

## Persistent psychotic symptoms after long-term heavy use of mephedrone: A two-case series

### *Síntomas psicóticos persistentes después del uso abusivo prolongado de mefedrona: una serie de dos casos*

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#### Abstract

Mephedrone (4-methylmethcathinone) is a synthetic stimulant drug of the cathinone class. Similar effects to those of cocaine and ecstasy are reported by users, with a high addictive potential. Given its increasing rate of consumption in Europe, it is getting more and more attention from the addiction field. In spite of that, little is known about the long-term consequences of prolonged heavy use. The two following cases might depict some of them.

Case 1 was a middle-age man who reported three years of intravenous use of mephedrone. He used to binge for several days in a row. Psychotic symptoms appeared after a few months, especially paranoid delusions. Sent to aftercare in a therapeutic community, delusions kept reappearing after prolonged abstinence. A good response to risperidone was observed.

Case 2 was a young man who used mephedrone heavily for two years, always snorted. Upon admission to the therapeutic community, the patient reported auditory hallucinations that partially remitted with olanzapine. Both cases showed a good insight and no personality deterioration.

Given its similarities to other substances that are known to induce psychotic symptoms, and the increasing consumption of mephedrone around Europe, similar cases are expected in the near future. Conventional antipsychotic treatment seems a reasonable pharmacological approach.

*Keywords:* mephedrone; cathinone; drug dependence; psychosis; heavy use; new psychoactive substances.

#### Resumen

La mefedrona (4-methylmethcathinone) es un estimulante sintético del grupo de las catinonas. Los usuarios refieren efectos similares a los de la cocaína y el éxtasis, con un potencial adictivo elevado. Dada la creciente tasa de consumo en Europa, cada vez recibe más atención desde el campo de las adicciones. No obstante, poco se sabe sobre las consecuencias a largo plazo de su consumo abusivo. Los dos siguientes casos pueden servir para mostrar alguna de ellas.

El caso 1 es un hombre de mediana edad, quien refería un consumo intravenoso de mefedrona de 3 años de duración. Su patrón de uso consistía en atracones que duraban varios días. Tras varios meses de consumo, aparecieron síntomas psicóticos, especialmente delirios paranoides. Tras ser enviado a una comunidad terapéutica, los síntomas psicóticos se continuaron produciendo pese a mantener una abstinencia prolongada. Se observó una buena respuesta a la risperidona. El caso 2 es un hombre joven, con un consumo abusivo de 2 años de duración, vía nasal. A su llegada a la comunidad terapéutica, el paciente refirió alucinaciones auditivas que remitieron parcialmente con olanzapina. Ambos casos mostraron una buena conciencia de enfermedad, así como ausencia de deterioro en su personalidad.

Dadas las similitudes bioquímicas con otras sustancias con potencial para inducir síntomas psicóticos, y el creciente consumo de mefedrona en Europa, casos similares son esperables en un futuro cercano. El uso de antipsicóticos convencionales parece una estrategia razonable de tratamiento.

*Palabras clave:* mefedrona; catinona; dependencia a sustancias; psicosis; consumo abusivo; nuevas sustancias psicoactivas.

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**M**ephedrone, a synthetic cathinone, was initially synthesized as early as 1929 (European Monitoring Center for Drugs and Drug Addiction, 2010). However, its appearance in the context of human recreational consumption dates back only a few years. It displays strong stimulant and entactogen effects, similar to those of cocaine and MDMA (Winstock et al., 2011). Its addictive potential remains high, with some cases of dependence already reported in the literature (Bajaj, Mullen & Wylie, 2010).

Noteworthy, its consumption has dramatically increased in the past few years, reaching, in some countries, levels similar to those of other stimulants, such as cocaine, amphetamines and ecstasy (European Monitoring Center for Drugs and Drug Addiction, 2010). Despite all that, little is known in the actual literature about mephedrone use disorders, its natural history, treatment or adverse effects in the long run.

The biggest population-based study to date (Winstock et al., 2011), with a cross sectional design conducted with club drug users, excluded the investigation of psychotic symptoms associated with its consumption. However, given its biochemical similarity to other psychosis-inducing substances, as well as the specific body of evidence emerging around synthetic cathinones, it would be reasonable to expect such symptoms in the context of mephedrone consumption. As it is the case with other drugs, it would be also relevant to investigate whether psychotic symptoms are related to intoxication, withdrawal or whether they may persist after prolonged abstinence (and in such instances, the risk or association with illnesses such as schizophrenia).

To try to shed some light into these questions, we present two cases of mephedrone addiction with long-term heavy use, who presented persistent psychotic symptoms after prolonged abstinence, treated in a therapeutic community.

### Case 1

A 40 year old, white, single male, with university education and a stable high-qualified job came to our rehabilitation centre accompanied by his family. No previous psychiatric history, neither personal nor familial, was reported. Only occasional cocaine use figured among his substance use records. Three years ago, after a relationship break-up, the patient started using mephedrone. Initially snorted, it soon became an intravenous use, usually associated with sexual activity. The patient reported a heavy use, being able to binge for five consecutive days, usually two to three times per month. The usual amount he used in a day of binge was between 1 and 3 grams.

After a severe deterioration in both his psychological and physical health status, with the emergence of persecution and reference delusions, the patient started an outpatient treatment. Given the lack of success in achieving and maintaining abstinence, he was transferred to our Therapeutic

Community, where he spent 4 months. Upon admission, no antipsychotics were administered, given the fast remission of his delusional ideas once he became fully abstinent. The insight the patient displayed about them was fairly good. However, in the last weekend-permissions before discharge, he reported delusional beliefs again. They lasted only a few minutes, and again, his insight was good, so no medication was considered necessary. Finally, once back in the community, these brief, self-limited psychotic symptoms, mainly delusional beliefs of persecution and reference, kept reappearing. Therefore, risperidone 1 mg each night was prescribed, with complete remission up until the moment of writing this paper, three months after discharge of our therapeutic community.

### Case 2

A 26 year old, white, single male with university education and a high-qualified job came to our Therapeutic Community accompanied by his family after two years living abroad in the UK, where heavy use of mephedrone (always snorted, usually between 1 and 2 grams), on a daily basis, had taken place. The patient had no previous psychiatric history. Occasional use of cocaine was also reported. The patient described heavy use of alcohol in recent years. Upon admission, the patient reported auditory hallucinations, with no behavioural or affective impact. His insight regarding the origin of these psychotic symptoms was fairly good. High dose of olanzapine (up to 30 mg per day) was started, with gradual resolution of the hallucinations, although at the time of writing this paper, the patient is still in our Therapeutic Community and minor hallucinations of a few seconds duration are still present. No other psychotic symptoms were observed.

### Discussion

This report about the psychopathological consequences of long-term heavy-use of mephedrone is in line with previous publications outlining similar effects of mephedrone on heavy users (Dragogna, Oldani, Buoli & Altamura, 2014). Besides the usual consequences of addiction itself (social, organic and psychological deterioration) both cases presented persistent psychotic symptoms after months of abstinence to the substance. The fact that no previous psychiatric history existed in both cases, tentatively leads to a drug-related origin.

Given its biochemical similarities with amphetamines and other stimulants, and their well-known potential to induce psychotic symptoms (Bramness et al., 2012), it is not striking to observe such symptoms after long-term heavy use of mephedrone. A recent body of evidence is emerging, specifically related to synthetic cathinones, its biochemical and neurological toxicity, its behavioural consequences and its

psychiatric and physiological effects (Gregg & Rawls, 2014; Weaver, Hopper & Gunderson, 2015). Given its novelty, however, most of the data provided by this research is related to the acute consequences of consumption. The available evidence suggests that psychotic symptoms are related dysfunctions in the dopaminergic system (Martínez-Clemente et al., 2014). Besides dopamine, other systems such as the serotonergic might also be relevant parts in the overall toxicity of the drug.

Despite the novelty and the short-term nature of these findings, a tentative comparison with the case of methamphetamine might be made to foresee the long-term consequences of mephedrone use, since methamphetamines, biochemically related to synthetic cathinones, are one of the drugs with the highest potential to induce psychotic symptoms beyond intoxication, withdrawal and prolonged abstinence (Lichlyter, Purdon & Tibbo, 2011).

Given the increasing rate of consumption in Europe, especially in the UK (European Monitoring Center for Drugs and Drug Addiction, 2010), and the highly addictive properties of the substance (Weaver et al., 2015), one should consider that the implications might be relevant, as more and more cases are expected in the years to come. Indeed, there are already some reports suggesting that club drugs are one of the most prevalent substances seen in the Emergency Department (Nogué, Amigó & Galicia, 2014)

Although one suffered from delusions and the other from hallucinations, it is also worth mentioning that insight remained partially good in both case studies, and no personality deterioration, more ascribed to schizophrenia-like psychosis, was observed. The duration of consumption had been 3 and 2 years, respectively, therefore it remains unknown what would have happened if heavy use would have continued unchanged. In this scenario, it could be useful to think of a critical consumption threshold, assuming that, beyond a critical point, consumption might lead to persistent psychotic symptoms, and if continued, a chronic psychotic illness might ensue (Lichlyter et al., 2011).

Case series must be interpreted with caution, given their relevant limitations. The most relevant are its observational nature and the lack of control subjects. Therefore, it is not possible to fully establish a real and valid connection between drug use and the symptoms observed. For example, it can not be ruled out that drug use and symptoms onset were merely related by chance. Moreover, two other serious limitations must be taken into account when interpreting this report. First, as it is not implemented in routine clinical practice, upon admission, no toxicological evidence was gathered regarding the actual presence of mephedrone in patients' urine. Therefore, this report is based on patients' self-reports. Although this fact may diminish validity, it is a common methodological approach in the addiction field. Second, both patients had also used cocaine in the past, also a well-known psychosis-inducing substance. Nonetheless,

both reported mephedrone to be, by far, their main substance of abuse. This fact reasonably allows for the described psychopathological symptoms to be subscribed to mephedrone. There remains also the possibility of an alcohol-related origin for the hallucinations of case 2, which should then be labelled as alcohol hallucinosis. However, given the relatively young age of the patient and that no withdrawal or intoxication symptoms were observed during his stay in the Clinic, we considered it reasonable to discard this diagnosis.

Finally, regarding the treatment of psychotic symptoms associated with mephedrone, the little evidence this case series offers suggests that second generation antipsychotics, as in other substance-induced psychotic symptoms, might be useful.

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## Conflict of interests

None of the authors have any conflict of interest to disclose regarding the present report.

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