

The Phantom Menace: Novel Psychoactive Substances and the UK Armed Forces

Key Points

- Novel psychoactive substances (NPS) are compounds synthesised to mimic the effects of recreational drugs
- Research in the UK and the USA suggests that the use of NPS is becoming more prevalent amongst Armed Forces Personnel
- Civilian population data suggest that young males (16-24) are most likely to misuse NPS
- There is no unifying NPS toxidrome; identification of the subtype of NPS will greatly assist the military clinician in targeting supportive treatment
- NPS misuse may result in long term psychiatric and physical ill health; hence their use is entirely incompatible with Service Life

Introduction

Novel psychoactive substances (NPS) encompass a large group of synthesised compounds specifically designed to mimic traditional recreational drugs. Current UK Armed Forces compulsory drug testing (CDT) does not screen for these substances, making them tempting to the small proportion of UK Armed Forces personnel who indulge in recreational drug use. The acute and chronic sequelae of NPS misuse are widely variable, and associated with high morbidity. In this paper, we discuss NPS pharmacology and clinical presentation. We recommend a standard management plan for the Military Physician encountering a service person who has misused NPS. Finally, we reflect on the legal, ethical and military consequences of NPS misuse for both the service person misusing NPS, and the Military Physician providing their care.

What are Novel Psychoactive Substances (NPS) and who uses them?

Novel psychoactive substances (NPS), better known as “designer drugs” (or colloquially as “legal highs”), are substances produced to mimic the effects of taking a traditional illegal recreational drug (1). They can be broadly categorised by effect as synthetic cannabinoids, stimulant type drugs (notably synthetic cathinones), hallucinogenic type drugs, opioid type drugs and tranquiliser type drugs, and are traded under a variety of street names and descriptors (2). Until the enactment of the May 2016 Psychoactive Substances Act, NPS were readily available for legal purchase on high streets in “head shops” and over the Internet (3); hence the

misnomer “legal highs”. Despite the 2016 ban, NPS remain available, illegally, on the Internet and via illicit drug dealers (4).

It is difficult to quantify NPS use. A European survey of >13 000 young adults (those aged 15 to 24) in 2014 indicated that 8% had tried NPS (1). Another source, surveying young adults (aged 16 to 24) in England and Wales in 2014, estimates around 360,000 of this cohort had tried NPS in their lifetime, while 174,000 had used NPS in the last year(2). Accurate data on use of NPS within the UK is difficult to capture due to poor response rates from those surveyed, and the nebulous nature of NPS themselves. These are frequently rebranded and may contain a mixture of substances unbeknownst to the self-reporting user (1,3, 5, 6). The Home Office review of NPS use and social impact notes that the majority of those taking NPS are already using illicit drugs (1).

Novel psychoactive substances use in the UK Armed Forces is even more difficult to define. Armed Forces personnel are subject to randomised compulsory drug testing, which tests urine for “traditional” drugs of abuse as defined in the Misuse of Drugs Act 1971 (e.g. cocaine, heroin, ecstasy, anabolic steroids and lysergic acid diethylamide (LSD)) A freedom of information request to the Ministry of Defence (MoD) for the period October 2015-2016 reported that 660 UK Armed Forces personnel tested positive for illicit drugs on CDT. During that time period, both “traditional” recreational drugs and NPS were recovered from UK Military bases, including Metandienone, and Mephedrone(7). In 2007, one report noted that the cost to the British Army of drug related discharges was more than the number of personnel killed on active duty and more than the number killed in the Iraq and Afghanistan wars (8).

Currently, the UK Armed Forces CDT does not include NPS, and until recently, no tests were available (9). Joint Service Publication (JSP) 835 clearly states that drugs of abuse, including NPS, are not tolerated within the UK Armed Forces. Use of NPS by personnel will almost always result in administrative or disciplinary action, including discharge from the Armed Forces (though single Services may choose to retain personnel under exceptional circumstances)(9) Disciplinary action would relate to unfitness to work or misconduct through the use of drugs (10). It is easy to imagine that the small number of personnel inclined to misuse drugs would choose to avoid detection by using NPSs.

The Home Office have identified compulsory drug testing as a motivating factor for NPS use (1). One expert hypothesises that a reduction in UK Armed Forces personnel testing positive for cocaine in 2009 was due to this cohort switching to the then legal drug mephedrone (11). A similar displacement was hypothesised when compulsory drug tests (CDT) were first introduced in to the UK Armed Forces (and UK Prisons (12)). The introduction of CDTs with punitive sanctions saw soldiers switch from Class B drugs, like cannabis, to Class A drugs (such as cocaine) that could be eliminated from their system in a shorter period of time, thus circumventing a positive CDT (8).

While there is little data pertaining to the use of NPS among UK Armed Forces personnel, there is evidence to suggest NPS use is prevalent in the United States military; a comparable cohort. A number of high profile cases show synthetic cannabinoid, and to a lesser extent synthetic cathinone use is prevalent across the US Army, Air Force and Navy (13-15) in all ranks (16). One paper reports >100 discharges from the US military for NPS use between June 2011 and January 2012(17), whilst another reported that in 2012, 2.5% of 10,000 US Army drug tests that had initially registered as negative flagged as positive when tested for synthetic cannabinoids (18). These findings neatly illustrate how the use of NPS avoids a positive CDT, and may lead to under-reporting for NPS use.

A study examining hospital admissions of US service personnel due to substance misuse, found that 8.3% (13 of 155) had used "Bath Salts" (a stimulant type drug) and 7.7% (12 of 155) had used "Spice" (a synthetic Cannabinoid). The majority of patients in this study were male and aged under 30 (11). According to the Home Office young males aged between 16-24 were not only significantly more likely (three times more likely) than females to take NPS (2). Ministry of Defence biannual diversity statistics for October 2016 indicate that young male recruits make up 22.28% of the UK regular Armed Forces (33, 470 males aged 16-24) (19). Military physicians in primary and acute care should be aware of the potential for NPS misuse within the UK Armed Forces population, particularly among the young, male recruits.

Acute presentation of NPS

The presentation of NPS in the primary or acute care setting may be far more varied than the presentation of "traditional" drugs of misuse. This is due, in part, to the variation in chemical content of NPS (even when

branded identically)(4), and also the relative strength of these compounds compared to “traditional” drugs (20). Table 1 illustrates the pharmacology of the four categories of NPS discussed in this paper. Table 2 illustrates the subtypes of NPS, their street names, and systemic effects.

NPS Subtype	Receptor	Methods of Administration	Time to onset of High	Length Of "High"
SYNTHETIC CANNABINOIDS	CB1 receptor in Brain, GI tract, Lungs, Kidney CB2 receptors in Brain (14)	Smoking	~ 10 mins	2-6 hours (16)
STIMULANT TYPE DRUGS	↑ DA, 5HT, NA within the synapse Inhibits MAO (↓ DA, 5HT, NA reuptake within synapse) (21)	Intranasal, Intravenous	30-90 mins	2-8 hours (17, 26-28)
HALLUCINOGEN TYPE DRUGS				
• PHENYETHYLAMINES (inc. 2C series)	Partial agonists at 5HT2A serotonin receptor (22-23)	Orally, sublingually (from blotting paper), intranasal, intramuscular, intravenous, <i>per vaginum</i> , <i>per rectum</i> , smoked.	0-15 mins	15-90 mins (22)
• BROMO-DRAGONFLY	Full agonist at 5HT1, 5HT2 & α1 adrenergic receptors (24-26)		≥ 6hrs (high risk redosing)	Several days (29)
• METHOXETAMINE	↓DA reuptake NMDA glutamate receptor antagonist Agonist at muscarinic cholinergic and 5HT2 receptors (30-31)		~10 mins	2.5-5hrs (31)
OPIOID TYPE DRUGS	Agonists at μ & κ opioid receptors	Oral, subcutaneous injection, intravenous	Agent dependent	Agent dependent
TRANQUILIZER TYPE DRUGS	Agonists at the GABA _A receptor	Orally, sublingually (from blotting paper), intravenous, transdermal patches, spray (33-35)	Agent dependent Phenazepam 4-6 hrs Etizolam 30 mins-2hrs Pyrazolam 1-1.5 hrs	Agent dependent ~8hrs 15-60 hrs 16-18hrs

Key: CB = Cannabinoid receptor, DA = Dopamine, 5HT = Serotonin, NA = Noradrenaline, MAO = Monoamine Oxidase, NMDA = N-Methyl-D-aspartate, GABA = *gamma*-Aminobutyric acid

Table 1: Pharmacology and pharmacokinetics of the subtypes of Novel Psychoactive Substances

Drug Class	Street names*	Desired effect	Toxidrome				
			CNS	CVS	GS	Metabolic & Renal	Other
Synthetic Cannabinoids	Spice, K2, Black Mamba, Clockwork Orange, Ecstasy Damnation, Psyclone, Sensate, Abyss, Magic Dragon, K92 Genie, Yacatan Fire (2, 9, 35, 36)	Euphoria, relaxation, disinhibition, altered consciousness (2)	Anxiety/panic, psychosis, short term memory impairment, seizures, hallucination, movement disorders, self-mutilation, suicidal ideation (2, 2035, 36-37)	Tachycardia, hypertension, chest pain, ischaemia (including troponin +ve STEMI), dysrhythmias (35, 38-39)	Nausea, Emesis/Hyperemesis (2, 13, 20,35, 38)	Hyperthermia, hypo/hyperkalaemia, acute kidney injury, rhabdomyolysis, acidosis, hyperglycaemia, other electrolyte disturbances (27, 35,41)	Nystagmus, xerostomia, mydriasis, conjunctival hyperaemia (35, 41)
Stimulant type drugs (Synthetic Cathinones, Piperazines and Mephedrone)	Bath salts, BZP, <i>meph, m-cat, MCAT, Miaow, miaew, 4-mmc, bubbles, white magic, plant feeder</i> , NRG-1, Benzo Fury, MDAI, Bloom, Ivory Wave, Charge+, Sextacy (2, 17, 42)	Euphoria, sexual stimulation, empathy, increased work capacity (2, 21)	Confusion, agitation, seizures, psychosis, paranoia, panic, muscle spasms, vertigo, tinnitus, short term memory impairment, parkinsonism, motor automatisms, cerebral oedema, violent behaviour, depression, suicidal ideation, dependency 2, 23 - 26	Tachycardia, hypertension, chest pain, S-T ECG changes, dysrhythmias, myocardial infarction, myocarditis, syncope (2, 21, 27, 42)	Nausea, vomiting, abdominal pain, loss of bowel control (27, 42)	Hyperthermia, hyponatraemia, hypokalaemia, acidosis, acute kidney injury, rhabdomyolysis, Serotonin Syndrome (2,21, 27, 42)	Hepatic failure, disseminated intravascular coagulation, injection site injuries (including necrotising fasciitis), rash, compartment syndrome, spontaneous subcutaneous emphysema, abscesses, body odour (2, 21, 27, 42)
Hallucinogen type drugs (Phenylethylamines, Bromo Dragonfly and Methoxetamine)	Bromo-Dragonfly, 2C-B, BOMe2CC, Boom, C-Boom, Cimb-82, Special K, Mexxy, M-ket, MEX, Kmax, Special M, MA, legal ketamine, Minx, Jipper, Roflcopter (2, 3, 5, 22 27)	Hallucinations, sense of peace, emotional stimulation, amphetamine-like stimulation, dissociation (2, 3, 22-25)	Confusion, self-harming/bizarre behaviour, agitation, acute and delayed seizures, increased muscle tone, clonus, headache, flashbacks, paranoia, cerebellar ataxia (22-26,309)	Tachy or bradycardia, hyper/hypotension, dysrhythmias, heart murmurs, coronary vasospasm, heart failure. <i>Bromo Dragonfly: vasoconstriction (+/- irreversible peripheral ischaemia) (2, 22-36,)</i>	Nausea, vomiting, diarrhoea, stomach lining irritation (22-26, 30)	Hyperthermia, metabolic acidosis, acute kidney injury, rhabdomyolysis, Serotonin Syndrome, dysuria (230, 43-44)	Pulmonary oedema, respiratory depression, hepatic impairment, mydriasis, disseminated intravascular coagulation, diaphoresis, bruxism (30, 43)
Opioid type drugs	AH-7921, Doxylam, W 15 7, W 18, W 19 (2, 45-46)	Euphoria, hallucinations (46)	Nightmares, anxiety, agitation, dysphoria, depression, paranoia (46)	Possible cardiotoxicity; Prolonged QT, widened QRS (46)	Nausea, Vomiting (46)	Potential for rhabdomyolysis post injection (46)	Respiratory depression , pulmonary oedema, injection site soft tissue infections, miosis (46)
Tranquiliser type drugs	Xany, Etizolam, Phenazepam, Pyrazolam (47-53)	Relaxation, Anxiolytic	Drowsiness, hypotonia, in-coordination, ataxia, dysarthria, nystagmus, coma (47-53)	Hypotension, bradycardia (47-53)	n/a	Hypothermia, rhabdomyolysis (47-52)	Respiratory depression (47-53)

Key: CNS = Central Nervous System, CVS = Cardiovascular System, GS = Gastrointestinal System

Table 2: Illustrating categories of NPS, some street names, and how they present in the acute setting

Synthetic Cannabinoids

Synthetic cannabinoids are manufactured chemicals that are sprayed on to plant matter and consumed in a similar way to marijuana (most commonly smoking). However, whilst the consumption of marijuana has relatively predictable results (euphoria, relaxation, hunger), synthetic cannabinoids are often more potent, and present in a more variable manner (54) (see Table 2). Case studies report that in addition to the “desirable” effects of euphoria and altered consciousness, substance users may experience psychological effects ranging from anxiety and memory loss to violent psychosis (2, 20, 35). In some cases, psychosis has persisted for months after the initial ingestion of the synthetic cannabinoid, requiring treatments with antipsychotic medication and hospitalisation (55). Research suggests that the risk for psychosis increases for individuals with a history of mental illness (56). Recent MoD statistics suggest the rate of mental disorders among UK Armed Forces personnel is higher than the UK general population at 2.9% (57). Hence, it may be argued that Armed Forces personnel who misuse synthetic cannabinoids may be at greater risk of developing psychosis.

Cardiovascular side effects are commonly reported, and range from tachy/bradycardias and hypertension, to chest pain, dysrhythmias, ischaemia, and troponin positive ST segment elevation myocardial infarction (35, 39-40). One case series reports three 16 year olds who presented with myocardial infarction after smoking the synthetic cannabinoid K2. All three had structurally normal hearts (40).

Gastrointestinal effects of synthetic cannabinoids include nausea, vomiting and hyperemesis (2, 14, 36, 38). “Cannabinoid hyperemesis syndrome” is a cycle of nausea, abdominal pain, and vomiting normally associated with heavy marijuana use. Recently, cannabinoid hyperemesis syndrome has also been associated with the misuse of synthetic cannabinoids (39). In two cases reported, nausea and vomiting were the initial symptoms in a Spice induced fatal rhabdomyolysis. Both young male patients died within a week of synthetic cannabinoid ingestion, despite critical care interventions (41). Acute kidney injury has also been linked to the ingestion of synthetic cannabinoids (58). This deleterious effect on the kidneys may also contribute to the electrolyte and acid base disturbances which have been observed in synthetic cannabinoid users (35, 41, 58).

Whilst relatively few papers report deaths from ingestion of synthetic cannabinoids or their sequelae, they may cause considerable physical and psychiatric morbidity in those taking them (36, 58-61). The symptoms

arising from synthetic cannabinoid use may have serious implications for Armed Forces Personnel and their immediate and long term fitness for duty. As illustrated in Table 2, there is no obvious toxidrome indicating synthetic cannabinoid intoxication. The CDT does not identify synthetic cannabinoids or their metabolites, and formal toxicology screening may be of little use, particularly if the synthetic cannabinoid is a new compound (59, 61-62). Treatment is largely supportive (fluids for acute kidney injury, antipsychotics for psychosis)(59, 62). In Figure 1, we suggest an approach to the assessment and management of UK Armed Forces personnel who may be intoxicated with NPS.

Figure 1

Stimulant Type Drugs

Stimulant type drugs, including synthetic cathinones such as mephedrone, are often marketed as “bath salts” or “plant food” (17, 28, 42). Cathinones are naturally found in the leaves of the African khat plant, and chewed as a stimulant in some cultures (2). Mephedrone (4-methyl-*N*-methylcathinone) deserves an individual mention, as it has been linked to a significant number of fatalities. One study reports 30 deaths related to mephedrone in people aged 16-24 in the UK over a 4 year period (28). Another paper reports 62 mephedrone associated deaths in the UK over 2 years, attributed to both acute toxicity and fatal self harm under the influence of the drug (27).

Unlike traditional stimulant drugs (e.g. cocaine), synthetic cathinones have qualities mimicking ecstasy and amphetamines, causing euphoria, sexual stimulation, empathy, increased alertness and capacity for work, and hallucinations (2, 17, 28). The pharmacokinetic and clinical characteristics of these substances are illustrated in Tables 1 & 2.

The neurological and psychiatric sequelae of using synthetic cathinones are varied, and range from motor dysfunction to severe psychosis. Cathinone toxicity has been associated with extreme behaviours, often referred to as excited delirium syndrome. This causes a hyperdopaminergic state linked to violent behaviour, agitation, and can lead to self-mutilation, homicidal activity and sudden death (63-65), . Fatalistic self-harm caused by depression or psychosis is one of the main causes of death among cathinone users (64-66). US military data, implicating synthetic cathinone use in both suicide and murder-suicide, is of particular interest (14, 42). This is particularly relevant to UK Armed Forces populations, as, unlike most UK citizens, they have relatively easy access to weapons systems (such as rifles and hand guns).

Due to their stimulation of the sympathetic nervous system, the cardiovascular effects of synthetic cathinones may be readily anticipated. Tachycardia and hypertension are common, as is chest pain and ST segment changes (which may be rate related or due to coronary vasospasm in a younger cohort). Narrow complex tachycardias, ventricular tachycardia (VT), ventricular fibrillation (VF) and myocardial infarction are also reported (21, 42, 67). Two case reports discuss asystolic cardiac arrest as a result of ingesting synthetic cathinones; in both cases, the subjects were young (28 and 44 years of age) and male. One died following 30 minutes of resuscitation effort and was found to have pulmonary oedema. The other was successfully resuscitated but died on intensive care 24 hrs later, as a result of cerebral and pulmonary oedema (68-69).

Gastrointestinal effects of synthetic cathinones are non-specific; and may not be as diagnostically helpful as the metabolic and renal sequelae of synthetic cathinone abuse. Hyperthermia is a widely reported side effect of synthetic cathinone abuse; both as an individual sign and as part of the serotonin syndrome. Temperatures ≥ 41.5 °C have been recorded (21, 27). In severe cases, rhabdomyolysis, acute kidney injury, lactic acidosis and deranged electrolytes are reported; of note, hypokalaemia and hyponatraemia, which undoubtedly contribute to cerebral oedema. Individuals thus compromised invariably need critical care intervention, and may require renal replacement therapy (2, 17, 27, 68). Synthetic cathinones have the potential to create a metabolic “perfect storm”, affecting multiple organs in an unpredictable manner and requiring intensive medical intervention in order to avoid death.

Mainstays of treatment for synthetic cathinone toxicity include benzodiazepines and antipsychotics, which is symptomatic and focuses on reducing sympathetic overstimulation (64, 70). Currently, no antidote exists to counteract synthetic cathinone toxicity (71). Continued abstinence from the drug is vital. For those who develop single or multi-organ failure, early intervention with critical care input is key, including aggressive cooling and electrolyte replacement (25, 29, 42).

Longer term sequelae of synthetic cathinone abuse are difficult to predict. Case studies report that regular users of synthetic cathinones may exhibit psychiatric symptoms for weeks to months post ingestion (27, 29). Physical ill health is again difficult to predict; however, it can be hypothesised that those misusing synthetic

cathinones could face chronic cardiac or renal impairment. Such behaviours and sequelae are incompatible with a career in the UK Armed Forces.

Hallucinogen type drugs

The hallucinogen type NPS may be considered as three subcategories due to their differing pharmacology, described in Table 1. All of these NPSs are ingested for their hallucinogenic and emotionally stimulating properties; however, their distinctive pharmacology determines the severity and potential lethality of their sequelae.

Adverse effects of the hallucinogen type drugs are shown in Table 2. Neuro-psychiatric side effects are common, and seizures may follow ingestion of all three drugs. Bromo dragonfly has been reported to cause delayed onset seizures taking place >8 hrs post ingestion (23-26, 30-31, 43, 45, 72).

Gee *et al* report on a case series of 10 patients who took 2C series phenylethylamines; common findings were hypertension (8/10) and tachycardia (10/10; ranging from 100 to 175 bpm) (23). Due to their action at the 5HT_{2A} serotonin receptor, coronary vasospasm and peripheral vasoconstriction would be anticipated. These have been reported, but the degree to which they affect the vasculature is highly variable (due to the partial agonism at 5HT_{2A} receptors), and depends on the dose and chemical taken (22, 72). In contrast, Bromo Dragonfly's potent action at the 5HT₁ and 2 receptors and the α ₁ adrenoceptor greatly increase the risk of vasospasm, and peripheral vasoconstriction resistant to vasodilators has been reported, leading to gangrene and amputation of extremities. It is hypothesised that vasospasm following Bromo Dragonfly ingestion contributes to acute kidney injury and ischaemic hepatitis in these patients (25-26, 45). Methoxetamine users may also present with hypertension and tachycardia. ST segment elevation myocardial ischaemia (in a 21 year old male) is reported (44).

All of the hallucinogenic NPS compounds may induce gastrointestinal upset in the form of nausea, vomiting or diarrhoea (22-26, 29-30). As illustrated in Table 2, the serotonergic effects of all three drugs may induce hyperthermia (reported frequently), Serotonin syndrome, and subsequently rhabdomyolysis, acute kidney injury (potentially requiring renal replacement therapy) and metabolic acidosis (30, 43-45). Interestingly,

methoxetamine is often marketed to ketamine misusers as “bladder friendly” (i.e. lacking the lower urinary tract symptoms that ketamine will typically cause.) Animal studies indicate that this is not the case, and methoxamine may be just as irritating to the urinary tract as ketamine (71).

Opioid type drugs

There is little information surrounding the misuse of synthetic opioids, although the effects of taking them are somewhat more familiar to the clinician (Table 2). As with “conventional” opioids such as heroin or morphine, those taking these drugs may experience nightmares, agitation, paranoia, anxiety and depression. There is potential for them to cause cardiotoxicity in the form of QT prolongation or widening of the QRS (see Figure 2). If opioid type drugs are injected, injection site soft tissue infections, abscesses or rhabdomyolysis may occur (46). However, the key danger of opioid type NPS is their potency. The “W series” of synthetic opioids are pure μ -agonists, with W-18 being the most potent. They all have the potential to cause rapid respiratory depression and death (45). Miosis and respiratory depression may give the clinician a clue to the substance taken, but toxicologists predict that extremely high doses of naloxone would be needed to reverse the effects of these drugs (45, 46). In the age of online shopping, the Military Physician should consider the source of opioid in service personnel presenting in this manner, and be aware of the potent opioid analogues available for purchase on the internet.

Tranquiliser type drugs

The tranquiliser type drugs used as recreational substances are benzodiazepines without license in the UK (such as etizolam and phenazepam), and benzodiazepine analogues created for research purposes or specifically for the NPS black market (such as pyrazolam). These NPS are taken recreationally for their relaxing and anxiolytic properties. They act at the GABA benzodiazepine receptor, and vary widely in their potency, onset of action and half-life.

The tranquiliser type NPS are taken as standalone recreational drugs, but are also used in combination with other “traditional” drugs and/or NPS. A proportion of recreational substances marketed as “traditional” drugs or NPS have been found to be contaminated with tranquiliser type drugs (51, 52) and NPS have been found in products marketed and sold as benzodiazepine replacements (74). Due to their benzodiazepine like properties, the effects of tranquiliser type NPS are easy to predict; however, the duration of action and

potency are less certain. Case series of deaths in Scotland between 2010-14 found 228 cases where phenazepam was detected in post mortem femoral blood samples. Phenazepam was the cause of death in two cases, and contributed to death in 54 cases (53).

CNS effects of the tranquiliser type NPS include sedation, ataxia, dysarthria, hypotonia, nystagmus, and coma. The immobility caused by CNS depression may result in rhabdomyolysis and hypothermia, and these should be considered in patients where tranquiliser type NPS use is suspected. As with conventional benzodiazepine overdoses, bradycardia and hypotension may also be predicted (47-50).

Treatment for intoxication with a tranquiliser type NPS is largely supportive. Hypotension should be corrected with IV fluids. Flumazenil may be considered; due to the variable potency and half-life of these agents, a flumazenil infusion may be necessary (47-50).

Management for the Military Acute Care Practitioner

Management of NPS consumption, in military personnel may be challenging for the Military Acute Care Practitioner, particularly when multiple substances are taken concurrently. Whilst their intoxication may be apparent, their diagnosis and the acute and chronic sequelae may be less obvious. NPS are often more potent than traditional illicit drugs (due to their full agonist action at receptors) (75-76), and routine laboratory screening may not be helpful in the acute phase. In this diagnostic “fog of war”, an identification of the class of agent ingested may help the Military Acute Care Practitioner to treat the patient pro-actively (see Figure 1).

Activated Charcoal and Intralipid

The benefit of gastric decontamination in NPS misuse is uncertain. Trial of NPS is only advocated in patients who have taken NPS orally (in pill form), within an hour of presentation, who are not vomiting, and who are able to protect their own airway (44, 46-48, 79).

The use of Intralipid (20%) has been proposed to counteract the effects of lipid soluble molecules on the brain (78). There have been several case reports where patients have been resuscitated from mixed overdoses

(psychotropic medications, antihypertensives, and a combination of both agents) following the administration of Intralipid. The agents taken in these cases included diazepam, temazepam, citalopram, quetiapine, sertraline, bupropion and lamotrigine (79-80). There is no evidence as yet that Intralipid is useful in the management of NPS toxicity, however, these cases indicate that Intralipid might be of benefit where high doses of benzodiazepines have been ingested. One review suggests that Intralipid may be of benefit where the patient has taken a lethal dose of cardiotoxic agents or sustained a cardiac arrest secondary to these drugs (80). However, administration of Intralipid should be weighed against potential side effects (allergic reactions, blood dyscrasias, deranged liver function, clotting disorders, hyperlipidaemia and pancreatitis (80).) Its use may interfere with laboratory assays and routine blood tests, which can impede treatment of the patient, particularly in the context of multiorgan failure (79).

Discussion

Current evidence suggests that the use of NPS amongst members of the civilian population is relatively low. However, research indicates two types of NPS, synthetic cannabinoids and synthetic cathinones, have become increasingly popular among US military personnel (14, 15, 81), a comparable group to the UK Armed Forces. The available evidence would suggest the UK Armed Forces are a high risk group for NPS misuse, particularly the young male recruits, some of whom (approximately 1.34%) would be classed as vulnerable adults (19).

For the small number of UK Armed Forces personnel who chose to misuse recreational drugs, NPS present a cheap, easily available alternative to “traditional” recreational drugs. They have the added benefit of being undetectable on current CDT batteries, and may be more potent than traditional drugs. We know that young, male Armed Forces recruits, particularly those within lower ranks, are at increased risk of misusing alcohol, illicit drugs and prescription medications. Self-reported drug seeking behaviour in comparable cohorts of young civilian men indicates that there is a strong link between traditional drug seeking behaviour and NPS misuse (1). Complex patterns of polysubstance use may increase the adverse side effects experienced by the user, including mortality, and present unique diagnostic challenges to military clinicians, with an unclear clinical picture of intoxication and toxicity (82).

Little is known about the long-term harms produced by NPS; however many of the acute harms are incompatible with a career in the UK Armed Forces. It may be argued that NPS seeking behaviour in UK Armed Forces personnel is a maladaptive coping mechanism for meeting the demands placed on them by a military life and career. Alcohol is commonly misused within the UK Armed Forces community: between January 2012 and November 2016, 6,443 UK Armed Forces personnel were diagnosed with alcohol misuse or dependence (83). The penalties for alcohol misuse within the UK Armed Forces are not as immediately punitive as those for misusing recreational drugs, and there is a strong culture of rehabilitation, although it may be argued that this is due to the cultural acceptability of alcohol in the UK. Illicit drug misuse in UK Armed Forces personnel will almost always result in discharge.

All forms of substance use are higher among young male soldiers in the lower ranks who have recently been deployed (84-89); a group that is also at a higher risk of developing long-term mental health problems (e.g. depression, PTSD, suicidal ideation) (74, 890). As more soldiers now survive their injuries, increasing numbers of deployed military personnel are returning from combat with a range of comorbid physical and mental health issues that have complicated interrelationships with substance use and dependence. There is a high concurrence of problematic substance use with PTSD, depression, anxiety, traumatic brain injury, pain, survivor guilt and suicidal ideation (86, 88, 91-97) all of which undermine the physical fitness and mental readiness of active military personnel and may actually contribute to harmful and criminal behaviours (98-99).

The misuse of NPS by military personnel is incompatible with the physical fitness and mental readiness needed for a successful career in the UK Armed Forces. This misuse has been associated with sequelae ranging from impaired memory, to critical illness, death and danger to others (14, 36, 55, 560, 9100, 101-103). Although there have been no reported cases where NPS misuse has impacted a soldier's performance in the battlefield, there are incidents recorded during training and on combat missions that illustrate the incompatibility of using NPS and active duty in the Armed Forces (14). We can surmise the detrimental effect of even one individual misusing NPS in a combat environment, where their ability to function in teams, mental readiness and physical capabilities may be impaired. During peacetime the effects of NPS misuse on an individual may negatively impact on the safety of others (e.g. drivers of heavy machinery or vehicles, handling live ammunition or explosives). Likewise, there is potential for harm to civilians; a pilot under the influence of NPS may maim or

kill passengers and civilians on the ground. Finally, there is potential for damage to UK Armed Forces assets, such as aircraft, tanks, armoured vehicles and vessels, if personnel are operating under the influence of NPS.

The UK Armed Forces have a duty of care to protect personnel classed as vulnerable adults (those aged 16-18 and all personnel in Phase 1 training). This is particularly pertinent at a time when there is increasing pressure to increase the age of recruitment to over 18 (104). It may be argued that young, male Armed Forces personnel are particularly vulnerable to misusing NPS, and it is questionable whether dismissal from the Armed Forces is morally acceptable or whether rehabilitation should be the first course of action. It may be surmised that discharge from the UK Armed Forces for NPS Misuse dismisses the most damaged soldiers with more complex mental health needs, and that this may have negative implications for their function as civilians, and their future employment chances (8).

Conclusion

Novel psychoactive substances present a challenge to the military physician and to the UK Armed Forces. Currently, there are no routine screening tests for these substances. Military Acute Care Practitioners should be aware of the acute presentations of common types of NPS, and cogniscent of their potentially devastating physical and psychiatric sequelae. Early involvement of specialist secondary care teams may be needed. Prolonged supportive care may be necessary due to the potency of many of these agents.

Only a small number of military personnel have been identified as recreational drug users; however, whilst NPS remain undetectable, they may prove tempting to this small population. On their own, NPS may undermine both the health of soldiers and the capabilities of the UK Armed Forces. The misuse of NPS may be part of a larger issue of substance use and dependence among active military personnel, particularly young males. Whilst the misuse of “traditional” recreational drugs may be forgiven under exceptional circumstances, the dangerous and unpredictable sequelae of taking NPS make the practice, in general, incompatible with service life.

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Legends

Figure 1: Figure illustrating an approach to the assessment and management of a service person who has taken Novel Psychoactive Substances

Figure 2: Figure illustrating prolonged QTc and widening of the QRS complex in a patient who overdosed on amitryptaline. Similar cardiotoxicity may be observed following ingestion of opioid type novel psychoactive substances. Reproduced with permission from www.lifeinthefastlane.com (72)

