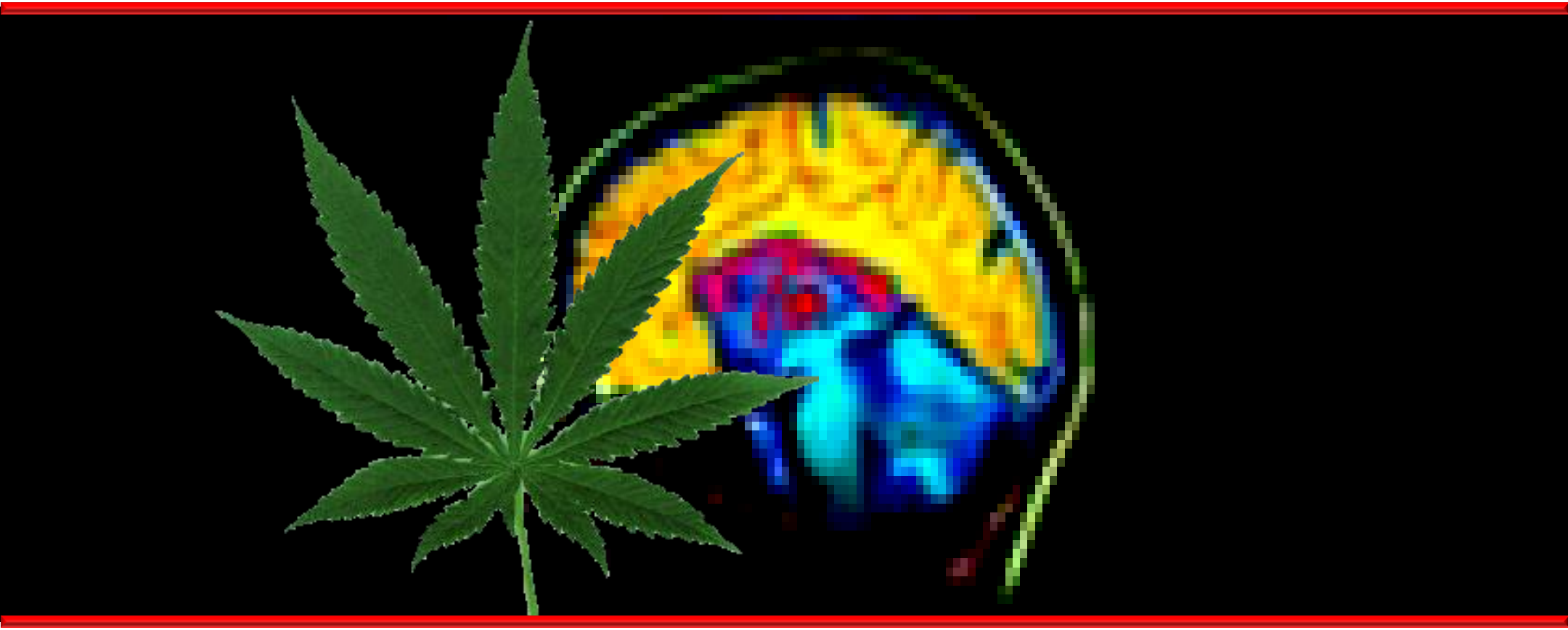
Effects of Marijuana On Brain, Body & Behavior



Nora D. Volkow, MD
Director
National Institute on Drug Abuse

Marijuana is the Most Commonly Used Illicit Drug In the U.S.

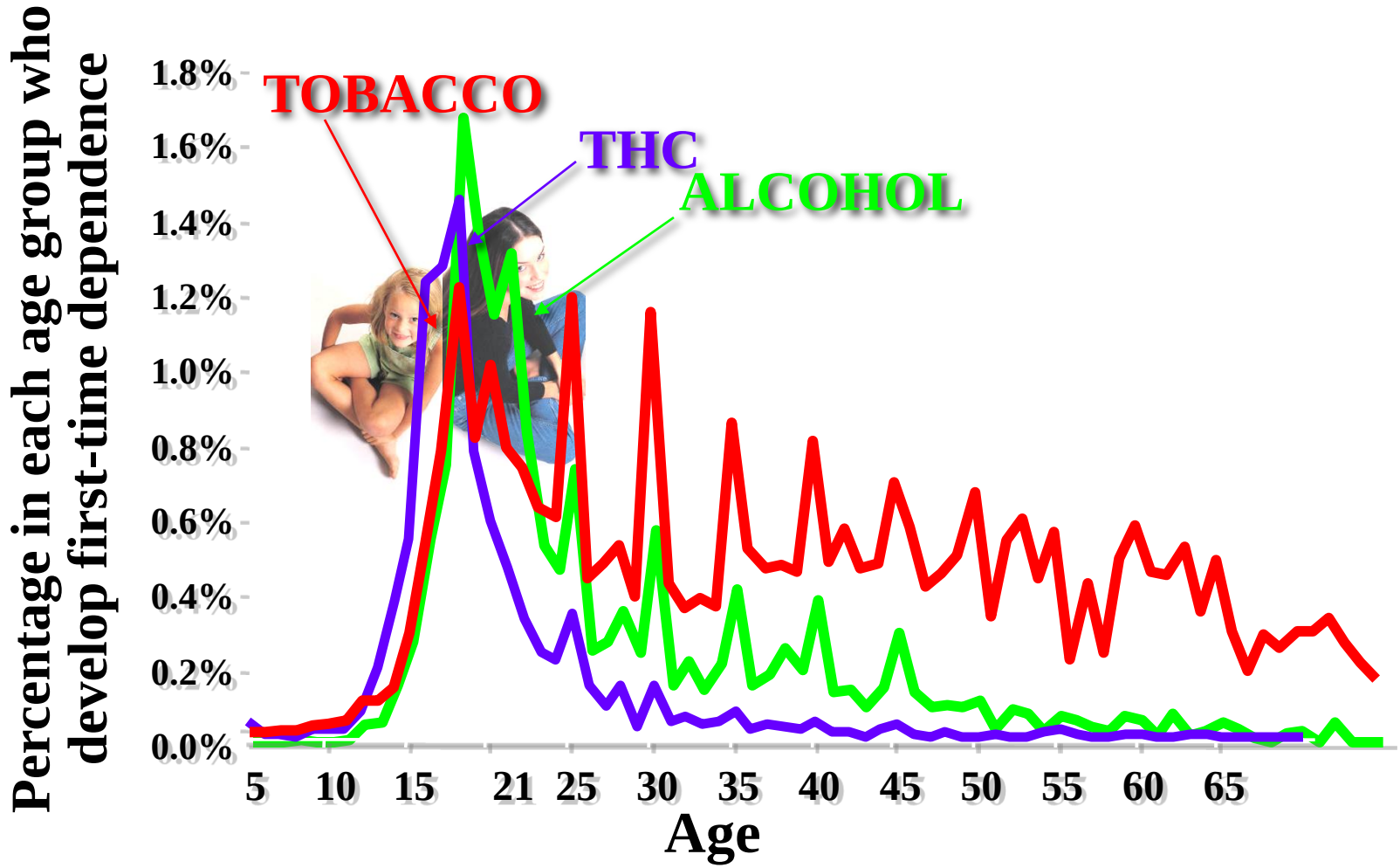
- **Over 111 million Americans have tried it at least once**
- **An estimated 2.4 million Americans used it for the first time in 2012**

Tetrahydrocannabinol (THC)
Active Ingredient in Marijuana

2012 National Survey on Drug Use and Health, SAMHSA, 2013.

ADDICTION IS A DEVELOPMENTAL DISEASE

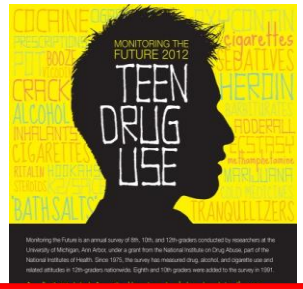
it starts in adolescence and childhood

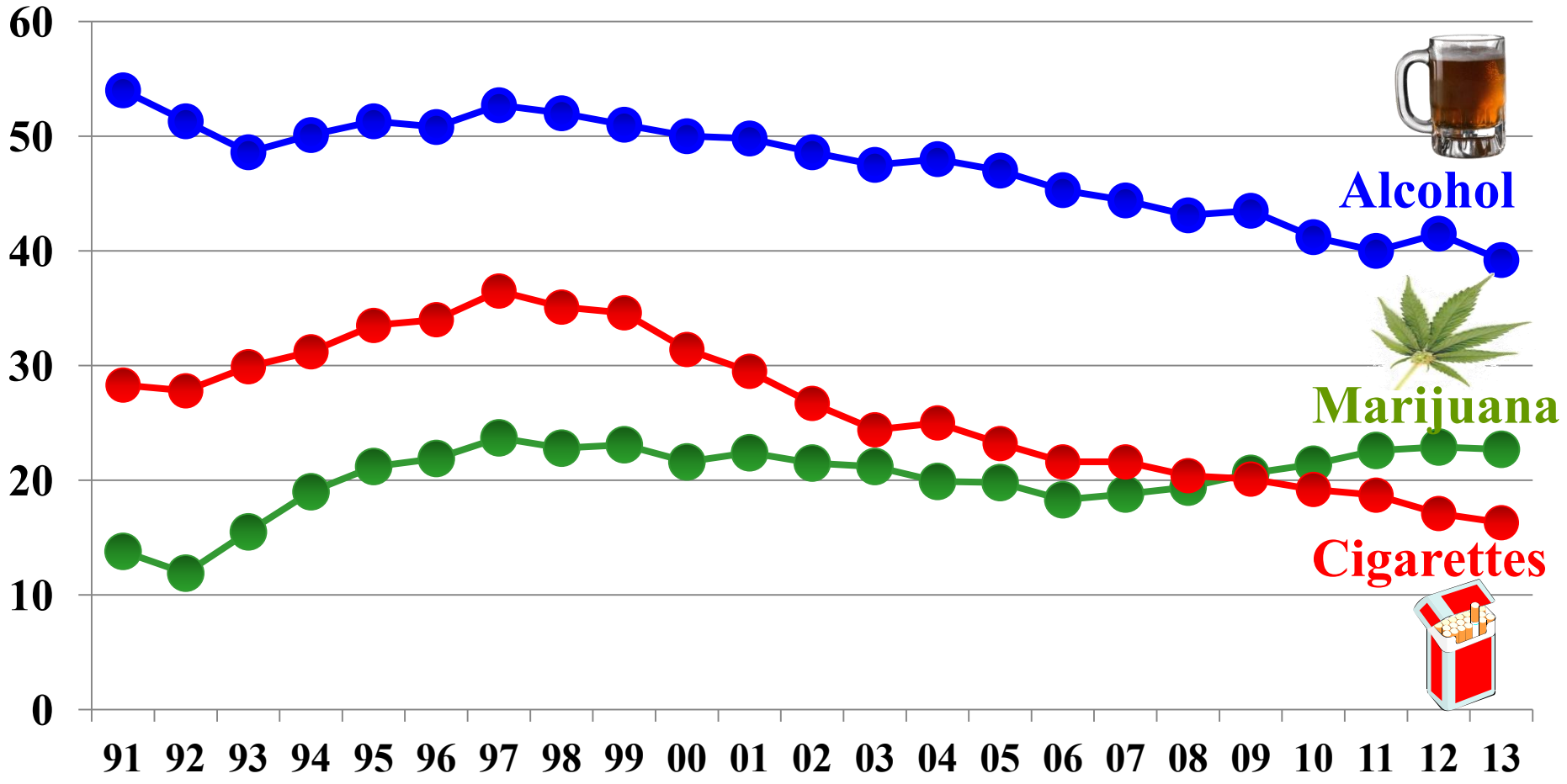


Age at tobacco, at alcohol and at cannabis use dependence as per DSM IV

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

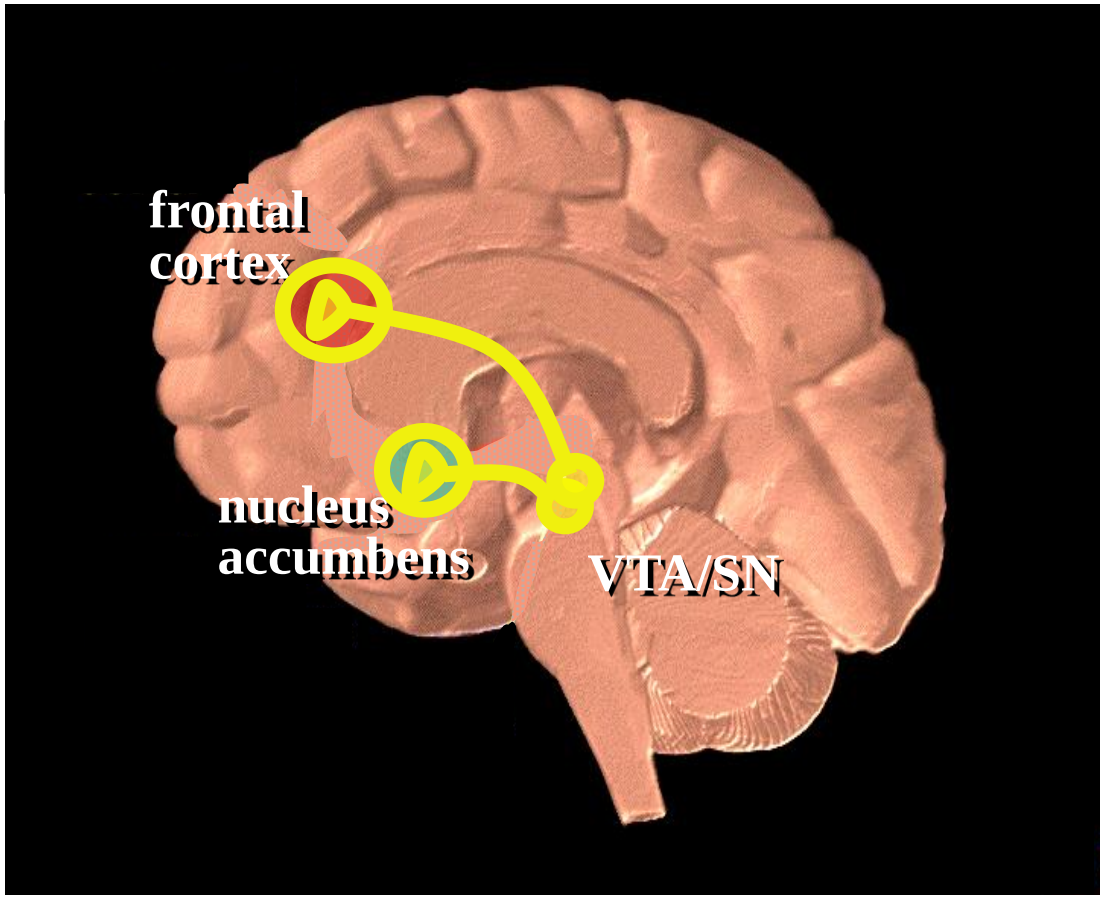
Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes, Marijuana and Alcohol



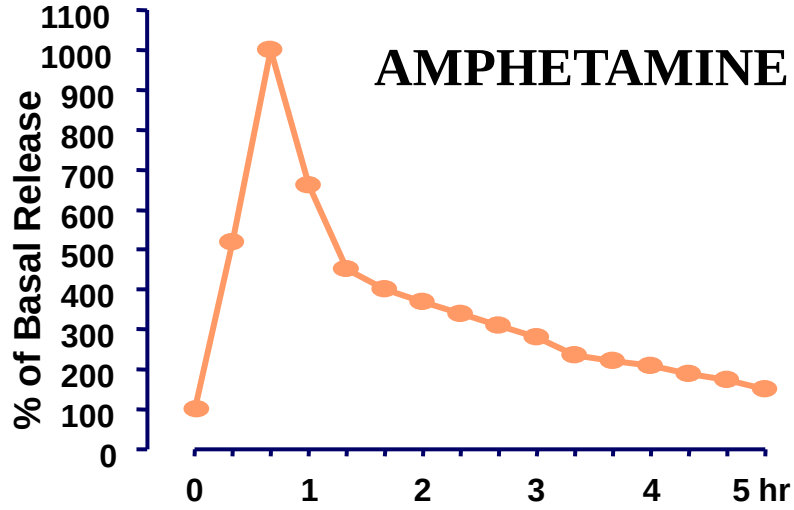


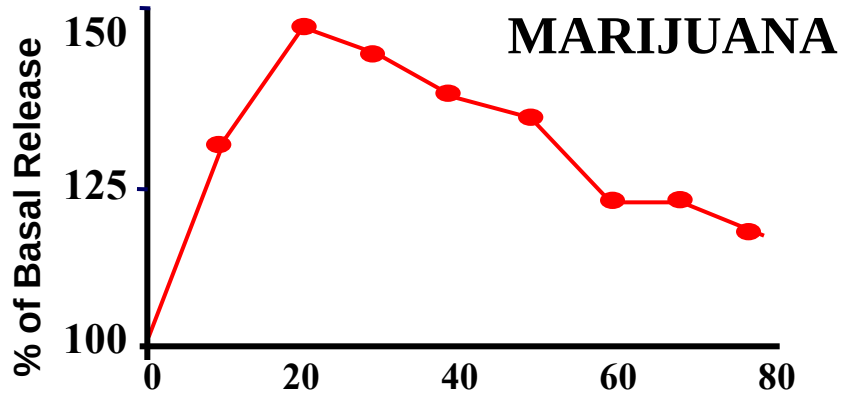
SOURCE: University of Michigan, 2013 Monitoring the Future Study.

Natural and Drug Reinforcers Increase Dopamine in NAc

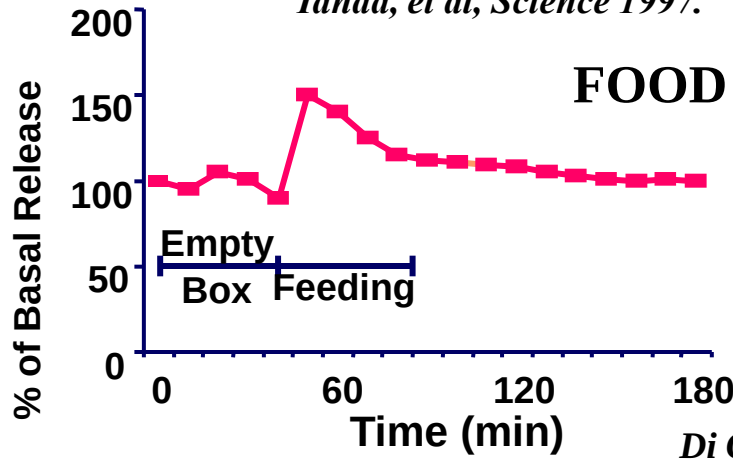


Drugs of abuse increase DA in the Nucleus Accumbens, which is believed to trigger the neuroadaptions that result in addiction



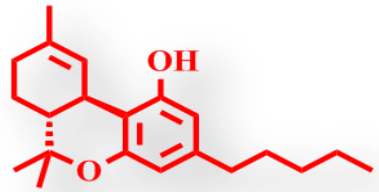


Tanda, et al, Science 1997.



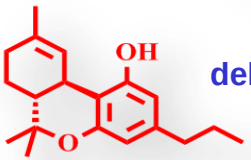
Di Chiara et al.

Constituents of MJ and the Cannabinoid System



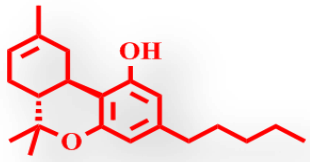
Δ^9-THC

delta-9-tetrahydrocannabinol



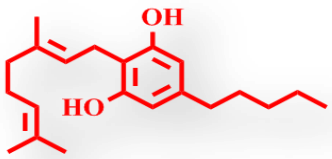
Δ^9-THCV

delta-9-tetrahydrocannabivarin



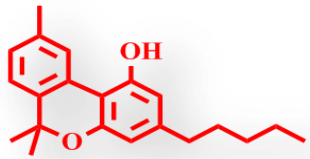
Δ^8-THC

delta-8-tetrahydrocannabinol



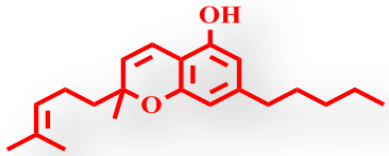
CBG

cannabigerol



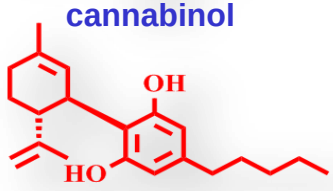
CBN

cannabinol



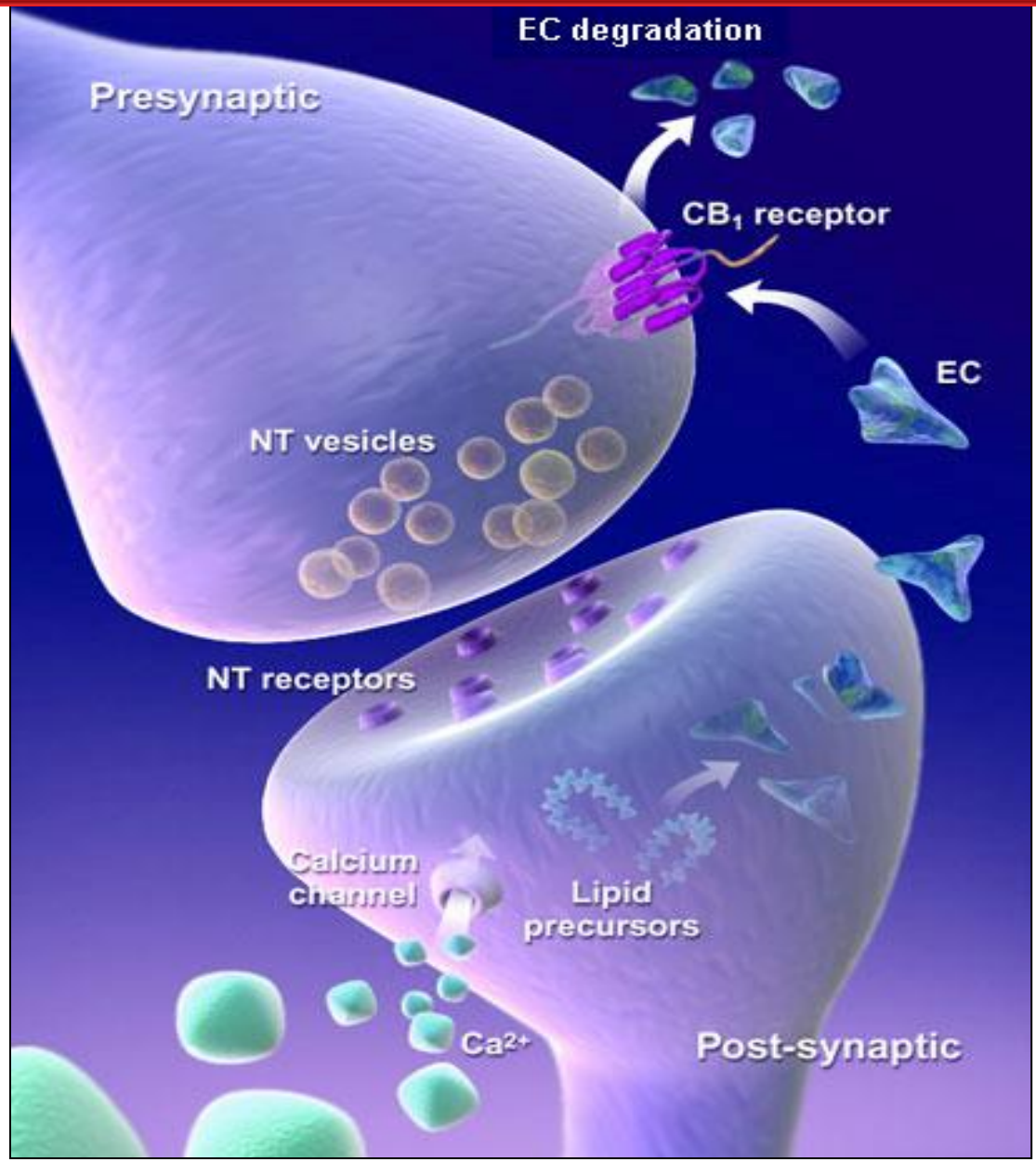
CBC

cannabichromene



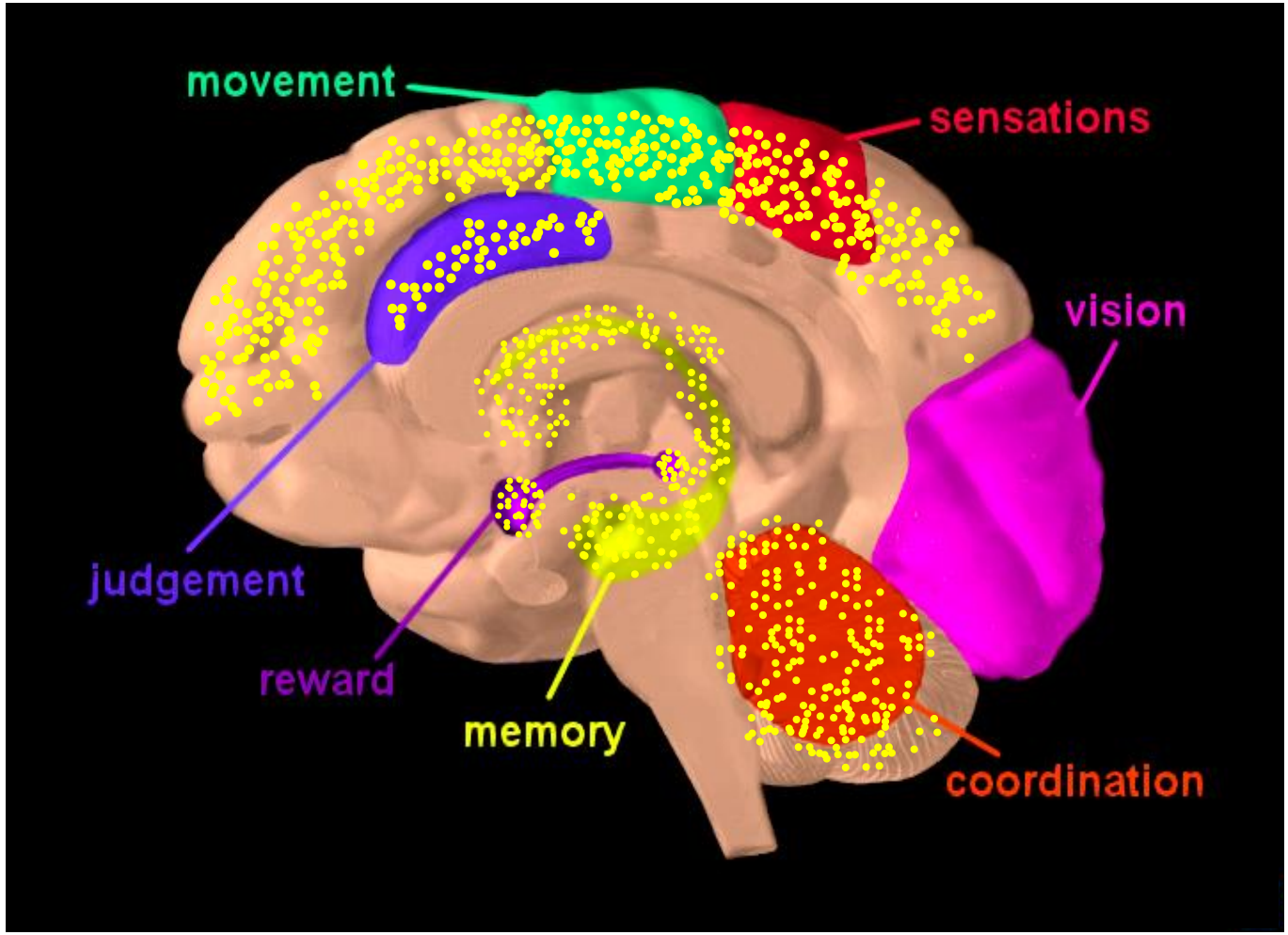
CBD

cannabidiol



Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

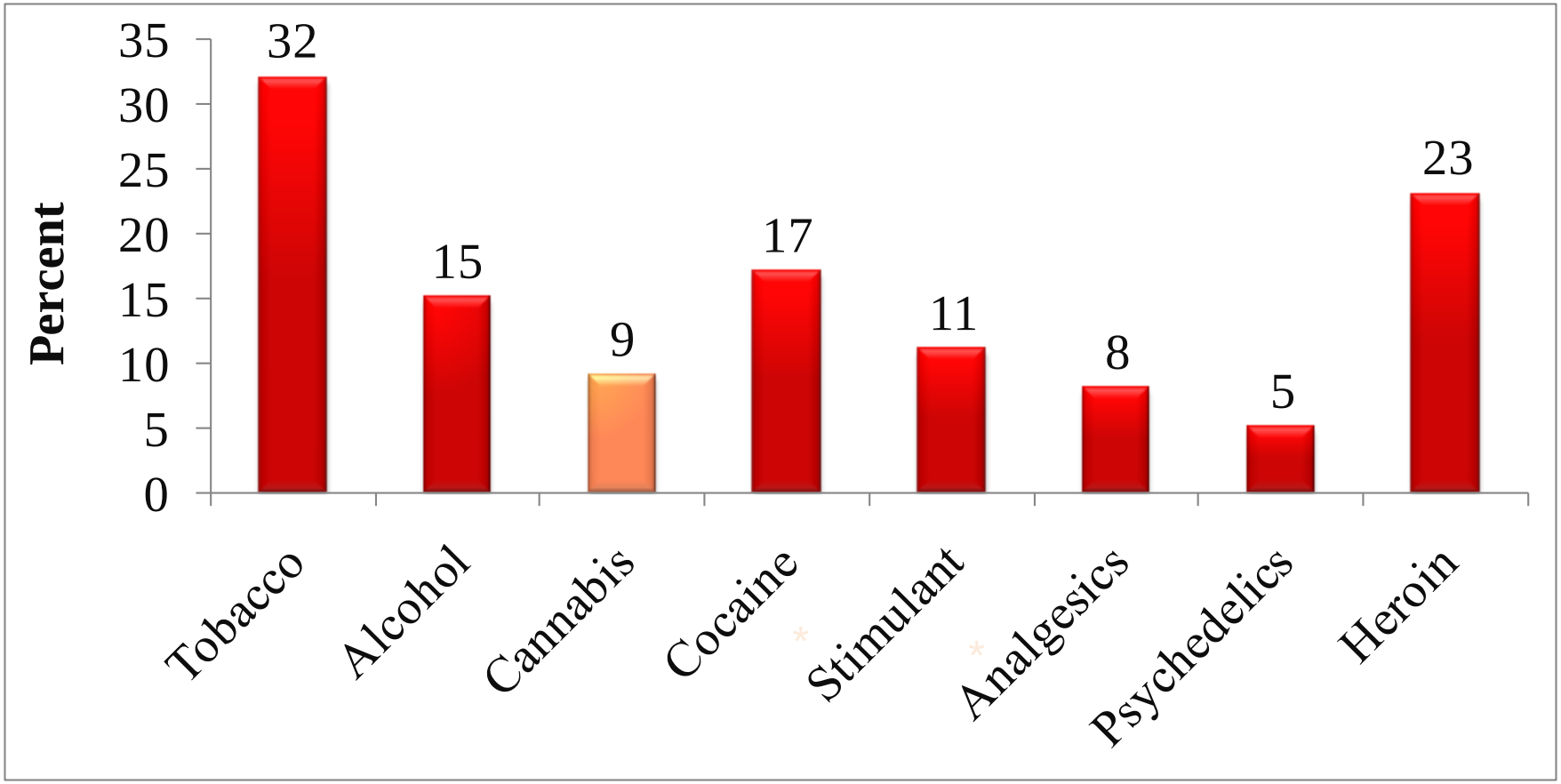
- Brain Development
- Memory and Cognition
- Motivational Systems & Reward
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia



Long Term Effects of Marijuana

Addiction: About 9% of users may become dependent, 1 in 6 who start use in adolescence, 25-50% of daily users

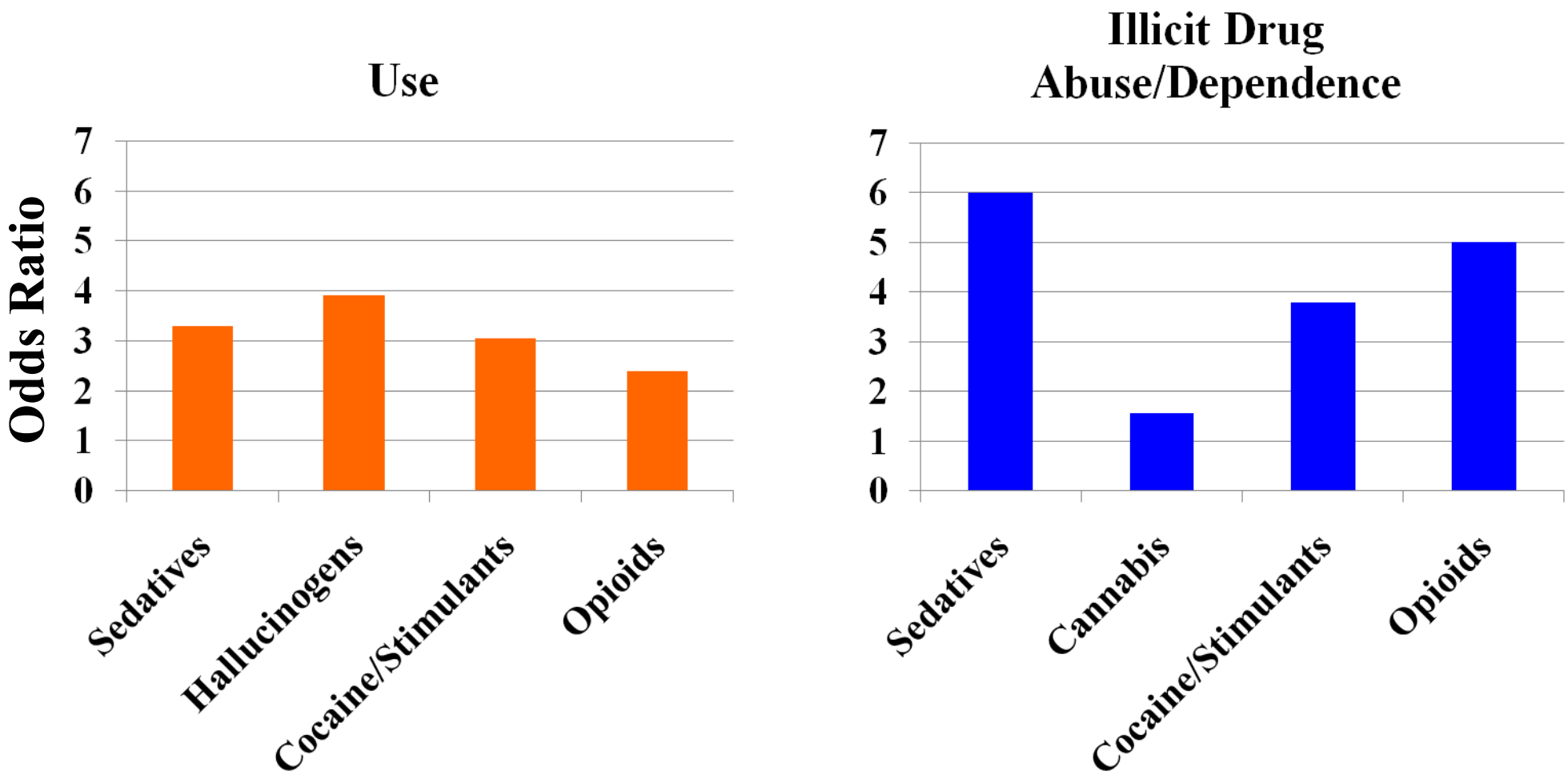
Estimated Prevalence of Dependence Among Users



**** Nonmedical Use***

Source: Anthony JC et al., 1994

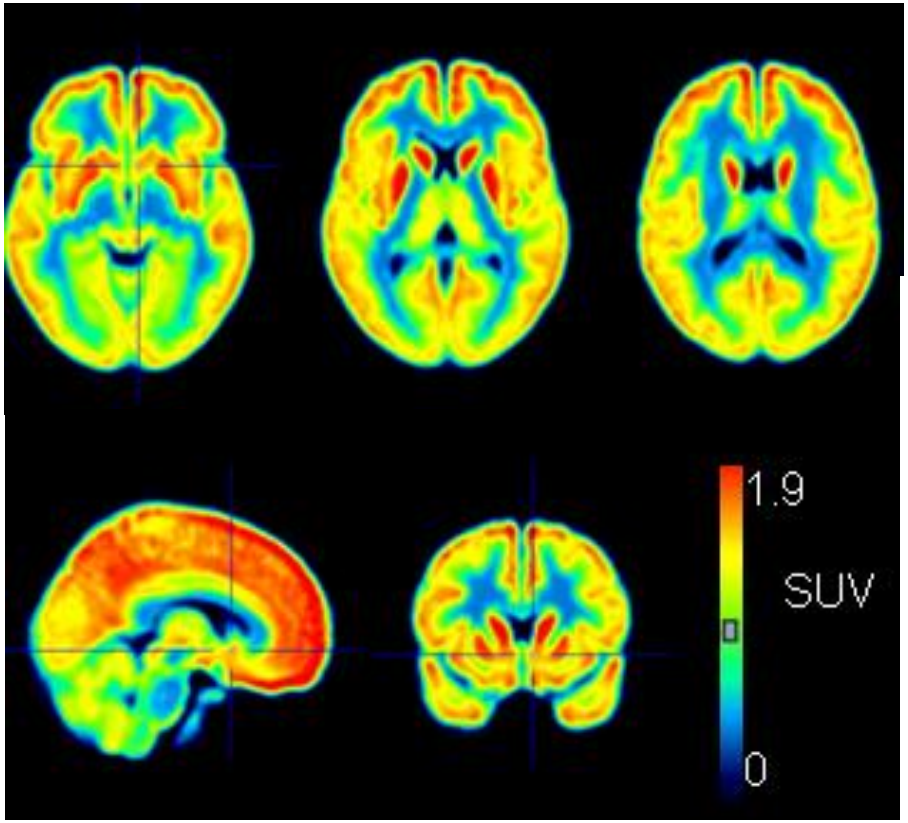
Drug Use Outcomes in Twin Pairs (n =234) Discordant for Cannabis Use Before Age 17



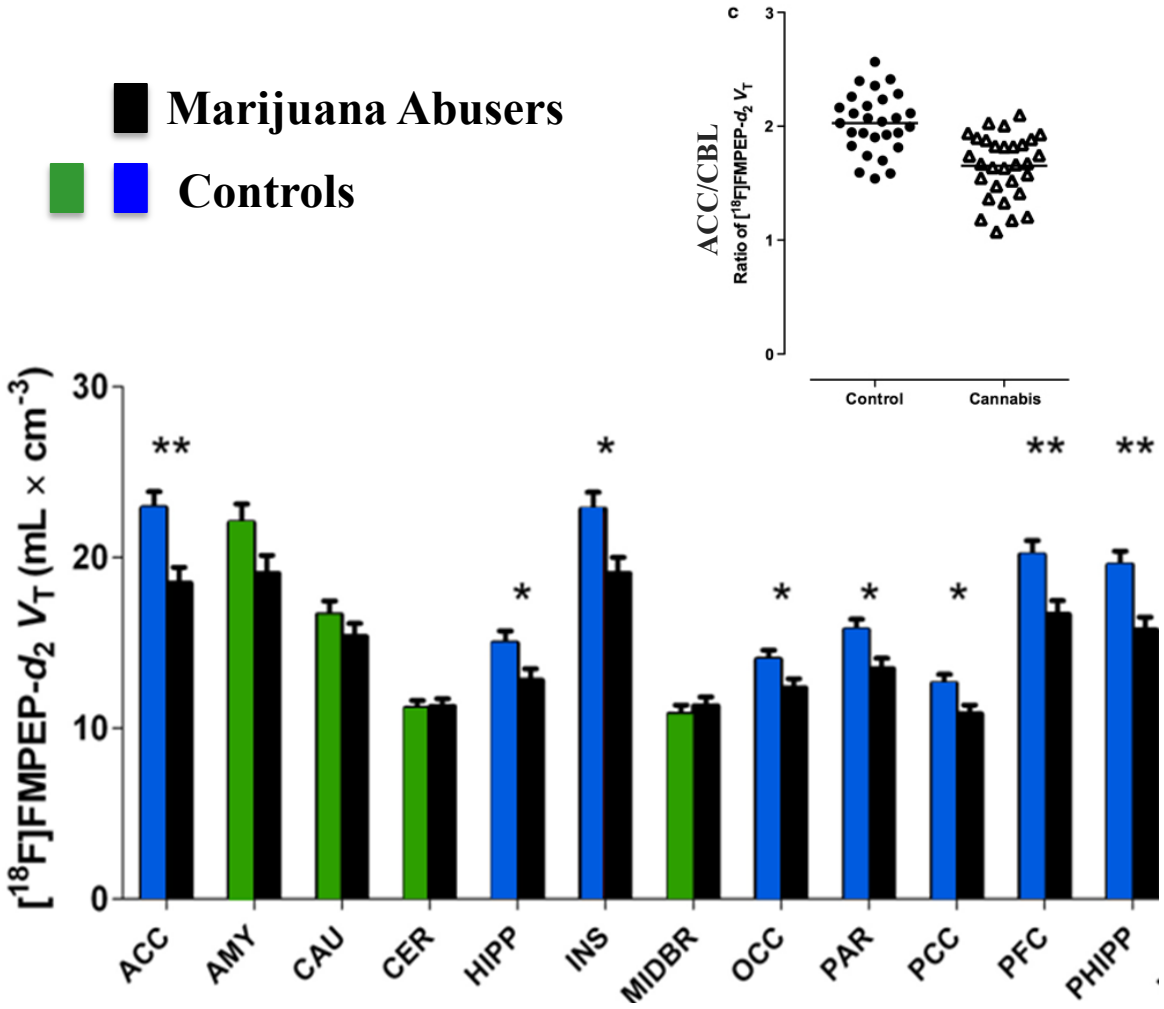
Source: Lynskey, MT et al., JAMA, 289, pp. 427-433, 2003.

Does marijuana use negatively affect the brain?

Cannabinoid CB1 Receptors in Human Brain are Downregulated in Marijuana Abusers

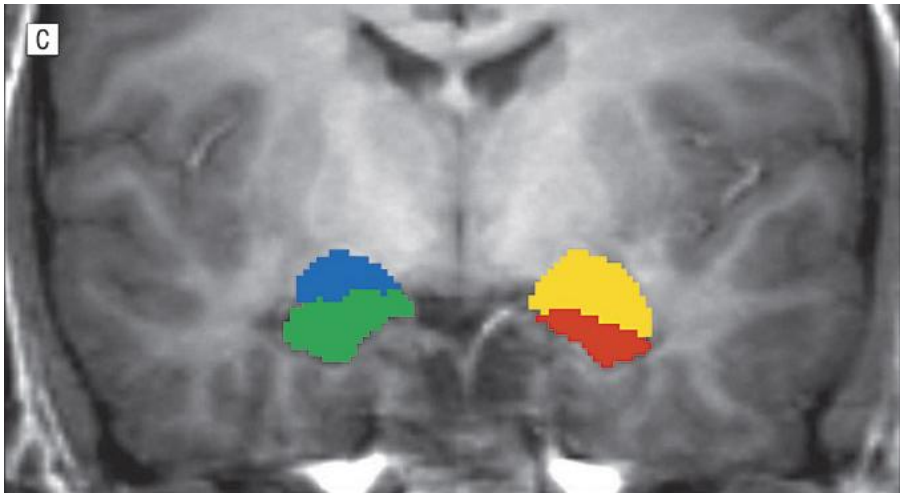


Van Loere et al., 2007.



Hirvonen et al., Mol Psychiatry 2013

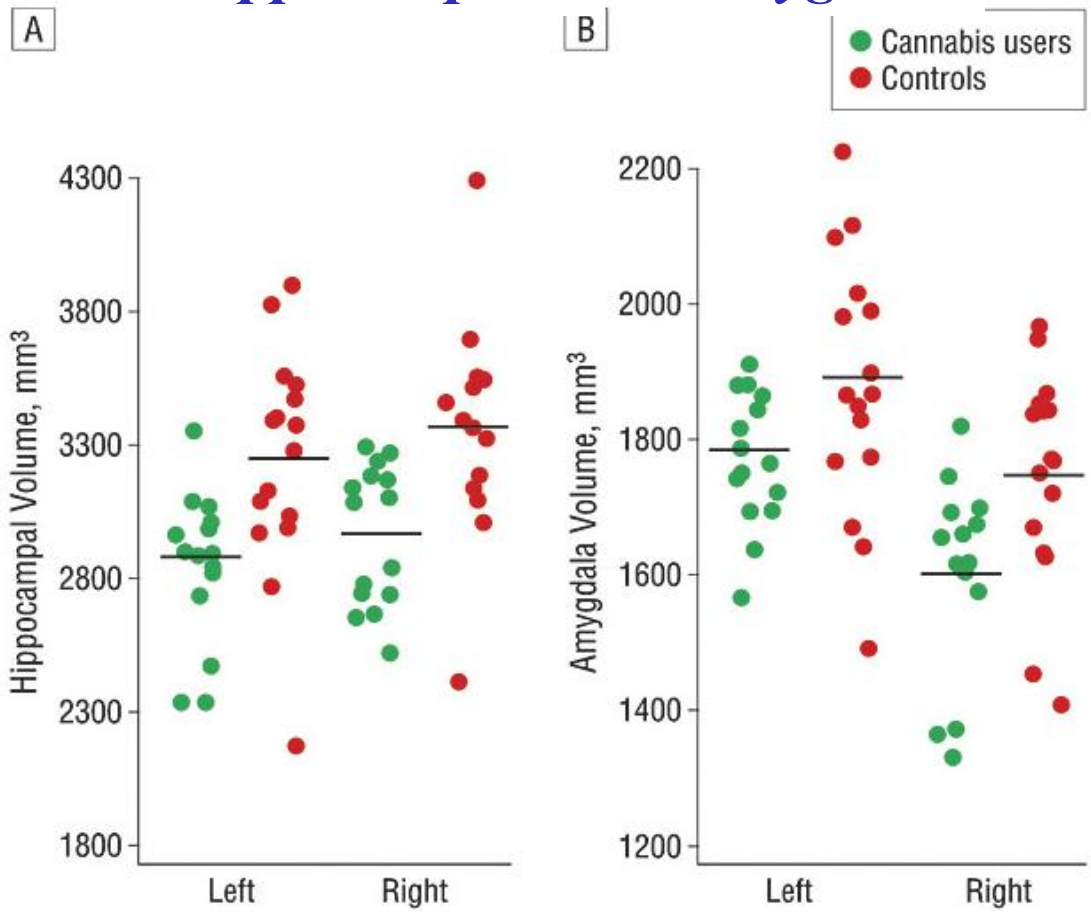
Brain abnormalities associated with long-term heavy cannabis use



L (yellow) and R (blue) amygdala
L(red) and R(green) hippocampus

morphology and function of hippocampus has been linked to reduced memory performance in heavy cannabis users

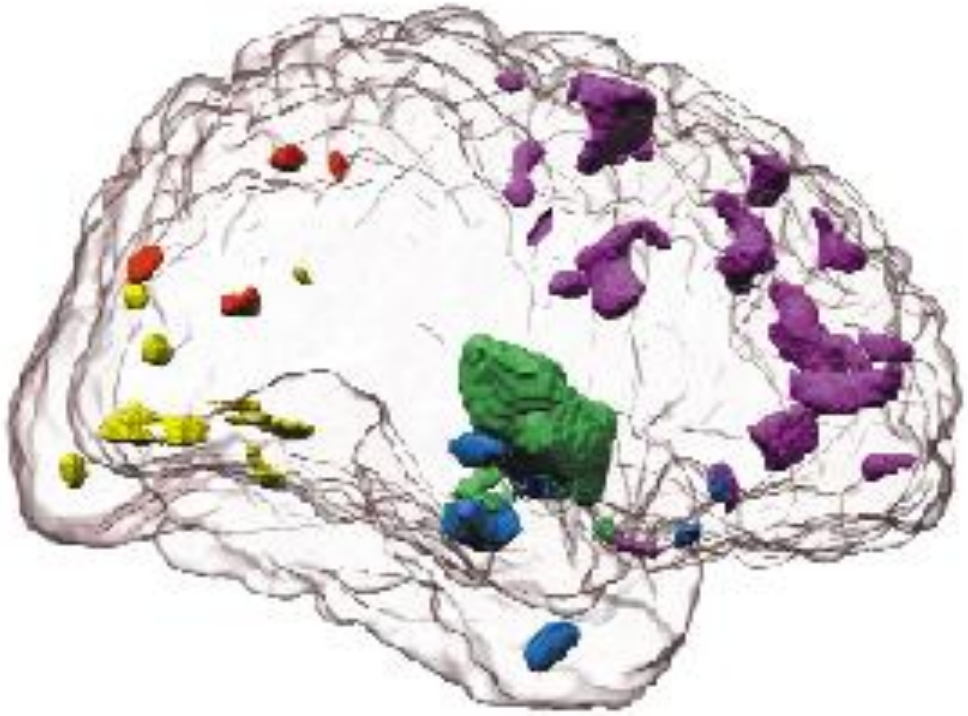
Hippocampus ***Amygdala***



Hippocampal and amygdalar volumes were smaller in cannabis users than in controls.

Yucel et al., Arch Gen Psychiatry. 2008 Jun;65(6):694-701.

BRAIN DEVELOPMENT & THC

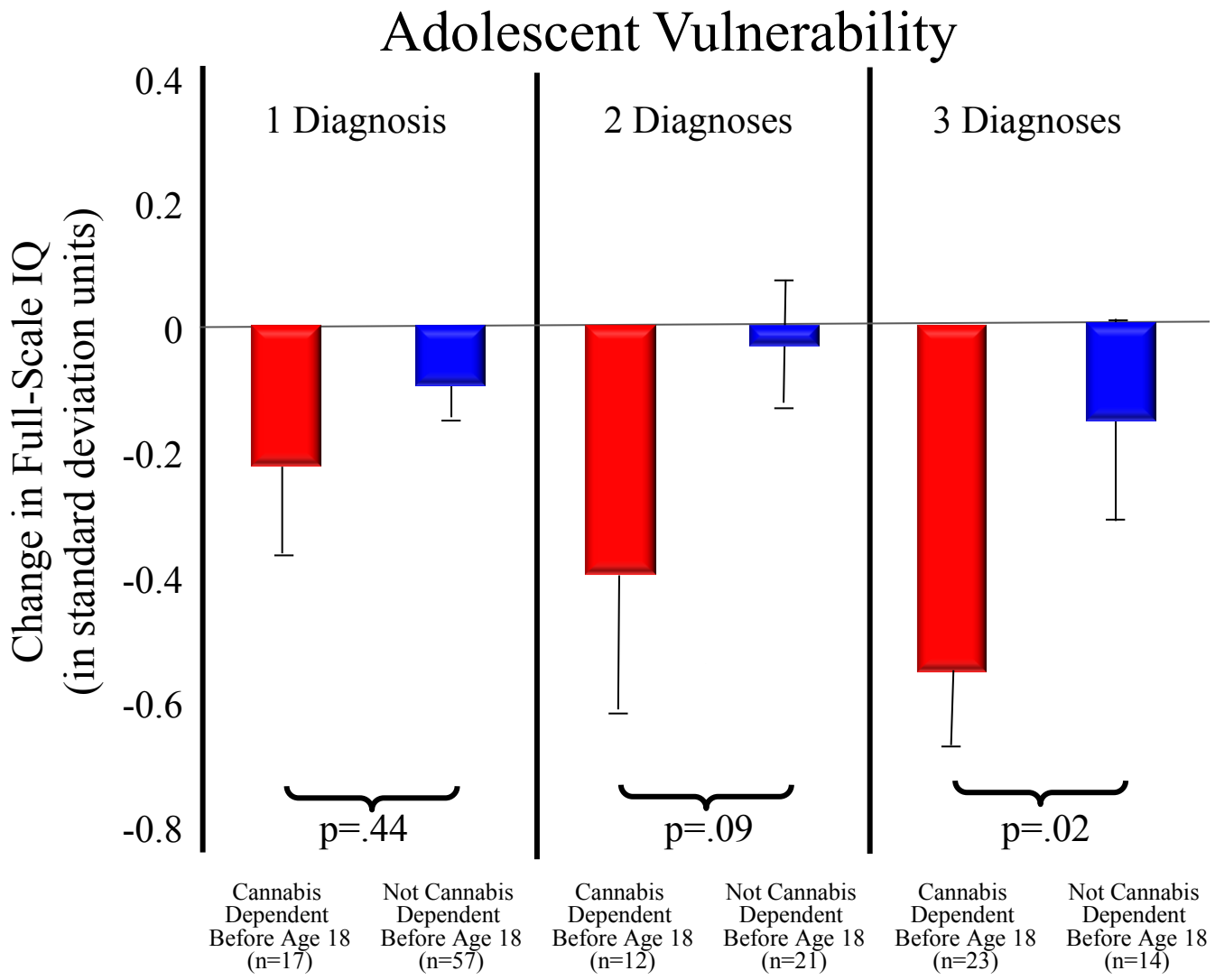


Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife

Dunedin prospective study of 1037 Ss born 1972/73,

Tested for IQ at age 13 and 38y.

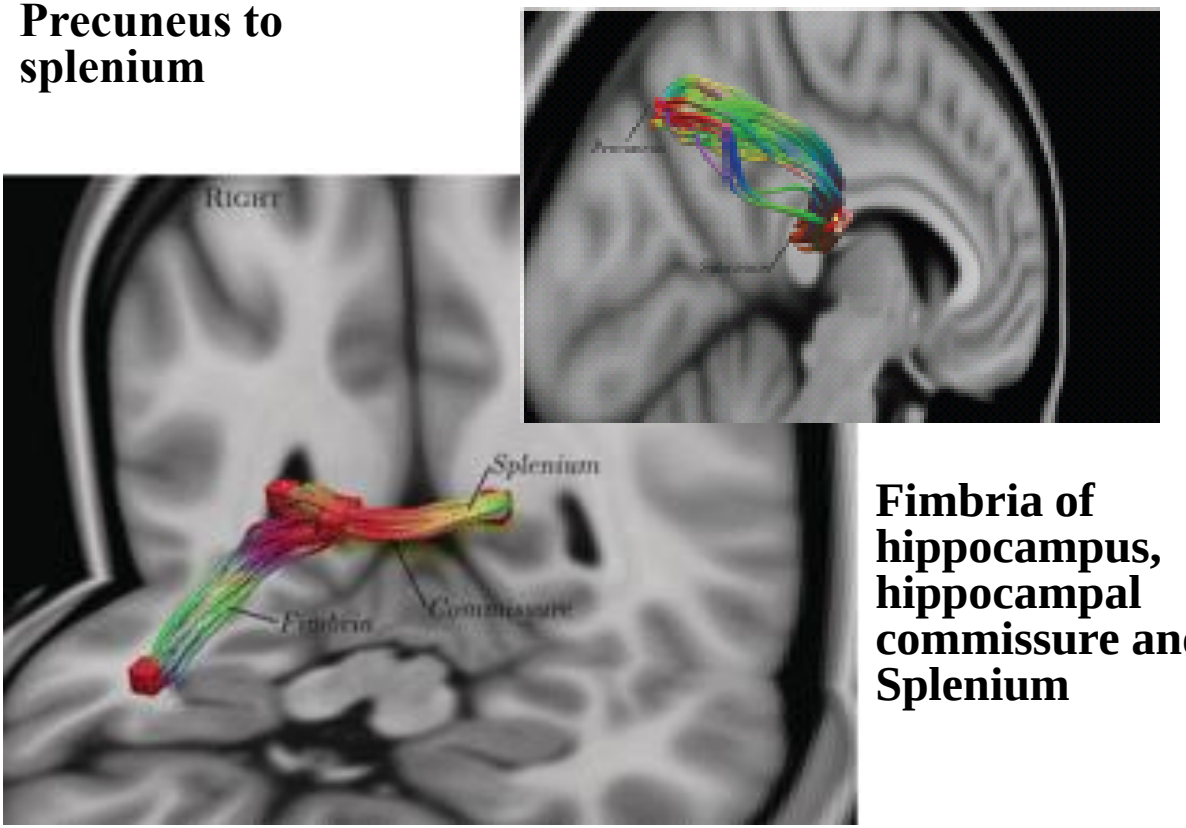
Tested THC use ages 18, 21, 26, 32 and 38y



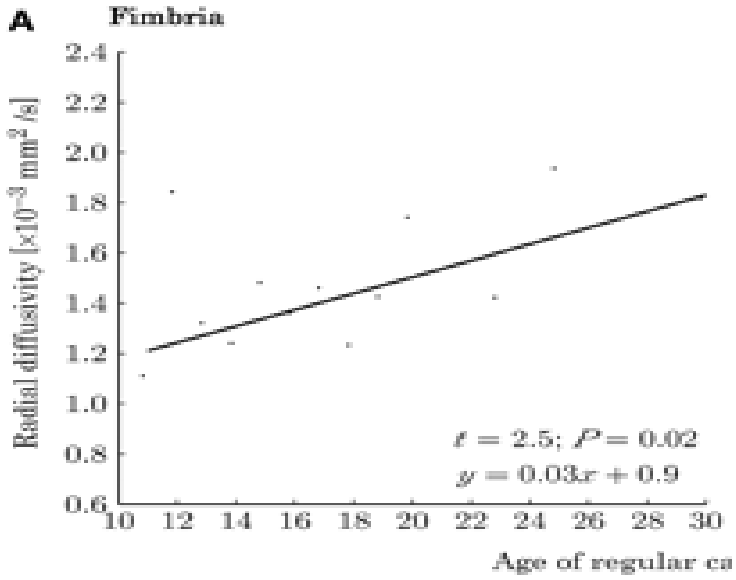
Source: Meier MH et al., PNAS Early Edition 2012.

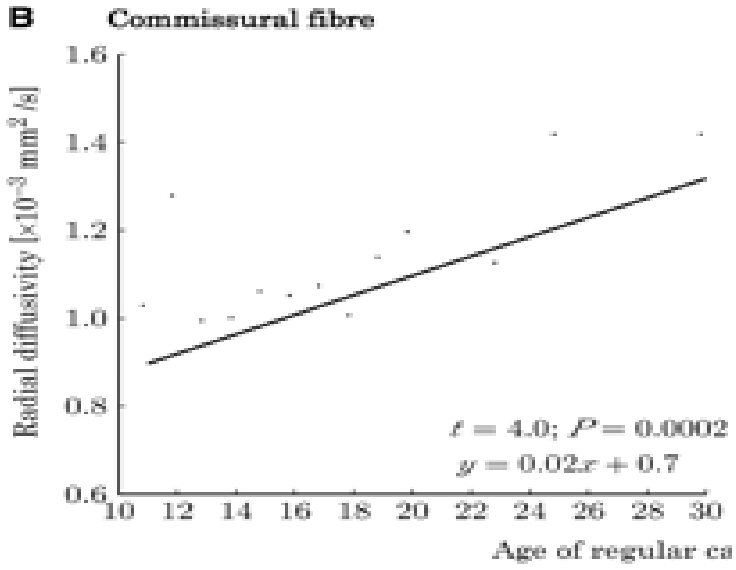
Early (<18y) Long-Term Cannabis Use Decreases Axonal Fiber Connectivity

Precuneus to splenium



Fimbria of hippocampus, hippocampal commissure and Splenium

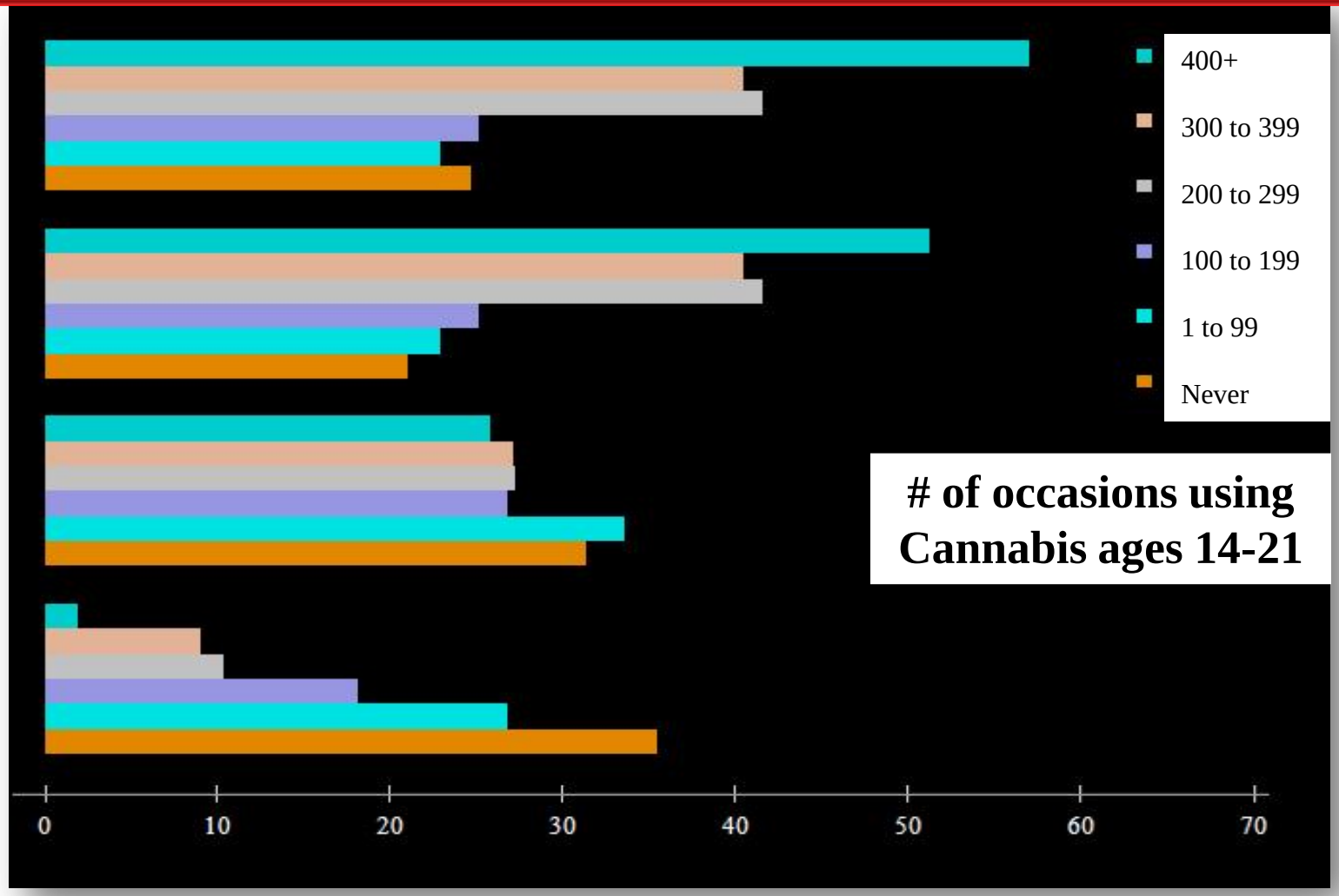




Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33). ***Zalesky et al Brain 2012.***

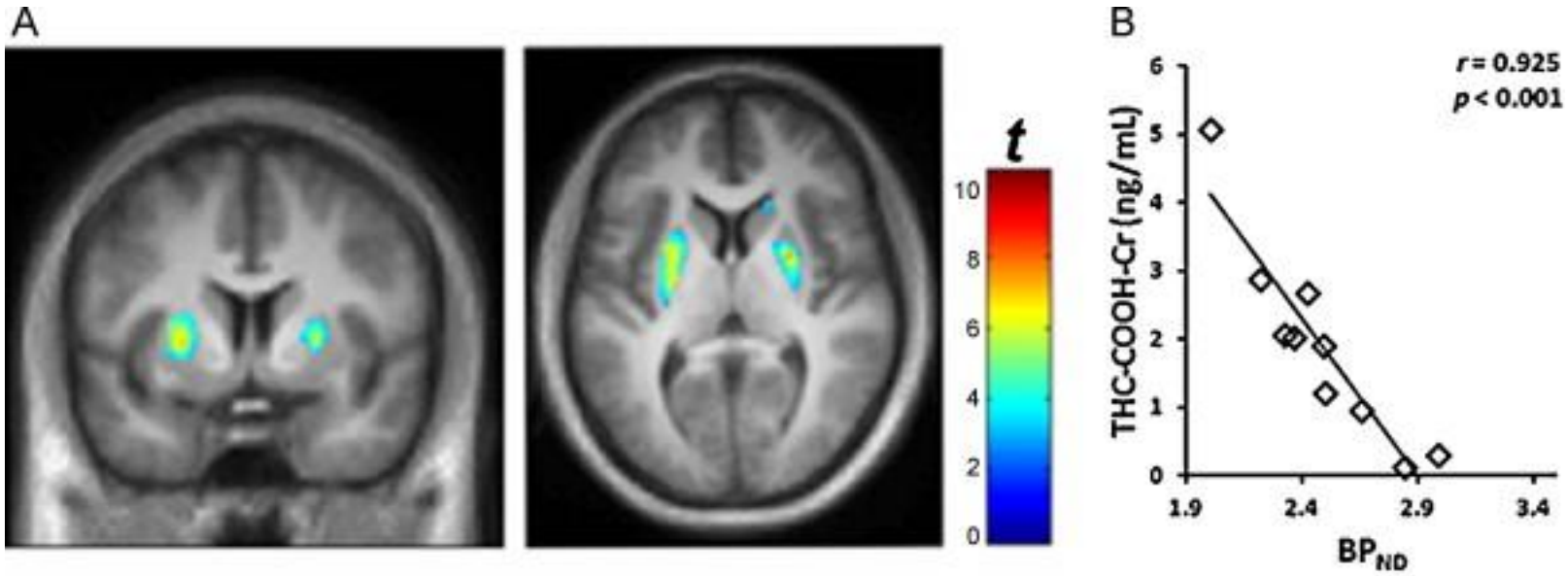
AMOTIVATION & THC

Cannabis Use and Later Life Outcomes Are Dose Dependent



Source: Fergusson and Boden. Addiction, 103, pp. 969-976, 2008.

Correlations between Urine Concentration of THC and D2R availability (RAC BP_{ND}) in Cannabis Users (n = 10)

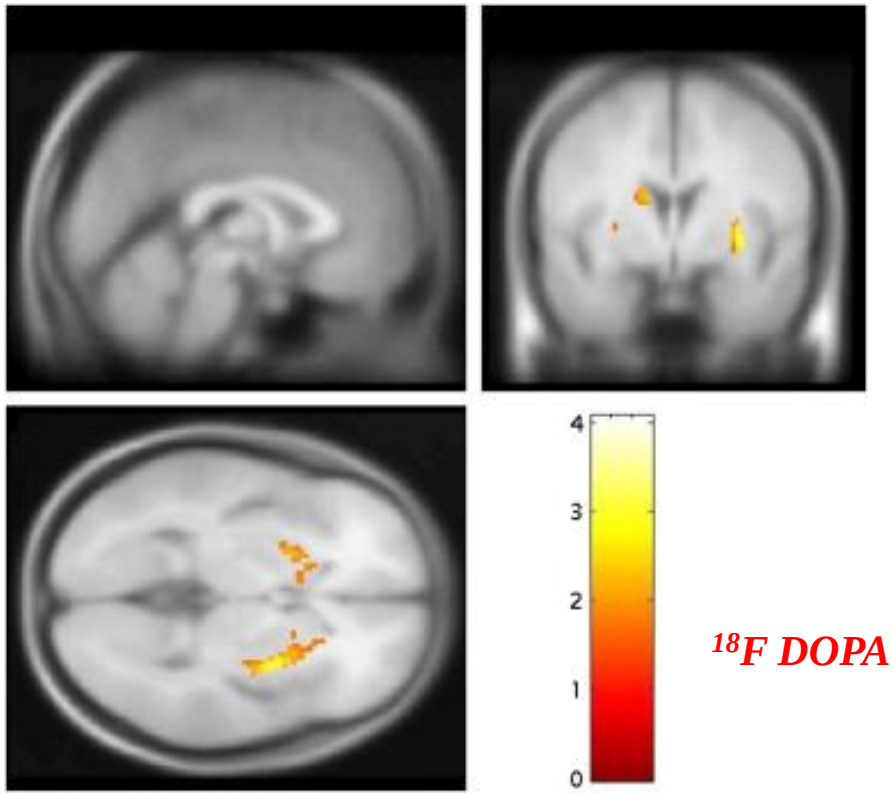


Marijuana abusers with heavier consumption had lower Striatal D2R

Albrecht DS et al., Drug and Alcohol Depend 2013;128:52-57.

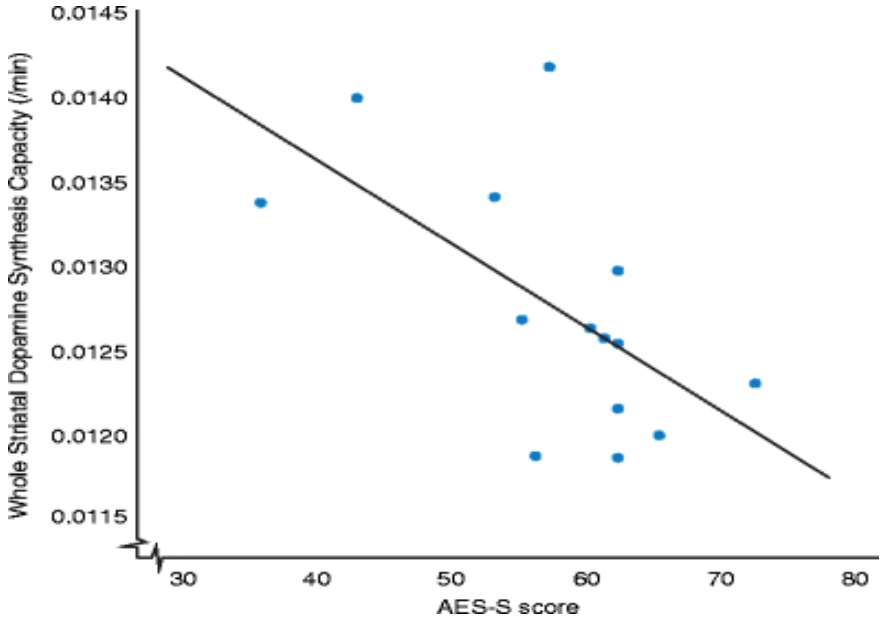
DA Synthesis Capacity in Cannabis Abusers

Reduced striatal DA synthesis capacity in cannabis users relative to controls



^{18}F DOPA

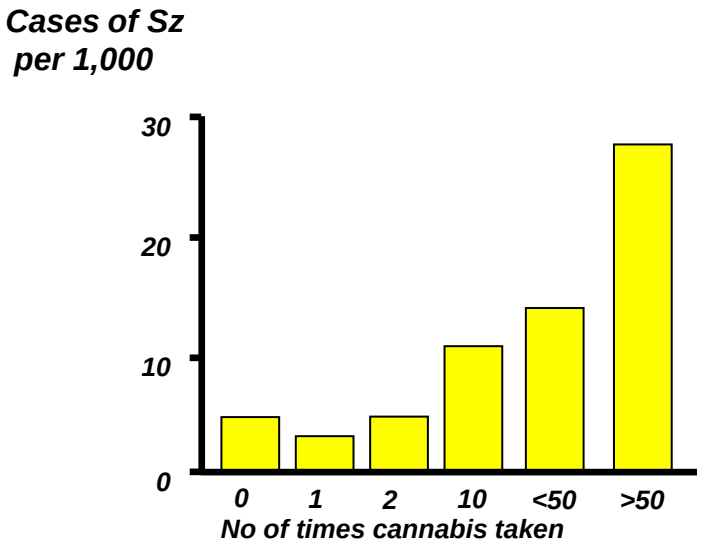
Striatal DA synthesis and apathy (AES-S score)



Bloomfield et al., Psychopharm 2014.

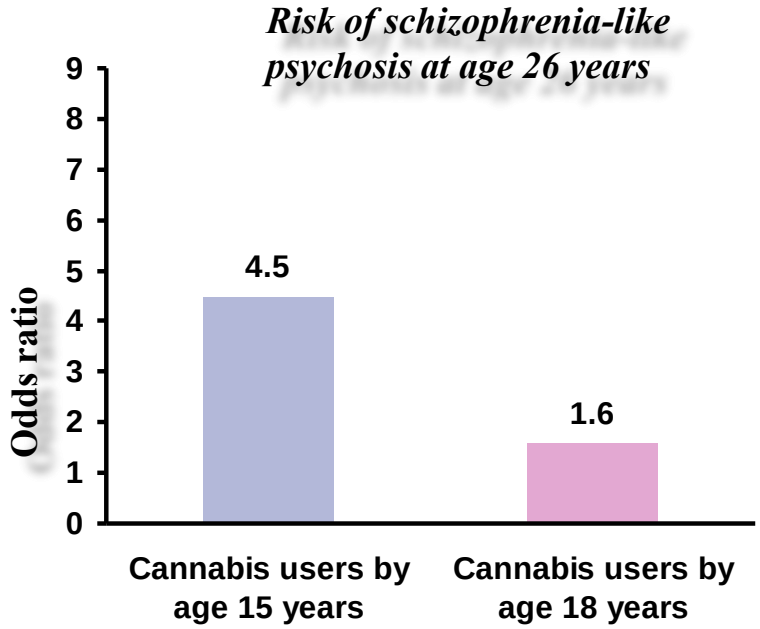
Cannabis-associated psychosis

CANNABIS AND SCHIZOPHRENIA
Study of Swedish Conscripts (n=45 570)



Andréasson et al Lancet, 1987

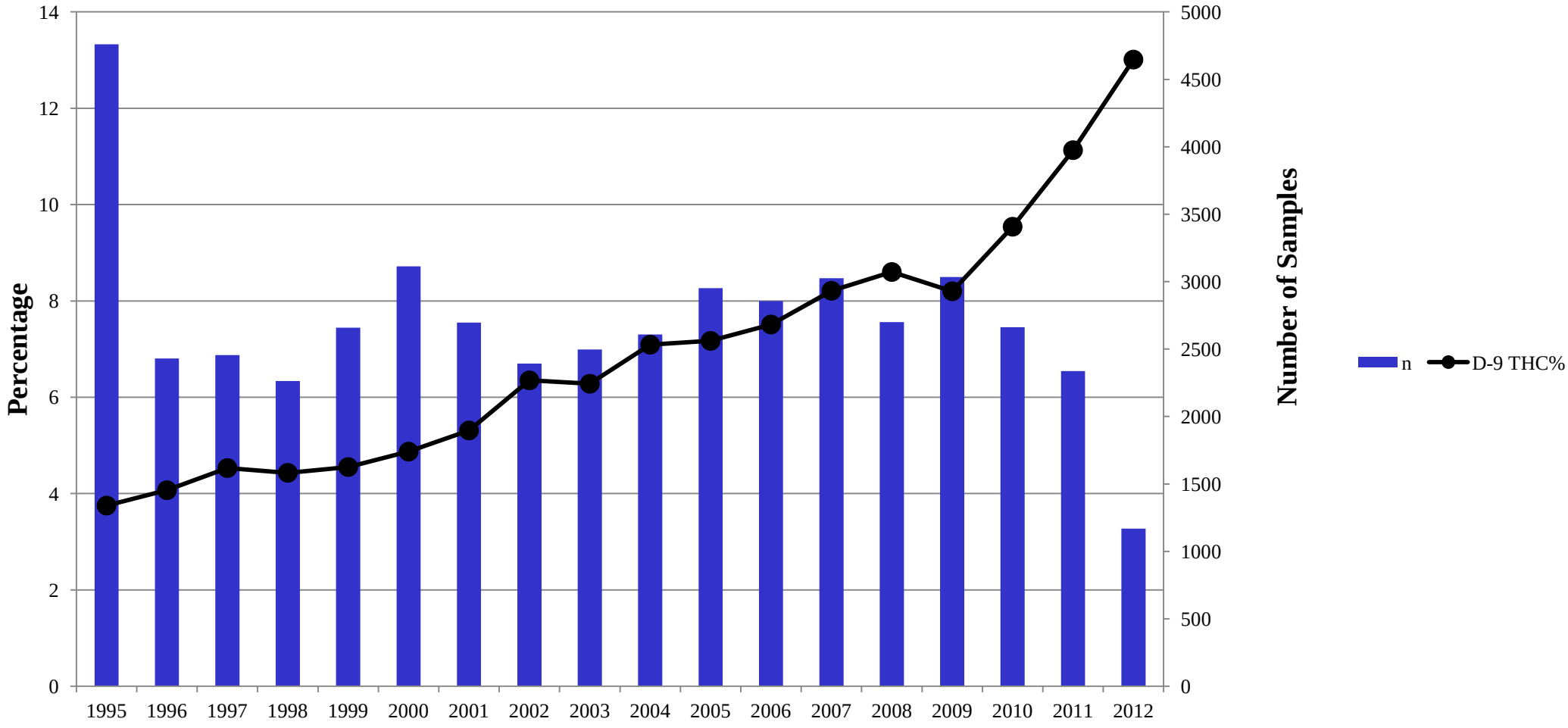
CANNABIS AND SCHIZOPHRENIA-Like
Longitudinal prospective Dunedin study (n=1037)



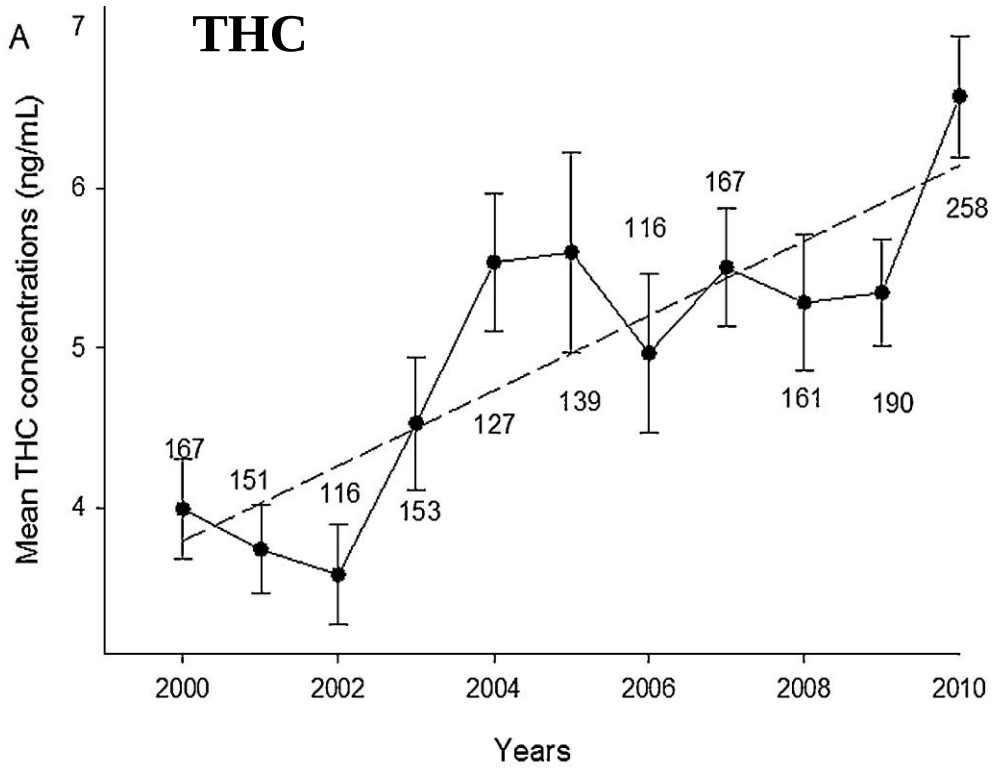
Arseneault et al BMJ 2002

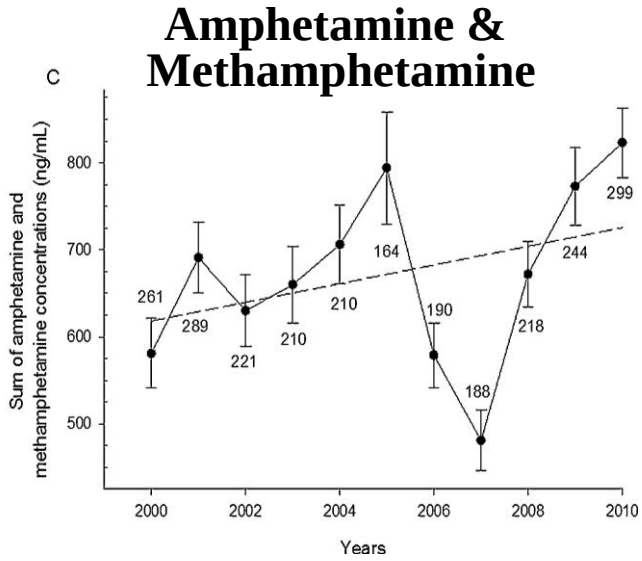
THC OF TODAY

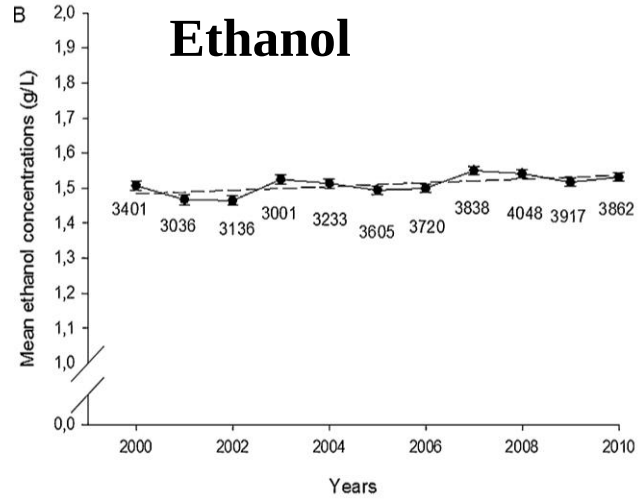
Average Delta-9 THC Concentration Per Year



Mean Concentrations of THC, Ethanol & Amphetamines In Whole Blood Samples From Drivers Apprehended By The Police Suspected Of Driving Under The Influence



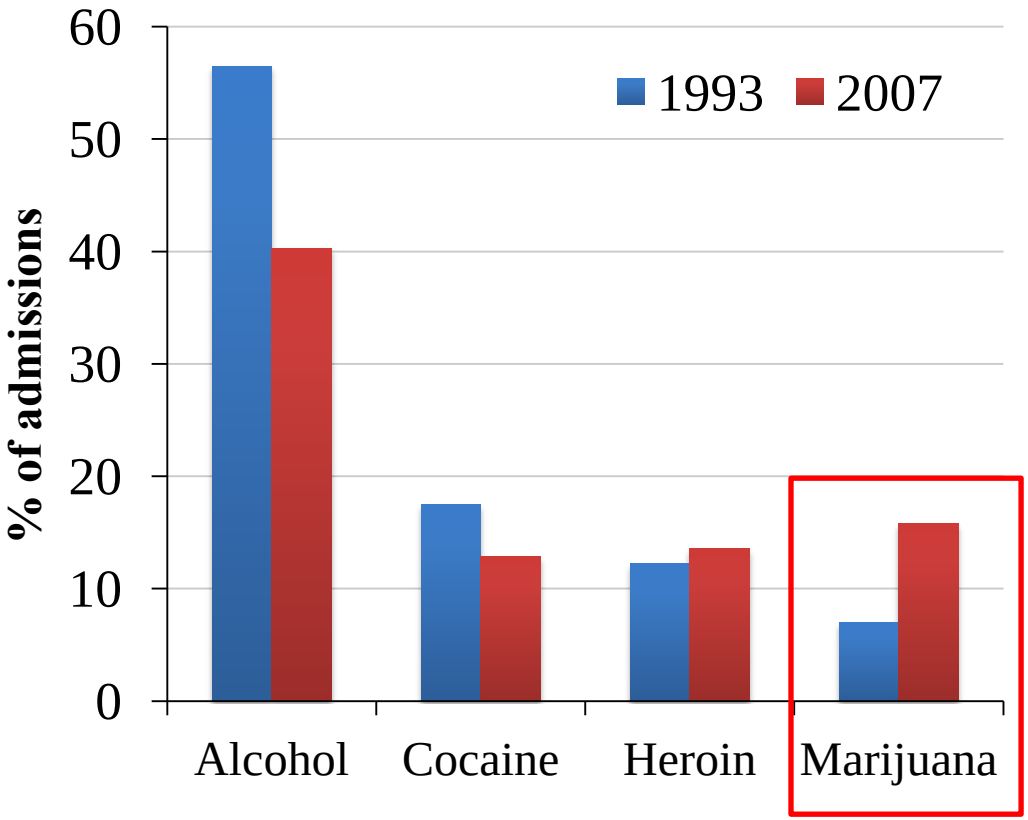




Vindenes V et al.,Forensic Sci Internati 2013; 226(1–3): 197-201.

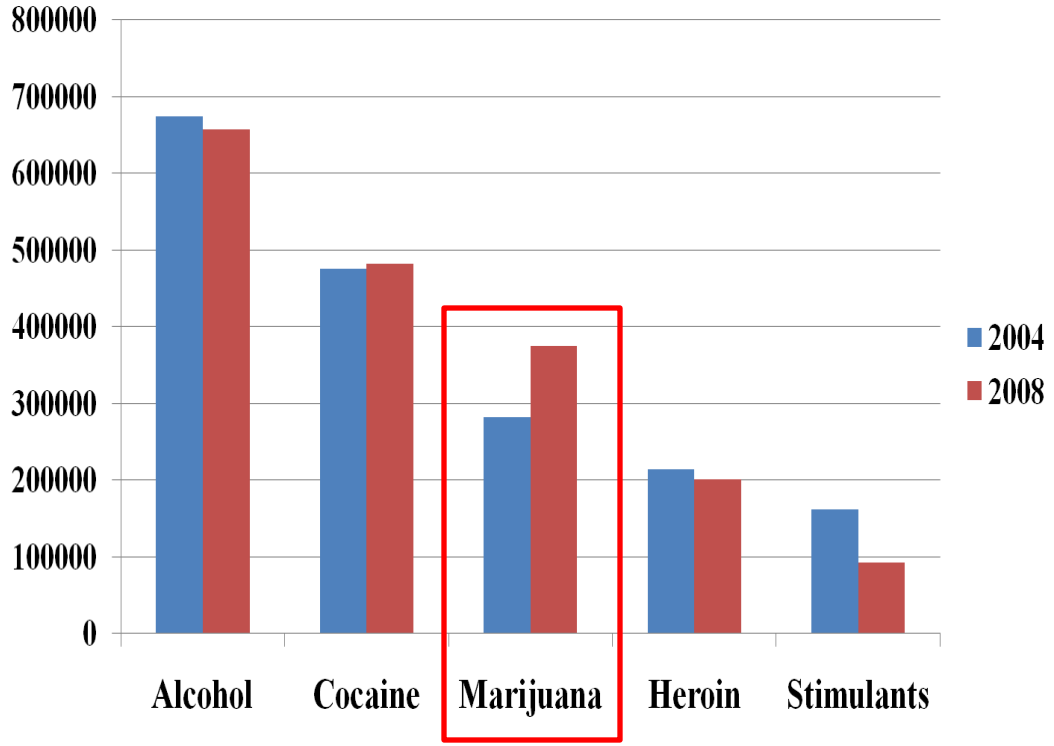
Increased Marijuana Treatment Admissions

1993 and 2007



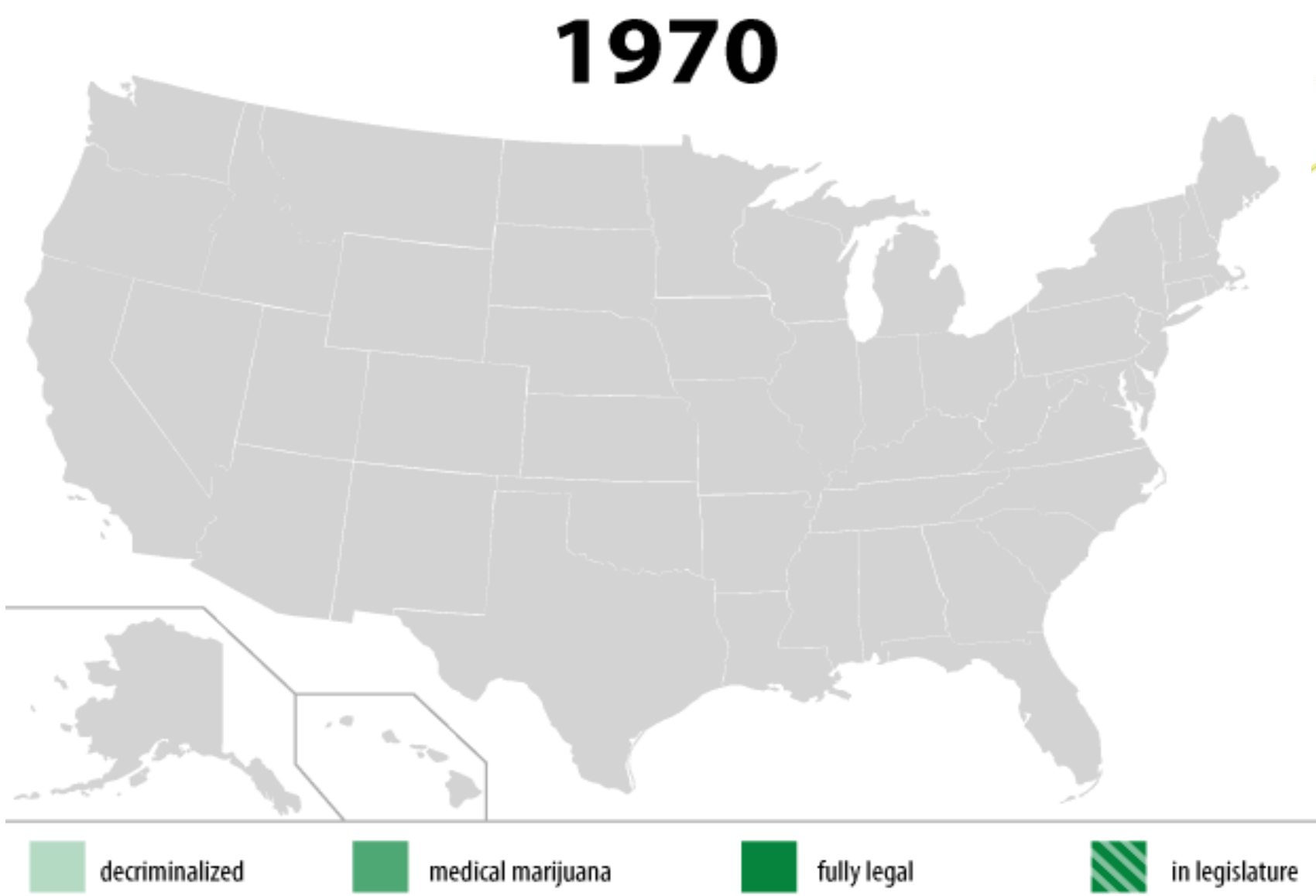
Source: SAMHSA, TEDS 1993 & 2007.

Emergency Department Visits Involving Selected Drugs: 2008



Source: SAMHSA, 2008 DAWN.

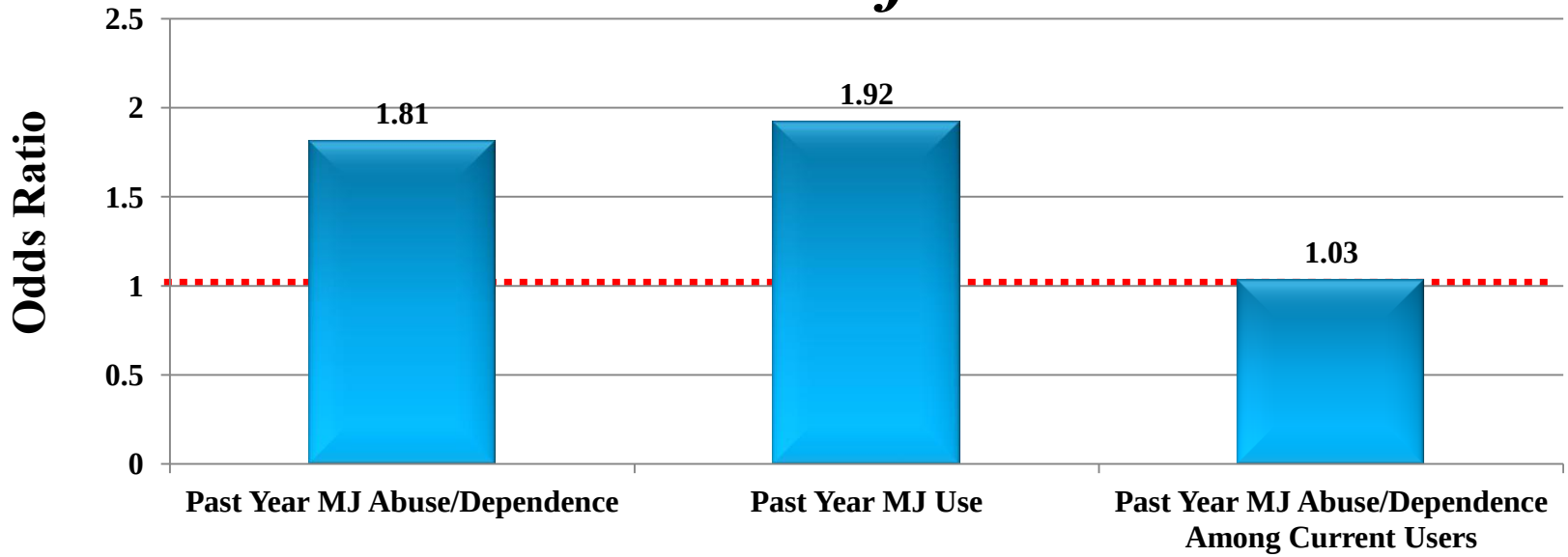
Changes in Marijuana Policy in the USA



Map Of States That Legalized Marijuana By 2004

passed laws legalizing MJ

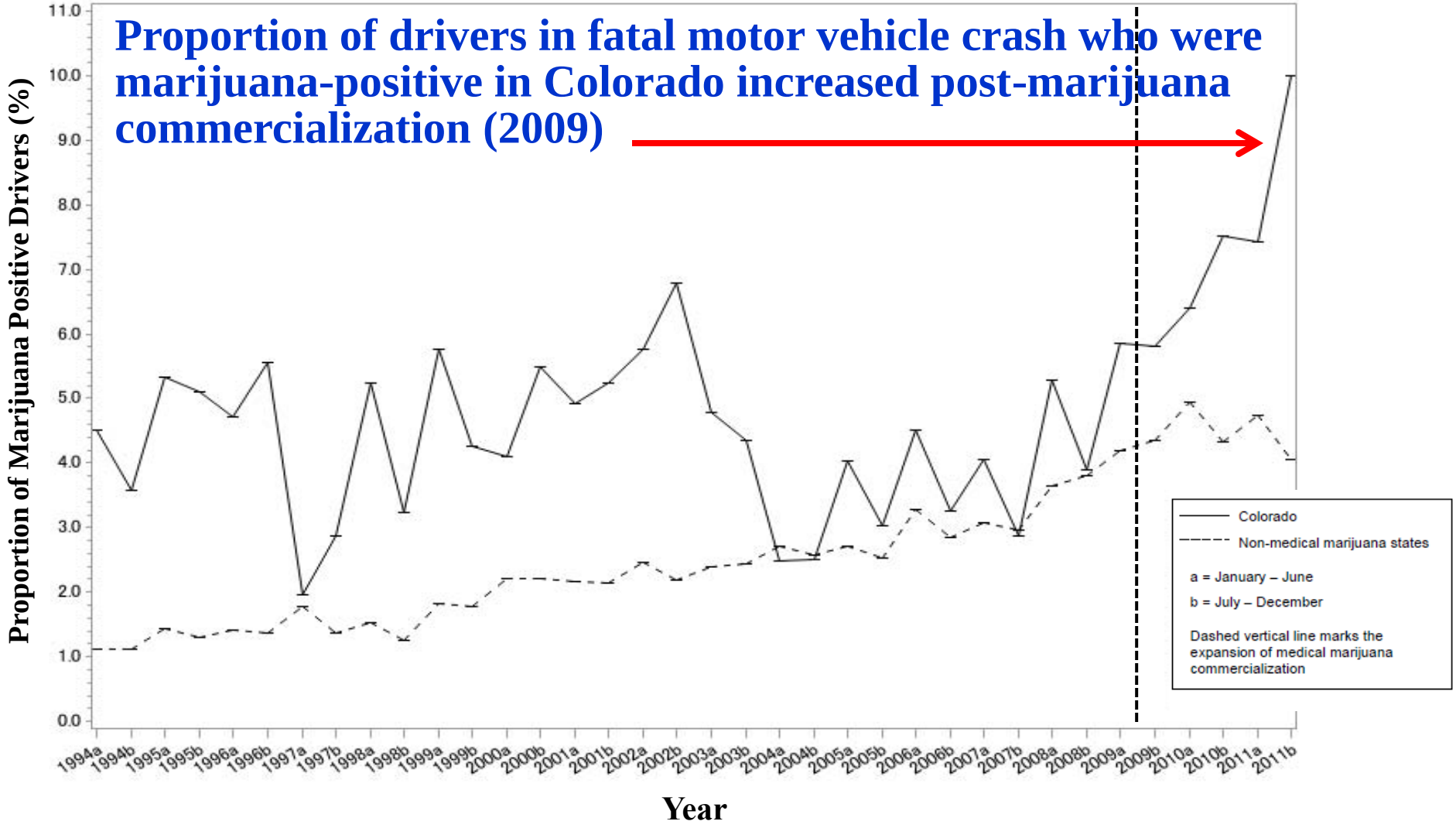
Outcomes of Interest



NESARC: National Epidemiologic Survey on Alcohol and Related Conditions

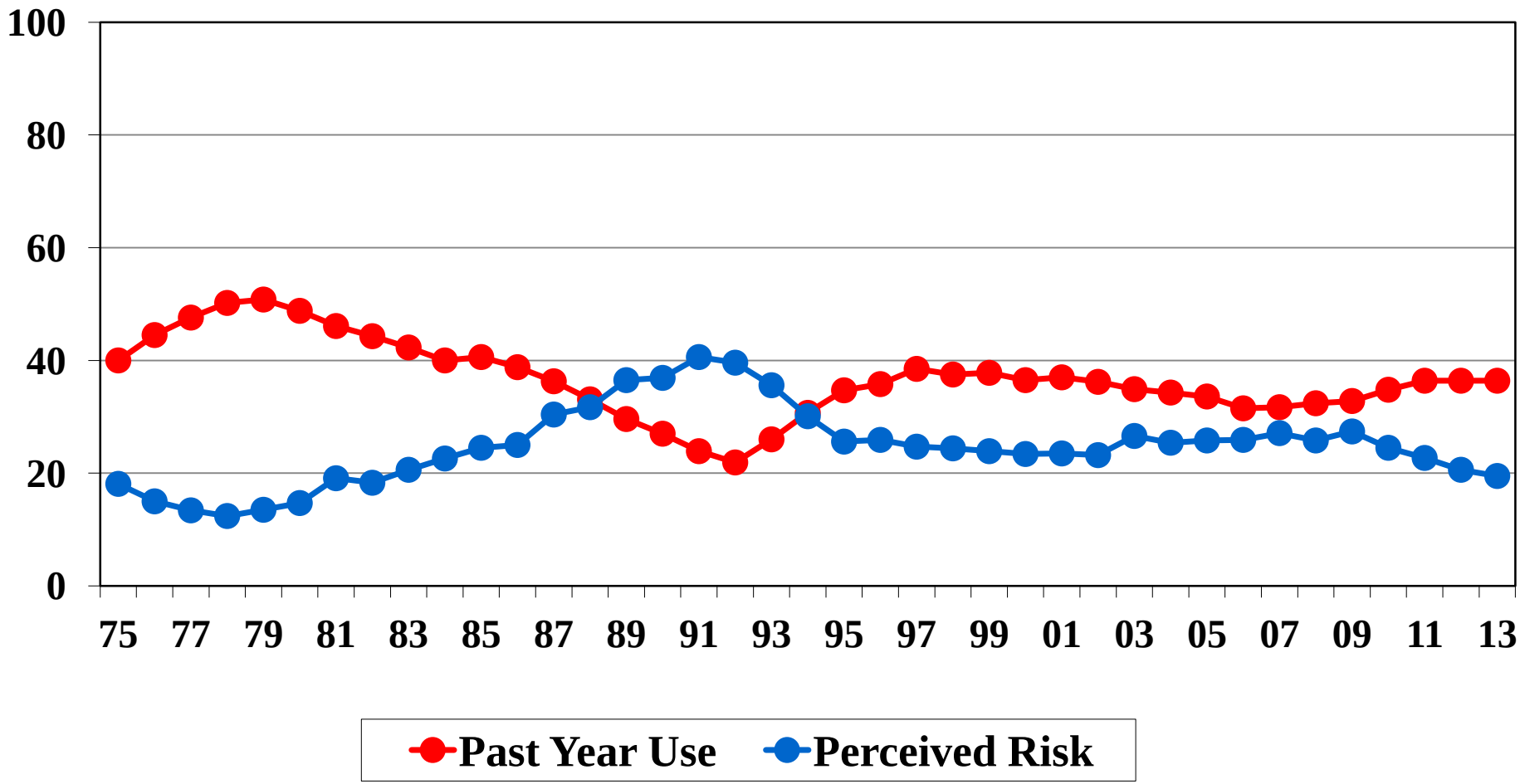
Cerda M et al. Drug and Alcohol Dependence 2012; 120: 22 – 27.

Proportion Of Drivers In A Fatal Motor Vehicle Crash Who Were Marijuana-Positive In Colorado and 34 States Without Medical Marijuana Laws From 1994-2011



Salomonsen-Sautel S et al., Drug and Alcohol Dependence 2014, http://dx.doi.org/10.1016/j.drugalcdep.2014.04.008

12th Graders' Past Year Marijuana Use vs. Perceived Risk of Occasional Marijuana Use



SOURCE: University of Michigan, 2013 Monitoring the Future Study