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Short Communication

AN "ACCIDENTAL" ACUTE PSYCHOSIS WITH ECSTASY USE

Guillaume Vaiva, M.D., Ph.D.*
Virginie Boss, M.D.**
Daniel Bailly, M.D.***
Pierre Thomas, M.D., Ph.D.****
Philippe Lestavel, M.D.*****
Michel Goudemand, M.D.******

Abstract—Over the last 10 years, Europe has witnessed the development of the ecstasy phenomenon; this term is used to describe several products sharing more or less the same effects. The most widely used and hence the most well known is 3,4 MDMA, but MDA, MDEA, MBDB and even 2CB or nexus are available. The psychopathological consequences of MDMA use in man are relatively poorly understood. The case reported here involves an acute psychotic episode with residual symptoms after six months, with a sudden onset at least 12 hours after taking alcohol and ecstasy without realising it, in an individual with no previous psychopathology other than a moderate anxiety disorder. Twelve cases of acute psychotic episodes after taking ecstasy have been reported in the literature; two after taking the drug on two occasions and one after a single use. No authors have examined the previous mental state or possible previous psychopathology with any precision. The present subject had not displayed any previous psychotic behavior when tested with a proven standardized interview technique; this was confirmed by his peers and his family. He did, however, show signs of social phobia. Although the personality of an individual is a factor in taking a drug, and probably in the quality of the psychotropic effects experienced, a host of arguments favor the appearance of psychotic symptoms *de novo*, which were probably related to direct toxicity by MDMA and/or its metabolites on the serotoninergic neurons.

Keywords—acute psychosis, drug abuse, ecstasy, emergency psychiatry, social phobia

*Department of Psychiatry and Emergency Department, CHRU de Lille, Université de Lille II, Lille, France.
**Department of Psychiatry, CHRU de Lille, Université de Lille II, Lille, France.
***Department of Psychiatry, CHRU de Lille, Université de Lille II, Lille, France.
****Department of Psychiatry, CHRU de Lille, Université de Lille II, Lille, France.
*****Emergency Department, CHRU de Lille, Université de Lille II, Lille, France.
******Department of Psychiatry, CHRU de Lille, Université de Lille II, Lille, France.
Please address correspondence and reprint requests to: Dr Guillaume Vaiva, Clinique Michel Fontan, Université de Lille II, 6 rue du Professeur Laguesse, 59037 Lille cedex, France. Email: gvaiva@chru-lille.fr

The last 10 years or so in Europe have seen the development of the "ecstasy" phenomenon, which is the symbol of recreational drugs in general. Users, either alone or in private parties, are on the increase. The phenomenon is most common in England and in the Netherlands, with an estimated incidence of 13% to 18% amongst the 18-to-25 year olds (Webb et al. 1996), which may reach 52% in "exposed populations," such as individuals who go to techno night clubs (Millman & Beeder 1994). In France, the prevalence is uncertain, but estimated to be at least 5% of males between 18 and 23 years old (Coste 1997).

Several substances with more or less the same effects are grouped together by the term ecstasy, the best-known one being 3,4-methylenedioxymethamphetamine (MDMA), but there are also N-demethylated derivative (MDA), methylenedioxyethylamphetamine (MDEA), N-methyl-benzodioxazolylbutanamine (MBDB) and 4-bromo-2,5-dimethoxyphenylethylamine (2-CB or Nexus).

The psychopathological consequences of MDMA use in man are poorly understood (Bailly 1999). On the basis of a series of cases reported in the literature, acute psychosis, chronic psychosis similar to paranoid delusions, flash-back phenomena similar to that with LSD, anxiety/panic states and depressive mood disorders may occur (INSERM 1998). The authors report the case of a young man who presented with his first-ever acute psychotic episode after taking a single dose of ecstasy without realising it. It was possible to examine his previous history, as well as his personality structure.

CLINICAL CASE

A 26-year-old man was admitted to the emergency room after attacking seven automobile drivers, pulling them out of their vehicles and destroying their car radios. He exhibited severe violence, which was not oriented and was incongruous. He had delusions: the mechanisms were intuitive and interpretative, the themes were supernatural, with reference delusions and an intense sense of persecution. At times, rapid mood changes were observed, mainly linked to the conviction that he had committed rape. He did not have hallucinations, but had some illusions.

The physical examination showed tachycardia (107 beats per minute), a blood pressure of 130/90, and a temperature of 38.2°C (signs confirming amphetamine intoxication). The toxicologic analysis done two days later

showed the following: (1) in the blood, no trace of toxic substances, no psychotropes and a serum alcohol of zero; and (2) in the urine, a positive sample for amphetamine-like substances (analysed by EMIT, or Enzyme Multiplied Immunoassay Technique), but negative for other drugs, including benzodiazepines and cannabis.

This young man had just obtained his private pilot's licence and had celebrated the event in the company of his peers. The party had taken place two days earlier, in a trendy night club where alcohol and techno music continued all night. His comrades had slipped a white round tablet with a horse-shaped emblem in the middle into a glass with an alcoholic drink, without his knowledge. They had bought it in the club for 100 French Francs as an ecstasy tablet. They had not noticed any problems during the night, and were quite satisfied with the effects of the product. The young graduates had left each other the next morning, drunk, but without any other ill effects. At the same time, a joint operation by the police and customs officials ended with seizure of a stock of identical pills (with an emblem shaped like a horse's head) in the Lille conurbation. There was a strong suspicion that certain night clubs in the city, including the one at which the patient had been, were getting rid of their drug stocks. Toxicological analysis of the pills showed that they contained 3,4-methylenedioxymethamphetamine.

The patient was treated with amisulpride (600mg/day) and cyamemazine (150mg/day during the 10 days of his hospitalisation). Two months after he was initially seen and treated in the emergency room, he wanted to contact the drivers he had attacked so that he could apologize. When he returned to the emergency room, he remembered all the details of his hospital stay without any errors. He said that at the time of his actions, he was convinced that he was taking part in a "role-playing game," to which he had to adhere completely. He only remembered part of what had happened at the beginning of the incident. His friends had left him and did not want to take him home. He had then walked along the street for one or two hours, gripped by intense agitation. He then returned to the night club and was thrown out because his behavior was violent and threatening towards the disk-jockey. He had very strong delusions: as soon as he heard the dance music, he saw it as a signal from something threatening that he had to eliminate. When he was arrested by the police, he was in the process of attacking motorists in order to destroy their car radios.

With his consent and the participation of his parents, a semi-structured evaluation interview (the MINI for DSM IV) was performed. At the time of the interview, he fulfilled the criteria for a mild major depressive episode. No other disorders were noted on Axis I, although some psychotic symptoms were still present (blunted affect, avolition, a lack of energy and interest, and incomplete judgement of the delusion). He was still taking 600mg/day of amisulpride. Previous to this incident, he fulfilled the criteria for a "social phobia" disorder of moderate intensity, without any disorder on Axis I or Axis II. The young man had a reserved, timid, inhibited temperament, but this did not affect his relationship or affective exchanges noticeably. He did not have a schizoid or borderline personality. He did not smoke, only drank alcohol occasionally, and did not take drugs (he had smoked cannabis once or twice when 19 years old). These facts were confirmed by his parents, as well as by the very comprehensive medical report from his pilot's school (the last examination had been one month before the acute episode).

The case reported here is therefore that of an acute psychotic episode, with residual symptomatology six months later, in an individual without any previous psychopathology other than moderate anxiety; it occurred suddenly following absorption of toxic substances (alcohol and ecstasy) at least 12 hours after he took an ecstasy tablet given without his knowledge.

DISCUSSION

Twelve cases of acute psychotic episodes after ecstasy ingestion have been reported in the literature. Two of them occurred after a single dose (McGuire, Cope & Fahy 1994; Gouxoulis et al. 1993) and one after two doses (Series et al. 1994). No author was able to examine the previous history of the individuals accurately, nor any possible psychopathological history. This patient had no previous history of psychosis as measured by a standardized validated interview; this was confirmed by his peers and family. He did, however, fulfil the DSM-IV criteria for social phobia. Retrospectively, the authors noted the extent of his psychomotor disinhibition with ecstasy, which seemed to be proportional to the intensity of his previous social inhibition. This point does not explain the psychotic episode.

From a neurobiologic point of view, acute psychotic disorders are often related to dysfunction of the mesolimbic dopaminergic system (Davis et al. 1991). During the first three hours, the effect of absorption of MDMA is a massive release of the serotonin, dopamine and noradrenaline stocks (White et al. 1996;Wilson et al. 1993; Schimdt & Kehne 1990); later, an acute hyposerotoninergic state is present (White et al. 1996). In our observation, the psychotic disorder in this case appeared at least 12 hours after taking ecstasy, during the reduction phase of the intoxication. Toxicological analysis of the blood was negative (this detection is only positive for 24 hours; see Verebey, Alrazy & Jarre 1988).

Like other authors, our hypothesis is that serotoninergic dysregulation affects the dopaminergic system (Rutty & Milroy 1997; White et al. 1996). Sudden disappearance of serotoninergic feedback on the dopaminergic pathways may contribute to an increase in the mesolimbic hyperdopaminergic state. In animals, it has been shown that serotonin depletion induced by MDMA unmasks the

effects of a hyperdopaminergic state (Baker & Makhay 1996). In addition, although it has not been mentioned much in the literature, MDMA disturbs dopaminergic function either directly (White et al. 1996; Schmidt & Kehne 1990), or through the peptidergic systems (neurotensin, substance P, dynorphines; Hanson 1989). A consistent series of arguments therefore suggest that there is a sudden central hyperdopaminergic state, which may be related to the appearance, sometimes *de novo*, of an acute psychotic disorder.

Other authors have described a lesion in the serotoninergic neurons by making a parallel with toxic effects described in animals, in particular in primates, with MDMA use (McGuire, Cope & Fahy 1994; Ricaurte & McCann 1992). Degradation of the serotoninergic cell bodies and nerve endings has been suggested to occur with high doses and/or repeated doses of MDMA. Other authors show the large variations in MDMA and MDA metabolism; the genetically determined "slow metabolizers" may therefore be particularly vulnerable to this type of toxicity, even after a single dose (Demirkiran, Jankovic & Dean 1992).

From the published cases, psychotic disorders following absorption of ecstasy appear to have become chronic (McGuire, Cope & Fahy 1994; Creighton, Black & Hyde 1991; McGuire & Fahy 1991; Schifano 1991). Most of the cases occurred in individuals who either abused multiple substances or were chronic ecstasy users. In a case like the one reported here, in an individual with good general health who is not a drug user and has an acute episode following a single dose, the prognosis should be good. Similarly, a team from Milan has described the experience of three friends who had a brief psychotic episode following ingestion of substances containing ecstasy. These episodes resolved completely after rehydration and anxiolytic treatment (Alciati et al. 1999). However, at six months' follow-up, our patient still has symptoms, albeit mild, that were not present before the intoxication. The patient and his psychiatrist do not envisage changing or stopping his antipsychotic treatment.

The nature of these symptoms remains difficult to interpret: (1) his mild depressive state may have contributed to his symptomatology, but does not explain the poor judgement occurring with the delirium; and (2) the symptoms described may be the result of a Parkinsonian syndrome, caused by the neuroleptics given after the incident. This hypothesis is the most difficult one to prove, since the intensity of the initial delusional symptoms and the violence exhibited by these patients often mean that treatment with neuroleptics is maintained for a long time, at considerable doses. The fact that this patient is very robust may have influenced the medical staff not to reduce the treatment too quickly. We can therefore not exclude the possibility that the symptomatology observed may have been caused by prolonged neuroleptic treatment. However, in this difficult diagnosis, the poor judgement associated with the delirium, and the feeling of strangeness which he continued to experience, do not allow the hypothesis that mild psychotic symptoms were present to be eliminated.

CONCLUSION

In Europe, the consumption of ecstasy is on the increase, especially from greater private use. The detailed clinical features of ecstasy intoxication still need to be defined, in particular the outcome. The context of psychotic episodes with ecstasy still needs further study, in order to improve knowledge about the premorbid state, and in particular about the personality profile. Nevertheless, although these factors may play a role in the first dose of the drug being taken and probably in the type of psychotropic effects felt, many arguments are in favor of the appearance of psychotic disorders *de novo*, probably due to direct toxicity of MDMA and/or its metabolites on the serotoninergic neurons. Biological vulnerability factors may be involved. The present observations show that these "accidental" acute psychotic episodes do not always have a favorable prognosis.

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