Ecstasy abuse: an Irish perspective

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The last two decades have seen a transformation in the way young people socialise. In addition to tobacco and alcohol, an increasing number of young people take recreational drugs including ecstasy (3, 4-methylenedioxymethamphetamine [MDMA]) as part of their night out. A key factor in the increasing use of recreational drugs is their association with nightclubs, dance music and 'raves'. The popularity of ecstasy is due to its positive effects on mood and feeling of well-being, and the fact that most young people perceive it to be a safe drug.

However, there have been a substantial number of reports of severe acute toxicity and death.[1] The rate of ecstasy use by teenagers in Ireland is amongst the highest in Europe (ESPAD, 1999) with 1 in 20 16 year olds reported to have taken ecstasy.[2] Although less prevalent than cannabis, ecstasy and amphetamines are the second most commonly used drugs in the general population.

In the latter half of the 1990s, there was a decreasing trend in those presenting to treatment services with problematic ecstasy use, from 7.4% in 1995 to 3.5% in 1998. This trend did not continue however, and there was an increase in the proportion of people to 5.9% in 2000 presenting with ecstasy problems.[3] After cannabis, ecstasy is the drug that features next in prosecutions and drug seizures data in Ireland. Ecstasy seizures come mostly from street or dance events, rather than from point of entry to the country. The number of seizures recorded by Gardai increased quite considerably from 534 in 1996 to 1,910 in 2000.[3]

History

Ecstasy was first synthesised and patented in Germany by Merck in 1914. The intention was to market it as an appetite suppressant, but the drug was never released onto the market for this indication. However, there are published reports of the use of MDMA as an adjunct to psychotherapy, as it was said to enhance the 'therapeutic alliance by inviting self-disclosure and promoting trust'.[4] Since the mid-1980s, ecstasy had become popular as a recreational drug and, by

1987, deaths involving MDMA use were being described. (There are now a substantial number of reports in the literature implicating MDMA with severe acute toxicity problems or death.[1])

At the same time, reports were beginning to appear that the drug and its demethylated metabolite, 3,4-methylenedioxyamphetamine (MDA) had long-term neurotoxic effects on laboratory animals.[5] These reports have done little to prevent the widespread use of ecstasy as one of the most popular illicit recreational drugs.

In 1985, the US Drug Enforcement Administration restricted the therapeutic use of MDMA, placing it on Schedule 1 of its Restricted Drugs List. It is classified similarly in Ireland (Schedule 1 of the Misuse of Drugs Act, 1977) and the UK (Class A under the Misuse of Drugs Act).

Abuse patterns

Ecstasy is most commonly ingested in tablet form; however, the actual composition of tablets varies greatly. An examination of tablets sold as ecstasy in Europe between 1995 and 1997 reveals that of 69 tablets, 30 contained MDMA, with doses ranging from 2mg to 149mg and another eight contained a mixture of substances including amphetamines, ephedrine, caffeine and aspirin. Overall, approximately 10% of drugs sold as ecstasy contain no active ingredient.

A more recent study conducted in the UK reported that concentrations of MDMA varied 70-fold between tablets. This is an important confounding factor for research into the effects of ecstasy use.

The total amount consumed per occasion varies greatly among users. The most common dosage is one to two tablets per night, but case reports have indicated doses as high as 10 tablets. Tolerance to the psychoactive properties of MDMA develops rapidly; therefore some individuals use increasing amounts of ecstasy to reinforce the psychoactive effects.

Pharmacology

Ecstasy is the popular name for 3,4-methylenedioxy-methamphetamine (MDMA). As the name implies, MDMA is a derivative of methamphetamine (known by such street names as speed, crystal and meth) and its parent compound, amphetamine. Its structure also resembles that of mescaline giving it some hallucinogenic properties. MDMA is an indirect monoaminergic agonist, stimulating the release and inhibiting the reuptake of serotonin.

The psychostimulant properties of ecstasy are observed 20 to 60 minutes after ingestion and its effects last from two to four hours. It is widely distributed, easily crosses the blood/brain barrier, is hepatically metabolised by CYP2D6 and is renally excreted. The pharmacokinetics of MDMA are nonlinear: a small increase in dosage leads to a disproportionate rise in drug plasma concentration, thus possibly explaining why some individuals develop acute toxic reactions after apparently normal doses.[6] Approximately 10% of Caucasians are deficient in CYP2D6 and this may make those individuals more susceptible to adverse reactions.

Effects of ecstasy

Single doses of MDMA have been administered to volunteers in double-blind, placebo-controlled trials, although most findings of the effects of ecstasy are based on recreational MDMA users. The desired effects for which MDMA is used are a feeling of euphoria and postponement of fatigue, sharpened sensory perception, greater sociability and a heightened sense of closeness to other people.

Due to the fact that MDMA causes increased arousal and alertness, it is usually accompanied by adverse effects such as trismus, bruxism and restlessness. Homeostatic control of body temperature is adversely affected due to altered hypothalamic control, leading to an increase in body temperature, sweating and dehydration.[7] This has led to reports of death due to hyperthermia, hyponatraemia due to water intoxication, the syndrome of inappropriate antidiuretic hormone (SIADH) and disseminated intravascular coagulation (DIC).[1]

Serotonin syndrome

Ecstasy may induce the serotonin syndrome which is caused by a drug-induced excess of intrasynaptic 5-hydroxytryptamine (5-HT). The symptoms include behavioural hyperactivity, mental confusion, agitation, hyper-reflexia, hyperpyrexia, tachycardia, shivering, clonus, myoclonus and tremor; it can be fatal.

It is difficult to estimate the morbidity of these reactions, which raises the question of which factors influence the development of serotonergic overactivity. One crucial factor is dosage, while others include individual sensitivity, variations in drug metabolism, tolerance, environmental factors and the concomitant use of other psychoactive drugs which affect 5-HT.[8]

Long-term effects

The long-term serotonergic damage caused by MDMA was first demonstrated in laboratory animals in the mid-1980s. When rats were treated with successive doses of MDMA, they developed a pronounced loss of 5-HT axon terminal markers.[9,10] Serotonergic changes have been shown in a variety of indices, with dose-dependent reductions in 5-HT, 5-hydroxyindole acetic acid (5-HIAA), tryptophan hydroxylase and 5-HT uptake sites or neuronal transporters.

There are numerous indications of serotonergic damage in humans. In a positron emission tomography (PET) scan study, McCann et al (1998) documented a reduced density of 5-HT transporter sites, which correlated with the extent of past ecstasy use.[11] These serotonergic deficits were found across a wide range of brain regions. Significantly lower levels of cerebrospinal fluid (CSF) serotonin and its metabolites have also been found in abstinent ecstasy users.[12] This evidence would suggest that repeated ingestion of MDMA may produce long-term reductions in serotonergic activity and degeneration of serotonergic terminals in humans.

Psychiatric changes

Acute psychiatric effects from MDMA occur and include

mood alteration and visual hallucinations. Chronic use may lead to longer-term adverse psychiatric effects such as major depression, panic disorder, psychosis and aggression.[13,14]

In a study, Parrott et al (2000) assessed 50 young adults in an Irish town where drug use was prevalent. On the standard psychiatric self-rating questionnaire (SCL-90), heavy ecstasy users reported significantly higher scores than nonusers on the following factors: general anxiety, phobic anxiety, hostility, obsessionality, paranoid ideation, psychoticism, somatisation, altered appetite, restless sleep and impulsiveness.

Concentration difficulties, memory disturbance and other cognitive impairments have been demonstrated by many different research studies, which would suggest a reason for clinical concern.[15]

Conclusion

Ecstasy consumption is of growing concern, especially in the young population and is, at present, second only to cannabis use in this population in a number of European countries including Ireland. One area of concern was outlined in a study carried out in Dublin by Gervin et al (2000) where the authors found an association between heroin smoking by 'chasing the dragon' to 'come down' off the effects of ecstasy. One-quarter of the study's sample population cited this as their main reason for commencing opiates.[16]

There is a considerable body of evidence that ecstasy use not only may have acute adverse effects but repeated use may also have serious long-term consequences. Although subtle at first, its effects may develop into major neuropsychiatric syndromes over the lifetime of an otherwise healthy individual. Even if these long-term effects are confined to a small proportion of susceptible individuals, the negative consequences of MDMA exposure could develop into a major public health problem given the large number of young people who use it. In order to prevent this, it is important that comprehensive educational programmes are developed to educate this young population about the many long-term adverse effects of taking ecstasy.

References

1. Schifano F. A bitter pill. Overview of ecstasy-related fatalities. *Psychopharmacology* 2004; 173: 242-8
2. Hibell B, Anderson B, Bjarnason T et al. ESPAD: the European School Survey Project on alcohol and other drugs 1997. www.espad.org/reports.html
3. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). National Report, 2002. www.emcda.eu.int/
4. Grinspoon L, Bakalar J. Can drugs be used to enhance the psychotherapeutic process? *Am J Psychotherapy* 1986; 40: 393-404
5. Ricaurte GA, Yuan J, McCann UD. MDMA-induced serotonin neurotoxicity: studies in animals. *Neuropsychobiology* 2000; 42: 5-10
6. De la Torre R, Farre M, Ortuno J et al. Non-linear pharmacokinetics of MDMA in humans. *British Journal of Clinical Pharmacology* 2000; 49: 104-9
7. Davison D, Parrott AC. Ecstasy in recreational users: self-reported psychological and physiological effects. *Hum Psychopharmacol Clin Exp* 1997; 12: 91-7
8. Gillman PK. Serotonin syndrome: history and risk. *Fundum Clin Pharmacol* 1998; 12: 482-91
9. Ricuarte GA, Bryan G, Strauss L, Seiden LS, Schister CR. Hallucinogenic amphetamine selectively destroys brain serotonin nerve terminals. *Science* 1985; 229: 986-8
10. Schmidt CJ, Wu L, Lovenberg W. MDMA: a potentially neurotoxic amphetamine analogue. *Eur J Pharmacol* 1986; 124: 175-8
11. McCann UD, Szabo Z, Scheffel U, Dannals RF, Ricaurte GA. Positron emission tomographic evidence of toxic effect of MDMA on brain serotonin neurones in humans. *Lancet* 1998; 352: 1433-7
12. McCann UD, Ridenour A, Shaham Y, Ricaurte GA. Serotonin neurotoxicity after MDMA: a controlled study in humans. *Neuropsycopharmacology* 1994; 20: 129-38
13. Keenan E, Gervin M, Dornan A, O'Connor J. Psychosis and recreational use of MDMA. *Irish Journal of Psychological Medicine* 1993; 10 (3): 162-3
14. Schifano F. Chronic atypical psychosis associated with MDMA ('ecstasy') abuse. *Lancet* 1991; 338: 1335
15. Parrott AC, Lees A, Garnham NJ, Jones M, Wesnes K. Cognitive performance in recreational users of MDMA or 'ecstasy': evidence for memory deficits. *Journal of Psychopharmacology* 1998; 12: 79-83
16. Gervin M, Hughes R, Bamford L, Smith B, Keenan E. Heroin smoking by 'chasing the dragon' in young opiate users in Ireland: stability and associations with use to 'come down' off ecstasy. *Journal of Substance Abuse Treatment* 2001; 20: 297-300

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