ADDICTION E SALUTE MENTALE NELLA POPOLAZIONE
DAI 16 AI 25 ANNI
17 Dicembre 2019
OPI Brescia

NPS e Dipendenze Comportamentali

Chi aiuta gli operatori sanitari?

Pierluigi Simonato, MD, PhD, Psychiatrist

University of Hertfordhire (UK)
Casa di Cura Parco dei Tigli (Italy)

Background

The Dual Diagnosis Problem: a network

Dual Diagnosis Unit

- Dr. Gloria Pessa; Dr. Davide Mioni; Dr. Pierluigi Simonato
- Dr. Laura Bulsis; Dr. Angelica Cucco; Dr. Silvia Rossato; Dr. Francesca Rascio
- Trained nurses

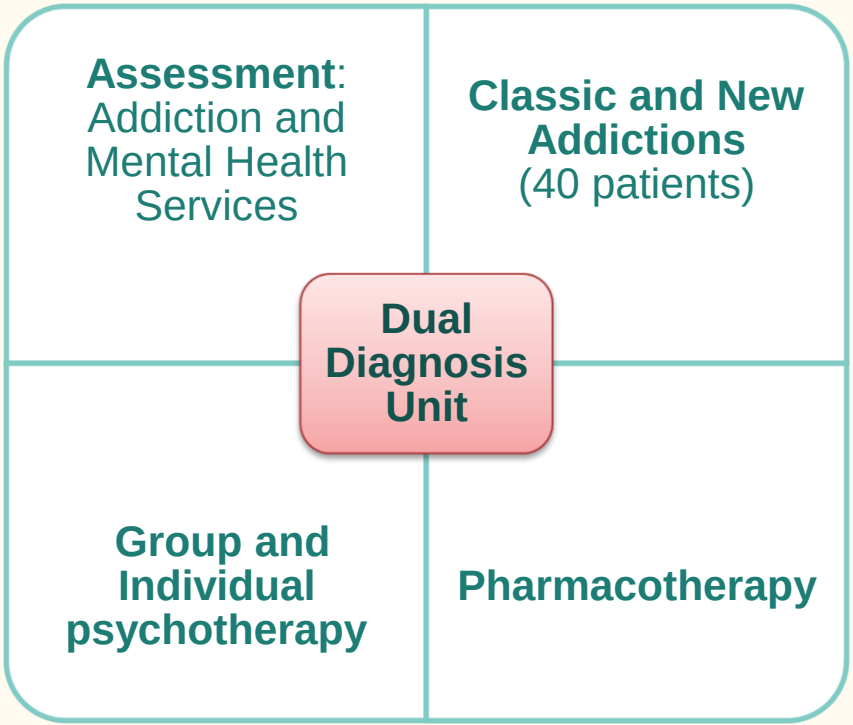
National and International collaborations

- Mental Health and Addiction Services
- Prof. Ornella Corazza, Prof. Fabrizio Schifano, University of Hertfordshire
- Prof. Giovanni Martinotti, Dr. Rita Santacroce, University of Chieti
- Prof. Giuseppe Bersani, La Sapienza , Roma
- Prof. H. Bowden Jones, Imperial College London

Psychiatric features, classic drugs, novel products

casa di cura
parco dei tigli

- North east of Italy (Padova-Venice)
- 40 inpatients
- **All regions of Italy**
- Convention with the National Health System
- Clinical Director: Prof. Giulia Perini
- 30 days recovery



In this presentation

Part 1: NPS

Part 2: NPS and PUI (Problematic Use of Internet)

Part 3: NPS, PIEDs and Exercise Addiction

Part 1

NPS: Novel Psychoactive Substances

NPS: Novel Psychoactive Substances

“New narcotic or psychotropic drug” which is not scheduled under Conventions of 1961 or 1971 but which may pose a public health threat.

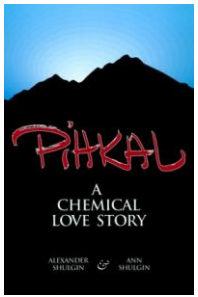
“New” means recently available: many NPS are not completely “unknown”, but their use constitutes a novelty.

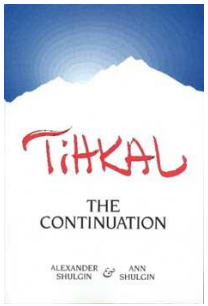
They are sold online.

Advisory Council on the Misuse of Drugs , Novel Psychoactive Report (2011)

Corazza, O., Assi, S., Simonato, P., Corkery, J., Bersani, F. S., Demetrovics, Z., ... & Deluca, P. (2013). Promoting innovation and excellence to face the rapid diffusion of novel psychoactive substances in the EU: the outcomes of the ReDNet project. *Human Psychopharmacology: Clinical and Experimental*, *28*(4), 317-323.

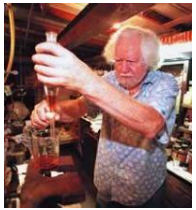
Background – Back to the Future





Ann and Alexander Shulgin designed over 200 compounds; anecdotally their inspiration started with an experience with Mescaline (Peyote Cactus).

- **PiHKAL (‘60).** Phenethylamines such as MDMA, MMDA, DOM, 2C-B, 2C-E…
- **TiHKAL (’70)**. Tryptamines such as: DMT, Ibogaine, LSD, 5Meo-DMT,…
- **Shulgin Index.** Pharmacology of 1300 compounds, with about 130 of the most active and studied compounds from PiHKAL investigated in depth.



NPS as a Galaxy: sometimes words have two meanings

Chemical Analogues:
They are **similar but different effects**; structural derivatives with few chemical modifications

- E.g.: MDMA is a chemical analogues of methamphetamine

Mimetics:
chemically different but they mimic the pharmacological effects; they bind the same CNS receptors

- E.g.: Spice drugs are mimetics of THC

Designer drugs:
manufactured with minor modifications; new substances with similar effects

- E.g.: synthetic opioids (AH-7921)

Legal highs:
umbrella term for many unregulated substances: they are the new alternatives to controlled drugs, with strong marketing strategies.

- It's a misleading term (Corazza, 2012)

- Where are they "legal"? Are they really "safe"? Do they contain contaminants?

Different Groups

Difficult to be Update!

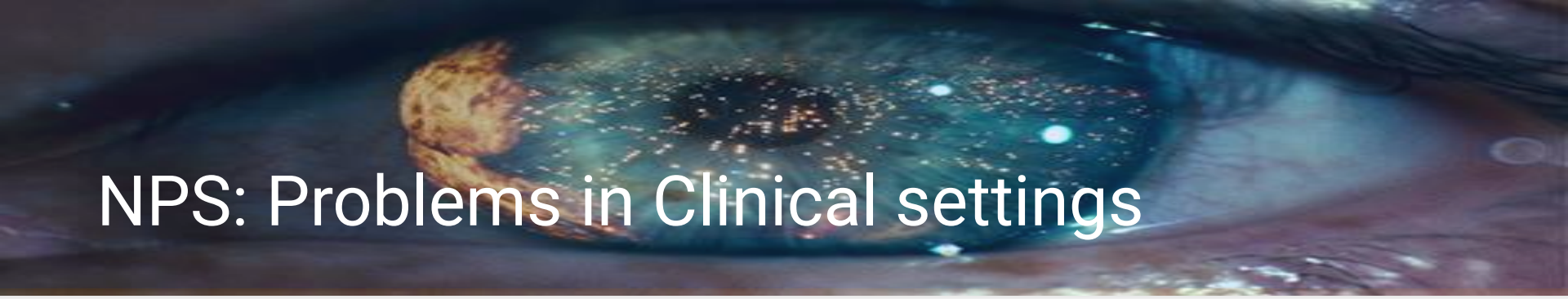
Not universally agreement to categorise them

NPS mimic existing established recreational drugs!!

- **Synthetic cathinones**
- **Spice drugs**
- **Synthetic tryptamines**
- **PCP/ketamine-like compounds**
- **Ethno-drugs**
- **Synthetic analogues**
- **Medical products**
- **PIEDs**

Schifano, F. (2015). Novel psychoactive substances (NPS): clinical and pharmacological issues. *Drugs and Alcohol Today*, *15*(1), 21-27.

At least one new psychoactive substance appears on the illicit drug market every week
400 identified substances / 4000 molecules.



NPS: Problems in Clinical settings

Unpredictable effects

Present in clinical and ER settings

Difficult assessment in traditional health services

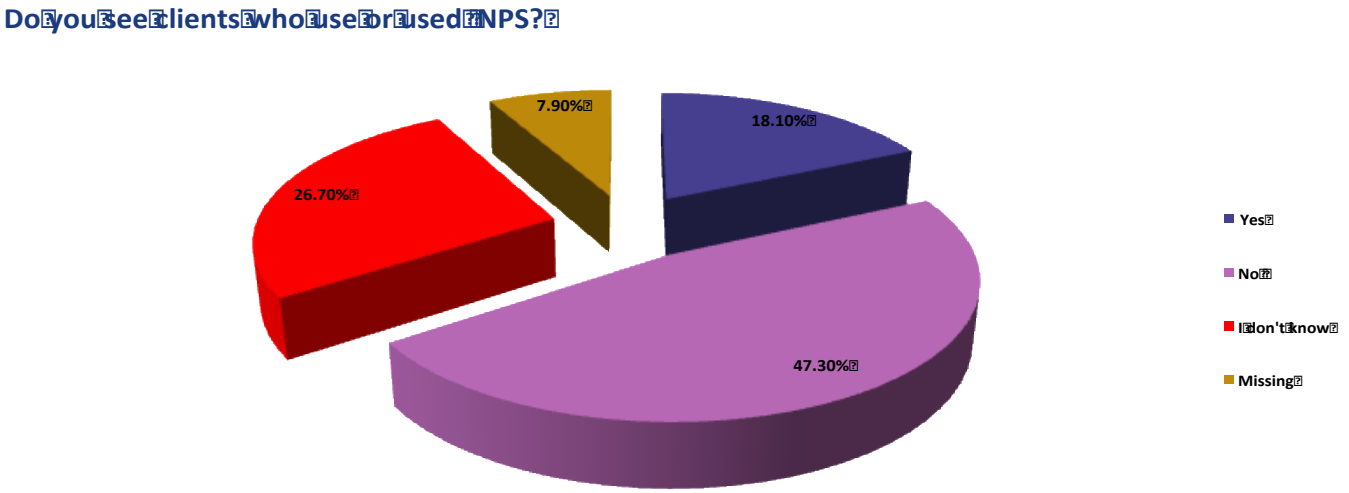
Different populations (e.g. clubbers and psychonauts)

Risk of misdiagnosis (e.g. psychotic symptoms)

Helander, Anders, et al. "Detection of new psychoactive substance use among emergency room patients: Results from the Swedish STRIDA project." Forensic science international 243 (2014): 23-29.

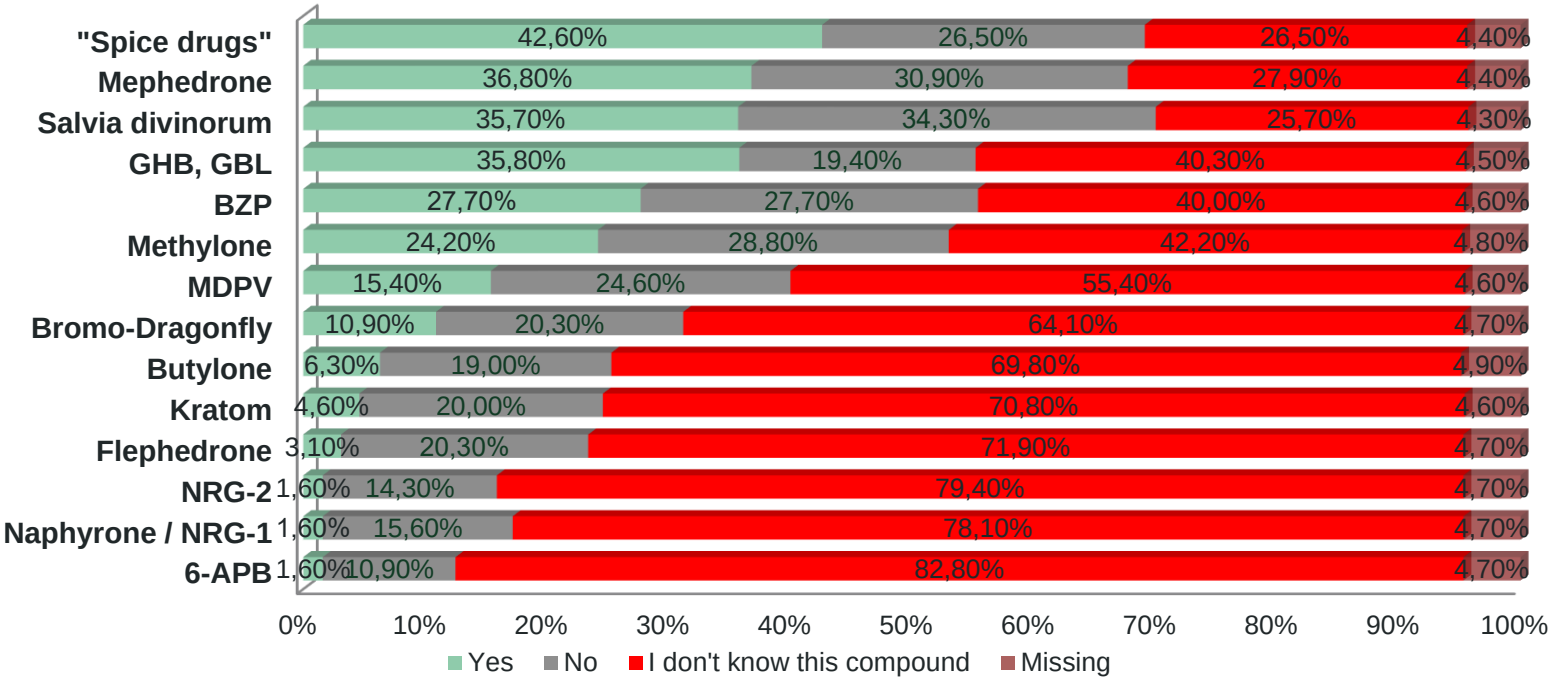
Schifano, F., Orsolini, L., Duccio Papanti, G., & Corkery, J. M. (2015). Novel psychoactive substances of interest for psychiatry. *World Psychiatry*, *14*(1), 15-26.

Physicians and assessment : results from the Italian survey for health professional



Simonato P, Corazza O, Santonastaso P et al. **Novel psychoactive substances as a novel challenge for health professionals: results from an Italian survey** Human Psychopharmacology: Clinical and Experimental, Volume 28, Issue 4, pages 324–331, July 2013

Physicians and assessment: most used NPS



thebmj

BMJ 2017;356:i6848 doi: 10.1136/bmj.i6848 (Published 25 January 2017)

PRACTICE

CLINICAL UPDATES

Novel psychoactive substances: types, mechanisms of action, and effects

Derek K Tracy [1 2], David M Wood [3 4], David Baumeister [5]

[1]Oxleas NHS Foundation Trust, London; [2]Cognition, Schizophrenia and Imaging Laboratory, Department of Psychosis Studies, the Institute of Psychiatry, Psychology and Neuroscience, King's College London; [3]Clinical Toxicology, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners, London, UK; [4]School of Life Sciences and Medicine, King's College London, London, UK; [5]Department of Psychology, the Institute of Psychiatry, Psychology and Neuroscience, King's College London

1) Stimulant NPS

2) Cannabinoids NPS

3) Hallucinogenic NPS

4) Depressant NPS

1. STIMULANT NPS

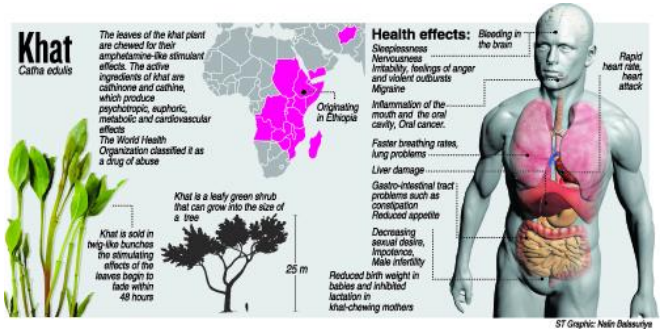
- **Euphoria, wellbeing, "high"**

- Many compounds: related to amphetamines and cocaine, related to MDMA
- Increase **serotonin, dopamine, noradrenaline** (neuronal reuptake pump/ active releaser)

- **Agitation, anxiety, hyper vigilance**, cardiovascular toxicity, seizures, renal disease, respiratory failure

- Psychiatric consequences: **impulsive behaviour, cognitive impairment, lability in mood**

Synthetic cathinones

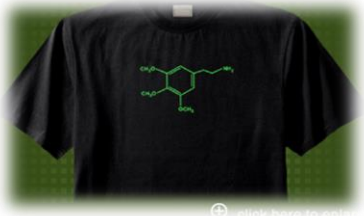


- Cathinones derivate from **Catha edulis (khat plant)**: cathinone is considered the prototype of this group, with amphetamine like effects

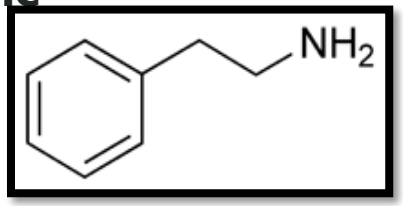
- **Synthetic cathinones** (e.g. mephedrone) **has been developed from this substance** (1920s ---- 2000s) (e.g. mephedrone was discovered in 1929 but appeared online in 2007) Examples: *butylone; EC; 3 and 4 FMC; mephedrone; ephedrone; MDPV; methylone; naphyrone; pyrovalerone* …

- **Synthetic cathinones are closed related to phenethylamines** (amphetamine, methamphetamines, mescaline, MDMA..)

Phenethylamines



Phenethylamines: stimulant /entactogenic / hallucinogenic compounds



Controlled: amphetamine, methamphetamine, MDMA, mescaline
"Ring –substituted"

- **2-c Series** (2C-E; 2C-I; 2c-c NBOME ; **25 I- NBOME**)
- **D Series** (DOM, DOI)
- BenzoDifurans (**Bfly**)
- Others **(5APB**; **6APB**; PMA and PMMA)

Actions:

SSRA : **Selective Serotonin Releasing Agents**

2. Cannabinoid NPS

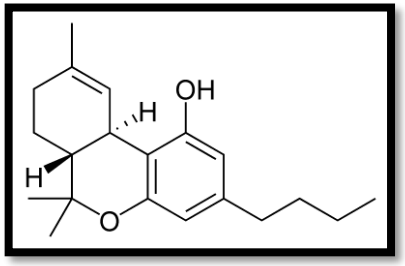
- **150 Synthetic cannabinoid** receptor agonists (!) (Spice drugs)

- Relaxation, "stoned"
- **Full agonists, without CBD**: different from cannabis !!!

- Stimulating/sedative compounds, anxiogenic/anxiolytic drugs, paranoia, psychotic symptoms, agitation, cardiovascular toxicity , renal and pulmonary issues (...)

- Higher potential for addiction and withdrawal effects

Synthetic Cannabinoids



Synthetic Cannabinoids: analogues of TetraHydroCannabinol (THC); **they are the first NPS**, the second used substance in high schools.

- HU 210 : first synthesized in ‘88
- CP compounds : developed in ’80 as analgesic
- AminoAlkylindoles compounds: **JWH compounds** and **AM serie**
- **AKB-48 and similar**

They are full agonist of CB 1 and 2; severe effects without the protective effect of CBD (Cannabidiol).

Human Psychopharmacology:
Clinical & Experimental

Special Issue on Novel Psychoactive Substances

"Spiceophrenia": a systematic overview of "Spice"-related psychopathological issues and a case report

Duccio Papanti ✉, Fabrizio Schifano, Giulia Botteon, Francesca Bertossi, Jason Mannix, Daniela Vidoni, Matteo Impagnatiello, Elisabetta Pascolo-Fabrici, Tommaso Bonavigo

First published: 23 July 2013 | https://doi.org/10.1002/hup.2312 | Cited by: 80

3. Hallucinogenic NPS

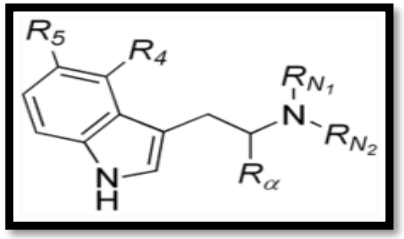
DISSOCIATIVES (ketamine and PCP like compounds) [**Methoxetamine**]

- Death, impulsive and aggressive behaviours, psychotic symptoms

PSYCHEDELICS [5MeoDALT, **NBOMe** and 2C group]

- Psychedelic effects: mystical experiences, synaesthesia
- Agonist of **5-HT2a** (not only)
- Agitation, hallucinations, tachycardia, hypertension, hyperthermia, rhabdomyolysis, serotonin syndrome, and seizure

Tryptamines



Tryptamines : mono amine alkaloids, hallucinogenic and psychedelic compounds; they may be found in plants/animals/fungi.

Psylocybin and psilocin (magic mushrooms); DMT , DET

Bufotenin (5HO DMT) from Bufo Alvarius (Colorado River Toad)

NPS:

- **Ayahuasca**

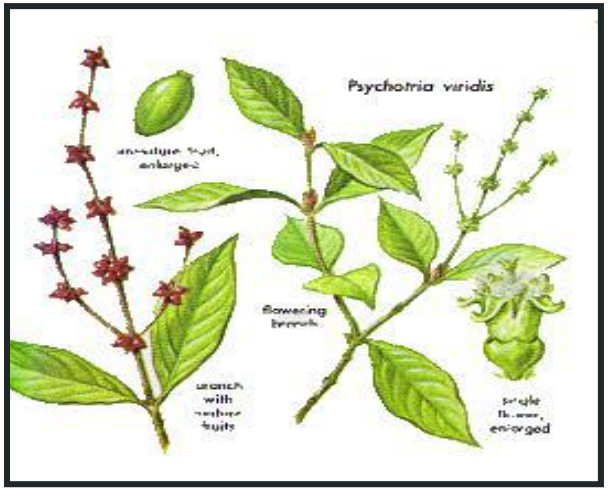
- **5 MeO DMT** (Alpha O): synthesized in '39, discovered in nature in '59 (Yopo snuff); it's a sacrament in the Church of the Tree of Life; euphoric effects, NDE and no hallucinations
- **5-MeO DiPT** (Foxy Methoxy)
- Alpha – MT

Actions:

SSRA: Selective Serotonin Releasing Agents

Botanical Sources of **Ayahuasca**

Banisteriopsis caapi
“ayahuasca”
(Malpighiaceae)



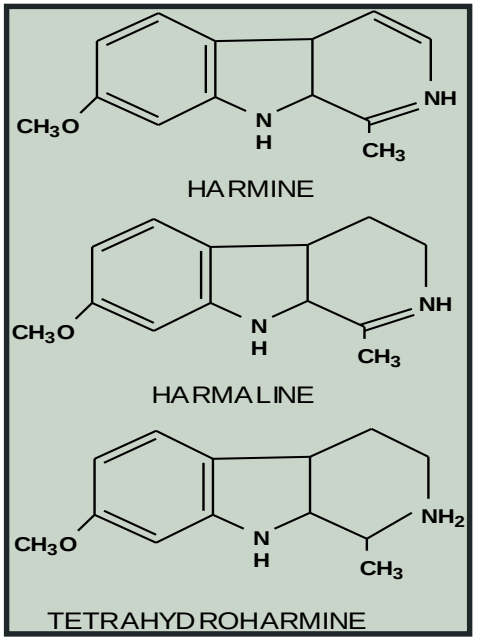
Psychotria viridis
“chacruna”
(Rubiaceae)

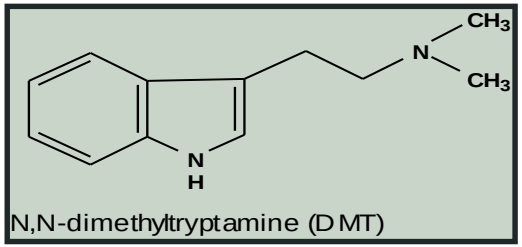
Traditionally, ayahuasca is a decoction prepared from the stems of B. caapi and the leaves of either Psychotria viridis or Diplopterys cabrerana

Diplopterys cabrerana
“chagro-ponga”
(Malpighiaceae)

Chemistry of Ayahuasca

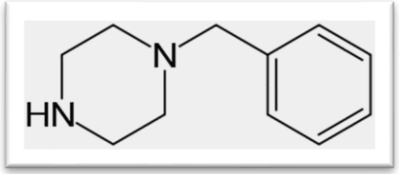
The vine Banisteriopsis caapi contains three ß-carbolines as **major active constituents.** Harmine and harmaline are potent, reversible, **selective inhibitors of MAO-A.** Tetrahydroharmine is weaker as an MAOI but relatively potent as a serotonin uptake inhibitor.





The leaf admixtures, Psychotria viridis or Diplopterys cabrerana **contain the potent, short-acting hallucinogen, DMT**.
DMT is orally inactive unless taken in conjunction with an MAO inhibitor

Piperazines



Piperazines: they are stimulants, "failed pharmaceuticals"; potential therapeutic agents never brought to market.

Antihelminthic drugs ('50); Antidepressants ('70)

BZP :**<u>Alternatives to MDMA and methamphetamines or adulterant in other preparations</u>**

BZP

MCPP (widespread, entactogenic, metabolite of trazodone)

TFMPP; MBZP

Actions: increase serotonin levels (5ht transporter, non selective agonists of 5ht receptors)

brain sciences

MDPI

Review

Hallucinogen Persisting Perception Disorder: Etiology, Clinical Features, and Therapeutic Perspectives

Giovanni Martinotti [1,2], Rita Santacroce [1,2,*], Mauro Pettorruso [3], Chiara Montemitro [1], Maria Chiara Spano [1], Marco Lorusso [1], Massimo di Giannantonio [1] and Arturo G. Lerner [4,5]

1 Department of Neuroscience, Imaging and Clinical Sciences, University "G. d'Annunzio", 66100 Chieti, Italy; giovanni.martinotti@gmail.com (G.M.); chiara.montemitro@gmail.com (C.M.); m.chiara.spano@gmail.com (M.C.S.); doloma2012@gmail.com (M.L.); digiannantonio@unich.it (M.d.G.)
2 Department of Pharmacy, Pharmacology, Postgraduate Medicine, University of Hertfordshire, Herts AL10 9AB, UK
3 Institute of Psychiatry and Psychology, Catholic University of Sacred Heart, 00168 Rome, Italy; mauro.pettorruso@hotmail.it
4 Lev Hasharon Mental Health Medical Center, Pardessya 42100, Israel; alerner@lev-hasharon.co.il
5 Sackler School of Medicine, Tel Aviv University, Ramat Aviv 69121, Israel
* Correspondence: rita.santacroce82@gmail.com; Tel.: +39-0871-355-6914

Received: 4 February 2018; Accepted: 13 March 2018; Published: 16 March 2018

4. Depressant NPS

Similar to classic drugs: clinicians are not aware of their consumption!
Can be sold as other NPS!

BENZODIAZEPINES [diclazepam and flubromazepam]

- modulators of the GABA receptor, enhancing inhibitory signalling in the central nervous system
- There are reports of NPS benzodiazepine induced **confusional states** lasting several days. **Acute withdrawal** may cause seizures.

DRUG TESTING AND ANALYSIS

REVIEW | Free Access

The emergence of new psychoactive substance (NPS) benzodiazepines: A review

Correction(s) for this article

Kieran R. Manchester, Emma C. Lomas, Laura Waters, Fiona C. Dempsey, Peter D. Maskell

First published: 04 May 2017 | https://doi.org/10.1002/dta.2211 | Cited by: 16

NPS BDZ

- Phenazepam (Russia)
- Etizolam (Japan)
- Pyrazolam (no country)
- Flubromazepam
- Diclazepam
- Meclonazepam
- Nifoxipam
- Adinazolam

TABLE 2 Benzodiazepine patent years and EMCDDA report years

Compound	Year patented	Year reported to the EMCDDA
3-hydroxyphenazepam	Not reported	2016[37,46]
4-chlorodiazepam (Ro5–4864)	1964[131]	2016[40]
Adinazolam	1976[132]	2015[35]
Bromazolam	1976[133]	2016[39]
Clonazolam	1971 [194]	2014[35]
Cloniprazepam	Not reported	2015[134]
Desalkylflurazepam	Not reported	2016[39]
Deschloroetizolam	1998 [196]	2014[34]
Desmethylflunitrazepam (fonazepam)	1963 [197]	2016[38]
Diclazepam	1964 [198]	2013[33]
Etizolam	1978 [199]	2011[30]
Flubromazepam	1962 [200]	2013[33]
Flubromazolam	1978 [201]	2014[34]
Flunitrazolam	Not reported	2016[38]
Flutazolam	1970 [202]	2015[37]
Meclonazepam	1975 [203]	2014[34]
Metizolam	1988 [204]	2015[35]
Nifoxipam	1985 [205]	2014[34]
Nimetazepam	1963 [206]	2007[17]
Nitrazolam	1971 [194]	2015[35]
Phenazepam	1974 [207]	2007[17]
Pyrazolam	1979 [208]	2012[32]

OPIODS [AH-7921 MT-45 **novel fentanyl** drugs]

- Little is known about any specific subjective effects of NPS opioids to differentiate them from established recreational opioids

- Animal data suggest AH-7921 has a higher overdose risk than morphine

Neuropharmacology 134 (2018) 121–132

Contents lists available at ScienceDirect

Neuropharmacology

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

Invited review

Fentanyl, fentanyl analogs and novel synthetic opioids: A comprehensive review

Patil Armenian [a, *], Kathy T. Vo [b], Jill Barr-Walker [c], Kara L. Lynch [d]

[a] Department of Emergency Medicine, University of California, San Francisco-Fresno, 155 N Fresno St., Fresno, CA 93701, USA
[b] Department of Emergency Medicine, University of California, San Francisco, California Poison Control System, San Francisco Division, UCSF Box 1369, San Francisco, CA 94143-1369, USA
[c] University of California, San Francisco, 1001 Potrero Avenue, Library, San Francisco, CA 94110, USA
[d] Department of Laboratory Medicine, University of California, San Francisco, 1001 Potrero Avenue, Clinical Chemistry, San Francisco, CA 94110, USA

Fentanyl and synthetic opioids

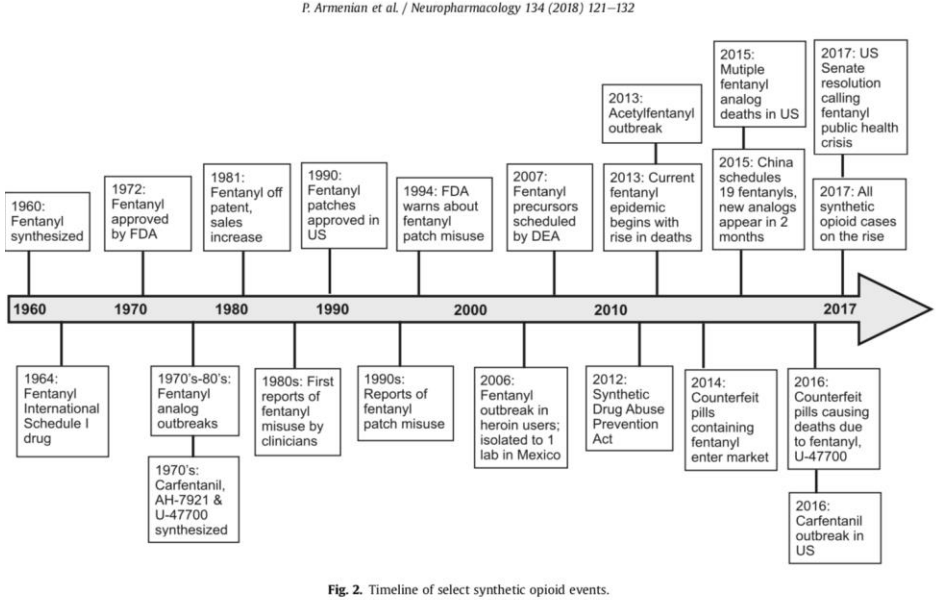


Fig. 2. Timeline of select synthetic opioid events.

Table 1
DEA and UN scheduling of synthetic opioids.

Synthetic Opioid	DEA (US)	Date (DEA)	UN
alpha-methylfentanyl	Schedule I	9/22/1981	Schedule I
sufentanil	Schedule II	5/25/1984	Schedule I
3-methylfentanyl	Schedule I	9/22/1986	Schedule I
alfentanil	Schedule II	1/23/1987	Schedule I
3-methylthiofentanyl	Schedule I	5/29/1987	Schedule I
acetyl-alpha-methylfentanyl	Schedule I	5/29/1987	Schedule I
alpha-methylthiofentanyl	Schedule I	5/29/1987	Schedule I
beta-hydroxyfentanyl	Schedule I	5/29/1987	Schedule I
para-fluorofentanyl	Schedule I	5/29/1987	Schedule I
thiofentanyl	Schedule I	5/29/1987	Schedule I
beta-hydroxy-3-methylfentanyl	Schedule I	1/8/1988	Schedule I
carfentanil	Schedule II	10/28/1988	NS
remifentanil	Schedule II	11/5/1996	Schedule I
acetyl fentanyl	Schedule I	7/17/2015	Schedule I
beta-hydroxythiofentanyl	Schedule I	5/12/2016	NS
butyryl fentanyl	Schedule I	5/12/2016	NS
AH-7921	Schedule I	5/15/2016	Schedule I
thiafentanil	Schedule II	8/26/2016	NS
U-47700	Schedule I	11/14/2016	NS
furanyl fentanyl	Schedule I	11/29/2016	NS
4-fluoroisobutyryl fentanyl	Schedule I	5/3/2017	NS
MT-45	NS		Schedule I

The synthetic opioids problem

- Fentanyl
- Fentanyl analogues

Fentanyl and fentanyl analogs are full agonists at the m-opioid receptor and potencies of these medications, typically in relation to morphine, are described throughout the medical literature. However, sound evidence supporting statements of potency are lacking.

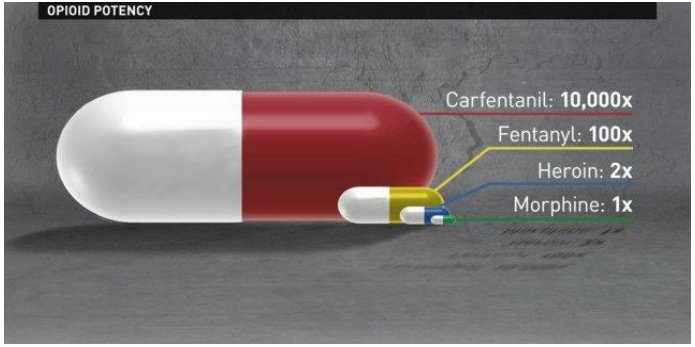
Fenanyl's potency being approximately 50-100 times the potency of morphine or carfentanil's potency being **10,000 times** that of morphine

- Novel synthetic opiods

- AH 7921, U47700, MT 45

Novel synthetic opioids have not been studied in humans and therefore, pharmacokinetic data does not exist. In general, novel synthetic opioids are highly selective for the m-receptor.

Such models revealed that U-47700 is 7.5 times more potent in binding to opioid receptors than morphine



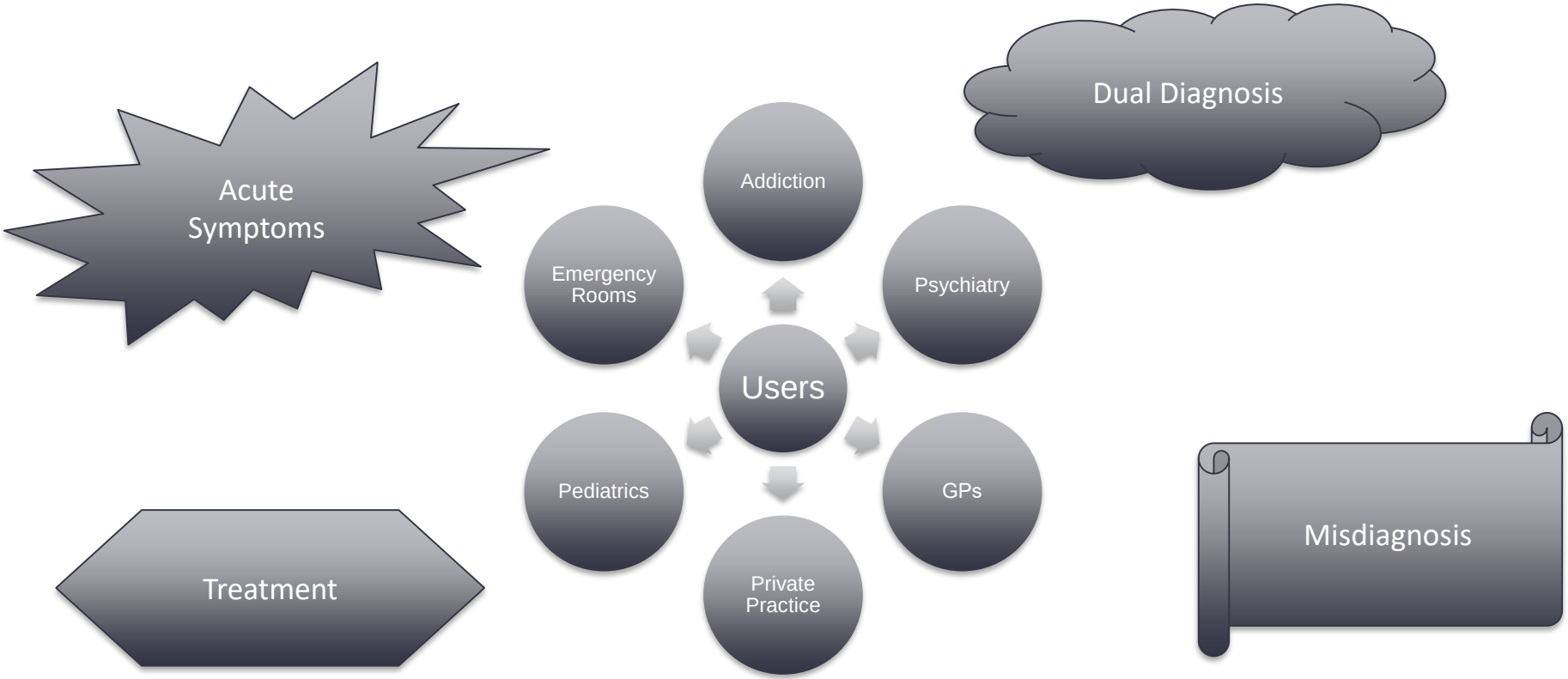
Opioid Crisis

Lethal Opioid Doses

Opioid	FDA	Relative Potency	Lethal Dose
Morphine	✓	1x	1 Pea
Heroin	✓	2x	1 Sunflower Seed
Fentanyl	✓	100x	1 Sesame Seed
Sufentanil	✓	500x	1 Grain of Sand
Carfentanil	✗	10,000x	0.5 Grains of Salt

Clearvue Data

NPS and Clinical Impact



brain sciences

MDPI

Editorial

Recent Changes in Drug Abuse Scenarios: The New/Novel Psychoactive Substances (NPS) Phenomenon

Fabrizio Schifano

Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit, University of Hertfordshire, Hertfordshire AL10 9AB, UK; f.schifano@herts.ac.uk

Received: 7 December 2018; Accepted: 9 December 2018; Published: 13 December 2018

The clinical Role of NPS: psychosis

- **(a) increased central dopamine levels**, typically seen with novel psychedelic phenethylamines, novel stimulants and synthetic cathinones;
- **(b) significant cannabinoid CB1 receptor activation**, which is associated with high potency synthetic cannabimimetics;
- **(c) 5-HT2A receptor activation**, seen with latest generation phenethylamines, tryptamine derivatives and hallucinogenic plants;
- **(d) antagonist activity at n-methyl-D-aspartate/NMDA receptors**, observed with ketamine, methoxetamine/MXE, and their latest derivatives;
- **(e) k-opioid receptor activation**, which is typically associated with both Salvia divinorum and Mitragyna speciosa/'Kratom' intake.

Are clinicians aware of NPS?

Difficult assessment in traditional health services

Different populations: clubbers, psychonauts , psychiatric patients [a]

Unpredictable effects and risk of misdiagnosis

Assessment, management, treatment[b]

Martinotti, Giovanni, et al. "Novel psychoactive substances in young adults with and without psychiatric comorbidities." *BioMed research international* 2014 (2014).

Novel Psychoactive Treatment: UK Network (Neptune): Guidance on the clinical management of acute and chronic harms of Club Drugs and Novel Psychoactive Substances

UNODC Early Warning Advisory on New Psychoactive Substances

[Log on or register

Home About

- What are NPS?
- NPS Substance Groups
  - Aminoindanes
  - Other substances
  - Phencyclidine-type substances
  - Phenethylamines
  - Piperazines
  - Plant-based substances
  - Synthetic cannabinoids
  - Synthetic cathinones
  - Tryptamines

June 2019 - UNODC: Commission on Narcotic Drugs decision on international control of four fentanyl analogues enters into force

VIENNA, Austria - June 2019. The decision adopted by the Commission on Narcotic Drugs during its 62nd Session from 18 to 22 March 2019 to add Cyclopropylfentanyl, Methoxyacetylfentanyl, Orthofluorofentanyl (2-Fluorofentanyl) and Parafluorobutyrylfentanyl (4-Fluorobutyrfentanyl) to Schedule 1 of the Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol, was communicated by the Secretary-General on 23rd of May 2019 to all States Members of the United Nations, to non-member States Parties to the Conventions, to the World Health Organization and to the International Narcotics Control Board and thereby entered into force on that date.

UNODC Early Warning Advisory on New Psychoactive Substances

Home About

- What are NPS?
- NPS Substance Groups
  - Aminoindanes
  - Other substances
  - Phencyclidine-type substances
  - Phenethylamines
  - Piperazines
  - Plant-based substances
  - Synthetic cannabinoids
  - Synthetic cathinones
  - Tryptamines
- Legal Responses
- Resources
- Global SMART Programme
- EWA Partners
- **Latest News on NPS**
- ICE-Portal

December 2018 - WHO: World Health Organization recommends 9 NPS for scheduling

VIENNA, Austria – December 2018: At the reconvened sixty-first session of the Commission on Narcotic Drug
Organization (WHO) announced the scheduling recommendations on new psychoactive substances reviewed at th
Dependence (ECDD) held in Geneva from 12 to 16 November 2018. In total, thirteen substances were critically re
scheduling:

Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol:
Cyclopropylfentanyl - Schedule I
Methoxyacetylfentanyl - Schedule I
Ortho-fluorofentanyl (2-Fluorofentanyl) - Schedule I
Parafluoro butyrfentanyl (4-Fluorobutyrfentanyl) - Schedule I

Convention on Psychotropic Substances of 1971:
ADB-FUBINACA - Schedule II
FUB-AMB (MMB-FUBINACA, AMB-FUBINACA) - Schedule II
ADB-CHMINACA - Schedule II
CUMYL-4CNBINACA - Schedule II
N-ethylnorpentylone (Ephylone) - Schedule II

The WHO recommended pregabalin, tramadol and Paramethoxybutyrfentanyl (4-Methoxybutyrfentanyl) for surve

UNODC Early Warning Advisory on New Psychoactive Substances

[Log on or register

Home About

- What are NPS?
- NPS Substance Groups
  - Aminoindanes
  - Other substances
  - Phencyclidine-type substances
  - Phenethylamines
  - Piperazines
  - Plant-based substances
  - Synthetic cannabinoids
  - Synthetic cathinones
  - Tryptamines
- Legal Responses
- Resources
- Global SMART Programme
- EWA Partners
- **Latest News on NPS**
- ICE-Portal

March 2019 - UNODC: Nine substances and three precursors "scheduled" at the 62nd Session of the Commission on Narcotic Drugs

VIENNA, Austria – March 2019: At its 62nd regular session from 18 to 22 March 2019, the Commission on Narcotic Drugs decided to place nine substances and three precursors under international control. Following recommendations by the WHO, nine substances were added to the relevant schedules of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol and the Convention on Psychotropic Substances of 1971. Moreover, following recommendations by the INCB, three precursors, which can be used in the illicit manufacture of amphetamine-type stimulants, were added to Table I of the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988.

Added to the Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol:

1. Cyclopropylfentanyl - Schedule I
2. Methoxyacetylfentanyl - Schedule I
3. Orthofluorofentanyl (2-Fluorofentanyl) - Schedule I
4. Parafluorobutyrylfentanyl (4-Fluorobutyrfentanyl) - Schedule I

Added to the Convention on Psychotropic Substances of 1971:

5. ADB-FUBINACA - Schedule II
6. FUB-AMB (MMB-FUBINACA, AMB-FUBINACA) - Schedule II
7. ADB-CHMINACA - Schedule II
8. CUMYL-4CN-BINACA - Schedule II
9. *N*-Ethylnorpentylone (ephylone) - Schedule II

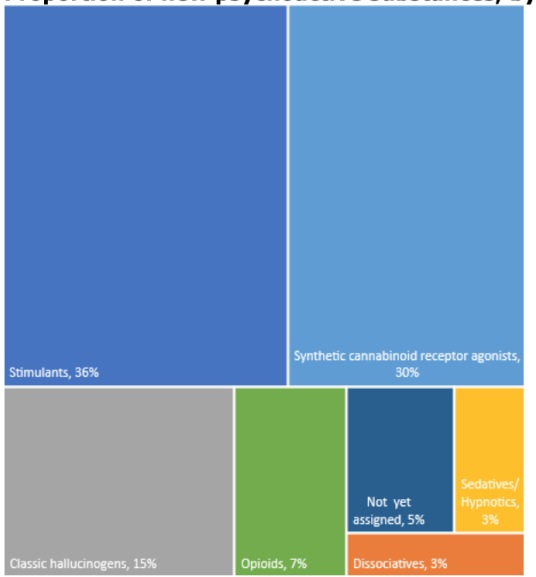
Added to the Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988:

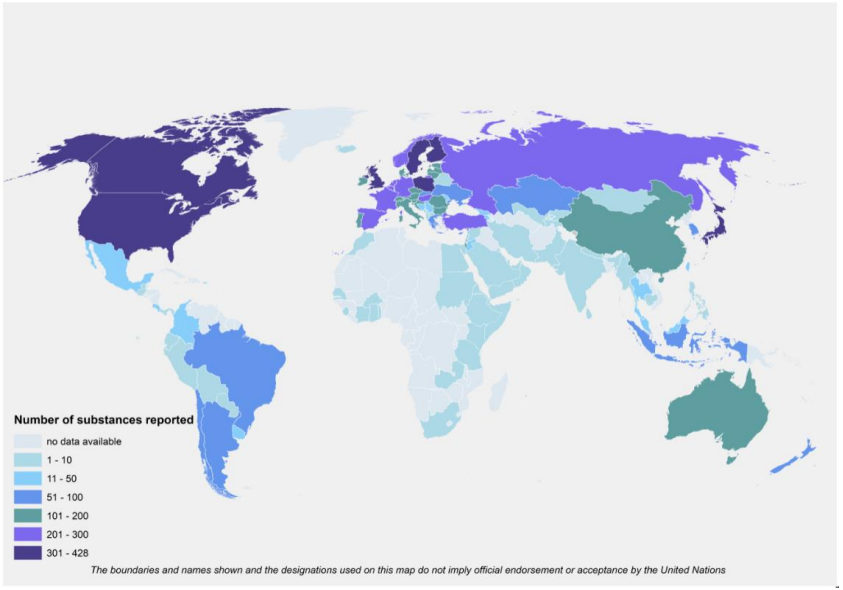
1. *3,4-MDP-2P-methylglycidate* (PMK glycidate) (all stereoisomers) - Table I
2. *3,4-MDP-2P-methylglycidic acid* (PMK glycidic acid (all stereoisomers) - Table I
3. *Alpha-phenylacetoacetamide (APAA) (including its optical isomers)* - Table I

How widespread are NPS?

NPS have become a global phenomenon with 119 countries and territories from all regions of the world having reported one or more NPS. Up to December 2018, 888 substances have been reported to the UNODC Early Warning Advisory (EWA) on NPS by Governments, laboratories and partner organisations. NPS available on the market have similar effects as substances under international control such as cannabis, cocaine, heroin, LSD, MDMA (ecstasy) or methamphetamine. Looking at the effects of NPS that have been reported until December 2018, the majority are stimulants, followed by synthetic cannabinoid receptor agonists and classic hallucinogens.

Proportion of new psychoactive substances, by psychoactive effect group, up to December 2018:

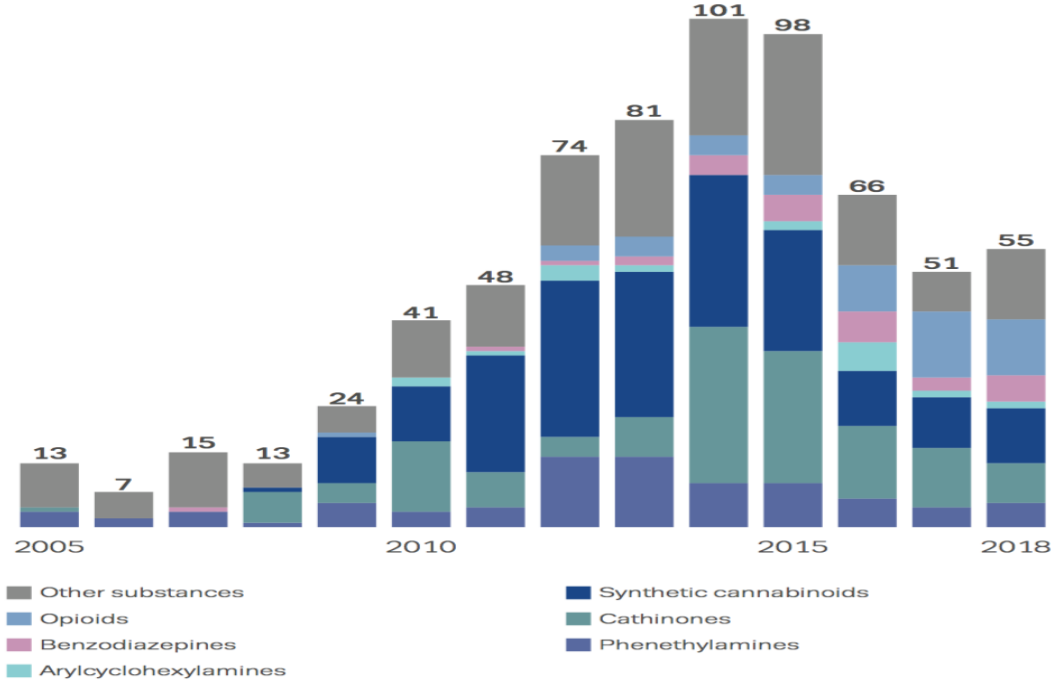




Source: UNODC Early Warning Advisory on NPS, 2019.

Note: The analysis of the pharmacological effects comprises NPS registered up to December 2018. Plant-based substances were excluded from the analysis as they usually contain a large number of different substances, some of which may not have been known and whose effects and interactions are not fully understood.

Number and categories of new psychoactive substances notified to the EU Early Warning System for the first time, 2005-18



New accelerated EU procedures to identify and respond to new psychoactive substances appearing in the European Union

New legislative package

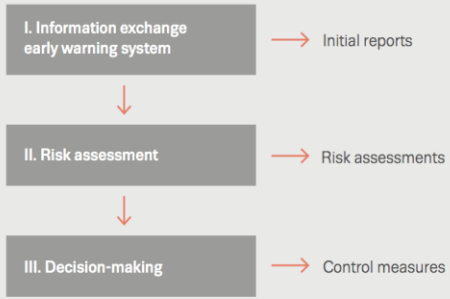
Regulation

Regulation (EU) 2017/2101 amends Regulation (EC) 1920/2006 providing for information exchange on, and an early warning system and risk assessment procedure for, new psychoactive substances

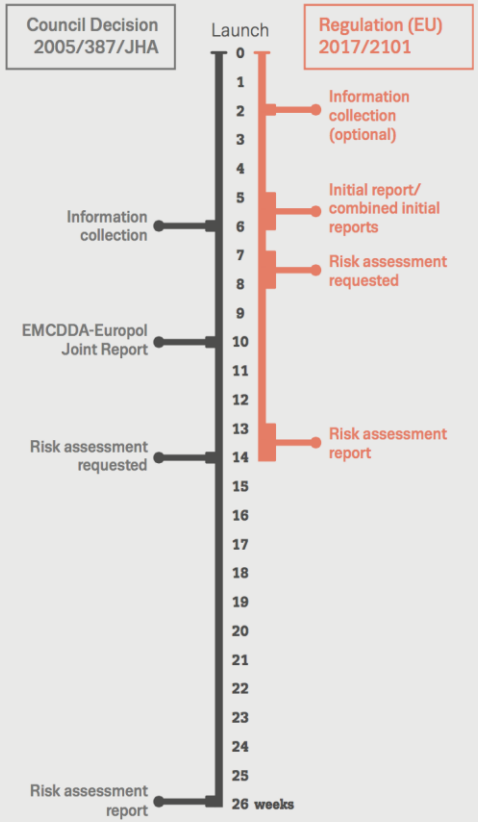
Directive

Directive (EU) 2017/2103 amends Council Framework Decision 2004/757/JHA in order to include new psychoactive substances in the definition of 'drug' and repeals Council Decision 2005/387/JHA

Unchanged three-step approach



Shorter deadlines



Specific NPS-related legislation

Austria: **The New Psychoactive Substances Act**

In 2011, the New Psychoactive Substances Act (Federal Act on the Protection against health hazards defines a 'new psychoactive substance' as "a substance or preparation which has, when applied, the (1)). Under the Act, the Federal Minister of Health has the authority to specify individual NPS or class control, whenever this is needed to prevent their distribution and avoid the health hazards that may ar specification: "1. it can be assumed that they will be distributed with a view to being misused by certa state of scientific knowledge and experience, they may pose a health hazard to the consumers or such

Ireland: **The Criminal Justice (Psychoactive Substances) Act 2010**

The Criminal Justice (Psychoactive Substances) Act came into effect on 23 August 2010 to deal with th export or advertise a psychoactive substance (this is intended to include any such importation or expor

Romania: **Law 194/2011 of 10 November 2011**

A law to control NPS in Romania was passed in 2011. Under the new legislation, a specific permit is re to those caused by substances controlled under drug laws. These effects are defined as those prov 'causing dependency', but no specific reference to 'harmful' substances is made. The unauthorized dis imprisonment, but not the possession for personal use.

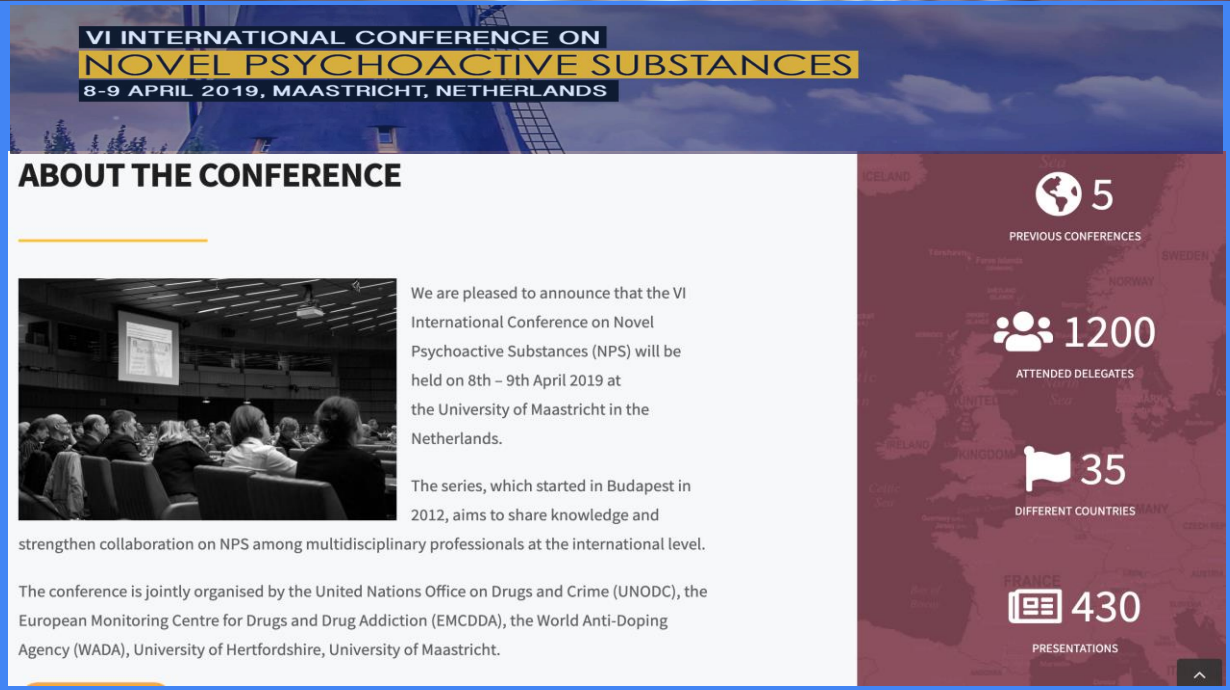
New Zealand: Market Restrictions/Pre-market authorization. **The Psychoactive Substances A**

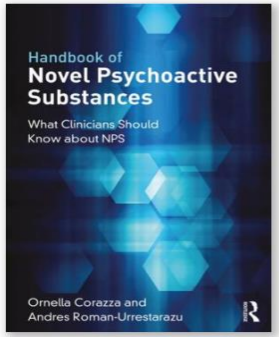
The importation, manufacture, sale, supply, or possession of a psychoactive substance or approved p individual who uses the substance or product is subject to requirements similar to those imposed up new approach aims to balance the demand for access to such substances with the risk of likely harm t proof whereby manufactures will be required to have their products assessed in order to prove that these products will include age restrictions and place-of-sale restrictions on the sale of approved produ for approved products; health-warning requirements for approved products; signage, storage, and offences relating to the sale of approved products by or to persons under the age of 18 years and the p Authority to recall approved products in certain circumstances.

United Kingdom: **The Psychoactive Substances Act 2016**

The Psychoactive Substances Act makes it an offence to produce, supply, offer to supply, possess v psychoactive substances; that is, any substance intended for human consumption that is capable of p imprisonment. It excludes legitimate substances, such as food, alcohol, tobacco, nicotine, caffeine an drugs, which continue to be regulated by the Misuse of Drugs Act 1971. It also exempts healthcare ac on the basis that persons engaged in such activities have a legitimate need to use psychoactive substa notices, premises notices, prohibition orders and premises orders (breach of the two orders will be a graded response to the supply of psychoactive substances in appropriate cases. Moreover, it provide search premises in accordance with a warrant, and to seize and destroy psychoactive substances.

NPS: The International Conferences





Handbook of Novel Psychoactive Substances

What Clinicians Should Know about NPS

Edited By ***Ornella Corazza, Andres Roman-Urrestarazu***

Edition	1st Edition
First Published	2018
eBook Published	10 October 2018
Pub. location	New York
Imprint	Routledge
DOI	https://doi.org/10.4324/9781315158082
Pages	408 pages
eBook ISBN	9781315158082
Subjects	Behavioral Sciences, Medicine, Dentistry, Nursing & Allied Health

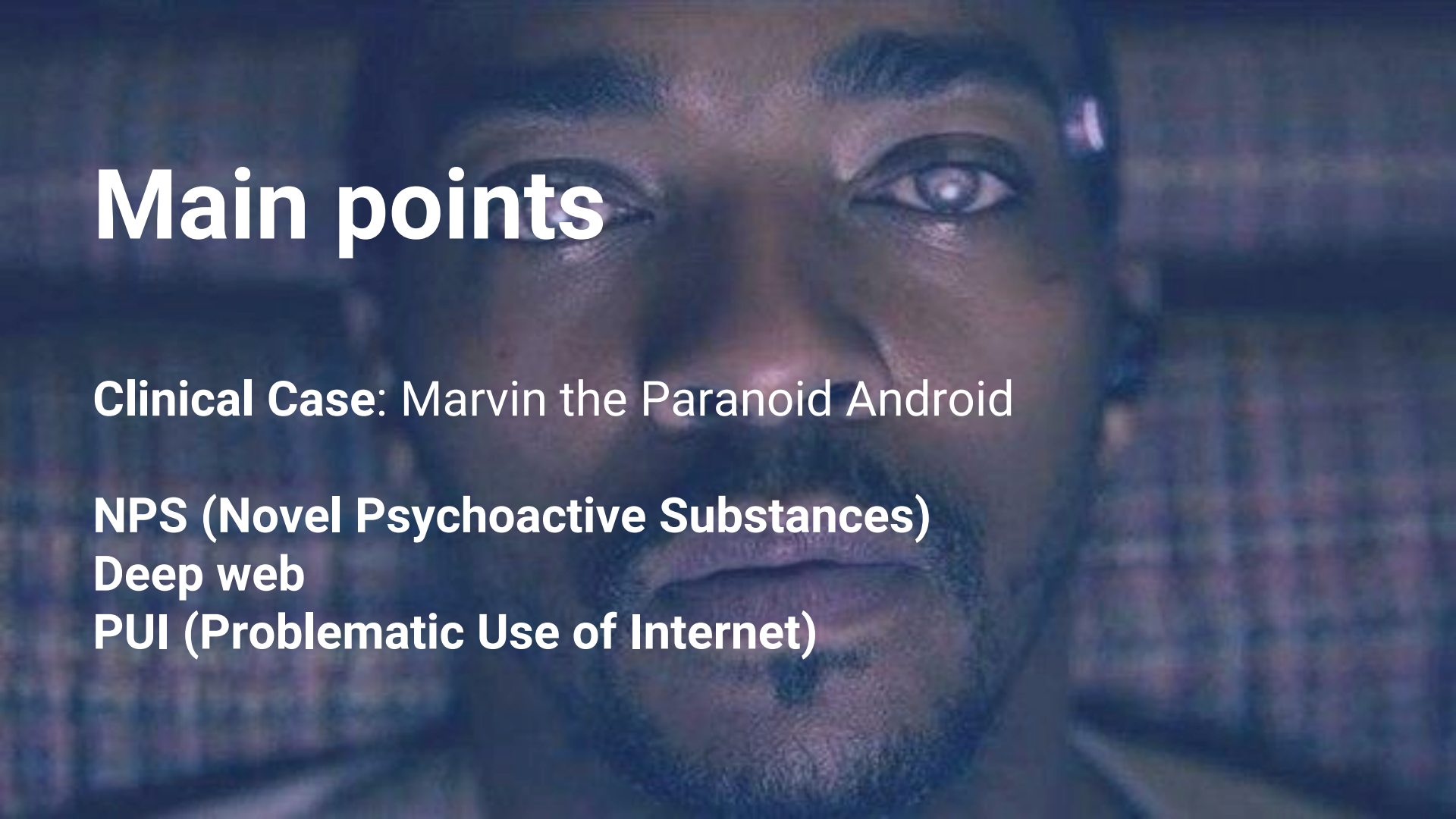
Part 2

NPS and PUI (Problematic Use of Internet)

PUI and novel forms of substance misuse: a controversial relation

Pierluigi Simonato
MD, Psychiatrist , PhD

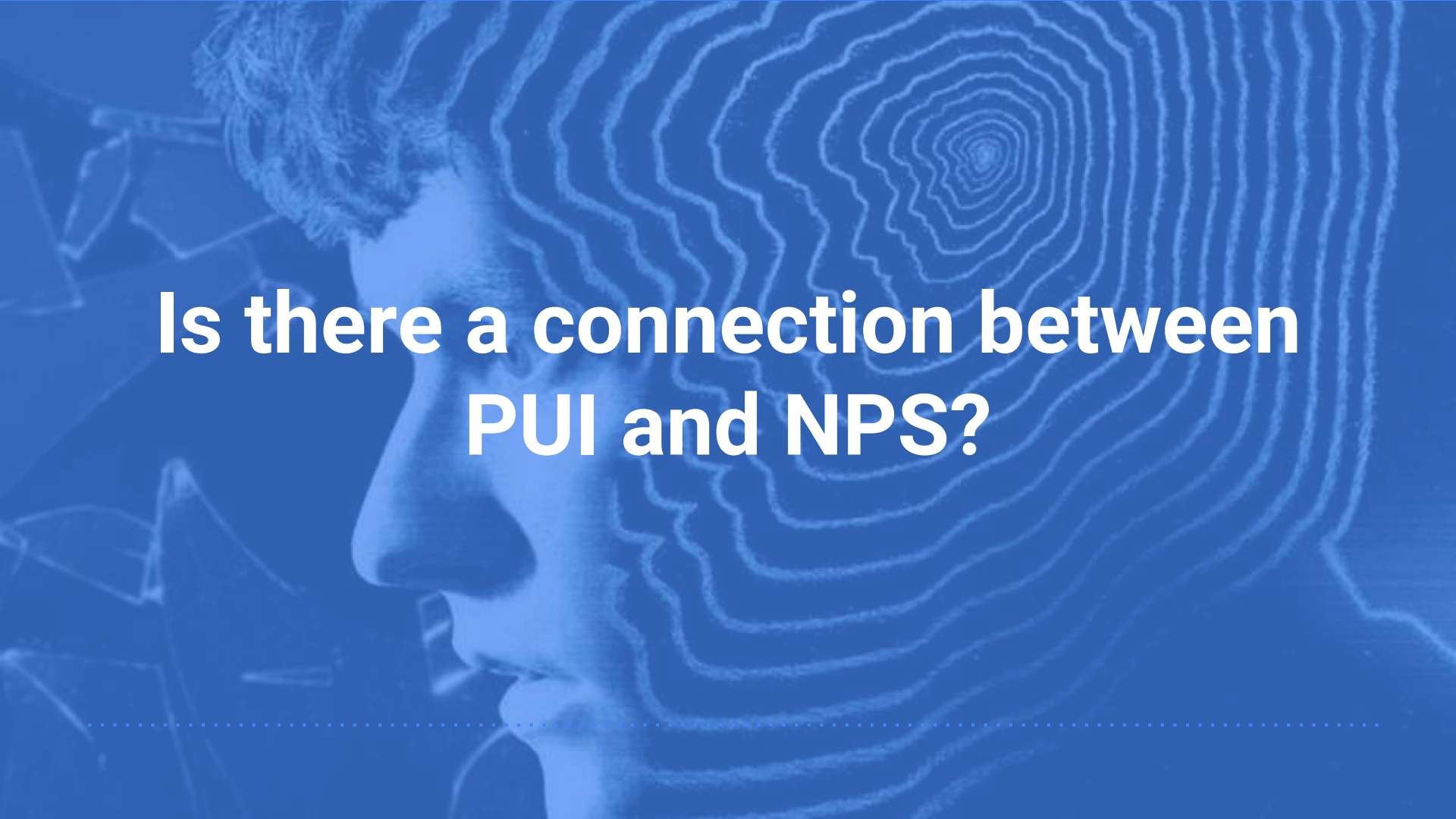
University of Hertfordshire (UK)
Casa di Cura Parco dei Tigli (Italy)



Main points

Clinical Case: Marvin the Paranoid Android

NPS (Novel Psychoactive Substances)
Deep web
PUI (Problematic Use of Internet)


Is there a connection between PUI and NPS?

Clinical Case: Paranoid Android

Case Reports

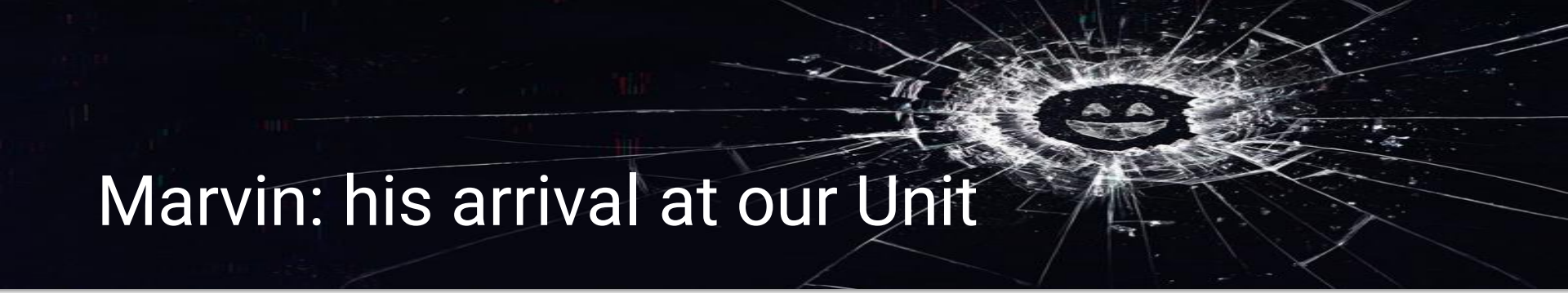
“Marvin, the Paranoid Android”: The Case of an Alpha-PVP User in the Expanding Galaxy of NPS

Simonato Pierluigi, Bulsis Laura, Negri Attilio, Bansal Gurjeet K, Pessa Gloria, Mioni Davide, Giuseppe Borgherini, Martinotti Giovanni, Schifano Fabrizio, Giulia Perini & Corazza Ornella ...show less

Pages 306-313 | Received 16 May 2017, Accepted 03 Jan 2018, Published online: 16 May 2018

Download citation https://doi.org/10.1080/02791072.2018.1447172 Check for updates

The Hitchhiker's Guide to the Galaxy series by Douglas Adams



Marvin: his arrival at our Unit

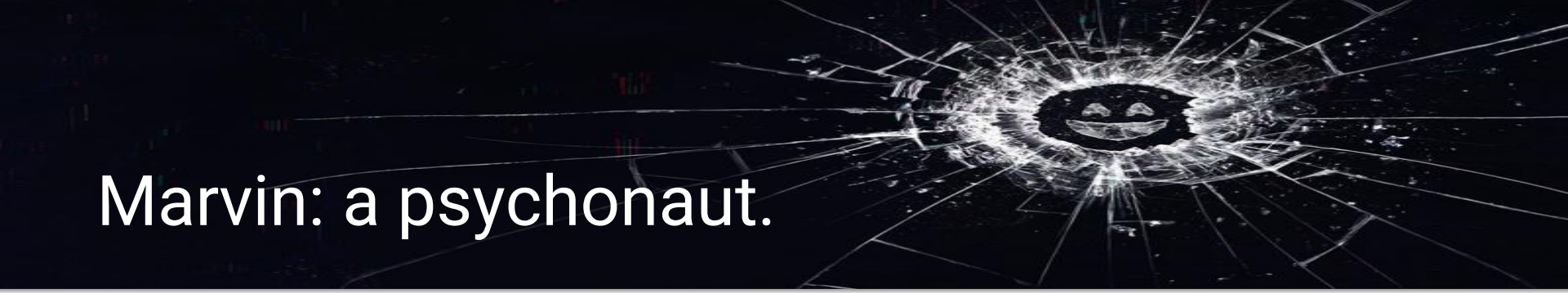
- **28 years old**, single, studied at Liceo Scientifico, attempted **2 years University** (Tecniche Erboristiche)
- **Substances induced psychosis** (previous) and **depressive mood** (last weeks): reality check at the arrival seemed to be stable, **without evidence of delusions/hallucinations**
- Patient **was followed only by the Mental Heath Service** when he arrived at our Unit (Treatment: Risperidone 4 mg/die ; Venlafaxine 75 mg/die ; Delorazepam mg1/die)
- He had two previous hospitalisation

Marvin: anamnestic events

16 y.o.: intense use of THC (cannabis and skunk) with first psychotic episode with visual and auditory hallucinations – Mental Health Service

Not followed by Local Addiction Service (at the time)

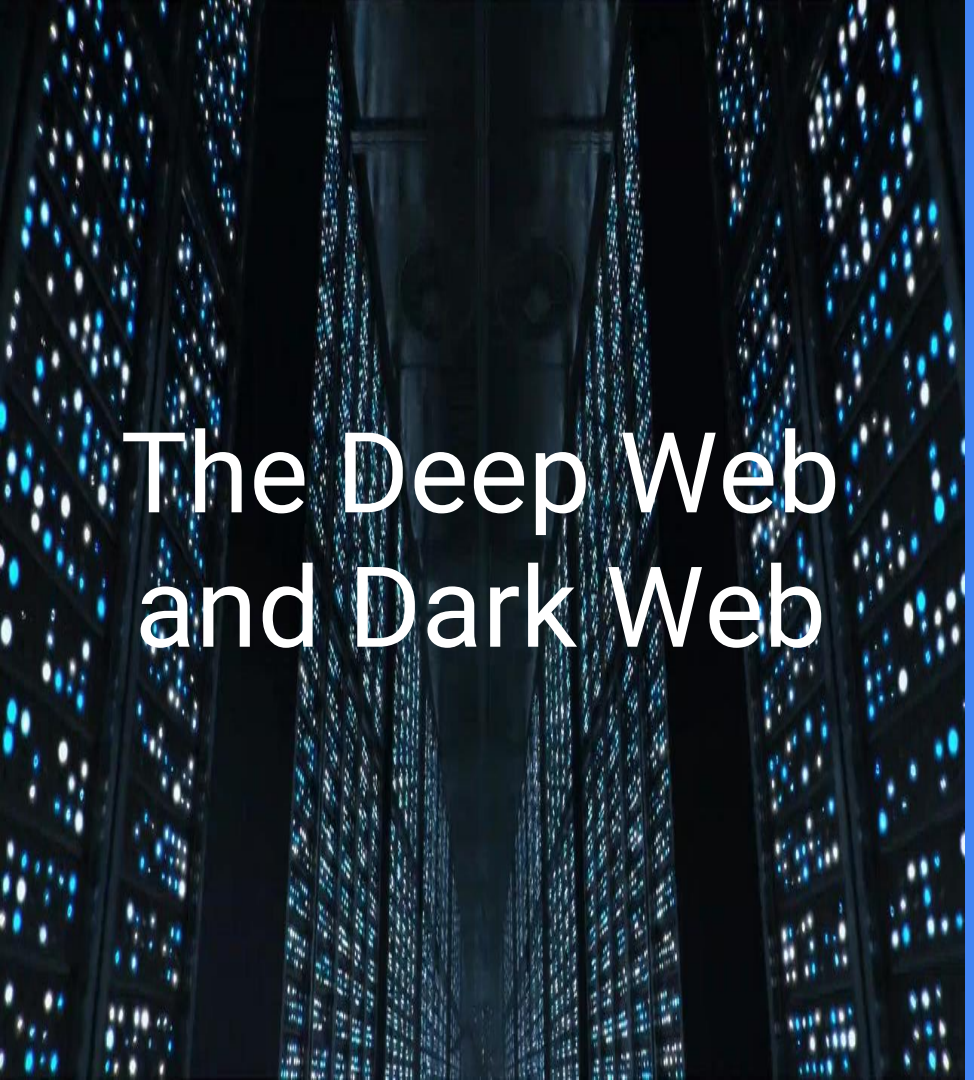
He revealed (after strong security reassurances) **a strong use of NPS starting from 18 years old**



Marvin: a psychonaut.

He became a psychonaut. He surfed the web **compulsively** to

- **Explore the drug market**
- **Inform himself on novel compounds** available online
- Find the **best substance** for himself
- **Search in the open/closed webfora** and **the dark net** (he didn't want to reveal the exact sites !)
- **Buy novel substances**
- **Review NPS that he tried**
- **Avoid legal actions** (anonymous package, neighbours address)



The Deep Web and Dark Web

The Deep/Dark web

- **The deep web is the part of World Wide Web content not indexed** by standard search engines.
- **The dark web is a “secret and anonymous” part** where you can buy drugs, weapons or other illegal materials.
- **Most of online drug marketplaces**, particularly those selling illegal substances, are located on the **“dark net of the deep web.”**

Van Buskirk, J., Griffiths, P., Farrell, M., & Degenhardt, L. (2017). Trends in new psychoactive substances from surface and “dark” net monitoring. *The Lancet Psychiatry*, *4*(1), 16-18.

What does it mean? (McGuigan, 2011)

- The traditional search engines see only a small amount of the information that is available whereas **the deep web is several orders of magnitude larger than the surface web.**
- **It has been estimated by Google that the amount of Internet is 5.000.000 of terabyte.**
- **While Google is able to find 200 terabyte.**
- **We are talking of 0.004%of the data.**

Corazza, O., & Roman-Urrestarazu, A. Novel Psychoactive Substances.

Mack, R. (2019). Combating the Illicit Goods Trade on the Dark Web.


SURFACE WEB
- Publicly available websites
- Search engines
DEEP WEB
- Medical information
- Legal documents
- Scientific reports
- Subscription info
- Various databases
- Government Intel
- Company specific repositories
DARK WEB
- Illegal websites and information
- Tor-encrypted websites
- Websites that sell drugs
- Private communication forums

Gulati, S., Sharma, S., & Agarwal, G. (2018). The Hidden Truth Anonymity in Cyberspace: Deep Web. In *Intelligent Computing and Information and Communication* (pp. 719-730). Springer, Singapore.

Who are the e-psychonauts?

- **New populations of users:** attitude towards **self-experimentation**
- They are **“invisible” to traditional health services** (Addiction services)
- They consider themselves **different from “junkies”**
- They are the “latest generation of drug users”: **educated and informed**
- **They post their experiences online**
- “Psychonauts” refers to users of **different drug categories** (synthetic cannabinoids, opioids, dissociatives, etc.)

Schifano, F., Napoletano, F., Chiappini, S., Guirguis, A., Corkery, J. M., Bonaccorso, S., ... & Vento, A. (2019). New/emerging psychoactive substances and associated psychopathological consequences. *Psychological medicine*, 1-13.

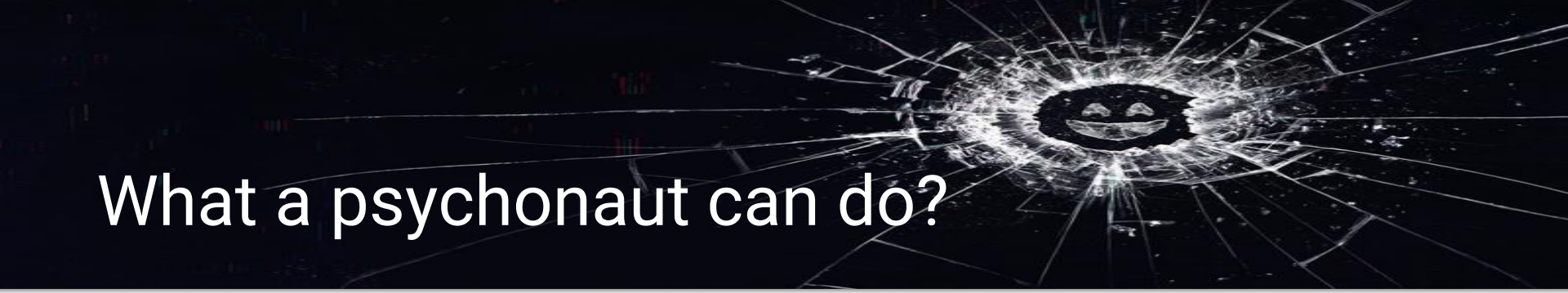
Orsolini, L., Chiappini, S., Corkery, J. M., Guirguis, A., Papanti, D., & Schifano, F. (2019). The use of new psychoactive substances (NPS) in young people and their role in mental health care: a systematic review. *Expert review of neurotherapeutics*

Who are the e-psychonauts?

- A definition is not available: **we do not have a clear psychopathological profile**

- The web has become a **strategic source of information** about the spread of **new substances**, their effects and possible risks (Soussan and Kjellgren, 2014a, b; Davey et al., 2012; Deluca et al., 2012).

Orsolini, L., Ciccarese, M., Papanti, D., De Berardis, D., Guiguis, A., Corkery, J., & Schifano, F. (2019, January). Psychedelic fauna for psychonaut hunters. In *European Neuropsychopharmacology* (Vol. 29, pp. S472-S473).
Orsolini, L., Papanti, G. D., Francesconi, G., & Schifano, F. (2015). Mind navigators of chemicals' experimenters? A web-based description of e-psychonauts. Cyberpsychology, Behavior, and Social Networking, 18(5), 296-300.

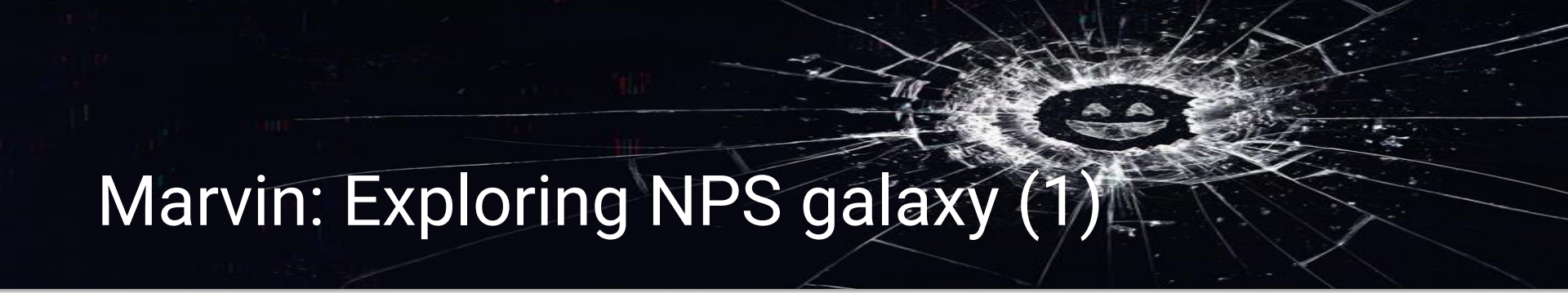


What a psychonaut can do?

- Anonymize himself (e.g. Tor)
- Search for substances (e.g. Grams)
- Read the description of the product (e.g. Sellers review, drug fora)
- Buy the compounds (e.g. crypto-currencies)
- Receive the anonymous package
- Review the sellers and the product

Orsolini, L., Papanti, G. D., Francesconi, G., & Schifano, F. (2015). Mind navigators of chemicals' experimenters? A web-based description of e-psychonauts. *Cyberpsychology, Behavior, and Social Networking*, *18*(5), 296-300.

.



Marvin: Exploring NPS galaxy (1)

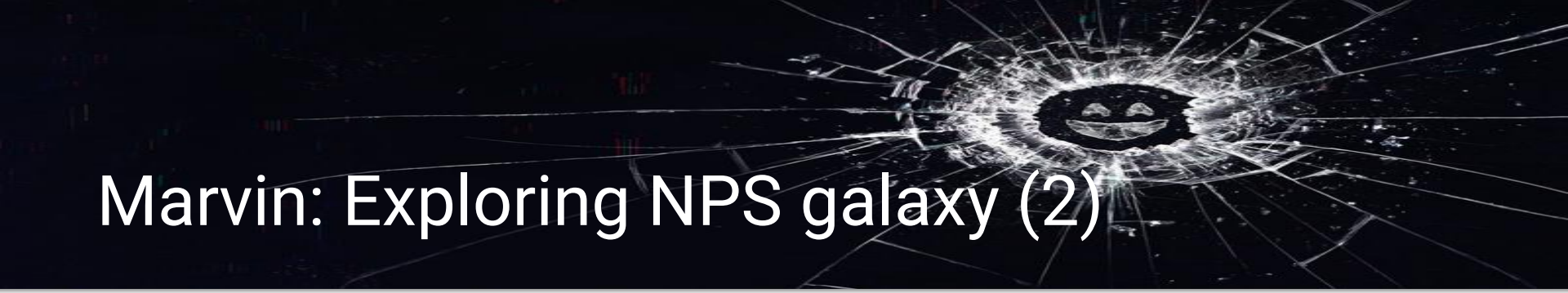
JWH 2210 (not AH): alone; dissolved in alcohol, 1g → 15 mg per dose

4 HO Met [4-hydroxy-N,N-ethyl-methyltryptamine] : 15-20 mg ; tried 1 time; laugh and low mood ; he observed that he was using anti-psychotic medications

2 C-E [4-ethyl-2,5-dimethoxyphenethylamine] : 18 mg ; tried once , no effects

MDPV: low dosage; dissolved in water; two times , he observed a middle stimulation

Kratom : 1 time , sweating , middle visual effects , miosis , heat
Amanita muscarina
Salvia divinorum: few times



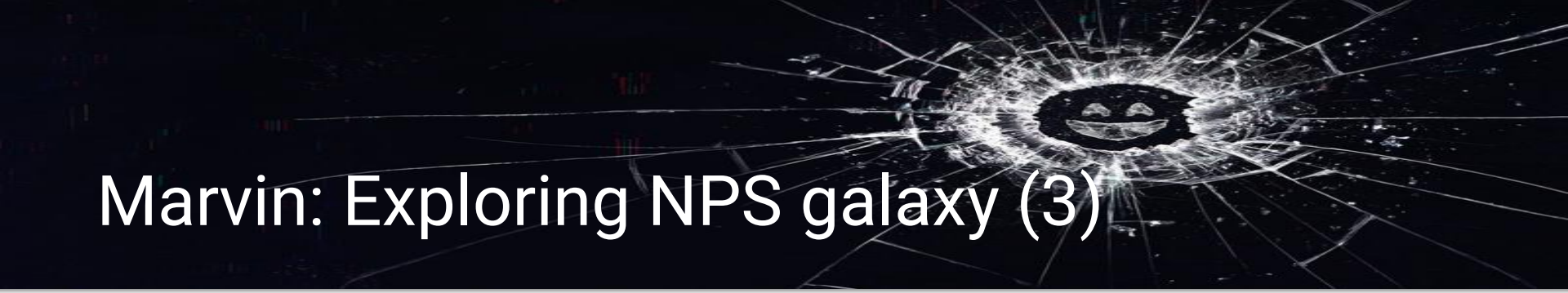
Marvin: Exploring NPS galaxy (2)

Ketamine : 3- 4 times, pleasant effects but he perceived it ‘harmful’.

Methoxetamine: ‘another planet’, 1 time at 50 mg, powerful, few seconds of psychotic experience.

Pentedrone (α-methylamino-valerophenone): 2-3 times, middle effect

Ethyl-phenidate: ‘strange effect’, dissociative symptoms.



Marvin: Exploring NPS galaxy (3)

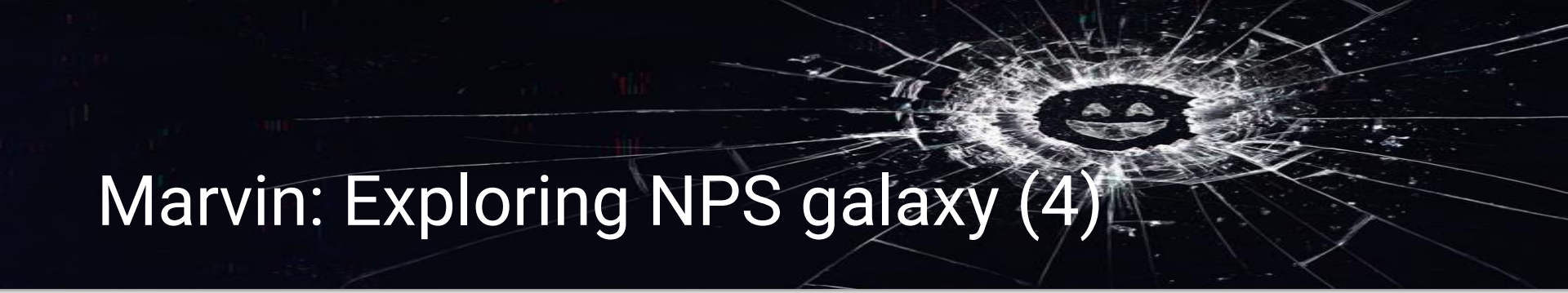
25 C and I NBOME: 2 times , stimulant effect

Oxycodone: 1 time

AH-2971

MT-45

DMT: 1 time, vaporized



Marvin: Exploring NPS galaxy (4)

Alpha PVP (α-Pyrrolidinopentiophenone)

- Powder form: insufflated or smoked, **every day for 3-4 days**, for 5-6 months Dosage till **300 - 400 mg** [suggested dosage in online fora is 25 - 30 mg]
- Effects : **Stimulation (+++)**, **mental (euphoria)**; **physical (energy)** ; sexual (arousal)
- **'Panic attacks'**: especially after at high dosage **Hyperpyrexia: 40°C**
- **Delusions** (Ekbom's syndrome, persecutory delusion)

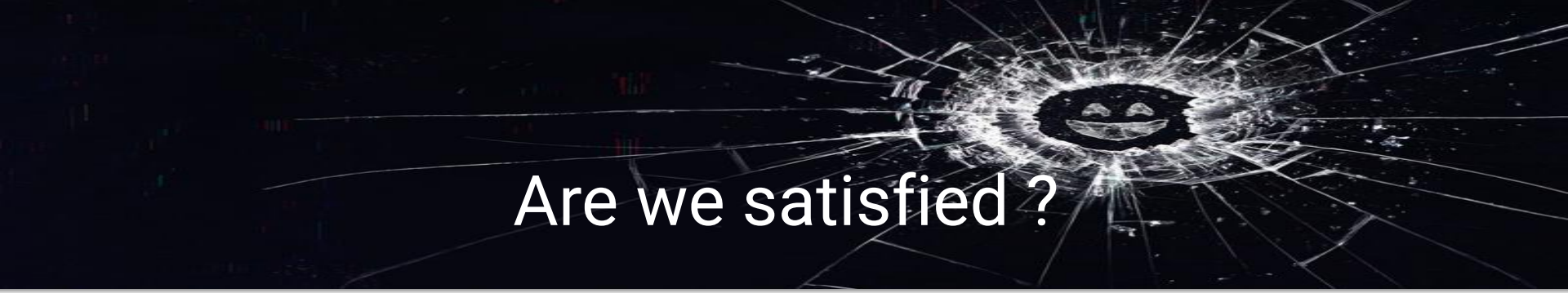
- **Arrival at psychiatric ward and then at our Unit where he revealed the use of compounds for the first time**

Marvin: Assessment phase (we can use current classifications*)

- **Stimulant (NPS) and cannabis dependence**
- **Psychotic episode induced by substances**
- **Schizoid Personality Disorder**

He participated to the Program (40 days) with individual and group psychotherapy; change of AD, he progressively integrated to the group changing his mind about NPS.

(***Clinical interviews, SCID I II; SCL-90; MMPI-2**)



Are we satisfied ?

Psychiatric disturbances?

Personality ? What about “Dark traits”*?

(Machiavellianism, psychopathy, narcissism, sadism)

Addictions? What is the role of Internet ?

* Kircaburun, K., Jonason, P. K., & Griffiths, M. D. (2018). The Dark Tetrad traits and problematic online gaming: The mediating role of online gaming motives and moderating role of game types. *Personality and Individual Differences*, *135*, 298-303.

.

PUI : Problematic Use of Internet

- **Problematic Use of the Internet (PUI)** is an **umbrella term.**

- According to literature there's **a range of repetitive impairing behaviors** (excessive and compulsive video gaming, compulsive sexual behaviour, buying, gambling, streaming or social networks use).

- **The actual scientific effort is bringing together scientists** and clinicians from across different fields (impulsive, compulsive, and addictive disorders) **to better understand the phenomenon** [European Cooperation in Science and Technology (**COST**) Action Programme (CA 16207)]

Fineberg, N. A., Demetrovics, Z., Stein, D. J., Ioannidis, K., Potenza, M. N., Grünblatt, E., ... & Grant, J. E. (2018). Manifesto for a European research network into Problematic Usage of the Internet. *European Neuropsychopharmacology*, *28*(11), 1232-1246.
.

- **There's a great debate about it.**

- A **spectrum of Internet usage**, from **controlled** to **uncontrolled**, is recognized (Billieux et al., 2017).

- **Psychiatry is beginning to acknowledge PUI.**

- **Key point**: **"old" psychopathological phenomena that have been reconfigured** and **others are intrinsically linked to cyberspace.**

Aboujaoude, E. (2010). Problematic Internet use: an overview. *World Psychiatry*, *9*(2), 85-90.

Spada, M. M. (2014). An overview of problematic Internet use. *Addictive behaviors*, *39*(1), 3-6.

Two potential processes:

(1) **Problematic Internet Use may predispose to develop psychiatric disease**

(1) **Psychiatric patients can develop Problematic Internet Use** as a coping strategy

The studies, so far, were not designed or statistically powered to detect the **nature of the association** (cause, effect, or independent).

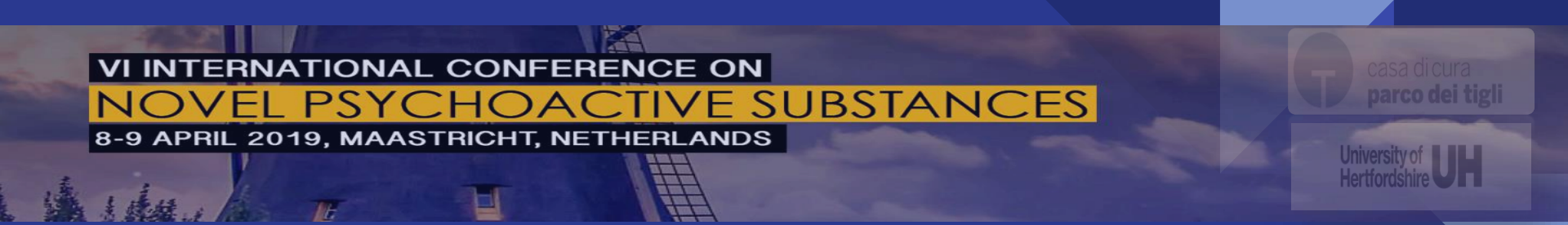
Our work as clinicians is challenging.

Our clients are changing.
Our environment is changing.


Be ready.

Part 3

NPS, PIEDs and Exercise Addiction



The health risks of looking fit. Supplement use, appearance anxiety and exercise addiction

Pierluigi Simonato
MD, PhD, Psychiatrist

Dual Diagnosis Unit - Parco dei Tigli, Padova (Italy)
School of Life and Medical Sciences University of Hertfordshire (UK)

PLOS ONE

RESEARCH ARTICLE

The emergence of Exercise Addiction, Body Dysmorphic Disorder, and other image-related psychopathological correlates in fitness settings: A cross sectional study

Ornella Corazza[1,2]*, Pierluigi Simonato[1,3], Zsolt Demetrovics[4], Roisin Mooney[1], Katinka van de Ven[5], Andres Roman-Urrestarazu[6,7], Lili Rácmolnár[4], Ilaria De Luca[1], Eduardo Cinosi[1,8], Rita Santacroce[1,9], Massimo Marini[10], David Wellsted[1], Keith Sullivan[1], Giuseppe Bersani[2], Giovanni Martinotti[1,9]

1 Centre for Clinical & Health Research Services, School of Life and Medical Sciences, University of Hertfordshire, Hatfield, United Kingdom, **2** Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Rome, Italy, **3** Dual-Diagnosis Unit, Clinic Parco dei Tigli, Padova, Italy, **4** Department of Clinical Psychology and Addiction, Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary, **5** Social Policy Research Centre, University of New South Wales, Sydney, Australia, **6** Institute of Public Health, University of Cambridge, Cambridge, United Kingdom, **7** Department of International Health, Maastricht University, Maastricht, Netherlands, **8** Hertfordshire Partnership University NHS Foundation Trust, Hatfield, United Kingdom, **9** Department of Neuroscience, Imaging, and Clinical Science, University of Chieti Pescara, Chieti, Italy, **10** Department of Psychiatry, University of Padua, Padua, Italy

The setting of the Keep Fit Study

- A large cross-sectional sample **(N=1711)** was surveyed in fitness settings using the **Exercise Addiction Inventory** (EAI), **Appearance Anxiety Inventory** (AAI) and Rosenberg's Self Esteem Scale (RSE)
- Questions surrounding the **use of fitness supplements**.
- Participants were over 18 years old with membership to a **fitness club**. To recruit a suitable sample, a snowballing technique was used.
- Four countries
- https://humanenhancementdrugs.com

Overall 1711 participants were recruited from the **United Kingdom (377), Italy (494), Netherlands (189) and Hungary (651).**

The sample consisted of **both female (66.3%) and male participants**, and had a mean age of 30 (±10.26).

Most respondents were **employed (63.6%)**, while 29% were students, 5.3% unemployed and 1.2% retired at the time of the survey.

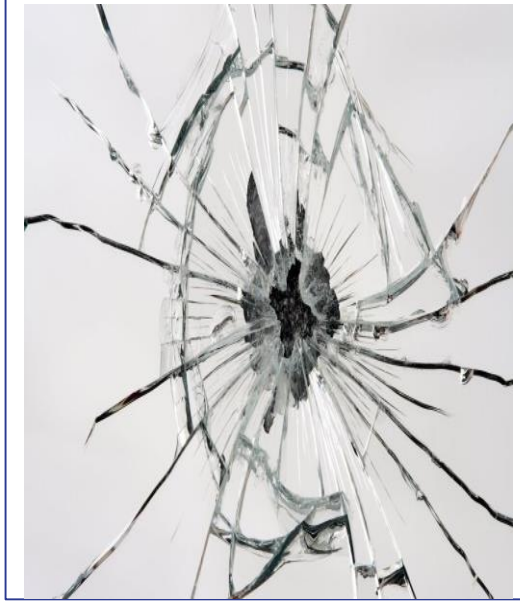
The overall sample was engaged in a **heterogeneous class of fitness activities**, including walking (53.3%), running (79.2%) and body weight exercises (28.7%).

Table 1. Sample description (N= 1711) with specification of demographics and types of physical activities

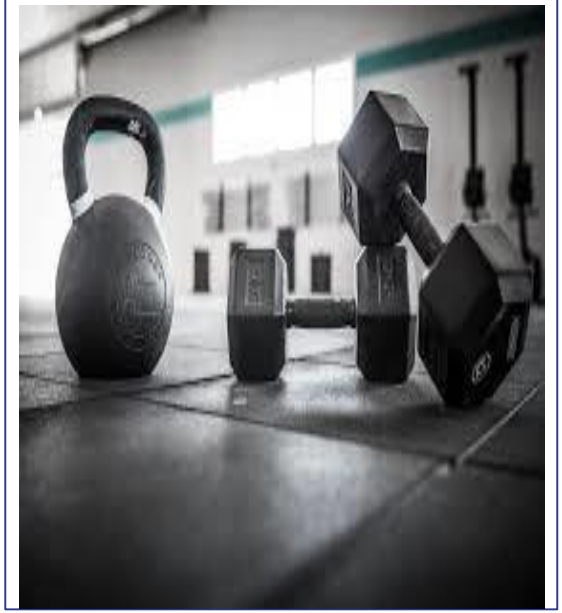
General information (n=1711)		n	Percentage	Male		Type of activities*	
Country	Hungary	651	38%	11.4%		Walking	53.3%
	Italy	494	28.9%	48%		Running	79.2%
	UK	377	22%	46.9%		Body-lifting	28.7%
	Netherlands	189	11%	47.1%		Lift- weights	27.2%
						Swimming	19.6%
Age	m=30.17± 10.26					Hockey	17.9%
						Riding	16.9%
						Hiking	12.8%
Gender	Male		577	33.7%		Gymnastics	11.3%
	Female		1134	66.3%		Football	8.9%
						Yoga	8.7%
						Bike fast	8.6%
						Aerobics	8.6%
						Resistance	8.4%
Occupation	Employed		1091	64.3%		Martial arts	7.8%
	Student		496	29.2%		Skipping Rope	7.0%
	Unemployed		89	5.2%		Volleyball	6.7%
	Retired		20	1.2%		Rugby	5.7%
						Basketball	4.5%
						Tennis	4.3%

The problem

BDD



EA



PIEDS

What is the **BDD (Body Dysmorphic Disorder)**?

Body dysmorphic disorder (BDD) is a common, **severe disorder** characterized by distressing or impairing **preoccupation with perceived imperfections in one's physical appearance** and time-consuming **rituals** (e.g., excessive mirror checking, cosmetic surgery seeking) aimed at checking, hiding, or fixing "flaws."

BDD has similarities to OCD (Phillips et al., 2007, Phillips et al., 2010) and is **classified as an obsessive-compulsive and related disorder** in the fifth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association, 2013)

Although OCD and BDD share many similarities, they also have important differences, such as poorer insight and more frequent **comorbidity with depression and substance use disorders in BDD.**

Major depressive disorder is the most common comorbid disorder in BDD (lifetime rates of 75–82%), and depressive symptoms (e.g., anhedonia, low energy, difficulty concentrating, hopelessness) can thwart one's motivation or engagement in CBT.

Hardardottir, Hrefna et al. "Body dysmorphic disorder: Symptoms, prevalence, assessment and treatment." *Laeknabladid* 105.3 (2019): 125-131.

Greenberg, Jennifer L., et al. "Predictors of Response to Cognitive-Behavioral Therapy for Body Dysmorphic Disorder." *Behavior Therapy* (2019).

In adult population–based studies, the **point prevalence rates range from 0.7% to 2.4%** on the basis of DSM-III-R or DSM-IV criteria (Bouman et al., 2017, Franca et al., 2017, Mollmann et al., 2017, Morselli et al., 2016). Other studies report rates in the general population that are as high as 5.8% (Mollmann et al., 2017).

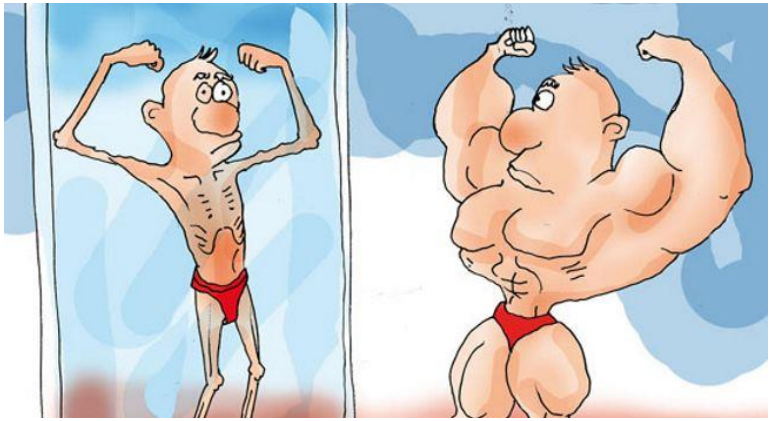
In **aesthetic specialties**, rates are noticeably higher, with a reported prevalence of 6.7% among general dermatology patients, **14.0% among cosmetic dermatology patients**, 10% in the maxillofacial setting, and **21% in patients seeking rhinoplasty** (Bouman et al., 2017, Brito et al., 2016, Locatelli et al., 2017).

Most studies report **a higher prevalence in women**, although two reviews report equal prevalence in men and women with differentiating factors being the areas of preoccupation.

Historically, the literature has cited **BDD as a clear contraindication to cosmetic surgeries and procedures** (Lee et al., 2017).

Muscle dysmorphia (MD), a condition in which the principal symptom is a marked preoccupation with one's body being insufficiently muscular, has been the subject of considerable **nosological debate in recent years.**

In the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM5), **it is currently classified as a subtype of body dysmorphic disorder (BDD)**



Sreshta, Nina, et al. "Muscle dysmorphia." *Body Dysmorphic Disorder: Advances in Research and Clinical Practice* (2017): 81.

AAI

Comparison of appearance

Repetitive check

Avoiding behaviours

Camouflaging

Avoiding reflective surfaces

….

Appearance Anxiety Inventory

Please tick the box that best describes the way you have felt about your appearance of a specific feature OVER THE PAST WEEK, INCLUDING TODAY

Name_____ Date_____

		Not at all 0	A little 1	Often 2	A lot 3	All the time 4
1	I compare aspects of my appearance to others					
2	I check my appearance (e.g. in mirrors, by touching with my fingers, or by taking photos of myself)					
3	I avoid situations or people because of my appearance					
4	I brood about past events or reasons to explain why I look the way I do					
5	I think about how to camouflage or alter my appearance					
6	I am focussed on how I feel I look, rather than on my surroundings					
7	I avoid reflective surfaces, photos, or videos of myself					
8	I discuss my appearance with others or question them about it					
9	I try to camouflage or alter aspects of my appearance					
10	I try to prevent people from seeing aspects of my appearance within particular situations (e.g., by changing my posture, avoiding bright lights)					

Veale, David, et al. "The Appearance Anxiety Inventory: Validation of a process measure in the treatment of body dysmorphic disorder." *Behavioural and Cognitive Psychotherapy*42.5 (2014): 605-616.

What is **EA (Exercise Addiction)**?

Exercise addiction falls within the field of **behavioural addictions**, similar to gambling disorder, but due to the **lack of sustained and methodologically rigorous evidence for exercise addiction as a morbidity**, **the disorder is not listed as a mental dysfunction** in the latest (fifth) edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5)

Pattern of behaviour in which there's a loss of control of the exercise: the subject acts compulsively, exhibits dependence, and experiences negative consequences to health as well as in his or her social and professional life.

Several terminologies are used for describing exercise addiction, including: *exercise dependence*, *compulsive exercise*, *obligatory exercise*, and *exercise abuse* .

Szabo, Attila, et al. "Focus: addiction: methodological and conceptual limitations in exercise addiction research." *The Yale journal of biology and medicine* 88.3 (2015): 303.

Bircher, Julianna, et al. "Exercise addiction and personality: a two-decade systematic review of the empirical literature (1995-2015)." *Baltic Journal of Sports and Health Sciences* 3.106 (2017): 19-33.

Exercise has been widely considered to be beneficial to health (Biddle & Mutrie, 2007; Warburton, Nicol, & Bredin, 2006). **When done without limit, however, exercise can be harmful**; it can become a compulsive and addictive form of exercise behaviour, particularly when it is performed for body image improvements or as a stress reliever (Griffiths, 1996; Terry, Szabo, & Griffiths, 2004).

The Four Phases Model of the exercise addiction (Freimuth et al., 2011) :
1- Recreational exercise (pleasure)
2- At-risk exercise (escape)
3- Problematic exercise (daily life)
4- Exercise addiction (main activity)

Exercise addiction researchers provided valid tools to assess the prevalence of EA, which is low, ranging **between 0.3% and 0.5% among the general adult population** (Mónok et al., 2012), and between 3.0% and 6.0% among athletes or **regular exercisers** (Szabo et al., 2016). Nonetheless, this prevalence rate may reach over 20% in elite **endurance athletes** such those participating in triathlon and/or ironman races (Blaydon & Lindner, 2002; Youngman & Simpson, 2014). Studies suggest that men generally show higher scores in EA than women.

Dumitru, Delia & Dumitru, Teona & J. Maher, Anthony. (2018). A systematic review of exercise addiction: Examining gender differences. 10.7752/jpes.2018.03253.

EAI

1. Salience
2. Mood modification
3. Tolerance
4. Withdrawal symptoms
5. Conflict
6. Relapse.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Exercise is the most important thing in my life	1	2	3	4	5
Conflicts have arisen between me and my family and/or my partner about the amount of exercise I do	1	2	3	4	5
I use exercise as a way of changing my mood (e.g. to get a buzz, to escape, etc.)	1	2	3	4	5
Over time I have increased the amount of exercise I do in a day	1	2	3	4	5
If I have to miss an exercise session I feel moody and irritable	1	2	3	4	5
If I cut down the amount of exercise I do, and then start again, I always end up exercising as often as I did before	1	2	3	4	5

Szabo, Attila, and Mark D. Griffiths. "The exercise addiction inventory: A new brief screening tool." *Addiction research and theory* 12.5 (2004): 489-499.

PIEDS (Performance and Image Enhancing Drugs)

PIEDS are used to make us look and feel better.

More than a billion people apply, ingest or inject performance and image enhancing drugs and substances (PIEDS) daily to swell muscle mass, shed fat, sustain endurance, resist fatigue, stimulate energy, improve mood, tolerate pain, deflate inflammation, enhance relaxation, promote concentration, sharpen reactions, maintain alertness, reduce fluid, control steadiness, augment body shape, induce euphoria and strengthen confidence.

Whilst anabolic-androgenic steroids (AAS) have been studied since the 1980s [48], **an increasingly wide range of fitness enhancing products are advertised online** with misleading marketing strategies, such as drastically improving one's appearance in a faster and 'safer' way than traditional medicines or method.

It's an unexplored field: new context and aims, relationship with social context, relationship with Behavioural Addictions, relationship with sports.

PIEDS are enlisted as NPS.

Corazza, Ornella, et al. "The diffusion of performance and image-enhancing drugs (PIEDs) on the internet: the abuse of the cognitive enhancer piracetam." *Substance Use & Misuse* 49.14 (2014): 1849-1856.

Brennan, Rebekah. An Ethnopharmacological Study of The Injecting Use of Performance and Image Enhancing Drugs (PIED) Volumes I & II. Diss. Waterford Institute of Technology, 2018.

Smith, Aaron, et al. Performance and Image Enhancing Drugs and Substances: Issues, Influences and Impacts. Routledge, 2018.

PIEDS (Performance and Image Enhancing Drugs)

- **Muscle drugs** (e.g. AAS, hormones, GHB, CJC-1295)
- **Weight loss drugs** (e.g. diuretics, MHRA, sibutramine)
- **Image enhancing drugs** (e.g. Melanotan I II, finasteride)
- **Sexual enhancers** (e.g. Viagra, Tribulus terrestris)
- **Cognitive enhancers** (e.g. Piracetam, Modafinil)
- **Mood and behavioural enhancers** (e.g. diazepam, stimulants)

Evans-Brown, M (2012). Human Enhancement Drugs: The emerging challenges to public health.

Fitness products in the Keep Fit study

We asked about “Fitness products” (**39.8%**)

- Supplements
- Pharmaceuticals
- Legal
- Illegal

- **Online** and Fitness Shop

- **Side effects** (**8.6%**)

Type of Fitness Product * (n=657)	Percentage	**Source of purchase**	
Proteins	63.3%	Fitness Shop	48.6%
Vitamins	52.5%	Online	31.3%
Aminoacids	39.1%	Pharmacy	8.3%
Caffeine products	29.8%	Food Store	3.8%
Fish Oil	29.7%	Other source	8.0%
Mineral salts	13.1%		
Teas	12.8%		
Herbal products	9.4%	**Source of information**	
Antioxidants	8.2%	Online	41.4%
NO	8.2%	Friends	18.9%
Ginseng	7.9%	Personal Trainer	14.6%
Guaranà	7.0%	Magazine	10.5
Steroids	5.9%	Medical professionals	4.5%
Diuretics	4.9%	Family	3.7%
Thyroid hormones	3%	Other	6.3%
Laxatives	2.3%		
Amphetamine-like products	2.3%		
GH	1.8%	**Experienced side-effects**	
Sibutramine	1.1%	Yes	8.6%

** Multiple choice*

Keep Fit : results

Exercise Addiction Inventory (EA) and Appearance Anxiety Inventory (BDD)

EA and BDD

An average score of 18.51±4.2 was reported in the **Exercise Addiction Inventory** with no significant differences between male and female.

- **EA was detected in 11.7% of the overall sample**, considering the cut-off of the scale (24 points) as suggested in literature.
The latter was **higher amongst male (15%)**, who scored over 24 points in the Exercise Addiction Inventory.

The **Appearance Anxiety Inventory** indicated an **alarmingly high prevalence of appearance anxiety** and low body satisfaction across the four countries.

- On the Appearance Anxiety Inventory, **38.5% of the overall was found at risks of BDD.**

Table 2. Exercise Addiction Inventory (EAI), Appearance Anxiety Inventory (AAI), Rosenberg Self-Esteem (RSE) scores and use of fitness supplements with specification of gender differences

	Sample	Male	Female		Over Cut Off		
EAI	m=18.51±4.2	m=18.44±4.38	m=18.65±3.97	n.s.	**11.7% (n=191)**	Male=81 (15%) Female=110 (10%)	$\chi2$=8.25 p<0.001
AAI	m=18.14±5.7	m=18.07±5.87	m=18.28±5.58	n.s.	**38.5% (n=577)**	Male=108 (21.4%) Female= 468 (47.2%)	$\chi2$=93.87 p<0.001
RSE	m=12.33±2.48	m=12.19±2.53	m=12.58±2.37	f=8.86 p<0.001			
Fitness supplements	Yes 39.8% (n=657)	Yes 51.3%	Yes 34.2%	$\chi2$=44.47 p<0.001	Note: Results seem influenced by country		Hungary Yes 52.3% (n=332) $\chi2$= 155 p<0.001

Note: m= mean; $\chi2$ = chi square; f= ANOVA

EAI and AAI in the four countries

Table 3. Exercise Addiction Inventory (EAI) and Appearance Anxiety Inventory (AAI) results per country

	Netherlands	Hungary	UK	Italy	
EAI over cut-off (scored over 24)	20.9%	9.3%	16.1%	7.9%	X=31.53 p<0.001
AAI over cut-off (scored over 19)	38.1%	51.5%	30.0%	29.5%	X=64.29 p<0.001

Fitness supplements users

Users vs Non Users

Respondents who declared the use of fitness supplements **scored significantly higher ($p<0.001$) in both the Appearance Anxiety Inventory and the Exercise Addiction Inventory** (Table 4) with an average score of m=19.62 in the Exercise Addiction Inventory, m=18.91 in the Appearance Anxiety Inventory scale and m=12.27 in the Rosenberg Self-Esteem scale.

However, no significant difference was recorded in the Rosenberg Self-Esteem scale. Across the sample, a higher prevalence of EA was found among those using fitness enhancing products compared to non-users (m=19.62±4.24 vs 17.78±4.24 $p<0.001$) across both the male and the female sample (Table 4).

Table 4. Fitness supplements users vs non-users: differences considering to Exercise Addiction Inventory, Appearance Anxiety Inventory, Rosenberg Self-Esteem and their country

	Users (n=657)	Non Users	
EAI	m=19.62±4.24	m=17.78±4.24	f=75.89; p<0.001
AAI	m=18.91±5.88	m=17.63±5.62	f=17.99 p<0.001
RSE	m=12.27±2.52	m=12.38±2.44	n.s.
Hungary	52.3%	$\chi2$= 155 p<0.001	
Netherlands	52.2%		
UK	41.3%		
Italy	16.9%		

What can we say about BDD, EA and PIEDs use?

Three different logistic models were created according to the gender of participants (Table 6).

1. Across the whole sample, **EA emerged as a strong predictor of the consumption of fitness supplements**. This risk appeared to be over three times higher in those reporting Exercise Addiction Inventory scores over the cut-off (p<0.001, **OR = 3.03** with a Confidence Interval (CI) ranging from 2.15 to 4.28.

2. The risk of using supplements was much higher in the **male sample** reporting Exercise Addiction Inventory score over the clinical cut-off (OR = 3.25, CI 1.81-5.86). In those cases where EA was identified, the risk of using sport supplements was over five times higher, **making EA the strongest predictor for this group.**

3. Although EA was also a significant predictor for supplement use, but to a lesser extent in the **female group** (OR= 2.50), two additional psychopathological factors emerged: **Appearance Anxiety (OR = 1.5**; CI 1.20-2.12) and **low self-esteem** as measured by the Rosenberg Self-Esteem scale (OR = 1.08; CI 1.02-1.15).

Table 6. Logistic regression models with specification of gender

		B	ES	Wald	df	Sig	Odds Ratio (OR)	Confidence Interval (CI)	
								Min	Max
Model I: fitness supplements (whole sample)	Age	.000	.006	.000	1	.989	1.000	.989	1.011
	RSE total	.030	.023	1.796	1	.180	1.031	.986	1.078
	EA over the Cut Off (1)	**1.111**	**.175**	**40.061**	**1**	**.000**	**3.037**	**2.153**	**4.283**
	AAI over the Cut off (1)	.243	.116	4.352	1	.037	1.275	1.015	1.602
	Constant	1.118	.362	9.526	1	.002	.327		
Model II: fitness supplements (male)	Age	.010	.009	1.167	1	.280	1.010	.992	1.027
	RSE total	-.073	.037	3.810	1	.051	.930	.864	1.000
	EA over the Cut Off (1)	**1.182**	**.300**	**15.508**	**1**	**.000**	**3.259**	**1.810**	**5.868**
	AAI over the Cut off (1)	.455	.240	3.592	1	.058	1.577	.985	2.525
	Constant	-.852	.608	1.963	1	.161	.427		
Model III: fitness supplements (female)	Age	-.006	.008	.596	1	.440	.994	.980	1.009
	RSE total	**.083**	**.030**	**7.827**	**1**	**.005**	**1.087**	**1.025**	**1.152**
	EA over the Cut Off (1)	**.918**	**.226**	**16.541**	**1**	**.000**	**2.504**	**1.609**	**3.898**
	AAI over the Cut off (1)	**.469**	**.145**	**10.389**	**1**	**.001**	**1.598**	**1.202**	**2.125**
	Constant	1.297	.466	7.740	1	.005	.273		

What can we understand so far….

In our study **a medium level of EA was recorded across the whole sample** (Table 2) indicating higher exposure to physical injuries and withdrawal symptoms, like depression, anxiety and mood swings. Higher levels of EA of clinical concern (**over the clinical cut-off score**) were found among the **11.7%** of the sample, **especially male** ($p<0.001$).

Overall participants were **concerned about their physical appearance**. This was confirmed by the high risk of manifesting a BDD among the sample that was significantly **higher amongst females** (Table 2).

This result was much higher not only than the scores reported among the general population (where BBD prevalence ranges from 0.7% to 2.3%), but also of those found among at risk populations.

What can we understand so far….

A **large percentage (39.8%)** of respondents reported the use of different **fitness products**.

The diffusion of fitness products, especially PIEDs, remains marginally studied and regulated, and deserves prompt responses from authorities informed by evidence base.

Online advertising (41.4%) and peer-pressure (14.6%) appeared to be key drivers for the use of sporting and muscular enhancing products at gyms.

Medical supervision for the use of these substances was sought only by 4.5% of the sample.

What can we understand so far….

The applied logistic regression models revealed for the first time **an association between the consumption of fitness supplements and the level of EA across sample**, suggesting a **predictability of use** (Table 6).

Although preliminary, these findings indicate that intake of fitness enhancing products could be **motivated by such underlying psychopathological and image-disturbance features.**

The statistical significance of **EA** was particularly high for **males**, where the risk of fitness supplements intake was from 1.8 to 5.8 times higher than that reported among females (Table 6).

Conversely, the substance intake by the **female group** was more influenced by **appearance anxiety and self-esteem.**

Such **gender differences** underlying the intake of fitness supplements must be explored very carefully in future analysis.

Limitations

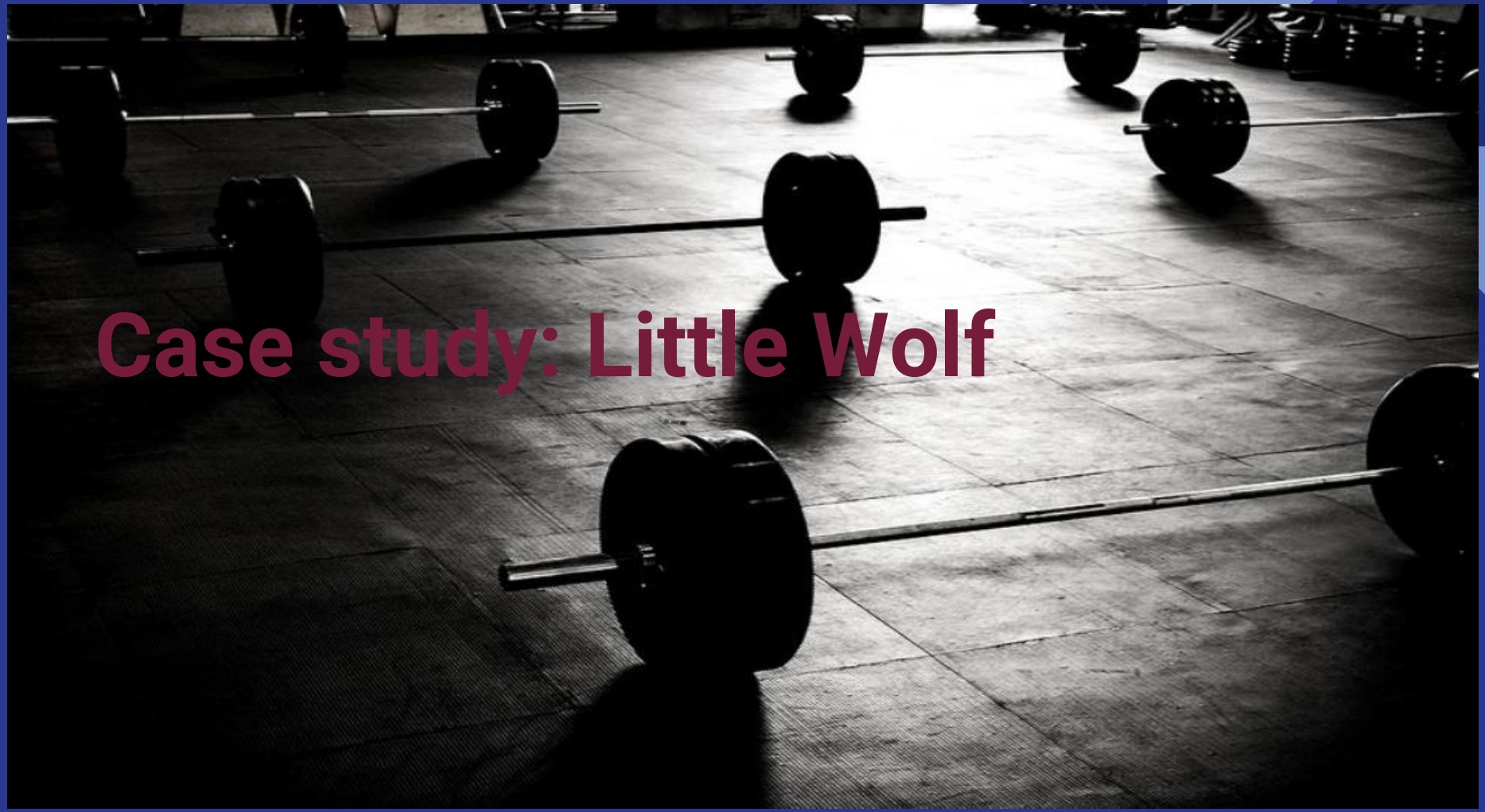
Although Keep Fit made a significant contribution to the field, authors remain aware of the study limitations, which can be summarised as follows:

(a) the assessment of a non-stratified population with different recruitment procedures among countries

(b) the absence of a structured psychiatric interview able to assess the emerged underlined pathologies;

(c) the use of fitness products was self-reported and not validated by any biological testing;

(a) the lack of information on the frequency and duration of the exercise and use of fitness products.



Case study: Little Wolf

Case study

Admission in our Unit: **cocaine**
Treatment: Valproic Acid (not compliance); Alprazolam
Age: **33 years old**
Anamnestic features:

- Normal childhood, family
- Studies: Liceo Scientifico
- Jobs: several, different low level jobs; last one: logistic administration
- Previous issues: misuse of ecstasy as recreational drug, psychotherapy and psychiatric support (24-27 yo), **not main psychiatric events**
- Persistent problems with cocaine through years , nasal consumption

Case study: the assessment

AAI: scoring of 23 (cut-off 19 points)

- Important anxiety regarding the **physical aspect**; presence of a undiagnosed BDD; important bulling history starting 13 years old.
- The physical appearance became the only way to appreciate.
- At 16 yo started gym, several activities, bodybuilding
- Statement of the father: “You will be healed when you close the mirror in the closet”
- Great attention to aliment and supplement

Case study: the assessment

EAI:

- Over the clinical cut-off of the scale (24) (cut off 24)
- Training twice day during our recovery
- **Training 6 times** at week during his routine: the key motivation was to fell better and fell accepted
- He follow several Bodybuilders and athletes online

Case study

PIEDS

To enhance his performance he used in the meantime amino acids, protein and creatine but they did not produce desire effects.

When he was 30 years old, his use of NPS increased and he started with androgen and anabolic steroid (AAS):

- SUSTANON 250 mg /TESTOVIS 100mg (testosterone proprionate)
- WINSTROL (Stanozolol) 2mg cpr
- DECA DURABOLIN (Nandrolone) 25 mg im

- DIANABOL (**methandrostenolone**) 5 -15 mg cpr
- TRENBOLONE im

Case study

The use of PIEDs was recommended by his personal trainer and a nurse;

1-2 times in the year, 3-6 weeks

They also suggested a cycle of 2 or 3 AAS with **blood exams every 3 months**; interestingly **he never had side effects**.

He never took growth hormone (GH) even if he desired it.

Case study

- He was interviewed with ASI (Addiction Severity Index),SCL-90-R test/re-test (Symptom Checklist), BDI-II (Beck Depression Inventory), AUDIT (Alcohol use disorders identification test), SCID-5-PD(Structured Clinical Interview for DSM-5).
- The interview with SCID-5-PD, revealed a **personality disorder**, **Body Dismorfic Disorder** (BDD) and **a stimulants use disorder** (cocaine).

- **AAI : 23 EAI; 24**

Case study

Choose of a correct pharmacotherapy: not gain loss; **SSRI high dosage**, (not mood stabiliser) [Vortioxetine 20 mg; Trazodone 150 mg]

- Suggest a personal psychotherapy CBT
- Continue with the local Addiction Service

In the second recovery in our unit, the patient scored lower in the AAI and EAI, declared less anxiety especially towards his body and decided to start a community program according with SERD.

…. We cannot forget….

World Health Organization

Health Topics | Countries | News | Emergencies

Global Strategy on Diet, Physical Activity and Health

- Diet, Physical Activity & Health
- Global strategy development
- Childhood overweight & obesity
- Documents & publications
- Related links

Physical Activity and Adults

Recommended levels of physical activity for adults aged 18 - 64 years

In adults aged 18–64, physical activity includes leisure time physical activity (for example: walking, dancing, gardening, hiking, swimming), transportation (e.g. walking or cycling), occupational (i.e. work), household chores, play, games, sports or planned exercise, in the context of daily, family, and community activities. In order to improve cardiorespiratory and muscular fitness, bone health, reduce the risk of NCDs and depression:

Photo: V. Collazos

1. Adults aged 18–64 should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week or do at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity.
2. Aerobic activity should be performed in bouts of at least 10 minutes duration.
3. For additional health benefits, adults should increase their moderate-intensity aerobic physical activity to 300 minutes per week, or engage in 150 minutes of vigorous-intensity aerobic physical activity per week, or an equivalent combination of moderate- and vigorous-intensity activity.
4. Muscle-strengthening activities should be done involving major muscle groups on 2 or more days a week.

Journal List › World Psychiatry › v.15(2); 2016 Jun › PMC4911759

World Psychiatry
OFFICIAL JOURNAL OF THE WORLD PSYCHIATRIC ASSOCIATION (WPA)

World Psychiatry. 2016 Jun; 15(2): 176–177.
Published online 2016 Jun 5. doi: 10.1002/wps.20331

PMCID: PMC4911759
PMID: 27265709

Physical activity and mental health: evidence is growing

Stuart Biddle [1]

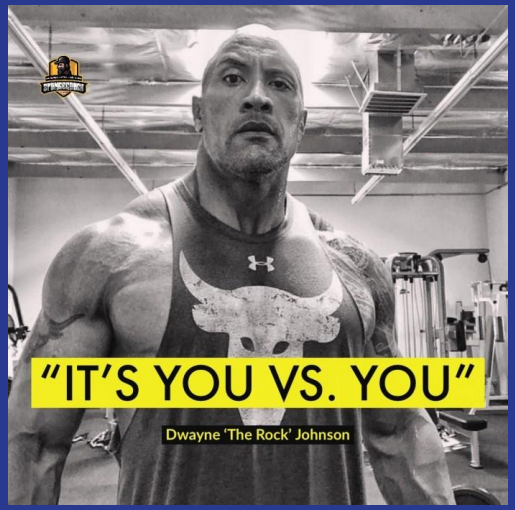
ELSEVIER

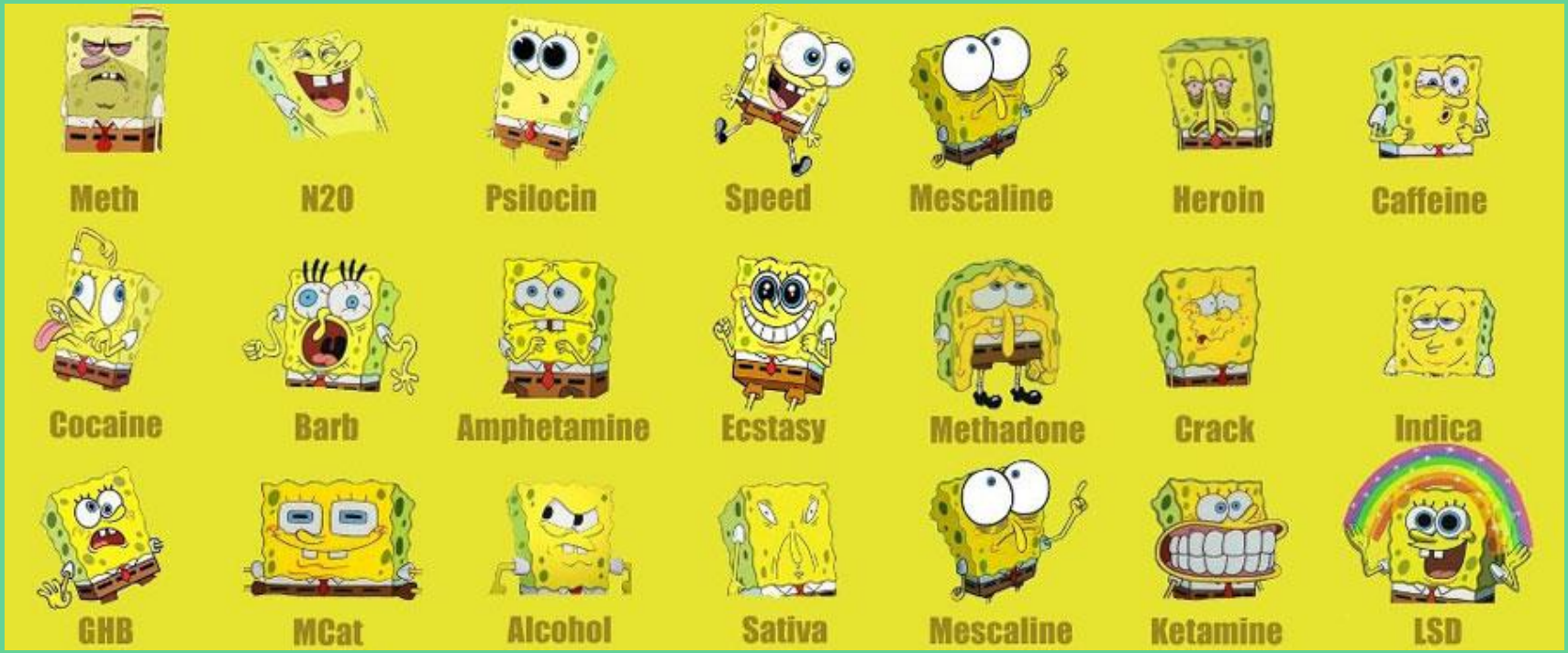
Mental Health and Physical Activity
Available online 11 December 2018
In Press, Corrected Proof

Physical activity and depression, anxiety, and self-esteem in children and youth: An umbrella systematic review

Leila Pfaeffli Dale [a], Leigh Vanderloo [b, c], Sarah Moore [d, e], Guy Faulkner [a]

Show more


"IT'S YOU VS. YOU"
Dwayne 'The Rock' Johnson



Thanks for you attention