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The age of novel psychoactive substances

Novel psychoactive substances (NPS) are compounds which are designed to mimic existing recreational drugs. The emergence of NPS has changed the landscape of the synthetic drug market. Previously, the market had a limited number of compounds which belonged to a small number of chemical groups; now NPS has shifted the market to one which possesses hundreds of compounds. The European Monitoring Centre for Drugs and Drug Addiction is currently monitoring 730 substances, with more being identified each year.

In the past, NPS used to evade anti-drug laws and were therefore called "legal highs". Manufacturers achieved this by tweaking the pharmacological structures of existing compounds to create new substances. To tackle this problem and ensure that "legal highs" became illegal, different countries passed laws to create a blanket ban on NPS. For example, in the UK and Ireland, the 2016 Psychoactive Substances Act makes it an offence to produce or supply, but not possess (unless an individual is in prison) current and future NPS. In the United States, the Synthetic Drug Abuse Prevention Act of 2012 bans synthetic cannabinoids, synthetic cathinone and hallucinogenic drugs. This Act puts these NPS drugs under Schedule 1 of the Controlled Substance Act. A Schedule 1 substance is defined as a drug that has a high potential for abuse, no accepted medical use in the US and is not classed as safe. Despite these laws, the supply, use or possession of these substances has not decreased. In fact, the strength and price of NPS have increased since the act.

NPS can be categorized into six groups based on their similarity to established recreational drugs. The six groups of NPS are: stimulants, cannabinoids, classic hallucinogens*, dissociatives*, sedatives/hypnotics** and opioids**. Stimulants and cannabinoids being the most common.^{1,2}

Stimulants

Stimulants mimic the effects of traditional psychostimulants such as 3,4-methylenedioxymethamphetamine (MDMA), cocaine and amphetamines, producing a sense of euphoria and wellbeing by increasing the synaptic levels of serotonin, dopamine and/or noradrenaline. Stimulants include synthetic cathinones or "SCs" (Mephedrone, bath salts), substituted phenylethylamines (2C agents) and piperazines (BZP). Most stimulants are typically sold in a powder or pill format, however, SCs are often sold under the disguise of plant food or bath salts —hence the street name. SCs are normally snorted or ingested orally (wrapped in cigarette paper "bombing" or dissolved in water "whizzy water"). 1,2,3

Synthetic cannabinoids

NPS variants of cannabinoids are termed synthetic cannabinoid receptor agonists (SCRAs). The common street names for SCRAs include "Spice" and "K2" these synthetic cannabinoids are often packaged into foil sachets and sold as incense. SCRAs are usually solids or oils sprayed onto

 $^{^{\}star}$ dissociatives and classical hallucinogens can be merged into a Hallucinogenic NPS group

^{**}note opioid and sedatives can be merged into depressant NPS

Forensic



herbal mixtures which are smoked. Liquid SCRAs can be used in electronic cigarettes and vaporizers. 1,2,3

Classic hallucinogens/psychedelics

Psychedelics are known as classic hallucinogenics, however despite the name they do not produce hallucinations but a range of "psychedelic effects". These effects include perceptual alternations and quasi-mystical experiences that can be categorized under oceanic boundlessness (positive emotions ranging from heightened mood to sublime happiness and serenity or grandiosity) and anxious ego-dissolution (thought disorder and loss of autonomy and self-control associated with arousal, anxiety and paranoid ideations).¹

Dissociatives

Dissociatives are a type of hallucinogen that distort visual and auditory perceptions causing the perception of an absence of time, weightlessness and disconnection from the physical body. All of these effects lead to detachment and potent psychedelic experiences. Dissociatives can be inhaled, swallowed or injected, with effects that can range from milder effects than ketamine to stronger effects experienced with phencyclidine (PCP).^{1,3}

Sedatives/ hypnotics

Sedatives are known as central nervous system depressants and are designed to slow down the function of the human brain. These drugs have a significant inhibitory and relaxing effect on the brain and mimic varying sedating and antianxiety drugs. They are the least understood of the NPS. One of the reasons for this is that the clinical symptoms are so similar to the established recreational drug that it is difficult to identify their exposure in a clinical setting. ^{2,4,5}

Synthetic opioids

Little is known about the specific subjective effects of novel opioids compared to the established recreational opioids. Fewer NPS opioids appear in isolation, and they are normally sold as part of cannabinoid smoking mixtures. Those that do appear in isolation are AH-7921, doxylam, nortilidine, and desomorphine; normally these opioids are sold as "research chemicals" or "legal opioids". All of them have opioid receptor activity, with AH-7921 having the same potency as morphine. 1,3

Novel psychoactive substances – Availability, trends and concerns

The darknet uses custom software and hidden networks superimposed onto the architecture of the Internet. It can be used for the sale of restricted goods as it has a low risk of detection, making it an "attractive" platform for obtaining NPS,⁶ with online purchases of NPS increasing according to a 2016 Global Drug Survey (GDS).⁷

According to the last World Drug Report 2018, synthetic cannabinoids and SCs represent the largest class of NPS. This poses a problem as synthetic cannabinoids are most likely to lead to emergency medical treatment than any other.⁷

In summary, NPS are on the rise globally and with it an increase in the incidence of intoxication and death. The major limitation of these drugs is the lack of identification tools – which exacerbates the difficulty for medical practitioners to identify the best treatment route and for forensic staff to identify illegal substances. A lack of prosecution encourages an increase in NPS drug use.

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