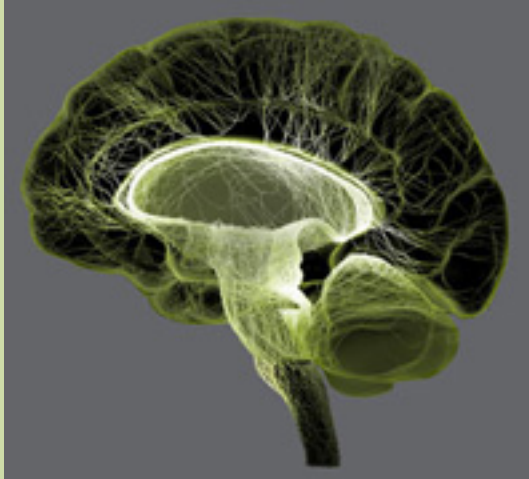
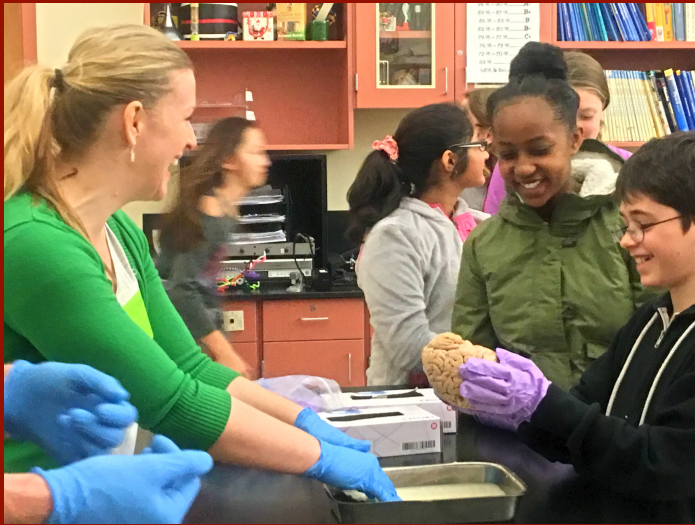


# Art, Pain & Cannabinoids



- **Bill Griesar, Ph.D.**
  - Neuroscience, WSU Vancouver
  - Psychology, Portland State University
  - Behavioral Neuroscience, OHSU
  - NW Noggin
- **Jeff Leake, M.F.A.**
  - Neuroscience, WSU Vancouver
  - NW Noggin
- **Ram Kandasamy**
  - Neuroscience, WSU Vancouver
  - NW Noggin
- **Cole Taylor Dawson**
  - Neuroscience, WSU Vancouver
  - NW Noggin

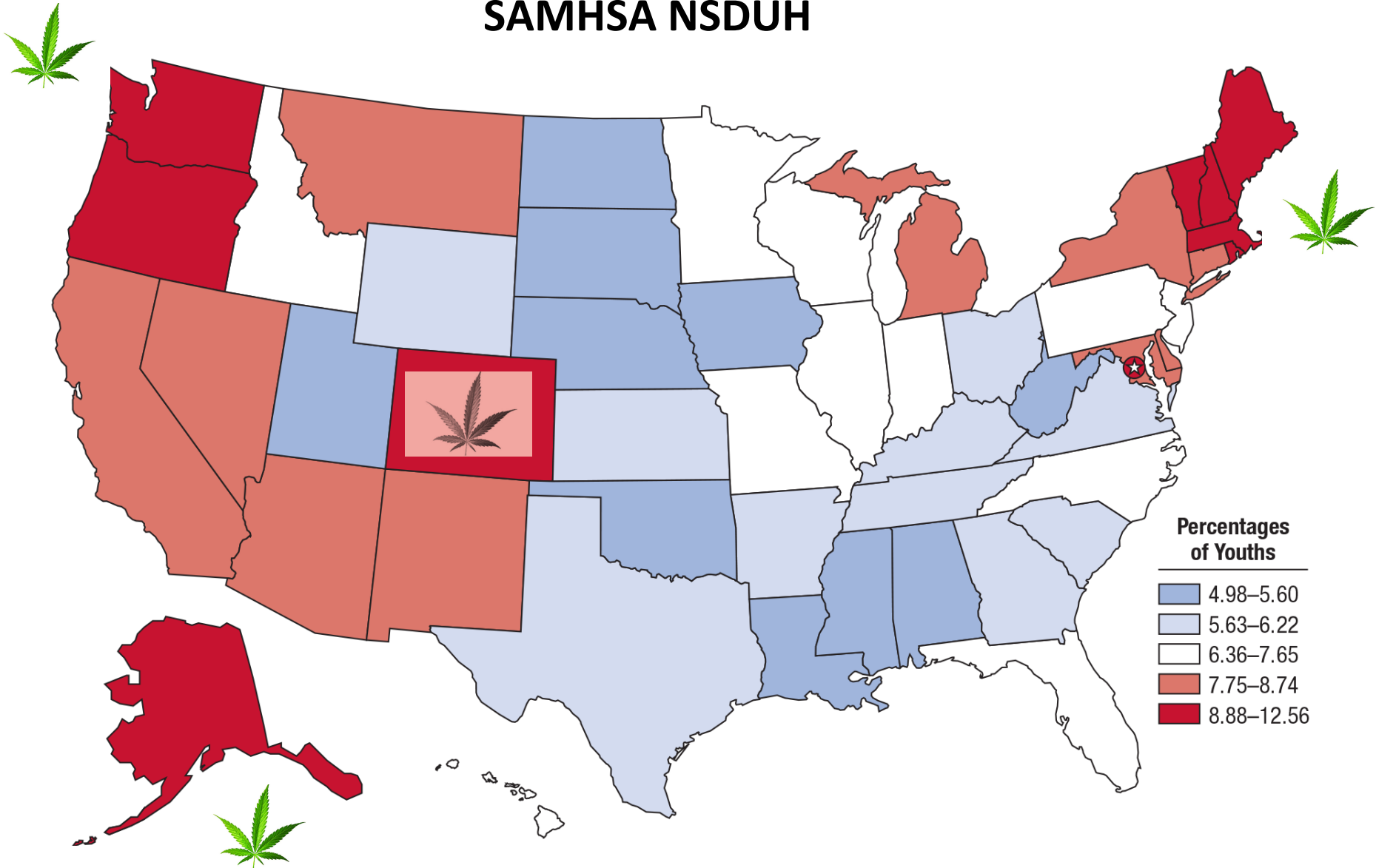
# nwnoggin.org



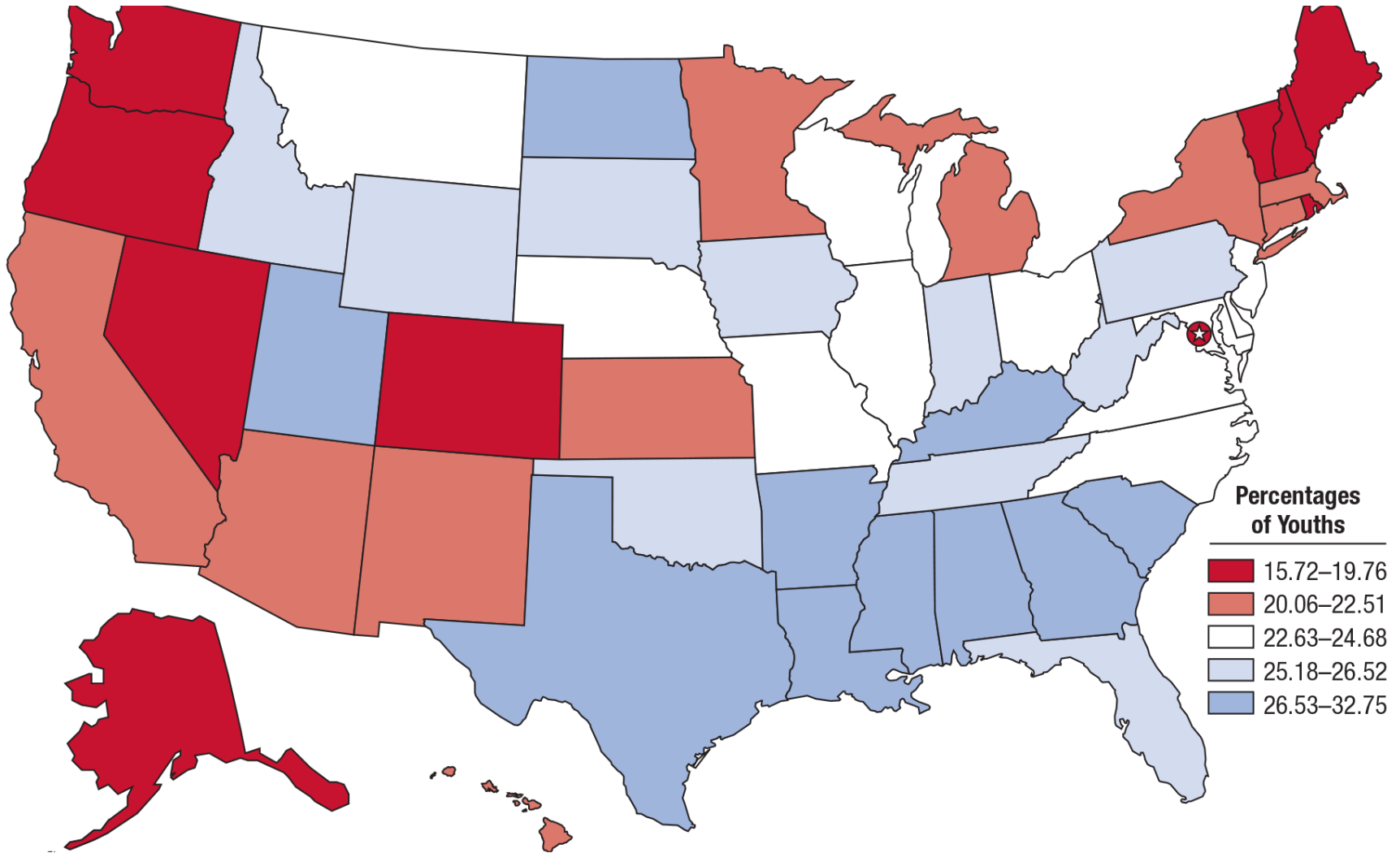
# We talk often about drugs



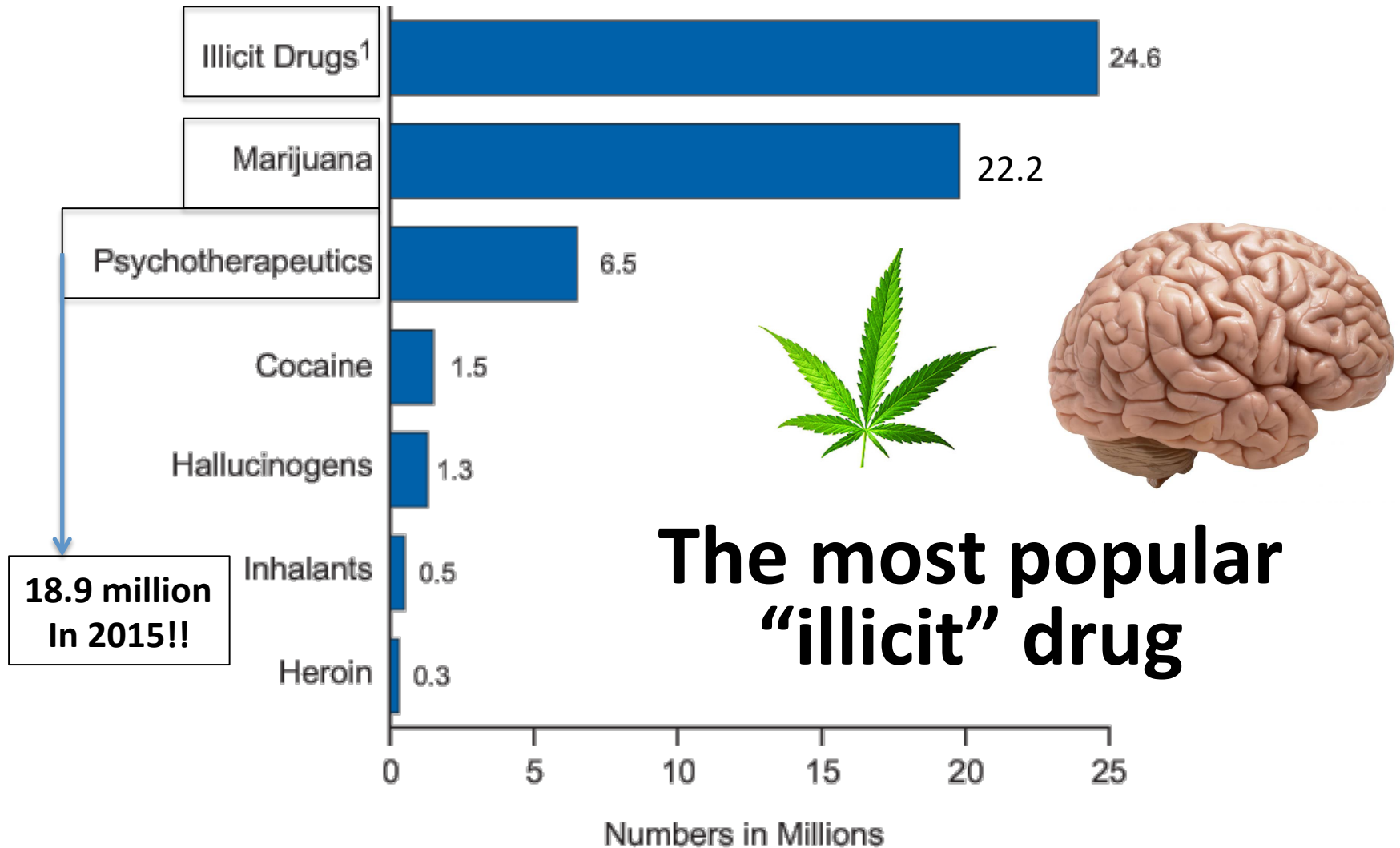
# Marijuana use in the past month among youths aged 12 to 17, by state: percentages, annual averages, 2013-2014; SAMHSA NSDUH



# 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



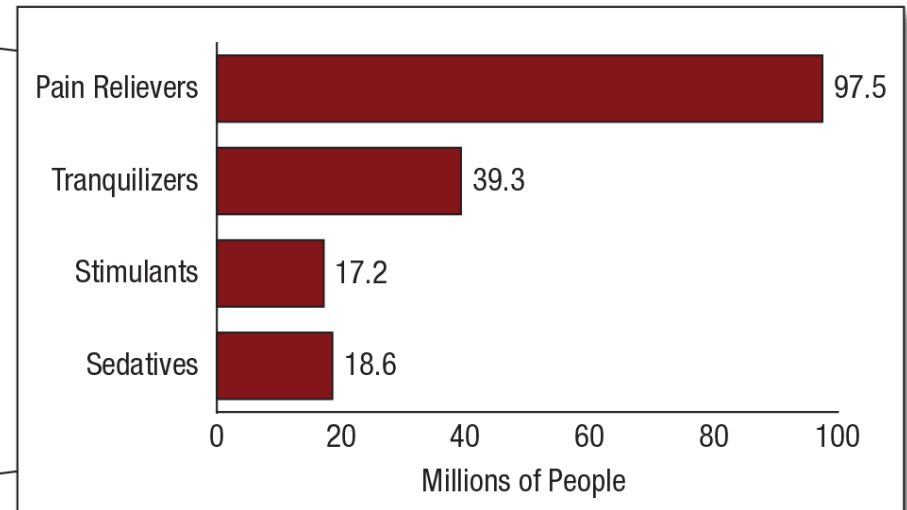
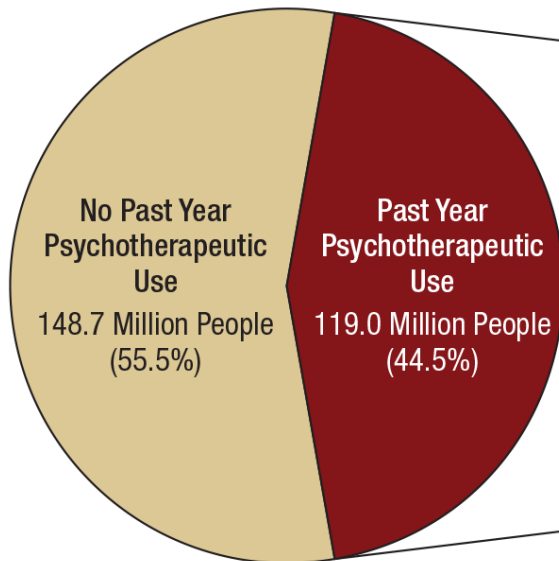
# Past Month Illicit Drug Use among Persons 12 or Older: 2014



SOURCE: Substance Abuse and Mental Health Services Administration, Health & Human Services (2015)  
<http://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.htm>

# NSDUH Report on Prescription Psychotherapeutics 2015

In 2015, **119.0 million Americans** aged 12 or older *used* prescription psychotherapeutic drugs in the past year, representing **44.5 percent** of the population. (SAMHSA)

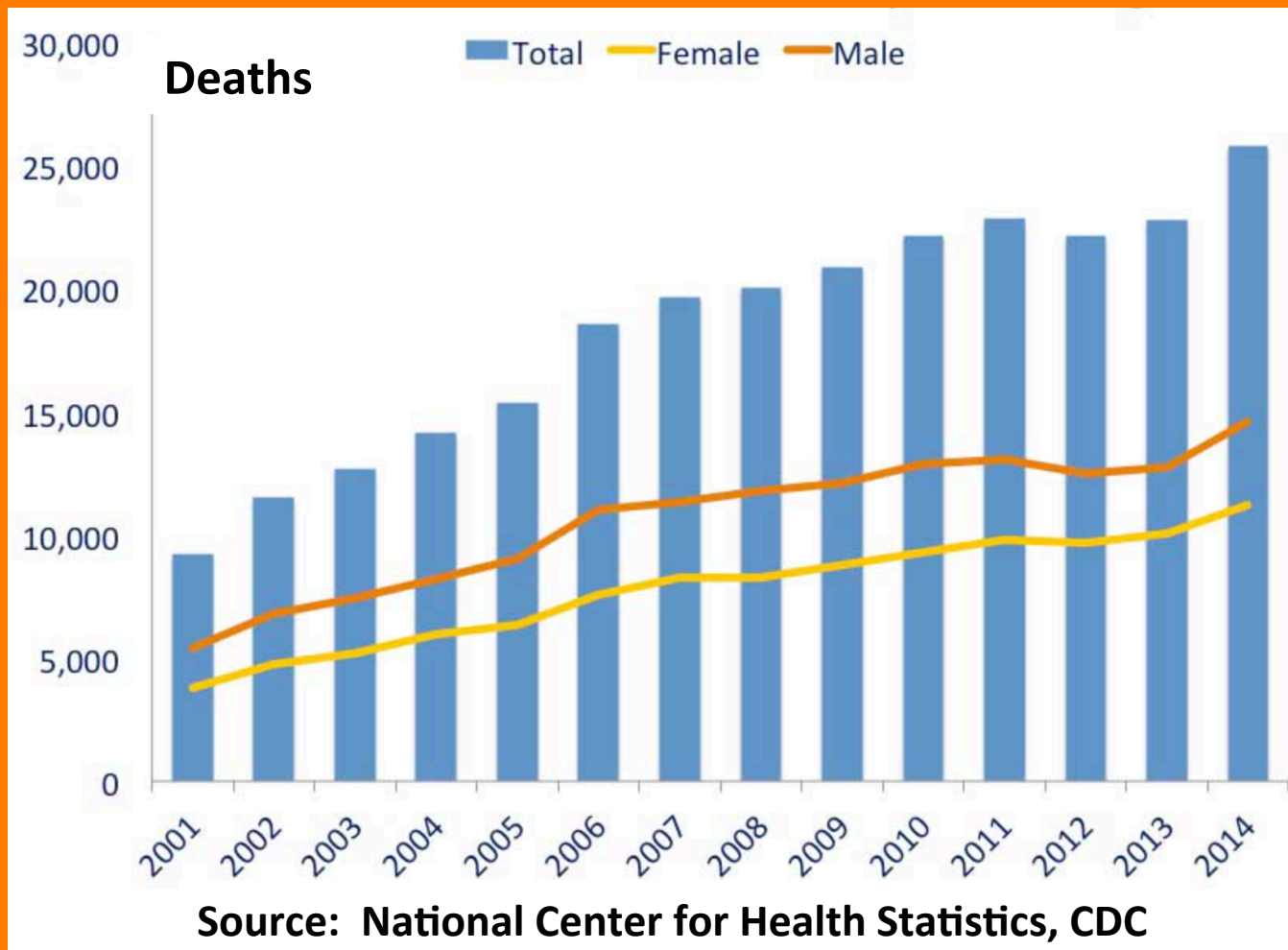


Report issued in September, 2016

# Opioids are addictive, and kill

“In 2014, more than 28,000 people died from opioid overdose, and at least half of those deaths involved a prescription opioid. Many more became addicted to prescription and illegal opioids.”

- NIH

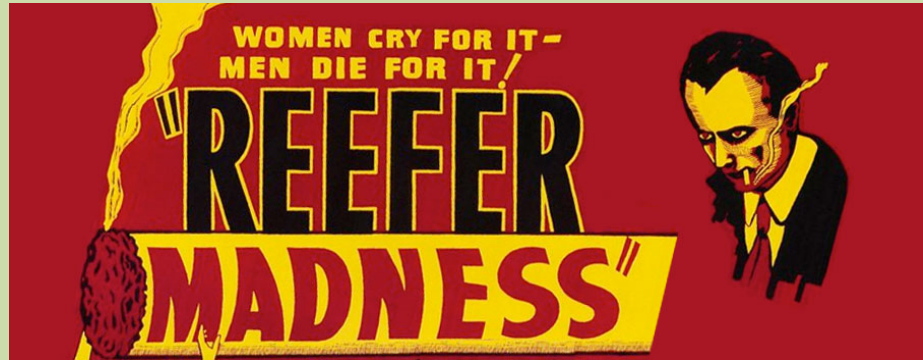


SOURCE: <https://medlineplus.gov/magazine/issues/fall16/articles/fall16pg12-14.html>





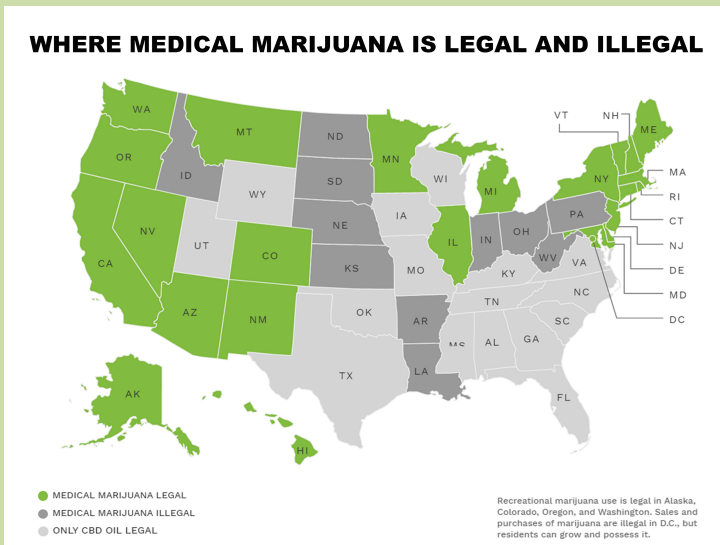
- Harry Anslinger, first Commissioner of Narcotics, Bureau of Narcotics
- *“Those who are habitually accustomed to use of the drug are said to develop a delirious rage after its administration, during which they are temporarily, at least, irresponsible and liable to commit violent crimes.”*



## A history of demonization



- **Jeff Sessions**, nominee for Attorney General, United States
- *“Good people don’t smoke marijuana...”*
- *“The KKK was OK until I found out they smoked pot...”*
  - *New York Times (11/17/16)*
  - [https://www.nytimes.com/2016/11/17/us/politics/specter-of-race-shadows-jeff-sessions-potential-trump-nominee-for-cabinet.html?mtrref=undefined&\\_r=1](https://www.nytimes.com/2016/11/17/us/politics/specter-of-race-shadows-jeff-sessions-potential-trump-nominee-for-cabinet.html?mtrref=undefined&_r=1)

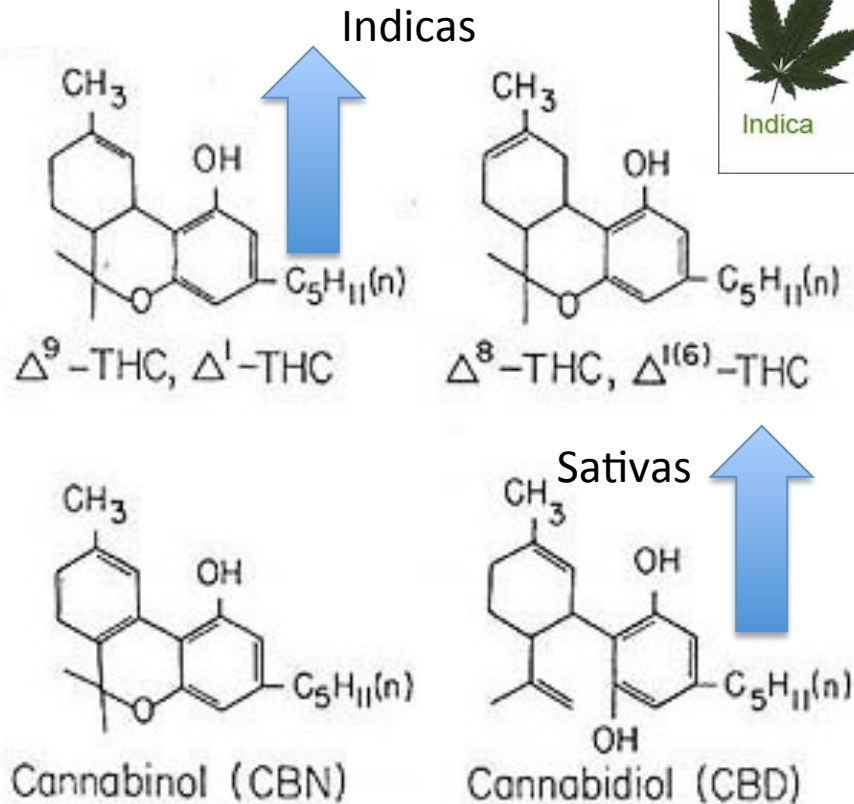


(SOURCE: Brookings Institution)


# A history of demonization

# Cannabis contains cannabinoids

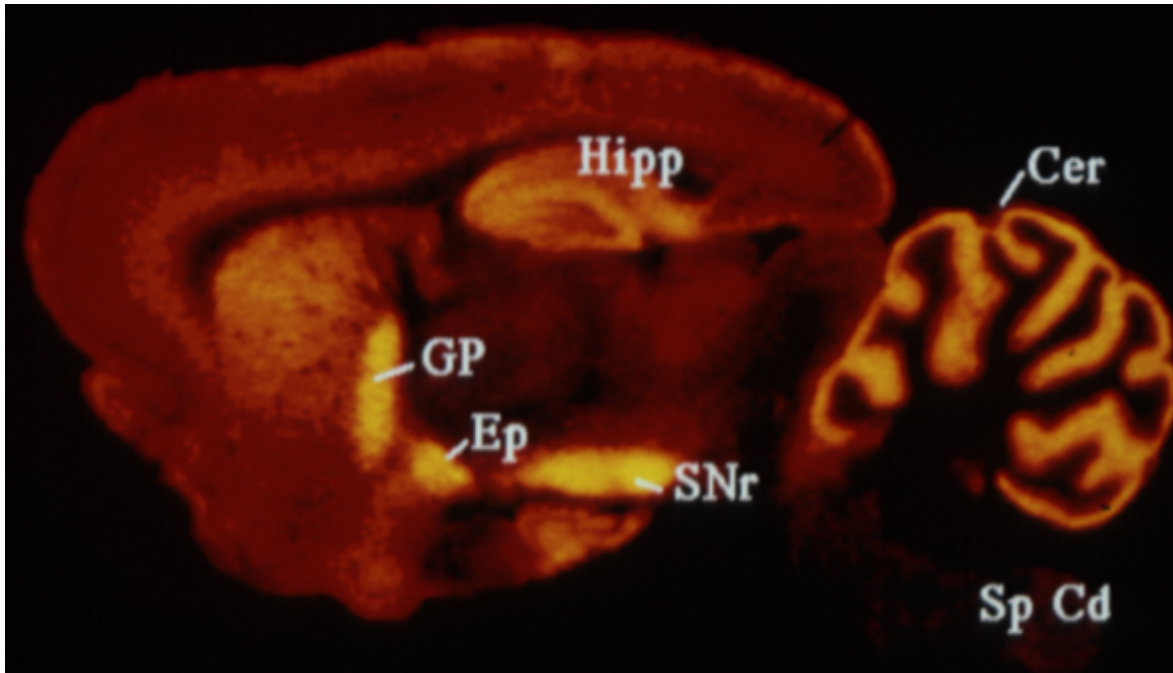
SOURCE: Cannabis, a complex plant: different compounds and different effects on individuals, Atakan (2012)



- More than 100!
- Concentrated in resin
- *Lots of variability*, depending on strain, other factors...

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

# Cannabinoids act at cannabinoid receptors: CB1 and CB2



## CB1 Receptors

*Abundant!*

Cerebellum

Basal ganglia

Hippocampus

Brainstem

Spinal cord

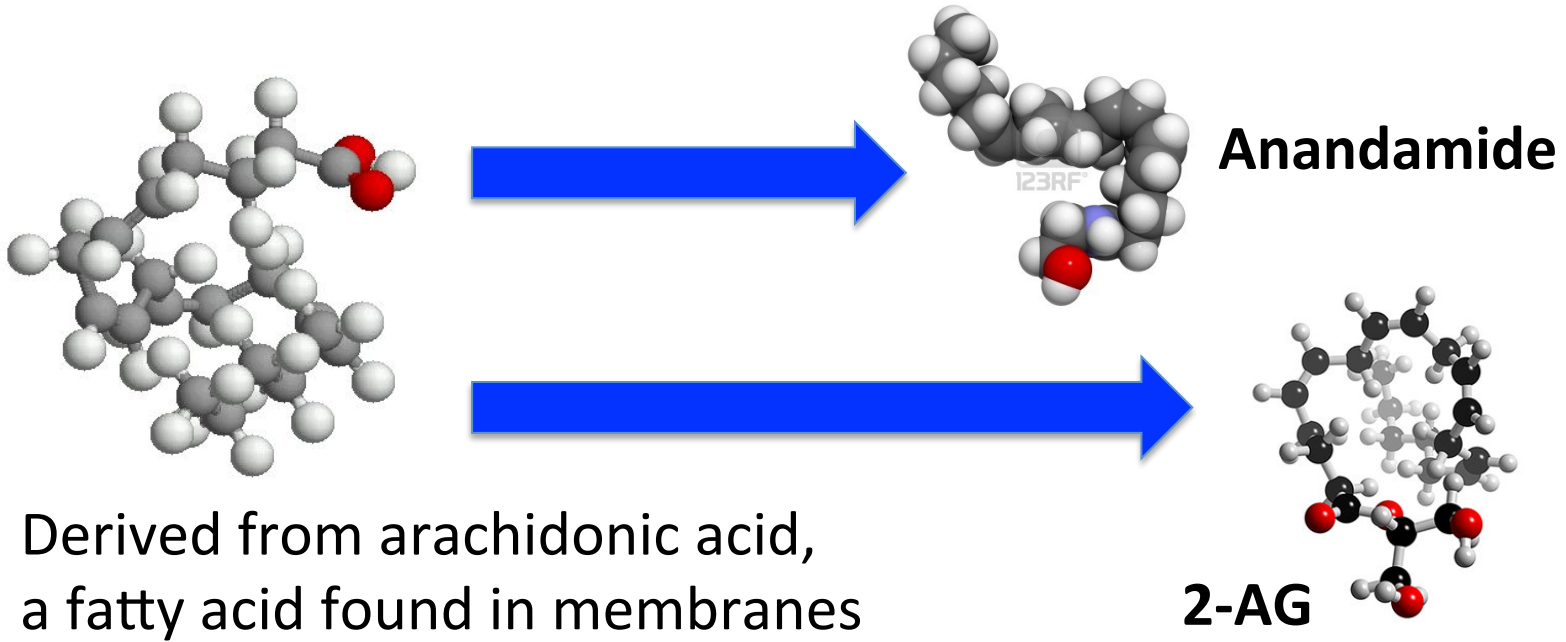
Neocortex

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

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

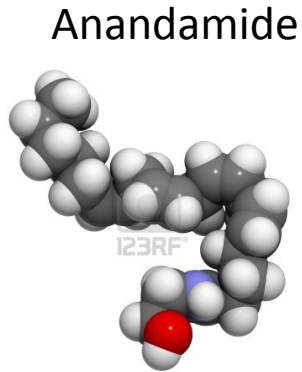
# Endogenous cannabinoid neurotransmitters

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



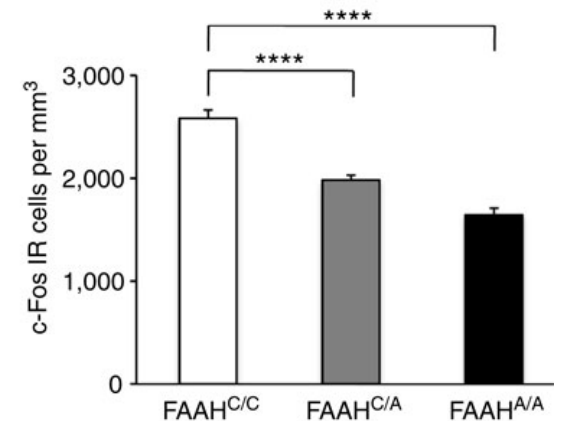
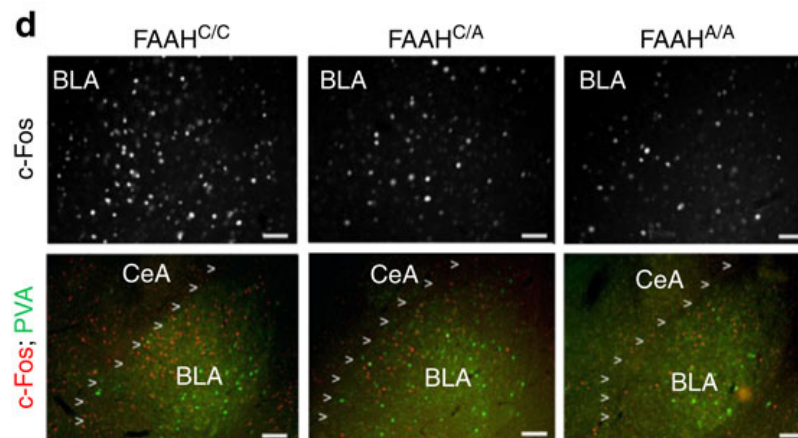
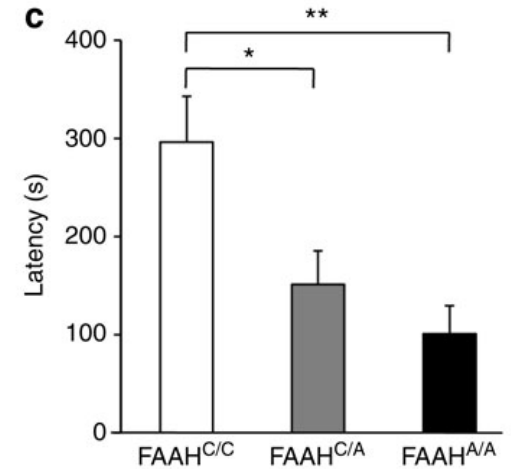
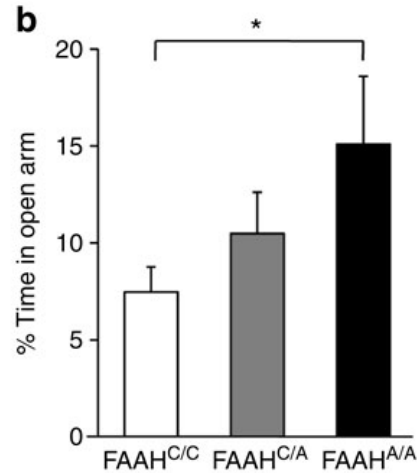
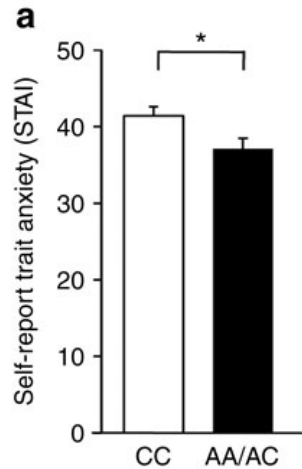
# Anxiety: Genetic protection?

Decreased anxiety in humans and mice with FAAH C385A



Breakdown by  
FAAH; several  
Forms (A, C)

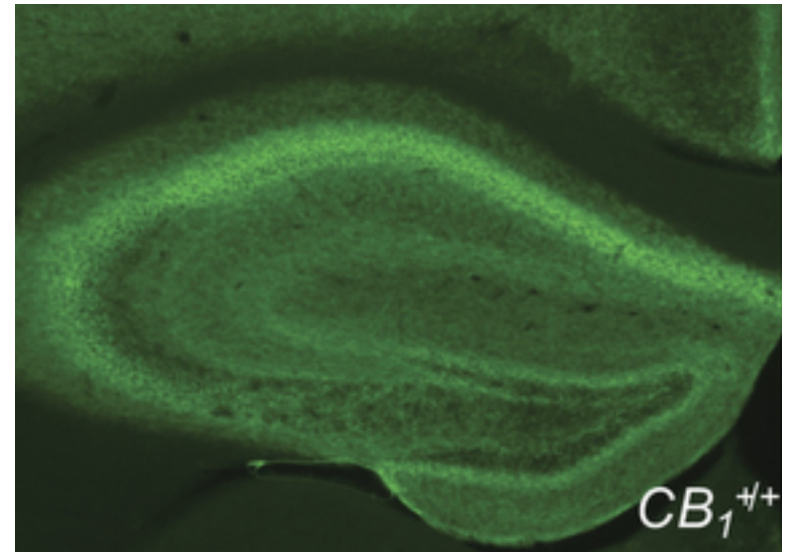
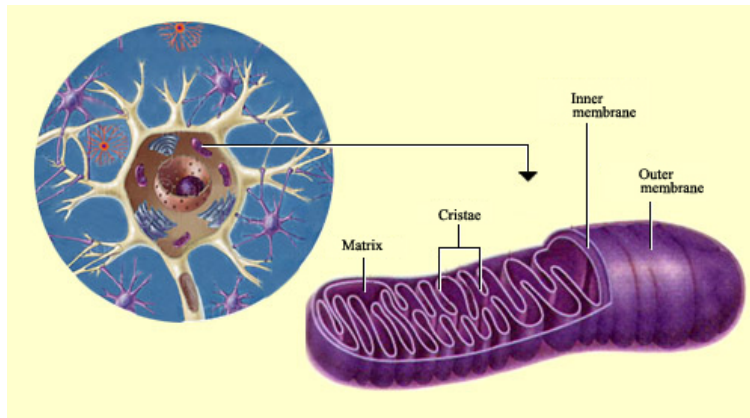
A less common;  
Less effective at  
breakdown



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

# A cannabinoid link between mitochondria and memory

Etienne Hebert-Chatelain, et al  
Nature (2016)



Cellular activity depends on mitochondria  
Mitochondria site of cellular respiration (ATP)  
Mitochondria have many CB1 receptors (mtCB1)  
Cannabinoid action at mtCB1 inhibits respiration  
Hippocampus starved of energy (less ATP)  
*A mechanism for amnesia..?*

# Risks of chronic adolescent use

Volkow et al (2014), NEJM

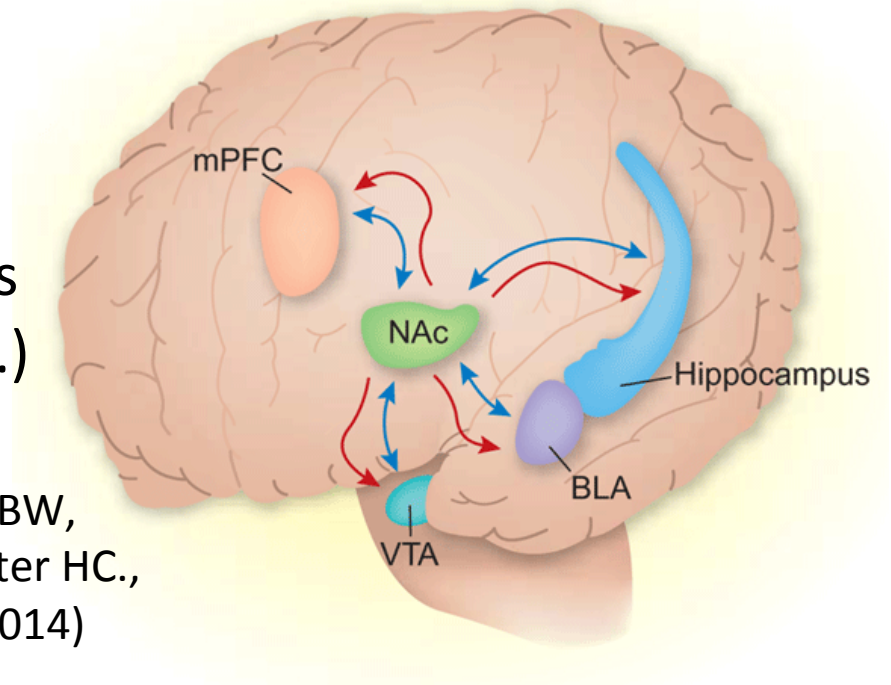
- **Cognitive impairment:** IQ drop
- **Risk of dependence:** 9% of those who experiment; 1 in 6 of those who start using in adolescence, and 25 – 50% of those who smoke daily...
- **Changes in functional connectivity**
- **Increased risk of anxiety and depression, and schizophrenia/psychosis** in those 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...***

