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Depressive symptomatology in young adults with a history of MDMA use: a longitudinal analysis

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Abstract

Research suggests that methylenedioxymethamphetamine (MDMA)/'ecstasy' can cause serotonin depletion as well as serotonergic neurodegradation that may result in depression. This longitudinal study used the Beck Depression Inventory (BDI-II) to assess depressive symptomatology every six months over a two-year period among a community sample of young adult MDMA/'ecstasy' users ($n = 402$). Multilevel growth modeling was used to analyze changes in BDI scores. Between baseline and 24 months, the mean BDI score declined from 9.8 to 7.7. Scores varied significantly across individuals at baseline and declined at a rate of 0.36 points every six months. Persons with higher baseline scores were more likely to have their scores decrease over time. Several factors were significantly associated with score levels, independent of time: gender – men's scores were lower than women's; ethnicity – whites' scores were lower than those of non-whites; education – persons with at least some university education had scores that were lower than those without any college experience; benzodiazepines – current users' scores were higher than non-users'; opioids – current users' scores were higher than non-users'; and cumulative ecstasy use – people who had used MDMA more than 50 times had scores that were higher than persons who had used the drug less often. The results reported here show low levels of depressive symptoms among a sample that, after 24 months, consisted of both current and former MDMA users. The low and declining mean scores suggest that for most people MDMA/'ecstasy' use does not result in long-term depressive symptomatology.

Keywords

MDMA, ecstasy, substance abuse, depressive symptomatology, depression, BDI, longitudinal analysis

Introduction

The presence of depressive symptomatology in people who have used methylenedioxymethamphetamine (MDMA)/'ecstasy' has been the subject of much research. Both short and longer term symptoms of depression reported in MDMA users have been attributed to serotonin depletion and/or serotonergic neurodegradation (Green *et al*., 2003; Morton, 2005). Alarmingly, findings from research on non-human primates have suggested that even a single, moderate dose of the drug can cause damage to the serotonergic system (Ricaurte *et al*., 1988).

The Beck Depression Inventory (BDI) (Beck *et al*., 1961) is one of the most commonly used instruments to screen for depression in research involving MDMA/'ecstasy' users. This research has consisted primarily of cross-sectional studies that have employed early editions of the BDI, versions in which scores of 9 or less were considered suggestive of minimal or no depression, and scores in the 10–16 range were considered indicative of mild depression (Beck *et al*., 1961; Beck and Steer, 1993). In general, these studies have been conducted with relatively small samples that were recruited through convenience or snowball sampling techniques. For example, research in England compared chronic MDMA/'ecstasy' users ($n = 29$), who reported using the drug at least 100 times, with non-MDMA users ($n = 29$), and found that the mean score of the former (9.2, SD = 5.9) was significantly higher than that of the latter (5.2, SD = 3.9), independent of gender. Participants were recruited through a peer-oriented convenience sampling technique (MacInnes *et al*., 2001). Using a convenience sample, which consisted entirely of men, researchers in Holland compared heavy MDMA/'ecstasy' users (48 or more use occasions in the last two years) ($n = 21$), moderate users (12–48 occasions) ($n = 21$), and non-MDMA users ($n = 20$), and found mean BDI scores of 7.0

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(SD = 6.3), 3.9 (SD = 3.3), and 3.0 (SD = 3.7), respectively. The results of BDI score analysis, which controlled for confounding factors such as level of education and attention-deficit disorder in youth, revealed no significant statistical differences between the groups (Verkes *et al*., 2001). Research in England with a convenience sample compared current MDMA/'ecstasy' users ($n = 30$), former MDMA/'ecstasy' users ($n = 20$), poly-drug users with no MDMA history ($n = 30$), and people with no history of illicit drug use ($n = 30$) (Roiser and Sahakian, 2004). Ex-users had the highest mean score at 12.6 (SD = 9.5), followed by current users at 7.9 (SD = 6.5), poly-drug users at 6.0 (SD = 5.4), and non-users at 3.8 (SD = 2.8). Analysis revealed some differences between the groups. Both current users and former users had significantly higher BDI scores than the drug naïve controls; however, their scores were not significantly higher than the poly-drug users. Higher frequencies of MDMA use, defined as number of times the drug was used per month during users' highest regular use period, correlated with higher BDI scores. Another study conducted in Holland, again with a convenience sample, compared current moderate users (less than 50 tablets in lifetime) ($n = 15$), current heavy users (more than 50 tablets) ($n = 23$), former heavy users ($n = 16$), and poly-drug but MDMA naïve users ($n = 15$), and found median BDI scores of 2.0, 5.0, 5.5, and 1.0, respectively (de Win *et al*., 2004). Although significant differences were noted between some groups, the BDI scores for all groups were within normal limits. A study based on a convenience sample of young adults living in Minnesota compared users ($n = 26$) with non-MDMA users ($n = 26$) and found statistically significant differences in BDI scores between the groups (Hanson and Luciana, 2004). The mean score for users was 8.7 (SD = 8.3) while for non-users it was 3.6 (SD = 3.3).

Several cross-sectional studies have used the BDI-II, the latest edition of the instrument, which was developed to better match DSM-IV criteria for major depressive episode (MDE). BDI-II scores of 13 or less suggest minimal or no depression (Beck *et al*., 1996). One of these studies was conducted in Australia with a small sample recruited through advertising posters. It compared individuals with a history of MDMA/'ecstasy' use ($n = 17$) to those with no MDMA use history ($n = 15$), and found the users' mean BDI score (12.4, SD = 9.4) was significantly higher than non-users' (5.5, SD = 4.6) (McCardle *et al*., 2004). Another BDI-II study conducted in Louisiana compared users ($n = 32$), aged 18–45 years, to ecstasy naïve controls ($n = 32$) recruited from introductory psychology classes at a state university, and found no differences between them. The mean score for both groups was 10.3 even though the user group had significantly more experience with a wide assortment of psychoactive drugs, including alcohol and nicotine (Guillot and Greenway, 2006). Finally, we conducted a cross-sectional study with young adults in Ohio who were current MDMA/'ecstasy' users ($n = 402$), the same sample upon which this article is based. The mean BDI-II score for the sample was 9.8 (SD = 8.9, range 0–48). We also found that 14.4% of the sample had scores ≥ 20, indicating symptoms of moderate to severe depression (Falck *et al*., 2006a).

To the best of our knowledge, only one study has employed the BDI in a pre–post fashion with MDMA/'ecstasy' users. Curran and Travill (1997) compared recent users ($n = 12$) and non-users ($n = 12$), all of whom were recruited through a snowball sampling at a dance club in England. The results showed that mean BDI scores increased from 3.5 (SD = 3.5) on the night of MDMA use to 11.8 (SD = 7.2) four days later. The mean BDI score among the non-users on the fifth day was 6.9 (SD = 4.1), essentially unchanged from baseline. This study established the acute, post-ecstasy use depressed mood (or washout/offset period), which the authors suggested was caused by serotonergic depletion. At least two other studies, both using the Symptom Checklist-90-Revised (SCL-90-R), have examined changes in depressive symptoms over time among people with a history of MDMA use. One study, conducted with participants recruited in the Hamburg, Germany, area who were followed for 18–24 months, found no significant differences in depressive symptoms between current ($n = 18$) and former ($n = 16$) MDMA users, poly-drug using controls ($n = 17$), and drug-naïve controls ($n = 15$) (Thomasius *et al*., 2006). The other study, also conducted in Germany, with 38 users, some of whom continued to use and some who became MDMA/'ecstasy' abstinent, found no significant difference in depressive symptoms after 18 months (Daumann *et al*., 2004). All three of these studies were conducted with small samples recruited through convenience sampling techniques.

To extend current research and better understand depressive symptomatology among MDMA users over the long term, we administered the BDI-II longitudinally to a comparatively large sample of young adults to answer the following questions: 1) Over a 2-year timeframe, are there statistically significant changes in BDI-II scores among people with a history of MDMA use?; 2) Does the rate of change vary across individuals?; and 3) What factors influence BDI-II scores as well as variation in their rate of change?

Methods

Sampling

Participants in this study were 402 people recruited in the Columbus, Ohio, metropolitan area over a 13-month period (May 2002 through May 2003), who agreed to participate in a natural history study focusing on MDMA and other drug use by young adults. To be eligible for a baseline interview, participants had to be between 18 and 30 years old; an Ohio resident; not involved in a formal drug abuse treatment program within the past 30 days; able to give an address and telephone number at which they could be contacted for follow-up; and report having used MDMA at least once in the past six months. A respondent-driven sampling plan was used to recruit participants (Heckathorn, 1997; Heckathorn *et al*., 2002). More detail on the sampling methodology is available elsewhere (Carlson *et al*., 2005; Wang *et al*., 2005). Informed consent was obtained from all participants following a protocol approved by the university's Institutional Review Board. The study also operated under a federal grant of confidentiality issued by the U.S. Department of Health and Human Services/National Institute on Drug Abuse.

The baseline sample consisted of 258 men and 144 women. In terms of race/ethnicity, 328 (81.6%) were white, and the remainder were classified as non-white. The mean age of participants was 20.9 years (median = 20 years; range = 18–30). About 22% of the sample had less than a high school education, 36.1% had completed high school, and 52.7% had some college or a college degree. Nearly half the sample had used MDMA on 10 or fewer times. As previously reported elsewhere, MDMA/'ecstasy' use ranged from 1 to 1000 occasions, the mean was 36.2, the median was 11.2, and the mode was 10 (Falck *et al*., 2006a).

Data collection

Baseline questionnaires were administered face-to-face by trained interviewers in a field-site office. The questionnaire was largely interviewer-administered but also contained short segments administered by the participants themselves. It consisted of standardized and author-generated items. Data were collected on a variety of topics including, but not limited to, sociodemographic and drug use variables. The BDI-II was self-administered by participants about one hour into the baseline interview. Given the concerns about the post-MDMA use washout period influencing the baseline interview (Curran and Travill, 1997; Curran, 2000), participants were asked not to participate in an interview within three days of last having used the drug. Follow-up interviews were scheduled at six-month intervals after baseline. Follow-up interviews lasted less than an hour and focused on collecting information on participants' drug use practices, with particular emphasis on MDMA use. The BDI-II was administered at the beginning of the follow-up interviews.

Measures

The dependent measure in this study was the BDI-II score. The BDI-II screens for and measures the severity of symptoms of depression that have occurred in the last two weeks. It consists of 21 items, each with a four-point (0–3) response scale. Scores can range from 0 to 63, with higher scores reflecting a greater severity of symptoms. Scores from 0 to 13 suggest no to minimal depression, 14–19 mild depression, 20–28 moderate depression, and scores above 29 suggest severe depression (Beck *et al*., 1996).

Sociodemographic characteristics (gender, age, ethnicity, and education) were treated as fixed explanatory variables, while lifetime occasions of MDMA use and the frequency of other non-medical drug use in the last 30 days were treated as time-varying covariates. Other non-medical drugs included marijuana, hashish, heroin, non-prescribed opioids, non-prescribed tranquilizers, cocaine HCl, crack cocaine, amphetamine, methamphetamine, ketamine, phencyclidine, LSD, and psilocybin. Days of drinking alcohol to intoxication/drunkenness in the previous 30 was also considered. The use of all drugs, except cannabinoids and alcohol, was measured dichotomously (use, no use in the last 30 days). Frequency of cannabinoid use was measured as a three category variable (no use, use on 1–20 days, use on 21 or more days). Alcohol use was similarly measured (no drunkenness, drunkenness on 1–10 days, drunkenness on 11 or more days).

Analysis

Internal consistency of the BDI-II was assessed at each measurement point with Cronbach's alpha coefficient. As longitudinal data are hierarchically structured, that is, repeated measures nested within individuals, a multi-level modeling technique, growth modeling, was used to analyze the data (Raudenbush and Bryk, 2002). Inter-individual changes and intra-individual variations in the changes were assessed simultaneously in the model, which was run with SAS Proc Mixed (SAS Institute, 2004). The model was specified as the following:

$$y_{it} = \beta_{0i} + \beta_{1i} T_{it} + \sum \beta_p Z_{pit} \quad (1)$$

$$\beta_{0i} = \gamma_{00} + \sum \gamma_{0k} X_{ki} + u_{0i} \quad (2)$$

$$\beta_{1i} = \gamma_{10} + \sum \gamma_{1k} X_{ki} + u_{1i} \quad (3)$$

$$y_{it} = \gamma_{00} + \sum \gamma_{0k} X_{ki} + \gamma_{10} T_{it} + \sum \gamma_{1k} T_{it} \cdot X_{ki} + \sum \beta_p Z_{pit} + (u_{0i} + T_{it} \cdot u_{1i} + e_{it}) \quad (4)$$

where the intercept and slope coefficients β_{0i} and β_{1i} in equation 1 of the growth model were specified as random, indicating that the initial level and rate of change in BDI-II scores vary across individuals. Time-varying explanatory variables Z_{pit} were included in the level 1 equation of the model as covariates, and their interactions with time were also tested. The fixed variables X_{ki} were included in the level 2 equations (i.e., equations 2 and 3) to predict variations in β_{0i} and β_{1i}, respectively. In the combined model equation 4, the cross-level interactions between time and variables X_{ki} tell how the rate of change in BDI scores was associated with individual sociodemographic characteristics and how the effects of sociodemographic characteristics on y_{ij} vary over time. In the interest of parsimony, drugs with similar pharmacological effects were grouped together for the analysis. Thus, marijuana was combined with hashish, heroin with other opioids, cocaine HCl with crack, amphetamine with methamphetamine, ketamine with phencyclidine, and LSD with psilocybin.

Results

The analysis was based on 402 observations at baseline, 348 at six months, 339 at 12 months, 326 at 18 months, and 292 at 24 months. Table 1 shows the drug use practices of the sample over the course of the study. About 15% of the sample at baseline (T_0) reported having used MDMA/'ecstasy' on more than 50 occasions. At the 24-month follow-up (T_4), 14% of those people who completed the interview reported having used the drug on more than 50 occasions. In fact, the proportion of the sample falling into each MDMA frequency of use category was largely static over the course of the study, even though as the study progressed participants moved into new frequency categories based on cumulative occasions of

Table 1 Drug use practices over 24 months

	T_0 ($N = 402$)	T_1 ($N = 348$)	T_2 ($N = 339$)	T_3 ($N = 326$)	T_4 ($N = 292$)
Cumulative MDMA/'ecstasy' use					
<10	168 (41.8)	140 (40.2)	134 (39.5)	124 (38.0)	116 (39.7)
10–50	175 (43.5)	156 (44.8)	154 (45.4)	151 (46.3)	135 (46.2)
50+	59 (14.7)	52 (14.9)	51 (15.0)	51 (15.6)	41 (14.0)
		30-day drug use			
Alcohol drunkenness					
No use	61 (15.3)	57 (17.1)	43 (13.5)	53 (17.3)	48 (17.4)
1–10	265 (66.4)	207 (62.2)	233 (73.0)	201 (65.5)	184 (66.7)
10+	73 (18.3)	69 (20.7)	43 (13.5)	53 (17.3)	44 (15.9)
Cannabinoids					
No use	52 (12.9)	58 (16.7)	83 (24.6)	81 (24.9)	88 (30.2)
1–20	183 (45.5)	161 (46.3)	146 (43.2)	143 (44.0)	124 (42.6)
20+	167 (41.5)	129 (37.1)	109 (32.3)	101 (31.1)	79 (27.2)
Tranquilizers					
No use	202 (50.3)	262 (75.3)	258 (76.1)	258 (79.1)	245 (83.9)
Use	200 (49.8)	86 (24.7)	81 (23.9)	68 (20.9)	47 (16.1)
Heroin					
No use	391 (97.3)	332 (95.4)	329 (97.1)	314 (96.3)	286 (98.0)
Use	11 (2.7)	16 (4.6)	10 (3.0)	12 (3.7)	6 (2.1)
Other opioids					
No use	276 (68.7)	254 (73.0)	255 (75.2)	247 (75.8)	228 (78.1)
Use	126 (31.3)	94 (27.0)	84 (24.8)	79 (24.2)	64 (21.9)
Crack					
No use	395 (98.3)	344 (98.9)	335 (98.8)	322 (98.8)	291 (99.7)
Use	7 (1.7)	4 (1.2)	4 (1.2)	4 (1.2)	1 (0.3)
Cocaine HC1					
No use	291 (72.4)	267 (76.7)	269 (79.4)	263 (80.7)	236 (80.8)
Use	111 (27.6)	81 (23.3)	70 (20.7)	63 (19.3)	56 (19.2)
Methamphetamine					
No use	355 (88.3)	325 (93.4)	320 (94.4)	312 (95.7)	281 (96.2)
Use	47 (11.7)	23 (6.6)	19 (5.6)	14 (4.3)	11 (3.8)
Amphetamine					
No use	351 (87.3)	312 (89.7)	310 (91.5)	298 (91.4)	270 (92.5)
Use	51 (12.7)	36 (10.3)	29 (8.6)	28 (8.6)	22 (7.5)
LSD					
No use	382 (95.0)	319 (91.7)	317 (93.5)	317 (97.2)	286 (97.9)
Use	20 (5.0)	29 (8.3)	22 (6.5)	9 (2.8)	6 (2.1)
Psilocybin					
No use	342 (85.1)	308 (88.5)	318 (93.8)	301 (92.3)	273 (93.5)
Use	60 (14.9)	40 (11.5)	21 (6.2)	25 (7.7)	19 (6.5)
Ketamine					
No use	338 (84.1)	336 (96.6)	335 (98.8)	324 (99.4)	290 (99.3)
Use	64 (15.9)	12 (3.5)	4 (1.2)	2 (0.6)	2 (0.7)
PCP					
No use	402 (100.0)	347 (99.7)	339 (100.0)	326 (100.0)	292 (100.0)
Use	—	1 (0.3)	—	—	—

The number of people responding to the 30-day drug use practice questions may not equal the total *n* for a given follow-up period because of missing values.

MDMA/'ecstasy' use. For other drugs, use is not cumulative, and represents only use in the 30 days prior to the completing the interview. Thus, for instance, 41.5% of the sample used cannabis on 21 or more days in the 30 days before the baseline interview, while 27.2% reported using it at that frequency at the 24-month interview.

Table 2 shows the mean BDI-II scores by time period. Overall, scores decreased from 9.8 (SD = 8.9) at baseline to 7.7 (SD = 8.0) at 24 months. In addition, the BDI-II scores had a high internal consistency over time with Cronbach's alpha coefficients ranging from 0.91 to 0.92.

Table 3 shows the results of the multi-level analysis. The change in BDI scores over time was statistically significant. BDI-II scores declined, on average, at a rate of 0.36 points every six months, controlling for covariates. However, inter-individual variation in the rate of change in BDI scores was not explained by sociodemographics. As such, the interaction effects in equation 4 are not reported in the table. This also indicates that the effects of individual sociodemographics on the BDI score remained unchanged over time. Several sociodemographic characteristics were significantly associated with variation in the initial BDI scores: men's scores were significantly lower than women's; whites' scores were lower than non-whites; and participant's with at least some university education had lower scores than those without college experience.

The initial (i.e., baseline) level and the rate of change in BDI scores varied significantly across individuals (see lower panel of table). Some of the time-varying drug use practices had a significant effect on BDI scores. Specifically, participants who had used MDMA on more than 50 occasions had significantly higher scores than those who had used less often. Current users of non-prescribed benzodiazepines and current users of non-prescribed opioids also had significantly higher BDI scores than did non-users of drugs in these classes. None of the interactions between time and time-varying covariates were found to be statistically significant and therefore are not reported in Table 3. The proportional reduction in mean squared error was used to measure the variance explained at both level 1 and level 2 (Snijders and Bosker, 1994). The level 1 $R^2_1 = 0.13$ and the level 2 $R^2_2 = 0.20$. That is, about 13% of the intra-individual variance and 20% of the inter-individual variance were explained by the model.

Table 4 shows baseline and 24-month mean BDI scores of those people who reported no use of MDMA after their initial interviews and those who reported additional occasions of use. The group that continued to use MDMA/'ecstasy' had higher scores at baseline as well as at 24 months, although scores still fell into the range suggesting no to minimal depression.

Table 2 Mean BDI-II scores over 24 months

Time	N	Mean	SD
Baseline	402	9.8	8.9
6 months	348	8.8	8.1
12 months	338	8.3	7.8
18 months	325	8.1	8.3
24 months	285	7.7	8.0

Table 3 Results of multilevel analysis – predictors of change in BDI-II scores over 24 months

Parameter		Estimate	P value
Fixed effect			
Intercept		13.44	0.0001
Time		−0.36	0.0033*
Men		−2.95	0.0001*
Whites		−1.94	0.0288*
Age		0.17	0.2006
College education		−2.39	0.0007*
MDMA/'ecstasy' (10–50)		−0.40	0.4994
MDMA/'ecstasy' (50+)		2.11	0.0138*
Cannabinoids (1–20)		0.39	0.3959
Cannabinoids (20+)		0.83	0.1210
Opioids		0.91	0.0167*
Cocaine HCl/crack cocaine		0.58	0.1440
Methamphetamine/amphetamine		0.20	0.6801
Ketamine/PCP		−0.02	0.9815
LSD/psilocybin		−0.04	0.9254
Tranquilizers		0.92	0.0444*
Alcohol drunkenness (1–10)		−0.68	0.1141
Alcohol drunkenness (10+)		−0.51	0.3420
Random effect	Variance component	Z value	P value
Initial level	44.37	10.49	<0.0001*
Rate of change	2.45	6.27	<0.0001*
Covariance between initial level and rate of change	−4.65	−4.42	<0.0001*

*Statistically significant.

Table 4 Mean BDI-II scores of continuing and currently abstemious MDMA/'ecstasy' users at baseline and 24 months

	N	Mean	SD	Min	Max
Abstemious					
T_0	195	8.6	8.2	0	40
T_4	122	6.3	7.5	0	41
Continuing					
T_0	207	10.9	9.3	0	48
T_4	163	8.7	8.3	0	42

Discussion

To the best of our knowledge, this is the first longitudinal study to use standardized instrumentation with a large sample to explore depressive symptomatology among MDMA/'ecstasy' users. The findings are strengthened by the sampling methodology we used because it produced a sample that is likely to be more representative of an ecstasy user population than virtually any other study published to date, save the birth registry studies in Germany by Lieb *et al.* (2002) and in Holland by Huizink *et al*. (2006). Although the BDI-II is a screening tool, and not a clinical assessment, it has been used worldwide in studies of MDMA users. It also has excellent internal reliability with MDMA users. Overall, our results show low and declining levels of depressive symptoms among a sample that, 24 months into the study, consisted of both active and currently abstemious MDMA users. These findings suggest that most people who have used the drug do not experience significant levels of depressive symptomatology in the long term. The data also show that people who used MDMA on more than 50 occasions had significantly higher levels of depressive symptoms than those who used less often. The results of this longitudinal study replicate many of the findings of our earlier cross-sectional study of depressive symptomatology with this sample (Falck *et al*., 2006a).

Several sociodemographic variables were significantly associated with BDI-II scores. Men had lower scores than women; whites had lower scores than non-whites, and participants with at least some university education had lower scores than those without such experience. Finding that men had lower levels of depressive symptomatology is consistent with at least one other study involving MDMA users as well as general population studies which have shown that men are less likely than women to experience high levels of depressive symptoms or major depressive disorder (MDD) (Robins *et al*., 1991; Kessler *et al*., 1994; Milani *et al*., 2004). Why whites and persons with at least some college education had lower levels of symptoms than their reference groups is unclear. It is also not known why BDI-II scores declined every six months (0.36 points per period), controlling for covariates. In addition, the inter-individual variation in the rate of change in BDI scores over time is unexplained. Further research is needed on these issues.

Having crossed the threshold of 50 occasions of MDMA use during the two-year observation period had a significant effect on BDI-II scores. Consistent with other studies (MacInnes *et al*., 2001; de Win *et al*., 2004), higher levels of MDMA use (50 or more occasions) were associated with significantly higher scores. The higher scores may be explained, in part, by recent research that has suggested serotonergic damage occurs with frequent use, higher dosage use, more total uses, or clinically dysfunctional use (Hanson and Luciana, 2004). In addition, a meta-analysis of 25 studies concluded that increases in symptomatology were associated with higher lifetime levels of MDMA consumption (Sumnall and Cole, 2005). It is, however, still unclear whether depressive symptoms, regardless of level or severity, are necessarily, or solely, related to MDMA use. First, other research with this same sample has shown that more than three-fourths of the people who had used MDMA more than 50 times also reported drug histories that included amphetamine and methamphetamine use (Carlson *et al*., 2005). This complicates attribution of depressive symptomatology to MDMA because amphetamine analogs can be toxic to serotonin neurons and cause other brain damage (Fleckenstein *et al*., 2000). Second, the possibility that MDMA used in combination with other drugs produces neurotoxic effects cannot be discounted (Green *et al*., 2003). Third, and perhaps most importantly, in another study with this sample we found that nearly three-fourths of those who had a lifetime history of MDE or MDD experienced their initial episode before their first use of MDMA (Falck *et al*., 2006b). At least one other research group has reported similar findings (Lieb *et al.*, 2002). A drug that produces euphoria, enhances social interaction, increases empathy, and is called 'ecstasy,' is, not surprisingly, likely to appeal to young people who have been affected by depression. Consequently, future research on depression and other psychological problems among MDMA users would be enhanced greatly by considering the temporal relationships between the onset of the disorders being studied and the initiation of use of MDMA as well as other drugs.

Finding that participants who used opioids, including heroin, had significantly higher BDI scores is largely consistent with previous research that has shown high levels of depressive disorder among heroin users (Darke and Ross, 1997, 2002). Finding that individuals who used non-prescribed benzodiazepines had higher scores is not surprising, particularly if the drugs were used in response to sleep problems or anxiety, common symptoms of depression (Goodwin and Hasin, 2002; Roeloffs *et al*., 2002).

A relationship between cannabis and depressive symptomatology has been noted by some researchers. For example, Daumann *et al*. (2004) attributed the depressive symptomatology reported by MDMA/'ecstasy' users in their study to regular cannabis use, not MDMA. Morgan *et al*. (2002), in their study, which compared current, former, non-MDMA poly-drug users with drug-naïve controls, suggested that psychopathology, including depressive symptoms as measured by the SCL-90-R, was linked to the extent of cannabis use in the past year, with more use associated with higher scores. Alternatively, MacInnes *et al*. (2001), in their study of chronic MDMA users who had been MDMA/'ecstasy' abstinent for at least two weeks, found no association between the current use of cannabis and symptoms of depression. The earlier cross-sectional study of the baseline behaviors of the sample reported on here revealed no association between recent cannabis use and serious depressive symptomatology, which was defined as a BDI-II score ≥20 (Falck *et al*., 2006a). The results of this study affirm our earlier findings and extend them by showing no significant association between cannabis use and changes in depressive symptomatology. Clearly, more research is needed to sort out the conflicting results on the role cannabis plays in the development of depressive symptoms among current and former MDMA/'ecstasy' users.

A particularly interesting finding is that the mean BDI-II scores at 24 months for those who reported no MDMA use after the baseline interview ($n = 122$), as well as those who did ($n = 163$), were both in the no to minimal depression range, 6.3 and 8.7, respectively. It is worth noting that these scores are lower than the mean scores (12.6) obtained from the college students ($n = 120$) in an introductory psychology class used by Beck *et al*. (1996) to assess the diagnostic discrimination capabilities of the BDI-II. Thus, our data add some strength to the argument that for many people MDMA/'ec-

stasy' use may not result in clinically meaningful depressive symptomatology (Cole and Sumnall, 2002; Sumnall and Cole, 2005).

This study has several limitations. First, even though the BDI was administered at regular intervals over a two-year period, it may have missed episodes of depressive symptoms that occurred outside of its two-week screening window. Second, while low BDI-II scores (≤13) suggest no or minimal levels of depression, it is possible that subclinical depression, which may be a precursor to MDE/MDD, may exist within this score range. Similarly, it is also possible that the BDI is not sensitive enough to detect subtle changes in somatic, affective, or cognitive states that are caused by damage to the serotonergic system. Third, although the BDI is widely used to screen for depression in normal populations, the meaning of differences in scores, even when they fall into the same diagnostic category, is uncertain. This is complicated by the fact that there are several instances of multiple measures for the same symptom in the instrument. For instance, six separate BDI-II items measure the DSM-IV criterion for feelings of worthlessness and guilt. Fourth, this study is based heavily on self-reports of behaviors. Biological assays were not used to confirm MDMA/'ecstasy' use. Given the eligibility criteria for MDMA use, it is unlikely urine testing would have produced meaningful data; hair analysis was and remains prohibitively expensive with large samples. Consequently, there is no certainty that the MDMA/'ecstasy' participants thought they were taking was actually MDMA. Thus, BDI scores cannot be conclusively associated with MDMA use. Nevertheless, findings from other researchers have shown a high level of agreement between self-reports of MDMA use and the results of biochemical assays. For example, Stuerenburg *et al.* (2002) reported a 91.3% concordance rate between self-reported MDMA use and MDMA identified by hair analysis in 107 users. Pichini *et al*. (2006) studied 34 users and reported a similarly high rate of agreement.

Conclusion

Our findings suggest for most people MDMA/'ecstasy' use is not associated with clinically meaningful depressive symptomatology in the long term. These results, coupled with those of other studies that have found that many users with a history of MDE/MDD experienced these problems before initiating MDMA use, also raise questions about the nature of the relationship between MDMA use and symptoms of depression. Additional research using more sensitive instrumentation would perhaps shed more light on this critically important issue.

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