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Effect of ecstasy use on neuropsychological function: a study in Hong Kong

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Abstract *Rationale:* Previous studies on the effects of ecstasy on neuropsychological performance have often recruited small sample sizes. *Objectives:* The present study was conducted to validate previous findings regarding the effects of ecstasy consumption on neuropsychological performance. *Method:* A comprehensive neuropsychological investigation was conducted in 100 abstinent ecstasy users and 100 matched non-user counterparts on standardized measures of working memory, verbal and non-verbal memory, verbal and figural fluency, and selective and switching attention. *Results:* Abstinent ecstasy users were impaired on verbal and non-verbal memory, complex attention, and verbal fluency, but not on working memory, relative to their non-user counterparts. Of particular interest was the fact that abstinent ecstasy users performed better on figural fluency relative to their non-user counterparts. In addition, only cumulative ecstasy consumption correlated with neuropsychological performances among abstinent ecstasy users. Canonical discriminant analysis yielded verbal and visual memory, switching attention, and verbal fluency as potential core neuropsychological variables for differentiating abstinent ecstasy users from non-users. Levels of depression and general non-verbal intelligence, as measured by the Beck Depression Inventory and the test of non-verbal Intelligence, respectively, were not likely to affect these findings, since these measures were matched between ecstasy users and non-users. *Conclusions:* These findings suggest that previous ecstasy consumption can affect a wide range of neuropsychological performance, though figural fluency may be subsequently enhanced as a result of the phenomenon of "cortical disinhibition." Furthermore, measures of verbal and visual memory, switching attention, and verbal fluency may be particularly useful for differentiating abstinent ecstasy users from non-users.

Keywords 3,4-Methylenedioxymethamphetamine · Ecstasy · Neuropsychological function · Cognitive function · Drug

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3,4-Methylenedioxymethamphetamine (MDMA, "ecstasy") has recently become an increasingly popular drug at rave parties in Hong Kong. Previous studies have shown that MDMA leads to diffuse serotonin depletion and degeneration of serotonergic axon terminals in animals including non-human primates (Ricaurte et al. 1985, 1988a, 1992; Schmidt et al. 1986; Stone et al. 1986; Battaglia et al. 1987, 1988; Schmidt 1987; O'Hearn et al. 1988; Wilson et al. 1989; Molliver et al. 1990), whereby such neurotoxic effects of MDMA may be long term in non-human primates (Ricaurte et al. 1988a,b, 1992; Fischer et al. 1995; Aguirre et al. 1997; Hatzidimitrou et al. 1999). Abstinent MDMA human users had lower levels of 5-hydroxyindoleacetic acid (5-HIAA, found in cerebrospinal fluid and detectable in urine), which were observed to relate positively to delayed visual memory perfor-

mance (Bolla et al. 1998). Specificity of 5-HIAA has been previously demonstrated in abstinent MDMA human users who had lower levels of CSF 5-HIAA, but not of homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) (McCann et al. 1999). Serotonergic neuroendocrine dysfunction (e.g. disregulated release of cortisol) is also related to memory span performance in MDMA human users (Verkes et al. 2001).

Neuroimaging studies have suggested that MDMA consumption in abstinent MDMA users lowers their global densities of 5-hydroxytryptamine (5-HT) transporter sites most noticeably in the hypothalamus, as well as other cortical and subcortical brain structures (McCann et al. 1998; Obrocki et al. 1999; Reneman et al. 2000). However, these findings were not replicated in later studies (Reneman et al. 2001; Thomasius et al. 2003) with ecstasy users who had much longer periods of abstinence. Gamma et al. (2000) have also demonstrated that healthy volunteers who are administered a single oral dose of MDMA (1.7 mg/kg) have decreased regional cerebral blood flows (rCBFs) in the limbic, paralimbic, central frontal, and temporal areas. However, Chang and colleagues (2000) administered two oral doses of MDMA within 1 week and found that abstinent MDMA users had reduced rCBF only after, but not before MDMA administration in various brain regions. Nevertheless, MDMA has been found to affect the brain diffusely, with both cortical and subcortical brain structures affected, thus leading to possible impairments on a wide range of neuropsychological functions (e.g. Gouzoulis-Mayfrank et al. 2000; Rodgers 2000; Bhattachary and Powell 2001).

Neuropsychological function of MDMA users

Many studies on the neuropsychological effects of MDMA have been conducted with abstinent MDMA users. Various mood changes, including impulsivity and anxiety, have been reported by MDMA users in previous studies (Solowij et al. 1992; Gamma et al. 2000; see Morgan 2000 for a comprehensive review). In terms of neuropsychological functions, MDMA users have been found to be impaired on verbal working memory in some studies (Curran and Travill 1997; Verkes et al. 2001), but not in others (Morgan 1998; Parrott and Lasky 1998; McCann et al. 1999; Gouzoulis-Mayfrank et al. 2000; Rodgers 2000). Furthermore, no group differences were observed between abstinent MDMA users, polydrug users, and healthy volunteers on tasks related to central executive functioning (Morgan 1998; Wareing et al. 2000). Hence, MDMA users seem to be impaired on verbal working memory. Abstinent MDMA users are also impaired, relative to healthy volunteers, in terms of immediate and delayed verbal memory (Bolla et al. 1998; Morgan 1999; Gouzoulis-Mayfrank et al. 2000; Rodgers 2000; Bhattachary and Powell 2001). Verbal memory performance in abstinent MDMA users has been negatively associated with levels of 5-HIAA depletion (Bolla et al. 1998) and cumulative MDMA consumption (Morgan 1999; Gouzoulis-Mayfrank et al. 2000). In contrast to these findings on verbal memory performance, abstinent MDMA users were found to be significantly impaired only in terms of delayed but not immediate visual memory (Bolla et al. 1998; Rodgers 2000).

Previous studies have found no differences between MDMA users and healthy volunteers on basic visual, auditory, and complex reaction time tasks (Rodgers 2000), though abstinent MDMA users have been found to be impaired on complex attention tasks (e.g. McCann et al. 1999; Gouzoulis-Mayfrank et al. 2000). These findings suggest that MDMA may mostly affect complex attention, while sparing basic attention processes.

Abstinent MDMA users have been found to be impaired, relative to healthy volunteers, on verbal fluency in some studies (e.g. Bhattachary and Powell 2001), but not in others (e.g. Gouzoulis-Mayfrank et al. 2000). This discrepancy on verbal fluency performance in MDMA users may be due to the fact that Bhattachary and Powell (2001) employed both regular and abstinent MDMA users, whereas Gouzoulis-Mayfrank et al. (2000) employed only abstinent users. A speculative explanation may be that there is a fluctuation in verbal fluency performance immediately upon MDMA intake. As no study has examined visual fluency performance in MDMA users, this was addressed in the present study.

Neuropsychological impairments in MDMA users have been related to MDMA consumption in previous studies. For example, cumulative MDMA consumption is negatively related to immediate and delayed story recall performance in MDMA users (Bhattachary and Powell 2001). In contrast, chronological age and sex were unrelated to delayed verbal recall (Reneman et al. 2000). Nonetheless, cumulative MDMA consumption has been identified as the strongest predictor of memory functioning in MDMA users, relative to cannabis usage, general intelligence, and time since MDMA was last taken (Bhattachary and Powell 2001), though this was not supported by other studies where these latter studies showed similar memory impairments between MDMA and cannabis subgroups (Dafters et al. 1999; Rodgers 2000; Croft et al. 2001). That is, it remains unclear whether MDMA contribute specifically to the observed memory impairments in previous studies. The total number of MDMA exposures was also negatively related to complex attention in abstinent MDMA users (McCann et al. 1999), whereas duration of MDMA usage is negatively related to divided attention (Gouzoulis-Mayfrank et al. 2000). The length of the period of abstinence from MDMA has an effect on recall performance, where better recall performance for MDMA users seems to be associated with a longer period of abstinence (Morgan 1999).

The present study

Although many studies have been conducted on ecstasy users in terms of their neuropsychological performance, consumption of alcohol, nicotine, and other drugs were often reported for ecstasy users in previous studies (e.g.

Curran and Travill 1997; Morgan 1998, 1999; Rodgers 2000; Wareing et al. 2000; Bhattachary and Powell 2001; Verkes et al. 2001). In light of the effect of consuming alcohol (Talland 1965; Tarter 1976; Kapur and Butters 1977; Parker and Noble 1977; Parsons and Farr 1981; MacVane et al. 1982; De Renzi et al. 1984; Shelton et al., 1984; Walsh 1985; Ryan and Butters 1986; Grant 1987; Bowden 1988; Akshoomoff et al. 1989), other drugs such as marijuana (Weingartner et al. 1972; Darley et al. 1973; Braff et al. 1981) and cocaine (Washton and Stone 1984; Mittenberg and Motta 1993), and multiple drugs (Grant et al. 1978a,b; McCaffrey et al. 1988; Sweeney et al. 1989) on neuropsychological performance, the extent to which concomitant alcohol and other drugs affect the findings of previous studies regarding ecstasy usage and neuropsychological performance is largely unknown. Gouzoulis-Mayfrank and colleagues (2000) showed that there were distinct neuropsychological profiles for users of both MDMA and cannabis that were different from that for users of cannabis only. The neuropsychological profiles for MDMA and cannabis users in their study accurately classified 90.4% of the users who took MDMA and cannabis, while also correctly classifying cannabis-only users (85.7%) and healthy volunteers (92.6%) (Gouzoulis-Mayfrank et al. 2000). In response to Parrott and Lasky's (1998) suggestion to control better the history of other substance use in drug studies, the present study examined a large sample of ecstasy users who did not report any history of substance abuse or smoking. This group of ecstasy users was identifiable, since the use of ecstasy has only recently become a popular trend in Hong Kong for individuals with different backgrounds, including those who had no prior exposure to nicotine, alcohol, or other, illicit drugs. Specifically, it was expected that ecstasy users would be impaired on verbal and visual memory, complex attention, and verbal fluency.

Materials and methods

Participants

Two hundred participants, 100 abstinent ecstasy users and 100 non-users (gender ratio=1:1) in Hong Kong were recruited from local bars and dance clubs for this study using Solowij et al.'s (1992) "snowball" sampling technique from July 2001 through November 2001. These participants were screened from an initial total of 572 individuals, where 165 had regular alcohol consumption (one drink per week for over 6 months or longer within the last 2 years), 82 smoked regularly (10 cigarettes per week for over 6 months or longer within the last 2 years), 83 were polydrug users, and 42 had a combination of alcohol, nicotine, or polydrug consumption. No demographic or clinical data were collected from these excluded participants. Exclusion criteria included self-reports of: (1) having previously smoked or consumed alcohol on a regular basis, (2) a history of illicit substance use, (3) consumed other pharmacological drugs on a regular basis (e.g. pain relievers), (4) a history of neurological or psychiatric illness(es), and (5) a history of head injury. All ecstasy users in our study reported an orange appearance of the tablets taken during the period of 2000 through 2001. As reported by Cheng et al. (2003), ecstasy tablets in Hong Kong during this time period contain approximately 50% MDMA, with ketamine as a common additive in these tablets.

The performances of the 100 abstinent ecstasy users were compared with the 100 non-users on a wide range of neuropsychological measures administered in a quiet room inside a local office building. Informed consent was obtained and debriefing was provided for all participants in this study. None of the participants was paid for their participation in this study. Ethics approval was obtained from the research committee of the University of Hong Kong. This study was conducted in accordance with the Principles of Helsinki.

Neuropsychological measures

For the purpose of this study, a battery of neuropsychological tests was selected based on previously published normative data on Hong Kong Chinese (Lee et al. 2002b) as well as the recommendation of Lee et al. (2002a) regarding memory assessment.

Test of non-verbal intelligence (TONI-3) This measure was used as a screening measure of non-verbal intelligence that is free of language and cultural bias (Brown et al. 1997). It consists of five practice items and 45 test items of abstract/figural problem solving with different formats and novel figures for each item. A total score was derived by summing all the scores for each individual test item.

Beck depression inventory (BDI) A Chinese-adopted version of the Beck Depression Inventory (Beck 1987) was used as a measure for clinical depression. In the present study, the reliability (as indicated using Cronbach's alpha) of this measure was 0.88.

Forward and backward digit span test (FDST and BDST) The FDST is a measure of working memory, or more specifically of the ability to retain short-term, verbal materials (Wechsler 1987). Digits of varying length (from 2 to 15 in this study) were presented to the participant. The participant was then asked to recall the digits verbally. There were two sets of different digits for each digit length. This test was terminated when the participant failed to correctly recall both sets of digits for a particular digit length, with their score being derived directly from the most recent digit length for which the digits were recalled correctly. The BDST differed from the FDST in that the former required the participant to recall the digits in the reverse order from which they were originally presented (Wechsler 1987).

Chinese auditory verbal learning test (CAVLT) This measure was developed to measure verbal learning and memory

domain. Rey (1959) first introduced the original version of this test, which was later modified and adapted for use with English-speaking participants (Taylor 1959; Lezak 1979). The test consists of five successive presentations of 15 words (list A), with each trial being followed by a free-recall test. Upon completion of the fifth presentation, an interference list of 15 words (list B) was presented, followed by a free-recall test of that list. Immediately following this, a post-interference free-recall test of the words from list A was administered without further presentation of those words (immediate recall). The participants were required to recall words from list A again after a 30-min delay. Each trial was designed to assess immediate memory span and learning memory. Immediate recall was calculated by summing the number of correct items recalled from list A over five consecutive trials (CAVLT-immed). Delayed recall was calculated from the number of correct items recalled from list A after a 30-min delay (CAVLT-del). A score for delayed recognition was calculated based on the number of items correctly identified as belonging to list A (CAVLT-recog).

Aggie figures learning test (AFLT) This measure was used as a non-verbal measure of learning and memory (Majdan et al. 1996). The test format was constructed according to that for CAVLT, using 15 abstract figures that did not lend themselves to verbal encoding. Administration and scoring procedures are much like those employed for CAVLT. Separate scores for immediate recall, delayed recall, and delayed recognition were calculated and are represented as AFLT-immed, -del, and -recog, respectively.

Color trails test (CTT) This is a measure of attention developed by D'Elia et al. (1996), and previously validated for use in Hong Kong by Lee and Chan (2000a). Forms 1 (CTT1) and 2 (CTT2) were administered, in which the participants were asked to connect circles that were numbered from 1 to 8 on the practice trails and 1 to 25 on the test trials, in an ascending manner (e.g. "1" followed by "2"). Form 2 differs from form 1 in that the former requires the participant to connect circles of alternating colors, yet retain the numerical progression as in form 1. Completion time (in seconds) was recorded for all participants on test trials only.

Stroop test (ST; Chinese version) This is a measure of selective attention adapted from Regard's (1981) version of the Stroop test. A previously validated Chinese translation of the Victoria Version of this test was used in the present study (Lee and Chan 2000b). This version contains three subtests: (1) color dots (D), color of non-color words (W), color words that conflict with the color in which they are presented (C). Reaction times (in seconds) are recorded separately for these subtests. The difference between the reaction times obtained for C and D was used to assess the magnitude of the Stroop effect.

Symbol digit modalities test (SDMT) This is a measure of complex scanning and visual tracking originally developed by Smith (1982). It consists of 110 test items. The participants were required to match a symbol (based on a symbol-digit key) with a number within 90 s. While both verbal and written administration of this measure were performed, only the scores obtained on the verbal administration of this measure were used in order to reduce the psychomotor demands of this measure. The total number of correct symbol-digit pairings was calculated for all participants.

Verbal fluency test (VFT; Chinese version) This measure was used to measure verbal fluency by indicating the spontaneous production of words of a given category within 1 min (Benton et al. 1983). The categories fruits and vegetables (VFT-fruit) were combined together to avoid confusion among our Chinese participants. In addition, animals (VFT-animal) and instruments (VFT-instrument) were used as separate categories in this measure. VFT-fruit was administered first, followed by VFT-animal, and then VFT-instrument. The inter-rater reliability (intra-class correlation coefficient) of this measure was 0.95 between two raters on 50 protocols.

Ruff figural fluency test (RFFT) This is a measure of non-verbal fluency that requires participants to generate as many unique designs as possible within 1 min for each of the five parts of the measure (Ruff 1996). Each part contains a different configuration of dots with which the participants are required to generate unique designs. The total scores for the total number of unique designs (RFFT-unique) and repeated designs (RFFT-per) summed across all parts of this measure were calculated for all participants.

Statistical analyses

Descriptive statistics were calculated for chronological age and education in years, MDMA dosage used per week (tablet), duration of MDMA usage (month), time since last dosage was taken (months), and scores on the TONI-3 and the BDI. One-way analysis of variance (ANOVA) was performed in order to identify differences between MDMA users and non-users in terms of their demographic characteristics and neuropsychological performance. Bivariate correlations were performed to examine the relationships between MDMA cumulative dose (calculated as MDMA dosage per week×duration of MDMA usage×4), abstinence (months since MDMA was last taken), and neuropsychological performance. Stepwise canonical discriminant analysis was performed to identify which of the neuropsychological measures in this study could accurately classify ecstasy users and non-users on the basis of performance scores. However, CTT1 and CTT2 (n=79) were not entered for this analysis in order to maintain equal sample sizes for all neuropsychological measures. All statistical analyses were corrected for multiple comparisons by setting the cutoff for P-values at 0.001.

Table 1 Demographic and clinical characteristics. *Abstinence* months since ecstasy was last taken, *TONI-3* Test of Non-Verbal Intelligence, *BDI* Beck Depression Inventory

	Ecstasy users	Ecstasy non-users	*F*	*P*
Age (years)	28.46 (5.71); range=18–45	28.82 (5.78); range=18–45	0.20	0.66
Education (years)	10.53 (1.75); range=6–16	10.66 (1.94); range=7–16	0.25	0.63
Ecstasy dosage per week (tablet)	3.70 (0.86); range=2–5	0.00 (0.00)	–	–
Duration of ecstasy usage (months)	2.38 (0.49); range=2–3	0.00 (0.00)	–	–
Cumulative dosage (tablet)	35.84 (13.21); range=16–60	0.00 (0.00)	–	–
Abstinence	2.23 (0.51); range=1–3	0.00 (0.00)	–	–
TONI-3	28.99 (3.49); range=22–38	29.24 (3.37); range=22–38	0.27	0.61
BDI	1.31 (1.15); range=0–4	1.48 (1.01); range=0–5	1.23	0.27

Values represent arithmetic means and values in brackets represent the corresponding standard deviations. Dashes indicate that a particular cell is not applicable
Cumulative dosage = (ecstasy dosage per week×duration of ecstasy usage×4)

Results

Demographic characteristics and information pertaining to ecstasy usage for all participants are summarized in Table 1. Ecstasy users and non-users were not significantly different from each other with respect to chronological age, years of education, and scores on the TONI-3 and the BDI ($P>0.05$).

The results obtained from the ANOVA showed that ecstasy users were significantly impaired compared to non-users with respect to verbal (CAVLT-immed, -del, and -recog) and non-verbal memory (AFLT-immed, -del, and -recog), switching attention (SDMT-verbal), verbal fluency (VFT-fruit, -animal, and -instrument), and figural fluency (RFFT-unique). However, ecstasy users performed similarly to non-users with respect to working memory (FDST and BDST) and attentional control (CTT1 and CTT2) ($P>0.05$). It is important to note that differences on ST (selective attention) and RFFT-perserve (perseveration tendencies) between ecstasy users and non-users were statistically significant only prior to controlling for multiple comparisons. An interesting finding of the present study was that ecstasy users were superior to their non-user counterparts in terms of RFFT-unique (see Table 2).

In addition, the results from Pearson's correlations indicated that while cumulative ecstasy dosage was negatively related to AFLT (del and recog) and RFFT-unique, positively related to RFFT-perserve, but not significantly

Table 2 Differences on neuropsychological measures between ecstasy users and non-users (n=200). *FDST* forward digit span test, *BDST* backward digit span test, *CAVLT* Chinese-Rey auditory verbal learning test, *AVLT* Aggie figures learning test, *ST* Stroop test, *CTT1* and *CTT2* form 1 and 2 of the color trails test, *SDMT* symbol digit modalities test, *VFT* word fluency test, *RFFT* Ruff figural fluency test, *immed* immediate recall, *de* delayed recall, *recog* delayed recognition

Neuropsychological function	Measure	Ecstasy users	Ecstasy non-users	*F*	*P*
Working memory	FDST	9.38 (1.01)	9.57 (1.03)	0.50	0.19
	BDST	6.66 (0.96)	6.75 (1.02)	0.22	0.52
Verbal memory	CAVLT (immed)*	5.20 (0.80)	10.51 (1.45)	1,665.62	<0.001
	CAVLT (del)*	5.28 (1.57)	13.52 (1.26)	1,427.60	<0.001
	CAVLT (recog)*	5.64 (1.93)	12.80 (1.22)	1,168.70	<0.001
Non-verbal memory	AFLT (immed)*	5.44 (1.58)	6.54 (2.00)	177.47	<0.001
	AFLT (del)*	5.45 (1.57)	8.81 (1.99)	175.70	<0.001
	AFLT (recog)*	12.63 (1.24)	13.70 (1.44)	31.81	<0.001
Attention	ST	13.70 (2.38)	13.03 (0.86)	7.05	0.01
	CTT1	27.62 (3.33)	27.42 (3.11)	0.17	0.69
	CTT2	64.44 (6.92)	63.88 (7.04)	0.28	0.60
	SDMT-verbal*	60.97 (4.43)	66.30 (3.00)	99.24	<0.001
Verbal fluency	VFT-fruit*	16.93 (2.14)	19.31 (1.92)	68.40	<0.001
	VFT-animal*	13.54 (2.10)	18.40 (1.42)	369.50	<0.001
	VFT-instrument*	11.28 (1.61)	12.13 (0.79)	22.39	<0.001
Figural fluency	RFFT-unique*	111.52 (11.76)	97.91 (6.12)	105.30	<0.001
	RFFT-per	14.75 (7.04)	12.50 (6.30)	5.67	0.02

Values represent arithmetic means and values in brackets represent the corresponding standard deviations. Degrees of freedom used in all analyses under this table was (1, 198), except for CTT1 and CTT2 which was (1, 177)
Asterisks denote statistically significant differences

Table 3 Relationship between ecstasy and neuropsychological performance (n=100). *Abstinence* months since ecstasy was last taken, *FDST* forward digit span test, *BDST* backward digit span test, *CAVLT* Chinese-Rey auditory verbal learning test, *AVLT* Aggie figures kearning test, *ST* Stroop test, *CTT1* and *CTT2* form 1 and 2 of the color trails test, *SDMT* symbol digit modalities test, *VFT* word fluency test, *RFFT* Ruff figural fluency test, *immed* immediate recall, *del* delayed recall, *recog* delayed recognition

Cumulative dosage = (ecstasy dosage per week×duration of ecstasy usage×4)
Asterisks denote statistically significant correlations

Neuropsychological function	Measure	Cumulative dosage	*P*	Abstinence	*P*
Working memory	FDST	0.09	0.38	−0.18	0.07
	BDST	−0.10	0.32	−0.10	0.30
Verbal memory	CAVLT (immed)	−0.19	0.06	0.06	0.56
	CAVLT (del)	−0.31	0.002	−0.13	0.19
	CAVLT (recog)	−0.10	0.34	−0.13	0.20
Non-verbal memory	AFLT (immed)	−0.13	0.21	−0.00	0.99
	AFLT (del)	−0.33*	<0.001	0.07	0.48
	AFLT (recog)	−0.34*	<0.001	−0.09	0.38
Attention	ST	−0.06	0.54	−0.03	0.76
	CTT1	0.18	0.08	0.19	0.06
	CTT2	0.02	0.88	0.01	0.90
	SDMT-verbal	0.13	0.18	−0.08	0.44
Verbal fluency	VFT-fruit	−0.22	0.03	0.12	0.25
	VFT-animal	−0.18	0.07	−0.01	0.89
	VFT-instrument	−0.07	0.49	0.04	0.67
Figural fluency	RFFT-unique	−0.50*	<0.001	0.18	0.07
	RFFT-per	0.43*	<0.001	−0.06	0.57

related to C-RAVLT (del) and WFT-fruit. Period of abstinence from ecstasy was not related to any neuropsychological measures used in this study (P>0.05). These results are summarized in Table 3.

As revealed by stepwise canonical discriminant analysis, only measures of verbal memory (CAVLT-immed, -del, and -recog), non-verbal memory (AFLT-del), ST, and verbal fluency (VFT-animal) could accurately classify participants in this study as either ecstasy users or non-users (99% accuracy for MDMA users, 100% accuracy for non-users, P<0.001).

Discussion

In accordance with previous studies, our findings indicate that abstinent ecstasy users are impaired, relative to non-users, on verbal (Bolla et al. 1998; McCann et al. 1999; Morgan 1999; Gouzoulis-Mayfrank et al. 2000; Reneman et al. 2000; Rodgers 2000; Bhattachary and Powell 2001) and non-verbal memory (Bolla et al. 1998; Rodgers 2000), selective and switching attention (McCann et al. 1999), and verbal fluency (Bhattachary and Powell 2001), but not on working memory and attentional control (Morgan 1998; Parrott and Lasky 1998; McCann et al. 1999; Gouzoulis-Mayfrank et al. 2000; Rodgers 2000). In contrast to one previous study (Gouzoulis-Mayfrank et al. 2000), no difference was found between ecstasy users and non-users on auditory attention (BDST). This may reflect a difference between the sample selection used by Gouzoulis-Mayfrank and colleagues (2000) and that used in the present study. However, there was a marked enhancement of figural fluency performance in ecstasy users relative to non-users. According to the present authors, none of the previous studies investigated ecstasy users' performance in this particular neuropsychological domain. Parrott (2000, 2001) has suggested that the neurocognitive profile of ecstasy users is consistent with a "reduced cortical inhibition." The observed enhancement of figural fluency performance among abstinent ecstasy users in the present study may have resulted from cognitive disinhibition, whereby the spontaneous generation of abstract figures was facilitated by such disinhibition. By convention, figural fluency performance rests primarily on an individual's ability to spontaneously generate abstract figures within certain rule restrictions. However, ecstasy users may be less distracted by these restrictions, and thus produce abstract figures more freely when completing measures such as the RFFT. As this was partially supported by the fact that our ecstasy group had slightly higher perseverative errors on RFFT, cognitive disinhibition may be a possible explanation for the enhanced performance observed in these ecstasy users. Future studies should perhaps examine the effects of ecstasy consumption on figural fluency performance. Another point worth mentioning is that the proposed cognitive disinhibition among ecstasy users enhanced figural (non-verbal) fluency, but affected verbal fluency in the same manner. That is, verbal fluency performances among abstinent ecstasy users in the present study were impaired, relative to their non-user counterparts. Since verbal fluency and figural fluency measures differ from each other conceptually on a verbal–non-verbal axis, ecstasy may selectively affect the different neural pathways necessary for these two neuropsychological functions. Previous lesion studies have provided some support in favor of distinct neural regions underlying verbal (Tucha et al. 1999) and figural fluency performance (Ruff et al. 1994). The level of depression (as measured by the BDI) and general non-verbal intelligence (as measured by the TONI-3) do not explain this enhancement of figural fluency since the abstinent ecstasy users in the present study were matched in terms of their depression and non-verbal intelligence.

As previous studies have shown (McCann et al. 1999; Morgan 1999; Gouzoulis-Mayfrank et al. 2000; Bhattachary and Powell 2001), cumulative dosage of ecstasy intake and period of abstinence are negatively related to neu-

ropsychological performance in ecstasy users. However, the present study found similar relationships between previous ecstasy consumption and neuropsychological performance, but not for period of abstinence from ecstasy. This finding may suggest that period of abstinence from ecstasy is a less sensitive measure of neuronal impairment than cumulative previous ecstasy consumption among ecstasy users. Nevertheless, ecstasy may affect neuropsychological performance in a dose-response manner, though further laboratory-controlled studies are needed to verify this claim. More importantly, the associations between ecstasy consumption, the period of use, and neuropsychological performance in this study were of moderate magnitude. This may reflect the fact that the sample consisted of individuals who had taken ecstasy and no other drugs (e.g. nicotine and alcohol), unlike previous studies, which included those with concurrent cigarette, alcohol, and polydrug consumption in their samples (e.g. Bolla et al. 1998). In particular, orbitofrontal disregulation has been suggested to be related to drug abuse tendencies (London et al. 2000). As noted earlier, the present finding of an enhanced figural fluency may provide some evidence of an intact orbitofrontal system in light of the recruitment for the present study of abstinent users who had used ecstasy only. Furthermore, the relationships between cumulative ecstasy consumption and neuropsychological performance were strongest for figural fluency, then non-verbal memory (recognition and delayed), then delayed verbal memory, and then verbal fluency, while attention performance was uncorrelated with ecstasy usage. This strong correlation between figural fluency performance and ecstasy consumption, relative to other neuropsychological measures, may suggest that ecstasy consumption primarily affects the frontal brain regions of abstinent ecstasy users. This has been supported to some degree in previous neuroimaging studies on ecstasy users (Chang et al. 2000; Gamma et al. 2000) where decreased rCBFs in various brain regions (including the frontal lobes) were found. As suggested in a review by Parrott (2000), future studies on ecstasy users should obtain better data on psychoactive drug histories, should better explain individual variability, and should clinically control the prior drug use of participants.

The fact that verbal and non-verbal memory, along with verbal fluency, were the most distinguishable variables between ecstasy users and non-users is worthy of discussion here. In light of the practical constraints in terms of financial and administrative resources in clinics devoted to helping individuals with substance-abuse problems, practitioners may opt to assess these particular neuropsychological domains (verbal and non-verbal memory, and verbal fluency) during the initial assessment of ecstasy users. Furthermore, the fact that these particular neuropsychological domains emerged as the most useful for distinguishing between ecstasy users and non-users may have direct implications on building a model of neuropsychological assessment specifically for ecstasy users. Such a model would allow researchers and practitioners to have a better framework and gain a better understanding of the consequences of ecstasy consumption for neuropsychological performance, as well as develop guidelines for core assessment and intervention programs for these individuals. The present findings have shown some promising results for the proposed model of assessment that includes memory and fluency functions. However, the relative inability of measures of attention to distinguish ecstasy users from non-users does not render them useless. Rather, the relative subordination of attentional performance to memory and verbal and figural fluency in terms of its ability to identify ecstasy users may reveal unique aspects of the neuropsychological effects of ecstasy. Alternatively, the resources subserving ecstasy users' performance on attentional measures may be substituted through other intact neuroanatomical networks that are relatively spared after ecstasy consumption. It is important to note that CTT1 and CTT2 were excluded from the stepwise discriminant analysis in the present study, which may have appeared to be useful for distinguishing between ecstasy users and non-users. However, in light of the absence of a statistical difference between these groups of individuals on the CTT, it is unlikely that this would have affected the present results. Future studies may help clarify these issues.

Although standard laboratory tests were not performed to ascertain the presence and absence of other drug usage in the present sample, the current authors believe that there are no a priori reasons for the participants to make false claims about their history of drug and other substance usage based on their motivation to participate in this study. It is interesting to note that personality profiles of ecstasy users in the present study may have affected the present results, though these were not formally assessed in this study. That is, in light of the recent trend of ecstasy use in Hong Kong, there may be personality differences between those ecstasy users and non-users. Moreover, the present findings are generally congruent with those reported in previous studies. Nevertheless, the present findings argue strongly against the use of ecstasy and highlight the negative effects of ecstasy consumption on a wide range of neuropsychological functions in humans. It would also be interesting to examine these functions using neuroimaging methodologies (McCann et al. 1998; Obrocki et al. 1999; Reneman et al. 2000), as well as to contrast animal models based on different variants of ecstasy to delineate the structural components that are primarily responsible for these neuropsychological consequences of ecstasy.

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