

Symptoms of anxiety and depression in childhood and use of MDMA: prospective, population based study

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Abstract

Objective To investigate whether using ecstasy (3,4-methylenedioxymethamphetamine, MDMA) is preceded by symptoms of behavioural and emotional problems in childhood and early adolescence.

Design Prospective, longitudinal, population based study

Setting The Dutch province of Zuid-Holland.

Participants A sample of 1580 individuals, followed up across a 14 year period, from childhood into adulthood.

Main outcome measures The first assessment took place in 1983 before MDMA appeared as a recreational drug in the Netherlands and included the child behaviour checklist to obtain standardised parents' reports of their children's behavioural and emotional problems. Use of the drug was assessed with the composite international diagnostic interview 14 years later.

Results Eight syndrome scales of childhood behaviour were examined. Scores in the deviant range for the scales designated as anxious or depressed in childhood were significantly related to use of MDMA in adolescents and adults, resulting in an increased risk (hazard ratio 2.22, 95% confidence interval 1.20 to 4.11, $P=0.01$).

Conclusions Individuals with childhood symptoms of anxiety and depression may have an increased tendency to use MDMA in adolescence or young adulthood. Its effects are supposed to include enhanced feelings of bonding with other people, euphoria, or relaxation. Especially individuals with symptoms of anxiety or depression may be susceptible to these positive effects.

Introduction

In the Netherlands, ecstasy (3,4-methylenedioxy-methamphetamine, MDMA) became available at dance parties from 1985 onwards. The lifetime prevalence of users aged 20-24 increased from 6.2% in 1997 to 13.2% in 2001, and the prevalence of MDMA use in the preceding month also increased, from 1.9% in 1997 to 2.9% in 2001.¹ Several studies have indicated that using MDMA is associated with emotional health problems, such as depression, psychotic symptoms, and anxiety disorders.²⁻⁵ These may represent two pathways: either emotional problems are a consequence of using MDMA, or emotional problems lead to ecstasy use—for example, in order to “self medicate” symptoms. These pathways are not mutually exclusive. Most authors argue for the first option and refer to neurotoxic effects of MDMA on serotonergic neurones. However, one study has shown that the first use of MDMA was secondary to phobias, somatoform disorders, dysthymia, and panic disorder or agoraphobia.³

We investigated whether use of MDMA is preceded by symptoms of behavioural and emotional problems

in childhood and early adolescence. We assessed MDMA use in a sample of 1580 individuals, followed up for a period of 14 years, from childhood into adulthood. The first assessment took place in 1983 before MDMA appeared as a recreational drug in the Netherlands. This offered a unique opportunity to investigate if a pathway exists from behavioural and emotional problems leading to MDMA use.

Methods

Participants

This study was part of an ongoing longitudinal study that started in 1983 in the Dutch province of Zuid-Holland. A random sample of 2600 children and adolescents aged 4-17 was drawn from municipal registers that list all residents. Of the 2447 parents contacted, 2076 (84.8%) cooperated. After the first measurement (1983), the sample was approached again in 1985, 1987, 1989, 1991, and 1997.^{6,7}

In 1997 we reassessed 1580 individuals with the computerised version of the composite international diagnostic interview⁸ to determine psychiatric diagnoses. The response rate was 79%. Scores for 1983 from the child behaviour checklist scores were similar for dropouts and for children who remained in the study.

Procedures

In 1983 the child behaviour checklist (CBCL)⁹ was used to obtain standardised parent reports of their children's behavioural and emotional problems in the preceding six months. The checklist includes 120 problem items, and eight syndrome scores are derived: withdrawn, somatic complaints, anxious or depressed, social problems, thought problems, attention problems, delinquent behaviour, and aggressive behaviour. We dichotomised syndrome scores on the CBCL as deviant and non-deviant (see bmj.com).

At follow-up, in 1997, we used the lifetime version of the composite international diagnostic interview (CIDI), version 2.1,⁸ to assess use of MDMA. This instrument allows for the standardised assessment of psychiatric symptoms, syndromes, and diagnoses of a wide range of substance use and mental disorders, along with information about onset, duration, and clinical and psychosocial severity. We defined lifetime use of MDMA as having used the drug on at least five occasions, to indicate only those users who progressed from experimentation with the drug to more regular use. We also assessed age at first use (onset).

Statistical analyses

We conducted Cox regression analyses to determine whether behavioural and emotional problems in child-

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hood or early adolescence, measured in 1983, were a risk factor for later use of MDMA. We defined survival time in years as age at onset of use of MDMA, or, if this did not occur, as the age at the final assessment, in 1997. We computed hazard ratios that indicate a considerable association between behaviour and emotion in 1983. We adjusted for possible cohort effects by fitting stratified Cox regressions, in which we used age groups in 1983 as strata, and further adjusted for the possible effects of socioeconomic status and tested for interaction effects of sex with the predictors (see bmj.com).

Results

Descriptive analyses

The mean age of participants was 9.9 in 1983 (range 4-17) and 24.5 in 1997 (range 18-33). In 1997, 98 study participants (4.7% of the total sample)—64 male and 34 female—reported using MDMA on at least five occasions. Table 1 shows the numbers of participants in the deviant range groups.

Ninety MDMA users (92%) had also experimented with other drugs, most commonly with cannabis, 58 with cocaine (59%), and 43 with psychedelic drugs (44%). Most (59) MDMA users had tried cannabis only once (60%), whereas of those who used both cocaine and ecstasy, 63 tried cocaine two to four times (64%) and those who used psychedelic drugs and MDMA used these on two to four occasions (49%, n = 48) or even on at least five occasions (49%, n = 48).

Survival analyses

On the basis of the associations shown in table 2 for separate Cox regression analyses, we included predictors with P values < 0.10 in the next model. Scores within the deviant range of the anxious or depressed syndrome scale and delinquent behaviour syndrome scale in 1983 were used as predictors in the multivariate model. This was stratified for age, and adjusted for socioeconomic status and sex. The final model included only one significant predictor—scores within the deviant range of the anxious or depressed syndrome scale at baseline (1983) on MDMA use, resulting in an increased risk on later MDMA use (hazard ratio 2.22, 95% confidence interval 1.20 to 4.11, P = 0.01).

Table 1 Number (percentages) of subjects in deviant range groups and number of subjects within deviant range groups that reported to have used ecstasy in 1997

CBCL scale in 1983	Boys in deviant range*	Boys in deviant range, using MDMA in 1997†	Girls in deviant range*	Girls in deviant range, using MDMA in 1997†
Withdrawn	60 (8)	4 (7)	68 (8)	2 (3)
Somatic complaints	39 (5)	3 (8)	34 (4)	0 (0)
Anxious/depressed	61 (8)	9 (15)	58 (7)	3 (5)
Social problems	66 (9)	2 (3)	79 (9)	2 (3)
Thought problems	26 (4)	3 (12)	16 (2)	0 (0)
Attention problems	95 (13)	6 (1)	75 (9)	1 (1)
Delinquent behaviour	92 (13)	13 (14)	56 (7)	0 (0)
Aggressive behaviour	99 (14)	8 (8)	87 (10)	0 (0)

In 1983, 1016 boys and 1060 girls were included in the study, and in 1997, 732 male subjects and 848 female subjects. At follow-up in 1997, 64 (9%) male subjects and 34 (4%) female subjects used MDMA.

*The percentages reflect the number of individuals with scores in the deviant range of the respective syndrome scales divided by the number of (male or female) individuals in 1997.

†The percentages reflect the number of individuals who used MDMA in 1997 divided by the number of individuals with scores in the deviant range of the respective syndrome scales.

Table 2 Separate Cox regression analyses for each syndrome on the childhood behaviour checklist (CBCL)

CBCL scale in 1983	Hazard ratio (95% CI)	P value
Withdrawn	0.97 (0.43 to 2.24)	0.95
Somatic complaints	0.73 (0.23 to 2.30)	0.58
Anxious or depressed	2.22 (1.20 to 4.11)	0.01
Social problems	0.73 (0.27 to 2.00)	0.54
Thought problems	1.64 (0.51 to 5.22)	0.40
Attention problems	0.86 (0.39 to 1.87)	0.70
Delinquent behaviour	1.81 (1.00 to 3.28)	0.05
Aggressive behaviour	0.94 (0.45 to 1.95)	0.87

Associations were stratified for age and adjusted for socioeconomic status and sex.

Associations are shown between each CBCL syndrome scale measured in 1983 and MDMA use measured in 1997.

Discussion

We found evidence for an increased risk for use of MDMA in individuals who scored in the deviant range of the anxious or depressed score of the child behaviour checklist in 1983. These problems in childhood and early adolescence preceded the use of MDMA, since measurement took place before MDMA appeared in the Netherlands.

Comparison with other studies

These findings partly confirm previous findings of Lieb et al, who showed that subjects with emotional disorders such as phobia, and somatoform conditions at baseline (age 14-24) showed a significantly increased risk of starting to use MDMA during a four year follow-up period,³ though assessment of MDMA use was retrospective and may have been subject to recall bias.

We found an effect of symptoms of anxiety and depression on later MDMA use for male and female participants. This finding contradicts other, mostly cross sectional, studies showing the strongest association between depressive and anxiety symptoms and substance use in young women.^{10 11} However, these associations have been examined in clinical samples, including individuals with more serious psychiatric and substance use disorders than our population based sample.

Meaning of the study

Although we performed multiple tests, the results imply that individuals with childhood symptoms of anxiety and depression may have an increased tendency to use MDMA since the drug's effects are supposed to include enhanced feelings of bonding with other people, euphoria, or relaxation. Alleviation of depressed mood, desire for an altered state of mind, desire to escape, and self medication are among often mentioned reasons to use MDMA.

Possible reasons for using MDMA

In animals, chronic exposure to MDMA results in inhibition of serotonin reuptake into the neurone and serotonin synthesis, and destruction of serotonergic axon terminals.¹² This decreased availability of serotonin in the central nervous system has been proposed as the basis for the symptoms of depression.^{13 14} However, our findings show that individuals who already had depressive symptoms in childhood or adolescence have an increased risk of starting to use MDMA. This may still affect the serotonin system,

What is already known on this topic

The use of ecstasy (3,4-methylenedioxymethamphetamine, MDMA) is associated with emotional health problems, such as depression, psychotic symptoms, and anxiety disorders

Insight into temporal pathways that explain links between emotional problems and ecstasy use is lacking

What this study adds

Individuals with childhood symptoms of anxiety and depression may have an increased tendency to use ecstasy in adolescence or young adulthood

Focusing on these vulnerable individuals in future studies will increase our insight into the potential harmful effects of MDMA on brain neurotransmitter systems and associated psychopathology

which may increase the risk of these individuals developing a mood disorder later. Other mechanisms may be involved, for example, a common underlying genetic vulnerability may account for both symptoms of mood disorders and the propensity to use drugs such as ecstasy; depression in parents has been shown to be associated with depression and substance use disorders in offspring.

Other factors may account for the increased tendency to use MDMA such as peer pressure, the desire to party, novelty seeking, other drug use of adolescents, social roles in peer groups, substance use of parents, and bad parenting practices.

Conclusion

Our findings give evidence for a temporal pathway, in which childhood symptoms of anxiety and depression may precede use of MDMA. The reward mechanisms involved in the plausible "self medication" attempts of vulnerable individuals need to be examined, to prevent

adolescents and young adults from using MDMA regularly.

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A memorable patient

When a medical qualification is not good enough

I was born into a medical family, and I clearly recollect saying, at the age of 4, that I was going to be a doctor like my father: this predated my older sister's and brother's decisions to read medicine. My father had joined his father in general practice, and two of his brothers also became GPs. My mother, whose parents were both medically qualified, was in the same year at medical school as my father and was also a partner in the practice.

Patients certainly appreciated the continuity of family care, though I was to learn that their approbation concealed underlying expectations.

I received a call during a Tuesday evening surgery some 25 years ago, requesting advice about a patient. This woman was in her late 60s and had had a visit the day before from my GP registrar for diarrhoea and a presumptive diagnosis of gastroenteritis. He had examined her and suggested fluids and symptomatic treatment. She was staying with a friend outside the practice area, but I agreed that, if she could be brought home, I

would visit her after surgery. This I duly did and could not find anything to suggest any other pathology; I duly noted her dry tongue and thirst, which I attributed to mild dehydration.

Her friend took her back so as to look after her and called in a deputy GP the next day, and his own doctor the day after, who admitted her to hospital, where, she was to tell me later, it took another day to make the diagnosis. I went to see her after she was discharged and apologised for the delay in her receiving appropriate treatment. I said my only defence was that new onset, non-ketotic diabetic hyperglycaemia was uncommon and at least four other doctors had also failed to make the diagnosis.

She replied that she could forgive all the others, but not me—I should have done better because I was a Houghton.

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