

4-MTA: a new synthetic drug on the dance scene

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Abstract

4-MTA (*p*-methylthioamphetamine) is a new synthetic sulphur derivative of amphetamine that has been associated with six deaths since it was first identified in Europe in 1997. Sold as 'ecstasy' or 'Flatliners', the drug like MDMA is a potent serotonin releaser. Using a self-nominated sampling methodology we accessed over 1000 dance drug users through a magazine survey. Ten percent of respondents thought that they had used 4-MTA. Those with experience of 4-MTA tended to come from a sub-population of heavy 'ecstasy'-users. Responses to the effects of the drug were mixed, although about a quarter of those who believed that they had tried 4-MTA thought that they would use it again. © 2002 Published by Elsevier Science Ireland Ltd.

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1. Introduction

1.1. Background

4-MTA (*p*-methylthioamphetamine, 4-methylthioamphetamine) is a new synthetic stimulant drug that has recently been identified as a substance of abuse within the dance club scene in Europe. Usually sold as tablets, 4-MTA has been marketed as both ecstasy and as a novel drug in its own right under the name 'Flatliners' in the UK and has appeared as tablets marked 'S-5' or 'MK' in other European countries (EMCDDA, 1999). Typically white tablets scored across the middle on one side have been reported to contain 100–140 mg of 4-MTA.

4-MTA was first identified in Europe in 1997 and to date seizures have been made in the UK, Netherlands and Belgium (Groombridge, 1998). Of particular concern is that since its first identification in 1997, there have been at least five deaths in the UK and one in the Netherlands (EMCDDA, 1999) some of which have received publicity in the popular press. Further there

have been a number of serious physical complications reported in association with its use including respiratory depression (Huang et al., 1992). In all but one case, other psychoactive substances are thought to have played a role. Possession has recently been controlled by legislation following recent recommendation by the Advisory Council on the Misuse of Drugs in the UK and in Europe (EMCDDA, 1999).

4-MTA is a psychoactive (thio-substituted) sulphur analogue of amphetamine. The compound is optically active and the exact composition will depend on the synthetic route used to synthesize it. Although little is known about the action of 4-MTA in humans, other sulphur analogues have been prepared and have predicted potency of 30 times that of mescaline (Nichols and Shulgin, 1976). It is thus highly probable that other thio-derivatives will become available for illicit sale.

Initially synthesized with anti-depressant potential in mind its pharmacological effect is similar to that of 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy'), leading to an acute release of serotonin (5-HT). Its mechanism of action includes (in addition to the direct release of serotonin) the inhibition of Monoamine Oxidase-A activity (Li et al., 1996). These combinations of actions are responsible for the potential of 4-MTA to induce the serotonin syndrome (hyperserotonergic state)

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(Lane and Baldwin, 1997). Adverse effects have included nausea, nystagmus, hyperthermia, thirst, shivering, confusion, memory loss, sweating, intoxication and amnesic effects (EMCDDA, 1999). Although there have been no systematic studies of 4-MTA in man, anecdotal evidence suggests that risk of adverse events may be increased by the slow onset of effects (>1 h) compared to MDMA and the possibility that users take more ‘pills’ in the belief that the initial tablet was of poor quality or of a small dose.

There are no clinical data on the neuropsychological effects of 4-MTA in humans. However, limited animal work and anecdotal reports indicate that 4-MTA is empathic (of the entactogen drug class) but with a slower onset of action and of longer lasting effects than MDMA. A small number of users have experienced a combination of a peaceful and calm feeling but with a stimulating effect that is neither energising nor psychedelic, but strongly hampers sleep. Other effects include feeling drunk and dizzy (EMCDDA, 1999).

To our knowledge, there have been no epidemiological studies assessing the prevalence of use of 4-MTA among drug users associated with the dance music scene in the UK. Consequently, the pattern of use, and the quality of experience with the drug are not known. This paper reports some initial UK epidemiological data on 4-MTA use in a non-treatment sample that use ‘dance drugs’.

Identifying and engaging drug users from non-treatment (‘hidden’) populations in research studies are problematic and obtaining access to a large sample is often difficult (Griffiths et al., 2000). Previous studies have used snowballing techniques (Callow, 1996; Topp et al., 1999), privileged access interviewing (Beck and Rosenbaum, 1994; Brown et al., 1995; Williamson et al., 1996) research advertisements and questionnaires in magazines (Winstock et al., 2001a; Petridis and Sherlock, 1996). All of these survey methodologies have their limitations and conventional survey techniques also tend to perform poorly in this area. Thus convincing random samples of ‘hidden drug users’ are rarely available, if ever.

Despite these problems, there has been increased interest in studying and tracking patterns of drug use using non-random sampling methods within the dance scene. Research of this nature has recently become a focus for advisory groups such as the Office of National Drug Control Policy (ONDCP) in the United States (McCaffrey, 1998).

Thus as part of a wider study exploring current patterns of drug misuse and harm reduction methods employed by ‘clubbers’ we have investigated the use of ‘Flatliners’ thought to contain 4-MTA to assess its prevalence, associated pattern of use and reported desirability.

2. Method

2.1. Subjects and setting

Our subjects were a self-nominated sample of regular drug users who responded to a 13-item self-completion questionnaire placed in ‘Mixmag’, a popular UK media publication whose primary target audience is one interested in the dance music scene. This publication is targeted at those involved in the dance music scene and with a circulation of about 50,000 is one of the UK’s largest, Rave’ music and other such dance music forms have previously been shown to be associated with the use of drugs such as MDMA and other stimulant drugs (Forsyth et al., 1997; Saunders, 1997).

It was hoped that association with a magazine that has credibility in the youth market would produce a higher response than advertising in more generalist publications.

2.2. Measurements

Use of other substances in particular alcohol was also significant. We used the fiveitem Alcohol Use Disorders Identification Test (AUDIT) (Piccinelli et al., 1997), which detects harmful use of alcohol (cut-off score of 5 being indicative of harmful drinking) to gauge alcohol consumption.

3. Results

3.1. Subjects

One thousand one hundred and fifty-one subjects responded, of whom 689 respondents (60.5%) were male, and 462 (39.5%) were female. The mean age of all respondents was 23.9 years (\pm S.D. 5.49), with male respondents being significantly older (24.6 years vs. 22.9 years, respectively, $P < 0.001$). The majority of the sample were employed (65%, 745), nearly one-third (27%, 308) were students, with only 6.0% (72) unemployed. The mean demographics for Mixmag readers based on the magazines marketing data was; age 21–23 years, 70% male, 30% female, with 70% being employed and 30% being students. This suggests that the sample broadly reflected the demographics of the readers of the magazine as a whole and hence by inference a sub-population of the dance music scene.

3.2. Awareness and perception of 4-MTA

Just over three-quarters (868/1151, 75.7%) of the respondents reported having heard of ‘Flatliners’ or 4-MTA. Subjects were asked what they had heard about the drug. Just over half (438/868; 50.5%) said reports of

the effects of its use had been predominantly negative, 2.6% (23/868) predominately positive, whilst the remainder (390/868, 46.6%), reported hearing that 'Flatliners' had both good and bad effects.

3.3. Availability and associated patterns of use

Just over a quarter (241/868, 27.8%) of those who had ever heard of 'Flatliners', (4-MTA) had been offered tablets purporting to contain 4-MTA. A total of 116 subjects (116/1151, 10.0%) reported ever having used 'Flatliners', of whom 71 (61.7%) were male. The mean number of times 'Flatliners' had been used was 3.2, with 87 subjects (7.6%) reporting use within the last 30 days. The mean age of first use was 20.8 years (S.D. 4.4 years).

Users of 'Flatliners' tablets reported significantly more days of ecstasy use within the last 30 days (5.8 vs. 4.1 days, $P < 0.0005$), higher typical levels of ecstasy tablets consumed per session (3.9 vs. 2.7 tablets, $P < 0.0005$), higher maximum number of tablets ever taken in a session (8.7 vs. 5.6 tablets, $P < 0.0005$) and, a greater number of consecutive days on which ecstasy tablets had been taken (5.2 vs. 3.1 days, $P < 0.0005$) when compared to those subjects who reported never having used 'Flatliners'. Additionally in our respondents female users of 'Flatliners' had significantly more days of amphetamine use in the last month than their male counter parts (4.3 vs. 2.2 days, respectively, $P < 0.05$), but male users reported significantly more days of cannabis use within the last 30 days (18.0 vs. 11.8 days, $P < 0.05$).

Use of other substances in particular alcohol was also significant in our subjects. The fiveitem AUDIT with a cut-off score of 5 being indicative of harmful drinking was used to gauge alcohol consumption (Piccinelli et al., 1997). We found that 72% of all respondents (825/1151) scored ≥ 5 , whilst the mean score of those who said that they used 'Flatliners' was 8.

3.4. Reported effects and desirability

Of those who reported ever having taken 'Flatliners' one quarter reported 'really good' effects, one half reported the experience as 'OK', with the remaining quarter reporting effects as 'not good' or 'very unpleasant'. Most users reported having taken one tablet, though 17 subjects (14.7%) reported taking three or more tablets during an evening (range 1–10). Of those who had tried 'Flatliners', approximately 25% (29/116) thought they would try the drug again, 40% thought they would not, with the remainder being undecided.

4. Discussion

4.1. Limitations of study

This study is subject to significant methodological limitations. Caution needs to be exercised when reviewing these findings since it is not possible to be certain that all tablets identified by respondents as 'Flatliners' did indeed contain 4-MTA. Identification of illicitly produced tablets on the basis of superficial inspection is impossible, although in the case of 4-MTA, these tablets may have a faint particular odour presumably due to the sulphur content of the compound (Poortman-van der Meer, 1998). However, the comparatively poor ratings in terms of experience given to 'Flatliners' seems to suggest that the tablets did, at least, contain something other than the most common ingredient of tablets sold as 'ecstasy', MDMA.

The fact that a significant percentage of respondents had purchased a distinct brand of pill known as 'Flatliners' (believed to contain 4-MTA) is suggestive that they existed at least as an identified, distinct drug product on the dance drug scene. Although there is wide variation in content of 'ecstasy' pills (Winstock and King, 1996; Wolff et al., 1996), to our knowledge tablets scored in the particular topographical appearance of 'Flatliners' were not found to contain psychoactive compounds other than 4-MTA in the period 1997–1999.

In the present study, the sample was self-nominating and thus subject to bias and certainly cannot be said to be representative of UK dance drug users. There is no information as to how the responders differed from non-responders. However, the broad similarity of demographics between responders and other readers of the MixMag publication does suggest some degree of congruence between the two samples. It may be that those readers with the greatest interest and involvement in drug use may have been more likely to respond. It is likely that this sample therefore better represents the 'heavier end' of drug use in the dance music scene, than those dance music enthusiasts whose drug use is less intense.

A bias towards more intensive users does not compromise the validity of the sample in this particular study since its aim was to explore patterns of drug consumption among regular users, who may have a greater likelihood of using 'Flatliners'. Although the prevalence of current 'Flatliner' (tablets thought to contain 4-MTA) use reported by this sample cannot be extrapolated to the majority of young peoples' drug use in any general sense, it does suggest that within at least a particular part of the youth population, numbers of young people have been exposed to a new and potentially dangerous synthetic stimulant. Further data analysis on the drug use patterns of the subjects in this study

and further discussion on the methodological limitations can be found elsewhere (Winstock et al., 2001b).

4.2. Summary

Magazine surveys can be a useful source of detecting new drug trends in dance drug using populations. In our study three-quarters of a sample of over 1000 dance drug users reported having heard of the drug, whilst 10% reported having used 'Flatliners', with only a minority reporting a negative experience. Although the sample is non-random we obtained access to a large group of regular drug users actively involved in the dance music scene and within a short space of time. In doing this we have obtained some initial epidemiological data on both the prevalence and associated patterns of use of 'Flatliners' (tablets which are believed to contain 4-MTA—a new synthetic drug).

'Flatliners' (tablets which contain 4-MTA) were apparently quite widely available among those drug users who are involved in the dance music scene. Our users tended to be those who habitually consumed high levels of 'ecstasy' tablets as well as other substances, notably alcohol. In contrast to anecdotal reports, over three-quarters of respondents reported their experience of 'Flatliners' as either very positive or at least 'OK'. The variation in reported effects, although possibly attributable to inconsistent 'Flatliner' pill composition, may also reflect individual pharmacogenetic variation. There is believed to be far more variation in the ability to metabolise thio-substituted compounds than the equivalent oxy-substituted ones (Nichols and Shulgin, 1976). This may explain the spectrum of effects reported by users from no effect to a marked psychoactive effect (Shulgin and Shulgin, 1991). As a derivative of amphetamine metabolism by the cytochrome P450 'super family' of oxidative liver enzymes is possible and may in part explain this variability since the activity of these enzymes can be altered by prior xenobiotic exposure, by its genetics and by co-administered drugs (Cho et al., 1999).

The reported long acting nature of 4-MTA, its prolonged empathic effect and apparent inhibition of sleeplessness may have contributed to the positive effects reported after consumption of a 'Flatliner' tablet. Less than half of our subjects reported that they would not take it again. Although the majority of respondents reported the use of only one tablet (believed to contain 4-MTA), there were small groups who reported use of multiple tablets, which may be a risk factor for serious adverse events. The combination of 4-MTA with other drugs such as MDMA, amphetamines, alcohol and ephedrine products may increase the risks of serious problems consequent upon its use. Similarly certain tyramine rich foods could induce serious adverse inter-

actions due to MAOI effects in susceptible individuals (EMCDDA, 1999).

Given the relatively short time the 4-MTA has been identified as being available to recreational users, it is particularly worrying that the number of serious incidents implicating its use is high compared to that of MDMA. Ecstasy (MDMA) has been associated with a few hundred deaths across the whole of Europe in the last 10 years, with even more conservative estimates regarding the risk of death following the consumption of MDMA from countries such as Scotland (Gore, 1999).

This is however, one of the first instances where media concern about 'dangerous' or 'contaminated pills' is perhaps warranted. The appearance and early identification of tablets that contain potentially more dangerous compounds such as 4-MTA may be seen as supportive of the Dutch policy of 'pill testing', which successfully alerted users to the presence of atropine in a batch of ecstasy pills in 1997 (DIMS, 1998). 4-MTA is however only one example of many new synthetic drugs that has been identified within the dance music scene. For instance, in Australia there have been several fatalities related to the use of *p*-methoxyamphetamine (PMA, Byard et al., 1998; Byard, 1999), which shares not only the stimulant and hallucinogenic effects of MDMA but also its risk of hyperthermia (and hyperpyrexia).

However, while such methods (media exposure) may alert monitoring agencies and users to more 'dangerous' constituents, by implication a result confirming the presence of MDMA in an illicit tablet appears to give a 'shine of safety' to a drug that has been associated with a wide range of physical and psychiatric problems (Cohen, 1996; Topp et al., 1999; Curran and Travill, 1997), as well as numerous fatalities (Milroy et al., 1996; Dar and McBrien., 1996) many of which may have been idiosyncratic and thus not predictable from the composition of the tablet. Further some rapid 'colour reagent' detection kits commonly employed in clubs, based on the Marquis test (a mixture of sulphuric acid and formaldehyde) is not responsive to the presence of 4-MTA (Winstock et al., 2001b). Clearly some formal laboratory based method is required to monitor those drugs on the 'dance scene'.

In summary early detection and dissemination of information about the risks of new synthetic compounds through club outreach workers, magazines and the media should be considered as a means of raising the awareness of drugs that may prove to be far more dangerous in terms risk of mortality than ecstasy. 4-MTA (believed to be present in tablets called 'Flatliners') may be the first of many novel stimulant compounds that are marketed in an attempt to bypass current legislation and precursor control while at the same time providing sought after effects. The appearance and use of 'Flatliners' tablets also demonstrates the

ease of branding a new drug to a receptive, drug curious population. Continued vigilance will be required to detect new synthetic compounds that may find their way into the dance drug scene, perhaps under the guise of an already familiar tablet.

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