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ORIGINAL INVESTIGATION

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Ecstasy (MDMA): are the psychological problems associated with its use reversed by prolonged abstinence?

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Abstract *Rationale:* Chronic, regular recreational use of ecstasy (MDMA) is associated with psychopathology, elevated behavioural impulsivity and persistent impairment of memory performance. *Objective:* The aim of the present study was to investigate which of these sequelae persist after at least 6 months of abstinence from ecstasy. *Methods*: Four groups of participants were compared: 18 current regular recreational ecstasy users, 15 ex-regular ecstasy users who had abstained from using the drug for an average of 2 years, 16 polydrug users who had never taken ecstasy and 15 drug-naive controls. *Results*: There were no significant group differences in age, education level, or pre-morbid intelligence and, generally, the use of illicit drugs other than ecstasy was not significantly different among the three drug-using groups. Both current and ex-ecstasy users exhibited elevated psychopathology and behavioural impulsivity compared with polydrug users and drug-naive controls, but current ecstasy users exhibited a broader range of psychopathology than ex-users. Both groups of ecstasy users also exhibited impaired working memory and verbal recall performance compared with drug-naive controls, but only ex-users exhibited impaired verbal recall relative to polydrug users. Regression analysis indicated that psychopathology was primarily predicted by the extent of previous consumption of cannabis rather than ecstasy, whereas the majority of the cognitive deficits were only predicted by the extent of previous ecstasy use. *Conclusions*: Selective impairments of neuropsychological performance associated with regular ecstasy use are not reversed by prolonged abstinence. This is consistent with evidence that ecstasy has potent and selective neurotoxic effects on brain serotonergic systems in humans.

Keywords 3-4-Methylenedioxymethamphetamine · MDMA · Ecstasy · Psychopathology · Cognitive performance · Memory

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Introduction

Recreational use of the potent and selective serotonin (5-HT) neurotoxin ecstasy (3,4-methylenedioxymethamphetamine, MDMA) has become increasingly widespread (Tasker et al. 1999; Johnston et al. 2000; Morgan 2000). Recent neuroimaging studies suggest that extensive exposure to ecstasy results in persistent depletion of 5-HT in humans (McCann et al. 1998; Semple et al. 1999; Reneman et al. 2000). Furthermore, there are reports that regular, frequent use of ecstasy is associated with sleep disorders, depressed mood and elevated anxiety, trait impulsiveness and hostility (Allen et al. 1993; Morgan 1998a, 1998b, 2000; Gerra et al. 1998, 2000; Gamma et al. 2000; Parrott et al. 2000; Wareing et al. 2000). Moderate ecstasy users have been reported to exhibit persistent impairments of episodic memory (Morgan 1999; Rodgers 2000) and elevated behavioural impulsivity (Morgan 1998a, 1998b). Other persistent cognitive deficits, including deficits in attention and working memory, have only been reported to occur in heavy users (McCann et al. 1999; Gouzoulis-Mayfrank et al. 2000; Morgan 2000; Verkes et al. 2001; Wareing et al. 2000).

The present study sought to further investigate the latter findings and determine which, if any, of these psychological impairments persist after at least 6 months of abstinence from ecstasy. Psychopathological status was assessed with a General Health Questionnaire (GHQ; Goldberg 1978), an Impulsiveness, Venturesomeness, and Empathy questionnaire (IVE; Eysenck and Eysenck 1991) and a psychiatric symptom checklist – the SCL-90-R (Derogatis 1997). Two neuropsychological

measures that have already proved sensitive to the selective cognitive impairments associated with regular ecstasy use (Morgan 1998a, 1998b) were employed. These were a measure of behavioural impulsivity: the Matching Familiar Figures test (MFF20; Cairns and Cammock 1978) and a measure of everyday memory function: the story recall component of the Rivermead Behavioural Memory Test (RBMT; Wilson et al. 1985). Other neuropsychological measures were also employed to explore executive function and working memory performance in ecstasy users. These included: two tests of verbal fluency, a digit cancellation test, the Trail-Making Test (1946), the Stroop test (Stroop 1935) and the Subtracting Serial Seven's test (Smith 1967).

On the basis of the literature, it was predicted that both current ecstasy users and ex-ecstasy users would exhibit elevated psychopathology and selective deficits in cognitive performance compared with polydrug users who had never used ecstasy and with control participants who had never taken illicit drugs. However, there is tentative evidence of remission of anxiety and hostility after a year of abstinence from ecstasy (Gerra et al. 2000; Wareing et al. 2000), while deficits in working memory appear to persist for at least 6 months after abstinence (Wareing et al. 2000). Thus, it was expected that heavy ecstasy users who had been abstinent for more than 6 months would exhibit less psychopathology on the SCL-90-R than current heavy users. However, it was also predicted that ex-ecstasy users would continue to exhibit selective deficits in cognitive performance relative to a group of polydrug users, who had used similar amounts of other illicit substances, and to drug-naive control subjects. Specifically, it was predicted that current and ex-ecstasy users would exhibit impaired recall performance in the RBMT and elevated behavioural impulsivity in the MFF20 relative to both polydrug users and drug-naive controls. Finally, it was hypothesised that there would be dose–response relationships between the degree of impairment of cognitive function and the extent of previous exposure to ecstasy.

Methods

Participants

Subjects were recruited using the 'snowball' technique (Solowij et al. 1992). The data collectors (LM, LF and JR) informed acquaintances about the study, and they spread word of it among their acquaintances. Every participant completed a consent form and questionnaires about their age, gender, educational level, medical history and past and present use of both legal and illicit drugs. Potential participants were excluded from the study if they were pregnant or had any of the following conditions: current or previous asthma, heart disease, epilepsy, dyslexia, eating disorders, schizophrenia, major depressive disorder, alcoholism or opiate dependence; or had previous loss of consciousness that had lasted for more than 2 min. Participants who passed the initial screening were then administered the National Adult Reading Test (NART; Nelson 1982) to provide an estimate of premorbid I.Q. and to ensure that their knowledge of English was adequate (they had to obtain more than 25 correct answers to participate). Sixty-four subjects participated in the study: 18 (9 male, 9 female) current heavy recreational ecstasy users who had taken ecstasy more than twenty times in their lifetime and also used other illicit drugs; 15 (4 male, 11 female) heavy recreational ecstasy users who had been abstinent from ecstasy for at least 6 months but had continued to use other illicit drugs; 16 (8 male, 8 female) polydrug controls who had never taken ecstasy, but, otherwise, had similar drug-use histories; and 15 (6 male, 9 female) drug-naive control subjects (see Table 1 for patterns of ecstasy use). The study was approved by the Psychology Department ethics committee. All participants provided signed informed consent and were paid £5 (pounds sterling) each for participating.

Assessment measures

Psychopathological status was assessed using a 12-item GHQ (Goldberg 1978), the 54-item IVE (Eysenck and Eysenck 1991), and the 90-item SCL-90-R (Derogatis 1997). Cognitive performance was assessed using the MFF20 (Cairns and Cammock 1978), the story recall component of the RBMT (Wilson et al. 1985), Trail-Making Test (TMT, Army Individual Test Battery 1946), colour-word version of the Stroop test (Stroop 1935) and the Subtracting Serial Sevens test (SSS; Smith 1967). Participants were also administered a digit cancellation test that involved marking every occurrence of the number 5 which was distributed randomly among 400 two-digit numbers in a 20×20 array, and two tests of verbal fluency. The first of these was the Controlled Oral Word Association test (COWA; Benton and Hamsher 1976) and the second was a category fluency task. In the COWA task, participants had 60 s to generate as many different words as they could (excluding proper nouns) beginning with the letters F, A and S. In the category fluency test, participants had 90 s to name as many different examples of fruit as possible, followed by another 90 s to name as many different examples of vegetables as possible. The brief news story component of the RBMT, which comprised five sentences containing 65 words, and 21 ideas, was recorded on audiotape. A tape recorder was also used to record participants' responses to the Stroop task, the COWA task, the category fluency task and the SSS task.

Procedure

Participants were required to abstain from using alcohol for at least 10 h, cannabis for at least 24 h, and any other illicit drugs for

Table 1 Ecstasy use in the two user groups: mean±SD

	Current ecstasy users		Ex-ecstasy users	
n	Male 9	Female 9	Male 4	Female 11
Estimated lifetime dose (tablets)	513±470	93±65	336±248	577±884
Tablets taken in previous month	1.8±2.3	1.2±1.1	0.0±0.0	0.0±0.0
Average dose per session	2.6±1.0	1.8±0.6	1.6±0.8	1.7±0.7
Maximum dose per session	6.7±3.7	3.4±1.6	4.2±2.6	2.8±1.5
Duration of use (years)	6.4±2.5	2.4±1.3	3.5±1.9	4.3±1.5
Time since last dose (weeks)	5.1±3.9	3.0±2.5	110±58	113±97

at least 1 week before testing. On the test day, participants were administered a personal-details questionnaire, a general drug-use history questionnaire (and, in the case of the ecstasy-users, an additional questionnaire about their patterns of ecstasy use), then the NART, GHQ, IVE and SCL-90-R. They were then instructed to listen to the brief audio-taped news story taken from the RBMT and write down as much of what they had just heard as possible, verbatim, immediately after the story had been presented. After the immediate recall test, participants completed the other tests in the following order: Stroop, MFF20, verbal and category fluency, TMT, SSS and digit cancellation – see Morgan (1998b) for details of MFF20 procedure and Lezac (1983) for other test procedures. The dependent variables for the Stroop, TMT and digit cancellation tests were completion time and the number of errors (including omissions) committed. The dependent variables for the SSS test were the number of subtractions in 90 s and errors committed. The dependent variable for the verbal and category fluency tasks was the number of correct items generated. Finally, the dependent variables for MFF20 were the mean latency to first response, the total number of errors committed, and a I score (Salkind and Wright 1977) calculated by subtracting the standardised score of the mean latency from the standardised score of the number of errors committed (Z_e–Z_l). After they had completed these tests, 40–50 min after the RBMT story had been presented, participants were again asked to write down as much of the story as possible, to produce a delayed recall score. Recall was scored in the standard way (Wilson et al. 1985) with one point being given for each of the 21 ideas recalled perfectly or a close synonym and half a point for partial recall or a partial synonym.

Statistical analysis

SPSS (version 10) one-way analysis of variance (ANOVA) was used to compare personal details, drug histories, NART, gender differences, GHQ, IVE, and SCL-90-R scores, and the measures of cognitive performance of the four groups. The Kruskal-Wallis test was employed in cases where the group differences in self-reported past consumption of illicit drugs violated the homogeneity of variance assumption. A two-way ANOVA, with one repeated factor (immediate and delayed recall) and one between factor (group) was used to compare RBMT recall performance. Planned comparisons were employed to compare the means of the four groups. Pearson's product moment correlation coefficient was employed to investigate correlations between dependent variables and dose–response relationships. Stepwise linear regression analyses were performed to determine which measures of past use of illicit drugs were predictive of subsequent psychopathology and cognitive impairment. The number of grams of amphetamine and cocaine, cannabis joints, psilocybin mushrooms, LSD trips and popper hits consumed in the year before testing, average and maximum doses of ecstasy consumed on a single occasion, and the estimated total number of ecstasy tablets consumed were all entered as independent variables. Finally, to further control for group differences in the use of illicit drugs other than ecstasy, the data were re-analysed using analysis of covariance to determine whether any measures of the latter measurements of illicit drug use were statistically significant covariates and, if so, what effect they had on the statistical significance of group differences.

Results

Participant details and drug use histories

One-way ANOVA of the personal characteristics of participants in the four experimental groups (current ecstasy users, ex-users, polydrug controls and drug-naive controls) indicated that they were not significantly different in terms of their age, gender ratio, education level achieved, height, weight, or estimated pre-morbid IQ. However, drug-naive control subjects smoked fewer cigarettes, and ex-ecstasy users consumed less alcohol than participants in the other groups (Table 2). The reported duration of use of cannabis, amphetamine, cocaine, LSD, psilocybin mushrooms or poppers was not significantly different among current ecstasy users, ex-users and polydrug controls. Parametric statistical analysis also indicated that there were no significant group differences between the reported consumption of cannabis or psilocybin mushrooms in the year prior to testing. Although the number of current ecstasy users who reported having consumed amphetamine, LSD and poppers in the year prior to testing was more than double that of ex-ecstasy users and polydrug users (Table 3), non-parametric analysis using the Kruskal-Wallis test indicated no statistically significant group differences in the use of these drugs. There was however, a significant group difference in reported past consumption of cocaine – ex-ecstasy users reported significantly less cocaine use than current ecstasy users or polydrug using controls. Furthermore, five current ecstasy users reported that they had taken between 3 and 15 benzodiazepine tablets in the year prior to testing, and three reported that they had taken between 1 and 10 tablets of ketamine, while only one ex-ecstasy user reported that they had used benzodiazepines, and none reported having used ketamine. None of the polydrug controls reported using either drug in the year prior to testing.

Gender differences

Male subjects consumed more alcohol per week than females ($F_{1,54}$=10.78, P=0.002), and male current ecstasy users consumed more ecstasy in their lifetimes ($F_{1,16}$=7.04, P=0.017) over a longer period ($F_{1,16}$=18.91, P<0.001) than females (Table 1). There were no other gender differences in participants' drug histories, GHQ

Table 2 Personal characteristics: frequencies, mean±SD

	Current ecstasy users	Ex-ecstasy users	Polydrug controls	Drug-naive controls
n (Male, Female)	18 (9, 9)	15 (4, 11)	16 (8, 8)	15 (6, 9)
Age	23.4±3.2	24.7±2.5	22.1±3.3	22.4±4.1
Education[a]	2.61±0.7	2.67±0.6	3.00±0.0	2.73±0.6
I.Q[b]	116.6±6.8	114.2±4.4	116.4±6.6	114.5±5.9
Cigarettes per week	76.4±54.4	66.2±53.0	43.3±44.3	11.3±24.4*
Alcohol units per week	21.2±15.0	8.9±4.6	25.5±19.6	20.9±10.9*

[a] 1=GCSE, 2=A-level, 3=HND+
[b] Pre-morbid IQ estimated from National Adult Reading Test scores
* Groups significantly different at the 0.05 probability level

Table 3 Other illicit drug use in the three user groups: number of participants (*n*) reporting any use in the year prior to testing; mean±SD

	Current ecstasy users	Ex-ecstasy users	Polydrug controls
n	18	15	16
Cannabis (*n*)	17	11	14
Joints smoked in past year	519±794	785±1484	590±1442
Duration of use (years)	5.4±4.0	7.2±3.5	5.3±2.93
Psilocybin mushrooms (*n*)	12	4	3
Number consumed in past year	75.3±90.8	30.8±57.4	30.0±70.4
Duration of use (months)	39.5±52.2	27.2±31.0	16.1±34.4
Cocaine (*n*)	11	3	4
Grams consumed in past year	2.14±3.4	0.15±0.3	2.56±6.1
Duration of use (months)	27.1±37.4	18.7±25.0	4.7±8.4
Amphetamine (*n*)	9	3	4
Grams consumed in past year	29.9±56.4	4.6±15.4	2.6±6.5
Duration of use (months)	42.4±45.5	45.3±28.8	26.0±25.1
LSD (*n*)	8	3	4
Trips in past year	8.5±18.2	2.71±6.9	0.40±0.8
Duration of use (months)	53.3±59.0	40.1±32.8	16.7±31.7
Poppers (*n*)	5	2	1
Hits in past year	10.4±38.6	1.7±6.2	15.6±62.3
Duration of use (months)	3.1±4.3	1.2±2.1	0.9±2.6

Table 4 Statistically significant group differences (planned comparisons). *Planned comparisons (assuming equal variances) significant at the 0.05 probability level, **planned comparisons (assuming equal variances) significant at the 0.01 probability level. None of the current versus ex-ecstasy user planned comparisons or polydrug control versus drug-naive control planned comparisons were statistically significant

	Current users vs controls	Ex-ecstasy users vs controls	Current users vs polydrug	Ex-ecstasy users vs polydrug
i) Measures of psychopathology: SCL-90-R measure				
Global severity index	**	*	**	
Positive symptom distress index	*	*	*	*
Somatisation	**	*	*	
Obsessive–compulsive	**	*	*	
Anxiety	**		**	
Phobic anxiety	*		*	
Inter-personal sensitivity	*	*	*	*
Depression	*		*	
Paranoid ideation	*		*	
Altered appetite/restless sleep	*	*	*	*
ii) Measures of cognitive performance: neuropsychological measure				
RBMT recall	*	**		*
MFF20 latencies	**	*	*	
MFF20 errors	**	**	**	*
SSS errors	**	*		
TMT (B) errors	*		*	

or SCL-90-R scores or any measure of cognitive performance. However, males scored significantly higher on IVE venturesomeness ($F_{1,60}$=8.83, P=0.004), while females scored significantly higher on empathy ($F_{1,60}$= 4.79, P=0.032).

Group differences

Measures of psychopathology

Two participants failed to answer all of the IVE questions, and three (one current ecstasy user, one polydrug control and one drug-naive control) failed to complete the SCL-90-R and were excluded from the analysis. One-way ANOVA indicated that there were no significant group differences in GHQ or IVE measures (although there was a trend towards elevated impulsiveness scores in ecstasy users relative to drug-naive controls). However, there were significant group differences for the SCL-90-R Global Severity Index (GSI) ($F_{3,57}$=4.35, P=0.008) and Positive Symptom Distress Index (PSDI) ($F_{3,57}$=3.82, P=0.015) scores (Fig. 1a, b), and on scores on eight of the ten specific SCL-90-R factors. These were: somatisation ($F_{3,57}$=4.70, P=0.005), obsessive–compulsive ($F_{3,57}$=4.33, P=0.008), anxiety ($F_{3,57}$= 4.26, P=0.009), phobic anxiety ($F_{3,57}$=3.21, P=0.029), inter-personal sensitivity ($F_{3,57}$=3.57, P=0.019), depression ($F_{3,57}$=2.90, P=0.043), paranoid ideation ($F_{3,57}$= 2.86, P=0.045) and altered appetite and restless sleep ($F_{3,57}$=3.69, P=0.017), e.g. Fig. 1c, d. There were no significant group differences in psychoticism or hostility.

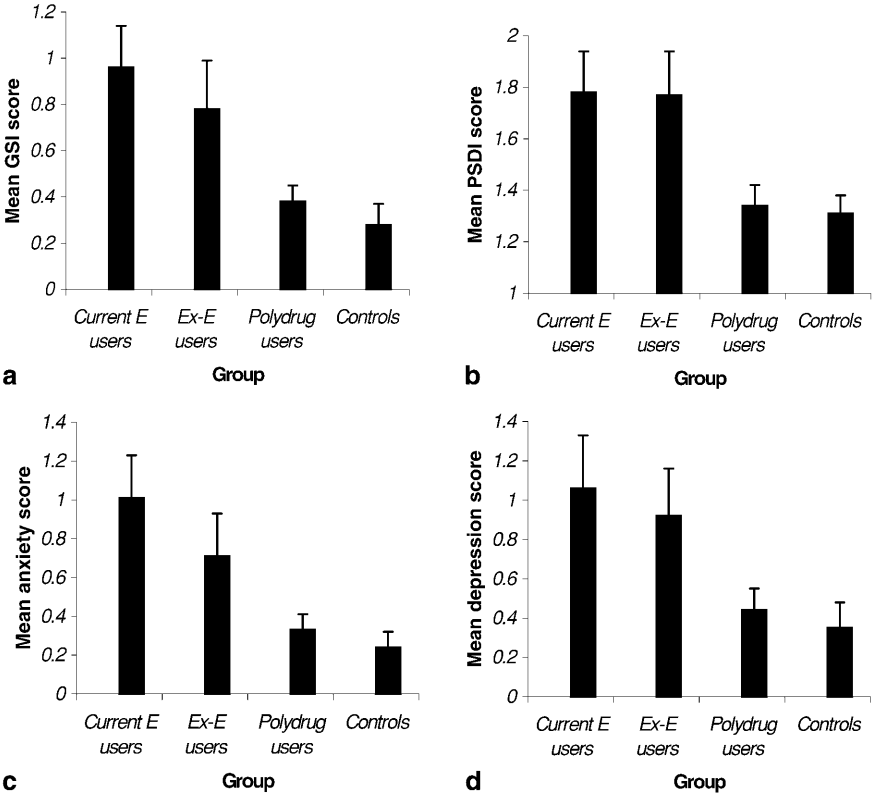

Fig. 1 Group differences in SCL-90-R psychopathology scores. **a** Mean global severity index scores. **b** Mean positive symptom distress index scores. **c** Mean anxiety scores. **d** Mean depression scores

Planned comparisons indicated that, although there were no significant differences between current and ex-users on any SCL-90-R measure, current ecstasy users exhibited significantly elevated scores on the majority of measures relative to polydrug users and drug-naive controls, whereas ex-ecstasy users only exhibited elevated scores on a subset of SCL-90-R measures relative to polydrug users and drug-naive controls (Table 4).

Measures of neuropsychological performance

Three participants failed to complete the Stroop test (one ex-ecstasy user, one polydrug user and one drug-naive control), two (one ex-ecstasy user and one polydrug control) failed to complete the SSS and fluency tests, and one ex-ecstasy user failed to complete the TMT, MFF20 and RBMT tests. These participants were excluded from the analysis. There were no statistically significant group differences in executive functions indicated by verbal fluency, digit cancellation or Stroop test performance. There were also no group differences in TMT performance (A) or in the completion times for TMT (B) and the number of SSSs in 90 s. However, there was a trend towards a statistically significant group difference in the category fluency test ($F_{3,62}$=2.71, P=0.053) – ecstasy users tended to generate significantly fewer items for both categories. The ecstasy user groups also exhibited elevated impulsivity as indicated by significant group differences in latencies to first response ($F_{3,62}$=3.80, P=0.015), total number of errors committed ($F_{3,62}$=7.42, P<0.001; Fig. 2a, b) and the composite I score for the MFF20 ($F_{3,62}$=7.34, P<0.001). Furthermore, there were statistically significant group differences in the number of errors committed in the TMT (B) ($F_{3,62}$=2.75, P=0.050) and the SSS test ($F_{3,61}$=3.17, P=0.031) – ecstasy users exhibited the worst performance in both tests (Fig. 2c, d). Finally, ecstasy users exhibited impaired memory performance as indicated by a highly statistically significantly group difference in RBMT recall performance ($F_{3,59}$=4.21, P=0.009). Immediate recall performance was considerably better than delayed recall performance ($F_{1,59}$=50.42, P<0.001), but there was no interaction between groups and time of testing (Fig. 3a, b). Planned comparisons indicated that there were no significant differences between current and ex-users on any neuropsychological measure but confirmed that both current ecstasy users and ex-ecstasy users exhibited significantly impaired cognitive performance relative to drug-naive controls. Furthermore, although current and ex-ecstasy users committed significantly more errors than polydrug users in the MFF20 test, only ex-ecstasy users exhibited significantly impaired RBMT recall performance compared with polydrug users (Table 4).

Correlational analyses

Measures of psychopathology

GHQ scores correlated significantly with SCL-90-R GSI scores (r=0.491, P<0.001) and PSDI scores (r=0.463,

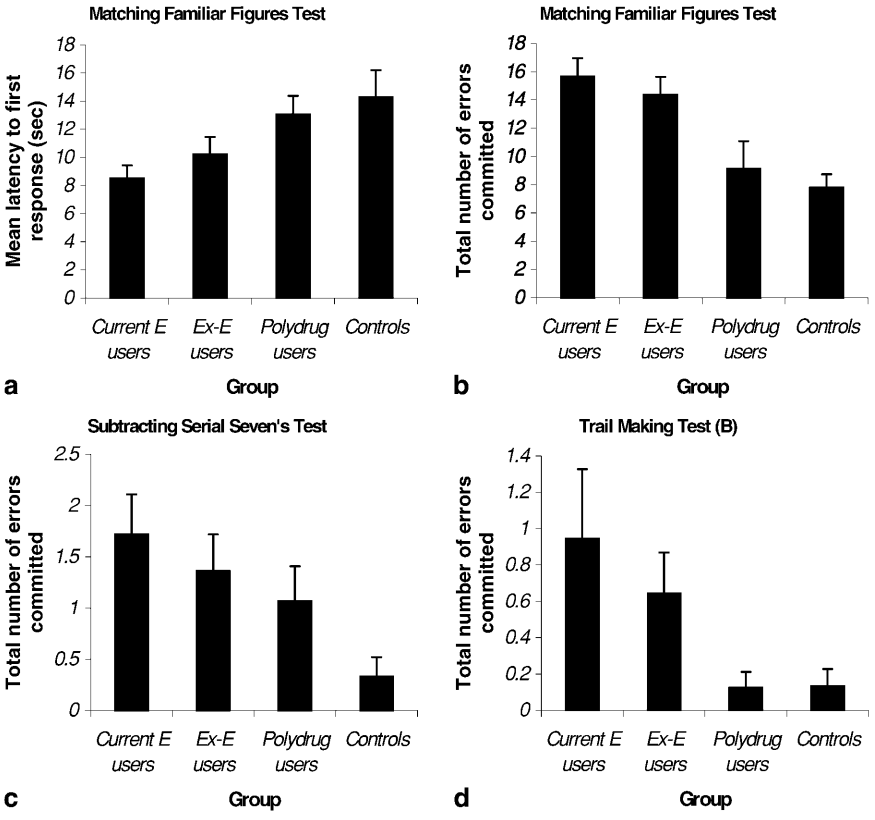

Fig. 2 Group differences in cognitive performance. **a** Latencies to first response in the Matching Familiar Figures test. **b** Total number of errors committed in the Matching Familiar Figures test. **c** Total number of errors committed in the Subtracting Serial Seven's test. **d** Total number of errors committed in the Trail Making Test (**b**)

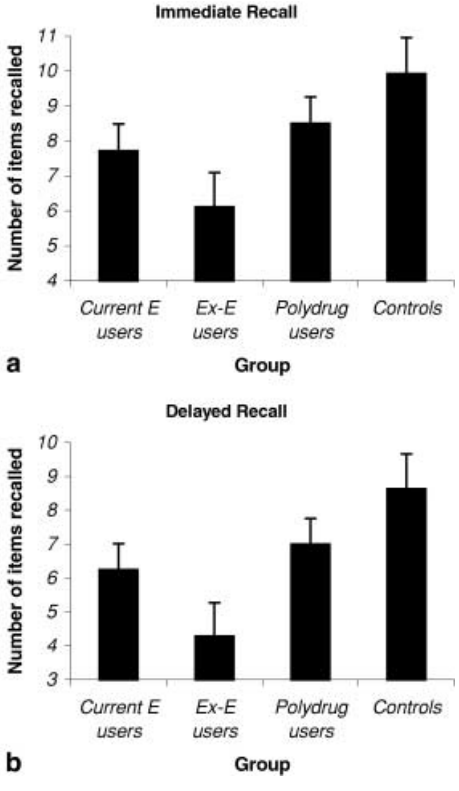

Fig. 3 Group differences in memory performance. **a** Immediate recall in the paragraph recall component of the Rivermead Behavioural Memory Test. **b** Delayed recall in the same test

P<0.001). Furthermore, scores on all SCL-90-R factors were highly inter-correlated, and all except somatisation scores correlated significantly at the *P*<0.001 probability level with GHQ scores.

Measures of neuropsychological performance

MFF20 latencies to first response were highly negatively correlated with the number of errors committed (r=–0.570, *P*<0.001). However, neither MFF20 measure correlated significantly with any other measure of cognitive performance. Furthermore, cognitive performance in the RBMT, MFF20, TMT (B), SSS, and category fluency tests was not significantly correlated with GHQ scores, IVE scores or any of the SCL-90-R scores.

Measures of illicit drug use

Estimated lifetime consumption of ecstasy correlated with the average (r=0.568, *P*<0.001) and maximum number of ecstasy tablets (r=0.396, *P*=0.001) that users reported consuming on a single occasion. The average dose was also highly correlated with the maximum dose of ecstasy (r=0.890, *P*<0.001). However, the only measure of other illicit drug use that correlated with measures of ecstasy consumption was the reported number of LSD trips taken in the year prior to testing. This was significantly correlated with the average (r=0.568, *P*<0.001) and maximum reported doses of ecstasy (r=0.396, *P*=0.001).

Dose–response relationships

The estimated lifetime consumption of ecstasy by current users correlated negatively with their immediate (r=–0.586, P=0.011) and delayed (r=–0.541, P=0.021) recall performance, while the estimated lifetime consumption of ex-ecstasy users was not correlated with their recall performance. However, the number of errors committed in the MFF20 was positively correlated with the reported average dose of ecstasy consumed by all ecstasy users (r=0.382, P=0.034).

Stepwise regression analyses

Measures of psychopathology

No measure of past ecstasy consumption predicted SCL-90-R GSI and PSDI scores, or any of the SCL-90-R factor scores, whereas previous cannabis use predicted most of these scores. The reported number of cannabis joints consumed in the year prior to testing predicted overall GSI (R square =0.431, P<0.001) and PSDI (R square =0.231, P<0.001) scores. The number of cannabis joints consumed also predicted specific anxiety (R square =0.427, P<0.001), depression (R square =0.363, P<0.001), obsessive–compulsive (R square =0.305, P<0.001), inter-personal sensitivity (R square =0.370, P<0.0010, hostility (R square =0.313, P<0.001) and altered appetite and restless sleep (R square =0.273, P<0.001) factor scores. However, some SCL-90-R factor scores were predicted by past use of other drugs in addition to cannabis. Somatisation and psychoticism were predicted by the reported number of cannabis joints, and the number of popper hits consumed in the year prior to testing (R square for cannabis only =0.310, P<0.001, and =0.398, P<0.001, respectively; R square for cannabis + poppers =0.395, P<0.001, and =0.507, P<0.001, respectively). Phobic anxiety was predicted by the reported number of cannabis joints and number of grams of amphetamine consumed in the year prior to testing (R square for cannabis only =0.413, P<0.001; R square for cannabis + amphetamine =0.536, P<0.001). Finally, paranoid ideation was predicted by the reported number of cannabis joints and number of grams of cocaine consumed in the year prior to testing (R square for cannabis only =0.378, P<0.001; R square for cannabis + cocaine =0.445, P<0.001).

Measures of neuropsychological performance

In contrast to measures of psychopathology, most measures of neuropsychological performance were only predicted by measures of previous ecstasy use. Immediate and delayed recall were only significantly predicted by estimated lifetime consumption of ecstasy tablets (R square =0.150, P=0.005, and =0.174, P=0.002, respectively). MFF20 errors, mean latencies to first response and I scores were only significantly predicted by the average dose of ecstasy (R square =0.361, P<0.001; =0.170, P=0.005; 0.321, P<0.001, respectively). SSS errors were only predicted by the maximum dose of ecstasy (R square =0.190, P=0.001). The exception, however, was that TMT (B) errors were only predicted by the number of LSD trips and number of psilocybin mushrooms consumed in the year before testing (R square for LSD only =0.271, P<0.001; R square for LSD + psilocybin mushrooms =0.359, P<0.001).

Analysis of covariance

The reported number of cannabis joints consumed in the year prior to testing proved to be a statistically significant covariate for all of the SCL-90-R measures of psychopathology and only group differences in GSI, somatisation, obsessive–compulsive, anxiety, phobic anxiety, and altered appetite and restless sleep remained statistically significant when past cannabis use was treated as a covariate. The reported number of LSD trips and popper hits experienced in the year prior to testing also proved to be statistically significant covariates for the majority of SCL-90-R measures, while cocaine and amphetamine use were statistically significant covariates for paranoid ideation and phobic anxiety, respectively. Furthermore, none of the group differences in SCL-90-R measures remained statistically significant when all of these measures of illicit drug consumption were treated as covariates simultaneously.

In contrast, none of the latter measures of illicit drug use was a statistically significant covariate of any of the neuropsychological measures that had been proven to differentiate between groups. Only past consumption of psilocybin mushrooms proved to be a significant covariate ($F_{1,52}$=10.17, P=0.002) of the number of errors committed in the TMT (B) and the previously borderline group difference in errors in this test was no longer statistically significant when past use of mushrooms was treated as a covariate.

Discussion

The results of the present study showed that current and ex-ecstasy users exhibited significantly elevated psychopathology relative to both polydrug users and drug-naive controls. Planned comparisons indicated that the SCL-90-R scores of current ecstasy users were not significantly different to those of ex-ecstasy users. However, there was tentative evidence that current users exhibited a broader range of psychopathology than ex-ecstasy users. These findings are generally in agreement with those of Parrott et al. (2000) and tentative evidence of the remission of anxiety after a year of abstinence from ecstasy (Wareing et al. 2000). However, stepwise regression analyses indicated that elevated scores on all of these SCL-90-R measures were primarily predicted by

measures of the extent of recent cannabis use, instead of previous ecstasy consumption. Some SCL-90-R factors were also predicted by the recent use of other illicit drugs, in addition to cannabis, but no measure of ecstasy consumption proved to be a significant predictor of current psychopathology. Furthermore, reported past use of many illicit drugs other than ecstasy proved to be statistically significant covariates for SCL-90-R measures, and none of the group differences in SCL-90-R measures remained statistically significant if all of these measures of drug consumption were treated as covariates simultaneously. Thus, psychopathology in regular ecstasy users may be associated more with their polydrug use generally, rather than with their ecstasy use.

The present findings are in agreement with reports that psychopathology in young adults is associated with substance abuse. For example, use of cannabis has been associated with co-morbid or concurrent psychopathology both in cross-sectional (Deykin et al. 1986) and longitudinal (Johnson and Kaplan 1990; Miller-Johnson et al. 1998) studies. It is difficult, however, to interpret the causality of the relationship between polydrug use and psychopathology. There are three possible ways of accounting for the relationship between substance abuse and mental health problems. First, the two may be associated because they share overlapping aetiologies for the two distinct outcomes. Second, individuals with psychopathology may be more predisposed to consume illicit substances either in an attempt to self-medicate their distress (Deykin et al. 1986; McGuire et al. 1994; Khantzian 1997) or through differential association with a sub-culture that uses drugs. The third possibility is that polydrug use causes psychopathology. The authors of a recent longitudinal study of cannabis use concluded that the primary causal direction leads from psychopathology to cannabis use in adolescents. However, they concluded that the reverse occurs in young adults and that the use of cannabis, alcohol and cigarettes at age 18 years elevated the risk of later mental disorder at age 21 years (McGee et al. 2000). If heavy use of cannabis does play a causal role in the aetiology of psychopathology, it is noteworthy that, in the present study, cannabis users who had never taken ecstasy (polydrug users) exhibited significantly less psychopathology and ex-ecstasy users displayed a narrower range of psychopathology. Thus, although the extent of past ecstasy use did not predict mental health problems in the present study, it is possible that regular ecstasy use may exacerbate psychopathology in young adults.

Despite the elevated psychopathology observed in current and ex-ecstasy users, and significant positive correlations between GHQ scores and SCL-90-R scores, the results indicated that there were no significant group differences between GHQ scores. This finding fails to support a previous report from this laboratory (Morgan 1998b) but does suggest that the GHQ is less sensitive than the SCL-90-R to individual differences in affective state associated with previous exposure to ecstasy. In the present study, there were also no significant group differences in impulsiveness, venturesomeness and empathy questionnaire (IVE) scores, although there was a trend towards elevated impulsiveness scores in ecstasy users relative to drug-naive controls. Again this fails to support previous reports that regular ecstasy users exhibited elevated IVE impulsiveness scores compared with control participants (Morgan 1998b; Parrott et al. 2000). However, there are other reports from this laboratory that relatively light ecstasy users did not differ from drug-naive controls in relation to IVE impulsiveness (Morgan 1998a) or mood (Morgan 1998a, 1998b).

In contrast to the SCL-90-R findings, regression analyses indicated that impaired neuropsychological performance by ecstasy users in the SSS, MFF20 and RBMT tests was only predicted by measures of past consumption of ecstasy. Furthermore, no measure of past consumption of cannabis, amphetamine, cocaine, LSD, psilocybin mushrooms or poppers proved to be statistically significant covariates of measures of performance on any of these neuropsychological tests. This suggests that the mechanisms underlying the aetiology of the cognitive deficits in ecstasy users are distinct from those underlying the aetiology of psychopathology. There was one exception, however. Regression analyses indicated that TMT (B) errors were only predicted by the extent of previous consumption of hallucinogenic drugs (LSD and psilocybin mushrooms), and the group difference in the number of errors committed in the TMT (B) was not statistically significant when past reported consumption of psilocybin mushrooms was treated as a covariate. It is difficult to interpret the clinical significance of elevated error rates in this test, however. McCaffrey et al. (1989) investigated the stability of performance errors in the TMT in poly-substance abusers and concluded that the transient nature of the errors raised questions about its utility as an indicator of central nervous system dysfunction.

In the present study, the average latency to first response of current ecstasy users in the MFF20 test was significantly briefer than that of drug-naive controls and polydrug controls, and they also committed more errors in this test than either polydrug users or drug-naive controls. Furthermore, the number of errors committed by all ecstasy users was positively correlated with the average dose of ecstasy that they reported consuming on a typical occasion. These findings support previous reports from this laboratory (Morgan 1998a, 1998b, 1999, 2000). Furthermore, the high latency-error correlation attained for the MFF20 in the present study supported the rationale for the derivation of an I score for each participant – a composite behavioural index of impulsivity (Salkind and Wright 1977). The I scores of both current and ex-ecstasy users in the present study were also significantly elevated compared with those of drug-naive controls and polydrug controls. The latter findings suggest that ecstasy users exhibit a trade-off towards greater speed at the cost of less accuracy in this type of cognitively demanding visual discrimination task.

Ex-ecstasy users, who had been abstinent for at least 6 months, also committed more errors in the MFF20 test

than either polydrug users or drug-naive controls, but only exhibited significantly shorter latencies than drug-naive controls. Thus, although there was some tentative evidence of a partial remission of faster responding in ex-ecstasy users, there was no statistically significant evidence of remission of inaccuracy after abstinence from ecstasy for at least 6 months and an average of 2 years.

The exact relationship between self-report measures of trait impulsiveness and behavioural measures of impulsivity is unclear, however, because further analysis showed that performance on the IVE and MFF20 was not correlated (r=0.21, P=0.11). This suggests that the scores provided by these measures probably reflect different constructs of impulsivity – for further discussion of this issue see Morgan (1998b) and Evenden (1999). MFF20 performance was also not correlated with performance in any other neuropsychological test. Thus, although it has been speculated that MFF20 performance might reflect deficits in visual discrimination, attention, working memory and/or central executive function – in addition to providing a behavioural measure of impulsivity (Morgan 2000), the present study provides no evidence to support this view. Nevertheless, the SSS and TMT tests are believed to tap working memory and/or central executive function to some degree. Thus, the fact that ecstasy users exhibited elevated error rates in both of these tests, as well as in the MFF20, suggests that they may exhibit a general tendency to perform less accurately than non-users when they are under time pressure in cognitively demanding tasks.

Other results from the present study suggest that the neuropsychological deficits in ecstasy users were relatively circumscribed. Although there was a trend towards a statistically significant group difference in the total number of items generated for both categories of the category fluency test, there were no group differences in verbal fluency, digit cancellation or Stroop test performance. There were also no group differences in TMT (A) performance or in the completion times for TMT (B) and the number of SSSs in 90 s. The lack of any group differences in verbal fluency in the present study is in agreement with previous reports (Klugman et al. 1999; Wareing et al. 2000). The lack of other deficits in neuropsychological performance is consistent with previous reports that ecstasy users are unimpaired in many aspects of cognitive processing (Krystal et al. 1992; Parrott et al. 1998; Parrot and Lasky 1998; Morgan 1998b, 1999, 2000; Rodgers 2000).

Contrary to a previous report from this laboratory (Morgan 1999), the recall performance of current ecstasy users in the present study was not found to be significantly impaired compared with that of polydrug users. This finding may simply reflect the use of a smaller sample of current ecstasy users in the present study. However, the latter finding agrees with other recent reports that immediate recall was not impaired relative to cannabis-using controls (Gouzoulis-Mayfrank et al. 2000; Rodgers 2000). Despite the use of smaller samples in the present study, the recall of current ecstasy users was significantly impaired compared with that of drug-naive control subjects. This supports previous reports that ecstasy users exhibit impaired recall when compared with drug-naive controls (Parrott and Lasky 1998; Parrott et al. 1998; Schifano et al. 1998; Klugman et al. 1999; McCann et al. 1999; Morgan 1999; Gouzoulis-Mayfrank et al. 2000; Reneman et al. 2000) and is in agreement with the regression analyses that indicated that impaired recall performance was specifically predicted by measures of past ecstasy use.

A more striking finding was that, despite the fact that in all other neuropsychological tests the cognitive performance of ex-ecstasy users was equal to or less impaired than that of current users, the recall performance of ex-ecstasy users was significantly impaired relative to polydrug users, while that of current users was not. This is consistent with a report by Wareing et al. (2000) and suggests that deficits in episodic memory performance do not recover after abstinence from ecstasy for at least 6 months and an average of 2 years. There were also statistically significant dose–response relationships between the extent of lifetime exposure to ecstasy and the degree of impairment of recall performance. This is consistent with previous reports of statistically significant dose–response relationships between the extent of memory impairment and the degree of previous exposure to ecstasy (Bolla et al. 1998; Semple et al. 1998; Morgan 1999; Gouzoulis-Mayfrank et al. 2000). Finally, the finding that recall performance was not correlated with GHQ scores, IVE scores or any of the SCL-90-R scores suggests that impaired recall performance is not secondary to individual differences in mood or personality.

In summary, the present findings indicate that regular use of ecstasy is associated with elevated psychopathology – although further analysis indicated that this psychopathology was primarily predicted by the extent of previous consumption of cannabis rather than ecstasy. In contrast, the selective neuropsychological deficits observed in ecstasy users appear to be largely attributable to the extent of previous exposure to ecstasy. Furthermore, abstinence from regular use of ecstasy for an average of 2 years did not reverse behavioural impulsivity or impairments in working memory or verbal recall performance. Thus, regular ecstasy users are at significant risk of protracted neuropsychological impairments. Impulsivity appears to be distinct from other neuropsychological deficits, but none of the neuropsychological deficits observed in ecstasy users was related to psychopathological status. There was also evidence of significant dose–response relationships between measures of past exposure to ecstasy and measures of neuropsychological impairment. These findings are consistent with evidence that MDMA causes persistent impairment of memory performance in rats (Marston et al. 1999) and evidence that ecstasy has potent and selective neurotoxic effects on central nervous system serotonergic systems in humans (McCann et al. 1998; Semple et al. 1999; Morgan 2000; Reneman et al. 2000).

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