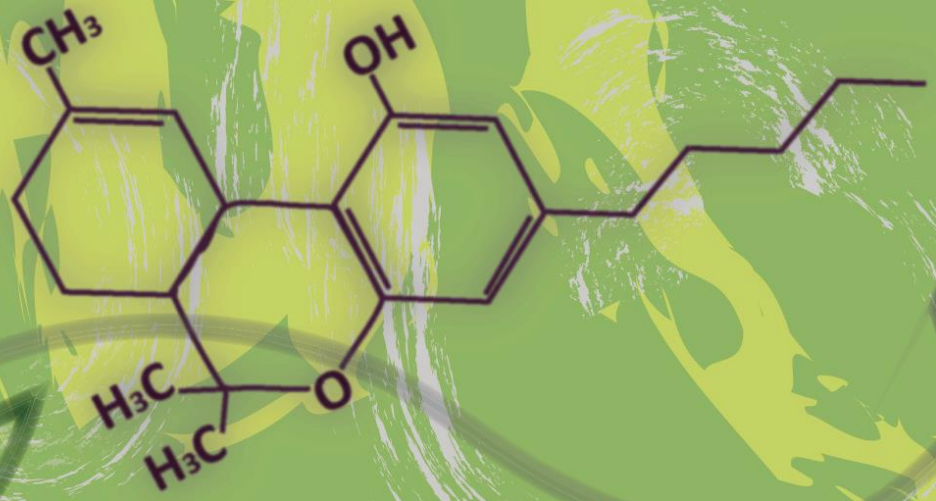
THE HIGHS AND LOWS OF MEDICAL MARIJUANA



Outline

Part I: *Nick Jikomes*
- The cannabis plant
- Cannabinoids & psychoactivity

Part II: *John Hatch*
- Marijuana and human health

Part III: *Kayla Davis*
- Public policy and medical marijuana

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ShannonKringen.com

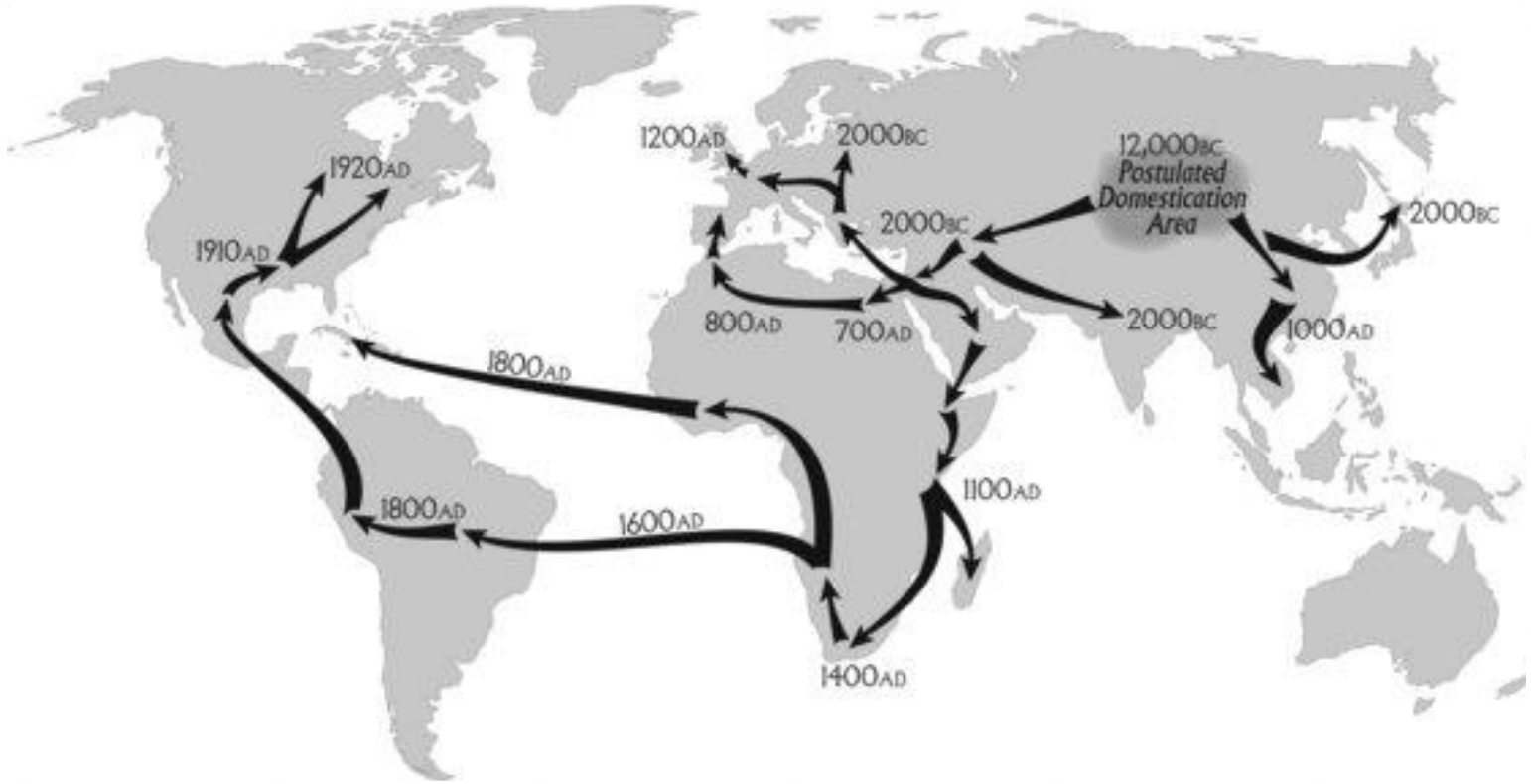








The cannabis plant: history



Historical uses:

- **Fiber**
- **Food**
- **Medicine**
- **Religious/ritual**
- **Recreation**

- **Ancient China:** surgical anesthetic
- **Ancient Egypt:** pain relief
- **Ancient India:** anxiety
- **Roman Empire:** labor pains

Warf (2014)

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The cannabis plant: basics

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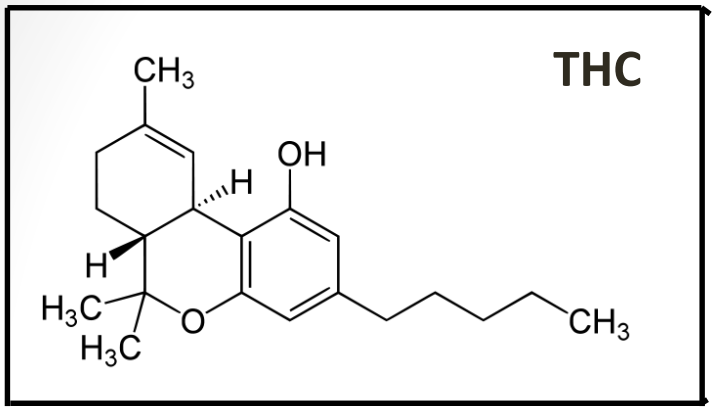
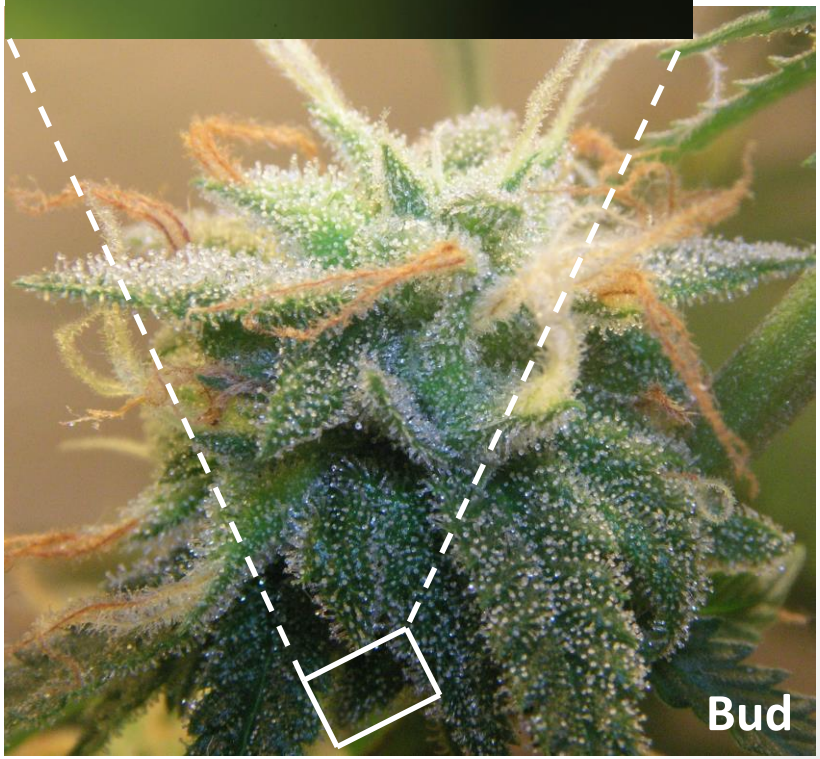
leafscience.com

The cannabis plant: buds & trichomes





- **Bud:** trimmed portion of female flower; cultivated by humans.
- **Trichomes:** hair-like outgrowths that secrete *terpenes* and *cannabinoids.*
- **Cannabinoids:** a diverse class of chemical compounds that act on *cannabinoid receptors*.

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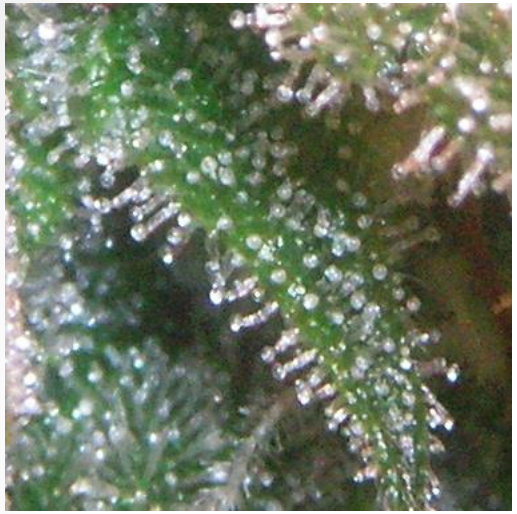
The cannabis plant: why does it contain psychoactive compounds?



Cannabis sativa

Drosera capensis

Solanum scabrum

Solanum quitoense

Common functions of trichomes:

- Defend against insect herbivores *
- Defend against frost in colder habitats
- Minimize water loss in windy habitats *
- Prevent overheating in dry, open habitats *
- Attract pollinators or prey

Ecological role of psychoactive plant compounds :

- Defense: many used as insecticides
- Caffeine, nicotine

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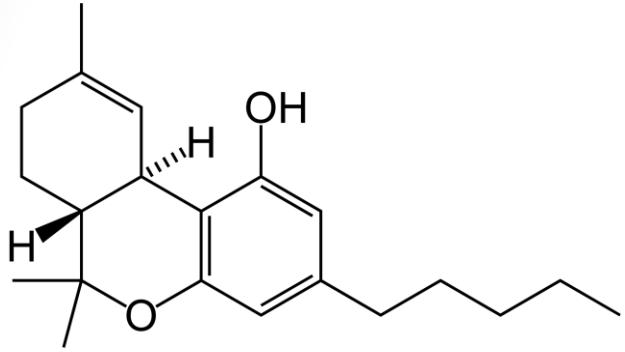
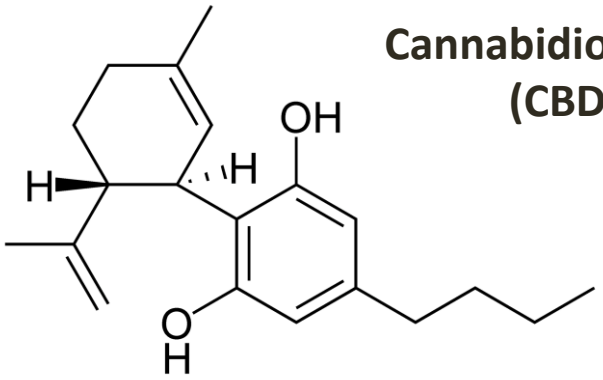
The cannabis plant: break for questions

Cannabinoids: plant cannabinoids

Δ^9-Tetrahydrocannabinol (THC)



Major *psychoactive* molecule in marijuana



Cannabidiol (CBD)

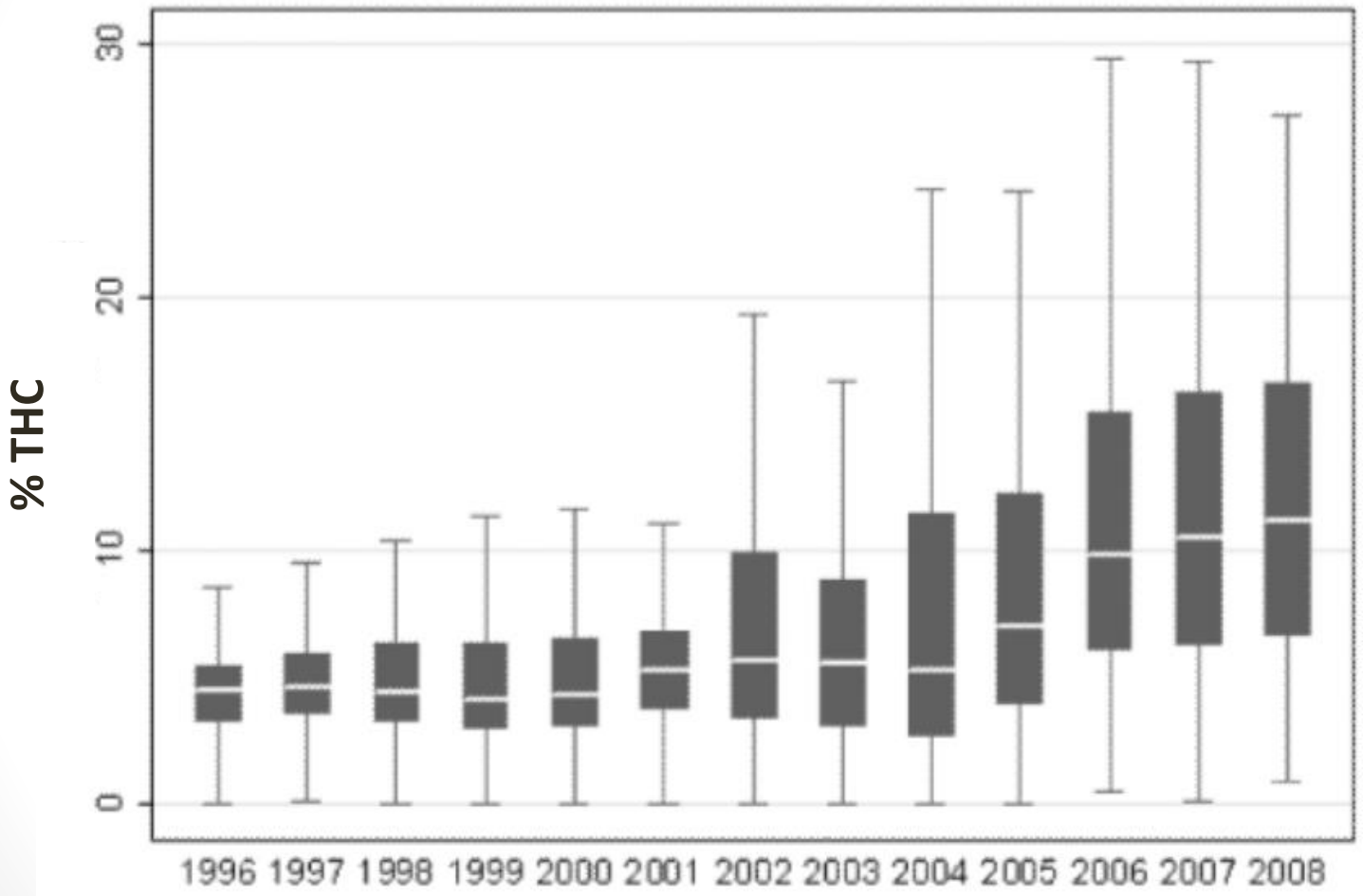
***Non-psychoactive* cannabinoid with many medically useful properties**

- Antiemetic (reduced nausea/vomiting)
- Anticonvulsant (suppresses seizure activity)
- Anti-inflammatory
- Anti-oxidant
- Anxiolytic
- Anti-tumoral
- Anti-psychotic

* Based mostly on animal studies, not human clinical trials

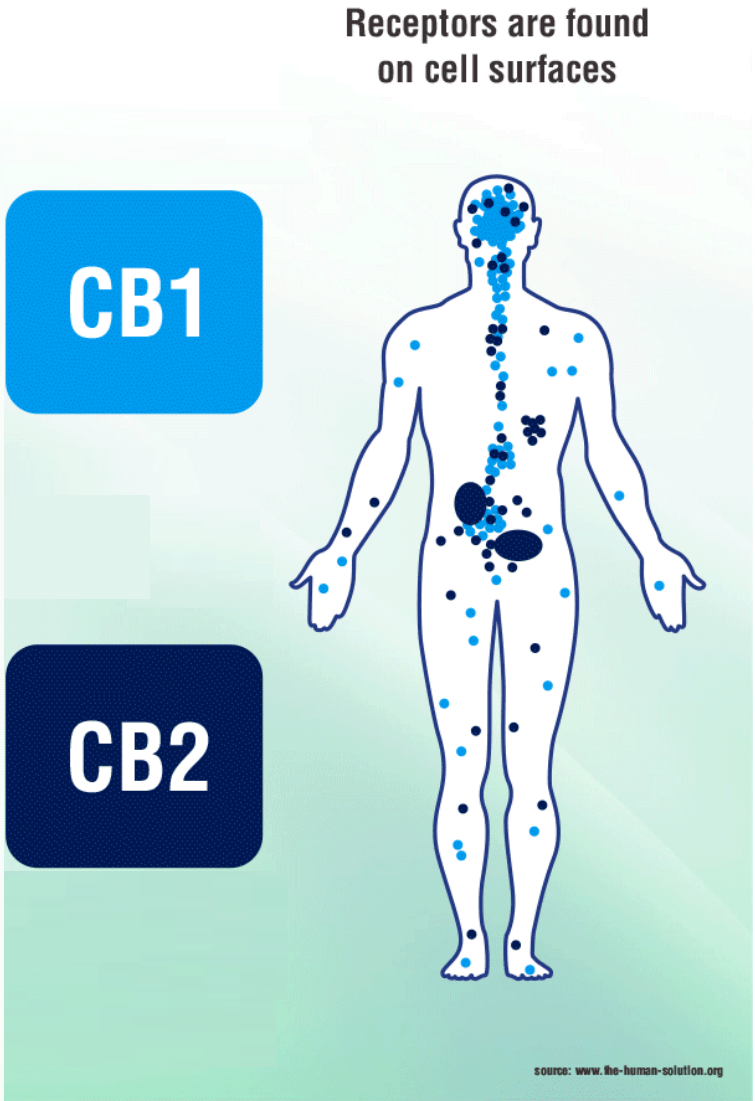
British Journal of Clinical Pharmacology

Cannabinoids: plant cannabinoid variability



liq.wa.gov

Cannabinoids: the human endocannabinoid system



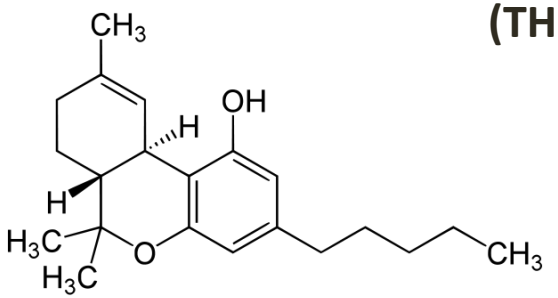
- **CB1 receptor:** found on neurons throughout the central and peripheral nervous system.
- **CB2 receptor:** found largely outside the nervous system, including the immune and gastrointestinal systems.
- **Psychoactive effects** of marijuana are largely due to **CB1 activation** by **THC**.

Cannabinoids: endogenous cannabinoids

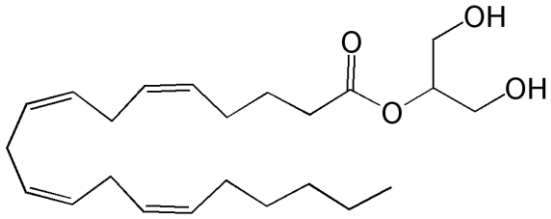
Plant cannabinoids (phytocannabinoids)

Endogenous cannabinoids (endocannabinoids)

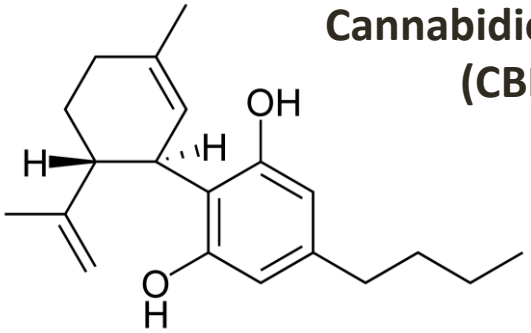
Δ^9-Tetrahydrocannabinol (THC)



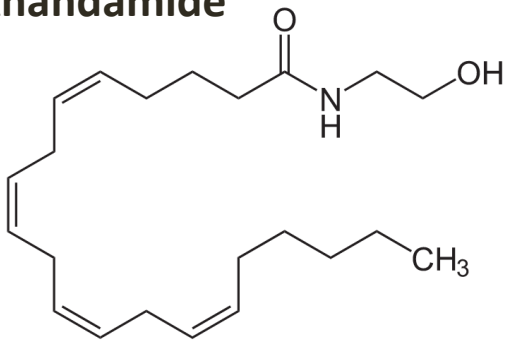
2-Arachidonylglycerol (2-AG)



Cannabidiol (CBD)



Anandamide



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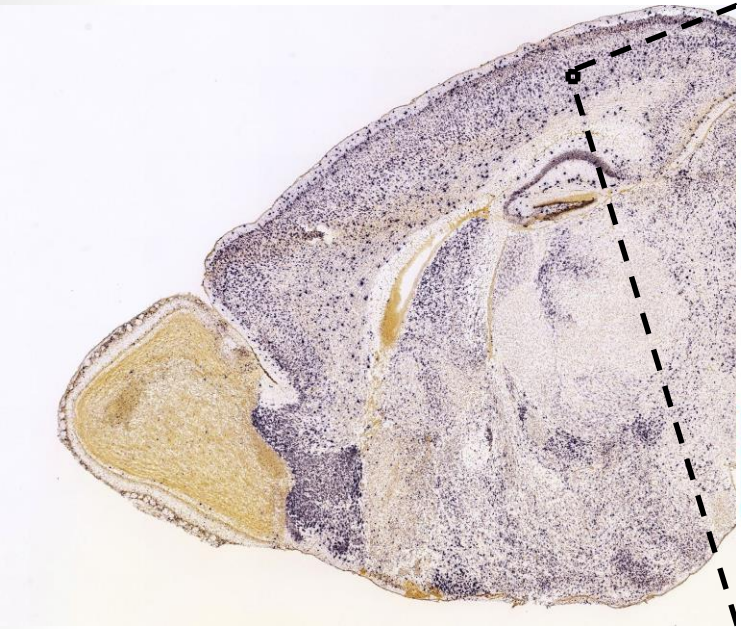
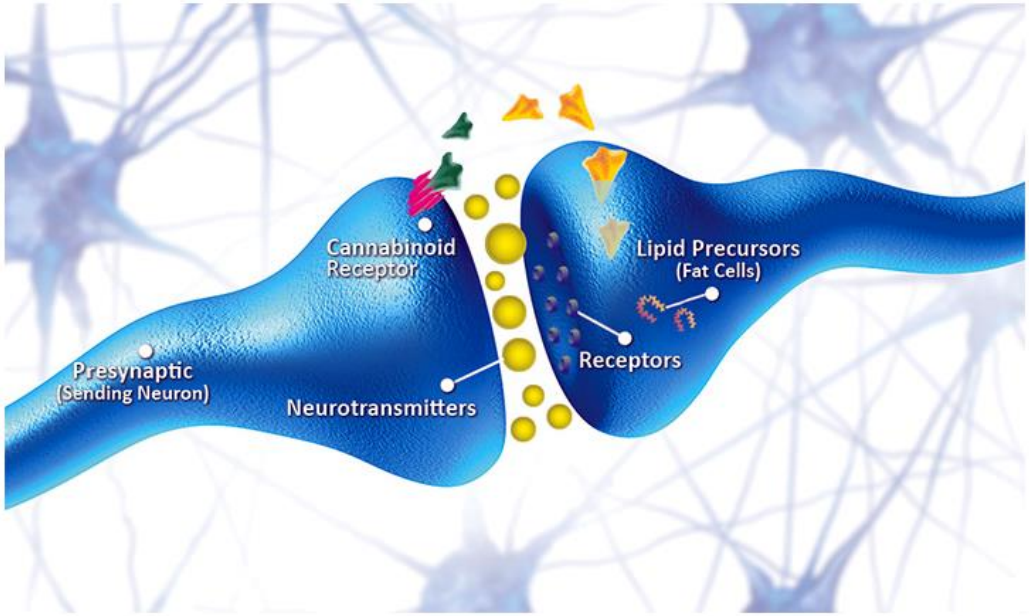
Cannabinoids: effects on mammalian nervous system





- **CB1** is one of the most **widely expressed** receptors in the mammalian brain
- Cannabinoids act as **retrograde signals** sent from "receiver" to "sender" neuron.

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Allen Brain Atlas
Cannavest.com

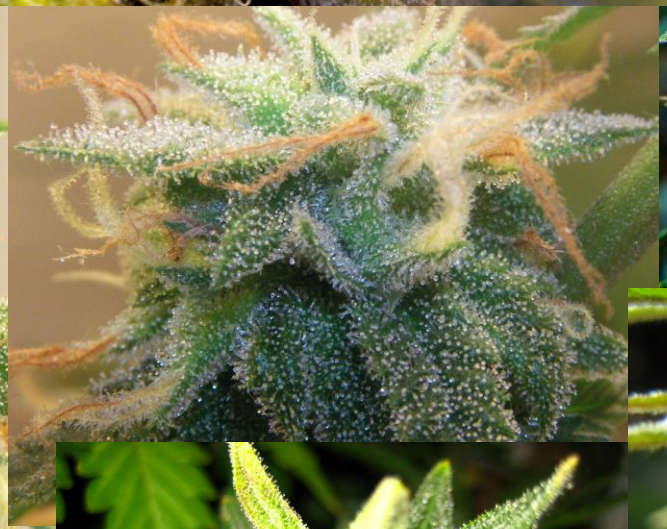
Cannabinoids: variability in psychoactive properties

Psychoactive properties (user reported)	**Medicinal uses (claimed)**
• "Euphoric" "uplifting" • Increases energy, creativity; induces a "mental high"	• Depression/mood disorders • ADHD • Fatigue
• "Relaxing," "sedating" • Promotes relaxation; induces a "body high"	• Anxiety • Insomnia • Chronic pain • Muscle spasms • Nausea • Inflammation • Low appetite

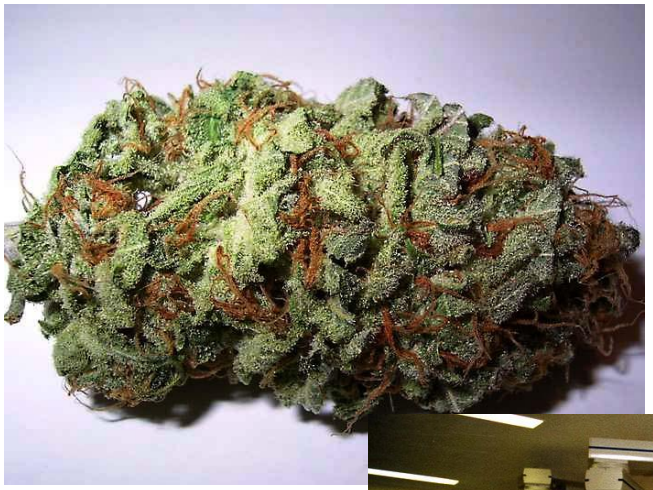
Hillig & Mahlberg (2004)







Cannabinoids: break for questions



Part II: Marijuana and Human Health

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Two Distinct Concepts

- Risks associated with recreational use
- Benefits associated with therapeutic use

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Recreational Use: Risks

Claim	Science Says…
Marijuana causes respiratory damage	???
Marijuana causes cognitive decline	???
Marijuana causes schizophrenia	???
Marijuana can cause dependency	???

Wikimedia Commons

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Respiratory Damage

- Cannabis smoke contains many harmful chemicals also found in tobacco smoke:
  - Tar
  - Carbon monoxide
  - Ammonia
  - Hydrogen Cyanide
  - Arsenic
  - Formaldehyde
  - Carcinogens
    - Polyaromatic hydrocarbons

Wikimedia Commons
BA Moore et al. *JGIM* 2004
S Sidney et al. *Cancer Causes & Control* 1997

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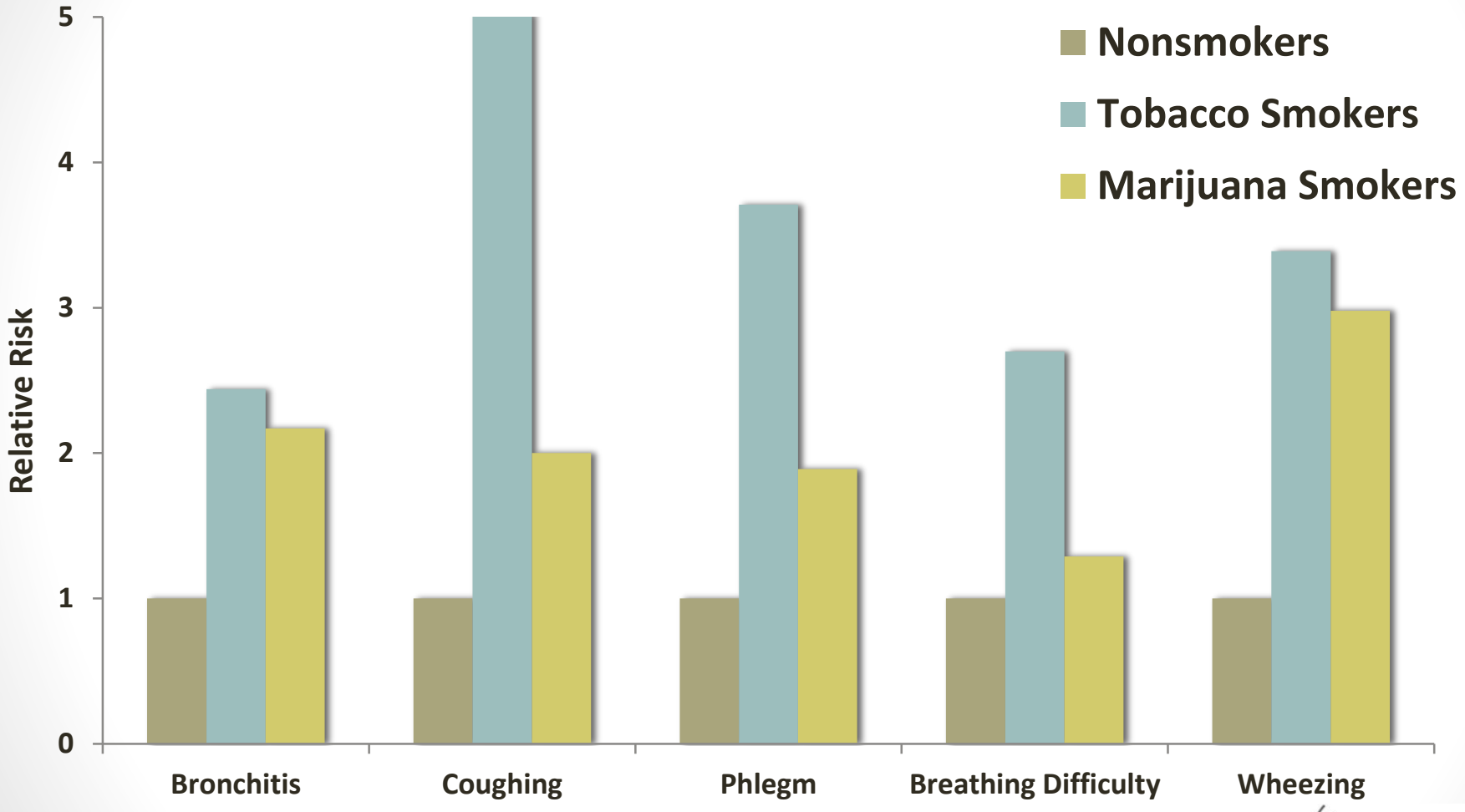
Respiratory Damage



BA Moore et al. *JGIM* 2004
S Sidney et al. *Cancer Causes & Control* 1997

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Verdict

Claim	Science Says…
Marijuana causes respiratory damage	✓
Marijuana causes cognitive decline	???
Marijuana causes schizophrenia	???
Marijuana can cause dependency	???

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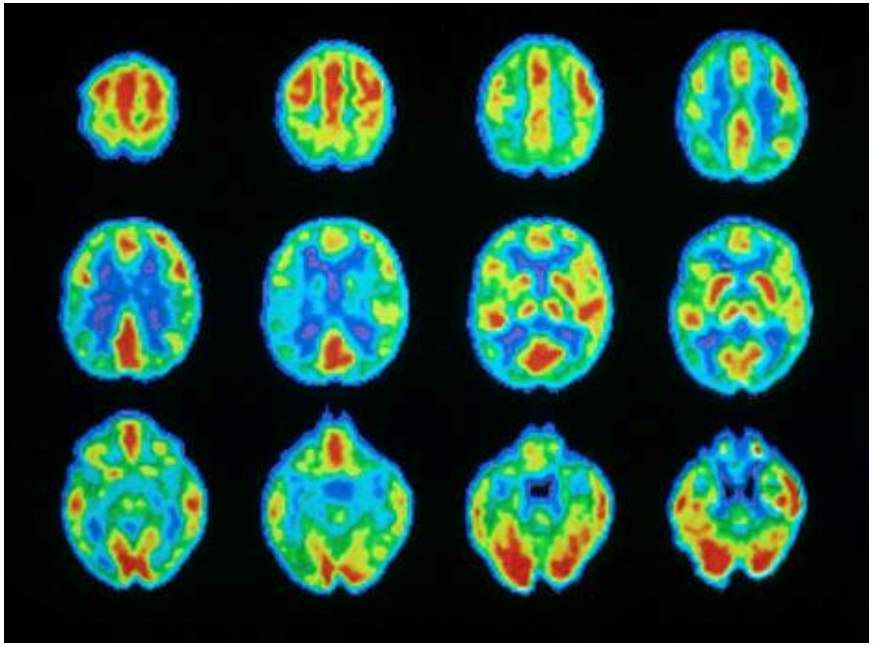
Two Key Risk Factors

Age

- Brain *development* continues through adolescence.

Frequency of use

- *Plasticity* means that the brain changes itself in response to experiences.



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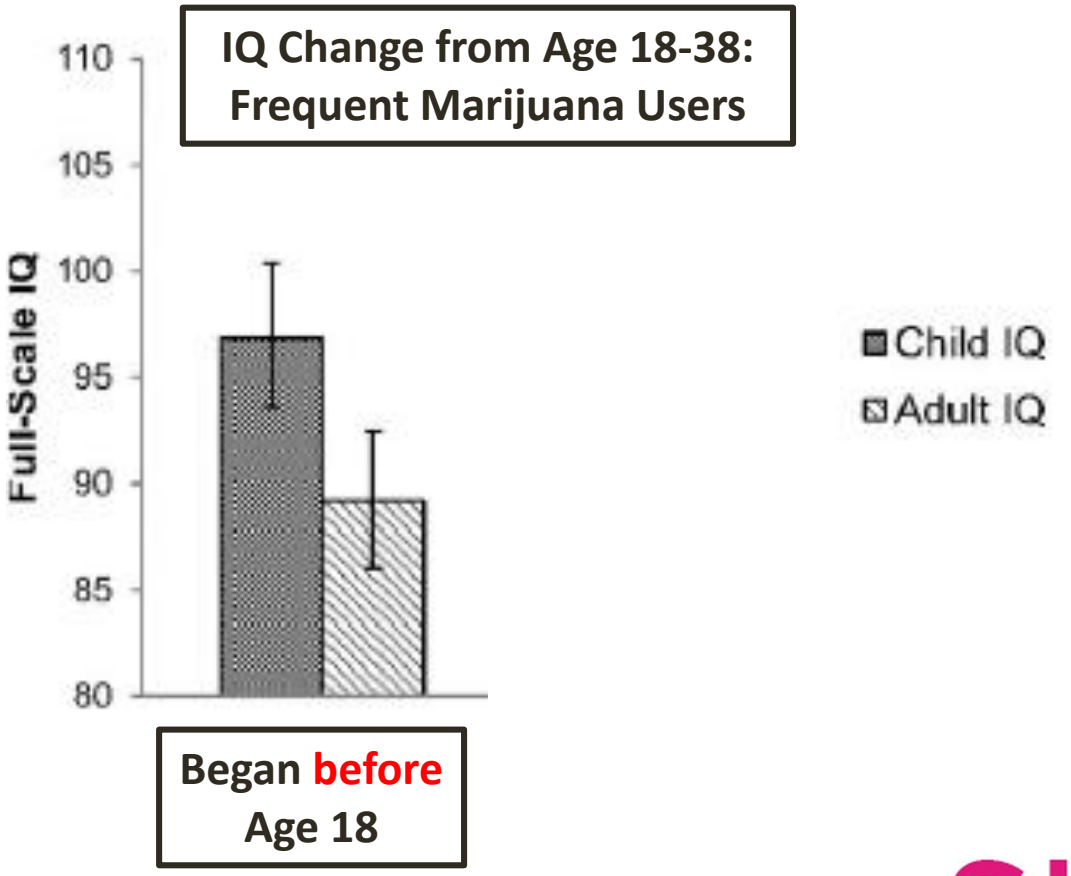
Cognitive Decline

- Significant changes in IQ only for heavy users who begin use during adolescence.



MH Meier et al. *PNAS* 2012

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Verdict

Claim	Science Says…
Marijuana causes respiratory damage	✓
Marijuana causes cognitive decline	
Adolescent/frequent use	✓
Adult/occasional use	✗
Marijuana causes schizophrenia	???
Marijuana can cause dependency	???

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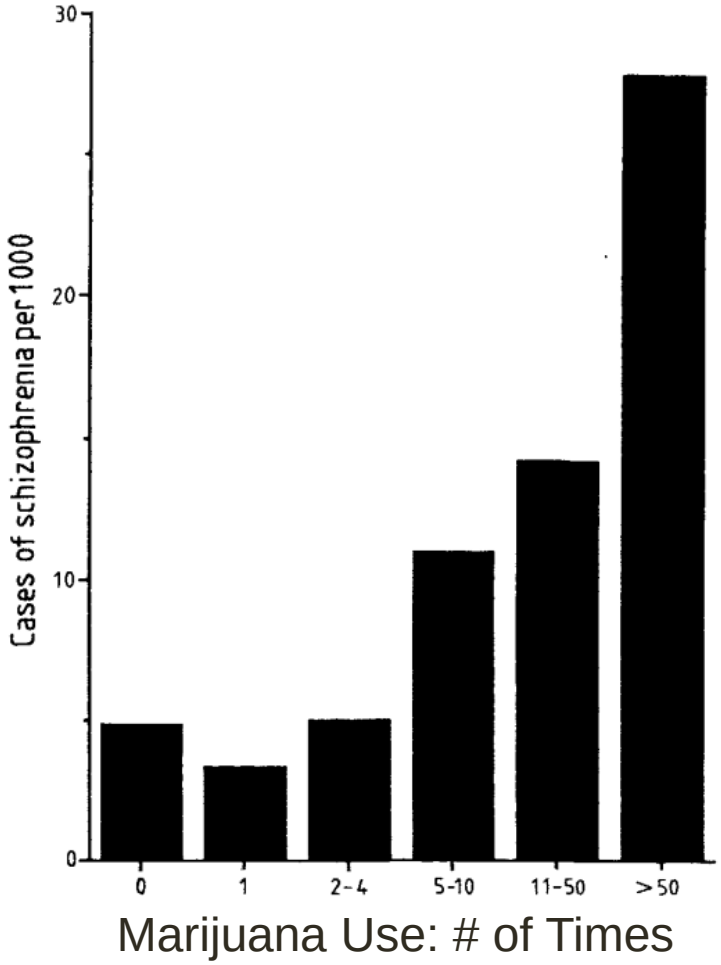
Schizophrenia

- Early data suggested that cannabis use may cause schizophrenia



Marijuana Use → **Schizophrenia**

Schizophrenia → **Marijuana Use**

Marijuana Use

Schizophrenia

S Andreasson et al. *The Lancet* 1987

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Verdict

Claim	Science Says…
Marijuana causes respiratory damage	✓
Marijuana causes cognitive decline	
Adolescent/frequent use	✓
Adult/occasional use	✗
Marijuana causes schizophrenia	**Needs More Research!**
Marijuana can cause dependency	???

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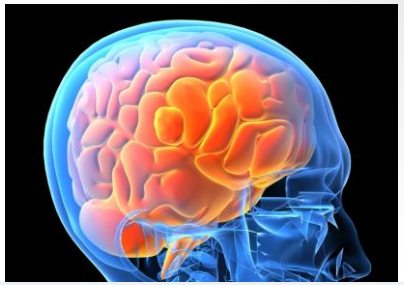
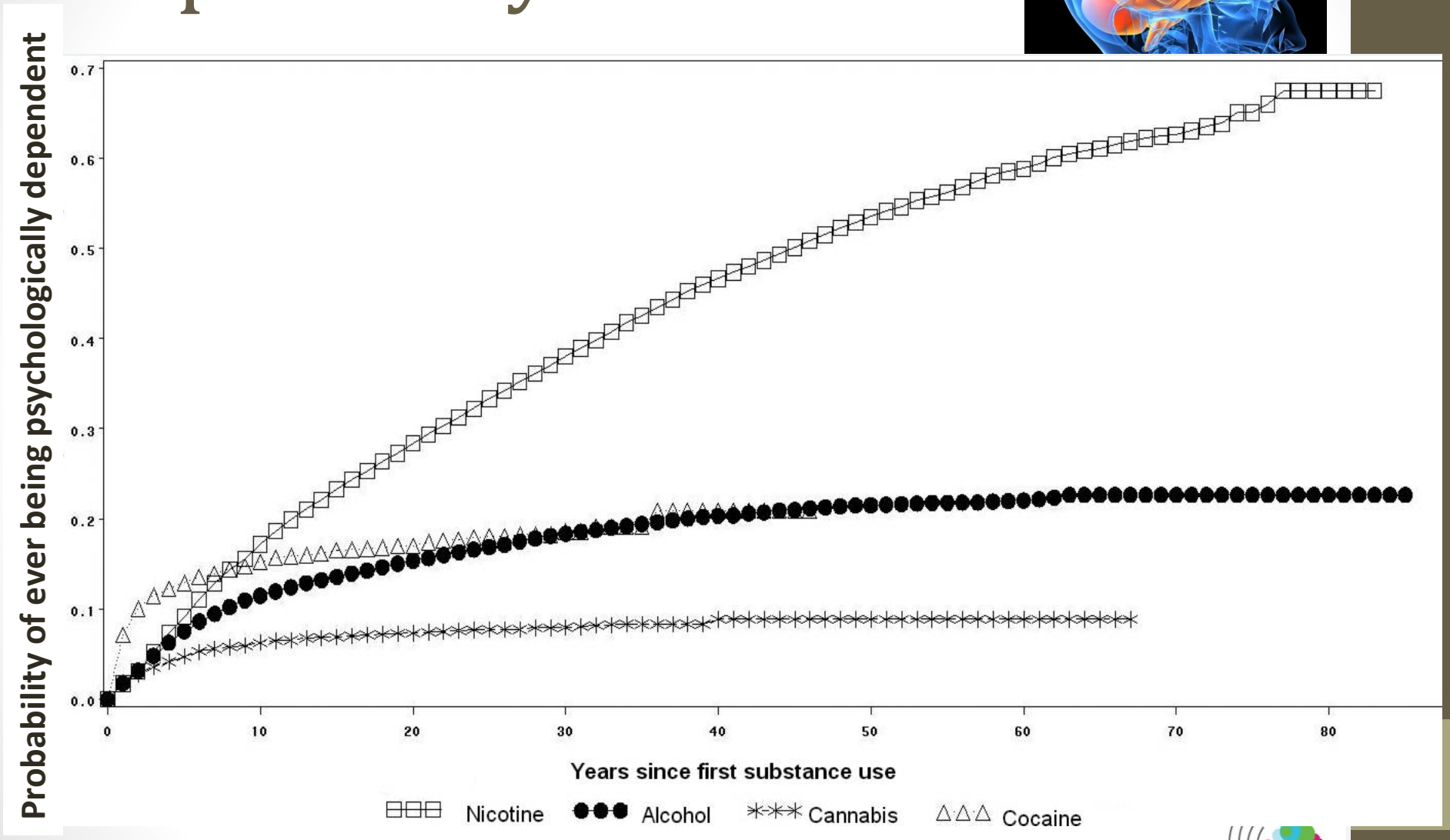
Dependency





C Lopez-Quintero et al. *Drug Alcohol Depend.* 2011

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Verdict

Claim	Science Says…
Marijuana causes respiratory damage	✓
Marijuana causes cognitive decline	
Adolescent/frequent use	✓
Adult/occasional use	✗
Marijuana causes schizophrenia	Need More Research!
Marijuana can cause dependency	✓

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Questions?

- Next up: therapeutic applications of marijuana and cannabinoids.

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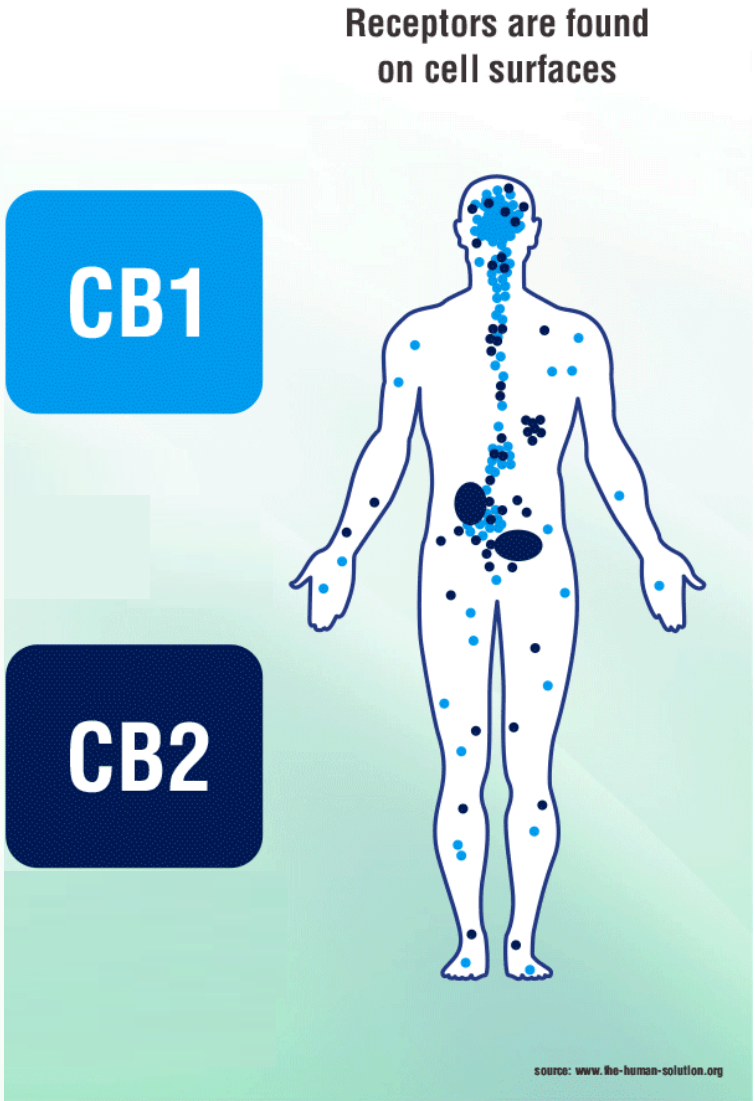
Reminder: the endocannabinoid system



- **CB1 receptor:** found on neurons throughout the central and peripheral nervous system.
- **CB2 receptor:** found largely outside the nervous system, including the immune and gastrointestinal systems.

Potential Therapeutic Uses

Can marijuana treat:	Science Says…
Chronic Pain?	???
Glaucoma?	???
Cachexia?	???
Seizures & Epilepsy?	???
Cancer?	???

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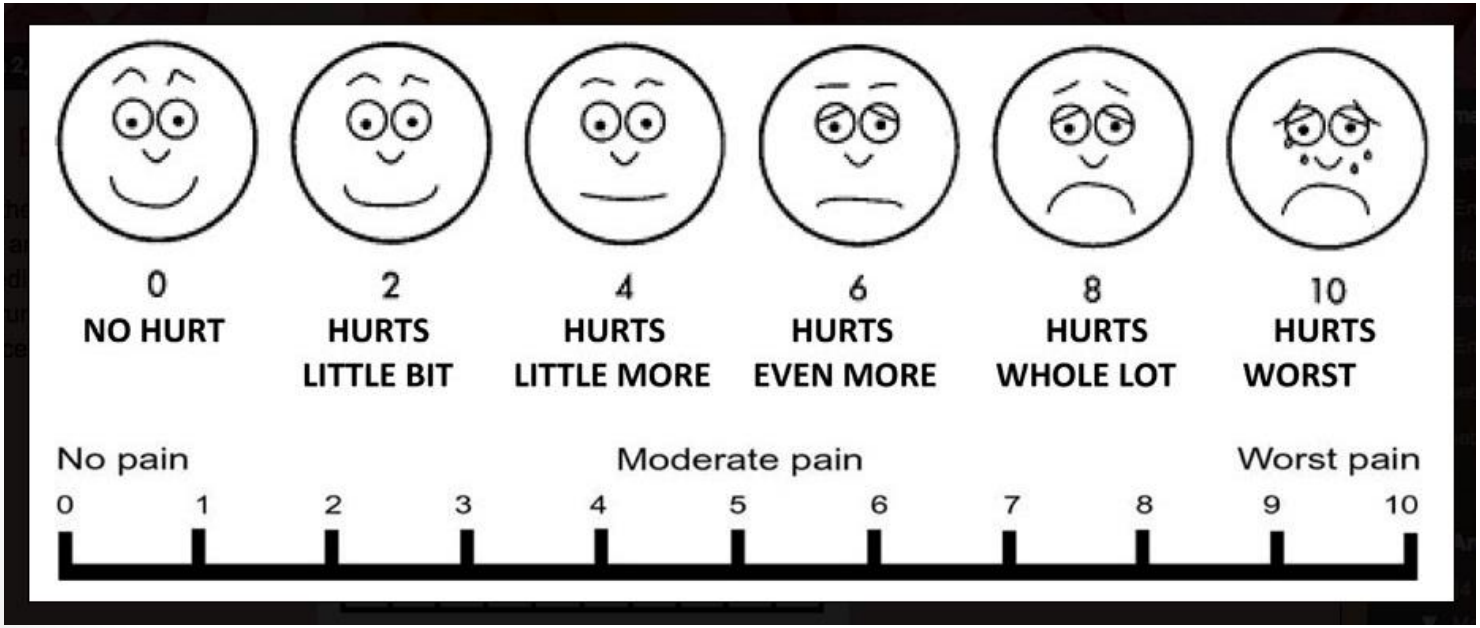
Chronic Pain

- Oldest documented medicinal use of marijuana.
- Best for long-term pain issues, like nerve damage after surgery.
- Functions differently than most (or all) prescription painkillers.
- Not all strains are created equal!



Wikimedia Commons
MC Lee et al. *Pain* 2013

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Verdict

Can marijuana treat:	Science Says…
Chronic Pain?	✓
Glaucoma?	???
Cachexia?	???
Seizures & Epilepsy?	???
Cancer?	???

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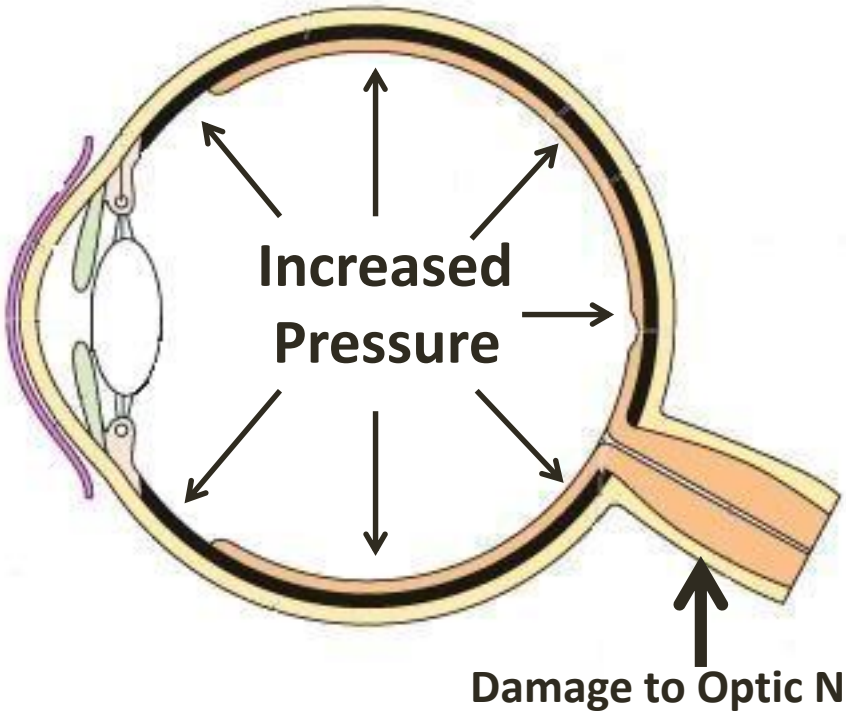
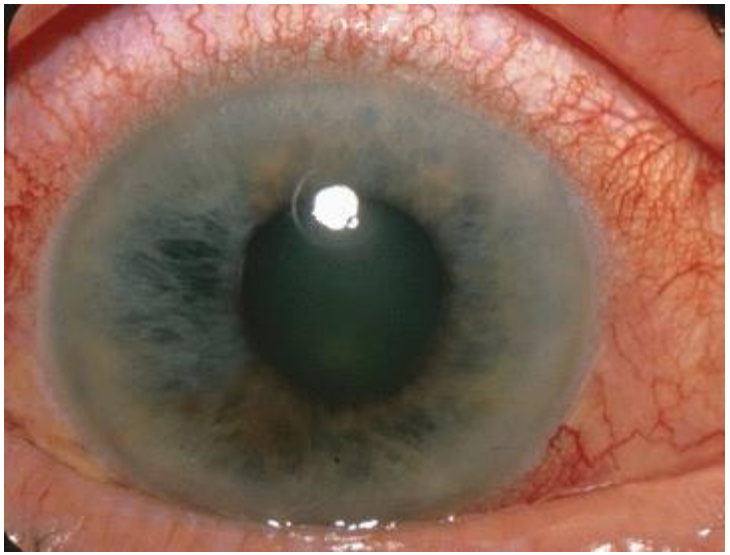
Glaucoma





- Cannabinoids reduce pressure- may be effective due to:
  - Less secretion of fluid.
  - Better drainage of fluid.
  - Fewer damaging cellular reactions in the nerve.
- CB1 and CB2 receptors are present in the eye- new t possible!

Wikimedia Commons

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Verdict

Can marijuana treat:	Science Says…
Chronic Pain?	✓
Glaucoma?	✓
Cachexia?	???
Seizures & Epilepsy?	???
Cancer?	???

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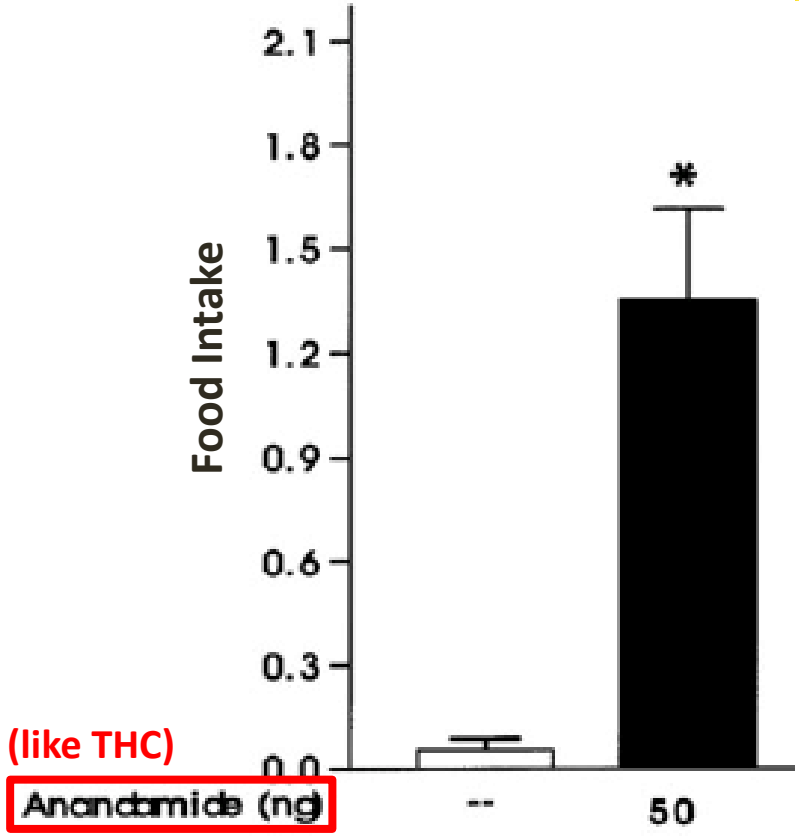
Nausea & Appetite

- "The munchies" have therapeutic benefits for people suffering from cachexia.
  - Chemotherapy
  - HIV/AIDs



Activates CB1 (like THC)

Jamshidi et al. *BJP* 2009

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Verdict

Can marijuana treat:	Science Says…
Chronic Pain?	✓
Glaucoma?	✓
Cachexia?	✓
Seizures & Epilepsy?	???
Cancer?	???

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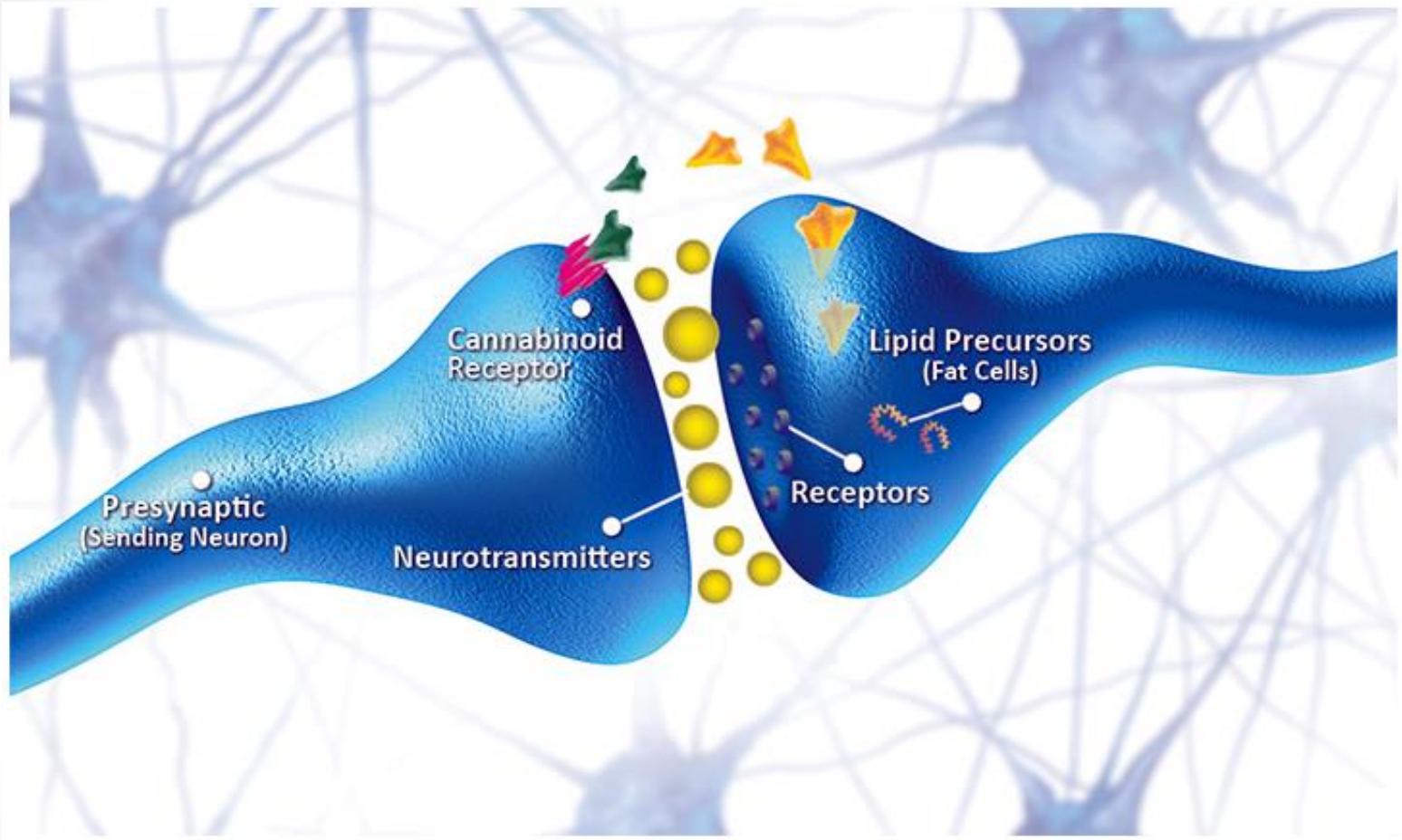
Seizures & Epilepsy



- Result from excessive neural transmission.
- **CBD** in particular may protect against these disorders.

Van der Stelt et al. *Neuromol. Med.* 2005
Devinsky et al. American Epilepsy Society Annual Meeting, April 2015

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Verdict

Can marijuana treat:	Science Says…
Chronic Pain?	✓
Glaucoma?	✓
Cachexia?	✓
Seizures & Epilepsy?	✓
Cancer?	???

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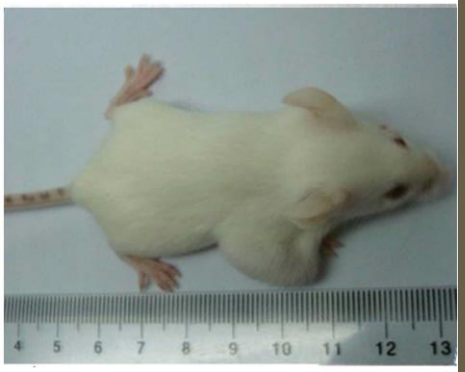
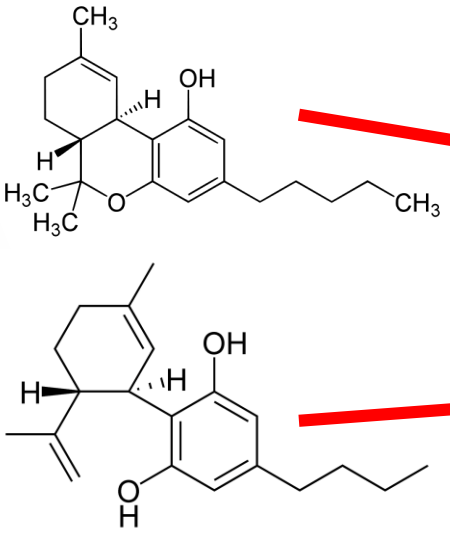
Cancer



- **Cancer**: Uncontrolled cell division leads to tumor growth.

- Cannabis and related compounds have been shown to inhibit tumor growth *in vitro*.
- THC and cannabinoids may be:
  - Anti-mitogenic (reduce cell division)
  - Anti-angiogenic (reduce blood vessel growth)
  - Pro-apoptotic (induce controlled cell death)
- But we don't understand the mechanisms!



Wikimedia Commons
X Lan et al. *IJMM* 2012

Verdict

Can marijuana treat:	Science Says…
Chronic Pain?	✓
Glaucoma?	✓
Cachexia?	✓
Seizures & Epilepsy?	✓
Cancer?	**Needs More Research!**

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Questions?

- Next up: Marijuana and public policy.

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How does policy control marijuana research?

Kayla Davis

History of Drug laws in USA

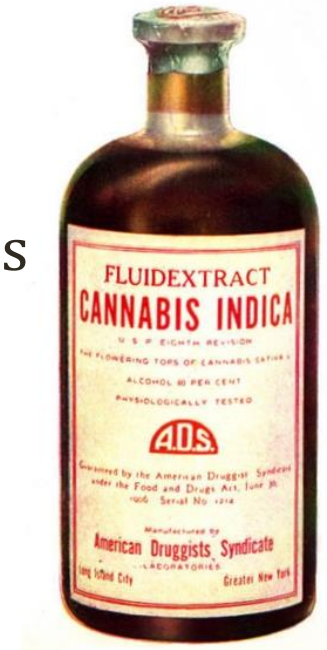
1611 Jamestown settlers bring Hemp to North America

1850 Marijuana listed in US pharmacopeia

1906 Pure Food and Drugs Act requires labeling of Medicines

1911 Massachusetts outlaws cannabis

1930 Pharmaceutical companies sell cannabis extract and cannabis cigarettes



https://commons.wikimedia.org/w/index.php?title=File:Drug_bottle_containing_cannabis.jpg&redirect=no

Propaganda Time. Reefer Maddness Original Trailerr 1936. YouTube. Youtube.com 3 Oct 2011, 9 Sept, 2015.

Marijuana becomes criminal

1937 The Marijuana Tax Act is passed

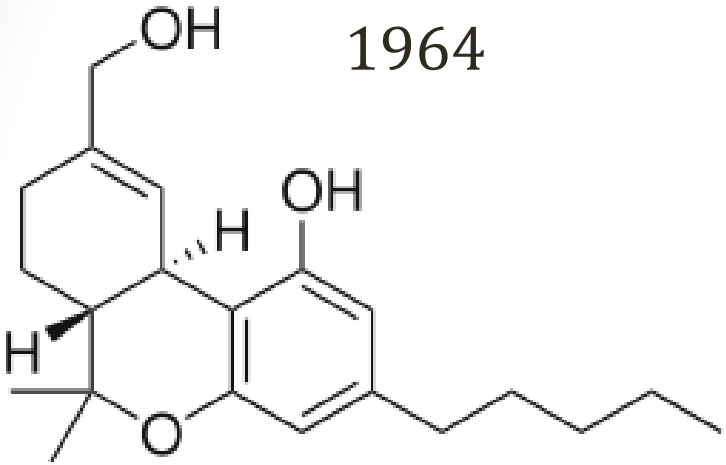
First marijuana seller convicted under federal law

1942 Marijuana is removed from US pharmacopeia

1951 Boggs Act sets 2-5 year minimum penalty

1956 Minimum penalty extended 2-10 years and maximum $20,000 fine

Research Regulation



1964

http://gallery.marihemp.com/public_domain_free/miss1

Break for questions

Schedule 1 controlled substance

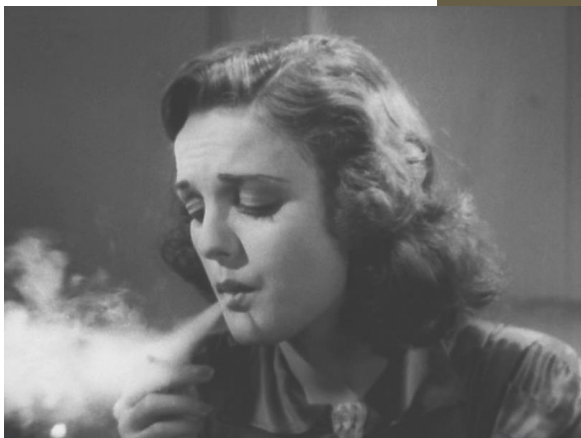
LSD MDMA Mescaline

Peyote Marijuana Heroin

Schedule 2 controlled substance

Cocaine Vicodin

Methamphetamine Oxycodone

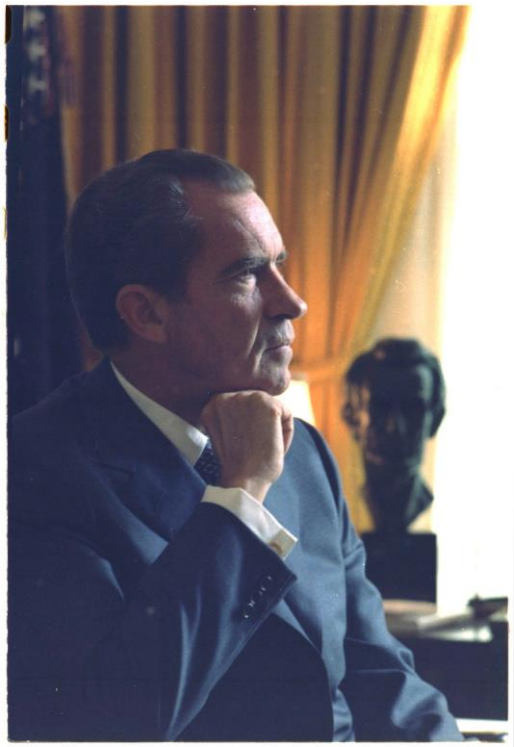


War on Drugs

1972 National Commission on Marijuana and Drug Abuse recommends decriminalizing marijuana

1973 DEA established

1978 Investigational New Drug Compassionate Use Program



Wikimedia Commons

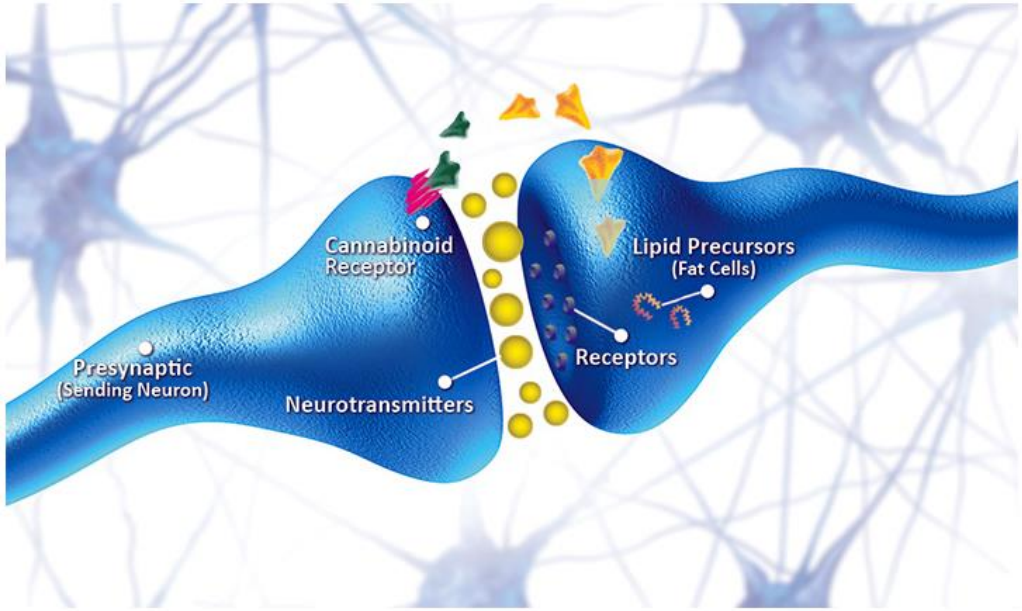
Investigational New Drug Compassionate Use Program

- Provides FDA-approved medical marijuana to patients
- Thirty patients enrolled at peak
- Shut down in 1992 as response to Bush administration's "get tough on drugs" initiative
- Four patients are still enrolled

Decriminalization ends.. for awhile

1980 Ronald Reagan is elected President

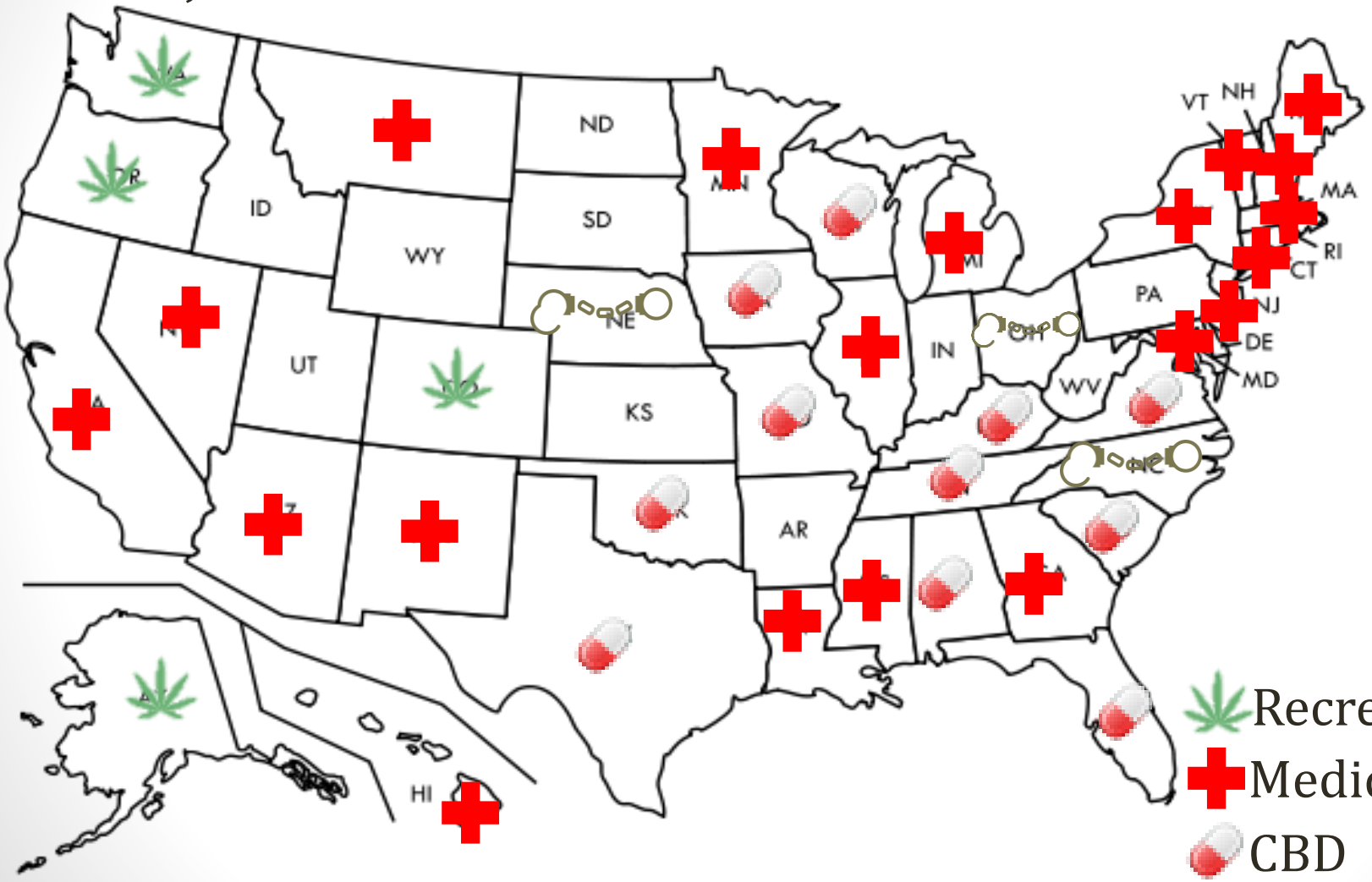
1990 and 1992 Endocannabinoids and cannabinoid receptors are discovered



http://www.reagan.utexas.edu/archives/photographs/photo.html

State Marijuana Laws

- Twenty-three states and Washington, DC, allow the use of marijuana to treat certain medical conditions.



https://commons.wikimedia.org/wiki/File:Blank_US_map_borders_labels.svg

Marijuana in Massachusetts

2008 Massachusetts votes to decriminalize marijuana

2012 63% of voters approved legalization of medical marijuana

2015 First dispensary opens

2015 Ballot question to end marijuana prohibition cleared

Break for questions

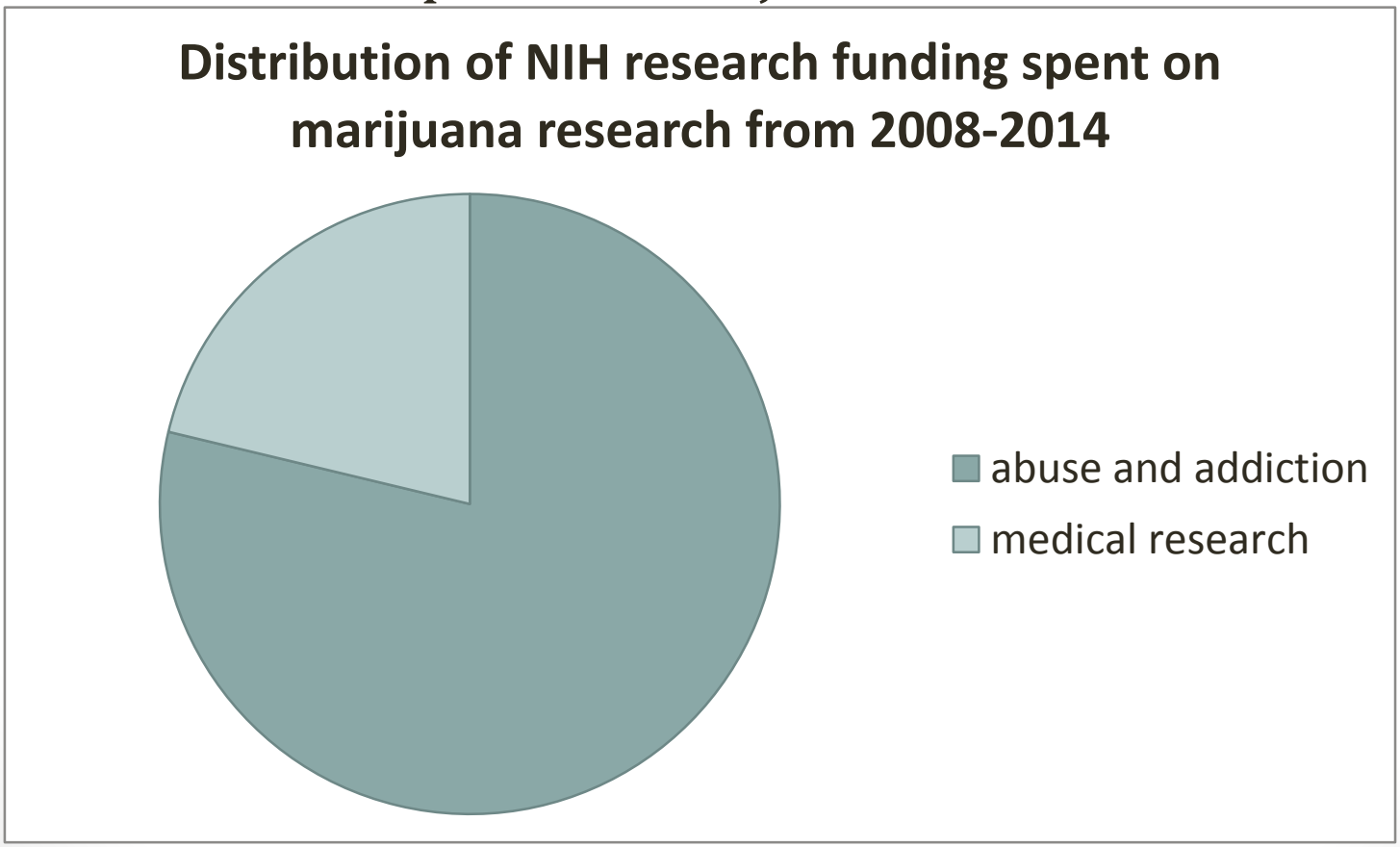
Marijuana use statistics

- 7% of Americans reported using marijuana within the past month.
- **7,100** new marijuana users every day in 2011
- 42% of Americans have reported trying marijuana
- 4.2 million people met the criteria for abuse of or dependence on this drug

Marijuana Research

- From 2008-2014 the NIH budget was approximately $120.6 billion.

- $1.4 billion was spent on marijuana research



Medical Marijuana Research

2014 28 active grants funded by NIH

Autoimmune disease	1
Inflammation	2
Pain	6
Psychiatric Disorder	2
Seizures	1
Withdrawal, Dependence	13

2015 49 new grants funded by NIH

115 clinical trials
72 marijuana abuse

The future of Marijuana research

- Rescheduling

Thank you!

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Harvard Medical School
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Division of Medical Sciences

The Harvard Graduate School of Arts and Sciences (GSAS)

The Harvard Graduate Student Council (GSC)

The Harvard/MIT COOP

NIDA process

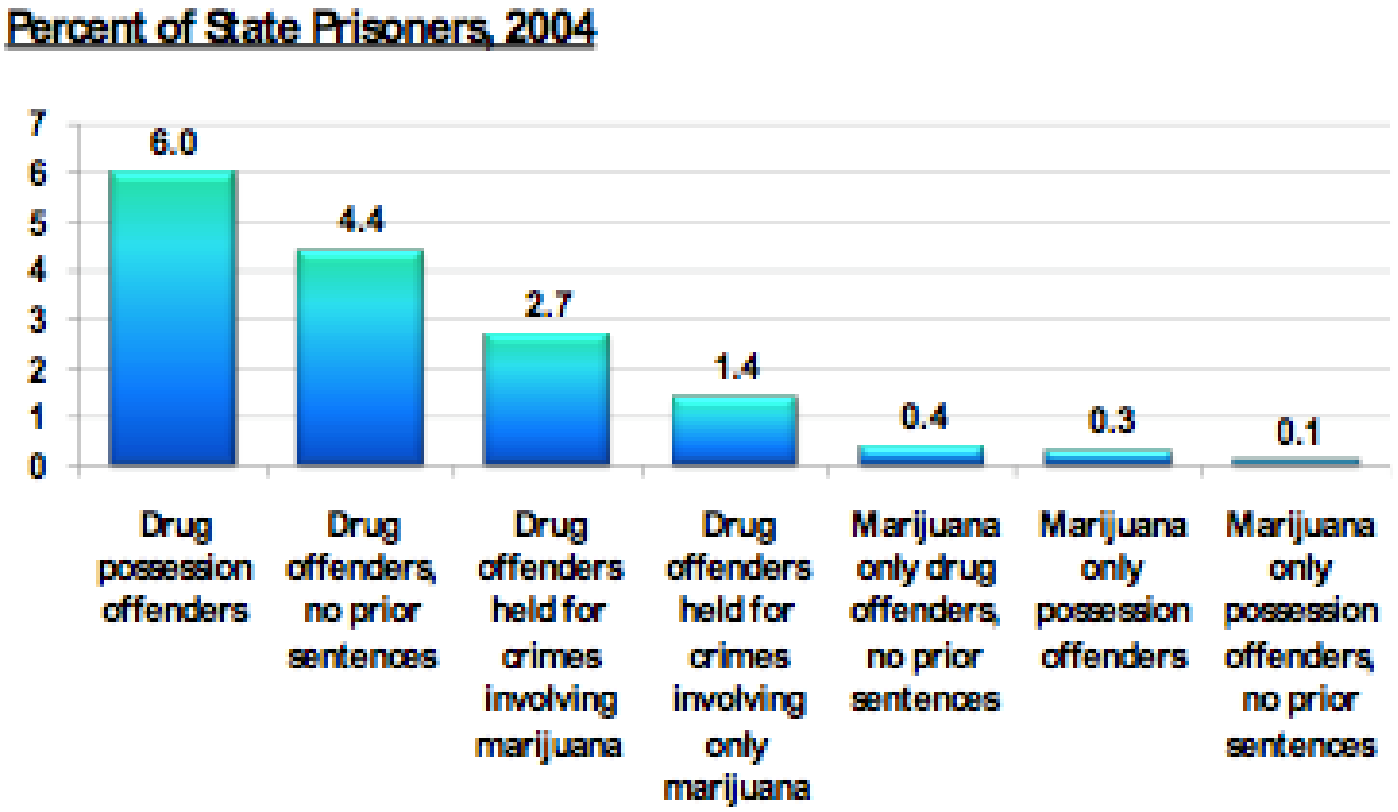
- NIH funded projects
  - Demonstrate scientific validity and ethical soundness through NIH review
  - Active-status Investigational New Drug application
  - A DEA registration for marijuana

- Non- NIH funded Human research projects
  - Demonstrate scientific validity and ethical soundness through FDA Investigational New Drug process
  - A DEA registration for marijuana

- Contact NIDA to place an order

E1

Drug Possession Offenders in State Prisons



Source: Bureau of Justice Statistics, 2004 *Survey of Inmates in State Correctional Facilities*. Unpublished special tabulations (February 2006).

12/2010