Ecstasy: A Drug in Expansion with Multiple Risks

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ABSTRACT

In 1993, in France, the increase in seizures of the drug by customs was an impressive 133,521 doses which represents an increase of 860% in one year. The drug, which first appeared in the United Kingdom and then in the United States, is being spread over Europe by vast movements of hippie populations (eg travellers or Ravers) and appears in night clubs or at parties in tablet form. The largest source of “Ecstasy” is now Holland and Thailand.

Recent studies have shown that the reputation of being an inoffensive drug, which has helped the spread of ecstasy, is no longer true. Its insidious effects on behaviour and personality have made ecstasy an important factor in traffic accident mortalities.

INTRODUCTION

Ecstasy, also known as “love drug” or “E”, is a synthetic derivative of amphetamine: 3,4, methylene dioxy-methyl amphetamine (MDMA). Used in 1914 as an anorexic agent, then as a mood modifying agent, in the last ten years MDMA and related molecules, such as 3,4 methylene dioxy amphetamine (MDA) and its “sister” 3,4 methylene dioxy-ethyl-amphetamine (MDEA, “eve”) have become a family of euphoric drugs with rapid growth. These molecules cause tolerance and psychic, but not physic, dependence.

EPIDEMIOLOGY OF ECSTASY

Customs seizures carried out in France in 1993 have shown that “Ecstasy” was a drug with rapid growth, although less used than other drugs at the present time. Table 1 indicates the quantities of drug seizures in 1993. Results are expressed in tons and kilograms, with the increase percentage vs. 1992.

Table 1
Quantities of Drug Seizures in 1993 vs 1992

<table>
<thead>
<tr>
<th></th>
<th>Cannabis</th>
<th>Cocaine</th>
<th>Heroine</th>
<th>Crac</th>
<th>Amphetamines</th>
<th>Ecstasy (doses)</th>
<th>L.S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>45.8 T</td>
<td>1.7 T</td>
<td>385 kgs</td>
<td>5 kgs</td>
<td>43 kgs</td>
<td>133,521</td>
<td>43061 T</td>
</tr>
<tr>
<td>+9%</td>
<td>+5.5%</td>
<td>+18%</td>
<td>+11.7%</td>
<td>+225%</td>
<td>+869%</td>
<td>+235%</td>
<td></td>
</tr>
</tbody>
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These numbers represent approximately only 10% of all drug traffic. The main network comes from Eastern European countries in which failed industries have found a new channel for basic chemical production in making methylenedioxy amphetamine and drug trafficking is now facilitated by the opening up of European boarders. The main producers are Latvia and Bulgaria, who export drugs to the Persian gulf and Poland, then on to Scandinavian countries (20% of Ecstasy come from Poland). Drug turnaround is concentrated in Warsaw, Budapest, Prague and Sofia, there is also an important traffic through Thailand. Ecstasy, now widely distributed in Europe and in the USA, is finding its way into France via the Netherlands, the UK, Belgium, Germany, Sweden and Denmark, all of which have a large consumption of this drug.

A international UN report on narcotic trafficking in 1994 pointed to Vienna as harbouring certain factors which facilitated the circulation of Ecstasy (Le Monde, 2/3/93, p.12).

There is a flourishing ‘narco-tourism’ in Dutch frontier towns such as Maastricht, Heerlen, Venlo, Enschede etc, where dealers and users can easily find soft and hard drugs. Furthermore, traffic is facilitated by Dutch law which authorises the sale of soft drugs. However, the discrimination between soft and hard drugs is difficult to apply in these boarder towns where numerous “coffee-shops” are allowed to sell narcotics (30g cannabis for each client ...).

The migratory communities of the 1970s, eg the “hippies”, organised rock festivals during which drugs were consumed in large quantities. At the present day several dissident movements have been listed: ‘Ravers’ (party goers), New Age Travellers associated with ‘divine’ mysticism, who are joined by anarchists squatters etc.

In the South of France, there are many discotheques where Ecstasy is regularly used and in the Paris suburbs a laboratory making Ecstasy was broken up.

The distribution of Ecstasy is also greatly facilitated by a fairly simple synthesis process, moderate price and a distribution network which is practically inaccessible for the police, moreover the benefits of consumption are overshadowed by its falsely innocuous reputation.

**NEUROBIOLOGY OF ECSTASY**

The main neurological effects of Ecstasy are medical in increasing serotonin (5-HT) extra cellular level in the central nervous system, especially in striatum and hippocampus, as shown in rat brain homogenates (Doman et al, 1991). This extra cellular serotonin increase is due to presynaptic end nerves release of serotonin and its uptake blocked by MDMA. In addition, MDMA inhibits competitively serotonin catabolism by mono-oxydase A (MAO A) which is responsible of extra cellular degradation. (K = 22mM) Concentration response curves for MDMA inhibition of MAO show an IC50 44mM versus an IC50 of 370mM for MAO B. So MDMA is a preferential inhibitor of MAO A, (increasing extra cellular 5HT). Reciprocally fluoxetine (Prozac) inhibits MAO B (IC50 = 80mM) which increases the intra cellular content of serotonin (Leonardi, 1994)).

Ecstasy damage on brain sertonic neurones in humans have been recently studied (McCann, 1994): 30 MDMA users and 28 controls have been compared for the measurement of biological and behavioural indexes of central 5HT function. Measure obtained after two
weeks of drug abstinence included monoamine metabolites in cerebral spinal fluid (CSF) and personality tests in which serotonin is implicated (ie. impulsiveness and aggressivity) gave the following results: lower levels of 5 hydroxy indolacetic acid in MDMA users than in controls (p=0.01). Lower scores on personality measures of impulsiveness (p = 0.04) and indirect hostility (p=0.09) in users. These results mean that the serotonin brain system has a role in modulating aggressive personality traits and acting aggressively.

Metabolism and Analysis of MDMA

In microsomal preparations, MDMA has shown to be demethylated by the enzyme debrisoquine hydroxylase in dihydroxymethyl amphetamine (DHMA) this enzyme belongs to the cyt.p450 system. Incubation of MDMA isomers with human microcosms has demonstrated that their demethylation is deficient in some poor metabolizer phenotypes. This may induce genetically determined difference in toxicity (Tucker, 1994)

Amphetamine derivated molecules are relatively stable in blood and urine so they can be detected in non-degraded form by gas on H.P.L chromatography and by mass spectrography (Rudler, 1988). The immuno-enzymatic method in urine provided by Roche Laboratories permits a group molecule detection. The delay for detection in urine is about 24-48 hours.

TOXICITY OF ECSTASY

The direct toxicity of MDMA in several animal species is now well established; human toxicity is still being investigated. In rodents, myelinic degeneration of the central nervous system, in 5HT1 terminal nerves, has been demonstrated. (Dornan et al, 1991) In dogs, overdosage resulted in death from hypothermia, hyperbactacidemia, candida hypertension and tachycardia (Dawis, 1994).

In male rats, the repeated septemic administration of MDMA produced a rapid, transient outburst of copulatory behaviour, also ejaculation latency and the post-ejaculatory interval were lengthened (Darnan et al, 1991)

In humans, MDMA toxicity could be distinguished in immediate or in short-term actions and delayed actions, concerning mainly mental disorders. In fact, effects could be intricated so that unexpected pathologic disorders emerged.

Descriptions of systemic toxicity induced by MDMA are now widely available. Classical symptoms are: dilated pupils, agitation, excitement, delusions, incontinence, tachycardy, depression and death by heart failure or arrhythmiae breathing problems (Cregg, 1994).

Some particular cases have also been described:

• one case of a patient with intra-cranial haemorrhage was associated with MDMA ingestion (Hughes, 1993)

• two cases of aplastic anaemia following exposure to Ecstasy have been reported. Anaemia regressed spontaneously 7-9 weeks after presentation. These results, after studies on bone marrow culture, suggest that drug toxicity is transient or affects a mature cell progenitor as its target . (Marsch et al, 1994)

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• another case concerned a man who was admitted with hypothermia, rhabdomyolysis disseminated intravascular coagulation (Tehan et al, 1993).

Another effect of MDMA neurotoxicity could be sleep disturbance. All night polysomnograms of MDMA users compared to those of controls have shown a decrease of some 19 minutes total sleep in users; stage 2 sleep was principally affected. This neurotoxicity is thought to involve serotonin neurones (Allen et al, 1993).

Neuropsychiatric sequelae have been known for approximately a decade. In 1991, the “Lancet” reported the main mental disorders observed in MDMA long term users (Lancet, vol 338, p. 1335, Nov 1991). These disorders were: aggressive outbursts, anxiety, mood swings, paranoid delusions, delusions of bodily changes, delusions of having AIDS. All these behaviour patterns are thought to be influenced by serotonin (Steele, 1994).

Other psychiatric disorders reported are, obsessive compulsive behaviour and paranoid psychosis which appeared sometimes after abuse of MDA, MDMA or MDEA (Cassidy, 1994). Plus panic attacks, chronic depersonalisation and derealisation (dissociation syndrome).

These psychotic symptoms may be clinically similar to those of psychotic patients with no history of substance use. (McGuire, 1994). Although paranoid or dissociative psychosis are known to rise after chronic Ecstasy use (Keenan, 1993) a case was reported where a 21 year old female patient, suffered a psychotic depersonalisation disorder with a suicidal tendency after the first intake of only two tablets of Ecstasy. Symptoms decreased slowly taking six months in spite of a serotonin reuptake inhibition treatment (Wodarz, 1993). This observation is correlated with some preclinical studies which showed that such inhibitors (fluoxetine - Prozac) seemed not to block Ecstasy induced psychosis effects, although they suppressed systemic toxicity and short term neurotoxicity in humans (McCann, 1993).

Traffic accidents caused by consumption of Ecstasy or its derivatives are at the present time underestimated, few cases have been reported in literature: however, two cases of accidental deaths resulted from MDMA use that induced an episode of bizarre and risky behaviour (Dowling, 1987). There was a case of a 26 year old male who died from severe brain contusion after falling from a moving car during an attempt at car surfing. Toxicological urine screening showed positive signs of amphetamine, blood analysis indicated a MDMA level of 0.63mg/l and a blood alcohol concentration of 1.23mg/l. (Hooft, 1994).

REFERENCES

Allen RP, Mc Cann UD, Ricaurte GA. Persistent effects of racemic 34 methylenedioxymethamphetamine MDMA ecstasy of human sleep. Sleep (Rochester, 16 (6), p 560-4, 1993.


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