

LJMU Research Online

Fisk, JE, Montgomery, C and Hadjiefthyvoulou, F

Visuospatial working memory impairment in current and previous ecstasy/polydrug users

http://researchonline.ljmu.ac.uk/id/eprint/1087/

Article

Citation (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

Fisk, JE, Montgomery, C and Hadjiefthyvoulou, F (2011) Visuospatial working memory impairment in current and previous ecstasy/polydrug users. Human Psychopharmacology: Clinical and Experimental, 26 (4-5). pp. 313-321. ISSN 0885-6222

LJMU has developed LJMU Research Online for users to access the research output of the University more effectively. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LJMU Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain.

The version presented here may differ from the published version or from the version of the record. Please see the repository URL above for details on accessing the published version and note that access may require a subscription.

For more information please contact researchonline@ljmu.ac.uk

Visuospatial working memory impairment in current and previous ecstasy/polydrug users

Dr John E. Fisk¹, Dr Catharine Montgomery², Ms Florentia Hadjiefthyvoulou¹

¹University of Central Lancashire, Preston PR1 2HE, United Kingdom

²Liverpool John Moores University, Liverpool L3 3AF, United Kingdom

Running Head: Visuospatial working memory in ecstasy users

Corresponding author:

Professor John E Fisk, PhD
Department of Psychology
University of Central Lancashire
Preston PR1 2HE
United Kingdom
Tel 44 (0) 1772 894465
Fax 44 (0) 1772 892925

e-mail: jfisk@uclan.ac.uk

Key words: ecstasy; cocaine; spatial working memory; substance misuse

Acknowledgements

The authors declare that, except for income received from their primary employers, this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors are not aware of any conflict of interest and do not have any financial interest in this piece of research.

ABSTRACT

Objective. Previous research suggests that ecstasy users are impaired in processing visuo-spatial information. However, for the most part the deficits observed appear to involve the recall and recognition of complex visual and geometric patterns. The present research sought to determine whether ecstasy use was associated with deficits in serial spatial recall and visuo-spatial working memory (VSWM). Methods. Thirty-eight current ecstasy/polydrug users, 16 previous ecstasy/polydrug users, and 52 non ecstasy users completed serial simple spatial recall and VSWM tasks. Results. Both current and previous users of ecstasy exhibited deficits on the VSWM task. Following controls for group differences in aspects of cannabis and cocaine use, the overall group effect fell to just below statistical significance. However the difference contrast comparing users with nonusers continued to demonstrate a statistically significant ecstasy-related VSWM deficit. **Conclusions**. Ecstasy users were impaired in processing visuo-spatial information especially under conditions of high processing demand. The results are consistent with ecstasy-related impairment either in the short term posterior parietal and occipital area store or the DLPFC processes which augment it under conditions of higher processing demands. Further research is needed to pinpoint the actual source of the ecstasy/polydrug-related VSWM deficits that have been observed here and elsewhere.

INTRODUCTION

The purpose of the present study is to establish whether ecstasy users might be impaired in visuo-spatial processing, more specifically the visuo-spatial working memory system. There is an emerging body of evidence to suggest that ecstasy use may be associated with visuo-spatial deficits. Much of the existing research has focussed on recall and recognition. For example, Gouzoulis-Mayfrank et al. (2000) found that users exhibited deficits on the immediate recall (but not the subsequent learning) of previously presented complex visual stimuli. Ecstasy/polydrug users have also been found to be less accurate in a visual discrimination matching to sample task (McCann et al., 2007). Deficits have also been observed on a simple visual recall task (Fox et al. 2001). Furthermore Yip and Lee (2005) observed deficits among ecstasy/polydrug users in the immediate and delayed recall of complex visual stimuli (and in figural fluency) and de Sola Llopis et al. (2008) found that heavy users were impaired relative to non users on a similar measure.

In relation to recognition, Verkes et al. (2001) found that both heavy and moderate ecstasy users were impaired relative to nonusers in their ability to recognise previously presented (serially and simultaneously) geometric figures. Similarly Gouzoulis-Mayfrank et al. (2000) found that ecstasy users were impaired in identifying targets (previously memorised complex visual stimuli) from similar non targets. Fox et al. (2002) also found that ecstasy users did significantly worse in a pattern recognition task (selecting a previously seen stimulus paired with a novel stimulus).

However, not all studies have found ecstasy-related impairments. For example, McCann et al. (1999) failed to observe ecstasy-related deficits in the recognition of a previously presented matrix type figure and likewise, the recall of complex geometric figures was found to be unaffected by ecstasy use (Bhattachary & Powell, 2001). More recently, in a

longitudinal prospective study, Schilt et al. (2007) found that, relative to those who did not become ecstasy users, individuals who subsequently started using ecstasy were unimpaired in the immediate and delayed recall and learning of complex figures. Similarly, Bedi and Redman (2008) found that individual differences on the combined copying, immediate and delayed recall scores of the Rey Complex Figures test were unrelated to any aspect of ecstasy or other illicit drug use and Halpern et al. (2004) also failed to observe ecstasy-related deficits on the same measure. Finally, Rodgers (2000) found that ecstasy users were unimpaired on a measure of immediate visual memory (a composite based on the recognition of abstract designs, the reproduction of simple geometric figures, and visual associative learning: pairing colours with abstract line drawings). Thus to summarise, the evidence for ecstasy-related deficits in the recall and recognition of visual stimuli is mixed.

Aside from the possibility of deficits in recall and recognition, a number of studies have focussed on more prefrontal tasks which utilise executive resources. Here again there is a degree of ambiguity in the results. In relation to the ability to mentally rotate objects McCann et al. (1999) and Schilt et al. (2007) failed to observe ecstasy-related deficits although in a later study McCann et al. (2007) did observe ecstasy-related impairments in mental rotation. Furthermore, utilising a spatial working memory task in which participants search for tokens hidden in a computer generated array of spatial locations, ('boxes'), Fox et al. (2002) found that ecstasy users produced more errors (by returning to a box where a previous token was hidden or looking repeatedly in the same empty box for a concealed token in a single trial). Furthermore performance was especially impaired on the more difficult trials with more boxes. Using the same measure, Semple et al. (1999) found that while users did not differ significantly from nonusers (which the authors attributed to limited statistical power) there was a significant association between lifetime ecstasy use and the number of errors on the task. Aside from spatial working memory, in their study, Fox et al.

(2002) found that although visuo spatial associative learning (pairing complex abstract stimuli with specific spatial locations) was unimpaired there was in fact a trend whereby ecstasy users performed worse at the more difficult levels (Fox et al., 2002).

The Corsi blocks procedure is a long standing paradigm used for assessing an individual's simple spatial span. Results have been inconsistent in relation to ecstasy use with deficits among users being identified by Verkes et al. (2001) and Hanson and Luciana (2010). However, ecstasy users in Gouzoulis-Mayfrank et al.'s (2000) study did not show impairment on this measure. More interestingly backward spatial span is believed to rely more heavily on prefrontal executive resources and a number of studies have tested ecstasy users on this measure. For example, while heavy users (but not light users) were significantly impaired on backward span, this was no longer significant following controls for a family history of substance abuse (Halpern et al. 2004). However, in de Sola Llopis et al.'s (2008) longitudinal study ecstasy users were worse on the backward span measure and although the difference only approached significance at baseline, linear mixed models analysis for the longitudinal aspect over 0-24 months, showed that ecstasy users exhibited a significant backward span deficit. More recently Hanson and Luciana (2010) compared polydrug users with non drug controls finding that the former group were impaired on a spatial working memory measure but that the level of ecstasy use was unrelated to the magnitude of the impairment.

There is some evidence therefore of the effects of ecstasy use on visual processing. However, previous research has tended to focus on recall and recognition of visual stimuli which presumably recruit occipital and medial-temporal resources rather than pre-frontal processes. Furthermore the tests of visuo-spatial working memory that have previously been used have generally not captured the full range of processes which have been explored in the verbal domain. For example, VSWM involves not only the maintenance of static visual stimuli but also involves the processing of dynamic sequential spatial information and

manipulating the contents of temporary visual stores. Neuroimaging (fMRI) research suggests that the maintenance aspects are supported by a limited capacity store in the posterior parietal and occipital cortices with the incremental processing component loading on more anterior locations in the prefrontal cortex (Martin et al., 2008). In previous research from our own laboratory (Wareing et al., 2004; 2005) we demonstrated that while ecstasy/polydrug users performed similarly to non ecstasy users on simple span tasks, i.e., recalling a sequence of spatial locations, when a processing component was added, in which participants were required to make a visual judgement while simultaneously maintaining a sequence of spatial locations, an ecstasy/polydrug related deficit was apparent. Furthermore, it is noteworthy that this deficit persisted in previous users of the drug. However, these studies suffered from a number of limitations. First, the spatial stimuli were displayed in a matrix arrangement. This has been shown to facilitate verbal recoding (Brown et al., 2006) leaving open the question as to whether the deficits that were observed were actually visuospatial in nature. Second, it has also been shown that matrix displays allow the utilisation of structural information from long term memory, for example, visuo-spatial templates (Dean et al., 2008), thus the deficits observed might have reflected group differences in the ability to retrieve this information.

The present study utilises a spatial working memory measure which is an analogue of the verbal working memory measures that have been developed such as operation span (Miyake et al., 2000). Like operation span it requires the retention of serial order information and it includes a secondary processing task. It also relates to existing measures of serial spatial memory in that it uses a Corsi type irregular display. Thus participants are required to maintain a spatial sequence of increasing length while simultaneously performing a visual discrimination task. Using the same measure, Fisk and co-workers have previously demonstrated a spatial working memory deficit among adult dyslexics and among older

adults (Fisk 2004; Smith-Spark et al. 2007). In the present study, ecstasy/polydrug users are predicted to exhibit a deficit specifically on the spatial working memory measure with simple spatial span expected to reveal no drug-related deficits. Thus an interaction is predicted between user group and spatial working memory (SWM) processing demands (simple span=low demand; SWM task =high demand). This expectation will be tested in a mixed ANOVA design. The deficit is predicted to be present in both current and former ecstasy/polydrug users compared to nonusers and the two user groups are expected to perform similarly.

METHOD

Participants

Thirty-eight current ecstasy/polydrug users (Males=19, Females=19), 16 previous ecstasy/polydrug users who had not used ecstasy for at least 6 months (Males=1, Females=15), and 52 non ecstasy users (Males=8, Females=44) 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). Individuals with a medical diagnosis of drug dependence or those injecting illicit drugs were excluded from the study. Current pattern and history of drug use for the three groups is displayed in Table 1. For current ecstasy/polydrug users, median period of abstinence was 40, 2, 3, and 2.5 weeks for amphetamine, cannabis, cocaine and ecstasy respectively. For previous ecstasy/polydrug the equivalent abstinence figures were 260, 28, 12, and 60 weeks for amphetamine, cannabis, cocaine and ecstasy respectively. For non ecstasy users median period of abstinence was 24 and 8 weeks for cannabis and cocaine respectively.

<<Insert Table 1 about here>>

Inspection of Table 2 reveals that the three groups were similar in terms of average age and years of education. Overall group differences were statistically significant for the Ravens (IQ) measure, p<.05, and for alcohol, p<.01, and tobacco consumption, p<.05. Difference contrasts revealed that non users consumed significantly less alcohol and tobacco compared to ecstasy/polydrug users, p<.05 in both cases. On the Ravens measure current users scored significantly higher than previous users and they also smoked significantly fewer cigarettes per day, p<.01. Compared to those currently using, previous users had fewer years of education and consumed fewer units of alcohol although these differences only approached statistical significance.

<<Insert Table 2 about here>>

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., Fisk et al., 2005). These data were used to estimate the total lifetime use for each drug (e.g. ecstasy, cannabis, amphetamines, cocaine etc). Period of abstinence, frequency of use, and recent use (in the previous 10 and 30 days) 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 recorded.

Spatial Working Memory Span. The test was developed by Fisk (2004) as a measure of visuo-spatial working memory and has been used subsequently for this purpose (e.g., Smith-Spark & Fisk, 2007). Twelve Corsi style boxes appear on a PC monitor, in a random array, with a line running horizontally across the middle of the screen so that there is an even distribution of 6 boxes in each half of the screen. Five of the boxes are highlighted for three seconds, four of which contain Xs and one of which contains Os. First, the participants were

required to indicate whether there were more highlighted boxes in the top half or the bottom half of the screen by pointing to one of two boxes positioned respectively in the top right hand corner and the bottom right hand corner. In addition, participants were asked to remember the location of the box that was highlighted with Os and after the Corsi style pattern was removed, to record the position of the 'O' cell in an answer booklet. They did this by writing a 1 in the appropriate location. There were three trials of this type after which the number of consecutive Corsi displays increased to two, each one containing 12 boxes in the same spatial arrangement, five of which were highlighted. As each display was presented the participant was required to point to the top or bottom according to where the majority of boxes were located. The participant was also required to remember the location of the 'O' cell in each Corsi display and after the displays were removed to indicate the locations in the answer book by writing in the appropriate locations a 1 for the 'O' cell from the first display and a 2 for the 'O' cell from the second display. As the task proceeded the number of Corsi displays presented consecutively increased by 1 every three trials. After each display the participant completed the pointing task and after all of the displays in that particular trial had been presented the participant recorded the position of the 'O' filled cells in order in the answer book by writing 1, 2, 3, etc. In total there were six levels to the task with the number of Corsi displays presented in a trial gradually increasing from one to six. In order to achieve a particular level, the participant was required to be correct in at least two of the three trials. The response was deemed to be correct if the locations of the 'O' filled cells, and their serial order were successfully recalled, and the pointing component of the task had been completed correctly. The maximum level that was achieved was defined as the participant's spatial working memory span.

Simple spatial span. Participants were presented with a random pattern consisting of 12 blank squares arranged in a Corsi-type fashion on a computer monitor. On each trial, a

certain number of squares would be highlighted (filled with Xs) in sequence each for two seconds. As each new square was highlighted the previous one went blank. Participants then attempted to recall the position of each of the squares so highlighted. They did this by indicating the positions of the squares and the order in which they were filled in an answer book provided for this purpose. For the first three trials only one position was highlighted. Subsequently for each block of three trials the number of positions highlighted increased by one. Thus there were three trails with two positions, three trails with three positions, three trials with four positions etc. The participant proceeded to the next level until he/she failed to recall the positions on at least two out of three trials. The participants simple spatial span was the maximum level achieved.

Procedure

Participants were informed of the general purpose of the experiment and their right to withdraw any time. Informed consent was obtained verbally after which the drug use questionnaire was administered first, followed by the Raven's Progressive Matrices intelligence test, and the age/education questionnaire. Next the simple spatial span task was administered after which participants completed a practice version of the spatial working memory task. This consisted of three trials at level one, followed by three trials at level two. After this, the full version of the spatial working memory task was administered. 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 which conforms to the ethical guidelines of the British Psychological Society and the Declaration of Helsinki (as amended in Seoul in 2008)¹.

Design and Statistics

A mixed design was employed with drug users as the between participants factor (current, previous, and non ecstasy user) and processing demands the within participants factor (simple spatial versus spatial working memory). This was followed by a series of ANCOVAs with spatial working memory as the dependent variable, drug user as the between participants

independent variable and various other variables introduced as covariates. Differences between the groups were investigated through difference (reverse Helmert) contrast analyses in which nonusers were compared with all ecstasy/polydrug users, and current ecstasy/polydrug users with previous ecstasy/polydrug users.

RESULTS.

Spatial Span and Spatial Working Memory

The main analysis with processing demands (simple spatial versus spatial working memory) within participants, and user group (current, previous, and non ecstasy user) between participants, revealed a significant main effect of processing demands with lower span scores evident under conditions of high demand, F(1,103)=41.22, p<.001. The overall group effect was also statistically significant, F(2,103)=3.80, p<.05. Difference contrasts revealed that non users scored significantly higher than the combined user groups, p<.01, while current and previous users did not differ significantly from each other, p>.05. As predicted the interaction between working memory processing demands and user group was statistically significant, F(2,103)=3.32, p<.05. Inspection of Figure 1 and Table 3 reveals that, as anticipated, the relative impairment among users was most evident under conditions of high working memory processing demands. In order to explore the basis of the interaction, a between participant ANOVA was conducted with the spatial working memory scores as the dependent variable. The overall effect of group was statistically significant, F(2,103)=4.32, p<.05 and as predicted, difference contrasts revealed that non users achieved higher spatial working memory scores than the combined current and previous user groups, p<.01, which in turn did not differ significantly from each other, p>.05. No group difference had been predicted for the simple spatial span scores. However, the main effect of group did in fact approach statistical significance, F(2,103) = 2.71, p=.071, and Tukey's post hoc test revealed

that the difference between previous users and the other two groups approached statistical significance, p= .093 for previous versus current, and p= .073 for previous versus nonusers. In both cases previous users had lower simple span scores.

<<Insert Table 3 and Figure 1 about here>>

Statistical control for IQ, weekly alcohol, and daily cigarette consumption

The groups differed significantly on the IQ, alcohol, and cigarette measures and these were in turn correlated with spatial working memory (p<.05 for IQ and cigarettes, and p=.055 for alcohol). ANCOVA was conducted with group between participants, the spatial working memory score as the dependent variable, and with the IQ, alcohol, and cigarette measures entered as covariates. The overall group effect remained statistically significant, F(2,94)=5.16, p<.01, and furthermore, difference contrasts continued to show that non users achieved significantly higher scores than the combined current and previous user groups, p<.01, which in turn did not differ significantly from each other, p>.05. As covariates, the IQ and alcohol measures accounted for statistically significant variance in the SWM scores with F values of 4.17, p<.05, and 10.58, p<.01, respectively on 1,94 degrees of freedom. Daily cigarette consumption also approached significance as a covariate, F(1,94)=3.20, p=.077.

Unexpectedly, previous users exhibited a degree of impairment on the simple span measure. Furthermore, IQ and alcohol consumption were significantly correlated with simple span, p<.001, and p<.05 respectively. Therefore ANCOVA was conducted with group between participants, the simple spatial span score as the dependent variable, and with alcohol consumption and IQ entered as covariates. The overall group effect no longer approached significance F(2,95)=1.65, p>.05. As covariates, the IQ and alcohol measures accounted for statistically significant variance in the simple spatial span scores with F values of 20.19, p<.001, and 4.85, p<.05, respectively on 1,95 degrees of freedom. Thus it appears

that the difference observed between previous users and the other two groups was substantially attributable to group differences in IQ and alcohol consumption.

Statistical control for aspects of cannabis and cocaine use

In order to evaluate the extent to which cannabis or cocaine use might have been responsible for the ecstasy/polydrug related SWM deficits noted above, ANCOVA was again conducted with group between participants and the spatial working memory score as the dependent variable. The current frequency of cocaine use and the total lifetime use for both cannabis and cocaine were found to be significantly correlated with SWM, p<.05 in all cases, and were entered as covariates. The overall group effect approached statistical significance, F(2,85)=2.59, p=.081, and the difference contrasts continued to show that non users achieved significantly higher scores than the combined current and previous user groups, p<.05, which in turn did not differ significantly from each other, p>.05.

DISCUSSION

The present results demonstrate that both current and previous ecstasy users exhibit impairments in visuo-spatial working memory performance. The present study's focus on dynamic visuo-spatial processing is rare among the existing substance abuse research literature. To date the focus has been on more static visual processes with a very substantial emphasis on visual recall. Thus a number of studies have found ecstasy related deficits in the ability to recall, reconstruct or recognise previously viewed complex visual or geometric stimuli (Back-Madruga et al., 2003; Bolla et al., 1998; Fox et al., 2001; Gouzoulis-Mayfrank et al., 2000; Verkes et al., 2001). In one or two cases the deficits observed appear to be dose related (Back-Madruga et al., 2003; Bolla et al., 1998; Fox et al., 2001). In some instances while recognition was unimpaired, ecstasy users took longer to confirm the identity

previously seen visual targets (Gouzoulis-Mayfrank et al., 2000; Verkes et al., 2001). These ecstasy-related impairments may reflect the adverse effects of the drug on occipital processes. Indeed there is evidence that ecstasy use may be associated with changes in the occipital lobe. For example, in an early EEG study Dafters et al. (1999) found that the integrity of the visual association pathway spanning the occipital-parietal-temporal areas was compromised in ecstasy users. In other research, Chang et al. (2000) conducted a neuroimaging study with a sample of 21 ecstasy users. Two to three weeks following the administration of MDMA, rCBF among a subsample of eight users was reduced relative to baseline across a range of neural locations including the basal ganglia, the visual cortex, superior parietal and the dorsolateral prefrontal cortex (DLPFC). The authors proposed that the subacute effects of MDMA were to increase extracellular serotonin which due to the neurotransmitter's vasoconstrictive effects may have given rise to reduced rCBF. More recently, using PET scanning, Buchert et al. (2004) showed that compared with polydrug controls and nonusers of illicit drugs, current ecstasy users had significantly reduced serotonin transporter availability in a number of regions including the occipital lobe (as well as the medial temporal lobes and pre central sulcus, mesencephalon, and basal ganglia). The reduction in the occipital lobe was dose related and larger than in the other regions

The potential effects of ecstasy on aspects of vision may also be explored through experimental protocols. For example, ecstasy users have been found to respond differently to the tilt after-effect illusion consistent with atypical lateral inhibition of occipital neurons (Brown et al. 2007; Dickson et al., 2009). Other research has utilised transcranial magnetic stimulation (TMS). For example, TMS of the occipital cortex gives rise to subjective light sensations at specific thresholds determined by the minimum stimulator output intensity required to reliably produce the sensation. These thresholds were significantly lower in ecstasy users compared with controls and were negatively correlated with the frequency of

ecstasy use consistent with a dose related effect (Oliveri & Calvo, 2003). Thus to summarise it is possible that the deficits observed among ecstasy users in the recall, reproduction and recognition of visual stimuli may be attributable the effects of the drug on occipital processes.

By way of contrast visuo-spatial working memory as assessed in the present study involves considerably more than the ability to recall or recognise static visual displays. It involves the temporary storage, maintenance, processing and manipulation of visuo-spatial information in pursuit of goal related behaviours and is more reliant on prefrontal cortical resources (Cabeza & Nyberg, 2000). The absence of any ecstasy-related deficit on the simple Corsi span measure suggests that basic serial processing of spatial sequences appears to remain substantially intact. It has been shown that short visual sequences, consisting of up to three locations, can be stored and maintained in a limited capacity store in the posterior parietal and occipital cortices while longer sequences and irregular spatial arrangements such as the Corsi design require DLPFC resources which augment the posterior store perhaps by facilitating chunking or by temporarily storing excess spatial information (Martin et al., 2008). Thus the present results suggest that among ecstasy users this network is able to cope with basic visuo-spatial maintenance tasks. This is not to say that the posterior store is intact. It may well be that the capacity of the store is reduced in ecstasy/polydrug users and that performance is maintained by recruiting additional DLPFC resources. However working memory tasks of the kind reported here require the concurrent maintenance and processing of information and are known to make greater demands on DLPFC resources which are involved in updating the contents of the posterior store and organising the potentially conflicting demands of the task (Chase et al., 2008; McCarthy et al., 1996). It appears therefore that these additional demands result in a deterioration in performance among ecstasy/polydrug users. While such decrements have previously been demonstrated in the processing of verbal material (Fisk & Montgomery, 2009; Montgomery et al., 2005), the

present study provides additional evidence to show that visuo-spatial processing is also affected.

While no group differences were expected on the simple Corsi type span measure, previous users registered lower scores on this task relative to nonusers and current users. However the overall group effect fell just short of statistical significance and in any event appeared to be due to group differences in IQ and alcohol consumption rather than being attributable to ecstasy use.

A number of limitations are evident in the present research. First, following statistical controls for concurrent cannabis and cocaine use, the overall group effect was reduced to a trend and although the difference contrasts continued to indicate that ecstasy/polydrug users were significantly impaired relative to nonusers, the possibility that the deficits observed might in part be attributable to illicit drugs other than ecstasy or to some pre existing condition predating the initiation of drug use cannot be excluded. Second, there was a pronounced gender imbalance between the groups with females predominating among nonusers and previous ecstasy/polydrug users and males more prevalent among current users. Third, it must be acknowledged that as with most studies in this area no objective measure of recent drug use such as urinalysis or hair analysis was used.

In summary both current and previous ecstasy users exhibited deficits in the spatial working memory task. With respect to the difference contrasts, the deficits remained statistically significant following the removal of the variance associated with cannabis and cocaine use. In view of the existing research evidence of ecstasy-related impairment in the processes supported by the occipital and posterior parietal areas, it is possible that DLPFC resources are recruited to bolster the capacity of the posterior store thereby reducing the available capacity needed to cope with the additional processing demands which characterises the SWM task.

REFERENCES

- Back-Madruga C, Boone KB, Chang L, Grob CS, Lee A, Nations H, & Poland RE. 2003.

 Neuropsychological effects of 3,4-methylenedioxymethamphetamine (MDMA or ecstasy) in recreational users. *Clin Neuropsychol* **17**: 446-459.
- Bedi G, Redman J. 2008. Ecstasy use and higher-level cognitive functions: Weak effects of ecstasy after control for potential confounds. *Psychol Med* **38**: 1319-1330.
- Bhattachary S, & Powell JH. 2001. Recreational use of 3,4-methylenedioxymethamphetamine (MDMA) of 'ecstasy': Evidence for cognitive impairment. *Psychol Med* **31**: 647-658.
- Bolla KI, McCann UD, & Ricaurte GA. 1998. Memory impairment in abstinent MDMA ('Ecstasy') users. *Neurology* **51**: 1532-1537.
- Brown J, Edwards M, McKone E, & Ward J. 2007. A long-term ecstasy-related change is visual perception. *Psychopharmacology (Berl)* **193**: 437-446.
- Brown LA, Forbes D, & McConnell J. 2006. Limiting the use of verbal coding in the Visual Patterns Test. *O J Exp Psychol* **59**: 1169-1176.
- Buchert R, Thomasius R, Wilke F, Petersen K, Nebeling B, Obrocki J, Schulze O, Schmidt U, & Clausen M. 2004. A voxel-based PET investigation of the long-term effects of 'ecstasy' consumption on brain serotonin transporters. *Am J Psychiatry* **161**: 1181-1189.
- Cabeza R, Nyberg L. 2000. Imaging Cognition II: An Empirical Review of 275 PET and fMRI Studies. *J Cogn Neurosci* **12**: 1-47.
- Chang L, Grob CS, Ernst T, Itti L, Mishkin FS, Jose-Melchor R, & Poland RE. 2000. Effect of ecstasy 3,4-methylenedioxymethamphetamine (MDMA) on cerebral blood flow: A co-registered SPECT and MRI study. *Psychiatry Res* **98**: 15-28.

- Chase HW, Clark L, Sahakian BJ, Bullmore ET, & Robbins TW. 2008. Dissociable roles of prefrontal subregions in self-ordered working memory performance.

 Neuropsychologia 46: 2650-2661.
- Dafters RI, Duffy F, O'Donnell PJ, & Bouquet C. 1999. Level of use of 3,4-methylenedioxymethamphetamine (MDMA or Ecstasy) in humans correlates with EEG power and coherence. *Psychopharmacology (Berl)* **145**: 82-90.
- de Sola Llopis S, Miguelez-Pan M, Peña-Casanova J, Poudevida S, Farré M, Pacifici R, Böhm P, Abanades S, Verdejo García A, Langohr K, Zuccaro, P, de la Torre R. 2008. Cognitive performance in recreational ecstasy polydrug users: A two-year follow-up study. *J Psychopharmacol* 22: 498-510.
- Dean GM, Dewhurst SA, & Whittaker A. 2008. Dynamic visual noise interferes with storage in visual working memory. *Exp Psychol* **55**: 283-289.
- Dickson C, Bruno R, & Brown J. 2009. Investigating the role of serotonin in visual orientation processing using an 'ecstasy' (MDMA)-based research model.

 *Neuropsychobiology 60: 204-212.
- Fisk JE (2004). The relative magnitudes of age related deficits in verbal and visuo-spatial working memory [abstract]. *Proceedings of the British Psychological Society* **12**: 169.
- Fisk JE, & Montgomery C. 2009. Evidence for selective executive function deficits in ecstasy/polydrug users. *J Psychopharmacol* **23**: 40-50.
- Fisk JE, Montgomery C, Wareing M, & Murphy P. 2005. Reasoning deficits in ecstasy (MDMA) polydrug users. *Psychopharmacology (Berl)* **181**: 550-559.
- Fox HC, McLean A, Turner JJD, Parrott AC, Rogers R, Sahakian BJ. 2002.

 Neuropsychological evidence of a relatively selective profile of temporal dysfunction in drug-free MDMA ('ecstasy') polydrug users. *Psychopharmacology (Berl)* **162**: 203-214.

- Fox HC, Parrott AC, & Turner JJD. 2001. Ecstasy use: Cognitive deficits related to dosage rather than self-reported problematic use of the drug. *J Psychopharmacol* **15**: 273-281.
- Gouzoulis-Mayfrank E, Daumann J, Tuchtenhagen F, Pelz S, Becker S, Kunert H-J, Fimm B, & Sass H. 2000. Impaired cognitive performance in drug free users of recreational ecstasy (MDMA). *J Neurol Neurosurg Psychiatry* **68**: 719-725.
- Halpern JH, Pope HG Jr, Sherwood AR, Barry S, Hudson JI, Yurgelun-Todd D. 2004.

 Residual neuropsychological effects of illicit 3,4-methylenedioxymethamphetamine

 (MDMA) in individuals with minimal exposure to other drugs. *Drug Alcohol Depend*75: 135-147.
- Hanson KL, Luciana M. 2010. Neurocognitive impairments in MDMA and other drug users: MDMA alone may not be a cognitive risk factor. J Clin Exp Neuropsychol **32**: 337-349.
- Martin R, Houssemand C, Schiltz C, Burnod Y, & Alexandre F. 2008. Is there continuity between categorical and coordinate spatial relations coding? Evidence from a grid/no-grid working memory paradigm. *Neuropsychologia* **46**: 576-594.
- McCann UD, Mertl M, Eligulashvili V, & Ricaurte GA. 1999. Cognitive performance in (±) 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy') users: A controlled study. *Psychopharmacology (Berl)* **143**: 417-425.
- McCann UD, Peterson SC, Ricaurte GA. 2007. The effect of catecholamine depletion by alpha-methyl-para-tyrosine on measures of cognitive performance and sleep in abstinent MDMA users. *Neuropsychopharmacology* **32**: 1695-1706.
- McCarthy G, Puce A, Constable RT, Krystal JH, Gore JC, & Goldman-Rakic P. 1996.

 Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cereb Cortex* **6**: 600-611.

- Montgomery C, Fisk JE, Newcombe R, & Murphy PN. 2005. The differential effects of ecstasy/polydrug use on executive components: Shifting, inhibition, updating and access to semantic memory. *Psychopharmacology (Berl)* **182**: 262-276.
- Oliveri M, & Calvo G. 2003. Increased visual cortical excitability in ecstasy users: A transcranial magnetic stimulation study. *J Neurol Neurosurg Psychiatry* **74**: 1136-1138.
- Raven J., Raven J.C., & Court JH. 1998. *Manual for Raven's Progressive Matrices and Vocabulary Scales*. Oxford, UK: Oxford Psychologists Press SPM1-SPM95.
- Rodgers J. 2000. Cognitive performance amongst recreational users of ecstasy.

 *Psychopharmacology (Berl) 151: 19-24.
- Schilt T, de Win MML, Koeter M, Jager G, Korf DJ, van den Brink W, & Schmand B. 2007.

 Cognition in novice ecstasy users with minimal exposure to other drugs: A prospective cohort study. *Arch Gen Psychiatry* **64**: 728-736.
- Smith-Spark JH, & Fisk JE. 2007. Central executive functioning in developmental dyslexia. *Memory* 15: 34-56.
- Solowij N, Hall W, & Lee N. 1992. Recreational MDMA use in Sydney: a profile of ecstasy users and their experiences with the drug. *B J Addict* **87**: 1161-1172.
- Verkes RJ, Gijsman HJ, Pieters MSM, Schoemaker RC, de Visser S, Kuijpers M, Pennings EJM, de Bruin D, Van de Wijngaart G, Van Gerven JMA, & Cohen AF. 2001.

 Cognitive performance and serotonergic function in users of ecstasy. *Psychopharmacology (Berl)* **153**: 196-202.
- Wareing M, Fisk JE, Murphy P, & Montgomery C. 2005. Visuo-spatial working memory deficits in current and former users of MDMA ('Ecstasy'). *Hum Psychopharmacol* **20**: 115-123.

- Wareing M, Murphy P, & Fisk JE. 2004. Visuospatial memory impairments in users of MDMA ('ecstasy'). *Psychopharmacology (Berl)* **173**: 391-397.
- Yip JTH, Lee TMC. 2005. Effect of ecstasy use on neuropsychological function: A study in Hong Kong. *Psychopharmacology (Berl)* **179**: 620-628.

Endnotes

¹ In order to address the concerns of the illicit drug users within our sample in relation to protecting their identity and anonymity, consent was obtained verbally rather than in writing.

Table 1. Indicators of Drug Use for Ecstasy Users and Nonusers

	Current Users			Previous Users			Non-Ecstasy Users			
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D.	n	
Lifetime Dose										
Amphetamine (grams)	95.50	124.74	12	469.33	410.47	3	-	-	-	
Cannabis (joints)	3009.15	4465.89	33	2321.85	4173.90	13	145.44	270.53	17	
Cocaine (lines)	1347.84	1836.88	25	366.22	505.20	9	763.50	1175.96	4	
Ecstasy (tablets)	699.71	1288.82	38	161.13	268.59	16	-	-	-	
Use in Previous 30 Days										
Amphetamine (grams)	0.50	1.17	12	0	0	3	-	-	-	
Cannabis (joints)	18.95	45.44	33	2.54	6.81	13	4.12	13.55	17	
Cocaine (lines)	10.60	14.22	25	4.44	10.67	9	2.00	4.00	4	
Ecstasy (tablets)	6.11	12.49	38	0	0	16	-	-	-	
Use in Previous 10 Days ¹										
Amphetamine (grams)	1.00	_	1	-	-	-	-	-	-	
Cannabis (joints)	3.33	3.60	18	1.50	0.71	2	5.00	1.41	2	
Cocaine (lines)	16.83	12.27	6	8.00	0.00	2	16.00	-	1	
Ecstasy (tablets)	1.43	0.53	7	-	-	-	-	-	-	
Frequency of use (times per week)										
Amphetamine	0.12	0.29	12	0	0	4	-	_	-	
Cannabis	1.11	1.88	33	0.33	0.85	13	0.53	1.26	17	
Cocaine	0.41	0.49	25	0.28	0.39	8	0.58	0.49	4	
Ecstasy	0.38	0.49	38	0.02	0.06	16	-	_	-	
Weeks since last use										
Amphetamine	78.30	114.37	15	346.67	150.11	3	-	-	-	
Cannabis	28.20	76.39	33	59.66	76.96	12	91.44	141.87	18	
Cocaine	17.55	54.81	32	28.75	35.31	9	7.11	5.92	5	
Ecstasy	5.47	6.73	38	114.44	99.99	16	-	-	-	
Alcohol (units per week)	18.30	12.64	38	12.53	9.46	15	9.58	9.49	48	
Tobacco (Cigarettes per day)	6.88	4.81	16	16.14	11.65	7	6.25	5.88	12	

^{1.} Data relate to only those individuals actually using within the previous 10 days

Table 2. Average age, intelligence, years of education for ecstasy user and nonusers.

	Current Users			Previous Users			Non-Ecstasy Users			p		
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D. 1	n Gro	ıp Non user	Current	
										versus	versus	
										user	previous	
Age (years)	21.45	2.53	38	22.25	4.73	16	20.92	2.91	52 ns	ns	ns	
Intelligence (Ravens, max=60)	45.76	8.34	37	40.31	12.44	16	46.21	7.07	52 < .05	.070	<.05	
Education (years)	15.58	2.40	38	14.38	3.93	16	15.65	1.51	51 ns	ns	.088	

Table 3. Simple spatial and spatial working memory scores for ecstasy user and nonusers.

	Curr	Current Users			Previous Users		Non-Ecstasy Users			p		
	Mean	S.D.	n	Mean	S.D.	n	Mean	S.D. n	Group	Non user versus user	Current versus previous	
Spatial Span Spatial Working Memory	3.55 2.05	1.03 1.41	38 38	2.81 2.00	1.64 1.46	16 16	3.56 2.83	1.11 52 1.34 52	.071 <.05	ns <.01	<.05 ns	

Figure 1: Simple Spatial and Spatial Working Memory Span

