

Pre-publication manuscript of:

**Fisk, J.E., & Montgomery, C. (2009).** Sleep impairment in ecstasy/polydrug and cannabis-only users. *The American Journal on Addictions*, 18, 430-437. ISSN: 1055-0496 (5950 words) DOI: 10.1080/10550490903077762

Sleep impairment in ecstasy/polydrug and cannabis-only users

Running Head: Sleep impairment

John E. Fisk<sup>1</sup>, Catharine Montgomery<sup>2</sup>

<sup>1</sup>University of Central Lancashire

<sup>2</sup>Liverpool John Moores University

Corresponding author:

Professor John E Fisk, PhD

Department of Psychology

University of Central Lancashire

Preston PR1 2HE

United Kingdom

Tel 44 (0) 1772 894465

Fax 44 (0) 1772 892925

e-mail: jfisk@uclan.ac.uk

### Abstract

The present study investigated aspects of sleep quality in ecstasy and cannabis users. Two-hundred and twenty seven participants (117 ecstasy/polydrug users, 53 cannabis users and 57 drug naive participants) took part. The participants completed measures of daytime sleepiness, and indicators of sleep quality. The results demonstrated that ecstasy/polydrug users viewed themselves as being more evening types and having poorer sleep quality than cannabis users and drug naive participants. They were also more likely to have missed out on a night's sleep. The reported differences in sleep type may reflect ecstasy-related serotonergic dysfunction resulting in problems with shifting circadian rhythms.

Key words: ecstasy; cannabis; sleep; Karolinska; Epworth

## Introduction

There is a considerable body of research evidence indicating that ecstasy users are subject to a range of sleep-related problems. Current users whose drug use was largely limited to ecstasy reported poorer sleep quality and more sleep time compared with nonusers possibly due to short-term post intoxication effects. However, the same study<sup>[1]</sup> found that abstinent ecstasy-only users also suffered from sleep impairment reporting significantly more night-time awakenings compared to nonusers. As these individuals had been abstinent for at least 28 days and on average for over 500 days it appears that sleep problems were a longer term consequences of taking the drug. Other post intoxication effects include sleeplessness<sup>[2]</sup> and longer term problems including sleep disturbance and sleep deprivation have been reported by ecstasy users<sup>[3,4]</sup>. Evidence of sleep disturbance (from the SCL-90) has been found in both heavy<sup>[5]</sup> and light users of ecstasy<sup>[6]</sup> and problems appear to persist long after the last occasion of use<sup>[7]</sup>. Furthermore, a substantial minority (around 40%) of Parrott et al's<sup>[8]</sup> ecstasy-using sample identified poor sleep when off drug as a consequence of their ecstasy use showing that even relatively short periods of abstinence are associated with sleep problems.

Laboratory studies have also demonstrated a range of sleep problems among ecstasy users (see Schierenbeck et al<sup>[5]</sup> for a review). For example, Allen et al<sup>[9]</sup> studied the sleep patterns of ecstasy users via EEG and found that they exhibited reduced total sleep time and more specifically less non-REM sleep. McCann et al<sup>[10]</sup> found that MDMA users had lasting reductions in the serotonin metabolite CSF 5-hydroxyindoleacetic acid (5-HIAA). They also exhibited changes in sleep patterns and personality. Animal studies have also demonstrated how MDMA gives rise to neurotoxicity and consequent sleep disturbance. For example, the administration of MDMA to adult male rhesus monkeys was associated with pronounced elevated activity levels three to four days following administration and disruption of the sleep-wake cycle<sup>[11]</sup>. Rats were found to exhibit long-term changes in the regulation of circadian rhythms, motor activity and sleep generation following the administration of MDMA<sup>[12]</sup>.

Aside from the effects of MDMA and ecstasy on sleep quality there is also abundant evidence that cannabis has been associated with sleep problems in both animal and human studies<sup>[5]</sup>. Santucci et al<sup>[13]</sup> found that the administration of a cannabinoid receptor antagonist to rats increased the time spent in wakefulness reducing slow-wave sleep duration and delaying REM sleep onset. The authors suggest that the results are consistent with the existence of an endogenous cannabinoid system which has a role in regulating the sleep wake cycle. In a human study Tassinari et al<sup>[14]</sup> found that administration of a single heavy oral dose of THC to cannabis naïve participants caused severe intoxication and sleep impairment with a decrease in slow wave sleep and the disappearance of REM stages. Nicholson et al<sup>[15]</sup> observed that following the night time administration of  $\Delta$ -9-tetrahydrocannabinol (THC), the following day there was a reduction in sleep latency, increased sleepiness, and mood changes. It has been demonstrated that sleep problems are common withdrawal symptoms when cannabis users attempt to stop using the drug. In a study from Budney et al<sup>[16]</sup>, current users experienced sleep difficulties and strange dreams which persisted for at least 45 days after the last ingestion of cannabis. Following cessation of cannabis use the same range of symptoms including sleep problems and strange dreams were observed by Arendt et al<sup>[17]</sup> among a group of abstinent individuals seeking treatment for cannabis dependence.

In a previous study<sup>[18]</sup> we sought to establish whether ecstasy/polydrug users experienced more daytime sleepiness compared with non ecstasy users and if so whether this was responsible for the range of cognitive deficits previously observed among the ecstasy-using sample. Few significant differences in day time sleepiness were observed between users and nonusers and there was no evidence that the cognitive deficits we observed were mediated by group differences in day time sleepiness. Our previous study<sup>[18]</sup> failed to address a number of potentially important issues. First we failed to consider whether there might be any differences between the groups in different aspects of perceived sleep quality such as morning wakefulness, perceived sleep type (morning or evening type), the prevalence of missing a night's sleep and the number of hours typically slept each night. Second, we did not thoroughly consider the extent to which the sleep problems that were identified might have

been due to cannabis use rather than ecstasy. In view of the evidence presented above this remains a distinct possibility. The present study attempts to address these omissions. It is intended to compare drug naïve, cannabis only, and ecstasy/polydrug users on the various sleep measures.

The aim of the present study therefore is to assess sleep quality in ecstasy polydrug users and cannabis users. As ecstasy users frequently co administer cannabis, and also in much of the ecstasy literature, control participants were cannabis users, this raises questions as to whether the deficits that have been observed were due to cannabis or to ecstasy. It is also unclear whether different aspects of sleep quality are adversely affected as well as daytime sleepiness. The present study sought to investigate these issues by comparing perceptions of sleep quality among ecstasy/polydrug users, cannabis users and drug naïve individuals. It was predicted that the two drug using groups will report poorer sleep quality and morning alertness, greater daytime tiredness and less sleep time. No prediction is made in relation to the sleep type measure.

## METHOD

### Participants.

In total, 227 individuals were included in the study. There were 117 (53 females) ecstasy/polydrug users, 53 (36 females) cannabis-only users, and 57 (43 females) nonusers of illicit drugs. Participants were initially recruited through direct approach to Liverpool John Moores University undergraduate students. Subsequently, word of mouth referral was used with most participants being recruited by this means. Most participants were students (81%), with a further 8 and 7% respectively in full and part-time employment. Background data for the illicit drug using groups are set out in Table 1. Inspection of the Table reveals the extent of poly substance use among the ecstasy/polydrug group. It is also worthy of note that cannabis use among this group is far more pronounced compared to the cannabis-only group.

The average age of the drug naïve group was 20.91 years (s.d. 1.80), years of education was 15.37 (s.d. 1.96), and the Ravens score 47.61 (s.d. 5.39).

<<Insert Table 1 about here>>

### Measures

Drug Use Questionnaire. Patterns of drug use and other relevant lifestyle variables were investigated via means of a background questionnaire. The questionnaire gauged the use of ecstasy and other drugs. In relation to illicit drugs, participants were asked a range of questions including the last time that they had used each drug and the amount consumed in the previous 30 days. Participants were also questioned concerning their history of drug use, and these data were used by the experimenters to estimate total lifetime use of each drug.

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.

Miss a night’s sleep. Participants were asked: ‘Do you sometimes miss a night’s sleep or have much less sleep than normal?’ A ‘yes’ or ‘no’ response was obtained.

Hours sleep per night. Participants were asked: ‘How long do you usually sleep on a typical night?’ and responded indicating the number of hours.

The Epworth Sleepiness Scale (ESS) represents the likelihood of dozing off during the day in various situations with scores exceeding 10 indicative of some form of sleep disorder<sup>[19]</sup>. 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 (see, for example, Gillberg et al<sup>[20]</sup>). 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<sup>1</sup>.

Participants completed a range of other measures the results of which have been reported elsewhere<sup>[18]</sup>. They are included in the present paper for completeness.

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.

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 our previous paper<sup>[18]</sup>.

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. The two fluency measures were standardised and averaged to form a single standardised composite measure of letter fluency.

Using the present sample, our previous study<sup>[18]</sup> revealed that ecstasy/polydrug users were significantly impaired on these aspects of executive functioning, relative to a non ecstasy-using group which included both cannabis only and drug naïve users. The present study has separated out cannabis only and drug naïve persons. On this basis, computation span scores were associated with a statistically significant overall



group difference,  $F(2,222) = 5.19$ ,  $p < .01$ , with Dunnett's  $t$  post hoc test revealing that the ecstasy/polydrug users performed significantly worse than cannabis only,  $p < .05$ , and drug naïve persons,  $p < .01$ . The consonant updating task was also associated with significant group effect,  $F(2,133) = 3.40$ ,  $p < .05$ , with Dunnett's  $t$  post hoc test revealing that the ecstasy/polydrug users performed significantly worse than cannabis only and drug naïve persons,  $p < .05$  in both cases. Lastly the Chicago World Fluency test yielded a significant group difference,  $F(2,88) = 6.49$ ,  $p < .01$ , with Dunnett's  $t$  post hoc test revealing that the ecstasy/polydrug users performed significantly worse than cannabis only and drug naïve persons,  $p < .01$  in both cases.

### Procedure

Written informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Committee of Liverpool John Moores University and the research was conducted in accordance with the ethical guidelines of the British Psychological Society. Participants completed the measures in a single session lasting between three to four hours<sup>2</sup>.

### Design

Drug using group with three levels (drug naïve, cannabis only, and ecstasy/polydrug) served as the independent variable. Dependent variables were the various sleep measures together with the two measures of daytime sleepiness.

## RESULTS

In all groups the majority of participants indicated that they occasionally missed a night's sleep however at 91% the proportion was significantly higher among ecstasy/polydrug users compared to cannabis-only (81%) and drug naïve (75%),  $\chi^2$  ( $df=2$ ;  $N=224$ ) = 7.98,  $p < .05$ . In terms of the means and inter-quartile range, inspection of Table 2 reveals that ecstasy-polydrug users were more likely to describe themselves as 'evening types'. Higher

scores on the sleep quality measure indicate poorer quality and on this basis drug naïve individuals appear to report better sleep quality compared to the other two groups.

<<Insert Table 2 about here>>

Since the data were ordinal in nature nonparametric tests were utilised. Inspection of Table 3 reveals that the group differences were statistically significant for the sleep type and approached significance for the sleep quality measure. Pairwise comparisons revealed that drug naïve individuals had significantly lower scores on the sleep type and sleep quality measures compared to ecstasy/polydrug users. Thus drug naïve persons were less likely to view themselves as evening types and believed that they had better sleep quality. Pairwise comparisons also revealed that cannabis-only users had significantly lower scores on the sleep type measure compared to ecstasy/polydrug users. Thus cannabis-only users were also less likely to view themselves as evening types.

Looking at the proportion of participants describing themselves as definitely evening types, this was 11% among drug naïve persons which is similar to the proportion in the general population<sup>[21]</sup>. Among cannabis only users the proportion was 21%, while among ecstasy/polydrug users it was 37%. Definitely morning types were 4, 2, and 3% respectively for drug naïve, cannabis only, and ecstasy/polydrug compared with approximately 10% in the general population.

<<Insert Table 3 about here>>

No statistically significant group differences emerged on the remaining sleep measures. However, the pairwise difference between drug naïve and ecstasy/polydrug users on the Karolinska measure administered at the beginning of testing approached significance,  $p=.065$  two tailed, as did the pairwise difference between cannabis only and ecstasy/polydrug users at the end of testing,  $p=.066$  two tailed. Drug naïve individuals were less tired than ecstasy/polydrug at the beginning of testing while interestingly cannabis only users were more tired than ecstasy/polydrug at the end of testing.

Inspection of Table 1 reveals that the standard deviation in relation to the periods of abstinence for cannabis and ecstasy was very large and there were substantial discrepancies

between the respective medians and means in relation to the time elapsed since last use. Thus the groups contained participants who differed greatly in terms of the period of abstinence. It is possible that the drug-related effects on the different sleep measures may vary according to the length of abstinence and that the relationship may not be a monotonic one. With regard to ecstasy, in order to examine this possibility, participants were divided into different groups depending on their period of abstinence. Four such groups were formed, and these were selected so as to conform as closely as possible to the four quartiles constituting the distribution. Thus the four groups represented progressively increasing periods of abstinence. The first quartile comprised persons who had been abstinent for less than a week; the second more than one but less than three weeks; the third more than three but less than 12 weeks, and the fourth more than 12 weeks. These four groups were compared with cannabis only users and drug naïve persons on the measures of interest. The Kruskal Wallis test revealed that the overall group effect was nonsignificant for the two Karolinska measures, the Epworth Sleepiness Scale, morning tiredness, sleep quality and hours of sleep per night, with  $\chi^2$  values ( $N=225$ ,  $df=5$ ) ranging between 0.80 and 8.07,  $p>.15$  in all cases. The sleep type measure was associated with a statistically significant group difference,  $\chi^2$  ( $N=225$ ,  $df=5$ ) = 16.70,  $p<.01$ . The trends across the groups are displayed in Figure 1. Subsequent Mann-Whitney U analyses revealed that the first, third and fourth quartiles differed significantly from the drug naïve group,  $p<.024$ ,  $.016$ , and  $.001$ , respectively. The first, third and fourth quartiles also differed significantly from cannabis only users,  $p<.042$ ,  $.022$ , and  $.004$ , respectively. In all three cases ecstasy users were more likely to describe themselves as evening types compared to the cannabis only and drug naïve groups. Focussing on ecstasy users, the Jonckheere-Terpstra Trend test failed to reveal a statistically significant trend with increasing duration of abstinence, J-T statistic = 0.877,  $p>.05$ .

<<Insert Figure 1 about here>>

While cannabis only users did not differ significantly from drug naïve persons on any of the measures, it is possible that such differences might emerge as periods of abstinence from cannabis vary. In order to examine this possibility, cannabis only users were divided

into four different groups (again based as closely as possible on quartiles) according to their period of abstinence. The first quartile comprised persons who had been abstinent for less than a week; the second more than one but less than four weeks; the third more than four but less than 20 weeks, and the fourth more than 20 weeks. Comparison of these four groups and drug naïve persons on the measures of interest yielded no statistically significant group differences on any of the sleep measures with  $\chi^2$  values ( $N=106$ ,  $df=5$ ) ranging between 2.06 and 7.10,  $p>.13$  in all cases via the Kruskal Wallis test.

In order to establish whether or not the cognitive deficits in ecstasy/polydrug users that were noted above were mediated by the significant group differences in sleep type, sleep quality and missing a night's sleep, these three variables were included as covariates in the analyses of the cognitive measures with user group (drug naïve, cannabis-only, ecstasy/polydrug) again as the between participant independent variable. Following control for the sleep measures ecstasy/polydrug users continued to exhibit deficits on all of the cognitive measures: for computation span,  $F(2,216) = 5.73$ ,  $p<.01$ , for consonant updating,  $F(2,127) = 4.44$ ,  $p<.05$ , and for the Chicago World Fluency test  $F(2,83) = 6.72$ ,  $p<.01$ .

## DISCUSSION

Among the measures included in the present study, only the sleep type indicator yielded an overall statistically significant group difference. In terms of the pairwise comparisons, on the sleep quality measure, drug naïve individuals achieved significantly lower scores compared with the ecstasy/polydrug group indicating that the drug naïve group judged their sleep quality to be better than the ecstasy/polydrug users. On the sleep type measure both drug naïve and cannabis only users were significantly less inclined to describe themselves as definitely evening types compared to ecstasy/polydrug users. All of these pairwise comparisons remained statistically significant at the Bonferroni corrected alpha level of .016. In relation to duration of abstinence, at unadjusted alpha levels, three of the four

quartiles contained significantly more individuals who were likely to describe themselves as evening types. The remaining quartile consisting of those who had been abstinent for one to three weeks, did not exhibit this tendency. However, with full Bonferroni correction ( $\alpha = .006$ ), only the group displaying the longest period of abstinence from ecstasy differed statistically from the cannabis only and drug naïve persons<sup>3</sup>.

This difference in sleep type is particularly interesting. Over a third of ecstasy/polydrug users described themselves as definitely evening types, compared with just 10% in the general population<sup>[21]</sup> and 11% of drug naïve persons in the present study. In the animal literature, MDMA and other serotonin-related drugs such as fenfluramine have been shown to interfere with the body's ability to "reset" its circadian clock in rats<sup>[22]</sup>. Although this decrement was slightly reduced at 20 weeks following administration, the deficits were still present, and the authors suggest that this is due to serotonergic degeneration caused by ecstasy and fenfluramine. This is further supported by Colbron et al<sup>[23]</sup> who found that repeated exposure to MDMA in hamsters altered the ability of the circadian clock to phase shift. Thus it is possible that this difference in sleep type reflects a transient ecstasy-related shift in circadian rhythms in human ecstasy users. However, the proposition that ecstasy use causes individuals to become evening types must be treated with a degree of caution. It is equally possible that these individuals were evening types prior to the initiation of drug use. Future studies would do well to adopt longitudinal designs in which premorbid characteristics can be properly assessed.

Statistically significant differences in self-reported sleep quality were also observed, with ecstasy/polydrug users reporting poorer sleep quality than drug naïve persons. This is in line with previous studies in ecstasy users where "restless sleep" has frequently been cited<sup>[3, 8, 24, 25]</sup>.

On the Karolinska measure drug naïve individuals were less tired compared to ecstasy/polydrug users at the beginning of testing and cannabis users were more tired than ecstasy/polydrug users at the end of testing. However, even on a one-tailed basis, neither of these two differences was statistically significant following Bonferroni correction. In our

previous study<sup>[18]</sup>, ecstasy/polydrug users were found to differ significantly from the control group on the Karolinska measure at the beginning of testing. However, no significant difference was found in the present study despite the fact that the data were largely the same. In our previous study the control group contained cannabis only users, while in the present study these have been separated out as a distinct group. Furthermore, the present sample contained an additional 13 ecstasy/polydrug users and an additional 10 non-ecstasy users, recruited after the close of the previous study. The differences between the two studies highlight the potential importance of separating out different polydrug categories.

While statistically significant group differences were observed on the sleep type, sleep quality and missing a night's sleep measures, none of these appear to have mediated the significant ecstasy/polydrug -related group deficits that were observed on the cognitive measures which all remained significant following the inclusion of the relevant sleep measures as covariates. This would seem to suggest that the cognitive deficits do not arise from sleep deprivation, or restless sleep nor do they appear to reflect morningness-eveningness differences which might be associated with differential time of day effects in relation to testing.

The fact that most of the sleep measures yielded no overall statistically significant group differences is surprising as it has been suggested that, in part, the cognitive deficits displayed by ecstasy users may reflect differences in lifestyle, for example Cole and Sumnall<sup>[26]</sup> suggest that the lifestyle of an ecstasy user is one of constant circadian disruption, which has been responsible for similar cognitive deficits in aircrew (Chou et al. 2000 cited in Cole and Sumnall<sup>[26]</sup>). In the present study, if this were the case then one would expect that ecstasy users would report fewer average hours of sleep per night and greater subjective sleepiness. However, this was not the case. It is possible that the heterogeneous nature of the ecstasy/polydrug group might have been a factor in explaining the absence of sleep impairment. Interestingly Carhart-Harris et al<sup>[1]</sup> did not observe significant sleep problems in their ecstasy/polydrug group. The sleep-related deficits that were observed in that study were limited to ecstasy-only users. Carhart-Harris et al have suggested that the sedative effects of

cannabis might have counteracted the potential for sleep disturbance among the ecstasy/polydrug group and this may also have been the case in the present study.

There were a number of limitations with the present study. Firstly, we had to rely on self-reports of previous drug use. While other ecstasy use studies have also relied on self-report measures<sup>[27, 28, 29, 30]</sup> clearly it would have been desirable to use objective testing methods (e.g. urine, hair). The data were accumulated over a period of years and while all participants completed a subset of measures, during the various phases of the project new cognitive measures were introduced and others were removed from the test battery. While all three groups experienced this changing pattern in equal measure, we cannot guarantee that the demands of the test procedure were equivalent in terms of their potential to give rise to fatigue over the entire duration of the project. Having said this, the length of the test session remained fairly constant throughout averaging between three and four hours with a break roughly half way through.

To summarise, ecstasy/polydrug users and cannabis-only users and drug naïve persons performed similarly on most of the sleep measures. Most notable was the difference in sleep type between the ecstasy/polydrug users and the other two groups. Future research should seek to investigate this concept of a circadian shift in human users of the drug and also the apparent differences in morningness/eveningness as a construct<sup>[31]</sup>.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## References

1. Carhart-Harris RL, Nutt DJ, Munafo M, Wilson SJ (in press) Current and former ecstasy users report different sleep to matched controls: a web-based questionnaire study. *Journal of Psychopharmacology*: published online June 18, 2008 as doi:10.1177/0269881108089599.
2. Baylen CA Rosenberg H (2006) A review of the acute subjective effects of MDMA/ecstasy. *Addiction* 101: 933-947.
3. Huxster JK, Pirona A, Morgan MJ (2006) The sub-acute effects of recreational ecstasy (MDMA) use: a controlled study in humans. *Journal of Psychopharmacology* 20(2): 281-290.
4. Montoya AG, Sorrentino R, Lukas SE, Price BH (2002) Long-term Neuropsychiatric Consequences of "Ecstasy" (MDMA): A review. *Harvard Rev Psychiatry* 10: 212-220
5. Schierenbeck T, Riemann D, Berger M, Hornyak M. (2008). Effect of illicit recreational drugs upon sleep: Cocaine, ecstasy and marijuana. *Sleep Medicine Reviews*, 12, 381-389.
6. Dughiero G, Schifano F, Forza G (2001) Personality dimensions and psychopathological profile of Ecstasy users. *Human Psychopharmacology: Clinical and Experimental: Special issue: The human psychopharmacology of MDMA or 'Ecstasy'* 16: 635-639
7. Soar, K.; Parrott, A. C.; Fox, H. C.; (2004) Persistent neuropsychological problems after 7 years of abstinence from recreational ecstasy (MDMA): A case study. *Psychological Reports* 95: 192-196



8. Parrott AC, Rodgers J, Buchanan T, Ling J, Heffernan T, Scholey AB (2006)  
Dancing hot on ecstasy: physical activity and thermal comfort ratings are associated with the memory and other psychobiological problems reported by recreational MDMA users. *Human Psychopharmacology Clin Exp* 21: 285-298
9. Allen R, McCann UD, Ricaurte GA (1993) Persistent Effects of (+)3,4-Methylenedioxymethamphetamine (MDMA, "Ecstasy") on Human Sleep Sleep 16(6): 560-564
10. McCann UD, Ricaurte GA (1995) On the neurotoxicity of MDMA and related amphetamine derivatives. *Journal of Clinical Psychopharmacology* 15: 295-296.
11. Insel TR, Battaglia G, Johannessen JN, Marra S (1989) 3,4-Methylenedioxymethamphetamine ('Ecstasy') selectively destroys brain serotonin terminals in rhesus monkeys. *Journal of Pharmacology and Experimental Therapeutics* 249: 713-720.
12. Balogh B, Molnar E, Jakus R, Quate L, Olverman HJ, Kelly PAT, Kantor S, Bagdy G (2004) Effects of a single dose of 3,4-methylenedioxymethamphetamine on circadian patterns, motor activity and sleep in drug-naïve rats and rats previously exposed to MDMA. *Psychopharmacology* (2004) 173: 296–309
13. Santucci V, Storme J-J, Soubrié P, Le Fur G (1996). Arousal-enhancing properties of the CB1 cannabinoid receptor antagonist SR 14176A in rats as assessed by electroencephalographic spectral and sleep-waking cycle analysis. *Life Sciences*, 58: PL103-PL110.
14. Tassinari CA, Ambrosetto G, Peraita-Adrado MR, Gastaut H (1999) The neuropsychiatric syndrome of  $\Delta^9$ -THC and cannabis intoxication in naïve subjects: A clinical and polygraphic study during wakefulness and sleep. In: Nahas GG, Sutin KM, Harvey D, Agurell S, Pace N, Marihuana and Medicine. Totowa, NJ, US: Humana Press, pp. 649-664.

15. Nicholson AN, Turner C, Stone BM, Robson PJ (2004) Effect of  $\Delta$ -9-tetrahydrocannabinol and cannabidiol on nocturnal sleep and early-morning behavior in young adults. *Journal of Clinical Psychopharmacology* 24: 305-313.
16. Budney AJ, Moore BA, Vandrey RG, Hughes JR (2003) The time course and significance of cannabis withdrawal. *Journal of Abnormal Psychology* 112: 393-402.
17. Arendt M, Rosenberg R, Foldager L, Sher L, Munk-Jorgensen P (2007) Withdrawal symptoms do not predict relapse among subjects treated for cannabis dependence. *The American Journal on Addictions* 16: 461-467.
18. Montgomery C, Fisk JE, Wareing M, Murphy PN (2007). Self reported sleep quality and cognitive performance in ecstasy users. *Human Psychopharmacology: Clinical and Experimental* 22: 537-548.
19. Johns M, Hocking B (1997) Daytime sleepiness and sleep habits of Australian workers. *Sleep* 20: 844-849.
20. Gillberg M, Kecklund G, Akerstedt T (1994). Relations between performance and subjective ratings of sleepiness during a night awake. *Sleep* 17: 236-241.
21. Smith CS, Reilly C, Midkiff K (1989). Evaluation of three circadian rhythm questionnaires with suggestions for an improved measure of morningness. *Journal of Applied Psychology*, 74, 728-738
22. Biello SM, Dafters RI (2001) MDMA and fenfluramine alter the response of the circadian clock to a serotonin agonist in vitro. *Brain Research* 920: 202-209.
23. Colbron S, Jones M, Biello SM (2002) MDMA alters the response of the circadian clock to a photic and non-photic stimulus. *Brain Research* 956: 45-52.
24. Parrott AC, Sisk E, Turner JJD (2000) Psychobiological problems in heavy “ecstasy” (MDMA) polydrug users. *Drug and Alcohol Dependence* 60: 105-110.
25. Topp L, Hando J, Dillon P, Roche A, Solowij N (1999) Ecstasy use in Australia: patterns of use and associated harm. *Drug and Alcohol Dependence* 55:105-115

26. Cole JC, Sumnall HR (2003) Altered states: the clinical effects of Ecstasy.  
Pharmacology & Therapeutics 98: 35– 58.
27. 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.
28. Morgan MJ (1998) Recreational use of “ecstasy” (MDMA) is associated with  
elevated impulsivity. Neuropsychopharmacology 19: 252-264.
29. Morgan MJ (1999) Memory deficits associated with recreational use of “ecstasy”  
(MDMA). Psychopharmacology 141: 30-36.
30. Rodgers J (2000) Cognitive performance amongst recreational users of “ecstasy”.  
Psychopharmacology 151: 19-24.
31. Horne JA, Ostberg O (1976) Self-Assessment Questionnaire to Determine  
Morningness-Eveningness in Human Circadian Rhythms. International Journal of  
Chronobiology 4: 97-110

## Figure Captions

Figure 1:

Sleep Type According to Period of Abstinence from Ecstasy From Most Recent (1st Quartile) to Most Abstinent (4th Quartile) Compared to Cannabis Only Users and Drug Naïve Persons.

Table 1. Age, Years of Education, Intelligence, and Measures of Illicit Drug Use for Cannabis-Only and Ecstasy/Polydrug users.

	Cannabis-Only Users				Ecstasy/Polydrug Users			
	Median	Mean	S.D.	n	Median	Mean	S.D.	n
Age	21	20.96	1.76	53	21	21.68	1.95	117
Years of education	16	15.39	2.03	53	16	15.10	2.80	117
Ravens Progressive Matrices	50	49.63	4.85	52	48	47.68	6.04	114
Ecstasy								
Lifetime dose (tablets)	-	-	-	-	187	328.55	449.68	117
Current use (tablets taken in previous 30 days)					1	3.09	4.84	116
Weeks since last use					3	23.30	52.84	117
Cannabis								
Lifetime dose (joints)	76	631.26	1091.21	33	1052.5	3159.49	4597.49	87
Current use (joints taken in previous 30 days)	1	8.55	26.95	32	9.5	37.10	62.46	86
Weeks since last use	4	31.51	70.25	52	0.57	24.46	76.82	97
Cocaine								
Lifetime dose (grams)					22	53.29	88.47	47
Current use (grams taken in previous 30 days)					1	1.39	1.88	45
Weeks since last use					3	14.20	36.67	91
Amphetamine								
Lifetime dose (grams)					6	72.95	136.87	33
Current use (grams taken in previous 30 days)					0	0.33	1.26	23
Weeks since last use					52	99.00	118.02	44

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.

Table 2. Indicators of various sleep attributes and cognitive functions among drug naïve, cannabis-only and ecstasy/polydrug users

	Drug Naïve					Cannabis Only					Ecstasy/Polydrug				
	Mean	s.d	Median	25Pctl	75Pctl	Mean	s.d	Median	25Pctl	75Pctl	Mean	s.d	Median	25Pctl	75Pctl
Sleep Measures															
Sleep Type	3.58	0.96	4	3	4	3.56	1.04	4	3	4	4.02	1.01	4	4	5
Sleep Quality	1.69	0.63	2	1	2	1.92	0.79	2	1	2	1.99	0.85	2	1	2.5
Hours Sleep per Night	8.06	1.07	8	8	9	8.02	1.33	8	7	9	7.97	1.47	8	7	9
Morning State	2.55	0.69	3	2	3	2.54	0.73	3	2	3	2.66	0.74	3	2	3
Epworth Sleepiness Scale	6.40	3.25	6	4	9	6.83	3.42	7	4	9	6.54	3.38	6	4	9
Karolinska Sleepiness Scale (beginning)	4.26	1.36	4	3	5	4.74	1.63	5	3	6	4.85	1.57	5	3	6
(end)	5.50	1.64	6	4	7	6.01	1.42	6	5	7	5.49	1.53	6	4	7
Cognitive Measures															
Computation	4.59	1.58				4.42	1.32				3.84	1.68			
Span															
Letter Updating	4.15	0.65				4.18	0.63				3.83	0.81			
Chicago Word Fluency	0.27	1.03				0.26	0.27				-0.40	0.84			

Sleep Type: 1 – definitely morning type; 2 – more morning; 3 – neither; 4 – more evening; 5 – definitely evening type.

Sleep Quality: 1 – very well; 2 – satisfactory; 3 – not very well; 4 very badly.

Morning Tiredness: 1 – very alert; 2 – fairly alert; 3 – fairly tired; 4 – very tired

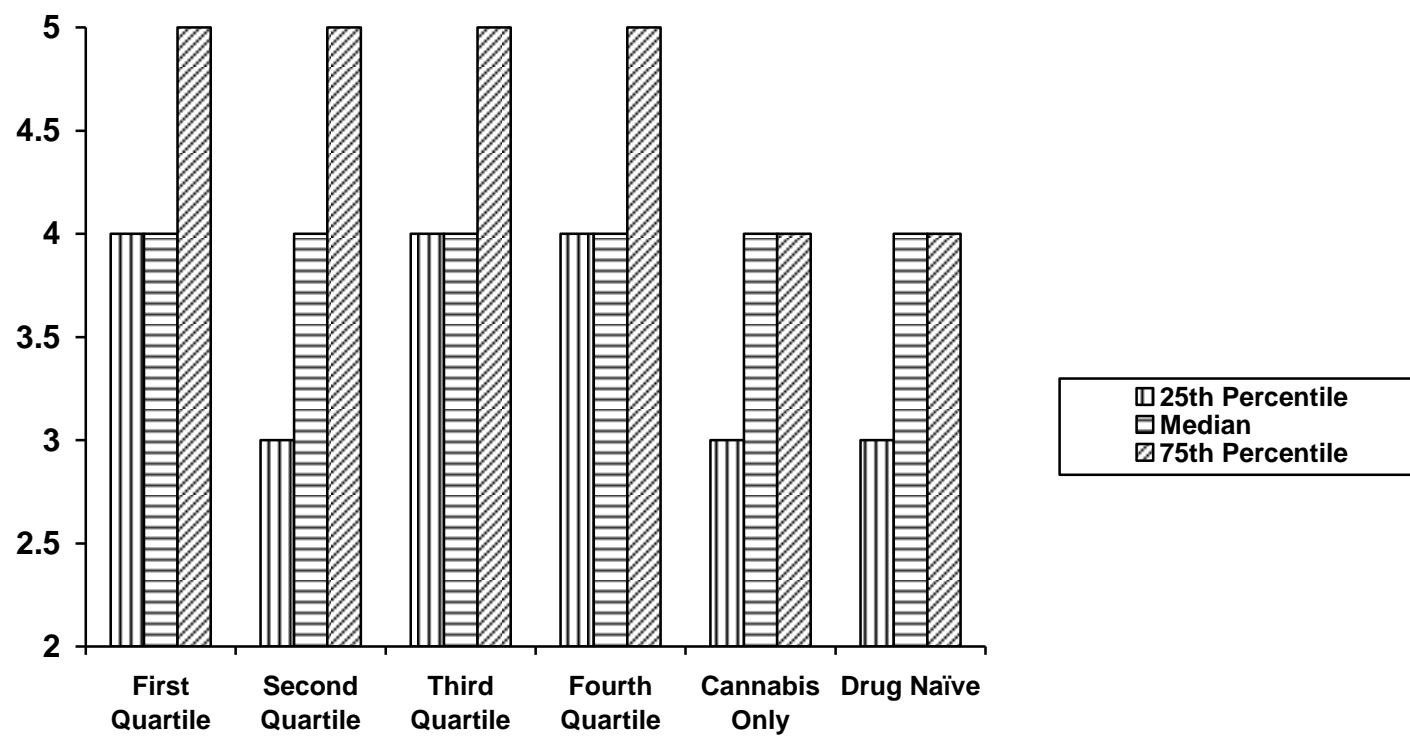
The Epworth and Karolinska Data and the cognitive measures were reported in our previous paper<sup>[18]</sup>.

Table 3

Inferential statistics corresponding to the drug use group effects and pairwise comparisons for the various sleep measures.

	Overall Effect $\chi^2$ (df=2; N=224)	Drug Naïve versus Cannabis Only Mann-Whitney U	Drug Naïve versus Ecstasy/Polydrug Mann-Whitney U	Cannabis Only versus Ecstasy/Polydrug Mann-Whitney U
Sleep Type	13.45**	1381.00	2342.00**	2232.00**
Sleep Quality	4.78 <sup>†</sup>	1210.00	2613.00*	2924.00
Hours Sleep per Night	0.48	1377.50	3020.50	2944.00
Morning State	1.00	1429.00	2987.00	2827.50
Epworth Sleepiness Scale	0.51	1367.00	3216.00	2794.00
Karolinska Sleepiness Scale (beginning)	3.26	558.50	1099.50 <sup>†††</sup>	1542.50
Karolinska Sleepiness Scale (end)	3.43	551.00	1354.50	1259.50 <sup>††</sup>

\*\*  $p < .01$ ; \*  $p < .05$ ; <sup>†††</sup>  $p = .065$ ; <sup>††</sup>  $p = .066$ ; <sup>†</sup>  $p = .091$ , all two tailed.





---

<sup>1</sup> The Karolinska measure was not administered during the early stages of our research programme. Therefore the data that were reported correspond to 34 drug naïve, 39 cannabis only and 82 ecstasy/polydrug users.

<sup>2</sup> A small number of participants were unable to complete the test session due to other commitments. These individuals returned on a subsequent occasion to complete the test battery.

<sup>3</sup> Full Bonferroni correction is only one means of controlling for inflated Type one error. It is worthy of note that the number of pairwise comparisons that might be expected to produce alpha values exceeding .05 purely by chance (the error rate per experiment) is less than one ( $8 \times .05 = 0.4$ ). Thus the fact that six of the eight comparisons were associated with alpha values less than .05 suggests that the sample as a whole is disproportionately characterised by evening types.