Street Drug Pharmacology 2017

J. Randall Webber, MPH, CADC
JRW Behavioral Health Services
www.randallwebber.com

www.linkedin.com
Emerging Drugs of Abuse discussion group

Psychoactivity = ability to affect mood, thinking, perception and/or behavior

CONTROLLED SUBSTANCES

- Schedules I-V
- Schedule I: High potential for abuse, tendency to produce dependence, no accepted medical use in US
- Schedules II-V: Potential for abuse, tendency to produce dependency, does have accepted medical application

SCHEDULE I SUBSTANCES

- LSD
- Heroin
- Cannabis
- PCP

SCHEDULE II SUBSTANCES

- Morphine
- Cocaine
- Short-acting barbiturates
- Amphetamines

DRUG NAMES

- Chemical (7-chloro-1,3-dyhydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one
- Generic: diazepam
- Brand : Valium
- Street: No common street names for Valium

Potency, purity & misrepresentation of street drugs

- **potency** = strength, compared to some other drug of a similar type.
- **purity** = the major determinant of potency.
  - The more pure the drug, the more potent.
  - Street drugs are seldom pure, but are commonly misrepresented in one of three ways

DRUG MISREPRESENTATION

- **adulteration:** (to adulterate = to "step on"/"hit"/"dance on" "cut" a drug).
- **Substitution/misrepresentation-1:** None of the alleged drug is present, but another drug/drugs is/are.
- **substitution/misrepresentation -2:** None of the alleged drug is present, and neither is any other drug or active substance.

The Problem with Pill Identifications:

New York City May 2000 Amphetamine

Chicago May 2000 MDMA

Portland Oct 2000 MDMA

Tucson AZ July 2000 PMA

TIME FACTORS

- Onset of action: How quickly does the drug produced it's effect?
- Duration of action: How long does the drug's effect last?
- Residual effects: After-effects, extended drug reaction, flashbacks

METHOD OF ADMINISTRATION

- Ingestion (oral): slower onset/longer duration
- Insufflation (sniffing/snorting): faster onset/shorter duration
- Intravenous (I.V.) Injection: faster onset (seconds)/shortest duration
- Smoking: fastest onset/shortest duration

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Abscesses Associated with I.V. Injection

THE “RUSH” OR “FLASH”

A highly pleasurable sensation produced by the instantaneous effect of i. v. injection or smoking*

* If entire dose administered at once

METABOLISM AND EXCRETION

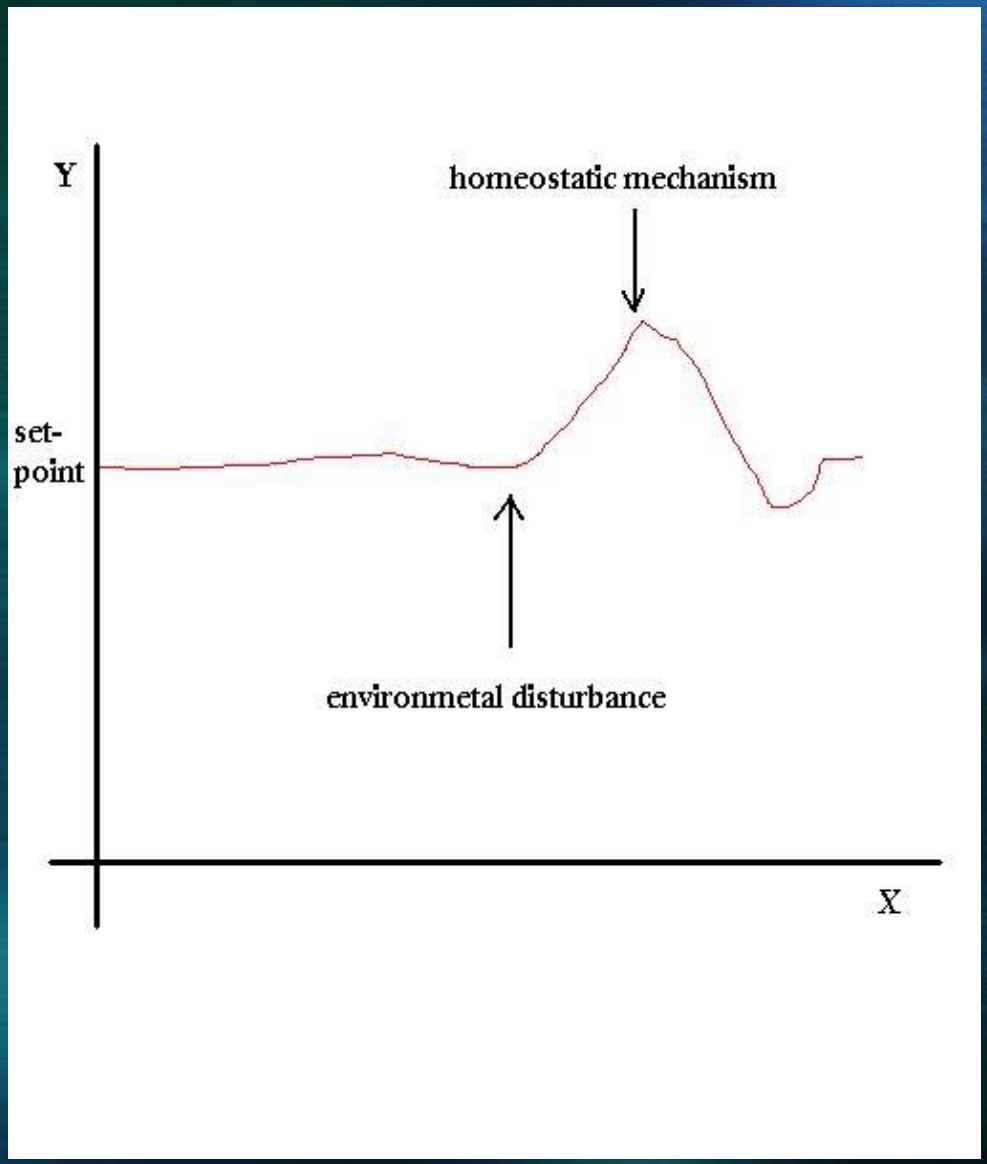
- The break-down of a drug into simpler substances
- The removal of the drug from the body

TOLERANCE

Homeostasis

The human body's natural tendency to move toward a state of equilibrium or constancy

SET POINT RESPONSE TO DRUG USE



TOLERANCE

- Need to increase the dose of a drug in order to obtain the desired effect
- Decreased effect of drug after repeated administration
- Dependent on prior dosage level
- Develops in hours (cocaine), days (LSD), or weeks

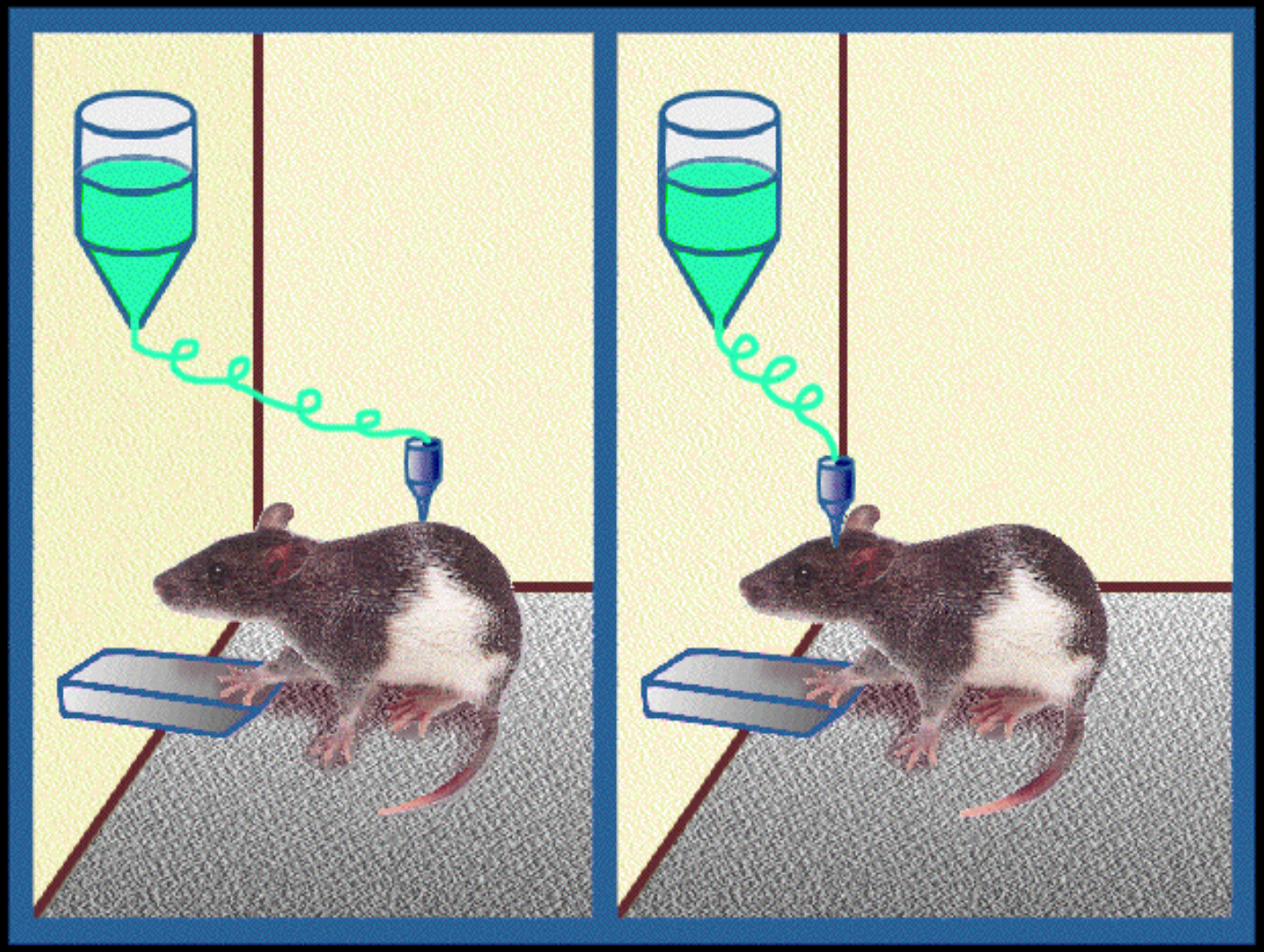
ADDICTION POTENTIAL

- What percentage of first-time users will enjoy the effect of the drug enough that they will seek it out again?
- If an individual uses the drug on a regular basis, how likely is it that s/he will become dependent on the substance?

ADDICTION POTENTIAL

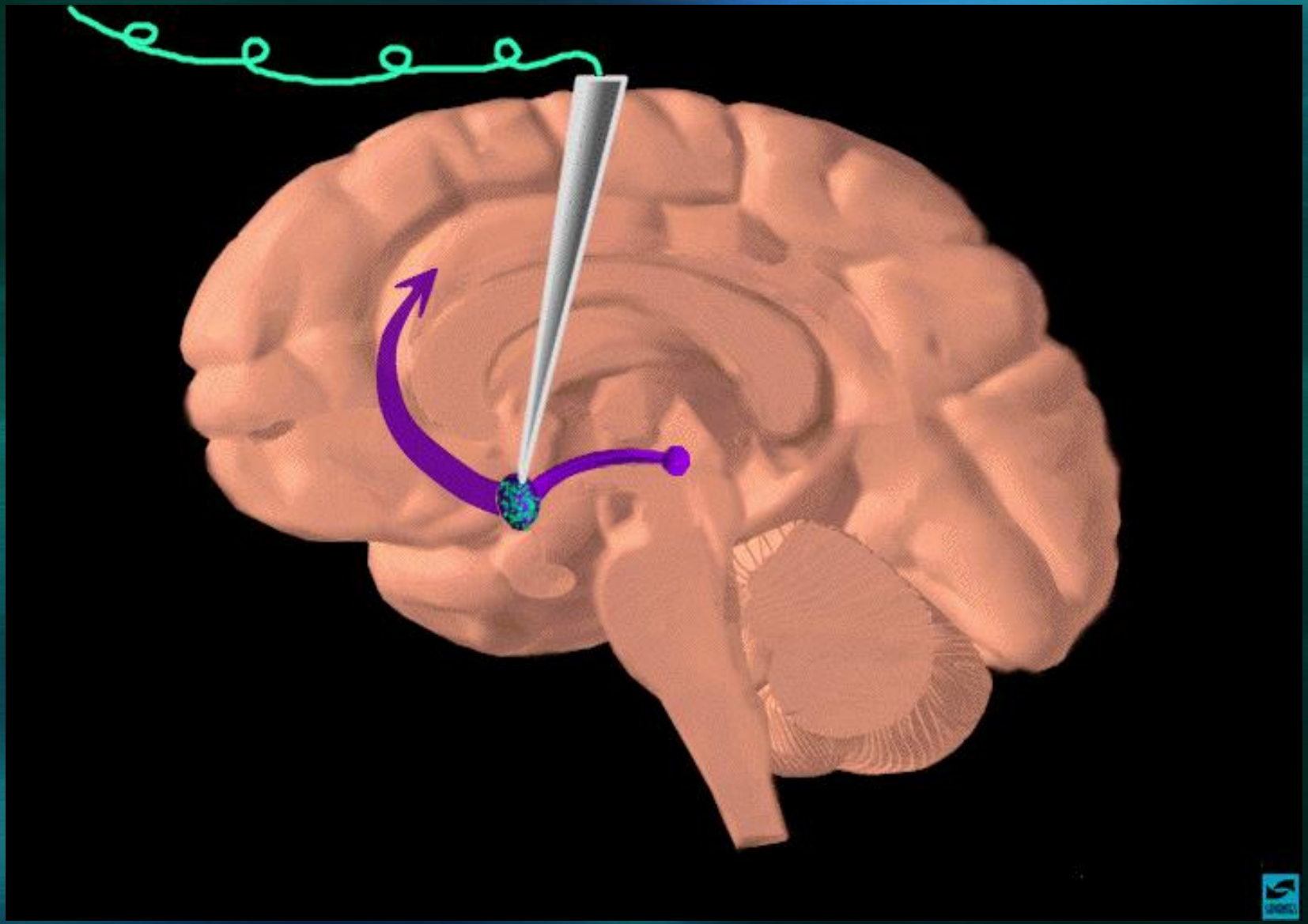
- After being introduced to the drug, do sub-human animals (e.g., monkeys, rats, mice) seek out opportunities to self-administer the substance? Do they do so to the exclusion of eating, consuming water and engaging in reproductive behavior?

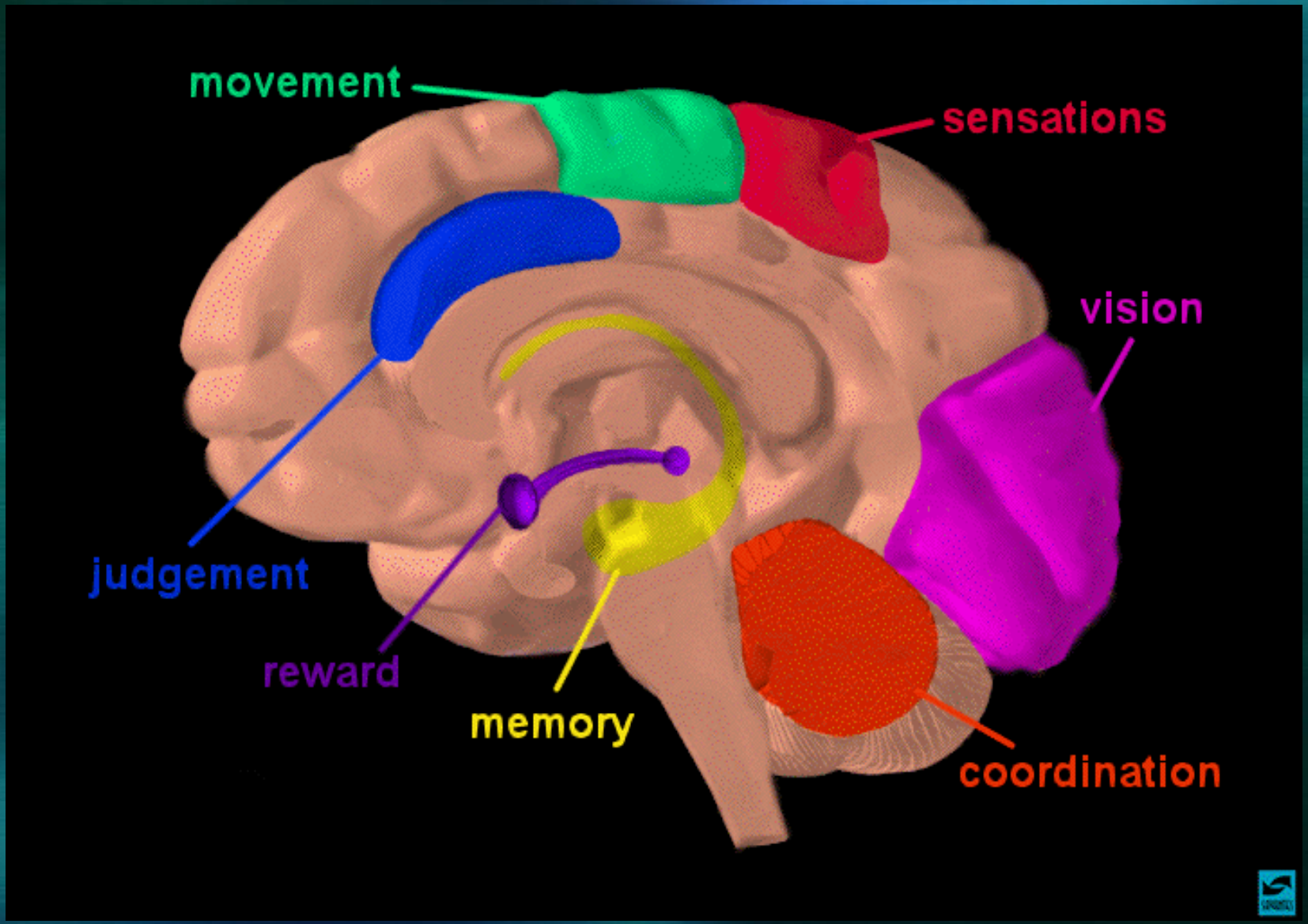
ADDICTION POTENTIAL CAN BE PREDICTED IN PART BY OBSERVING ANIMAL SELF-ADMINISTRATION

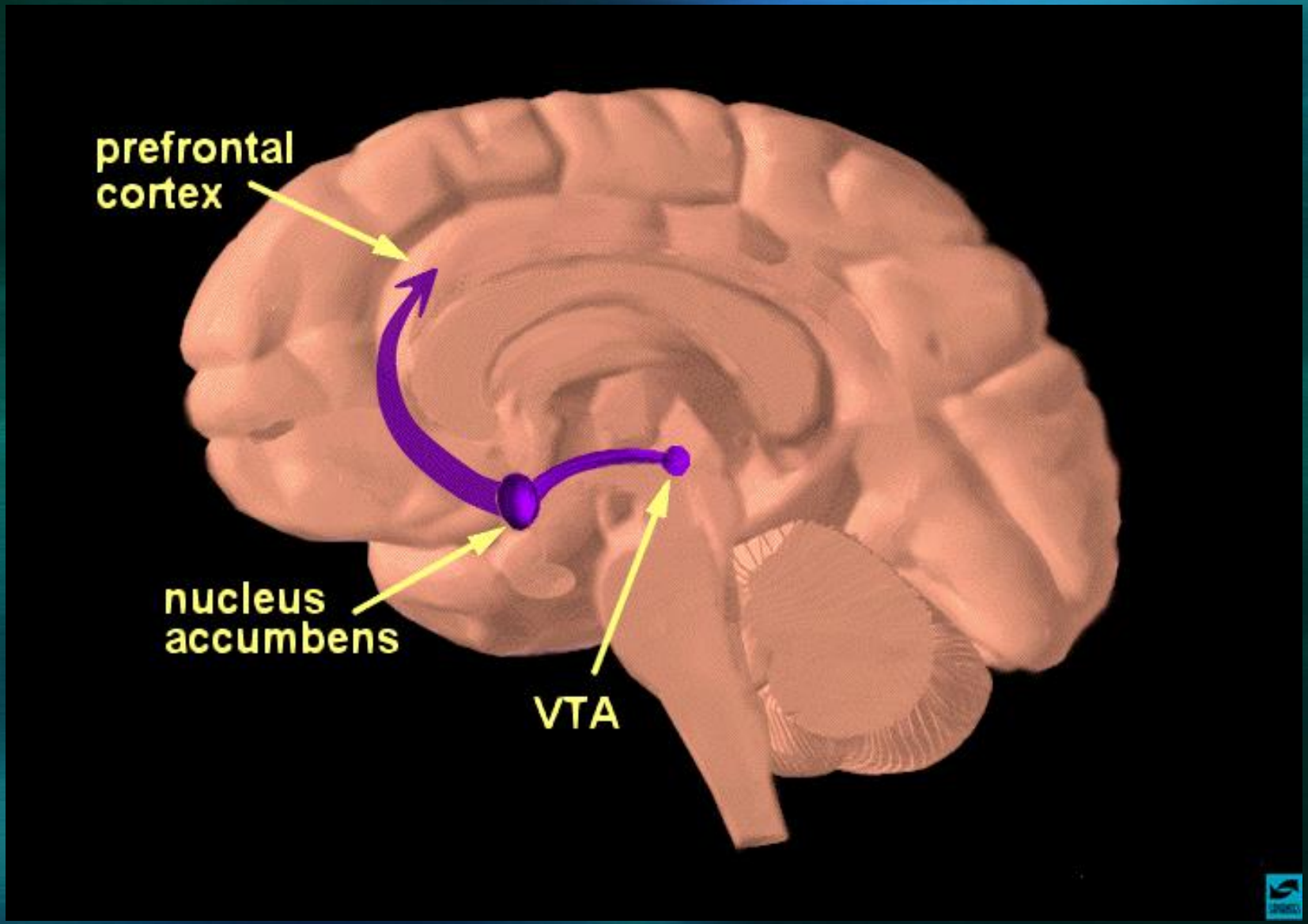


ADDICTION POTENTIAL

- Ability to stimulate the brain's reward circuits
- Ability to meet a individualized neurochemical need
- Physical dependency potential
- Intensity of withdrawal symptoms




movement
sensations
vision
judgement
reward
memory
coordination


prefrontal
cortex
nucleus
accumbens
VTA

ADDICTION POTENTIAL

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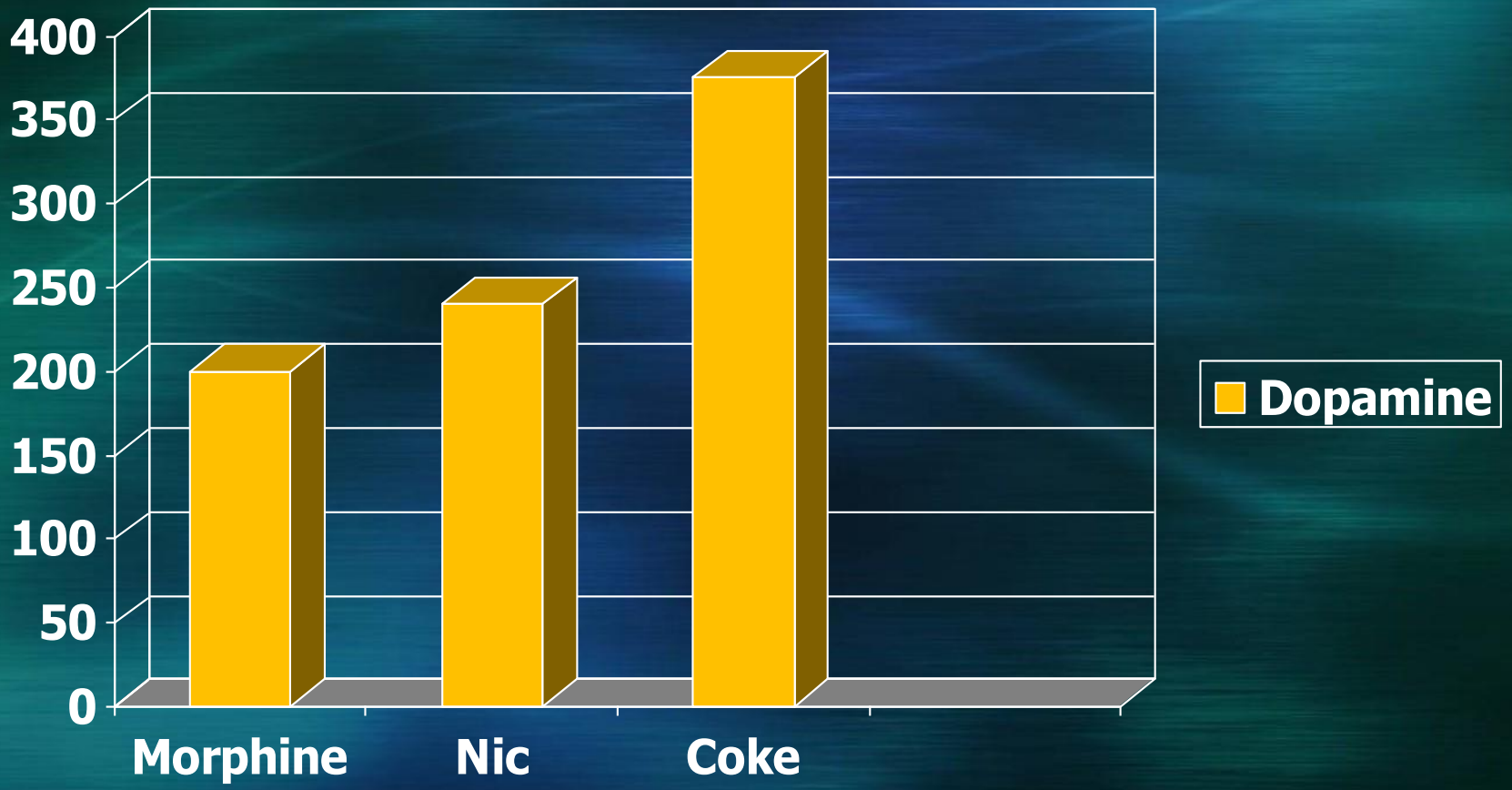
Neurotransmitters

- Serotonin (5-HT)
- Norepinephrine (NE)
- Dopamine (DA)
- Acetylcholine (Ach)
- Glutamate (GLU)
- Gamma amino butyric acid (GABA)
- N-methyl-D-aspartate (NMDA)

Dopamine Levels in the Shell of the Nucleus Accumbens (% of baseline)



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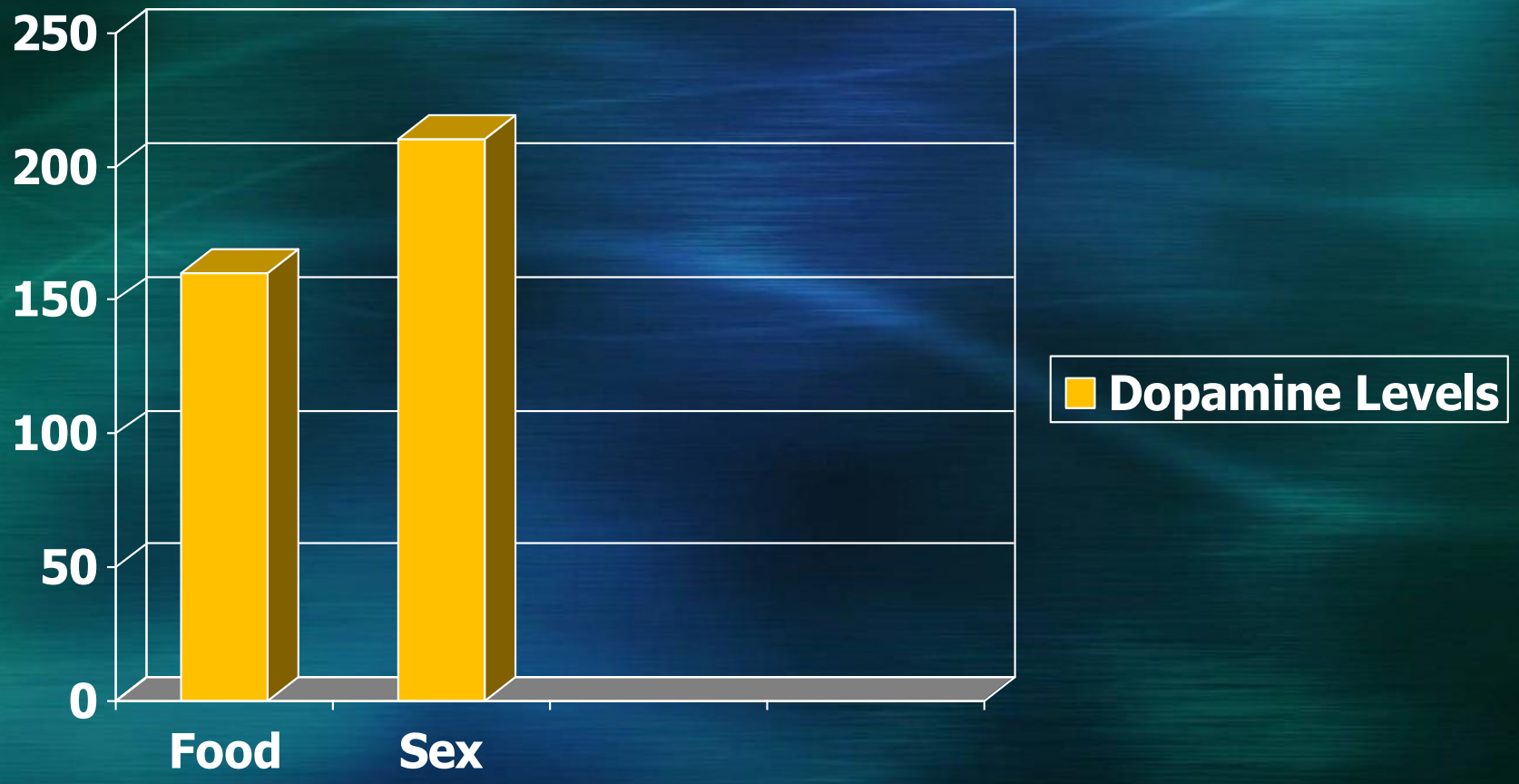

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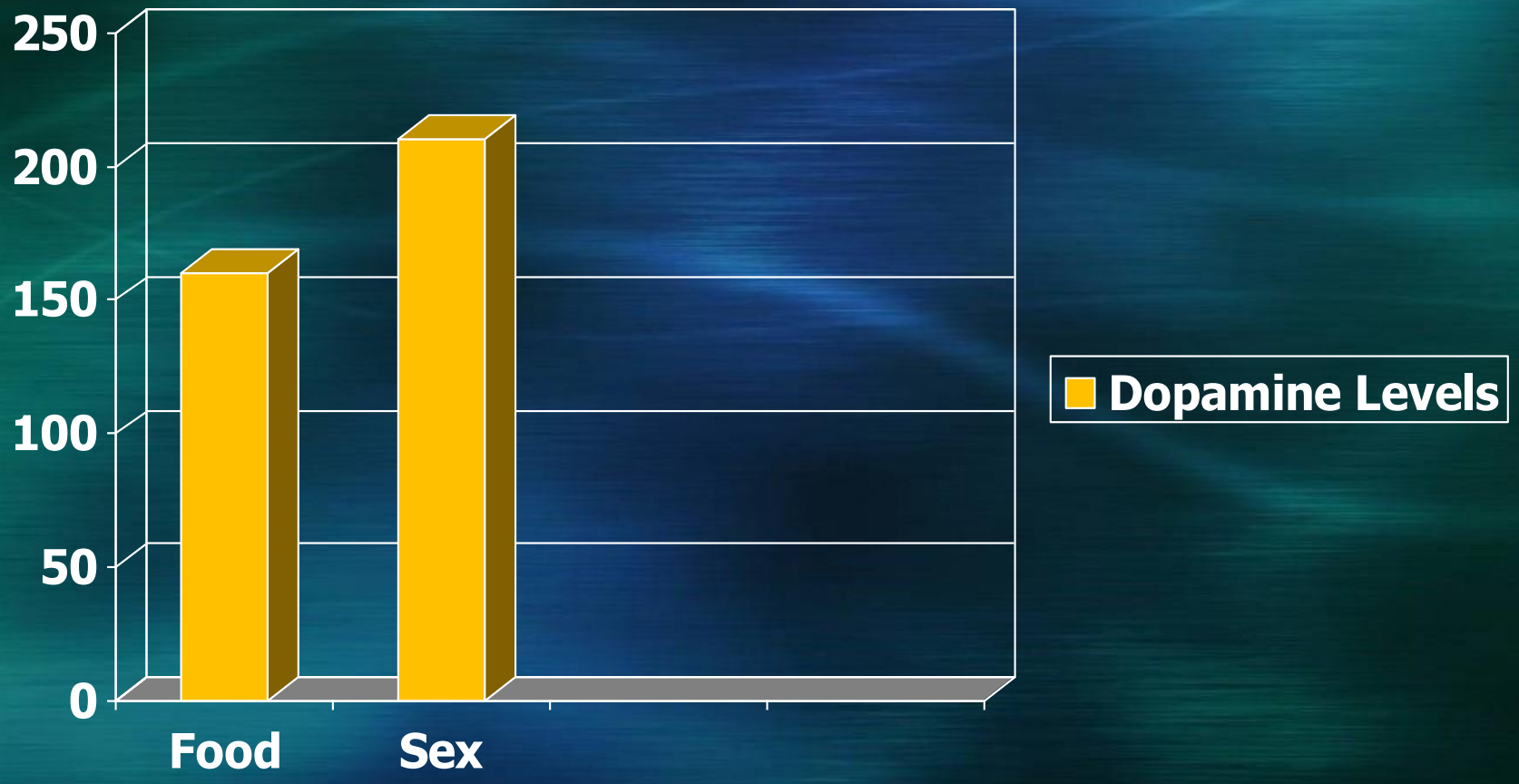

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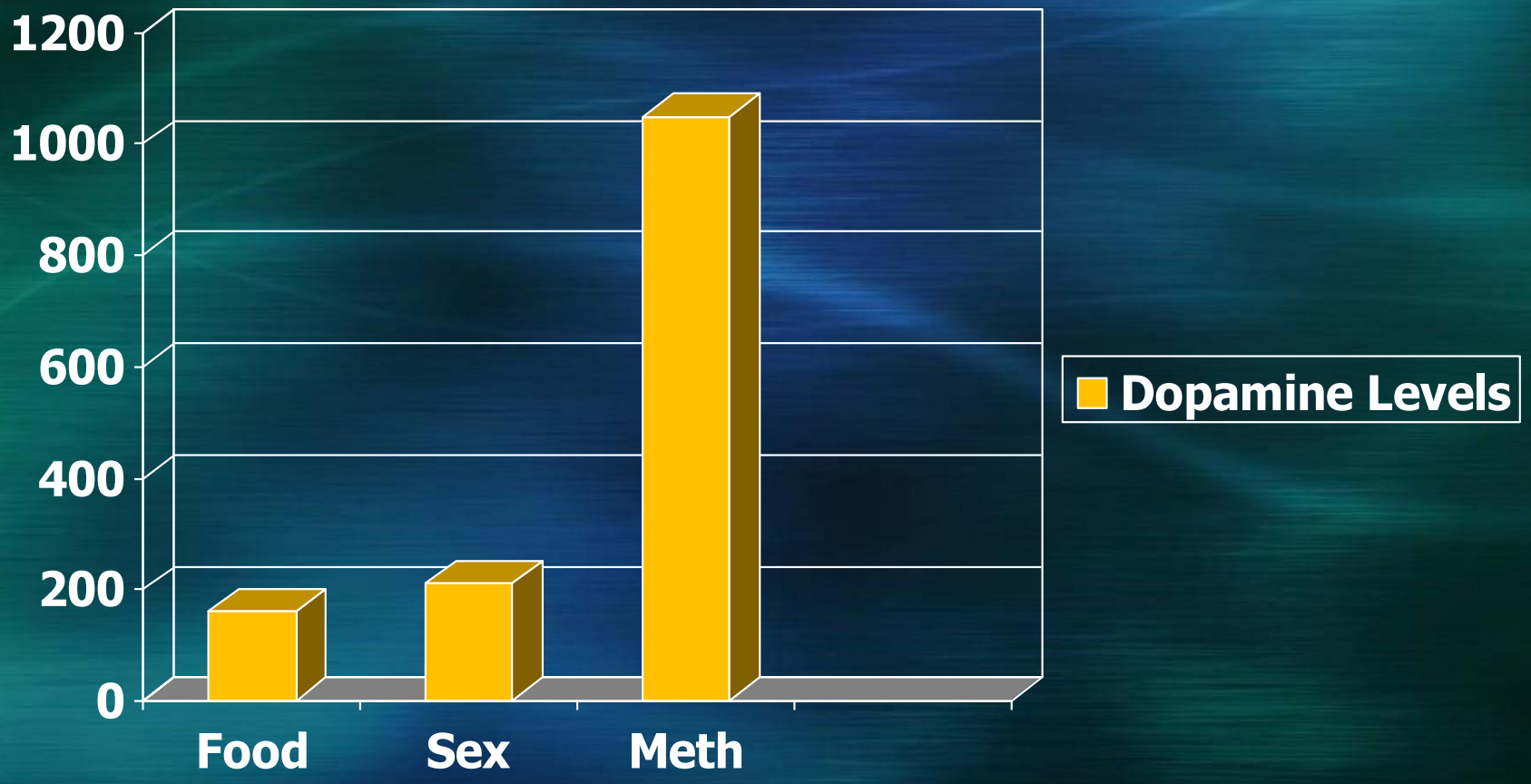
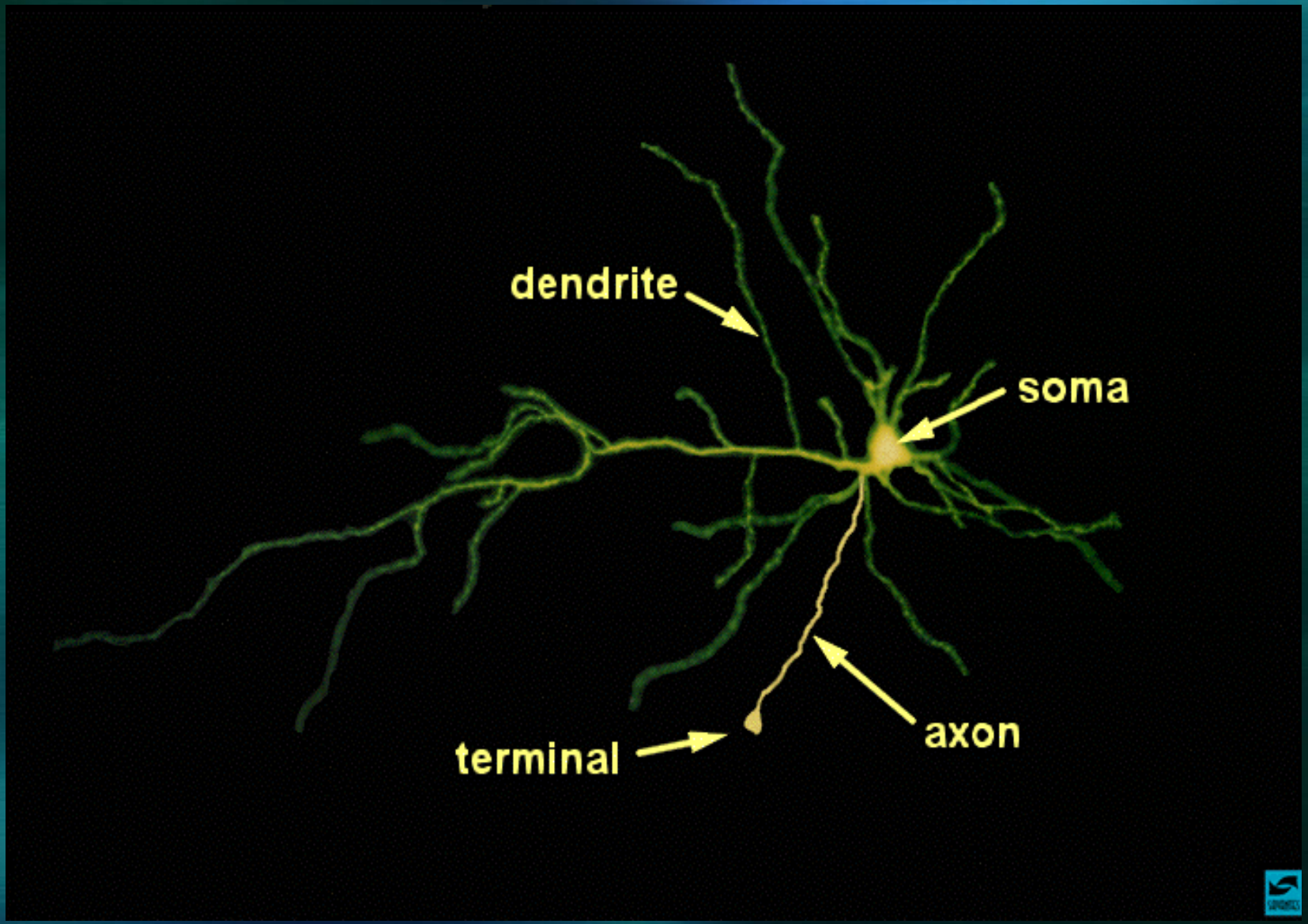
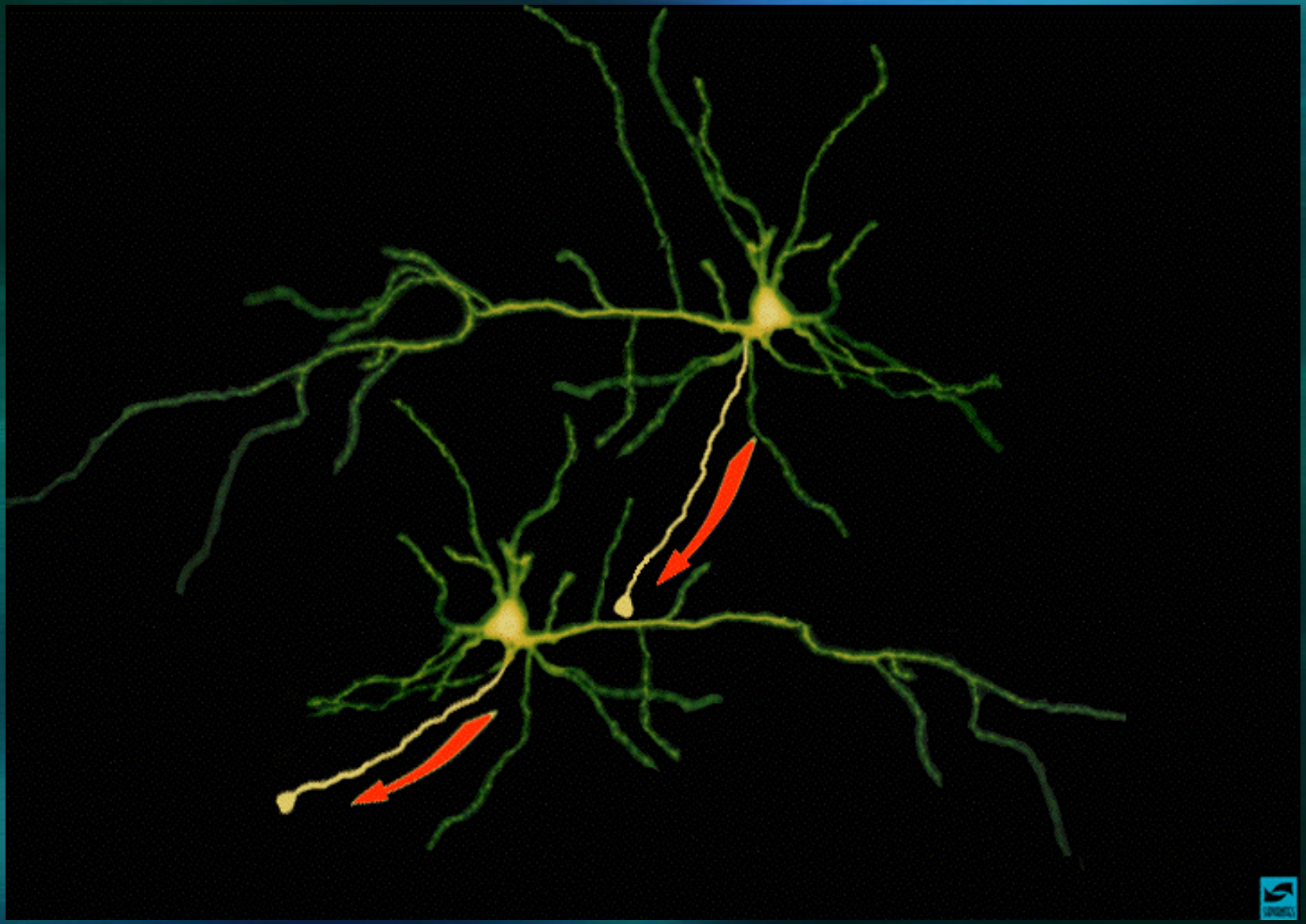
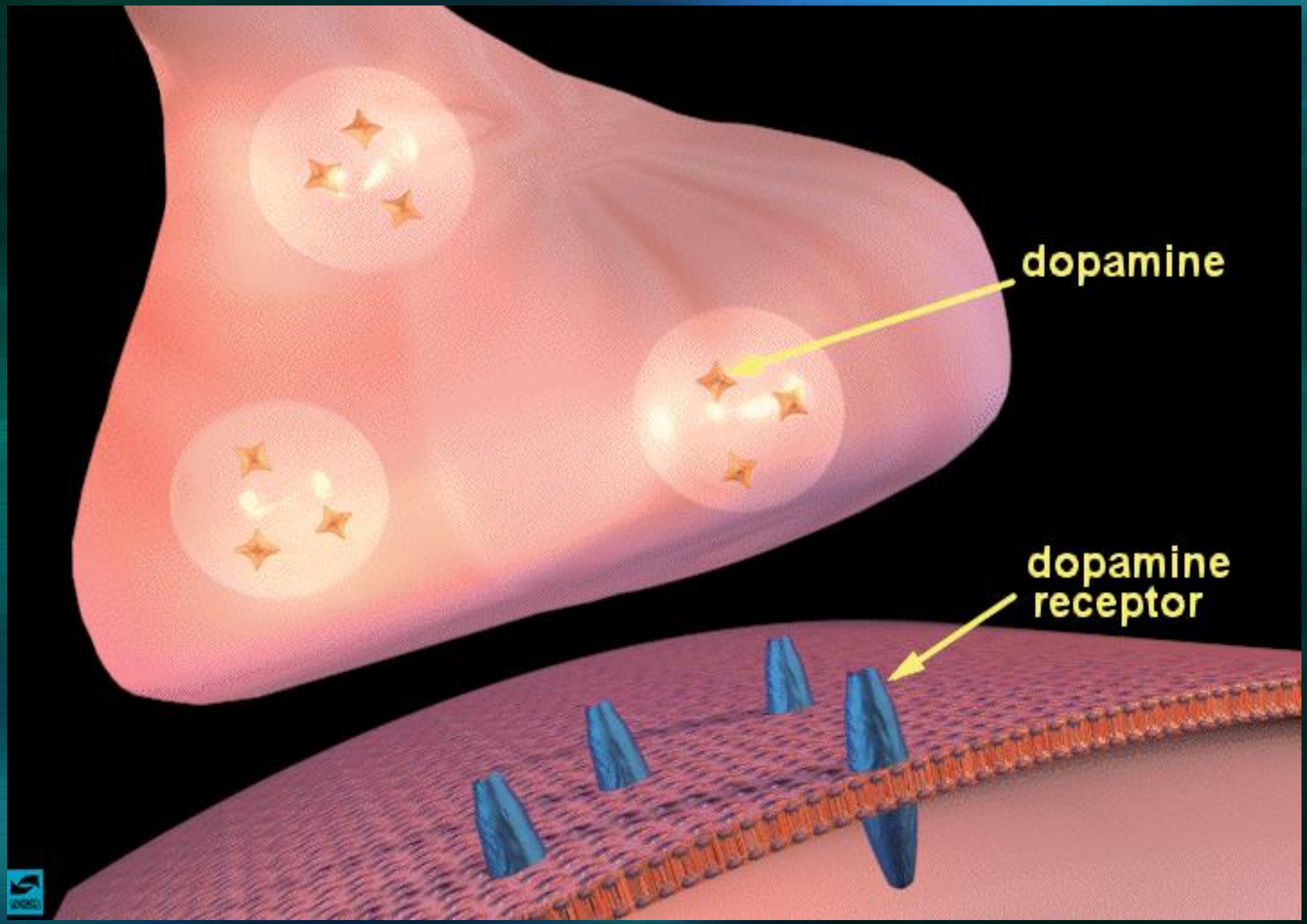
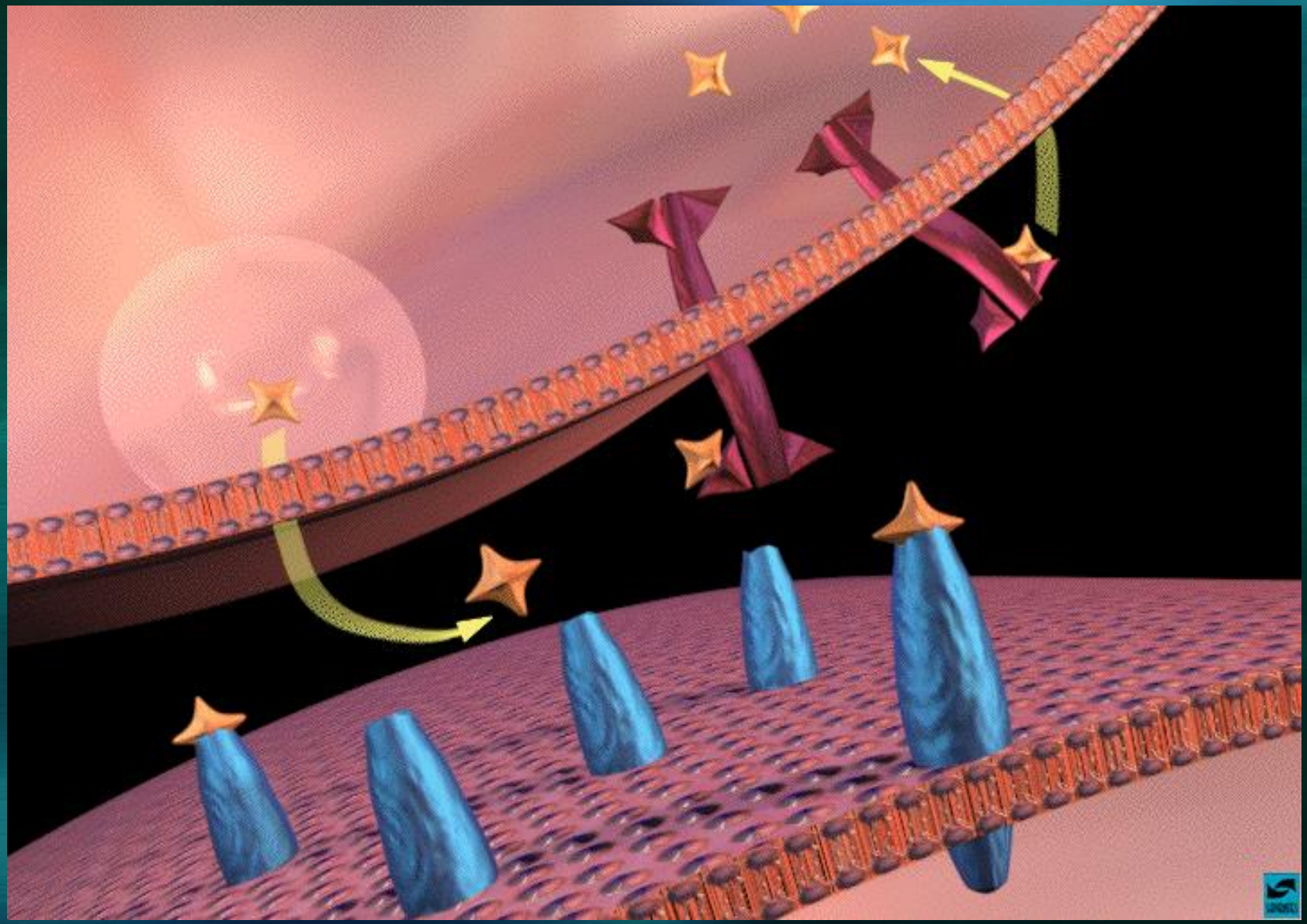



dendrite
soma
terminal
axon




dopamine
dopamine receptor



NEUROTRANSMITTERS

- Naturally-occurring brain chemicals
- Many psychoactive drugs resemble neurotransmitters:

NEUROTRANSMITTERS

DRUG	NEUROTRANSMITTER
LSD	Serotonin
Methamphetamine	Norepinephrine
heroin	Endorphins

NEUROTRANSMITTERS

DRUG	NEUROTRANSMITTER
THC	Anandamide
PCP	Receptor site identified but not associated neurotransmitter

TOXICITY

- Ability to produce physical damage to the human body
- Long-range = months, years
- Short-range = days, weeks
- Physical vs behavioral

TOXICITY

- Physical
- Behavioral
- Acute Vs Long-Term

PSYCHIATRIC IMPAIRMENT

- Ability of drug to produce negative changes in thinking, learning, perception, mood or behavior
- Acute vs chronic

PSYCHIATRIC IMPAIRMENT

- Short-term
- Long-term
- Affective Disorders
- Thought Disorders

“Krokodil”:

A Media Rumor Runs Wild

A lesson in how to divert attention from real problems

Krokodil patient in Russia

Krokodil: A Timeline

- 2010: News reports from Russia
- November 2012: “Krokodil” implicated in overdose death in Oklahoma. Autopsy showed only morphine
- Oklahoma Bureau of Narcotics: Accounts of “Krokodil” in the media “should be taken with a grain of salt.”
- September 23, 2013: 2 patients in Arizona diagnosed with krokodil-related medical conditions. No laboratory evidence of desomorphine found
- Early October, 2013: 2 cases reported in Utah. Still no laboratory evidence of desomorphine exists anywhere in US

- October 14, 2013: Krokodil reported in Joliet, Illinois. The media frenzy begins

Intravenous Drug User in Great Britain (Picture used in a report on Krokodil broadcast by ABC affiliate WLS-TV in Chicago)


НИЖНИЙ НОВГОРОД

Krokodil: A Timeline

- Reports greeted with skepticism by Linkedin.com “Emerging Drugs of Abuse” discussion group
- Media continues to report stories despite lack of analytical findings
- US DEA makes finding krokodil top priority for 200 agents in five states. Only heroin found.

October 27, 2013: A Voice of Rationality

Chicago Tribune

Suspected krokodil a false alarm

Negative tests lead to further skepticism

October 27, 2013|By Andy Grimm, Chicago Tribune reporter

(Anthony Souffle, Chicago Tribune)

The hunt for krokodil continues as tests conducted in recent days on a suspected sample of the so-called flesh-eating drug came back negative, federal officials said.

An announcement two weeks ago by a Joliet doctor who said he treated three patients who showed the telltale rotting flesh associated with the toxic, home-brewed opiate — made from mixing codeine tablets with solvents like gasoline or acids — has sparked media coverage. A week later, a Crystal Lake hospital reported treating a krokodil user, and reports have cropped up across the country.

But whether the U.S. faces a horrifying new drug or merely an urban legend is hard to say, and confirmation of cases may not come for months or years, if ever.

Jack Riley, special agent in charge of the Drug Enforcement Administration's Chicago office, said doctors and victims in the Chicago area have been interviewed by law enforcement.

In a sweep modeled after the agency's successful search for the source of deadly fentanyl-tainted heroin some six years ago, 200 DEA agents across five states have made finding krokodil a top priority, Riley said.

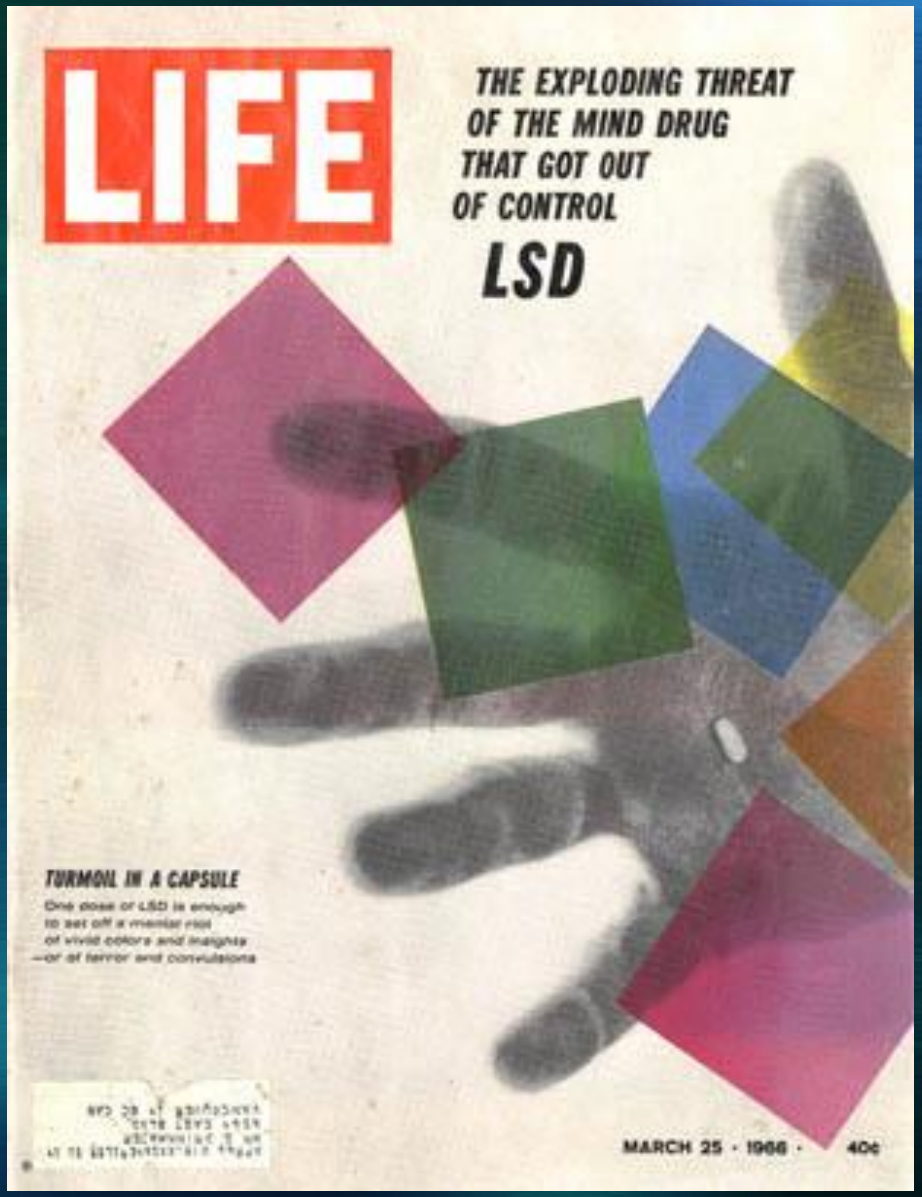
"We have run quite a few buys in the city and suburbs," Riley said "What the lab tells us is it's just heroin."

Some experts in law enforcement and public health say it's unlikely the drug will be widely used beyond the remote areas of Russia and eastern Europe where it became popular a decade ago.

Krokodil is a myth. So what?

- “Krokodil” symptoms probably caused by bacterial infection such as necroticizing faciititis ("flesh-eating disease“)
  - Transmitted by dirty hypodermic needles
  - Drug users could have been told free sterile syringes available legally at needle exchanges
- Waste of time and resources
- Loss of credibility
- What is something real shows up. Like….

March 25, 1966



Important “basics”

- What is the drug’s addiction potential?
- Does the drug produce tolerance?
- What are typical physical dependence withdrawal symptoms?
- What is the drug’s potential for producing immediate and long-term physical toxicity?
- Does the drug produce psychiatric impairment? Short-term? Chronic?

Stimulants

- Cocaine
- Amphetamine (Adderall)
- Lisdexamfetamine (Vyvanse)
- Methamphetamine
- Methylphenidate (Ritalin/Concerta)

Stimulants: Basics

- High addiction potential
- Tolerance develops
- Withdrawal symptoms minimal
- Moderate to high potential for immediate physical toxicity
- Moderate potential for long-term toxicity
- Moderate to high potential for acute psychiatric impairment
- Low to moderate potential for chronic psychiatric impairment

CNS Stimulants (Cocaine)

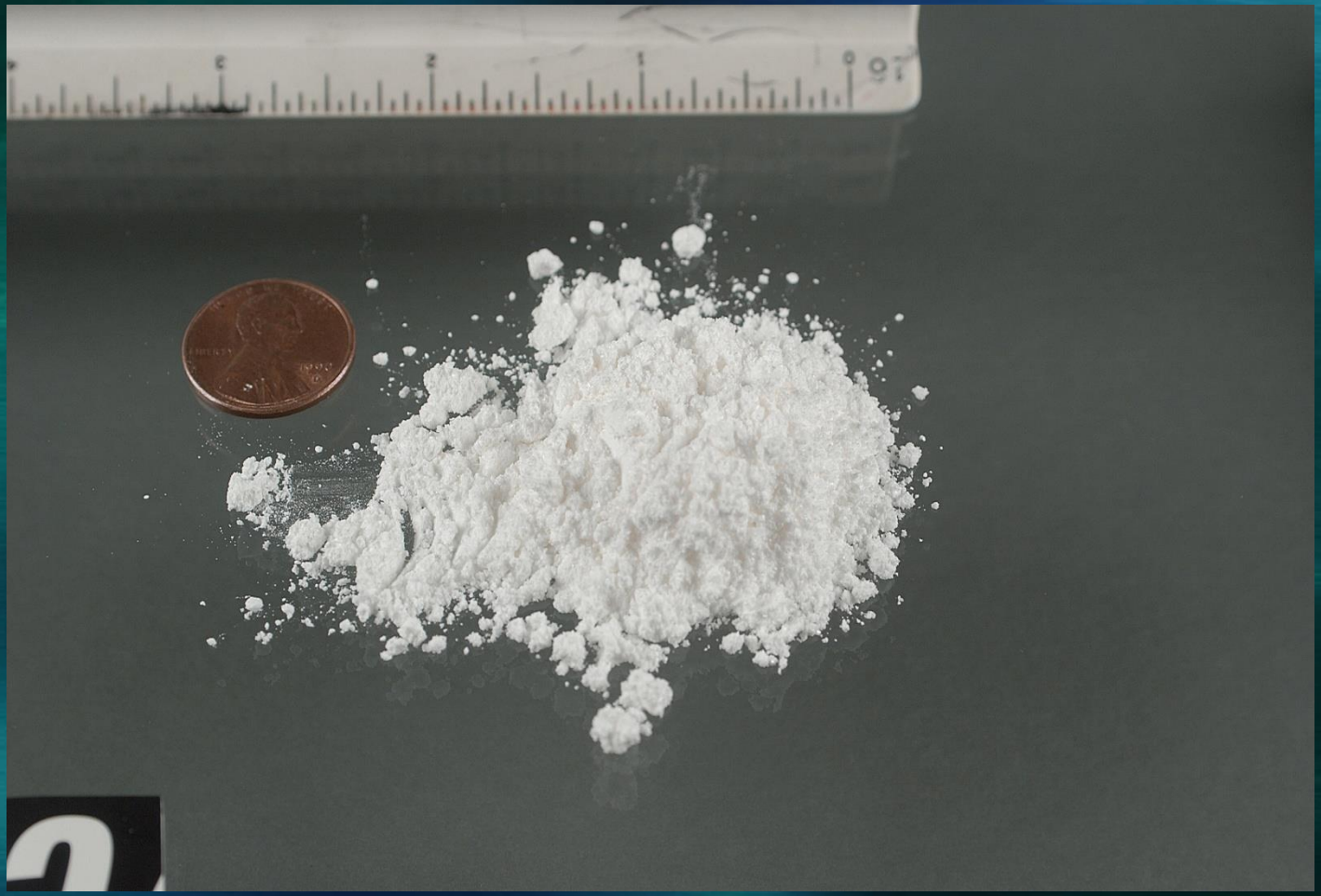
- Local anesthesia
- coca (Erythoxlum Coca)
- cocaine hydrochloride (hcl) ("coke", "toot", "nose/nose candy", "blow", "freeze", "snow", "girl", "white lady", "la mujer blanca")
- alkaloidal cocaine ("free base", "crack", "rock/ready rock", "basuco")

ERYTHROXYLOM COCA FLOWER

COCA FARMER

MAKING COCAINE

Cocaine Hcl



COCAINE PARAPHERNALIA

VIALS OF CRACK

MORE CRACK

Cocaine Vs. Amphetamine

- Cocaine:
  - Short-acting drug, with a duration of 5-60 minutes.
  - Cocaine can be snorted, injected or smoked, but it is relatively ineffective when swallowed.
  - Tolerance to cocaine can develop and then disappear in a matter of hours.
  - When snorted tends to do much more severe damage to the nasal area.
  - Produces *local anesthesia*

Stimulants

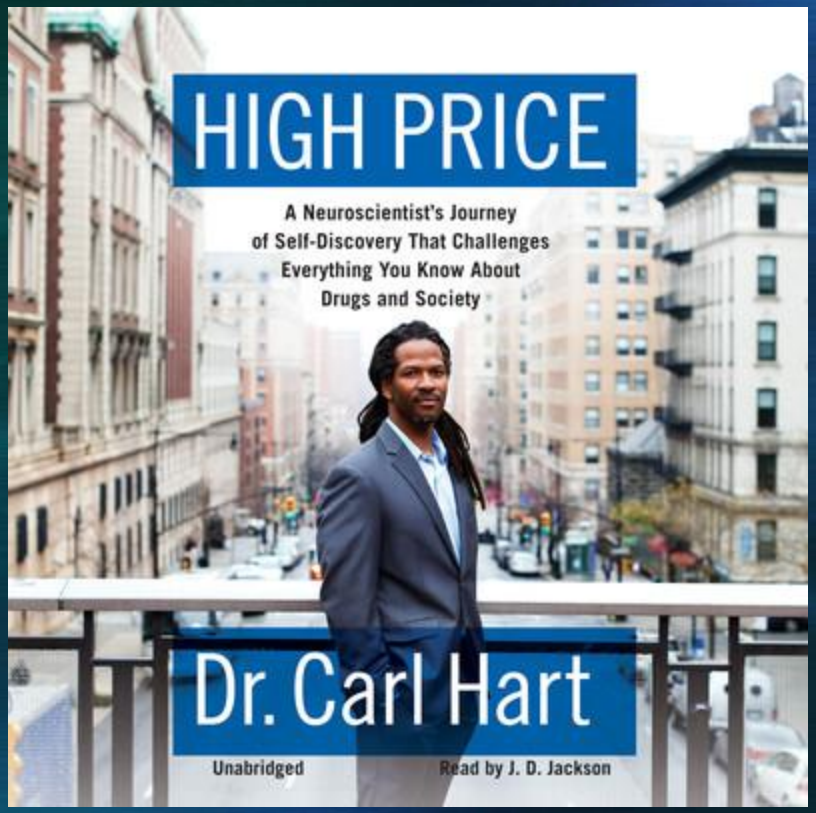
- Cocaine
- Amphetamine (Adderall)
- Lisdexamfetamine (Vyvanse)
- Methamphetamine
- Methylphenidate (Ritalin/Concerta)

Adderall/Other ADD Medications

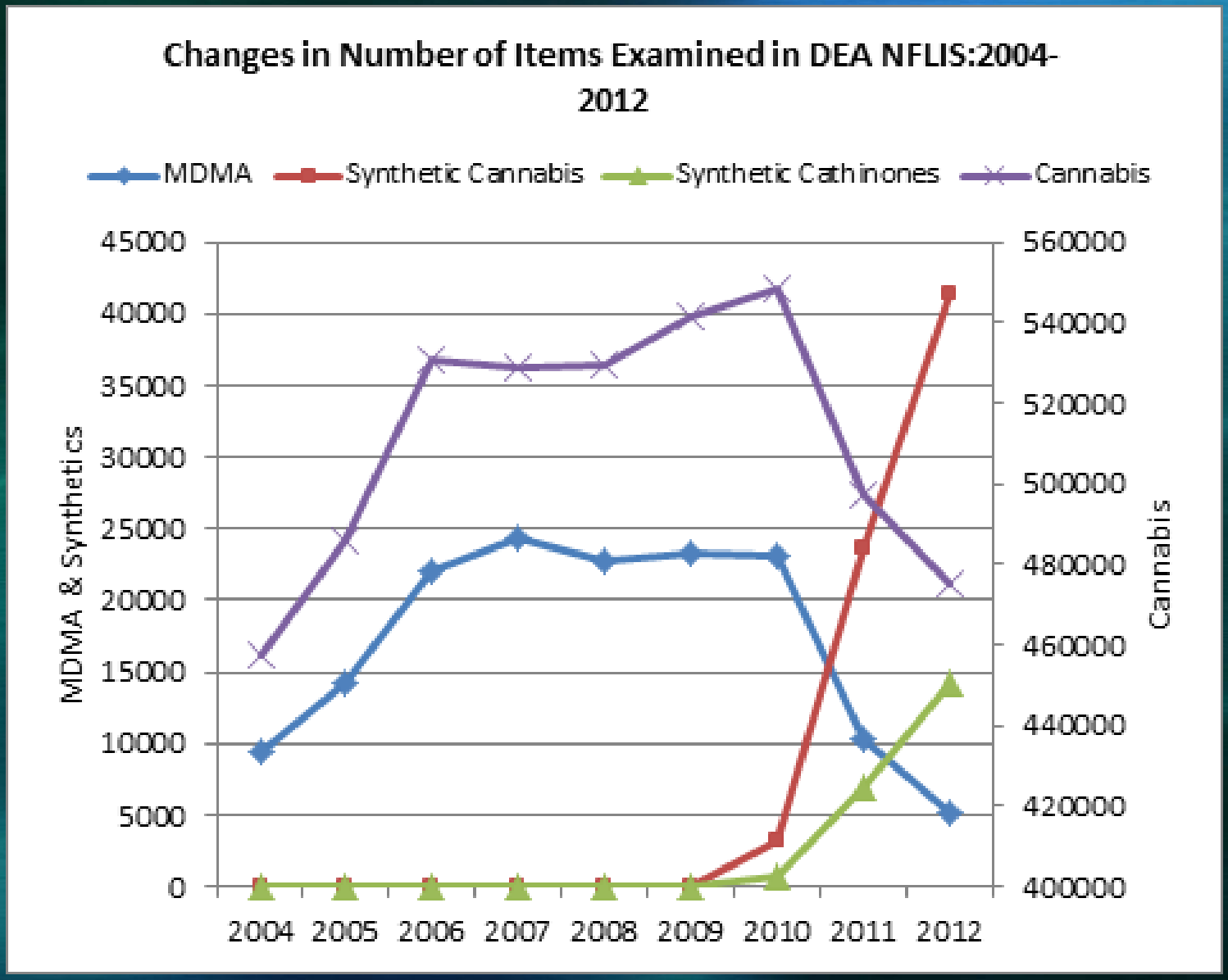
- By senior year, nearly two-thirds of college students are offered Adderall or other “study drugs”, and nearly one-third have accepted
- *Journal of Clinical Psychiatry*: 67% increase 2006 to 2011 in ER visits by adults ages 18-25

Stimulants

- Amphetamine (Adderall)
- Lisdexamfetamine (Vyvanse)
- Methamphetamine
- Methylphenidate (Ritalin/Concerta)
- Cocaine


HIGH PRICE
A Neuroscientist's Journey of Self-Discovery That Challenges Everything You Know About Drugs and Society
Dr. Carl Hart
Unabridged
Read by J. D. Jackson

Stimulants:
Synthetic Cathinones


Changes in Number of Items Examined in DEA NFLIS:2004-2012
MDMA
Synthetic Cannabis
Synthetic Cathinones
Cannabis
MDMA & Synthetics
Cannabis
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
560000
540000
520000
500000
480000
460000
440000
420000
400000
2004
2005
2006
2007
2008
2009
2010
2011
2012

Khat

- Native to tropical East Africa and the Arabian Peninsula
- Fresh leaves/tops chewed or consumed as tea
- Stimulation and euphoria
- Part of social culture in many countries (coffee, tea, coca or khat?)


EGYPT
SAUDI ARABIA
OMAN
CHAD
ERITREA
YEMEN
SUDAN
DJIBOUTI
ETHIOPIA
CENTRAL
AFRICAN
REPUBLIC
SOMALIA
UGANDA
DEM. REP.
OF THE CONGO
KENYA
RWANDA
BURUNDI
TANZANIA
INDIAN OCEAN

Khat cultivation in Yemen

Women in Somalia Selling Khat/Quat

Khat

- Native to tropical East Africa and the Arabian Peninsula
- Fresh leaves/tops chewed or consumed as tea
- Stimulation and euphoria
- Part of social culture in many countries (coffee, tea, coca or khat?)

Khat

- Coca--------Cocaine
- Khat---------Cathinone (Schedule I)
- Cathinone: Structure similar to amphetamines

BATH SALTS*

* Contain schedule I substances as of October 2011

HUFF POST ADDICTION & RECOVERY

Bath Salts: The 'Cannibal' From Miami's Alleged Dangerous Drug Of Choice

Posted: 05/30/2012 10:58 am Updated: 05/31/2012 10:39 am

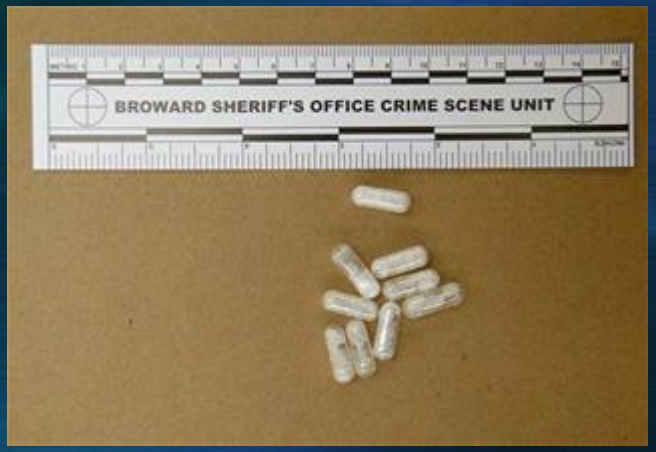
Rudy Eugene, 31, the so-called “Miami Cannibal who was fatally shot as he chewed on another man's face in a gruesome attack over the weekend, is suspected to have been high on a drug known as "bath salts."

Miami cannibal case: NO bath salts or other street drugs found in his system, only marijuana

The Miami-Dade County Medical Examiner's released the toxicology results Tuesday on 31-year-old Rudy Eugene. Lab results found marijuana in his system, but not any other street drugs, alcohol or prescription drugs.

newser
READ LESS KNOW MORE

How Flakka Can Turn Man to Cannibal



No evidence exist that the person had taken “flakka”/alpha-PVP

“White Blizzard”

Possible Substances in "Bath Salts"

- **All related to cathinone/methcathinone**
  - **4 – Methylmethcathinone (Mephedrone, M-Cat, Meow, 4-MMC)**
  - **3,4 – Methylenedioxymethcathinone (Methylone, MDMC)**
  - **3,4 – Methylenedioxypyrovalerone (MDPV)**
  - **Alpha-PVP**
  - Pentedrone
  - Butylone
  - Pentylone

Possible Substances in “Bath Salts”

- **All related to cathinone/methcathinone**
  - **Ethylone**
  - Buphedrone
  - 4-MEC
  - 3,4-DMMC
  - Isopentadrone
  - pyrovalerone

Mephedrone

Mephedrone

- (4-methylmethcathinone /(4-MMC) or 4-methylephedrone)
- Do not confuse with methadone or methylone
- Onset:
  - Oral: 15–45 minutes
  - Insufflation (nasal/“snorting”): 10 minutes
  - i.v. injection (rare): 30 seconds
- Duration:
  - Oral/Nasal: 2-3 hours
  - Intravenous: 30 minutes

UNODC
United Nations Office on Drugs and Crime

VOLUME 15
M.arch

GLOBAL SMART UPDATE

Special Segment
Injecting use of synthetic drugs

2016

Mephedrone

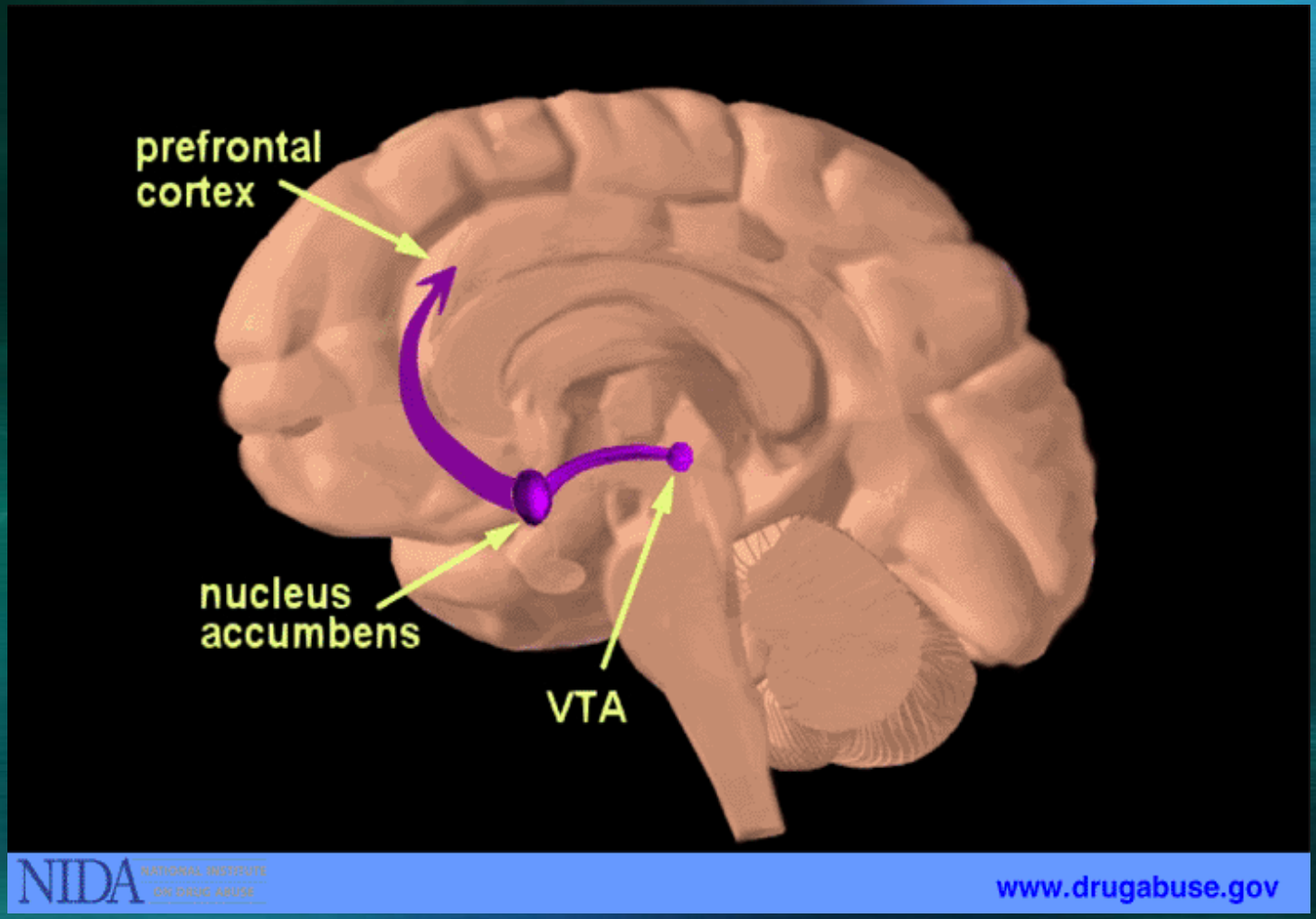
- Controlled under federal analog act
- No formal published studies effects on humans
- A few animals studies that could be applied to humans

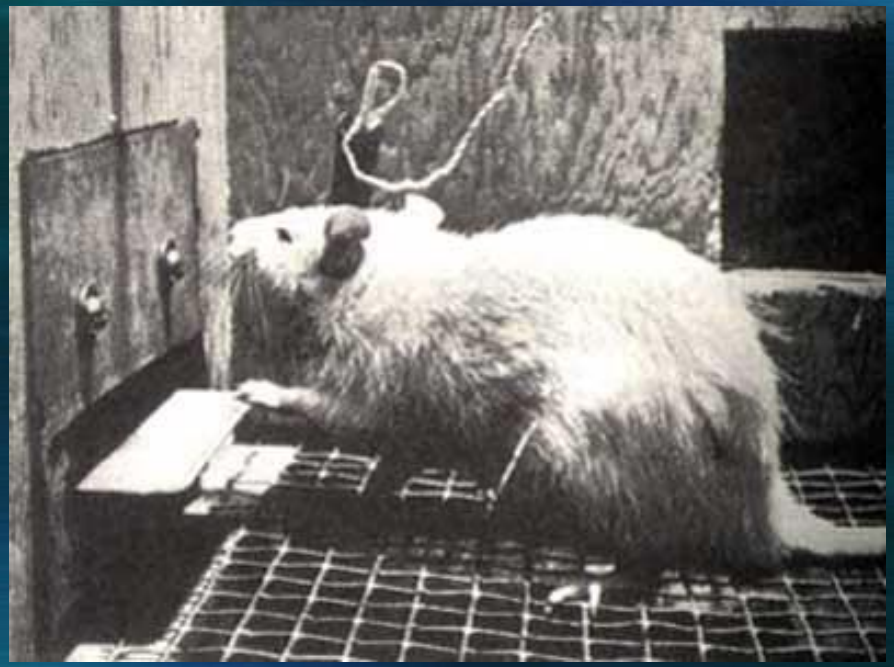
Mephedrone Research

- UK Study:
  - Users w/ previous cocaine experience:
    - Better quality and longer lasting high
    - Less addictive
- Malanga, et. al. (2012)

Mephedrone: Addiction Potential

- Dr. C.J. Malanga at University of North Carolina
- Effect of mephedrone and cocaine on intracranial self-stimulation (ICSS)


prefrontal cortex
nucleus accumbens
VTA
NIDA
NATIONAL INSTITUTE ON DRUG ABUSE
www.drugabuse.gov



Mephedrone and Intracranial Self-Stimulation

- Animals allowed to self-administer mephedrone decrease their ICSS
- Like cocaine, mephedrone makes ICSS less desirable
- Consistent with user self-reports

MDPV

MDPV Addiction Potential

- August 2013 journal *Neuropharmacology*
- Animal self-administration
- Found to be more rewarding than methamphetamine

Methylone

Methylone

- One of the most common synthetic cathinones
- Similar to MDMA/"ecstasy"
- Was an ingredient (along with MDMA) in one of two "Molly" overdoses at the Zoo Music Festival in New York over the 2013 Labor Day weekend
- Has appeared in "Molly" samples in other parts of the country

Hallucinogens/Psychedelics

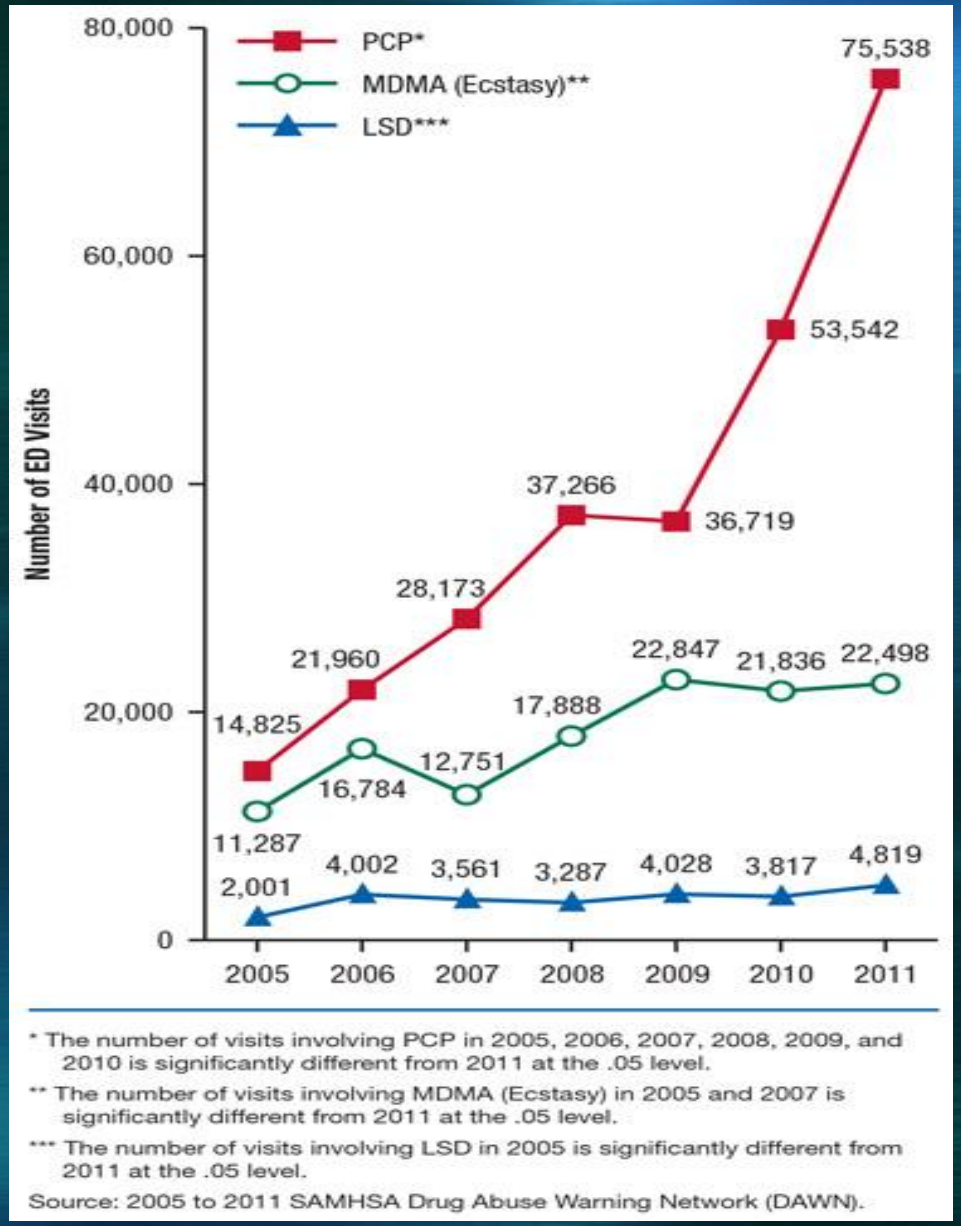
Psychedelics/hallucinogens: Basics

- Addiction potential low
- Tolerance develops rapidly
- Withdrawal symptoms absent or extremely minimal
- Low potential for immediate or long-term physical toxicity
- Moderate potential for acute psychiatric impairment
- Low potential for chronic psychiatric impairment

Hallucinogens/Psychedelics

- LSD
- Psilocybin
- Relatively safe

- NBOMe series-Not so much



+410%

ED visits involving PCP, LSD and MDMA: 2005-2011

Hallucinogens

- Lower risk
  - LSD
  - Psilocybin
  - Peyote/mescaline
- Higher risk
  - Anticholinergics
  - NBOMe compounds

Hallucinogens (Lower risk)

- Addiction potential low
- Tolerance develops rapidly
- Short- and long-term physical toxicity potential low
- Psychiatric impairment low to moderate
- Neurochemical mechanism of action:
  - Stimulation of serotonin subreceptors (5HT2A)
  - Increase in glutamate

LSD Vs Psilocybin

- Psilocybin rarer
- Psilocybin duration shorter than LSD (4-6 hours Vs 8-12)

Hallucinogens (Lower risk)

- Effects (desired):
  - Hallucinations
  - Perceptual distortions
  - “Morphing”
  - Synesthesia
  - Altered body image
  - Altered experience of time and space
  - Consciousness expansion
  - Mystical experiences

Hallucinogens (Lower risk)

- Effects (side)
  - Slight increase in body temperature
  - Nausea (rare)
  - Blurred vision (rare)
  - Slightly increased/decreased blood pressure
  - Slight elevation of pulse
  - Dilated pupils

Hallucinogens (Lower risk)

- Effects (Undesired)
  - Panic
  - Fear of insanity
  - Paranoia
  - Frightening hallucinations
  - Depersonalization
  - Derealization

Low risk hallucinogens: Therapeutic Uses

- Terminal cancer patients

Anticholinergics

Anticholinergic hallucinogens

- Jimsom weed
- Deadly nightshade
- Angel's trumpet
- Stinkweed
- Belladonna alkaloids
  - Atropine
  - Scopolamine
  - Hyoscyamine

Anticholinergics

- Hot as a hare
- Dry as a bone
- Blind as a bat
- Red as a beet
- Mad as a hatter

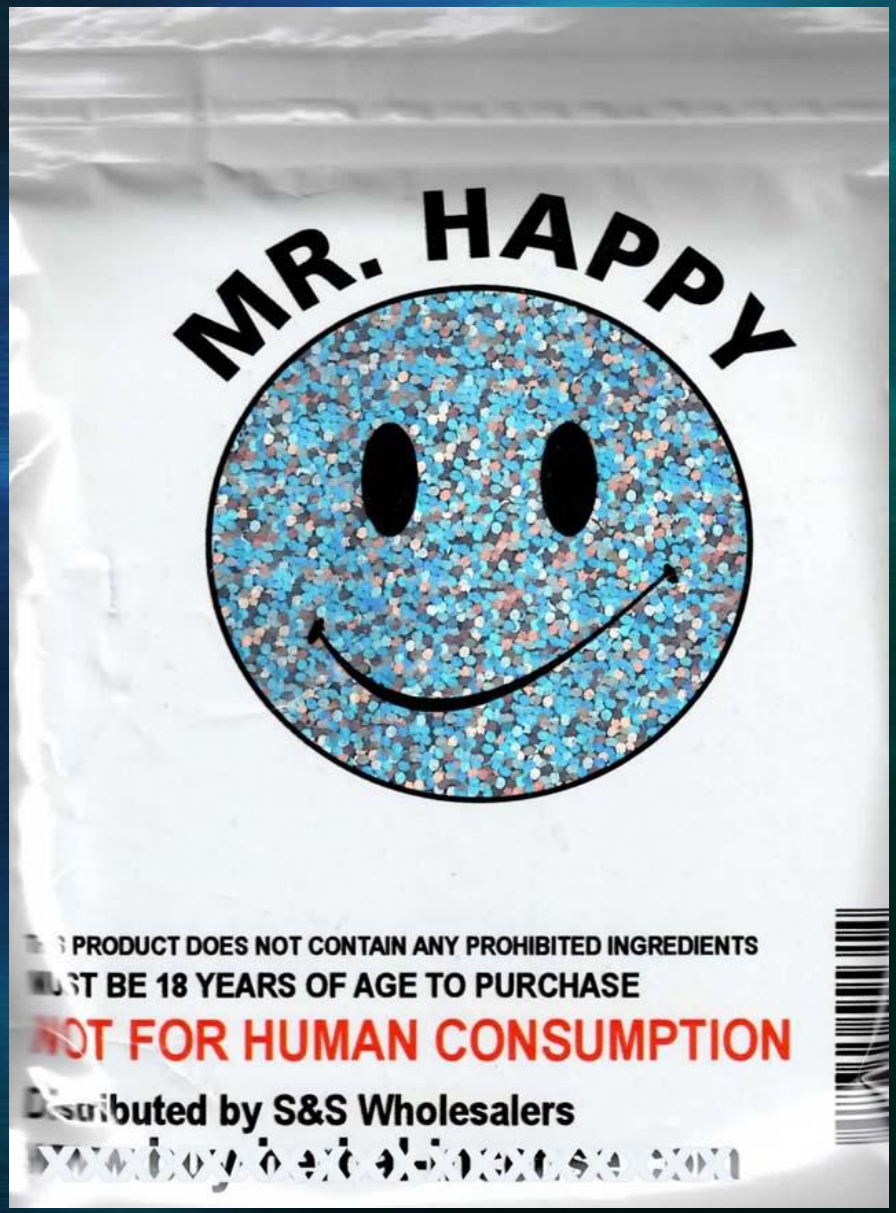
Synthetic Phenethylamines (NBOMe Compounds)

Submissions to Forensic Laboratories

- Alabama, Arkansas, California, Colorado, Connecticut, Florida, Georgia, Iowa, Indiana, **Illinois**, Kansas, Kentucky, Louisiana, Maryland, Maine, Minnesota, **Missouri**, New Hampshire, New Jersey, New Mexico, North Dakota, Nebraska, Nevada, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, Wisconsin, and Wyoming.

25I-NBOmE


25I-NBOMe
4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine


MR. HAPPY
PRODUCT DOES NOT CONTAIN ANY PROHIBITED INGREDIENTS
ST BE 18 YEARS OF AGE TO PURCHASE
NOT FOR HUMAN CONSUMPTION
buted by S&S Wholesalers

25I-NBOMe

- "N-Bomb", "Smiles," "25I"
- Similar to LSD in potency and effects
  - Strong open- and closed-eye visuals (trails, color shifts, brightening)
  - Mood lift/euphoria
  - Mental and physical stimulation
- 12-16 hour duration
- May be sold as LSD or "fake mescaline"
- Not active orally
- Taken sublingually, nasally ("snorting" or drops), buccally
- May show up as "blotter"

25I-NBOMe

- Disorientation, confusion, panic, psychosis reported
- Dystonia: Twisting and repetitive movements or abnormal postures.
- Medical reports of fatal seizures (unusually high doses)

25B-NBOMe

- “New nexus”, “Nova”, “Cimbi-36”
- Dose 250-500 micrograms
- Also not effect orally
- Reports from users of:
  - Typical psychedelic effects (visuals, oneness with the universe, magical experiences)
  - Extremely high pulse (≥ 180 bpm)
  - High blood pressure with facial redness, headache and “feelings like I was going to explode”
  - Panic/dissociation lasting from a few minutes to hours

25C-NBOMe

- More of the same
- Greatest danger is “serotonin syndrome”

Serotonin Syndrome (Mild)

- Agitation
- Increased heart rate
- Shivering
- Sweating
- Dilated pupils
- Myoclonus (intermittent tremor or twitching)
- Over responsive reflexes

Serotonin Syndrome (Severe)

- High blood pressure
- Severe hyperthermia (possibly as high as 106 °)
- Kidney dysfunction, damage and failure
- Seizures
- Multiple life-threatening blood clots
- Hypervigilance

NBOMe Substances: One User's Opinion

- From drugsforum.com (September 2013):

  These are all **very novel compounds with an extremely short and limited history of human use**. You can gather research on each from (others') perspective (Internet comments) or you can do the research on yourself. **Proceed with care and patience, the safety profile of these compounds is completely unknown, and similar compounds have shown to be potentially deadly.**

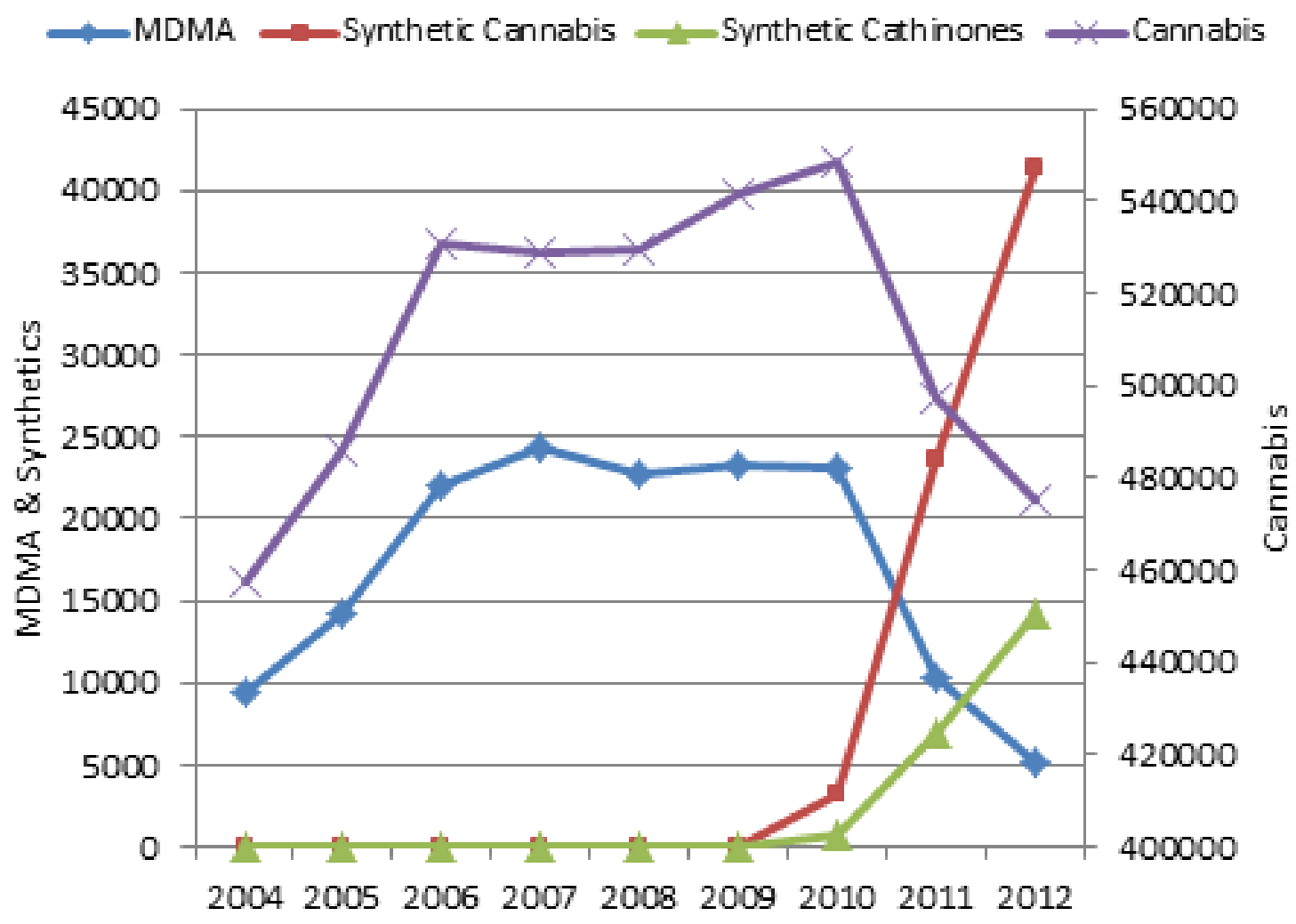
Good golly Miss Molly Who are you today?

- Pop quiz: What is “Molly”?

MDMA

- “Ecstasy”
- “Molly”
- “Flat”/”Chicago Mints” (Chicago)

Changes in Number of Items Examined in DEA NFLIS:2004-2012



The New York Times

Overdoses of ‘Molly’ Led to Electric Zoo Deaths

By James C. McKinley Jr. September 12, 2013 6:06 pm

(One of the deceased) had taken a fatal mix of MDMA and **methylone**, a closely related stimulant that is also often sold under the name molly. Methylone is one of several stimulants and psychedelic drugs often used by drug dealers to cut MDMA, law enforcement officials said.

The New York Times

Overdoses of ‘Molly’ Led to Electric Zoo Deaths

By James C. McKinley Jr. September 12, 2013 6:06 pm

A third New Yorker died on July 15 of an **overdose of methylone** after attending a different electronic dance music concert on Governors Island, the medical examiner’s office said.

February 23, 2015

12 hospitalized due to MDMA overdose on Wesleyan campus

Dr. Mark Neavyn, chief of toxicology at Hartford Hospital: **"When we see these people in the emergency department and they claim to have taken Molly, we don't pay attention to that word anymore**.

Dissociative anesthetics

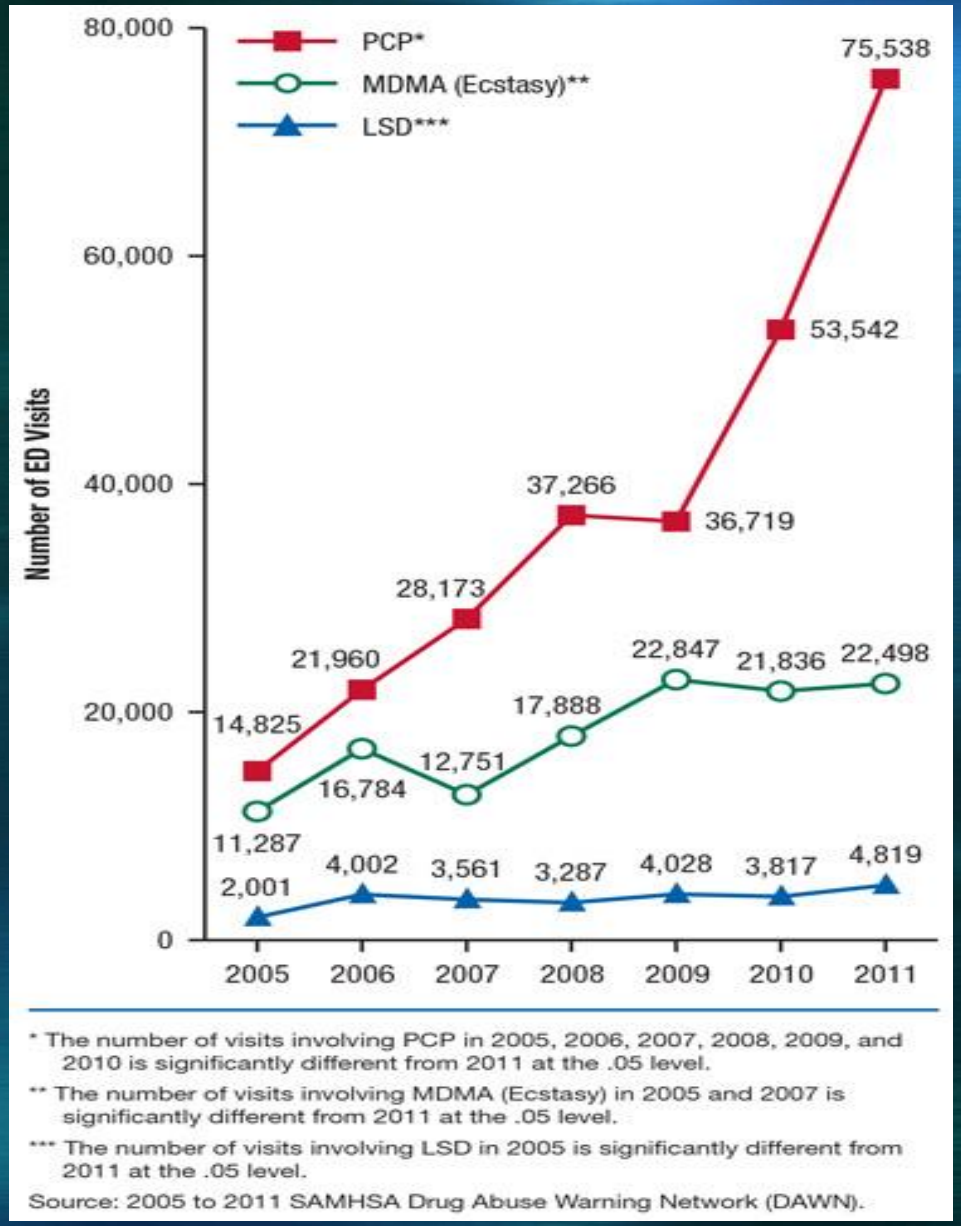
- Phencyclidine (PCP)
- Ketamine
- Dextromethorphan (DXM)

Dissociative anesthetics: Basics

- Addiction potential low to moderate
- Tolerance develops
- Withdrawal symptoms mild
- Moderate to high potential for immediate physical toxicity
- Potential for long-term physical toxicity varies
- Potential for acute and chronic psychiatric impairment moderate to high
- NMDA/glutamate antagonist

PCP

- Angel dust
- Sherms
- Dips
- Fry
- Embalming fluid



+500%

ED visits involving PCP, LSD and MDMA: 2005-2011

PCP

- Oral (rare)
- Intranasal
- Smoked (on marijuana, mint, parsley)
- i.v. (rare)

PCP

- (Not used medically)
- Floating feeling
- Sedation
- Euphoria
- Confusion
- Disorientation
- Depersonalization
- Derealization
- Loss of ego boundaries
- Panic

PCP

- Bizarre behavior
- Aggressive behavior
- Hallucinations (rare)

PCP

- Numbness
- Ataxia
- Increased blood pressure
- Nystagmus
- Seizures

Ketamine (Ketalar)

- “Special K”
- Intravenous anesthetic
- Post-operative pain management with an opioid
- Also used in veterinary medicine
- Many of the same effects as PCP
- Fewer negative effects
- Short-acting (20-60 minutes)

Ketamine

- Addiction rare in U.S., More Common in Europe
- Heavy use $\rightarrow\rightarrow\rightarrow\rightarrow$ Severe bladder infection/destruction

Ketamine: Treatment of depresssion

- Single sub-anesthetic dose
- Provides relief for 1-2 weeks

DXM

- Dextromethorphan
- In OTC cough medicines
- Often kept behind counter
- Robotussin DM
- Coricidin cough and cold = “Skittles”, “3-C”
- Similar to ketamine and PCP, but less intense effects except in large doses
- “Robotripping”

CANNABIS

Cannabis

- Endocannabinoids
  - CB_1 CB_2
- Marijuana
  - THC
  - CBD
  - Other cannabinoids
- Hashish
- Concentrates
  - Hash oil
  - Shatter
  - Wax

Hash oil/BHO (Up to 90% THC)

Hashish (Up to 65% THC)

Shatter (Up to 90% THC)

Wax (Up to 90% THC)

Cannabis

- Effects:
  - Euphoria
  - Dreaminess
  - Introspective mood
  - Hilarity
  - Heightened perception

Cannabis

- Effects (side):
  - Bloodshot eyes
  - Forgetfulness
  - Increased pulse
  - Dry mouth

Cannabis

- Effects (undesired):
  - Confusion
  - Paranoia
  - Derealization
  - Depersonalization
  - Panic
  - Anxiety
  - Psychosis (rare)

Marijuana: Respiratory effects

- Substantial evidence:
  - Association between long-term cannabis smoking and worse respiratory symptoms and more frequent chronic bronchitis episodes
- Moderate evidence:
  - *Cessation* of cannabis smoking and improvements in respiratory symptoms.
  - *No* statistical association between cannabis smoking and the incidence of lung cancer.

Marijuana and cancer

- Moderate evidence:
  - *No* statistical association between cannabis smoking and the incidence of lung cancer.
  - *No* statistical association between cannabis use and the incidence of head and neck cancers.
- Limited evidence:
  - Statistical association between current, frequent, or chronic cannabis smoking and non-seminoma-type testicular germ cell tumors.

Marijuana: Respiratory effects

- Limited evidence:
  - Association between occasional cannabis smoking and an increased risk of developing chronic obstructive pulmonary disease (COPD) when controlled for tobacco use
- Insufficient evidence
  - To support or refute a statistical association between cannabis smoking and hospital admissions for COPD.
  - To support or refute a statistical association between cannabis smoking and asthma development or asthma exacerbation.

Marijuana: Cancer

- Insufficient evidence:
  - Esophageal, prostate, cervical, bladder, penile, anal cancer, non-Hodgkin lymphoma.
  - Parental cannabis use and a subsequent risk of developing acute myeloid leukemia/acute non-lymphoblastic leukemia, acute lymphoblastic leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring.

Cannabis & Immune Function

- There exists a paucity of data on the effects of cannabis or cannabinoid-based therapeutics on the human immune system.
- There is insufficient data to draw conclusions concerning the effects of cannabis smoke or cannabinoids on immune competence.
- There is limited evidence to suggest that regular exposure to cannabis smoke may have anti-inflammatory activity.
- There is insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and adverse effects on immune status in individuals with HIV.

Cannabis and Pregnancy

- Smoking cannabis during pregnancy is linked to lower birth weight in the infant
- The relationship between smoking cannabis during pregnancy and other pregnancy and childhood outcomes is unclear.

Cannabis and cognition

- Recent cannabis use impairs the performance in cognitive domains of learning, memory, and attention. Recent use may be defined as cannabis use within 24 hours of evaluation.
- A limited number of studies suggest that there are impairments in cognitive domains of learning, memory, and attention in individuals who have stopped smoking cannabis.
- Cannabis use during adolescence is related to impairments in subsequent academic achievement and education, employment and income, and social relationships and social roles.

The potency problem

- Marijuana only available from U.S. government's marijuana farm
- Government marijuana averages 6% THC
- Street marijuana can reach 40% THC or more

Injury and death

- Cannabis use prior to driving increases the risk of being involved in a motor vehicle accident.
- In states where cannabis use is legal, there is increased risk of unintentional cannabis overdose injuries among children.
- It is unclear whether and how cannabis use is associated with all-cause mortality or with occupational injury.

User-suggested warnings for legal marijuana

- Risk of harm to mental health and psychological functioning
- Risk of operating machinery while under the influence
- Short-term physical side effects
- Responsible use
- Long-term negative physical effects
- Dependence, addiction, or abuse.

Cannabis

- Cannabis hyperemesis syndrome (CHS)
  - Vomiting
  - Abdominal pain
  - May be relieved by hot showers (?)

Medical marijuana

- Modest effects:
  - In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective antiemetics.
  - In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms
  - •In adults with multiple sclerosis (MS) related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.

Cannabis: Basics

- Addiction potential low to moderate
- Tolerance develops to some symptoms of intoxication
- Physical dependence withdrawal symptoms mild
- Immediate and long-term physical toxicity potential appears moderate to low
- Immediate psychiatric impairment potential low to moderate/chronic psychiatric impairment may be moderate for adolescents

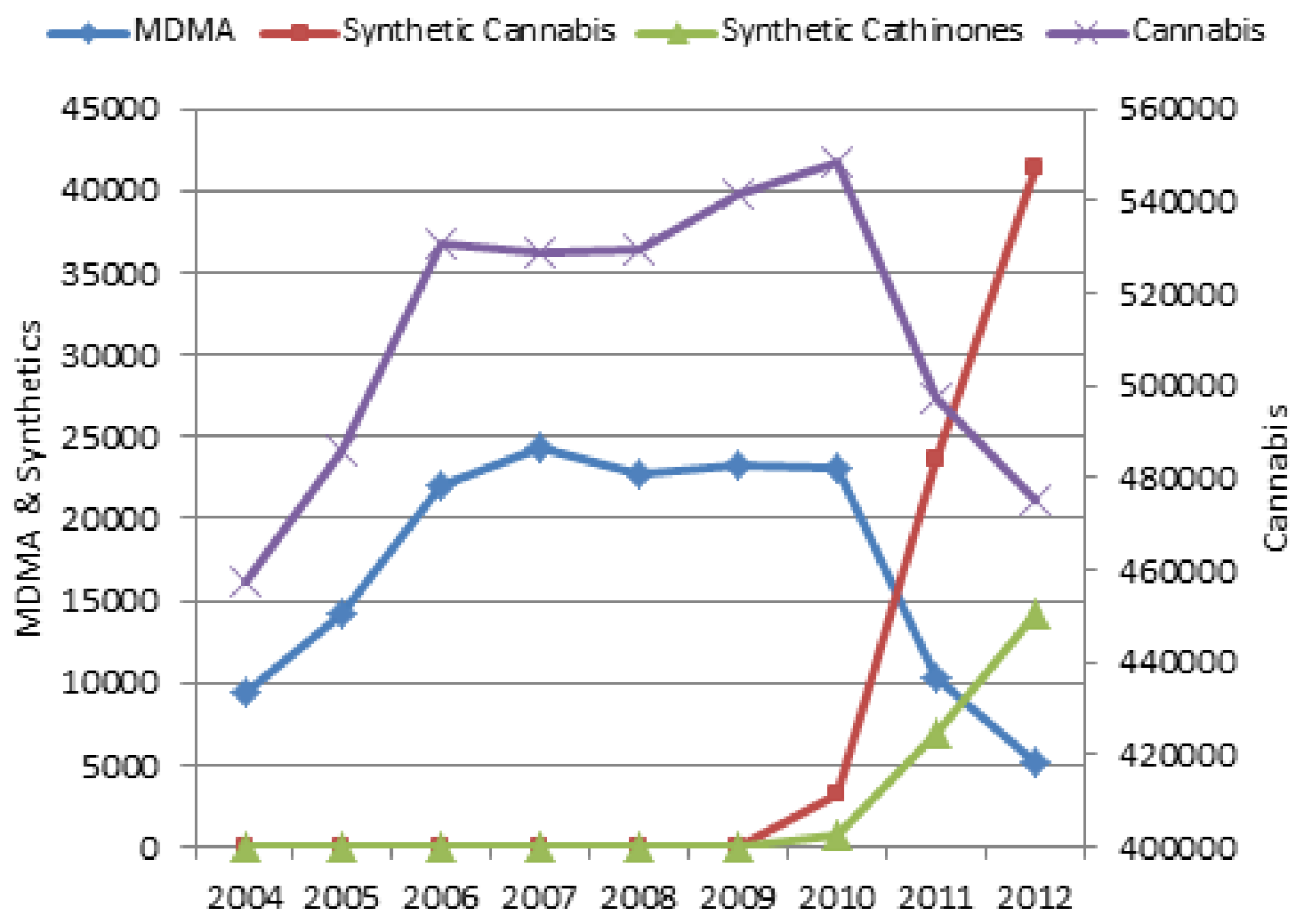
Cannabinoids

- Δ9-Tetrahydrocannabinol (THC)
- Endocannabinoids
- **Synthetic cannabinoids**

Synthetic Cannabinoids

“K2”, “Spice”, “herbal incense”, “synthetic marijuana”

Changes in Number of Items Examined in DEA NFLIS:2004-2012



Herbal Incense

- Crushed, non-psychoactive herbal/plant matter treated with one or more synthetic cannabinoids
  - First Generation: “K2”, “Spice”, “Black Mamba”, “Red Dragon”
  - Second Generation: “K3”, “Splice”, “Apocalypse”, “Destiny”, “Cloud Ten”, “Head Trip”, house mixes

Herbal incense Pharmacology

- Hundreds of synthetic cannabinoids (similar to both Δ9-THC and endogenous cannabinoids) have been created
- Potency ranges from hundreds of times *more* potent than THC to over 1000x *less* potent
- Most common psychoactive ingredients in herbal incense were JWH series
- Synthesized in the 1990s by Dr. John W. Huffman at Clemson University

First Generation Herbal Incense: Typical Effects

- Cannabis-like intoxication
- Dreaminess
- Euphoria
- Introspective mood
- Hilarity
- Forgetfulness
- Heightened sensory perception

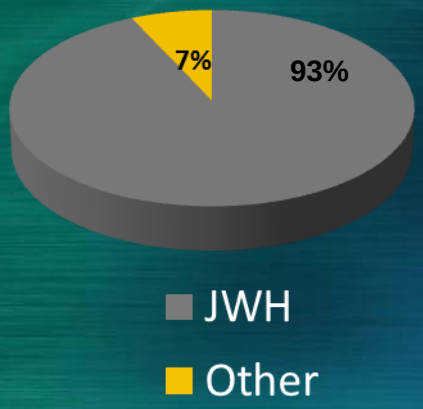
THESE ARE THE EFFECTS MOST COMMONLY REPORTED BY USERS

First Generation Herbal Incense: Other Effects

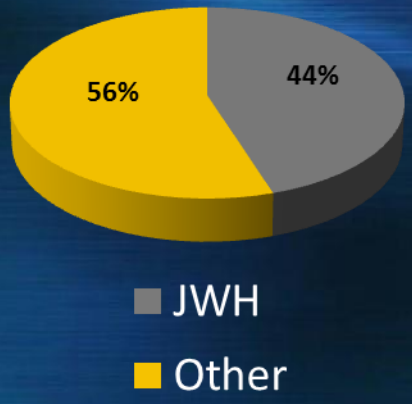
- Severe anxiety (may persist after herbal incense use is discontinued)
- Panic attacks
- Dissociation (e.g., derealization)
- Racing thoughts
- Hallucinations
- Rapid pulse (tachycardia)
- Seizures (*Journal of Addiction Medicine*, Sept 2012)

Rapid Growth in Number of Synthetic Cannabinoids Identified by DEA

19 variations in 2010
N=2,386



47 Variations in 2011
N=23,688



61 Variations in 2012
N=41, 458

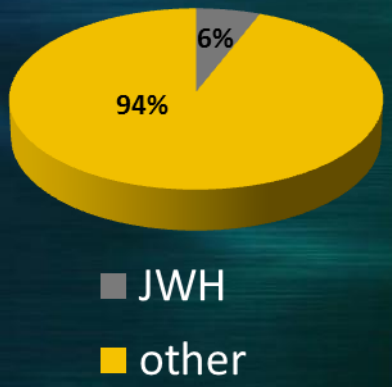


Fig. 1 Synthetic Cannabinoids in the U.S. NFLIS Toxicology Labs as of 9/27/13

The New Era:
Herbal Incense Becomes Pure Synthetic Cannabinoids

Calls to Poison Control Centers

- Data from the American Association of Poison Control Centers' "National Poison Data Center"
- 2010: 2,874 calls
- 2016 (January-July): 1,682

New Synthetic Cannabinoids

- AM-2201
  - Doses can be as low as 500 micrograms (1/2000th of a gram & 1/56,000th of an ounce)
  - Users' experiences (experienced outside observer) at 10 mg (1/100 of a gram)
    - Blacked out (unconscious)
    - Vomiting
    - Trouble breathing
    - Clenching every muscle in their bodies
    - (One person) Acting psychotic and screaming at the top of his lungs
    - (All three): Confusion for another hour or so

New Synthetic Cannabinoids

- XLR-11
  - Potent CB_1 & CB_2 agonist
  - First identified by laboratories in 2012 as an ingredient in synthetic cannabis smoking blends
  - A novel compound invented specifically for grey-market recreational use
  - Banned in New Zealand July 2012
  - Placed in Schedule I by DEA May 2013
  - Toxicity
    - Linked to acute kidney injury in some users

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

Morbidity and Mortality Weekly Report (*MMWR*)

February 15, 2013

Acute Kidney Injury Associated with Synthetic Cannabinoid Use — Multiple States, 2012

Rapid Growth in Number of Synthetic Cannabinoids Identified by DEA

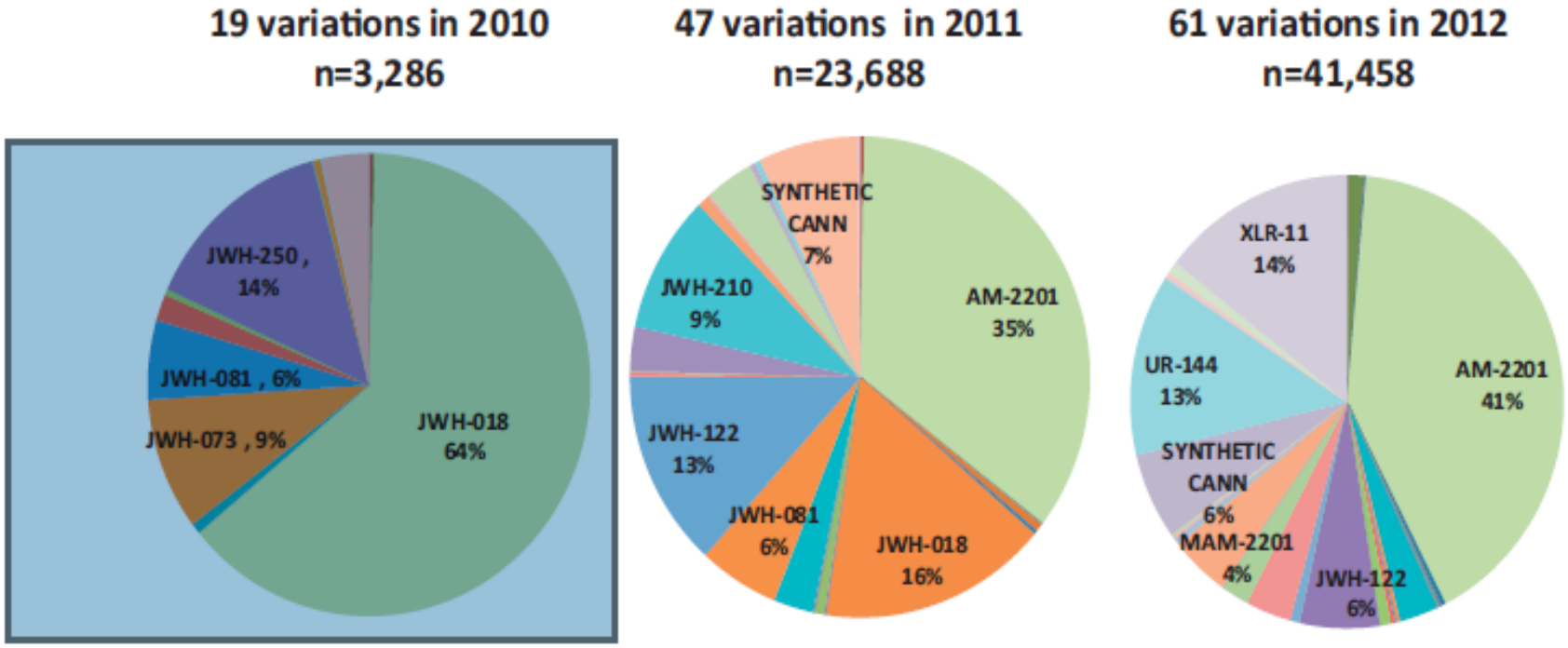


Fig. 1. Synthetic cannabinoids identified in U.S. NFLIS Toxicology Labs as of 9/7/13.

New Synthetic Cannabinoids

- UR-144
  - Placed in Schedule I by DEA May 2013
  - Users' experience:
    - Very mellow and enjoyable
    - A blissful glow…intellectually and artistically stimulating (then with more) Catapulted into another dimension where the stakes are high. On trial in front of God.
    - The familiar becomes strange and different, an alternate reality
    - The woods…..large and deep….the weeds actively malevolent, almost alive
    - I had no idea these chemicals could do something that intense. Thought the entire world was ending and I losing my mind.
    - Extreme addiction & depression after only half a week of use. Also major anxiety lasting for 2 days

Additional Synthetic Cannabinoids

- THJ-2201
- 5F-PB-22
- AB-CHMINACA
- AB-PINACA
- MAB-CHMINACA

SC ER Visits and Deaths: March-May 2015

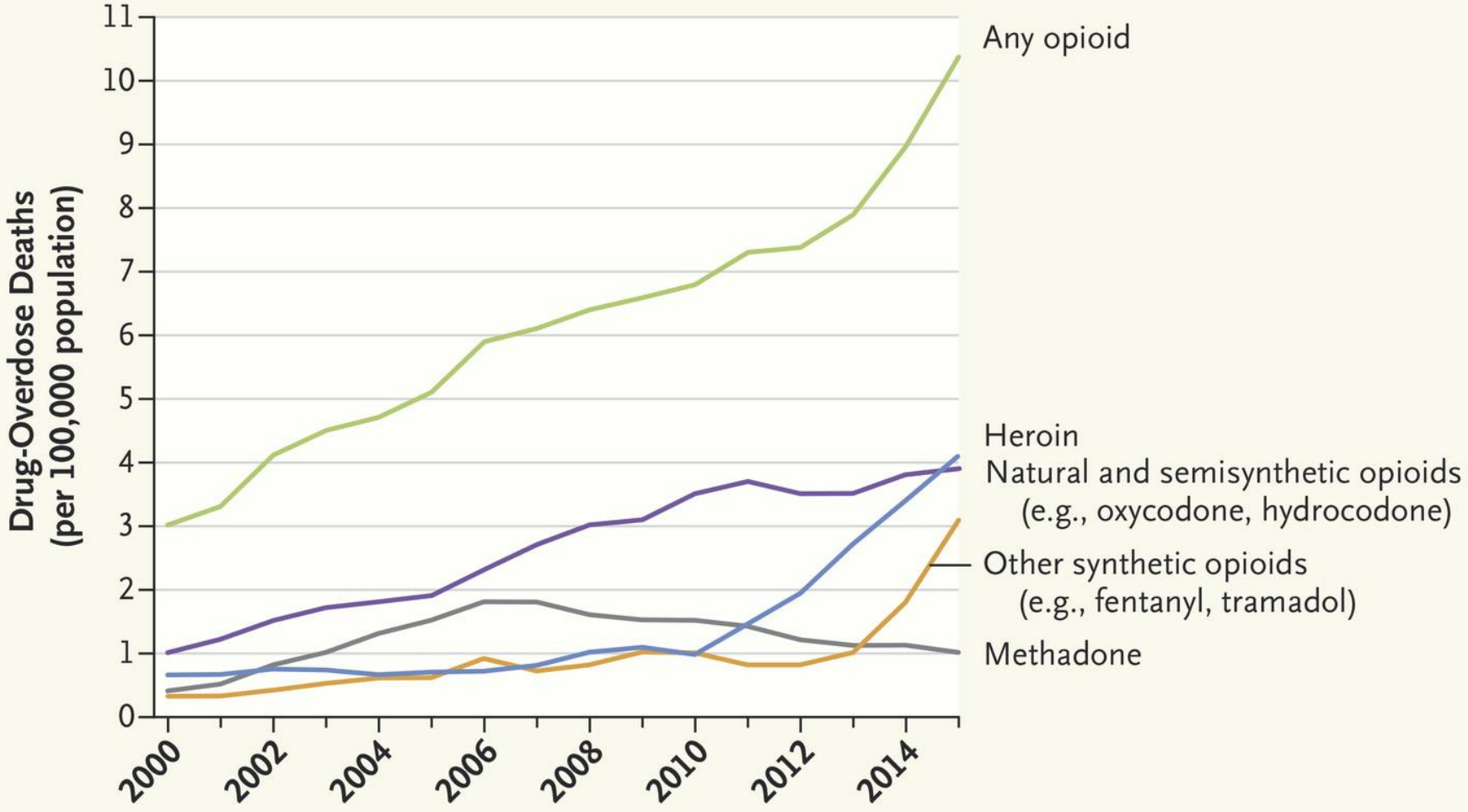
- Mississippi Department of Public Health
  - 1200 ER visits
  - 17 deaths
- Alabama Department of Public Health
  - 1000 1200 ER visits
  - 5 deaths

Opioids: Basics

- Addiction potential high
- Tolerance develops
- Physical dependence withdrawal symptoms moderate to serious/not life-threatening
- Immediate physical toxicity potential (overdose) moderate to high
- Long-term physical toxicity potential low
- Acute and chronic psychiatric impairment potential low

Opioids

- **Heroin**
- **Hydrocodone/Vicodin/Norco**
- **Oxycodone (OxyContin/Percodan)**
- **Hydromorphone (Dilaudid)**
- **Oxymorphone (Opana)**
- **Fentanyl (Sublimaze)**
- UR-47700
- Other synthetic opioids


Drug-Overdose Deaths
(per 100,000 population)
11
10
9
8
7
6
5
4
3
2
1
0
2000
2002
2004
2006
2008
2010
2012
2014
Any opioid
Heroin
Natural and semisynthetic opioids
(e.g., oxycodone, hydrocodone)
Other synthetic opioids
(e.g., fentanyl, tramadol)
Methadone

Press Release

DEA ISSUES NATIONWIDE ALERT ON FENTANYL AS THREAT TO HEALTH AND PUBLIC SAFETY

WASHINGTON, DC – The United States Drug Enforcement Administration (DEA) today issued a nationwide alert about the dangers of fentanyl and fentanyl analogues/compounds. Fentanyl is commonly laced in heroin, causing significant problems across the country, particularly as heroin abuse has increased.

- **According to DEA, Chicago white heroin is fentanyl laced with heroin**

CBS St. Louis

KMOX NewsRadio 1120

Drug Blamed for Prince's Death Spreading on St. Louis-Area Streets

Brian Kelly (@brpkelly)

June 8, 2016 9:08 AM

Opioids

- March 2016: Fentanyl found in “hydrocodone” and “oxycodone” tablets
- October 2015: Fentanyl found in fake Xanax tablets
- Prince had fake hydrocodone tablets containing fentanyl

Opioids

- Heroin
- Hydrocodone/Vicodin/Norco
- Oxycodone (OxyContin/Percodan)
- Hydromorphone (Dilaudid)
- Oxymorphone (Opana)
- Fentanyl (Sublimaze)
- **UR-47700**
- **Other synthetic opioids (e.g., carfentanil)**

Opioid effects

- Sedation (“nodding”)
- Euphoria
- Pain relief
- Constipation
- Constricted pupils

Opiate Withdrawal

- Signs of w/d:
  - **Drug hunger (craving)**
  - **Dilated pupils**
  - **Yawning**
  - **Lacrimation (eyes tear)**
  - **Rhinitis (runny nose)**
  - **Fever**
  - **Restlessness**
  - **Stomach, leg and back cramps**

Opiate Withdrawal

- Signs of w/d:
  - **Insomnia**
  - **Nausea**
  - **Diarrhea**
  - **Vomiting**
  - **Chills/cold flashes with goose bumps ("cold turkey“)**
  - **Sweating**
  - **Leg spasms (“kicking the habit”)**

Opiate Withdrawal

- Signs of w/d:
  - **Rapid pulse**
  - **Increased blood pressure**
  - **Anxiety**
  - **Depression**
  - **Muscle and bone pain**

Medication-Assisted Treatment

Medication-Assisted Treatment

Providing opioid agonist or partial agonist medication as an adjunct to psychosocial treatment in order to improve engagement, retention and outcomes.

Treating Opiate Dependency: A Dilemma

- Physical dependence and craving are major barriers to abstaining from opiate use
- Detoxifying addicts with increasingly smaller doses of heroin or morphine is not an effective approach
- “Cold turkey” withdrawal is painful and unpleasant and often results in relapse

Using Medication to suppport opiate dependence treatment

PROFILE FOR POTENTIAL PSYCHOTHERAPEUTIC AGENT

- Effective after oral administration
- Long biological half-life (>24 hours)
- Minimal side effects during chronic administration
- Safe, no true toxic or serious adverse effects
- Efficacious for a substantial % of persons with the disorder

opiate Agonist Treatment of Addiction - Payte - 1998

Medications used to treat opiate dependency

- Methadone
- Clonidine
- Buprenorphine
- Naltrexone

CNS depressants

- Addiction potential moderate to high
- Tolerance develops
- Physical dependence withdrawal symptoms moderate to severe/life-threatening
- Physical toxicity (overdose) potential high/other immediate & long-term physical toxicity low
- Low potential for psychiatric impairment

CNS depressants: Withdrawal symptoms

- Tremor
- Agitation
- Insomnia
- Sweating
- Elevated pulse and blood pressure
- Sensory hypersensitivity
- (Stomach cramps)
- (Nausea/vomiting)
- Seizures

CNS depressants

- Addiction potential moderate to high
- Tolerance develops
- Physical dependence withdrawal symptoms moderate to severe/life-threatening
- Physical toxicity (overdose) potential high/other immediate & long-term physical toxicity low
- Low potential for psychiatric impairment

Sedative-Hypnotics

- Barbiturates (Rare, but physically dangerous)
- Non-barbiturates
  - Ambien
  - Lunestra
  - (Rozeram)
  - Restoril (tenazepam)

Benzodiazepines

- Xanax (alprazolam)
- Klonopin (clonazepam)
- Valium (diazepam)
- Ativan (lorazepam)

Purple Drank

- Drank
- Syrup
- Sizzup
- Lean

Sippin Syrup

Slow your roll

PURPLE DRANK

ima grip and sip

WARNING!

THIS BEVERAGE MAY BE EXTREMELY RELAXING AND CALMING

Purple Drank

The Nutritional Supplement of Champions

IMPORTANT QUESTIONS

WHAT ARE THESE DRUGS?

WHAT EFFECTS DO THEY HAVE?

WHAT ARE THE DANGERS?

WHAT IS THEIR ADDICTION POTENTIAL?

ARE THEY IN MY COMMUNITY?