

## **Demographics and Self-Reported Effects of Illicit Ecstasy Use**

**Lisa Jerome, Ph.D., and Matthew Baggott, B.A.**

### **Introduction and Overview**

This chapter discusses surveys that examine the demographics of ecstasy use and the effects of ecstasy as retrospectively described by illicit ecstasy users. Findings from these retrospective studies are compared with findings from clinical studies. Throughout this report, the term “ecstasy” is used instead of “MDMA” whenever the identity of the consumed drug is in question.

Surveys of ecstasy users are useful for documenting patterns of drug use and common effects of ecstasy in uncontrolled settings. Yet they are limited by both the questions researchers ask and the participants, who may not have experienced the full range of rewarding and adverse drug effects. Therefore, the therapeutic potential of MDMA is better documented in reports of its use in psychotherapy, as described in Chapter 2. Similarly, adverse effects of ecstasy are more adequately documented in the case reports and studies described in Chapters 5 and 6.

Ecstasy use is highest among individuals between the ages of 16 and 25, with the drug most strongly associated with dance and “rave” sub-cultures. However, ecstasy use is not limited to one age group or sub-culture. In the United States, prevalence of ecstasy use in the last year was estimated to be 3.1% for eighth graders, and 8.2% for 12 graders in 2000, and estimated to be 5.5% for college students, and 3.6% for young adults (ages 19-28) in 1999.

In surveys of ecstasy users, commonly reported effects of ecstasy are generally consistent with effects seen in clinical MDMA studies, as described in Chapter 2. Commonly reported acute psychological effects of ecstasy include increases in positive mood, energy, feelings of closeness to others, anxiety, and difficulty concentrating as well as alterations in perception in several modalities. Jaw clenching, sweating, dry mouth, nausea, and insomnia are the most commonly reported acute physiological effects of ecstasy. Reported short-term sequelae, defined here as effects occurring from 24 hours to a week after using ecstasy, include reduced energy, depressed mood, irritability, and anxiety. However in some surveys, users of illicit ecstasy reported ecstasy-induced hallucinations and increases in sexual arousal, two effects either not reported or contradicted by descriptions appearing in other reports. Differences between clinical studies and retrospective surveys are probably due to a variety of factors, including differences in measurement techniques, differences in respondents’ understanding of terms used in measures, and the varying identity, potency, and purity of illicit ecstasy. Comparisons of the effects of ecstasy, amphetamines, and psychedelics/hallucinogens by experienced users support the hypothesis that MDMA has novel psychopharmacological effects.

Few of the reports reviewed in this chapter assessed possible long-term effects of ecstasy use and only a minority of volunteers in these reports described long-term benefits or difficulties. Most users of illicit ecstasy report decreased drug effects (short-term tolerance) when one dose of ecstasy is rapidly followed by another. However, lasting decrease of drug effects (long-term tolerance) has not been confirmed by all studies asking respondents about this phenomenon.

Two reports of co-administration of ecstasy with selective serotonin uptake inhibitors have somewhat conflicting findings, although both suggest that serotonin uptake inhibitors reduce many of the acute effects of ecstasy.

**Table 3.1: Estimated Prevalence of Ecstasy Use in the United States**

	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
<b>% Using at Least Once</b>										
<b>8th Grade</b>	-	-	-	-	-	3.4	3.2	2.7	2.7	4.3
<b>10th Grade</b>	-	-	-	-	-	5.6	5.7	5.1	6.0	7.3
<b>12th Grade</b>	-	-	-	-	-	6.1	6.9	5.8	8.0	11.0
<b>College Students</b>	2.0	2.9	2.3	2.1	3.1	4.3	4.7	6.8	8.4	-
<b>Young Adults (19-28 yo)</b>	3.2	3.9	3.8	3.8	4.5	5.2	5.1	7.2	7.1	-
<b>% Using in Last Year</b>										
<b>8th Grade</b>	-	-	-	-	-	2.3	2.3	1.8	1.7	3.1
<b>10th Grade</b>	-	-	-	-	-	4.6	3.9	3.3	4.4	5.4
<b>12th Grade</b>	-	-	-	-	-	4.6	4	3.6	5.6	8.2
<b>College Students</b>	0.9	2	0.8	0.5	2.4	2.8	2.4	3.9	5.5	-
<b>Young Adults (19-28 yo)</b>	0.8	1	0.8	0.7	1.6	1.7	2.1	2.9	3.6	-
<b>% Using in Last 30-Days</b>										
<b>8th Grade</b>	-	-	-	-	-	1.0	1.0	0.9	0.8	1.4
<b>10th Grade</b>	-	-	-	-	-	1.8	1.3	1.3	1.8	2.6
<b>12th Grade</b>	-	-	-	-	-	2.0	1.6	1.5	2.5	3.6
<b>College Students</b>	0.2	0.4	0.3	0.2	0.7	0.7	0.8	0.8	2.1	-
<b>Young Adults (19-28 yo)</b>	0.1	0.3	0.3	0.2	0.4	0.3	0.6	0.8	1.3	-

Data taken from the 2000 Monitoring the Future survey (Johnston et al. 2000a; Johnston, 2001)

### **Demographics of Ecstasy Use: History and Current Trends**

Non-medical use of MDMA apparently began in the early 1970s, sometimes under the name “MDM”. Seizures of MDMA were reported in Chicago in 1970 (Sreenivasan 1972) and 1972 (Gaston and Rasmussen 1972). However, MDMA use is only sporadically documented until about the mid-1970s. Around 1976, MDMA began to be used as an adjunct in psychotherapy and commercial manufacture of MDMA commenced in the Boston area. In 1983, a group based in Texas began to manufacture and distribute MDMA, aggressively promoting the drug and selling it openly at bars. Use of MDMA continued to spread in the United States until concerns about its widespread use and the neurotoxicity of a related drug led to its placement into Schedule I of the Controlled

Substances Act in 1985. In Europe, use of MDMA was closely associated with the “Acid House” dance sub-culture originating on the Spanish island of Ibiza circa 1985. Acid House evolved into the “rave” scene, which spread to the United States in the early 1990s.

Initially, ecstasy use was restricted to a few distinct sub-cultures. Early ecstasy-using groups described in the scientific literature include college students, young professionals engaged in the club or party circuit, aficionados of the Grateful Dead musical group, gay men, and the spiritually-minded people sometimes referred to as “New Age seekers” (Beck 1994; Lewis and Ross 1995; Peroutka et al. 1987; Solowij et al. 1992; Watson and Beck 1991). Later reports describe ecstasy use in “rave” sub-cultures (Boys 1997; Forsyth 1996; van de Wijngaart et al. 1999), high school students (Forsyth et al. 1997; Pedersen and Skrondal 1999; Schuster et al. 1998; Wright and Pearl 1990; 1995; 2000), college students (Conner et al. 1998; Meilman et al. 1990; Schuster et al. 1998; Webb et al. 1998; Webb et al. 1996), gay men (Klitzman et al. 2000), drug users (Robson and Bruce 1997; Schifano et al. 1998; Williamson et al. 1997), and central European prostitutes (Kurova 1998).

The most extensive data on ecstasy use in the United States are collected by the Monitoring the Future (MTF) survey, conducted by researchers at the University of Michigan (Johnston et al. 2000a; b). This annual survey of representative high school students and young adults has included questions on ecstasy use since 1991 for young adults and 1996 for high schools. Reported prevalence of ecstasy use in each annual MTF survey is summarized in **Table 3.1**. Demographic information on ecstasy users from the 1999 MTF survey is summarized in **Table 3.2**.

Several reports have focused on adolescents’ use of ecstasy. According to the 1999 Monitoring the Future survey of youth and young adults in the United States, 4.3% of 8<sup>th</sup> graders, 7.3% of 10<sup>th</sup> graders and 11% of 12<sup>th</sup> graders surveyed reported having used ecstasy at least once. While most U.S. high school students report using ecstasy only once or twice, some are regular users. Extent of ecstasy use by U.S. high school students is summarized in **Table 3.3**. The percentage of high school students who had reportedly tried ecstasy was lower (approximately 3%) in a sample of 10,812 Norwegian high school students (Pedersen and Skrondal 1999). In one survey, approximately 13% of 274 British high school students indicated that they knew someone who had used ecstasy (Pedersen and Skrondal 1999; Wright and Pearl 1995; 2000). In contrast, the 1999 MTF survey found that an estimated 26.7% of high school seniors in the United States reported having friends who took ecstasy and 2.7% reported that most or all of their friends took ecstasy.

Reported ecstasy use by university students varies from over a third of a sample of 369 undergraduates (Peroutka 1987) to 12% of a sample of 400 undergraduates attending a small private university in the U.S. (Meilman et al. 1990). As can be seen in **Table 3.1**, 8.4% of U.S. college students are estimated to have used ecstasy at least once. The ages of volunteers participating in the studies described in this document range from the early

teens to the mid-40s. However, a majority of participants are between the ages of 18 and 25, reflecting the demographics of ecstasy use.

**Table 3.2: Demographics of Ecstasy Users (Age 19-32) in the United States**

	Percent of Population Using:		
	At Least Once	In Last Year	In Last 30-Days
<b>Total</b>	6.8	2.8	1.0
<b>Gender</b>			
<b>Male</b>	8.3	3.4	1.6
<b>Female</b>	5.6	2.3	0.6
<b>Modal Age:</b>			
<b>19-20</b>	7.9	4.9	1.5
<b>21-22</b>	7.8	4.6	1.4
<b>23-24</b>	7.6	3.3	0.9
<b>25-26</b>	6.4	3.4	1.9
<b>27-28</b>	5.5	1.8	0.8
<b>29-30</b>	6.6	0.7	0.3
<b>31-32</b>	5.5	0.8	0.5
<b>Region:</b>			
<b>Northeast</b>	8.3	4.5	1.0
<b>North Central</b>	2.6	1.1	0.4
<b>South</b>	7.0	2.5	1.0
<b>West</b>	9.8	3.9	1.8
<b>Population Density:</b>			
<b>Farm/Country</b>	4.4	2.6	1.2
<b>Small Town</b>	5.4	2.5	0.6
<b>Medium City</b>	6.3	2.4	0.7
<b>Large City</b>	7.3	3.0	1.7
<b>Very Large City</b>	10.5	3.6	1.3

Data taken from the 1999 Monitoring the Future survey  
(Johnston et al. 2000b)

Most surveys of alcohol and drug use have found that males are more likely than females to use alcohol and other substances (Forsyth 1996; Forsyth et al. 1997; Pedersen and Skrondal 1999; Schuster et al. 1998; Williamson et al. 1997). The gender disparity in ecstasy use is less apparent than it is for most other substances (Boys et al. 1999; Boys 1997; Robson and Bruce 1997; Topp et al. 1999), though a survey of Norwegian high school students found the gender disparity to be greatest for ecstasy use (Pedersen and Skrondal 1999). A randomly selected sample of 3021 residents of the Munich area, ages 14 – 25, suggests that the prevalence of ecstasy use there increases with age for men, but not for women (Schuster et al. 1998). In studies in which ethnicity is reported, most illicit ecstasy users are found to be white or of European descent (Solowij et al. 1992; Topp et al. 1999; Webb et al. 1998; Williamson et al. 1997). Several researchers found that ecstasy users had attained slightly more formal education than users of other drugs (Boys 1997; Hammersley et al. 1999; Topp et al. 1999). The 1999 Monitoring the Future survey found that prevalence of ecstasy use in the last year among U.S. college students is now somewhat higher than among non-college-student peers (5.5% versus 3.9%).

**Table 3.3: Estimated Frequency of Ecstasy Use by U.S. High School Students**

<b>% Reporting Use At Least Once</b>	<b>Grade:</b>		
	<b>8th</b>	<b>10<sup>th</sup></b>	<b>12th</b>
No occasions	97.3	94.0	92.0
1-2 occasions	1.6	3.2	4.6
3-5 occasions	0.3	1.0	1.3
6-9 occasions	0.3	0.7	0.6
10-19 occasions	0.2	0.4	0.9
20-39 occasions	0.1	0.3	0.4
40 or more	0.2	0.3	0.4
<b>% Reporting Use in Last Year</b>			
No occasions	98.3	95.6	94.4
1-2 occasions	0.8	2.6	3.3
3-5 occasions	0.3	0.8	0.9
6-9 occasions	0.3	0.5	0.4
10-19 occasions	0.1	0.3	0.5
20-39 occasions	0.1	0.1	0.2
40 or more	0.1	0.2	0.2
<b>% Reporting Use in Last 30-Days</b>			
No occasions	99.2	98.2	97.5
1-2 occasions	0.4	0.5	1.7
3-5 occasions	0.1	0.1	0.4
6-9 occasions	0.0	0.1	0.2
10-19 occasions	0.1	0.1	*
20-39 occasions	*	0.0	0.1
40 or more	0.2	0.1	*

Data taken from the 1999 Monitoring the Future survey (Johnston et al. 2000a)

Polydrug use is the norm amongst ecstasy users in most studies (Boys et al. 1999; Boys 1997; Curran and Travill 1997; Davison and Parrott 1997; Forsyth 1996; Hammersley et al. 1999; Lenton et al. 1997; Parrott and Stuart 1997; Pedersen and Skrondal 1999; Solowij et al. 1992; van de Wijngaart et al. 1999). Most ecstasy users report experience with cannabis, psychostimulants, and hallucinogens (Forsyth 1996; Hammersley et al. 1999; Lenton et al. 1997; Parrott and Stuart 1997; Schifano et al. 1998; Schuster et al. 1998; Solowij et al. 1992; Topp et al. 1999; van de Wijngaart et al. 1999).

While the reported frequency of ecstasy use varies, the most commonly reported rate of use is that of several times a month (Cohen 1995; Curran and Travill 1997; Davison and Parrott 1997; Forsyth 1996; Hammersley et al. 1999; Lester et al. 1992; Parrott and Lasky 1998; Peroutka et al. 1988; Schifano et al. 1998; Schuster et al. 1998; Siegel 1986; Solowij et al. 1992; Topp et al. 1999; Williamson et al. 1997). The typical interval between use reported by participants in some studies extended from once every few months to once a month (Hammersley et al. 1999; Lester et al. 1992; Solowij et al. 1992). However, respondents in other surveys reported using ecstasy from once a week to once every two weeks (Boys et al. 1999; Schifano et al. 1998; Williamson et al. 1997). It appears that longer intervals between use were more prevalent during the late 1980s and early 1990s, with intervals decreasing in length during the mid-1990s.

Most users of illicit ecstasy reported using approximately one tablet per occasion (Schifano et al. 1998; Solowij et al. 1992; Topp et al. 1999). Two early studies requesting estimated amount of MDMA contained per dose reported that the typical estimated amount of ecstasy used on each occasion ranged from 50 mg to 390 mg (Lester et al. 1992; Siegel 1986). The average dose was estimated to be between 100 mg and 150 mg (Lester et al. 1992; Siegel 1986). Some people used lower doses on occasion, while others used extremely high doses. When samples were formally assessed for contents in one study, it was found that the actual doses were usually smaller than estimated by volunteers (Siegel 1986). Many participants have combined ecstasy with other drugs on at least one occasion (Forsyth 1996; Parrott and Lasky 1998; Solowij et al. 1992; Topp et al. 1999). Cannabis, amphetamines, LSD and nitrates are the substances that were most commonly combined with ecstasy. At least two studies found that a large minority of respondents combined ecstasy with alcohol (Solowij et al. 1992; Topp et al. 1999), but other depressants were rarely, if ever, used along with ecstasy (Forsyth 1996; Topp et al. 1999). Cannabis is frequently smoked before and after using ecstasy at dance events (Forsyth 1996).

### **An Overview of Retrospective or Uncontrolled Studies Addressing Drug Effects**

Researchers have sought to examine the acute and sub-acute effects of ecstasy through by conducting interviews or surveys with non-medical ecstasy users. Some reports were gathered from individuals who used MDMA non-medically before it was made a controlled substance (Buffum and Moser 1986; Siegel 1986; Watson and Beck 1991), but the majority rely on information gathered from presumably illicit ecstasy users (Cohen 1995; Curran and Travill 1997; Davison and Parrott 1997; Lester et al. 1992; Parrott and

Lasky 1998; Parrott and Stuart 1997; Peroutka 1989; Schifano et al. 1998; Solowij et al. 1992). A few researchers have gathered information from a specific group of individuals, such as psychiatrists (Liester et al. 1992), university students (Peroutka et al. 1988), in-treatment drug users (Parrott and Stuart 1997; Schifano et al. 1998), and rave attendees (van de Wijngaart et al. 1999). Individuals participating in these studies were either drawn from a randomly selected sample (Cohen 1995; Peroutka et al. 1988) or selected through “snowball sampling” (Curran and Travill 1997; Davison and Parrott 1997; Liester et al. 1992; Parrott and Lasky 1998; Parrott and Stuart 1997; Solowij et al. 1992). In one study, participants were drawn from consecutive admissions to a drug treatment clinic (Schifano et al. 1998).

There are some important limitations to retrospective and non-experimental investigations of the effects of ecstasy. These include self-selected samples of participants, uncontrolled settings of drug use, and the unknown identity, purity, and potency of illicit ecstasy. A sample of illicit ecstasy users is liable to be self-selected, raising the issue of whether people who choose to take ecstasy differ in their experience of the drug than people in general. Some authors have tried addressing this issue by comparing people who have only used the drug a few times with those who have used it more often (Peroutka et al. 1988; Solowij et al. 1992). While ecstasy is frequently taken at dance events, the settings where it is taken vary, possibly influencing the nature of the drug experience. Lastly, the identity, potency, and purity of illicit ecstasy tablets used by participants cannot be assessed in most retrospective studies. Some researchers attempt to gauge the identity of the material by requesting samples of the material (Siegel 1986) or conducting urine samples on selected participants (van de Wijngaart et al. 1999), but this can only confirm the identity of recently consumed ecstasy. In most cases, the identity of illicit ecstasy remains unknown. Hence the reported effects of ecstasy may be affected by variance in the identity, potency, and purity of illicit ecstasy.

Researchers investigating the reported effects of ecstasy in illicit or non-medical users have had different goals. Some researchers wished to measure the acute and sub-acute effects of ecstasy (Curran and Travill 1997; Davison and Parrott 1997; Liester et al. 1992; Parrott and Lasky 1998; Peroutka et al. 1988) while others sought to compare ecstasy with other drugs, such as amphetamine and LSD (Parrott and Stuart 1997; Siegel 1986; Solowij et al. 1992). Some researchers were seeking information about a specific drug effect (Buffum and Moser 1986; Watson and Beck 1991) or specific outcomes, such as adverse events that occurred subsequent to ecstasy use (Schifano et al. 1998; Topp et al. 1999). Since different researchers possessed different goals and sometimes interviewed or surveyed different populations, the measures used and the comparisons performed in each study are not identical.

Because of these considerations, the authors were unsuccessful in attempts to create a single table summarizing the effects attributed to ecstasy in all studies. However, **Table 3.4** provides a summary of reported effects of ecstasy in one representative survey.

## Acute Psychological Effects Reported in Retrospective Studies

Commonly reported acute subjective effects include euphoria, happiness, increased energy, increased peacefulness, feeling close to others, empathy, increased sociability, increased anxiety, confusion, difficulty concentrating, increased insight, changed perceptions of color, and visual hallucinations. Less commonly reported acute psychological effects of ecstasy are sensual feelings, agitation, depressed mood, and changed perception of time, being distant from others, and altered tactile perceptions. Feelings of euphoria and increased energy were the most commonly mentioned across studies, with each receiving mention in 6 out of 12 studies (Euphoria: Cohen 1995; Schifano et al. 1998; Siegel 1986; Solowij et al. 1992; van de Wijngaart et al. 1999; Watson and Beck 1991). Energy: Cohen 1995; Curran and Travill 1997; Davison and Parrott 1997; Parrott and Stuart 1997; Solowij et al. 1992; van de Wijngaart et al. 1999).

**Table 3.4: Effects of Ecstasy Reported by 100 Undergraduates**

Acute Effects: Psychological	n / 100 Reporting Effect	Acute Effects: Physiological	n/100 Reporting Effect
Sense of “closeness” with other people	90	Trismus	75
Increased alertness	50	Tachycardia	72
Luminescence of objects	42	Bruxism	65
Difficulty concentrating	38	Dry mouth	61
Parasthesias	35	Tremor	42
Hot or cold flashes	33	Palpitations	41
Increased sensitivity to cold	27	Diaphoresis (sweating)	38
Dizziness / Vertigo	24	Insomnia	31
Visual hallucinations	20		
Blurred vision	20		
Sub-Acute Effects: Psychological	n / 100 Reporting Effect	Sub-Acute Effects: Physiological	n/ 100 reporting Effect
Drowsiness	36	Muscle aches or fatigability	32
Sense of “closeness” with others	22	Tight jaw muscles	21
Depression	21	Headache	17
Difficulty concentrating	21	Dry mouth	14
Anxiety, worry or fear	12		
Irritability	12		

Table adapted from Peroutka et al., 1988 and based on responses from 100 volunteers, ages 18-25, who had used ecstasy 1-38 times. Drug effects were selected by respondents from a list prepared by the researchers.

Anxiety was mentioned across 5 of 11 studies. Feeling social, feeling close to others, confusion, and visual hallucinations were mentioned in 4 of 12 studies. Feelings of dissociation, possibly similar to experiences produced by hallucinogens, were reported in two studies (Siegel 1986; van de Wijngaart et al. 1999). Users were more likely to report feelings of dissociation after very high doses of ecstasy (an estimated 500 mg and higher) (Siegel 1986).

Despite the potential for gathering inaccurate information in retrospective studies, the majority of the psychological effects reported by illicit ecstasy users are similar to those reported by participants in clinical MDMA studies (Cami et al. 2000; Grob et al. 1996; Vollenweider et al. 1998a). Increases in positive mood, energy, difficulty concentrating, and alterations in perception have been documented in both types of study. This suggests that while the identity of illicit ecstasy tablets is often uncertain, the effects of illicit ecstasy are fairly similar to those reported for MDMA.

To this date, controlled clinical studies have not formally measured increases in empathy or feelings of closeness to others associated with MDMA/ecstasy, although spontaneous remarks by volunteers about increased empathy or sociability have been noted (Cami et al. 2000; Grob et al. 1996; Vollenweider et al. 1998a; 1999a). Retrospective studies of illicit ecstasy users appear to offer stronger support for MDMA-induced increases in empathy, sociability, or feelings of closeness to others. Some researchers conducting retrospective surveys specifically requested information about empathy or closeness to others (Peroutka et al. 1988; Siegel 1986). Others asked volunteers to describe the effects of ecstasy within a structured interview (Liester et al. 1992). At least four studies found support for increased feelings of closeness to others, sociability, or empathy. Participants in at least one study reported feeling more friendly (Davison and Parrott 1997; Parrott and Stuart 1997), less aggressive (Liester et al. 1992), and less defensive (Liester et al. 1992) acutely after taking ecstasy. Illicit ecstasy users sampled from different populations reported increased empathy, friendliness, or sociability as acute effects of ecstasy, including psychiatrists (Liester et al. 1992), undergraduates (Peroutka et al. 1988) and people seeking treatment for substance abuse (Schifano et al. 1998). The reported increases in closeness to others, sociability and empathy appear to be unique to MDMA and a few structurally related analogues (Gouzoulis-Mayfrank et al. 1998; Nichols 1986) and support the proposed classification of MDMA as a member of a novel pharmacological class, called “entactogens” (Nichols 1986). Perhaps because of their training and focus on observing and analyzing thought and emotion, the psychiatrists surveyed seemed to be especially attentive to acute ecstasy-induced increases in insight and decreases in fear and defensiveness. Assuming that a majority of illicit ecstasy sold contains MDMA, it appears that the reputed entactogenic effects of MDMA occur across a variety of settings.

A surprisingly high number of individuals surveyed in these studies reported experiencing hallucinations, particularly visual hallucinations (Peroutka et al. 1988; Schifano et al. 1998; Siegel 1986; Solowij et al. 1992). The percentage of respondents reporting ecstasy-induced hallucinations varies from “rare” in the work of Solowij and Hall (1992) to 43% in the survey conducted by Siegel (1986). Participants in one survey

described most of these hallucinations as simple flashes of light or the appearance of an object in periphery vision that vanishes upon inspection (Peroutka et al. 1988). Sometimes volunteers reported seeing simple geometric forms, especially with closed eyes (Solowij et al. 1992). While these experiences were similar to those reported in clinical studies (Downing 1986; Vollenweider et al. 1998a), experiencing more complex forms, as reported among the ecstasy users in Siegel's sample (1986) did not occur in any of the clinical studies. The high prevalence of visual hallucinations in retrospective surveys may be due to users purchasing other drugs sold as ecstasy. Differences in dose may also influence the frequency of hallucinations. Estimated doses taken by illicit ecstasy users are often higher than those employed in clinical MDMA studies (Liester et al. 1992; Siegel 1986). In addition, some surveys or interviews may not have presented participants with a clear definition of a hallucination. In these cases, respondents may have classified visual illusions or alterations in perception as hallucinations.

An investigation of sexual behavior after MDMA in men and women found that ecstasy reportedly increased receptivity to sexual behavior but decreased the occurrence of sexual behavior (Buffum and Moser 1986). Men's sexual responses were reportedly particularly dampened by ecstasy. In contrast, a survey of 500 ecstasy users conducted five years later found that 83% of the respondents reported sexual arousal as an acute effect of ecstasy (Cohen 1995). Despite the larger number of respondents in the survey conducted by Cohen, the items contained in the survey designed by Buffum and Moser address specific sexual feelings and behaviors. Thus, it seems likely that the earlier study (Buffum and Moser 1986) is a more accurate reflection of the acute effects of ecstasy on sexual behavior. Acute decreases in libido have also been reported in uncontrolled and controlled clinical studies of MDMA (Greer and Tolbert 1986; Vollenweider et al. 1998a).

### **Acute Physiological Effects of Ecstasy Reported in Retrospective Studies**

Retrospective surveys can only provide indirect documentation of the physiological effects of ecstasy and must rely on the possibly faulty perceptions and memories of volunteers. Furthermore, without objectively measuring certain parameters, such as heart rate and body temperature, it is impossible to ascertain the degree to which they are acutely altered by ecstasy. Despite these limitations, the reported physiological and somatic effects of ecstasy are similar to those documented in controlled clinical studies. These effects have been assessed in seven studies of ecstasy users (Cohen 1995; Curran and Travill 1997; Davison and Parrott 1997; Liester et al. 1992; Peroutka et al. 1988; Siegel 1986; Solowij et al. 1992) and one study of in-patient ecstasy-using substance abusers (Schifano et al. 1998). Jaw clenching, sweating, nausea, dry mouth, and insomnia are the most frequently reported physiological effects of illicit ecstasy. Other physiological effects reported in more than one study are increased heart rate, increased body temperature, dilated pupils, loss of appetite, tremor, headaches, and blurred vision. Most of the reported side effects of ecstasy are similar to those produced by psychostimulants, and nearly all are reported to be mild or moderate in nature.

The physiological effects of ecstasy most commonly reported in these studies also match those documented by medical personnel treating adverse events subsequent to ecstasy use. For example, tachycardia, dilated pupils, and hypertension were the most frequently cited physiological complaints, while agitation, excitement, and hallucinations were the most commonly reported psychological complaints in a series of consecutive cases contacting the National Poisons Information Center in Ireland (Clegg and Tracey 1993). A more complete review of medical reports of the adverse effects of ecstasy is presented in a separate document.

In summary, clinical MDMA studies offer a more accurate picture of the acute effects of MDMA in humans than retrospective studies. However, surveys of illicit users appear to be very consistent with the findings reported in clinical studies and reports of complaints brought to medical personnel. This suggests that the effects of MDMA in uncontrolled settings and in larger doses than those used in clinical studies are not dramatically different from the effects documented in clinical studies. While clinical MDMA studies have not yet formally measured ecstasy-induced increases in feelings of empathy, sociability, and closeness to others, surveys of illicit ecstasy users provide evidence for these effects.

### **Sub-Acute and Long-term Effects of Ecstasy Reported in Retrospective Studies**

Surveys of ecstasy users have often included measures of effects that arise after the acute effects of ecstasy have subsided. Most studies focus on the effects appearing from up to a day after taking ecstasy to a week after use (Curran and Travill 1997; Davison and Parrott 1997; Lester et al. 1992; Parrott and Lasky 1998; Solowij et al. 1992; van de Wijngaart et al. 1999). Other researchers have focused specifically on long-term effects, defined as effects those occurring from two weeks to years after ecstasy use (Schifano et al. 1998; Watson and Beck 1991). Information on sub-acute and long-term effects appears to be combined in some papers (Cohen 1995), and information on both types of effects has been reported separately by other researchers (Lester et al. 1992; Peroutka et al. 1988; Solowij et al. 1992).

Studies have varied in the methods and the time frame used for measuring drug effects occurring after the acute effects have subsided. Some researchers differentiate between effects occurring up to 24 hours after taking ecstasy and effects occurring a few days to a week later (Curran and Travill 1997; Parrott and Lasky 1998; Peroutka 1987). Some measures appear to be ambiguous in reference to time frame, but are likely to be interpreted as referring to effects appearing immediately after the acute effects have subsided (Davison and Parrott 1997). Effects occurring up to a week after use will be treated as sub-acute effects.

### **Sub-acute Sequelae Reported After Ecstasy Use**

When short-term sequelae are defined as any effects that appear up to a week after the acute effects of ecstasy have subsided, the most commonly reported short-term sequelae in surveys of ecstasy users are depressed mood, insomnia, irritability, anxiety, being less

alert, and tight jaw. Fatigue, drowsiness, having a decreased appetite, continued feelings of closeness to others, and muscle aches were also reported in at least two of twelve studies. Short-term effects reported in only one study were headache, continued difficulty concentrating, continued decrease in anxiety, and a continued reduction in defensiveness. Psychiatrists who had taken MDMA / ecstasy seemed to experience the greatest number of positive short-term effects (Liester et al. 1992). They reported that the increased sociability and reduction in anxiety initiated by the drug continued after the acute effects had subsided. Several researchers wrote that residual effects disappeared from one to three days after ecstasy use (Peroutka et al. 1988; Siegel 1986; Solowij et al. 1992).

The sub-acute drug effects documented in clinical MDMA studies (Liechti et al. 2000a; Liechti et al. 2000b; Liechti and Vollenweider 2000a; Vollenweider et al. 1998a) compare well with the short-term effects of ecstasy recalled by illicit ecstasy users. In clinical studies, decreased energy, decreased clear-headedness, moderately increased negative mood, and physiological effects such as decreased appetite, are reported after MDMA exposure. Some physical complaints appear to be more common in illicit ecstasy users than in volunteers in clinical MDMA studies. Illicit ecstasy users have reported muscle aches (Peroutka et al. 1988; van de Wijngaart et al. 1999) and back pain (Cohen 1995) shortly after using ecstasy, while these effects were not as commonly reported in clinical studies of the effects of MDMA. The muscle aches and back pain reported by illicit ecstasy users are probably at least partially due to physical activity, such as dancing, performed during the acute effects of ecstasy, and are probably not solely due to the effects of MDMA.

### **Long-term Sequelae Reported After Ecstasy Use**

Some researchers define a long-term effect as any effect that either appears or persists a week after using ecstasy, while others define it as any effect that appears and persists many months after ecstasy use. Hence it is not clear whether all of the long-term effects reported in retrospective studies have occurred at the same point in time. Comparing across studies, the most commonly reported long-term effects of using ecstasy were increases in anxiety and dysphoric mood, increased sensitivity to emotion, changes in spiritual practices or increased spirituality and changes in life values, all reported in two out of 12 studies. While increased impulsivity is listed as a long-term effect in two different studies (Liester et al. 1992; Schifano et al. 1998), the percentage in one study (Liester et al. 1992) is very small (5%, or one individual). Long-term sequelae reported in only one study include a persistent increase in social function and reduction in defenses in the sample of psychiatrists (Liester et al. 1992), jaw clenching when anxious in one individual in a sample of undergraduates (Peroutka et al. 1988), flashbacks, frequent headaches and stomach aches in a sample of 500 ecstasy users (Cohen 1995) and psychotic symptoms in 28% of a sample of drug users consecutively admitted to a drug treatment program (Schifano et al. 1998).

Schifano and colleagues sought to discover the number of psychiatric conditions that occurred after ecstasy use (Schifano et al. 1998). After interviewing 150 ecstasy-using

patients admitted to a drug treatment program, Schifano and colleagues found that 12% of individuals had anxiety disorders, 32% had mood disorders and 28% had psychotic disorders, with time between last use and diagnosis varying across the sample. However, due to the retrospective nature of the study and to non-random sampling, it is not possible to conclude that these diagnoses have any relation to ecstasy use. Individuals in this study are not necessarily representative of ecstasy users in general. Instead, they represent a segment of the drug-using population that desires medical or psychiatric help in relation to their drug use. A second study (Curran and Travill 1997), using a different design, also reported an increase in anxiety and depressed mood after ecstasy use. Five days after taking ecstasy at a club, participants had higher anxiety and depression scores than they had when assessed at the club or one day after taking ecstasy. These same ecstasy users had higher anxiety or depression scores at five days after the first assessment than people who had used alcohol at the first assessment. None of the participants in this study were diagnosed with an affective disorder, although their scores on the Beck Depression Inventory scores were comparable to those occurring in mild to moderate clinical depression. It should also be noted that other researchers categorize effects occurring five days after ecstasy use as short-term effects, (Liester et al. 1992; Peroutka et al. 1988).

Because of a hypothesized association with serotonergic function, mood is often measured in studies comparing illicit ecstasy users with people who have not used ecstasy (Gamma et al. 2000b; Gerra et al. 2000; Morgan 1998; Parrott and Lasky 1998). An increase in depressed mood or dysphoria after ecstasy use has been reported in some studies that compare ecstasy users with individuals who have not used ecstasy (Gamma et al. 2000b; Gerra et al. 1998). However, other studies have not found an association between depressed mood or depression and ecstasy use (Morgan 1998; Parrott and Lasky 1998). Likewise, studies that have sought to detect decreases in cognitive or emotional function in ecstasy users have also failed to find an association between depressed mood and ecstasy use (Dafters et al. 1999; Krystal et al. 1992). It appears that retrospective studies are more consistent in reporting depressed mood after ecstasy use than are studies that compare illicit ecstasy users with non-users. Decreases in positive mood or increases in depressed mood may be time-limited effects of ecstasy use, a hypothesis supported by the findings of Parrott and Lasky (1998). Ecstasy users in this study felt more depressed two days after having used ecstasy than did people who had not used ecstasy, but both groups reported relatively similar moods seven days after ecstasy administration and at baseline. Depressed mood appears to be a commonly reported sub-acute effect of ecstasy use, but only one retrospective study has found a relationship between ecstasy use and affective disorders diagnosed after ecstasy use (Schifano et al. 1998). Researchers wishing to draw stronger conclusions about the presence of persistent depressed mood after ecstasy use may need to employ more specific measures of depression and larger samples or prospective study designs.

In contrast to studies focusing on possible long-term adverse effects of ecstasy, Watson and Beck sought to study the link between spirituality, religious behavior and ecstasy / MDMA use by conducting qualitative interviews with 100 ecstasy users (Watson and Beck 1991). Although they found that some individuals used ecstasy in their spiritual

practices, the authors do not provide figures indicating the percentage of their sample engaged in spiritual practices involving ecstasy/MDMA. Because their study is retrospective, the link between ecstasy use and increased or changed spiritual beliefs or activity can only be considered an association. As is the case with the study of Schifano and colleagues, it is unclear as to whether ecstasy use is directly related to long-term changes in spiritual activities or whether this is an artifact of self-selected sampling. However, a retrospective study of 20 psychiatrists who had used ecstasy indicated that 46% changed their religious or spiritual practices for over a week after taking ecstasy (Liester et al, 1992).

Comparisons between these studies and clinical MDMA trials are difficult to make. To date, only one uncontrolled clinical study has described long-term psychological effects of MDMA. In this study, long-term effects were defined as those occurring two weeks to two years after MDMA administration, which took place in the context of psychotherapy (Greer and Tolbert 1986). There are some similarities between the findings in this study and the findings of retrospective studies. A little over half of the participants in the clinical study reported changes in life goals subsequent to MDMA-assisted psychotherapy, and a little under half reported that they had changed their spiritual or physical practices subsequent to MDMA-assisted therapy. Most of these changes were viewed positively. However, one of the participants experienced intensified anxiety subsequent to MDMA-assisted psychotherapy, but he viewed this as a necessary development and did not regret having been part of the study. Since MDMA was administered in the course of psychotherapy, both reported benefits and reported problems occurring after MDMA administration may also relate to the therapeutic session or preexisting issues rather than to the direct effects of MDMA.

In summary, commonly reported short-term sequelae after ecstasy use include depressed mood, insomnia, irritability, anxiety, decreased alertness, and jaw tension. Because of the lack of a clear definition as to what constitutes a long-term effect and because few clinical studies have measured long-term effects after MDMA administration, only tenuous conclusions can be made about long-term effects occurring after taking ecstasy or MDMA. While problems and benefits have been reported to persist for more than a week after taking ecstasy, it is not clear whether the drug was directly involved in producing these effects. However, studies of illicit ecstasy users suggest that at least some individuals may experience changes in interpersonal relations or life goals that they perceive to be positive or beneficial and other individuals may experience increases in anxiety or depression. Further research is needed to address the issue of potential long-term effects occurring after use of ecstasy or MDMA. Researchers should clearly define the onset times and durations that qualify effects as "long-term". Prospective studies of potential ecstasy or MDMA users are needed as well. Researchers may then be able to identify and assess any long-term benefits or problems seen after ecstasy use.

### **Comparisons Between Ecstasy, Hallucinogens and Psychostimulants**

Individuals familiar with the effects of amphetamines, hallucinogens, and ecstasy were asked to compare the effects of each of the three drug classes with the others in two

**Table 3.5: Frequently Reported Effects of Ecstasy, Amphetamines, and Hallucinogens**

‘MAIN’ EFFECTS		
Ecstasy	Amphetamines	Hallucinogens
Talkative	Energetic	Strange thoughts*
Open minded	Talkative	Open minded
Closeness to others*	Alert*	Enlightened
Happiness *	Confident	Insightful
Easy going*	Clear thinking	Restless
Accepting*	Attentive	Accepting
Sensual*	Increased self esteem	Energetic
Euphoria*	Open minded	Easy going
Confident	Easy going	Talkative
Carefree	Accepting	Happiness

  

‘SIDE’ EFFECTS		
Ecstasy	Amphetamines	Hallucinogens
Loss of appetite	Loss of appetite	Visual illusions
Dry mouth	Insomnia	Visual hallucinations
Rapid heartbeat	Rapid heartbeat	Loss of appetite
Jaw tension	Jaw tension	Insomnia
Insomnia	Grinding teeth	Confusion
Grinding teeth	Dry mouth	Poor concentration
Hot and cold flushes	Palpitations	Auditory hallucinations
Sweating / sweaty palms	Irritability	Anxiety
Poor concentration	Desire to urinate	Mental instability
Desire to urinate	Tremors	Rapid heartbeat

Table adapted from Solowij & Hall, 1992 and based on responses from 46 / 100 volunteers experienced with all three drug classes. Drug effects were selected by respondents from a list prepared by the researchers. Asterisks indicate those main effects that distinguished each drug category from the rest, significant at  $P \leq .001$ .

surveys of illicit ecstasy users (Parrott and Stuart 1997; Solowij et al. 1992). MDMA shares structural and pharmacological characteristics with both amphetamines and hallucinogenic phenethylamines, such as mescaline. Amphetamine produces most of its effects through acting on the dopaminergic and noradrenergic systems, whereas classical hallucinogens share an affinity for 5HT<sub>2A</sub> receptors. Because MDMA possesses both dopaminergic and noradrenergic effects and has an affinity for the 5HT<sub>2A</sub> receptor (Battaglia and De Souza 1989), researchers have sought to compare the effects of ecstasy,

psychostimulants, and hallucinogens (Parrott and Stuart 1997; Solowij et al. 1992). Comparisons from one of these studies are summarized in **Table 3.5**.

Participants in both drug comparison studies reported that ecstasy shared some similarities with psychostimulants (Parrott and Stuart 1997; Solowij et al. 1992). Like amphetamines, ecstasy was reported to make users talkative, and many of the acute physiological effects, such as loss of appetite and jaw tension, were reported for both ecstasy and amphetamines (Solowij et al. 1992). Both ecstasy and amphetamines reportedly produce increases in energy, confidence, and elation (Parrott and Stuart 1997). While ecstasy apparently produces greater feelings of emotional composure than amphetamine or LSD, the degree of composure associated with ecstasy is closer to that of amphetamine than LSD (Parrott and Stuart 1997). Illicit ecstasy users reported that ecstasy and hallucinogens also produce some similar effects (Parrott and Stuart 1997; Solowij et al. 1992). Both ecstasy and hallucinogens reportedly produce difficulties in concentration and increases in open-mindedness and feelings of acceptance (Solowij et al. 1992). When compared with each other and with amphetamine, both ecstasy and LSD were associated with decreased clear-headedness (Parrott and Stuart 1997).

Unlike psychostimulants or hallucinogens, ecstasy was reported to produce increases in agreeableness (Parrott and Stuart 1997), feelings of closeness to others, happiness, feeling easy going, and sensual feelings (Solowij et al. 1992). Ecstasy alone is highly rated along these dimensions. Thus, ecstasy is rated as being similar to amphetamines and hallucinogens by experienced drug users, but it is also reported to possess some distinguishing features as well.

The adverse effects of ecstasy have been compared with those of amphetamine and cocaine powder. Experienced drug users familiar with all three drugs rated ecstasy as producing effects that were more severe than those associated with cocaine but less severe than those associated with amphetamine (Williamson et al. 1997). Volunteers in this study and that of Solowij and Hall (1992) rated the adverse effects associated with ecstasy as mild to moderate in severity.

### **Decline in Drug Effects After Repeated Use or “Loss of Magic”**

Four studies addressed the issue of changes in the effects of ecstasy arising after repeated use (Davison and Parrott 1997; Lester et al. 1992; Peroutka et al. 1988; Solowij et al. 1992). In some cases, items referring to changes in effects after repeated use were only posed to individuals who had used ecstasy more than three (Solowij et al. 1992) or five times (Peroutka et al. 1988). Participants indicated whether the effects of ecstasy grew more intense or less intense over time. All studies that requested information about tolerance reported that participants had found that taking another dose immediately after the first dose produced fewer positive effects and greater negative effects (Davison and Parrott 1997; Peroutka et al. 1988; Solowij et al. 1992).

These studies also investigated the possibility of a general decline in the effects of ecstasy with each successive use, sometimes referred to as “loss of magic.” Scientific evidence

for a decrease in the intensity of effects with repeated use of ecstasy is currently inconclusive and may depend upon at least two factors. Volunteers in two of the four studies listed above reported that the effects of ecstasy decreased with repeated use (Peroutka et al. 1988; Solowij et al. 1992). Volunteers in one of the four studies reported no decline in the intensity of drug effects over time (Liester et al. 1992). People participating in another one of the four studies reported that any decline in the effects of ecstasy experienced over repeated use was related more to growing familiarity with the effects of the drug than to an actual decline in effects (Davison and Parrott 1997). Participants reporting a decline in drug effects with repeated use attributed this decline to the effects of the drug itself, to the quality of ecstasy, and to familiarity with the effects (Peroutka et al. 1988; Solowij et al. 1992). Participants in the study that did not find a decline in drug effects after repeated use also had the longest reported average interval between each use (Liester et al. 1992), with the minimum interval between instances of use being "several weeks." The reduction in the effects of ecstasy over successive uses may be due in part to frequency of use, with a decline in drug effects associated with more frequent use. It is also possible that expectations about drug effects play a role in the reported decline in drug effects, with novelty-seeking users growing disappointed with ecstasy once they become familiar with the drug's effects (Davison and Parrott 1997; Solowij et al. 1992).

### **Coadministration of Ecstasy with SSRIs in Illicit Ecstasy Users**

Several researchers have collected cases of individuals who have taken MDMA or ecstasy in combination with a selective serotonin reuptake inhibitor, or SSRI. Two retrospective studies discuss the effects of coadministration of SSRIs along with ecstasy in illicit users. One collection of case reports (McCann and Ricaurte 1993) found that four individuals who took fluoxetine (Prozac) before taking ecstasy experienced less negative effects with only minor attenuation of the positive effects of ecstasy. Subsequent publications suggest that this report is incorrect (Liechti et al. 2000a; Liechti and Vollenweider 2000b; Stein and Rink 1999). A later case report found that both the positive and the negative effects of ecstasy were greatly reduced in two individuals who took citalopram (Celexa) and ecstasy (Stein and Rink 1999). The findings in the second report are confirmed by a controlled clinical study that compared the effects of MDMA given alone with the effects produced after pre-treatment with citalopram (Liechti et al. 2000a; Liechti and Vollenweider 2000b). Taken together, the two reports and the definitive clinical study suggest that serotonin release is involved in producing many of the subjectively experienced effects of MDMA.

### **Other Avenues of Investigating the Effects of Ecstasy / MDMA**

A few researchers and therapists have attempted to reproduce some or all of the effects of hallucinogenic drugs through post-hypnotic suggestion (Greer and Tolbert 1990; Masters and Houston 1972). Self-hypnosis was used to reproduce the analgesic effects of MDMA in a cancer patient (Greer and Tolbert 1990). Currently, there are no controlled studies using hypnotically induced re-creations of the effects of MDMA, but there is one published report of an attempt to recreate the subjective effects of MDMA through

hypnotic induction. Hastings (1994) sought to reproduce the effects of ecstasy via post-hypnotic suggestion, with four individuals who had previous experience with MDMA or ecstasy serving as volunteers in this study. Volunteers were asked to report what they experienced during the period of post-hypnotic suggestion and to compare it with their experience with ecstasy, though statistical comparisons were not used to test the strength of these comparisons. It appears that Hastings was partially successful in reproducing the effects of ecstasy in his volunteers, particularly in the realms of “bodily experience” and “energy.” Three of the four participants reported that their experience was nearly identical to their last experience with ecstasy, while one of the participants reported that the effects were different from his or her last experience with ecstasy, but pleasant nonetheless.