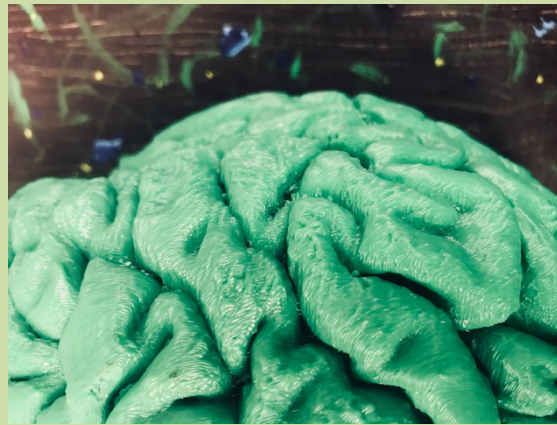
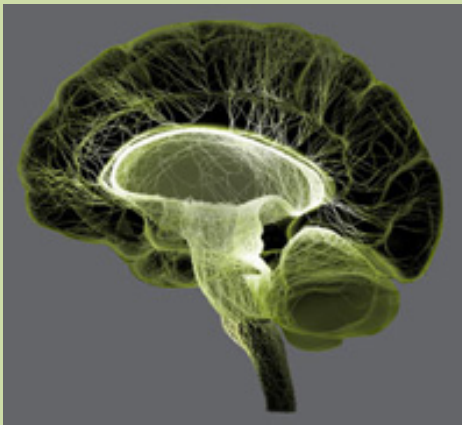


# Cannabis, Pain, Bias & Brain

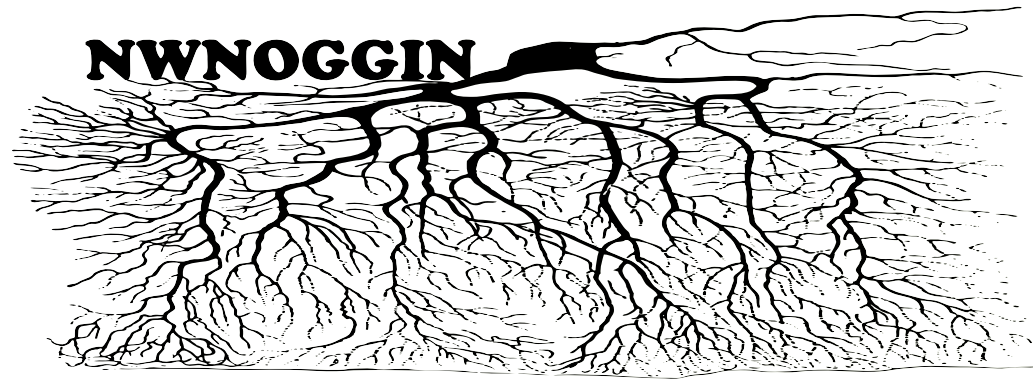


- **Bill Griesar, Ph.D.**
- **Jeff Leake, MFA**
  - Psychology, University Studies
    - **Portland State University**
  - Behavioral Neuroscience
    - **Oregon Health & Science University**
  - **NW Noggin, [nwnoggin.org](http://nwnoggin.org)**



Joos van Craesbeeck  
"The Smoker" 1635

# NWNOGGIN

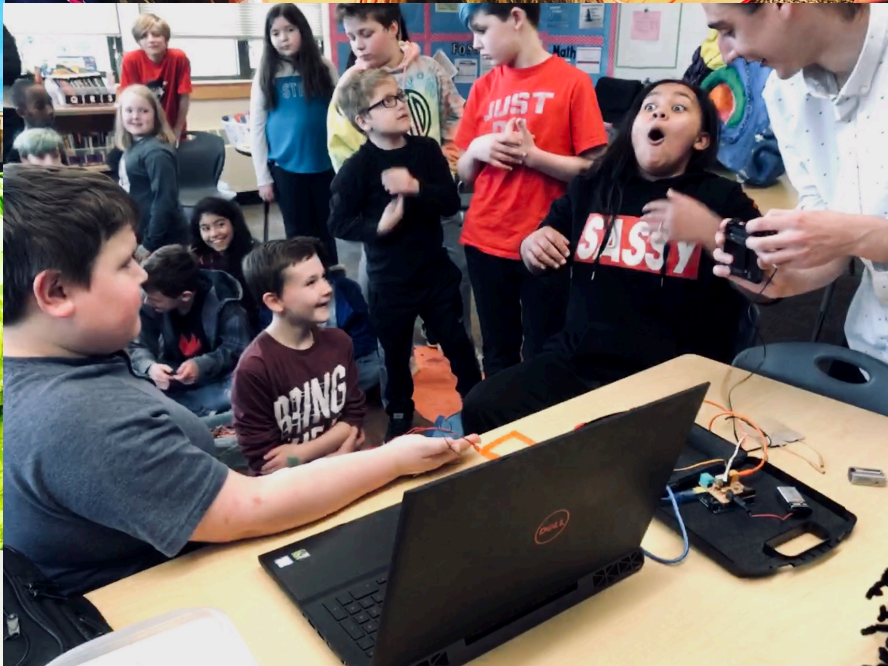


[nwnoggin.org](http://nwnoggin.org)

Arts integrated neuroscience  
outreach for K-12 & community



# TODAY @ Ardenwald Elementary!



Sleep  
Anxiety  
Depression  
ADHD  
Autism  
Development  
Perception  
Drugs  
Memory  
Language  
Bias

*What you do  
has relevance  
GO PLACES*





**We all pay for research**



More support  
Greater understanding  
Less confirmation bias  
Increased participation  
New ideas, directions  
FUN!

**Connections matter**

# BUILD NEW CONNECTIONS

*Oh the places you'll go!*



- **Academic priority K-12, urban/rural communities, tribal majority schools**
  - Not always well-funded or valued, often ignored, subjected to standardized testing that primarily benefits others. Complex brain development underway, unacknowledged diversity, prevalence of mental health issues ...
- **Homeless youth (p:ear), incarcerated youth (MacLaren Correctional Facility)**
  - *“It’s like people see me as an object, not as a human being”*
- **Young graduate researchers, undergraduates (PSU, OHSU, PNCA,...)**
  - *How does my research relate to the world? How can I explain it?*
  - *Where can I go from here? How do I connect kids from K-12 schools?*
- **Artists: Painters, Dancers, Storytellers, Musicians**
  - *How does my work relate to other fields? How do I connect with new audiences?*
  - *How is my practice influenced and enriched by discoveries about the brain?*
- **Area businesses (BioGift, Intel, Velo Cult, Retirement homes, Hospitals)**
  - *How can we better connect with everyone in our community?*
- **Members of the public**
  - *Why are my taxes spent on research? Art? What are we discovering? Making?*

# We get *many* questions about marijuana from students & public!

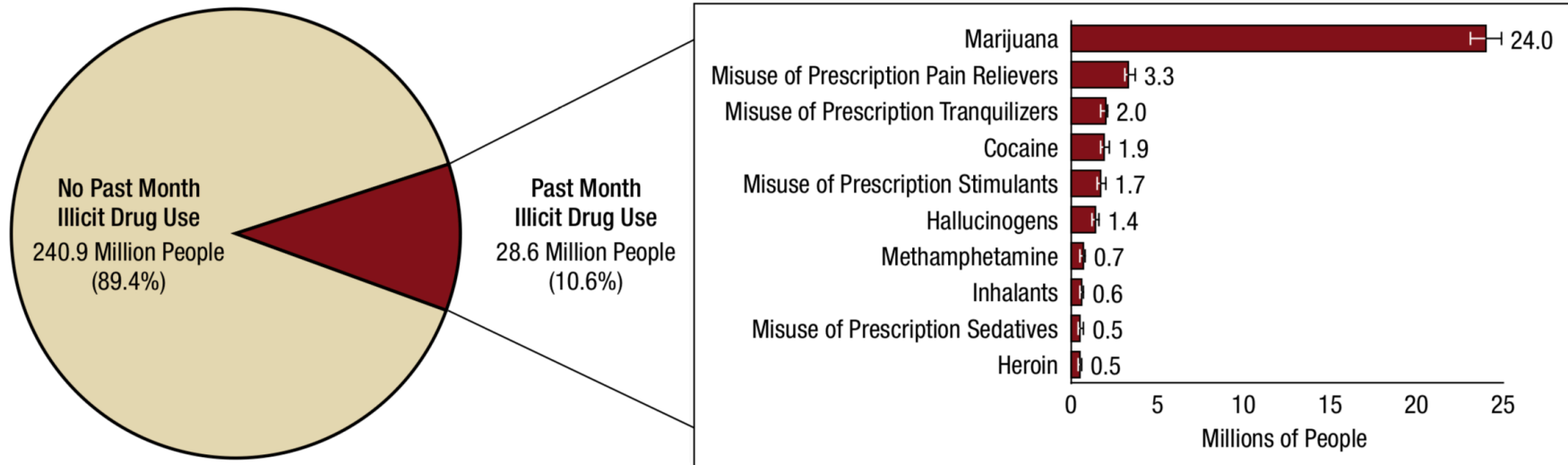




# Marijuana: the most commonly used “illicit” drug



Figure 15. Numbers of Past Month Illicit Drug Users among People Aged 12 or Older: 2016



Note: Estimated numbers of people refer to people aged 12 or older in the civilian, noninstitutionalized population in the United States. The numbers do not sum to the total population of the United States because the population for NSDUH does not include people aged 11 years old or younger, people with no fixed household address (e.g., homeless or transient people not in shelters), active-duty military personnel, and residents of institutional group quarters, such as correctional facilities, nursing homes, mental institutions, and long-term care hospitals.

Note: The estimated numbers of current users of different illicit drugs are not mutually exclusive because people could have used more than one type of illicit drug in the past month.

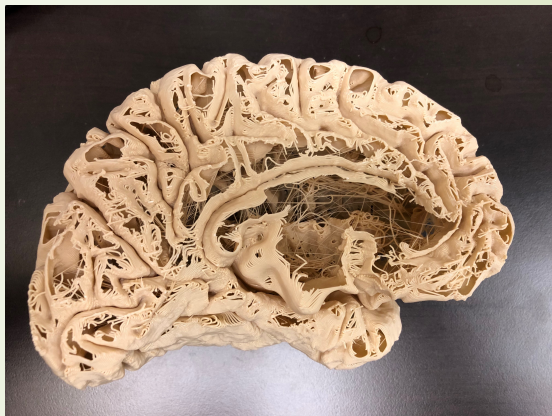
SOURCE: [Substance Abuse and Mental Health Services Administration, Health & Human Services \(2016\)](#)



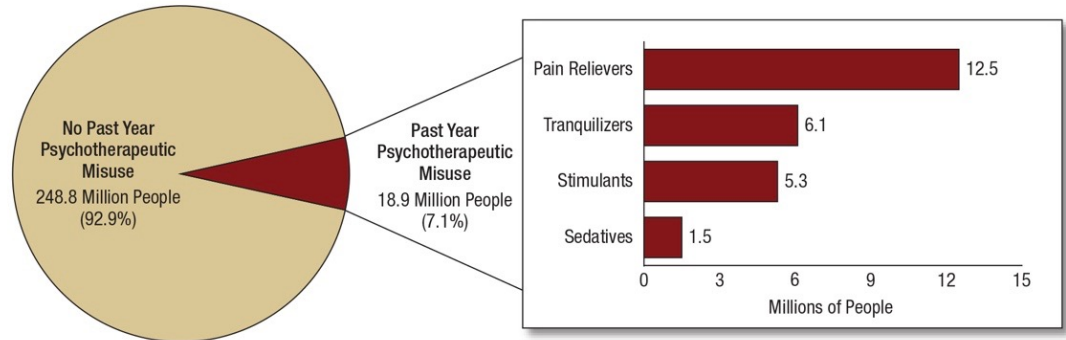
**SAMHSA: “Misuse of prescription psychotherapeutic drugs is second only to marijuana as the nation's most prevalent illicit drug use issue.”**

**According to the US government, everyone using marijuana is an illicit misuser**

# Misuse of Prescription Drugs



**Figure 6. Numbers of Past Year Prescription Psychotherapeutic Misusers among People Aged 12 or Older: 2015**



D

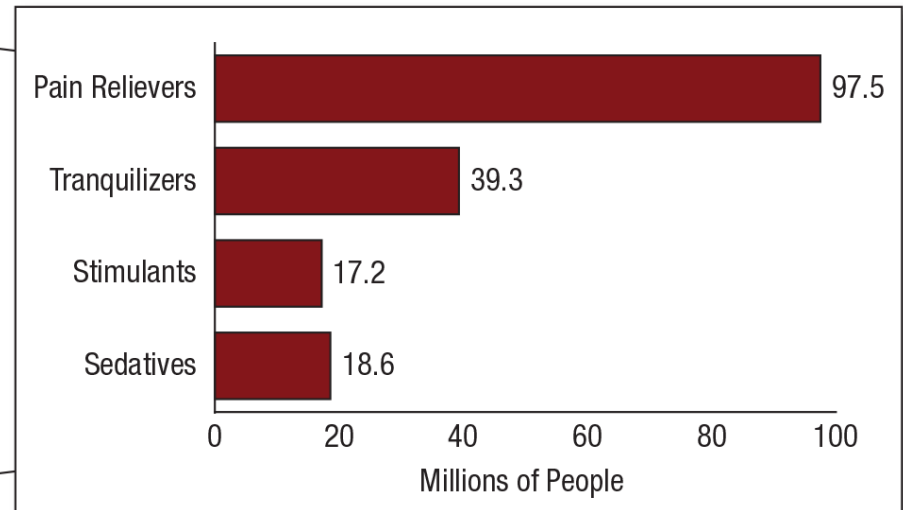
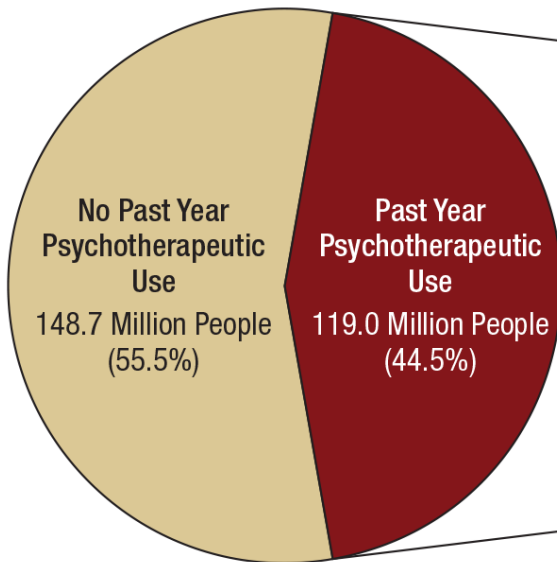
Note: Estimated numbers of people refer to people aged 12 or older in the civilian, noninstitutionalized population in the United States. The numbers do not sum to the total population of the United States because the population for NSDUH does not include people aged 11 years old or younger, people with no fixed household address (e.g., homeless or transient people not in shelters), active-duty military personnel, and residents of institutional group quarters, such as correctional facilities, nursing homes, mental institutions, and long-term care hospitals.

Note: The estimated numbers of past year misusers of different psychotherapeutics are not mutually exclusive because people could have misused more than one type of psychotherapeutic in the past year.

The Substance Abuse and Mental Health Services Administration (SAMHSA) estimates that **18.9 million Americans “misused” prescription drugs in 2015**, including opioids.

# 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 this population.** (SAMHSA)



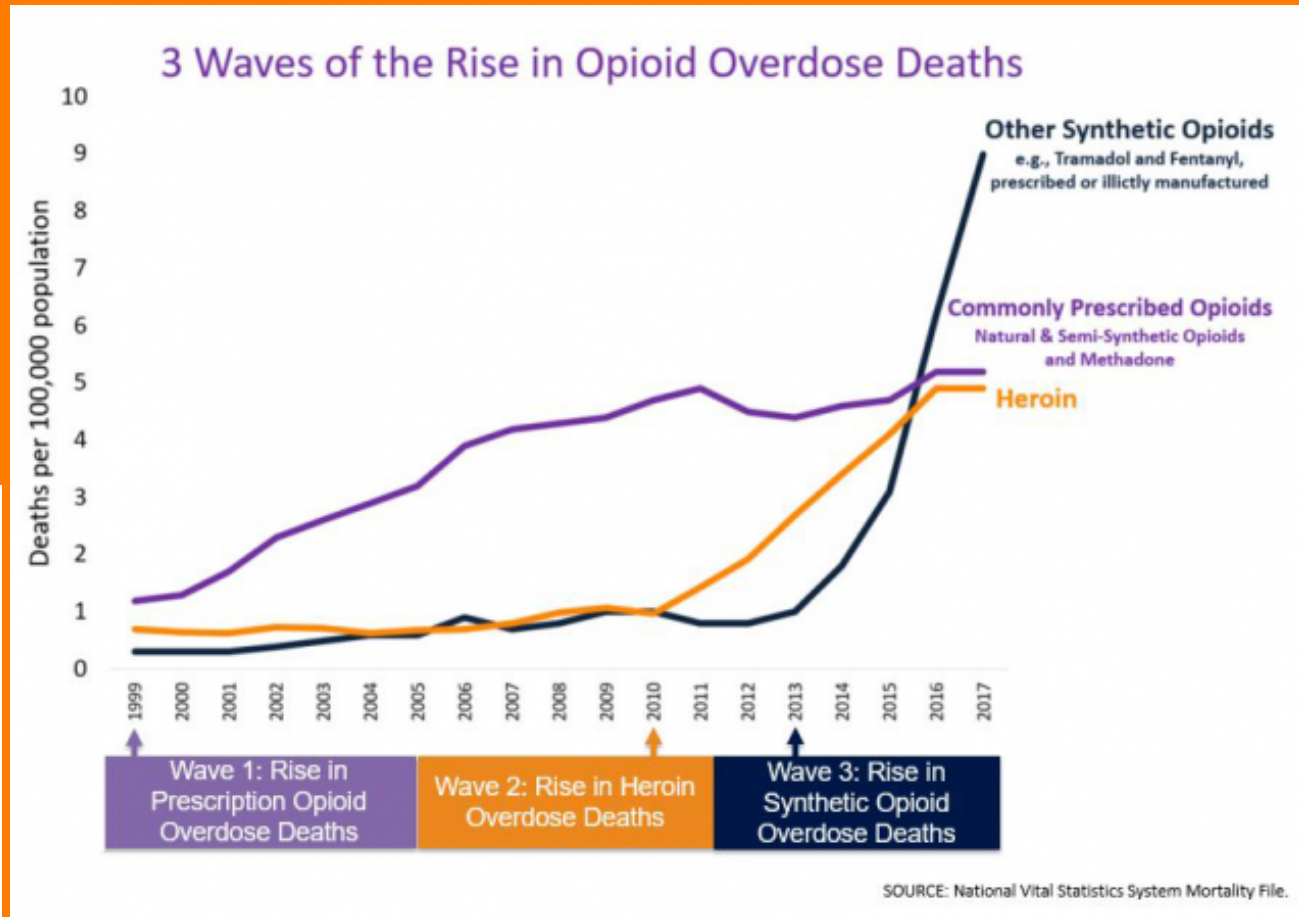
Report issued in September, 2016

# Meanwhile...

## Opioids are addictive, and kill

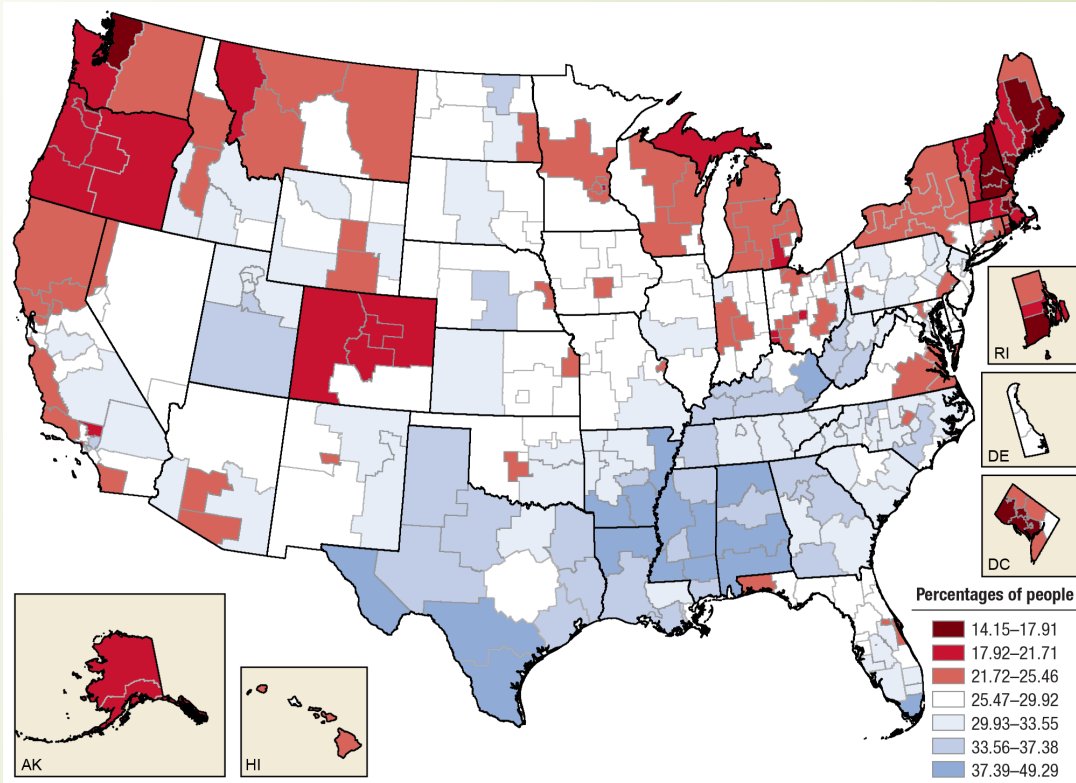
*“From 1999-2017, almost 400,000 people died from an overdose involving any opioid, including prescription & illicit opioids.”*

-CDC



Source: [Centers for Disease Control](https://www.cdc.gov)

# Oregonians aren't too concerned about occasional marijuana use

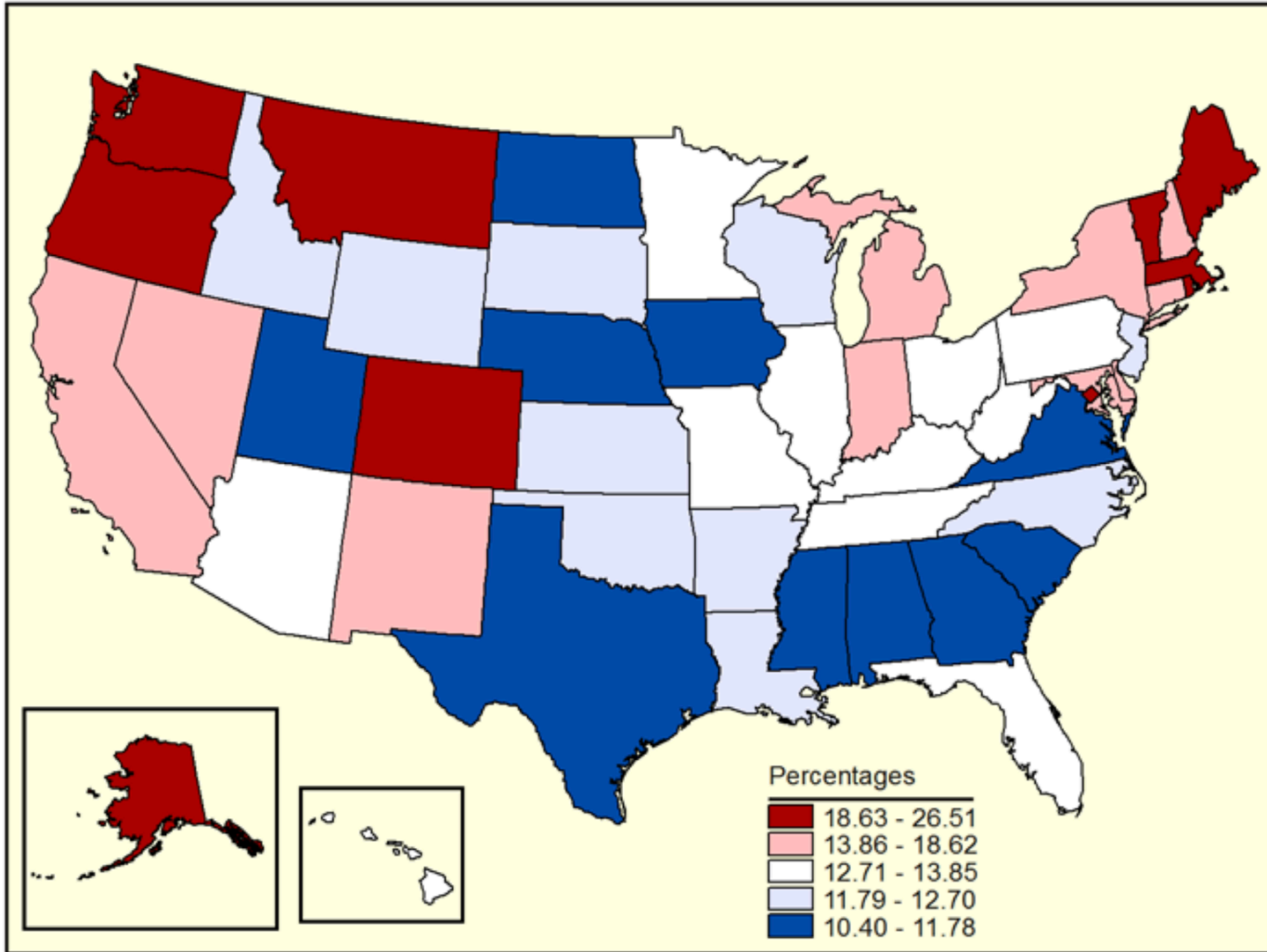


Perceptions of great risk of harm from smoking marijuana once a month among youths aged 12 to 17, by state: percentages, annual averages, 2012 to 2014; [SAMHSA](#)

*“Epidemiological data indicate that in the general population marijuana use is not associated with increased mortality” - [NIH](#)*

# Notice anything..?

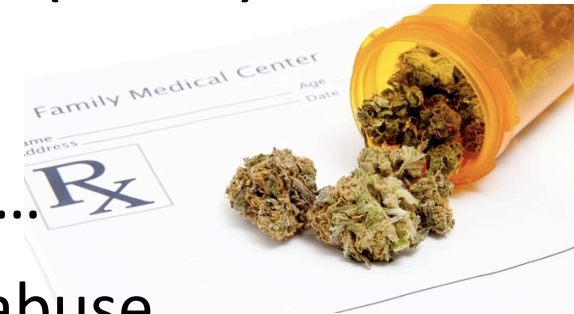
**Figure 2a** *Marijuana Use in the Past Year among Individuals Aged 12 or Older, by State: Percentages, Annual Averages Based on 2016 and 2017 NSDUHs*



Source: SAMHSA, Center for Behavioral Health Statistics and Quality, NSDUH, 2016 and 2017.

# 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...

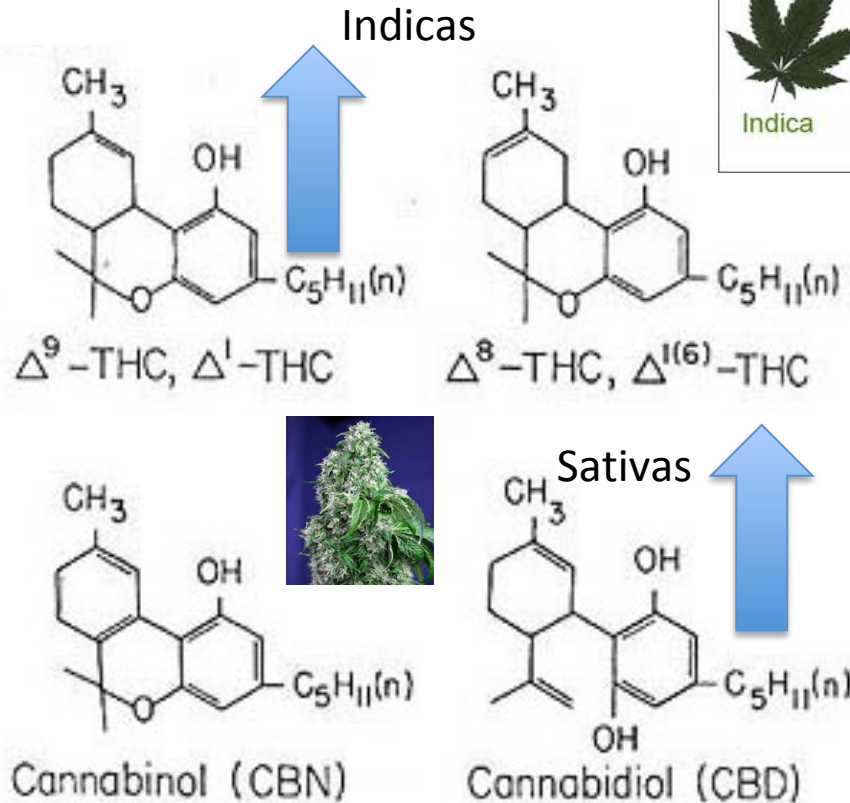



**Marijuana is *still* a  
Schedule I substance**

**Makes it more difficult to conduct research funded  
by the National Institute on Drug Abuse (NIDA)**

# Cannabis contains cannabinoids

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



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

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



# Method of drug administration matters



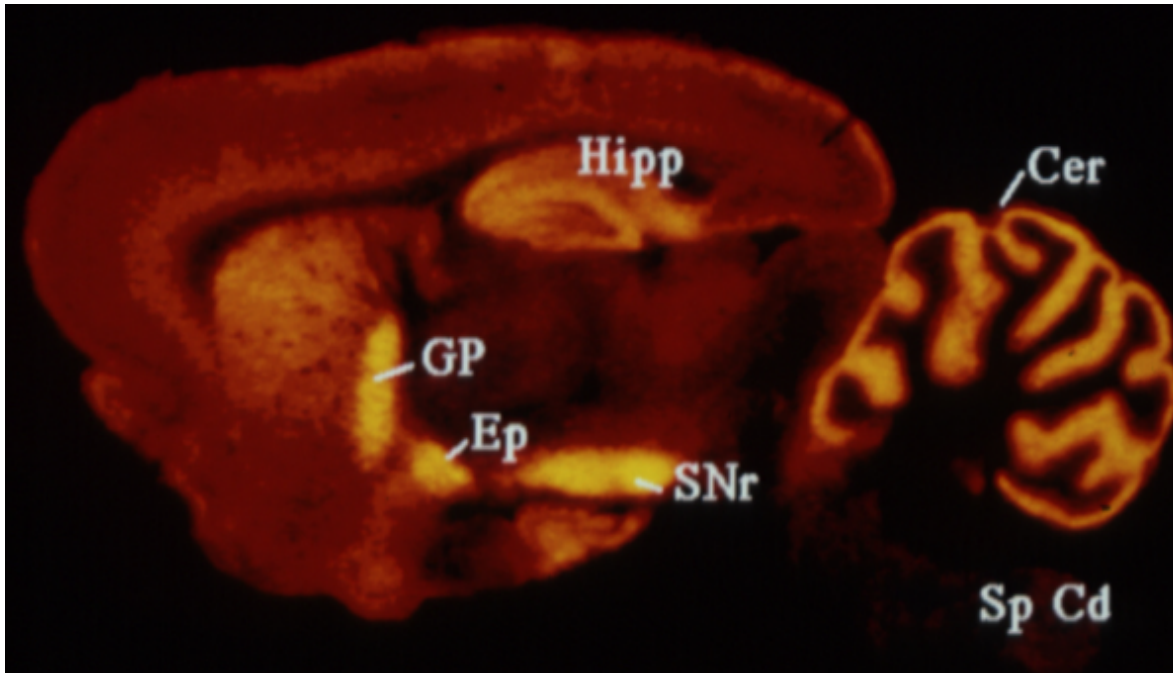
Burning vaporizes cannabinoids, which reach the brain in seconds. Oral administration delivers less THC, CBD, CBN, etc. more slowly...

## 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



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

## CB1 Receptors

*Abundant!*

Cerebellum

Basal ganglia

Hippocampus

Brainstem

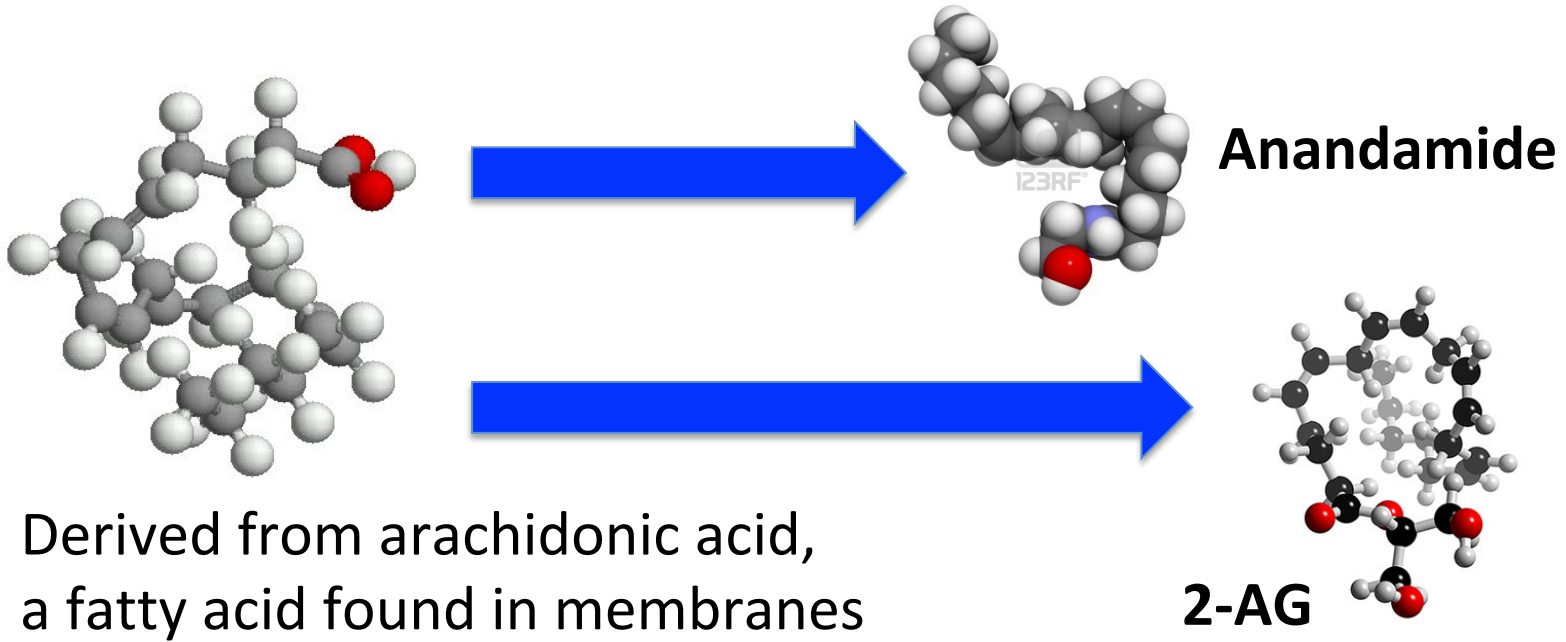
Spinal cord

Neocortex

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

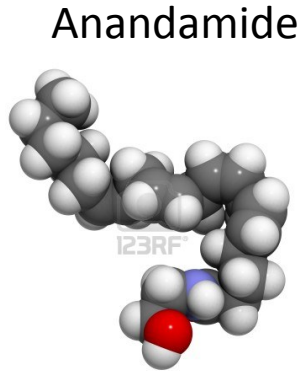
# Endogenous cannabinoid neurotransmitters

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



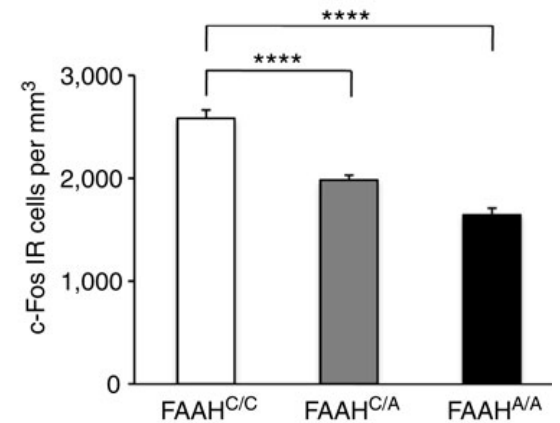
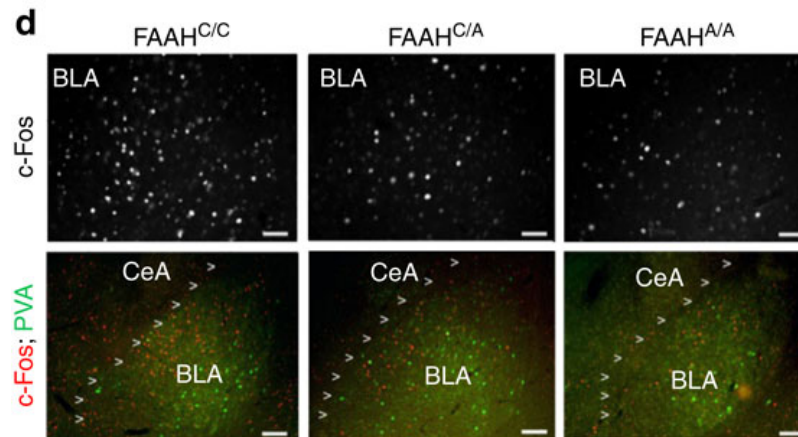
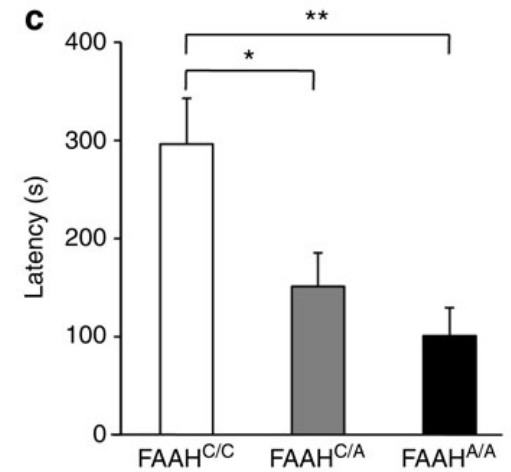
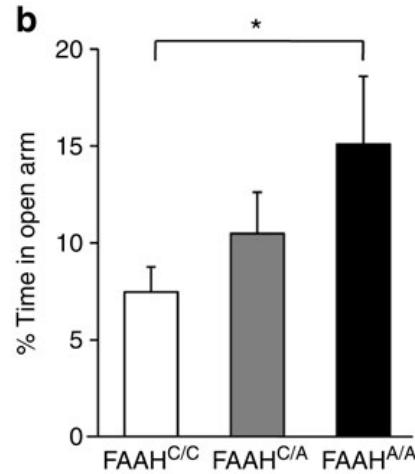
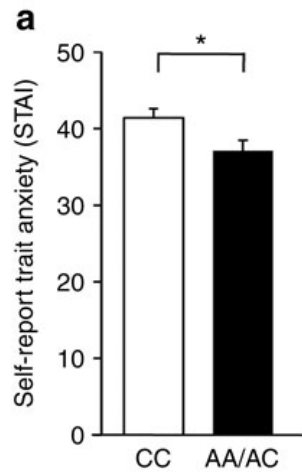
# Anxiety: Genetic protection?

Decreased anxiety in humans and mice with FAAH C385A



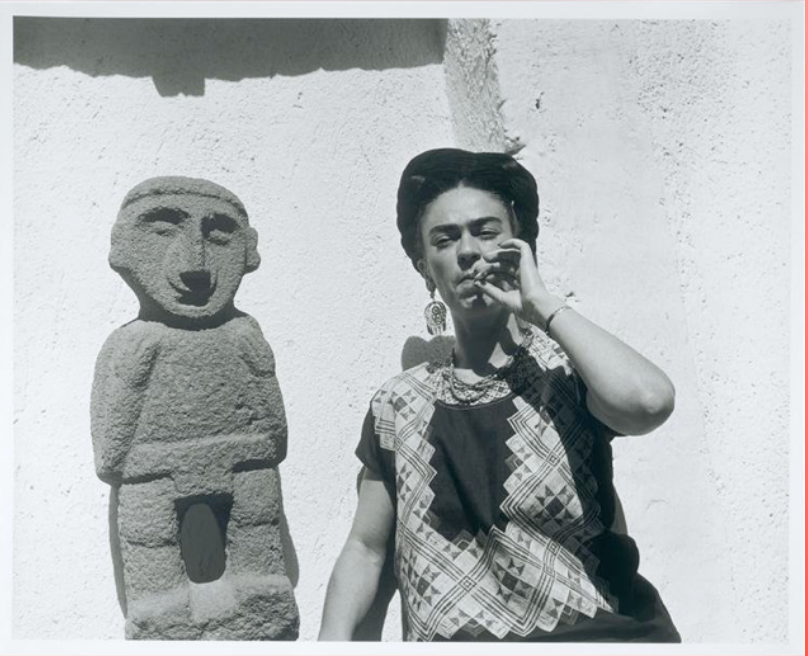
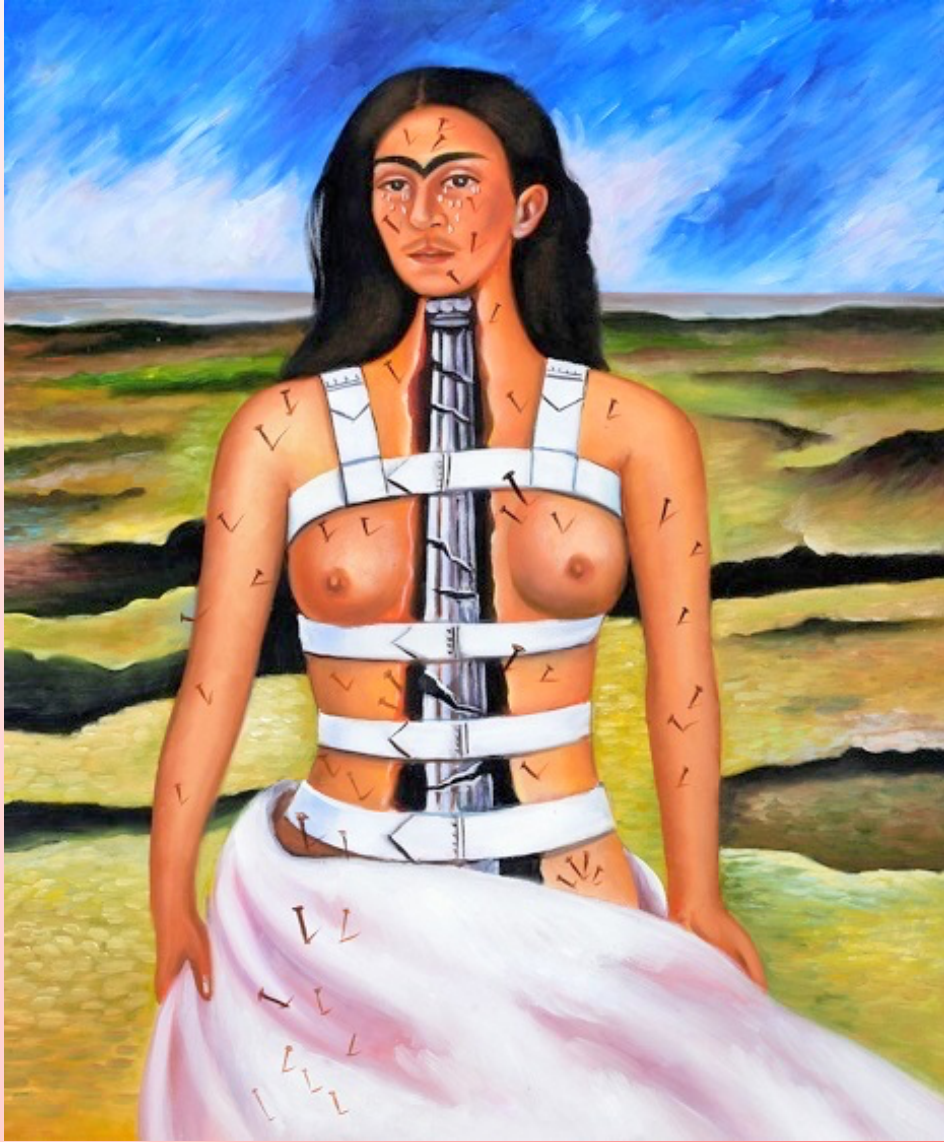
Breakdown by  
FAAH; several  
Forms (A, C)

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)

# Pain



Artist Frida Kahlo survived a bus accident in 1925, which broke her spinal column, collarbone, ribs, pelvis and right leg, crushed and dislocated her right foot, dislocated her shoulder, and left her w/terrible, psychologically debilitating bouts of chronic pain.

# Cannabinoids reduce pain

...inhaled cannabis is consistently effective in reducing chronic non-cancer pain. Oral cannabinoids seem to improve some aspects of chronic pain (sleep, general quality of life), or cancer chronic pain, but they do not seem effective in acute postoperative pain, abdominal chronic pain, or rheumatoid pain...inhaled cannabis seems to be more tolerable and predictable than oral cannabinoids. Cannabis or cannabinoids are not universally effective for pain. Continued research on cannabis constituents and improving bioavailability for oral cannabinoids is needed..."

[Cannabis and Cannabinoids for Chronic Pain \(2017\)](#)

**Marijuana legalization means fewer opioid prescriptions and deaths ([Source](#))**

# More therapeutic effects



- **Appetite stimulation**  
(e.g., Foltin, 1988; Grotenhermen, 2012)  
*Why is this therapeutic?*
- **Nausea relief**  
(e.g., Parker et al (2011); “The anti-emetic effect of cannabinoids has been shown across a wide variety of animals that are capable of vomiting in response to a toxic challenge.” Also studies referenced by the National Cancer Institute at [cancer.gov](http://cancer.gov); though chronic use linked to hyperemesis syndrome; Soriano-Co M, 2010)



# STILL MORE therapeutic effects



- Multiple sclerosis
  - E.g., “Current status of cannabis treatment of multiple sclerosis,” Deutsch et al (2008)
- Epilepsy
  - E.g., “The case for medical marijuana in epilepsy,” Maa (2014)
- Cancer
  - E.g., “The combination of cannabidiol and  $\Delta 9$ -THC enhances the anticancer effects of radiation in an orthotopic murine glioma model,” Scott et al (2014)



# Marijuana impairs cognition, memory, motor coordination



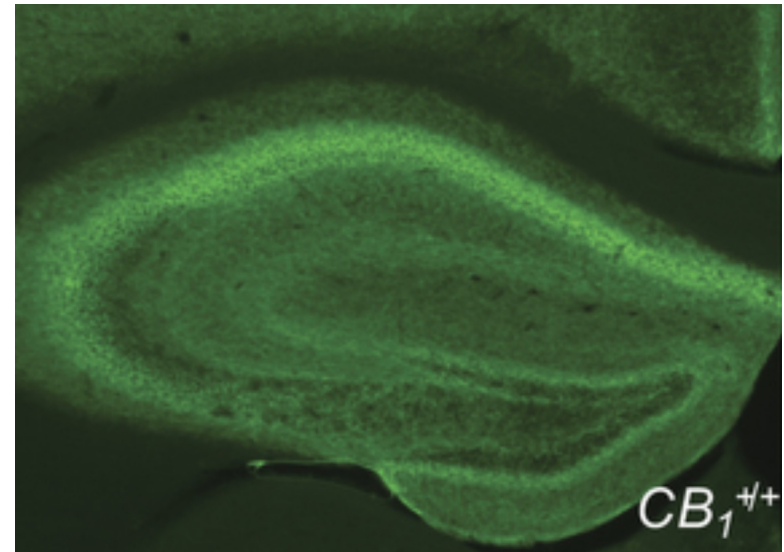
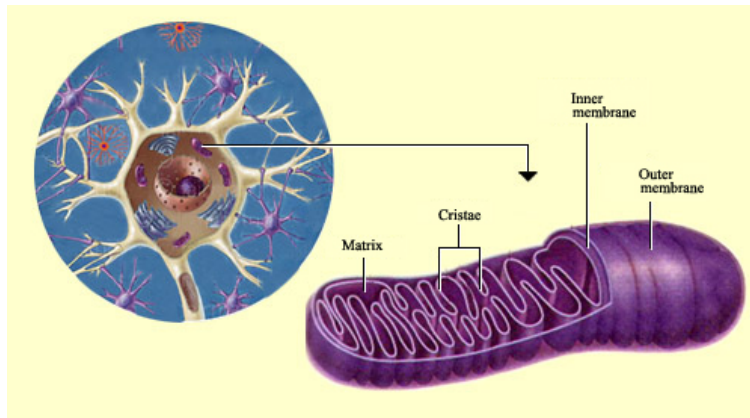
- Deficits in acute verbal and spatial memory (e.g., Curran et al, 2002)
- Deficits in working/short-term memory (Schoeler 2013)
- Cannabis and alcohol both impair skills critical for driving (Sewell RA et al, 2009)
- Differential effects on socialization (Atakan, 2012)



# 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..?*



**Noggin @ p:ear**

# Police at p:ear

*“If one really wishes to know how justice is administered in a country, one does not question the policemen, the lawyers, the judges, or the protected members of the middle class. One goes to the unprotected – those, precisely, who need the law’s protection most! – and listens to their testimony.”*

—[James A. Baldwin](#)



# Marijuana and Bias

**From Will Kendall, the Art Director at p:ear:**

“I witnessed a couple of youth leaving the p:ear space with a green marijuana container in hand. I asked them to a) keep their weed cancelled in our space and b) if they did plan on smoking to go at least two blocks from the p:ear space. They agreed to both requests easily and even had a sense of appreciation that I was not judging them for what they were about to do.”

“Shortly after leaving both youth came back into p:ear and were quickly followed by a police officer saying ‘come here,’ and ‘get over here.’ The youth walked to the far side of our space to avoid interactions with the police but were followed by the officer who multiple times reached out to try grabbing the youth, who avoided contact...The youth agreed to go, but as he got outside the officer immediately tried to physically detain him. It was at this point that the youth was unreachable as his past trauma was triggered and he was in full fight mode. Shortly after, more police cars arrived and the youth was detained by five officers and placed in the back of the car.”



- 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



# A history of demonization

Jeff Sessions

Attorney General, U.S  
(2017-2018)

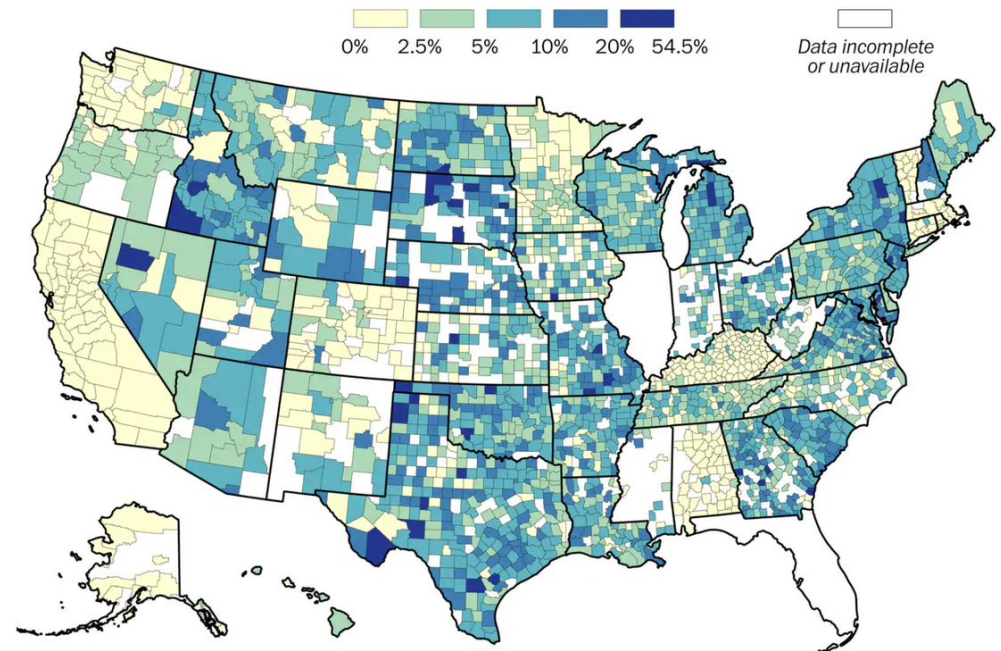
*"Good people don't smoke marijuana..."*

*"The KKK was OK until I found out they smoked pot..."*

[New York Times](#)

## The burden of marijuana enforcement

Marijuana possession arrests as share of all arrests reported to the FBI in 2016



Source: NACJD analysis of FBI Uniform Crime Reporting data

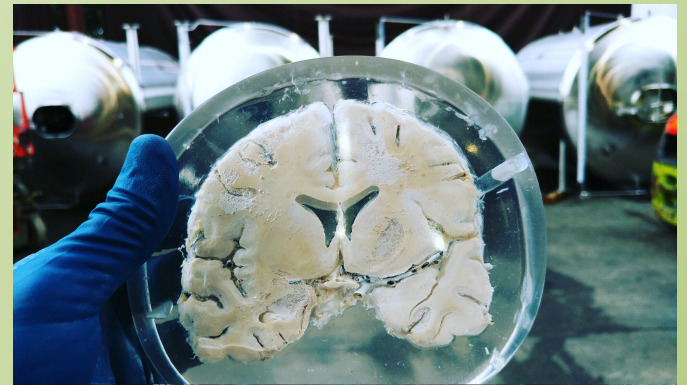
THE WASHINGTON POST

**In an inordinate number of American counties, marijuana arrests are a significant portion of what the police do every day.**

[SOURCE](#)

# *Jeff Sessions' last act as AG...*

*"...signed an order making it more difficult for the Justice Department to investigate & implement reform at police departments with patterns of abuse, questionable shootings, racism, & other constitutional violations..."* – [Washington Post](#)





# Risks of chronic adolescent use

Volkow et al (2014), NEJM

- **Cognitive impairment:** Small drop in IQ (from Meier, M.H. et al. (2012))
- **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...”*

# Can we trust NIDA-funded marijuana research?

“We had them smoke it in the lab, then studied their mood and cognition,” recalls [Dr. Hutchinson](#)... “And what they told me was ‘that was disgusting, what are you giving me? I would never, ever smoke that stuff.’” -[NPR](#)

Low-Quality Cannabis



High-Quality Cannabis



- [Scientists Frustrated with Low Quality Weed from the Government](#)
- [Research grade marijuana supplied by the National Institute on Drug Abuse is genetically divergent from commercially available Cannabis](#)

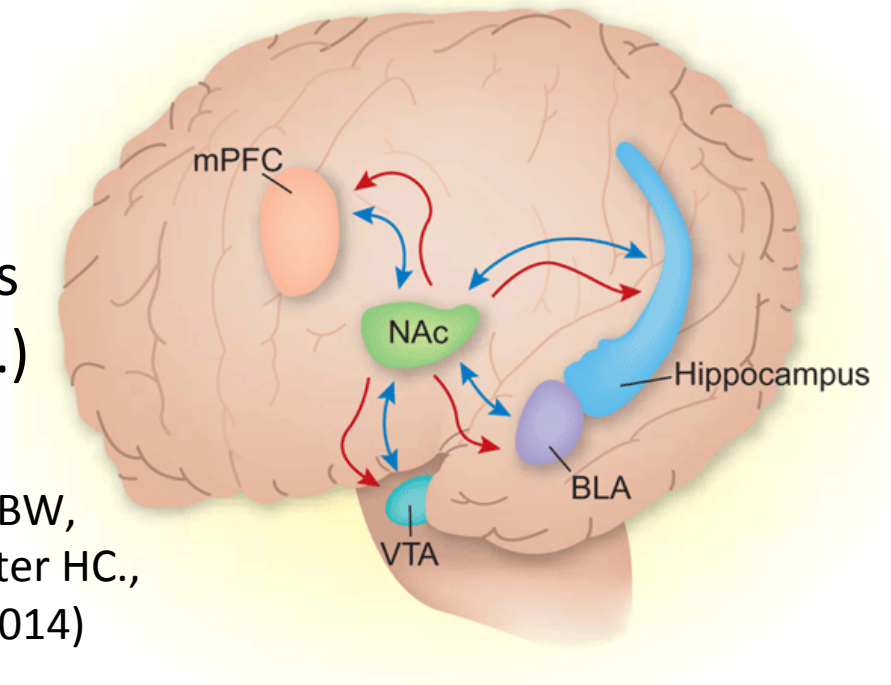


**NIDA has only *one* DEA-certified supplier, the University of Mississippi, known for shipping freeze-dried, re-hydrated samples...**

# Also...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..?*

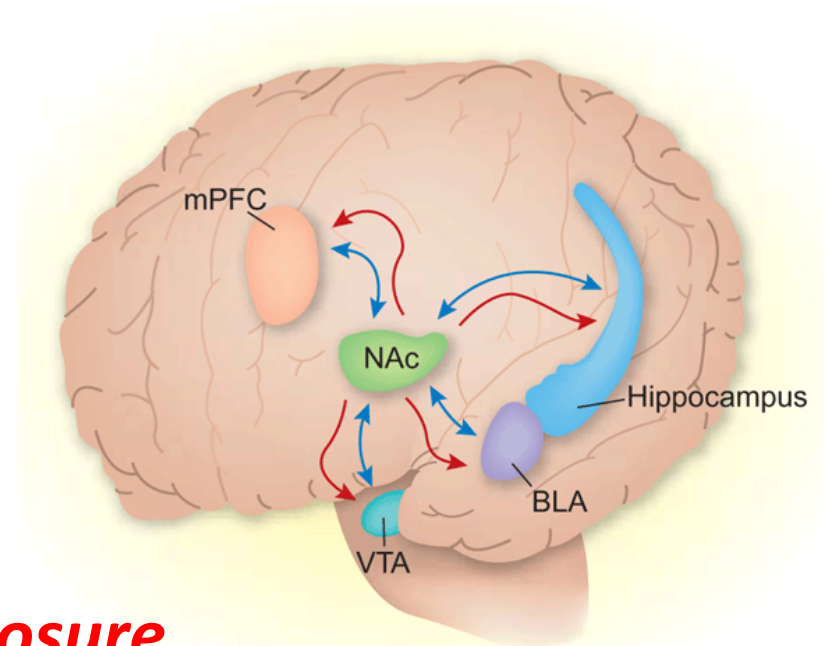
- **Daily Marijuana Use *Is Not Associated* with Brain Morphometric Measures in Adolescents or Adults**

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

Same journal

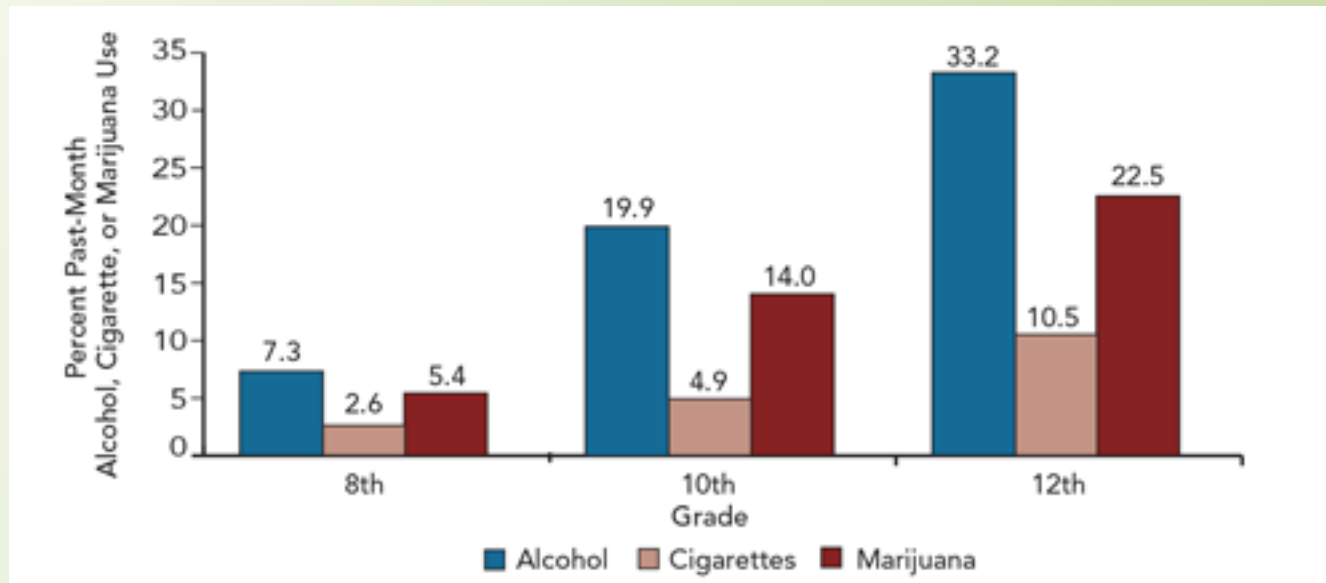
Different research group

***\* Controlled for alcohol exposure...***



# More adolescents use alcohol than cigarettes or marijuana

ALCOHOL in adolescence...  
Causes many deaths  
Causes many injuries  
Impairs judgment  
Increases the risk of assault  
Impacts brain development



SOURCE: Johnston, L.D.; Miech, R.A.; O'Malley, P.M.; et al. *Monitoring the Future National Survey: Trends in 30-Day Prevalence of Use of Various Drugs in Grades 8, 10, and 12, 2015*. Available at: <http://monitoringthefuture.org/data/16data/16drtbl3.pdf>.

# How we can do better



Marijuana research, de-scheduling, legalization, education  
Check our own bias, and privilege  
Lower the emotional temperature  
Go places, listen, learn and contribute  
Invest in more affordable housing, education, enrichment,  
and open, healing community spaces instead of enforcement