iversen, 2008; Parrott *et al*., 2004). Consequently, although the plasma elimination half-life is as little as 28 hours for chronic users and 56 hours for occasional users (Parrott *et al*., 2004), tissue elimination half-life is more prolonged and can take approximately 7 days (Ashton, 2001; Parrott *et al*., 2004), while total elimination of δ^9-tetrahydrocannabinol and its metabolites may take up to 30 days (Ashton, 2001; Iversen, 2008; Parrott *et al*., 2004).

1.2.2 Pharmacodynamics

The effects of cannabis are mediated through specific cannabinoid receptors. These receptors are broadly classified into two types, the CB_1 receptors which are found predominantly within the central nervous system (CNS) (Gérard, Mollereau, Vassart and Parmentier, 1990; Matsuda, Lolait, Brownstein, Young and Bonner, 1990) and the CB_2 receptors which are found predominantly within tissues of the immune system (Munro, Thomas and Abu-Shaar, 1993). Although endogenous ligands (endocannabinoids) which naturally interact with these receptors have been identified (Ameri, 1999; Ashton, 2001; Grotenhermen, 2003; Iversen, 2008; Parrott *et al*., 2004), the focus of the present thesis relates to the psychoactive effects of exogenous cannabinoids (phytocannabinoids) administered via preparations derived from the plant *Cannabis sativa* and mediated primarily through the binding of δ^9-tetrahydrocannabinol to the CB_1 receptors within the central nervous system. The present thesis will, therefore, focus on the pharmacodynamics of this interaction.

The CB_1 receptors are distributed throughout the central nervous system though their density in different regions varies greatly with highest concentrations being found in the basal ganglia, cerebellum, hippocampus and cerebral cortex (Egertová and Elphick, 2000; Glass, Dragunow and Faull, 1997; Herkenham, Lynn, Johnson, Melvin, De Costa and Rice, 1991; Herkenham, Lynn, Little, Johnson, Melvin, De Costa and Rice, 1990). Furthermore, the CB_1 receptors are predominantly localised on pre-synaptic axon terminals suggesting that cannabinoids play a role in the modulation of neurotransmitter release (Ameri, 1999; Egertová and Elphick, 2000; Elphick and Egertová, 2001; Katona, Sperlágh, Maglóczky, Sántha, Köfalvi, Czirják, Mackie, Vizi and Freund, 2000).

Binding of δ^9-tetrahydrocannabinol to the CB_1 cannabinoid receptors initiates several responses. The first of these is to inhibit the activity of the enzyme adenylate cyclase (Howlett and Fleming, 1984) resulting in the decreased production of the second messenger cyclic adenosine monophosphate (cAMP) (Ameri, 1999; Demuth and Molleman, 2006; Elphick and Egertová, 2001) thereby disrupting neurotransmitter release through a reduction in A-type potassium channel phosphorylation by protein kinase A (Demuth and Molleman, 2006; Elphick and Egertová, 2001). Secondly, activation of CB_1 receptors inhibits N-type (Mackie and Hille, 1992) and Q-type (Mackie, Lai, Westenbroek and Mitchell, 1995) calcium channels and activates inwardly rectifying potassium channels (Mackie *et al*., 1995) thereby reducing the flow of calcium ions and stimulating the flow of potassium ions into the synaptic bouton. This leads to neuronal hyperpolarisation and inhibition of neurotransmitter release into the synapse (Demuth and Molleman, 2006; Parrott *et al*., 2004). The diverse localisation of the CB_1 cannabinoid receptors within the central nervous

system means that a wide array of neurotransmitter systems are potentially disrupted by the use of cannabis, including those of the neurotransmitters acetylcholine, norepinephrine, dopamine, 5-hydroxytryptamine (serotonin), γ-aminobutyric acid (GABA), glutamate, D-aspartate and cholecystokinin (Egerton, Allison, Brett and Pratt, 2006; Pertwee, 2008; Pertwee and Ross, 2002). Consequently, cannabis use disrupts a wide array of physiological and psychological behavioural systems.

1.3 Physiological and psychological effects of cannabis use

As described previously, cannabis has a long history of use for medicinal purposes (Iversen, 2008) and its use was advocated for a wide variety of ailments (Ben Amar, 2006; Earleywine, 2002; Parrott *et al*., 2004; Zuardi, 2006) before its use declined during the early 20th century following the advent of more reliable medicines and legal restrictions which limited its use (Iversen, 2008; Zuardi, 2006). Interest in the therapeutic use of cannabis continued, however, and research from clinical trials has extolled the efficacy of cannabis across a range of conditions. For example, in a review of clinical trials, Ben Amar (2006) found cannabinoids to be effective both as an antiemetic in the treatment of nausea and vomiting associated with chemotherapy and as an appetite stimulant in combating loss of appetite and associated progressive weight loss during the advanced stages of cancer and cachexia (wasting syndrome) associated with Acquired Immune Deficiency Syndrome (AIDS). Ben Amar's review also noted the promising beneficial effect of cannabinoids in reducing spasticity and muscle spasms associated with multiple sclerosis (MS) and spinal cord injuries, reducing motor and verbal tics associated with Tourette's syndrome and as an anticonvulsant in the treatment of epilepsy. Despite the positive therapeutic potential of cannabis, however, concerns remain over the adverse effects associated

with its use which can be broadly categorised as either acute effects due to cannabis intoxication or as non-acute effects which persist beyond the initial period of intoxication.

1.3.1 Acute adverse effects of cannabis use

Acute cannabis intoxication is associated with feelings of euphoria and relaxation accompanied by perceptual distortions and a loosening of social inhibitions (Hall and Degenhardt, 2009). However, cannabis can also produce feelings of severe anxiety and can induce panic attacks, paranoia and psychosis (Ashton, 2001). Physiologically, cannabis intoxication increases heart rate (tachycardia) and supine blood pressure, and induces vasodilation and postural hypotension (Ashton, 2001; Jones, 2002; Sidney, 2002). While these effects pose no major problems for healthy users, individuals with underlying cardiovascular disease may be at increased risk of myocardial infarction (heart attack) and stroke (Ashton, 2001; Jones, 2002; Sidney, 2002). In addition, cannabis intoxication is associated with impaired attention (Solowij and Pesa, 2010), learning (Solowij and Pesa, 2010), memory (Ranganathan and D'Souza, 2006; Solowij and Pesa, 2010), working memory and executive processing, including deficits in decision-making, risk-taking, inhibition and verbal fluency (Crean, Crane and Mason, 2011; Solowij and Pesa, 2010). Cannabis intoxication is also associated with deficits in speed of information processing, reaction time, perceptual-motor co-ordination and an increased risk of road traffic accidents if users drive while intoxicated (Ashton, 2001; Hall and Degenhardt, 2009; Kalant, 2004).

It is possible that the acute effects associated with cannabis intoxication are transient and recover once δ^9-tetrahydrocannabinol and its metabolites have been eliminated from the body. Of more significance are the non-acute effects that persist beyond the initial period of intoxication.

1.3.2 Non-acute adverse effects of cannabis use

Frequent, long-term (chronic) use of cannabis can lead to tolerance and dependence (Hall and Degenhardt, 2009). This can occur either as a consequence of a reduction in the number of cannabinoid receptors (down-regulation) or as a consequence of a reduction in the sensitivity of the receptors to the effects of δ^9-tetrahydrocannabinol (desensitisation) (Grotenhermen, 2003; Iversen, 2008; Martin, Sim-Selley and Selley, 2004; Villares, 2007).

The composition of smoke from cannabis joints is similar to that from tobacco (Tashkin, Baldwin, Sarafian, Dubinett and Roth, 2002). The smoke from cannabis joints, however, contains greater concentrations of the carcinogenic polycyclic aromatic hydrocarbons (PAHs) benzanthracene and benzopyrene (Ashton, 2001; Tashkin *et al*., 2002) and produces greater amounts of tar and higher concentrations of carboxyhaemoglobin than smoke from tobacco cigarettes (Wu, Tashkin, Djahed and Rose, 1988). Consequently long-term, frequent cannabis use is associated with an increased incidence of respiratory disorders such as bronchitis (Ashton, 2001; Kalant, 2004; Tashkin *et al*., 2002) and emphysema (Ashton, 2001), and is further associated with increased risk of lung cancer (Aldington, Harwood, Cox, Weatherall, Beckert, Hansell, Pritchard, Robinson and Beasley, 2008). Furthermore, increased levels of carboxyhaemoglobin as a consequence of carbon monoxide inhalation are

associated with the development of atherosclerosis, a major contributory factor in the aetiology of coronary heart disease (Astrup, 1973).

Cannabis use is associated with an increased risk of schizophrenia (Arseneault, Cannon, Witton and Murray, 2004; Degenhardt, Tennant, Gilmour, Schofield, Nash, Hall and McKay, 2007; Hall and Degenhardt, 2008; Kalant, 2004; Moore, Zammit, Lingford-Hughes, Barnes, Jones, Burke and Lewis, 2007), anxiety (Crippa, Zuardi, Martín-Santos, Bhattacharyya, Atakan, McGuire and Fusar-Poli, 2009; Kalant, 2004; Moore *et al*., 2007) and depression (Degenhardt, Hall and Lynskey, 2003; Kalant, 2004; Moore *et al*., 2007; van Laar, van Dorsselaer, Monshouwer and de Graaf, 2007). Although establishing causality remains elusive, some studies have suggested that the temporal dynamics are such that cannabis use predicts an increase in psychotic symptoms (Degenhardt *et al*., 2007) and depression (van Laar *et al*., 2007) but that symptoms of psychosis and depression do not predict cannabis use (Degenhardt *et al*., 2007).

Long-term, frequent use of cannabis is associated with a range of cognitive impairments including deficits in attention (Jacobsen, Mencl, Westerveld and Pugh, 2004; Medina, Hanson, Schweinsburg, Cohen-Zion, Nagel and Tapert, 2007; Messinis, Kyprianidou, Malefaki and Papathanasopoulos, 2006; Solowij, Stephens, Roffman, Babor, Kadden, Miller, Christiansen, McRee and Vendetti, 2002), learning (Croft, Mackay, Mills and Gruzelier, 2001; Grant, Gonzalez, Carey, Natarajan and Wolfson, 2003; Harvey, Sellman, Porter and Frampton, 2007; Nestor, Roberts, Garavan and Hester, 2008), and executive functioning, including deficits in decision-making (Bolla, Eldreth, Matochik and Cadet, 2005; Whitlow, Liguori, Livengood,

Hart, Mussat-Whitlow, Lamborn, Laurienti and Porrino, 2004), inhibition (Battisti, Roodenrys, Johnstone, Pesa, Hermens and Solowij, 2010; Bolla, Brown, Eldreth, Tate and Cadet, 2002; Solowij *et al*., 2002), problem solving (Bolla *et al*., 2002), planning (Medina *et al*., 2007) and verbal fluency (Croft *et al*., 2001; McHale and Hunt, 2008; Messinis *et al*., 2006). Deficits in speed of information processing (Fried, Watkinson and Gray, 2005; Kelleher, Stough, Sergejew and Rolfe, 2004; Wadsworth, Moss, Simpson and Smith, 2006), manual dexterity (Bolla *et al*., 2002; Croft *et al*., 2001) and psychomotor speed (Bolla *et al*., 2002; Medina *et al*., 2007; Messinis *et al*., 2006) associated with frequent, long-term use of cannabis also persist beyond the initial period of acute intoxication. Furthermore, while some studies have shown cannabis users to have lower intelligence quotient than non-users (Fried *et al*., 2005; Messinis *et al*., 2006) other studies have found no significant differences (Bolla *et al*., 2005; Croft *et al*., 2001; Fisk and Montgomery, 2008; Solowij *et al*., 2002).

The most consistently reported deficits among users, however, relate to memory performance (Bolla *et al*., 2002; Croft *et al*., 2001; Grant *et al*., 2003; McHale and Hunt, 2008; Medina *et al*., 2007; Messinis *et al*., 2006; Nestor *et al*., 2008; Rodgers, 2000; Solowij and Battisti, 2008; Solowij and Pesa, 2010; Solowij *et al*., 2002). One area that has so far been relatively neglected in terms of research, however, relates to memory functioning within an everyday context, an important aspect of which is prospective memory.

1.4 Prospective Memory

1.4.1 Definition and classification of prospective memory

Prospective memory is an important aspect of memory functioning in the real world which describes the process of remembering to carry out an intended task at an appropriate time at some point in the future (McDaniel and Einstein, 2007), for example, remembering to meet a friend or colleague, remembering to post a letter on your way home or remembering to take medication. The successful realisation of such intentions is characterised by distinct phases (Ellis, 1996; Ellis and Freeman, 2008; Kliegel, MacKinlay and Jäger, 2008) during which the intention is successfully formed and encoded, then retained over a period of time during which the individual continues with their activities, and is finally executed when the appropriate retrieval context (*when*) is recognised (cue identification) and the intended task (*what*) is recalled (intention retrieval). The retrieval context that triggers execution of the intention can be the occurrence of a specific event (event-based), for example, passing a post box triggers the intention to post a letter, the elapse of a specific period of time (time-based), for example, intending to meet a friend at 7pm or to take a cake out of the oven in 15 minutes, or the completion of an activity (activity-based), for example, finishing a meal triggers the intention to take medication after eating (McDaniel and Einstein, 2007).

As described previously, cannabinoid receptors are widely distributed throughout the central nervous system (Egertová and Elphick, 2000; Glass *et al*., 1997; Herkenham *et al*., 1990, 1991). It is conceivable, therefore, that the neurobiological correlates of prospective memory may be susceptible to the psychopharmacological effects of

cannabis. It is necessary, therefore, to appreciate the neurobiological underpinnings of prospective memory.

1.4.2 The neurobiology of prospective memory

Initial speculation for the involvement of the frontal lobes in prospective memory is derived from case studies of patients with lesions. For example Shallice and Burgess (1991) presented evidence from three patients with damage to the frontal lobes in which the errors made were analogous to prospective memory failure. Specifically, the patients typically forgot tasks they had to do and frequently had to return to shops to buy items they had forgotten to buy on their first visit. More recently, research has noted that patients with lesions of the prefrontal cortex show impaired performance in event-based, but not time-based, prospective memory tasks (Cheng, Wang, Xi, Niu and Fu, 2008) while patients with lesions of the thalamus show impairments in time-based, but not event-based prospective memory tasks (Cheng, Tian, Hu, Wang and Wang, 2010).

Recent studies have employed functional neuroimaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) to examine haemodynamic changes in order to determine those regions of the brain activated during the execution of a prospective memory task. Such studies have led to a general consensus that prospective memory is mediated by brain structures within the anterior (rostral) prefrontal cortex known as Brodmann area 10.

For example, in the first study to employ neuroimaging techniques Okuda, Fujii, Yamadori, Kawashima, Tsukiura, Fukatsu, Suzuki, Ito and Fukuda (1998) employed

positron emission tomography to examine changes in regional cerebral blood flow. In this study they noted that the execution of a prospective memory task was associated with increased blood flow in the right dorsolateral prefrontal cortex (Brodmann areas 8 and 9), right ventrolateral prefrontal cortex (Brodmann area 47), left frontal pole (Brodmann area 10), left anterior cingulate gyrus (Brodmann area 24), left parahippocampal gyrus (Brodmann area 28) and the midline medial frontal lobe (Brodmann area 8).

Research by Burgess, Quayle and Frith (2001) also employed positron emission tomography to examine changes in regional cerebral blood flow, this time under two different prospective memory conditions. In the first condition there was an expectation of a target cue which did not subsequently appear while in the second condition the target cue did appear. Relative to a baseline measure, increased blood flow was observed bilaterally in the frontal pole (Brodmann area 10), in the right dorsolateral prefrontal cortex (Brodmann areas 45 and 46), in the right inferior parietal cortex (Brodmann areas 7, 19, 39 and 40) and in the precuneus with decreased blood flow in the left fronto-temporal region (Brodmann areas 38 and 47 and insula) when prospective memory stimuli were expected suggesting that these regions were associated with the maintenance of an intention. When a prospective memory stimulus occurred and was acted upon increased blood flow was observed in the thalamus with decreased blood flow in the right dorsolateral prefrontal cortex suggesting that these regions were associated with the realisation of an intention.

In subsequent research, Burgess, Scott and Frith (2003) manipulated the complexity of the on-going task and the prospective memory task in order to examine whether

the observed haemodynamic changes were simply a function of increased difficulty of the prospective memory tasks relative to the baseline on-going task. Burgess *et al*. found no evidence of task difficulty as a potential explanation for the previously observed pattern of haemodynamic changes since reduced regional cerebral blood flow was observed during more effortful tasks than during less effortful tasks. Of particular interest, however, was the observation that during the prospective memory conditions decreased blood flow was observed in the left superior medial regions of the anterior (rostral) prefrontal cortex (Brodmann area 10) which was accompanied by an associated increase in blood flow in more lateral regions and in the right dorso-medial thalamus. Burgess *et al*. therefore postulated that the anterior prefrontal cortex was involved in the switching of attention between external stimuli and the internal cognitive representations of the intention. Specifically, Burgess *et al*. proposed that the medial regions of the anterior prefrontal cortex were involved in suppressing internally generated thought and directing attention towards external stimuli while lateral regions were involved in maintaining it.

A subsequent study utilising functional magnetic resonance imaging to explore brain activity while performing tasks that alternated between phases that relied on attention directed towards external stimuli (stimulus-oriented thoughts) and phases that relied on cognitions that were not directed towards external stimuli (stimulus-independent thoughts) also noted differential activation of medial and lateral regions of the anterior prefrontal cortex. In this study, Gilbert, Frith and Burgess (2005) observed sustained activation of medial regions during the stimulus-oriented phases and transient activation of right lateral regions when attention was switched between

stimulus-oriented and stimulus-independent phases regardless of the direction of the switch.

As described above, the successful realisation of intentions is characterised by two distinct processes involving the recognition of the appropriate retrieval context (cue identification) and the retrieval of the intended task (intention retrieval) sometimes referred to as the prospective and retrospective components respectively (Ellis, 1996; Ellis and Freeman, 2008; Kliegel *et al*., 2008). The neurobiology associated with these different aspects of prospective memory was explored by Simons, Schölvinck, Gilbert, Frith and Burgess (2006) who employed functional magnetic resonance imaging to examine the pattern of haemodynamic changes associated with the identification of the cue and the subsequent retrieval of the intention. In addition to the consistent pattern of lateral activation and medial deactivation in the anterior prefrontal cortex (Brodmann area 10) across both cue identification and intention retrieval, Simons *et al*. noted greater activation bilaterally in a less lateral region of the anterior prefrontal cortex and in the posterior cingulate cortex and precuneus during intention retrieval and greater activation of the medial anterior prefrontal cortex (Brodmann area 10) and the anterior cingulate cortex (Brodmann area 32/11 and 25) during cue identification.

More recently, Okuda, Fujii, Ohtake, Tsukiura, Yamadori, Frith and Burgess (2007) employed positron emission tomography and focused on the anterior prefrontal cortex as their region of interest to explore the specific pattern of haemodynamic changes associated with event-based and time-based prospective memory retrieval contexts. During execution of the time-based prospective memory task increased

blood flow was observed in the anterior medial frontal lobe (Brodmann area 10), anterior cingulate gyrus (Brodmann area 32/10) and right superior frontal gyrus (Brodmann area 9/10). In comparison, execution of the event-based prospective memory task was accompanied by activation in the lateral left superior gyrus (Brodmann area 10) and deactivation bilaterally in the medial frontal lobe and anterior cingulate cortex.

Evidence from electrophysiological studies examining event-related potentials have identified greater negativity over the frontal polar region associated with intention formation, N300 negativity over the occipital-parietal region associated with the detection of prospective memory cues, a late positivity complex associated with retrieval of the intention from memory, and a frontal slow wave reflecting disengagement from the on-going activity when the cue was detected (West and Ross-Munroe, 2002). Furthermore, utilising magnetoencephalography (MEG) to assess the localisation of brain activity during the execution of prospective memory, Martin, McDaniel, Guynn, Houck, Woodruff, Bish, Moses, Kičić and Tesche (2007) noted activation in the posterior parietal cortex during the prospective memory task that was associated with the initial noticing of the target cue and activation in the hippocampal formation during both the prospective and the retrospective memory tasks associated with a memory search for the intended action to be performed. In addition, Martin *et al*. noted activation in the frontal lobes across all conditions.

To summarise, evidence from studies of patients with lesions (Cheng *et al*., 2008; Shallice and Burgess, 1991), neuroimaging (Burgess *et al*., 2001, 2003; Gilbert *et al*., 2005; Okuda *et al*., 1998, 2007; Simons *et al*., 2006) and electrophysiological

studies of event-related potentials (Martin *et al*., 2007; West and Ross-Munroe, 2002) point to the execution of prospective memory being mediated by structures within the anterior prefrontal cortex and hippocampal formation. Understanding the susceptibility of these structures to the psychopharmacological effects of cannabis is important in understanding the potential effects of cannabis use on prospective memory.

1.4.3 Neurobiological vulnerability of the prefrontal cortex and hippocampus to the psychopharmacological effects of cannabis

As described previously, cannabinoid receptors are known to be widely distributed throughout the central nervous system with highest concentrations being found in the cerebral cortex and hippocampus (Egertová and Elphick, 2000; Glass *et al*., 1997; Herkenham *et al*., 1990, 1991), including the prefrontal cortices and hippocampal formation implicated in the execution of prospective memory (Burgess *et al*., 2001, 2003; Cheng *et al*., 2008; Gilbert *et al*., 2005; Martin *et al*., 2007; Okuda *et al*., 1998, 2007; Shallice and Burgess, 1991; Simons *et al*., 2006; West and Ross-Munroe, 2002). It seems reasonable to assume, therefore, that these regions will be particularly susceptible to any neurotoxicity associated with cannabis use.

Indeed, evidence from studies utilising structural magnetic resonance imaging (MRI) have suggested that frequent, heavy cannabis use is associated with structural abnormalities. For example, compared to non-users, cannabis users have been shown to exhibit altered tissue density in both white and gray matter, specifically in hippocampal regions (Demirakca, Sartorius, Ende, Meyer, Welzel, Skopp, Mann and Hermann, 2011; Matochik, Eldreth, Cadet and Bolla, 2005). This reduced tissue

volume may be associated with neuronal apoptosis (Chan, Hinds, Impey and Storm, 1998) and is associated with increasing duration of cannabis use (Yücel, Lubman, Velakoulis, Wong, Wood, Condello, Brewer and Pantelis, 2006; Yücel, Solowij, Respondek, Whittle, Fornito, Pantelis and Lubman, 2008). In addition, research has suggested that commencement of cannabis use before the age of 17 years while brain maturation is on-going is associated with reductions in cortical gray matter volume and increases in white matter volume (Wilson, Mathew, Turkington, Hawk, Coleman and Provenzale, 2000). It must be noted, however, that other studies have found no evidence of alterations to tissue volume (Block, O'Leary, Ehrhardt, Augustinack, Ghoneim, Arndt and Hall, 2000; Jager, Van Hell, De Win, Kahn, Van Den Brink, Van Ree and Ramsey, 2007).

In addition, neuroimaging techniques have provided evidence of altered regional cerebral blood flow in the prefrontal cortices and hippocampal regions in cannabis users compared to non-users. For example, Lundqvist, Jönsson and Warkentin (2001) noted decreased blood flow in the right prefrontal, right superior frontal and right central regions using ^{133}Xe-inhalation. Using magnetic resonance imaging, however, Sneider, Pope, Silveri, Simpson, Gruber and Yurgelun-Todd (2006, 2008) noted increased rather than decreased blood volume in the right frontal, left temporal and cerebellum. Other studies which have employed positron emission tomography and functional magnetic resonance imaging techniques to examine regional blood flow during cognitive task performance have also noted cannabis related alterations in blood flow even in the absence of task performance differences.

For example, functional magnetic resonance imaging to examine regional cerebral blood flow in cannabis users during an associative learning task has shown increased activation in the parahippocampal gyrus during the encoding phase (Becker, Wagner, Gouzoulis-Mayfrank, Spuentrup and Daumann, 2010; Nestor *et al*., 2008) which is accompanied by reduced activation of the right superior temporal gyrus, bilateral superior frontal gyrus and right middle frontal gyrus (Nestor *et al*., 2008). Jager *et al*. (2007), however, noted decreased activation of parahippocampal regions and the right dorsolateral prefrontal cortex during learning and decreased anterior cingulate cortex activations during retrieval associated with cannabis use. Schweinsburg, Nagel, Schweinsburg, Park, Theilmann and Tapert (2008) noted decreased activation of the right dorsolateral prefrontal cortex and increased activation of the right posterior parietal cortex while Kanayama, Rogowska, Pope, Gruber and Yurgelun-Todd (2004) noted increased activation of the prefrontal cortex and anterior cingulate associated with spatial working memory tasks while decreased activation in the anterior cingulate cortex has been noted during Stroop task performance (Gruber and Yurgelun-Todd, 2005).

In addition, positron emission tomography has shown decreased cerebral blood flow in the dorsolateral, left medial and right ventral prefrontal cortices during verbal memory tasks (Block, O'Leary, Hichwa, Augustinack, Boles Ponto, Ghoneim, Arndt, Hurtig, Watkins, Hall, Nathan and Andreasen, 2002) while reduced activation of the anterior cingulate cortex and left dorsolateral prefrontal cortex and increased hippocampal activation has been observed during Stroop task performance (Eldreth, Matochik, Cadet and Bolla, 2004). Alterations to blood flow have also been noted during the Iowa Gambling task with observations of increased activation in the

cerebellum and decreased activation in the right dorsolateral prefrontal cortex (Bolla *et al*., 2005).

Although the evidence of altered patterns of metabolic activity has shown equivocal findings in terms of the regions of interest showing significant increases or decreases in activation there is compelling evidence that neural functioning, particularly within the prefrontal cortex and hippocampus may be susceptible to interference as a consequence of the psychopharmacological effects of cannabis use.

1.5 The effect of cannabis use on prospective memory

In recent years research has focused on the impact of recreational drug use on prospective memory. Such research has associated deficits in prospective memory with excessive use of alcohol both in adults (Heffernan, Ling and Bartholomew, 2004; Heffernan, Moss and Ling, 2002) and teenagers (Heffernan and Bartholomew, 2006), binge drinking in teenagers (Heffernan, Clark, Bartholomew, Ling and Stephens, 2010), acute alcohol intoxication (Leitz, Morgan, Bisby, Rendell and Curran, 2009; Paraskevaides, Morgan, Leitz, Bisby, Rendell and Curran, 2010), tobacco use (Heffernan, Ling, Parrott, Buchanan, Scholey and Rodgers, 2005; Heffernan, O'Neill and Moss, 2010), ecstasy use (Heffernan, Jarvis, Rodgers, Scholey and Ling, 2001; Heffernan, Ling and Scholey, 2001; Rendell, Gray, Henry and Tolan, 2007; Rodgers, Buchanan, Scholey, Heffernan, Ling and Parrott, 2003; Zakzanis, Young and Campbell, 2003), ecstasy/polydrug use (Hadjiefthyvoulou, Fisk, Montgomery and Bridges, 2011a, 2011b, 2011c) and methamphetamine use (Iudicello, Weber, Grant, Weinborn, Woods and the HIV Neurobehavioral Research Centre Group, 2011; Rendell, Mazur and Henry, 2009).

To date relatively few studies have investigated the effect of cannabis use on prospective memory performance. In the first published study Rodgers, Buchanan, Scholey, Heffernan, Ling and Parrott (2001) developed an on-line version of the Prospective Memory Questionnaire (PMQ; Hannon, Adams, Harrington, Fries-Dias and Gipson, 1995) to gauge the number of failures reported by participants across long-term episodic, short-term habitual and internally cued aspects of prospective memory. The utilisation of a web-based design to gather data provided access to a large number of participants with 488 participants completing the study, and thereby allowed the authors to employ regression analysis to ascertain the contribution made by cannabis use to reported deficits in prospective memory. The authors noted that cannabis use was associated with increased reports of failures in short-term habitual and internally cued, but not long-term episodic, aspects of prospective memory. This study, however, was not without methodological limitations. In particular, the study employed a self-report measure of prospective memory performance which may be prone to inaccuracies due to a failure of participants to accurately remember that they have forgotten to carry out an intended task. In addition, a subsequent report by Buchanan, Ali, Heffernan, Ling, Parrott, Rodgers and Scholey (2005) noted that the factorial structure of the on-line version of the Prospective Memory Questionnaire differed from that of the equivalent pencil and paper version. Specifically, those items contained within the scales measuring deficits in short-term habitual and internally cued aspects of prospective memory did not load onto discrete factors but instead appeared to be measuring more than one factor. This casts doubt on the integrity of the findings of Rodgers *et al*. who reported deficits only in these aspects.

A further limitation of this study was that Rodgers *et al*. (2001) did not control for the potential effect of anxiety and depression. This may be important because, as previously described, research has noted an association between cannabis use and symptoms of anxiety and depression (Crippa *et al*., 2009; Degenhardt *et al*., 2003; Kalant, 2004; Moore *et al*., 2007; van Laar, *et al*., 2007) and this has two important implications for the study by Rodgers *et al*. Firstly, research has suggested that both anxiety and depression affect prospective memory performance (Harris and Menzies, 1999; Kliegel and Jäger, 2006; Rude, Hertel, Jarrold, Covich and Hedlund, 1999). Secondly, self-reports may be particularly susceptible to the negative self-appraisals associated with anxiety and depression (Bedi and Redman, 2008; Cuttler and Graf, 2008, 2009; Rabbitt, Maylor, McInnes, Bent and Moore, 1995). Since the use of other recreational drugs, particularly use of alcohol and tobacco, have been found to affect prospective memory (Heffernan and Bartholomew, 2006; Heffernan *et al*., 2002, 2004, 2005; Heffernan, Clark *et al*., 2010; Heffernan, O'Neill and Moss, 2010; Leitz *et al*., 2009; Paraskevaides *et al*., 2010), a further criticism of this study is that Rodgers *et al*. did not control for use of these other recreational drugs.

More recently Montgomery and Fisk (2007) administered the traditional pencil and paper version of the Prospective Memory Questionnaire (Hannon *et al*., 1995) to gauge prospective memory failures in 28 ecstasy-polydrug users and 35 non-users. The authors noted that cannabis use was common among both the ecstasy-polydrug users and the non-users and utilised regression analysis to ascertain the contribution of both cannabis use and ecstasy use to reported deficits in prospective memory. The authors concluded that use of cannabis, but not ecstasy, was a significant predictor of reported deficits in long-term episodic, short-term habitual and

internally cued aspects of prospective memory. These findings were not entirely consistent with the earlier findings of Rodgers *et al*. (2001) who found cannabis use to be associated with deficits in short-term habitual and internally cued aspects of prospective memory and ecstasy use to be associated with deficits in long-term episodic aspects of prospective memory. As in the study by Rodgers *et al*., this study by Montgomery and Fisk can be criticised for its utilisation of a self-report measure of prospective memory performance and although Montgomery and Fisk controlled for use of alcohol by including it as a predictor, like Rodgers *et al*., they did not control for the potential effect of anxiety and depression which, as described above, may be important because of their association with cannabis use, with prospective memory, and with negative self-appraisal.

A further criticism of this study lies in its utilisation of regression analysis despite the relatively small sample size. According to Green (1991), as a rule-of-thumb, a minimum acceptable sample size of $50 + 8m$ (where m is the number of predictors) is required to test the overall fit of the regression model and a sample size of $104 + m$ is required to test the individual predictors, assuming a medium effect size between criterion and predictors. Employing these criteria, Montgomery and Fisk (2007) would require a minimum sample of 90 participants to test the fit of the model and a minimum of 109 participants to test the significance of individual predictors within the model. In addition to criticisms of the use of regression analysis with the small sample size, a further criticism of this study stems from the authors' interpretation of the regression models which for both long-term episodic and short-term habitual aspects of prospective memory were not significant. In other words the models proposed by Montgomery and Fisk did not significantly explain the deficits observed

thereby making predictions of the contribution of cannabis use to the deficits somewhat irrelevant (Howell, 2010).

Subsequent research by Fisk and Montgomery (2008) also employed the traditional pencil and paper version of the Prospective Memory Questionnaire (Hannon *et al*., 1995) to compare prospective memory failures in 27 cannabis users who had abstained for at least 24 hours prior to testing and did not use any other illicit recreational drugs with 20 non-users. On this occasion the authors employed multivariate analysis of covariance to determine any differences between cannabis users and non-users in terms of the number of prospective memory failures reported. After statistically controlling for alcohol consumption which differed significantly between cannabis users and non-users and fluid intelligence scores where the difference between users and non-users approached significance, the authors concluded that cannabis users reported significantly more failures in short-term habitual and internally cued, but not long-term episodic, aspects of prospective memory. This finding was consistent with those reported by Rodgers *et al*. (2001) who also found cannabis use to be associated with self-reported deficits in both short-term habitual and internally cued aspects of prospective memory but were not entirely consistent with those of Montgomery and Fisk (2007) who reported that cannabis use was also associated with reports of deficits in long-term episodic prospective memory. However, as argued previously, the interpretation of the regression analysis by Montgomery and Fisk was not appropriate due to the non-significant regression models for long-term episodic prospective memory. As in previous studies by Rodgers *et al*. and Montgomery and Fisk, this study by Fisk and Montgomery can be criticised for utilisation of a self-report measure of prospective

memory and failure to consider the potential effect of anxiety and depression which may have confounded the findings.

In the first published study to employ an objective measure of prospective memory performance McHale and Hunt (2008) employed the Belonging sub-test of the Rivermead Behavioural Memory Test (RBMT; Wilson, Cockburn and Baddeley, 1991) to assess event-based prospective memory and employed both short-interval and long-interval tasks to assess time-based prospective memory in 18 cannabis users who had abstained for at least 24 hours prior to testing, 20 tobacco users and 20 non-users. In the short-interval task participants pressed a timer 10 minutes after the instruction while the long-interval task required participants to post a stamped addressed envelope to the researchers two days after their participation. The authors found no significant differences between cannabis users, tobacco users and non-users in event-based prospective memory. In the time-based tasks, however, McHale and Hunt found that the delay between the expected and the actual execution of the short-interval task was significantly longer for cannabis users than for both tobacco users and non-users and significantly fewer of the cannabis users remembered to return the envelope to the researchers in the long-interval task. These findings corroborate those of Montgomery and Fisk (2007) who found that cannabis use was associated with self-reported deficits in long-term episodic and short-term habitual aspects of prospective memory. Neither Rodgers *et al*. (2001) or Fisk and Montgomery (2008) found cannabis use to be associated with self-reported deficits in long-term episodic prospective memory which contradicts the findings of McHale and Hunt. Rodgers *et al*. noted, however, that cannabis use correlated negatively with use of strategies to assist remembering. It is possible therefore, that in the long-interval task tobacco

users and non-users employed some strategy upon leaving the study, for example making a note in a diary, to assist their remembering which could explain their better performance in the task. The fact that it is impossible to know precisely what strategies participants may employ outside of the laboratory environment is an inherent disadvantage of the utilisation of naturalistic tasks to ascertain memory impairments and is a criticism of McHale and Hunt's study.

Unlike the previous studies which relied upon self-reports of prospective memory failures which may be prone to inaccuracies due to a failure of participants to remember that they have forgotten to carry out an intended task, this study by McHale and Hunt (2008) has the advantage of employing an objective measure of prospective memory. However, as in the studies by Fisk and Montgomery (2008), Montgomery and Fisk (2007) and Rodgers *et al*. (2001), the study by McHale and Hunt can be criticised as it did not control for the potential effect of anxiety and depression which may be important because of their association both with cannabis use and with prospective memory. Although McHale and Hunt included tobacco users as a comparison group, they did not control for the potential effect of alcohol and, since use of alcohol has been found to adversely affect prospective memory (Heffernan and Bartholomew, 2006; Heffernan *et al*., 2002, 2004; Heffernan, Clark *et al*., 2010; Leitz *et al*., 2009; Paraskevaides *et al*., 2010), McHale and Hunt can be further criticised for not controlling for the use of this recreational drug.

More recently, Hadjiefthyvoulou *et al*. have utilised a range of objective and self-report measures to assess prospective memory in ecstasy-polydrug users and non-users. In the first of their studies, Hadjiefthyvoulou *et al*. (2011a) assessed event-

based, mid- and long-term time-based, and self-reported prospective memory in 42 ecstasy-polydrug users and 31 non-users. In this study the authors administered the belonging, appointment and message tests of the Rivermead Behavioural Memory Test, although the version employed is unclear as the authors report in text that the second edition (RBMT-II; Wilson, Cockburn and Baddeley, 2003) was employed but the version referenced by the authors is the extended version (RBMT-E; Wilson, Clare, Baddeley, Cockburn, Watson and Tate, 1999). A laboratory-based paradigm in which prospective memory tasks had to be completed either in response to a message on the screen during a perceptual processing speed task or at specified times during the testing procedure and a naturalistic paradigm in which participants had to post test results to the researchers were also employed. In addition, the authors utilised both the Prospective Memory Questionnaire (Hannon *et al*., 1995) and the Prospective and Retrospective Memory Questionnaire (PRMQ; Crawford, Smith, Maylor, Della Sala and Logie, 2003). The authors noted that the deficits in ecstasy-polydrug users compared to non-users remained statistically significant after controlling for use of cannabis thereby suggesting that cannabis was not an important contributor to the deficits. This finding appeared to contradict previous findings which have noted deficits associated with cannabis use (Fisk and Montgomery, 2008; McHale and Hunt, 2008; Montgomery and Fisk, 2007; Rodgers *et al*., 2001). However, inspection of the relationships between different aspects of drug use and prospective memory revealed significant associations between both lifetime and frequency of cannabis use and prospective memory. Although the associations with lifetime use disappeared after controlling for other drug use, associations with frequency of use remained suggesting that cannabis use may play some role in the deficits observed.

In their second study, Hadjiefthyvoulou *et al*. (2011c) administered the Cambridge Prospective Memory Test (CAMPROMPT; Wilson, Emslie, Foley, Shiel, Watson, Hawkins, Groot and Evans, 2005) to assess event-based and time-based prospective memory in 29 ecstasy-polydrug users, 12 cannabis users and 18 non-users. The authors reported no significant differences between the cannabis users and the non-users in either event-based or time-based prospective memory. These findings corroborate those of McHale and Hunt (2008) in terms of event-based prospective memory but not in terms of time-based prospective memory. As Hadjiefthyvoulou *et al*. recruited only twelve cannabis users, however, it is possible that this study lacked sufficient power to detect significant differences, particularly if the effect was small. The findings of Hadjiefthyvoulou *et al*. (2011c) also appeared to contradict the previous findings of Fisk and Montgomery (2008), Montgomery and Fisk (2007) and Rodgers *et al*. (2001) which noted deficits associated with cannabis use. Again, however, inspection of the relationships between different aspects of drug use and prospective memory revealed that frequency of use was significantly associated with deficits in time-based prospective memory while frequency of use and consumption within the previous 30 days were significantly associated with deficits in event-based prospective memory. These findings thereby suggest that cannabis use is associated with deficits in prospective memory.

Finally, a recent study by Montgomery, Seddon, Fisk, Murphy and Jansari (in press) utilised a non-immersive virtual reality paradigm to assess prospective memory and executive functioning in 20 cannabis users who did not use any other illicit drugs and had abstained from use for a period of at least 5 days and 20 non-users. During the task, participants played the role of an office worker and performed routine tasks

associated with the role. Montgomery *et al*. found that planning and prospective memory in both event-based and time-based contexts were significantly poorer in cannabis users than in non-users and that these deficits were correlated with dose, frequency and duration of use and total use of cannabis. These findings corroborate the time-based deficits associated with cannabis use noted by McHale and Hunt (2008) and highlight the need to consider the cognitive processes underlying prospective memory. For example, as previously described, successful realisation of intended tasks is characterised by distinct phases (Ellis, 1996; Ellis and Freeman, 2008; Kliegel *et al*., 2008). These phases draw upon specific cognitive processes. For example, during the first phase the intention is successfully formed (planning) and the association between the retrieval context (*when*) and the intended task (*what*) encoded (associative learning) while the execution of the intention relies upon recognition of the appropriate retrieval context (attention/monitoring of the environment) and recall of the intended task (retrospective memory).

1.6 Rationale for thesis

Cannabis is the most commonly used illicit recreational drug in the United Kingdom among teenagers and young adults (MacLeod and Page, 2011; Smith and Flatley, 2011; Toner and Freel, 2010). In addition, first initiation to cannabis use among young adults typically occurs as young as 15 years (Hoare and Moon, 2010). This may be important because brain development occurs during adolescence and it is possible that those individuals who commence cannabis use during this critical period may be more vulnerable to the deleterious neurocognitive effects of cannabis. Of particular importance is the potential impact of cannabis use on cognition within everyday situations where any deficits may impact upon an individual's quality of

life by adversely affecting their ability to effectively plan and organise their daily activities or adhere to medical regimes. From the review of the literature exploring the effect of cannabis use on prospective memory outlined above there is a consensus that cannabis use has a detrimental impact upon an individual's ability to remember to perform such daily intentions. The findings of these studies, however, may be criticised on the basis of a number of potential methodological limitations.

The first of these criticisms stems from the utilisation of self-report measures of prospective memory within many of these studies. Such measures may be prone to inaccuracies for two reasons. In the first instance, asking individuals with memory problems to reflect on their memory failures creates a paradox which may lead these individuals to underestimate of the extent of their problems simply because they have failed to accurately remember that they have forgotten to carry out a task. Secondly, such measures have been heavily criticised as a consequence of their poor correlation with objective measures of ability (Bedi and Redman, 2008; Chan, Wang, Ma, Hong, Yuan, Yu, Li, Shum and Gong, 2008; Uttl and Kibreab, 2011).

A further criticism stems from the failure of these studies to control for symptoms of anxiety and depression. This may be important because previous research has noted an association between cannabis use and symptoms of anxiety and depression (Crippa *et al*., 2009; Degenhardt *et al*., 2003; Kalant, 2004; Moore *et al*., 2007; van Laar *et al*., 2007) and this has two important implications. Firstly, research has suggested that prospective memory is adversely affected by symptoms of anxiety and depression (Harris and Menzies, 1999; Kliegel and Jäger, 2006; Rude *et al*., 1999). Secondly, research has suggested that self-reports may be particularly

susceptible to negative self-appraisals associated with symptoms of anxiety and depression (Bedi and Redman, 2008; Cuttler and Graf, 2008, 2009; Rabbitt *et al*., 1995). Indeed, this may explain some of the inconsistencies these studies have encountered in their findings in relation to the specific aspects of prospective memory affected by cannabis use.

Since the use of other recreational drugs, in particular the use of alcohol and tobacco, have been reported to adversely impact upon prospective memory (Heffernan and Bartholomew, 2006; Heffernan *et al*., 2002, 2004, 2005; Heffernan, Clark *et al*., 2010; Heffernan, O'Neill and Moss, 2010; Leitz *et al*., 2009; Paraskevaides *et al*., 2010), a further criticism of many of these studies stems from their failure to control for use of these recreational drugs.

In the light of these methodological limitations the aim of the programme of research undertaken in this thesis was to evaluate an objective measure for the assessment of prospective memory and to employ this tool to examine the effect of cannabis use on prospective memory in order to mitigate the limitations associated with the utilisation of self-report measures. In examining the effect of cannabis use on prospective memory the present thesis aimed to further extend previous research by controlling for symptoms of anxiety and depression and the use of other recreational drugs which may adversely impact upon prospective memory.

Furthermore, the present thesis aimed to extend previous research to explore the nature of any deficits observed in terms of attempting to elucidate the underpinning neurobiological processes that might be particularly susceptible to the

psychopharmacological effects of cannabis use. Specifically, the present thesis explored whether deficits recovered on cessation of cannabis use, whether deficits were related to the dose and duration of cannabis use and whether the age of commencement of cannabis use affected prospective memory.

As the successful realisation of intended tasks is characterised by distinct phases (Ellis, 1996; Ellis and Freeman, 2008; Kliegel *et al*., 2008) which draw upon specific cognitive processes the present thesis also explored the underlying prospective memory processes that may be particularly susceptible to the psychopharmacological effects of cannabis. Specifically, the thesis examined whether prospective memory deficits were due to deficits associated with the initial encoding of the task and its associated cue or to deficits in the retrieval of the intention. The thesis further explored whether deficits occurred as a consequence of failures in the recognition of the appropriate retrieval context (*when*) or failure to recall the intended task (*what*). Finally, the present programme of research explored whether time-based or event-based retrieval contexts were more susceptible to the psychopharmacological effects of cannabis.

Chapter 2

Psychometric properties of a prospective memory video procedure

2.1 Rationale

As outlined in chapter one, previous studies investigating the effect of cannabis use on prospective memory (Fisk and Montgomery, 2008; Montgomery and Fisk, 2007; Rodgers *et al*., 2001) have predominantly utilised self-report measures of prospective memory, in particular the Prospective Memory Questionnaire (Hannon *et al*., 1995). The use of such self-report measures is not without its limitations, however. For example, such measures may be prone to inaccuracies for two reasons. Firstly, asking individuals with memory problems to reflect on their memory failures creates a paradox which may lead these individuals to underestimate of the extent of their problems simply because they have failed to remember that they have forgotten to carry out a task. Secondly, self-reports may be particularly susceptible to negative self-appraisals associated with anxiety and depression (Bedi and Redman, 2008; Rabbitt *et al*., 1995). Indeed, this may explain some of the inconsistencies such studies have encountered in their findings in relation to the specific aspects of prospective memory affected by cannabis use. In addition, such measures have been criticised as a consequence of their poor correlation with objective measures of ability (Bedi and Redman, 2008; Chan *et al*., 2008; Uttl and Kibreab, 2011).

In order to accurately reflect prospective memory ability it is important to employ more objective measures of performance. These can be divided into naturalistic tasks and laboratory tasks. Naturalistic tasks are those tasks which take place within the context of the individual's everyday life. For example, typical naturalistic tests

of prospective memory require participants to post a letter to the researcher on a specified date or to telephone the researcher at a specific time. Such paradigms lack the ability to control for confounding variables such as the use of strategies to assist remembering, for example making a note in a diary. This may subsequently lead to an underestimation of the extent of prospective memory deficits. Furthermore, tasks which rely on the execution of only one or two tasks may be too simplistic and may potentially allow non-clinical individuals with mild prospective memory deficits to attain maximal performance (ceiling effect). The use of laboratory tasks to infer performance in the real-world, however, has received criticism because of a lack of ecological validity (Chaytor and Schmitter-Edgecombe, 2003; Spooner and Pachana, 2006). For example, typical laboratory tests of prospective memory employ paradigms such as that developed by Einstein and McDaniel (1990) which require participants to press a particular key on a computer keyboard when a particular word or category of word, for example animals, appears on the screen during an on-going task such as a short-term memory task or a lexical decision task. Such tasks do not reflect salient real-world prospective memory tasks and therefore lack ecological validity.

Two commercially available laboratory tasks that have attempted to retain ecological validity are the Rivermead Behavioural Memory Test (Wilson *et al*., 1991) and the Cambridge Prospective Memory Test (Wilson *et al*., 2005). The Rivermead Behavioural Memory Test comprises twelve everyday memory tasks of which three are specific prospective memory tasks. These include the belonging test which requires participants to remember to ask for the return of a personal belonging, the appointment test which requires participants to ask the time of their next

appointment when an alarm sounds, and the message test which requires participants to remember to deliver a message envelope. However, the simplicity of the test as a consequence of the inclusion of only three tasks allows the possibility that non-clinical individuals with mild prospective memory deficits may attain maximal performance and this has led to criticism of the test as a consequence of its lack of sensitivity (Spooner and Pachana, 2006). Furthermore, Mills, Kixmiller, Gillespie, Allard, Flynn, Bowman and Brawn (1997) found no significant correlation between scores on the prospective memory tasks of the Rivermead Behavioural Memory Test and actual performance completing a number of assigned tasks thereby suggesting that the prospective memory tasks lacked validity. In comparison, the more recently developed Cambridge Prospective Memory Test comprises six tasks which measure prospective memory with three tasks specifically gauging time-based prospective memory where the task is performed at specified times and three tasks gauging event-based prospective memory where the task is performed in response to a particular event. Although comprising more tasks and providing a more sensitive scoring system than the Rivermead Behavioural Memory Test, this test also has the potential for non-clinical individuals with mild prospective memory deficits to perform at, or near, maximal capacity. This is because the test permits the use of strategies to assist remembering and therefore individuals who experience problems remembering may be more likely to use this opportunity to improve their performance, particularly in a situation where they know their ability is under scrutiny. Indeed, Hadjiefthyvoulou *et al*. (2011c) noted that scores achieved across the event-based prospective memory tasks were negatively skewed suggesting a lack of sensitivity as described by Spooner and Pachana (2006) in relation to the Rivermead Behavioural Memory Test.

Within the field of recreational drug use research these tests have the disadvantage that participants must be tested individually in a face-to-face situation and users of illicit drugs may be reluctant to participate under these circumstances. One measure which may help to alleviate this problem by allowing participants to be tested in small groups which provide a measure of anonymity to such participants is the Prospective Remembering Video Procedure (PRVP) described by Titov and Knight (2001). This procedure utilises a naturalistic task with a shopping scenario that simulates an individual walking through a busy shopping area with natural distractions in the form of fragments of conversations and street musicians as well as pedestrians going about their business. In examining convergent validity of their video procedure with performance in the real-world utilising an *in vivo* version of the same task, Titov and Knight (2000, 2001) found no significant differences between performance in the video procedure and performance in the *in vivo* task and scores on the two versions were strongly correlated suggesting that the Prospective Remembering Video Procedure was a reliable predictor of real-world prospective memory functioning.

Such a task was developed by Forster (2003) as part of her undergraduate thesis to assess prospective memory in dyslexics and this task has been utilised subsequently to assess prospective memory in patients with eating disorders (Seed, Dahabra, Heffernan, Robertson, Foster, Venn, Froom and Williams, 2004) and in teenagers who binge drink (Heffernan, Clark *et al*., 2010). The psychometric properties of this particular video procedure, however, have never been assessed. Before employing any psychological measure it is important to understand the reliability and validity of the measure and to establish normative data. With this goal in mind, the aim of the

present series of studies was to assess the psychometric properties of this prospective memory video procedure by examining both the internal consistency and factorial structure of the task and by gathering evidence of convergent validity against existing measures of prospective memory. The distribution of scores was also examined to ensure that the task was capable of discriminating between those individuals with good prospective memory and those with poor prospective memory and to ensure that the task was not too easy or too difficult.

2.2 Study 1: Reliability, factorial structure and item analysis

The aim of this first study was to evaluate the psychometric properties of a video procedure for the assessment of prospective memory by examining both the internal consistency and factorial structure of the task and examining the distribution of the scores attained to ensure that the task was capable of discriminating between those individuals with good prospective memory and those with poor prospective memory and to ensure that the task was not too easy or too difficult.

2.2.1 Methodology

2.2.1.1 Design

The study employed a correlation design to assess the internal consistency and the factorial structure of a prospective memory video procedure. The measures were the individual responses (correct/incorrect) for each of the location-action combinations comprising the prospective memory video procedure and the total number of correctly recalled location-action combinations.

2.2.1.2 Participants

An opportunity sample of 1057 undergraduates between the ages of 18 and 24 years studying at universities in the northeast of England completed the prospective memory video procedure. The sample comprised 399 males with a median age of 19 years and 658 females also with a median age of 19 years.

2.2.1.3 Measures

A prospective memory video procedure as described by Titov and Knight (2001) provided an objective measure of prospective memory performance. The task in the present study (adapted from Forster, 2003) involved the presentation of a list of seventeen intentions comprising specific locations, for example "at HMV", and associated actions that were either tasks to perform at that location, for example "at HMV buy a CD" or questions to be answered, for example "at the flower stall what colour is the stall's canopy?". A shopping simulation was then presented as a ten minute video depicting an unfamiliar shopping area and focusing on shop fronts and passers-by that provided location cues and distractions during which the previously presented intentions were recalled as a series of location-action combinations when the appropriate cue appeared on the video. For each intention, one point was awarded if the location-action combination was correctly recalled with no points if only one member of the combination was correctly identified, thus providing a score between zero and seventeen with higher scores indicating better prospective memory.

2.2.1.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. Participants were then informed that a list of locations and associated tasks to be performed at that location would be read out and that without writing anything down while the list was being read they were to try to remember as many of the intentions as they could. When the participants were happy to continue the list of locations and associated actions to be remembered (appendix A) was read aloud at a steady pace. The list was repeated and participants were reminded that the aim of the task was to recall the items at the appropriate time and therefore as they watched the video they were to record both the location and the associated action on the response sheet provided only when they reached the appropriate location cue on the video. After verifying that participants understood the task requirements, the video was played. On completion of the video procedure, participants were debriefed and thanked for their participation.

2.2.2 Results

2.2.2.1 Distribution of scores

A Kolmogorov-Smirnov test for normality indicated that scores on the prospective memory video procedure were not normally distributed [$D(1057) = 0.09$, $p < 0.001$]. Examination of the frequency distribution (Figure 2.1), however, suggested that the

distribution of scores was not severely skewed and confirmed that performance on the task was not subject to ceiling or floor effects.

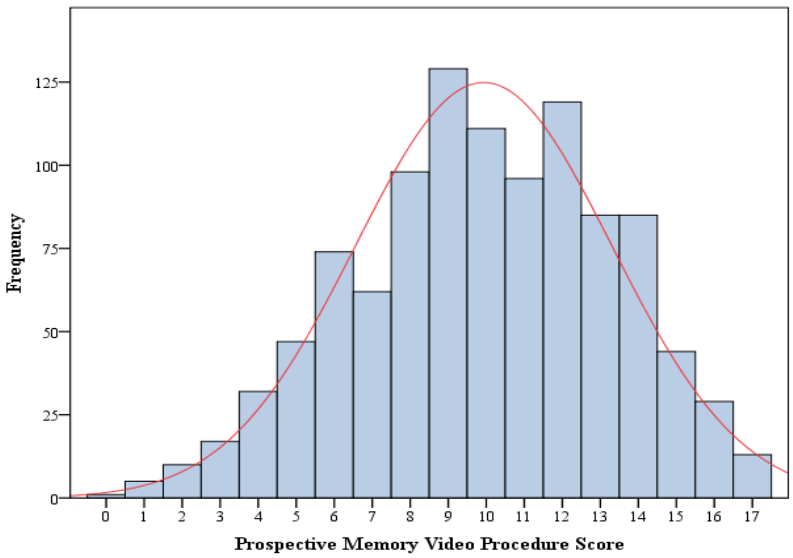

Figure 2.1. Distribution of scores on the prospective memory video procedure

2.2.2.2 Reliability and Factorial Structure

Cronbach's alpha suggested that the video procedure was sufficiently reliable with the seventeen items comprising the procedure showing an acceptable degree of internal consistency ($\alpha = 0.73$). Principal component analysis (PCA) was conducted on the seventeen items making up the video procedure to determine the factorial structure of the task. The suitability of the data was verified utilising Kaiser-Meyer-Olkin's (KMO) measure of sampling adequacy (KMO = 0.85) and Bartlett's test of sphericity indicated that correlations between items were appropriate for principal component analysis [χ^2 (136) = 1490.60, $p < 0.001$]. Four factors with eigenvalues greater than one were extracted which explained 38.16% of the variance within the data. According to Field (2009), however, Kaiser's recommendation to retain all factors with eigenvalues greater than one often overestimates the number of factors

present. Field goes on to argue that Kaiser's criterion is accurate with fewer than 30 items if all extraction communalities exceed 0.7 or with sample sizes greater than 250 if the average extraction communality is 0.6 or greater but advocates the use of a scree plot in all other circumstances provided the sample size is greater than 200. In the present study the average extraction communality was 0.38 therefore the one-factor solution suggested by the scree plot (Figure 2.2) was accepted.

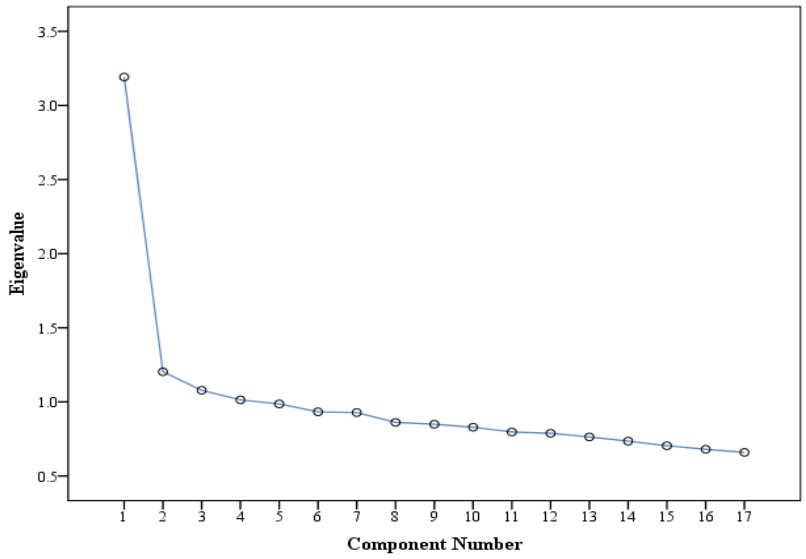

Figure 2.2. Scree plot of factors extracted following principal components analysis of the prospective memory video procedure items

2.2.2.3 Item Analysis

The difficulty of each of the seventeen items comprising the prospective memory video procedure was examined by considering the proportion of participants who answered the item correctly (Table 2.1). Scrutiny of these item difficulties suggested that two items, "at HMV buy a CD" and "at Burger King buy a milkshake", which were correctly recalled by more than 80% of participants appeared to be too easy and one item, "at the mobile phone stall ask for directions to the station" which was correctly recalled by fewer than 20% of participants appeared to be too difficult. A

test is considered to be acceptable, however, if the item difficulties average 0.5 (McIntire and Miller, 2007) and therefore, as the average item difficulty in the present study was 0.58, the prospective memory video procedure was considered appropriate.

Table 2.1. The proportion of participants correctly recalling each item comprising the prospective memory video procedure

Item	Proportion correctly recalling the item (%)	Item	Proportion correctly recalling the item (%)
Halifax	65	Wallis	50
Dixon	55	Mobile phone stall	19
Pushchair	62	H Samuel	69
Bench	50	Thornton	74
Boots	52	Orange	76
WH Smith	71	Link	47
HMV	91	Man asking for change	50
Burger King	83	Picture stall	30
Flower stall	50		

In order to ascertain the utility of the items comprising the prospective memory video procedure it is important to consider whether the items are able to sufficiently discriminate between individuals with good prospective memory and individuals with poor prospective memory (item discrimination). On the basis of a median split, participants who correctly recalled fewer than 10 intentions during the prospective memory video procedure were categorised as having poor prospective memory and those who correctly recalled more than 10 intentions were categorised as having good prospective memory. Across all items, a higher proportion of those with poor prospective memory compared to those with good prospective memory failed to

correctly recall the item and a higher proportion of those with good prospective memory compared to those with poor prospective memory correctly recalled the item (Table 2.2). Furthermore, across all of the items, Chi-square tests of association indicated that these associations between prospective memory ability and the correct recall of the item were significant.

Table 2.2. The proportion of individuals with good prospective memory (high scorers) and poor prospective memory (low scorers) failing to correctly recall and correctly recalling each item comprising the prospective memory video procedure

Item	Proportion failing to correctly recall the item (%)		Proportion correctly recalling the item (%)		Chi-Square statistics
	Low Scorers	High Scorers	Low scorers	High Scorers	
Halifax	52.42	15.50	47.58	84.50	χ^2 (1) = 143.60, p < 0.001
Dixon	63.37	25.05	36.63	74.95	χ^2 (1) = 140.71, p < 0.001
Pushchair	57.89	18.47	42.11	81.53	χ^2 (1) = 155.59, p < 0.001
Bench	72.84	27.18	27.16	72.82	χ^2 (1) = 197.27, p < 0.001
Boots	73.05	25.27	26.95	74.73	χ^2 (1) = 216.07, p < 0.001
WH Smith	47.58	12.31	52.42	87.69	χ^2 (1) = 139.99, p < 0.001
HMV	17.05	2.55	82.95	97.45	χ^2 (1) = 56.13, p < 0.001
Burger King	30.32	6.37	69.68	93.63	χ^2 (1) = 90.35, p < 0.001
Flower stall	71.79	27.18	28.21	72.82	χ^2 (1) = 188.30, p < 0.001
Wallis	73.05	25.90	26.95	74.10	χ^2 (1) = 210.32, p < 0.001
Mobile phone stall	92.00	68.37	8.00	31.63	χ^2 (1) = 83.30, p < 0.001
H Samuel	50.95	12.53	49.05	87.47	χ^2 (1) = 160.92, p < 0.001
Thornton	40.21	12.74	59.79	87.26	χ^2 (1) = 91.56, p < 0.001
Orange	38.32	9.77	61.68	90.23	χ^2 (1) = 105.38, p < 0.001
Link	74.74	29.51	25.26	70.49	χ^2 (1) = 193.87, p < 0.001
Man asking for change	68.42	32.70	31.58	67.30	χ^2 (1) = 120.75, p < 0.001
Picture stall	89.26	48.41	10.74	51.59	χ^2 (1) = 184.29, p < 0.001

2.2.3 Summary of findings and conclusions

The aim of the present study was to evaluate the psychometric properties of a video procedure for the assessment of prospective memory. Specifically, this first study examined the internal consistency and the factorial structure of the video procedure and examined the distribution of scores attained on the task to ensure that the task was capable of discriminating between individuals with good prospective memory and those with poor prospective memory and to ensure that the task was not too easy or too difficult.

In relation to these objectives, the findings suggested that the prospective memory video procedure was a reliable measure with the seventeen items comprising the procedure showing an acceptable degree of internal consistency and principal component analysis further suggested that these items loaded onto a single factor suggesting that the items measured the same underlying construct. Scrutiny of the individual items comprising the video procedure suggested that while the majority of the items were within acceptable bounds in terms of the proportion of respondents correctly recalling the intention (item difficulty), two items appeared to be less difficult and one item appeared to be more difficult. The average item difficulty over the test as a whole, however, suggested that the task difficulty was appropriate and the distribution of scores attained by participants further suggested that the prospective memory video procedure was sufficiently complex to prevent ceiling effects whilst at the same time avoiding floor effects due to the task being too difficult. Furthermore, all items were able to discriminate between individuals with good prospective memory and those with poor prospective memory.

2.3 Study 2: Convergent validity with existing self-report measures

The findings documented in study one suggested that the prospective memory video procedure was a reliable objective measure which was not prone to ceiling effects in non-clinical populations and that the factorial structure of the task was such that all items appeared to measure the same construct. A limitation of this study, however, was that it did not provide evidence that the construct measured by the procedure was indeed prospective memory. The aim of the present study, therefore, was to gather evidence of convergent validity of the video procedure with existing measures of prospective memory. Specifically, the present study examined the relationship between scores on the video procedure and self-reports of prospective memory deficits utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995) and the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003). As the prospective memory video procedure measures prospective remembering and the Prospective Memory Questionnaire (Hannon et *al*., 1995) and the prospective memory subscale of the Prospective and Retrospective Memory Questionnaire (Crawford, *et al*., 2003) measure prospective memory failures, it was predicted that there would be an inverse relationship between scores on the prospective memory video procedure and each of these measures.

2.3.1 Methodology

2.3.1.1 Design

The study employed a correlation design to gather evidence of convergent validity of the video procedure with existing self-report measures of prospective memory. The measures were the number of location-action combinations correctly recalled during

the video procedure, the number of prospective memory failures reported on each of the Prospective Memory Questionnaire (Hannon *et al*., 1995) subscales and the number of prospective memory failures reported on the prospective memory subscale of the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003). The presentation of the measures was held constant across all participants.

2.3.1.2 Participants

Of the 1057 participants who completed study one, an opportunity sample of 640 participants also completed the present study. The sample comprised 224 males with a median age of 19 years and 416 females also with a median age of 19 years.

2.3.1.3 Measures

The prospective memory video procedure described in study one was employed to objectively gauge prospective memory performance. Cronbach's alpha confirmed that the reliability of the video procedure was acceptable in the present study (α = 0.72).

The Prospective Memory Questionnaire (Hannon *et al*., 1995) was employed as an existing self-report measure of prospective memory ability against which the prospective memory video procedure could be evaluated. This questionnaire (appendix B) gauged the number of prospective memory failures reported across three aspects of prospective memory ability with fourteen items related to long-term episodic prospective memory, fourteen items related to short-term habitual prospective memory and ten items related to internally cued prospective memory.

Long-term episodic prospective memory describes situations where the task is completed hours or days after a cue to perform it and occurs irregularly, for example, "in the last year I forgot to send a card for a birthday or anniversary" or "in the last week I forgot to meet a friend on time". Short-term habitual prospective memory describes situations where the task is completed within minutes of a cue to perform it and occurs routinely, for example, "in the last week I forgot to lock the door when leaving my apartment or house" or "in the last week I forgot to button or zip some part of my clothing as I was dressing". In contrast, internally cued prospective memory describes situations where the task had no obvious external cue to elicit remembering, for example, "in the last week I forgot what I wanted to say in the middle of the sentence" or "in the last week I forgot what I came into a room to get". On each subscale the participant responded along a nine-point scale which ranged from one (never forgot) to nine (much forgetting). A mean score was calculated for each of the subscales thus providing three scores between one and nine with higher scores indicating poorer prospective memory. Cronbach's alpha confirmed acceptable reliability in the present study for the long-term episodic ($\alpha = 0.81$), short-term habitual ($\alpha = 0.75$) and internally cued ($\alpha = 0.81$) subscales.

The Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) was also employed as an existing self-report measure of prospective memory ability against which the prospective memory video procedure could be evaluated. This questionnaire (appendix C) gauged the number of memory failures reported across long-term and short-term and across self-cued and environmentally cued aspects of both prospective memory and retrospective memory ability. The questionnaire comprises eight items related to prospective memory, for example, "do you decide to

do something in a few minutes' time and then forget to do it?" (short-term, self-cued) or "do you forget to buy something you planned to buy, like a birthday card, even when you see the shop?" (long-term, environmentally cued) and eight items related to retrospective memory, for example, "do you fail to recognise a character in a radio or television show from scene to scene?" (short-term, environmentally cued) or "do you fail to recall things that have happened to you in the last few days?" (long-term, self-cued). On each of the subscales the participant responded along a five-point scale which ranged from one (never forgot) to five (very often forgot). A total score was calculated for each subscale thus providing two scores between eight and forty with higher scores indicating poorer prospective memory. Cronbach's alpha confirmed acceptable reliability in the present study for both the prospective ($\alpha = 0.80$) and the retrospective ($\alpha = 0.73$) memory subscales.

2.3.1.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. The procedure detailed in study one for the completion of the prospective memory video procedure was adopted for the present study. On completion of the video procedure participants completed the Prospective Memory Questionnaire (Hannon *et al.*, 1995) and the Prospective and Retrospective Memory Questionnaire (Crawford *et al.*, 2003), both of which contained instructions for

completion. Following the completion of all tasks the participants were debriefed and thanked for their participation.

2.3.2 Results

2.3.2.1 Convergent validity with the Prospective Memory Questionnaire

As the data obtained from the Prospective Memory Questionnaire (Hannon *et al*., 1995) were of ordinal level, non-parametric Spearman's rho tests of correlation were conducted to ascertain the existence of any relationship between the scores obtained utilising the prospective memory video procedure and the number of long-term episodic, short-term habitual and internally cued prospective memory failures reported utilising this questionnaire. These tests indicated significant correlations between scores on the video procedure and reports of prospective memory failures in long-term episodic [r (640) = -0.11, p = 0.004, r^2 = 0.01] and short-term habitual [r (640) = -0.13, p = 0.001, r^2 = 0.02] but not internally cued [r (640) = -0.004, p = 0.92] aspects of prospective memory.

2.3.2.2 Convergent validity with the Prospective and Retrospective Memory Questionnaire

As the data obtained from the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) were of ordinal level, non-parametric Spearman's rho tests of correlation were conducted to ascertain the existence of any relationship between the scores obtained utilising the prospective memory video procedure and the number of prospective memory and retrospective memory failures reported utilising this questionnaire. These tests indicated no significant relationship between scores on

the video procedure and reports of memory failures in either prospective memory [r (640) = 0.03, p = 0.41] or retrospective memory [r (640) = -0.06, p = 0.11].

2.3.3 Summary of findings and conclusions

The aim of the present study was to gather evidence of convergent validity of the video procedure with existing measures of prospective memory. Specifically, the present study examined the relationship between scores on the video procedure and self-reports of prospective memory deficits utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995) and the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003). The findings indicated small correlations between scores on the video procedure and reports of deficits in long-term episodic and short-term habitual but not internally cued aspects of prospective memory utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995) and found no relationship between scores on the video procedure and reports of deficits in prospective memory utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003).

The small correlations observed in the present study were not unexpected as previous research has consistently noted weak correlations between self-reports of prospective memory deficits and objective measures of ability (Bedi and Redman, 2008; Chan *et al*., 2008; Uttl and Kibreab, 2011). Similarly, the absence of a relationship with self-reports of deficits in internally cued prospective memory was not unexpected due to the nature of the video procedure which comprises environmental cues rather than being internally cued. Nor was the absence of a relationship with self-reports of deficits in retrospective memory when utilising the Prospective and Retrospective

Memory Questionnaire (Crawford *et al*., 2003) unexpected as Crawford *et al*. (2003) argue that prospective memory and retrospective memory relate to separate constructs. The absence of a relationship between scores on the video procedure and self-reports of prospective memory deficits when utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003), however, was unexpected. This may reflect a lack of construct validity within this particular questionnaire as Uttl and Kibreab (2011) noted that the scores on the prospective memory subscale were more highly correlated with the scores on the retrospective memory subscale than with the scores on other self-report measures of prospective memory leading them to suggest that this questionnaire measures a general memory factor rather than distinct components of prospective and retrospective memory.

2.4 Study 3: Convergent validity with existing objective measures

The findings documented in study two provided only weak evidence of convergent validity of the video procedure with existing self-report measures of prospective memory. Self-report measures have been criticised, however, as a consequence of their poor correlation with objective measures of ability (Bedi and Redman, 2008; Chan *et al*., 2008; Uttl and Kibreab, 2011). The aim of the present study, therefore, was to gather evidence of convergent validity of the video procedure against an existing objective measure of prospective memory. As both the prospective memory video procedure and the Cambridge Prospective Memory Test (Wilson *et al*., 2005) measure prospective remembering, it was predicted that there would be a direct relationship between overall scores attained utilising these measures. In addition, as the prospective memory video procedure comprised event-based cues it was further predicted that there would be a direct relationship between scores on the prospective

memory video procedure and scores for the event-based tasks on the Cambridge Prospective Memory Test (Wilson *et al*., 2005) with no relationship between scores on the prospective memory video procedure and scores for the time-based tasks.

2.4.1 Methodology

2.4.1.1 Design

The study employed a correlation design to gather evidence of convergent validity of the video procedure with an existing objective measure of prospective memory. The measures were the number of location-action combinations correctly recalled during the video procedure and scores based upon execution of the time-based and the event-based tasks during the Cambridge Prospective Memory Test (Wilson *et al*., 2005). Half of the participants completed the video procedure followed by the Cambridge Prospective Memory Test while the remainder completed the Cambridge Prospective Memory Test followed by the video procedure.

2.4.1.2 Participants

Of the 1057 participants who completed study one, an opportunity sample of 80 participants also completed the present study. These participants had not completed study two. The sample comprised 25 males with a median age of 20 years and 55 females with a median age of 19 years.

2.4.1.3 Measures

The prospective memory video procedure described in study one was employed to objectively gauge prospective memory performance. Cronbach's alpha confirmed

that the reliability of the video procedure was acceptable in the present study (α = 0.73).

The Cambridge Prospective Memory Test (Wilson *et al*., 2005) was employed as an existing objective measure of prospective memory ability against which the video procedure could be evaluated. The test required participants to perform three tasks at specified times during the test, for example "in seven minutes…." and three tasks in response to a particular event, for example "when the alarm sounds…." whilst engaged in a concurrent activity which involved the completion of a series of puzzles and quizzes over a testing period of 25 minutes. Prompts were provided in the event that the participants failed to spontaneously perform the task at the appropriate time or performed an incorrect action. Points for the completion of tasks were awarded on a sliding scale according to the protocol described in the test manual with a maximum of six points awarded if the task was spontaneously performed in response to the appropriate event or time cue. Four points were awarded if one prompt was required prior to execution of the correct response and two points were awarded if two prompts were required. One point was awarded if an incorrect response was carried out following two prompts with zero points being awarded if the participant made no response and indicated that they could not remember what it was they had been asked to do even after prompts. The scores for the three event-based tasks and the three time-based tasks were totalled separately to provide two scores between zero and eighteen. An overall prospective memory performance score was also calculated by summing the time-based and the event-based scores, thus providing a score between zero and thirty-six. In all three instances a higher score indicated better prospective memory. Cronbach's alpha indicated that the reliability of the test

in the present study was lower than traditionally recommended ($\alpha = 0.56$). However, as alpha is dependent upon the number of items (Cortina, 1993; Streiner, 2003), this may be due to the low number of items contained within the task.

2.4.1.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested individually and were randomly selected to complete either the prospective memory video procedure followed by the Cambridge Prospective Memory Test or to complete the Cambridge Prospective Memory test followed by the video procedure. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were allocated a unique identifier to ensure anonymity. The procedure detailed in study one for the completion of the prospective memory video procedure was adopted for the present study and the Cambridge Prospective Memory Test (Wilson *et al*., 2005) was completed according to the protocol described in the test manual. Following the completion of all tasks the participants were debriefed and thanked for their participation.

2.4.2 Results

Shapiro-Wilk tests for normality indicated that the scores obtained utilising the Cambridge Prospective Memory Test (Wilson *et al*., 2005) were not normally distributed in terms of time-based prospective memory [$W(80) = 0.90$, $p < 0.001$], event-based prospective memory [$W(80) = 0.91$, $p < 0.001$] or in terms of overall prospective memory score [$W(80) = 0.94$, $p = 0.001$]. As data transformations must be performed on all variables within a statistical analysis (Field, 2009) and because

the data were normally distributed in terms of prospective memory video procedure scores [W (80) = 0.98, p = 0.15], transformation was not appropriate as correcting the skew within the Cambridge Prospective Memory Test scores would have generated skew within the prospective memory video procedure scores. Non-parametric Spearman's rho tests of correlation were therefore conducted to ascertain the existence of relationships between the scores obtained utilising the prospective memory video procedure and scores obtained utilising the Cambridge Prospective Memory Test (Wilson *et al*., 2005). These tests indicated significant correlations between scores on the video procedure and scores for time-based prospective memory [r (80) = 0.33, p = 0.003, r^2 = 0.11], event-based prospective memory [r (80) = 0.21, p = 0.03, r^2 = 0.05 *one-tailed*] and overall prospective memory score [r (80) = 0.33, p = 0.003, r^2 = 0.11].

2.4.3 Summary of findings and conclusions

The aim of the present study was to gather evidence of convergent validity of the video procedure with existing measures of prospective memory. Specifically, the present study examined the relationship between scores on the video procedure and scores obtained on the Cambridge Prospective Memory Test (Wilson *et al*., 2005). The findings indicated a moderate correlation between scores on the video procedure and total prospective memory scores and a small correlation with scores for event-based prospective memory suggesting that the two tasks measured the same underlying construct. The findings also indicated a moderate correlation between scores on the video procedure and scores for time-based prospective memory which was somewhat surprising given that the video procedure comprises event-based and not time-based retrieval cues.

2.5 Overall summary of findings and conclusions

The aim of the present series of studies was to evaluate the psychometric properties of a video procedure for assessing prospective memory. Specifically, the studies documented examined the reliability of the video procedure in terms of its internal consistency and examined the factorial structure of the measure and the distribution of scores attained on the task. These studies also gathered evidence in the form of convergent validity against existing measures of prospective memory to ascertain that the construct measured by the tool was indeed prospective memory.

In relation to these objectives, the findings of the present series of studies suggested that the prospective memory video procedure is a reliable measure with the items comprising the procedure showing an acceptable degree of internal consistency. Furthermore, the items loaded onto a single factor, and correlations with existing measures of prospective memory provided evidence, albeit weak evidence, that the construct measured by the task was indeed prospective memory. All items appeared to contribute to the utility of the task in discriminating between individuals with good prospective memory and those with poor prospective memory. Furthermore, examination of item difficulty and the distribution of scores suggested that the task was sufficiently complex to prevent ceiling effects among non-clinical populations with mild prospective memory deficits whilst at the same time avoiding floor effects due to the task being too difficult.

Chapter 3

Does cannabis use affect prospective memory processes?

3.1 Rationale

As described in chapter one few studies have investigated the effects of cannabis use on prospective memory performance and at the time of planning the current study only one of these studies had been published. In this published study Rodgers *et al*. (2001) utilised an on-line version of the Prospective Memory Questionnaire (Hannon *et al*., 1995) to gauge self-reported prospective memory failures and concluded that cannabis use was associated with increased reports of failures in short-term habitual and internally cued, but not long-term episodic, aspects of prospective memory. As indicated in chapter one, however, this study was not without methodological limitations. Specifically, the question mark over the validity of the on-line version of the Prospective Memory Questionnaire, the utilisation of a self-report measure of prospective memory performance which may be prone to inaccuracies, and a failure to control for the potential effects of anxiety, depression and use of other recreational drugs, particularly use of alcohol and tobacco. In the light of these limitations, the present study had three aims. The first was to examine self-reported prospective memory failures associated with cannabis use in a replication of the study by Rodgers *et al*. utilising the traditional pencil and paper version of the Prospective Memory Questionnaire (Hannon *et al*., 1995) in order to overcome the limitations of the on-line version in relation to its psychometric characteristics. The second aim was to extend the findings of Rodgers *et al*. by incorporating the video procedure evaluated in chapter two as an objective measure of prospective memory to compare users and non-users in order to overcome the limitations of self-reported assessment

of memory failures. The final aim was to extend the findings of Rodgers *et al*. by controlling for anxiety, depression and use of other recreational drugs in addition to the use of strategies to assist remembering. In the light of the self-reported deficits noted by Rodgers *et al*. (2001) it was predicted that cannabis users would report more prospective memory failures than non-users. Since previous research has shown objectively measured deficits in memory and executive functions in cannabis users (Battisti *et al*., 2010; Bolla *et al*., 2002; Croft *et al*., 2001; Grant *et al*., 2003; McHale and Hunt, 2008; Medina *et al*., 2007; Messinis *et al*., 2006; Nestor *et al*., 2008; Rodgers, 2000; Solowij and Battisti, 2008; Solowij and Pesa, 2010; Solowij *et al*., 2002) it was also predicted that these self-reported deficits would translate to objectively observed deficits and that cannabis users would recall significantly fewer intentions than non-users on the prospective memory video procedure.

3.2 Methodology

3.2.1 Design

The study employed a quasi-experimental independent measures design utilising pre-existing groups of cannabis users who had declared use of cannabis within the previous year and non-users who had never smoked cannabis. The dependent measures were the number of location-action combinations correctly recalled during the prospective memory video procedure and the number of prospective memory failures reported on each of the Prospective Memory Questionnaire (Hannon *et al*., 1995) subscales. The number of strategies used to assist remembering, level of anxiety and depression, and use of alcohol, tobacco and any other recreational drugs

in addition to cannabis use were also measured and controlled for during analysis of the data. The presentation of the measures was held constant across all participants.

3.2.2 Participants

An opportunity sample of 143 undergraduates between the ages of 18 and 24 years studying at universities in the northeast of England participated. Data from 23 participants who reported the use of illicit recreational drugs in addition to their use of cannabis and 9 participants whose use of additional illicit recreational drugs was unknown were excluded. Data from a further 6 participants who reported use of cannabis within 24 hours prior to testing, 3 participants who had used cannabis only once and 12 participants who no longer smoked cannabis and had not smoked for more than one year were also excluded. The remaining sample of 90 participants comprised 45 cannabis users who had used cannabis within the previous year (20 males and 25 females with a median age of 19 years) and 45 non-users (17 males and 28 females also with a median age of 19 years). There was no significant difference in the proportion of males and females within the cannabis users and non-users [χ^2 (1) = 0.41, p = 0.52]. Based upon the 62.22% of cannabis users who disclosed information relating to their cannabis use, the cannabis users smoked a median of 2 joints per week (range: 1 joint every 6 months to 20 joints per week), had used cannabis for a median of 3 years (range: 6 months to 6 years) and had abstained from use for a median of 10.50 days (range: 24 hours to 7 months).

3.2.3 Measures

The prospective memory video procedure described in chapter two was employed to objectively gauge prospective memory performance. Cronbach's alpha confirmed

that the reliability of the video procedure was acceptable in the present study (α = 0.68).

The Prospective Memory Questionnaire (Hannon *et al*., 1995) described in chapter two was employed to gauge the number of prospective memory failures across long-term episodic, short-term habitual and internally cued aspects of prospective memory. An additional subscale, the techniques to assist remembering scale, was utilised to gauge the use of strategies designed to assist remembering. As with the prospective memory subscales described in chapter two, the participant responded along a nine-point Likert scale which ranged from one (never used the strategy) to nine (much use of the strategy). A mean score was calculated providing a score between one and nine with higher scores indicating greater use of strategies to assist remembering. Cronbach's alpha confirmed that reliability was acceptable in the present study for the long-term episodic (α = 0.82), short-term habitual (α = 0.79) and internally cued (α = 0.74) prospective memory scales and for the techniques to assist remembering scale (α = 0.82).

The Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) comprises two subscales with seven items related to generalised anxiety and seven items related to loss of interest and diminished pleasure aspects of depression and was employed to gauge levels of anxiety and depression experienced by cannabis users and non-users during the previous week. Responses to each item were scored along a four-point Likert scale ranging from zero to three such that higher scores indicated more severe symptoms. A total score for each subscale was calculated, thus providing two scores between zero and twenty-one. Cronbach's alpha indicated that the reliability

of the items related to anxiety was acceptable in the present study ($\alpha = 0.81$), however, reliability of the items related to depression in the present study was lower than traditionally recommended ($\alpha = 0.53$).

A substance use questionnaire developed for the current programme of research (appendix D) provided details of cannabis use, including the number of joints smoked, duration of use, and details of last use. In addition, the questionnaire ascertained estimates of weekly consumption of alcohol (in terms of units of alcohol where one unit is defined as half a pint (284ml) of standard beer, one 25ml measure of spirits or one standard (125ml) glass of wine), tobacco (in terms of the number of cigarettes smoked) and any other illicit recreational drugs in addition to cannabis. Details of duration of use and last use were also ascertained. No additional measures of drug use were employed.

3.2.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. The procedure detailed in chapter two for the completion of the prospective memory video procedure was adopted for the present study. On completion of the video procedure, participants completed the Prospective Memory Questionnaire (Hannon *et al.*, 1995), the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) and finally the substance use questionnaire, all of which

contained instructions for their completion. Following the completion of all tasks the participants were debriefed and thanked for their participation.

3.3 Results

3.3.1 Participant demographics

Table 3.1 shows the median age, weekly consumption of alcohol, number of cigarettes smoked per week, number of strategies used to assist remembering and the median anxiety and depression scores of cannabis users and non-users.

Table 3.1. Median age, weekly consumption of alcohol, number of cigarettes smoked per week, number of strategies used to assist remembering, anxiety score and depression score of cannabis users and non-users (range in brackets)

	Cannabis Users	Non-Users
Age (years)	19.00 (5.00)	19.00 (3.00)
Units of alcohol consumed	30.00 (95.50)	12.00 (70.00)
Number of cigarettes smoked	1.00 (180.00)	0.00 (60.00)
Number of strategies used	3.29 (6.86)	3.21 (5.08)
Anxiety score	8.00 (19.00)	7.00 (16.00)
Depression score	3.00 (10.00)	2.00 (8.00)

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of age [$W(45) = 0.77$, $p < 0.001$ for users and $W(45) = 0.77$, $p < 0.001$ for non-users], alcohol consumption [$W(44) = 0.84$, $p < 0.001$ for users and $W(44) = 0.82$, $p < 0.001$ for non-users] or tobacco consumption [$W(37) = 0.64$, $p < 0.001$ for users and $W(43) = 0.29$, $p < 0.001$ for non-users]. Although Levene's tests for the

assumption of homogeneity of variance between cannabis users and non-users revealed no violation of the assumption in terms of age [F (1, 88) = 0.08, p = 0.78] or alcohol consumption [F (1, 86) = 1.77, p = 0.19], the assumption was violated in terms of the number of cigarettes smoked per week [F (1, 78) = 10.62, p = 0.002]. In addition, the data obtained in relation to the number of strategies used to assist remembering and levels of anxiety and depression were of ordinal level. Therefore, non-parametric Mann-Whitney U tests were performed to ascertain any significant differences between cannabis users and non-users in terms of age, use of strategies to assist remembering, level of anxiety or depression and weekly consumption of alcohol and tobacco. These tests revealed no significant differences between cannabis users and non-users in terms of age [U = 986.50, p = 0.82], number of strategies used to assist remembering [U = 1008.50, p = 0.97], or level of anxiety [U = 999.50, p = 0.92] or depression [U = 872.50, p = 0.25]. Cannabis users, however, consumed significantly more alcohol (median = 30 units, range = 95.50) than non-users (median = 12 units, range = 70.00) [U = 391.50, p < 0.001] and smoked significantly more tobacco (median = 1 cigarette, range = 180) than non-users (median = 0 cigarettes, range = 60) [U = 469.00, p < 0.001].

3.3.2 Self-reported prospective memory

In terms of the number of self-reported prospective memory deficits utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995), the median number of long-term episodic, short-term habitual and internally cued prospective memory failures reported by cannabis users and non-users is shown in Figure 3.1.

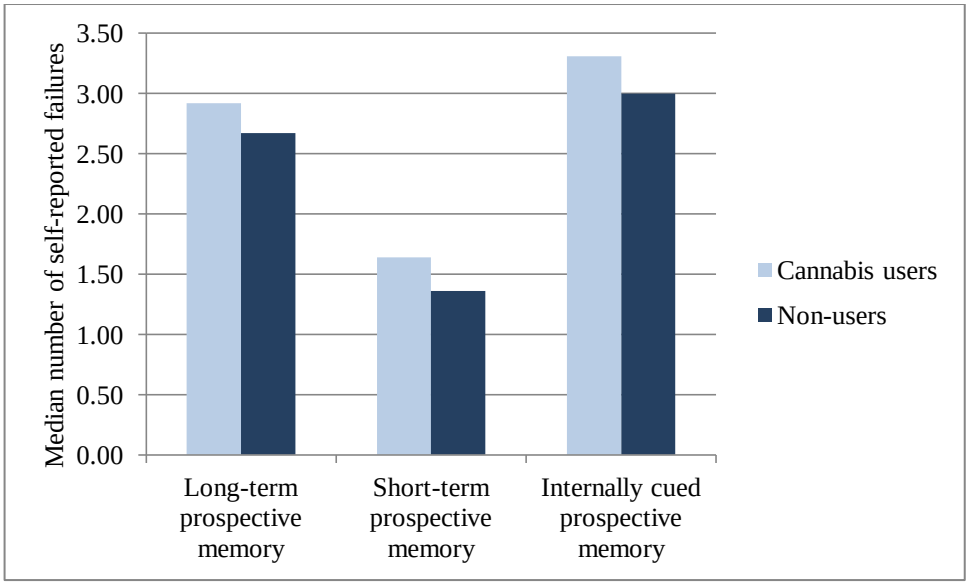

Figure 3.1. The median number of long-term episodic, short-term habitual and internally cued prospective memory failures reported by cannabis users and non-users

As the data obtained in relation to the number of long-term episodic, short-term habitual and internally cued prospective memory failures were of ordinal level, non-parametric Mann-Whitney U tests were performed to ascertain the presence of any significant differences between cannabis users and non-users in terms of self-reported prospective memory failures. These tests revealed no significant effect of cannabis use on the number of self-reported failures in long-term episodic [U = 886.00, p = 0.31], short-term habitual [U = 816.50, p = 0.11] or internally cued [U = 849.50, p = 0.25] aspects of prospective memory.

3.3.3 Objectively measured prospective memory

In terms of objectively measured prospective memory, the mean number of location-action combinations correctly recalled by cannabis users and non-users during the prospective memory video procedure is shown in Figure 3.2.

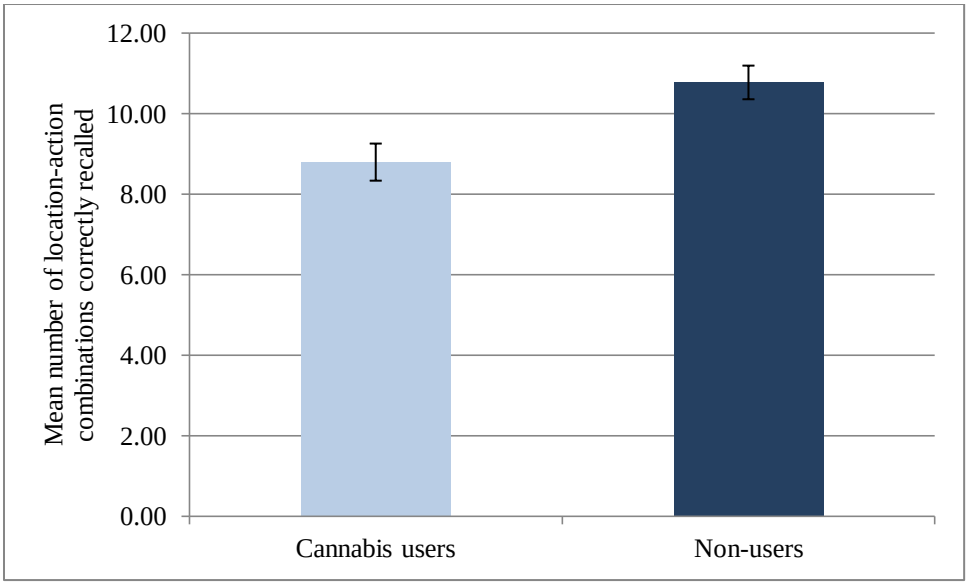

Figure 3.2. The mean number of location-action combinations correctly recalled by cannabis users and non-users during the video procedure (±1 standard error)

Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure [W (45) = 0.98, p = 0.72 for users and W (45) = 0.97, p = 0.29 for non-users]. Furthermore, Levene's test for the assumption of homogeneity of variance between users and non-users indicated that the assumption was not violated [F (1, 88) = 0.67, p = 0.41] and the data obtained were of ratio level. Bonferroni corrected Spearman's rho tests of correlation indicated no significant relationships between prospective memory video procedure scores and age [r (90) = 0.09, p = 1.00], number of strategies used to assist remembering [r (90) = 0.18, p = 0.58], level of anxiety [r (90) = 0.09, p = 1.00] or depression [r (90) = -0.24, p = 0.16], number of units of alcohol consumed [r (88) = -0.15, p = 0.98], or number of cigarettes smoked [r (80) = -0.09, p = 1.00]. There was therefore no justification for the inclusion of any of these factors as covariates. Analysis of variance performed to ascertain the presence of any significant differences between cannabis users and non-

users in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure revealed a significant effect of cannabis use on prospective memory with cannabis users correctly recalling significantly fewer location-action combinations (mean = 8.80, standard deviation = 3.09) than non-users (mean = 10.78, standard deviation = 2.80) [F (1, 88) = 10.10, p = 0.002, η_p^2 = 0.10].

3.4 Summary of findings and conclusions

The present study had three aims. The first of these was to examine self-reported prospective memory failures associated with cannabis use in a replication of the study by Rodgers *et al* (2001) utilising the traditional pencil and paper version of the Prospective Memory Questionnaire (Hannon *et al*., 1995) in order to overcome the limitations of the on-line version in relation to its psychometric characteristics. The second aim was to extend the findings of Rodgers *et al*. by incorporating the prospective memory video procedure as an objective measure of prospective memory to compare users and non-users in order to overcome the limitations of self-reported assessment of memory failures. The final aim was to extend the findings of Rodgers *et al*. by controlling for anxiety, depression and use of other recreational drugs in addition to use of strategies to assist remembering. In relation to these aims the results obtained revealed no significant differences in the number of self-reported prospective memory failures across long-term episodic, short-term habitual or internally cued aspects of prospective memory. Cannabis users, however, correctly recalled significantly fewer location-action combinations than non-users during the objectively measured prospective memory video procedure. Furthermore, there were no significant relationships in the present study between prospective memory video

procedure scores and age, number of strategies used to assist remembering, level of anxiety and depression, number of units of alcohol consumed or number of cigarettes smoked.

The findings of the present study suggested that cannabis use has a detrimental effect on prospective memory in young adults though cannabis users appear to be unaware of any impairment. This study was the first to employ an objective measure of prospective memory performance and was also the first study to report no significant difference in self-reported deficits associated with cannabis use. These findings therefore need to be confirmed in a second, independent cohort.

Chapter 4

Does prospective memory recover on cessation of cannabis use?

4.1 Rationale

The findings of the study documented in chapter three (Bartholomew, Holroyd and Heffernan, 2010) suggested that cannabis use has a detrimental effect upon prospective memory performance in young adults. It is important, however, to distinguish whether the deficits observed are simply a consequence of the residual effects of acute intoxication or are more prolonged, persisting even after the elimination of the drug and its metabolites from the body.

Previous research has suggested that cognitive deficits associated with cannabis use may recover following abstinence. For example, Pope, Gruber, Hudson, Huestis and Yurgelun-Todd (2001, 2002) noted that cognitive deficits observed in current heavy cannabis users following 7 days abstinence were not evident at 28 days abstinence. Furthermore, Pope *et al*. (2001) found that former users did not differ from controls across any of the cognitive domains tested. McHale and Hunt (2008) also noted that deficits in verbal fluency were more pronounced in recent users than in abstinent users who had not used within the seven days preceding the study. Unfortunately, as these abstinent users had used within the four weeks preceding the study it is not possible to ascertain whether these deficits would have remained with a prolonged period of abstinence. Other studies, however, have reported evidence of deficits persisting beyond 28 days of abstinence (Bolla *et al*., 2002; Medina *et al*., 2007). To date, no studies have explored this phenomenon in relation to prospective memory processes. The first aim of the present study, therefore, was to extend the study

reported in chapter three (Bartholomew *et al*., 2010) to include previous users in order to ascertain whether the prospective memory deficits observed in current cannabis users recover upon cessation of cannabis use.

In addition, the prospective memory deficits observed by Bartholomew *et al*. (2010) were noted with an objective but not with a self-report measure of prospective memory suggesting that perhaps cannabis users were not aware of any deficits. This study was the first study to employ an objective measure of prospective memory and was also the first study to report no significant difference in self-reported deficits associated with cannabis use. These findings therefore need to be confirmed in a second, independent cohort and this was the second aim of the present study.

In light of the findings reported in chapter three (Bartholomew *et al*., 2010) it was predicted that current cannabis users would correctly recall fewer location-action combinations during the prospective memory video procedure than non-users. In addition, as previous research has suggested that cognitive deficits associated with cannabis use recover following abstinence (McHale and Hunt, 2008; Pope *et al*., 2001, 2002) and that former users do not differ from controls (Pope *et al*., 2001) it was predicted that previous cannabis users would not differ from non-users in terms of the number of location-action combinations recalled during the prospective memory video procedure. As the elimination of δ^9-tetrahydrocannabinol and its metabolites occurs gradually as the δ^9-tetrahydrocannabinol stored in adipose tissues leaks back into the bloodstream (Ashton, 2001; Iversen, 2008; Parrott *et al*., 2004), it was further predicted that if prospective memory recovers following cessation of use there would be a direct correlation between length of abstinence and the number

of location-action combinations correctly recalled during the prospective memory video procedure and an inverse correlation between length of abstinence and the number of deficits reported.

4.2 Methodology

4.2.1 Design

The study employed a quasi-experimental independent measures design utilising pre-existing groups of current cannabis users who had declared use of cannabis within the previous year, previous cannabis users who had not used cannabis for at least one year, and non-users who had never smoked cannabis. The dependent measures were the number of location-action combinations correctly recalled during the prospective memory video procedure, the number of prospective memory failures reported on each of the Prospective Memory Questionnaire (Hannon *et al*., 1995) subscales and the number of prospective memory failures reported on the prospective memory subscale of the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003). The number of strategies used to assist remembering, level of anxiety and depression, and use of alcohol, tobacco and any other recreational drugs in addition to cannabis use were also measured and controlled for during analysis of the data. The presentation of the measures was held constant across all participants.

4.2.2 Participants

An opportunity sample of 207 undergraduates between the ages of 18 and 24 years studying at universities in the northeast of England participated. Data from 51 participants who reported the use of illicit recreational drugs in addition to their use

of cannabis and 6 participants whose use of additional illicit recreational drugs was unknown were excluded. Data from a further participant who reported use of cannabis within 24 hours prior to testing and 20 participants whose last use was unknown were also excluded. The remaining sample of 129 participants comprised 43 current cannabis users who had used cannabis within the previous year (18 males and 25 females with a median age of 19 years), 43 previous cannabis users who had not used cannabis for at least one year (18 males and 25 females with a median age of 19 years) and 43 non-users (18 males and 25 females with a median age of 19 years). Based upon the 55.81% of current cannabis users who disclosed information relating to their cannabis use, the current users smoked a median of 0.29 joints per week (range: 1 joint every 6 months to 8 joints per week), had used cannabis for a median of 2 years (range: 1 year to 7 years) and had abstained from use for a median of one month (range: 24 hours to 7 months). Based upon the 30.23% of previous users who disclosed information relating to their cannabis use, the previous users smoked a median of 0.23 joints per week (range: 1 joint per year to 20 joints per week), had used cannabis for a median of one year (range: 1 week to 3 years) and had abstained from use for a median of 2 years (range: 1 year to 5 years).

4.2.3 Measures

The prospective memory video procedure described in chapter two was employed to objectively gauge prospective memory performance. Cronbach's alpha confirmed that the reliability of the video procedure was acceptable in the present study (α = 0.64).

The Prospective Memory Questionnaire (Hannon *et al*., 1995) described in chapter two was employed to gauge the number of prospective memory failures across long-term episodic, short-term habitual and internally cued aspects of prospective memory. The techniques to assist remembering scale described in chapter three was also utilised to gauge the use of strategies designed to assist remembering. Cronbach's alpha confirmed that reliability was acceptable in the present study for the long-term episodic ($\alpha = 0.83$), short-term habitual ($\alpha = 0.71$) and internally cued ($\alpha = 0.82$) prospective memory scales and for the techniques to assist remembering scale ($\alpha = 0.75$).

The Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) described in chapter two was also employed to gauge the number of prospective memory failures across long-term, short-term, self-cued and environmentally cued aspects of prospective memory. Cronbach's alpha confirmed that reliability was acceptable in the present study for the long-term prospective memory ($\alpha = 0.69$), short-term prospective memory ($\alpha = 0.78$), self-cued prospective memory ($\alpha = 0.69$) and environmentally cued prospective memory ($\alpha = 0.69$) subscales.

The Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) described in chapter three was employed to gauge levels of anxiety and depression experienced by cannabis users and non-users during the previous week. Cronbach's alpha indicated acceptable reliability in the present study for the items related to anxiety ($\alpha = 0.79$) and the items related to depression ($\alpha = 0.61$).

The substance use questionnaire described in chapter three provided details of cannabis use and ascertained estimates of weekly consumption of alcohol, tobacco and any other illicit recreational drugs in addition to cannabis. Details of duration of use and last use were also ascertained. No additional measures of drug use were employed.

4.2.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. The procedure detailed in chapter two for the completion of the prospective memory video procedure was adopted for the present study. On completion of the video procedure, participants completed the Prospective Memory Questionnaire (Hannon *et al*., 1995), the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003), the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) and finally the substance use questionnaire, all of which contained instructions for their completion. Following the completion of all tasks the participants were debriefed and thanked for their participation.

4.3 Results

4.3.1 Participant demographics

Table 4.1 shows the median age, weekly consumption of alcohol, number of cigarettes smoked per week, number of strategies used to assist remembering and the median anxiety and depression scores of current cannabis users, previous cannabis users and non-users.

Table 4.1. Median age, weekly consumption of alcohol, number of cigarettes smoked per week, number of strategies used to assist remembering, and scores for anxiety and depression in current cannabis users, previous cannabis users and non-users (range in brackets).

	Current users	Previous users	Non-users
Age (years)	19.00 (4.00)	19.00 (5.00)	19.00 (5.00)
Units of alcohol consumed	22.00 (98.00)	16.00 (54.00)	10.00 (55.00)
Number of cigarettes smoked	0.50 (100.00)	0.00 (120.00)	0.00 (140.00)
Number of strategies used	3.00 (4.27)	2.71 (4.71)	3.14 (4.86)
Anxiety score	8.00 (17.00)	6.00 (13.00)	6.00 (15.00)
Depression score	3.00 (8.00)	3.00 (10.00)	2.00 (9.00)

Although Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of alcohol consumption among previous users [$W(41) = 0.95$, $p = 0.07$], the data were not normally distributed among current users [$W(43) = 0.84$, $p < 0.001$] or non-users [$W(41) = 0.87$, $p < 0.001$]. Shapiro-Wilk tests further revealed that the data were not normally distributed in terms of age [$W(43) = 0.85$, $p < 0.001$ for current users, $W(43) = 0.67$, $p < 0.001$ for previous users and $W(43) =$

0.74, $p < 0.001$ for non-users] or tobacco consumption [W (41) = 0.59, $p < 0.001$ for current users, W (41) = 0.66, $p < 0.001$ for previous users and W (42) = 0.24, $p < 0.001$ for non-users]. Although Levene's tests for the assumption of homogeneity of variance between cannabis users, previous users and non-users revealed no violation of the assumption in terms of age [F (2, 126) = 0.04, p = 0.96] or alcohol consumption [F (2, 122) = 2.59, p = 0.08], the assumption was violated in terms of the number of cigarettes smoked per week [F (2, 121) = 9.16, $p < 0.001$]. In addition, the data obtained in relation to the number of strategies used to assist remembering and levels of anxiety and depression were of ordinal level. Therefore, non-parametric Kruskal-Wallis tests were performed to ascertain any significant differences between current users, previous users and non-users in terms of age, use of strategies to assist remembering, level of anxiety or depression and weekly consumption of alcohol and tobacco. These tests revealed no significant differences between current users, previous users and non-users in terms of age [H (2) = 1.71, p = 0.43], number of strategies used to assist remembering [H (2) = 0.19, p = 0.91], or level of anxiety [H (2) = 4.52, p = 0.10] or depression [H (2) = 1.04, p = 0.59]. There were, however, significant differences in the number of units of alcohol consumed [H (2) = 12.84, p = 0.002] and the number of cigarettes smoked [H (2) = 12.86, p = 0.002]. Bonferroni corrected Mann-Whitney U tests revealed that non-users consumed significantly fewer units of alcohol (median = 10 units, range = 55) than both previous users (median = 16 units, range = 54) [U = 517.50, p = 0.01] and current users (median = 22 units, range = 98) [U = 526.50, p = 0.003] with no significant difference between current users and previous users [U = 841.00, p = 1.00]. These tests also revealed that non-users smoked significantly fewer cigarettes per week (median = 0, range = 140) than both previous users (median = 0, range =

120) [U = 591.50, p = 0.01] and current users (median = 0.50, range = 100) [U = 547.50, p = 0.003] with no significant difference between current users and previous users [U = 824.00, p = 1.00].

4.3.2 Self-reported prospective memory

In terms of the number of self-reported prospective memory deficits utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995) the median number of long-term episodic, short-term habitual and internally cued prospective memory failures reported by current cannabis users, previous cannabis users and non-users is shown in Figure 4.1.

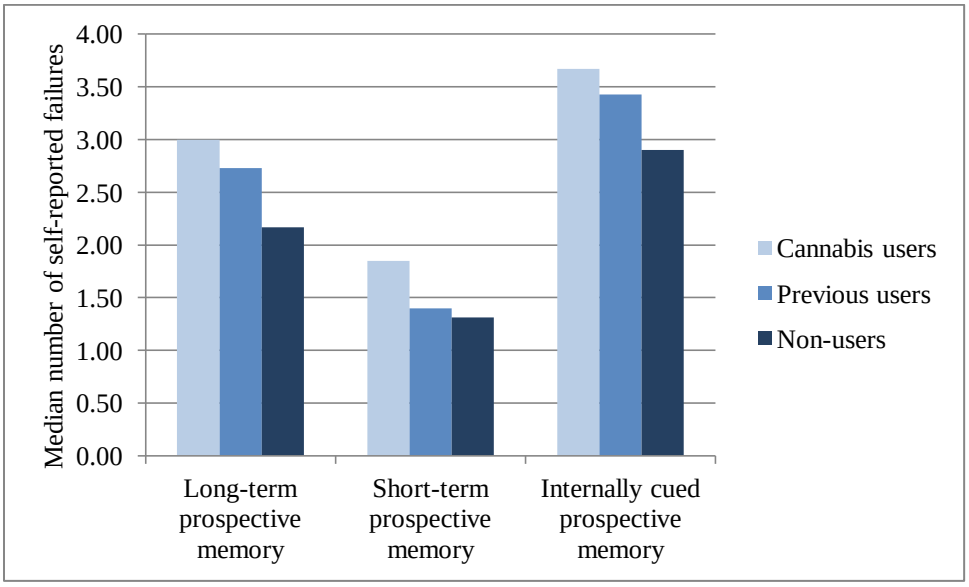

Figure 4.1. The median number of long-term episodic, short-term habitual and internally cued prospective memory failures reported by current cannabis users, previous cannabis users and non-users.

As the data obtained in relation to the number of long-term episodic, short-term habitual and internally cued prospective memory failures were of ordinal level, non-parametric Kruskal-Wallis tests were performed to ascertain the presence of any

significant differences between current users, previous users and non-users in terms of self-reported prospective memory failures when utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995). These tests revealed no significant effect of cannabis use on internally cued prospective memory [H (2) = 0.89, p = 0.64]. There was, however a significant effect of cannabis use on long-term episodic [H (2) = 9.40, p = 0.009, E^2 = 0.07] and short-term habitual [H (2) = 13.48, p = 0.001, E^2 = 0.09] aspects of prospective memory. Bonferroni corrected Mann-Whitney U tests indicated that current users reported more long-term episodic failures (median = 3.00, range = 5.42) than non-users (median = 2.17, range = 5.63) [U = 589.00, p = 0.012] with no significant differences between current users and previous users (median = 2.73, range = 4.05) [U = 759.50, p = 0.46] or between previous users and non-users [U = 702.50, p = 0.17]. These tests also indicated that current cannabis users reported more short-term habitual failures (median = 1.85, range = 4.31) than both previous users (median = 1.40, range = 3.07) [U = 597.00, p = 0.015] and non-users (median = 1.31, range = 2.00) [U = 533.00, p = 0.003] with no significant difference between previous users and non-users [U = 827.50, p = 1.00].

In terms of the number of self-reported prospective memory deficits utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) the median number of long-term, short-term, self-cued and environmentally cued prospective memory failures reported by current cannabis users, previous cannabis users and non-users is shown in Figure 4.2.

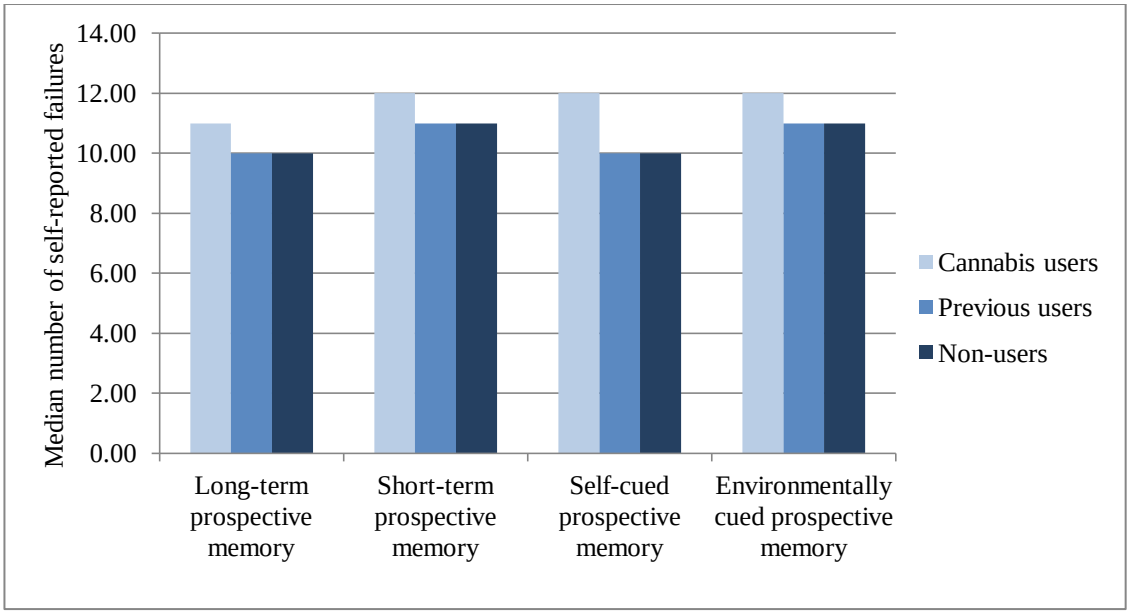

Figure 4.2. The median number of long-term, short-term, self cued and environmentally cued prospective memory failures reported by current cannabis users, previous cannabis users and non-users.

As the data obtained in relation to the number of long-term, short-term, self-cued and environmentally cued prospective memory failures were of ordinal level, non-parametric Kruskal-Wallis tests were performed to ascertain the presence of any significant differences between current users, previous users and non-users in terms of self-reported prospective memory failures when utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003). These tests revealed no significant effect of cannabis use on the number of long-term [H (2) = 3.46, p = 0.18], short-term [H (2) = 5.39, p = 0.07], self-cued [H (2) = 4.01, p = 0.14], or environmentally cued [H (2) = 5.07, p = 0.08] aspects of prospective memory.

4.3.3 Objectively measured prospective memory

In terms of objectively measured prospective memory, the mean number of intentions in the form of location-action combinations correctly recalled by current

users, previous users and non-users during the prospective memory video procedure is shown in Figure 4.3.

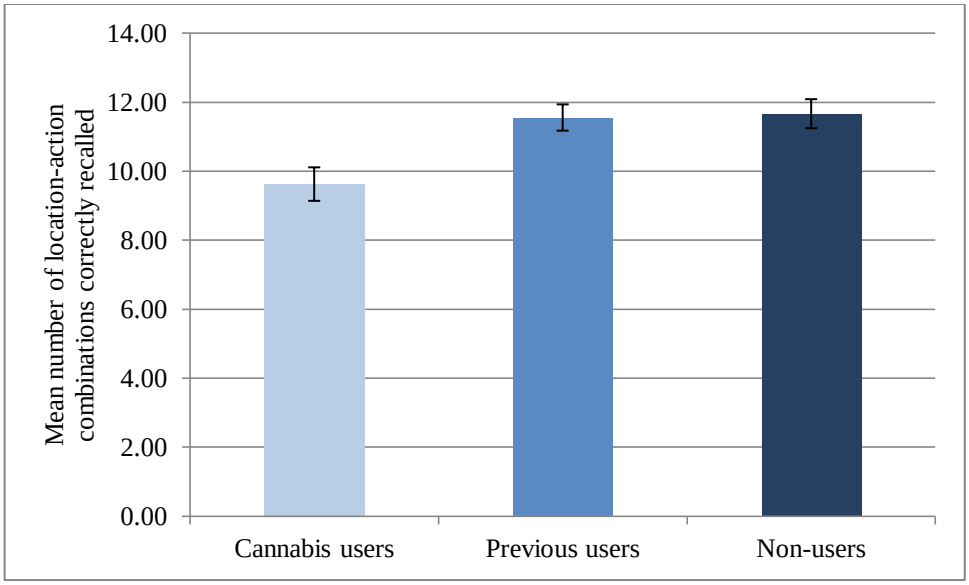

Figure 4.3. The mean number of location-action combinations correctly recalled by current cannabis users, previous cannabis users and non-users during the video procedure (± 1 standard error).

Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure [W (43) = 0.96, p = 0.16 for current users, W (43) = 0.96, p = 0.19 for previous users and W (43) = 0.96, p = 0.14 for non-users]. Furthermore, Levene's test for the assumption of homogeneity of variance between current users, previous users and non-users indicated that the assumption was not violated [F (2, 126) = 1.91, p = 0.15] and the data obtained were of ratio level. Bonferroni corrected Spearman's rho tests of correlation indicated no significant relationships between prospective memory video procedure scores and age [r (129) = -0.06, p = 1.00], number of strategies used to assist remembering [r (129) = 0.01, p = 1.00, level of anxiety [r (128) = 0.03, p = 1.00] or depression [r (128) = -0.05, p =

1.00], number of units of alcohol consumed [r (125) = -0.04, p = 1.00], or number of cigarettes smoked [r (124) = -0.10, p = 1.00]. Although there was no justification for retaining these factors, their inclusion did not adversely affect the observed power and therefore, to remain conservative, these factors were retained as covariates. Analysis of covariance performed to ascertain the presence of any significant differences between current users, previous users and non-users in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure, after statistically controlling for age, strategies to assist remembering, anxiety, depression, units of alcohol consumed and number of cigarettes smoked, revealed a significant effect of cannabis use on prospective memory [F (2, 110) = 7.14, p = 0.001, η_p^2 = 0.12]. Bonferroni corrected pairwise comparisons indicated that current users correctly recalled fewer location-action combinations (mean = 9.63, standard deviation = 3.19) than both previous users (mean = 11.56, standard deviation = 2.50) (p = 0.006) and non-users (mean = 11.67, standard deviation = 2.76) (p = 0.002) with no significant difference between previous users and non-users (p = 1.00).

4.3.4 Relationship between prospective memory and length of abstinence

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of the length of abstinence from cannabis use [W (86) = 0.80, p < 0.001]. Spearman's rho tests of correlation were therefore conducted to ascertain any relationships between prospective memory and length of abstinence.

In terms of self-reported prospective memory utilising the Prospective Memory Questionnaire (Hannon *et al.*, 1995) Spearman's rho tests of correlation revealed

significant relationships between length of abstinence and reports of deficits in long-term episodic [r (86) = -0.21, p = 0.03 r^2 = 0.04 *one-tailed*] and short-term habitual [r (86) = -0.22, p = 0.02, r^2 = 0.05 *one-tailed*] aspects of prospective memory such that reports of problems decreased as length of abstinence increased. There was no relationship between length of abstinence and internally cued aspects of prospective memory [r (86) = -0.14, p = 0.20]. In terms of self-reported prospective memory utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) Spearman's rho tests of correlation revealed significant relationships between length of abstinence and reports of deficits in long-term [r (86) = -0.19, p = 0.04 r^2 = 0.04 *one-tailed*], short-term [r (86) = -0.25, p = 0.01, r^2 = 0.06 *one-tailed*], self-cued [r (86) = -0.26, p = 0.01, r^2 = 0.07 *one-tailed*] and environmentally cued [r (86) = -0.20, p = 0.03, r^2 = 0.04 *one-tailed*] aspects of prospective memory such that reports of problems decreased as length of abstinence increased.

In terms of objectively measured prospective memory utilising the prospective memory video procedure the Spearman's rho test of correlation indicated a small but significant direct correlation such that increased length of abstinence was associated with better prospective memory [r (86) = 0.26, p = 0.01, r^2 = 0.07 *one-tailed*].

4.4 Summary of findings and conclusions

The present study had two aims. The first of these was to extend previous findings to include previous users in order to ascertain whether the prospective memory deficits observed in cannabis users recover upon cessation of cannabis use. The second aim was to confirm the findings reported in chapter three (Bartholomew *et al*., 2010) in a second, independent cohort.

In relation to these aims, the present findings confirmed the inconsistency of self-report measures in assessing prospective memory failures with two different measures, the Prospective Memory Questionnaire (Hannon *et al*., 1995) and the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003), providing conflicting evidence. In particular, cannabis users reported significantly more failures than non-users in long-term episodic prospective memory and significantly more failures than both previous users and non-users in short-term habitual prospective memory when utilising the Prospective Memory Questionnaire (Hannon *et al*., 1995) but there were no significant differences between current users, previous users and non-users in long-term, short-term, self-cued or environmentally cued aspects of prospective memory when utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003). Current cannabis users, however, correctly recalled significantly fewer intentions in the form of location-action combinations than both previous users and non-users during the objectively measured prospective memory video procedure. Furthermore, previous users who had not used for at least one year did not differ from non-users in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure.

The findings of the present study confirmed the findings noted by Bartholomew *et al*. (2010) in chapter three that cannabis use has a detrimental effect on prospective memory in young adults and further suggested that these deficits recover following cessation of cannabis use.

Chapter 5

Relationship of prospective memory deficits to dose and age of onset

5.1 Rationale

Previous studies described within the current programme of research suggested that cannabis use has a detrimental effect on prospective memory performance in young adults. These studies independently, however, were unable to evaluate whether the deficits observed were related to dose and duration of use due to a high proportion of cannabis users who preferred not to disclose information relating to their cannabis use and because the majority of users were relatively low-dose users with short duration of use. Previous evidence that the neurocognitive effects of cannabis use are dose-related is somewhat equivocal. For example, some studies have suggested that cognitive deficits are related to the number of joints smoked per week (Bolla *et al*., 2002), duration of cannabis use (Solowij *et al*., 2002), frequency of use (Rodgers *et al*., 2001) and to cumulative lifetime use (Montgomery and Fisk, 2007). Other studies, however, have found no such relationships (Pope *et al*., 2001, 2002). In the light of these contradictory findings, the first aim of the present series of studies was to examine whether the prospective memory deficits observed in cannabis users were related to the number of joints smoked per week, to the duration of cannabis use and to the estimated lifetime consumption of cannabis.

In addition, first initiation to cannabis use among young adults typically occurs as young as 15 years (Hoare and Moon, 2010). This may be important because brain development occurs during adolescence and early adulthood and it is possible that those individuals who commence cannabis use during this critical period may be

more vulnerable to the deleterious neurocognitive effects of cannabis. Indeed, research has supported this notion noting that early-onset of cannabis use is associated with cognitive deficits (Battisti *et al*., 2010; Ehrenreich, Rinn, Kunert, Moeller, Poser, Schilling, Gigerenzer and Hoehe, 1999; Pope, Gruber, Hudson, Cohane, Huestis and Yurgelun-Todd, 2003). Furthermore, commencement of cannabis use before the age of 17 years while brain maturation is on-going is associated with reductions in cortical gray matter volume and increases in white matter volume (Wilson *et al*., 2000). No research has investigated this phenomenon in relation to prospective memory processes. As previous research has categorised early-onset as commencement of use before the age of 17 years and late-onset as commencement of use after the age of 17 years (Ehrenreich *et al*., 1999; Pope *et al*., 2003; Wilson *et al*., 2000), the second aim of the present studies was to examine whether prospective memory performance in early-onset users who commenced use before the age of 17 years differed from that of late-onset users who commenced use after the age of 17 years.

5.2 Study 1: Relationship of deficits to dose and duration of cannabis use

The aim of the present study was to examine whether the prospective memory deficits observed in cannabis users were related to the number of joints smoked per week, duration of cannabis use and to estimated lifetime consumption of cannabis. In the light of equivocal evidence that the neurocognitive effects of cannabis use are dose-related (Bolla *et al*., 2002; Montgomery and Fisk, 2007; Pope *et al*., 2001, 2002; Rodgers *et al*., 2001; Solowij *et al*., 2002) no predictions were made regarding the direction of any relationships between the various metrics of cannabis use and prospective memory performance.

5.2.1 Methodology

5.2.1.1 Design

The study employed a correlation design utilising pre-existing cannabis users who had declared use of cannabis within the previous year. The measures were the number of location-action combinations correctly recalled during the prospective memory video procedure, the number of cannabis joints smoked per week, the duration of cannabis use and an estimate of cumulative lifetime cannabis use. Level of anxiety and depression, and use of alcohol, tobacco and any other recreational drugs in addition to cannabis use were also measured and controlled for during analysis of the data. The presentation of the measures was held constant across all participants.

5.2.1.2 Participants

An opportunity sample of 52 undergraduates between the ages of 18 and 24 years studying at universities in the northeast of England participated. Data from 20 participants who reported the use of illicit recreational drugs in addition to their use of cannabis and one participant whose use of additional illicit recreational drugs was unknown were excluded. Data from a further 7 participants who preferred not to disclose the number of joints smoked, one participant who did not declare the duration of their cannabis use and 3 participants who did not declare their last use of cannabis were also excluded. The remaining sample of 20 participants was supplemented by 26 participants who completed the study described in chapter three, 24 participants who completed the study described in chapter four, 24 participants who completed the study described in chapter six and 23 participants who completed

the study described in chapter seven. The final sample of 117 participants comprised 51 males with a median age of 19 years and 66 females with a median age of 19 years. Participants smoked a median of 0.58 joints per week (range: 1 joint every 6 months to 20 joints per week), had used cannabis for a median of 2 years (range: 2 months to 7 years) with a median estimated lifetime use (number of joints smoked per year multiplied by the number of years of use) of 52 joints (range: 2 joints to 3120 joints) and had abstained from use for a median of 21 days (range: 24 hours to 8 months).

5.2.1.3 Measures

The prospective memory video procedure described in chapter two was employed to objectively gauge prospective memory performance. Cronbach's alpha confirmed that the reliability of the video procedure was acceptable in the present study ($\alpha = 0.70$).

The Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) described in chapter three was employed to gauge levels of anxiety and depression experienced during the previous week. Cronbach's alpha indicated that the reliability of the items related to anxiety was acceptable in the present study ($\alpha = 0.85$), however, reliability of the items related to depression in the present study was lower than traditionally recommended ($\alpha = 0.51$).

The substance use questionnaire described in chapter three provided details of cannabis use and ascertained estimates of weekly consumption of alcohol, tobacco and any other illicit recreational drugs in addition to cannabis. Details of duration of

use and last use were also ascertained. No additional measures of drug use were employed.

5.2.1.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. The procedure detailed in chapter two for the completion of the prospective memory video procedure was adopted for the present study. On completion of the video procedure participants completed the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) and the substance use questionnaire, both of which contained instructions for their completion. Following the completion of all tasks the participants were debriefed and thanked for their participation.

5.2.2 Results

Kolmogorov-Smirnov tests for normality revealed that the data were not normally distributed in terms of age [D (117) = 0.26, $p < 0.001$], alcohol consumption [D (115) = 0.18, $p < 0.001$] or tobacco consumption [D (106) = 0.29, $p < 0.001$]. In addition, the data obtained in relation to levels of anxiety and depression were of ordinal level. Therefore, Spearman's rho tests of correlation were performed to examine any relationship between these factors and performance in the prospective memory video procedure. These tests revealed no significant relationship between performance in the prospective memory video procedure and age [r (117) = -0.08, p

= 0.38], level of anxiety [r (117) = 0.03, p = 0.75] or depression [r (117) = -0.14, p = 0.13], alcohol consumption [r (115) = -0.12, p = 0.21] or tobacco consumption [r (106) = -0.04, p = 0.66]. Therefore, there was no need to statistically control for these factors in subsequent analyses.

Kolmogorov-Smirnov tests for normality revealed that the data were not normally distributed in terms of the number of joints smoked per week [D (117) = 0.28, p < 0.001], duration of cannabis use [D (117) = 0.22, p < 0.001] or estimated lifetime consumption of cannabis [D (117) = 0.32, p < 0.001]. Spearman's rho tests of correlation were therefore performed to ascertain whether scores on the prospective memory video procedure were related to the dose and/or duration of cannabis use. These tests revealed no significant relationship between performance in the prospective memory video procedure and number of cannabis joints smoked per week [r (117) = 0.04, p = 0.69], duration of cannabis use [r (117) = -0.12, p = 0.19] or estimated lifetime use of cannabis [r (117) = 0.001, p = 0.99].

5.2.3 Summary of findings and conclusions

The aim of the present study was to explore whether the prospective memory deficits observed in cannabis users were related to the number of joints smoked per week, duration of cannabis use and to estimated lifetime consumption of cannabis. In relation to this aim, the findings presented found no evidence that the prospective memory deficits were related to the dose or the duration of cannabis use.

The present findings did not support earlier research which suggested that deficits were related to the number of joints smoked per week (Bolla *et al*., 2002), duration

of cannabis use (Solowij *et al*., 2002) and to cumulative lifetime use (Montgomery and Fisk, 2007). It should be noted, however, that the participants in the present study had much lower levels of cannabis use than participants in these earlier studies and this may explain the lack of a relationship between scores on the prospective memory video procedure and cannabis dose and duration of use in the present study.

5.3 Study 2: The effect of age of onset of use on prospective memory

The aim of the present study was to examine whether prospective memory performance in early-onset cannabis users who commenced use before the age of 17 years differed from that of late-onset users who commenced use after the age of 17 years. Since previous research (Battisti *et al*., 2010; Ehrenreich *et al*., 1999; Pope *et al*., 2003) has shown early-onset of cannabis use to be associated with cognitive deficits it was predicted that these deficits would extend to prospective memory and that early-onset users would correctly recall fewer location-action combinations than late-onset users during the prospective memory video procedure.

5.3.1 Methodology

5.3.1.1 Design

The study employed a quasi-experimental independent measures design utilising pre-existing cannabis users who commenced cannabis use before the age of 17 years and cannabis users who commenced cannabis use after the age of 17 years. The dependent measure was the number of location-action combinations correctly recalled during the prospective memory video procedure. Level of anxiety and depression, and use of alcohol, tobacco and any other recreational drugs in addition

to cannabis use were also measured and controlled for during analysis of the data. The presentation of the measures was held constant across all participants

5.3.1.2 Participants

Of the 117 participants who completed study one, 90 completed the present study. The sample comprised 47 early-onset users who commenced cannabis use before the age of 17 years (20 males and 27 females with a median age of 19 years and a median age of first use of 16 years) and 43 late-onset users who commenced use after the age of 17 years (18 males and 25 females also with a median age of 19 years and a median age of first use of 18 years). There was no significant difference in the proportion of males and females within the early-onset users and the late-onset users [χ^2 (1) = 0.004, p = 0.95]. The early-onset users smoked a median of one joint per week (range: 1 joint every 6 months to 20 joints per week), had used cannabis for a median of 3 years (range: 1 year to 7 years) with a median estimated cumulative lifetime use of 144 joints (range: 6 joints to 3120 joints) and had abstained from use for a median of 14 days (range: 24 hours to 8 months). The late-onset users smoked a median of 0.46 joints per week (range: 1 joint every 6 months to 10 joints per week), had used cannabis for a median of one year (range: 2 months to 5 years) with a median estimated lifetime use of 36 joints (range: 2 joints to 520 joints) and had abstained from use for a median of 21 days (range: 2 days to 8 months).

5.3.1.3 Measures

The prospective memory video procedure described in chapter two was employed to objectively gauge prospective memory performance. Cronbach's alpha confirmed acceptable reliability of the video procedure in the present study ($\alpha = 0.71$).

The Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) described in chapter three was employed to gauge levels of anxiety and depression experienced by early-onset users and late-onset users during the previous week. Cronbach's alpha indicated that the reliability of the items related to anxiety was acceptable in the present study ($\alpha = 0.86$), however, reliability of the items related to depression in the present study was lower than traditionally recommended ($\alpha = 0.55$).

The substance use questionnaire described in chapter three provided details of cannabis use and ascertained estimates of weekly consumption of alcohol, tobacco and any other illicit recreational drugs in addition to cannabis. Details of duration of use and last use were also ascertained. No additional measures of drug use were employed.

5.3.1.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. The procedure detailed in chapter two for the completion of the prospective memory video procedure was adopted for the present study. On completion of the video procedure participants completed the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) and the substance use questionnaire, both of which contained instructions for their completion. Following the completion of all tasks the participants were debriefed and thanked for their participation.

5.3.2 Results

5.3.2.1 Participant demographics

Table 5.1 shows the median age, weekly consumption of alcohol, number of cigarettes smoked per week, weekly cannabis consumption, duration of cannabis use, estimated lifetime cannabis use, and median anxiety and depression scores for early-onset users and late-onset users.

Table 5.1. Median age, weekly consumption of alcohol, number of cigarettes smoked per week, weekly cannabis consumption, duration of use, estimated lifetime cannabis use, and scores for anxiety and depression in early-onset users and late-onset users (range in brackets).

	Early-Onset Users	Late-Onset Users
Age (years)	19.00 (3.00)	19.00 (5.00)
Age at commencement of use (years)	16.00 (3.50)	18.00 (3.50)
Units of alcohol consumed	25.00 (99.00)	25.00 (86.50)
Number of cigarettes smoked	3.00 (90.00)	2.25 (180.00)
Number of joints smoked	1.00 (19.96)	0.46 (9.96)
Duration of use (years)	3.00 (6.00)	1.00 (4.83)
Estimated lifetime use (joints)	144.00 (3114.00)	36.00 (518.00)
Anxiety score	7.00 (12.00)	5.00 (19.00)
Depression score	2.00 (8.00)	2.00 (9.00)

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of age [$W(47) = 0.82$, $p < 0.001$ for early-onset users and $W(43) = 0.79$, $p < 0.001$ for late-onset users], alcohol consumption [$W(46) = 0.83$, $p < 0.001$ for

early-onset users and W (42) = 0.85, p < 0.001 for late-onset users], tobacco consumption [W (43) = 0.74, p < 0.001 for early-onset users and W (38) = 0.60, p < 0.001 for late-onset users], cannabis consumption [W (47) = 0.64, p < 0.001 for early-onset users and W (43) = 0.55, p < 0.001 for late-onset users], duration of use [W (47) = 0.89, p < 0.001 for early-onset users and W (43) = 0.66, p < 0.001 for late-onset users], estimated lifetime consumption [W (47) = 0.64, p < 0.001 for early-onset users and W (43) = 0.59, p < 0.001 for late-onset users] or last use [W (47) = 0.61, p < 0.001 for early-onset users and W (43) = 0.74, p < 0.001 for late-onset users]. Although Levene's tests for the assumption of homogeneity of variance between early-onset users and late-onset users revealed no violation of the assumption in terms of age [F (1, 88) = 0.01, p = 0.92], alcohol consumption [F (1, 86) = 0.13, p = 0.72], or last use [F (1, 88) = 1.37, p = 0.24], the assumption was violated in terms of tobacco consumption [F (1, 79) = 4.49, p = 0.04], weekly cannabis consumption [F (1, 88) = 5.15, p = 0.03], duration of use [F (1, 88) = 4.61, p = 0.04] and estimated lifetime use [F (1, 88) = 9.99, p = 0.002]. In addition, data obtained in relation to level of anxiety and depression were of ordinal level.

Therefore, non-parametric Mann-Whitney U tests were performed to ascertain any significant differences between early-onset users and late-onset users in terms of age, level of anxiety and depression, and consumption of alcohol, tobacco and cannabis. These tests revealed no significant differences between early-onset users and late-onset users in terms of level of anxiety [U = 824.00, p = 0.13], or depression [U = 939.00, p = 0.56], alcohol consumption [U = 953.50, p = 0.92], tobacco consumption [U = 797.50, p = 0.85], or last use of cannabis [U = 941.50, p = 0.58]. Early-onset users, however, were younger (median = 19 years, range = 3) than late-onset users

(median = 19 years, range = 5) [U = 495.00, p < 0.001], smoked more cannabis per week (median = 1 joint, range = 19.96) than late-onset users (median = 0.46 joints, range = 9.96) [U = 721.00, p = 0.02], had used cannabis for longer (median = 3 years, range = 6) than late-onset users (median = 1 year, range = 4.83) [U = 165.50, p < 0.001] and had higher estimated lifetime use (median = 144 joints, range = 3114) than late-onset users (median = 36 joints, range = 518) [U = 426.50, p < 0.001].

5.3.2.2 Effect of early-onset versus late-onset of cannabis use

Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure [W (47) = 0.96, p = 0.14 for early-onset users and W (43) = 0.96, p = 0.09 for late-onset users]. Furthermore, Levene's test for the assumption of homogeneity of variance between early-onset users and late-onset users indicated that the assumption was not violated [F (1, 88) = 0.59, p = 0.44] and the data were of ratio level. Bonferroni corrected Spearman's rho tests of correlation indicated no significant relationships between prospective memory video procedure scores and age [r (90) = -0.06, p = 1.00], level of anxiety [r (90) = 0.05, p = 1.00] or depression [r (90) = -0.16, p = 1.00], alcohol consumption [r (88) = -0.21, p = 0.50], tobacco consumption [r (81) = -0.07, p = 1.00], weekly cannabis consumption [r (90) = 0.05, p = 1.00], duration of use [r (90) = -0.11, p = 1.00], estimated lifetime use [r (90) = 0.003, p = 1.00] or last use [r (90) = -0.08, p = 1.00]. There was therefore no justification for the inclusion of any of these factors as covariates. Analysis of variance performed to ascertain the presence of any significant differences between early-onset users and late-onset users in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure

revealed no significant effect of the age of commencement of use on prospective memory [F (1, 88) = 0.76, p = 0.39].

5.3.3 Summary of findings and conclusions

The present study explored whether prospective memory performance in early-onset cannabis users who commenced use before the age of seventeen years at a time when the adolescent brain is developing differed from performance in late-onset users who commenced use after the age of seventeen years. The findings presented found no significant difference between early-onset users and late-onset users and thereby found no evidence that prospective memory deficits were related to the age at which cannabis use commenced.

The present findings did not support earlier research which has suggested that early-onset of cannabis use has a detrimental impact on cognition (Battisti *et al*., 2010; Ehrenreich *et al*., 1999; Pope *et al*., 2003). It should be noted, however, that the participants in the present studies had much lower levels of cannabis use than participants in these earlier studies and this may explain the present findings.

5.4 Overall summary of findings and conclusions

The present series of studies had two aims. The first of these was to examine whether the prospective memory deficits observed in cannabis users were related to the number of joints smoked per week, duration of cannabis use and to estimated lifetime consumption of cannabis. The second aim was to examine whether prospective memory performance in early-onset cannabis users differed from that of late-onset users. In relation to these aims the results obtained revealed no significant

relationship between prospective memory video procedure scores and the number of cannabis joints smoked per week, duration of use, or estimated lifetime consumption of cannabis. Furthermore, the prospective memory performance of early-onset users did not significantly differ from that of late-onset users. The findings of the present series of studies, therefore, found no evidence to suggest that prospective memory deficits observed were related to dose and/or duration of cannabis use or to the age at which cannabis use commenced.

Chapter 6

The effect of cannabis use on prospective memory encoding and retrieval processes

6.1 Rationale

Previous studies described within the current programme of research have suggested that cannabis use has a detrimental effect on prospective memory performance in young adults and have further suggested that these deficits may recover following cessation of cannabis use. Furthermore, these studies have suggested that the deficits observed are not related to the quantity of cannabis smoked or to the duration of cannabis use. In order to better understand the psychopharmacological mechanisms by which cannabis use affects prospective memory it is necessary to elucidate the precise nature of the deficits observed. In order to do this it is necessary to consider the processes underlying prospective memory.

As described in chapter one the successful realisation of intentions is characterised by distinct phases during which the intention is successfully formed and encoded, then retained over a period of time during which the individual continues with their activities, and is finally executed when the appropriate retrieval context is recognised and the intended task is recalled (Ellis, 1996; Ellis and Freeman, 2008; Kliegel, *et al*., 2008). Deficits can therefore arise as a consequence of failure in the encoding of the association between the appropriate retrieval context (*when*) and the intended task to be performed (*what*) or as a consequence of the failure to recall the intention.

Previous research has noted deficits in both visual recognition and delayed visual recall in cannabis users (McHale and Hunt, 2008) suggesting that either encoding or retrieval processes could be affected. To date, however, no research has explored this phenomenon in relation to prospective memory encoding and retrieval. Furthermore, McHale and Hunt utilised different tests of recognition and recall making it impossible to ascertain whether the information to be recalled had initially been encoded. The first aim of the present study, therefore, was to explore whether the prospective memory deficits observed in cannabis users were due to deficits associated with the encoding of the task and its associated cue and/or to deficits in the retrieval of the intention.

In order to explore this issue the present study therefore employed a recognition task designed specifically for use with the prospective memory video procedure to ascertain whether those items not recalled during the prospective memory video procedure were recognised and hence had been encoded. One problem that can arise within recognition tasks, however, is the potential for individuals to simply respond to all possible stimuli. In this way the participant achieves a perfect score having failed to miss any of the targets. Indeed, Ilan, Smith and Gevins (2004) noted that acute cannabis intoxication was associated with an increase in the number of false recognitions made suggesting that cannabis use impaired sensitivity to targets. In order to mitigate this problem the present study measured the number of false recognitions (false alarms) in addition to the number of correct recognitions (successful hits) in order to estimate each participant's ability to discriminate between different stimuli (sensitivity) and their tendency to respond in a particular

way irrespective of the stimulus that was presented (response bias) (Macmillan and Creelman, 1991).

In addition, the successful retrieval of intentions is dependent upon the successful recognition of the appropriate retrieval context (*when*) and the successful recall of the intended task to be performed (*what*) (Ellis, 1996; Ellis and Freeman, 2008; Kliegel, *et al*., 2008). Consequently, failure to successfully execute intentions can arise as a consequence of failure in either, or both, of these aspects. Evidence from neuroimaging studies have further noted differential activations within the anterior prefrontal cortex and anterior cingulate cortex associated with these different aspects of prospective memory retrieval (Simons *et al*., 2006). However, no research to date has investigated whether the retrieval deficits observed in cannabis users arise as a consequence of problems associated with the recognition of the appropriate retrieval context (cue identification) and/or deficits in the recall of the intended task to be performed (intention retrieval). The second aim of the present study therefore was to address this hiatus with two objectives. Firstly, the study explored whether cannabis users made more errors than non-users in identifying the appropriate cue to act during the prospective memory video procedure. Secondly, the study explored whether cannabis users made more errors than non-users in recalling the task to be performed during the prospective memory video procedure.

In relation to the first aim, as previous findings described within the present thesis have suggested that cannabis use has a detrimental effect on prospective memory video procedure scores it was predicted that cannabis users would recall fewer location-action combinations than non-users. Furthermore, as McHale and Hunt

(2008) noted deficits in visual recognition associated with cannabis use it was predicted that cannabis users would recognise fewer intentions than non-users.

In relation to the second aim, since the successful execution of intended tasks relies upon noticing the target cue (Kliegel, Guynn and Zimmer, 2007), a process that requires attending to stimuli in the environment and previous research has indicated deficits in attention associated with cannabis use (Jacobsen *et al*., 2004; Medina *et al*., 2007; Messinis *et al*., 2006; Solowij *et al*., 2002) it was predicted that cannabis users would make more cue identification errors during the prospective memory video procedure than non-users. Additionally, since the execution of intended tasks requires that, having noticed the cue, a memory search is conducted to retrieve the intended task (Kliegel *et al*., 2007) and previous research has indicated deficits in the retrospective recall of information (Bolla *et al*., 2002; Croft *et al*., 2001; Grant *et al*., 2003; McHale and Hunt, 2008; Medina *et al*., 2007; Messinis *et al*., 2006; Nestor *et al*., 2008; Rodgers, 2000; Solowij and Battisti, 2008; Solowij and Pesa, 2010; Solowij *et al*., 2002), it was predicted that cannabis users would make more task retrieval errors during the prospective memory video procedure than non-users.

6.2 Methodology

6.2.1 Design

The study employed a quasi-experimental independent measures design utilising pre-existing groups of cannabis users who had declared use of cannabis within the previous year and non-users who had never smoked cannabis. The dependent measures were the number of location-action combinations correctly recalled during

the prospective memory video procedure, the number of correct location-action combinations identified during the recognition task (successful hits), the number of the novel location-action combinations identified during the recognition task (false alarms), the number of cue identification errors made during the prospective memory video procedure and the number of task retrieval errors made during the video procedure. Level of anxiety and depression, and use of alcohol, tobacco and any other recreational drugs in addition to cannabis use were also measured and controlled for during analysis of the data. The presentation of the measures was held constant across all participants.

6.2.2 Participants

An opportunity sample of 86 undergraduates between the ages of 18 and 24 years studying at universities in the northeast of England participated. Data from 15 participants who reported the use of illicit recreational drugs in addition to their use of cannabis and one participant whose use of additional illicit recreational drugs was unknown were excluded. Data from a further participant whose last use of cannabis was unknown and 9 participants who no longer smoked cannabis and had not smoked for more than one year were also excluded. The remaining sample of 60 participants comprised 30 cannabis users who had used cannabis within the previous year (16 males and 14 females with a median age of 19 years) and 30 non-users (16 males and 14 females with a median age of 18 years). Based on the 80% of cannabis users who disclosed information relating to their cannabis use, the cannabis users smoked a median of one joint per month (range: 1 joint every 6 months to 4 joints per week), had used cannabis for a median of one year (range: 1 year to 4 years) and had abstained from use for a median of 2 months (range: 5 days to 7 months).

6.2.3 Measures

The prospective memory video procedure described in chapter two was employed to objectively gauge prospective memory performance. In the present study, however, the focus was also on the type of error made by participants. Therefore, utilising the categorisation method described by Woods, Twamley, Dawson, Narvaez and Jeste (2007), errors were recorded as (a) a cue identification error if the participant failed to recognise the cue, (b) a task substitution error if the participant recognised the cue but carried out an incorrect task, (c) a content loss error if the participant recognised the cue but failed to recall the task to be performed, or (d) a time loss error if the participant recognised the cue and carried out the correct task but at the incorrect time during the video sequence. In addition to the number of correct location-actions recalled as described in previous studies, the total number of each type of error made was calculated to provide four scores between zero and seventeen. Cronbach's alpha confirmed that reliability of the video procedure was acceptable in the present study ($\alpha = 0.75$).

The Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) described in chapter three was employed to gauge levels of anxiety and depression experienced by cannabis users and non-users during the previous week. Cronbach's alpha indicated acceptable reliability in the present study for the items related to anxiety ($\alpha = 0.78$) and depression ($\alpha = 0.59$).

A recognition task (appendix E) developed for the study was employed to determine whether the locations and their associated actions had been successfully encoded. The task included the seventeen location-action combinations participants were

required to remember during the video procedure interspersed with seventeen novel location-action combinations related to the locations encountered within the video sequence but which had not been identified as intentions to remember. Participants were required to indicate which of the listed combinations represented those combinations they had been asked to remember during the video procedure. The number of location-action combinations correctly recognised (successful hits) and the number of novel location-action combinations incorrectly recognised (false alarms) during the task were recorded thus providing two scores between zero and seventeen. These scores were then converted to proportions of successful hits (hit rate) and false alarms (false alarm rate) and indices of sensitivity (d') and response bias (β) calculated.

The substance use questionnaire described in chapter three provided details of cannabis use and ascertained estimates of weekly consumption of alcohol, tobacco and any other illicit recreational drugs in addition to cannabis. Details of duration of use and last use were also ascertained. No additional measures of drug use were employed.

6.2.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested in small groups of six to eight participants per session in a spacious room. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. As the focus of the prospective memory video procedure in the

present study was on the errors made, the procedure followed differed slightly from that adopted in previous studies. As in previous studies, participants were informed that a list of locations and associated tasks to be performed at that location would be read out and that without writing anything down while the list was being read they were to try to remember as many of the intentions as they could. When the participants were happy to continue the list of locations and associated actions to be remembered was read aloud at a steady pace. The list was repeated and participants were reminded that the aim of the task was to recall the items at the appropriate time and therefore as they watched the video they were to record both the location and the associated action on the response sheet provided only when they reached the appropriate location cue on the video. In addition, participants were told at this point that there may be occasions where they recognised a location and remembered that they had to do something at that location but were unable to remember what it was that they had to do or that they may remember tasks that they needed to carry out but be unable to remember where they were to carry out the task. Participants were instructed that in the event of either of these situations arising they should write what they remembered in the appropriate column on the response sheet and leave the corresponding column blank. After verifying that participants understood the task requirements, the video was played. On completion of the video procedure participants completed the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994), the substance use questionnaire, and finally the recognition task, all of which contained instructions for their completion. Following the completion of all tasks the participants were debriefed and thanked for their participation.

6.3 Results

6.3.1 Participant demographics

Table 6.1 shows the median age, weekly consumption of alcohol, number of cigarettes smoked per week, and the median anxiety and depression scores of the cannabis users and non-users.

Table 6.1. Median age, weekly consumption of alcohol, number of cigarettes smoked per week, and scores for anxiety and depression in cannabis users and non-users (range in brackets).

	Cannabis Users	Non-Users
Age (years)	19.00 (3.00)	18.00 (2.00)
Units of alcohol consumed	25.00 (52.00)	12.00 (48.00)
Number of cigarettes smoked	4.00 (70.00)	0.00 (5.00)
Anxiety score	5.00 (10.00)	5.50 (11.00)
Depression score	2.00 (7.00)	1.00 (7.00)

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of age [$W(30) = 0.84$, $p < 0.001$ for users and $W(30) = 0.70$, $p < 0.001$ for non-users], alcohol consumption [$W(29) = 0.93$, $p = 0.04$ for users and $W(29) = 0.90$, $p = 0.01$ for non-users] or tobacco consumption [$W(25) = 0.61$, $p < 0.001$ for users and $W(24) = 0.37$, $p < 0.001$ for non-users]. Although Levene's tests for the assumption of homogeneity of variance between cannabis users and non-users revealed no violation of the assumption in terms of age [$F(1, 58) = 0.46$, $p = 0.50$] or alcohol consumption [$F(1, 56) = 0.07$, $p = 0.79$], the assumption was violated in terms of the number of cigarettes smoked per week [$F(1, 47) = 8.41$, $p = 0.01$]. In

addition, the data obtained in relation to levels of anxiety and depression were of ordinal level.

Therefore, non-parametric Mann-Whitney U tests were performed to ascertain any significant differences between cannabis users and non-users in terms of age, level of anxiety or depression and weekly consumption of alcohol and tobacco. These tests revealed no significant differences between cannabis users and non-users in terms of age [$U = 387.50$, $p = 0.30$], level of anxiety [$U = 389.50$, $p = 0.37$] or depression [$U = 350.00$, $p = 0.13$]. Cannabis users, however, consumed significantly more alcohol (median = 25 units, range = 52) than non-users (median = 12 units, range = 48) [$U = 245.00$, $p = 0.01$] and smoked significantly more tobacco (median = 4 cigarettes, range = 70) than non-users (median = 0 cigarettes, range = 5) [$U = 58.50$, $p < 0.001$].

6.3.2 Prospective memory retrieval

The mean number of location-action combinations correctly recalled by cannabis users and non-users during the prospective memory video procedure is shown in Figure 6.1.

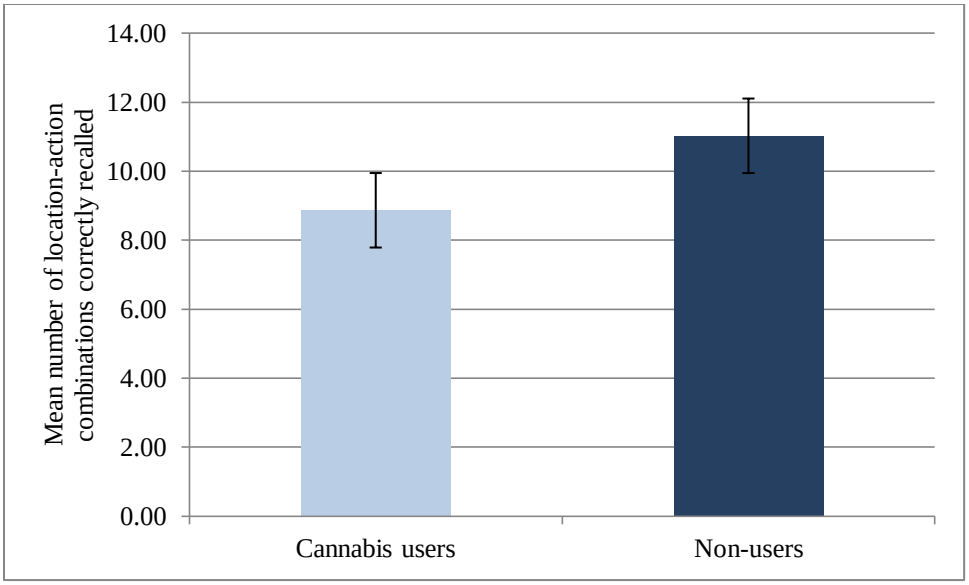

Figure 6.1. The mean number of location-action combinations correctly recalled by cannabis users and non-users during the video procedure (± 1 standard error).

Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure [W (30) = 0.97, p = 0.53 for users and W (30) = 0.98, p = 0.71 for non-users]. Furthermore, Levene's test for the assumption of homogeneity of variance between users and non-users indicated that the assumption was not violated [F (1, 58) = 3.46, p = 0.07] and the data obtained were of ratio level.

Bonferroni corrected Spearman's rho tests of correlation indicated no significant relationships between prospective memory video procedure score and level of anxiety [r (60) = 0.15, p = 1.00] or depression [r (60) = -0.08, p = 1.00], alcohol consumption [r (58) = -0.29, p = 0.14] or the number of cigarettes smoked per week [r (49) = -0.23, p = 0.54]. There was no justification, therefore, for the inclusion of these factors as covariates. There was, however, a significant relationship between prospective memory video procedure score and age [r (60) = -0.43, p = 0.005]. As

the assumption of homogeneity of regression was not violated [F (1, 56) = 0.003, p = 0.96] age was included as a covariate. Analysis of covariance performed to ascertain the presence of any significant differences between cannabis users and non-users in terms of the number of location-action combinations correctly recalled during the prospective memory video procedure revealed that, after controlling for age, there was a significant effect of cannabis use on prospective memory with cannabis users correctly recalling significantly fewer location-action combinations (mean = 8.87, standard deviation = 3.93) than non-users (mean = 11.03, standard deviation = 2.62) [F (1, 57) = 5.18, p = 0.03, η_p^2 = 0.08].

6.3.3 Prospective memory encoding

The median number of location-action combinations correctly recognised (successful hits) and falsely recognised (false alarms) by cannabis users and non-users during the recognition task is shown in Figure 6.2.

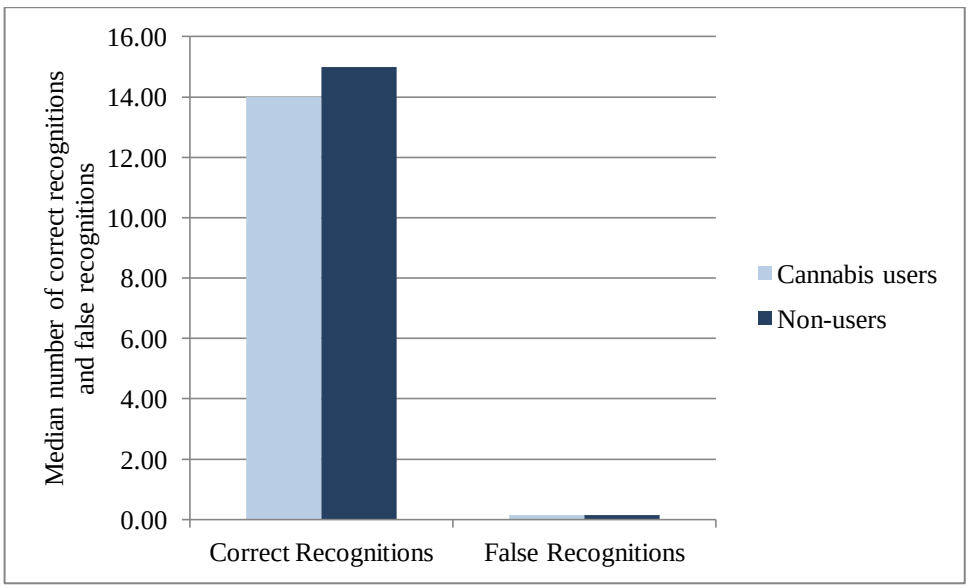

Figure 6.2. The median number of correct and false recognitions made during the recognition task by cannabis users and non-users.

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of the number of correct recognitions made [W (30) = 0.86, p = 0.001 for cannabis users and W (30) = 0.82, p < 0.001 for non-users], the number of false recognitions [W (30) = 0.48, p < 0.001 for users and W (30) = 0.55, p < 0.001 for non-users], sensitivity [W (30) = 0.87, p = 0.002 for non-users], or response bias [W (30) = 0.82, p < 0.001 for users and W (30) = 0.90, p = 0.01 for non-users]. Levene's tests for the assumption of homogeneity of variance between users and non-users indicated that the assumption was not violated in terms of the number of correct recognitions [F (1, 58) = 3.19, p = 0.08], the number of false recognitions [F (1, 58) = 0.13, p = 0.72], sensitivity [F (1, 58) = 0.35, p = 0.56], or response bias [F (1, 58) = 2.18, p = 0.15] and the data were of ratio level. As data transformations must be performed on all groups within a statistical analysis (Field, 2009) and because the data were normally distributed in terms of sensitivity among cannabis users [W (30) = 0.95, p = 0.14], transformation was not appropriate as correcting the skew within the non-users would have generated skew within the users. In addition, data transformations failed to correct the skew in terms of the number of false alarms and response bias, therefore, non-parametric Mann-Whitney U tests were performed to ascertain the presence of any significant differences between cannabis users and non-users in terms of their encoding of the intentions. These tests revealed no significant effect of cannabis use on the number of correct recognitions [U = 364.50, p = 0.20] or on the number of false recognitions [U = 440.00, p = 0.87]. Furthermore, there was no significant effect of cannabis use on sensitivity [U = 385.50, p = 0.34] or response bias [U = 415.00, p = 0.60].

6.3.4 Cue identification errors

The mean number of cue identification errors made by cannabis users and non-users during the prospective memory video procedure is shown in Figure 6.3.

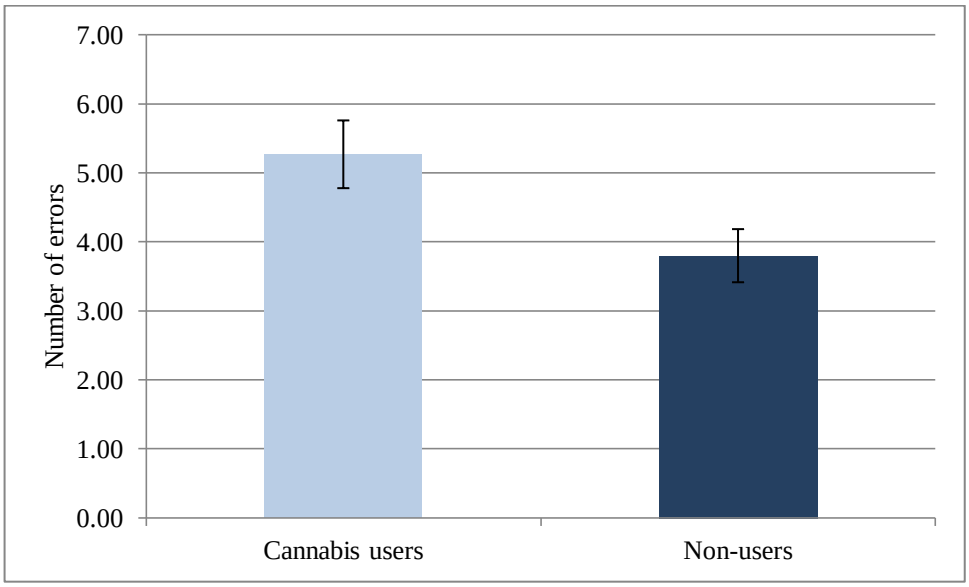

Figure 6.3. The mean number of cue identification errors made by cannabis users and non-users during the video procedure (± 1 standard error).

Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of the number of cue identification failures made during the prospective memory video procedure [W (30) = 0.97, p = 0.50 for users and W (30) = 0.95, p = 0.18 for non-users]. Furthermore, Levene's test for the assumption of homogeneity of variance between users and non-users indicated that the assumption was not violated [F (1, 58) = 1.46, p = 0.23] and the data obtained were of ratio level. Bonferroni corrected Spearman's rho tests of correlation indicated no significant relationships between the number of cue identification failures made during the prospective memory video procedure and age [r (60) = 0.29, p = 0.13], level of anxiety [r (60) = -0.19, p = 0.75] or depression [r (60) = -0.02, p = 1.00], alcohol consumption [r (58) = 0.33, p = 0.07] or number of cigarettes smoked per week [r

(49) = 0.27, p = 0.31]. There was therefore no justification for the inclusion of these factors as covariates. Analysis of variance performed to ascertain the presence of any significant differences between cannabis users and non-users in terms of the number of cue identification failures made during the prospective memory video procedure revealed a significant effect of cannabis use on cue identification with cannabis users making significantly more no response errors (mean = 5.27, standard deviation = 2.69) than non-users (mean = 3.80, standard deviation = 2.11) [F (1, 58) = 5.53, p = 0.02, η_p^2 = 0.09].

6.3.5 Task retrieval errors

The median number of task retrieval errors in terms of task substitution, content loss and time loss errors made by cannabis users and non-users during the prospective memory video procedure is shown in Figure 6.4.

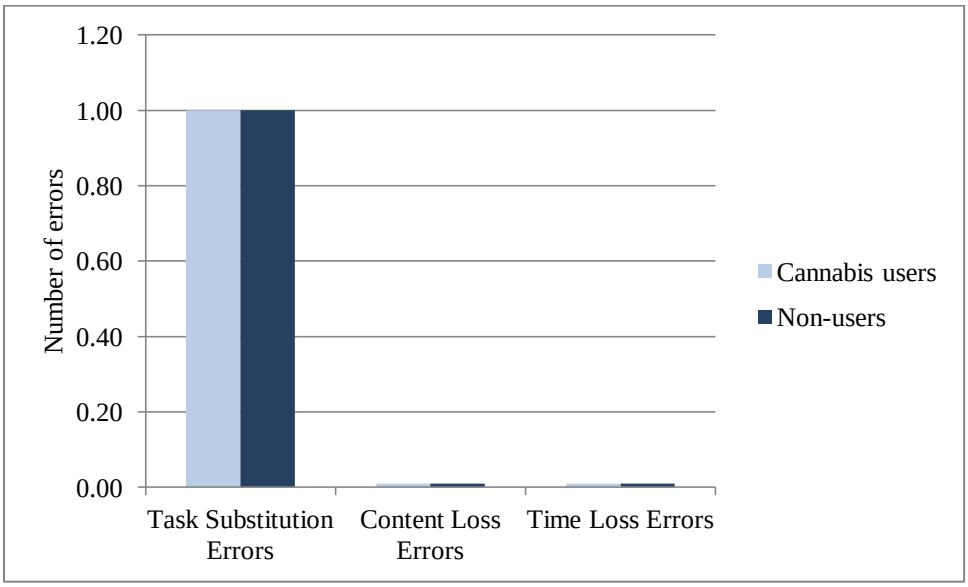

Figure 6.4. The median number of task retrieval errors made by cannabis users and non-users during the video procedure

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of the number of task substitution [W (30) = 0.89, p = 0.004 for users and W (30) = 0.87, p = 0.002 for non-users], content loss [W (30) = 0.67, p < 0.001 for users and W (30) = 0.74, p < 0.001 for non-users] or time loss [W (30) = 0.42, p < 0.001 for users and W (30) = 0.49, p < 0.001 for non-users] errors made during the prospective memory video procedure. Although Levene's tests for the assumption of homogeneity of variance between users and non-users indicated that the assumption was not violated in terms of the number of task substitution errors [F (1, 58) = 0.22, p = 0.64] or the number of time loss errors [F (1, 58) = 0.16, p = 0.69], the assumption was violated in terms of the number of content loss errors [F (1, 58) = 7.96, p = 0.007]. Data transformations failed to correct the skew in terms of the number of content loss and time loss errors. Therefore, although the data obtained were of ratio level, due to the marked degree of skew within the data and violation of the assumption of homogeneity of variances, non-parametric Mann-Whitney U tests were performed to ascertain any significant differences between cannabis users and non-users in terms of the number of task substitution, content loss and time loss errors made during the prospective memory video procedure. These tests revealed no significant effect of cannabis use on the number of task substitution errors [U = 432.00, p = 0.78], the number of content loss errors [U = 403.50, p = 0.45] or the number of time loss errors [U = 423.00, p = 0.54].

6.4 Summary of findings and conclusions

The first aim of the present study was to examine whether the deficits observed in cannabis users were due to deficits associated with the encoding of the task and its associated cue or to deficits in the retrieval of the intention. Cannabis users recalled

significantly fewer intentions in the form of location-action combinations during the prospective memory video procedure than non-users confirming once again that cannabis use has a detrimental effect on prospective memory retrieval. There were no differences, however, in the number of location-action combinations correctly recognised by cannabis users and non-users during the recognition task suggesting that the intentions had been initially encoded. Furthermore, there were no significant differences in the number of novel location-action combinations identified (false recognitions) by cannabis users and non-users suggesting that the performance of the cannabis users during the recognition task could not be explained by differences in sensitivity to the cues or to biased responding.

The findings of the present study therefore suggested that the prospective memory deficits in cannabis users were associated with deficits in processes involved in the retrieval of the intention rather than deficits in processes associated with the encoding of the task and its associated cue.

The second aim of the present study was to explore whether the retrieval deficits observed in cannabis users arise as a consequence of problems associated with the recognition of the appropriate retrieval context (cue identification) or deficits in the recall of the intended task to be performed (intention retrieval). In examining the errors made, cannabis users and non-users did not differ significantly in the number of task retrieval errors made, either in terms of carrying out an incorrect task (task substitution) or failing to recall the task to be performed (content loss). Nor did cannabis users and non-users differ in terms of carrying out a correct intention at an

inappropriate time. Cannabis users did, however, make more cue identification failures than non-users.

The findings of the present study therefore suggested that the cannabis-related prospective memory retrieval deficits arose as a consequence of problems associated with the recognition of the appropriate retrieval context in which to perform the intention rather than to failures in the retrieval of the task to be performed. In addition, these findings suggest that cannabis use may exert a detrimental impact within the medial anterior prefrontal cortex and/or the anterior cingulate cortex (Simons *et al*., 2006). As the anterior cingulate cortex is implicated in inhibition (Battisti *et al*., 2010; Gruber and Yurgelun-Todd, 2005), the present findings may therefore reflect an inability to effectively inhibit attention to distracting stimuli in the environment causing the individual to miss relevant cues.

Of further note was the observation that there were no occasions where participants recalled a task but failed to identify the location for the task. This finding supports the 'noticing and search' model which suggests that the successful execution of intended tasks relies initially upon noticing the target cue which then subsequently stimulates a memory search in order to retrieve the intention (Kliegel *et al*., 2007).

Chapter 7

Does cannabis use affect time-based prospective memory?

7.1 Rationale

Previous studies documented within this thesis have suggested that cannabis use has a detrimental effect on prospective memory performance in young adults. All of these studies employed a prospective memory video procedure based on an original idea by Titov and Knight (2001) to objectively assess prospective memory deficits and consistently found that current cannabis users recalled significantly fewer location-action combinations than non-users. The video procedure utilised in these studies, however, assesses only event-based prospective memory retrieval contexts where the intended task is performed in response to the occurrence of a specific event, for example, remembering to post a letter when you pass a post box. This is in contrast to time-based prospective memory retrieval contexts where the intended task is performed at a specific time or following the elapse of a specific duration of time, for example, remembering to meet a friend at 7pm or remembering to take a cake out of the oven in 15 minutes time.

At the initial time of planning the present study no research had investigated whether cannabis use affects prospective memory in time-based retrieval contexts. Since beginning data collection, however, McHale and Hunt (2008) have assessed time-based and event-based prospective memory in cannabis users, tobacco users and non-users. As described in chapter one this study noted that the delay between the expected and the actual execution of the short-interval task was significantly longer for cannabis users than for both tobacco users and non-users and significantly fewer

of the cannabis users remembered to return the envelope to the researchers in the long-interval task. Although McHale and Hunt employed a laboratory-based task to assess prospective memory over short time intervals they utilised a naturalistic task to assess prospective memory over long intervals. This may be important because previous research has noted that cannabis users are less likely than non-users to employ strategies to assist remembering (Rodgers *et al*., 2001). It is possible therefore, that in the long-interval task tobacco users and non-users employed some strategy upon leaving the study, for example making a note in a diary, to assist their remembering which could explain their better performance in the task. The fact that it is impossible to know precisely what strategies participants may employ outside of the laboratory environment is an inherent disadvantage of naturalistic tasks. Furthermore, in both the short-interval and the long-interval tasks there was only one occurrence of the prospective memory target. As described in chapter two, such tasks may be too simplistic with the potential for non-clinical individuals with mild deficits to attain maximal performance. It would therefore be advantageous to examine this phenomenon under controlled laboratory conditions with a more sensitive test of prospective memory and this was the first aim of the present study.

In addition, McHale and Hunt (2008) found no significant differences between cannabis users, tobacco users and non-users in event-based prospective memory. These findings do not corroborate those described in chapter three (Bartholomew *et al*., 2010), chapter four or chapter six of the present thesis which all noted cannabis related deficits during an event-based prospective memory video procedure. This discrepancy needs to be investigated further and this was the second aim of the present study. As described in chapter two, the Rivermead Behavioural Memory

Test (Wilson *et al*., 1991) utilised by McHale and Hunt has received criticism due to a lack of sensitivity (Spooner and Pachana, 2006), a problem that is compounded in McHale and Hunt's study by the use of only one of the available prospective memory sub-tests. Therefore the present study attempted to overcome this lack of sensitivity by utilising the more recently developed Cambridge Prospective Memory Test which assesses performance in both time-based and event-based retrieval contexts (Wilson *et al*., 2005).

As McHale and Hunt (2008) reported deficits in time-based prospective memory, it was predicted that non-users would perform better than cannabis users on the time-based tasks in the present study. On the basis of findings recorded throughout this thesis which have consistently suggested that cannabis use has a detrimental effect on event-based prospective memory, it was predicted that non-users would also perform better than cannabis users on the event-based tasks in the present study.

7.2 Methodology

7.2.1 Design

The study employed a quasi-experimental independent measures design utilising pre-existing groups of cannabis users who had declared use of cannabis within the previous year and non-users who had never smoked cannabis. The dependent measures were the scores based upon the number of time-based and event-based prospective memory tasks successfully completed during the Cambridge Prospective Memory Test (Wilson *et al*., 2005). Pre-morbid intelligence, level of anxiety and depression, and use of alcohol, tobacco and any other recreational drugs in addition

to cannabis use were also measured and controlled for during analysis of the data. The presentation of the measures was held constant across all participants.

7.2.2 Participants

A sample of 79 young adults between the ages of 18 and 24 years participated. The sample was derived predominantly through opportunity sampling of undergraduates studying at universities in the northeast of England and supplemented via snowball sampling. Data from 19 participants who reported the use of illicit recreational drugs in addition to their use of cannabis and 10 participants who no longer smoked cannabis and had not smoked for more than one year were excluded. The remaining sample of 50 participants comprised 25 cannabis users who had used cannabis within the previous year (9 males and 16 females with a median age of 19 years) and 25 non-users (3 males and 22 females also with a median age of 19 years). There was a significant difference in the proportion of males and females within the cannabis users (36% males and 64% females) and non-users (12% males and 88% females) [χ^2 (1) = 3.95, p = 0.05]. Based on the 92% of cannabis users who disclosed information relating to their cannabis use, the cannabis users smoked a median of 0.92 joints per week (range: 1 joint per month to 10 joints per week), had used cannabis for a median of 2 years (range: 9 months to 7 years) and had abstained from use for a median of 14 days (range: 2 days to 7 months).

7.2.3 Measures

The Cambridge Prospective Memory Test (Wilson *et al*., 2005) described in chapter two was utilised to gauge the effectiveness of prospective memory in time-based and

event-based retrieval contexts. Cronbach's alpha confirmed that the reliability of the test was acceptable in the present study ($\alpha = 0.64$).

The Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) described in chapter three was employed to gauge levels of anxiety and depression experienced by cannabis users and non-users during the previous week. Cronbach's alpha indicated acceptable reliability in the present study for the items related to anxiety ($\alpha = 0.81$) and the items related to depression ($\alpha = 0.62$).

As some of the cannabis users recruited did not meet the entry requirements for undergraduate study, the National Adult Reading Test (Nelson and Willison, 1991) was employed to estimate pre-morbid intelligence in order to control for any differences between the cannabis users and non-users. The test comprised 50 words of increasing level of difficulty which participants read aloud. These words were irregular in that they did not follow the general rules of pronunciation. Correct pronunciation, therefore, could only be achieved if the participant knew and recognised the word in its written form. The number of incorrectly pronounced words was recorded to provide an error rate score between 0 and 50 which was converted to an estimated IQ score.

The substance use questionnaire described in chapter three provided details of cannabis use and ascertained estimates of weekly consumption of alcohol, tobacco and any other illicit recreational drugs in addition to cannabis. Details of duration of use and last use were also ascertained. No additional measures of drug use were employed.

7.2.4 Procedure

The study protocol was approved by the School of Life Sciences ethics committee. Participants were tested individually. The nature of the task was explained and participants were provided with an opportunity to ask for further clarification of the task requirements. After providing informed consent the participants were each allocated a unique identifier to ensure anonymity. The Cambridge Prospective Memory Test (Wilson *et al*., 2005) was completed according to the protocol described in the test manual with two exceptions. The first was that reference to the use of strategies during the test in the initial instructions was removed. This change was implemented because research has indicated that cannabis users are less likely to use strategies than non-users (Rodgers *et al*., 2001) which could exaggerate deficits in users compared to non-users. In addition, individuals who experience problems remembering may be more likely to use this opportunity to improve their performance, particularly in a situation where they are aware their ability is under scrutiny. The second exception was that the instruction to "change to another task" was amended to read "complete this questionnaire". At this point the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) was placed on the table in front of the participant. This change was implemented to clearly differentiate the execution of the intention from simply turning the page when the current task had been completed. The substance use questionnaire was completed during the interval between the alarm signalling the end of testing and the completion on the final task and the National Adult Reading Test (Nelson and Willison, 1991) was administered according to the protocol described in the test manual on completion of the final task of the Cambridge Prospective Memory Test. Following the completion of all tasks the participants were debriefed and thanked for their participation.

7.3 Results

7.3.1 Participant demographics

Table 7.1 shows the median age, weekly consumption of alcohol, number of cigarettes smoked per week, estimated IQ, and the median anxiety and depression scores of cannabis users and non-users.

Table 7.1. Median age, weekly consumption of alcohol, number of cigarettes smoked per week, estimated IQ, and scores for anxiety and depression of cannabis users and non-users (range in brackets).

	Cannabis Users	Non-Users
Age (years)	19.00 (3.00)	19.00 (3.00)
Units of alcohol consumed	20.00 (36.50)	3.50 (37.50)
Number of cigarettes smoked	1.75 (50.00)	0.00 (60.00)
Estimated IQ	110.00 (19.00)	113.00 (14.00)
Anxiety score	5.00 (12.00)	6.00 (17.00)
Depression score	2.00 (8.00)	1.00 (6.00)

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of age [$W(25) = 0.86$, $p = 0.003$ for users and $W(25) = 0.78$, $p < 0.001$ for non-users], alcohol consumption [$W(25) = 0.80$, $p < 0.001$ for non-users] or tobacco consumption [$W(24) = 0.71$, $p < 0.001$ for users and $W(24) = 0.22$, $p < 0.001$ for non-users]. Although Levene's tests for the assumption of homogeneity of variance between cannabis users and non-users revealed no violation of the assumption in terms of age [$F(1, 48) = 0.83$, $p = 0.37$] or alcohol consumption [$F(1, 48) = 0.07$, $p = 0.79$], the assumption was violated in terms of the number of cigarettes smoked per

week [F (1, 46) = 7.13, p = 0.01]. In addition, the data obtained in relation to levels of anxiety and depression were of ordinal level. Therefore, non-parametric Mann-Whitney U tests were performed to ascertain any significant differences between cannabis users and non-users in terms of age, level of anxiety or depression and weekly consumption of alcohol and tobacco. These tests revealed no significant differences between cannabis users and non-users in terms of age [U = 220.00, p = 0.06] or level of anxiety [U = 245.50, p = 0.19]. Cannabis users, however, reported significantly more symptoms of depression (median = 2, range = 8) than non-users (median = 1, range = 6) [U = 187.00, p = 0.01], consumed significantly more alcohol (median = 20 units, range = 36.50) than non-users (median = 3.50 units, range = 37.50) [U = 85.50, p < 0.001] and smoked significantly more tobacco (median = 1.75 cigarettes, range = 50) than non-users (median = 0 cigarettes, range = 60) [U = 100.50, p < 0.001].

Shapiro-Wilk tests for normality revealed that the data were normally distributed in terms of estimated IQ [W (25) = 0.97, p = 0.56 for users and W (25) = 0.92, p = 0.06 for non-users]. Furthermore, Levene's test for the assumption of homogeneity of variance between cannabis users and non-users indicated that the assumption was not violated [F (1, 48) = 1.48, p = 0.23] and the data obtained were of ratio level. Therefore, analysis of variance was performed to ascertain any significant difference between cannabis users and non-users in terms of estimated IQ. This test revealed that cannabis users had a significantly lower estimated IQ (mean = 109.84, standard deviation = 4.19) than non-users (mean = 112.40, standard deviation = 4.59) [F (1, 48) = 4.24, p = 0.05].

7.3.2 Time-based and event-based prospective memory

The median scores based on the number of time-based and event-based prospective memory tasks successfully completed during the Cambridge Prospective Memory Test (Wilson *et al.*, 2005) by cannabis users and non-users is shown in Figure 7.1.

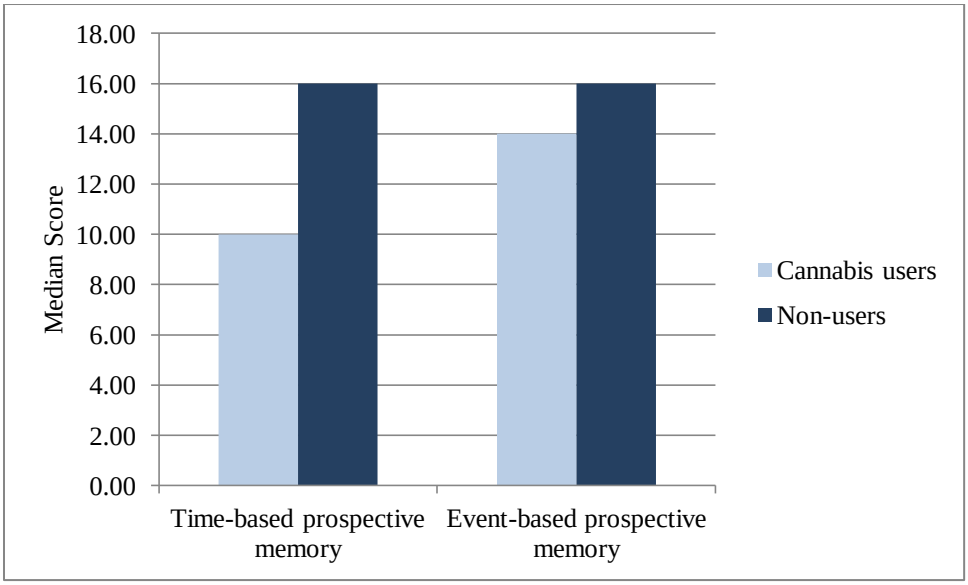

Figure 7.1. Median time-based and event-based prospective memory scores of cannabis users and non-users.

Shapiro-Wilk tests for normality revealed that the data were not normally distributed in terms of scores for time-based prospective memory [W (25) = 0.92, p = 0.045 for users and W (25) = 0.78, p < 0.001 for non-users] or for event-based prospective memory [W (25) = 0.91, p = 0.03 for users and W (25) = 0.90, p = 0.02 for non-users]. Furthermore, Levene's tests for the assumption of homogeneity of variance between users and non-users indicated that the assumption was violated in terms of scores for both time-based prospective memory [F (1, 48) = 7.11, p = 0.01] and event-based prospective memory [F (1, 48) = 5.59, p = 0.02]. Data transformations failed to correct the skew in both time-based and event-based prospective memory

and in view of the violation of assumptions of normality and homogeneity of variance, Mann-Whitney U tests were performed to ascertain the presence of any significant differences between cannabis users and non-users in terms of time-based prospective memory and event-based prospective memory. These tests revealed a significant effect of cannabis use on time-based prospective memory with cannabis users performing significantly poorer (median score = 10, range = 16) than non-users (median score = 16, range = 11) [U = 161.50, p = 0.001, r_g = 0.48, *one-tailed*]. These tests also revealed a significant effect of cannabis use on event-based prospective memory with cannabis users performing significantly poorer (median score = 14, range = 16) than non-users (median score = 16, range = 8) [U = 224.00, p = 0.04, r_g = 0.28, *one-tailed*].

7.4 Summary of findings and conclusions

The present study had two aims. The first of these was to explore the effect of cannabis use on time-based prospective memory. The second aim was to investigate the discrepancy between the findings of McHale and Hunt (2008) and previous findings documented within the present thesis in relation to event-based prospective memory.

In relation to these aims, the present study found that cannabis users performed significantly poorer than non-users on both time-based and event-based prospective memory tasks. As the size of the effect was larger for time-based prospective memory scores these findings suggested that prospective memory within time-based retrieval contexts may be more susceptible to the psychopharmacological effects of cannabis use than event-based prospective memory.

The findings of the present study in relation to the effect of cannabis use on time-based prospective memory support the findings of McHale and Hunt (2008) who noted poorer performance in cannabis users on both short-interval and long-interval time-based tasks. The present findings do not, however, support the findings of Hadjiefthyvoulou *et al*. (2011c) published since completion of the empirical research undertaken within the present thesis which found no difference between cannabis users and non-users in relation to time-based prospective memory deficits.

In relation to the second aim, the present findings support the findings of previous studies documented within the present thesis which suggest that cannabis use has a detrimental effect on event-based prospective memory. The present findings do not, however, support the findings of McHale and Hunt (2008) or the recently published findings of Hadjiefthyvoulou *et al*. (2011c), both of which found no difference between cannabis users and non-users in relation to event-based prospective memory deficits.

In addition, Okuda *et al*. (2007) noted differential haemodynamic changes associated with event-based and time-based prospective memory retrieval contexts. During the execution of time-based tasks blood flow in the anterior medial frontal lobe, anterior cingulate gyrus and right superior frontal gyrus is increased while the execution of event-based tasks is accompanied by increased blood flow in the lateral left superior gyrus and decreased blood flow bilaterally in the medial frontal lobe and anterior cingulate cortex. The present findings therefore suggest that the medial anterior prefrontal cortex, the anterior cingulate gyrus and/or the superior frontal gyrus may be particularly susceptible to the psychopharmacological effects of cannabis use.

Chapter 8
Discussion

The programme of research documented within this thesis had three major aims. The first was to evaluate the psychometric properties of a video procedure in an effort to validate an objective measure of prospective memory. The second aim was to utilise this measure in order to examine whether cannabis use affected prospective memory in young adults. The final aim was to explore the nature of any cannabis-related deficits observed in an attempt to better understand the mechanisms underpinning the psychopharmacological effects of cannabis use.

8.1 Psychometric properties of the prospective memory video procedure

In relation to the first aim, the findings documented in chapter two suggested that the prospective memory video procedure had good internal consistency and the factorial structure of the task was such that all items appeared to measure the same construct initially described as prospective memory. Evidence that the task did indeed measure the construct prospective memory was provided in the form of convergent validity between the prospective memory video procedure and existing measures of prospective memory.

In terms of convergent validity with the Prospective Memory Questionnaire (Hannon *et al*., 1995) this evidence was weak with self-reports of deficits in both long-term episodic and short-term habitual aspects of prospective memory showing only small correlations with the performance on the video procedure. This finding was not unexpected and supports previous research which notes weak correlations between

self-reports of prospective memory deficits and objective measures of ability (Bedi and Redman, 2008; Chan *et al*., 2008; Uttl and Kibreab, 2011). There was no relationship between performance on the prospective memory video procedure and self-reports of deficits in internally cued prospective memory. This was not unexpected due to the nature of the video procedure which comprises environmental cues rather than being internally cued and instead provides evidence of divergent validity.

The evidence of convergent validity with the Cambridge Prospective Memory Test (Wilson *et al*., 2005) was much stronger with moderate correlations observed between prospective memory scores obtained utilising this task and performance on the video procedure suggesting that the two measures assessed the same construct of prospective memory. The finding that scores for time-based prospective memory, were more strongly correlated with performance on the video procedure than scores for event-based prospective memory was somewhat surprising, however, given the nature of the video procedure which comprised event-based, but not time-based, target cues.

The data presented in chapter two failed to find evidence of convergent validity between self-reports of deficits in prospective memory utilising the Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) and performance on the video procedure. Uttl and Kibreab (2011), however, noted that scores on the prospective memory subscale for this questionnaire were more highly correlated with scores on the retrospective memory subscale than with scores on other self-report measures of prospective memory. Uttl and Kibreab therefore suggested that the

Prospective and Retrospective Memory Questionnaire appeared to measure a single general memory factor rather than distinct components of prospective and retrospective memory and this may explain the lack of convergent validity observed.

In pilot studies, Titov and Knight (2001) found that participants were able to successfully recall more than 25 instructions to buy items during their video procedure because of the high association between the location and the action. This led to the recommendation to introduce tasks to do, for example, "ask for directions to the station" and questions to be answered, for example, "what colour is the stall's canopy?" which have low association between the location and the action in order to increase the difficulty of the task and reduce ceiling effects. The present task included five buy items, seven do items and five questions to be answered. Scrutiny of the individual items comprising the video procedure suggested that while the majority of the items were within acceptable bounds in terms of item difficulty, two items appeared to be less difficult (both were buy items with high association) and one item appeared to be more difficult (a do item with low association). The average item difficulty over the test as a whole, however, suggested that the task difficulty was appropriate and the distribution of scores attained by participants further suggested that the prospective memory video procedure was sufficiently complex to prevent ceiling effects whilst at the same time avoiding floor effects due to the task being too difficult. The utility of the procedure is further enhanced as all items were able to discriminate between individuals with good prospective memory and those with poor prospective memory.

Whilst the prospective memory video procedure shows promise as a reliable and valid tool for the assessment of prospective memory, further evidence is warranted. For example the finding that scores on the time-based prospective memory tasks of the Cambridge Prospective Memory Test (Wilson *et al*., 2005) were more highly correlated with the prospective memory video procedures scores than scores on the event-based tasks is problematic in establishing the validity of the prospective memory video procedure which, in its present form, measures only event-based prospective memory. In addition, the studies within the present thesis did not gather evidence of discriminant validity. This is important because prospective memory draws upon a number of cognitive processes such as planning, associative learning, attention/monitoring of the environment and retrospective memory which may share variance with the task.

8.2 The effect of cannabis on self-reported prospective memory

The findings presented within this thesis in relation to self-reported prospective memory deficits associated with cannabis use were mixed. The study documented in chapter three found no significant difference between cannabis users and non-users in terms of the number of long-term episodic, short-term habitual or internally cued prospective memory failures reported when utilising the Prospective Memory Questionnaire (Hannon *et* al., 1995) while the study described in chapter four noted that cannabis users reported more failures in long-term episodic and short-term habitual, but not internally cued, aspects of prospective memory than non-users. The evidence was further confounded by the findings in chapter four which found no significant difference between cannabis users and non-users in terms of the number of prospective memory failures reported when utilising the more recently developed

Prospective and Retrospective Memory Questionnaire (Crawford *et al*., 2003) although the scales measuring short-term and environmentally cued aspects of prospective memory both indicated a trend.

The findings of these two studies did not fully support the findings of Rodgers *et al*. (2001) or those of Montgomery and Fisk (2007) and Fisk and Montgomery (2008) published since the completion of these studies. The failure of Buchanan *et al*. (2005) to replicate the factorial structure of the Prospective Memory Questionnaire (Hannon *et al*., 1995) on-line and their subsequent recommendation to exclude the short-term habitual and internally cued subscales of the on-line Prospective Memory Questionnaire, however, casts doubt on the integrity of the findings of Rodgers *et al*. who reported deficits only on these aspects. Similarly, although Montgomery and Fisk (2007) employed the traditional pencil and paper version of the Prospective Memory Questionnaire their findings should also be interpreted with caution. In particular, these authors reported cannabis to be a significant predictor of deficits in long-term episodic and short-term habitual aspects of prospective memory. As noted in chapter one, however, in both instances the model from which they drew their conclusions was not significant. In other words, the models the authors proposed did not significantly explain the deficits observed thereby making predictions of the contribution of cannabis use to the deficits somewhat irrelevant and erroneous.

Differences in the recruitment of participants may have contributed to the differences in findings as the present studies recruited undergraduates studying at universities in the northeast of England while the study by Rodgers *et al*. (2001) recruited participants from much broader demographic backgrounds via specific drug-related

websites. Furthermore, the present studies excluded participants who had declared use of any illicit recreational drugs in addition to cannabis use thus establishing a 'pure' cannabis using group while many of the participants recruited by both Rodgers *et al*. and Montgomery and Fisk (2007) also used ecstasy. Although Rodgers *et al*. noted differential effects of cannabis and ecstasy on prospective memory performance and Montgomery and Fisk noted that impairments were associated with use of cannabis but not ecstasy it is possible that the prospective memory deficits observed were associated with the long-term use of other recreational drugs or a consequence of an interaction between the different drugs being used. This does not, however, explain the difference in findings of the present studies and those of Fisk and Montgomery (2008) who also established a cannabis group who did not use other illicit recreational drugs. A further point of note was that the participants in both of the present studies were slightly younger (median age of 19 years) than those in the studies of Rodgers *et al*. (modal age of 21 to 25 years), Montgomery and Fisk (mean age of 21.5 years) and Fisk and Montgomery (mean age of 20 to 22 years for non-users and 21 years for users). It is possible, therefore, that the cannabis users in the present studies had used cannabis for shorter duration and consequently exhibited less severe deficits than those in the studies of Fisk and Montgomery, Montgomery and Fisk and Rodgers *et al*. leaving them unaware of any memory problems.

The findings documented within the present thesis supplement the growing body of evidence confirming inconsistencies of self-report measures in assessing prospective memory failures.

8.3 The effect of cannabis on objectively measured prospective memory

The findings documented within chapter three suggested that cannabis use affected prospective memory in young adults with cannabis users correctly recalling fewer location-action combinations during the prospective memory video procedure than non-users. This finding was confirmed in subsequent studies documented in chapter four and chapter six.

At the time of commencing this programme of research the present studies were the first to investigate prospective memory deficits associated with cannabis use using an objective measure of prospective memory. These findings do not support those of McHale and Hunt (2008) or those of Hadjiefthyvoulou *et al*. (2011c) published since the completion of these studies who found no differences between cannabis users and non-users in event-based prospective memory.

A potential explanation for this difference in findings relates to task complexity. In the study by McHale and Hunt (2008), participants were required to remember only one intention while participants in the study by Hadjiefthyvoulou *et al*. (2011c) were required to remember three event-based and three time-based intentions. By comparison, the prospective memory video procedure utilised in the studies within the present thesis required participants to remember to carry out seventeen intentions as part of a shopping scenario. It is possible that both McHale and Hunt and Hadjiefthyvoulou *et al*. failed to find any differences because the tasks were too simple. Furthermore, Hadjiefthyvoulou *et al*. noted that the scores for event-based prospective memory in their study demonstrated a negative skew. This suggests that the scores were subject to a ceiling effect which, as noted by Uttl (2005), may give

rise to null effects. In addition, as the study by McHale and Hunt recruited only eighteen participants and the study by Hadjiefthyvoulou *et al*. recruited only twelve participants it is possible that both of these studies lacked sufficient power to detect significant differences, particularly if the effect was small. The current findings do, however, substantiate previous research suggesting that cannabis use has detrimental effects on cognitive processes, particularly in relation to memory (Bolla *et al*., 2002; Croft *et al*., 2001; Grant *et al*., 2003; McHale and Hunt, 2008; Medina *et al*., 2007; Messinis *et al*., 2006; Nestor *et al*., 2008; Rodgers, 2000; Solowij and Battisti, 2008; Solowij and Pesa, 2010; Solowij *et al*., 2002).

8.4 The nature of prospective memory deficits

In relation to the third aim, the studies described in chapters four to seven explored the nature of the prospective memory deficits observed. This may be important in helping to elucidate the mechanisms underpinning the neurobiological impact of cannabis use on prospective memory.

The findings documented in chapter four suggested that the prospective memory deficits observed in current cannabis users recover following cessation of use with those who had previously used cannabis but who had not smoked for at least one year performing as well as those who had never smoked cannabis. Although this phenomenon has not previously been investigated in relation to prospective memory, these findings provide support for earlier research (McHale and Hunt, 2008; Pope *et al*., 2001, 2002) which also noted that cognitive deficits recover following a period of abstinence. It should be noted, however, that prospective memory performance of the previous users in the present study had not been assessed prior to their cessation

of use and it is therefore possible that these participants may have exhibited fewer deficits during their period of cannabis use. Furthermore, those classified as previous users who disclosed information relating to their cannabis use (30.23%) indicated that their use had been light and of relatively short duration (76.92% smoked one joint or less per week and all had used cannabis for three years or less). It is possible, therefore, that any deficits incurred as a consequence of cannabis use were not sufficiently severe to induce permanent damage.

Chapter five documented two studies. The first of these studies explored whether the cannabis-related prospective memory deficits were related to the number of cannabis joints smoked per week, duration of cannabis use, and to estimated lifetime cannabis use. The second study explored whether prospective memory performance in early-onset cannabis users who commenced use before the age of 17 years at a time when the adolescent brain is developing differed from performance in late-onset users who commenced after the age of 17 years. The findings presented in these studies found no evidence that the prospective memory deficits were related to the number of joints smoked per week, duration of use, estimated lifetime consumption or to the age at which cannabis use commenced.

The present findings do not support earlier research which has suggested that deficits were related to the number of joints smoked per week (Bolla *et al*., 2002), duration of cannabis use (Solowij *et al*., 2002), frequency of use (Rodgers *et al*., 2001) and to cumulative lifetime use (Montgomery and Fisk, 2007). It should be noted, however, that the participants in the present studies had much lower levels of cannabis use than participants in these earlier studies. For example, the present participants

smoked a median of 0.58 joints per week, had used cannabis for a median of 2 years and had an estimated lifetime consumption of 52 joints compared to participants in the study by Bolla *et al*. who smoked an average of 48.50 joints per week, used on average 5.80 days per week and had used for an average of 4.80 years. Similarly, participants in the study by Solowij *et al*. had used for an average of 17.10 years and used on a median of 27.90 days per month, while in the study by Rodgers *et al*. 18.64% used between one and four times per month, 9.84% used between five and twenty times per month, and 10.86% used more than twenty times per month and in the study by Montgomery and Fisk the average cumulative lifetime use of cannabis among the ecstasy-polydrug users was 4087.89 joints and among the non-ecstasy users was 1277.76 joints. This was also the case in relation to age of commencement of use where participants in the present study had lower levels of cannabis use than participants in earlier studies (Battisti *et al*., 2010; Ehrenreich *et al*., 1999; Pope *et al*., 2003). For example, early-onset users in the present study had smoked a median of one joint per week for a period of 3 years with an estimated lifetime consumption of 144 joints while late-onset users had smoked a median of 0.46 joints per week for a period of one year with an estimated lifetime consumption of 36 joints compared to participants in the study by Pope *et al*. where early-onset users had an average of 17368 and late-onset users an average of 12480 lifetime episodes and participants in the study by Battisti *et al*. who had used cannabis on at least fifteen days per month for a period of three years.

In order to gauge total lifetime use of cannabis the present study multiplied the number of joints by the duration of use. This method, however, assumes that a constant level of consumption has been maintained over the duration of use. This is

highly unlikely to be that case and therefore provides, at best, only a crude estimate of lifetime consumption.

Although this study found no significant differences between early-onset and late-onset cannabis users, the study was potentially confounded by a number of factors. Firstly, the dose and duration of cannabis use was greater for early-onset users. Therefore, had any differences emerged it would have been impossible to ascertain whether the difference was due to the age of onset or due to the increased dose and duration of use. Secondly, previous studies exploring the effect of age of onset of cannabis use on cognitive processes (Ehrenreich *et al*., 1999; Pope *et al*., 2003; Wilson *et al*., 2000) has categorised early-onset use as commencement of use before the age of 17 years and late-onset use as commencement of use after the age of 17 years. It could be argued, however, that since neural development continues into early adulthood, all participants within the study were engaged in cannabis use during a period when the brain may be particularly vulnerable to the deleterious neurocognitive effects of cannabis. Although comparison across studies becomes difficult when not comparing like-with-like, future studies may wish to reconsider this criterion for categorisation as early- or late-onset.

Having established that the prospective memory deficits associated with cannabis use recovered on cessation of cannabis use but did not appear to be related to the quantity or duration of cannabis use or associated with the age at which cannabis use commenced, the focus turned to the nature of deficits in terms of the processes underlying prospective memory affected by cannabis use. For example, the successful realisation of intentions is characterised by distinct phases during which

the intention is formed and encoded, then retained over a period of time during which the individual continues with their activities, and is finally executed when the appropriate retrieval context is recognised and the intended task is recalled (Ellis, 1996; Ellis and Freeman, 2008; Kliegel *et al*., 2008). The studies documented within chapter six set out to explore the nature of cannabis-related prospective memory deficits in relation to where they occur within these phases.

The first objective of the study documented in chapter six was to explore whether the cannabis-related prospective memory deficits arise as a consequence of failure in the encoding of the association between the retrieval context (*when*) and the intended task (*what*) or as a consequence of failure to recall the intention. Cannabis users recalled significantly fewer location-action combinations during the prospective memory video procedure than non-users, confirming once again that cannabis use has a detrimental effect upon prospective memory retrieval. There were, however, no significant differences in the number of location-action combinations correctly recognised by cannabis users and non-users during the recognition task. Furthermore, there were no significant differences in the number of novel location-action combinations identified (false recognitions) by cannabis users and non-users suggesting that the performance of the cannabis users during the recognition task could not be explained by differences in sensitivity to the cues or to biased responding. These findings suggested that the association between the appropriate retrieval context (*when*) and the intended task (*what*) had been adequately encoded and stored (and therefore were equivalently available for retrieval) across both users and non-users. Although these findings suggested that the deficits observed during the prospective memory video procedure arose as a consequence of problems in

retrieval processes it is possible that despite adequate encoding and storage the quality of the representation may not have been equivalent across users and non-users and this may have mediated the deficits observed in the retrieval of the intended tasks during the prospective memory video procedure. Future studies should investigate this potential explanation of the current findings.

These findings do not corroborate earlier research which has suggested that cannabis use has a detrimental impact upon visual recognition (McHale and Hunt, 2008). The cannabis users in the present study, however, consumed lower levels of cannabis (a median of one joint per month for a median of one year) than those in McHale and Hunt's study (used on average three times a week with an average of two joints per session) and this may explain the difference in findings between the two studies.

The second objective of the study documented in chapter six was to explore prospective memory retrieval processes. As described above, the successful retrieval of intentions is dependent upon the successful recognition of the appropriate retrieval context (*when*) and the successful recall of the intended task to be performed (*what*) (Ellis, 1996; Ellis and Freeman, 2008; Kliegel *et al*., 2008). Consequently, failure to successfully execute intentions can arise as a consequence of failure in either, or both, of these aspects. The findings documented in chapter six of the present thesis indicated that cannabis users and non-users did not differ significantly in the number of task retrieval errors. Cannabis users did, however, make significantly more errors than non-users in identifying the appropriate retrieval context. These findings therefore suggested that the cannabis-related prospective memory deficits observed during the prospective memory video procedure were attributable to failures in

recognition of the appropriate cue to perform the prospective memory task. As cannabis use has a detrimental impact upon attention (Harvey *et al*., 2007; Jacobsen *et al*., 2004; Medina *et al*., 2007; Messinis *et al*., 2006; Solowij *et al*., 2002) this may explain the present findings.

Of further note was the observation that there were no occasions where participants recalled a task but failed to identify the location for the task. This finding supports the 'noticing and search' model which suggests that the successful execution of intended tasks relies initially upon noticing the target cue which then subsequently stimulates a memory search in order to retrieve the intention (Kliegel *et al*., 2007).

In the final study of the current programme of research the focus was on the retrieval context that triggers execution of the intention. While previous studies utilised a prospective memory video procedure to assess prospective memory in event-based retrieval contexts where the intended task is performed in response to a specific event, the study documented in chapter seven focused on prospective memory in time-based retrieval contexts where the intended task is performed at a specific time or following the elapse of a specific duration of time. The findings presented indicated that cannabis users performed significantly poorer than non-users in both time-based and event-based prospective memory tasks. As the magnitude of the effect was greater for time-based prospective memory performance than for event-based prospective memory performance, the findings suggested that time-based prospective memory was particularly susceptible to the psychopharmacological effects of cannabis.

In relation to event-based prospective memory, the findings of the present study did not support the findings of McHale and Hunt (2008) or Hadjiefthyvoulou *et al*. (2011c) who noted no difference between cannabis users and non-users. The present findings do, however, corroborate those described in chapter three, chapter four, and chapter six of the present thesis which all noted cannabis-related deficits during an event-based prospective memory video procedure and those of Montgomery *et al*. (in press) who noted deficits in both time-based and event-based prospective memory utilising a virtual reality paradigm.

As described above, a potential explanation for this discrepancy relates to task complexity. In the study by McHale and Hunt, participants were required to remember only one intention while participants in the study by Hadjiefthyvoulou *et al*. and the study documented in chapter seven were required to remember three event-based and three time-based intentions. By comparison, the prospective memory video procedure utilised in previous studies within the present thesis required participants to remember to carry out seventeen intentions as part of a shopping scenario. It is possible that McHale and Hunt failed to find any differences because the tasks were too simple. Furthermore, as the study by McHale and Hunt recruited only eighteen users and the study by Hadjiefthyvoulou *et al*. recruited only twelve users it is possible that both of these studies lacked sufficient power to detect significant differences, particularly if the effect was small. Indeed, although the study documented in chapter seven recruited twenty-five users, analysis utilising G*Power indicated that, based on a partial eta squared (η_p^2) effect size from previous studies within the present thesis and a significance level of 0.05, a sample size of at least 65 participants would be required to achieve a minimum power of 0.75.

In relation to time-based prospective memory, the findings of the present study supported the findings of McHale and Hunt (2008) and Montgomery *et al*. (in press) who also reported time-based prospective memory deficits associated with cannabis use. The findings do not, however, support the findings of Hadjiefthyvoulou *et al*. (2011c) published since completion of the empirical studies within the present thesis. As Hadjiefthyvoulou *et al*. recruited only twelve cannabis users, however, it is likely that this study lacked sufficient power to detect a significant effect.

The findings documented within chapters four to seven suggested that the deficits observed in current cannabis users recover on cessation of cannabis use and that prospective memory in time-based retrieval contexts was more vulnerable to the effects of cannabis use than retrieval in event-based contexts. Furthermore, the findings presented suggested that these deficits arise as a consequence of problems in retrieval of the intentions rather than problems in their encoding and that these retrieval problems arise as a consequence of failures in cue identification rather than problems retrieving the task to be performed. The findings presented found no evidence that the prospective memory deficits observed were related to the number of joints smoked per week, duration of use, estimated lifetime consumption or to the age at which cannabis use commenced.

8.5 Neurobiology of prospective memory

As discussed in chapter one, studies employing functional neuroimaging techniques to determine those regions of the brain activated during the execution of prospective memory tasks have led to a general consensus that prospective memory is mediated by brain structures within the anterior (rostral) prefrontal cortex or Brodmann area

10 (Burgess *et al*., 2001, 2003; Gilbert *et al*., 2005; Okuda *et al*., 1998). In addition, such studies have identified those regions of the brain activated during specific prospective memory processes.

For example, in addition to the consistent pattern of lateral activation and medial deactivation in the anterior prefrontal cortex (Brodmann area 10) associated with the maintenance and realisation of intentions, Simons *et al*. (2006) noted a less lateral bilateral activation of the anterior prefrontal cortex (Brodmann area 10) during the retrieval of the intended task (intention retrieval) and activation of the medial anterior prefrontal cortex (Brodmann area 10) and the anterior cingulate cortex (Brodmann area 32/11 and 25) during recognition of the appropriate retrieval context (cue identification).

The findings of the study documented in chapter six suggested that the cannabis-related prospective memory deficits observed during the prospective memory video procedure were attributable to failures in the recognition of the appropriate cue to perform the prospective memory task rather than to failures in the retrieval of the task to be performed. These findings therefore suggest that cannabis use may exert a detrimental impact within the medial anterior prefrontal cortex (Brodmann area 10) and/or the anterior cingulate cortex (Brodmann area 32/11 and 25). As the anterior cingulate cortex is also implicated in inhibition (Battisti *et al*., 2010; Gruber and Yurgelun-Todd, 2005), the present findings may reflect an inability to effectively inhibit attention to distracting stimuli in the environment causing the individual to miss relevant cues.

In addition, Okuda *et al*. (2007) noted activation in the anterior medial frontal lobe (Brodmann area 10), anterior cingulate gyrus (Brodmann area 32/10) and right superior frontal gyrus (Brodmann area 9/10) during time-based prospective memory tasks while activations in the lateral left superior gyrus (Brodmann area 10) and deactivation bilaterally in the medial frontal lobe and anterior cingulate cortex were noted during event-based prospective memory tasks.

The findings of the study documented in chapter seven suggested that time-based prospective memory may be more susceptible than event-based prospective memory to the effects of cannabis use. These findings therefore suggest that the anterior medial frontal lobe (Brodmann area 10), the anterior cingulate gyrus (Brodmann area 32/10) and/or the right superior frontal gyrus (Brodmann area 9/10) may be particularly susceptible to the deleterious effects of cannabis use.

8.6 Neurobiological vulnerability to cannabis use

The deficits observed in the studies presented within this thesis suggest that cannabis use disrupts prospective memory processes. Cannabinoid receptors are known to be widely distributed throughout the central nervous system with highest concentrations being found in the cerebral cortex and hippocampus (Egertová and Elphick, 2000; Glass *et al*., 1997; Herkenham *et al*., 1990, 1991), including the prefrontal cortices and hippocampal formation implicated in the execution of prospective memory (Burgess *et al*., 2001, 2003; Gilbert *et al*., 2005; Okuda *et al*., 1998, 2007; Simons *et al*., 2006). The precise mechanism by which cannabis impairs prospective memory processes remains unknown although several potential explanations have been proposed.

One potential explanation is that disruption to prospective memory processes may be mediated through structural abnormalities associated with frequent, heavy cannabis use. Evidence for this position from studies utilising structural magnetic resonance imaging, however, is somewhat equivocal. For example, research has noted that commencement of cannabis use before the age of 17 years is associated with reduced cortical gray matter volume and increased white matter volume (Wilson *et al*., 2000) and that age of first use predicts enlarged tissue volume in the amygdala (Yücel *et al*., 2006) while increasing duration of cannabis use in heavy cannabis users is associated with reduced amygdala volumes (Yücel *et al*., 2008). Research has also noted that, compared to non-users, cannabis users exhibited altered tissue density in both white and gray matter, specifically in hippocampal regions (Demirakca *et al*., 2011; Matochik *et al*., 2005) which may be associated with neuronal apoptosis (Chan *et al*, 1998) and that this reduced hippocampal tissue volume is associated with increasing duration of cannabis use (Yücel *et al*., 2006, 2008). Furthermore, cannabis use is associated with increased mean diffusivity in the corpus callosum suggesting the presence of structural abnormalities which interrupt communication between the cerebral hemispheres (Arnone, Barrick, Chengappa, Mackay, Clark and Abou-Saleh, 2008). Other studies, however, have found no evidence of alterations to tissue volume (Block *et al*., 2000; Jager *et al*., 2007).

A second potential explanation is that disruption to prospective memory processes is mediated through haemodynamic changes associated with frequent, heavy cannabis use. For example, positron emission tomography and functional magnetic resonance imaging techniques have provided evidence of altered regional cerebral blood flow in the prefrontal cortices and hippocampus in cannabis users compared to non-users

(Becker *et al*., 2010; Block *et al*., 2002; Bolla *et al*., 2005; Eldreth *et al*., 2004; Gruber and Yurgelun-Todd, 2005; Jacobsen *et al*., 2004; Jager *et al*., 2007; Kanayama *et al*., 2004; Lundqvist *et al*., 2001; Nestor *et al*., 2008; Schweinsburg *et al*., 2008; Sneider *et al*., 2006, 2008). This suggests that cannabis use may interfere with cortical metabolism in those regions implicated in the execution of prospective memory tasks.

Alternatively, since the cannabinoid receptors are located on pre-synaptic axon terminals (Ameri, 1999; Egertová and Elphick, 2000; Katona *et al*., 2000) it is possible that the observed deficits are a consequence of modulation of those neurotransmitters associated with memory. For example, in rats, exposure to δ^9-tetrahydrocannabinol decreases extracellular levels of γ-aminobutyric acid (GABA) and increases extracellular levels of dopamine and glutamate in the prefrontal cortex (Pistis, Ferraro, Pira, Flore, Tanganelli, Gessa and Devoto, 2002) while reducing extracellular concentrations of acetylcholine in the hippocampus (Nava, Carta, Colombo and Gessa, 2001). In humans, exposure to δ^9-tetrahydrocannabinol reduces γ-aminobutyric acid release in hippocampal interneurons (Katona *et al*., 2000).

In relation to these three postulated mechanisms, the findings documented in chapter four which suggested that the prospective memory deficits observed in current cannabis users recover following cessation of use appear to support the notion of transient effects such as alterations in regional cerebral blood flow and/or neurotransmission rather than more permanent structural abnormalities. It is important to note, however, that prospective memory performance of the previous users in this study had not been assessed prior to their cessation of use and it is

therefore possible that these participants may have exhibited fewer deficits during their period of cannabis use. Furthermore, those classified as previous users who disclosed information relating to their cannabis use (30.23%) indicated that their use had been light and of relatively short duration (76.92% smoked one joint or less per week and all had used cannabis for three years or less). It is possible, therefore, that any deficits incurred as a consequence of cannabis use were not sufficiently severe to induce permanent structural damage.

8.7 Susceptibility of prospective memory to the effects of mood

Previous research has presented evidence of differential effects of mood upon prospective memory. Specifically, deficits in event-based prospective memory have been associated with heightened anxiety states (Harris and Menzies, 1999; Kliegel and Jäger, 2006) while deficits in time-based prospective memory have been associated with depression (Kliegel and Jäger, 2006; Rude *et al*., 1999). This literature formed the basis of the rationale within the present thesis to consider the potential effect of mood on prospective memory task performance.

The studies documented within the present thesis found no evidence of a relationship between the event-based prospective memory and anxiety across any of the studies. In addition, only one study noted a relationship between event-based prospective memory and depression, the effect of which was removed following correction for multiple outcomes. Only one study explored the relationship between time based prospective memory and mood and this study found no relationship between time-based prospective memory and either anxiety or depression. It would appear therefore that anxiety and depression have little effect on prospective memory.

8.8 Limitations and future research

Titov and Knight (2000, 2001) have shown video procedures for the assessment of prospective memory to be reliable and ecologically valid measures which show high predictive validity with *in-vivo* prospective memory performance. Data presented within this thesis provides further evidence that the prospective memory video procedure provides an objective measure of prospective memory which is reliable and which is not prone to ceiling effects in non-clinical populations with mild memory deficits. The utilisation of such procedures, however, is not without limitations. For example, while the number of intentions to be remembered enhanced the reliability and the sensitivity of the task, it has been argued that this places a heavy retrospective memory load on the individual (Phillips, Henry and Martin, 2008) and risks the task becoming a vigilance task (Ellis and Kvavilashvili, 2000; Maylor, 2008). Kelemen, Weinberg, Alford, Mulvey and Kaeochinda (2006), however, argue that increasing the number of prospective memory targets does not alter the nature of the task.

Furthermore, the prospective memory video procedure has a heavy associative learning component as a consequence of necessitating the encoding of seventeen locations and their associated tasks. This may be important within the current context because research has noted cannabis-related deficits in paired associative learning (Bolla *et al*. 2002; Croft *et al*., 2001). In addition, although some studies have found no deficits in associative learning associated with cannabis use (Fisk and Montgomery, 2008; Harvey *et al*., 2007) other research has pointed to alterations in neural metabolism during associative learning encoding even in the absence of performance deficits (Becker *et al*., 2010; Jager *et al*., 2007; Nestor *et al*., 2008).

In addition, some theorists have argued that the task does not contain a concurrent on-going task that must be interrupted and therefore does not meet the criteria for a prospective memory task (Ellis and Kvavilashvili, 2000; McDaniel and Einstein, 2007). The lack of a concurrent task potentially allows participants to rehearse the intentions to be remembered during the task. In the real-world, however, natural distractions often take the place of an explicit on-going task. Indeed, the Virtual Week (Rendell and Craik, 2000) does not require participants to engage in an on-going task as the authors argue that the design of the task is such that it reflects typical activities. In order to mitigate this criticism, however, future research paradigms wishing to employ such video procedures may wish to develop an ecologically valid concurrent task. For example, having participants assess the aesthetic qualities of the shops passed (Farrimond, Knight and Titov, 2006), count the number of bicycles and strollers (McDermott and Knight, 2004), or listen to a concurrent radio news bulletin (Potvin, Rouleau, Audy, Charbonneau and Giguère, 2010) provides opportunities for participants to become engrossed within an on-going activity and prevent potential rehearsal of the intentions. Future research paradigms may also wish to manipulate the level of distraction within the simulated environment and to explore different environments, for example, an office or factory, a university campus or a hospital ward.

Although the present protocol for the prospective memory video procedure reiterated the task instructions and asked participants to verify that they understood what was required, it was felt that the timeframe between presentation of the intentions and commencement of the task was too short and did not replicate real-world shopping scenarios. Future research paradigms could, for example, include an additional

segment of video simulating the journey to the shopping area (Knight, Harnett and Titov, 2005; Titov and Knight, 2001) in order to more accurately reflect real-world situations. A further limitation of the video procedure is that passage through the task is governed by the researcher with little interaction from the participant. Virtual reality tasks such as the Removal Task (Brooks, Rose, Potter, Jayawardena and Morling, 2004), Virtual Street (Titov and Knight, 2005) and JAAM (Jansari, Agnew, Akesson and Murphy, 2004) may help to mitigate both of these limitations.

In a pilot study, Titov and Knight (2001) noted that the inclusion of concurrent time-based tasks distracted participants such that they ignored one task while performing the other. The decision was therefore taken not to include time-based tasks within the current prospective memory video procedure paradigm. This limits the content validity of the task and future research paradigms may wish to incorporate time-based tasks in order to more fully encompass the range of tasks associated with prospective remembering.

Despite being a commercially available validated measure of generalised anxiety and symptoms of loss of interest and diminished pleasure aspects of depression, the depression scale of the Hospital Anxiety and Depression Scale (Snaith and Zigmond, 1994) utilised within the present programme of research consistently lacked an acceptable level of reliability. This was somewhat surprising as Bjelland, Dahl, Haug and Neckelmann (2002) in a review of studies assessing the reliability and validity of this scale noted that most factor analyses demonstrated the appropriate two factor solution and internal consistency statistics between 0.68 and 0.93 for the anxiety scale and between 0.67 and 0.90 for the depression scale. As Cronbach's

alpha is dependent upon the number of items (Cortina, 1993; Streiner, 2003), this may be due to the low number of items contained within the task. However, as the anxiety scale which comprises the same number of items did not suffer from this problem then this may need closer inspection. As this measure was employed in the current research only to ensure no significant differences between the groups, the low reliability coefficient was less critical than would be required for clinical decisions. Future research paradigms, however, may wish to consider utilising an alternative measure.

Since the Hospital Anxiety and Depression Scale was administered towards the end of each of the testing sessions, it is possible that any anxiety experienced by participants in the lead up to their participation may have dissipated by the time they completed the scale due to having completed most of the tests. While this applies equally to both cannabis users and non-users it is possible that scores may have been affected. Future research paradigms may wish to consider assessing mood prior to the commencement of testing.

The present thesis made the assumption that, as all participants (with the exception of those recruited to the study documented in chapter seven) were university undergraduates and had met the entry requirements of their programme, IQ would be similar across groups. This assumption may not be truly accurate and future paradigms should consider matching participants on IQ.

The studies documented within the present thesis primarily comprised cannabis users with light use and relatively short duration of use. Future research paradigms may

therefore wish to extend the current protocol to include participants with heavier and more prolonged use to ascertain whether longer-term use is more detrimental to prospective memory processes than short-term use. In addition, the purity and strength of the cannabis preparations used by the participants was not taken into account in the present studies. This may be important because it is possible that those participants who smoke preparations containing greater quantities of δ^9-tetrahydrocannabinol may experience more severe impairments than those who smoke preparations containing smaller quantities. This could be taken into consideration when gathering recreational drug use information although this may be difficult to achieve in practice as most users will tend to consume whatever can be sourced at the time. Consequently, as was the case in the current programme of research, many users will not be aware of the particular strain of cannabis being used and also the strain being used may differ from one use to another.

Studies within the present thesis were also limited by the utilisation of a quasi-experimental design. Such an approach was necessary as it would not be ethically responsible, given the psychoactive nature of cannabis, to randomly allocate non-users. However, non-random allocation on the basis of a pre-existing characteristic introduces the potential for other pre-existing differences to confound the findings. Furthermore, the recruitment of undergraduates undermines the ability to generalise the findings beyond the undergraduate population. Many chronic cannabis using adolescents disengage from education and this may explain the pattern of cannabis use observed with predominantly low dose and short duration of use.

The programme of research undertaken within the present thesis was not funded and this led to two important limitations. Firstly, it meant that it was not possible to employ biological measures of cannabis use and abstinence. This may have impacted upon the reliability of dose-related analyses from self-reported estimates of use. Secondly, it meant that it was not possible to employ neuroimaging techniques to ascertain the neurobiological vulnerability of prospective memory processes to cannabis use. Instead, the conclusions drawn from the present series of findings in relation to the impact of cannabis use on neurobiological processes underpinning prospective memory are somewhat speculative due to the reliance on a review of the literature exploring the neurobiology of prospective memory in healthy adults and the literature exploring the neurobiological vulnerability to cannabis use. Future paradigms which are not subjected to the financial constraints incurred in the present programme of research may wish to extend the current protocol to incorporate neuroimaging techniques such as positron emission tomography and functional magnetic resonance imaging to explore the pattern of haemodynamic changes associated with prospective memory in cannabis users.

Executive processes can be categorised functionally into processes required for planning, attention switching (set-shifting), monitoring and updating of information, and inhibition of responses (Miyake, Friedman, Emerson, Witzki, Howerter and Wager, 2000). As neuroimaging studies have revealed that executive functioning is subserved by prefrontal and parietal regions (Collette and Van der Linden, 2002; Collette, Van der Linden, Laureys, Delfiore, Degueldre, Luxen and Salmon, 2005; Wager and Smith, 2003) it seems reasonable to presume that deficits in prospective memory are underpinned by deficits in executive functioning. Indeed, research has

indicated that the successful realisation of intentions relies on executive processes particularly in relation to planning and monitoring (Kliegel, Altgassen, Hering and Rose, 2011; Kliegel, Eschen and Thöne-Otto, 2004; Kopp and Thöne-Otto, 2003; Marsh and Hicks, 1998; Martin, Kliegel and McDaniel, 2003). Although previous research has suggested that cannabis use has a detrimental effect on executive functioning (Battisti *et al*., 2010; Bolla *et al*., 2002; Bolla *et al*., 2005; Croft *et al*., 2001; McHale and Hunt, 2008; Medina, *et al*., 2007; Messinis *et al*., 2006; Solowij *et al*., 2002; Whitlow *et al*., 2004) these studies did not examine prospective memory. Although Fisk and Montgomery (2008) assessed executive processes, associative learning and prospective memory in the same cohort, they found no significant differences between cannabis users and non-users in either associative learning or executive functioning despite finding self-reported evidence of prospective memory deficits. Two possible conclusions can be drawn from this, either the cannabis users exaggerated the extent of their problems as a consequence of their perceptions about the impact of the drug (stereotype threat) or the executive function tasks utilised lacked ecological validity in terms of their application to real-world performance. Future research paradigms may therefore wish to employ more ecologically valid measures of executive functioning in order to ascertain the extent to which executive functioning deficits subserve prospective memory deficits in cannabis users.

8.9 Conclusions

The present thesis documents a series of quasi-experimental studies comparing cannabis users and non-users in order to examine the effect of cannabis use on prospective memory and explore the nature of any deficits observed in an attempt to

better understand the mechanisms underpinning the effects of cannabis use. The findings across all of the studies documented suggested that cannabis use, even in relatively light users with short duration of use, has a detrimental effect on prospective memory in young adults although users did not appear to be aware of these deficits. In addition, the findings presented suggested that the deficits observed in current cannabis users recover on cessation of cannabis use and that time-based prospective memory was more vulnerable to the effects of cannabis use than event-based prospective memory. Furthermore, the findings presented suggested that these deficits arise as a consequence of problems in retrieval of the intentions rather than problems in their encoding and that these retrieval problems arise as a consequence of failures in cue identification rather than problems retrieving the task to be performed. The findings presented found no evidence that the prospective memory deficits observed were related to the number of joints smoked per week, duration of use, estimated lifetime consumption or to the age at which cannabis use commenced. Although the scale of the deficits appeared trivial with cannabis users recalling, on average, only two items fewer than non-users, the magnitude of the effect was moderate suggesting practical significance, particularly as the deficits were observed in independent cohorts comprising cannabis users with light use and relatively short duration of use.

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Appendices

Appendix A: Prospective Memory Video Procedure

A list of locations and associated tasks will be read out to you. Without writing anything down while the list is being read you are to try to remember as many of these as you can. A short video will then be played during which you will see the locations where you have been asked to perform a particular task. When you see an appropriate location cue, write the location and the task on the response sheet provided. Do you have any questions?

Location	**Associated Action**
At the Link	What instrument is the man playing?
At the Orange shop	Buy a £10 top-up voucher
When the man asking for change	Check your pockets for 20p
At Dixon's	Ask the price of Play Station 2
At the picture stall	Who is the famous bear?
At Halifax	Check whether your loan cheque has cleared
The first man pushing a pushchair	Use your mobile to send a text
At WH Smith	Ask if there are any job vacancies
At the flower stall	What colour is the stall's roof?
At Burger King	Buy a milkshake
At Boots	What is the boy wearing on his face?
At Thornton's	Buy a bag of toffee
At the mobile phone stall	Ask for directions to the station
The woman sitting on the bench	Ask her the time
At H Samuel	Buy a watch battery
At Wallis	How many phone boxes are there outside?
At HMV	Buy a CD

Appendix B: Prospective Memory Questionnaire (Hannon *et al.*, 1995)

Section A

For each item, circle the position along the scale that best indicates your forgetting during the indicated time interval. For example, if you forgot to water your plants approximately 3 times in the last month you would respond as indicated below:

In the last month I forgot to water my plants:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

If an item does not apply to you during the specified time please circle NA next to the item. For example, if you have no plants you would respond as indicated below:

In the last month I forgot to water my plants:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

Please be sure to respond to each question and answer to the best of your knowledge.

1. In the last **month** I missed appointments I had scheduled:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never 3 times 6 or more times

2. In the last **month** I forgot to follow a change in my usual routine:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

3. In the last **year** I forgot to send a card for a birthday or anniversary:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never 3 times 6 or more times

4. In the last **week** I forgot to make an important phone call:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

5. In the last **month** I told someone something that I did not mean to tell:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

6. In the last **month** I forgot to return something I borrowed:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

7. In the last **week** I forgot to pick up items I needed when shopping:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

8. In the last **week** I forgot to meet a friend on time:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

9. In the last **week** I forgot to pass on a message to someone:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

10. In the last **week** I forgot to run an errand I meant to do:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never 3 times 6 or more times

11. In the last **week** I forgot to return a phone call:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

12. In the last **month** I forgot to make an appointment I needed to make (e.g., doctor or dentist):

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

13. In the last **month** I forgot to write an important letter:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

14. In the last **month** I forgot to return books to the library by the due date:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

15. In the last **month** I forgot to tip when I finished dinner at a restaurant:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

16. In the last **week** I forgot to turn my alarm clock off when I got up in the morning:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

17. In the last **week** I forgot to lock the door when leaving my apartment or house:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

18. In the last **month** I forgot to take my keys out of my car before locking the doors:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

19. In the last **week** I forgot to button or zip some part of my clothing as I was dressing:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

20. In the last **month** I forgot to pay the bill when finishing a meal at a restaurant:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

21. In the last **month** I forgot to put a stamp on a letter before mailing it:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

22. In the last **week** I forgot to comb my hair in the morning:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

23. In the last **week** I forgot to put on deodorant after showering or bathing:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

24. In the last **week** I forgot to flush the toilet:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

25. In the last **month** I forgot to get the groceries out of the car when I got home from the store:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

26. In the last **week** I forgot to lock up my house, bike, or car:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

27. In the last **week** I forgot to shower or bathe:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

28. In the last **month** I forgot to cash or deposit my paycheque before my account ran out of money:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

29. In the last **week** I forgot what I wanted to say in the middle of a sentence:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

30. In the last **week** I forgot to say something important I had in mind at the beginning of a conversation:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

31. In the last **week** I forgot what I came into a room to get:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

32. In the last **week** I started to do something, and then forgot what it was I wanted to do:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

33. In the last **month** I forgot to bring something I meant to take with me when leaving the house:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

34. In the last **week** I got part way through a chore and forgot to finish it:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

35. In the last **month** I was driving and temporarily forgot where I was going:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

36. In the last **month** I dialled someone on the phone and forgot who I had called by the time they answered:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

37. In the last **month** I started writing a note or letter and forgot what I wanted to say:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

38. In the last **month** I started to write a cheque and forgot to whom it was to be paid:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦ NA

never twice 4 or more times

Section B

For each item, circle the position along the scale that best indicates the number of times you have used that particular strategy **in the last week**.

39. I make lists of things I need to do:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

40. I write myself reminder notes:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

41. I make a grocery list whenever I go shopping for food:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

42. I plan my daily schedule in advance so I will not forget things:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

43. I repeat things I need to do several times to myself in order to remember:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

44. I use external reminders like tying a string around my finger to help me remember to do things:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

45. I rehearse things in my mind so I will not forget to do them:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

46. I lay things I need to take with me by the door so I will not forget them:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

47. I make post-it (sticky notes) reminders and place them in obvious places:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

48. I create mental pictures to help me remember to do something:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

49. I put things in piles so I know which ones to do first and which can wait:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

50. I lay in bed at night and think of things I need to do the next day so I won't forget to do them:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

51. I try to do things at a regular time so I will remember to do them:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

52. I keep an appointment book updated in order to remember to do things:

¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦-----¦

never twice 4 or more times

Appendix C: Prospective and Retrospective Memory Questionnaire (Crawford *et al.*, 2003)

For each item please circle the response that most accurately describes your forgetting. For example, if you rarely forget something you decide to do in a few minutes time, your response will be:

Never Rarely Sometimes Quite Often Very Often

1. Do you decide to do something in a few minutes' time and then forget to do it?
   Never Rarely Sometimes Quite Often Very Often
2. Do you fail to recognize a place you have visited before?
   Never Rarely Sometimes Quite Often Very Often
3. Do you fail to do something you were supposed to do a few minutes later even though it's there in front of you, like take a pill or turn off the kettle?
   Never Rarely Sometimes Quite Often Very Often
4. Do you forget something that you were told a few minutes before?
   Never Rarely Sometimes Quite Often Very Often
5. Do you forget appointments if you are not prompted by someone else or by a reminder such as a calendar or diary?
   Never Rarely Sometimes Quite Often Very Often
6. Do you fail to recognize a character in a radio or television show from scene to scene?
   Never Rarely Sometimes Quite Often Very Often
7. Do you forget to buy something you planned to buy, like a birthday card, even when you see the shop?
   Never Rarely Sometimes Quite Often Very Often
8. Do you fail to recall things that have happened to you in the last few days?
   Never Rarely Sometimes Quite Often Very Often
9. Do you repeat the same story to the same person on different occasions?
   Never Rarely Sometimes Quite Often Very Often
10. Do you intend to take something with you, before leaving a room or going out, but minutes later leave it behind, even though it's there in front of you?
    Never Rarely Sometimes Quite Often Very Often
11. Do you mislay something that you have just put down, like a magazine or glasses?
    Never Rarely Sometimes Quite Often Very Often
12. Do you fail to mention or give something to a visitor that you were asked to pass on?
    Never Rarely Sometimes Quite Often Very Often
13. Do you look at something without realising you have seen it moments before?
    Never Rarely Sometimes Quite Often Very Often
14. If you tried to contact a friend or relative who was out, would you forget to try again later?
    Never Rarely Sometimes Quite Often Very Often
15. Do you forget what you watched on television the previous day?
    Never Rarely Sometimes Quite Often Very Often
16. Do you forget to tell someone something you had meant to mention a few minutes ago?
    Never Rarely Sometimes Quite Often Very Often

Appendix D: Substance Use Questionnaire

The following questions relate to any substances you may use. Please answer all questions as truthfully and accurately as you can (remember your answers are completely anonymous).

---

1. Have you ever drunk alcohol? Yes ☐$_1$ No ☐$_2$ **If no please go to question 2**
   a. How many units do/did you usually drink in an average week (1 unit = ½ pint of beer or lager, 1 standard glass of wine, 1 measure of spirits or 1 alcopop)? _____
   b. How many years have you been drinking/did you drink alcohol? _____
   c. How long is it since your last alcoholic drink? _____

2. Have you ever smoked tobacco? Yes ☐$_1$ No ☐$_2$ **If no please go to question 3**
   a. How many cigarettes do/did you usually smoke each week? _____
   b. How many years have you been smoking/did you smoke tobacco? _____
   c. How long is it since your last cigarette? _____

3. Have you ever used cannabis? Yes ☐$_1$ No ☐$_2$ **If no please go to question 4**
   a. What form of cannabis do/did you use?
      Herbal cannabis/marijuana ☐$_1$
      Cannabis resin/Hashish ☐$_2$
      Cannabis oil ☐$_3$
   b. How often do/did you use cannabis?
      Less than once per month ☐$_1$
      At least once per month ☐$_2$
      Weekly ☐$_3$
      Daily ☐$_4$
   c. How much cannabis do/did you use (e.g. 20 joints/month)? _____
   d. What variety of cannabis do/did you use? _____
   e. How many years have you been using/did you use cannabis? _____
   f. How long is it since you last used cannabis? _____

4. Have you ever used other recreational drugs? Yes ☐$_1$ No ☐$_2$ **If no please go to end**
   Which recreational drugs do/did you use?

Recreational drug used?	Frequency of use (daily, weekly, monthly, less than once per month)?	Amount used?	Duration of use?	Last use?
e.g. Ecstasy	Less than once per month	1 pill/3 mths	2 years	2 weeks ago

(Please continue overleaf if you need more space)

Thank you for your assistance.

Appendix E: Recognition Task

Below is a list of locations and tasks to perform at that location, some of which you were asked to remember as part of the video task and some are not. Please place a tick next to the ones you were asked to remember.

	Location	**Action**
	Man asking for change	Check your pockets for 20p
	Clinton Cards	What occasion is being advertised?
	Pavers Shoes	Hand in your CV
	Woolworth	Buy pick 'n' mix sweets
	Wallis	How many phone boxes are outside
	Boots	What is the boy wearing on his face?
	Body Shop	Buy body lotion
	Game	Buy PlayStation 2 game
	Flower stall	What colour is the stalls canopy?
	Halifax	Check whether loan check has cleared
	H Samuel	Buy a watch battery
	Jessop	Price digital cameras
	Bonmarche	How many phone boxes outside?
	Dixons	Ask price of PlayStation 2
	Woman who says "nice day today"	Ask the time
	Card Store	Ask directions to nearest post box
	Flower Stall	Buy flowers for your mum
	First man with pushchair	Use mobile to send a text
	Picture stall	Who is the famous bear?
	Etam	Exchange jumper
	The Link	What instrument is the man playing?
	HMV	Buy a CD
	Girl with dog	What colour is the woman's jacket?
	Man playing instrument	Give him 20p
	Woman sitting on bench	Ask her the time
	Mobile phone stall	Ask directions to the station
	Burger King	Buy a milkshake
	Waterstone	Buy a £10 book token
	Thornton	Buy a box of toffees
	Tiny	How many people are outside?
	Newspaper barrow	Use mobile to phone a friend
	The Orange shop	Buy a £10 top-up voucher
	Vodafone	Buy a £5 top-up voucher
	WH Smith	Ask about job vacancies

Appendix F: Breakdown of participation across different studies

Chapter	2a	2b	2c	3	4	5a	5b	6	7
2a	1057	640	-						
		-	80						
3				45 CU 45 NU		26 CU	22 CU		
4					43 CU 43 PU 43 NU	24 CU	16 CU		
5a						20 CU	15 CU		
6						24 CU	17 CU	30 CU 30 NU	
7						23 CU	20 CU		25 CU 25 NU

Key:

CU = Current cannabis user (within the last year)

PU = Previous cannabis user (at least one year since last use)

NU = Non-user (never used)