8. Is there an ecstasy (MDMA) dependence syndrome?

Louisa Degenhardt, Raimondo Bruno and Libby Topp

8.1. Introduction

This chapter considers whether there is sufficient evidence to support the concept of an ecstasy dependence syndrome. Most people who use psychoactive substances do so without experiencing problems, but a minority of users experience difficulties controlling their use. Here, we begin by explaining the requirements for a valid psychiatric diagnosis, and discuss the concept of "drug dependence" and its theoretical basis. We then review the animal and human literature on the topic and discuss the issues arising from this literature.

The evidence for an MDMA dependence syndrome is the subject of debate[1] [2] for reasons that will become clearer in this Chapter. In the following sections, existing evidence on these aspects of the diagnosis of "ecstasy dependence" will be considered. Much of what is known about the natural history and course of ecstasy use careers is derived from cross-sectional convenience samples, and there remains a significant gap in current knowledge of this area.

8.2. What makes a valid psychiatric diagnostic entity?

It is useful to begin by outlining the features of what is considered a "valid" psychiatric diagnostic entity[3]. In most areas of medicine the underlying pathogens of disease are well understood and there are "gold standard" biological tests for the disease. This is not the case in psychiatry, where the mechanisms underlying psychiatric illness, although becoming clearer, are complex and relatively incompletely described and diagnosis depends upon the pattern of symptoms and behaviour reported by and observed in individuals.

A number of features have been proposed to characterise a valid psychiatric diagnosis[3-6]. These include that the diagnostic entity:

a) predicts a patient's prognosis (relative to someone who does not meet such diagnostic criteria);
b) is independent of other diagnoses;
c) predicts treatment response if the patient is treated for the disorder;
d) predicts the course over time; and
e) is related to neurobiology.

There is good evidence to support the validity of dependence syndromes for drugs such as alcohol and heroin. Indeed, the concept of "dependence" was developed from observations made by clinicians treating alcohol users who appeared to be suffering from alcohol-related harms that were related to, but importantly different from, impaired control over alcohol use itself.

8.3. What is "drug dependence"?

Most people who use psychoactive drugs do so without experiencing any problems, but some do develop problems related to their use[7] [8]. The conceptualisation and measurement of these problems has undergone considerable change over the past four decades, with the emergence of the concept of a substance "dependence syndrome", derived from Edwards and colleagues' work on alcohol dependence [9].

In 1977, Edwards and colleagues suggested that alcohol dependence could be conceptualised as a cluster of symptoms occurring in heavy drinkers that were distinguishable from alcohol-related problems[10]. Seven symptoms were regarded as major indicators of the alcohol dependence syndrome:

- Narrowing of the behavioural repertoire surrounding drug use taking behaviours;
- Salience of drinking (alcohol use given priority over other activities);
- Subjective awareness of a compulsion (experiencing loss of control over alcohol use, or an inability to stop using);
- Increased tolerance (using more alcohol to get the same effects, or finding that the same amount of alcohol has less effect);
- Repeated alcohol withdrawal symptoms (such as fatigue, sweating, diarrhoea, anxiety, trouble sleeping, tremors, stomach ache, headache, hallucinations, fever);
- Relief or avoidance of withdrawal symptoms by further drinking; and
- Rapid reinstatement of dependent drinking after abstinence.

These features can be seen to fall into the categories of behavioural indicators (e.g. salience of drinking and awareness of compulsion) and more neurobiological signs (e.g. tolerance and withdrawal). The concept of a dependence syndrome has since been extended to other drugs such as cannabis, tobacco, amphetamines, opioids and sedatives.

These diagnoses have been shown to have good validity in terms of predicting prognosis[11], treatment response and course over time. There is also supporting neurobiological evidence of a dependence syndrome for these drugs.

The most recent operationalisation of the dependence syndromes is in the DSM-IV[12] and ICD-10[13] classification systems[14]. These criteria are summarised in Table 8.1 and 8.2. Both systems

require a cluster of three or more indicators that a person experiences a loss of control over their drug use and/or physical or psychological cravings for a drug to avoid a dysphoric state.

Table 8.1: DSM-IV dependence criteria

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more of the following:

1. Tolerance, as defined by either:
    a. a need for markedly increased amounts of the substance to achieve intoxication or the desired effect;
    b. markedly diminished effect with continued use of the same amount of the substance;
2. Withdrawal, as manifested by either of the following:
    a. A characteristic withdrawal syndrome for the substance;
    b. The same or a closely related substance is used to relieve or avoid withdrawal symptoms;
3. the substance is taken in larger amounts of for a longer period than intended;
4. there is a persistent desire or unsuccessful efforts to cut down or control substance use;
5. a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects;
6. important social, occupational or recreational activities are reduced or given up because of substance use;
7. substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.

Source: American Psychiatric Association[12]

Table 8.2: Criteria for past year ICD-10 drug dependence

Three or more of the following present together at some time during the previous year:

- A strong desire or sense of compulsion to take the substance;
- Difficulties in controlling drug use in terms of its onset, termination, or levels of use;
- A physiological withdrawal state when substance use has ceased or has been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
- Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses;
- Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
- Continued use despite clear evidence of overtly harmful consequences.

Source: World Health Organization [13]

8.4. Theoretical models of drug dependence

Animal models of drug dependence have been developed. Different psychoactive substances certainly act in different ways upon the brain[15-19], but two major pathways in the brain have been implicated as common pathways upon which most drugs of dependence act[18 20 21]. These are the mesolimbic-frontocortical dopaminergic pathway (which extends from the ventral tegmental area (VTA) to the nucleus accumbens and prefrontal cortex) and the endogenous opioid receptor

system. Both acute and chronic use of multiple drugs including alcohol, opiates, nicotine, cannabinoids and amphetamines[22] affect the dopaminergic pathway.

8.4.1. Neuroadaptation

Neuroadaptation refers to changes in the brain that occur after repeated administration that oppose the acute effects of substance use in order to maintain homeostasis in brain systems and thereby maintain a level of brain functioning that is similar to its nondrug state. This may be of two types: *within-system adaptations*, where the changes occur at the site of the substance's action, and *between-system adaptations* which are changes in different mechanisms that are triggered by the substance's action. When substances are repeatedly administered, changes occur in the chemistry of the brain to oppose the substance's effects. When substance use is discontinued, the adaptations are no longer opposed; and hence the brain's homeostasis is disrupted[23 24].

According to this hypothesis, neuroadaptation explains the development of tolerance to the effects of a substance and the experience of withdrawal when substance use abruptly stops[23]. While traditionally, conceptualisations of substance dependence focused on physical withdrawal symptoms, such as diarrhoea or fever, contemporary formulations have emphasised more motivating psychological symptoms, such as dysphoria, depression, irritability and anxiety.

It has been hypothesised that these negative motivational symptoms are manifestations of neurobiological changes that signal "not only…the beginning of the development of dependence, but may also contribute to vulnerability to relapse and may also have motivational significance" (p.53)[18]. This approach hypothesises that after chronic substance use, changes occur in brain systems such as the dopamine reward system and the endogenous opioid system, which maintain substance use and make it difficult to cease use[18].

8.4.2. Behavioural models

Behavioural models of addiction focus on directly observable behaviour. One class of behavioural model concentrates upon the fact that behaviour is maintained (or made more likely) by the consequences (reinforcers) of such behaviour [25]. Drug self-administration is then an example of *instrumental behaviour* because the activities of persons (or animals in an experiment) are instrumental in obtaining the consequences (the substance's effects).

Research with animal subjects has shown that when many psychoactive drugs are available, drug-naïve animals will self-administer them, often to excess[26]. This finding has been replicated with many species of animal, using different drugs and a variety of routes of administration[16 26]. This observation has led to the development of the *operant reinforcement model* of substance use. Substances might be reinforcing in two general ways: through the direct effects of substances upon some sort of reinforcement system in the brain; or through their effects upon other reinforcers (such as social or sexual reinforcers, or through removing aversive stimuli such as distress or dysphoric moods) or behavioural effects (such as increased attention) [16].

Another group of behavioual theories use *classical conditioning* to explain the development and persistence of addictive behaviour [27 28]. According to *cue exposure theory*, cues for substance use are important in the development and maintenance of addictive behaviour [27 29]. A cue that has been present when substances were administered will be more likely to elicit a conditioned response (*cue reactivity*), which is thought to underlie craving. Cue reactivity may explain why someone who was dependent upon a substance but has been abstinent for some time experiences strong cravings when exposed to drug-related cues [27].

There are numerous other theories of the processes involved in the development of dependence[30 31], and it is clear that there is some interaction between the processes identified in the behavioural models and those in the neuroadaptation or neurobiological models of the development of dependence. The operationalisation of the dependence syndrome in the DSM-IV and ICD-10 includes both neuroadaptation and behavioural components. This takes into account that for some drug classes (and for some individuals) either aspect may be more prominent in the development of dependence.

8.5. Complicating Issues

As noted in Chapter 2, pills sold as "ecstasy" may not contain any MDMA at all. This means that persons developing regular or "dependent" use of the drug "ecstasy" may not always be taking MDMA. Although the importance of expectancies in the subjective experience of acute drug effects has been established, the way in which this might facilitate dependent use is as yet unexplored.

Related to this is the possibility that some (or many) pills sold as ecstasy may contain methamphetamine, not MDMA[32] (see Chapter 3). Regular users may therefore be developing dependence upon methamphetamine instead of, or as well as, MDMA. Previous research has attempted to control for the effects of other drug use, including methamphetamine[1 33], but this "other drug use" is what *users believed to be methamphetamine.*

8.6. Animal evidence on the dependence potential of MDMA

The first question that arises about the nature of the MDMA dependence syndrome is the extent to which there is evidence from animal models to support the dependence potential of MDMA. There is evidence that MDMA induces dopaminergic activity in the mesolimbic 'reward' pathway (Robeldo et al, 2004b), but that this is dampened by antagonistic neurotransmitter release in other parts of the reward system due to the drug's activity at serotonergic receptors [34]. Behavioural studies with rodents show that the drug is reinforcing using classical conditioning assessments such as conditioned place preference methods [35] . However, operant conditioning studies where animals need to work progressively harder to receive a dose of the drug show that MDMA is a less potent reinforcer of behaviour than cocaine or methamphetamine [36 37].

Similarly, typical physical or dysphoric signs of a physical dependence syndrome (such as withdrawal) do not develop in animals chronically treated with MDMA [38]; and there are neurobiological reasons why this may be the case. Together, animal studies to date have shown that although MDMA is rewarding, it may be less rewarding than other illicit drugs. As such, it may be the case that MDMA has weaker effects on biological reward systems, and hence the biological neuroadaptive responses to these actions may also be attenuated. This suggests that the course of "dependence" upon ecstasy may differ from other drugs of dependence such as opioids, where the disorder is often chronic, where users are at high risk of developing dependent use, and among whom demand for treatment for such use is high (e.g. [39]).

8.7. Evidence for an "ecstasy dependence" syndrome in humans

For many years, it was thought that it was not possible to become dependent upon ecstasy (MDMA)[40]. This might have been in part because some of the characteristic features of the classic drug dependence syndrome were not common among regular MDMA users. After ecstasy began to be used recreationally, most users used the drug irregularly, in quite specific contexts (e.g. nightclubs), use was time limited (e.g. confined to a weekend evening), and there was little injection of the drug (a route of administration often associated with dependence risk[41]).

As the prevalence of ecstasy use has increased over time in the general population[42] [43], some features of use have been documented that may reflect the development of problematic ecstasy use patterns. Now among regular ecstasy users in Australia, for example, some users report very frequent use[44], significant minorities report experimenting with injection of the drug[45], many users report "bingeing", i.e. using the drug continuously for more than 48 hours[44]. Use is also extending into a wide range of contexts, with the traditional nightclub environment now just one of many common use locations[44]. Users perceive risks[46] and harms[44] [47] associated with their ecstasy use. It is therefore perhaps not surprising that the literature on problematic and putatively dependent ecstasy use has expanded considerably since the mid 1990s.

8.7.1. Current diagnostic classification

In leading psychiatric diagnostic classification systems, there is no ecstasy dependence syndrome included, but it is possible to classify an ecstasy-dependent person as dependent upon hallucinogens and/or amphetamines[12]. This classification has important implications because the dependence syndrome described for each of these drug types differs both nosologically and empirically.

Amphetamine dependence includes a withdrawal syndrome as one of the criteria[12]. Amphetamine withdrawal symptoms include craving the drug, fatigue, psychological distress (irritability, depression, anxiety, disturbed sleep, and problems with concentration) and physical problems that may include sweating, decreased appetite, and body aches[48].

The DSM-IV diagnostic criteria for amphetamine dependence have been shown to be unifactorial[48], as are those for other drugs such as alcohol, opiates and cocaine[49]. There is now

good evidence for an amphetamine dependence syndrome[48 50 51], which typically occurs after a period of sustained regular use. Daily use is particularly risky[52 53], but weekly users are still at risk of developing dependence[54]. Dependence has been associated with mental health, physical, occupational, relationship, financial and legal problems[55-60].

Hallucinogen dependence does not include a withdrawal syndrome as one of the criteria[12]. Considerably less work has investigated the nature and validity of the hallucinogen syndrome. Existing evidence suggests that the syndrome is less severe than for amphetamines, and that hallucinogen dependence is not unifactorial, but conforms to a two-factor structure[61].

8.7.2. Case studies of ecstasy dependence

In 1999, Jansen reported three cases of ecstasy dependence in the literature[62]. Two cases involved persons who had access to large amounts of high purity MDMA, whose use escalated markedly as their tolerance to the effects grew, and for whom the costs of greater use did not present a problem)[62]. The third case involved escalating use by a person suffering from post-traumatic stress disorder (PTSD) who found that MDMA helped him overcome the emotional detachment that had been a core feature of his PTSD. He devoted increasingly large proportions of his income to fund purchase of the drug as his use became more frequent and tolerance increased[62].

Each of these individuals displayed key phenomena of drug dependence. They developed clear tolerance to the effects of the drug; they spent increasing amounts of time using and getting over the effects of using ecstasy; other activities were neglected; they perceived harms related to their use; they had attempted to cease use without success; and they reported mild withdrawal symptoms in the comedown period[62]. All three also had other drug use disorders and one had comorbid mental health problems.

Notably, in two of these cases, there was extremely ready access to the drug. For the other, the symptoms of a pre-existing psychiatric disorder may have played some role in increasing the initial rewarding effects of the drug.

8.7.3. Studies of "ecstasy dependence" among users

There have been a handful of studies examining "dependence" among ecstasy users. All of these have involved the use of interviews designed to measure dependence on different classes of drugs.

An early study[1] found that among a sample of 185 regular ecstasy users (median of 12 days (range 2-100) of use in the past six months), 64% had met criteria for lifetime ecstasy dependence, as assessed by the Composite International Diagnostic Interview (CIDI). Dependent persons typically met criteria for dependence during their heaviest use period. The frequency of such use was not necessarily high: during this heaviest period, 66% were using only one or two days per week, and 25% were using between one to three days per month[1]. Reported "withdrawal" symptoms were highly prevalent, leading the authors to observe the difficulty in distinguishing withdrawal symptoms from the sub-acute 'comedown' effect from dysphoria relating to the absence of the drug which is reversible on reinstatement of use[1].

Nonetheless, those who met criteria for dependence reported greater levels of financial, relationship and social problems; more anxieties about their drug use; higher levels of criminal behaviour; and higher health risk behaviours than those who were not dependent. Multivariate analyses found that these associations were not explained by other drug use[1].

A small US study using the CIDI to assess DSM-IV ecstasy dependence found that among 52 ecstasy users, 43% met criteria for lifetime dependence upon the drug[63]. No information on patterns of use or correlates was provided[63]. Very high self-reported rates of withdrawal symptoms (59%) and "continued use despite knowledge of harm" (63%) were found.

One Washington study of "rave" attendees using the CESAR Arrestee Drug Screener (CADS) found that 17% screened positively for probable ecstasy dependence[64]. Multivariate analyses found that sex, race and other drug use were the strongest predictors of ecstasy dependence[64].

A very small study of US university students who used ecstasy (n = 26) found that around half (n = 14) met criteria for ecstasy abuse or dependence[65]. Those meeting criteria for abuse or dependence reported more lifetime and past year occasions of use, as well as heavier use within each session; but those *without* a use disorder reported more frequent and heavier use in the past month[65].

A novel "ecological momentary assessment" design was used a in a recent study[66]. 22 regular ecstasy-using participants wore wristbands for six weeks and reported on drug use and craving regularly across the period. The researchers found that although craving for ecstasy was low

overall, craving for ecstasy increased over the 24 hours before use, and was higher on Friday nights before the weekends on which ecstasy was used compared to those Fridays when it was not[66].

A study of 200 Taiwanese juvenile justice detainees who used ecstasy (63% had used ecstasy 20 times) measured ecstasy "dependence" using the amphetamine dependence questions from the Kiddie epidemiologic version of the Schedule for Affective Disorders and Schizophrenia (K-SADS-E) [67]. They found that 22% met criteria for "dependence"; 36% reported no dependence symptoms. The most commonly reported dependence symptoms were continued use despite knowledge of problems (37%) and spending considerable time using and recovering from the effects of the drug (30%).

The largest study of dependence among ecstasy users thus far included 1,662 regular Australian users and examined the Severity of Dependence (SDS) [68]. The SDS is a five item self-report scale assessing compulsion to use a drug (the "psychological" component of dependence), with items relating to impaired control over drug taking, preoccupation with a given drug and anxieties about drug taking [53] [69]. Among those who screened positive for dependence upon ecstasy according to the SDS (18% of the sample), 49% used the drug once or twice per week; while 34% used just one to three times per month; only 2% of those who screened positive for ecstasy dependence (n = 7) were using it at least every second day [68]. Nonetheless, the reported financial, legal and work-related harms of ecstasy were more common among this group, as were sexual risk behaviours, overdose, and help seeking behaviours, compared to those who did not screen positively for dependence. Further stratified analyses suggested that, despite high levels of concurrent methamphetamine use, these associations were independent of problematic methamphetamine use.

A German study found that 16% of current ecstasy users met criteria for DSM-IV ecstasy dependence when assessed using a standardised assessment interviews to assess DSM-IV dependence[70]. Finally, a German population-based study of young adults, which assessed drug dependence using the CIDI, which found that small proportions of the young adult population in Germany (0.4%) met criteria for past year ecstasy/hallucinogen/stimulant dependence[71].

8.7.4. The structure of the ecstasy dependence syndrome

Two studies have examined the structure of the ecstasy dependence syndrome, both conducted in Australia. DSM-IV dependence criteria for ecstasy were examined by Topp et al (1997). A bi-

factorial structure was identified, with independent components defined as *'compulsive use'* (use despite problems, giving up important activities because of ecstasy, unsuccessful attempts to stop, withdrawal and excessive time spent obtaining or using) and *'escalating use'* (tolerance, and using more or for longer than intended).

In a 2008 study by Bruno and colleagues, the factor structure of the SDS applied to ecstasy was examined [68]. Multiple studies have shown that the SDS has good test-retest reliability, high internal consistency, and construct validity for opioids, cocaine and amphetamines [69]. The scale is unidimensional for opioids, amphetamine and cocaine and has high diagnostic utility in detecting DSM dependence [50 69 72 73]. In this study [68], dependence upon ecstasy did not have a unifactorial structure, but rather, two related factors provided a good fit to this data, which were defined as 'compulsive use' and 'escalating use'. The same factors were identified ten years earlier by Topp and colleagues using DSM-IV dependence syndrome items.

The two-dimensional structure of the dependence syndrome found in studies of ecstasy users, together with the findings from animal literature, could suggest that the biological basis for a dependence syndrome similar to other drugs, although attenuated, could be present, but that other issues, for example, behavioural reinforcements, may additionally play a strong role in the syndrome [68]. These findings, although limited to the context of users in one country, did comprise a very large (n = 1658) national sample of users; they certainly suggest that the continued classification of ecstasy dependence within the same diagnostic code as amphetamines is not warranted. There is debate as to the categorisation of ecstasy dependence in future revisions of the DSM [74] and evidence certainly suggests that a separate category may be warranted for ecstasy.

These findings carry two important implications. Firstly, the dependence syndrome does not appear to be of the same nature as for drugs such as alcohol, opioids and amphetamine, suggesting a different series of underlying causes, perhaps with a less clear biological basis; this is consistent with the mixed findings from animal research. Secondly, regardless of the nature of any dependence syndrome, some users clearly experience problems related to their use, which cause them distress, and for which they might request help.

8.7.5. The course of ecstasy dependence

Only one study has assessed the prognosis of persons who met diagnostic criteria for ecstasy dependence, using a structured diagnostic interview for DSM-IV[71]. This was a German

population-based study of young adults. The study had a mean follow up period of just over three years and ecstasy use and dependence were assessed each time. The researchers found that those meeting criteria for DSM-IV ecstasy dependence at baseline were highly likely to have remitted three years later – 93% were no longer dependent at follow up[71]. Of this 93%, 50% were no longer using the drug, and of the 43% still using, the majority did not meet criteria for a use disorder. The authors suggested that ecstasy dependence might constitute a "transient phenomenon"[71].

Returning to the criteria for a useful diagnostic entity outlined in Section 8.2, the transience of this syndrome suggests that in contrast to a valid clinical entity, "ecstasy dependence" as assessed in that survey failed to provide useful predictive information about course.

8.7.6. Treatment seeking for ecstasy-related problems

Some users do present for treatment because their ecstasy use has become problematic for them. Routine data collections in Australia[44 75] and the United States[76] have documented persons requesting treatment of their ecstasy use. In Australia, the numbers are very small (less than 1% of all episodes), considering the prevalence of MDMA use in the general population compared to heroin and cocaine use [42]. Ecstasy is more often noted as a secondary drug of concern[44]. This is consistent with surveys of ecstasy users, which consistently find that although some ecstasy users report concerns about their ecstasy use, treatment seeking is very low for this group[44 70].

One study of clients presenting for drug treatment in Texas, United States examined 38,350 treatment episodes between 1988-2003 for persons admitted with problems with so-called "club drugs" (e.g. ecstasy, GHB and ketamine) and compared them with users of alcohol or other drugs[76]. Club drug users were more impaired on five of six Addiction Severity Index (ASI) indices at admission, and they were more likely to have a broader range of heavier, polydrug use patterns. Treatment completion rates were higher for this group than alcohol or other drug clients. At follow-up 90 days after discharge, club drug users continued to report more ASI problems. The authors noted the higher levels of co-occurring mental health and other drug use problems for ecstasy users seeking treatment[76], suggesting that these problems might be more important drivers for presentation to treatment services.

The above data suffer significant limitations, and should not be taken to estimate treatment demand nor treatment need. A reliance on routine data collections to estimate treatment need presupposes that existing drug treatment systems are accessible to, known about, and attractive

to ecstasy users who are in need of help in addressing their drug use or the problems associated with this use. It is quite likely that existing treatment services that are oriented to persons with alcohol, opioid and stimulant drug problems are much less attractive to people with MDMA problems..

These data do suggest, however, that in contrast to alcohol and other drug clients, problematic use of ecstasy alone may be a less significant reason for entering treatment. Problems related to the use of other drugs and mental health may play more of a role in the presentation of MDMA users for treatment. Chapters 9 and 10 examine the evidence on comorbid drug use and mental disorders among ecstasy users.

8.8. Summary and implications

The beginning of this Chapter outlined the core features of a "valid" diagnostic entity, and evidence for those features has been reviewed for ecstasy. The evidence for an ecstasy dependence syndrome is limited in scope and by weak study designs. Animal evidence relevant to the topic suggests that MDMA may be a less potent reinforcer than other drugs but it does nonetheless have dependence potential. This suggests that a) the physiological basis of an ecstasy dependence syndrome might be relatively weaker in comparison to other drugs with very clear and marked dependence potential (e.g. opioids), and b) other factors related to the behavioural and psychological aspects of reward and dependence may make a relatively greater contribution for ecstasy than for other drugs of dependence.

Human evidence suggests that this is the case. Some people do report problems controlling and concern about their use, but the notable lack of case reports of severe tolerance or withdrawal syndromes in the literature suggests that physical features play a more limited role than psychological ones. Although tolerance has been reported, as has withdrawal, the existing literature is based on self-report and there is insufficient data to distinguish between the sub-acute effects of ecstasy intoxication and a "true" withdrawal syndrome. Controlled studies of withdrawal are required to investigate this further.

There is insufficient data to allow a rigorous evaluation of the validity of any "ecstasy dependence syndrome". Prospective studies are required to assess stability of the diagnosis over time, as are multi-method assessments of "dependence" that are not reliant on a single assessment method. Existing studies examining the structure of ecstasy dependence suggest that the nature of dependence upon ecstasy is different to drugs such as alcohol, methamphetamine and opioids. A two factor structure has been identified, as has been the case for hallucinogens, with factors reflecting "compulsive use" and "escalating use" factors.

Regardless of the nature of any MDMA dependence syndrome, there is clear evidence that some ecstasy users become concerned about their use. Although presentation for treatment of ecstasy use appears relatively uncommon compared to the prevalence of its use in the general population, it does occur. Much more study is required but evidence suggests that co-occurring drug use and mental health problems may play a role in presentation for treatment.

8.9. References

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