

Part 2: Hallucinogens

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Nomenclature

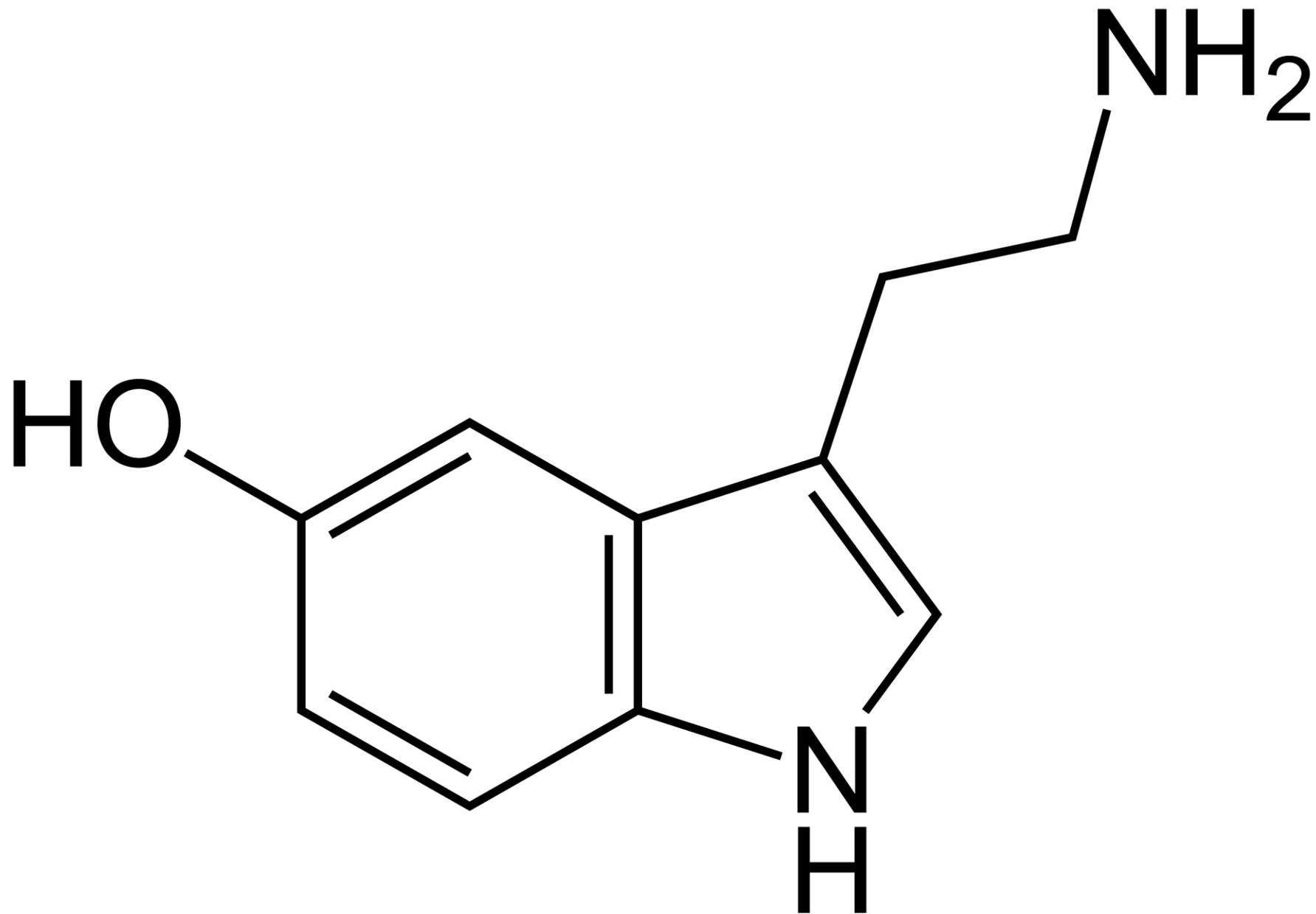
- Hallucinogen
- Psychedelic [makes manifest the hidden realities of the mind]
- Psychotomimetic
- Entheogen [Generates the God within]

Hollister's Criteria

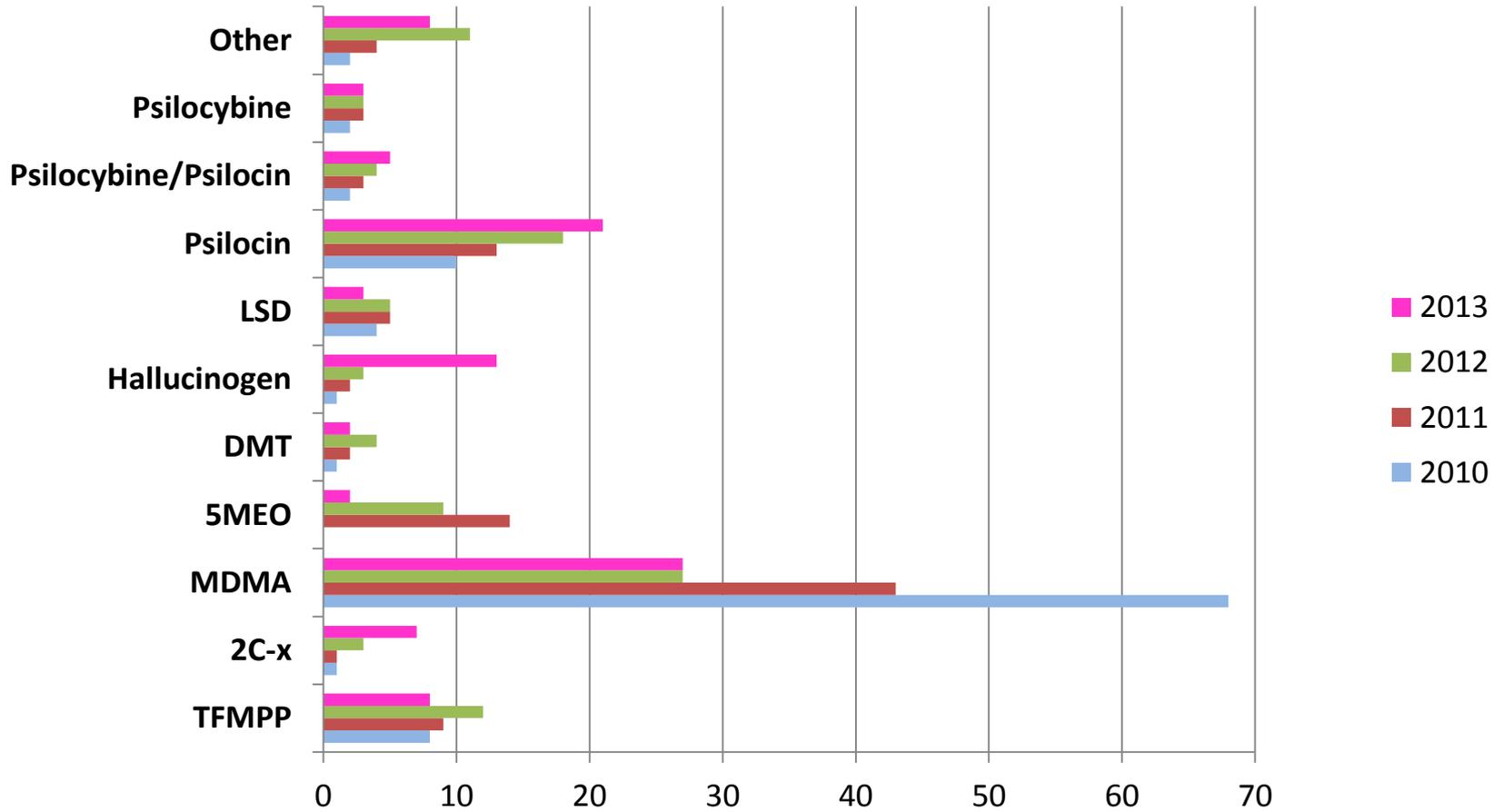
- Changes in thought, perception, and mood predominate
- Intellectual and memory impairments minimal
- Stupor, narcosis, or excessive stimulation NOT integral effects
- Minimal autonomic nervous system side effects
- Addictive craving **absent**

Classic hallucinogens

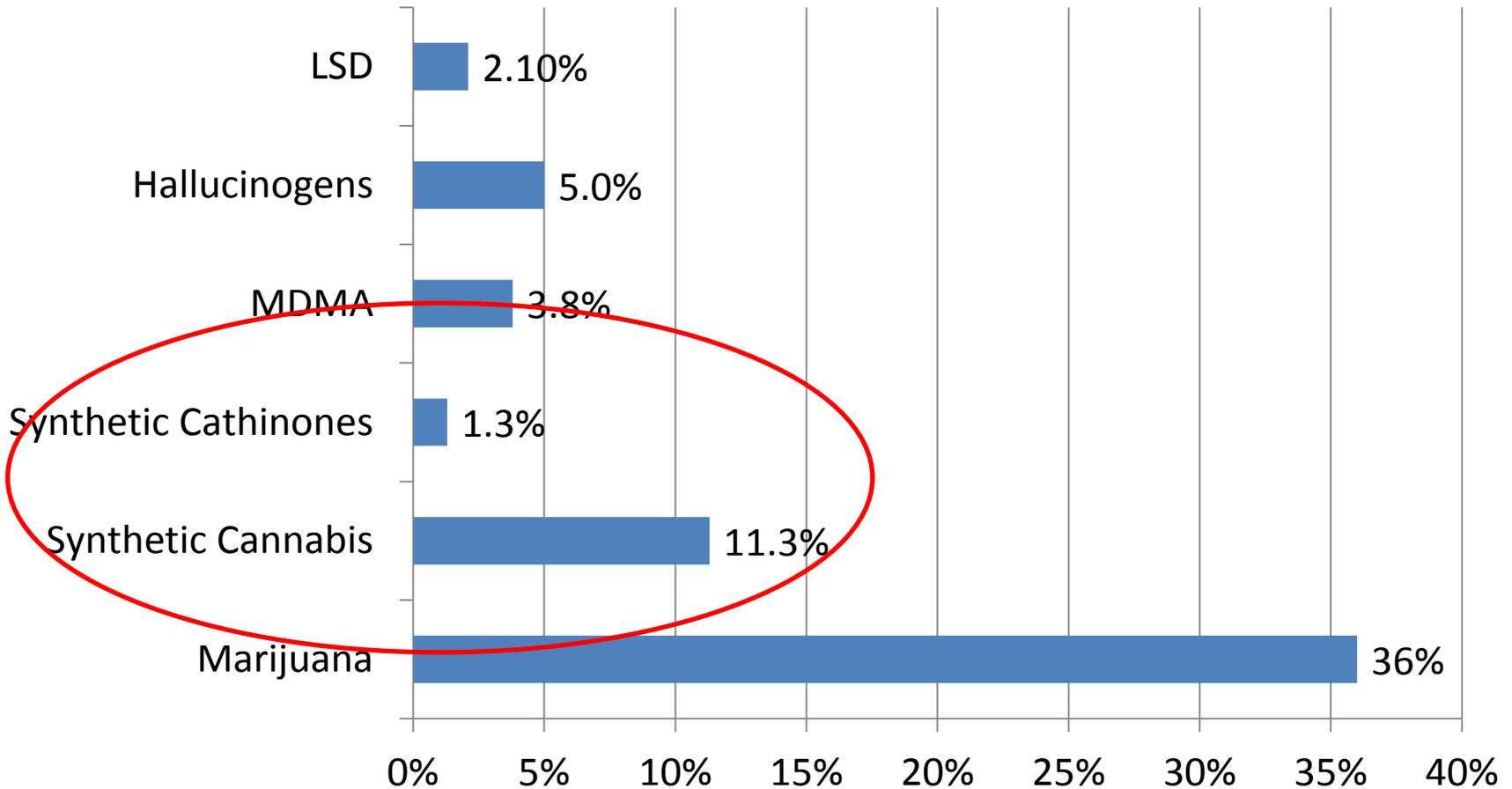
- Hollister's criteria **PLUS**
 1. Bind at 5-HT₂ serotonin receptors
 2. are recognized by animals trained to discriminate 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) from vehicle.



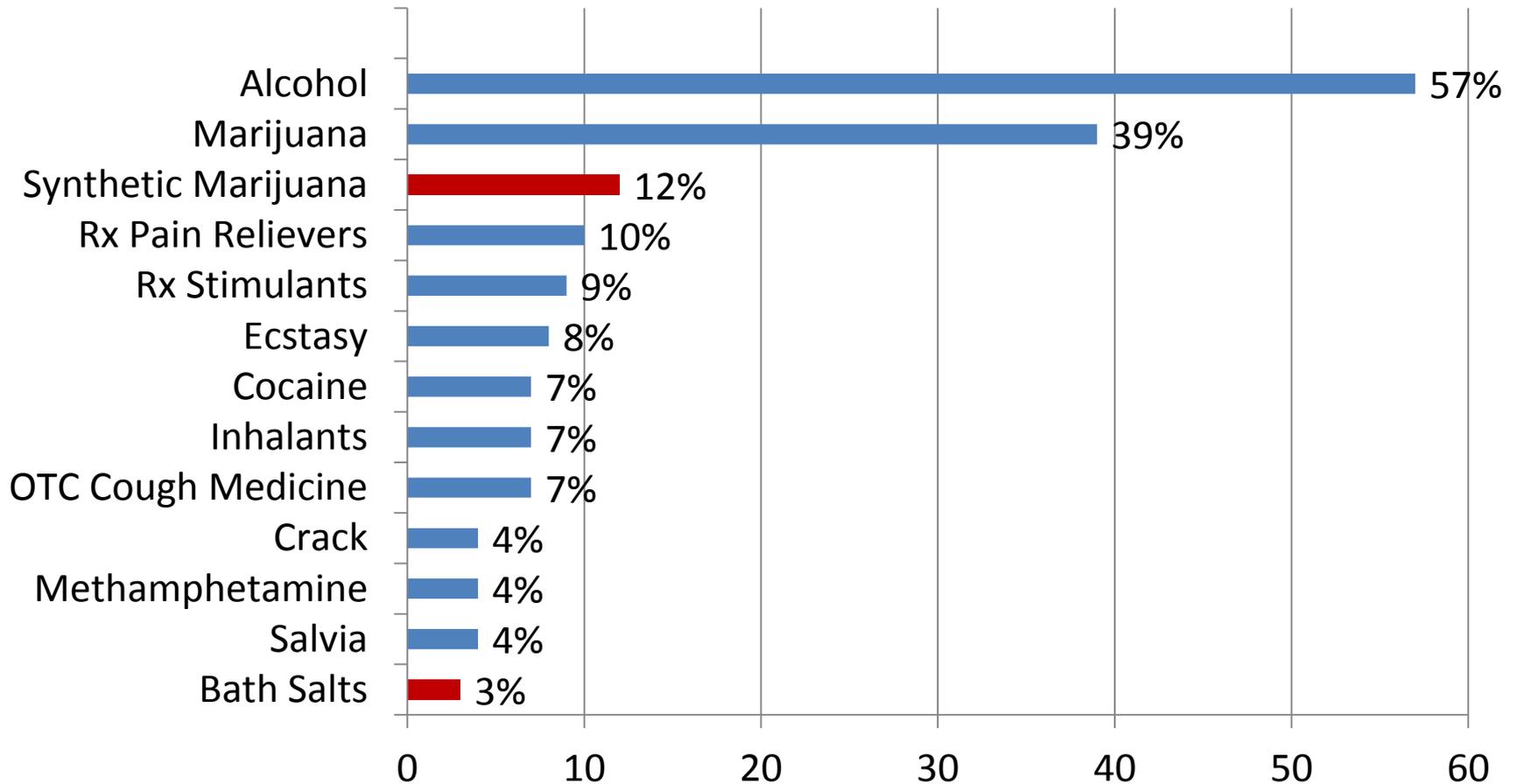
Prevalence



Past Year Drug Use by 12th Grade Students: MTF, 2012



Percentage of U.S. Students (Grades 9 to 12) Reporting Past Year Alcohol and Other Drug Use, 2012 (N=3,884)



SOURCE: Adapted by CESAR from The Partnership for a Drug-Free America and the MetLife Foundation, *The Partnership Attitude Tracking Study (PATS): Teens and Parents, 2013*.

Prevalence

- Lifetime: 14.8%
- Past year: 1.8%
- Age 12-17: 4.1% lifetime/3.0% past year
- Males: 18.5%/2.3%
- Females: 11.3%/1.3%
- Caucasian: 17.8/1.9
- Black/African American: 6.6%/1.4%
- AI/AN: 28.3%/6.6%
- Asian: 5.5%/0.8%
- Hispanic/Latino: 9.5%/1.7%

Effects of hallucinogens- Somatic

- Dizziness
- Weakness
- Tremors
- Parasthesias
- Drowsiness
- Nausea
- Blurred vision

Effects of hallucinogens- perceptual

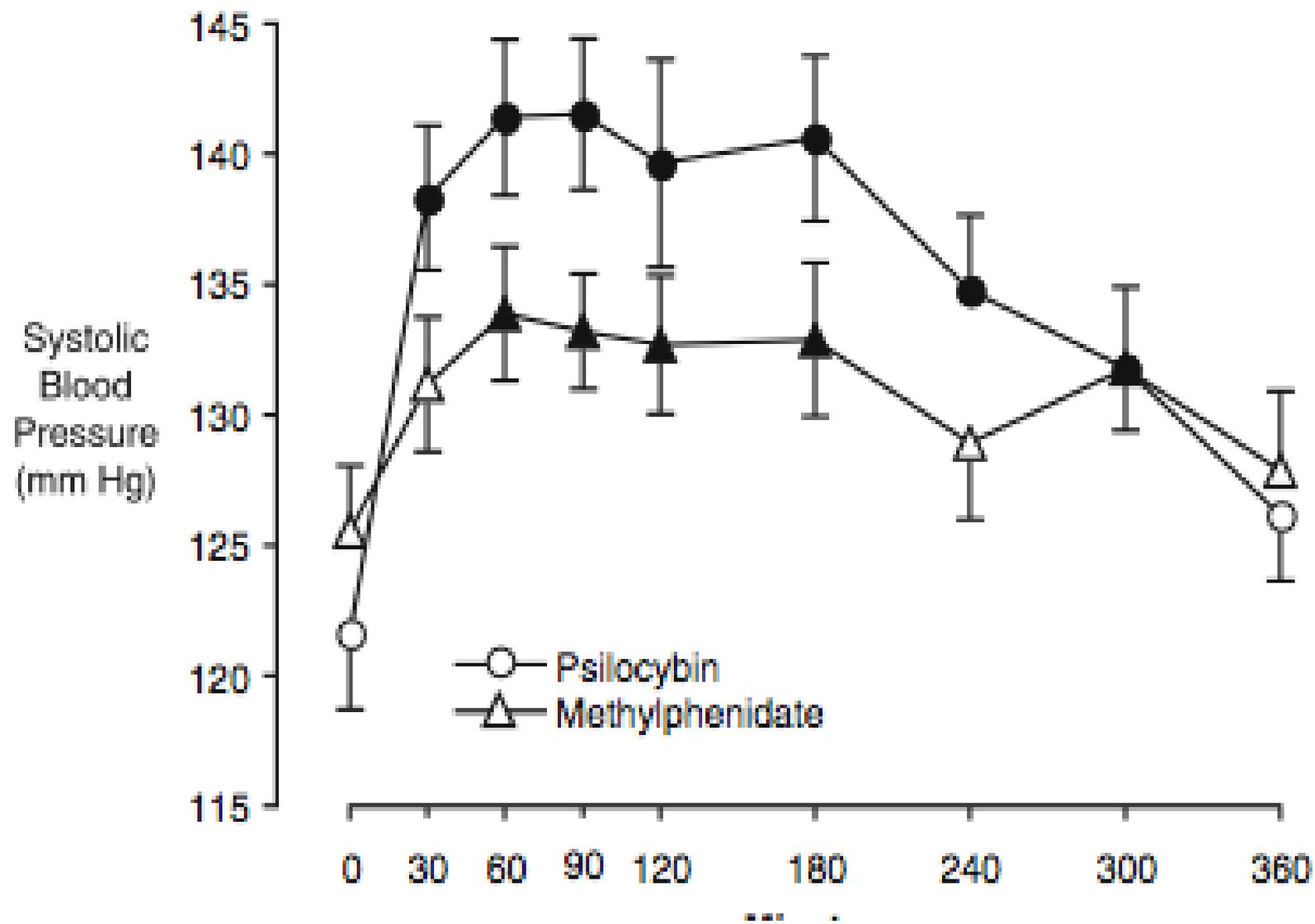
- Altered shapes and colors
- Difficulty focusing on objects
- Heightened sense of hearing
- Synesthesia- tasting colors, seeing music etc.
- Illusions
- True hallucinations- less common
- Altered sense of time

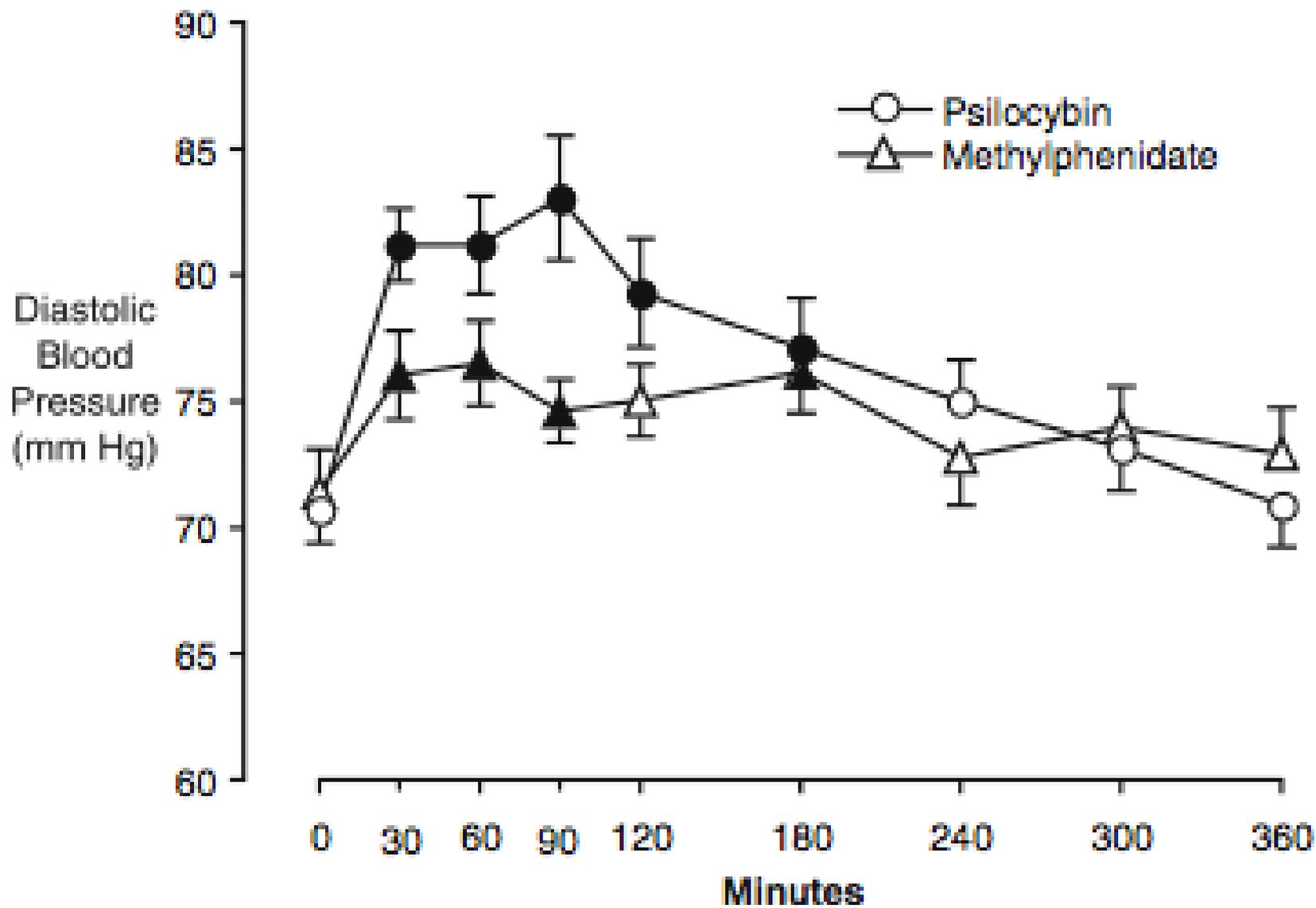
Other notable effects of hallucinogens

- Affective component- alterations in mood
- Anxiety/tension
- Depersonalization
- Dream-like state
- Difficulty expressing thoughts

Four stages of hallucinogenic experience

- Perceptual
- Biographical
- Symbolic
- Spiritual





“Bad trips”

- Challenging experiences
- Affective, perceptual
- Highly dependent on “set” and “setting”
- Use grounding techniques [deep breathing]
- Usually amenable to “talking down”
- May use benzodiazepines or antipsychotics for more difficult experiences

Classification

- Two subtypes of arylalkylamines
 1. Indolelalkylamines- Bind to 5-HT_{2A}, 2B, 2C, 1A
 2. Phenylalkylamines- selective for 5-HT_{2A}

Note: Arylalkylamines can also be stimulants or empathogens based on their molecular structures

**INDOLEALKYLAMINES:
SUBSTITUTED TRYPTAMINES**

DMT [N,N- Dimethyltryptamine]



DMT [N,N- Dimethyltryptamine]

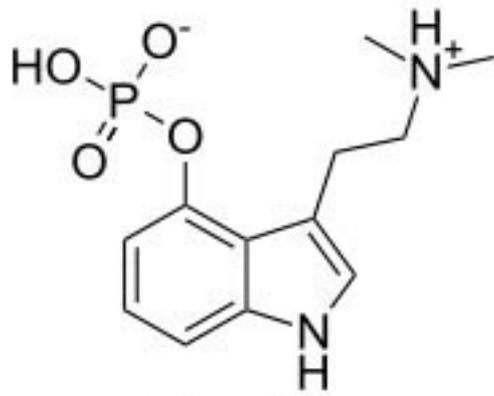
- Prototypical of this subtype
- Naturally occurring [Sonoran desert toads, Mimosa hostillis, phalaris grass etc.]
- Rapid onset of action [5 minutes, or less]
- Brief duration of action [30 minutes]
- Characteristic odor
- Smoked or injected
- Not orally stable
- Released by pineal glands during times of stress
- Dream states; near death experiences

Ayahuasca

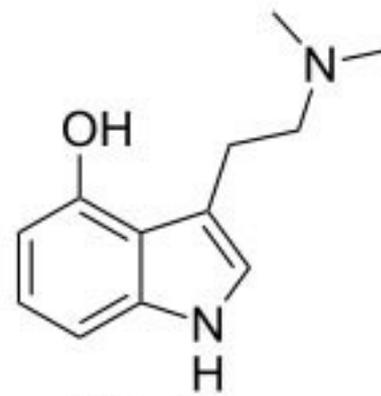
- DMT + harmaline [MAOI]
- *Psychotria viridis* + *Banisteriopsis caapi*
- Ceremonial uses among indigenous populations in the Amazon
- Ceremonial uses among the mestizo religions [uniao de vegetal, santa]

Psilocybin and Psilocin

- Tryptamines that naturally occur in certain types of mushrooms
- “shrooms”
- Cross-Tolerance with LSD
- Rapid tolerance build up
- Onset within 30 minutes
- 4-6 hours duration of effects
- Psilocybin metabolized to psilocin, the psychoactive alkyloid
- Nausea, panic attacks, anxiety are common adverse effects
- Mild BP elevation usually observed



Psilocybin

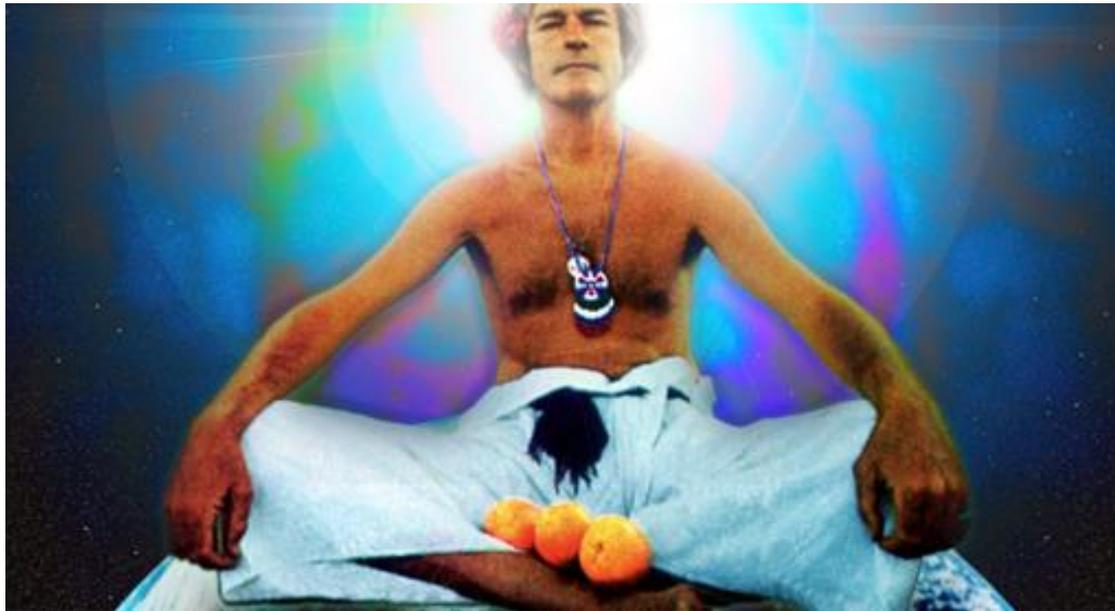


Psilocin

Indolealylamines-lysergamides



Indolealylamines-lysergamides



Indolealylamines-lysergamides

turn on

tune in

drop out

Indolealylamines-lysergamides

- LSD [lysergic acid diethylamide]
- Does not occur naturally
- Synthesized by Albert Hoffman [1938]
- “... affected by a remarkable restlessness, combined with a slight dizziness. At home I lay down and sank into a not unpleasant intoxicated[-]like condition, characterized by an extremely stimulated imagination. In a dreamlike state, with eyes closed (I found the daylight to be unpleasantly glaring), I perceived an uninterrupted stream of fantastic pictures, extraordinary shapes with intense, kaleidoscopic play of colors. After some two hours this condition faded away.”

Indolealylamines-lysergamides

- Highly potent
- Water soluble, clear white odorless crystals
- Sheets of thin blotter paper with dried solution of LSD [most common]
- Sugar cubes [“Dropping acid”]
- Pills [“microdots”], or thin gelatin squares [“windowpanes”]

Indolealylamines-lysergamides

- Onset 30-60 minutes
- Peak 2-4 hours
- Duration 8- 12 hours

Indolealkylamines- Beta-carbolines

- Harmaline, harmine
- Bind to, but do not activate 5-HT_{2A}
- Not psychedelic
- Act as MAOI
- Component of ayahuasca and “pharmahuasca”

PHENYLALKYLAMINES

Phenylalkylamines

- Largest group of classic hallucinogens
- Mescaline [peyote, San pedro]
- 2-CB [“nexus”]
- DOM, DOB, DMA, MDA, many others

Peyote

- Sacramental use within Native American Church
- Grows within a 50 mile distance of Rio Grande along US-Mexico border, and in hills north of Mexico City
- Buttons harvested from top of peyote cactus
- Onset 30-60 min: nausea, increased respiration rate, minor perceptual changes
- Next several hours [5-10]: classic hallucinogen effects

DOM

- Very potent
- Results from structural modification of mescaline-like substances
- Used as model hallucinogen in drug discrimination studies

MDA

- Stimulant + hallucinogenic effects
- Modified to form MDMA [“ecstasy”]- stimulant + empathogenic effects

Endless combinations are possible

- By changing the molecular structure, you can get hallucinogen, empathogen, stimulant, or a combination of these three!

Alexander “Sasha” Shulgin

- Discovered, synthesized, and personally tested over 200 psychoactive substances for their psychedelic properties
- Authored PIHKAL, TIHKAL [Phenylethylamines and Tryptamines I Have Known and Loved]
- Popular creations include the DOx creations [DOB, DOM], and 2C series [2CB, 2CI]

“Magical half dozen”

- DOM
- 2-CB
- 2-CE
- 2C-T-2
- 2C-T-7
- [mescaline]

2C-phenylethylamines

- A broad range of compounds that share a common phenylethan-2-amine structure.
- 2 C-X can be snorted or dissolved into a liquid and placed on blotter paper under the tongue.
- May last 6-10 hours; onset takes 15 min- 2 hours

2C-phenylethylamines

- Almost all of the 2C-phenethylamines are produced in Asia, principally China, but some small labs in the U.S. are capable of producing 2C (usually 2C-B).
- In 2011, DEA offices throughout the country began noting the increasing availability and abuse of 2C at raves and in nightclubs, particularly by teenagers and young adults.
- NFLIS labs nationwide identified 253 reports of phenethylamines in 2010, 336 in 2011, 828 in 2012, and 230 through May 2013.

2C-B [“Nexus”]

- Used by underground therapists in 1970s
- Create a warm atmosphere, ego weakening, therapeutic rapport
- `My body was flooded with orgasms - practically from just breathing. The love-making was phenomenal, passionate, ecstatic, lyric, animal, loving, tender, sublime....I am aware of every muscle and nerve in my body, unbelievably erotic, quiet and exquisite, almost unbearable..'
- Sold over the counter as a sexual enhancer worldwide until 1993
- Popular at raves; banned by DEA

2C-B [“Nexus”]

- ‘When I take Nexus, I merge with the music, become one with the crowd, and fuse with the whole of Planet Earth. This isn't a drug, it's a trance-dance sacrament.’
- ‘a cross between the warm, lovey-dovey feeling produced by Ecstasy and the visual patterning you get when you take magic mushrooms’
- ‘I tried it once and all that happened was that I felt jittery, disorientated and strung out for the entire evening.’

2C-I

- Became popular between 2001-2005
- Strong stimulant component, with associated hallucinogen and empathogen components
- Often delayed effect [users taking multiple doses as a result]
- Users report virtually no nausea, vomiting or muscle cramps [as opposed to 2C-T-2 and 2C-T-7]
- ‘deeper, more purely psychedelic and less sensory’ compared to 2C-B

2C-C-NBOMe, 2C-I-NBOMe, 25-I-NBOMe, Mescaline-NBOMe

- New class of 2C drugs
- NO history of human consumption prior to 2010
- Linked to several hospitalizations and deaths
- Usually result of people taking upto 10x the recommended doses
- “N-Bomb”, “Smiles”

2C-C-NBOMe, 2C-I-NBOMe, 25-I-NBOMe, Mescaline-NBOMe

- Strongly active at the **sub-milligram dose (a Super Potent drug)**
- Most 25I and 25C is sold as **pure powder**
 - Weighing and handling pure high-potency chemicals such as LSD or 25I-NBOMe should be performed wearing eye protection, gloves, and a filter mask
- Perhaps the greatest risk of the wide availability of pure NBOMe powders is **confusing one white powder for another**, or simply **misunderstanding the difference** between one psychedelic or stimulant drug and another
- In 2011, 10 items of the NBOMe family were seized and identified in NFLIS forensic laboratories, as compared to 447 in 2012.

2C-C-NBOMe, 2C-I-NBOMe, 25-I-NBOMe, Mescaline-NBOMe

- Effective November 15, 2013, the United States Drug Enforcement Administration (DEA) made the synthetic phenethylamines 25I-NBOMe, 25C-NBOMe, and 25B-NBOMe Schedule I, illegal drugs under the Controlled Substances Act (CSA) for the next two years.
- Plan to make them permanently illegal

Hallucinogen Persisting Perception Disorder (HPPD)

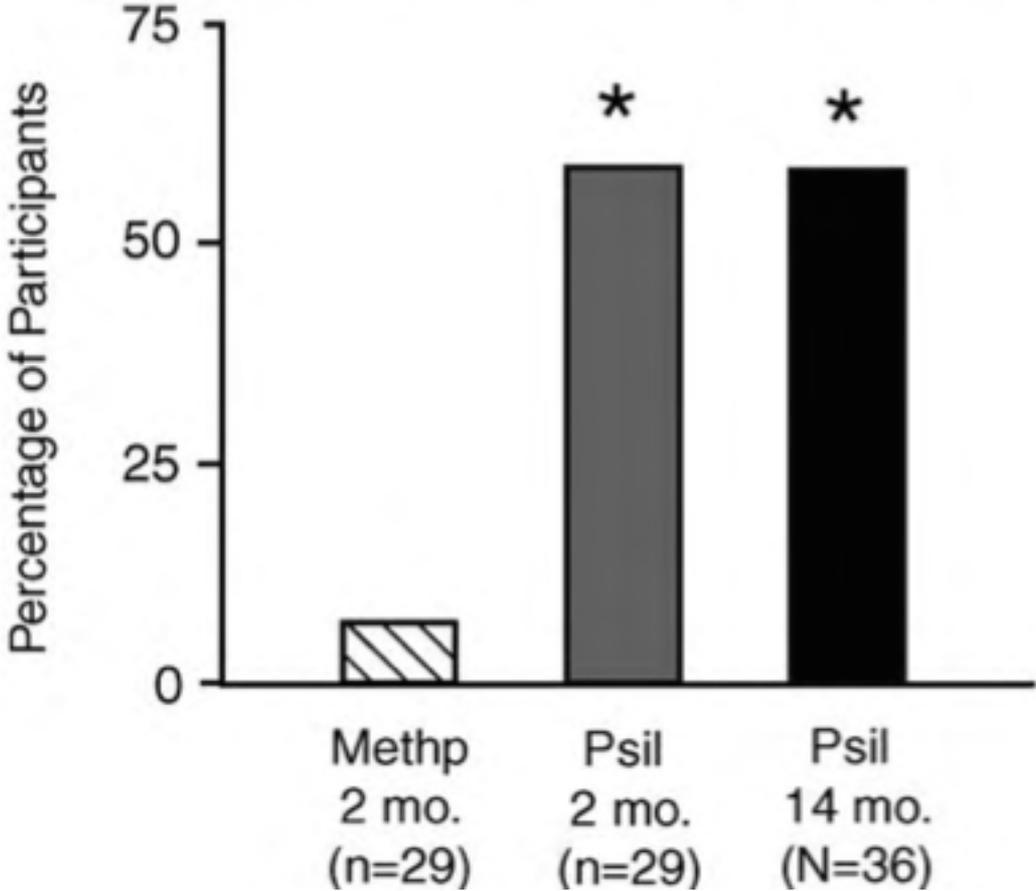
- Re-experiencing of perceptual symptoms experienced while intoxicated following cessation of use = flashbacks
- Unrelated to dose or number of exposures
- Usually resolves within 1-2 years of last use
- Can be triggered by other substance use

POSSIBLE THERAPEUTIC USES

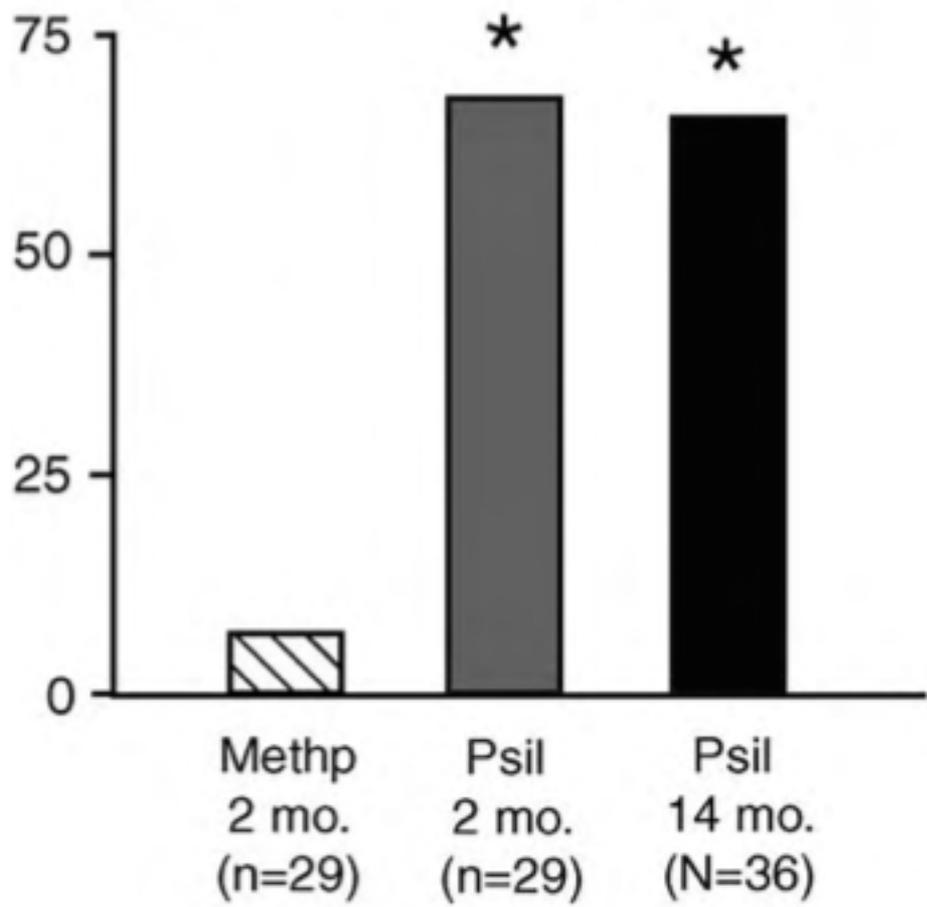
Psilocybin and Mystical Experiences

- Double blind study done at Johns Hopkins University
- At 14 month follow up:
 - 58% rated the psilocybin-occasioned experience as being among the five most personally meaningful experiences
 - 67%- five most spiritually significant experiences of their lives
 - 64% indicated that the experience increased well-being or life satisfaction

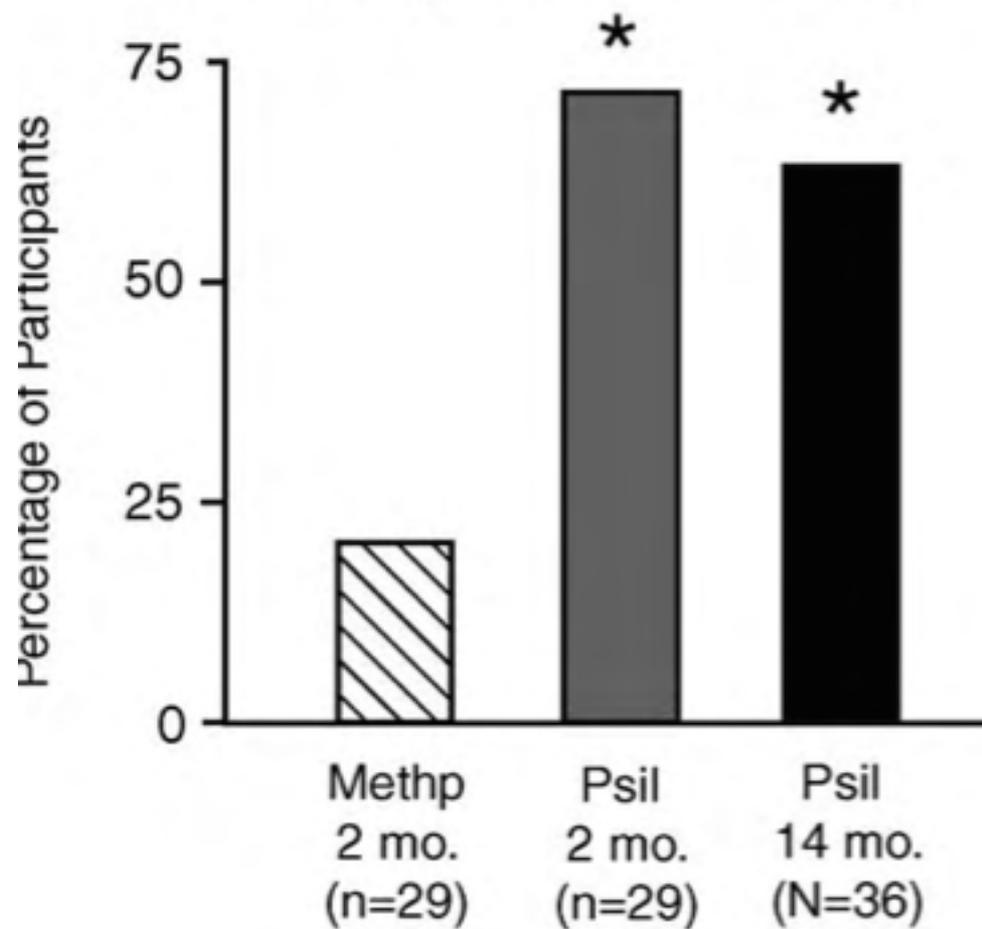
**Among the Top 5 Personally
Meaningful Experiences of Lifetime**



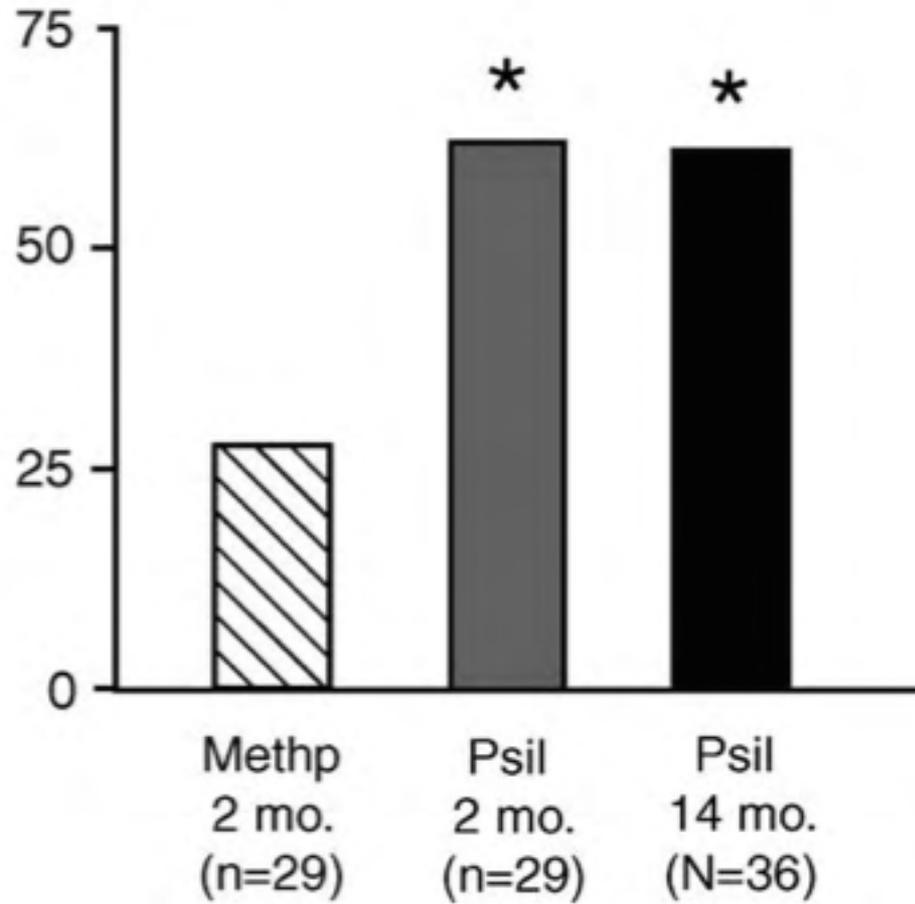
Among the Top 5 Spiritually Significant Experiences of Lifetime



Increased Current Personal Well-Being or Life Satisfaction



Positive Behavior Change



Other Notable investigations

- Large double blind, placebo controlled trial of psilocybin and cancer related anxiety at Johns Hopkins, New York University, and Harbor-UCLA
- Small study of Psilocybin and OCD at University of Arizona

Psychedelics and Addiction Treatment

- Over one hundred years ago William James described the phenomenon of sudden transformative change of a religious or spiritual nature, which was often accompanied by changes in behavior such as the abrupt onset of sobriety in alcoholics
- More recently, William R. Miller and others have elucidated the nature of what has been termed “quantum change”

Psychedelics and Addiction Treatment

- Over 30 studies evaluating LSD for treatment of alcoholism between 1950-1970
- Most studies plagued with methodology
- However, some of the best-designed studies (e.g. (Hollister, Shelton, & Krieger, 1969; Ludwig, Levine, Stark, & Lazar, 1969) appear to show an effect on drinking of 1-3 months duration following a single dose of LSD in a supportive environment
- Recent meta-analysis: NNT of 6 [slightly less than naltrexone!!]

Psychedelics and Addiction Treatment

- hallucinogenic drug experiences, undergone in a relatively structured supportive setting, may provide a useful model of quantum change
- Such carefully tailored and purposeful experiences (as opposed to misuse or “recreational” use) may be associated with reduced use of other substances

Psychedelics and Addiction Treatment

- Ibogaine for heroin and alcohol dependence
- Ketamine for heroin and alcohol dependence
- Cross-sectional studies consistently show reduced rates of alcohol dependence among
 - Native American Church [Peyote]
 - US and Brazilian religions using ayahuasca

Psychedelics and Addiction Treatment

- University of New Mexico psilocybin for treatment of alcohol dependence [PI: Michael Bogenschutz]
- Safety and feasibility study completed
- Double blind placebo controlled study with N=180 under way, with NYU as a second research site
- <https://www.youtube.com/watch?v=uX5MrmR86mk>

Conclusions

- Classic hallucinogens exert their actions through agonism at the 5-HT₂ serotonin receptor
- Classic hallucinogens have a major effect on thought, perception and mood
- Classic hallucinogens do not induce addictive craving
- There are many new and emerging hallucinogens whose actions and effects are poorly understood, and may pose a risk to public safety
- There are potential therapeutic applications of classic hallucinogens