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Fisk, JE, Montgomery, C and Murphy, PN (2009) The Association Between the Negative Effects Attributed to Ecstasy Use and Measures of Cognition and Mood Among Users. EXPERIMENTAL AND CLINICAL PSYCHOPHARMACOLOGY. 17 (5). pp. 326-336. ISSN 1064-1297

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The association between the negative effects attributed to ecstasy use and measures of cognition and mood among users.

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Abstract

Objectives: In self reports, abstinent ecstasy/polydrug users claim that they experience certain ongoing affective and psychological changes including elevated anxiety, arousal and depression. In addition, various aspects of cognition (e.g. everyday memory, reasoning, executive functioning) appear to be affected. The present paper investigated the link between these two psychological sequelae. *Methods:* 95 ecstasy/polydrug users completed tests of reasoning, intelligence, information processing speed, executive functioning, and everyday memory. Affect was measured via a mood adjective checklist. Adverse effects attributed to ecstasy were measured via responses to adjectives reflecting changes in users since they started using the drug. In addition, indicators of sleep quality and daytime sleepiness were obtained. *Results:* Users attributed a number of adverse effects to ecstasy, namely heightened irritability, depression, paranoia and deteriorating health. Adverse effects were significantly and negatively correlated with aspects of intelligence, everyday memory and sleep quality. Length of use of ecstasy use was positively correlated with adverse effects. *Conclusions:* While many users attribute a number of adverse affects to their use of ecstasy it remains unclear whether these self perceptions are a corollary of the psychopharmacological effects of the drug or reflect factors which in fact predate its use.

Keywords: ecstasy, mood, adverse effects, intelligence

The present research is concerned with those individuals who consume the street drug ecstasy, usually along with a range of other illicit substances. The main ingredient of ecstasy is 3, 4-methylenedioxymethamphetamine (MDMA). In a review of the literature, Parrott (2004) notes that since the late 1990s, in terms of psychoactive ingredients, chemical analysis reveals that most ecstasy tablets consisted of between 80-100% MDMA with the typical dose increasing during the first half of the present decade. Previous research from our laboratory has revealed that ecstasy/polydrug users are impaired on a range of cognitive measures compared to non-ecstasy using controls (Montgomery, Fisk, & Newcombe, 2005a; Montgomery, Fisk, Newcombe, & Murphy, 2005b; Montgomery, Fisk, Newcombe, Wareing & Murphy, 2005c; Montgomery, Fisk, Wareing & Murphy, 2007). However, it has sometimes proved difficult to establish a link between indicators of the level of ecstasy use (e.g. measures of lifetime use) and cognitive outcomes. It is possible that different patterns of drug taking may be associated with different levels of risk. For example, it may be the case that those persons who take ecstasy while engaging in excessive physical activity for prolonged periods of time in hot environments without adequately monitoring fluid intake are at particular risk from ecstasy-related neurotoxicity, (Parrott, Rodgers, Buchanan, Ling, Heffernan, & Scholey, 2006). Alternatively it may be the number of tablets typically taken on each occasion of use (Thomasius, Petersen, Buchert, Andresen, Zapletalova, Wartberg, et al. 2003) which determines the neurotoxic potential. Individual differences in enzyme regulated metabolic processes have also been implicated in adverse effects related to ecstasy use (Schifano, 2004). It is clear that not all ecstasy users suffer adverse effects as a consequence of using the drug and there is no obvious way of determining which

users will exhibit performance deficits. One possible means of identifying those at risk may be to directly ask users whether or not ecstasy has had any adverse effects on different aspects of their behaviour.

A number of studies have revealed that ecstasy/polydrug users report various adverse psychiatric and affective symptoms (e.g., Parrott, Buchanan, & Scholey, 2002). What is less clear is whether or not these are a consequence of using ecstasy or whether they reflect some pre-existing disposition, or a combination of these two factors. For example, an individual may report themselves as being generally depressed (perhaps as a consequence of circumstances pre-dating ecstasy use) and use ecstasy as a form of self medication so as to temporarily improve their mood state. An additional explanation for self-reported ecstasy-related deficits may be that those individuals who volunteer to participate in studies of substance abuse do so because they already suspect (rightly or wrongly) that ecstasy might have harmed them in some way. Deficits may therefore be perceived rather than real (Bedi & Redman, 2008). This self-selection bias might be because of exposure to press reports or other sources of information which purport to link drug use with adverse outcomes.

It is also worthy of note that some researchers have failed to find evidence of increased psychopathology among ecstasy users. For example, while 40% of Murphy, Wareing, and Fisk's (2006) sample reported an increase in adverse reactions, e.g., confusion, paranoia, and depression, since commencing ecstasy use, 42% actually reported a reduction in negative experiences. Morgan (1998) found no differences in self-reported mood, anxiety, and aggression, between ecstasy users, polydrug controls and non-drug users and Dafters, Duffy, and O'Donnell (1999) found that there was no relationship between the amount of ecstasy consumed during the previous 12 months and measures of depression and positive and negative affectivity. Furthermore

Thomasius et al (2003) reported that adverse symptoms were associated with polydrug use in general rather than specifically ecstasy use. Similar findings were reported by Bedi, Van Dam and Redman (2008) who also note that responses to self-report checklists may reflect transient sub-acute post-intoxication effects rather than clinically significant psychiatric problems. Findings from another recent study which utilised a longitudinal design revealed that while a positive association existed between self reported depression and lifetime ecstasy use, the levels reported were not clinically significant and declined in both current and abstinent ecstasy users over a 24 month period (Falck, Wang & Carlson, 2008).

Nonetheless, a number of studies using self-report measures do report adverse ecstasy-related effects. Parrott and Lasky (1998) observed that two days after consuming ecstasy, users were more depressed, unsociable, and ill-tempered, compared to nonusers. Ecstasy users also felt more abnormal and experienced unpleasant feelings to a greater degree than controls. Relative to controls, Curran and Travill (1997) reported that while ecstasy users exhibited an elevated mood state on-drug, five days later they exhibited mood impairment and heightened depression. Similarly, Gamma, Buck, and Berthold (2001) found that ecstasy users were more depressed relative to nonusers and more recently a longitudinal study revealed that they exhibited elevated anxiety, obsessive/compulsive tendencies and impaired interpersonal sensitivity on the SCL-90 measure (Thomasius, Zapletalova, & Petersen, 2006). These deficits were evident in both current and former ecstasy users and persisted over the duration of the study.

Parrott et al's (2002) ecstasy-using respondents indicated that they had suffered depression, memory problems, anxiety, mood fluctuation, poor concentration, and physical problems (infections, tremors/twitches and weight loss) as

a consequence of their ecstasy use. The likelihood of reporting symptoms increased with the extent of ecstasy use. Ecstasy users were also found to be significantly more depressed compared to controls in a study by McCardle, Luebbers, and Carter (2004) and more recently, Lamers, Bechara, and Rizzo (2006) found that relative to cannabis only and drug naïve controls, ecstasy/polydrug users were significantly more depressed and exhibited higher levels of anxiety. Finally, Curran, Rees, and Hoare (2004) and Hoshi, Pratt, and Mehta (2006) found that ecstasy users were more likely to attribute aggressive meanings to ambiguous sentences compared to nonusers.

Relatively few studies have examined the mediating role of psychological affect in underpinning ecstasy-related cognitive deficits. McCardle et al (2004) found that ecstasy-related deficits in recall remained statistically significant following statistical controls for group differences in depression. However, it remains unclear whether the adverse emotional and affective changes specifically attributed to ecstasy use are associated with adverse outcomes in other aspects of cognition.

To summarise, there is evidence for ecstasy-related impairment in aspects of psychological affect and psychological health (e.g., Parrott et al, 2002) which in some instances co-occurs with deficits in aspects of cognition (Thomasius et al, 2006). Adverse psychopathology is not always evident (Bedi & Redmond, 2008) nor are cognitive deficits always found (McCardle et al, 2004). It is apparent therefore that adverse outcomes are not present in all ecstasy users and it may be that those who self-report adverse effects arising from ecstasy use in aspects of mood, concentration, and emotional expression may be the same group who experience cognitive and other deficits. Aside from the evidence that psychiatric conditions such as schizophrenia are associated with specific forms of cognitive impairment, it has also been documented that sub-clinical levels of depression and anxiety are associated with

cognitive impairment (e.g. Ramponi, Barnard, & Nimmo-Smith, 2004; Sedek & von Hecker 2004). It may be that ecstasy-related deficits in cognition and affect are concentrated among those who self-report adverse effects of using the drug.

Therefore, various cognitive and affective measures were analysed including those where ecstasy-related deficits have previously been observed in order to establish whether scores on these were negatively related to the number of self-reported adverse reactions to the drug.

It was predicted that indicators of recent and longer term ecstasy use would be positively related to the number of adverse reactions. No association between the use of other drugs and self-reported adverse reactions to ecstasy was predicted. Adverse reactions were predicted to be negatively associated with performance in other aspects of cognition including intelligence, memory, and executive functioning. Adverse reactions were also predicted to be associated with diminished psychological affect, impaired general health and sleep quality, and psychophysiological measures including arousal.

Method

Design

Correlational analysis is used with the number of adverse ecstasy-related effects reported being correlated with respectively, recent and longer term patterns of drug use, indicators of intelligence, aspects of executive functioning, measures of day time sleepiness and physiological arousal, aspects of psychological affect and everyday memory functioning. Since predictions are directional in nature, one-tailed probability values are reported.

Participants

This study makes use of an existing database that was constructed over the period 2002 to 2007. The database includes 95 ecstasy/polydrug users (53 males, 42 females; mean age 21.56, S.D. 1.92), individuals who currently use or who have previously used ecstasy. In terms of illicit drugs, three participants had used only ecstasy, a further 17 had used ecstasy and one other drug, while the remainder were polydrug users in the sense that they used ecstasy along with two or more of the following: cocaine, cannabis, and amphetamine. This database enabled us to explore differences between ecstasy users and nonusers in a range of cognitive functions and the results of this research have been reported elsewhere (e.g., Montgomery et al 2005a; 2005b; 2005c; 2007). However, we have never before examined how self perceptions among abstinent users regarding the effects of their ecstasy use, relate to outcomes on other important psychological constructs and that is the purpose of the present paper. The participants whose data are included in our database were recruited via direct approach to university students, and by the snowball technique. Participants were requested to refrain from ecstasy use for at least 7 days prior to testing and were also requested not to use any other illicit drug for at least 24 hours prior to testing. Mean lifetime ecstasy dose is 328.02 tablets (SD 415.68) and mean frequency of use 0.39 times per week (SD 0.44), although at the time of testing 21 users were long term abstinent (no use in last 6 months).

Materials/ Measures

Measures of Intelligence and Processing Speed. Analogical reasoning was assessed via word pair analogies (based on the SATS analogy quiz). Participants are presented with two capitalised words (e.g. MASON: STONE), and the five possible

answers in which the one of the word pairs reflected a similar analogy (e.g. Carpenter: Wood). There are 30 items and participants receive a total score for the number of analogies correctly inferred from the word pairs.

Fluid intelligence was measured via Raven's Progressive Matrices (Raven, Raven, & Court, 1998), and premorbid intelligence was assessed via the National Adult Reading Test (NART- Nelson, 1982). The processing speed task involves the comparison of pairs of stimuli with the participant required to determine whether the pairs were the same or different as quickly as possible (see Wareing, Fisk, Montgomery, Murphy, & Chandler, 2007 for a complete description). Processing speed has been associated with intelligence scores with fast processors typically scoring higher on intelligence tests (e.g., Stough, Nettelbeck, Cooper, & Bates, 1995).

Measures of Executive Functioning (see Montgomery et al 2005b for full descriptions).

Measures of the separable components of executive functioning were administered relating to the updating, switching, access, and inhibition component processes (Fisk & Sharp, 2004). Computation span is an indicator of the updating component process and involves the serial recall of digit sequences. The sequences are presented simultaneously with a dual task. Participants achieve a span score analogous to digit span which corresponds to the maximum number of digits recalled in the correct order subject to the requirement that the dual task is completed without error.

Letter updating involves presenting participants with sequences of consonants which vary in length (four different sequence lengths are used). In each trial the participant is unaware of the number of letters that will be presented. The task is

tailored to the participant's span, such that at the end of each sequence they are asked to recall 'n' letters, where 'n' is equal to their span (i.e., 4, 5, or 6 letters).

Two tasks measure the switching component of executive functioning. In the plus-minus task participants solve a number of simple arithmetic problems alternating between addition and subtraction. In the number letter task, participants alternately classify number letter pairs as vowel/consonant or odd/even.

The Chicago Word Fluency test is believed to measure the efficiency of access to semantic memory. Within fixed time limits, participants write down as many words as possible beginning with the letter S and as many four letter words beginning with the letter C. Semantic fluency is administered in a similar manner except that participants are asked to produce as many animal names as possible.

In the random letter generation task participants are asked to produce letters in a random sequence by imagining that they are drawing the letters of the alphabet from a hat, speaking each letter produced aloud and then replacing it and repeating the procedure. The task is repeated three times with letters produced at 4, 2, or 1 second intervals and is believed to load on the inhibition executive component process.

These measures of executive functioning have been used extensively in the past (see for example, Fisk & Sharp, 2004).

Real World Memory Measures (see Fisk & Montgomery, 2008, for full descriptions).

Four self-report real-world memory measures were administered. The Everyday Memory Questionnaire (EMQ; Sunderland, Harris, & Baddeley, 1983) is a self-report measure of memory lapses in everyday activities. The Cognitive Failures Questionnaire (CFQ; Broadbent, Cooper, FitzGerald, & Parkes, 1982) measures the prevalence of attentional lapses in everyday contexts. The Cognitive Failures

Questionnaire for Others is completed by the participant's 'significant other' and assesses the extent to which that person believes that the participant exhibits attentional lapses. Prospective memory is assessed using the Prospective Memory Questionnaire (PMQ), (Hannon, Adams, Harrington, Fries-Dias, & Gipson, 1995). The PMQ provides measures of three aspects of PM short-term habitual PM, long-term episodic PM, and internally cued PM. In addition, 14 questions make up the "techniques to remember" scale, which provides a measure of the number of strategies used to aid remembering. The reliability and validity of the CFQ, EMQ and PMQ have been documented previously (see, for example, Hannon et al, 1995; Royle & Lincoln, 2008; Wallace, 2004).

Measures of Sleep Quality and Wakefulness.

The Epworth Sleepiness Scale (ESS) measures the likelihood of dozing off during the day in various situations (Johns & Hocking, 1997). The Karolinska Sleepiness Scale (KSS; Gillberg, Kecklund, & Akerstedt, 1994) measures the participant's state of sleepiness at a given moment in time. The remaining questions set out below assessed various aspects of sleep quality. No specific time frame was specified in relation to these. Thus they reflect general perceptions.

The sleep type indicator assesses the extent to which individuals view themselves as morning types or evening types. Participants read the following statement: "We hear about people who 'feel better in the morning' or who 'feel better in the evening'. Which of these two types do you think you are?" Participants respond by selecting one of the following alternatives scored 1 to 5 respectively: A. definitely a 'morning' type; B. more 'morning' than 'evening'; C. neither one nor the other; D. more 'evening' than 'morning'; E. definitely an 'evening' type.

Sleep quality is assessed by the following question: “How well do you normally sleep at night?” Participants respond by selecting one of the following alternatives scored 1 to 4 respectively: A. very well; B. satisfactorily; C. not very well; D. very badly.

Morning tiredness is assessed by the following question: “How refreshed do you usually feel in the mornings?” Participants respond by selecting one of the following alternatives scored 1 to 4 respectively: A. very alert; B. fairly alert; C. fairly tired; D. very tired.

Psychological Affect

Mood adjective checklist: Anxiety, depression/hedonic tone, and arousal are measured by means of a mood adjective checklist (see Matthews, Jones, & Chamberlain, 1990; Wareing, Fisk, & Murphy, 2000). Of the 18 words on the checklist, six words map onto each of these three constructs. For each word participants rate themselves as either: not at all, slightly, moderately, very, or extremely, with high scores indicative of higher levels of perceived arousal, anxiety, and depression.

Drug Use

Patterns of drug use and other relevant lifestyle variables are investigated via means of a background questionnaire (Montgomery et al, 2005b; Murphy et al, 2006). Ecstasy users are asked if they believe that since using ecstasy they have changed in any way. They respond to each of the following words: caring (-), paranoid (+), alert (-), depressed (+), sociable (-), aggressive (+), happy (-), healthy (-), moody (+), patient (-), irritable (+), confident (-), sad (+), loving(-), and confused (+), using a five point scale: much more 5, more 4, no change 3, less 2, and much less 1. The number of words eliciting adverse reactions is calculated. Responses of 4 or 5 to words

suffixed with (+) constitute an adverse reaction as do responses of 1 or 2 to words suffixed with (-). Ecstasy users are also asked to respond 'Yes' or 'No' to the following questions: 'Do you take any sort of precautions when using ecstasy?', 'When under the influence of ecstasy do you take rest breaks when dancing?', 'When under the influence of ecstasy do you monitor your fluid intake?', and 'Is there a maximum number of ecstasy tablets you will take in one session?'

In relation to drug use, participants are asked a range of questions including duration of use, and the last time that they had used each drug. Participants are also questioned concerning their history of drug use, i.e., when they began taking specific illicit drugs and the last occasion when each drug was consumed. The amount consumed of each drug during the previous 10 and 30 days is also assessed. Participants also indicate the number of different illicit drugs that they had previously consumed.

Procedure

Participants are informed of the general purpose of the studies, and written informed consent is obtained. The tasks are administered under laboratory conditions, and a computer running MS-DOS is used for the computer based tasks. Participants are fully debriefed, paid £20 in store vouchers, and given drugs education leaflets. The studies were approved by the Liverpool John Moores University Research Ethics Committee, and were administered in accordance with the ethical guidelines of the British Psychological Society.

Results

The average number of reported adverse reactions was 2.89 (s.d. 2.86). The median was 2 and the range was 0 to 11. While kurtosis was not a problem, $z=0.11$, $p>.05$, the distribution was severely positively skewed, $z=3.83$, $p=.0001$. Following

transformation (taking the inverse), skewness was reduced but remained problematic, $z=2.97$, $p=.0015$. For this reason non parametric tests were used. Twenty six percent of the sample reported no adverse effects, 27% one or two, 21% three or four, and 25% five or more adverse effects. Inspection of Table 1 reveals that a substantial proportion of the sample indicated that ecstasy had made them more paranoid and/or less healthy (over 40% in both cases), over 30% in each case indicated that ecstasy had made them more moody and/or more irritable, and over 20% less patient and/or more confused. In all of these cases, the other users predominantly reported no change and there were only one or two users reporting positive changes. However on some of the other aspects of behaviour substantial number of users reported positive outcomes, for example that ecstasy had made them more caring, sociable, happy, and confident. While cumulatively almost half of the participants reported three or more adverse effects, it is noteworthy that the modal response to each individual question was 'no change'.

Examination of Table 2 reveals that there was no significant relationship between the number of reported adverse ecstasy-related effects and the amounts of the various illicit drugs consumed during the previous 10 days (although in two cases the correlations were associated with p values of .053 and .063). Among those ecstasy users who smoked tobacco there was a positive correlation between the number of cigarettes consumed in the previous 10 days and the number of adverse reactions reported. There was no association between the amount of various illicit drugs consumed within the previous 30 days and reported adverse reactions. Inspection of Table 3 reveals that there was a positive association between the length of ecstasy use and reported adverse reactions. The period of abstinence for various illicit drugs was unrelated to reported adverse reactions. However, the association between the number

of reported adverse reactions and the period of abstinence from cannabis use was associated with a probability of .065.

Measures of intelligence (Ravens progressive matrices and analogical reasoning) were significantly and negatively related to the reported number of adverse reactions associated with ecstasy use (see Table 4). Emotional intelligence was also negatively related to the number of reported adverse reactions. However, this relationship has been explored in depth in other research from our laboratory (Craig, Fisk, Montgomery, Murphy, & Wareing, in press) and will not be discussed further here. The association between the number of errors on the processing speed task and the number of reported adverse reactions although nonsignificant was associated with a probability of .057, with those reporting more adverse reactions committing more errors. None of the measures of executive functioning were significantly associated with the number of reported adverse reactions, although the association between one of the measures of the switching component executive process and the number of adverse reactions produced a probability of .064. Those reporting more adverse reactions exhibited a larger switch cost (indicative of a greater degree of impairment). However, the association with the other measure of the switching process was not significant.

Inspection of Table 5 reveals that reported adverse reactions to ecstasy were significantly associated with short-term prospective memory (PM) problems. Furthermore, the number of reported adverse effects was positively correlated with everyday memory problems and also with the number of techniques used to aid PM recall. While in both cases the relationships were not statistically significant, they were associated with probability values of .060 and .063 respectively. The outcomes evident in Table 6 demonstrate that higher levels of reported adverse effects are

associated with sleep problems. High scores on the Karolinska, Epworth, sleep quality and morning alertness measures are indicative of sleep problems. Thus the positive correlation between these measures and the number of reported adverse effects indicated that those reporting more adverse effects were subject to impaired sleep and increased daytime tiredness. Indeed over 20% of the present sample had a score of 10 and above on the Epworth measure which is consistent with clinical levels of sleep impairment. Aside from increased daytime sleepiness, those reporting more adverse effects also had significantly lower levels of self-reported physiological arousal and in terms of their present state-of-mind, they described themselves as significantly more anxious and depressed.

Discussion

The present study assessed a range of adverse effects reported by users of ecstasy. It was found that ecstasy users reported certain psychological changes, which they attributed to their ecstasy use. Use of ecstasy was associated with increased paranoia, deteriorating health, heightened depression, increased moodiness and irritability, impatience and confusion. Some aspects of intelligence, real world (prospective) memory function, and general psychological affect (state anxiety and depression) also appear to be subject to a greater degree of impairment among those users reporting more adverse reactions. There was also a significant positive correlation between tobacco use and reported adverse effects indicating that as adverse effects increased, so did amount of tobacco consumed in the previous 10 days.

The types of adverse effects noted in the present study have been associated with cognitive deficits in other populations. For example, non-ecstasy using depressed individuals frequently exhibit memory impairments (e.g. Austin, Mitchell &

Goodwin, 2000). Thus it may be that ecstasy causes adverse effects, which in turn cause prospective memory failures, anxiety and depression. While it is possible that these affective states might have preceded the use of the drug, in the present case, our participants specifically attributed them to ecstasy use. Therefore the present results raise the possibility that ecstasy use gives rise to adverse reactions in some users which may in turn cause them to report elevated levels of depression and anxiety as well as memory impairment. However, due to our reliance on self-reports and the retrospective nature of our study, it is not possible to make a definitive statement in this regard.

The incidence of reported adverse effects supports previous research where ecstasy has been implicated. For example, Parrott and Lasky (1998) reported elevated depression and irritability; Curran and Travill (1997) likewise reported mood impairment and elevated depression. Curran et al. (2004) also reported increased perceived aggression following ecstasy use. However, the present study differs from previous research as the adverse effects reported by the ecstasy users were directly attributed to their ecstasy use. In addition, the median abstinence period was 3 weeks, with ¼ of the sample reporting abstinence for six months or more, indicating that these adverse effects are likely to persist for longer periods of time. The persistence of reported adverse effects might indicate that ecstasy use produces lasting changes to these aspects of behaviour. However, other possibilities must be acknowledged, for example, it may be that the individuals in question exhibit underlying psychopathology which possibly predates ecstasy use and which they mistakenly attribute to the drug.

Also worthy of note was the significant correlation between length of ecstasy use and adverse effects indicating that adverse effects increased with increasing length

of use. Other studies looking at various negative consequences of ecstasy use (e.g. adverse effects on memory) have found that length of use is an important factor. For example in a longitudinal study, Zakzanis and Young (2001) found that continued administration of ecstasy use over a 1-year period was associated with a decrease in memory performance. Similarly Croft, Klugman, Baldeweg, and Gruzelier (2001) and Wareing et al. (2000) found that long-term users of ecstasy are at particular risk of brain and cognitive dysfunction respectively.

Time since last use of ecstasy showed no relationship to reported adverse effects. This is consistent with the possibility that the adverse effects are an enduring consequence of using the drug rather than a sub-acute transient effect. However, the absence of a significant association between the period of abstinence and reported adverse effects might also be consistent with the possibility that they reflect some underlying psychopathology predating ecstasy use and mistakenly attributed to the drug. As for the other drugs that were considered, with one exception there was no significant correlation between time since last use and ecstasy-related adverse effects. The exception was cannabis where a negative correlation between adverse effects and time since last use was very close to significance. This is consistent with a significant reduction in anxiety over time since last cannabis use we have reported in another sample (Murphy, Erwin, Wareing, Blackman, Yanulevitch, Keane, et al, 2008).

The statistically significant correlation between adverse effects and amount of tobacco smoked in the last 10 days could be explained in a number of ways. It may be that those ecstasy users who are experiencing adverse effects smoke more to alleviate their symptoms. Alternatively, it may be that the use of tobacco actually exacerbates the adverse effects experienced. Smoking has been found to be highly comorbid with clinical and sub-clinical anxiety and depression: two of the adverse effects noted in

the present study. However it remains unclear whether smoking is a response to, or a cause of, these other factors (Gilbert & Gilbert, 1995; Morrell & Cohen, 2006; Parrott & Kaye, 1999; Parrott, Morinan, Moss, & Scholey, 2004). Nicotine may be associated with heightened or diminished anxiety depending on the sub-type and neural location of particular nicotinic (nAChR) receptors, whether the effects of nicotine treatment are to activate or desensitize these receptors, and the knock-on effects on the major neurotransmitters including dopamine. Thus whether outcomes are anxiogenic and anxiolytic is believed to depend on the specific neural pathways that are implicated (Picciotto, Brunzell, & Caldarone, 2002) and in the present context the situation is further complicated by the direct pharmacological action of ecstasy on serotonergic and dopaminergic systems. Therefore outcomes may be variable and finely balanced depending on the combined effects of MDMA and nicotine on specific neural pathways.

While the specific neuropsychopharmacological mode of action remains uncertain, it is clear that individuals do smoke to alleviate feelings of anxiety and depression. For example, sensitivity to anxiety-related symptoms (i.e., perceiving them as indicative of a loss of control and illness) may predispose individuals to smoking and it has been argued that despite its effects on physiological arousal, subjectively, nicotine has anxiolytic properties for those exhibiting anxiety sensitivity (Stewart, Karp, Pihl, & Peterson, 1997). Scheitrum and Akillas (2002) have proposed that smoking is a form of self medication which can have stimulatory or anxiolytic properties depending on the individual's personality and their underlying level of trait anxiety. Thus within this broader context, the results reported here are consistent with the possibility that users in the present sample smoked to alleviate the ecstasy-related adverse effects that they were experiencing.

Nonetheless, the possibility that smoking was a response to some pre-existing depressed or anxious state or that cigarettes were somehow directly responsible for the negative feelings experienced by users cannot be excluded. If this were the case then users might possibly misattribute their adverse reactions to ecstasy use when in fact they were pre-existing or due to the effects of nicotine. However, we re-examined the relationship between reported adverse effects and anxiety and depression excluding all those ecstasy users who smoked cigarettes. Although this reduced the sample size to just 30 participants (thereby increasing the likelihood of a Type 2 error), the correlations between adverse reactions and the two affect measures remained statistically significant, $r = .344$ and $r = .332$ for anxiety and depression respectively, $p < .05$ in both cases. Thus it appears that the positive association between reported adverse effects and respectively depression and anxiety is not limited to ecstasy users who consume nicotine but is also prevalent among non smoking ecstasy users.

An additional finding emerging from our results was the association between ecstasy related adverse effects and reported sleep problems. Research suggests that the chronic use of ecstasy causes sleep disturbances and sleep deprivation (Baylen & Rosenberg, 2006; Montoya, Sorrentino, Lukas, & Price, 2002). In the present study the adverse effects attributed to ecstasy use were significantly associated with reported sleep problems and with depressed mood. Sleep deprivation has itself been associated with negative affect in a recent human study. Those who were sleep deprived experienced significantly greater negative outcomes in relation to subjective vigour, fatigue and depression (as assessed by the Profile of Mood States questionnaire). Furthermore, relative to those who were simply sleep deprived, those who were both sleep deprived and required to perform moderate intermittent exercise

during the period of deprivation were found to be particularly prone to negative mood disturbance (Scott, McNaughton, & Polman, 2006). Again the association between negative mood, sleep deprivation and exercise would appear to be especially relevant to ecstasy users given the particular circumstances in which the drug is consumed.

In the sleep literature individuals have been classified according to whether they see themselves as morning or evening types (Horne & Ostberg, 1976). In a recent study, Selvi, Gulec, Agargun, and Besiroglu (2007) found that morning types were more susceptible to adverse mood effects (depression) following sleep deprivation with evening types showing no adverse mood effects. In the present study however, morningness-eveningness was not significantly correlated with the adverse effects associated with ecstasy. Thus, it appears that the adverse effects that were prevalent among users and the negative mood states associated with them are not mediated or exacerbated by this aspect of sleep type.

In our previous research we have documented a number of instances where ecstasy/polydrug users exhibited performance decrements relative to non ecstasy users (Montgomery & Fisk, 2007; Montgomery et al 2005b; 2007). If these deficits were more evident in those users who reported adverse effects then in the present sample it might expected that a significant correlation would exist between self-reported adverse effects and scores on those measures where deficits have been previously documented. This expectation was supported by the significant correlations with some measures of function (e.g. prospective memory, depression, anxiety, arousal, sleep quality). However, there was no significant correlation between previously well documented (e.g. updating- Montgomery et al. 2005b) decline in aspects of executive function and adverse effects. Conversely, areas where we have not previously documented differences between ecstasy polydrug users and nonusers **were**

significantly correlated with adverse effects (e.g. aspects of intelligence). It is unclear why this dissociation occurred and clearly further research may be needed to shed light on these contrasting outcomes. It may be that those apparent ecstasy-related deficits which occur independently of reported adverse effects are not actually a consequence of ecstasy use but perhaps reflect some pre-existing difference between users and nonusers which has its origins before the initiation of drug use. Consistent with this possibility, in the context of the longer term consequences of cannabis use Pope (2002) has emphasised the importance of considering whether or not the apparent differences between users and nonusers might reflect pre-morbid conditions perhaps in sociodemographic factors, personal dispositions, or underlying psychopathology.

There were a number of limitations to the present study. As with much research in this area we relied on self-reports to confirm recent use/abstinence. Similarly, we asked individuals to estimate their use of various drugs and clearly individuals may have been inaccurate when reporting these values. Due to constraints on resources it was not possible to resort to physiological testing methods such as hair analysis, urinalysis or breathalysers. While this would have been preferable, it is commonplace in research among ecstasy users to rely on self report measures (e.g. Fox, McLean, Turner, Parrott, Rogers, & Sahakian, 2002; Morgan 1999). Nonetheless, even if our participants were accurate in their self reports, it is possible that recent use may have in some way affected their responses. For example, Pope, Gruber, Hudson, Huestis, & Yurgelun-Todd (2001) have noted that residual amounts of cannabinoids remain present in the system for up to 30 days after the last use of cannabis.

A further limitation was the use of the snowball method of recruitment. While this is common among researchers operating in the substance abuse area (e.g., Solowij, Hall, & Lee, 1992) it does have its limitations. First it is open to self-selection bias in the sense that those users who are willing to participate in research of this kind may not be representative of users in general. Second, a condition of ethical approval for the study was that users would be properly informed, debriefed and provided with drug education leaflets. While the information provided was generally neutral in tone, and the information sources listed generally adopted a harm reduction approach, it was stated that the experimenters did not condone the use of illicit drugs. Furthermore it was stated that the purpose of the study was to establish whether illicit drug users performed differently on various measures and the extent to which any differences observed were attributable to ecstasy or to the effects of other drugs. While we did not explicitly mention deficits or impairment the information provided may have encouraged participation from those persons who were already concerned about aspects of their use (Bedi, & Redman, 2008).

For example, as a direct result of reading about the background to our research, or through prior exposure to negative information sources in the media or via friends and personal contacts, users may have approached our study with the preconception that ecstasy is harmful. These expectations may have affected the responses that were produced with users endorsing adverse effects not because they actually experienced them but because they believed that they should. Alternatively they may have misattributed pre-existing or unrelated conditions to ecstasy use. Cole, Michailidou, Jerome, & Sumnall (2006) have demonstrated that inducing such stereotype threat may actually cause users to perform worse on cognitive measures.

Thus again given our method of recruitment our sample may not have been representative of ecstasy users in general.

In summary, the present paper found that ecstasy/polydrug users reported a range of adverse psychological effects which they attributed to ecstasy use. These adverse effects were significantly correlated with length of use of ecstasy raising the possibility that adverse effects are a long-term consequence of using the drug. Future research should seek to further investigate the link between reported adverse effects and measures of psychological functioning. In the present paper executive function measures were not correlated with adverse effects while some everyday memory measures, and some mood measures were. Thus future research should seek to elucidate this link while at the same time attempting to address some of the methodological limitations evident in research of this kind.

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Table 1

Number of ecstasy users indicating changes in behaviour

| Ecstasy has made me: | Much Less | Less | No Change | More | Much More |
|----------------------|-----------|------|-----------|------|-----------|
| Caring | 0 | 3 | 73 | 16 | 3 |
| Paranoid | 1 | 2 | 53 | 35 | 4 |
| Alert | 1 | 15 | 71 | 6 | 2 |
| Depressed | 0 | 2 | 66 | 25 | 2 |
| Sociable | 0 | 3 | 43 | 41 | 8 |
| Aggressive | 2 | 6 | 76 | 9 | 2 |
| Happy | 0 | 8 | 66 | 16 | 5 |
| Healthy | 3 | 39 | 50 | 3 | 0 |
| Moody | 0 | 1 | 62 | 32 | 0 |
| Patient | 1 | 21 | 68 | 5 | 0 |
| Irritable | 0 | 0 | 66 | 28 | 1 |
| Confident | 0 | 6 | 56 | 25 | 8 |
| Sad | 0 | 3 | 79 | 13 | 0 |
| Loving | 0 | 0 | 75 | 17 | 3 |
| Confused | 0 | 0 | 71 | 23 | 1 |

Table 2

Correlations between Reported Adverse Effects of Ecstasy and the amount the major Psychoactive Drugs consumed in the previous 10 or 30 days.

| | Median | Inter-quartile Range | Correlation with Adverse Reactions Measure (Spearman's rho) | p | n |
|------------------------------------|--------|----------------------|---|------|----|
| Amount Consumed (previous 10 days) | | | | | |
| Ecstasy (tablets) | 0 | 1 | -.159 | .063 | 94 |
| Alcohol (units) | 17 | 20.5 | -.026 | .405 | 89 |
| Amphetamine (grams) | 0 | 0 | -.044 | .340 | 91 |
| Cannabis (joints) | 0 | 2.13 | .168 | .053 | 94 |
| Cocaine (grams) | 0 | 0 | -.001 | .497 | 94 |
| Tobacco (cigarettes) | 0 | 77.50 | .339 | .004 | 60 |
| Amount Consumed (previous 30 days) | | | | | |
| Ecstasy (tablets) | 1 | 4 | -.013 | .449 | 93 |
| Amphetamine (grams) | 0 | 0 | -.044 | .340 | 91 |
| Cannabis (joints) | 3 | 24 | .115 | .139 | 90 |
| Cocaine (grams) | 0 | 1 | .048 | .340 | 78 |

Table 3

Correlations between Reported Adverse Effects of Ecstasy and respectively Length of Use and period of Abstinence for the Main Psychoactive Drugs

| | Median | Inter-quartile Range | Correlation with Adverse Reactions Measure (Spearman's rho) | p | n |
|--|--------|----------------------|---|------|----|
| Length of use (weeks): | | | | | |
| Ecstasy | 152 | 163 | .237 | .011 | 94 |
| Alcohol | 372 | 156 | -.029 | .392 | 93 |
| Amphetamine | 128 | 216 | .103 | .284 | 33 |
| Cannabis | 266 | 193 | .098 | .199 | 76 |
| Cocaine | 120 | 132 | .107 | .184 | 73 |
| Tobacco | 380 | 194 | .159 | .099 | 67 |
| Weeks since last use: | | | | | |
| Ecstasy | 3 | 11 | .026 | .402 | 94 |
| Alcohol | 0.14 | 0.22 | -.112 | .142 | 93 |
| Amphetamine | 24 | 96 | .107 | .277 | 33 |
| Cannabis | 0.57 | 2.86 | -.175 | .065 | 76 |
| Cocaine | 3 | 13.14 | .011 | .465 | 73 |
| Tobacco | 0.01 | 0.14 | -.135 | .137 | 67 |
| Number of Different Illicit Drugs Consumed | 3 | 1 | .190 | .033 | 94 |

Table 4
 Correlations between Reported Adverse Effects of Ecstasy and respectively Measures of Intelligence and Executive Functioning

| | Median | Inter-quartile Range | Correlation with Adverse Reactions Measure (Spearman's rho) | p | n |
|---------------------------------------|--------|----------------------|---|------|----|
| Intelligence | | | | | |
| Ravens Progressive Matrices | 48.5 | 8 | -.184 | .038 | 94 |
| NART | 28 | 9 | -.020 | .426 | 94 |
| Analogical Reasoning | 12.5 | 8.75 | -.283 | .038 | 40 |
| Emotional Intelligence | 120 | 15.75 | -.329 | .005 | 60 |
| Processing Speed | -0.08 | 0.79 | .007 | .480 | 55 |
| Processing Speed (errors) | -0.10 | 0.71 | .216 | .057 | 55 |
| Executive Functioning | | | | | |
| Computation Span (updating) | 4 | 3 | .014 | .446 | 94 |
| Letter Updating | 3.92 | 1.12 | .007 | .481 | 55 |
| Plus-Minus (switching) | 1.43 | 0.38 | -.023 | .441 | 43 |
| Number-Letter (switching) | 1.64 | 0.29 | .235 | .064 | 43 |
| Letter Fluency (access) | -.050 | 1.27 | .161 | .207 | 28 |
| Semantic Fluency (access?) | -.130 | 1.50 | -.210 | .141 | 28 |
| Random Letter Generation (inhibition) | -0.10 | 0.53 | -.078 | .230 | 93 |

Table 5
 Correlations between Reported Adverse Effects of Ecstasy and Measures of Real World memory

| | Median | Inter-quartile Range | Correlation with Adverse Reactions Measure (Spearman's rho) | p | n |
|-----------------------------------|--------|-------------------------|--|------|----|
| Everyday Memory | 91 | 44 | .212 | .060 | 55 |
| Cognitive Failures (self-report) | 45 | 20 | .130 | .165 | 58 |
| Cognitive Failures (other-report) | 13 | 13 | .179 | .152 | 35 |
| Prospective Memory (Total) | 2.47 | 1.05 | .267 | .038 | 45 |
| Long Term | 2.64 | 1.46 | .191 | .105 | 45 |
| Short Term | 1.14 | 0.57 | .290 | .027 | 45 |
| Internally Cued | 2.80 | 1.36 | .121 | .215 | 45 |
| Techniques | 2.71 | 2.04 | .232 | .063 | 45 |

Table 6

Correlations between Reported Adverse Effects of Ecstasy and respectively Measures of Sleep Quality, Tiredness, Health, and Psychological Affect

| | Median | Inter-quartile Range | Correlation with Adverse Reactions Measure (Spearman's rho) | p | n |
|--|--------|----------------------|---|------|----|
| Sleep Type (Morning or Evening) | 4 | 1 | -.022 | .415 | 95 |
| Sleep Quality | 2 | 1 | .194 | .030 | 95 |
| Hours sleep per night | 8 | 2 | -.076 | .231 | 95 |
| Morning Alertness | 3 | 1 | .275 | .004 | 95 |
| Epworth Daytime Sleepiness | 6 | 5 | .174 | .047 | 93 |
| Karolinska Daytime Sleepiness (start of testing) | 5 | 2 | .202 | .057 | 63 |
| Karolinska Daytime Sleepiness (end of testing) | 5.5 | 3 | .344 | .003 | 62 |
| Arousal | 20 | 5.5 | -.264 | .005 | 93 |
| General Health (Self Report) | 4 | 1 | -.298 | .002 | 95 |
| Anxiety | 12 | 6 | .414 | .000 | 93 |
| Hedonic Tone/Depression | 13 | 4 | .329 | .001 | 93 |