

ORIGINAL INVESTIGATION

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Memory deficits associated with recreational use of “ecstasy” (MDMA)

Received: 12 January 1998/Final version: 14 May 1998

Abstract Evidence from both animal, and human, studies suggests that repeated administration of 3,4-methylenedioxymethamphetamine (MDMA; “ecstasy”) produces lasting decreases in serotonergic activity. Serotonin is believed to play a modulatory role in a variety of psychological processes, including learning and memory. There are recent reports that polydrug users, who have used ecstasy recreationally, exhibit selective impairments in memory. However, these studies did not compare ecstasy users with polydrug users who had not taken ecstasy, leaving open the possibility that the memory deficits may be associated with a history of use of other illicit drugs. The present study used the Rivermead Behavioural Memory test to investigate immediate and delayed recall in: 25 polydrug-users who had taken more than 20 tablets of ecstasy (MDMA group), 22 participants (polydrug controls) who had never taken ecstasy, but, otherwise has personal characteristics (e.g. age, gender, education, height, weight), and illicit drug use histories, that were generally not significantly different from those of the MDMA group, and 19 participants who had not used illicit drugs but who also had similar personal characteristics (non-drug controls). Participants in the MDMA group recalled significantly fewer ideas (approximately 75% of the number of ideas recalled by participants in either of the other two groups), in both immediate and delayed recall conditions. The two illicit drug-using groups did differ in their estimated IQ scores and their duration of use of LSD, but only the latter proved to be a statistically significant covariate, and the difference in recall performance between the MDMA and polydrug controls groups remained statistically

significant when this variable was treated as a covariate. The present findings provide the first evidence that deficits in memory performance in recreational ecstasy users are primarily associated with past exposure to ecstasy, rather than with the other legal and illicit drugs consumed by these individuals, and are consistent with reduced serotonergic modulation of mnemonic function as a result of long-term neurotoxic effects of MDMA in humans.

Key words MDMA · Serotonin · Neurotoxicity · Memory

Introduction

Recreational use of the illicit drug “ecstasy” (3,4-methylenedioxymethamphetamine or MDMA) has increased dramatically in recent years. It is estimated that, in the UK alone, 750 000 ecstasy tablets are taken each weekend and more than a million people have taken the drug (Cook 1995). Media reports of severe acute toxicity and death following ingestion of ecstasy, particularly when taken at “raves”, coupled with the scale of the current epidemic of recreational use of this drug, have prompted widespread popular concern. Such concern may be misplaced, to some degree, however, since the number of individual tragedies attributed to the acute toxicity of ecstasy represents only a minute fraction of the total population of recreational ecstasy users, whereas preclinical (e.g. Steele et al. 1994; Green et al. 1995; Simantov and Tauber 1997), evidence suggests that a much more significant proportion of this population may eventually be at risk of long-term neurotoxicological effects (decreased brain 5-HT and 5-HIAA concentrations and suspected 5-HT axon terminal degeneration), particularly in the hippocampus (Fischer et al. 1995; Aguirre et al. 1997; Frederick and Paule 1997), a brain region that is believed to play an

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important role in learning and memory. Studies with humans have corroborated this view. Recreational ecstasy users have been reported to exhibit significantly lower CSF 5-HIAA levels (Ricaurte et al. 1990; McCann et al. 1994), and in a recent PET study, ecstasy users were found to have reduced 5-HT transporter binding in all brain regions, compared to controls (Szabo et al. 1997).

Despite this evidence, the possible long-term psychological sequelae of ecstasy use in humans have received relatively little attention from researchers, partly because controlled laboratory studies of the effects of repeated administration of ecstasy are precluded for legal and ethical reasons. Some evidence has emerged, however, from studies of recreational users, that suggests that recreational use of ecstasy is associated with memory impairment. Krystal et al. (1992) reported a pattern of mild-to-moderate impairment in the initial and delayed paragraph test of the Wechsler Memory Scale in a sample of nine individuals with extensive ecstasy-use histories. The latter finding is supported by a recent report of significant decrements in working memory in ecstasy users compared with alcohol users, and a trend in the same direction for prose recall (Curran and Travill 1997), and a report that both novice and more experienced recreational ecstasy users were impaired on tests of immediate and delayed recall compared to non-users, but were not impaired on other neuropsychological tests (Parrott 1997). There were some methodological problems with the earlier studies, however. In the first study, some of the participants had psychiatric histories, all had been administered tryptophan prior to testing and performance of recreational "ecstasy" users was compared with age-matched norms rather than with that of a control group of non-users (Krystal et al. 1992), while in the two more recent studies of recreational ecstasy users, data on other illicit drug use were not collected (Curran and Travill 1997; Parrott 1997). Furthermore, previous investigations of the psychological sequelae of recreational ecstasy use have failed to control adequately for the possible long-term influence of other drugs, both legal and illicit, on behaviour. This is a problem because, generally, recreational ecstasy users are polydrug users.

One strategy that can be adopted to identify the psychological sequelae associated with ecstasy use specifically, as distinct from those associated with the use of illicit drugs generally, is to compare the performance of ecstasy users not only with that of participants who have never taken any illicit drugs, but also with a third group of polydrug users who have never taken ecstasy, but otherwise have drug histories that are similar to recreational ecstasy users. The present study employed this design, and the Rivermead Behavioural Memory Test (RBMT – Wislon et al. 1985), a short, reliable and valid test of everyday memory (Wilson et al. 1989), to investigate whether a his-

tory of recreational ecstasy use, rather than polydrug use generally, is specifically associated with deficits in immediate and delayed recall performance.

Materials and methods

Participants

Sixty-six university students or graduates participated in the study: 25 recreational ecstasy users (MDMA group), 22 polydrug controls, and 19 non-drug controls. All participants were recruited by poster advertisements, and word of mouth, over a period of 3 months, and were first screened for eligibility by interviews. They were recruited so that the personal characteristics (e.g. age, gender ratio, education, height and weight) of the participants in each of the three experimental groups were similar (see Table 1). Individuals also had to be in good health. Exclusionary criteria included: current pregnancy, current or previous asthma, heart disease, epilepsy, migraine, viral encephalitis, meningitis, dyslexia, eating disorders, schizophrenia, major depressive disorder, alcoholism, or opiate dependence. Individuals recruited into the MDMA group were required to have used ecstasy on at least 20 occasions. Those recruited into the polydrug control group were required to have no history of ecstasy exposure, but otherwise, had to have a drug-use history that was, generally, not significantly different from that of the MDMA participants. Finally, non-drug control participants had to have no history of use of illicit drugs.

Screening

Initial screening of potential participants was conducted either by a telephone or face-to-face interview. Potential participants who did not meet any of the exclusionary criteria, and claimed to have a suitable drug use history, were then formally assessed with a personal details questionnaire and a general drug use questionnaire. Prospective MDMA group members were also given a specific ecstasy-use questionnaire that requested information on: the duration of usage, the last time used, the amount (number of tablets) used in the previous month, the frequency of use, the average and maximum amounts taken per session, and an estimate of total lifetime consumption. They were also requested to identify the number of each type of tablet they had ever taken with the aid of a list of available "brands". Participants who passed this screening process were administered the New Adult Reading Test (NART – Nelson and O'Connell 1978) to provide an estimate of premorbid IQ, and to ensure that their knowledge of English was adequate for completion of the experimental tasks (they had to obtain more than 25 correct answers to participate). Finally, except for nicotine, all participants were required to abstain from taking any psychoactive drug (include alcohol) on the day of the study. Two participants were excluded from the study: one non-drug control participant due to recent alcohol intoxication and one MDMA participant who had taken antidepressants on the day of the study.

Test procedure

On the test day, participants were instructed to listen to a brief audio-taped news story, taken from the Rivermead Behavioural Memory Test (RBMT) and then write down as much of what they has heard as possible, word for word, immediately after the story had been presented. The story comprised five sentences containing 65 words and 21 "ideas". The RBMT was followed by a battery of neuropsychological tests, the results of which have been reported elsewhere (Morgan 1998). These tests included two

successive “Tower of London” (TOL) tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB, Paul Fray Ltd) and an intervening 20-item Matching Familiar Figures Test (MFF20 – Caims and Cammock 1978). After they had completed these tests, and 40–50 min after RBMT story had been presented, participants were again asked to write down as much of the story as possible. Recall was scored in the standard way, with one point being given for each of the 21 ideas recalled perfectly or a close synonym, half a point for partial recall or partial synonym. One-way analysis of variance was used to compare the personal characteristics and drug histories of participants in the three experimental groups. A repeated measures analysis of variance with two levels (immediate and delayed recall) was used to compare memory performance. Post hoc analyses of group differences were conducted with Duncan’s multiple range test (using a *P* value of 0.05 as a cut-off for statistical significance). Pearson’s product moment correlation coefficient was used to explore correlations between drug history and recall performance variables. Finally, analysis of covariance was employed in conjunction with the repeated measures analysis of immediate and delayed recall to identify, and control for, any independent variables that might be significant covariates. The study was approved by the local health authority ethics committee and participants provided signed informed consent.

Results

One-way analysis of variance of the personal characteristics of participants in the three experimental groups (MDMA, polydrug control and non-drug control) indicated that they were not significantly different in terms of their: age, gender ratio, education level achieved, height, or weight (see Table 1). Further analysis of the self-reported drug use histories of participants in the

Table 1 Means (standard deviations) for personal characteristics

	Non-drug control (<i>n</i> = 19)	Polydrug control (<i>n</i> = 22)	MDMA (<i>n</i> = 25)
Age	21.74 (2.94)	22.86 (4.52)	22.28 (2.51)
Gender ^a	1.58 (0.50)	1.68 (0.48)	1.48 (0.51)
Height (cm)	172.3 (7.91)	170.3 (8.48)	172.3 (8.88)
Weight (kg)	67.4 (10.8)	64.4 (14.2)	65.1 (9.9)
Education ^b	2.68 (0.58)	2.95 (0.21)	2.80 (0.50)
NART	37.5 (4.15)	39.1 (4.73)	35.9 (2.52) ^c

^aMales coded as 1, Females as 2

^b1 = GCSE, 2 = A-level, 3 = HND

^cSignificant difference between groups at the 0.05 level

two polydrug-using groups (MDMA and polydrug controls) showed that they were not significantly different in terms of their average consumption of: alcohol, cigarettes, and cannabis per week; or amphetamine, LSD, psilocybin mushrooms, inhalants (“poppers”), and cocaine in the previous year; or their duration of use of: alcohol, cigarettes, cannabis, amphetamine, psilocybin mushrooms, inhalants, and cocaine (see Table 2). Although the average consumption of cocaine appeared to differ between groups, only a small minority of participants in either group had ever used this drug, and the apparent difference (and its lack of statistical significance) was largely attributable to the fact that only two of the MDMA participants were regular heavy users (i.e. used more than 10 g a year).

There were some statistically significant differences between the groups, however. The NART (estimated

Table 2 Means (SD) for self-reported drug consumption

	Control	Polydrug	MDMA
<i>Alcohol (units)</i>			
Consumed per week	14.97 (12.9)	42.95 (36.7)	34.94 (23.3)
Duration of use (years)	5.79 (3.5)	8.52 (4.8)	7.90 (2.5)
<i>Cigarettes</i>			
Consumed per week	36.75 (55.3)	67.33 (84.4)	65.80 (55.1)
Duration of use (years)	3.18 (3.3)	6.15 (6.1)	6.07 (4.2)
<i>Cannabis (joints)</i>			
Consumed per week	0.00 (0.0)	9.28 (11.5)	13.74 (11.6)
Duration of use (years)	0.00 (0.0)	5.52 (4.8)	6.14 (2.8)
<i>Amphetamine (g)</i>			
Consumed in previous year	0.00 (0.0)	12.09 (32.1)	23.68 (42.1)
Duration of use (years)	0.00 (0.0)	2.73 (3.7)	4.32 (2.6)
<i>Psilocybin mushrooms</i>			
Consumed in previous year	0.00 (0.0)	112.3 (234)	203.6 (267)
Duration of use (years)	0.00 (0.0)	1.25 (1.9)	2.44 (2.5)
<i>LSD (“trips”)</i>			
Consumed in previous year	0.00 (0.0)	2.68 (6.1)	2.63 (4.2)
Duration of use (years)	0.00 (0.0)	1.43 (2.1)	3.19 (2.2) ^a
<i>Inhalants (“hits”)</i>			
Consumed in previous year	0.00 (0.0)	176.0 (766)	30.03 (109)
Duration of use (years)	0.00 (0.0)	1.18 (2.7)	2.02 (2.6)
<i>Cocaine (g)</i>			
Consumed in previous year	0.00 (0.0)	0.27 (1.3)	2.60 (6.9)
Duration of use (years)	0.00 (0.0)	0.27 (1.1)	1.36 (2.6)

^aIndicates significant difference between MDMA and polydrug groups at the 0.05 probability level

Table 3 Group means (standard deviations) of number of RBMT ideas recalled

	Non-drug group	Polydrug group	MDMA group
<i>n</i> per group	19	22	25
Immediate recall	8.29 (2.87)	8.09 (1.86)	6.14 (2.23) ^a
Delayed recall	7.61 (2.74)	7.23 (1.90)	5.36 (2.48) ^a

^a Significantly different from the other two groups at the 0.01 level

IQ) scores for the three groups were different ($F_{2,63} = 4.19$, $P = 0.020$), and re-analysis of the data from only the two groups of participants who had used illicit drugs (MDMA and polydrug groups) revealed that the NART scores of polydrug participants were significantly higher than those of the MDMA participants ($F_{1,45} = 8.96$, $P = 0.004$). There was also one statistically significant difference between the duration of use of one of the less frequently used illicit drugs – LSD. Participants in the MDMA group had used LSD for a significantly longer period than those in the polydrug group ($F_{1,45} = 7.81$, $P = 0.008$). There were also group differences in the number of participants who had used benzodiazepines, barbiturates and ketamine. Eight participants in the MDMA group reported occasional use of benzodiazepines (although only one reported having taking any within the 2 weeks prior to testing), two reported occasional use of barbiturates, and two reported having taken ketamine with ecstasy, while none of the participants in the polydrug control group reported having taken these drugs.

Repeated measures analysis of variance indicated that there was a highly statistically significant group effect on recall ($F_{2,63} = 6.28$, $P = 0.003$), and, as expected, immediate recall performance was considerably better than delayed recall performance ($F_{1,63} = 30.62$, $P = 0.000$), while there was no interaction between groups and time of testing. Analysis of the data from the MDMA and polydrug groups alone revealed that there was a marked impairment of the recall performance of MDMA participants compared to polydrug participants ($F_{1,45} = 10.06$, $P = 0.003$), that immediate recall performance was better than delayed recall performance ($F_{1,63} = 21.19$, $P = 0.000$), and that there was no statistically significant interaction between groups and time of testing (see Table 3).

As indicated earlier, the NART scores of polydrug participants were significantly higher than those of the MDMA participants. However, NART scores did not correlate with immediate ($r = -0.015$, $P = 0.942$), or delayed ($r = 0.057$, $P = 0.786$), recall performance within the MDMA group, or with immediate ($r = 0.283$, $P = 0.202$) or delayed ($r = 0.314$, $P = 0.155$), recall performance within the polydrug group.

Average consumption of cannabis per week did not differ significantly between the participants in the MDMA group and those in the polydrug group. There

was, however, a statistically significant negative correlation between the cannabis consumption and the immediate recall ($r = -0.376$, $P = 0.009$), but not delayed recall, across participants in the two groups combined. Cannabis consumption also correlated negatively with immediate recall ($r = -0.476$, $P = 0.016$), but not delayed recall, within the MDMA group, although it did not correlate with either measure for participants in the polydrug group. Further analysis indicated, however, that cannabis consumption was not a significant covariate ($t = -1.943$, $P = 0.058$) when the recall performance of the MDMA group was compared to that of the polydrug group.

Participants in the MDMA group used LSD for a significantly longer period than those in the polydrug group. Within the MDMA group, duration of use of LSD showed a trend towards a positive correlation with the estimated lifetime consumption of ecstasy ($r = 0.381$, $P = 0.060$), and correlated negatively with delayed recall ($r = -0.412$, $P = 0.041$), but not immediate recall, and did not correlate with either measure of recall performance for participants within the polydrug group. In an analysis of covariance, duration of use of LSD proved to be a significant covariate ($t = -2.086$, $P = 0.043$) for recall performance, but the difference between the recall of the MDMA and polydrug groups remained statistically significant ($F_{1,44} = 4.98$, $P = 0.031$).

None of the other measures of consumption, or duration of use, of alcohol, tobacco, cannabis, amphetamine, cocaine, LSD, psilocybin mushrooms, or inhalants, proved to be significant covariates in relation to recall. Furthermore, within the MDMA group, repeated measures ANOVA indicated that there was no difference in recall performance between participants who had taken benzodiazepines, barbiturates or ketamine, and those who had not.

Participants in the MDMA group reported having taken an average of 50 ecstasy tablets in their lifetime, although estimates of total individual consumption ranged from the minimum entry requirement of 20 tablets to more than 160. Correlational analysis indicated that immediate and delayed recall performance were highly correlated ($r = 0.809$, $P = 0.000$), but neither measure was correlated with reported total lifetime consumption of ecstasy. On the other hand, there was a trend towards statistically significant negative correlations between immediate recall performance and the average amount of ecstasy consumed per session ($r = -0.367$, $P = 0.071$), and the duration of use of ecstasy in years ($r = -0.355$, $P = 0.082$), and there was a statistically significant correlation between a composite of these two measures (average per session \times duration of use) and immediate recall ($r = -0.466$, $P = 0.019$). However, none of these measures was correlated with delayed recall.

The average time since last use of ecstasy in the MDMA group was approximately 65 days, but this

ranged from less than a week (five participants) to more than 6 months (three participants). To investigate the relationship between the period elapsed since ecstasy was used and the degree of memory impairment, the MDMA group was divided into three categories: those who had taken ecstasy within the previous month, those who had last used it between 1 and 6 months prior to testing, and those who had not used it for at least 6 months. Analysis of these data with repeated measures ANOVA indicated a highly statistically significant effect of time elapsed since last use of ecstasy on recall performance ($F_{2,22} = 6.46$, $P = 0.006$). Post hoc analyses with Duncan's multiple range test indicated that the recall performance of participants who had not taken ecstasy for at least 6 months was statistically significantly better than that of those who had taken ecstasy within the previous month, and those who had taken it between 1 and 6 months prior to testing (see Table 4).

Finally, in response to the ecstasy questionnaire item: "In what kind of environment do you normally take ecstasy?", only one participant reported that they usually consumed the drug alone, eight reported that they usually consumed it in a small group, and 16 reported that they usually consumed it in a large group. Twenty-one of the 25 participants in the MDMA group (11 male and ten female) responded positively to the following item: "From your own experience, would you say that there are any long-term side effects from using ecstasy". The "side effects" they identified included: heightened anxiety (12 participants), depression (seven), mood swings (six), loss of appetite (five), sleep problems (five), reduced ability to concentrate (four), impaired memory (four), mental slowness (three), and paranoia (two). In response to the item: "Do you view ecstasy to be safe drug?", five participants responded "yes", eight responded "no", and 12 indicated that they were "not sure". Counter-intuitively, all of those who responded "yes" to this item also reported that they believed that anxiety, and other long-term side effects, were associated with the recreational use of ecstasy.

Discussion

The results of the present study show that deficits in recall performance were primarily associated with a history of recreational use of ecstasy. The immediate and delayed recall performance of ecstasy users was markedly impaired compared to participants in the other two control groups, even though they had similar personal characteristics (age, gender ratio, height, weight, and education level achieved), and their self-reported histories of consumption of other drugs (alcohol, cigarettes, cannabis, amphetamine, LSD, inhalants, psilocybin mushrooms, and cocaine), and duration of use of most of these drugs, was not significantly

Table 4 Means (SD) of number of ideas recalled for sub-groups of the MDMA group defined by period elapsed since last use of ecstasy

Period since last use:	MDMA sub-groups		
	<1 month	1–6 months	> 6 months
<i>n</i> per group	13	9	3
Immediate recall	6.04 (2.18)	5.33 (1.87)	9.00 (1.32) ^a
Delayed recall	5.62 (2.31)	3.78 (1.33) ^a	9.00 (1.80) ^a

^a Significantly different from the other MDMA sub-groups at the 0.05 level

different from participants in the polydrug control group.

There were some differences between the participants in the two groups that reported use of illicit drugs. NART (estimated IQ) scores of polydrug participants were significantly higher than those of the MDMA participants, but these scores did not correlate with either measure of recall performance within the two drug groups, and the difference between the means for these two groups was only 3 IQ points. Participants in the MDMA group had also used LSD for a significantly longer period than those in the polydrug group, and the duration of use of LSD also proved to be a significant covariate for recall performance. However, the difference between the recall of the MDMA and polydrug groups remained statistically significant when duration of LSD use was treated as a covariate. Finally, some MDMA participants reported occasional use of benzodiazepines, barbiturates, and ketamine, while none of the participants in the polydrug group had taken these drugs. However, the recall performance of those who had taken these drugs was not different from those who has not. Thus, the results indicate that these differences had little effect on the statistical significance of the association between impaired recall performance and a history of recreational use of ecstasy.

The results also provided some tentative evidence of relationships between measures of consumption of ecstasy and severity of impairment of recall performance. There were trends towards statistically significant negative correlations between immediate recall performance and both, the average amount of ecstasy consumed per session, and the duration of use of ecstasy in years, and a composite of these two measures was found to correlate negatively with immediate recall, but not delayed recall, performance. The results also indicated that the impairment of memory performance associated with recreational use of ecstasy was a long-lasting phenomenon (at least 6 months), although there was tentative evidence of recovery of memory performance in a small group of three ecstasy users who abstained from taking it for more than 6 months.

The present findings are generally congruent with previous investigations of memory performance in recreational ecstasy users (Krystal et al. 1992; Curran

and Travill 1997; Parrott 1997), although the design of the previous studies prohibited an assessment of the possible long-term influence of other drugs on memory performance.

There were limitations with the present study, however. Because, for legal and ethical reasons, there was no control over drug administration, and biochemical assays of MDMA consumption were not available, there was no objective confirmation of the dose or purity of MDMA taken. Tablets sold as "ecstasy" can contain MDA (3,4-methylenedioxy-amphetamine), MDEA (3,4-methylenedioxy-ethylamphetamine), or mixtures of a range of other compounds (e.g. caffeine, ephedrine, selegiline, amphetamine, ketamine, LSD — Saunders 1995; Wolff et al. 1995). However, although some tablets sold as "ecstasy" contain little or no MDMA, the majority do contain MDMA, or the related compound MDEA, and since participants in the present study reported having taken an average of 50 ecstasy tablets, of which the most common were the "white dove" type which typically contain 88–140 mg MDMA (Wolff et al. 1995), it would seem reasonable to conclude that they had indeed consumed a significant quantity of MDMA.

Another issue concerns whether ecstasy use causes memory impairment, or whether a poor memory simply reflects a pre-existing trait of ecstasy users. If the latter were the case, however, there should be no effect of average dose consumed, duration of use, or period elapsed since last use, of ecstasy on memory performance. Since there was tentative evidence of such effects, the present data suggest that ecstasy use may, indeed, cause memory impairment. This view is supported by the subjective assessments of participants in the MDMA group, the majority of whom reported that they believed that recreational ecstasy use resulted in long-term side effects, which included: elevated anxiety, depression, mood swings, reduced ability to concentrate and impaired memory. Generally, therefore, the present data may be consistent with pre-clinical evidence that, in rodents and non-humans primates, MDMA produces reductions of brain 5-HIAA concentrations and 5-HT uptake site densities in the hippocampus region, which has been implicated in mnemonic processes in humans (Valenstein et al. 1987). Furthermore, the present data agree with pre-clinical evidence that neurotoxic damage to this region can persist for many months (Fischer et al. 1995; Frederick and Paule 1997).

In previous studies, that have employed the same design (Morgan 1998), little difference has generally been observed between groups in measures of mood and cognitive performance (IQ, TOL, spatial span), although it was found (and replicated in the present investigation), that the MDMA group committed significantly more errors than the polydrug controls in the MFF20, a behavioural measure of impulsivity. Previous investigators have also reported that recre-

ational ecstasy users were unimpaired on other neuropsychological measures (Krystal and Price 1992; Parrott 1997). Thus, the lasting psychological sequelae of ecstasy use in young adults appear to fall within two reasonably specific categories: 1) elevated impulsivity, and 2) impaired memory performance.

It has been suggested that more general cognitive impairments may not be evident in young people because of sufficient neural reserve (Hunter 1988). If, however, 5-HT function declines with age (e.g. McEntee and Crook 1991), then impaired recall performance may be one of the earliest signs of the development of more global, age-related, cognitive impairment associated with a history of recreational ecstasy-use. Furthermore, even if, as the present data tentatively suggest, mnemonic function in young recreational ecstasy users does eventually recover with abstinence, an age-related decline in serotonergic function may result in re-emergence of impaired mnemonic function in later life. Clearly, further research with older participants with a long history of ecstasy use, as well as young participants who have not used ecstasy for many months, is indeed to clarify the long-term clinical implications of impairment of immediate and delayed recall performance in young recreational ecstasy users.

Acknowledgements Thanks to Professor Paul Willner and Robert Sykes for their comments on this manuscript, and to Clare Edwards, Richard Green, Laura Grundy and Rachel Hunter for their contributions to the recruitment and assessment of participants.

References

- Aguirre N, Frechilla D, Garcia-Osta A, Lasheras B, Del Rio J (1997) Differential regulation by methylenedioxy-methamphetamine of 5-hydroxytryptamine 1A receptor density and mRNA expression in rat hippocampus, frontal cortex, and brainstem. *J Neurochem* 68:1099–1105
- Caims E, Cammock T (1978) Development of a more reliable version of the Matching Familiar Figures Test. *Dev Psychol* 13:555–560
- Cook A (1995) Ecstasy (MDMA): alerting users to the dangers. *Nursing Times* 91:32–33
- Curran HV, Travill RA (1997) Mood and cognitive effects of 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy"): week-end "high" followed by mid-week "low". *Addiction* 92:821–831
- Fischer C, Hatzidimitriou G, Wlos J, Katz J, Ricaurte G (1995) Reorganization of ascending 5-HT axon projections in animals previously exposed to the recreational drug 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy"). *J Neurosci* 15:5476–5485
- Frederick DL, Paule MG (1997) Effects of MDMA on complex brain function in laboratory animals. *Neurosci Biobehav Rev* 21:67–78
- Green AR, Cross AJ, Goodwin GM (1995) Review of the pharmacology and clinical pharmacology of 3,4-methylenedioxy-methamphetamine (MDMA or Ecstasy). *Psychopharmacology* 119:247–260
- Hunter A (1988) Serotonergic involvement in learning and memory. *Biochem Soc Transact* 17:79–81

- Krystal JH, Price LH, Opsahl C, Ricaurte GA, Heninger GR (1992) Chronic 3,4-methylenedioxymethamphetamine (MDMA) use: effects on mood and neuropsychological function. *Am J Drug Alcohol Abuse* 18:331–341
- McCann UD, Ridenour A, Shaman Y, Ricaurte GA (1994) Serotonin neurotoxicity after MDMA (“ecstasy”): a controlled study in humans. *Neuropsychopharmacology* 10:129–138
- McEntee WJ, Crook TH (1991) Serotonin, memory, and the aging brain. *Psychopharmacology* 103:143–149
- Morgan MJ (1998) Recreational use of “ecstasy” (MDMA) is associated with elevated impulsivity. *Neuropsychopharmacology* 19:252–264
- Nelson H, O’Connell A (1978) Dementia: the estimation of pre-morbid intelligence levels using the New Adult Reading Test. *Cortex* 14:234–244
- Parrott AC (1997) MDMA, mood, and memory: the agnosia of the ecstasy. *Br Psychol Soc Proc* 5:49
- Ricaurte GA, Finnegan K, Irwin I, Langston JW (1990) Aminergic metabolites in cerebrospinal fluid of humans previously exposed to MDMA: preliminary observations. *Ann NY Acad Sci* 600:699–710
- Saunders N (1995) “Ecstasy And The Dance Culture”. Neal’s Yard Publishing, London, UK
- Simantov R, Tauber M (1997) The abused drug MDMA (Ecstasy) induces programmed death of human serotonergic cells. *FASEB* 11:141–146
- Steele TD, McCann UD, Ricaurte GA (1994) 3,4-Methylenedioxymethamphetamine (MDMA, “Ecstasy”): pharmacology and toxicology in animals and humans. *Addiction* 89:539–551
- Szabo Z, Scheffel U, McCann U, Dannals RF, Ravert HT, Mathews WB, Musachio JL, Ricaurte GA (1997) Reductions of 5-HT transporters in MDMA users observed using PET with [¹¹C]-[+]-McN5652. *Soc Neurosci Abstr* 23:23
- Valenstein E, Bowers D, Verfaellie M, Heilman KM, Day A, Watson RT (1987) Retrosplenial amnesia. *Brain* 110:1631–1646
- Wilson B, Cockburn J, Baddeley A (1985) *The Rivermead Behavioural Memory Test*. Thames Valley Text, Reading, UK
- Wilson B, Cockburn J, Baddeley A, Alan D (1989) The development and validation of a test battery for detecting and monitoring everyday memory problems. *J Clin Exp Neuropsychol* 11:855–870
- Wolff K, Hay AWM, Sherlock K, Conner M (1995) Contents of “ecstasy”. *Lancet* 346:1100–1101