

‘Substance misuse; aspetti neuropsicofarmacologici e clinici’

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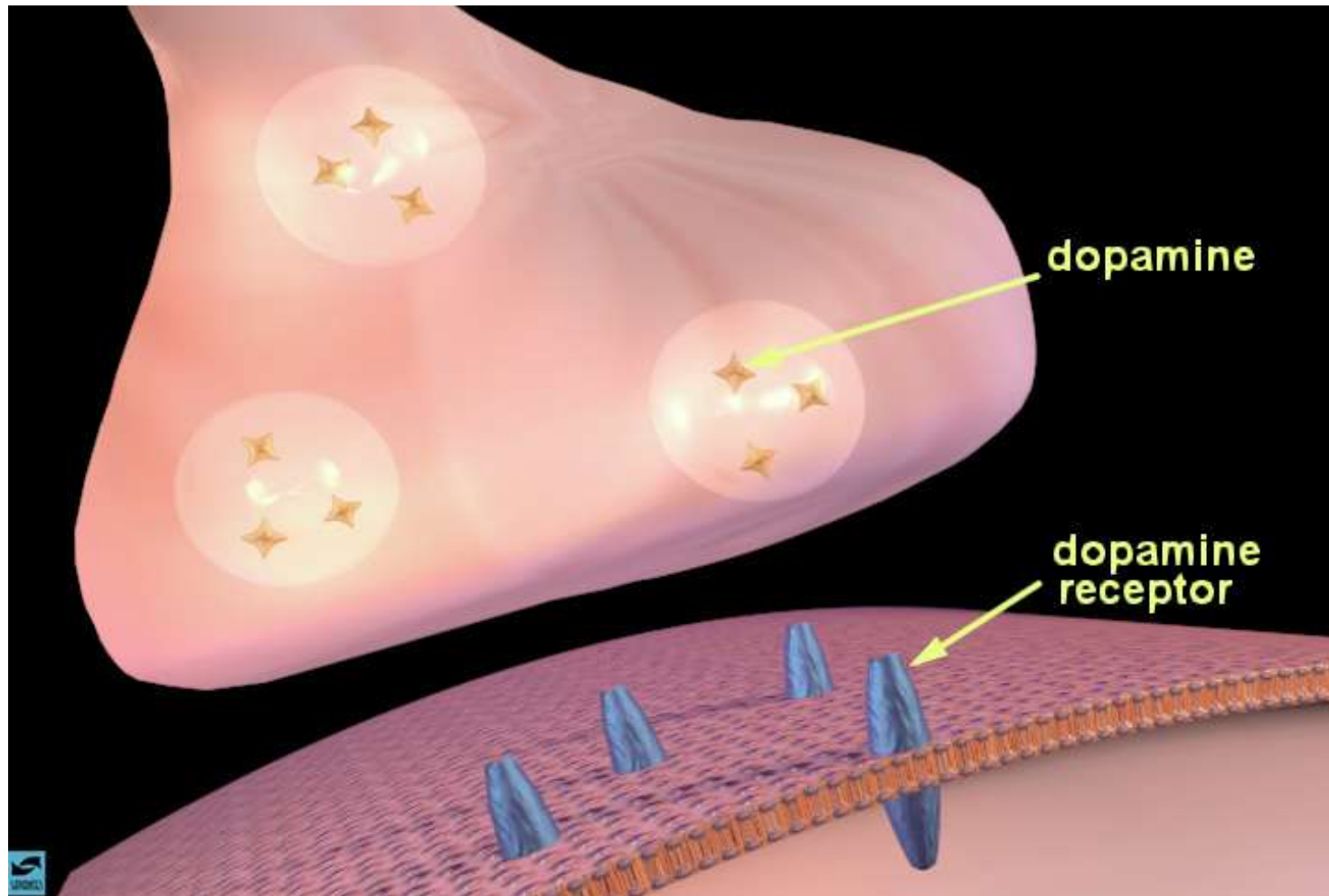
University of Hertfordshire (UK)

Hertfordshire Partnership NHS Foundation Trust

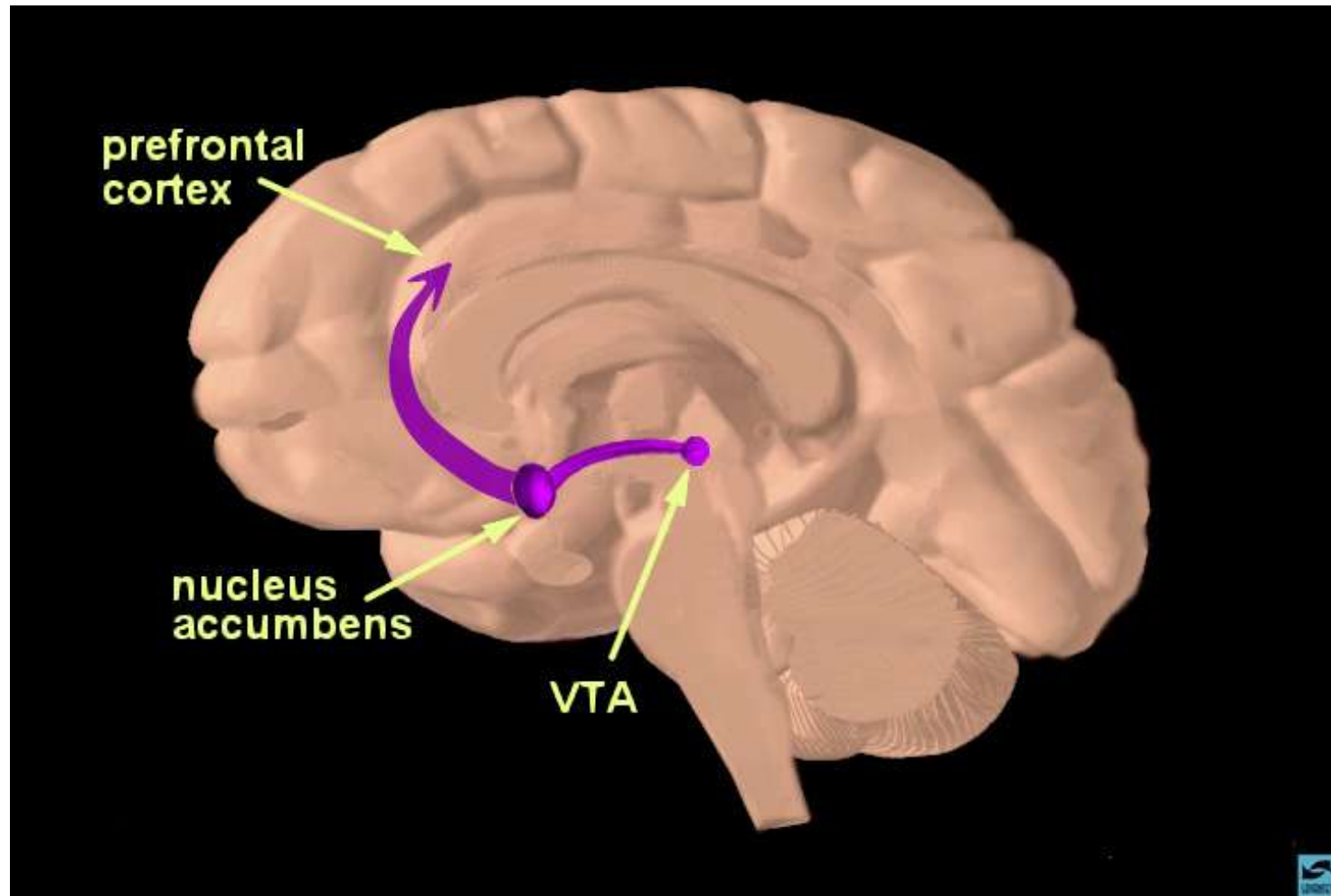
(2012)



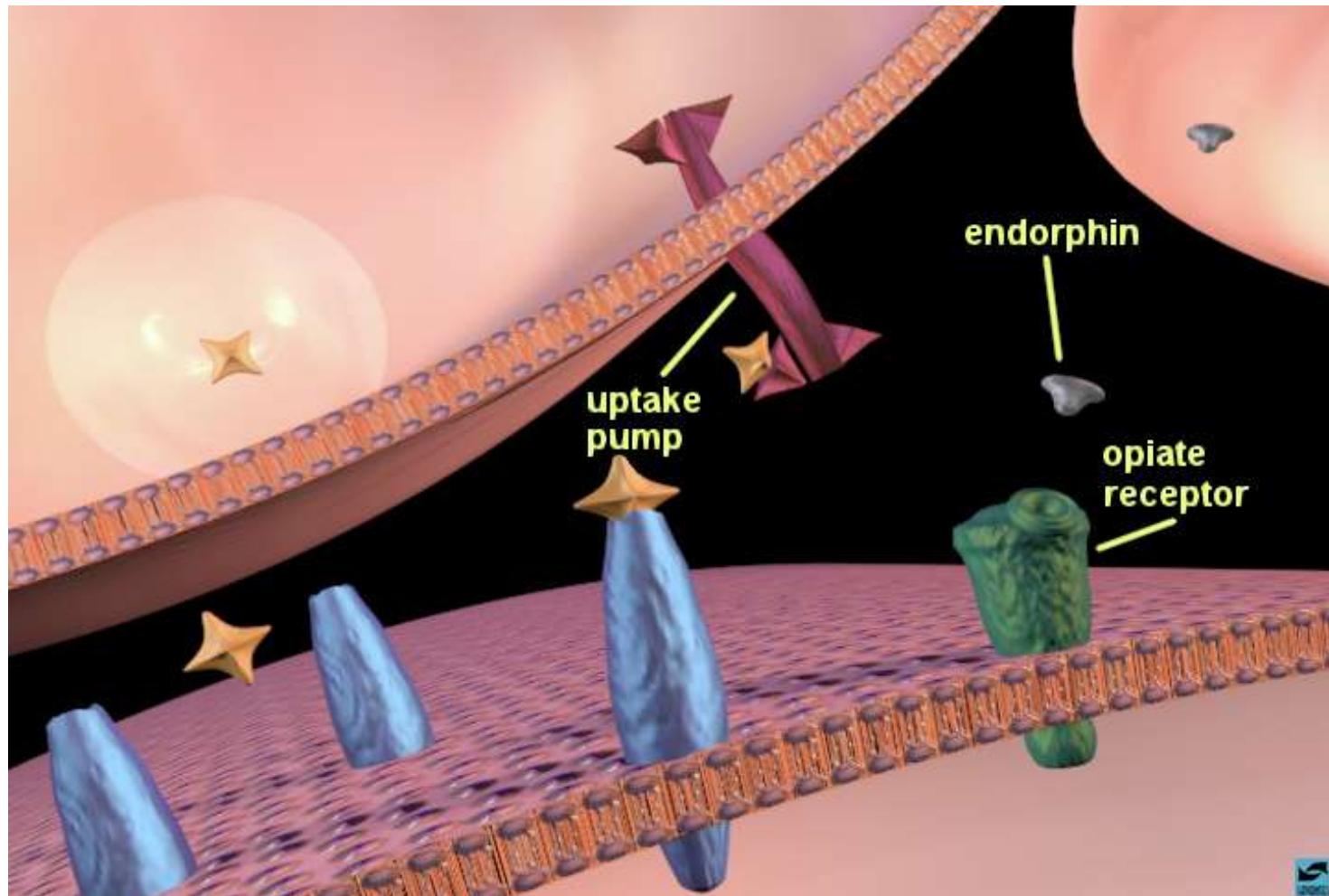
The synapse transmission



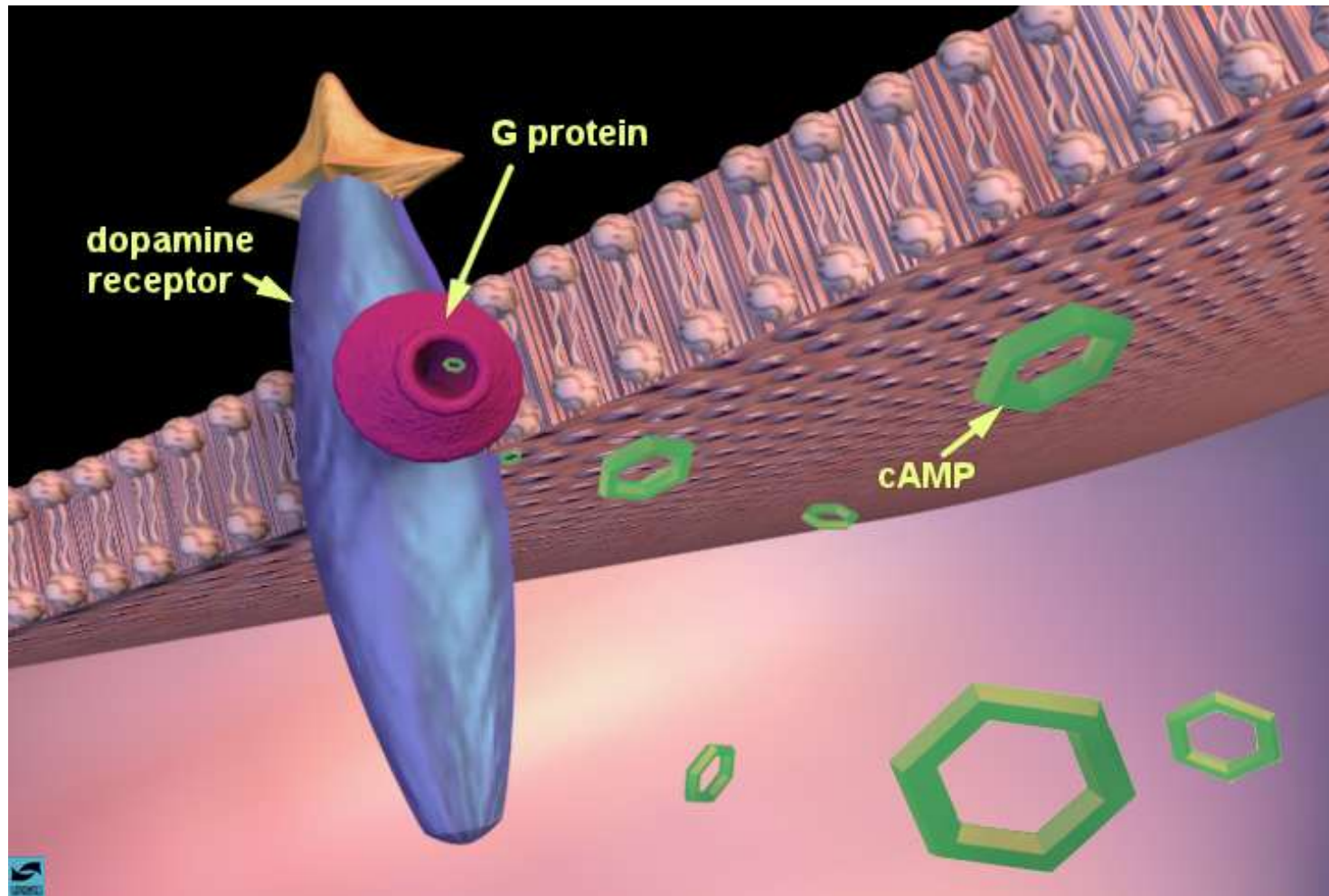
The reward pathway



DA neurotransmission



Dopamine and the production of cyclic AMP



Polypharmacy use



- alcohol is taken with ecstasy at the beginning of the night to get a stronger/better high (MDMA, whilst in the presence of alcohol, shows more significant physiopathological effects. Other options: pre-party packages containing SSRIs; moclobemide
- Cocaine, amphetamines and/or additional ecstasy tablets are taken to maintain arousal and a state of alertness (the MDMA entactogenic effects fade away in 2 – 4 hours).
- Finally, opiates and/or high (i.e. sedatives) dosages of alcohol are taken in the last part of the night to calm down before going home since the untoward after-effects of ecstasy (namely: irritability and restlessness) persist well beyond the end of the empathogenic and entactogenic pleasurable effects.

History of a psychonaut; case report no.1

SUMMARY

Uppers: Cocaine; Amphetamines; Cathinones

Downers: Benzodiazepines✓; Opiates✓; Alcohol✓
Barbiturates; Kava-Kava

All Arounders: LSD; Mescaline; DMT; Yage; Ayahuasca
PCP; Ketamine; MDMA; MDA; THC✓;
Ibogaine.

(✓ current use).

Case Report no. 2; list of the psychoactive substances an 18 yr old was purchasing online (alphabetical order):

- **Amisulpride**
- Bupropion
- Caffeine tablets/Minikikke
- Cannabis seeds
- Codeine
- D,L-phenylalanine
- **Ephedrine hydrochloride**
- **Gabapentin**
- **GBL and GHB**
- Ginseng
- Isopropyl nitrate
- **Kava-kava**
- **Ketamine**
- **Methylphenidate**
- Niacinamide
- Nitrous oxide
- Phenelzine
- Phenylalanine
- **Pregabalin**
- Rhodiola rosea
- **Salvia divinorum**
- **Selegiline**
- Sildenafil/Viagra

- Tryptophan
- Various antihistamine drugs
- Various benzodiazepines

More in particular, he was giving his preference to the following **combinations**:

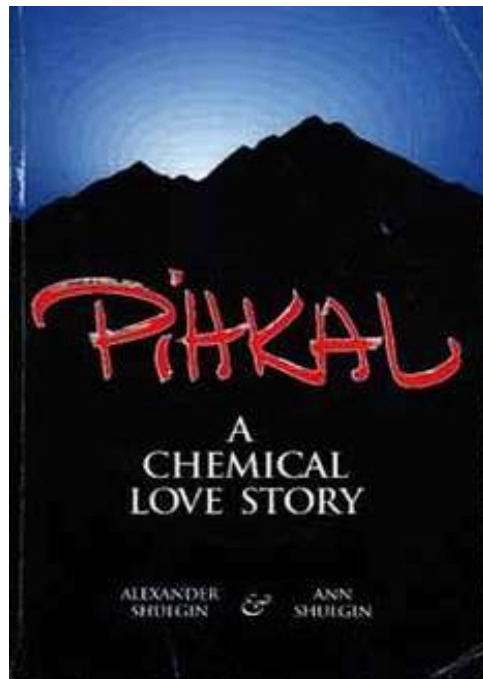
- **Methylphenidate plus clonazepam**
- Selegiline plus benzodiazepines plus cannabis plus SSRIs
- Cannabis plus benzodiazepines
- **GHB plus benzodiazepines**

Case report no. 3

- 17-yr-old
- **MDPV/bath salts**(snorted); £15-£30 for 1g; 300 doses in the last year or so
- **Mephedrone/meow meow/miao miao** (snorted); £7 for 1g (he once did 18g in a day!)
- **dimethocaine** (snorted); like cheap cocaine with 90 mins rush; £180 for 25g
- **6-APDB** (6-(2-Aminopropyl)-2,3-dihydrobenzofuran) or also marketed as **Benzo Fury**, snort/bomb white crystals; £20 for 1g
- **5-IaI/NRG-2** (5-Iodo-2-aminoindane); snorted and felt like MDMA
- **MDAi/whoof whoof/bau bau** (snorted); white powder; £10 for 1g; tried 2 or 3 doses.

PIHKAL Phenethylamines I Have Known And Loved

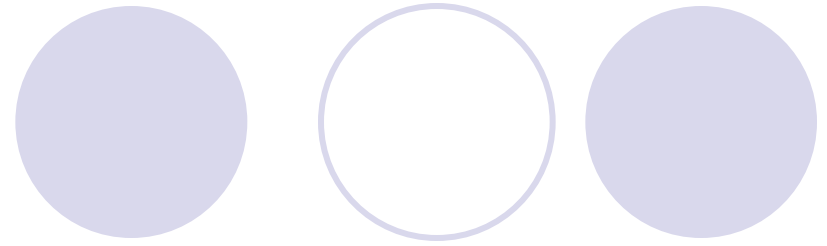
1991; 179 PEAs



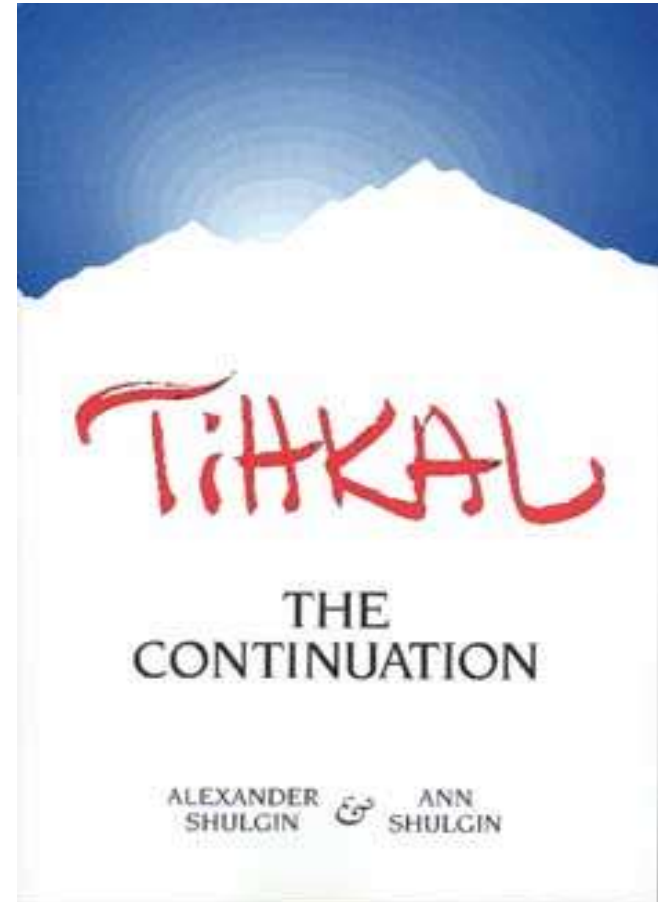
‘Entactogens/empathogens’: the XTC-like drugs

- **MDA** (‘love drug’, the parental compound of MDMA)
- **MDEA** (‘Eve’, which has effects similar to those of MDMA)
- **MBDB** (‘TNT’)
- **2-CB** (‘nexus’)
- **BOD** (allegedly providing yourself with ‘...16 hours of inner strength, good mood and contentedness’)
- **DOB** (reported to be 33 times more powerful than MDMA itself; effects would last for up to 24 hours)
- **4-MTA** (‘flatliners’; likely to be the result of the work of some researchers who were looking for new serotonergic agents)
- **2C-T-7** (‘Blue Mystique’; created by A Shulgin and also one of his personal favourites). There is a complete series of 2C-T compounds (which includes **2Ci**, **2C-T-2** etc), either been synthesized already or just theorised

Tryptamines



- **Tryptamines I Have Known And Loved (1997)**
- **64** psychoactives described)
- Shulgin & Shulgin: **The Shulgin Index** 2011
- **120** novel psychoactives



Psychonauts' suggested combinations of psychedelics

- '.....Similar to combining **DMT/DPT/5-MeO-DMT with ketamine**, combining **4-acetoxy-DET with ketamine** also provides an incredible synergy. Highly recommended for the **cosmic-mystical near-death inclined!..... Xenon gas while on mushrooms or LSD** comes in at a close second. '

PSYCHONAUT WEB MAPPING PROJECT

● Project Details

- 2-year EC funded (January 2008 – December 2009)
- Principal Investigator:
 - » Professor Fabrizio Schifano, University of Hertfordshire and HPFT Trust
- Project Manager:
 - » Dr Paolo Deluca, IoP, London
- Associated Partners:
 - » UK: St George's University of London (Main Beneficiary)
 - » Finland: A-Clinic Foundations (A-Klinikka)
 - » Norway: Bergen Clinics Foundation
 - » Italy: Servizio Salute Regione Marche
 - » Belgium: De Sleutel
 - » Spain: IMIM-IMAS
 - » Germany: University of Duisberg-Essen
 - » UK: University of Hertfordshire
- 14 Collaborating Partners from 10 countries



Results

- Database:
 - **419** novel compounds and combinations in total
 - **30%** herbal compounds
 - **35%** chemical compounds (includes well known pharmaceutical products)
 - **35%** odd/idiosyncratic combinations
 - » Chemical
 - » Herbal
 - » Pharmaceutical
 - » Combination
 - » NK
- Thesaurus of slang terms and region specific language (multilingual)



Results

- Some 50 technical folders uploaded, including:

Herbal	Chemical	Pharmaceutical	Combination
Ephedra	2C-B	Benzydamine	Happy Caps
Gotu Kola	4-AcO-MET	GBL, GHB, 1,4-BD	Minikikke/Superkikke
Ikhathazo	5-MeO-AET	Pregabalin	Spice
Jurema	5-MeO-MiPT		
Kanna	Bromodragonfly		
Wild Dagga	Herkinorin		
Phalaris	HU-210		
Salvia	JWH-018		
Sinicuichi	JWH-073		
Syrian rue	MDPV		
	Mephedrone		



Identifying Emerging Trends

- Spice

- Smoking blend containing synthetic cannabinoids e.g., JWH-018
- Appeared in or around 2004; now some 140 plus different 'spice' drugs available



- Schifano, F., Corazza, O., Deluca, P., Davey, Z., et al. Psychoactive drug or mystical incense? Overview of the online available information on Spice products. *International Journal of Culture and Mental Health*, 2009.
- » Mustata, C., Torrens, M., Pardo, R., Perez, C., The Psychonaut Web Mapping Group., & Farre, M. (2009). Spice drugs: Cannabinoids as a new designer drugs [Spanish]. *Adicciones*, 21(3), 181- 186.



Piperazines

50 Piperazine mentions; 2006 – 3, 2007 – 9, 2008 – 18, 2009 – 16, 2010 – 4 (so far). Note: can expect 2009 figures to increase as inquests are completed.

Typically other substances involve combination of some of the following: alcohol, amphetamines/MDMA, cocaine, GHB/GBL, ketamine & sometimes opiates or benzodiazepines

Piperazine combinations:

2006 – BZP & TFMPP 2, BZP 1

2007 – BZP & TFMPP 4, BZP 4, CPP 1

2008 – BZP & TFMPP 4, BZP 14

2009 – BZP & TFMPP 11, BZP 3, TFMPP 1, 1 – tox det awaited

2010 – BZP & TFMPP

Implicated in death – 3 solely piperazines; 26 with other drugs and/or alcohol

Identifying Emerging Trends

- Ivory Wave (Vanilla Sky)

- One of several products currently being marketed as “**bath salts**”
- Appeared in or around April 2009
- NA/DA reuptake inhibitor; 4x more powerful than methylphenidate?
- Was purported to contain the cocaine analogue (-)-2- β -Carbomethoxy-3- β -(4-fluorophenyl)tropane (β -CFT, WIN-35,428) as well as MDPV (Methylenedioxypyrovalerone; **MDPV**)



Identifying Emerging Trends

- Google Insights Search – Ivory Wave



Not enough search volume to show results.

Not enough search volume to show results.





MDPV (MethyleneDioxyPyroValerone) lethality risk

- 57 year-old male died in January 2010 in Inner London.
- Cause of death: Coronary artery disease in the presence of MDPV. Open verdict.
- Toxicology (SGUL): PM blood MDPV 0.01mg/l; opened packet of “Ivory Wave” bath salts – positive for MDPV and lidocaine.
- PM – Focally severe coronary artery atheroma. As significance of presence in MDPV in blood is unknown, pathologist gave disease in presence of drug as cause of death.

Finnish media reports of deaths where MDPV found at PM, but unable to get any details.

FSS MDPV seizures: Q4 2008 = 1; Q3 2009 = 3; Q4 2009 = 25; Q1 2010 = 7

Identifying Emerging Trends

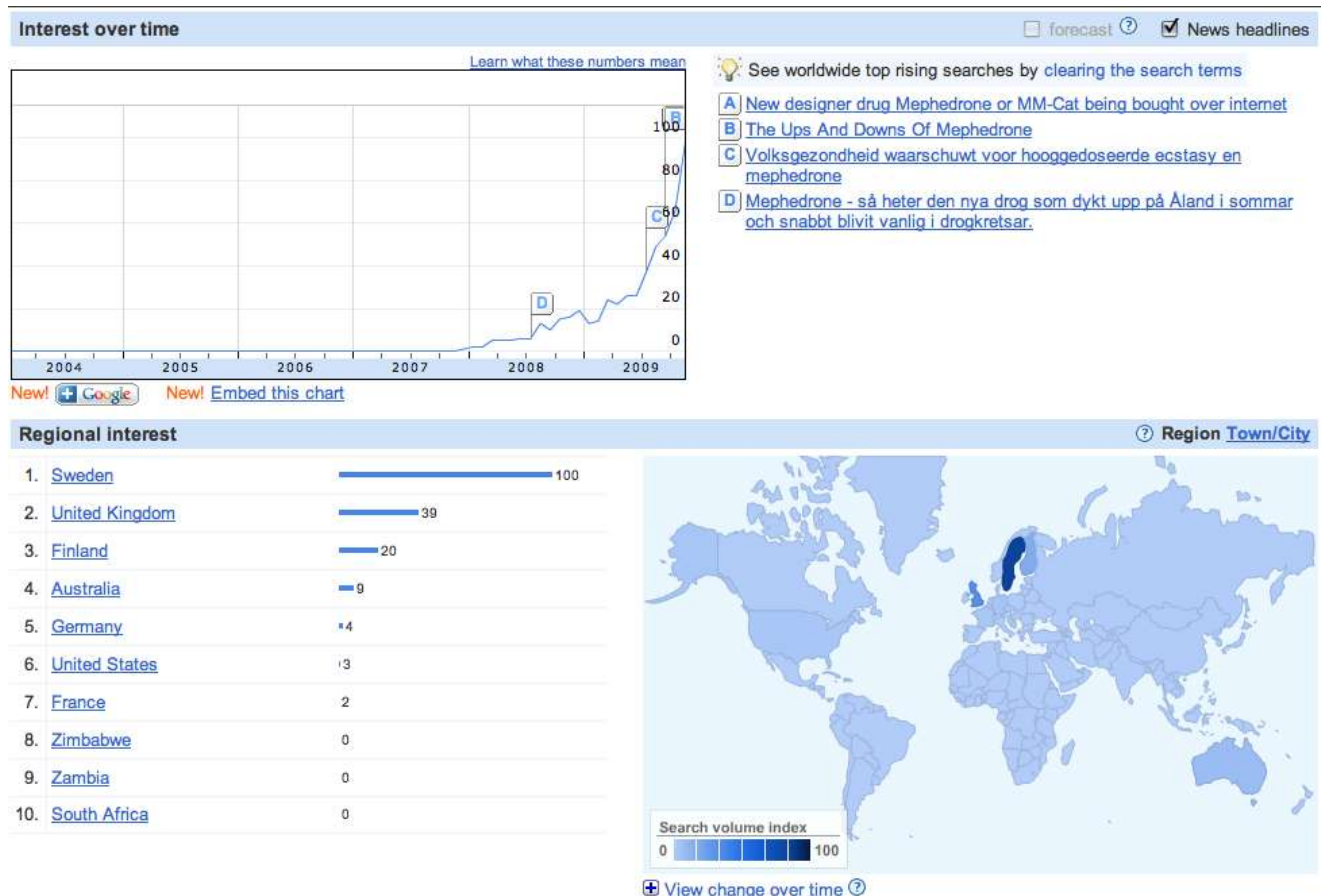
● Mephedrone (Schifano et al, Psychopharmacology 2011)

- Research chemical → 4-Methylmethcathinone
- Appeared in or around 2007
- Stimulant compared variously to amphetamine, ecstasy, and cocaine
- Miaow, 4-MMC, MMCat/MCAT, MD3, Roxy, Krabba, Mefedron, and various trade names
- Sold as powder or in capsules
- Sold as “plant feeder” and/or “not for human consumption”



Identifying Emerging Trends

- Google Insights Search – Mephedrone

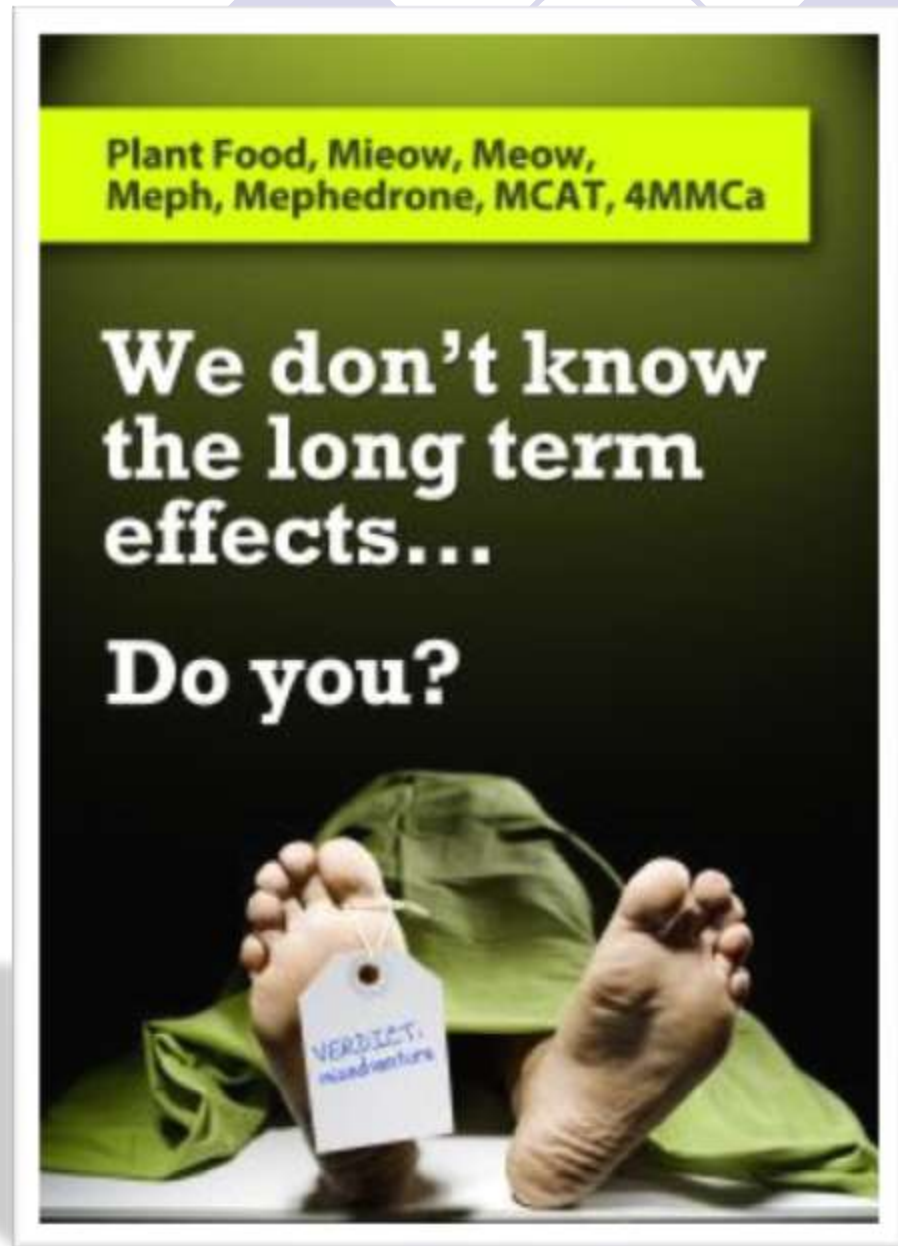


Mephedrone
= a cause for concern?

128 suspected;
25 cases not found; 13 still
pending;
90 cases meph identified at
PM;
69 inquests completed; data
fully available for 62 cases.

14/62 (23%) hanged
themselves
18/62 (29%) meph alone

(Schifano et al, Psychopharmacology –Berlin,
2011; Corkery, Schifano and Ghodse, in press)



Possible further challenges ahead

- **NRG-1**/naphyrone (stimulant; may inhibit reuptake of: 5-HT; NA; and DA) (Schifano and Albanese, in press)
- **NRG-2/5-lal**
- **NRG-3 and NRG-4** (?????)
- **N-Joy** (spice drugs); **Infinity** (?????)
- **B-fly** (powerful hallucinogenic drug; 5-HT2 agonist??)
- **Herkinorin** (mu, delta and k opioid receptor agonist; a truly unique hallucinogenic drug: similar to Salvinorin A but with opiate/opioid-like properties incl. tolerance and dependence)
- **Mytragina speciosa** ('Kratom'; an opiate/opioid-like drug from herbal origin)
- **Pregabalin** (sedative; potential for misuse not even mentioned in the product characteristics; Schifano et al, in press; EMCDDA, 2010)
- **Benzydamine/Tantum Rosa** (hallucinogenic indole; 5-HT2 agonist??)
- **Cocaine 'add ons': tropacocaine** (prolongs cocaine duration effects but possesses antiACh activities as well); **levamisole** (agranulocytosis risks; inhibits catabolism of DA and NA)

Breaking news from the web....(1)

Product	Active Constituent	Information
Methoxetamine (aka MXE, or MKET)	2-(3-methoxyphenyl)-2-(ethylamino)cyclohexanone	Analogue of Ketamine.
MDAI (Sparkle, Mindy)	5,6-Methylenedioxy-2-aminoindane	Developed in the 1990s by David E. Nichols at Purdue University. Similar to MDMA. Analysis of 2 products purported to contain MDAI found that one contained mephedrone and the other had an inorganic composition. Neither contained MDAI.
2M2B	2-methyl-2-butanol	Psychoactive properties unclear
AM-694	1-(5-fluoropentyl)-3-(2-iodobenzoyl)indole	Cannabinoid.
5IAI (AMY)	5-Iodo-2-aminoindane	Developed in the 1990s by David E. Nichols at Purdue University. Related to MDAI and MMAI.
2AI		To be better understood
Dimethocaine/DMC		stimulant properties similar to, but less potent than, cocaine
MDAT (aka HEX.TC.1)	6,7-Methylenedioxy-2-aminotetralin	Developed in the 1990s by David E. Nichols at Purdue University. MDMA-like.
5-MeO-DALT	<i>N,N</i> -diallyl-5-methoxytryptamine	Psychedelic tryptamine from Shulgin. Closely related to 5-Meo-DPT and DALT. A death in Cambridge where someone walked in front of a lorry whilst under the influence of a large dose of 5-MeO-DALT has been reported.

Breaking news from the web....(2)

4-MeO-PCP	4-Methoxyphencyclidine	Has been around since at least 2008. Dissociative anaesthetic with hallucinogenic and sedative effects. Ketamine-like re potency with slightly different effects.
DMAA	Dimethylamylamine	Was an ingredient in NZ party pills after the BZP ban. Stimulant.
5ID	Combination	Advertised as a combination between 5-IAI and DMAA: "New exciting chemical 5ID is now available at DiscoFoodStore.co.uk, a blend of two high purity compounds designed to give you maximum satisfaction in your lab research...It's a combination of two tried and tested research chemical's, 5-IAI and DMAA. . Unlike other research chemicals this particular mix is available right now only from DiscoFoodStore."
ECX	1-EthynylCyclohexanol	CNS depressant with effects comparable to ethanol. From 1one (maybe only) site advertising ECX: "1-EthynylCyclohexanol ECX - in stock from the 1st December! Apologies for the delay, we're just awaiting the best packaging for this interesting chemical."
MBZP	1-methyl-4-benzylpiperazine	Derivative of BZP.

Breaking news from the web....(3)

X-20-3	Combination	<p>From website: "X-20-3" is a balanced cocktail of two different, non neurotoxic, chemicals and has been tested lots of times."</p> <p>According to another site: "x-20-3 is a carefully balanced blend of three chemicals, 2 of which are mdmai and mdai the thrid is yet to be disclosed."</p> <p>Third site: X-20-3 is more formally known as, 6-(2-aminopropyl)benzofuran & 5,6-Methylenedioxy-2-aminoindane & 6,7-Methylenedioxy-2-aminotetralin.</p>
Jolly Green Granules (GG, JGG)	?	? Also sold – Jolly Bombs and Jolly Crystal Bombs and Green Genie Kryptonite
NRG2	?	? Also sold – Energy-2. In January 2011 one shop stated that "This product will be discontinued shortly we are selling all our stock of cheap."
NRG3	?	? Also sold – Energy-3
Nopaine		<p>Advertised in freebase and HCL form.</p> <p>"Smokable cocaine replacement that gives a dopamine rush similar to freebased cocaine....[or] Nasal or oral cocaine replacement that gives a dopamine rush similar to cocaine Hcl."</p>
White minds		Wholesaler http://whiteminds.co.uk/ psychoactive properties unclear
A3 (aka A3A, A3a Methano)		Advertised as mephedrone replacement. Reportedly 1,5-Methano-1H-3-benzazepine,2,3,4,5-tetrahydro-, hydrochloride. The following warning on one site: "Warning: This product is at least 3 times more potent of any other product sold on this site. This means reduce your plants dosage by at least a third (and wait for the results"
E3 (Eric-3)		Advertised as mephedrone replacement (compound from Eric-1234) – also available E1, E2, E3, E4, E5, E6, E7

Breaking news from the web....(4)

M3OW		Advertised as new mephedrone
R.U.C.H		From a website selling: "Research ultra chemical high Or R.u.c.h is a Special blended chemical which will provide your plants with a high euphoric feeling. It will also help relieve the tiredness of your greenery."
MADCAT		From a website selling: "A new Research Chemical which has been proven to be the closest thing to the last RC . Mad CAT is a legal green powder "
C1C		Stimulant RC from wide mouth frog
3-MeO-PCE	Methoxieticyclidine	Advertised as the "non-ketone" version of MXE. Ketamine-like
MPA	Methiopropamine	Also advertised as 'Methedrene'
Synthacaine		
RCS-4		Also known as BTM-4, SR-19. Coming out in Feb 2011. Psychoactive properties unclear
MDMAI	5,6-Methylenedioxy- <i>N</i> -methyl-2-aminoindane	Developed in the 1990s by David E. Nichols, a non-neurotoxic SSRA; a cyclized analogue of MDMA? Advertised as coming soon
5-APB	5-(2-aminopropyl)benzofuran	Advertised as an analogue of 6-APB
NBOMe-MESCALINE	N-benzyloxymethyl-3,4,5-trimethoxyphenethylamine	Developed by David E. Nichols. Samples made available online in December 2010, with more stock expected in early-mid February
2DPMP		On sale; pipradrol
D2PM		Back in stock 2 February 2011 pipradrol-like drug

ReDNet Project

Recreational Drugs' European Network: an ICT prevention service addressing the use of novel compounds in vulnerable individuals

- Aims

- Develop and pilot drug prevention and drug information services using different ICT tools (including SMS, Virtual Worlds, Facebook, YouTube, and Smartphone applications)
- Use the information already contained in the Psychonaut Web Mapping Database to develop these services, together with input from the target groups

- Target Groups

- Young people (16-24) and those misusing drugs who generally don't have access to appropriate information and or treatment services
- ***Professionals in contact with this group (including health professionals, educators, social services etc)***

- Project details

- 2-year EU funded (**start date: April 1st, 2010**)
- Project Lead: Prof. Fabrizio Schifano (University of Hertfordshire)
- 10 associated partners from 8 countries and 15 collaborating partners from 12 countries

