

Recreational ecstasy use and depression

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Abstract

Research in laboratory animals has shown that 3,4-methylenedioxymethamphetamine (MDMA or ecstasy) destroys serotonergic axons in the brain at certain doses. Serotonin is known to take part in the regulation of mood in humans. Many researchers have hypothesized that if recreational ecstasy use destroys serotonergic axons, then a corresponding decline in the mood of ecstasy users should be seen. The purpose of the present study was to look at the relationship between recreational ecstasy use and depression as measured by the Beck Depression Inventory-II. No significant differences were found between

Beck Depression Inventory-II scores of heavy ecstasy users and ecstasy-naïve college students. No significant relationships were found between Beck Depression Inventory-II scores and any of the measures of ecstasy use. Most ecstasy users who had been diagnosed with a psychiatric disorder reported that being diagnosed preceded their use of ecstasy.

Keywords

3,4-methylenedioxymethamphetamine, MDMA, ecstasy, Beck Depression Inventory, serotonin, depression

Introduction

In several studies, 3,4-methylenedioxymethamphetamine (MDMA or ecstasy) has been shown to damage serotonin (5-hydroxytryptamine, 5-HT) pathways in rodents and non-human primates (Commins *et al.*, 1987; O'Hearn *et al.*, 1988; Wilson *et al.*, 1989; Ricaurte *et al.*, 1992). Since MDMA has been shown to be neurotoxic to other animals, many researchers have hypothesized that MDMA is also neurotoxic to humans, although at what dose neurotoxicity is likely to occur is still a matter of controversy (Vollenweider *et al.*, 1999; McCann and Ricaurte, 2001; Vollenweider *et al.*, 2001). Brain imaging studies consistently have revealed less serotonin transporter (SERT) binding in heavy ecstasy users (ecstasy users who had used 100 or more tablets of ecstasy on average) in comparison to ecstasy-naïve controls. Some have revealed modest regional brain differences of approximately 5 to 15% (Semple *et al.*, 1999; Reneman *et al.*, 2001a; Reneman *et al.*, 2001b; Buchert *et al.*, 2003; Thomasius *et al.*, 2003; Buchert *et al.*, 2004), while others have revealed greater differences of approximately 10 to 70% (McCann *et al.*, 1998; McCann *et al.*, 2005). In contrast, brain imaging studies have not revealed any differences in SERT binding in the brains of moderate ecstasy users (ecstasy users who had used a maximum of 50 tablets of ecstasy) or heavy ecstasy users who had been abstinent for 20 weeks or longer (Reneman *et al.*, 2001a; Reneman *et al.*, 2001b;

Buchert *et al.*, 2003; Thomasius *et al.*, 2003; Buchert *et al.*, 2004). Although only one study has employed a moderate ecstasy use group of participants (Reneman *et al.*, 2001b), the lack of differences in SERT binding between moderate ecstasy users, polydrug controls, and drug-naïve controls may indicate that a lower use of MDMA is not sufficient to cause neurotoxicity. Also, the lack of differences in SERT binding between polydrug controls, drug-naïve controls, and heavy ecstasy users who had been abstinent for 20 weeks or longer suggests that at least some recovery had taken place.

Serotonin is known to take part in the regulation of mood in humans. Many researchers have hypothesized that if recreational ecstasy use destroys 5-HT axons, then a corresponding decline in the mood of ecstasy users should be seen. Several studies have investigated this possibility through use of the Symptom Checklist 90 (SCL-90), the Symptom Checklist 90 Revised edition (SCL-90-R), or the Beck Depression Inventory (BDI). Eight out of ten studies that have used the SCL-90 or the SCL-90-R have not found significantly higher depression scores in ecstasy users in comparison to control participants (Parrott *et al.*, 2000; Daumann *et al.*, 2001; Dughiero *et al.*, 2001; Parrott *et al.*, 2001; Daumann *et al.*, 2004; Milani *et al.*, 2004; Halpern *et al.*, 2004; von Geusau, 2004). Interestingly, Morgan *et al.* (2002) initially found significantly higher SCL-90-R depression scores in current heavy ecstasy users in comparison to drug-naïve and polydrug controls,

but these differences were no longer significant after treating cannabis use as a covariate. Thomasius *et al.* (2003) found significantly higher depression scores in both current and former heavy ecstasy users (abstinent from ecstasy use for at least 20 weeks) in comparison to drug-naïve controls, but neither group of ecstasy users had significantly higher scores than polydrug controls. The evidence from studies that have used the BDI in measuring depression in ecstasy users has been somewhat mixed. MacInnes *et al.* (2001) found that heavy ecstasy users had significantly higher depression scores than drug-naïve controls. In contrast, Verkes *et al.* (2001) failed to find significantly higher depression scores in heavy ecstasy users in comparison to mostly drug-naïve controls. In another study, de Win *et al.* (2004) failed to find significantly higher depression scores in moderate or heavy ecstasy users in comparison to polydrug controls, but the researchers did find significantly higher scores in former heavy ecstasy users. Roiser and Sahakian (2004) found that both current and former heavy ecstasy users (abstinent from ecstasy use for at least 1 year) had significantly higher depression scores in comparison to drug-naïve controls, but neither group of ecstasy users had significantly higher scores than polydrug controls. Finally, de Almeida and Silva (2005) found that ecstasy users had significantly lower depression scores than polydrug controls. The BDI-II was constructed in order to match better the criteria for a major depressive episode as found in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Beck *et al.*, 1996). Although several studies have used the SCL-90, the SCL-90-R, or the BDI in measuring depression in ecstasy users, only one study has used the BDI-II (McCardle *et al.*, 2004). In this particular study, ecstasy users scored significantly higher on the BDI-II than mostly drug-naïve controls.

The purpose of the present study was to look at the relationship between recreational ecstasy use and depression. The BDI-II scores of ecstasy users were compared with those of ecstasy-naïve controls (participants who had never used ecstasy but who may have used other illicit substances). Also, the relationship between BDI-II scores and various conditions of ecstasy use (ecstasy total lifetime consumption, period of abstinence from ecstasy, and most ecstasy consumed within 12 hours) was examined. Finally, the presence of psychiatric disorders was examined in the ecstasy user group in order to determine if those disorders more commonly preceded or followed the initial use of ecstasy.

Method and materials

Participants

After obtaining approval from the Institutional Review Board of the University of Louisiana at Lafayette, 32 ecstasy users between the ages of 18 and 45 were recruited via word of mouth and the Internet. Information about the study was presented on an Internet forum centred in Louisiana (ravers.org). Contact was established through e-mail or telephone. Thirty-two ecstasy-naïve controls were recruited from introductory psychology classes at the university. Credits towards course completion were awarded for participation.

Materials

Every participant completed a personal history questionnaire, a drug use questionnaire (Roiser and Sahakian, 2004), the BDI-II (Beck *et al.*, 1996), and the Shipley Institute of Living Scale (Zachary, 1991). The personal history questionnaire investigated gender, age, psychiatric background, and current use of medications for depression. The drug use questionnaire asked all participants to report their total lifetime usage of a wide array of substances, and ecstasy users were asked specifically about period of abstinence from ecstasy and most ecstasy used in 12 hours. Much like its predecessor, the BDI-II is a self-report instrument that measures the presence and severity of depressive symptoms in adults and adolescents 13 years of age or older, and its reliability and validity have been supported by a number of studies (Beck *et al.*, 1996; Steer and Clark, 1997; Storch *et al.*, 2004). The Shipley Institute of Living Scale (SILS) is composed of a Vocabulary subtest and an Abstraction subtest, and it has received a great deal of empirical support as a valid and reliable test of general intelligence, or IQ (Zachary *et al.*, 1985; Weiss and Schell, 1991). It was designed for the purpose of assessing cognitive deterioration (Shipley, 1940). In theory, cognitive deterioration is likely to have a more noticeable effect on an individual's ability to reason abstractly, whereas the ability to recall learned information is not as likely to decline. Thus, the Vocabulary subtest was constructed as a measure of premorbid intelligence, and the Abstraction subtest was constructed as a measure of postimpairment capability.

Procedure

All participants read and were given a copy of the informed consent. The Shipley Institute of Living Scale was administered first, followed by the BDI-II, personal history questionnaire, and drug use questionnaire. Following the administration of the tests and questionnaires, all participants were given a copy of the debriefing form. Those being prescribed any anti-depressant medication as defined by the National Institute of Mental Health (2002) were excluded in order to ensure that psychotropic drugs taken specifically for the alleviation of depression did not influence results. Any participant who used ecstasy within the last week was excluded. This was done to control for any sub-acute effects of ecstasy use. Finally, anyone who reported illicit drug use on the day of testing was excluded.

Statistical analysis

A chi-square analysis was performed in order to assess whether gender differed between groups. Group comparisons were conducted using the nonparametric Wilcoxon rank sum test. Within the ecstasy user group, the nonparametric Pearson's rho was used to investigate relationships between ecstasy use variables (ecstasy lifetime consumption, period of abstinence from ecstasy, and most ecstasy consumed within 12 hours) and BDI-II scores.

Results

Group comparisons revealed that the ecstasy user and ecstasy-naïve groups did not differ significantly in terms of gender, SILS Vocabulary scores, SILS Abstraction scores, or current IQ. Ecstasy users were significantly older than non-users. Demographics as well as the medians, means and standard deviations of SILS subscores and IQ scores for each of the two groups are presented in Table 1.

Control participants were mostly free of illicit drugs, with only

eight participants admitting to some level of cannabis use. Ecstasy users reported significantly higher lifetime total drug use than controls for all drugs, including alcohol and nicotine. The ecstasy user group had used an average of 688 tablets of ecstasy, with individual lifetime totals ranging from 20 to 8760 tablets. Furthermore, 75% of ecstasy users reported a lifetime total of 100 or more tablets. The median for most ecstasy used in 12 hours was six tablets, and the average maximum dose in a 12 hour time period was approximately nine tablets of ecstasy. Medians, means and standard deviations of recreational drug use for each of the two groups are presented in Table 2.

BDI-II scores did not differ significantly between the ecstasy user and control groups. Furthermore, no significant correlations were found between any of the conditions of ecstasy use (ecstasy total lifetime consumption, period of abstinence from ecstasy, and most ecstasy consumed within 12 hours) and BDI-II scores. Medians, means and standard deviations of BDI-II scores for each of the two groups are presented in Table 3.

With regard to psychiatric diagnosis, 25% of ecstasy users indicated that they had been diagnosed with a psychiatric disorder (four with major depression, two with posttraumatic stress disorder, one with bipolar disorder, and 1 with generalized anxiety disorder). Out of this subset of eight ecstasy users, seven stated that they had been diagnosed with a psychiatric disorder before ever having taken ecstasy. The ecstasy user in this study who was diagnosed with major depression after having used ecstasy stated that he experienced depression as a direct result of a 4 month drug binge involving the use of large amounts of LSD, ecstasy, and heroin, and stated that he began this drug binge shortly after a death in the family.

Table 1 Demographics, SILS subscores, and IQ scores

	Ecstasy-naïve controls	Ecstasy users
<i>n</i>	32	32
Age (mean)	21.4 (4.5)	23.5 (5.6)*
Age (median)	20.0	22.0
Gender (M/F)	15/17	19/13
SILS Verbal (mean)	27.4 (4.2)	29.4 (5.1)
SILS Verbal (median)	26.0	30.0
SILS Abstraction (mean)	29.6 (5.5)	31.4 (6.7)
SILS Abstraction (median)	30.0	32.0
IQ (mean)	101.5 (8.9)	104.6 (11.2)
IQ (median)	101.0	105.5

Standard deviations are reported in parentheses next to each of the means.

* $p < 0.01$.

Table 2 Recreational drug use

	Ecstasy-naïve controls			Ecstasy users		
	<i>p</i>	Md	Mean	<i>p</i>	Md	Mean
Alcohol lifetime drinks	27	70	334 (605)	31	1040	3089 (4675)***
Nicotine lifetime cigarettes	13	0	2236 (6975)	28	14 235	27 037 (33 414)***
Cannabis lifetime joints	8	0	74 (282)	32	2190	3579 (4394)***
Cannabis last month joints		0	1 (4)		2	12 (26)***
Cannabis abstinence weeks		48	137 (263)		2	29 (59)*
Psilocybin lifetime uses	0	0	0	26	6	10 (14)***
Amphetamine lifetime grams	0	0	0	28	20	56 (92)***
LSD lifetime hits	0	0	0	29	14	107 (250)***
Ecstasy lifetime tabs	0	0	0	32	256	688 (1563)***
Ecstasy abstinence weeks	–	–	–		7	38 (70)
Most ecstasy in 12 hrs		0	0		6	9 (7)***
Amyl Nitrate lifetime hits	0	0	0	9	0	16 (57)**
Ketamine lifetime grams	0	0	0	17	1	9 (23)***
Cocaine lifetime grams	0	0	0	30	27	283 (823)***
Opiate lifetime grams	0	0	0	15	0	55 (294)***

For substance use variables, number of users is followed by the median (Md) and the mean. Standard deviations are reported in parentheses next to each of the means.

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

Table 3 BDI-II scores

	Ecstasy-naïve controls	Ecstasy users
Mean	10.3 (8.8)	10.3 (8.0)
Median	7.0	9.0

Standard deviations are reported in parentheses next to each of the means.

Discussion

In the current study, ecstasy users were compared to a group of mostly drug-naïve college students. Both groups completed the SILS, the BDI-II, a personal history questionnaire, and a drug use questionnaire. Gender and age were similar across groups. Ecstasy users were significantly older than non-users. However, the mean difference in age between groups was only 2.1 years. While studies suggest that adolescents and the elderly may score higher than young and middle-aged adults on the BDI (Beck *et al.*, 1988), the age of participants in the current study all fell in the normal adult range from 18 to 43. Intelligence was similar between the two groups, and there was no evidence for cognitive deterioration in the ecstasy user group. No differences in depression scores were found between the two groups.

All of the ecstasy users in the current study reported frequent past or present ecstasy use. The average lifetime total use was about 700 tablets of ecstasy, with 75% of users reporting that they had used at least 100 tablets. Approximately 60% of ecstasy users had consumed a maximum of six or more tablets of ecstasy in a 12 hour time period. Cole *et al.* (2002) noted that the average dose of MDMA found in samples obtained from drug seizures in the UK from 1991 to 2001 ranged from as high as approximately 100 mg to as low as approximately 70 mg. Assuming that these tablets contained an average of 70 to 100 mg of MDMA, six tablets of ecstasy would amount to a 420 to 600 mg dose of MDMA in a 12 hour time period. Such a dose would be at least equal to a 5 mg/kg dose of MDMA for a person weighing 84 kg (185 lbs) or less. A single oral dose of 5 mg/kg of MDMA has been shown to significantly reduce 5-HT content in the brains of squirrel monkeys as measured 2 weeks later (Ricaurte *et al.*, 1988). If humans are as sensitive to the neurotoxic effects of MDMA, then it is possible that many users in this study caused damage to their serotonin pathways as a result of their ecstasy use. In light of this, one may wonder why ecstasy users failed to display higher depression scores than ecstasy-naïve controls. Depression is a complex construct and involves more than serotonin functioning alone. Accordingly, the level of 5-HT neurotoxicity possibly experienced by the ecstasy users may not have been sufficient to cause decrements in mood. Another potential explanation is that the negative effects of 5-HT neurotoxicity may have been offset by long-term positive effects of MDMA on mood. Some researchers have indicated that some ecstasy users have reported long-lasting improvements in self-awareness, self-esteem, openness in communication,

and insight into personal problems (Greer and Tolbert, 1986; Grinspoon and Bakalar, 1986; Verheyden *et al.*, 2003). Finally, there may be differences in mood between ecstasy users and non-users, but limitations of verbal self-report data may limit the sensitivity of the BDI-II. Of course, the viability of these potential explanations await further research.

Reviewing the literature suggests that ecstasy users tend to score somewhat higher than control participants on tests of depression. However, mean scores tend to be not much higher than mean scores for college students and the general population (Rizley, 1978; Dobson and Breiter, 1983; Gotlib, 1984; Robbins and Tanck, 1984; Lightfoot and Oliver, 1985; Baron and Hanna, 1990; Robinson *et al.*, 1990; Beck *et al.*, 1996; Steer and Clark, 1997; Whisman and Perez, 2000; Al-Musawi and Nu'man, 2001; Dozois, 2003; Storch *et al.*, 2004). In accord with previous studies, the ecstasy user and ecstasy-naïve college student groups in the present study each had a mean score of about ten on the BDI-II. Interestingly, Falck *et al.* (2006) also found a mean BDI-II score of about ten in a large sample ($n = 402$) of ecstasy users. In relation to these findings, Sumnall and Cole (2005) determined that the average depression scores of ecstasy users have not been clinically meaningful in any of the studies that have used the SCL-90, SCL-90-R, or BDI.

Of the ecstasy users in the current study, 25% reported being diagnosed with a psychiatric disorder, with 88% of that subset stating that they were diagnosed before ever having taken ecstasy. Looking at mood disorders alone, 16% of ecstasy users reported having been diagnosed with either major depression or bipolar disorder, with 80% of that subset stating that they had been diagnosed before ever having taken ecstasy. These percentages are roughly comparable to those reported in the study by de Win *et al.* (2004) in which 32% of ecstasy users were diagnosed with a mood disorder at some point in their lives, with 71% reporting that their mood disorder preceded their first use of ecstasy. Also consistent with results of the current study, Lieb *et al.* (2002) found that 88% of ecstasy users diagnosed with a mental disorder reported the onset of the mental disorder as previous to their first use of ecstasy. In regard to mood disorders alone, Lieb *et al.* noted that 53% of those diagnosed reported the onset of the mood disorder as being previous to their first use of ecstasy. Furthermore, Lieb *et al.* followed up on individuals who had not used ecstasy by the time of the initial point of assessment, and they found that those who had been diagnosed with a mental disorder previously were nearly twice as likely to have used ecstasy 3 to 4 years later. The evidence that is currently available seems to indicate that ecstasy users who have received a psychiatric diagnosis are likely to display mental health symptoms prior to using ecstasy. Unfortunately, the current study cannot compare the frequency of psychiatric diagnosis in college students with that of ecstasy users since only ecstasy users were asked about their past psychiatric history.

One limitation to the present study, as well as others of a similar research design, is that retrospective studies rely on self-reports of drug use, which may be inaccurate due to imperfect memory or dishonesty. Urine analysis could have disconfirmed recent ecstasy use but was not utilized in this study. Second, ecstasy consumption is not completely synonymous with MDMA

consumption. ecstasy tablets vary in content, and both the purity and typical dose of MDMA found within ecstasy tablets have been debated (Cole *et al.*, 2002; Parrott, 2004). This allows for the possibility that the ecstasy users in the current study were sold substances being passed off as MDMA that are less detrimental to mood.

In summary, the levels of depression in a group of heavy ecstasy users were not found to be significantly different from those in college students. This is consistent with previous research, which has indicated that ecstasy users and college students score about the same on tests of depression. Also consistent with previous research, ecstasy users in the current study reported that major depression and other psychological disorders were more likely to precede ecstasy use. While MDMA-induced neurotoxicity is an important area of study, the results of this study suggest that, on average, levels of depression found in ecstasy users are not clinically meaningful as measured by the BDI-II.

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