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1 **CASE REPORT**2 **Obsessive-compulsive disorder followed by psychotic episode in long-**
3 **term ecstasy misuse**4 **CARLO MARCHESI, MATTEO TONNA & CARLO MAGGINI**5 *Department of Neuroscience, Psychiatric Division, University of Parma, Italy*6 **Abstract**

7 *Aim.* We report the case of two young subjects who developed an obsessive-compulsive disorder (OCD) during a heavy use
8 of ecstasy. After several months of discontinuation of the drug, major depression with psychotic features developed in one
9 subject and a psychotic disorder in the other individual. No mental disorder preceded the use of ecstasy in any subject.
10 *Findings.* A familial and personality vulnerability for mental disorder was revealed in one subject, but not in the other, and
11 all physical, laboratory and cerebral NMR evaluations showed normal results in both patients. Remission of OCD and
12 depressive episode or psychotic disorder was achieved after treatment with a serotonergic medication associated with an
13 antipsychotic. *Conclusions.* The heavy long-term use of ecstasy may induce an alteration in the brain balance between
14 serotonin and dopamine, which might constitute a pathophysiological mechanism underlying the onset of obsessive-
15 compulsive, depressive and psychotic symptoms. The heavy use of ecstasy probably interacted with a vulnerability to
16 psychiatric disorder in one subject, whereas we cannot exclude that an “ecstasy disorder” ex novo affected the other
17 individual.

18 **Key words:** *Ecstasy, obsessive-compulsive disorder, major depression, psychosis, serotonin*19 **Introduction**

20 The use of ecstasy (MDMA) can induce acute
21 psychological effects including: (1) generally, eu-
22 phoria and reduction of negative thoughts; (2)
23 sometimes, hyperactivity, flight of ideas, insomnia,
24 hallucinations, depersonalisation, anxiety, agitation
25 and bizarre behaviour; (3) occasionally, panic at-
26 tacks, delirium, or brief psychotic episodes (Green
27 2003).

28 In addition, MDMA shows long-term effects,
29 which outlast the actual drug experience by months
30 or years, such as cognitive impairment, greater
31 impulsivity, panic attacks, recurrent paranoia, hallu-
32 cinations and severe depression (Kalant 2001; Green
33 2003).

34 An increase in serotonin (5-HT) and dopamine
35 (DA) release is the major mechanism underlying the
36 acute mental effects of ecstasy (Kalant 2001),
37 whereas the long-term effects have been suggested
38 to depend on a decrease of serotonergic function.

39 This damage has been clearly demonstrated
40 in animal experiments (Green 2003; Gouzoulis-
41 Mayfrank and Daumann 2006). In humans, one

postmortem study (Kish et al. 2000) reported severe
depletion (50–80%) of striatal 5-HT and 5-HIAA in
the brain of a 26-year-old male subject who had
regularly taken MDMA for 9 years. Moreover,
several studies found a reduction of 5-HIAA in the
cerebrospinal fluid of ecstasy users, and brain ima-
ging studies suggested a brain damage and glial
proliferation in heavy MDMA users (Gouzoulis-
Mayfrank and Daumann 2006). Therefore, some
evidence suggests that a long-term effect of MDMA
might induce brain alterations, particularly involving
the serotonergic system. However, some metho-
dological problems suggest caution to infer a causal
relationship between MDMA use, cerebral altera-
tions and the onset of psychopathological conditions
(Curran 2000).

We present the clinical history of two patients who
showed the onset of obsessive-compulsive disorder
(OCD) after a long period of use of ecstasy alone.
Moreover, many months after discontinuation of
MDMA, a depressive episode with psychotic fea-
tures developed in one patient and a psychotic
disorder in the other.

Correspondence: Carlo Marchesi, MD, Dipartimento di Neuroscienze, Sezione di Psichiatria, Università di Parma, Strada del Quartiere 2, 43100 Parma, Italy. Tel.: +39 521 703523 508. Fax: +39 521 230611. E-mail: carlo.marchesi@unipr.it

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Case one

A 16-year-old girl used ecstasy for 1 year (four to five tablets per week; total lifetime intake of about 200 tablets). After the first 2–3 months of MDMA consumption, the patient began to spend most of her time performing complex rituals before leaving or after returning home. The compulsive behaviour was associated with obsessive thoughts: obsessive phobias, numerical, symmetry and order obsessions, over-crowding of thoughts accompanied by poor insight and resistance. The disorder significantly interfered with her daily life: even automatic activity such as writing or walking became influenced by exact, compulsive rules. The great interference of compulsive behaviour led the patient to abandon the school. She discontinued MDMA use because she considered ecstasy responsible for the OCD. After discontinuation, the OCD improved but did not disappear. Three months later, the patient was hospitalised for the onset of a severe depressive episode with psychotic features and worsening of the OCD. Anamnestic information did not report the existence of mental disorders before the ecstasy use. Moreover, clinical evaluation showed the presence of major depression and delusional disorder in relatives. Finally, the patient was diagnosed, using the Structured Interview for DSM-IV personality disorders (Pfohl et al. 1997), as affected by a borderline personality disorder. All physical, laboratory and cerebral NMR evaluations failed to show abnormal results. After 2 months of treatment with an antidepressant (clomipramine) and an antipsychotic (olanzapine), remission of depressive episode and OCD was achieved.

Case two

A 23-year-old man started to use MDMA at 20 years of age and stopped the drug use after more than 2 years of consumption (one to two tablets per week for a total lifetime intake of about 150 tablets) because of the sudden onset of obsessions of contamination. The obsessions were associated with a compulsive potomanic behaviour, justified by the patients the need for “inner” purification. The severity of symptoms induced a water intoxication and the patient was hospitalised in a medical ward. After discharge, the obsessions of contamination worsened and were associated with different and complex compulsive acts of purification which caused great interference in his daily life; particularly, he was unable to work and to attend his daily activities. Eight months after MDMA discontinuation, a psychotic disorder developed and the patient was hospitalized in a psychiatric clinic. All

physical, laboratory and cerebral NMR evaluations failed to show abnormal results. Anamnestic information and clinical evaluations did not support the existence of a mental or a personality disorder before the use of ecstasy. Moreover, no mental disorder was found in any relative. He was treated with an antipsychotic (risperidone) and a serotonergic antidepressant (sertraline). A complete remission of both psychotic and obsessive-compulsive symptoms was achieved only after 1 year of treatment.

Discussion

These case reports raise the question about the causal relationship between ecstasy misuse and onset of mental disorders. It is not easy to answer the question of whether MDMA induced psychopathological conditions in these subjects. However, we must take into account several findings.

No mental disorder affected the two patients before the use of ecstasy. Therefore, we can exclude that they used ecstasy as a self-medication for a pre-existing depressive or anxiety disorder, as suggested by previous studies (Curran 2000; Lieb et al. 2002; Huizink et al. 2006).

During the abuse of ecstasy, the two patients did not use any other drugs. Almost only poly-drug abusers were evaluated in previous studies investigating psychopathological effects of ecstasy. Concomitant opiate and alcohol addiction was found to be a risk factor for developing mental disorders in ecstasy users (Schifano et al. 2000).

The two patients first developed OCD after long-term use of ecstasy. In agreement with this finding, in a previous study Parrott et al. (2001) observed higher scores in OC subscale of SCL-90 in heavy ecstasy poly-drug users than in control subjects; more recently (Lieb et al. 2002), the prevalence of OCD was found to be twice as frequent in MDMA users than in non-users. However, the onset of OCD followed the drug abuse in only a minority (16%) of ecstasy users.

A dysfunction of the serotonergic system has been hypothesized to underline the development of OCD in non-addicted subjects (Aouizerate et al. 2004; Chamberlain et al. 2005). In fact, the specific treatment response to serotonergic medications and the transient exacerbation of symptoms after a pharmacological challenge with specific 5HT agonists suggest that an imbalance of 5HT is involved in the pathogenesis of OCD (Zohar et al. 2000; Micallef and Blin 2001).

A psychotic depressive episode or a psychotic disorder developed in the patients some months after MDMA discontinuation. Previous studies reported a high prevalence (nearly 30%) of depression

in MDMA users (Schifano et al. 1998; Topp et al. 1999; Lieb et al. 2002). Interestingly, in a high percentage (40%) of the ecstasy users major depression developed after drug abuse (Lieb et al. 2002). Also psychosis is a well-documented psychopathological condition associated with MDMA use (McGuire et al. 1994; Schifano et al. 1998; Topp et al. 1999; Curran et al. 2004). However, psychosis induced by ecstasy use is generally a short-lasting disorder (Topp et al. 1999; Curran et al. 2004), whereas in our patient the psychotic symptoms remitted after 1 year of treatment.

The association between OCD and major depression or psychotic disorder is a well-documented clinical condition in non-addicted patients (Aouizerate et al. 2004; Chamberlain et al. 2005). Recently, this association has been investigated in neurophysiological, neuropsychological and neuroimaging studies (Aouizerate et al. 2004; Poyurovsky et al. 2004; Chamberlain et al. 2005; Bottas et al. 2005). The 5HT/DA dysfunction in cortical-striatal-thalamic-cortical pathways has been suggested as a possible pathophysiological mechanism underlying the association between obsessive-compulsive, depressive and psychotic symptoms in non-addicted patients.

Acutely, MDMA is known to increase 5HT and DA activity, whereas long-term use decreases 5HT function (this effect was observed after using ecstasy 25 times) (McCann et al. 1998). The long-term effect on the DA system appears to be more controversial (Green et al. 2003; Goñi-Allo et al. 2006). Therefore, the MDMA effect on the serotonergic and probably on the dopaminergic system might be involved in the onset of psychopathological conditions, such as major depression, anxiety and psychotic disorders, in ecstasy users. In accord with this hypothesis, a higher incidence of these disorders was found in subjects with pre-existing MDMA misuse (Lieb et al. 2002), particularly in heavy users (Schifano et al. 1998).

Mental disorders do not develop in all ecstasy users. Therefore, a pre-disposition to psychiatric illnesses may need to exist for psychopathological symptoms to develop in some ecstasy users.

In view of these observations, a specific causal role as a primary risk factor for the onset of mental disorders in our patients cannot be attributed to ecstasy with certainty, even though heavy use of the drug lasted several months and was followed by mental disorders. However, in one of our patients ecstasy misuse probably interacted with a vulnerability to psychiatric disorders. In fact, the girl was affected by a borderline personality disorder which predisposes people to suffer from several mental disorders, such as substance abuse, depression,

anxiety and eating disorders (Skodol et al. 2002; Lieb et al. 2004). Moreover, this patient also showed a familial vulnerability to major depression and psychotic disorder (Shih et al. 2004). In contrast, the young man did not show any personality or familial predisposition to mental disorders. However, we cannot exclude that this patient might have been vulnerable to psychotic disorders, because his psychotic disorder lasted much longer than the usual ecstasy-induced psychosis (Curran et al. 2004). Therefore, the onset of the mental disorder in the girl was probably induced by the interaction between ecstasy misuse and personality and familial vulnerability rather than representing an *ex novo* "ecstasy disorder". In contrast, it is difficult to say whether an *ex novo* "ecstasy disorder" affected the young man.

Conclusion

Our case reports suggest that the assessment of personality and psychiatric family history in ecstasy users might be a useful clinical tool: (1) to identify a predisposition for the development of mental disorders; (2) to verify the association between ecstasy abuse and the onset of a specific mental disorder in vulnerable individuals; and (3) to clarify whether ecstasy may induce mental disorders in absence of other risk factors.

Statement of interest

The authors have no conflict of interest with any commercial or other associations in connection with the submitted article.

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