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An investigation of the subacute effects of ecstasy on neuropsychological performance, sleep and mood in regular ecstasy users

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Abstract

The aim of this study was to differentiate the subacute from the chronic effects of ecstasy. Regular ecstasy users who subsequently chose to take ecstasy (experimental group: E, *N* = 16) were compared with regular ecstasy users who opted not to (control group: C, *N* = 16). Groups were assessed with neuropsychological and psychometric measures at drug-free baseline before ecstasy use and 1 and 4 days after use. Ecstasy users who consumed ecstasy (E) did not differ from those who did not (C) in relation to age, estimated IQ, personality or past substance use, including ecstasy. At baseline, E reported being more energetic, lively and cheerful whereas the day after ecstasy use they reported being more muddled, afraid, sad and dejected than C. However, this was not significant after controlling for sleep deprivation. Mood returned to baseline within 3 days and there were no group differences in Beck depression inventory scores at any of the three testing sessions. There were no subacute effects of ecstasy on working memory, story recall, impulsivity, or decision-making. However, at baseline and the day after use ecstasy users made poorer decisions, and were less sensitive to punishment, in the Somatic marker sensitivity test. These findings suggest that previous reports of marked subacute effects of ecstasy use may have been confounded by chronic polydrug use before use, co-substance use and sleep disturbances after use.

Key words

cognition; ecstasy; MDMA; mood; sleep; subacute

Introduction

Recreational use of "ecstasy" (3,4-methylenedioxymethamphetamine, MDMA) has become increasingly widespread and is associated with "clubbing" at weekends (e.g. Topp, *et al.* 1999; Winstock 2001). In the UK, regular ecstasy users typically take between one and two tablets characterised by high MDMA purity levels (Parrott, 2004). Tolerance to its positive effects develops rapidly (Solowij, *et al.* 1992; Davison and Parrott 1997; Cottler, *et al.* 2001; Morgan, *et al.* 2002; Verheyden, *et al.* 2003; Parrott 2005). The acute effects of pharmaceutically pure MDMA, tested in the laboratory, last for 3–6 h and are reported to include an affective state of enhanced mood and well-being, heightened openness and a sense of closeness to other people (Liechti, *et al.* 2000a; Vollenweider, *et al.* 1998). Similarly, the acute effects of "street" ecstasy include mood elevation and a variety of perceptual, prosocial and aesthetic effects (e.g. Sumnall, *et al.* 2006). Subsequently, only a minority of participants report experiencing negative physiological and psychological symptoms in the 3 to 5 days after administration of pharmaceutically pure MDMA (Vollenweider, *et al.* 1998; Liechti and Vollenweider 2000a, b; Liechti, *et al.* 2000b). On the other hand, naturalistic studies suggest that a greater proportion of "street" ecstasy users experience more intense subacute effects that can disrupt mood and cognition up to 8 days after consumption of "street" ecstasy (Curran and Travill 1997; Parrott and Lasky 1998; Verheyden, *et al.* 2002; Curran, *et al.* 2004; Hoshi, *et al.* 2004).

However, a variety of methodological limitations have undermined the validity of the latter findings. In particular, all of these studies except one (Parrot and Lasky 1998) failed to collect baseline measures prior to drug consumption. Although Parrot and Lasky (1998) did include drug-free baseline measurements, pre-drug group differences in memory recall and the mood symptom "sad" were not included as covariates in the analyses, which might have confounded the

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interpretation of their findings. Hence, on the basis of the latter naturalistic studies, it is impossible to differentiate whether the observed differences between the experimental groups are indeed a genuine subacute effect of the drug or are at least partly attributable to chronic effects of ecstasy. It is now widely accepted that chronic use of ecstasy and other substances by regular ecstasy users is associated with persistent perturbations of mood and selective cognitive deficits (e.g. Morgan 1998a, 1998b, 1999, 2000; Morgan, *et al.* 2002, 2006). Thus, the latter naturalistic studies failed to control for possible existing chronic effects of past regular ecstasy consumption by not including a control group of matched ecstasy users who had abstained from using ecstasy on the night out. It should also be noted that a drug-naive control group would be redundant when attempting to differentiate the genuine subacute effects from the chronic effects of ecstasy.

The studies by Curran and colleagues (Curran and Travill, 1997; Curran, *et al.* 2004) and Parrott and Lasky (Parrott and Lasky, 1998) also failed to control for other confounding factors such as inter-session drug consumption or sleep deprivation. Sleep deprivation and disrupted circadian rhythm are known to be associated with a decline in neuropsychological performance and depression (Durmer and Dinges 2005; Tsuno, *et al.* 2005) and ecstasy is well known for its potent stimulant properties, which may result in subsequent sleep disruption and insomnia (e.g. Allen, *et al.* 1993; Liechti, *et al.* 2000b; Liechti and Vollenweider 2000a).

In a recent study, we attempted to cater for the latter design limitations by comparing two groups of ecstasy users: those who subsequently voluntarily consumed ecstasy and those who did not. These two groups were assessed at baseline prior to some of them taking ecstasy and then over the days after use (Huxster, *et al.* 2006). Contrary to the earlier reports of profound and long-lasting unpleasant subacute effects of ecstasy, we found that after controlling for co-use of alcohol with ecstasy, and the subacute effects of ecstasy on sleep, the effects on mood remained marginally statistically significant while the subacute effects on cognitive impairment did not. However, short-comings of our latter study included a lack of objective neuropsychological measures of cognitive performance and confirmatory assays of self-reported drug history during the testing period.

Therefore, the aim of the present study was to differentiate the subacute from the chronic effects of ecstasy by extending our latter study to include objective measures of cognitive performance and assays of recent drug use. Two groups of young adults (aged 19–30 years) were compared: 16 regular ecstasy users who voluntarily decided to take ecstasy later that night after baseline assessment and 16 regular ecstasy users who voluntarily opted not to take ecstasy after baseline assessment. At baseline full drug-use histories, measures of personality and estimated pre-morbid IQ were collected to determine whether there were any pre-existing differences between the two groups. Each participant completed parts of a battery of psychometric and neuropsychological measures three times: an initial drug-free baseline assessment prior to ecstasy use, the subsequent day (24-h later) and then 3 days later. The baseline assessment usually took place on a Friday or a Saturday evening between 6.00 pm and 9.00 pm. In order to confirm self-reported drug history, we collected oral–serum fluid samples at each testing session. Finally, we also collected daily measures of sleep and all other substance use to control for confounding by the effects of other substances on the subacute effects of ecstasy.

Materials and methods

Participants

Volunteers, 19 males and 13 females, aged 19–30 years (mean ± SD = 22.81 ± 2.94) were recruited via email advertisements at the University of Sussex, distribution of flyers at local nightclubs and the "snowball" technique (Solowij, *et al.* 1992). The experiment was advertised as a study investigating clubbing lifestyles with no mention of ecstasy in order to avoid a selection bias and encouraging and promoting drug use. All selected participants were regular recreational ecstasy users who reported using the drug at least once a month. They were allocated to one of the two experimental groups on a post hoc basis according to whether they reported ecstasy use after baseline assessment. Exclusion criteria included a history of treatment for epilepsy, schizophrenia, bipolar disorder, anxiety and depression; intravenous drug use; or any serious current medical condition that required medication. All participants reported that they were not under the influence of drugs or alcohol at the time of testing and were requested to provide written informed consent and were paid £20 for participating. The study was approved by the University of Sussex, Psychology Department Ethics Committee.

Study design

A mixed between and within factor design was used with ecstasy users who voluntarily chose to use ecstasy between drug-free baseline assessment and the second testing session that took place 24 h later ($N = 16$) and those who chose to abstain for this period ($N = 16$) as the between conditions and 3 days of assessment as repeated measures. The experimenter (AP) met with each participant individually in the participant's home. Participants were administered a number of questionnaires and counterbalanced neuropsychological tests.

Questionnaires and neuropsychological tests

Personal details A 10-item questionnaire that covered: gender, age, height, weight, parents occupations, educational level, current medication, smoking status and personal and family psychiatric history.

National adult reading test (NART; Nelson 1982) This test provides an estimate of pre-morbid IQ and ensures that their knowledge of English is adequate.

Rivermead behavioural memory test (RBMT; Wilson,* et al. *1985) A taped prose passage taken from the RBMT containing 65 words was played to participants who then wrote down all they could recall immediately and then again after 30 min delay. In order to minimise test–retest effects, parallel forms of four different stories matched for difficulty and length were randomly administered to each participant at each testing session.

General drug history questionnaire Participants were asked to indicate if they had ever used alcohol, tobacco or any of a list of illicit drugs including marijuana, ecstasy, cocaine, amphetamine, LSD and opiates. If they had they were required to indicate age of first use, total duration of use, time since last use, frequency of use and usual dose per session.

Past 24 h and 3-day sleep and drug-use questionnaire Participants were asked to rate the quality of their sleep and record the duration of the previous nights' sleep in hours and drug consumption during the last 24 h on the day after baseline and over the following 3 days on the last day of testing.

Mood visual analogue scales (MVAS) This questionnaire consisted of 16 visual analogue measures of current mood state.

Beck depression inventory (BDI; Beck,* et al. *1961) The BDI is a 22-item self-report depression inventory.

Serial seven subtractions (SSS) task This task measured concentration and working memory. The subject was asked to serially subtract as many sevens from a given three-digit number as they could in 120 s.

Matching familiar figures (MFF20; Cairns and Cammock, 1978) test This is a behavioural measure of impulsivity that involves the simultaneous presentation of a stimulus figure and an array of six similar alternatives, all except one of which differed on one or more details. The participant is required to select the figure that exactly matches the stimulus as quickly and as accurately as possible. Three dependent variables were analysed: (1) the mean latency to first response; (2) the total number of errors committed and (3) an "I score" – calculated by subtracting the standard score of the mean latency to first response from the standard score of the total number of errors committed (Ze – Zl).

Somatic marker sensitivity test (SMST) (Peterson,* et al. *1996) This is a computerised analogue of the variably reinforced card playing task described by Bechara, *et al.* (1994). Subjects are presented with four "decks" of cards A′, B′, C′ and D′, and are provided with 200 points. The task comes to an end after 100 card selections (although subjects are not informed of this arbitrary end point). For two decks (A′ and B′), choosing a card was followed by a high financial gain, but at unpredictable points, the selection of a card was followed by a high financial penalty, so that in the long run, these decks were disadvantageous. For the other two decks (C′ and D′), the immediate financial gain was smaller, so that in the long run, these decks were more advantageous.

Drug screening Screening for drugs was carried out with Intercept® devices provided by Altrix Healthcare plc., Warrington, UK. Assays were screened for cannabis, cocaine, opiates and methamphetamine and its derivatives. MDMA concentration was determined by GC/MS.

Subjective acute effects of ecstasy were assessed with 24 VASs.

Summary of testing schedule

- Day 0: Consent form, personal details questionnaire, general drug-use questionnaire, MVAS, BDI, NART, SSS, RBMT, MFF20, past 24-h sleep questionnaire, drug screening, SMST.
- Day 1: Past 24-h sleep and drug-use questionnaire, MVAS, BDI, SSS, RBMT, ecstasy effects questionnaire, MFF20, drug screening, SMST.
- Day 4: Past 3-day sleep and drug-use questionnaire, MVAS, BDI, SSS, RBMT, MFF20, Drug screening, SMST, payment and debriefing (Figure 1).

Statistical analysis

All data were analysed with SPSS (version 11.0). One-way ANOVA's and independent samples *t*-tests were used to test for group (ecstasy use versus no use) differences in age, gender ratio, education, estimated IQ, personality, psychopathology and past and subsequent substance use. The data were analysed with two-way repeated measures ANOVA's with ecstasy group as a between factor and repeated measures on the day before ecstasy use and subsequent two testing days after use were used to assess group differences and changes in mood, neuropsychological performance and sleep. The Greenhouse–Geisser correction was employed if Mauchly's test indicated significant deviation from the assumption of sphericity. Potential confounding variables, including sleep duration and quality, were treated as covariates where appropriate. Pearson's product moment correlation coefficient was employed to investigate correlations between dependent variables and dose–response relationships. Bonferroni correction was employed in cases of multiple hypothesis testing.

Results

Baseline measures

Table 1 details the personal characteristics for subsequent ecstasy users (ecstasy) and non-users (control). There were no group differences for any of these measures.

Table 1 Personal details

	Ecstasy ($N = 16$)	Control ($N = 16$)
Age mean (± SD)	22.81 (±2.94)	22.62 (±3.34)
Males (N)	10	9
Females (N)	6	7
University level education (N)	11	11
Current cigarette smokers (N)	14	14
Used alcohol in last 24 h (N)	12	11
Used cannabis in last 24 h (N)	10	12
Estimated IQ	114.81 (3.79)	115.42 (3.14)

Table 3 Participants' ecstasy consumption history means (±SD)

	Ecstasy ($N = 16$)	Control ($N = 16$)
Age at first use	16.85 (1.42)	17.39 (2.35)
Duration of use in years	5.5 (2.5)	5.6 (2.9)
Frequency of use per month	2.1 (1.9)	2.1 (2.9)
Average dose per session (tablets)	2.3 (1.1)	2.6 (2.3)
Weeks since last use	2.9 (3.9)	7.2 (9.9)
Calculated lifetime use*	419.9 (764.6)	647.6 (1690.9)

Symbol * derived from usual dose * frequency * duration.

Table 2 summarises the substance use history means (±SD) for ecstasy users (ecstasy) and non-users (control). There were no significant group differences for any of these measures. Of the 32 participants, all had used alcohol and ecstasy, 31 had used cannabis, 27 had used cocaine, 21 ketamine, 26 psilocybin mushrooms, 23 "poppers", 23 amphetamine, and 21 LSD.

Table 3 shows that no participants had taken ecstasy for at least 6 days prior to day 1 of the study. There were no group differences in ecstasy use history (see Table 3).

Mood

MVAS data There was a significant day by group interaction for the items sad [F (2, 58) = 3.154, $P = 0.05$], afraid [F (2, 58) = 3.236, $P = 0.04$], placid [F (2, 58) = 3.664, $P = 0.03$] and dejected [F (1.458, 42.283) = 3.647, $P = 0.03$]. Ecstasy users were significantly more sad, afraid, placid and dejected than controls on the day after use than on the other days (see Figure 2). There was also a main effect of day for the items muddled [F (1.535, 44.511) = 11.409, $P = 0.001$], lively [F (2, 58) = 14.286, $P = 0.001$], energetic [F (2, 58) = 10.352, $P = 0.001$] and cheerful [F (2, 58) = 3.554, $P = 0.035$] and a significant day by group interaction for the same items: muddled [F (1.535, 20.669) = 3.670, $P = 0.03$], lively [F (2, 58) = 6.586, $P = 0.003$], energetic [F (2, 58) = 3.793, $P = 0.02$] and cheerful [F (2, 58) = 5.164, $P = 0.009$]. Finally, a main effect of group was found for the item hungry [F (1, 29) = 8.973, $P = 0.006$] showing that ecstasy users were significantly hungrier than controls during all three testing sessions (Figure 2).

Table 2 Substance use history means (±SD)

Substance	Ecstasy ($N = 16$)	Control ($N = 16$)
Alcohol (units per week)	23.9 (15.6)	24.7 (30.1)
Nicotine (cigarettes per week)	52.1 (46.3)	41.6 (27.6)
Cannabis (joints lifetime)	10332 (15861)	7826 (8649)
Cocaine (grams lifetime)	68.5 (16 2.6)	59.6 (115.2)
Amphetamine (grams lifetime)	40.7 (72.0)	97.8 (158.4)
Ketamine (grams lifetime)	165.4 (465.4)	46.2 (57.9)
LSD ("trips" lifetime)	65.8 (112.2)	44.2 (103.9)
Mushrooms ("hits" lifetime)	24.8 (27.1)	35.3 (73.8)
Poppers ("hits" lifetime)	364.9 (613.3)	47.1 (71.9)

BDI The mean (SD) BDI scores for day 0, 1 and 4 for controls were 7.3 (5.6), 4.6 (2.9) and 5.1 (4.8). The mean (SD) BDI scores for day 0, 1 and 4 for ecstasy users were 3.8 (3.6), 3.6 (4.7) and 3.4 (3.6). There were no main effects of group, day and no group by day interaction.

Sleep measures

Quality of sleep There was no main effect of the quality of sleep rating across nights, no effect of group and no significant interaction between group and rating of quality of sleep across nights. However, quality of sleep the night after baseline was positively correlated with both immediate [$r = 0.431$, $P = 0.022$] and delayed [$r = 0.447$, $P = 0.017$]. RMBT recall the following day.

Hours of sleep Two ecstasy users failed to report the number of hours they slept on day 3, 4 and 5. There was a significant

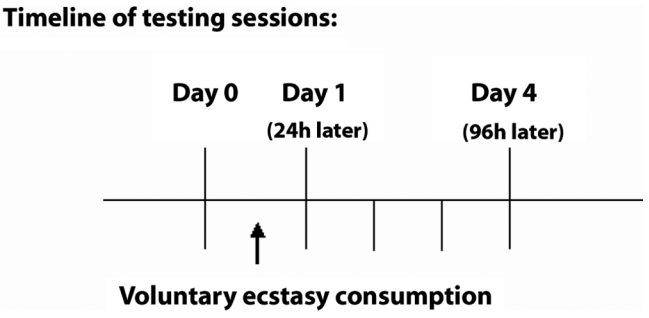

Figure 1 Each participant was tested three times: an initial drug-free baseline assessment: day 0; the subsequent day: day 1 (24 h later); and then 3 days later: day 4 (96 h later). Sixteen participants opted to voluntarily consume ecstasy on the night between testing sessions day 0 and day 1.

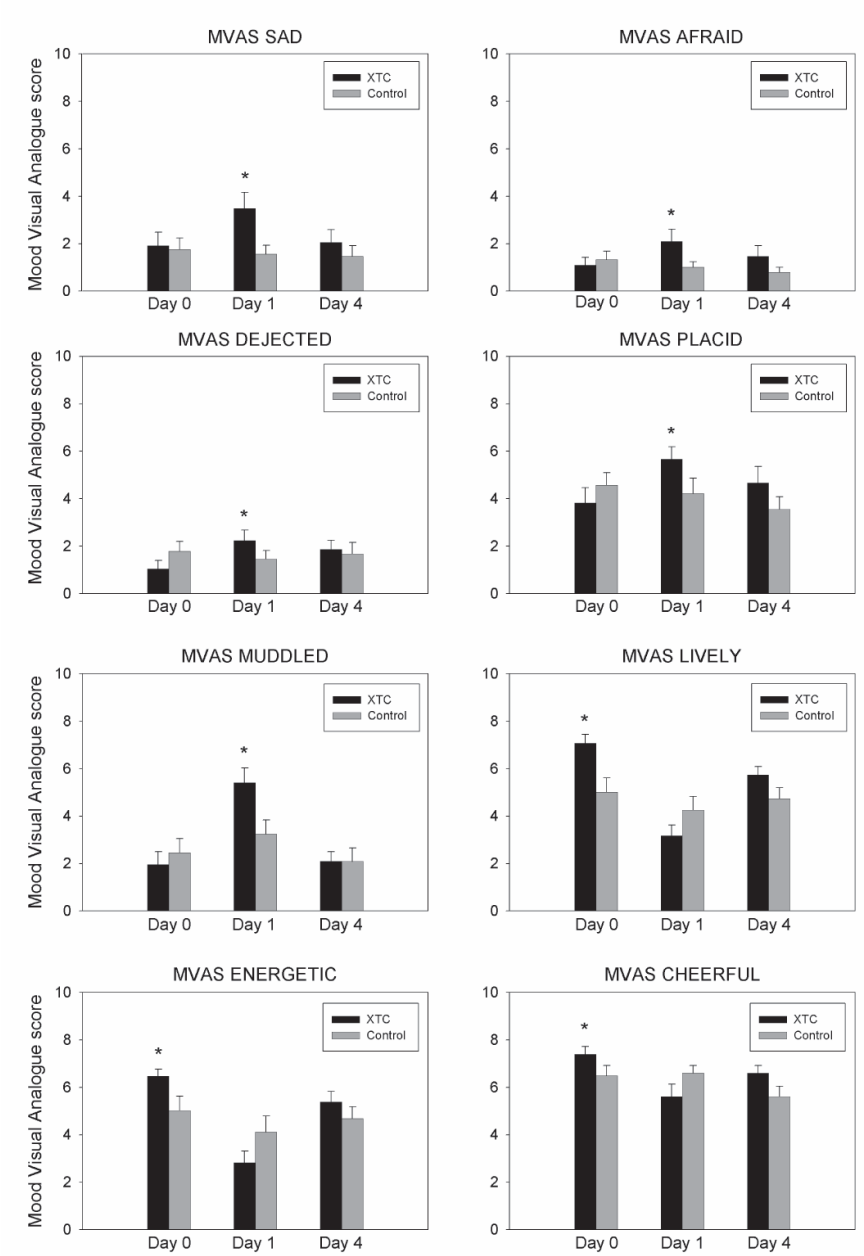

Figure 2 Means (SEM) for MVAS. ANOVA of MVAS with group (ecstasy group "XTC" versus controls) as the between factor and the three assessment days as the within factor yielded a day by group interaction for the items sad [F (2, 58) = 3.154, P = 0.05], afraid [F (2, 58) = 3.236, P = 0.04], placid [F (2, 58) = 3.664, P = 0.03], dejected [F (1.458, 42.283) = 3.647, P = 0.03], muddled [F (1.535, 20.669) = 3.670, P = 0.03], lively [F (2, 58) = 6.586, P = 0.003], energetic [F (2, 58) = 3.793, P = 0.02] and cheerful [F (2, 58) = 5.164, P = 0.009].

main effect of day [F (4, 112) = 9.397, P = 0.001] and group [F (1, 28) = 18.05, P = 0.001] (see Figure 3). There was no interaction between group and hours slept during the five nights starting from the night prior to baseline assessment to the night prior to day 4.

Mood and sleep Pearson's product moment correlations were conducted to explore possible relationships between the 22 MVAS items reported on day 1 and the number of hours slept between day 0 and day 1 (night of consumption). Non-significant correlations are not reported.

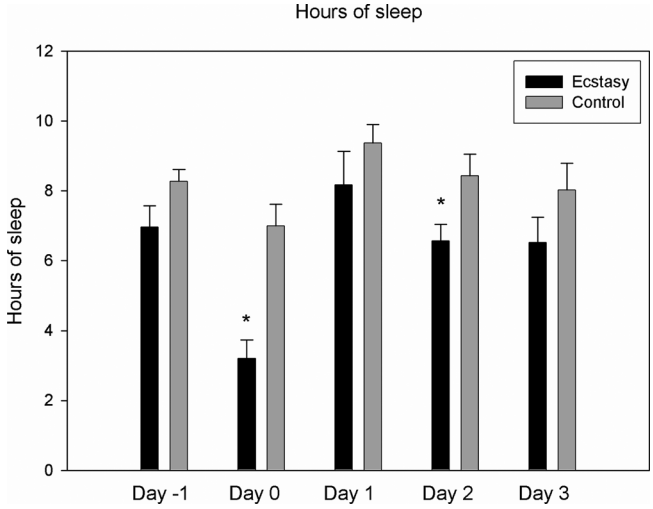

Figure 3 Means (SEM) hours of sleep. Day 1 indicates the night preceding baseline assessment on day 0. ANOVA of hours of sleep with group as the between factor and hours of sleep over five nights as the within factor indicated a main effect of day [F (4, 112) = 9.397, P = 0.001] and a main effect of group [F (1,28) = 1019.09, P = 0.001]. There was no interaction between group and hours of sleep over these five nights.

Hours of sleep as a covariate Several MVAS items on day 1 were positively correlated with sleep disruption between day 0 and day 1 (see Table 4). After exclusion of data from two participants who failed to report their sleep hours, a two-way repeated measures ANCOVA of self-reported mood (MVAS) with hours of sleep as a covariate yielded no main effect of group, no main effect of day and no group by day interaction.

Cognitive performance

SSS task There were no main effects of group, day or group by day interaction either for the total number of subtractions or for the total number of errors (see Table 5).

Rivermead behavioural memory test Repeated measures ANOVA with group as the between factor and immediate and delayed recall over the 3 testing days as the within factor, and with quality of sleep on the night before the second RMBT test treated as a covariate, showed a statistically significant effect of day [F (5, 125) = 2.761, P = 0.021] with both groups performing better on day 4 than on the two previous testing sessions (see Figure 4), but no significant effect of group or interaction between group and day of testing.

MFF test 20 There was a main effect of day [F (2, 60) = 13.285, P = 0.001], and a main effect of group on this measure [F (1, 30) = 4.426, P = 0.045], for the average total numbers of errors committed. After Greenhouse–Geisser correction for significant sphericity, there was a significant main effect of day for mean latencies to first response [F (1.277, 38.305) = 45.822, P < 0.001]. There was no interaction between group and testing day for any of the MFF20 measures (including derived "I" score measures of impulsivity) (see Figure 5).

SMST There was a significant main effect of choice of deck [F (1.679, 90) = 71.501, P = 0.001], a main effect of testing day [F (3, 60) = 3.374, P = 0.041], and interactions between group and choice of deck [F (3, 90) = 3.086, P = 0.019], choice of deck and testing day [F (6, 180) = 143.254, P = 0.001] and group, testing day and choice of deck [F (6, 180) = 6.386, P = 0.001]. There was also a main effect of day [F (1.175, 60) = 23.809, P = 0.001] and an interaction between group and the total number of points gained [F (1.175, 60) = 6.616, P = 0.011] (see Figure 6).

Drug screening An initial screening analysis of oral–serum assays confirmed that all ecstasy users accurately reported the use of MDMA between baseline and day 1. A similar analysis of oral–serum assays of the non-using participants proved that they too were all accurate in their reported abstinence. Subsequent GC/MS analyses indicated that the mean concentration of MDMA found in ecstasy users' oral fluid was 351.06 ng/ml (SD 606.87 ng/ml). Only two participants had traces of the metabolite MDA. The mean concentration of MDA was 11.63 ng/ml (SD 25.35 ng/ml). The concentration of MDMA and the number of pills ecstasy users reported consuming on the night out [r = −0.039 P = 0.823] was not significantly correlated.

Subjective effects of ecstasy No significant relationships were found between the concentrations of MDMA, MDA or number of ecstasy tablets consumed on the night before testing and the self reported acute subjective effects of ecstasy.

Subjective effects and past ecstasy use history The subjective effects of ecstasy were assessed the day after use in the group that used ecstasy. The effects "happy" [r = −0.777, P = 0.001] and

Table 4 Pearson's r correlations between MVAS on day 1 and number of hours of sleep between day 0 and day 1 (night of consumption)

	Drowsy	Cheerful	Energetic	Tired	Lively	Muddled	Sad
Numbers of hours of sleep on the night of consumption	r = –.517, P = 0.002	r = .512, P = 0.003	r = .540, P = 0.001	r =–.529, P = 0.002	r = .606, P < 0.001	r = –.460, P = 0.008	r = –.471, P = .007

Table 5 SSS total and error means (±SD)

	Total day 0	Errors day 0	Total day 1	Errors day 1	Total day 4	Errors day 4
Control	23.18 (12.10)	2.12 (1.70)	26.87 (12.21)	2.31 (1.85)	29.31 (15.90)	1.75 (2.20)
Ecstasy	33.00 (13.87)	1.18 (0.98)	34.06 (14.46)	1.31 (1.19)	33.43 (14.85)	1.56 (2.06)

"sociable" [$r = -0.746$, $P = 0.001$], were negatively correlated with the usual dose of ecstasy consumed in the past by participants in this group. The item "anxious" was positively correlated with the usual dose of ecstasy [$r = 0.714$, $P = 0.002$]. The items "irritable" [$r = -0.640$, $P = 0.008$] and "aggressive" [$r = -0.628$, $P = 0.001$] were negatively correlated with age of first use. Finally, "nervous" was positively correlated with the estimated total lifetime consumption of ecstasy [$r = 0.677$, $P = 0.004$].

Alcohol and other drug consumption

Between day 0 and day 1 There was no difference in the amount of alcohol, cannabis or any other illicit drug consumed by ecstasy users and controls on the night prior to the second testing day. Ecstasy users consumed an average of 2.09 (1.11 SD) ecstasy tablets between day 0 and day 1.

Between day 1 and day 4 There was a significant difference between ecstasy users and controls for alcohol consumption between day 1 and day 4 [F (1, 31) = 4.195, $P = 0.045$] with controls drinking more alcohol than ecstasy users over these 3 days. There were no group differences in consumption of any other illicit drug.

Discussion

In the present study, participants who reported that they used ecstasy (confirmed by immunoassays of oral–serum samples), reported elevated negative mood symptoms the day after use (sad, dejected, afraid, placid and muddled) when compared to controls who did not take ecstasy (confirmed by immunoassays). However, the negative mood scores of the ecstasy using group were not significantly different from those of the

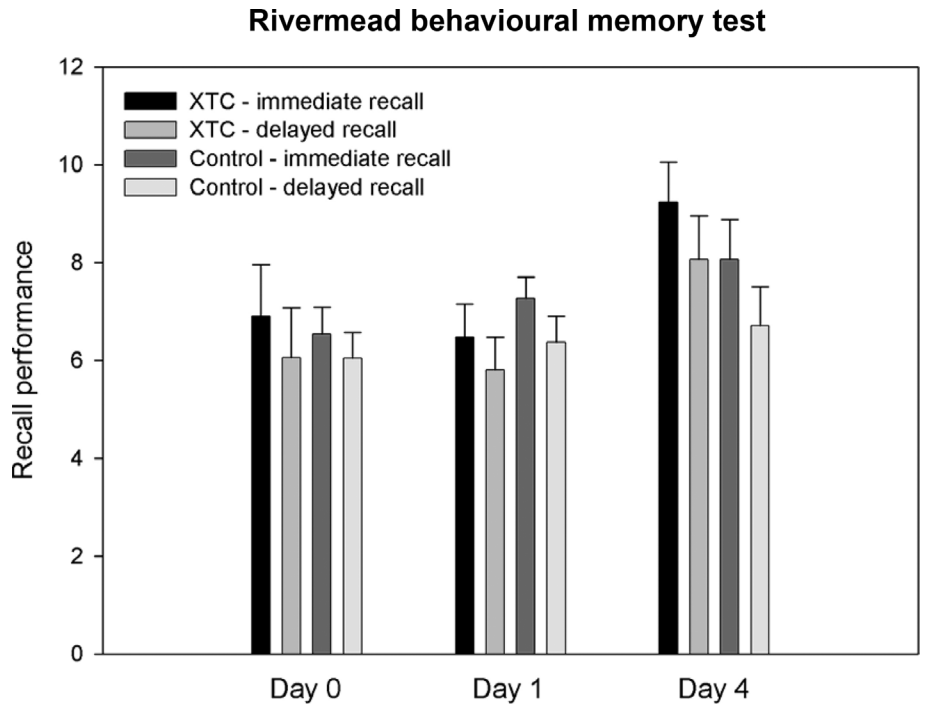

Figure 4 Means (SEM) of immediate and delayed recall performance (RBMT). ANOVA with group as between factor and 3 testing days and time of testing as within factors yielded an effect of day [F (2, 58) = 5.207, $P = 0.008$] and an effect of time of testing [F (1, 29) = 38.637, $P = 0.006$]. There was no interaction between group and day of testing or between group and time of testing.

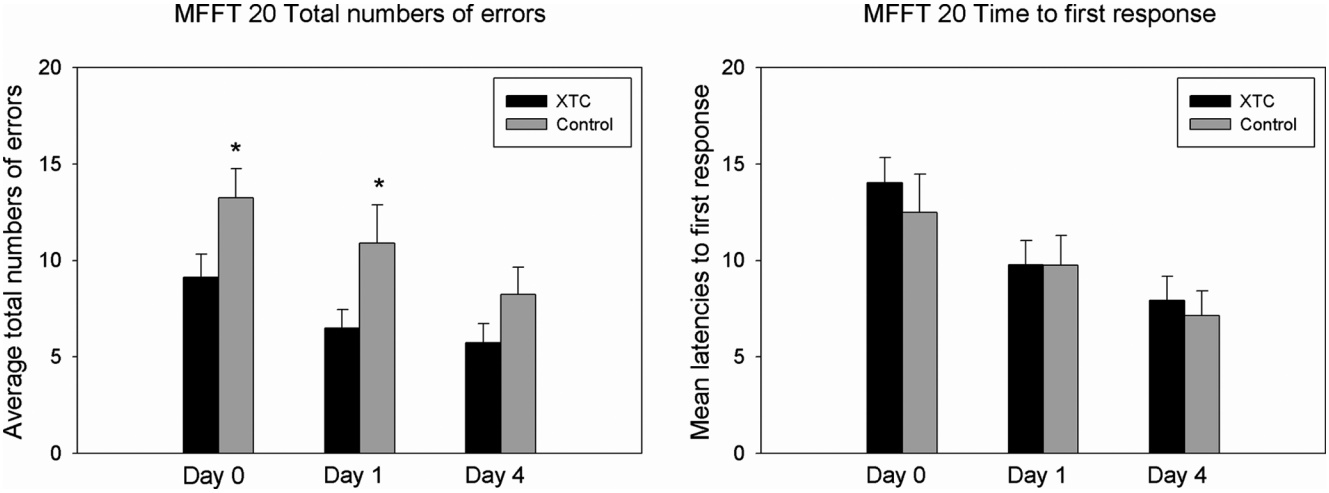

Figure 5 Means (SEM) of MFF20 performance. ANOVA with group as between factor and the 3 assessment days as the within factor yielded a main effect of day [F (2, 60) = 13.285, P = 0.001] on the total numbers of errors committed as well as a main effect of group on this same measure [F (1, 30) = 4.426, P = 0.045] and an effect of day for the mean latencies to first response [F (1.277, 38.305) = 45.822, P = 0.005]. There was no interaction between group and test day on both MFF20 measures.

non-users at follow up assessment 3 days later. Furthermore, no group differences in mood were found with the BDI across the three testing sessions. These findings are not consistent with reports that ecstasy produces markedly depressed mood for a period up to 2 to 4 days after ecstasy consumption (Curran and Travill 1997; Verheyden, *et al.* 2002; Curran, *et al.* 2004). However, Hoshi, *et al.* (2004) did not find a group difference between ecstasy users and controls in BDI scores 4 days after ecstasy consumption. This may be attributable to the BDI itself. Sumnall and Cole (2005) suggested that such self-report scales used may be heavily confounded by the somatic effects of substance misuse. Furthermore, the BDI has been reported to lack test–retest reliability. Beck suggested not re-administering the BDI within a short interval as the scores could be spuriously inflated due to memory factors (Beck 1961) and Groth-Marnat (1990) reported that controversy exists over whether the revised BDI is measuring trait or state variables. Instead, our VAS results are more in line with Parrott and Lasky (1998) who found that 2 days after ecstasy use participants reported feeling more depressed, abnormal and unsociable than at baseline, but returned to pre-use levels by 5 days after consumption. However, these investigators did not statistically control for baseline differences in ecstasy use or other substance use either before or during their study.

Another methodological problem common to earlier studies of the subacute effects of ecstasy is that investigators failed to control for confounding factors such as inter-session drug consumption or sleep deprivation (Curran and Travill 1997; Parrot and Lasky 1998; Verheyden, *et al.* 2002; Curran, *et al.* 2004). The cumulative impact of intense physical effort due to prolonged dancing, poor diet and disrupted sleep due to the stimulant properties of ecstasy may inevitably result in depressed mood. In the present study, ecstasy using participants also reported sleeping less the day after use and feeling significantly more sad, afraid, placid and dejected than controls. We (Huxster, *et al.* 2006) have previously reported that after controlling for co-use of alcohol with ecstasy, and the subacute effects of ecstasy on sleep, the subacute effect on mood remained marginally statistically significant but the subacute effects on cognitive impairment did not. However, in the study, we did not measure hours of sleep deprivation and only asked participants to report how restless their sleep was. In the present study, we also determined how many hours participants slept throughout the study. As is clear from Figure 3, the ecstasy using group reported significant reductions in hours slept the night after use when compared to the ecstasy users who opted not to take the drug and when sleep deprivation was controlled for, the negative mood observed on day 1 became non-significant between the two groups. The lack of group differences in mood 4 days after use, and even the day after use – when hours of sleep deprivation were controlled for – suggests that subsequent ecstasy use, which in regular ecstasy users would typically occur 7 days after baseline assessment, is not related to relief of withdrawal symptoms as suggested by previous investigators (e.g. Topp, *et al.*, 1999; Cottler, *et al.*, 2001).

The present study also showed that, after controlling for sleep quality on day 2 where appropriate, ecstasy consumption had few subacute effects on cognition in a population of regular ecstasy users. Participants who chose to consume ecstasy showed no direct impairment in working memory, immediate and delayed recall or decision-making performance when compared to similar regular ecstasy users who chose not to use ecstasy. The results of the MFF test (MFF20) and the SMST, showed a

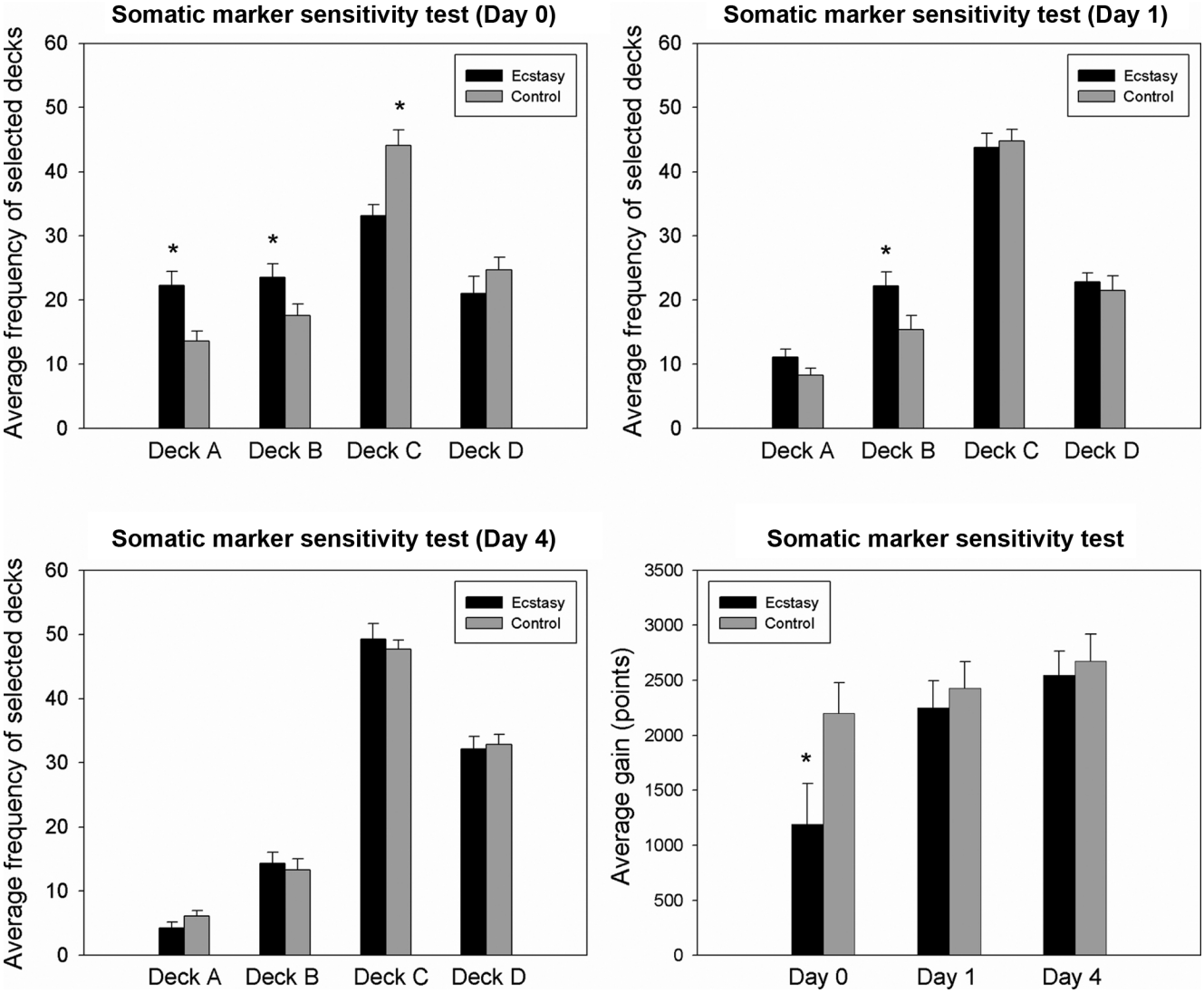

Figure 6 Means (SEM) of SMST performance. Choice of higher reward and high penalty cards from decks A and B were disadvantageous in the long term, while choice of cards from decks C and D were ultimately advantageous. ANOVA of the mean frequency of selected decks with deck and day of testing as within factors and group as a between factor yielded a main effect of deck [F (1.679, 90) = 71.501, P = 0.001], a main effect of testing day [F (3, 60) = 3.374, P = 0.041], an interaction between group and deck [F (3, 90) = 3.086, P = 0.019], an interaction between deck and testing day [F (6, 180) = 143.254, P = 0.001] and an interaction between group, testing day and deck [F (6, 180) = 6.386, P = 0.001]. ANOVA of the average gain with group as between factor and the total number of points gained on each testing session indicated a main effect of day [F (1.175, 60) = 23.809, P = 0.001] and an interaction between group and points gained [F (1.175, 60) = 6.616, P = 0.011]. Asterisks indicate significant differences between the XTC and control groups at P = 0.05.

significant test–re-test effect for both groups. In the MFF20, both groups responded faster and more accurately over each successive testing session. However, subsequent ecstasy users were more accurate on the two first testing sessions than controls. This may be attributable to anticipatory arousal enhancing accuracy at baseline, which would then persist into the second session because the same test materials were used across all three sessions. This is possible because participants who went on to use ecstasy reported elevated arousal at baseline, which may have been associated with their intention to use ecstasy after assessment. Immediate and delayed recall in ecstasy users did not differ from controls. However, again both groups performed better on day 4 than on the two previous testing sessions. The results of the SMST showed that subsequent ecstasy users were

more likely to make poor decisions and were less sensitive to punishment than controls at baseline before ecstasy use. However, both groups preferred safer bets on each successive testing session and by day 4 there were no group differences in performance on the task. These results suggest that ecstasy users can learn new cognitive tasks and compensate for initially impaired baseline performance despite recent ecstasy consumption. Nevertheless, such compromised decision-making prior to taking the drug could contribute to the development of a pattern of abusive use of ecstasy.

The usual dose of ecstasy consumed per session was positively correlated with self-reported subjective ecstasy effects on sadness and anxiety and negatively correlated with happiness and sociability. These correlations might reflect the development of tolerance to the subjective effects of ecstasy. However, no significant correlations were found between the concentrations of MDMA and the number of tablets consumed and the self-reported subjective effects of ecstasy. The concentration of MDMA and the self-reported number of ecstasy tablets consumed was also not correlated. Such relationships are probably highly dependent on the purity of the ecstasy tablets, the time elapsed between ecstasy consumption and immunoassay collection or individuals' specific metabolic systems (de la Torre, *et al.* 2005). The strengths of the current study include the collection of sleep duration data, objective measures of cognitive performance and assays of recent drug use. However, there were some methodological shortcomings. Although both groups did not differ in terms of: age, premorbid IQ, personality and self-reported past drug history, there was a gender imbalance with more males than females in both groups. This may be pertinent because Verheyden, *et al.* (2002) reported that female ecstasy users were more likely to be affected by the residual mood effects of ecstasy than male ecstasy users. Further information on participants' activities between day 0 and day 1 would also have been desirable. Although both groups reported spending the night out "clubbing", we did not collect data about the exact time of consumption of each ecstasy tablet, club ambient temperature, extent of physical activity and dietary intake.

In conclusion, the present findings generally extend and corroborate our previous report (Huxster, *et al.* 2006), which employed the same design and suggest that the subacute effects of ecstasy in regular ecstasy users has an indirect impact on mood, which is partly mediated by its disrupting effects on participants' normal sleep pattern. Furthermore, the present findings also suggest that ecstasy consumption has only modest subacute effects on neuropsychological performance. Previous reports of substantial negative subacute effects of ecstasy in regular users may have therefore been partly attributable to, the perhaps more clinically significant, chronic sequelae of regular ecstasy use. The present evidence of relatively modest and transient negative subacute effects of ecstasy is likely to be relevant to a more accurate characterisation of the abuse liability of this drug. Further research is required to investigate the role of positive outcome expectancies, mood and anticipatory cravings prior to ecstasy use by regular users.

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