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Abstract

Previous research has shown that heavy users of ecstasy may suffer impaired cognitive functioning, and the present study set out to investigate whether such impairment might also be found in light users or ex-users of ecstasy. Sixty subjects, comprising 20 current light users, 20 ex-users, and 20 non-users of ecstasy, were tested on an extensive battery of cognitive tests. Current light users of ecstasy achieved significantly lower scores on the overall cognitive test battery than did the non-users ($p=0.011$), though there were no significant differences on any individual subtests. However, the scores obtained by the ex-users of ecstasy did not differ significantly from those of the non-users. It was concluded that current light users of ecstasy show a small but significant cognitive impairment, but that no such impairment is detectable in ex-users who had abstained from the drug for at least 6 months.

Introduction

Ecstasy (MDMA) is a recreational drug used by young people. There have been concerns raised about possible neurotoxic effects it may have in humans, especially acute effects such as hyperthermia and water intoxication. However, there is also concern about possible long-term neurotoxic effects such as psychopathology and cognitive impairment. Previous research indicates that ecstasy may have a detrimental effect on cognitive functioning in heavy users. A large number of studies have shown significant impairment of recall performance in regular and heavy users of ecstasy (Parrott et al. 1998, Morgan 1999, Rodgers 2000, Morgan et al. 2002, Gouzoulis-Mayfrank et al. 2005, Quednow et al. 2006, Ward 2006). These studies have shown impairment of both long-term and short-term memory. Further studies focussing on the components of short-term working memory (WM) have shown impairments in current and previous ecstasy users on tests of both verbal WM (Wareing et al. 2004) and visuo-spatial WM (Wareing et al. 2005).

One important issue in ecstasy research concerns whether the observed memory impairments are permanent or whether they are reversible. Morgan et al. (2002) reported that the memory impairments observed in regular ecstasy users was not reversed by prolonged abstinence, since the impairment remained at a similar level in a group of ex-users of ecstasy who had abstained from the drug for at least 6 months. Gouzoulis-Mayfrank et al. (2005) found that even 18 months of abstinence from ecstasy produced no improvement in memory performance, and Ward et al. (2006) reported memory impairments persisting for up to 2 years after cessation of ecstasy use.

One central problem affecting the study of cognitive impairment associated with ecstasy use is that most ecstasy users tend to use other drugs too, so it can be difficult to isolate the effects of any one drug (Parrott et al. 2003, Gouzoulis-Mayfrank & Daumann 2006). Morgan et al. (2002) have employed regression analysis to deduce that, in polydrug users, cognitive impairment was mainly related to previous ecstasy use, whereas psychopathology (notably anxiety, depression, hostility, and sleep disorders) was more closely related to previous cannabis use. However, these conclusions remain tentative and the currently available data does not permit a clear separation of the effects of different drugs in common concurrent use.

Another area which has yet to be fully investigated is the effect of ecstasy on cognition in relatively light or occasional users. Many young people make fairly infrequent use of the drug, and it is important out find out whether they are also at risk of significant cognitive impairment. The aim of the present study was to investigate the extent of cognitive impairment in light users of ecstasy.

Method

Design and procedure
Current light ecstasy users (n=20), previous light ecstasy users (n=20) and ecstasy naive controls (n=20) were assessed on a wide range of cognitive tests. For the purposes of this study, light ecstasy use is defined as taking less than two tablets at a time once a month, whereas exceeding this amount would be defined as heavy ecstasy use. Previous ecstasy users were defined as individuals who had used ecstasy in the past but who had not taken this drug for at least 6 months. Ecstasy-naïve controls were defined as individuals who had never taken ecstasy.
All participants were administered an extensive range of cognitive tests (see *materials* below) and they also completed a questionnaire to ascertain their demographic status, lifestyle & drug use history. Participants were assured in advance that their replies would be treated with total confidentiality.

Participants
The sample comprised 32 males and 28 females, of mean age 25.4 (sd = 3.8) years. The three groups were equated for sex, age, SEG & education, and there were no significant differences between the groups in these variables.

Materials
All subjects completed a verbal memory test with both immediate and delayed recall (Lovatt et al, 2000), and the Automated Performance Test System (APTS: Hodgson & Golding 1991), which is a computerised cognitive test battery. The subtests of the APTS and the verbal memory test are listed below in the order in which they are administered:

- Verbal memory test (immediate recall)
- Tapping (ATAP). Measures non-dominant hand motor control and motivation.
- Four Choice Visual Reaction Time (AREACT). Tests perceptual speed alongside a simple decision making task.
- Code Substitution (ACODES). A visual search technique, measuring short-term memory for symbolic visual information and the ability to encode and decode such information rapidly.
- Grammatical Reasoning (AREASON). A test of verbal, logical and reasoning ability.
- Pattern Comparison (PATRNC) Using a visual search technique, this test provides a measure of perceptual speed and accuracy.
- Sternberg Memory (STERNB). A test of short-term memory using numerical items.
- Tapping (BTAP). Retested at the end to provide a check for the effects of fatigue and loss of motivation.
- Verbal memory test (delayed recall)

Results

Table 1 shows the history of ecstasy use reported by the current user and ex-user groups, and table 2 shows the history of use of other drugs by all three groups.

Insert table 1 here

Insert table 2 here

Table 3 shows the mean scores and standard deviations for the three groups of participants on each of the cognitive tests.

Insert table 3 here

A global analysis of the pattern of cognitive test results indicated that current light users performed worse than controls on most of the cognitive tests (11/13 tests), though on two tests they performed better than controls (2/13 tests). This overall pattern of worse cognitive performance in current light users was significant (Binomial p=0.011, 1-tail).

Ex-users performed worse on some test (7/13 tests) and better on other tests (6/13 tests) than controls, but their overall performance did not differ significantly from controls (Binomial, NS, 1 tail).

An ANOVA carried out on individual subtests revealed no significant differences between the groups on any of the tests, but differences between current users and controls approached significance (p = 0.05 - 0.10) for 2 out of the 13 performance tests, namely Pattern recognition and Sternberg memory, with current users being worse than controls in both cases.

Factor analysis revealed significant patterns of correlation between memory and scores on the cognitive test battery for all participants.

Discussion

The results show that current light users of ecstasy show a slight impairment in their overall cognitive performance when compared with ecstasy-naive controls. The difference between these two groups was significant when compared for overall cognitive performance across the whole battery of tests, but there were no significant impairments on any individual cognitive tests. Given that previous studies using similar sample sizes have shown fairly severe impairment in heavy ecstasy users (eg Morgan et al. 2002, Gouzoulis-Mayfrank et al. 2005, Quednow et al. 2006, Ward 2006) , the present findings suggest that occasional light use of ecstasy does not seem to produce cognitive impairment of the same order. Furthermore no cognitive impairment was found in this study in the ex-users of ecstasy when compared with controls. This finding contrasts with that reported by most studies of heavy ecstasy users, who are consistently found to show cognitive impairments persisting over many months (Morgan et al. 2002, Gouzoulis-Mayfrank et al. 2005, Ward et al. 2006). The findings of the present study would thus tentatively suggest that light ecstasy users are not at high risk of significant long-term cognitive impairment. However, it is possible that the failure to find significant long-term impairment among ex-users in the present study may simply reflect a lower level of initial impairment. In other words, the severity of long-term impairment is in proportion to the low level of impairment in current light users.

One major problem with studies of this kind, as explained in the introduction, is that users of ecstasy are likely to be users of other drugs too (Parrott et al. 2003, Gouzoulis-Mayfrank & Daumann 2006), and indeed this was found to be the case in the present study (see table 2). The light users and ex-users of ecstasy in this sample were much more likely than controls to report having used other drugs such as cannabis, LSD, cocaine, and amphetamines. Consequently ascribing the small effects observed here to ecstasy use is inevitably somewhat tentative, as the effects are likely to be confounded with those of the other drugs. However, one observation which may mitigate this confounding factor in the present study is that the ex-users and current users were almost identical in their pattern of use of other drugs, thus leaving ecstasy use as the only major variable distinguishing these two groups.

It can be concluded from the present study that light users of ecstasy do suffer a small but significant cognitive impairment, but that this impairment falls below significance in abstinent ex-users.

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Table 1. History of ecstasy use reported by the user and ex-user groups.

	Ex-user (n = 20)		Current user (n = 20)	
	Mean	*SD*	*Mean*	*SD*
Number of years used	5.53	2.83	4.73	3.10
Last used days	666	543.1	49	31.0
Av. tabs per night	1.38	0.54	1.28	0.63
Av. tabs per year	8.00	5.26	7.28	4.68
Total tabs lifetime	64.7	58.35	55.05	56.0

Table 2. History of use of other drugs reported by all three groups.

	Control (n = 20)		Ex-user (n = 20)		Current user (n = 20)	
	occasional	regular	occasional	regular	Occasional	regular
solvents	0	0	2	0	3	0
alcohol	2	17	2	18	2	18
caffeine	4	15	4	16	2	18
nicotine	8	6	8	12	5	14
cannabis	12	3	10	10	8	10
LSD	1	0	10	0	13	0
cocaine	2	2	15	1	15	0
amphetamine	5	0	16	0	16	0
opiates	0	0	3	0	2	0
ketamine	0	0	2	0	2	0
others (anabolic steroids)	1	0	6	0	5	0

Table 3. Cognitive tests: the mean scores and standard deviations for the three groups.

SUBTEST	CONTROL		EX-USER		CURRENT USER	
	Mean	SD	Mean	SD	Mean	SD
verbal memory immediate	8.60	2.04	8.70	2.58	8.25	2.73
verbal memory delayed	6.95	2.74	7.20	2.55	6.50	2.88
tapping (1)	65.35	14.97	74.56	18.23	61.10	23.64
tapping (2)	66.15	13.86	75.10	17.01	62.80	23.73
reaction time (sec)	0.61	0.13	0.56	0.12	0.61	0.12
acodes no. Correct	47.65	8.81	45.35	8.45	44.15	12.80
acodes speed of correct (sec)	2.40	0.38	2.49	0.37	2.39	0.34
areason no. correct	22.50	8.07	21.16	7.49	21.30	9.76
areason speed of correct (sec)	3.63	0.98	3.75	0.85	3.75	1.09
paterc no. correct	98.05	27.34	95.15	14.66	81.45	29.03
paterc speed of correct (sec)	1.29	0.33	1.22	0.20	1.24	0.19
sternb no. correct	55.10	9.95	53.20	7.65	47.10	16.21
sternb speed of correct (sec)	1.24	0.24	1.33	0.20	1.27	0.22