The Nature of Ecstasy-Group Related Deficits in Associative Learning.

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Running head: Impaired learning in ecstasy-polydrug users.

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Abstract

Rationale/Objectives: Research has revealed associative learning deficits among users of ecstasy; the present study explored the component processes underlying these deficits. *Methods:* 35 ecstasy users and 62 non-ecstasy users completed a computer-based, verbal paired-associates learning task. Participants attempted to learn eight sequentially presented word pairs. After all eight had been presented, the first member of each pair was displayed and participants attempted to recall the second. Eight trials were administered. Correct responses on each trial, forgetting at various levels of learning, perseveration errors and the rate at which the associations were learned (trials to completion) were all recorded. *Results:* MANOVA revealed that ecstasy users performed worse overall and subsequent ANOVAs showed that users performed significantly worse on virtually all measures. Regression analysis revealed that over half of the ecstasy-group related variance in trials to completion was attributable to group differences in initial learning and forgetting. In relation to forgetting, it appears that cannabis use may be an important determinant. In relation to rate of learning (trials to completion) and initial learning, both ecstasy and cannabis may be implicated. *Conclusions:* There appears to be abundant evidence of associative learning deficits among ecstasy users. However, it appears that a range of illicit drugs including cannabis and ecstasy may contribute to these deficits.

Keywords: ecstasy, MDMA, learning, paired associate learning, cannabis.

Introduction.

Developing an understanding of relationships between concepts is a fundamental aspect of human learning. One key aspect of this is associative learning, which involves forming appropriate links between previously unrelated phenomena. The working memory system in general, and the executive in particular are essential components in learning new skills before they become automatic, so that learning and the acquisition of knowledge is dependent on working memory (Tanji & Hoshi, 2001). The term associative learning describes the process by which an organism develops or reinforces connections between stimulus representations (Rose et al, 2001). Ecstasy users have been shown to exhibit deficits in aspects of working memory functioning (e.g., Fisk et al, 2004; Wareing, et al, 2004) and in view of the role of working memory and executive processes in supporting associative learning it is possible that users might also experience impairments in learning processes.

Much of the research in this domain has focussed on animal learning and to date the results have been equivocal. While some studies have found MDMA-related deficits in aspects of learning (Broening et al, 2001; Frederick et al, 1995; Taylor & Jentsch, 2001; Williams et al, 2003) others have not (Frederick & Paule 1997; Ricaurte et al, 1993; Romano & Harvey 1994; Winsaeur et al, 2002). In a study examining learning in rats, Robinson et al (1993) found that the extent of 5HT denervation (72.6%) was not sufficient to produce marked deficits (this may be a sign of neurocompensatory changes). More generally, it is possible that the apparent lack of MDMA-related deficits in some animal studies is because the tasks are too simple, and they do not mirror learning in humans.

Although some studies in humans have investigated associative learning, this is an area that is still under investigated as a number of tasks used relate more to

immediate and delayed recall, rather than the learning of associations. Gouzoulis-Mayfrank et al (2003) used the word-pair learning test of the LGT-3 test battery, which requires participants to memorise 20 word pairs consisting of a Turkish word and it's German translation. In the retrieval phase, participants had to identify the correct Turkish word corresponding to each German word (out of 5 possible answers). Heavy ecstasy users performed worse than non-users in the delayed recall of the word pairs, but not the immediate recall component. However, the effect was reduced to below statistical significance after control for general knowledge scores.

Croft et al (2001) studied the relative contributions of ecstasy and cannabis to spatial and non-spatial Paired Associates Learning (PAL). Participants were required to learn associations between six spatial pairs (spatial) and six colour pairs (non-spatial). The task began with the participant guessing, then learning the prompted association through feedback from the experimenter (yes/no). The task finished when the participant correctly reported 18 consecutive associations, and the number of guesses required to get to this point was the score (maximum allowed was 180). No significant differences were observed between the ecstasy/cannabis group and the cannabis only group. A combined drug-user group performed significantly worse than controls on the non-spatial PAL. ANCOVA revealed that this effect was more due to cannabis than ecstasy. However, the average cannabis abstinence period was only 17 hours so it was possible that participants were still intoxicated. Also, Croft et al's participants only had a modest lifetime dose of ecstasy.

Fox et al (2002) also used a spatial PAL task in which participants were required to learn the spatial locations of abstract patterns. In the test trials participants were first required to learn six pattern-location pairs and then in the next trial eight pairings. No significant group differences were observed in the number of errors, the

number of presentations required per trial, or the memory score (total number of patterns successfully located on initial presentation). The group by trial interaction approached significance, and post hoc tests revealed that the ecstasy group made a greater number of errors on the 8 pair trials. Rodgers (2000) found that ecstasy users were unimpaired during the initial learning phase of the verbal and visual paired associates sub-tasks of the Wechsler Memory Scale. However, subsequent deficits in the delayed recall of the verbal and visual paired associates were apparent among ecstasy users but not among cannabis-only users.

In addition to deficits in associative learning, basic verbal learning deficits have also been observed using the Rey Auditory Verbal Learning Test (RAVLT). During trials 1-5, a list of 15 words is read to participants, and they are then required to recall as many words as possible in any order; in trial 6 this is repeated with a new list of words (interference). Trial 7 requires participants to again recall the original list. Finally, participants are given a list of words containing those from the first list with phonemic and semantic distractors, and required to circle words that appeared in the first list. McCardle et al (2004) found that ecstasy users performed significantly worse than non-users on delayed recall (trial 7), and Reneman et al (2000) found that ecstasy users recalled significantly fewer words than non-users. Ecstasy-related deficits were also observed on trial 1, the total number of words recalled and trials 6 and 8 in ex-ecstasy users compared to drug-naïve controls (Thomasius et al, 2003).

A problem with research in this area is that the ecstasy-related deficits observed may be at least in part, attributable to cannabis or the concomitant use of other drugs. Croft et al (2001) used a battery of neuropsychological tests to compare a group of cannabis only users, a combined ecstasy and cannabis group, and a control group. No significant differences were observed between the ecstasy/cannabis and the

cannabis only groups. However, a combined drug-using group (merging the cannabis only and ecstasy/cannabis group) performed worse than controls on working memory (forward and backward digit span), information processing, and learning and recognition memory. The authors concluded that cannabis, not ecstasy, was responsible for the deficits. However, the lifetime ecstasy dose of Croft et al's participants was only 41.9 tablets, which is relatively modest compared to other studies (e.g. Morgan et al's 2002 study in which users consumed over 500 tablets). While Croft et al's results appear to implicate cannabis use, Gouzoulis-Mayfrank et al (2000) found an ecstasy/cannabis group (with an average lifetime dose of 93.4 tablets) to be impaired relative to a cannabis-only and a non-user group in selective attention, a verbal learning task, immediate visual recall, logical thinking and general knowledge. However, more recently Dafters et al (2004) found that combined ecstasy-cannabis users, although worse than drug free controls on various measures of episodic memory (free recall and story recall), did not differ significantly from cannabis only users on any of the measures that were administered. Furthermore, unlike Croft et al's study, Dafters et al included both a heavy and light ecstasy user group, both of which performed similarly and did not differ from the cannabis-only users. This being the case, Dafters et al (2004) maintain that that the memory impairments obtained were due to cannabis rather than ecstasy. In relation to the present study, it is important therefore to consider the extent to which cannabis and other drugs might contribute to any apparent ecstasy-group related deficit in associative learning.

Thus the aim of the present study is to determine if users of ecstasy exhibit deficits in associative learning while attempting to control for the potentially confounding effects of other elicit drugs. In addition to the measures used by other

researchers (mainly immediate and delayed recall of words) the test used in the present study assesses various measures of forgetting, perseverative errors, and the speed with which all associations are learned (trials to completion) which have not yet been systematically investigated in ecstasy research. The number of pairs repeated correctly on trial one gives a measure of initial learning, and the number of trials required for a participant to learn all associations ("trials to completion") gives an overall indication of speed of learning. Forgetting at each level will also be recorded, whereby forgetting a response that had previously been recalled correctly once would indicate forgetting at level one, forgetting a response that had previously been recalled two times would be forgetting at level two, and so on. In addition, the number of perseverative errors will be recorded (i.e. giving the same incorrect response on two or more consecutive trials). It is expected that ecstasy users will perform worse than controls in paired associate learning, more specifically, they will correctly recall fewer pairs on trial 1, forget more items, make more perseverative errors, and take more trials to learn all associations. An overall deficit in associative learning may provide further support for impaired executive function since optimal learning requires the effective use of strategies and self-monitoring meta processes. Furthermore, an increased number of perseverative responses might be associated with a failure to inhibit previously incorrect responses or with an inability to shift mental set. Recalling fewer pairs on trial one may in part reflect hippocampal/medial temporal lobe impairment, while forgetting well-learned material would suggest a retrieval deficit.

Method

Design and Analysis.

Dependent variables were various measures of associative learning including trials to completion, initial learning (number of correct responses in trial 1),

perseverative responses, and forgetting at various levels of learning. The independent variable was ecstasy user group (users versus non-users). MANOVA was used supplemented by separate univariate analyses for each dependent variable. Subsequently, for each of the dependent variables, various measures of amphetamine, cannabis and cocaine use including lifetime use, frequency of use, average weekly dose, amount consumed in the previous 30 days and a categorical user-nonuser variable were included as covariates. Following this, in order to establish whether heavy ecstasy users were impaired relative to light users a second MANOVA was conducted with estimated level of lifetime ecstasy use between participants (heavy user- more than 200 tablets, light user - fewer than 200 tablets, and non ecstasy user) and the same dependent variables as indicated above.

In addition to these analyses, the relationship between aspects of illicit drug use and associative learning performance was assessed through bivariate correlation. This was done separately for measures of ecstasy, cannabis, cocaine and amphetamine use. For each of these, it was expected that measures of use would be inversely correlated with the measures of learning performance. For each illicit drug five separate measures of use were correlated with the five measures of learning performance yielding a total of 25 correlations. Given that the drug use measures were inter-correlated as were the learning measures, full Bonferroni correction is inappropriate (Uitenbroek, 2004). An adjusted Bonferroni significance level of .01 was computed based on application of the procedure set out by Uitenbroek (2004).

In order to establish which of the learning processes shared variance with the ecstasy-user group variable, hierarchical regression analysis was used. In all cases, trials to completion was the dependent variable. The ecstasy user group related variance was estimated first by entering this measure as the sole independent variable.

Next, measures of initial learning, perseverative responses and forgetting at various levels were entered as independent variables in separate regressions. In each case the measure of learning performance was entered first followed by ecstasy user group to establish how much of the ecstasy user-group related variance was accounted for by each learning sub-process.

Participants

Participants were initially recruited through direct contact with under-graduates from Liverpool John Moores University, and through the snowball technique (Solowij et al, 1992). 62 non-ecstasy users (44 female, mean age 21.3) and 35 ecstasy users (15 female, mean age 21.66) were recruited. Participants reported that they had abstained from ecstasy use for at least 7 days (mean = 12.16 weeks), and other psychoactive drugs for at least 24 hours prior to testing. Participants were paid 15 UK pounds in store vouchers for their participation.

Materials.

Patterns of drug use and other relevant lifestyle variables were investigated by means of a background questionnaire. The questionnaire gauged the use of ecstasy and other drugs, as well as age, years of education, general health, and other relevant lifestyle variables. In relation to other drugs, participants were asked a range of questions including frequency and duration of use and the last time that they had used each drug. Participants were also questioned concerning their history of drug use, and using a technique developed by Montgomery et al (in press) these data were used to estimate total lifetime use for each drug. Average weekly dose and the amount of each drug consumed within the previous 30 days were also assessed. Fluid intelligence was

measured via Raven's Progressive Matrices (Raven et al 1998), and pre-morbid intelligence was assessed via the National Adult Reading Test (NART, Nelson, 1982).

Associative Learning. This was assessed via a verbal paired associates task. Participants were presented sequentially with the same eight word pairs (taken from Fisk, 2003) on a computer screen. For example,

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After each presentation, the participant was prompted with the first member of each pair and required to recall the second member. Eight such trials were administered. The order of presentation was randomised and changed for each trial. Measures included the number of correct responses in trial 1 (a measure of initial learning), forgetting at various levels, the number of trials required to learn all associations, and the number of perseverative errors (giving the same incorrect answer consecutively).

Sleep quality. A screening questionnaire and the Epworth Sleepiness Scale (ESS- Johns, 1991) were used to investigate any group differences in sleep quality. The ESS is a measure of subjective daytime sleepiness and contains eight items, which a participant has to score on a scale of 0 (would never doze off in this situation) to 3 (high chance of dozing off in this situation). A total score of all eight items was used in the analysis. The screening questionnaire contained a number of questions on sleep quality, e.g., hours per night, "how refreshed do you feel in the morning", in addition to relevant lifestyle questions relating to cigarette and alcohol consumption.

Procedure.

The tests were administered under controlled laboratory conditions. A computer running on MS-DOS was used for the associative learning task. Tasks were administered in the following order: Health/education questionnaire, ecstasy and drug use background questionnaire, sleep questionnaires, associative learning, NART and finally Raven's progressive matrices. Overall, testing took two to three hours per person. The study was approved by the Ethics Committee of Liverpool John Moores University, and was administered in accordance with the ethical guidelines of the British Psychological Society.

Results

Average age, years of education, fluid intelligence, premorbid intelligence and other background variables for the two groups are set out in Table 1. Statistical tests (ANOVA, t-test) revealed that there were no significant differences between the groups regarding these variables, so they are not discussed further.

<Insert table 1 about here>

Inspection of Table 2 reveals that the use of other drugs was commonplace among the ecstasy group, but was restricted mainly to the use of cannabis among the control group. The Ecstasy users had a lifetime dose of cannabis nearly twice that of the controls (2128 joints compared to 1082 joints), in addition to using it more frequently (2.45 times per week, compared to 0.77 times), and having smoked more in the last 30 days (17.52 joints compared to 7.91 joints). There were significant group differences in the amount smoked in the last 30 days $t(37.74) = 2.07$, and the frequency of use $t(32.56) = 3.20$, $p<.05$ in both cases. However the difference in lifetime use was not statistically significant: $t(41.31)=1.80$, $p>.05$. (As Levene's test was significant, degrees of freedom have been adjusted accordingly.) The ecstasy

group reported an average total lifetime dose of ecstasy of 315 tablets; of amphetamine, 4 grams (n=8); and of cocaine, 18.96 grams (n=15). The average frequency of use for ecstasy was 0.4 times per week, and for cocaine, 0.26 times per week (n=15).

<Insert table 2 about here>

Ecstasy users performed worse on all measures of associative learning. Users required more trials to learn the pairings; they scored lower on the measure of initial learning (the number of correct responses on Trial 1); and they made more perseverative responses. However, Table 3 reveals that the group differences were less pronounced for the measures of forgetting. Indeed, the means reported in the Table indicate that once the material had been learned to a moderate degree, forgetting was a rare event among both users and nonusers. Thus, for example, once a response had been successfully learned for four or more consecutive trials, there was no occurrence of forgetting in the nonuser group and only seven of the 35 users forgot a previously learned response. MANOVA revealed that the ecstasy-related group difference on the measures of associative learning was statistically significant, $F(7,89) = 4.64$, $p<.001$. Furthermore, subsequent univariate analyses revealed significant group differences on each of the measures with the exception of forgetting at levels 2 and 4 (see Table 3).

<Insert Table 3 about here>

It is possible that some or all of these effects might have been attributable to the effects of other drugs. To address this possibility, the preceding analysis was repeated five times with different measures of amphetamine, cannabis, and cocaine

use as covariates. In the first analysis, measures of lifetime use of each of these other drugs were included; in the second, the number of times each drug was consumed each week; in the third, the amount of each drug consumed within the last 30 days; in the fourth, the average weekly dose (i.e., total amount consumed divided by the length of use in weeks); and in the fifth, categorical variables in which users and non users of each individual drug were coded as 0 or 1 respectively. Thus each of the analyses contained specific measures of amphetamine, cannabis, and cocaine use as covariates. This was done for the multivariate data yielding 5 multivariate outcomes and for each of the seven measures of associative learning yielding 35 univariate analyses in total. The results are set out in Table 4. In the analyses, the multivariate effect of ecstasy user group and the univariate ecstasy user group effects on trials to completion and perseverative errors remained statistically significant. The same was true in relation to forgetting at level three although this result needs to be treated with caution as all non-ecstasy users scored zero on this measure. Somewhat less reliable were the group differences in initial learning where measures of the frequency of other drug use and the categorical other drug use/non use covariates reduced the ecstasy-related group differences to below statistical significance. Similarly, ecstasy-group related differences in forgetting were reduced to below statistical significance following control for total lifetime use and average weekly dose of the other drugs.

<Insert table 4 about here>

In relation to the cannabis measures that were included in each of the 35 ANCOVA analyses referred to in the previous paragraph, homogeneity of regression was obtained in 31 out of 35 cases, $p > .05$ for the covariate by ecstasy user group interaction. The exceptions were: (i) in relation to the cannabis user group covariate, for the initial learning measure; (ii) again in relation to the cannabis user group

covariate, for the forgetting at level 4 measure; (iii) regarding the average weekly dose of cannabis covariate, for the forgetting at level 3 measure; and (iv) in relation to the frequency of cannabis use covariate, for the forgetting at level 1 measure. For these exceptional cases, the covariate by ecstasy user group interactions were all statistically significant; $p<.05$ in all cases.

Since the number of cocaine and amphetamine users among the non-ecstasy user group was small, it was not possible to properly test for homogeneity of regression in relation to the cocaine and amphetamine measures. Given these limitations, we cannot entirely rule out the possibility that other drugs may have played a part in accounting for the results obtained here. Indeed the correlations set out in Table 5 reveal that various aspects of other drug use were correlated with associative learning processes. Assuming a value of $\alpha = .01$, forgetting, both for well learned and for less well-learned material, was significantly correlated with total lifetime dose and average weekly dose of cannabis. Perseverative responses were significantly correlated with the frequency of amphetamine use. Initial learning was significantly correlated with lifetime cannabis use, the frequency of cannabis and cocaine use, cannabis use during the previous 30 days, and the average weekly dose of ecstasy. Consistent with the results of the MANOVA, the ecstasy user group variable was significantly correlated with all measures of learning performance.

<Insert table 5 about here>

In relation to possible ecstasy dosage effects, Table 6 reveals that for the most part while both ecstasy user groups performed worse than non-users, there is little difference between the high lifetime ecstasy dose and the low lifetime ecstasy dose user groups. MANOVA with level of ecstasy use as the independent variable (high lifetime dose n=18, low lifetime dose n=17, non user n=62) and the seven measures of

learning performance as dependent variables yielded a significant multivariate effect of level of ecstasy use $F(14,178) = 5.19$, $p<.001$. Table 6 reveals that significant differences were also obtained for each of the component learning measures. Pairwise comparisons revealed that non users performed significantly better than both user groups in trials to completion, $p<.05$ via Tukey's test. Equally non users were significantly better than heavy users on the initial learning measure, $p<.05$. Non users were also significantly better than light users on all of the forgetting measures, $p<.05$. The only significant differences between the two ecstasy user groups were for forgetting at levels 2, 3, and 4 where paradoxically light users performed significantly worse then heavy users, $p<.05$, via Tukey's test.

<Insert Table 6 about here>

Regarding the ecstasy-group related variance in trials to completion, it is important to emphasise that the ecstasy-group related variance potentially arises from a range of sources. In addition to using ecstasy, a range of other drugs was also used and there may also be premorbid differences between the two groups, as well as differences in psychological affect. Thus the ecstasy-group related variance might have arisen from any one of these sources. The focus here is to establish which sub-processes were responsible for the difference in overall learning performance among this group of poly-substance abusers.

Table 7 reveals that the ecstasy-group related variance amounted to 21.8% of the total variance in associative learning (as indicated by the R squared increment of .218). In subsequent analyses, ecstasy use was entered in the regression equation following the inclusion of each specific learning sub-process. This makes it possible to establish how much of the ecstasy-group related variance was accounted for by each of the learning sub-processes. Inspection of Table 7 reveals that following

statistical control for group differences in initial learning (as measured by the number of correct responses in Trial 1), the residual ecstasy-group related variance amounts to 8.6%. Thus over half of the ecstasy-group related variance is accounted for by individual differences in the level of initial learning. Three other regression models were evaluated. Prior control for group differences in perseverative responses reduced the ecstasy-related variance from 21.8% to 13.4%. Inclusion of forgetting at level one and at higher levels in the first stage of the hierarchy removed at least half of the ecstasy-group related variance in both cases.

<Insert Table 7 about here>

Discussion.

As expected, the results demonstrated an ecstasy-group related deficit in associative learning. The ecstasy user group performed worse on all measures of associative learning, they required more trials to learn the associations, achieved fewer correct responses on trial one, produced more perseverative responses, and demonstrated a greater propensity to forget previously learned responses, especially those that were not well learned. Furthermore, when indices of cannabis, cocaine, and amphetamine use (lifetime dose, frequency of use, average weekly dose, amount consumed in the last 30 days, and a categorical variable of user/non-user) were included as covariates, the ecstasy-group related deficits in trials to completion and perseverations remained significant. However, differences in initial learning fell to below statistical significance with control for other drug use (frequency of use, user/non-user). In addition, group differences in forgetting were reduced to below statistical significance following control for lifetime, and average weekly dose of other drugs.

As some of the apparent ecstasy-group related effects were reduced to below statistical significance following controls for the use of other drugs and since homogeneity of regression was not obtained in all cases or could not be tested, the possibility that other drugs might affect associative learning performance cannot be excluded. Indeed the correlations obtained in the present study suggest that cannabis use may affect a number of aspects of learning performance. However, the correlations set out in Table 5 do need to be treated with caution. Most of them were modest in scale so that the variables in question shared only a relatively small amount of variance with the learning measures. Furthermore, the Bonferroni correction that was used is based on the assumption that it is appropriate to consider expectations for each illicit drug separately; hence the procedure is based on a total of 25 comparisons where both the outcome variables and the predictor variables were intercorrelated. If a more conservative Bonferroni correction procedure was employed, then with 100 independent correlations, a value for $\alpha = .0005$ would be appropriate. At this level only two of the correlations would be statistically significant, specifically, perseverative responses with the frequency of amphetamine use and the ecstasy user-nonuser variable with trials to completion.

It was noteworthy that the apparent ecstasy-group effect does not appear to be directly related to the level of lifetime ecstasy use, since MANOVA revealed that, relative to nonusers, heavy ecstasy users were no more impaired than light ecstasy users. This outcome is not readily explained. It may be that no straightforward relationship exists between the total number of tablets taken and the risk of a neurotoxic dose (O'Shea et al 1998). Rather the likelihood of MDMA related impairment is associated with the co-occurrence of a number of factors, which are not necessarily related to the total number of tablets consumed such as the number of

tablets ingested on a single occasion and the conditions (ambient temperature, level of hydration, background sound level) prevailing at the time (O'Shea et al 1998). Thus an individual who typically consumes a modest dose, relatively infrequently but over a long period of time may have a high lifetime dose but not demonstrate any substantial learning deficits.

Turning to the results of the regression analysis, it was revealed that ecstasy user group accounted for approximately 22% of the total variance in trials to completion. All of the component measures of learning performance substantially reduced the ecstasy-group related variance. The greatest degree of attenuation was achieved by the level of initial learning (number correct in trial 1). The various measures of forgetting each reduced the ecstasy group related variance by about one half while for perseverative responses the degree of attenuation was around 40%. Thus the ecstasy-group related effect appears to be mediated through all of the learning sub processes. Taken together with the results of the MANOVA, the robustness of the group difference in trials to completion following the various ANCOVA analyses is consistent with an ecstasy-mediated effect in relation to this aspect of learning. However, it is at least possible that some of the attenuation produced by the level of initial learning and by forgetting may have been due to other drugs such as cannabis. Such a possibility would be consistent with Dafters et al (2004) and Croft et al's (2001) results linking cognitive deficits to cannabis use rather than ecstasy. However, in relation to the other learning measures, statistical controls for group differences in various measures of cannabis consumption did not eliminate the overall ecstasy related group difference.

There are a number of limitations of the present study that need to be acknowledged. In a quasi-experimental design such as that adopted in the present

study, it is possible that the groups may have differed on some variable other than ecstasy. Some possibilities can be excluded such as intelligence (NART and Raven's) and aspects of sleep quality. However others such as general health, nutrition, or some premorbid condition cannot be ruled out. Furthermore, we relied on self-reports of drug use and so it is possible that there were inaccuracies in this data. There is also no guarantee of the purity of drugs used, and the quantitative amounts per tablet, gram etc (Cole et al 2002). Furthermore, due to limited resources, we were unable to provide an objective measure of recent drug use (e.g. from hair and urine samples). However, most published studies testing cognitive deficits among ecstasy users have not used these techniques (e.g. Fox et al, 2002; Morgan, 1998; Morgan, 1999; Parrot and Lasky, 1998, Rodgers, 2000, Wareing et al, 2000). All participants reported being drug free for 24 hours, and ecstasy free for at least 7 days (average abstinence period was actually 12 weeks), and we have no reason to believe this information to be false (participants were not informed that they would be excluded prior to testing).

In conclusion, the present study further supports evidence for cognitive deficits in ecstasy users. Individual differences in initial learning, perseverative responses and forgetting all appear to be important determinants of verbal associative learning deficits in these individuals. However, while some of these impairments appear to be related to ecstasy use, others may be attributable to other drugs such as cannabis.

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Table 1

Age, Years of Education, Intelligence, and Sleep Quality for Ecstasy Users and Non Ecstasy Users

	Ecstasy Users		Non Ecstasy Users	
	Mean	S.D.	Mean	S.D.
Age (Years)	21.66	1.64	21.30	1.79
Years of Education	15.77	1.88	15.36	2.12
Ravens Progressive Matrices (maximum 60)	49.94	4.55	48.13	5.27
NART (maximum 50)	28.91	5.98	29.76	5.80
Hours Sleep per Night	8.11	1.56	8.01	1.27
Epworth Sleep Scale (Maximum 24)	6.38	3.38	5.97	3.03
Self Report Health *	3.74	0.74	3.84	0.81

* The self report health measure scores range from 1 (very poor) to 5 (very good)

Table 2.

Indicators of Drug Use Among Ecstasy Users and Non Ecstasy Users

	Ecstasy Users			Non Ecstasy Users		
	Mean	S.D.	n	Mean	S.D.	n
Total Use						
Ecstasy (tablets)	315.30	330.10	35			
Amphetamine (grams)	4.00	3.86	8	4.00	-	1
Cannabis (joints)	2128.71	2401.96	26	1082.54	1439.33	18
Cocaine(grams)	18.96	22.03	15	-	-	
Frequency of Use (times per week)						
Ecstasy	0.40	0.34	35			
Amphetamine	0.04	0.04	5	-	-	
Cannabis	2.45	2.40	25	0.77	0.90	18
Cocaine	0.26	0.23	15	-	-	
Amount Used During Previous 30 Days						
Ecstasy (tablets)	3.38	3.58	34			
Amphetamine (grams)	1.20	2.68	5	-	-	
Cannabis (joints)	17.52	18.26	24	7.91	11.03	16
Cocaine(grams)	1.23	1.77	13	-	-	
Average Weekly Dose						
Ecstasy (tablets)	1.67	1.31	35			
Amphetamine (grams)	0.10	0.20	8	0.01	-	1
Cannabis (joints)	7.75	8.73	25	5.11	9.94	18
Cocaine(grams)	0.14	0.24	15	-	-	

Table 3

Performance on Associative Learning Measures for Ecstasy Users and Non-Ecstasy Users.

	Ecstasy Users		Non Ecstasy Users		F (1,95)
	Mean	S.D.	Mean	S.D.	
Trials to Completion	6.11	1.94	4.32	1.46	26.54***
Number of Correct Responses in Trial 1	2.97	2.01	4.32	2.01	10.14**
Number of Perseverative responses	0.69	1.16	0.16	0.66	8.13**
Number Forgotten at:					
Level 1	0.86	1.03	0.39	0.75	6.61*
Level 2	0.26	0.66	0.10	0.35	2.47
Level 3	0.14	0.36	0.00	0.00	10.12**
Level 4	0.06	0.24	0.00	0.00	3.68

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

Table 4

Ecstasy User Group Effect (F values) on Measures of Associative Learning Following Statistical Controls for Various Measures of Amphetamine, Cannabis, and Cocaine Use[1].

	Covariate Measures:				
	Total Use	Times used per week	Amount Consumed in the previous 30 days	Average Weekly Dose	Ever Used[2]
Multivariate Effect (d.f. = 7,85)	3.16*	4.16***	5.20***	4.10***	3.64**
Trials to Completion	18.71***	18.06***	21.78***	23.76***	15.45***
Number of Correct Responses in Trial 1	6.21*	2.65	4.27*	7.70*	0.73
Number of Perseverative responses	4.17*	7.54**	12.26***	8.13**	4.52*
Forgetting: Number Forgotten at level 1	2.30	5.80*	6.95**	3.75	7.23**
Forgetting: Number Forgotten at level 2	2.26	5.98*	4.94*	2.74	6.05*
Forgetting: Number Forgotten at level 3	5.53*	16.76***	18.83***	7.28**	7.72**
Forgetting: Number Forgotten at level 4	3.39	0.73	0.53	3.82	6.84*

1. Separate measures relating to the use of each of the three drugs were entered as covariates in each analysis. For all univariate analyses, degrees of freedom were 1,91. Unless otherwise noted, the units were as follows: cannabis - number of joints; amphetamine and cocaine – grams. Nonusers of the drug in question were coded as zero on the particular measure concerned.
2. Categorical variable coded 0 = user, 1 = nonuser

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

Table 5
Correlations Between Various Measures of Learning Performance and Measures of Illicit Drug Use.

	Trials to Completion	Initial Learning	Perseverative Responses	Forgetting Level 1	Forgeting Levels 2-7
Total Use					
Ecstasy	.193	-.226	.162	.146	-.045
Cannabis	.281*	-.242*	-.039	.309*	.360*
Cocaine	.092	-.155	.274	.047	-.012
Amphetamine	.085	.058	.172	.093	.074
Frequency					
Ecstasy	.218	-.173	.004	.189	.066
Cannabis	.165	-.320*	-.102	-.016	.057
Cocaine	.169	-.248*	.139	.148	-.014
Amphetamine	.143	.107	.331*	.085	-.058
Use in Last 30 Days					
Ecstasy	.226	-.127	.075	.154	.082
Cannabis	.198	-.279*	-.052	-.037	.000
Cocaine	.092	-.154	.036	.109	-.038
Amphetamine	-.054	.106	-.040	.051	-.035
Average Weekly Dose					
Ecstasy	.234	-.260*	.149	.100	-.038
Cannabis	.235	-.230	-.032	.266*	.305*
Cocaine	.042	-.107	.113	.005	.014
Amphetamine	-.033	.103	-.002	.057	-.025
User/Non User					
Ecstasy	-.466**	.310*	-.281*	-.259*	-.281*
Cannabis	-.221	.245*	.013	-.075	-.100
Cocaine	-.302*	.345*	-.202	-.075	-.078
Amphetamine	-.167	.184	-.072	-.078	-.143

N=97

** p<.001; * p< .01; one tailed.
A Bonferroni corrected significance level of $\alpha = .01$ was used

Table 6

Performance on Associative Learning Measures for Ecstasy Users with High and Low Lifetime Dose and Non-Ecstasy Users.

	High lifetime ecstasy dose >200 tablets[1]		Low lifetime ecstasy dose ≤ 200 tablets[2]		Non ecstasy user		F (1,95)
	Mean	S.D.	Mean	S.D.	Mean	S.D.	
Trials to Completion	5.67	1.28	6.59	2.40	4.32	1.46	14.92***
Number of Correct Responses in Trial 1	2.67	1.81	3.29	2.20	4.32	2.01	5.49**
Number of Perseverative responses	0.67	1.28	0.71	1.05	0.16	0.66	4.03*
Number Forgotten at:							
Level 1	0.72	0.83	1.00	1.22	0.39	0.75	3.75*
Level 2	0.06	0.24	0.47	0.87	0.10	0.35	4.75*
Level 3	0.00	0.00	0.29	0.47	0.00	0.00	16.15***
Level 4	0.00	0.00	0.12	0.33	0.00	0.00	5.17**

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

1. n=18; mean lifetime number of tablets consumed = 520, range = 219 to1682
2. n=17; mean lifetime number of tablets consumed = 98, range = 15 to192

Table 7.

Variance in Associative Learning Uniquely Associated with Ecstasy User Group Following Statistical Controls for the Effects of Other Independent Variables

Regression Model	Independent Variables in the Model Prior to the Inclusion of Ecstasy User Group	Total R squared	R squared increment associated with Ecstasy User Group
0	None	.218	.218***
1	Number of Correct Responses in Trial 1	.454	.086***
2	Number of Perseverative responses	.304	.134***
3	Number Forgotten at level 1	.445	.109***
4	Number Forgotten at levels 2, 3 and 4	.405	.091***

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