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Working memory deficits in current and previous users of MDMA ('ecstasy')

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Current and previous users of the drug MDMA ('ecstasy') were tested on measures of central executive functioning, information processing speed, and on self-report measures of arousal and anxiety. The results were compared with those for a control group who did not use MDMA. Relative to the control group, both user groups were found to be impaired in some aspects of central executive functioning. Also, there were significant group differences on the measures of anxiety (users were more anxious) and on arousal (previous users scoring higher on the arousal measure relative to current users). Users processed information as quickly as non-users but less accurately. Some possible mediators of the above group differences are discussed.

The class A drug 3,4-methylenedioxymethamphetamine, generally known as MDMA or 'ecstasy', is an amphetamine-based stimulant with hallucinogenic properties which induces an acute increase in levels of the neurotransmitters 5-hydroxytryptamine (serotonin) and dopamine. The immediate effects of its use include elation and a high energy state (Curran & Travill, 1997) which may be taken to indicate enhanced subjective arousal. MDMA has been found to cause the destruction of serotonergic axons and terminals in animals (Fischer, Hatzidimitriou, Wlos, Klatz, & Ricaurte, 1995) and humans (e.g. McCann, Szabo, Scheffel, Dannals, & Ricaurte, 1998). While the long-term psychological effects of MDMA use are still to be established, there is evidence for disturbances of mood (e.g. anxiety, depression and irritability), appetite and sleep, which have primarily been attributed to serotonergic dysfunction (Parrott & Lasky, 1998).

While evidence of emotional disturbance is emerging, the effects of the drug on cognitive functioning remain unclear. Morgan (1999) has discovered memory deficits among MDMA users affecting both immediate and delayed recall. However, previous research has tended to focus on episodic memory and more specifically on recall. The primary aim of the present study is to establish if users and previous users of MDMA exhibit impairments in more basic level cognitive processes such as working memory functioning, information processing speed, anxiety and arousal. The present study makes use of Baddeley's model of working memory and in particular focuses on the central executive component. This mechanism is believed

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to be involved in planning, monitoring and controlling action sequences, accessing long-term memory, strategy selection, and inhibiting inappropriate response patterns controlling dual task performance (Baddeley, 1996).

Turning now to affect, while MDMA use has been linked with increased anxiety and other affective dysfunctions, its relationship to arousal levels is less clear. While subjective reports of its immediate effect indicate heightened subjective arousal, Curran and Travill (1997) reported a pattern of mood change (most notably depression) in the five days after MDMA use consistent with diminished arousal. Although the direction of any potential effect remains unclear, differences in arousal compared to non-MDMA using controls might reasonably be predicted.

In the context of the issues set out above, it is unclear whether any potential effects of MDMA on mood and cognitive functioning are long term or whether they cease when the individual stops taking the drug. In an attempt to address these aspects, the present study compares current users, previous users and non-users.

To summarize, for all three participant groups (current users, previous users and non-users), various measures of central executive functioning were obtained along with measures of information processing speed, anxiety and arousal. The following specific hypotheses are addressed:

H1 Consistent with a central executive deficit, MDMA users will be less effective in a random letter generation task. Random letter generation (see below) is an established indicator of central executive functioning (see Baddeley, 1996).

H2 Arousal levels in current, previous and non-users will differ significantly and users will exhibit higher anxiety levels.

The potential moderating effects of arousal and anxiety on any group differences in central executive functioning were also investigated.

Method

Participants

In all, 30 individuals took part in the study (10 non-users, 10 current users and 10 previous users). Participants were recruited using the 'snowball' technique (individuals agreeing to take part in the study contact their friends and acquaintances who in turn contact other users, thereby creating a 'snowball' effect). Previous users were defined as those who had stopped taking MDMA at least six months previously. Current users were those who reported that they were still regularly[1] taking the drug. Non-users were those who stated that they had never taken MDMA. Various measures of MDMA use and the use of other drugs can be found in Table 1. Each group contained equal numbers of males and females.

Measures

Information was gathered through pencil and paper tasks. Participants were tested on word span, Brook's spatial matrix task, a visual memory task and for verbal fluency. None of these tests resulted in statistically significant group differences and they are not reported further.[2] The remaining tests were as follows.

[1] For both current users and previous users all consumed at least one MDMA tablet per month. In fact, Table 1 reveals that most consumed on a weekly or twice weekly basis.

[2] Further details are available from the corresponding author.

Table 1. Age, years of education, health and indicators of MDMA and other drug use among participants

	Previous users		Current users		Non-users	
Measure	*M*	SD	*M*	SD	*M*	SD
Age (years)	22·60	2·22	22·20	2·20	22·60	2·12
Years of education	12·60	0·84	12·20	1·03	12·30	0·67
Self-report health[a]	2·50	0·85	2·80	0·92	1·70	0·48
Length of MDMA use (years)	3·90	1·20	4·10	1·37	—	—
Number consumed in one session	3·40	1·60	3·25	0·86	—	—
Number of days on which MDMA is consumed per year	96·60	72·83	101·20	40·05	—	—
Number of days since MDMA was consumed	323·25	130·05	8·20	5·75	—	—
Percentage of participants using:						
Amphetamines	60·00	—	70·00	—	0·00	—
Cocaine	10·00	—	0·00	—	0·00	—
LSD	60·00	—	30·00	—	0·00	—
Marijuana	70·00	—	60·00	—	0·00	—
Any of the above	100·00	—	100·00	—	0·00	—

[a] Self-report measure ranging from 1 = very good to 5 = very poor.

Central executive functioning. This was assessed through a random-letter generation task (Baddeley, 1996). Participants were asked to speak aloud consonants (i.e. no vowels) in a random sequence.[3] They were told to avoid repeating the same letter sequence, to avoid producing alphabetical sequences, and to try to speak each letter with the same overall frequency. Individuals attempted to produce three sets of 100 letters : one set at the rate of one letter every 4 s, another set at one every 2 s, and the third set at one every 1 s. (Signals at each of these frequencies were recorded onto audio cassettes.) The order in which participants produced the sequences (i.e. 4-, 2- or 1-s intervals) was randomized. Responses were recorded on an answer sheet by the experimenter.

This task yielded three performance measures: redundancy[4] which measures the extent to which each letter occurs with the same overall frequency; the number of letters produced at each of the production rates (participants often suffer lapses at the faster rates and so produce fewer letters); and the number of vowel intrusions. Each of these three measures was obtained at all three production rates (4 s, 2 s and 1 s).

State anxiety and arousal. These were measured through scales devised by Warr and co-workers (see e.g. Fisk & Warr, 1996). The scales are applicable to a range of situations of varying specificity (e.g. ranging from how one feels about a particular task, or one's feelings about life as a whole, etc.). The focus in the present study was on the participant's state in the experimental setting.

Information processing speed. Participants were presented with a booklet containing stimuli, each one consisting of two rows of letters. They were given 30 s to classify as many rows as possible as 'the same' or 'different' (by writing the letter 'S' or 'D' next to each pair). Half of the rows were the same, and in half one of the letters was different. Letters (all consonants) were randomly chosen as was the position

[3] Baddeley (1996) noted that one problem with the standard version of the random generation task is that individuals frequently adopt simplifying strategies such as spelling out words. The requirement to avoid producing vowels avoid this problem.

[4] Redundancy is expressed as a percentage and is calculated using the procedure set out in Baddeley (1966).

of the non-identical letter within each string. The task was repeated three times with the length of the rows increased from 3 to 6 to 9 consonants. For each stimulus length (3, 6 and 9) a record was made of the total number of pairs classified and the proportion classified correctly. This indicator of information processing speed is based on similar measures employed elsewhere (e.g. by Fisk & Warr, 1996).

Other measures. A number of other measures were also taken. These included period of MDMA use (in years), frequency of use (days per year), the number of tablets ingested in a single event (e.g. in an evening out), the number of days since an ecstasy tablet had last been ingested, which other drugs had been taken in addition to MDMA, whether the individual was currently taking prescription medications, a 5-point self-report health measure (scoring 1 = very good; 2 = good; 3 = average; 4 = poor; and 5 = very poor), and the number of years of education.

Procedure

Participants were tested individually. The anxiety/arousal questionnaire was administered first, followed by the background data/drug use questionnaire, the information processing speed measure, the word fluency test, and the random generation task. Considerable importance was attached to ethical considerations: for example, consultations with the 'Drugline' organization in Manchester were undertaken before the study commenced and at the end of the session all participants were given a Drugline leaflet which highlighted some of the dangers involved with using illegal drugs.

Results

Background measures

Table 1 reveals that all users were taking at least one other psychoactive drug in addition to MDMA. There were significant group differences in the self-report health measure ($F(2,27) = 5{\cdot}39$, $p < {\cdot}05$ (users, particularly current users, rated their health status worse than non-users)). There were no significant differences between users and non-users with regard to age and years of education. However, non-users differed from users in that they did not consume other drugs.

Central executive measures

MDMA users found the random letter generating task a difficult one. Indeed, two previous users found the task to be sufficiently unpleasant that for ethical reasons they were not asked to complete it at the 1-s rate. In the analyses reported below, the data for these two individuals at the 2- and 4-s rates have also been excluded. Scores for the different aspects of the random measure are set out in Table 2. A high score for redundancy and for the number of vowel intrusions is indicative of poor central executive performance. In contrast, a high score for number of letters generated is indicative of efficient central executive performance. The data were analysed using MANOVA with group (previous user, current user and non-user) as the sole independent variable. Consistent with Hypothesis 1, this yielded an overall multivariate effect of group ($F(18,36) = 5{\cdot}73$, $p < {\cdot}001$ for Pillai's Trace). Univariate analyses revealed that, consistent with Hypothesis 1, there are more vowel intrusions among the two MDMA groups relative to the control group. The main effect of group was statistically significant at each three production rates (see Table 2). Also

consistent with prediction, MDMA users generated fewer letters and exhibited a higher degree of redundancy. However, Table 2 reveals that in both cases the difference was statistically significant only at the 1-s production rate.

Table 2. Measures of central executive functioning, information processing speed, and affect for MDMA users and non-users

	Previous users		Current users		Non-users		
	M	SD	*M*	SD	*M*	SD	$F(2,25)^a$
Random generation score							
1-s rate							
Letters produced	59·50	24·09	65·20	23·69	94·40	7·73	8·57**
Redundancy (%)	21·58	24·01	11·21	4·71	5·51	1·57	3·41*
Vowel	5·50	4·50	5·40	2·72	1·60	1·78	5·02*
2-s rate							
Letters produced	84·90	18·19	92·00	9·83	99·10	1·10	2·50
Redundancy (%)	10·65	8·66	7·77	4·19	6·15	2·66	1·99
Vowel	3·00	2·79	5·00	2·75	0·80	0·79	8·83**
4-s rate							
Letters produced	97·80	5·03	99·00	2·16	100·00	0·00	1·12
Redundancy (%)	7·77	10·34	6·29	4·53	4·18	2·47	0·66
Vowel	2·30	1·95	4·30	2·41	0·50	1·27	9·46**
Information processing speed							
Number of stimuli classified							
Three-letter	20·00	2·00	18·90	5·61	22·70	3·02	2·57
Six-letter	14·90	3·67	14·60	4·62	15·50	2·17	0·16
Nine-letter	11·70	3·23	12·90	4·65	12·50	1·72	0·32
Percentage correct							
Three-letter	97·98	3·71	96·72	4·54	98·82	1·90	0·88
Six-letter	94·47	6·41	88·23	13·29	94·93	2·77	1·86
Nine-letter	77·47	8·83	75·20	12·03	95·89	4·42	15·94***
Affect measures							
Anxiety	12·10	1·29	13·10	2·28	10·90	0·74	4·91*
Arousal	22·80	2·15	17·20	4·34	20·50	2·07	8·57**

***$p < .001$; **$p < .01$; *$p < .05$.

[a] For information processing speed, anxiety, and arousal: $F(2,27)$.

Information processing speed

The number of comparisons and the percentage correct for the three stimulus set sizes (3, 6 and 9 letters) are shown in Table 2. A MANOVA was carried out with the six information processing speed measures as dependent variables; this revealed a statistically significant effect of group (non-users outperformed the two user groups: $F(12,46) = 2·20$, $p < .05$ for Pillai's Trace). However, univariate analyses revealed

that the group difference was statistically significant only for the percentage correct at the nine-letter level (Table 2).

Arousal and anxiety

With regard to anxiety, Table 2 reveals that non-users were the least anxious. On average, current users scored highest on the measure with previous users scoring marginally lower. In terms of arousal, current users show the lowest levels, previous users are highest, with non-users occupying an intermediate position. Consistent with Hypothesis 2, for both anxiety and arousal the main effect of group was statistically significant (see Table 2). However, subsequent comparison of condition means revealed that with regard to anxiety, only the difference between current and non-users was significant ($p < \cdot 05$, via Tukey's test). For arousal, only the difference between previous and current users was significant ($p < \cdot 01$, via Tukey's test). The difference between current and non-users was just short of statistical significance.

Potential confounding effects of health, anxiety, arousal and other drugs

It is possible that group differences in the self-report health, anxiety and arousal measures and in the use of other drugs might be responsible for some of the significant group differences in central executive functioning and information processing speed. ANCOVAs were conducted for each of those variables in Table 2 associated with significant group differences. For the relevant central executive and information processing speed measures, health, anxiety, arousal, LSD, marijuana and amphetamine use were included separately as covariates (in the case of the last three, these were scored 1 if the participant used the particular drug and 0 if they did not). In each case, group (with three levels: current users, previous users and non-users) was included as the sole independent variable. Six such analyses were conducted and in all but one case (the number of vowel intrusions at the 1-s rate) the group difference remained statistically significant following control for the above covariates. Over all six ANCOVAs homogeneity of regression was achieved in 28 of 36 cases.[5] A subsequent ANCOVA revealed that group differences in arousal remained statistically significant following control for health, LSD, marijuana and amphetamine use (homogeneity of regression was achieved in all cases). However, group differences in anxiety were reduced to below statistical significance following control for the same covariates (again, homogeneity of regression was achieved in all cases). Thus, to summarize, on the whole the major group differences noted in Table 2 associated with MDMA use remain statistically significant following control for health, anxiety, arousal and other drug use.

[5] The exceptions were in the ANCOVA for letters generated at the 1-s rate where all but two of the covariates interacted significantly with group. In the ANCOVA for vowel intrusions (1-s) rate, anxiety and marijuana interacted significantly with group. Similarly the analysis for redundancy (1-s rate) showed a significant interaction between anxiety and group while that for information processing speed (percentage correct, 9-letter stimuli) showed a significant interaction between marijuana and group.

Discussion

In the random generation task, users generated fewer letters, exhibited a greater degree of redundancy and made more vowel intrusion errors compared with non-users. Baddeley (1996) notes that random generation places a continual strain on the central executive and as such is relatively demanding of cognitive resources. With this in mind these results are consistent with Morgan's (1998) observation that MDMA users appear to be unable to cope with high levels of cognitive demand. Furthermore, previous users appear to be as affected as current users, suggesting that the effects persist after the individual has ceased taking MDMA.[6]

With regard to information processing speed, the results show that current and previous users process information as quickly as non-users; however, they are significantly less accurate at least for the more complex (longer stimulus length) items. It appears, therefore, that users maintain parity with non-users at the expense of making more errors.

Anxiety levels were higher among both user groups. However, these results need to be treated with some caution since anxiety levels in the present study are noticeably lower than those reported elsewhere (e.g. Fisk & Warr, 1996)[7] and the group differences observed here were no longer statistically significant following control for health and use of other drugs.

Turning to the outcomes associated with arousal, the level reported by non-users is similar to that reported elsewhere for similar aged persons (e.g. Fisk & Warr, 1996). Relative to this the arousal levels of current users were lower, while those of previous users were elevated. These results are consistent with findings reported elsewhere. For example, Curran and Travill (1997) report 'mid week lows' (p. 821) among current users while in studies of non-human primates, Fischer *et al*. (1995) found that exposure to MDMA, in addition to destroying certain serotonergic pathways, actually caused the abnormal re-growth of others in areas of the brain believed to affect arousal levels. However, these observations, while potentially important, need to be treated with caution since both user groups, while differing significantly from each other, did not differ significantly from non-users.

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[6] This observation is dependent on the fact that previous users replied honestly when they indicated that they were no longer taking the drug.

[7] Fisk and Warr (1996) report on average anxiety score of 14·03 for similar aged persons. Non-users in the present study produced an average score of 10·90.

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