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RESEARCH REPORT

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# Mephedrone: use, subjective effects and health risks

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## ABSTRACT

**Aims** To assess the patterns of use, subjective effect profile and dependence liability of mephedrone, supported by corroborative urine toxicology. **Design** Cross-sectional structured telephone interview. **Setting** UK-based drug users associated with the dance music scene. **Participants** A total of 100 mephedrone users, recruited through their involvement with the dance music scene. **Measurements** Assessment of pattern of use, acute and after effects, DSM dependence criteria and gas chromatography-mass spectrometry urinalysis. **Findings** Mephedrone consumption results in typical stimulant-related subjective effects: euphoria, increased concentration, talkativeness, urge to move, empathy, jaw clenching, reduced appetite and insomnia. Thirty per cent of the sample potentially met criteria for DSM-IV dependence and there was evidence of a strong compulsion to use the drug (47% had used the drug for 2 or more consecutive days). Self-reported recent consumption of mephedrone was confirmed by toxicological analysis in all of the 14 participants who submitted a urine sample. **Conclusion** Mephedrone has a high abuse and health risk liability, with increased tolerance, impaired control and a compulsion to use, the predominant reported dependence symptoms.

**Keywords** Abuse, cathinone, dependence, legal highs, mephedrone, risks, toxicology.

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## INTRODUCTION

[1]The β-keto-amphetamine mephedrone (4-methylmethcathinone) is a synthetic stimulant with little, if any, reported use before 2007 [1]. A phenethylamine derivative, mephedrone has a close chemical relationship to cathinone, the psychoactive chemical compound present in the khat plant [2]. Against a background of early reports in Australia, the United States and several countries in northern Europe, the United Kingdom experienced a rapid increase in mephedrone distribution and consumption in 2009–10.

To gather initial data on the health risks of mephedrone, we included several questions on this drug in our annual online sentinel drug user survey among a population of experienced polydrug users who are members of the dance music scene in the United Kingdom (see [3,4] for a detailed description of our methodology). In a recent paper in this journal, we reported a basic description of the use of mephedrone [4]. Our data indicated that, despite previous obscurity, in 2009 mephedrone had been taken by 43% of a total of 2220 respondents: it was ranked as the sixth most frequently used drug that year [after alcohol, tobacco, cannabis, cocaine and 3,4-methylenedioxymethamphetamine, (MDMA)] and was perceived to produce a 'better high' than cocaine.

Users of new or emergent drugs are a relatively hidden population and may be difficult to access using traditional approaches. Online surveys are valuable in providing a rapid illustration of an emergent substance in the drug scene, but limitations include the lack of scope for detailed questioning. Moreover, for new or emergent substances, it is difficult to assess the validity of reports because the substance may acquire several colloquial names with no assurance for the user of the precise nature of the substance's contents. To gain further insights into the health risks of mephedrone, we invited participants in our 2009 online survey to consent to a personal telephone interview with the following aims: to (i) describe initiation to mephedrone and patterns of use;

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(ii) assess a comprehensive set of acute and withdrawal effects; and (iii) assess the prevalence of dependence symptoms. We also conducted a toxicological analysis of urine samples taken following mephedrone use and submitted by participants for analysis. This paper presents the main findings from the study.

## METHOD

### Design and sample characteristics

This was a cross-sectional, structured telephone survey with a urine toxicological analysis of cathinone compounds. Of a total of 947 users of mephedrone who completed our online survey in 2009, 218 had expressed interest in further research contact and had provided contact details. We continued to contact and secure personal telephone interviews with this group until our target of 100 users was reached. The average time to complete interview was 25 minutes; standard deviation (SD) = 6.3. All participants were aged 18 years or older (mean age, 25.1 years, 23 female, and 86% in employment or education), and reported using mephedrone at least once in the previous 12 months. There was a high life-time prevalence of MDMA and cocaine use (96% and 92%, respectively), in keeping with the sample that they had been drawn from [4]. All interviews were conducted between February and 10 April 2010, following initial contact and eligibility screening. Participants were offered a £20 high street store voucher for their participation in the study. The study protocol was approved by the joint ethics committee of the South London and Maudsley NHS Foundation Trust and the Institute of Psychiatry.

### Procedure

On completion of the interview we asked the participant if they intended to use mephedrone again within the next month. Those reporting this intention were asked if they would be willing to take a sample of their urine a day after mephedrone use and send it to the study laboratory, for analysis of cathinones and other drugs. Among the 47 participants who intended to use mephedrone again in the next month, 26 (55%) consented to provide a urine sample. We received a total of 14 samples (54%) for analysis. We developed a confirmatory procedure using gas chromatography-mass spectrometry (GC-MS) for the following 10 methylcathinone compounds: Cath, MC, EC, 4-MMC, 2-FMC, 3-FMC, 4-FMC, DMC (dimethylcathinone), 4-MAB (4-methoxymethylaminobutyrone) and 4-MoxyMC (4-methoxymethcathinone). Cath and MC standards were purchased from Sigma-Aldrich Co. (Dorset, UK) 4MMC was purchased from LGC Standards (Middlesex, UK) and all other compounds were synthesized at Kingston University, London.

### Brief structured telephone interview

We created a brief, structured telephone interview schedule based on, but extending, our previous online survey question set. Through cognitive and pilot testing, we developed a 20-minute interview with 61 items. We generated a set of 28 typical stimulant or empathogenic drug effects (positive/negative and physical/psychological) and 12 withdrawal symptoms. Participants were asked to report how often during mephedrone use they had experienced each effect using a Likert-type rating scale ('never', 'once', 'sometimes', 'most of the time'; scored 0–3) and the average intensity (strength) of each effect reported ('mild', 'moderate' or 'intense'; scored 1–3). For the risk profile in this report, we present the basic prevalence of each effect (experienced 'once' or more frequently) and we computed the product of the frequency and intensity of effect ratings to create a variable with a score range from 0–9, with three equivalent scores: once × moderate and sometimes × mild; once × intense and most of the time × mild; and sometimes × intense and most of the time × moderate.

As an index of mephedrone-related negative consequences and harm, the participant was asked if s/he had experienced a persistent desire or strong urge to take the drug, had been concerned about taking the drug, or whether friends or family expressed concern to them about their mephedrone use. We included seven dependence items adapted from DSM-IV-TR for use in the study [5]. For brevity, we recognized that we would not be able to include a formal clinical diagnosis of dependence in the interview (e.g. using the Composite International Diagnostic Interview [6]). We also excluded the four DSM drug abuse items for brevity, and also because mephedrone was a legal substance at the time of the survey and the item concerning recurrent substance-related legal problems would not clearly apply. Each of three study interviewers (two research workers based at the Institute of Psychiatry (IoP), one IoP postgraduate) received training in the administration of the interview by study coordinators A.W. (psychiatrist) and J.M. (psychologist).

### Statistical analysis

Given the small and non-probability sample, we report descriptive statistics only (PASW, version 18; SPSS Inc., Chicago, IL, USA). Analytical chemistry was performed using liquid chromatography-mass spectrometry and confirmed by GC-MS.

## RESULTS

### Mephedrone initiation and typical session

Eighty-eight participants first used mephedrone in 2009 (the remainder using first between 2008 and 2010). Participants' first mephedrone session lasted for a median of 6 hours [interquartile range (IQR) 4–10], in which a median of four doses were taken (IQR 2–7), with each dose being on average 97 mg and, across the session, a median of 500 mg mephedrone (IQR 200–1000) was consumed. On this first occasion of use 89 participants reported drinking alcohol, 17 used cocaine, 23 used MDMA, 34 used cannabis and 24 used ketamine. At interview, participants reported using mephedrone for an average of 6.1 months (SD = 3.1). Participants were then asked to consider how their use had changed since first using mephedrone, and we recorded how much on average they used as first dose in recent typical session of use. During a typical session, the majority (83 of 100) administered their first dose (average first dose 125 mg) as a 'line' (79% intranasally, 9.9% by wrapping in a cigarette paper and swallowing, and the remainder by tipping some mephedrone powder into a drink). There were no reports of mephedrone taken by injection. The typical session lasted for a median of 10 hours (IQR 6–16), during which a median of 5.5 doses were taken (IQR 3–10), with a median interval of 60 minutes between doses (IQR 30–90; five participants did not answer this question), and median total of 1000 mg consumed (IQR 250–1275). During this typical session 82 participants reported drinking alcohol, 36 used cannabis, 35 used ketamine, 26 used cocaine and 23 used ecstasy. None reported using mephedrone alone and the average group size of co-users was 10 (SD = 8). Forty-seven participants reporting using mephedrone continuously for 48 hours or more; and among these participants the median number of continuous using days was 3 (IQR 2–4 days). In the previous 4 weeks, participants reported taking a total median of 1500 mg (IQR 500–4000; no report from two participants).

### Acute and withdrawal effect profile

We recoded the frequency of having experienced each symptom into a dichotomous variable of ever having experienced a symptom or not (the prevalence). We then calculated the strength of each symptom as the product of the actual frequency and the intensity, and reported the mean for each item on this composite score. The prevalence (ranked) and average strength of the acute effects of mephedrone and related withdrawal effects are shown in Table 1. Increased energy, euphoria and talkativeness were the most prevalent and intense acute effects, while tiredness, insomnia, nasal congestion and impaired concentration were the most prevalent withdrawal-related effects (with nasal congestion the most intense effect).

**Table 1** Mephedrone: prevalence and average frequency × intensity of acute and withdrawal-related effects ($n = 100$).

| *Acute effect* | *n* | *Frequency × intensity of effect (mean, SD)*[a] |
|---|---|---|
| Increased energy | 99 | 6.4 (2.4) |
| Euphoria | 97 | 5.9 (2.6) |
| Talkativeness | 96 | 7.1 (2.7) |
| Urge to move, do things | 94 | 6.1 (2.8) |
| Empathy | 92 | 5.4 (3.0) |
| Jaw clenching, bruxism | 89 | 5.1 (3.0) |
| Body sweats | 81 | 4.4 (3.2) |
| No appetite for food | 81 | 5.3 (3.5) |
| Heart racing | 80 | 3.8 (2.8) |
| Restless or anxious | 74 | 3.3 (2.9) |
| Increased sexual desire | 66 | 3.1 (3.1) |
| Forgetting things | 63 | 3.5 (6.4) |
| Overheating | 62[b] | 2.8 (4.9) |
| Tremor in extremities | 58 | 2.6 (2.9) |
| Blurred vision | 53 | 1.8 (2.2) |
| Improved concentration | 50 | 1.6 (2.1) |
| Paranoia | 41 | 1.4 (2.1) |
| Panic | 35 | 1.2 (2.7) |
| Shortness of breath | 34 | 1.9 (2.0) |
| Headache | 31 | 1.4 (2.5) |
| Agitated | 41 | 1.4 (2.0) |
| Visual hallucinations | 27 | 0.8 (1.5) |
| Extremities cold or numb | 24 | 0.9 (1.9) |
| Vomiting | 23 | 0.8 (1.7) |
| Auditory hallucinations | 22 | 0.5 (1.2) |
| Chest pain | 17 | 0.8 (2.1) |
| Skin blue or red | 14 | 0.5 (1.5) |
| Angry or aggressive | 10 | 0.2 (0.9) |
| Skin rash | 6 | 0.3 (1.2) |
| *Withdrawal effect* | *n* | *Frequency × intensity of effect (mean, SD)* |
| Tiredness | 90 | 1.6 (2.1) |
| Insomnia at end of session | 82 | 2.1 (1.2) |
| Nasal congestion | 78 | 4.7 (3.4) |
| Unable to concentrate | 66 | 2.9 (2.8) |
| Irritable | 64 | 2.5 (2.6) |
| Lost memory of mephedrone session | 59 | 2.5 (2.8) |
| Depression | 57 | 2.3 (2.8) |
| Emotional | 56 | 2.2 (2.9) |
| Anxiety | 51 | 2.1 (2.7) |
| Unusual sweat odour | 42 | 2.3 (3.3) |
| Increased appetite | 33 | 1.3 (2.4) |
| Urge or cravings to use mephedrone | 25 | 1.4 (3.0) |

[a]Product of frequency × intensity of effect (range 1–9). [b]Missing data for one participant. SD: standard deviation.

**Table 2** DSM-IV dependence symptoms for mephedrone ($n = 100$).

| *Symptom (question stem: 'Since you have been taking mephedrone:')* | *n endorsed (%)* |
|---|---|
| Usual dose no longer has desired effect[a] | 53 (54.1) |
| Taken mephedrone or other stimulant to relieve withdrawal effects[a] | 12 (12.2) |
| Taken for longer or in larger amounts than intended | 61 (62.2) |
| Wanted to cut down or stop but had not been successful | 14 (14.3) |
| Much time obtaining, taking or recovering from | 20 (20.4) |
| Important social, occupational or recreational activities given up | 7 (7.1) |
| Continue to take in spite of physical/psychological problems | 24 (24.5) |

[a]Positive symptom taken for endorsement of either item. Note: missing data for two participants on all items.

**Reported DSM-IV dependence symptoms and intention to use next month (Table 2)**

While 20 participants (20.4%) reported no dependence symptoms, 29 (29.5%) reported three or more symptoms and therefore reached an indicative threshold for possible clinical diagnosis of stimulant dependence. Thirty-three (33.7%) were concerned about their mephedrone use, 22 (22.4%) reported a persistent desire or strong urge to use and 15 (15.3%) participants reported that family or friends had expressed concern over their use. Mephedrone consumption was confirmed by GC-MS in all 14 samples submitted. Other concurrent reported drug use was also confirmed in 10 cases (most commonly cocaine, alcohol, ketamine, cannabis and methylone). (Table 3)

## DISCUSSION

To our knowledge, this is the first study to conduct a personal interview with mephedrone users on patterns of

**Table 3** Results of urine toxicology following self-reported use ($n = 14$).

| *Sample no.* | *Mephedrone used, previous 24 hours (mg)* | *Other drugs used previous 24 hours (mg)* | *Results of GC-MS* |
|---|---|---|---|
| 1 | 2000 | – | Mephedrone (+) |
| 2 | 500 | Cocaine (500) | Mephedrone (+)<br>Cocaine (–) |
| 3 | 1000 | Methylone (2000) | Mephedrone (+)<br>Methylone (+) |
| 4 | 1000 | MDMA (100) | Mephedrone (+)<br>MDMA (+) |
| 5 | 2000 | MDMA[a]<br>Cocaine (500) | Mephedrone (+)<br>TFMPP[b]<br>MeOPP[c]<br>Benzylpiperazine (BZP)<br>Ketamine |
| 6 | 500 | – | Mephedrone (+)<br>TFMPP<br>BZP[d] |
| 7 | 3000 | – | Mephedrone (+) |
| 8 | 500 | – | Mephedrone (+) |
| 9 | 500 | MDMA (500) | Mephedrone (+)<br>MDMA (+) |
| 10 | 500 | Cocaine (2000) | Mephedrone (+)<br>Cocaine (+)<br>Ketamine (+) |
| 11 | 1000 | Cocaine (500) | Mephedrone (+) |
| 12 | 2000 | Cocaine (500) | Mephedrone (+) |
| 13 | 500 | Cocaine (500)<br>Ketamine (500) | Mephedrone (+)<br>Ketamine (+) |
| 14 | 500 | – | Mephedrone (+) |

[a]Participant reported taking 'five pills'. [b]3-Trifluoromethylphenylpiperazine, a piperazine stimulant. [c]MeOPP (para-methoxyphenylpiperazine), a piperazine stimulant. [d]Benzylpiperazine, an amphetamine-like stimulant. MDMA: 3,4-methylenedioxymethamphetamine; GC-MS: gas chromatography-mass spectrometry.

use, subjective effects and health risks. Our study is also novel for the inclusion of a toxicological analysis of mephedrone in urine.

The subjective reports from our participants point to a health risk profile common to the stimulant class with a presumed mechanism of action that involves the release and inhibition of re-uptake of monoamine neurotransmitters [7]. The reported risk profile suggests a relatively low incidence of aggressive behaviours at the doses consumed typically by the subjects in this study. The relatively low incidence of adverse effects (compared to sought-after effects) may be due to mephedrone's low potency and short duration of action, the latter permitting titration of dosing and effect. This is not to suggest that the use of mephedrone is without risk. There have been reports of some serious and excessive sympathomimetic reactions from taking this substance, including extreme agitation, aggression, panic, dehydration, confusion, overheating, seizures, cardiovascular dysregulation and paranoid episodes [8].

The indication that mephedrone has a dependence liability is also a matter of concern. Around 30% of our participants experienced three or more DSM-IV dependence criteria. The predominant symptoms were increased tolerance (the study did not ask about within session development of tolerance), impaired control, continuing to take mephedrone despite physical and psychological problems and a strong urge to use the substance. These symptoms were also reflected in the prevalence of using mephedrone for 2 or more consecutive days (47% of our sample). The authors recognize that the process used to assess dependence does not produce a dependence diagnosis, but we suggest that the findings are strongly indicative of mephedrone's dependence potential.

The emerging profile is of a stimulant drug which induces a strong and repeated compulsion to use. This aspect of the drug has also been observed by research groups in the Netherlands and Scotland [8,9].

We readily acknowledge several study limitations. This is a very small sample of self-nominating drug users with uncertain generalizability to the wider using population. We also acknowledge the possibility of recall bias when reflecting on changes in doses used over time, the uncertain reliability when estimating typical doses and the possibility that the reported effect profiles may be contaminated by polysubstance use. The strengths of the study relate to the value in conducting a rapid assessment of new and emerging drug trends. Sentinel samples from target populations can provide valuable insights into new drug use trends [10], and are often the only practical method by which to collect a first impression of a substance's risk profile. There is value in communicating basic data as quickly as possible to inform users, policy and research audiences. Our use of a toxicology analysis also pointed to complete concordance between self-report and detection of the mephedrone in urine. The discordant results for the presence of cocaine in samples 2, 5 and 11–13, where there was reported use, may reflect the low purity of cocaine currently variable in the United Kingdom (the average purity of street level cocaine has fallen from 51.2% in 2003 to 20.3% in 2009 [11]). We also consider it likely that in a social setting it may not be possible for subjects who may have used other substances to differentiate cocaine from other similar stimulants—including ephedrine and mephedrone.

Turning to the implications of this study, it is unknown how the consumption of other stimulant drugs, as well as ketamine and alcohol, can modify the effects of mephedrone, the drug's pattern of health risk behaviours or its metabolism. It is likely that combined stimulant consumption will increase the risk of toxicity. Concurrent consumption of alcohol may lead to greater disinhibition, memory impairment and the possibility of increased health risk behaviours. Harm reduction advice and interventions offered to users of cocaine and other amphetamine-type stimulants hold promise for this population [12]. Although mephedrone was classified as a controlled substance in the United Kingdom in April 2010, it is unlikely that it will disappear from the drug scene. There is evidence that users have migrated from purchasing the drug from online distributors to buying it from street dealers. Further, there has also been a significant increase in price, and the consistency and purity of the substance is uncertain [13]. In time, it is likely that individuals with mephedrone use disorder will present for psychosocial treatment to the National Health Service and other services.

## Declarations of interest

None.

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