

DR. CATHELIJNE LYPHOUT

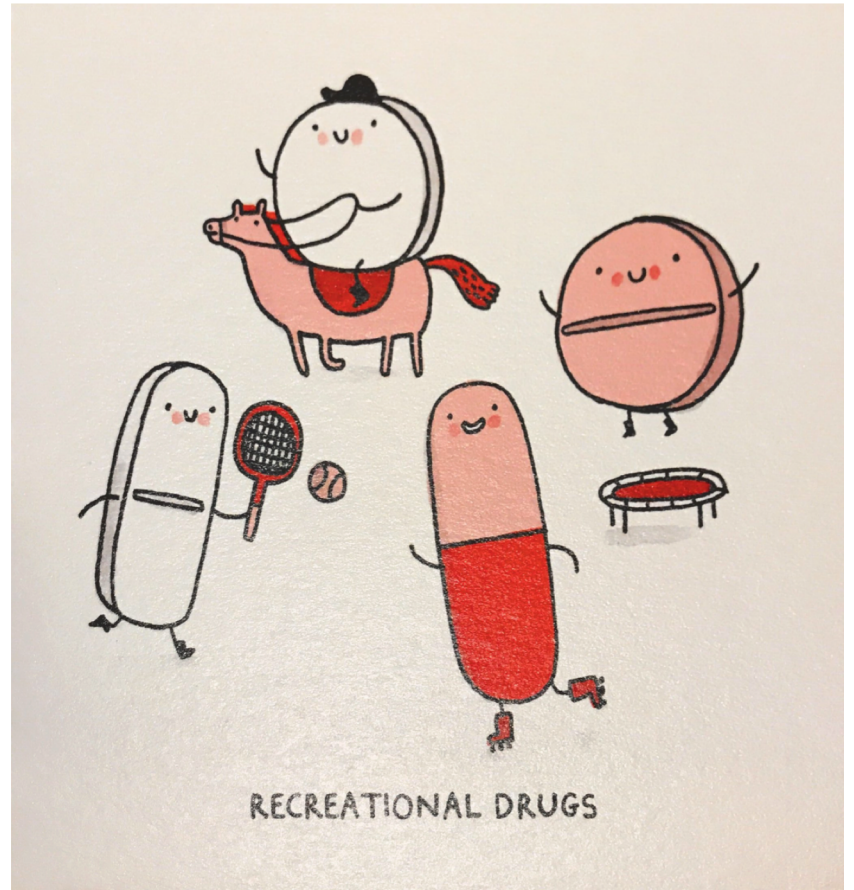
22/02/2018

WHAT'S NEW IN DRUGS?

RECENTE TRENDS IN RECREATIONEEL DRUGGEBRUIK

RECREATIONEEL DRUGGEBRUIK

- KLASSIEKE DRUGS
- NOVEL PSYCHOACTIVE SUBSTANCES / DESIGNER DRUGS
 - RESEARCH CHEMICALS
 - HERBALS
- NIET-MEDISCH GEBRUIK VAN GENEESMIDDELEN
- INHALANTIA



WETGEVING

- KB 24 februari 1921 betreffende het verhandelen van verdovende middelen
- KB 31 december 1930 houdende regeling van de slaapmiddelen en de verdovende middelen en betreffende risicobeperking en therapeutisch advies
- 1961: UN Single Convention on Narcotic Drugs (NY, implementatie in België in 1969)
- 1971: UN Convention on Psychotropic Substances (Wenen)
- KB 22 januari 1998 houdende regeling van sommige psychotrope stoffen en betreffende risicobeperking en therapeutisch advies.

BELGISCHE WETGEVING

- September 2016: Generieke wetgeving

(KB 06.09.2017 houdende de regeling van verdovende middelen en psychotrope stoffen)

- Overnemen van reeds gedefinieerde “yellow list”: stoffen opgenomen bij het **verdrag van 1961**
- Lijsten I, II, III en IV van de “green list”: stoffen opgenomen bij het **verdrag van 1971**
- **Classificatie op basis van een gemeenschappelijke chemische basisstructuur**
- Wettelijk kader voor GBL (gamma-butyrolactone) en 1,4-BD (1,4-butanediol)

BELGIAN EARLY WARNING SYSTEM ON DRUGS (BEWSD)

- Hoofddoelen
 - Snelle detectie van NPS in België
 - Monitoring van de samenstelling van illegale drugs
 - Monitoring van hoog-risico trends over zijn samenstelling
 - Inschatting van gezondheidsrisico
- Gebaseerd op rapportering door laboratoria
- Communicatie aan
 - een professioneel netwerk
 - de bevolking: enkel ingeval van hoog risico

ews@druglijn.be

KLASSIEKE DRUGS



Narcotics

Even termed as 'Opioids' and originally derived from substance 'Opiates' and its common form includes morphine and heroin



Cocaine

Cocaine is a strong stimulant mostly used as a recreational drug. It is commonly snorted, inhaled, or injected into the veins.



Hallucinogens

Produces sensory hallucinations involving any of the 5 body senses. Common types of hallucinogens include LSD, PCP and peyote



Inhalants

Drugs that are to be inhaled and are available either as a Gas or Solvent. Most common Inhalant products like nail polish and gasoline



Amphetamines

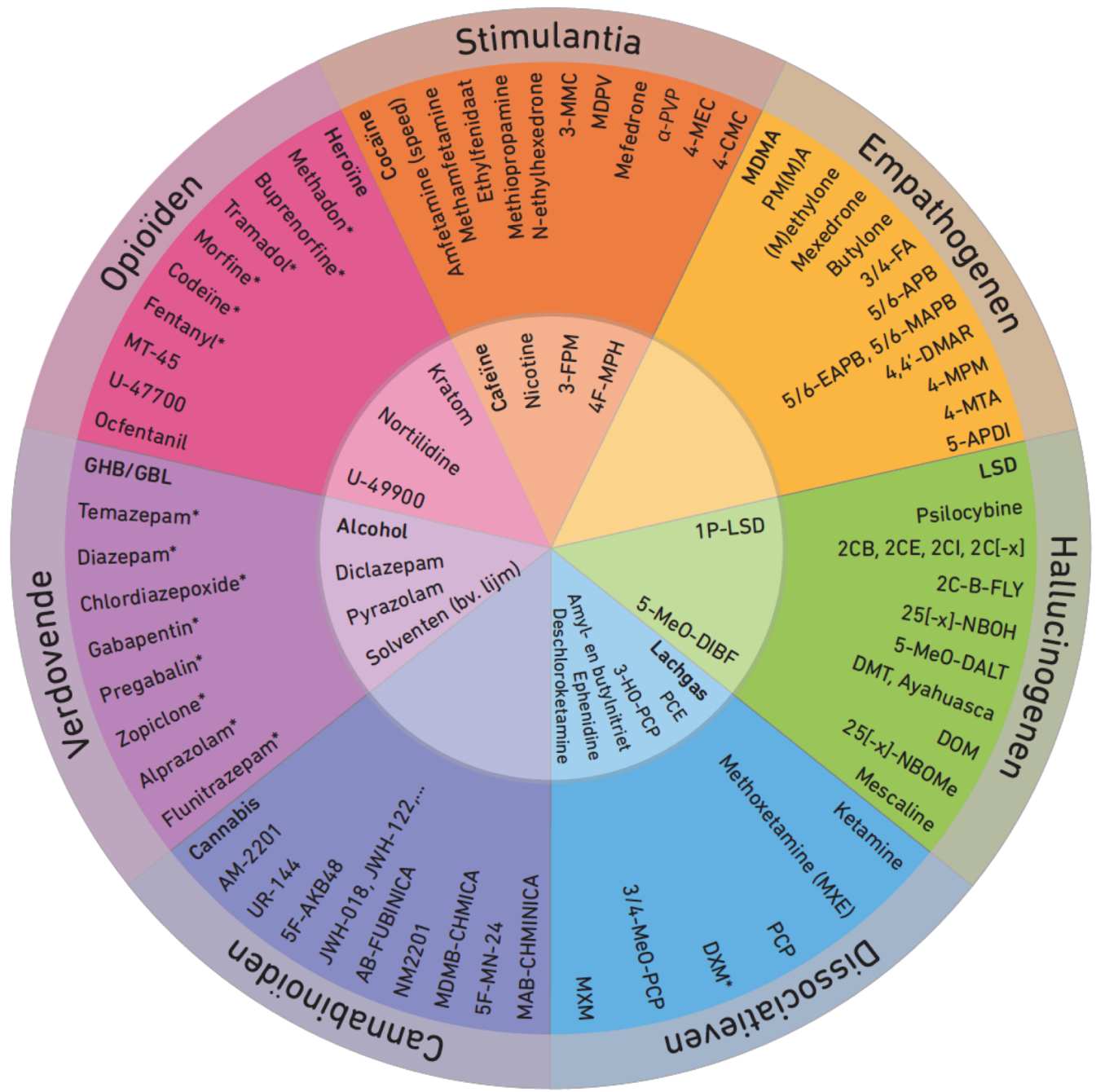
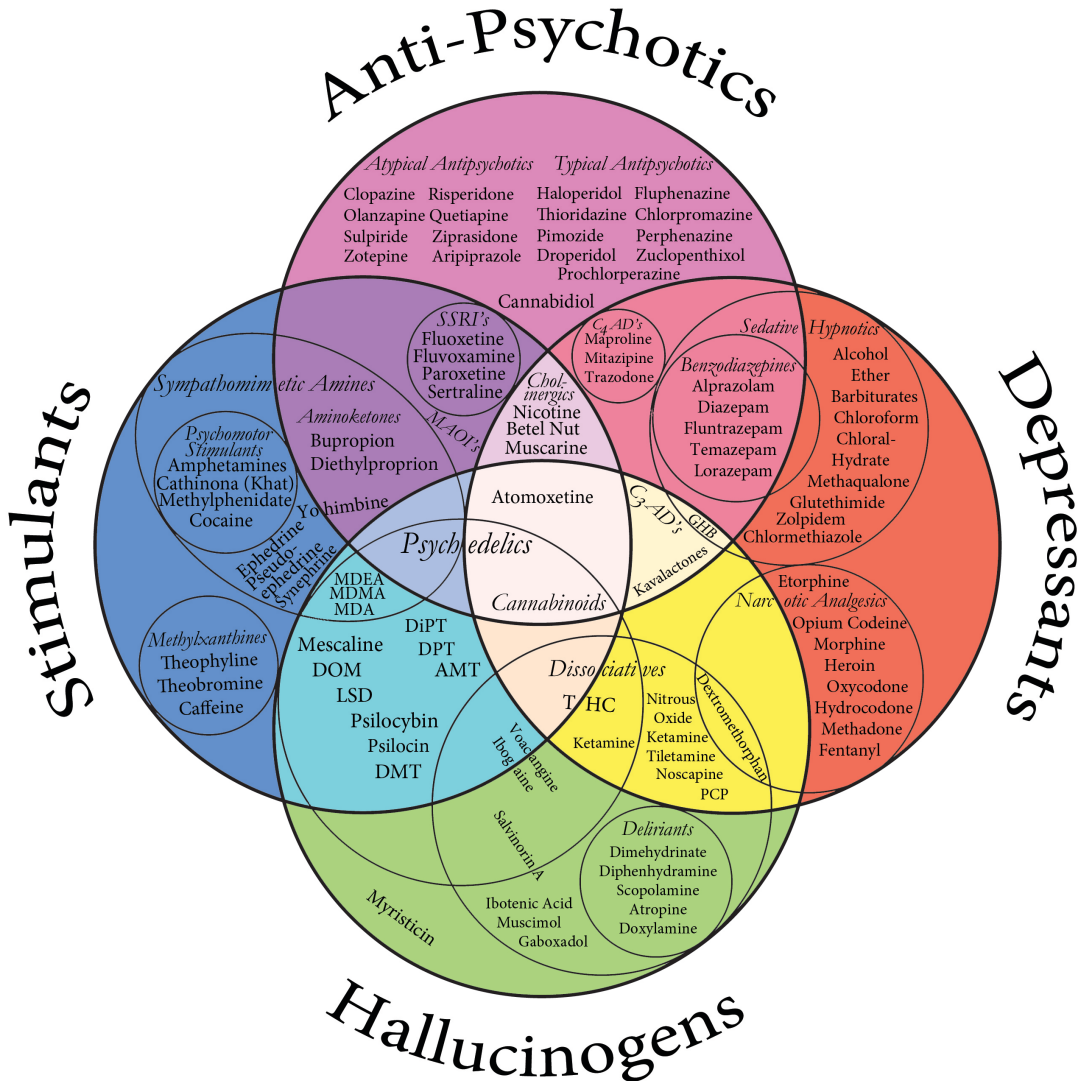
Boosts alertness and increases activity of the central nervous system, the most abused form of stimulants are amphetamines



Cannabis

Marijuana use has been legalized in certain states by prescription because of its psychoactive effects.

<http://drugs.tripsit.me>



2-Methylamino-1-p-tolyl
 Not for human consumption
 For technical use only.

MXE **BENZO FURY**

RESEARCH CHEMICAL PELLETS

Ca. 99.9%
 Purity: 99.4%
 Batch: 001
 Sample: 1g

Xn, R22

METHOXYAMINE

CC1=CC=C(C=C1)CN(C)C

THE FULL BUZZ

5-IAI

NOT FOR HUMAN CONSUMPTION

copyrightthefullbuzz.com

18

200mg CONCENTRATED SAMPLE PACK

100% LEGAL IN THE UK

100% LIDOCAINE FREE

NEW... Ivory WAVE

WAVE

BLACK MANIBA

18

PHENAZEPAM

PURE CHEMICALS OFFICIAL PRODUCT

7-bromo-5

KANNA 3g

NOT FOR HUMAN CONSUMPTION

(a)

CUBA

WTF

NEXT GENERATION HERBAL POTPOURRI

4g

Does not contain AM 2201 or any DEA Banned Substance

(b)

CUBA Mr. Nice Guy

NOT FOR HUMAN CONSUMPTION
 WIF IS SOLD AS POTPOURRI. STROKE THE FURRY BAG

THIS POTPOURRI DOES NOT CONTAIN AM 2201, JWH-081, JWH-019, JWH-018, JWH-073, HU-211, JWH-015, JWH-200, JWH-250, HU-210, CP47, 497 ALONG WITH STIMULANT BZP AND RTFMPP

NOT FOR CONSUMPTION. NOT FDA APPROVED.

6 96969 69670 7

SCAN THIS TO REGISTER FOR FREE PRODUCT GIVEAWAYS
 WWW.MR-NICE-GUY.COM

CONCENTRATED BATH SALTS

For an invigorating, energizing and truly Scentual experience

SYNTHETIC CANNABINOID RECEPTOR AGONISTS (SCRA'S)

- Eerste gerapporteerd gebruik in 2004
- Toegevoegd aan plantaardig materiaal
 - weken
 - sprayen
 - (crystalijn poeder toevoegen)
- Gewoonlijk gerookt, ook soms ingestie



naturally occurring cannabinoids

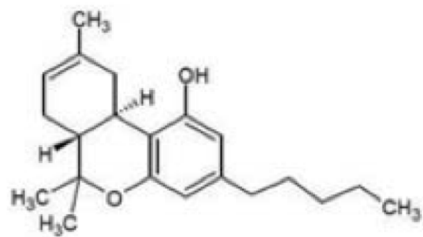
synthetic cannabinoids

classic cannabinoids

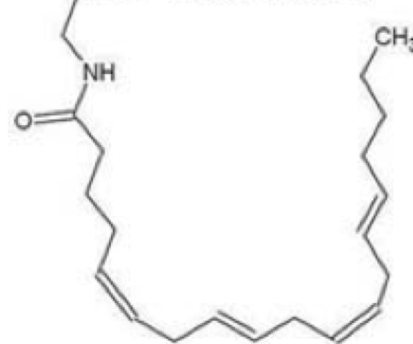
eicosanoids

used as medication

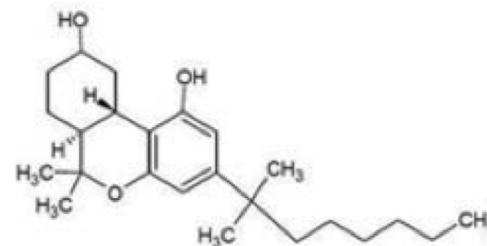
Δ^9 -tetrahydrocannabinol



anandamide



nabilone



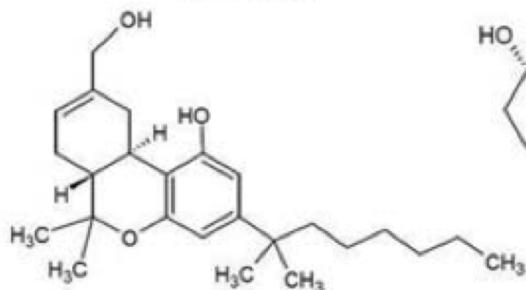
synthetic cannabinoids as drugs of abuse

classic cannabinoids

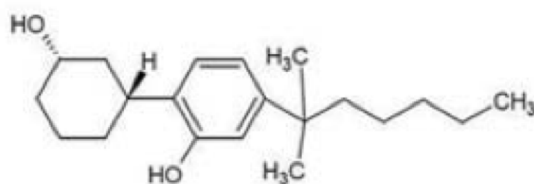
non-classic

aminoalkylindoles

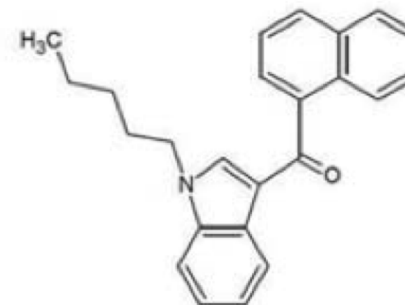
HU-210



CP47,497



JWH-018



SYNTHETIC CANNABINOID RECEPTOR AGONISTS (SCRA'S)

- Bootst de effecten van THC na
- Potente full cannabinoid receptor agonisten
- Meeste zijn zeer potente cannabinoid receptor type I (CBI) agonisten
- Weinig kennis over de farmacologische eigenschappen
- Brede chemische diversiteit



SYNTHETIC CANNABINOID RECEPTOR AGONISTS (SCRA'S)

- Meest voorkomende benamingen
 - Spice
 - K2
- AM-2201
- MDMB-CHMICA
- AB-FUBINACA
- MAM-2201
- XLR-11 (5F-UR-144)
- JWH-018



SYNTHETIC CANNABINOID RECEPTOR AGONISTS (SCRA'S)

- Beperkte data over toxiciteit bij mensen
- Producten die worden **verkocht als** synthetische cannabinoïden bevatten vaak **verschillende chemicaliën** in **verschillende concentraties**
 - << heel moeilijk om product-gerelateerde specifieke effecten vast te stellen
- Cardiovasculaire problemen
- Psychologische stoornissen
- Carcinogeen potentieel van sommige metabolieten
- Verslaving en ontwenningssymptomen werden reeds gerapporteerd

Acute toxicity due to the confirmed consumption of synthetic cannabinoids: clinical and laboratory findings

Maren Hermanns-Clausen^{1*}, Stefan Kneisel^{2*}, Bela Szabo³ & Volker Auwärter²

	N=29
Restlessness/agitation	41%
Hallucinations	38%
Vertigo	24%
Anxiousness	21%
Tachycardia	76%
Hypertension	34%
Dyspnoea	21%
Nausea/vomiting	28%
Mydriasis	38%

BRIEF COMMUNICATION

Severe Toxicity Following Synthetic Cannabinoid Ingestion

J. LAPOINT^{1,2,3}, L. P. JAMES⁴, C. L. MORAN⁵, L. S. NELSON^{1,2,3}, R. S. HOFFMAN^{1,2,3}, and J. H. MORAN^{6,7}

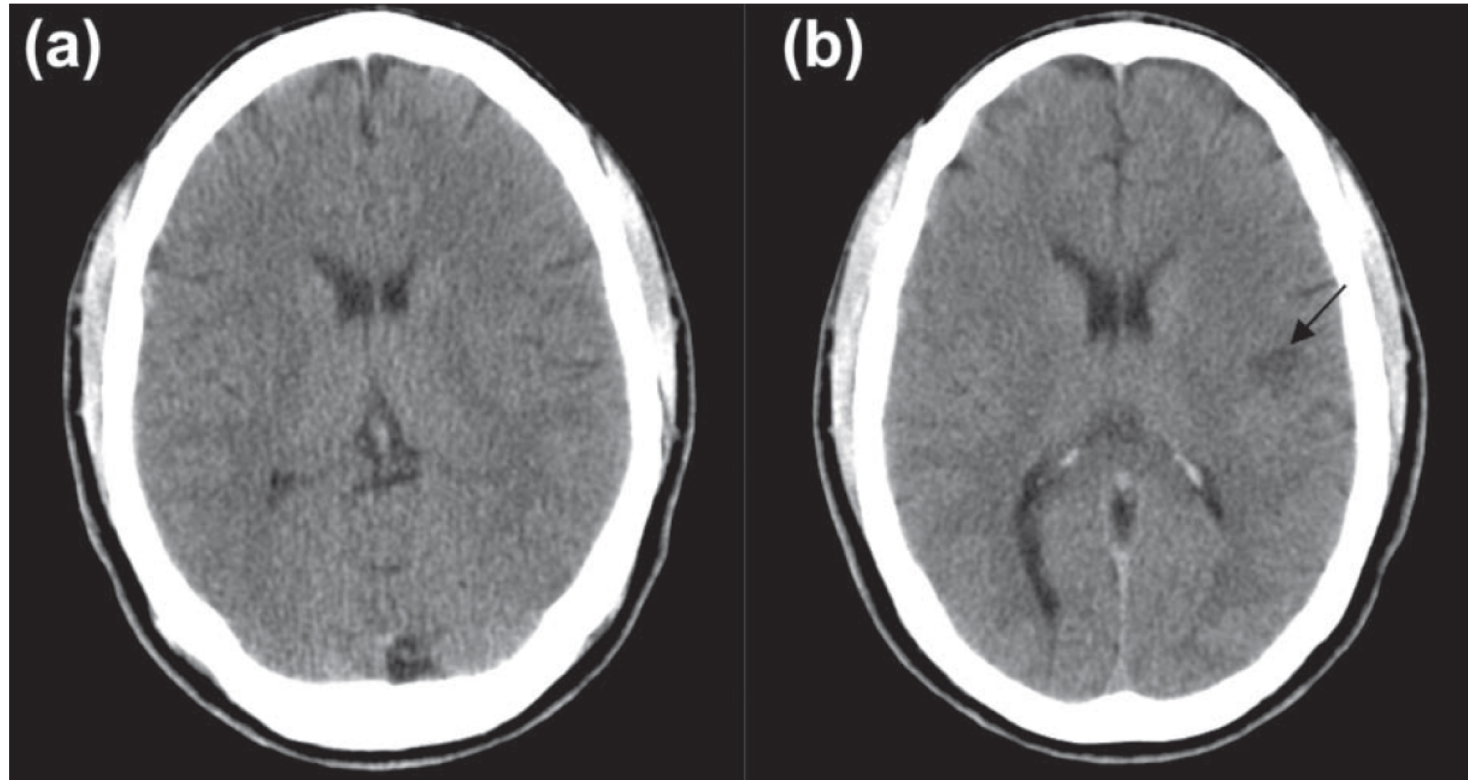
Conclusion

We describe a patient with **repetitive seizures and supraventricular tachycardia** following confirmed ingestion of the synthetic cannabinoid JWH-018. Clinicians should consider synthetic cannabinoid exposure in the differential diagnosis of patients who present with agitated delirium and seizures following recreational drug abuse.

BRIEF COMMUNICATION

A case of acute cerebral ischemia following inhalation of a synthetic cannabinoid

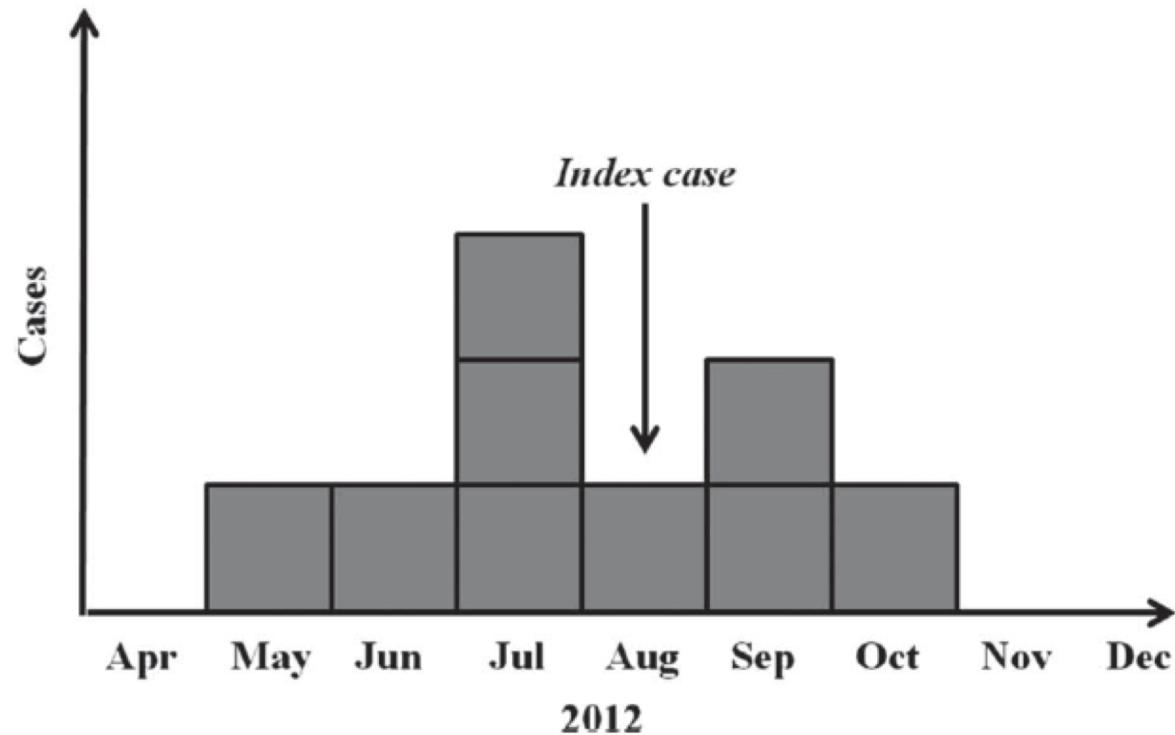
M. TAKEMATSU,¹ R. S. HOFFMAN,² L. S. NELSON,^{2,3} J. M. SCHECHTER,^{4,5} J. H. MORAN,⁶ and S. W. WIENER^{4,5}



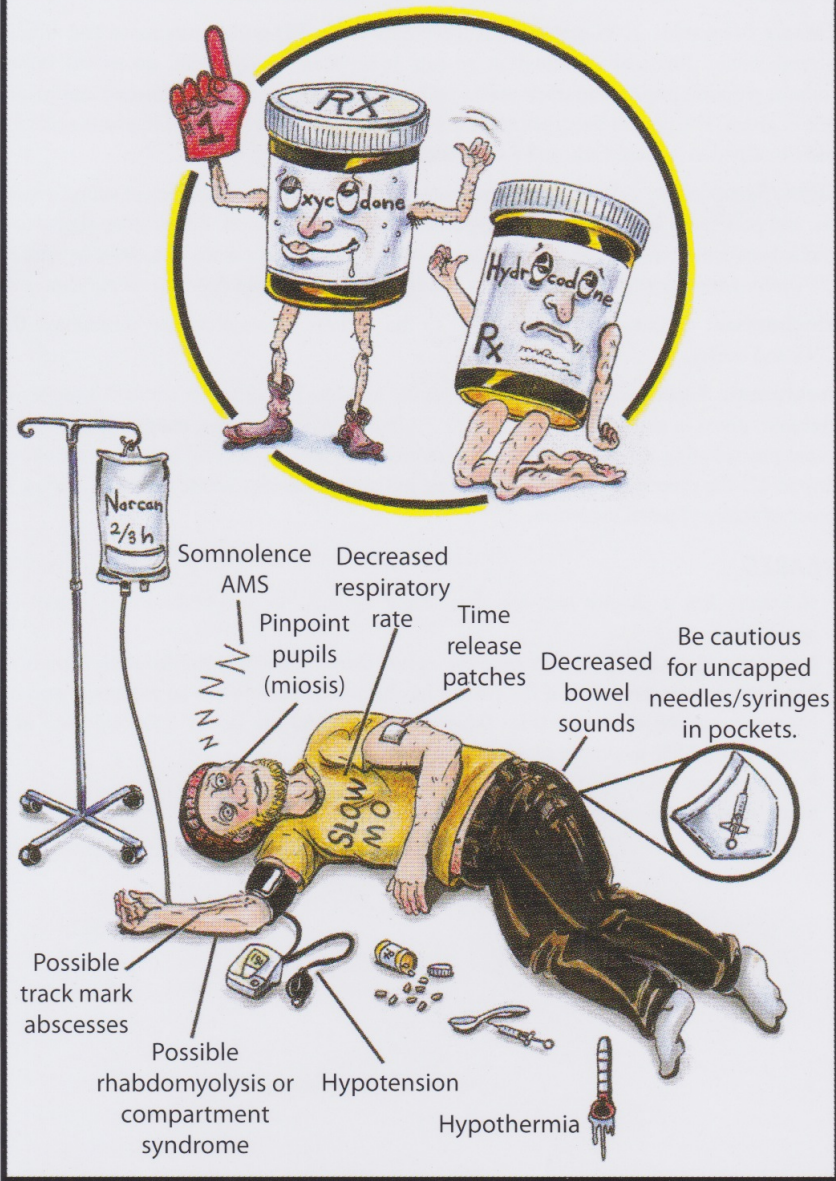
CRITICAL CARE

Acute kidney injury associated with smoking synthetic cannabinoid

G. L. BUSER,^{1,2} R. R. GERONA,³ B. Z. HOROWITZ,⁴ K. P. VIAN,⁵ M. L. TROXELL,⁶ R. G. HENDRICKSON,⁴ D. C. HOUGHTON,⁶ D. ROZANSKY,⁷ S. W. SU,⁸ and R. F. LEMAN¹



Opiate Toxidrome



OPIOID TOXICODROOM

- **Somnolentie tot coma**
- **Vertraagde ademhaling tot ademhalingsstilstand (bradypnoe)**
- Vertraagde hartslag (bradycardie)
- Verminderde peristaltiek (hypoperistalsis)
- **Miose**
- Perifere vasodilatatie: **Hypotensie**
- **Hypothermie**

Complicaties

- Niet-pulmonair acuut longoedeem
- QT verlenging bij methadon
- Rhabdomyolyse!



OPIOID TOXICODROOM

- Morfine
- Heroïne
- Methadon
- Opioiden op voorschrift (oa. Oxycodon: oxycontin® / oxynorm®)
- Fentanyl ea.
- Fentanils: nieuwe fentanylderivaten (NPS)

- Paraphernalia
- Cave: patches

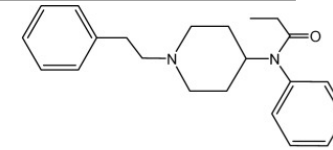
- AD: Naloxone (Narcan)
 - Normaalgezien: IV per 40mcg titreren / IM 400mcg (tot 0,4-2mg)
 - Bij NPS vaak hoge doses nodig! (tot 10mg beschreven!)



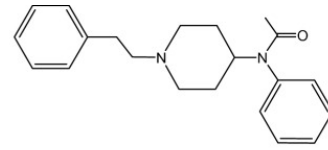
SYNTHETIC OPIOIDS

- Mainly fentanyl derivatives
- compounds with different chemical structures
 - AH-7921
 - MT-45
 - **U-47700 (U4)**

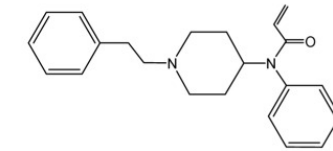
Acetylfentanyl
 Acryloylfentanyl
Carfentanyl
 α-methylfentanyl
3-methylfentanyl
 Furanylfentanyl
 4-fluorobutyrylfentanyl
 4-methoxybutyrylfentanyl
 4-chloroisobutyrylfentanyl
 4-fluoroisobutyrylfentanyl
 Tetrahydrofuranylfentanyl
 Cyclopentylfentanyl
Ocfentanil



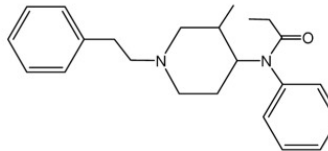
Fentanyl



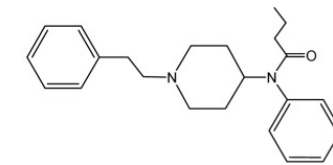
Acetylfentanyl



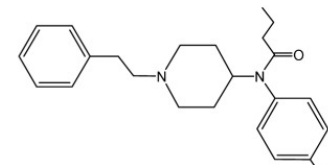
Acryloylfentanyl



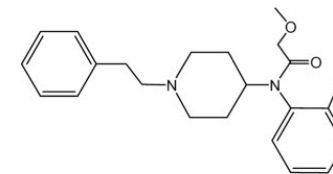
3-Methylfentanyl



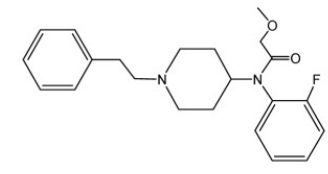
Butyrylfentanyl



4-Fluorobutyrylfentanyl



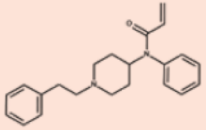
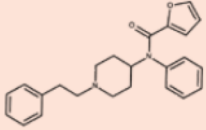
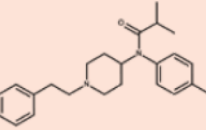
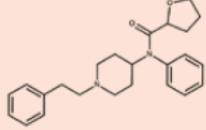
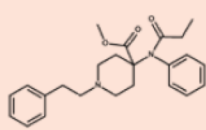
Furanylfentanyl



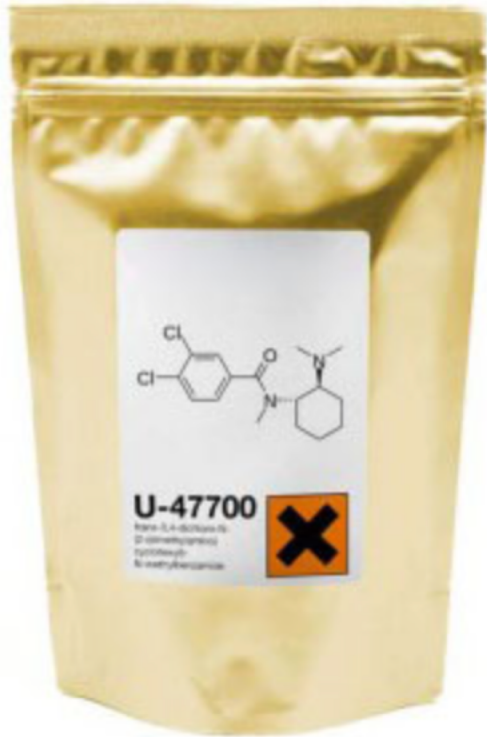
Ocfentanil

Slang:
 China white
 China girl
 Persian white
 Egg white
 Crocodile
 Synthetic heroin

Key findings of the risk assessments of acryloylfentanyl, furanylfentanyl, 4-fluoroisobutyrylfentanyl (4F-iBF), tetrahydrofurfanylfentanyl (THF-F) and carfentanil

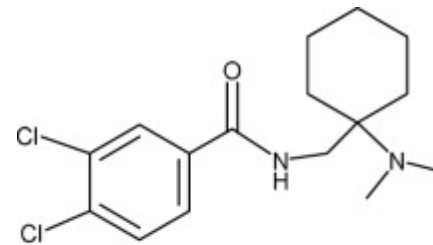
Common name	Acryloylfentanyl	Furanylfentanyl	4F-iBF	THF-F	Carfentanil
Chemical name	<i>N</i> -(1-phenethylpiperidin-4-yl)- <i>N</i> -phenylacrylamide	<i>N</i> -phenyl- <i>N</i> -[1-(2-phenylethyl)piperidin-4-yl]furan-2-carboxamide	<i>N</i> -(4-Fluorophenyl)- <i>N</i> -(1-phenethylpiperidin-4-yl)isobutyramide	<i>N</i> -Phenyl- <i>N</i> -[1-(2-phenylethyl)piperidin-4-yl]oxolane-2-carboxamide	Methyl 1-(2-phenylethyl)-4-[phenyl(propanoyl)amino]piperidine-4-carboxylate
Chemical structure					
Category	Synthetic opioid	Synthetic opioid	Synthetic opioid	Synthetic opioid	Synthetic opioid
Pharmacology	μ- opioid receptor agonist	μ- opioid receptor agonist	μ- opioid receptor agonist	μ- opioid receptor agonist	μ- opioid receptor agonist
Formal notification to the EU Early Warning System	7 July 2016	3 November 2015	26 August 2016	23 December 2016	12 February 2013
Number of deaths	47	23	20	14	61
Number of countries where associated deaths occurred	3	6	2	1	8
Number of seizures by law enforcement	162	143	24	53	801
Number of countries where it has been seized	5	14	4	1	7
Total quantity seized	113 g of powder 1 495 ml liquid 896 tablets	1 036 g powder 6 g plant material 1 559 ml liquid 45 tablets	379 g powder 208 ml liquid 6 727 tablets	99 g powder 950 ml liquid	3.3 kg powder

SYNTHETIC OPIOIDS

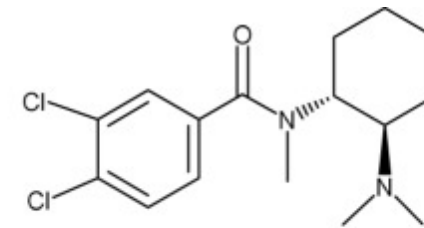


Risico

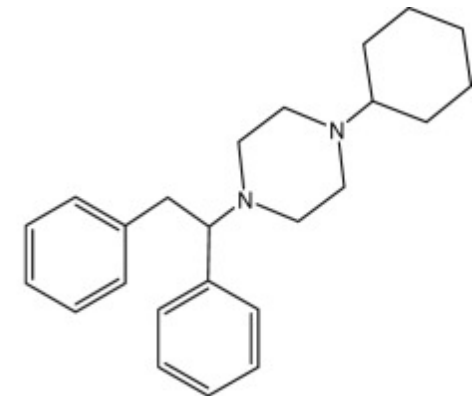
- Opioid toedroom
- Heel krachdig – nauwe therapeutie index
- Vaak verkocht als / gemixt door heroïne
- Hoge doses van naloxone nodig



AH-7921



U-47700

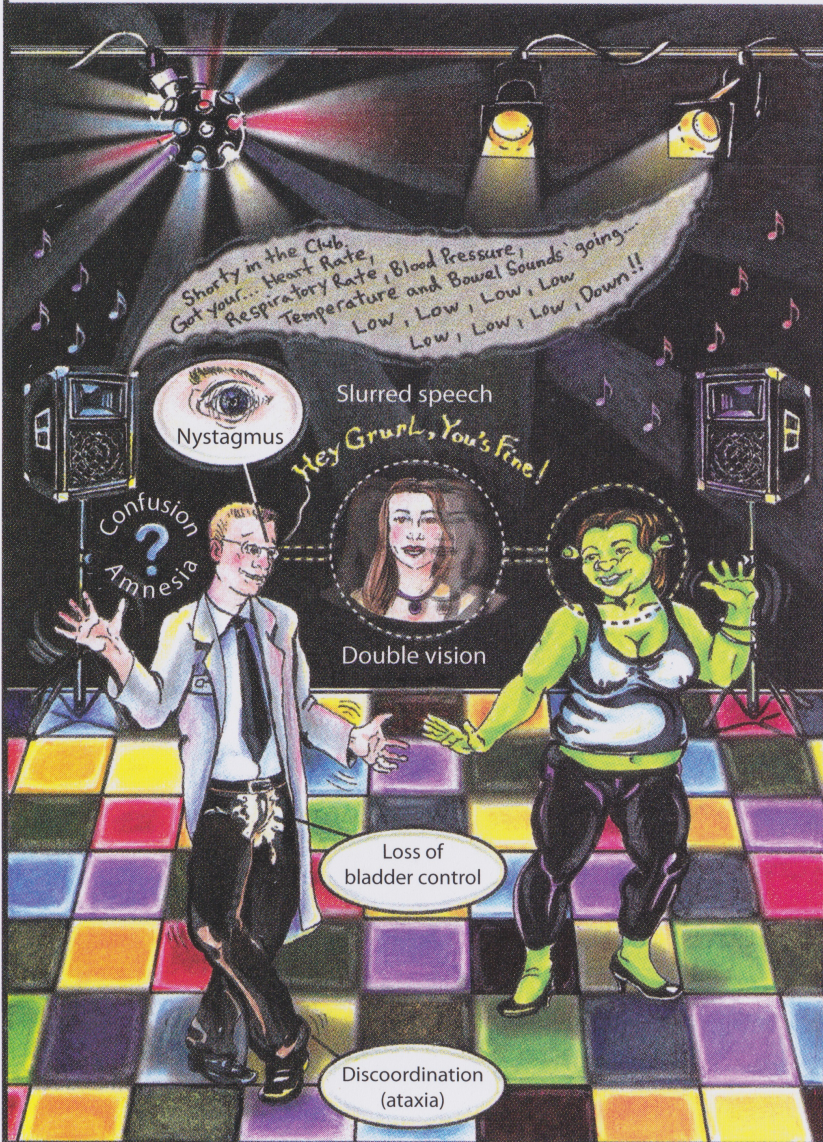


MT-45

ADVIEZEN VOOR MEDISCH PERSONEEL BIJ VERMOEDEN NPS-OPIOIDEN

- Gebruik steeds handschoenen + evt. masker
- Open geen zakjes met onbekend poeder (gevaar voor aerogene verspreiding)
 - Meegeven aan politie – meenemen voor analyse (UZ Gent)
- Vermijd contact met ogen / neus / mond / huid
- Was de huid met koud water en zeep
 - Alcogel onvoldoende (kan opname via de huid versterken)
 - Zeker voor het eten / naar het toilet / roken
- Bij vermoeden intoxicatie
 - Verwijderen van de bron
 - Handschoenen, geen mond-op-mond beademing
 - Zuurstof + BLS (ALS) zn
 - Naloxone (MUG)

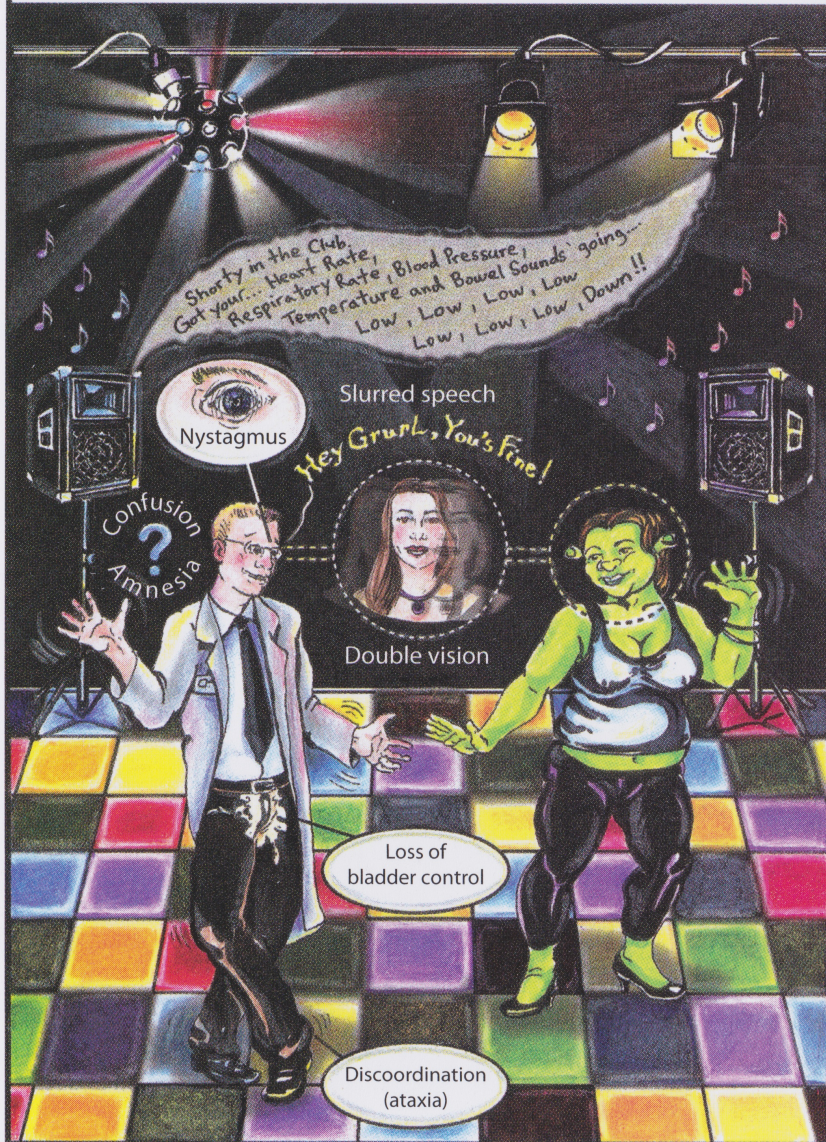
Hypnosedative Toxidrome



SEDATIEF – HYPNOTISCH TOXICODROOM

- **Verminderde ademhaling – wegvallen van tonus in keel**
- **Verminderd bewustzijn tot coma**
- **Vertraagde hartslag (bradycardie)**
- **Lage bloeddruk (hypotensie)**
- **Verminderde coordinatie**
- Mompelende spraak
- Lethargie
- Disinhibitie
- Verminderde spiertonus
- Nystagmus (vnl horizontaal)

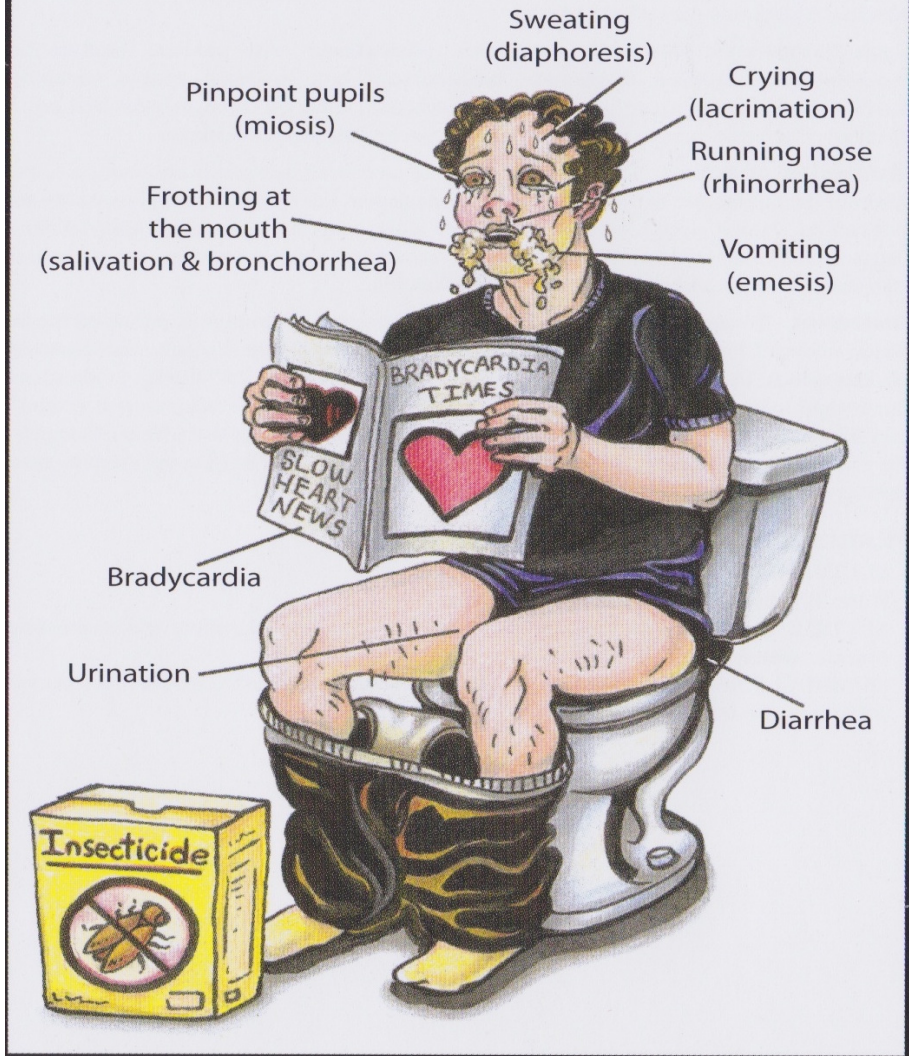
Hypnosedative Toxidrome



SEDATIEF – HYPNOTISCH TOXICODROOM

- Alcohol
- Benzodiazepines/Z-drugs
- GHB/GBL ('liquid XTC')
- Anti-epileptica
- Barbituraten
- Baclofen (! Lazarussyndroom)
- Clonidine

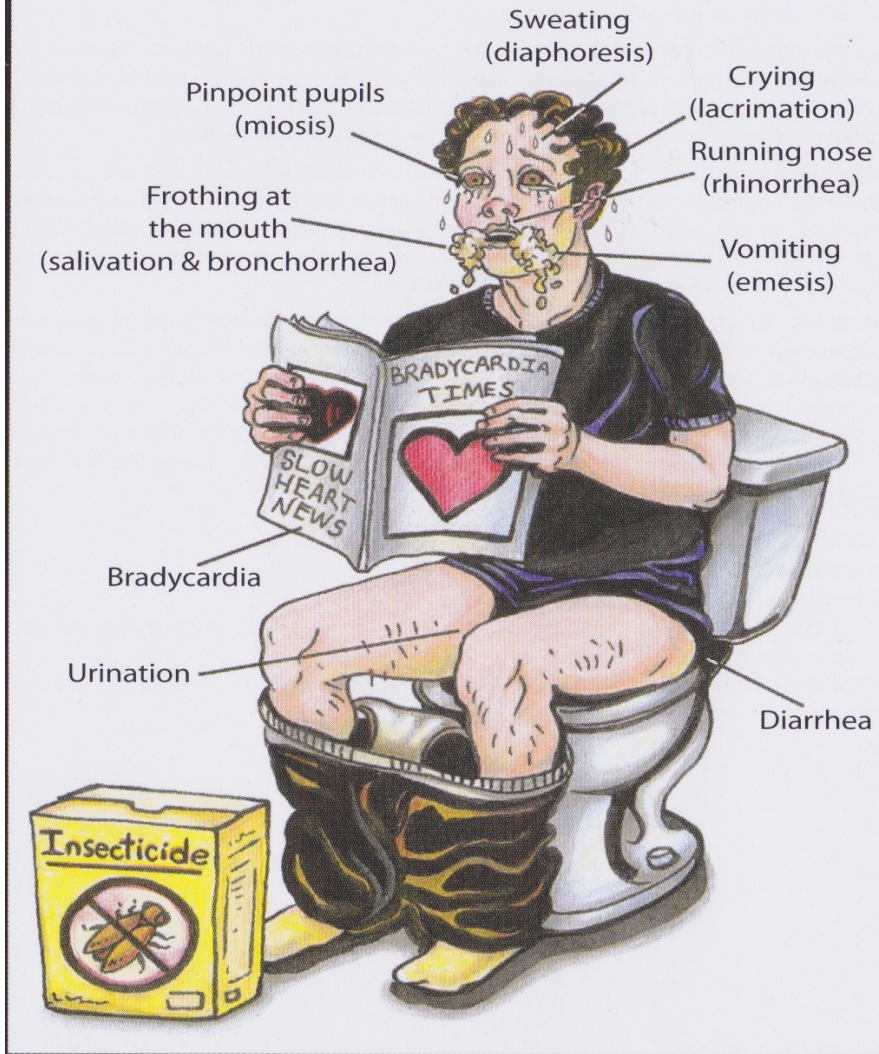
Cholinergic Toxidrome



CHOLINERG TOXICODROOM

- Miose (kleine pupillen)
- Trage hartslag (bradycardie)
- Zweeten
- Tranen
- Loopneus
- Braken
- Speekselvloed
- Longoedeem
- Toename mictie
- Diarree

Cholinergic Toxidrome



CHOLINERG TOXICODROOM

Bronnen:

Organofosfaten

- Chemische oorlogsvoering

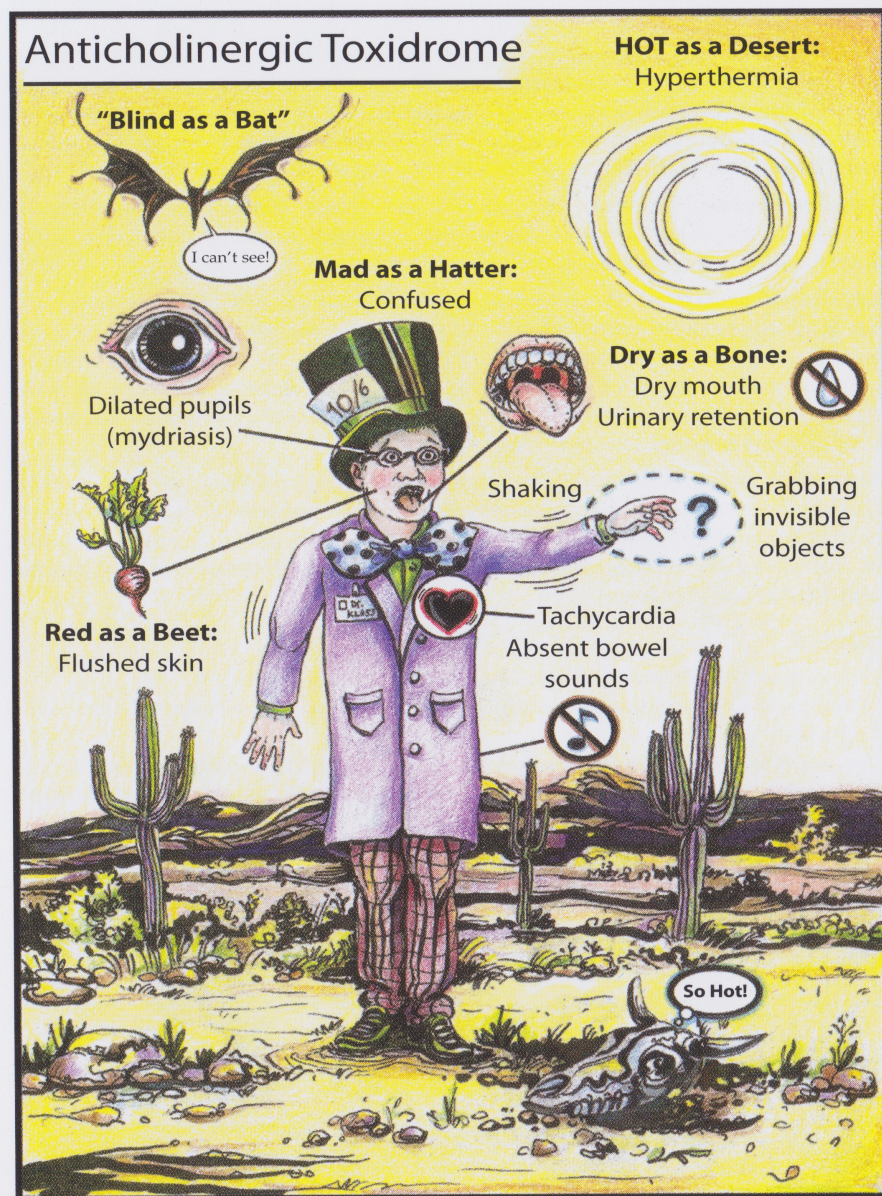
Sarin (metro Japan)

Soman (WO II)

VX (Kim Jong-nam)

...

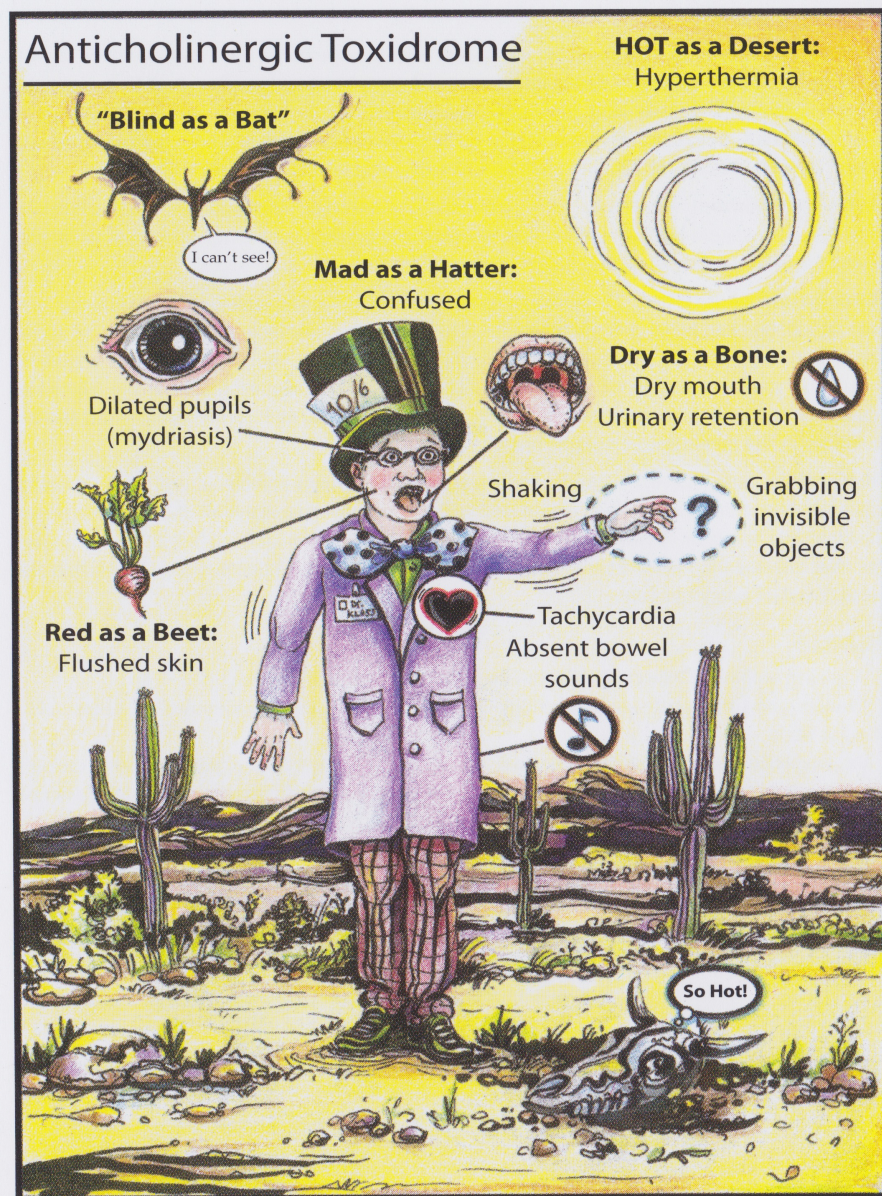
- Insecticiden



ANTICHOLINERG TOXICODROOM

- Mydriase
- Droge mucosa
- Tachycard
- Hypertherm
- Hypertens
- Hypoperistaltiek
- Droge warme huid
- Urinaire retentie!
- **Delirium, verminderde coordinatie, verward, hallucinaties**
- **Stuipen**

‘Dry as a bone, ret as a beat, hot as a hare, mad as a hatter, and blind as a bat’



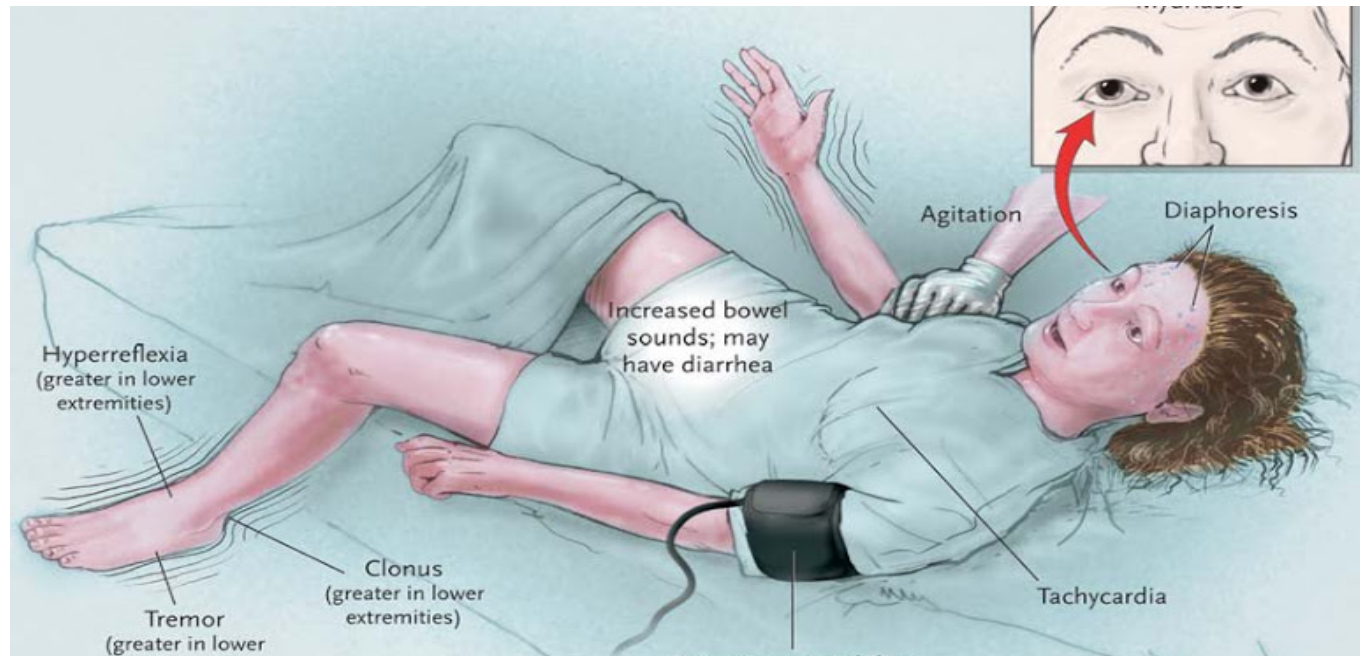
ANTICHOLINERGIC TOXICODROOM

- Anticholinergica
 - Atropine
 - Scopolamine (versneden heroïne)
- Antihistaminica
- TCA
- Anti-parkinson medicatie
- Antipsychotica
- Carbamazepine
- ...

‘Dry as a bone, red as a beet, hot as a hare, mad as a hatter, and blind as a bat’

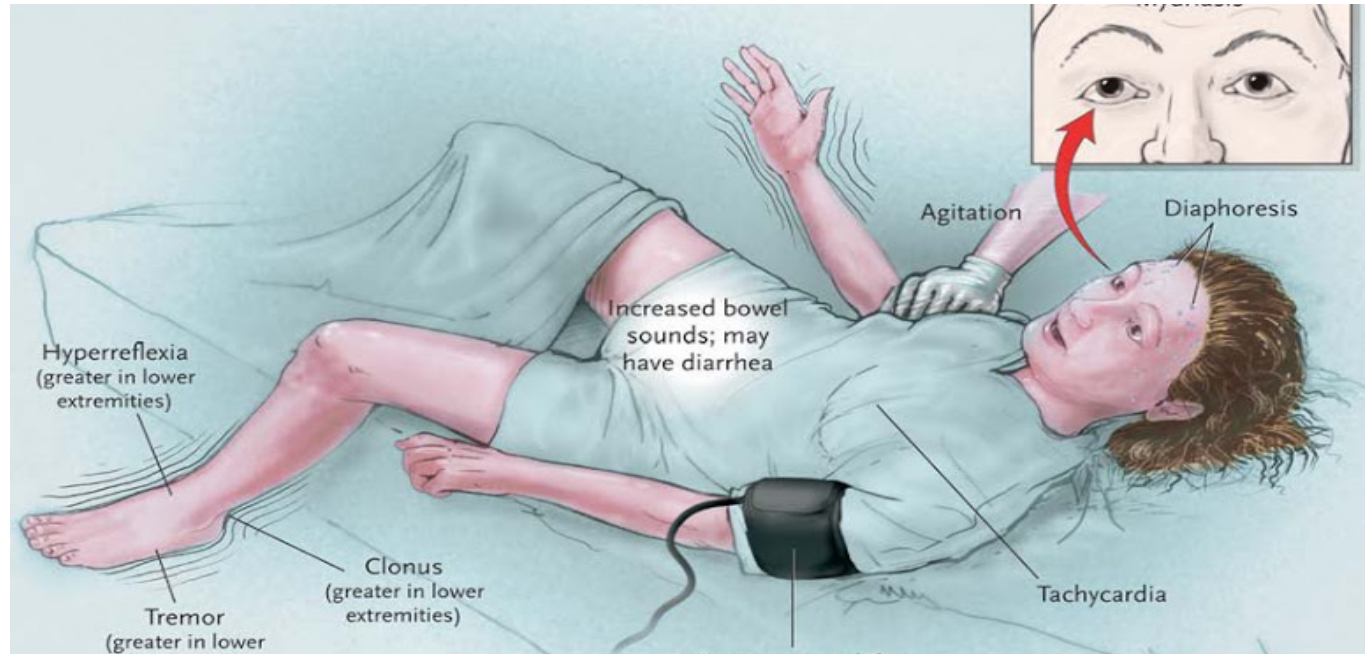
SEROTONINERG SYNDROOM

- Agitatie
- Zweeten
- Versnelde hartslag (tachycardie)
- Toename van darmgeruisen (hyperperistalsis)
- Clonus
- Beven (Tremor)
- Toegenomen reflexen (hyperreflexie)



DD/ maligne neuroleptisch syndroom

SEROTONINERG SYNDROOM

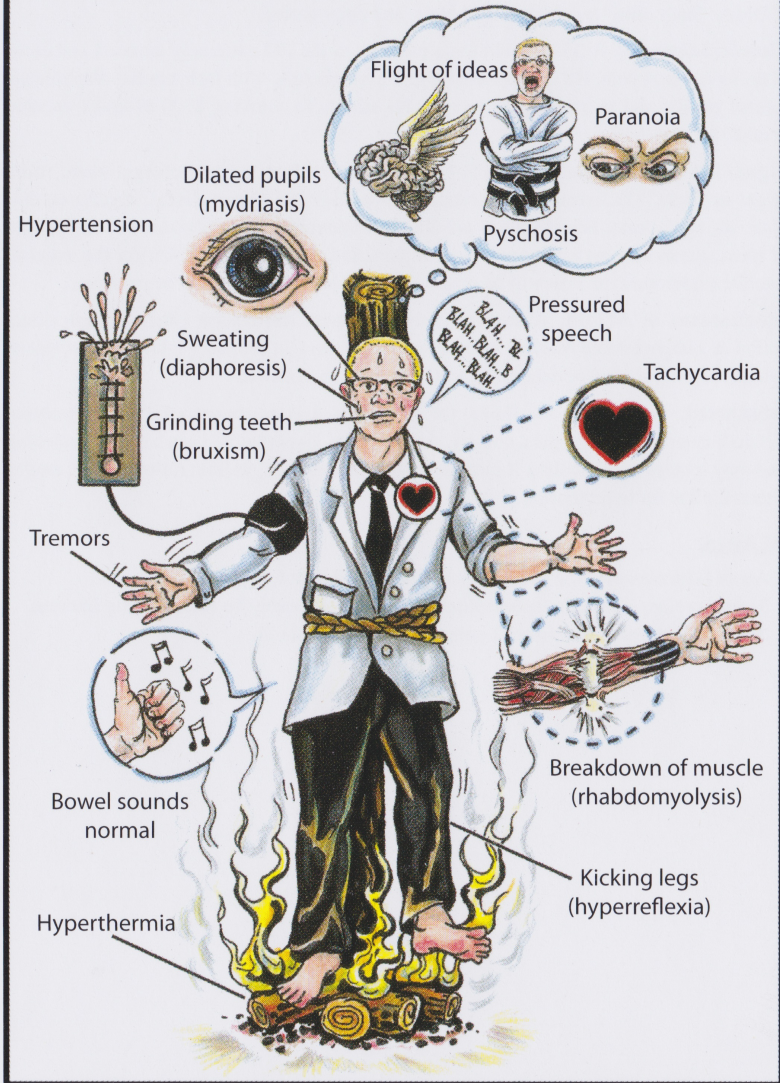


LSD
Cocaine
MDMA (ecstasy)
Tramadol
(Fentanyl)

SSRI (antidepressiva)
TCA (antidepressiva)
MAO-I
Lithium

DD/ maligne neuroleptisch syndroom

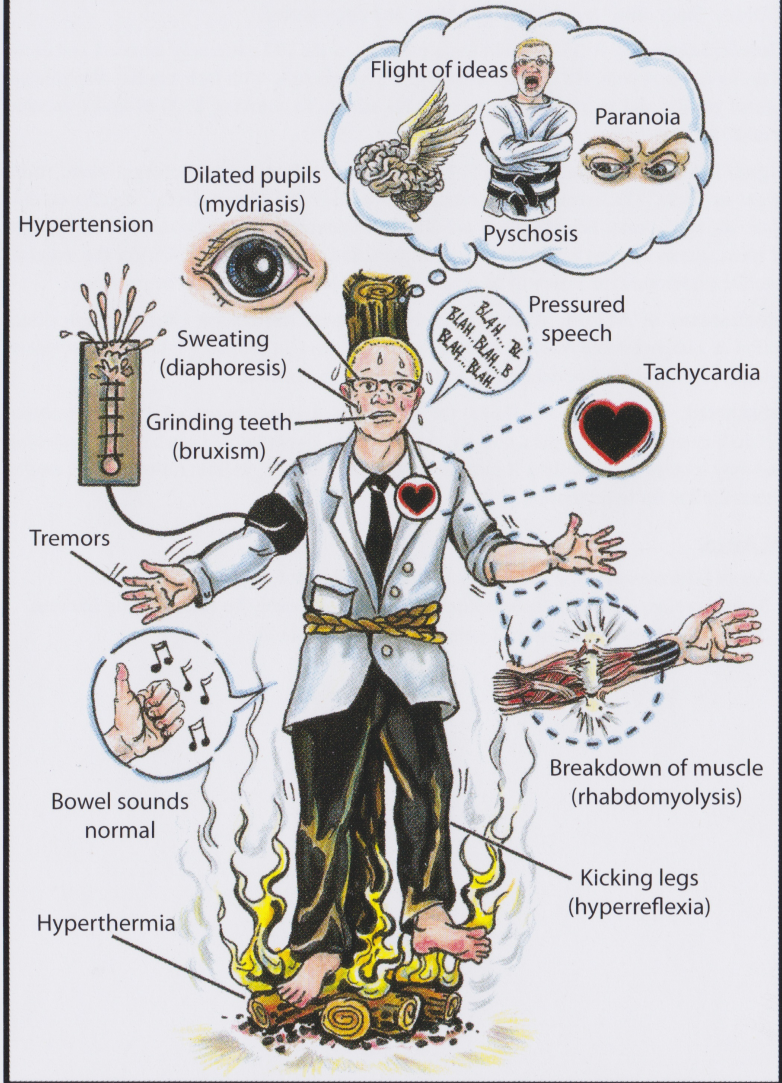
Sympathomimetic Toxidrome



SYMPATHOMIMETISCH TOXICODROOM

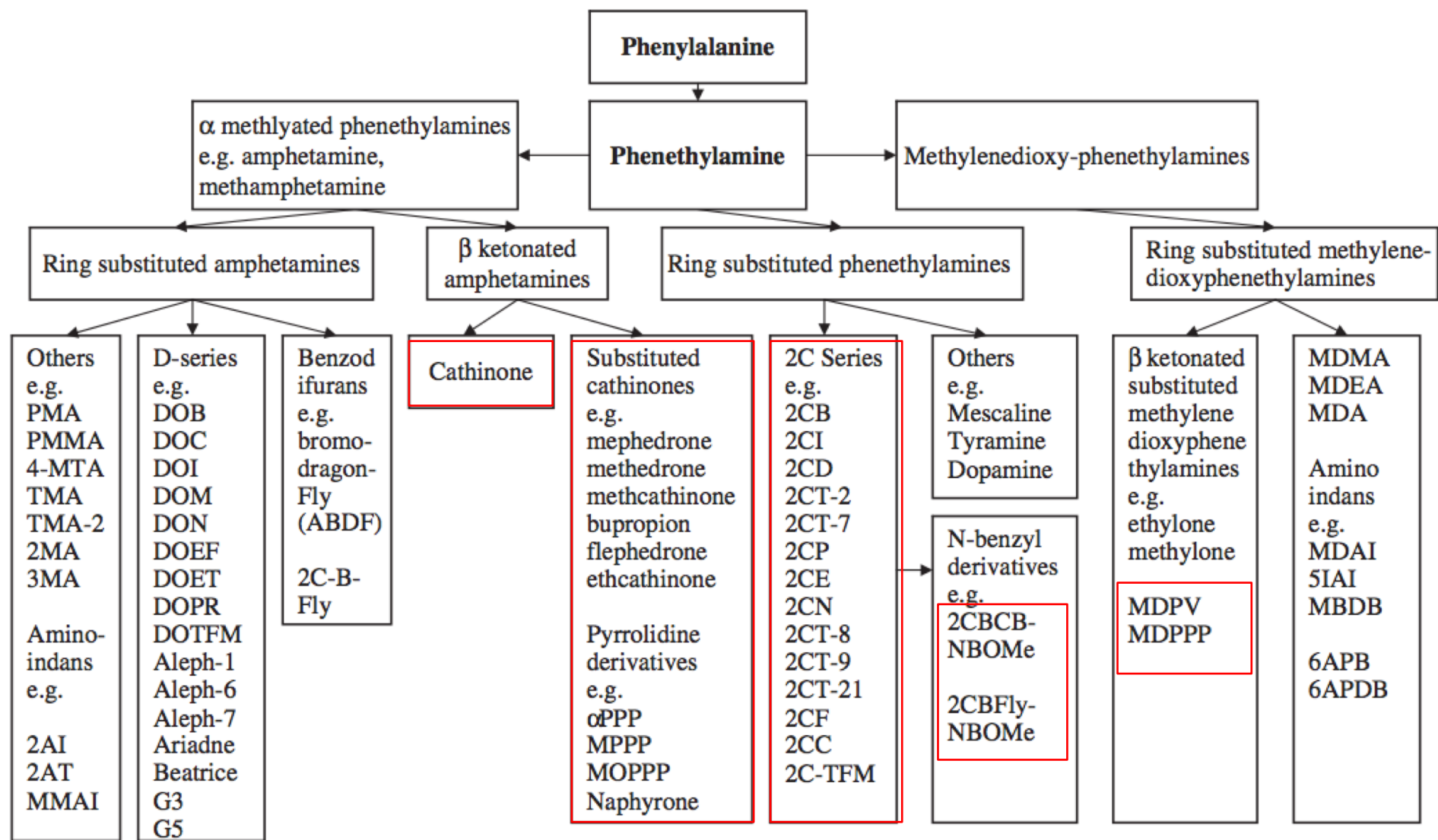
- Hyperadrenerg: **'fight or flight'** mode
- Versnelde hartslag (tachycardie)
- Verhoogde bloeddruk (hypertensie)
- Verhoogde temperatuur (hyperthermie)
- Vergrootte pupillen (mydriasis)
- Toegenomen reflexen (hyperreflexie)
- Zweeten
- Drukke spraak, 'flight of ideas', paranoia
- Bruxism, tremor

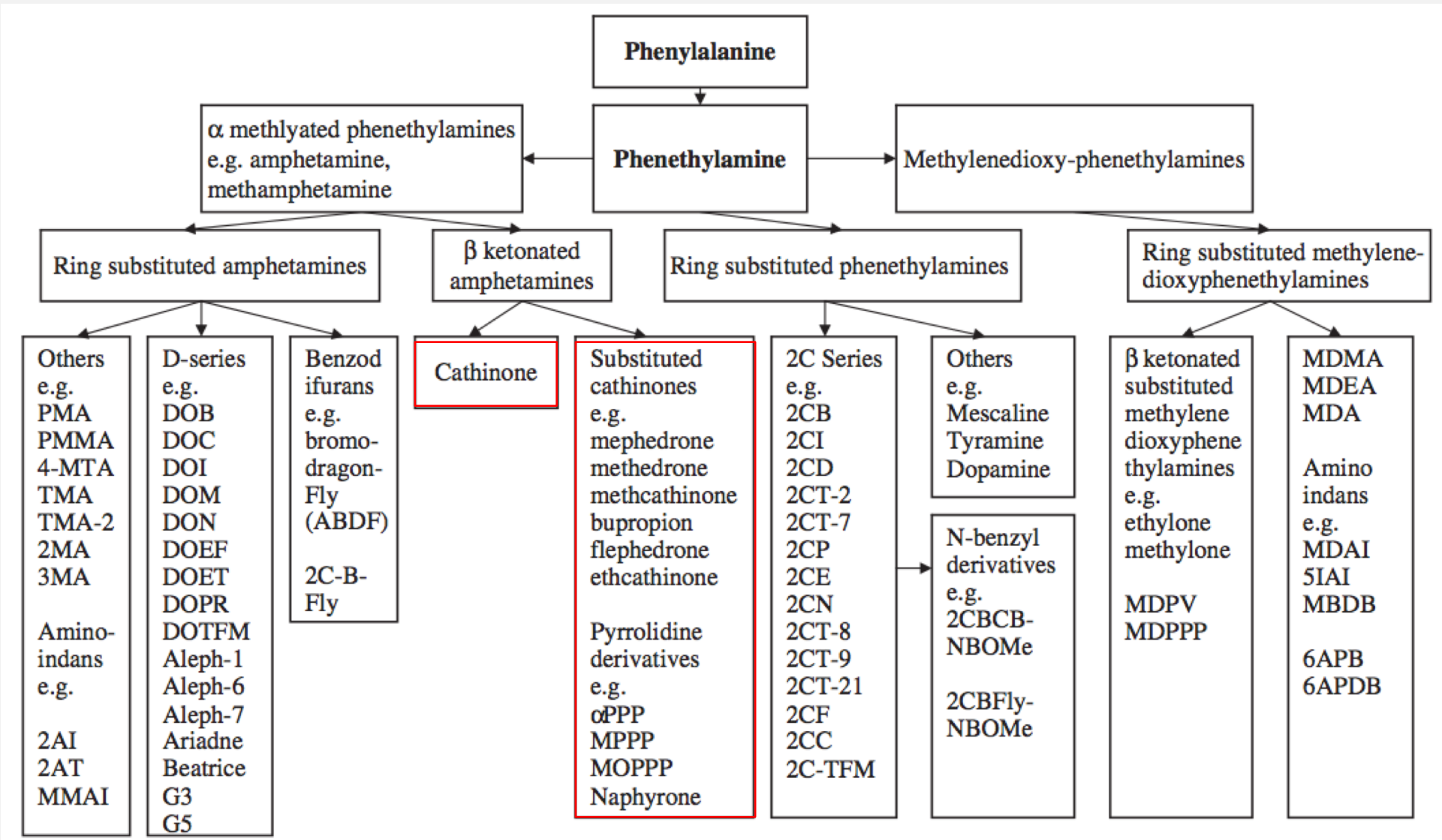
Sympathomimetic Toxidrome



SYMPATHOMIMETISCH TOXICODROOM

- Amphetamines
- MDMA
- Speed
- Cocaine
- Epinephrine
- Methylphenidate (Rilatine)
- MAO-I
- Cathinones 'Bath salts'



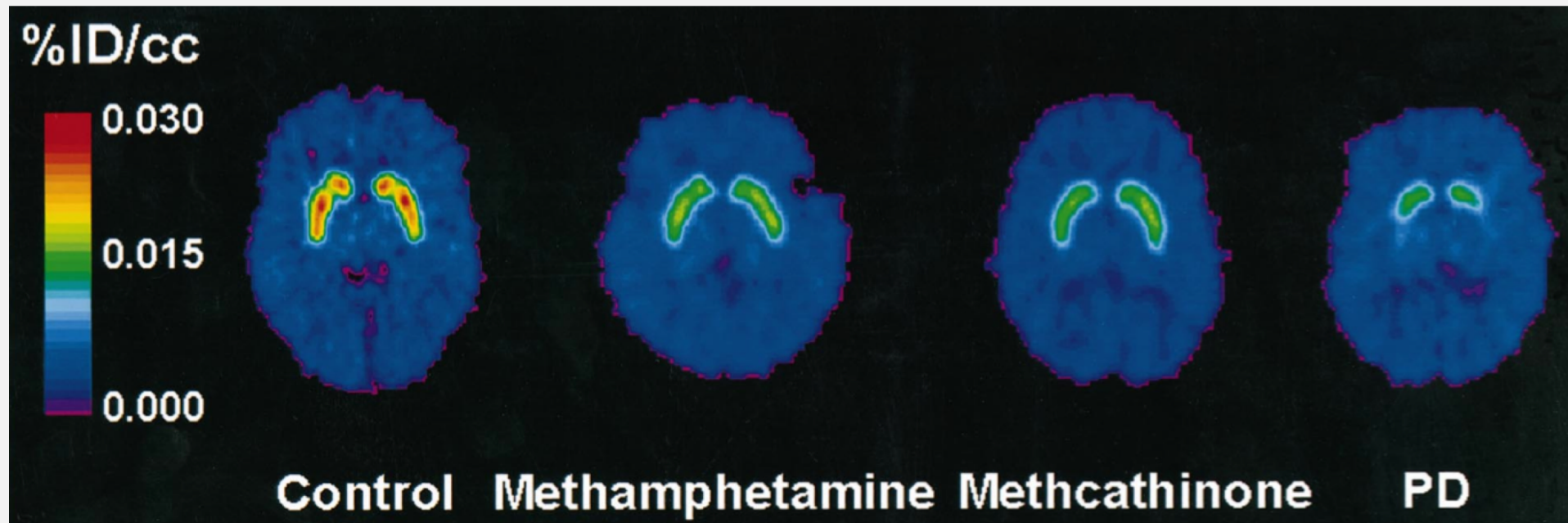


SYNTHETIC CATHINONES

- First detected in 2008
- Stimulant drug
- Ring-substituted phenylethylamines with a substitution of a ketone group at the β -carbon position
 - different R-group substitutions = a large list of synthetic cathinones,
 - many of them are identical except for the β -carbon
- Very little knowledge about the pharmacokinetics and pharmacodynamics
- Act on the central nervous system
 - promoting release of monoamine neurotransmitters
 - most likely inhibit their reuptake

Reduced Striatal Dopamine Transporter Density in Abstinent Methamphetamine and Methcathinone Users: Evidence from Positron Emission Tomography Studies with [^{11}C]WIN-35,428

Una D. McCann,¹ Dean F. Wong,² Fuji Yokoi,² Victor Villemagne,² Robert F. Dannals,² and George A. Ricaurte³



MEPHEDRONE

- MCAT, meow meow, 4-MMC, meph
- Bijna een klassieke drug in bepaalde landen
- Meestal in poedervorm (ook tabletten)
- Nasaal (70%) / oraal (30%) / rapportering van IV gebruik
- Zeer verslavend
- Stimulerend effect
- Vasoconstrictief
- Uitgesproken agitatie / agressie
- Hyponatremie with encephalopathie

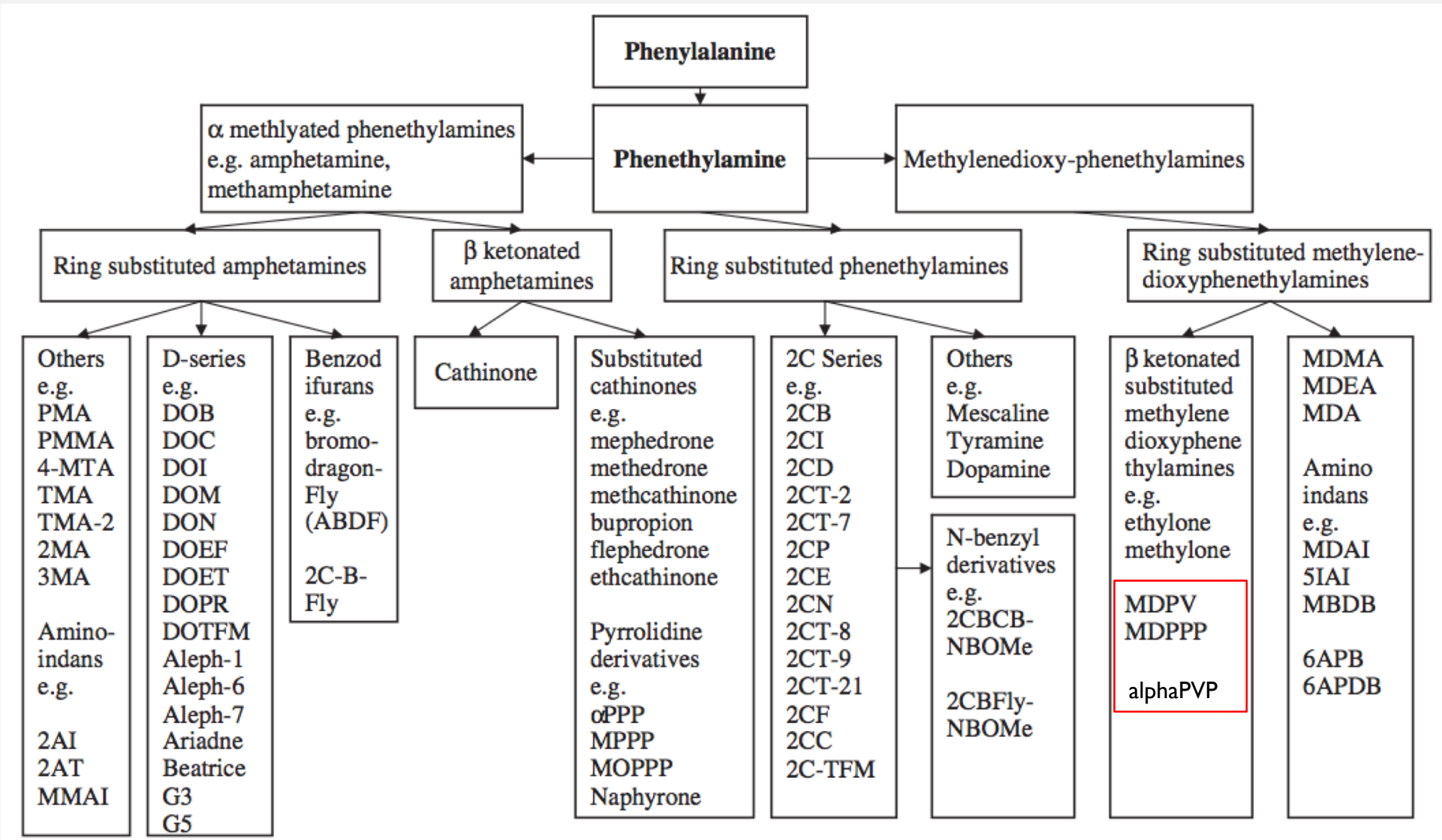
OVER 18'S ONLY **MCAT** OVER 18'S ONLY
(99.9% Pure Mephedrone)
Plant Extract - Research Chemical
PROBABLY THE BEST PLANT FOOD IN THE WORLD

1 Gram =	£15
2 Grams =	£25
3 Grams =	£35
4 Grams =	£45
5 Grams =	£55

HURRY WHILE STOCKS LAST!!!

For bulk orders of 100 grams or more please ask!

The advertisement features a pink background with a white polka-dot pattern. A central photograph shows a pile of white, crystalline powder on a dark surface. A blue banner with white text is positioned at the bottom right of the ad.



MDPV

Norepinephrine-dopamine reuptake inhibitor

Extreme stimulatie met euforie, disinhibitie en sexuele opwinding

Dwangmatig gebruik

Vals positieve resultaten voor PCP





ALPHA-PVP

- Flakka / zombie drug / \$5 insanity
- Norepinephrine-dopamine reuptake inhibitor
- Sterke stimulerende drug: agitatie, paranoia en hallucinaties
- Sexuele opwinding
- Oraal, intranasaal, verstuiven, intraveneus, rectaal, sublinguaal

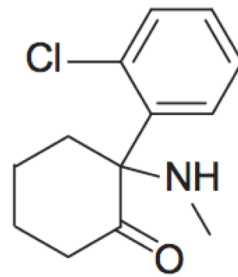
PIPADROL & DERIVATIVES

- Example of rediscovered 'failed' pharmaceuticals
 - e.g. pipradrol was marketed in '50s as an antidepressant
- Limited published literature
- User reports describe CNS stimulant effects
- Long duration of action with prolonged neuropsychiatric symptoms
- Oral route, nasal insufflation, rectal use
- No published studies on abuse and dependency potential

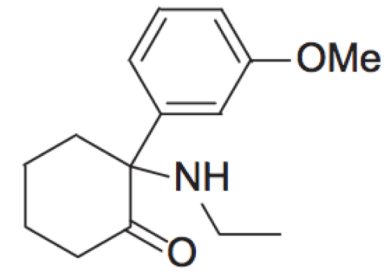
TRYPTAMINES

- Hallucinogenic effects produced predominantly through agonism at 5HT_{2A} receptors
- Some exhibit stimulant activity resulting in agitation, tachyarrhythmias, hyperpyrexia and death
- Oral route, smoking, nasal insufflation, (iv)
- Ayahuasca = South American brew made from plants and containing DMT + MAO inhibitors
- Current data suggest low potential for dependence

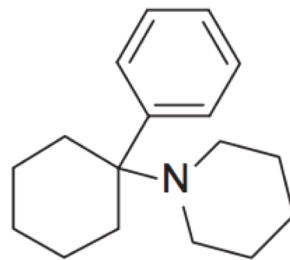
KETAMINE & ANALOGUES



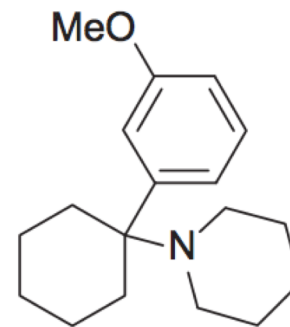
Ketamine



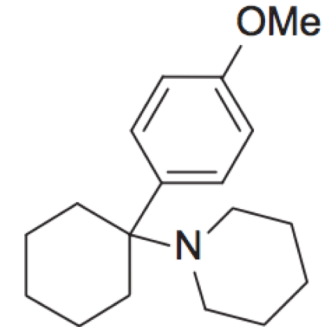
Methoxetamine



PCP-phencyclidine



3-MeO-PCP



4-MeO-PCP

DRUGS OF ABUSE (DOA) SCREENING

- Ketamine:
 - Dissociatief anaestheticum, vnl. voor veterinair gebruik
 - Phencyclidine (PCP) analoog
 - Kleurloze, geurloze vloeistof of poeder (DFSA)
 - Gebruik als recreatieve drug: zeer snel effect, “out of body” ervaring, “superhuman strength” zonder pijnperceptie ↔ ataxie, agitatie, angst, paranoia, delirium, hallucinatie
 - Screening met immunoassays: gevoeligheid ontoereikend (vnl. POCT), interferentie met quetiapine
 - UZ Gent: ketamine, norketamine en dehydronorketamine in urine en serum met LC-HR-MS

KETAMINE & ANALOGUES

[BMJ Case Rep.](#) 2012 Sep 30;2012. pii: bcr2012006447. doi: 10.1136/bcr-2012-006447.

Ketamine bladder syndrome: an important differential diagnosis when assessing a patient with persistent lower urinary tract symptoms.

[Srirangam S¹](#), [Mercer J.](#)

Author information

1 Department of Urology, East Lancashire Hospitals NHS Trust, Blackburn, UK.

Abstract

The recreational use of ketamine is increasing in popularity due to its dissociative and paralytic effects, ease of availability and low cost. However, serious and frequently irreversible damage to the urinary tract is a recently recognised side effect of recreational ketamine use. The authors present a case of a young male patient with a 2-year history of troublesome lower urinary tract symptoms and a 5-year history of ketamine consumption. Medical management of such patients is largely limited to analgesia alone, and cessation of ketamine use before irreversible damage occurs remains the best means of avoiding the radical reconstructive surgery required in end-stage disease. This case and an accompanying review of the available literature illustrate the importance of early recognition of ketamine bladder syndrome in recreational users.

Three months of methoxetamine administration is associated with significant bladder and renal toxicity in mice.

Dargan PI¹, Tang HC, Liang W, Wood DM, Yew DT.

Author information

1 Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners , London , UK.

Abstract

CONTEXT.: Methoxetamine is a ketamine analogue that has recently emerged as a novel psychoactive substance. Chronic ketamine use is associated with significant bladder and renal toxicity. Methoxetamine has been marketed as "bladder friendly", but there is no data to be able to substantiate this claim.

OBJECTIVE: To characterise the patterns of bladder and renal toxicity associated with 3 months of methoxetamine administration in an animal model.

MATERIALS AND METHODS: Two-month-old Institute of Cancer Research mice were administered 30 mg/kg methoxetamine intraperitoneally (n = 5) or saline (n = 3 control) for 3 months. The animals were then sacrificed and histological examination, immunocytochemistry using polyclonal anti-CD4 antibodies and sirius-red staining for collagen were performed.

RESULTS: The kidneys of methoxetamine-treated animals showed inflammatory cell infiltration, tubular cell necrosis and glomerular damage ($1.9 \pm 0.3\%$ shrunken glomeruli in control, $9.8 \pm 0.8\%$ in methoxetamine-treated mice ($p < 0.0001$); $2.9 \pm 0.3\%$ tubular cell degeneration in control, $20.4 \pm 1.1\%$ in methoxetamine-treated mice ($p < 0.0001$)). There was a greater density of mononuclear cells in the bladder lamina propria and submucosa in methoxetamine-treated mice (43.0 ± 2.1 per $250 \times 250 \mu\text{m}$) than controls (7.1 ± 1.2 per $250 \times 250 \mu\text{m}$), $p < 0.001$. CD4-positive staining was seen in the bladder submucosa and lamina propria of all methoxetamine-treated mice and muscle-layer of two methoxetamine-treated mice; these changes were not seen in the control mice. There was an increase in sirius-red collagen in the bladder sub-mucosa and muscle-layer in the methoxetamine-treated mice compared with control mice.

DISCUSSION: This study has shown that 3 months of daily 30 mg/kg intra-peritoneal methoxetamine results in significant bladder and renal toxicity in mice. Changes in the bladder included inflammatory changes with subsequent fibrosis and changes in the kidney were seen at both a tubular and glomerular level. These changes are similar to those seen in comparable animal models of chronic ketamine administration. Further work is required to determine the time course of the onset of these effects and whether the effects are reversible with methoxetamine cessation.



Clinical Toxicology (2012), 50, 438–440
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DOI: 10.3109/15563650.2012.683437

informa
healthcare

BRIEF COMMUNICATION

Methoxetamine associated reversible cerebellar toxicity: Three cases with analytical confirmation

JENNIFER E. SHIELDS¹, PAUL I. DARGAN², DAVID M. WOOD², MALGORZATA PUCHNAREWICZ³,
SUSANNAH DAVIES³, and W. STEPHEN WARING¹

¹*Acute Medical Unit, York Teaching Hospital NHS Foundation Trust, York, UK*

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³*Analytical Services International Ltd., St. George's University of London, London, UK*



ANNUAL DEATHS

Tobacco	435,000
Poor Diet/Exercise	365,000
Alcohol	85,000
Prescription Drugs	32,000
Motor Vehicle Crashes	26,347
Homicide	20,308
Aspirin	7,600
Peanuts	100
Kratom	0



KRATOM: Safer Than Peanuts!



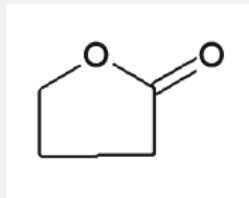
HERBALS

	Khat	Kratom	Salvia divinorum
Origin	Plant (horn of Africa, Arabian peninsula)	Tree (South-East Asia)	Plant (Mexico)
Use	Chewing leaves and shoots	Chewing or smoking leaves, powder swallowed or brewed in tea	Chewing or smoking leaves, drinkable infusion, inhaling vaporized extract
Constituents	Cathinone, cathine alkaloids	Many alkaloids incl. mitragynine	Salvinorin A
Effects	CNS stimulant	CNS stimulant, sedative at high doses	Intense hallucinations

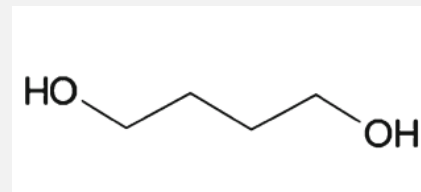
GHB, GBL EN 1,4-BD

- GHB, γ -hydroxyboterzuur
- Precursoren: γ -butyrolacton (GBL), 1-4-butaandiol (1,4-BD)
- Gesynthetiseerd in jaren '60 als structuuranaloog van neurotransmitter GABA
- Endogeen aanwezig als precursor en metaboliet van GABA
- Initieel gebruikt als anestheticum en spierversterkend middel, maar verlaten o.w.v. neveneffecten en misbruik
- Momenteel op markt voor behandeling van narcolepsie met cataplexie (Xyrem[®])
- GHB, GBL en 1,4-BD populair als partydrug o.w.v. stimulerend effect ('liquid ecstasy')

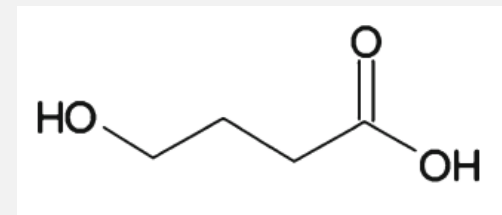
GBL



1,4-BD



GHB



GHB, GBL EN 1,4-BD

- populair als partydrug o.w.v. stimulerend effect ('liquid ecstasy')
- Kleurloze vloeistof
- Effect afhankelijk van dosis: van euforie en relaxatie tot sedatie, coma en amnesie -> DFSA

- Screening: enzymatische assays (interferentie door ethanol)
- Confirmatie: GC/MS (of LC/MS)

- Snelle metabolisatie (plasma $T_{1/2} < 1u$), kort detectievenster
- Differentiatie tussen endogeen aanwezig en exogeen toegediend GHB: cut-off in bloed (5 mg/L) en urine (6 mg/L)

BEHANDELING

- Meestal geen specifieke behandeling of antidota (excl. opioïden)
- Behandeling gebaseerd op symptomen: supportieve zorgen
- ABC aanpak
- Benzodiazepines = eerstelijnsbehandeling in alle geagiteerde, derierende, stuipende en/of hypertherme patiënten
- Toxin-geïnduceerde hyperthermie = actieve en agressieve koeling
- Psychosociale zorg!

DIAGNOSTIEK

- Labo

- Nierfunctie alle NPS
- CK's alle NPS
- Leverfunctie alle NPS
- Troponine ECG afwijkingen

SCRA en cathinones: overweeg

- ECG

- SCRA en cathinones

- RX thorax

- Sedativa vermoeden aspiratie

- CT hersenen

- Bij focale neurologie: protocol CVA (vasospastisch)
- Exclusie trauma capitis: à blanc

DIAGNOSTIEK

- New Psychoactive Substances (NPS)
 - Uitdagingen voor laboratoriumdiagnostiek:
 - Beperkte kennis over chemische structuur en metabolisatie/PK
 - Geen (synthetische cannabinoïden, fentanylanalogen) of beperkte (synthetische cathinones) kruisreactiviteit met bestaande immunoassays voor klassieke DOA
 - Immunoassays ontwikkeld/in ontwikkeling voor specifieke NPS, research only
 - Lage concentraties en snel metabolisme: GC-MS screening onvoldoende gevoelig
 - Niet opgepikt met targeted LC-MS screening als bibliotheek niet up-to-date is
 - LC-HR-MS

SAMENVATTING

- Toenemend aantal NPS
 - Voornamelijk synthetische cannabinoïden
 - Beperkte kennis over hun gebruik en risico's
 - Moeilijk om bij te blijven
- Gevaar van nieuwe sterke opioïden
- Acute toxiciteit lijkt gelijkaardig aan de 'klassieke' drugs
 - Maar 'toegevoegde' onverwachte eigenschappen
 - Management is waarschijnlijk gelijkaardig aan de op heden gebruikte behandelingen

MOTIEVEN VOOR GEBRUIK

- Verminderde beschikbaarheid van klassieke drugs
- competitieve prijzen
- Moeilijk te detecteren in routine drugsscreening
- legal status in vele landen
- specifieke kwaliteiten van bepaalde NPS

DRUGS OF ABUSE (DOA) SCREENING

- Meestal immunoassays, ook enzymatische testen (GHB)
- Specifieke drugs of metabolieten: cocaïne, THC, GHB, LSD, methadon
- Groepen van drugs: amfetamines, opiaten, benzodiazepines, barbituraten
- (Semi-)automatisatie of POCT:



DRUGS OF ABUSE (DOA) SCREENING

- Indicaties voor aanvragen van DOA screening:
 - Diagnose van onverklaard coma
 - Ondersteuning bij bevestiging van hersendood en beoordeling van mogelijkheid tot orgaandonatie
 - Documentatie van eerder druggebruik
 - Medicolegale of forensische context
- Zelden urgent
- Vanuit klinisch standpunt onnodig ter confirmatie van gekende intoxicatie bij asymptomatische patiënt

DRUGS OF ABUSE (DOA) SCREENING

- Kennis van eigenschappen en beperkingen van DOA screening is essentieel voor adequate interpretatie:

- Kennis van gehanteerde cut-offs
- Detectietijden in urine en bloed:

Moeller *et al.*, Mayo Clin Proc, 2017

Drug	Bloed	Urine
Amfetamine	12u	48u
Barbituraten	1-7d	1-21d
Benzodiazepine	6-48u	3-30d
Cocaine	24u	2-4d
Cannabinoïden	2-14d	3- >30d
Morfine/codeïne	12u	48u
Heroïne	6u	48u
Methadon	24u	3d
GHB	<6u	<12u

DRUGS OF ABUSE (DOA) SCREENING

- Kennis van eigenschappen en beperkingen van DOA screening is essentieel voor adequate interpretatie:
 - Kennis van gehanteerde cutoffs:
 - Concentratie waarbij screeningsresultaat als positief beschouwd wordt en confirmatietest volgt
 - Dikwijls opgesteld in context van workplace drug testing: vals positieven vermijden, hogere cutoff
 - Klinische context: cutoff ev. verlagen om vals negatieven te vermijden
 - Cutoffs bepaald voor volwassen populatie, bij kinderen cutoff ev. door sterker verdunde urine

DRUGS OF ABUSE (DOA) SCREENING

- Kennis van eigenschappen en beperkingen van DOA screening is essentieel voor adequate interpretatie:
 - Kennis van gehanteerde cut-offs
 - Detectietijden in urine en bloed
 - Kruisreactiviteiten
 - Mate waarin een component (geneesmiddel, drug, metaboliet, endogene molecule) een signaal kan genereren in een assay
 - Immunoassays: uitgedrukt als de equivalente concentratie van de component die eenzelfde signaal genereert als de target van de assay bij de cut-off (of als % kruisreactiviteit vergeleken met een standaardcomponent)
 - Verschillen tussen assays van verschillende producenten
 - Inconsistente en onvolledige documentatie in bijsluiters

TABLE 4. Summary of Agents Contributing to Results by Immunoassay^a

Substance	Potential positives (includes true- and false-positives)	Potential medications that may not be detected
Alcohol ^{2,4}	Short-chain alcohols (eg, isopropyl alcohol)	Not applicable
Amphetamines ²⁵⁻⁵⁰	l-Methamphetamine (Vick's inhaler) ^b l-Deprenyl ^f Amantadine Aripiprazole Atomoxetine Benzphetamine Bupropion Clobenzorex ^d Chlorpromazine Desipramine Dextroamphetamine Dimethylamylamine Ephedrine Fenproporex ^d Isometheptene Isoxsuprine Labetalol Metformin Methylphenidate Methamphetamine MDMA Phentemine Promethazine Pseudoephedrine Phenylephrine Phenylpropanolamine Ranitidine Ritodrine Selegiline Thioridazine Trazodone Trimipramine Trimethobenzamide	Not applicable
Benzodiazepines ⁵¹⁻⁵⁹	Efavirenz Oxaprozin Sertraline	Alprazolam Clonazepam Lorazepam
Cannabinoids ^{17,60-70}	Baby wash products Dronabinol Efavirenz NSAIDs Proton pump inhibitors	Nabilone Synthetic cannabinoids
Cocaine ⁷¹⁻⁷³	Coca leaf tea Topical anesthetics containing cocaine	Not applicable

TABLE 4. Summary of Agents Contributing to Results by Immunoassay^a

Substance	Potential positives (includes true- and false-positives)	Potential medications that may not be detected
Opioids/opiates/heroin ^{17,18,74,90}	Dextromethorphan Diphenhydramine ^e Doxylamine ^e Heroin Opiates (codeine, hydromorphone, hydrocodone, morphine) Poppy seeds Quinine Quinolones Rifampin Verapamil and metabolites ^e	Buprenorphine Fentanyl Meperidine Methadone Oxycodone Oxymorphone Tramadol
Phencyclidine ^{17,74,91-100}	Dextromethorphan Diphenhydramine Doxylamine Ibuprofen Imipramine Ketamine Lamotrigine MDPV Meperidine Mesonidazine Thioridazine Tramadol Venlafaxine, O-desmethylvenlafaxine	Not applicable
Tricyclic antidepressants ¹⁰¹⁻¹¹¹	Carbamazepine ^f Cyclobenzaprine Cyproheptadine ^f Diphenhydramine ^f Hydroxyzine ^f Quetiapine	Not applicable
Synthetic cannabinoids ¹¹²	Lamotrigine	Not applicable

DRUGS OF ABUSE (DOA) SCREENING

- Vervalste medicatie:

Case



www.saferparty.ch

Xanax®



Vorsicht: Falschdeklarierte Xanax-Tablette

Logo	XANAX
Gewicht	173.9 mg
Grösse	15.5 x 3.6 mm
Dicke	3.6 mm
Bruchrille	ja
Farbe	weiss
Inhaltsstoffe	Flualprazolam: Qual. Cyproheptadin: Qual. Zwei Unbekannte
Getestet in	Zürich (DIZ), 01. März 2019



DRUGS OF ABUSE (DOA) SCREENING

- Weerspiegelt niet de publieke indruk
- Spiking met sedativa of recreatieve drugs is zeldzaam maar niet onbestaand
- Meestal veel hogere ethanolemie dan verwacht via anamnese

- Greene et al. (Londen):
 - Ethyl in 89.7% van de gevallen (mean 1.65, range 0.04-3.1g/L) - 60% klinisch significante ethanolemie (>1.5g/L)
 - Recreativele drugs in 12 pt (15%), waarvan 7 ontkend
 - Medicatie in 13 pt, slechts 1 onverklaard

DRUGS OF ABUSE (DOA) SCREENING

- De wet van 7 februari [2014](#) voegt de verplichting voor alle Belgische laboratoria toe om de analyseresultaten op een automatische wijze door te sturen naar het BEWSD, zelfs indien deze deel uitmaken van een gerechtelijk onderzoek.
- ZN stuurt BEWSD vervolgens een '[alert](#)' door naar het professionele netwerk.
- Dit netwerk bestaat uit alle laboratoria uit België maar ook hulp – en spoeddiensten, politie en parket, drughulpverlening, etc.
- Specifieke databank dat elektronisch toegankelijk is voor geregistreerde experts.
- Op basis van deze informatie rapporteert het BEWSD jaarlijks over de zuiverheid van de verschillende illegale drugs, drug-intoxicaties en eventuele overlijdens die gelinkt kunnen worden aan het gebruik van drugs.
- Deze informatie heeft als doel het drugsbeleid in ons land te sturen. Bovendien wordt het gedeeld met internationale partners, waaronder [EMCDDA](#), [Europol](#) en [UNODC](#).