

AGORA' PENITENZIARIA 2016
XVII Congresso Nazionale SIMSPe-ONLUS

DIAGNOSI E GESTIONE DELLE DIPENDENZE IN AMBITO PENITENZIARIO:
«EFFETTO PSICOTROPO DI VECCHIE E NUOVE SOSTANZE DI ABUSO
E POSSIBILI INTERAZIONI FARMACOLOGICHE»

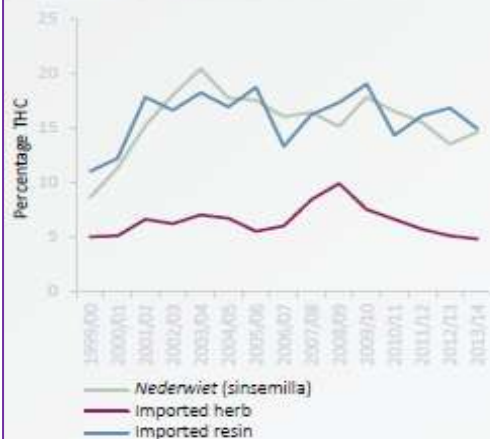
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VECCHIE E NUOVE SOSTANZE DI ABUSO...

UNODC, World Drug Report 2015: «IS CANNABIS BECOMING MORE HARMFUL?»

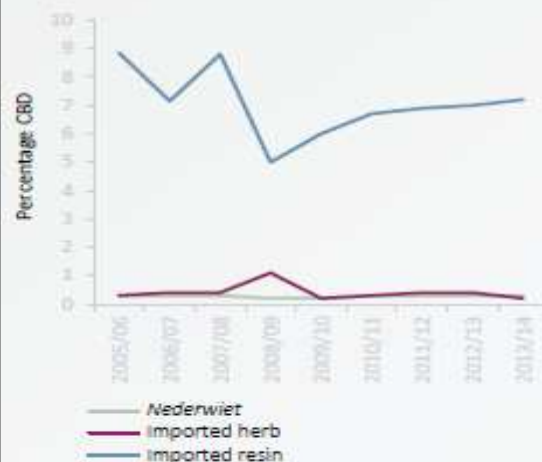
«Vecchie» sostanze

Trends in mean potency (percentage of THC) of cannabis products sold in "coffee shops" in the Netherlands, 1999-2014



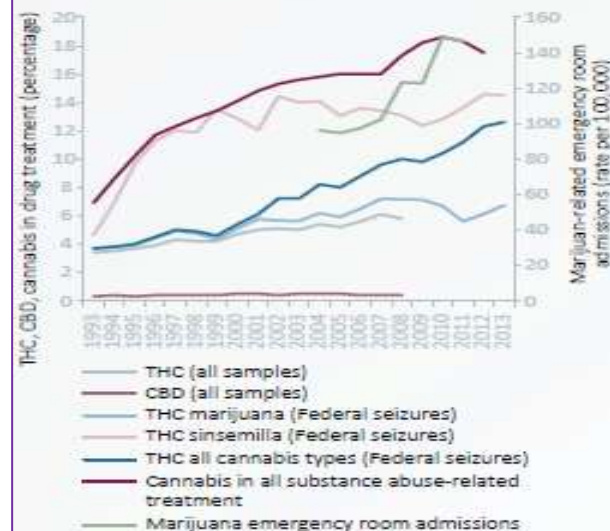
Source: Trimbos Institute.

Trends in median CBD content of cannabis products sold in "coffee shops" in the Netherlands, 2005-2014



Source: Trimbos Institute.

THC and CBD content in cannabis samples, cannabis-treatment admissions and marijuana-related hospital emergencies, United States, 1993-2013



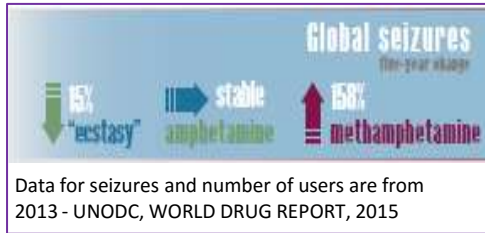
Sources: Z. Mehmedic and others, "Potency trends of Δ^9 -THC and other cannabinoids"; and SAMHSA.

(In Australia) «...The shift towards increasing use of cannabis with **high THC and low CBD** content has also been linked to an increase in drug treatment demand and in the risk of cannabis dependence and vulnerability to psychosis, but there is little evidence of the direct impact of potency»

(Swift et al., 2013; UNODC, 2015)

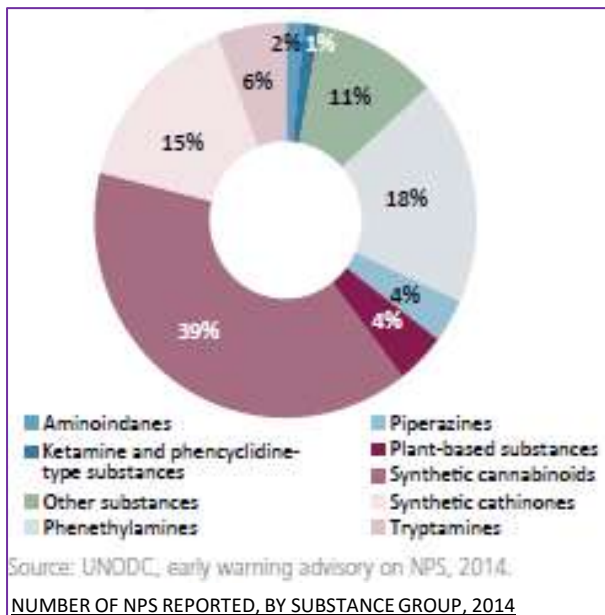
UNODC, World Drug Report 2015: «**ATS** Amphetamine-Type Stimulants and **NPS** New Psychoactive Substances: **SYNTETIC DRUGS** »

«Nuove» sostanze



ATS = gruppo di psicostimolanti sinteticamente derivati, i cui principali composti sono amfetamine e metamfetamine ma anche methcathinone (o kat o efedrone, prodotta da efedrina e pseudoefedrina), fenetillina, efedrina, pseudoefedrina, metilfenidato, MDMA or 'Ecstasy' (WHO) – ecstasi fu sintetizzata nel 1912

Nel 2014: globalmente gli ATS sono stati il secondo gruppo di sostanze usate dopo i cannabinoidi (Illicit Drug data Report 2014-15)



NPS = 'a new narcotic or psychotropic drug, in pure form or in preparation non controllato dalla United Nations Single Convention on Narcotic Drugs del 1961 o dalla United Nations Convention on Psychotropic Substances del 1971 ma che pone una minaccia pubblica comparabile a quella posta dalle sostanze elencate in queste Convenzioni' – queste sostanze sono psicoattive nel senso che stimolano o deprimono il SNC (Council Decision 2005/387/JHA)" – EMCDDA, 2016.

Al dicembre 2014: 541 sostanze disponibili sul mercato classificate come NPS da UNODC – gruppo più rappresentato: Cannabinoidi Sintetici (dalla scoperta dei recettori CB1 e CB2, anni 80, c'è stata una continua evoluzione della famiglia dei CS, la loro crescita sul mercato si è caratterizzata per l'introduzione di successive continue modificazioni strutturali - the **transient nature** of the NPS + the **challenge of diversity**) – UNODC, WORLD DRUG REPORT, 2015

TUTTO IL RESTO E' NUOVO !!

MERCATO

?

VENDITA

ACQUISTI

USO



...EFFETTO PSICOTROPO...

❖ THE PROXIMAL MECHANISMS OF DRUGS EFFECTS →

Drug	Primary (proximal) target	Brain effects
Alcohol	Agonist at GABA and antagonist at glutamate receptors	Increases GABA Blocks NMDA glutamate receptors
Benzodiazepines	Agonists at benzodiazepine site on GABA-A receptor	Increase GABA
GHB	GHB and GABA-B receptor agonist	Mimics GABA Inhibits dopamine release
Ketamine	NMDA glutamate receptor antagonist	Blocks glutamate
Caffeine	Antagonist at adenosine A2 receptor	Reduces sedation Increases noradrenaline
Khat	Releases ephedrine, a dopamine releaser	Mild increase in noradrenaline and dopamine
Cannabis	Cannabis CB1 receptor agonist	Stimulates endo-cannabinoid signalling, leading to a change in cortical and memory functions
Cocaine	Blocks dopamine reuptake site	Greatly increases dopamine
Amphetamines (dexamphetamine and methyl)	Release dopamine and block reuptake	Greatly increase dopamine and noradrenaline
Nicotine	Agonist at (nicotinic) acetylcholine receptors	Slightly increases dopamine
MDMA	Blocks serotonin and dopamine reuptake	Increases serotonin and dopamine function
Mephedrone	Release dopamine and block reuptake	Increase dopamine, and serotonin
Hallucinogens	Agonists at serotonin 5-HT _{2A} receptors	Change across-cortex signalling
Heroin and other opioids	Agonists at endorphin receptors	Produce euphoria, reduce pain

Agonist = drug that activates or stimulates a receptor; Antagonist = drug that blocks a receptor.

(NEPTUNE, 2015)

CANNABINOIDI SINTETICI: «sostanze con strutture chimiche differenti, agonisti di CB1 E CB2 ad alta affinità (il THC è un agonista parziale di CB1 e CB2 ma il THC high è associato al legame CB1 e gli effetti del THC sono modulati da altri composti naturali es. cannabidiolo e cannabivarina), sostanze con strutture chimiche differenti che spesso interagiscono con recettori diversi dai CB - Schifano et al., 2016

«Sebbene gli effetti di *AMFETAMINA* e *METAMFETAMINA* siano molto simili, la metamfetamina è resa molto più potente dalla sua struttura chimica» - Illicit Drug Report 2014-15

«La molecola della *METAMFETAMINA* è strutturalmente simile a quella della *AMFETAMINA* e del neurotrasmettitore DA ma è molto diversa da quella della *COCAINA* – questi stimolanti hanno simili effetti comportamentali e psicologici ma sono evidenti importanti differenze nei meccanismi di base del loro funzionamento» - N.I. on Drug Abuse, 2013

«I singoli *CATINONI* hanno effetti e livelli di potenza diversi sui circuiti DA, NE, 5HT - Schifano et al., 2016



...EFFETTI DESIDERATI vs
EFFETTI AVVERSI...

...EFFETTI A BREVE TERMINE vs
EFFETTI A LUNGO TERMINE...

Le sostanze possono essere classificate secondo criteri differenti, in base alla struttura chimica, all'attività farmacologica e agli effetti psicologici – una possibilità è quella di valutare gli effetti di una sostanza lungo la **dimensione SEDAZIONE/STIMOLAZIONE** e lungo la **dimensione ALTERAZIONI DELLA PERCEZIONE SI'/NO**

Neurotoxicity of Synthetic Cannabinoids JWH-081 and JWH-210

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Forensic Science International 260 (2016) 91–98

Contents lists available at ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forensic

Synthetic cannabinoid drug use as a cause or contributory cause of death

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ARTICLE INFO

Article history:
Received 15 September 2015
Received in revised form 17 December 2015
Accepted 20 December 2015
Available online 7 January 2016

Keywords:
Synthetic cannabinoids
Intoxication
Toxicology
Cause and manner of death

ABSTRACT

Adverse effects associated with synthetic cannabinoid use include agitation, psychosis, seizures and cardiovascular effects, all which may result in a lethal outcome. We report the collection of data from 25 medical examiner and coroner cases where the presence of synthetic cannabinoids was analytically determined. Participating offices provided case history, investigative and relevant autopsy findings and toxicology results along with the cause and manner of death determination. This information, with the agency and cause and manner of death determinations blinded, was sent to participants. Participants offered their opinions regarding the likely contribution of the toxicology findings to cause and manner of death. The results show that some deaths are being attributed to synthetic cannabinoids, with the highest risk areas being behavioral toxicity resulting in excited delirium, trauma or accidents and as contributing factors in subjects with pre-existing cardiopulmonary disease. While insufficient information exists to correlate blood synthetic cannabinoid concentrations to effect, in the absence of other reasonable causes, the drugs should be considered as a cause or contributory cause of death based on history and circumstances with supporting toxicological data.

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Case Series of Synthetic Cannabinoid Intoxication from One Toxicology Center

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Section Editor: Rick A. McPherson, DO

Submission history: Submitted December 17, 2015; Accepted February 22, 2016

Electronically published April 26, 2016

Full text available through open access at http://es.cholomship.org/uc/uciem_westjem

DOI: 10.5811/westjem.2016.2.29519

Synthetic cannabinoid use has risen at alarming rates. This case series describes 11 patients exposed to the synthetic cannabinoid, MAB-CHMINACA who presented to an emergency department with life-threatening toxicity including obtundation, severe agitation, seizures and death. All patients required sedatives for agitation, nine required endotracheal intubation, three experienced seizures, and one developed hyperthermia. One developed anoxic brain injury, rhabdomyolysis and died. A significant number were pediatric patients. The mainstay of treatment was aggressive sedation and respiratory support. Synthetic cannabinoids pose a major public health risk. Emergency physicians must be aware of their clinical presentation, diagnosis and treatment. [West J Emerg Med. 2016;17(3):290–294.]

Table 2 User reported clinical effects of synthetic cathinones [17, 25, 28, 30, 62]

(Prosser et al., J Med Toxicol 8:33-42, 2012)

Cardiovascular	Palpitations, shortness of breath, chest pain
ENT	Dry mouth, epistaxis, nasal pain, "nose burns", oropharyngeal pain, tinnitus
Gastrointestinal	Abdominal pain, anorexia, nausea, vomiting
Genitourinary	Anorgasmia, erectile dysfunction, increased libido
Musculoskeletal	Arthralgias, extremity changes—coldness, discoloration, numbness, tingling, muscular tension and cramping
Neurologic	Aggressiveness, bruxism, dizziness, headache, lightheadness, memory loss, tremor, seizures
Ophthalmologic	Blurred vision, mydriasis, nystagmus
Pulmonary	Shortness of breath
Psychological	Anger, anxiety, auditory and visual hallucinations, depression, dysphoria, empathy, euphoria, fatigue, formication, increased energy, increased and decreased concentration, loquaciousness, panic, paranoia, perceptual distortions, restlessness
Other	Body odor "mephedrone stink", diaphoresis, fever, insomnia, nightmares, skin rash

These are self-reported symptoms by users of synthetic cathinones. It is possible that these effects are not all related to cathinone use as many users take these substances simultaneously with other drugs and ethanol. Additionally due to lack of reliability and consistency of products, users may not be aware of what drug they have actually taken. Please see text for more information

Amphetamine-Type Central Nervous System Stimulants Release Norepinephrine More Potently Than They Release Dopamine and Serotonin

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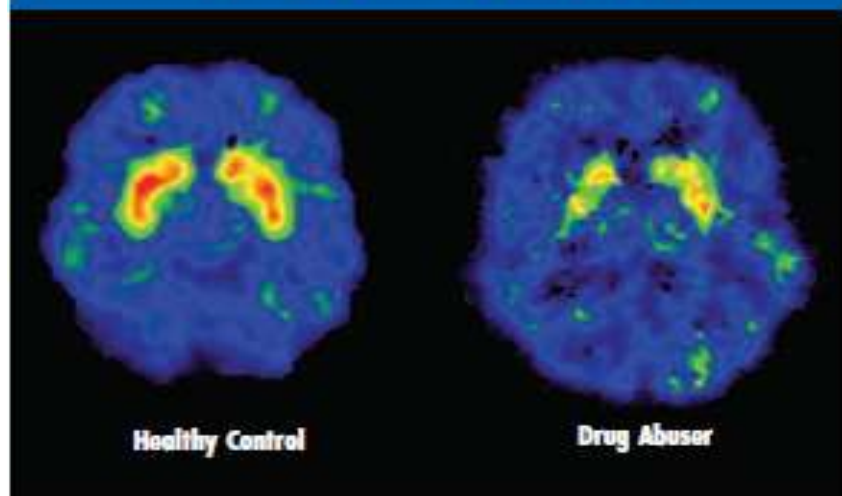
Performance enhancement at the cost of potential brain plasticity: neural ramifications of nootropic drugs in the healthy developing brain

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DECREASED DOPAMINE TRANSPORTERS IN A METHAMPHETAMINE ABUSER^{1B}



NATIONAL INSTITUTE ON DRUG ABUSE – NIH Pub. No. 14-5605 Printed April 2007, Revised February 2008, August 2010, July 2014

Neuropsychopharmacology (2012) 37, 1081–1082
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 www.neuropsychopharmacology.org

Commentary

What Matters in Measuring Methamphetamine-Related Cognitive Impairments: 'Abnormality Detection' Versus 'Everyday Import'?

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Neuropsychopharmacology (2012) 37, 1081–1082; doi:10.1038/npp.2011.309

...INTERAZIONI FARMACOLOGICHE E CURA.....

- Gli abusatori possono presentarsi ai servizi di **PRONTO SOCCORSO** senza fornire (sufficienti) informazioni rispetto alle sostanze assunte
- E' facile che i test standard utilizzati per i dosaggi risultino negativi
- E' *impossibile disporre di linee di indirizzo* per il trattamento dei sintomi (dist. del comportamento e psicologici) correlati con l'assunzione delle alcune centinaia di sostanze oggi disponibili

- *Soggetti con patologie* cardiologiche, neurologiche e psichiatriche, soprattutto se in terapia, sono a rischio severo di effetti avversi - l'uso di stimolanti può correlarsi ad ischemia coronarica da trattarsi secondo gli schemi tradizionali (i betabloccanti sono controindicati perchè potrebbero aggravare i sintomi, spt la vasocostrizione e l'ipertensione)
- Talora le condizioni cliniche hanno *carattere di emergenza/urgenza* e possono essere necessari sedazione profonda e ventilazione assistita
- L'ipertermia va trattata come urgenza (grave rischio di rhabdomiolisi)

- I pz con sintomi meno severi dovrebbero essere valutati e trattati come per i sintomi legati a qualunque altra sostanza di abuso e possono beneficiare anche solo di interventi supportivi
- Data la complessa e sconosciuta farmacologia delle sostanze eventualmente assunte e le frequenti associazioni, *quando sia necessario un trattamento farmacologico* le benzodiazepine sono la 1 scelta spt per l'agitazione correlata all'uso di stimolanti e di catinoni sintetici (spesso sono necessarie somministrazioni successive e questo è un problema nel caso di assunzione di alcool) - le benzodiazepine anche riducono il rischio di episodi epilettici
- Quando le benzodiazepine non siano sufficienti, sono indicati il propofol e/o gli antipsicotici (sebbene alogperidolo, olanzapina, ziprasidone possano abbassino la soglia epilettica, limitino lo sfiebramento e contribuiscano alle disritmie)

- Intervento clinico *per lo più sintomatico*
- Necessario monitoraggio stretto per le molte eccezioni legate anche alla nostra scarsa conoscenza delle sostanze – es. sindrome serotoninergica – es. tossicità cerebellare da methoxetamina – es. danno renale acuto da cannabinoidi sintetici – es. infarto ischemico da cannabinoidi sintetici
- Quando possibile rivolgersi al Centro Antiveleni!

