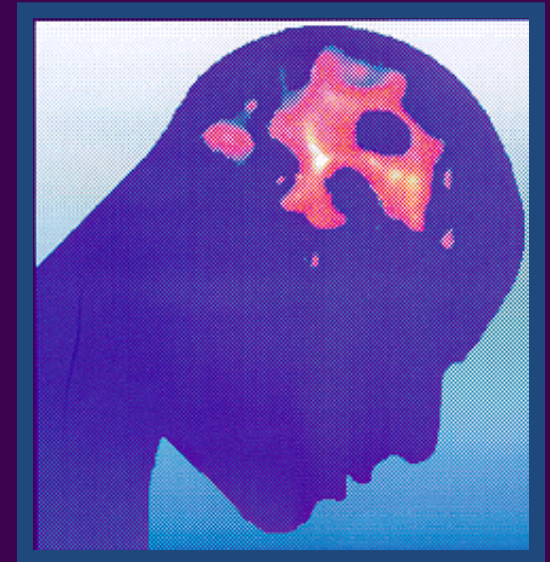
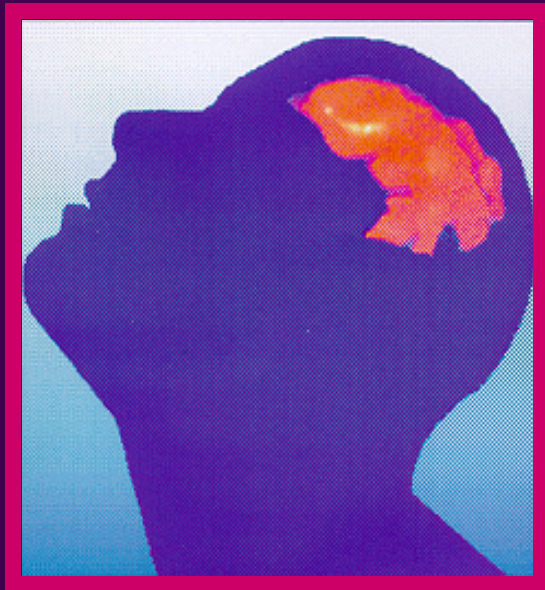
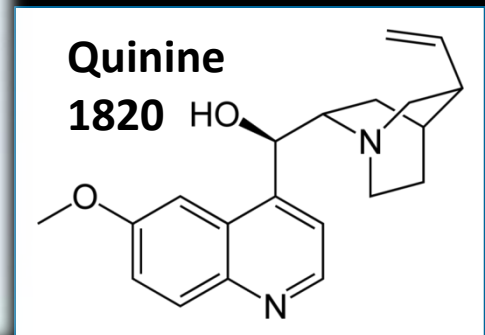
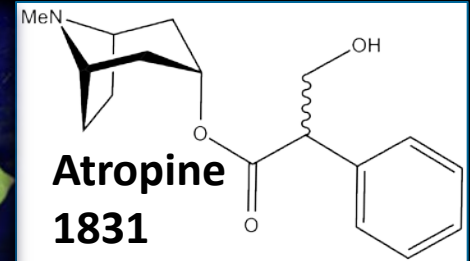
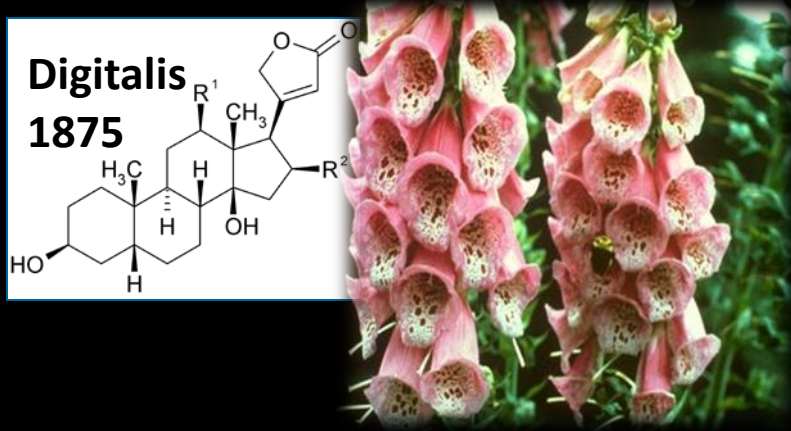


# SYNTHETIC DESIGNER DRUGS



**Bertha K. Madras, PhD**  
Professor of Psychobiology  
Department of Psychiatry  
Harvard Medical School

# Modern Drugs Were Isolated from Plants

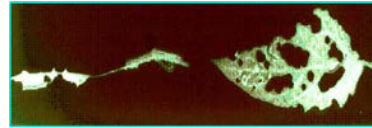
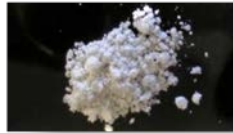
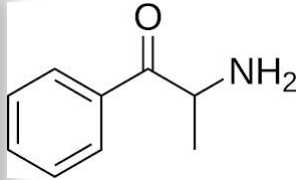




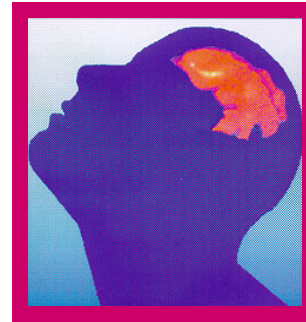
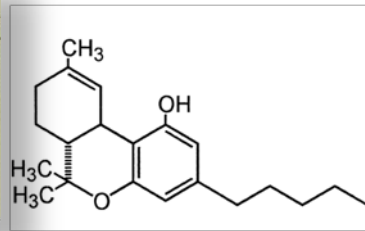
# Certain Plants Also Yielded Pleasurable Sensations



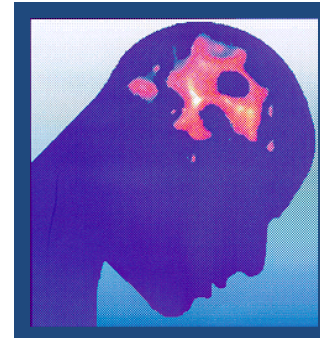
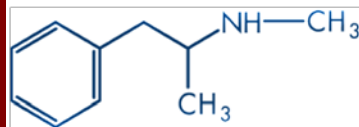
**Cathinone**



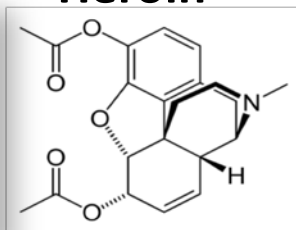
**Δ-9-tetrahydrocannabinol (THC)**



**Methamphetamine**



**Heroin**



# Goals

- **What are Designer Drugs?**
- **What Drives Designer Drug Markets?**
- **Trends?**
- **Are Designer Drugs Legal?**
- **Who Uses “Bath Salts”, Synthetic Cannabinoids, and Why?**
- **Effects and Harmful Effects?**
- **Summary**

# What Are Designer Drugs?

## Categories

- **Bath salts:** stimulants hallucinogens, entactogens, “empathogens”
  - These are not bath salts!!!!!! They are chemicals.
- **“Spice”, “K2” Cannabinoids:** marijuana-like chemicals
- **“Dragonflys”:** Hallucinogens
- **Morphine-like:** Krokodil
- **Tryptamines:** Hallucinogens

# A Myriad of Designer Drugs

## DISSOCIATIVES

Methoxetamine  
Ketamine  
Phencyclidine

## Hallucinogens

DOB Aleph-2 DOM  
2C-D 2C-B 2CT-2  
2-CE 2C-C 2C-I  
2C-T-2 2C-T-4 2C-N  
2C-P

## CATHINONES

Cathinone  
Methcathinone  
Mephedrone  
Flephedrone  
Pyrovalerone MDPV  
Pentylone Naphyrone

## SYNTHETIC CANNABINOIDS

CP 47,497 CP 55,940  
Cannabicyclohexanol  
JWH-007, -018, -073, -081,  
-098, -122, -164, -210,  
UR-144 XLR-11 UR

## PIPERAZINES

BZP MDBP mCPP  
TFMPP MeOPP

## HALLUCINOGENIC AMPHETAMINES

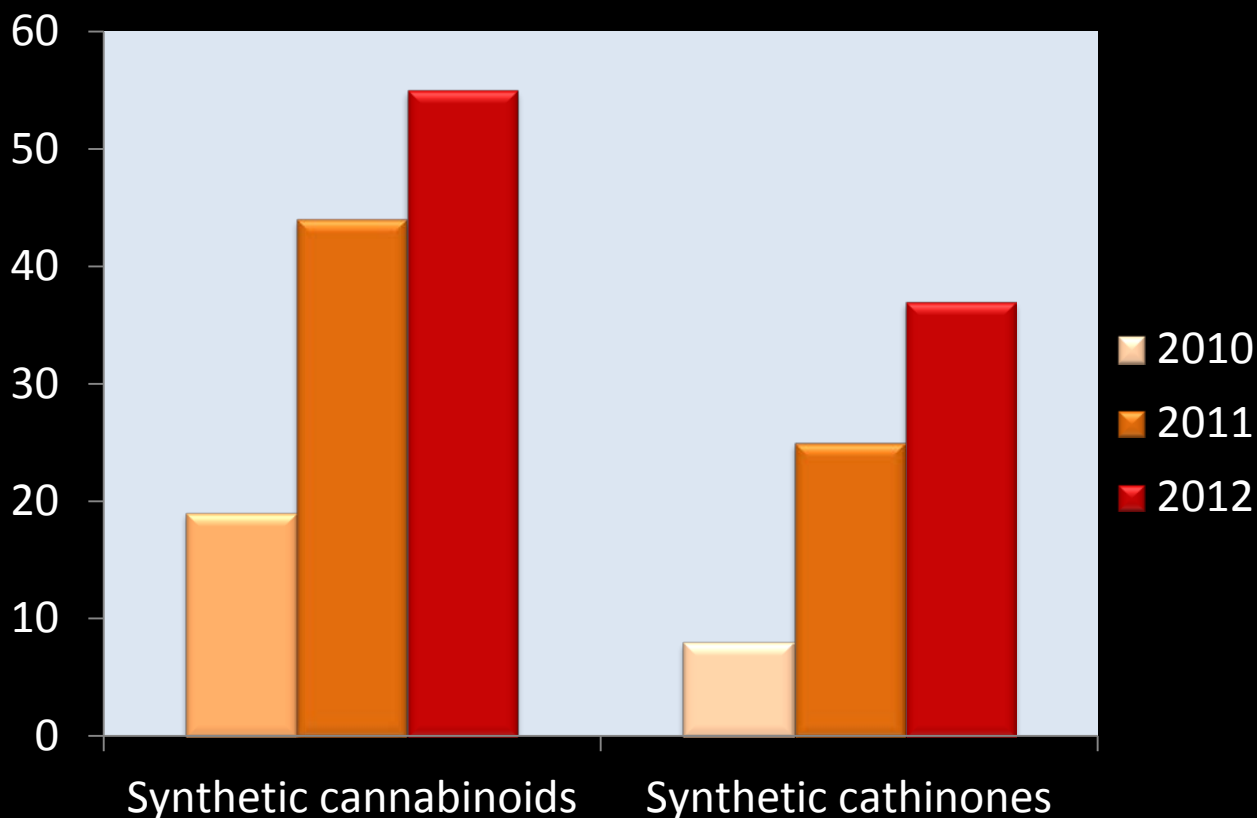
(rigid dragonflies)  
2C-Bfly Br-Fly  
Br-dragonfly TCB-2

## MDMA -related

PFA PFMA 6-APB  
MDAI 5-IAI  
MDAT

# National Trends: Unique Type of Synthetic Drugs

NFLIS (2010-2012)

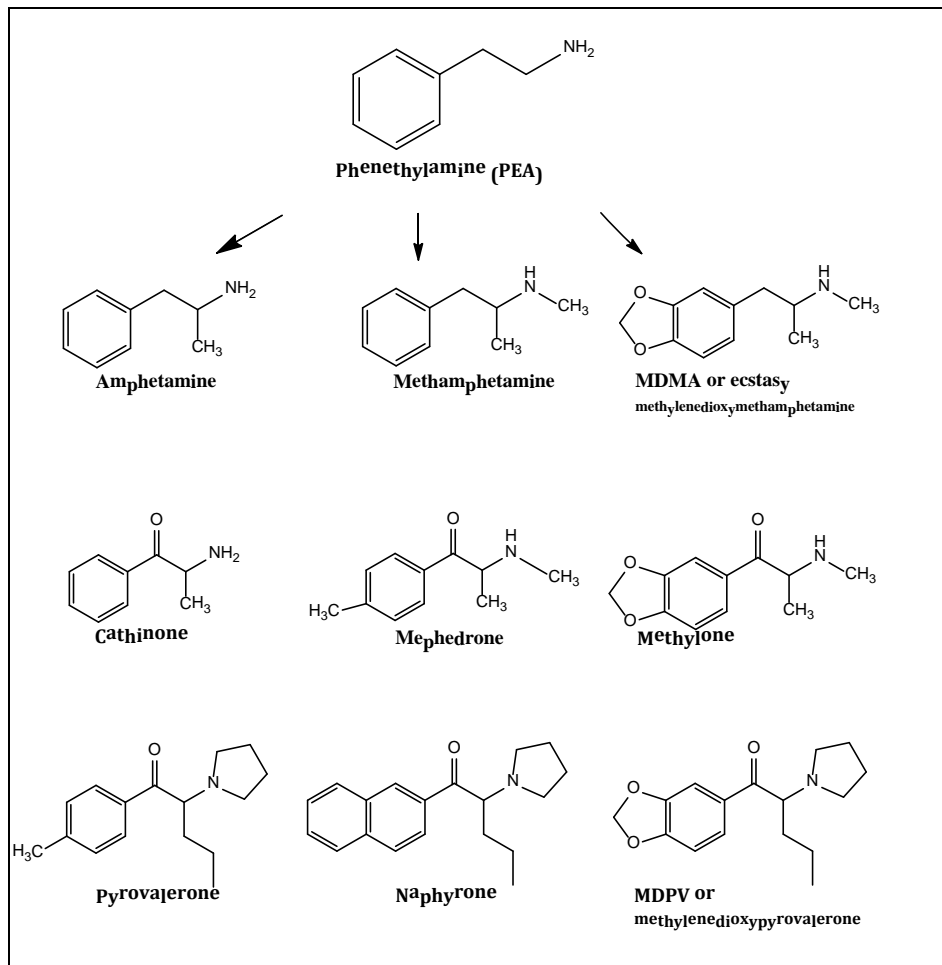


Source: US DEA, Office of Division Control, National Forensic Laboratory Information System, 2012



# What Are Designer Drugs?

## Bath salts



**ARE NOT**  
**Skin cleansers,**  
**perfumes or**  
**soothing lotions**

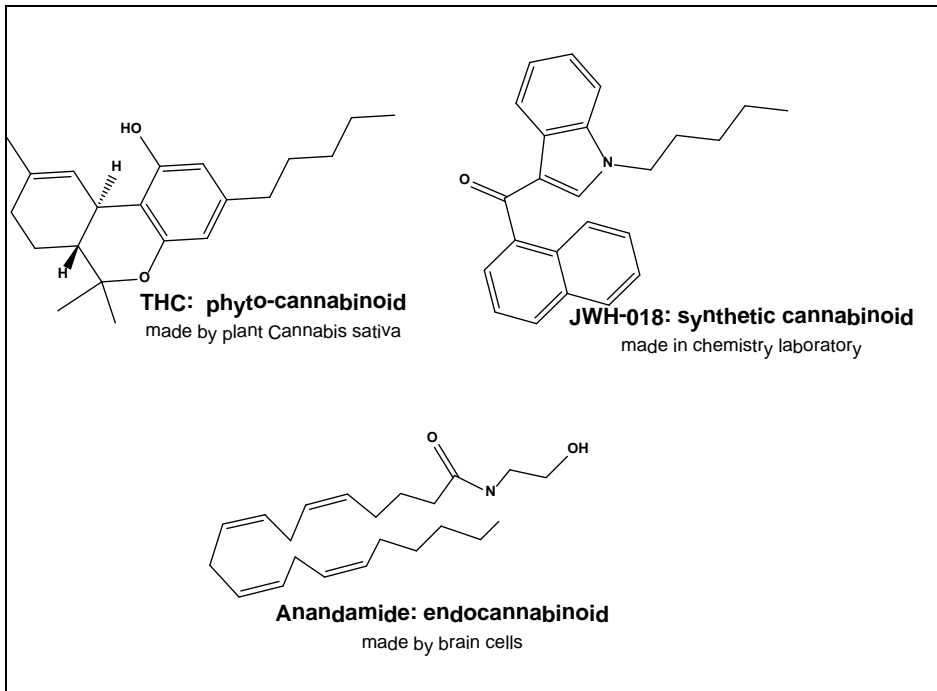


# Bath salts: how to recognize

- **If sold as “Bath salts” warning signs:**
  - Is it in a small packet?
  - Is it labeled: “not for human consumption”?
  - Is it labeled “not illegal”?
  - Is it labeled “adults only” ?
- **If sold as “plant food”, “fertilizer”**

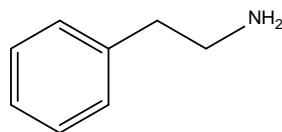
# What Are Designer Drugs?

## Marijuana-like

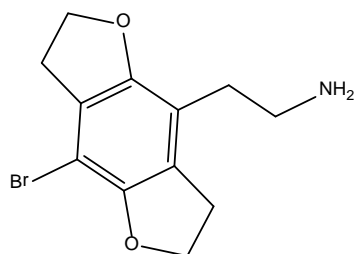


# What Are Designer Drugs?

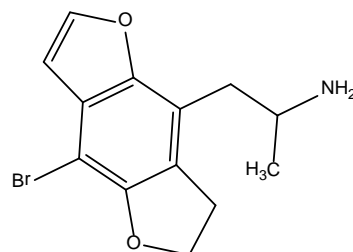
## Dragonfly



Phenethylamine (PEA)



2C-Bfly



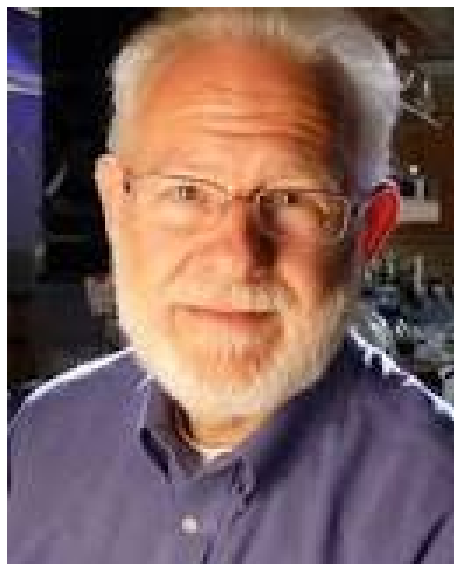
Br-Dragonfly

# Krokodil

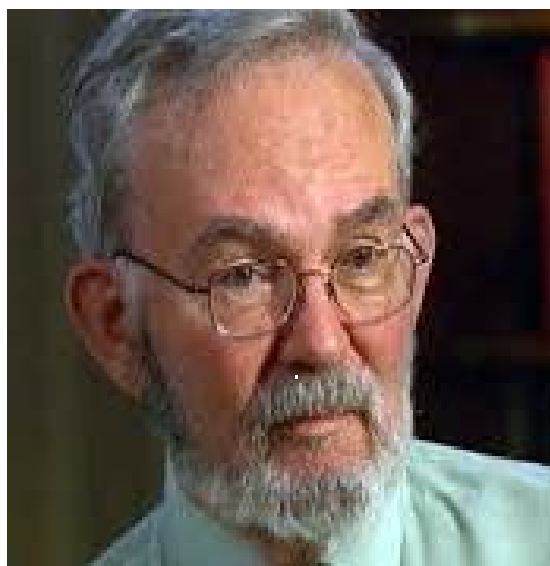
- **Desmorphine** : Russian, response to tight heroin supply
- **Synthesis**: Simple with codeine, iodine, red phosphorus.
- **Purity**: Highly impure, contaminated with toxic, corrosive byproducts
- **Psychoactive effects**: Similar to heroin, shorter duration; brain damage
- **Notoriety**: produces severe tissue damage, phlebitis, gangrene
- **Life expectancies**: short



# Where Did Designer Drugs Come From?



**Dr. David Nichols**



**Dr. John W Huffman**



**Dr. Alexander Shulgin**

ACS Chemical Neuroscience  
Research Article  
pubs.acs.org/chemneuro

**Extensive Rigid Analogue Design Maps the Binding Conformation of Potent *N*-Benzylphenethylamine 5-HT<sub>2A</sub> Serotonin Receptor Agonist Ligands**

Jose L. Juncosa, Jr., Martin Hansen, Lisa A. Bonner, Juan Pablo Cueva, Rebecca Maglathlin, John D. McCorvey, Danuta Marona-Lewicka, Markus A. Lill, and David E. Nichols<sup>a</sup>

Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue University, West Lafayette, Indiana 47907, United States

**Supporting Information**

**ABSTRACT:** Based on the structure of the superpotent 5-HT<sub>2A</sub> agonist 2-(4-bromo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine, which consists of a ring-substituted phenethylamine skeleton modified with an *N*-benzyl group, we designed and synthesized a small library of constrained analogues to identify the optimal arrangement of the pharmacophoric elements of the ligand. Structures consisted of diversely substituted tetrahydroisoquinolines, piperidines, and one benzazepine. Based on the structure of (SS)-9b, which showed the highest affinity of the series, we propose an optimal binding conformation. (SS)-9b also displayed 124-fold selectivity for the 5-HT<sub>2A</sub> over the 5-HT<sub>2C</sub> receptor, making it the most selective 5-HT<sub>2A</sub> receptor agonist ligand currently known.

**KEYWORDS:** serotonin, 5-HT<sub>2A</sub>, agonist, rigid analogue, hallucinogen, molecular model

Chemical structures and data:  
BrC1=CC=C(C=C1C2=CC(OC)=C(C=C2)NCC3C4C(CCC5C(C4)N(CCC5)C6=CC=CC=C6)C7=CC(OC)=C(C=C7)C8=CC=CC=C83  $5\text{-HT}_{2A} K_i = 0.19 \pm 0.01 \text{ nM}$  (21-fold selectivity over 5-HT<sub>2C</sub>)  
BrC1=CC=C(C=C1C2=CC(OC)=C(C=C2)NCC3C4C(CCC5C(C4)N(CCC5)C6=CC=CC=C6)C7=CC(OC)=C(C=C7)C8=CC=CC=C83  $5\text{-HT}_{2A} K_i = 2.5 \pm 0.1 \text{ nM}$  (124-fold selectivity over 5-HT<sub>2C</sub>)

Contents lists available at SciVerse ScienceDirect  
Drug and Alcohol Dependence  
journal homepage: www.elsevier.com/locate/drugalcdep

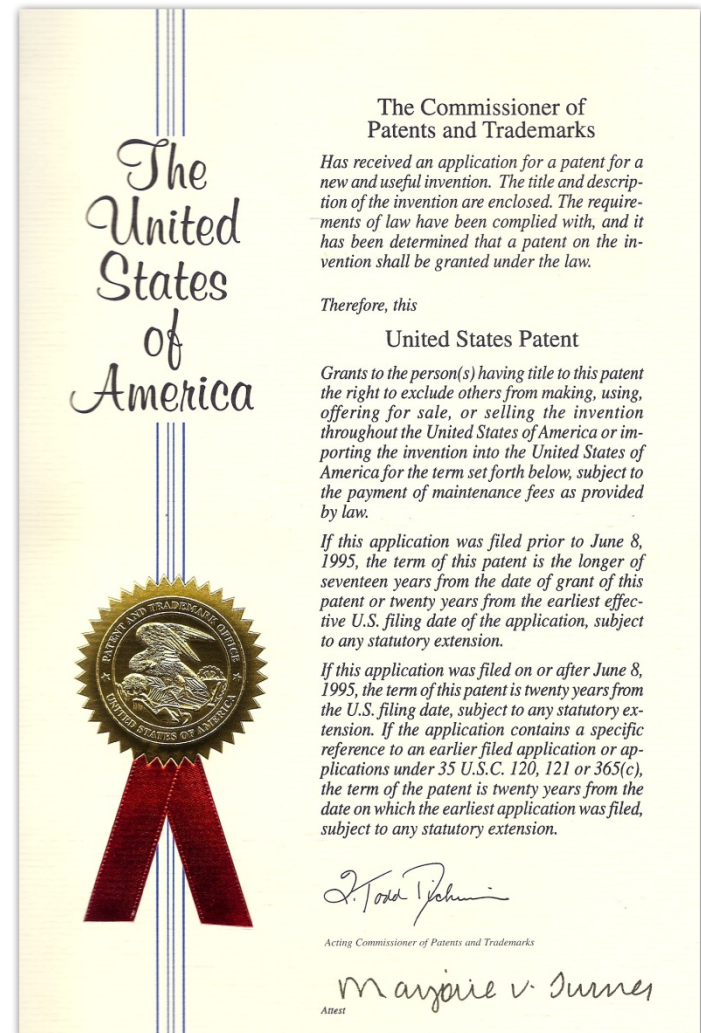
**1-Pentyl-3-phenylacetylindoles and JWH-018 share *in vivo* cannabinoid profiles in mice**

Jenny L. Wiley<sup>a,b,\*</sup>, Julie A. Marusich<sup>a</sup>, Billy R. Martin<sup>b</sup>, John W. Huffman<sup>c,d</sup>

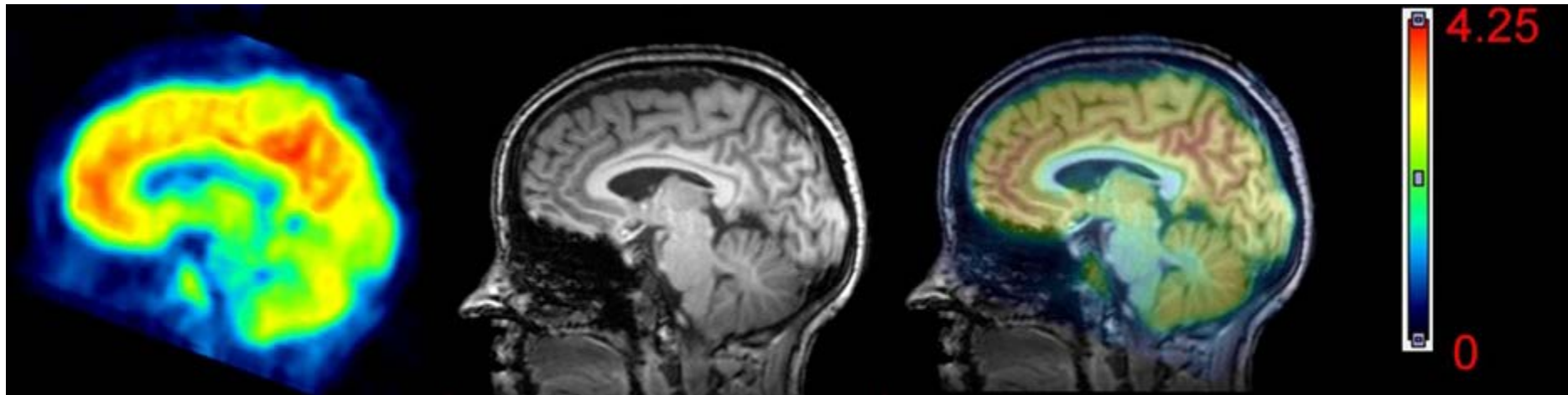
<sup>a</sup> RTI International, Research Triangle Park, NC 27709-2194, USA  
<sup>b</sup> Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298-0613, USA  
<sup>c</sup> Department of Chemistry, Clemson University, Clemson, SC 29634-0973, USA  
<sup>d</sup> P.O. Box 605, Dillsboro, NC 28725-0605, USA

# Why do Medicinal Chemists Compound?

- New medications
- Basic science
- Publish research
- Publish patents



# Marijuana distribution (CB<sub>1</sub>) in Human Brain



Red, yellow regions have high concentrations of CB<sub>1</sub> cannabinoid receptor

PET image CB<sub>1</sub>      MRI defines anatomy      MRI, PET combined

Terry et al., Quantitation of cannabinoid CB<sub>1</sub> receptors in healthy human brain using positron emission tomography and an inverse agonist radioligand. Neuroimage 48 362, 2009

# How Did Legitimate Chemical Research Evolve into Illegal Drug Production?

ACS Chemical Neuroscience  
Research Article  
pubs.acs.org/chemneuro

## Extensive Rigid Analogue Design Maps the Binding Conformation of Potent *N*-Benzylphenethylamine 5-HT<sub>2A</sub> Serotonin Receptor Agonist Ligands

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Contents lists available at SciVerse ScienceDirect

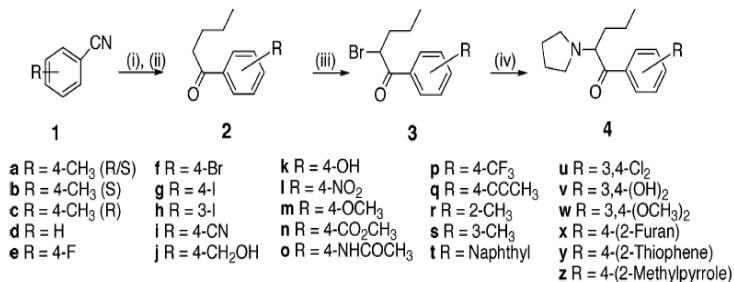
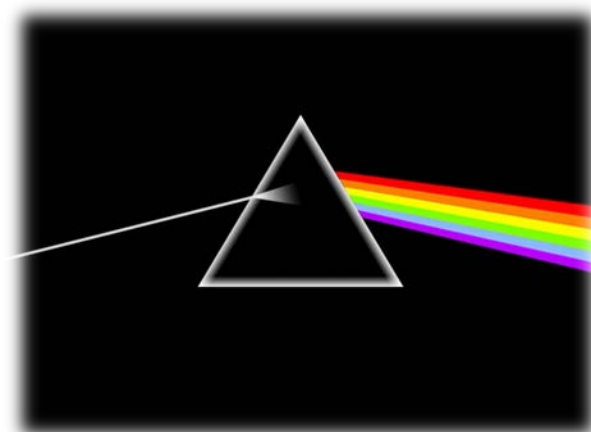
## Drug and Alcohol Dependence

journal homepage: [www.elsevier.com/locate/drugalcdep](http://www.elsevier.com/locate/drugalcdep)

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<sup>a</sup> RTI International, Research Triangle Park, NC 27709-2194, USA  
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<sup>c</sup> Department of Chemistry, Clemson University, Clemson, SC 29634-0973, USA  
<sup>d</sup> P.O. Box 605, Olinboro, NC 28725-0605, USA





# What Drives Designer Drugs?

- **Internet: sales, production, information**
- **Deceptive Marketing**
- **Grey zone legal status**
- **Evade drug tests**

*To have novel*

- feelings
- sensations
- experiences

**AND**

*To share them*



Vivian Felsen

*To evade  
drug testing*





*To evade legal  
issues*



Vivian Felsen

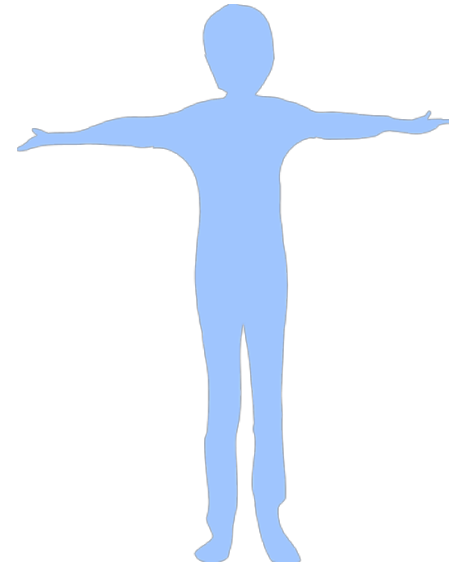


# A Human Experiment without Informed Consent



*Marketed to teens and young adults*

- Unknown composition of matter
- No consistency in manufacturing
- Not tested for human consumption
- Unknown actions in brain or body
- Unknown dosage, drug interactions



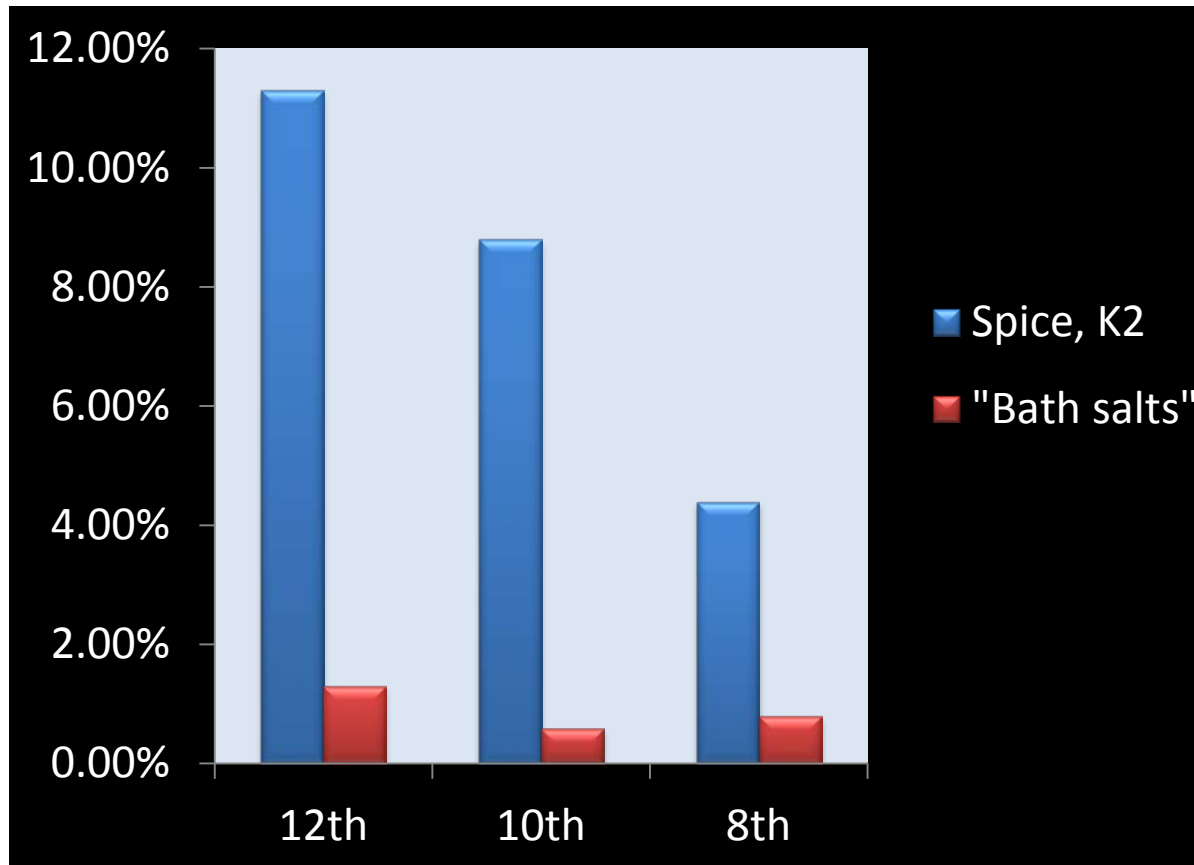
# Trends?

## EU Psychonaut Web Mapping Project of “legal highs”

- > 200 discussion forums, social media, online shops, websites (YouTube, eBay, Google, Google Insight)
- > 410 substances/products
- Information is valuable, as scientific data are scarce
- “Spice”, mephedrone, naphyrone, MDAI, MDPV were tracked from single source country to spread
- *After made illegal, online searches decrease*

# Trends: Synthetic Marijuana, Bath Salts?

## High School Students



Synthetic marijuana

**10<sup>th</sup>, 12<sup>th</sup> graders**

**2<sup>nd</sup> most widely used  
drug after marijuana**

**8<sup>th</sup> graders**

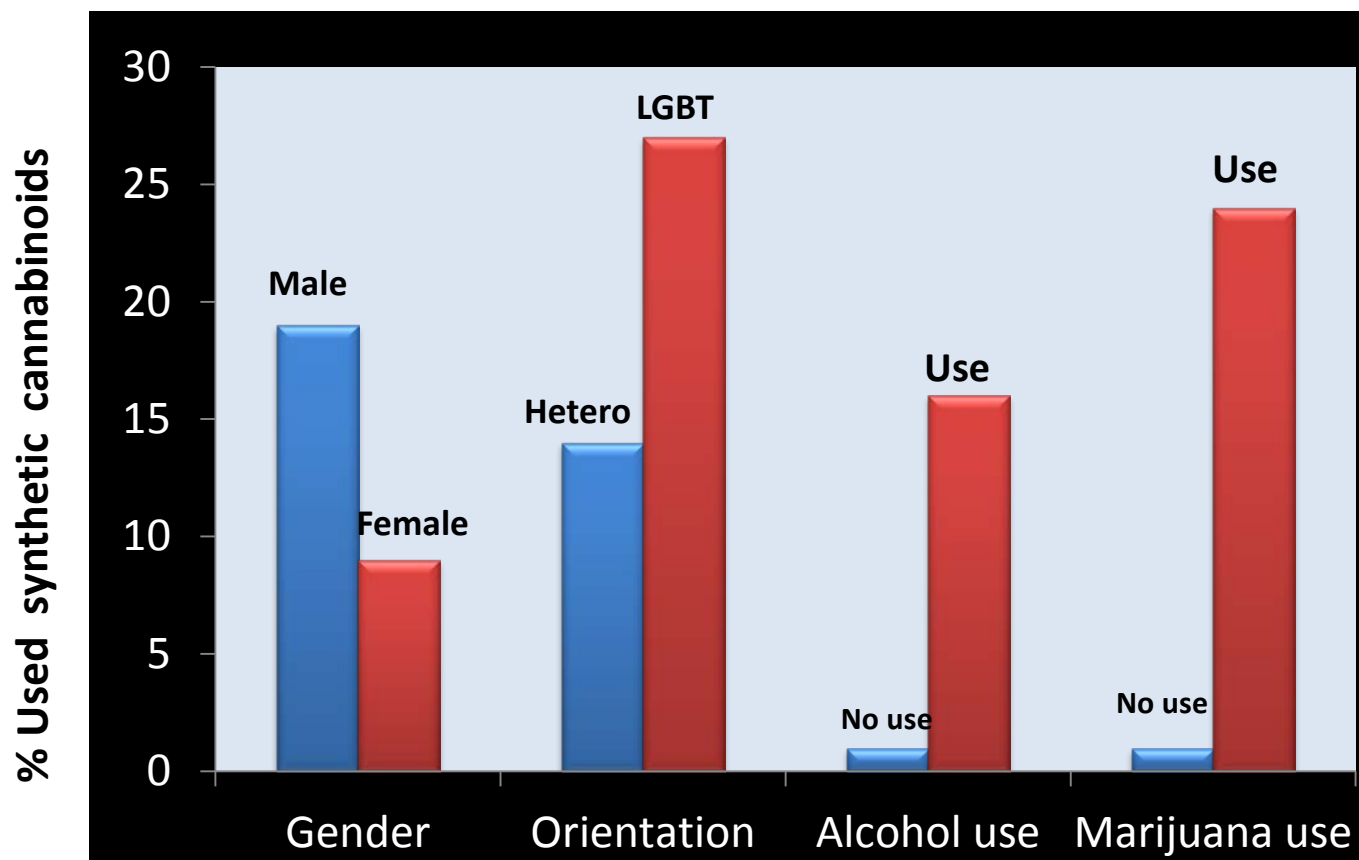
**3<sup>rd</sup> most widely used  
drug after marijuana,  
inhalants**

Source: Monitoring the Future, Dec 2012

# Trends, Synthetic Marijuana

## College Students

**% Undergraduate Students Reporting Synthetic Cannabinoid Use  
2011-2012 (n=2,349 students at a large Southeastern University)**



Adapted by CESAR from Stogner, J.M. and Miller, B.L., "A Spicy Kind of High: A Profile of Synthetic Cannabinoid Users," *Journal of Substance Use*, Advance online publication (doi:10.3109/14659891.2013.770571), 2013. For more information, contact Dr. Stogner at [stogner@email.unc.edu](mailto:stogner@email.unc.edu).



# **Legal Status**

## **Rationale for Legal Restrictions**

- 1. Actual or potential for abuse, addiction**
- 2. Significant psychoactive effects**
- 3. Risk to public health**
  - **Driving under influence, suicides, homicides, drugs abused to evade drug screens, overdose illness, deaths**
- 4. Analogs currently controlled, same reasons**

# **Are Designer Drugs Legal?**

## **Federal level**

- **October 2011: DEA controlled three synthetics, mephedrone, 3, 4-methylenedioxypyrovalerone (MDPV) , and methyldone, sold as “bath salts” “plant food”.**
- **March 1 2012: DEA extended control of five “fake marijuana” products (JWH-018, JWH-073, JWH-200, CP-47,497, cannabicyclohexanol.**
- **June 2012: 26 synthetic drugs, including 15 synthetic cannabinoids, placed under Controlled Substance Act.**
- **Possession, sale of these chemicals, or products that contain them, illegal in the United States.**

# Are Designer Drugs Legal?

## State level

**New Jersey:** bans six chemicals used to make designer drug 'bath salts'

Investigation: Ban on Bath Salts, Designer Drugs is Working Dramatically

**ARKANSAS: STATE HEALTH OFFICER ACTS TO BAN DESIGNER DRUG**

**Nebraska** ban on synthetic designer drugs advances

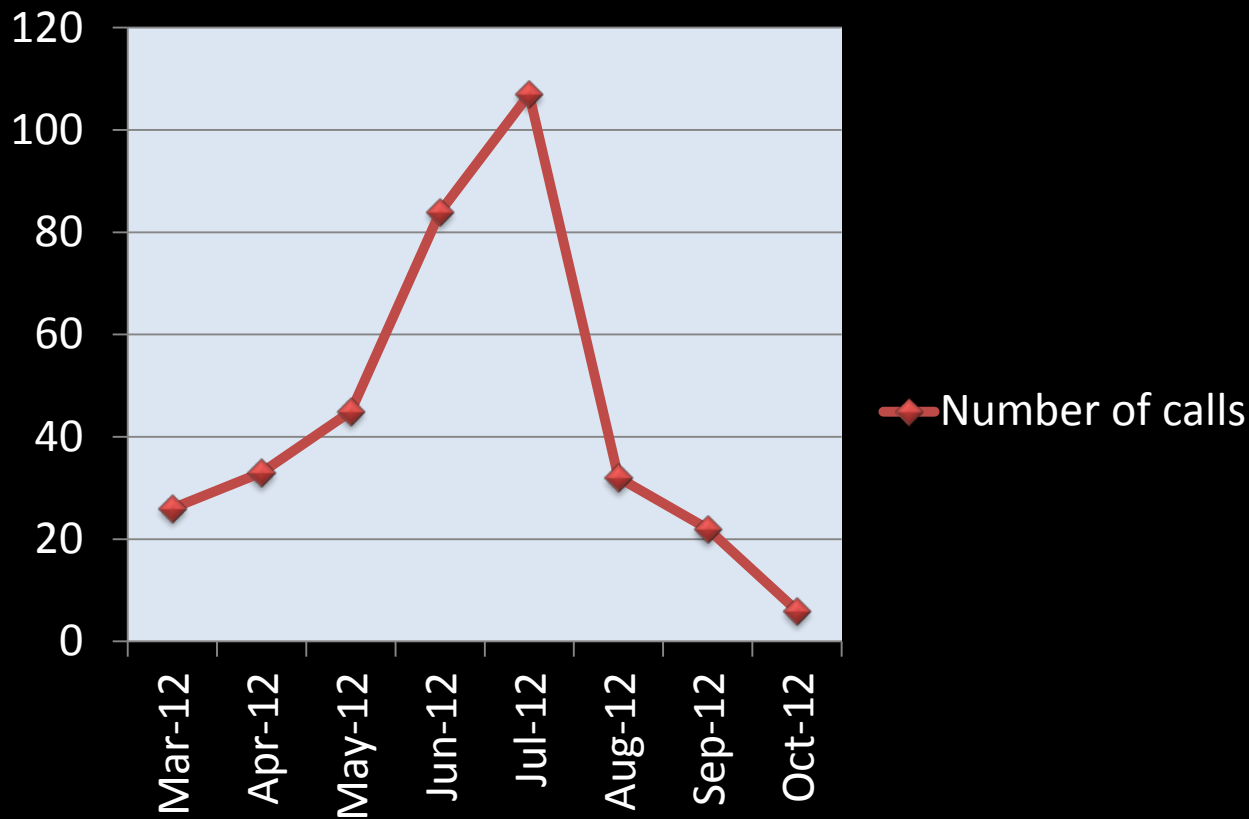
**Ohio:** Senator Burke working to ban designer drugs.

**Florida:** House Committee Passes Bill to Ban 27 Substances Used in Designer Drugs

**Michigan:** Bills banning synthetic designer drugs headed to Gov. Snyder

# Calls to Poison Control Centers Decline After Drugs Scheduled (FL)

**Illegal Status Reduces Use**



# “Bath Salts”

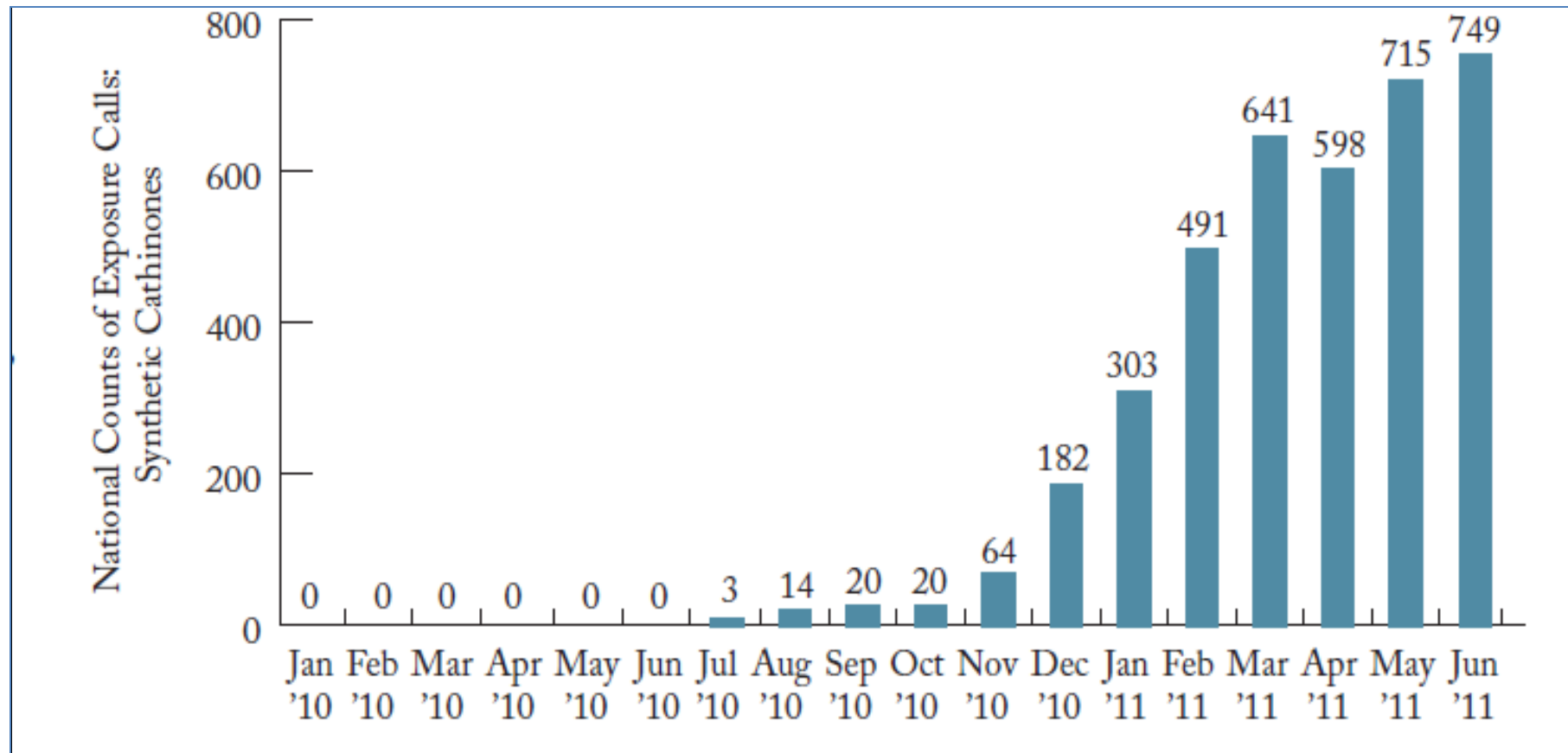




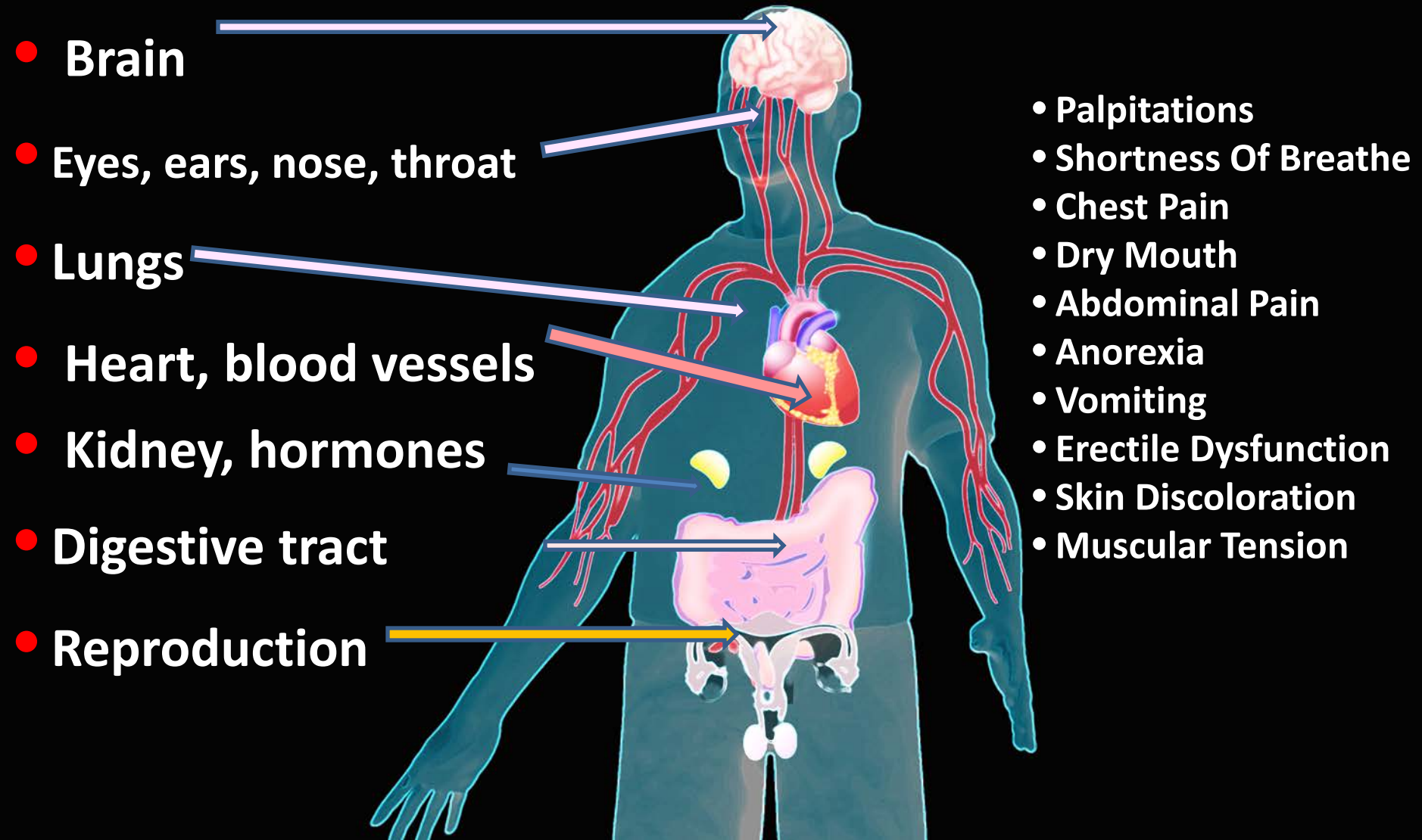
# “Bath Salts” Contain Designer Stimulants

DRUG NAME	DESCRIPTION
<b>Mephedrone</b>	4-methyl-methcathinone; “Miaow” Similar to cocaine and MDMA (ecstasy)
<b>Methylone</b>	$\beta$ -MDMA: 3,4-methylenedioxy-methcathinone; “Explosion” Similar to cocaine and MDMA (ecstasy)
<b>MDPV</b>	3,4-methylenedioxyprovalerone; MDPV; “NRG-1” (Brandt, 2010); “Ivory Wave” Stimulant with rapid onset; 2-4 hour duration of action
<b>BZP</b>	1-benzyl-piperazone Similar to amphetamine 1/10 potency of <i>d</i> -methamphetamine

# Cathinones Trends: Calls to Poison Control Centers Jan 2010 – June 2011



# “Bath Salts” Affect Many Organs



# “Bath Salts”, Psychoactive Effects

- **Psychoactive effects:** Aggression, dizziness, memory loss, seizures, blurred vision, anxiety, hallucinations, depression, dysphoria, euphoria, fatigue, increased energy and decreased concentration, panic and paranoia.
- **Addiction:** Mephedrone user survey; 50% considered it addictive, ~ 50% reported continuous use for > 48 h, and > 30% fulfilled 3+ criteria for abuse/addiction (DSM-IV).
- **Addiction:** Another survey (n=1,006); 17.5% of users reported addiction symptoms
  - highest frequency of daily use falling in the 11-15 year old age range.



# **“Bath Salts” Case Reports**

---

- **Man repeatedly stabs himself in face**
- **University student runs head-on into traffic and killed**
- **Daughter attacks 71 year old mother with machete**
- **Mother leaves 2 year old on highway median and carries 5 year old**
- **Man runs into police station thinking someone hiding under his car**
- **Man jumps from 3<sup>rd</sup> story window fleeing from non-existent person**
- **Couple destroy home walls trying to stab imaginary people**
- **Man flees car he thinks is melting and chased by electricity**
- **19 year old man arrested pointing 3 rifles at family members**
- **Woman driving with toddler arrested after banging head on steering wheel**
- **Man arrested for disorderly conduct eats dirt while handcuffed**
- **Man rams stolen car into front door of store and steals bath salts**
- **Man arrested at grocery store after damage and drinking hand sanitizer**
- **Man makes 911 call being chased by people with rifles**

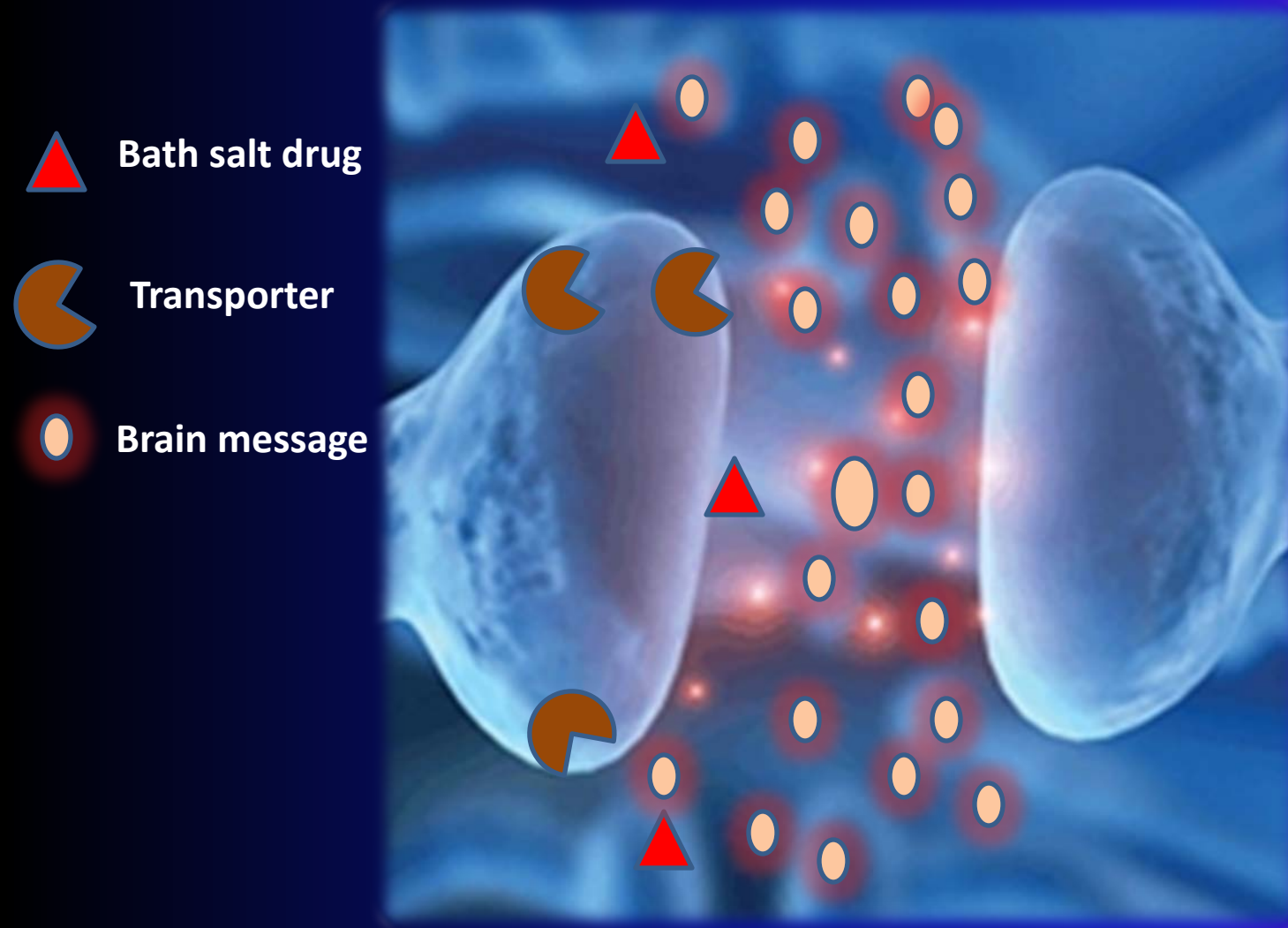
# Bath Salts: Medical Effects

Organ system	Effects
Cardiovascular	Palpitations, tachycardia, chest pain, vasoconstriction, myocardial infarct.
Psychological	Aggression, anger, anxiety, agitation, auditory visual hallucinations, depression, dysphoria, empathy, euphoria, fatigue
Neurological	Seizures, tremor, dizziness, memory loss, cerebral edema, headaches, lightheaded
Musculoskeletal	Arthralgia, coldness, numbness, discoloration, numbness, tingling of limbs, muscular tension, cramping
Gastrointestinal	Abdominal pain, anorexia, nausea, vomiting
Pulmonary	Shortness of breathe
Ears, nose, throat	Dry mouth, nasal pain, tinnitus

# Clinical Symptoms in Patients Admitted to ED (n=236)

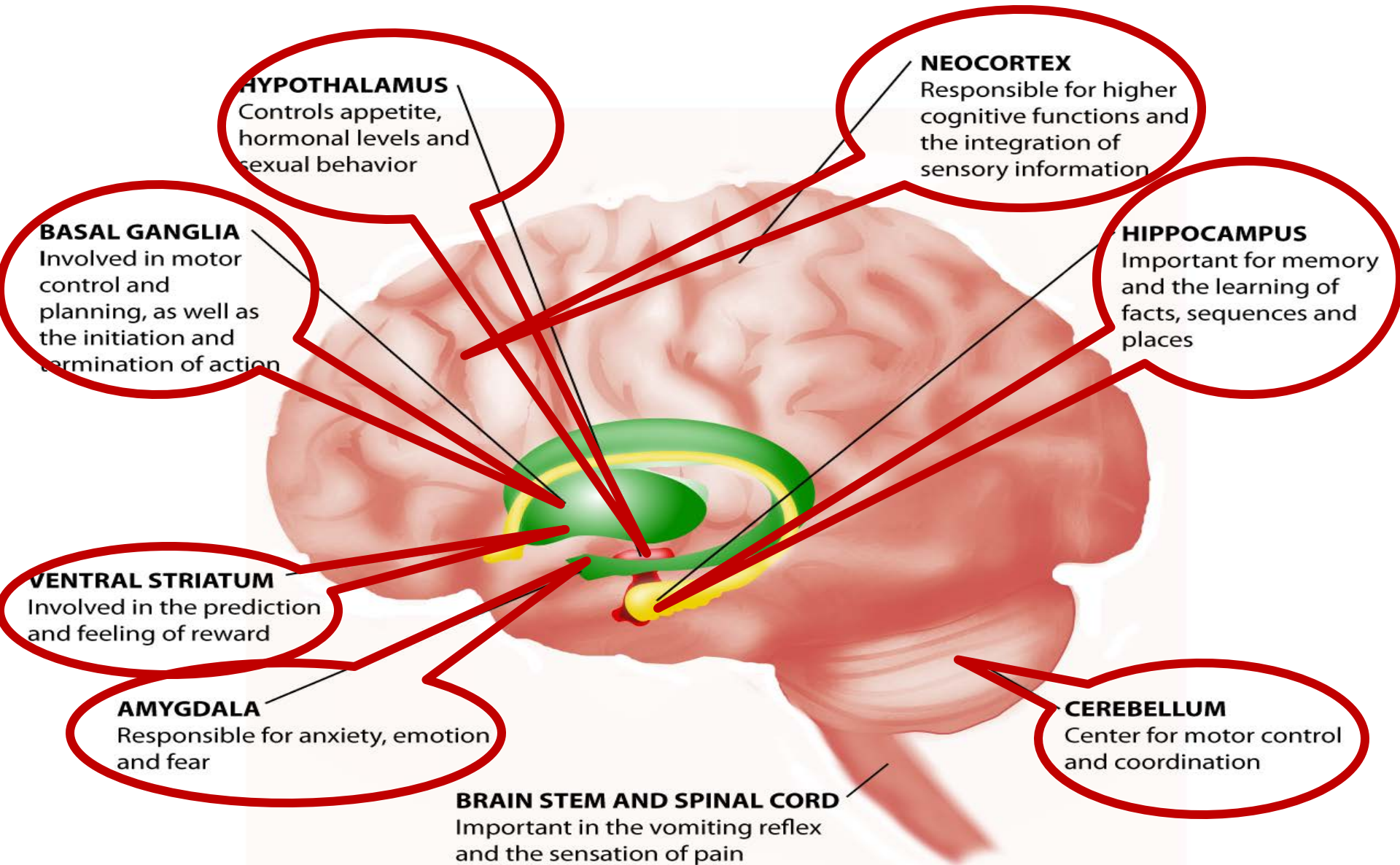
Agitation	82%
Combative/Violent behavior	57%
Tachycardia	56%
Hallucinations	40%
Paranoia	36%
Confusion	34%
Myoclonus/Movement disorders	19%
Hypertension	17%
Chest pain	17%
CPK elevations	9%

# Biology of “Bath Salts”





# Bath Salts Likely Affects Many Brain Regions



# **“Bath Salts”: Summary**

---

- **Cathinones do not all confer same effects or health risks.**
- **They engender risks and adverse consequences:**
  - (a) emergency department mentions
  - (b) persistence of effects after 24 hours
  - (c) addictive potential
  - (d) **psychiatric, cardiovascular effects**
  - (e) deaths

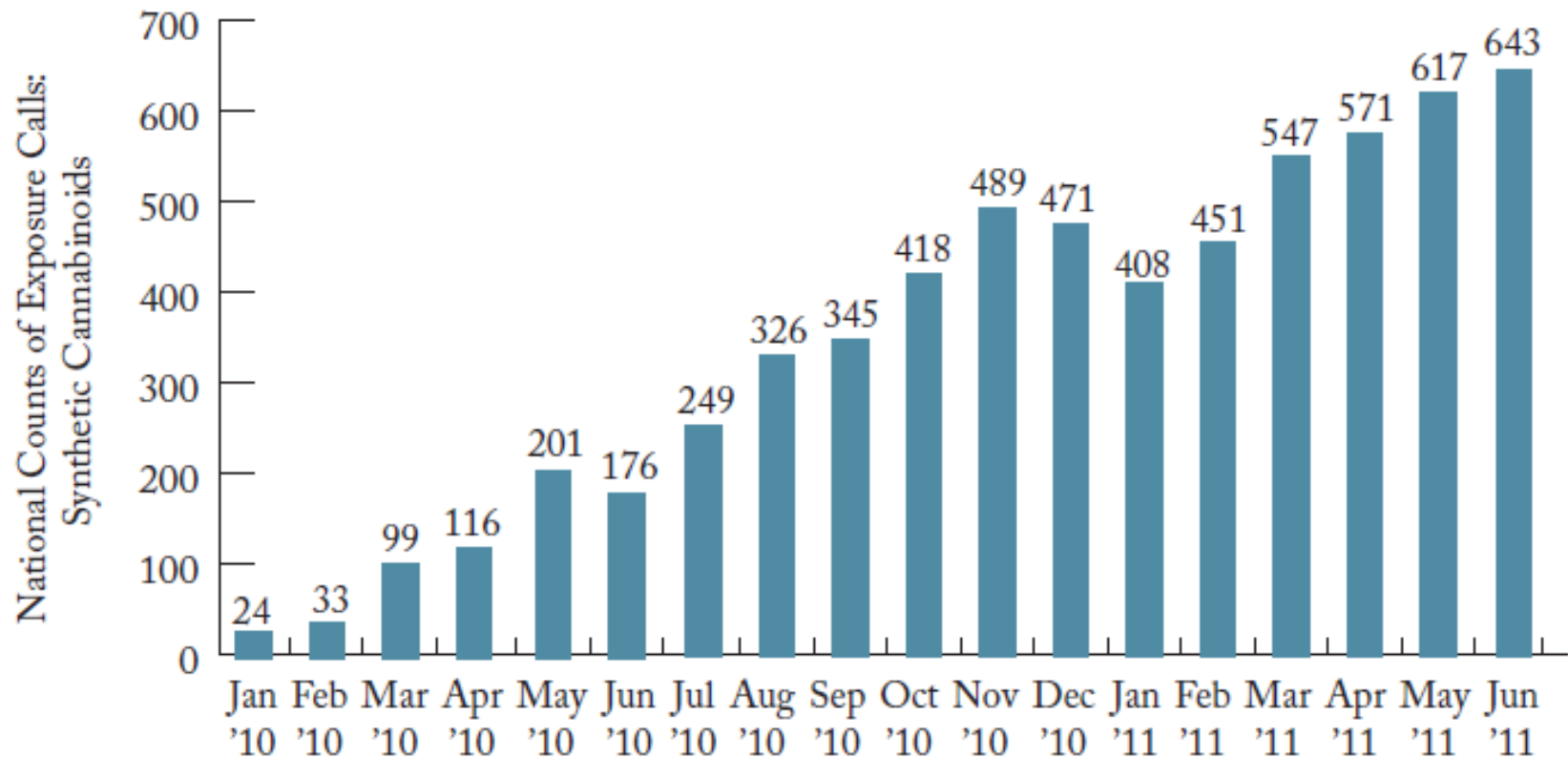
# Synthetic Cannabinoids (Marijuana)

## K2; Spice

Bliss  
Black Mamba  
Blaze  
Bombay Blue  
Genie  
Spice  
JWH -018  
JWH -073, -250  
“herbal smoking  
mixture”  
“incense”  
“herbal blends”  
“air freshener”  
“not for human  
consumption”.



# Calls to Poison Control Center for Synthetic Cannabinoids Jan 2010-June 2011





# K2, Spice overview

---

- **What:** Synthetic forms of marijuana
- **What:** Mixture of dried, shredded plants sprayed with THC-like chemicals; THC is the most active constituent of marijuana. Strong clove smell
- **Onset time:** 5-15 minutes (smoked)
- **Duration:** 1- 8+ hours
- **Effects:** Many
- **Comparison with marijuana:** effects may be extreme of smoked marijuana *or different.*

# Comparison of Marijuana and Synthetic Cannabinoids

## Cannabis ~= Synthetic Cannabinoids

- High heart rate
- Red eyes
- Anxiety
- Mild sedation
- Hallucinations
- Acute psychosis
- Memory deficits

## Symptoms More Typical of Synthetics

- Seizures
- Low blood potassium
- High blood pressure
- Nausea/vomiting
- Agitation
- Violent behavior
- Coma

SOURCES: Hermanns-Clausen et al. (In Press), *Addiction*; Rosenbaum et al. (2012). *Journal of Medical Toxicology*; Forrester et al. (2011). *Journal of Addictive Disease*; Schneir et al. (2011). *Journal of Emergency Medicine*.

# Psychoactive Effects

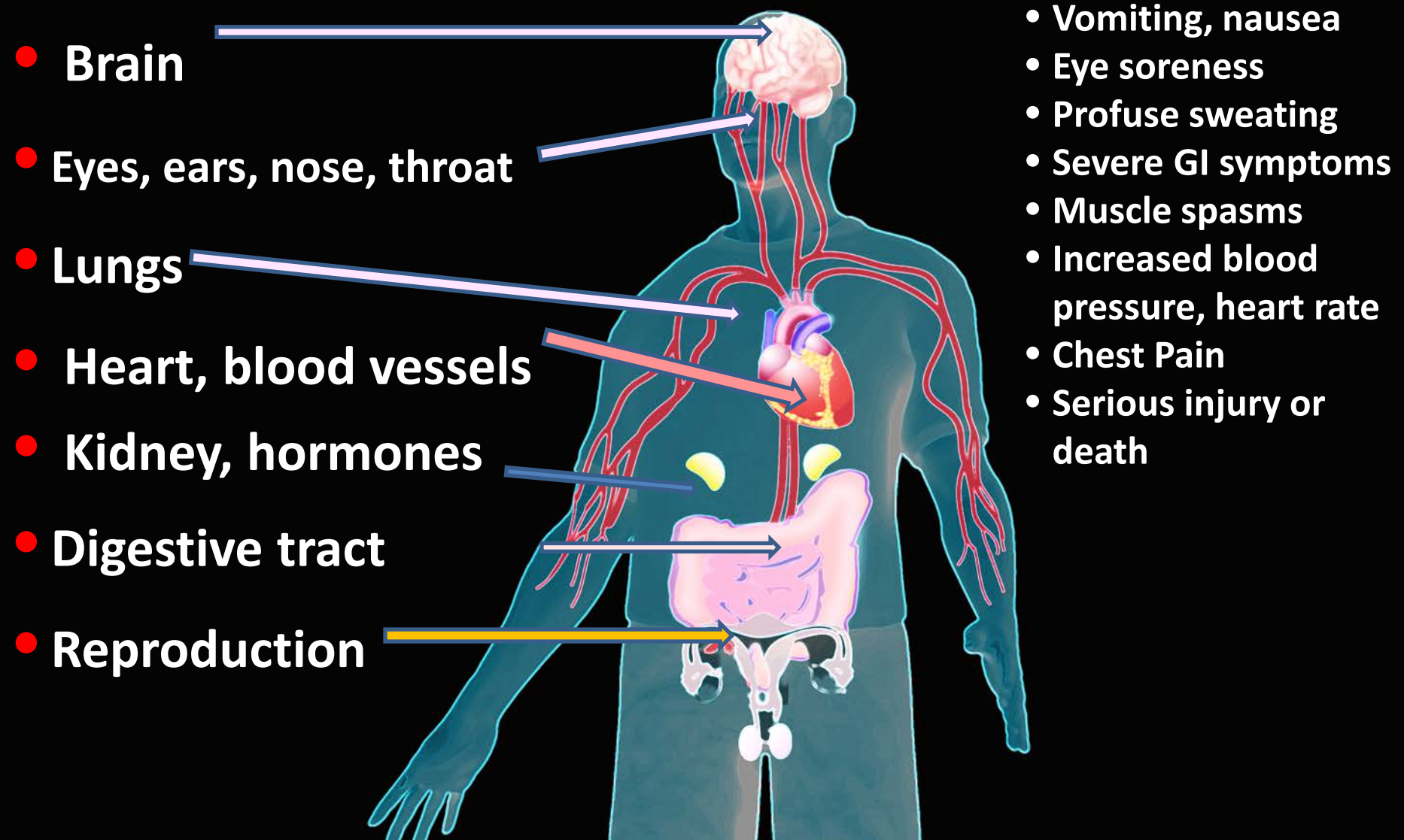
## Positive Psychoactive Effects

- Pleasant
- Euphoria
- Relaxation
- Sedation

## Negative Psychoactive Effects

- Severe paranoia, endangering self, others
- Agitation, delirium
- Headaches
- Anxiety, panic attacks
- Loss of control
- Confusion, hallucinations, psychosis
- Suicidal thoughts
- Seizures, tremors
- Impaired short-term memory concentration
- Persistent psychosis

# “K2, Spice” Affect Many Organs



# Adverse effects of cannabinoids

- **Abusers in ER seek treatment for addiction**
- **Multiple deaths associated with these alone or combined**

Organ system	Effects
Psychological	Anxiety, aggression, agitation, confusions, dysphoria, paranoia, irritation, panic attack, hallucinations
Neurological	Seizures, loss of consciousness
Cardiovascular	Tachycardia, hypertension, chest pain, cardiac ischemia
Metabolic	Hypokalemia, hyperglycemia
Gastrointestinal	Nausea, vomiting
Autonomic, other	Fever, mydriasis conjunctivitis,



# Acute Kidney Injury Associated with Synthetic Cannabinoid Use

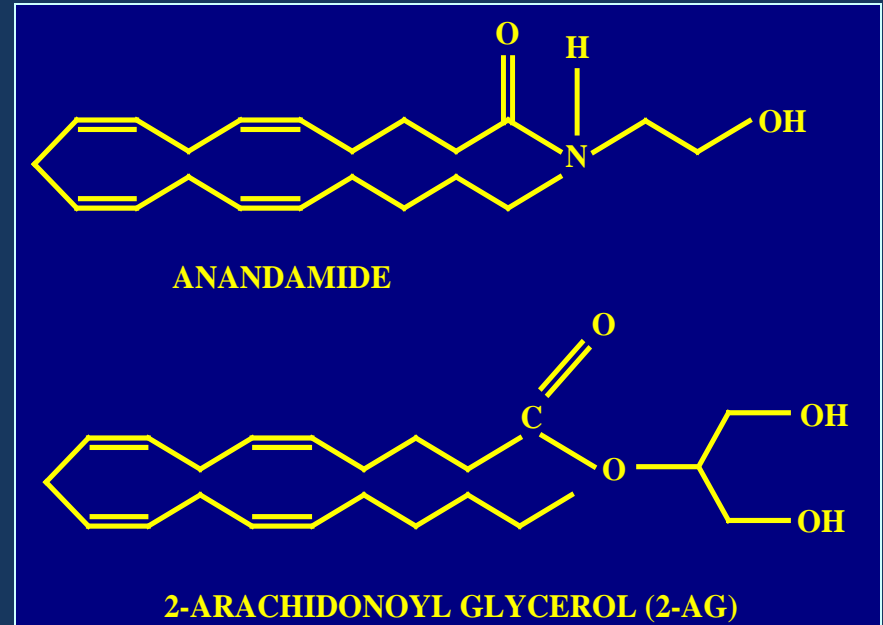
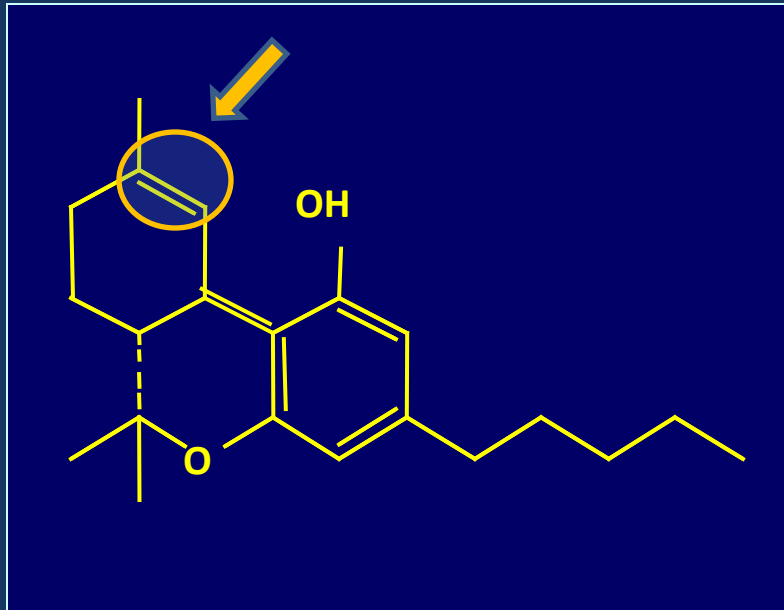
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# Biology of Synthetic Cannabinoids

## Plants, Brain, Tissues, Produce Cannabinoids

Marijuana plant makes  
~ 80 phytocannabinoids  
THC =#1

Brain, other organs make Endocannabinoids  
Anandamide: arachidonylethanolamide  
2-AG: 2-arachidonylglycerol  
7 or more made in brain and in other tissues



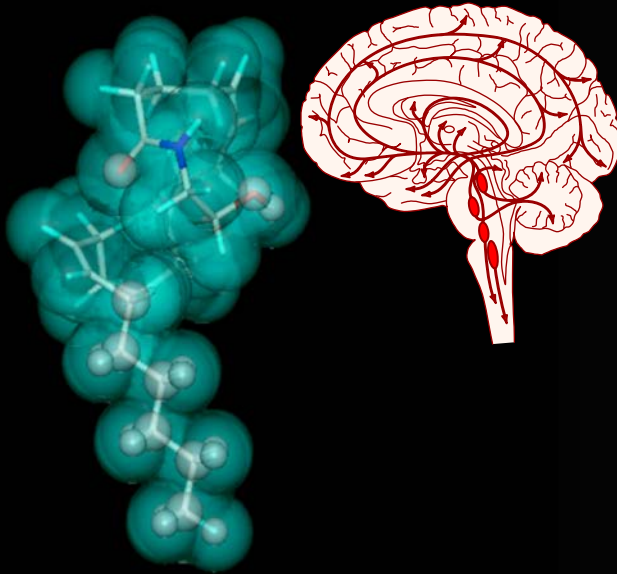
**Synthetic cannabinoids: 1,000s made by chemists**

$\Delta$ 9-THC (Gaoni & Mechoulam, 1964)

# $\Delta^9$ -THC, others, endocannabinoids target similar cannabinoid receptors

## Endocannabinoid

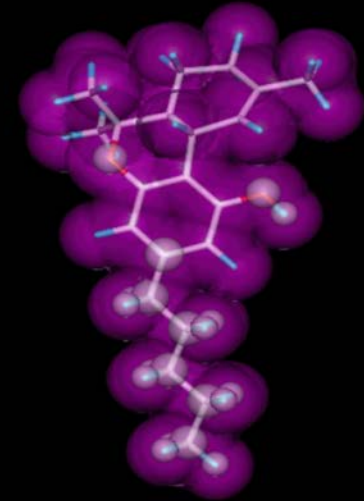
made by the brain



**Anandamide**

## Drug

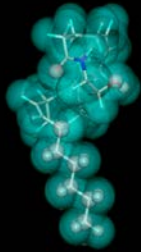
THC made by the plant, Cannabis Sativa



**THC**

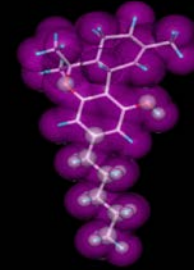
# Brain Cannabinoid System

## Controls Communication



**Anandamide**

- Modulates brain communication by reducing chemical messages
- Critical for brain development
- Controls chemical messages critical for pleasure, mood, pain, appetite, motivation, memory



**THC**

- THC, synthetics affect anandamide control of brain signals
- THC, synthetics' effects are prolonged, more powerful, different

# Addiction

- **Addiction to JWH-018, JWH-200, JWH-073, CP-47,497, cannabicyclohexanol:** physiological and psychological dependence *liability* similar to that of marijuana and THC.
- **Physical and psychological withdrawal:** elevated blood pressure, restlessness, drug craving, nightmares, sweating, nausea, tremor and headache, palpitation, insomnia, headache, diarrhea, vomiting.



# Summary

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- “Spice” and “K2”, widely used by high school and college students, are emerging public health challenges.
- Their rapid rise in popularity,
  - ready access from multiple sources
  - production of acute psychological distress
  - toxicity
  - potentially long term harmful effects
  - ability to evade standard drug tests, require a massive public education campaign and strategies for deterrence in healthcare systems are needed to respond to this emerging threat.

# Hallucinogens

1. Phenethylamines : similar to mescaline
2. Dragonfly: 2C-Bfly, Br-fly, Br-dragonfly)
3. SalvinorinA: *5.9% among 12<sup>th</sup> graders*
4. Smiles:
5. Dissociative anesthetics: methoxetamine, ketamine, PCP
6. DMAA (1,3-dimethylamylamine): “party pills”, weight loss, sports performance supplements.

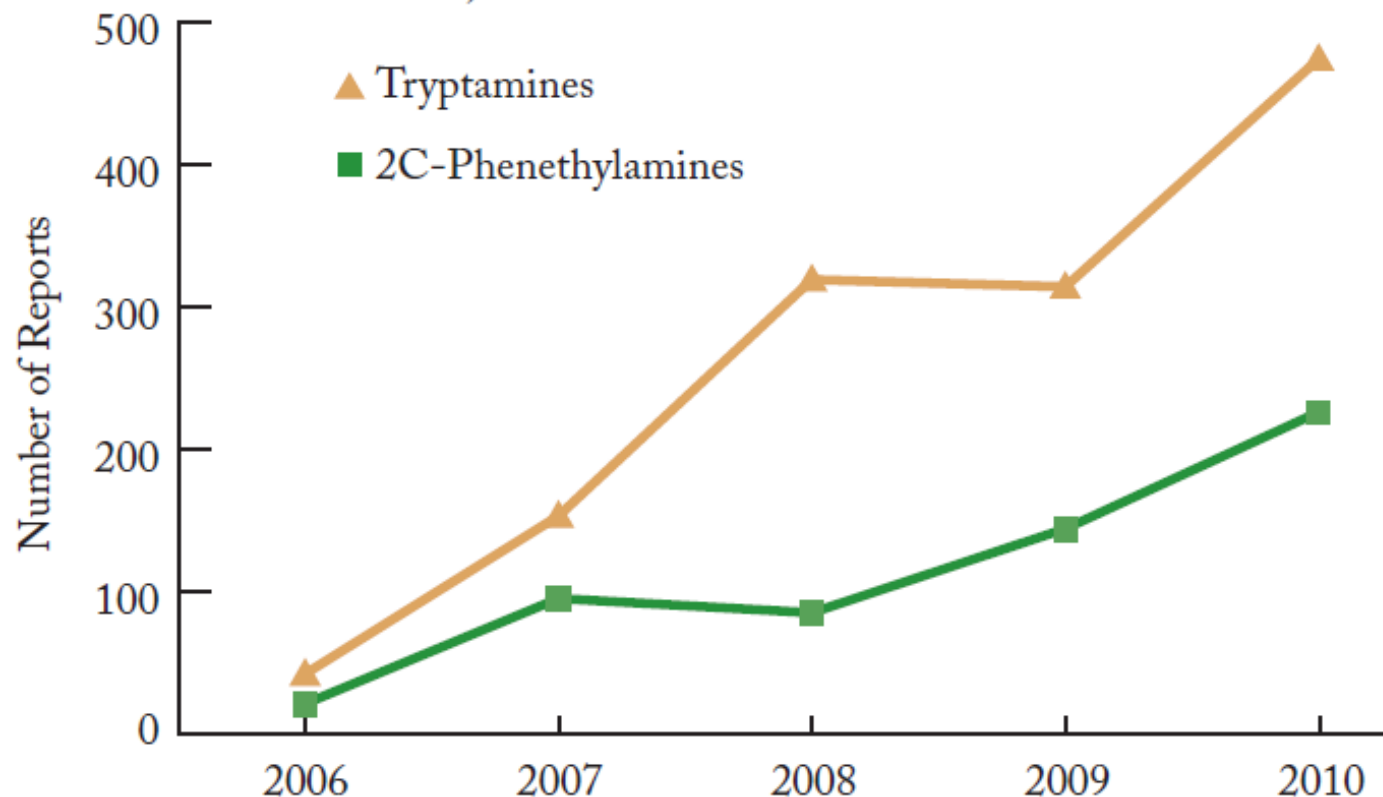
# Smiles or 25-I



- **“Smiles” or “25-I”:** analog of 2C-B: drug is the newest of "research chemicals" available for purchase online.
- 25-I's chemical makeup varies from batch to batch, effects similar to LSD, 2C-I, and 2C-B, all banned under federal law.
- **Psychoactive effects:** hallucinations, in some cases severe brain hemorrhaging, death.
- **Trend in Connecticut:** among high school and college students.
- **Public awareness:** Unaware of potentially fatal side effects.

# Dragonfly

**Figure 1** 2C-Phenethylamine and Tryptamine Reports to NFLIS, 2006-2010



# Dragonfly Shopping Cart

2C	Chemical name	Dosage	Duration (h)
2C-B	4-Bromo-2,5-dimethoxyphenethylamine	12–24 mg	4–8
2C-C	4-Chloro-2,5-dimethoxyphenethylamine	20–40 mg	4–8
2C-D	4-Methyl-2,5-dimethoxyphenethylamine	20–60 g	4–6
2C-E	4-Ethyl-2,5-dimethoxyphenethylamine	10–25 mg	8–12
2C-G	3,4-Dimethyl-2,5-dimethoxyphenethylamine	20–35 mg	18–30
2C-G-3	3,4-Trimethylene-2,5-dimethoxyphenethylamine	16–25 mg	12–24
2C-G-5	3,4-Norbornyl-2,5-dimethoxyphenethylamine	10–16 mg	32–48
2C-I	4-Iodo-2,5-dimethoxyphenethylamine	14–22 mg	6–10
2C-N	4-Nitro-2,5-dimethoxyphenethylamine	100–150 mg	4–6
2C-P	4-Propyl-2,5-dimethoxyphenethylamine	6–10 mg	10–16
2C-SE	4-Methylseleno-2,5-dimethoxyphenethylamine	~100 mg	6–8
2C-T	4-Methylthio-2,5-dimethoxyphenethylamine	60–100 mg	3–5
2C-T-2	4-Ethylthio-2,5-dimethoxyphenethylamine	12–25 mg	6–8
2C-T-4	4-Isopropylthio-2,5-dimethoxyphenethylamine	8–20 mg	12–18
2C-T-7	4-Propylthio-2,5-dimethoxyphenethylamine	10–30 mg	8–15
2C-T-8	4-Cyclopropylmethylthio-2,5-dimethoxyphenethylamine	30–50 mg	10–15
2C-T-9	4-(t)-Butylthio-2,5-dimethoxyphenethylamine	60–100 mg	12–18
2C-T-13	4-(2-Methoxyethylthio)-2,5-dimethoxyphenethylamine	25–40 mg	6–8
2C-T-15	4-Cyclopropylthio-2,5-dimethoxyphenethylamine	>30 mg	Several hours
2C-T-17	4-(s)-Butylthio-2,5-dimethoxyphenethylamine	60–100 mg	10–15
2C-T-21	4-(2-Fluoroethylthio)-2,5-dimethoxyphenethylamine	8–12 mg	7–10





# Dragonfly Deaths

- 2Cs are designer drugs emerging as new drugs of abuse.

Table 2 Deaths from 2C reported in the media

Age/sex	Agent	Route	Dose	Symptoms
20-year-old male [35]	2C-T-7	Snorted	35 mg	Vomiting, hallucinations, agitation, violence/aggression, nasal bleeding, possible seizure activity, pulmonary edema, cardio/pulmonary arrest
17-year-old male [36]	2C-T-7	Snorted	Unknown	Agitation, violence, aggression, possible hyperthermia (temp. of 40.5 °C), seizures, Cardio-pulmonary arrest
Unknown male [37]	2C-T-7; 200 mg MDMA	Unknown	Unknown	Agitation, aggression, violence, seizures, hallucinations, cardio/pulmonary arrest, cerebral hemorrhage
22-year-old male male [38]	2C-T-21	ingestion	Unknown (dipped tip of tongue into powder)	Hyperthermia (108 °C), seizures, coma
19-year-old male male [34, 44]	2C-T	Snorted	Unknown	Aggressive/agitation, hyperthermia, DIC, multi-organ failure
17-year-old male male [39, 40]	2C-LNBOMe	Ingestion	Unknown, mixed with chocolate	Hyperventilation, foaming at the mouth
18-year-old male [39, 40]	2C-LNBOMe	Unknown	Unknown	Unknown

Information is taken from what reported in the media and therefore accuracy cannot be verified

# Methoxamine and methylhexanamine

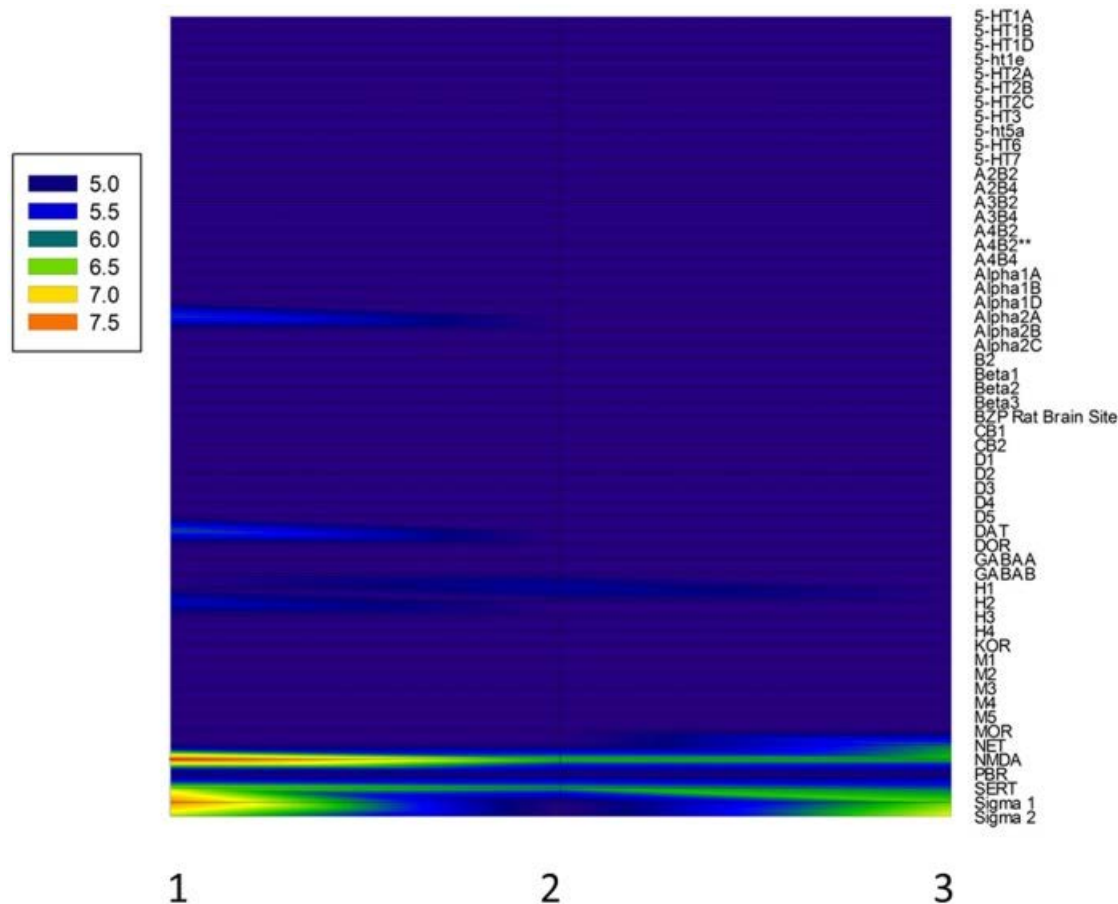
## Methoxamine

- 2011
- Dissociative, pain suppression
- Sold as ketamine derivative
- Similar to PCP
- 5-7 hour duration
- Deaths

## Methylhexanamine

- Stimulant
- Dietary supplement market
- Cathinone replacement
- DMAA FDA challenges for safety evidence
- Deaths

# Methoxetamine and 3,4-methoxy analogues of PCP target NMDA receptors



# Summary

## Designer drugs: a rapidly expanding threat to public health

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- A vast array of new drugs are being introduced
- Contents, doses of substances unknown
- Drug interactions unknown
- Short-, long-term effects unknown
- Toxicity reports are increasing rapidly
- Effects on developing brain unknown
- Routine drug testing currently not feasible
- Legal status for many uncertain

# Summary

## Designer drugs: a rapidly expanding threat to public health

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- Impact on brain function, behavior, organ systems, is unacceptably high
- Preclinical research on each drug (100's) is not feasible unless massive scale-up of research funding
- Drug combinations challenge research
- We are engaged in a massive human experiment, which will require years to resolve



# What Concerned People Can Counsel

- **Avoid consuming drugs that affect thinking, feelings, judgment.**
- **The adolescent brain is fragile as it is not fully formed.**
- **No one knows what a street drug contains, how much, impurities, toxins.**
- **Intoxication is risky, for health, for making unsafe or unhealthy choices.**
- **Any drug, legal or not, if not prescribed / used for medical purposes, can be unsafe.**
- **No one knows long term effects of designer drugs.**

# Faustian Bargains

## Drug Use and Drug Policy

Pleasure

Full, legal access

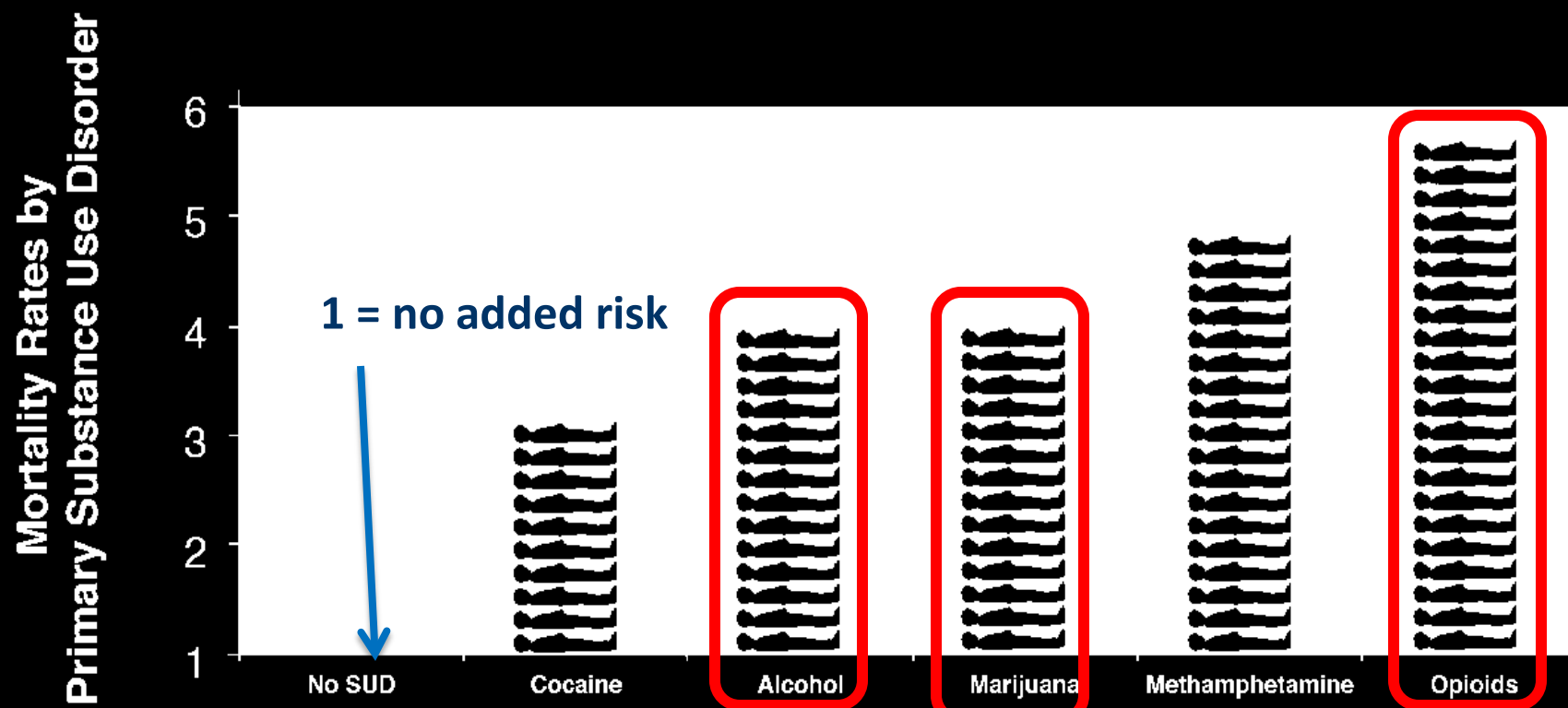


Pain

Medical, social,  
economic, legal, costs

# Death Rates 3-5 Times Higher in Addicted Patients

## Standardized Mortality Rates of Patients with a Primary Substance Use Disorder (SUD)



adapted from: Callaghan RC, Cunningham JK, Verdichevski M, Sykes, J, Jaffer SR, Kish SJ. (2012) All-cause mortality among individuals with disorders related to the use of methamphetamine: A comparative cohort study. *Drug Alcohol Depend.* doi:10.1016/j.drugalcdep.2012.03.004