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ORIGINAL INVESTIGATION

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Recreational ecstasy/MDMA and other drug users from the UK and Italy: psychiatric symptoms and psychobiological problems

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Abstract *Rationale*: Recreational drug use is increasingly widespread amongst young people, but there are concerns that psychoactive drugs may be associated with psychiatric symptoms or psychobiological problems. *Objectives*: To assess the psychiatric health status of a large, non-clinical sample of young adults from Italy and the UK, and relate it to their use of ecstasy/MDMA and other recreational drugs. *Methods*: The UEL Recreational Drug Use Questionnaire was completed by 768 young people (mean age 21.7 years) from four European cities. The subjects comprised 150 non-drug users, 185 alcohol/tobacco users, 97 cannabis and alcohol/tobacco users, 102 illicit polydrug but not ecstasy users, 115 light (<20 times) ecstasy polydrug users, and 119 heavy (>20 times) ecstasy polydrug users. The unpaid volunteers completed the SCL-90 self-rating inventory for psychiatric symptoms when off drug, with 30 additional questions covering positive moods and life experiences. *Results*: Heavy ecstasy polydrug users reported significantly higher scores than non-drug users on several SCL-90 factors, including phobic anxiety, obsessive–compulsive behaviour, anxiety, psychoticism, somatisation, and significantly higher rates of 'loss of sex interest or pleasure'. Self-rated symptom scores increased in line with greater drug use, so that polydrug users who had never taken ecstasy also reported a variety of psychobiological impairments. In contrast, positive moods and life experiences were broadly similar across subgroups. *Conclusions*: The recreational use of ecstasy/MDMA is associated with a range of psychiatric symptoms and psychobiological problems. However, these problems are not specific to ecstasy users but are also evident in other recreational polydrug users.

Keywords MDMA · Ecstasy · Drug · Serotonin · Anxiety · Depression

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Introduction

Ecstasy or MDMA (3,4-methylenedioxymethamphetamine) is popular as an illicit recreational drug. It is readily available in the UK (Saunders 1995; Webb et al. 1996), mainland Europe (Schifano 1998; Schuster et al. 1998; Verkes et al. 2001), America (Cohen 1998; McCann et al. 2000) and most westernised countries (Parrott 2001a). Around 13% of British university students admit to having taken it (Webb et al. 1996), while the age of first use has gradually declined (Schuster et al. 1998). MDMA is 'neurochemically messy', being primarily an indirect serotonin agonist but also boosting dopamine and other monoamines (McDowell and Kleber 1994). The acute boost in neurotransmitter activity can generate profound feeling of euphoria and well-being (Cohen 1998; Parrott 2001a, 2001b), although depression and anhedonia generally follow in the days afterwards, due to monoaminergic depletion (Curran and Travill 1998; Parrott and Lasky 1998). The acute stimulation induced by MDMA can generate various physiological changes including hyperthermia, hyponatremia and cardiac, hepatic and renal problems. These adverse reactions are increased in the hot and crowded conditions of dances/raves and can occasionally prove fatal (McCann et al. 1996; Cohen 1998).

Repeated dosing with MDMA causes serotonergic neural damage in laboratory animals, with loss of the distal axon projections to the higher brain regions (Ricaurte et al. 1992). Neuronal damage can occur at dose levels within the range used by humans (Ricaurte et al. 2000), so that the consequences of its recreational use are of concern. Abstinent regular ecstasy users have been shown to display reduced levels of 5-HT neuronal transporters and other serotonergic markers (McCann et al. 1996, 1998, 2000; Verkes et al. 2001). Memory problems have been consistently demonstrated (Krystal et al. 1992; Parrott and Lasky 1998; Parrott et al. 1998; Morgan 1999; Verkes et al. 2001), together with deficits in higher cognitive processing (Morgan 1998; Parrott 2000a, 2001a; Verkes et al. 2001). Various psychiatric and psy-

chobiolgical problems have also been noted, including depression, psychotic breakdown, anxiety, phobic anxiety, sleep disturbance, impulsivity and various eating disorders (McCann et al. 1996; Schifano 1998). However, most of the psychiatric evidence has come from individual case studies, so it might be that abreactions only occur in susceptible individuals (Saunders 1995).

In an attempt to estimate the occurrence of psychiatric symptoms and psychobiological problems in young recreational drug users, we previously surveyed a non-clinical cohort of young people from a town in Ireland where recreational drug use was prevalent (Parrott et al. 2000a). The heavy ecstasy users reported significantly higher scores on several SCL-90 psychiatric symptom scales than non-users, while scores for the light ecstasy users were generally intermediate (Parrott et al. 2000a). However, the heavy ecstasy users had also used a wide range of psychoactive drugs, such as amphetamine and cocaine. Thus, it was unclear whether it was the ecstasy or the polydrug use in general that was most problematic. The present study was designed to address this question by comparing subgroups with increasing use of psychoactive drugs: non-drug users; alcohol and/or nicotine users; cannabis users; illicit polydrug users who had never taken ecstasy; light ecstasy polydrug users, and heavy ecstasy polydrug users. The participants were assessed in four European cities: Rome, Padova, Manchester and London, and thus came from various socio-cultural backgrounds. Finally, we also assessed positive feelings and life experiences. Many young people take recreational drugs in the belief that they will make their lives more exciting and pleasurable. Advocates for the use of recreational drugs also criticise researchers for focusing on the problematic side of drugs and presenting a biased impression of their overall effects (Saunders 1995). We therefore wanted to generate some empirical data on this topic.

Table 1 Group characteristics and self-report drug use (mean±SD; percentages of drug users). The means regarding cannabis-use refer to the following classification: 1= non users; 2= moderate users; 3= heavy users. Other illicit drugs represent lifetime consumption. Zero drug-use groups were excluded from the analysis of variance (ANOVA) test

	Group						
	Non-drug users *n*=150	Alcohol and/or tobacco users *n*=185	Cannabis, alcohol and/or tobacco users *n*=97	Polydrug users; no ecstasy *n*=102	Light ecstasy polydrug users *n*=115	Heavy ecstasy polydrug users *n*=119	ANOVA group effect
Gender (male/female/ underclared)	40%/59%/1%	54%/45%/1%	58%/40%/2%	70%/28%/2%	59%/39%/2%	80%/18%/2%	
Age (years)	18.8±4.8	21.5±4.4	21.7±4.3	22.7±4.6	22.7±4.6	23.6±4.2	***
Alcohol (units per week)	0	11.0±14.7 (89%)	20.5±28.3 (80%)	21.0±28.5 (78%)	24.2±32.6 (84%)	29.1±42.6 (77%)	***
Tobacco (cigarettes per week)	0	26.9±51.5 (37%)	66.4±69.6 (98%)	80.9±69.4 (77%)	67.2±63.3 (73%)	66.5±79.4 (66%)	***
Cannabis	0	0	2.6±0.5 (100%)	2.7±0.4 (84%)	2.8±0.4 (84%)	2.9±0.3 (91%)	***
Amphetamine	0	0	0	10.9±35.7 (48%)	17.6±56.5 (64%)	124.1±233.8 (83%)	***
Cocaine	0	0	0	21.4±77.5 (54%)	23.5±99.3 (72%)	78±158.8 (80%)	***
LSD	0	0	0	7.5±50.1 (34%)	5.9±14.6 (51%)	72.6±234.5 (81%)	***
Magic mushroom	0	0	0	2.4±7.3 (28%)	2.5±9.9 (39%)	11.5±51.1 (54%)	
Barbiturate/ benzodiozepine	0	0	0	47.7±229 (14%)	73.1±445.4 (17%)	43±256.7 (27%)	
Opiate	0	0	0	261.2±993.5 (18%)	102.7±609.5 (24%)	108.5±565.6 (27%)	
Anabolic	0	0	0	0.6±4.5 (4%)	4.0±19.3 (5%)	4.4±33.3 (3%)	
Solvent	0	0	0	6.7±51 (16%)	1.8±9.9 (17%)	6.4±28.4 (18%)	
Popper	0	0	0	9.6±51.8 (38%)	5.7±17.8 (36%)	17.5±44.8 (42%)	
Ketamine	0	0	0	0.0±0.0 (1%)	0.1±0.0 (4%)	1.8±5.8 (24%)	

**P<0.01, ***P<0.001

Materials and methods

Participants

The participants comprised young people from four European cities: Rome and Padua in Italy, London and Manchester in the UK. They were approached in venues where young people congregate: clubs, cafes, city squares, college campuses. The aims of the study were explained, and each volunteer was asked to sign a written agreement form which contained a description of the study. Seven hundred and sixty-eighty volunteers with a mean age of 21.7 years provided full data; their characteristics are summarised in Table 1.

Drug usage patterns

Each participant completed the UEL Drug History Questionnaire (Parrott et al. 2000a), which covered the use of various recreational drugs. For each drug a yes/no response was required to indicate whether it had ever been taken; estimates of weekly consumption of tobacco/nicotine, alcohol and cannabis were requested, as well as lifetime consumption estimates for amphetamine, cocaine, ecstasy/MDMA, opiates, magic mushrooms, benzodiazepines, poppers, anabolic steroids and other drugs. The responses were used to categorise each volunteer into one of six subgroups (Table 1). Non-drug users were those who took less than one unit of alcohol per week and did not smoke tobacco. Alcohol/nicotine users were defined as those who took at least one unit of alcohol per week and/or smoked tobacco. Cannabis users had taken cannabis but not any other illicit drug. Polydrug users had taken an illicit drug other than cannabis, but not ecstasy/MDMA. Light ecstasy polydrug users had taken MDMA between 1 and 20 times. Heavy ecstasy polydrug users had taken MDMA on more than 20 occasions. The consumption rates for each drug type are shown in Table 1. Weekly consumption rates are shown for alcohol and tobacco, while cannabis users were categorised as non-users, moderate users or heavy users. For all other drugs, the values represent mean lifetime number of occasions used.

Assessment measures

The SCL-90 self-rating scale covered various psychiatric symptoms and psychobiological dimensions: depression, anxiety, somatisation, obsessive–compulsive behaviour, interpersonal sensitivity, hostility, phobic anxiety, psychoticism, paranoid ideation and ‘additional scales’ covering psychobiological problems such as altered appetite and disturbed sleep (Derogatis 1997). Example questions are: “feeling easily annoyed or irritated?” (anger–hostility subscale) and “feelings of worthlessness?” (depression subscale). Each question was rated on a four-point scale: not at all (0), a little bit (1), quite a bit (2), moderately (3) and extremely (4). The response indicated whether that feeling or complaint had been experienced over the past 4 weeks, when not under the effects of drugs. The SCL-90 questionnaire has been used in previous studies of recreational ecstasy users (Schifano et al. 1998; Parrott et al. 2000a), with Schifano using an Italian translation which was again used here. Thirty questions were added to cover positive moods and life experiences in four areas. Example questions are: “feeling satisfied with my life?” (positive life experience); “feeling happy?” (positive mood); “having good time with friends?” (sociability); “feeling healthy and proficient?” (positive psychobiology).

Procedure and data analysis

Most participants completed the questionnaires in the presence of the investigator, who was available to answer questions, although some participants took their questionnaires away for completion (to be returned by post). The study protocol was passed by the UEL ethics committee. The questionnaire data was analysed using one-way analysis of variance (ANOVA) between subgroups, using SPSS for Windows. This was followed by monotonic (first-order) polynomial contrasts, with groups ordered according to increasing drug use (as defined above). This statistic calculated whether the SCL-90 scores changed as a monotonic/linear function of drug usage.

Results

Table 1 presents the recreational drug consumption patterns for each subgroup. It shows that, as drug use widened, so usage intensified. Thus, the heavy ecstasy users had the most extensive experience of many of the other psychoactive drugs, both legal and illicit (Table 1). Group mean scores for all the dependent variables are shown in Table 2. The ANOVA group effect was significant for: somatisation, obsessive–compulsive behaviour, anxiety, anger–hostility, phobic anxiety, psychoticism, MDMA side effects and total negative scales. In every case the monotonic/linear polynomial function was also significant, with pathology scores increasing as psychoactive drug use widened/intensified (Table 2). There were no significant ANOVA group effects for the four positive scales, although the first-order polynomial function for ‘positive moods’ was significant, with slightly lower scores in all three polydrug users subgroups (Table 2).

Discussion

There was a close relationship between the extent of recreational drug use and high scores on many of the psychiatric symptom scales. The highest SCL-90 scores were reported by the polydrug users, the lowest scores by the non-drug and/or legal drug users (Table 2). We believe this is the first study to report a direct relationship between the extent of recreational drug use and psychiatric symptoms in a non-clinical cohort of young people. Our participants were not attending drug clinics, nor were they being assessed because of psychiatric complaints. Given the current prevalence of drug taking, these findings suggest that there are many young people who are experiencing psychiatric symptoms and psychobiological problems related to their use of recreational drugs (Webb et al. 1996; Schuster et al. 1998). In contrast, positive life experiences were generally similar across subgroups, with none of the ANOVA group effects being significant. Self-ratings of life contentment, sociability and positive psychobiological functioning, were generally similar across groups, although positive moods were somewhat lower amongst the polydrug users (Table 2). The findings from the different subgroups will now be discussed.

The ecstasy/MDMA subgroup findings agree with previous reports of psychiatric and/or psychobiological problems, where depression, suicide, psychoticism, paranoia, phobic anxiety, obsessive–compulsive disorder, food cravings and sleep impairments have each being described in individual case studies (Green et al. 1995;

Table 2 SCL-90 questionnaire group mean scores (±SD)

	Group							
	Non-drug users	Alcohol and/or tobacco users	Cannabis, alcohol and/or tobacco users	Polydrug users; no ecstasy	Light ecstasy polydrug users	Heavy ecstasy polydrug users	ANOVA group effect	Polynomial linear function
SCL-90 negative scales								
Somatisation	0.56±0.9	0.51±0.5	0.64±0.5	0.70±0.6	0.69±0.6	0.67±0.5	**	**
Obsessive–compulsive	0.78±0.5	0.77±0.6	0.99±0.6	1.06±0.7	1.08±0.8	1.12±0.7	**	***
Sensitivity	0.81±0.3	0.77±0.7	0.79±0.6	0.85±0.6	0.80±0.7	0.79±0.7	–	–
Depression	0.81±0.6	0.79±0.7	0.83±0.6	0.91±0.7	0.86±0.7	0.93±0.7	–	–
Anxiety	0.65±0.5	0.69±0.5	0.78±0.6	0.81±0.6	0.80±0.6	0.88±0.6	*	***
Anger–hostility	0.69±0.6	0.78±0.8	0.98±0.8	1.05±0.8	1.02±0.9	1.07±0.9	***	***
Phobic anxiety	0.22±0.3	0.26±0.5	0.32±0.4	0.32±0.4	0.38±0.5	0.37±0.5	*	**
Paranoid ideation	0.91±0.7	0.84±0.7	0.94±0.8	1.19±0.7	1.04±0.8	0.88±0.6	–	–
Psychoticism	0.43±0.5	0.44±0.5	0.58±0.5	0.63±0.5	0.63±0.6	0.60±0.5	*	***
Negative psychobiology	3.95±3.0	4.17±3.5	4.87±3.4	4.54±3.6	4.85±3.8	5.05±4.1	–	**
MDMA side effects	0.96±0.7	0.96±0.7	1.14±0.7	1.19±0.8	1.26±0.7	1.22±0.7	**	***
Total negative	7.55±5.0	7.69±5.4	8.84±5.2	9.57±5.4	9.59±6.6	9.55±5.6	*	***
SCL-90 positive scales								
Sociability	2.16±0.6	2.25±0.7	2.16±0.8	2.03±0.7	2.22±0.7	2.17±0.8	–	–
Positive moods	2.21±0.7	2.28±0.7	2.18±0.8	2.09±0.7	2.12±0.8	2.12±0.8	–	*
Positive psychobiology	2.71±0.8	2.87±0.8	2.74±0.9	2.56±0.8	2.75±0.8	2.69±0.9	–	–
Positive life experiences	2.20±0.8	2.24±0.9	2.02±0.8	2.00±0.9	2.15±0.8	2.11±0.9	–	–
Total positive	9.41±2.4	9.65±2.7	9.10±2.8	8.76±2.7	9.23±2.8	9.07±2.9	–	–

*P<0.05, **P<0.01, ***P<0.001

McCann et al. 1996, 2000; Cohen 1998; McGuire 2000). These abreactions are probably not unusual or atypical. In a systematic survey of 150 ecstasy users attending a drug dependency clinic, psychiatric symptoms were significantly more frequent in the more experienced ecstasy users (mean lifetime use: 47 tablets) than in the novice users (3 tablets; Schifano et al. 1998). Significantly raised SCL-90 scores were also found in a non-clinical investigation of young adults from Ireland. The worst symptom profiles were reported by the heavy ecstasy users, the best by the non-users, while SCL-90 scores for the light ecstasy users were generally intermediate. The pattern of symptoms reported by the ecstasy/MDMA users was very similar to that found here (Parrott et al. 2000a). In the present study, the depression scores did not differ significantly across groups, although there was a trend for higher scores amongst the heavy drug users (Table 2). However several of the heavy ecstasy users responded positively to the depression subscale question for: 'loss of sex interest or pleasure' (4% of non-users, compared with 14% of heavy ecstasy users: P<0.05). Topp et al. (1999) reported that 12.2% of their Australian recreational ecstasy users complained of 'loss of sex urge', although they did not have control group data. Repeated MDMA administration causes neurotoxicity in laboratory animals (Ricaurte et al. 2000), and serotonergic nerve damage has been indicated in regular ecstasy users (McCann et al. 1998; Verkes et al. 2001). Serotonin is involved in a wide range of functions, including mood, pleasure, cognition, impulsivity, aspects of psychotic behaviour, sleep and sex. Hence the current psychobiological impairments may reflect serotonergic neural damage, which may be long lasting. The cognitive/memory deficits displayed by abstinent ecstasy users (Parrott et al. 1998; Verkes et al. 2001) seem to remain long after drug use has discontinued (Wareing et al. 2000; Parrott 2001a).

Adverse symptom profiles were also evident amongst the polydrug users who had never taken ecstasy/MDMA (Table 2). This group comprised recreational users of amphetamine, cocaine, LSD, magic mushrooms and other drugs, so it was not surprising that they showed functional deficits (see later). However, their adverse symptom profiles emphasise the difficulty of interpreting the ecstasy subgroup findings. Thus, the adverse profiles for the ecstasy subgroups (Table 2) may be due to MDMA, polydrug use or the numerous lifestyle factors that surround recreational drugs (irregular circadian patterns, intermittent periods of rest and recuperation, poor diet, heat stress, sympathetic overactivity). It is likely that these factors contribute together in complex ways, so that while some individuals develop numerous problems, others may remain comparatively unimpaired. Future studies should attempt to unravel the complex interactions between these different factors. The cannabis user group was generally intermediate between the polydrug user groups and the legal/non-user groups (Table 2). This is consistent with the extensive literature on cannabis, which shows that psychiatric problems can often develop with regular cannabis use (McGuire et al. 1994). Our us-

ers were moderate/heavy users of cannabis (Table 1), and, thus, some degree of psychobiological deficit was not unexpected. The two groups reporting the lowest SCL-90 scores were the non-drug users and the 'legal' users of alcohol and/or nicotine. The slightly younger mean age of the non-users should be noted, also the fact that none of them came from Manchester. The alcohol/nicotine group mainly comprised light drinkers, whose weekly alcohol consumption was around half that reported by the heavier drug users (Table 1). Comparatively few were cigarette smokers, with far higher rates of tobacco smoking amongst the cannabis and polydrug users. One of the most interesting findings was how the use of all psychoactive drugs, both legal and illicit, increased in parallel (Table 1).

It should be emphasised that the current findings only reflect associations, and do not indicate causation. Two contrasting explanations need to be discussed. Recreational drug use may be most prevalent in those with pre-existing problems or the drugs may be causing the problems (McCann et al. 1996; McGuire 2000). There is some support for each explanation. Many individuals with personality disorders or other psychiatric problems take recreational drugs. Impulsivity is closely associated with drug experimentation and risky patterns of drug taking, while some young schizophrenics and others with mental health problems also take recreational drugs. This has led to the suggestion that psychiatric problems amongst illicit drug takers reflect the emergence of pre-existing dispositions (Saunders 1995). However, various aspects of the current findings do not support that model. For instance, it is unlikely that individuals with pre-existing phobic anxiety would decide to become heavy stimulant/MDMA polydrug users attending raves or large dance clubs. They might be expected to avoid psychoactive drugs with their potentially disruptive effects or consume relaxants such as alcohol in less-threatening environments. Similar arguments can be proposed for some of the other disorders identified in Table 2, such as generalised anxiety and obsessive–compulsive disorder. The high levels of phobic anxiety and obsessional–compulsive symptoms with intensive drug use are more consistent with drug causation as the explanation. They also agree with many of the published case studies, where psychiatric disorders often develop in recreational drug users with no known psychiatric history or predisposition (Soar et al. 2001). It should also be noted that membership of each drug usage category was not fixed beforehand; everyone was in a state of potential transition across categories. Each polydrug user was originally a non-drug user until they progressed through the different usage categories, generally in the following order: tobacco/alcohol; cannabis; occasional illicit; heavy polydrug. The current findings show that as an individual moves up the drug-usage scale, self-reported positive moods and experiences remain unchanged, while psychiatric symptoms and psychobiological problems increase (Table 2).

Advocates for recreational drugs suggest that their effects are beneficial, generating feelings of excitement, pleasure and emotional closeness (Saunders 1995). However, although recreational drugs have some positive effects – which is why they are taken – these are generally counterbalanced by parallel detrimental changes. Thus, the energy and excitement produced by cocaine is accompanied by emotional tension, suspiciousness and/or paranoia, so that acute adverse reactions are quite usual (Angrist 1987). Alcohol and benzodiazepines also have a mixture of positive and negative effects. Although often leading to feelings of sociability and relaxation, they may cause anger and aggression, and generally impair psychomotor and cognitive skills (Ashton 1994). The acute after effects also contribute to the negative overall profile. The on-drug experience is generally followed by a period of neurochemical depletion, when unpleasant moods predominate. Thus, regular smokers suffer from irritability and restlessness between cigarettes, as their plasma nicotine level falls. Indeed, the repeated experience of adverse moods over the day helps explain why nicotine dependency leads to heightened stress and depression, and why quitting leads to long-term mood gains (Parrott 1999, 2000b). All psychoactive drugs have potentially damaging effects when used regularly (Angrist 1987; Ashton 1994; McGuire et al. 1994; Curran and Travill 1997; Parrott 1999; McGuire 2000). Thus, it is not surprising that psychobiological problems are most frequent in those who use most drugs (Table 1 and Table 2).

The current study has a number of methodological limitations. The data were based upon self-reports, so that both the drug-use values and the SCL-90 responses may contain inaccuracies. The accuracy of self-report measures clearly needs further empirical investigation, while a related issue is the uncertain nature of the pharmacological constituents of illicit drug tablets (Curran 2000). However, given the meaningfulness of the current findings, and their consistency with other findings, these problems are probably a source of random rather than systematic error. The current report is also limited to overall group effects. Our extensive data set is being subjected to a more comprehensive series of analyses in order to systematically assess individual drugs, drug combinations, age and gender and cross-cultural factors. The preliminary findings from each city have been reported as conference papers (Milani et al. 2000a; Parmar et al. 2000; Turner et al. 2000), together with the overall sample (Parrott et al. 2000b) and ecstasy subgroup findings (Milani et al. 2000b). Each city showed the same general pattern, with significantly greater SCL-90 pathology scores for the polydrug users. There were some slight differences, which reflected subtle variations in participant characteristics across cities. We also noted some interesting differences in polydrug combinations. Thus, heavy ecstasy users in Italy tended to combine it with large amounts of alcohol, whereas in the UK the use of other CNS stimulants was more popular (reports in preparation). We are also assessing gender differences more systematically and investigating how drug use changes as a function of age (Milani, unpublished observations).

In relation to this, we are planning a prospective study to investigate the relationship between pre-morbid factors

and the development of drug-related problems. We intend to follow a group of young people over several years in order to gauge how changes in drug use relate to psychobiological integrity and well being. Such prospective studies are crucially needed since current knowledge on ecstasy/MDMA is limited to cross-sectional comparisons (Curran 2000; McCann et al. 2000; Parrott 2000a; Verkes et al. 2001; although see Zakzanis and Young 2001). The current findings also have implications for health education. Drug education packages should explain how and why psychoactive drugs are associated with problems rather than benefits. Clear information based on scientific findings would be far more persuasive than emotive messages, such as "just say no", which fail to provide any objective reasons for avoiding drugs. Finally, there are concerns over the long-term effects of drugs such as ecstasy/MDMA. Given their widespread use at even younger ages (Schuster et al. 1998), it is likely that drug-related disorders may become an increasing problem over time.

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