Reasoning deficits in ecstasy (MDMA) polydrug users.

John E. Fisk and Catharine Montgomery

Liverpool John Moores University

Michelle Wareing and Philip N. Murphy

Edge Hill College of Higher Education

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Corresponding author:

Dr John E Fisk

School of Psychology

Liverpool John Moores University

15-21 Webster Street

Liverpool L3 2ET

United Kingdom

Telephone: 44 (0) 151 231 4035; Fax: 44 (0) 151 231 4245

e-mail: j.e.fisk@livjm.ac.uk

ABSTRACT.

Objectives. Previous research has shown that ecstasy users are impaired in thinking and reasoning. The present study sought to explore the possibility that syllogistic reasoning errors in ecstasy users were due to an inability to construct a model of the premises due to working memory limitations. Methods. Twenty-nine ecstasy users and 25 non-ecstasy user controls completed syllogistic reasoning problems varying in difficulty. Results. On the easier problems both groups performed at well above chance although nonusers achieved significantly more correct responses. Consistent with existing research, on the more difficult problems, errors by nonusers were characterised by incorrect conclusions suggesting that while nonusers have the working memory capacity to construct a single model of the premises, this is not an exhaustive representation and usually results in an erroneous conclusion. On the other hand for all problem types ecstasy users, rather than produce incorrect responses, were more likely to fail to generate a conclusion. Conclusions. The present results are consistent with the possibility that ecstasy users with their reduced working memory capacity may experience difficulty in constructing even a single model of the premises. While this might be attributable to the effects of MDMA neurotoxicty, many of the ecstasy users in the present study were polydrug users. Thus the possibility that other drugs including cannabis and cocaine might contribute to the present results cannot be excluded.

INTRODUCTION.

Ecstasy has been a popular recreational drug since the 1980's. Its key psychoactive ingredient, MDMA (3,4-Methlylenedioxymethamphetamine) disrupts brain functioning by blocking the reuptake of serontonin and to a lesser extent by promoting the release of dopamine (Morgan, 2000). Ecstasy use has been associated with a range of cognitive deficits including working memory impairments (see Morgan, 2000, for a review). Since aspects of working memory have been implicated in reasoning performance (Fisk & Sharp, 2002; Gilhooly et al, 1999; Gilinsky & Judd, 1990), it is possible that ecstasy users might be impaired in reasoning. Evidence of such impairment has been forthcoming from our own laboratory with ecstasy users performing significantly worse on measures of syllogistic reasoning relative to nonusers (Montgomery, et al, in press). The purpose of the present paper is to further explore the basis of reasoning deficits in ecstasy users.

In relation to working memory and executive functioning, evidence has emerged suggesting that ecstasy users score lower than non-user controls on measures of these constructs. From our own laboratory, Fisk et al (2004) found that ecstasy users scored significantly lower than nonusers on a measure of verbal working memory performance. Similar findings were obtained by Wareing et al (2004a) and ecstasy-related deficits in visuo-spatial working memory were observed in another study (Wareing et al, 2004b). While these studies are consistent with ecstasy-related impairment, other researchers have failed to find group-related differences. For example, Fox et al (2002) found no evidence of deficits on the strategy component of a visuo-spatial working memory task. Similarly, Simon and Mattick (2002) found that ecstasy users were unimpaired on the working memory measure of the Weschler

Memory Scale III (WMS III). More recently, in a follow-up study Gouzoulis-Mayfrank et al (in press) found that continued use of ecstasy was not associated with any further deterioration in measures of executive functioning including backward digit span and the 2 back test. However, users who had ceased using ecstasy did not show any improvement in these measures. One possible explanation for the discrepant results may be that ecstasy-related deficits only become apparent on tasks that load heavily on working memory and executive resources.

In relation to reasoning, prior to Montgomery et al's study, this aspect of cognition had not been systematically assessed in relation to possible ecstasy-related effects. Some studies examined logical thinking and decision-making. For example, Gouzoulis-Mayfrank et al (2000) found that ecstasy-cannabis users performed significantly worse than both cannabis only, and non-users in tests of logical thinking (LPS-4 test) and problem solving (mosaic test). McCann et al (1999) found that ecstasy users were impaired relative to nonusers in tests of logical reasoning. From our own laboratory, Montgomery et al (in press) found that ecstasy users were impaired in syllogistic reasoning, producing fewer correct responses than nonusers. The syllogisms used varied in terms of their difficulty. Users were impaired on the least difficult problems. However, on the more difficult problems both users and nonusers performed at little above chance level.

Among the different measures of reasoning competence, syllogistic reasoning is perhaps one of the best known (Evans et al, 1999; Johnson-Laird, 1983). Like other forms of reasoning, syllogistic deduction requires a participant to draw valid inferences from a set of premises. For Example,

Given that: Some A are B,

and

No B are C

It follows that: Some A are not C.

Johnson-Laird (1983) maintains that reasoning involves constructing mental models of the premises and testing conclusions against these models. Constructing a single model may be sufficient to solve some problems, while others may require up to three models. The construction and temporary retention of these models uses up cognitive resources, in particular working memory. One-model problems place the smallest demands on the working memory system, more complex problems as well as those that have no valid conclusions, require the construction of either two or three models to derive a solution and place the largest demands on the working memory system. Beyond working memory, syllogistic reasoning is also believed to utilise other resources, for example relations between linguistic concepts such as 'all', 'some' and the logical operator 'not', as well as spatial representations of class inclusion relationships (see, for example, Ford, 1995).

Our earlier findings (Montgomery et al, in press) leave a number of questions unanswered. While ecstasy users did perform significantly worse than nonusers on the one-model syllogisms, contrary to expectations, there was no group difference on the more difficult three-model syllogisms and syllogisms for which there was no valid conclusion (NVC). As these load more heavily on working memory resources it had been expected that they would be associated with a more pronounced ecstasy-related deficit. Our results might be explained in terms of Evans and co-workers' account of syllogistic reasoning (Evans et al, 1999; Handley et al, 2000; Newstead et al, 1999; Newstead et al, 2002). According to Evans, individuals generally construct only a single mental model of the premises and fail to search for alternatives. For both one-

model and more complex syllogisms, the premises need to be retained so that alternative possible conclusions can be accepted or rejected in the context of the initial mental model and the contents of working memory updated as necessary. The ecstasy related deficit that was evident on the one-model problems appears to be consistent with some degree of impairment in this process. When attempting the NVC/three model problems, according to Evans et al (1999), individuals again construct only a single model, which does not provide an exhaustive representation of the implications of the premises. Therefore in the case of our previous study (Montgomery et al, in press) with both users and nonusers, constructing just a single model, most inferences derived from it would be likely to be erroneous and group differences would therefore not be expected on these NVC/three model problems.

Accepting Evans et al's account of reasoning performance, the ecstasy-related deficit on the less difficult one-model syllogisms is consistent with the possibility that ecstasy users may lack the working memory resources to construct even a single model from the premises. As noted above working memory deficits have been established in ecstasy users. Wareing et al (2004a) found that ecstasy users were impaired on the computation span measure, which is an established measure of verbal working memory capacity (Fisk & Sharp, 2004). Deficits among ecstasy users have also been observed in visuo-spatial working memory (Wareing et al 2004b). Thus it is clearly possible that ecstasy users may find it more difficult to construct the single mental model needed to derive a solution. If this proves to be the case, then rather than produce incorrect conclusions to syllogisms, ecstasy users might be expected to be more likely to generate no conclusion at all. Producing an incorrect conclusion requires the ability to construct at least some model of the premises albeit an invalid

one. According to Evans et al this is what typically occurs when individuals are confronted with three model syllogisms.

If ecstasy users are less able to produce the single model required to derive a solution, then for one-model problems, it is predicted that users will obtain fewer correct conclusions and that errors will be characterised by a failure to generate a response rather than an incorrect response. For three model problems it is predicted that while nonusers will be capable of producing a response, since it is likely to be based on only a single model it is likely to be incorrect. On the other hand it is predicted that a significant number of ecstasy users will be unable to produce any response on the three model problems due to their inability to form the necessary model of the premises. Thus a different pattern of errors is predicted for the user and nonuser groups. In our previous study we failed to consider this aspect. The present study is designed to address this omission as well as to replicate our previous findings.

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. For example, Croft et al (2001) found no significant differences on a range of cognitive measures between individuals who used both ecstasy and cannabis and cannabis-only users. However, the 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. Simon and Mattick (2002) failed to find any evidence of ecstasy-related deficits on the WMS III, on a short form measure of intelligence, and on vocabulary subtest of the WAIS III. However, there was an inverse relationship between immediate visual recall and frequency of cannabis use. 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. Both Croft et al and Dafters et al concluded that cannabis, not ecstasy, was responsible for the deficits. 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 reasoning performance.

METHOD.

Participants.

Twenty-nine ecstasy users (mean age 22.55, S.D. 3.79, range 20-37) and 25 non-ecstasy user controls (mean age 20.84, S.D. 1.37, range 20-25) were recruited. Participants were initially recruited through direct approach to undergraduate students at Liverpool John Moores University. Students were asked if they were willing to be involved in a study examining the effects of ecstasy and cannabis on aspects of cognitive functioning. Subsequently participants were recruited through the "snowball technique" (Solowij et al, 1992). Those participating in the study were asked to abstain from taking illicit drugs for at least seven days prior to testing. None of the participants took part in our previous study on syllogistic reasoning. Participants were paid 15 UK pounds in store vouchers for their participation.

Materials.

A background questionnaire used by Wareing et al (2004a) assessed the use of ecstasy and other drugs, as well as age, years of education, other lifestyle variables and a

measure of psychological health. Fluid intelligence was measured through Raven's progressive matrices (Raven et al, 1998).

Syllogistic reasoning: Participants attempted to generate solutions for four one-model syllogisms, four three-model syllogisms, and four syllogisms for which there was no valid conclusion (NVC). The syllogisms used in the study were presented in random order. Participants were introduced to the concept of a syllogism, and examples (concrete and abstract) were provided. Examples and explanations were also provided for some correct and incorrect inferences, and Venn diagrams were used for purposes of illustration. Participants were told to generate as many conclusions as possible for each pair of premises. They were told that no pair generated more than two valid conclusions, some only generated one, and some had no valid conclusions. In addition, they were provided with a list of the eight possible solutions that can be generated over all the pairs of premises. The syllogisms were presented in a booklet, in abstract form as in the examples set out above. In each case, the two premises were printed, followed by the instruction to 'Please write down all valid conclusions'. Two boxes were provided underneath for the participant to record their responses. A response was deemed correct if it followed necessarily from the premises or in the case of the NVC syllogisms, if the participant indicated that no valid conclusions were possible. Errors were classified as either an incorrect conclusion when they did not follow logically from the premises or 'no response' when the individual failed to produce any conclusion. The syllogisms were the same as those used by Fisk and Sharp (2002) and Montgomery et al (in press). According to Johnson-Laird (1983), NVC syllogisms require either two or three mental models in order to derive the correct solution. In the present study, two of the NVC syllogisms were two-model and

two were three-model. Therefore, in terms of the number of models required, three-model syllogisms and NVC syllogisms were the hardest, and one-model the easiest.

Procedure.

Participants were informed as to the nature of the study and provided written consent. The tests were administered under controlled laboratory conditions. They were administered in the following order: Health/education questionnaire, background drug use questionnaire, syllogistic reasoning test, and Ravens progressive matrices. A range of other measures was also administered the results of which are outside the scope of the present study and which have been reported elsewhere, for example, random letter generation (Wareing et al, 2002; Fisk et al, 2004), a mood adjective checklist, sleep quality questionnaire, and the Epworth Sleepiness Scale (Wareing 2005). Rest breaks were incorporated as necessary, and testing was terminated if participants showed signs of discomfort. After all the measures had been administered, participants were debriefed, paid 15 UK pounds in store vouchers, and provided with drug education leaflets. 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.

Design and Analysis

The data were analysed for skewness, kurtosis, and homogeneity of variance. Following the procedure outlined by Tabachnick and Fidell, with regard to skewness, a value for z was computed by dividing the skewness statistic by its standard error. In relation to kurtosis a value for z was computed by taking the square root of the ratio of the kurtosis statistic to its standard error. According to Tabachnick and Fidell, for

samples of this size, the computed z values should be evaluated conservatively in both cases, so that ratios yielding z values exceeding 3.00, p<.001, are indicative of a departure from normality (Tabachnick & Fidell, 2001). Homogeneity of variance was initially evaluated using Levene's test. Since this measure is considered oversensitive, in situations where homogeneity was not obtained a value for F_{max} (the ratio of the largest cell variance to the smallest) was calculated. According to Tabachnick and Fidell (2001, p80) a value for F_{max} as large as 10 is acceptable given the ratio of the sample sizes for the two groups in the present study.

Where normality and homogeneity of variance was obtained, mixed ANOVA was used with user group (ecstasy users versus nonusers) between participants and error type (incorrect versus non response) and level of difficulty (one model, NVC and three model) within participants. Dependent variables included the number of correct conclusions generated and the number of errors for the one-model, NVC, and three-model problem types. Errors were further classified according to whether they were characterised by an incorrect conclusion or a failure to produce a conclusion. Where normality was not achieved, ecstasy user group differences were evaluated by the Mann Whitney U test.

The relationship between various measures of amphetamine, cannabis, cocaine, and ecstasy use and measures of syllogistic reasoning errors will be investigated through bivariate correlation.

RESULTS.

<u>Background variables</u>. Examination of Table 1 reveals that ecstasy users were significantly older than nonusers, consumed alcohol significantly more frequently, and ingested significantly more units per week. However the two groups did not differ

in terms of years of education, the self-report health measure, and Raven's measure of fluid intelligence. Ecstasy users had consumed on average a total of 362 tablets. The average length of use was 211 weeks and the average weekly dose just under two tablets.

<insert Table 1 about here>

With regard to the use of other drugs most ecstasy users were also regular users of cannabis and a substantial minority of ecstasy users also used cocaine and amphetamine (Table 2). However in relation to amphetamine none of the participants were currently using the drug. Among non-ecstasy users, the use of other drugs was rare and largely limited to cannabis. Eight non-ecstasy users who had used cannabis occasionally in the past were unable to provide an estimate of their use. Two of the non-ecstasy users had also previously used amphetamine and cocaine on an occasional basis but again were unable to quantify the amount.

<insert Table 2 about here>

Syllogistic reasoning.

In relation to the number of correct responses, the NVC and three model responses exhibited substantial positive skewness yielding statistics of 1.428 and 1.580 respectively, both with standard error of 0.325. The resulting ratios both yield z values exceeding 3.00, p<.001, which are indicative of a departure from normality for samples of this size. Regarding the one model correct responses, skewness was non significant, p>.05. For all three variables (one model, NVC and three model correct responses), kurtosis was nonsignificant, p>.01 in one case and p>.05 in the remaining two cases. Similarly homogeneity of variance was obtained, p>.05 in all three cases via Levene's test.

With regard to the six syllogistic reasoning error measures, tests for normality revealed that kurtosis was not significant for any of these, p > .01 in one case and p > .05 in the remaining five cases. Similarly only one of the six error response variables exhibited substantial positive skewness yielding a statistic of 1.43 with standard error of 0.325, z = 4.37, p < .001, which is indicative of a departure from normality. For the remaining five measures p > .001 in one case and p > .05 for the other four. Using Levene's test, homogeneity of variance was obtained for five of the six measures, p > .05. In the case of NVC non responses, Levene's test was significant F(1,51) = 4.34, p = .042. However, even in this case a value for $F_{max} = 3.069$ was obtained, which is acceptable given the ratio of the sample sizes for the two groups.

The mean number of correct syllogistic reasoning responses for the ecstasy user and nonuser groups are set out in Table 3. As expected, performance on the three model and NVC syllogisms was poor. Of the ecstasy user group, 75% failed to get any answers correct on the three model syllogisms. For the NVC syllogisms 62% failed to get any correct. For non-ecstasy users, 44% failed to achieve any correct answers for the three model problems, while the equivalent figure for the NVC problems was 60%. For the one-model syllogisms, Table 3 reveals that on average ecstasy users and non-ecstasy users achieved 3.14 and 4.64 correct answers respectively. In relation to the one-model correct responses, where normality and homogeneity of variance were obtained, ANOVA revealed that users performed significantly worse than nonusers, F(1,52) = 7.83, p<.01, partial $\eta^2 = .131$. Normality was not obtained in relation to NVC and three model correct responses. In these cases, Mann Whitney U test showed that nonusers also achieved more correct responses than users on the three model syllogisms, U = 245.50, p<.05. However the group difference on the NVC syllogisms was non-significant, U = 340.50, p>.05.

<insert Table 3 about here>

The different types of errors committed by ecstasy users and nonusers for the one model, NVC and three model problems are summarised in Table 4. Consistent with prediction, nonusers tended to generate more incorrect responses while ecstasy users generally failed to produce any response. In view of the fact that seventeen of the 18 tests for violations of normality and homogeneity were non-significant, syllogistic reasoning errors were analysed using repeated measures ANOVA. Type of error (incorrect versus no response) and problem type (one model, NVC, three model) were within participants and ecstasy user group was between participants. Consistent with expectation, reasoning errors among non-ecstasy users were characterised by incorrect responses, while among ecstasy users, reasoning errors were characterised by a failure to respond. This produced a significant interaction between error type and ecstasy user group, F(1,51) = 12.27, p<.001, partial $\eta^2 = .194$. This was qualified by a significant three way problem type by error type by ecstasy user group interaction, F(1.68,85.63) = 4.10, p < .05, partial $\eta^2 = .074$ (since Mauchley's test of sphericity was significant, degrees of freedom have been adjusted using the Greenhouse-Geisser epsilon value). Compared to nonusers, ecstasy users were less likely to produce a response for all problem types. In relation to incorrect responses, nonusers produced more for the three model and NVC problems but there was little difference between the groups for the one model problems.

<insert Table 4 about here>

In view of the significant group differences in average age and in the two measures of alcohol consumption (Table 1), these three variables were entered as covariates and the analysis of syllogistic reasoning errors was repeated. Consistent with the main analysis, the group by error type interaction remained statistically

significant, F(1,45) = 5.04, p<.05, with nonusers tending to produce incorrect responses while ecstasy users tended to fail to produce a response. Homogeneity of regression was obtained for all three covariates, F<1 (age and frequency of alcohol use) and F(1,46) = 3.48, p>.05 (units of alcohol) for the respective group by covariate interactions.

<u>Potential effects of other drugs</u>. As noted above many of the ecstasy users in the present study were polydrug users having consumed cannabis, amphetamine and cocaine in addition to ecstasy. There were too few users of these other drugs among the non-ecstasy user group to conduct ANCOVA as tests for homogeneity of regression would be unreliable. This leaves open the possibility that the effects observed in the present study might be due to the cocktail of illicit drugs consumed by the ecstasy user group. To address this possibility various measures of illicit drug use were correlated with the total number of incorrect syllogistic reasoning responses and with the number of non-responses. In addition measures of alcohol use were also included. The results are set out in Table 5. All of the measures of ecstasy use were significantly correlated with incorrect responses and non-responses on the syllogistic reasoning task. As the level of ecstasy use increased, the number of non-responses also increased while the number of incorrect responses decreased. With regard to cannabis, total lifetime use, and average weekly dose were significantly correlated with the syllogistic reasoning error outcomes with the nature of the correlations being the same as was the case for the ecstasy measures. Frequency of cannabis use was negatively correlated with the number of incorrect syllogistic responses as was the equivalent ecstasy measure. Interestingly, average weekly dose of cocaine and the cocaine user/nonuser variable were significantly correlated with the syllogistic reasoning error measures. Despite the relatively large number of significant

correlations in Table 5, it is worthy of note that after full Bonferroni correction (with α = .0015625) only three of the correlations remained statistically significant. All three involved the number of non-responses on the syllogistic reasoning task and the corresponding drug use variables were the total lifetime use of ecstasy, average weekly dose of ecstasy, and the user/nonuser ecstasy group variable. The correlations between the frequency of ecstasy use and syllogistic non-responses and the average weekly dose of cocaine and non-responses were just short of significance, with p = .0017375, and p = .0015695 respectively.

<insert Table 5 about here>

DISCUSSION.

As expected, ecstasy users achieved fewer correct responses on the one-model problems relative to nonusers. This replicates our previous findings (Montgomery et al , in press). In the present study nonusers managed to do significantly better on the three model problems also. This contrasts with our previous study in which no deficits were obtained on the three model problems. In the present study the nonuser group obtained a mean of 1.08 correct answers on these problems compared to ecstasy users who only managed to obtain a mean of 0.45. In our previous study the equivalent figures were 0.81 and 0.82 for nonusers and users respectively. Thus relative to the outcomes obtained in our previous study, the significance difference on the three model problems obtained here is due to a slightly higher level of performance among the nonusers and a rather larger diminution in the ecstasy users' performance.

If ecstasy users were less able to produce the single model necessary to generate a conclusion, then relative to nonusers, they would be more likely to produce no response in both the one model and the NVC/three model contexts. On the other

hand nonusers would be expected to achieve more correct solutions on the one-model problems where a single model is sufficient to achieve a valid conclusion. However, on the three model and NVC problems where the initial model of the premises is insufficient to produce a valid response they would make more incorrect responses compared to users. These expectations were fulfilled and overall, ecstasy users did exhibit more non-responding relative to nonusers, while nonusers made more incorrect responses on the more difficult NVC and three model problems relative to users.

These findings suggest that ecstasy users with their reduced working memory capacity (Fisk et al, 2004; Wareing et al 2004a; 2004b) are less able to retain the premises in working memory and as a consequence experience difficulty in forming the initial model necessary to draw a conclusion. The present results also add to the growing body of research evidence favouring Evans et al's (1999) account of syllogistic reasoning processes. It appears that only those with above average working memory capacity are able to go beyond the initial model of the premises when confronted with more complex reasoning problems (Handley et al, 2000; Newstead et al, 2002) and the results of the present study suggests that ecstasy users are far less likely to be found among this group. It remains to be seen which aspects of working memory and executive functioning are involved in syllogistic reasoning performance. Miyake et al (2000) and Fisk and Sharp (2004) have proposed that the executive processes underpinning the operation of working memory are separable. The processes identified include updating, switching, inhibition, and access to semantic memory. It would be desirable to repeat the present study with measures of these four processes to establish which aspects of executive functioning might be implicated in ecstasy-related syllogistic reasoning deficits. Recent findings from our laboratory

suggest that the updating and semantic access executive processes are especially susceptible to ecstasy-related impairment (Montgomery et al 2005).

At a psychopharmacological level, it is possible that the impairments in reasoning performance observed in ecstasy users could be associated with ecstasy related neurotoxicity especially in the prefrontal cortex which is known to play an important role in supporting reasoning and working memory processes (see for example, Goel et al, 2000). For example, using PET neuroimaging, McCann et al (1998), showed that compared to non-users, ecstasy users had significantly lower densities of 5HT transporter sites in diverse brain regions including the frontal cortex, pariental cortex, cingulate cortex, and in subcortical structures including the caudate, putamen, and cerebellum (these sub-cortical structures have also been implicated in syllogistic reasoning performance; Goel et al, 2000). Further, the decreases observed were positively correlated with the extent of ecstasy use. Neural injury in ecstasy users was also assessed by Reneman et al (2002a) using single-voxel (1H) MR spectroscopy imaging. N-Acetylasportate (NAA)/Creatine (CR), NAA Choline (CHO), and Myoinositol (MI) CR ratios were measured in the frontal, occipital, and parietal cortices. These ratios serve as a marker for neuronal loss or dysfunction. Although no significant differences between ecstasy users and nonusers were found in the occipital and parietal cortex, ecstasy users did exhibit a reduction of NAA/Cr and NAA/Cho ratios in the frontal cortex. Furthermore, the level of the reduction in the frontal cortex was significantly correlated with the extent of ecstasy use. In another study using SPECT imaging, post-synaptic 5-HT_{2a} receptor densities were examined (Reneman et al, 2002b). Compared to previous ecstasy users and controls, current ecstasy users had significantly lower binding ratios in the frontal, parietal, and occipital cortices. By way of contrast, previous users showed significantly higher in

binding ratios in certain brain areas perhaps due to a compensatory up-regulation of post-synaptic 5-HT_{2a} receptors due to low synaptic 5-HT levels. Thus to sum up the ecstasy-related reasoning deficits that were observed in the present study might be a consequence of MDMA related neurotoxicity affecting those neural areas that are believed to support reasoning processes.

The ecstasy users in the present study were polydrug users while the use of drugs among the non-ecstasy group was largely limited to cannabis. Thus caution needs to be exercised in attributing the effects observed here solely to ecstasy use. Nonetheless, the correlations set out in Table 5 are consistent with various aspects of ecstasy use playing an important role in accounting for the results that were obtained. We had predicted that use of ecstasy would be associated with an increased propensity to produce no response in the reasoning task. Consistent with this prediction, all of the various measures of ecstasy use were positively correlated with the number of nonresponses. With regard to the number of incorrect responses, we had predicted that these would be more prevalent among nonusers since ecstasy users would be less able to produce the single model of the premises which in the three model and NVC contexts gives rise to an incorrect response. The correlations were consistent with this prediction. As measures of ecstasy use increased, and presumably the capacity to generate a single model of the premises decreased, so the likelihood of an incorrect response decreased (instead users were more likely to generate no response at all). Thus correlations for the ecstasy user variables were negative with increased use associated with a reduced level of incorrect responses.

Measures of cannabis and cocaine use were also correlated with syllogistic reasoning errors. While none of these correlations remained statistically significant following Bonferroni correction, it is worthy of note that at the unadjusted $\alpha = .05$

level, five of the eight cannabis measures were significantly correlated with the syllogistic reasoning errors. However, assuming that the type one errors were distributed randomly, the error rate per experiment (Howell, 1997) would indicate that no more than one of the cannabis measures should have been significantly correlated with the syllogistic reasoning errors. The fact that the actual number of potential type one errors involving cannabis exceeds the expected error rate per experiment is consistent with the possibility that aspects of cannabis use might have contributed in part to the current findings.

Returning to the different patterns of errors evident in the responses of participants, one possible explanation for the prevalence of non-responses among the ecstasy user group might have been a general lack of motivation. This however appears to be unlikely. Ecstasy users performed as well as nonusers on the Raven's progressive matrices task, which is at least as demanding as syllogistic reasoning. They were also unimpaired in random letter generation (see Fisk et al., 2004), which is also a cognitively demanding task. Thus the non-responding evident in the syllogistic reasoning task appears to reflect something other than a general motivational deficit. A further possible explanation for the prevalence of non responses is that ecstasy users did not understand the task. However, the average number of correct responses achieved by ecstasy users on the easier one model syllogisms was 3.14 which is considerably above the single correct response which might have been achieved by chance¹. Thus it appears that ecstasy users did have an adequate understanding of the task and that the non-responses must be due to some other factor, e.g., difficulty in constructing a model of the premises.

Given that the present study does demonstrate that ecstasy users are impaired in syllogistic reasoning, it is appropriate to consider the likely implications of this

deficit. According to Piaget's notion of formal operational thought (Inhelder & Piaget, 1958) and Johnson-Laird's (1983) mental models perspective, the ability to solve syllogisms is indicative of a broader capacity for logical thought which supports reasoning in everyday contexts. Indeed individual differences in syllogistic reasoning performance were found to be significantly correlated with SAT mathematics scores among college students (Stanovich & West, 1998) and with cognitive ability scores in 10 to 13 year old children (Kokis et al, 2002). Furthermore abilities in conditional reasoning (Piburn 1990) and syllogistic reasoning (Watters & English, 1995) have been linked with the development of scientific reasoning skills in elementary school children. Thus the ecstasy-related deficits observed in the present study and in our previous one may potentially have implications for ecstasy users in terms of their level of educational attainment and their capacity for decision making in every day contexts where it is necessary to make inferences about real events.

A number of limitations were evident in the present study, for example, in relation to the correlations, we were reliant on individuals being willing and able to provide an accurate account of their previous drug use. Furthermore since it was not possible to quantify the amounts of each psychoactive drug present within the tablets or joints consumed a further source of error was introduced. Thus it must be acknowledged that the interpretation of the correlations that were observed is constrained by the accuracy of this data. Additionally, because of limited resources, we were unable to use urine, saliva, or hair samples to confirm recent patterns of drug use. However, the drug use questionnaire was designed to check the internal consistency of the information provided and it is equally worthy of note that most of the published studies that have probed cognitive deficits among ecstasy users have <u>not</u> resorted to urine, hair, or saliva testing (e.g., Fox et al, 2002; Morgan, 1999; Parrott

& Lasky, 1998; Rodgers, 2000). Nonetheless, this remains a potential limiting factor in interpreting our findings.

Aside from the issue of drug testing, other limitations evident in studies of the present kind need to be acknowledged. For example, lifestyle differences and premorbid factors cannot be excluded as possible sources of group differences in studies of this nature. Ecstasy users may experience altered sleep patterns. They may neglect their diet and their physical health and all of these factors have the potential to impair cognitive functioning (Cole et al, 2002). Other psychosocial factors need to be acknowledged. It may be that ecstasy users arrived at the laboratory with the expectation that they would perform worse on the cognitive measures that were to be administered and that this expectation became a self-fulfilling prophecy. Croizet et al (2004) have shown that stereotype threat can cause groups to under-perform when they believe that the measures assessed are associated with group-related deficits. When these prior expectations were removed, Croizet et al found that group members no longer exhibited impairment. Although Croizet et al's research did not involve drug users, the possibility of stereotype threat cannot be entirely excluded in relation to the ecstasy users tested in the present study. Apart from these potentially confounding factors it is also important not to over generalise from the present findings. For example, given that word of mouth referral was used as the primary means of recruiting participants, our ecstasy-user group may not be entirely representative of all ecstasy users, especially those who consume the drug in settings that are unlike those frequented by those individuals constituting the present sample.

Despite these caveats, the present study along with our previous one, does suggest that this population of polydrug users are susceptible to reasoning deficits which may be associated with difficulties in making everyday decisions in contexts

where a number of information sources need to be integrated in a logical manner, for example, financial decisions, or career choices. They might also exhibit an impaired ability to weigh up the pros and cons of conflicting arguments and might also be impaired in academic contexts where the acquisition of complex inter-related concepts is necessary.

References.

- Cole J, Sumnall H, Grob, C (2002) Sorted: Ecstasy facts and fiction. The Psychologist 15: 464-467
- Croft RJ, Mackay AJ, Mills ATD, Gruzelier JGH (2001) The relative contributions of ecstasy and cannabis to cognitive impairment. Psychopharmacology 153: 373-379
- Croizet JC, Despres G, Gauzins ME, Huguet P, Leyens JP, Meot A (2004) Stereotype threat undermines intellectual performance by triggering a disruptive mental load. Personality and Social Psychology Bulletin 30: 721-731
- Dafters RI, Hoshi R, Talbot AC (2004) Contribution of cannabis and MDMA ("ecstasy") to cognitive changes in long term polydrug users.

 Psychopharmacology 173: 405-410
- Evans JStBT, Handley SJ, Harper CNJ, Johnson-Laird PN (1999) Reasoning about necessity and possibility: A test of the mental model theory of deduction.

 Journal of Experimental Psychology: Learning, Memory and Cognition 25: 1495-1513
- Fisk JE, Montgomery C, Murphy P, Wareing M (2004) Evidence of executive deficits among users of MDMA (Ecstasy). British Journal of Psychology 95: 457-466
- Fisk JE, Sharp C (2002) Syllogistic reasoning and cognitive ageing. Quarterly Journal of Experimental Psychology 55A: 1273-1293
- Fisk JE, Sharp C (2004) Age-related impairment in executive functioning: Updating, inhibition, shifting, and access. Journal of Clinical and Experimental Neuropsychology 26: 874-890

- Ford M (1995) Two modes of mental representation and problem solution in syllogistic reasoning. Cognition 54: 1-71
- Fox HC, McLean A, Turner JJD, Parrott AC, Rogers R, Sahakian BJ (2002)

 Neuropsychological evidence of a relatively selective profile of temporal dysfunction in drug-free MDMA ("ecstasy") polydrug users.

 Psychopharmacology 162: 203-214
- Gilhooly KJ, Logie RH, Wynn V (1999) Syllogistic reasoning tasks, working memory and skill. European Journal of Cognitive Psychology 11: 473-498
- Gilinsky AS, Judd BB (1994) Working memory and bias in reasoning across the life span. Psychology and Aging 9: 356-371
- Goel V, Buchel C, Frith C, Dolan RJ (2000) Dissociation of mechanisms underlying syllogistic reasoning. Neuroimage 12: 504-514
- Gouzoulis-Mayfrank E, Fischermann T, Rezk M, Thimm B, Hensen G, Daumann J

 (in press) Memory performance in polyvalent MDMA (ecstasy) users who

 continue or discontinue MDMA use. Drug and Alcohol Dependence
- Gouzoulis-Mayfrank E, Daumann J, Tuchtenhagen F, Pelz S, Becker S, Kunert HJ, Fimm B, Sass H (2000) Impaired cognitive performance in drug-free recreational ecstasy (MDMA) users. Journal of Neurology Neurosurgery and Psychiatry 68: 719-725
- Handley SJ, Dennis I, Evans JStBT, Capon A (2000) Individual differences and the search for counterexamples in syllogistic reasoning. In W Schaeken, G De Vooght, A Vandierendonck, G d'Ydewalle (Eds) Deductive Reasoning and Strategies. Mahwah, NJ: Lawrence Erlbaum
- Howell DC (1997) Statistical Methods for Psychology (4th ed.). Belmont CA:

 Duxbury

- Inhelder B, Piaget J (1958) The Growth of Logical Thinking from Childhood to Adolescence. London: Routledge
- Johnson-Laird PN (1983) Mental Models. Cambridge, UK: Cambridge University

 Press
- Kokis JV, Macpherson R, Toplak ME, West RF, Stanovich KE (2002) Heuristic and analytic processing: Age trends and associations with cognitive ability and cognitive styles. Journal of Experimental Child Psychology 83: 26-52
- McCann UD, Szabo Z, Scheffel U, Dannals RF, Ricaurte GA (1998) Positron emission tomographic evidence of toxic effect of MDMA ('Ecstasy') on brain serotonin neurons in human beings. Lancet 352 (9138): 1433-1437
- McCann UD, Mertl M, Eligulashvili V, Ricaurte GA (1999) Cognitive performance in (±) 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy") users: a controlled study. Psychopharmacology 143: 417-425
- Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD (2000)

 The unity and Diversity of executive functions, and their contributions to complex "frontal lobe" tasks: A latent variable analysis. Cognitive Psychology 41: 49-100
- Montgomery C, Fisk JE, Newcombe R, Murphy PN (2005). The Differential Effects of MDMA ("ecstasy") on Executive Components: Shifting, Inhibition, Updating and Access to Semantic Memory. Manuscript submitted for publication.
- Montgomery C, Fisk JE, Newcombe R, Wareing M, Murphy P (in press). Syllogistic reasoning performance in MDMA (Ecstasy) users. Experimental and Clinical Psychopharmacology

- Morgan MJ (1999) Memory deficits associated with recreational use of "ecstasy" (MDMA). Psychopharmacology 141: 30-36.
- Morgan MJ (2000) Ecstasy (MDMA): a review of its possible persistent psychological effects. Psychopharmacology 152: 230-248
- Newstead SE, Handley SJ, Buck E (1999) Falsifying mental models: Testing the predictions of theories of syllogistic reasoning. Memory and Cognition 27: 344-354
- Newstead SE, Thompson VA, Handley SJ (2002) Generating alternatives: A key component in human reasoning? Memory and Cognition 30: 129-137
- Parrott AC, Lasky J (1998) Ecstasy (MDMA) effects upon mood and cognition:

 Before, during and after a Saturday night dance. Psychopharmacology 139:

 261-268
- Piburn MD (1990) Reasoning about logical propositions and success in science.

 Journal of Research in Science Teaching 27: 887-900
- Raven J, Raven JC, Court JH (1998) Manual for Raven's Progressive Matrices and Vocabulary Scales. Oxford UK: Oxford Psychologists Press
- Reneman L, Endert E, de Bruin K, Lavalaye J, Feenstra MG, de Wolff F, Booij J

 (2002b) The acute and chronic effects of MDMA ('Ecstasy') on cortical 5-HT

 2A receptors in rat and human brain. Neuropsychopharmacology 26: 387-396
- Reneman L, Majoie CB, Flick H, den Heeten GJ (2002a) Reduced N-acetylaspartate levels in the frontal cortex of 3,4- methylenedioxymethamphetamine (Ecstasy) users: preliminary results. American Journal of Neuroradiology 23: 231-237.
- Rodgers J (2000) Cognitive performance amongst recreational users of "ecstasy".

 Psychopharmacology 151: 19-24

- Simon NG, Mattick RP (2002) The impact of regular ecstasy use on memory function. Addiction 97: 1523-1529
- Solowij N, Hall W, Lee N (1992) Recreational MDMA use in Sydney: a profile of ecstasy users and their experiences with the drug. British Journal of Addiction 87: 1161-1172
- Stanovich KE, West RF (1998) Who uses base rates and P(D|~H)? An analysis of individual differences. Memory and Cognition 26: 161-179
- Tabachnick BG, Fidell LS (2001) Using Multivariate Statistics, (4th Ed.). Boston MA USA: Allyn and Bacon
- Wareing M (2005) Working Memory and Executive Deficits Among MDMA ('Ecstasy') Users. Unpublished PhD thesis
- Wareing M, Fisk JE, Murphy P (2002) Little evidence for central executive impairment among light/moderate users of MDMA. Proceedings of the British Psychological Society 10: 107.
- Wareing M, Fisk JE, Murphy P Montgomery C (2004a) Verbal working memory deficits in current and previous users of MDMA. Human Psychopharmacology: Clinical and Experimental 19: 225-234
- Wareing M, Murphy P, Fisk JE (2004b) Visuospatial memory impairments in users of MDMA ('ecstasy'). Psychopharmacology 173: 391-397
- Watters JJ, English LD (1995) Children's application of simultaneous and successive processing in inductive and deductive reasoning problems: Implications for developing scientific reasoning skills. Journal of Research in Science

 Teaching 32: 699-714

Table 1.

Performance on background variables and indicators of ecstasy use.

Variables.	Ecstasy User		Nonuser		t
	Mean	S.D.	Mean	S.D.	-
Age	22.55	3.78	20.84	1.37	2.27*
Education (years)	15.03	2.86	15.20	2.04	-0.24
Ravens Total Score (fluid intelligence)	47.48	6.34	48.08	5.25	-0.37
Self report health	3.72	0.80	3.96	0.68	1.16
Alcohol (units per week)	27.86	20.58	14.90	12.55	2.82**
Frequency of Alcohol Consumption (times per week) ¹	3.21	1.81	1.91	1.02	3.24**
Ecstasy Use					
Lifetime Use: Number of Ecstasy Tablets consumed	361.90	391.36			
Frequency (times per week)	0.33	0.25			
Length of Use (weeks)	210.57	133.02			
Weeks since last use	23.22	46.03			
Average weekly dose (tablets)	1.98	1.92			

^{1.} Three ecstasy nonusers failed to indicate their frequency of alcohol use

^{**} p<.01; * p<.05.

Table 2: Use of other illicit drugs

	Ecstasy Users		Non-Ecstasy Users			
	Mean	S.D	n	Mean	S.D.	n
<u>Lifetime Use</u> Amphetamine (g)	170.20	242.02	10	-	-	-
Cannabis (joints)	3319.43	3430.05	21	546.40	606.66	5
Cocaine (g)	68.81	67.96	10	-	-	-
Frequency (current users only) Times per week						
Amphetamine	1.18	1.86	9	-	-	-
Cannabis	2.82	3.00	20	0.80	1.25	5
Cocaine	0.42	0.34	10	-	-	-
Length of Use (we	akc)					
Amphetamine	103.73	87.14	11	78.00	110.31	2
Cannabis	298.38	145.67	23	189.37	140.68	13
Cocaine	116.88	65.51	12	151.00	142.84	2
Average Weekly d Amphetamine (g)	<u>ose</u> 2.33	4.52	10	-	-	-
Cannabis (joints)	13.00	14.65	20	2.43	3.76	5
Cocaine (g)	1.31	1.98	10	-	-	-

Table 3

Correct Syllogistic Responses for ecstasy users and non-users

Ecstasy Users		Non Ecstasy Users	
Mean	S.D.	Mean	S.D.
3.14	1.94	4.64	2.00**
0.79	1.21	0.71	1.12
0.45	0.95	1.08	1.26*
	Mean 3.14 0.79	Mean S.D. 3.14 1.94 0.79 1.21	Mean S.D. Mean 3.14 1.94 4.64 0.79 1.21 0.71

^{*} p<.05; ** p<.01

Table 4
Syllogistic Reasoning Errors for ecstasy users and non-users

Error type	Ecstasy	Users	Non Ecsta	asy Users
Models	Mean	S.D.	Mean	S.D.
Incorrect				
One-model	1.14	1.38	0.92	1.21
NVC	3.48	2.61	5.17	2.16
Three-model	3.28	2.43	4.75	1.94
Total	7.90	4.59	10.83	3.92
No Response				
One-model	3.72	1.62	2.38	1.53
NVC	2.93	2.19	1.41	1.25
Three-model	4.28	2.03	2.21	1.61
Total	10.93	5.08	6.00	3.49

Table 5

Correlation coefficients between various measures of illicit drug use and syllogistic reasoning errors.

Measure/	n	Syllogistic	Syllogistic
Illicit Drug		Reasoning Incorrect	Reasoning Non-
		Responses	Responses
Total Use		•	•
Ecstasy	53	381**	.540***
Cannabis	41	360**	.363**
Cocaine	43	071	.160
Amphetamine	50	066	.140
Frequency			
Ecstasy	52	292*	.398**
Cannabis	40	343*	.242
Cocaine	42	202	.256
Amphetamine	48	.022	.045
Alcohol	51	320*	.335*
Average			
Weekly Dose			
Ecstasy	53	324**	.468***
Cannabis	40	263*	.290*
Cocaine	42	288*	.445**
Amphetamine	49	.012	.060
Alcohol	53	230*	.246*
User/Non User			
Ecstasy	53	.344**	492***
Cannabis	53	030	.106
Cocaine	53	.279*	389**
Amphetamine	53	.053	122

Notes: In the case of total use, frequency, and average weekly dose, a value of zero was entered for nonusers of the drug in question. For the User/Nonuser variable, users were coded zero and nonusers '1'.

^{***} p<.001; ** p<.01; * p<.05; one tailed, unadjusted for multiple comparisons.

The mean of 3.14 was significantly greater than 1 the number which might have been achieved by chance, t(28) = 5.93, p<.001.