THE EFFECT OF ECSTASY/POLYDRUG USE ON PROSPECTIVE MEMORY AND EXECUTIVE PROCESSES

by

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Abstract

The purpose of this thesis was to examine the range of prospective memory and executive function deficits in ecstasy/polydrug users and the role of these processes in accounting for the observed prospective memory performance deficits. Using a variety of laboratory and self-report measures of prospective memory and a self-report measure of executive function, ecstasy/polydrug users were tested in laboratory settings on measures of event and time-based, short and long term prospective memory as well as on a wide range of executive function components. It was found that ecstasy/polydrug users in relation to non-users experience more general prospective memory problems as ecstasy/polydrug-related deficits were evident on both time and event-based and short and long-term prospective memory. Ecstasy/polydrug users also demonstrated deficits on executive processes suggesting that recreational drug users are impaired in a broader range of executive function and ecstasy/polydrug-related deficits are not restricted to the three-model component of executive function. It was also found that executive dysfunction is associated with poorer time-based prospective memory and perhaps some of the drug related prospective memory deficits are mediated by drug related executive function impairment. Finally, although few prospective memory or executive function performance deficits were evident among cannabis-only users a trend was evident in all investigations; ecstasy/polydrug users perform the worst, cannabis-only users at intermediate levels and drug-naïve perform the best. The most striking finding of the present thesis was that the recreational use of cocaine was associated with PM deficits; an association that consistently emerged in all studies of PM performance. The outcomes of the present thesis provide a fruitful direction for future research.

Abbreviations

5-HT	5-Hydroxytryptamine
5-HIAA	5-Hydroxyindoleaceticacid
ABI	Aquired Brain Injury
ADHD	Attention/deficit hyperactive disorder
ANOVA	Analysis of Variance
ASD	Autism Spectrum Disorder
BA	Broadmann's area
BD	Bipolar Disorder
BRIEF	Behavioural Rating Inventory Executive Function
CAMPROMPT	Cambridge Prospective Memory Test
CANTAB	Cambridge Neuropsychological Test Battery
CE	Central Executive
CFQ	Cognitive Failures Questionnaire
CSF	Cerebrospinal Fluid
DEX	Dysexecutive Questionnaire
EEG	Electroencephalograph
EF	Executive Function
EMQ	Everyday Memory Questionnaire
FAB	Frontal Assessment Battery
fMRI	Functional Magnetic Resonance Imaging
HKLLT	Hong Kong List Learning Test
MANCOVA	Multivariate Analysis of Covariance
MANOVA	Multivariate Analysis of Variance
MCQ	Memory Compensation Questionnaire
MDA	Methylenedioxyamphetamine
MDD	Major depressive disorder
MDMA	Methylenedioxymethamphetamine
OCD	Obsessive Compulsive Disorder
PASAT	Paces Auditory Serial Addiction Task
PFC	Prefrontal Cortex
PM	Prospective Memory
PMQ	Prospective Memory Questionnaire
PRMQ	Prospective Retrospective Memory Questionnaire
PRVP	Prospective Remembering Video Procedure
PTA	Post Traumatic Amnesia
RAVLT	Rey Auditory Verbal Learning Test
RBMT	Rivermead Behavioural Memory Test
rCBF	Regional Cerebral Blood Flow
RM	Retrospective Memory
RNG	Random Number Generation

ROCF	Rey-Osterrieth Complex Figure
ROI	Regions Of Interest
SAS	Supervisory Attentional System
SERT	Serotonin Transporter
SPECT	Single Photon Emission Computed Tomography
TBI	Traumatic Brain Injury
THP	Tryptophan Hydroxylase
TMT-B	Trail Making Test-B
TOH	Tower Of Hanoi
TOL	Tower Of London
TWTE	Test-Wait-Test-Exit
VSWM	Visuospatial Working Memory
WCST	Wisconsin Card Sorting Task
WM	Working Memory
WMS-R	Wechsler Memory Scale-Revised
WWW	World Wide Web

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Chapter 1: Thesis Overview

The aim of this thesis is to provide an insight into the impact of ecstasy/polydrug use on aspects of cognition such as Prospective Memory and Executive Functioning that are involved in our everyday activities and play a crucial role in our day-to-day functioning. In Chapter 2 the psychological processes that underline remembering to perform an intended action are discussed. A concise account of the classification of prospective memory, the major theoretical models and the neuroanatomical basis of prospective memory is provided. Chapter 3 evaluates the multidimentional construct of executive processes by exploring the most established executive function models and their biological underpinnings.

Chapter 4 explores the effect of Ecstasy (MDMA) on the brain and its biological underpinnings in both animal and human studies. Chapter 5 provides a concise account of prospective memory deficits in recreational users of ecstasy throughout the literature. It also discusses the different experimental approaches adopted to investigate the effect of ecstasy use on this important aspect of day-to-day memory functioning. Chapter 6 explores the plethora of studies investigating the effect of recreational drug use on the three major components of executive function, updating, shifting and inhibition. It therefore summarises most important findings in this area in order to establish a coherent understanding of the ecstasy-related effect on different components of executive function.

Chapters 7, 8, 9 and 10 are the empirical chapters of this thesis that investigate prospective memory and executive processes in ecstasy/polydrug users. Chapter 7 investigates the impact of ecstasy/polydrug use on real world memory i.e., everyday memory, cognitive failures and prospective memory adopting both laboratory-based and self-report measures of prospective memory. In chapter 8 the range of laboratory measures of prospective memory is augmented by the use of the CAMPROMPT test battery in order to investigate the impact of illicit drug use on event and time-based prospective memory in a sample of cannabis only, ecstasy/polydrug and drug naïve controls. Measures of retrospective memory and learning are also administered in this chapter. Chapter 9 investigates the impact of recreational use of ecstasy on executive processes using a self-report measure of executive function; the Behavioural Regulation Index of Executive Function-Adult Version (BRIEF-A). In chapter 10 both prospective memory and executive function measures are adopted in order to investigate the role of executive processes in accounting for prospective memory deficits observed in ecstasy/polydrug users.

The final chapter is the general discussion of the findings from all four empirical chapters. Consequently, Chapter 11 discusses the findings of this thesis in terms of their implications for recreational drug users, identifies possible limitations and provides directions for future research.

Chapter 2: Real World Memory and Prospective Memory

Chapter Overview

The purpose of this chapter is to explore the distinct form of memory known as prospective memory and evaluate its impact on everyday functioning. Although the concept of prospective memory has been investigated extensively for the past 30 years, it still remains somehow elusive. Different definitional approaches have been discussed in the literature debating the role of retrospective memory in prospective remembering and the importance of non-cognitive components (such as motivation, reward or conflicting goals) in the successful completion of prospective memory tasks (Einstein & McDaniel, 1996). The different approaches and theoretical models are therefore discussed in this chapter.

When people complain about how poor their memory is, they don't usually refer to the intricacies in remembering the title of a film they watched days ago or remembering a newspaper article. They usually refer to their everyday cognitive lapses and the failure to recognise acquaintances, forget important events that occurred the previous day, forget the location of familiar objects around the house or forget to take essential objects when leaving the home or office and so on. These aspects of memory lapses fall under the term real world memory and refer to everyday memory (Sunderland *et al.,* 1983) and cognitive failures (Broadbent *et al.,* 1982). An additional aspect of the term real world memory involves the

ability to remember to attend a meeting, pass on a message or perform everyday intended actions such as remembering to buy milk from the store; an aspect that has been coined as Prospective memory (PM). According to Brandimonte, Einstein and McDaniel (1996) PM refers to the ability to perform activities in the future or simply to "remember to remember". The focus of memory research was traditionally on the recollection of past events and information or retrospective memory (RM). One of the most important reasons as to why PM has gained increased attention in recent years (Crawford *et al.*, 2003; Kliegel *et al.*, 2000; 2001; 2005; Marsh & Hicks, 1998) is the extent to which PM lapses can interfere with an individual's everyday functioning. For example, forgetting to buy milk from the store on your way home or forgetting to pick up your dry-cleaning seems inconsequential. Forgetting to take your medication, miss important appointments or interviews, however, can have serious consequences.

Loftus in 1971 was the first researcher to focus on PM. Subsequent research in this new memory field was very slow due to the fact that only a few researchers were interested in this aspect of memory. A milestone for PM was the publication of the first book on the topic in 1996 by Brandimonte, Einstein and McDaniel which although focusing on only the main developments in the area, identified important aspects for future research. From then on, PM has generated considerable interest and has become an important research focus for some researchers (McDaniel & Einstein, 2000; Einstein & McDaniel, 2005)

2.1 Prospective Memory and delayed intentions

According to the literature, PM is the ability to perform activities in the future (Brandimonte, Einstein & McDaniel, 1996; Kliegel *et al.,* 2001; Kliegel *et al.*, 2005) and represents a form of explicit episodic memory that involves the completion of intentions that cannot be realized when initially formed (Ellis, 1996). The ability to retain, recall and realise intentions is an important aspect in everyday memory failures, more specifically in PM (Eldridge, Sellen and Bekeian, 1991; Terry, 1988). Evidence from diary studies suggests that nearly half (West, 1984) or even up to 70% (Terry, 1988) of memory failures in the real world context involve the forgetting of intentions rather than the forgetting of information. Consequently, in order to capture the multidimentional concept of PM, understanding the role of delayed intentions is essential. According to Kvavilashvili and Ellis (1996), delayed intentions are the ones that must be retained and recalled at another moment in the future.

Ellis (1996) distinguishes five phases that are involved in the realization of a delayed intention; *Formation and encoding of intention and action* (associated with the retention of an action i.e., *what* you want to do, an intent i.e., *the decision* to do something and the retrieval context describing the criteria for recall i.e., *when* the intention and action should be retrieved), *Retention Interval* (refers to the delay between encoding and the initiation of a potential performance interval), *Performance Interval* (refers to the performance interval or period when the intended action should be retrieved), *Initiation and Execution of Intended Action* and *Evaluation of Outcome*.

Ellis (1996) also suggested that for the realization of a delayed intention both prospective and retrospective components are important and that the first phase of the model (formation and encoding of intention and action) forms the retrospective component of the intention and the remaining phases the prospective component. In relation to this, Crawford *et al.,* (2003) argued that PM is concerned with the timing of when things are to be remembered as opposed to RM that is concerned with what should be remembered, and although PM is distinct but not entirely independent of RM, both memory processes are essential to carry out a successful PM task. This chapter, however, will be concentrating on the PM component and its distinct variations.

2.2 Classification of Prospective Memory

As a cognitive construct, PM is more rigorously defined than the typical characterization "remembering to do something in the future" (Marsh & Hicks, 1998). Hereby, in order to capture the many cognitive variables that affect prospective remembering different classes of PM tasks have been proposed through the literature. For example, Kvavilashvili and Ellis (1996) classified PM tasks according to variations in (a) the encoding phase (i.e., importance or pleasantness of task), (b) the retrieval phase (i.e., event- vs time- based tasks), (c) the storage/retention phase (i.e., short- vs long- term delay) and (d) the performance phase (i.e., short or long). Other suggested classes of PM tasks also refer to the complexity of the PM activity (Einstein *et al.,* 1992) and whether the task is habitually or infrequently performed (Harris, 1980). Other important variables affecting prospective remembering include the retrieval context and the

strategies people adopt for remembering (Harris, 1980). Regardless of the importance of these variables the most widely investigated aspect of PM tasks has been the retrieval phase; the focus of the present thesis.

2.3 Retrieval phase

Einstein and McDaniel (1990), proposed that the retrieval phase of PM can be divided into two main classes; time-based PM and event-based PM. Retrieval phase is probably the most researched and debatable phase of prospective remembering and involves the way in which delayed intentions are realized i.e., cued by the monitoring of time or cued by external environmental factors; hence the concept of both time-based tasks and event-based tasks.

2.3.1 Time-based Prospective Memory

The term time-based PM is given for the type of retrieval of a delayed intention, that requires time monitoring i.e., an intention to be performed at a particular time or after a specific amount of time has passed (McDaniel & Einstein, 2000). The best known experiment on time-based PM is the study by Ceci and Bronfenbrenner in 1985 that explored the development of time-based PM in 10 and 14 year old children. In their study, children had to remove cupcakes from the oven after a delay of 30 minutes while they were engaged in a popular video game in a room with a clock for time monitoring. Children had to carry out the task either in a familiar context (their home) or in a laboratory. The authors found that, overall, children checked the clock more often in the laboratory setting and that

the task success was higher in the laboratory than in their familiar context. However, according to the authors, the number of clock checks cannot predict task success as younger children in the familiar context checked the clock more often than older children but success rate was higher in older children. Instead it was the effective and strategic allocation towards the end of the baking period that lead toward the successful completion of the task. Therefore, those children with better PM performance tended to intensify their time monitoring activities more towards the end of the baking period. Consequently, this investigation suggests age-related changes in the development of time-based PM and that strategic clock checking is adaptive and increases PM task success rate.

Craik (1986) went on to suggest that retrieval performance depends on self-initiated or attention demanding processes as opposed to being dependent on environmentally cued automatic processes. Given that the attentional resources essential for processing task relevant information decline with age (Hasher &Zack, 1979), Craik predicted that age-related changes in performance will be larger on PM tasks than on other types of memory processes. Einstein and McDaniel (1990;1996), however, argued that relative to event-based PM, time-based PM performance is more dependent on self-initiated resource demanding processes and therefore that age-related performance would be more pronounced in time-based PM rather than event-based. Although their view was supported by the outcome of some studies (Einstein *et al.,* 1995; Park *et al.,* 1997) a number of other investigations have shown that older adults perform better than younger adults on time-based tasks given that assessment occurs in the context of their everyday life (Martin, 1986; Maylor, 1990; Rendell & Craik, 2000; West, 1988).

By way of contrast, Birt (2001), in a meta-analysis showed larger age effects on time-based task than on event-based tasks. It is difficult to draw definitive conclusions from these studies as the literature is somewhat contradictory as to whether age-related differences are more common in event- or time-based tasks.

Context importance

Confusion in the literature might be attributed to the fact that the context in which memory performance is assessed is largely ignored. Hereby, in Birt's meta-analysis, it was found that the age effect is larger for time-based rather than event-based tasks; a result that is consistent with Einstein and McDaniel's (1990) prediction. In relation to this, studies on aging have shown that time-based PM performance is affected because self-initiated processing is impaired in older adults whereas event-based task performance is not affected (Einstein *et al.,* 1995; Katai *et al.,* 2003; Kliegel *et al.,* 2001; Khan *et al.,* 2007). Another interesting finding from Birt's meta-analysis was that naturalistic studies (i.e., in the context of a familiar setting and everyday life) showed a reverse age effect suggesting that older adults are more successful than young adults on time-based tasks when those tasks are performed in the context of their everyday life.

In order to understand the importance of the context in which memory performance is assessed, Einstein and McDaniel (1990;1996) have pioneered two computer based paradigms (one event-based and one time-based) to mimic real-life prospective remembering when people are busily engaged in other activities. Accordingly, in their time-based laboratory paradigm participants monitor a clock

and respond at fixed intervals while completing an attention demanding task. Much of the literature in this area uses these paradigms to assess time-based and event-based prospective remembering in a laboratory environment.

Task importance

Another factor affecting the performance of PM, in particular time-based PM, is the perceived importance of the delayed intention. Some studies suggest that the importance of the task can affect performance and therefore the successful completion of the delayed intention (Ellis, 1988; Kvavilashivili, 1987; Meacham & Singer, 1977; Kliegel et al, 2001). Diary studies have reported that successful remembering was higher for important appointments (Andrzejewski *et al.*, 1991) and that there was a positive relationship between recollection of the intention and the perceived importance of the intention (Ellis,1988). Meacham and Singer (1977) also suggested that high-incentive is predictive of better performance. Participants who were given a monetary incentive to return four prepaid postcards on specified dates performed better than participants with no incentive. Similarly, Kvavilashvili (1987) demonstrated a significant positive effect of task importance on PM performance. As a way of contrast, Goschke and Kuhl (1993) reported that subjective importance of delayed intentions had no effect on their recall. Kliegel *et al.* (2000), in a series of experiments labelled a time-based PM task as important as opposed to a cover task. Their findings suggested that the importance of the task leads to a selective increase of attention allocation towards the PM task, particularly during the last period before the completion of the task. They also suggested that the accuracy of prospective remembering can be influenced by

affecting attention allocation at specific phases of the process when the importance of the task is manipulated.

In relation to this, Kliegel *et al.* (2001), in a second experiment investigated the assumption that event-based PM is an automatic process and does not rely on attentional resources. It was found that PM performance was unaffected even with an addition of a task that increased overall demands of the ongoing activities. In addition to this they found that at least some event-based PM tasks are mediated by relatively automatic processes and require very little attention for successful performance. In terms of task importance, the authors found that importance has an effect on the time-based but not event-based PM tasks. Furthermore, the importance of the task improved PM to the degree the task requires the strategic allocation of attentional resources.

2.3.1.1 Theoretical models of time-based prospective memory

According to Coren and Ward (1989), attentional resources support the process of monitoring. Humans have a limited attentional capacity so higher cognitive load can negatively affect monitoring of time in time-based tasks. To investigate this assumption, Khan, Sharma and Dixit (2008) explored the relationship between cognitive load and event- and time-based PM. They found that performance deteriorated in both PM tasks as the cognitive load increased. Nevertheless, performance under an event-based task showed less error compared to the time-based task suggesting that monitoring is more crucial for time-based PM.

Although it is clear that retrieval in time-based PM is fundamentally different from that in event-based (Einstein & McDaniel 1996), there are only a few empirical studies that examined the nature of retrieval in time-based tasks (Ceci &Bronfenbrenner, 1985; Cicogna *et al.,* 2005; Cook *et al.,* 2005; Einstein *et al.,* 1995; Park *et al.,* 1997; Redell & Craik, 2000). One finding that emerged from the existing literature involves the participant's time monitoring behaviour prior to the critical time to remember. More specifically, it has been suggested that the frequency of rehearsal in a time-based task is positively correlated with PM performance (Harris & Wilkins, 1982; Einstein *et al.,* 1995; Park *et al.,* 1997). Prior to the emphasis on attentional resources, in order to explain these findings an early theoretical account was offered by Harris and Wilkins (1982): *the Test-Wait-Test-Exit (TWTE)* model of time-based PM.

This model proposes that people encode a future task and then wait until the time is appropriate to carry out the intended task. For example, a person needs to 'test and wait' until the time is appropriate to take the cookies out of the oven before they burn. When the action is carried out, then the 'test and wait' cycle is stopped ('exit'). Consequently, successful performance is dependent on monitoring the time during the critical period. This contrast with the more recent perspectives on time-based PM, as described in later studies (Einstein *et al.,* 1995; Park *et al.,* 1997) in which the time monitoring aspect is a self-initiated process that requires attentional resources.

Despite the insights provided by these two models the main question remains: What is the nature of these self-initiated processes? Harris and Wilkins suggested

that the intention spontaneously pops into a person's mind or is triggered by some incidental cues in the environment. An experiment, where time references in a film made participants aware of their PM tasks, supports another theoretical model of time-based prospective memory proposed by Wilkins and Baddeley (1978), the *"random walk" model*. This model underlines the significance of incidental external or internal cues in remembering intentions. In contrast to this model Wilkins and Baddeley proposed that our mind is a multidimentional semantic space and a trace is formed in this space when an intention is formulated. Our thoughts, however, do not remain in this space throughout the delayed interval; instead they move in various parts of this area randomly and depend on the stimuli we come across in the environment and the activities that we are engaged in. If near the time of the execution of the intention, those thoughts accidentally wander around the trace of the intention then it is likely that we realise that we should carry out an intention, thus successfully carrying out the PM task. This model does not therefore regard the retrieval of the intention as a self-initiated process. Instead, it proposes that the timely remembering of intentions depends entirely on incidental factors.

In order to investigate which of the two models is correct and therefore determine what brings a time-based PM task into our minds during the retention interval, Kvavilashvili and Fisher (2007) conducted a series of three studies. The authors first investigated self-report rehearsal processes in naturalistic time-based PM tasks and compared them with event-based PM tasks. The participants were expected to phone the experimenter at a prearranged time (time-based) or after a text message (event-based). Participants also recorded the details of occasions

when they thought about the intention during a seven day delay interval (long delay interval). It was found that the intention is either triggered by incidental cues or periodically pops into one's mind for no apparent reason. This opposes previous literature and suggests that rehearsal and retrieval of time-based PM could be a more automatic process than previously thought.

Kvavilashvili and Fisher (2007) also emphasized the importance of the storage/retention phase in the successful completion of a time-based PM task. They suggested that the process of retrieval (i.e., automatic/self-initiated) can depend on storage/retention phase. For example, most laboratory studies have used short time delays (Sellen *et al.,* 1997), so participants are likely to keep the task in mind for the entire delay period. Therefore retrieval processes in short-term laboratory tasks can be regarded as self-initiated and deliberated. On the other hand, remembering time-based PM tasks in everyday life with long delay intervals cannot occur in the same way, as people are engaged in more activities during the delay period. In addition, self-initiated rehearsals, occurring when people are engaged in planning their daily activities, were reported in few cases regardless of age, and were lower than rehearsals triggered by incidental cues. These results suggest that a great variety of cues, such as internal or external incidental cues or cues completely unrelated to the intention, can act as triggers and promote successful prospective remembering.

These findings are therefore more in line to Harris and Wilkins (1982) model of TWTE. Kvavilashvili and Fisher (2007) also suggest that retrieval of event- and time-based PM is not mediated by fundamentally different processes and that

thoughts about the task/intention occur via three different routes in both event-based and time-based PM: i.e., by rehearsal prompted by incidental external or internal cues, by self-initiated planning thoughts or by no apparent triggers. This suggests that the difference between event- and time-based PM is more quantitative than qualitative since representations of event-based tasks have low level of activation that is sufficient to trigger remembering with the occurrence of a target and/or event in the environment. On the contrary, the activation levels in time-based tasks may be greater and fluctuate over time leading in periodic conscious thoughts about the task.

2.3.2 Event-based Prospective Memory

Beyond the context of time-based PM, event-based PM has been studied extensively in its own right. The term event-based PM tasks refers to the situation where the intended action is performed at the occurrence of an external or environmental cue or event (Einstein & McDaniel, 1990). The authors in their laboratory paradigm of event-based PM, tried to mimic real life event cued prospective remembering by giving their participants one or two words to remember and instructing them to press a key whenever the target words appeared while they were busily involved in an ongoing task. Although the laboratory paradigms of event-based and time-based PM are very useful in assessing PM under laboratory condition in a naturalistic manner, they do not completely capture more complex PM situations in which several delayed actions are planned to be executed (Kliegel *et al.*, 2000).

In relation to this Ellis (1996) suggested that the more complex situations are likely to include planning processes such as forming a daily plan of activity. Laboratory tasks, however, do not involve such planning. In an attempt to investigate the potential role of the complexity of processes involved in many PM activities such as developing a plan, remembering the plan and remembering to execute the plan sometime in the future, Kliegel, McDaniel, and Einstein (2000), used a six element laboratory task based on a paradigm by Shallice and Burgess (1991). In this experiment participants had to work within constraints on six subtasks to maximise their total points. This paradigm required the participants to engage with a range of processes that included making a plan, retaining the intended plan and executing a series of multiple intentions. The PM component of this task was that participants had to initiate the six subtasks on their own at a specific point during the test. It was found that the planning and executing of PM tasks have to be distinguished, since formulating a plan did not overlap substantially with the manner in which PM tasks were executed.

The involvement of Retrospective Memory (RM) in the execution of PM tasks needs to be addressed when performing a PM task as the literature suggests that both the prospective elements and RM are crucial for successful prospective remembering (Crawford *et al.*, 2005). Kvavilashvili (1987) found that remembering an intention at an appropriate moment and remembering content or facts acquired in the past might be considered as two separate forms of memory, suggesting that RM and PM are somehow different.

According to the literature, the retrieval context plays a key role in prospective remembering. McDaniel and Einstein (1992) argue that distinctive cue words, as opposed to background words, can increase PM performance. For example, more specific cues such as the word "tiger" can trigger better performance than more general cues such as "animal", given that the cue is relevant to the task (Einstein *et al.,* 1995). An important question when investigating cues is whether noticing a cue is an automatic response or whether conscious attentional resources are essential (Marsh & Hicks, 1998). These possibilities have been associated with a lot of conflicting evidence throughout the literature and two theories have been developed to explain this type of PM retrieval. The first theory assumes that attentional and/or working memory resources need to be allocated to monitoring the environment for the occurrence of the target event (Smith, 2003). Consequently, in order to successfully retrieve an intention, strategic, resource-demanding processes must be employed before the occurrence of the target event. The second theory supports a multiprocess model of PM retrieval that involves several processes (McDaniel & Einstein, 2000). The different approaches to understand the processes involved in event-based PM are discussed below.

2.3.2.1 Theoretical Models of event-based PM

Similarly to time-based PM, a number of theoretical models have been proposed to understand the underlying mechanisms that lead to successful event-based retrieval. According to Guynn (2003), in laboratory PM tasks, the monitoring

process involves a recognition check to evaluate whether the cue presented is the correct one for performing the intended action. If the recognition check indicates that the cue represents a target event then the intended action is executed. Failure to carry out the intention is therefore, due to the person's failure to initiate a recognition check (in other words failure to monitor) or due to the failure of the recognition check to identify the event as a target. This theory is therefore based on two main assumptions; that monitoring processes require capacity demanding attentional processes and that monitoring processes are essential for prospective remembering to occur. If this is the case then the resource demanding processes required for PM will reduce the attentional resources available for performing ongoing activity and consequently lower the performance success of the ongoing task. This assumption is supported by a number of studies (Cohen *et al.,* 2008; Einstein *et al.,* 2005; Marsh *et al.,* 2003; Smith, 2003). A specific mechanism proposed to support monitoring is *the supervisory attentional system* (SAS; Shallice & Burgess, 1991) which monitors for a cue signalling the appropriateness of executing the intended action. When a cue is detected the SAS switches attention to the intended action. This suggests that the realisation of an intended action is an attentional process supported by executive attentional systems and not memory processes per se.

By way of contrast, McDaniel and Einstein (2000) proposed a different multiprocess theory suggesting that because of the PM demands in everyday life it is adaptive to have a cognitive system to aid PM retrieval through several processes. So, in addition to the resource demanding processes such as monitoring, prospective remembering can sometimes be spontaneously elicited by

features of the target cue even without resources dedicated to the intention. McDaniel and Einstein (2004) maintain that this spontaneous retrieval in event-based PM can involve a number of processes such as the *reflexive-associative hypothesis*, in which the cue is strongly associated with the intention during planning and the intention is performed reflexively.

In relation to this, Guynn, McDaniel and Einstein (2001) proposed an alternative to conscious cue-focused account based on a memory model proposed by Moscovitch (1994); an *"automatic-associative" memory system* that consciously attends to external cues which in turn interact with memory traces previously associated with those cues. If there is enough interaction between the external cue and a memory trace then the system delivers awareness of the information associated with the cue, thus mediating PM retrieval. As opposed to cue focus theory, the target event is not necessarily recognised as a cue; it simply stimulates a reflexive associative process bringing the intended action into awareness. The entire pattern implicates both cue-focused and reflexive associative process and more generally supports a multidimensional framework of PM (McDaniel and Einstein, 2000).

As previously discussed, some researchers argue that PM declines with age and a number of experiments using event-based PM to appear support this assertion (see review Henry *et al.,* 2004). However, other studies report no age differences in event-based PM (Einstein and McDaniel, 1990). In an attempt to understand this anomalous pattern, Einstein and McDaniel (2005) used the multiprocess point of view and suggested that age differences depend on whether the PM task uses focal

or non-focal target events. According to Einstein and McDaniel (2005) a focal PM cue is the one that stimulates the spontaneous retrieval of an intention without the need to employ strategic monitoring processes. With non-focal targets attention-demanding processes (i.e., monitoring) are essential for prospective remembering and according to Craik (1986) these resources decline with age. Conversely, focal targets require spontaneous retrieval which is assumed to stay relatively intact with age. To support this assumption, Rendell and Craik (2000) found minimal age-related declines in event-based PM when the event was focal. In contrast, when the event was non-focal the age differences were more pronounced.

According to McDaniel, Guynn, Einsten and Breneiser (2004), spontaneous retrieval, as opposed to monitoring, can occur even when no resources are devoted to monitoring for the target during or prior to the occurrence of the target. To support this, Einstein *et al.*'s (1995) results from a study comparing performance on event-based PM tasks between older and younger adults suggest a large automatic component to event-based PM. Marsh and Hicks (1998) suggested that these mixed findings can be explained by the character of the demands that the tasks place on working memory and that poorer event-based PM performance depends on an attention demanding component and therefore might be correlated with measures of central executive functioning.

To support this view, the *notice-search model* (Kliegel *et al.,* 2001; Logie *et al.*, 2004) has also been proposed. This model suggests that for successful PM, familiarity and probe search are required. When people encounter the PM cue they get a sense of familiarity (noticing) which may then prompt a more conscious

probe of memory (search) to determine what the cue means. Therefore, there are two stages in a successful event-based PM task: the stage of noticing or a feeling of familiarity and the search stage. Burgess (2000b) suggested that PM task completion requires many of the skills that are commonly described as executive processes. Successful completion of intentions rely on the operation of a number of different cognitive processes including attention, action control and memory (Dobbs & Reeves, 1996; Ellis, 1996). In particular the literature on PM addresses an important debate on the attentional or strategic demands of PM task retrieval evaluating the notice-search (strategic component) and automatic activation models. According to West and Craik (1999) older adults are more prone to lapses of intention and are believed to suffer from attentional or executive deficits. These failures are associated with changes in neural activity in a region thought to be responsible for the implementation of cognitive control. It is therefore reasonable in order to further understand the underlying mechanisms of PM to look at changes in neural activities during the realisation of PM tasks.

2.4 Neuroanatomical basis of event-based and time-based PM

Many investigations of PM implicate the role of the frontal lobes, more specifically the involvement of the prefrontal cortex (PFC), in the realisation of delayed intentions. Processes in both event- and time-based PM can be linked with frontal lobe activity. This evidence is coming from patients with frontal lobe dysfunction (Fuster, 1997) and age-related literature (McFarland & Glisky, 2009). Although the literature has been somehow elusive as to whether age is responsible for greater decline in time-based or event-based PM, a vast body of research

agrees that younger adults perform better than older adults in PM tasks that require self-initiated processing; i.e., time-based PM tasks (Einstein *et al.*, 1995; Einstein *et al.*, 1997; Maylor, 1996; McDaniel *et al.*, 2004; Park *et al.*, 1997). Time-based PM tasks, although requiring many of the same processes of event-based PM, have greater monitoring demands and are more likely to be entirely self-initiated (Craik, 1986; Einstein and McDaniel, 1990; 1996).

As discussed previously, time-based PM tasks require the formation of an association between cue and intention, the maintenance of this intention over a delayed period, the division of attention between tasks, monitoring the environment for a cue and the interruption and inhibition of ongoing activities. Fuster (1997) showed that these operations are impaired in frontal lobe patients; thus implicating the role of the frontal lobe in time-based PM tasks. Age-related declines in frontal lobe functions have also been showed by West (1996). Support for age-related declines comes from a range of studies. For example, morphological evidence shows disproportional volume loss in the PFC in relation to other brain areas in older adults (Raz *et al.*, 2005).

Neuroimaging studies also suggest that the anterior PFC and more specifically Broadmann's area10 (BA10) is likely to be of central importance to PM (Okuda *et al.*, 1998; Burgess *et al.*, 2001,2003; Simons *et al.*, 2006). In particular, Okuda *et al.* (1998) employing Positron Emission Tomography (PET) examined the functional neuroanatomy of PM by examining changes in regional cerebral blood flow (rCBF). They found increased activity in the left frontal pole, the ventrolateral PFC (BA 8/9/47) and anterior cingulate (BA24) during a PM task.

Burgess, Quayle and Frith (2001) also found increased activation in BA10 (bilaterally) across several cognitive tasks. In their study activation during an ongoing task was compared to activation in two PM conditions (i.e., cue identification and intention retrieval). Increased activation relative to a control task in bilateral frontal pole, right lateral, prefrontal and parietal cortex was observed. The same authors in a later study (2003) extended their previous findings by showing that this bilateral activation of lateral BA10 that is associated with retrieving a delayed intention was accompanied by a deactivation in medial BA10. In relation to this, an activation was observed in lateral BA10, lateral parietal cortex and precuneus. Den Ouden *et al.* (2005) found that these increased activations were associated with holding an intention during an ongoing task.

Furthermore, Simons, Scholvinck, Gilbert, Frith and Burgess (2006) measured brain activity (using functional magnetic resonance imaging [fMRI], and a combination of two different PM tasks: words and shapes) while manipulating the demands on either recognizing the appropriate context to act (cue identification) or remembering the action to be performed (intention retrieval). A consistent pattern of hemodynamic changes was found in both PM conditions in anterior prefrontal cortex (BA10), with lateral BA10 activation accompanied by medial BA10 deactivation. These effects were more pronounced when demands on intention retrieval were high. This is consistent with the hypothesis that anterior prefrontal cortex (area 10) supports the biasing of attention between external events (e.g., identifying the cue amongst distracting stimuli) and internal thought processes (i.e., maintaining the intention and remembering the intended actions). These results suggest that whilst cue identification and intention retrieval may be

behaviourally separable, they share at least some common neural basis in anterior prefrontal cortex. PM related activation was also evident in areas outside anterior PFC region such as lateral PFC and parietal cortex. The anterior cingulate cortex was also activated to a greater extent in a cue identification PM task and the posterior cingulate and precuneus showed greater activation in the intention retrieval task (Simon et al 2006; Okuda et al 1998; Burgess et al 2001).

Further evidence for the involvement of the PFC in PM comes from Okuda et al (2002) who looked at PET activation during a time-based PM task. Participants had to clasp their hands either at a time point (time-based) or after a cue (event-based) while performing a mental arithmetic task. Both conditions increased rCBF in frontal and medial temporal regions. The authors however did not compare brain activity between the two tasks or examine decreases in rCBF thus it was unclear if the two tasks made differential demands upon rostral prefrontal brain activity consistent with the age-related literature. Reanalysing Okuda's et al's 2002 data Okuda *et al.*, (2007) observed significant rCBF increases in the left superior frontal gyrus (including lateral BA10) for the time-based PM relative to the event-based task. Deactivations within rostral PFC were evident in the medial BA10 as rCBF decreased during the event-based PM task in comparison to the ongoing activity alone. The authors also found that the decrease in medial BA10 during time-based PM was not as significant as in the event-based PM suggesting that deactivation in medial BA10 during PM task are specific to event-based PM. Okuda *et al.* (2007) also found that during time-based PM the right superior frontal gyrus, anterior medial frontal lobe and anterior cingulate gyrus were more active and that the left superior frontal gyrus was more active in the event-based

condition. The results suggest the involvement of multiple brain regions of rostral prefrontal cortex in both time- and event-based PM.

To conclude, there is growing evidence that the frontal lobes and more specifically the PFC are not the only brain regions that are involved in the realisation of delayed intentions. Regions such as the right dorsolateral and ventrolateral prefrontal cortices, the left frontal pole and medial frontal regions and the left parahippocampal region (Okuda *et al.*, 1998) provide the neuroanatomical basis for PM.

2.5 Chapter summary

The literature on PM has yet to reach a consensus and there are many theoretical models that have been proposed to identify the underlying mechanisms through which intentions in either time-based or event-based actions are retrieved and the factors affecting this retrieval. What is undisputable is the important role of PM in our everyday environment and the need for more investigation in the area. All in all, having discussed the most established theoretical models of both event- and time-based PM and the role of the frontal lobes in the execution of PM tasks, it can be tentatively concluded that time-based PM tasks are reliant on self-initiated processes whereas event-based tasks are considered to be dependent on more automatic processes. On the whole, the research literature has suggested that executive processes such as planning, monitoring or attention are essential for PM performance. It is therefore reasonable to assume that there is an association between executive processes and prospective remembering.

This assumption can be supported by evidence suggesting that PM processes such as dividing attention, monitoring the environment for a cue, associating a cue for intention and interrupting an ongoing activity may also involve planning which is thought to depend on the frontal lobes (Lezak 1982; Shallice, 1982). PM as it has been previously discussed depends on self-initiated and attention demanding resources and therefore PM performance can be correlated with measures of central executive functioning (Marsh and Hicks, 1998). In relation to this, Martin, Kliegel and McDaniel (2003) found that executive processes in older adults were significantly correlated with performance on three PM tasks. To support this view, additional studies have implicated the role of executive processes in PM performance (Kliegel *et al.,* 2000; Kliegel *et al.,* 2008).

More direct evidence of the involvement of executive processes in PM comes from neuroimaging studies that suggest regions of the frontal lobe (such as rostral prefrontal cortex) are involved in supporting both event-based and time-based PM tasks (Burgess *et al.,* 2003; Martin *et al.,* 2003; Okuda *et al.,* 2007; Simons *et al.,* 2006). According to Okuda *et al.* (2007) these regions are involved in the attentional and executive control aspects of PM functions. Having said that, it will be sensible to evaluate the term executive function and, essentially, its involvement to prospective memory processes. Consequently, the next chapter will look in depth the central executive system and the possible involvement of it in PM performance.

Chapter 3: Executive Function

Chapter overview

Over the last few decades the term executive function has received increased attention. Early models of executive function were restricted to cognitive abilities using a unitary framework while specific components of executive function were not identified and the biological basis of this term was limited to frontal lobes. Nowadays, executive functions are known to represent a rather complex, interrelated set of cognitive abilities critical for adaptive function. Despite the plethora of research and speculation concerning executive functioning the term itself and the conceptualization of it still remains somewhat elusive. The purpose of this chapter is to provide an up to date perspective of executive processes by exploring the most established executive function models and their biological underpinnings.

3.1 What is Executive Function (EF)?

Before discussing the theoretical models which may be found within the literature on EF, it is essential to define the concept. Many definitions have been proposed through the years by different researchers that have influenced research and clinical practices. For example, Lezak (1995) defines EF as a group of superior abilities of organisation and integration; such as anticipating and establishing goals, designing plans and programs, self-regulation and monitoring of tasks.

Similarly, Welsh and Pennington (1988) suggest that EF is "the ability to maintain an appropriate-solving set for attainment of a future goal" (pp. 201). However, according to Gioia, Isquith, Guy and Kenealy (2000), EF is not restricted to cognitive processes but is also characterised by emotional responses and behavioural actions; something that these constructs fail to capture. EF is therefore better described as a collection of interrelated tasks or processes that are responsible for goal-directed or future-orientated behaviour with the executive system acting as the "conductor" that controls, organises and directs cognitive ability, emotional responses and behaviour (Gioia *et al.,* 2001). Having said that, Gioia *et al.* (2000), identified the key elements of EF that include the anticipation and deployment of attention, impulse control and self-regulation, initiation of activity, working memory, mental flexibility and utilisation of feedback, planning ability and organization and selection of efficient problem-solving strategies.

3.2 Theoretical models of Executive Function

In order to understand the critical role of executive functioning in our everyday lives, researchers throughout the years have tried to provide a theoretical framework of this complex term in order to comprehend how executive dysfunction affects our everyday life and determine the different neural pathways underpinning EF. Although a number of theoretical models of EF have been proposed, no one model has been uniformly accepted. Early attempts to conceptualise EF resulted in unitary models such as Baddeley's (1986) "Working memory" model or Norman and Shallice's (1986) "supervisory acting system". However, later research demonstrated that the unitary view is too simplistic and

that the term EF is more likely to be composed of distinct but interrelated components (Baddeley, 2000; Miyake *et al.,* 2000). Findings that frontal lobe patients rarely exhibit global executive dysfunction provide evidence for fractionation of EF (Bigler, 1988; Pennington & Ozonoff, 1996). In light of this new evidence, concepts such as the central executive have been modified in an attempt to fractionate the overall construct to derive subcomponents constituting the various control systems. Before discussing fractionated accounts of executive functioning a description of Baddeley's working memory model will be outlined (Baddeley, 2000).

3.2.1 Working memory model

Baddeley's model proposes that working memory plays a key role in complex activities and is consisted of four major components; the central executive system, the phonological loop, the visuospatial sketchpad and the episodic buffer. Baddeley (2000) defines working memory as "a limited capacity system allowing the temporary storage and manipulation of information necessary for such complex processes as comprehension, learning and reasoning" (pp. 418). Figure 1 represents Baddeley's (2000) Working memory model.

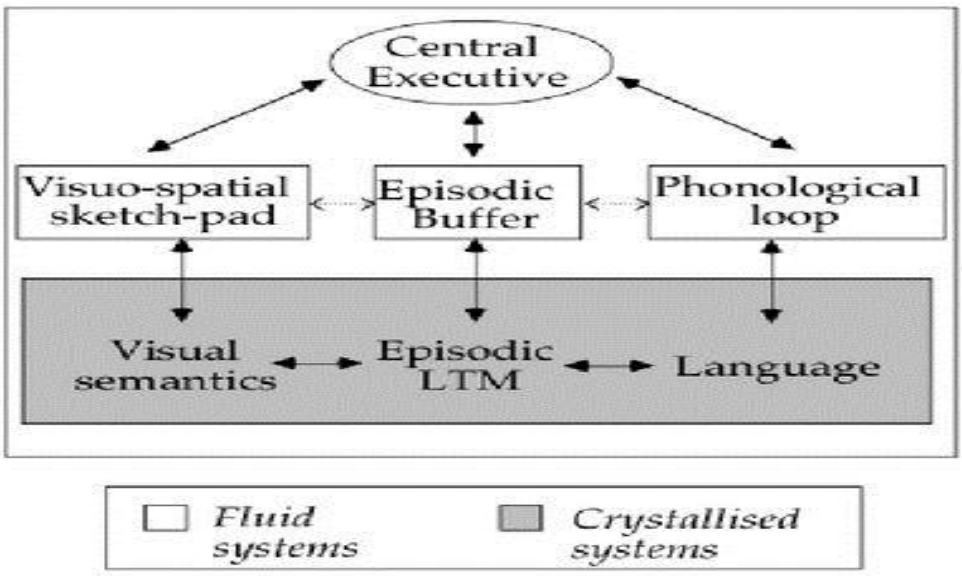

Figure 1. Working Memory model (Baddeley, 2000).

According to this model, working memory consists of the "central executive" system that is a limited capacity attentional system and two slave systems; the phonological loop and the visuo-spatial sketch pad (See Figure 1). The shaded areas represent 'crystallized' cognitive systems that are responsible for accumulating long-term knowledge (e.g., language and semantic knowledge), whereas unshaded systems represent 'fluid' capacities (e.g., attention and temporary storage) and are unchanged by learning, other than indirectly via the crystallized systems (Cattell, 1963). The episodic buffer according to Baddeley (2000) is a third slave system that links information across domains to form visual, spatial and verbal information with chronological order (i.e., memory of a story). The episodic buffer is also speculated to have links with long-term memory.

According to Baddeley (1996, 2000), the "central executive" has four main functions. Firstly, it is responsible for selective attention in that it selectively

evaluates a relevant piece of information while ignoring irrelevant information and distractions. Impairment of the central executive therefore results in the failure to evaluate targeted events/stimuli and maintain goal-directed behaviour as the actions of the central executive are influenced by distractions or irrelevant information. Secondly, the central executive is capable of coordinating two or more simultaneous activities by managing sufficient working memory resources across the tasks. The third function of the central executive is the ability to switch attention and respond to a task or situation that requires mental flexibility prevailing habitual or stereotyped behaviours. Impairment of this can result in rigid performance and perseverative behaviour. Finally, the central executive is responsible for retrieving information from long-term memory a crucial function for responding to the demands of the environment.

The Phonological Loop has the ability to temporarily maintain and manipulate speech based information. It is therefore responsible for retaining verbal and acoustic information using a temporary store and an articulatory rehearsal system. Visuo-spatial sketch pad on the other hand, is responsible for holding and manipulating visuospatial information while the episodic buffer is controlled by the central executive and provides space for temporary storage of information. It also has the ability to integrate information from the two slave systems and long-term memory to create a unitary episodic event (Baddeley, 2000).

While Baddeley's model specifies distinct functions for the central executive, it is unclear as to whether these are performed by a single unitary system or by a collection of discrete and separable executive resources. Furthermore, although

the working memory construct has been studied extensively and is considered to be a well validated model which offers a coherent conceptual framework for describing executive processes and although it accounts for specific patterns of executive impairments, nonetheless it neglects important elements of executive functioning such as goal setting, reasoning and planning.

3.2.2 Miyake *et al.*'s model of Executive Function

Another theoretical model of EF that has received increased attention is Miyake *et al.*'s (2000) model which proposes that the central executive is fractionated with three components performing separate tasks with varying degrees of competence. Miyake *et al.* proposed the separability of three executive functions: shifting, updating and inhibition and their contribution to higher level complex executive tasks. The authors focused on these three executive components not only because they have been widely discussed in the literature and there are a number of well-studied cognitive tasks (such as Wisconsin Sorting Card Task (WCST) and Tower of Hanoi (TOH)) that tap each target function, but also because these three components are likely to be implicated in the performance of complex executive tasks. The first component of this model has been proposed as being crucial for understanding the failures of cognitive control in brain-damaged patients and laboratory tasks where the participant is required to shift between tasks. In other words, *'shifting'*, is responsible for shifting back and forth between several tasks or mental sets (Monsell, 1996) and is considered to be an important aspect of executive control (Norman and Shallice, 1986).

The second component of this model refers to 'updating' or '*updating and monitoring of working memory representations*' (Miyake *et al.,* 2000, pp. 56). This component is responsible for the monitoring and coding of information relevant to the current task, revising items in working memory by replacing old information that is no longer needed, and incorporating new relevant information. Therefore, updating does not passively store information in working memory but actively manipulates this information (Morris & Jones, 1990). The third component is known as '*inhibition*' and refers to the ability to consciously inhibit dominant, automatic responses when necessary (Miyake *et al.,* 2000).

In order to measure performance on these three components of EF and determine whether these components are indeed separable Miyake *et al.* used a wide variety of cognitive tasks that have been extensively used in the literature. They administered a total of nine tasks that have been linked to one of the three components as well as five complex tasks commonly used as measures of executive functioning. The authors used statistical analysis to examine whether these three components are functionally separable or are separate facets of a unitary system. Confirmatory factor analysis indicated that the three components are moderately correlated with each other, but they are clearly separable. Additionally, structural equation modelling showed that the three EFs contribute differently to performance on complex prefrontal executive tasks. For example, performance on the WCST was primarily related to the shifting component, the Tower of Hanoi (TOH) to the inhibition component, operation span to updating, and Random Number Generation (RNG) to both inhibition and updating. Miyake *et al.*'s results therefore suggest both the unity and diversity of EF.

Evidence for this view comes from clinical observations showing differences in performance among executive tasks. For example, some patients show impairments on the WSCT but not on the TOH, while others show the opposite pattern (Shallice, 1988; Godefroy *et al.*, 1999). Further evidence for the fractionisation of EF comes from individual differences studies examining a wide range of populations on the WCST and TOH such as normal young adults (Lehto, 1996), normal elderly adults (Robbins *et al.*, 1998), brain-damaged adults (Burgess *et al.*, 1998) and children with neurocognitive pathologies (Welsh *et al.*, 1991). Although the individual differences are evident there is a consistent pattern across these studies showing that intercorrelations between the different executive tasks are low suggesting that the central executive system is not unitary but fractionated.

Therefore, Miyake *et al.*'s model proposes that EF are fractionated but also overlapping to a modest degree. It also suggests that EF is underpinned by different neural pathways supporting separable sub-processes that are selectively impaired in patients with specific types of executive dysfunction.

3.3 Assessment of Executive Function

It has become evident that patients with frontal lobe damage, as with the pioneering case of Phineas Gage, show severe problems in the control and regulation of their behaviour and have difficulties functioning in their everyday life. Although some patients do not demonstrate impairments on all cognitive tasks they may show some impairment on more complex frontal lobe or executive

function tasks. Some of these tasks include the WSCT and the TOH. Despite their complexity these tasks have become the primary research tools for studying the organisation and role of EF in neuropsychological studies with patients of brain damage. These EF tasks have provided the basis for the nature of the cognitive deficits observed in frontal lobe patients. A vast amount of laboratory-based tasks have, therefore, been designed through the years to measure not only specific components of EF such as updating, shifting and inhibition, as previously discussed, but more complex EF functions. This section will provide a concise account of the most established laboratory-based measures of EF that have been used extensively in the literature.

3.3.1 Laboratory-based measures of Executive Function

Most laboratory measures of EF have been developed to capture impairments in the most prominent components of EF; inhibition, update and shifting. The most widely used tests to measure inhibition, among other, are the Stroop task and the stop-signal task. The Stroop task, developed by Stroop (1935), has been used in research on EF extensively throughout all these years with only minor variation. Miyake *et al.* (2000) has adapted the Stroop Task for computer administration to measure levels of inhibition. Participants are required to verbally name the colour of a stimulus as quickly as possible with reaction times measured by a voice key. The task is comprised of 72 trials where asterisks are printed in one of six colours (red, green, blue, orange, yellow or purple), 60 trials with a colour word printed in a different colour and 12 trials with coloured words printed in the same colour. The different trial types are mixed so the participants are required to consciously

inhibit dominant, automatic responses. This test has been used extensively in the literature to measure executive dysfunction and cognitive control in patients with major depressive disorder (MDD; Hammar *et al.*, 2010), obsessive compulsive disorder (OCD; Rao *et al.*, 2010), in children with ADHD (Barkley *et al.*, 1992; Lufi, Cohen, & Parish-Plass, 1990) as well as in aging populations (Mittenberg *et al.*, 1989; Ludwig *et al.*, 2010). Other tests for inhibition have also been used widely in the literature such as the stop-signal task (Logan, 1994; Miyake *et al.*, 2000) and the antisaccade task (Roberts *et al.*, 1994; Miyake *et al.*, 2000) to name a few.

With regard to shifting, laboratory-based measures include the plus/minus task, where participants need to alternately add and subtract a number from a series of two digit numbers as quickly and accurately as possible, measuring this way the cost of shifting between the operations (Jersil, 1927; Spector and Biederman, 1976; Miyake *et al.*, 2000). The cost of shifting is calculated as the difference between the number of correct answers given in the alternating list and the average of those in the addition and subtraction lists within the given time period. Other measures of shifting include the number/letter task (Rogers & Monsell, 1995; Miyake *et al.*, 2000) and the local global task (Navon 1977; Miyake *et al.*, 2000).

In terms of updating tasks the keep tract task (Yntema, 1963; Miyake *et al.*, 2000), tone monitoring task (Miyake *et al.*, 2000) and the letter memory task (Morris & Jones, 1990) are among the most popular laboratory-based measures

that have been used in the literature. These tasks require the individual to effectively monitor and update working memory representations.

More complex EF tasks include the Wisconsin Card Sorting Test (WCST; Grant & Berg, 1948; Heaton *et al.,* 1981; Kimberg *et al.,* 1997), the Tower of Hanoi (TOH; Borys *et al.,* 1982; Humes *et al.,* 1997) or its variant, the Tower of London (TOL; Phillips *et al.,* 1999), random number generation (Towse and Neil, 1998) and the operation span task (Turner & Engle, 1989). The WCST was primarily designed to measure flexibility whilst the TOH measures planning ability and working memory. These complex tasks have been used extensively in the literature to measure executive dysfunction in patients with autism (for example, Bennetto *et al.,* 1996; Ozonoff, 1995), and ADHD (Barkley, Grodzinsky, & DuPaul, 1992).

It is evident from the literature that a wide variety of laboratory-based tasks of EF have been designed to tap the most discussed components of EF and have been used extensively in measuring executive impairments in a wide variety of populations. Although laboratory-based measures of EF are still very popular when testing executive impairment, in the last decade self-report measures of EF have also been designed to examine executive impairment with relation to the everyday environment. One of the better known self-report measures of EF that has been used extensively in the literature both with clinical and non-clinical population is the *Behavioural Rating Inventory of Executive Function- Adult (BRIEF-A)*.

3.3.2 Self-report measures of Executive Function: The BRIEF-A

For many years the assessment of EF was dependent on laboratory-based measures. Although offering strong internal validity, control over extraneous variables and the possibility of examining the component EF processes set out above, laboratory measures are limited in terms of their ecological validity and in their ability to capture executive processes as they are manifested in the everyday environment (Gioia *et al.*, 2008). Relying on only laboratory-based measures of EF can lead to a limited and incomplete assessment given the fact that EF plays an important role in the direction and control of real-world behaviour (Gioia & Isquith, 2004). Furthermore, laboratory measures of EF capture only individual executive components operating in isolation over a short-time frame in contrast to the integrated multidimensional priority-based decision making that is usually demanded in real-world situations (Goldberg & Podell, 2000).

In order to overcome the restrictions that, despite their internal validity, laboratory-based measures possess, several self-report measures have been developed that are specifically designed to capture individuals' EF in their everyday environment. Therefore, these measures offer an ecologically valid component that includes more internally valid measures that assess executive performance in an everyday environment and offer a more broad idea of EF components that laboratory-based measures fail to offer in a single assessment.

A prominent self-report measure of executive functioning is the BRIEF-A, which consists of nine subscales each including questions which involve everyday activities which contain an executive component. The BRIEF has been used

extensively in research with ADHD patients (Chang *et al.*, 2009; Jarratt *et al.*, 2005; Mahone & Hoffman, 2007; Toplak *et al.*, 2009) autism spectrum disorders (Gilotty *et al.*, 2002; Chan *et al.*, 2009) and frontal lobe patients (Malloy & Grace 2005). The BRIEF-A has been developed to capture the behavioural manifestations of executive dysfunctions. It simultaneously assesses multiple inter-related domains of EF that have been commonly discussed in the literature. The nine scales of the BRIEF include Inhibition, Shifting, Emotional Control, Self-monitor, Initiate, Working Memory, Plan/Organisation, Task Monitor, and Organization of Materials. Bodnar, Prahme, Cutting, Denckla, and Mahone (2007) argue that everyday instruments such as the BRIEF, measure subtle individual differences in discrete real world processes and unlike many laboratory tests are unrelated to, and not contaminated by overall differences in general ability measures such as IQ.

The reliability and validity of the BRIEF in assessing executive functions has been demonstrated in a number of studies. For example, a study of executive functions among epileptic participants by Slick, Lautzenhiser, Sherman and Eyrl (2006) found that the majority of the sample exhibited selective deficits on particular subscales of the BRIEF. Slick et al's results were also consistent with earlier studies (e.g., Gioia et al 2000) in that with one or two qualifications, factor analysis revealed the existence of the same two higher level factors: Behaviour Regulation and Metacognition. Gioia et al (2002) also investigated the psychometric properties of the BRIEF in a mixed clinical sample of children. They reported that children with ADHD had significantly higher scores on almost all scales of the BRIEF in comparison to the control group. Their results again

demonstrate that executive processes are best characterised as fractionated as opposed to unitary, although in this case the nine subscales were found to map onto three higher level constructs. Elevated scores on the BRIEF were also demonstrated in children and adolescents with moderate to severe traumatic brain injury (TBI) (Mangeot *et al.,* 2002) and children with autism (Gilotty *et al.,* 2002). Chang *et al.*(2009) using the BRIEF-A found that students with ADHD faced significantly more difficulties in the self-monitor and task monitor scales when compared to the control group. This evidence suggests that the BRIEF-A can capture effectively the behavioural manifestations of EF in a variety of populations.

The utility of the BRIEF in clinical settings has been demonstrated in a number of other studies. For example, Toplak et al (2009) found that for those diagnosed with ADHD, assessments by significant others (teachers and parents) were correlated with performance on executive function tests, although at the level of individual component processes the BRIEF ratings did not invariably map uniquely onto their equivalent performance test measures. The BRIEF ratings however did prove to be better predictors of an ADHD diagnosis compared to the objective performance test outcomes which did not account for any unique variance in the diagnostic classification. Most of the aforementioned research relates to assessments of executive function by significant others. In a recent review, Walker and D'Amato (2006) provide evidence for the psychometrical integrity of the self-report version of the measure. Their review demonstrates that results from the self-report measure do provide a psychometrically valid indicator of executive functioning.

In an attempt to examine neuropsychological activities, executive dysfunctions and their association in children with autism spectrum disorders (ASD), Chan *et al.*, (2009) found that children with ASD showed significantly poorer EF in everyday activities using the BRIEF and had lower frontal perfusion patterns than normal children. In addition, frontal cordance values (an indirect measure of brain perfusion assessed using EEG) were significantly associated with executive dysfunctions in the Hong Kong list learning test (HKLLT), delayed intrusions, object recognition, false alarms and the BRIEF. The reliability of the BRIEF in assessing EF has been demonstrated in many studies (Malloy & Grace, 2005). According to Walker and D'Amato (2006), the BRIEF serves as a valuable addition to the neuropsychological assessment batteries and provides important information regarding the decision making process of adolescents. In an attempt to evaluate methods of assessing inhibitory control (a variable that is known to be central to the executive function construct), Bodnar *et al.* (2007) found that the BRIEF appears to measure different elements of inhibitory control than those assessed by computerised continuous performance tests. The BRIEF is designed to tap component executive processes within an everyday context and reflects the application of processes outside the laboratory and it is not therefore necessarily directly related to laboratory measures of executive processes.

Indeed a number of studies have failed to find a significant relationship between the BRIEF subscales and laboratory-based neuropsychological measures. For example, in a sample of children with traumatic brain injury (TBI), Vriezen and Pigott (2002) found that while outcomes on the BRIEF were correlated with

measures of IQ they were not significantly related to outcomes on tests such as the WCST, TMT-B and verbal fluency. In another study utilising a sample consisting of children and adolescents with ADHD, Tourette's syndrome and normal controls, BRIEF ratings were found to be unrelated to word fluency, and Tower of London performance although ratings on the BRIEF inhibition component scale and performance on a go/no-go task were significantly related (Mahone et al, 2002). More recently Conklin et al (2008) found that while children with TBI were impaired on both backward digit span and the BRIEF, the outcomes on the two measures were unrelated to each other (Conklin et al, 2008). Similarly Rabin et al (2006) examined individuals with amnesic mild cognitive impairment, older persons with cognitive complaints, and healthy controls, on a laboratory based neuropsychological test battery while also administering the BRIEF (self-report and significant other). Again while the clinical groups were significantly impaired on a number of the laboratory tests including learning, immediate and delayed recall, and on a number of the BRIEF sub scales, performance on the two classes of measures was largely unrelated.

However, a number of other studies have found associations between BRIEF ratings and laboratory measures of executive function. For example, event related potential measures of error monitoring processes in a non-clinical population were found to be correlated with the task monitoring scale of the BRIEF (Chang et al, 2009). Similarly in both an autistic spectrum disorder sample and a control group, anterior cordance (an EEG indicator of the adequacy of cerebral perfusion) was found to be negatively correlated with the metacognition, behaviour regulation and global BRIEF scales. Furthermore in both groups the BRIEF scores were

significantly correlated with the number of intrusions in a word learning/recall task and false alarms in the recognition of line drawings (Chan et al, 2009).

Other researchers have also obtained analogous results. For example, in a mixed clinical group which also included normal controls, scores on the metacognitive BRIEF scale were significantly correlated with performance on a set shifting task (in which participants were required to alternate their response focussing on either stimulus shape or colour). Furthermore, verbal fluency performance was correlated with a number of the BRIEF component scales including working memory and inhibition (Anderson et al, 2002).

The BRIEF has certainly been useful in predicting the behavioural correlates of clinical conditions, for example Mares et al (2007) found that the planning and organisation and inhibition scales were predictive of behavioural problems associated with ADHD. Similarly Feifer and Rattan (2007) found that the BRIEF was better at measuring self-regulation in children with emotional disturbances compared to more traditional measures of executive functioning such as the WCST and the category test (categorising visual stimuli to one of four categories according to some defining common characteristic). In a sample of older children and adolescents with TBI and an orthopaedic injury control group, Mangeot et al (2002) found that there was a linear relationship between the severity of the TBI and performance on the aggregate and the two higher level BRIEF scales (based on parental ratings).Furthermore, scores on the BRIEF were significantly related to performance on a working memory test in which the participant was presented with three consonants and a number, and after counting down from the latter were

required to recall the former. The BRIEF scores were also found to be predictive of parental ratings of behavioural adjustment and adaptive functioning. Taking this literature into consideration it is clear that BRIEF-A is a reliable self-report measure that can capture behavioural manifestations of EF as effectively as laboratory-based measures.

3.4 Biological basis of Executive Function

In order to fully comprehend the term EF, it is essential to explore the neural substrates of executive functioning and determine the cerebral areas associated with each executive process. Initially, the neural substrates of EF were thought to be mediated by the frontal lobes due to the fact that patients with lesions in the frontal lobe demonstrated executive dysfunction (Burgess and Shallice, 1996a,b; Owen *et al.,* 1990; Shallice, 1982). Nevertheless, there is also evidence suggesting that patients with non-frontal lesions can show executive dysfunction similar to frontal patients (Andres & Van der Linden, 2000). This evidence indicates that frontal lesions do not necessarily predict executive dysfunction and that executive processes are not exclusively based upon a network of prefrontal regions. In relation to this, recent neuroimaging studies reveal that executive functioning relies on a dispersed cerebral network involving frontal and posterior associative cortices (Collette & Van der Linden, 2002) and that each executive process is associated with specific prefrontal cerebral areas (Collette *et al.,* 2005) supporting the idea that EF are fractionated.

Goldman-Rakic (1996) suggested the involvement of the dorsorateral frontal regions in spatial information and the ventrolateral frontal regions in non-spatial information. In relation to this, Owen (2000) proposed that the dorsolateral frontal cortex is activated in memory situations that require monitoring of responses and understanding of information such as free recall or backward digit span, whilst the ventrolateral frontal cortex plays a crucial role in encoding and retrieval strategies. The role of mid-dorsolateral, mid-ventrolateral and dorsal anterior cingulate cortex was also linked with processes such as response selection, working memory maintenance and stimulus retrieval while the rest of the frontal cortex remained insensitive to these task demands (Duncan and Owen, 2000). Collette and Van der Linden (2002) also found activations during a wide range of executive tasks in some prefrontal areas such as Broadmann's area (BA) 9/46 and 10 and the anterior cingulate gyrus. Other frontal (BA 6,8,44,45 and 47) and parietal regions (BA 7 and 40) were also activated during executive tasks.

Wager and Smith (2003) also showed that specific EF are associated with specific cerebral regions. For instance, the right inferior prefrontal cortex (BA 10 and 47) is activated during mental operation of switching and inhibition while the superior frontal cortex (BA 6,8, and 9) is activated during working memory updating. The role of posterior parietal cortex (BA 7) and medial prefrontal cortex (BA 32) is also linked with executive functioning during storage and attention tasks. This evidence supports the view that EFs are fractionated and are not restricted to frontal regions.

Further evidence for the diversity and unity of executive functions comes from Collette *et al.* (2005) who investigated Miyake *et al.*'s (2000) three component model of EF. The authors observed increased rCBF in the posterior regions located in the left superior parietal gyrus and in the right intraparietal sulcus during the execution of executive tasks specific to updating, shifting and inhibition. Increased rCBF was also observed in the left middle and inferior frontal gyri. These areas are involved in the running of several executive processes thus demonstrating the unity of EF.

In order to further demonstrate the diversity of executive processes Collette *et al.* (2005) observed specific activation in cerebral areas during each executive process. With regard to the updating component several frontal areas were activated such as frontopolar (BA10), superior (BA6), middle (BA9/46), inferior (BA44/45) and orbitofrontal (BA11) cortices as well as in the intraparietal sulcus and cerebellum. These results are consistent with previous studies that explored the neural substrate of the updating component (Collette and Van der Linden, 2002). Collette *et al.* (2005) also found that the left frontopolar gyrus (BA 10) is associated more specifically with the updating component than any other EF. In support of this the frontopolar cortex has been found to be associated with the evaluation and selection of internally generated information; an essential process for updating (Christoff & Gabrielli, 2000).

Collette *et al.* (2005) also found activations in specific brain areas during performance of shifting tasks. Those activations were observed in the right supramarginal gyrus, left precuneus, left superior parietal cortex, the right

intraparietal sulcus and left, middle and inferior frontal gyri. Previous research also suggests that the intraparietal sulcus is associated with increased activity in the prefrontal areas in shifting tasks (Dove *et al.*, 2000; Sohn *et al.*, 2001). Finally, Collette *et al.* (2005) demonstrated that activation during inhibition tasks was observed in common cerebral areas already found in the conjunction of the three executive processes and also activity in the right inferior frontal gyrus (BA 45). They also showed that the right orbitofrontal gyrus (BA11) and the right middle/superior frontal gyrus (BA10) are more closely associated with inhibitory processes than updating and shifting.

In conclusion, the evidence discussed suggests the involvement of a variety of cerebral areas in the execution of executive processes. Additionally, it demonstrates both the unity of EF by the activation of common cerebral areas during the performance of all three executive tasks but also the diversity of EF by the activation of component specific cerebral areas.

3.5 The role of executive processes in Prospective memory

In Chapter 2 the assumption that there is an association between executive processes and prospective remembering was made. Evidence for this assumption comes from studies demonstrating that PM processes such as dividing attention, monitoring the environment for a cue, associating a cue for intention and interrupting an ongoing activity, may also involve planning and therefore the frontal lobes (Lezak, 1982; Shallice, 1982). Also, Marsh and Hicks (1998) have argued that PM depends on self-initiated and attention demanding resources so

PM performance can be correlated with measures of central EF. Both neuropsychological (Martin *et al.,* 2003; Kliegel *et al.,* 2000; Kliegel *et al.,* 2008) and neuroimaging (Burgess *et al.,* 2003; Okuda *et al.,* 2002; Simons *et al.,* 2006; Okuda *et al.* 2007) evidence suggest the involvement of executive processes in PM performance since regions of the frontal lobe, such as the rostral prefrontal cortex, are involved in both the performance of PM and EF.

In order to examine the effect of external alerting in complex situations Manly *et al.* (2002) used a modification of the six elements test (Shallice and Burgess, 1991) called the hotel test. These tests have been demonstrated to be more sensitive to real-life problems with EF than traditional tests such as the WCST. The six elements test and the hotel test require the participant to carry out simple subtasks in a limited time period. The participant needs to divide the available time evenly across the tasks in order to attempt at least something from each task. The purpose of these tests is therefore not to successfully complete all tasks but to apply an effective strategy. The authors used the hotel test with Acquired Brain Injury (ABI) patients to test the effect of external alerting in complex situations, thus reflecting, everyday demands. They found that test performance was no different between the ABI patients and the control group in the alerted condition (where participants had prompts) as opposed to the control condition where ABI patients performed worse than controls. These studies on alerting strategies provide evidence that by providing external support (i.e., a cue) for monitoring processes, significant improvements in performance can be seen (Fish *et al.,* 2007).

Although these studies use different paradigms they all require goal management with an important PM component. According to Fish *et al.* (2007), any situation in which an intention is formed in order to successfully carry out a task and which cannot be executed immediately but in the near future, can be considered as requiring PM. This retrieval of the intention and the performance of the intention, as discussed in the previous chapter, can either be time-based (cued by the passage of time) or event- based (cued by an external event). In order to successfully remember to carry out the task in the near future, it is important to retrieve that memory at the appropriate time and according to Norman and Shallice (1986), this is very likely to depend on attentional or executive systems. Also, in complex tasks/situations in which several activities run simultaneously, additional planning and monitoring processes maybe required (Fish *et al.*, 2007). Although strategic and automatic processes are involved in PM retrieval (Einstein *et al.*, 2005), it is likely that the extent to which executive processes are involved in PM retrieval is dependent on the specific requirements of the task (Glisky, 1996). For instance, time-based prospective tasks are more likely to rely on EF than event-based tasks as they require a higher degree of self-initiated retrieval (Einstein *et al.*, 1995).

Having evaluated the role of EF in PM retrieval it is then possible that executive dysfunction is correlated with poor PM performance. It is therefore essential when studying PM performance to evaluate the role of executive resources as well. Fish *et al.* (2007) examined the contribution of executive monitoring towards the completion of a PM task in people with differing brain injuries and PM difficulties. After a period of brief training, the participants were required to make

telephone calls to a voicemail service at four set times each day over a period of 10 days. On five randomly selected days, eight text messages with the cue word "STOP" were sent to the participants' mobile telephones (but not within an hour of the target time) in order to investigate whether executive monitoring improves PM performance. Remarkable improvements were observed on cued days, hence demonstrating modulation of PM performance using cues, suggesting that such strategies are useful to remediate some negative consequences of executive dysfunctions.

Further evidence supporting the role of EF in PM performance comes from the definition of PM. Einstein and McDaniel (1990) propose that there are two components during a PM task; the retrospective component and the prospective component. The retrospective component is a typical memory function whilst the prospective component relies mainly on executive processes. Furthermore, in a multitask PM paradigm, Kliegel *et al.* (2000) showed that individual differences in executive functioning (e.g., working memory and inhibition) predicted the successful initiation and execution of a complex PM task while retrospective memory did not. In a later study, Kopp and Thone-otto (2003) tried to separate the cognitive processes involved in PM by testing patients with specific cognitive deficits in an event-based PM task. They found that patients with brain injury and impaired performance on neuropsychological tests of EF performed worse in the PM task than patients with no executive dysfunction thus supporting the role of EF in PM performance.

Executive functions are an integral part of PM performance. PM tasks create the need to monitor the environment in order to detect the relevant cue. This means that attention needs to be divided between monitoring and performing the ongoing task. According to Smith and Jonides (1999), such activity relies on executive processes like monitoring and working memory. It is therefore reasonable to assume that impairments on EF such as inhibition and working memory might predict poor PM performance because patients with impaired EF allocate more resources to the ongoing task in order to compensate for their executive deficits thus reducing the available resources for monitoring cues.

Another possible mechanism through which EF plays a role in PM is in maintaining the activation level of the mental representation of the future intention. According to Goschke and Kuhl (1993), delayed intentions are held in a higher activational state than other mental representations so they can be retrieved more easily when the cue occurs. In relation to this, Einstein and McDaniel (1996) maintain that the cue first creates a sense of familiarity (noticing) that is followed by a memory search for the content of the intention. Therefore, noticing depends on how easily the mental representation of the intention comes to mind.

To conclude, there is growing evidence that the successful performance of a PM task is heavily dependent on executive processes and that executive dysfunction predicts poor PM performance. Further research for the exact role and the extent to which executive processes contribute to successful PM performance is essential as both executive processes and PM play a crucial role in our everyday functioning.

3.6 Chapter summary

Although the research on EF is plentiful, the term EF still remains somewhat elusive as different definitions have been proposed throughout the years and different theoretical models have been devised to explain this complex term and evaluate whether EF are unitary or fractionated. In this chapter the most influential models that provide evidence for the fractionisation of EF have been discussed as well as the different approaches to measure executive dysfunction in clinical cases. The most widely used laboratory-based measures of assessing EF and the importance of using self-report measures that are able to capture the behavioural manifestations of EF in the everyday environment were also discussed. The biological underpinnings of EF and especially the involvement of the frontal lobes and their crucial role in our everyday environment and in PM performance were also evaluated.

A new line of investigation linking these theoretical constructs is concerned with how the common mechanisms supporting EF and PM operate in recreational drug users. More specifically, existing research suggests that ecstasy/polydrug users perform worse on both PM and EF tasks in comparison to drug naïve persons (Montgomery *et al.*, 2005; Fisk & Montgomery, 2009b). Given that recreational drugs such as ecstasy, cannabis and cocaine are widely used and that both EF and PM play an important role in the everyday functioning, it is crucial to examine the possible effects of recreational drug use on these cognitive processes. The subsequent chapters will therefore evaluate the effect of ecstasy/polydrug use on EF and PM performance and discuss the different approaches of measuring executive dysfunction and prospective remembering among recreational users.

Chapter 4: MDMA Neurotoxicity in humans

Chapter overview

3,4 methylenedioxymethamphetamine (MDMA) or Ecstasy is the drug of choice for a large number of recreational drug users. Ecstasy is known to have both stimulant and hallucinogenic properties and animal studies suggest that ecstasy can damage serotonergic nerve terminals in the brain. A growing body of research indicates that the use of ecstasy can have deleterious effects upon memory ability and has been associated with a range of cognitive deficits. The purpose of this chapter is to explore the effect of Ecstasy on the brain and the biological underpinnings of this complex drug.

4.1 What is MDMA?

3,4 methylenedioxymethamphetamine or MDMA is a ring-substituted amphetamine derivative and is also structurally related to mescaline; a hallucinogenic compound (Green *et al.,* 2003). MDMA was originally created in Germany in 1914 as a precursor agent for therapeutically active compounds (Cohen, 1998). Shulgin and Nickols (1978) reported that MDMA has psychoactive properties in humans and in the 1980s the drug was used in psychotherapy to increase patients' self-esteem and help therapeutic

communication. However, increased heart-rate and blood-pressure as well as transient anxiety were observed with acute administration (Greer & Straoussman, 1985). Ecstasy was classed as an illegal drug in the US in 1985 due to its high abuse potential, lack of clinical application and evidence that 3,4-methylenedioxyamphetamine (MDA), a related compound and major MDMA metabolite, induced serotonergic nerve terminal degeneration in rat brain (Ricaurte *et al.,* 1985). MDMA was also classed an illegal drug in the United Kingdom under the Misuse of Drugs Act (1971). Nevertheless, it has become a popular recreational drug used at "rave" and "techno" parties to help people dance all night. This established ecstasy as a party drug (Green *et al.,* 2003). Ecstasy comes in a variety of colours and shapes in the form of tablets and can vary in purity. Tablets, however, have been found to contain between 80 and 150mg of MDMA (Green *et al.,* 2003). The acute effects of ecstasy include a relaxed, euphoric state that leads to emotional openness, empathy and decreased negative thoughts and inhibitions (Parrott & Stuart, 1997), hence its appeal as a recreational drug.

Due to the increased popularity of ecstasy, research has aimed to determine the acute and long-term effects of the drug in animals and humans. These studies have been conducted to examine the effects of MDMA on the brain and determine the extent to which ecstasy disrupts normal brain functioning. The subsequent sections provide a concise account of both animal and human studies on MDMA neurotoxicity.

4.2 MDMA neurotoxicity in animals

Many of the acute and physiological effects of MDMA are consistent with increased serotonin (5-HT) release. Most, if not all, animal studies suggest that MDMA disrupts the normal regulation of serotonin (5-HT) in animal brain. MDMA is a serotonergic agonist (McDowell and Kleber, 1994) and MDMA administration to rats induces an acute and rapid release of 5-HT (Yamamoto *et al.,* 1995; Nixdorf *et al.,* 2001; Mechan *et al.,* 2002a). In addition, Gudelsky and Nash (1996) demonstrated a dose-related increase in extracellular 5-HT concentration in the striatum and medial prefrontal cortex (PFC) following the administration of MDMA in rats. MDMA also inhibits the activity of tryptophan hydroxylase (TPH), an enzyme required for serotonin synthesis (Stone *et al.,* 1987a,c; 1988; Johnson *et al.,* 1992). More specifically, TPH activity starts to decline in the neostriatum, frontal cortex, hippocampus and hypothalamus within 15 minutes of MDMA administration (Stone *et al.,* 1987) and remained inhibited for another 2 weeks after a single dose of MDMA (Schmidt and Taylor, 1987).

Serotonergic changes have also been demonstrated with dose-dependent reductions in 5-HT, 5-HIAA (the main metabolite of serotonin), TPH and serotonin uptake sites or neuronal transporters (e.g., SERT) in a variety of animal species and are often long-lasting (Fischer *et al.,* 1995). This comes from evidence that MDMA-treated rats develop a pronounced loss of serotonin axon terminal markers (Ricaurte *et al.,* 1985; Schmidt *et al.,* 1986). Further research suggests that MDMA-treated animals develop a persistent loss of not only serotonin but also 5-HIAA, TPH and 5-HT transporters (Schmidt, 1987; Ricaurte *et al.,* 1988a,b,c). This evidence suggests a distal axotomy of central 5-HT

neurons (McCann, 1998). The loss of these axonal markers in primates is long-lasting (Ricaurte *et al.,* 1988a, b, c) and in some brain regions might even be permanent (Ricaurte *et al.,* 1992; Fischer *et al.,* 1995).

Animal studies also provide evidence of regional differences in sensitivity to the neurotoxic effects of MDMA. For instance, areas with increased number of serotonergic terminals, such as the cerebral cortex, show more severe deficits than brain regions containing fibres of passage (e.g., hypothalamus) or cell bodies (e.g., brainstem) (Commins *et al.,* 1987; Steele *et al.,* 1994). Consequently, repeated administration of MDMA in animals produces long-lasting degeneration of serotonergic axons and decrease in brain 5-HT and 5-HIAA concentrations in areas such as the neocortex, hippocampus, caudate nucleus, putamen and many thalamic nuclei (Ricaurte *et al.,* 1992; Fischer *et al.,* 1995; Hatzidimitriou *et al.,* 1999).

Because MDMA is a complicated compound neurochemically, it affects a range of neurotransmitters in addition to serotonin such as dopamine. For example, there is evidence to suggest that MDMA disrupts dopamine levels by increasing its release from cerebral tissue (Yamamoto and Spanos, 1988; Colado *et al.,* 1999a; Nixdorf *et al.,* 2001). Yamamoto and Spanos (1988) by placing voltametry electrodes in the caudate and nucleus accumbens in rats found dose-dependent release of dopamine in both brain areas, suggesting that MDMA also alters dopamine levels in animals. Although MDMA disturbs both serotonin and dopamine levels in cerebral areas in animals, the effect on serotonin levels is much more prominent (Yamamoto and Spanos, 1988; Colado *et al.,* 1999a;

Nixdorf *et al.,* 2001). The exact mechanism of neuronal damage is unknown. However some investigations suggested that neuronal damage may be related to ecstasy-induced release of dopamine (Stone *et al.,* 1988) and oxidative stress (Colado *et al.,* 1997a,b; Aguirre *et al.,* 1999; Shankaran *et al.,* 1999a,b; Yeh, 1999).

4.3 MDMA neurotoxicity in humans

As discussed previously, it is evident that repeated administration of high doses of MDMA can produce long-term reductions in serotonergic activity and the degeneration of serotonin neurons in animals. It is therefore possible that this neurotoxic potential of MDMA is present in humans as well (McCann, 1998; Morgan, 2000). A growing body of empirical investigations support the proposition that MDMA is also neurotoxic in humans and there are numerous indications of serotonergic damage in the human brain. The potential neurotoxic effect of MDMA in humans can be evaluated indirectly by measuring the concentration of 5-HIAA in cerebrospinal fluid (CSF) in recreational users of ecstasy. Lower levels of CSF 5-HIAA were observed in ecstasy users compared to polydrug users that have never used ecstasy (Ricaurte *et al.,*1990; McCann *et al.,* 1994; Bolla *et al.,* 1998).

Psychological effects of MDMA such as positive mood and euphoria can be explained by the effects of MDMA on neurotransmitters such as serotonin and dopamine. Liechti and Vollenweider (2001) attributed positive mood after

MDMA use in humans to the release of serotonin and the euphoric effects to the release of dopamine in the brain. In addition, human studies have shown that some of the psychological effects of MDMA, including positive mood, extroversion and elevated sensory perception, are blocked by selective serotonin reuptake inhibitors supporting the involvement of 5-HTT(5-hydroxy- tryptamine, the serotonin transport protein) in the mechanism of action of MDMA (Farre *et al.,* 2007). MDMA also has physiological effects in both animals and humans that include the homeostatic control of body temperature. MDMA-treated rats face hypothermia in a cold environment and they are overheated under high temperatures (Gordon *et al.,* 1991). The same effect is observed in MDMA users in that they report increased body temperature including excess sweating and dehydration (Davison and Parrott, 1997).

Further support for the involvement of MDMA in serotonin levels is the evidence that recreational MDMA users face "serotonin syndrome" which according to Gillman (1999) is caused by an excess of intrasynaptic 5-HT as a result of adverse drug reaction. The symptoms of "serotonin syndrome" include behavioural hyperactivity, mental confusion, agitation, fever, tachycardia, shivering and tremor. Most MDMA users display mild signs of the serotonin syndrome such as hyperactivity, mental confusion, hyperthermia and jaw clenching (Davison and Parrott, 1997; Parrott and Lasky, 1998). Therefore, it is evident from this research that MDMA alters serotonin levels in both animals and humans.

4.3.1 Neuroimaging and neuropsychological evidence

More evidence for the neurotoxic potential of MDMA and its effect on serotonergic systems in various brain areas emerges from neuroimaging studies in humans. Because of the relative absence and the availability of postmortem human brain material, only one marker of brain serotonin neuronal number is used in human studies that can be assessed in living human brain. This marker is known as the SERT (the site on serotonin neurons which takes released serotonin back into the neuron). Neuroimaging studies of brain serotonin neuronal integrity in ecstasy users therefore employ radioligands that bind to this transporter (e.g., McCann *et al.,* 1998; Semple *et al.,* 1999). Single photon emission computed tomography (SPECT) and PET have been used in the literature to provide evidence for the neurotoxic effects of MDMA. These neuroimaging studies employed radioligand-based methodology designed to detect binding to SERT, with the assumption that decreased levels of SERT will reflect decreased number of serotonin neurons/nerve endings (Kish, 2002).

Postmortem human brain (Little *et al.,* 1998) and SPECT (Jacobsen *et al.,* 2000; Staley *et al.,* 2001) studies have reported above-normal levels of brain SERT in human users of cocaine and in tobacco smokers suggesting that brain levels of SERT might change following exposure to some drugs independently of any changes in levels of nerve terminals. This method of investigation is therefore useful in detecting MDMA-related changes.

For example, reduced densities of serotonin transporter sites were observed in ecstasy users during a PET scan across a wide range of brain regions such as hypothalamus, cingulate cortex, frontal cortex, occipital and parietal cortex. In addition, this decrease was positively correlated with the extent of prior ecstasy use (McCann *et al.,* 1998). Decreased global brain volume and increased percentage of CSF was also observed in ecstasy users with longer duration of use (Chang *et al.,* 2000).

Semple *et al.* (1999) using SPECT with a 5-HT radioligand investigated heavy ecstasy users that remained abstinent for 3 weeks and ecstasy-naive controls. Ecstasy users showed reduction of cortical 5-HT transporter binding in comparison to the control group but had a normal dopamine receptor binding; highlighting once again the effect of MDMA on serotonin levels. The authors also suggested that at least some of the loss of transporter density might be temporary and related to the last use of MDMA. Another SPECT study looking at cortical 5-HT2A receptor densities demonstrated that MDMA users that remained abstinent for an average of 4.6 months had significantly up regulated 5HT2A receptor densities in the occipital cortex compared to an ecstasy-naive control group (Reneman *et al.,* 2000). These neuroimaging studies provide further support in that heavy ecstasy users exhibit persistent serotonergic changes.

More evidence for neuronal damage in a condition restricted to damage to nerve terminals (but no cell body loss) can only be obtained by postmortem brain examination. In such examination the levels of all markers of serotonin nerve terminal integrity (e.g., serotonin, tryptophan hydroxylase, and SERT) are

decreased if nerve terminal loss has occurred (Kish, 2002). Kish et al (2000) found after an autopsy of a chronic MDMA user that striatal levels of serotonin and those of its metabolite 5-hydroxyindoleacetic acid were severely depleted by 50 to 80% in the brain whereas concentrations of dopamine were within the normal control range. The authors therefore suggested that MDMA exposure in humans can cause decreased tissue stores of serotonin and the behavioural effects of this drug can be caused by massive release and depletion of brain serotonin.

In a more recent study, Kish et al (2010) measured protein levels of SERT and the rate-limiting serotonin-synthesizing enzyme tryptophan hydroxylase (TPH) in autopsied brain of a high-dose MDMA user. As compared with control values, SERT protein levels were markedly reduced in the striatum (caudate, putamen) and occipital cortex and less affected in frontal and temporal cortices. TPH protein was also severely decreased in caudate and putamen. The magnitude of the striatal SERT protein reduction was greater than the SERT binding decrease typically reported in imaging studies. These findings therefore extend imaging data based on SERT binding and suggest that high-dose MDMA exposure could cause loss of two key protein markers of brain serotonin neurones, a finding compatible with either physical damage to serotonin neurones or down regulation of components within.

Having established the role of MDMA in potentially giving rise to neurotoxic lesions of the central serotonergic system, it is necessary to specify which systems are most affected in order to try and explain the behavioural manifestations observed in recreational users of ecstasy. As mentioned above, Reneman *et al.*

(2000) found that the 5-HT2A receptor binding was significantly elevated in the occipital cortex of heavy ecstasy users compared to a control group suggesting that the occipito-parietal region of the cortex may be altered by extensive MDMA exposure. Chang *et al.* (2000) in their study found no significant differences in rCBF between abstinent heavy ecstasy users and controls. However, within 3 weeks of administration of total dose of 3.5 mg/kg of MDMA, rCBF remained decreased in the visual cortex, the caudate, superior parietal and dorsolateral frontal regions. Ecstasy use was also associated with decreased EEG coherence specifically in relation to the visual association pathways (Dafters *et al.*, 1999). Reduced coherence levels are associated with dysfunctional connectivity in the brain suggest disturbances in alertness mechanisms. These findings may explain why heavy ecstasy users show deficits in attention and tasks that demand visual discrimination (Morgan, 2000).

Reduced glucose metabolic uptake was also observed in MDMA users using PET in the hippocampus, amygdala and cingulate cortex bilaterally (Obrocki *et al.*, 1999). Furthermore, in a recent study Kish et al (2010b) explored the different brain areas affected by MDMA use and the possibility that structural brain differences might account for serotonin transporter binding changes. The authors measured a brain serotonin transporter binding in 50 drug free controls and 49 chronic abstinent ecstasy users. A magnetic resonance image for positron emission tomography image co-registration and structural analyses was developed. It was found that serotonin transporter binding in ecstasy users was significantly decreased throughout all cerebral cortices and hippocampus and that the decrease was related to the extent of drug use (i.e., years, maximum dose).

Serotonin transporter binding, however, was normal in basal ganglia and midbrain.

Also, voxel-based analyses confirmed a cortical serotonin transporter binding loss with occipital cortex most severely affected. Magnetic resonance image measurement revealed no overall regional volume differences between the groups. A slight left-hemispheric biased cortical thinning was, however, detected in methamphetamine-using ecstasy users. The ecstasy group also reported subnormal mood and demonstrated generally modest deficits on some tests of attention, executive function and memory, with the latter associated with serotonin transporter decrease. The authors also found that low dose (one to two tablets/session) chronic ecstasy/polydrug users might display a highly selective mild to marked loss of serotonin transporter in cerebral cortex/hippocampus that is unrelated to recent use of other drugs or other potential confounds. The striking sparing of serotonin transporter-rich striatum observed in this study suggests that serotonergic neurons innervating cerebral cortex are more susceptible (for unknown reasons) to ecstasy than those innervating subcortical regions. The authors therefore concluded that the behavioural problems in some ecstasy users during abstinence might be related to serotonin transporter changes limited to cortical regions.

The evidence for ecstasy-related decreases in serotonin transporter binding in the hippocampus is crucial since the hippocampus is important for memory functioning (Hatzidimitriou *et al.,* 1999). It is therefore logical to assume that memory functioning is affected in recreational users of ecstasy. Given that lesions

of the 3 corticothalamic circuits, the dorsolateral prefrontal circuit, the lateral orbitofrontal circuit and the anterior cingulate circuit are associated with executive function deficits and disinhibition (Cumming, 1993), findings from PET, SPECT and EEG studies support the notion that extensive exposure to MDMA may potentially cause, amongst other things, impairments in learning, episodic memory, working memory and attention (Morgan, 2000).

4.4 Is MDMA neurotoxic?

The available human and animal data indicates that recreational use of MDMA is associated with loss of serotonin (5-HT), its major metabolite (5-HIAA), its biosynthetic enzyme (TPH) and its presynaptic transporter (SERT). These losses are persistent after weeks of abstinence and thus are not only due to the short-term pharmacological effects of MDMA. Although, human data is limited, there is sufficient animal data to suggest that MDMA causes long-lasting decreases in 5-HT, 5-HIAA, TPH and SERT in a variety of brain regions (such as the hippocampus, frontal cortex, etc). It is therefore possible that MDMA has the potential to damage serotonergic axon terminals and produce a 5-HT distal axotomy. This evidence has been interpreted by several researchers and has been referred to as ‘MDMA neurotoxicity’.

However, during the last few years, several studies have questioned the neurotoxic potential of MDMA to 5-HT terminals. Such conclusions were based on results from western blot studies of the SERT protein showing no change in SERT protein abundance regardless of large decreases in 5-HT concentrations; what up to that date, had been considered a neurotoxic MDMA treatment in rats

(Baumann *et al.*, 2007; Wang *et al.*, 2004; 2005). Another argument put forward by some researchers to question the 5-HT neurotoxic potential of MDMA is the failure of some studies to demonstrate changes in Glial fibrillary acidic protein (GFAP) expression after several treatment regimens with MDMA known to deplete central 5-HT concentrations (Wang *et al.*, 2004; 2005). GFAP is the major protein constituent of astroglial intermediate filaments and has been used as a marker to detect neuronal degeneration (O'Callaghan & Miller, 1993). No changes in GFAP expression found in these studies are therefore indicative of no neurotoxicity induced by MDMA treatment. Grob (2000) and Kalia (2000) also argue that the lack of reactive gliosis in animals exposed to ecstasy suggests absence of MDMA-induced neurotoxicity. These findings therefore raise doubts among some investigators as to whether MDMA "serotonergic neurotoxicity" involves distal axotomy or alternatively a long-lasting down regulation of 5-HT synthesis and SERT expression by the serotonergic neurons (see Puerta & Aguirre, 2011 for a review).

4.5 Chapter summary

Despite the controversy in the literature as to whether MDMA has neurotoxic potential or not, there is abundance of evidence that recreational use of ecstasy causes long-lasting cognitive and behavioural problems in ecstasy users (see Zakzanis *et al.*, 2007 for a review). A relatively new line of investigation suggests that recreational users of ecstasy are impaired in particular memory functions such as prospective remembering (Heffernan *et al.*, 2001a,b; Montgomery *et al.*, 2007), memory and learning (Parrott *et al.*, 1998; Schifano *et al.*, 1998; Morgan, 1999; Bolla *et al.*, 1998; Gouzoulis-Mayfrank; 2000) and

cognitive/executive functioning (Fox *et al.*, 2001; Schifano *et al.*, 1998; Morgan *et al.*, 1999; McCann *et al.*, 1999a; Gouzoulis-Mayfrank, 2000). The following two chapters will evaluate the effects of ecstasy use on prospective memory and executive functioning that are important factors to everyday functioning.

Chapter 5: Prospective Memory deficits in ecstasy/polydrug users

Chapter overview

A plethora of research has evaluated the effect of ecstasy in humans and its effects on various cognitive domains and memory processes (Morgan, 1998; 1999; Gouzoulis-Mayfrank et al., 2000). Ecstasy-related research on memory function has mainly focused on learning, verbal memory, implicit and episodic memory. It is therefore of interest to investigate the extent to which the impairments that have been observed impact memory functioning in an everyday context. An important aspect of day-to-day memory functioning is Prospective Memory (PM). PM, as previously discussed, refers to remembering to execute a particular behaviour in the future. For example, remembering to pass on a message or meet a friend or pick up milk from the store on your way home. A relatively new line of investigation suggests that PM is impaired in recreational users of ecstasy (Heffernan et al., 2001a, b; Montgomery and Fisk, 2008; Fisk and Montgomery, 2008). This chapter will, therefore, provide a concise account of PM deficits in recreational users of ecstasy.

5.1 Ecstasy use and memory functioning

Ecstasy use has long been associated with neurocognitive deficits (Halpern *et al.*, 2004; Yip & Lee, 2005) and a growing body of research indicates that ecstasy can have deleterious effects upon memory ability (Parrott and Lasky, 1998; Morgan, 1999; 2000; Rodgers, 2000). Lasting impairments in explicit memory are observed in human studies following repeated use of ecstasy (Bolla *et al.*, 1998; McCann *et al.*, 1999; Morgan, 1999; Reneman *et al.*, 2000). Ecstasy users are therefore impaired on neuropsychological measures of memory that require the intentional recollection of an episode or previous experiences (Tulving and Markowitsch, 1998).

Measuring the effect of ecstasy on explicit memory, Bolla *et al.* (1998) compared the performance of abstinent ecstasy users and controls (non-ecstasy users) on the Rey- Auditory Verbal Learning Test (RAVLT), the Wechsler Memory Scale Revised (WMS-R) and Rey-Osterrieth Complex Figure Test (ROCF). The authors found that ecstasy users were impaired in immediate verbal and delayed visual memory in comparison to controls and also that the impairment was greater with increased use of ecstasy. Immediate and delayed recall was also investigated in ecstasy users using subtests of the Rivermead Behavioural Memory Test (RBMT; Wilson *et al.*, 1985). Ecstasy users recalled significantly fewer ideas from a short passage read out to them in both immediate and delayed recall conditions than the control group (Morgan, 1999). Decreased recall in ecstasy users was also observed immediately after presentation and after a delay in a computerised battery of cognitive tasks (Parrott *et al.*, 1998). Zakzanis and Young (2001) examined the neurotoxic potential of continued ecstasy use and its consequences

over a year. In a longitudinal study 15 ecstasy users completed the RBMT on two occasions. The findings indicated that continued use of ecstasy was associated with progressive decline in terms of immediate and delayed recall. There is therefore adequate evidence to support the proposition that explicit memory impairments are present in ecstasy users.

Memory, however, is not a unitary system and as a consequence other memory components are likely to be affected by the neurotoxic properties of ecstasy, for example PM. Since PM can be conceptualised as a complex cognitive operation drawing on explicit memory and varying in both difficulty level and in terms of the component processes drawn upon (Gilsky, 1996), it is very likely that PM is also impaired in recreational users of ecstasy.

5.2 Prospective Memory deficits in Ecstasy/polydrug users: Evidence from self-report measures

It has been long established that recall and recognition are impaired in users of ecstasy and the extent to which these impairments impact memory functioning in an everyday context has been researched in recent years. An important aspect of day-to-day functioning is PM; remembering to do things at some point in the future. PM is a relatively new line of investigation (Brandimonte *et al.,* 1996; Ellis *et al.,* 1996) that has received increased attention. Research over the years has suggested that the neurotoxic effects of ecstasy disrupt normal PM functioning. Heffernan *et al.* (2001a) were the first to examine PM in ecstasy/polydrug users using self-report measures of PM, specifically the Prospective Memory Questionnaire (PMQ; Hannon *et al.,* 1995).

The PMQ is a self-report measure of PM that requires participants to record the number of times their PM failed within a period of time. It consists of three subscales measuring short-term habitual, long-term episodic and internally cued PM. The PMQ also measures the number of strategies people use to aid remembering. This has been proven a useful scale in estimating the effectiveness of PM in the context of personality differences (Heffernan and Ling, 2001) and age-related differences (Heffernan and Elmirghani, 2000). The PMQ has also been used with brain damaged patients to evaluate PM performance (Hannon *et al.,* 1995) and in recent years has been used extensively to explore self-perceived PM deficits in regular users of ecstasy, cannabis, alcohol and tobacco (Heffernan *et al.,* 2001a,b;2005; 2010a,b; Rodgers *et al.,* 2001;2003; Fisk and Montgomery, 2008; Montgomery and Fisk, 2008). It is therefore, a powerful tool in detecting PM deficits in a variety of populations.

Using the PMQ, Heffernan *et al.* (2001a) investigated the effect of ecstasy use on PM for the first time in a sample of 30 regular users (who had taken ecstasy 10 or more times per month) and 31 ecstasy free controls. Ecstasy users were impaired on all three subscales of the PMQ; short-term habitual PM, long-term episodic PM and internally cued PM in comparison to the control group whilst no significant difference was observed between the two groups for the techniques to remember scale. Therefore, ecstasy users reported global impairments in PM in comparison to the control group. These impairments remained even after controlling for the use of other drugs such as cannabis and cocaine as well as tobacco and alcohol; suggesting that ecstasy is responsible for the PM deficits.

In a subsequent study, Heffernan *et al.* (2001b) using the PMQ replicated previous findings that ecstasy users face global impairments of PM, an effect that is unrelated to the use of any other drug. In a different experiment (Heffernan *et al.*, 2001b) the authors tested a different group of 30 regular ecstasy users and 37 non-ecstasy users to examine whether PM and the Central Executive (CE) system are linked. Participants were assessed on their PM using the PMQ and on their EF by a verbal fluency task. Unlike previous findings, ecstasy users were only impaired on the short-term habitual and long-term episodic aspects of PM and not on internally cued PM. Ecstasy users in comparison to the non-ecstasy group performed worse on the verbal fluency task. The fact that ecstasy users showed corresponding impairments in both measures of PM and EF support the notion that PM and CE are somehow linked.

Finally, in a third study the authors (Heffernan *et al.*, 2001b) administered the Cognitive Failures Questionnaire (CFQ; Broadent *et al.*, 1982) to 15 ecstasy users, 15 cannabis users and 15 drug naïve persons to measure self-perceived day-to-day cognitive slips. No significant differences were observed between the three groups suggesting that ecstasy users do not perceive their cognitive performance to be worse than the other two control groups. These findings on cognitive performance are in line with Rodgers *et al.* (2000) who also found no differences between ecstasy users, cannabis users and drug naïve persons on the CFQ. Collectively these studies, therefore, suggest that ecstasy/polydrug users are impaired in both PM and EF but do not produce more cognitive slips.

These results for cognitive performance are somehow peculiar since cognitive impairment is evident in ecstasy users on objective measures (Fox *et al.*, 2001; Parrott and Lasky, 1998; Morgan, 1999; 2000; Gouzoulis-Mayfrank *et al.*, 2000). Despite these impairments being apparent ecstasy users do not report more cognitive failures in their everyday lives. A possibility as to why self-report measures of cognitive failures do not show significant impairments can be referred to as the 'memory paradox', in which people experiencing memory impairment are not able to remember and thus report cognitive slips. Another possibility may be that ecstasy users utilise compensatory strategies to aid day-to-day functioning but that such strategies are unavailable during the performance of more objective laboratory based tasks. It is therefore possible that ecstasy users perceive only some aspects of memory impairment such as PM (Heffernan *et al.*, 2001a; b).

A problem with investigations in the area of recreational drug use is the small sample sizes evident in most studies due to the difficulties associated with recruiting larger samples. Overcoming this difficulty, Rodgers *et al.* (2001) used the World Wide Web (WWW) to assess memory in recreational users of ecstasy and to investigate the different effects of ecstasy and cannabis on memory functioning. They administered two self-report questionnaires; the PMQ to assess PM and the Everyday Memory Questionnaire (EMQ; Sunderland *et al.*, 1983) to assess common memory lapses in everyday activities, such as returning to check whether you have done something you meant to do or repeating a story or a joke. The EMQ has been proven useful in the area of recreational drug use (Heffernan *et al.*, 2001b; Montgomery and Fisk, 2008; Fisk and Montgomery, 2008) and

smoking (Heffernan *et al.,* 2005). Drug use was assessed using the Recreational drug use questionnaire (Parrott, 2000) in a sample of 488 people.

Findings revealed a clear double dissociation between the ecstasy and cannabis. Consequently, it was found that cannabis was associated with reports of 'here and now' cognitive problems in short-term and internally cued PM and everyday memory. Conversely, ecstasy was associated with reports of long-term memory problems that were more related to storage and retrieval difficulties. Findings on RM that delayed recall is the most impaired memory function in ecstasy users (Rodgers *et al.,* 2000) support the results of this study. Also, these storage deficits might be due to serotonergic neural damage in the hippocampus due to extensive exposure to ecstasy (Parrott, 2000). Rodgers *et al.* (2001) also found that the errors made in completing the questionnaires were associated with the history of ecstasy use. This may be explained as a manifestation of greater impulsitivity and less reflective behaviour observed in abstinent ecstasy users (Morgan, 1998) and may be related to serotonergic axonal loss in the frontal cortex (McCann *et al.,* 2000).

Reviewing the results of their previous study, Rodgers *et al.* (2003), controlled for other recreational drugs co-used using statistical analysis and found that effects on PM were restricted to the use of ecstasy and cannabis rather than any other drug. They also found that greater ecstasy use is associated with more difficulties in self-reports of long-term PM and that cannabis use predicts self-reports of failures in everyday memory with greater use corresponding with more reported problems. Since cannabis and ecstasy contribute to day-to-day functioning problems

differently it is possible that different recreational drugs affect human memory in distinct ways.

In order to evaluate the role of cannabis in real-world memory (everyday memory, cognitive failures and PM), Fisk and Montgomery (2008) assessed cannabis users on self-report measures of everyday memory, cognitive failures and PM as well executive components and associative learning. Cannabis users were impaired on all three aspects of real-world memory in relation to the control group. The findings of this study are broadly consistent with those of Rodger *et al.* (2001) in terms of the role of cannabis in everyday memory deficits and PM. Fisk and Montgomery's (2008) study, unlike Rodgers *et al.,* found that cannabis only users exhibited deficits in all aspects of PM and were also impaired on measures of cognitive slips, i.e., the CFQ.

The different pattern of PM outcomes reported in the two studies might be a product of the different characteristics of the two samples and may be that the effects of cannabis in the context of polydrug use are different from those evident in cannabis only users. The absence of cannabis related deficits in EF and associative learning is somewhat surprising since real-world memory processes and especially PM are known to be dependent on prefrontal executive resources (Marsh and Hicks; 1998; McDaniel *et al.,* 1999). The authors suggested that these findings can be explained by the type of assessment. For example, cannabis users appear to perform sufficiently in a laboratory setting whilst in a less controlled environment outside the laboratory where more distractions are present users might demonstrate impairment. It is therefore essential to administer more

ecologically valid EF tasks in real-world contexts, capable of capturing cannabis related impairments.

Further evidence for the effect of ecstasy use on PM comes from additional studies utilising self-report measures. Montgomery and Fisk (2008) in a study to evaluate real-world memory processes in ecstasy/polydrug users administered self-report measures of everyday memory, cognitive failures and PM in a laboratory setting. They also administered an objective measure of cognitive failures i.e., the 'CFQ for others' and laboratory measures of EF to explore the assumption that there is a link between PM and EF. The authors found that ecstasy/polydrug users were impaired relative to non-ecstasy users on the CFQ, EMQ and on long-term episodic and internally cued PM as well as on a working memory task. Also, ecstasy/polydrug users were rated less favourably by their significant others on the CFQ for others measure compared to non-ecstasy users. The authors also found no interaction between the source of the CFQ scores (self or others) and ecstasy/polydrug use suggesting that users are aware of their cognitive slips and therefore a self-report assessment of cognitive failures is consistent with ratings from a close family member or a friend. Ecstasy/polydrug users were also impaired on the WM task. However, following regression analysis WM capacity did not emerge as a significant predictor of memory deficits, highlighting the limited importance of WM capacity as a mediator of difficulties in everyday memory in ecstasy/polydrug users. When controlling for the use of other recreational drugs, cannabis emerged as the most important predictor of PM and everyday memory deficits in ecstasy/polydrug users. In fact, the authors found that with the exception of the CFQ for others, cannabis emerged as the only

significant predictor for everyday and prospective memory deficits. It is therefore evident that cannabis is also an important predictor of PM and real world deficits in ecstasy/polydrug users.

In addition to cannabis, tobacco and alcohol have also been suggested to affect memory performance. Ling, Heffernan, Buchanan, Rodgers, Scholey and Parrott (2003) examined the effects of alcohol on two aspects of memory performance; PM and everyday memory. Data were collected using the WWW and participants completed the PMQ and EMQ. After controlling for the use of other drugs and strategies used to aid remembering it was found that alcohol was associated with impairments in long-term PM and with an increased number of cognitive failures. Both short-term and long-term PM failures, using the PMQ, were also found in a number of studies, (e.g., Heffernan and Bartholomew, 2006; Heffernan *et al.*, 2006) supporting these findings. In a recent study, Heffernan *et al.* (2010b) measured PM using the Prospective Retrospective Memory Questionnaire (PRMQ; Crawford *et al.*, 2003) in 50 alcohol only users; 29 non-binge drinkers and 21 binge drinkers. The PRMQ shows high internal consistency and provides a self-report measure of memory slips in everyday life. It consists of 16 items, 8 for PM (4 short-term and 4 long-term PM) and 8 for RM. In addition to the PRMQ, the authors also used an objective measure of PM, the Prospective Remembering Video Procedure (PRVP), based on previous research (Seed *et al.*, 2005). The test consists of a 10 minute video clip containing footage of a shopping district in Scarborough. The view presented in the video was a mixture of shop fronts, passers-by and retail stalls. Before watching the video participants were asked to remember specific actions or items associated with particular location on the

video. Participant then had to write down each action-location combination on a response sheet whilst viewing the video and not before. There were 18 location-action/item associations and a higher score indicated better PM functioning.

Findings suggested that binge drinkers and non-binge drinkers did not differ in their PM lapses on PRMQ. However, binge drinkers recalled significantly less location-action/item combinations than non-binge drinkers in the PRVP. The findings suggest that poorer PM performance is associated with binge drinking. It also raises the need to administer objective measures of PM since the PRMQ was unable to detect obvious PM failures present in the objective PM task.

Tobacco use has also been implicated with difficulties in PM. Heffernan *et al.* (2005) investigated the effect of tobacco in 2 aspects of real-world memory, long-term PM and everyday memory in a web based study using the PMQ and EMQ. A large sample size of 763 people took part in the investigation. Illicit drugs such as ecstasy, cannabis and LSD as well as alcohol use were controlled for in the study. In general the authors found that cigarette smokers reported significantly worse long-term PM than non-smokers. Findings also revealed that there were differences between light and heavy smokers suggesting that nicotine may have a dose dependent impact upon PM. A significant ANOVA group effect on the EMQ was also observed although the trend for greater memory errors amongst the heavier smokers was not significant. The findings of this study suggest that there are selective memory deficits associated with smoking and that smoking is a factor affecting long-term PM.

It is therefore evident that ecstasy is not the only substance that can affect PM performance. The major concern with studies in the area of recreational drug use is the variety of drugs in addition to ecstasy that recreational users of ecstasy consume. Given the difficulty in recruiting ecstasy only users most studies in the area recruit ecstasy/polydrug users, i.e., people who consume a variety of drugs in addition to ecstasy. This is a concern as the use of other illicit drugs such as cannabis, cocaine, amphetamines and LSD will have an effect on neuropsychological functioning (Gouzoulis-Mayfrank *et al.*, 2000; Fox *et al.*, 2001; 2003; Parrott, 2001; 2003; 2006; Rodgers *et al.*, 2003; Heffernan *et al.*, 2005). It is therefore evident from the literature that ecstasy/polydrug users face difficulties in PM, everyday memory and cognitive failures. Although most studies in the area have effectively used self-report measures to detect PM deficits the use for more objective PM measures are essential since objective measures might be more sensitive in capturing PM difficulties.

5.3 Prospective Memory deficits in Ecstasy/polydrug users: Evidence from laboratory measures

Studies in the area of recreational drug use have typically used self-report measures to capture PM deficits in ecstasy/polydrug users. Whilst self-report measures have been proven to be a powerful tool in detecting PM deficits in recreational users of ecstasy, laboratory-based measures are essential as they offer a more objective assesment of ecstasy-related deficits. Only a limited number of studies have used laboratory-based measures to test PM performance in ecstasy/polydrug users and where such measures have been employed they have

been rather artificial and contrived in nature for example the 'Virtual week' (Rendell and Craik, 2000).

5.3.1 'Virtual week'

The 'virtual week' is a board game where participants move around the board with the roll of a dice. The times of the day that people are typically awake are marked on the board. Participants are required to circuit the board seven times as a simulation of a week in their life, with each circuit representing a day. As participants move around the board they need to choose their daily activities (10 event cards for each virtual day) and then remember to execute them (PM tasks). Thus each day of the virtual week includes 10 PM tasks; four regular tasks, four irregular tasks and two time-check tasks. The four regular tasks simulate the tasks occurring when one undertakes routine duties. Two of these are time-based (monitored by passing a particular time on board) and the other two are event-based (triggered by information on an event card). The four irregular tasks simulate occasional tasks that occur in everyday life and two of them are time-based and the other two event-based. Finally, the two time-check tasks require the participant to 'break set' from the game activity and monitor real time on a stop clock and also indicate when a specified period of time has passed. Correct scores indicate that the target item is remembered at the correct time. Late items are scored when the item is remembered after the correct time but before the end of the virtual week. Wrong items are marked when tasks are incorrectly recalled or recalled at the incorrect time. Tasks that are not remembered at any time are

marked as missed. The 'Virtual week' by the inclusion of regular and irregular tasks varies the role of RM in PM processes.

As previously mentioned, PM also involves a retrospective memory component (Cohen *et al.,* 2001; McDaniel and Einstein, 1992) that is impaired in ecstasy users (Bolla *et al.,* 1998; Morgan, 1999; 2000; Kalechstein *et al.,* 2007). It is therefore important to distinguish between regular and irregular PM tasks in the 'Virtual week' as regular PM tasks impose fewer demands on RM (remembering what needs to be done) thus permitting an assessment of whether PM failures are restricted to the retrospective component or these difficulties extend to the PM component. Also the distinction between time and event-based PM tasks is important as the two types of PM tasks rely on different neural pathways and mechanisms. For example, time-based PM tasks are believed to rely upon internal control mechanisms as no external mnemonic aid is employed and this is more dependent on self-initiated mental activities such as time monitoring. On the other hand, event-based PM tasks are considered to be more automatic processes.

In order to investigate the distinction between time-based and event-based PM and the role of RM component in ecstasy users Rendell *et al.* (2007) have employed 'virtual week' to investigate PM in ecstasy/polydrug users. Measures of perceived sleep quality, psychopathology and cannabis consumption were also taken to determine any possible contributory factors to PM impairments. The results demonstrated that ecstasy use was significantly associated with increased difficulties in PM and that the magnitude of this deficit did not vary as a function of task type. Additionally, they found that PM deficits are not secondary to the

effects of cannabis use, sleep quality or increased psychopathology. The authors also distinguished users as frequent and infrequent users and found that although both groups performed significantly worse than the control group, the extent of PM failures was associated with the extent of ecstasy exposure. It was therefore suggested that more frequent users of ecstasy performed worse than infrequent users in the laboratory-based measure of PM.

In relation to the role of RM, Rendell et al's (2007) study suggested that RM failures are not sufficient to account for the magnitude of the PM impairments observed, as the regular tasks have minimal demands on RM and yet were significantly impaired. Also, in this study the majority of errors included misses (i.e., failures to respond) or late responses rather than wrong content (i.e., forget what was supposed to be done). Consequently, this study suggests that ecstasy/polydrug users are impaired in their time and event-based PM and that these impairments in PM are not because of RM failure.

The 'Virtual week' has also been used to investigate the effects of other recreational drugs. For example, Rendell *et al.* (2009) found that long-term abstinent methamphetamine users were also impaired on the measure in comparison to a drug naive control group. Impairments were also evident in measures of verbal learning, delayed recall (RAVLT), forward and backward digit span, and the Hayling sentence completion task (believed to load on the inhibitory executive process). Interestingly, the extent of the methamphetamine-related effect in PM was found to co-vary substantially with the degree of impairment on the Hayling task (Rendell *et al.,* 2009). The virtual week paradigm has also

featured in a number of other studies. For example, Leitz *et al.* (2009) demonstrated that performance on the measure was impaired following the acute administration of alcohol. This deficit was eliminated when individuals were asked to simulate the required actions at the time of encoding (by imaging the full sensory aspects of the context in which the action was to be completed; Paraskevaides *et al.,* 2010).

The paradigm has also been used to investigate the basis of PM deficits in individuals with mild cognitive impairment and dementia (Thompson *et al.*, 2010), multiple sclerosis (Rendell *et al.*, 2007b) and schizophrenia (Henry *et al.*, 2007). Therefore, although somewhat contrived and artificial in nature, the 'Virtual week' provides a more objective measure of PM that detects PM deficits in a variety of populations augmenting the traditional self-report measures that have been employed by most of the studies in the area of recreational drug use.

Although self-report ecstasy-related PM deficits are well documented (Heffernan *et al.,* 2001a,b; Rodgers *et al.,* 2001;2003) the use of self-report measures or of single PM tasks are of limited value as performance cannot be discriminated beyond being correct or incorrect on a limited number of one-off trials (Zakzanis *et al.,* 2003). These studies therefore provide relatively limited information regarding the extent, scope or implications of problems experienced by ecstasy users. They also fail to investigate the conditions under which PM failures are most likely to occur (Rendell *et al.,* 2007). The 'virtual week' is an attempt to overcome the limitations that self-report measures retain and affords the

opportunity to distinguish event and time-based PM and also to investigate the role of RM in PM failures.

Whilst the virtual week paradigm has its advantages, the test clearly has an associative learning component. For example, before the PM element can be completed, the participant is required to learn each of the ten particular responses associated with specific locations on the board and to select the appropriate response from among the set of available alternatives each time a PM action is triggered. Also, some responses are common to different tasks making it easier for the participant to complete the task. Montgomery *et al.* (2005) have demonstrated that ecstasy users are impaired on paired associative learning. It is therefore possible that some of the deficits observed on the 'virtual week' might be attributable to associative learning rather than the PM components. In fact, just over half of the virtual week PM sub-tasks are regular and more repetitive in nature and thus more readily learned. It is the remaining more irregular tasks that have a more substantial learning requirement. In Rendell *et al.*'s (2007a) study, ecstasy users performed worse on these irregular virtual week tasks recording 65% of the level of correct responses achieved by non-users while for regular tasks the percentage was 83%. This suggests that performance is indeed adversely affected by the learning component. Nevertheless, there was no statistically significant interaction between user group and task type with users demonstrating a significant deficit overall. Thus, while group differences in learning may partially account for the virtual week results the outcomes obtained are nonetheless consistent with an ecstasy-related PM deficit.

5.3.2 Rivermead Behavioural Memory Test (RBMT)

In another attempt to offer a more objective perspective for PM failures in ecstasy users, Zakzanis *et al.* (2003) have employed the RBMT (Wilson, 1991) to test event and time-based PM. Fifteen abstinent (2 weeks) ecstasy users and 17 non-ecstasy users completed the RBMT. The authors tested PM memory using three of the subscales of the RBMT asking participants to remember to ask for a belonging at the end of the test session, ask a specific question when an alarm clock sounded and deliver a message at a specific point during testing. Ecstasy users remembered to successfully carry out these delayed intentions on significantly fewer occasions compared to the control group. It was also suggested that the ability to recall a future appointment is related to the frequency of ecstasy use.

Understanding the important contribution of cannabis in memory functioning and specifically to PM, McHale and Hunt (2008) investigated cognitive function in short-term abstinent cannabis users employing measures of phonemic verbal fluency, visual recognition, immediate and delayed recall and PM. Cannabis users were compared against a drug free control group and a tobacco using control group. Cannabis users compared to both control groups, demonstrated deficits on verbal fluency, visual recognition, delayed (but not immediate) visual recall and also short-term and long-term PM. This study is one of the few studies in the area of recreational drug use that has employed simple laboratory measures for measuring PM. The authors measured both time and event-based PM using the belonging subtest (remember to ask for a belonging at the end of the test session) of the RBMT (Wilson, 1991) to measure event-based PM. Time-based PM was measured using short interval (10 minutes) and long-interval (2 days) tasks. The

short interval task required the participant to press a timer exactly 10 minutes after being instructed to do so. The long-interval task required the participant to post an envelope exactly 2 days after the date of the test session. Results suggested that cannabis users were impaired in both short and long interval time-based PM in comparison to the control groups but not on the event-based task.

The RBMT has been extensively used to measure everyday memory performance in age-related literature (Melendez-Moral *et al.,* 2010; Fraser and Glass, 1999), autism spectrum disorder (Jones *et al.,* 2011), Schizophrenia (Guaiana *et al.,* 2004; Tyson *et al.,* 2005), dementia (Glass, 1998); TBI (Anderson *et al.,* 1999; Wills *et al.,* 2000) and post-traumatic stress disorder (PTSD; Moradi and Neshat, 1999). It has also been used in measuring event-based and time-based PM (using three sub-tests) in a number of studies within the area of recreational drug use (Zakzanis *et al.,* 2003; McHale and Hunt, 2008) and with elderly people (Cockburn and Smith, 1994). In addition, it has been used in a few studies to measure immediate and delayed recall in ecstasy/polydrug users (Morgan, 1999; Zakzanis and Young, 2001). The RBMT has therefore been proven to be a powerful tool in detecting both everyday and PM difficulties in clinical and non-clinical populations. Validity and reliability of this laboratory-based measure has been documented in a number of studies (e.g., Man *et al.,* 2009; Wilson *et al.,* 1989).

5.3.3 Cambridge Prospective Memory Test (CAMPROMPT)

Another laboratory measure that distinguishes event and time-based PM is the CAMPROMPT (Wilson *et al.,* 2005). The CAMPROMPT is a more up-to-date

test battery that is sensitive to individual differences both within clinical and normal populations (Fleming *et al.,* 2008; Groot *et al.,* 2002; Wilson *et al.,* 2005). It is a standardised neuropsychological test that relates to Einstein and McDaniel's (1990) paradigm (see Chapter 2). It consists of a total of six PM tasks, three cued by time and three cued by events. Participants are asked to work on some distractor tasks such as word-finder puzzles or a general knowledge quiz for a twenty minute period while they had to remember to perform the PM tasks. The participants are allowed to spontaneously use strategies, such as taking notes, to help them remember. Total scores are generated on both time-based and event-based subscales with higher scores reflecting better PM performance. The validity and reliability of the CAMPROMPT has been documented in a number of studies (i.e., Fleming *et al.,* 2008; Groot *et al.,* 2002; Wilson *et al.,* 2005).

For instance, in a study by Groot, Wilson, Evans and Watson (2002) performance on an earlier version of the CAMPROMPT was found to be significantly poorer for a group of TBI patients in comparison to a control group. Groot *et al.* (2002) also found that the CAMPROMPT correlated significantly with measures of memory, attention and executive functioning. A later edition of the CAMPROMPT has since been published and is considered a highly valid tool for measuring PM in the TBI population. For example, Fish *et al.* (2007) used the CAMPROMPT to measure PM deficits in individuals with non-progressive brain injury and Fleming *et al.* (2008) assessed PM performance in adults with severe TBI using the CAMPROMPT**'s** time-based and event-based sub-scales as well as the incidence of note-taking. The authors concluded that patients with longer periods of post-traumatic amnesia (PTA) and EF impairment display poorer

PM. Additionally, the CAMPROMPT has also been used to measure PM deficits in individuals with bipolar disorder (BD; Lee *et al.* 2010).

In a more recent study Heffernan *et al.* (2010a) investigated whether persistent smoking leads to impairments in self-report and objective measures of PM. Eighteen smokers and 22 non-smokers were assessed on the PRMQ questionnaire and on the CAMPROMPT. After controlling for ecstasy, cannabis and alcohol, results suggested that the two groups did not differ significantly in PM or RM as assessed by the PRMQ. Nevertheless, smokers were worse in terms of total recall on the CAMPROMPT recalling significantly fewer time-based, and event-based elements in comparison to the non- smoking group.

On the whole, these findings suggest that the CAMPROMPT is a more sensitive objective tool in detecting PM deficits than traditional self-report measures and demonstrates the importance of not relying solely on self-report measures, but the need to use laboratory tests to detect PM impairment. Nevertheless, the greatest advantage of the CAMPROMPT is that, as opposed to the RBMT, it is more sensitive in detecting PM problems in non-clinical population.

5.4 Chapter summary

It is evident from the literature that ecstasy/polydrug users are impaired on measures of PM. Most studies in the area have employed self-report measures to capture any possible PM deficits in recreational users of ecstasy (Heffernan *et al.*, 2001a,b; Rodgers *et al.*, 2001;2003; Montgomery and Fisk, 2008; Fisk and

Montgomery, 2008). Although self-report measures are found to be reliable in detecting PM difficulties it is possible that self-perceptions might be distorted. For instance, drug users may arrive at the laboratory with the expectation that they will underperform (Cole *et al.,* 2006; Bedi & Redman, 2008). This expectation can affect their responses on self-report measures exaggerating the extent of any deficits present. Also, since the questionnaires assess memory, people experiencing memory impairment might not be able to remember and thus report memory lapses.

Furthermore, self-report measures of PM fail to capture the distinction between time-based and event-based PM tasks (retrieval phase) and concentrate on the storage/retention phase of PM i.e., action to be performed in the short or long-term. Although, objective measures such as the 'virtual week' have been employed in recent years to overcome this limitation, they have been rather artificial and contrived. In particular, the 'virtual week' paradigm although undoubtedly possessing a PM component, also involves associative learning in which ecstasy users are known to show impairment (Montgomery *et al.,* 2005) making it unclear whether the deficits observed are due to the PM or learning aspects. Consequently, the need to employ more ecologically valid measures to assess PM is essential. In order to address some of these limitations this research will include simple laboratory measures of PM (event and time-based PM tasks as well as short-term and long-term PM tasks) that are designed to be more naturalistic and where the PM component is less obvious to the participant including the CAMPROMPT (see Chapter 7 and 8). Although CAMPROMPT

seems to be rather artificial as a laboratory measure, its main advantage is that it's useful and reliable with non-clinical population as opposed to the RBMT.

As well as the obvious PM impairments in recreational users of ecstasy, neuropsychological evidence suggests that Executive Functions (EF) is also impaired in ecstasy/polydrug users (Fox *et al.*, 2001; Fisk *et al.*, 2004). In view of the potential role of EF in underpinning PM performance, the next chapter will evaluate the impact of the recreational use of ecstasy on measures of executive functioning.

Chapter 6: Executive dysfunction in Ecstasy/polydrug users

Chapter overview

It is evident from the previous chapter that PM is impaired in recreational users of ecstasy. Other lines of investigation suggest that ecstasy users also face other cognitive deficits. The working memory system in general and the executive system in particular appear to be affected by the neurotoxic effects of ecstasy. Although a lot of studies have investigated the effect of ecstasy on the executive processes, it remains unclear why ecstasy users may be impaired in some executive function tasks and not others. Most studies in the area have used laboratory measures to assess executive dysfunction in ecstasy users that map onto Miyake et al's (2000) theoretical perspective of executive function. This chapter will therefore explore the plethora of studies investigating the effect of recreational drug use grouping them according to Miyake et al's three major components of EF, updating, shifting and inhibition. Previews reviews on the impact of ecstasy on EF suggested that ecstasy-related deficits do not appear on all cognitive tasks or in all studies (Morgan, 2000; Parrott, 2000; Murphy et al., 2009). It is therefore essential to summarise the most important findings in this area in order to establish a coherent understanding of the ecstasy-related effect on different components of EF. This chapter will therefore provide a concise account of ecstasy–related deficits on the multidimentional construct known as EF and the components affected by the neurotoxic effects of ecstasy.

Executive functions, as previously discussed, are a group of higher level abilities of organisation and integration. EF have been neuroanatomically associated with different neural pathways involving the PFC (Roberts *et al.,* 1994). These are believed to be underpinned by both serotonin and dopamine systems and are potentially compromised by the disruption of these systems (Kish, 2002). Functional neuroimaging studies have shown that the majority of these metabolic reductions (e.g., reduction in the concentration of serotonin transporters SERT) due to the use of ecstasy are concentrated in the dorsolateral and parietal prefrontal regions (Cohen *et al.,* 1996). It is therefore possible that recreational users of ecstasy demonstrate executive dysfunction during neuropsychological assessment. In fact, plenty of neuropsychological evidence suggests that ecstasy users face difficulties in different aspects of EF (Fisk *et al.,* 2004; Fisk & Montgomery, 2009b; Montgomery *et al.,* 2005; 2007; Montgomery & Fisk, 2008; Morgan, 2000; Wareing *et al.*, 2004;).

6.1 Recreational use of ecstasy and working memory

The term WM, according to Baddeley (2000), combines short-term storage processes with other aspects of cognitive activity such as learning and reasoning. WM is responsible for the storage and retrieval of task-related material as well as additional processing relevant to the task (Shah & Miyake, 1999). The allocation of processing resources necessary for the successful completion of a task is part of the executive function of WM and plays a central role in recruiting cognitive resources needed for the person to manage the demands of a task (Murphy *et al.*,

2009). WM is known to involve both executive and non-executive processes. Specific executive processes of WM have been identified by different techniques i.e. logical deduction (Baddeley, 1996), latent variable analysis (Miyake *et al.*, 2000; 2001) and exploratory factor analysis (Fisk & Sharp, 2004) on data from tasks likely to utilize executive processes. The key executive processes that have been identified include the updating of WM, shifting mental set, the inhibition of prepotent responses and access to semantic long-term memory.

A number of neuropsychological studies showed that the severity of ecstasy use can selectively affect WM (Bolla *et al.*, 1998; Fox *et al.*, 2001; Gouzoulis-Mayfrank *et al.*, 2000; Verdejo-Garcia *et al.*, 2005). Several processes are known to load heavily on the WM components; it is therefore possible that these processes are also affected by the neurotoxic effects of ecstasy. For example, aspects of WM have been implicated in reasoning performance (Fisk & Sharp, 2002; Gilhooly *et al.*, 1999; Gilinsky & Judd, 1994), and consistent with this ecstasy use appears to impair reasoning processes (Fisk et al, 2005). Other studies have demonstrated ecstasy/polydrug related impairment in tasks believed to load on updating (Fisk *et al.*, 2004; Montgomery *et al.*, 2007; Wareing *et al.*, 2004), access to long-term memory (Fisk *et al.*, 2004; Montgomery *et al.*, 2007; Montgomery *et al.*, 2005), and visuospatial WM (Fisk & Montgomery, 2009b; Montgomery & Fisk, 2008). It is therefore possible that ecstasy users are impaired in these constructs.

6.1.2 Updating of WM and access to long term memory

Recreational use of ecstasy is known to have adverse effects on the process of updating WM and access to long-term memory. For example, Wareing *et al.* (2004) measured updating in a sample of 42 current ecstasy users, 17 former users and 31 non-ecstasy users using a reading span and a computational span task. Both user groups showed deficits on both measures of updating in comparison to the non-ecstasy user group, an effect that remained after controlling for age, other drug use and passive memory storage differences. Similarly, Fisk *et al.* (2004) found updating impairments using the computation span measure in ecstasy/polydrug users in comparison to non-ecstasy users even after controlling for the use of other drugs.

Also, Montgomery *et al.* (2007) assessed 103 ecstasy users and 103 non-ecstasy users on two updating tasks (i.e., the computation span and consonant updating task) and a task measuring access to long-term memory (i.e., Chicago word fluency task). After controlling for age, IQ, levels of sleepiness and the concurrent use of other drugs the authors found that ecstasy users reported deficits on all three EF tasks implicating the recreational use of ecstasy with impairments in updating and access to long-term memory. Current ecstasy users in comparison to former users, also demonstrated deficits in updating tasks (i.e., the computational span); an effect that was unrelated to information processing speed difficulties (Wareing *et al.,* 2007).

6.1.3 Visuospatial Working Memory (VSWM)

Although deficits in updating and access to long-term memory are clear, visuospatial deficits are not as clear cut among ecstasy users. Even though evidence suggests that ecstasy use is associated with visuospatial deficits, much of the existing research has focussed on visual recall and recognition and not VSWM. A number of studies have found ecstasy-related deficits in the ability to recall, reconstruct or recognise previously viewed complex visual stimuli (e.g., Bolla *et al.,* 1998; Gouzoulis-Mayfrank *et al.,* 2000; Fox *et al.,* 2001; Verkes *et al.,* 2001). Although these ecstasy-related impairments on visual processing are useful in providing information of the adverse effects of recreational use of ecstasy, such processes recruit occipital and medial temporal resources rather than prefrontal processes (Dafters *et al.,* 1999; Chang *et al.,* 2000).

Instead, VSWM involves more than just the ability to recall or recognise visual information. It involves the temporary storage, maintenance, processing and manipulation of visuospatial information in search of goal-related behaviours and is more dependent on prefrontal cortical resources and therefore on executive processes (Cabeza & Nyberg, 2000). A number of studies have demonstrated that VSWM is affected by the recreational use of ecstasy (e.g., Fox *et al.,* 2002; Wareing *et al.,* 2005). For example, Fox *et al.* (2002) assessed VSWM using a spatial WM task in a sample of ecstasy/polydrug users and non-ecstasy users. Ecstasy/polydrug users in comparison to the non-ecstasy user group performed significantly worse on the spatial WM task consistent with ecstasy-related VSWM deficits. Using the same measure, Semple *et al.* (1999) found that although users did not differ significantly from nonusers, there was a significant association

between lifetime ecstasy use and the number of errors on the task. Furthermore, in a study measuring updating and VSWM in current and former ecstasy users against a non-ecstasy user group, both user groups demonstrated deficits in VSWM and updating (Wareing *et al.,* 2005). VSWM deficits using a VSWM span task were also demonstrated in ecstasy/polydrug users in relation to non-ecstasy users (Wareing *et al.,* 2004).

De Sola LLopis (2008) also measured VSWM in a community sample with follow-ups at 6, 12 and 24 months. Thirty seven ecstasy/polydrug users, 23 cannabis-only users and 34 drug naïve controls completed the Corsi block tapping task (specifically the backward sequence span). The author found that, at baseline, heavy ecstasy/polydrug users (with total lifetime of ecstasy use more than 100 tablets) showed visuospatial memory impairments that persisted even after 24 months. Finally, a recent study that sought to determine whether ecstasy use is associated with deficits in serial spatial recall and VSWM in a sample of current ecstasy/polydrug users, previous ecstasy/polydrug users and non-ecstasy users found that both current and previous ecstasy users exhibit impairments in VSWM performance (Fisk *et al.,* 2011). It is therefore evident that VSWM performance is problematic in ecstasy users.

Although VSWM deficits are evident in ecstasy users, simple visuospatial memory impairments are not so clear cut. While some studies identified ecstasy-related visuospatial memory deficits using the Corsi blocks paradigm (e.g., Verkes *et al.,* 2001; Hanson & Luciana, 2010) some others failed to show impairments using the same paradigm (e.g., Gouzoulis-Mayfrank *et al.,* 2000;

Reneman *et al.,* 2006). No visuospatial memory deficits in ecstasy users were also demonstrated in a number of other studies that employed the simple spatial span task as a measure of visuospatial memory (e.g., Fisk & Montgomery, 2009; Montgomery & Fisk, 2008; Morgan, 1998). For example, Montgomery and Fisk (2008) assessed the process of updating the contents of visuospatial memory in a large sample of ecstasy/polydrug users and non-ecstasy users. It was found that although ecstasy users showed updating deficits, their performance did not differ from the non-ecstasy user group in the spatial span test. Similar findings were observed on a later study by the same authors. Both heavy and light user groups in this study as opposed to the non-ecstasy user group demonstrated deficits on measures of updating. Nevertheless, the performance of the three groups did not differ on the measure of simple spatial span (Fisk & Montgomery, 2009).

It is therefore evident from the aforementioned research that although ecstasy users seem to be underperforming in measures of VSWM, ecstasy-related deficits are not as evident in simple visuospatial memory tasks. A possible explanation for these results may be that ecstasy-related deficits are evident on tasks loading heavily on WM and executive resources (Fisk *et al.,* 2005). For instance, tests such as the spatial span involve only a modest processing requirement and a relative small memory load. It is therefore possible that ecstasy-related deficits are not evident on these tasks because of their low WM load. On the other hand, tasks that involve dual task performance such as verbal or visual judgements combined with serial recall (e.g., the spatial working memory span) are thought to involve an increased memory load and are more dependent on WM resources. Consequently, ecstasy-related deficits are more apparent.

6.2 Shifting

Shifting between tasks or mental sets refers to the ability to shifting back and forth between multiple tasks, operations, or mental sets (Monsell, 1996). It can also referred as ‘‘attention switching’’or ‘‘task switching,’’ and it is an important function in understanding both failures of cognitive control in brain-damaged patients and laboratory tasks that require participants to shift between tasks (Monsell, 1996). Models of attentional control, such as the supervisory attentional system (SAS) (Norman & Shallice, 1986), often assume that the ability to shift between tasks or mental sets is an important aspect of executive control. The most common explanation of this EF is that the Shifting process involves the disengagement of an irrelevant task set and the active engagement of a relevant task set (Miyake *et al.*, 2000). Relatively few studies have been contacted to investigate the performance of ecstasy users for the shifting component of EF. The most common laboratory tasks for assessing shifting in ecstasy users include the Trail Making Task-B (TMT-B), the Plus/minus task, the number/letter task and the WCST.

A few studies have employed the TMT-B to measure shifting in ecstasy users. This test requires the participant to connect numbers and letters in an alternating pattern (e. g., 1-A-2-B-3-C etc.) in as little time as possible. As TMT-B requires attentional switching between the letters and numbers, it is more cognitively demanding and thus requires more time. Semple *et al.* (1999) used the TMT-B to measure shifting in ecstasy users. The authors failed to find any ecstasy-related differences between 10 regular ecstasy users and 10 polydrug users. Also, comparing a sample of 30 current heavy ecstasy users, 31 former ecstasy users, 29

polydrug controls and 30 drug naive controls, Thomasius *et al.* (2003) observed no significant differences using the TMT-B task. This was supported by McCardle *et al.* (2004) who found no ecstasy-related group differences on the TMT-B in a sample of 17 ecstasy users compared to 15 non-ecstasy user controls. Furthermore, Morgan *et al.* (2002) used the TMT-B task to assess executive function in four groups: 18 current ecstasy users, 15 former ecstasy users, 16 polydrug controls (with similar drug use histories to the ecstasy groups) and 15 drug naive controls. Although completion times for TMT-B did not differ significantly between the groups, ecstasy users did commit significantly more errors on this task (current users committed slightly more than previous users although this was non-significant).

With regards to the plus/minus task (Jersild, 1927; Spector & Biederman, 1976; Miyake *et al.*, 2000), three lists two-digit numbers are given to the participant. On the first list participants are instructed to add 3 to each two-digit number as quickly and accurately as possible. On the second list participants need to subtract 3 from each number, and finally on the third list the participants are required to alternate between adding and subtracting 3 from the two-digit numbers. The cost of shifting is calculated as the difference between the number of correct answers given in the alternating list and the average of those in the addition and subtraction lists within the given time periods. In terms of the number/letter task (Rogers & Monsell, 1995), participants are presented with a number/letter pair (e.g. 8F) usually in one of four squares on a computer screen. Participants need to indicate whether the number was odd or even when the number–letter pair is presented in the top two squares and also whether the letter was a consonant or a

vowel when the number–letter pair was presented in the bottom two squares. The trials within the first two blocks required no task switching, whereas half of the trials in the third block required participants to shift between these two types of categorization operations. Similar to the plus–minus task, the shift cost for this task is the difference between the average response times of the trials in the third block that required a mental shift and the average response times of the trials in which no shift is necessary.

The only study in the area of recreational drug use that used the plus/minus and number/letter tasks to measure shifting is Montgomery *et al.* (2005). The authors assessed shifting performance using these tasks in 51 ecstasy/polydrug users and 42 non ecstasy university students. No significant difference in performance between the two groups on any of the shifting tasks was observed suggesting that recreational use of ecstasy leaves the shifting component of EF unimpaired. Similar findings were also observed in a number of other studies using the Wisconsin Card Sorting Task (WCST; e.g., Fox *et al.,* 2001; Thomasius *et al.,* 2003; McCann *et al.,* 2007). As discussed in chapter 3, the WCST (Grant & Berg, 1948; Heaton *et al.,* 1981; Kimberg *et al.,* 1997) requires participants to sort cards depending on colour, shape or number. The criterion for sorting changes without warning and the participant needs to be able to shift attention to find the new sorting criterion. Failure of the participant to shift attention (i.e., number of errors until realising the new criterion) is indicative of shifting impairment.

On the whole, no significant differences between ecstasy users and the non-ecstasy control group were observed using the WCST. For instance, no shifting

deficits using the WCST were present between 20 abstinent ecstasy users with self-reported ecstasy-related problems, 20 non-problematic users and 20 controls with some polydrug use (Fox *et al.*, 2001). Thomasius *et al.* (2003) also measured executive shifting in 30 current ecstasy users, 31 former ecstasy users, 29 polydrug users and 30 drug-naïve controls using the WCST. Age, education, IQ, psychopathology as well as alcohol, tobacco and concurrent drug use were controlled in the study. Ecstasy users showed no performance deficits in the WCST with both user groups making significantly fewer errors than polydrug controls leaving open the question as to which drug is responsible for deficits in executive shifting. Reneman *et al.* (2006) and McCann *et al.* (2007) measuring shifting using the WCST also failed to find performance deficits between ecstasy users and non-ecstasy controls.

Traditionally, studies in the area of recreational drug use recruit participants that are polydrug users because of the difficulty to recruit a sample of ecstasy users. The only study that reported ecstasy-related deficits on the WCST and the shifting component of EF in abstinent ecstasy users was the study of Halpern *et al.* (2004). The authors recruited participants from a region in USA where cultural and religious norms minimises the exposure to other drugs including alcohol. Consequently, 11 heavy ecstasy-only users, 12 moderate ecstasy-only users and 16 drug naïve controls completed the WCST. Age, gender, parental education, parental household income, family substance abuse history and family psychiatric history were controlled using regression analysis. Heavy users demonstrated shifting deficits when age, gender and family of origin variables were controlled.

This evidence therefore suggested that recreational use of ecstasy might have an effect on executive shifting.

6.3 Inhibition

The third executive component is inhibition. Inhibition refers to the ability to consciously inhibit dominant, automatic, or current responses when necessary. A popular measure of inhibition in the area of recreational drug use has been the Stroop Task (Stroop, 1935). During the task participants are required to verbally name the colour of a stimulus as quickly as possible while the reaction times are measured. The task is comprised of 72 trials where asterisks are printed in one of six colours (red, green, blue, orange, yellow or purple), 60 trials with a colour word printed in a different colour and 12 trials with coloured words printed in the same colour. The different trial types are mixed so the participants are required to consciously inhibit dominant, automatic responses. No ecstasy-related deficits on this task were reported in any of the studies.

For example, Gouzoulis-Mayfrank *et al.* (2000) found no performance deficits on the Stroop task between a sample of ecstasy users, cannabis-only users and drug naïve controls. Morgan *et al.* (2002) also administered the Stroop Task to measure inhibition in a sample of 18 current ecstasy/polydrug users, 15 former ecstasy/polydrug users, 16 polydrug users and 15 drug naïve controls. No significant differences in the Stroop Task were observed between the four groups suggesting that inhibition does not appear to be impaired in recreational ecstasy users. Inhibition was also measured with regard to ecstasy dosage. For instance,

the stroop task was administered to a sample of moderate ecstasy users, heavy current ecstasy users, former ecstasy users and polydrug controls (Reneman *et al.*, 2006). Once again no performance deficits on the Stroop were observed between the groups suggesting that ecstasy exposure also leaves the inhibition component of EF unimpaired.

Contrasting with the aforementioned findings, some studies have reported significant group differences using the Stroop Task (Croft *et al.*, 2001; Yip & Lee, 2005; Dafters, 2006). For example, Croft *et al.* (2001) assessed inhibition in a sample of 11 ecstasy/cannabis users, 18 cannabis users and 31 near-drug-naïve controls. The authors found that higher MDMA consumption predicted slower speed processing in the Stroop task. However, these findings were equivocal since the initial ANOVA showed no significant main effect for processing speed across their 3 groups while a subsequent ANCOVA analysis with both user groups combined and measures of cannabis and ecstasy use as covariates established that ecstasy was more strongly related to the performance deficits than cannabis. Homogeneity of regression results were not reported in this analysis. Yip and Lee (2005) also reported deficits on the Stroop tasks between ecstasy users and drug naïve controls. This is a rare study as the ecstasy user group was characterised solely by ecstasy use and no other recreational drug including tobacco and alcohol. In this study discriminant function analysis significantly classified ecstasy users with 99% accuracy based on response time. However, after controlling for multiple comparisons, users' task performance was not significantly worse than that of drug naïve controls. Also, ecstasy consumption

did not correlate with task performance. It is therefore appears that the findings of this study are equivocal.

The tower of London (TOL) is another common measure of inhibition that has featured in the recreational drug use literature. This measure requires the participants to move coloured balls between different pegs in order to achieve a a pre-specified goal configuration in the smallest number of moves. The number of moves made to complete the task is a measure of inhibition, i.e., fewer moves is indicative of better inhibition performance. Morgan (1998) in a series of two studies administered the TOL in a sample of 16 ecstasy/polydrug users, 12 non-ecstasy users and 16 drug naïve controls for study one and to 25 ecstasy/polydrug users, 20 non-ecstasy polydrug controls and 19 drug naïve controls for study two. No significant group differences were observed in either of the studies suggesting that the inhibition component (measured by TOL) is not impaired in recreational users of ecstasy. No inhibition deficits were also observed in a later study using the TOL between ecstasy/polydrug users and polydrug controls (Fox *et al.*, 2002).

Despite these non-significant results, some studies have reported ecstasy-related deficits on the inhibition component using the TOL. For instance, Fox *et al.* (2001) found impairments on the inhibition component in a sample of self-reported problematic ecstasy users in comparison to non-problematic users and non-ecstasy controls. More specifically, problematic ecstasy users showed significantly longer solution times compared to controls with some level of polydrug use, whilst non-problematic users showed significantly longer initial planning times than both the control group and problematic users. Nevertheless,

no performance deficits were reported for the number of errors or trials completed. Finally, although De Sola Llopis (2008) found no intergroup differences for the total number of movements or for initiation time, estimated lifetime ecstasy use was significantly correlated with the total number of movements suggesting that ecstasy use is associated with performance on the task.

6.4 Differential effects of ecstasy, cocaine, and cannabis use on Executive Function

Although it is evident from the EF literature that ecstasy impairs the updating component and tasks that load on WM, the ecstasy-related deficits on inhibition and shifting are less evident. Recent neuropsychological studies have investigated the differential effects of ecstasy, cannabis and cocaine on executive components in order to determine whether these executive components are susceptible to other recreational drugs (Verdejo-Garcia & Perez-Garcia, 2007; Verdejo-Garcia *et al.*, 2005; Fernandez-Serrano *et al.*, 2010; Madoz-Gúrpide *et al.*, 2011). For instance, Verdejo-Garcia *et al.* (2005) investigated the severity of consumption of different drugs and neuropsychological performance on tasks sensitive to executive components of working memory, response inhibition, cognitive flexibility, and abstract reasoning. Thirty-eight polysubstance abusers completed the different tasks along with a severity of drug consumption interview. Using multiple regression analyses the authors found that severity of ecstasy use had an impact on working memory and abstract reasoning indices whilst severity of cocaine use was associated with the inhibitory control index. Severity of cannabis use was associated with the cognitive flexibility index.

Verdejo-Garcia and Perez-Garcia (2007) also suggested that chronic use of cocaine has adverse effects on executive functioning. In their study two groups of participants were recruited i.e., abstinent polysubstance users and drug free controls. Polysubstance users were further subdivided based on their drug of choice (cocaine vs heroin). Tests of fluency, working memory, reasoning, inhibitory control, flexibility, and decision making were administered. It was found that abstinent polysubstance users had clinically significant impairments on all executive components. In fact, cocaine polysubstance users had more severe impairments than heroin users and controls on measures of inhibition (using the Stroop Task) and shifting (using the go/no go and category test). Indeed, greater severity of drug use predicted poorer performance on updating measures. These finding therefore suggest that chronic drug use is associated with widespread impairment on executive components, with cocaine use inducing more severe deficits on inhibition and shifting.

Further evidence for the involvement of cocaine in EF comes for a recent study that investigated the relationship between executive deficits and three measures of severity of cocaine use: years of use, quantity used, and frequency of use. Twenty-four cocaine users were compared with twenty-seven community controls on several neuropsychological tests of EF. Chronic cocaine users in comparison to the drug naïve controls performed worse on measures of attention and working memory, set-shifting abilities, cognitive test of mental flexibility and response inhibition and the WCST. All three aspects of cocaine use were associated with most of the EF measures suggesting that increased cocaine use is associated with more EF problems (Madoz-Gúrpide *et al.,* 2011).

Besides the aforementioned cocaine-related effect on several executive components, the use of cannabis can also affect adversely EF. For example, the use of cannabis was also implicated in deficits on the updating component. Montgomery *et al.* (2005) showed that in relation to non-ecstasy users, ecstasy users demonstrated deficits on updating and access to long-term memory tasks. The authors also found that cannabis use was negatively correlated with updating performance while cocaine use was associated with long-term memory access. Also, chronic cannabis users have shown WM deficits on several measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB) including Rapid Visual Information Processing, Pattern Recognition Memory, Spatial Recognition Memory, Spatial Span, Spatial Working Memory and Visuospatial Paired Associate Learning (Harvey *et al.,* 2007; Solowij *et al.,* 2008). Furthermore, long-term cannabis users were found to be impaired on measures of inhibition (such as the Stroop task, Go/NoGo and a variety of decision-making and gambling tasks) (Solowij *et al.,* 2002; Bolla *et al.,* 2002; 2005; Smith *et al.,* 2004; Hester *et al.,* 2009).

It is therefore apparent that different drugs affect executive components in distinct ways. Although the recreational use of ecstasy only affects the updating component and tasks loading on WM, it leaves the inhibition and shifting components intact. Other recreational drugs such as cocaine and cannabis, however, have adverse effects on these components. It is therefore crucial to evaluate the contribution of these drugs when investigating executive functioning in ecstasy/polydrug users.

6.5 Chapter summary

In summary, it is evident from the existing literature that ecstasy-related deficits exist in laboratory measures of EF. Although, it seems that the updating component and in general tasks that load on WM are susceptible to the effects of ecstasy, there is little evidence to date to suggest that ecstasy use is associated with impairment on executive shifting or executive inhibition. It is therefore necessary to further investigate the effect of recreational drug use on these components using different laboratory or self-report measures that map on the construct components of executive shifting and executive inhibition. It is also evident from the ecstasy-related EF literature that assessment of EF is restricted to laboratory measures, that although offer strong internal validity, control over extraneous variables and the possibility of examining the component EF processes individually, laboratory measures are limited in terms of their ecological validity and in their ability to capture executive processes as they are manifested in the everyday environment (Gioia *et al.*, 2008).

In order to further investigate the effect of recreational use of ecstasy on executive components and provide an alternative method of assessment, the present investigation will use a self-report measure of EF; the BRIEF-A. As previously discussed in chapter 3, the BRIEF-A is a self-report measure of executive functioning which consists of nine subscales each including questions which involve everyday activities and contain an executive component. The BRIEF-A has been developed to capture the behavioural manifestations of executive dysfunction in the various interrelated domains of the construct that have been commonly discussed in the literature. It is also argued that the BRIEF-A,

measures subtle individual differences in discrete real world processes and unlike many laboratory tests it is unrelated to, and not contaminated by overall differences in general ability measures such as IQ (Bodnar *et al.,* 2007).

Having evaluated the current literature in ecstasy/polydrug use and its adverse effects on PM and EF, the following chapters will further investigate the ecstasy/polydrug-related effect on these processes. The present investigations will also address the identified grey areas in the literature of PM and EF in terms of assessing these multidimentional constructs. Consequently, chapters that follow will evaluate the impact of recreational use of ecstasy on prospective remembering and executive functioning by utilising different assessment approaches as opposed to the traditional measures adopted throughout the literature and assess components that have previously been neglected in the area of recreational drug use.

Chapter 7: Everyday and prospective memory deficits in ecstasy/polydrug users

Chapter overview

This chapter investigates the impact of ecstasy/polydrug use on real world memory i.e. everyday memory, cognitive failures and PM. Both laboratory-based and self-report measures of PM were administered to a sample of ecstasy/polydrug users and non-ecstasy users in order to determine whether ecstasy-related deficits were present. Self-report measures of cognitive failures and everyday memory were also administered. Everyday memory deficits were present in ecstasy/polydrug users. Also, deficits were observed on both laboratory and self-report measures of PM within the ecstasy/polydrug user population in comparison to non-ecstasy users. This study extends previous research by showing that PM deficits observed in recreational users of ecstasy are real and not attributed to self-misperceptions. Ecstasy/polydrug-related deficits were observed on both time and event-based PM and are not task specific. Surprisingly, recreational use of cocaine was also highly associated with PM deficits.

7.1 Introduction

An important aspect of memory that has received increased attention in recent years is known as real world memory. In the present study, real world memory is assessed in terms of three separate but related aspects: everyday memory, cognitive failures and PM. Everyday memory and cognitive failures refer to an individual's inability to remember to carry out simple everyday tasks, for example, forgetting the location of familiar objects around the house or workspace, failing to recognise acquaintances or to recollect important events that occurred previously. PM involves remembering to carry out a particular behaviour sometime in the future, for example, returning a library book on time, passing on a message or taking medication on time.

Previous investigations have demonstrated a link between the use of recreational drugs and real world memory problems. For example, ecstasy/polydrug users (Montgomery & Fisk, 2008) and cannabis-only users (Fisk & Montgomery, 2008) showed deficits in a variety of self-report real world memory measures. Evidence for PM impairments in ecstasy/polydrug users (Heffernan *et al.,* 2001a; 2001b) and cannabis users (McHale and Hunt, 2008) have also been demonstrated in other studies. It also appears that PM impairments might be drug specific and that cannabis is associated with "here and now" memory deficits in short-term habitual and internally cued PM and ecstasy with long-term PM problems (Rodgers *et al.,* 2001; 2003).

Most studies in the area of recreational drug use have investigated PM performance using self-report measures of PM (Heffernan *et al.,* 2001a; 2001b;

Fisk & Montgomery, 2008; Montgomery & Fisk, 2008; Rodgers *et al.,* 2001; 2003). Although these self-report measures are well validated and have been proven to be a powerful tool in detecting PM deficits in recreational drug users, they reflect participants' self-perceptions concerning their memory ability. It is therefore possible that these self-perceptions are distorted. For example, drug users may arrive at the laboratory with the expectation that they will underperform (Cole *et al.,* 2006; Bedi and Redman, 2008), an expectation that can affect their responses on self-report measures exaggerating the extent of any deficits present. It is also possible that people experiencing memory impairment might not be able to remember and thus report their memory lapses.

Nevertheless, the most important limitation of self-report measures is that they somehow fail to capture the distinction between time-based and event-based PM tasks. Instead, self-report measures focus on the period over which the PM task is executed i.e., the short-term or the long-term. From the existing self-report literature it is not clear whether ecstasy/polydrug users are impaired in event-based, time-based PM tasks or on both types of PM task. It is therefore crucial to explore this as these two types of task utilise neural processes that are in part separable. Neuroimaging evidence suggests that event-based tasks utilise the frontopolar cortex including Broadmann area 10 (BA10; Burgess *et al.,* 2003; Gilbert *et al.,* 2005). Whilst time-based tasks not only activate the frontopolar cortex, they also activate more diverse regions including the anterior medial frontal regions, the right superior frontal gyrus and the anterior cingulate (Okuda *et al.,* 2007).

Although, as previously discussed in Chapter 5, objective measures such as the 'virtual week' have been employed to overcome this limitation (Rendell *et al.*, 2007), they have been rather artificial and contrived in nature. There is a need to employ more ecologically valid measures to assess PM because if ecstasy/polydrug users are differentially affected on time and event-based PM tasks, this will provide further information on which specific neural locations are susceptible to specific drug-related effects.

In order to address the aforementioned limitations this investigation will include laboratory measures of event and time-based PM as well as short-term and long-term PM in addition to the existing self-report measures of real world memory. These simple laboratory measures are designed to be more naturalistic, with the PM component being less obvious to the participant. Along with the designed laboratory measures of PM the Rivermead Behavioural Memory Test (RBMT-II; Wilson *et al.* 1999) will be administered. The RBMT is a laboratory measure of everyday memory that includes three PM tasks and it has been extensively used in the literature with a variety of populations (Anderson *et al.,* 1999; Fraser and Glass, 1997; Guaiana *et al.,* 2004; Jones *et al.,* 2011; Melendez-Moral *et al.,* 2010; Tyson *et al.,* 2005; Wills *et al.,* 2000) but seldom if ever in the area of recreational drug use. Ecstasy/polydrug-related deficits were predicted on all measures.

7.2 Method

Design

All measures were analysed using a between participant design with user group at two levels (ecstasy users, non-ecstasy users) as the controlled variable. Observed variables included background measures such as age, intelligence, years of education, self-report health and consumption of cigarettes per day and units of alcohol per week. The recreational drugs cannabis and cocaine were also observed in terms of their total lifetime of use, frequency, current use and average use. Any group differences between these background variables were investigated by a series of independent sample t-tests. Where group differences reached significance, a further analysis was carried out using MANCOVA with the relevant background measure as a covariate.

A series of two MANCOVAs was used to look at group differences for the laboratory-based and self-report measures separately where the self-report measures in one occasion and the laboratory-based measures on the other occasion were used as the dependent variables. Lifetime and frequency of cannabis use as well as alcohol and tobacco consumption were used as covariates in both cases. Pearson's correlation coefficients were calculated between the real world memory measures and weeks since last use of the four most consumed drugs i.e. ecstasy, cannabis, cocaine and amphetamines. Regression analyses were also conducted with the lifetime use and frequency of use of the major drugs as

independent variables. Pearson's correlation coefficients were also calculated between laboratory and self-report measures.

Participants

Forty two ecstasy/polydrug users (mean age= 21.67, Males=14, Female=28) and thirty one non-users (mean age= 21.03, Males=5, Females=26) took part in this investigation completing a range of both self-report and laboratory based PM measures. All participants completed a drug history questionnaire before taking part, describing their pattern of drug use. Measures of alcohol and smoking were also accessed in the drug use history questionnaire. Participants were recruited via direct approach to university students and the snowball technique i.e., mouth to mouth referral (Solowij, 1992). All participants were university students attending Liverpool John Moores University or the University of Central Lancashire. Due to the nature of the studies, there is some overlap in terms of the participants in some of the chapters. Please refer to appendix 1 for specific number of participants overlapping in each study.

Materials

The prior history of ecstasy consumption and the beliefs and behaviours associated with ecstasy were assessed using the background drug use questionnaire (see appendix 2 for a copy of the questionnaire). Participants were also questioned concerning their previous use of other drugs, and using a technique employed by Montgomery *et al.* (2005), these data were used to estimate the total lifetime use for each drug (e.g., ecstasy, cannabis,

amphetamines, cocaine, etc.). Length of use, average weekly dose and the amount of each drug consumed within the previous 10, 30, and 90 days was also assessed. Fluid intelligence was measured via Raven's Progressive Matrices (Raven *et al.*, 1998). A further questionnaire assessed the number of years of education, the participant's age and gender and their cigarette and alcohol consumption (see appendix 3 for the questionnaire).

Self-report measures of Prospective memory

Prospective memory Questionnaire (Hannon et al, 1995)

The Prospective Memory Questionnaire (PMQ) is an established self-report measure (Hannon *et al.,* 1995) using a Likert-type scale to indicate likelihood of the occurrence of a memory lapse in set period of time. The PMQ provides measures of three aspects of PM on a scale of 1-9 for each aspect (1 revealing little forgetting, 9 revealing a great deal of forgetting). Fourteen questions measure short-term habitual PM, e.g., "I forgot to turn my alarm clock off when I got up this morning". Fourteen items measure long-term episodic PM, e.g., "I forgot to pass on a message to someone". Ten questions measure internally cued PM, e.g., "I forgot what I wanted to say in the middle of a sentence". In addition, 14 questions make up the "techniques to remember" scale, which provides a measure of the number of strategies used to aid remembering. For each of the four scales, a total score is calculated by summing the responses in each section and dividing them by the number of items in each section (14 for ST-habitual, LT episodic and strategies and 10 for internally cued). Thus high scores being

indicative of much forgetting and many strategies used to aid remembering. For a copy of the questionnaire please see appendix 4.

Prospective and Retrospective Memory Questionnaire (PRMQ; Crawford et al., 2003)

The PRMQ provides a measure of memory slips in everyday life. It consists of sixteen items, eight related to PM failures e.g. 'Do you decide to do something in a few minutes' time and then forget to do it?' and another eight related to RM e.g. 'Do you fail recognising a place you have visited before?'. Participants were asked to say how often these things happened to them on a 5-point scale: very often, quite often, sometimes, rarely or never resulting in minimum and maximum scores of 8 and 40 with higher scores indicative of PM difficulties. For a copy of the questionnaire please see appendix 5.

Everyday Memory Questionnaire (EMQ; Cornish, 2000; Sunderland et al., 1983)

The EMQ is a self-report measure of memory lapses in everyday activities. It consists of twenty seven statements with responses made on a 9-point scale ranging from 'not at all in the last six months' to 'more than once a day'. Examples of items include 'forgetting where you put something' or 'finding a television story difficult to follow'. A total score for everyday memory is calculated by adding the responses to all items with higher EMQ score being indicative of more everyday memory difficulties. For a copy of the questionnaire please see appendix 6.

Cognitive failures questionnaire (CFQ; Broadbent et al., 1982)

The CFQ is a twenty five item measure of cognitive failures or of everyday attentional deficits. Items include 'do you fail to notice signposts on the road?'. or 'do you forget what you came to the shops to buy?'. Responses are made on a 5-point scale with zero corresponding to 'never' and four to 'very often'. A maximum possible score of 100 can be obtained, with higher scores being indicative of more everyday attentional deficits. For a copy of the questionnaire please see appendix 7.

The reliability and validity of the PMQ, CFQ and EMQ have been previously evaluated (Hannon *et al.,* 1995; Royle and Lincoln, 2008; Wallace, 2004).

Laboratory-based measures of PM

Prospective memory pattern recognition test

This test is based on the processing speed task (Fisk & Warr, 1996) which was amended so as to provide a laboratory-based measure of prospective memory by the addition of a concurrent prospective memory element. In the pattern comparison speed task, the stimulus is a matrix potentially consisting of a basic grid of nine cells (three across and three down). Line segments define the borders of each cell and the target patterns are made up of three, six, or nine such line segments randomly selected from the basic grid. Two patterns are displayed, one in the top and one in the bottom half of the screen. The objective is to classify as

many pairs as "the same" or "different" within a fixed time period. Participants were asked to classify the pairs as quickly as possible by pressing the "/" key on the keyboard if the two patterns are the same, and the "z" key if they are different. The two patterns are identical in half of the trials but differ by one line segment only in the other half. For the first 30 seconds, patterns consisted of three line segments, for the next 30 seconds they comprised six line segments, and for the third 30 seconds they were made up of nine line segments. For each level of complexity (three, six, or nine segments), the computer keeps a record of the number of correct responses. This task was repeated three times. The PM element added to this test required the participant to remember to press the F1 key at the end of each trial when the message "please wait a moment" appeared. Participants were told that this was in order to save their scores on the task. Failure to press F1 resulted in the score for that segment being reported as 'error' in the screen display at the end of the task. The number of times the participant forgot to press F1 for each trial was calculated producing a laboratory event-based PM measure.

Prospective memory fatigue test

At the beginning of the test session, participants were told that they should provide an indication of their level of fatigue (using the Karolinska sleepiness scale; Gillberg *et al.,* 1994) every 20 minutes throughout the experiment. If the 20 minute period passed during the completion of a task, participants were asked to complete the questionnaire immediately after. Responses were recorded and the percentage of remembering to complete the Karolinska sleepiness scale was calculated for the first and second half of the session, as well as for the

participant's overall performance, producing three measures of medium-term time-based PM. On occasions where the participant forgot to ask for the questionnaire, he/she was reminded to fill in the Karolinska sheet.

Long-term recall PM

A list of 15 words was presented five times, orally, using an audio recording device. At the end of each trial the participant wrote down as many words as he/she could recall from the list. No time constraint was imposed for recalling the items and the total number of correct words recalled was calculated for each trial. A long-term PM element was added to the recall test. Participants had to remember to return an answer sheet containing the words that they were able to recall to the experimenter after a delay of one, two, and three weeks from the time of testing. Three prepaid envelopes were provided for this purpose. Participants scored 1 if the envelope was returned and 0 otherwise. This data was collected separately for each week but the total number of envelops returned (out of three) by each participant was used as the score for long-term PM.

These laboratory tasks were based on paradigms developed by Mathias and Mansfield (2005) and Einstein *et al.* (1995).

Rivermead Behavioural Memory Test (RBMT; Wilson et al., 1999)

The RBMT-II combines laboratory-based measures of memory and assessments obtained by questionnaire and observation. It aims to provide equivalents of

everyday memory situations, thereby avoiding some of the weakness of questionnaires, rating scales and checklists. There are twelve components to the RBMT each attempting to provide an objective measure of one of a range of everyday memory problems reported and observed in patients with memory difficulties. A full description of the RBMT-II may be found elsewhere (Wilson *et al.,* 1999). In the present study only the three subtasks relating to PM were used:

1) *Remembering a hidden belonging*: Something of minimal value (a pen or pencil in this study) is requested from the participant and placed in a specified location. The participant is required to ask for his belonging and to remember the location when the examiner says "We have now finished this test". Participants receive a score of 2 if the belonging and location are recalled correctly, 1 if after prompt, or 0 if neither object nor location is remembered.

2) *Remembering an appointment*: a timer is set for 20 minutes. The participant is told that when the alarm clock rings he/she should ask a pre-arranged question (e.g., 'What time does this session end'). A profile score of 2 is given if the appointment is recalled correctly, 1 if after prompt or 0 if it is not recalled at all.

3) *Delivering a message:* A path around the room is traced, and an envelope marked "message" is left at a specific location by the experimenter. The participant is required to pick up the envelope and leave it in the right place on the route both immediately and after a delay. A single score was awarded ranging from zero to three depending on the number of errors made over the two attempts. For a copy of the RBMT score sheet please see Appendix 8.

Procedure

Participants were informed of the general purpose of the experiment and verbal consent was obtained. All tests were administered under laboratory conditions and the participant had the right to withdraw from the experiment at any time. The drug history Questionnaire was firstly administered followed by Ravens, Health/Age/Education questionnaire, Prospective Memory questionnaires (Crawford *et al.,* 2005 and Hannon *et al.,* 1995), Prospective Memory Pattern recognition Task, Recall PM task and the RBMT-II. The fatigue prospective memory task was administered throughout the session. Participants were fully debriefed, paid 20 UK pounds in Tesco store vouchers and given drug education leaflets. The study was approved by the Ethics committee of the University of Central Lancashire.

7.3 Results

Demographic and background variables

The scores for background measures such as age, years of education, intelligence, and cigarette and alcohol consumption are summarised in Table 7.1. A series of t-tests revealed that no significant differences between the two groups were present in age, fluid intelligence and years of education. Although the number of cigarettes consumed per day by smokers did not differ significantly between the two groups, tobacco use was more prevalent among ecstasy/polydrug users than non-ecstasy users. In fact, over half of ecstacy/polydrug users were current cigarette smokers and less than one third of non-ecstasy users currently smoked

cigarettes. Ecstasy/polydrug users consumed significantly more units of alcohol per week $t(69)= 3.56$, $p<0.001$, than non-ecstasy users.

Table 7.1. Demographical and Background Drug Use Variables for Users and Nonusers

	Ecstasy/Polydrug Users			Non Ecstasy Users			
	Mean	S.D.	N	Mean	S.D.	N	p
Age (years)	21.67	3.61	42	21.03	3.25	31	ns
RavensProgressive Matrices (maximum 60)	43.31	10.90	41	44.87	7.57	31	ns
Years of Education	13.98	4.22	41	14.48	2.99	31	ns
Cigarettes per day	9.76	8.68	21	6.33	6.65	9	ns
Alcohol (Units per week)	15.07	9.90	41	7.17	8.28	30	<.001
Total Use							
Ecstasy (Tablets)	668.88	1234.67	42	-	-	-	-
Amphetamine (grams)	196.00	254.78	13	-	-	-	-
Cannabis (joints)	3259.49	4571.12	39	243.00	323.14	10	<.001
Cocaine (lines)	1270.71	1762.69	28	255.00	343.65	2	-
Frequency of Use (times per week)							
Ecstasy	0.25	0.32	42	-	-	-	-
Amphetamine	0.10	0.27	14	-	-	-	-
Cannabis	1.02	1.79	39	0.86	1.59	10	ns
Cocaine	0.41	0.51	27	0.54	0.65	2	-
Weeks Since Last Use:							
Ecstasy	31.56	63.73	42	-	-	-	-
Amphetamine	118.90	160.04	16	-	-	-	-
Cannabis	30.40	71.08	39	71.80	88.73	10	ns
Cocaine	23.65	57.23	32	6.33	2.89	3	-
Number Ever Used							
Amphetamine			17			0	
Cannabis			40			10	
Cocaine			33			3	

With respect to illicit drug use, the majority of ecstasy/polydrug users had in the past, or were currently consuming cocaine and most of them were cannabis users. Less than half of ecstasy/polydrug users had a history of amphetamine use. Statistical analyses revealed that there were no significant differences between the two groups in the frequency of cannabis and cocaine use. No statistical difference was observed in the amount of total cocaine consumed between the two groups. Ecstasy/polydrug users, however, smoked significantly more joints in total than non-ecstasy users $t(39.43)=4.08$, $p<0.001$ thus having greater lifetime exposure to cannabis. Given the limited use of cocaine and amphetamines among the non-ecstasy user group it was not meaningful to statistically analyse group differences for these substances.

Before analysing the data for the laboratory and self-report measures of real world memory data screening was performed to identify any possible outliers. Univariate outliers for the real world memory measures were identified and corrected according to Tabachnick and Fidell (2007). The transformed values were used to carry out the statistical analysis. A multivariate outlier was also identified and that particular person was excluded.

Laboratory-based measures

Outcomes for both laboratory and self-report measures of real world memory for ecstasy/polydrug users and non-ecstasy users are summarised in Table 7.2.

Table 7.2. Scores on laboratory and self-report measures of real world memory for ecstasy/polydrug users and non-ecstasy users (one-tailed)

	Ecstasy/ Polydrug Users		Non Ecstasy Users		P	p covariates: cannabis use	p Covariates: cannabis smoking, and alcohol use
	Mean	S.D.	Mean	S.D.			
LABORATORY MEASURES							
RBMT-II							
Appointment	1.55	0.77	1.65	0.61	ns	ns	ns
Belonging	1.19	0.77	1.65	0.61	<.01	<.05	<.05
Message	1.90	0.30	1.90	0.30	ns	ns	ns
Fatigue PM Task (% recalled)							
First half of test session	50.44	36.04	72.20	25.57	<.01	<.01	<.05
Second half of test session	9.48	16.26	44.62	39.52	<.001	<.001	<.001
Processing Speed PM Task Errors	1.60	2.41	0.61	1.23	<.05	<.05	<.05
Long Term Recall PM Task (max 3)	0.81	1.21	1.29	1.16	<.05	ns	ns
SELF-REPORT MEASURES							
Everyday Memory	94.51	36.13	79.42	31.77	<.05	<.05	<.05
Prospective Memory (Hannon et al)							
Short Term	1.53	0.69	1.27	0.38	<.05	<.05	ns
Long Term	2.81	1.00	2.47	0.88	ns	ns	ns
Internally Cued	2.62	0.96	2.39	0.95	ns	ns	ns
Techniques to Remember	2.74	1.10	3.32	1.58	<.05	ns	ns
Cognitive Failures	43.40	14.20	40.00	12.71	ns	ns	ns
Prospective Memory (Crawford et al)	22.63	4.96	20.26	5.52	<.05	<.05	ns

Regarding the laboratory measures, inspection of Table 7.2 reveals that ecstasy/polydrug users were impaired on all but two of the measures. The two groups did not differ significantly in one event-based and one time-based PM task in the RBMT-II. With regard to the time-based PM tasks, ecstasy/polydrug users, with the exception of the appointment test of the RBMT-II, were impaired in relation to the non-ecstasy users. In fact, ecstasy/polydrug users forgot to complete the fatigue task on more occasions than the control group, especially in the second half of the test session. For example, the completion rate for ecstasy/polydrug users in the first half of the session was only around 50% as opposed to non-ecstasy users' rate that was as high as 72%. The difference between the two groups was more striking in the second half of the session where ecstasy/polydrug users remembered to complete the fatigue task an average of 9% of the time as opposed to non-ecstasy users who completed around 45% of occasions, almost five times more often than ecstasy/polydrug users. Impaired time-based PM performance is also evident on the long-term measure. For example, during the three weeks following testing, non-ecstasy users posted back almost 50% more delayed response sheets compared to ecstasy/polydrug users. These group differences were, however, were less evident on the time-based RBMT-II appointment task.

In terms of the event-based PM tasks, ecstasy/polydrug users once again demonstrated more difficulties performing the tasks than non-ecstasy users as they performed worse on the RBMT-II belonging task and the event-based processing speed task. More specifically, ecstasy/polydrug users forgot to press the F1 key almost three times more than the control group in the processing speed task.

Surprisingly, no performance difference was observed in the RBMT-II message task between the two groups.

In terms of statistical analysis, MANOVA with the seven laboratory measures of PM as dependent variables and the ecstasy/polydrug user group between participants as the independent variable revealed a statistically significant group effect $\Lambda = 0.59$, $F(7,65)=6.49$, $p<0.001$, partial $\eta^2=0.411$. Univariate analysis revealed that all but two of the individual measures yielded statistically significant group differences with ecstasy/polydrug users consistently performing worse than non-ecstasy users. More specifically, ecstasy/polydrug users performed worse on the RBMT-II belonging task ($F(1,71)=7.36$, $p<0.01$, partial $\eta^2 =0.094$), the fatigue task (first half: $F(1,71)=8.23$, $p<0.01$, partial $\eta^2 =0.104$ and second half: $F(1,71)=27.11$, $p<0.001$, partial $\eta^2 =0.276$), the long-term recall PM task ($F(1,71)=2.90$, $p<0.05$, partial $\eta^2 =0.039$) and the processing speed PM task ($F(1,71)=4.31$, $p<0.05$, partial $\eta^2 =0.057$). No significant differences were present in the RBMT-II appointment task or the RBMT-II message task. The values for means and standard deviations for all laboratory measures of PM for both groups are summarised in Table 7.2.

Following the inclusion of the covariates relating to lifetime cannabis use (joints) and the current frequency of cannabis use (times per week), the multivariate group effect remained statistically significant $\Lambda = 0.662$, $F(7,62)=4.52$, $p<0.001$, partial $\eta^2=0.338$. When the previously significant dependent variables were considered separately they remained significant with the exception of the long term recall PM task $F(1,68)=0.72$, $p=0.201$, partial $\eta^2=0.010$. Following the inclusion of two

more covariates relating to alcohol consumption (units per week) and tobacco use (cigarettes per day) the multivariate group effect once again remained statistically significant $\Lambda = 0.71$, $F(7,58)=3.41$, $p<0.01$, partial $\eta^2=0.292$. The inclusion of the four covariates reduced the ecstasy/polydrug user group effect size by 11.6%. In the univariate analyses three out of the seven dependent variables remained statistically significant while the long term recall PM task was no longer statistically significant $F(1,64)=0.12$, $p=0.37$, partial $\eta^2=0.002$. Inspection of table 7.2 suggests that with regard to the laboratory measures, ecstasy/polydrug users remained impaired in relation to the non-ecstasy user group even following the inclusion of the covariates in almost all the measures. It can therefore be concluded that the deficits in the ecstasy/polydrug group are more likely to be attributed to ecstasy.

Self-report measures of real world memory

Results for the self-report measures of real world memory in ecstasy/polydrug users and non-ecstasy users are summarised in Table 7.2. With the exception of cognitive failures, it is evident from looking at Table 7.2 that ecstasy/polydrug users experience a greater occurrence of real world memory problems than non-ecstasy users. MANOVA with the seven self-report measures of real world memory as the dependent variables and the ecstasy/polydrug user group between participants revealed a statistically significant group effect $\Lambda = 0.76$, $F(7,58)=2.68$, $p<0.01$, partial $\eta^2=0.245$. In terms of the univariate analyses, the difference in performance between the two groups was statistically significant for the four out of the seven real world memory measures with ecstasy/polydrug users performing

worse than the non-ecstasy users on all occasions. In more detail, ecstasy/polydrug users scored higher than non-ecstasy users, thus had higher number of memory slips, in their self-perceived everyday memory ($F(1,64)=3.21$, $p<0.05$, partial $\eta^2=0.048$), short term PM ($F(1,64)=3.21$, $p<0.05$, partial $\eta^2=0.048$) and overall PM performance ($F(1,64)=3.38$, $p<0.05$, partial $\eta^2=0.050$). Also, non-ecstasy users were able to use significantly more techniques to aid their remembering than ecstasy/polydrug users ($F(1,64)=2.99$, $p<0.05$, partial $\eta^2=0.045$). No significant differences between the two groups were present in the long-term PM, internally cued PM or cognitive failures. The values for means and standard deviations for all measures of real world memory for both groups are summarised in Table 7.2.

After the inclusion of the two measures of cannabis use as covariates (lifetime and frequency of cannabis use) the multivariate group effect for the self-report measures of real world memory remained statistically significant ($\Lambda= 0.79$, $F(7,56)=2.18$, $p<0.05$, partial $\eta^2=0.214$) although the significance was reduced to 0.05. Inspection of the univariate analyses showed that all previously significant self-report measures remained significant but one. The techniques used to remember scale from the PMQ was no longer statistically significant $F(7,62)=2.36$, $p=0.06$, partial $\eta^2=0.037$. Following the addition of the other two covariates, alcohol consumption and tobacco use, the multivariate group effect was no longer statistically significant $\Lambda= 0.831$, $F(7,52)=1.51$, $p=0.09$, partial $\eta^2=0.169$. In the univariate analyses, only the everyday memory measure remained statistically significant $F(1,58)=3.39$, $p<0.05$, partial $\eta^2=0.055$ while the other three measures were reduced to below significance: short-term PM,

$F(1,58)=0.80$, $p=0.19$, partial $\eta^2=0.014$; techniques used to remember $F(1,58)=1.81$, $p=0.09$, partial $\eta^2=0.030$ and PM performance in the PRMQ $F(1,58)=2.1$, $p=0.07$, partial $\eta^2=0.035$. In multivariate terms three out of the four covariates produced a statistically significant effect on the self-report real world memory measures: lifetime cannabis use $\Lambda= 0.77$, $F(7,52)=2.20$, $p<0.05$, partial $\eta^2=0.230$; tobacco use $\Lambda= 0.73$, $F(7,52)=2.75$, $p<0.05$, partial $\eta^2=0.270$ and alcohol consumption $\Lambda= 0.745$, $F(7,52)=2.49$, $p<0.05$, partial $\eta^2=0.251$.

Relationship between period of abstinence and memory

It is possible that some of the drug-related deficits observed in the real world memory measures are a product of short-term post intoxication effects. It is therefore important to investigate any possible correlations between weeks since last use for the four main illicit drugs and each of the real world memory measures. Table 7.3 summarises the aforementioned correlations.

Inspection of Table 7.3 reveals that for most of the real world memory measures the correlations were not statistically significant. Although no ecstasy/polydrug effect was evident in Table 7.2, performance on the RBMT-II appointment task was negatively correlated with the period of abstinence for amphetamines $r=-.526$, $p<0.05$ suggesting that participants abstaining for a longer period perform better on the time-based PM task.

Table 7.3. Correlations between Real World memory Measures and Duration of Abstinence for the Major Illicit Drugs

	Weeks Since Last Use:			
	Ecstasy	Cannabis	Cocaine	Amphetamine
LABORATORY MEASURES				
RBMT-II				
Appointment	-.089	.025	.001	-.526*
Belonging	.137	.082	.030	.078
Message	.001	.175	.066	.212
Fatigue PM Task (% recalled)				
First half of test session	.336*	.281	.248	.405
Second half of test session	.113	.124	-.128	.192
Processing Speed PM Task Errors	-.037	-.182	-.029	-.174
Long Term Recall PM Task (max 3)	-.173	.053	.074	-.010
SELF-REPORT MEASURES				
Everyday Memory	-.028	-.048	-.126	-.243
Prospective Memory (Hannon et al)				
Short Term	-.119	-.043	.165	-.210
Long Term	-.034	-.023	-.033	-.154
Internally Cued	.044	-.155	-.027	-.043
Techniques to Remember	.024	-.110	-.084	.218
Cognitive Failures	-.556***	-.147	-.070	-.305
Prospective Memory (Crawford et al)	-.151	-.113	-.026	-.119

*** p<.001; * p<.05 one-tailed

Similarly, performance on cognitive failures was highly correlated with the period of abstinence in relation to ecstasy use r=-.556, p<0.001 suggesting that a longer period of abstinence causes fewer self-reported cognitive failures. A relationship between the first half of the fatigue test and the period of abstinence from ecstasy was also observed r=.336, p<0.05 suggesting that the longer the period of abstinence from ecstasy the better the performance on the time-based PM task.

Relationship between aspects of drug use and real world memory measures

The relationship between the lifetime use and frequency of use for the four major illicit drugs i.e., ecstasy, cannabis, cocaine and amphetamines and the real world memory measures was investigated. Regression analyses were conducted with either the frequency or lifetime use of the four major drugs as the independent variables and each real world memory measure in turn as the dependent variable. Table 7.4 summarises the simple and semi partial correlation coefficients from these regression analyses.

For the frequency of use and lifetime use nonusers of each drug were coded as zero. Regression analyses were only conducted in those cases where the simple correlation between the drug use measure and the real world memory measure was statistically significant. Inspection of Table 7.4 reveals that total lifetime use of ecstasy and cocaine are related with several laboratory measures of PM, suggesting that as the level of use increases so does the PM deficit. More specifically, total lifetime use of ecstasy was correlated with the RBMT-II belonging task, the second half of the fatigue PM task and the processing speed PM task. Lifetime use of cocaine was correlated with the RBMT-II appointment task, the RBMT-II belonging task, the second half of the fatigue task and the processing speed PM task. Lifetime use of cannabis was also found to be correlated with the RBMT-II belonging task, the second half of the fatigue PM task and the long term recall PM task.

Table 7.4. Correlations between Real World memory Measures and Lifetime Use and Frequency of Use for the Major Illicit Drugs

		Lifetime Use		Frequency	
Real World Memory Measure	Drug	Simple	Semi Partial	Simple	Semi Partial
Laboratory Measures					
RBMT-II					
Appointment	Cocaine	-.258*	-.288*	-.265*	-.210
Belonging	Ecstasy	-.300**	-.106		
	Cannabis	-.233*	-.052		
	Cocaine	.408***	-.238*	.482***	-.440***
Message	Cannabis			-.264*	-.273*
Fatigue PM Task (% recalled)					
First half of test session	Ecstasy			-.238*	-.163
	Cannabis	-.203	-.124	-.247*	-.203
	Cocaine	-.204	-.072	-.244*	-.101
Second half of test session	Ecstasy	-.231*	-.118	-.267*	-.167
	Cannabis	-.254*	-.178		
	Cocaine	-.213*	-.033		
Processing Speed PM Task Errors	Ecstasy	.284*	.177	.227*	.143
	Cocaine	.283*	.146	.277*	.154
Long Term Recall PM Task (max 3)	Cannabis	-.212*	-.132	-.289*	-.220
	Cocaine	-.191	-.154	-.330**	-.271*
Self-Report Measures					
Everyday Memory					
ProspectiveMemory (Hannon et al)					
Short Term	Ecstasy	.304**	.279*		
	Cannabis			.265*	.218*
Long Term					
Internally Cued	Ecstasy	.377**	.361**	.271*	.181
	Amphet-amine			.249*	.127
Techniques to Remember					
Cognitive Failures	Ecstasy	.292*	.212	.350**	.251*
	Cocaine	.237*	.027		
	Cannabis	.251*	-.185		
ProspectiveMemory (Crawford et al)	Ecstasy	.330**	.188	.253*	.100
	Cocaine	.249*	.097		
	Amphet-amine	.229*	.183		

*** p<.001; ** p<.01; * p<.05; one-tailed

In terms of frequency of use, cocaine was correlated with almost all the laboratory measures of PM whilst the frequency of use for ecstasy was only correlated with three out of the seven laboratory measure. Frequency of use for cannabis was also correlated with three PM laboratory measures. More specifically, frequency of ecstasy use was correlated with the fatigue PM task at both times of the test session and the processing speed PM task. Frequency of cocaine use was correlated with the RBMT-II appointment task, the RBMT-II belonging task, the first half of the fatigue PM task, the processing speed PM task and the long term recall PM task. Finally, cannabis was correlated with the RBMT-II belonging task, the first half of the fatigue PM task and the long term recall PM task. Increased frequency of use of is therefore associated with a greater degree of PM impairment. Although the major characteristic of the ecstasy/polydrug group is ecstasy use it appears that cocaine is also implicated in the observed PM deficits.

As far as the self-report measures of real world memory are concerned it appears that lifetime use of ecstasy is responsible for most of the self-report measures, whereas the total lifetime use of cocaine is not as prominent in the self-report measures as in the laboratory measures of PM. Consequently, short term and internally cued PM were correlated with total lifetime use of ecstasy; cognitive failure was correlated with lifetime use of ecstasy, cannabis and cocaine and PM performance from the PRMQ with ecstasy, cocaine and amphetamines in terms of total lifetime use.

Similarly, frequency of use for ecstasy was correlated with three of the real world memory measures i.e., internally cued PM, cognitive failures and PM performance while frequency use of cocaine was not correlated with any of the self-report measures. Frequency of cannabis use was associated with short term PM while frequency of amphetamine use was correlated with internally cued PM. No association with any aspect of drug use was observed in everyday memory or techniques use to remember. The significant correlations suggest that increased frequency of use is associated with higher scores on the self-report measures consistent with more real world memory problems.

Table 7.4 also displays the semi partial correlation values from the regression analyses. A semi partial correlation coefficient represents the correlation between the dependent variable (real world memory measure) and a predictor (lifetime or frequency of use for the four illicit drugs) that has been residualized with respect to all other predictors in the equation with the dependent variable remaining unaltered. After removing variance that the specific predictor has in common with the other predictors, the semi partial expresses the correlation between the residualized predictor and the unaltered dependent variable. It therefore assesses the specific effect of each independent variable on the dependent variable.

It was found that the lifetime use of cocaine is primarily responsible for the deficits observed in the RBMT-II appointment and belonging tasks, as the semi partial correlations were statistically significant. On the other hand, lifetime use of ecstasy is responsible for difficulties in short-term and internally cued PM in the self-report measures. Frequency of cocaine was also associated with

impairments in the RBMT-II appointment task and the long-term recall PM task suggesting that the use of cocaine affects both event and time-based PM. Frequency of cannabis use was also responsible for the deficits in the RBMT-II message task and the self-report short- term PM, while frequency of ecstasy use was only associated with cognitive failures performance, although this measure was not statistically significant between the two groups.

It is evident from looking at the correlations in Table 7.4 that, although some of the simple correlations were statistically significant for most real world memory measures most, of the semi partial correlations did not reach statistical significance. This means that although the drug-related effect is evident on the particular real world memory measure it is not possible to identify which of the four drugs is likely to be primarily responsible.

Inter-correlations between laboratory measures of PM and self-report real world memory measures

Disregarding the drug-related differences it would be reasonable to assume that laboratory measures of PM will be correlated with each other and with the self-report measures of PM. Nevertheless, such correlations cannot be perfect as each laboratory task has different performance aspects. For example, some laboratory tasks measure the time-based aspect of PM and some other the event-based. These tasks also differ in terms of the period over they need to be executed either in the short-term or the long-term. Furthermore, self-report measures of PM do not distinguish the event-based and time-based PM components.

Table 7.5 summarises the inter-correlations between the laboratory measures of PM and self-report real world memory measures. Inspection of Table 7.5 reveals that most of the laboratory measures are inter-correlated with the exception of the long-term recall PM task which is not correlated with any of the other laboratory measures of PM. In addition, some laboratory measures such as the fatigue PM task and the processing speed PM task correlated with a number of self-report measures of real world memory. Finally, Table 7.6 reveals that self-report measures of real world memory were also correlated with each other.

Table 7.6. Inter Correlations between the Self Report Measures of Real World Memory

	Everyday Memory	Prospective Memory				Cognitive Failures
		Short Term	Long Term	Internally Cued	Techniques	
SELF-REPORT MEASURES						
Everyday Memory						
Prospective Memory (Hannon et al)						
Short Term	.049					
Long Term	.442***	.246*				
Internally Cued	.455***	.379***	.507***			
Techniques to Remember	.254*	.211*	.366**	.577***		
Cognitive Failures	.477***	.280**	.357**	.513***	.289**	
Prospective Memory (Crawford et al)	.615***	.145	.412***	.521***	.328**	.707***

*** p<.001; ** p<.01; * p<.05; one-tailed

Table 7.5 Inter Correlations between the Laboratory and Self Report Measures of Real World Memory

	RBMT-II			Fatigue PM Task		Processing Speed PM Task	Long Term Recall PM Task
	Appointment	Belonging	Message	First Half	Second Half		
LABORATORY MEASURES							
RBMT-II							
Appointment							
Belonging	.334**						
Message	-.021	.200*					
Fatigue PM Task (% recalled)							
First half of test session	.238*	.291**	.056				
Second half of test session	.266*	.263*	.122	.425***			
Processing Speed PM Task Errors	-.220*	-.270*	-.049	-.206*	-.185		
Long Term Recall PM Task (max 3)	.010	.087	.004	-.018	-.172	-.135	
SELF-REPORT MEASURES							
Everyday Memory	-.018	-.041	.140	-.063	-.141	-.033	-.103
Prospective Memory (Hannon et al)							
Short-Term	-.096	-.128	-.003	-.230*	-.120	.392***	-.071
Long-Term	-.069	-.155	-.139	-.053	-.312**	-.006	-.182
Internally Cued	-.021	-.037	-.014	-.077	-.175	-.024	.038
Techniques to Remember	-.041	.072	-.048	.024	-.002	.035	.200*
Cognitive Failures	-.174	-.161	.007	-.223*	-.323**	.108	.086
Prospective Memory (Crawford et al)	-.279**	-.190	-.003	-.201*	-.281**	-.008	.035

*** p<.001; ** p<.01; * p<.05; one tailed

7.4 Discussion

The impact of ecstasy/polydrug use in everyday and PM was investigated in the present study. Previous investigations in the area demonstrated that recreational users of ecstasy suffer from deficits in real world memory including everyday memory, cognitive failures and most noticeably in their PM performance (Heffernan *et al.,* 2001a; 2001b; Rodgers *et al.,* 2001; 2003; Montgomery & Fisk, 2008; Fisk & Montgomery, 2008). Although previous research has demonstrated consistently that real world memory problems are evident in ecstasy/polydrug users, PM assessment mode was largely restricted to self-report measures that assess the self-perception of the participant in relation to their possible memory lapses. The need for more objective measures was therefore crucial in order to determine whether the reported deficits by ecstasy/polydrug users are real rather than imagined. The present investigation is therefore assessing real world memory processes with a variety of both objective laboratory measures and self-report measures to determine whether these drug-related deficits previously reported are real, rather than imagined, and consequently confirm or otherwise the validity of the self-reported measures.

In terms of the laboratory measures, multivariate analysis showed that on the whole ecstasy/polydrug users were impaired on the PM laboratory measures; an effect that remained statistically significant after controlling for total lifetime and frequency of cannabis use, tobacco and alcohol use. When looking at the PM measures individually, it was evident that ecstasy/polydrug users performed worse in all cases compared to non-ecstasy users. All measures, but two (one event and

one time-based PM task), reached statistical significance demonstrating that the differences in performance between the two groups represent meaningful differences. Ecstasy/polydrug users seem to experience greater difficulties in event-based, time-based and long term PM than non-ecstasy users. Subsequently, the present study extends previous research in which ecstasy/polydrug users were impaired in their PM performance (Heffernan *et al.*, 2001a; 2001b; Rodgers *et al.*, 2001; 2003; Montgomery & Fisk, 2008; Fisk & Montgomery, 2008).

Only a few studies have used the RBMT to investigate the ecstasy-related deficits on PM. For example, Zakzanis *et al.* (2003) administered the RBMT in a group of ecstasy/polydrug users and non-ecstasy users. Unlike the present study, Zakzanis *et al.* observed ecstasy-related deficits on the appointment and message PM scale of the RBMT but not on the belonging scale. However, it is likely that these deficits on the two subscales of the RBMT were due to confounding factors as their ecstasy/polydrug user group scored significantly less on the WAIS-III vocabulary sub-test compared to the control group. To the best knowledge of the author, the present study is the first one to demonstrate ecstasy-related deficits on the belonging subscale of the RBMT. Although the RBMT has been consistently used to detect memory lapses in clinical populations, it has been criticised as lacking the sensitivity to detect memory problems in non-clinical populations (Spooner & Pachana, 2006). Thus it may be that the test was not appropriate for the university based sample of recreational drug users and the absence of impairments in the two subtests might be attributed to the limited sensitivity of the test rather than the lack of ecstasy/polydrug related impairments.

In terms of the three remaining laboratory tests of PM i.e., the fatigue PM task, processing speed PM task and the long-term recall PM task ecstasy/polydrug users performed significantly worse on all three measures in comparison to the control group and after controlling for covariates all but the long-term recall PM task remained statistically significant. More specifically it was found that ecstasy/polydrug users remembered to ask for a fatigue questionnaire on fewer relevant occasions than non-ecstasy users, they made more errors on the processing speed PM task and returned fewer envelops during the three-week period following testing. These findings suggest that ecstasy/polydrug users experience more general PM problems as deficits were evident on both the retrieval phase (time and event-based PM tasks) and storage/retention phase (short and long-term PM). This also suggests that ecstasy/polydrug-related deficits demonstrate a general feature of PM performance rather than task-specific aspects.

It appears, that in terms of the laboratory PM performance the observed deficits are more likely to be attributed to the effect of ecstasy/polydrug use rather than cannabis as previously suggested (McHale & Hunt, 2008). This is consistent with previous findings with studies using self-report measures of PM (Heffernan *et al.*, 2001a; 2001b; Montgomery & Fisk, 2007; Rodgers *et al.*, 2001; 2003). What is also evident from the present findings is that the deficits observed in ecstasy/polydrug users are real rather than imagined and they are evident on both time and event-based PM and also short and long-term PM.

Although the present study is among the first to use a variety of laboratory tasks and naturalistic PM tasks, previous research using the 'virtual week' paradigm also revealed ecstasy-related deficits in event and time-based PM performance (Rendell *et al.*, 2007). As previously discussed in Chapter 5 the 'virtual week' is a board game where the participant is required to complete previously learned tasks at specific times during the game. While this test differentiates event and time-based PM it clearly has an associative learning component since the participant needs to learn each response paired with specific location on the board before carrying out the PM task. Consequently, the deficits observed during the game might at least in part be attributed to associative learning impairments rather than difficulties in PM performance. This is possible as previous investigations suggest that associative learning is impaired in ecstasy/polydrug users (Montgomery *et al.*, 2005b). Therefore, the laboratory measures used in the present study required minimal learning and retrospective memory. This ensures that the deficits in performance observed on these tasks are less likely to be attributed to associative learning or retrospective memory problems.

Although the ecstasy/polydrug group differences remained statistically significant after the inclusion of aspects of cannabis use as covariates, further analysis revealed that cannabis is negatively associated with PM performance. For instance, the frequency of cannabis use was associated with performance on the RBMT message task performance although the two groups did not differ statistically in the main analysis. In fact, after the shared variance with the other drugs was excluded the effect of cannabis remained statistically significant. Cannabis was also correlated with the fatigue PM task at both times of the test

session. For the first half of the session, both frequency and total lifetime use of cannabis were associated with poorer PM performance; an effect that nevertheless did not remain statistically significant after the exclusion of shared variance with the other drugs. Total lifetime use of cannabis was also associated with poorer performance in the second half of the session. Finally, both lifetime and frequency of cannabis use were associated with the long term recall PM task suggesting that cannabis use contributes to poorer long-term PM.

In terms of the recreational use of ecstasy, it was found that lifetime use of ecstasy was negatively associated with the RBMT belonging task, the second half of the fatigue PM task and the processing speed task whilst frequency of ecstasy use was negatively associated with the first half of the fatigue task and the processing speed PM task. Nevertheless, after excluding the shared variance of the other drugs none of these associations reached significance suggesting that ecstasy use is not uniquely responsible for the effects observed. These findings are somewhat surprising given those reported by Rodgers *et al.,* (2001; 2003) who found that ecstasy use was associated with long term PM deficits while cannabis use was associated with short-term PM.

Another surprising finding in the present study is the effect of cocaine on PM performance. There was clear evidence that cocaine use is associated with performance on a number of laboratory measures of PM. To the best of the author's knowledge the present study is the first to link recreational use of cocaine with PM deficits. Either total lifetime, or frequency use of cocaine or both, were associated with performance on all PM tasks with the exception of the RBMT

message task. In fact, lifetime use of cocaine shared unique variance with the appointment and belonging subtests of the RBMT and frequency of cocaine use with the long term recall PM task suggesting that recreational use of cocaine might be responsible for the observed performance deficits.

As far as the self-report measures are concerned, the drug-related effects were less evident. Although ecstasy/polydrug users as a group reported PM deficits, the specific drugs responsible for these deficits were less clear. Also the effect of cocaine was less evident than in the laboratory measures. Lifetime use of ecstasy and frequency of cannabis use seemed to be associated with self-perceived short-term PM while both lifetime and frequency of ecstasy were associated with internally cued PM. Although ecstasy/polydrug users did not appear to experience difficulties in cognitive failures, lifetime use of ecstasy, cannabis and cocaine were associated with a greater incidence of cognitive failures. In addition, in terms of PM performance on the whole, lifetime use of ecstasy, cocaine and amphetamines emerged as predictors of self-reported PM deficits. Nevertheless, no specific aspect of use for any of the drugs emerged as uniquely responsible for the observed self-reported deficits.

To conclude, the present study intended to determine the impact of ecstasy/polydrug use on aspects of real world memory such as everyday memory, cognitive failures and prospective memory. Ecstasy/polydrug associated deficits were observed on both laboratory and self-report measures of prospective memory. Ecstasy/polydrug users were impaired on all PM laboratory measures with the exception of one event and one time-based PM task from the RBMT-II.

Ecstasy/polydrug related deficits were also observed in some of the self-report measures of PM and in the EMQ while no deficits were observed in the self-report measures of cognitive failures. It can therefore be assumed that ecstasy/polydrug users possess some self-awareness of their memory lapses. An unexpected finding was that the recreational use of cocaine can be associated with prospective memory deficits. Further research is needed, to clarify whether the cocaine related deficits are limited to the ecstasy/polydrug population or whether they might be present among those persons whose recreational use is largely confined to cocaine.

Chapter 8: Ecstasy/polydrug related deficits on the Cambridge Prospective Memory Test (CAMPROMPT)

Chapter overview

It is evident from the previous investigation that ecstasy/polydrug users experience difficulties in PM performance; an effect evident on both laboratory and self-report measures. It is therefore apparent that PM deficits in ecstasy/polydrug users are real rather than imagined. In the present study, as an extension to the previous investigation, the range of laboratory measures of PM was augmented by the use of the CAMPROMPT test battery in order to investigate the impact of ecstasy/polydrug use on event and time-based PM in a sample of cannabis only, ecstasy/polydrug and drug naïve controls. Measures of retrospective memory and learning were also administered in order to establish whether ecstasy/polydrug deficits in PM were mediated by group differences in these processes. Ecstasy/polydrug users performed significantly worse on both event and time-based PM tasks in comparison to both cannabis-only and drug naïve groups. Furthermore, it was found that better retrospective memory was associated with greater PM performance. Nevertheless, this association did not mediate the drug-related effects that were observed. Consistent with previous findings, recreational use of cocaine was linked once again to PM deficits.

8.1 Introduction

Previous investigations into the effect of illicit drug use on PM found that PM performance is impaired after the recreational use of ecstasy (Heffernan *et al.*, 2001a; 2001b; Rodgers *et al.*, 2001; 2003; Montgomery & Fisk, 2007). The previous investigation, in an attempt to overcome the limitations of previous studies, administered simple laboratory measures of PM as opposed to the previously adopted self-report PM measures to establish whether reported impairments in PM are real rather than imagined. It also distinguished differences in event and time-based PM since previous research has mostly investigated drug-related impairments in the storage/retention phase i.e., short and long-term PM. It was found that PM deficits are evident both on self-report and laboratory based measures and are apparent on both the retrieval (time and event-based) and storage/retention phase (short and long-term).

Evidence suggests that PM is dependent on medial temporal-hippocampal processes as well as PFC resources. Evidence for this comes from several clinical studies. For instance, Adda *et al.* (2008) observed PM impairment in a clinical group with medial temporal sclerosis. More specifically, they found that patients with left hemisphere lesions were also impaired in delayed verbal recall on the Rey Auditory Verbal Learning Task (RAVLT) suggesting that PM performance is correlated with verbal learning ability. A number of studies using this measure suggested that recreational users of ecstasy are also impaired on their verbal learning ability. For example, Fox *et al.* (2001) administered the Auditory Verbal Learning task to examine learning of verbal material in short-term and long-term ecstasy users and polydrug controls. Both ecstasy user groups recalled

significantly fewer words on the initial three recall trials as well as on the delayed recall trial in comparison to the polydrug control group with long-term ecstasy users performing the worst. Ecstasy-related impairments on verbal learning were also observed using the RAVLT in other studies (Reneman *et al.,* 2000; Quednow *et al.,* 2006) while memory and learning impairments are evident in ecstasy/polydrug users in a number of other studies (Parrott *et al.,* 1998; Parrott & Lasky, 1998; Bolla *et al.,* 1998; Rodgers *et al.,* 2000).

Evidence also suggests that PM performance is correlated with episodic memory after alcohol administration (Leitz *et al.,* 2009) and retrospective memory in general (Martin *et al.,* 2007; Goto and Grace, 2008). Retrospective memory refers to remembering past events or experiences and according to Einstein and McDaniel (1990) PM has a retrospective component responsible to retain the basic information about action and context. It is therefore possible that impairments in PM can lead to RM and verbal learning difficulties. Evidence for this association between RM and PM comes from both neuroimaging and animal studies. For example, Martin *et al.* (2007) using magnetoencephalography found that during retrospective and prospective memory tasks the hippocampal region was activated longer in comparison to the control condition. Conversely, other regions were differentially involved as PM tasks were linked with activations in the posterior parietal lobe in comparison to the retrospective and control conditions.

In an animal study utilising a PM paradigm it was found that while rats searched for food rewards in a radial maze the retrospective component while dependent on

hippocampal processes also required PFC resources without which the prospective component could not be activated (Goto & Grace, 2008). In the same study the dopaminergic system appeared to be differentially involved with the two components. Specifically, D1 receptors were associated with the retrospective component while D2 receptors supported the prospective component. Since ecstasy is known to have an effect on both the serotonergic and dopaminergic systems, it is possible that disruption of dopaminergic processes as a consequence of using ecstasy might therefore be responsible for the PM deficits observed in recreational drug users.

Although PM deficits among illicit drug users are apparent in self-report studies (Heffernan *et al.*, 2001a; 2001b; Rodgers *et al.*, 2001; 2003; Montgomery & Fisk, 2008) apart from the more objective PM measures introduced in the previous Chapter differences in performance between recreational drug users and drug naïve persons have yet to be established using laboratory based measures. One of the few studies to look at PM performance in cannabis users utilising simple laboratory measures found that when asked to wait 10 minutes before pressing a timer, relative to controls users were less likely to remember to do so. Furthermore, compared to the control group they were also less likely to remember to post an envelope back to the experimenter two days after the test session (McHale & Hunt, 2008).

A recent laboratory measure of PM is the 'virtual week' (Rendell *et al.*, 2007). As discussed in previous chapters, the virtual week paradigm is a board game in which the participant needs to remember to execute previously learned tasks as

they progress around the board. Some tasks are triggered by external environmental factors (i.e., event-based tasks) while others are cued by the passage of time (i.e., time-based tasks). It is therefore a measure that examines event and time-based PM performance and it has been proven useful in detecting PM deficits among abstinent ecstasy users (Rendell *et al.,* 2007a), long-term abstinent methamphetamine users (Rendell *et al.,* 2009), following acute alcohol administration (Leitz *et al.,* 2009), and in clinical populations including those with multiple sclerosis (Rendell *et al.,* 2007b) and schizophrenia (Henry *et al.,* 2007).

Although the 'virtual week' has been proven to be a powerful laboratory measure in detecting PM impairments in a variety of populations as noted previously it clearly possess an associative learning component as the participants need to learn the responses paired with each location on the board before completing the PM task. Therefore it is not clear that the observed deficits specifically reflect PM performance or are attributable to associative learning impairments that are known to be present in recreational users of ecstasy (Montgomery *et al.,* 2005).

In the previous Chapter, overcoming this limitation, simple laboratory measures of PM that did not involve a learning component were used. The RBMT (Wilson *et al.,* 1999) was also used with only one of the three PM tasks reaching significance. As the RBMT has been criticised as lacking the sensitivity to detect memory problems in non-clinical populations, it was not included in the present investigation. Instead, a more up-to-date test battery was employed. The Cambridge Prospective Memory Test (CAMPROMPT; Wilson *et al.,* 2005) is a laboratory measure of PM that examines event and time-based PM within both

clinical and non-clinical populations (Fleming *et al.,* 2008; Groot *et al.,* 2002; Wilson *et al.,* 2005). Extending the previous investigation the CAMPROMPT was consequently adopted in the present study as an additional more up-to-date measure of event and time-based PM. Measures of verbal learning were also administered in order to capture possible learning impairments in recreational drug users. Rey's Auditory Verbal Learning Test (RAVLT; based on Rey, 1964) was employed for this purpose.

In addition to the CAMPROMPT and the learning measure, as an extension to the previous investigation a RM measure will be administered in order to uncover whether ecstasy/polydrug users are impaired in RM performance and the extent to which these impairments affect PM performance. Unlike the previous study, a cannabis only user group in addition to the ecstasy/polydrug user group is included in order to examine the direct effect of cannabis on memory in general and PM in particular. It is expected that both drug user groups will performed worse on all memory measures compared to the drug-naïve group while no prediction is made for the PM performance between the ecstasy/polydrug and cannabis only user groups.

8.2 Method

Design

A between-participant design with the three groups (cannabis-only, ecstasy/polydrug and drug-naïve) as independent variables and the CAMPROMPT time and event-based PM scores as the dependent variables was

employed. The background variables, retrospective memory and learning measures were also evaluated for differences between the three groups. Pearson's correlation coefficients were calculated between the PM measures and the other measures. Also, regression analyses were conducted with the time and event-based PM measures as the dependent variables in order to determine any unique drug, retrospective memory or learning contributions to PM performance.

Participants

Twenty-nine ecstasy/polydrug users (12 females), twelve cannabis-only users (7 females) and eighteen drug naïve (16 females) took part in the investigation. All participants were university students from the University of Central Lancashire or Liverpool John Moores University and they were recruited via direct approach or via the snowball technique, i.e., mouth to mouth referral (Solowij *et al.*, 1992).

Materials

In common with the previous investigation, the prior history of ecstasy and other drug consumption was assessed using the background drug use questionnaire (Montgomery, *et al.*, 2005). Estimates of the total lifetime use, length of use, average weekly dose and the amount of each drug consumed within the previous 10, 30, and 90 days were also calculated. Fluid intelligence was measured via Raven's Progressive Matrices (Raven *et al.*, 1998) and a further questionnaire assessed the number of years of education, the participant's age and gender and their alcohol and cigarette consumption.

Prospective and retrospective memory questionnaire (PRMQ; Crawford et al., 2005).

The PRMQ provides a self-report measure of prospective and retrospective memory slips in everyday life. It consists of sixteen items, eight referring to prospective memory failures time and eight concerning retrospective failures. Only the retrospective component was used in this study. For full a description of the measure refer to Chapter 7.

Rey Auditory Verbal Learning Test (RAVLT; based on Rey, 1964).

The RAVLT is a test developed to evaluate verbal learning and memory. A list (List A) of 15 words was presented to the participant orally, with the aid of an audio recording device, for five consecutive times. At the end of each trial the participant was asked to write down as many words as possible from the list. After the fifth trial, an interference list (List B), also consisting of 15 words was read to the participant after which she/he was asked to recall as many words as possible from the interference list. Immediately following this the participant was again asked to recall the words from list A without hearing it again (trial 6). Next after a 20-minute interval, the participant was asked to remember the words from list A (trial 7) after which a recognition test was administered. For the recognition test a list consisting of the 15 words from list A and 15 distracter words was read to the participant and the individual was asked to indicate whether the word belonged to list A or not. A number of outcome measures were produced, first the total number of words correctly recalled over trials one to five, second a measure of

proactive interference (number correct on trial one minus number correct on the interference list), third retroactive interference (number correct on trial five minus number correct on trial six) and fourth, a measure of decay (number correct on trial five minus number correct on trial 7). For a copy of the questionnaire please refer to appendix 9.

Memory compensation questionnaire (MCQ; Dixon, de Frias & Bäckman, 2001)

The MCQ is a 44 item self-report measure assessing the variety and number strategies the participant uses to compensate for deficient memory performance. The MCQ is comprised of seven subscales: external (e.g., "Do you use shopping lists when you go shopping?"); internal (e.g., "Do you take your time to go through and reconstruct an event you want to remember?"): time (e.g., "Do you ask people to speak slowly when you want to remember what they are saying?"); reliance (e.g., "When you want to remember an important appointment do you ask somebody else (for example, spouse or friend) to remind you?"); effort (e.g., "Do you put in a lot of effort when you want to remember an important conversation with a person?"); success (e.g., "When you want to remember a newspaper article is it important to you to remember it perfectly?"); and change (e.g., "Do you use such aids for memory as notebooks or putting things in certain places more or less often today compared to *5-10* yrs ago?"). Responses for each item are presented on a 5-point scale, with higher scores representing more frequent use of the specified compensatory behavior (1=*never*, 5=*always*) with some items being reverse scored. For a copy of the questionnaire please refer to appendix 10.

The Cambridge Prospective Memory Test (CAMPROMPT) (Wilson et al., 2005).

The CAMPROMPT is a laboratory measure of PM that consists of a total of six prospective memory tasks, three cued by time and three cued by events. Participants were asked to work on some distractor tasks such as word-finder puzzles or a general knowledge quiz for a twenty minute period while they had to remember to perform the prospective memory tasks. Two of the three time-based tasks were cued by a countdown kitchen timer. In the first time-based task the participant had to remind the experimenter not to forget his/her mug or keys when there were seven minutes left to the end of the session. In the second time-based task, when the timer showed sixteen minutes the examiner asked the participant to remember that "in seven minutes time" he/she had to stop whichever task was they were on and change to another. The third time-based task was cued by a clock. The participant was asked at a specific time (e.g., ten past eleven; 5 minutes after the 20 minute session) to remind the examiner to ring the reception/garage.

For the event-based tasks the participant was asked: 1) to return a book to the examiner when he/she came to a question about the television program 'EastEnders' during the general knowledge quiz; 2) to return an envelope with "MESSAGE" written on it when he/she was reminded that there were five minutes left in the test; and finally, 3) when the examiner informed him/her that the session was over, to remind the examiner to pick up five objects that had been hidden at the beginning of the session. Six points were awarded for each subtask that was successfully completed, unaided. If the task was completed after a single general prompt from the experimenter then 4 points were awarded. Alternatively,

participants were awarded two points if a second more specific prompt was required, one point if after prompting, the required action was completed on the second attempt and no points if the participant failed to complete the required action after prompting. Total scores were then generated on time-based and event-based subscales, each scoring a maximum of 18, with higher scores reflecting better prospective memory performance. The validity and reliability of the CAMPROMPT has been documented previously (e.g., Fleming *et al.,* 2008; Groot *et al.,* 2002; Wilson *et al.,* 2005). For a copy of CAMPROMPT's score sheet please refer to appendix 11.

Procedure

Participants were informed of the purpose of the investigation and their right to withdraw at any time. After verbal consent had been obtained the tests were administered under laboratory conditions. The drug-use questionnaire (Montgomery *et al.,* 2005) was administered first followed by the Raven's progressive matrices (Raven *et al.,* 1998), the age/education questionnaire, the PRMQ (Crawford *et al.,* 2005) and the MCQ (Dixon de Frias, & Bäckman, 2001) questionnaires. Finally, the RAVLT and the CAMPROMPT (Wilson *et al.,* 2005) tests were administered. Participants were fully debriefed, paid £20 in Tesco store vouchers and given drug education leaflets. The University of Central Lancashire's ethics committee approved the study.

8.3 Results

Data screening revealed that no univariate outliers were present in the two PM measures. Where outliers were present, in the other memory measures, were replaced by the next highest/lowest score on the particular measure, plus/minus one according to Tabachnick and Fidell (2007). No multivariate outliers were detected in any of the dependent measures. However, the distribution of the event-based measure was negatively skewed. Following the data transformation procedure recommended by Tabachnick and Fidell (2007), the event-based scores were reflected and the square root was taken. This means that trends in the transformed variable are reversed so that higher scores are indicative of worse performance.

As it is evident from Table 8.1, with the exception of cigarette consumption, the three groups did not statistically differ in terms of their background measures such as age, IQ, years of education and alcohol consumption. The proportion of cigarette smokers in the groups varied significantly ($\chi 2$ (N=53, df=2) = 8.09, p=.017) as almost half of the ecstasy/polydrug users and cannabis only users were smokers, while only one drug-naïve reported cigarette consumption.

Table 8.1 Age, intelligence, years of education, cigarette and alcohol use by group.

	Ecstasy/Polydrug Users			Cannabis-Only Users			Nonusers			P[1]
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	N	
Age (years)	21.17	1.79	29	21.92	1.56	12	20.44	2.28	18	ns
Ravens Progressive Matrices (maximum 60)	39.21	8.39	29	40.25	7.35	12	40.72	8.90	18	ns
Years of Education	15.27	2.44	26	14.92	4.06	12	16.00	2.00	18	ns
Cigarettes per day	7.42	4.48	12	9.00	3.58	6	15.00	-	1	.017
Alcohol (Units per week)	13.41	12.08	27	15.18	12.95	11	9.47	14.70	15	ns

[1] For one-way ANOVA, except cigarettes where chi-squared test was used

Table 8.2 summarises the means and standard deviations for the most prevalent illicit drugs used by the ecstasy/polydrug group and the amount of cannabis used by the cannabis-only group in the last 30 days, their frequency of use, total lifetime use and weeks since last use. The amount of cannabis consumed by the two groups in the four aspects of drug use did not differ significantly although there were some noteworthy differences in the means, for example, the average lifetime dose was higher among the ecstasy/polydrug users.

Table 8.2. Indicators of Illicit Drug Use

	Ecstasy/Polydrug Users			Cannabis-Only Users			p[1]
	Mean	S.D.	n	Mean	S.D.	N	
Total Use							
Ecstasy (Tablets)	640.86	1284.99	29	-	-	-	-
Cannabis (joints)	3048.84	5297.53	25	2242.58	3307.71	12	ns
Cocaine (lines)	1037.89	1282.60	19	-	-	-	-
Amount Consumed in Previous 30 Days							
Ecstasy (Tablets)	3.14	8.28	29	-	-	-	-
Cannabis (joints)	26.08	45.80	25	22.25	33.05	12	ns
Cocaine (lines)	8.16	12.74	19	-	-	-	-
Frequency of Use (times per week)							
Ecstasy	0.24	0.43	29	-	-	-	-
Cannabis	1.87	2.52	25	1.86	2.71	12	ns
Cocaine	0.28	0.36	19	-	-	-	-
Weeks Since Last Use:							
Ecstasy	47.00	76.32	29	-	-	-	-
Cannabis	20.34	37.13	25	73.32	113.69	12	ns
Cocaine	15.40	24.36	22	-	-	-	-

1. Mann-Whitney U test

A series of one-way ANOVAs were conducted in order to investigate the effect of ecstasy/polydrug and cannabis-only use on the PM, RM, learning and memory compensation strategies. Table 8.3 summarises the outcomes of these comparisons. Inspection of Table 8.3 reveals that in comparison to the two illicit drug use groups, the drug naïve group performed significantly better on both time and event-based PM tasks. In fact the drug naïve group consistently performed better on all of the measures. Post-hoc analysis revealed that both cannabis-only users and drug naïve performed significantly better than ecstasy/polydrug users on the event-based PM task while cannabis-only users and drug naïve performed

similarly since the difference did not reach significance. For the time-based PM task the drug-naïve group performed significantly better than the ecstasy/polydrug user group whilst no difference in performance was observed between the ecstasy/polydrug and cannabis-only user group or cannabis-only and drug naïve group.

Furthermore, the drug naïve group also performed better on the self-report measures of retrospective memory than all the other groups. However, pairwise comparisons revealed that the only difference that reached significance was the one between ecstasy/polydrug users and drug naïve, with non-users reporting better retrospective memory. In terms of the memory compensation questionnaire, ecstasy/polydrug users made significantly less use of external memory aids in relation to drug naïve on the MCQ external scale. Performance on the same scale almost reached significance between cannabis only and drug naïve participants. No significant differences between the three groups were present on the RAVLT measure.

Table 8.3. Outcomes for the Prospective Memory, Executive Functions, and Memory Measures by Group.

	Ecstasy/Polydrug Users			Cannabis-Only Users			Nonusers			F	Pairwise Comparisons (Tukey's test)[1]		
	Mean	S.D.	N	Mean	S.D.	n	Mean	S.D.	n		E/PU vs CO	E/PU vs. Non	CO vs. Non
CAMPROMPT													
Event-Based PM	12.48	3.27	29	15.08	2.39	12	16.00	1.68	18	10.40***	.019	.000	
Event-basedPM[2]	2.46	0.69	29	1.90	0.59	12	1.66	0.50	18	10.10***	.027	.000	
Time-Based PM	10.45	3.94	29	12.33	5.65	12	15.11	3.51	18	6.79**		.001	
Retrospective Memory Questionnaire	21.63	7.09	27	19.83	5.77	12	16.65	4.33	17	3.48*		.029	
MCQ													
External	25.18	7.61	28	24.25	9.30	12	30.67	4.84	18	3.96*		.041	.055
Internal	31.32	5.98	28	29.25	6.84	12	33.17	7.88	18	1.21			
Time	14.18	3.39	28	12.67	4.64	12	15.11	3.86	18	1.48			
Reliance	14.79	4.28	28	15.25	4.20	12	13.22	4.86	18	0.95			
Effort	20.61	4.01	28	20.67	3.87	12	21.33	4.19	18	0.19			
Success	14.04	3.29	28	12.83	3.95	12	13.18	3.91	17	0.58			
Change	19.93	3.89	28	21.50	3.45	12	20.33	4.51	18	0.64			
RAVLT													
Learning T1-T5	39.04	9.38	28	40.58	11.11	12	45.22	9.60	18	2.21			
Proactive	0.89	1.77	28	1.58	1.38	12	0.94	1.47	18	0.83			
Retroactive	1.57	2.41	28	2.00	1.86	12	1.39	1.46	18	0.33			
Decay	2.00	2.17	27	2.00	1.76	12	1.22	1.26	18	1.10			

***p<.001; ** p<.01; * p<.05.

1.Only statistically significant differences or differences approaching statistical significance are reported.

2.This is the transformed variable where higher scores are indicative of worse performance.

In order to investigate any possible associations between the PM and the rest of the memory functions, correlations were employed. Table 8.4 summarises the correlations between event and time-based PM tasks and the retrospective memory measures, the MCQ and the RAVLT measure. Inspection of table 8.4 revealed that the event-based measure, as expected, was significantly correlated with the time-based PM measure. It was also correlated with the two retrospective memory measures; the Crawford *et al.*'s retrospective component of the PRMQ and the recall score of the RAVLT over trial 1-5 suggesting that better retrospective memory performance predicts better event-based PM performance. Event-based PM also approached significance with the reliance scale of the MCQ suggesting that as reliance on others as an aid to memory increases, PM performance decreases. Similarly, time-based PM was highly correlated with Crawford *et al.*'s retrospective component while the recall score on the RAVLT over trials 1-5 approached significance. This demonstrates once again that better retrospective memory performance is associated with better time-based PM performance.

In order to evaluate the unique contributions of each predictor to PM performance, two regressions were employed with the scores on the event and time-based PM tasks as the dependent variables. Variables previously statistically significant in the correlation analysis were included as predictors. Results from the regression analyses are summarised in Table 8.4.

Table 8.4. The Relationship between Time and Event-Based PM and Memory Functions

Correlate/IV	Simple Correlation		Semi-partial correlations from regression	
	Event-Based PM[1]	Time-Based PM	DV = Event-Based PM[1]	DV = Time-Based PM
CAMPROMPT				
Event-Based PM[1]		-.523***		
Time-Based PM	-.523***			
RetrospectiveMemory	.270*	-.381**	-.026 ***	-.361 *
Questionnaire				
MCQ				
External	-.075	.052		
Internal	-.003	.007		
Time	-.084	-.068		
Reliance	.258†	-.184		
Effort	-.193	-.064		
Success	.019	.008		
Change	.035	-.021		
RAVLT				
Learning T1-T5	-.273*	.244*	-.239†	.217†
Proactive	.008	-.042		
Retroactive	.095	.033		
Decay	.152	-.060		
Ecstasy/polydrug vs all others			.453**	.228
Cannabis-only vs all others			-.265	-.073

***p<.001; ** p<.01; * p<.05; † p<.10. (0ne-tailed)

1. This is the transformed variable where higher scores are indicative of worse performance.

Inspection of Table 8.4 reveals that the retrospective components of the self-report measure was statistically significant in both event and time-based PM suggesting that better retrospective memory may predict better time and event-based PM performance.

Ecstasy/polydrug users (compared to all other participants) and cannabis-only users (compared to all other participants) were also added as predictors in the regression analyses. In terms of ecstasy/polydrug use, the semi-partial correlation was statistically significant in the event-based PM task reflecting the ecstasy/polydrug related PM deficit. No significance was observed on the time-based PM with ecstasy/polydrug use as the predictor or in either time or event-based PM with cannabis only use as a predictor.

The polydrug consumption amongst the ecstasy group makes it difficult to clearly attribute the PM impairments to specific drugs. In an effort to address this issue, simple and partial correlations were employed between different aspects of drug use and the two PM measures. The simple and semi-partial correlation coefficients are summarised in table 8.5. With respect to time-based PM, only the frequency of cannabis use was correlated with time-based PM suggesting the involvement of this aspect of cannabis use in time-based PM. Consequently, no semi-partial correlations were calculated for the time-based PM task.

Unlike time-based PM, several significant correlations were observed for event-based PM. In fact, all aspects of drug use i.e., total lifetime use, frequency and amount of drug consumed in the last 30 days, were significantly correlated with event-based PM for cannabis, cocaine and ecstasy with the exception of the amount of ecstasy consumed in the last 30 days. However, when controls for the use of other drugs were entered aspects of ecstasy use were no longer significant with event-based PM suggesting that ecstasy is not responsible for the event-based PM impairments. Aspects of cannabis and cocaine yielded statistically

significant correlations after controlling for the use of other drugs. In fact, two aspects of cannabis use remained significant while all three aspects of cocaine use remained statistically significant for the event-based PM suggesting that impairments in PM performance might be attributable to cocaine and cannabis use rather than ecstasy use.

Table 8.5. The Relationship between Time and Event-Based PM and Indicators of Illicit Drug Use

	Event-Based PM[2]		Time Based PM
	Simple Correlation	Semi-Partial Correlation[1]	Simple Correlation
Cannabis			
Total Lifetime Use	.214*	-.197	-.152
Consumed in last 30 days	-.215*	-.221*	-.152
Frequency	.301**	-.382**	-.279*
Cocaine			
Total Lifetime Use	.308**	-.305**	-.131
Consumed in last 30 days	.299**	-.312**	-.130
Frequency	.419**	-.453***	-.120
Ecstasy			
Total Lifetime Use	.209*	-.037	-.155
Consumed in last 30 days	-.170	-.074	-.058
Frequency	.215*	-.103	-.064

***, p<.001; ** p<.01; * p<.05; one tailed.

[1] Controlling for the use of other drugs on the measure in question, e.g., the correlation between total use of cannabis and PM controlling for the total use of cocaine and total use of ecstasy.

[2]Correlation for the transformed variable.

8.4 Discussion

The aim of the present investigation was to examine PM performance in a sample of ecstasy/polydrug, cannabis only users and drug naïve university students on an additional PM laboratory measure that is more sensitive in detecting PM differences in normal populations as opposed to the RBMT employed in Chapter 7 which is most effective with clinical populations. The CAMPROMPT battery was administered in order to confirm and extend previous retrieval phase impairments between recreational users of ecstasy and non-ecstasy users. As a further extension to the previous investigation, in addition to the typical ecstasy/polydrug user group, a cannabis-only user group and a drug-naïve group were recruited to look at the effect of cannabis as opposed to previous polydrug-related effects. Learning and RM measures were also administered in order to investigate the extent to which these processes are associated with PM performance.

In terms of performance on the CAMPROMPT, ecstasy/polydrug users were impaired on both the event and time-based PM tasks in relation to the drug naïve group. Ecstasy/polydrug users also performed significantly worse than cannabis-only users in the event-based PM task. Although it was evident on both time and event-based measures that ecstasy/polydrug users performed the worst, cannabis only users achieving intermediate levels and drug naïve performing the best, the cannabis only user group did not differ significantly from the drug naïve group. The ecstasy/polydrug related effect observed in the present investigation is in line

with previous research using self-report measures (Heffernan *et al.*, 2001a; 2001b; Rodgers *et al.,* 2001; 2003; Montgomery and Fisk, 2007) and laboratory measures of PM (Rendell *et al.*, 2007). The present findings were also in line with PM deficits in laboratory measures observed in the previous chapter. Furthermore, the present findings further demonstrate CAMPROMPT's efficacy in detecting individual differences in PM performance among non-clinical populations (Groot *et al.,* 2002; Wilson *et al.,* 2005).

With regards to the non PM measures, ecstasy/polydrug related deficits were not as evident. Ecstasy/polydrug related deficits were only observed on the retrospective memory component of the PRMQ with drug naïve performing significantly better than the ecstasy/polydrug users. Also, in terms of memory compensation strategies, the non-user group were significantly more likely to report using external memory aids in everyday contexts. On the whole for the non PM measures, cannabis-only users did not differ significantly from the drug naïve group in any of these measures suggesting that deficits in these measures are not attributed to the recreational use of cannabis. For the sample as a whole, individual differences on both PM measures were significantly correlated with performance on the RM component of the PRMQ and the retrospective component of the RAVLT (recall scores for trials 1-5) suggesting better RM is associated with better PM performance. This finding is consistent with previous research connecting PM performance with medial temporal function (Martin *et al.*, 2007; Adda *et al.*, 2008).

In order to establish the extent to which drug-related deficits on PM tasks were mediated by deficits in RM, regression analyses were employed. For the time-based task, the variable representing ecstasy/polydrug use and the variable representing cannabis-only use were not statistically significant as predictors. This leaves open the question of whether drug use or individual differences adversely affect time-based PM. Conversely, ecstasy/polydrug use yielded statistically significant results in event-based PM suggesting that ecstasy/polydrug use adversely affect event-based PM.

While the ecstasy/polydrug related deficits are evident on PM measures, which drug or drugs are responsible for these deficits is not very clear. In order to determine the contribution of each illicit drug semi-partial correlations controlling for the use of other drugs revealed that no aspect of ecstasy use is actually significant as a predictor of PM performance. What is somehow surprising is that although the cannabis-only group did not appear to be significantly impaired in comparison to the drug naïve group, recreational use of cannabis among the whole sample was significantly correlated with event-based PM even after controlling for the use of other drugs. More specifically, frequency of cannabis use and the amount consumed in the last 30 days were associated with poorer event-based PM performance. These findings implicate the recreational use of cannabis with PM impairments and are in line with previous investigations in which cannabis-related deficits have been observed (Rodgers *et al.,* 2003; Fisk & Montgomery, 2008; McHale & Hunt, 2008).

A striking finding in the present investigation is the contribution of cocaine in determining event-based PM performance. All aspects of cocaine were associated with poorer event-based PM performance. Specifically, total lifetime use, frequency of use and amount of cocaine consumed in the last 30 days remained statistically significant as predictors of event-based PM performance even after controlling for concurrent use of other drugs. This replicates the cocaine-related deficits observed in the previous investigation. To the best knowledge of the author, the present and the previous study are the first to link recreational use of cocaine with PM deficits. Although the effect of cocaine is obvious in these two studies, the mechanism through which cocaine might adversely affect PM performance remains unclear.

A methodological issue that needs to be considered is the relatively small sample size in the present study which means that the results of the regression analyses need to be treated with caution. Nonetheless, the present results are potentially informative as a guide for which variables might be incorporated into future research utilising larger samples.

To conclude, the present study intended to determine the impact of ecstasy/polydrug use and cannabis use on event-based and time-based prospective memory using the CAMPROMPT. Measures of RM and learning were also administered in order to study the extent to which retrospective memory and learning account for the prospective memory deficits in recreational drug users. Relative to both drug naive participants and cannabis only users, ecstasy/polydrug users performed significantly worse on the event-based PM task while no

significant differences in performance were observed between the cannabis user and drug naïve groups. However, consistent with the results of the previous study, recreational use of cocaine was significantly correlated with event-based prospective memory performance, demonstrating the need for a systematic investigation of the potential role of cocaine in accounting for the PM deficits that have been observed here and in other studies. Having established the impact of ecstasy/polydrug use on PM, the next chapter will investigate the potential effect of ecstasy/polydrug use on measures of EF.

Chapter 9: Self-report measures of executive dysfunction among recreational drug users

Chapter overview

The purpose of the present chapter is to investigate the effect of the recreational use of ecstasy on EF. A relatively new line of investigation evaluates the integrity of EF in relation to recreational drug use and more specifically in relation to ecstasy/polydrug use. Several studies in the area have revealed that ecstasy/polydrug users exhibit deficits on a number of laboratory tests of EF (see Murphy et al., 2009 for a review). These studies, however, have been restricted to Miyake et al.'s (2000) three components of EF i.e., shifting, inhibition and updating. Laboratory measures of EF, regardless their validity and reliability, are potentially limited in terms of their ecological validity with regard to everyday functioning. Consequently, the present study aims to extend previous reports of executive dysfunction in ecstasy/polydrug users by investigating the extent to which executive deficits are manifested in everyday life using the self-report measure of EF BRIEF-A in a university based sample of ecstasy/polydrug, cannabis-only and drug naïve individuals. It was found that compared to drug naive, ecstasy/polydrug users performed significantly worse on those subscales measuring inhibition, monitoring emotional regulation and self, initiating action, working memory, planning, task monitoring and organisational ability. However, further intergroup comparisons revealed that for the most part ecstasy/polydrug users did not differ significantly from cannabis only users who in turn did not differ from non-illicit drug users.

9.1 Introduction

According to Gioia, Isquith and Guy (2001), EF is a collection of interconnected tasks or processes that are responsible for goal directed or future orientated behaviour in the everyday or "Real world" environment. The executive system has been referred to as the conductor which controls, organises and directs cognitive activity, emotional responses and behaviour. Although the concept of EF has recently received increased attention it still remains somehow elusive. A number of theoretical models of EF have been proposed; however, no model has been uniformly accepted. Early attempts to conceptualize EF resulted in unitary models such as the "Central Executive" (Baddeley, 1986). After findings showing that patients rarely exhibit global executive dysfunction (Bigler, 1988), Miyake *et al.* (2000) suggested that EF is fractionated into 3 separable components; shifting, inhibition and updating (a more detailed account of theoretical models of EF can be found in chapter 3).

A relatively new line of investigation evaluates the integrity of EF in relation to recreational drug use, specifically ecstasy/polydrug use. MDMA is known to have neurotoxic effects on serotonergic axon terminals in both animals and humans (Green *et al.,* 2003) and in view of the important role played by serotonin in regulating prefrontal neural processes (Morgan, 2000) executive dysfunction among ecstasy users is possible. Several studies utilising laboratory-based measures have demonstrated deficits in aspects of executive functioning among ecstasy users (Fox *et al.*, 2001; Montgomery *et al.*, 2007; Montgomery & Fisk, 2008; Verdejo-Garcia *et al.,* 2005; Wareing *et al.,* 2007; also see Chapter 6 for an extensive review). Further evidence for the fractionisation of EF comes from

evidence suggesting that suggested that it is the updating component of working memory and not shifting and inhibition elements that are sensitive to the effects of ecstasy (Fisk & Montgomery, 2009; Fisk *et al.,* 2004; McCann *et al.,* 2007; Montgomery *et al.,* 2005; Reneman *et al.,* 2006).

The assessment of EF has largely been restricted to laboratory-based measures. Although laboratory measures of EF possess strong internal validity, enable control over extraneous variables and the possibility to examine individual component processes separately, they are limited in terms of their ecological validity with regard to everyday functioning (Gioia *et al.,* 2008). Therefore, relying on only laboratory-based measures can lead to a limited and incomplete assessment given that executive functions play a key role in the direction and control of real-world behaviour (Gioia & Isquith, 2004). Consistent with this view, Goldberg and Podell (2000) argue that laboratory measures of EF only capture narrow aspects of the executive system and not the multidimensional aspects of decision making that characterise real world situations.

In order to overcome the limitations of laboratory-based measures, self-report measures have been developed that are specifically designed to provide an indicator of an individual's executive functioning in the everyday environment. These measures offer ecologically valid and internally consistent indicators of executive processes in an everyday context and provide a broader perspective compared to that provided by one-off laboratory-based measures obtained in a single assessment. Among such everyday measures is the Behavioural Rating

Inventory of Executive Function (BRIEF), which includes questions related to everyday activities in familiar contexts that participants can readily relate to.

The BRIEF has been developed to capture the behavioural manifestations of executive dysfunction in the various interrelated domains of the construct that have been commonly discussed in the literature (Bodnar *et al.*, 2007). It also provides an indicator of nine separate aspects of executive functioning: Inhibition, Shift, Emotional Control, Self-Monitor, Initiate, Working Memory, Plan/Organisation, Task-Monitor, and Organization of Materials. Bodnar *et al.* (2007) argue that everyday instruments such as the BRIEF, measure subtle individual differences in discrete real world processes and unlike many laboratory tests are unrelated to, and not contaminated by overall differences in general ability measures such as IQ. The BRIEF has been used in a wide range of contexts, for example, in research focussing on Attention Deficit/ Hyperactivity Disorder (ADHD) (Chang *et al.*, 2009; Gioia et al, 2002; Jarratt *et al.*, 2005; Mahone & Hoffman, 2007; Toplak *et al.*, 2009); bipolar disorder (Shear *et al.*, 2002), autism spectrum disorders (Gilotty *et al.*, 2002; Gioia *et al.*, 2002; Chan *et al.*, 2009), childhood epilepsy (Sherman *et al.*, 2006), frontal lobe lesions (Malloy & Grace 2005) and traumatic brain injury (Gioia *et al.*, 2002; 2004).

The reliability and validity of the BRIEF in assessing EF has been demonstrated in a number of studies (Slick *et al.*, 2006; Gioia *et al.*, 2000; Gioia *et al.*, 2002; Toplak *et al.*, 2009; Bodnar *et al.*, 2007; Walker & D'Amato, 2006) and it is extensively discussed in Chapter 2.

Assessments of EF using laboratory measures are valuable in providing evidence that ecstasy users are impaired on some aspects of executive functioning such as updating and access to semantic memory while other processes such as inhibition and set shifting remain unimpaired to recreational use of ecstasy. Conversely, the use of self-report measures of EF such as the BRIEF that are able to tap behavioural manifestations of executive functioning in the everyday environment would allow a more comprehensive view of the nature of executive deficits in ecstasy/polydrug users.

Consequently, the present investigation predicts that ecstasy/polydrug users will perform worse on the BRIEF measure compared to cannabis-only users and drug naïve. Since evidence from previous investigations (Fisk & Montgomery, 2009a; Montgomery *et al.,* 2005) suggest that ecstasy/polydrug use rather than cannabis use is associated with executive deficits it is predicted that the cannabis-only and nonuser group in the present study will not differ significantly from each other.

9.2 Method

Design

A between participants design was employed with drug use as the independent variable (with three levels, ecstasy/polydrug, cannabis only, and drug naïve). Dependent variables were the nine component subscales of the BRIEF-A (i.e., inhibit, shift, emotional regulation, self-monitor, initiate, working memory, plan, task monitor and organise). Correlation and linear regression analyses were also

employed in order to investigate each recreational drug's possible contribution to executive dysfunction.

Participants

Sixty five ecstasy/polydrug users (36 females) 19 cannabis-only users (13 females) and 38 non-users of illicit drugs (31 females) took part in this investigation. This sample of participants also completed some of the measures from previous studies. See appendix 1 for participants overlap table. Participants were recruited via direct approach to university students and the snowball technique i.e., word-of-mouth referral (Solowij *et al.,* 1992). All participants were university students attending the University of Central Lancashire (UCLAN) or Liverpool John Moores University (LJMU).

Materials

The background drug-use questionnaire used in the previous investigations was administered to assess the prior history of illicit drug consumption and estimate the total lifetime use for each drug (e.g., ecstasy, cannabis, cocaine, amphetamines etc.), frequency of use as well as the period of abstinence. Fluid intelligence was measured via Raven's Progressive Matrices (Raven *et al.,* 1998). The participant's age and gender, the number of years of education as well as their current use of alcohol and cigarettes were also assessed. A self-reported measure of EF was administered to capture the participant's views of their own EF in their everyday environment. The self-reported measure of executive functions is described below.

Behaviour Rating Inventory of Executive Function- Adult Version (BRIEF-A) (Roth et al., 2005)

The BRIEF-A is a 75 item measure which provides indicators of nine separate aspects of EF. Eight items measure Inhibition (the ability to resist or control impulses), e.g., "I tap my fingers or bounce my legs". Six items measure the Shift process (being able to shift attention, change strategies, act flexibly) e.g., "I have trouble changing from one activity to another". Ten items measure Emotional Control (the individual's ability to control their emotions), e.g., "I have angry outbursts". Six items measure Self-monitoring (insensitivity, inability to infer the feelings and emotions of others, behaving in a thoughtless manner), e.g., "I don't notice when I cause others to feel bad or get mad until is too late". Eight items measure Initiate (having the impetus to begin tasks, generate ideas and develop strategies), e.g., "I need to be reminded to begin a task even when I am willing". Eight items measure Working Memory, (the temporary storage and maintenance of information while working on ongoing tasks) e.g., "I have trouble concentrating on tasks (such a chores, reading or work)". Ten items measure Planning/Organisation (setting goals and developing tactics to achieve them, anticipation of future events and the preparation of strategies to deal with them), e.g., "I get overwhelmed by large tasks". Six items measure Task Monitoring (the ability to appraise task requirements and avoid making careless mistakes), e.g., "I make careless errors when completing tasks" and finally eight items measure the Organization of Materials (disorganised, untidy), e.g., "I am disorganized". For each item participants respond on a three point likert scale; Never, Sometimes and

Often. On each of the subscales higher scores are indicative of more executive dysfunction. An additional three scales measure the validity and reliability of the participant's responses, for example, 'infrequency' i.e., the extent to which the respondent endorses items which are usually rejected by the vast majority of people, e.g., "I forget my name". Scores on certain other items are combined to form indicators of 'negativity' and 'inconsistency'. For each of the nine scales, a total score is generated by adding the scores for each of relevant the questions. For a copy of the questionnaire please refer to appendix 12.

Procedure

Participants were firstly informed of the general purpose of the investigation and their right to withdraw from the experiment at any time. After verbal consent had been obtained, the tests were administered in a quiet laboratory. The drug-use questionnaire was administered first, followed by Ravens Progressive Matrices, and the BRIEF-A (Roth *et al.*, 2005). At the end of the experiment, participants were fully debriefed, paid £20 in Tesco store vouchers, and given drug education leaflets. The University of Central Lancashire's Ethics Committee approved the study.

9.3 Results

Using the criteria suggested by Tabacknick and Fidell (2007) there were no univariate outliers. A multivariate outlier was detected and the participant was excluded from the analysis. Regarding the distribution of the BRIEF subscales, the scores did not deviate significantly from normal and the z scores associated

with the statistics in relation to skewness and kurtosis were consistent with normality for samples of this size (Tabachnick & Fidell, 2007).

With regard to the validity of the BRIEF, the three validity subscales were considered. Inspection of the negativity scores revealed that three cases exceeded the score of six, which according to the instruction manual merits further investigation. Nevertheless, inspection of the remaining indicators for these cases was within acceptable bounds and therefore not excluded from the analysis. In terms of the infrequency scales, three cases exceeded the score of three. However, after inspection of the cases' scores on the other validity scales the cases were retained. One case was excluded from the analysis as the inconsistency score was unusually high.

Table 9.1 below summarises the means and standard deviations of background and demographic variables including the amount of alcohol and tobacco consumption for the three groups.

Table 9.1. Demographical Variables for Illicit Drug Users and Nonusers

	Ecstasy/Polydrug Users			Cannabis-Only Users			Nonusers			p[1]
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n	
Age (years)	21.38	2.85	65	21.84	3.58	19	20.50	2.21	38	ns
Ravens Progressive Matrices (maximum 60)	42.59	9.08	64	42.32	7.23	19	43.11	8.67	38	ns
Years of Education	14.75	3.43	64	15.05	2.55	19	14.97	2.51	38	ns
Cigarettes per day	8.83	7.60	29	6.63	4.37	8	9.67	7.99	6	ns
Alcohol (Units per week)	13.91	9.93	64	15.00	14.15	18	8.34	11.80	35	.039

1. For one-way ANOVA

Inspection of Table 9.1 revealed that the three groups did not differ significantly on any of the background variables with the exception of alcohol consumption. On further analysis, Tukey's post-hoc test revealed that ecstasy/polydrug users consumed significantly more units of alcohol per week than drug naïve ($p<0.05$). Although mean alcohol consumption was higher in cannabis-only users than ecstasy/polydrug users, Tukey's post-hoc test revealed that this difference was not statistically significant. No other pairwise comparisons yielded statistically significant results. Table 9.2 summarises the background drug use variables for the ecstasy/polydrug and cannabis-only user groups. The total lifetime use, frequency of use and the total amount consumed in the last thirty days for each of the major illicit drugs are summarised.

Inspection of Table 9.2 revealed that although there are noticeable differences in various indicators of cannabis consumption, only total lifetime use of cannabis reached significance. It is worth noticing that the polydrug group, besides the use of ecstasy and cannabis, was also characterised by regular use of cocaine. An inspection of other recreational drugs reported by polydrug users (such as amphetamines, poppers, ketamine and LSD) revealed that the small amount of ecstasy/polydrug users that reported such use described their use as 'occasional' in the past three months. Consequently, these drugs were not included in the analysis.

Table 9.2. Background Drug Use Variables for Illicit Drug Users

	Ecstasy/Polydrug Users			Cannabis-Only Users			p[1]
	Mean	S.D.	N	Mean	S.D.	N	
Total Use							
Ecstasy (Tablets)	613.54	1148.52	65	-	-	-	-
Cannabis (joints)	3034.90	4748.40	58	1412.89	2804.90	19	0.020
Cocaine (lines)	1099.93	1572.44	42	-	-	-	-
Amount Consumed in Previous 30 Days							
Ecstasy (Tablets)	3.58	7.38	65	-	-	-	-
Cannabis (joints)	21.83	45.39	58	13.68	28.10	19	ns
Cocaine (lines)	8.38	12.98	42	-	-	-	-
Frequency of Use (times per week)							
Ecstasy	0.25	0.37	65	-	-	-	-
Cannabis	1.40	2.20	58	1.37	2.45	19	ns
Cocaine	0.31	0.42	41	-	-	-	-
Weeks Since Last Use:							
Ecstasy	37.78	71.40	65	-	-	-	-
Cannabis	25.47	60.42	58	73.05	101.22	19	ns
Cocaine	20.29	47.72	48	-	-	-	-

1 For Mann-Whitney U test

MANOVA was conducted to investigate the effect of ecstasy/polydrug and cannabis-only use on EF. Thus, Table 9.3 summarises the results of the primary analysis. Multivariate analysis of variance with the nine subscales of the BRIEF as the dependent variables and the three groups as the independent variables was conducted revealed a statistically significant group effect, $\Lambda = .707$, $F(18,202) = 2.13$, $p=0.006$, partial $\eta^2 = .159$. Univariate analysis revealed that all subscales of the BRIEF were statistically significant, with the exception of the shift subscale (see Table 9.3 for the statistical results of univariate analysis). Tukey's post-hoc analysis revealed that, as predicted, ecstasy/polydrug users performed significantly worse than drug naïve on all but two (shift and emotional regulation) subscales of the BRIEF.

It was also predicted that cannabis-only users would not differ significantly than drug naïve; a prediction that was supported with the exception of the emotional regulation subscale that reached significance. However, ecstasy/polydrug users did not differ significantly from cannabis-only users on any of the EF apart from the inhibit subscale. The significance levels for the pairwise comparisons are also summarised in Table 9.3.

Table 9.3. Performance on the Self Report BRIEF-A Measure for Ecstasy/Polydrug, Cannabis-Only, and Nonusers of Illicit Drugs.

BRIEF subscale	ecstasy/polydrug users		cannabis-only users		drug-naïve		Group overall effect			pairwise comparisons			
	Mean	SD	Mean	SD	Mean	SD	F(2,109)	P	partial η2	Ecstasy/polydrug users vs drug naïve	ecstasy/polydrug users vs cannabis only users	cannabis only users vs drug naïve	p covariate of alcohol
Inhibit	15.67	2.95	14	2.89	13.94	2.86	4.79	0	0.081	0.009	0.048	ns	0.038
Shift	9.95	2.57	9.24	2.33	10.21	2.41	0.87	Ns	0.016	ns	ns	ns	ns
emotional regulation	17.15	4.45	15.41	4.89	18.76	4.09	3.45	0.018	0.06	ns	ns	0.016	0.008
self monitor	10.38	2.37	9.76	2.33	9.09	2.04	2.98	0.028	0.052	0.022	ns	ns	ns
Initiate	15.05	3.19	14.06	2.36	13.15	2.56	4.79	0	0.01	0.004	ns	ns	ns
working memory	14.84	3.37	14.24	3.19	13.29	2.66	2.63	0.039	0.046	0.031	ns	ns	ns
Plan	17.86	4.44	16.76	3.54	15.65	3.18	3.52	0.017	0.061	0.013	ns	ns	ns
task monitor	11.34	2.41	10.71	1.83	10.03	1.8	4.08	0.01	0.07	0.007	ns	ns	ns
Organise	15	4.04	14.29	4.13	12.5	3.29	4.64	0.006	0.078	0.004	ns	ns	ns

Since the groups differed significantly in their alcohol consumption, a multivariate analysis of covariance was conducted to look at the effect of the covariate on the EF. In multivariate terms, the overall group effect remained statistically significant after the inclusion of the covariate, $\Lambda = .740$, $F(18,192) = 1.73$, $p=0.037$, partial $\eta^2 = .140$. This suggests that alcohol does not affect the performance of EF. Also, the effect size was only reduced by 1.9% suggesting that most of the variance was explained. In the univariate analysis however, with the exception of inhibit and emotional regulation, the rest of the EF were decreased to below significance.

As with the previous investigations (Chapters 7 and 8), the ecstasy/polydrug user group was characterised by recreational use of cocaine and cannabis. It is therefore necessary to try and determine the contribution of each of the main illicit drugs to executive dysfunction. Correlational analyses were therefore conducted to observe any associations between the individual illicit drugs and the nine EFs. Table 9.4 summarises the Pearson's correlation coefficients for the lifetime and frequency of use for ecstasy, cannabis and cocaine for each EF.

Table 9.4. Simple correlations and semi-partial correlations (from regression) between BRIEF subscales and aspects of drug use

		Lifetime use		Frequency	
BRIEF subscale	Drug	Simple	semi partial	Simple	semi partial
Inhibit	Ecstasy	.196*		.283**	.213*
	Cocaine			.207*	
Shift					
Emotional regulation					
self-monitor	Ecstasy	.205*		.213*	
	Cannabis			.195*	
	Cocaine	.222*	.170*	.202*	
Initiate	Ecstasy			.214*	
	Cannabis			.211*	
working memory	Cannabis			.183*	
Plan	Ecstasy	.221*		.200*	
task monitor	Ecstasy	.182*		.195*	
Organise	Ecstasy	.200*			

*$p<0.05$, **$p<0.01$, (one-tailed)

Inspection of Table 9.4 reveals that lifetime use of ecstasy is positively correlated with five out of the nine EFs. Consequently, ecstasy is associated with deficits in inhibit, self-monitor, planning, task-monitor and organise subscales. The self-monitor subscale was also significantly correlated with total lifetime use of cocaine whilst no component of EF was associated with total lifetime use of cannabis. However, when the variance in relation to the total use of other drugs was excluded using regression analysis, total lifetime use of ecstasy was reduced to below significance suggesting that the deficits in EF are not uniquely attributed to the use of ecstasy. Surprisingly, the only semi-partial correlation that reached significance was the total lifetime use of cocaine for the self-monitor subscale, suggesting that recreational use of cocaine is responsible for the impairment in that aspect of EF.

In terms of frequency of use, ecstasy was predominantly associated with EF since five out of the nine components of EF were significantly correlated. Frequency of cannabis use was significantly correlated with three components of EF and frequency of cocaine use with only two components. Nevertheless, when the variance in relation to the frequency of use of other drugs was excluded the only association that was statistically significant was that between the frequency of ecstasy use and the inhibit EF component. It can therefore be assumed that the deficits observed on the inhibit component of EF are related to the frequency of ecstasy use.

9.4 Discussion

The aim of the present study was to investigate the effect of ecstasy/ polydrug use and cannabis use on executive functioning with regards to the everyday environment. The present investigation assessed a broader range of EFs as opposed to the traditional three-component model often adopted in this area. In comparison to drug naïve, ecstasy/polydrug users performed significantly poorer on all subscales of the BRIEF with the exception of shift and emotional regulation. When ecstasy/polydrug users were compared with the cannabis-only group, only the inhibit subscale of the BRIEF produced a statistically significant difference with ecstasy/polydrug users performing worse. When evaluating the role of cannabis use in executive functioning, cannabis-only users were compared to the drug naïve sample and although cannabis only users performed generally worse than the drug naïve in all subscales of the BRIEF, the only component of

EF that reached significance was emotional regulation. Similar to the previous studies on PM, a trend is evident with ecstasy/polydrug users performing the worst, cannabis users performing at intermediate levels and the drug naïve group performing the best.

Which drug is primarily responsible for the observed deficits in executive functioning is therefore not clear. In order to answer this question correlational and regression analyses were employed to look at any associations between the different components of EF and recreational drug use. These analyses revealed that total lifetime and frequency of ecstasy use were associated with most executive components while the equivalent measures for the other drugs were generally not. Nevertheless, when the variance of other drugs was excluded the only component that yielded significant differences in frequency of use was the inhibit component. It is therefore possible that the inhibit component is particularly sensitive to the recreational use of ecstasy. This is a surprising finding as a number of previous laboratory-based investigations suggested that it is the updating component of working memory and not the shifting and inhibition elements that are sensitive to the effects of ecstasy (Fisk *et al.,* 2004; Montgomery *et al.,* 2005; Reneman *et al.,* 2006; McCann *et al.,* 2007).

It is also possible that laboratory measures of EF are less sensitive in detecting impairments in the inhibition component of EF as opposed to self-report measures of executive functioning. Consistent with this view Bodnar *et al.* (2007) found that the BRIEF appears to measure different elements of the inhibition construct than those assessed by computerised performance tests; thus explaining why as

opposed to laboratory measures of inhibition this aspect of EF is impaired on the BRIEF. The findings of the present investigation therefore suggest that the inhibition component of EF is impaired in ecstasy/polydrug users with respect to their everyday environment. It also suggests that the reported failures in this component are attributed to the recreational use of ecstasy.

Consistent with Bodnar *et al.*'s view, Toplak *et al.* (2009) have in fact observed that certain of the BRIEF subscales (e.g. switching/shifting) do not appear to map straightforwardly onto the equivalent laboratory measures. In terms of switching (shifting), previous laboratory-based research has generally failed to uncover ecstasy-related deficits (see Murphy *et al.,* 2009 for a review). These findings were replicated in the present study since deficits were not observed on the BRIEF shift subscale.

In terms of working memory, findings are less straightforward. The BRIEF's WM subscale relates most closely to the updating executive process within Miyake *et al.*'s conceptualisation (see Friedman et al, 2008). Previous laboratory-based investigations of WM suggest that ecstasy/polydrug users are impaired on tests loading on this process (Montgomery *et al.,* 2005; Fisk *et al.* 2009; also see Murphy *et al.* 2009 for a review).

While the present results also showed that ecstasy/polydrug users had poorer WM scores compared to cannabis-only user group, the difference did not reach statistical significance. Despite this, the difference between the ecstasy/polydrug group and the drug naïve group was statistically significant; a finding consistent

with the laboratory outcomes. The remaining BRIEF subscales do not readily map onto the laboratory measures underpinning Miyake *et al.*'s conseptualisation of fractionated EF. The present study revealed ecstasy/polydrug related deficits on a number of the other BRIEF subscales including planning, initiation, organisation, and self and task monitoring. It is possible that these impairments reflect separate aspects of another key executive function: the effective maintenance of goal directed behaviour. Consequently, the present results potentially identify an additional aspect of EF which might be subject to ecstasy/polydrug related effects. Further investigation of this, possibly through the use of appropriate self-report measures and laboratory tests, might possibly establish a useful direction for further research.

Nevertheless, the present findings need to be interpreted with caution with regards to the drug-related deficits observed. It is worth mentioning that in the present investigation cannabis consumption was higher in the ecstasy/polydrug user group than the cannabis-only group. It is therefore possible that the observed deficits in executive components are in fact attributed to cannabis use. This would account for why cannabis users were impaired (although not significantly) whilst ecstasy/polydrug users with higher levels of cannabis consumption were significantly impaired. Whilst previous research using laboratory measures of EF failed to find cannabis-related deficits (Fisk & Montgomery, 2008), the present findings, raise the possibility that although cannabis users perform adequately in laboratory settings, executive deficits may be present in their everyday lives. Evidence supporting this possibility comes from other non-laboratory measures. For instance, Verdejo-Garcia *et al.* (2006) found that performance on two self-

report aspects associated with prefrontal lobe neural functioning i.e., an executive component (panning, WM and mental flexibility) and an apathy component (loss of energy, poor initiation and reduced affective expression) were associated with the severity of cannabis use.

Furthermore, more evidence for the importance of administering self-report measures of EFs that capture the behavioural manifestations of EF in day-to-day functioning and the involvement of cannabis use comes from a recent internet study using the Webexec. The Webexec (Buchanan *et al.,* 2010) is a short self-report measure of problems with EF that is specifically designed for internet-mediated research. This brief self-report measure of EF generates a global score of executive functioning; reflecting the participant's overall experience of executive problems instead of measuring specific aspects. The measure was correlated with three cognitive tasks (i.e., reverse digit span, semantic fluency and semantic fluency with inhibition) and also with scores on the Dysexecutive questionnaire (DEX) indicating good validity. The authors also used this measure to assess executive dysfunction in recreational drug users. The findings suggested that participants with higher cannabis consumption reported more executive problems and also that scores on the Webexec were correlated with PMQ's long-term PM scale. Further evidence for the involvement of cannabis use in deficits in EF comes from recent neuropsychological assessment. For example, Fontes *et al.* (2011) using the Frontal Assessment Battery (FAB; a neuropsychological instrument evaluating EF), found that abstinent chronic cannabis users performed as poorly controls.

Brain imaging studies might also be informative for the potential presence of cannabis-related deficits in aspects of EF or the lack of it. Neuroimaging evidence suggests that although there are no differences between cannabis users and nonusers in tests of WM and visuo-auditory selective attention, neuroimaging analysis focussing on specific regions of interest (ROI) revealed differences in brain activity between users and nonusers in the superior parietal cortex (Jager *et al.,* 2006). In a subsequent fMRI study, during an associative learning task Jager *et al.* (2007) found no structural differences in the particular ROI whilst lower activation levels among frequent cannabis users were present in the medial temporal structures (especially the para-hippocampal area) and the right DLPFC. These findings therefore suggest that the neural structures and processes that support performance on EF tasks do not function similarly in cannabis users and nonusers and although this appears to be non-problematic in laboratory tasks, in more everyday settings such as those assessed by the BRIEF and other self-report measures, cannabis-related deficits may be more apparent.

Many ecstasy/polydrug users in the present investigation were also regular users of cocaine. Correlational analysis suggested that a number of components were associated with the recreational use of cocaine and in the case of self-monitor, lifetime use of cocaine appeared to be the only drug use measure uniquely accounting for deficits in that aspect of executive functioning. While to the best of the author's knowledge no previous studies of cocaine users have used self-report executive measures, other research using laboratory-based tasks have produced inconsistent results. For instance, in some studies cocaine users have been found to be impaired on laboratory measures of the switching component of EF such as

the trailing making test (TMT-B) and the Wisconsin Card Sort Test (WCST) (Beatty *et al.*, 1995; Berry *et al.*, 1993; Rosselli *et al.*, 2001) while others failed to demonstrate impairment on the same tasks (Gillen *et al.*, 1998; Goldstein *et al.*, 2004; Verdejo-García & Pérez-García, 2007).

Similar inconsistent findings were also observed on the inhibitory processes; while some studies have found cocaine-related impairments on the Stroop task (Rosselli *et al.*, 2001; Verdejo-García & Pérez-García, 2007), some others suggest that recreational use of cocaine leaves performance on the Stroop task unimpaired (Berry *et al.*, 1993; Goldstein *et al.*, 2004). Mixed results have also been observed on the WM component of EF in relation to recreational use of cocaine. For example, cocaine users were found to be impaired on paced auditory serial addition task (PASAT) after three days of abstinence but not after a further two week period of abstinence (Berry *et al.*, 1993). Furthermore, Verdejo-García and Pérez-García (2007) found that substance dependent polydrug users whose drug of choice was cocaine were impaired on the number letter re-sequencing task, on forward and backward digit, and on spatial span known to load on the WM component. Contradicting these findings, Gonzalez *et al.* (2004) found that cocaine users performed similarly to controls on a combined deficit score for the PASAT and the WMS-III number-letter sequencing task. Evidence for EF deficits on laboratory-based tasks among recreational cocaine users is therefore unclear and inconsistent. Furthermore, the fact that in the present study cannabis-only users reported a degree of executive dysfunction (although not at a significant level) suggests that cocaine is unlikely to account for the full range of deficits that were observed here.

Furthermore, alcohol consumption should not be disregarded in the present study as groups differed significantly in their levels of alcohol consumption. Since previous investigations have linked alcohol abuse with executive dysfunction, it is possible that some of the deficits observed on the BRIEF are attributable to effects of alcohol rather than drug use per se. For example, according to Scheurich (2005) new approaches concerning EF found response inhibition and decision-making impairments amongst those consuming alcohol but normal performance in simple working memory tasks. Also, alcohol abuse in early and middle adolescence was found to be associated with deficits in verbal recall and visuo-spatial functioning (Brown *et al.,* 2000) while comparison of crack cocaine addicted persons, alcoholics, and controls revealed deficits in neuropsychological tests of attention and executive functioning with deficits being particularly prevalent among the alcoholic participants (Goldstein *et al.,* 2004).

Similarly, Loeber *et al.* (2009) found that alcohol dependent patients did worse than healthy controls on tasks believed to load on attention/EFs, however the decrement decreased with increasing length of abstinence. Although the mechanisms that may underlie such everyday cognitive impairments associated with binge drinking are not yet fully understood, it is possible that alcohol-dependent patients use additional and generally higher-order executive functions to compensate for deficient task performance. The compensatory mechanisms might help to explain why performance on cognitive tasks may appear to be unimpaired on basic cognitive domains (Scheurich, 2005).

To conclude, the present study intended to determine the impact of ecstasy/polydrug use on executive functioning using the self-report BRIEF-A measure. Relative to drug naive persons ecstasy/polydrug users performed significantly worse on all subscales, with the exception of the ability to shift mental set and to regulate emotions. However, for the most part, ecstasy/polydrug users did not differ significantly from cannabis only users, leaving open to question which specific aspect of polysubstance use contributed the effects that were observed.

Chapter 10: The role of executive processes in accounting for prospective memory deficits in ecstasy/polydrug users

Chapter Overview

The purpose of the present chapter is to investigate the role of executive processes in accounting for prospective memory deficits observed in ecstasy/polydrug users. The effect of ecstasy/polydrug and cannabis use is investigated in three previously administered laboratory measures of PM. The three general scales from the self-report measure of EF BRIEF-A (i.e., Behavioural regulation index (BRI), metacognition index (MI) and the global executive composite (GEC)) were also used to investigate the hypothesis that executive processes are in fact responsible for the PM deficits observed in ecstasy/polydrug users. Findings suggested that in comparison to drug naïve, ecstasy/polydrug users were impaired on all three laboratory measures of PM. It was also found that executive processes were correlated with time-based PM measures. It is therefore possible that deficits in PM performance are associated with deficits in executive processes and perhaps some of the drug related PM deficits are mediated by drug related EF impairment.

10.1 Introduction

PM, as discussed in previous chapters, refers to the ability to remember to execute previously scheduled activities. It is therefore crucial for the management of everyday life. Ellis (1996) argues that at the initiation of a PM task, the intention to do something, the intended action and the retrieval context need to be encoded together. So the intention is held in memory over a short-term or long-term delay period. Consequently, when an action is to be retrieved, ongoing activity needs to be inhibited in order to switch and execute the intended action. PM failures can occur at different stages during this process. For example, retention of the action or retrieval context may fail or retrieval of the action at the appropriate time or event may be missed. These two stages are characterized as the retrospective component of PM (remembering what needs to be executed) and the prospective component of PM (remembering when to do something).

According to Einstein and McDaniel (1990), the retrospective component is a classic memory function whilst the prospective component depends mainly on EF. Supporting this view, Marsh and Hicks (1998) argued that PM depends on self-initiated and attention demanding resources and therefore PM performance can be expected to be correlated with measures of central executive functioning. Similarly, Martin *et al.* (2003) found that executive processes in older adults were significantly correlated with performance on three PM tasks. Furthermore, additional studies have implicated the role of executive processes in PM performance (Kliegel *et al.*, 2000; Kliegel *et al.*, 2008). Both neuropsychological

(Martin *et al.,* 2003; Kliegel *et al.,* 2000; Kliegel *et al.,* 2008) and neuroimaging (Burgess *et al.,* 2003; Okuda *et al.,* 2003; Simons *et al.,* 2006; Okuda *et al.,* 2007) evidence suggest the involvement of executive processes in PM performance since regions of the frontal lobe, such as the rostral prefrontal cortex, are involved in both the performance of PM and EF.

More evidence for the role of executive processes in PM performance comes from studies demonstrating an association between EF and PM performance. For instance, in a multitask PM paradigm, Kliegel *et al.* (2000) showed that individual differences in executive functioning (e.g., working memory and inhibition) predicted the successful initiation and execution of a complex PM task while retrospective memory did not. In a later study, Kopp and Thone-otto (2003) tried to separate the cognitive processes involved in PM by testing patients with specific cognitive deficits in an event-based PM task. They found that patients with brain injury and impaired performance on neuropsychological tests of EF performed worse in the PM task compared to patients with no executive dysfunction, thus supporting the role of EF in PM performance.

A possible explanation for the important role of executive processes in PM performance could be that PM tasks create the need to monitor the environment in order to detect the relevant cue. This means that attention needs to be divided between monitoring and performing the ongoing task. According to Smith and Jonides (1999), such activity relies on executive processes like monitoring and working memory. It is therefore reasonable to assume that impairments on EF such as inhibition and working memory might predict poor PM performance

because patients with impaired EF allocate more resources to the ongoing task in order to compensate for their executive deficits, thus reducing the available resources for monitoring cues.

Also, in complex tasks/situations in which several activities run simultaneously, additional planning and monitoring processes maybe required (Fish *et al.,* 2007). It is also argued that the extent to which executive processes are involved in PM retrieval might be dependent on the specific requirements of the task (Glisky, 1996). For example, time-based PM is more likely to depend on executive processes than event-based PM, as time-based tasks require a higher degree of self-initiated retrieval (Einstein *et al.,* 1995).

A new line of investigation linking these theoretical constructs is concerned with how the common mechanisms supporting EF and PM operate in recreational drug users. More specifically, existing research including findings in previous chapters of this thesis suggest that ecstasy/polydrug users perform worse on both PM and EF tasks in comparison to drug naïve persons (Heffernan *et al.,* 2001a; b; Rodgers *et al.,* 2001; 2003; Montgomery *et al.,* 2005; Fisk *et al.,* 2009). In previous studies (Chapters7-9), the integrity of prospective remembering and executive functioning was evaluated in ecstasy/polydrug users. It is evident from these studies that ecstasy/polydrug users demonstrate impairments on both PM performance and executive processes. Given that executive processes such as planning, monitoring or attention are essential for PM performance, it is therefore reasonable to assume that there is an association between executive processes and prospective remembering within the same cohort of ecstasy/polydrug users. This

assumption can be supported by evidence suggesting that PM processes such as dividing attention, monitoring the environment for a cue, associating a cue for intention and interrupting an ongoing activity may also involve planning which is thought to depend on the frontal lobes (Lezak, 1982; Shallice, 1982).

It is therefore apparent that there is growing evidence that the successful performance of a PM task is heavily dependent on executive processes and that executive dysfunction predicts poor PM performance. Further research for the exact role and the extent to which executive processes contribute to successful PM performance is essential, as both executive processes and PM play a crucial role in our everyday functioning.

Consequently, the aim of this investigation is to confirm the ecstasy/polydrug related PM deficits observed in Chapter 7 by adding data from other participants to the sample used in Chapter 7. Apart from the bigger sample size, the present study adds a cannabis-only user group in order to investigate the effect cannabis use on laboratory measures of PM. Finally, the present investigation also aims to evaluate the role of executive processes in PM deficits in recreational drug users and determine whether ecstasy/polydrug-related deficits in PM can be attributed to drug related differences in EF. Taking into consideration previous research from other laboratories and also from present findings, it is predicted that ecstasy/polydrug users in comparison to drug naïve will demonstrate ecstasy/polydrug related deficits in all three laboratory measures of PM. It is also predicted that cannabis-only users will perform worse than drug naïve in the

measures of PM and that ecstasy/polydrug-related deficits in PM can be attributed to drug-related differences in EF.

10.2 Method

Design

A between participant design (MANOVA) with drug use as the independent variable (at three levels i.e., ecstasy/polydrug, cannabis-only and drug naïve) and the three laboratory measures of PM (Fatigue PM task, PM pattern recognition task and long-term PM recall task) was employed. Alcohol consumption was included as a covariate in order to test for any alcohol-related effects. Correlational and regression analyses were also employed to investigate any possible associations between the laboratory measures of PM and the BRIEF general scales and whether these associations are drug-related. Correlation and regression analyses were also used to examine the effect of each of the three major illicit drugs on PM.

Participants

Seventy four Ecstasy/polydrug users (Female= 42), twenty-one cannabis only users (female=13) and forty drug naïve (female=33) took part in this investigation. As in Chapter 9, these participants also completed some of the tasks discussed in previous investigations. The table summarising the participants overlapping in each chapter can be found in appendix 1. Participants were recruited via direct approach to university students and the snowball technique i.e., word-to-mouth

referral (Solowij *et al.,* 1992). All participants were university students attending the University of Central Lancashire or Liverpool John Moores University. Demographic details are summarised in Table 10.1.

Materials

As with the previous investigations the background drug history questionnaire was administered in order to assess history of illicit drug use, fluid intelligence was measured via Raven's Progressive Matrices (Raven *et al.,* 1998) and a further questionnaire was used to assess participant's age, gender, education as well as their alcohol and smoking consumption. Three laboratory measures of PM were administered in order to assess event-based PM (i.e., PM pattern recognition task), time-based PM (i.e., Fatigue PM task) and long-term PM (i.e., Long-term recall PM task). The three laboratory measures of PM were those used in the previous study and a detailed description can be found in Chapter 7. In order to assess executive functioning, the three general scales of the self-report measure BRIEF-A were used in this investigation.

Behaviour Rating Inventory of Executive Function- Adult Version (BRIEF-A) (Roth et al., 2005)

The BRIEF-A is a 75 item measure which provides indicators of nine separate aspects of executive functions. These aspects of executive function include inhibition, shifting, emotional control, self-monitoring, initiate, working memory, plan and organisation, task monitor and organization of materials. Description of these scales can be found in Chapter 9. Besides the nine components of EF and

the reliability scales, the BRIEF-A provides, three general scales i.e., the Behavioural Regulation Index (BRI), the Metacognition Index (MI) and the Global Executive Composite (GEC). The BRI represents the adult's ability to maintain appropriate regulatory control of his/her behaviour and emotional responses. Appropriate emotional regulation enables metacognitive processes to successfully achieve problem solving and also support appropriate self-regulation. A score for BRI is generated by adding the scores from the inhibit, shift, emotional control and self-monitor subscales of the BRIEF-A. The MI represents the person's ability to systematically solve problems via planning and organisation while sustaining these task-completion efforts in active working memory. Also, this index can be interpreted as a person's ability to cognitively manage attention and problem solving. A score for this index is generated by adding scores from the initiate, working memory, plan/organization, task-monitor and organisation of materials subscales of the BRIEF-A. Finally, GEC is a summary score incorporating all the nine scales of the BRIEF-A and represents an accurate reflection of a person's level of executive dysfunction.

Procedure

Participants were informed of the general purpose of the experiment and verbal informed consent was obtained. All tests were administered under laboratory conditions and the participant had the right to withdraw at any time from the experiment. The MDMA Questionnaire was administered first followed by Ravens, Health/Age/Education questionnaire, Prospective Memory Pattern recognition Task, Recall PM task and the BRIEF-A. The fatigue prospective memory task was administered throughout the session. Participants were fully

debriefed, paid 20 UK pounds in Tesco store vouchers and given drug education leaflets. The study was approved by the Ethics committee of the University of Central Lancashire.

10.3 Results

With regards to data screening, using the criteria suggested by Tabacknick and Fidell (2007), where univariate outliers were present they were replaced by the next highest/lowest score on the particular measure, plus/minus one. Where multivariate outliers were detected, the participants were excluded from the analysis. Regarding the distribution of the BRIEF subscales, the scores did not deviate significantly from normal and the z scores associated with the statistics in relation to skewness and kurtosis were consistent with normality for samples of this size (Tabachnick and Fidell, 2007).

As it is evident from Table 10.1, with the exception of alcohol consumption, the three groups did not differ significantly in terms of their age, intelligence, years of education or cigarette consumption.

Table 10.1. Age, intelligence, years of education, cigarette and alcohol use by group.

	Ecstasy/Polydrug Users			Cannabis-Only Users			Nonusers			P[1]
	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	
Age (years)	21.42	2.96	74	21.42	3.51	21	20.55	2.24	40	ns
Ravens Progressive Matrices (maximum 60)	41.90	10.00	73	42.19	7.57	21	43.10	8.46	40	ns
Years of Education	14.97	3.03	70	15.19	3.14	21	15.56	2.25	40	ns
Cigarettes per day	9.22	7.35	36	7.00	4.24	9	9.67	7.99	6	ns
Alcohol (Units per week)	14.80	10.76	71	13.75	13.93	20	8.24	11.51	37	<.05

[1]For one-way ANOVA

Table 10.2 summarises the means and standard deviations for the most prevalent recreational drugs used by the ecstasy/polydrug group and the amount of cannabis used by the cannabis-only group. Measures include the amount consumed in the last 30 days, the frequency of use, total lifetime use and weeks since last use. It is worth noticing that the polydrug group, besides the use of ecstasy and cannabis, was also characterised by regular use of cocaine. An inspection of other recreational drugs reported by polydrug users such as amphetamines, poppers, ketamine and LSD revealed that the small amount of ecstasy/polydrug users that reported such use described their use of the aforementioned drugs as 'occasional' in the past three months. Consequently, these drugs were not included in the analysis.

Non parametric statistical analysis was also employed to examine possible differences between different aspects of cannabis consumption between the two groups. As is evident from Table 10.2, the total lifetime use of cannabis differed significantly between the two groups with ecstasy/polydrug users consuming twice as much cannabis as the cannabis-only group.

Table 10.2. Indicators of Illicit Drug Use

	Ecstasy/Polydrug Users			Cannabis-Only Users			p[1]
	Mean	S.D.	N	Mean	S.D.	N	
Total Use							
Ecstasy (Tablets)	694.86	1300.39	74	-	-	-	-
Cannabis (joints)	3044.69	4756.85	67	1348.24	2678.53	21	<.019
Cocaine (lines)	1219.98	1593.54	50	-	-	-	-
Amount Consumed in Previous 30 Days							
Ecstasy (Tablets)	5.53	15.26	74	-	-	-	-
Cannabis (joints)	19.70	42.65	67	13.14	26.83	21	ns
Cocaine (lines)	12.24	23.31	50	-	-	-	-
Frequency of Use (times per week)							
Ecstasy	0.27	0.42	74	-	-	-	-
Cannabis	1.30	2.09	67	1.33	2.35	21	ns
Cocaine	0.42	0.59	49	-	-	-	-
Weeks Since Last Use:							
Ecstasy	36.44	67.97	74	-	-	-	-
Cannabis	25.55	58.76	67	68.58	97.40	21	ns
Cocaine	20.18	45.63	57	-	-	-	-

1. Mann-Whitney U test

Multivariate analysis of variance (MANOVA) was employed in order to investigate the effect of ecstasy/polydrug and cannabis-only use on the three laboratory measures of PM. Table 10.3 summarises the means and standard deviations of the three groups as well as the overall effect and pairwise comparisons.

As can be seen from Table 10.3, inspection of the means reveals that ecstasy/polydrug users consistently perform worse than cannabis-only users who in turn perform worse than drug naïve on all laboratory measures of PM. In fact, the multivariate group effect was statistically significant $\Lambda = .518$, $F(6,258) = 16.62$, $p<0.001$, partial $\eta^2 = .280$ suggesting an overall difference in PM performance across the three groups. In univariate terms, the three groups differed significantly on all three laboratory measures of PM. Tukey's post-hoc analysis revealed that performance on the fatigue PM task differed significantly between ecstasy/polydrug users and drug naïve as well as between cannabis-only and drug naïve groups, with ecstasy/polydrug and cannabis-only performing worse respectively. No significant differences were observed in performance of the fatigue PM task between ecstasy/polydrug users and cannabis-only users.

With regards to the PM pattern recognition task ecstasy/polydrug users performed significantly worse i.e., committed more errors than the drug naïve group while no significant group pairwise differences were observed between ecstasy/polydrug users and cannabis only or between cannabis only and the drug naïve control group.

Table 10.3. Scores on laboratory measures of PM for ecstasy/polydrug, cannabis only and drug naïve (one-tailed)

	Ecstasy/Polydrug Users		cannabis-only users		drug naïve		F	Pairwise Comparisons (Tukey's test)			Covariates: units of alcohol
	Mean	S.D.	Mean	S.D.	Mean	S.D.		E/PU vs CO	E/PU vs. Non	CO vs. Non	
PM fatigue task	33.06	22.14	45.56	20.11	73.23	23.57	41.39***	ns	<0.001	<0.001	37.20***
PM pattern recognition task	2.15	2.98	0.67	1.06	0.54	1.12	7.41**	ns	<0.01	ns	6.17**
Long-term PM task	0.59	1.04	1.05	1.16	1.59	1.27	10.05***	ns	<0.001	ns	6.17**

***p<.001; ** p<.01; * p<.05; P values at one-tailed

Ecstasy/polydrug-related performance deficits were also observed on the long-term PM recall task where ecstasy/polydrug users remembered to post back significantly fewer envelopes than non-recreational drug users.

Since the groups differed significantly in their alcohol consumption, a multivariate analysis of covariance was conducted to look at the effect of this covariate on the three laboratory measures of PM. In multivariate terms, the overall group effect remained statistically significant after the inclusion of the covariates, $\Lambda = .549$, $F(6,242) = 14.10$, $p<0.001$, partial $\eta^2 = .259$. This suggests that alcohol consumption did not affect the performance on measures of PM. Also, the effect size was only reduced by 2.1% suggesting that most of the variance was explained. The group effect for each of the PM task also remained statistically significant in the univariate analysis suggesting that PM performance is not affected by differences in alcohol consumption.

As with previous investigations, the ecstasy/polydrug user group was characterised by recreational use of cocaine and cannabis. It is therefore necessary to determine the contribution of each of the main illicit drugs to PM performance. Correlation analysis was therefore conducted to observe any associations of the illicit drugs and the three laboratory measures of PM. Table 10.4 summarises the Pearson's correlation coefficients for the lifetime, frequency and current use for ecstasy, cannabis and cocaine for each of the PM tasks.

Table 10.4. Simple and partial correlations between aspects of drug use and PM measures

	Fatigue PM task (Time-based PM)		PM pattern Recognition task (Event-based PM)		Long-term PM recall task (Long-term PM)	
	Simple Correlation	Semi-partial Correlation	Simple Correlation	Semi-partial Correlation	Simple Correlation	Semi-partial Correlation
Cannabis						
Total Lifetime Use	.002	-.162	-.182*	-.084	-.194*	-.178*
Consumed in last 30 days	.037	-.200*	-.204**	.005	-.212**	-.237**
Frequency	.150*	-.185*	-.210**	.122	-.205**	-.224*
Cocaine						
Total Lifetime Use	.223**	-.206**	-.279**	.151*	-.212**	-.194*
Consumed in last 30 days	.173*	-.117	-.197*	.045	-.210**	-.217**
Frequency	.419**	-.164*	-.273**	.099	-.259**	-.235**
Ecstasy						
Total Lifetime Use	.197**	-.017	-.184*	.131	-.085	.061
Consumed in last 30 days	.189*	-.013	-.196**	.092	-.137	.108
Frequency	.173*	-.075	-.263**	.067	-.153*	.040

***p<.001; ** p<.01; * p<.05; P values at one-tailed

With regards to the fatigue PM task, all three aspects of cocaine and ecstasy were associated with performance deficits in this time-based PM measure. Only frequency of cannabis was associated with the fatigue PM task. Nevertheless, when the variance of other drugs on the measure in question was excluded using regression analysis, two out of the three aspects of cannabis use were statistically significant suggesting that the frequency and current use of cannabis is associated with deficits in time-based PM performance. Total lifetime use and frequency of use of cocaine semi-partial correlations were also statistically significant after controlling for the use of other drugs while no aspect of ecstasy use yielded any statistically significant associations with the fatigue PM task following controls for other drug use.

With respect to the PM pattern recognition test significant associations were observed in all aspects of use for three drugs during correlation analysis. However, during regression analysis total lifetime use of cocaine appeared to be the only aspect of drug use significantly associated with performance deficits in the event-based PM task. Finally, for the long-term PM task all aspects of cannabis and cocaine use as well as the frequency of ecstasy use produced significant correlations with the measure. When the variance of other drugs was excluded from the analysis the three aspects of cocaine and cannabis use accounted for statistically significant unique variance while no aspect of ecstasy use was actually significant. It is therefore evident from these results that it is cannabis and cocaine rather than ecstasy that are responsible for the observed deficits in PM performance.

The purpose of this investigation was also to evaluate the role of executive processes in PM deficits and also determine whether these deficits in executive functioning can account for the PM deficits in ecstasy/polydrug users. In order to do this, the three general scales of the BRIEF-A (used in the previous chapter) were correlated with the three laboratory measures of PM. Regression analyses, with the BRIEF-A MI and BRI scales as predictors, was also employed in order to determine whether executive processes are responsible for the PM deficits in ecstasy/polydrug users and cannabis only users. Table 10.5 summarises the simple correlations from correlation analysis and the semi-partial correlations from regression analysis.

Table 10.5. Simple and semi-partial correlations for EF and PM measures in ecstasy/polydrug and cannabis only users

Correlate/IV	Simple correlation			Semi-Partial correlation		
	Fatigue PM task	PM pattern recognition task	long-term PM task	Fatigue PM task	PM pattern recognition task	long-term PM task
Model 1						
BRI	-0.078	-0.083	-0.108			
MI	-0.277**	0.046	-0.017	-.271*		
Model 2						
GEC	-0.205*	-0.007	-0.069			
Ecstasy/polydrug vs all others				.576***	-.290**	.337***
Cannabis-only vs all others				.331***		

***p<.001; ** p<.01; * p<.05; P values at one-tailed

As it is evident from Table 10.5, only the Metacognition index and the Global Executive Composite scale of the BRIEF-A are significantly correlated with the fatigue PM task, suggesting that impairments in executive processes are associated with impairments in time-based PM. Regression analysis with the laboratory measures of PM as dependent variables and the BRIEF BRI and MI as predictors also revealed that MI shared statistically significant unique variance

with the fatigue PM task (only significant associations are displayed in Table 5 for regression analysis). Another regression was also employed to determine whether ecstasy/polydrug-related deficits in PM can be attributed to drug related differences in EF. In order to do this, Ecstasy/polydrug users (compared to all other participants), cannabis-only users (compared to all other participants) and the BRIEF GEC score were added as predictors in the regression analyses. The three laboratory measures of PM were the dependent variables.

Regression analysis revealed that ecstasy/polydrug users (relative to all other participants) accounted for statistically significant unique variance in all PM tasks reflecting the ecstasy/polydrug-related PM deficits. Therefore, it appears that the ecstasy/polydrug effect on laboratory measures of PM cannot be entirely attributed to drug-related differences in executive functioning. Cannabis-only users (relative to all other participants) also accounted for statistically significant unique variance in the PM fatigue task reflecting cannabis-related PM deficits. It is also worth noting that the GEC was significantly correlated with the Fatigue PM Task, although not significant in the regression analysis. This suggests that GEC shares variance in common with either one or the other of the drug use predictors or both and the Fatigue PM. It is therefore possible that some of the ecstasy-related (or cannabis-related) variance in Fatigue PM might co-vary with GEC related variance in Fatigue PM. If this is the case, then it can be argued that there is a possible link between polydrug use, EF and PM, with perhaps some of the drug related PM deficits mediated by drug related EF impairment. However, this interpretation should be treated with caution.

It is evident that executive processes are correlated with the time-based PM task. What is interesting to look at will be which of these executive components are correlated with the fatigue PM task and also whether specific executive components can be associated with performance deficits in the other PM measures. In order to do this the nine subscales of the BRIEF-A were correlated with the PM measures. Table 10.6 summarises the simple correlations.

Table 10.6. Correlations between individual components of Executive Functions and PM measures

Executive Components	Fatigue PM task	Long-term PM recall task	PM pattern recognition task
Inhibit	-0.162*	-0.183*	-0.092
Shift	-0.090	0.034	0.039
Emotional regulation	0.074	0.007	-0.102
Self-monitor	-0.181*	-0.199*	-0.040
Initiate	-0.248**	-0.025	0.020
Working memory	-0.208*	0.018	0.045
Plan	-0.171*	-0.003	0.072
Task monitor	-0.256**	0.043	0.018
Organise	-0.213**	-0.100	0.008

** p<.01; * p<.05; P values at one-tailed

Inspection of Table 10.6 revealed that for the fatigue PM task all but two individual components of executive function were significantly correlated with performance in time-based PM task. Also, the inhibit and self-monitor scales were significantly correlated with the long term PM recall task suggesting that worse performance on executive functions predicts poor PM performance. No significant correlations were observed on the PM pattern recognition task suggesting that executive processes are only involved in time-based PM tasks.

10.4 Discussion

The aim of the present study was to reproduce findings from Chapter 7 that ecstasy/polydrug users are impaired in their PM performance. It also aimed to evaluate the role of executive processes in accounting for these PM deficits. On the whole, ecstasy/polydrug users in comparison to drug naïve performed significantly worse on all three laboratory measures of PM; a finding that is consistent with results from Chapter 7. These findings are also in line with previous investigations implicating ecstasy/polydrug use with PM impairments using self-report measures (Heffernan *et al.,* 2001; Rodgers *et al.,* 2001; 2003; Montgomery *et al.,* 2005; Fisk *et al.,* 2009). It can therefore be concluded that ecstasy/polydrug users underperform in time and event-based as well as long-term PM tasks.

The performance of recreational drug users whose drug choice was cannabis was also assessed in the present investigation. Although cannabis users performed worse than non- users of illicit drugs in all PM tasks, the only comparison that reached significant difference was the performance on the fatigue PM task where cannabis-only users remembered to complete a questionnaire every twenty minutes on less occasions than the drug naïve. Consistent with the previous studies, a trend is evident; ecstasy/polydrug users perform the worst on the PM tasks, cannabis-only users perform at intermediate levels and drug naïve perform the best.

Nevertheless, it is worth noting that in the present investigation the level of cannabis consumption in the ecstasy/polydrug user group was significantly higher than the one in the cannabis-only group. In fact, ecstasy/polydrug users consumed more than twice the amount of cannabis than the cannabis-only group. It is therefore possible that the observed deficits in PM performance are in fact attributed to cannabis use. This would account for why cannabis users were impaired in the PM pattern recognition task and long-term PM recall task (although not significantly) whilst ecstasy/polydrug users with higher levels of cannabis consumption were significantly impaired. Previous research on cannabis-related deficits in PM performance demonstrated that cannabis users are impaired in their PM performance. For example, Fisk and Montgomery (2008) found cannabis-related deficits in a sample of cannabis only users compared to controls on all subscales of the PMQ (i.e., long-term episodic, short-term habitual and internally cued PM as well as on the techniques aiding remembering). Similarly, McHale and Hunt (2008) demonstrated that abstinent cannabis users exhibit performance deficits on the long and short-term interval PM. Consequently, the present findings in relation to drug-related differences need to be interpreted with caution.

The ecstasy/polydrug user group was also characterised by recreational use of cocaine in addition to cannabis. In order to further investigate cocaine and cannabis-related interactions, correlation and regression analyses were employed. With regards to the fatigue PM task, for the most part aspects of ecstasy and cocaine use were significantly correlated with the time-based PM measure. However, when the variance of the other drugs was excluded (using regression

analysis) no aspect of ecstasy use yielded a significant association with the PM measure. Instead, all aspects of cocaine use (i.e., total lifetime use, frequency of use and the amount consumed in the last 30 days) produced significant associations. Most aspects of cannabis use were also significantly associated, suggesting that it is the recreational use of cocaine and cannabis rather than ecstasy use that are responsible for deficits in time-based PM performance.

Similarly, no aspect of ecstasy use was associated with poor performance on the long-term PM recall task while aspects of cannabis and cocaine produced significant associations. Finally, although all aspects of all three drugs were significantly correlated with performance on the PM pattern recognition task, regression analysis revealed that only lifetime use of cocaine was significantly associated with poor performance on the event-based task thus suggesting that impaired performance in the event-based PM task is attributable to the recreational use of cocaine. This is not a surprising result as cocaine was linked to impaired PM performance in all previous studies of this thesis. It can therefore be concluded that it is the recreational use of cocaine and cannabis rather than ecstasy that are responsible for poor overall PM performance.

It is therefore evident that ecstasy/polydrug users are indeed impaired in their PM performance and that for the most part recreational use of cannabis and cocaine is responsible for these deficits. What is not very clear is the role of executive processes in these PM performance deficits. It is known that PM is dependent on prefrontal executive processes as well as the medial temporal-hippocampal processes that support memory functions (Goldstein & Polkey, 1992; Kliegel *et*

al., 2005; West, 1996). PM processes such as dividing attention, monitoring the environment for a cue, associating a cue for intention and interrupting an ongoing activity may also involve planning that clearly draws on the prefrontal cortices and consequently on executive resources (Lezak, 1982; Shallice, 1982; Marsh & Hicks, 1998; McDaniel *et al.,* 1999; Whyte *et al.,* 2006).

It is therefore possible that ecstasy/polydrug-related deficits in PM are originating from deficits in executive functioning. The findings of the present investigation provide evidence for this assumption. It was found that the general scales of the BRIEF-A i.e., the Metacognition Index and the Global Executive Composite scales were significantly associated with the fatigue PM task suggesting that better EF performance predicts better PM performance. It was also suggested that there is a possible link between polydrug use, EF and PM, with perhaps some of the drug related PM deficits mediated by drug related EF impairment. Nevertheless, this interpretation should be treated with caution.

With regards to the role of executive processes in PM, looking at the individual components of EF from the BRIEF-A all but two scales were significantly correlated with the fatigue PM task. The inhibit and self-monitor subscales of the BRIEF-A were also significantly correlated with the long-term PM recall task suggesting that executive dysfunction is correlated with poor PM performance. Since no significant correlations were observed between EF and the event-based measure, it can be concluded that it is the time-based component of PM that rely on executive processes and not the event-based PM component. This is in line with Einstein et al's (1995) view that time-based prospective tasks are more likely

to rely on EF than event-based tasks. A possible explanation for this is that although strategic and automatic processes are involved in PM retrieval (Einstein *et al.,* 2005), it is likely that the extent to which executive processes are involved in PM retrieval is dependent on the specific requirements of the task (Glisky, 1996). For instance, time-based prospective tasks are more likely to rely on EF than event-based tasks as they require a higher degree of self-initiated retrieval (Einstein *et al.,* 1995). This could explain why deficits in executive functions are associated with deficits in time-based PM and not event-based PM.

The ecstasy/polydrug user group was also characterised by higher level of alcohol consumption. MANCOVA analysis with alcohol consumption as a covariate revealed that the overall group effect remained statistically significant, suggesting that alcohol consumption was not responsible for the deficits in PM performance. Nevertheless, alcohol consumption should not be overlooked, since previous investigations have linked alcohol abuse with executive dysfunction, it is possible that some of the deficits observed on the BRIEF are attributable to effects of alcohol rather than drug use (Brown *et al.,* 2000; Loeber *et al.,* 2009; Goldstein *et al.,* 2004).

Despite deficits in EF, alcohol also has adverse effects on PM performance (Heffernan *et al.,* 2010; Montgomery *et al.,* 2011). In relation to this, Montgomery *et al.* (2011) found that acute alcohol intoxication selectively impairs executive function and PM. In their study, participants in the alcohol condition performed worse on the planning, prioritisation, creativity and adaptability executive subscales and also on the time-based and event-based PM

tasks. However, alcohol did not impair the selection executive function task or the action-based PM task. Consistent with alcohol-related deficits in PM, Heffernan *et al.* (2010) also found that binge drinkers were impaired on a video based prospective memory task. Heffernan *et al.* (2003) examined the effects of alcohol on two aspects of memory performance; PM and everyday memory. Data was collected using the WWW and participants completed the PMQ and EMQ. After controlling for the use of other drugs and strategies used to aid remembering, it was found that alcohol was associated with impairments in long-term PM and with an increased number of cognitive failures. Both short-term and long-term PM failures using the PMQ were also found in a number of studies (e.g., Heffernan and Bartholomew, 2006; Heffernan *et al.,* 2006) supporting these findings. Finally, the level of alcohol consumption and tobacco should be kept in mind as several investigations suggest that these legal substances are related with PM deficits (Heffernan *et al.,* 2003; Heffernan & Bartholomew, 2006; Heffernan *et al.,* 2006; Heffernan *et al.,* 2010).

To conclude, the present study aimed to investigate the impact of ecstasy/polydrug use on PM and the role of executive processes in accounting for these PM deficits. Relative to drug naïve, ecstasy/polydrug users were impaired on all three laboratory measures of PM. Furthermore, executive processes were correlated with time-based PM measures. It is therefore possible to assume that deficits in PM performance are attributed to deficits in executive processes and perhaps some of the drug related PM deficits are mediated by drug related EF impairment. Recreational use of cannabis and cocaine was also associated with

laboratory measures of PM leaving open to question which drug is primarily responsible for the observed deficits in PM performance.

Chapter 11: General Discussion

The aim of the present thesis was to investigate the impact of ecstasy/polydrug use on prospective memory and executive processes. The role of executive processes in accounting for prospective memory deficits in ecstasy/polydrug users was also explored.

11.1 Prospective memory deficits in ecstasy/polydrug users

Previous investigations on the effects of ecstasy/polydrug use on prospective memory demonstrated that ecstasy/polydrug users are impaired on self-report measures of prospective memory (Heffernan *et al.*, 2001a; b; Rodgers *et al.*, 2001; 2003; Montgomery & Fisk, 2007; Fisk & Montgomery, 2008) raising the possibility that that PM performance is adversely affected by the neurotoxic effects of ecstasy.

Limitations of the existing literature on Prospective Memory performance

With the exception of a few studies (e.g. Rendell *et al.*, 2007; Zakzanis *et al.*, 2003; McHale & Hunt, 2008) the majority of investigations in the area of recreational drug use have used self-report measures to assess PM performance. Although self-report measures of PM have been extensively used in the literature and have been proven to be a powerful tool in detecting PM deficits in a variety of populations, they reflect participants' self-perceptions concerning their memory ability. These self-perceptions might therefore be distorted since people

experiencing memory impairments might not be able to remember and thus report their memory lapses.

Nonetheless, the most important limitation of self-report measures is that they fail to fully capture the distinction between time-based and event-based PM tasks. Instead, the scope of self-report measures is restricted to the period over the PM task is executed i.e., the short-term or the long-term. From the existing literature it is clear that ecstasy/polydrug users report deficits in both long and short-term PM (Heffernan *et al.,* 2001a; b; Rodgers *et al.,* 2001; 2003). However, it is not clear whether ecstasy/polydrug users are impaired in event-based, time-based PM task or both. It is therefore crucial to explore this as these two types of tasks utilise neural processes that are in part separable (Burgess *et al.,* 2003; Gilbert *et al.,* 2005; Okuda *et al.,* 2007).

These studies of self-report measures, despite their utility in detecting general PM deficits, provide relatively limited information regarding the extent, scope or implications of problems experienced by ecstasy/polydrug users. They also fail to investigate the conditions under which PM failures are most likely to occur (Rendell *et al.,* 2007). Although some investigations have tried to overcome these limitations by administering laboratory measures of PM (e.g., Rendell *et al.,* 2007) where these measures were used they have tended to be rather artificial and contrived in nature. In addition, they also appear to possess an associative learning component and that aspect of cognition is known to be impaired in recreational users of ecstasy (Montgomery *et al.,* 2005) making it difficult to determine the

extent to which any deficits that are observed are attributable to the PM component.

Research Aim

The aim of this thesis with regards to PM failures in ecstasy/polydrug users was to administer a number of naturalistic simple laboratory measures that require minimum learning and with the PM component being less obvious to the participant. Using both self-report and simple laboratory measures of PM a series of investigations (Chapters 7, 8 and 10) assessed the impact of ecstasy/polydrug use on both the storage/retention phase (i.e., the period over which the action is executed; short -term or long-term) and the retrieval phase (i.e., whether the action is triggered by monitoring time -time-based PM- or by external environmental factors -event-based PM-). These particular aspects have been under investigated in the area of recreational drug use.

11.1.1 Evidence from laboratory measures

On the whole, a variety of laboratory measures of PM have been used during the investigations. In order to measure retrieval phase (i.e. event and time-based PM) a number of laboratory measures were employed. For example, in Chapter 7 event-based PM was measured by employing the PM processing speed task where the participant was required to perform an action when presented with a cue. The RBMT was also administered to the participants and three of the subtests were used to measure time-based and event-based PM. With regards to time-based PM,

the Fatigue PM task was designed where the participant was required to monitor time and remember to ask for a questionnaire every twenty minutes throughout the test session. This test was also useful in assessing short-term PM as the period over which the action needed to be executed was of limited duration. Long-term PM was assessed by asking the participant to complete a simple recall test and to post their answers back to the experimenter at weekly intervals over the three-week period following testing.

In Chapter 8, time and event-based PM were assessed by the use of the CAMPROMPT test battery: a laboratory measure of event and time-based PM. Chapter 10 confirmed findings from Chapter 7 assessing event-based, time-based and long-term PM using the same laboratory measures with a larger sample. In addition, using a self-report measure of EF the role of executive processes in accounting for PM deficits was investigated.

Chapter 7 revealed that, on the whole, ecstasy/polydrug users were impaired on all PM laboratory measures. When looking at these PM measures individually, it was evident that ecstasy/polydrug users in comparison to non-ecstasy users underperformed in all cases. All measures, but two (one event and one time-based PM task from the RBMT), reached statistical significance demonstrating that the differences in performance between the two groups were meaningful. More specifically, on the PM processing speed test measuring event-based PM, ecstasy/polydrug users forgot to press a key on the computer when presented with the relevant cue on more occasions than non-ecstasy users. They also remembered to ask for a questionnaire assessing their level of fatigue (the fatigue PM task

measuring time-based PM) on fewer occasions than non-ecstasy users. Similarly, they forgot to post back their delayed recall responses in a prepaid envelope (long-term PM task) more often than non-ecstasy users. It is therefore evident that ecstasy/polydrug users seem to experience greater difficulties in event-based, time-based, short-term and long-term PM than non-ecstasy users.

With regards to the RBMT, ecstasy/polydrug users performed significantly worse than non-ecstasy users only on one of the three PM subtests of this measure: the RBMT belonging test measuring time-based PM. To the best knowledge of the author, the present study is the first one to demonstrate ecstasy-related deficits on the belonging subscale of the RBMT. For example, Zakzanis *et al.* (2003) administered the RBMT in a group of ecstasy/polydrug users and non-ecstasy users. Unlike the present study, Zakzanis *et al.* observed ecstasy-related deficits on the appointment and message PM scale of the RBMT but not on the belonging scale. Although ecstasy-related deficits were observed on the two subscales it is possible that these deficits were due to confounding factors as their ecstasy/polydrug users scored significantly less on the WAIS-III vocabulary sub-test compared to the control group. Unlike Zakzanis et al's study the present groups did not differ in background variables such as age, IQ, gender or years of education. Although the RBMT has been consistently used to detect memory lapses in clinical populations, it has been criticised as lacking the sensitivity to detect memory problems in non-clinical populations (Spooner & Pachana, 2006). Thus, it may be that the test was not appropriate for the university based sample of recreational drug users and the absence of impairments in the two subtests might

be attributed to the limited sensitivity of the test rather than the lack of ecstasy/polydrug related impairments.

Consistent with the results obtained in Chapter 7, using a different measure, the CAMPROMPT, Chapter 8 revealed that once again ecstasy/polydrug users were impaired on event and time-based PM. Unlike the RMBT, the CAMPROMPT has been developed for use with non-clinical populations and is better able to detect the subtle differences that may be present in these groups. In comparison to the drug naïve control group, ecstasy/polydrug users performed significantly poorer on both time and event-based scales of the CAMPROMPT supporting ecstasy/polydrug-related deficits on the retrieval phase found on the previous investigation (Chapter 7). In this study, the effect of the recreational use of cannabis on the retrieval phase (time and event-based PM) was also assessed by recruiting a cannabis-only user group. Although previous investigations suggest that the recreational use of cannabis is associated with PM deficits (McHale & Hunt, 2008), in this study cannabis-only users did not differ significantly from the drug naïve control group in event or time-based PM performance.

However, what is noteworthy is that although the cannabis-only group did not appear to be significantly impaired in comparison to the drug naïve group, recreational use of cannabis among the whole sample was significantly correlated with event-based PM even after controlling for the use of other drugs. More specifically frequency of cannabis use and the amount consumed in the last 30 days were associated with poorer event-based PM performance. These findings link the recreational use of cannabis with PM impairments and are in line with

previous investigations in which cannabis-related deficits have been observed (Rodgers *et al.*, 2003; Fisk & Montgomery, 2008; McHale & Hunt, 2008). The possibility that the observed deficits in ecstasy/polydrug users are in fact attributable to higher levels of cannabis consumption should therefore not be discarded. Nevertheless, a trend is evident from this investigation. In terms of PM performance, ecstasy/polydrug users perform the worst, followed by cannabis-only users performing at intermediate levels and drug naïve controls performing the best.

Chapter 10 also revealed ecstasy/polydrug-related deficits in laboratory measures of PM using a larger sample size (using participants from both Chapters 7 and 8). Ecstasy/polydrug users consistently performed worse than the drug naïve control group on all the laboratory measures of PM (i.e., PM fatigue task, PM pattern recognition task and long-term recall PM task) consistent with previous literature in the area of recreational drug use (Heffernan *et al.*, 2001a; b; Rodgers *et al.*, 2001; 2003; Rendell *et al.*, 2007). The increased sample size in Chapter 10 relative to Chapter 7 allowed the inclusion of a cannabis only group. The trend for PM performance in ecstasy/polydrug users, cannabis-only users and drug naïve was similar to that observed in the CAMPROMPT. Once again ecstasy/polydrug users performed worse on laboratory measures on PM, cannabis-only users performed at intermediate levels and drug naïve performed the best.

Contribution of recreational use of cannabis to Prospective Memory performance

Although it is evident from the three studies of PM that ecstasy/polydrug users perform poorly in laboratory measures of PM in comparison to all the other groups (non-ecstasy, cannabis-only and drug naïve controls), what is less evident is which drug is primarily responsible for the observed deficits in PM performance. Further investigation looking at different aspects of drug use was therefore employed across the studies in order to establish a relationship between aspects of drug use and PM performance.

With regards to the contribution of recreational use of cannabis on PM performance, cannabis was associated with a number of laboratory measures of PM. For example, both frequency of cannabis use and amount consumed in the last 30 days was associated with poorer performance on the fatigue PM task and event-based scale of the CAMPROMPT, frequency of use with the RBMT message task while all three aspects of cannabis use (lifetime, frequency and amount consumed in the last 30 days) were associated with poorer performance on the long-term recall PM task. It is therefore evident that recreational use of cannabis is involved in time and event-based and long-term PM performance. These findings are not surprising as previous investigations have linked the recreational use of cannabis with PM deficits (Rodgers *et al.,* 2003; Fisk & Montgomery, 2008; McHale & Hunt, 2008). However, the present studies augment previous findings by demonstrating which aspects of cannabis use appear

to be related to PM performance and by the inclusion of more naturalistic and purer laboratory measures of the PM construct.

Contribution of recreational use of cocaine in Prospective Memory performance

A surprising revelation in the series of investigations on PM performance presented here was the fact that no aspect of ecstasy use was correlated with any of the laboratory measures of PM. Instead, in all three investigations there was clear evidence that recreational use of cocaine is associated with performance on a number of laboratory measures. In fact, either total lifetime or frequency of use of cocaine or both were associated with performance on all PM tasks (RBMT appointment and belonging tasks, Fatigue PM task, PM processing speed task and Long-term recall PM task) except the RBMT message task. Indeed, the recreational use of cocaine shared unique variance with the appointment and belonging subtests of the RBMT and the long-term recall task. With regards to the CAMPROMPT, recreational use of cocaine was also associated with the event-based PM scale but not with the time-based PM. Actually, all three aspects of cocaine use were associated with poorer event-based PM performance. Total lifetime use, frequency of use and amount of cocaine consumed in the last 30 days remained statistically significant as predictors of event-based PM performance even after controlling for the use of other drugs.

More evidence for the involvement of recreational use of cocaine in PM deficits come from the last study of this thesis (Chapter 10) that, using a larger sample

size, revealed cocaine-related deficits in the fatigue PM task, PM processing speed task and the long-term recall task. It is therefore evident that recreational use of cocaine plays an important role in the observed PM deficits in ecstasy/polydrug users. Although no previous investigation has linked cocaine use with PM deficits, the mechanism through which the recreational use of cocaine might impact PM performance can be explained neuroanatomically.

As discussed in previous chapters, PM performance is dependent on prefrontal executive resources. In fact, several studies demonstrated that event-based PM tasks utilise the frontopolar cortex and more specifically Broadmann area 10 (BA10; Burgess *et al.*, 2003) and the left superior frontal gyrus (Okuda *et al.*, 2007). On the other hand, time-based PM tasks activate various regions including the anterior medial frontal regions, the right superior frontal gyrus and the anterior cingulate. Similarly to the event-based tasks, time-based tasks also activate the BA10 and the superior frontal gyrus (Okuda *et al.*, 2007). BA10 is known to support several executive functions and in most specifically those that involved updating contents of working memory (Collette *et al.*, 2005). Consequently, updating deficits may be associated with PM deficits in both time and event-based. A number of studies suggested that cocaine users are in fact impaired in different measures of working memory i.e., impairments were observed on the paced auditory serial addiction task (PASAT; Berry *et al.*, 1993), the number letter re-sequencing task and on forward and backward digit and spatial span (Verdejo-Garcia & Perez-Garcia, 2007). This can therefore explain the observed cocaine-related deficits on PM performance in the present study.

Another explanation for the cocaine-related deficits in PM comes from studies looking at dopaminergic activity in the PFC in those areas known to support executive processes. A number of studies suggest that cocaine has an effect on dopamine levels thereby influencing behaviour (Heien *et al.*, 2005; Zhang *et al.*, 2005; Sidiropoulou *et al.*, 2009). More specifically, according to neuroimaging evidence, cocaine users experience hypoactivation in the mesencephalon where dopamine cell bodies are located and projections originate. In relation to a control group, cocaine users also exhibit a deactivation in regions with high levels of dopamine projections such as the putamen, anterior cingulate, parahippocampal gyrus and amygdala (Tomasi *et al.*, 2007). This deactivation in dopamine projection regions was associated with a compensatory hyperactivation in cortical regions enhancing executive functions. Nonetheless, Tomasi *et al.* found that the activation of these cortical regions (prefrontal and parietal cortices) during the performance of a working memory task was less in cocaine users than in non-users. It is therefore possible that prior history of cocaine use can interrupt dopaminergic operations in the PFC causing executive dysfunction and therefore impairment in PM performance.

Further evidence for the involvement of dopamine in PM performance comes from studies investigating Parkinson's disease which is characterised by disruption of dopaminergic functioning in the cortico-striatal pathway. For example, a recent study demonstrated that the administration of L-dopa significantly improves PM performance in a sample of Parkinson's patients in comparison to an unmedicated condition (Costa *et al.*, 2008). Since it is known that both cocaine and ecstasy potentially disrupt the functioning of dopaminergic

systems, it is possible that the PM deficits observed in Chapters 7, 8 and 10 of this thesis are due to impaired dopaminergic processes in the cortico-striatal pathway.

Summary of laboratory measures of PM

Summarizing the findings from laboratory measures of PM, it is evident that ecstasy/polydrug users underperform in objective measure of PM. Consequently, the present series of investigations extend previous research using self-report measures in which ecstasy/polydrug users were impaired in their PM performance (Heffernan *et al.,* 2001a; 2001b; Rodgers *et al.,* 2001; 2003; Montgomery & Fisk, 2007; Fisk & Montgomery, 2008). The ecstasy/polydrug related effect observed in the present investigations is also consistent with recent research using laboratory measures of event and time-based PM (Rendell *et al.,* 2007). The present findings also augment the existing literature demonstrating the efficacy of the CAMPROMPT measure in capturing individual differences in PM performance among non-clinical populations (Groot *et al.,* 2002; Wilson *et al.,* 2005). It is also clear that reported PM deficits in ecstasy/polydrug users are real rather than imagined since the self-reported impairments have been confirmed by the outcomes of the laboratory measures. What is also worthy of note is that the recreational use of ecstasy was not associated with any laboratory measure of PM in any of the three investigations reported here. Instead, recreational use of cocaine appeared to be the main predictor for the observed PM deficits in ecstasy/polydrug users.

11.1.2 Evidence from self-report measures of real world memory

11.1.2.1 Prospective memory

In addition to the variety of laboratory measures that were administered, a number of self-report measures that have been used extensively in the literature to assess PM performance in ecstasy/polydrug users were also employed. For instance, in Chapter 7 two questionnaires were employed to assess participants' perceptions of their PM performance. The PMQ questionnaire assessed short-term PM, long-term PM, internally cued PM and techniques people employ to help them remember. The PRMQ was also administered to measure overall PM performance.

It was revealed that in comparison to the non-ecstasy user group, ecstasy/polydrug users reported more deficits on the short-term PM scale and also used fewer techniques to help them remember. Although findings from previous studies are in line with the reported deficits on the short-term PM scale of the PMQ (Heffernan *et al.,* 2001a; b; Rodgers *et al.,* 2001; 2003; Montgomery & Fisk, 2007) the lack of deficits on the long-term PM and internally cued PM scales are inconsistent with previous literature (Heffernan *et al.,* 2001a; Rodgers *et al.,* 2001; 2003; Montgomery & Fisk, 2007). In terms of the PRMQ, ecstasy/polydrug users reported general PM problems as opposed to the non-ecstasy user group suggesting that on the whole ecstasy/polydrug users perceive their PM performance to be impaired.

11.1.2.2 Everyday memory

In Chapter 7, ecstasy/polydrug users also reported their everyday memory ability to be impaired relative to non-ecstasy users. This provides further evidence for ecstasy/polydrug-related deficits in everyday memory performance found in a number of previous investigations (Heffernan *et al.*, 2001b; Montgomery & Fisk, 2008; Fisk & Montgomery, 2008).

11.1.2.3 Cognitive failures

However, on a different self-report measure administered in Chapter 7, no differences in the incidence of self-perceived cognitive failures was observed between ecstasy/polydrug and non-ecstasy users. While at variance with the results obtained on some of the other self-report measures, this is not unprecedented as previous studies in the area have failed to find deficits in everyday cognitive lapses using the CFQ (Rodgers *et al.*, 2000; Heffernan *et al.*, 2001b).

Contribution of other drugs in self-report measures of real world memory

Although ecstasy/polydrug users as a group reported real world memory deficits, the specific drugs responsible for these deficits were less clear. For instance, lifetime use of ecstasy and frequency of cannabis use were positively associated with self-perceived short-term PM while lifetime use of ecstasy was positively associated with internally cued PM. Although ecstasy/polydrug users did not appear to experience difficulties in cognitive failures, lifetime use of ecstasy was

positively associated with cognitive failures. Furthermore, in terms of PM performance on the whole, lifetime use of ecstasy, cocaine and amphetamines were positively associated with the self-reported PM deficits. These positive associations suggest that increased frequency and lifetime use is related with higher scores on the self-report measures consistent with more real world memory problems. Nevertheless, most of the semi-partial correlations did not reach statistical significance meaning that it is not possible to identify which of the four drugs is likely to be primarily responsible for the real world memory deficits in ecstasy/polydrug users.

Also, the effect of the recreational use of cocaine was less evident in the self-report measures of real world memory as opposed to the prominent role of cocaine in relation to the outcomes on the laboratory measures of PM. It is therefore clear that although the use of cocaine appears to affect the outcomes on the laboratory PM measures there appears to be less awareness of this link in the self-perceptions of cocaine users.

11.2 Executive dysfunction in ecstasy/polydrug users

Limitations of the existing literature

Ecstasy/polydrug-related deficits have been demonstrated in aspects of executive functioning in several investigations (see Murphy *et al.*, 2009 for a review). Although ecstasy/polydrug-related EF deficits have been established, assessment of EF in the area of recreational drug use has been restricted to laboratory-based

measures that despite their obvious advantages are limited in terms of their ecological validity with regard to everyday functioning (Gioia *et al.,* 2008). Also, laboratory measures of EF capture only narrow aspects of the executive system and not the multidimensional aspects of decision making that characterise real-world situations (Goldberg & Podell, 2000). Therefore, relying on only laboratory-based measures can lead to a limited and incomplete assessment given that executive functions play a key role in the direction and control of real-world behaviour (Gioia & Isquith, 2004).

Research aim

While laboratory measures are of vital importance in identifying the processes and interrelationships underpinning EF, self-report measures such as the BRIEF-A contextualise executive processes placing them in the naturalistic real world environments in which PM behaviour is manifested. Compared to the low level component processes that characterise laboratory measures, the component scales comprising the BRIEF-A provide a broader more effective operationalization of the EF construct potentially making it easier to identify which aspects of EF are relevant to successful PM performance. As a first step, Chapter 9 administered the BRIEF-A, thereby obtaining data for the nine aspects of EF that have been commonly discussed in the literature.

11.2.1 Evidence from the BRIEF

This investigation revealed that in comparison to drug naïve, ecstasy/polydrug users demonstrated deficits on all subscales of the BRIEF, with the exception of shift and emotional regulation. Evaluating the role of cannabis use in executive functioning cannabis-only users were compared to the drug naïve sample and although cannabis only users performed generally worse than drug naïve in all subscales of the BRIEF the only component of EF that reached significance was emotional regulation. Similar to the previous studies on PM, a trend is evident in EF performance as well; ecstasy/polydrug users performing the worst following cannabis users performing at intermediate levels and drug naïve performing the best. The present findings are broadly in line with previous literature questioning the integrity of EF in ecstasy/polydrug users (e.g., Fox *et al.,* 2001; Verdejo-Garcia *et al.,* 2005; Montgomery *et al.,* 2007; Wareing *et al.,* 2007; Montgomery & Fisk, 2008).

Contribution of recreational drugs

With regards to which drug or drugs are associated with EF performance, Chapter 9 revealed that aspects of ecstasy use rather than any other drug were associated with most executive components. Nevertheless, when the variance of other drugs was excluded only the inhibit EF component yielded a statistically significant (adverse) association specifically with the frequency of ecstasy use. It is therefore possible that the inhibit component is sensitive to the recreational use of ecstasy.

This was unexpected as a number of previous investigations using laboratory-based measures suggested that it is the updating component of working memory and not the shifting and inhibition elements that are sensitive to the effects of ecstasy (Fisk *et al.,* 2004; Montgomery *et al.,* 2005; Reneman *et al.,* 2006; McCann *et al.,* 2007). A possible explanation as to why laboratory measures of inhibition appear unaffected by ecstasy use while the self-report measure is associated with ecstasy-related deficits may be that the BRIEF measures different elements of the inhibition construct than those assessed by computerised performance tests (Bodnar *et al.,* 2007).

The potential role of recreational cannabis use in accounting for the EF deficits observed in this investigation should not be disregarded since cannabis consumption in the ecstasy/polydrug user group was generally significantly greater than that of the cannabis-only group. It is therefore possible that the observed deficits in executive components are in fact attributed to cannabis use. This might explain why cannabis users were impaired (although not significantly) whilst ecstasy/polydrug users with higher levels of cannabis consumption were significantly impaired. The present findings raise the possibility that although cannabis users perform adequately in laboratory settings, in a less controlled environment i.e., their everyday lives, they might demonstrate executive dysfunction. Chapter 9 also revealed ecstasy/polydrug related deficits on a number of the other BRIEF subscales including planning, initiation, organisation, and self and task monitoring. It is possible that these impairments reflect separate aspects of another key executive function: the effective maintenance of goal directed behaviour.

11.3 The role of executive processes in accounting for Prospective Memory deficits in ecstasy/polydrug users

What is evident from the empirical chapters of this thesis is that ecstasy/polydrug users are impaired in measures of PM and EF. What is less evident is the role of executive processes in accounting for these ecstasy/polydrug-related PM deficits. PM processes such as dividing attention, monitoring the environment for a cue, associating a cue for intention and interrupting an ongoing activity may also involve planning that clearly draw on prefrontal cortices and consequently on executive resources (Lezak, 1982; Shallice, 1982; Marsh & Hicks, 1998; McDaniel *et al.,* 1999; Whyte *et al.,* 2006). It is therefore possible that the observed ecstasy/polydrug-related deficits in PM are originating from ecstasy/polydrug-related deficits in executive functioning.

Chapter 10 provides evidence for this assumption since the general scales of the BRIEF-A (i.e., the metacognition index and the Global Executive Composite scales) were significantly associated with the fatigue PM task suggesting that deficits in EF performance predicts poorer time-based PM performance. Chapter 10 also revealed a possible link between polydrug use, EF and PM, with perhaps some of the drug related PM deficits mediated by drug related EF impairment. Nevertheless, this interpretation should be treated with caution.

Given that no association was found between EF and the event-based measure, it is reasonable to assume that it is the time-based component of PM that rely on executive processes and not the event-based PM component. This provides evidence for Einstein *et al.*'s (1995) view that time-based prospective tasks are

more likely to rely on EF than event-based tasks as they require a higher degree of self-initiated retrieval (Einstein *et al.,* 1995).

11.4 The role of Retrospective Memory in Prospective Memory deficits

Since PM has a retrospective component, responsible for retaining the basic information about the required action and the contextual cue (Einstein & McDaniel, 1990) it is possible that impairments in PM observed in ecstasy/polydrug users might stem from RM and verbal learning difficulties. Since neuroimaging evidence suggesting that the hippocampal region and the dopaminergic system are involved in both retrospective and prospective memory (Martin *et al.*, 2007; Goto & Grace, 2008) it is possible that ecstasy/polydrug users are also impaired in their RM and verbal learning. Findings from Chapter 8 revealed that ecstasy/polydrug users in comparison to drug naïve reported RM problems and that these problems in RM (both in the retrospective component of the PRMQ and RAVLT) are associated with both event and time-based PM. Since RM plays an important role in PM performance the present findings raise the need for further research. Unlike previous research (Reneman *et al.,* 2000; Quednow *et al.,* 2006) the present thesis failed to find any ecstasy/polydrug related deficits on verbal memory.

11.5 Implications of present findings and contribution to the existing literature

Findings from the present investigations of PM performance provide further evidence for ecstasy/polydrug-related deficits in short and long-term PM

previously reported in self-report studies. It is therefore evident that deficits in the storage/retention phase are real in ecstasy/polydrug users and not falsely perceived. In this thesis ecstasy/polydrug users reported deficits on the short-term PM scale of the PMQ. However, they appeared unaware of their long-term PM deficits that were apparent on the objective measure. It is therefore possible that laboratory measures of PM are more efficient in capturing PM deficits than the traditional self-report measures. Although on the subjective measures, ecstasy/polydrug users reported general PM impairment, on its own this does not fully explore the nature of deficits in the retrieval phase (i.e., event and time-based PM); a phase that has been under-investigated in the area of illicit drug use. Evidence from the laboratory measures of event and time-based PM employed in this thesis provide evidence for ecstasy/polydrug-related deficits in the retrieval phase and also that PM deficits in recreational drug users are not task specific; instead they consistently underperform in all PM measures.

The evidence for such deficits on objective measures and the significant association between these and the outcomes on subjective measures provides support for the efficacy of self-report measures in detecting general PM impairments. However, it is clear from the present results that self-report measures are ineffective in assessing important components of the PM construct, such as event and time-based PM. The results reported here demonstrate that both of these are clearly impaired in recreational drug users.

An important advantage of the laboratory measures of PM employed in this thesis is that they require minimum learning. This contrasts with other laboratory tasks

that have been used in this area that require a greater degree of learning. This is an important improvement since associative learning is impaired in ecstasy/polydrug users (Montgomery *et al.,* 2005) and reported deficits on these laboratory measures (for example the Virtual Week; Rendell *et al.,* 2007) might be attributed to associative learning impairments rather than PM problems. Consequently, the present thesis provides objective evidence for ecstasy/polydrug related deficits in PM performance in both the retrieval and storage/retention phase suggesting that reported PM deficits in ecstasy/polydrug users are real rather than imagined and highlights the importance of employing objective measures in assessing PM performance in the area of recreational drug use.

Another important contribution to the existing knowledge of PM problems in recreational drug users is the revelation that recreational use of cocaine is associated with PM deficits. In fact, aspects of cocaine use were associated with performance on all PM tasks and for the most part recreational use of cocaine shared unique variance with most laboratory measures of PM. The present thesis has therefore implicated the recreational use of cocaine, for the first time, in accounting for the PM deficits observed in ecstasy/polydrug users. Another surprising revelation was the fact that recreational use of ecstasy was not associated with any of the laboratory measures of PM, instead recreational use of cocaine emerged as the primary contributor to PM deficits. This is an important finding since previous literature has attributed PM impairments in ecstasy/polydrug users to the recreational use of ecstasy. It is therefore possible that these impairments are in fact attributable to the recreational use of cocaine and not exclusively to the effects of ecstasy use. The effects of cocaine use,

although evident on objective measures of PM, were not as evident on the self-report measures of PM within the same cohort of ecstasy/polydrug users. This, once again emphasises the importance of using more objective measures of PM performance in studies of recreational drug users.

While the importance of using objective measures of PM performance has been emphasised, the present thesis employed a self-report measure of EF performance in the everyday environment as opposed to the laboratory measures employed in previous studies in the area. Ecstasy/polydrug users underperformed on most components of the BRIEF including the inhibit component. This is an interesting finding as previous investigations have failed to observe deficits on laboratory measures mapping on the inhibit component. It is therefore possible that self-report measures of EF are more capable of detecting the behavioural manifestations of EF in the everyday environment. The reason for the reported ecstasy/polydrug-related deficits on the inhibit component is that the BRIEF may measure different elements of the inhibition construct than those assessed by computerised performance tests (Bodnar *et al.,* 2007). This therefore not only emphasizes the utility of the BRIEF in capturing the behavioural manifestations of EF but also the need for employing measures of EF that characterise real-world situations in recreational drug-users.

Also, the present findings identify another key executive function: the effective maintenance of goal directed behaviour. Consequently, this thesis potentially identifies an additional aspect of executive function which might be subject to the

adverse effects of recreational use of ecstasy, providing a useful direction for further research.

Finally, the present thesis has evaluated the contribution of executive processes and retrospective memory in PM performance in ecstasy/polydrug users. Findings provide evidence that the observed ecstasy/polydrug-related deficits in PM (time-based PM) are originating from ecstasy/polydrug-related deficits in executive functioning. There was also evidence to support that problems in RM are associated with both event and time-based PM. These findings therefore emphasize the need to investigate the contribution of such processes to PM performance within the population of recreational drug users.

To conclude, given the role of PM and EF in a person's day-to-day functioning, perhaps the most important implication of the findings of this thesis is that the recreational use of illicit drugs may have serious consequences for the everyday functioning of users. The evidence for PM and EF deficits found in this thesis in ecstasy/polydrug users suggests that recreational drug use adversely affects performance on key everyday activities. For example, while forgetting to pass on a message, post an envelope or meet a friend may often be inconsequential, forgetting to take your medication, missing important appointments or interviews, can have serious consequences. The possibility that some of the important processes that are essential for day-to-day functioning might be impaired in ecstasy/polydrug users is a clear cause for concern.

11.6 Limitations

As with most studies in this area, there are a number of limitations. For example, the ecstasy/polydrug user group was characterised by the recreational use of cannabis and cocaine in addition to ecstasy. Due to the quasi-experimental design of the studies the concurrent use of other illicit drugs may have contributed to group differences in both PM and EF. Although the employment of statistical procedures that excluded the variance attributable to other drugs went some way to overcoming this limitation (as in previous studies in the area), it is not possible to totally control for confounding effects of this nature.

Also, the purity of MDMA tablets obviously cannot be guaranteed. Although a review by Parrott (2004) reports that the MDMA content of ecstasy tablets retrieved from amnesty bins in nightclubs was approaching 100%, from a lifetime perspective it is not possible to be definitive as to the amount of MDMA and other chemical compounds present in ecstasy tablets. Similarly to MDMA, cocaine and cannabis purity cannot be guaranteed either. For example, potency of cannabis (i.e., THC content) varies widely in the UK (Potter *et al.,* 2008). Within the UK two distinct types of cannabis are circulating. One form contains floral and foliar material from outdoor grown pollinated female plants; referred to as herbal cannabis or marijuana. The second form, and most frequently used, is predominantly grown indoors using all-female plants and highly technical equipment and is referred to as skunk. The investigations in this thesis, as with most neuropsychological studies in the area, do not discriminate between the two available forms of cannabis dried-plant material. This is a potential limitation as

previous studies demonstrated that the content of THC and other major cannabinoids varies widely in illicit cannabis (ElSohly *et al.*, 2000).

Similarly, purity of cocaine cannot be guaranteed either. According to Schifano and Corkery (2008), however, purity of cocaine powder has remained fairly stable in the UK during 1990-2004 with mean purity levels varying between 42- 60% within this timeframe (as reported by Police and may reflect what is available in the street market).

A further limitation of the present investigations was the lack of objective measures of recent drug use such as hair or urine analysis. Instead, a self-report measure of history of drug use was administered. Although this is clearly a limitation, previous studies in the area have not used these techniques and have relied on self-report measures instead (Morgan, 1999; Heffernan *et al.* 2001a; b; Rodgers *et al.*, 2001; 2003; Fisk & Montgomery, 2007). Also, the drug use history questionnaire (Montgomery *et al.*, 2005b) employed in this investigation provided a number of checks for internal consistency, verifying the reliability of the information provided by participants. Nonetheless future research would benefit from the inclusion of objective measures of recent drug use.

Another possibility is that the apparent ecstasy/polydrug related deficits may not necessarily be a consequence of illicit drug use but instead be due to pre-existing differences between the groups originating before the onset of illicit drug use. For example, there has been evidence of PM deficits (Kliegel *et al.,* 2006) and executive dysfunction (Barkley, 1997) in children with ADHD. Executive

dysfunction has also been demonstrated in patients with unipolar depression (see Fossati, 2002 for a review). In relation to this, Pope (2002) has emphasized the importance of considering differences in sociodemographic factors, personal dispositions and underlining psychopathology between users and non-users. It is therefore possible that impairments observed on PM and EF performance, are not necessarily attributed to the use of illicit drugs. Furthermore, lifestyle differences or the effects of illicit drug use on other physiological processes such as altered sleep patterns and cognitive deficits (Fisk & Montgomery, 2009b) might be the actual cause of the observed deficits. The contribution of alcohol consumption and tobacco in PM and executive processes should also be kept in mind as several investigations suggest that these legal substances are related with PM deficits (Heffernan *et al.,* 2003; Heffernan and Bartholomew, 2006; Heffernan *et al.,* 2006; Heffernan *et al.,* 2010). Although the series of investigations in this thesis have tried to control for alcohol consumption, the possible involvement of alcohol in the observed deficits should not be disregarded.

11.7 Future directions

In reflecting on the research questions addressed in this thesis, several interesting findings that potentially provide a useful direction for future research were observed. With regards to PM in recreational drug users, the present thesis emphasized the importance of using more objective measures of PM rather than self-report measures since laboratory measures of PM were more sensitive in detecting PM deficits in ecstasy/polydrug users. It also provided further evidence for the effect of ecstasy/polydrug use on the time and event-based PM that is

under-investigated in the area of illicit drug use. It is therefore evident from the findings of this thesis that recreational drug users face a range of PM deficits that are not restricted to the storage/retention phase (i.e., short and long-term PM). Hence, this provides a useful direction for future research as it is essential to investigate the whole range of PM deficits experienced by ecstasy/polydrug users using more objective measures in order to further establish the scope, extent or implications of such deficits in PM.

Another finding from the present thesis that merits further investigation is the potential role of executive processes and RM in accounting for the observed deficits in PM in recreational drug users. Although the present thesis provides evidence for the contribution of EF and RM in PM performance, further research is essential to identify the extent of which these processes affect PM performance. Consequently, a wider range of laboratory measures of PM that are less artificial in nature and require minimum contribution of executive processes and RM in order to identify whether drug-related deficits in PM are not a result of drug-related deficits in executive processes and/or RM are crucial.

In terms of EF in ecstasy/polydrug users, an alternative assessment was introduced in the present thesis. The efficacy of the BRIEF to capture deficits on the inhibit scale while previous laboratory measures of the components failed to do so, outlines the importance of employing different assessment methods to measure executive dysfunction in ecstasy/polydrug users. The findings of the present thesis in relation to EF also suggest that ecstasy/polydrug users are impaired in a wider range of EF than previously thought. In fact, ecstasy/polydrug

users demonstrated a range of EF deficits with regards to the everyday environment. Impairment on a number of BRIEF subscales including planning, initiation, organisation, and self and task monitoring were also revealed. Therefore this thesis identifies another key executive function: the effective maintenance of goal directed behaviour that might be subject to the adverse effects of recreational use of ecstasy. Further investigation of this possibility through the use of appropriate self-report measures and laboratory tests might constitute a fruitful direction for further research.

Perhaps the most striking revelation of the present investigations on PM performance in ecstasy/polydrug users is the contribution of recreational use of cocaine in the observed PM deficits. Evidence demonstrated that all laboratory measures of PM were associated with the recreational use of cocaine, and for the most part cocaine shared unique variance with most of these measures. This revelation provides a fundamental direction for further research in order to understand the origin of ecstasy/polydrug related deficits in PM performance. Consequently, further research is essential in order to determine the exact role played by cocaine in PM performance amongst recreational drug users and also to clarify whether the cocaine-related deficits are limited to the ecstasy/polydrug population or whether they might be present among those persons whose recreational use is largely confined to cocaine.

11.8 Overall summary

The aim of this thesis was to expand on previous research as to the impact of ecstasy/polydrug use on prospective remembering and executive functioning. Evidence from a series of investigations suggests that ecstasy/polydrug users experience more general PM problems as ecstasy/polydrug-related deficits were evident on both the retrieval phase (time and event-based PM tasks) and storage/retention phase (short and long-term PM). This also suggests that ecstasy/polydrug-related deficits demonstrate a general feature of PM performance rather than task-specific aspects. These deficits on both laboratory measures of PM and (some) self-report measures of real world memory therefore suggest that ecstasy/polydrug users possess some self-awareness of their memory lapses. The findings of the present thesis with relation to laboratory measures of PM also emphasize the importance of employing more objective measures to assess PM in the area of recreational drug use. An unanticipated finding in the present thesis was that the recreational use of cocaine was associated with PM deficits; an association that consistently emerged in all studies of PM performance.

Ecstasy/polydrug users also demonstrated deficits on executive processes using the self-report measure BRIEF suggesting that recreational drug users are impaired in a broader range of EF with regards to the everyday environment and ecstasy/polydrug-related deficits are not restricted to three-model component of EF. The present thesis also identified another key executive function: the effective maintenance of goal directed behaviour that appears to be susceptible to the adverse effects of recreational use of ecstasy. It was also revealed that

ecstasy/polydrug users face RM problems and that these problems in RM are associated with both event and time-based PM. Furthermore, evidence to suggest that executive dysfunction is associated with poorer time-based PM performance was suggested. It is therefore possible that deficits in PM performance are associated with deficits in executive processes and perhaps some of the drug related PM deficits are mediated by drug related EF impairment.

Finally, although few PM or EF performance deficits were evident among cannabis-only users, a trend is evident in all investigations of PM and EF; ecstasy/polydrug users perform the worst, cannabis-only users at intermediate levels and drug-naïve perform the best. All in all, ecstasy/polydrug related deficits are evident on both prospective remembering and executive processes. The outcomes of the present thesis, despite addressing some of the grey areas in the literature of PM and EF in relation to recreational drug use, also provide a fruitful direction for future research.

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APPENDIX 1: PARTICIPANTS OVERLAP TABLE

This table shows the number of participants overlapping in chapters 7-10

	Chapter 7	Chapter 8
Chapter 7 (PMQ, PRMQ, RBMT, CFQ, EMQ, PM fatigue, PM procspeed, PM long)	-	-
Chapter 8 (CAMPROMPT, RAVLT, MCQ, RM)	-	-
Chapter 9 (BRIEF-A)	37EP	28EP
	7CO	12CO
	20DN	18DN
Chapter 10 (BRIEF-A, PM fatigue, PM procspeed, PM long)	37EP	28EP
	7CO	12CO
	20DN	18DN

EP= Ecstasy/polydrug users

CO= Cannabis-only users

DN= Drug naïve

APPENDIX 2: DRUG HISTORY QUESTIONNAIRE

Participant Number _____ Height _____

Weight _____

Gender _____

Age _____

1. Have you ever used the drug ecstasy? Yes/No*

(If 'No' please move on to Question 16)

2. How long have you been taking ecstasy? _____ Months _____ Years

3. How aware are you that using the drug ecstasy may have harmful long term effects on your health?

(*Please tick relevant answer*)

Very aware ____

Quite aware ____

Unsure ____

Quite unaware ____

Very unaware ____

Can you explain below what these harmful effects may be?

4. Are you concerned about the possible dangers of using ecstasy?

(*Please tick relevant answer)*

Extremely Concerned ____

Very Concerned ____

Concerned ____

Slightly Concerned ____

Not Concerned ____

5. How do you find out information about ecstasy?
(Please tick all relevant answers)

TV-News		Radio	
TV-Specialist Programes\Debate		Drug Agencies	
Daily Newspaper		Drug Leaflets	
Music Magazines		Friends	
Magazine		Clubs	
Other			

6. Where do you usually take ecstasy?
(Please tick relevant boxes)

Pubs/Bars	
Night-clubs	
Rave Events	
Private House/Flat	
Parties	
Own Home	
Friends Home	
Other	

7. What activities do you participate in when under the influence of ecstasy?
(Please tick relevant boxes)

Dancing	
Listen to Music	
Talking	
Driving	
Sexual Behaviour	
Drinking	
Smoking	
Other	

8. Do you take any sort of precautions when using ecstasy? Yes\No
(E.G. Vitamins)

*If **yes** please give details*

9. Are you aware that medical advice suggests that you should take precautions when using ecstasy? Yes___ No ____

*If **yes** can you explain below what precautions should be taken and why*

10. When under the influence of ecstasy:

(a) Do you take regular rest-breaks when dancing Yes--- No---

(b) Do you monitor your fluid intake Yes--- No---

(c) Is there anything else you do Yes--- No---

*If **yes** please give details*

11. Is there a maximum number of ecstasy tablets you will take in one session? Yes--- No---

If **Yes**, what is the maximum number _____

12. What factors decide when you have taken enough ecstasy tablets in one session? (***Please give details below***)

13. Do you believe that since using ecstasy you have changed in any way?

Please look at the following list very carefully

(For example, if you believe that since using ecstasy you have become more caring then tick caring under the heading MORE. If however you feel that you have become less caring then tick caring under the heading LESS. If you feel that you have not become any more or less caring the tick caring under the heading NO CHANGE)

	MUCH MORE	**MORE**	**NO CHANGE**	**LESS**	**MUCH LESS**
CARING					
PARANOID					
ALERT					
DEPRESSED					
SOCIABLE					
AGGRESSIVE					
HAPPY					
HEALTHY					
MOODY					
PATIENT					
IRRITABLE					
CONFIDENT					
SAD					
LOVING					
CONFUSED					

Any other changes _____

14. What has stopped you taking ecstasy in the past?
(Please tick relevant boxes)

Bad Experience (You)	
Bad Experience (Other)	
Work/College	
Parents	
Short Term Health (Physical)	
Long Term Health (Physical)	
Death	
Responsibilities	
Prison	
Psychological Problems (Short Term - in the last 1 month)	
Anxiety	
Depression	
Flashbacks	
Panic Attacks	
Paranoia	
Psychological Problems (Long Term - continuing after 1 month)	
Anxiety	
Depression	
Flashbacks	
Panic Attacks	
Paranoia	
Other (please specify)	

15. From the following list, please indicate what type of other drugs you use **at the same time** as ecstasy and the frequency of use.

(Please tick all relevant boxes)

Drug	Always	Frequently	Occasionally	Never
Alcohol				
Amphetamine				
Cannabis				
Cocaine				
Crack				
DMT				
GHB				
Herbal E				
Heroin				
Ketamine				
LSD (Acid\Blotters)				
LCB				
Mushrooms				
Poppers				
Prozac				
Salvia Divindrum				
Tranquillisers				
Tobacco				
Viagra				
Other				

16. From the following list, please indicate what type of other drugs you **have used in the last three months** use and the frequency of use.

(Please tick all relevant boxes)

Drug	Always	Frequently	Occasionally	Never
Alcohol				
Amphetamine				
Cannabis				
Cocaine				
Crack				
DMT				
GHB				
Herbal E				
Heroin				
Ketamine				
LSD (Acid\Blotters)				
LCB				
Mushrooms				
Poppers				
Prozac				
Salvia Divindrum				
Tranquillisers				
Tobacco				
Viagra				
Other				

17. From the following list, please indicate which types of drugs you have used in the past. Please indicate when you **first began using** and when you **last used** the drug.

Drug	**When did you first use?**	**When did you last use? (Please circle one only)**				
	mm/yr.	**Hours Previous**	**Days Previous**	**Weeks Previous**	**Months Previous**	**Years Previous**
Ecstasy (MDMA)			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Alcohol			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Amphetamine			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Cannabis			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Cocaine			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Crack			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
DMT			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
GHB			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Herbal E			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Heroin			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Ketamine			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
LSD (Acid\Blotters)			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
LCB			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Mushrooms			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Poppers			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Prozac			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Salvia Divindrum			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Tranquillisers			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Tobacco			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Viagra			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10
Other			0 1 2 3 4 5 6	1 2 3	1 2 3 4 5 6 7 8 9 10 11	1 2 3 4 5 6 7 8 9 10

If less than a day, indicate hours previous

18. Please list any controlled substances, prescription medications, and alcohol you have consumed **in the last 10 days?** Please list ALL occasions during the last 10 days.

Substance	**Form, e.g., skunk, rocky, tablets, powder**	**Days/ hours previous**	**Amount taken**			
			Grams	**Cost**	**Units** *e.g. bags/wraps*	**Dose** *e.g. joints, line*

19. How would you describe you current pattern of **ecstasy** use?

_____ times per week OR

_____ times per month OR

_____ times per year OR

_____ previous user (more than 6 months since last used)

Please estimate your pattern of use from the first year of taking the drug to present use

- Fill in the year you began taking ecstasy
- Select an average month of use within that year
- Estimate the total number of ecstasy tablets you would normally have taken during one session
- Indicate frequency of use, e.g., number of times per week/month/year

Continue to fill in each consecutive year regardless of whether you used ecstasy or not. If you have not used for a particular year, continue to enter the year and specify a month, and then enter zero in the space provided for the total number of tablets taken.

Year	**Month**	**Total number of tablets taken in one session**	**Frequency of use**	**Route of Administration**
e.g. Year 1 1993	June	1	One a Week	e.g. swallow, sniff, inject
This year	Last 30 days		How many times?	

20. How would you describe you current pattern of **Amphetamine** use?

_____ times per week OR

_____ times per month OR

_____ times per year OR

_____ previous user (more than 6 months since last used)

In what form do you take amphetamine?
Powder (amphetamine sulphate) _____

Tablets (please indicate type) _____

Other _____

Please estimate your pattern of use from the first year of taking the drug to present use

- Fill in the year you began taking amphetamine
- Select an average month of use within that year
- Estimate the total number of amount of powder you would normally have taken during one session
- Indicate frequency of use, e.g., number of times per week/month/year

Year	**Month**	**Total amount taken in one session**	**Frequency of use**	**Route of administration**
e.g. Year 1 1993	June	e.g. 1	One a Week	e.g. swallow, sniff, inject
This year	Last 30 days		How many times?	

21. How would you describe you current pattern of **Cannabis** use?

_____ times per week OR

_____ times per month OR

_____ times per year OR

_____ previous user (more than 6 months since last used)

In what form do you take Cannabis?

Joints _____

Other _____

Please estimate your pattern of use from the first year of taking the drug to present use

- Fill in the year you began taking Cannabis
- Select an average month of use within that year
- Estimate the total number of joints you would normally have taken during one session
- Indicate frequency of use, e.g., number of times per week/month/year

Year	**Month**	**Total number of joints in one session**	**Frequency of use**	**Route of administration**
e.g. Year 1 1993	June	e.g. 1	One a Week	e.g. Smoke, Swallow,
This year	Last 30 days		How many times?	

22a. **Other drug regularly used:** Please estimate your pattern of use from the first year of taking the drug to present use.

_____ times per week OR

_____ times per month OR

_____ times per year OR

_____ previous user (more than 6 months since last used)

Which Drug? _____

In what form? _____

Please estimate your pattern of use from the first year of taking the drug to present use

- Fill in the year you began taking the drug
- Select an average month of use within that year
- Estimate the total amount you would normally have taken during one session
- Indicate frequency of use, e.g., number of times per week/month/year

Year	**Month**	**Total amount in one session**	**Frequency of use**	**Route of administration**
e.g. Year 1 1993	June	e.g. 1	One a Week	e.g. Smoke, Swallow, Inject, Snort
This year	Last 30 days		How many times?	

22b. **Other drug regularly used:** Please estimate your pattern of use from the first year of taking the drug to present use.

_____ times per week OR

_____ times per month OR

_____ times per year OR

_____ previous user (more than 6 months since last used)

Which Drug? _____

In what form? _____

Please estimate your pattern of use from the first year of taking the drug to present use

- Fill in the year you began taking the drug
- Select an average month of use within that year
- Estimate the total amount you would normally have taken during one session
- Indicate frequency of use, e.g., number of times per week/month/year

Year	**Month**	**Total amount in one session**	**Frequency of use**	**Route of administration**
e.g. Year 1 1993	June	e.g. 1	One a Week	e.g. Smoke, Swallow, Inject, Snort
This year	Last 30 days		How many times?	

23. How many years of full time education have you completed from primary school to date?

_____Years

24. From the following list, please indicate if you have obtained any of the following educational qualifications?

Qualification	**Y\N**	**Details**
CSE		
GCE		
GCSE		
A LEVEL		
NVQ		
GOV. EMPLOYMENT TRAINING SCHEME		
CRAFT\TRADE (EG CITY & GUILD)		
HND		
DEGREE		
OTHER		
NONE		

25. Do you have any convictions for drugs Yes--- No---
*If **yes**, would you please give details below?*
E.g. year of conviction, type of drug, type of offence

26. Do you have any other convictions Yes--- No---
*If **yes**, would you please give detail below?*
E.g. year of conviction, type of offence

27. What are your current living circumstances?
(Please tick relevant box)

Live Alone	
Parental Home	
Live with partner	
Marriage Partner	
Single Parent Family	
Live with Friends	
No Fixed Abode	
Other	

28. On Average approximately how much alcohol do you normally consume?
(E.g. 1 unit = 1 glass of wine; 1 measure of spirit pint of beer)

Daily	
Weekly	
Fortnightly	
Monthly	
Other	

29. Have you ever experienced or been hospitalised for any of the following conditions?

- Neurological *Yes/No
- Heart *Yes/No
- Respiratory *Yes/No

If **yes, can you please explain what they were.*

30. Have you ever been diagnosed as suffering from any of the following conditions?

- Diabetes *Yes/No
- Anxiety *Yes/No
- Depression *Yes/No
- Flashbacks *Yes/No
- Panic Attacks *Yes/No
- Paranoia *Yes/No
- Phobias *Yes/No
- Schizophrenia *Yes/No

If **yes, did you receive treatment? - Please give details*

31. Are you currently taking any prescription drugs *Yes/No

*If yes, please give the name of the drug _____

32. Do you consider yourself to be in good health?
(Please tick relevant box)

Very Good	
Good	
Average	
Poor	
Very Poor	

33. What is your current employment status?
(Please tick relevant box)

Employed full-time	
Employed part-time	
Unemployed	
Self-employed	
Student	
Other. e.g. Sick, Disabled, Homemaker	

APPENDIX 3: BACKGROUND INFORMATION QUESTIONNAIRES

Participant Number:

HEALTH/EDUCATION QUESTIONNAIRE. Your answers to the questions below will provide us with brief details of your health status and educational background. The tests you will carry out today will just be used to measure individual differences in performance and will not be used for the purpose of diagnosing any medical condition.

1. What is your age in years?

2. How would you rate your overall health on a scale from 1 = *poor* to 5 = *excellent* with 3 = *average* ?

3. How many prescription medications do you take each week?

4. How many times in the past 5 years have you been hospitalised or received other treatment for cardiovascular or neurological problems (e.g., heart attacks, stroke, or high blood pressure)?

5. Please indicate the number of years that you have been in FULL TIME education from your first infant school to the present date.

Participant:

1. We hear about people who 'feel better in the morning' or who 'feel better in the evening'. Which of these two types do you think you are?

   A. definitely a 'morning' type
   B. more 'morning' than 'evening'
   C. neither one nor the other
   D. more 'evening' than 'morning'
   E. definitely an 'evening' type

2. How well do you normally sleep at night?

   A. very well
   B. satisfactorily
   C. not very well
   D. very badly

3. How long do you usually sleep on a typical night?

   Approx. ..... hours

   From ..... til .....

4. How refreshed do you usually feel in the mornings?

   A. very alert
   B. fairly alert
   C. fairly tired
   D. very tired

5. Do you sometimes miss a night's sleep, or have much less sleep than normal?

   Yes
   No

   If 'Yes', what is the reason for this?.....

6. Do you have any medical or other reason which regularly prevents you from getting a good night's sleep?

   Yes
   No

   If 'Yes', please give details .....

7. Do you smoke?

Yes
No

If 'Yes', how many cigarettes per day? .....

8. How often do you usually drink alcohol?

A. every day
B. 4-5 days a week
C. 2-3 days a week
D. once a week
E. less than once a week

9. How many units of alcohol do you normally drink in a week?
(1 unit =1 glass wine; 1 measure spirits; 1/2 pint beer)

Approx. ..... units/week

10. Do you drink coffee?

Yes
No

If 'Yes', how many cups in a day? .....

11a How many hours sleep have you had in the last 24 hours? .....

11a How many hours sleep have you had in the last 72 hours (3 days)? .....

12 Are you currently taking any medication?

Yes
No

If 'yes', please give details. .....

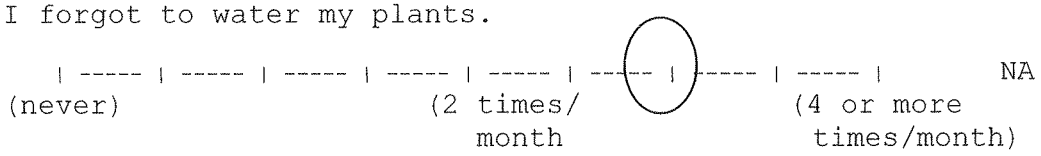
APPENDIX 4: PROSPECTIVE MEMORY QUESTIONNAIRE

Participant Number:

PROSPECTIVE MEMORY QUESTIONNAIRE

The following questionnaire has been developed to test how well you remember to do things. Please answer each question to the best of your knowledge. For each item select the place on the line which best indicates your behaviour during the past week or month or year. For each item circle the slash you select as demonstrated in the example below:

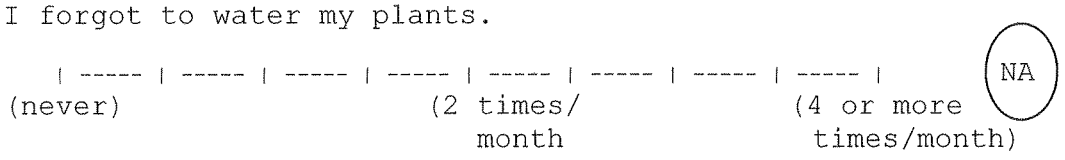
I forgot to water my plants.



The person responding to the above question forgot to water his/her plants approximately 3 times during the past month.

If the item does not apply to you during the time specified, circle NA next to the item (for not applicable). For example, if you have no plants, you would respond as demonstrated below:

I forgot to water my plants.



Again, be sure to respond to each item. Thank you very much for your cooperation!

1. I missed appointments I had scheduled.

|------|------|------|------|------|------|------|------| NA

(never) (3 times/ month) (6 or more times/month)

2. I forgot to follow a change in my usual routine.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

3. I forgot to send a card for a birthday or anniversary.

|------|------|------|------|------|------|------|------| NA

(never) (3 times/ year) (6 or more times/year)

4. I forgot to make an important phone call.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

5. I told someone something that I did not mean to tell.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

6. I forgot to return something I borrowed.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

7. I forgot to pick up items I needed when shopping.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

8. I forgot to meet a friend on time.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

9. I forgot to pass on a message to someone.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

10. I forgot to run an errand I meant to do.

|------|------|------|------|------|------|------|------| NA

(never) (3 times/ week) (6 or more times/week)

11. I forgot to return a phone call.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

12. I forgot to make an appointment I needed to make (e.g., doctor or dentist).

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

13. I forgot to write an important letter.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

14. I forgot to return books to the library by the due date.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

15. I forgot to tip when I finished dinner at a restaurant.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

16. I forgot to turn my alarm clock off when I got up in the morning.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

17. I forgot to lock the door when leaving my apartment or house.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

18. I forgot to take my keys out of my car before locking the doors.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

19. I forgot to button or zip some part of my clothing as I was dressing.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

20. I forgot to pay the bill when finishing a meal at a restaurant.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

21. I forgot to put a stamp on a letter before mailing it.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

22. I forgot to comb my hair in the morning.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

23. I forgot to put on deodorant after showering or bathing.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

24. I forgot to flush the toilet.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

25. I forgot to get the groceries out of the car when I got home from the grocery store.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

26. I forgot to lock up my house, bike, or car.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

27. I forgot to shower or bathe.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

28. I forgot to cash or deposit my paycheck before my account ran out of money.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

29. I forgot what I wanted to say in the middle of a sentence.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

30. I forgot to say something important I had in mind at the beginning of a conversation.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

31. I forgot what I came into a room to get.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

32. I started to do something, and then forgot what it was I wanted to do.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

33. I forgot to bring something I meant to take with me when leaving the house.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

34. I got part way through a chore and forgot to finish it.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

35. I was driving and temporarily forgot where I was going.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

36. I dialed someone on the phone and forgot who I had called by the time they answered.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

37. I started writing a note or letter and forgot what I wanted to say.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

38. I started to write a check and forgot to whom it was to be paid.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ month) (4 or more times/month)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

40. I write myself reminder notes.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

47. I make Post-It (sticky notes) reminders and place them in obvious places.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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.

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

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

|------|------|------|------|------|------|------|------| NA

(never) (2 times/ week) (4 or more times/week)

APPENDIX 5: PROSPECTIVE RETROSPECTIVE MEMORY QUESTIONNAIRE

Crawford et al PM Questionnaire

Please read carefully each statement listed below decide how much each item describes you recently. Indicate your response for each item by circling the number that corresponds to your choice. Please circle **one** answer for each statement.

	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?	1	2	3	4	5
2. Do you fail to recognize a place you have visited before?	1	2	3	4	5
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?	1	2	3	4	5
4. Do you forget something that you were told a few minutes before?	1	2	3	4	5
5. Do you forget appointments if you are not prompted by someone else or by a reminder such as a calendar or diary?	1	2	3	4	5
6. Do you fail to recognize a character in a radio or television show from scene to scene?	1	2	3	4	5
7. Do you forget to buy something you planned to buy, like a birthday card, even when you see the shop?	1	2	3	4	5
8. Do you fail to recall things that have happened to you in the last few days?	1	2	3	4	5
9. Do you repeat the same story to the same person on different occasions?	1	2	3	4	5
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?	1	2	3	4	5
11. Do you mislay something that you have just put down, like a magazine or glasses?	1	2	3	4	5
12. Do you fail to mention or give something to a visitor that you were asked to pass on?	1	2	3	4	5
13. Do you look at something without realising that you have seen it moments before?	1	2	3	4	5
14. If you tried to contact a friend or relative who was out, would you forget to try again later?	1	2	3	4	5
15. Do you forget what you watched on television the previous day?	1	2	3	4	5
16. Do you forget to tell someone something you had meant to mention a few minutes ago?	1	2	3	4	5

APPENDIX 6: EVERYDAY MEMORY QUESTIONNAIRE

EVERYDAY MEMORY QUESTIONNAIRE

Sunderland, Harris & Baddeley (1983)

Rate the frequency with which you make each memory lapse using the scale 1-9.

1. Not at all in the last six months
2. About once in the last six months
3. More than once in the last sixmonths but less than once a month
4. About once a month
5. More than once and month but less than once a week
6. About once a week
7. More than once a week but less than once a day
8. About once a day
9. More than once a day

1. Forgetting where you put something. Losing things around the house. ☐
2. Failing to recognise places that you are told you have often been to before. ☐
3. Finding a television story difficult to follow. ☐
4. Not remembering a change in your daily routine, such as a change in the place where something is kept, or a change in the time something happens. Following your old routine by mistake ☐
5. Having to go back to check whether you have done something you meant to do. ☐
6. Forgetting when something happened; for example, forgetting whether something happened yesterday or last week. ☐
7. Completely forgetting to take things with you, or leaving things behind and having to go back for them. ☐
8. Forgetting that you were told something yesterday or a few days ago, and maybe having to be reminded about it. ☐
9. Starting to read something (a book or an article in a newspaper, or magazine) without realising you have already read it before. ☐
10. Letting yourself ramble on to speak about unimportant or irrelevant things. ☐
11. Failing to recognise, by sight, close relatives or friends that you meet frequently. ☐
12. Having difficulty picking up a new skill. For example, having difficulty in learning a new game or in working some new gadget after you have practiced once or twice. ☐
13. Finding that a word is 'on the tip of your tongue'. You know what it is but cannot quite find it. ☐
14. Completely forgetting to do things you said you would do, and things you planned to do. ☐
15. Forgetting important details of what you did or what happened to you the day before. ☐
16. When talking to someone, forgetting what you have just said. Maybe saying, "What was I just talking about?" ☐
17. When reading a newspaper or magazine being unable to follow the thread of a story; losing track of what it is about. ☐

18. Forgetting to tell somebody something important . Perhaps forgetting to pass on a message or remind someone of something. ☐
19. Forgetting important details about yourself, e.g. your birthday or where you live ☐
20. Getting details of what someone had told you mixed up and confused. ☐
21. Telling someone a story or joke that you have told them once already. ☐
22. Forgetting details of things you do regularly, whether at home or at work. For example, forgetting details of what to do, or forgetting at what time to do it. ☐
23. Finding that the faces of famous people, seen on television or in photographs, look unfamiliar. ☐
24. Forgetting where things are normally kept or looking for them in the wrong place. ☐
25. (a) Getting lost or turning in the wrong direction on a journey, a walk or in a building where you have OFTEN been before. ☐
    (b) Getting lost or turning in the wrong direction on a journey, a walk or in a building where you have ONLY BEEN ONCE OR TWICE BEFORE. ☐
26. Doing some routine thing twice by mistake. For example, putting two lots of tea in the teapot, or going to brush/comb your hair when you have just done so. ☐
27. Repeating to someone what you have just told them or asking them the same question twice. ☐

TOTAL ☐

APPENDIX 7: COGNITIVE FAILURES QUESTIONNAIRE

Cognitive Failure Questionnaire.

Participant Number:

The following questions are about minor mistakes which everyone makes from time to time, but some of which happen more than others. We want to know how often these things have happened to you over the last six months. Please circle the appropriate number.

	Very Often	Quite Often	Occasionally	Very rarely	Never
1. Do you read something and find you haven't been thinking about it and must read it again?	4	3	2	1	0
2. Do you find you forget why you went from one part of the house to the other?	4	3	2	1	0
3. Do you fail to notice signposts on the road?	4	3	2	1	0
4. Do you find that you confuse right and left when giving directions?	4	3	2	1	0
5. Do you bump into people?	4	3	2	1	0
6. Do you find that you forget whether you've turned off a light or fire or locked the door?	4	3	2	1	0
7. Do you fail to listen to people's names when you are meeting them?	4	3	2	1	0
8. Do you find that you say something and realise that it might be taken as insulting?	4	3	2	1	0
9. Do you fail to hear people speaking to you when you are doing something else?	4	3	2	1	0
10. Do you lose your temper and regret it?	4	3	2	1	0
11. Do you leave important letters unanswered for days?	4	3	2	1	0
12. Do you find you forget which way to turn on a road you know well but rarely use?	4	3	2	1	0
13. Do you fail to see what you want in a supermarket (although it's there)?	4	3	2	1	0
14. Do you find yourself suddenly wondering whether you've used a word correctly?	4	3	2	1	0
15. Do you have trouble making up your mind?	4	3	2	1	0
16. Do you find you forget appointments?	4	3	2	1	0
17. Do you forget where you put something like a newspaper?	4	3	2	1	0

Please turn over to complete the questionnaire.

	Very Often	Quite Often	Occasio nally	Very rarely	Never
18. Do you find you accidentally throw away the thing you want and keep what you meant to throw away- as in the example of throwing away the matchbox and putting the used match in your pocket?	4	3	2	1	0
19. Do you daydream when you ought to be listening to something?	4	3	2	1	0
20. Do you forget people's names?	4	3	2	1	0
21. Do you start doing one thing at home and get distracted into doing something else?	4	3	2	1	0
22. Do you find you can't quite remember something although it's "on the tip of your tongue"?	4	3	2	1	0
23. Do you find you forget what you came to the shops to buy?	4	3	2	1	0
24. Do you drop things?	4	3	2	1	0
25. Do you find you can't think of anything to say?	4	3	2	1	0

Thank you very much for your time in participating in this study.

APPENDIX 8: RBMT SCORE SHEET

TVTC
Thames Valley Test Company

RBMT-II

The Rivermead Behavioural Memory Test II

Procedural guide and scoring sheet

- This scoring sheet provides a summary procedure to ensure that the test is consistently carried-out in the correct order.
- Please follow the instructions in the Manual for detailed procedural and scoring guidance.

Subject and test details

Name				
Date of birth				
Date of test				
Assessment	1 ☐	2 ☐	3 ☐	4 ☐
Version	A (Red) ☐	B (Blue) ☐	C (Green) ☐	D (Yellow) ☐

• 1 and 2 First and Second Name

Action

Present the portrait for 'Remembering a name'.

A Catherine Taylor
B Henry Fisher
C Pauline Roberts
D Philip Goodwin

• 3 Belonging

Action

Hide a belonging for 'Remembering a hidden belonging'.

A Desk drawer
B Cupboard
C Filing cabinet
D Brief case or bag

• 4 Appointment

Action

Set the timer for 'Remembering an appointment'.

A 'When do I have to see you again?'
B 'When does this session end?'
C 'When will I know the results of the test?'
D 'What time do we finish today?'

• 5 Pictures

Action

Present the ten presentation cards for 'Picture recognition'.

• 6a Story (immediate)

Action

Read the prose passage from the test materials or Story Sheet. Then ask the subject to recall the prose passage.

Response

Adopt your own technique (e.g. underlining and encircling) for recording each of the 21 'ideas' correctly recalled or partially recalled against the appropriate passage on the Story Sheet.

Scoring

Scoring is based on points awarded for the number of 'ideas' correctly recalled. You should therefore count and calculate *after* the test has been completed.

☐ *Raw Score*
Each 'idea' recalled word-perfect or using a close synonym = 1
Each 'idea' partially recalled, or recalled with approximate synonym = ½
(Maximum = 21)

☐ *Standardized Profile Score*

Raw Score	≤3.5	4–5.5	≥6
Standardized Profile Score	0	1	2

Screening Score
Score later

• 5 Pictures

Action

Present the 20 recognition cards for 'Picture recognition'.

Response

Tick/check each picture identified correctly ('yes' responses). Record false positives separately.

1	2	3	4	5	6	7	8	9	10

Total ☐

Record the number of false positives ☐

Scoring

☐ *Raw Score*
Subtract the number of false positives from the total number of pictures correctly identified
(Maximum = 10)

☐ *Standardized Profile Score*

Raw Score	≤8	9	10
Standardized Profile Score	0	1	2

○ *Screening Score*
All ten pictures identified correctly with no false positives = 1
(Otherwise = 0)

Harcourt Assessment
32 Jamestown Road
London NW1 7BY

• 7 Faces

Action

Present the five presentation cards for 'Face recognition'.

• 8a Route (immediate)

Action

Demonstrate the route for 'Remembering a short route' (immediate). (Leave the 'Message' envelope for 'Remembering to deliver a message' at the location marked by an asterisk below.) Then ask the subject to reproduce the route. Record the subject's responses below. (The subject's response to 'Remembering to deliver a message' should be recorded in the next section.)

Response

A	B	C	D	Subject's Route
Chair	Door	Window	Table	
Door	Window*	Table	Chair	
Window	Table	Chair*	Door*	
Table*	Chair	Door	Window	
Chair	Door	Window	Table	

* message left here

Scoring

(Please refer to the relevant section in pages 6 and 7 of the Manual for details on scoring)

☐ *Raw Score*
(Maximum = 11)

☐ *Standardized Profile Score*

Raw Score	≤8	8–9	11
Standardized Profile Score	0	1	2

○ *Screening Score*
All stages of the route recalled in the correct order (i.e. raw score of 11) = 1
(Otherwise = 0)

• 9a Message (immediate)

Action

When demonstrating the route, leave the 'Message' envelope for 'Remembering to deliver a message' (immediate) at the location marked by an asterisk above.

Response

Tick/check as appropriate:

'Message' envelope picked-up spontaneously ☐

picked-up after prompt ☐

left at correct location ☐

Scoring

☐ *Raw Score*
'Message' picked-up spontaneously = 2
picked-up after prompt = 1
left at correct location = another 1
(Maximum = 3)

Standardized Profile Score
Score later

Screening Score
Score later

• 7 Faces

Action

Present the ten recognition cards for 'Face recognition'.

Response

Tick/check each face identified correctly ('yes' responses).

Record false positives separately.

1	2	3	4	5

Total ☐

Record the number of false positives ☐

Scoring

☐ *Raw Score*
Subtract the number of false positives from the total number of faces correctly identified
(Maximum = 5)

☐ *Standardized Profile Score*

Raw Score	≤3	4	5
Standardized Profile Score	0	1	2

○ *Screening Score*
All five faces identified correctly with no false positives = 1
(Otherwise = 0)

• 10 and 11 Orientation and Date

Action

Ask the ten questions for 'Orientation' and 'Date' in the order given below:

Response

Record the subject's responses in the spaces provided:

1 Year	2 Month	3 Day of week
4 Date	5 Place	6 City or town
7 Age	8 Year born	9 Prime Minister

10 President

Scoring

☐ *Raw Score*
Score one point for each correct response.
- Total number of correct responses to Orientation questions **i.e. excluding Date**

(Maximum = 9)
- Correct Date

(Maximum = 1)

Standardized Profile Score
- Orientation questions

☐

Raw Score	≤7	8	9
Standardized Profile Score	0	1	2

Raw Score	≤ Two days out	One day out	Correct
Standardized Profile Score	0	1	2

Screening Score
- Orientation questions

All nine Orientation questions answered correctly = 1
(Otherwise = 0)
- Date

Correct Date given = 1
(Otherwise = 0)

• 4 Appointment

Action

Engage the subject in conversation until the timer sounds for 'Remembering an appointment'. Prompt if necessary.

A 'When do I have to see you again?'
B 'When does this session end?'
C 'When will I know the results of the test?'
D 'What time do we finish today?'

Response

Tick/check as appropriate:

Subject asked appropriate question spontaneously
after prompt
Subject remembered that something had to be asked but could not remember what it was

Scoring

Raw Score
Subject asked appropriate question spontaneously = 2
after prompt = 1
Subject remembered that something had to be asked but could not remember what it was = 1
(Maximum = 2)

Standardized Profile Score

Raw Score	0	1	2
Standardized Profile Score	0	1	2

Screening Score
Appropriate question asked without prompt when timer sounded = 1
(Otherwise = 0)

• 6b Story (delayed)

Action

Ask the subject to recall the prose passage for 'Delayed prose recall'. Give opening prompt if necessary.

Response

Record each of the 'ideas' correctly recalled or partially recalled against the appropriate passage on the Story Sheet.

Scoring

Score exactly as for 'Immediate prose recall' *but deduct one point if the subject needed an opening prompt.*

Each 'idea' recalled word-perfect or using a close synonym = 1
Each 'idea' partially recalled, or recalled with approximate synonym = ½
(Maximum = 21)

Standardized Profile Score

Raw Score	≤1.5	2–3.5	≥4
Standardized Profile Score	0	1	2

Screening Score
If the subject recalled at least six 'ideas' on 'Story (immediate)' and at least four 'ideas' on 'Story (delayed)' = 1
(Otherwise = 0)

• 8b Route (delayed)

Action

Ask the subject to reproduce the route for 'Remembering a short route' (delayed). Record each of the stages reproduced correctly below. (The subject's response to 'Remembering to deliver a message' (delayed) should be recorded in the next section.)

Response

A	B	C	D	Subject's Route
Chair	Door	Window	Table	
Door	Window*	Table	Chair	
Window	Table	Chair*	Door*	
Table*	Chair	Door	Window	
Chair	Door	Window	Table	

* message left here

Scoring

(Please refer to the relevant section on pages 6 and 7 of the Manual for details on scoring)

Raw Score
(Maximum = 11)

Standardized Profile Score

Raw Score	≤8	8–9	11
Standardized Profile Score	0	1	2

Screening Score
All stages of the route recalled in the correct order (i.e. raw score of 11) = 1
(Otherwise = 0)

• 9b Message (delayed)

Action

Remind the subject, if necessary, about the 'Message' envelope for 'Remembering to deliver a message' (delayed). The location is marked by an asterisk above.

Response

Tick/check as appropriate:

'Message' envelope picked-up spontaneously
picked-up after prompt
left at correct location

Scoring

Raw Score
'Message' picked-up spontaneously = 2
picked-up after prompt = 1
left at correct location = another 1
(Maximum = 3)

Standardized Profile Score

The Standardized Profile Score for 'Remembering to deliver a message' is based on the sum of the Raw Scores obtained for the **immediate and delayed** recalls (therefore maximum Raw Score = 6).

Sum of Raw Scores	≤4	5	6
Standardized Profile Score	0	1	2

Screening Score

If the subject spontaneously picked-up the 'Message' envelope and left it at the correct location in the **immediate and delayed** recalls = 1
(Otherwise = 0)

• 1 and 2 First and Second Name

Action

Re-present the portrait for 'Remembering a name'.
Give first letter prompt if necessary.

A Catherine Taylor
B Henry Fisher
C Pauline Roberts
D Philip Goodwin

Response

Tick/check as appropriate

First Name recalled without prompt
recalled with prompt
Second Name recalled without prompt
recalled with prompt

Scoring

Raw Score

- First Name recalled without prompt = 2
  recalled with prompt = 1
  (Maximum = 2)
- Second Name recalled without prompt = 2
  recalled with prompt = 1
  (Maximum = 2)

Standardized Profile Score

The Standardized Profile Score for 'Remembering a name' is based on the sum of the Raw Scores obtained for the recall of the **First and Second Names** (therefore maximum Raw Score = 4).

Raw Score	≤2	3	4
Standardized Profile Score	0	1	2

Screening Score

- If the subject recalled the First Name without prompt = 1
  (Otherwise = 0)
- If the subject recalled the Second Name without prompt = 1
  (Otherwise = 0)

• 3 Belonging

Action

Inform the subject that 'We have finished this test'.
Wait for recall of 'Remembering a hidden belonging'.
Prompt if necessary.

A Desk drawer
B Cupboard
C Filing cabinet
D Brief case or bag

Response

Tick/check as appropriate:

Place recalled without prompt
recalled with prompt
Item recalled without prompt
recalled with prompt

Scoring

Raw Score

Place recalled without prompt = 2
recalled with prompt = 1
Item recalled without prompt = 2
recalled with prompt = 1
(Maximum = 4)

Standardized Profile Score

Raw Score	≤2	3	4
Standardized Profile Score	0	1	2

Screening Score

If the subject spontaneously recalled the item and the place where it was hidden = 1
(Otherwise = 0)

Score summary

	Standardized Profile Score (2,1 or 0)	Screening Score (1 or 0)
1 First Name		
2 Second Name		
3 Belonging		
4 Appointment		
5 Pictures		
6a Story immediate		
6b delayed		
7 Faces		
8a Route immediate		
8b delayed		
9 Message (immediate & delayed)		
10 Orientation (not including date)		
11 Date		
Total		
	maximum = 24	maximum = 12

APPENDIX 9: REY'S AUDITORY VERBAL LEARNING TASK QUESTIONNAIRE

Participant Number:

RAVLT

	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Serial Position	**Interference**		Trial 6	Trial 7 (20 minute delay
Plum							**Hawk**			
Door							**Oil**			
Sage							**Salt**			
Ball							**Mile**			
Corn							**Wool**			
Lily							**Plate**			
Flute							**Saw**			
Spoon							**Eye**			
Rain							**Rope**			
Rock							**Oak**			
Silk							**Pear**			
Foot							**Sock**			
Frog							**Gold**			
Horse							**Jazz**			
Trout							**Inch**			
Intrusions										
TOTAL CORRECT										

Participant Number:

	Yes	No
Ant	_ _ _	____
Frog	____	_ _ _
Nail	_ _ _	____
Plum	____	_ _ _
Wine	_ _ _	____
Bed	_ _ _	____
Trout	____	_ _ _
Bus	_ _ _	____
Sage	____	_ _ _
Herb	_ _ _	____
Spoon	____	_ _ _
China	_ _ _	____
Ball	____	_ _ _
Horse	____	_ _ _
Book	_ _ _	____
Flute	____	_ _ _
Corn	____	_ _ _
Rain	____	_ _ _
Opal	_ _ _	____
Milk	_ _ _	____
Fork	_ _ _	____
Lily	____	_ _ _
Rock	____	_ _ _
Door	____	_ _ _
Shoe	_ _ _	____
Silk	____	_ _ _
Aunt	_ _ _	____
Chair	_ _ _	____
Foot	____	_ _ _
Rake	_ _ _	____

	Hit (solid line, column 1)	Correct Rejection (solid line, column 2)	Miss (dashed line, column 2)	False Alarm (dashed line, column 1)
Total Score				

APPENDIX 10: MEMORY COMPENSATION QUESTIONNAIRE

Memory Compensation Questionnaire (MCQ)

Roger A. Dixon and Lars Bäckman

Dixon, R.A., Garrett, D.D., & Bäckman, L. (in press). Principles of compensation in cognitive neuroscience and neurorehabilitation. In D.T. Stuss, G. Winocur, & I.H. Robertson (Eds.), *Cognitive neurorehabilitation*. Cambridge: Cambridge University Press.

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Contact: rdixon@ualberta.ca, vlslab@ualberta.ca

Date:_____/_____/_____
d m y

Participant #: _____
Scorer's Initials:_____

MEMORY QUESTIONNAIRE

Directions

Different people use their memory in different ways in their everyday lives. For example, some people make shopping lists, whereas others do not. Some people are good at remembering some things, whereas others are not. In this questionnaire, we would like you to tell us about how you use your memory. There are no right or wrong answers to these questions because people are different. Please take your time and answer each of these questions to the best of your ability.

Each question is followed by five choices. Read the choices carefully for each question. Choose one of the choices and draw a circle around the letter corresponding to that choice. Mark only one number for each question.

Some of the questions ask how often you do certain things that may be related to your memory. For example:

Do you make a list of things to be accomplished during the day?

1. Never
2. Seldom
3. Sometimes
4. Often
5. Always

In this example you could choose any one of the answers. Choose the one that comes closest to what you usually do. Don't worry if the time estimate is not exact or if there are some exceptions.

Keep these points in mind

(1) Please answer every question, even if it doesn't seem to apply to you very well.
(2) Answer as honestly as you can what is true for you. Please do not mark something because it seems like the "right thing to say".

1.	Do you use shopping lists when you go shopping?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
2.	Do you ask people to speak slowly when you want to remember what they are saying?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
3.	When you want to remember an important appointment do you ask somebody else (for example, spouse or friend) to remind you?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
1.	Do you put in a lot of effort when you want to remember an important conversation with a person?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
5.	When you want to remember a story do you read it more than once?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
6.	When you are reading a book, do you use a bookmark to indicate where you stopped reading last time?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never

7.	Do you put in effort when you want to memorize a funny story?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
8.	When you want to remember a newspaper article is it important to you to remember it perfectly?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
9.	When an interesting T.V. program is going to be on in the next few days do you ask somebody else to help you remember (for example, spouse or friend)?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
10.	Do you concentrate a lot to learn something you really want to remember?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
11.	When you want to remember a newspaper article do you read it more slowly?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
12.	When you want to remember an event such as a birthday, do you ask somebody else (for example, spouse or friend) to help you remember?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always

13.	Do you post notes on a board or other prominent place to help you remember things for the future (for example, meetings or dates)?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
14.	When you want to remember the name of a particular person, do you ask somebody else (for example, spouse or friend) to help you remember?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
15.	When you are reading something that really interests you (and that you want to remember) do you slow down your reading speed?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
16.	When you want to remember a conversation is it important to you to remember it perfectly?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
17.	Do you sometimes ask someone (for example, spouse or friend) to help you remember when you are going to start a trip?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
18.	Do you put things (for example, glasses or keys) in particular places to remember where they are for future purposes?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never

19.	Do you ask other people (for example, spouse or friend) to help you remember things more or less often today compared to 5 - 10 years ago?	1. Much more often 2. More often 3. No difference 4. Less often 5. Much less often
20.	Do you try hard when you want to remember an important telephone number?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
21.	Do you put things in obvious places (for example, briefcase in front of the door) in order to remember them when you're going out?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
22.	When you want to remember something from a T.V. program do you use "memory tricks" like grouping or repeating to yourself?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
23.	Do you take your time to go through and reconstruct an event you want to remember?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
24.	Do you write down appointments (for example, with the hairdresser or the dentist) in a notebook or calendar?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never

25.	Before an important day do you think about or plan the things you have to do?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
26.	Do you spend a lot of time on " memory tricks" or other aids for memory in your daily life?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
27.	Do you note birthdays in a notebook or calendar in order to remember them?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
28.	Do you repeat telephone numbers to yourself in order to remember them well?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
29.	Do you spend more or less time learning important things today compared to 5 - 10 years ago (for example, reading things more slowly or reading them more than once)?	1. Much more time 2. More time 3. No difference 4. Less time 5. Much less time
30.	Do you write down telephone numbers in a calendar or notebook in order to remember them?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never

31.	When you want to remember the name of a person do you try to associate the name with the person's face?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
32.	Do you concentrate when you want to learn the name of a person you have just met?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
33.	When you want to remember something that happened in a particular day do you review and reconstruct the events of that day in order to help you remember?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
34.	Do you use such aids for memory as notebooks or putting things in certain places more or less often today compared to 5 - 10 years ago?	1. Much less often 2. Less often 3. No difference 4. More often 5. Much more often
35.	When you want to remember an event that took place when you were a child, is it important for you to remember it as perfectly as possible?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
36.	Do you use letters as cues (in other words, go through the alphabet) when you want to remember the name of a person, a city, or something else?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always

37.	Do you put in effort when you want to remember the time of an important meeting?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
38.	When you want to remember something do you try to relate it to something else you know well in order to remember it better?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
39.	If you want to remember a funny story is it important to you to remember it perfectly?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
40.	Do you use mental images or pictures to remember some types of information?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always
41.	Do you put in effort and concentrate to remember important things more or less often today compared to 5 - 10 years ago?	1. Much more often 2. More often 3. No difference 4. Less often 5. Much less often
42.	Is it important for you to remember things perfectly (as verbatim as possible)?	1. Never 2. Seldom 3. Sometimes 4. Often 5. Always

43.	Do you repeat important appointments to yourself in order to remember them as well as possible?	1. Always 2. Often 3. Sometimes 4. Seldom 5. Never
44.	Is it more or less important to you to remember things perfectly today compared to 5 – 10 years ago?	1. Much more important 2. More important 3. No difference 4. Less important 5. Much less important
45.	Do you use memory tricks such as repeating things to yourself or grouping things in categories more or less often today compared to 5 - 10 years ago?	1. Much less often 2. Less often 3. No difference 4. More often 5. Much more often

Coding For the Compensations Questionnaire

Notes:

- All of the questions for this questionnaire are coded in the same manner, regardless of the response choices for each question.
- The is no scoring required for this questionnaire
- Composite variables are created at a later date when they are required for analysis (the details are given later in this manual)
- If the participant does NOT answer one of the questions, a value of "99" is entered for that variable
- The value of "98" is not applicable for this task, since the participants should answer all of the questions
- If a participant circles 2 responses, then enter "99" into the computer for that question.
- If a participant circles 2 responses and then scribbles one of them out, then enter the response that has not been scribbles out for that question
- If the participant has included handwritten comments beside a question, it may be possible to use the comments to determine an answer that was previously ambiguous (e.g. if the participant has circled 2 answers, but has made a comment that directs his or her answer towards a certain response). In this case, it is important to check with the lab co-ordinator(s) if you are unclear as to how to proceed
- The coding method is as follows:

1= 1 2= 2 3= 3 4= 4 5= 5	So, if a participant were to select response '4,' (either "often" or "seldom") then his or her response would be entered as '4' in the data

- **Note:** This coding method has changed from previous waves, where a response of '1' was coded as '0,' a response of '2' as '1,' etc.

- A listing of the variable names for each question is given below

id particpant's id

c1 Do you use shopping lists when you go shopping?

c2 Do you ask people to speak slowly when you want to remember what they are saying?

c3 When you want to remember an important appointment do you ask somebody else (for example, spouse or friend) to remind you?

c4 Do you put in a lot of effort when you want to remember an important conversation with a person?

c5 When you want to remember a story do you read it more than once?

c6 When you are reading a book, do you use a bookmark to indicate where you stopped reading last time?

c7 Do you put in effort when you want to memorize a funny story?

c8 When you want to remember a newspaper article is it important to you to remember it perfectly?

c9 When an interesting T.V. program is going to be on in the next few days do you ask somebody else to help you remember (for example, spouse or friend)?

c10 Do you concentrate a lot to learn something you really want to remember?

c11 When you want to remember a newspaper article do you read it more slowly?

c12 When you want to remember an event such as a birthday, do you ask somebody else (for example, spouse or friend) to help you remember?

c13 Do you post notes on a board or other prominent place to help you remember things for the future (for example, meetings or dates)?

c14 When you want to remember the name of a particular person, do you ask someone else (for example, spouse or friend) to help you remember?

c15 When you are reading something that really interests you (and that you want to remember) do you slow down your reading speed?

c16 When you want to remember a conversation is it important to you to remember it perfectly?

c17 Do you sometimes ask someone (for example, spouse or friend) to help you remember when you are going to start a trip?

c18 Do you put things (for example, glasses or keys) in particular places to remember where they are for future purposes?

c19 Do you ask other people (for example, spouse or friend) to help you remember things more or less often today compared to ***5***-***10*** yrs ago?

c20 Do you try hard when you want to remember an important telephone number?

c21 Do you put things in obvious places (for example, briefcase in front of the door) in order to remember them when you're going out?

c22 When you want to remember something from a T.V. program do you use "memory tricks" like grouping or repeating to yourself?

C23 Do you take your time to go through and reconstruct an event you want to remember?

c24 Do you write down appointments (for example, with the hairdresser or the dentist) in a notebook or calendar?

c25 Before an important day-do you think about or plan the things you have to do?

c26 Do you spend a lot of time on "memory tricks" or other aids for memory in your daily life?

c27 Do you note birthdays in a notebook or calendar in order to remember them?

c28 Do you repeat telephone numbers to yourself to remember them well?

c29 Do you spend more or less time learning important things today compared to ***5***-***10*** yrs ago (for example, reading things more slowly or reading them more than once)?

c30 Do you write down telephone numbers in a calender or notebook in order to remember them?

c31 When you want to remember the name of a person do you try to associate the name with the person's face?

c32 Do you concentrate when you want to learn the name of a person you have just met?

c33 When you want to remember something that happened in a particular day do you review and reconstruct the events of that day in order to help you remember?

c34 Do you use such aids for memory as notebooks or putting things in certain places more or less often today compared to ***5***-***10*** yrs ago?

c35 When you want to remember an event that took place when you were a child, is it important for you to remember it as perfectly as possible?

c36 Do you use letters as cues (in other words, go through the alphabet) when you want to remember the name of a person, a city, or something else?

c37 Do you put in effort when you want to remember the time of an important meeting?

c38 When you want to remember something do you try to relate it to something else you know well in order to remember it better?

c39 If you want to remember a funny story is it important to you to remember it perfectly?

c40 Do you use mental images or pictures to remember some types of information?

c41 Do you put in effort and concentrate to remember important things more or less often today compared to ***5***-***10*** yrs ago?

c42 Is it important for you to remember things perfectly (as verbatim as possible)?

c43 Do you repeat important appointments to yourself in order to remember them as well as possible?

c44 Is it more or less important to you to remember things perfectly today compared to ***5-10*** yrs. ago?

c45 Do you use memory tricks such as repeating things to yourself or grouping things in categories more or less often today compared to ***5***-***10*** years ago?

Compensation Composite Variables

Notes:

- The following pages contain a listing of the composite variables that are derived from the Compensation questionnaire for data analysis purposes.
- The first part of this section names the raw data variables that need to be reverse-coded prior to the creation of the new composite variables.

The following variables need to be reverse coded:

c5, c6, c7, c9, c14, c15, c16, c18, c19, c20, c22, c24, c26, c28, c29, c30, c33, c37, c38, c39, c41, c43, c44

Therefore, the variables will now be coded as follows:

a choice of ‘1' will receive a code of ‘5,’ a choice of ‘2' will receive a code of ‘4,' etc.

The new variable names are as follows:

c5r, c6r, c7r, c9r, c14r, c15r, c16r, c18r, c19r, c20r, c22r, c24r, c26r, c28r, c29r, c30r, c33r, c37r, c38r, c39r, c41r, c43r, c44r

Special Note:

- The variables will have a suffix attached to them to reflect which wave of testing they are from. **For example,** “mia1rw5' means that this variable was used for the data from the group of participants in sample 1 wave 5.

- the suffixes may be changed to reflect each wave of testing

The Compensation Questionnaire Composite Variables

Composite Variable Name	Variables in the Composite
External (cqext)	c1, c6r, c13, c18r, c21, c24r, c27, c30r
Internal (cqint)	c22r, c23, c25, c28r, c31, c33r, c36, c38r, c40, c43r
Time (cqtime)	c2, c5r, c11, c15r, c26r
Relative (cqrel)	c3, c9r, c12, c14r, c17
Effort (cqeffo)	c4, c7r, c10, c20r, c32, c37r
Success (cqsuc)	c8, c16r, c35, c39r, c42
Change (cqchan)	c19r, c29r, c34, c41r, c44r, c45

COMPENSATION QUESTIONNAIRE: DATA ENTRY INSTRUCTIONS

COMMENTS: The Compensation questionnaire is an indicator of how Participants use their memory.

Instructions for Data entry:

1. NO SCORING required for this task.

2. Enter the response that has been circled by the Participant (ex. 1-5) into the correct column in the SPSS data file.

3. “99" = NO RESPONSE given.

4. “98" = is NOT APPLICABLE for this task because Participant is supposed to answer every question, except in the case where “NO RESPONSE” is given as mentioned above.

5. If a Participant circles 2 responses, then enter “99" into the computer for that question.

6. If a Participant circles 2 responses and then scribbles one of them out, then enter the response that has not been scribbled out for that question.

7. DO NOT compute values (this will be done later by a data analyst).

Special Note: In some cases, the Participant may have handwritten comments beside some of the questions in the questionnaires. In the case where Participants have circled 2 responses or have circled one response and partly another (ex. they circled “a” and then started to circle “c” and stopped half-way), the Participants’ handwritten comments, in some cases, help determine which response the Participant may have intended to circle. When dealing with scoring situations such as this, be sure to ask the Lab Co-ordinators what decision should be made if you are not clear.

APPENDIX 11: CAMPROMPT SCORE SHEET

CAMPROMPT Record Form

Name _____ _____ Hospital number _____

Date of birth _____

Date of test _____

Assessment ☐ First ☐ Second

Version ☐ A ☐ B

Ability Band ☐ Below average (< 90) ☐ Average (90-110) ☐ Above Average (111+)

SUMMARY OF SCORES

		Time	Event
(12)	Book/map		
(13)	Change task/pen		
(14)	Take keys/mug		
(15)	Give message		
(16)	Objects and locations		
(17)	Ring garage/reception		
	Total time-based		
	Total event-based		
	Overall total score		
	Classification		

Score conversion

Score A = 6
Score B = 4
Score C = 2
Score D = 4
Score E = 2
Score F = 1
Score G = 1
Score H = 0

Tester's own record of five small objects and where hidden:

Harcourt Assessment

TVTC Thames Valley Test Company

(The following summary is provided to help the tester keep track of the correct procedure. It is not a substitute for the detailed instructions provided in the manual, pages 11-21, which must be followed at all times.)

Put a mark against each of the items from 1-11 as a sign the correct procedure has been followed. Circle examinee's responses for items 12-17.

1. Read the introductory information from the manual, pages 1-8.

2. Show, name and hide the five objects, as described in the manual, page 12.

3. Demonstrate beeper, set timer and press START, as in manual, page 13.

4. Reminder not to forget keys (mug), as in manual, page 13.

5. Instructions about EastEnders (Coronation Street) quiz question and giving book (map), as in manual, page 13.

6. Tell examinee to begin the puzzles.

7. At **18 minutes** give message card and envelope, as in manual, page 13.

8. At **16 minutes** give instructions about changing task (pen) in seven minutes, as in manual, page 13.

9. Adjust clock hands under table and note time.

10. At **15 minutes** put clock on table and give instructions re time and ringing garage (reception), as in manual, page 14.

11. At **13 minutes** give Quiz Question sheet A or B and instruction, as in manual, page 14.

[1] 12. Watch until examinee has done **quiz question 14**, the one about EastEnders (Coronation Street). Examinee should then give the book/map, as in manual, page 14.

a)	examinee spontaneously carries out some task	
	gives book/map	Score A
	wrong task, prompt, gives book/map	Score B
	wrong task, prompt, still wrong task	Score C
b)	no response	
	prompt, gives book/map	Score D
	prompt, wrong task, prompt, gives book/map	Score E
	prompt, wrong task, prompt, wrong task	Score F
c)	no response	
	prompt, 'no', prompt, gives book/map	Score G
	prompt, 'no', prompt, 'no'/wrong task	Score H

[2] 13. At **nine minutes** examinee should change task (pen), as in manual, page 15.

a) examinee spontaneously carries out some task
changes task/pen — Score A
wrong task, prompt, changes task/pen — Score B
wrong task, prompt, still wrong task — Score C

b) no response
prompt, changes task/pen — Score D
prompt, wrong task, prompt, changes task/pen — Score E
prompt, wrong task, prompt, still wrong task — Score F

c) no response
prompt, 'no', prompt, changes task/pen — Score G
prompt, 'no', prompt, 'no'/wrong task — Score H

[3] 14. At **seven minutes** examinee should remind you to take your keys (mug), as in manual, page 16.

a) examinee spontaneously carries out some task
'take keys/mug' — Score A
wrong task, prompt, 'take keys/mug' — Score B
wrong task, prompt, still wrong task — Score C

b) no response
prompt, 'take keys/mug' — Score D
prompt, wrong task, prompt, 'take keys/mug' — Score E
prompt, wrong task, prompt, still wrong task — Score F

c) no response
prompt, 'no', prompt, 'take keys/mug' — Score G
prompt, 'no', prompt, 'no'/wrong task — Score H

[4] 15. At **five minutes *'There are five minutes left.'*** Examinee should give message, as in manual, page 17.

a) examinee spontaneously carries out some task
gives message — Score A
wrong task, prompt, gives message — Score B
wrong task, prompt, still wrong task — Score C

b) no response
prompt, gives message — Score D
prompt, wrong task, prompt, gives message — Score E
prompt, wrong task, prompt, wrong task — Score F

c) no response
prompt, 'no', prompt, gives message — Score G
prompt, 'no', prompt, 'no'/wrong task — Score H

[5] 16. At **0** alarm goes off, ***'We have finished this test.'*** Examinee should now tell you about the five objects and their locations, as in manual, page 18.

a) examinee spontaneously carries out some task
objects and locations — Score A
wrong task, prompt, objects and locations — Score B
wrong task, prompt, wrong task — Score C

b) no response
prompt, objects and locations — Score D
prompt, wrong task, prompt, objects and locations — Score E
prompt, wrong task, prompt, wrong task — Score F

c) no response
prompt, 'no', prompt, objects and locations — Score G
prompt, 'no', prompt, 'no'/wrong task — Score H

[5b] Examinee should tell you about the five objects and their locations. If not ***'Can you remember what they were and where they were hidden?'***, as in manual, page 20.

Record examinee's responses and whether or not prompts were needed either for object or for location.

_____ _____ _____

_____ _____

_____ _____

_____ _____

_____ _____

[6] 17. At * (the time you specified – ***five minutes after end time***) examinee should remind you to ring the garage/reception, as in manual, page 20.

a) examinee spontaneously carries out some task
ring garage/reception — Score A
wrong task, prompt, ring garage/reception — Score B
wrong task, prompt, wrong task — Score C

b) no response
prompt, ring garage/reception — Score D
prompt, wrong task, prompt, ring garage/reception — Score E
prompt, wrong task, prompt, wrong task — Score F

c) no response
prompt, 'no', prompt, ring garage/reception — Score G
prompt, 'no', prompt, 'no'/wrong task — Score H

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APPENDIX 12: BRIEF-A

Behavior Rating Inventory of Executive Function- Adult Version (BRIEF-A) Questionnaire

Participant Number:
Date:
Gender: Male Female
Age:
Date of Birth:
Years of Education:
Level of education: Less than High School
High School
College
Master's Degree
Doctorate
Other

During the past month, how often has each of the following behaviors been a *problem*?

N=Never S=Sometimes O=Often

1	I have angry outbursts	N	S	O
2	I make careless errors when completing tasks	N	S	O
3	I am disorganized	N	S	O
4	I have trouble concentrating on tasks (such as chores, reading or work)	N	S	O

5	I tap my fingers or bounce my legs	N	S	O
6	I need to be reminded to begin a task even when I am willing	N	S	O
7	I have a messy closet	N	S	O
8	I have trouble changing from one activity or task to another	N	S	O
9	I get overwhelmed by large tasks	N	S	O
10	I forget my name	N	S	O
11	I have trouble with jobs or tasks that have more than one step	N	S	O
12	I overreact emotionally	N	S	O
13	I don't notice when I cause others to feel bad or get mad until its too late	N	S	O
14	I have trouble getting ready for the day	N	S	O
15	I have trouble prioritizing activities	N	S	O
16	I have trouble sitting still	N	S	O
17	I forget what am I doing in the middle of things	N	S	O
18	I don’t check my work for mistakes	N	S	O
19	I have emotional outbursts for little reason	N	S	O
20	I lie around the house a lot	N	S	O
21	I start tasks (such as cooking, projects) without the right materials	N	S	O
22	I have trouble accepting different ways to solve problems with work, friends, or tasks	N	S	O
23	I talk at the wrong time	N	S	O
24	I misjudge how difficult or easy tasks will be	N	S	O
25	I have problems getting started on my own	N	S	O
26	I have trouble staying on the same topic when I am talking	N	S	O
27	I get tired	N	S	O
28	I react more emotionally to situations than my friends	N	S	O
29	I have problems waiting for my turn	N	S	O
30	people say that I am disorganized	N	S	O
31	I lose things (such as keys, money, wallet, homework, etc.)	N	S	O
32	I have trouble thinking of a different way to solve a problem when I am stuck	N	S	O
33	I overreact to small problems	N	S	O
34	I don't plan ahead for future activities	N	S	O
35	I have a short attention span	N	S	O

36	I make inappropriate sexual comments	N	S	O
37	when people seem upset with me, I don't understant why	N	S	O
38	I have trouble counting to three	N	S	O
39	I have unrealistic goals	N	S	O
40	I leave the bathroom a mess	N	S	O
41	I make careless mistakes	N	S	O
42	I get emotionally upset easily	N	S	O
43	I make decisions that get me into trouble (legally, financially, socially)	N	S	O
44	I am bothered with having to deal with changes	N	S	O
45	I have difficulty getting excited about things	N	S	O
46	I forget instructions easily	N	S	O
47	I have good ideas but I cannot get them on paper	N	S	O
48	I make mistakes	N	S	O
49	I have trouble getting started on tasks	N	S	O
50	I say things without thinking	N	S	O
51	my anger is intense but ends quickly	N	S	O
52	I have trouble finishing tasks (such a s chores, work)	N	S	O
53	I start things at the last minute (such as assignments,chores, tasks)	N	S	O
54	I have difficulty finishing a task on my own	N	S	O
55	people say that I am easily distracted	N	S	O
56	I have trouble remembering things, even for a few minutes (such as directions, phone numbers)	N	S	O
57	people say I am too emotional	N	S	O
58	I rush through things	N	S	O
59	I get annoyed	N	S	O
60	I leave my room or home a mess	N	S	O
61	I get disturbed by unexpected changes in my daily routine	N	S	O
62	I have trouble coming up with ideas for what to do with my free time	N	S	O
63	I don't plan ahead for tasks	N	S	O
64	people say that I don't think before acting	N	S	O
65	I have trouble finding things in my room, closet, or desk	N	S	O
66	I have problems organizing activities	N	S	O

67	after having a problem I don't get over it easily	N	S	O
68	I have trouble doing more than one thing at a time	N	S	O
69	my mood changes frequently	N	S	O
70	I don't think about consequences before doing something	N	S	O
71	I have trouble organizing work	N	S	O
72	I get upset quickly or easily over little things	N	S	O
73	I am impulsive	N	S	O
74	I don't pick up after myself	N	S	O
75	I have problems completing my work	N	S	O

APPENDIX 13: PEER REVIEWED PUBLICATION FOR PROSPECTIVE MEMORY (1)

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Original Paper

Everyday and prospective memory deficits in ecstasy/polydrug users

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Abstract

The impact of ecstasy/polydrug use on real-world memory (i.e. everyday memory, cognitive failures and prospective memory [PM]) was investigated in a sample of 42 ecstasy/polydrug users and 31 non-ecstasy users. Laboratory-based PM tasks were administered along with self-reported measures of PM to test whether any ecstasy/polydrug-related impairment on the different aspects of PM was present. Self-reported measures of everyday memory and cognitive failures were also administered. Ecstasy/polydrug associated deficits were observed on both laboratory and self-reported measures of PM and everyday memory. The present study extends previous research by demonstrating that deficits in PM are real and cannot be simply attributed to self-misperceptions. The deficits observed reflect some general capacity underpinning both time- and event-based PM contexts and are not task specific. Among this group of ecstasy/polydrug users recreational use of cocaine was also prominently associated with PM deficits. Further research might explore the differential effects of individual illicit drugs on real-world memory.

Keywords

cannabis, cocaine, cognitive failures, ecstasy, everyday memory, prospective memory

Introduction

An important topic of investigation that has received increasing attention in recent years concerns real-world memory processes (i.e. everyday memory, prospective memory (PM) and cognitive failures). Examples of everyday memory problems and cognitive failures might include, for example, forgetting the location of familiar objects around the house, forgetting to take essential objects when leaving the home or office, failing to recognize acquaintances, or forgetting important events that occurred the previous day. Prospective memory (PM) involves remembering to execute a particular behaviour at some point in the future, for example, remembering to attend a meeting, meet a friend or pass on a message. Previous investigations from our laboratory in which we evaluated the integrity of real-world memory processes in ecstasy/polydrug (Montgomery and Fisk, 2007) and cannabis-only users (Fisk and Montgomery, 2008) have shown that users of illicit substances exhibit deficits in real-world memory on a range of measures. Evidence of ecstasy/polydrug- (Heffernan et al., 2001a,b) and cannabis-related (McHale and Hunt, 2008) impairment has emerged in other studies. Furthermore impairments may be specific to particular drugs. For example, Rodgers and co-workers found that cannabis was related to short-term and internally cued PM deficits while ecstasy was related to deficits in long-term PM (Rodgers et al., 2001, 2003).

Most of the research into real-world memory functioning among users of illicit substances has utilized self-reported measures (Fisk and Montgomery, 2008; Heffernan et al., 2001a,b; Montgomery and Fisk, 2007; Rodgers et al., 2001, 2003). However, it is possible that self-perceptions may be distorted. For example, drug users may arrive at the laboratory with the expectation that they will under-perform (Bedi and Redman, 2008; Cole et al., 2006). This may affect their responses on self-reported measures causing them to imagine or overstate the magnitude of any deficits that might be present. Clearly it would be desirable to confirm the results obtained through self-reported measures utilizing laboratory measures of the relevant constructs. To date relatively few studies in this area have used laboratory tests of PM. Where such tests have been included they have been rather artificial and contrived in nature. For example the 'virtual week' is a board game completed in the laboratory in which the participant is required to complete previously learned tasks at specific points as they progress around the board. Deficits were observed on this measure among currently abstinent ecstasy users including those who used infrequently (Rendell et al., 2007). While this test undoubtedly possesses a PM component it has been acknowledged that more ecologically valid measures are needed (Will et al., 2009). In order to address some

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of these limitations, the present research will include laboratory measures of PM which are designed to be more naturalistic and where the PM component is less obvious to the participant.

Cognitive failures and PM are known to utilize prefrontal executive processes including the working memory system. Neuroimaging studies have revealed the involvement of the frontopolar cortex (Brodmann area 10 [BA10]) and neighbouring prefrontal areas during the performance of PM tasks (Okuda et al., 2007). Other research utilizing dual-task methodology (Marsh and Hicks, 1998) cognitive ageing paradigms (McDaniel et al., 1999) and Parkinson's-related deficits (Kliegel et al., 2005) has also linked PM functioning to prefrontal lobe capacity. Therefore, if ecstasy or other illicit drugs are associated with real-world memory deficits among currently abstinent users, then this would provide evidence consistent with a disruption of the processes supported by these specific neural locations and in particular BA10.

Prospective memory tasks may be defined as either event-based or time-based. For example, some predefined external event may trigger the retrieval of the intention to act, or alternatively the trigger may be the elapse of a given period of time. Self-reported measures do not adequately capture this distinction and thus while there is evidence of self-reported ecstasy/polydrug-related deficits in PM it is not clear whether users exhibit deficits on one or both types of task. This is an important question since there is evidence to suggest that the two classes utilize neural processes that are at least in part separable. For example, Burgess et al. (2003) and Gilbert et al. (2005) have shown that event-based tasks utilize the frontopolar cortex, including BA10. More recently positron emission tomography (PET) scanning has revealed that while the left superior frontal gyrus was involved in both types of tasks, different areas within this structure were found to be activated. Furthermore, in addition to the frontopolar cortex, the time-based tasks also activated more diverse regions including anterior medial frontal regions, the right superior frontal gyrus and the anterior cingulate (Okuda et al., 2007). Thus, if ecstasy/polydrug users are differentially affected on time- and event-based PM tasks then this would provide further information on which specific neural locations are susceptible to specific drug-related effects.

To address these issues laboratory-based and self-reported measures of PM and real-world memory were administered. Ecstasy/polydrug-related deficits were predicted on all measures.

Method

Participants

Forty-two ecstasy/polydrug users (14 males, 28 females) and 31 non-users (five males, 26 females) took part in this investigation. Participants were recruited via direct approach to university students and the snowball technique, i.e. word-of-mouth referral (Solowij et al., 1992). All participants were university students attending Liverpool John Moores University (LJMU) or the University of Central Lancashire (UCLAN).

Materials

The prior history of illicit drug consumption was assessed using a background drug-use questionnaire which has been used extensively in previous research from our laboratory (e.g., Montgomery et al., 2005b). These data were used to estimate the total lifetime use for each drug (e.g. ecstasy, cannabis, amphetamines, cocaine, etc). Period of abstinence and frequency of use were also assessed. Fluid intelligence was measured via Raven's Progressive Matrices (Raven et al., 1998) and the number of years of education, the participant's age and gender, and their current use of cigarettes and alcohol were assessed.

Self-reported measures of real-world memory

Everyday memory: The Everyday Memory Questionnaire (EMQ) (Cornish, 2000; Sunderland et al., 1983) is a self-reported measure of memory lapses in everyday activities. The measure consists of 27 statements with responses made on a nine-point scale ranging from 'not at all in the last six months' to 'more than once a day'. Examples of statements include: 'forgetting where you put something'; 'finding a television story difficult to follow'. A total score is calculated by summing the responses to all items.

Cognitive failures: The Cognitive Failures Questionnaire (CFQ) (Broadbent et al., 1982) is a 25-item measure of everyday attentional deficits. Questions include 'Do you fail to notice signposts on the road?' and 'Do you forget what you came to the shops to buy?'. Responses are made on a five-point scale with zero corresponding to 'never' and four to 'very often' yielding a maximum possible score of 100.

Prospective Memory Questionnaire: The Prospective Memory Questionnaire (PMQ) (Hannon et al., 1995) is a self-reported measure indicating the likelihood of a memory lapse in given time period. The PMQ provides measures of three aspects of PM on a scale of 1–9 for each aspect (1 revealing little forgetting, 9 revealing a great deal of forgetting). Fourteen questions measure short-term habitual PM, e.g. 'I forgot to turn my alarm clock off when I got up this morning'. Fourteen items measure long-term episodic PM, e.g. 'I forgot to pass on a message to someone'. Ten questions measure internally cued PM, e.g. 'I forgot what I wanted to say in the middle of a sentence'. In addition, 14 questions make up the 'techniques to remember' scale, which provides a measure of the number of strategies used to aid remembering. For each of the four scales, an average score is calculated by summing the responses and dividing by the number of items in that section (14 for ST-habitual, LT episodic and strategies and 10 for internally cued). Thus, higher scores are indicative of more forgetting and many strategies used to aid remembering.

The Prospective and Retrospective Memory Questionnaire (PRMQ): The Prospective and Retrospective Memory Questionnaire (PRMQ) (Crawford et al., 2003) provides a measure of memory slips of this kind in everyday life. It consists of 16 items, eight related to PM failures, e.g. 'Do you decide to do something in a few minutes' time and then forget to do it?'. Participants were asked to say how often these things happened to them on a five-point scale, very often,

quite often, sometimes, rarely, never, resulting in minimum and maximum possible scores of eight and 40.

The reliability and validity of the CFQ, EMQ and PMQ have been documented previously (see, for example, Hannon et al., 1995; Royle and Lincoln, 2008; Wallace, 2004).

Laboratory measures of prospective memory

Prospective memory pattern recognition test: This test is based on a processing speed task (see, e.g., Fisk and Warr, 1996) which was amended so as to provide a laboratory-based measure of PM by the addition of a parallel PM element. In the pattern comparison speed task, participants indicated as quickly as possible whether two patterns appearing on the computer screen were the same or different by pressing respectively the '/' key or the 'Z' key on the keyboard. After each 30-second period the patterns increased in complexity and for each level of complexity the computer kept a record of the number of correct responses. The PM element of this test required the participant to remember to press the 'F1' key at the end of each 30-second period when the message 'please wait a moment' appeared. Participants were told that this was in order to save their scores on the task. Failure to press F1 resulted in the score for that segment being reported as an 'error' in the screen display at the end of the task. This task was repeated three times. The number of times the participant forgot to press F1 for each trial was calculated producing a laboratory event-based PM measure.

Prospective memory fatigue test: At the beginning of the test session, participants were told that they should provide an indication of their level of fatigue (using the Karolinska Sleepiness Scale; see Gillberg et al., 1994) every 20 minutes throughout the experiment. If the 20-minute period elapsed during the completion of a task, participants were asked to complete the fatigue measure immediately after. The percentage of occasions on which the participant remembered to complete the Karolinska sleepiness scale was calculated. This was done for the first and second half of the test session thereby producing two measures of medium-term time-based PM. On each occasion, participants who forgot were reminded to fill in the questionnaire.

Long-term recall prospective memory: A list of 15 words was presented five times, orally, using an audio recording device. At the end of each trial the participant had to write down as many words as they could recall from the list. No time constraint was imposed in this regard. A long-term PM element was added to the recall test. Participants had to remember to return an answer sheet to the experimenter with the words that they were able to recall after a delay of 1, 2 and 3 weeks from the time of testing. Three prepaid envelopes were provided for this purpose. Participants scored 1 if the envelope was returned and 0 otherwise. This data was collected separately for each week but the score was the total number of sheets returned (out of a maximum of three).

These laboratory tasks were based on similar paradigms devised by Mathias and Mansfield (2005) and Einstein et al. (1995).

Rivermead Behavioural Memory Test (RBMT-II): A full description of the RBMT-II may be found elsewhere (Wilson et al., 1999). In the present study only the three subtasks relating to PM were used:

(1) *Remembering a hidden belonging*. A small object (a pen or pencil in this study) was requested from the participant and placed in a specified location. The participant was told to remember to retrieve the belonging later doing so when the examiner said the words: 'We have now finished this test'. Participants received a score of two if the belonging and location was recalled correctly, one if after a prompt and zero if neither object nor location was remembered.
(2) *Remembering an appointment*. A timer was set for 20 minutes. The participant was told that when the alarm clock rang they should ask a pre-arranged question (e.g., 'What time does this session end'). A profile score of two is given if the question is recalled correctly, one if after a prompt or zero if it is not recalled at all.
(3) *Delivering a message*. Having first observed the experimenter, the participant was required to replicate a short route around the test room depositing a message at a specified location on the way. This was done immediately and after a delay and a single score was awarded ranging from zero to three depending on the number of errors made over the two attempts.

Procedure

Participants were informed of the general purpose of the experiment and their right to withdraw any time. After consent had been obtained the tests were administered under laboratory conditions. The drug-use questionnaire was administered first followed by the Ravens intelligence test, the age/education questionnaire, and the PM questionnaires (Crawford et al., 2003; Hannon et al., 1995). Next the PM pattern recognition task, the recall PM task and the RBMT-II tasks were administered. The fatigue PM task was administered throughout the session. Participants were fully debriefed, paid £20 in Tesco store vouchers and given drug education leaflets. The University of Central Lancashire's Ethics Committee approved the study.

Results

Demographic and background variables

Inspection of Table 1 reveals that the ecstasy/polydrug users did not differ from non-ecstasy users on most of the demographic and background drug use variables. Ecstasy/polydrug users consumed significantly more units of alcohol per week compared with non-ecstasy users. Although the number of cigarettes consumed per day by smokers did not differ significantly between the groups, tobacco use was more prevalent among ecstasy/polydrug users with over one-half of the group currently smoking while less than one-third of non-ecstasy users currently smoked cigarettes.

With regard to illicit drug use, a majority of the ecstasy/polydrug group had in the past or were currently consuming

Table 1. Demographical and background drug use variables for users and non-users

	Ecstasy/polydrug users			Non-ecstasy users			
	Mean	SD	*n*	Mean	SD	*n*	*p*-value
Age (years)	21.67	3.61	42	21.03	3.25	31	ns
Ravens Progressive Matrices (maximum 60)	43.32	10.90	42	44.87	7.57	31	ns
Years of Education	15.05	3.15	42	15.63	1.57	31	ns
Cigarettes per day	9.45	8.60	22	6.33	6.65	9	ns
Alcohol (Units per week)	14.85	10.11	41	7.17	8.28	30	<0.01
Total Use							
Ecstasy (Tablets)	668.88	1234.67	42	–	–	–	–
Amphetamine (grams)	196.00	254.78	13	–	–	–	–
Cannabis (joints)	3259.49	4571.12	39	243.00	323.14	10	<0.001
Cocaine (lines)	1270.71	1762.69	28	255.00	343.65	2	–
Frequency of Use (times per week)							
Ecstasy	0.25	0.32	42	–	–	–	–
Amphetamine	0.10	0.27	14	–	–	–	–
Cannabis	1.02	1.79	39	0.85	1.59	10	ns
Cocaine	0.41	0.51	27	0.54	0.65	2	–
Weeks Since Last Use[a]							
Ecstasy	4	26	42	–	–	–	–
Amphetamine	46	254	16	–	–	–	–
Cannabis	2	23	39	18	154	10	ns
Cocaine	4	18.5	32	8	5	3	–
Number Ever Used							
Amphetamine			17			0	
Cannabis			40			10	
Cocaine			33			3	
Ecstasy			42			0	

[a]For weeks since last use, median and inter-quartile range are reported.

cocaine and almost all were cannabis users. Around 40% of the group were also amphetamine uses. However, the correlation between estimated lifetime use of ecstasy and cannabis, $r = 0.041$ ($p > 0.05$, $n = 39$), was not statistically significant while that between lifetime ecstasy and cocaine use approached significance, $r = 0.332$ ($p = 0.084$, $n = 28$). Estimated lifetime use of cocaine and cannabis was also not significantly related $r = 0.172$ ($p > 0.05$, $n = 29$). Among non-ecstasy users the use of illicit drugs was largely confined to cannabis, although three of the group had also used cocaine. Given the limited use of cocaine and amphetamine among non-ecstasy users it was not meaningful to statistically analyse group differences in these substances. However, ecstasy/polydrug users had significantly greater total lifetime exposure to cannabis compared with non-ecstasy users.

Laboratory-based prospective memory measures

With regards to the laboratory measures of PM, examination of Table 2 reveals that ecstasy/polydrug users were impaired on all but two of the measures. With regard to the time-based tasks, remembering to complete the fatigue task proved problematic for ecstasy/polydrug users especially during the second half of the test session. Overall the completion rate among ecstasy users was only 51% of that achieved by non-users. From a longer-term perspective during the three weeks following testing non-users posted back 77% more delayed recall response sheets compared with users. However, on the time-based RMBT-II appointment task, group differences were less evident.

With regard to the event-based tasks, although ecstasy/polydrug users and non-ecstasy users performed similarly on the RMBT-II message task, ecstasy users performed worse on the RMBT-II belonging task. Similarly users were between two and three times more likely to forget to press the 'F1' key during the processing speed task.

Multivariate analysis of variance (MANOVA) with the seven laboratory measures of PM as dependent variables and ecstasy/polydrug user group between participants revealed a statistically significant effect of group, $\Lambda = 0.598$, $F(7,65) = 6.25$, $p < 0.001$, partial $\eta^2 = 0.402$. As can be seen in Table 2, univariate analyses revealed that all but two of the individual measures yielded statistically significant group differences with ecstasy/polydrug users consistently performing worse than non-ecstasy users. Following the inclusion of covariates relating to lifetime cannabis use (joints) and frequency of cannabis use (times per week), the multivariate group effect remained statistically significant, $\Lambda = 0.671$, $F(7,62) = 4.34$, $p < 0.001$, partial $\eta^2 = 0.329$. Following the inclusion of two further covariates relating to alcohol consumption (units per week) and tobacco use (cigarettes per day), again the multivariate group effect was significant, $\Lambda = 0.712$, $F(7,58) = 3.34$, $p < 0.01$, partial $\eta^2 = 0.288$.

Table 2. Scores on laboratory and self-reported measures of real-world memory for users and non-users

	Ecstasy/polydrug users		Non-ecstasy users			*p* Covariates: cannabis use	*p* Covariates: cannabis smoking, and alcohol use
	Mean	SD	Mean	SD	*p*-value		
LABORATORY MEASURES							
RBMT-II							
Appointment	1.55	0.77	1.65	0.61	ns	ns	ns
Belonging	1.19	0.77	1.65	0.62	<0.01	<0.05	<0.05
Message	1.83	0.50	1.87	0.50	ns	ns	ns
Fatigue PM Task (% recalled)							
First half of test session	50.44	36.04	72.20	25.57	<0.01	<0.01	<0.05
Second half of test session	9.48	16.26	44.62	39.52	<0.001	<0.001	<0.001
Processing Speed PM Task Errors	1.64	2.55	0.61	1.23	<0.05	<0.05	<0.05
Long-term Recall PM Task (max 3)	0.95	1.32	1.68	1.30	<0.05	ns	ns
SELF-REPORTED MEASURES							
Everyday Memory	94.51	36.13	79.42	31.77	<0.05	<0.05	<0.05
Prospective Memory (Hannon et al., 1995)							
Short Term	1.53	0.72	1.27	0.38	<0.05	<0.05	ns
Long Term	2.81	1.00	2.47	0.88	ns	ns	ns
Internally Cued	2.62	0.96	2.39	0.95	ns	ns	ns
Techniques to Remember	2.74	1.10	3.32	1.58	<0.05	ns	ns
Cognitive Failures	43.40	14.20	40.00	12.71	ns	ns	ns
Prospective Memory (Crawford et al., 2003)	22.63	4.96	20.56	5.52	<.05	<.05	Ns

Thus, the inclusion of the four covariates reduced the ecstasy/polydrug user group effect size by 28%. However, none of the covariates were statistically significant as predictors of the dependent variables, $F < 1.20$, for the multivariate effect, in all cases. Inspection of Table 2 reveals that in univariate terms four of the seven dependent variables produced statistically significant group differences following inclusion of the covariates. Thus, with regard to the laboratory measures, ecstasy/polydrug users remained impaired relative to non-ecstasy users even following the inclusion of the covariates. This suggests that the deficits among this group are more likely to be attributable to ecstasy.

Self-reported real-world memory measures

Outcomes for the self-reported measures of real-world memory may be found in Table 2. With just one exception, it is clear that ecstasy/polydrug users exhibit higher scores on all of the measures consistent with a greater incidence of real-world memory problems. MANOVA with the seven self-reported measures of real-world memory as dependent variables and ecstasy user group between participants revealed a statistically significant effect of group, $\Lambda = 0.756$, $F(7,58) = 2.68$, $p < 0.05$, partial $\eta^2 = 0.244$. Inspection of Table 2 reveals that in terms of the univariate analyses, the difference between the two groups was statistically significant for four of the seven dependent variables. The inclusion of the two measures of cannabis use as covariates reduced the multivariate effect to borderline significance, $\Lambda = 0.786$, $F(7,56) = 2.18$, $p = 0.05$, partial $\eta^2 = 0.214$. Furthermore when all four covariates were included (the two measures of cannabis use plus the tobacco and alcohol use indicators) the multivariate effect was no longer statistically significant $\Lambda = 0.826$, $F(7,52) = 1.57$, $p > 0.05$, partial $\eta^2 = 0.174$ and inspection of Table 2 reveals that only one of the univariate analyses continued to yield a statistically significant group difference: the everyday memory measure. In multivariate terms, two of the four covariates produced a statistically significant effect on the self-reported real-world memory measures, total cannabis use, $\Lambda = 0.769$, $F(7,52) = 2.23$, $p < 0.05$, partial $\eta^2 = 0.231$; and tobacco use $\Lambda = 0.723$, $F(7,52) = 2.84$, $p < 0.05$, partial $\eta^2 = 0.277$.

Relationship between period of abstinence and memory

It is possible that some of the drug-related deficits observed in the real-world memory measures may have been due to short-term post-intoxication effects. For the four main illicit drugs, Table 3 contains the correlations between weeks since last use and each of the real-world memory measures. Inspection of Table 3 reveals that for the most part the correlations not were statistically significant. With regard to the cognitive failures measure, although no ecstasy/polydrug effect was evident in Table 2, it is clear that performance on the task is correlated with the period of abstinence specifically in relation to ecstasy. Those abstaining for a longer period self-reported fewer cognitive failures.

Table 3. Correlations between real-world memory measures and duration of abstinence for the major illicit drugs

	Weeks since last use			
	Ecstasy	Cannabis	Cocaine	Amphetamine
LABORATORY MEASURES				
RBMT-II				
Appointment	−0.089	0.025	0.001	−0.526*
Belonging	0.137	0.082	0.030	0.078
Message	0.001	0.175	0.066	0.212
Fatigue PM Task (% recalled)				
First half of test session	0.336*	0.281	0.248	0.405
Second half of test session	0.113	0.124	−0.128	0.192
Processing Speed PM Task Errors	−0.037	−0.182	−0.029	−0.174
Long-term Recall PM Task (max 3)	−0.174	0.025	0.074	−0.011
SELF-REPORTED MEASURES				
Everyday Memory	−0.028	−0.048	−0.126	−0.243
Prospective Memory (Hannon et al., 1995)				
Short Term	−0.119	−0.043	0.165	−0.210
Long Term	−0.034	−0.023	−0.033	−0.154
Internally Cued	0.044	−0.155	−0.027	−0.043
Techniques to Remember	0.024	−0.110	−0.084	0.218
Cognitive Failures	−0.556***	−0.147	−0.070	−0.305
Prospective Memory (Crawford et al., 2003)	−0.151	−0.113	−0.026	−0.119

***$p < 0.001$; *$p < 0.05$ one-tailed.

Relationship between aspects of drug use and the memory measures

Table 4 contains the simple Pearson's correlation coefficients between the laboratory and self-reported measures of real-world memory on the one hand and lifetime use and frequency of use of the four main illicit drugs on the other (for non-users of a particular drug, lifetime and frequency of use have been coded as zero). Only those correlations that were statistically significant at $p < 0.05$ one-tailed are displayed. Examination of Table 4 reveals that total lifetime use of both ecstasy and cocaine are related to several of the laboratory measures indicating that as the level use increases, the real-world memory deficits increase in magnitude. With regard to frequency of use, cocaine is significantly correlated with five of the seven laboratory measures of real-world memory while the frequency of ecstasy use is significantly correlated with just three. In all cases increased frequency of use is associated with a greater degree of memory impairment. While the defining characteristic of the polydrug group is ecstasy use, clearly it appears that cocaine is also implicated in the real-world memory deficits identified here.

With regards to the self-reported measures of real-world memory, correlations with lifetime use are generally larger in absolute magnitude for ecstasy compared with cocaine. Similarly, in relation to frequency of use, while ecstasy yields significant correlations for three of the real-world memory measures, only one is statistically significant in relation to cocaine use. For all of the statistically significant correlations, increased use is associated with higher scores on the self-reported measures consistent with more real-world memory problems.

While it would have been potentially informative to conduct regression analyses with the measures of lifetime use and frequency of use for each drug as predictors and the measures of real-world memory as dependent variables, this was not possible. The sample size was inadequate given the number of predictors and the predictors were substantially intercorrelated reflecting the degree of polysubstance abuse within the ecstasy/polydrug group. Indeed all but two of the predictors possessed tolerances of less than 0.5 rendering testing and interpretation of the regression coefficients problematic (Tabachnick and Fidell, 2001).

However, while the standardized regression coefficients are not especially informative in the present context, a comparison of the simple correlation and semi-partial correlation coefficients does provide an indication of which variables share statistically significant unique variance with the real-world memory measures. Thus, where the simple correlations were statistically significant the semi-partial correlation between that drug-use measure and the real-world memory performance was computed controlling for the use of the other drugs on the measure in question. Thus, in relation to the RBMT-II belonging measure lifetime and frequency of cocaine use appear to be important determinants. For the RBMT-II message measure the frequency of cannabis use, and for the long-term recall PM task the frequency of both cocaine and cannabis use account for statistically significant unique variance. Of the self-reported measures lifetime ecstasy use is significantly associated with unique variance in the short-term and internally cued Hannon et al. (1995) PM measures and frequency of ecstasy use with the cognitive failures measure. The frequency of cannabis use shares unique variance with the short-term PM measure.

Table 4. Correlations between real-world memory measures and lifetime use and frequency of use for the major illicit drugs

		Lifetime Use		Frequency	
Real-world Memory Measure	Drug	Simple	Semi Partial	Simple	Semi Partial
Laboratory Measures					
RBMT-II					
Appointment	Cocaine	−0.258*	−0.288*	−0.265*	−0.210†
Belonging	Ecstasy	−0.300**	−0.106		
	Cannabis	−0.233*	−0.052		
	Cocaine	−0.408***	−0.238*	−0.482***	−0.440***
Message	Cannabis			−0.264*	−0.273*
Fatigue PM Task (% recalled)					
First half of test session	Ecstasy			−0.238*	−0.163†
	Cannabis	−0.203*	−0.124	−0.247*	−0.203†
	Cocaine	−0.204*	−0.072	−0.244*	−0.101
Second half of test session	Ecstasy	−0.231*	−0.118	−0.267*	−0.167†
	Cannabis	−0.254*	−0.178†		
	Cocaine	−0.213*	−0.033		
Processing Speed PM Task Errors	Ecstasy	0.284*	0.177†	0.227*	0.143
	Cocaine	0.283*	0.146	0.277*	0.154
Long-term Recall PM Task (max 3)	Cannabis	−0.276*	−0.173†	−0.260*	−0.207*
	Cocaine	−0.254*	−0.161	−0.330**	−0.271*
Self-Reported Measures					
Everyday Memory					
Prospective Memory (Hannon et al., 1995)					
Short Term	Ecstasy	0.304**	0.279*		
	Cannabis			0.265*	0.218*
Long Term					
Internally Cued	Ecstasy	0.377**	0.361**	0.271*	0.181†
	Amphetamine			0.249*	0.127
Techniques to Remember					
Cognitive Failures	Ecstasy	0.292*	0.212†	0.350**	0.251*
	Cocaine	0.237*	0.027		
	Cannabis	0.251*	−0.038		
Prospective Memory (Crawford et al., 2003)	Ecstasy	0.330**	0.188†	0.253*	0.100
	Cocaine	0.249*	0.097		
	Amphetamine	0.229*	0.183†		

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; †$p < 0.10$; one-tailed.

Semi-partial correlation is a conservative procedure in which the pooled variance between the real-world memory measure and two or more of the drug-use variables is excluded. For a number of the real-world memory measures some of the simple correlations with drug use were statistically significant while none of the semi-partial correlations proved to be so. Thus, in these cases there is a significant drug-related effect but it is not possible to identify which drug was likely to be primarily responsible. For example, with respect to processing speed task PM errors, total use of ecstasy yields a correlation of 0.284, which implies that the shared variance between the two measures was over 8%. However following control for total use of the other drugs, the semi-partial correlation was reduced to 0.177, implying that total ecstasy use shared just over 3% of the variance with the processing speed task PM errors measure after the overlapping effects of the other drugs were eliminated. The equivalent figures for total use of cocaine were 8% and 2%. Thus, in this case, while there is evidence of potential cocaine and ecstasy-related effects, similar patterns of use for these two drugs in those persons exhibiting different degrees of PM deficits make it impossible to identify which drug may be associated with outcomes on this PM measure.

Inter-correlations between the prospective memory and real-world memory measures

Ignoring for the moment drug-related differences, it would be reasonable to expect that the laboratory measures of PM would be correlated with each other. However, the correlations would not be expected to be perfect since each task would have performance aspects specific to it. Furthermore, the separate tasks reflect different aspects of PM functioning such as event-based versus time-based tasks and in the latter case PM deficits may be reflected with respect to both short-term and longer-term phenomena. Inspection of Table 5 reveals that with the exception of the long-term

Table 5. Inter-correlations between the laboratory and self-reported measures of real-world memory

	RBMT-II			Fatigue PM Task		Processing Speed PM Task	Long-term Recall PM Task
	Appointment	Belonging	Message	First Half	Second Half		
LABORATORY MEASURES							
RBMT-II							
Appointment							
Belonging	0.334**						
Message	−0.021	0.200*					
Fatigue PM Task (% recalled)							
First half of test session	0.238*	0.291**	0.056				
Second half of test session	0.266*	0.263*	0.122	0.425***			
Processing Speed PM Task Errors	−0.220*	−0.270*	−0.049	−0.206*	−0.185†		
Long-term Recall PM Task (max 3)	0.026	0.190†	0.060	0.073	−0.028	−0.182†	
SELF-REPORTED MEASURES							
Everyday Memory	−0.018	−0.041	0.140	−0.063	−0.141	−0.033	−0.094
Prospective Memory (Hannon et al., 1995)							
Short Term	−0.096	−0.128	−0.003	−0.230*	−0.120	0.392***	−0.135
Long Term	−0.069	−0.155	−0.139	−0.053	−0.312**	−0.006	−0.096
Internally Cued	−0.021	−0.037	−0.014	−0.077	−0.175†	−0.024	0.046
Techniques to Remember	−0.041	0.072	−0.048	0.024	−0.002	0.035	0.241*
Cognitive Failures	−0.174†	−0.161†	0.007	−0.223*	−0.323**	0.108	−0.044
Prospective Memory (Crawford et al., 2003)	−0.279**	−0.190†	−0.003	−0.201*	−0.281**	−0.008	−0.048

***$p < .001$; **$p < .01$; *$p < .05$; †$p < .10$; one-tailed.

Table 6. Inter-correlations between the self-reported measures of real-world memory

	Everyday Memory	Prospective Memory				Cognitive Failures
		Short Term	Long Term	Internally Cued	Techniques	
SELF-REPORTED MEASURES						
Everyday Memory						
Prospective Memory (Hannon et al., 1995)						
Short Term	0.049					
Long Term	0.442***	0.246*				
Internally Cued	0.455***	0.379***	0.507***			
Techniques to Remember	0.254*	0.211*	0.366**	0.577***		
Cognitive Failures	0.477***	0.280**	0.357**	0.513***	0.289**	
Prospective Memory (Crawford et al., 2003)	0.615***	0.145	0.412***	0.521***	0.328**	0.707***

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; one-tailed.

recall task, where two of the outcomes only approached significance, the remaining laboratory tasks did reveal a number of statistically significant inter-correlations. Furthermore, for each of the laboratory tasks performance was correlated with the scores obtained on one or more of the self-reported measures. Finally, not surprisingly, Table 6 reveals that the outcomes for the self-reported measures were also correlated with each other.

Discussion

In multivariate terms ecstasy/polydrug users were found to be impaired on the laboratory-based PM measures. The group-related effect remained statistically significant following controls for lifetime and frequency of cannabis use and current use of tobacco and alcohol. In terms of the individual laboratory measures, ecstasy/polydrug users exhibited poorer performance in all cases. These deficits were statistically significant on all but two of the measures (the two exceptions were the RBMT appointment and message subscales) and remained statistically significant in four of the seven measures following controls for cannabis, alcohol and tobacco use. In demonstrating that ecstasy/polydrug users were impaired on a variety of PM tasks the present study extends previous research in which ecstasy users have been found to exhibit impairment on a range of cognitive tasks, for example, selective deficits have been observed in aspects of verbal and visuospatial executive functioning, on the Tower of Hanoi, and Tower of London tasks, as well as on the Stroop measure (for a review, see Murphy et al., 2009). Ecstasy users have also exhibited performance decrements in aspects of deductive reasoning (Fisk et al., 2005).

Returning to the findings of the present study, with regard to the RBMT-II, only the belonging sub-scale yielded statistically significant group differences. To the best of our knowledge the present study is the first to demonstrate a deficit on the RBMT belonging scale (ecstasy users scored lower on this scale in Zakzanis et al.'s (2003) study, however the difference was not statistically significant). There have been few studies investigating ecstasy-related deficits on the RBMT PM measures. Zakzanis et al. (2003) observed ecstasy-related deficits on the 'appointment' and 'message' PM RBMT component measures while neither of these yielded statistically significant differences in the present study. It is possible that the deficits observed by Zakzanis et al. (2003) might have been due to confounding factors. For example, their ecstasy users scored significantly lower on the WAIS-III vocabulary sub-test compared with the control group.

The three remaining laboratory-based tasks, i.e. the fatigue PM task (remembering to periodically complete the fatigue measure during the test session), the processing speed PM task (remembering to press 'F1' to store the participant's scores), and the long-term recall PM task (remembering to mail the delayed recall test in the successive weeks following the test session) all yielded consistent ecstasy/polydrug-related deficits which for the most part remained statistically significant following the inclusion of the covariates. Furthermore, deficits were evident on both time-based (fatigue PM task) and event-based PM tasks (RBMT-II belonging; processing speed PM task) which suggests that the ecstasy/polydrug deficit reflects some general feature of PM task performance rather than more task-specific aspects.

Thus, it appears that some aspects of ecstasy use or some other characteristic of the ecstasy-using group gives rise to PM deficits independent of any effects which might be attributable to cannabis use. This is consistent with the results of those studies which have used self-reported measures and have found ecstasy-related deficits, for example, those from our own laboratory (Montgomery and Fisk, 2007) and elsewhere (Heffernan et al., 2001a,b; Rodgers et al., 2001, 2003). The present results suggest that these deficits are likely to be real rather than imagined and are evident in both time- and event-based PM contexts. Ecstasy-related deficits were also evident on both short-term (fatigue) and long-term (weekly word recall) PM tasks although in the latter case the deficit was no longer significant following controls for group differences in cannabis use. These results are perhaps somewhat at odds with those reported by Rodgers et al. (2001, 2003) who found that, on the basis of self-reports, ecstasy use was associated with long-term deficits while cannabis use was associated with short-term. While the present study is among the first to use a range of laboratory-based and naturalistic PM measures, previous research using the 'virtual week' paradigm did reveal ecstasy-related deficits with users performing worse than non-users on time- and event-based PM components of the task. Furthermore, the deficits were present in both frequent and infrequent users (Rendell et al., 2007). In a subsequent study, methamphetamine users also exhibited deficits on this task (Rendell et al., 2009). As noted above the 'virtual week' is a board game conducted in the laboratory in which the participant is required to complete previously learned tasks at specific points as they progress around the board. While this test has its merits, before the PM element can be completed it is necessary to learn each of the particular responses that is paired with specific locations on the board. Thus, the test has a substantial associative learning component. Montgomery et al. (2005a) have demonstrated that ecstasy users are impaired on paired associative learning and so it is possible that the deficits evident on the virtual week might be attributable to this aspect rather than the PM components. In the present study, the retrospective memory element was minimal and little learning was necessary. Thus, the PM deficits observed here are less likely to be due to associative learning problems.

While it is noteworthy that the ecstasy/polydrug group differences remained statistically significant following the inclusion of the cannabis use measures as covariates there are indications that cannabis use may be negatively associated with PM. For example the frequency of cannabis use accounted for unique variance in the long-term recall PM task with more frequent users returning fewer recall answer sheets in the weeks following testing. Furthermore, while there was no ecstasy/polydrug-related difference on the RBMT message score, the frequency of cannabis use again was associated with unique variance on this task with more frequent users achieving lower scores. Furthermore the cannabis use measures were significantly correlated with a number of the other laboratory PM tasks with greater lifetime exposure and increased frequency of use associated with poorer PM performance. However, in these cases the effects were reduced to below statistical significance when the shared variance with the other drug use measures was excluded.

Among ecstasy/polydrug users there was clear evidence that cocaine use was associated with adverse outcomes on a number of the laboratory tests of PM. As far as the authors are aware the present study is the first to link recreational use of cocaine with PM deficits. Either lifetime, or frequency of use, or both, were associated with performance on all but one of the laboratory measures of PM and one or other of these aspects of use were found to share unique variance with three of the PM laboratory measures. As noted above PM performance is dependent on pre-frontal executive resources. Of particular relevance to the present paper, a number of studies have shown that event-based PM tasks utilize the frontopolar cortex, i.e. BA10 (Burgess et al., 2003; Gilbert et al., 2005) and the left superior frontal gyrus (Okuda et al., 2007). Similarly while time-based PM tasks activated more diverse regions including anterior medial frontal regions, the right superior frontal gyrus and the anterior cingulate, they also utilized BA10 and the superior frontal gyrus (Okuda et al., 2007). Thus, the cocaine-related deficits observed on both the time- and event-based laboratory PM tasks might be arise from the effects of the drug on the processes supported by BA10.

Neuroimaging studies in normal populations have revealed that the dorsolateral prefrontal cortex including BA10 supports a broad range of executive functions and in particular those which involve updating the contents of working memory (Collette et al., 2005). This raises the possibility that cocaine use is associated with specific executive function deficits which in turn give rise to PM deficits. Few studies of cocaine users have focused on this particular component executive process. Deficits among cocaine users have been observed on the paced

auditory serial addition task (PASAT) (Berry et al., 1993; but see also Gonzalez et al., 2004). Furthermore, substance-dependent polydrug users whose drug of choice was cocaine were found to be impaired on a number letter re-sequencing task, and on forward and backward digit and spatial span (Verdejo-García and Pérez-García, 2007). These tasks all require the contents of working memory to be updated and the results are therefore consistent with a cocaine-related deficit in the updating component process.

At the neurotransmitter level dopaminergic activity in the prefrontal cortex is known to underpin executive processes. Equally cocaine is known to influence behaviour through its effects on dopamine expression (Heien et al., 2005; Sidiropoulou et al., 2009; Zhang et al., 2005). Unifying these separate aspects, Tomasi et al.'s (2007) fMRI results demonstrated that compared to controls, cocaine users exhibited hypoactivation in the mesencephalon, where dopamine cell bodies are located and projections originate, together with a deactivation in dopamine projection regions (putamen, anterior cingulate, parahippocampal gyrus and amygdala). These outcomes were associated with a compensatory hyperactivation in cortical regions involved with executive functions (prefrontal and parietal cortices). However, during the performance of a task loading on working memory resources the activation of these prefrontal regions was less than that observed in non-users. Interestingly, those users with urine samples positive for cocaine were significantly less likely to exhibit these tendencies relative to abstinent users. Thus, Tomasi et al. (2007) argue that a prior history of cocaine use disrupts the operation of those dopaminergic systems in the prefrontal cortex which underpin executive functioning. One manifestation of this disruption may be the cocaine-related deficit in PM functioning which could stem from impairment to the updating executive process due the possible susceptibility of BA10 to dopamine-mediated deficiency.

A further possibility is that cocaine might give rise to impairment in medial temporal and hippocampal processes. Fox et al. (2009) observed deficits in various aspects of performance on the Rey Auditory Verbal Learning Task (RAVLT) among cocaine-dependent individuals receiving treatment as inpatients. Deficits in learning and recall were related to between group self-reported stress levels and among cocaine users with raised early morning cortisol levels. Fox et al. argue that the stress-related increase in cortisol levels and associated memory deficits are potentially symptomatic of hippocampal damage among cocaine-dependent individuals. Such deficits might potentially affect the recall component of PM performance and if present among recreational cocaine users might therefore provide an explanation for the results obtained here.

While the laboratory PM measures demonstrated clear drug-related effects, outcomes in relation to the self-reported measures were less clear-cut. Although the ecstasy/polydrug group exhibited impairment this was substantially attenuated following the inclusion of the other measures as covariates. It may be that although ecstasy/polydrug users as a whole are aware of their PM problems they may be uncertain as to which illicit drug is responsible for their perceived deficits.

As with most studies in this area, there are a number of limitations. Owing to the quasi-experimental design of the study the concurrent use of other illicit drugs may have contributed to group differences in PM as the two groups also differed significantly on these variables. Also, the purity of MDMA tablets obviously cannot be guaranteed (but see Parrott, 2004) and as with previous studies in this area (Heffernan et al., 2001a,b; Morgan, 1999) no objective measure of recent drug use such as urinalysis was employed. A further limitation of research of this kind is that the apparent ecstasy/polydrug-related deficits may not necessarily be a consequence of illicit drug use but perhaps reflect some pre-existing difference between users and non-users which had its origins before the initiation of drug use. Consistent with this possibility, in the context of the longer-term consequences of cannabis use Pope (2002) has emphasized the importance of considering whether or not the apparent differences between users and non-users might reflect pre-morbid conditions perhaps in sociodemographic factors, personal dispositions, or underlying psychopathology. A further possibility is that the effects observed here may not have a direct pharmacological basis but instead be related to lifestyle differences or may be due to the effects of drugs on aspects of physiological functioning, for example sleep quality (but see Fisk and Montgomery 2009; Montgomery et al., 2007).

To conclude, the current study intended to determine the impact of ecstasy/polydrug use on aspects of real-world memory such as everyday memory, cognitive failures and PM. Ecstasy/polydrug associated deficits were observed on both laboratory and self-reported measures of PM. Ecstasy/polydrug users were impaired on all PM laboratory measures with the exception of one event- and one time-based PM task from the RBMT-II. Ecstasy/polydrug-related deficits were also observed in some of the self-reported measures of PM and in the EMQ while no deficits were observed in the self-reported measures of cognitive failures. We can therefore assume that ecstasy/polydrug users possess some self-awareness of their memory lapses. An unanticipated finding was that the recreational use of cocaine can be associated with PM deficits. Further research is needed to clarify whether the cocaine-related deficits are limited to the ecstasy/polydrug population or whether they might be present among those persons whose recreational use is largely confined to cocaine.

Disclosure/Conflict of Interest

The authors declare that, except for income received from their primary employers, no financial support or compensation has been received from any individual or corporate entity over the past three years for research or professional service and there are no personal financial holdings that could be perceived as constituting a potential conflict of interest. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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APPENDIX 14: PEER REVIEWED PUBLICATION FOR PROSPECTIVE MEMORY (2)

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ORIGINAL INVESTIGATION

Prospective memory functioning among ecstasy/polydrug users: evidence from the Cambridge Prospective Memory Test (CAMPROMPT)

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Abstract
Rationale Prospective memory (PM) deficits in recreational drug users have been documented in recent years. However, the assessment of PM has largely been restricted to self-reported measures that fail to capture the distinction between event-based and time-based PM. The aim of the present study is to address this limitation.
Objectives Extending our previous research, we augmented the range laboratory measures of PM by employing the CAMPROMPT test battery to investigate the impact of illicit drug use on prospective remembering in a sample of cannabis only, ecstasy/polydrug and non-users of illicit drugs, separating event and time-based PM performance. We also administered measures of executive function and retrospective memory in order to establish whether ecstasy/polydrug deficits in PM were mediated by group differences in these processes.
Results Ecstasy/polydrug users performed significantly worse on both event and time-based prospective memory tasks in comparison to both cannabis only and non-user groups. Furthermore, it was found that across the whole sample, better retrospective memory and executive functioning was associated with superior PM performance. Nevertheless, this association did not mediate the drug-related effects that were observed. Consistent with our previous study, recreational use of cocaine was linked to PM deficits.
Conclusions PM deficits have again been found among ecstasy/polydrug users, which appear to be unrelated to group differences in executive function and retrospective memory. However, the possibility that these are attributable to cocaine use cannot be excluded.

Keywords Ecstacy · Cocaine · Cannabis · Prospective memory · CAMPROMPT

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Introduction

Prospective memory (PM) involves remembering to execute a particular behaviour at some future point in time, which may be in the short or long term, for example remembering to turn off the lights when leaving a room or remembering to attend a meeting, meet a friend or pass on a message. Self-report measures of this construct have been developed (e.g. Crawford et al. 2003; Hannon et al. 1995), and in previous research from our laboratory, Fisk and co-workers have demonstrated apparent impairments on these measures among ecstasy/polydrug users (Montgomery and Fisk 2007) and cannabis-only users (Fisk and Montgomery 2008). Other researchers have also reported deficits on self-report PM measures among users of illicit drugs (Heffernan et al. 2001a, b; Rodgers et al. 2001, 2003) and studies from our own laboratory and elsewhere have revealed deficits among illicit drug users in laboratory measures of PM (Hadjiefthyvoulou et al. 2010; Rendell et al. 2007a; Rendell et al. 2009).

Unsurprisingly, given their role in supporting memory functions in general, evidence suggests that PM is dependent on medial temporal–hippocampal processes. For example, in a clinical group with medial temporal sclerosis, Adda et al. (2008) found that PM performance was

impaired and that among those with left hemisphere lesions the degree of impairment was correlated with that in delayed (7 day) verbal recall on the Rey Auditory Verbal Learning Task (RAVLT). Leitz et al. (2009) found that PM performance was significantly correlated with episodic memory recall following acute administration of alcohol. In another recent study utilising magnetoencephalography, Martin et al. (2007) found that that the hippocampal region was activated longer during both retrospective and prospective memory tasks relative to a control condition. Interestingly, other regions were also differentially implicated, since compared to the retrospective and control tasks, the PM task was associated with earlier onset of activation in the posterior parietal lobe. In an animal study by Goto and Grace (2008), in which rats searched for food rewards in a radial maze, prospective and retrospective memory elements of PM were explored. The results suggested that the retrospective aspect, although requiring hippocampal input, also recruits PFC resources before the prospective component can be activated. Furthermore, the dopaminergic system appeared to differentially support this process with the D1 receptor apparently supporting the former aspect and the D2 receptor the latter prospective component. Since ecstasy impacts both serotonergic and dopaminergic processes, this raises the possibility that disruption of dopaminergic processes might be responsible for the PM deficits that have been observed in human drug users.

Aside from its reliance on medial temporal structures, PM is known to utilise prefrontal executive processes including the working memory system. Neuroimaging studies have revealed the involvement of the frontopolar cortex (Brodmann area 10) and neighbouring prefrontal areas during the performance of PM tasks (Okuda et al. 2007). Other research utilising dual-task methodology (Marsh and Hicks 1998), cognitive ageing paradigms (McDaniel et al. 1999) and Parkinson's-related deficits (Kliegel et al. 2005) has also linked PM functioning to prefrontal-lobe capacity.

It is worthy to note that prospective memory functions may be defined as either event-based or time-based. For example, some predefined external event may trigger the retrieval of the intention to act, or alternatively, the trigger may be the elapse of a given period of time. There is evidence to suggest that the two classes utilise neural processes that are at least in part separable. For example, Burgess et al. (2003) and Gilbert et al. (2005) have shown that event-based tasks utilise the frontopolar cortex, including Brodmann area 10 (BA10). Similar findings were reported by Fleming et al. (2008) in patients with frontally based traumatic brain injury, particularly in relation to event-based PM. More recently, PET scanning has revealed that while the left superior frontal gyrus was involved in both types of tasks, different areas within this structure were found to be activated. Furthermore, in addition to the frontopolar cortex, the time-based tasks also activated more diverse regions, including anterior medial frontal regions, the right superior frontal gyrus and the anterior cingulate (Okuda et al. 2007). Given the clear dependence of PM on medial temporal/hippocampal processes and on the PFC, it is also clearly of relevance that ecstasy/polydrug-related deficits have been observed on tasks supported by these structures, including aspects of executive functioning (see Murphy et al. 2009 for a review). It would therefore be of value to determine whether or not the drug-related deficits in medial temporal processes and in PFC functions are responsible for the ecstasy/polydrug-related deficits that have been observed in PM.

While a number of researchers have used self-report measures to investigate PM deficits among illicit drug users (Heffernan et al. 2001a, b; Montgomery and Fisk 2007; Rodgers et al. 2001, 2003), to date, relatively few studies in this area have used laboratory tests of prospective memory. McHale and Hunt (2008) administered two simple laboratory tests: remembering to press a timer 10 min after being instructed to do so and remembering to post an envelope back to the experimenter 2 days after the test session. Cannabis users were found to be impaired on both of these measures. A popular recent addition to laboratory measures of PM is the 'virtual week' paradigm. This PM test is a board game completed in the laboratory, in which the participant is required to execute previously learned tasks at specified points as they progress around the board at specific times or in conjunction with specific events. This measure has featured in a number of studies. For example, deficits were observed on this measure among currently abstinent ecstasy users including those who used infrequently (Rendell et al. 2007a). Long-term abstinent methamphetamine users were also found to be impaired on the measure relative to a drug naive control group (Rendell et al. 2009). Furthermore, impairments were also evident in measures of verbal learning and delayed recall (RAVLT), forward and backward digit span and the Hayling Sentence Completion Task (believed to load on the inhibitory executive process). The extent of the methamphetamine-related effect in PM was found to co-vary substantially with the degree of impairment on the Hayling task (Rendell et al. 2009). In other research utilising the virtual week, Leitz et al. (2009) demonstrated that performance was impaired following the acute administration of alcohol. However, in a subsequent study, the deficit was eliminated when individuals were instructed simulate the required actions at the time of encoding (by imaging the full sensory aspects of the context in which the action was to be completed; Paraskevaides et al. 2010). The measure has also been used to investigate the basis of PM deficits in individuals with mild cognitive impairment and dementia (Thompson et al. 2010), multiple sclerosis (Rendell et al. 2007b) and schizophrenia (Henry et al. 2007).

While the virtual week paradigm has its merits, before the PM element can be completed, it is necessary to learn each of the ten particular responses that is paired with specific locations on the board and select the appropriate response from among the set of available alternatives each time a PM action is triggered. This is made easier by the fact that some responses are common to different tasks. However, the test clearly has an associative learning component, and Montgomery et al. (2005a) have demonstrated that ecstasy users are impaired on paired-associative learning. Thus, it is possible that some of the deficits evident on the virtual week might be attributable to this aspect rather than the PM components. That said, it is worthy of note that just over half of the virtual week, PM sub-tasks are regular and more repetitive in nature, and thus, more readily learned. It is the remaining more irregular tasks that have a more substantial learning requirement. Interestingly, ecstasy users performed worse on these irregular virtual week tasks, recording 65% of the level of correct responses achieved by non-users, while for regular tasks, the percentage was 83% (computed from Table 2; Rendell et al. 2007a). This suggests that performance is indeed adversely affected by the learning component. Nonetheless, it must be acknowledged that there was no statistically significant interaction between user group and task type with users demonstrating a significant deficit overall. Thus, while group differences in learning may partially account for the virtual week results, the outcomes obtained are nonetheless consistent with an ecstasy-related PM deficit.

In our previous study (Hadjiefthyvoulou et al. 2010), in order to minimise the learning requirement, we used a small number of more simple PM tasks, for each of which only a single stimulus–response paring needed to be learned. We also used the Rivermead Behavioural Memory Test (RBMT; Wilson et al. 1999) battery, which includes three separate PM tasks. In our study, only one of the three RBMT PM measures produced statistically significant ecstasy/polydrug-related deficits. However, the RBMT has been criticised as lacking the sensitivity to detect memory problems in non-clinical populations (Spooner and Pachana 2006). Thus, it may be that the test was not appropriate for the university-based sample of recreational drug users, which was featured in our previous study. A more up-to-date test battery that is sensitive to individual differences, both within clinical and normal populations, is the Cambridge Prospective Memory Test (CAMPROMPT; Fleming et al. 2008; Groot et al. 2002; Wilson et al. 2005). The purpose of the present study is to confirm and extend our previous findings utilising the more sensitive CAMPROMPT measure. At the same time, we will take measures of executive functioning and retrospective memory in order to establish the extent to which any ecstasy/polydrug deficits in PM that are uncovered are mediated by deficits in those memory and executive functions that are known to underpin PM processes. This aspect was not addressed in our previous study. A further innovation in the present study is the inclusion of a cannabis-only control group (i.e. individuals whose illicit drug use is restricted to cannabis). Using self-report measures, we (Fisk and Montgomery 2008) have previously documented PM deficits among cannabis-only users (relative to non-users of illicit drugs). However, we have not previously assessed a cannabis-only user group on laboratory measures of PM and not in relation to ecstasy/polydrug users. It is expected that both illicit drug-using groups will perform worse than non-users of illicit drugs on the CAMPROMPT measures. No prediction is made in relation to PM differences between the two illicit drug-using groups.

Method

Design and analytical strategy

A between-participants design was employed with drug-using group with three levels (ecstasy/polydrug, cannabis-only and non-users of illicit drugs) as the independent variable. The dependent variables were the CAMPROMPT time and event-based PM scores. Background variables and the executive and recall measures were also assessed for group differences.

Pearson's correlation coefficients were calculated between the PM measures and the executive and recall measures, respectively. Regression analyses were conducted with the PM measures as dependent variables. In each regression, those variables that were significantly correlated with the PM measures and any background measures, yielding statistically significant drug-related differences, were included as predictors. Since the drug use IV had nominal level of measurement, it was not possible to include it directly in the regression. Following the procedure outlined by Tabachnick and Fidell (2007), group differences were incorporated into the regression by constructing two dichotomous variables. In the first, ecstasy/polydrug users were coded as '1' and all other persons coded as '0'; in the second, cannabis-only users were coded as '1' with all other persons coded as '0'. In this way, it was possible to establish whether each group accounted for statistically significant unique variance while controlling for the effects of the other predictors.

Participants

Twenty-nine ecstasy/polydrug users (12 females), 12 cannabis-only users (7 females) and 18 non-users of illicit drugs (16 females) took part in this investigation (for

demographic details, see Table 1). The gender composition differed significantly between the groups with females predominating among the non-illicit user group and males among the ecstasy/polydrug users, $\chi 2$ (N=59, DF=2) = 10.40, p<0.01. Participants were recruited via direct approach to university students and the snowball technique, i.e. word-of-mouth referral (Solowij et al. 1992). All participants were university students attending the University of Central Lancashire (UCLAN) or Liverpool John Moores University (LJMU).

Materials

A background drug-use questionnaire that has been previously employed by us (Montgomery et al. 2005b) assessed the history of illicit drug use and estimated the total lifetime use, frequency of use, recent consumption, as well as the period of abstinence for each drug (e.g. ecstasy, cannabis, amphetamines, cocaine etc.). Fluid intelligence was measured via Raven's Progressive Matrices (Raven et al. 1998), and a further questionnaire assessed the participant's age and gender, the number of years of education and their current use of alcohol and cigarettes.

Prospective and retrospective memory questionnaire (PRMQ; Crawford et al. 2003). The PRMQ provides a self-report measure of prospective and retrospective memory slips in everyday life. It consists of 16 items, 8 referring to prospective memory failures, e.g. 'Do you decide to do something in a few minutes time and then forget to do it?' and 8 concerning retrospective failures, e.g. "Do you fail to recognize a place you have visited before?". Participants were asked to specify "how often these things happened to them on a 5-point scale" very often, quite often, sometimes, rarely, never. Ratings were subsequently assigned numerical values of 5 (very often) to 1 (never). A total score for each subscale (prospective memory and retrospective memory) was also calculated with minimum score of 8 and maximum score of 40, with higher scores indicative of more memory problems.

Rey Auditory Verbal Learning Test (RAVLT; based on Rey 1964). The RAVLT is a test developed to evaluate verbal learning and memory. A list (list A) of 15 words was presented to the participant orally, with the aid of an audio recording device, for five consecutive times. At the end of each trial, the participant was asked to recall as many words as possible from the list. After the fifth trial, an interference list (list B), also consisting of 15 words, was read to the participant, after which she/he was asked to recall as many words as possible from the interference list. Immediately following this, the participant was again asked to recall the words from list A without hearing it again (trial 6). Next, after a 20-min interval, the participant was asked to remember the words from list A (trial 7), after which a recognition test was administered. For the recognition test, a list consisting of the 15 words from list A and 15 distracter words was read to the participant, and the individual was asked to indicate whether the word belonged to list A or not. A number of outcome measures were produced; first, the total number of words correctly recalled over trials one to five; second, a measure of proactive interference (number correct on trial 1 minus number correct on the interference list); third, retroactive interference (number correct on trial 5 minus number correct on trial 6); and fourth, a measure of decay (number correct on trial 5 minus number correct on trial 7).

Memory compensation questionnaire (MCQ; Dixon et al. 2001). The MCQ is a 44-item self-report measure assessing the variety and number strategies the participant uses to compensate for deficient memory performance. The MCQ is comprised of seven subscales: external (e.g. "Do you use shopping lists when you go shopping?"); internal (e.g. "Do you take your time to go through and reconstruct an event you want to remember?"); time (e.g. "Do you ask people to speak slowly when you want to remember what they are saying?"); reliance (e.g. "When you want to remember an important appointment, do you ask somebody else (for example, spouse or friend) to remind you?"); effort (e.g. "Do you put in a lot of effort when you want to remember an important conversation with a person?"); success (e.g. "When you want to remember a newspaper article, is it important to you to remember it perfectly?"); and change (e.g. "Do you use such aids for memory as notebooks or putting things in certain places more or less often today compared to 5–10 year ago?"). Responses for each item are presented on a five-point scale, with higher scores representing more frequent use of the specified compensatory behaviour (1=*never*, 5=*always*) with some items being reversely scored.

Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) (Roth et al. 2005). The BRIEF-A is a 75-item measure of executive function. For each item, the participant responds on a three-point scale: never, sometimes and often. The measure provides indicators of nine aspects of executive functions. These map onto two higher level indices the Behavioral Regulation Index (BRI) and the Metacognitive Index (MI). The BRI refers to the ability of the individual to maintain appropriate regulatory control of their own behaviour and emotional responses and is comprised of four subscales: inhibit (e.g. "I tap my fingers or bounce my legs"); shift (e.g. "I have trouble changing from one activity to another"); emotional control (e.g. "I have angry outbursts"); and self-monitor (e.g. "I don't notice when I cause others to feel bad or get mad until it is too late"). The MI refers to the individual's ability to systematically solve problems through effective planning and organization. It relates directly to the ability to engage in active problem solving across a variety of contexts and is

comprised of five subscales: initiate (e.g. "I need to be reminded to begin a task even when I am willing");working memory ("I have trouble concentrating on tasks (such as chores, reading or work)"); plan/organize (e.g. "I get overwhelmed by large tasks"); task monitor (e.g. "I make careless errors when completing tasks"); and organization of materials (e.g. "I am disorganized"). For both the BRI and the MI, higher scores are indicative of more executive dysfunction.

The Cambridge Prospective Memory Test (CAMPROMPT) (Wilson et al. 2005). The CAMPROMPT is a laboratory measure of prospective memory that consists of a total of six prospective memory tasks, three cued by time and three cued by events. Participants were asked to work on some distractor tasks such as word-finder puzzles or a general knowledge quiz for a 20-min period while they had to remember to perform the prospective memory tasks. The participants were allowed to spontaneously use strategies, such as taking notes, to help them remember. Two of the three time-based tasks were cued by a countdown kitchen timer, and the participant had to remind the experimenter not to forget his/her mug or keys when there were 7 min left to the end of the session. In the second task, when the timer showed 16 min, the examiner asked the participant to remember that "in 7 minutes time", he/she had to stop whichever task they were on and change to another. The third time-based task was cued by a clock. The participant was asked at a specific time (e.g. 10 past 11; 5 min after the 20-min session) to remind the examiner to ring the reception/garage. For the event-based tasks, the participant was asked: (1) to return a book to the examiner when he/she came to a question about the television program 'EastEnders' during the general knowledge quiz; (2) to return an envelope with "MESSAGE" written on it when he/she was reminded that there were 5 min left in the test; and finally, (3) when the examiner informed him/her that the session was over, to remind the examiner to pick up five objects that had been hidden at the beginning of the session. Six points were awarded for each subtask that was successfully completed, unaided. If the task was completed after a single general prompt from the experimenter, then four points were awarded. Alternatively, participants were awarded two points if a second more specific prompt was required, one point if after prompting, the required action was completed on the second attempt and no point if the participant failed to complete the required action after prompting. Total scores were then generated on time-based and event-based subscales, each scoring a maximum of 18, with higher scores reflecting better prospective memory performance. The validity and reliability of the CAMPROMPT has been documented in a number of studies (i.e. Fleming et al. 2008; Groot et al. 2002; Wilson et al. 2005).

Procedure

Participants were informed of the purpose of the investigation and their right to withdraw at any time. After consent had been obtained, the tests were administered under laboratory conditions. The drug-use questionnaire (Montgomery et al. 2005b) was administered first followed by the Raven's progressive matrices (Raven et al. 1998), the age/education questionnaire, the PRMQ (Crawford et al. 2003), the MCQ (Dixon et al. 2001) and the BRIEF-A (Roth et al. 2005) questionnaires. Finally, the RAVLT and the CAMPROMPT (Wilson et al. 2005) tests were administered. Participants were fully debriefed, paid £20 in Tesco store vouchers and given drug education leaflets. The University of Central Lancashire's Ethics Committee approved the study. Data for the BRIEF-A obtained in the present study have been included with similar data that were collected previously by us from another group of participants and are the subject of a separate publication (Hadjiefthyvoulou et al. 2010). Participants also performed a range of other tasks that are beyond the scope of the present investigation.

Results

As is apparent from inspection of Table 1, with the exception of tobacco smoking, the groups did not differ

Table 1 Age, intelligence, years of education, cigarette and alcohol use by group

	Ecstasy/polydrug users			Cannabis-only users			Nonusers			p^a
	Mean	SD	Number	Mean	SD	Number	Mean	SD	Number	
Age (years)	21.17	1.79	29	21.92	1.56	12	20.44	2.28	18	ns
Raven's progressive matrices (maximum 60)	39.21	8.39	29	40.25	7.35	12	40.72	8.90	18	ns
Years of education	15.27	2.44	26	14.92	4.06	12	16.00	2.00	18	ns
Cigarettes per day	7.42	4.48	12	9.00	3.58	6	15.00	–	1	.017
Alcohol (units per week)	13.41	12.08	27	15.18	12.95	11	9.47	14.70	15	ns

[a] For one-way ANOVA, except cigarettes where chi-squared test was used

significantly on any of the background variables. The proportion of smokers differed significantly between the groups, $\chi 2$ (N=53, df=2)=8.09, p=0.017; however, the expected frequency in one of the cells, 3.94, was below the critical value of 5, thus, although there are clear differences between the groups with 40–50% of illicit drug users regularly smoking and only one nonuser, the statistical significance of this outcome cannot be confirmed by chi-square. The daily consumption of cigarettes did not differ significantly between ecstasy/polydrug and cannabis-only users, t (16) = 0.75, p>0.05. Indicators of illicit drug use may be found in Table 2. It is clear that the ecstasy/polydrug group used a range of other illicit substances in addition to ecstasy, including cannabis, cocaine and ketamine. Furthermore, for all of the measures of drug use, the median was substantially less than the mean; indeed, in all cases, the measures exhibited a positive skew, with a small minority of users demonstrating relatively high levels of use, while the majority were clustered around the median. Members of both illicit drug-using groups had also used poppers (amyl nitrate) during the preceding 3 months (as had one individual among the non-illicit drug users). It is worthy of note that the various indicators of cannabis use did not differ significantly between the two illicit drug-using groups.

Data screening revealed that there were no univariate outliers on the PM scores. However, the distribution of the event-based PM measure deviated significantly from normal exhibiting a negative skew. Following the data transformation procedure recommended by Tabachnick and Fidell (2007), the event-based scores were reflected and the square root was taken. This means that trends in the transformed variable are reversed so that higher scores are indicative of worse performance. Subsequent tests revealed that the distribution of the transformed variable did not deviate significantly from normal. Table 3 contains both the untransformed and the transformed event-based PM measure. However, the analyses reported below relate to the latter.

Inspection of Table 3 reveals that compared to the other two groups, non-illicit drug users displayed better PM performance on both the time and event-based measures. The ecstasy/polydrug users' scores were the worst, while cannabis-only users' scores were between those of the other two groups. These trends were associated with statistically significant overall group differences. Subsequent post-hoc tests revealed that with respect to the event-based PM

Table 2 Indicators of illicit drug use

	Ecstasy/polydrug users				Cannabis-only users				p[1]
	Median	Mean	SD	Number	Median	Mean	SD	Number	
Total use									
Ecstasy (tablets)	194	640.86	1284.99	29	–	–	–	–	–
Cannabis (joints)	728	3048.84	5297.53	25	1,118	2242.58	3307.71	12	ns
Cocaine (lines)	416	1037.89	1282.60	19		–	–	–	–
Amount consumed in previous 30 days									
Ecstasy (tablets)	0	3.14	8.28	29	–	–	–	–	–
Cannabis (joints)	1	26.08	45.80	25	0.50	22.25	33.05	12	ns
Cocaine (lines)	2	8.16	12.74	19	–	–	–	–	–
Frequency of use (times per week)									
Ecstasy	0.04	0.24	0.43	29	–	–	–	–	–
Cannabis	0.25	1.87	2.52	25	0.15	1.86	2.71	12	ns
Cocaine	0.06	0.28	0.36	19	–	–	–	–	–
Weeks since last use:									
Ecstasy	12	47.00	76.32	29	–	–	–	–	–
Cannabis	4	20.34	37.13	25	7.50	73.32	113.69	12	ns
Cocaine	6	15.40	24.36	22	–	–	–	–	–
Use of other drugs during the previous 3 months	Percent				Percent				
Amphetamine	3				0				
Ketamine	31				8				
LSD	3				0				
Magic mushrooms	3				0				
Poppers	45				17				

[a] For Mann–Whitney U test

Table 3 Outcomes for the prospective memory, executive functions and memory measures by group

	Ecstasy/polydrug users			Cannabis-only users			Nonusers			*F* value	Pairwise comparisons (Tukey's test)[a]		
	Mean	SD	Number	Mean	SD	Number	Mean	SD	Number		E/PU vs CO	E/PU vs. Non	CO vs. Non
CAMPROMPT													
Event-based PM	12.48	3.27	29	15.08	2.39	12	16.00	1.68	18	na			
Event-based PM[b]	2.46	0.69	29	1.90	0.59	12	1.66	0.50	18	10.10***	0.027	0.000	
Time-based PM	10.45	3.94	29	12.33	5.65	12	15.11	3.51	18	6.79**		0.001	
BRIEF													
Behaviour regulation	54.50	10.83	24	48.91	11.79	11	50.43	7.57	14	1.38			
Metacognition	73.96	13.59	24	70.55	12.30	11	65.69	15.82	16	1.66			
Retrospective memory questionnaire	21.63	7.09	27	19.83	5.77	12	16.65	4.33	17	3.48*		0.029	
MCQ													
External	25.18	7.61	28	24.25	9.30	12	30.67	4.84	18	3.96*		0.041	0.055
Internal	31.32	5.98	28	29.25	6.84	12	33.17	7.88	18	1.21			
Time	14.18	3.39	28	12.67	4.64	12	15.11	3.86	18	1.48			
Reliance	14.79	4.28	28	15.25	4.20	12	13.22	4.86	18	0.95			
Effort	20.61	4.01	28	20.67	3.87	12	21.33	4.19	18	0.19			
Success	14.04	3.29	28	12.83	3.95	12	13.18	3.91	17	0.58			
Change	19.93	3.89	28	21.50	3.45	12	20.33	4.51	18	0.64			
RAVLT													
Learning T1-T5	39.04	9.38	28	40.58	11.11	12	45.22	9.60	18	2.21			
Proactive	0.89	1.77	28	1.58	1.38	12	0.94	1.47	18	0.83			
Retroactive	1.57	2.41	28	2.00	1.86	12	1.39	1.46	18	0.33			
Decay	2.00	2.17	27	2.00	1.76	12	1.22	1.26	18	1.10			

***$p<0.001$; **$p<0.01$; *$p<0.05$

[a] Only statistically significant differences or differences approaching statistical significance are reported

[b] This is the transformed variable where higher scores are indicative of worse performance

measure, ecstasy/polydrug users performed significantly worse than the other two groups, which in turn, did not differ significantly from each other. The only statistically significant pairwise difference on the time-based PM measure was with respect to the ecstasy/polydrug group, which performed significantly worse than the non-illicit drug users group.

With regard to the BRIEF-A, the MCQ and the RAVLT measures, two univariate outliers were identified, one on the decay score of the RAVLT and the other on the change score of the MCQ. These were replaced by the next highest/lowest score on the particular measure, plus/minus one (Tabachnick and Fidell 2007). On the basis of Mahalanobis distance, no multivariate outliers were detected. Examination of Table 3 reveals that there were statistically significant group differences on only two of the non-PM measures. First, the groups differed significantly on Crawford et al. (2003) self-report retrospective memory measure, with ecstasy/polydrug users scoring significantly worse than non-illicit drug users (neither of the other pairwise comparisons were statistically significant). Second, non-illicit drug users made significantly more use of external memory aids compared to ecstasy/polydrug users. The difference between the nonusers and cannabis-only users on the same measure approached significance.

For the sample as a whole, correlations between the PM and the other measures are set out in Table 4. The event-based PM measure was significantly correlated with the time-based measure (as might be expected). It was also significantly correlated with two of the retrospective memory measures: the Crawford et al. (2003) self-report measure and the recall score on the RAVLT over trials 1–5. Unsurprisingly, better retrospective memory performance was associated with better PM performance (High scores on the Crawford et al. measure are indicative of retrospective memory problems, while the reverse is true of the time-based and untransformed event-based PM measures. Hence, the correlation with the Crawford et al. measure is negative in the former case and positive in relation to the transformed event-based PM measure.) The correlation between the 'Reliance' subscale on the MCQ and the event-based PM measure approached statistical significance: as reliance on others as an aid to memory increased, so PM performance decreased. Interestingly, the event-based PM measure was not significantly correlated with either of the BRIEF-A composite scales. The time-based PM measure, like the event-based, was significantly correlated with the Crawford et al. (2003) self-report retrospective memory measure, and with the recall score on the RAVLT over trials 1–5, the correlation approached significance; in both cases, better retrospective memory was associated with better time-based PM performance. The correlation between the time-based PM measure and the BRIEF-A metacognitive index also approached statistical significance. Higher executive functioning was associated with better time-based PM performance.

In order to evaluate the unique contributions of each of the predictors to PM performance, two regressions were run with respectively the transformed event-based PM measure and the time-based PM measure as dependent variables. Variables were included as predictors if they were significantly correlated (in bivariate terms) with the dependent variable or if they were associated with significant group differences on the dependent measure. In instances where the univariate or bivariate outcomes approached statistical significance, the variables in question were also included as predictors. The results for the regression analyses are set out in the penultimate two columns of Table 4. None of the individual predictors for time-based PM were statistically significant; however, the overall model accounted for statistically significant variance (r^2=0.285, p<0.05). The likely implication of this is that there was a degree of overlapping variance with pairs or larger combinations of predictors sharing pooled variance with the dependent variable, making it impossible to allocate statistically significant unique variance to any one predictor. More specifically, it is possible that the statistically significant drug-related PM effects apparent in the ANOVA are in part mediated by drug-related differences on the other predictors, in particular, aspects of retrospective memory.

Switching the focus to event-based PM, the regression model accounted for statistically significant variance, (r^2= 0.378, p<0.01). Of the individual predictors, the recall score on the RAVLT over trials 1–5 approached statistical significance; unsurprisingly, better recall was associated with better PM performance. Of the other predictors, ecstasy/polydrug users (relative to other participants) accounted for statistically significant unique variance (reflecting the ecstasy/polydrug-related PM deficit). Thus, it appears that the ecstasy/polydrug effect on event-based PM cannot be entirely attributed to drug-related differences in retrospective memory and executive functioning. Surprisingly, the dichotomous gender variable was also statistically significant as a predictor. Given the manner in which the variable was coded and the sign of the beta weight, this would suggest that females were performing worse than males on the event-based PM task. Paradoxically, a subsequent t test revealed no statistically significant gender difference on the event-based PM task, t (57) = 0.13, p>0.05. However, further examination of the gender differences within the drug-using groups showed that the gender deficit was only apparent among ecstasy/polydrug users. Among other participants, females were actually performing better. This raised the possibility of an interaction between gender and ecstasy/polydrug use in determining event-based PM scores. In order to test this

Table 4 The relationship between time and event-based PM and executive and memory functions

Correlate/IV	Simple correlation		Standardised beta weight and (squared semi-partial correlation from regression)		
	Event-based PM[a]	Time-based PM	DV=event-based PM[a]	DV=time-based PM	DV=event-based PM[a]
CAMPROMPT					
Event-based PM[1]		−0.523****			
Time-based PM	−0.523****				
BRIEF					
Behaviour regulation	0.184	−0.105			
Metacognition	0.130	−0.248*		0.034 (0.001)	
Retrospective memory questionnaire	0.270**	−0.381***	0.019 (0.000)	−0.361 (0.038)	−0.026 (0.000)
MCQ					
External	−0.075	0.052	−0.172 (.014)	0.097 (0.003)	−0.154 (0.012)
Internal	−0.003	0.007			
Time	−0.084	−0.068			
Reliance	0.258*	−0.184	0.180 (0.021)		0.194 (0.024)
Effort	−0.193	−0.064			
Success	0.019	0.008			
Change	0.035	−0.021			
RAVLT					
Learning T1-T5	−0.273**	0.244*	−0.239 (0.051)*	0.217 (0.040)	−0.208 (0.038)*
Proactive	0.008	−0.042			
Retroactive	0.095	0.033			
Decay	0.152	−0.060			
Gender			0.314 (0.060)**	−0.090 (0.004)	0.012 (0.000)
Ecstasy/polydrug versus all others			0.555 (0.138)***	−0.277 (0.034)	0.218 (0.011)
Ecstasy/polydrug versus all others by Gender interaction			–	–	0.423 (0.053)**
Cannabis-only versus all others			0.095 (0.005)	−0.130 (0.009)	0.037 (0.001)
			r^2=0.378	r^2=0.285	r^2=0.431
			F(7,47) = 4.09, p<0.01	F(7,41) = 2.34, p<0.05	F(8,46) = 4.36, p<0.001

****p<0.001; ***p<0.01; **p<0.05; *p<0.10

[a] This is the transformed variable where higher scores are indicative of worse performance

possibility, the regression was repeated, this time, in addition to the ecstasy/polydrug and gender variables, their product was included as an independent variable in order to establish whether or not there was a statistically significant interaction. The results are set out in the final column of Table 4, inspection of which reveals that in this expanded model, only the interaction between gender and ecstasy/polydrug use accounts for statistically significant unique variance. Given the manner in which the dichotomous variables were coded, the positive beta coefficient indicates that female ecstasy/polydrug users were especially impaired on the event-based CAMPROMPT task. By way of clarification subsequent analyses revealed that the mean scores for female ecstasy/polydrug users was 65% higher than that for female non-ecstasy users, while the equivalent difference for males was just 16% (as noted above higher scores are indicative of poorer event-based PM performance).

The incidence of polydrug use among the ecstasy users makes it difficult to unambiguously attribute the impairments evident in PM to specific illicit drugs. In an attempt to address this issue, Table 5 contains the simple and partial correlation coefficients between aspects of drug use on the one hand and the two PM measures on the other. Where an individual does not use a specific drug, their usage has been coded as zero. Inspection of the Table reveals that only one aspect of drug use is correlated with time-based PM, i.e. the current frequency of cannabis use. In view of this outcome, no partial correlations were calculated for time-based PM. By way of contrast, virtually all aspects of drug use were correlated with event-based PM. However, when controls for the use of other illicit drugs were entered, aspects of ecstasy use were no longer significantly correlated with event-based PM; rather, it was aspects of cannabis and cocaine use which yielded statistically significant correlations.

The illicit drug users among our sample were requested to refrain from cannabis use for 24 h prior to testing and from cocaine, ecstasy and other drug use for 7 days prior to testing. In order to address the possibility that the PM differences that we observed were due to post-intoxication effects, we excluded all individuals who indicated that they had consumed ecstasy, cocaine or cannabis during the 10 days prior to testing. This reduced the size of the cannabis-only group, thereby reducing statistical power such that three-way group comparisons were not meaningful. For this reason, the non-illicit drug users and cannabis-only users were merged to form a single group (drug naive/cannabis only $n=25$; ecstasy/polydrug $n=14$). For the event-based PM task, the corresponding means (standard deviations) for the ecstasy/polydrug and combined drug naive/cannabis-only users were respectively 2.20 (0.73) and 1.69 (0.47) which differed significantly, $F(1,37) = 7.10$, $p< 0.05$. For the time-based PM task, the equivalent figures were respectively 10.92 (3.65) and 14.40 (4.65) which again differed significantly, $F(1,37) = 5.78$, $p<0.05$. Thus, the ecstasy/polydrug-related PM deficits remained statistically significant following removal of those persons who indicated that they had used illicit drugs during the previous 10 days.

Discussion

On the event-based PM measure, ecstasy/polydrug users were impaired relative to both cannabis-only and nonusers of illicit drugs. This group was also impaired relative to nonusers on the time-based measure. While a trend was evident on both measures with ecstasy/polydrug users performing worse, cannabis-only users achieving intermediate levels of performance and non-illicit drug users

Table 5 The relationship between time and event-based PM and indicators of illicit drug use

	Event-based PM[a]		Time-based PM
	Simple correlation	Partial correlation[b]	Simple correlation
Cannabis			
Total lifetime use	0.246*	0.208	−0.154
Consumed in last 30 days	0.259*	0.230*	−0.158
Frequency	0.338**	0.390**	−0.286*
Cocaine			
Total lifetime use	0.339**	0.328**	−0.139
Consumed in last 30 days	0.257*	0.261*	−0.126
Frequency	0.403**	0.416***	−0.133
Ecstasy			
Total lifetime use	0.261*	−0.002	−0.160
Consumed in last 30 days	0.210	−0.036	−0.058
Frequency	0.268*	−0.028	−0.065

***$p<0.001$; **$p<0.01$; *$p< 0.05$; one-tailed

[a] Correlation for the transformed variable

[b] Controlling for the use of other drugs on the measure in question, e.g. the correlation between total use of cannabis and PM controlling for the total use of cocaine and total use of ecstasy

performing best, cannabis-only users did not differ significantly from nonusers of illicit drugs on either PM measure. The ecstasy/polydrug-related deficit observed here in relation to non-illicit drug users is consistent with previous findings from our own and other laboratories using self-report (Hadjiefthyvoulou et al. 2010; Heffernan et al. 2001a, b; Montgomery and Fisk 2007; Rodgers et al. 2001, 2003) and laboratory measures (Hadjiefthyvoulou et al. 2010; Rendell et al. 2007a). They also demonstrate the utility of the CAMPROMPT measure in detecting individual differences in PM performance among non-clinical populations augmenting the existing literature in this regard (Groot et al. 2002; Wilson et al. 2005).

For the most part, ecstasy/polydrug deficits were not evident on the other measures that were administered. Deficits were only evident on the retrospective memory questionnaire and nonusers of illicit drugs were significantly more likely to report using external memory aids in everyday contexts. Cannabis-only users did not differ significantly from either of the other two groups on any of the non-PM measures.

For the sample as a whole, individual differences on both PM measures were significantly correlated with outcomes on the retrospective memory questionnaire and with the RAVLT recall scores for the first five trials. In both cases, better retrospective memory was associated with better PM performance. Scores on the BRIEF-A metacognitive index were also related to performance on the time-based PM task with better executive functioning associated with improved PM performance; however, this trend only approached statistical significance two-tailed (although given the directional nature of the anticipated effect, the outcome is statistically significant on a one-tailed basis). These findings are consistent with the outcomes reported above linking PM performance with medial temporal functioning (Adda et al. 2008; Martin et al. 2007) and with PFC processes (e.g. Okuda et al. 2007).

In order to establish the extent to which drug-related deficits on the PM tasks were mediated by deficits in retrospective memory and executive functions, regressions were run with each of the PM variables as the criterion. For the time-based PM task, the dummy variable representing the effects of ecstasy/polydrug use was not statistically significant as a predictor. Indeed, although the model as a whole accounted for statistically significant variance, none of the individual predictors were statistically significant. This suggests that any effects associated with ecstasy/polydrug use covary with individual differences in the other predictors and with the criterion leaving open the question of whether drug use per se adversely affects time-based PM.

The regression analysis for event-based PM yielded different results with only ecstasy/polydrug use and gender, accounting for statistically significant unique variance. A further regression revealed that the two predictors, in fact, significantly interacted, such that the ecstasy/polydrug-related deficit was most pronounced amongst female users. Indeed, neither of the main effects was statistically significant in the amended model. Of the other predictors in the model, the RAVLT recall scores for the first five trials approached statistical significance. It is noteworthy that the sum of the squared semi-partial correlation coefficients (0.139) is far less than the overall R-squared value (0.431), indicating that most of the explained variance in the criterion reflects the overlapping effects of two or more predictors.

The emergence of gender-specific illicit drug-related effects is not without precedent. For example, women who were heavy users of cannabis were impaired relative to female light users on visuo-spatial memory, while no such deficit emerged among male cannabis users (Pope et al. 1997). Gender was also found to moderate the extent of ecstasy-related deficits in design fluency (with female users exhibiting a deficit, while male users actually performed better than controls), although it was not a moderating factor on deficits observed in verbal learning (Medina et al. 2005). Reneman et al. (2001) found that female ecstasy users exhibited a larger reduction in serotonin transporter densities relative to males. However, in a subsequent study in which ecstasy users were found to be impaired in various aspects of memory performance, female users were not significantly more affected than male users (Reneman et al. 2006). It is also worthy of note that the gender–drug use interaction only emerged on event-based PM tasks and not on the time-based PM measure. Thus, the apparent gender difference observed in the present study should be treated with a degree of caution.

While deficits in aspects of PM are clearly evident among ecstasy/polydrug users, what is less clear is which illicit drug or drugs may be responsible for these deficits. It is striking that when the use of other drugs is controlled through partial correlation, no aspect of ecstasy use is statistically significant as a predictor of PM performance. It is also worthy of note that while cannabis-only users were not significantly impaired relative to non-illicit drug users, they did performance worse on both PM measures compared with controls, and cannabis use among the whole sample was significantly correlated with event-based PM even following statistical controls for the effects of other illicit drugs. Higher levels of consumption during the previous 30 days and increasing frequency of use were associated with poorer event-based PM performance. Thus, the present results suggest that cannabis use does adversely affect PM performance, although the effect may be accentuated among polydrug users. The present results augment those of other studies in which cannabis-related PM deficits have been observed, (e.g. Fisk and Montgomery 2008; McHale and Hunt 2008; Rodgers et al. 2003).

A striking feature of the present results was that cocaine use was significantly correlated with event-based PM performance even following statistical controls for the use of other illicit drugs. Increasing lifetime dose, greater consumption during the previous 30 days and an increased frequency of use are all associated with poorer event-based PM performance. This replicates the results of our previous study (Hadjiefthyvoulou et al. 2010), this time, with a different sample and with an alternative laboratory-based PM measure. As far as we are aware, the present study and our previous one are the first to link the recreational use of cocaine with prospective memory deficits. The mechanisms through which cocaine might adversely affect PM functions remain unclear. On the basis of the results from their fMRI study, Tomasi et al. (2007) argue that a prior history of cocaine use disrupts the operation of those dopaminergic systems in the prefrontal cortex, which underpin executive functioning. Given the key role of executive functions in supporting PM processes, this might account for the adverse association between cocaine use and PM functioning.

It is also noteworthy that PM deficits have been observed in Parkinson's patients (Kliegel et al. 2005), and since the disease is characterised by disruption of dopaminergic functioning in the corticostriatal pathway, this is consistent with a direct role for dopamine in supporting PM functions. Evidence, consistent with this proposition, emerged in a recent study by Costa et al. (2008), in which administration of L-dopa significantly improved PM performance in a sample of Parkinson's patients relative to an unmedicated condition. As noted above, animal studies have also suggested a direct role for mesocortical dopaminergic systems in supporting prospective memory processes (Goto and Grace 2008). Since it is known that both cocaine and ecstasy potentially disrupt the functioning of dopaminergic systems, it is possible that the basis of the prospective memory deficits observed in the present study reside in impaired dopaminergic processes in the corticostriatal pathway.

A further possibility is that cocaine might give rise to impairment in medial temporal and hippocampal processes. In a recent study, Fox et al. (2009) found that performance on various aspects of the RAVLT was impaired among an inpatient cocaine-dependent group. Relative to controls, deficits were related to self-report stress levels and within the cocaine-dependent group with raised early morning cortisol levels. Fox et al. attribute the stress-related increase in cortisol levels and the associated memory deficits to hippocampal damage stemming from cocaine use. If this were the case, in the present context, the recall component of PM performance might be compromised among recreational cocaine users, thereby accounting for the results obtained here.

A number of limitations can be identified for this study. First, as with many studies in this area, no objective measure of recent drug use, such as urinalysis or hair analysis, was used. Thus, the period of abstinence cannot be objectively verified. Also, the purity of the ecstasy tablets or any other consumed drug cannot be guaranteed, making it still more difficult to attribute the effects observed here to specific psychoactive drugs. Another important factor that should not be overlooked is that the apparent ecstasy/polydrug-related deficits may not necessarily be a consequence of illicit drug use but instead be due to pre-existing differences between users and nonusers originating before the onset of illicit drug use. In addition, the possibility that current lifestyle differences or the effects of illicit drug use on other physiological processes (e.g. impaired sleep quality) might be the actual cause of the deficits observed in the current study cannot be entirely excluded. A methodological issue that needs to be considered is the relatively small sample size in the present study, which means that the results of the regression analyses need to be treated with caution. Indeed, before definitive statements can be made regarding the relative importance of individual predictors, the regression analysis would need to be replicated with a substantially larger sample. Nonetheless, the present results are potentially informative as a guide for which variables might be incorporated into future research, utilising larger samples. Other methodological aspects of the present study might warrant a different approach in future research. For example, we used a self-report measure of executive functioning rather than laboratory-based measures. It might have been desirable to incorporate laboratory-based tests of executive functioning; however, recent conceptualisations of executive functioning have emphasised the non-unitary nature of these processes, identifying four or more separable processes: updating, inhibition, switching and access to semantic memory (Fisk and Sharp 2004; Miyake et al. 2000) each with a number of specific measures. Furthermore, ecstasy/polydrug users appear to be differentially affected on each of these (Montgomery et al. 2005b). Thus, the inclusion of such a comprehensive test battery would have substantially expanded the length of the test session and was not possible given the resource constraints of the present study. Nonetheless, future research might incorporate such measures, perhaps utilising latent variable analysis, in order to evaluate the potential role of the various executive component processes with respect to a range of different PM measures.

To conclude, the present study intended to determine the impact of ecstasy/polydrug use and cannabis use on event-based and time-based prospective memory using the CAMPROMPT. Measures of executive functioning and retrospective memory were also administered in order to study the extent to which executive processes account for the prospective memory deficits in recreational drug users.

Relative to both drug-naive persons and cannabis-only users, ecstasy/polydrug users performed significantly worse on both event-based and time-based prospective memory tasks, while no significant differences in performance were observed between the cannabis user and nonuser groups. However, consistent with the results of our previous study, recreational use of cocaine was significantly correlated with event-based prospective memory performance, demonstrating the need for a systematic investigation of the potential role of cocaine in accounting for the PM deficits that have been observed here and in other studies.

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