

## Strap: Legal highs

### Title: Novel Psychoactive Substances (NPS): no longer legal, not always highs

Standfirst: Use of legal highs amongst students is on the rise. As counsellors it is difficult to stay abreast of what young people are using and the effects that substances can have. **John Turner** and **Kirstie Soar** guide us through some of the terminology and the effects commonly reported and highlight appropriate responses from counsellors.

“I was at a club – this guy gave me something and I took it – I’ve been feeling really woozy ever since. Now I’m really worried about what it was and what it might be doing to me.”

“Smoking ‘spice’ or whatever it was, has had such an awful effect on me. Even now a year later I can’t shake the paranoia and anxiety, and just feel I’ve lost part of my sanity because of the way the experience made me feel and the things I think I saw. I wish I could go back, and it makes me cry to think of other people my age and younger, especially kids, going through this” (experience of a young man who tried a synthetic cannabis-like novel psychoactive, taken from an online chat forum).

It’s not uncommon for clients to have experimented with substances of one kind or another and to want to talk about this in sessions. Staying abreast of the myriad of substances available and their possible impact is a challenge for us all, and has become more so in recent years with the rise of novel psychoactive substances.

Since the early 2000s the rebranding of rarely used psychoactive substances as legal alternatives to banned drugs, and the creation of novel/new psychoactive substances (NPS), has dramatically gathered pace.<sup>1</sup> In Europe alone the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is currently attempting to keep records on the manufacture, distribution, use and effects of 450 NPS, with an additional 101 new substances being reported as available in one or more of the 28 member states in the year 2014 to 2015 alone.<sup>1</sup>

Previously referred to as ‘legal highs’, NPS are now more tightly controlled in the UK following the introduction of the Psychoactive Substances Bill in May 2016. Under this change to UK law it is now illegal to manufacture, sell and use all psychoactive substances (these being substances “capable of producing a psychoactive effect”,), except for named exemptions which include caffeine, nicotine, alcohol, various medicines and food-related products.<sup>3</sup> However, with concerns about how this new legislation will be enforced, mixed regulation across the EU and other countries worldwide, and the simple fact that illegal drug use is widespread, it is likely that NPS use will remain relatively commonplace. An illustrative example of this relates to use of mephedrone, once a ‘legal high’ but banned in the UK in early 2010. A study monitoring use in the same London club venues both before and after the ban, showed use and self-reported preferences for mephedrone as being sustained and even increased after the drug had become illegal<sup>4</sup>.

Current knowledge of NPS is limited, and understanding the exact effects of individual drugs, for acute use, chronic consumption and when used in combinations

with other substances, is challenged by the ever changing contexts of availability, quality of product and evolution of new drugs. What is clear is that NPS use amongst younger populations in the UK has grown considerably. For example, recent evidence found that almost one third (31 per cent) of participants in a study of 446 users of an online young adult UK student general forum (The Study Room), reported using an NPS.<sup>5</sup> Taken together we have a worrying situation where large numbers of predominantly younger individuals are experimenting with these poorly understood compounds. Given this landscape practitioners especially are faced with having to work with and support individuals who may be experiencing problems related to or exacerbated by NPS use. We suggest therefore, that the best way forward in this context is to utilise a combination of the limited knowledge we do have about individual NPS, often gleaned from case studies and small scale research, with the broader understanding that we already have of different drug class effects. Many of these NPS were designed to mimic and replace illegal drugs, and so this stance is a reasonable foundation for working intelligently with clients; perhaps especially so in non-clinical settings such as schools, colleges and universities, where currently little direct guidance for counsellors exists, but where drug experimentation is commonplace. As with so many issues, awareness informs compassion and understanding and helps in coping with the anxieties we may feel when working with issues beyond our own direct experience.

### Types and classes of NPS

Looking at the NPS which have entered the legal and illegal drug markets in recent years, the EMCDDA describe most as belonging to one of 5 main drug groups based on the molecular chemical family to which they belong: stimulatory phenethylamines and piperazines; hallucinogenic tryptamines; cathinone analogues; and synthetic cannabinoids.<sup>2</sup> Not all identified NPS fit these established categories and so some are more broadly classified as 'others'; these may include plant based NPS, and drugs which mimic the dissociative anaesthetic ketamine. It is by the EMCDDA categorisation that we refer to NPS groupings here. However, it is important to note that there are inconsistencies in classification of NPS in the research literature and clinical guidance, and across EU countries. Indeed the usefulness to front line clinicians and practitioners in classifying these varied substances based on their molecular structure is not especially clear, and users themselves tend to categorise NPS based on their psychotropic effects. Classification is made even more complex by NPS vendors who use suggestive marketing in their packaging or brand names; alluding more to the overall effect of the NPS as a stimulant, psychedelic, sedative etc. rather than categorising them by their drug molecular similarities.<sup>6</sup> Despite the UK ban, and closure of shops selling direct to consumers, international online sellers are likely to remain ubiquitous for the time being, and so these 'branding issues' will persist.

Table 1 below lists the five EMCDDA drug groups and provides a few illustrative examples of NPS for each. The table excludes details of 'street' or product names, as these are changeable and unpredictable, and so of considerably less utility to practitioners in non-specialist settings, compared to the reported experiences and behaviours of the user.<sup>7</sup> The table also lists possible problems that may be evident following sustained use, high doses or which might present in more susceptible individuals, and those with other psychological problems, current or historical.

**Table 1: Examples of NPS categorised by their perceived pharmacological effects/actions (and in line with EMCDDA drug group classifications)**

Category	Examples of NPS	Effects	Potential psychological problems
<b>Phenethylamines</b>	NBOM-e subtypes (e.g. 25n, 25b); 2C-B ; 2C-I; 5-APB; 6-APB	Stimulant and/or hallucinogenic	hallucinations, agitation
<b>Piperazines</b>	mCPP; BZP; TFMPP; MBZP	Stimulant	psychosis, panic attacks, hallucinations, insomnia, anxiety, agitation
<b>Tryptamines</b>	DMT; AMT; 4-OH-MET; 5-Meo-DALT; 4-OH-DiPT	Hallucinogenic and stimulant properties	hallucinations
<b>Cathinones</b>	Mephedrone; Methyldone; Methcathione; MDPV ; MDPPP	Stimulant and empathogenic effects (MDMA/ecstasy-like)	agitation, psychotic symptoms, hallucinations, risk of dependency
<b>Synthetic cannabinoids (cannabis-like)</b>	Spice; JWH-018; AB-FUBINACA	Depressant, sedative, hallucinogenic, but some stimulant properties	agitation, aggression, paranoid thinking, anxiety, hallucinations, psychotic symptoms, addiction, confusion
<b>Others</b>	5-APDB 6-APDB	Stimulant (derivative of MDA)	psychosis, panic attacks, hallucinations, insomnia, anxiety, agitation
	3-MeO-PCP	Ketamine-like (derivative of PCP)	derealisation, distorted reality, hallucinations, confusion, agitation, depressive thoughts
	MXE	Ketamine-like effects, stimulant, depressant, anti-depressant, hallucinogenic, and analgesic effects.	
	Salvia divinorum	Hallucinogenic	hallucinations, alterations in reality, panic attacks, paranoid thoughts

In terms of prevalence, the growth of alternatives to cannabis (synthetic cannabinoids) has been reported to have shown the most dramatic increases in types and demand in recent data sets.<sup>2</sup> However, these same data also show that stimulant types are being produced at a comparable level, if the very wide range of different new stimulant substances are summed across the separate classes.

Because these two groups of NPS (synthetic cannabinoids and the mixed stimulant types) are clearly the most widely used the rest of this article will concentrate a little more on what is known about their effects, and about the possible problems that may arise from use.

*Synthetic cannabinoids:* Synthetic cannabinoids are generally sold and consumed as a cannabis-like leaf product, often consisting of the psychoactive chemical sprayed onto herbs (e.g. thyme, mint), which can be smoked, vaporised or ingested in the same fashion as cannabis. These NPS are designed as alternatives to cannabis and its main psychoactive ingredient  $\Delta$ -9-tetrahydrocannabinol (THC), and appear to be largely consumed to induce comparable states of relaxation, euphoria and altered consciousness.<sup>8</sup> The synthetic cannabinoids vary considerably in their chemical structure but all appear to act as agonists at endocannabinoid receptors in the central nervous system, producing overall effects similar to THC.<sup>9</sup> However, many appear to be associated with more psychosis-like and agitation effects, and to produce greater sympathomimetic effects (e.g. raised heart rate, palpitations, sweating, muscle tension etc.) compared to organic cannabis. For example, Papaneti and colleagues' systematic review of the widely popular synthetic cannabinoid varieties known as 'Spice', found increased prevalence of hallucinations and psychotic symptoms following both acute and chronic use.<sup>10</sup> Winstock and Barratt investigated adverse experiences relating to synthetic cannabinoid products in 950 people who had used synthetic cannabinoids in the last year, with 2.4 per cent having reportedly sought emergency medical treatment, noting prominent increased anxiety and agitation.<sup>11</sup> Those who sought medical treatment were usually significantly younger (average age 20) than those who did not (average age 23), and this suggests potential age differences in anxiety-related responses to synthetic cannabinoids in users.

These negative effects may in part be due to the fact that the synthetic cannabinoids, as simple THC analogues, lack the more complex pharmacological profile attributable to other psychoactives naturally found in cannabis, most importantly cannabidiol (CBD). CBD has been reported to have both anxiolytic and antipsychotic effects. Fortunately, for most individuals adversely affected, the effects of synthetic cannabinoids appear to be short lasting and to resolve upon drug cessation and so may need little more than short-time monitoring and supportive care.<sup>12</sup> Nonetheless, the effects of long term exposure and follow-up profiles of affected users are under-researched, although one study has shown evidence of prolonged psychosis in a small subset of users.<sup>12</sup> In addition, although work looking in detail at the issue of dependence on synthetic cannabinoids is limited, case study work,<sup>13</sup> and a survey study<sup>8</sup> have suggested some users may have significant symptoms and find discontinuation problematic. Given that many of these drugs exert similar or more powerful central effects compared to THC, it is certainly not surprising that signs of dependency may be observable in some regular users.<sup>9</sup>

*Stimulant type NPS:* The majority of stimulant type NPS are sold in powdered form (sometimes under the guise of plant food or bathing products) or as tablets, with users tending to snort, ingest or smoke the substance. The reasons for taking NPS with stimulant effects mirror those generally given for use of other legally available and illicit stimulants. Amongst other effects, these substances are commonly reported to induce euphoria, create a sense of energy and general stimulation, to enhance cognitive states and to facilitate social interaction and sexual experiences.<sup>14</sup> As with many other psychostimulants, in addition to recreational use it is possible that many of these substances, possibly at lower doses, could be seen by some users as aiding study/work, reducing fatigue and need for sleep, and as enhancing

concentration and performance. Additionally, it is also worth noting that as with most other stimulants (especially amphetamine-type stimulants; ATS), NPS stimulants are also likely to have strong anorectic effects, though comparative effects of different types on appetite suppression has not yet been systematically documented.

With the phenethylamine based substances, the core chemical structure is designed to mimic that of more purely stimulant drugs such as amphetamine, methamphetamine and cocaine; and as such this group of compounds are often classed as ATS.<sup>15</sup> However, similar to most potent stimulants, many of the phenethylamine NPS appear to have some hallucinogenic properties. With regards to negative effects, high levels of intoxication have been associated with anxiety, insomnia, aggression, paranoia and psychosis, effectively mirroring effects frequently seen with high doses of amphetamine. Many users also appear to show a hangover from use (or 'come down') often lasting several days after use, with experiences such as mood disturbance, irritability and restlessness, and somatic symptoms such as pain and fatigue.<sup>15</sup>

The piperazines also produce similar effects to amphetamine. As such, in addition to the stimulant effects of heightened arousal and cognitive states, they are associated with often powerful sympathomimetic effects, which at high doses are capable of creating severe agitation and adverse cardiovascular symptoms (referred to as the sympathomimetic toxidrome).<sup>16</sup> There is some evidence that piperazine compounds have at times been mis-sold as ecstasy/MDMA, and so users' reports of what they believe they have taken may show a mismatch with their descriptions of adverse effects which instead relate more to exposure to a piperazine. Piperazines appear more likely to cause hallucinatory experiences than many other NPS stimulants, and more so than ecstasy, so user reports of this effect may help practitioners to better establish what might have been taken.

Current understanding of the effects of cathinones (originally derived from the khat plant) is largely based on studies looking at mephedrone, as the most widely used of all drugs in this class. This substance, and other cathinones, share similar properties to both MDMA/ecstasy and methamphetamine/amphetamine, although they are generally seen as less potent. However, overlap in effects with these drugs has been argued to make mephedrone, and most likely the other cathinones, both particularly appealing to young people and club goers, and to have a high potential for dependence.<sup>15</sup> The recent guidance from the Novel Psychoactive Treatment UK Network (NEPTUNE) also highlights reports of co-use of mephedrone with methamphetamine in club settings, and in particular this combination being used as part of the 'Chem Sex' scene in London, largely amongst men who have sex with men.<sup>15</sup> This may be especially worrying as the combination of these two psychostimulants may enhance the negative effects of both drugs when used individually. More generally negative effects associated with cathinone use again mimic those seen with other stimulants, though severe effects are most likely associated with longer periods of use and/or use of high doses and combinations with other substances.<sup>16</sup>

Table 2: Some considerations for practitioners working with clients who use or may have used NPS

<b>Questions/considerations</b>	<b>Comment</b>
<b>1. Is the individual aware of changes to UK law? There are no 'legal highs' anymore</b>	The ubiquity of products online may give the false impressions that some/all substances they can buy are legal in the UK – none of them are, and so they may be breaking the law
<b>2. If they've been taking NPS, what effects have they experienced?</b>	The user may think they know what they have taken, but they cannot be certain, so the effects can help to at least ascertain class
<b>3. Need to establish whether any distress reported has a history beyond or prior to NPS use</b>	As with other substance use assessments it is important to try to establish the origins of the client's distress and advise about the role their NPS and other drug use might be having
<b>4. Screen for dependence</b>	Does the use of any NPS type/class show evidence of meeting dependence criteria?
<b>5. Need to discuss extent of use, combined use and raise awareness of pertinent issues</b>	Use of multiple types of NPS and other substances can be managed in the same fashion as other complex drug use patterns, taking into consideration the classes being used. Multiple use of different stimulants and combinations of powerful stimulants with alcohol are of particular concern for general health and wellbeing, as well as linked to areas such as aggression, affective problems and sexual risk taking
<b>6. General health and wellbeing</b>	As for other substance use – ask about weight change, poor performance in study/work, poor skin condition, chest pains/breathing problems, stomach upsets, etc. With obvious intoxication or significant poor health symptoms immediate hospital/emergency services support should be sought
<b>7. Financial/legal complications</b>	With changes to legislation, continued NPS use may see a rise in people charged with related offences; possible pricing adjustments; debts linked to dependence
<b>8. General lack of knowledge about NPS</b>	As with other substances (but perhaps exacerbated by the sheer numbers/types) users of illicit substances cannot be sure of content or strength of substances purchased. We also know very little about the consequences of use, especially long-term use

## Conclusion

Research documenting the physical and psychological effects experienced by regular and current users of NPS (who have not experienced severe effects to the point of hospitalisation) is limited, with most data relating to prevalence of use through demographic research. Studies to date do however raise significant concerns about the harm related to use of many of these substances. Synthetic cannabinoids may trigger or amplify negative psychological symptoms seen with regular cannabis use, through their often more potent effects, producing in some users severe anxiety, troubling hallucinations and possibly even psychosis. The wide range of stimulant-like NPS also appear problematic for some individuals, producing significant negative mood changes, psychosis, dependence and increasing rates of sexual risk-taking and regretted sex. Although not covered in detail here, other NPS classes may also be problematic, for example with hallucinatory/psychedelic types capable of producing profound hallucinations which, as with classic hallucinogens, might lead to flashback type experiences and possibly more persistent problems.

The extent of these problems in users is currently difficult to determine, and the sheer numbers of substances available, discerning which have been taken, at what doses and in which combinations complicates understanding immeasurably. Adding to this, the recent legal changes in the UK, and changes in legislation which will and have already taken place in other countries, will naturally make studying these substances even more problematic, and ultimately the work of front line workers more difficult. What is clear is that we can learn from previous examples of changes in controls over substances, and that in general once a psychoactive substance appears and gains some popularity, its use is unlikely to disappear. To help practitioners understand the use of NPS we can at least look to the fact that most of these substances have been designed to mimic, at least in part, the effects of 'classic' recreational drugs, and so there is much we can understand by mapping across from this wider knowledge base, alongside new information as it becomes available: from bodies such as the EMCDDA and NEPTUNE<sup>15</sup>, as well as from the academic literature base. What we know so far about many NPS, and importantly, the categories of drug to which they belong, can help to inform current practices of UK practitioners and front line staff (see for example the suggested guidance in table 2). In turn, the experiences of these staff will also be a key part in helping to map the changes in the NPS market and in expanding our understanding of the nature and extent of problems in users.

## About the authors

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MDMA/ecstasy use in clubbers and young pregnant women (the effects on their infant's development) and use of multiple recreational substances.

Dr Kirstie Soar is a Principal Lecturer at the University of East London, specialising in drug research. Her work has examined the short and long term consequences of MDMA/ecstasy use, polydrug use and most recently the effects of recreational (non-addicted) cocaine use on cognitive functioning. Other recent projects have explored the use of alcohol gels, cannabis vaping and e-cigarettes.

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PQs:

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