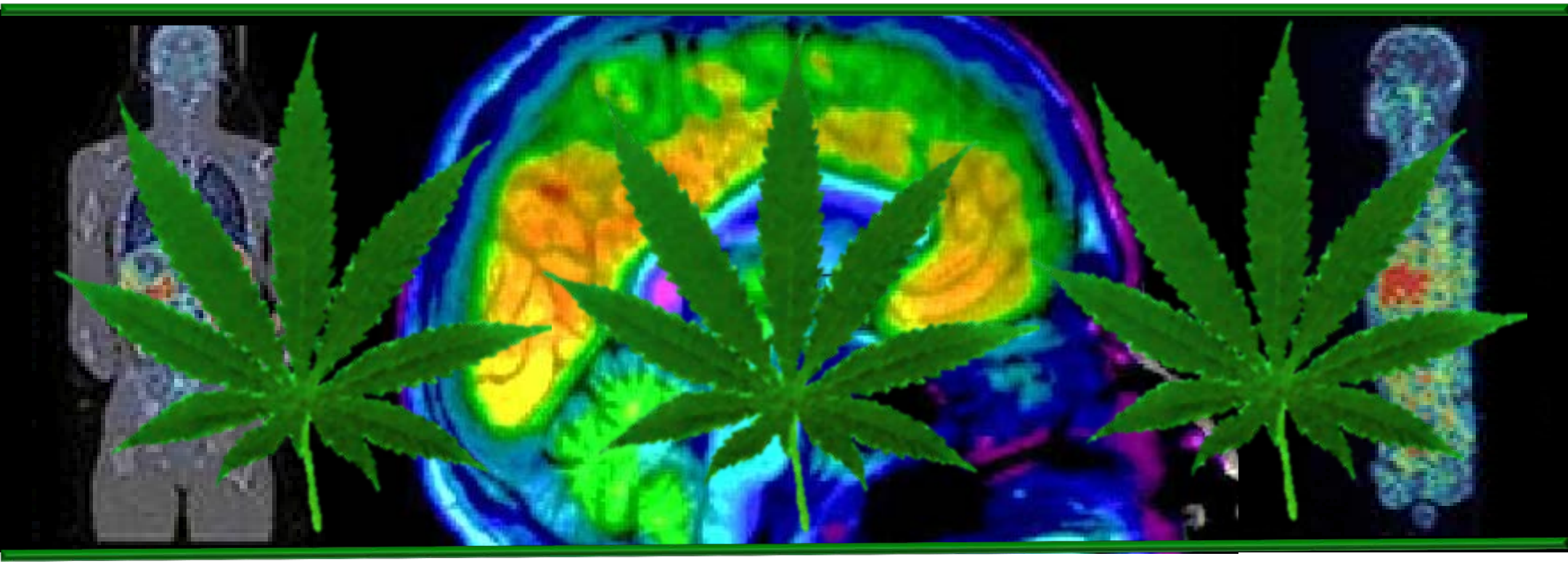
MARIJUANA

Health Effects on the Brain & Body

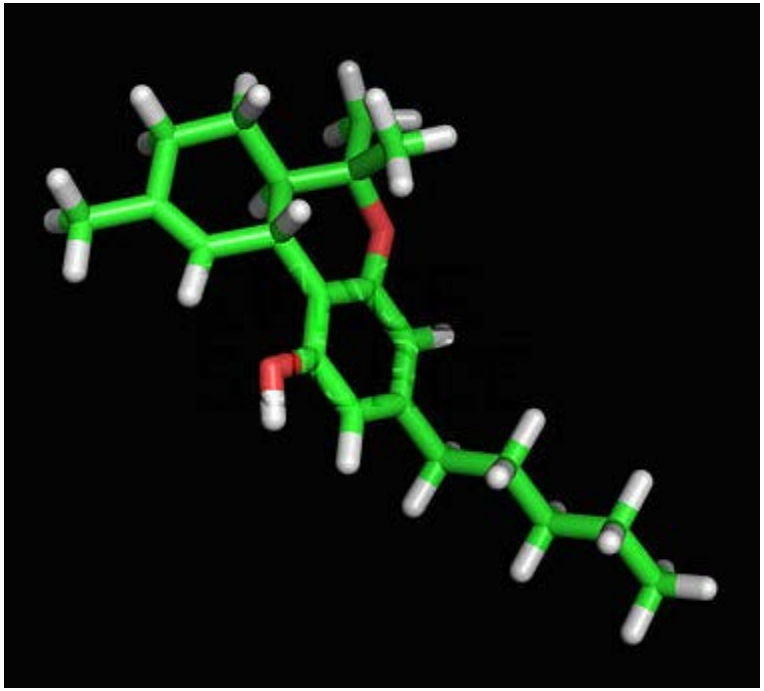


Nora D. Volkow, MD
Director
National Institute
on Drug Abuse

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

- Over 114 million Americans have tried it at least once

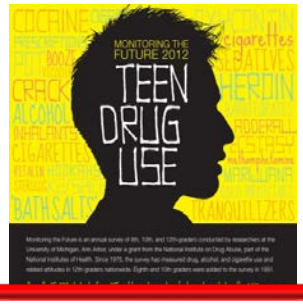
- An estimated 2.4 million Americans used it for the first time in 2013

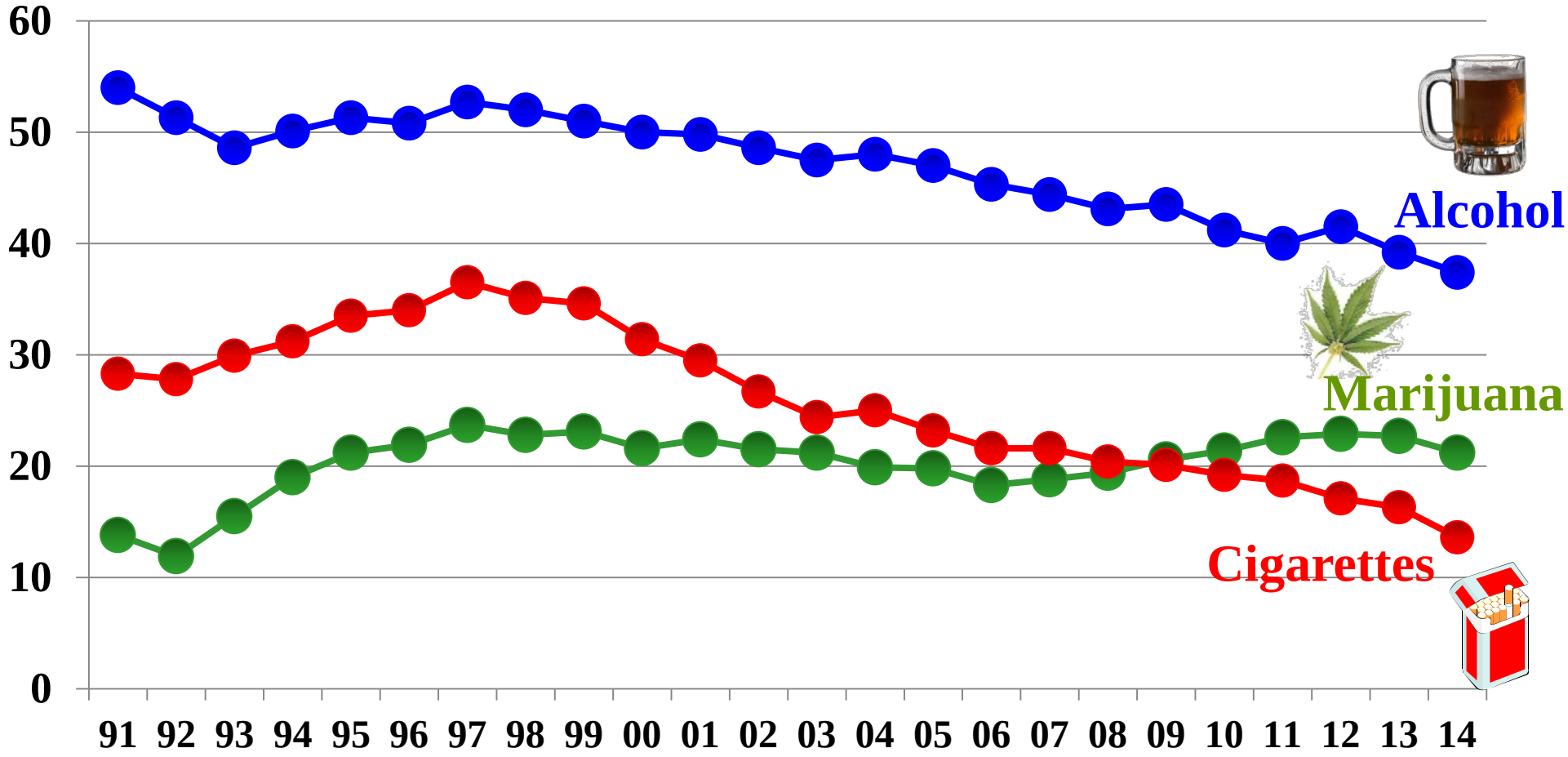


Tetrahydrocannabinol (THC)
Active Ingredient in Marijuana

2013 National Survey on Drug Use and Health, SAMHSA, 2014.

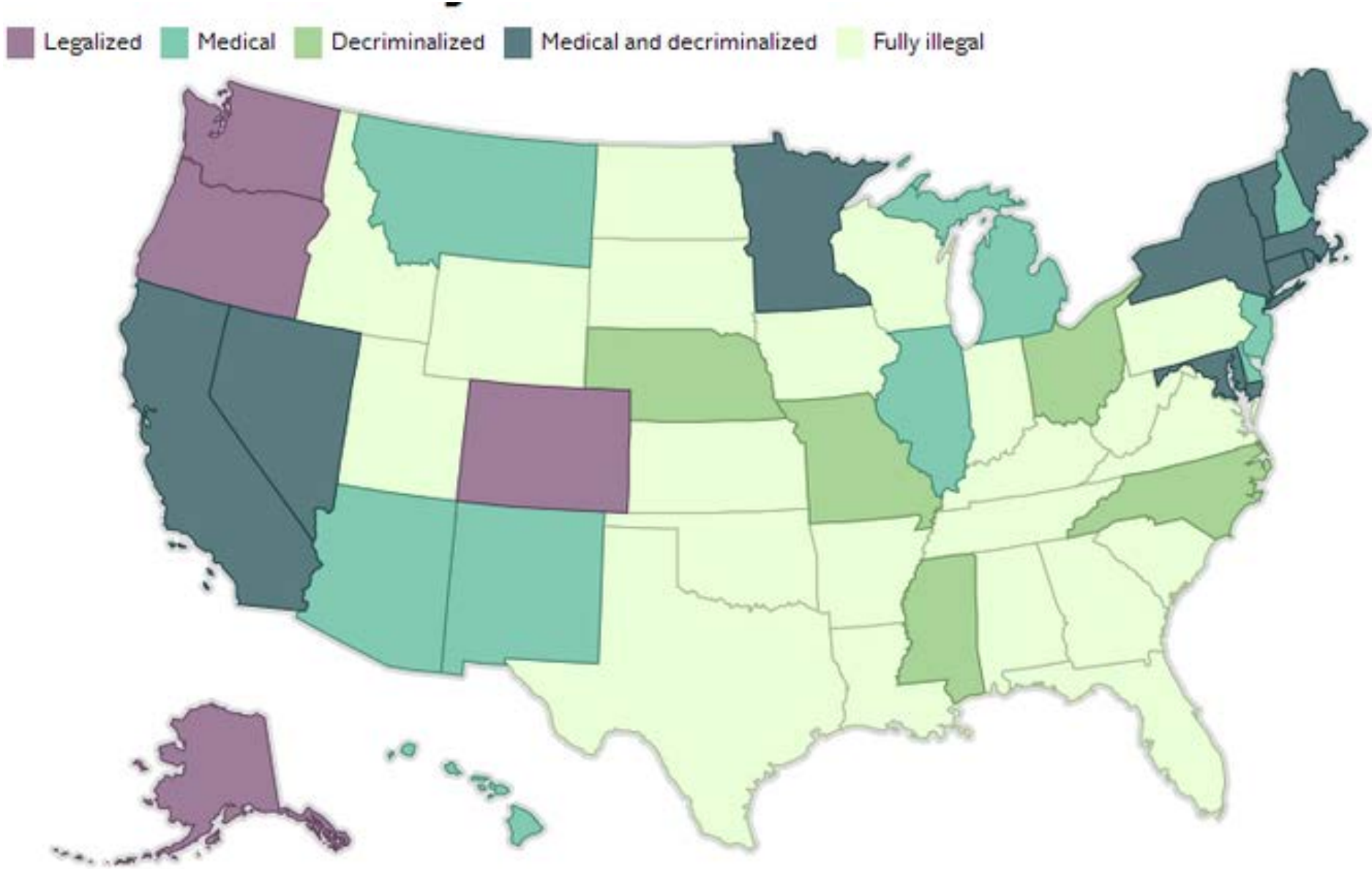
Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes, Marijuana and Alcohol





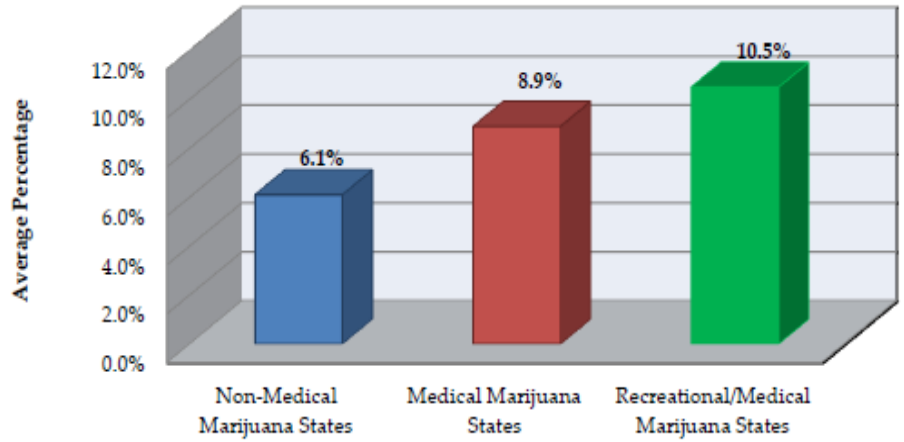
SOURCE: University of Michigan, 2014 Monitoring the Future Study.

Status of Marijuana Laws in the United States



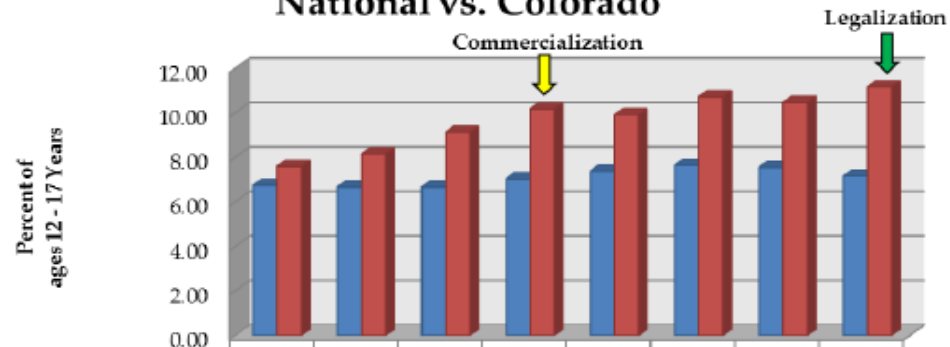
Source: NORML, Drug Policy Alliance, and the Marijuana Policy Project

Average Past Month Use by 12 to 17-Year-Olds, 2013



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

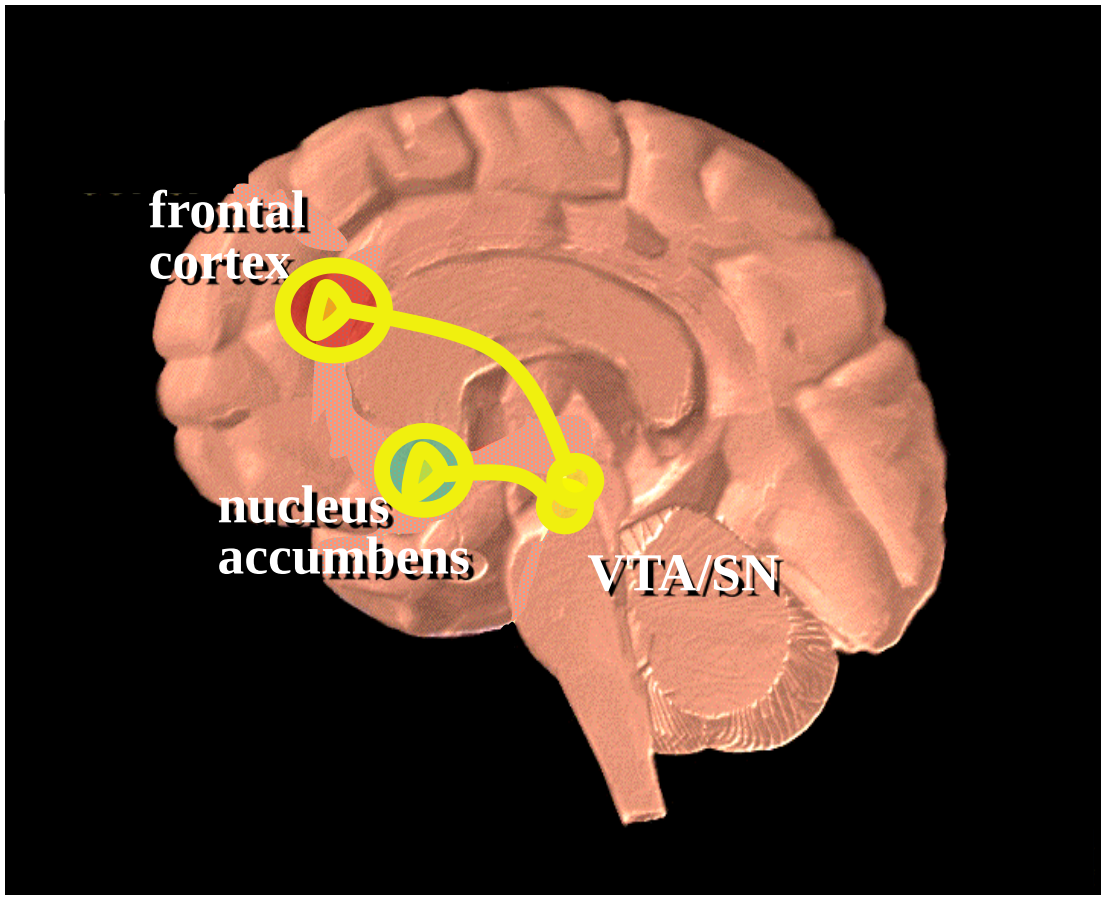
Youth (Ages 12 to 17 Years) Past Month Marijuana Use National vs. Colorado



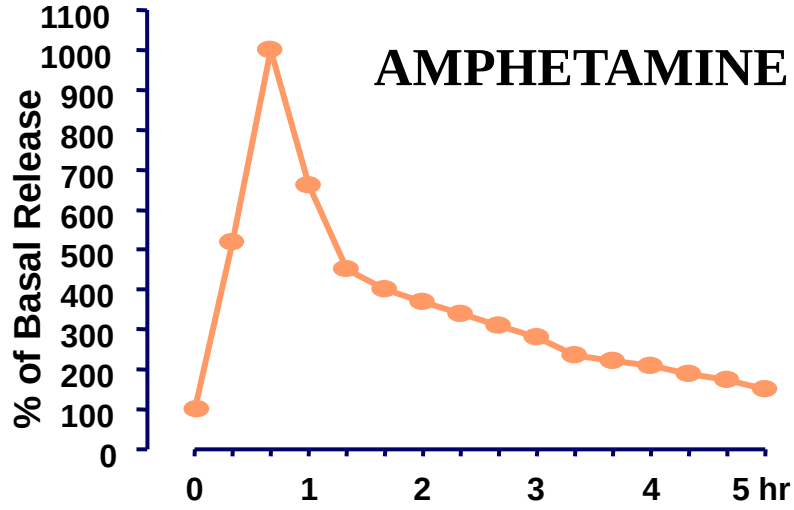
	2006	2007	2008	2009	2010	2011	2012	2013
National Average	6.74	6.67	6.67	7.03	7.38	7.64	7.55	7.15
Colorado Average	7.60	8.15	9.13	10.17	9.91	10.72	10.47	11.16

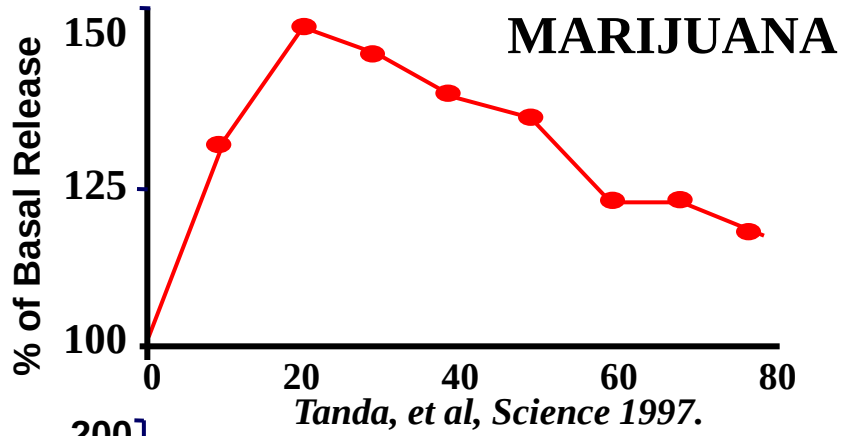
E: SAMHSA.gov, National Survey on Drug Use and Health, 2006-2013

Natural and Drug Reinforcers Increase Dopamine in NAc

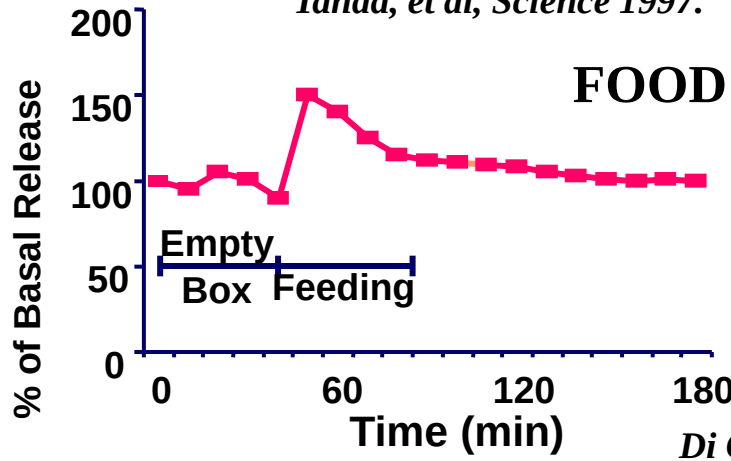


Drugs of abuse increase DA in the Nucleus Accumbens, which is believed to trigger the neuroadaptions that result in addiction



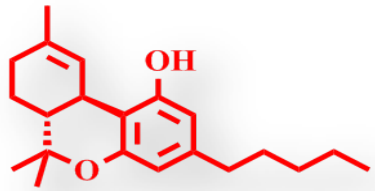


Tanda, et al, Science 1997.



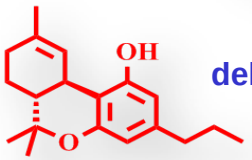
Di Chiara et al.

Constituents of MJ and the Cannabinoid System



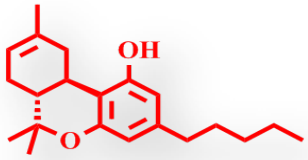
Δ^9-THC

delta-9-tetrahydrocannabinol



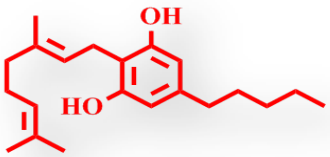
Δ^9-THCV

delta-9-tetrahydrocannabivarin



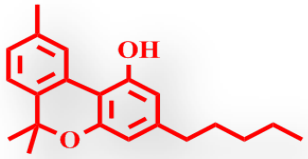
Δ^8-THC

delta-8-tetrahydrocannabinol



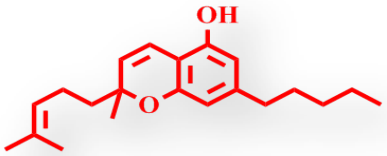
CBG

cannabigerol



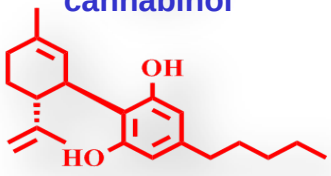
CBN

cannabinol



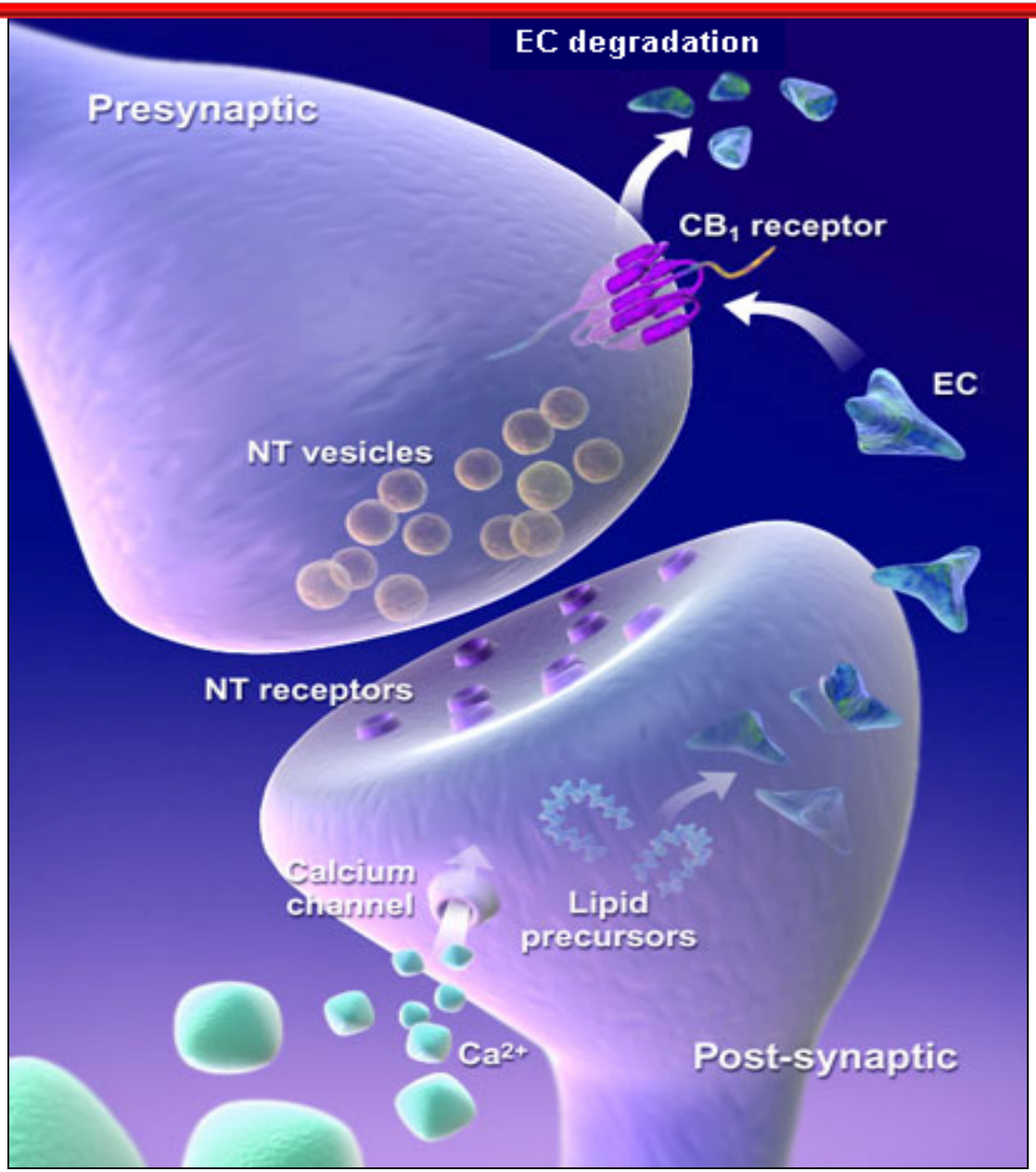
CBC

cannabichromene



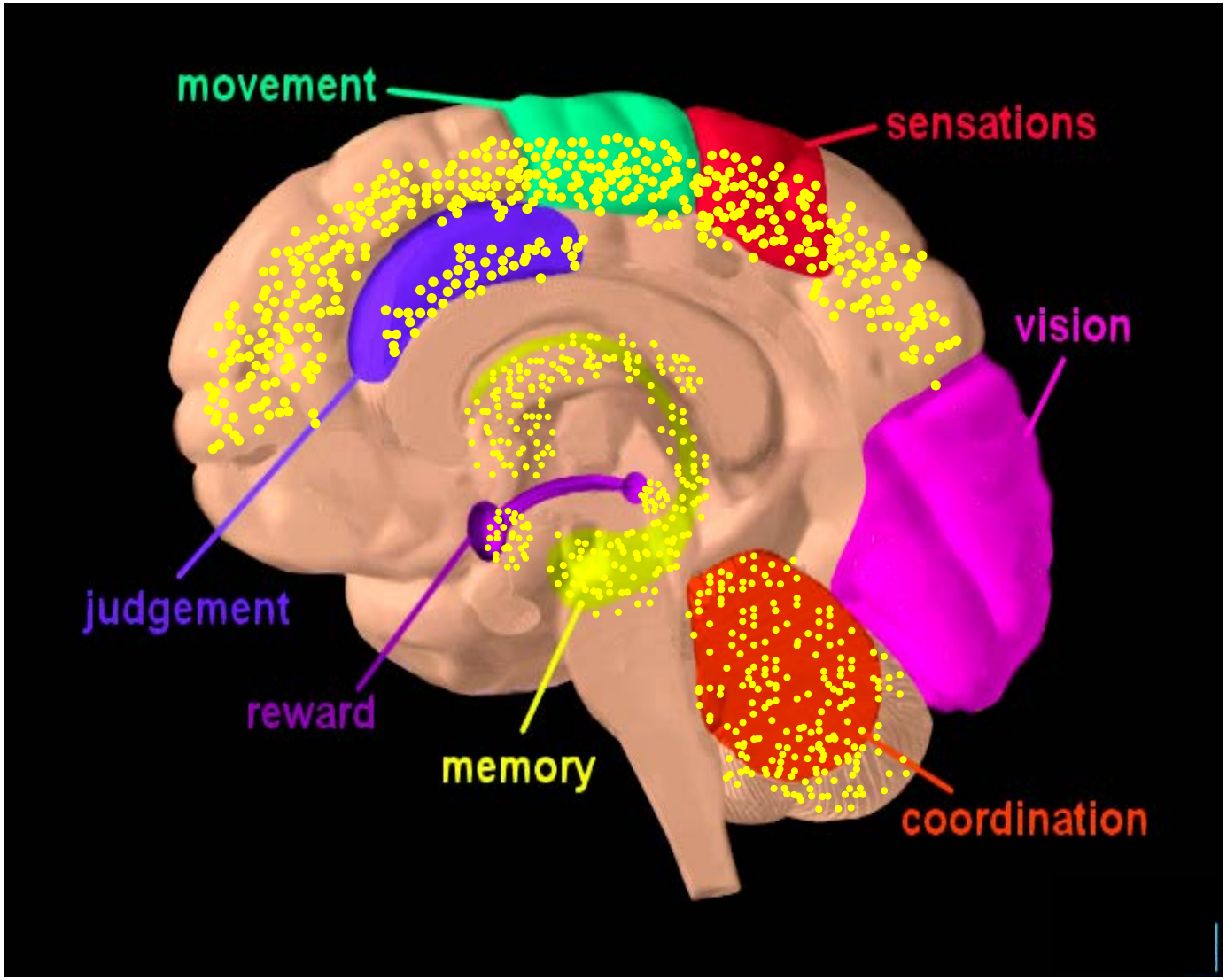
CBD

cannabidiol



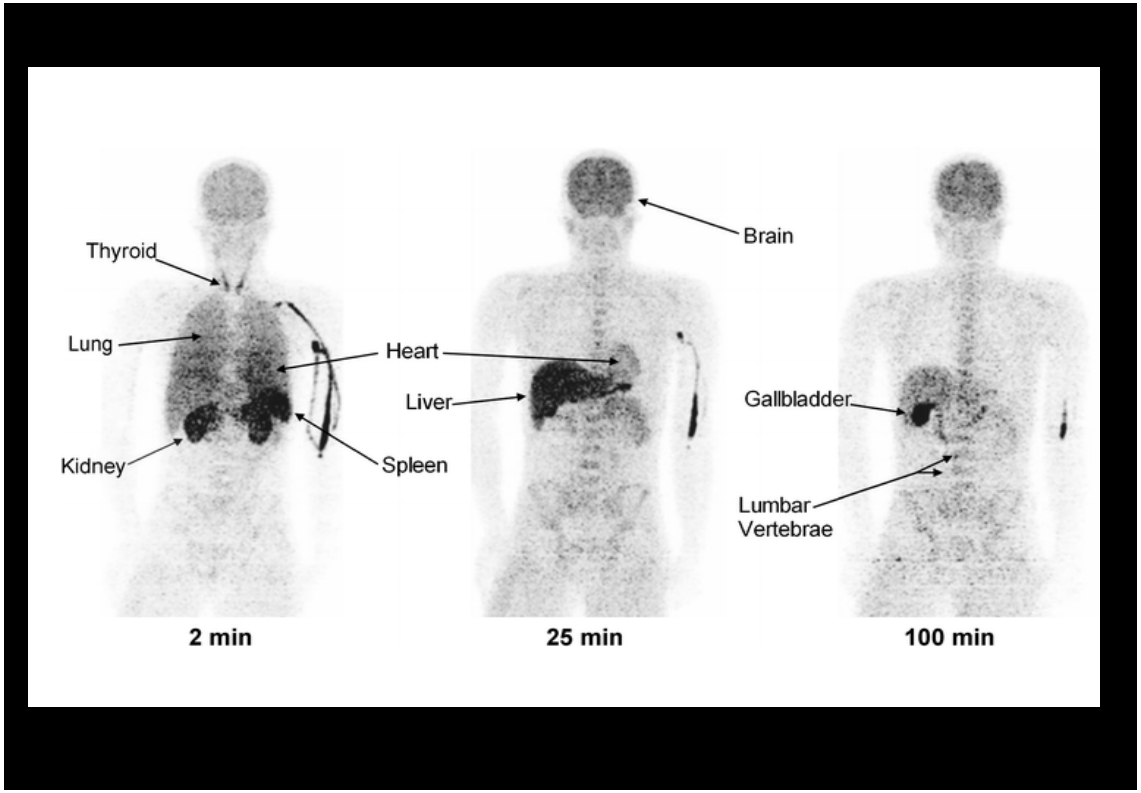
Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

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



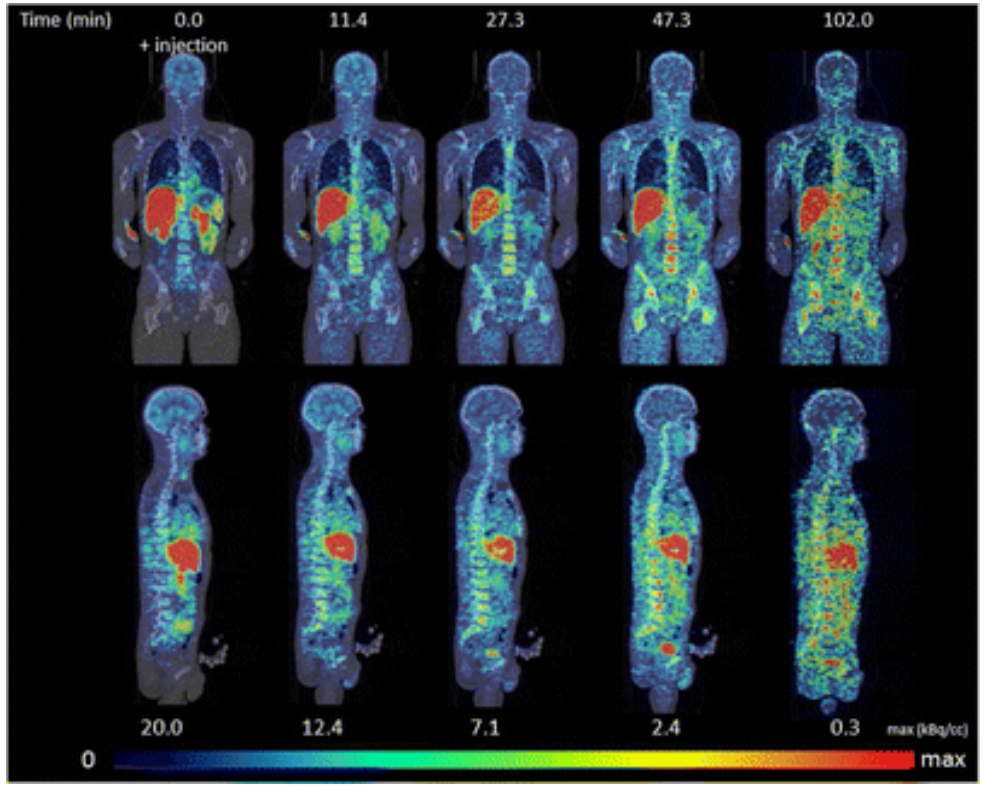
Cannabinoid Receptors Are Also Located Throughout the Body

Whole Body Distribution of CB1 Receptors (2, 25, and 100 min after injection of 11C-MePPEP)



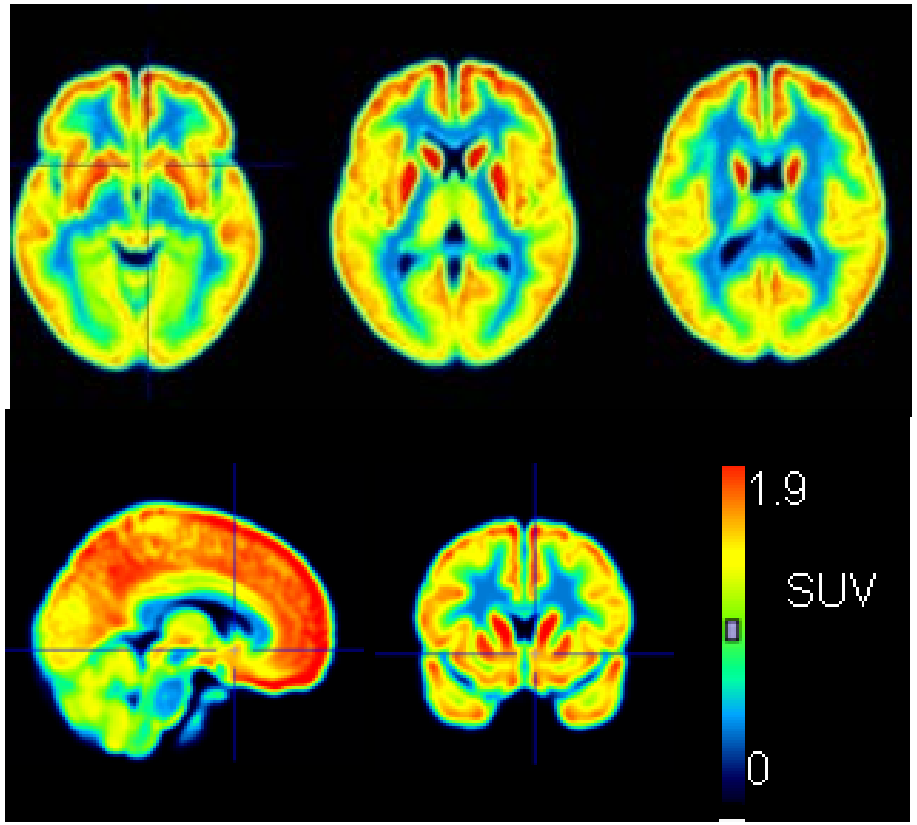
Terry et al., Eur J Nucl Med Mol Imaging. 2010

PET images of [11C]-NE40 (CB2R radioligand)

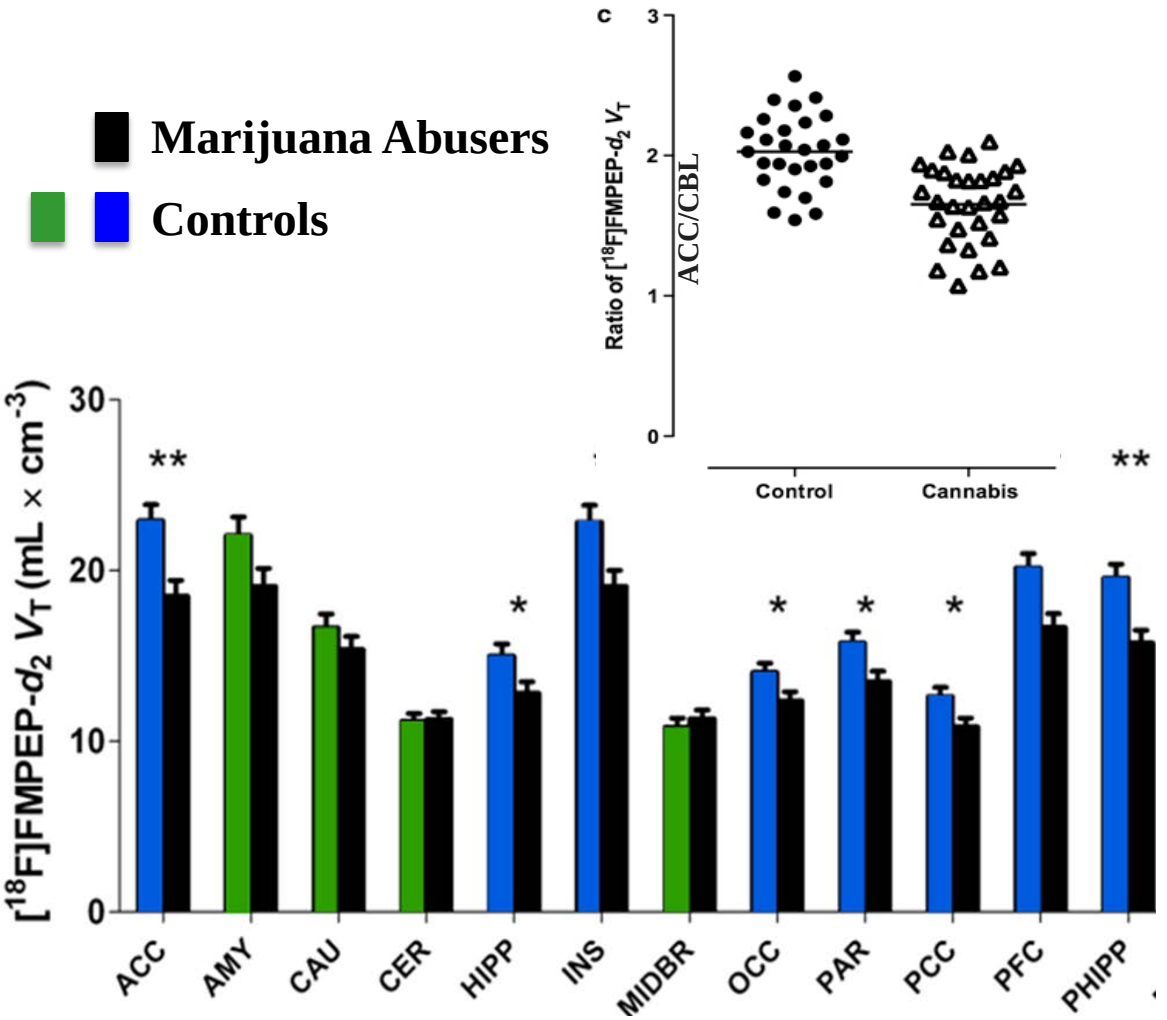


Ahmad et al., Mol Imaging Biol. 2013 A

Cannabinoid CB1 Receptors in Human Brain are Downregulated in Marijuana Abusers

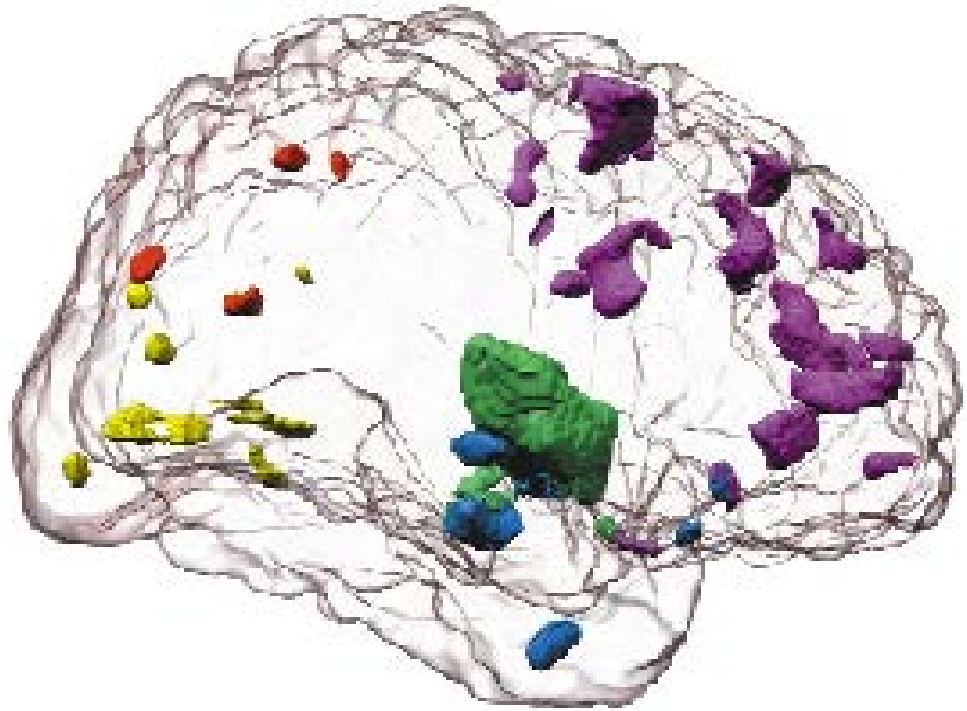


Van Loere et al., 2007.



Hirvonen et al., Mol Psychiatry 2013.

Does Marijuana Use negatively affect the developing brain and an individual's personal trajectory into adulthood?

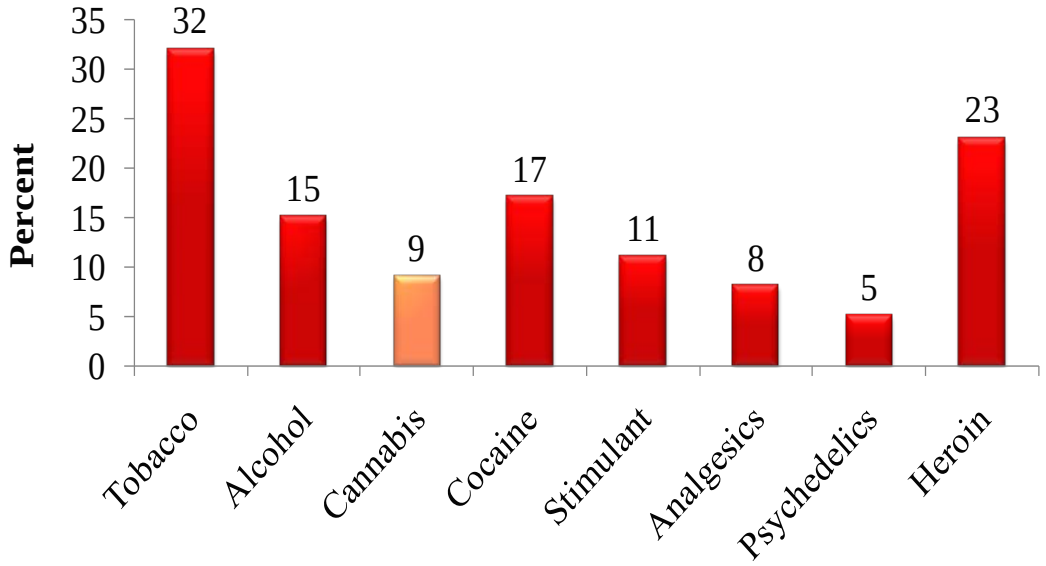


Long Term Effects of Marijuana

Addiction:

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

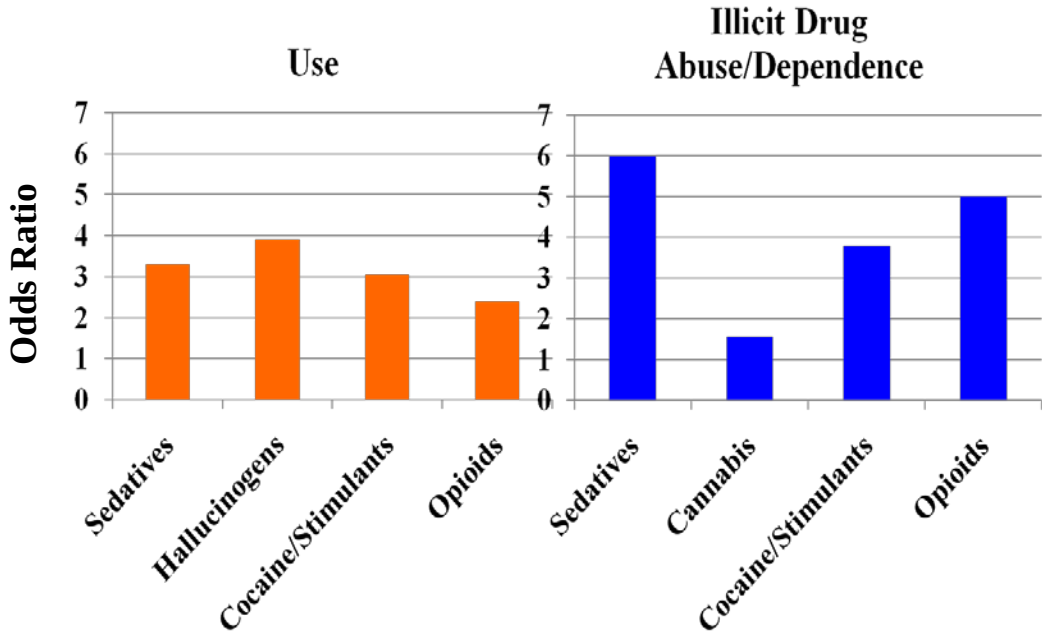
Estimated Prevalence of Dependence Among Users



**** Nonmedical Use***

Source: Anthony JC et al., 1994

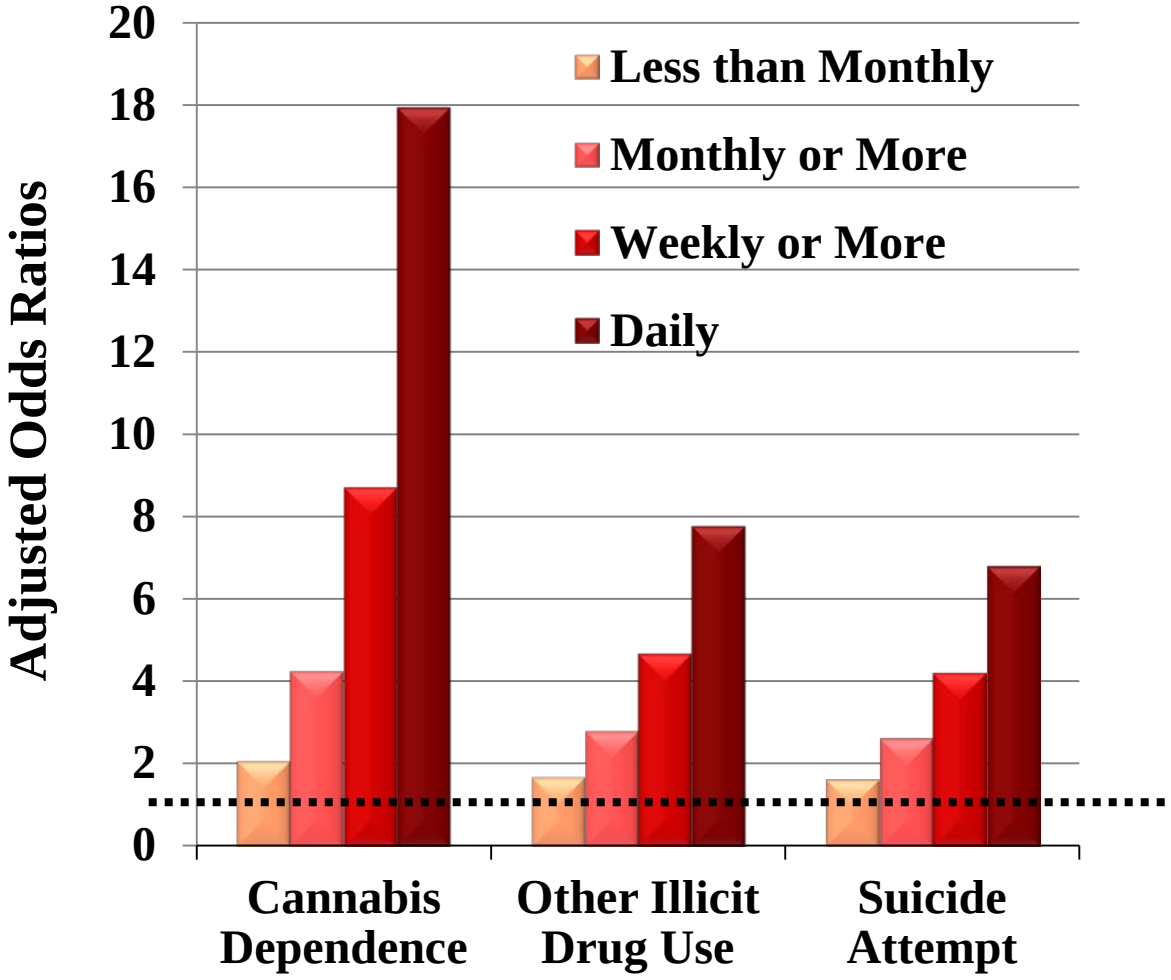
Drug Use Outcomes in Twin Pairs (n =234) Discordant for Cannabis Use Before Age 17

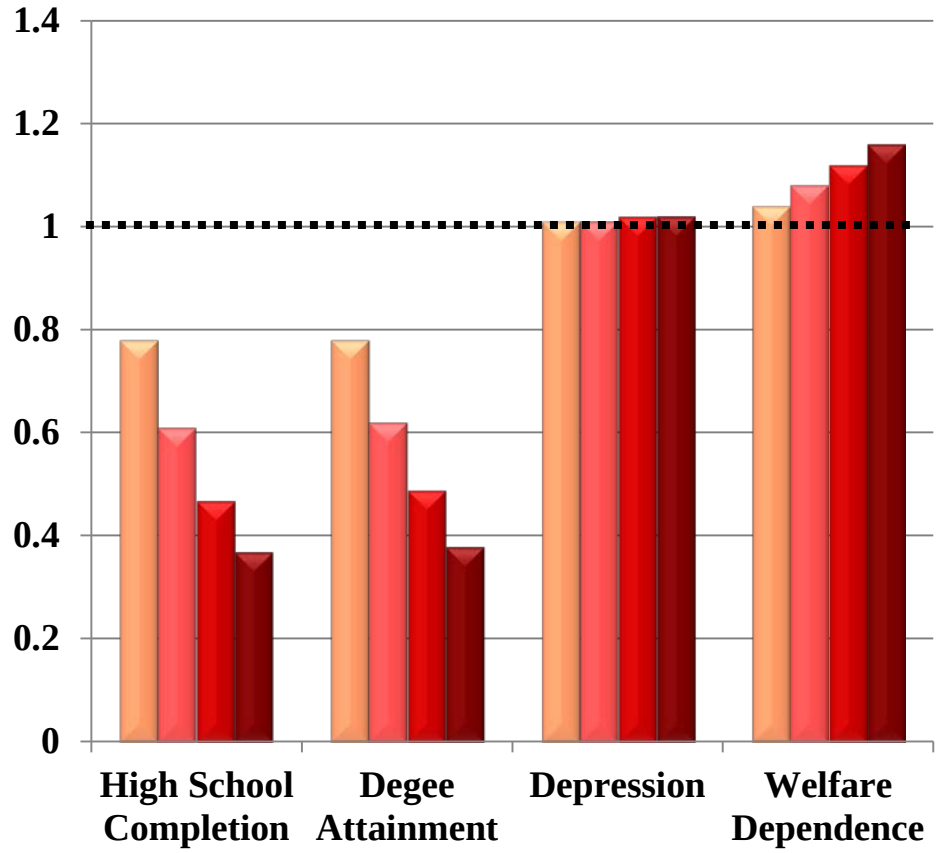


Source: Lynskey, MT et al., JAMA, 289, pp. 427-433, 2003.

Frequency Of Cannabis Use Before Age 17 Years and Adverse Outcome (30years age) (n=2500-3700)

Consistent and dose-response association were found between frequency of adolescent cannabis use and adverse outcomes





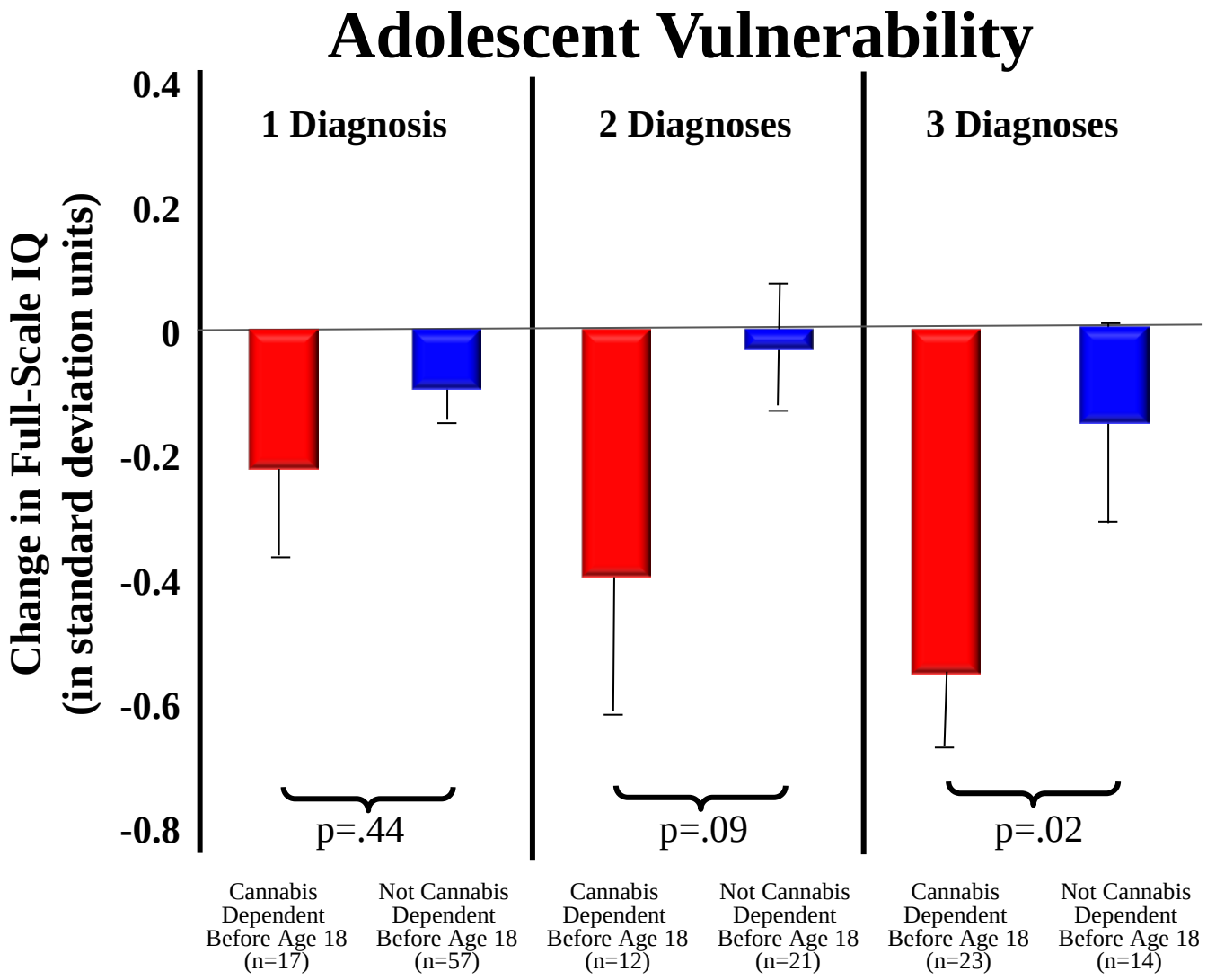
Silins E et al., The Lancet September 2014.

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.

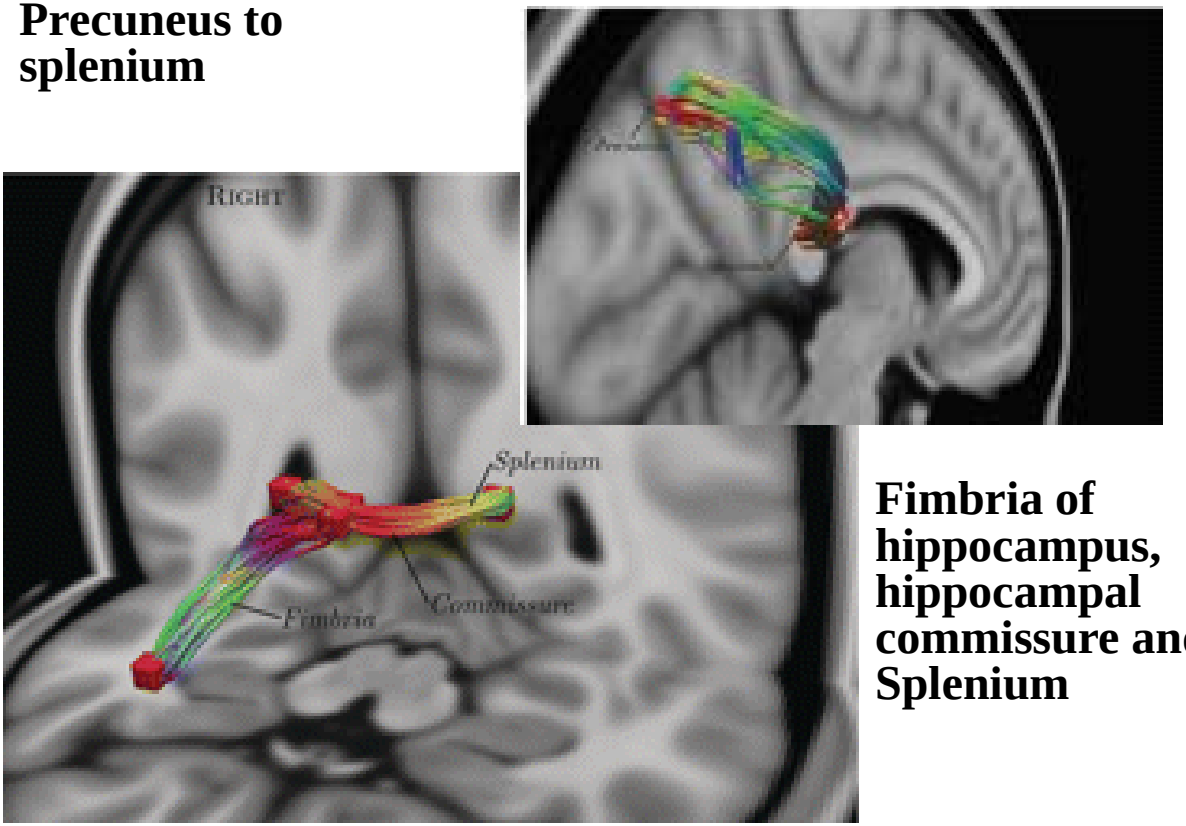
Tested THC use ages 18, 21, 26, 32 and 38y



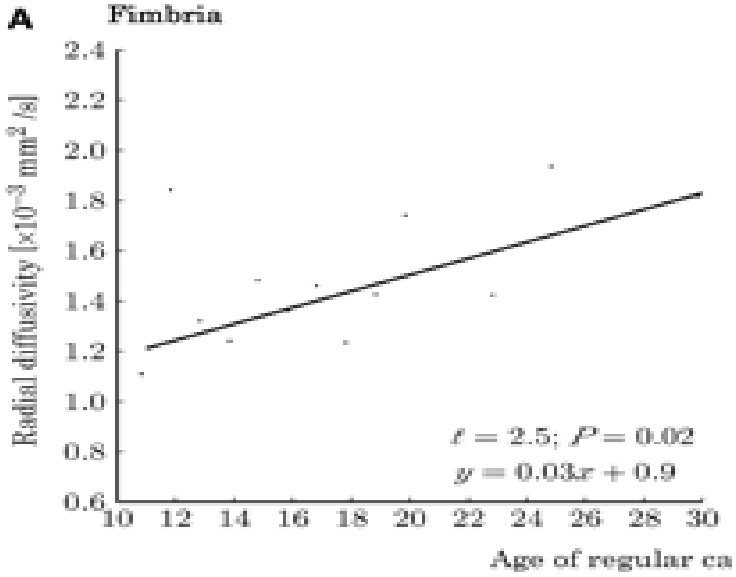
Source: Meier MH et al., PNAS Early Edition 2012.

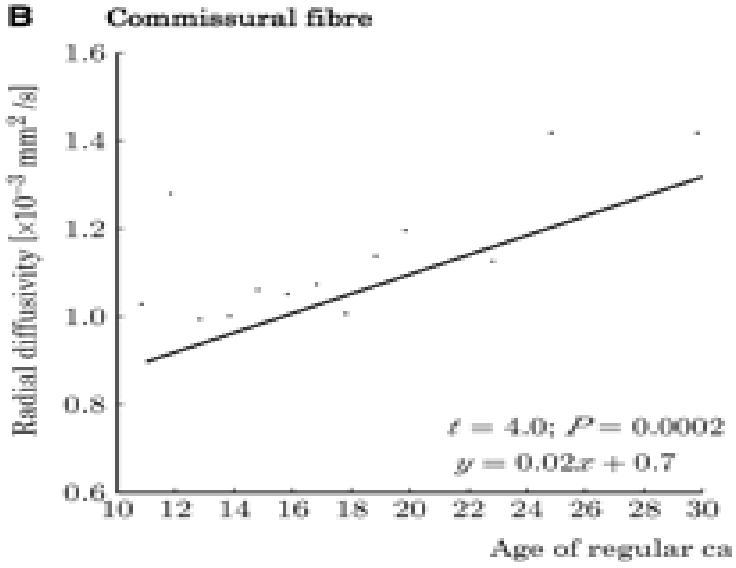
Early (<18y) Long-Term Cannabis Use Decreases Axonal Fiber Connectivity

Precuneus to splenium



Fimbria of hippocampus, hippocampal commissure and Splenium

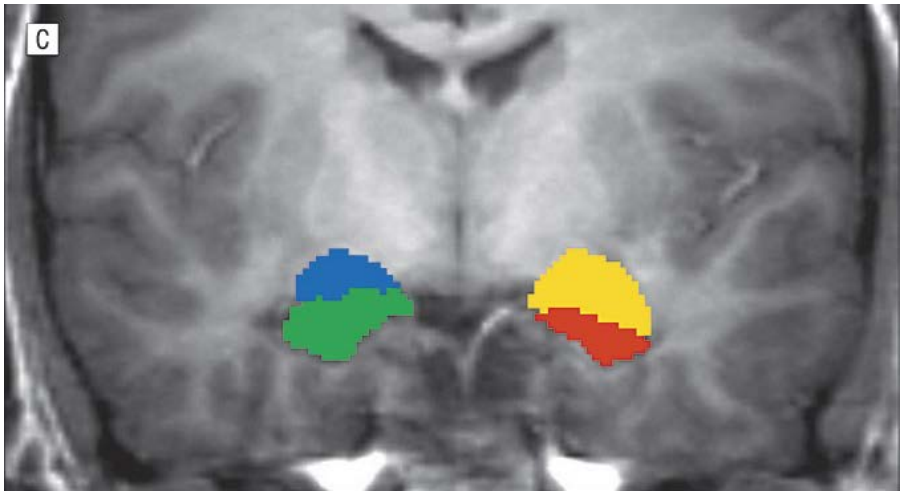




Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33). ***Zalesky et al Brain 2012.***

Effects of THC on Mental Illness

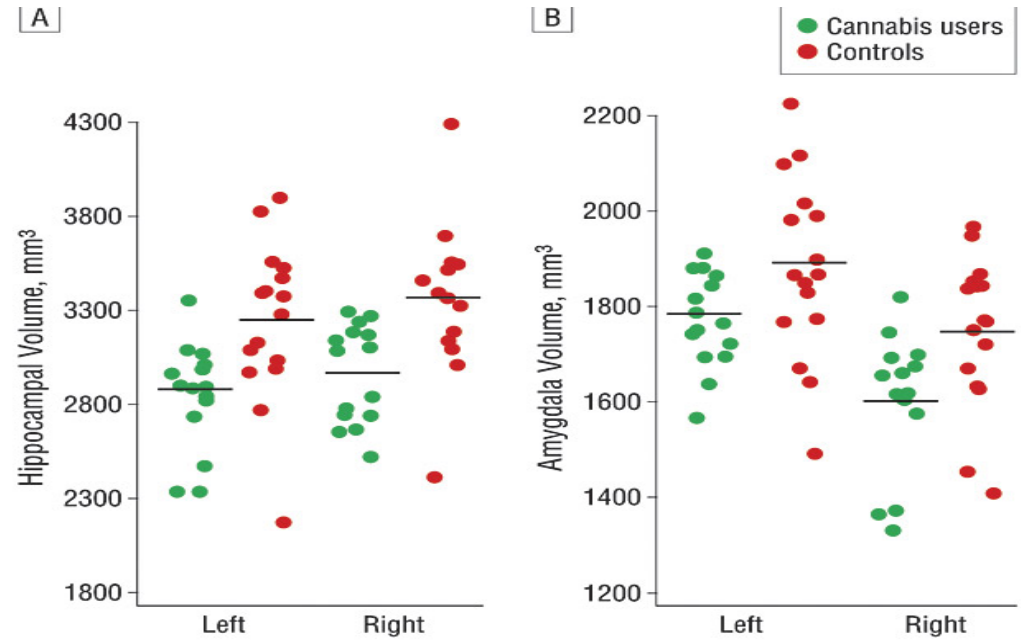
Brain abnormalities associated with long-term heavy cannabis use



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

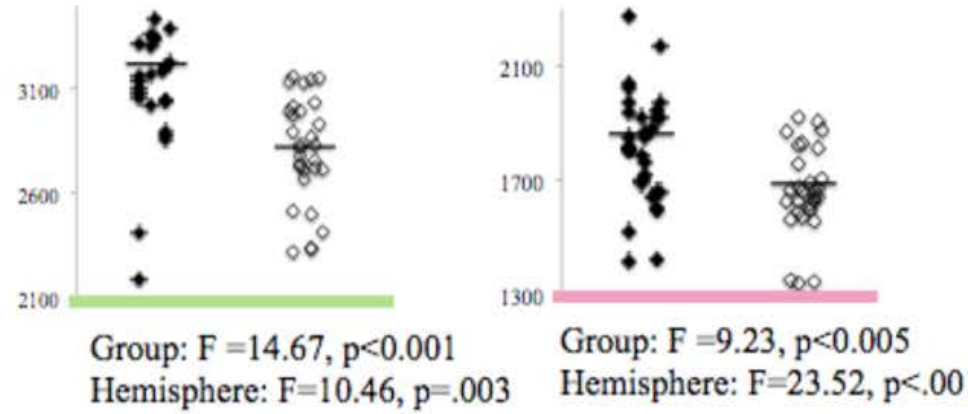
Hippocampus and amygdala volumes are smaller in cannabis users than controls and this has been linked with *impaired memory performance*

Hippocampus ***Amygdala***



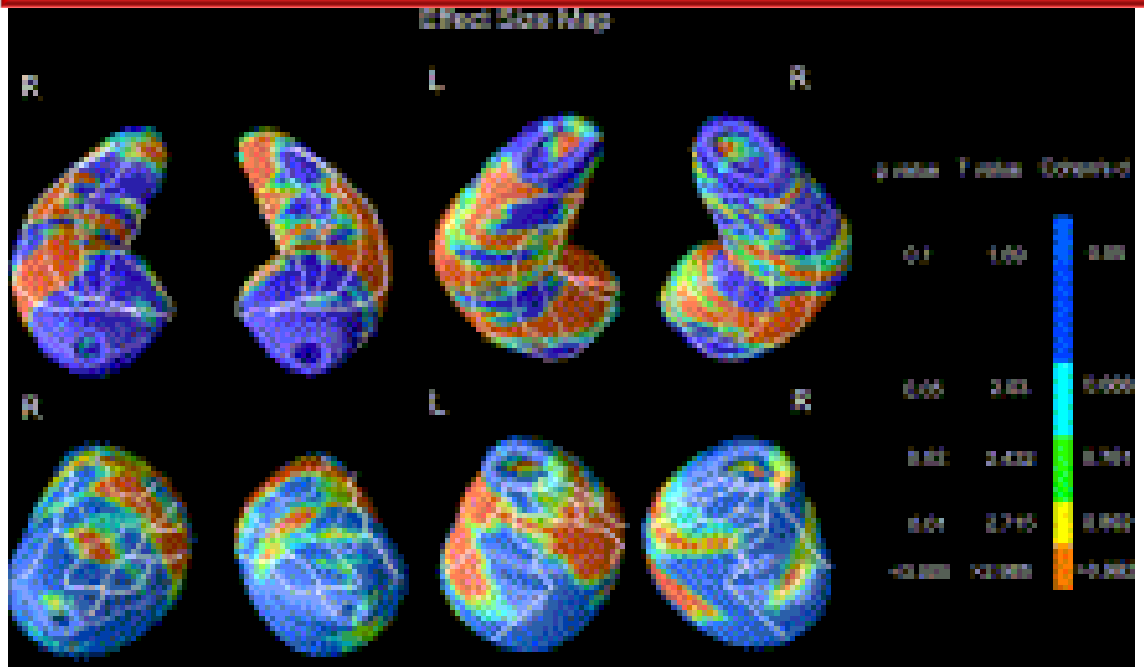
Yucel et al., Arch Gen Psychiatry. 2008

Hippocampus ***Amygdala***



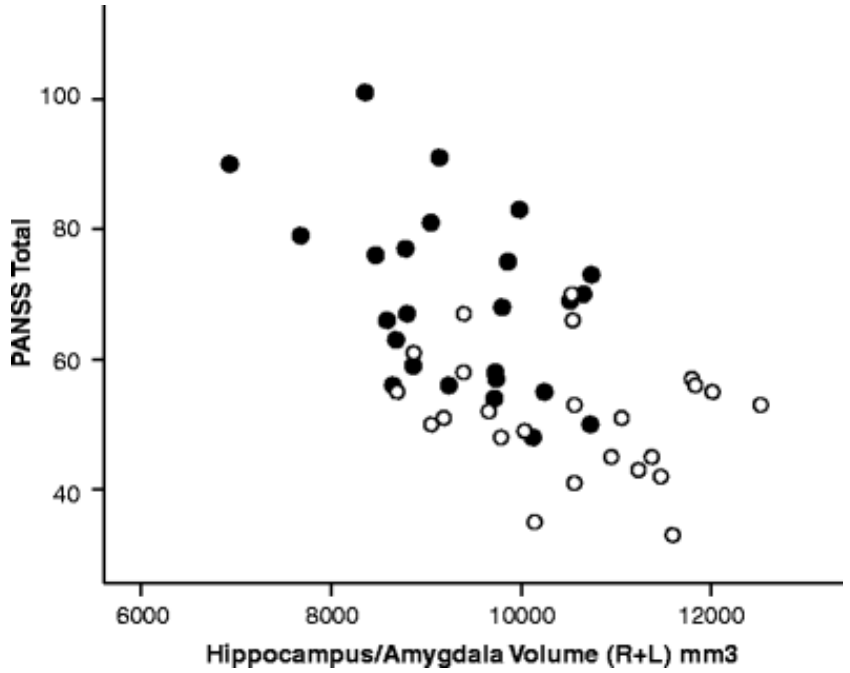
Lorenzeti et al.., Biological Psychiatry 2015

Schizophrenics have Smaller Hippocampus and Amygdala



Areas in Hippocampus and Amygdala where volumes were smaller in schizophrenics than controls

Prestia et al., Am J Geriatr Psychiatry 2015.



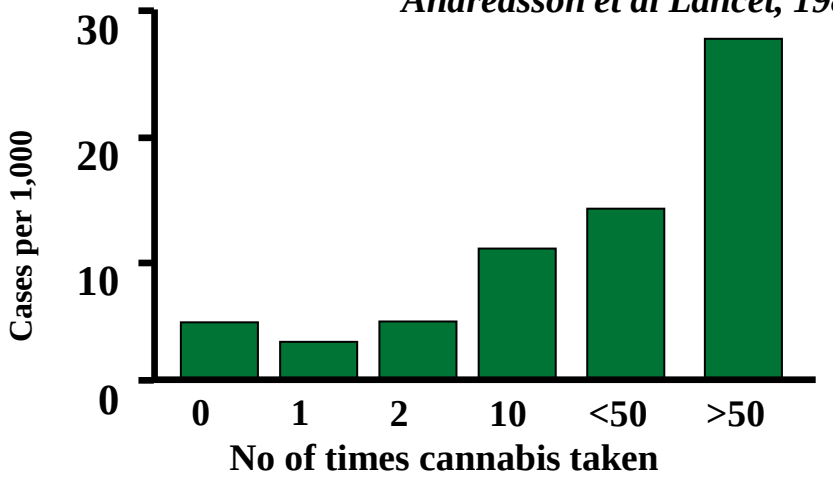
Hippocampus/Amygdala volumes correlated with psychosis in schizophrenics (closed) and bipolar patients (open)

Watson et al., Brain Imaging Behav. 2012.

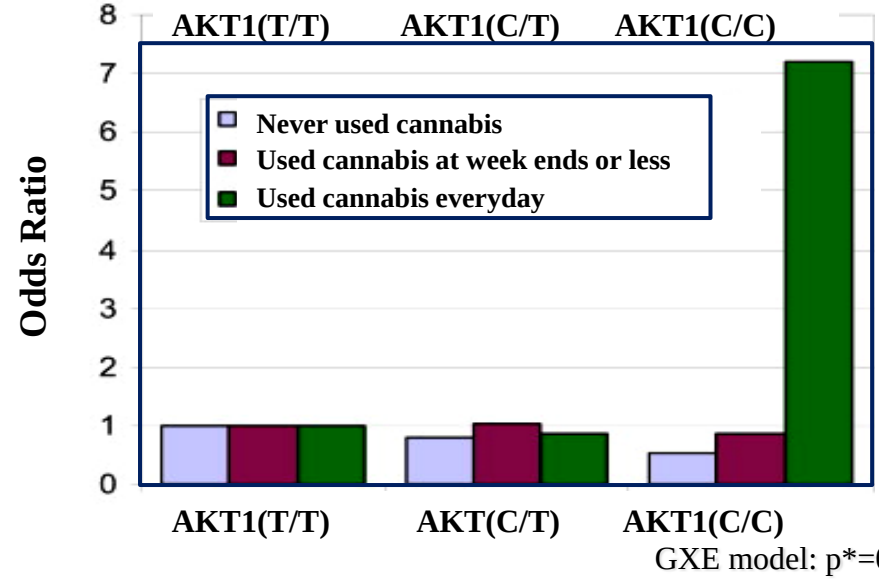
Cannabis-Associated Psychosis

Study of Swedish Conscripts (n=45570)

Andréasson et al Lancet, 1987.



Regular Cannabis Use Increases Schizophrenia Risk in those with AKT1

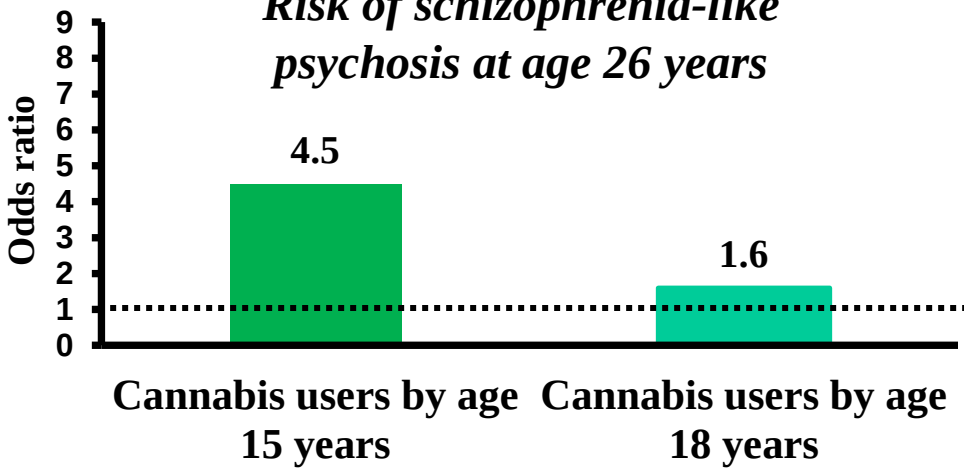


GXE model: p*=0.014

Di Forti et al., Biological Psychiatry, 2012.

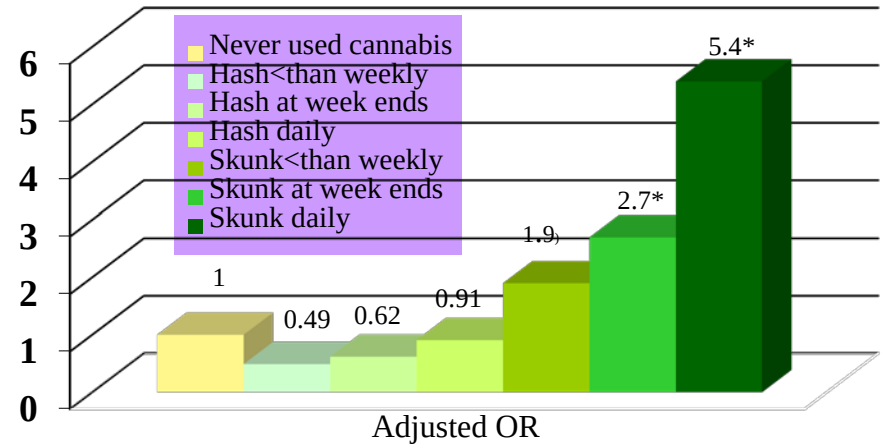
Prospective Dunedin study (n=1037)

Risk of schizophrenia-like psychosis at age 26 years



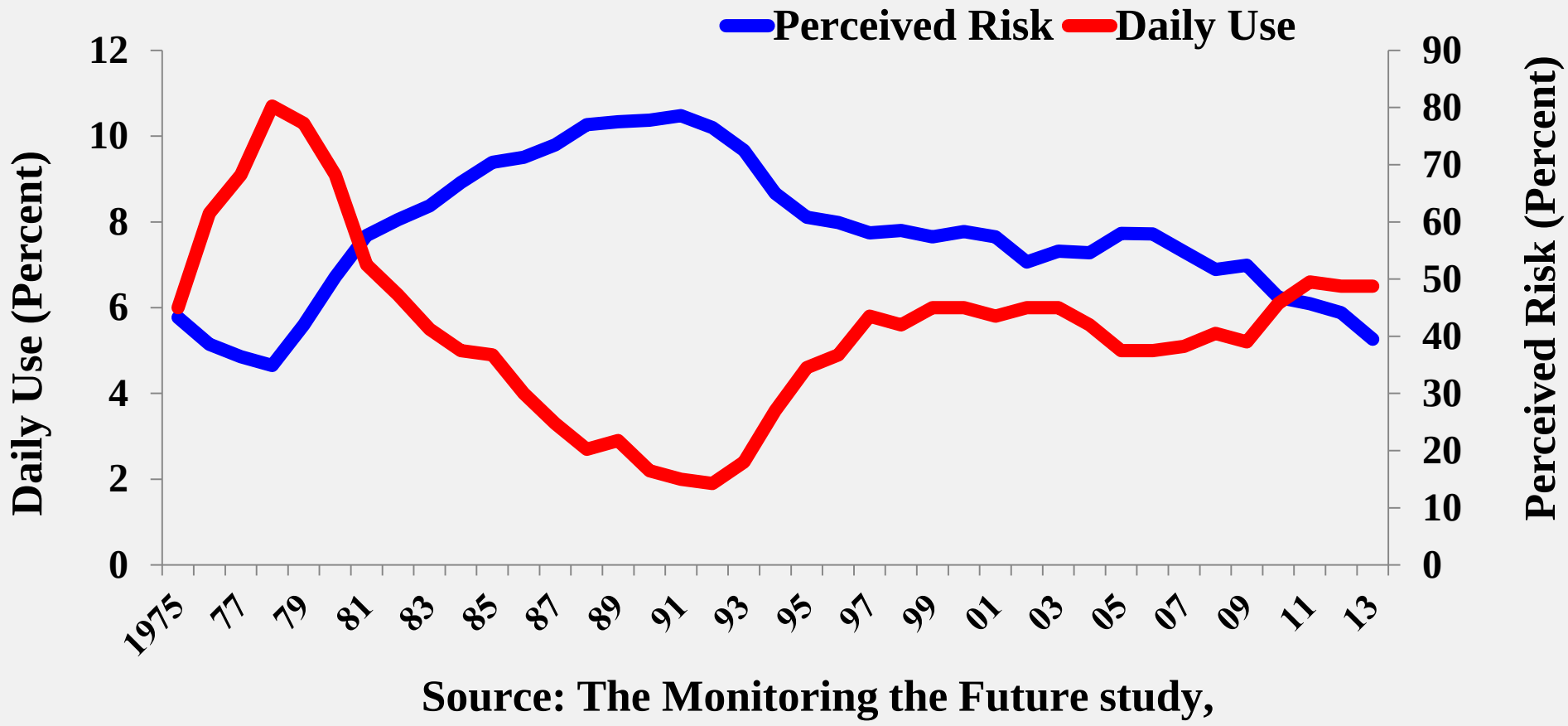
Arseneault et al BMJ 2002

Effect of High Potency Cannabis on Risk of Psychosis



Di Forti M et al., The Lancet published online February 18, 2015.

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



SOURCE: University of Michigan, 2013 Monitoring the Future Study

NIDA NATIONAL INSTITUTE ON DRUG ABUSE
The Science of Drug Abuse & Addiction

EXAMPLES OF RISK AND PROTECTIVE FACTORS

Risk Factors	Domain	Protective Factors
Early Aggressive Behavior	Individual	Self-Control
Poor Social Skills	Individual	Positive Relationships
Lack of Parental Supervision	Family	Parental Monitoring and Support
Substance Abuse	Peer	Academic Competence
Drug Availability	School	Anti-Drug Use Policies
Poverty	Community	Strong Neighborhood Attachment

Reduce these

Elevate these

Prevention Programs Should

Enhance Protective Factors & Reduce Risk Factors

Adolescent Brain Cognitive Development National Longitudinal Study

NIDA, NIAAA, NCI, NICHD, NIMH, NIMHD, NINDS, OBSSR, ORWH

Ten year longitudinal study of 10,000 children from age 10 to 20 years to assess effects of drugs on individual brain development trajectories