



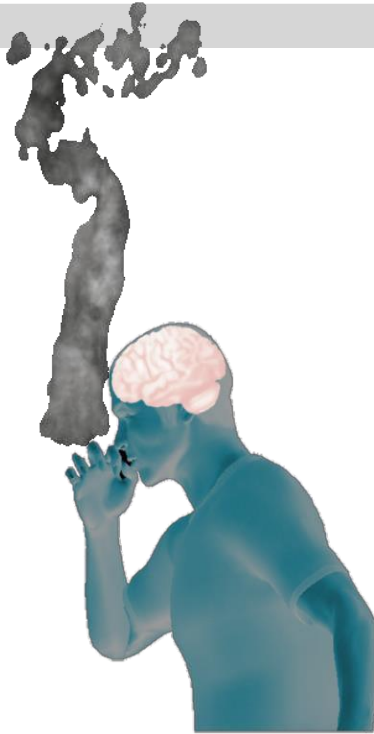
**INTER-AMERICAN DRUG ABUSE  
CONTROL COMMISSION  
CICAD**

Secretariat for Multidimensional Security

**SIXTY-FIFTH REGULAR SESSION OF CICAD  
May 8 - 10, 2019  
Buenos Aires, Argentina**

**OEA/Ser.L/XIV.1.65  
CICAD/doc.2468/19  
6 May 2019  
Original: English**

**MARIJUANA AND MEDICINE**



# Marijuana and Medicine



**OAS** | More rights  
for more people



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Harvard Medical School  
Department of Psychiatry  
McLean Hospital



Nations at crossroad

Nations at crossroad



# Cannabinoid System in Body



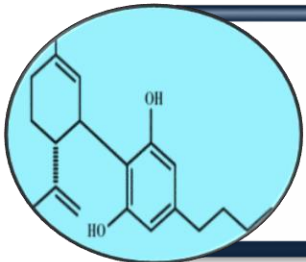
## Marijuana and the Brain



## How are Medicines Assessed?



## Marijuana as Medicine



# Cannabinoids as Medicine: the future

# Cannabinoid System in the Body

## CB1 receptors

### BRAIN

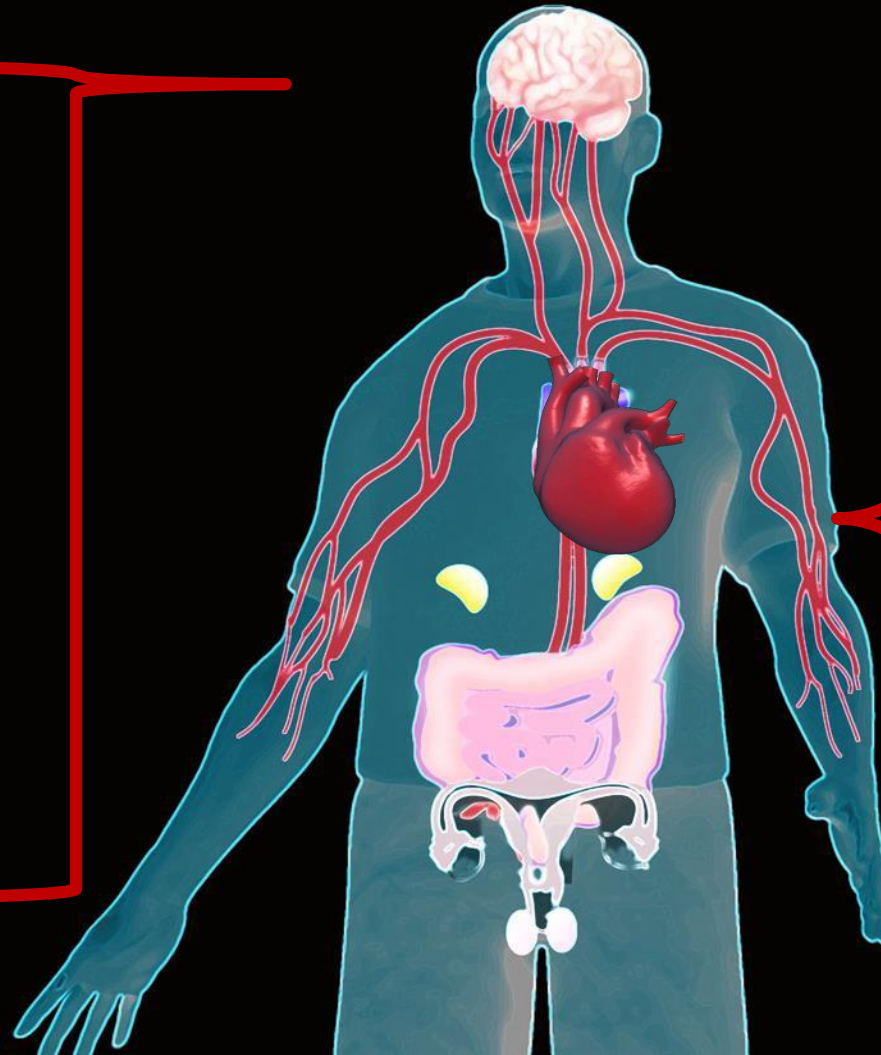
Heart  
Pancreas  
Muscle  
Testis, ovaries  
Uterus  
Prostate  
Vascular tissue  
Immune cells

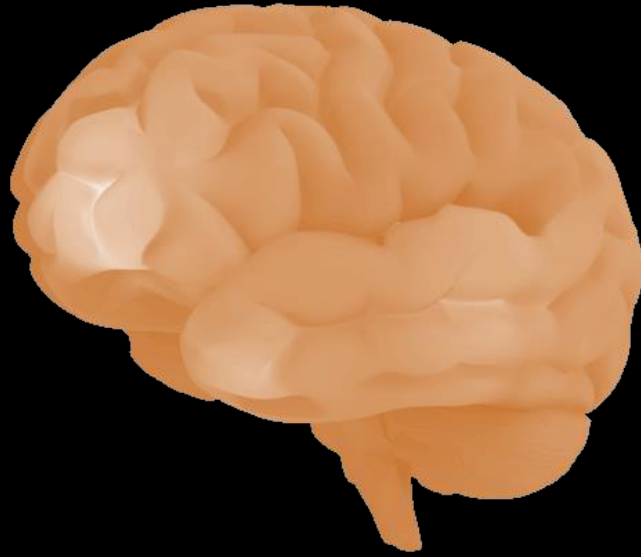
## CB2 receptors

### BLOOD CELLS

### IMMUNE CELLS

Brain  
Heart  
Adrenal  
Intestinal tract  
Pancreas  
Bone  
Smooth muscle  
Reproductive organs





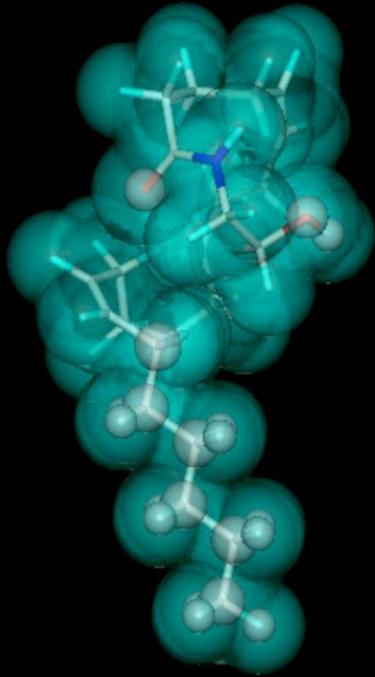
# Marijuana and the Brain



# The Brain Makes Cannabinoids

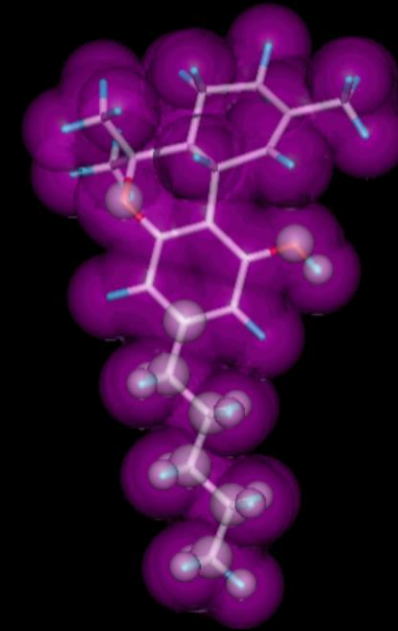
## THC Is an “Imposter” of Brain Cannabinoids

Made by the brain



**Anandamide**

Made by marijuana



**THC**

# How Are Medications Approved?





# Basic Criteria for a Medicine

**Pure?**

**Safe?**

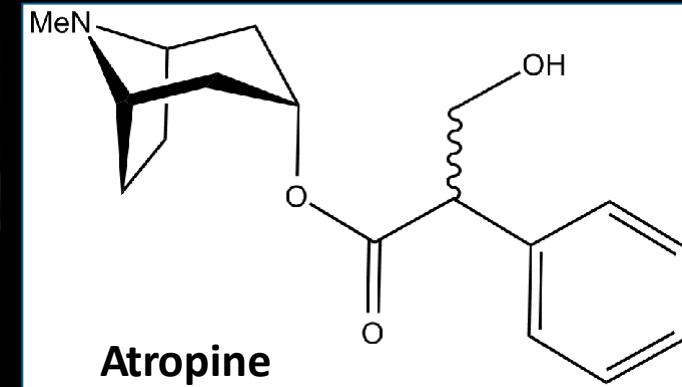
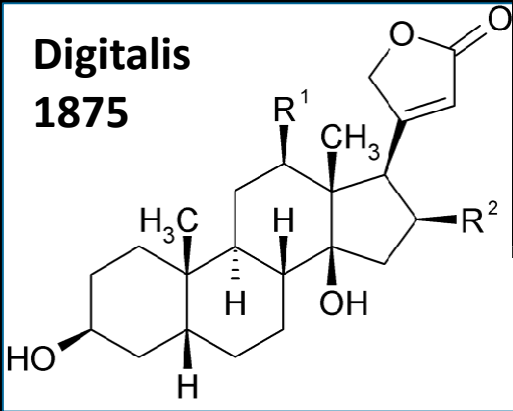
**Effective?**

# 1. Randomized Clinical Trials



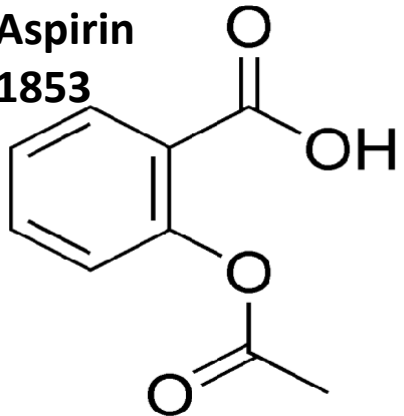
## 2. Pure Products Isolated from Plants

**Digitalis**  
1875

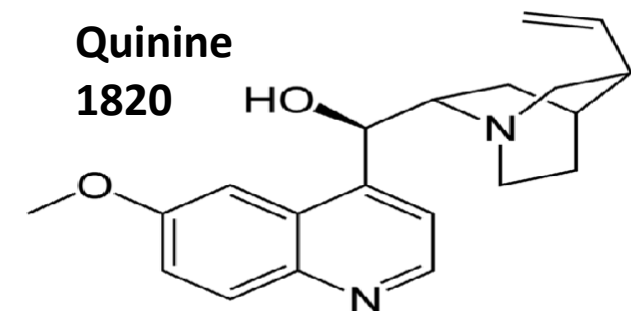


- Highly purified and defined
- Treat specific illness
- Mechanism of action
- Controlled, consistent, regulated doses
- Variations to improve drug possible

**Aspirin**  
1853



**Quinine**  
1820







# Marijuana and Medicine

**Can Marijuana  
be Approved as  
a Drug?**



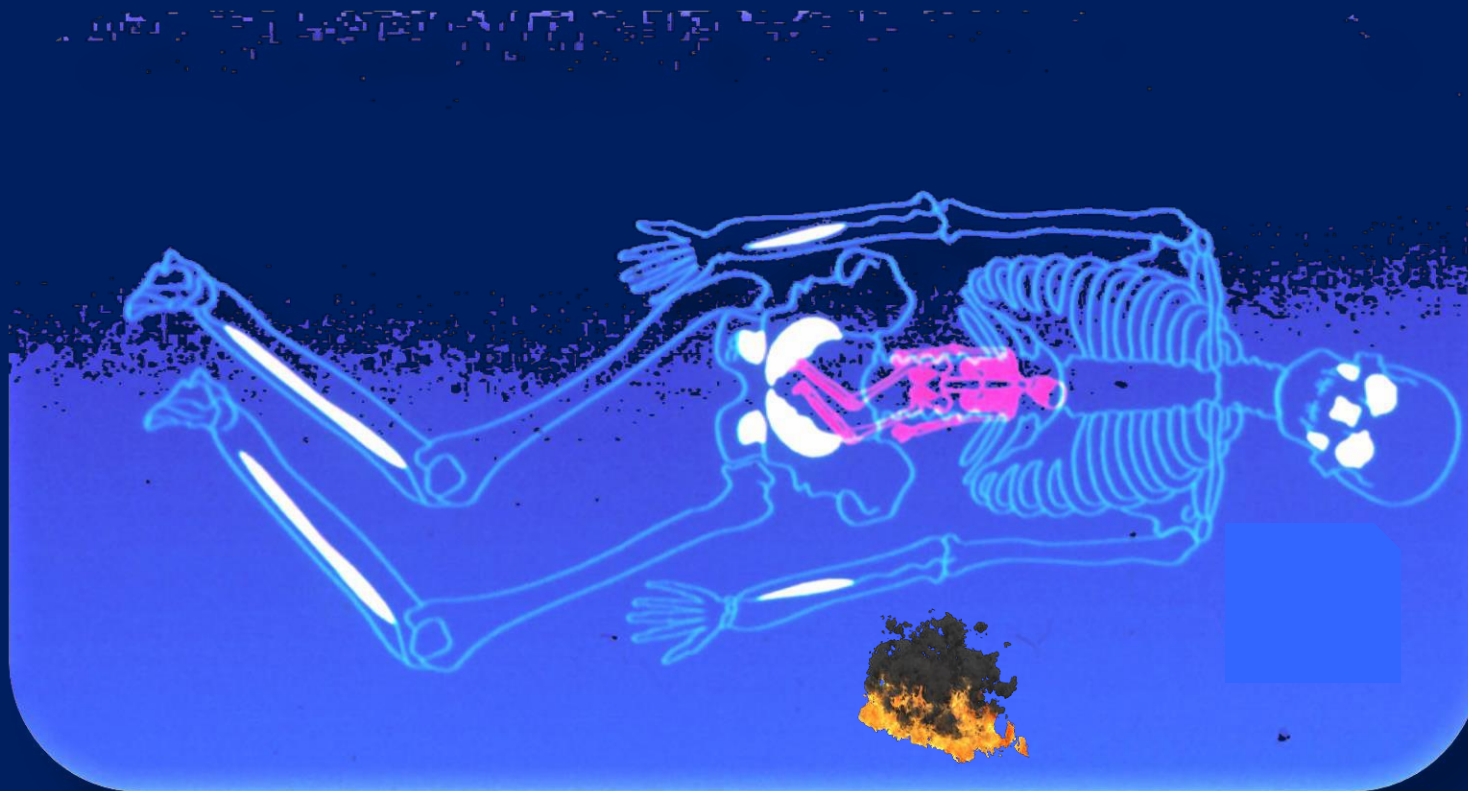
**Is Marijuana  
Effective in  
Medical  
Conditions?**



**Is Marijuana  
Safe?**

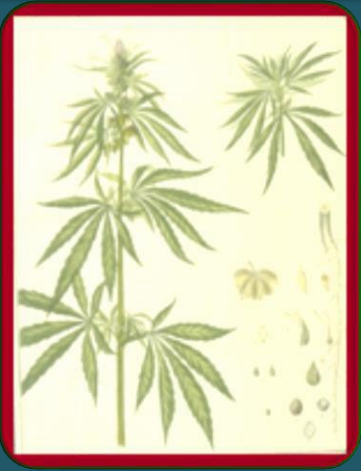
# **Can Marijuana be Approved as a Medicine?**

# Marijuana as a Medicine

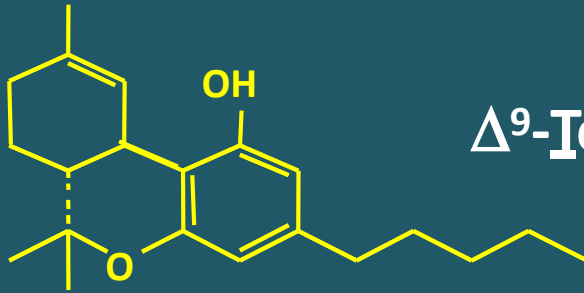


Sources: Zias J, Stark H, Sellgman J, Levy R, Werker E, Breuer A, Mechoulam R. Early medical use of cannabis. *Nature*. 1993 May 20;363(6426):215; Brownstein MJ, A brief history of opiates, opioid peptides, and opioid receptors. *Proc. Natl. Acad. Sci. USA* Vol. 90, pp. 5391-5393, June 1993. Helen Askitopoulou, Ioanna A Romoutski, and Elini Konsolaki, "Archaeological Evidence of the Use of Opium in the Minoan World" in *International Congress Series* 1242, (December 2002): 23-29

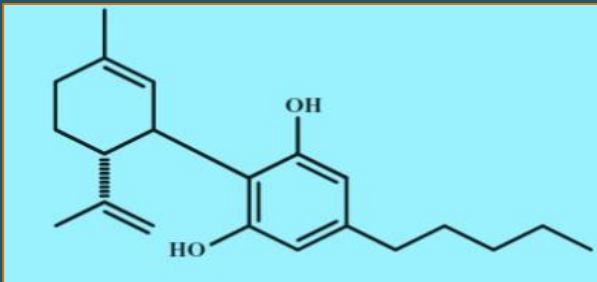
# Marijuana is not a Pure Compound



Marijuana contains > 700 chemicals  
104 Phytocannabinoids made by plant



$\Delta^9$ -Tetrahydrocannabinol (THC) is main chemical



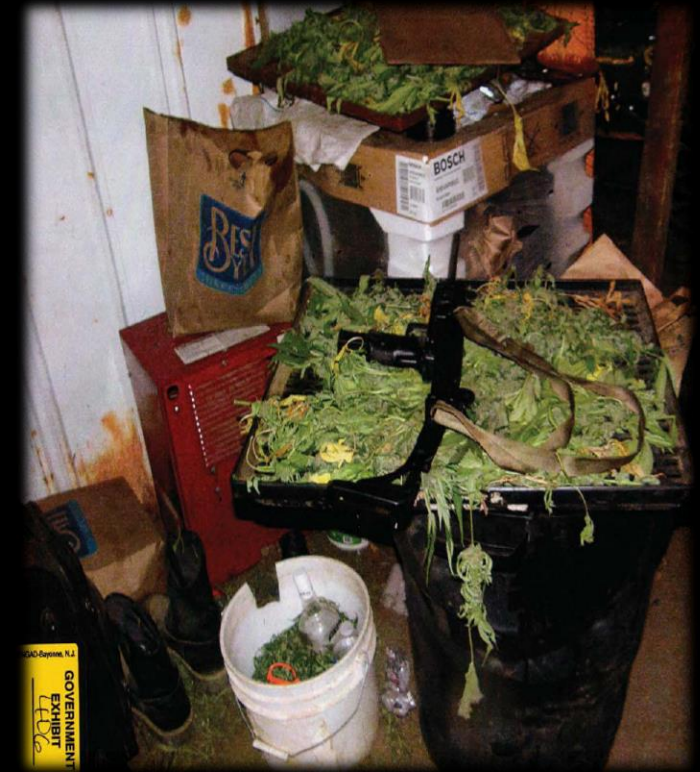
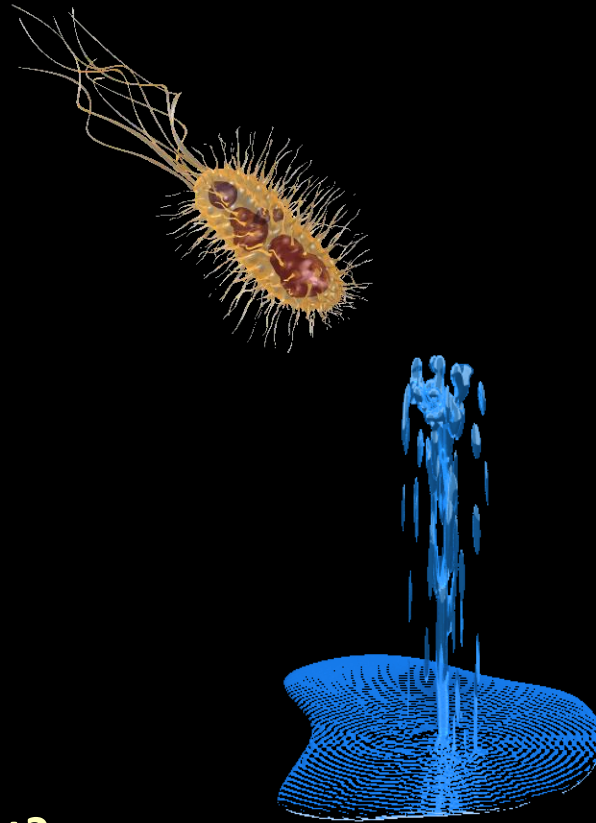
Cannabidiol is second most important cannabinoid



# Is Marijuana Pure: not Contaminated with Microbes, Chemicals?

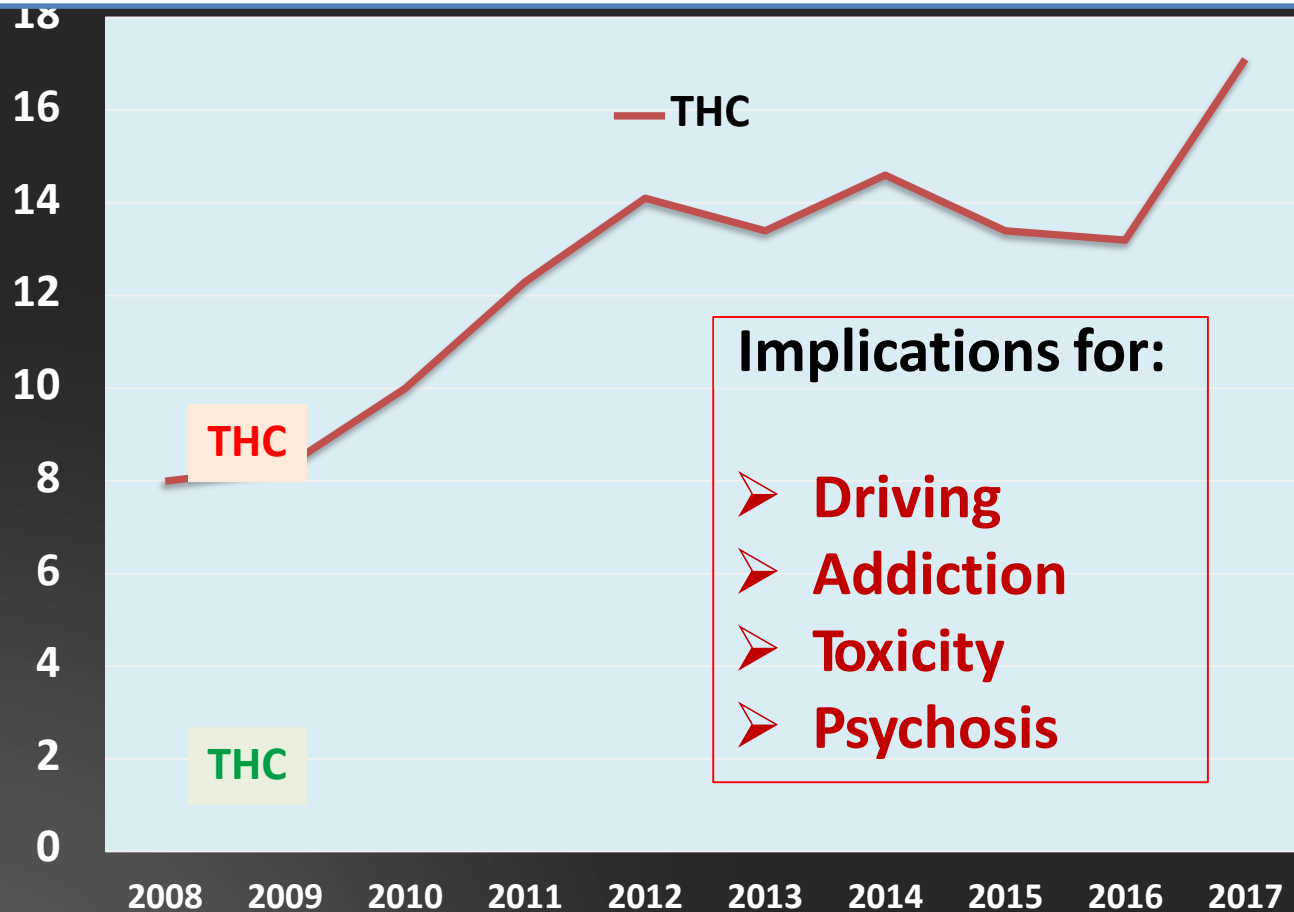
## Variables

- Soil
- Water
- Temperature
- Bacteria
- Viruses
- Animal Waste
- Insecticides
- Pesticides
- Herbicides
- Insects
- Toxic Chemicals
- Active Compounds
- Heavy Metals
- Drug Content of plant?

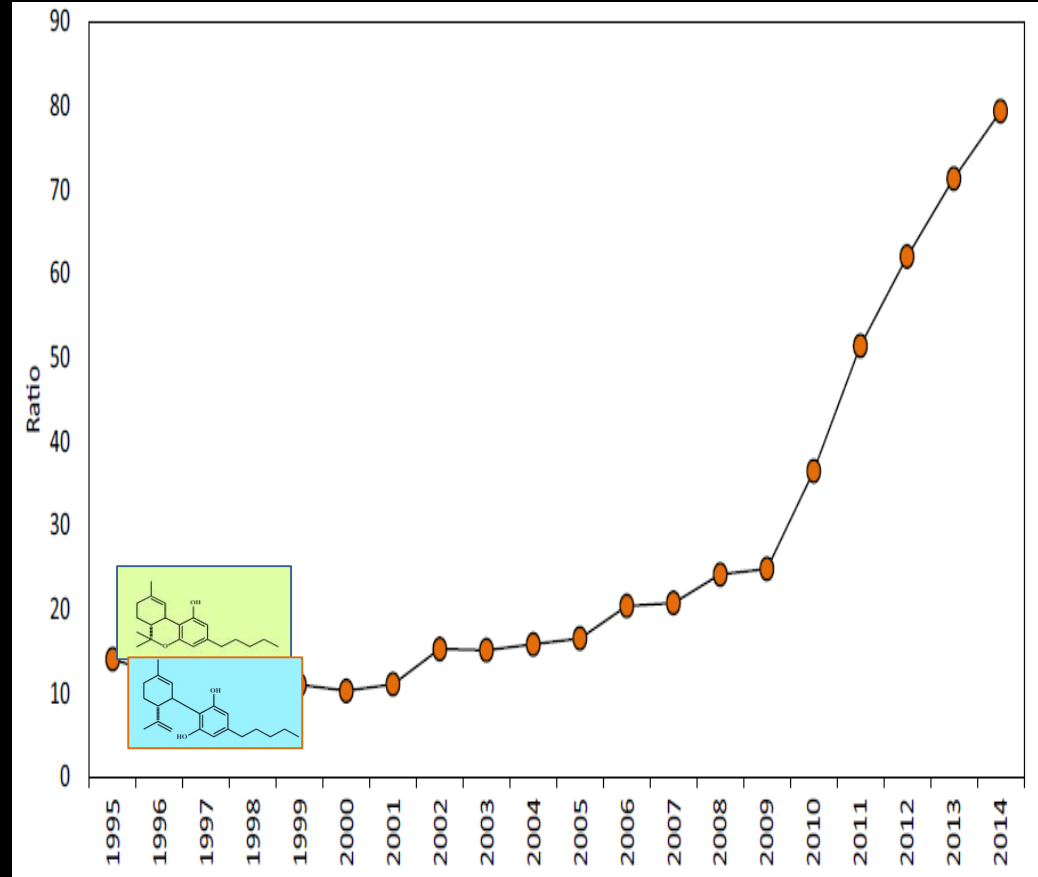


# Safe and Effective Dose Range?

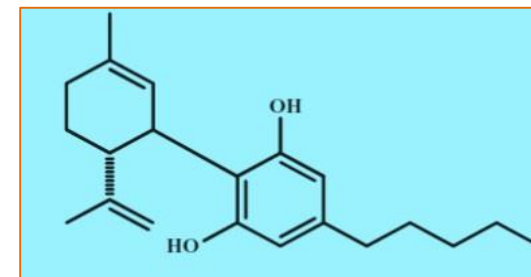
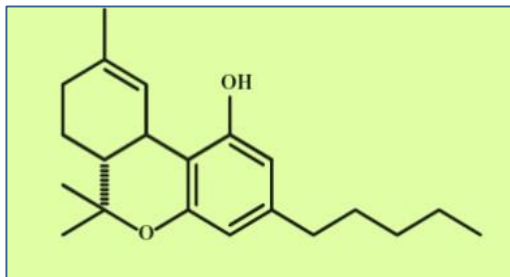
## THC dose is rising



## THC:CBD Ratio Falling



# THC and CBD Differ Markedly



EFFECT		CBD
Addiction	YES	NO For treatment?
Intoxication	YES	NO (anti?)
Impairs cognition	YES	NO (anti?)
Anxiety	YES	Anxiolytic (?)
Psychotomimetic	YES	Anti-psychotic (?)
Seizures	YES and NO	Anti-convulsant
Receptors	CB1, CB2 partial agonist, others	Allosteric antagonist CB1,CB2, Δ,μ, FAAH (?), TRPV-1,2(?) 5-HT1A

# Is Marijuana Effective?

# Effective AND Safe for a Specific Disease? No

## CALIFORNIA

Cancer, glaucoma, HIV/AIDS, AIDS, anorexia, arthritis, cachexia, cancer, chronic pain, glaucoma, migraine, persistent muscle spasms, including spasms associated with multiple sclerosis, seizures, including seizures associated with epilepsy, severe nausea; Chronic pain, persistent muscle spasms, HIV/AIDS, Chronic pain, AIDS, Hepatitis C, Crohn's disease,

Alzheimer's disease, cachexia or wasting syndrome, severe, and chronic pain, severe nausea, seizures (including epilepsy), severe or persistent muscle spasms (including multiple sclerosis), PTSD

## ILLINOIS

40 chronic diseases and conditions: cancer, glaucoma, positive status for HIV/AIDS, hepatitis C, amyotrophic lateral sclerosis, Crohn's disease, agitation of Alzheimer's disease, cachexia/wasting syndrome, muscular dystrophy, severe fibromyalgia, spinal cord disease (not limited to arachnoiditis), Tarlov cysts, hydromyelia syringomyelia, Rheumatoid arthritis, fibrous dysplasia, spinal cord injury, traumatic brain injury and post concussion syndrome, Multiple Sclerosis, Arnold-Chiari malformation and Syringomyelia, Spinocerebellar Ataxia (SCA), Parkinson's Disease, Tourette Syndrome, Myoclonus, Dystonia, Reflex Sympathetic Dystrophy, RSD (Complex Regional Pain Syndromes Type I), Causalgia, CRPS (Complex Regional Pain Syndrome Type II), Neurofibromatosis, Chronic inflammatory Demyelinating Polyneuropathy, Chronic Inflammatory Demyelinating Polyneuropathy, Sjogren's Syndrome, Lupus, Interstitial Cystitis, Myasthenia Gravis, Hydrocephalus, nail-patella syndrome or residual limb pain; or the treatment of these conditions."

## CONNECTICUT

Cancer, glaucoma, positive status for HIV/AIDS, Parkinson's disease, multiple sclerosis, damage to the nervous tissue of the spinal cord with objective neurological indication of intractable spasticity, epilepsy, cachexia, wasting syndrome, Crohn's disease, posttraumatic stress disorder, or... any medical condition, medical treatment or disease approved by the Department of Consumer Protection..

# Is Marijuana Effective for a Specific Disease?

- Andrade C. Cannabis and Neuropsychiatry, 2: The Longitudinal Risk of Psychosis as an Adverse Outcome. J Clin Psychiatry. 2016 Jun;77(6):e739-42.
- Andrae MH, et al., Inhaled Cannabis for Chronic Neuropathic Pain: A Meta-analysis of Individual Patient Data. J Pain. 2015 Dec;16(12):1221-32
- Belendiuk KA, Baldini LL, Bonn-Miller MO. Narrative review of the safety and efficacy of marijuana for the treatment of commonly state-approved medical and psychiatric disorders. Addict Sci Clin Pract. 2015 Apr 21;10(1):10.
- Benbadis SR, et al, Medical marijuana in neurology. Expert Rev Neurother. 2014 ec;14(12):1453-65.
- Farrell M., et al, Should doctors prescribe cannabinoids? BMJ 2014; 348: pp. g2737
- Gibbs M, et al, Cannabis use and mania symptoms: a systematic review and meta-analysis. J Affect Disord. 2015 Jan 15;171:39-47
- Gloss D, Vickrey B. Cannabinoids for epilepsy. Cochrane Database Syst Rev. 2014 Mar 5;3:CD009270.
- Harrison AM, et al, Systematic Review of the Use of Phytochemicals for Management of Pain in Cancer Therapy. Biomed Res Int. 2015;2015:506327.

Dementia  
Neurological diseases  
Multiple sclerosis  
Psychiatric disorders  
Epilepsy

## EVIDENCE FOR MEDICAL MARIJUANA WEAK

- Lutge EE, et al, The medical use of cannabis for reducing morbidity and mortality in patients with HIV/AIDS. Cochrane Database Syst Rev. 2013
- Martín-Sánchez E, et al, . Systematic review and meta-analysis of cannabis treatment for chronic pain. Pain Med. 2009 Nov;10(8):1353-68.
- McLoughlin BC, et al Cannabis and schizophrenia. Cochrane Database Syst Rev. 2014 Oct 14;(10):CD004837.
- Phillips TJ, et al. Pharmacological treatment of painful HIV-associated sensory neuropathy: a systematic review and meta-analysis of randomised controlled trials. PLoS One. 2010 Dec 28;5(12):e14433.
- Richards BL, et al Neuromodulators for pain management in rheumatoid arthritis. Cochrane Database Syst Rev. 2012 Jan 18;1:CD008921
- van den Elsen GA, et al., Efficacy and safety of medical cannabinoids in older subjects: a systematic review. Ageing Res Rev. 2014 Mar;14:56-64.
- Whiting PF et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA. 2015 Jun 23-30;313(24):2456-73
- Wilkinson ST, et al, A Systematic Review of the Evidence for Medical Marijuana in Psychiatric Indications. J Clin Psychiatry. 2016 Aug;77(8):1050-64.
- Yadav V, , et al., Summary of evidence-based guideline: complementary and alternative medicine in multiple sclerosis: report of the guideline development subcommittee of the American Academy of Neurology. Neurology. 2014 Mar 25;82(12):1083-92.

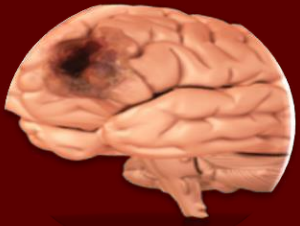
Arthritis  
Chronic neuropathic pain  
Medical, psychiatric illnesses  
Movement disorders  
AIDS  
Bowel diseases

**Is Marijuana Safe?**

**What are side effects?**



# Heavy Marijuana Use: Risks for Young People



**B**rain  
changes



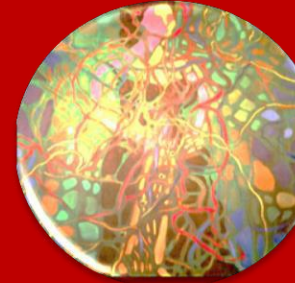
**A**ddiction



**D**eficits



**A**motivation



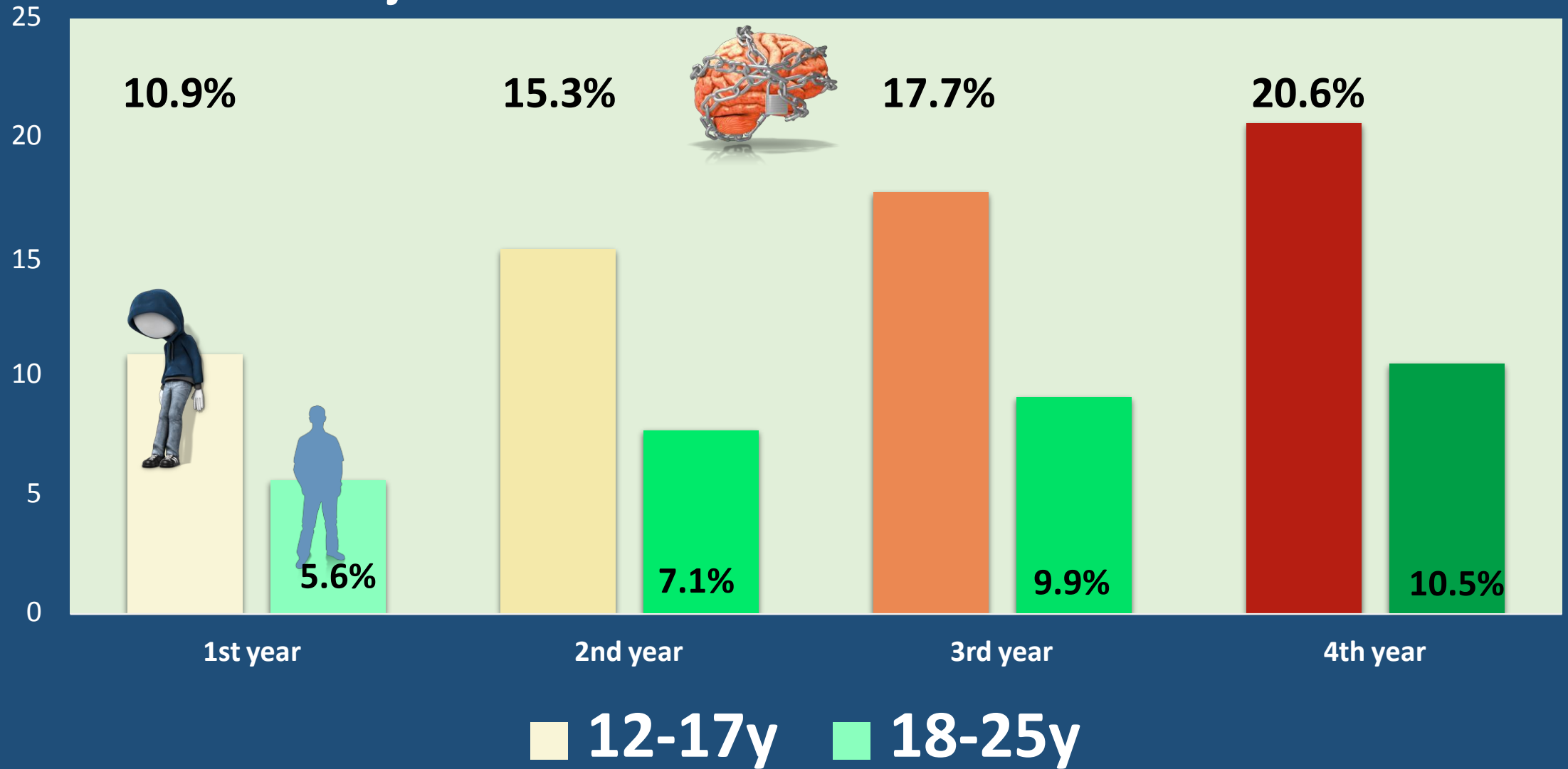
**P**sychosis



**S**afety

One Month of Marijuana Abstinence in Adolescents and Young Adults is Associated with Improved Memory (Schuster, J Clinical Psychology, 2018)

## % Marijuana Use Disorder After First Year of Use



Han B, Compton WM, Blanco C, Jones CM. Time since first cannabis use and 12-month prevalence of cannabis use disorder among youth and emerging adults in the United States. *Addiction*. 2019 Apr;114(4):698-707

12-month prevalence of cannabis use disorder among US youth aged 12-17 and emerging adults aged 18-25 varied by time since first cannabis use. (n=100,000 12-25; Past 12-month cannabis use disorder was assessed using DSM-IV criteria)

# Marijuana Impairs Brain Function



## Impaired learning, memory

- Verbal IQ; Memory; Errors
- Word associations
- Perseveration



## Impaired motor function

- Balance, coordination
- Sports, driving, motor



## Impaired decision making

- Risky sexual behavior (STDs)
- Driving alone or with impaired driver
- Impaired executive function

Crean RD, Crane NA, Mason BJ. *An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions*. Journal of Addiction Medicine 2011;5:1-8;Pope HG Jr, et al. Early-onset cannabis use and cognitive deficits: what is the nature of the association? Drug Alcohol Depend. 2003 Apr 1;69(3):303-10.; Pope and Yurgelun-Todd (1996) Solowij et al. 2002, Fletcher et al., 1996,McHale and Hunt,2008; Porter, & Frampton, 2007 et al., 2002; Harvey et al, 2007; Solowij & Pesa, 2010 ; Novaes et al. 2008; Battisti et al., 2010 ; Schweinsburg A. D., Brown S. A., Tapert S. F. The influence of marijuana use on neurocognitive functioning in adolescents. Curr Drug Abuse Rev 2008; 1: 99; Lisdahl K. M., Wright N. E., Medina-Kirchner C., Maple K. E., Shollenbarger S. Considering cannabis: the effects of regular cannabis use on neurocognition in adolescents and young adults. Curr Addict Rep 2014; 1: 144–56.



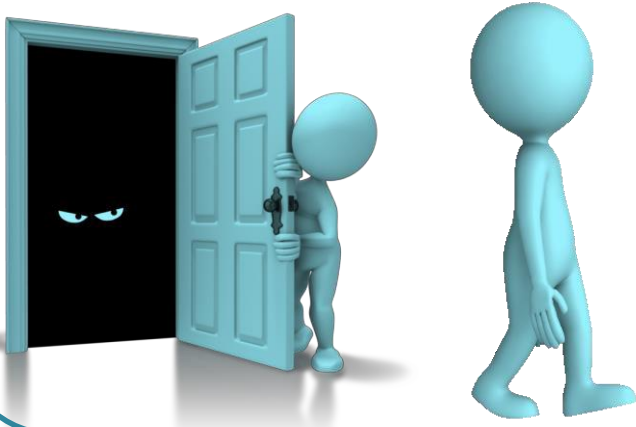


**Marijuana is a  
Hazard for  
Mental Health**

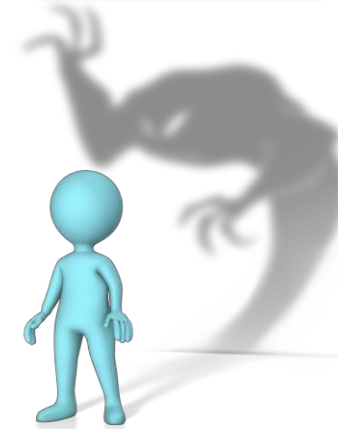


# THC and Psychosis

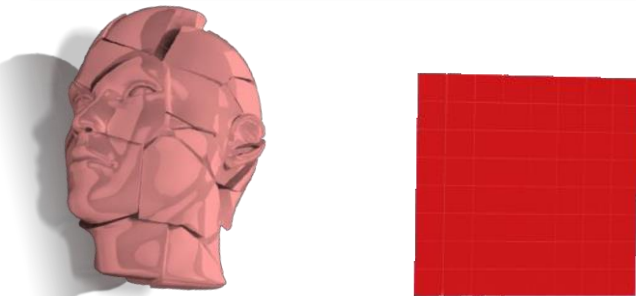
## Suspiciousness



## Paranoia



## Conceptual disorganization



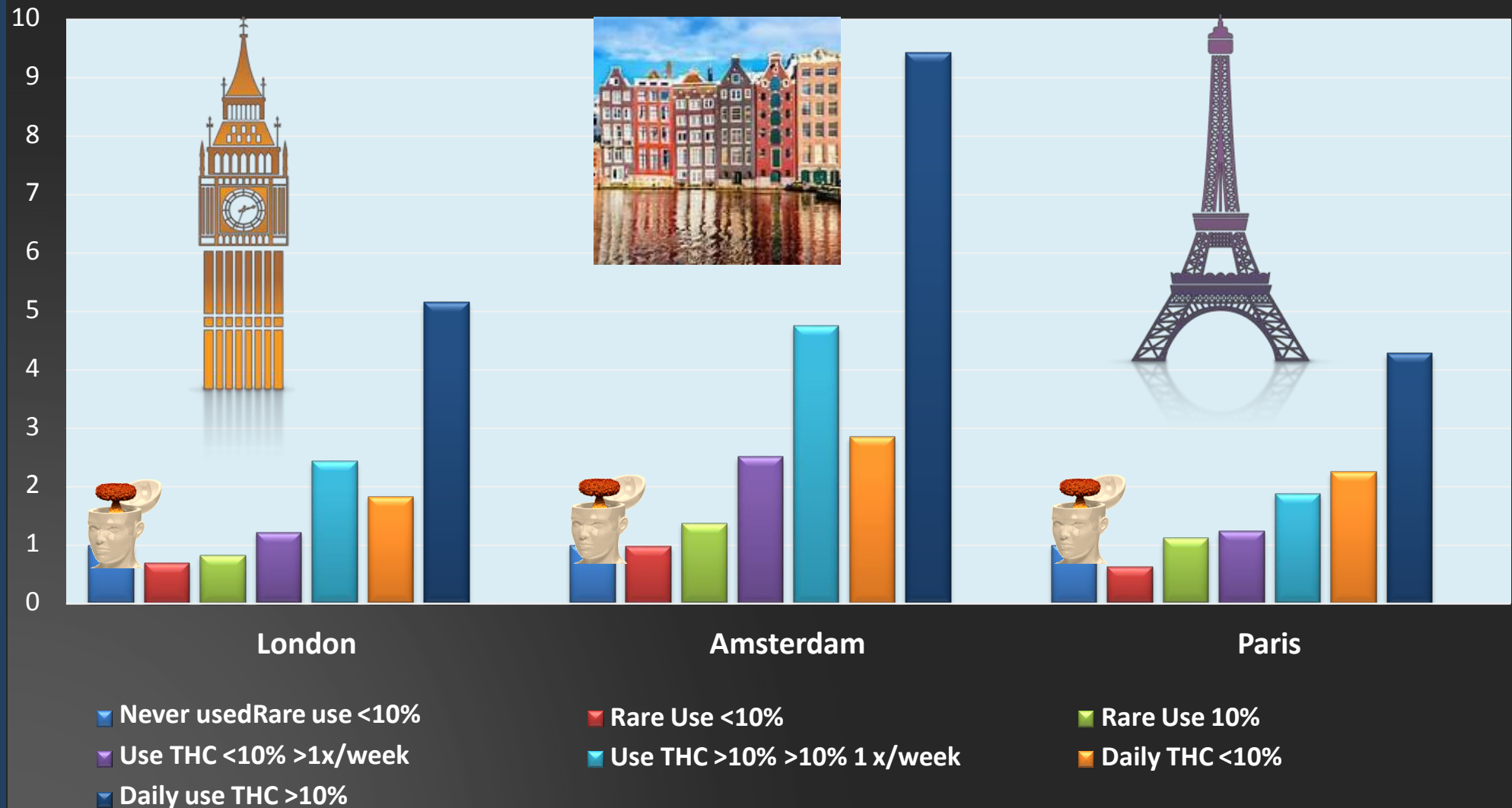
## Perceptual alterations



# Psychotic Disorders as Function of THC dose, Frequency of Use: A tale of 3 cities

The contribution of  
cannabis use to  
variation in the  
incidence of psychotic  
disorder across Europe  
(EU-GEI):

Di Forti et al  
[www.thelancet.com/p](http://www.thelancet.com/p)  
sychiatry Published  
online March 19, 2019





# If Marijuana is Recommended It Should Be Held to Medical Standards

Approved Medications	Marijuana
Well-studied, national standards	No comparable evidence
Prescribed by clinicians	Recommended by bud-tenders
Quality evidence required	No quality evidence required
Products regulated dose, purity, route	Unregulated smoke, vapors, oils, edibles, creams

Caputi TL, Humphreys K. Medical marijuana users are more likely to use prescription drugs medically and non-medically. *J Addict Med*. 2018;12(4):295-299.

Bonn-Miller MO, Loflin MJE, Thomas BF, Marcu JP, Hyke T, Vandrey R. Labeling accuracy of cannabidiol extracts sold online. *JAMA*. 2017;318(17):1708-1709.



# Pure THC, CBD Approved for Medical Conditions

## NOT Marijuana For Any Form of Medical Condition

- **Dronabinol:** weight loss in AIDS; nausea for chemotherapy
- **Nabilone:** weight loss in AIDS; nausea with cancer chemotherapy
- **Syndros (dronabinol oral solution):** cancer and AIDS
- **Cannabidiol (CBD) Epidiolex:** rare childhood seizures
- **Sativex:** Europe, Canada

# Does Marijuana Fulfill Criteria?

**Purity: NO**

A specific medical condition to use marijuana **NO**

**Dose, Standard doses: NO**

What patients may benefit; tested in children **NO**

**Quality control: NO**

Reported adverse effects – acute and chronic **NO**

**Clinical trials: LIMITED**

How the drug should be taken (oral, intravenous?) **NO**

The safe drug dose for a specific medical condition **NO**

**Safety, side effects: NO**

How the drug is made (pill, liquid) **NO**

Active and inactive ingredients **NO**

The background of the slide features a warm, golden-brown color palette. At the top center, a bright, glowing sun emits several rays of light that fan out across the frame. Below the sun, two hands are positioned palms up, holding a realistic, dark grey human brain. The brain is the central focus, resting on the hands. The overall composition suggests a theme of care, protection, and the value of the human mind.

# **In Defense of our Brains The Repository of our Humanity**

**Bertha K Madras**