

Past 12-month and lifetime comorbidity and poly-drug use of ecstasy users among young adults in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions

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Abstract

Background: Ecstasy use is prevalent among young people and often co-occurs with other drug use, but little is known about the past 12-month and lifetime psychiatric comorbidity and specific additional drug abuse among young adult ecstasy users in the general population. To provide this information, we compared current ecstasy users to former users, other illicit drug users, and non-illicit drug users.

Method: Data were gathered in a face-to-face survey of the United States conducted in the 2001–2002 (NESARC). Participants were household and group quarters residents aged 18–29 years ($n = 8666$). We measured current ecstasy use defined as any use in the past year; former ecstasy use as use prior to the past year only; other lifetime drug use included any drug other than ecstasy; lifetime non-illicit drug use as no illicit drug use. Associations were determined for nine other classes of illicit drugs, eight personality disorders, and seven mood and anxiety disorders.

Results: Of current ecstasy users, 44% used >3 other classes of illicit drugs in the past year, compared to 1.6% of non-ecstasy drug users. Current ecstasy use was associated with current anxiety (OR = 3.7), specifically panic disorder (OR = 7.7) and specific phobia (OR = 4.1), also alcohol abuse (OR = 21.6) and dependence (OR = 4.1) and any personality disorder (OR = 5.1) compared to non-illicit drug users.

Conclusions: Results indicate important differences in comorbidities of current and former ecstasy users compared to other drug users and lifetime non-illicit drug users that may affect phenotype definitions and etiologic studies. Ecstasy use may represent a distinct population of drug users for which unique treatments may be necessary.

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1. Introduction

Since emerging onto the illicit drug landscape in the 1980s, ecstasy (3,4-methylenedioxy-*N*-methyl-amphetamin, MDMA) has become endemic in the population of drug users, especially among young adults. Ecstasy use has increased among young people over the past decade in the U.S., peaking in 2001 (Johnston et al., 2007a; Landry, 2002; Martins et al.,

2005). Estimates of the current (past-year) prevalence of ecstasy use among young adults in the U.S. and abroad range from 3% to 6%, with lifetime estimates around 10% (Degenhardt et al., 2004; Johnston et al., 2007b; von Sydow et al., 2002; Wu et al., 2006). While initially perceived as relatively harmless (Downing, 1986), there is now a wide literature indicating the harmful physiological and psychological after-effects of ecstasy use (Substance Abuse and Mental Health Services Administration, 2002). Short- and long-term psychiatric consequences and correlates of ecstasy use remain understudied in the general population.

The active ingredient in ecstasy pills, MDMA, has been shown to have effects similar to both hallucinogens and

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amphetamines, in terms of rewarding effects as well as unpleasant side effects and after-effects of use (Burgess et al., 2000; Dumont and Verkes, 2006; Parrott, 2006). Besides physical symptoms, studies have indicated that the post-acute effects of ecstasy use can include symptoms of depression, anxiety, anhedonia, insomnia, and appetite disturbance (Verheyden et al., 2003a). Long-term consequences of ecstasy use have not been firmly established in human studies (Burgess et al., 2000; Thomasius et al., 2006), although animal studies indicate that ecstasy may lead to long-term increases in anxiety and social behavior deficits (Clemens et al., 2005; Clemens et al., 2007).

Epidemiological and behavioral research on ecstasy users have mainly focused on small populations (e.g. “rave” cultures) in urban settings (Fendrich et al., 2003; Gross et al., 2002). While symptoms of depression and anxiety following ecstasy use have been reported in most but not all of these selected small samples (Thomasius et al., 2005), little has been done to establish the extent to which ecstasy use in the general population is comorbid with other psychiatric disorders, as defined by DSM-IV (American Psychiatric Association, 1994). The most comprehensive study to date, the Early Developmental Stages of Psychopathology (EDSP) Study in Germany, found that young adult ecstasy and related (i.e. amphetamine, stimulant) users were more likely to exhibit major depressive disorder, panic attacks, phobia, and generalized anxiety disorder, compared with other illicit drug users (Lieb et al., 2002). However, the sample was drawn in 1994 in Munich and combined ecstasy users with other amphetamine and stimulant users; whether these results generalize to young adults in the U.S. sampled recently and specifically having used ecstasy is unknown. Further, no study to our knowledge has compared the prevalence of Axis II disorders among individuals who have and have not used ecstasy. The association between ecstasy use and Axis II disorders is important to establish because Axis II disorders increase the likelihood of incident drug use (Degenhardt et al., 2007) and a more chronic course of drug use disorders (Compton et al., 2003; Dawson et al., 2005). Thus, the specific sets of comorbidities common among ecstasy users may have implications for treatment and intervention development.

In addition to increased psychiatric symptoms associated with ecstasy use, epidemiologic evidence indicates that ecstasy use rarely occurs in isolation from other drugs (Gross et al., 2002; Martins et al., 2005; Scholey et al., 2004; Wu et al., 2006). The specific drugs commonly used by ecstasy users in the general population, however, are understudied. This is important for both treatment and policy, as the toxicity of poly-drug use can increase due to drug interactions (Parrott, 2006). Data from the National Household Survey of Drug Use and Health indicated that almost all ecstasy users (>98%) also use alcohol and marijuana, but there may also be an excess of binge drinking, cocaine, stimulant, and pain reliever use among ecstasy using groups (Martins et al., 2005; Wu et al., 2006). Information about current patterns of drug use among former ecstasy users is additionally important to understand how poly-drug use in ecstasy users evolves after the cessation of ecstasy use.

This study aims to add to the literature on the specific current and lifetime comorbidities and poly-drug use profiles of

ecstasy users in the general population by utilizing a large, nationally representative sample of young adults assessed for a wide range of DSM-IV Axis I and Axis II disorders. Further, because ecstasy use has been associated with poly-drug use in previous studies, we compared ecstasy users to all other users of illicit drugs that did not use ecstasy to determine if there were characteristics that differentiated ecstasy users from illicit drug users in general. Specifically, we: (1) estimated current and lifetime rates of use of other substances among current and past ecstasy users and other illicit drug users, including alcohol use and binge drinking; (2) compared the prevalence of lifetime and past-year DSM-IV Axis I and Axis II disorders (American Psychiatric Association, 1994) between current (last 12 months) ecstasy users, past ecstasy users, illicit drug users that never used ecstasy, and lifetime non-illicit drug users. Adults aged 18–29 were assessed in this sample as this age group has the highest prevalence of ecstasy use, even when compared to adolescents (Martins et al., 2005; Wu et al., 2006).

2. Methods

2.1. Sample

Data were drawn from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative United States survey of civilian non-institutionalized participants aged 18 and older, sampled cross-sectionally and interviewed in person. Details of the sampling frame are described elsewhere (Grant et al., 2003a, 2004a,b). The National Institute on Alcohol Abuse and Alcoholism (NIAAA) sponsored the study and supervised the fieldwork, conducted by the U.S. Bureau of the Census. Details of interviewing, training, and field quality control can be found elsewhere (Grant et al., 2003b). Young adults, Hispanics, and African-Americans were oversampled, and rates were weighted to the 2000 decennial census in terms of age, race, sex, and ethnicity and were further weighted to adjust for sampling probabilities. The study achieved an overall response rate of 81%.

The present analysis includes the subset of the sample aged 18–29 ($N=8666$). In the NESARC, 90.3% (S.E. = 3.6) of current ecstasy users were aged 18–29; thus, restricting the sample to this age group reduced potential confounding due to age in our analyses. Of the 8666, 49.8% was male. Whites comprised 61.3% of the sample, African-Americans, 13.1%, Hispanics, 18.1%, Asian or Pacific Islander, 5.6%, and American Indians and Alaska Natives, 1.9%.

2.2. Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV; Grant et al., 2001), a state-of-the-art structured diagnostic interview, was administered to the NESARC participants using computer-assisted software with built-in skip, logic, and consistency checks. This instrument was specifically designed for experienced lay interviewers and was developed to advance measurement of substance use and mental disorders in large-scale surveys.

2.2.1. Ecstasy and other drug use. The sample was divided into four mutually exclusive groups corresponding to the four categories we analyzed: current ecstasy users (i.e. respondents who reported using ecstasy in the past 12 months, $n=116$), lifetime but not current ecstasy users (i.e. respondents who reported ever using ecstasy, but reported no ecstasy use in the past 12 months, $n=242$), lifetime users of any other illicit drugs but not ecstasy ($n=2028$), and lifetime non-illicit drug users ($n=6280$). Lifetime non-ecstasy illicit drug users combine current and former users; this group was chosen to serve as a general reference to the ecstasy groups but is not compared specifically to current and former ecstasy users. The lifetime non-illicit drug use group includes but is not limited to alcohol and tobacco users. Use of ten specific drug classes was assessed in the

Table 1

Demographic characteristics of current ecstasy users, former ecstasy users, non-ecstasy lifetime illicit drug users, and lifetime never illicit drug users, NESARC 2001–2002

	Current ecstasy users (<i>N</i> = 116), % (S.E.) ^a	Former ecstasy users (<i>N</i> = 242), % (S.E.) ^a	Any other illicit drug users (<i>N</i> = 2028), % (S.E.) ^a	Never drug users (<i>N</i> = 6280), % (S.E.) ^a	<i>p</i> -Value (chi square test)
Sex					
Male	65.8 (4.7)	60.8 (3.5)	54.8 (1.2)	47.2 (0.8)	***
Female	34.2 (4.7)	39.2 (3.5)	45.2 (1.2)	52.8 (0.8)	
Race/ethnicity					
White	76.6 (4.5)	80.1 (3.0)	68.8 (2.1)	57.5 (2.1)	***
Black	4.2 (1.7)	2.1 (0.8)	11.6 (1.0)	14.4 (0.9)	
Hispanic	12.0 (3.0)	9.1 (1.9)	13.5 (1.6)	20.3 (1.9)	
Other	7.3 (3.2)	8.7 (2.2)	6.2 (0.8)	7.9 (0.9)	
Education					
Less than HS	13.3 (3.3)	13.2 (2.5)	14.6 (0.9)	16.0 (0.8)	NS
HS	41.6 (6.1)	25.1 (3.6)	28.8 (1.4)	29.4 (0.8)	
At least some college	45.1 (5.4)	61.7 (4.2)	56.6 (1.5)	54.7 (0.9)	
Marital status					
Married/cohabit	12.8 (4.0)	30.5 (3.4)	34.1 (1.3)	37.4 (0.9)	***
Widow/divorce/sep	3.8 (1.6)	5.4 (2.4)	4.6 (0.6)	3.3 (0.3)	
Never married	83.5 (4.2)	64.1 (3.9)	61.3 (1.4)	59.3 (0.9)	
Personal income					
\$0–19,999	50.7 (5.7)	26.7 (3.5)	34.2 (1.4)	33.2 (0.9)	***
\$20,000–34,999	15.4 (3.7)	24.1 (3.3)	22.9 (1.1)	22.2 (0.6)	
\$35,000–69,999	17.0 (4.3)	32.3 (3.6)	28.1 (1.2)	30.1 (0.7)	
\$70,000 or more	16.9 (4.5)	16.9 (2.8)	14.9 (1.3)	14.5 (0.8)	
Urbanicity					
Urban	88.5 (3.7)	88.8 (3.0)	81.4 (2.0)	82.4 (1.6)	NS
Rural/other	11.5 (3.7)	11.2 (3.0)	18.6 (2.0)	17.6 (1.6)	
Region					
Northeast	22.3 (6.1)	26.1 (5.3)	15.4 (2.9)	18.6 (3.8)	***
Midwest	15.0 (4.4)	13.4 (3.2)	27.9 (3.6)	22.3 (3.4)	
South	33.6 (6.2)	30.4 (5.0)	30.1 (3.2)	37.5 (3.8)	
West	29.2 (6.6)	30.2 (5.6)	26.6 (4.0)	21.6 (4.0)	
Current insurance status					
Private insurance	55.2 (5.4)	57.3 (3.7)	57.8 (1.4)	57.7 (1.3)	NS
Medicaid	3.2 (1.7)	5.1 (1.4)	7.1 (0.8)	6.8 (0.5)	
Medicare or veterans	5.0 (2.5)	1.5 (0.8)	2.7 (0.4)	3.4 (0.4)	
None	36.6 (5.1)	36.1 (3.8)	32.3 (1.3)	32.0 (1.2)	

NS, not significant.

^a S.E. refers to standard error.*** *p* < 0.001.

AUDADIS-IV. Respondents were given common examples of each class of drug; lifetime use of the drug was first established, and past-year use was subsequently established. Specific questions were included in the AUDADIS-IV to establish ecstasy use. Respondents were first asked about lifetime use of any hallucinogen; ecstasy was given as an example of a hallucinogen. Those respondents with a lifetime report of any hallucinogen use were asked specific separate questions about lifetime ecstasy use (*N* = 358) and past-year ecstasy use (*N* = 116).

2.2.2. *Axis I and Axis II disorders.* Alcohol abuse and dependence diagnoses were made according to DSM-IV (American Psychiatric Association, 1994). The reliability and validity of alcohol dependence diagnosis has been extensively documented in the U.S. and abroad (Hasin et al., 2007). Mood disorders included DSM-IV primary major depressive disorder (MDD), bipolar I, bipolar II, and dysthymia. Anxiety disorders included DSM-IV primary panic disorder with and without agoraphobia, social and specific phobias and generalized anxiety disorder. Diagnostic methods used in the AUDADIS-IV are described in detail elsewhere (Grant et al., 2004a, 2005; Hasin et al., 2005). In DSM-IV, “primary” excludes substance-induced disorders or those due to medical conditions; specific AUDADIS questions about the chronological relationship between

intoxication or withdrawal and the full psychiatric syndrome implement DSM-IV criteria differentiating primary from substance-induced disorders. MDD diagnoses also ruled out bereavement. Personality disorders (PDs), assessed on a lifetime basis, included DSM-IV avoidant, dependent, obsessive-compulsive, paranoid, schizoid, and antisocial personality disorders (APD). DSM-IV PD diagnoses require long-term patterns of social/occupational impairment and exclusion of substance-induced cases; AUDADIS-IV PD diagnoses were made accordingly (Compton et al., 2005; Grant et al., 2004b, 2005).

Test–retest reliability for AUDADIS-IV mood, anxiety, and personality diagnoses in general population and clinical settings was good to fair (0.40–0.62) (Grant et al., 1995, 2003b; Hasin et al., 1997). Test–retest reliabilities of AUDADIS-IV personality disorders (not measured in prior surveys) compare favorably with those in patient samples using semi-structured personality interviews (Grant et al., 2004b).

2.2.3. *Socio-demographic variables.* We examined the following potential correlates of ecstasy use for inclusion as control variables: gender, race/ethnicity, education, marital status, personal income, urbanicity, region, and current insurance status (see Table 1).

Table 2
Poly-drug use of, former and current ecstasy users, as well as non-ecstasy lifetime illicit drug users, NESARC 2001–2002

	Current ecstasy users (N = 116), % (S.E.) ^a	Former ecstasy users (N = 242), % (S.E.) ^a	Any other illicit drug users (N = 2028), % (S.E.) ^a	p-Value (chi-square test)
Past-year use of				
Any alcohol	98.4 (1.3)	95.4 (1.4)	90.3 (0.8)	***
Binge drinking ^b	62.3 (5.9)	45.2 (4.2)	29.1 (1.3)	***
Sedatives	23.5 (5.0)	16.0 (3.0)	5.2 (0.6)	***
Tranquilizers	34.2 (5.1)	10.0 (2.1)	4.6 (0.6)	***
Opioids	33.8 (4.9)	21.9 (3.0)	11.1 (1.0)	***
Amphetamines	20.6 (4.4)	9.1 (1.9)	2.7 (0.4)	***
Cannabis	85.6 (3.7)	47.1 (4.2)	31.5 (1.2)	***
Cocaine	38.1 (5.0)	10.1 (2.3)	1.8 (0.4)	***
Inhalants	12.9 (3.8)	3.2 (1.2)	0.6 (0.2)	**
Heroin	3.4 (2.5)	0.6 (0.5)	0.1 (0.1)	NS
Other	1.5 (1.5)	0.0 (0.0)	0.1 (0.0)	NS
More than one illicit drug	91.3 (3.0)	32.3 (3.7)	11.1 (0.8)	***
More than two illicit drugs	66.5 (5.1)	17.3 (2.9)	4.5 (0.6)	***
More than three illicit drugs	44.3 (5.7)	9.7 (2.2)	1.6 (0.3)	***
Lifetime use of				
Any alcohol	98.8 (1.2)	99.3 (0.5)	97.2 (0.4)	***
Binge drinking ^b	89.2 (3.2)	86.4 (2.4)	72.9 (1.2)	***
Sedatives	36.5 (6.2)	35.8 (3.7)	12.0 (1.0)	***
Tranquilizers	44.3 (5.8)	33.7 (3.3)	11.8 (1.0)	***
Opioids	45.7 (5.8)	45.1 (4.0)	21.2 (1.2)	***
Amphetamines	32.7 (5.3)	37.2 (3.9)	11.0 (0.9)	***
Cannabis	97.7 (1.6)	97.6 (1.0)	90.5 (0.8)	***
Cocaine	52.6 (5.1)	54.0 (4.3)	11.7 (0.9)	***
Inhalants	26.4 (5.5)	25.4 (3.3)	6.9 (0.7)	***
Heroin	5.0 (2.7)	3.8 (1.4)	0.3 (0.1)	**
Other	1.5 (1.5)	4.2 (1.7)	0.4 (0.2)	**
More than one illicit drug	97.9 (1.6)	98.9 (0.7)	37.7 (1.4)	***
More than two illicit drugs	78.2 (4.6)	77.4 (3.4)	19.5 (1.2)	***
More than three illicit drugs	58.5 (5.5)	59.4 (3.9)	12.0 (1.0)	***

NS, not significant.

^a S.E. refers to standard error.

^b Any instance of 5+ drinks for men or 4+ drinks for women.

*** $p < 0.0001$.

** $p < 0.01$

2.3. Statistical analysis

Four groups were established for the present analysis: current ecstasy users ($N = 116$), former ecstasy users ($N = 242$), lifetime non-ecstasy illicit drug users ($N = 2028$), and lifetime non-illicit drug users ($N = 6280$). Associations between these four groups and demographics (Table 1) and poly-drug use (Table 2) were established with cross tabulation; chi-square tests were used to test statistical significance (at $\alpha < 0.01$ level). To establish the associations with psychiatric disorders, drug use group (4-level) was used as the main predictor and the binary outcome of psychiatric disorder was used as the outcome (Table 3), independent mood and anxiety disorders, and Table 4, personality disorders). Logistic regressions were performed controlling for sex, race/ethnicity, marital status, family income, and urbanicity (99% confidence intervals estimated to account for multiple testing). To adjust for the complex sample design of the NESARC all analysis were conducted using SUDAAN (Research Triangle Institute, 2004).

3. Results

3.1. Demographic characteristics

Lifetime ecstasy use is associated with being male ($\chi^2 = 35.9$, d.f. = 3, $p < 0.01$), White ($\chi^2 = 58.6$, d.f. = 9, $p < 0.01$), and from

the Northeast ($\chi^2 = 46.2$, d.f. = 9, $p < 0.01$) (see Table 1). Current ecstasy use is associated with being never married ($\chi^2 = 28.2$, d.f. = 6, $p < 0.01$) and being in the lowest income category ($\chi^2 = 33.8$, d.f. = 9, $p < 0.01$).

3.2. Current use of other substances

Almost all respondents drank at least one drink in the past year, with current ecstasy users most likely to both drink any alcohol and binge drink in the past year (see Table 2). Among current ecstasy users, 91.3% used at least one additional illicit drug (other than ecstasy) in the past year, 66.5% used at least two additional drugs, and 44.3% used at least three additional drugs in the past year (Table 2). Among former ecstasy users, 32.3% used more than one additional drug in the past year, and 11.1% of non-ecstasy drug users have used more than one additional drug in the past year. Among former ecstasy and lifetime non-ecstasy illicit drug users, 57.5% and 41.6% (respectively) used one or more illicit drugs in the past year ($p < 0.01$ for the difference in proportion). The most commonly used drug in the past year

was cannabis, followed by cocaine and tranquilizers for current ecstasy users, and opioids for former ecstasy users and other drug users.

3.3. Lifetime use of other substances

Current ecstasy users were the group most likely to use alcohol and binge drink in their lifetime compared to other groups (Table 2). Among the illicit drugs, cannabis was the most commonly used among current ecstasy users, followed by cocaine and tranquilizers. Among former ecstasy users and other drug users, cannabis was most likely to be used on a lifetime basis, followed by opiates. The proportion of current and former ecstasy users using two or more additional drugs (78.2% vs. 77.4%) or three or more additional drugs (58.5% vs. 59.4%) was similar and much higher than other illicit drug users.

3.4. Comorbid psychiatric disorders

3.4.1. Current Axis I disorders. Table 3 shows the likelihood of each Axis I disorder based on drug use status. Current ecstasy users were likely to have a current anxiety disorder (OR = 3.7), specifically panic disorder (OR = 7.7) and specific phobia (OR = 4.1) than non-illicit drug users. Additionally, current ecstasy use was strongly associated with having a current alcohol disorder (OR = 22.6) compared to lifetime non-illicit drug users; specifically, current ecstasy use was strongly associated with alcohol abuse (OR = 21.6).

In contrast to current ecstasy use, former use was associated with having a current mood disorder (OR = 3.5) and having current major depression (OR = 2.6), as compared to non-illicit drug users.

Lifetime non-ecstasy drug use was associated with all measured current Axis I disorders compared to non-illicit drug users. Further, lifetime non-ecstasy drug use was the only drug class associated with current mania (OR = 1.6).

3.4.2. Lifetime Axis I disorders. For current and former ecstasy users, associations with lifetime Axis I disorders were generally similar to the results for current disorders (Table 4), save that current ecstasy use was not associated with lifetime dysthymia and former ecstasy use was not associated with lifetime generalized anxiety disorder. Non-ecstasy drug use was associated with every lifetime Axis I disorder measured, compared to non-illicit drug users.

3.4.3. Axis II disorders. Current and former ecstasy users had higher odds of any personality disorder, specifically antisocial and paranoid personality disorders, compared to non-illicit drug users (Table 5). Current ecstasy users also had higher odds of histrionic personality disorder (OR = 6.4) and schizoid personality disorder (OR = 3.4) as compared to non-illicit drug users. Non-ecstasy drug use was significantly associated with every measured personality disorder compared to non-illicit drug users (Table 5).

4. Discussion

Results indicated that poly-drug use was ubiquitous among current and former ecstasy users, especially cannabis, cocaine, tranquilizers, and opiates. Both current and former ecstasy users had a higher rate of poly-drug use compared to non-ecstasy illicit drug users. Current ecstasy use was most strongly related to current panic disorder and specific phobia but unrelated to depression, whereas former ecstasy use had higher current and lifetime prevalence of major depression compared to never drug users. Further, there is a strong relationship between current ecstasy use and alcohol disorders, especially alcohol abuse. Finally, both current and former ecstasy use is associated with some Axis II disorders compared to non-illicit drug users, including anti-social personality, histrionic, and paranoid personality disorders. Non-ecstasy drug users, by contrast, had a higher prevalence of every measured Axis I and Axis II disorder (save for dependent personality disorders) compared to non-illicit drug users.

Overall, these findings suggest that while illicit drug users generally have higher risk of all psychopathology, current and former ecstasy users may have different current and lifetime comorbidities than other drug users. Our findings generally concur with those of Lieb et al. (2002) in showing a higher prevalence of panic and phobia among current ecstasy users, despite differences in the exposure definition across study (i.e., ecstasy or related substances in the Lieb et al., 2002 analysis). Additionally, our finding that former ecstasy users had a high prevalence of current major depression (whereas there is no difference between current ecstasy users and lifetime non-users in the prevalence of current major depression) may be indicative of long-term adverse effects of ecstasy use. Laboratory studies have indicated that psychological well-being may be impaired and depressive symptoms reported up to 2.5 years after the cessation of heavy ecstasy use (De Win et al., 2004; Gerra et al., 2000; MacInnes et al., 2001; Thomasius et al., 2003, 2005; Verheyden et al., 2003b). However, our finding that the prevalence of depression is not elevated in current ecstasy users warrants further investigation into a possible delayed effect of ecstasy on a full-spectrum depression diagnosis. While studies generally concur that in the short-term, ecstasy users experience symptoms of depression (Parrott, 2006), it is possible that the development of a clinically relevant depression diagnosis may develop over a longer period of time. Further, the high comorbidity across psychiatric diagnoses limits the ability to tease apart effects due to ecstasy use from effects due to use of other substances and psychiatric diagnoses. Longitudinal studies will be able to better test hypotheses about the relationship between depression and ecstasy use in the general population.

Comorbid personality disorders often predict less successful treatment and a more chronic course of substance abuse/dependence (Compton et al., 2003; Dawson et al., 2005). Therefore, the associations between personality disorders and drug use, and the personality disorders unique to ecstasy use, are important indicators that may be useful to develop more effective treatments. Additionally, the prevalence of lifetime treatment-seeking among ecstasy users was higher than the general

Table 3
Prevalence and odds of current DSM-IV Axis I disorders comparing current ecstasy users, former ecstasy users, and other illicit drug users to lifetime non-illicit drug users, NESARC 2001–2002

	Mood disorders									
	Any mood disorder		Major depression		Dysthymia		Mania or hypomania			
	% (S.E.) ^a	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (<i>N</i> = 116)	14.7 (3.4)	1.4 (0.7–2.9)	6.0 (6.0)	1.2 (0.4–3.4)	4.6 (4.6)	4.2 (1.2–15.7)	1.3 (1.3)	0.4 (0.1–2.2)		
Former ecstasy users (<i>N</i> = 242)	27.8 (3.3)	3.5 (2.2–5.5)	11.3 (2.5)	2.6 (1.3–5.2)	3.8 (1.3)	4.0 (1.3–12.2)	3.8 (1.3)	1.4 (0.5–3.7)		
Any other illicit drug users (<i>N</i> = 2028)	21.6 (1.2)	2.4 (1.9–3.0)	10.6 (0.9)	2.4 (1.8–3.3)	3.3 (0.5)	3.10 (1.7–5.5)	4.9 (0.5)	1.6 (1.1–2.4)		
Never drug users (<i>N</i> = 6280)	10.4 (0.5)	1.0	5.0 (0.3)	1.0	1.1 (0.2)	1.0	2.8 (0.3)	1.0		
	Anxiety disorders									
	Any anxiety disorder		Panic disorder		Social phobia		Specific phobia		Generalized anxiety disorder	
	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (<i>N</i> = 116)	24.2 (24.2)	3.7 (1.8–7.5)	7.9 (7.9)	7.7 (2.5–23.9)	3.9 (3.9)	2.1 (0.6–7.8)	19.1 (19.1)	4.1 (1.8–9.4)	3.2 (3.2)	2.7 (0.7–10.2)
Former ecstasy users (<i>N</i> = 242)	19.1 (3.0)	2.5 (1.4–4.6)	7.8 (1.8)	7.6 (3.4–17.1)	4.9 (1.4)	2.8 (1.1–6.7)	11.2 (2.5)	2.0 (1.0–4.3)	4.4 (1.4)	3.6 (1.3–9.8)
Any other drug users (<i>N</i> = 2028)	18.1 (1.1)	2.2 (1.7–2.8)	4.1 (0.5)	3.4 (2.0–5.8)	5.6 (0.6)	2.7 (1.8–4.0)	11.5 (1.0)	1.9 (1.4–2.6)	3.7 (0.5)	2.8 (1.7–4.6)
Never drug users (<i>N</i> = 6280)	9.5 (0.6)	1.0	1.3 (0.2)	1.0	2.1 (0.2)	1.0	6.4 (0.5)	1.0	1.3 (0.2)	1.0
	Alcohol disorders									
	Any alcohol use disorder		Alcohol abuse		Alcohol dependence					
	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (<i>N</i> = 116)	69.5 (69.5)	22.6 (11.5–44.3)	52.7 (52.7)	21.6 (10.7–43.6)	16.7 (16.7)	4.1 (1.8–9.4)				
Former ecstasy users (<i>N</i> = 242)	47.6 (4.1)	9.3 (5.6–15.2)	28.0 (3.5)	8.4 (5.2–13.7)	19.6 (3.1)	4.7 (2.6–8.5)				
Any other illicit drug users (<i>N</i> = 2028)	31.3 (1.3)	4.8 (3.8–6.0)	19.0 (1.2)	5.1 (3.9–6.8)	12.3 (0.8)	2.9 (2.2–3.9)				
Never drug users (<i>N</i> = 6280)	8.4 (0.5)	1.0	4.1 (0.3)	1.0	4.3 (0.4)	1.0				

^a S.E. refers to standard error.

^b Odds ratio adjusted for sex, race/ethnicity, marital status, personal income, urbanicity, and region.

Table 4
Prevalence and odds of lifetime DSM-IV Axis I disorders comparing current ecstasy users, former ecstasy users, and other illicit drug users to lifetime non-illicit drug users, NESARC 2001–2002

	Mood disorders									
	Any mood disorder		Major depression		Dysthymia		Mania or hypomania		Bipolar	
	% (S.E.) ^a	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (<i>N</i> = 116)	22.8 (4.2)	1.4 (0.7–2.7)	8.2 (2.6)	0.8 (0.3–2.2)	5.8 (2.2)	3.0 (1.0–9.3)	5.5 (2.2)	1.2 (0.4–3.6)	10.1 (3.2)	1.3 (0.8–5.0)
Former ecstasy users (<i>N</i> = 242)	42.1 (4.0)	3.6 (2.3–5.8)	18.6 (2.9)	2.2 (1.3–3.8)	6.2 (1.6)	3.5 (1.5–8.3)	9.1 (2.2)	2.1 (1.0–4.4)	18.1 (2.9)	2.5 (1.6–5.9)
Any other illicit drug users (<i>N</i> = 2028)	34.5 (1.5)	2.6 (2.1–3.2)	18.3 (1.1)	2.2 (1.7–2.8)	6.9 (0.7)	3.7 (2.4–5.6)	8.7 (0.7)	2.0 (1.4–2.7)	12.7 (0.9)	1.9 (1.3–3.1)
Never drug users (<i>N</i> = 6280)	17.1 (0.8)	1.0	9.6 (0.5)	1.0	2.0 (0.2)	1.0	4.3 (0.3)	1.0	4.8 (0.4)	1.0
	Anxiety disorders									
	Any anxiety disorder		Panic disorder		Social phobia		Specific phobia		Generalized anxiety disorder	
	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (<i>N</i> = 116)	25.3 (4.9)	2.7 (1.3–5.4)	9.0 (3.1)	4.2 (1.4–12.1)	4.5 (1.9)	1.3 (0.4–4.2)	19.9 (4.7)	3.5 (1.6–7.9)	3.2 (1.6)	1.6 (0.4–6.1)
Former ecstasy users (<i>N</i> = 242)	26.6 (3.5)	2.6 (1.5–4.5)	11.7 (2.2)	5.4 (2.7–10.7)	8.5 (2.4)	2.5 (1.1–6.1)	12.4 (2.6)	1.9 (0.9–3.7)	5.2 (1.5)	2.4 (0.9–6.1)
Any other illicit drug users (<i>N</i> = 2028)	22.9 (1.4)	2.0 (1.6–2.5)	7.2 (0.8)	3.0 (2.0–4.5)	8.2 (0.8)	2.2 (1.6–3.0)	14.0 (1.1)	1.9 (1.4–2.5)	5.7 (0.8)	2.6 (1.7–3.9)
Never drug users (<i>N</i> = 6280)	13.0 (0.6)	1.0	2.6 (0.2)	1.0	3.8 (0.3)	1.0				
	Alcohol disorders									
	Any alcohol use disorder		Alcohol abuse		Alcohol dependence					
	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b				
Current ecstasy users (<i>N</i> = 116)	80.2 (4.4)	20.1 (9.2–43.9)	59.8 (5.7)	15.2 (7.7–30.2)	20.4 (4.4)	2.7 (1.2–5.8)				
Former ecstasy users (<i>N</i> = 242)	77.7 (3.1)	15.7 (9.7–25.4)	57.8 (3.5)	13.8 (9.3–20.5)	19.8 (3.1)	2.2 (1.3–4.0)				
Any other illicit drug users (<i>N</i> = 2028)	58.7 (1.3)	6.9 (5.7–8.4)	35.6 (1.3)	5.8 (4.7–7.2)	23.1 (1.2)	3.0 (2.4–3.7)				
Never drug users (<i>N</i> = 6280)	17.0 (0.8)	1.0	8.2 (0.5)	1.0	8.8 (0.5)	1.0				

^a S.E. refers to standard error.

^b Odds ratio adjusted for sex, race/ethnicity, marital status, personal income, urbanicity, and region.

Table 5
Prevalence and odds of DSM-IV Axis II disorders comparing current ecstasy users, former ecstasy users, and other illicit drug users to lifetime non-illicit drug users, NESARC 2001–2002

	Any personality disorder		Antisocial personality disorder		Avoidant personality disorder		Dependent personality disorder	
	% (S.E.) ^a	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (N = 116)	15.0 (0.6)	5.1 (2.7–9.6)	10.5 (10.5)	8.0 (2.7–23.5)	2.5 (2.5)	1.0 (0.2–4.9)	1.1 (1.1)	1.7 (0.1–28.2)
Former ecstasy users (N = 242)	32.3 (1.4)	3.1 (1.9–4.9)	8.5 (2.1)	6.6 (2.8–15.6)	4.3 (1.3)	2.0 (0.7–5.2)	2.1 (0.9)	3.3 (0.7–14.6)
Any other illicit drug users (N = 2028)	33.3 (3.3)	2.7 (2.3–3.3)	7.2 (0.8)	5.7 (3.6–8.9)	6.3 (0.8)	2.7 (1.8–3.9)	1.6 (0.5)	2.6 (1.1–6.1)
Never drug users (N = 6280)	46.6 (46.6)	1.0	1.3 (0.2)	1.0	2.5 (0.2)	1.0	0.6 (0.1)	1.0
	Obsessive compulsive personality disorder		Paranoid personality disorder		Schizoid personality disorder		Histrionic personality disorder	
	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b	% (S.E.)	AOR (99% CI) ^b
Current ecstasy users (N = 116)	12.4 (12.4)	2.1 (0.8–5.5)	14.9 (14.9)	4.4 (1.8–10.6)	8.6 (8.6)	3.4 (1.1–10.4)	16.3 (16.3)	6.4 (2.7–15.0)
Former ecstasy users (N = 242)	10.1 (1.9)	1.6 (0.9–3.0)	11.5 (2.4)	3.6 (1.8–7.3)	4.8 (1.5)	2.0 (0.8–5.2)	7.5 (1.8)	2.9 (1.3–6.6)
Any other illicit drug users (N = 2028)	12.2 (1.0)	1.9 (1.4–2.6)	11.2 (0.9)	2.8 (2.1–3.9)	7.3 (0.8)	2.7 (1.9–3.9)	6.1 (0.8)	2.2 (1.4–3.4)
Never drug users (N = 6280)	6.7 (0.4)	1.0	4.9 (0.3)	1.0	3.0 (0.3)	1.0	2.7 (0.3)	1.0

^a S.E. refers to standard error.

^b Odds ratio adjusted for sex, race/ethnicity, marital status, personal income, urbanicity, and region.

population of illicit drug users, which could signal the greater severity and higher poly-drug use among this group: 13.8% (S.E. = 3.7) of current ecstasy users and 18.4% (S.E. = 2.2) of former ecstasy users have ever utilized drug treatment services, compared to 7.1% (S.E. = 0.4) of non-ecstasy drug users ($\chi^2 = 22.7$, d.f. = 2, $p < 0.01$).

There was a strong link between current ecstasy use and current alcohol abuse. It is important to note that 62% of current ecstasy users engaged in binge drinking in the past year, results which are consistent with findings from Martins et al. (2005). Clinical studies indicate that specific combinations of drugs can interact to increase toxicity, with alcohol increasing the plasma level of ecstasy compared to ecstasy users consuming no alcohol (Hernandez-Lopez et al., 2002; Schifano et al., 1998). Additionally, we found that current ecstasy users were almost all illicit poly-drug users with a high prevalence of current cannabis, cocaine, opioid and/or tranquilizer use in addition to ecstasy use. The evidence regarding the combined effect of cannabis and ecstasy on both short- and long-term neuropsychological functioning is mixed, with some evidence indicating that cannabis might actually ameliorate the neurotoxicity of ecstasy use (Daumann et al., 2001; Parrott, 2004). The high prevalence of opioid use (e.g. prescription pain killer) is consistent with emerging evidence regarding the increase in the use of this drug among young adults in the United States in general (Substance Abuse and Mental Health Services Administration, 2004; Wu et al., 2006; Zacny et al., 2003); as preliminary data suggests higher prevalence of deep coma in emergency room patients positive for ecstasy and opiates compared to patients positive for ecstasy alone (Liechti et al., 2005), this is an important area for follow-up research.

It is alarming that 44% of current ecstasy users were using more than three classes of illicit drugs in addition to alcohol, and that current ecstasy use was strongly related to alcohol abuse. In combination with a high prevalence of unsafe behaviors such as driving after or while drinking that are indicative of an alcohol abuse diagnosis (Chou et al., 2006), these results indicate that young ecstasy users in the general population may be engaging in multiple risky behaviors. A wide literature has shown that poly-drug users, especially ecstasy users, are more likely to engage in risky sexual behavior and may progress more quickly to injection drug use (Galaif and Newcomb, 1999; Klitzman et al., 2002). Overall, these findings signal a need for target prevention and treatment programs that can specifically focus on the adverse consequences of risky behavior associated with poly-drug use, in particular, in the risky behaviors associated with combining ecstasy with alcohol use.

The strong connections between ecstasy and multiple other drug usage could suggest that the presence of ecstasy use in an individual may be a marker for a more severe subtype of drug user; thus, the presence of ecstasy use might be useful for phenotype definition, especially as studies have begun to define phenotypes based on the presence of multiple drug dependencies (Agrawal et al., 2005; Kendler et al., 2003). It is well established that there is inter-individual variation in the propensity for adverse effects due to ecstasy, and a number of polymorphisms affecting metabolism of ecstasy have been implicated including CYP2D6 and other CYP isoenzymes (Carmo et al., 2006; De la Torre et al., 2005; Lynch and Price, 2007; Yang et al., 2006). The genetic epidemiology of ecstasy use may be further enhanced by examining potential gene/gene or gene/environment interactions to produce anxiety and other psychiatric disorders.

Study limitations are noted. First, data specifically covering frequency or quantity of ecstasy use were not available from the NESARC. Prior studies showing associations of higher quantity or frequency with depression and anxiety symptoms (Verheyden et al., 2003b; Thomasius et al., 2006; Topp et al., 1999) suggest the possibility of a dose–response relationship between frequency or quantity of ecstasy use and the prevalence of psychiatric disorders. Thus, by including experimental as well as regular ecstasy users in this sample, we have likely provided a very conservative estimate of the association between ecstasy use and psychiatric disorders. This should be addressed further in future studies. Second, whether ecstasy and other drugs were taken on the same occasion or on separate occasions within a 1-year period is unknown. This would also be informative to add to future studies. Third, as in all large-scale epidemiologic surveys, information is based on self-report. Fourth, there is some indication that the degree of purity and intensity of ecstasy pills (i.e. amount of MDMA) varies substantially (Parrott et al., 2004; Spruit, 2001). While having this information would be helpful in understanding the correlates of ecstasy use, it is unlikely to be known even to the users, and the relationship between specific doses of 3,4-methylenedioxyamphetamine and acute reactions can only be studied in a laboratory setting.

Finally, we cannot make conclusions about the causal effect of ecstasy on risk of psychiatric disorders due to the cross-sectional nature of the study design and the high co-occurrence of poly-drug use among ecstasy users, although clues can be provided by the temporal relationship between age at onset of ecstasy use and onset of psychiatric disorders. Preliminary analyses among the lifetime ecstasy users in this sample indicated that the mean age at onset of any hallucinogen use (the most specific information available) was 18.0 years. The mean ages at onset of some disorders we studied were younger (social phobia, 13.0; specific phobia, 10.4; dysthymia, 14) while the mean ages at onset of other disorders were similar to the age at onset of hallucinogen use (from 17.0 for major depression to 19.0 for panic disorder). However, the purpose of this report is to provide an initial characterization of the co-occurrence of DSM-IV disorders and use of other drugs among ecstasy-using populations. Longitudinal designs, preferably with access to biological markers of ecstasy use, could better establish causality. Future research should implement these designs to establish the temporal order of ecstasy use and psychiatric disorders as well as the specific ecstasy effects on the onset of psychiatric disorders above that which results from factors common to use of any drugs (Gouzoulis-Mayfrank and Daumann, 2006).

The study also had important strengths, including a large sample size and a state-of-the-art diagnostic instrument including both Axis I and Axis II disorders. Further, this study represents the first sample of ecstasy users in the U.S. assessed for a range of DSM-IV Axis I disorders, and the first sample of ecstasy users internationally to be assessed for Axis II disorders. Thus, despite limitations of the design, this study represents an important addition to the literature on the epidemiology of ecstasy use in the general population. Given the high prevalence of poly-drug use as well as current and life-

time prevalence of psychiatric disorders among ecstasy users, prevention efforts geared toward reducing ecstasy use among young people need to incorporate information about the harmful interactive effects of poly-drug use (e.g. combining alcohol use with ecstasy use), and intervention efforts should incorporate programs to treat both comorbidity of psychiatric disorders and substance disorders. Finally, future research should establish the impact of multiple classes of drugs combined with ecstasy on both short- and long-term physical and psychological effects.

Conflict of interest

All authors declare that they have no conflicts of interest.

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