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Attentional Processes in Abstinent Methylenedioxymethamphetamine (Ecstasy) Users

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In recent years, methylenedioxymethamphetamine (MDMA or ecstasy) has gained great popularity among young adults. Although human research in abstinent users has focused primarily on memory function, little attention has been given to other neuropsychological functions that may have some bearing on memory performance, such as attention. Hence, the purpose of this study was to examine the effects of MDMA on attentional processes. Accordingly, 24 MDMA users and 30 matched normal controls were tested on the Wechsler Abbreviated Scale of Intelligence (WASI) and the Test of Everyday Attention (TEA). We found MDMA users to show generally no significant difference on attention tasks compared with controls with the exception of a single TEA subtest. More interestingly, we found some preliminary evidence to indicate that dosage, in terms of the number of tablets used, may be related to impairment on specific component attentional tasks. This finding brings to light the important relationship between poor attentional processes and drug-taking behaviors and their reciprocal relationship.

Key words: MDMA (ecstasy), attention, neuropsychology, substance abuse

Methylenedioxymethamphetamine (MDMA, or ecstasy) is one of the most popular drugs used among young adults today (Schuster, 1998). The drug has gained popularity because of its euphoric psychoactive effects. Recent investigations have shown that memory impairment is often a consequence of prolonged use in abstinent users (e.g., Morgan, 1999; Parrott, Lees, Garnham, Jones, & Wesnes, 1998; Reneman, Booij, Schmand, van den Brink, & Gunning, 2000; Ricaurte et al., 1993). In addition, human neuropsychological studies have recently shown that extensive use of MDMA could lead to long-term deficits in explicit memory processes (Bolla et al., 1998; McCann et al., 1999; Morgan, 1999; Parrott & Lasky, 1998; Parrott et al., 1998; Reneman et al., 2000; Wareing, Fisk, & Murphy, 2000; Zakzanis & Young, 2001).

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More specifically, Bolla et al. (1998) compared a group of abstinent MDMA users with controls on the Rey Auditory Verbal Learning Test, Wechsler Memory Scale–Revised (WMS–R), and Rey–Osterrieth Complex. They found impairment to be correlated to the amount of MDMA used (total milligrams per month). They also showed impairment in immediate verbal memory and visual memory. In addition, using a 1-year longitudinal design, Zakzanis and Young (2001) found a decline in immediate and delayed recall tasks on the Rivermead Behavioral Memory Test in a small sample of abstinent users. Moreover, Krystal, Price, Ricaurte, and Heninger (1992) found that a sample of 9 chronic abstinent MDMA users showed a mild to moderate memory impairment in both initial and delayed recall on the Logical Memory subtest of WMS–R. Curran and Travill (1997) found that abstinent MDMA users were impaired in terms of working memory on a prose recall task. Furthermore, Parrott (1997) showed that abstinent novice and chronic MDMA users were impaired on measures of immedi-

ate recall when compared with controls but did not show impairment in other neuropsychological domains. Finally, Morgan (1999) also showed that abstinent MDMA users recalled significantly fewer items on the short passage of prose on both immediate and delayed recall on the Rivermead Behavioral Memory Test.

Although most studies have found consequential evidence of memory impairment in abstinent MDMA users, some researchers have not replicated these findings. For example, Ricaurte et al. (1993) showed that selective damage to the 5-hydroxytryptamine system, like that produced by MDMA, is not sufficient to impair memory on its own. Similarly, Robinson, Castaneda, and Whishaw (1993) performed an experiment on rats to determine the effect of MDMA on memory processes. They found that MDMA-pretreated rats displayed a mild impairment in place navigation tasks, but once the rats discovered the goal location, MDMA-pretreated rats performed at control levels and showed no deficits in memory for spatial location. These competing results therefore indicate that memory disturbances in MDMA users are incomplete and that other possible moderating effects have yet to be delineated.

Direct behavioral evidence has led researchers to investigate the role of higher cognitive and executive functions. For example, Gouzoulis-Mayfrank et al. (2000) administered a comprehensive cognitive test battery to 28 abstinent ecstasy users who were concomitant cannabis users. The ecstasy group was compared with two equally sized matched cannabis user and nonuser control groups. All participants completed a session composed of both computerized and paper-and-pencil tests. The test battery included tests of attention, memory and learning, frontal lobe function, and general intelligence. The tests of attention included tonic and phasic alertness, selective visual attention, divided attention, intermodal integration, visual scanning, and cognitive interference. The results showed that the ecstasy group did not reveal impairment in simple reaction tasks of attention (tonic and phasic alertness). The ecstasy users did, however, display a significant impairment compared with one or both control groups on more complex attentional tasks (e.g., go and no-go task of selective attention, divided attention, and intermodal integration). Furthermore, low performance scores on measures of working memory, verbal memory, and divided attention were associated with individuals who had consumed greater doses of MDMA and cannabis. Moreover, Parrott et al. (1998) also examined a broader range of cognitive function in abstinent MDMA users. The authors assessed three groups of individuals: Ten MDMA users who had taken 10 tablets of ecstasy or more, 10 novice MDMA users who had consumed 1 to 9 tablets, and 10 non-MDMA users. All participants were tested with a computerized battery of cognitive tasks. The participants' performances on response speed and vigilance scores (i.e., simple reaction time, choice reaction time, and number vigilance) were similar across groups. The two MDMA groups, however, performed significantly lower than controls on immediate word recall and delayed word recall. Finally, Semple, Ebmeier, Glabus, O'Carroll, and Johnstone (1999) administered a battery of tests to abstinent MDMA users including the Cambridge Neuropsychological Test Automated Battery Spatial Working Memory test, Trail Making Test (Part B), phonemic word fluency, and the Stroop task to examine the effect of MDMA on executive functions. It was found that individuals with a higher dosage history of MDMA had a significant increase in errors on the Spatial Working Memory test. It was concluded that perhaps the decrease in performance on the Spatial Working Memory test may reflect the high density of MDMA-destroyed serotonin terminals found in the frontal lobes.

Given that the specificity of neuropsychological (dys)function is insufficiently defined and unresolved in MDMA users, it may be that a supervisory attentional system is responsible for disturbed and varying performance on measures of memory and executive function. For example, McCann et al. (1999) examined a range of psychomotor tasks with the aid of a computerized assessment battery of tests. They found that abstinent MDMA users showed impaired performances on sustained attention tasks such as arithmetic calculations and visual discrimination. In addition, Cami et al. (2000) examined the effect of MDMA directly on psychomotor activity in 8 healthy volunteers. The experiment was performed in a randomized double-blind crossover controlled trial. The participants were given MDMA at the time of testing that was similar in dosage used by MDMA users for recreational purposes (75 and 125 mg). The MDMA groups were compared with two control groups—an amphetamine (40 mg) and placebo group. The 125-mg MDMA group showed a mild decrease in response on a digit–symbol substitution test, which is an attention-demanding measure.

Accordingly, the purpose of this investigation was to determine the effects of MDMA on attentional processes in abstinent MDMA users. The following questions were posed: (a) Do MDMA users differ in terms of attentional processes compared with normal

matched controls? (b) Are there potential moderators of effect (e.g., number of times MDMA was used, duration of MDMA use, usual MDMA dose, frequency of MDMA use, time since last MDMA dose) that may be related to attention performance?

Methods

Participants

Twenty-four MDMA users and 30 control participants took part in the study. Participants were all fluent English-speaking individuals. Exclusion from the study was warranted when participants reported a past or current history of major medical illness (e.g., neurologic, renal, endocrine, or hematologic), current major psychiatric illness as determined by the structured clinical interview of the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; American Psychiatric Association, 1994; a positive drug screen for illicit or prescribed psychoactive drugs) or current alcohol dependence. Participants were also excluded if they reported a current pregnancy, migraine, dyslexia, or eating disorder. Most participants, however, reported erratic or highly erratic sleep habits typically coinciding with MDMA use. Hence, given that sleep deprivation is a noted finding in MDMA users and affects cognitive performance, we tested participants when they reported at least seven nights of 7 to 9 hr of continuous sleep. Moreover, all participants agreed to abstain from all drugs for at least 2 weeks before testing. Their drug-free status was confirmed by urine and blood drug screens. Given that the half-life of MDMA in animals is 1 to 2 hr, the 2-week period of abstinence was deemed long enough to rule out any withdrawal effects including sleep deprivation. Consent was obtained from each participant.

Participant characteristics are presented in Table 1. MDMA users and control participants did not differ significantly in terms of age, education, and gender.

Table 1. *Demographics*

	MDMA ($n = 24$)		Controls ($n = 30$)	
Parameter	***M***	***SD***	***M***	***SD***
Age	22.7	3.7	22.5	5.2
Education	15.7	0.8	15.7	1.0
Gender Male/Female	11/13		15/15	

Note: MDMA = methylenedioxymethamphetamine.

Procedure

Participants completed the following neuropsychological measures after outlining their characteristic MDMA and other recreational drug use.

Wechsler Abbreviated Scale of Intelligence (WASI)

To assess general intelligence, we used two subtests from the WASI (Wechsler, 1997) that represent both performance (i.e., matrix reasoning) and verbal ability (i.e., vocabulary). Together, they can be used to obtain a prorated IQ, and they have elaborate psychometric properties (see Wechsler, 1997).

The Matrix Reasoning subtest consists of a series of visual pattern matching and analogy problems pictured in nonrepresentational designs. It requires the participant to conceptualize spatial, design, and numerical relationships ranging from the very obvious and concrete to the very complex and abstract (Lezak, 1995).

As a measure of semantic memory, participants completed the Vocabulary subtest of the WASI in which they were required to provide definitions of words in an incremental order of difficulty. However, this task is also highly susceptible to educational level achieved (Lezak, 1995).

The Test of Everyday Attention (TEA)

The TEA (see Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994) provides norm-referenced scores on tests that are sensitive to selective attention, sustained attention, attentional switching, and divided attention. One of the strengths of the TEA is that it mainly uses relatively familiar everyday materials and is therefore plausible and acceptable to participants. It was, however, designed with the latest evidence on separable attentional systems in the brain in mind, and Robertson et al. (1994) provided a brief summary of the theoretical background of the test.

Map Search. This subtest examines a participant's ability to circle as many symbols (restaurants, garages, and gas stations) as they can on a Philadelphia map. First, participants are asked to circle with a red marker as many symbols as they can on the map for 1 min (Map Search I); then participants are given a blue marker to circle any additional symbols that can

be found on the map for a second minute (Map Search II). The total number of symbols circled in a 1- and 2-min time span are recorded.

Elevator Counting. Participants are required to count a series of single tones that each symbolize a floor. The floor count obtained at the end of each series is compared with the correct floor counts. On the basis of this comparison, a score of 1 will be recorded for correct responses and 0 for incorrect responses. This subtest is used as a baseline measure.

Elevator Counting With Distraction. During this subtest, participants are required once again to count a series of elevator tones, as in the previous subtest, and instructed to ignore the higher pitch distracter tones. A score of 1 is recorded for correct responses and 0 for incorrect counts.

Visual Elevator. This is a visual representation of the Elevator Counting subtest. Participants are asked to count a series of elevator icons and to change direction on the basis of the arrow icons embedded within each series, either in the up or down direction and reversing count when necessary to determine the floor reached at the end of each series. The floor count and the time taken to complete each series are recorded. A score of 1 is recorded for correct responses and 0 for false counts. Furthermore, the total amount of time on the correct responses is noted.

Elevator Counting With Reversal. During this subtest, participants are instructed to listen to three different tones: low, middle, and high. The middle tones are to be counted as floors as was instructed on the Elevator Counting subtest. The high and low pitch tones depict the up and down arrows as in the Visual Elevator subtest. Participants are given similar instructions to count the middle tones and to change direction either in the up or down direction and reversing count when necessary to determine the floor count at the end of each series. Participants are awarded a score of 1 for correct responses and 0 for false responses.

Telephone Search. This subtest entails that participants search through a telephone directory looking at services such as plumbers, restaurants, and hotels and circle services with double symbols (two squares, two stars, two circles, or two crosses) embedded beside the name of various companies. The total number of correctly circled symbols and the time taken to complete the task are recorded.

Telephone Search While Counting. During this subtest, participants are asked to examine another telephone directory and to circle the double symbols placed beside the company name; however, during this subtest participants are instructed to simultaneously listen to a series of single elevator tones while searching through the telephone directory. Participants are asked to pay equal attention to both tasks. The floor counts for each series, the total number of correctly circled symbols, and the time taken to complete the task are all recorded.

Results

MDMA and Other Drug Use

To provide an estimate of the intensity, frequency, and duration of MDMA use, detailed information about prior MDMA use was obtained from a structured interview that ascertained the number of milligrams per capsule of MDMA generally taken at one time (each capsule was assumed to equal 100 mg on the basis of previously published estimates; see Bolla et al., 1998), the number of times that MDMA was taken per month, and the total number of months of MDMA use. A dose variable—a combination of intensity and frequency—was also calculated by multiplying the self-reported milligrams ingested in a single MDMA session (which could last hours and involve several separate doses of MDMA) by the number of MDMA sessions per month (Bolla et al., 1998). Table 2 summarizes the characteristics of MDMA use in the user group. Table 3 illustrates other recreational drug exposure in the MDMA user and nonuser groups. It can be seen from the table that the control participants had similar drug-taking histories compared with the MDMA users (with the important exception of MDMA itself).

Statistical Analyses

Independent sample *t* tests were used to detect differences among groups on the neuropsychological battery. To articulate the magnitude of these differences, Cohen's (1988) effect size *d* was also computed among groups and converted to overlap distribution percentages (see Zakzanis, 1998). Briefly, *d* is a pure number, one free of our original measurement unit with which to index what can be alternatively called the degree of departure from the null hypothesis of the

alternative hypothesis or the effect size we wish to detect. This is typically accomplished by standardizing the raw effect size as expressed in the measurement unit of the dependent variable by dividing it by the common standard deviation of the measures in their respective populations, the latter also in the original measurement unit (Cohen, 1988; also see Zakzanis, in press). Moreover, Cohen's *d* can be converted into nonoverlap distribution percentages in which the effect size is transformed into a graphical representation of the effect on the degree of overlap between control and experimental groups. Cohen (1988) provided the percentiles of nonoverlap U_3 corresponding to various values of *d* (values obtained from a normal distribution table are essentially equivalent to Cohen's U_3 tabled values). Hence, the percentage of MDMA users that exceed the upper half of cases for the control group in terms of neuropsychological test scores are expressed as non-OL%.

Table 4 includes the mean performance, standard deviation, independent sample *t* test comparisons and their significance along with Cohen's effect size among groups. From the table, it can be seen that a large effect with corresponding statistical significance was found on the TEA Map Search 2 subtest ($d = 0.82$ OL% = 50) in which approximately half of the MDMA users performed more poorly than the worst performing non-MDMA user. No other test variable reached significance in terms of magnitude of effect.

We conducted a correlational analysis to determine whether any of the moderator variables were related to MDMA use. The correlational analysis revealed significant negative correlations between dosage and TEA subtests Map 1, Visual Elevator 2, and Elevator Counting With Reversal. Furthermore, a significant negative correlation was also found between number of MDMA tablets used and the

Table 2. *Characteristics of MDMA Users*

Characteristic	MDMA	*M* Range
Number Times Used	22.3	2–100
Duration of Use (in Years)	14.7	0.5–12
Usual Dose, mg[a]	1.3	0.5–2
Frequency of Use (per Month)	1.7	0.5–4
Time Since Last Dose (in Weeks)	25.8	2.0–120

[a]The number of capsules ingested per day, assuming that 100 mg is equal to one capsule.

Table 3. *Other Types of Recreational Drug Use*

	MDMA		Non-MDMA	
Drug	Freq.	%	Freq.	%
Non-MDMA Amphetamine	6	25	6	20
Cocaine	5	21	7	23
Benzodiazepines	1	4	0	0
LSD, Other Hallucinogens	13	54	8	27
Cannabis	20	83	16	53
Organic Solvents/Inhalants	3	12	1	3
Opiates	7	29	1	3
PCP and Related Drugs	4	17	3	10
Alcohol	23	96	25	83
Nicotine	18	75	12	30

Note: LSD = lysergic acid diethylamide; PCP = phencyclinide.

Table 4. *Neuropsychological Results of MDMA and Non-MDMA Users*

	MDMA		Non-MDMA			
Test	*M*	*SD*	*M*	*SD*	*d*	*p*
WASI						
Matrix Reasoning	27.8	3.8	28.0	3.2	.06	.83
Vocabulary	59.0	6.6	60.2	3.7	.09	.80
TEA						
Map Search 1	11.8	2.1	11.3	2.2	.23	.40
Map Search 2	8.2	2.4	10.5	3.2	.82	.00
Elevator Counting	11.9	1.9	11.3	2.3	.29	.36
Elevator Counting with Distraction	11.4	2.6	11.7	2.4	.12	.7
Visual Elevator (Accuracy)	12.5	3.5	11.6	3.1	.27	.34
Elevator Counting with Reversal	11.0	2.4	11.1	2.5	.04	.97
Telephone Search	13.0	3.9	13.3	3.1	.09	.76
Telephone Search with Counting	10.4	3.4	9.5	3.0	.28	.34

Note: *d* = Cohen's effect size (MDMA *M*/Non-MDMA/pooled *SD*/2); *p* = probability; WASI = Wechsler Abbreviated Scale of Intelligence; TEA = Test of Everyday Attention.

TEA subtest Telephone Search While Counting. The results of this correlational analysis are detailed in Table 5.

Discussion

The purpose of this investigation was to determine the effects of MDMA on attentional processes in abstinent MDMA users. It was found that MDMA users differed from nonusers on the Map Search 2 subtest of the TEA. As this subtest examines a participant's ability to circle as many additional symbols (restaurants, garages, and gas stations) as possible on a Philadelphia map that were missed (Map Search 2) after first circling the symbols that can be found on the map (Map Search 1), the significant difference among groups may have occurred for several reasons (e.g., attention to detail, fatigue) given that MDMA users did not show striking abnormalities on the test measure, such as neglect.

Moreover, we found several relationships between MDMA-taking behavior and attentional processes. For example, it appears that dosage is related to several attentional processes as articulated with the Map Search 1, Visual Elevator 2, and Elevator Counting With Reversal on the TEA. In addition, it appears that the number of MDMA tablets taken over a lifetime is related to performance on the Telephone Search While Counting task of the TEA.

Taken together, our results illustrate little difference in attentional processes among groups. Indeed, on several of the attentional subtests the MDMA users actually had higher scores. However, when dose and total number of times MDMA was used were examined, more significant associations were found. This is most likely because the effects of MDMA on the brain are subtle and only seen at higher levels of use.

There were important limitations to the study, however. Additional research will have to resolve limitations that impede the validity of most human MDMA research. For instance, given that there is little quality control in street drugs, most investigations provide only an estimate at best when calculating each participant's MDMA intake. As such, for legal and ethical reasons, there was no control over MDMA administration or objective confirmation of the dose or purity of MDMA taken. In keeping with published reports of ecstasy content (Wolff, Hay, Sherlock, & Conner, 1995), however, we were able to deduce that all of our participants had indeed used MDMA in various amounts, given the type of ecstasy that was reportedly used. Moreover, published reports (e.g., Wolff et al., 1995) have noted that tablets sold as ecstasy can contain 3,4-methylenedioxy-amphetamine (MDA), 3,4-methylenedioxy-ethylamphetamine (MDEA), or mixtures of a range of other compounds (e.g., caffeine, ephedrine, selegiline, amphetamine, ketamine, and LSD-9). Although some tablets sold as ecstasy contain little or no MDMA, the majority does contain MDMA or the related compound MDEA (Morgan, 1999).

Another issue concerns the drug history of the participant sample; that is, self-report of drug-taking behavior in drug users is notoriously unreliable. As such, it remains unclear whether the reported use of MDMA and other drug exposures are gross underestimates or overestimates of actual drug use. Given that

Table 5. *Correlational Analysis*

Test	Number Times Used (Pearson Correlation)	Dosage (Pearson Correlation)
WASI		
Matrix Reasoning	–0.223	–0.157
TEA		
Map Search 1	–0.238	–0.528**
Map Search 2	–0.109	0.157
Elevator Counting	–0.085	–0.235
Elevator Counting With Distraction	–0.364	–0.317
Visual Elevator	–0.321	–0.513*
Elevator Counting With Reversal	–0.263	–0.443*
Telephone Search	–0.268	–0.246
Telephone Search With Counting	–0.524*	–0.334

Note: Dosage per pill was assumed to equal 100 mg based on previously published estimates; see Bolla et al. (1998). $N = 24$

* $p < .05$. ** $p < .01$.

this was a self-referred sample of users with an invested interest in its outcome, it is believed that the self-reported drug-taking behaviors of the participants can be loosely described as reliable. It is possible, however, that the attentional disturbance may be secondary to polydrug use and not MDMA itself. Indeed, attention-type deficits have been found in college students with heavy-drinking (e.g., Blume, Marlatt, & Schmaling, 2000) and marijuana (Pope & Yurgelun-Todd, 1996) histories. Although we excluded MDMA users with a positive drug screen for illicit or prescribed psychoactive drug or current alcohol dependence, the use, but not dependence, of polydrugs in the MDMA group and its effect on attentional function remains quantitatively unresolved and requires further examination.

Accordingly, we should emphasize the difficulty of drawing conclusions about the effects of MDMA in polydrug users. Although we would like to be able to draw neurochemical conclusions based on our observations among groups, given the contamination of the group through use of other substances and the relative paucity of information regarding the neurochemical effects of MDMA, our desire to relate MDMA use and attentional dysfunction should not be taken well beyond what can be foreseeably derived from our preliminary investigation.

Finally, premorbid personality characteristics and overlapping neurocognitive dysfunction may also make the interpretation of these findings difficult; that is, poor decision making and planning and difficulties in terms of volition and purposive action may contribute to substance abuse habit. Accordingly, a person premorbidly marked by poor executive function may be more inclined to abuse MDMA, thus making any cause–effect speculations imperceptible. It will be important for future research to keep these limitations in mind while trying to untangle the neuropsychology of MDMA.

In conclusion, although this investigation did not reveal significant deficiencies in attentional processes, it did find that MDMA dose and the total number of times used were related to poorer scores on several subtests of the TEA. As with previous studies, it may be that a certain threshold of total MDMA (alone or in combination with other illicit substances) must be crossed before notable deficits in neurocognition are found between users and nonusers. This study adds to the neuropsychology of MDMA by illustrating that attentional processes are also at risk in heavy users.

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