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ORIGINAL INVESTIGATION

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Self-reported psychopathological symptoms in recreational ecstasy (MDMA) users are mainly associated with regular cannabis use: further evidence from a combined cross-sectional/longitudinal investigation

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Abstract *Rationale:* 3,4-Methylenedioxymethamphetamine (MDMA, ecstasy) has become a widely used recreational drug among young people. This is of great concern, since MDMA is neurotoxic in animal studies and its use has been associated with psychological distress and a variety of self-reported psychiatric symptoms. However, exploring the origins of psychopathology in ecstasy users is hampered by the frequent polydrug use and by the cross-sectional design of all investigations, so far. *Objectives:* The present study combines a cross-sectional with a longitudinal approach to further clarify the impact of the use of other illicit drugs on psychopathological symptoms reported by ecstasy users. *Methods:* At baseline, we administered self-rating scales for impulsivity, sensation seeking and general psychological complaints to 60 recreational ecstasy users and 30 matched controls. From the initial sample of ecstasy users, 38 subjects were re-examined 18 months later. *Results:* At baseline, ecstasy users reported significantly more psychological complaints than controls. However, self-reported psychopathology was mainly associated with regular cannabis use. At follow-up, subjects who had abstained from ecstasy use during the follow-up period did not differ from those reporting continued consumption. In contrast, subjects with regular concomitant cannabis use during the follow-up period reported more anxiety, interpersonal sensitivity and obsessive-compulsive behaviour than cannabis-abstinent users. Finally, higher levels of obsessive-compulsive behaviour, interpersonal sensitivity, depression, anxiety, phobic anxiety and paranoid ideation were significantly correlated with the duration of regular interim cannabis use. *Conclusions:* The present findings suggest that self-reported psychopathology in ecstasy users is predominantly attributable to concomitant use of cannabis. Abstinence from cannabis and not ecstasy seems to be a reliable predictor for remission of psychological complaints in ecstasy users.

Keywords MDMA · THC · Cannabis · Ecstasy · SCL-90-R · Psychopathology

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Introduction

3,4-Methylenedioxymethamphetamine (MDMA, ecstasy) has become a widely used recreational drug among young people. According to a German epidemiological study, 5.1% of 14- to 15-year-olds and 7.1% of young adults have tried ecstasy at least once (Speck and Reimers 1999). Several studies in other western European countries and the USA indicate similar frequencies and suggest that the popularity of ecstasy is still on the rise (Ramsey and Spiller 1997; Abraham et al. 1998; Tasker et al. 1999; Johnston et al. 2000; Strote et al. 2002).

This is of great concern, since both anecdotal evidence and large naturalistic studies relate the use of ecstasy to a variety of psychopathological conditions and self-reported psychological problems such as anxiety, obsessive-compulsive behaviour, somatisation, panic attacks, eating disorders, depersonalisation, derealisation, flashbacks, hallucinations, paranoid delusions and other psychotic phenomena (Benazzi and Mazzoli 1991; Pallanti and Mazzi 1992; McGuire et al. 1994; Jansen 1997; Schifano et al. 1998). Furthermore, in group studies using standardised psychometric instruments, ecstasy users were shown to exhibit a broad range of psychopathology,

including high impulsivity, depression, anxiety, psychoticism, paranoia, obsessionality, hostility, altered appetite and sleep disturbances (Morgan 1998; Gamma et al. 2000; McCann et al. 2000; Milani et al. 2000; Parrott et al. 2000a, 2000b, 2001; Daumann et al. 2001; Dughiero et al. 2001; Morgan et al. 2002; Thomasius et al. 2003).

It has been suggested that MDMA's pharmacological properties may play a crucial role in the development of these psychological disorders in regular users (Parrott et al. 2001; Soar et al. 2001). MDMA has a well recognised neurotoxic potential upon central serotonergic systems in animal studies (Ricaurte et al. 1992, 2000). There is growing evidence that these toxic effects can be very long lasting or even permanent (Fischer et al. 1995; Hatzidimitriou et al. 1999) and may also occur in humans (McCann et al. 1998, 2000; Reneman et al. 2001). Serotonin (5-HT) is thought to be involved in the modulation of numerous functions including cognition and mood. In particular, 5-HT has been identified as a key neurotransmitter in the aetiology of depression and it plays an important role in other psychiatric disorders, including schizophrenia, anxiety and obsessive-compulsive disorder (Naughton et al. 2000).

However, exploring the origins of psychopathology in ecstasy users is hampered by the cross-sectional design of the investigations. Hence, it is unclear whether the psycho(patho)logical findings reflect a direct or indirect consequence of ecstasy use or whether it is rather a poor premorbid adjustment, which leads to drug abuse and increases the likelihood of developing a manifest psychiatric disturbance. In addition, the frequent polydrug use pattern of ecstasy users makes it very difficult to relate abnormal findings to the use of one substance alone. Schuster et al. (1998) reported that approximately 97% of ecstasy users consume additional illicit drugs, mainly cannabis and (meth)amphetamine, but also LSD, cocaine and psilocybin. Furthermore, it has been suggested that psychopathology in ecstasy users may be associated with polydrug, rather than ecstasy use (Parrott et al. 2001; Thomasius et al. 2003). In particular, there is some evidence that concomitant use of cannabis may play an important role in regard to self-reported psychological distress in ecstasy users (Daumann et al. 2001; Morgan et al. 2002).

Promising strategies to disentangle long-term sequelae of ecstasy use from pre-existing abnormalities and/or effects of other drugs include longitudinal studies with user populations and prospective studies of young people who are at risk of developing drug use. So far, only one recent investigation dealing with the relationship between ecstasy use and mental disorders has chosen such a prospective-longitudinal approach (Lieb et al. 2002). In this study, ecstasy users had significantly higher rates for almost all mental disorders according to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV). However, the authors concluded that mental disorders were more likely to precede rather than to follow the onset of ecstasy use (Lieb et al. 2002). The current investigation combines a cross-sectional with a longitudinal approach to clarify the impact of the use of ecstasy and other illicit drugs on psychopathological symptoms reported by ecstasy users, who did not have a current or previous axis I psychiatric diagnosis except for drug abuse, over a period of 18 months.

Materials and methods

Participants

At baseline (t_1), 60 ecstasy users were recruited directly in the dance scene by students who were involved in the study, via word-of-mouth and via the internet. This sample was fully independent from the sample of a previous investigation of our group (Daumann et al. 2001). Concomitant use of other typical club drugs (amphetamines, cocaine, cannabis and LSD) was tolerated. However, subjects were excluded if they reported substantial use of alcohol (defined as drunkenness occurring at a frequency of at least twice per month over 6 months or longer within the last 2 years), or regular use of other legal or illegal psychotropic drugs such as opiates and benzodiazepines (defined as use once per month or more frequently over 6 months or longer within the last 2 years). The control group (t_1) consisted of 30 healthy persons who were matched for age, sex and level of education with the MDMA users and had no previous or current history of alcohol or drug use other than moderate use of cannabis. We were able to re-examine 38 users 18 months after the initial examination (t_2). Twenty-two participants did not participate in the follow-up study. Fifteen subjects moved without giving notice of their new address, four participants simply lost interest in the study, one subject served a sentence as a consequence of drug dealing and two subjects developed a manifest psychiatric disorder and were, therefore, excluded from the follow-up.

For both baseline and follow-up, all ecstasy users agreed to abstain from drug use for at least 7 days prior to the study with the exception of cannabis. Because daily moderate cannabis use was part of the life style of many subjects and because cannabis screens may remain positive for several weeks after the last use (thus making it impossible to verify reported abstinence), we accepted that most subjects would only abstain from cannabis on the study day. All subjects underwent a structured interview according to the DSM-IV (SCID). In addition, we took a medical history and detailed history of drug use. Drug screens were performed on the study day with urine samples for stimulant amphetamines, methylenedioxyamphetamines (ecstasy), cocaine and its metabolite, marijuana, benzodiazepines, barbiturates and opiates. Exclusion criteria for all participants were: (1) a positive drug screen on the study day except for cannabis; (2) any current or previous axis I psychiatric diagnosis except for drug abuse in the user group; and (3) any organic brain disorder or relevant general medical condition requiring pharmacological treatment. After detailed description of the study to the subjects, written informed consent was obtained and subjects were paid for their participation. The study was in accordance with the Helsinki Declaration of 1975 and was approved by the local ethics committee at the RWTH Aachen.

Self-rating scales

Subjects completed the following self-questionnaires for the assessment of psychological dimensions which were already shown to be affected in ecstasy users in former studies (Daumann et al. 2001; Morgan et al. 2002; Thomasius et al. 2003).

Sensation Seeking Scale SSS V (Zuckerman et al. 1978)

This scale measures individual differences in sensation seeking along four dimensions: thrill and adventure seeking, experience seeking, disinhibition, and boredom susceptibility.

Barratt Impulsivity Scale BIS (Barratt 1985)

This self-questionnaire consists of three subscales: attentional impulsivity, motor impulsivity and non-planning impulsivity.

Symptom Checklist-90-Revised SCL-90-R (Derogatis 1994)

This broadly used checklist assesses primary symptom dimensions (somatisation, obsessive-compulsive behaviour, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism) and global indices of psychological distress (global severity index, positive symptom distress index and positive symptom total).

Statistical analyses

The cross-sectional demographic data and group differences regarding psychometric scores (t_1) were analysed by means of unpaired Student's *t*-test. In addition, self-reported psychopathology was correlated with the reported patterns of drug use. Longitudinal effects were computed in terms of change scores (t_2–t_1) regarding self-reported psychopathology. In order to obtain information about the impact of ecstasy and cannabis use on psychological symptoms different groups of users were defined on the basis of the reported drug use during the follow-up period. These groups were then compared by means of unpaired Students' *t*-test. In addition, psychometric change scores were correlated with the interim drug use. All procedures were performed using SPSS version 11.0 (SPSS Inc., Chicago, Ill., USA). Thresholds of $P<0.05$ were considered significant.

Results

Sociodemographic data and drug histories

Sociodemographic data are presented in Table 1. The two groups were identical in terms of sex distribution and they were similar in terms of age and level of education. The patterns of drug use at baseline (t_1) are presented in Table 2. All 60 drug users reported regular use of ecstasy. Forty-four users reported both concomitant regular amphetamine and cannabis use, and 17 users reported LSD consumption. In general, a higher extent of ecstasy use was most notably correlated with a higher extent of amphetamine use (estimated lifetime dose: $r=0.468$, $P<0.001$; duration of regular use: $r=0.548$, $P<0.001$; average frequency of use: $r=0.335$, $P=0.026$; age at onset of use: $r=0.699$, $P<0.001$) use but also with cannabis use (duration of regular use: $r=0.418$, $P=0.002$). The control group denied regular drug use except for mild cannabis use in eight subjects. The patterns of interim drug use from baseline to 18-month follow-up are presented in Table 3. Fifty percent of the former ecstasy users reported complete abstinence from ecstasy over the entire follow-up period. In addition, 50% of the sample reported abstinence from cannabis use during the follow-up period. Eight subjects reported both abstinence from cannabis and

Table 1 Demographic data of ecstasy users ($n=60$) and controls ($n=30$) at baseline (t_1)

	Ecstasy users	Controls
Mean age in years (mean±SD)	24.6±3.97	25.37±2.72
Men:women	42:18	21:9
Level of education		
Basic school-leaving exam after form 9 (*Hauptschulabschluß*)	6	3
Intermediate school-leaving exam after form 10 (*Realschule/ mittlere Reife*)	20	10
Highest school-leaving exam qualifying for admission to college/university after form 12 or 13 (*Fachabitur/Abitur*)	32	17
University degree (*Hochschulabschluß*)	2	–

Table 2 Patterns of lifetime drug use in ecstasy users ($n=60$) and controls ($n=30$) at baseline (t_1): mean values and standard deviations. *THC* tetrahydrocannabinol (cannabis); *x* subjects felt that they were unable to give a reliable estimate

	Ecstasy Ecstasy users	Cannabis		Amphetamine Ecstasy users	LSDE cstasy users
		Ecstasy users	Controls		
Subjects reporting use	60	44	8	44	17
Estimated lifetime dose	271.3±454.4 pills	x	x	137.3±352.2 g	44.6±142.6 trips
Duration of regular use (months)	28.5±29.5	56.6±47.3	20.4±38.7	24.3±28.4	12.0±34.7
Average frequency of use (days per month)	3.1±2.8	17.0±12.9	4.3±9.1	5.7±7.8	0.7±1.5
Average daily or one night dose	2.0±1.5 pills	633.0±600.5 mg	182.2±421.9 mg	396.±450.8 mg	0.5±1.0 trips
Age at onset of use	19.8±3.7	15.7±2.6	18.1±2.4	18.9±3.8	18.7±4.4
Time since last dose in days	218.3±374.9	20.3±81.5	16.7±19.6	212.6±375.0	682.2±705.3
THC-screen in urine sample on study day	–	31 positive/29 negative	4 positive/26 negative	–	–

Table 3 Patterns of drug use in ecstasy users (n=38) in the 18-month period between t_1 and t_2: mean values and standard deviations. *THC* tetrahydrocannabinol (cannabis); *x* subjects felt that they were unable to give a reliable estimate

	Ecstasy	Cannabis	Amphetamine	LSD
Subjects reporting use	19	19	6	4
Estimated interim dose	21.1±38.46 pills	x	17.7±38.3 g	6.68±24.1 trips
Duration of regular use (months)	8.95±2.11	11.4±8.7	5.0±8.3	0.9±3.8
Average frequency of use (days per month)	0.6±1.2	15.0±13.1	1.0±2.1	0.4±1.5
Average daily or one night dose	1.0±1.0 pills	447.2±379.0 mg	207.9±409.7 mg	0.2±0.3 trips
Time since last dose in days	206.1±431.9	20.1±61.5	33.0±29.8	97.5±96.0
THC-screen in urine sample on study day	–	17 positive/21 negative	–	–

Table 4 Significant correlations between drug use and psychometric scores in ecstasy users (n=60) at baseline (t_1). *x* subjects felt unable to give a reliable estimate; – no significant correlation

	Ecstasy	Amphetamine	Cannabis
Age at onset of use	Obsessive-compulsive behaviour (–0.30)*, interpersonal sensitivity (–0.32)*, depression (–0.30)*, paranoid ideation (–0.28)*	–	Motor impulsivity (–0.35)*
Estimated life-time dose	–	Depression (0.26)*, anxiety (0.39)*, phobic anxiety (0.29)*	x
Duration of regular use	–	–	–
Average frequency of use	–	Anxiety (0.29)*	Obsessive-compulsive behaviour (0.41)*, interpersonal sensitivity (0.32)*, depression (0.30)*, anxiety (0.36)*, aggression/hostility (0.46)**, phobic anxiety (0.37)**, paranoid ideation (0.37)**, psychoticism (0.29)*
Average daily or one night–dose		Depression (0.27)*, anxiety (0.33)*, phobic anxiety (0.29)*, psychoticism (0.35)*	Thrill/adventure seeking (0.32)*, obsessive-compulsive behaviour (0.26)*, depression (0.33)*, anxiety (0.29)*
Time since last dose	–	–	–

* P<0.05, **P<0.01 (significance of correlation)

ecstasy over the follow-up period. Interim consumption of amphetamine and LSD was reported only by few subjects.

Psychometric self-ratings

Cross-sectional analyses (t_1)

Group mean scores on each subscale of the SCL-90-R are illustrated in Fig. 1. With the exception of depression, ecstasy users reported significantly more complaints on every subscale. In addition, ecstasy users scored higher on the BIS non-planning impulsivity subscale (t=2.532, P=0.014) and the SSS V experience seeking subscale (t=2.630, P=0.011). Significant coefficients of correlation between drug use and psychometric scores at baseline are presented in Table 4. The age of onset of ecstasy use correlated with four subscales of the SCL-90-R. The extent of reported amphetamine use was mainly associated with depression and anxiety. Prior cannabis use, and most notably the frequency of use was positively correlated with sensation seeking and every subscale of the SCL-90-R with the exception of somatisation. Finally, when controlling for the frequency of cannabis use in terms of partial correlation analyses no association between ecstasy/amphetamine use and psychopathology remained significant.

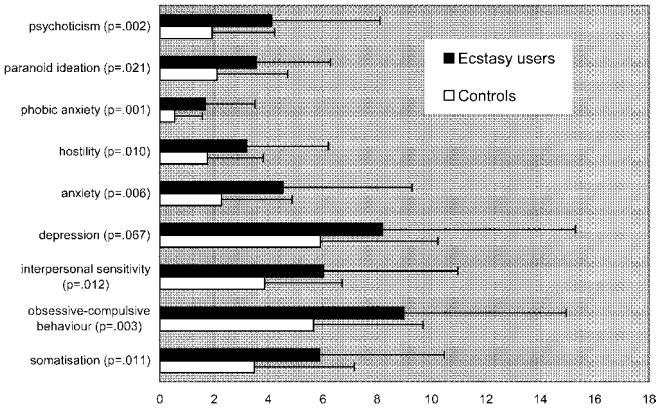

Fig. 1 Self-reported psychopathological symptoms (SCL-90-R subscales) at baseline (t_1): mean values and standard deviation in ecstasy users (n=60) and controls (n=30). P significance of group differences (Student's t-test)

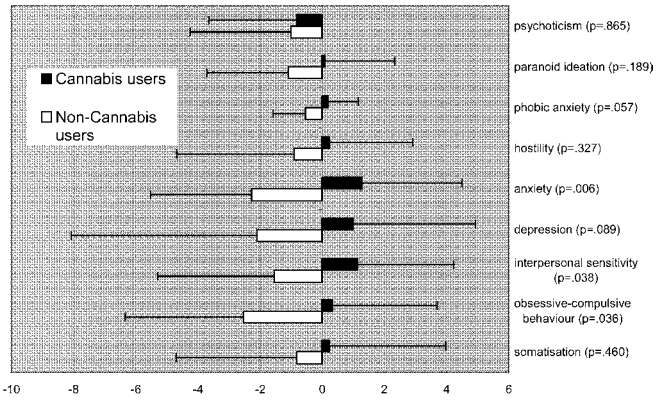

Fig. 2 Change scores ($t_2 - t_1$) in self-reported psychopathological symptoms (SCL-90-R subscales): mean values and standard deviation in cannabis users (present or former ecstasy users reporting concomitant cannabis use during the period from t_1 to t_2; n=19) and non-cannabis users (present or former ecstasy users reporting abstinence from cannabis use during the period from t_1 to t_2; n=19). P significance of group differences (Student's t-test)

Longitudinal analyses

Based on the reported interim drug use we first compared the psychometric change scores (t_2–t_1) of subjects who reported complete abstinence from ecstasy use with those who reported continued ecstasy use over the period of 18 months. In these group analyses, no significant differences were found (data not shown). Subsequently, we compared subjects with regular interim cannabis use to subjects who reported no cannabis use during the follow-up period. The groups did not differ in terms of impulsivity (BIS) and Sensation Seeking (SSSV). However, we found differences for several subscales of the SCL-90-R. Results of these group analyses are illustrated in Fig. 2. At follow-up, subjects with interim cannabis use scored higher on every subscale, whereas cannabis-abstinent participants scored lower with the exception of psychoticism. Group differences were significant for the subscales anxiety, interpersonal sensitivity and obsessive-compulsive behaviour. Finally, the use of ecstasy between baseline and follow-up was not associated with any psychopathological symptom. However, cannabis use, and particularly the duration of regular cannabis use during the follow-up period, was significantly correlated with several subscales of the symptom checklist (non-panning impulsivity: r=–0.51, P=0.005; obsessive-compulsive behaviour: r=0.34, P=0.041; interpersonal sensitivity: r=0.41, P=0.015; depression: r=0.35, P=0.037; anxiety: r=0.46, P=0.008; phobic anxiety: r=0.37, P=0.036; paranoid ideation: r=0.34, P=0.040). In addition, the extent of cannabis use was negatively associated with non-planning impulsivity (r=–0.38, P=0.032).

Discussion

The aim of the present investigation was to clarify the impact of different illicit drugs on psychopathology in recreational ecstasy users over a period of 18 months. At baseline, a battery of self-rating scales was administered to 60 ecstasy users with concomitant use of cannabis, amphetamines and LSD and 30 controls who were matched for age, sex and level of education. In agreement with former studies (Gamma et al. 2000; Daumann et al. 2001; Parrott et al. 2001; Thomasius et al. 2003), ecstasy users suffered more psychological complaints than controls, although we excluded participants with indication of a manifest, clinically relevant psychiatric disorder. However, elevated psychopathology was not associated with the extent of prior ecstasy use, but rather the extent of amphetamine consumption and, particularly, with the frequency of cannabis use.

From the initial sample of 60 users, we were able to assess 38 subjects after a follow-up period of 18 months. Notably, subjects who abstained from ecstasy use over this period of time did not differ from those reporting continued consumption. This finding contrasts with a previous study suggesting that abstinence from MDMA leads to an improved psychiatric status (Morgan et al. 2002). However, in this study conclusion was drawn from a cross-sectional comparison between current ecstasy users and ex-ecstasy users and not from a longitudinal study design. In the study by Morgan and co-workers (2002), current ecstasy users reported a 14-fold higher amount of cocaine, a 6-fold higher amount of amphetamine, and a 3-fold higher amount of LSD compared to the group of ex-ecstasy users. These differences in terms of drug use patterns might account for the subtended findings.

Subjects who continued using cannabis reported more anxiety, interpersonal sensitivity and obsessive-compulsive behaviour than subjects who abstained from cannabis use during the follow-up period. Furthermore, continued cannabis users tended to experience more depression and phobic anxiety. Moreover, higher levels of obsessive-compulsive behaviour, interpersonal sensitivity, depression, anxiety, phobic anxiety and paranoid ideation were associated with the duration of regular cannabis use.

These data are in line with, and extend, former studies with ecstasy users (Daumann et al. 2001; Lieb et al. 2002; Morgan et al. 2002). They strongly suggest that regular cannabis use is a crucial factor for the development and maintenance of psychopathological symptoms in ecstasy users. Only one recent study reported that the extent of ecstasy use was a better predictor of psychopathology than cannabis use (Thomasius et al. 2003). However, the authors also stated that cannabis use played an important role in regard to psychopathology in their sample (Thomasius et al. 2003). Based on our longitudinal data, abstinence from cannabis and not ecstasy seems to be a reliable predictor for improvement of psychological distress in ecstasy users, most notably anxiety, depression, interpersonal sensitivity and obsessive-compulsive be-

haviour. Indeed, there is a growing body of evidence from longitudinal studies that cannabis use is associated with a variety of psychopathological symptoms (Johnson and Kaplan 1990; Miller-Johnson et al. 1998; Arseneault et al. 2002). However, even on the basis of longitudinal data, it is difficult to draw the non-ambiguous conclusion that cannabis use *causes* psychopathology in ecstasy users. For example, individuals with psychological problems may be predisposed to use drugs as an attempt to self-medicate their complaints (Khantzian 1997). Furthermore, although these individuals may well recognise psychopathological symptoms, they might continue drug consumption either because they attribute psychological complaints to personal qualities or because of their strong adherence to a specific drug-using subculture. A recent longitudinal study suggested that psychopathology might lead to cannabis use in adolescents (McGee et al. 2000). However, in young adulthood, the causal direction seems to reverse, indicating that individuals continuing cannabis use put themselves at substantial risk for the development of further psychopathology over the years (McGee et al. 2000; Arseneault et al. 2002). Our data support the hypothesis that self-reported psychological complaints in ecstasy users remit with cannabis abstinence. This finding may implicate a causal link between cannabis use and psychopathology in this sample. Alternatively, it is also conceivable that individuals quit cannabis use because of psychosocial changes in their lives that might also account for growing psychological integrity and well-being. Therefore, further studies should include comprehensive interviews in order to obtain more details on the psychosocial background of ecstasy/cannabis users.

In this study, differences in terms of sensation seeking and impulsivity became evident only in the cross-sectional group analysis. In agreement with former studies (Morgan 1998; Daumann et al. 2001; Dughiero et al. 2001; Parrott et al. 2001), ecstasy users exhibited significantly elevated non-planning impulsivity and experience seeking. However, longitudinal analyses failed to detect any significant changes. Thus, it could be argued that sensation seeking and impulsivity might rather be premorbid personality traits that increase the likelihood for taking drugs than consequences of drug exposure. Surprisingly, the frequency of cannabis use was negatively associated with non-planning impulsivity. In our sample, 14 subjects reported regular cannabis use on a daily basis. Hence, it could be argued that the consumption of cannabis took over a central part in their lives, and as a consequence strong users may have lost interest in other activities. Most items of the non-planning impulsivity subscale (Barratt 1985) comprehend daily life activities (e.g. work, hobbies, travelling or spending money) that might have lost importance for strong cannabis users. Thus, it seems conceivable that the negative association between the frequency of cannabis use and non-planning-impulsivity might reflect a reduction in general activity levels rather than low impulsivity.

Although the combined cross-sectional/longitudinal design of this investigation might help to overcome some methodological shortcomings of open-trial studies there are still limitations that should be mentioned. Although correlation analyses revealed high associations between cannabis use and psychopathology, it is possible that concomitant use of stimulant amphetamines and LSD, which were consumed by single subjects between baseline and follow-up might also play a role. Larger samples have to be recruited to further clarify the impact of those drugs on self-reported psychopathology, for example, by means of correlation or regression analyses. Furthermore, both the drug history and the psychopathological symptoms were assessed by self-reports and, therefore, may contain inaccuracies. However, subjects were interviewed about their drug histories without knowledge of our inclusion and exclusion criteria to gain acceptance into the study, and they had no motivation to falsify their data consciously. Furthermore, previous studies with similar designs suggested that self-reports of illicit drug use are fairly reliable (Brown et al. 1992; Harrison et al. 1993). Finally, we cannot rule out the possibility of a selection bias at t_2 because 22 of 60 ecstasy users did not participate in the follow-up study. To our knowledge, two subjects of the initial sample developed manifest psychiatric disturbances during the follow-up period, and they were therefore excluded from follow-up. We cannot rule out the possibility that other participants who dropped out of the follow-up examination may also have developed psychiatric disorders. Hence, we may have underestimated the psychopathological consequences of ecstasy use because severely impaired individuals might be underrepresented.

In conclusion, the present findings suggest that self-reported psychopathology in ecstasy users is predominantly attributable to regular cannabis use. Abstinence from cannabis and not ecstasy seems to be an appropriate predictor for remission of psychological complaints in ecstasy users, most notably, anxiety, depression, interpersonal sensitivity and obsessive-compulsive behaviour. Furthermore, there is striking evidence for a significant relationship between the duration of regular cannabis exposure and various psychopathological symptoms. Accordingly, cross-sectional data on psychiatric distress in ecstasy users should be interpreted with caution. Thus, further prospective/longitudinal investigations including more comprehensive interviews concerning the psychosocial background might help to corroborate the hypothesis of a causal link between cannabis exposure and self-reported psychopathology in ecstasy users.

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References

Abraham MD, Cohen PDA, Jan van Til R, Langemeijer MPS (1998) Licit and illicit drug use in Amsterdam. III. Developments in drug use 1987–1997. CEDRO, Amsterdam

Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE (2002) Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. BMJ 325:1212–1213

Barratt ES (1985) Impulsivity subtraits: arousal and information processing. In: Spence JT, Izard CE (eds) Motivation, emotion and personality. Elsevier, North Holland

Benazzi F, Mazzoli M (1991) Psychiatric illness associated with "Ecstasy". Lancet 338:1520

Brown J, Kranzler HR, Del Boca FK (1992) Self-reports by alcohol and drug abuse inpatients: factors affecting reliability and validity. Br J Addict 87:1013–1024

Daumann J, Pelz S, Becker S, Tuchtenhagen F, Gouzoulis-Mayfrank E (2001) Psychological profile of abstinent recreational ecstasy (MDMA) users and significance of concomitant cannabis use. Hum Psychopharmacol Clin Exp 16:627–633

Derogatis LR (1994) Symptom Checklist-90-R: administration, scoring and procedures manual. Clinical Psychometrics Unit, Johns Hopkins School of Medicine, Baltimore

Dughiero G, Schifano F, Forza G (2001) Personality dimension and psychopathological profiles of ecstasy users. Hum Psychopharmacol Clin Exp 16:635–639

Fischer C, Hatzidimitriou G, Wlos J, Katz J, Ricaurte G (1995) Reorganization of ascending 5-HT axon projections in animals previously exposed to the recreational drug 3,4-methylenedioxymethamphetamine (MDMA, ecstasy). J Neurosci 15:5476–5485

Gamma A, Frei E, Lehmann D, Pascual-Marqui RD, Hell D, Vollenweider FX (2000) Mood state and brain electric activity in ecstasy users. Neuroreport 11:157–162

Harrison ER, Haaga J, Richards T (1993) Self-reported drug use data: what do they reveal? Am J Drug Alcohol Abuse 19:423–441

Hatzidimitriou G, McCann UD, Ricaurte GA (1999) Altered serotonin innervation patterns in the forebrain of monkeys treated with 3,4-methylenedioxymethampheta-mine seven years previously: factors influencing abnormal recovery. J Neurosci 19:5096–5107

Jansen K (1997) Adverse psychological effects. In: Saunders N (ed) Ecstasy reconsidered. Saunders, London

Johnson RJ, Kaplan HB (1990) Stability of psychological symptoms: drug use consequences and intervening processes. J Health Soc Behav 31:277–291

Johnston LD, O'Malley PM, Bachman JP (2000) Monitoring the future national survey results on adolescent drug use: overview of the key findings, 1999 (NIH publication number 00-4690). National Institute on Drug Abuse, Rockville

Khantzian EJ (1997) The self-medication hypothesis of substance abuse disorders: a reconsideration and recent applications. Harv Rev Psychiatry 4:231–244

Lieb R, Schuetz CG, Pfister H, von Sydow K, Wittchen H-U (2002) Mental disorders in ecstasy users: a prospective-longitudinal investigation. Drug Alcohol Depend 68:195–207

McCann UD, Szabo Z, Scheffel U, Dannals RF, Ricaurte GA (1998) Positron emission tomographic evidence of toxic effect of MDMA ("ecstasy") on brain serotonin neurons in human beings. Lancet 352:1433–1437

McCann UD, Eligulashvili V, Ricaurte GA (2000) 3,4-Methylenedioxymethamphetamine (ecstasy)-induced serotonin neurotoxicity: clinical studies. Neuropsychobiology 42:11–16

McGee R, Williams S, Poulton R, Moffitt T (2000) A longitudinal study of cannabis use and mental health from adolescents to early adulthood. Addiction 95:491–503

McGuire PK, Cope H, Fahy TA (1994) Diversity of psychopathology associated with use of 3,4-methylenedioxymethamphetamine ("ecstasy"). Br J Psychiatry 165:391–395

Milani R, Turner JJD, Parrott AC, Parmar R (2000) Recreational drug use and psychobiological problems, collaborative UK/Italy study (5): ecstasy (MDMA) polydrug user findings. J Psychopharmacol 14:A15

Miller-Johnson S, Lochman JE, Coie JD, Terry R, Hyman C (1998) Comorbidity of conduct and depressive symptoms at sixth grade: substance abuse outcomes across adolescents. J Abnorm Child Psychol 26:221–232

Morgan MJ (1998) Recreational use of "ecstasy" (MDMA) is associated with elevated impulsivity. Neuropsychopharmacology 19:252–264

Morgan MJ, McFie L, Fleetwood LH, Robinson JA (2002) Ecstasy (MDMA): are the psychological problems associated with its use reversed by prolonged abstinence? Psychopharmacology 159:294–303

Naughton M, Mulrooney JB, Leonard BE (2000) A review of the role of serotonin receptors in psychiatric disorders. Hum Psychopharmacol Clin Exp 15:397–416

Pallanti S, Mazzi D (1992) MDMA (ecstasy) precipitation of panic disorder. Biol Psychiatry 32:91–95

Parrott AC, Milani R, Parmar R, Turner JJD (2000a) Recreational drug use and psychobiological problems, collaborative UK/Italy study (1): overview and main findings. J Psychopharmacol 14:A14

Parrott AC, Sisk E, Turner JJ (2000b) Psychobiological problems in heavy "ecstasy" (MDMA) polydrug users. Drug Alcohol Depend 60:105–110

Parrott AC, Milani RM, Parmar R, Turner JD (2001) Recreational ecstasy/MDMA and other drug users from the UK and Italy: psychiatric symptoms and psychobiological problems. Psychopharmacology 159:77–82

Ramsey M, Spiller J (1997) Drug misuse declared: results of the 1996 British crime survey. Home Office, RSD, London

Reneman L, Lavalaye J, Schmand B, de Wolff FA, van den Brink W, den Heeten GJ, Booij J (2001) Cortical serotonin transporter density and verbal memory in individuals who stopped using 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy"). Arch Gen Psychiatry 58:901–906

Ricaurte GA, Martello AL, Katz JL, Martello MB (1992) Lasting effects of MDMA on central serotonergic neurons in nonhuman primates: neurochemical observations. J Pharmacol Exp Ther 261:616–622

Ricaurte GA, Yuan J, McCann UD (2000) 3,4-Methylenedioxymethamphetamine (ecstasy)-induced serotonin neurotoxicity: studies in animals. Neuropsychobiology 42:5–10

Schifano F, Di Furia L, Forza G, Minicuci N, Bricolo R (1998) MDMA (ecstasy) consumption in the context of poly-drug abuse: a report on 150 patients. Drug Alcohol Depend 52:85–90

Schuster P, Lieb R, Lamertz C, Wittchen HU (1998) Is the use of ecstasy and hallucinogens increasing? Eur Addict Res 4:75–82

Soar K, Turner JJD, Parrott AC (2001) Psychiatric disorders in ecstasy (MDMA users: a literature review focussing on personal predisposition and drug history. Hum Psychopharmacol Clin Exp 16:641–645

Speck A, Reimers S (1999) Forschungsinitiative zur zielgerichteten Ecstasy-Prävention—Repräsentativbefragung zum Drogenkonsum schleswig-holsteinischer SchülerInnen. Supported by the ministry for labor, health and social affairs of the state of Schleswig-Holstein. Available upon request from the Ministry

Strote J, Lee JE, Wechsler H (2002) Increasing MDMA use among college students: result of a national survey. J Adolesc Health 72:64–72

Tasker T, Raw M, McNeill A (1999) Drug realities: a summary of the results of the 1996 national drugs campaign survey. Health Education Authority, London

Thomasius R, Petersen K, Buchert R, Andresen, Zapletalova P, Wartberg L, Nebeling B, Schmoldt A (2003) Mood, cognition and serotonin transporter availability in current and former ecstasy (MDMA) users. Psychopharmacology 167:85–96

Zuckerman M, Eysenck SPG, Eysenck HJ (1978) Sensation seeking in England and America. J Consult Clin Psychol 46:477–482