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

John E. Fisk[1]*, Catharine Montgomery[2] and Florentia Hadjiefthyvoulou[1]

[1]*University of Central Lancashire, Preston, UK*
[2]*Liverpool John Moores University, Liverpool, UK*

Objective Previous research suggests that ecstasy users are impaired in processing visuospatial 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 visuospatial 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 the 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 visuospatial 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 dorsolateral prefrontal cortex 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. Copyright © 2011 John Wiley & Sons, Ltd.

KEY WORDS—ecstasy; cocaine; spatial working memory; substance misuse

INTRODUCTION

The purpose of the present study is to establish whether ecstasy users might be impaired in visuospatial processing, more specifically, the visuospatial working memory (VSWM) system. There is an emerging body of evidence to suggest that ecstasy use may be associated with visuospatial 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 nonusers 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 and 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

*Correspondence to: J. E. Fisk, PhD, Professor, Department of Psychology, University of Central Lancashire, Preston PR1 2HE, UK. Tel: +44(0) 1772 894465; Fax: +44(0) 1772 892925 E-mail: jfisk@uclan.ac.uk

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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 that 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 (SWM) 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 although 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 SWM, in their study, Fox *et al.* (2002) found that although visuospatial 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, although 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 the longitudinal study of de Sola Llopis *et al.* (2008), 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 and found that the former group were impaired on an SWM 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 prefrontal processes. Furthermore, the tests of VSWM that have previously been used have generally not captured the full range of processes that have been explored in the verbal domain. For example, VSWM involves not only the maintenance of static visual stimuli but also the processing of dynamic sequential spatial information and manipulating the contents of temporary visual stores. Neuroimaging (functional magnetic resonance imaging) 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 although ecstasy/polydrug users performed similarly to non ecstasy users on simple span tasks, that is, 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 on whether the deficits that were observed were actually

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visuospatial in nature. Second, it has also been shown that matrix displays allow the utilisation of structural information from long-term memory, for example, visuospatial 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 an SWM measure that 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 an SWM deficit among adults with dyslexia and among older adults (Fisk, 2004; Smith-Spark and Fisk, 2007). In the present study, ecstasy/polydrug users are predicted to exhibit a deficit specifically on the SWM measure with simple spatial span expected to reveal no drug-related deficits. Thus, an interaction is predicted between user group and SWM processing demands (simple span = low demand; SWM task = high demand). This expectation will be tested in a mixed analysis of variance design. The deficit is predicted to be present in both current and former ecstasy/polydrug users compared with nonusers, and the two user groups are expected to perform similarly.

METHOD

Participants

Thirty-eight current ecstasy/polydrug users (men = 19, women = 19), 16 previous ecstasy/polydrug users who had not used ecstasy for at least 6 months (men = 1, women = 15) and 52 non ecstasy users (men = 8, women = 44) took part in this investigation. The participants were recruited via direct approach to university students and via the snowball technique, that is, word-of-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, the median period of abstinence was 24 and 8 weeks for cannabis and cocaine, respectively.

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, $p < 0.05$; and for alcohol, $p < 0.01$; and tobacco consumption, $p < 0.05$. Difference contrasts revealed that nonusers consumed significantly less alcohol and tobacco compared with ecstasy/polydrug users, $p < 0.05$ in both cases. On the Ravens measure, current users scored significantly higher than previous users, and they also smoked significantly fewer cigarettes per day, $p < 0.01$. Compared with current users, previous users had fewer years of education and consumed fewer units of alcohol although these differences only approached statistical significance.

Materials

The prior history of illicit drug consumption was assessed using a background drug-use questionnaire that 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). 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 VSWM and has been used subsequently for this purpose (e.g. Smith-Spark and 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 six boxes in each half of the screen. Five of the boxes are highlighted for 3 s, 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, the 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 the number 1 in the appropriate location. There were three trials of this type, after which, the number of

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Table 1. Indicators of drug use for ecstasy users and nonusers

	Current users			Previous users			Non ecstasy users		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*
Lifetime dose									
Amphetamine (g)	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 (g)	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[a]									
Amphetamine (g)	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

[a]Data relate to only those individuals actually using within the previous 10 days.
SD, standard deviation.

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

	Current users			Previous users			Non ecstasy users			*p*		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Group	Nonuser versus user	Current versus 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	<0.05	0.070	<0.05
Education (years)	15.58	2.40	38	14.38	3.93	16	15.65	1.51	51	ns	ns	0.088

SD, standard deviation.

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 the number 1 for the 'O' cell from the first display and the number 2 for the 'O' cell from the second display. As the task proceeded, the number of Corsi displays presented consecutively increased by one every three trials. After *each* display, the participant completed the pointing task, and after *all* 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 and so forth. 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.

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The maximum level that was achieved was defined as the participant's SWM span.

Simple spatial span. The 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 2 s. As each new square was highlighted, the previous one went blank. The 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 and so forth. The participant proceeded to the next level until he or 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

The 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 SWM task. This consisted of three trials at level one, followed by three trials at level two. After this, the full version of the SWM task was administered. The 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 as the within-participants factor (simple spatial versus SWM). This was followed by a series of analyses of covariance with SWM 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 SWM) 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, $F_{(1,103)} = 41.22$, $p < 0.001$. The overall group effect was also statistically significant, $F_{(2,103)} = 3.80$, $p < 0.05$. Difference contrasts revealed that nonusers scored significantly higher than the combined user groups, $p < 0.01$, whereas current and previous users did not differ significantly from each other, $p > 0.05$. As predicted, the interaction between working memory processing demands and user group was statistically significant, $F_{(2,103)} = 3.32$, $p < 0.05$. 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 analysis of variance

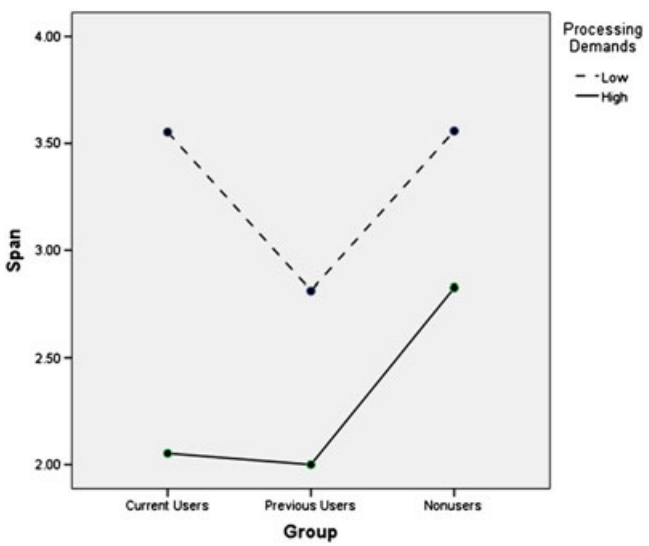

Figure 1. Simple spatial and spatial working memory span

[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.

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

	Current users			Previous users			Non ecstasy users			*p*		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Group	Nonuser versus user	Current versus previous
Spatial span	3.55	1.03	38	2.81	1.64	16	3.56	1.11	52	0.071	ns	<0.05
Spatial working memory	2.05	1.41	38	2.00	1.46	16	2.83	1.34	52	<0.05	<0.01	ns

SD, standard deviation.

was conducted, with the SWM scores as the dependent variable. The overall effect of group was statistically significant, $F_{(2,103)} = 4.32$, $p < 0.05$, and as predicted, difference contrasts revealed that nonusers achieved higher SWM scores than the combined current and previous user groups, $p < 0.01$, which in turn did not differ significantly from each other, $p > 0.05$. No group difference had been predicted for the simple spatial span scores. However, the main effect of group did in fact approach statistical significance, $F_{(2,103)} = 2.71$, $p = 0.071$, and Tukey's post hoc test revealed that the difference between previous users and the other two groups approached statistical significance, $p = 0.093$ for previous versus current and $p = 0.073$ for previous versus nonusers. In both cases, previous users had lower simple span scores.

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 SWM ($p < 0.05$ for IQ and cigarettes and $p = 0.055$ for alcohol). An analysis of covariance (ANCOVA) was conducted with group between-participants, the SWM score as the dependent variable, and with IQ, alcohol and cigarette measures entered as covariates. The overall group effect remained statistically significant, $F_{(2,94)} = 5.16$, $p < 0.01$, and furthermore, difference contrasts continued to show that nonusers achieved significantly higher scores than the combined current and previous user groups, $p < 0.01$, which in turn did not differ significantly from each other, $p > 0.05$. As covariates, the IQ and alcohol measures accounted for statistically significant variance in the SWM scores with F values of 4.17, $p < 0.05$ and 10.58, $p < 0.01$, respectively on 1,94 degrees of freedom. Daily cigarette consumption also approached significance as a covariate, $F_{(1,94)} = 3.20$, $p = 0.077$.

Unexpectedly, previous users exhibited a degree of impairment on the simple span measure. Furthermore, IQ and alcohol consumption were significantly correlated with simple span, $p < 0.001$ and $p < 0.05$, 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 $F_{(2,95)} = 1.65$, $p > 0.05$. As covariates, the IQ and alcohol measures accounted for statistically significant variance in the simple spatial span scores with F values of 20.19, $p < 0.001$ and 4.85, $p < 0.05$, 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 earlier, ANCOVA was again conducted with group between-participants and the SWM 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, $p < 0.05$ in all cases, and were entered as covariates. The overall group effect approached statistical significance, $F_{(2,85)} = 2.59$, $p = 0.081$, and the difference contrasts continued to show that nonusers achieved significantly higher scores than the combined current and previous user groups, $p < 0.05$, which in turn did not differ significantly from each other, $p > 0.05$.

DISCUSSION

The present results demonstrate that both current and previous ecstasy users exhibit impairments in VSWM performance. The present study's focus on dynamic visuospatial 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 (Bolla *et al.*, 1998; Gouzoulis-Mayfrank *et al.*, 2000; Fox *et al.*, 2001; Verkes *et al.*, 2001; Back-Madruga *et al.*,

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2003). In one or two cases, the deficits observed appear to be dose related (Bolla *et al.*, 1998; Fox *et al.*, 2001; Back-Madruga *et al.*, 2003). In some instances, although 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, regional cerebral blood flow 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 because of the neurotransmitter's vasoconstrictive effects, may have given rise to reduced regional cerebral blood flow. 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 precentral 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. For example, the transcranial magnetic stimulation 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 and 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 to the effects of the drug on occipital processes.

By way of contrast, VSWM, 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 visuospatial information in pursuit of goal-related behaviours and is more reliant on prefrontal cortical resources (Cabeza and 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, whereas 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 visuospatial 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 (McCarthy *et al.*, 1996; Chase *et al.*, 2008). It appears therefore that these additional demands result in a deterioration in performance among ecstasy/polydrug users. Whereas such decrements have previously been demonstrated in the processing of verbal material (Montgomery *et al.*, 2005; Fisk and Montgomery, 2009), the present study provides additional evidence to show that visuospatial processing is also affected.

Although 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

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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 SWM 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 that characterises the SWM task.

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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