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Procedural and declarative memory task performance, and the memory consolidation function of sleep, in recent and abstinent ecstasy/MDMA users

Mark Blagrove[1], Jennifer Seddon[1], Sophie George[2], Andrew C Parrott[1], Robert Stickgold[3], Matthew P Walker[4], Katy A Jones[1] and Michael J Morgan[2,5]

Abstract

Ecstasy/MDMA use has been associated with various memory deficits. This study assessed declarative and procedural memory in ecstasy/MDMA users. Participants were tested in two sessions, 24 h apart, so that the memory consolidation function of sleep on both types of memory could also be assessed. Groups were: drug-naive controls ($n = 24$); recent ecstasy/MDMA users, who had taken ecstasy/MDMA 2–3 days before the first testing session ($n = 25$), and abstinent users, who had not taken ecstasy/MDMA for at least 8 days before testing ($n = 17$). Procedural memory did not differ between groups, but greater lifetime consumption of ecstasy was associated with poorer procedural memory. Recent ecstasy/MDMA users who had taken other drugs (mainly cannabis) 48–24 h before testing exhibited poorer declarative memory than controls, but recent users who had not taken other drugs in this 48–24-h period did not differ from controls. Greater lifetime consumption of ecstasy, and of cocaine, were associated with greater deficits in declarative memory. These results suggest that procedural, as well as declarative, memory deficits are associated with the extent of past ecstasy use. However, ecstasy/MDMA did not affect the memory consolidation function of sleep for either the declarative or the procedural memory task.

Keywords

declarative memory, ecstasy (drug), learning, MDMA, memory consolidation, memory, procedural learning, procedural memory, sleep

Introduction

Ecstasy is the street name for [+/−]-3,4-methylenedioxymethamphetamine (MDMA). There have been many reports associating the use of ecstasy/MDMA with various memory deficits. This study aimed to examine the declarative and procedural memory performance of frequent ecstasy/MDMA users, 2–3 days after recreational use of ecstasy/MDMA, and during abstinence from ecstasy/MDMA, while controlling for various trait and state factors, including sleep length prior to testing. It also aimed to assess the change in memory across a 24-h period, so as to investigate the potential influence of ecstasy/MDMA on sleep-dependent memory consolidation.

Relative to drug-naive controls and polydrug controls, the most consistent neurocognitive deficit observed in recreational ecstasy/MDMA users has been poorer memory and learning (Morgan, 1999; Parrott and Lasky, 1998; Rogers et al., 2009; Zakzanis et al., 2007), although there are also negative findings (e.g. Back-Madruga et al., 2003). These memory deficits can persist after prolonged abstinence from ecstasy/MDMA (Morgan et al., 2002; Thomasius et al., 2005). The sub-acute effects of ecstasy/MDMA can also disrupt mood and cognition, with significant deficits 2–4 days after consumption, which are often followed by recovery from the sub-acute effect within approximately 7 days (Curran and Travill, 1997; Curran et al., 2004; Huxster et al., 2006; Jones et al., 2008; Parrott and Lasky, 1998, Verheyden et al., 2003). In order to separate out these sub-acute deficits from the longer-term chronic psychobiological deficits, we assessed two groups of frequent ecstasy/MDMA users: those who had taken ecstasy/MDMA in the previous 2–3 days, and those who had not taken any ecstasy/MDMA in the 8 or more days prior to testing. The first aim was to compare the performance of these two groups with controls on a

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declarative and a procedural memory task. The previous literature supports a prediction of deficits in ecstasy/MDMA users for the declarative task. The procedural task was included so as to augment the limited literature on the relationship between ecstasy/MDMA use and psychomotor performance, which does not support deficits on such tasks (Zakzanis et al., 2007), and because the specific task used, the Finger Tapping Task, is the standard task for the assessment of sleep-dependent memory consolidation.

The second aim was to assess whether ecstasy/MDMA affects the process of sleep-dependent memory consolidation. A period of sleep on the night after a procedural learning task can improve subsequent performance, despite no intervening task practice (Stickgold, 2005; Walker, 2005). This effect is not due to reduced sleepiness (Walker et al., 2002). The sleep effect is also seen for declarative memory tasks (Axmacher et al., 2008; Ellenbogen et al., 2009), but here usually refers to a smaller deficit in delayed recall performance after sleep than after a similar period spent awake (Born and Gais, 2003).

It was hypothesized that the sleep-dependent consolidation effect for declarative and/or procedural memory might be reduced or absent in ecstasy/MDMA users, because of the drug's disruptive effects upon sleep (Carhart-Harris et al., 2009; Huxster et al., 2006; Jones et al., 2008; Kirilly et al., 2008; Pirona and Morgan, 2010). The hypothesized decrement in procedural memory consolidation is also supported by the finding of an enhancement of memory consolidation during sleep, for the Finger Tapping Task, when acute selective serotonin reuptake inhibitor (SSRI) administration occurred in the period between learning and sleep (Rasch et al., 2009). SSRI administration generally augments serotonin activity (Beyer and Cremers, 2008), whereas serotonin deficiencies are claimed to follow ecstasy/MDMA usage (Thomasius et al., 2003; Walker et al., 2007), and may hence disrupt sleep-dependent procedural memory consolidation.

The third aim was to take account of three areas of confound present in naturalistic studies of recreational ecstasy/MDMA use. The first of these is the co-use of other drugs, which may themselves cause memory deficits (Croft et al., 2001; Gouzoulis-Mayfrank and Daumann, 2006; Lamers et al., 2006; Parrott, 2006). The use of illegal drugs in the 24 h before testing was therefore an exclusion criterion for the study. However, as there is evidence for ketamine (Morgan et al., 2004), cocaine (Schierenbeck et al., 2008) and cannabis (Pope et al., 2001) having cognitive effects that last longer than 24 h, after the initial analysis, using all participants, the data were reanalysed having temporarily excluded participants who reported any illegal drug use in the 48–24-h period before testing. The second area of confounds is pre-morbid intelligence and personality differences between ecstasy/MDMA users and non-users. The following traits which may act as confounds of memory performance, either directly or in interaction with drug use were proposed: Locus of Control (Blagrove and Akehurst, 2001), Conscientiousness (Saucier, 1994), and Morningness–Eveningness, a measure of preference that the individual has to do effortful or intense work in the morning compared with the evening. Self-reported usual time of maximum alertness was also recorded. A third type of confound was pre-test and during-test factors, such as length of sleep and alcohol/caffeine/nicotine use prior to testing, and sleepiness during testing.

To summarize, it was hypothesized that:

1. Declarative memory performance would be worse in recent and abstinent ecstasy/MDMA users compared with non-drug-using controls; and, with respect to the memory consolidation function of sleep,
2. Recent and abstinent ecstasy/MDMA users would exhibit a greater decrement in declarative memory performance, following sleep, than non-drug-using controls;
3. Recent and abstinent ecstasy/MDMA users would show a reduced improvement in procedural memory performance, following sleep, compared with non-drug-using controls.

No hypothesis was proposed about procedural memory performance being poorer in recent and abstinent ecstasy/MDMA users compared with non-drug-using controls, as the current limited literature on this does not support such a prediction. Also, the literature is unclear about the sub-acute effects of ecstasy/MDMA on memory, with some evidence that recent use is associated with memory deficits (Parrott and Lasky, 1998) while other evidence suggests that ecstasy/MDMA has no sub-acute effects on memory after controlling for baseline performance and other recent drug use (Pirona and Morgan, 2010). The study thus included both recent and abstinent ecstasy/MDMA groups, but no prediction was made about whether memory deficits in the recent ecstasy/MDMA group would exceed those of the abstinent group.

Method

Participants and drug conditions

Recruitment was by advertisements for individuals who frequently attend nightclubs: there was no mention of drugs in the advertisements. This ensured that participants had a similar nightclubbing social life, so that factors such as sporadic late nights and intense dancing were controlled for, but also that self-selection on the basis of drug use did not occur. Such controlling for lifestyle did, however, result in difficulty in finding non-drug taking controls who had never taken cannabis. It was thus decided to include in the control group participants who had occasionally taken cannabis, but who had not taken it within the last year. The exclusion criteria for all participants were: a history of epilepsy, schizophrenia, bipolar disorder, any intravenous drug use, or any serious current medical condition that requires or has required medication.

A total of 117 participants, all frequent night-clubbers, were recruited following telephone screening using participants' self-report for the exclusion criteria listed above. Of the 117 participants recruited, 38 were excluded due to not meeting the criteria for membership of the three experimental groups. A further eight were excluded due to reporting taking illegal drugs within the 24 h before either testing session. One participant (control) was excluded because of alcohol use an

hour prior to testing, and three recent ecstasy/MDMA users and one abstinent ecstasy/MDMA user were excluded due to their reported level of alcohol use in the evening/night prior to testing (reported units for these four participants = 40, 30, 21, and 30 respectively). The final sample thus totalled 66 participants, divided into three groups:

1. Control group ($n = 24$; mean age = 21.88 years (SD = 3.51, range 18–29 years); 11 males, 13 females). This comprised participants who reported having never taken ecstasy or MDMA nor any other illegal drugs, except for minor cannabis use (defined as lifetime consumption $\leq$10 joints) that was not within the last year. Nine in this group (37.5%) reported having used cannabis at least once.
2. Recent ecstasy/MDMA group ($n = 25$; mean age = 21.44 years (SD = 2.40, range 18–28 years); 10 males, 15 females). This comprised regular ecstasy/MDMA users (defined as taking ecstasy and/or MDMA at least twice per month) who reported taking ecstasy/MDMA 2–3 days before the first performance testing session. The group mean self-estimate of ecstasy/MDMA tablets consumed during the 2–3 days prior to testing = 2.88 (SD = 5.25, $n = 25$) and group mean self-estimate of MDMA consumed = 0.35 g (SD = 0.42, $n = 25$). Ten participants reported taking only ecstasy tablets, nine reported taking only MDMA powder, and six reported taking both ecstasy tablets and MDMA powder. The means for participants who reported using each form of MDMA are: ecstasy tablets, mean = 4.50 (SD = 6.03, $n = 16$), and MDMA powder, mean = 0.58 g (SD = 0.40, $n = 15$).
3. Abstinent ecstasy/MDMA group ($n = 17$; mean age = 22.29 years (SD = 3.26, range 18–29 years); 8 males, 9 females). This comprised regular (defined as above) ecstasy/MDMA users who reported not taking ecstasy or MDMA for 8 days or more before the first performance testing session. Period of abstinence from ecstasy/MDMA for this group ranged from 8–28 days before the first performance testing session.

Measures

1. Sleep questionnaire. This included questions on usual time of going to sleep and waking up on work and on rest days, and usual sleep quality ('during the last month, how would you rate your sleep quality overall: 1 = very good, 2 = fairly good, 3 = fairly bad, 4 = very bad').
2. Drug history questionnaire, combining the General Drug Use History Questionnaire (GDUQ); (Huxster et al., 2006) and the UEL Drug History Questionnaire (Parrott et al., 2000). This questionnaire recorded current frequency and usual dose of drugs consumed, and lifetime drug usage.
3. The previous 24 h drug use questionnaire. This assessed self-reported drug use, and caffeine, alcohol and nicotine use, in the 24 h prior to each performance testing session.
4. The 50 word, National Adult Reading Test (NART) (Nelson, 1982). This provides an estimate of pre-morbid full IQ.
5. The short mini-markers version of the Big-5 personality inventory (Saucier, 1994), to assess Conscientiousness.
6. The Composite Morningness Scale (Smith et al., 1989). This assesses preferred times of day for alert effortful activity. Higher scores represent Morningness.
7. Locus of Control questionnaire (Levenson, 1981). This assesses level of belief in whether events or aspects of one's life are under one's internal control.
8. Daily diary for recording drug use, sleep times and mood. The diary included, for each day, items recording any drugs taken during the day, and the quantities of these, time of going to bed, time taken to fall asleep, time of waking, and also items on self-assessed mood. For mood, participants completed two 10 cm visual analogue scales: (i) anchored as Very tense (score = 0) to Very relaxed (score = 100) and (ii) anchored as Very happy (score = 0) to Very sad (score = 100).
9. The Story Memory Subtest (version B) from the Rivermead Behavioral Memory Test (RBMT) (Wilson et al., 1985). This involves the participant listening to a 65-word newspaper-type story concerning the fighting of a fire. Free recall was assessed immediately, then after a delay of 20 min, and then 24 h later, and scored each time for recall of the 21 idea components.
10. The Finger Tapping Task (FTT) (Walker et al., 2002). The FTT involves typing the numbers 4-1-3-2-4 on a keypad for 12 trials of 30 s each, with a break of 30 s between each trial. Speed is calculated as the number of correct sequences typed in 30 s. The crucial comparison is between the mean speed of the last three trials on the first testing session and the mean speed of the first three trials on the second testing session, which was 24 h later. Error rate was also assessed.
11. The Stanford Sleepiness Scale (SSS) (Hoddes et al., 1973). This is a state measure of sleepiness, with items ranging from 1 = 'Feeling active, vital, alert, wide awake', to 7 = 'Almost in reverie, cannot stay awake, sleep onset appears imminent'.

Procedure

Institutional ethics approval was obtained and strict confidentiality of all data was guaranteed. Participants attended an initial questionnaire session at which written and informed consent was obtained from all participants. Participants then completed demographic details, the Sleep questionnaire, the Morningness Questionnaire, the NART, and the Drug history questionnaire. Hair assays were not used to confirm self-reports of ecstasy/MDMA use as ethical issues would have resulted from the holding of such objective evidence of illegal activity, and because it may have reduced the number of people willing to take part in the study. Substance dependence was not assessed. Participants then took home the daily diary for recording sleep times, mood and drug use. The diary was completed for 5–10 days, depending upon the period between the initial questionnaire session and the performance testing sessions.

The first performance testing session occurred the following week, usually in an afternoon but sometimes in the

early evening. The session comprised: the previous 24 h drug use questionnaire; the SSS; RBMT story presentation and immediate recall; FTT; Locus of Control questionnaire; 20 min delayed RBMT recall, and SSS.

The second testing session occurred exactly 24 h later. Due to the variability of sleep times for the illicit drug taking participants it was not possible to utilize the usual sleep-dependent memory consolidation design of 10:00 h and 22:00 h (i.e., wake condition) versus 22:00 h and 10:00 h (i.e., sleep condition) testing times. Tests: Previous 24 h drug use questionnaire; SSS; 24 h delayed RBMT recall; FTT; Big-5 mini-markers, and SSS. At this session the completed daily sleep and drug use diary was returned to the experimenters.

Participants were asked not to take illegal drugs in the 24 h prior to each performance testing session, and not to take alcohol for 12 h prior to testing. Anyone who did report doing so was tested and paid for their participation, but was not included in any of the analyses.

Statistics

The data were first analysed with SPSS version 13. The groups were compared for sleep, personality and drug use variables using one-way analyses of variance (ANOVAs) or Kruskal-Wallis/Mann-Whitney tests, depending upon normality of the data. Repeated measures ANOVAs for the RBMT and FTT scores were performed, with group as a between-subjects factor. Planned comparisons in these ANOVAs were between recent ecstasy/MDMA users and controls, and between abstinent ecstasy/MDMA users and controls, and the threshold p value for each of the two between groups comparisons is thus set at 0.025. Simple main effects were also computed at each of the test times. As the previous literature supports a prediction of deficits in declarative memory, one-tailed tests are used for the analysis of planned comparisons and simple main effects on the declarative task. Regressions of RBMT and of FTT performance on the continuous variable recency of ecstasy/MDMA use were then conducted. Recency of ecstasy/MDMA use was not normally distributed and so non-parametric rank regression was performed (Hettmansperger and McKean, 1998), using the RREG procedure on Minitab version 15 (Hollander and Wolfe, 1999). These regression analyses are reported immediately after the corresponding between-groups repeated measures ANOVAs. As an association was found between recency of ecstasy/MDMA use and RBMT score, the potential confounding variables (e.g. NART IQ, gender, mood, personality) were then investigated by being sequentially entered into the regression equation. The repeated measures ANOVAs were then re-run excluding participants who reported having taken illegal drugs in the period 48–24 h before testing, and the interaction found between recent ecstasy/MDMA use and recent other drug use on the RBMT was investigated further.

The repeated measures analyses were then further re-run using only participants who had obtained at least 7 h sleep prior to each of the two performance testing days. The group × test day interaction was computed for the two tasks in order to establish if the groups differed in the change of memory over the 24 h, i.e. to test whether ecstasy/MDMA use was associated with differences in sleep-dependent memory consolidation.

Multiple regressions were then performed to establish associations between lifetime drug use and mean scores on each of the memory tasks. Lifetime drug use variables and their residuals were not normally distributed, so these regressions were run with the non-parametric rank regression procedure on Minitab version 15. To avoid multicollinearity of drug use variables, the control group participants were not included in these lifetime drug use analyses. Lifetime usage of ecstasy tablets and of MDMA (grams) were entered first, other drug usage and demographic and personality variables were then entered stepwise with $p > 0.05$ set as the criterion for removal of variables from the regression, until the most predictive model was established in terms of the Jaecket–Hettmansperger–McKean test statistic HM (Hollander and Wolfe, 1999). Further analyses were also conducted with NART IQ, gender, sleep length and personality variables entered first into the regression equations, with drug variables entered second. Semi-partial correlations were also computed.

Results

Drug consumption, personality, sleep and mood analyses

Table 1 shows the lifetime drug histories and current drug use, including alcohol and tobacco, for the three groups. Drug frequency and usual dose refer to the past year; there is thus no cannabis frequency nor cannabis usual dose for the non-drug control group. The control and two ecstasy/MDMA groups did not differ significantly on alcohol frequency or usual alcohol dose. Number of cigarettes consumed per day was significantly lower for controls than for recent ecstasy/MDMA users (Mann-Whitney $U = 38.00$, $z = 3.41$, $p = 0.001$) and abstinent ecstasy/MDMA users (Mann-Whitney $U = 22.00$, $z = 3.23$, $p = 0.001$). The two ecstasy/MDMA groups did not differ significantly on reported lifetime use of any of the drugs. The only significant difference between the two ecstasy/MDMA groups in current drug use was in MDMA frequency, which was significantly higher for the recent ecstasy/MDMA group than for the abstinent group (Mann-Whitney $U = 88.50$, $z = 2.76$, $p = 0.005$).

Table 2 shows the group mean scores on the personality, sleep, and diary period mean mood and mood variability measures. The groups were significantly different on time of going to sleep at weekends and time of going to sleep on work days. The recent ecstasy/MDMA group was significantly lower in Morningness than was the control group, but the groups did not differ on self-reported usual time of maximum alertness, which for all groups was in the afternoon. None of the variables that we speculated might be confounds in the study (i.e. NART IQ; Conscientiousness; Locus of Control, Morningness and mean sleep length prior to testing) were significantly related to both group membership and to task performance (the only significant relationship between any of these variables and performance was between internal Locus of Control and mean RBMT score: $r = 0.27$, $p < 0.05$). Nevertheless, these five variables were introduced into the recency of ecstasy/MDMA use regression analyses to assess

Table 1. Lifetime and usual dose and frequency drug consumption for the control, recent ecstasy/MDMA and abstinent ecstasy/MDMA groups

	Controls $n = 24$	Recent ecstasy/MDMA $n = 25$	Abstinent ecstasy/MDMA $n = 17$
Alcohol ever (*n*)	24	25	17
Alcohol this year (*n*)	24	25	17
Alcohol usual dose (units)	8.42 (5.24)	12.48 (11.17)	10.24 (5.61)
Alcohol frequency	138.71 (74.07)	183.04 (82.23)	208.47 (110.78)
Tobacco ever (*n*)	12	25	16
Tobacco this year (*n*)	11	24	15
Tobacco, cigarettes per day	2 (1.55)	9.79 (7.56)**	7.30 (4.90)**
Cannabis ever (*n*)	9	25	16
Cannabis lifetime consumption (joints)	3.6 (2.9)	3771.1 (8057.1)	2969.3 (4764.0)
Cannabis this year (*n*)	0	22	11
Cannabis usual dose (joints)		2.93 (2.65)	2.15 (1.29)
Cannabis frequency (per year)		155.77 (149.65)	79.36 (101.09)
Ecstasy ever (*n*)	0	25	17
Ecstasy lifetime consumption (tablets)		268.8 (274.9)	422.1 (511.6)
Ecstasy this year (*n*)	0	23	16
Ecstasy usual dose (tablets)		3.48 (2.29)	3.31 (1.29)
Ecstasy frequency		40.22 (36.27)	39.25 (29.22)
MDMA ever (*n*)	0	23	17
MDMA lifetime consumption (g)		43.5 (49.0)	48.9 (102.4)
MDMA this year (*n*)	0	23	17
MDMA usual dose (g)		0.68 (0.30)	0.66 (0.45)
MDMA frequency		57.09 (57.53)*	23.69 (26.51)*
Cocaine ever (*n*)	0	24	15
Cocaine lifetime consumption (g)		47.6 (68.7)	55.6 (63.3)
Cocaine this year (*n*)	0	24	14
Cocaine usual dose (g)		0.86 (0.40)	0.98 (0.82)
Cocaine frequency		31.42 (35.32)	40.79 (40.39)
Amphetamine ever (*n*)	0	14	12
Amphetamine lifetime consumption (g)		18.2 (19.3)	47.4 (101.8)
Amphetamine this year (*n*)	0	11	4
Amphetamine usual dose (g)		0.98 (0.57)	1.00 (0.71)
Amphetamine frequency		23.64 (32.59)	53.75 (58.04)
Ketamine ever (*n*)	0	23	11
Ketamine lifetime consumption (g)		25.9 (73.8)	70.0 (151.0)
Ketamine this year (*n*)	0	22	10
Ketamine usual dose (g)		0.70 (0.66)	0.86 (0.69)
Ketamine frequency		16.52 (17.92)	21.10 (19.87)
Mushrooms ever (*n*)	0	16	10
Mushrooms lifetime consumption (hits)		7.4 (6.4)	12.2 (7.0)
Mushrooms this year (*n*)	0	8	4
Mushrooms frequency		2.75 (2.12)	2.25 (1.89)
LSD ever (*n*)	0	10	7
LSD lifetime consumption (tabs)		7.2 (9.4)	20.1 (30.0)
LSD this year (*n*)	0	5	4
LSD usual dose (tabs)		1.40 (0.55)	1.75 (0.50)
LSD frequency		2.60 (1.34)	3.00 (2.00)
Heroin (non-IV) ever (*n*)	0	1	1
Heroin lifetime consumption (g)		2.0	0.1
Poppers ever (*n*)	0	19	12
Poppers lifetime consumption (hits)		90.8 (150.3)	140.5 (276.1)
Poppers this year (*n*)	0	13	7
Poppers usual dose (hits)		8.38 (8.53)	8.86 (8.09)
Poppers frequency		9.92 (11.52)	13.29 (14.36)

Notes:
Usual dose and frequency refer to drug consumption over the past year.
Means and SDs include only participants who report having taken the drug during the period specified (lifetime or past year).
*Ecstasy groups differ from each other at $p = 0.005$, Mann Whitney.
**Each ecstasy group differs from controls at $p = 0.001$, Mann Whitney.

Table 2. Means of IQ, personality, sleep and diary mood variables for the control, recent ecstasy/MDMA and abstinent ecstasy/MDMA groups

	Controls $n=24$		Recent ecstasy/MDMA $n=25$		Abstinent ecstasy/MDMA $n=17$		ANOVA
	Mean	SD	Mean	SD	Mean	SD	$F(2,63)$
NART Full IQ	114.25	5.39	113.04[a]	4.60	117.24[a]	3.90	4.04*
Conscientiousness	39.83	2.97	39.44	4.41	40.88	3.92	0.74
Internal locus of control	34.38	5.75	30.68	3.79	31.74	8.04	2.56
Usual sleep quality	2.21	0.51	2.56	0.77	2.35	0.61	1.85
Time of going to sleep on work days	0:16	1:16	0:58	1:24	0:00	1:05	3.39*
Time of going to sleep on weekends[1]	1:32[bc]	1:23	3:23[c]	2:02	3:18[b]	1:28	8.76***
Time of waking on work days	8:42	1:17	9:22	1:36	8:51	1:14	1.52
Time of waking on weekends[1]	10:13	1:59	11:18	1:35	10:50	1:19	2.46
Morningness	31.46[b]	6.02	26.12[b]	5.40	27.47	6.03	5.49**
Time of maximum alertness	14:47	3:43	15:27	2:57	14:14	4:15	0.60
Mood across diary: happy/sad	36.59	9.49	35.37	15.38	39.33	10.06	0.54
Mood across diary: tense/relaxed	59.80	11.86	62.05	12.59	57.23	10.40	0.85
Variation in happy/sad across diary	17.38	5.99	17.33	7.91	17.31	7.10	0.00
Variation in tense/relaxed across diary	18.18	4.09	19.95	8.68	18.89	6.68	0.42
Sleep length on night before testing session 1	8:03	1:38	7:47	2:32	7:30	2:27	0.30
Sleep length on night before testing session 2	7:26	1:12	7:46	3:02	7:34	1:32	0.15

Note:
[1]Recent Ecstasy/MDMA $n=24$, Abstinent Ecstasy/MDMA $n=16$; ANOVA F has dfs (2,61).
*$p<0.05$.
**$p<0.01$.
***$p<0.001$.
[a]between groups comparison $p<0.025$, Dunnett test.
[b]between groups $p<0.01$, Dunnett test.
[c]between groups comparison $p=0.001$, Dunnett test.

whether they are confounds. Gender was also entered into the regression analyses, although there were no gender differences on any personality, drug consumption, IQ, sleep or performance (RBMT and FTT) variable.

There were no significant differences between the groups on alcohol consumption on the evening before each performance testing session, on time since last use of caffeine prior to the first testing session, on time since last use of nicotine prior to the first testing session, nor on mean mood variables (happy/sad and tense/relaxed) for the day of the first testing session (mood scores and time since last use of caffeine and nicotine were not collected on the second testing day). There was a significant difference between the groups on sleepiness at the start of the first session (controls, mean = 2.21 (SD = 0.83); recent ecstasy/MDMA, mean = 3.00 (0.87); abstinent ecstasy/MDMA, mean = 2.65 (1.32); ANOVA $F(2,63)=3.92$, $p=0.025$), but not at the end of that session nor at the start or end of the second session.

Memory performance analyses

The upper panel of Table 3 shows the means on the three RBMT recall testing times for the control, recent ecstasy/MDMA and abstinent ecstasy/MDMA groups. There was a significant effect of test time ($F(2,126)=30.49$, $p<0.001$), with significant decreases in recall between the immediate and 20 min delayed testing sessions (Sidak pairwise comparison, $p<0.001$) and between 20 min delayed testing and 24 h delayed testing (Sidak pairwise comparison, $p<0.05$). There was no interaction between group and change in recall across test times ($F(4,126)=1.23$). The three groups differed significantly from each other ($F(2,63)=3.22$, $p<0.05$), with a post hoc one-tailed Dunnett test for the main effect showing that recent ecstasy/MDMA users scored significantly worse than controls ($p<0.025$). Over the three test times the recent ecstasy/MDMA users recalled 76.1% of the level of control group recall.

Non-parametric rank regressions were performed to investigate the association between memory and recency of ecstasy/MDMA use. A continuous recency variable was computed as the reciprocal of the number of days since last use of ecstasy or MDMA. This varied from a maximum of 0.5 (reciprocal of 2 days) to 0 (meaning ecstasy or MDMA had never been consumed). This recency variable was entered into a regression as a predictor of the mean of the three RBMT test time scores, and the mean of the two FTT speed scores.

For all the participants taken together, recency of ecstasy/MDMA use predicted RBMT score with standardized beta = −0.217, $p=0.01$. When gender was entered into the regression the standardized beta for the recency variable = −0.220, $p<0.01$; the standardized beta for gender was not significant. When the Morningness, diary mood, variation in diary mood, NART IQ and pre-testing session sleep length variables from Table 2, and pre-testing session alcohol consumption and day of testing mood variables were entered into the regression, the recency of taking ecstasy/MDMA remained significantly associated with mean RBMT score with, in all cases, standardized beta being negative and of greater magnitude than 0.20, and with $p<0.025$. Negligible decreases in the size of the beta for the regression of RMBT

Table 3. Scores on Rivermead Behavioral Memory Test for (upper panel) controls, recent ecstasy/MDMA and abstinent ecstasy/MDMA groups, and for (lower panel) controls, recent ecstasy/MDMA users who reported no use of other illicit drugs 48–24 h before testing, and recent ecstasy/MDMA users who reported other illicit drug use 48–24 h before testing

		Immediate recall		20 min delayed recall		24 h delayed recall		Main effect planned comparison[a]
	n	Mean	SD	Mean	SD	Mean	SD	
Controls	24	9.56*	3.73	8.60	3.47	8.19*	3.67	$p < 0.025$
Recent ecstasy/MDMA users	25	7.48*	2.78	6.66	3.05	5.90*	2.99	
Abstinent ecstasy/MDMA users	17	8.91	2.72	8.03	2.67	8.09	2.37	
Controls	24	9.56*	3.73	8.60*	3.47	8.19**	3.67	$p < 0.01$
Recent ecstasy/MDMA users with other illicit drug use	16	6.78*	2.37	5.91*	2.16	5.13**	2.19	
Recent ecstasy/MDMA users without other illicit drug use	9	8.72	3.15	8.00	4.01	7.28	3.80	

Notes:
All participants reported no drug use in the 24 h before testing.
[a]one-tailed Dunnett test.
*and *groups differ $p < 0.025$, one-tailed Dunnett test.
**and **groups differ $p < 0.01$, one-tailed Dunnett test.

score onto recency of ecstasy/MDMA consumption occurred after entry of Locus of Control (beta for ecstasy/MDMA recency $= -0.17$, $p < 0.05$), mean sleepiness (beta for ecstasy/MDMA recency $= -0.19$, $p = 0.025$) and conscientiousness (beta for ecstasy/MDMA recency $= -0.20$, $p < 0.025$). In all cases where a potentially confounding variable was entered into the regression equation, the beta for the potential confounding variable was non-significant with $p > 0.1$. However, one confound did occur: when participants who reported having taken illicit drugs in the period 48–24 hours prior to testing were excluded from the regression, the standardized beta became negligible and non-significant (beta $= -0.01$). The drugs reported to have been consumed in this period were cocaine, ketamine, amphetamine and cannabis. Those who had taken illicit drugs in this period were 16 of the recent ecstasy/MDMA users and two abstinent ecstasy/MDMA users. The difference between the three groups on the repeated measures ANOVA also became non-significant ($F(2,45) = 0.20$) when these individuals were excluded.

To examine further this confound of other drug use, the lower panel of Table 3 reports the comparison of RBMT scores for the controls and for the recent ecstasy/MDMA users divided into those who did ($n = 16$) versus those who did not ($n = 9$) consume illicit drugs in the period 48–24 hours before testing. (As only two members of the abstinent ecstasy/MDMA users group had taken other illicit drugs in this 48–24 h period, further sub-group analysis was not possible for that group.) The controls and recent ecstasy/MDMA sub-groups differed on RMBT scores ($F(2,46) = 3.95$, $p < 0.05$), with recent ecstasy/MDMA users who had taken other drugs in the period 48–24 h before testing scoring significantly worse than controls (one-tailed Dennett test, $p < 0.01$), and with recent ecstasy/MDMA users who had not taken other drugs scoring worse than controls, but not significantly so.

Importantly, comparisons on various drug use variables between the recent ecstasy/MDMA users who used ($n = 16$) or did not use ($n = 9$) illicit drugs 48–24 h prior to testing (presented in Table 4) show that those who consumed these other drugs reported significantly less frequent use of ecstasy tablets, but similar usual dose of ecstasy tablets to the non-other drug use sub-group, and non-significantly higher frequency and usual dose of MDMA and cannabis, and higher lifetime cannabis usage. All other lifetime and usual drug use was very similar between the two sub-groups. Those who took illicit drugs in the 48–24 h prior to testing reported significantly higher use of MDMA in the 2–3 days prior to testing, but non-significantly fewer ecstasy tablets (median ecstasy tablets for those who took illicit drugs $= 0.25$; median ecstasy tablets for those who did not take illicit drugs $= 2.0$). There two sub-groups did not differ significantly in usual or pre-performance testing nicotine or alcohol use, in sleep length before either of the testing sessions, nor in sleepiness at the beginning or end of either testing session.

FTT speed on the first three trials of the second session (controls, mean $= 20.04$ (SD $= 5.22$); recent ecstasy/MDMA, mean $= 20.12$ (5.32), abstinent ecstasy/MDMA $= 21.35$ (6.12)) was significantly higher than on the last three trials of the first session (controls, mean $= 17.68$ (SD $= 5.09$); recent ecstasy/MDMA, mean $= 17.40$ (5.86); abstinent ecstasy/MDMA $= 19.10$ (5.65)), $F(1,61) = 34.11$, $p < 0.001$. This increase did not interact with group ($F(2,61) = 0.12$). The three groups did not differ significantly on FTT speed ($F(2, 61) = 0.44$) and regression analysis showed that recency of taking ecstasy/MDMA had a non-significant standardized beta ($= -0.06$) for predicting mean FTT speed score across the six trials. There was a significant decrease in errors between the testing sessions ($F(1,61) = 7.22$, $p < 0.01$), which did not interact with group ($F(2,61) = 0.05$), and the three groups did not differ on FTT errors ($F(2,61) = 0.81$).

Memory performance analyses across 24 h for participants who had at least 7 h sleep

In order to address the hypothesized effect of ecstasy/MDMA on sleep-dependent memory consolidation for RBMT performance, between-subjects repeated measures ANOVAs were run with the score on the second (20 min delayed memory) and third (24 h delayed memory) tests as the repeated measure, for individuals who had obtained at least 7 h sleep on

Table 4. Comparison of ecstasy, MDMA and cannabis consumption for recent ecstasy/MDMA users who took versus did not take illicit drugs[1] 48–24 h prior to testing

	Recent ecstasy/MDMA users who did not take illicit drugs 48–24 h prior to testing ($n = 9$)		Recent ecstasy/MDMA users who took illicit drugs[1] 48–24 h prior to testing ($n = 16$)		Comparison between groups (Mann-Whitney test)
	Mean	SD	Mean	SD	
Ecstasy lifetime usage (tablets)	252.78	155.76	277.75	328.27	n.s.
Ecstasy frequency (per year)	66.44	37.06	20.44	24.14	$p < 0.001$ U = 14.00 $z = 3.38$
Ecstasy usual dose (tablets)	2.94	2.70	3.34	2.29	n.s.
MDMA lifetime usage (g)	35.11	45.39	42.81	51.28	n.s.
MDMA frequency (per year)	43.33	39.04	57.69	66.05	n.s.
MDMA usual dose (g)	0.48	0.36	0.70	0.32	n.s.
Cannabis lifetime usage (joints)	1318	2799	4998	9583	n.s.
Cannabis frequency (per year)	63.00	71.41	178.75	166.61	n.s.
Cannabis usual dose (joints)	1.72	1.48	3.07	3.10	n.s.
Ecstasy tablets consumed 2–3 days prior to testing	2.94	2.96	2.84	6.28	n.s.
MDMA consumed 2–3 days prior to testing (g)	0.11	0.22	0.48	0.46	$p < 0.05$ U = 29.50 $z = 2.50$

Note:
[1]Drugs reported were: only amphetamine ($n = 1$), only ketamine ($n = 1$), only cocaine ($n = 2$), ketamine and cannabis ($n = 1$), cocaine and cannabis ($n = 3$) and only cannabis ($n = 8$).

each of the nights before the two testing sessions. Participants now included in the analysis are thus: controls, $n = 11$; recent ecstasy/MDMA users, $n = 13$; and abstinent ecstasy/MDMA users, $n = 10$. The means obtained are similar to those presented in Table 3 and so are not presented here. There was no interaction of test day with group ($F(2,31) = 1.53$), and thus no effect of ecstasy/MDMA on the memory consolidation function of sleep for the declarative task. These three groups differed significantly on RBMT recall ($F(2,31) = 5.63$, $p < 0.01$), with recent ecstasy/MDMA users scoring significantly worse than controls (one-tailed Dunnett test, $p < 0.005$). As with the complete sample, this significant group difference disappeared if individuals who reported having taken illicit drugs in the period 48–24 h prior to testing were excluded ($F(2,23) = 2.55$).

The FTT ANOVAs were then re-run for individuals who had obtained at least 7 h sleep on each of the nights before testing. Participants now included in the analysis are thus: controls, $n = 11$; recent ecstasy/MDMA, $n = 12$; abstinent ecstasy/MDMA, $n = 9$; *ns* differ from the RBMT analysis because two participants were unable to learn the task. The means obtained are similar to those presented for FTT above. The interaction of test day with group remained non-significant for the FTT speed ($F(2,29) = 0.09$) and error analyses ($F(2,29) = 0.13$). There was thus no effect of ecstasy/MDMA on the memory consolidation function of sleep for the procedural memory task.

Associations of memory with lifetime ecstasy/MDMA use

Non-parametric rank regressions were run to investigate the prediction of the mean RBMT and mean FTT scores by lifetime drug use. Lifetime usage was chosen as the long-term measure of total drug use as it had correlations with the two mean memory scores that, in general for the drugs reported, exceeded other possible total drug use measures, such as current frequency, current dose and the product of frequency and dose. Table 5 shows the non-parametric multiple regression results for lifetime drug use predictors of mean score on RBMT and FTT.

RBMT. Ecstasy lifetime usage and MDMA lifetime usage were first entered into the regression as predictors. As the continuous variable recency of use of ecstasy/MDMA and the dichotomous variable use of other illegal drugs 48–24 h before testing had been found to be related to RBMT score, these were also entered at this time. Both MDMA lifetime usage and recency of use of ecstasy/MDMA were found to have non-significant standardized betas and were hence removed from the regression: this resulted in Model 1. The next best predictor of RBMT score, cocaine lifetime usage, was then entered, which resulted in Model 2. Addition of any other lifetime drug usage or trait (e.g. personality, gender) or state (e.g. pre-testing mood, sleep length, or alcohol consumption) variable failed to add to the predictive value of the model, and all these other variables also had non-significant standardized betas when entered into the regression. RBMT score was thus predicted by lifetime ecstasy tablet usage, lifetime cocaine usage, and the consumption of illicit drugs other than ecstasy/MDMA 48–24 h before testing. Semi-partial correlations showed that the variance in declarative memory was marginally more associated with lifetime cocaine than lifetime ecstasy tablet usage.

Table 5. Regression results for predictors of mean scores on the Rivermead Behavioral Memory Test and the Finger Tapping Task for ecstasy/MDMA users ($n = 42$)

Dependent variable, model, and rejected predictors	Significant predictors	B[a]	SE[a]	Beta[a]	HM[b]	p[c]	Semi-partial correlation
RBMT							
Enter: Ecstasy lifetime usage; MDMA lifetime usage; recency of taking ecstasy/MDMA; use of illicit drugs 48–24 h before testing[d]							
Model 1							
	Ecstasy lifetime usage	−0.0023	0.0012	−.20	4.96	<0.05	−0.33
	Use of illicit drugs 48–24 h before testing	−2.3252	0.8921	−0.64	8.58	<0.005	−0.43
Rejected ($p > 0.05$): MDMA lifetime usage Recency of taking ecstasy/MDMA					10.73 (df = 2)	<0.005	
Enter: Cocaine lifetime usage							
Model 2							
	Ecstasy lifetime usage	−0.0018	0.0010	−0.15	4.23	<0.05	−0.27
	Use of illicit drugs 48–24 h before testing	−2.5202	0.7509	−0.69	11.37	<0.001	−0.46
	Cocaine lifetime usage	−0.0154	0.0058	−0.16	7.69	<0.01	−0.35
					19.25 (df = 3)	<0.001	
FTT speed							
Enter: Ecstasy lifetime usage; MDMA lifetime usage[de]							
Model 1							
Rejected ($p > 0.05$): MDMA lifetime usage	Ecstasy lifetime usage	−0.0052	0.0026	−0.17	4.99	<0.05	−.35

Notes:
RBMT Model 1, $F(2,39) = 4.68$; Model 2, $F(3,38) = 6.18$; FTT Model 1, $F(1,40) = 4.55$.
[a]Nonparametric rank regression statistics, with rank regression standardized beta.
[b]Jaecket–Hettmansperger–McKean nonparametric test statistic HM.
[c]HM statistic is converted to p by reference to Chi Square distribution (Hollander and Wolfe, 1999). HM has df = 1 unless otherwise stated.
[d]NART IQ, gender, sleep length, sleepiness, personality and consumption of alcohol, caffeine and nicotine were non-significant with $p > 0.1$ as predictors of RBMT score and FTT speed.
[e]Recency of taking ecstasy/MDMA and use of illicit drugs 48–24 h before testing were both non-significant with $p > 0.1$ as predictors of FTT speed.

FTT. Ecstasy lifetime usage and MDMA lifetime usage were first entered into the regression as predictors of FTT mean speed. Recency of use of ecstasy/MDMA and the dichotomous variable use of illicit drugs 48–24 h before testing were not predictive of FTT speed and were not entered into this regression. MDMA lifetime usage was found to have a negligible and non-significant beta (beta = −0.01) and so was removed. Model 1 thus had ecstasy lifetime usage as the significant predictor of FTT. The next largest predictor, cocaine lifetime usage, was then added, but it did not improve the predictive value of the model and the standardized beta for lifetime cocaine use was non-significant. Addition of any other lifetime drug usage or trait or state variable failed to add to the predictive value of the model, and all these variables had non-significant betas. FTT score was thus predicted only by lifetime ecstasy tablet usage.

Negligible changes to these RBMT and FTT regression results occurred when NART IQ, gender, sleep length and personality variables were entered first and held in the regression equations with drug variables entered second.

Discussion

Recent ecstasy/MDMA users showed a significant deficit in declarative verbal memory, on the RBMT, compared with non-drug controls. Recency of ecstasy/MDMA use, as a continuous variable that included recent, abstinent and non-ecstasy/MDMA users, was also significantly associated with poorer declarative memory. This association remained significant when prior alcohol consumption, prior sleep length, sleepiness during the task, NART estimated pre-morbid IQ, gender and specific personality variables were controlled for. The similarity between the groups in mood before the first testing session, and in mood and variation in mood across the diary period, indicates that mood was not a confound for the declarative memory performance results. The ecstasy/MDMA-using participants were heavier smokers than the

controls, but given that participants were not required to abstain from smoking, there should be minimal performance effects related to nicotine. Caffeine use prior to testing did not differ between groups, and so it was also unlikely to be a confound.

In a more detailed analysis, it was found that this association of recent ecstasy/MDMA use with poorer declarative recall was only significant for participants who also reported having used other illicit drugs 48–24 h prior to testing. Importantly, those individuals who used other illicit drugs did not have a greater usual use of ecstasy or MDMA than those who did not take other illicit drugs prior to testing. However, there were a number of differences between those participants who did and those who did not take other illicit drugs during the 48–24 h pre-test period that may account for the differences in RBMT score. Firstly, given that cannabis was the most prevalent illicit drug used in this 48–24 h period, it may be that the residual effects of cannabis lasted until testing. A second possibility follows from the finding that the ecstasy/MDMA-using participants who used illicit drugs in this period were heavier cannabis users. These participants may thus have had greater substance dependence for cannabis, and this may have impacted on their performance as a result of the required abstinence from all illicit drugs for 24 h before testing (Solowij and Battisti, 2008). Thirdly, it is possible that there was an interaction between the recent ecstasy/MDMA use and some or all of the other illicit drugs taken, which resulted in greater performance deficits. The latter possibility is consistent with investigators who have attributed memory deficits in ecstasy/MDMA users to the concurrent recent use of cannabis and other drugs (Croft et al., 2001; Gouzoulis-Mayfrank and Daumann, 2006; Lamers et al., 2006). It is also consistent with Pirona and Morgan (2010), who observed no sub-acute effects of ecstasy/MDMA on objective verbal recall performance, after controlling for sleep deprivation and concurrent use of other substances. However, finally, there was a significantly higher recent use of MDMA by those participants who took other illicit drugs prior to testing, and this may have contributed to the declarative memory deficits.

The procedural memory performance of recent and abstinent ecstasy/MDMA users did not differ from controls. This is consonant with Zakzanis et al. (2007), who concluded that ecstasy/MDMA does not cause motor skill deficits. However, the finding that the abstinent ecstasy/MDMA group did not show declarative memory deficits does appear to contradict Zakzanis et al. (2007) and many other reports (e.g. Reneman et al., 2001; Reneman et al., 2006; Thomasius et al., 2005). The latter findings, though, have not been completely consistent: for example, Reneman et al. (2001) reported that ecstasy/MDMA users recalled significantly fewer words than controls on delayed, but not immediate recall, and Thomasius et al. (2005) reported that only former ecstasy/MDMA users, and not current users, had significantly poorer verbal recall. Furthermore, although Reneman et al. (2006) reported that heavy current and also heavy former ecstasy/MDMA users performed significantly worse on memory tasks than controls, there was no evidence of memory deficits in moderate ecstasy/MDMA users. There are, however, numerous studies that have shown significant declarative memory deficits associated with chronic ecstasy/MDMA use (see review by Parrott, 2006; Indlekofer et al., 2009; Rendell et al., 2007).

Nevertheless, the present study did provide some evidence that ecstasy/MDMA consumption is implicated in chronic declarative and procedural memory deficits. Multiple regression indicated that lifetime usage of ecstasy tablets and of cocaine were predictors of deficits in declarative memory. The association of declarative memory deficits with lifetime ecstasy use is consistent with Thomasius et al. (2005), Schilt et al. (2008) and de Sola Llopis et al. (2008), and with the view that MDMA induces neurotoxicity (e.g. Gouzoulis-Mayfrank et al., 2003). Montgomery et al. (2007) had similarly found that lifetime ecstasy and cocaine use were associated with deficits in paired-associate learning, even after sleepiness was controlled for. The association with lifetime cocaine use may be consistent with evidence that cocaine disrupts the hypothalamic-pituitary-adrenal axis as a result of its action on 5-HT1A autoreceptors, such as the finding of down-regulation of 5-HT1A receptors in rat hypothalamus and dentate gyrus after 'binge'-pattern cocaine administration (Perrett et al., 1998). It has also been suggested that since psychostimulants are neurotoxic upon both serotonergic and dopaminergic neurons they may act synergistically with MDMA and enhance its long-term adverse effects (Gouzoulis-Mayfrank and Daumann, 2006). Multiple regression analysis also indicated that only lifetime usage of ecstasy tablets was a significant predictor of deficits in FTT procedural memory. This novel finding is consistent with preclinical evidence that 5-HT might modulate this type of learning at the level of the basal ganglia (e.g. Perez-Garcia and Meneses, 2008), and thus may be susceptible to MDMA-induced neurotoxicity. However, it is unclear why the reported lifetime consumption of ecstasy tablets was associated with declarative and procedural memory deficits, whereas lifetime consumption of grams of MDMA powder was not. This may indicate that estimations of powder MDMA use are less accurate than estimations of number of tablets consumed, either because powder mass may be difficult to assess, or because powders have more instances where they can be subject to adulteration than do tablets.

There was no support for the second and third hypotheses, of ecstasy/MDMA causing a deficit in sleep-dependent memory consolidation for the declarative and procedural tasks used here. Whether this holds for sleep-dependent memory consolidation of other declarative or procedural tasks remains to be determined. However, Tucker and Fishbein (2009) have recently demonstrated that post-sleep performance gains on a declarative paired associates task and on the procedural FTT are very similar regardless of whether subjects obtain a half night or a full night of sleep. It may thus be that the mild effects of ecstasy/MDMA on sleep length and quality are not sufficient to disrupt sleep-dependent memory consolidation for the tasks used in their and our studies.

Recent and abstinent ecstasy/MDMA users had lower Morningness than controls. Future research should assess whether this is a result of extreme evening preference types choosing to take ecstasy/MDMA, or whether this increased eveningness is a result of ecstasy/MDMA use. The latter is a

possibility as circadian rhythms are affected by MDMA in hamsters (Colbron et al., 2002) and rats (Balogh et al., 2004). However, it should be noted that Morningness scales in general, including the one used here, do confound individual differences in alertness across the day with habitual bed and wake times. Future work should thus address whether, relative to habitual wake up time, ecstasy/MDMA users and non-users differ in their pattern of alertness across the day. From the results here, all groups had their maximum alertness approximately 5.5–6 h after waking: frequent ecstasy/MDMA use does not therefore seem to be altering the pattern of alertness across the day.

The present study suffered from a number of methodological limitations. One was that we decided not to undertake assays to confirm substance use. Our rationale for this was that we considered it an unnecessary burden on participants, since recent studies involving serum checks have confirmed the accuracy of self-reported ecstasy/MDMA usage and abstinence (Parrott et al., 2008; Pirona and Morgan, 2010). Furthermore, Thomasius et al. (2003) reported very high concordance between self-reported ecstasy/MDMA use and the results of hair analyses. Also, Parrott (2004) noted the high purity of ecstasy tablets, so that taking 'ecstasy' tablets typically results in MDMA ingestion. There were other methodological limitations that are generic to naturalistic studies of ecstasy/MDMA users, including difficulties recruiting polydrug users who had never consumed ecstasy/MDMA and, as a consequence, difficulties statistically controlling for the possible influence of other illicit drugs. There was also the fundamental limitation inherent to all cross-sectional studies of being unable to infer causality.

One of the implications of the present findings is that ecstasy-induced neurotoxicity may result in procedural as well as declarative memory deficits, and therefore that limbic 5-HT/dopamine interactions may play a more prominent role in procedural memory than hitherto recognized. Ecstasy-induced neurotoxicity may also impact upon 5-HT and dopamine interactions in parallel, functionally segregated, cortico-striatal circuits thought to modulate aspects of impulsive responding (Fineberg et al., 2010; Morgan, 1998). Alternatively, since striatal dopamine transmission is implicated in both procedural learning (Willuhn and Steiner, 2009) and impulsivity (Fineberg et al., 2010), it is possible that the association between the extent of ecstasy use and procedural memory is due to pre-existing differences in impulsivity. The clinical implications of our observed association between deficits in procedural learning and the extent of lifetime ecstasy consumption might include an increased risk that regular ecstasy users will exhibit deterioration in the improvement of new simple motor skills. More generally, memory deficits will adversely affect numerous aspects of everyday functioning. For example, Reay et al. (2006) found that drug-free ecstasy/MDMA users had significantly poorer social intelligence, which was related to the MDMA-associated deficits in memory updating. Furthermore, Topp et al. (1999) noted many further deficits in ecstasy/MDMA users, including occupational stress and interpersonal difficulties, and these could also be related to or exacerbated by the additional stress of deficits in memory and cognition.

In summary, recent ecstasy/MDMA use was associated with significant declarative memory deficits, but only when there was also use of other illicit drugs, in particular cannabis, 48–24 h prior to testing. Caution is therefore required in interpreting earlier studies where recent use of other drugs has not been assessed or controlled. Recent ecstasy/MDMA use was not associated with procedural memory deficits. Higher levels of lifetime ecstasy tablet usage were significantly associated with declarative and procedural memory deficits. Finally, the recreational use of ecstasy/MDMA did not affect the memory consolidation function of sleep for the declarative and procedural tasks used in this study.

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