

Cognitive performance in recreational users of MDMA or 'ecstasy': evidence for memory deficits

A. C. Parrott¹, A. Lees¹, N. J. Garnham¹, M. Jones¹ and K. Wesnes²

¹Department of Psychology, University of East London, London E15 4LZ, UK and ²Cognitive Drug Research (CDR), Priory Court, Beech Hill, Reading RG7 2BJ, UK.

Cognitive task performance was assessed in three groups of young people: 10 regular users of 3,4-methylenedioxymethamphetamine (MDMA) who had taken 'ecstasy' 10 times or more; 10 novice MDMA users who had taken 'ecstasy' one to nine times; and 10 control subjects who had never taken MDMA. A computerized battery of cognitive tasks (Cognitive Drug Research system) was undertaken on a day when subjects were drug free. Performance on the response speed and vigilance measures (simple reaction time, choice reaction time, number vigilance), was similar across the three subgroups. However on immediate word recall and delayed word recall, both groups of MDMA users recalled significantly less words than controls. Animal research has shown that MDMA can lead to serotonergic neurodegeneration, particularly in the hippocampus and frontal cortex. Although the design of this study was far from ideal, these data are consistent with other findings of memory decrements in recreational MDMA users, possibly caused by serotonergic neurotoxicity.

Key words: cognition; 'ecstasy'; memory; methylenedioxymethamphetamine; performance; psychoactive drug; recreational drug

Introduction

3,4-Methylenedioxymethamphetamine (MDMA) or 'ecstasy', is widely used as an illicit recreational drug throughout Europe and America. In the UK it has been estimated that around half a million tablets of MDMA are taken each weekend (Saunders, 1995). Recreational MDMA users generally report feelings of elation, energy and confidence while on-drug, but feelings of depression, lethargy and irritability when coming down off-drug (Liestner *et al.*, 1992; Solowij *et al.*, 1992; Curran and Travill, 1997; Davison and Parrott, 1997). It can also generate hyperthermia and hyponatraemia (occasionally fatal), or induce various psychiatric disorders (Maxwell *et al.*, 1994; Series *et al.*, 1994; Steele *et al.*, 1994; Green *et al.*, 1995). There are also concerns over its long-term neurochemical effects, since it has been shown to cause serotonergic neurodegeneration in several animal species (Ricaurte *et al.*, 1992; Steele *et al.*, 1994; Frederick *et al.*, 1995; Green *et al.*, 1995; Frederick and Paule, 1997).

The physiological and subjective mood effects of MDMA have been investigated in a number of studies (Peroutka *et al.*, 1988; Liestner *et al.*, 1992; Solowij *et al.*, 1992; Davison and Parrott, 1997; Parrott and Stuart, 1997). However its effects upon cognitive task performance have rarely been studied. Krystal *et al.* (1992) measured the cognitive abilities of nine regular MDMA users, using a battery of neuropsychological tests. On most tasks their performance levels were as expected, but on the memory tasks their performance levels were lower than age-matched norms. Since the subjects were drug free when tested, these findings suggest that 'ecstasy' can have

enduring adverse effects on cognitive ability. Morgan (1998) also found that recreational MDMA users had impaired memory scores, in comparison with two control groups: non-drug users and recreational drug users who had never taken MDMA. Curran and Travill (1997) found that the acute self-administration of MDMA, was associated with a significant impairment in working memory and a trend towards impairment in prose recall. No other studies of the cognitive effects of MDMA seem to have been published (reviews: Green *et al.*, 1995; Steele *et al.*, 1994; McCann *et al.*, 1996). The current study was therefore undertaken to further investigate the cognitive consequences of MDMA use. Three subject groups were compared: regular MDMA users; novice MDMA users; and control subjects who had never taken MDMA. Subjects were tested on a cognitive test battery, on a day when they had not taken MDMA recently.

Methods

Subjects

Three groups of 10 subjects were assessed. The regular MDMA users stated that they had taken 'ecstasy' on 10 occasions or more; they comprised two females and eight males in the age range 18–25 years. The novice users stated that they had taken MDMA between one to nine times; they comprised five females and five males in the age range 20–25 years. The control subjects stated that they had never taken MDMA; they comprised six females and four males in the age range 21–30 years. Many of the subjects were university

students known personally to the researcher (AL), or friends of these contacts obtained via the 'snowball' technique (Solowij *et al.*, 1992). The subjects were unpaid.

Assessment measures

The assessment measures comprised a subset of tasks from the Cognitive Drug Research (CDR) computerized test battery (Parrott *et al.*, 1996). Each of the speeded tasks was presented for 3 min, given in the following order.

Choice reaction time 1

Either the word YES or NO appeared on the computer screen. When the YES stimulus appeared, the subject was required to press the YES response key as rapidly as possible. When the NO stimulus appeared, a corresponding NO response was required. (Note: this task was given as part of the initial training session. A second session was also given; see later.)

Immediate word recall

Fifteen words appeared on the middle of the computer screen at a rate of one word every 2 sec. Once the list finished, an on-screen instruction asked the subject to write down the words on a sheet of paper in front of them. The total number of words recalled was scored.

Simple reaction time

Subjects responded to the word YES on the computer screen, by pressing the YES response button as rapidly as possible. The inter-stimulus interval was varied randomly to reduce anticipation. The mean response time was automatically recorded.

Choice reaction time 2

This was identical to choice reaction time 1. The mean response time and percent correct responses were automatically recorded.

Number vigilance

A single target number was displayed on the right of the screen, while on the left a series of rapidly changing numbers was displayed. Each time the number on the left matched the target digit on the right, the subject was required to press the YES response button. Target detections and mean response time were scored automatically.

Sternberg task

Subjects viewed a series of five numbers appearing on the computer screen. Following this they were presented with a series of numbers, and required to press the YES button if the number had appeared in the original list, but the NO button if it had not appeared. Three lists of digits were presented. The mean response time was calculated automatically.

Delayed word recall

Subjects were instructed to write down all the words from the original (immediate recall) word list. The total number of words recalled was scored.

Ethical aspects and experimental procedures

The ethical aspects of human MDMA research are discussed by Curran (1998). It is important that undertaking a field study

such as this, should not be seen as providing tacit approval for the use of MDMA. Before being accepted into the study therefore, each subject was required to sign a written informed consent form. This stated that MDMA was an illegal drug, with a range of adverse side-effects, and that neither the experimenters nor the University condoned its use. Taking part in this study should therefore not be seen as providing any support or encouragement for the use of MDMA. The agreement also noted that taking part in the study was voluntary and that subjects could withdraw at any time. Finally the aims of the study were described: namely, to investigate the cognitive performance of recreational MDMA users and non-users.

Each subject arranged to come in for testing, on a day when they had not taken MDMA or any other illicit drug recently. They were tested individually in a laboratory cubicle. The experimenter collected both the drug data and cognitive data, and was therefore not 'blind' to the subject's drug grouping. The cognitive task package was explained, and the binary (yes/no) response keys demonstrated. An initial period for test familiarization and practice was given, with the first choice reaction time task being performed. This was then followed by the other cognitive tests. Afterwards each subject was thanked for participation and debriefed.

Results

The groups means (\pm SD) for the test battery are presented in Table 1, together with the ANOVA and Duncan test significance levels. Two cognitive tasks generated a significant ANOVA subgroup effect: immediate word recall ($p < 0.001$) and delayed word recall ($p < 0.01$). On immediate word recall, novice MDMA users recalled significantly less words than the controls (Duncan test: $p < 0.01$), while regular MDMA users also recalled less words than controls (Duncan test: $p < 0.05$; Table 1, Fig. 1). On delayed word recall, the MDMA subgroups again recalled less words than the controls (Duncan test comparisons both $p < 0.01$; Table 1, Fig. 1).

Discussion

The MDMA users were similar to non-users on the information processing speed measures: simple reaction time, choice reaction time, number vigilance response time and Sternberg task response time (Table 1). The index of sustained attention ability, target detections on number vigilance, was also similar across groups (Table 1). Thus the recreational use of MDMA was not associated with any alterations in the integrity of basic information processing. However both memory measures, immediate word recall and delayed word recall, were significantly impaired in the MDMA subgroups (Fig. 1). The overall cognitive profile for MDMA users, was therefore of impaired memory combined with unchanged information processing speed (Table 1). This profile was similar to that reported by Krystal *et al.* (1992, p.322). They tested nine regular MDMA users on a neuropsychological battery, and found unimpaired performance on most tests, but decrements on the memory tasks: 'Despite the absence of memory deficits

Table 1 Cognitive task performance in recreational MDMA users and non-users (group means \pm SD)

Cognitive task	Non-user controls (C)	Novice MDMA users (N)	Regular MDMA users (R)	ANOVA group effect	Duncan comparisons		
					CvsN	CvsR	NvsR
Simple reaction time (msec)	240 \pm 21	241 \pm 26	237 \pm 24	—	—	—	—
Choice reaction time 1 (CRT1)	410 \pm 57	378 \pm 47	399 \pm 58	—	—	—	—
CRT 1 (% Correct)	96.0 \pm 5.2	90.0 \pm 6.6	93.0 \pm 6.7	—	—	—	—
Choice reaction time 2 (CRT2)	393 \pm 45	380 \pm 46	413 \pm 49	—	—	—	—
CRT 2 (% Correct)	96.8 \pm 2.1	94.6 \pm 3.5	94.2 \pm 2.9	—	—	—	—
Number vigilance reaction time (msec)	380 \pm 32	389 \pm 35	384 \pm 25	—	—	—	—
Number vigilance (% Correct)	96.0 \pm 4.5	95.6 \pm 4.8	97.8 \pm 3.5	—	—	—	—
Sternberg task reaction time (msec)	672 \pm 95	553 \pm 95	740 \pm 256	—	—	—	*
Immediate word recall (n)	8.2 \pm 1.6	5.3 \pm 1.1	6.5 \pm 1.3	***	**	*	—
Delayed word recall (n)	6.9 \pm 1.6	4.6 \pm 1.0	5.1 \pm 1.4	**	**	**	—

Two-tailed probability levels: * p < 0.05; ** p < 0.01; *** p < 0.001.

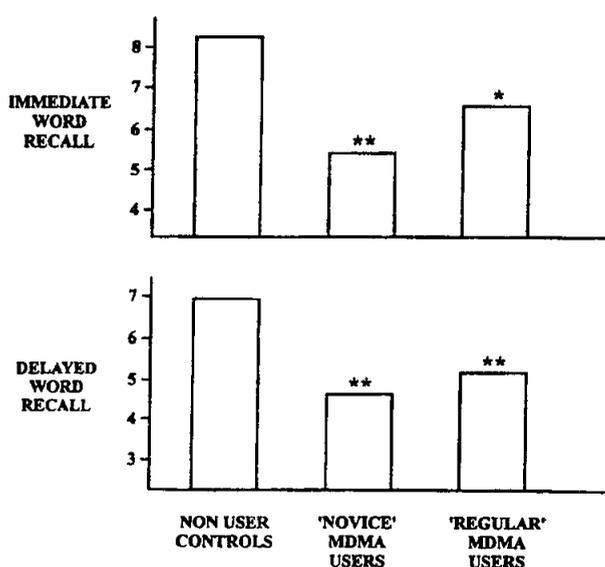


Figure 1 Immediate and delayed word recall in recreational MDMA ('ecstasy') users and non-users. * p < 0.05; ** p < 0.01 (Duncan test comparisons with controls)

on clinical examination, a pattern of mild to moderate impairment was observed on both the Initial and Delayed Paragraph Tests of the Wechsler Memory Scale'. However some limitations in Krystal's study should be noted. Firstly, they did not have a control group of non-users, but compared their data with age-matched norms. Secondly, several of their subjects had psychiatric histories prior to MDMA use. Thirdly, the study involved the administration of a tryptophan challenge prior to testing (Krystal *et al.*, 1992). Nevertheless despite these confounding factors, their findings were similar to those described here (Table 1). Memory impairments were also found in a study of recreational MDMA users from South Wales. They were tested on a neuropsychological test battery on a day when they were drug-free. Performance on several cognitive tasks was unimpaired, but significant decrements were evident in the memory measures (Morgan, 1998).

There are various possible explanations for this pattern of memory deficits. Firstly, they may be a direct result of MDMA administration. Curran and Travill (1997) found that the acute self-administration of MDMA was associated with poor cognitive task performance. If these detrimental effects remain over time, it would explain why cognitive decrements are found in MDMA users even when they are drug free. In particular, longer-term cognitive impairments may be caused by serotonergic neurodegeneration. Steele *et al.* (1994, p. 546) noted: 'The neurotoxic dose of MDMA in non-human primates approaches the dose of MDMA typically taken by recreational MDMA users (Ricaurte and McCann, 1992). This raises the concern that human MDMA users might also incur MDMA-induced serotonin damage'. Personality change has been reported in regular MDMA users (Saunders, 1995), with reduced scores on personality factors for impulsivity and indirect hostility (McCann *et al.*, 1994). These personality changes may reflect reduced serotonergic activity (McCann *et al.*, 1994), and the same explanation could be offered for the memory data. The frontal cortex and hippocampus are particularly rich in serotonin terminals and animal research has shown that their density is reduced following MDMA administration (Frederick *et al.*, 1995; Frederick and Paule, 1997). These brain areas are important for conscious awareness, planned action and memory storage. Thus MDMA-induced neurotoxicity in these regions, may be causing the current memory impairments (Fig. 1).

One difficulty with this explanation, is that recreational MDMA-users rarely report memory impairments. Millions of 'ecstasy' tablets have been taken over the past 10 years, and if the drug impairs memory, then complaints of poor memory should be more widespread. However many surveys of recreational MDMA users have not uncovered subjective evidence for memory impairments (Peroutka *et al.*, 1988; Krystal *et al.*, 1992; Solowij *et al.*, 1992; Davison and Parrott, 1997). Liester *et al.* (1992) noted that one of their 20 MDMA users complained of a poor memory, but this was described as a short-term effect. McCann and Ricaurte (1991) presented a case study of persistent neuropsychiatric abreaction to MDMA, which included severe memory problems. But in general, there are few descriptions of impaired memory in recreational MDMA users. This raises an alternative

explanation, namely that the memory deficits reflect a change in cognitive strategy. Drug users often state that their phenomenological experience becomes more immediate and non-verbal while on MDMA. They become more concerned with direct perception, and do not feel the necessity for labelling thoughts and feelings (Parrott, 1997). If this change towards a more phenomenal and less verbal cognitive style remained afterwards, it might help explain these verbal memory data. One test of this hypothesis, would be to also assess non-verbal memory skills (e.g. spatial and/or picture memory).

There were various design weaknesses in the current study, some of which are characteristic of other human MDMA field research. There was no control over which drugs had been taken, their purity or strength. The effects described here and elsewhere, can therefore only be attributed to tablets *believed by the user* to be MDMA (Table 1; Peroutka *et al.*, 1988; Krystal *et al.*, 1992; Liester *et al.*, 1992; Solowij *et al.*, 1992; Parrott, 1995, 1997; Curran and Travill, 1997; Davison and Parrott, 1997; Parrott and Stuart, 1997; Morgan, 1998). Thus while poor memory may reflect MDMA use, it may alternatively follow from impurities found in 'ecstasy' tablets (e.g. ketamine). This problem is debated elsewhere, and can best be answered by double-blind placebo-controlled studies (Parrott and Stuart, 1997; Curran, 1998). Another design weakness was that the subjects in each group were self-selected. This non-random group membership, means that the MDMA users and non-users may have differed in many other factors. In particular, the MDMA subgroups may have used more illicit drugs in general (e.g. cannabis, lysergic acid diethylamide, amphetamine). Detailed drug histories were not taken in this study, although they are going to be recorded in future studies. Another problem is that the subject groups may have differed in cognitive ability beforehand; thus the low memory task performance of the ecstasy users may be a random/chance effect. However this explanation seems unlikely, given the other findings of specific memory decrements in MDMA users (Krystal *et al.*, 1992; Morgan, 1998). Another weakness of the current study, was that while we asked subjects to come in for testing when they had not taken MDMA 'recently', we did not define this period of abstinence. The question of how long this period should be is now being addressed; we are monitoring the time-course of cognitive recovery following a dose of self-administered MDMA (Parrott and Lasky, unpublished).

Further MDMA field research is required, since placebo-controlled laboratory studies with human volunteers are unlikely to be sanctioned, particularly in the light of current findings. Several topics need to be addressed. The first relates to the effects of repeated MDMA exposure. Given the memory deficits of the novice MDMA users (Fig. 1), future studies should assess those who have taken MDMA just once or twice. This would help answer the question of how many times MDMA needs to be taken before cognitive decrements develop. Another topic is the time-course of neurochemical recovery following MDMA cessation. If a regular MDMA user stops taking 'ecstasy', how long will it take for their psychobiological functioning to return to baseline: weeks, months, years, or never? Krystal *et al.* (1992) found memory decrements in repeated MDMA users, despite a mean time of 66 days from their most recent 'ecstasy' tablet. While animal

research suggests that the neurochemical depletion following MDMA administration is prolonged (Ricaurte *et al.*, 1992; Green *et al.*, 1995). Another question relates to the exact nature of these cognitive/memory changes. A range of verbal and non-verbal memory tasks, together with measures of cognitive strategy, need to be assessed. Does the reduced memory reflect a genuine deficit, or a more subtle change in information processing strategy? Certainly the prospect of semi-permanent memory disabilities, caused by serotonergic neurotoxicity in young MDMA users, is extremely worrying.

Acknowledgement

The findings from this study were first presented at the Psychobiology Conference of the British Psychological Society, in September 1996.

Address for correspondence

A. C. Parrott
Department of Psychology
University of East London
London E15 4LZ
UK
Email: andy2@uel.ac.uk

References

- Curran H V, Travill R A (1997) Mood and cognitive effects of 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy'): week-end 'high' followed by mid-week low. *Addiction* 92: 821-831
- Curran H V (1998) Future perspectives for psychological research on MDMA ('ecstasy'). *J Psychopharmacol* 12: 105 (abstract)
- Davison D, Parrott A C (1997) Ecstasy (MDMA) in recreational users: self-reported psychological and physiological effects. *Hum Psychopharmacol* 12: 91-97
- Frederick D L, Paule M G (1997) Effects of MDMA on complex brain function in laboratory animals. *Neurosci Biobehav Rev* 21: 67-78
- Frederick D L, Ali S F, Slikker W, Gillam M P, Allen P R, Paule M G (1995) Behavioural and neurochemical effects of chronic methylenedioxymethamphetamine (MDMA) treatment in Rhesus monkeys. *Neurotoxicol Teratol* 17: 531-543
- Green A R, Cross A J, Goodwin G M (1995) Review of the pharmacology and clinical pharmacology of 3,4-methylenedioxymethamphetamine (MDMA or 'Ecstasy'). *Psychopharmacology* 119: 247-260
- Krystal J H, Price L H, Opsahl C, Ricaurte G A, Heninger G R (1992) Chronic 3,4-methylenedioxymethamphetamine (MDMA) use: effects on mood and neuropsychological function? *Am J Drug Alcohol Abuse* 18: 331-341
- Liester M B, Grob C S, Bravo G L, Walsh R N (1992) Phenomenology and sequelae of 3,4-methylenedioxymethamphetamine use. *J Nerv Ment Dis* 180: 345-352
- Maxwell D L, Polkey M I, Henry J A (1994) Hyponatraemia and catatonic stupor after taking 'ecstasy'. *BMJ* 307: 1399
- McCann U D, Ricaurte A (1991) Lasting neuropsychiatric sequelae of methylenedioxymethamphetamine ('ecstasy') in recreational users. *J Clin Psychopharmacol* 11: 302-305
- McCann U D, Ridenour A, Shaham Y, Ricaurte G A (1994) Serotonin neurotoxicity after 3,4-methylenedioxymethamphetamine (MDMA; ecstasy): a controlled study in humans. *Neuropsychopharmacology* 10: 129-138

- McCann UD, Slate SO, Ricaurte GA (1996) Adverse reactions with 3,4-methylenedioxyamphetamine (MDMA; 'ecstasy'). *Drug Safety* 15: 107-115
- Morgan MJ (1998) Lasting psychological sequelae of recreational use of MDMA ('ecstasy'): controlled studies in humans. *J Psychopharmac* 12: 105-106 (abstract)
- Parrott AC (1995) Psychoactive drugs of use and abuse: wobble, rave, inhale, or crave? *J Psychopharmac* 9: 390-391
- Parrott AC (1997) MDMA, mood and memory: the agnosia of the ecstasy. *Br Psychol Soc Proc* 5: 49
- Parrott AC (1998) The psychobiology of MDMA or 'ecstasy': symposium report. *J Psychopharmac* 12: 101-106
- Parrott AC, Stuart M (1997) Comparative mood effects of MDMA (ecstasy), LSD, and amphetamine, in polydrug users. *Hum Psychopharmac* 12 in press
- Parrott AC, Garnham NJ, Wesnes K, Pincock C (1996) Cigarette smoking and abstinence: comparative effects upon cognitive task performance and mood state over 24 hours. *Hum Psychopharmac* 11: 391-400
- Peroutka SJ, Newman H, Harris H (1988) Subjective effects of 3,4-methylenedioxyamphetamine in recreational users. *Neuropsychopharmacology* 1: 273-277
- Ricaurte GA, McCann UD (1992) Neurotoxic amphetamine analogues: effects in monkeys and implications for humans. *Ann NY Acad Sci* 648: 371-382
- Ricaurte GA, Martello AL, Katz JL, Martello MB (1992) Lasting effects of 3,4-methylenedioxyamphetamine (MDMA) on central serotonergic neurones in nonhuman primates: neurochemical observations. *J Pharmac Exp Ther* 261: 616-622
- Saunders (1995) Ecstasy and the dance culture. Neal's Yard Desktop Publishing, London
- Series H, Boeles S, Dorkins E, Peveler R (1994) Psychiatric complications of 'ecstasy'. *J Psychopharmac* 8: 60-61
- Solowij N, Hall W, Lee N (1992) Recreational MDMA use in Sydney: a profile of ecstasy users and their experience with the drug. *Br J Addict* 87: 1161-1172
- Steele TD, McCann UD, Ricaurte GA (1994) 3,4-Methylenedioxyamphetamine (MDMA, 'ecstasy'): pharmacology and toxicology in animals and humans. *Addiction* 89: 539-551