RESIDENTIAL SUBSTANCE ABUSE TREATMENT (RSAT)

Synthetic Drugs
December 19, 2018

Philip Barbour
TASC-IL

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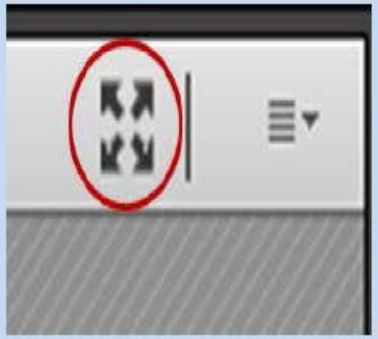
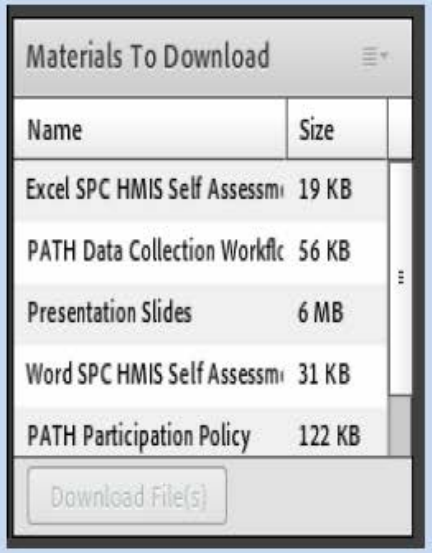


Presentation materials!

You can download a PDF version of today's presentation and additional resource materials from the "Materials To Download" box.



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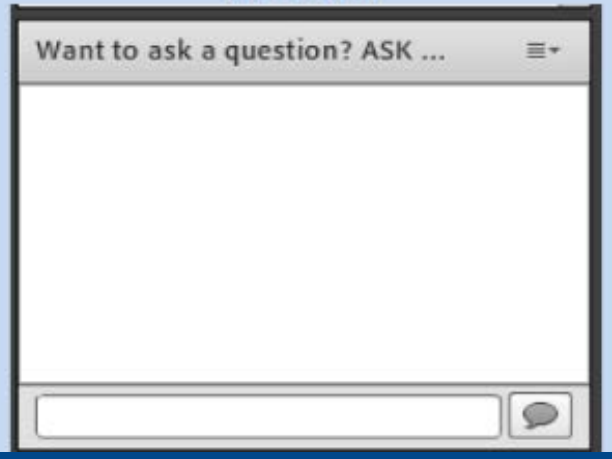


Chat with us!

If you have general comments, please post them in the participant chat box.

Synthetic Drugs

Philip Barbour

TASC-II
http://www2.tasc-il.org/

We Still Have an “Other Drug” Problem
What You Need to Know about Synthetic Drugs

Phillip Barbour / Master Trainer TASC

December 19, 2018

Training Collaborators

- South Southwest Addiction Technology Transfer Center
  - University of Texas at Austin, School of Social Work
- Pacific Southwest Addiction Technology Transfer Center
  - UCLA Integrated Substance Abuse Programs
- Centre for Addiction and Mental Health, Research Imaging Centre

Educational Objectives

At the end of this presentation, participants will be able to:

1. **Identify the key characteristics and effects of synthetic drugs, most notably synthetic cannabinoids and synthetic cathinones.**

2. **Describe the current information available on the availability and patterns of synthetic drug use in the United States.**

3. **List at least three strategies for communicating the dangers involved with synthetic drug use.**

4. **Review some recent legislation intended to stem the manufacturing of these synthetic drugs.**

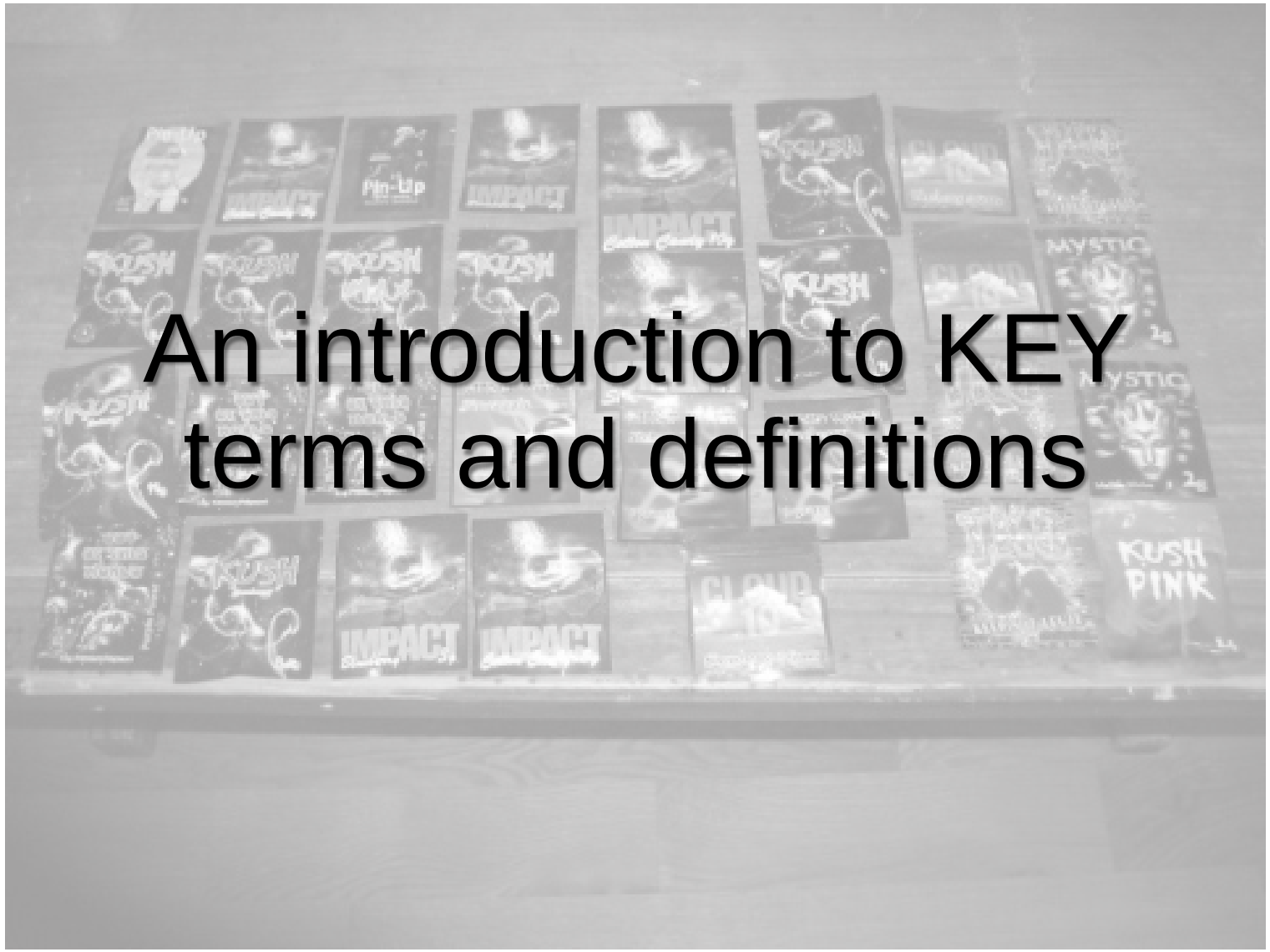
"Tales of Bath Salts and Zombie Cannibalism"

- Bath Salts made headlines in summer 2012 when a story of possible cannibalism was reported in Miami, FL
- The Miami-Dade Medical Examiner found no traces of bath salts, LSD, or synthetic marijuana in the perpetrator's system
- The sole psychoactive substance detected was cannabis (marijuana)

Have your heard these other media reports about "Bath Salts"?

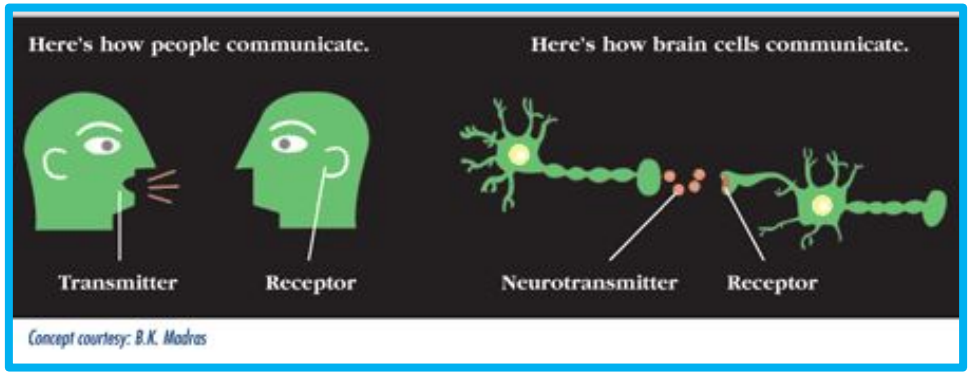
- The man who slashed himself to remove the "wires" in his body
- The mother who left her demon-ridden 2-year-old in the middle of the highway
- The 21-year-old son of a family physician who, after snorting bath salts once, shot himself following 3 days of acute paranoia and psychosis, including hallucinations of police squad cars and helicopters lined up outside his house to take him away

SOURCE: Slomski, A. (2012). *JAMA*.



An introduction to KEY terms and definitions

How Psychoactive Substances Work



- Because of their chemical structure, alcohol and drugs have dramatic effects on neurotransmitters in CNS

- Effects on:
  - Mental processes
  - Behavior
  - Perception
  - Alertness

SOURCE: NIDA. (2010). *Drugs, Brains, and Behavior: The Science of Addiction*.

Commonly Used Psychoactive Substances

SUBSTANCE	EFFECTS
Alcohol (liquor, beer, wine)	euphoria, stimulation, relaxation, lower inhibitions, drowsiness
Cannabinoids (marijuana, hashish)	euphoria, relaxations, slowed reaction time, distorted perception
Opioids (heroin, opium, many pain meds)	euphoria, drowsiness, sedation
Stimulants (cocaine, methamphetamine)	exhilaration, energy
Club Drugs (MDMA/Ecstasy, GHB)	hallucinations, tactile sensitivity, lowered inhibition
Dissociative Drugs (Ketamine, PCP, DXM)	feel separated from body, delirium, impaired motor function
Hallucinogens (LSD, mushrooms, Mescaline)	hallucinations, altered perception

SOURCE: National Institute on Drug Abuse.

The Top 8 Drug Types

There are eight different drug types, and each has its own set of effects and risks:

1. Stimulants
2. Depressants
3. Hallucinogens
4. Dissociatives
5. Opioids
6. Inhalants
7. Cannabis
8. Prescription drugs

https://easyread.drugabuse.gov/content/drugs-people-misuse

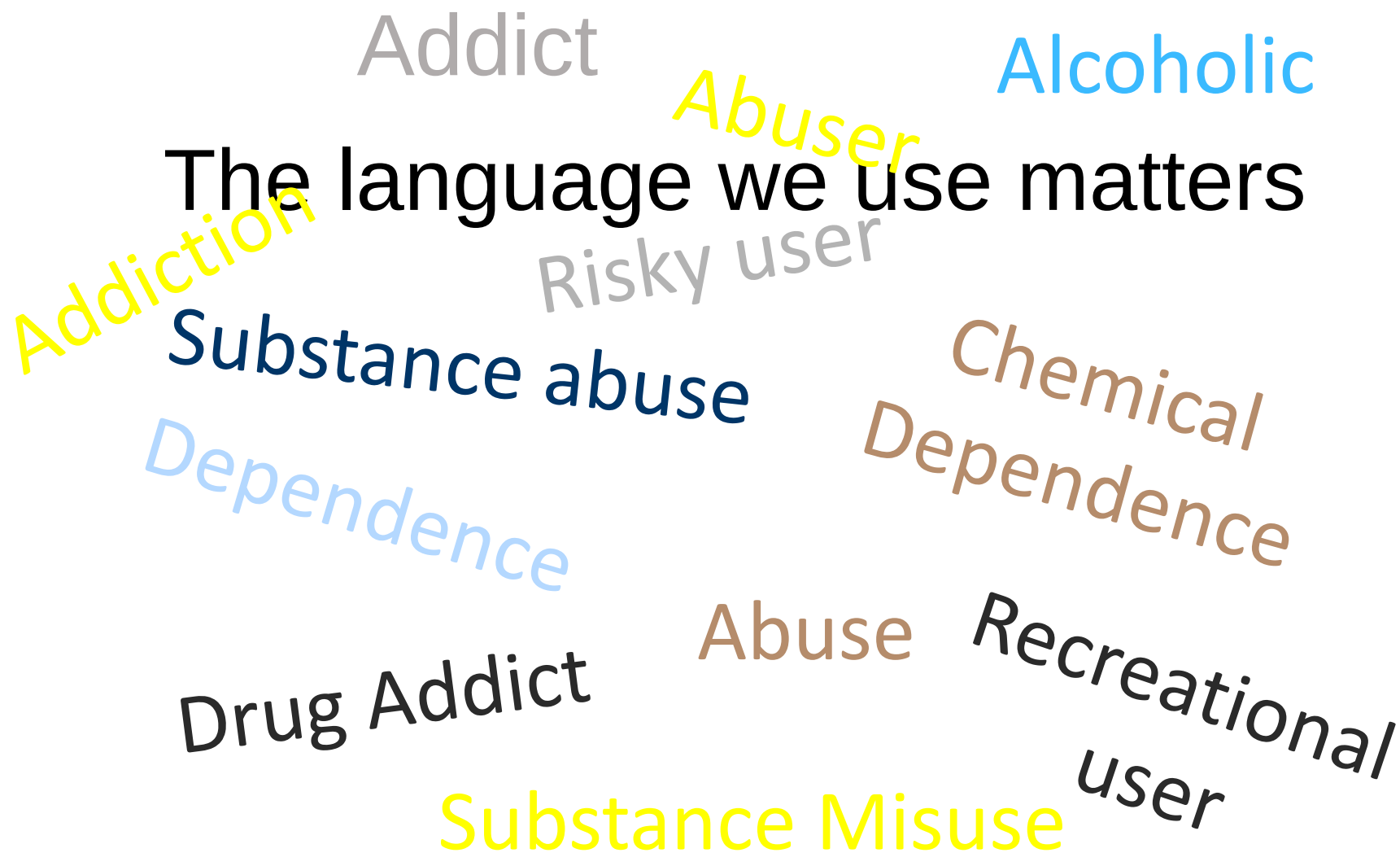
Keeping It Simple!

There are primality only 3 main drug classifications when it comes to prescription drugs.

- Central Nervous System drugs (CNS)
- Stimulants
- Opioids

https://www.drugabuse.gov/sites/default/files/cadchart.pdf

Substance Use Disorder (SUD)



What is a Substance Use Disorder?

A substance use disorder (SUD) is a continuum of problematic use of substances:

- On one end of the continuum are people who are using at risky levels. They may not be having problems yet, but are at risk of developing them if current level of use continues.
- On the other end, SUD is a complex, chronic, relapsing brain disease characterized by compulsive, and at times, uncontrollable drug craving, seeking, and use that persist even in the face of extremely negative consequences.

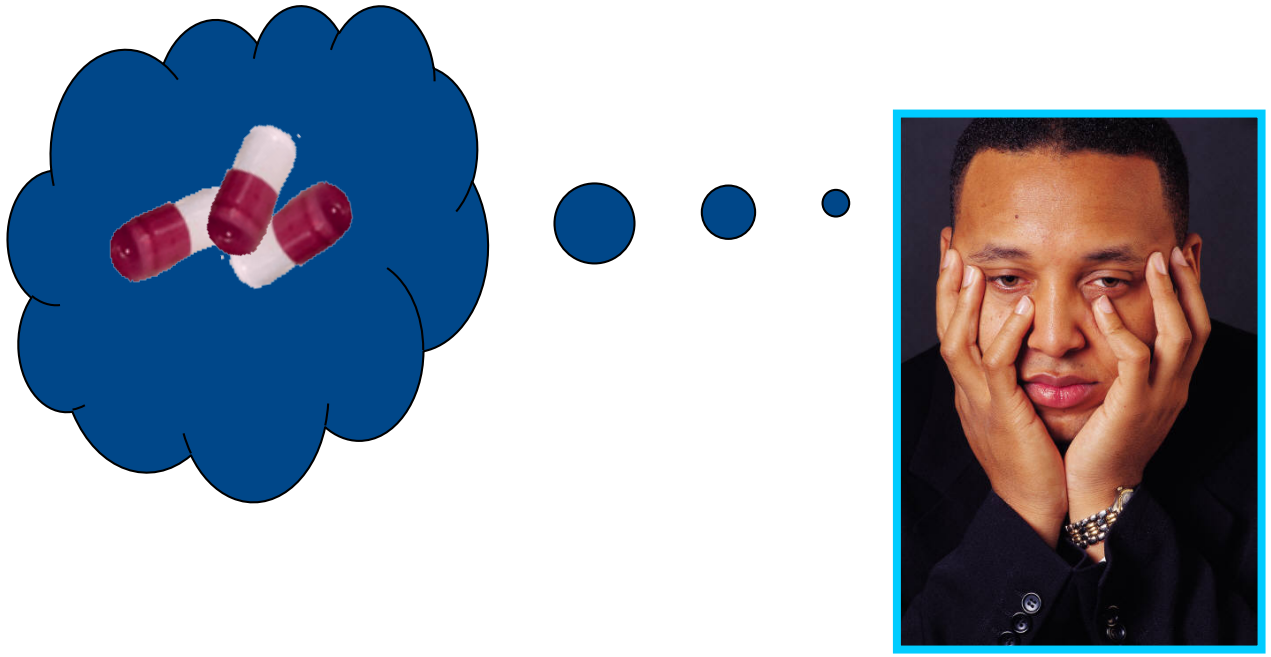
SOURCE: NIDA. (2010). *Drugs, Brains, and Behavior: The Science of Addiction*.

Some Additional Important Terminology

- **Psychological craving**
- **Tolerance**
- **Withdrawal symptoms**

Psychological Craving

Psychological craving is a strong desire or urge to use drugs. Cravings are most apparent during drug withdrawal.



Tolerance

Tolerance is a state in which a person no longer responds to a drug as they did before, and a higher dose is required to achieve the same effect.

SOURCE: Krasnegor, N.A. (Ed.). (1978). *Behavioral Tolerance: Research and Treatment Implications, NIDA Research Monograph 18*. Rockville, MD: Department of Health, Education, and Welfare.

Withdrawal

The following symptoms may occur when substance use is reduced or discontinued:

- **Tremors, chills**
- **Cramps**
- **Emotional problems**
- **Cognitive and attention deficits**
- **Hallucinations**
- **Convulsions**
- **Death**

SOURCE: APA. (2013). *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*.

A Review of synthetic DRUGS

Synthetic Drugs

- Not really “Spice,” “Bath Salts,” “Incense,” or “Plant Food”
- Chemically-based; not plant derived
- Complex chemistry
- Constantly changing to “stay legal”
- Need to prove “intended to use” to convict in some areas

Synthetic Cannabinoids

Spice vs. “Spice”

≠

Synthetic Cathinones

Bath Salts vs. “Bath Salts”

≠

Marijuana (Cannabis)

- Often called pot, grass, reefer, MJ, weed, herb
- A mixture of the dried, shredded leaves, stems, seeds, and flowers of *Cannabis* sativa—the hemp plant
- Most commonly used drug in the U.S.
- Delta-9-tetrahydrocannabinol (THC) is the main active ingredient in marijuana
- Common effects include: euphoria, relaxation, heightened sensory perception, laughter, altered perception of time, and increased appetite
- May also produce anxiety, fear, distrust, or panic, and can lead to severe mental health problems for some users.

SOURCE: NIDA. (2010). *NIDA DrugFacts: Marijuana*.

Synthetic Cannabinoids

- Wide variety of herbal mixtures
- Marketed as “safe” alternatives to marijuana
- Brand names include: “Spice,” “K2,” fake weed, “Yucatan Fire,” “Skunk,” “Moon Rocks,” herbal incense, “Crazy Clown,” “Herbal Madness”
- Labeled “not for human consumption”
- Contain dried, shredded plant material (inert) and chemical additives that are responsible for their psychoactive effects.

SOURCE: NIDA. (2012). *NIDA DrugFacts: Spice (Synthetic Marijuana).*

Synthetic Cannabinoids

- Mainly abused by smoking (alone or with marijuana); may also be prepared as an herbal infusion for drinking.
- Many of the active chemicals most frequently found in synthetic cannabis products have been classified by the DEA as Schedule I controlled substances, making them illegal to buy, sell, or possess.
- Multiple “generations” of drugs.

SOURCE: NIDA. (2012). *NIDA DrugFacts: Spice (Synthetic Marijuana)*.

Poll Question

When was **K2 (spice)** banned in the U.S.?

A. 1965
B. 1999
C. 2010
D. 2013

Poll Question

When was **K2 (spice)** banned in the U.S.?

A. 1965

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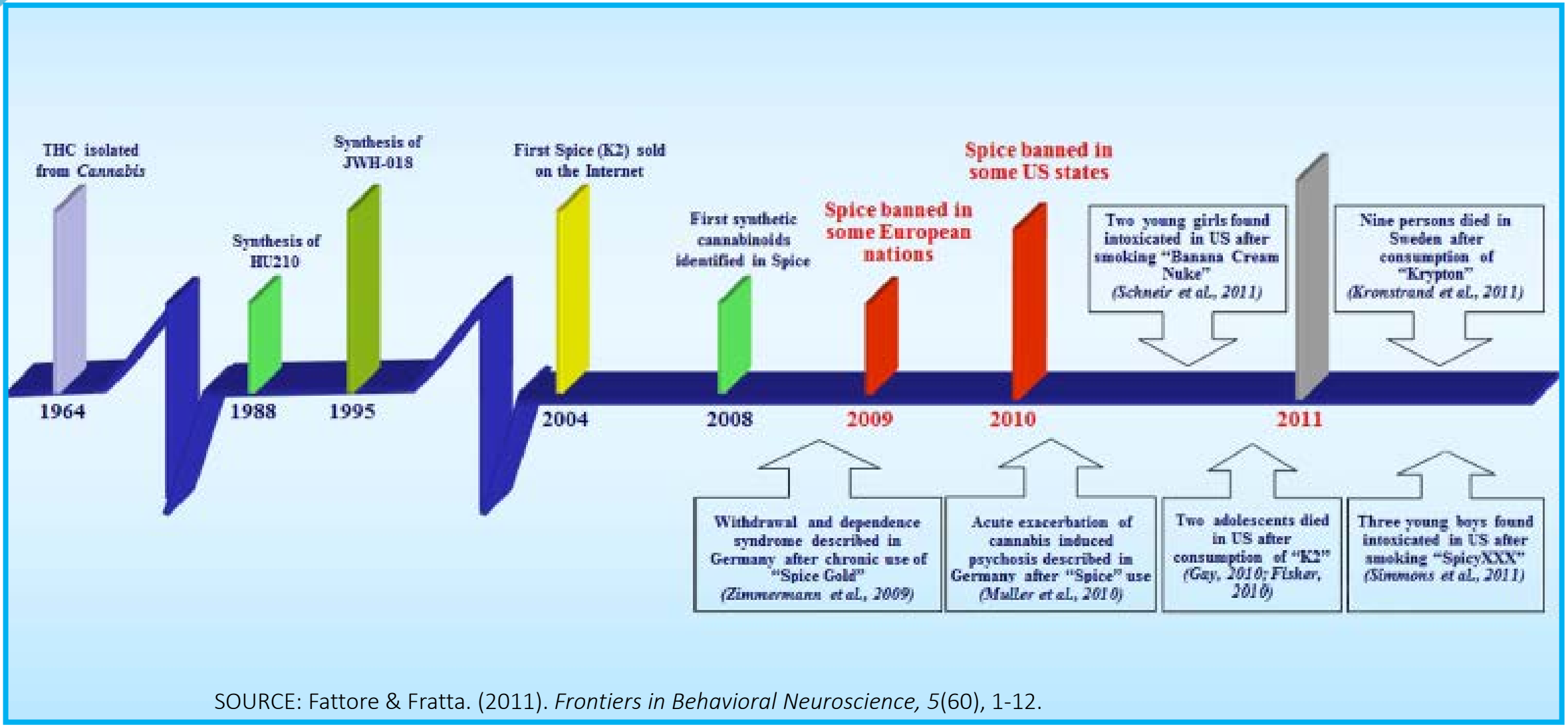
D. 2013

Timeline of Synthetic Cannabinoid Products



SOURCE: Fattore & Fratta. (2011). *Frontiers in Behavioral Neuroscience, 5*(60), 1-12.

Factors Associated with Synthetic Cannabinoid Popularity

- They induce psychoactive effects
- They are readily available in retail stores and online
- The packaging is highly attractive
- They are perceived as safe drugs
- They are not easily detectable in urine and blood samples

SOURCE: Fattore & Fratta. (2011). *Frontiers in Behavioral Neuroscience, 5*(60), 1-12.

In the News

- **July 2018 FDA:** Hundreds hospitalized due to contaminated synthetic cannabinoids
- Anticoagulants (thins the blood)
- Brodifacoum, which commonly is used in rat poison
- Believed to “extend the high”
- **August 2018 CCN:** 100 Cases in New Haven Connecticut , 56 Cases in Illinois

Khat

- Pronounced “cot”
- Stimulant drug derived from a shrub (*Catha edulis*) native to East Africa and southern Arabia
- Use is considered illegal, because one of its chemical constituents, cathinone, is a Schedule I drug
- Khat found in the U.S. often comes in by mail from Africa

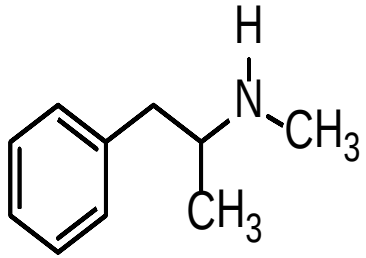
SOURCE: NIDA. (2011). *NIDA DrugFacts: Khat*.

Synthetic Cathinones

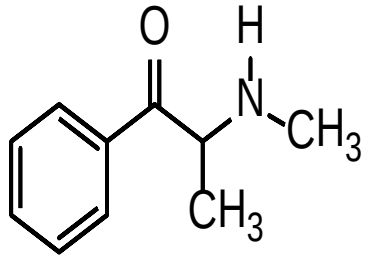
- Could be MDPV, 4-MMC, mephedrone, or methylone
- Sold on-line with little info on ingredients, dosage, etc.
- Advertised as legal highs, legal meth, cocaine, or ecstasy
- Taken orally or by inhaling
- Serious side effects include tachycardia, hypertension, confusion or psychosis, nausea, convulsions
- Labeled “not for human consumption” to get around laws prohibiting sales or possession

SOURCE: Wood & Dargan. (2012). *Therapeutic Drug Monitoring, 34*, 363-367.

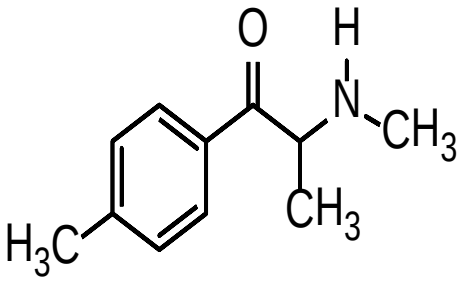
Synthetic Cathinones are β-keto ('bk') Analogs of Amphetamine



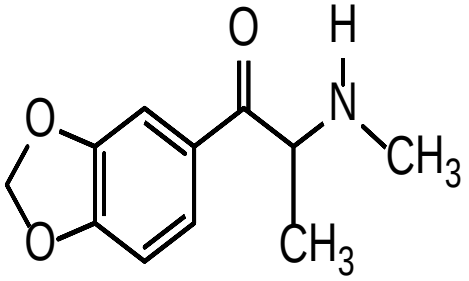
Methamphetamine



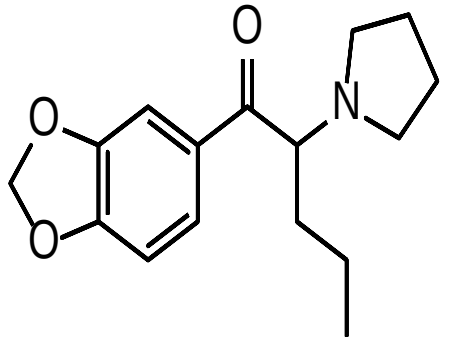
Methcathinone



4-Methylmethcathinone
(Mephedrone)



3,4-Methylenedioxmethcathinone
(Methylone)



3,4-Methylenedioxypyrovalerone
(MDPV)

Sources and Continuing Availability

- A number of synthetic marijuana and bath salt products appear to **originate overseas** and are manufactured in the **absence of quality controls** and **devoid** of governmental **regulatory oversight**.
- The large profits from sales, plus the fact that these chemicals can be easily synthesized to stay one step ahead of control, indicate there is **no incentive to discontinue retail distribution** of synthetic cannabinoid products under the current statutory and regulatory scheme.

SOURCES: ONDCP, 2012; EMCDDA, 2011.


The Effects of
Synthetic DRUGS

"People high on these drugs can get very agitated and violent, exhibit psychosis, and severe behavior changes…some have been admitted to psychiatric hospitals and have experienced continued neurological and psychological effects."

(Dr. Rick Dart, AAPCC President)

SOURCE: Dimond, D. *This Spice Can Kill You.* Posted 8/8/12 at 2:49 p.m.

Short-Term Effects of Synthetic Cannabinoids

- Loss of control
- Lack of pain response
- Increased agitation
- Pale skin
- Seizures
- Vomiting
- Profuse sweating
- Uncontrolled spastic body movements
- Elevated blood pressure
- Elevated heart rate
- Heart palpitations
- Bleeding from the eyes and ears

In addition to physical signs of use, users may experience severe paranoia, delusions, and hallucinations.

SOURCE: *Join Together Online*, December 4, 2012.

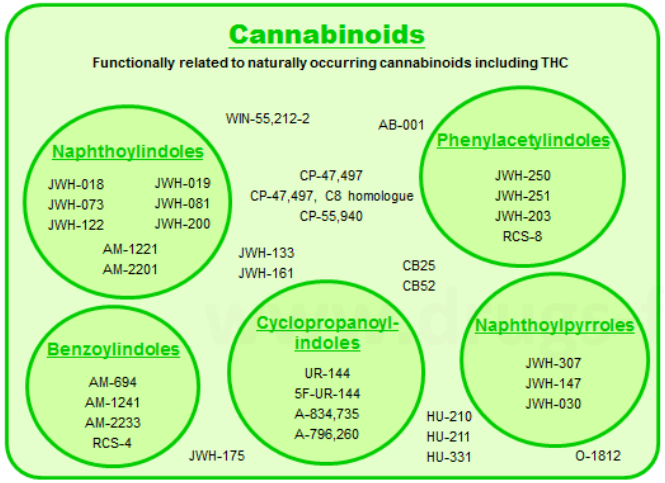
Cannabis vs. Synthetic Cannabinoids: Effects Seen in Clinical Cases

- **Most symptoms are similar to** cannabis intoxication:
  - Tachycardia
  - Reddened eyes
  - Anxiousness
  - Mild sedation
  - Hallucinations
  - Acute psychosis
  - Memory deficits
- Symptoms **not typically seen** after cannabis intoxication:
  - Seizures
  - Hypokalemia
  - Hypertension
  - 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*.

Synthetic Cannabinoids: Other Considerations

- Unlike cannabis, synthetic cannabinoids have no therapeutic effects
  - *Example: no cannabidiol (anti-anxiety), so mood effects unpredictable*

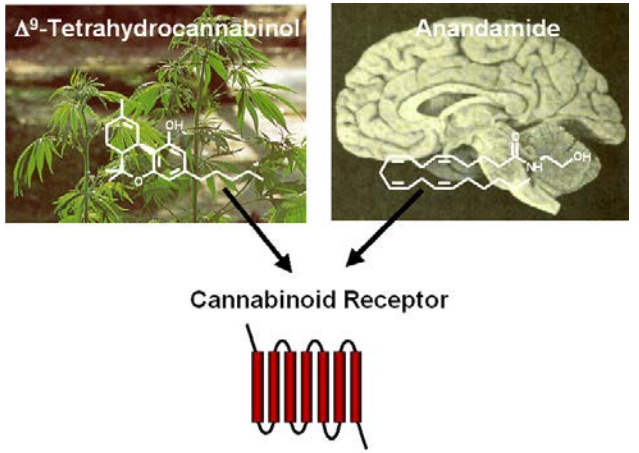


- Packets can contain other psychoactive substances: opioids, oleamide, harmine/harmaline (MAO-Is) that can interact with the synthetic cannabinoid
- Cancer-causing potential of inhaling smoke from these compounds unknown

SOURCE: Doris Payer, #CHSF2013.


The Neurobiology of
Synthetic Drug USE

Cannabinoids

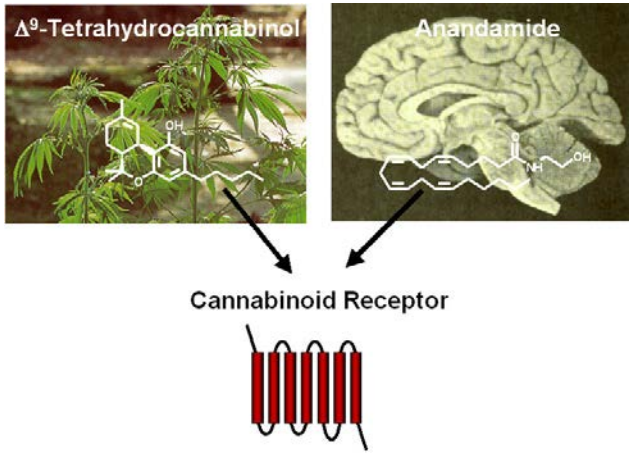


- Neurobiological Concerns:
  - Shown to induce dopamine release (although less directly than stimulants) → brain reward signal →potential for compulsive use/addiction
  - Shown to impact regions of the brain responsible for coordination, problem-solving, sense of time, motivation, etc. → impaired when high
  - Effects on regions underlying learning and memory → possible long-term effects
  - Possible link to psychosis and schizophrenia

SOURCE: Doris Payer, #CHSF2013.

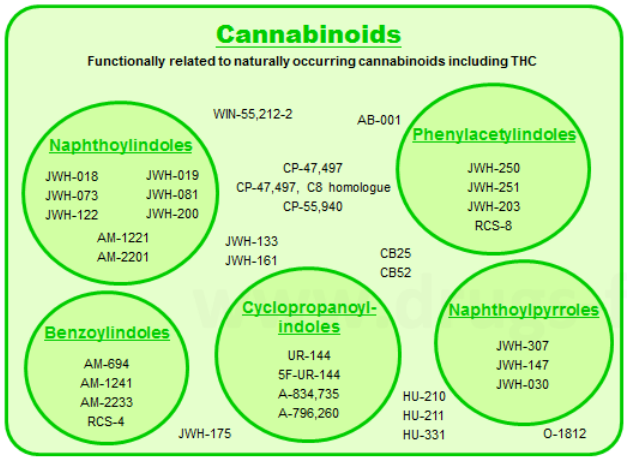
“Classic” Cannabinoids

- Endocannabinoid system
  (“endo” = within)
  Only recently discovered, unusual, not well understood
  - Receptors: CB1 (brain), CB2 (immune system)
  - Transmitters: Anandamide, 2-AG
- THC: binds to CB1 receptor
  - But not very well (low affinity) and not very good at inducing effects (partial agonist)
  - But unlike endocannabinoid transmitters, not degraded immediately, so CB1 activation is extended/exaggerated compared to anandamide



SOURCE: Doris Payer, #CHSF2013.

Synthetic Cannabinoids



- No structural similarity to THC, but same effects profile
  - Bind to CB1 and CB2 receptors
  - Same types of physical effects & impairments
  - In animals: signs of "high" similar, but at 2-14x lower dose
- The problem: Stronger & longer-lasting than THC
  - Better binding to receptors (high affinity/potency) AND each binding event has greater effect (full agonist)
    - 4x higher affinity for CB1, 10x for CB2
    - Longer half-life so effects longer lasting
  - Products of break-down (metabolites) also psychoactive
  - Together: More, more-likely, and longer-lasting adverse effects (especially if dosing is based on cannabis)

SOURCE: Doris Payer, #CHSF2013.

Synthetic Cannabinoids: "The Next Generation"

- New compound, URB-754: Does NOT bind to CB receptors itself, but inhibits enzyme that breaks down endocannabinoids
  - More endocannabinoid around → more binding to receptors
- AND, one "spice" sample was found to contain URB + a cathinone, which reacted with one another and together created a whole new psychoactive compound

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URB-754: A new class of designer drug and 12 synthetic cannabinoids detected in illegal products☆

Nahoko Uchiyama, Maiko Kawamura, Ruri Kikura-Hanajiri, Yukihiro Goda *

National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan

SOURCE: Doris Payer, #CHSF2013.

Stimulants

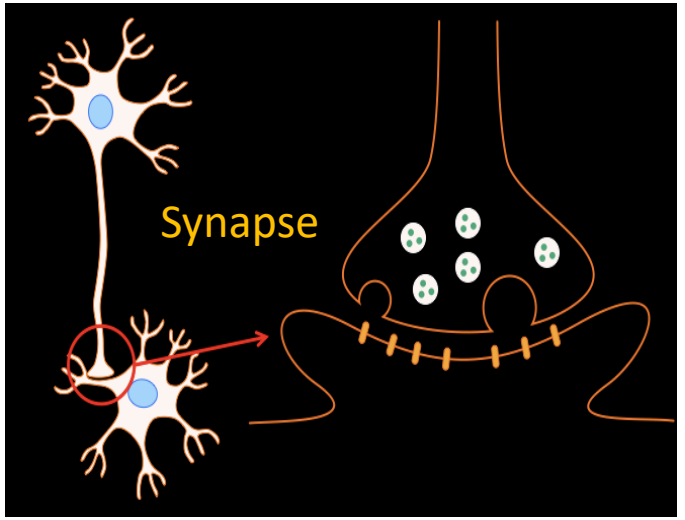
- Neurobiological Concerns
  - Addiction
    - Compulsive chase and use
  - Physical health
    - Cardio-vascular (heart rate, blood pressure, etc.)
    - Body temperature
    - Long-term brain changes
  - Mental state
    - Risky decisions, impaired judgment, impulsive acts, etc.

SOURCE: Doris Payer, #CHSF2013.

“Classic” Stimulants

Direct action on synapse

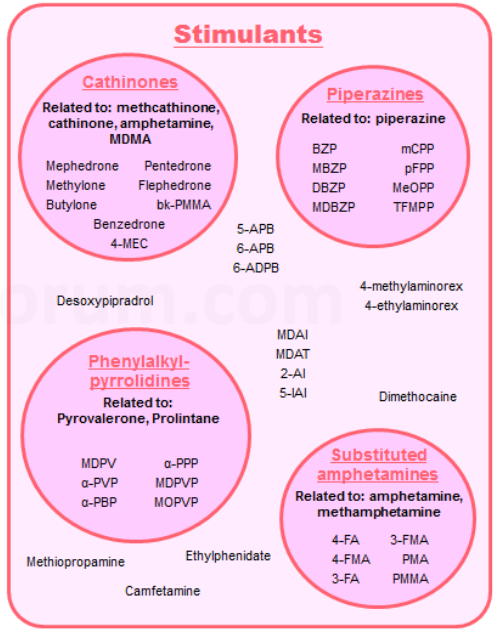
- Amphetamine, cathinone: induce dopamine release
- Cocaine, methylphenidate (Ritalin): block dopamine removal
- MDMA: additional effects on serotonin
  - Dopamine effects less strong, so less “reward,” so animals do not self-administer as much
  - Synthetic stimulants are variations on this theme, BUT: “*Very subtle structural modifications can yield profoundly different behavioural, neurochemical, and neurotoxicological effects*.”



SOURCE: Doris Payer, #CHSF2013.

Synthetic Stimulants

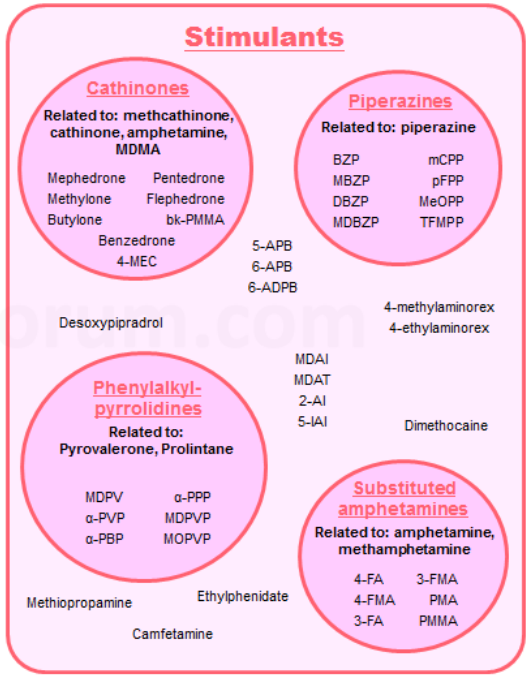
- In general: dopamine ↑ and animals like/want/work for drug
  - Sign of high abuse potential
  - Recreational use can progress easily to compulsive use



SOURCE: Doris Payer, #CHSF2013.

Synthetic Cathinones

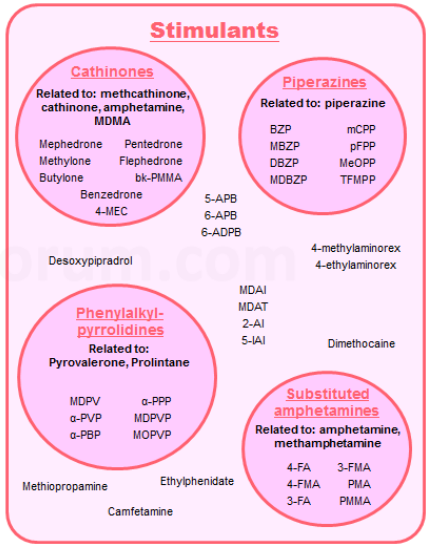
- Block transporters (removal)
  - Rank at **DAT**: MDPV/pyrovalerone >> cocaine, amphetamine/MA, methcathinone, naphyrone > mephedrone, butylone, methylone, etylone, flephedrone, MDEA > cathinone, MDMA, MBDB
  - Rank at **SERT**: MDEA, MDMA, naphyrone > MBDB, cocaine, ethylone, mephedrone, butylone >> rest
  - Rank at **NET** (fight/flight): MDPV, pyrovalerone > amph/MA, methcathinone > cathinone, mephedrone, flephedrone, naphyrone > MDMA, cocaine, methylone > MDEA, butylone, ethylone, MBDB



SOURCE: Doris Payer, #CHSF2013.

Synthetic Cathinones

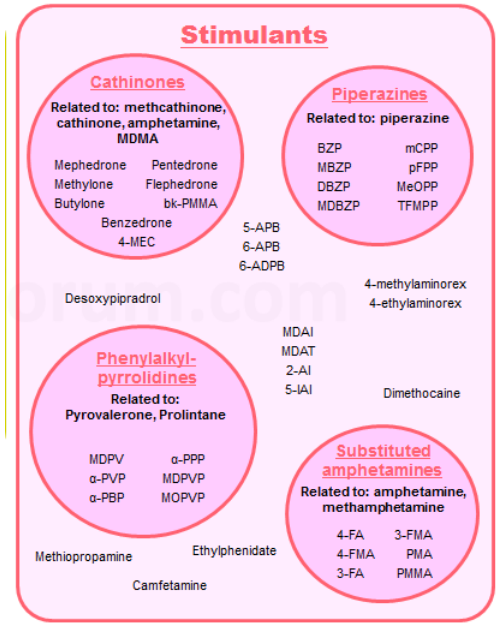
- Also release
  - **Dopamine**: Amph/MA, cathinone, methcathinone, mephedrone*, flephedrone > MDMA (potency low)
  - **Serotonin**: MDMA, MDEA, MBDB, methylone, ethylone, butylone, mephedrone
    - Amph/MA, methcathinone, flephedrone only at very high concentrations
- Pyrovalerone, naphyrone, MDPV: **NO** dopamine or serotonin release, but still extremely good at blocking removal – 10x cocaine



SOURCE: Doris Payer, #CHSF2013.

Synthetic Cathinones vs. “Classic” Stimulants

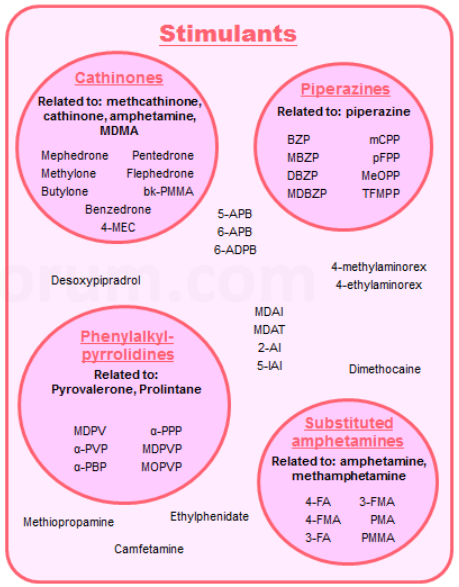
- Mephedrone originally thought to be more like MDMA than amphetamine b/c of serotonin effects, but dopamine release more like amphetamine
  → greater abuse liability
- In and out of brain faster than MDMA → greater potential for repeated binge use
- Effects on body temperature regulation different from MDMA: “Adverse effects cannot be extrapolated from previous observations on MDMA” (Shortall)
- MDPV: greater self-administration than even MA



SOURCE: Doris Payer, #CHSF2013.

Synthetic Stimulants: Physical Concerns

- Norepinephrine (fight/flight) system: hyper-active movement, body temperature regulation, cardio-vascular effects
- Especially MDPV
  - Better than cocaine (x10) at producing hyper-active movement, increased heart rate & blood pressure
  - Itself does not disrupt body temperature regulation (like MA or MDMA do), but heart rate/blood pressure interact with room temperature (Fantegrossi)
- Neurotoxicity ("brain damage"): some evidence for serotonin and dopamine depletion in animals
  - Mephedrone NOT toxic to dopamine cells (several reports)
  - **BUT: Mephedrone enhances toxic effects of amph/MA and MDMA! (Angoa-Perez) → co-administration frequent, even if accidental



SOURCE: Doris Payer, #CHSF2013.

THE EPIDEMIOLOGY OF SYNTHETIC DRUG USE

Compounds Encountered in the U.S.

233 New synthetic compounds from the 8 classes of drugs

Law Enforcement has encountered:

- 95 synthetic cannabinoids
- 51 synthetic cathinones
- 87 Other compounds (2C compounds, trytpamine, piperzines, etc.)

Synthetic Cannabinoid Data

American Association of Poison Control Center

These numbers reflect the closed human exposures to synthetic cannabinoid (THC homologs) reported to poison centers as of November 30, 2018. The numbers may change as cases are closed and additional information is received.

Year	Number of Cases
2011	6,968
2012	5,230
2013	2,668
2014	3,682
2015	7,797
2016	2,706
2017	1,959
2018	**1,843**

Emergency Room Visits Related to Synthetic Cannabis and Cathinones: DAWN, 2011

	% Male	% Under Age 21	% Sent to ICU or Sub. Abuse Treatment	% Discharged Home
Synthetic Cannabis	70%	55%	3%	78%
Synthetic Cathinones	76%	14%	12%	55%

SOURCE: OAS, SAMHSA-CSAT. (2013). Drug Abuse Warning Network, 2011 data.

In Summary: Key Points

Research is needed to better understand the side effects and long-term consequences associated with the use of synthetic cannabinoids and synthetic cathinones.

More toxicological identification of these new drugs, more information on the sources of them, as well as their distribution and patterns of use is needed to curtail future increases in use.

Resources for Continued Learning

- American Association of Poison Control Centers, www.aapcc.org
- Drug Enforcement Administration, www.dea.usdoj.gov
- European Monitoring Centre for Drugs and Drug Addiction, www.emcdda.europa.eu
- National Institute on Drug Abuse, www.nida.nih.gov
- Office of National Drug Control Policy, www.ondcp.org
- Pacific Southwest ATTC, www.psattc.org
- Refer to the *Synthetic Drugs Reference List***

Thank you for your time!

Questions?

Type your questions in the Q&A box on your screen

Speaker Contact Info:

Philip Barbour

pbarbour@tasc.org

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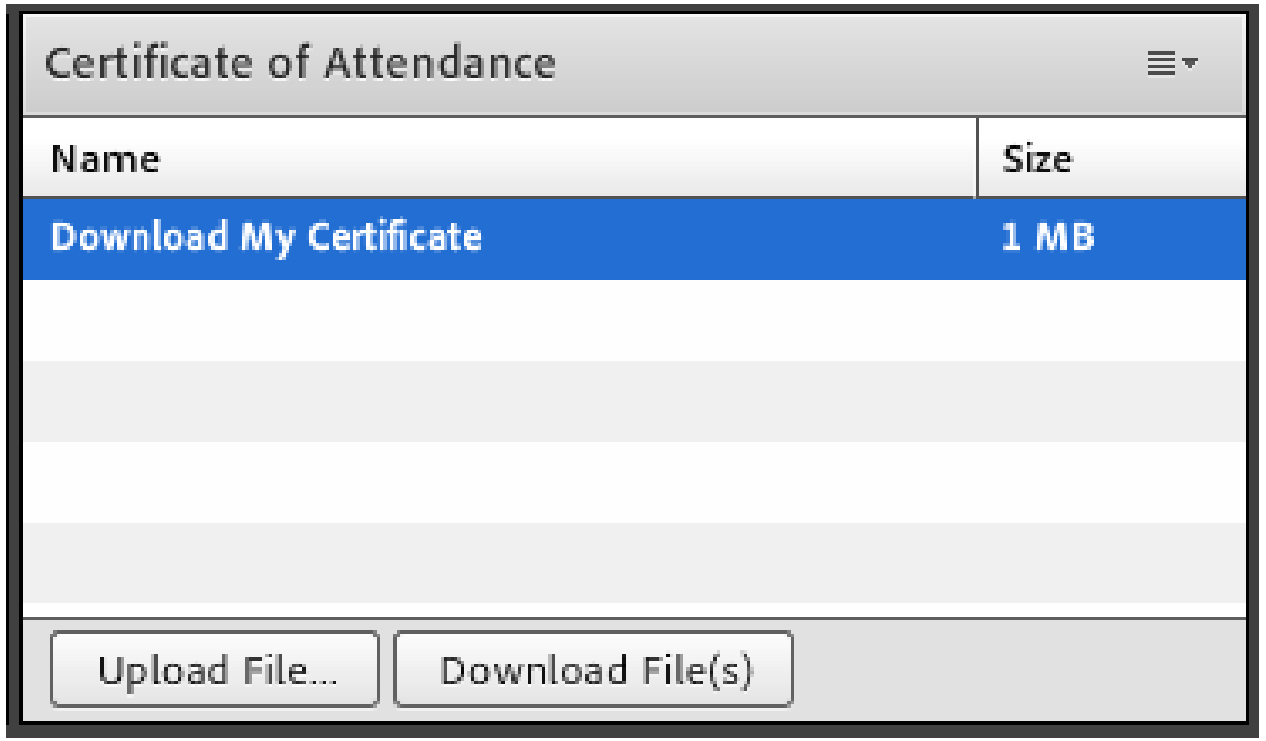

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- **Pass 10-question quiz with 7 correct answers**
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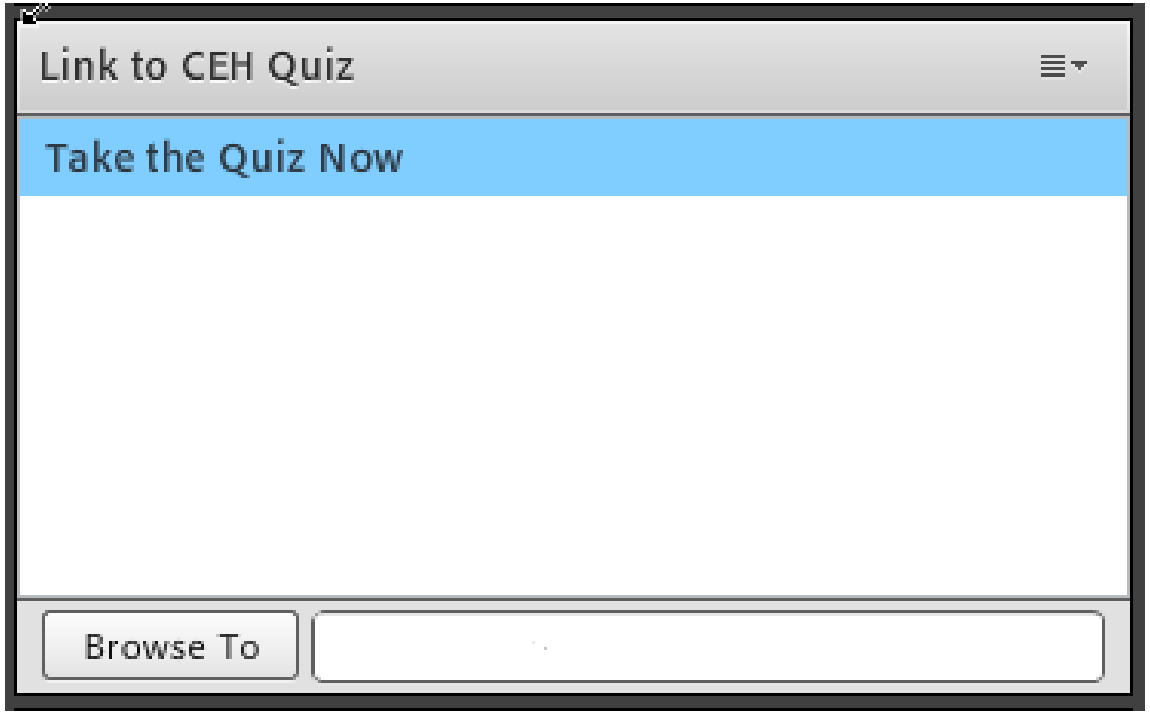

For more information on RSAT training and technical assistance please visit:

http://www.rsat-tta.com/Home

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