Everyday and prospective memory deficits in ecstasy/polydrug users

Running Head: prospective memory impairments

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Abstract

The impact of ecstasy/polydrug use on real world memory (i.e., everyday memory, cognitive failures and prospective memory) was investigated in a sample of 42 ecstasy/polydrug users and 31 non-ecstasy users. Laboratory-based prospective memory (PM) tasks were administered along with self-report measures of PM to test whether any ecstasy/polydrug-related impairment on the different aspects of PM was present. Self-report measures of everyday memory and cognitive failures were also administered. Ecstasy/polydrug associated deficits were observed on both laboratory and self-report 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.

Key Words: prospective memory, cognitive failures, everyday memory, ecstasy, cocaine, cannabis

An important topic of investigation that has received increasing attention in recent years concerns real world memory processes (i.e., everyday memory, prospective memory, 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 recognise 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, or 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 & Fisk, 2007) and cannabis-only users (Fisk & 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; 2001b) and cannabis related (McHale & 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 utilised self-report measures (Fisk & Montgomery, 2008; Heffernan et al 2001a; 2001b; Montgomery & 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 & Redman, 2008; Cole et al, 2006). This may affect their responses on self-report 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-report measures utilising laboratory measures of the relevant constructs. To date relatively few studies in this area have used laboratory tests of prospective memory. 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 of these limitations, the present research will include laboratory measures of prospective memory which are designed to be more naturalistic and where the PM component is less obvious to the participant.

Cognitive failures and prospective memory are 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 & 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-report 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 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). 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). 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 report 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 (Males=14, Females=28) and thirty one non users (Males=5, Females=26) took part in this investigation. Participants were

recruited via direct approach to university students and the snowball technique i.e. mouth to 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, 2005a). 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-report measures of Real World Memory

Everyday memory: The Everyday Memory Questionnaire (EMQ, Cornish, 2000; Sunderland et al. 1983) is a self-report measure of memory lapses in everyday activities. The measure consists of 27 statements with responses made on a 9-point scale ranging from "not at all in the last 6 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, Cooper, FitzGerald, & Parkes, 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 (Hannon et al, 1995): The Prospective Memory Questionnaire (PMQ) is a self-report 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; Crawford et al, 2005) provides a measure of memory slips of this kind in everyday life. It consists of sixteen items, eight related to prospective memory 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 5-point scale: Very often, quite often, sometimes, rarely, never, resulting in minimum and maximum possible scores of 8 and 40.

The reliability and validity of the CFQ, EMQ and PMQ have been documented previously (see, for example, Hannon et al, 1995; Royle & Lincoln, 2008; Wallace, 2004).

Laboratory measures of Prospective Memory

Prospective Memory Pattern Recognition Test. This test is based on a processing speed task (e.g., see Fisk & Warr, 1996) which was amended so as to provide a laboratory-based measure of prospective memory by the addition of a parallel prospective memory 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 prospective memory 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 '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 prospective memory 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, Kecklund, & Akerstedt, 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 prospective memory. On each occasion, participants who forgot were reminded to fill in the questionnaire.

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 had to write down as many words as he/she could recall from the list. No time constrain was imposed in this regard. A long-term prospective memory 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 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 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 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 question is recalled correctly, 1 if after prompt or 0 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 prospective memory questionnaires (Crawford et al. 2005 and Hannon et al.1995). Next the prospective memory pattern recognition task, the recall PM task and the RBMT-II tasks were administered. 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 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 to 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 a third of non-ecstasy users currently smoked cigarettes.

<<Insert Table 1 about here>>

With regard to illicit drug use, a majority of the ecstasy/polydrug group had in the past or were currently consuming 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, $r=.041$ ($p>.05$, $n=39$), was not statistically significant while that between lifetime ecstasy and cocaine use approached significance, $r=.332$ ($p=.084$, $n=28$). Estimated lifetime use of cocaine and cannabis was also not significantly related $r=.172$ ($p>.05$, $n=29$). 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 PM Measures.

With regard to the laboratory measures of prospective memory, 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 nonusers. From a longer-term perspective during the three weeks following testing non users posted back 77% more delayed recall response sheets compared to users. However, on the time based RMBT-II appointment task, group differences were less evident.

<<Insert Table 2 about here>>

With regard to the event-based tasks, although ecstasy/polydrug users and non-ecstasy users performed similarly on the RMBT-II message task, they 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.

MANOVA with the seven laboratory measures of prospective memory as dependent variables and ecstasy/polydrug user group between participants revealed a statistically significant effect of group, $\Lambda = .598$, $F(7,65) = 6.25$, $p<.001$, partial $\eta^2 = .402$. 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, $\Lambda = .671$, $F(7,62) = 4.34$, $p<.001$, partial $\eta^2 = .329$. 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, $\Lambda = .712$, $F(7,58) = 3.34$, $p<.01$, partial $\eta^2 = .288$. 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-Report Real World memory Measures

Outcomes for the self report 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-report measures of real world memory as dependent variables and ecstasy user group between participants revealed a statistically significant effect of group, $\Lambda = .756$, $F(7,58) = 2.68$, $p<.05$, partial $\eta^2 = .244$. 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, $\Lambda = .786$, $F(7,56) = 2.18$, $p=.05$, partial $\eta^2 = .214$. 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 $\Lambda = .826$, $F(7,52) = 1.57$, $p>.05$, partial $\eta^2 = .174$ 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-report real world memory measures, total cannabis use, $\Lambda = .769$, $F(7,52) = 2.23$, $p<.05$, partial $\eta^2 = .231$; and tobacco use $\Lambda = .723$, $F(7,52) = 2.84$, $p<.05$, partial $\eta^2 = .277$.

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 the Table 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 longer period self-reported fewer cognitive failures.

<<Insert Table 3 about here>>

Relationship between Aspects of Drug Use and the Memory Measures

Table 4 contains the simple Pearson's correlation coefficients between the laboratory and self-report 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 $p<.05$ 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 so 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.

<<Insert Table 4 about here>>

With regard to the self-report measures of real world memory, correlations with lifetime use are generally larger in absolute magnitude for ecstasy compared to cocaine. Similarly, in relation 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-report 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 & Fidell, 2001).

However, while the standardised 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-report measures lifetime ecstasy use is significantly associated with unique variance in the short-term and internally cued Hannon et al (1995) prospective memory measures and frequency of ecstasy use with the cognitive failures measure. The frequency of cannabis use shares unique variance with the short-term prospective memory measure

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 .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 .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 PM and Real World Memory Measures.

Ignoring for the moment drug-related differences, it would be reasonable to expect that the laboratory measures of prospective memory 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 prospective memory 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 recall task where two of the outcomes only approached significance the remaining laboratory tasks did reveal a number of statistically significant intercorrelations. Furthermore, for each of the laboratory tasks performance was correlated with the scores obtained on one or more of the self report measures. Finally, not surprisingly, Table 6 reveals that the outcomes for the self-report measures were also correlated with each other.

<<Insert Tables 5 and 6 about here>>

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 (see Murphy et al 2009, for a review). 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 to 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 prospective memory 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-report measures and have found ecstasy-related deficits, for example, those from our own laboratory (Montgomery & Fisk, 2007) and elsewhere (Heffernan et al 2001a; 2001b; 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

nonusers 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 (2005b) 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 prospective memory. As far as the authors are aware the present study is the first to link recreational use of cocaine with prospective memory deficits. Either lifetime, or frequency of use, or both, were associated with performance on all but one of the laboratory measures of prospective memory 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 utilise the frontopolar cortex, i.e., Brodmann area 10 (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 utilised 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 focussed 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 & 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 PFC 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 nonusers. 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 report 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 report 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. Due 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 (Morgan, 1999; Heffernan et al. 2001a and 2001b) 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 nonusers 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 emphasised the importance of considering whether or not the apparent differences between users and nonusers 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 & Montgomery in press; and 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 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. 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 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.

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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Table 1 Demographical and Background Drug Use Variables for Users and Nonusers

	Ecstasy/Polydrug Users			Non Ecstasy Users			p
	Mean	S.D.	n	Mean	S.D.	n	
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	<.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	<.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:							
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	

1. For weeks since last use, median and inter-quartile range are reported.

Table 2 Scores on Laboratory and Self-Report Measures of Real World Memory for Users and Nonusers

	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	0.62	<.01	<.05	<.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	<.01	<.01	<.05
Second half of test session	9.48	16.26	44.62	39.52	<.001	<.001	<.001
Processing Speed PM Task Errors	1.64	2.55	0.61	1.23	<.05	<.05	<.05
Long Term Recall PM Task (max 3)	0.95	1.32	1.68	1.30	<.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	0.72	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	20.56	5.52	<.05	<.05	Ns

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	-.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)	-.174	.025	.074	-.011
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

Table 4 Correlations between Real World Memory Measures and Lifetime Use and Frequency of Use for the Major Illicit Drugs

Real World Memory Measure	Drug	Lifetime Use		Frequency	
		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	-.276*	-.173†	-.260*	-.207*
	Cocaine	-.254*	-.161	-.330**	-.271*
Self-Report Measures					
Everyday Memory					
Prospective Memory (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*	-.038		
Prospective Memory (Crawford et al)	Ecstasy	.330**	.188†	.253*	.100
	Cocaine	.249*	.097		
	Amphet-amine	.229*	.183†		

*** p<.001; ** p<.01; * p<.05; † p<.10; one-tailed

Table 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)	.026	.190†	.060	.073	-.028	-.182†	
SELF-REPORT MEASURES							
Everyday Memory	-.018	-.041	.140	-.063	-.141	-.033	-.094
Prospective Memory (Hannon et al)							
Short Term	-.096	-.128	-.003	-.230*	-.120	.392***	-.135
Long Term	-.069	-.155	-.139	-.053	-.312**	-.006	-.096
Internally Cued	-.021	-.037	-.014	-.077	-.175†	-.024	.046
Techniques to Remember	-.041	.072	-.048	.024	-.002	.035	.241*
Cognitive Failures	-.174†	-.161†	.007	-.223*	-.323**	.108	-.044
Prospective Memory (Crawford et al)	-.279**	-.190†	-.003	-.201*	-.281**	-.008	-.048

*** p<.001; ** p<.01; * p<.05; † p<.10; one-tailed

Table 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