Self Reported Sleep Quality and Cognitive Performance in Ecstasy Users.

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Running Head: Sleep and cognition in ecstasy users.

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Abstract

Objectives: Research suggests that ecstasy users exhibit psychobiological changes relative to nonusers such as altered sleep patterns and cognitive deficits. In turn, it has been suggested that sleep quality may be a mediator of such cognitive deficits in ecstasy users. The present study sought to investigate this proposed relationship. *Methods:* Aspects of cognitive functioning in 104 ecstasy users and 103 nonusers obtained from our previous studies were reanalysed to explore the extent to which ecstasy-related group differences were attributable to differences in sleep quality. Cognitive function was assessed via the computation span test, consonant updating, paired associate learning, syllogistic reasoning and word fluency. Sleep quality was measured via the Epworth Sleepiness Scale (ESS), and the Karolinska Sleepiness Scale (KSS). *Results:* Ecstasy users performed worse than nonusers on all cognitive measures. While no differences were observed on the ESS, ecstasy users reported greater tiredness at the beginning of testing than nonusers. When the sleep variables were included as covariates, the effects of ecstasy on all cognitive measures remained significant. *Conclusions:* The results of the present study suggest little evidence for the mediating effects of sleep on cognitive function in ecstasy users.

Introduction

Research from our laboratory has previously demonstrated that ecstasy users are impaired on executive function (spatial working memory- Wareing et al. 2004, memory updating- Montgomery et al. 2005a, access to semantic memory- Montgomery et al. 2005a) and other working memory/executive based tasks (associative learning- Montgomery et al. 2005b, syllogistic reasoning- Fisk et al. 2005; Montgomery et al. 2005c). Similar findings have been observed by other authors (see Morgan, 2000, for a review of the literature). Apparent ecstasy-related deficits may be mediated by other drug use (Croft et al, 2001; Dafters et al 2004) although results from other studies suggest that ecstasy-related deficits remain following control for the use of other illicit drugs (Fisk et al, 2004; Reay et al 2006). Other potential mediators include lifestyle differences between users and nonusers such as exercise intensity, pre-morbid conditions and sleep-related impairments, (Cole et al, 2002; Cole & Sumnall, 2003; Huxster et al. 2006). However these have yet to be thoroughly explored.

With regard to the last of these potential mediators, previous research has shown that ecstasy users exhibit disturbed sleep patterns. Given that ecstasy users also exhibit cognitive deficits, the present study sought to investigate the extent to which such cognitive deficits are mediated by degraded sleep in ecstasy users. Primary evidence from subjective accounts of ecstasy users suggests that they are aware that they have less sleep when using than when not using ecstasy. Baylen and Rosenberg (2006) reviewed 24 studies of the acute subjective effects of ecstasy (i.e. occurring within 24 hours after use). Of the studies that assessed sleep, a range of between 9-85% of participants reported "sleeplessness" as a subjective effect of ecstasy. This is corroborated in another review where it is reported that the chronic use of ecstasy

causes sleep disturbances and sleep deprivation (Montoya et al. 2002). With ecstasy, the primary effects on sleep may be similar to those of other amphetamine analogues such as MDE; Gouzoulis et al. (1992) administered 140mg of MDE to sleeping participants, who awoke 60-120 minutes after administration, and stayed awake for 150+ minutes (resulting in a significant decrease in total sleep time). While it appears logical that disturbance of sleep may be a primary subjective effect of ecstasy due to its stimulant like properties, studies in ecstasy users also report that these effects may be longer lasting. Parrott et al. (2006) report that 40% of the 209 ecstasy users in their study attributed poor sleep when "off drug" to their use of ecstasy. Another recent study (Huxster et al. 2006) also found that the "restless sleep" factor of the SCL-90-R was elevated in ecstasy users, and users reported sleep disturbances for 48 hours after use.

Some studies looking at the longer lasting effects have also shown that ecstasy use is associated with decreases in sleep time. For example, Allen et al. (1993) assessed the sleep of ecstasy users via EEG. Abstinent users of ecstasy were found to have significantly less total sleep time, and also significantly less Non-REM sleep, which was due to an average of 37 minutes less sleep at stage 2. Contrasting with these findings, McCann et al. (unpublished, cited in McCann et al. 2000) found that ecstasy users actually have more efficient sleep, with increases in deeper sleep at stages 3 and 4 (although the authors state that the differences between this study and previous studies may be due to differences in characteristics of the users and their drug use).

The balance of the evidence set out above indicates that ecstasy users are subject to altered sleep patterns and impaired sleep quality. In turn, sleep deprivation and sleep disorders have been shown to adversely affect memory (see Maquet, 2001

for review). In a review of sleep deprivation studies, Harrison and Horne (2000) conclude that performance on tasks that utilise the frontal lobes is greatly affected by sleep deprivation. They have also shown that decision-making and reasoning are also impaired after one night of sleep loss (Harrison & Horne, 1999). More recently, Nilsson et al. (2005) found that after 31 hours sleep-deprivation, participants were impaired on the modified six-elements task (a test of executive function). Correspondingly, Lieberman et al. (2002) found that following sleep deprivation, executive and reaction time measures were all impaired. Compared to the pre-sleep-deprivation baseline, nearly all measures were degraded: participants' hits on a vigilance task decreased by almost half whereas reaction time increased; all visual reaction time measures were impaired, and spatial working memory was also significantly impaired (correct responses decreased, reaction time increased and time-out errors increased).

A number of explanations are possible for the ecstasy-related decrement in aspects of cognition. It is possible that the cognitive functioning of ecstasy users is degraded due to use of the drug, sleep deprivation/restless sleep, or a pre-existing cognitive deficit unrelated to ecstasy use. A number of different models of sleep-ecstasy-cognition interrelationships are possible. Firstly, ecstasy might impair sleep directly via psychopharmacological effects and the resulting sleep impairment might account for all or some of the observed cognitive deficits. Secondly, lifestyle differences might result in a person obtaining less sleep or suboptimal sleep. Such individuals might also co-incidentally consume ecstasy but the cognitive deficits associated with sleep impairment are a consequence of selecting a lifestyle which is characterised by less sleep and not due to ecstasy. Accordingly one study found that regular ecstasy users attributed their cognitive deficits to reduced sleep rather than

their use of ecstasy (Topp et al. 1999) and as summarised above, sleep deprivation impairs cognitive performance. Thirdly, it may be that ecstasy adversely affects cognition and sleep but the two effects are entirely unrelated.

Fortuitously, we have collected data on aspects of sleep quality throughout our programme of research, although for the most part we have yet to analyse this data. By pooling the data obtained in our previous research we are able to build up a large sample allowing us to more adequately investigate differences in sleep attributes between ecstasy users and nonusers and to investigate the potential mediating role of these in accounting for ecstasy-related deficits in other aspects of cognition. By way of summary, it was expected that ecstasy-related differences in sleep quantity and quality would mediate deficits in aspects of cognition including executive functioning, learning and reasoning.

Method

Participants.

In total, 207 individuals completed the Epworth Sleepiness Scale (ESS). There were 104 ecstasy users and 103 nonusers. Participants were initially recruited through direct approach to Liverpool John Moores University undergraduate students, including psychology majors and psychology-biology joint students. Subsequently, word of mouth referral was used with most participants being recruited by this means. Background data for each group are set out in Tables 1 and 2.

<<Insert Tables 1 and 2 about here>>

Measures

Measures of Daytime Sleepiness

The ESS represents the likelihood of dozing off during the day in various situations. Its validity and reliability as a measure of daytime sleepiness are well established (see for example, Chen et al, 2002; Johns, 1992; Johns, 2000; Vignatelli et al, 2003; Violani et al, 2003) with scores exceeding 10 indicative of some form of sleep disorder (Johns & Hocking, 1997). The ESS contains eight items, which a participant has to score on a scale of 0 (would never doze off in this situation) to 3 (high chance of dozing off in this situation). A total score over all eight items was used in the present analysis, with higher scores indicative of increased subjective daytime sleepiness.

The Karolinska Sleepiness Scale (KSS) measures the participant's state of sleepiness at a given moment in time. Participants are asked: 'Use the following scale to indicate how sleepy you are feeling at this moment. Write the number in the box.' Nine numerical response alternatives are listed vertically with verbal labels assigned to alternate numbers: 1. Extremely Alert; 2 ; 3 Alert; 4 ; 5 Neither Alert Nor Sleepy; 6 ; 7 Sleepy But Not Fighting Sleep; 8 ; 9 Extremely Sleepy, Fighting Sleep, Effort to Stay Awake. The participant selects the number which corresponds to their present state and writes it in a box situated at the bottom of the page. Thus responses range from 1 to 9 with higher numbers indicative of greater sleepiness. The measure was administered twice, once at the beginning of testing and a second time at the end of the session. The reliability and validity of the KSS as a real-time measure of daytime sleepiness are well established (see, for example, Gillberg et al, 1994; 1996; Harma et al, 2002). As we began administration of the measure after the start of our research programme a somewhat smaller sample, 69 ecstasy users and 63, nonusers completed the KSS. Details of this sub-sample may be found in Table3. Likewise, not all participants completed the remaining tasks which were administered at different times

during our research programme. The number of individuals completing each of the cognitive tasks set out below is indicated in Table 4.

<<Insert Tables 3 and 4 about here.>>

Executive Function Measures

Computation Span. Participants were required to solve a number of arithmetic problems (e.g., 4+7 = ?) by circling one of three multiple-choice answers as each problem was presented. They were also required to simultaneously remember the second digit of each presented problem. At the end of each set of problems the second digits had to be recalled in the order in which they were presented. The number of arithmetic problems that the participant had to solve, while at the same time remembering each second digit, gradually increased as the test proceeded. In order to proceed, the participant was required to be correct in at least two of the three trials at the current level. Computation span was defined as the maximum number of end digits recalled in serial order, with the added requirement that the corresponding arithmetic problems had been solved correctly. In order to take account of individual differences in the non-executive maintenance component of the task, the load on executive resources was computed as the percentage difference between the computation and digit span scores. Large percentage differences are indicative of poor executive functioning. Data for all of the participants who took part in Fisk et al's (2004) study were included in the present study and further details of the task may be found there.

Consonant Updating: In this computer-based task, the participant was presented with a random sequence of between 6 and 12 consonants on a computer screen. Twenty-four such lists were presented, and in each case, the participant was unaware of the number of consonants to be presented. The task was always to recall

the most recent six consonants in the order in which they were presented. The participant experienced six trials at each of the four list lengths: 6, 8, 10, and 12 items. The order in which the lists were presented was randomised. A single composite score of updating was calculated as in Fisk and Sharp (2004).

Chicago Word Fluency Test. Participants were instructed not to write any place names, peoples name or plurals in this test. Firstly participants were given five minutes to write down as many words as they could, beginning with the letter "S". Secondly, they were given four minutes to write down as many four-letter words beginning with "C" as they could. Scores for both letter fluency tasks were the number of appropriate words in each case. In the present study, the two fluency measures were standardised and averaged to form a single standardised composite measure of letter fluency.

Semantic Fluency: In the semantic fluency task, participants were required to recall as many animal names as they could think of. This could be different species, or breeds within species. Participants were given four minutes for this task. The score (which was standardised) was the number of appropriate words that were produced. Although not an executive function measure semantic fluency was included as a control for the letter fluency measure.

For both the word fluency and consonant updating tasks, data for all of the participants who took part in Montgomery et al's (2005a) study were included in the present study and further details of the tasks may be found there.

The executive function measures used in the present study are established indicators of prefrontal executive processes. Computation span has been used extensively in the cognitive ageing literature as a measure of executive functioning (e.g., Fisk & Warr, 1996; Salthouse & Babcock, 1991) and it is functionally similar to

the operation span measure used by Miyake et al (2000) in their study of executive processes. Consonant updating has also been employed by Miyake et al and others (e.g., Morris & Jones, 1990) as a measure of executive functioning and other researchers have demonstrated that these tasks utilise prefrontal executive resources (e.g., Collette et al, 2006; van der Linden et al 1999). The Chicago fluency task has long been known to load on prefrontal neural processes (Kolb & Whishaw, 1985; Parkin & Jarva, 1999; Warkentin & Passant, 1997).

Associative Learning Measures.

Learning was assessed through a verbal paired associates task. Participants were presented sequentially with the same eight word pairs (taken from Fisk, 2003) on a computer screen. After each presentation, the participant was prompted with the first member of each pair and required to recall the second member. Eight such trials were administered. The order of presentation was randomised and changed for each trial. Measures included the number of correct responses in trial 1 (a measure of initial learning), the number of correct responses subsequently forgotten and the number of trials required to learn all associations. Data for all of the participants who took part in Montgomery et al's (2005b) study were included in the present study and further details of the task may be found there.

Syllogistic reasoning

Abstract syllogisms were used, for example, given that:

Some A are B,

and

No B are C

Participants were expected to produce the following logical inference:

Some A are not C.

Syllogisms vary in difficulty with one-model problems being the easiest and three model the hardest. 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, requiring either 2 models or 3 models). There are eight possible inferences that can be drawn for the one model problems and four each for the NVC and three model problems. The three model and NVC responses were combined so as to produce a maximum score of 8 for these more difficult problems. The syllogisms were the same as those used by Montgomery et al (2005c) and Fisk and Sharp (2002) and further details of the task may be found there. Data for all of the participants who took part in Montgomery et al's (2005c) study were included in the present study.

Procedure

Full procedural details may be found in the original papers cited above. Written informed consent was obtained from all participants. Ethical approval was obtained form the Ethics Committee of Liverpool John Moores University and the research was conducted in accordance with the ethical guidelines of the British Psychological Society.

Design

The ESS was analysed in a between participant design with user group between participants (ecstasy users versus nonusers). The KSS was analysed in a mixed design with user group between participants and time of administration within participants

(participants completed the KSS at the beginning and again at the end of the testing session). The measures of cognitive functioning were analysed in a between participant design with user group between participants (ecstasy users versus nonusers). Subsequently the sleep measures were included as covariates and the analyses were repeated to establish the extent to which group-related cognitive deficits were mediated by group differences in sleep functioning. The relationship between the drug use indices, the sleep measures, and the cognitive outcome variables were explored through correlation (Spearman's rho, ρ).

Results

Inspection of Table 1 reveals that for the complete sample, the majority of ecstasy users were also current or previous users of cannabis and cocaine. A substantial minority had also used amphetamine in the past. Use of other drugs among non ecstasy users was rare and largely limited to cannabis. Although many non ecstasy users were using cannabis, the typical lifetime cannabis dose and level of recent use was far less than that of ecstasy users.

The indicators of daytime sleepiness are reported in Table 2. The Epworth sleepiness scale (ESS) represents the likelihood of dozing off during the day in various situations and is thus an indicator of daytime sleepiness. Scores exceeding 10 are thought to be indicative of some form of sleep disorder. The number of ecstasy users exceeding this score numbered 10, with exactly the same number of nonusers exceeding it. Thus the prevalence of high scores was identical for users and nonusers. Similarly in terms of the median scores, users and nonusers did not differ significantly.

Although the Karolinska measure utilises a rating scale it is widely treated in the research literature as conforming to interval level of measurement (see for example, Otmani, et al, 2005; Richter, et al, 2005; Swann et al, 2006; van den Berg et al 2005). In the present study, mixed ANOVA was applied with ecstasy user group between participants and time of administration as the within participant variable. This revealed a significant main effect of time of testing with participants indicating greater levels of tiredness on the second occasion of testing, $F(1,130) = 31.88$, $p<.001$. This was qualified by a significant time by group interaction, $F(1,130) = 4.32$, $p<.05$. Compared to nonusers, ecstasy users reported higher levels of tiredness at the beginning of testing, however, at the second occasion of testing there was little difference between the groups. The increase in tiredness between the two occasions of testing was greater for nonusers. Users began the session more tired but registered less change throughout the session. The main effect of group was non significant, $F < 1$.

In order to establish whether the group differences on the sleep quality and sleep type measures were responsible for the ecstasy-related deficits in other aspects of cognition we repeated our original analyses initially without any covariates and subsequently with the sleep measures as covariates. In relation to computation span the initial analysis revealed that ecstasy-related decrement was statistically significant, $F(1,205)=13.88$, $p<.001$, $\eta^2 = .063$. Following inclusion of the ESS as a covariate, the group difference remained statistically significant, $F(1,200)=15.16$, $p<.001$, $\eta^2 = .070$. For those participants completing the consonant updating task, nonusers achieved a slightly higher score compared to users, $F(1,62)=5.44$, $p<.05$, $\eta^2 = .081$. For this sample, ecstasy users registered significantly higher scores on the ESS. Following statistical controls for ESS, the ecstasy-related consonant updating deficit remained statistically significant, $F(1,60)=5.33$, $p<.05$, $\eta^2 = .082$.

On the composite letter fluency measure, the difference between the standardised scores indicates that ecstasy users produced fewer words. ANOVA with user group between participants and the semantic fluency score as a covariate revealed a statistically significant group difference, $F(1,96) = 10.48$, $p<.01$, $\eta^2 =098$. The effect remained significant following control for the ESS, $F(1,94) = 9.11$, $p<.01$, $\eta^2 =088$.

Ecstasy users were impaired on all aspects of learning. MANOVA with the three learning measures as dependent variables revealed that the multivariate effect was statistically significant, $\Lambda = 0.852$, $F(3,89) = 5.15$, $p<.01$. The effect remained significant following control for the ESS, $\Lambda = 0.859$, $F(3,87) = 4.77$, $p<.01$.

With regard to syllogistic reasoning, for both the easier one model and the more difficult two/three model problems, ecstasy users achieved fewer correct responses compared to nonusers. Mixed ANOVA with level of difficulty within participants and user group between participants revealed that the group difference was statistically significant, $F(1,81) = 5.74$, $p<.05$, $\eta^2 = .066$. The interaction between group and level of difficulty failed to reach significance, $F(1,81) = 2.15$, $p>.05$. For this sample, ecstasy users registered significantly lower scores on the Epworth measure indicating a lower prevalence of daytime sleepiness. Following statistical controls for the Epworth measure, the ecstasy-related reasoning deficit remained statistically significant, $F(1,79)=6.68$, $p<.05$, $\eta^2 = .078$. To summarise, there is no evidence that the variance attributable to the ESS mediated the ecstasy/polydrug-related cognitive deficits that we have observed previously in studies from our laboratory.

With one exception, there were too few participants completing the KSS as well as the other cognitive measures reported above, to allow the potentially

mediating role of group differences in this variable to be assessed. The exception was the computation span measure. The 69 users completing the Karolinska measure recorded a percentage processing cost of 43.03 (s.d. = 25.50) on the computation span measure compared with a 34.18% (s.d. = 22.93) cost for the 63 nonusers. Following control for group differences in the two Karolinska scores, this difference remained statistically significant, $F(1,128) = 4.47$, $p<.05$, with $\eta^2 = .034$ virtually unchanged from the level prior to inclusion of the covariates.

It is clear from Table 5 that the ESS was not significantly correlated with any of the cognitive measures. With regard to the Karolinska, for the most part, as noted above, too few participants completed both it and the cognitive measures so correlations with respect to these variables cannot be reported. However with regard to the computation span task where the sample size was adequate, correlations between this and the Karolinska measures were both near zero (ρ =-.013 and -.017 for the beginning and end of testing respectively, $p>.05$ in both cases). The ESS was significantly correlated with the Karolinska sleepiness measure at the second administration indicating that those participants who reported more fatigue at the end of testing also scored higher on the ESS.

<<Insert Table 5 about here.>>

With one exception, the ESS was not significantly correlated with any of the drug use measures reported in Table 5. Regarding the exception, higher levels of ecstasy use during the 30 days prior to testing were associated with <u>less</u> reported daytime sleepiness. In contrast to this, the Karolinska score at the start of testing was positively and significantly correlated with lifetime use of ecstasy and cannabis. Individuals with greater lifetime use were more likely to be tired at the start of testing.

Table 5 also contains the correlations between the cognitive measures and the measures of illicit drug use. The data on which these are based have been reported by us previously although in the present paper we have combined data from a number of previous studies (Fisk et al 2004; 2005; Montgomery et al 2005a; 2005b; 2005c). As we reported previously, lifetime ecstasy use is significantly associated with impairments in executive functioning (computation span, word fluency), associative learning, and syllogistic reasoning. Higher lifetime levels of cannabis use are negatively associated with aspects of executive functioning (computation span) and learning. Similarly increased lifetime exposure to cocaine is significantly associated with reduced executive functioning (letter updating and word fluency) and impaired associative learning. Inspection of Table 5 also reveals that the use of illicit drugs during the previous 30 days is also significantly associated with impairments in aspects of cognitive functioning. However, for the most part the magnitude of the correlations is less than the equivalent ones with the total lifetime use measures. This is consistent with the proposition that it is longer term exposure which is responsible for the impairments that are noted.

Discussion

As reported by us previously, ecstasy users performed significantly worse than nonusers on various measures of executive functioning. Users of the drug had a greater percentage processing cost on the computation span test, recalled fewer letters correctly on the verbal updating task, supplied fewer correct words on the Chicago word fluency measure, were impaired on a paired associates learning task (poorer initial learning, more forgetting and longer to learn all associations) and performed significantly worse on the syllogistic reasoning task (although the user group by

difficulty interaction was non-significant). There were few differences observed in the sleep measures in the present study. No significant group differences were obtained on the ESS. On the Karolinska measures, while ecstasy users reported feeling more tired than nonusers at the beginning of testing, there was little difference in subjective tiredness at the end of testing. Contrary to expectations, inclusion of the sleep measures as covariates in the analyses did not attenuate the ecstasy-related deficits in the various aspects of cognition which remained statistically significant, the effect sizes virtually unchanged.

Previous research in ecstasy users has found that users of the drug report disturbed sleep both as a primary subjective effect (Baylen & Rosenberg, 2006; Huxster et al. 2006; Montoya et al. 2002) and a longer lasting psychobiological complaint (Parrott et al. 2006). The present study found some support for sleep differences in ecstasy users. Ecstasy users began the test session significantly more tired than nonusers but reported little change throughout the test session. Nonusers on the other hand began the session less tired but experienced more incremental fatigue compared to users, over the testing session. Equal numbers of ecstasy users and nonusers were tested in the morning and afternoon sessions, so it is unlikely that the increased tiredness of ecstasy users prior to testing reflects straightforward time of day effects.

Irregular patterns of wakefulness and sleep are more characteristic of young adult populations and especially student populations (Cole et al 2002). It is possible that the increased feeling of tiredness at the beginning of testing might reflect an inability among some ecstasy users to adjust their circadian clock. Studies on rats have revealed that MDMA and other serotonin-related drugs such as fenfluramine interfere with the animal's ability to "reset" its circadian clock. The authors suggest

that this is due to serotonergic degeneration caused by ecstasy and fenfluramine (Biello and Dafters, 2001). This is further supported by Colbron et al. (2002) who found that repeated exposure to MDMA in hamsters altered the ability of the circadian clock to phase shift. These findings from animal studies are in line with research on human ecstasy users where "restless sleep" has frequently been cited as an effect of the drug (e.g. Huxster et al. 2006; Parrott et al. 2000; Parrott et al. 2006; Topp et al. 1999).

It has been suggested that, in part, the cognitive deficits displayed by ecstasy users may reflect differences in lifestyle, for example it has been suggested that the lifestyle of an ecstasy user is one of constant circadian disruption, which has been responsible for similar cognitive deficits in aircrew (Cole et al, 2002). The present study does provide some evidence of increased tiredness among ecstasy users in that the initial scores on the Karolinska measure were reduced. However, the absence of ecstasy-related differences on the ESS is surprising and casts some doubt on Cole et al's explanation of the cognitive deficits that have been observed in ecstasy users. In the present study, there was only limited evidence of sleep impairment and the inclusion of the sleep variables as covariates left the ecstasy-related effect sizes virtually unchanged with the group differences remaining significant.

There were a number of significant correlations between drug use indices and sleep quality. There were significant correlations between the initial Karolinska measure and both total cannabis use and total ecstasy use indicating that those who had a greater lifetime exposure to ecstasy and cannabis reported poorer sleep. The ESS was also significantly correlated with the Karolinska measure at the end of the test session in that those who were most tired at the end of the session tended to score higher on the ESS. The drug use indicators were also found to be correlated with the

cognitive measures in that higher levels of use were associated with cognitive impairment. However, caution is needed in interpreting the correlations set out in Table 5. Since the majority of ecstasy users also used cannabis and cocaine, the possibility that the drugs interact in some way to produce their effects cannot be ruled out. Furthermore, virtually all of the cocaine users were also ecstasy users so the significant correlations do not imply a simple direct relationship between cocaine use and cognitive outcomes.

Taken as a whole the results of the present study provide tentative support for one of the propositions made in the introduction. Three possible ecstasy-sleep-cognition relationships were proposed. Ecstasy-related deficits were observed in the various cognitive measures that were administered. There were also some differences in one of the sleep measures. However, little evidence was found for the mediating effects of sleep on cognitive deficits in ecstasy users. Consequently, as suggested in the introduction, it may be that ecstasy users exhibit impaired sleep quality, and impaired cognition, but the two are not related.

There were a number of limitations with the present study. Firstly, due to limited resources we had to rely on self-reports of previous drug use. Other studies have also relied on self-report measures of ecstasy use (e.g. Fox et al. 2002; Morgan 1998; Morgan 1999; Rodgers 2000). Nonetheless while the questionnaire we used has numerous checks for internal consistency and while we have no reason to doubt the responses of our participants, it would have been more desirable to supplement the self reports with objective measures of recent use (e.g. from urine or hair samples). Second, we used self report measures of sleep quality and it is possible that other more objective measures such as polysomnography might demonstrate that ecstasy

users do exhibit altered sleep patters and that these are related in some way to the cognitive impairments that have been observed.

Serotonergic neural pathways are known to be involved in sleep regulation and both directly and indirectly affect the integrity of cognitive processes. A corollary of this is that deficient brain serotonin activity is believed to be associated with sleep abnormalities, which in turn promote behavioral decline, psychiatric disorders, and deficiencies in the regulation of affective states (Markus et al, 2005; Voderholzer et al, 1998). Much of the research investigating the role of serotonin in sleep regulation has utilised polysomnography to explore the effects of manipulating the availability of the serotonin precursor tryptophan. Increasing its availability just before bedtime has been found to reduce feelings of sleepiness the following morning, enhance the capacity for sustained attention, and in poor sleepers enhance the speed of responding and reduce errors in a reaction time task (Markus et al, 2005). By way of contrast, tryptophan depletion led to increased wakefulness, decreased stage 2 sleep, and significant alterations in aspects of REM sleep, highlighting the important role of the serotonergic system in sleep maintainance and regulation (Huwig-Poppe et al, 1999; Voderholzer et al, 1998). Given that there is considerable evidence indicating reduced levels of serotonergic activity in abstinent ecstasy users (McCann et al 2000), future research might utilise the tryptophan challenge approach in order to accentuate and render more transparent the role that sleep disturbance might play in underpinning the ecstasy-related cognitive deficits that have been observed.

In conclusion while ecstasy users exhibited differences on some sleep measures these did not appear to mediate the cognitive deficits that were observed. Future research utilising more objective measures of sleep quality as well as pharmacological interventions might further clarify the extent to which sleep

impairments are responsible for the cognitive deficits that have been observed in ecstasy users.

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Table 1. Age, Years of Education, Intelligence, and Measures of Illicit Drug Use[A] for Current and Previous Users for those Participants Completing the Epworth Sleepiness Scale and the Background Sleep Attributes Questions

	Ecstasy Users			Non Ecstasy Users			T[B]
	Mean	S.D.	n	Mean	S.D.	n	
Age	21.68	1.96	104	21.11	1.66	103	2.29*
Ravens Progressive Matrices	47.77	6.15	102	48.53	5.31	102	0.35
NART	28.48	6.52	104	29.58	5.38	102	0.19
Ecstasy							
Lifetime dose (tablets)	349.97	464.41	104	-	-	-	
Current use (tablets taken in previous 30 days)	3.19	4.95	103	-	-	-	
Weeks since last use (mean/median)	19.35 (3)	43.46	104	-	-	-	
Cannabis							
Lifetime dose (joints)	3406.37	4710.24	80	763.10	1163.55	37	4.72***
Current use (joints taken in previous 30 days)	40.34	64.19	79	9.30	25.84	35	3.68***
Weeks since last use (mean/median)	21.01 (0.43)	73.91	91	24.06 (3.50)	56.36	56	-0.27
Cocaine							
Lifetime dose (grams)	48.60	78.91	40	-	-	0	
Current use (grams taken in previous 30 days)	1.52	1.98	38	-	-	0	
Weeks since last use (mean/median)	14.99 (3)	38.49	82	41.33 (8)	68.23	9	-1.14
Amphetamine							
Lifetime dose (grams)	77.46	140.12	31	4.00	-	1	
Current use (grams taken in previous 30 days)	0.36	1.31	21	-	-	0	
Weeks since last use (mean/median)	96.29 (46)	117.96	42	208.00 (260)	90.07	3	

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

Note A: The estimate of weeks since last use includes individuals who have used the drug in question on relatively few or on just a single occasion. Some individuals, especially infrequent users were unable to provide estimates for lifetime dose or current use.

Note B: t is calculated only where there are at least nine participants in each group

Table 2. Indicators of daytime sleepiness among ecstasy users and nonusers

	Ecstasy Users			Nonusers			Mann-Whitney U / t test
	25th Percentile	Median	75th Percentile	25th Percentile	Median	75th Percentile	
Epworth Daytime Sleepiness (maximum 24)	4	6	8	4	6.5	9	U = 4709.5, p >.05
Karolinska Sleepiness Scale (maximum 9; mean/standard deviation)							
First Administration		4.90	1.49		4.37	1.57	t = 2.01, p<.05
Second Administration		5.52	1.58		5.71	1.53	t = -0.71, p >.05

Table 3. Age, Years of Education, Intelligence, and Measures of Illicit Drug Use for Current and Previous Users for those Participants Completing the Karolinska Sleepiness Scale

	Ecstasy Users			Non Ecstasy Users			T[B]
	Mean	S.D.	n	Mean	S.D.	n	
Age	21.72	2.04	69	20.86	1.47	63	2.82**
Ravens Progressive Matrices	47.24	6.11	67	48.70	5.45	63	-1.43
NART	28.41	6.23	69	28.53	5.14	62	-0.13
Ecstasy [A]							
Lifetime dose (tablets)	337.40	493.26	69	-	-	-	
Current use (tablets taken in previous 30 days)	2.45	3.36	69	-	-	-	
Weeks since last use (mean/median)	24.24 (3)	49.37	69	-	-	-	
Cannabis [A]							
Lifetime dose (joints)	2830.18	4003.98	55	558.00	1012.21	25	3.94***
Current use (joints taken in previous 30 days)	34.75	55.18	55	9.98	30.78	24	2.54*
Weeks since last use (mean/median)	27.92 (0.43)	87.50	61	30.89 (6)	65.18	40	-0.18
Cocaine [A]							
Lifetime dose (grams)	52.40	85.37	25	-	-	0	
Current use (grams taken in previous 30 days)	0.73	0.84	25	-	-	0	
Weeks since last use (mean/median)	18.31 (3)	46.78	53	59.00 (30)	79.46	6	
Amphetamine [A]							
Lifetime dose (grams)	77.57	120.36	19	-	-	0	
Current use (grams taken in previous 30 days)	0.10	0.27	16	-	-	0	
Weeks since last use (mean/median)	117.13 (54)	136.71	24	182.00 (182)	110.31	2	

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

Note A: The estimate of weeks since last use includes individuals who have used the drug in question on relatively few or on just a single occasion. Some individuals, especially infrequent users were unable to provide estimates for lifetime dose or current use.

Note B: t is calculated only where there are at least nine participants in each group

Table 4. Executive Functioning, Associative Learning and Reasoning Outcomes for Ecstasy/polydrug Users and Nonusers

	Ecstasy Users			Non Ecstasy Users		
	Mean	S.D.	n	Mean	S.D.	n
Computation Span (% processing cost)	43.46	24.86	104	31.23	22.31	103
Consonant Updating (maximum six)	2.16	0.49	29	2.46	0.53	35
Word Fluency						
Chicago Word Fluency (standardised score)	-0.40	0.84	36	0.23	0.86	63
Semantic Fluency (standardised score)	-0.17	0.94	36	0.10	1.03	63
Paired Associate Learning						
Trials to Completion	5.63	1.65	30	4.32	1.43	63
Initial Learning	3.17	2.02	30	4.32	1.99	63
Forgetting	0.83	0.87	30	0.46	0.91	63
Syllogistic Reasoning						
One Model	3.78	1.96	32	4.92	1.86	51
Two/Three Model	1.31	1.82	32	1.76	1.62	51

Table 5 Correlations (Spearman's ρ) between aspects of cognitive functioning, daytime sleepiness and measures ecstasy use[A].

	Epworth Sleepiness Measure	Ecstasy		Cannabis		Cocaine	
		Total lifetime use	Current use[B]	Total lifetime use	Current use[B]	Total lifetime use	Current use[B]
Computation Span	.019	.239**	.116	.185*	.176*	.220**	.108
(Percentage cost)	n=206	n=207	n=206	n=172	n=193	n=154	n=182
Consonant Updating	.007	-.201	-.166	-.214	-.068	-.289*	-.206*
	n=63	n=64	n=63	n=53	n=59	n=49	n=56
Chicago Word Fluency	-.163	-.358**	-.293**	-.189	-.178	-.400**	-.312**
	n=98	n=99	n=98	n=80	n=92	n=79	n=90
Paired Associate Learning							
Trials to Completion	.025	.370**	.286**	.205	.245*	.404**	.225*
	n=92	n=93	n=92	n=75	n=86	n=75	n=84
Initial Learning	-.148	-.318**	-.150	-.334**	-.365**	-.299**	-.232*
	n=92	n=98	n=97	n=75	n=89	n=78	n=88
Forgetting	-.078	.318**	.216*	.192	.182	.316**	.232*
	n=92	n=98	n=97	n=75	n=89	n=78	n=88
Syllogistic Reasoning							
One Model	-.137	-.259*	-.137	-.056	-.086	-.174	-.204
	n=82	n=83	n=82	n=62	n=75	n=71	n=77
Two/Three Model	-.115	-.143	-.001	-.053	-.004	.020	.093
	n=82	n=83	n=82	n=62	n=75	n=71	n=77
Epworth Sleepiness Scale	-	-.091	-.161*	-.100	-.075	-.089	-.063
		n=203	n=202	n=169	n=190	n=151	n=178
Karolinska (start of session)	-.001	.260**	.125	.247**	.079	.126	.158
	n=132	n=132	n=132	n=110	n=123	n=96	n=116
Karolinska (end of session)	.344**	-.059	.043	-.007	-.061	-.010	-.012
	n=132	n=132	n=132	n=110	n=123	n=96	n=116

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

Note A: With regard to the total and current use estimates, scores for nonusers are entered as zero. Some participants were unable to estimate their pattern of use.

Note B: Current use refers to the amount consumed during the previous 30 days.