Modelling the adverse effects associated with ecstasy use.

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Running head: modelling ecstasy-related adverse effects.

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Abstract

Aims. Ecstasy, the street name for 3,4-meththylenedioxymethamphetamine, has been associated with a range of psychiatric symptoms and impaired psychological health in both problem and recreational users. The purpose of the present paper is to determine how these impairments are related to the history of polydrug use, and the conditions under which individuals ingest ecstasy.

Design. Associations between the variables of interest were investigated utilising negative binomial regression.

Setting. Liverpool and Preston in the North West of England.

Participants. A convenience sample of 159 recreational ecstasy/polydrug users, (80 males, 79 females). The sample was composed primarily of undergraduates.

Main Outcome Measures. The dependent variable was the number of reported ecstasy-related adverse effects. Independent variables included quantitative aspects of ecstasy and other drug use, and the various beliefs and behaviours associated with ecstasy use.

Results. The number of adverse effects was positively associated with lifetime exposure to ecstasy and negatively associated with period of abstinence from the drug. Adverse effects were more common among those who consumed ecstasy and alcohol concurrently, but were unrelated to other aspects of polydrug use. They were unaffected by whether the user took precautions when using the drug, and only weakly related to prior beliefs concerning the effects of ecstasy.

Conclusions. Greater lifetime exposure to ecstasy and consuming the drug concurrently with alcohol, increase the likelihood of experiencing adverse effects including paranoia, poor general health, irritability, confusion, and moodiness. Adverse effects decrease with the period of abstinence from the drug.

Evidence suggests that ecstasy use may adversely affect aspects of mood giving rise to heightened irritability, anxiety, and depression among currently abstinent users (e.g., Parrott and co-workers[1]). It is possible that different patterns of drug taking may be associated with different levels of risk. For example failing to take precautions when using ecstasy, such as monitoring fluid intake and keeping cool, may heighten the risks associated with the drug[2]. Alternatively the number of tablets typically taken on each occasion of use may determine the neurotoxic potential and the likelihood of experiencing adverse effects[3]. Since not all ecstasy users suffer adverse effects, the present paper will seek to determine which aspects of drug use might constitute a risk factor.

Ecstasy-related adverse effects, including depression, ill temper, mood impairment, anxiety, obsessive-compulsive and anti-social tendencies, have been observed in a number of studies[4-8]. These deficits were apparent relative to non users of illicit drugs and cannabis only users,[8] and have been observed to persist over time[9]. More subtle affective reactions have also been observed, for example, Curran et al.[10] and Hoshi et al.[11] found that ecstasy users were more likely to attribute aggressive meanings to ambiguous sentences, compared to nonusers. It is also noteworthy that such individuals have directly attributed their problems to ecstasy use and furthermore the likelihood of them reporting symptoms has been found to be dose-related[1].

It must be acknowledged that some researchers have failed to find evidence of increased psychopathology among ecstasy users or have attributed it to other factors[3, 12-15]. Even in those studies where adverse psychiatric and affective symptoms among ecstasy/polydrug users have been reported (e.g., Parrott et al.[1]), it remains unclear whether these are directly related to ecstasy use or whether they reflect some pre-existing condition, or a combination of both of these factors. For example, ecstasy is known to cause sleep

problems[16] and so the prior experience of sleep disturbance may in its own right affect the way in which ecstasy users respond. Thus it is important to investigate whether individuals who are experiencing negative affect do actually attribute this to their ecstasy use. On a more positive note, it may be that those who take precautions when using ecstasy and those who avoid bingeing on the drug (taking large numbers of tablets in a single session) are less likely to experience adverse effects. In view of the potential for harm to psychological health and the widespread prevalence of ecstasy use, it would be desirable to ask currently abstinent users to indicate directly how ecstasy in particular has affected their mood, social functioning and well being, and which aspects of their drug-using behaviour may have contributed to this.

Such a study was conducted recently by our laboratory.[17] We found that ecstasy users attributed a range of adverse effects to their use of the drug including heightened irritability, depression, paranoia and deteriorating health. Furthermore the length of ecstasy use was positively correlated with the reported number of adverse effects. However our previous study suffered from a number of limitations. Most importantly, we failed to consider the effects of the concurrent use of other drugs. For example, many ecstasy users take cannabis during the 'come down' phase in the hours immediately following their ecstasy use. Also users commonly report taking cocaine, alcohol, and tobacco, concurrently with ecstasy. It is possible therefore that some of the adverse effects that have been reported might be due to cocktail effects. Alternatively since cannabis has been shown to have neuroprotective qualities under certain conditions,[18] it is possible that those who take cannabis during the period immediately following ecstasy use might be less susceptible to self-reported adverse effects.

In the present study, we recruited additional participants thereby increasing our sample size substantially. We also made use of a technique that we overlooked in our previous investigation, i.e., negative binomial regression which is suited for count data with a

skewed distribution and a substantial number of zero scores. The utilisation of regression techniques allows us to consider how the number of reported adverse effects is related to a range of potential independent variables where the effects of the other variables are held constant. It is predicted that the number of adverse effects attributed to ecstasy use will be affected by, or associated with:

1. the duration of ecstasy use, the period of abstinence, the current frequency of use and the total number of pills consumed since first use;
2. whether ecstasy is consumed jointly with other drugs;
3. whether users are aware of the view that ecstasy causes long term health problems;
4. whether users are concerned about their ecstasy use and take precautions when ingesting the drug;
5. whether users limit the number of tablets taken in a single session;
6. the extent to which users experience sleep disturbance and health problems;
7. the levels of underlying anxiety and depression experienced by the user.

Method

Participants

This study makes use of an existing database that was constructed over the period 2002 to 2010. The database includes 159 ecstasy/polydrug users (80 males, 79 females; mean age 21.55, S.D. 2.47), individuals who currently use or who have previously used ecstasy. On average, participants had 15.49 (S.D. 2.56) years of full time education. Intelligence was assessed through Raven's Progressive Matrices[19] yielding an average score of 45.10 (S.D. 8.18) out of a maximum of 60. This did not differ significantly from the mean score of 46.42 (S.D. 7.01) from our sample of drug naive and non ecstasy users, $F(1,345)=2.65$, $p=.105$. The participants whose data are included in our database were recruited via direct approach to

university students, and by the snowball technique. Participants were requested to refrain from ecstasy use for at least 7 days prior to testing and were also requested not to use any other illicit drug for at least 24 hours prior to testing.

Measures

Drug Use

Patterns of drug use and other relevant lifestyle variables were investigated via means of a background questionnaire (e.g. Fisk et al.[18]). For each drug, participants reported the frequency and duration of their use and the last occasion of use. Participants were also questioned concerning their past drug use which enabled us to calculate an estimate of total lifetime use. Ecstasy users were asked 'Are you concerned about the possible dangers of using ecstasy?' responding on a five point scale from 0 = extremely concerned, to 4 = not concerned. They were also asked 'How aware are you that using ecstasy may have harmful long term effects?' responding on a five point scale from 0 = very aware, to 4 = not aware. Users also indicated the extent to which they used other drugs (alcohol, amphetamine, cannabis and cocaine) concurrently with ecstasy, responding on a four point scale from1 = never to 4 = always. Ecstasy users were also asked to respond 'Yes' or 'No' to the following questions: 'Do you take any sort of precautions when using ecstasy?', and 'Is there a maximum number of ecstasy tablets you will take in one session?'.

Using a measure developed by Murphy et al.[20] and Craig et al.[21] ecstasy users were asked if they believed that since using ecstasy they had changed in any way. They responded to each of the following words: caring (-), paranoid (+), alert (-), depressed (+), sociable (-), aggressive (+), happy (-), healthy (-), moody (+), patient (-), irritable (+), confident (-), sad (+), loving(-), and confused (+), using a five point scale: much more 5, more 4, no change 3, less 2, and much less 1. The number of words eliciting adverse reactions was calculated.

Responses of 4 or 5 to words suffixed with (+) constitute an adverse reaction as do responses of 1 or 2 to words suffixed with (-).

Epworth Sleepiness Scale (ESS) [22].

The ESS represents the likelihood of dozing off during the day in various situations (e.g. while watching TV). Participants are asked to rate eight such situations on a scale of 0 (would never doze off in this situation) to 3 (high chance of dozing off in this situation). The total score over all eight items is computed yielding possible minimum and maximum scores of 0 and 24 respectively. Higher scores are indicative of increased subjective daytime sleepiness[22] with scores exceeding 9 potentially indicative of a clinically significant sleep disorder[23].

Mood adjective checklist.

Anxiety and depression were measured by means of a mood adjective checklist.[24] Six words mapped onto each of these constructs (six words measuring arousal were not used in the present study). For each word participants rated themselves as either: not at all, slightly, moderately, very or extremely. The anxiety items were: tense, calm*, contented*, uneasy, worried, relaxed*; those covering depression were: enthusiastic*, sad, gloomy, depressed, happy*, cheerful*. Asterisked items were reverse scored. Maximum and minimum scores on the measures range from 6 to 30 with a midpoint of 18, and a total score for each measure was calculated by summing the responses. High scores are indicative of higher levels of perceived anxiety and depression.

Results

As is common in research of this nature most participants were polydrug users for whom ecstasy was their drug of choice. The extent of polydrug use is apparent in the trends reported in Table 1. The focus of the present study is the number of adverse effects reported by users. Responses for each of the specific effects are reported in Table 2. The items listed

in boldface type are those for which the number of negative responses exceeded the number of positive ones. For each participant, the number of items for which a negative response was made was summed and this provided the dependent variable. Thus a larger value corresponds to a greater number of perceived adverse effects.

Table 3 contains the descriptives for the variables of interest. Mean anxiety levels were 13.07 (S.D. 3.82), which is below the midpoint of the range and not significantly different from the mean of 12.53 (S.D. 2.90) for our sample of drug naive and non ecstasy users, $F(1,348)=2.26$, $p=.134$. The equivalent figures for the depression measure were 13.36 (S.D. 3.37) and 12.71 (S.D. 2.89) for ecstasy users and non users respectively, $F(1,347)=3.80$, $p=.052$. With regard to the Epworth daytime sleepiness measure, the mean value for ecstasy users was 6.88 (S.D. 3.66), however, 23% of users produced values exceeding 9 which is potentially indicative of a clinically significant sleep disorder.

Negative binomial regression with log link was conducted with the number of reported adverse effects as the dependent variable and the remaining variables listed in Table 3 entered into the model as covariates. Three separate analyses were conducted, the results of which are reported in Table 4. First, all predictors were entered into the model (see the left hand panel of Table 4). Overall the chi-squared value indicates that the full model was significantly better than the constant-only model. The extent to which alcohol was consumed at the same time as ecstasy was statistically significant as a predictor, with a greater incidence of this behaviour associated with the experience of more adverse effects. None of the other variables reflecting joint use of ecstasy and respectively amphetamine, cannabis and cocaine, significantly affected the number of reported adverse effects. In relation to aspects of ecstasy consumption, adverse effects significantly increased with total use of the drug but declined as the period of abstinence from the drug lengthened. Neither the current frequency of use nor the time elapsed since commencing ecstasy use were statistically significant as predictors.

Perhaps not surprisingly, those who were not overly concerned about their use of ecstasy reported significantly fewer adverse effects. Other significant outcomes were related to the Epworth measure of daytime sleepiness: those who experienced more tiredness were also likely to report more adverse effects. Equally those who felt healthier reported fewer adverse effects, while increased anxiety was positively associated with the measure.

Despite the apparent efficacy of the model in predicting the number of adverse effects, the Deviance/df parameter was greater than 1 indicating the possible presence of over-dispersion in the model. This remained the case after all of the non-significant predictors were excluded (the middle panel of Table 4). In order to deal with the problem of over-dispersion, a scaler dispersion parameter based on the deviance statistic was applied thereby giving rise to a compensatory increase the standard errors for the parameter estimates.[25,26] However, with the exception of the 'concern' predictor all other predictors remained statistically significant in the model (see the right hand panel of Table 4).

It is clear that a number of other illicit drugs were used more frequently than ecstasy and by implication consumed on separate occasions. In order to establish whether or not the propensity to report ecstasy-related adverse effects was associated with the use of these other drugs we introduced indicators of consumption for cannabis, cocaine, and alcohol respectively into the model. For cannabis and cocaine we included measures of total use, time since first use, period of abstinence and current frequency of use. None of these proved to be statistically significant as predictors. With regard to alcohol we included units consumed per week, time since first use and period of abstinence as predictors and again none of these proved to be statistically significant. The inclusion of these additional variables rendered health status statistically non-significant in two of the analyses. Weeks since last use of ecstasy was rendered non significant in the model containing aspects of cocaine use. Of the other predictors, concurrent alcohol use, total use of ecstasy and the anxiety measure were

statistically significant in all models. The daytime sleepiness measure was reduced to just below significance in the model containing aspects of cannabis use.

Discussion

The most commonly reported adverse effects were paranoia, impaired general health and moodiness with between 35 and 43% of the sample reporting these outcomes. Between 20 and 30% of the sample reported other specific adverse effects including reduced alertness, heightened aggression, depression, impatience, irritability, sadness and confusion. However, it is noteworthy that in almost all cases the most prevalent response was 'no change' indicating that the majority of ecstasy users did not associate specific adverse outcomes with their use of the drug. The implication of this is that where adverse effects are experienced for the most part they are limited in scope and most prevalent among a subset of users. Two aspects of ecstasy use proved to be associated with the number of reported adverse effects. Firstly, greater lifetime exposure to ecstasy was associated with an increased propensity to report adverse effects consistent with a dose-related effect. Secondly, the number of perceived adverse effects declined as the period of abstinence from the drug increased. A possible explanation for this is that recollection of the negative aspects of drug use diminishes as the time since the drug was last ingested increases. Neither the length of use nor the current frequency of use were statistically significant as predictors in the present study. Surprisingly, taking precautions and limiting the number of tablets ingested in a single session were not significantly associated with the reported number of adverse effects. Previous research has demonstrated that following ingestion, ecstasy gives rise to acute and potentially short term post-acute affective reactions[27]. However the present results suggest that the adverse effects were not due to short term post-acute factors, since ecstasy use during the previous 10 days was not statistically significant as a predictor.

The association between lifetime exposure and reported adverse effects is consistent with results reported elsewhere. For example Soar et al.[28] found that relative to nonusers and those who did not associate problems with their ecstasy use, those who viewed their use of the drug as problematic were impaired on a number of subscales of the Brief Symptom Inventory including somatisation, depression and anxiety. Consistent with the results of the present study, while problem users had greater lifetime exposure to ecstasy, they did not differ significantly in terms of length of use. In another study the likelihood of reporting mood fluctuations, depression and poor sleep also increased with lifetime dose[29].

While over 25% of ecstasy users in the present study said that ecstasy had made them more depressed, the self-report depression measure was not significantly associated with the total number of adverse effects in the present study. A number of previous studies have found no difference in depression between ecstasy users and non users. For example, Beck Depression Inventory (BDI) scores did not differ between heavy ecstasy users and ecstasy free controls in Guillot and Greenway's study,[30] and were only slightly elevated in heavier users in Falck et al's study[15]. In other studies of ecstasy/polydrug users, lifetime and recent ecstasy use were found to be unrelated to self-reported depression and instead recent stressful life events and aspects of polydrug and tobacco use were found to be important in this regard[31-34]. Thus while some users in the present study may believe that ecstasy has made them more depressed, overall the total number of adverse effects associated with the drug was not related to self-report depression. This is consistent with outcomes reported elsewhere in the literature where no direct link has been found between ecstasy use and depression.

By way of contrast, self reported levels of anxiety in the present study were significantly related to the total number of reported adverse effects. Heightened anxiety among ecstasy/polydrug users has been reported in a number of previous studies[8, 28,29]. However, the association with ecstasy use has not always been clear cut. Instead elevated

anxiety levels among ecstasy users were found to be associated with the use of other licit and illicit drugs or with other factors such as exposure to recent stressful life events.[31,32] The fact that in the present study there was an association between the number of adverse effects attributed to ecstasy and the individual's anxiety level suggests that the two constructs share statistically significant unique variance. Therefore the inconsistent findings among ecstasy users in relation to anxiety might be due to the fact that ecstasy has anxiogenic properties only among a subset of users, i.e. perhaps those who experience adverse effects, and this subset may not be equally represented in all samples.

One of the major findings in the present study was that the concurrent use of alcohol and ecstasy was positively associated with the total number of reported adverse effects. Research outcomes from animal studies have demonstrated that concurrent administration of alcohol (ethanol) and MDMA enhances the neurotoxic potential of the latter[35,36]. Among humans, studies have revealed that ecstasy and alcohol are frequently consumed together at dance club venues with users often bingeing on both substances,[37] and placing themselves at risk of serious physical harm and potentially death[38]. In an early study of drug-dependent ecstasy/polydrug users undergoing treatment, Schifano et al.[39] found that the presence of psychopathological symptoms (e.g. depression, psychotic disorders, cognitive disturbances, bulimic episodes, impulse control disorders, panic disorders and social phobia) was more evident among those who consumed alcohol and ecstasy together. More recently, in a review of the literature Gouzoulis-Mayfrank and Daumann[40] note that ecstasy is frequently consumed jointly with other drugs including alcohol and cannabis but also with stimulants such as amphetamine and cocaine. The present results confirm that ecstasy continues to be taken jointly with alcohol by a clear majority of users and that these persons are more likely to attribute adverse effects to the drug. To the best of our knowledge the present study is the first to demonstrate such an association among human recreational users. In view of the

enhanced neurotoxic potential demonstrated in animal studies and the acute risk of serious physical harm, this finding is of much potential concern.

It is noteworthy that many of our ecstasy/polydrug users were regular users of other common illicit drugs including cannabis, cocaine, and amphetamine. This is not uncommon in samples of this kind. For example, among Scholey et al's[41] large internet based sample, 61% of moderate ecstasy users and 81% of heavy ecstasy users had also consumed cocaine. The equivalent figures for amphetamine were 69% and 84% and for cannabis 72% and 68%. Interestingly the concurrent use of ecstasy with other drugs such as cannabis, cocaine and amphetamine was not associated with more reported adverse ecstasy-related effects in the present study.

In conclusion, ecstasy users were more likely to experience adverse effects if they had a larger lifetime dose and consumed the drug concurrently with alcohol. The use of other illicit drugs, both individually and concurrently with ecstasy, was unrelated to the prevalence of ecstasy-related adverse effects. Adverse effects were positively associated with daytime sleepiness and anxiety, but not depression. They also declined with the period of abstinence from the drug.

References

1. Parrott AC, Buchanan T, Scholey AB (2002) Ecstasy/MDMA attributed problems reported by novice, moderate and heavy recreational users. *Hum Psychopharmacol*. 2002; 17: 309-312.
2. Parrott AC, Rodgers J, Buchanan T, Ling J, Heffernan T, Scholey AB. Dancing hot on Ecstasy: physical activity and thermal comfort ratings are associated with the memory and other psychobiological problems reported by recreational MDMA users. *Hum Psychopharmacol*. 2006; 21: 285-298.
3. Thomasius R, Petersen K, Buchert R, Andresen B, Zapletalova P, Wartberg L, et al. Mood, cognition and serotonin transporter availability in current and former ecstasy (MDMA) users. *Psychopharmacology (Berl).* 2003; 167: 85–96
4. Parrott AC, Lasky J. Ecstasy (MDMA) effects upon mood and cognition: Before, during and after a Saturday night dance. *Psychopharmacology (Berl).* 1998; 139: 261-268.
5. Curran HV, Travill RA. Mood and cognitive effects of ± 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy'): Weekend 'high' followed by mid-week low. *Addiction.* 1997; 92: 821-831.
6. Gamma A, Buck A, Berthold T. No difference in brain activation during cognitive performance between Ecstasy (3,4-methylenedioxymethamphetamine) users and control subjects: A [H-sub-2¹-sup-5O]-positron emission tomography study. *J Clin Psychopharmacol.* 2001; 21: 66-71.
7. McCardle K, Luebbers S, Carter JD. Chronic MDMA (ecstasy) use, cognition and mood. *Psychopharmacology (Berl).* 2004; 173: 434-439.

8. Lamers CTJ, Bechara A, Rizzo M, Ramaekers JG. Cognitive function and mood in MDMA/THC users, THC users and non-drug using controls. *J Psychopharmacol*. 2006; 20: 302-311.
9. Thomasius R, Zapletalova P, Petersen K, Buchert R, Andresen B, Wartberg L, et al. Mood, cognition and serotonin transporter availability in current and former ecstasy (MDMA) users: The longitudinal perspective. *J Psychopharmacol*. 2006; 20: 211-225.
10. Curran HV, Rees H, Hoare T. Empathy and aggression: two faces of ecstasy? A study of interpretative cognitive bias and mood change in ecstasy users. *Psychopharmacology (Berl)*. 2004; 173: 425-433
11. Hoshi R, Pratt H, Mehta S. An investigation into the sub-acute effects of ecstasy on aggressive interpretative bias and aggressive mood- are there gender differences? *J Psychopharmacol*. 2006; 20: 291-301.
12. Morgan MJ. Recreational use of 'ecstasy' (MDMA) is associated with elevated impulsivity. *Neuropsychopharmacology*. 1998; 19: 252-264.
13. Dafters RI, Duffy F, O'Donnell PJ. Level of use of 3,4-methylenedioxymethamphetamine (MDMA or Ecstasy) in humans correlates with EEG power and coherence. *Psychopharmacology (Berl).* 1999; 145: 82-90.
14. Bedi G, Van Dam NT, Redman J. Ecstasy (MDMA) and high prevalence psychiatric symptomatology: Somatic anxiety symptoms are associated with polydrug, not ecstasy use. *J Psychopharmacol*. 2010; 24: 233-240.
15. Falck RS, Wang J, Carlson RG. Depressive symptomatology in young adults with a history of MDMA use: A longitudinal analysis. *J Psychopharmacol*. 2008; 22: 47-54.
16. Fisk JE, & Montgomery C. Sleep impairment in ecstasy/polydrug and cannabis-only users. *Am J Addict*. 2009; *18*, 430-437.

17. Fisk JE, Montgomery C, & Murphy P. The association between the negative effects attributed to ecstasy use and measures of cognition and mood among users. *Exp Clin Psychopharmacol*. 2009; 17, 326-336.

18. Fisk JE, Montgomery C, Wareing M, & Murphy P. The effects of concurrent cannabis use among ecstasy users: Neuroprotective or neurotoxic? *Hum Psychopharmacol*. 2006; 21:355-366.

19. Raven J, Raven JC, Court JH. Manual for Raven's progressive matrices and vocabulary scales. Oxford Psychologists Press, Oxford, UK; 1998.

20. Murphy PN, Wareing M. & Fisk JE. Users' perceptions of the risks and effects of taking MDMA (Ecstasy). *J Psychopharmacol.* 2006; 20, 447-455.

21. Craig L, Fisk JE, Montgomery C, Murphy PN, & Wareing M. Is emotional intelligence impaired in ecstasy-polydrug users? *J Psychopharmacol*. 2010; 24, 221-231.

22. Johns M, & Hocking B. Daytime sleepiness and sleep habits of Australian workers. *Sleep.* 1997; 20, 844-849.

23. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep*. 1992; 15, 376-381.

24. Matthews G, Jones DM, & Chamberlain GA. Refining the measurement of mood: the UWIST mood adjective checklist. *Br J Psychol.* 1990; 81, 17-42.

25. Allison PD. *Fixed Effects Regression Methods for Longitudinal Data Using SAS*. Cary, NC: SAS Institute Incorporated, Chapter 4; 2005

26. SAS Institute Inc. *SAS/STAT ® 9.2User's Guide, Second Edition*. Cary, NC: SAS Institute Inc. Chapter 51; 2009

27. Baylen CA. A review of the acute subjective effects of MDMA/ecstasy. *Addiction*. 2006; 101: 933-947

28. Soar K, Turner JJD, Parrott AC. Problematic versus non-problematic ecstasy/MDMA use: The influence of drug usage patterns and pre-existing psychiatric factors. *J Psychopharmacol*. 2006; 20: 417-424.

29. Rodgers J, Buchanan T, Pearson C, Parrott AC, Ling J, Heffernan T, et al. Differential experiences of the psychobiological sequelae of ecstasy use: Quantitative and qualitative data from an internet study. *J Psychopharmacol*. 2006; 20: 437-446.

30. Guillot C, Greenway D. Recreational ecstasy use and depression. *J Psychopharmacol*. 2006; 20: 411-416.

31. Scott RM, Hides L, Allen J, Burke R, Lubman DI. Depressive and anxiety symptomatology in ecstasy users: The relative contribution of genes, trauma, life stress and drug use. *Psychopharmacology (Berl).* 2010; 209: 25-36.

32. Medina KL, Shear PK. Anxiety, depression, and behavioral symptoms of executive dysfunction in ecstasy users: Contributions of polydrug use. *Drug Alcohol Depend*. 2007; 87: 303-311.

33. Durdle H, Lundahl LH, Johanson C-E, Tancer M. Major depression: The relative contribution of gender, MDMA, and cannabis use. *Depress Anxiety*. 2008; 25: 241-247.

34. de Win MML, Schilt T, Reneman L, Vervaeke H, Jager G, Dijkink S, et al. Ecstasy use and self-reported depression, impulsivity, and sensation seeking: A prospective cohort study. *J Psychopharmacol*. 2006; 20: 226-235.

35. Izco M, Orio L, O'Shea E, Colado MI. Binge ethanol administration enhances the MDMA-induced long-term 5-HT neurotoxicity in rat brain. *Psychopharmacology (Berl).* 2007; 189: 459-470.

36. Cassel J-C, Riegert C, Rutz S, Koenig J, Rothmaier K, Cosquer B, et al. Ethanol, 3,4-methylenedioxymethamphetamine (ecstasy) and their combination: Long-term

behavioral, neurochemical and neuropharmacological effects in the rat. *Neuropsychopharmacology*. 2005; 30: 1870-1882.

37. Winstock AR, Griffiths P, Stewart D. Drugs and the dance music scene: A survey of current drug use patterns among a sample of dance music enthusiasts in the UK. *Drug Alcohol Depend*. 2001; 64: 9-17.
38. Rivas-Vazquez, RA, Delgado L. Clinical and toxic effects of MDMA ('Ecstasy'). *Prof Psychol Res Pr*. 2002; 33: 422-425.
39. Schifano F, Di Furia L, Forza G, Minicuci N, Bricolo R. MDMA ('ecstasy') consumption in the context of polydrug abuse: A report on 150 patients. *Drug Alcohol Depend.* 1998; 52: 85-90.
40. Gouzoulis-Mayfrank E, Daumann J. The confounding problem of polydrug use in recreational ecstasy/MDMA users: A brief overview. *J Psychopharmacol*. 2006; 20: 188-193.
41. Scholey AB, Parrott AC, Buchanan T, Heffernan TM, Ling J, Rodgers J. Increased intensity of Ecstasy and polydrug usage in the more experienced recreational Ecstasy/MDMA users: A WWW study. *Addict Behav*. 2004; 29: 743-752.

Table 1. Indicators of Drug, Alcohol, and Tobacco Use

	N	Mean	s.d
Ecstasy			
Weeks since last use	159	26.77	57.88
Weeks since first use	159	200.25	122.55
Total consumption (tablets)	159	511.92	952.91
Frequency (times per week)	159	0.34	0.43
Alcohol			
Weeks since last use	158	0.54	1.31
Weeks since first use	158	399.30	149.53
Units consumed per week[1]	159	19.13	13.22
Tobacco			
Weeks since last use	108	12.34	52.84
Weeks since first use	108	387.07	166.88
Cigarettes consumed per day	85	9.98	6.93
Amphetamine			
Weeks since last use	52	91.60	124.96
Weeks since first use	52	266.23	201.82
Total consumption (grams)	43	131.39	224.93
Frequency (times per week)	38	0.08	0.19
Cannabis			
Weeks since last use	133	22.08	56.12
Weeks since first use	133	314.58	154.21
Total consumption (joints)	127	3049.35	4732.44
Frequency (times per week)	126	1.82	2.39
Cocaine			
Weeks since last use	125	13.74	32.36
Weeks since first use	127	170.50	113.52
Total consumption (grams)	87	108.04	166.80
Frequency (times per week)	87	0.46	0.69

1. *For example, 1 unit = 1 glass of wine; 1 measure of spirit, or half a pint of beer*

Table 2

Number of ecstasy users indicating changes in behaviour

Ecstasy has made me:	Much Less	Less	No Change	More	Much More
Caring	0	8	124	23	4
Paranoid	1	4	85	63	6
Alert	3	32	107	13	4
Depressed	0	6	113	37	3
Sociable	0	6	67	69	17
Aggressive	4	16	116	18	5
Happy	0	11	105	37	6
Healthy	7	61	84	7	0
Moody	0	6	98	52	3
Patient	2	36	113	8	0
Irritable	0	5	110	40	4
Confident	1	13	89	44	12
Sad	0	8	130	21	0
Loving	0	0	122	32	5
Confused	1	3	110	40	5

Table 3
Descriptive Statistics for the Variables in the Full Model (N=159)

	Mean	s.d
Adverse effects attributed to ecstasy (number)	3.00	2.72
Drugs used the same time as ecstasy[1]		
Alcohol	3.38	0.86
Amphetamine	1.33	0.61
Cannabis	2.26	1.02
Cocaine	2.06	0.89
Concerned about the effects of ecstasy[2]	2.28	0.97
Aware that ecstasy may have harmful long term effects[3]	0.82	0.76
Ecstasy		
Weeks since last use	26.77	57.88
Weeks since first use	200.25	122.55
Total consumption (tablets)	511.92	952.91
Frequency (times per week)	0.34	0.43
Consumption during the previous 10 days (tablets)	0.80	2.28
Health status[4]	3.67	0.81
Epworth Sleepiness Scale	6.88	3.66
Anxiety	13.07	3.82
Depression	13.36	3.37

1. Response scale: 1=never; 2=occasionally; 3=frequently; 4=always.
2. Response scale: 0=extremely concerned; 1=very concerned; 2=concerned; 3=slightly concerned; 4=not concerned.
3. Response scale: 0=very aware; 1=quite aware; 2=unsure; 3=not very aware; 4=not aware.
4. Response scale: 1=very poor; 2=poor; 3=average; 4=good; 5=very good.

Table 4. Inferential Statistics for Predictors in the Full and Reduced Models

	Full Model: All Predictors				Reduced Model				Reduced Model with Adjustment for Overdispersion			
	B	SE	Wald Chi Sq (df=1)	p	B	SE	Wald Chi Sq (df=1)	p	B	SE	Wald Chi Sq (df=1)	p
Drugs used the same time as ecstasy												
Alcohol	.283	0.09	10.18	.001	.318	0.08	15.28	.000	.318	0.09	11.23	.001
Amphetamine	.037	0.10	0.14	.704								
Cannabis	-.046	0.06	0.56	.453								
Cocaine	.060	0.09	0.47	.494								
Concerned about the effects of ecstasy	-.159	0.07	5.74	.017	-.147	0.07	5.05	.025	-.147	.08	3.71	.054
Precautions Taken	.121	0.14	0.81	.367								
Limit number of tablets per session	-.159	0.13	1.43	.232								
Aware that ecstasy may have harmful long term effects	.201	0.09	5.40	.020	.133	0.08	3.06	.080	.133	0.09	2.25	.134
Ecstasy												
Weeks since last use	-.005	0.00	7.73	.005	-.004	0.00	6.94	.008	-.004	0.00	5.10	.024
Weeks since first use	.000	0.00	0.04	.842								
Total consumption (tablets)	1.76E-4	0.63E-4	7.88	.005	1.59E-4	0.49E-4	10.59	.001	1.59E-4	0.57E-4	7.78	.005
Frequency (times per week)	-.291	0.23	1.64	.200								
Use in the previous 10 days	-.001	0.04	0.00	.986								
Health status	-.176	0.08	5.27	.022	-.177	0.07	5.80	.016	-.177	0.09	4.26	.039
Epworth Sleepiness Scale	.047	0.02	7.53	.006	.041	0.02	6.96	.008	.041	0.02	5.12	.024
Anxiety	.085	0.02	14.82	.000	.074	0.01	26.33	.000	.074	0.02	19.35	.000
Depression	-.020	0.03	0.58	.445								
Negative binomial	.110				.141				.141			
Chi Sq for full model			86.74 (df=17)	.000			82.04 (df=8)	.000			60.30 (df=8)	.000
Scalar for overdispersion			1.000				1.000				1.360	
Goodness of Fit (deviance/df)	1.463				1.360				1.000			