Psychopharmacology (2007) 194:371–379
DOI 10.1007/s00213-007-0837-5

ORIGINAL INVESTIGATION

Neurocognitive function in current and ex-users of ecstasy in comparison to both matched polydrug-using controls and drug-naïve controls

Rosa Hoshi · Kate Mullins · Catherine Boundy · Catherine Brignell · Paula Piccini · H. Valerie Curran

Received: 20 February 2007 / Accepted: 21 May 2007 / Published online: 1 July 2007

Abstract
Rationale Despite years of research and much controversy surrounding the effects of ecstasy use, findings are equivocal. Attempting to reduce methodological problems, such as concurrent use of other recreational drugs, could lead to a clearer picture of the effects of ecstasy use on cognitive function.
Objectives The aim of this study is to investigate the effects of both prolonged abstention from ecstasy use and current use on cognitive function while controlling for the regular use of other recreational drugs used by ecstasy users (alcohol, cannabis, cocaine, amphetamines and lysergic acid diethylamide).
Materials and methods A range of cognitive functions (including working memory, episodic memory, verbal learning and executive functions) was assessed in 109 participants: 25 current ecstasy users, 28 ex-ecstasy users (abstinent for at least 1 year), 29 polydrug-using controls (matched to both ecstasy-using groups for the use of other recreational drugs) and 27 drug-naïve controls.
Results There was an overall tendency for impaired verbal learning and memory in both current ecstasy users and polydrug controls. There was also evidence of reduced response inhibition in the current ecstasy users and polydrug controls, which appeared to be related to recency of drug use. However, the majority of tests showed no group differences.
Conclusions The results suggest that recreational drug use in general, rather than ecstasy use per se, can lead to subtle cognitive impairments and that recent drug use appears to impact strongest on cognitive performance. This study highlights the importance of controlling for the use of all recreational drugs and, in particular, recent drug use when investigating 'effects of ecstasy' on cognitive function.

Keywords Ecstasy · MDMA · Cognitive function · Polysubstance use · Recreational drug use

R. Hoshi (✉) · K. Mullins · C. Boundy · H. V. Curran
Clinical Psychopharmacology Unit, Sub-department of Clinical Health Psychology, University College London,
Gower Street,
London WC1E 6BT, UK
e-mail: rosahoshi@googlemail.com

C. Brignell
School of Psychology, University of Southampton,
Southampton, UK

P. Piccini
MRC Clinical Sciences Centre and Division of Neurosciences,
Hammersmith Hospital, Imperial College London,
London, UK

Introduction

±3,4-Methylenedioxymethamphetamine (MDMA) is a ring-substituted amphetamine derivative whose structure is similar to both amphetamine and the hallucinogen mescaline. MDMA is the main psychoactive compound in 'ecstasy' tablets that are used recreationally at dance clubs and raves for their acute effects, which include increased energy, euphoria and, uniquely, empathy. The continued widespread use of ecstasy has become a public health issue due to concerns about possible long-term effects in humans (e.g. EMCDDA 2005).

Preclinical research has consistently found evidence of serotonergic alterations after MDMA administration (see Green et al. 2003, for review). Evidence that 5-hydroxytryptamine (5-HT) may be involved in modulating aspects of cognitive function (e.g. Riedel et al. 1999) has stimulated research into the cognitive effects of MDMA in ecstasy

users. Although a wide range of impairments has been reported across numerous studies, findings remain equivocal. Among the more consistent results appear to be slight impairments on tasks tapping episodic memory and verbal learning (e.g. Bhattachary and Powell 2001; Morgan et al. 2002; Hanson and Luciana 2004), although subtle deficits have less frequently been reported on tests tapping executive functions (e.g. Verkes et al. 2001; Wareing et al. 2004; Fisk et al. 2005). Conflicting findings often reflect methodological problems inherent in the cross-sectional designs used to compare ecstasy users with 'controls', including premorbid differences, polydrug use among ecstasy users and lifestyle differences. Failure to match for the use of other recreational drugs could be particularly important given recent evidence that cannabis contributes to cognitive impairments observed in ecstasy users (e.g. Croft et al. 2001; Dafters et al. 2004). Importantly, however, many of the more recent studies *only* match groups for cannabis use and thus implicitly ignore the potential cognitive influences of the wide range of other recreational drugs [e.g. alcohol, amphetamines, cocaine and lysergic acid diethylamide (LSD)] that ecstasy users take.

Given the long-lasting serotonergic depletion found in monkeys (Hatzidimitriou et al. 1999), several studies have looked at long-term effects of ecstasy use in humans by testing abstinent users. Many of these studies report continuing impairments in ecstasy users after cessation but have minimum abstinence times of less than 1 year, suggesting that evidence of recovery, if it occurs, may not be apparent until after this length of time. In an interesting study, Gouzoulis-Mayfrank et al. (2005) retested 38 participants from a group of 60 ecstasy users originally tested 18 months previously. Of these, 21 reported abstinence or very sporadic use (1–5 ecstasy tablets) between the two test sessions, while the remaining 17 continued use. While they found no evidence of improved cognitive performance in the abstinent participants, they also found no evidence of deterioration in those who continued ecstasy use. However, it is important to note that the control group from the original study were not retested, making comparison difficult. In addition, a sampling bias may have contaminated the results as many of the participants who could not be retested were part of the 'heavy user' group at the original test session.

A recent UK study by Roiser et al. (2007) investigated cognitive function in 30 current and 20 ex-ecstasy users (abstinent for at least 1 year) compared with 30 polydrug controls (well matched for the use of other recreational drugs) and 30 drug-naïve controls. Interestingly, no significant differences were found between the three drug-using groups on performance on a variety of tests assessing working memory and decision-making. Perhaps more surprisingly, very few differences were observed between the drug-using groups and the drug-naïve controls, with only two subtests revealing group differences: ex-users were impaired compared to drug-naïve controls on one subtest assessing spatial ability (copying a pattern); and current users were quicker to perform mental rotations than controls. On the other hand, Yip and Lee (2005) investigated ecstasy users in Hong Kong and found deficits in current users compared to controls on almost all cognitive tests used, although reported ecstasy use was very low in comparison to the majority of other studies (a total of 16–60 tablets taken over 2–3 months), and almost no use of other recreational drugs was reported by participants. These results demonstrate the equivocal nature of the findings relating to cognitive performance in ecstasy users.

The present study was designed to investigate a broad range of cognitive functions in current ecstasy users and in ex-users abstinent for at least 1 year. A particular aim was to eliminate confounding variables in cross-sectional designs by recruiting a polydrug control group that was matched to both the ecstasy-using groups in use of all other recreational drugs. In addition, a drug-naïve control group matched with all other groups in terms of age, premorbid IQ, level of education, employment status and self-rated depression and anxiety was also assessed.

Materials and methods

Design and participants

Volunteers were screened and recruited into four groups to be compared in an independent group design: 25 current ecstasy users who take the drug at least once a month and have taken it on at least 25 occasions; 28 ex-ecstasy users who used to take the drug on a regular basis (on at least 25 occasions) but who had not taken it for at least 1 year; 29 polydrug users who had used a range of other recreational drugs (including cannabis, cocaine and amphetamines) but who had never taken ecstasy; and 27 drug-naïve controls who had no history of recreational drug use (apart from alcohol).

Participants were recruited through magazine advertisement and word of mouth. All gave written, informed consent. The study was approved by the institutional ethics committee. Inclusion criteria for all groups were that the participants were aged 25–50, not taking prescribed psychotropic medication or receiving psychological treatment, no current or history of drug addiction, not being depressed on the Structured Clinical Interview for DSM-IV (SCID), have a score of <18 on the Beck Depression Inventory (BDI; Beck 1978), have a score of <55 on the Spielberger Trait Anxiety Scale (STAI; Speilberger et al.

1970), no serious head injury in the past, not having drank more than three units of alcohol in the 24 h before testing and no use of recreational drugs for at least 3 days before testing. In addition, because of a linked Positron Emission Tomography (PET) study, all participants were male.

Procedure

The test session took approximately 1.5 h to complete. Most participants in three of the four groups (ex-users, polydrug and drug-naïve) were also scanned in a separate session for a PET study and provided hair samples for drug analysis (to be reported elsewhere). To assess recent drug use, all participants gave a urine sample before testing.

Cognitive assessments

Immediate and delayed prose recall A taped passage of prose was played (Rivermead Behavioural Memory Tests; Wilson et al. 1985), which participants were required to recall immediately after presentation and 30 min later.

The Buschke Selective Reminding task The Buschke Selective Reminding task (BSRT) was used to provide indices of verbal learning and forgetting over trials (Buschke and Fuld 1974). A list of 16 words was read aloud at a rate of 1/s, and the participant was required to repeat the list back to the experimenter. After being reminded only of the words they failed to recall, they attempted to recall the entire list again. This continued for three trials. After a 30-min delay, the participant is asked to recall the list again.

Go/No-go task This task tapped response inhibition. The task consisted of two blocks: a practice block of 30 stimuli and one block of 100 stimuli. Stimuli were eight characters of the alphabet. For the practice block, participants were instructed to respond, by pressing a designated key on the computer keyboard as quickly as possible, to each letter on the screen. Each letter appeared for 500 ms followed by an interstimulus interval (ISI) of 500 ms. In the main test block participants were instructed to respond by the same designated key press to all but two of the eight letters. These two letters constituted the 'No-go' trials. The proportion of 'Go' stimuli was 75% and of 'No-go' stimuli was 25%. Scores were recorded in terms of hits, false alarms (response inhibition errors) and reaction times.

Rapid visual information processing Rapid visual information processing (RVIP) was used to evaluate sustained attention and working memory (Wesnes and Warburton 1983). Single digits were presented on a computer screen at a rate of 100 digits per minute for 10 min. Participants were required to respond alternatively minute by minute to either three consecutive even numbers or three consecutive odd numbers. Eight target strings were presented per minute.

The Serial Sevens task This was used to tap working memory. A four-digit number was given to the participant, who was asked to subtract 7 from this number and continue to count backwards in sevens for 90 s. Number of correct subtractions and errors were recorded.

Semantic and phonemic verbal fluency Participants generated as many words as they could in 60 s beginning with the same letter (phonetic) or from the same category (semantic).

The Trail Making Test The Trail Making Test (TMT), a measure of scanning, visuomotor tracking, divided attention and cognitive flexibility was administered in the standard format (Reitan 1959). The time to complete trial A is subtracted from the time of trial B to remove the motor speed element and give a measure related to executive function.

CANTAB spatial working memory The CANTAB spatial working memory (SWM) is an assessment of the ability to retain and manipulate spatial information, a computer task administered in the standard way (Owen et al. 1990).

CANTAB Stockings of Cambridge The CANTAB Stockings of Cambridge (SOC) is a measure of planning and executive function, a computer task administered in the standard way (Owen et al. 1995).

Gibson's spiral maze This is a test of psychomotor performance requiring hand–eye coordination (Gibson 1977). Participants are told to draw round a maze on a piece of paper as quickly as possible without touching the sides. Time taken to complete the maze and errors (number of times the sides were touched) were recorded.

Mood assessments

Impulsivity was assessed using the Barratt Impulsiveness Scale (BS; Barratt and Patton 1983), and aggression was indexed using the Aggression Questionnaire (AQ; Buss and Perry 1992). At the end of the session, participants were given a short refreshment break and then completed an aggressive interpretative bias task (Hoshi et al. in press).

A semistructured interview was used to record participants' drug and alcohol use, and level of education and employment status was noted.

Statistical analysis

Statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) version 11. The majority of group differences were tested for significance with one-way analyses of variance (ANOVA). The prose recall task was analysed using repeated measure ANOVA with group as the between-subjects variable and time (immediate or delayed) as the within-subjects variable. Learning across trials in the Buschke Selective Reminding task was also analysed using a repeated measures ANOVA with group as the between-subjects variable and trial (1–3) as the within-subjects variable. Where data violated the assumptions of normality, Kruskal–Wallis tests were used. Post hoc comparisons were Bonferroni corrected, or in the case of variables compared using Kruskal–Wallis tests, individual Mann–Whitney *U* comparisons were carried out (α level Bonferroni corrected for multiple comparisons). Due to group differences in total BS score and the time since cannabis, cocaine and amphetamines had been used, these variables were included as covariates, and any significant changes this produced in results are reported. Chi-squared tests were used to compare level of education and employment status, as well as the number of people reporting having ever tried and those currently regularly using recreational drugs.

Results

Demographics

There were no significant differences between the groups in age, premorbid IQ (Spot the Word), self-rated aggression (AQ), depression (BDI) or anxiety (STAI; Table 1). A significant group difference was observed on self-rated impulsivity (BS total score) [$F_{(3,108)}=3.71$, $p=0.014$). Post hoc tests revealed that the current users rated themselves as more impulsive than drug-naïve controls ($p=0.007$). All groups had reached a similar level of education and had a similar distribution across types of employment status.

Drug and alcohol use

No differences were observed between the groups in terms of the time since alcohol was last used, years of regular use and lifetime occasions of use (Table 2). However, groups differed on age of first use [$F_{(3,107)}=5.61$, $p=0.001$] with current users ($p=0.001$) and polydrug controls ($p=0.023$) starting to drink at a younger age than controls, while there was a trend toward ex-users starting drinking younger than controls ($p=0.06$). Units of alcohol consumed in a typical session also differed across groups [$F_{(3,107)}=8.94$, $p<0.001$], with current users ($p<0.001$) and polydrug controls ($p<0.001$) drinking more units than control participants. Due to the significant group differences in units consumed in a typical session and age of first use of alcohol, these variables were entered as covariates but this did not significantly affect any of the results and thus are not reported.

Table 2 shows group data for use of cannabis, cocaine, amphetamine and LSD. As the majority of ex-users had stopped regularly using recreational drugs, the figures reflect patterns of use when taking the drug regularly. The only significant group difference apparent within the measures of cannabis use was length of time since last use ($\chi^2=8.66$, $p=0.003$) whereby current users had smoked cannabis more recently than both ex-users ($U=118.50$, $p=0.002$) and polydrug controls ($U=210.00$, $p=0.002$). Current regular (≥1 day per month) cannabis use was reported by 56% current users, 26% ex-users and 43% polydrug controls, while current regular use of cocaine was reported by 64% current users, 8% ex-users and 32% polydrug controls. Time since the last reported use of cocaine ($\chi^2=16.83$, $p=0.001$) and LSD ($\chi^2=21.48$, $p=0.001$) showed group differences. Current users had used cocaine more recently than ex-users ($U=118.50$, $p=0.001$) and LSD more recently than both ex-users ($U=76.00$, $p=0.001$) and polydrug controls ($U=38.00$, $p=0.001$). Participants were excluded if their urine sample tested positive for any drug apart from cannabis, and the following percentages of participants in each group tested positive for cannabis: ex-users, 18%; current users, 64%; polydrug users, 18%; and controls, 0%.

Several differences were observed between the ex-users and the current users in terms of patterns of ecstasy use (Table 3). As would be expected, the length of time since participants had used ecstasy was significantly longer in the ex-user group ($U=0.00$, $p<0.001$). In addition, ex-users had used ecstasy regularly for significantly fewer years than

Table 1 Mean (SD) for age, premorbid IQ (Spot the Word), depression (BDI), anxiety (STAI), aggression (AQ) and impulsivity (BS)

	Ex-users	Current users	Polydrug	Controls
Age (years)	29.50 (4.69)	28.64 (4.59)	31.93 (8.41)	32.04 (7.59)
Spot the Word	51.29 (3.73)	49.40 (4.26)	50.14 (4.36)	51.11 (3.53)
BDI	7.57 (5.49)	5.16 (3.40)	6.03 (4.17)	4.96 (5.47)
STAI	37.75 (9.67)	35.52 (7.55)	35.76 (6.93)	33.94 (8.44)
AQ	69.29 (17.17)	64.60 (15.48)	69.79 (15.20)	63.04 (18.03)
BS	53.64 (16.02)	60.80 (13.58)[a]	54.34 (14.75)	47.04 (15.44)

[a] Significantly higher than controls

Table 2 Mean (SD) for alcohol, cannabis, amphetamine and cocaine use

	Ex-users (EE)	Current users (CE)	Polydrug (PC)	Drug-naïve controls (C)	Significant comparisons
Alcohol					
Time since last use (days)	4.22 (4.81)	2.12 (1.56)	3.59 (2.91)	6.36 (14.69)	
Age of first use	14.66 (2.59)	13.76 (2.83)	14.47 (1.94)	16.33 (1.86)	CE > C PC > C
Years of regular use	10.91 (4.94)	9.34 (4.81)	14.43 (9.09)	12.38 (8.48)	
Number of days used in a typical month	10.43 (7.53)	13.28 (7.82)	10.88 (6.17)	7.90 (5.91)	
Amount used in a typical session (units)	6.98 (3.26)	8.84 (4.74)	9.29 (3.56)	4.44 (5.60)	CE > C PC > C
Cannabis					
Time since last use (days)	433.56 (719.57)	49.28 (147.08)	309.55 (517.95)		
Age of first use	16.65 (1.92)	16.12 (2.86)	16.04 (2.62)		
Years of regular use	8.34 (4.72)	9.93 (6.35)	10.37 (9.13)		
Number of days used in a typical month	16.70 (11.72)	16.35 (11.37)	17.73 (11.47)		
Amount used per month (oz.)	1.45 (1.72)	1.06 (1.16)	1.63 (1.884)		
Cocaine					
Time since last use (days)	777.90 (859.31)	27.52 (47.71)	560.08 (917.62)		EE > CE
Age of first use	21.66 (2.41)	20.84 (3.35)	22.52 (5.66)		
Years of regular use	3.46 (1.78)	4.01 (3.28)	4.64 (3.48)		
Number of days used in a typical month	6.92 (8.90)	3.48 (3.31)	5.03 (7.11)		
Amount used in a typical session (g)	1.74 (1.86)	0.58 (0.38)	0.91 (0.70)		
Amphetamine					
Time since last use (days)	2,445.62 (1,870.72)	842.08 (1,241.20)	2,142.20 (2,605.81)		
Age of first use	18.93 (2.17)	18.33 (3.82)	18.54 (3.61)		
Years of regular use	2.93 (2.30)	4.33 (5.90)	4.18 (5.63)		
Number of days used in a typical month	4.04 (5.43)	3.50 (2.37)	6.85 (7.18)		
Amount used in a typical session (g)	1.25 (1.00)	0.72 (0.43)	0.84 (0.49)		
LSD					
Time since last use (days)	1,754.05 (1,346.61)	522.09 (778.04)	2,802.68 (2,311.13)		EE > CE PC > CE
Age of first use	18.60 (3.15)	18.13 (3.72)	19.42 (4.24)		
Years of regular use	2.85 (1.65)	5.25 (4.17)	2.94 (1.67)		
Number of days used in a typical month	4.25 (3.58)	1.50 (0.58)	3.93 (4.03)		
Amount used in a typical session (trips)	1.70 (0.89)	1.60 (0.65)	1.00 (0.46)		

Table 3 Mean (SD) of ecstasy use

	Ex-users	Current users
Time since last use (days)	1,017.21 (789.26)	14.20 (9.50)*
Age of first use	19.39 (2.96)	18.20 (3.23)
Years of regular use	4.17 (2.73)	7.28 (4.70)*
Number of days used in a typical month	5.30 (3.17)	2.92 (2.16)*
Amount used in a typical session (tablets)	2.53 (1.44)	3.86 (2.39)*
Lifetime occasions	264.86 (233.98)	288.00 (420.88)
Highest number of tablets in one session	5.41 (3.84)	10.54 (8.39)*

*$p<0.01$

current users (U=208.00, p=0.001) and took fewer tablets on average per session (U=208.500, p=0.001). However, ex-users reported using ecstasy more frequently than current users (U=173.00, p=0.002). There was a significant difference in the highest number of ecstasy tablets participants reported using in one session (U=172.00, p=0.002), whereby current users reported higher numbers of tablets than ex-users.

Cognitive tests

Data for two participants (one ex-user and one control) on the RVIP, Go/No-Go, and SWM were lost, as well as the data for the SOC for these two participants and one current user, all due to computer failure.

Buschke selective reminding task A significant group difference was apparent on trial 1 of the task [$F_{(3,108)}$=6.56, $p<0.001$]. Post hoc tests indicated that both current users (p=0.004) and polydrug users (p=0.001) recalled fewer words than controls (Fig. 1a). A significant group difference was also found on the delayed trial (χ^3=11.03, p=0.002). Post hoc tests revealed that current users recalled fewer words than controls (U=162.50, p=0.001) and that both ex-users (U=264.00, p=0.053) and poly drug users (U=286.50, p=0.08) showed a trend toward recalling fewer words than controls (Fig. 1b). In addition, significant main effects of trial [$F_{(2,210)}$=221.07, $p<0.001$] and group [$F_{(1,105)}$=7.41, $p<0.001$] were found on learning across the first three trials of the task (Fig. 1c). Current users (p=0.001) and polydrug users (p=0.002) recalled fewer words at each trial than controls, while there was a trend toward ex-users remembering less than controls (p=0.056). There was no group × trial interaction.

Stockings of Cambridge A significant group difference was found in mean initial thinking time [$F_{(3,105)}$=3.41, p=0.02] with ex-users taking longer than current users (p=0.034; Fig. 2). After co-varying for self-rated impulsivity (BS total), there was no longer a significant group difference. There were no group differences in subsequent thinking time or in number of problems solved in the minimum moves.

Go/No-go A significant group difference was found in the total number of hits (χ^3=26.37, $p<0.001$). Post hoc tests revealed that the current users had fewer hits than both ex-users (U=97.51, $p<0.001$) and controls (U=172.00, p=0.004) and that the polydrug users also had fewer hits than the ex-users (U=154.50, $p<0.001$) and the controls (U=231.00, p=0.013; Fig. 3a). A group difference in reaction time to hits (χ^3=9.38, p=0.025) reflected current users having faster reaction times for hits than both ex-users (U=

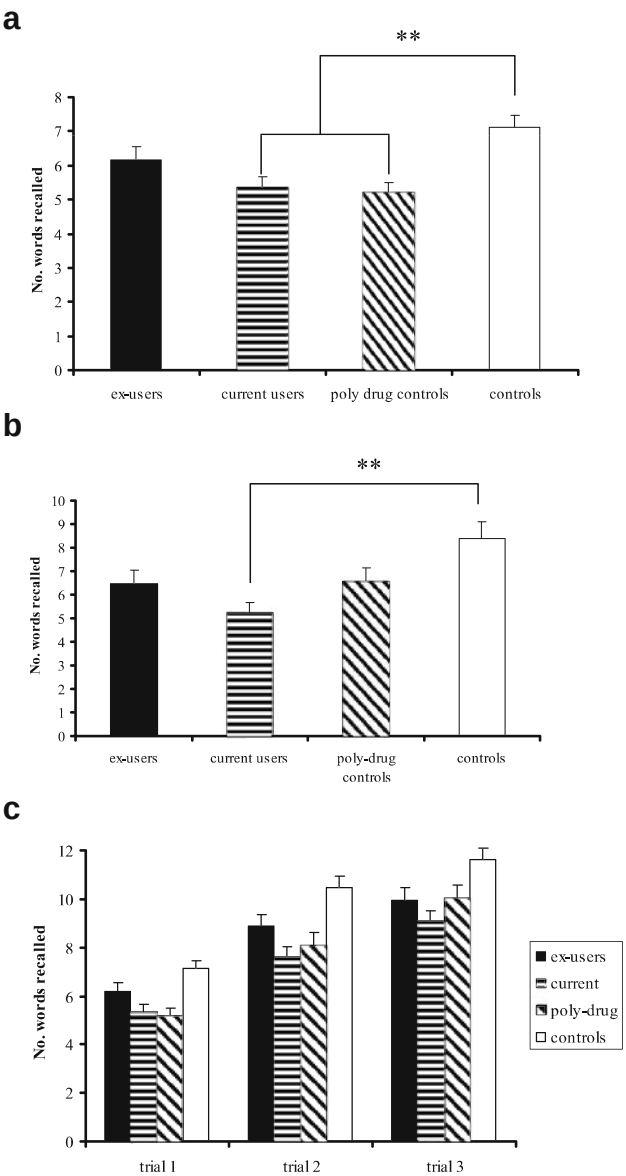

Fig. 1 Mean (SE) number of words recalled on BSRT **a** trial 1 **b** delayed trial **c** trials 1–3

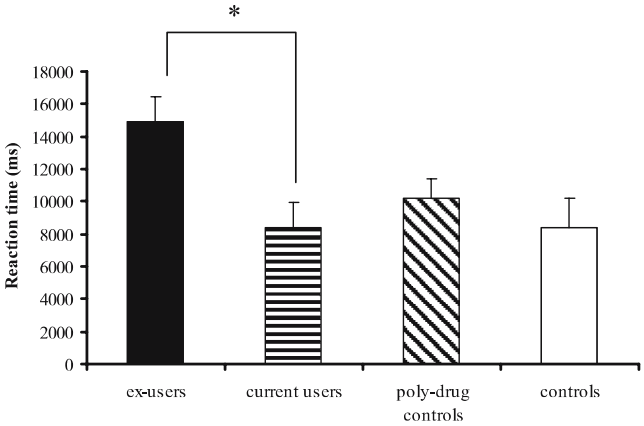

Fig. 2 Mean (SE) initial thinking time for the SOC task

222.00, p=0.034) and controls (U=184.00, p=0.008). Polydrug users had faster reaction times than controls (U=258.00, p=0.045) and tended to respond faster than ex-users (U=283.00, p=0.075; Fig. 3b). False alarms showed group differences [$F_{(3,106)}$=4.71, p=0.004] whereby polydrug users had more false alarms than both ex-users (p=0.017) and controls (p=0.008; Fig. 3c).

Other tasks

No significant group differences were found in immediate or delayed prose recall, RVIP, Serial Sevens, verbal fluency, SWM or the TMT.

As Roiser et al. (2007) found that self-reported impulsivity correlated with cognitive function in ecstasy users but not controls, BS scores were correlated with performance on BSRT, SOC and Go/No-go tasks. No significant correlations were found.

Discussion

This study showed a general tendency towards impaired learning and recall on the BSRT in all three drug-using groups and some evidence of impaired response inhibition on the Go/No-go task in current ecstasy users and polydrug users. In addition, ex-users had a longer initial thinking time on the SOC task than current users, indicating that they took longer to consider problems before starting to solve them. No group differences were observed on prose recall, RVIP, SWM, Serial Sevens, verbal fluency, TMT or Gibson's spiral maze.

Both current users and polydrug controls had a reduced hit rate on the Go/No-go task, while polydrug users also had significantly more commission of errors than ex-users and drug-naïve controls. Impaired performance on the Go/No-go task is thought to reflect deficits in response inhibition. Although poor response inhibition is often associated with drug use, this deficit appears only in two of the three drug-using groups. However, this discrepancy may be related to the patterns of *current* drug use that distinguish the groups. A higher proportion of current ecstasy users and polydrug users report current regular use of both cannabis and cocaine than ex-users. The fact that the majority of ex-users no longer take illicit drugs may have led to a reduction in impulsive behaviours.

The evidence of impaired learning and recall in the three drug-using groups is in accordance with the findings of other studies that both ecstasy users and polydrug controls have memory impairments compared to drug-naïve controls (e.g. Croft et al. 2001). This finding appears to implicate recreational drug use in general, rather than ecstasy use per se, in memory impairment. This is perhaps not surprising given the evidence that cannabis use has been found to lead

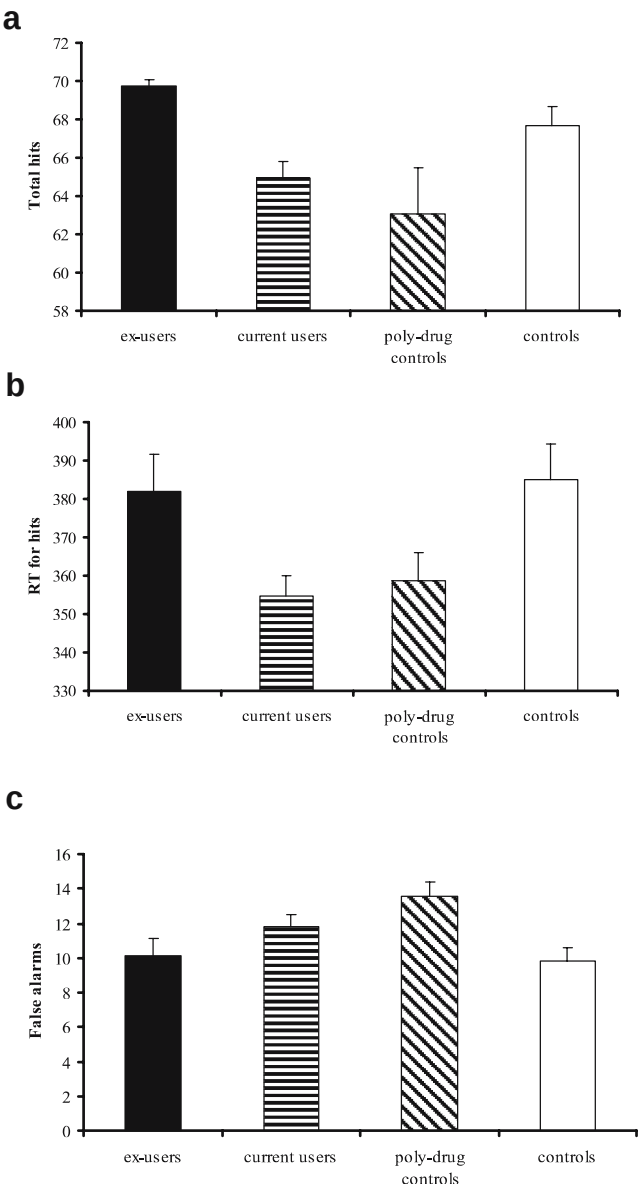

Fig. 3 Mean (SE) **a** number of hits **b** reaction time to hits **c** number of false alarms on the Go/No-go task

to memory impairments (see Lundqvist 2005, for review) and deficits have been observed for up to 28 days after abstinence (Solowij et al. 2002). As a much higher percentage of current users tested positive for cannabis in their urine, it is possible that the more significant cognitive deficits observed in the current users was due to residual effects of cannabis use. However, the drug-using groups in this study, unlike many previous studies, used other stimulants, and little is known about the effects of these on cognitive function. This highlights the crucial importance of matching groups for the use of *all* other recreational drugs, not just cannabis. The failure to do this may have led to many studies linking ecstasy use with cognitive deficits, whilst ignoring the use of other stimulants. Interestingly, in the present study, compared with controls, current users and the polydrug users had a significantly shorter memory span, while ex-users did not differ. Although this could be an indication of recovery in the ex-users, it is not possible to interpret this as recovery from impairments caused by ecstasy use because deficits were present in drug users who have never taken ecstasy. Rather, as current ecstasy users and polydrug controls report more *current* drug use than the ex-ecstasy users, it may indicate recovery from deficits caused by drug use in general.

The ex-user group took longer than current users to think about problems on the SOC task before starting to solve them. This could reflect the ex-users needing longer to work out the solution than current users, an interpretation that would fit with previous research finding cognitive deficits in ex-users (Curran and Verheyden 2003; Thomasius et al. 2003). However, after co-varying self-rated impulsivity scores, the group difference was no longer significant. Current users had somewhat higher BS scores than ex-users, so an alternative explanation may be that the current users are more impulsive than the ex-users and begin to solve the problem quicker. Although impulsivity has often previously been linked to ecstasy use, this result suggests that impulsivity is a trait associated with drug use in general.

In light of the large body of research reporting cognitive impairments in both previous and current ecstasy users, it may seem surprising that very few group differences were observed in the present study. However, recent studies that have attempted to minimise confounding variables have also found little evidence of group differences. As discussed above, Roiser et al. (2007) administered a battery of cognitive tests to four groups similar to those in the present study and found only two significant group differences, and the difference between current users and controls was no longer apparent after controlling for alcohol use. Essentially, the findings of the current study support the results of Roiser et al. (2007) in providing little evidence of cognitive impairment caused by ecstasy use per se. Overall, the results of research into cognitive effects of ecstasy use are inconsistent, and the present results appear to be in line with the majority that find no evidence of deficits in executive functions and working memory. In addition, the issue of publication bias must be taken into consideration. Dafters et al. (2004), who also found no evidence of cognitive impairment in ecstasy users, comment that it is likely that "failure to find evidence of MDMA's detrimental effects on cognition is under-reported due to the reluctance of scientific journals to publish nonsignificant results".

This study highlights the importance of matching groups for the use of *all* other recreational drugs, as well as other factors such as premorbid IQ and mood, when attempting to explore the effects of ecstasy use. It is extremely difficult, and thus time consuming, to recruit participants who use similar levels of cannabis, amphetamines and cocaine as ecstasy users but who have never taken ecstasy. This is reflected not only in the failure of other studies to match adequately but also the lack of research investigating the cognitive effects of *recreational* cocaine and amphetamine use: studies to date on these stimulants concentrate virtually exclusively on chronic addiction and withdrawal. This lack of information about the cognitive effects of other stimulant drugs and the established link between cannabis and memory impairments have lead to researchers citing cannabis as the most important drug to match for when investigating cognitive function in ecstasy users. The present study highlights the need to match for amphetamine and cocaine use. Not only are the drug-using groups in this study exceptionally well matched in terms of the use of all recreational drugs, but in addition, urine samples were taken to verify recent drug use.

It is, of course, difficult to control for confounding factors that are inherent in cross-sectional designs, such as premorbid differences in cognitive function. Further, our conclusions relate to *male* ecstasy users only. While a recent review found that there appeared to be gender differences in the acute and sub-acute effects of MDMA, there is no clear evidence of gender difference in cognitive function after regular ecstasy use (Allott and Redman 2007).

Researchers consistently suggest that cognitive deficits found in ecstasy users could be caused by the effects of MDMA consumption on 5-HT. However, the fact that the majority of preclinical studies find changes in serotonergic function in the absence of any functional changes indicates a far more complex relationship than the MDMA-induced neurotoxicity argument proposed by much of the research. Some fascinating new research found that polymorphisms of the 5-HT transporter gene was associated with cognitive performance in both the ecstasy users and controls tested, while patterns of decision making were altered only in one genetic subgroup of ecstasy users (Roiser et al. 2006). It is possible that these genetic variations may be associated with individual differences in vulnerability to MDMA-

induced changes in the serotonergic system and thus to changes in cognitive function. Although further research is required to investigate this possibility, it could reveal an intriguing explanation, in part at least, for the conflicting results in the ecstasy literature.

In conclusion, the present study provides evidence to suggest that recreational drug use, in particular *recent* drug use, may lead to subtle memory impairments, regardless of whether ecstasy has been used or not.

Acknowledgments RH was supported by a Medical Research Council (UK) studentship.

References

Allott K, Redman J (2007) Are there sex differences associated with the effects if ecstasy/3,4-methylenedioxymethamphetamine (MDMA)? Neurosci Biobehav Rev 31:327–347

Barratt E, Patton JH (1983) Impulsivity: cognitive, behavioural and psychophysiological correlates. In: Zuckerman M (ed) Biological basis of sensation feeling, impulsivity and anxiety. Erlbaum, Hillsdale, NJ

Beck AT (1978) The Beck Depression Inventory (BDI). The Psychological Corporation. Harcourt Brace Jovanovitz, Orlando, FL, USA

Bhattachary S, Powell JH (2001) Recreational use of 3,4-methylenedioxymethamphetamine (MDMA) or 'ecstasy': evidence for cognitive impairment. Psychol Med 31:647–658

Buschke H, Fuld PA (1974) Evaluating storage, retention and retrieval in disordered memory and learning. Neurology 11:1019–1025

Buss A, Perry M (1992) The aggression questionnaire. J Pers Soc Psychol 63:452–459

Croft R, Mackay A, Mills A, Gruzelier G (2001) The relative contributions of ecstasy and cannabis to cognitive impairment. Psychopharmacology 153:373–379

Curran H, Verheyden S (2003) Altered response to tryptophan supplementation after long-term abstention from MDMA (ecstasy) is highly correlated with human memory function. Psychopharmacology 169:91–103

Dafters R, Hoshi R, Talbot AC (2004) Contribution of cannabis and MDMA ("ecstasy") to cognitive changes in long-term poly-drug users. Psychopharmacology 173:405–410

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2005) News release no. 9: cocaine, amphetamines, ecstasy and cannabis: latest trends. Novermber 24, Lisbon

Fisk J, Montgomery C, Wareing M, Murphy PN (2005) Reasoning deficits in ecstasy (MDMA) polydrug users. Psychopharmacology 181:550–559

Gibson H (1977) Manual of the Gibson Spiral Maze, 2nd edn. Hodder, London, UK

Gouzoulis-Mayfrank E, Fischermann T, Rezk M, Thimm B, Henson G, Daumann J (2005) Memory performance in polyvalent MDMA (ecstasy) users who continue or discontinue MDMA use. Drug Alcohol Depend 78:317–323

Green A, Mechan AO, Elliot JM, O'Shea E, Colado IM (2003) The pharmacology and clinical pharmacology of 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy'). Pharmacol Rev 55:463–508

Hanson K, Luciana M (2004) Neurocognitive function in users of MDMA: the importance of clinically significant patterns of use. Psychol Med 34:229–246

Hatzidimitriou G, McCann U, Ricaurte G (1999) Altered serotonin innervation patterns in the forebrain of monkeys treated with 3,4-methylenedioxymethamphetamine seven years previously: factors influencing abnormal recovery. J Neurosci 19:5096–5107

Lundqvist T (2005) Cognitive consequences of cannabis use: comparison with abuse of stimulants and heroin with regard to attention, memory and executive functions. Pharmacol Biochem Behav 81:319–330

Morgan M, McFie L, Fleetwood L, Robinson J (2002) Ecstasy (MDMA): are the psychological problems associated with its use reversed by prolonged abstinence? Psychopharmacology 159:294–303

Owen A, Downes JJ, Sahakian BJ, Polkey CE, Robbins TW (1990) Planning and spatial working memory following frontal lobe lesions in man. Neuropsychologia 28:1021–1034

Owen A, Sahakian BJ, Semple J, Polkey CE, Robbins TW (1995) Visuo-spatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. Neuropsychologia 33:1–24

Reitan RM (1959) A manual for the administration and scoring of the Trail Making Test. Indiana University Press, Indianapolis, USA

Riedel W, Klaassen T, Deutz NEP, van Someren A, van Praag HM (1999) Tryptophan depletion in normal volunteers produces selective impairment in memory consolidation. Psychopharmacology 141:362–369

Roiser JP, Rogers RD, Cook LJ, Sahakian BJ (2006) The effect of polymorphism at the serotonin transporter gene on decision-making, memory and executive function in ecstasy users and controls. Psychopharmacology 118:213–227

Roiser J, Rogers RD, Sahakian BJ (2007) Neuropsychological function in ecstasy users: a study controlling for polydrug use. Psychopharmacology 189:505–516

Solowij N, Stephens RS, Roffman RA, Babor T, Kadden R, Miller M, Christiansen K, McRee B, Vendetti J (2002) Cognitive functioning of long-term heavy cannabis users seeking treatment. J Am Med Assoc 287:1123–1131

Speilberger C, Garsuch R, Lushene R (1970) Manual for the state-trait anxiety inventory. Consulting Psychologists Press, Palo Alto, California

Thomasius R, Petersen K, Buchert R, Andresen B, Zapletalova P, Wartberg L, Nebeling B, Schmoldt A (2003) Mood, cognition and serotonin transporter availability in current and former ecstasy users. Psychopharmacology 167:85–96

Verkes R, Gijsman H, Pieters M, Schoemaker R, de Visser S, Kuijpers M, Pennings E, de Bruin D, Van de Wijngaart G, Van Gerven J, Cohen A (2001) Cognitive performance and serotonergic function in users of ecstasy. Psychopharmacology 153:196–202

Wareing M, Murphy PN, Fisk JE (2004) Visuospatial memory impairments in users of MDMA ('ecstasy'). Psychopharmacology 173:391–397

Wesnes K, Warburton DM (1983) Effects of smoking on rapid visual information processing performance. Neuropsychobiology 9:229–233

Wilson, B, Cockburn J, Baddeley A (1985) The Rivermead Behavioural Memory test. Thames Valley Text, Reading, UK

Yip J, Lee TMC (2005) Effects of ecstasy use on neuropsychological function: a study in Hong Kong. Psychopharmacology 179:620–628