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An Investigation of Factors Associated with Depressive Symptoms among a Sample of Regular Ecstasy Consumers

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Key Words
Methylenedioxymethamphetamine · Depression · Psychopathology

Abstract
Aims/Objectives: Methylenedioxymethamphetamine affects the central serotonergic system, and there is some evidence for an association between ecstasy use (drugs sold as methylenedioxymethamphetamine) and depression. The aim of the present study was to investigate the incidence of self-reported depression and associated help-seeking among a sample of regular ecstasy users. A further aim was to examine the correlates of depressive symptomatology in this population. ***Materials and Methods:*** 100 regular ecstasy consumers (at least monthly use) were interviewed as part of the Ecstasy and Related Drug Reporting System in Tasmania, Australia. Participants were also administered epidemiological measures of depression (Center for Epidemiological Studies Depression Scale) and psychological distress (Kessler Psychological Distress Scale). ***Results:*** One quarter (23%) of participants self-reported recent experience of depression, a rate notably greater than the general population. However, only one third of these participants had attended a health professional for this issue. A range of drug use factors (e.g. frequency and quantity of ecstasy use, frequent cannabis or methamphetamine use, intravenous drug use, polydrug use, binge drug use, harmful alcohol use, and elevated psychological dependence scores for ecstasy and methamphetamine) were associated with high levels of depressive symptomatology. ***Conclusion:*** These findings are consistent with an association between depressive symptomatology and ecstasy and other drug use. Harm reduction strategies which target drug use factors such as those identified in this study may also aid in the reduction of the experience of depression. Considering the low levels of help-seeking among this population, improving awareness and access to information and treatment for depression may also be important.

Background

Animal research indicates that methylenedioxymethamphetamine or ecstasy is neurotoxic to the central serotonergic (5-HT) system and there is some evidence (though not conclusive) that ecstasy is also neurotoxic to the 5-HT system of humans [1]. Among other functions, the central 5-HT system is important for regulating mood in humans and thus it is possible that ecstasy use leads to an increase in the incidence of mood disorders such as depression. Consistent with this proposal, depression has been found to be associated with low 5-HT transporter densities [2].

Ecstasy use is associated with acute experience of dysphoria during the 'comedown' phase and during the days

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following methylenedioxymethamphetamine use [3–5] and many ecstasy consumers self-report experience of dysphoria or depression as a long-term consequence or side effect of ecstasy use [6, 7]. An elevated incidence of mental disorders (including depression and anxiety) and higher levels of depressive symptomatology is also a common finding among users of the drug [8–11].

While significantly higher levels of depression have been reported among either current or former ecstasy users relative to various control groups [12–20], other studies have failed to find differences [9, 21–28], or have reported a stronger association between depressive symptomatology and cannabis use [10, 21, 29, 30] or polydrug use generally [15, 19, 31]. Inadequate control groups or matching for drug use, small sample sizes, and different measures of depressive symptomatology or ecstasy use may account for many of the inconsistencies in this literature [32]. In a recent meta-analysis, it was concluded that there is a small association (effect size = 0.31) between depressive symptoms and use of ecstasy [33]. The magnitude of this relationship was not thought to be clinically relevant but it did remain after including only those studies that controlled for cannabis use.

The causal nature of the relationship between ecstasy use and depressive symptomatology has been difficult to establish. Cross-sectional research indicates that diagnosis of mood disorder typically precedes ecstasy use [8, 15, 25], and some longitudinal research suggests that depression in childhood or adolescence is associated with increased likelihood of ecstasy use in early adulthood [11, 34]. However, depression has also been reported subsequent to ecstasy use [11, 35] and some other longitudinal research findings suggest that depression does not predict future ecstasy use [36] or ecstasy use disorders [37].

The link between depression in ecstasy consumers and 5-HT function is also unclear. de Win et al. [15] found that although serotonin transporter (SERT) densities were reduced in current heavy ecstasy users relative to former users and controls, depressive symptoms did not correlate with SERT densities. In a PET study, Thomasius et al. [19] found elevated depression scores among recent as well as former ecstasy users relative to drug-naïve controls; however, differences in SERT availability were only observed in current but not former users. In a recent study, high depression scores among regular ecstasy consumers were associated with the presence of a particular SERT encoding gene, suggesting that genetics may play a role in susceptibility to depression [38].

Thus, while there is evidence that ecstasy and other drug users may be at risk of higher levels of depression, it has not been possible to fully disentangle this effect from other mitigating factors or to support the hypothesis that ecstasy plays a causative role in the manifestation of depression. From a public health perspective it may be more important to investigate the correlates rather than the presence of depressive symptomatology among ecstasy users, in order to best target harm reduction information to this population and to inform policy makers and clinicians working in this area. To date, few studies have systematically investigated the correlates of depressive symptomatology among ecstasy consumers to this end.

Whereas some studies have reported a relationship between ecstasy use and depressive symptomatology [15, 27, 31, 33, 39], others have reported a relationship between depressive symptoms and other drugs, such as cannabis [10, 27] and opiate use [40]. Female sex is associated with higher levels of psychological side effects or subacute depression among ecstasy users [5, 7], and elevated depressive symptomatology is observed among females relative to males in the general population [41] as well as ecstasy [40] and other polydrug user groups [23]. Non-drug factors such as dancing for extended periods of time are also associated with elevated levels of depression among ecstasy users [42].

The present study was conducted to investigate depressive symptoms among a sample of regular ecstasy consumers and to examine the relationship between depressive symptomatology, psychological distress, and self-reported mental health problems. A further aim was to investigate which demographic and drug use correlates of depression were most strongly associated with high levels of depressive symptomatology.

Materials and Methods

Participants and Procedures

Participants were 100 regular ecstasy users who were interviewed in Tasmania, Australia, as part of the 2007 Ecstasy and Related Drug Reporting System, a cross-sectional study designed to monitor trends in ecstasy and related drug markets in Australia [43]. Inclusion criteria required that participants be at least 16 years of age, have used ecstasy at least monthly in the preceding 6 months, and have resided in the Tasmanian capital city for the preceding year. Participants were recruited through a purposive sampling strategy [44] which included distribution of posters and flyers at various locations (e.g. cafés, bars, nightclubs, clothing stores, music stores, university), posting on internet forums, and peer referral. Participants contacted researchers, were screened for eligibility, and gave voluntary informed consent prior to participation in the study. Confidential face-to-face structured interviews were conducted in public locations (e.g. coffee shops, parks, university) between May and August 2007. Interviews took be-

tween 45 and 60 min to complete and were administered by trained interviewers. All participants were reimbursed 30 AUD for time and out-of-pocket expenses. Ethics approval was granted by the Tasmanian Social Sciences Human Research Ethics Committee. Full details of the interview content and methodology are available elsewhere [45].

Materials

The structured interview included demographic characteristics, patterns of ecstasy and other drug use, and the nature and incidence of risk behaviors and health harms associated with drug use. Participants also completed the Center for Epidemiological Studies Depression Scale (CES-D) [46] and the Kessler Psychological Distress Scale (K10) [47], and were asked if they had experienced any mental health problems during the 6 months preceding the interview. If participants had experienced mental health problems, they were asked to specify which mental health problems they had recently experienced and whether they had attended a health professional for such problems during this time.

The CES-D is a 20-item self-report scale designed to measure depressive symptoms in population surveys [46]. The scale taps dimensions of positive affect, depressed or negative affect, somatic symptoms, and interpersonal problems, and shows good psychometric properties [48]. Participants were asked to rate how often in the past week they had experienced each symptom (e.g. I felt depressed) on a 4-point scale ranging from 0 = rarely or none of the time to 3 = most or all of the time. Four positive affect items were reverse scored (e.g. I thought I was as good as other people) and total scores ranged from 0 to 60. A score of 16 or above was used to classify those with high levels of depressive symptomatology. This cutoff captured the upper quartile of the present sample and has demonstrated sensitivity (0.95) and specificity (0.70) for detecting diagnosable cases of major depression [49].

The K10 [47] is a 10-item questionnaire designed to measure the level of distress and severity associated with psychological symptoms in population surveys. Participants were asked to rate the extent to which they had experienced particular psychological symptoms (e.g. How often did you feel depressed?) in the preceding month, on a 5-point Likert scale ranging from 1 = all of the time to 5 = none of the time. K10 scores can be grouped into 4 categories of psychological distress: low (10–15), moderate (16–21), high (22–29) and very high (30–50) [50]. Data from the 1997 Australian National Survey of Mental Health and Wellbeing indicate that K10 scores of 22 or more have a specificity of 0.95 (correct rejection rate) and sensitivity of 0.55 (hit rate) for the identification of current DSM-IV diagnoses of anxiety or affective disorder, and scores of 30 or more have a sensitivity and specificity of 0.99 and 0.24, respectively [51]. In the present study, scores of 22 and above were classified as indicating 'high' levels of psychological distress.

Design and Data Analysis

All statistical analyses were conducted using SPSS 16.0.1 for Windows (SPSS Inc., 2007); χ^2 and Mann-Whitney U tests were used to examine differences between those with high (>16) and low (<16) CES-D scores on a range of variables. A series of backward stepwise logistic regression analyses were performed to investigate the associations between high CES-D scores, demographic characteristics, and patterns of ecstasy and other drug use.

Results

Demographic Characteristics of the Sample

The 100 participants had a median age of 23 years (range 17–40) and were predominantly male (54%). The majority of participants were heterosexual (93%) and all spoke English as their main language. Three quarters of the sample (79%) had completed secondary education (year 12), and the majority were either employed (46%) or currently studying (42%). Only a minority were currently in drug treatment (1%), and none had ever received a custodial sentence. On average participants had used ecstasy on a median of 12 days (range 6–100) in the preceding 6 months, with a median of 2 tablets (range 1–7) taken in a typical session of use.

CES-D and K10 Scores

The mean CES-D score was 13.2 (SD = 9.8) and the median score was 11 (range 0–47). Over one quarter (28%) of the sample had a score of 16 or more, indicating high levels of depressive symptomatology. The mean K10 score was 17.6 (SD = 5.6) and the median score was 17 (range 10–43). Over one tenth of the sample (15%) had K10 scores in the 'high' category, and 3% had scores in the 'very high' category, indicative of a possible diagnosis of an anxiety or affective disorder. There was a significant strong positive relationship between scores on the CES-D and K10 ($r = 0.812$, $p < 0.01$). Those with high category CES-D scores were significantly more likely to have 'high' or 'very high' K10 category (≥22) scores than those with low category CES-D scores (table 1).

CES-D Scores and Self-Reported Mental Health Problems

One third (35%) of the sample self-reported a mental health problem during the 6 months preceding the interview, most commonly experience of depression (23%) and/or anxiety (19%). However, only one third of those (12% of the sample) had visited a health professional in relation to mental health problems and just one fifth (7% of the sample) had been prescribed medication for a mental health problem in this time.

Those with high category CES-D scores were significantly more likely to report experience of a mental health problem during the 6 months preceding the interview relative to those with low category scores (table 1), with increased likelihood shown for depression but not anxiety. They were also significantly more likely to have attended a mental health professional or to have been prescribed medication for mental health problems during this time.

Table 1. Self-reported mental health problems in the 6 months preceding the interview among regular ecstasy consumers with low (<16) and high (≥16) CES-D scores

Variable, %	CES-D score <16 (n = 71)	CES-D score ≥16 (n = 28)	χ^2	OR (95% CI)
Experienced mental health problems	24	64	14.3***	5.7 (2.2–14.7)
Experienced depression	10	57	25.2***	12.2 (4.1–35.9)
Experienced anxiety	17	25	n.s.	
Accessed a mental health professional	3	36	20.4***	19.2 (3.8–95.4)
Prescribed medication for mental health	0	25	19.1***	23.3 (2.7–200.6)
K10 in 'very high' category (≤30)	0	12	8.1**	8.7 (1.0–88.2)
K10 in 'high' or 'very high' category (≤22)	2	62	45.8***	107.2 (12.8–899.1)

** $p < 0.01$; *** $p < 0.001$.

CES-D Scores and Demographic and Drug Use Characteristics

Table 2 shows demographic and drug use characteristics of regular ecstasy consumers with low or high category CES-D scores. Those with high category CES-D scores were significantly less likely to have completed year 12 of secondary education relative to those with low category CES-D scores. Those with high category CES-D scores had used ecstasy significantly more frequently and had used greater amounts in a typical session in the last 6 months relative to those with low scores. They were also more likely to report recent use of cannabis, frequent use of cannabis or methamphetamine (weekly or more often), daily tobacco use, use of more than 5 illicit drug types, binge use of stimulants (for 48 h continuously without sleep), typical use of methamphetamine with ecstasy, intravenous drug use, harmful levels of alcohol consumption [a score ≥16 on the Alcohol Use Disorder Identification Test (AUDIT)], and experience of dependence on ecstasy or methamphetamine according to the Severity of Dependence Scale (SDS) [52].

Prediction of CES-D Scores

Backward logistic regression was conducted to investigate the correlates of high CES-D scores (≥16) with the inclusion of all factors that differed significantly between the two groups (table 2). The resulting significant regression equation accounted for 37% of the variance in the prediction of CES-D category with the inclusion of the following independent predictors: recent injecting drug use, self-reported psychological ecstasy dependence (SDS score ≥4), consuming 2 or more pills on a typical occasion of ecstasy use, and engaging in harmful alcohol consumption (AUDIT score ≥16). This equation correctly predicted 74% of total cases and 39% of risk cases. A further regression equation was performed using only the frequency of use factors for ecstasy, cannabis, methamphetamine, and alcohol. Days of use for cannabis and methamphetamine were significant predictors of CES-D category accounting for 18% of variance and classifying 78% of total cases but only 22% of risk cases.

Discussion

Almost one quarter (23%) of the sample self-reported experience of depression during the 6 months preceding the interview. This is higher than a recent report of 6-month prevalence of depression (11%) in the general population [53] and the 12-month prevalence of affective disorder (6.2%) in an Australian normative study [41], but similar to levels of self-reported depression among other samples of ecstasy users [6, 7]. However, it should be noted that the above general population estimates were based on a diagnostic interview rather than self-report data, which may contribute to the discrepancy. Only one third of those self-reporting a mental health problem had visited a health professional in relation to mental health problems during the 6 months preceding the interview, and one fifth had been prescribed medication for a mental health problem in this time. A similar low rate of help-seeking has been found among young adults (aged 19–32) with psychopathology [54], with around one third (33.7%) having sought help for mental health problems. However, given the higher rates of psychopathology among ecstasy and other drug users relative to nonusers, a targeted approach to addressing low levels of help-seeking in this population may be particularly important.

Table 2. Demographic and drug use characteristics in ecstasy consumers with low (<16) and high (≥16) CES-D scores

Variable	CES-D score <16 (n = 71)	CES-D score ≥16 (n = 28)	χ^2 (Mann-Whitney U)	OR (95% CI)
Demographic characteristics				
Male, %	54	54	n.s.	
Younger (<23 years), %	54	43	n.s.	
Completed secondary education (year 12), %	86	61	7.6**	0.3 (0.1–0.7)
Unemployed, %	7	18	n.s.	
Full-time student, %	38	18	3.7; p = 0.053	0.4 (0.1–1.0)
Full-time work, %	25	29	n.s.	
Part-time work, %	21	14	n.s.	
Ecstasy and other drug use in last 6 months				
Median days used ecstasy	11	16	(653.5**)	1.0 (1.0–1.1)[1]
Median ecstasy pills used in typical session	1.5	2	(556.5**)	2.0 (1.2–3.3)
Used ecstasy weekly or more often, %	18	36	3.4; p = 0.065	2.4 (0.9–6.6)
Used 2 or more ecstasy pills in typical session, %	41	82	13***	7 (2–19)
Used alcohol, %	99	100	n.s.	
Used alcohol weekly or more often, %	93	82	n.s.	
Used cannabis, %	62	86	5.2*	3.7 (1.2–11.8)
Used cannabis weekly or more often, %	27	46	3.6; p = 0.060	2.4 (1.0–5.9)
Used methamphetamine, %	68	75	n.s.	
Used methamphetamine weekly or more often, %	3	18	6.9**	7.5 (1.3–41.3)
Used tobacco, %	72	79	n.s.	
Used tobacco daily, %	27	57	8.11**	3.6 (1.5–9.1)
Risky patterns of drug use in last 6 months				
Used drugs intravenously, %	1	14	6.9**	11.7 (1.2–109.6)
Used >5 illicit drug types, %	49	71	4.0*	2.6 (1.0–6.6)
Binged[2] on stimulants, %	27	64	12.1**	4.9 (1.9–12.5)
Typically binge drink with ecstasy, %	78	75	n.s.	
Typically use methamphetamine with ecstasy, %	6	32	12.7***	7.9 (2.2–28.6)
Risk of dependence				
'Harmful' alcohol consumption (AUDIT score ≥16), %	26	54	7.0**	3.3 (1.3–8.3)
Ecstasy SDS score ≥4, %	17	43	7.4**	3.7 (1.4–9.8)
Methamphetamine SDS score ≥4, %	9	25	4.8*	3.6 (1.1–11.9)

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

[1] The strength of this relationship does not change following correction for censored range of recent ecstasy use (6–180 days) when compared to other drugs (0–180 days).

[2] Use of stimulants for more than 48 h continuously without sleep.

Over one quarter (28%) of the sample had a CES-D score of 16 or more, indicating high levels of depressive symptomatology, and a possible diagnosis of depression. The mean CES-D score of 13 is comparable to the mean score of around 14 found for other young adult populations [55, 56]. Ecstasy users with high CES-D scores were significantly more likely to report high levels of psychological distress (K10 scores) relative to those with low scores. The mean K10 score of 18 in the current sample of regular ecstasy users is similar to the mean score of 14–16 reported among the general population [51, 57]. However, compared to the general population [41], a greater proportion of the present sample of ecstasy users had K10 scores categorized as 'high' (15 vs. 7%), with similar proportions categorized as 'very high' (4 vs. 3%). Thus, the present sample of ecstasy users were twice as likely to have K10 scores categorized as high relative to the general population.

Ecstasy users with high CES-D scores were also more likely to report experience of mental health problems (de-

pression rather than anxiety), to have attended a mental health professional, and to have been prescribed medication for mental health problems relative to those with low CES-D scores. Just three fifths (57%) of those with high CES-D scores indicated that they had experienced depression during the preceding 6 months. These findings suggest underrecognition of possible mental health problems among the remaining two fifths of this subsample. However, it should be noted that the CES-D is a screening instrument and while those with high scores are more likely to report depression, it is not possible to accurately predict clinical depression on the basis of high CES-D scores alone.

A range of correlates were associated with high levels of depressive symptomatology. Consistent with population level correlates of affective disorders [58], those with high CES-D scores were significantly less likely to have completed secondary education (year 12), or to be current full-time students. However, in contrast to the increased prevalence of affective disorders among females relative to males in the general population [41] and among ecstasy users [40], there were no sex differences in depressive symptomatology. Those with high CES-D scores had used ecstasy more frequently and in greater amounts, and were more likely to have recently used cannabis, to have used cannabis or methamphetamine more frequently (weekly or more often), and to have used tobacco daily in the preceding 6 months relative to those with low scores. They were also more likely to have engaged in risky drug use behaviors such as intravenous drug use, to consume a greater number of illicit drug types, and to report binge drug use (for 48 h continuously without sleep), typical use of methamphetamine with ecstasy, higher scores on dependence scales for both ecstasy and methamphetamine, and hazardous levels of alcohol consumption.

When just frequency of drug use was considered, frequency of use for cannabis and methamphetamine were more substantial predictors of depressive symptoms than frequency of ecstasy and alcohol use. However, when other patterns of drug use were considered, recent injecting drug use, self-reported psychological ecstasy dependence (SDS), consuming 2 or more pills on a typical occasion of ecstasy use, and engaging in harmful alcohol consumption (AUDIT score $\geq$16) were found to be the most substantial independent predictors of high CES-D scores. The present findings are generally consistent with previous research showing an association between depressive symptoms and cannabis use [10, 21, 29, 30] or polydrug use generally [15, 19, 31] among ecstasy users, and findings of a relationship between cannabis use and depression irrespective of concomitant ecstasy use [59]. However, the present results also suggest that other patterns of drug use, including ecstasy, alcohol and tobacco, are important correlates of depressive symptomatology in this population.

One limitation of the present study is that recent life events and subacute effects of recent ecstasy or other drug use may have affected depression scores at the time of the interview. For example, dysphoric mood is a well-known subacute side effect of ecstasy use that may continue for several days [7] and participants were not asked to abstain from drug use prior to the interview. Furthermore, there is an overlap between some symptoms of depression and substance use [40] and the CES-D has a higher false-positive rate among drug-dependent compared to other psychiatric patient groups [48]. However, no participant was classified in the high CES-D group due to reporting an array of symptoms for short duration (1–2 days in the preceding week): more than half of those classified in the high CES-D group (57%) had experienced at least 2 symptoms 'most or all of the time' (5–7 days in the preceding week) and the lowest scoring individual had experienced 3 of the 20 symptoms for a substantial period of the preceding week (3–4 days). As such, it is not likely that all of these cases can be accounted for by postacute anhedonic responses.

The aim of the present research was not to examine the causative relationship between depression and drug use, but to determine the correlates of depressive symptomatology among current ecstasy users. As such, this study yields useful information in terms of the development of harm reduction strategies for this population. Harm reduction messages that aim to reduce the incidence of risk factors (e.g. high frequency and quantity ecstasy use, binge drug use, frequency of cannabis and methamphetamine use, levels of drug dependence, harmful alcohol use, and intravenous drug use) may also aid in the reduction of the experience of depressive symptomatology. Conversely, it appears that depression occurs more often among ecstasy users than in the general population, and it is possible that improving the awareness of and access to treatment for depression in this population would contribute to a reduction of associated substance use problems.

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