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Current and former ecstasy users report different sleep to matched controls: a web-based questionnaire study

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Abstract

This study sought to test the association between ecstasy-use and abnormal sleep.
An anonymous web-based questionnaire containing questions on drug use and sleep was completed by 1035 individuals. From this large sample, a group of 89 ecstasy users were found who reported very little use of other drugs. This "ecstasy-only" group was further divided into two groups of 31 current users and 58 abstinent users. The subjective sleep of current and former ecstasy-only users was compared with that of matched controls. Patients were asked to rate their sleep according to: 1) sleep quality, 2) sleep latency, 3) night time awakenings and 4) total sleep time. Current ecstasy-only users reported significantly worse sleep quality ($P < 0.05$) and a greater total sleep time ($P < 0.001$) than controls. It was inferred that these differences might be due to recovery from the acute effects of the drug. Abstinent ecstasy-only users reported significantly more nighttime awakenings than controls ($P < 0.01$). These subjective findings are in agreement with the objective findings of previous studies showing persistent sleep abnormalities in ecstasy users.

Key words

5-HT; ecstasy; MDMA; serotonin; sleep

Introduction

Sleep abnormalities are often cited as a neurobiological symptom of chronic recreational ecstasy use (Morgan, 2000; Thomasius, *et al.*, 2004; McCann, *et al.*, 2000). It is widely recognised that the acute stimulant effects of 3,4-methylenedioxymethamphetamine (MDMA) disturb sleep. Users often report difficulty sleeping on ecstasy (Vollenweider, *et al.*, 1998; Topp, *et al.*, 1999) and describe vivid closed eye visual hallucinations and difficulty falling asleep when coming down from the drug (Topp, *et al.*, 1999; Curran, *et al.*, 2004). Some studies have documented subjective reports of lasting sleep abnormalities in former ecstasy users (Morgan, *et al.*, 2002; Soar, *et al.*, 2004; von Geusau, *et al.*, 2004), whereas other sleep enquiries have not found any evidence of persistent abnormalities (von Geusau, *et al.*, 2004, Montgomery, *et al.*, 2005).

Addressing the question with objective measures, data from two polysomnographic studies have been published comparing the sleep of abstinent ecstasy users with that of controls (Allen, *et al.*, 1993; McCann, *et al.*, 2007). Allen, *et al.* recorded the sleep of 23 abstinent (>14 days) ecstasy-polydrug users and compared this with that seen in 22 age, sex (but not "other" drug) matched controls. Ecstasy users had significantly less total sleep time than controls, although significant reductions were found exclusively in stage 2 sleep. In a more recent study, McCann, *et al.* recorded the sleep of 25 abstinent (mean 3.1 months) ecstasy-polydrug users and compared this with sleep in 23 age and education (but not sex or 'other' drug) matched controls. Consistent with the Allen study, ecstasy users had significantly less stage 2 sleep than controls. The authors of both studies suggested that the abnormal sleep might signify serotonergic damage resulting from ecstasy use.

A recent study in rats lends some support to this interpretation. Intraperitoneal injections of 15 mg/kg MDMA corresponded with abnormal sleep architecture and reduced 5-HT

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cell marker density 7 and 21 days after treatment (Kirilly, *et al*., 2008). Reduced latency to rapid eye movement (REM) sleep and increased sleep fragmentation were reported. These sleep changes are consistent with the expected effects of reduced serotonergic tone, and increased sleep fragmentation is consistent with the human polysomnography findings cited above. Importantly however, the sleep and serotonergic abnormalities recovered to non-significant levels after 180 days, suggesting good recovery from the toxic insult.

MDMA has been found to damage serotonergic cells in a variety of different animals by a number of different research teams (Battaglia, *et al*., 1987; Saadat, *et al*., 2004; Hatzidimitriou, *et al*., 1999). 5-HT is known to play an important role in sleep (Jouvet, 1999). The suprachiasmatic nucleus (SCN) of the hypothalamus, an area receiving the densest innervation of serotonergic cell fibres in the forebrain, plays a vital role in the control of the sleep–wake cycle (Ursin, 2002). Researches have found damage (Sabol and Seiden, 1998, Ricaurte, *et al*., 1992; Gardani, *et al*., 2005; Kirilly, *et al*., 2008) and abnormal recovery in the SCN of primates and rodents after heavy doses of MDMA (Sabol and Seiden, 1998; Fischer, *et al*., 1995; Ricaurte, *et al*., 1992). High doses of MDMA have been found to induce a prolonged dysregulation of the circadian rhythm in hamsters (Colbron, *et al*., 2002; Gardani, *et al*., 2005) and rats (Biello and Dafters, 2001).

There is a large amount of indirect evidence that MDMA induces serotonergic neurotoxicity in humans (Parrott, 2006). Several imaging studies have looked at the brains of human ecstasy users for evidence of 5-HT cell damage (McCann, *et al*., 1998; Semple, *et al*., 1999; Reneman, *et al*., 2001; Buchert, *et al*., 2004; McCann, *et al*., 2005). Arguably, the most incisive and methodologically sound are the recent positron emission tomography studies (Buchert, *et al*., 2004; McCann, *et al*., 2005). These studies discovered reductions in the densities of 5-HT transporters in both current and abstinent ecstasy users compared with controls. The 5-HT transporter has been shown to be a reliable marker of the integrity of the 5-HT neuron in animals (Scheffel and Ricaurte, 1990). It is important to note, however, that the human imaging studies also found evidence of recovery of 5-HT transporter densities with prolonged abstinence from ecstasy (Buchert, *et al*., 2004; McCann, *et al*., 2005). It has been hypothesised that MDMA-induced serotonergic neurotoxicity leads to lasting neuropsychological and neurobiological symptoms in recreational ecstasy users. Considering the importance of 5-HT for sleep modulation, it is likely that ecstasy-induced damage to the 5-HT system has implications for sleep.

This study sought to test the relationship between sleep and ecstasy use by collecting a large sample of ecstasy users and asking them about their sleep using a questionnaire designed for this purpose. On the basis of previous subjective and objective sleep studies using samples of ecstasy users, it was hypothesised that both current and abstinent ecstasy users would have poorer quality sleep compared with non-ecstasy controls.

Methods

Participants

A total of 1035 participants submitted acceptable forms. Duplicated forms and forms which raised suspicions of fabrication were deleted. Duplicated forms were easy to identify because responses were identical with those of previously submitted forms. Also, submissions sometimes contained the same email address but slightly different responses; in such cases, the latest form was used and any earlier submissions deleted. A small number of submission containing inconsistent, obscure or facetious responses were removed from the total sample. It is possible that some fabricated responses went undetected and were included in the total sample; this is a disadvantage of internet-derived samples that is difficult to combat. Of the 1035 participants who submitted forms, 857 had taken ecstasy at least once. Of the 857, 89 were regarded as predominantly 'ecstasy-only' users. Criteria for ecstasy-only use were: greater than 10 lifetime ecstasy pills, 10 or less lifetime uses of cocaine, crack cocaine, amphetamine, ketamine and opiates, and one or less uses of cannabis in the last month. Of the 89 ecstasy-only users, 31 were current users and 58 former/abstinent users. Ecstasy-users were categorised as 'abstinent' if they had not used the drug for over 28 days.

Procedure

The questionnaire, together with an introduction page, was assigned a secure web address within the University of Bristol Psychiatry department's web space (http://www.bris.ac.uk/psychiatry/secure/mdmaquest.html). Advertisements for the questionnaire webpage were placed on a number of websites and forums related to recreational drug use, youth culture and dance music. Additionally, small advertisement cards were distributed at dance music venues and record shops.

On accessing the website, participants were presented with an introduction page explaining the nature and purpose of the study. A link to a drug abuse help service was provided (http://www.bdp.org.uk/ecstasy.html). Individuals were encouraged to participate regardless of whether they had taken ecstasy or not. They were offered the incentive of a prize draw to win £50 of CD vouchers. Participants were reassured that their responses were completely anonymous and would be securely stored. Submitted forms were sent directly to a password protected email address. The questionnaire was available online for 6 months.

The questionnaire consisted of 62 questions. In addition to initial demographic questions, there were 10 questions specific to ecstasy use. Most of these questions were concerned with extent of use (e.g., 'What is the highest number of ecstasy pills you have taken in a single session?'). There were approximately 15 questions dedicated to polydrug use, including alcohol, and three questions on psychiatric and sleep medication. There were 11 self-constructed sleep questions. Most of the

questions in the questionnaire required numeric answers and some incorporated a Likert scale with selection buttons. In addition, there were opportunities for participants to elaborate on their answers. For example, text boxes were provided into which participants could describe specific aspects of their sleep. Finally, participants were encouraged to leave contact details in case of follow-up. Submitting the questionnaire was completed by clicking a 'submit' button with text alongside notifying that clicking would be considered a declaration of knowledgeable consent.

Data analysis

Mann–Whitney tests were used to compare the median values for a number of variables. Samples were not normally distributed, so Spearman's rank correlations were used for any correlational analyses.

Results

Summary

Current ecstasy-only users reported significantly worse sleep quality ($P < 0.05$) and a greater total sleep time ($P < 0.001$) than controls. Former ecstasy-only users reported significantly greater nighttime awakenings than controls ($P < 0.01$) and were significantly more likely than controls to be taking sleep medication ($P < 0.05$).

Demographics

Participants were reasonably well matched for age and sex. The current ecstasy-only group were significantly younger than the non-ecstasy control group (Table 1). In all the tables, the data for each ecstasy group is compared against the controls.

Drug use

The ecstasy-only groups were well matched with the control group for alcohol use. Significant differences were seen between both ecstasy-only groups and controls in use of amphetamine, cocaine and ketamine (Table 2). Only the current ecstasy-only group were currently using significantly more cannabis than controls. Although these differences are statistically significant, there is no evidence to suggest that such minimal use of any of these drugs would have an effect on long-term subjective sleep reports.

A significantly greater percentage of abstinent (but not current) ecstasy users than controls reported previous use of prescription medication for anxiety or depression. Conversely, a significantly greater percentage of current ecstasy users (but not abstinent ecstasy users) than controls reported current use of prescription medication for anxiety or depression. A significantly higher percentage of abstinent ecstasy users than controls reported current use of sleep medication. Although the use of sleep medication is a confounding variable, the removal of those subjects who claimed to be taking sleep medication had no effect on between-group comparisons of sleep.

Sleep

For the following sleep variables: sleep latency, sleep quality, number of awakenings, total sleep time, weekday wake up and fall asleep time, and fall asleep time when socialising, all responses were organised into groups of ordinal data. For *sleep latency*, the question was asked: 'how long does it usually take you to fall asleep?' Answers were sorted into the following groups, ordered 1–5: <10 min; 10–30 min; 30–60 min; 60–90 min; >90 min. For *sleep quality*, the question was asked 'In general, is your sleep:' The four possible responses were ordered 1–4: very unsatisfactory, moderately unsatisfactory, moderately satisfactory, very satisfactory. For number of awakenings, the question was asked: 'estimate the number of times you wake up during a typical nights sleep'. The six possible responses were ordered 1–5: <1, 1, 2, 3, >3. For *total sleep time*, the question was asked 'estimate how many hours sleep you get on weekdays'. The six possible responses were ordered 1–5: <5, 5–6, 6–7, 7–8, >8. For *fall asleep time* (*weekdays*), the question was asked: 'what time do you usually fall asleep on weekdays?' Answers were collected into five groups, ordered 1–5: before 10 p.m., 10 p.m. to 11:59 p.m.; 12 a.m. to 1:59 a.m.: 2 a.m. to 3:59 a.m.; later than 4 a.m. For *fall asleep time* (*when socialising*), the question was asked: 'what time do you usually fall asleep on nights when you have been socialising?' The same five categories of responses used in the previous question were used for this question. For *wake up time* (*weekdays*), the question was asked: 'what time do you usually wake up on weekdays?' Answers were collected into the following groups ordered 1–5: before

Table 1 Demographics

	Current ecstasy-only, $n = 31$	Abstinent ecstasy-only, $n = 58$	Ecstasy polydrug, $n = 242$	Non-ecstasy, $n = 178$
Mean age	22.4 (16–38)	26.9 (17–50)	27.2 (16–53)	27.9 (16–57)
Median age	22*	24.5	26	25
Sex (% females)	23	22	15	20

Range in brackets.

*Significant difference compared with non-ecstasy. $P < 0.05$ (Mann–Whitney).

Table 2 Drug use

	Current ecstasy-only, *n* = 31	*P*-values	Abstinent ecstasy-only, *n* = 58	*P*-values	E-polydrug, *n* = 242	*P*-values	Non-ecstasy, *n* = 178
Ecstasy mean lifetime pills	138.2 (12–1250)	NA	109.8 (12–1000)	NA	609 (12–10,000)	NA	0
Ecstasy mean highest pills taken in a single session	6.0 (2–20)	NA	4.4 (1–16)	NA	8.1 (1–50)	NA	0
Ecstasy mean days since last pill	8 (1–25)	NA	512 (28–3650)	NA	447 (28–3650)	NA	NA
Alcohol mean weekly units	15.1 (0–45)	0.26	16.5 (0–95)	0.63	23.7 (0–300)	0.020*	18.2 (0–100)
Cannabis mean occasions used in last month	0.4 (0–1)	<0.001***	0.1 (0–1)	0.07	35 (0–500)	<0.001***	0.06 (0–1)
Amphetamine mean lifetime uses	2.5 (0–8)	<0.001***	1.7 (0–10)	<0.001***	170 (0–10000)	<0.001***	0.3 (0–6)
Cocaine mean lifetime uses	1.4 (0–9)	<0.001***	1.5 (0–7)	<0.001***	292 (0–10000)	<0.001***	0.2 (0–6)
Ketamine mean lifetime uses	1.1 (0–7)	<0.001***	0.6 (0–8)	<0.001***	52 (0–6000)	<0.001***	0.04 (0–2)
Previous use of medication for anxiety or depression	20%	0.12	28%	<0.001***	28%	<0.001***	9%
Current use of medication for anxiety or depression	10%	0.033*	5%	0.26	7%	0.021*	2%
Current use of sleep medication	0%	0.56	7%	0.012*	5%	0.045*	1%

Range in brackets.

*Significant difference compared with non-ecstasy. $P < 0.05$ (Mann–Whitney).

***Significant difference compared with non-ecstasy. $P < 0.001$ (Mann–Whitney).

6:59 a.m.; 7 a.m. to 7:59 a.m.: 8 a.m. to 8:59 a.m.; 9 a.m. to 9:59 a.m.; after 10 a.m.

Comparing the sleep data for each ecstasy group against the controls, it was apparent that the current ecstasy-only group reported significantly worse sleep quality. Abstinent ecstasy-only users also had worse sleep quality but this difference did not reach significance (Figure 1). The mean values given in Chart 1 give an idea of the relative differences. Abstinent ecstasy users reported significantly more nighttime awakenings than non-ecstasy controls (Figure 2). Current ecstasy users reported sleeping significantly longer than non-ecstasy controls; this may be linked to recovery from the drug-induced sleep deprivation. In support of this inference, current ecstasy users reported falling asleep significantly later than controls on nights when they had been out socialising.

Given the hypothesised relationship between ecstasy use and lasting sleep disturbances, correlational analyses were carried out comparing the lifetime amount of ecstasy used and highest

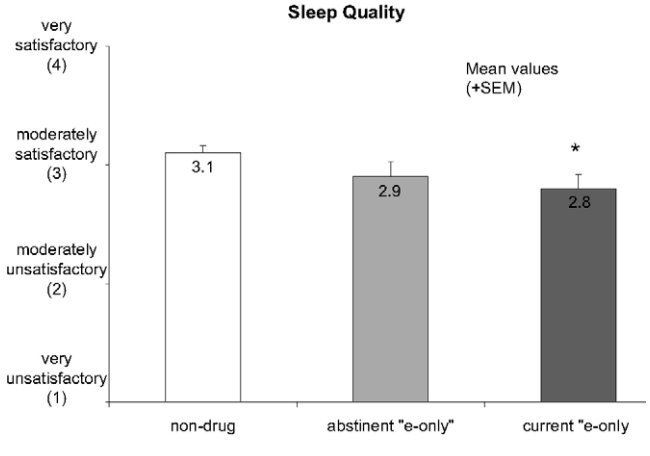

Figure 1 Both abstinent and current ecstasy users reported worse sleep than controls but this difference only reached significance for the current users.

*Significant difference compared with non-ecstasy. $P < 0.05$ (Mann–Whitney).

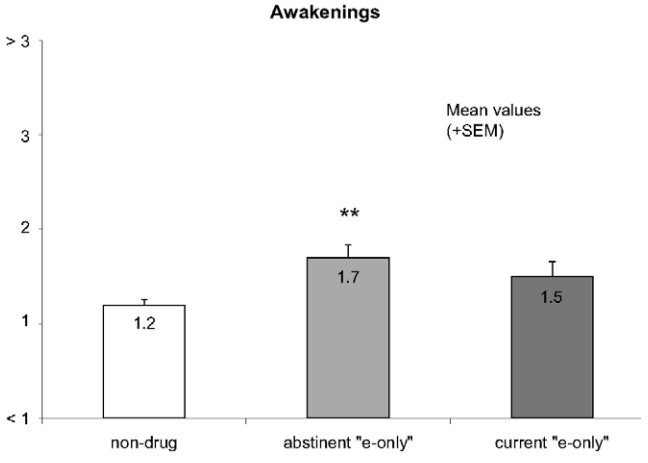

Figure 2 Abstinent ecstasy users but not current ecstasy users reported significantly more nighttime awakenings than controls.

**Significant difference compared with non-ecstasy. $P < 0.01$ (Mann–Whitney).

number of pills taken in a single session with all sleep variables. None of these analyses showed any statistically significant relationships, although there was a consistent trend towards heavier users reporting worse sleep.

Discussion

As mentioned in the 'introduction', sleep abnormalities are commonly cited as a possible neurobiological and/or neuropsychological side effect of ecstasy use. The results of this study provide some additional evidence to support this association. The large size of the original sample is useful in that it has allowed the extrication of a group of predominantly ecstasy-only users, a much sought after study group in ecstasy research. Using an ecstasy-only sample avoids the confounding variable of polydrug use. The vast majority of ecstasy users also take other drugs, many of which have been associated with acute and subacute sleep changes (Johanson, *et al.*, 1999; Comer, *et al.*, 2001; Morgan, *et al.*, 2006; Barratt, *et al.*, 1974). Previous studies that have looked at objective and subjective measures of sleep have used polydrug samples. In such cases, it is difficult to infer whether or not sleep changes are related to ecstasy or use of other drugs.

It is generally accepted that the acute effects of MDMA and the subacute recovery have consequences for sleep. The acute stimulant effects of MDMA induce a transient insomnia that is initially followed by fragmented sleep and complex closed eye visual hallucinations. The reported sleep of current ecstasy users was consistent with this pattern. The current ecstasy group reported poorer quality sleep than controls. The mean number of days of abstinence for this group was 8; some participants had even taken ecstasy the night before completing the questionnaire. It is likely, therefore, that their sleep reports were very much influenced by the acute effects of the drug and subsequent recovery. Despite the significantly poorer reported sleep of current ecstasy users, the median sleep quality rating was still 'moderately satisfactory'; thus, although sleep disruptions were clearly apparent, they were not severe.

In addition to reports of poorer sleep quality, the current ecstasy users also reported sleeping significantly longer than controls ($P \leq 0.001$). This may reflect recovery after drug- and social activity–related sleep deprivation. It may also be related to the life circumstances of the participants. Although the question was not asked, it seems likely that more of the non-ecstasy controls were either working or having to wake up for other obligations. This hypothesis is supported by the significantly later midweek wake up times of the current ecstasy-only group ($P \leq 0.001$). It is perhaps most likely that the current ecstasy-only group slept longer than controls simply because fewer of them were obliged to get up at a particular time.

Because the findings for the current ecstasy users might possibly have been related to their significantly younger age, we also carried out analyses after matching the age of the current ecstasy group with the control group by removing subjects over 45 years of age from the control group. This had no effect on the results. There was also no evidence of a relationship between sleep quality (or any other sleep variables) and age in any of the groups when analysed independently or when combined.

It is much easier to identify factors affecting sleep after recent use of ecstasy. It is much harder, however, to identify the causes of persistent sleep abnormalities in abstinent ecstasy users. Previous studies have reported differences in the sleep architecture of abstinent ecstasy uses compared with controls (Allen, *et al.*, 1993; McCann, *et al.*, 2007), but none of these studies have used ecstasy-only samples or matched for polydrug use. There is a tendency in such cross-sectional studies to ascribe any positive findings to neurological changes related to ecstasy use, but it is still contested whether low doses of MDMA are capable of causing neuronal damage when used recreationally by humans (e.g., Iversen, 2006) and whether the damage is sufficiently severe and persistent to affect sleep.

In this study, abstinent ecstasy users reported significantly more nighttime awakenings than controls. Current ecstasy users also reported a greater number of awakenings, but this difference did not reach significance. There are a number of possible explanations for the greater number of awakenings reported by abstinent ecstasy users. An argument has been repeatedly raised around non-prospective ecstasy studies that group differences may have existed before ecstasy use. To address this issue, we asked all ecstasy users whether their sleep was different now compared with how it was before they first took ecstasy; 55% of current users and 21% of abstinent users answered 'yes' (Table 3). Although a very small number in both groups claimed that their ecstasy use had improved their sleep, the vast majority stated that it had generally become more disturbed. We also asked those who had reported a change whether they believed it might be related to ecstasy; 82% of current users and 75% of abstinent users answered that it was either 'definitely' or 'possibly' related to ecstasy use.

It is unsurprising that so many current users reported that their sleep had been affected by ecstasy use (Table 4). It is more interesting however, that a reasonably large percentage (21%) of abstinent users also reported that their sleep is different now compared with how it was before they had ever taken

Table 3 Different sleep

	'Is your sleep different now compared to how it was before you started taking ecstasy?'	'Do you think this is related to ecstasy or something else?'
Current ecstasy-only, $n = 31$	'Yes' 55%	'Possibly or definitely related to ecstasy' 82%
Abstinent ecstasy-only, $n = 58$	'Yes' 21%	'Possibly or definitely related to ecstasy' 75%

Table 4 All sleep variables

Sleep quality	Population size	Very satisfactory	Moderately satisfactory	Moderately unsatisfactory	Very unsatisfactory	*t*-test *P* value v non-ecstasy
Current ecstasy only	*n* = 31	19%	52%	23%	7%	0.034*
Abstinent ecstasy only	*n* = 58	28%	47%	16%	10%	0.21
E-polydrug	*n* = 242	32%	40%	21%	7%	0.11
Non-ecstasy	*n* = 178	34%	48%	15%	3%	
How long to get to sleep (sleep latency)	<10 min	10–30 min	30–60 min	60–90 min	>90 min	
Current ecstasy only	39%	39%	19%	0%	3%	0.84
Abstinent ecstasy only	23%	47%	14%	4%	12%	0.059
E-polydrug	33%	42%	13%	6%	5%	0.37
Non-ecstasy	33%	48%	16%	2%	1%	
How many hours of sleep (total sleep time)	<5 h	5–6 h	6–7 h	7–8 h	>8 h	
Current ecstasy 'only'	3%	13%	29%	42%	13%	<0.001***
Abstinent ecstasy only	2%	10%	29%	41%	17%	0.12
E-polydrug	4%	17%	29%	35%	16%	0.86
Non-ecstasy	1%	15%	40%	28%	15%	
How many times wake up during night (awakenings)	<1	1	2	3	>3	
Current ecstasy only	32%	29%	16%	16%	7%	0.29
Abstinent ecstasy only	16%	44%	19%	9%	12%	0.008**
E-polydrug	32%	28%	18%	12%	10%	0.064
Non-ecstasy	33%	39%	16%	7%	5%	
Fall asleep time weekdays	Before 10 p.m.	10–11:59 p.m.	12–1:59 a.m.	2–3:59 a.m.	After 4 a.m.	
Current ecstasy only	3%	36%	32%	23%	7%	0.21
Abstinent ecstasy only	7%	32%	45%	14%	4%	0.60
Abstinent E-polydrug	1%	31%	49%	14%	4%	0.020*
Non-ecstasy	1%	38%	53%	7%	1%	
Fall asleep time socialising	Before 10 p.m.	10–11:59 p.m.	12–1:59 a.m.	2–3:59 a.m.	After 4 a.m.	
Current ecstasy only	0%	0%	6%	32%	61%	<0.001***
Abstinent ecstasy only	0%	4%	35%	33%	28%	0.19
E-polydrug	0%	0%	21%	44%	32%	<0.001***
Non-ecstasy	0%	10%	34%	38%	18%	
Wake up time weekdays	Before 7 a.m.	7–7:59 a.m.	8–8:59 a.m.	9–9:59 a.m.	After 10 a.m.	
Current ecstasy only	16%	29%	16%	12%	20%	0.007**
Abstinent ecstasy only	21%	26%	19%	14%	19%	0.014*
E-polydrug	23%	38%	17%	8%	13%	0.19
Non-ecstasy	29.2%	34.3%	18.5%	7.3%	9%	

All sleep variables and *P* values.

*Significant difference compared with non-ecstasy. $P < 0.05$ (Mann–Whitney).

**Significant difference compared with non-ecstasy. $P < 0.01$ (Mann–Whitney).

***Significant difference compared with non-ecstasy. $P < 0.001$ (Mann–Whitney).

ecstasy and that 75% of these associated the change with ecstasy use. We have no control group to compare these findings with and the retrospective nature of the data means we have no way of knowing whether their responses are sound. We also do not know whether the leading nature of the question and questionnaire in general kindled the association between ecstasy use and sleep changes. Nevertheless, the findings are interesting and provide some subjective support for the hypothesis that lasting sleep disturbances are a possible consequence of ecstasy use.

The argument that the greater number of awakenings in abstinent ecstasy users existed before ecstasy use cannot be completely discounted. Nighttime awakenings have been

shown to be associated with psychological and physiological factors such as anxiety, stress and arousal (Morin, *et al*., 2003). Significantly more abstinent ecstasy users than controls reported previous use of psychiatric medication ($P \leq 0.01$) but not current use. The proportion of ecstasy users diagnosed with psychiatric disorders is generally quite high: 25% (Guillot and Greenway, 2006); 32% (de Win, *et al*., 2004). Eighty-eight per cent of the former study claimed that their diagnosis was given before ecstasy use and 71% of the latter believed that the onset of symptoms took place before they first took ecstasy. The implication is that individuals susceptible to psychopathological symptoms have a predisposition to use ecstasy. The abstinent ecstasy group in this study had a significant history of psychiatric medication use ($P < 0.01$) and current ecstasy users reported significant current use of psychiatric medication ($P < 0.05$), suggesting a relationship exists between ecstasy-use and use of psychiatric medication.

In spite of these findings, it is problematic to infer that the greater number of awakenings seen in abstinent ecstasy users is the result of on-going psychological problems. The number of abstinent ecstasy users reporting current use of psychiatric medication is actually quite low (5%) and not significantly different from that of controls (2%). This suggests that overt psychological factors are probably not the direct cause of sleep disturbances in the case of former ecstasy users. Supporting this inference, the abstinent ecstasy-only group did not differ from controls on other sleep variables that might also be sensitive to psychological factors, that is, sleep quality, sleep latency and total sleep.

The question needs to be addressed whether the greater number of awakenings seen in abstinent ecstasy users is related to neurobiological changes induced by previous ecstasy use. MDMA has been found to cause damage to serotonergic cells in a variety of different animals by a number of different research teams (Battaglia, *et al*., 1987; Saadat, *et al*., 2004; Hatzidimitriou, *et al*., 1999; Kirilly, *et al*., 2008). Many researchers believe that MDMA is also likely to be a serotonergic neurotoxin in humans and that the doses of MDMA required to induce cell damage in animals are comparable with those used by recreational ecstasy users (McCann, *et al*., 2001, Mechan, *et al*., 2006, Meyer, *et al*., 2006). Given the large amount of indirect evidence supporting the case that MDMA does cause serotonergic damage in humans and that sleep does seem to be different in previous and present recreational ecstasy users, we can speculate that the relatively high number of nighttime awakenings seen in abstinent ecstasy users in this study may be related to serotonergic changes induced by MDMA. However, it is important to emphasise that nighttime awakenings was just one aspect of sleep; all the other main sleep variables (sleep latency, sleep quality, sleep hours) were not significantly different to controls. Also, the animal data does not support the hypothesis that MDMA has lasting effects on sleep fragmentation (Kirilly, *et al*., 2008). The finding of serotonergic damage and increased sleep fragmentation in MDMA treated rats was only significant at 7 days but not at 21 and 180. In fact, at 180 days, the MDMA treated rats had less fragmented sleep than saline treated rats. Thus, if ecstasy use does genuinely affect sleep in the long-term, then this effect is likely to be complex and subtle.

Discussion of the data for the ecstasy polydrug group has been deliberately kept to a minimum. This group is heterogeneous, reporting high use of a number of drugs in addition to ecstasy, including alcohol. Surprisingly, the ecstasy-polydrug group's reported sleep quality was not significantly different to that of controls. A large percentage of this group (60%) reported current cannabis use, with some reporting that they used the drug to help them fall asleep at night. Using cannabis as an aid to sleep is consistent with the sedating properties of cannabis in contrast to MDMA-induced arousal (Parrott, *et al*., 2007). It is hard to draw any conclusions about this group's reported sleep, given the variability and extent of its polydrug use and the lack of data on the duration of abstinence from these other drugs. It is worth making the point, however, that if there were a reliable linear relationship between the extent of ecstasy use and lasting sleep disturbances, then the polydrug group, whose ecstasy use was approximately six times higher than that of the ecstasy-only groups, would be expected to report significantly worse sleep than both controls and the more moderate ecstasy-only groups, but this was not the case. Analyses of the association between extent of ecstasy use and sleep variables across all ecstasy groups consistently showed suggestions of a trend in the direction of poorer sleep in heavier users, but these correlations were not strong and never reached significance.

Finally, it is important to address the serious limitations of subjective sleep measures. Clearly, subjective sleep measures do not have the same reliability as polysomnographic recordings. A recent study incorporating both subjective and objective sleep measures in cocaine users found large discrepancies between reported sleep and sleep recorded via polysomnography, with users tending to underestimate sleep disturbances (Morgan, *et al*., 2006). In addition to problems related to recall, subjective reports are vulnerable to biases such as denial and exaggeration. Without objective verification, we cannot know how honest or accurate the participants' responses were. Further polysomnography studies in both human and animal samples are required to improve our understanding of the relationship between ecstasy/MDMA use and sleep.

The fact that our data was derived via the Internet adds another level of unreliability to it. The great advantage of web-based questionnaires is their potential for attracting large study samples. A definite disadvantage, however, is the lack of control over who answers the questionnaire, where and when they answer it, how many times they answer it and whether they answer honestly and accurately.

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