

Transient psychotic episodes following recreational use of NRG-3

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The increased availability of novel psychoactive substances or ‘legal highs’ over the internet has made screening for recreational drug use much more difficult for doctors in recent years. Here, Drs Kihara and Day describe the case of a young male patient repeatedly presenting with transient psychotic episodes who eventually revealed that each episode had followed the use of NRG-3 obtained from the internet.



Negative attitudes, lack of awareness, and inadequate history taking with regard to alcohol and illicit drug use can present barriers to healthcare for patients. The growing trend in novel psychoactive substance use presents significant challenges for psychiatrists and physicians. Here, we describe a case of transient psychotic episodes associated with the use of the ‘legal high’, NRG-3.

Presentation

A 35-year-old, white British male presented to Accident and Emergency with visual hallucinations and agitation. He was previously well, with no past medical or psychiatric history. He lived with his wife and two sons, aged five and two years old. He had been the managing director of an inherited family business that had collapsed two years previously. He then became a house husband, pursuing an interest in property development while his wife worked as a primary school teacher.

He was admitted with suspected viral encephalitis. A CT head scan, lumbar puncture and serology were all normal. His symptoms resolved within a week and he was reviewed in the clinic one month

later. An EEG and HIV serology were normal. An MRI head scan revealed a soft tissue lesion, suspected to be a benign lipoma. No further imaging or investigations were deemed necessary. No illicit drug screening was recorded.

He remained well for a further three months, but then presented to primary care describing symptoms over the previous week. He reported passivity of volition, visual hallucinations and tingling sensations when touching the women he could see in the room. He described prosopagnosia and auditory hallucinations; hearing sexual moans and groans. His wife reported episodes when he was conscious but not responsive. Repeat EEG was normal. It was also noted that he seemed energetic despite sleep deprivation. He was referred to the Home Treatment Team for further assessment and was discharged after 10 days as his symptoms resolved with benzodiazepines. It was documented that there was no history of illicit drug use on a risk screening tool but no detailed drug and alcohol history was recorded.

He remained asymptomatic for a further six months, when he was referred for urgent assessment by his local Community Mental Health Team (CMHT). He reported vivid visual hallucinations, seeing people shooting at

him in his house, and tactile hallucinations, feeling metal objects being thrown at him. He reported seeing sexual encounters between his wife and other men and had been waking his wife in anger. He described depersonalisation and derealisation and had made errors with routine tasks such as dressing and making the bed. He had crossed a busy road when he saw the traffic light turn green and his wife was concerned for his safety.

During the assessment, he stated that he drank two bottles of wine most weekends and had smoked cannabis regularly in the past, but not since the birth of his first son. His symptoms were settling at the point of presentation and he was advised to take quetiapine 25mg for one night, then 50mg at night until he remained well for three to four days. His symptoms had completely subsided at follow-up two weeks later and he had stopped taking quetiapine after two days of treatment.

Shortly after this, his wife contacted his CMHT as he had not slept for two nights; he was agitated and sweating, and responding to visual hallucinations. He reported delusional perceptions and believed he was being persecuted by a black woman after seeing a black object. Olanzapine was started at 5mg every night for suspected psychosis and a sleep

deprived EEG was normal. One month later, he had stopped olanzapine and remained entirely asymptomatic.

Another four months later, he presented with anxiety, agitation, reduced sleep, olfactory hallucinations, visual hallucinations, secondary persecutory ideas and abnormal writhing movements. His wife called an ambulance and he was taken to a Place of Safety and admitted to a psychiatric ward. He was disorientated to time, place and person, confused, unable to engage in conversation and needed constant observation. He was afraid that his wife would be killed in a car crash and reported hearing his deceased father's voice. He sustained physical injuries from running into the walls in his room and jumping from the bed to the floor. His symptoms resolved over 48 hours with regular diazepam. There was no ongoing evidence of affective or psychotic symptoms and he was discharged.

Overall, there were five distinct episodes of psychotic symptoms requiring medical intervention and completely subsiding within a week. The patient finally disclosed that each episode was associated with the use of NRG-3 purchased from the internet and concealed from family members. He revealed this information during his most recent admission as his symptoms had been worse than previous episodes. He was adamant that he would refrain from recreational drug use in the future and was keen to share his history to serve as a warning to others.

Discussion

This case highlights two important areas. The first is the growing trend in the use of novel psychoactive substances or 'legal highs' as they are popularly known.¹

Modifications to existing drugs in research laboratories are a key part of the process of drug development, and a similar process has been followed with illicit drugs. This has led to a number of compounds appearing on the 'recreational' drug market as a way of avoiding government regulation of specific psychoactive compounds.

The cathinone class of drugs are abused for their psychostimulant and hallucinogenic effects, similar to cocaine or 3,4-methylenedioxy-methamphetamine (MDMA or ecstasy).² Cathinone itself is a naturally-occurring stimulant found in the leaves of khat, a plant (*Catha edulis*) grown and consumed in East Africa and the Arab peninsula. A variety of synthetic cathinones have been developed and sold as legal alternatives to cocaine or ecstasy, including 4-methylmethcathinone (mephedrone), 3,4-methylenedioxy-methcathinone (methylone), and 3,4-methylenedioxypropylone (MDPV).

Mephedrone use became prevalent in the UK in 2009, where it was (wrongly) linked with two deaths and reported prominently in the popular press. In common with other first-generation legal highs, *eg* piperazines, it was categorised under the Misuse of Drugs Act, 1971 (Amendment) Order as a class B controlled drug in April 2010. However, manufacturers continued to sell the product under different names,³ while other cathinone-related drugs were developed to avoid legal sanctions. NRG-3 is one such drug, with purported stimulant and mild hallucinogenic effects. It is often sold as containing 17- α ,21-dihydroxy-16- α -methylpregna-1,4,9(11)-triene-3,20-dione-21-acetate, but recent laboratory analysis of NRG-3 bought from the internet suggests that it often contains benzofuran (1-benzofuran-6-

ylpropan-2-amine), a compound of the phenethylamine and amphetamine classes.⁴

Synthetic cathinone use typically results in stimulant-related subjective effects: euphoria, increased energy, talkativeness, urge to move, reduced appetite and insomnia.⁵ Case reports of toxicity highlight agitation, paranoia, hallucinations and movement disorders, with episodes of psychosis that might be severe and last for several days.^{6,7} Our case illustrates these features well, and is consistent with other reported cases in responding to anxiolytic or antipsychotic medication, alone or in combination.

The second important point for discussion is the need for doctors to consider the use of non-prescribed drugs in patients presenting with medical or psychiatric problems. Although asking about drug use is part of any standard medical or psychiatric history, this case illustrates that this is often done in a brief or cursory manner, if at all. Studies of history taking about alcohol or illicit drug use by both physicians and psychiatrists have highlighted deficits.⁸⁻¹¹ For example, a survey of 200 cases admitted to six acute psychiatric wards in two London hospitals found three-quarters had no record of using alcohol or drugs in their notes.¹⁰ A recent study using an electronic case register of mental health patients to investigate khat use found that data on use of the drug was missing in 28 per cent of cases. Furthermore, when use was recorded it was rare to find information about quantity.¹² Such a deficit contributed to problems in managing our case.

Research suggests that negative attitudes towards alcohol or other drug use exert a significant influence on health professionals' willingness to intervene with alcohol-

Drug	Street Names	Legal status	Method of use	Effects
Synthetic cannabinoids	Annihilation, Black Mamba, Spice, Amsterdam Gold, X, Bombay Blue Extreme, Karma	Class B	Usually inhaled	Mimic effects of tetrahydrocannabinol (THC), the main active compound in cannabis
Mephedrone	Miaow miaow, Bubble, White Magic, MC, M-Cat, Bounce, 4-MMC	Class B	Oral ingestion	Stimulant Euphoria, anxiety, tachycardia
2-DPMP	Ivory Wave, Purple Wave, Vanilla Sky, D2PM	Class B	Nasal inhalation or oral ingestion	Stimulant
5-APB, 6-APB	Benzo Fury, White Pearl	Temporary banning order	Nasal inhalation or oral ingestion	Stimulant Anxiety, paranoia, increased body temperature
Naphyrone	NRG-1, NRG-2	Class B	Nasal inhalation or oral ingestion	Stimulant
Cathinone-related (benzofuran)	NRG-3	Legal	Nasal inhalation or oral ingestion	Stimulant, Mild hallucinogenic effects

Table 1. Summary of novel psychoactive substances and their properties

and drug-related issues, and can represent a significant barrier to healthcare for patients.¹³ The constructs of ‘role adequacy’ (having the necessary information and skills to identify and respond appropriately) and ‘role legitimacy’ (the extent to which management of these problems is felt to be the professional’s responsibility) have been highlighted as important,¹⁴ and are associated with support and perceived usefulness of education. Proude *et al.* found that individual feedback on performance with education about desired standards is effective in improving the quality of alcohol history taking in junior doctors.¹⁵

Screening for alcohol problems is facilitated by effective, validated screening tools such as the Alcohol Use Disorder Identification Test (AUDIT).¹⁶ However, screening for illicit drugs is more problematic, as use of combinations of drugs is increasingly common. The rapid increase in the number of available ‘legal highs’ has added to

this problem, fuelled by the ease of dissemination of information via the internet. Objective testing for illicit drugs is possible, but may be expensive and may not be easily available. The solution might be to ask about broad classes of illicit drugs such as depressants, stimulants and hallucinogens. It is important to ask specifically about substances bought from the internet, as the patient may not perceive that they are ‘drugs’ if they are not believed to be illegal.

The long-term effects of NRG-3 consumption are unknown and available information is largely from internet forums and users’ blogs. Recent trends in the development of substances branded as ‘herbal or legal highs’, designed specifically to bypass drug controls are concerning. In this case, we have witnessed serious adverse effects, extensive medical investigation and involvement of psychiatric services over a prolonged period of time, as well as significant distress to family members.

We hope that this case helps raise awareness among psychiatrists.

Declaration of interests

None declared.

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