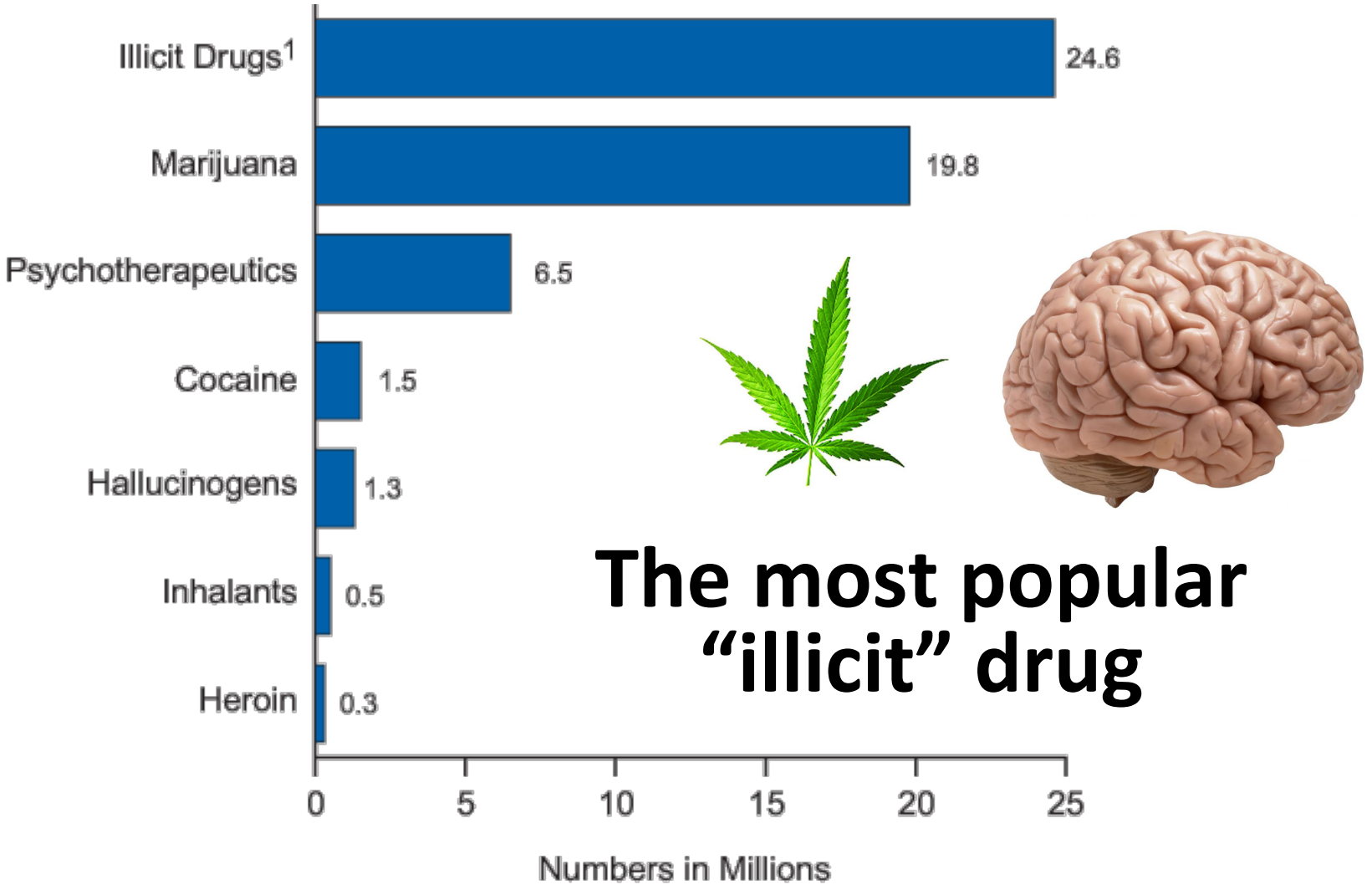
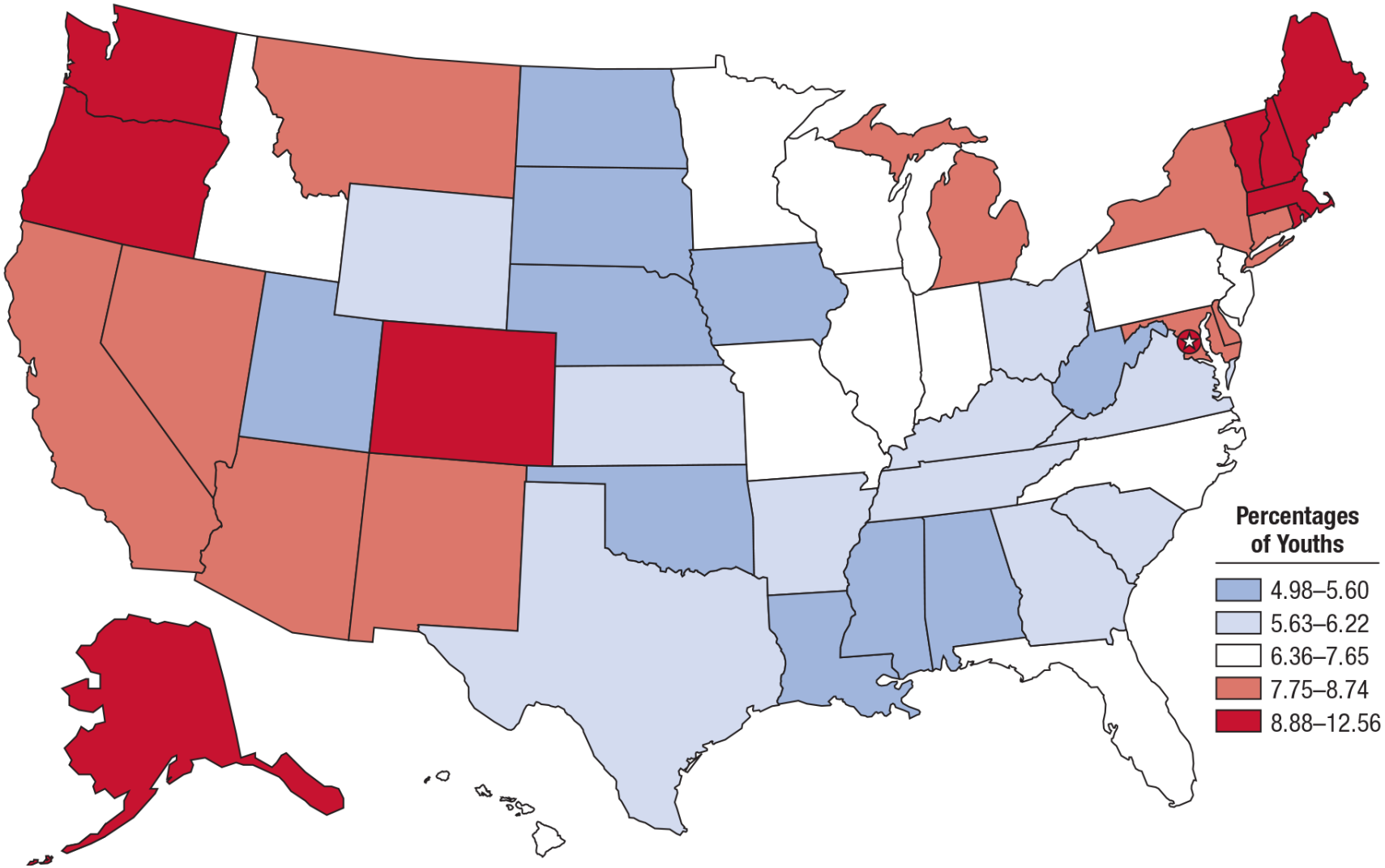
Past Month Illicit Drug Use among Persons Aged 12 or Older: 2013



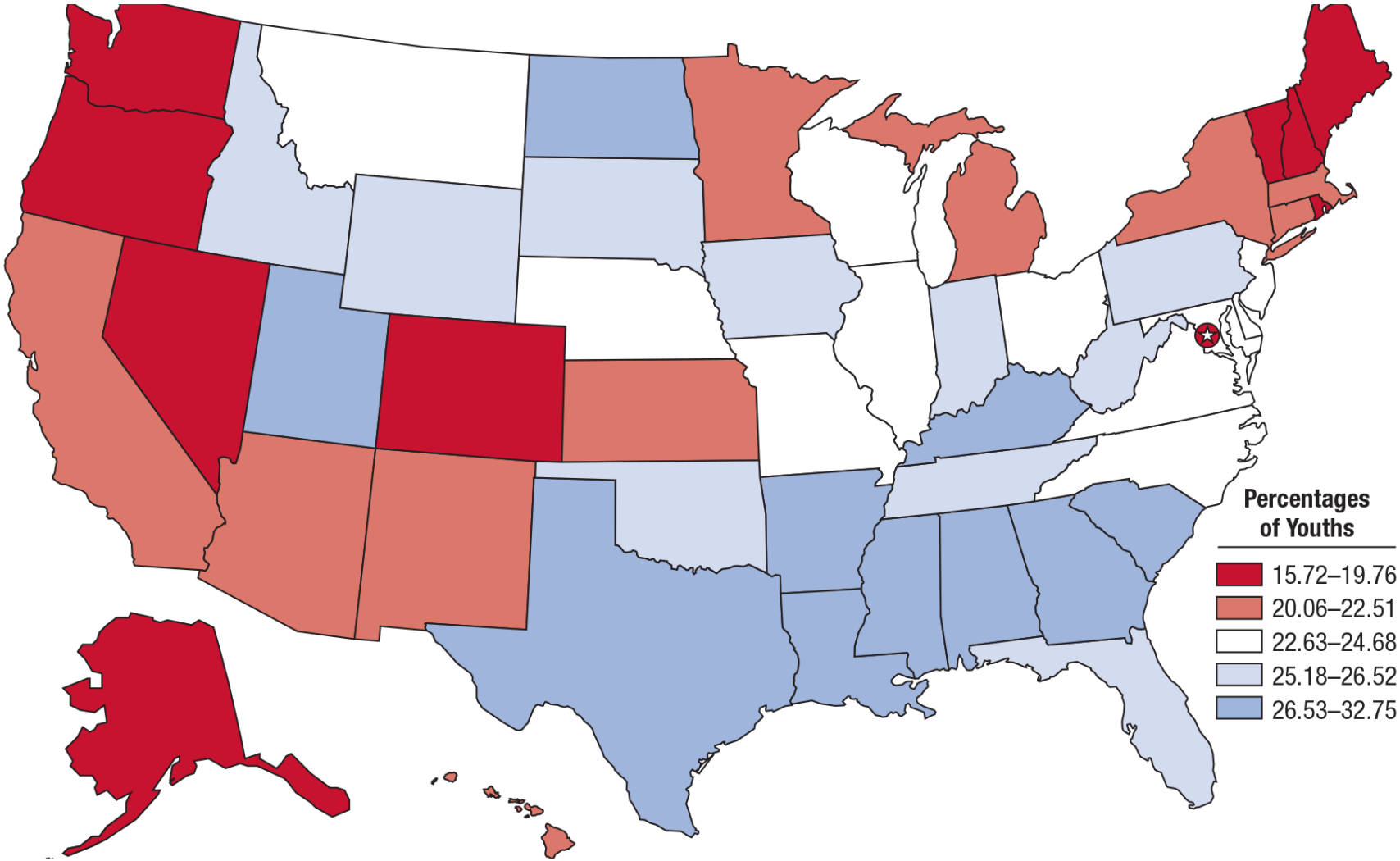
The most popular "illicit" drug

http://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.htm

Marijuana use in the past month among youths aged 12 to 17, by state: percentages, annual averages, 2013-2014; SAMHSA NSDUH



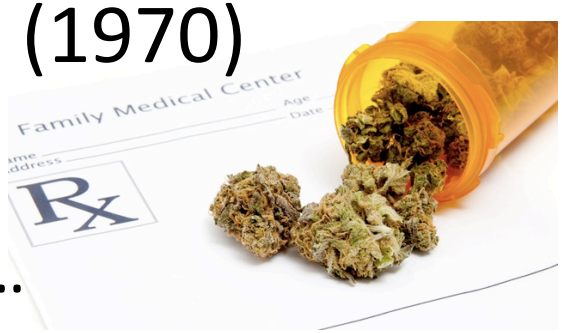
Perceptions of great risk of harm from smoking marijuana once a month among youths aged 12 to 17, by state: percentages, annual averages, 2013-2014; SAMHSA NSDUH



- **Harry Anslinger**, first Commissioner of Narcotics, Bureau of Narcotics
- "Those who are habitually accustomed to use of the drug are said to develop a ***delirious rage*** after its administration, during which they are temporarily, at least, irresponsible and liable to commit ***violent crimes***…"

A history of demonization

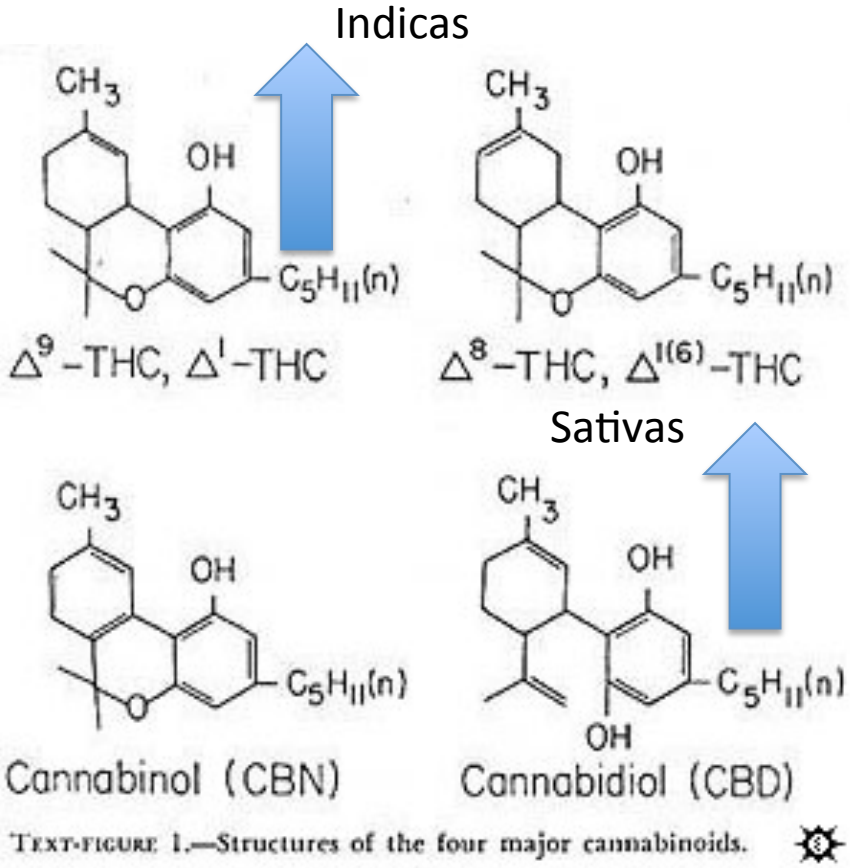
Controlled Substances Act (1970)



- The drug or other substance…
  1. …has a high potential for abuse
  2. …has no currently accepted medical use
- There is a lack of accepted safety for use of the drug…under medical supervision…

Marijuana is still a Schedule I substance

Cannabis contains cannabinoids



TEXT-FIGURE 1.—Structures of the four major cannabinoids.

- More than 60!
- Concentrated in resin
- Lots of differences, depending on strain, other factors…

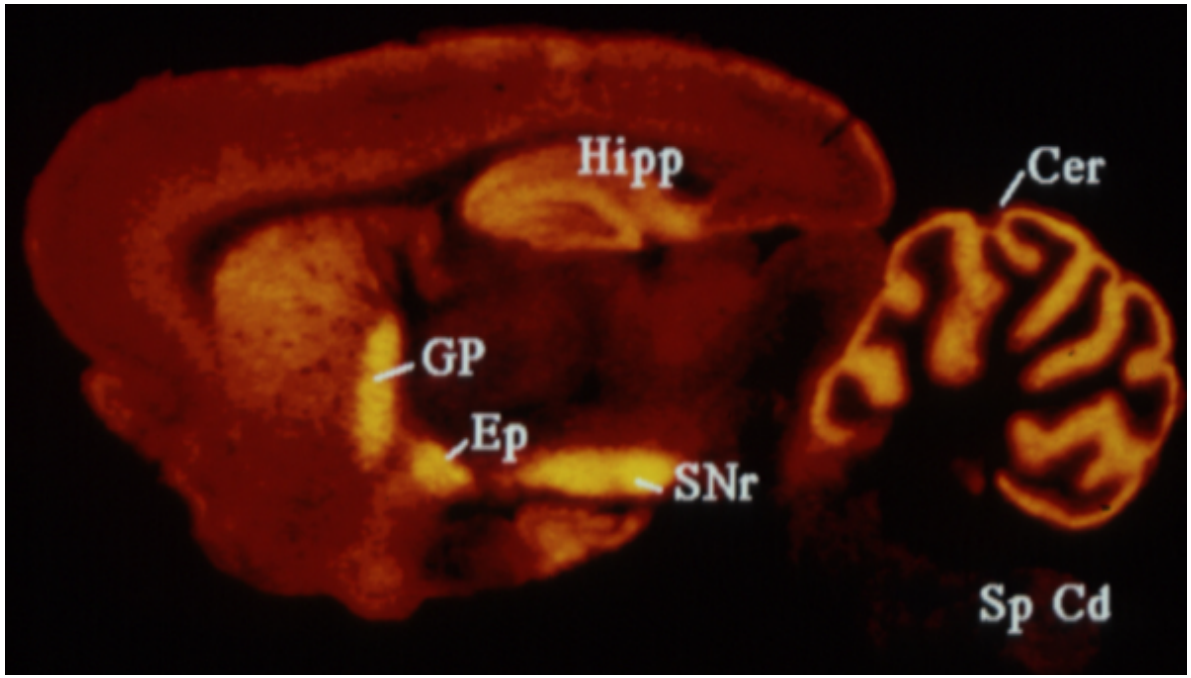
Method of drug administration matters

Burning vaporizes cannabinoids, which reach the brain in seconds.
Oral administration delivers less THC, CBD, CBN, etc. more slowly…

Marijuana is smoked…and eaten

"I strained to remember where I was or even what I was wearing, touching my green corduroy jeans and staring at the exposed-brick wall. As my paranoia deepened, I became convinced that I had died and no one was telling me…" New York Times, 6/3/13

Cannabinoids act at cannabinoid receptors: CB1 and CB2



(*Herkenham et al. (1991) J. Neurosci. 11: 563*)

<u>CB1 Receptors</u>

Abundant!

Cerebellum

Basal ganglia

Hippocampus

Brainstem

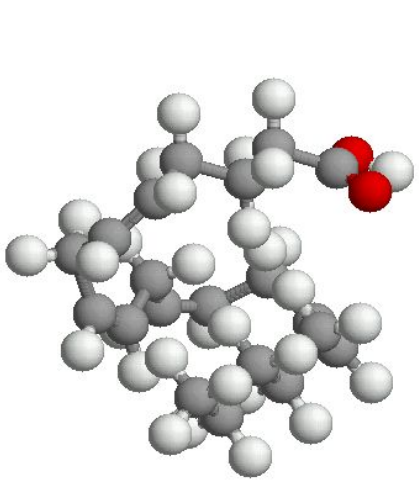
Spinal cord

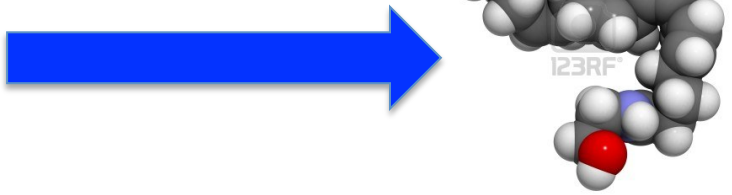
Neocortex

CNS expression in areas important for motor coordination, memory, pain, nausea, decision making…

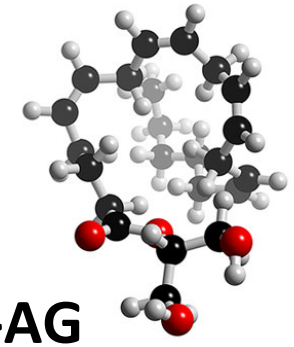
Endogenous cannabinoid neurotransmitters

If we have receptors for cannabinoids like THC, why are they there? What neurotransmitters act at these endogenous receptors..?





Anandamide



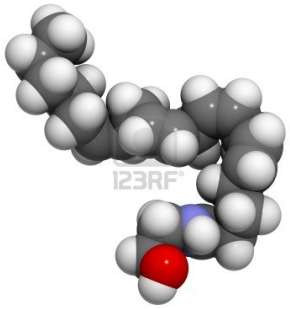
2-AG

Derived from arachidonic acid,
a fatty acid found in membranes

Anxiety: Genetic protection?

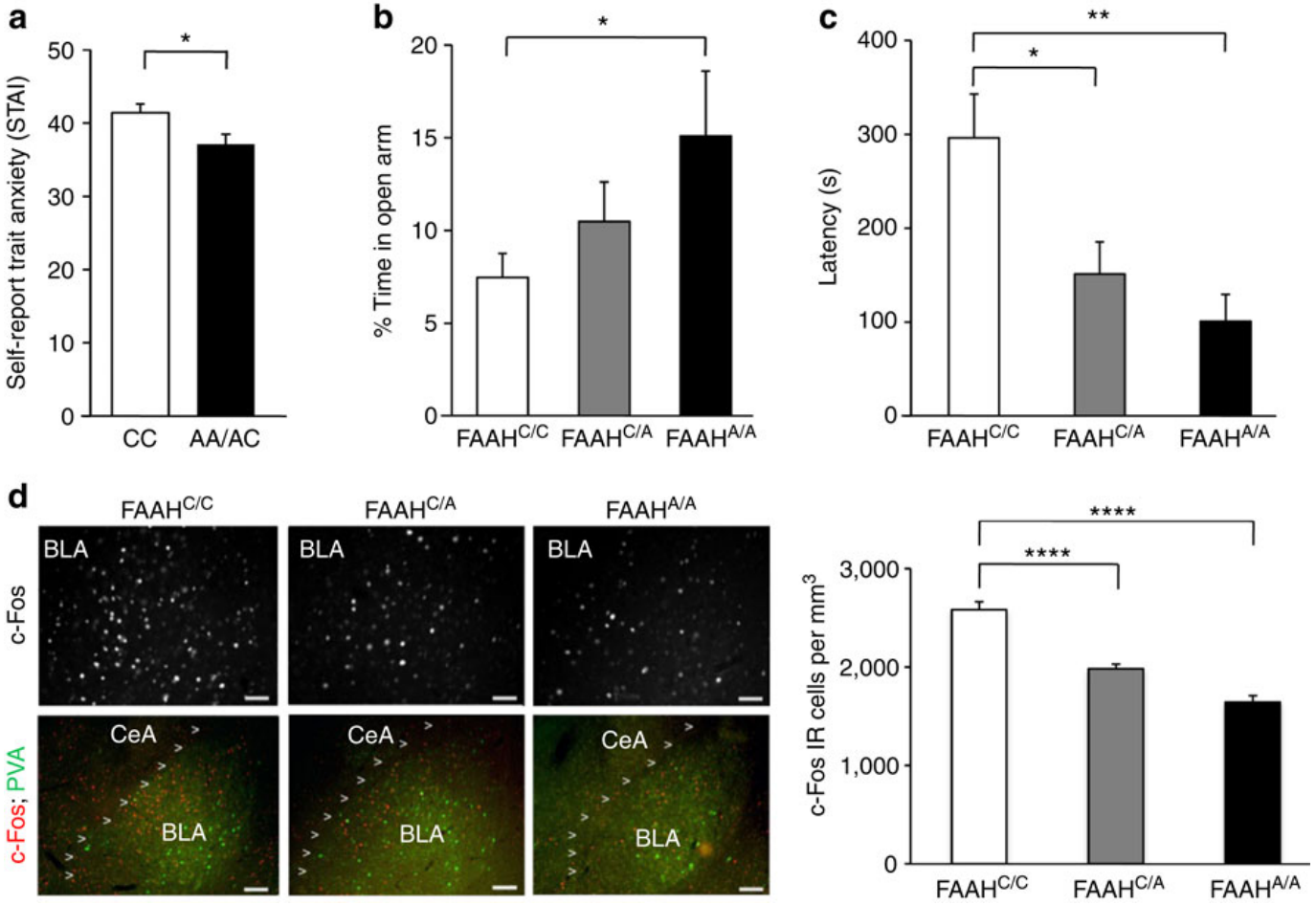
Decreased anxiety in humans and mice with FAAH C385A

Anandamide



Breakdown by FAAH; several Forms (A, C)

A less common; Less effective at breakdown

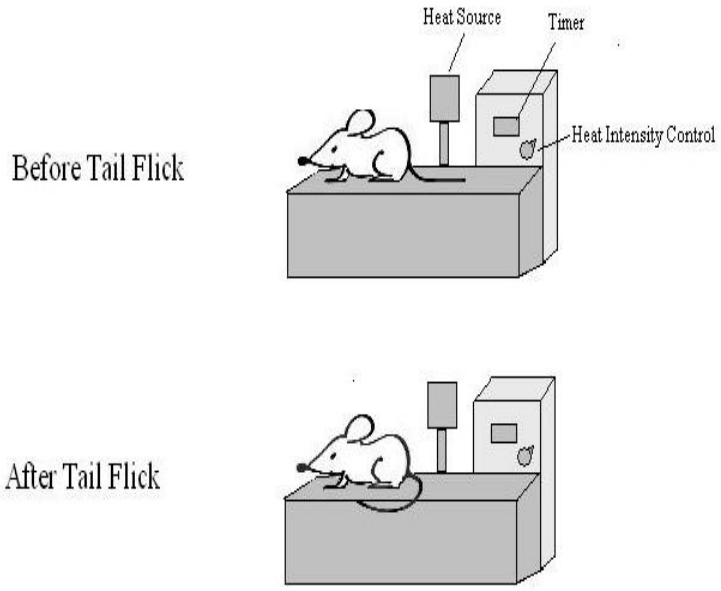


FAAH genetic variation enhances fronto-amygdala function in mouse and human, Nature Communications, Iva Dincheva et al (2015)

Cannabinoids reduce pain

A large body of literature indicates that cannabinoids suppress behavioral responses to acute and persistent noxious stimulation…
(Walker JM, Hohmann AG, 2005)

Co-administration of cannabinoids and opiates allows for pain relief with a lower opiate dose!
(e.g., Wilson AR, Maher L, Morgan MM, 2008)



More therapeutic effects

- **Appetite stimulation**

  (e.g., Foltin, 1988; Williams, 1988)

  Why is this therapeutic?

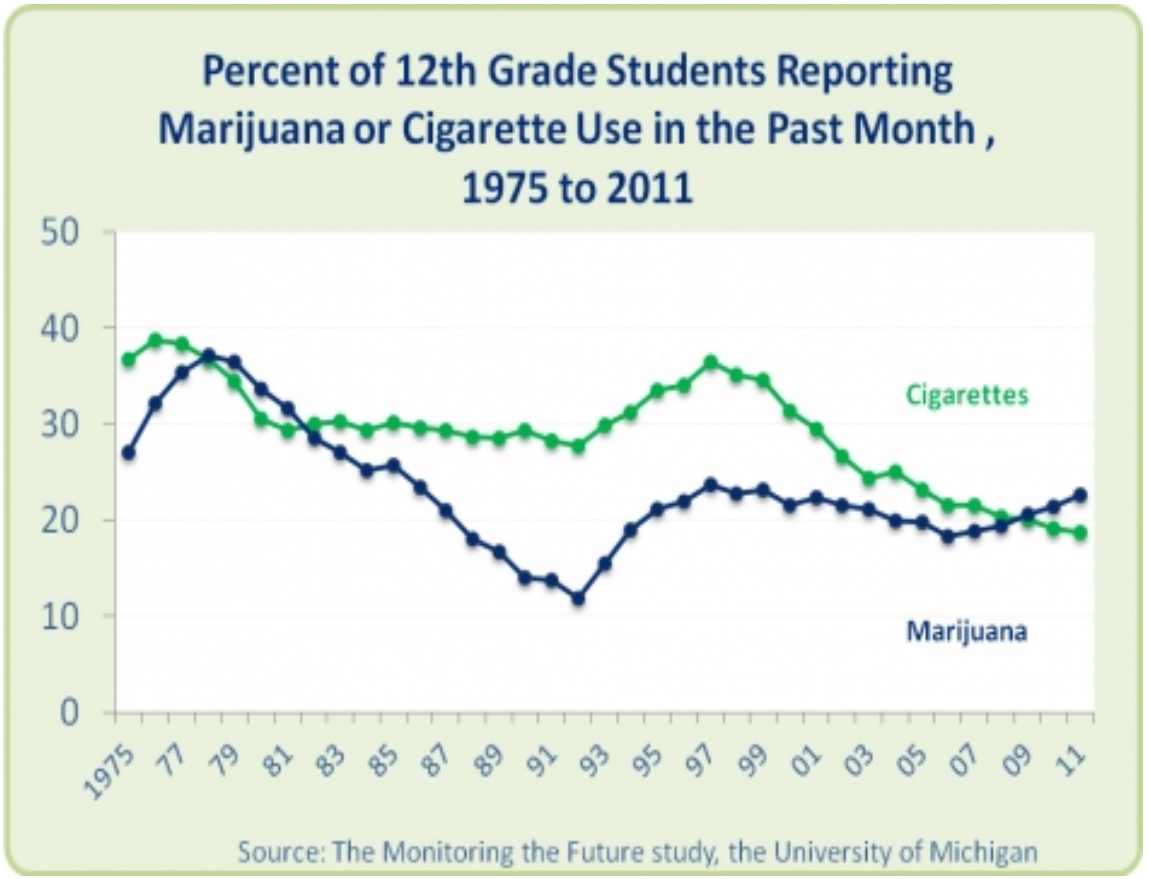
- **Nausea relief**

  (e.g., studies referenced by the National Cancer Institute at cancer.gov; though chronic use linked to hyperemesis syndrome; Soriano-Co M, 2010)

Marijuana impairs cognition, memory, motor coordination

- Deficits in verbal and spatial memory (e.g., Curran et al, 2002)
- With increasing cognitive demand, there is significantly reduced cognitive performance…
- Cannabis and alcohol both impair skills critical for driving (Sewell RA et al, 2009)
- Differential effects on socialization

Early chronic marijuana exposure linked to persistent cognitive deficits



http://www.drugabuse.gov/publications/topics-in-brief/marijuana

"…results suggest that adolescents are more vulnerable than adults to neurocognitive abnormalities associated with chronic heavy marijuana use…"

Schweinsburg et al (2008)

Risks of chronic adolescent use

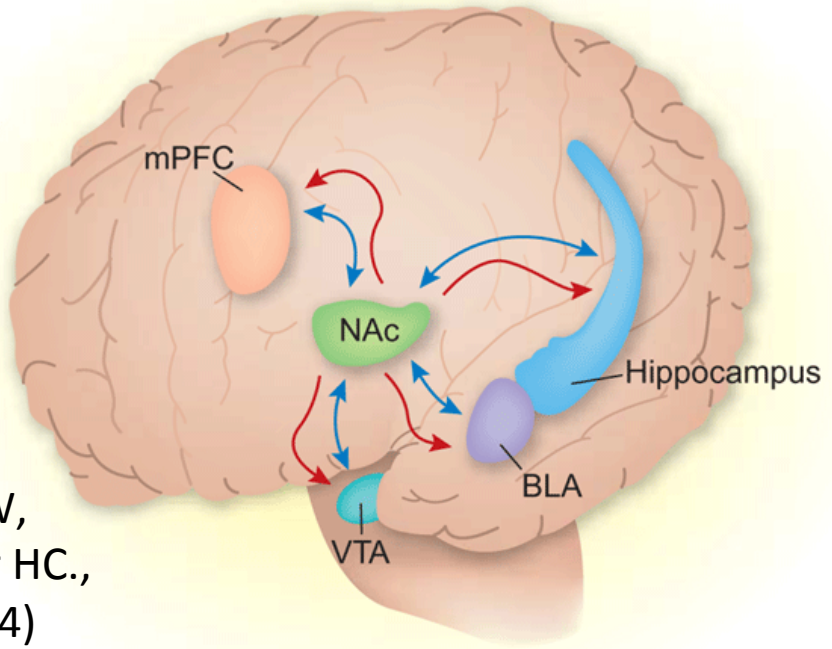
Volkow et al (2014), NEJM

- **Cognitive impairment**: IQ drop
- **Risk of dependence**: 9% of those who experiment; 1 in 6 of those who start using in adolescence, and 25 – 50% of those who smoke daily…
- **Changes in functional connectivity**
- **Increased risk of anxiety and depression, and schizophrenia/psychosis** in those with a preexisting genetic vulnerability (But from Volkow article: *"It is inherently difficult to establish causality in these types of studies because factors other than marijuana use may be directly associated with the risk of mental illness…")*
- **School performance**: "Early marijuana use is associated with impaired school performance…although reports of shared environmental factors… suggest that the relationship may be more complex…"

However…we're still learning

- **Cannabis use *is quantitatively associated* with nucleus accumbens and amygdala abnormalities in young adult recreational users.**

Nucleus accumbens, amygdala are part of motivational networks (what you seek, what you avoid…)

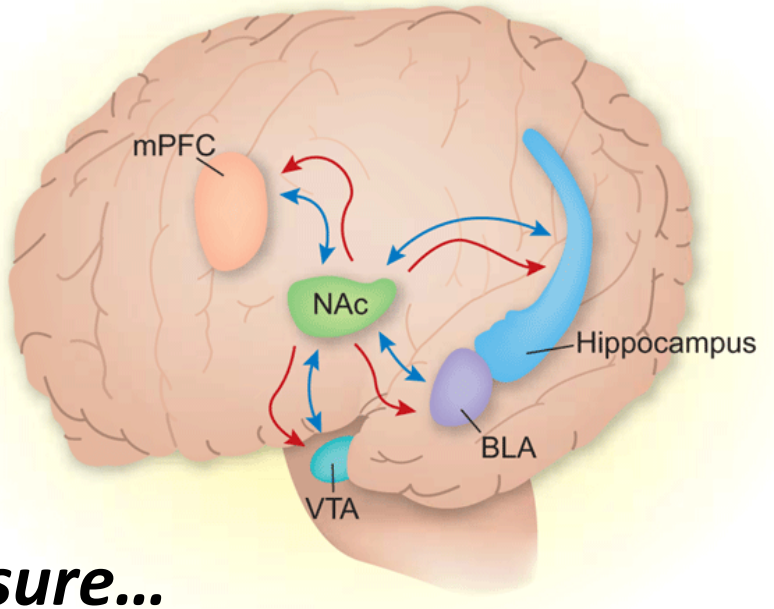


Gilman JM1, Kuster JK, Lee S, Lee MJ, Kim BW, Makris N, van der Kouwe A, Blood AJ, Breiter HC., J Neurosci. 2014 Apr 16;34(16):5529-38 (2014)

But wait - *which is it..?*

- **Daily Marijuana Use *Is Not Associated* with Brain Morphometric Measures in Adolescents or Adults**

Barbara J. Weiland, Rachel Thayer, Brendan E. Depue, Amithrupa Sabbineni, Angela Bryan, Kent E. Hutchison, The Journal of Neuroscience, 28 January 2015

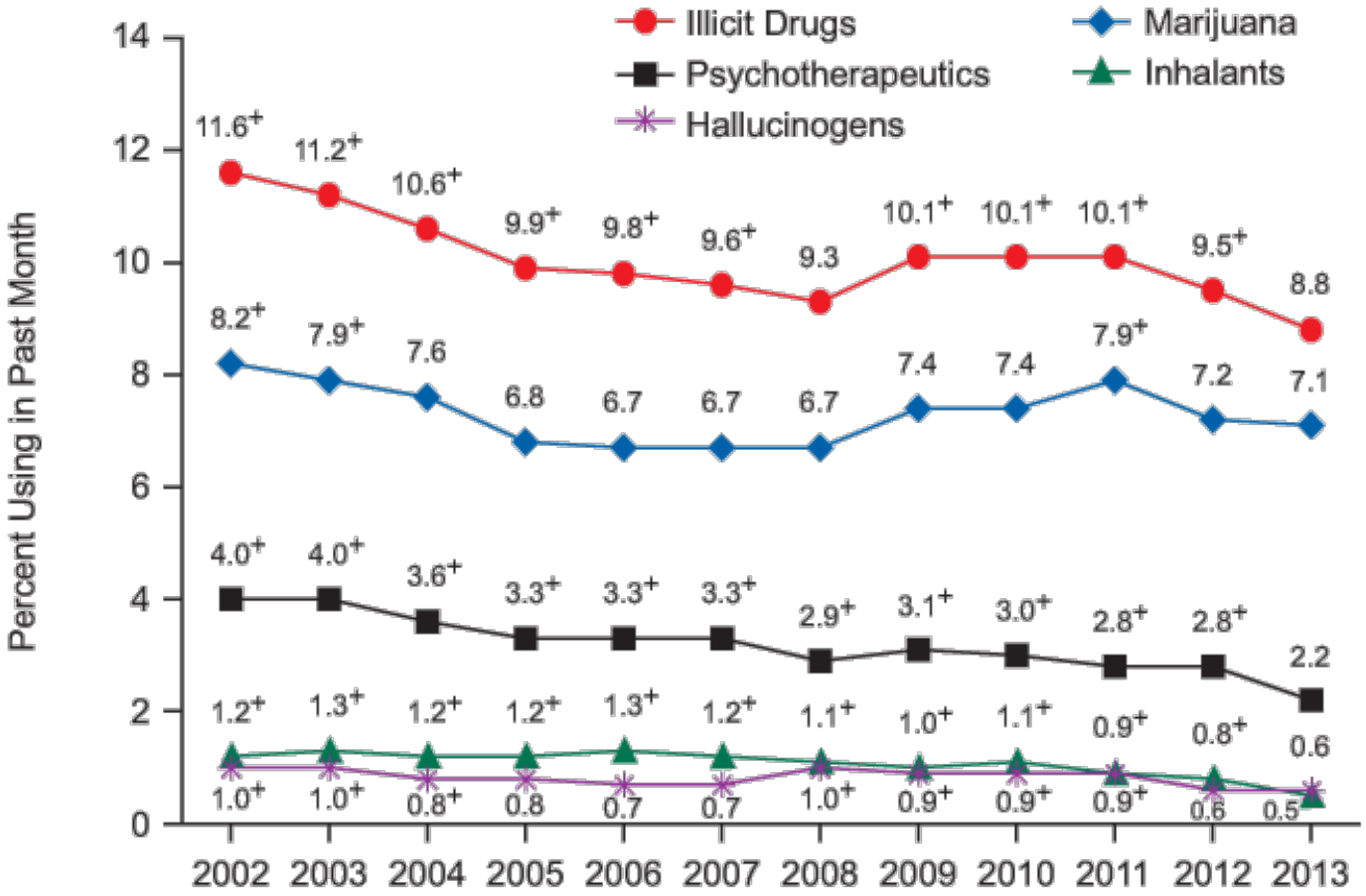


Same journal

Different research group

**** Controlled for alcohol exposure…***

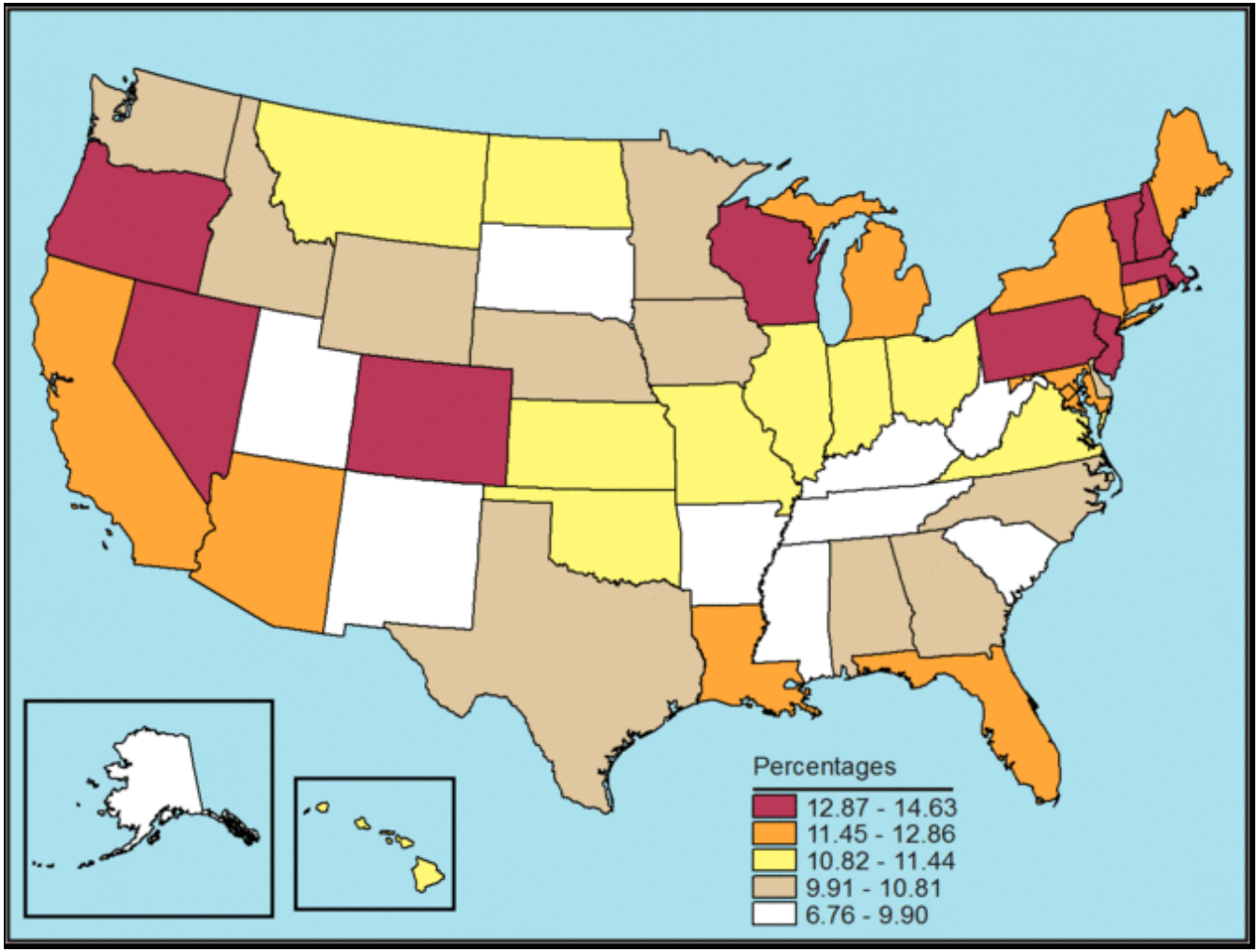
Past Month Illicit Drug Use



Youths Aged 12 to 17: 2002-2013

Substance Abuse and Mental Health Services Administration
National Survey on Drug Use and Health, 2013

Alcohol Use in the Past Month among Youths Aged 12 to 17, by State; SAMHSA NSDUH



Percentages, Annual Averages Based on 2013 and 2014 NSDUHs