Talking to Patients about Cannabis Use

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Outline

1. The History & The Science
2. The Politics
3. The Research
4. The New Age

1. The History & The Science

World History

- 8,000 BC: hemp cultivation in Japan
- Mentioned in texts since 2,727 BC (China)
  - Assyrians (Middle East), Ancient Greeks, Romans, Egyptians, medieval Arab society
- Used for arthritis, pain, inflammation, “mothers and children,” and in religious ceremonies and funerals

Cannabis sativa from Vienna Dioscurides, AD 512

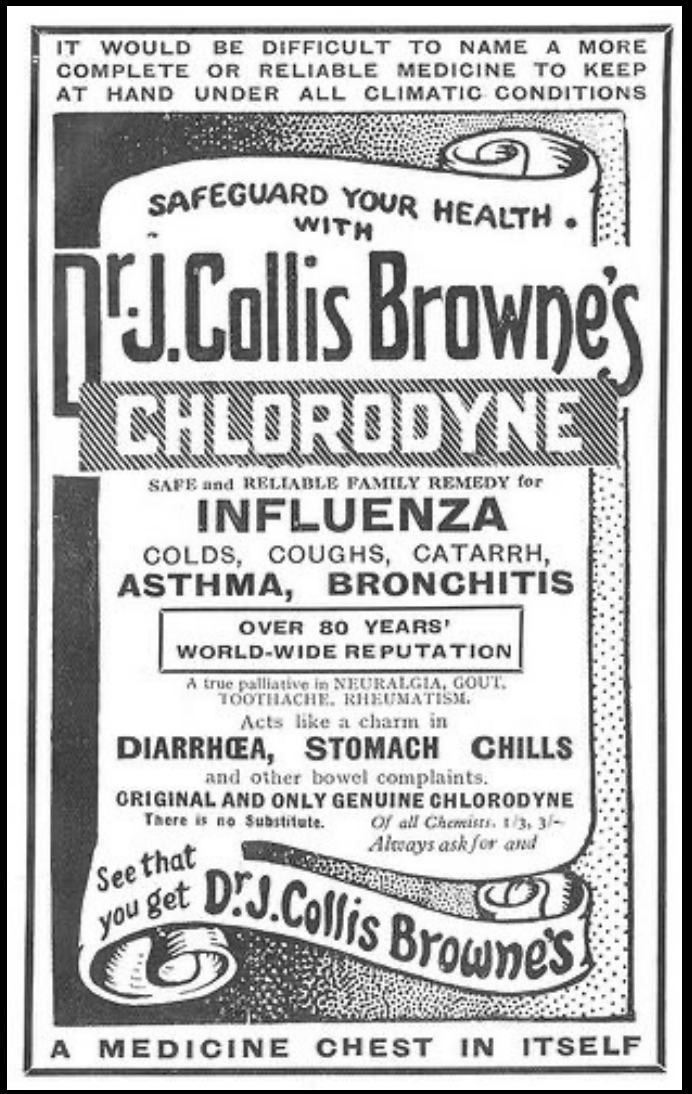
History in the U.S.

- Colonies were directed to grow hemp
- Widely used as a patent medicine in the late 1800s to early 1900s
- Listed in U.S. Pharmacopoeia 1851 - 1942

EXTRACTUM CANNABIS. *Extract of Hemp.*

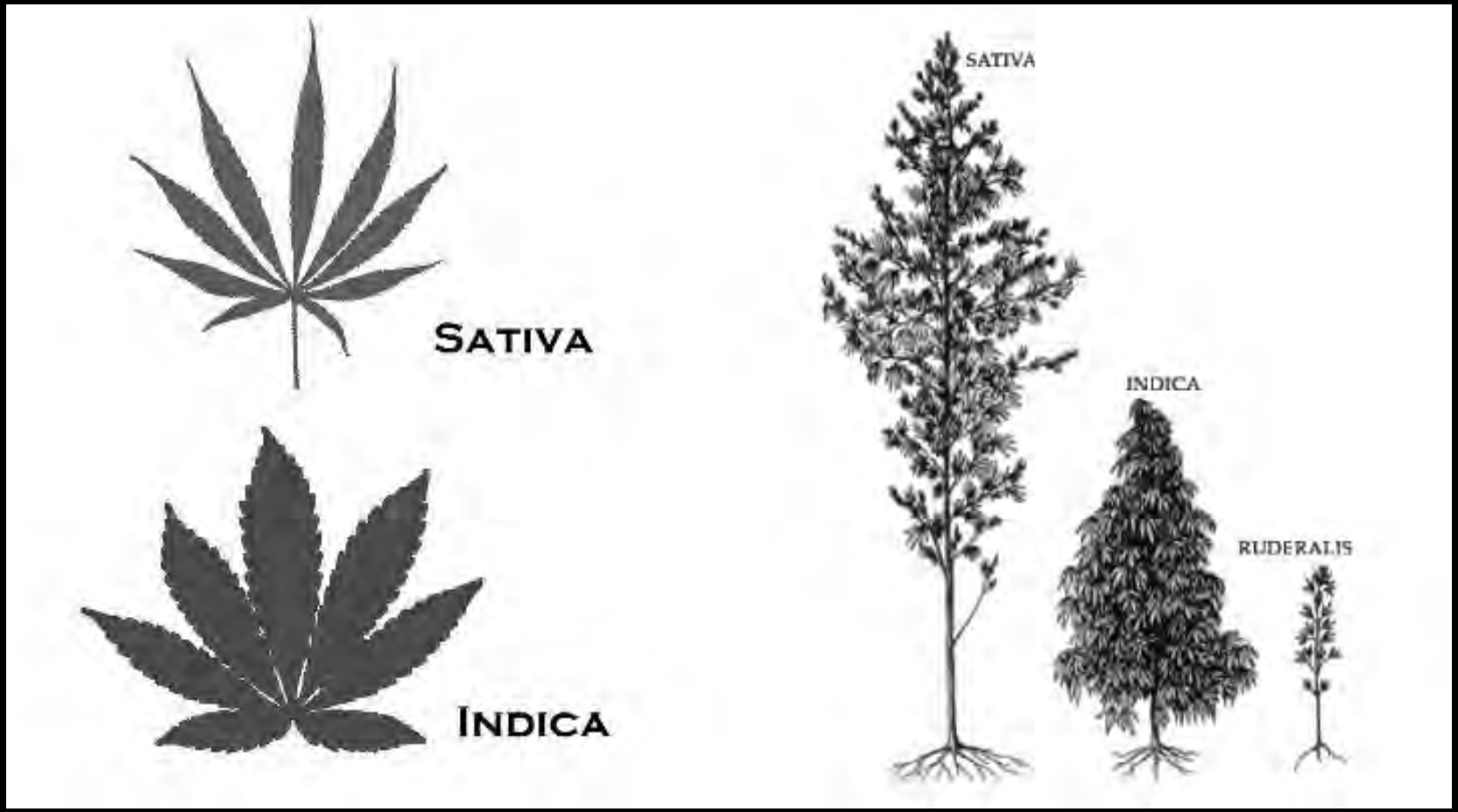
An alcoholic extract of the dried tops of Cannabis sativa—variety *Indica*.

U.S. Pharmacopoeia, 1851 (3rd Ed)



What's in a name?
Cannabis vs. Marijuana

Cannabis sativa



- *Cannabis sativa:* Equatorial countries (Columbia, Mexico)
- *Cannabis indica:* Subtropical countries (India, Pakistan)
- *Cannabis ruderalis:* Colder, northern regions (Russia, China)

Sativa

↑THC, ↓CBD

- "Head" high
- Energizing
- Increased alertness, creativity
- Reduces nausea
- Stimulates appetite

Indica

↓THC, ↑CBD

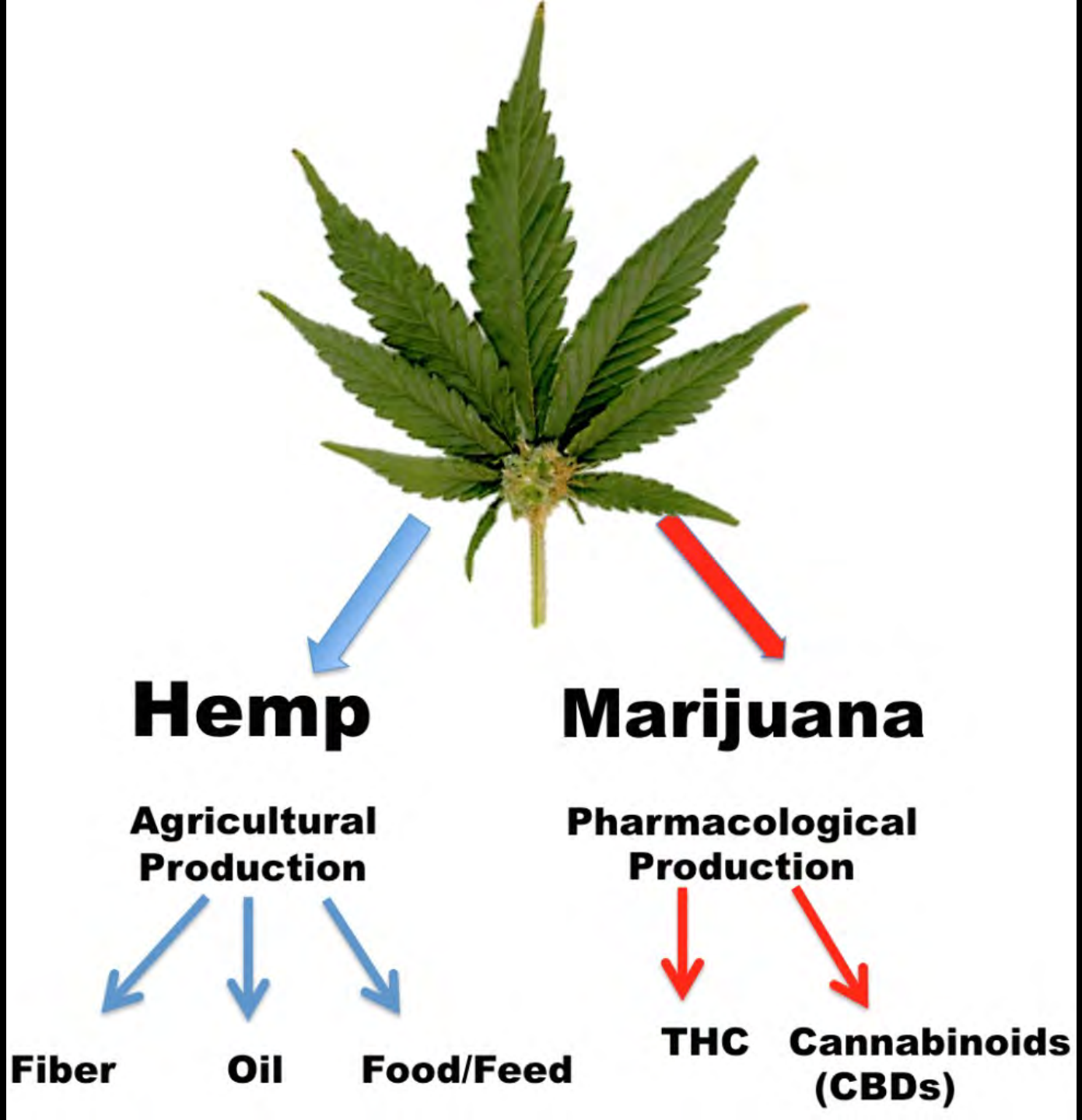
- "Body" high
- Muscle relaxant
- Pain relief
- Sleep aid
- Relieves anxiety
- Stimulates appetite

Ruderalis

↓THC, ↓CBD

- Autoflowering
- Bred with *Sativa* or *Indica* to minimize cultivator involvement

zambeza.com


Hemp
Marijuana
Agricultural Production
Pharmacological Production
Fiber
Oil
Food/Feed
THC
Cannabinoids (CBDs)

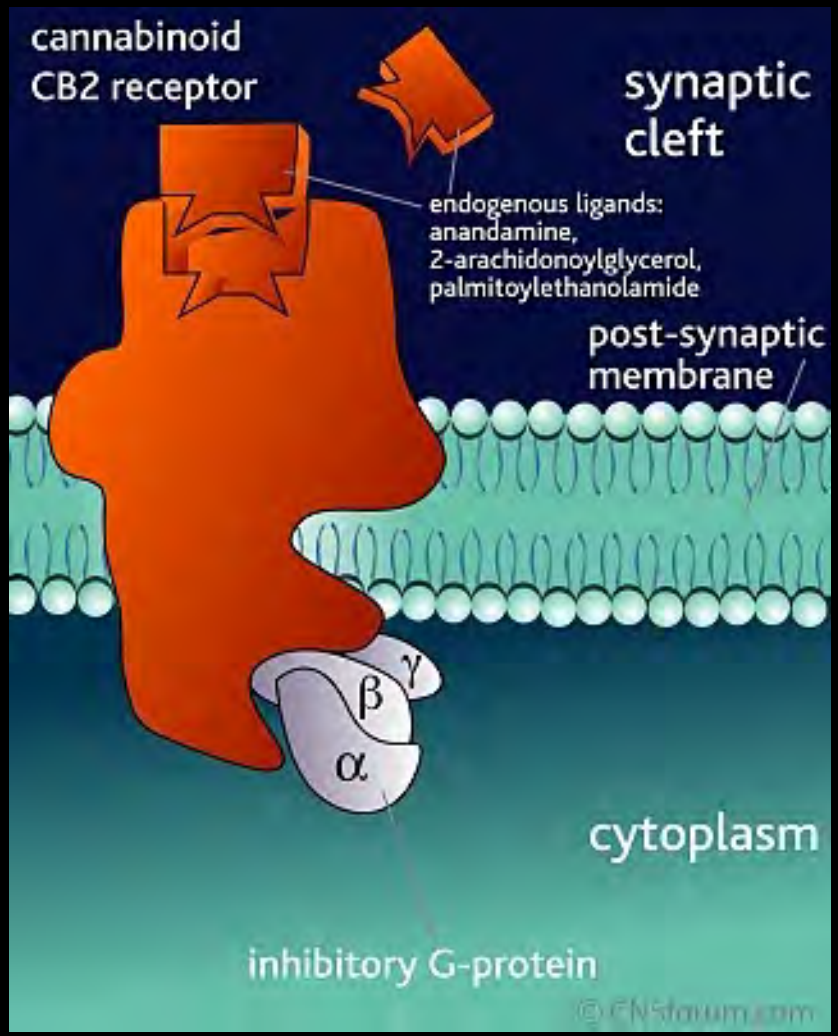
Industrial Hemp

↓↓THC, ↑CBD

- Nearly impossible to extract the THC
- Sustainable, durable
- Agricultural Improvement of 2018: removed hemp from CSA

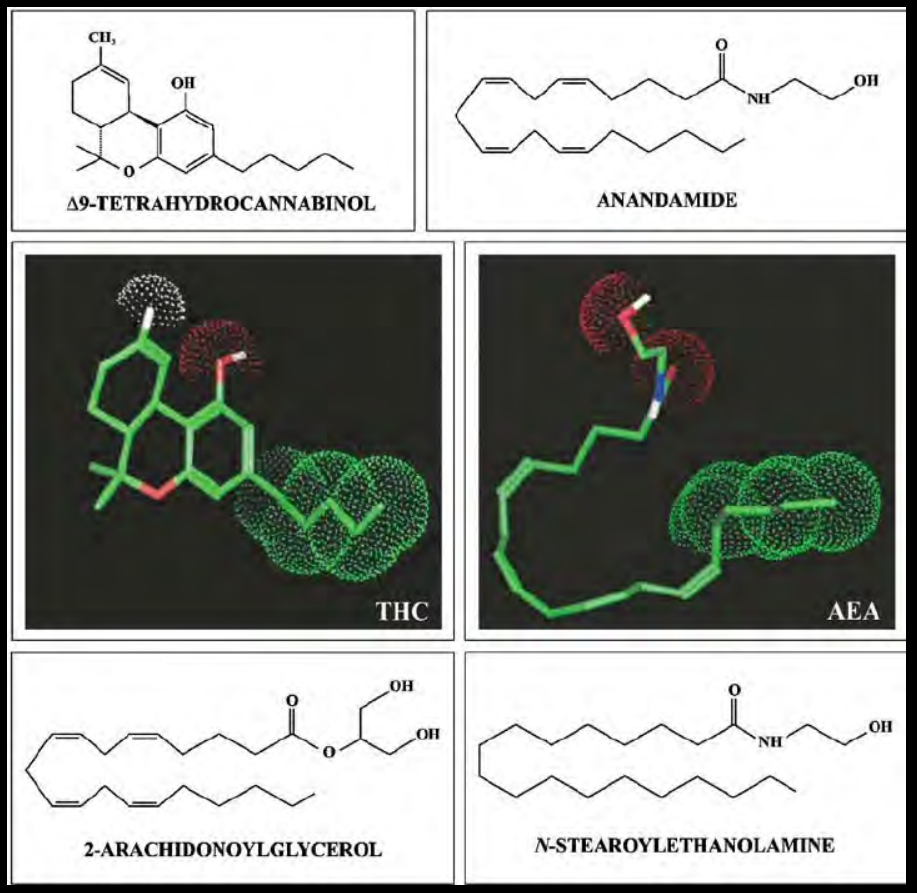
Cannabinoid receptors

- CB_1
  - Psychoactive; mostly in brain/CNS
  - Found on GABA interneurons and glutamatergic neurons
  - Low density in brainstem → no overdose risk
- CB_2
  - Found on peripheral immune cells (T cells, B cells, macrophages, etc)
  - Also on microglial, dendritic, and endothelial cells in the brain
  - Relief of pain
- There's more! (e.g., Vanilloid type 1)



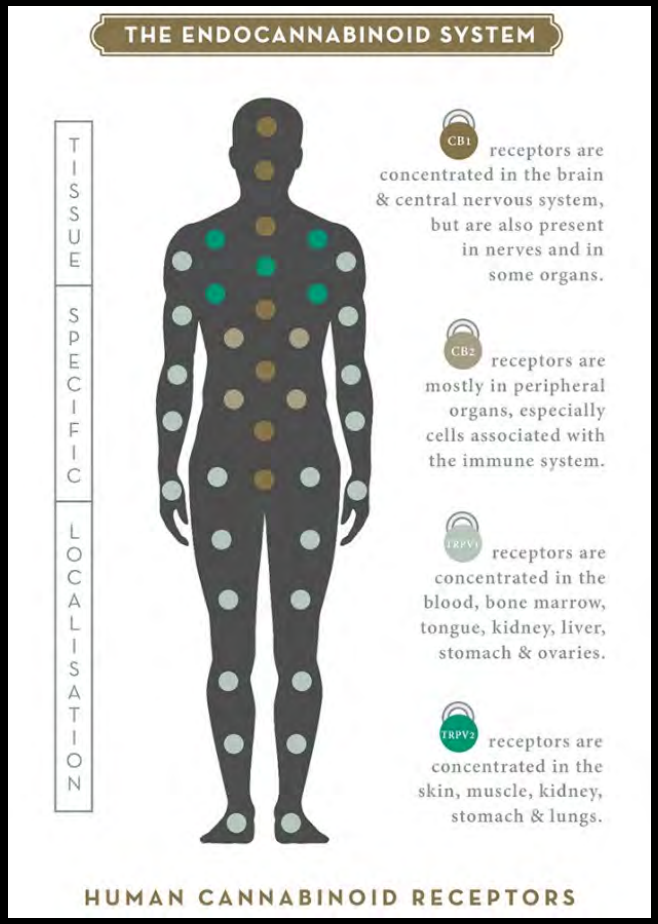
Endocannabinoids

- 5 discovered so far, but two are most studied:
  - Anandamide – THC-like
  - 2-AG – CBN-like
- Not stored in vesicles but produced "on demand" when ↑ Ca^{++}
- Function as antioxidants, vasodilators, anti-inflammatory agents, inhibitors of excitotoxicity, and play role in neurogenesis



Endocannabinoid System

- 600 million years old; most widespread receptor system in body
  - Every organ, gland, immune cell and connective tissue
- Lipid-based signaling system that regulates neurotransmitter release in response to neural activation
- "Body's supercomputer"'
  - Functions to keep every other bodily system in balance
  - Only neurotransmitter network to communicate with cells in 2 directions (ex: feedback from damaged organs)



Joe Dolce, *Brave New Weed*, 2016

Medium

Sept 30, 2016

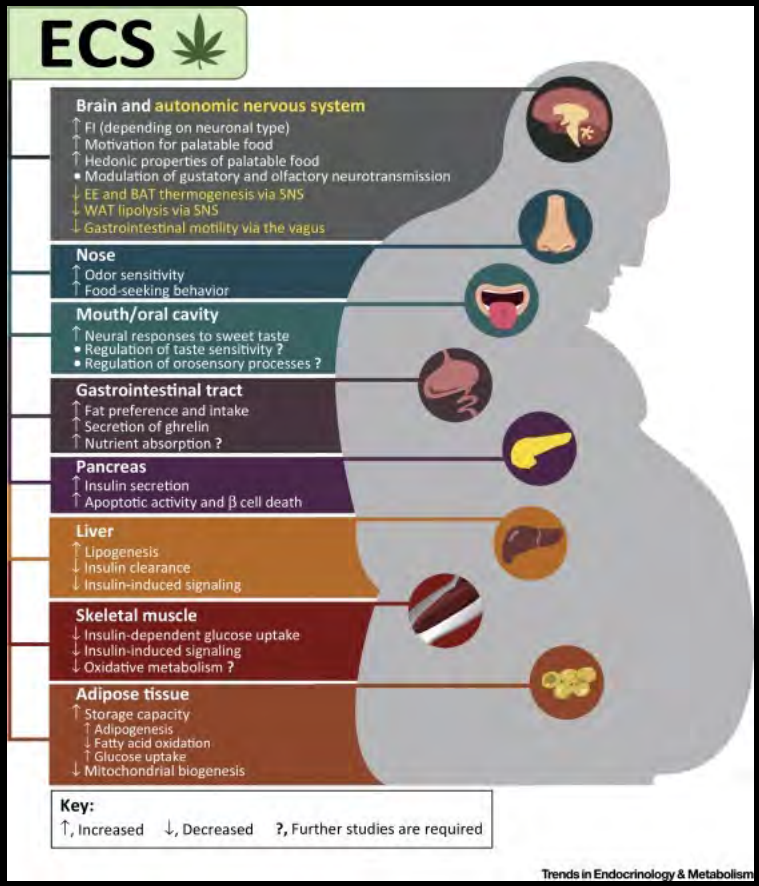
The Endocannabinoid System: What you need to know.

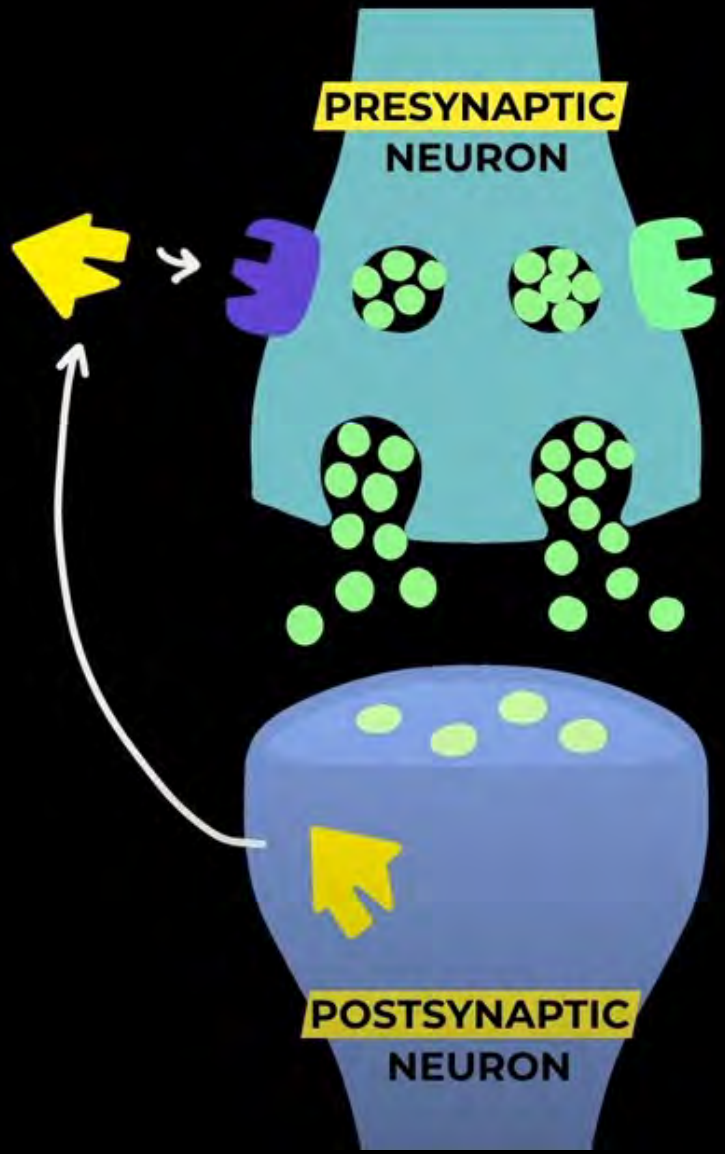
Medical schools don't teach it and most doctors have never heard of it. Still, the endocannabinoid system (ECS) is one of the most important system in our bodies. It is responsible for modulating every other body system from our bones to our central nervous system (CNS). You would think something so important would be more well known, but since it has been long association with cannabis, the ECS has been neglected by medical professionals and a complete mystery for most patients who may be suffering as a result of a dysfunction in their ECS.

ECS Function

- “Steadies the temperature in every room in the body’s house”

- Regulates the flow and balance of all organ systems
  - Maintains the heartbeat, stomach digestion, lung function, rate of bone healing
  - Rewards us for eating and having sex
  - Enables us to forget pain
  - Dispatches chemicals to protect troubled areas from further damage
    - i.e., when you break a bone or bang your head, endocannabinoids are the first responders





Rachel Knox,TED Talk: The ECS system and the revolution of one (2019).

The ECS Regulates 5 Basic Functions

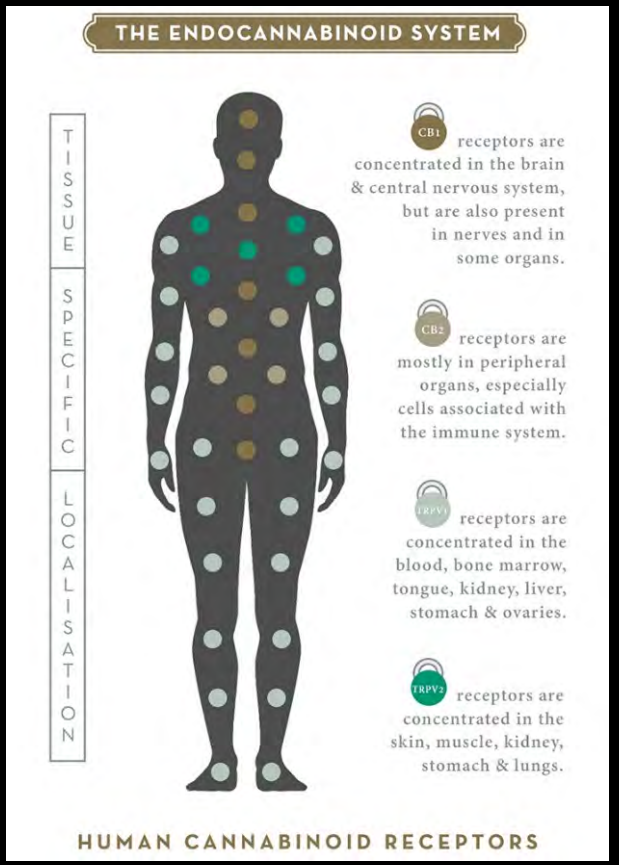
- Relaxing
- Eating
- Sleeping
- Forgetting
- Protecting our organs

The ECS Regulates 5 Basic Functions

- Relaxing
- Eating
- Sleeping
- Forgetting
- Protecting our organs

ECS Function

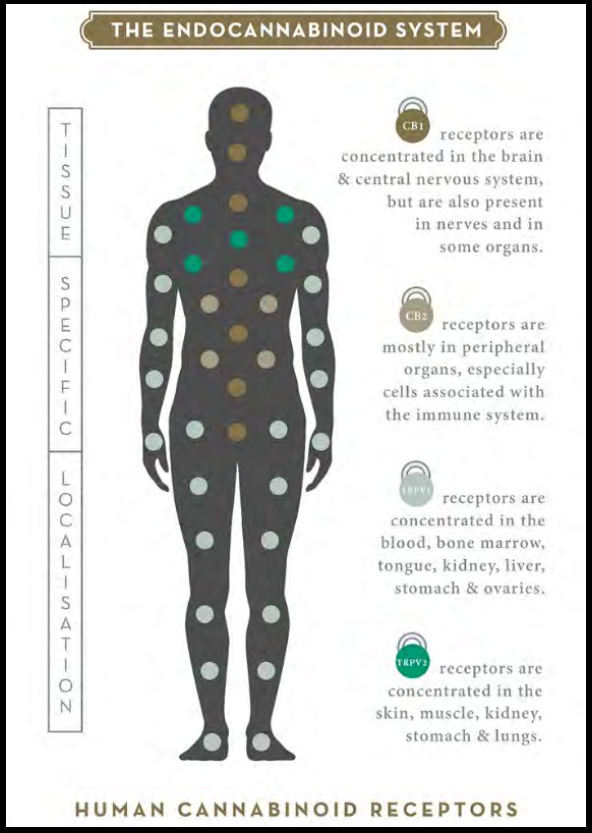
- Gastrointestinal activity
- Cardiovascular activity
- Pain perception
- Modulation of neurotransmitter release
- Maintenance of bone mass
- Protection of neurons
- Hormonal regulation
- Metabolism control
- Immune function
- Inflammatory reactions
- Inhibition of tumor cells



ECS Function

Marked increase in ECs with glutamate toxicity, shock-induced stress, trauma, etc

- Cancer
- Neuropathic/ inflammatory pain
- Multiple sclerosis
- Intestinal disorders
- Hemorrhagic/septic /cardiogenic shock
- PTSD
- TBI
- HTN
- Atherosclerosis
- Parkinson's disease



Bonni Goldstein, MD, *Cannabis Revealed,* 2016

Clinical Endocannabinoid Deficiency Syndrome

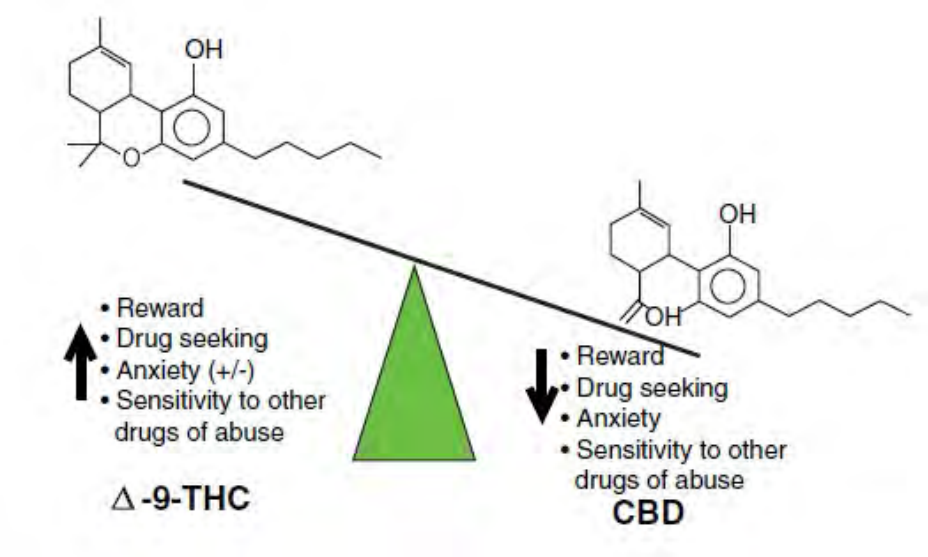
- Complex array of physical/mental conditions, typically misdiagnosed as discrete diseases (esp those with hyperalgesia)
  - Migraines
  - IBS
  - Fibromyalgia
- Likely includes:
  - Chronic pain disorders
  - Autoimmune disorders
  - GI issues
  - Mood disorders like anxiety, depression

Russo, Clinical Endocannabinoid Deficiency Reconsidered. Cannabis Cannabinoid Res, 2016.

Phytocannabinoids

- >120 have been isolated
- THC: partial CB1 agonist
- CBD: broad effects not fully established
  - indirectly activates CB1 receptor via ↑ anandamide
  - indirect agonist of 5-HT1A receptors
  - modulates multiple neurotransmitter systems

THC (tetrahydrocannabinol)
THCA (tetrahydrocannabinolic acid)
CBD (cannabidiol)
CBDA (cannabidiolic acid)
CBN (cannabinol)
CBG (cannabigerol)
CBC (cannabichromene)
CBL (cannabicyclol)
CBV (cannabivarin)
THCV (tetrahydrocannabivarin)
CBDV (cannabidivarin)
CBCV (cannabichromevarin)
CBGV (cannabigerovarin)
CBGM (cannabigerol monomethyl ether)
CBE (cannabielsoin)
CBT (cannabicitran)



Terpenes

A-PINENE

ANTI-INFLAMMATORY

BRONCHODILATOR

AIDS MEMORY

ANTI-BACTERIAL

also found in

pine needles

LINALOOL

ANESTHETIC

ANTI-CONVULSANT

ANALGESIC

ANTI-ANXIETY

also found in

lavender

BETA CARYOPHYLLENE

ANTI-INFLAMMATORY

ANALGESIC

PROTECTS CELLS LINING THE DIGESTIVE TRACT

also found in

black pepper

MYRCENE

CONTRIBUTES TO SEDATIVE EFFECT OF STRONG INDICAS

SLEEP AID

MUSCLE RELAXANT

also found in

hops

LIMONENE

TREATS ACID REFLUX

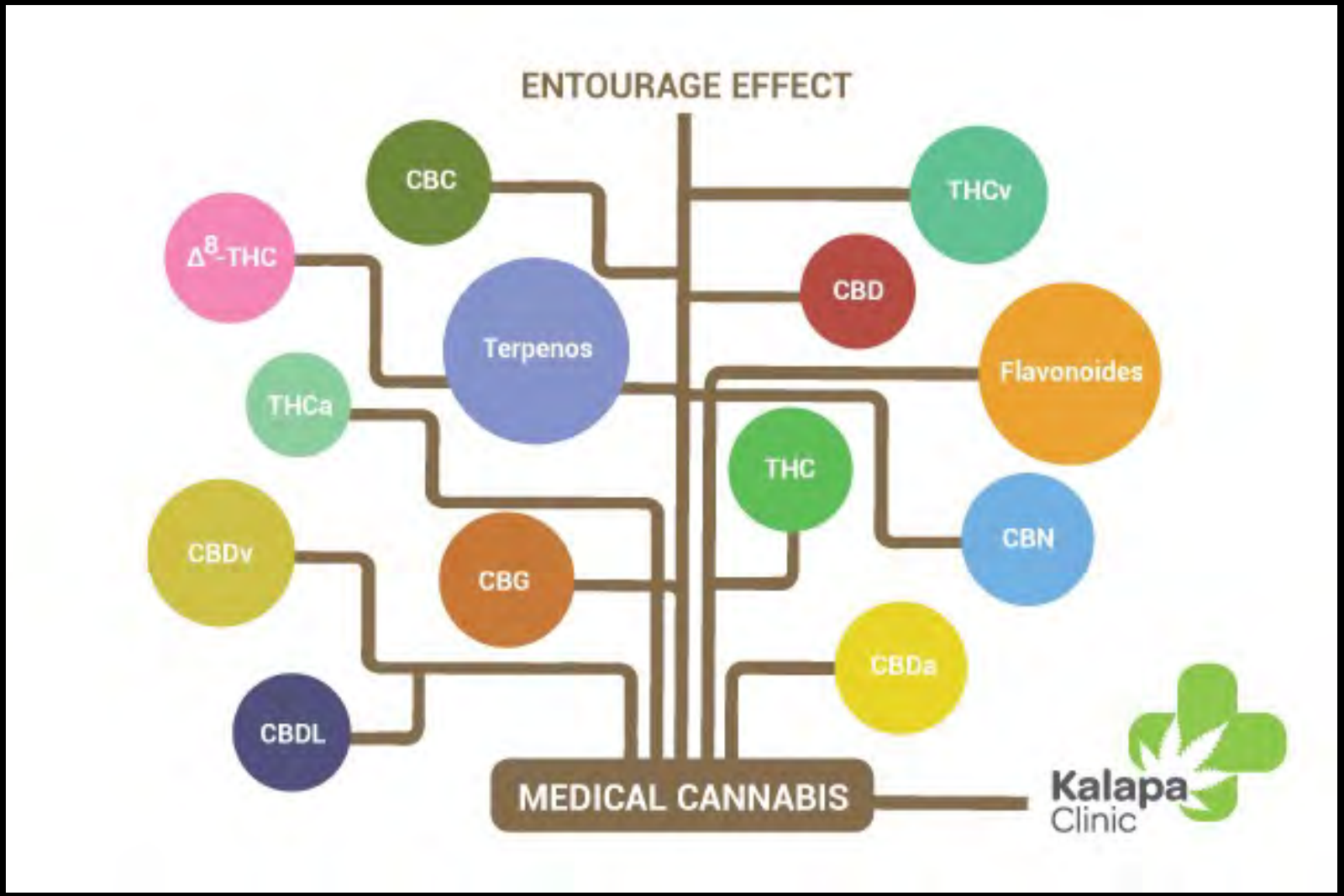
ANTI-ANXIETY

ANTIDEPRESSANT

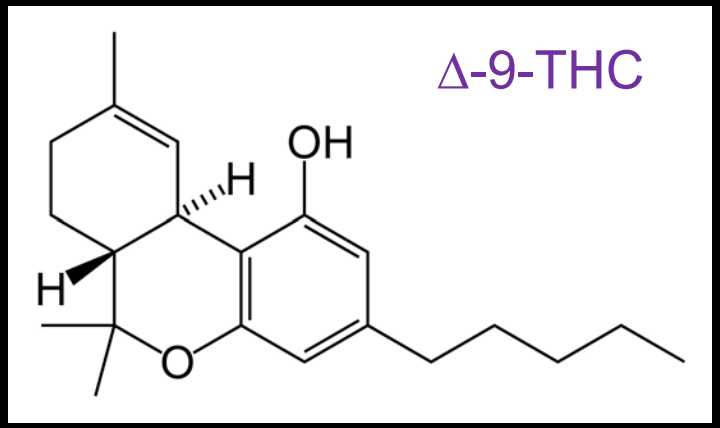
also found in

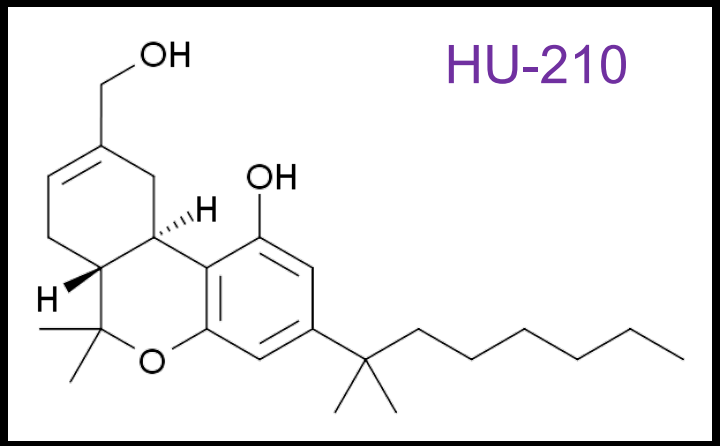
citrus

The Entourage Effect



A Word About Synthetic Cannabinoids





U.S. Patent No. 6,630,507

United States Patent **6,630,507**
Hampson , et al. **October 7, 2003**

**Please see images for: (Certificate of Correction) **

Cannabinoids as antioxidants and neuroprotectants

Abstract

Cannabinoids have been found to have antioxidant properties, unrelated to NMDA receptor antagonism. This new found property makes cannabinoids useful in the treatment and prophylaxis of wide variety of oxidation associated diseases, such as ischemic, age-related, inflammatory and autoimmune diseases. The cannabinoids are found to have particular application as neuroprotectants, for example in limiting neurological damage following ischemic insults, such as stroke and trauma, or in the treatment of neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease and HIV dementia. Nonpsychoactive cannabinoids, such as cannabidoil, are particularly advantageous to use because they avoid toxicity that is encountered with psychoactive cannabinoids at high doses useful in the method of the present invention. A particular disclosed class of cannabinoids useful as neuroprotective antioxidants is formula (I) wherein the R group is independently selected from the group consisting of H, CH.sub.3, and COCH.sub.3. ##STR1##

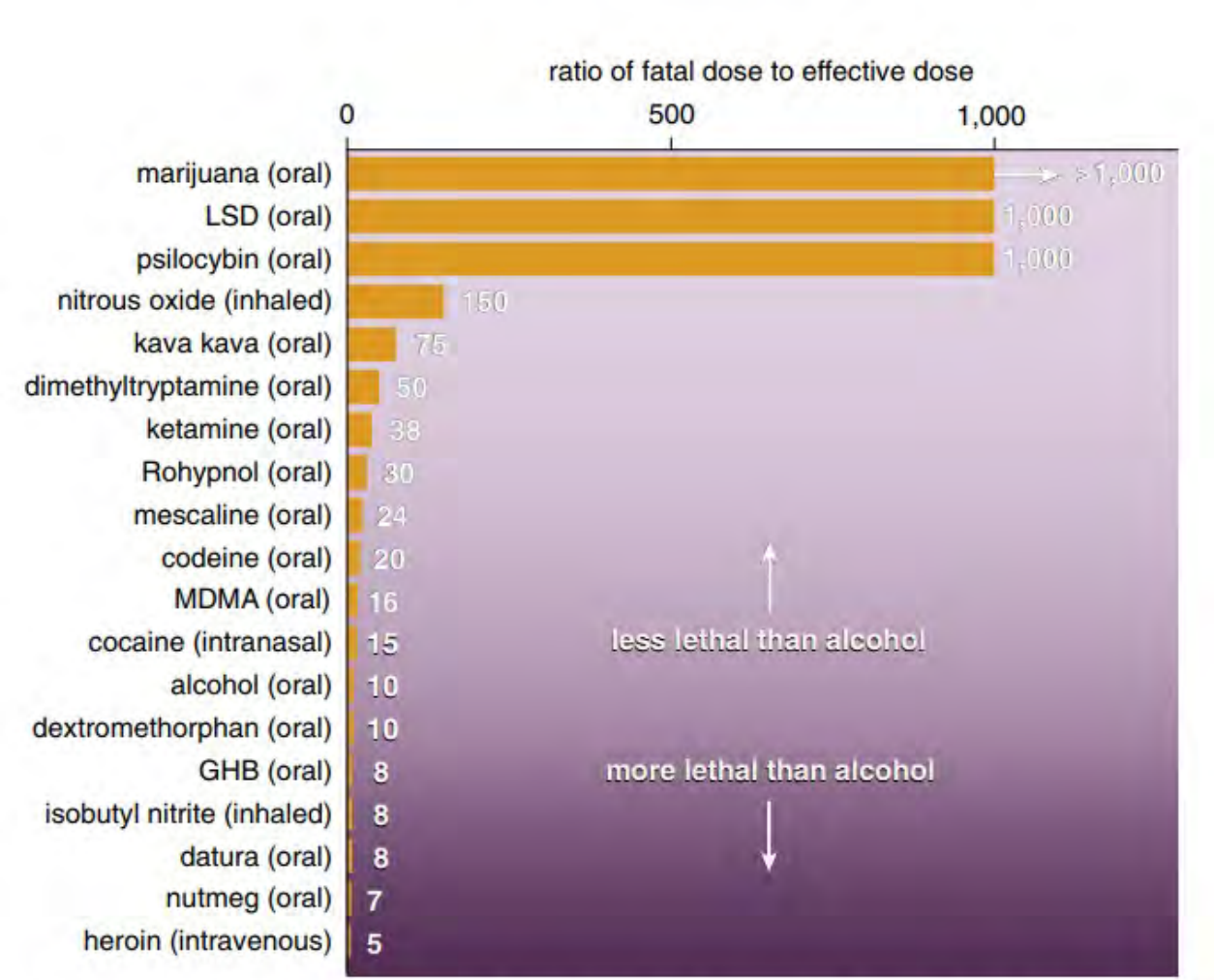
Inventors: **Hampson; Aidan J.** (Irvine, CA), **Axelrod; Julius** (Rockville, MD), **Grimaldi; Maurizio** (Bethesda, MD)
Assignee: **The United States of America as represented by the Department of Health and Human Services** (Washington, DC)
Family ID: **26767641**
Appl. No.: **09/674,028**
Filed: **February 2, 2001**
PCT Filed: **April 21, 1999**
PCT No.: **PCT/US99/08769**
PCT Pub. No.: **WO99/53917**
PCT Pub. Date: **October 28, 1999**

Current U.S. Class: **514/454**
Current CPC Class: A61K 31/35 (20130101)
Current International Class: A61K 31/35 (20060101); A61K 031/35 ()
Field of Search: ;514/454

FDA-Approved Synthetic Cannabinoids

FDA-Approved Cannabis-Derived CBD June 2018

Toxicity of Cannabis



Ranking psychoactive substances by their ratios of lethal dose to effective dose gives a general picture of how likely each is to precipitate an acute fatal reaction. By this measure, many illicit drugs are considerably safer than alcohol.

Gable RS, The Toxicity of Recreational Drugs, *American Scientist* 2006

Addictive Spectrum

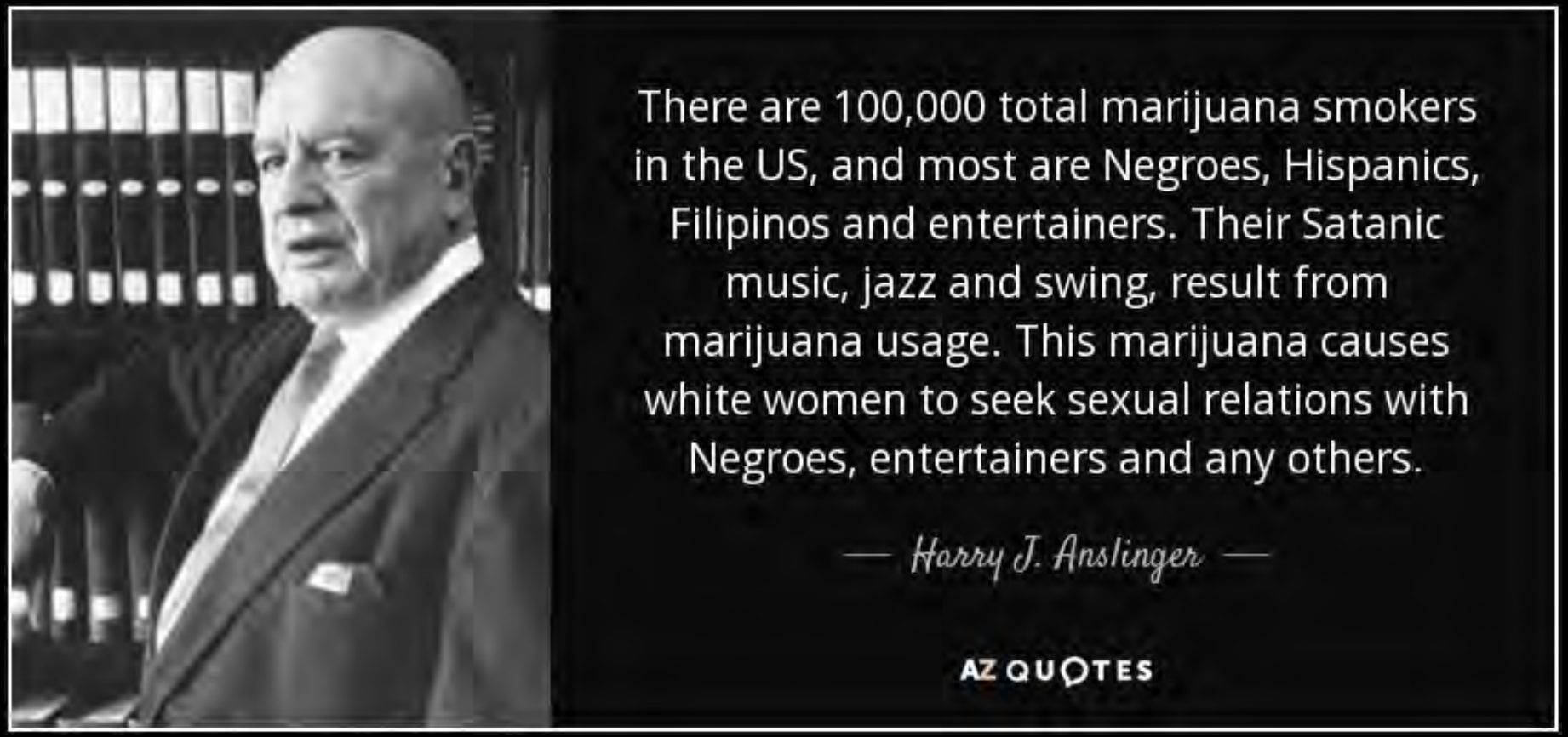
Out of everyone who has tried once, % who develop a use disorder:

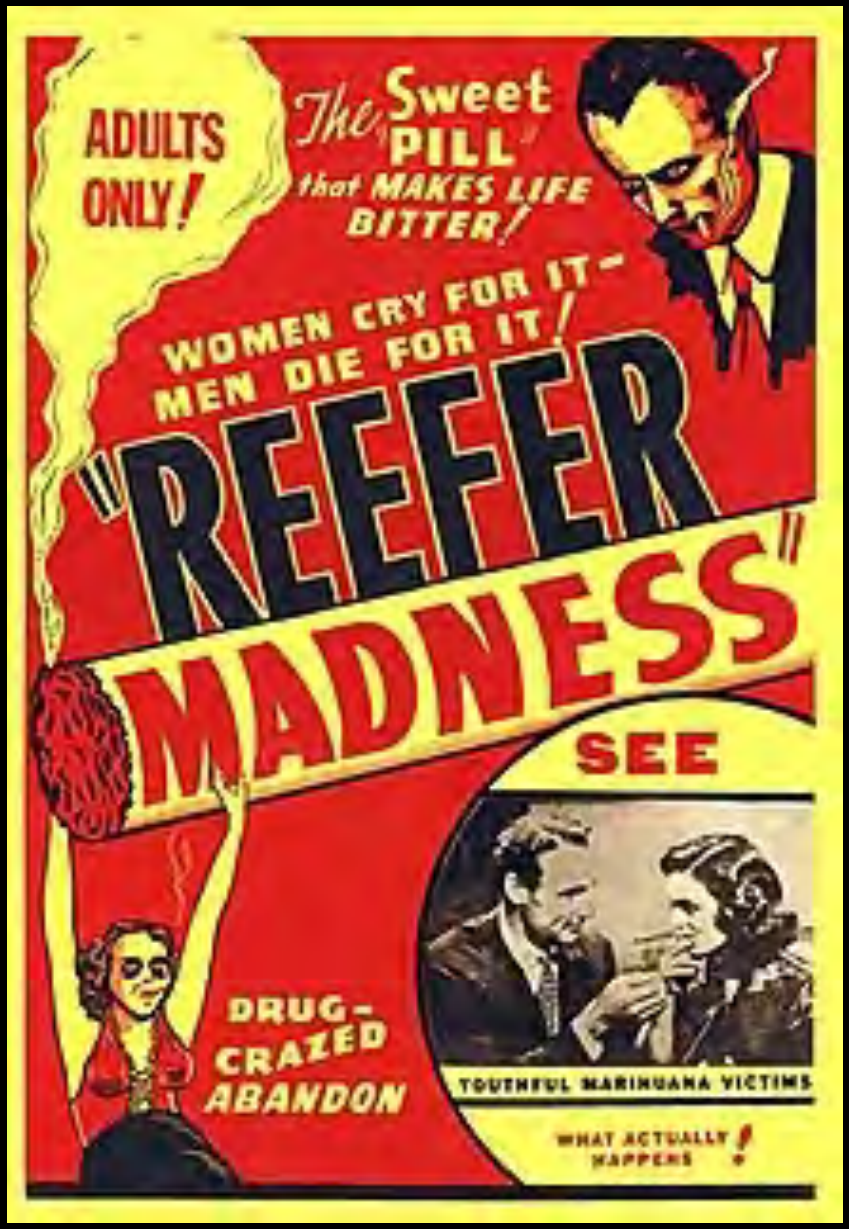
Nicotine: 32%
Heroin: 23%
Crack, IV cocaine: 23%
Intranasal cocaine: 17%
Alcohol: 15%
Cannabis: 9%
Sedative-hypnotics: 9%
~~Psychedelics: 4.9%~~
Inhalants: 3.7%

Anthony JC, Warner LA, Kessler KC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: basic findings from the National Comorbidity Survey. *Exp Clin Psychopharmacol.* 1994;2:244-268.

2. The Politics

Along came Harry Anslinger…

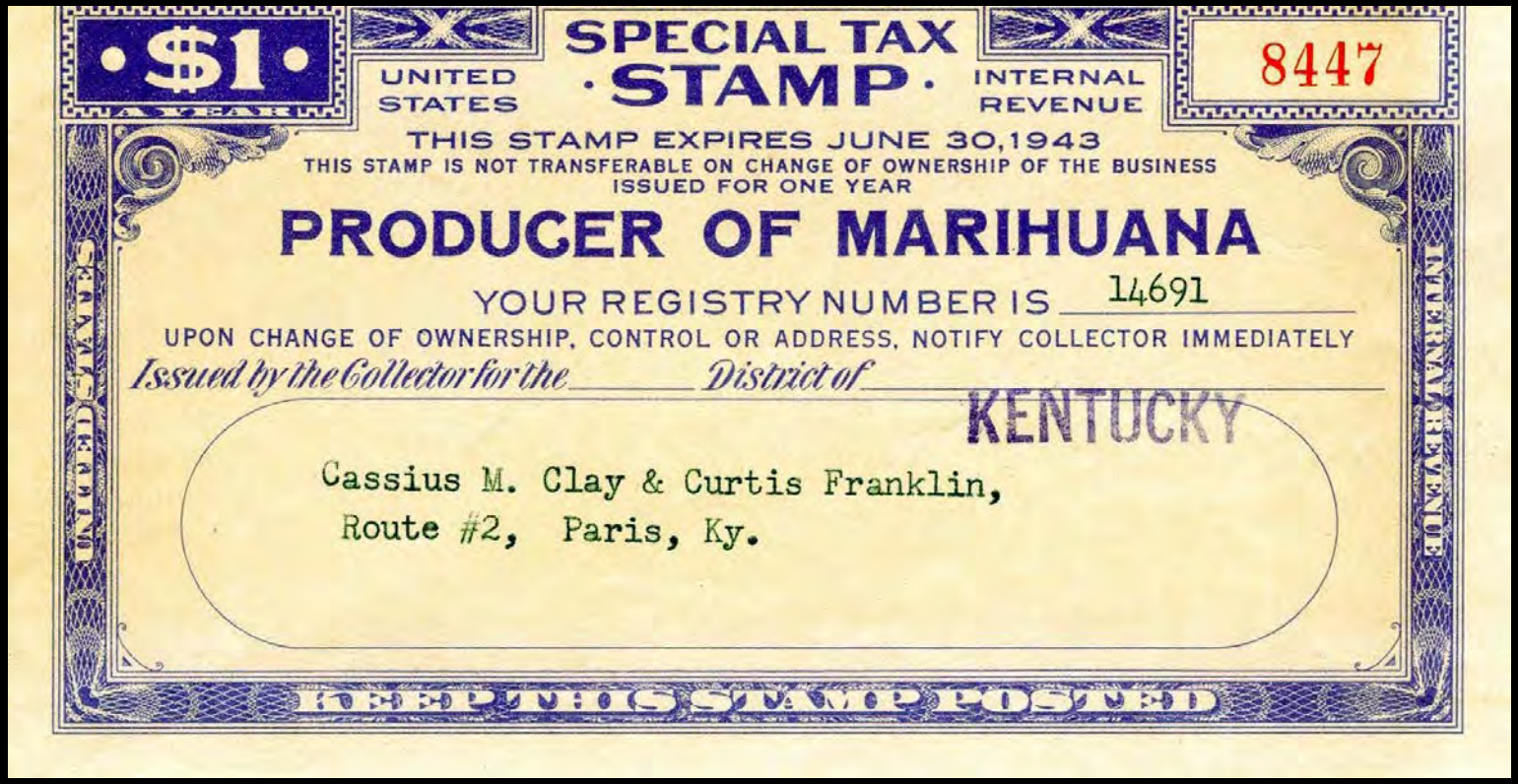



ADULTS ONLY!
The Sweet PILL that MAKES LIFE BITTER!
WOMEN CRY FOR IT—
MEN DIE FOR IT!
"REEFER MADNESS"
SEE
DRUG-CRAZED ABANDON
YOUTHFUL MARIHUANA VICTIMS
WHAT ACTUALLY HAPPENS!


Daring Drug Expose!
Horror Shame Despair!
MARIHUANA
WEED WITH ROOTS IN HELL
NOT RECOMMENDED FOR CHILDREN
SMOKE THAT GETS in YOUTH'S EYES!
LUST
CRIME
SORROW
HATE
SHAME
DESPAIR
WHAT HAPPENS AT Marihuana PARTIES?
MISERY
WEIRD ORGIES
WILD PARTIES
UNLEASHED PASSIONS!

1936

Marihuana Tax Act of 1937



$1 A YEAR

UNITED STATES · SPECIAL TAX STAMP · INTERNAL REVENUE

8447

THIS STAMP EXPIRES JUNE 30, 1943

THIS STAMP IS NOT TRANSFERABLE ON CHANGE OF OWNERSHIP OF THE BUSINESS

ISSUED FOR ONE YEAR

PRODUCER OF MARIHUANA

YOUR REGISTRY NUMBER IS 14691

UPON CHANGE OF OWNERSHIP, CONTROL OR ADDRESS, NOTIFY COLLECTOR IMMEDIATELY

Issued by the Collector for the ____ District of KENTUCKY

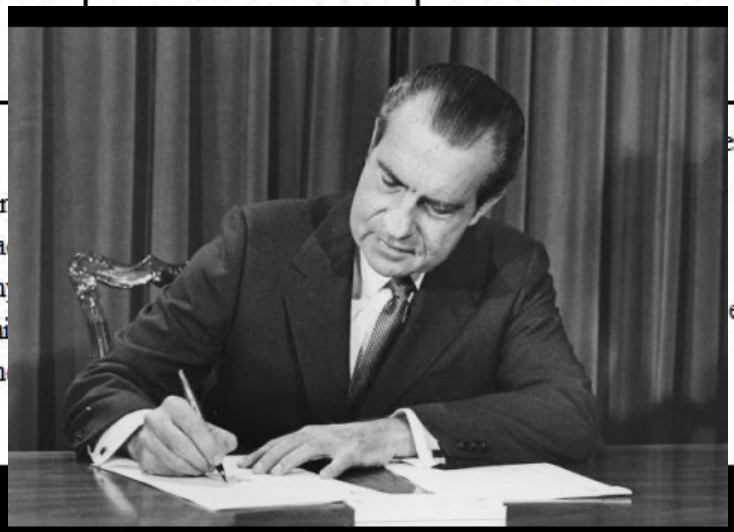
Cassius M. Clay & Curtis Franklin,
Route #2, Paris, Ky.

FOR INTERNAL REVENUE

FOR INTERNAL REVENUE STAMP POSTED

Controlled Substances Act of 1970

	Schedule I	Schedule II	Schedule III	Schedule IV	Schedule V
Potential for abuse	The drug or other substance has a high potential for abuse	The drug or other substance has a high potential for abuse	The drug or other substance has a potential for abuse less than the drugs or other substances in schedules I and II	The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule III	The drug or other substance has a low potential for abuse relative to the drugs or other substances in schedule IV
Medical use	The drug or other substance has no currently accepted medical use in treatment in the United States	The drug or other substance has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions	The drug or other substance has a currently accepted medical use in treatment in the United States	The drug or other substance has a currently accepted medical use in treatment in the United	The drug or other substance has a currently accepted medical use in treatment in the United
Consequences of abuse	There is a lack of accepted safety for use of the drug or other substance under medical supervision	Abuse of the drug or other substance may lead to severe psychological of physical dependence	Abuse of the drug or substance may lea moderate or low ph dependence or hi psychological depen		



Richard Nixon

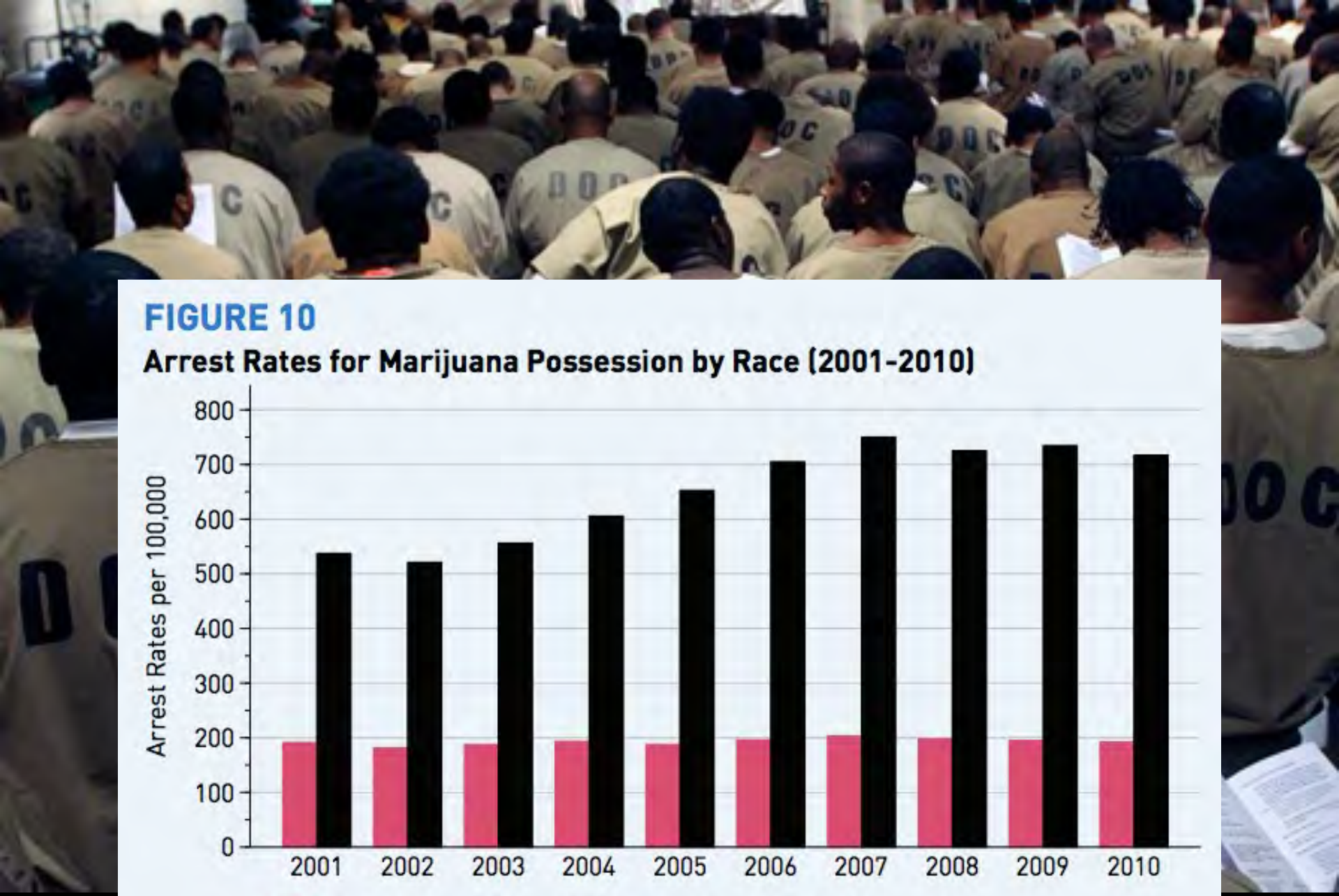
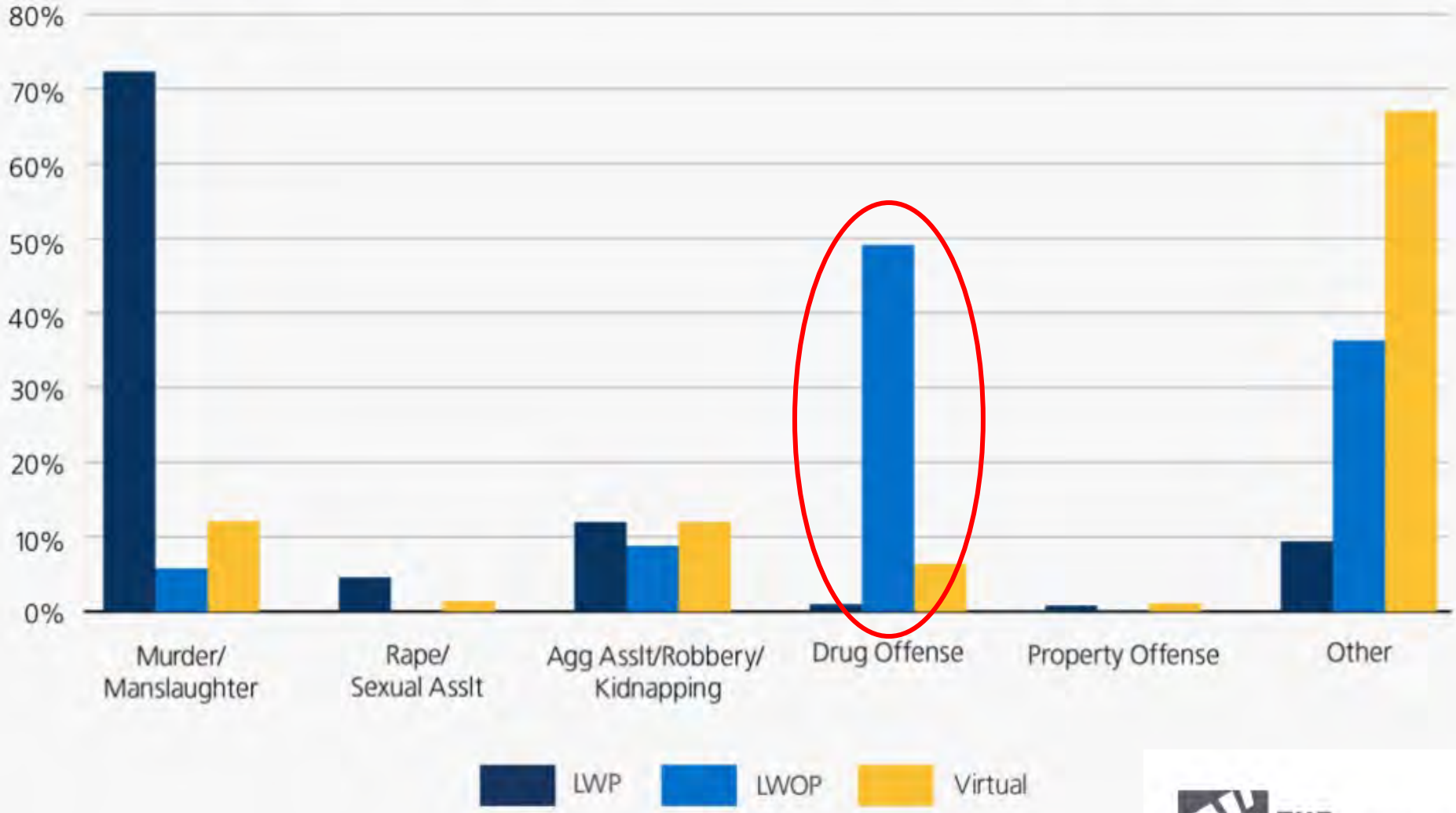


FIGURE 10

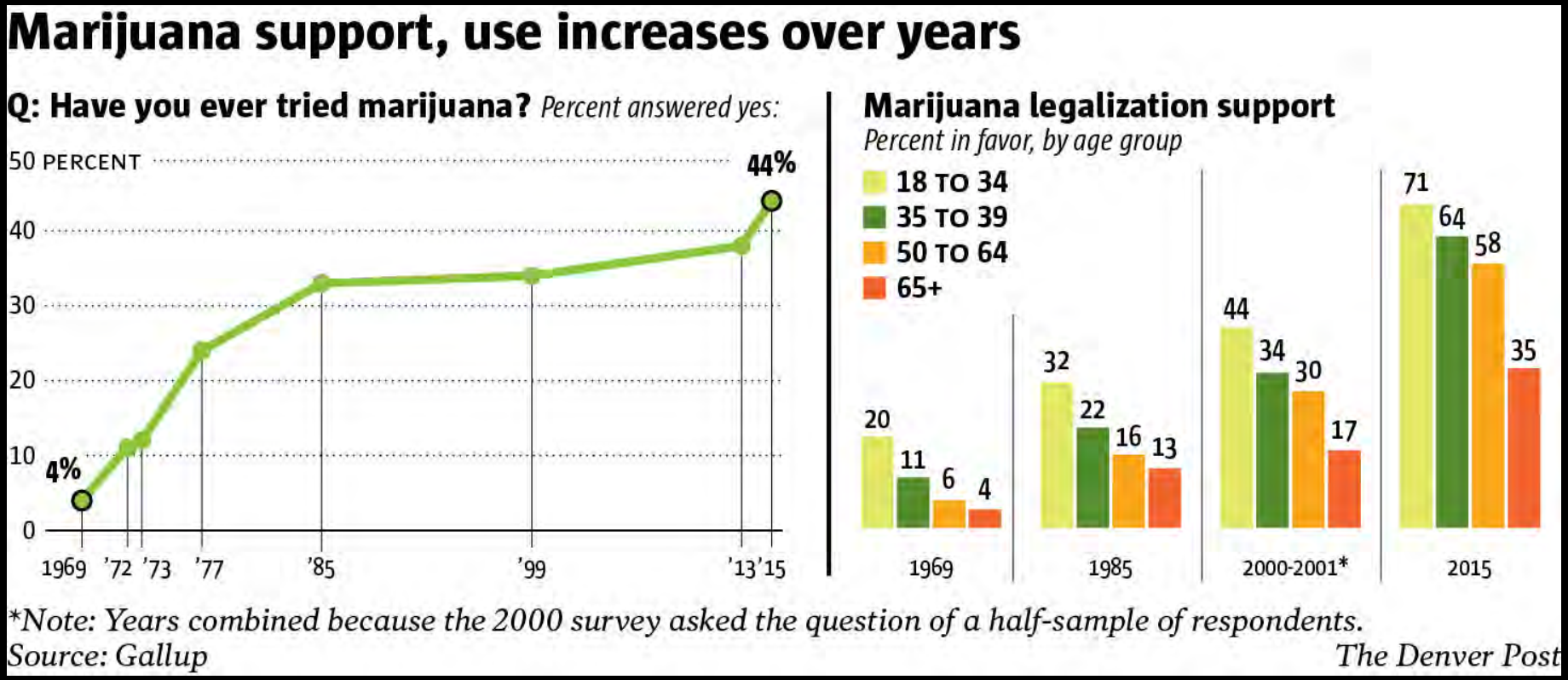
Arrest Rates for Marijuana Possession by Race (2001-2010)

Source: FBI/Uniform Crime Reporting Program Data and U.S. Census Data

Figure 5. Crime of Conviction among Federal Prisoners Serving LWP, LWOP, and Virtual Life Sentences, 2016



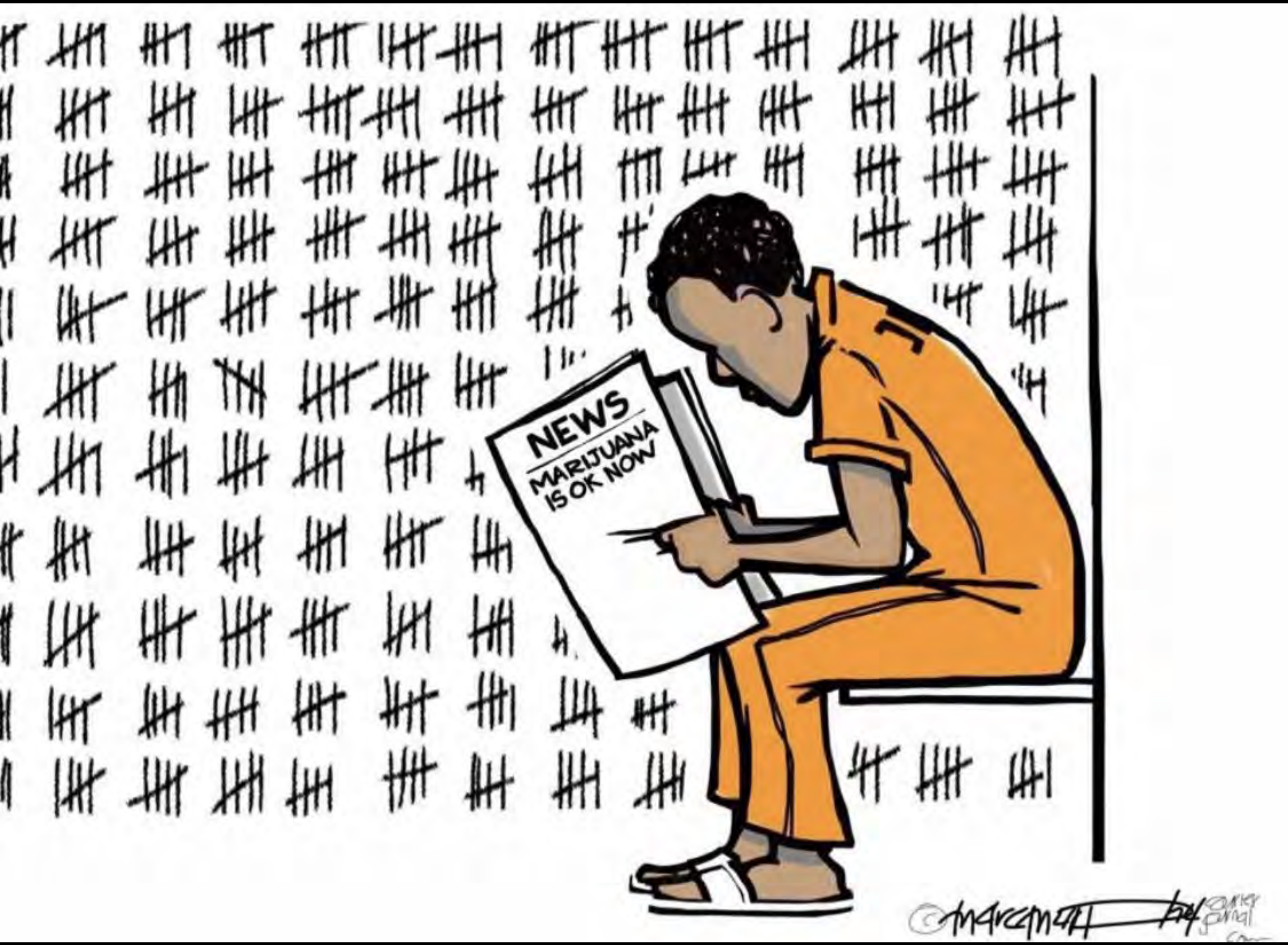
THE SENTENCING PROJECT

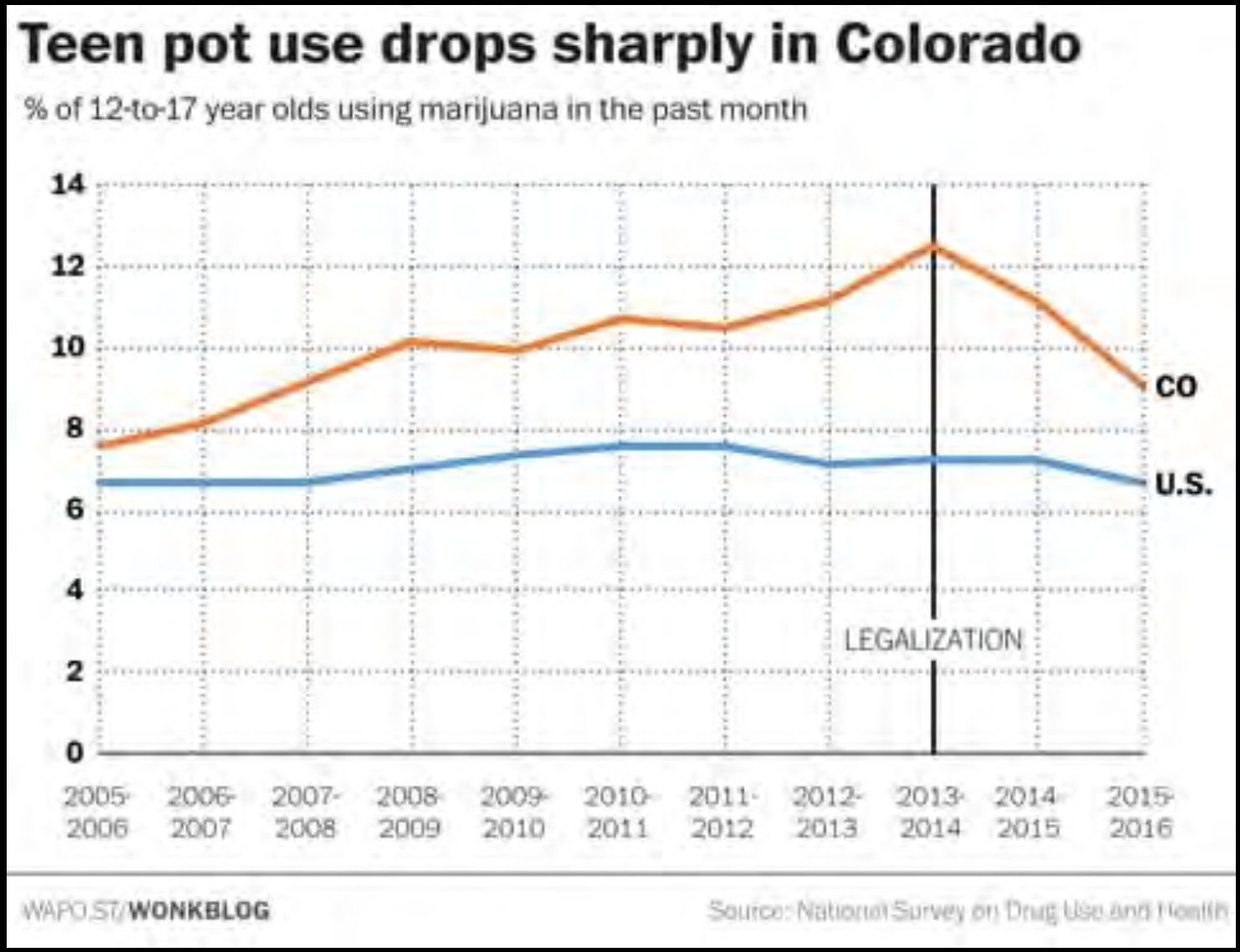


Cannabis use per total U.S. population:

0.05% → 4% → 52%

(1915) (1969) (2017)


NEWS
MARIJUANA IS OK NOW



Washington Post, December 2017

3. The Research

IN THE LAB

This scientist is testing a marijuana ingredient as a way to prevent relapse. It's a daunting task

By MEGAN THIELKING @meggophone / FEBRUARY 28, 2018

CBD for Opioid Use Disorder?

- Hurd: “Strong scientific basis” for using CBD for OUDs
  - Very safe and not rewarding
  - “Indisputable” evidence that they modulate anxiety
- ECS involved in stress responsivity & negative emotional states
  - CBD inhibits FAAH and ↑ anandamide → weak agonism at CB1 receptor leads to enhanced physiologic tone and reduced anxiety (strong agonism can cause anxiety/psychosis)
  - CBD reduces amygdala activity
- CBD reduces rewarding properties of opioids and withdrawal symptoms; reduces heroin-seeking behavior (a long-lasting effect)
- CBD normalizes heroin-induced impairment of CB1R and glutamate receptors in the striatum

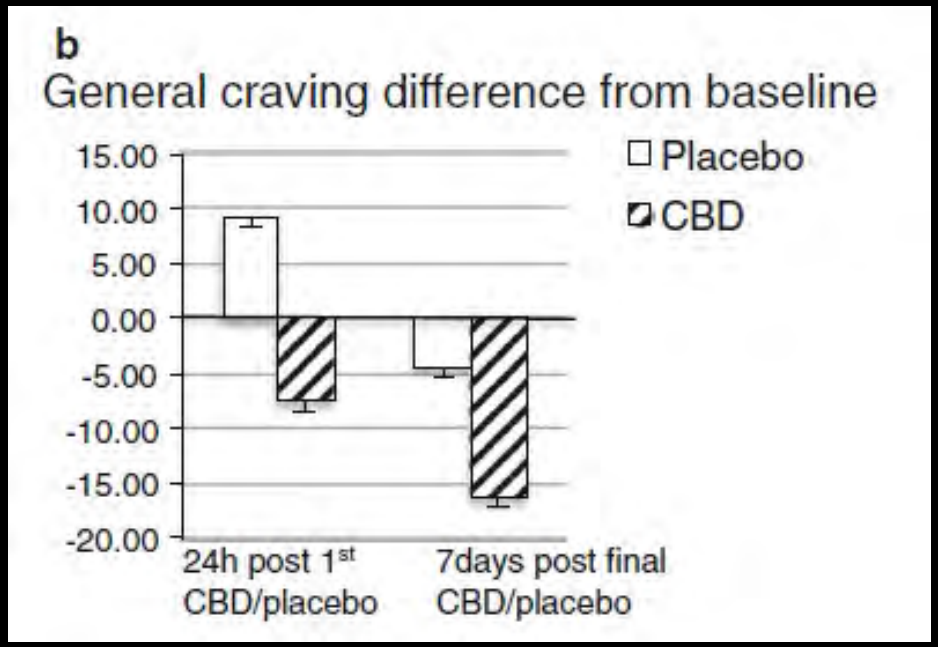
Hurd YL. Cannabidiol: Swinging the Marijuana Pendulum from ‘Weed” to Medication. Trends Neurosci 2017.

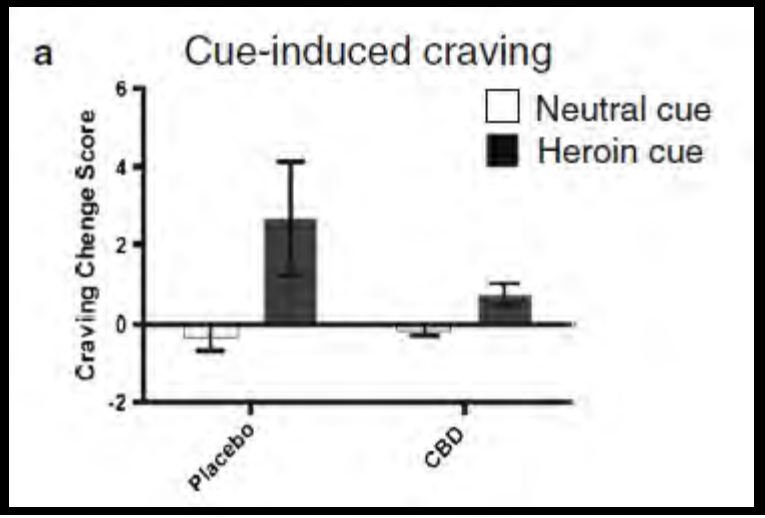
Neurotherapeutics (2015) 12:807–815
DOI 10.1007/s13311-015-0373-7

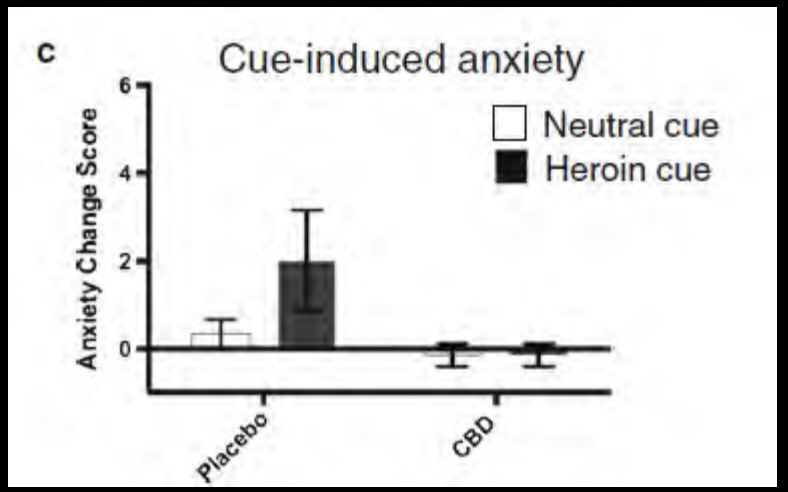
REVIEW

Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage

Yasmin L. Hurd[1] · Michelle Yoon[1] · Alex F. Manini[2] · Stephanie Hernandez[2] · Ruben Olmedo[2] · Maria Ostman[3] · Didier Jutras-Aswad[4]

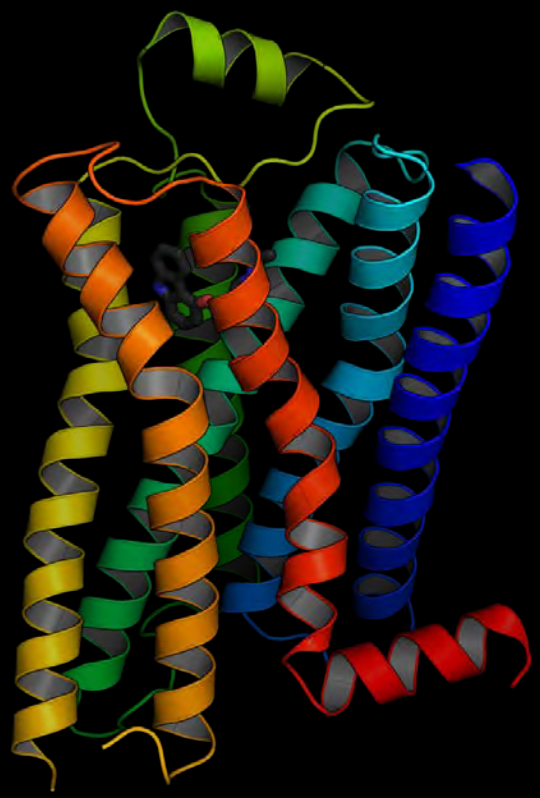






Cross-talk between EC and Opioid Systems

- Animals deficient in CB1 receptors have ↓ opioid reward
- Opioids regulate the release of ECs
- ECs alter opioid peptide levels
- EC + opioid receptors are expressed in the same cells in pathways implicated in addiction
- Both are G protein-coupled receptors with similar intracellular signaling cascades



June 2015

Original Investigation

JAMA®

Cannabinoids for Medical Use
A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

IMPORTANCE Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear.

OBJECTIVE To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids.

DATA SOURCES Twenty-eight databases from inception to April 2015.

STUDY SELECTION Randomized clinical trials of cannabinoids for the following indications: nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome.

DATA EXTRACTION AND SYNTHESIS Study quality was assessed using the Cochrane risk of bias tool. All review stages were conducted independently by 2 reviewers. Where possible, data were pooled using random-effects meta-analysis.

MAIN OUTCOMES AND MEASURES Patient-relevant/disease-specific outcomes, activities of daily living, quality of life, global impression of change, and AEs.

Evidence for Medical Cannabis

Whiting et al, 2015

- 79 trials (6,462 participants)
- Moderate-quality evidence:
  - Chronic pain
  - Spasticity
- Low-quality evidence:
  - Nausea/vomiting (chemotherapy)
  - Weight gain in HIV infection
  - Sleep disorders
  - Tourette's syndrome
- Adverse effects:
  - Dizziness, dry mouth, nausea, fatigue/drowsiness, somnolence, euphoria, vomiting, disorientation, confusion, loss of balance, hallucinations

U.S. Cannabis Research

- >20,000 experimental studies but few definitive clinical trials
- Lots of red tape for researchers in the U.S.
  - NIDA, DEA and FDA control access to cannabis since 1968

Federal Marijuana Farm, University of Mississippi

THC: 19 - 30%

THC: 8 - 13%

Dr. Sue Sisley, Scottsdale Research Institute, 2017

So after 45 years and 1,800 studies…

- No conclusive health-threatening dangers yet found
- Correlational studies:
  - Brain changes in adolescents
  - Long-term memory deficits / lower IQ
  - Addiction to more dangerous drugs
  - Increased incidence of psychosis

- NIDA's Alan Leshner: "congressional mandate forbids funding research to uncover benefits"
  - $66 million per year to determine harms of cannabis

West Indian Med J. 1991 Sep;40(3):120-3.

Five-year follow-up of rural Jamaican children whose mothers used marijuana during pregnancy.

Hayes JS[1], Lampart R, Dreher MC, Morgan L.

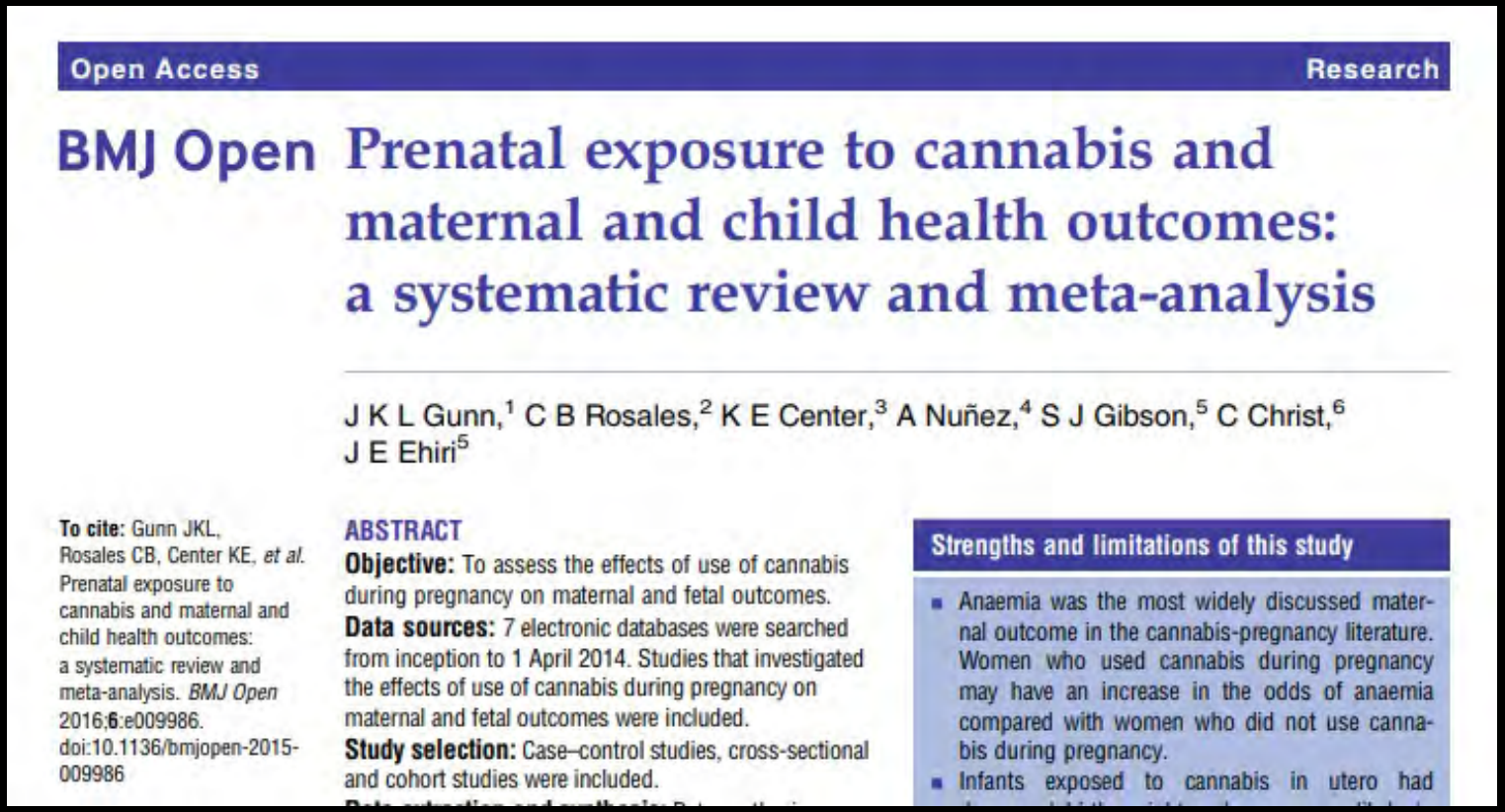
⊕ Author information

Abstract

This research provides data on the development of 59 Jamaican children, from birth to age 5 years, whose mothers used marijuana during pregnancy. Approximately one-half of the sample used marijuana during pregnancy and were matched with non-users according to age, parity, and socioeconomic status. Testing of the children was done at 1, 3, and 30 days of age with the Brazelton Neonatal Behavioral Assessment Scales and at ages 4 and 5 years with the McCarthy Scales of Children's Abilities. Data about the child's home environment and temperament were collected from direct observations as well as from standardized questionnaires. The results show no significant differences in developmental testing outcomes between children of marijuana-using and non-using mothers except at 30 days of age when the babies of users had more favourable scores on two clusters of the Brazelton Scales: autonomic stability and reflexes. The developmental scores at ages 4 and 5 years were significantly correlated to certain aspects of the home environment and to regularity of basic school (preschool) attendance.

Study author Dr. Melanie Dreher:

“No differences at all.”



Open Access Research

BMJ Open

Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis

J K L Gunn,[1] C B Rosales,[2] K E Center,[3] A Nuñez,[4] S J Gibson,[5] C Christ,[6] J E Ehiri[5]

To cite: Gunn JKL, Rosales CB, Center KE, *et al*. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. *BMJ Open* 2016;**6**:e009986. doi:10.1136/bmjopen-2015-009986

ABSTRACT

Objective: To assess the effects of use of cannabis during pregnancy on maternal and fetal outcomes.

Data sources: 7 electronic databases were searched from inception to 1 April 2014. Studies that investigated the effects of use of cannabis during pregnancy on maternal and fetal outcomes were included.

Study selection: Case–control studies, cross-sectional and cohort studies were included.

Strengths and limitations of this study

- Anaemia was the most widely discussed maternal outcome in the cannabis-pregnancy literature. Women who used cannabis during pregnancy may have an increase in the odds of anaemia compared with women who did not use cannabis during pregnancy.
- Infants exposed to cannabis in utero had

- 4 oz smaller
- 2x more likely NICU
- Moms more likely to have anemia

Many cannabis users are often tobacco or alcohol users; hence, determining a cannabis-only effect (excluding the presence of tobacco and alcohol) was currently not possible, as most studies did not exclude participants with poly-substance use. Future research in the area of cannabis and maternal and fetal health needs to exclude polysubstance use.

Publication Bias

THE LANCET

TERATOLOGY | VOLUME 334, ISSUE 8677, P1440-1442, DECEMBER 16, 1989

BIAS AGAINST THE NULL HYPOTHESIS: THE REPRODUCTIVE HAZARDS OF COCAINE

Gideon Koren • Heather Shear • Karen Graham • Tom Einarson

There were 58 abstracts on fetal outcome after gestational exposure to cocaine. Of the 9 negative abstracts (showing no adverse effect) only 1 (11%) was accepted, whereas 28 of the 49 positive abstracts were accepted (57%). This difference was significant. Negative studies tended to verify cocaine use more often and to have more cocaine and control cases.

Abstract

Article Info

Abstract

To examine whether studies showing no adverse effects of cocaine in pregnancy have a different likelihood of being accepted for presentation by a large scientific meeting, all abstracts submitted to the Society of Pediatric Research between 1980 and 1989 were analysed. There were 58 abstracts on fetal outcome after gestational exposure to cocaine. Of the 9 negative abstracts (showing no adverse effect) only 1 (11%) was accepted, whereas 28 of the 49 positive abstracts were accepted (57%). This difference was significant. Negative studies tended to verify cocaine use more often and to have more cocaine and control cases. Of the 8 rejected negative studies and the 21 rejected positive studies, significantly more negative studies verified cocaine use, and predominantly reported cocaine use rather than use of other drugs. This bias against the null hypothesis may lead to distorted estimation of the teratogenic risk of cocaine and thus cause women to terminate their pregnancy unjustifiably.

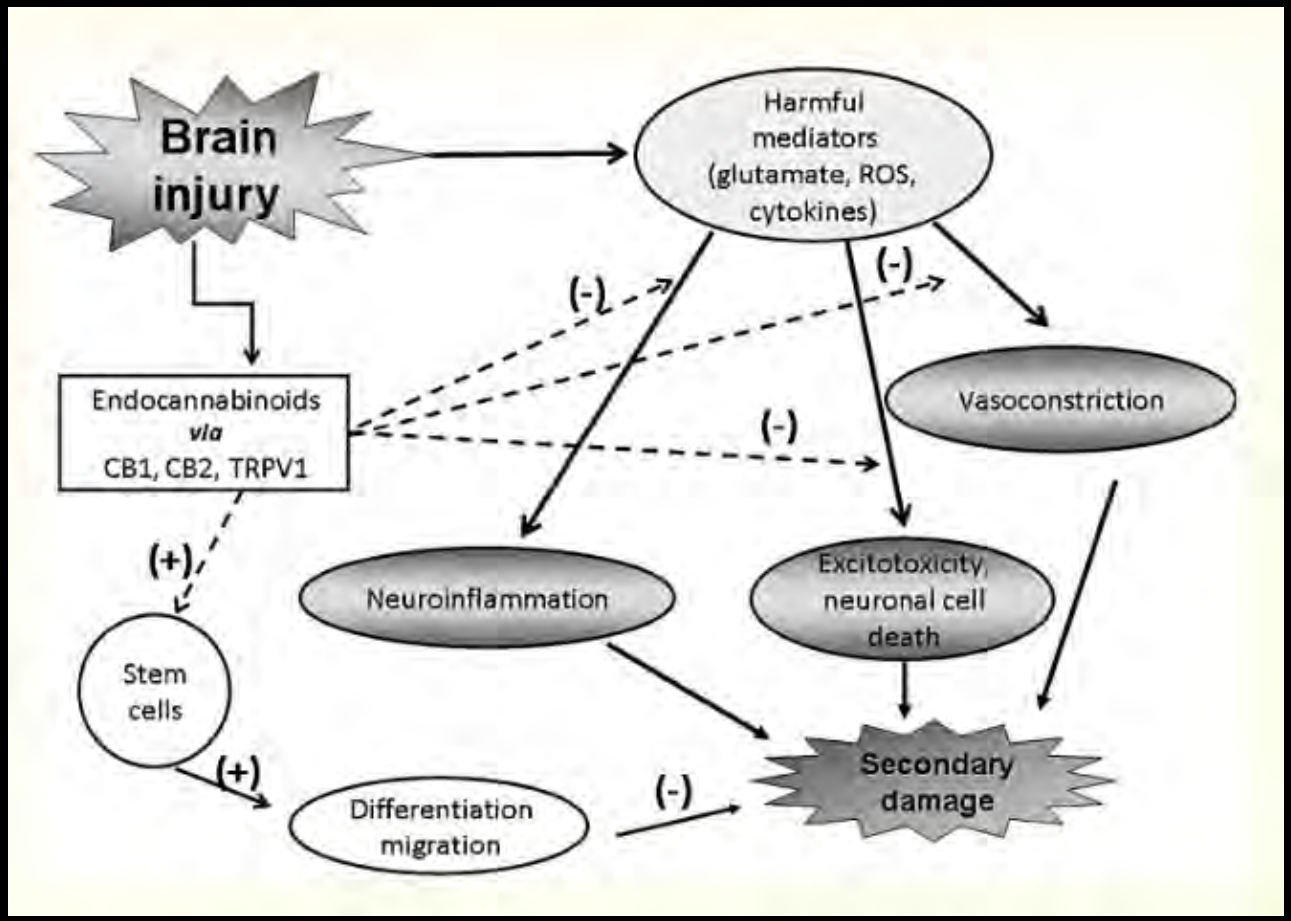
The Brain on Cannabis

- Large body of evidence from past few decades
- Observed in adults but most salient in adolescents
  - Cognitive decrements noted:
    - Verbal memory
    - Processing speed
    - Attention
    - Executive function

- fMRI studies show earlier onset of cannabis use related to altered activation during tasks requiring cognitive control and inhibition
- Linked to alterations in brain structure/function → but unclear consequences

Gruber et al, Frontiers in Pharmacology, 2018 Jan 17

Traumatic Brain Injury



Dr. Ester Shohami: IV CBD within 4 hours of TBI → significant recovery

Shohami et al. Endocannabinoids and traumatic brain injury. Br J Pharmacol 2011.

PTSD / Anxiety / Mood / Oh My?

- ECS plays a central role in the regulation of fear- and anxiety-related behavior
  - Baseline CB1 receptor activation (“tone”) normally constrains fear-related behavior & stress responses
  - Drugs that activate CB1 are anxiolytic
- In mice, CB1 activation:
  - impairs retrieval of aversive memories + enhances extinction
  - prevents the occurrence of PTSD-like behaviors after a stressor
- In humans:
  - Low-dose THC helped extinction of conditioned fear
  - PTSD associated w/ ↑ CB1 receptor availability and ↓ levels of peripheral ECs

Aug 2018

JAMA Psychiatry | Original Investigation

Effect of Cannabidiol on Medial Temporal, Midbrain, and Striatal Dysfunction in People at Clinical High Risk of Psychosis
A Randomized Clinical Trial

Sagnik Bhattacharyya, MBBS, MD, PhD; Robin Wilson, MBBS, MRCPsych; Elizabeth Appiah-Kusi, MSc; Aisling O'Neill, MSc; Michael Brammer, PhD; Jesus Perez, MBBS, MD, PhD; Robin Murray, DSc, FRCPsych, FRS; Paul Allen, PhD; Matthijs G. Bossong, PhD; Philip McGuire, MD, PhD, FRCPsych

Supplemental content

IMPORTANCE Cannabidiol (CBD) has antipsychotic effects in humans, but how these are mediated in the brain remains unclear.

OBJECTIVE To investigate the neurocognitive mechanisms that underlie the therapeutic effects of CBD in psychosis.

DESIGN, SETTING, AND PARTICIPANTS In this parallel-group, double-blind, placebo-controlled randomized clinical trial conducted at the South London and Maudsley NHS Foundation Trust

CONCLUSIONS AND RELEVANCE Cannabidiol may partially normalize alterations in parahippocampal, striatal, and midbrain function associated with the CHR state. As these regions are critical to the pathophysiology of psychosis, the influence of CBD at these sites could underlie its therapeutic effects on psychotic symptoms.

imaging (fMRI) while performing a verbal learning task.

MAIN OUTCOMES AND MEASURES Brain activation during verbal encoding and recall, indexed using the blood oxygen level–dependent hemodynamic response fMRI signal.

RESULTS Of the 16 participants in the CBD group, 6 (38%) were female, and the mean (SD) age was 22.43 (4.95) years; of 17 in the placebo group, 10 (59%) were female, and the mean (SD) age was 25.35 (5.24) years; and of 19 in the control group, 8 (42%) were female, and the mean (SD) age was 23.89 (4.14) years. Brain activation (indexed using the median sum of

nature medicine

Article | Published: 01 March 2000

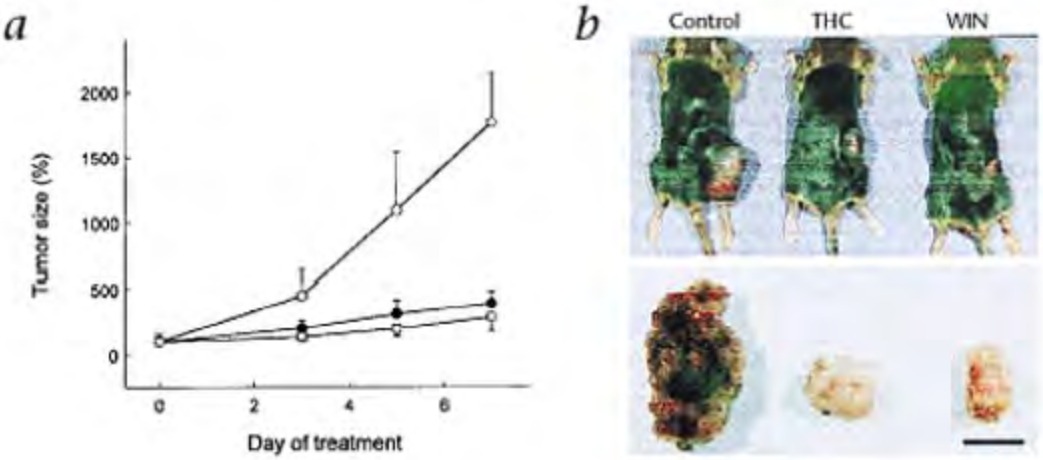
Anti-tumoral action of cannabinoids: Involvement of sustained ceramide accumulation and extracellular signal-regulated kinase activation

Ismael Galve-Roperh, Cristina Sánchez, María Luisa Cortés, Teresa Gómez del Pulgar, Marta Izquierdo & Manuel Guzmán

Nature Medicine **6**, 313–319 (2000) | Download Citation

- Andandamide & other cannabinoid agonists inhibit human breast cancer cell proliferation
- THC induces apoptosis in certain cancer cells

Figure 2: Cannabinoid-induced regression of malignant gliomas in Rag2$^{-/-}$ mice.

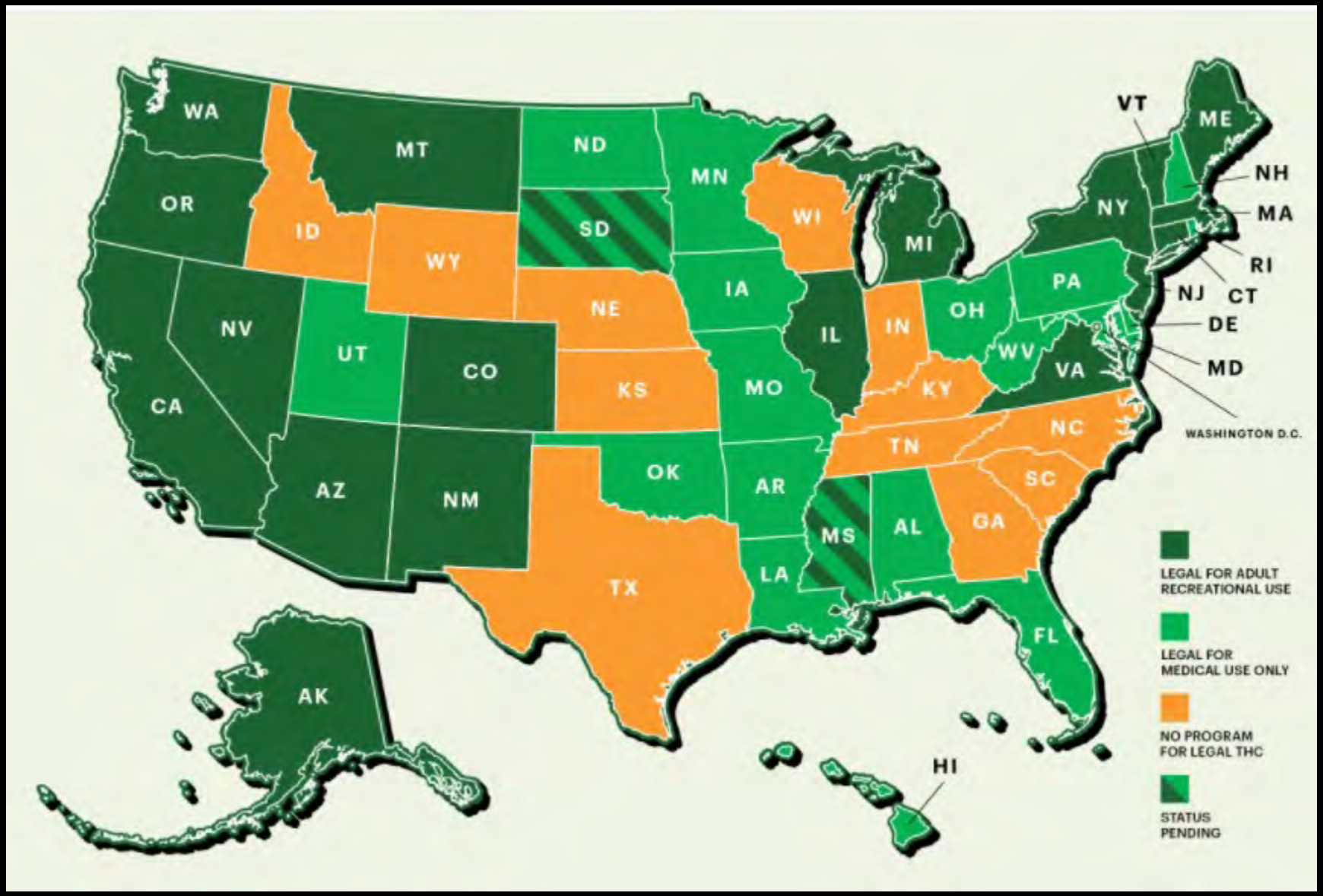


Cannabis as a “pharmacological treasure trove”

Raphael Mechoulam, PhD

> I can’t list all the physiological systems and conditions affected by cannabinoids because there are too many.
>
> DR. RAPHAEL MECHOULAM, THE CHEMIST WHO IDENTIFIED THE ENDOCANNABINOID SYSTEM

4. The New Age



Rollingstone.com

US Traffic Fatalities, 1985–2014, and Their Relationship to Medical Marijuana Laws

Julian Santaella-Tenorio, DVM, MSc, Christine M. Mauro, PhD, Melanie M. Wall, PhD, June H. Kim, MPhil, MHS, Magdalena Cerdá, DrPH, Katherine M. Keyes, PhD, Deborah S. Hasin, PhD, Sandro Galea, MD, DrPH, and Silvia S. Martins, MD, PhD

Results. On average, MML states had lower traffic fatality rates than non-MML states. Medical marijuana laws were associated with immediate reductions in traffic fatalities in those aged 15 to 24 and 25 to 44 years, and with additional yearly gradual reductions in those aged 25 to 44 years. However, state-specific results showed that only 7 states experienced post-MML reductions. Dispensaries were also associated with traffic fatality reductions in those aged 25 to 44 years.

reductions in those aged 25 to 44 years.

Conclusions. Both MMLs and dispensaries were associated with reductions in traffic fatalities, especially among those aged 25 to 44 years. State-specific analysis showed heterogeneity of the MML–traffic fatalities association, suggesting moderation by other local factors. These findings could influence policy decisions on the enactment or repealing of MMLs and how they are implemented. (*Am J Public Health.* 2017;107:336–342. doi:10.2105/AJPH.2016.303577)

between MMLs and different health outcomes. For example, a previous study showed that authorization of dispensaries in MML states was associated with treatment admissions in which marijuana is the primary substance of abuse.[11] One study to date has found evidence of dispensary legal provisions in MML states to be associated with an increase in traffic fatalities,[12] but

Substitution Hypothesis: Reduced prevalence of alcohol consumption

Am J Public Health, 2017

Original Investigation

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD, MS; Colleen L. Barry, PhD, MPP

Invited Commentary
page 1673

IMPORTANCE Opioid analgesic overdose mortality continues to rise in the United States, driven by increases in prescribing for chronic pain. Because chronic pain is a major indication for medical cannabis, laws that establish access to medical cannabis may change overdose

1999 and 2010. States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate (95% CI, −37.5% to −9.5%; *P* = .003) compared with states without

DESIGN, SETTING, AND PARTICIPANTS A time-series analysis was conducted of medical cannabis laws and state-level death certificate data in the United States from 1999 to 2010; all 50 states were included.

EXPOSURES Presence of a law establishing a medical cannabis program in the state.

MAIN OUTCOMES AND MEASURES Age-adjusted opioid analgesic overdose death rate per 100 000 population in each state. Regression models were developed including state and year fixed effects, the presence of 3 different policies regarding opioid analgesics, and the state-specific unemployment rate.

frontiers in Pharmacology

ORIGINAL RESEARCH
published: 17 January 2018
doi: 10.3389/fphar.2017.00983

The Grass Might Be Greener: Medical Marijuana Patients Exhibit Altered Brain Activity and Improved Executive Function after 3 Months of Treatment

Staci A. Gruber[1,2,3], Kelly A. Sagar[1,2,3], Mary K. Dahlgren[1,2,4], Atilla Gonenc[1,2,3], Rosemary T. Smith[1,2], Ashley M. Lambros[1,2], Korine B. Cabrera[1,2] and Scott E. Lukas[3,5]*

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OPEN ACCESS

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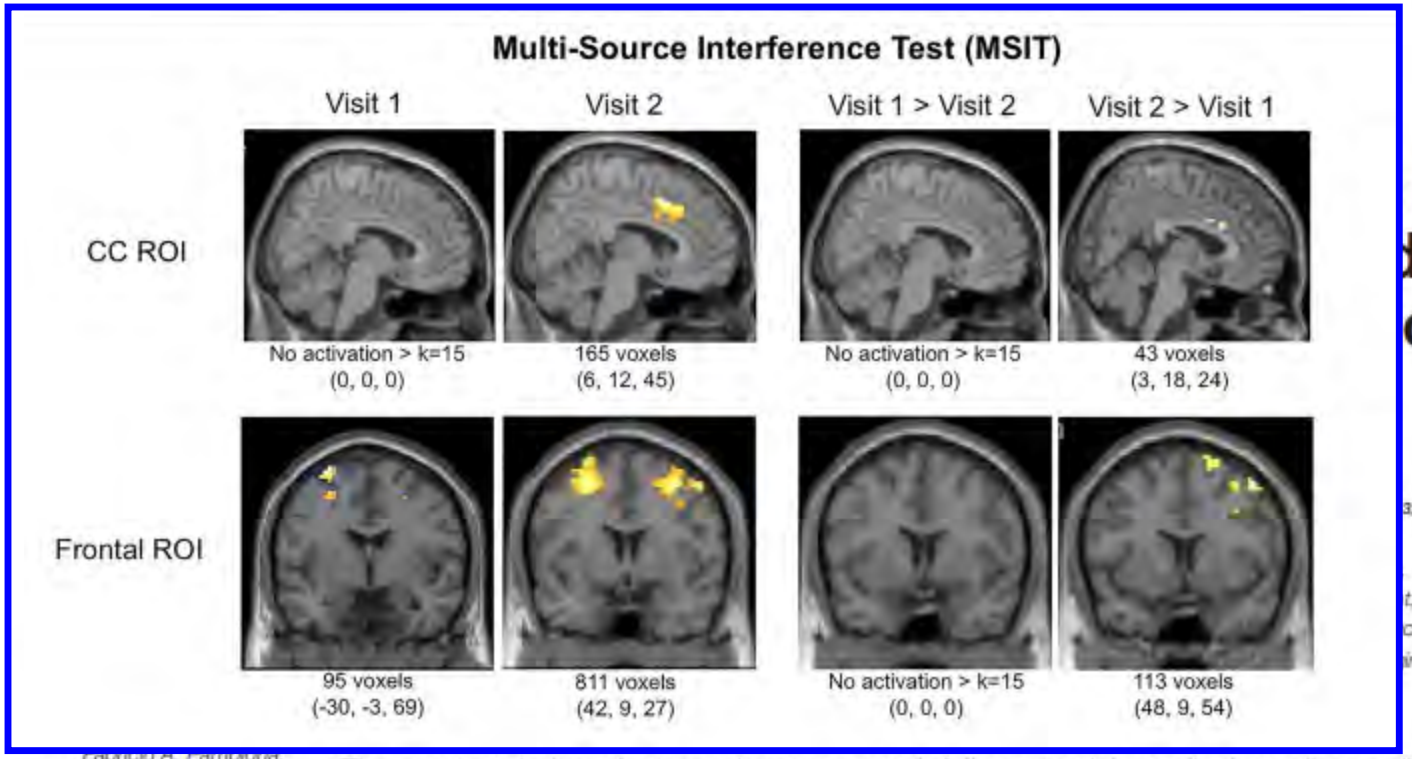
The vast majority of states have enacted full or partial medical marijuana (MMJ) programs, causing the number of patients seeking certification for MMJ use to increase dramatically in recent years. Despite increased use of MMJ across the nation, no studies thus far have examined the specific impact of MMJ on cognitive function and related brain activation. In the present study, MMJ patients seeking treatment for a variety of documented medical conditions were assessed prior to initiating MMJ treatment and

Frontiers in Pharmacology, Jan 2018

frontiers in Pharmacology

ORIGINAL RESEARCH
published: 17 January 2018
doi: 10.3389/fphar.2017.00983



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Frontiers in Pharmacology, Jan 2018

Medicinal Marijuana Program

SPOTLIGHT

NJ Medical Marijuana Dispensaries May Post Prices

Learn about this change and other developments in the Medicinal Marijuana Program.

More

Medicinal Marijuana Patient Overview

The Department has added five new categories of debilitating conditions effective March 27, 2018, which will expand the number of patients eligible to participate in the Medicinal Marijuana Program. Interested in how the program works but are not sure where to start? Learn about the patient process with our printable overview poster.

Physician's Statement

Debilitating Medical Condition: Check appropriate boxes.

- [ ] 1. Anxiety
- [ ] 2. Chronic Pain of Visceral Origin
- [ ] 3. Chronic Pain Related to Musculoskeletal Disorders
- [ ] 4. Migraine
- [ ] 5. Tourette's Syndrome
- [ ] 6. Seizure disorder, including epilepsy if resistant to conventional therapy
- [ ] 7. Intractable skeletal spasticity if resistant to conventional therapy
- [ ] 8. Glaucoma if resistant to conventional therapy
- [ ] 9. Amyotrophic lateral sclerosis
- [ ] 10. Multiple sclerosis
- [ ] 11. Terminal Cancer
- [ ] 12. Muscular dystrophy
- [ ] 13. Inflammatory bowel disease, including Crohn's disease
- [ ] 14. Terminal illness with prognosis of less than 12 months to live
- [ ] 15. Severe or Chronic pain, severe nausea or vomiting, cachexia or wasting syndrome which result from the condition or treatment of: Positive status for Human Immunodeficiency Virus (HIV), acquired immune deficiency syndrome, or cancer.
- [ ] 16. Post-Traumatic Stress Disorder (PTSD)
- [ ] 17. Opioid Use Disorder, as an adjunct to Medication Assisted Therapy

Please reach out to us!

Erin Zerbo: erin.zerbo@rutgers.edu

COE Listserv: bit.ly/coe-listserv

COE Website: bit.ly/mat-coe

24/7 MAT Provider Hotline: 844-HELP OUD