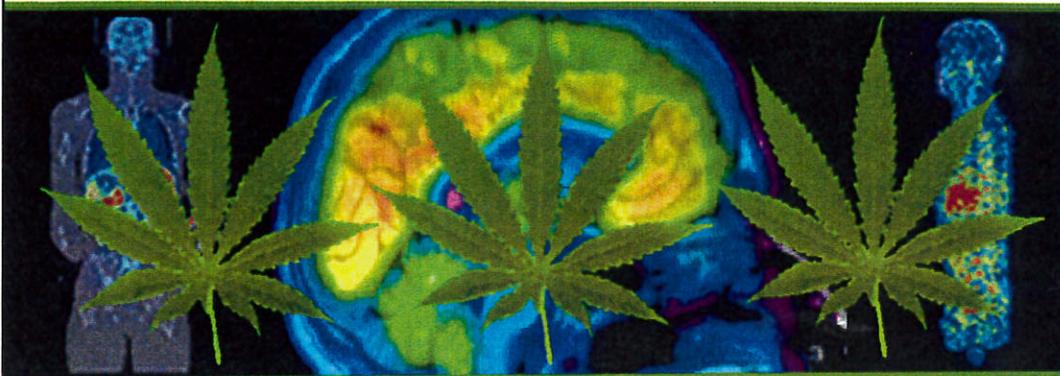


CBD - epileptic TX
 THC - no epileptic TX benefit

Effects of Cannabis on the Human Brain Therapeutic Potential



Nora D. Volkow, M.D.

Director

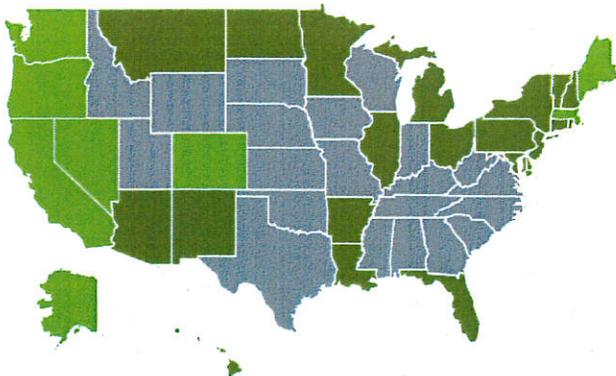
National Institute
 on Drug Abuse



@NIDAnews

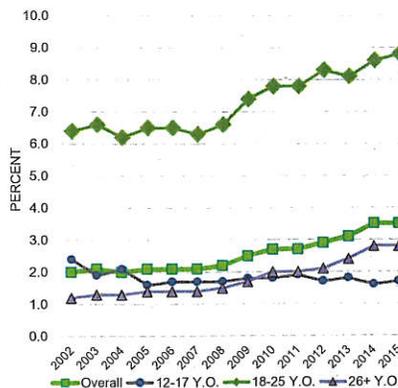
Legal Marijuana (28 states + DC)

Medical
 Recreational



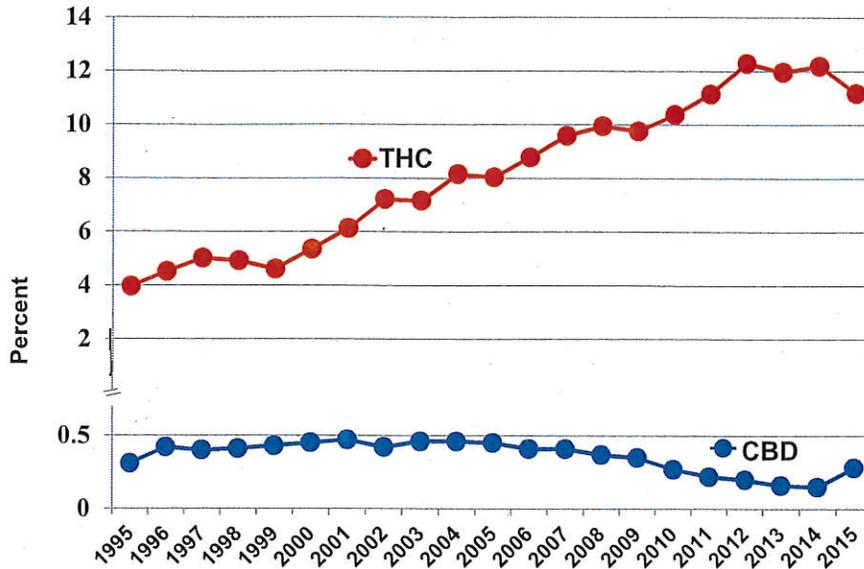
<http://www.governing.com/gov-data/safety-justice/state-marijuana-laws-map-medical-recreational.html>

Daily or Near Daily Marijuana Use



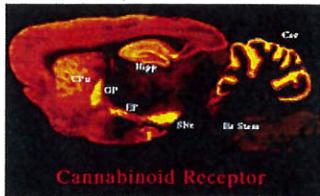
SAMHSA, National Survey on
 Drug Use and Health, 2016.

THC and CBD Potency of Non-Domestic Cannabis Samples, 1995 to 2015



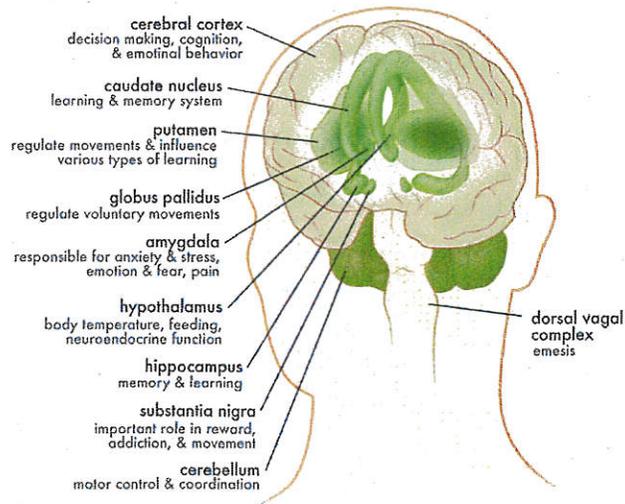
POTENCY MONITORING PROGRAM QUARTERLY REPORT NUMBER 131 -- NIDA Contract Number: N01 DA-15-7793

Cannabinoid Receptors Are Located Throughout the Brain

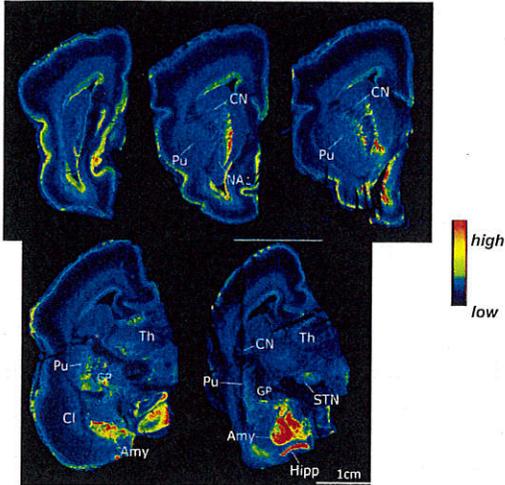


Regulation of:

- Brain Development
- Memory and Cognition
- Movement Coordination
- Pain Regulation & Analgesia
- Immunological Function
- Appetite
- Motivational Systems & Reward

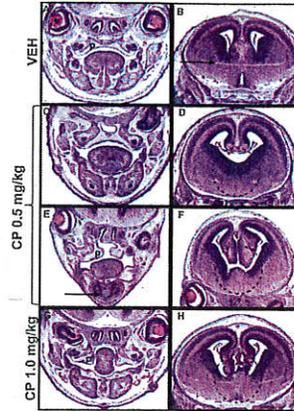


CB₁R mRNA Expression in Human Fetal Brain



Wang et al, *Neuroscience*, 2003

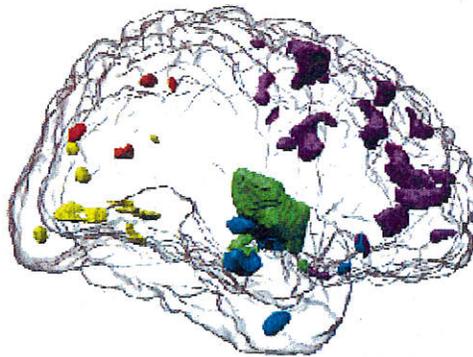
A Potent Cannabinoid Agonist (CP-55,940) Causes Brain Malformations in Fetal Mice

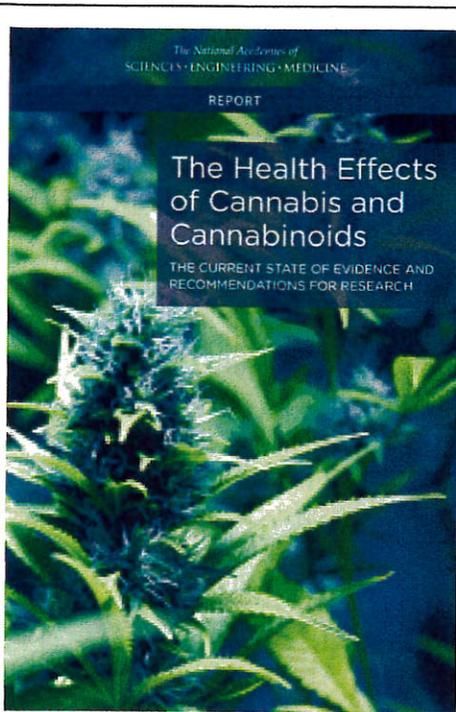


CP 55,940-treated fetal mice showing abnormalities of the brain, eyes, palate, and mandible. CP 55,940 is 45-times more potent than THC.

Marcoita et al., *Neurotox Teratology*, 2015.

Marijuana and the adolescent brain





National Academy of Sciences Report

Released: January 12, 2017

PURPOSE:

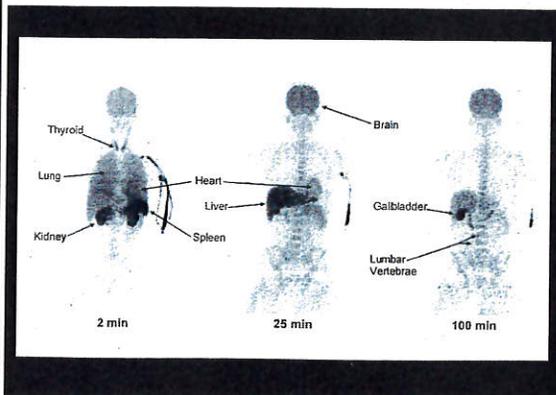
To provide a comprehensive review of the current evidence regarding the health effects of using cannabis and cannabis-derived products

RECOMMENDATIONS:

1. Address Research Gaps
2. Improve Research Quality
3. Improve Surveillance Capacity
4. Address Research Barriers

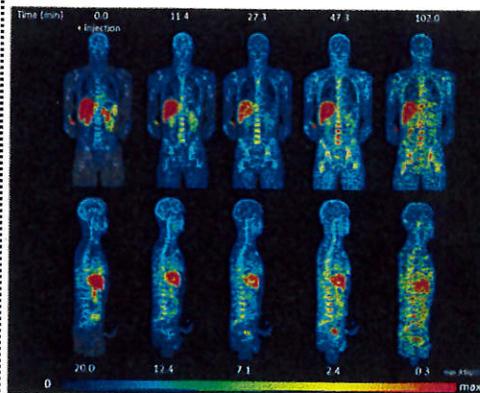
Cannabinoid Receptors Are Also Located Throughout the Body

Whole Body Distribution of CB1 Receptors (2, 25, & 100 min after injection of ^{11}C -MePPEP)



Terry et al., *Eur J Nucl Med Mol Imaging*. 2010.

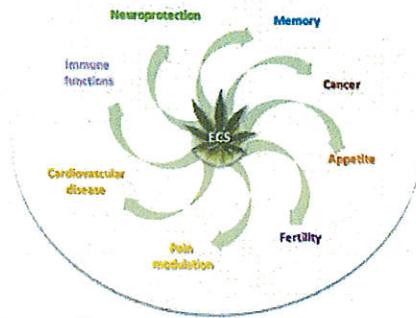
PET images of ^{11}C -NE40 (CB2R radioligand)



Ahmad et al., *Mol Imaging Biol*. 2013 A

Targeting the Cannabinoid System for Therapeutic Purposes

- **Exogenous compounds**
 - **Phytocannabinoids**
 - THC, CBD, combinations
 - **Synthetic cannabinoids**
 - Dronabinol
- **Endogenous manipulation**
 - FAAH inhibitors
 - MAGL inhibitors
 - Allosteric modulators
- **Receptor targets**
 - CB1, CB2, TRPV1, PPAR, 5-HT, peripheral, others...



Strength of the Evidence For Marijuana/Cannabinoid Medical Applications

Strongest Evidence

- Nausea (Cancer chemotherapy)
- Spasticity & Pain (MS)
- Appetite Stimulant (AIDS-associated wasting)
- **Pain esp. neuropathic**
- Glaucoma (decreases intraocular pressure; no evidence it slows disease progression; & short acting)

Modest Evidence

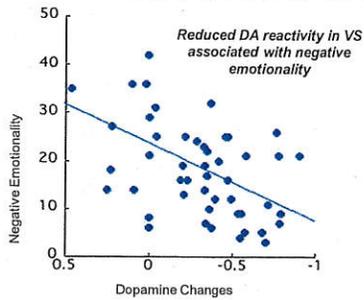
- Anticonvulsant (CBD)
- Anti-inflammatory (CBD)
- Antitumor (THC/CBD) (animal models/cell cultures: glioblastoma; breast cancer cells; others (mechanisms: apoptosis; inhibition of tumor angiogenesis))

Weakest Evidence

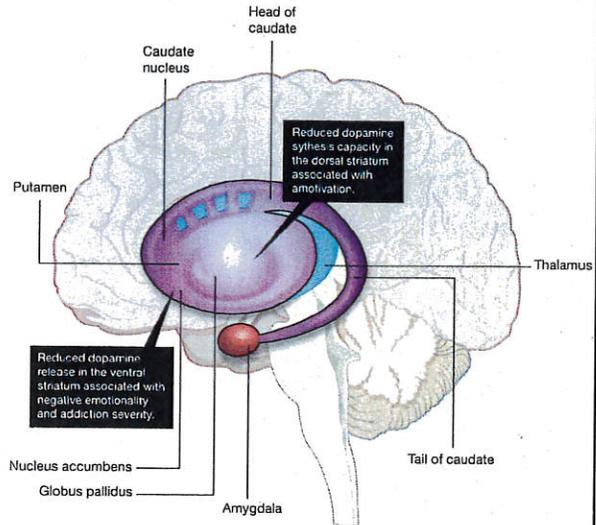
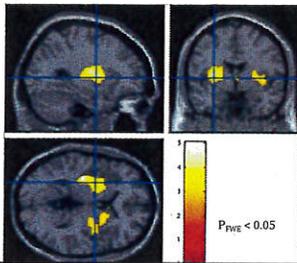
- PTSD
- ADHD
- Alzheimer's
- Depression



Marijuana: Effects on Dopaminergic systems involved with reward and motivation



Controls > Cannabis Users



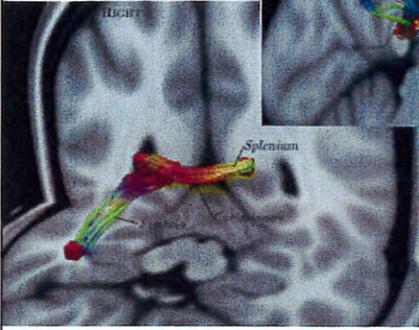
Volkow et al., PNAS 2014; Van de Giessen et al Molecular Psychiatry 2016

Marijuana and mental illness



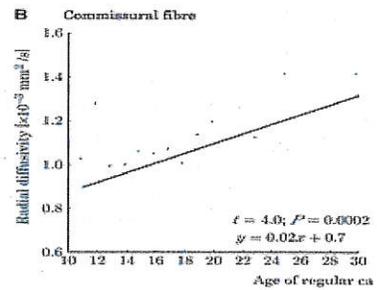
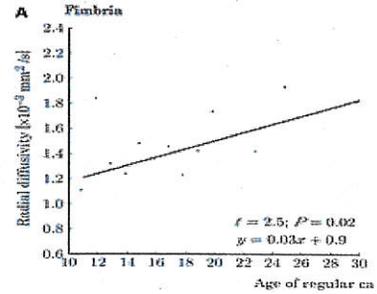
Early (<18y) Long-Term Cannabis Use Decreases Axonal Fiber Connectivity

Precuneus to splenium



Fimbria of hippocampus, hippocampal commissure and Splenium

Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) compared to controls (N=33). Zalesky et al Brain 2012.



Marijuana and the adult brain

