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

*Secretariat for Multidimensional Security*

**FIFTY-FIFTH REGULAR SESSION**  
**April 29 - May 1, 2014**  
**Washington, D.C.**

**OEA/Ser.L/XIV.2.55**  
**CICAD/doc.2105/14**  
**29 April 2014**  
**Original: English**

**EFFECTS OF MARIJUANA  
ON BRAIN, BODY & BEHAVIOR  
WILSON COMPTON, NATIONAL INSTITUTE ON DRUG ABUSE**

# Effects of Marijuana On Brain, Body & Behavior



**Wilson M. Compton, MD, MPE**  
**Deputy 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
- What about the rates among adolescents?



Tetrahydrocannabinol (THC)  
Active Ingredient in Marijuana

# 2013 Monitoring the Future Study

## Prevalence of Past Year Drug Use Among 12<sup>th</sup> graders

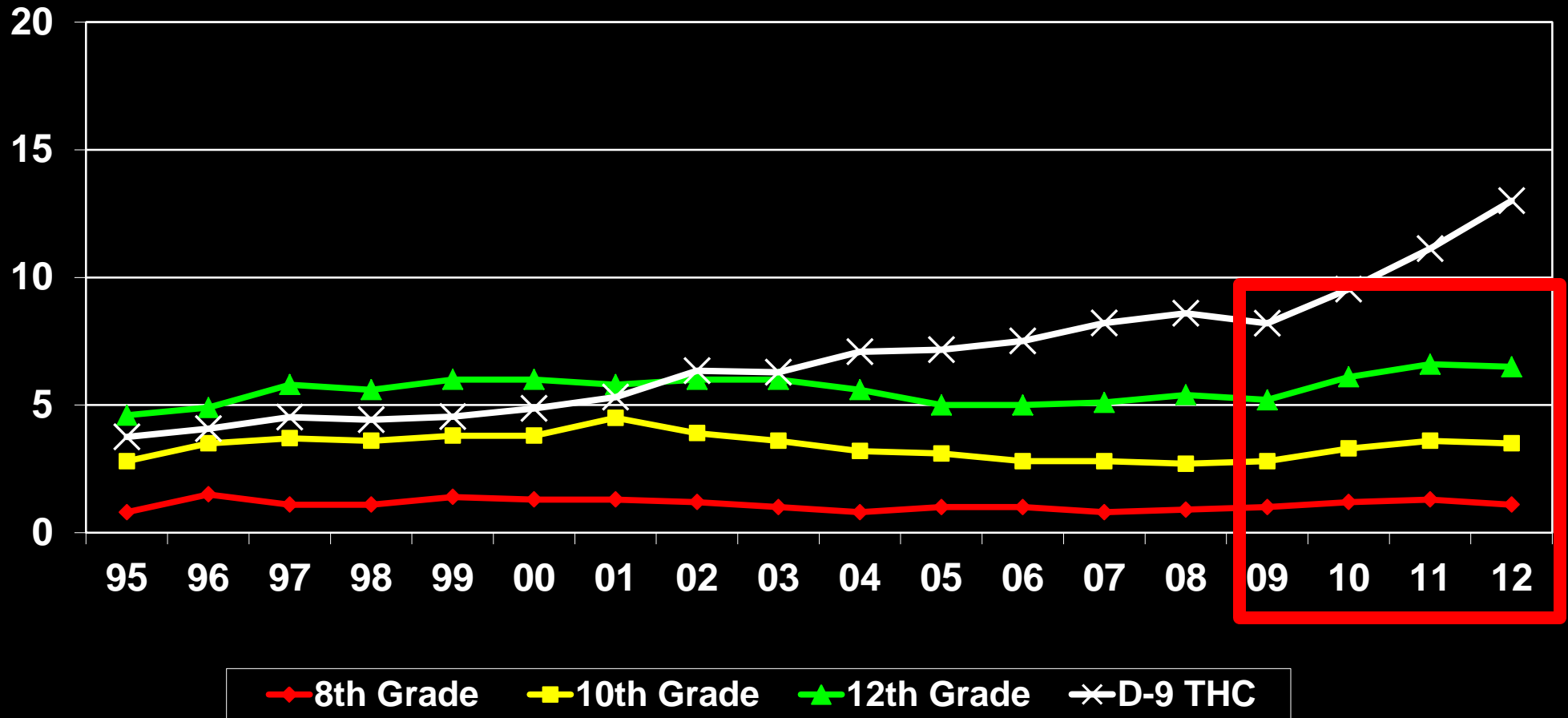
Drug	%	Drug	%
Alcohol	62.0	Sedatives*	4.8
Marijuana/Hashish	36.4	Tranquilizers*	4.6
Hookah	21.4	Hallucinogens	4.5
Small cigars	20.4	MDMA (Ecstasy)	4.0
Amphetamines*	8.7	Hall other than LSD	3.7
Synthetic Marijuana	7.9	OxyContin*	3.6
Snus	7.7	Salvia	3.4
Adderall*	7.4	Cocaine (any form)	2.6
Narcotics o/t Heroin*	7.1	Inhalants	2.5
Vicodin*	5.3	Ritalin*	2.3
Cough Medicine*	5.0	LSD	

\* Nonmedical use

Categories not mutually exclusive

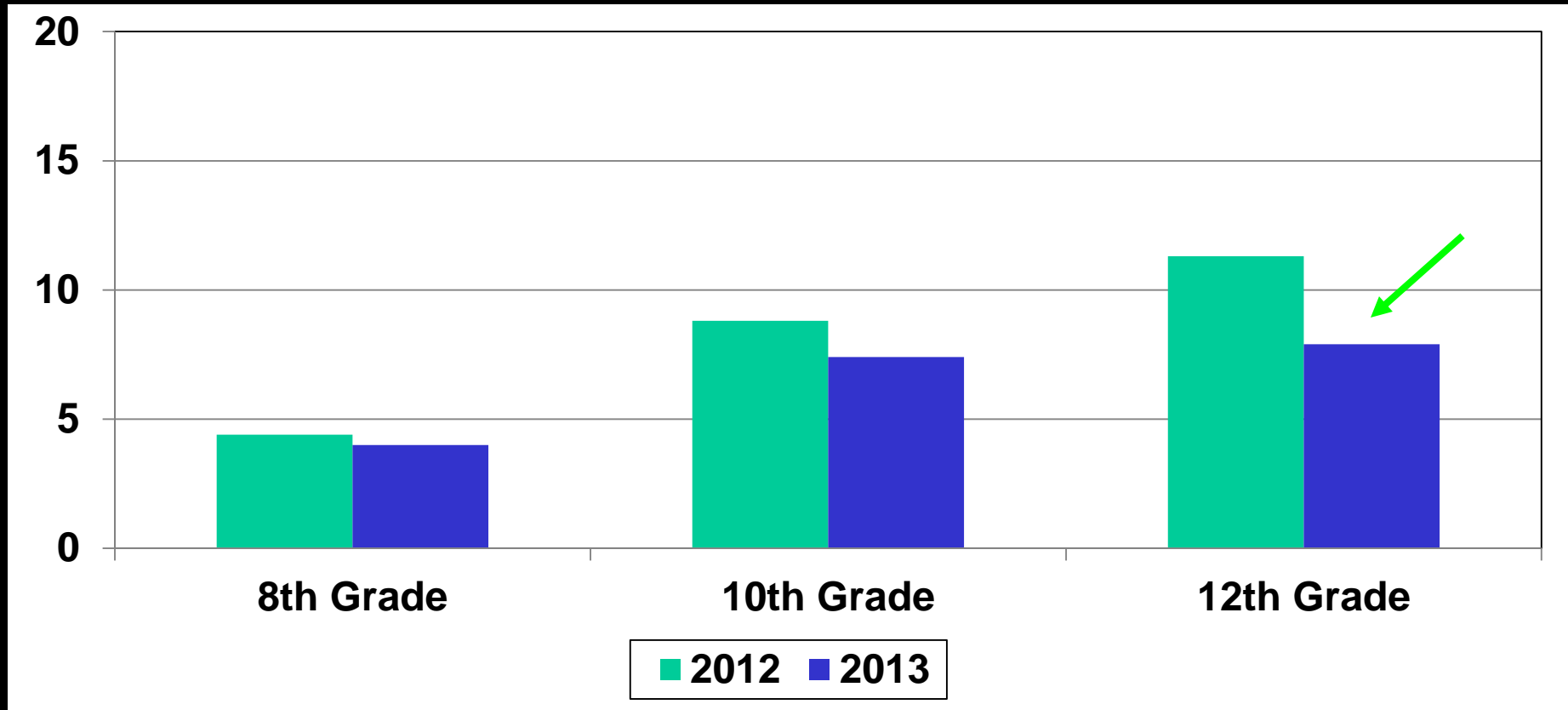
Source: University of Michigan, 2014

# Percent of Students Reporting Daily Use of Marijuana, by Grade and Potency (% THC-D9)



SOURCE: University of Michigan, 2013 Monitoring the Future Study, and University of Mississippi Marijuana Project (potency data)

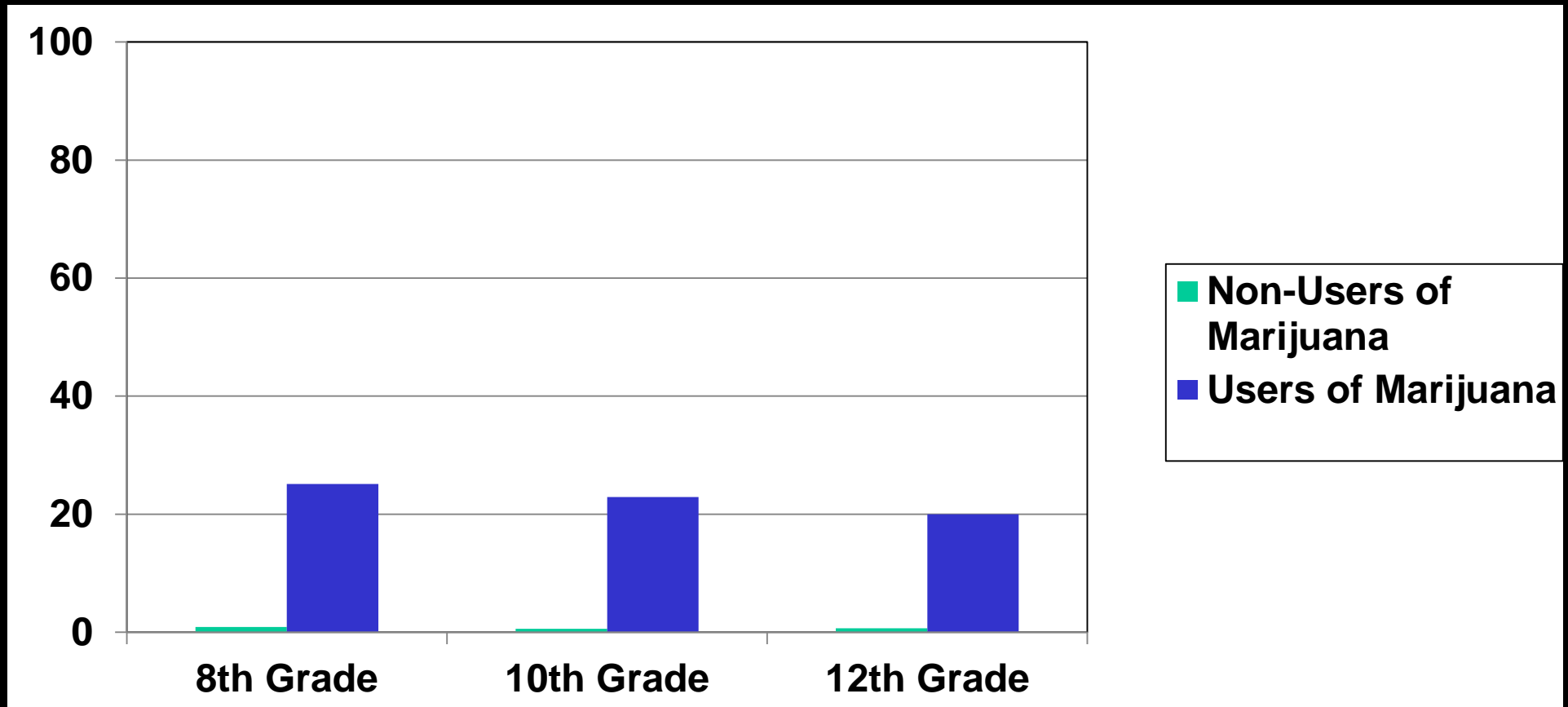
# Percent of Students Reporting Use of Synthetic Marijuana in Past Year, by Grade



Denotes significant difference  
between 2012 and 2013

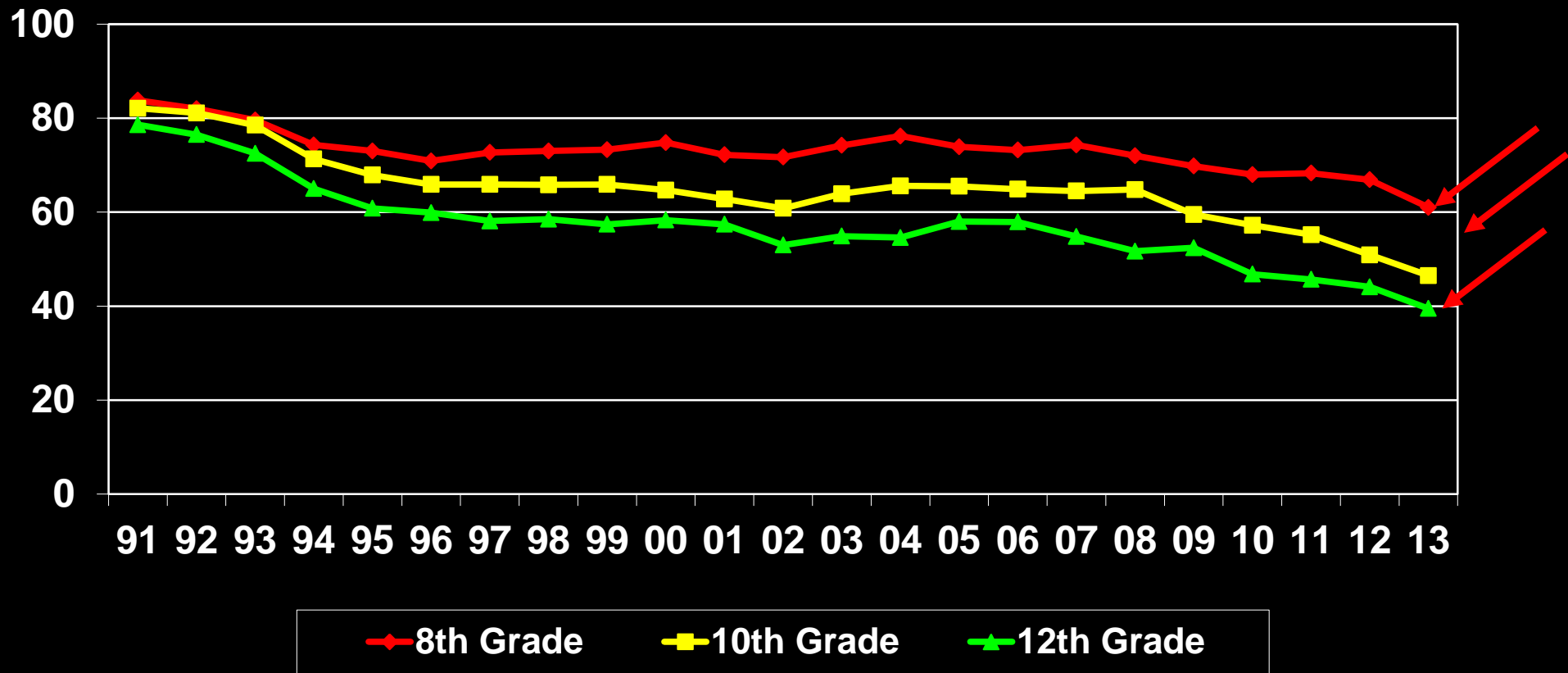
SOURCE: University of Michigan, 2013 Monitoring the Future Study

# Percent Reporting Using Synthetic Marijuana in Past Year, By Past-Year Use of Marijuana



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

# Percent Perceiving Great Risk of Smoking Marijuana Regularly

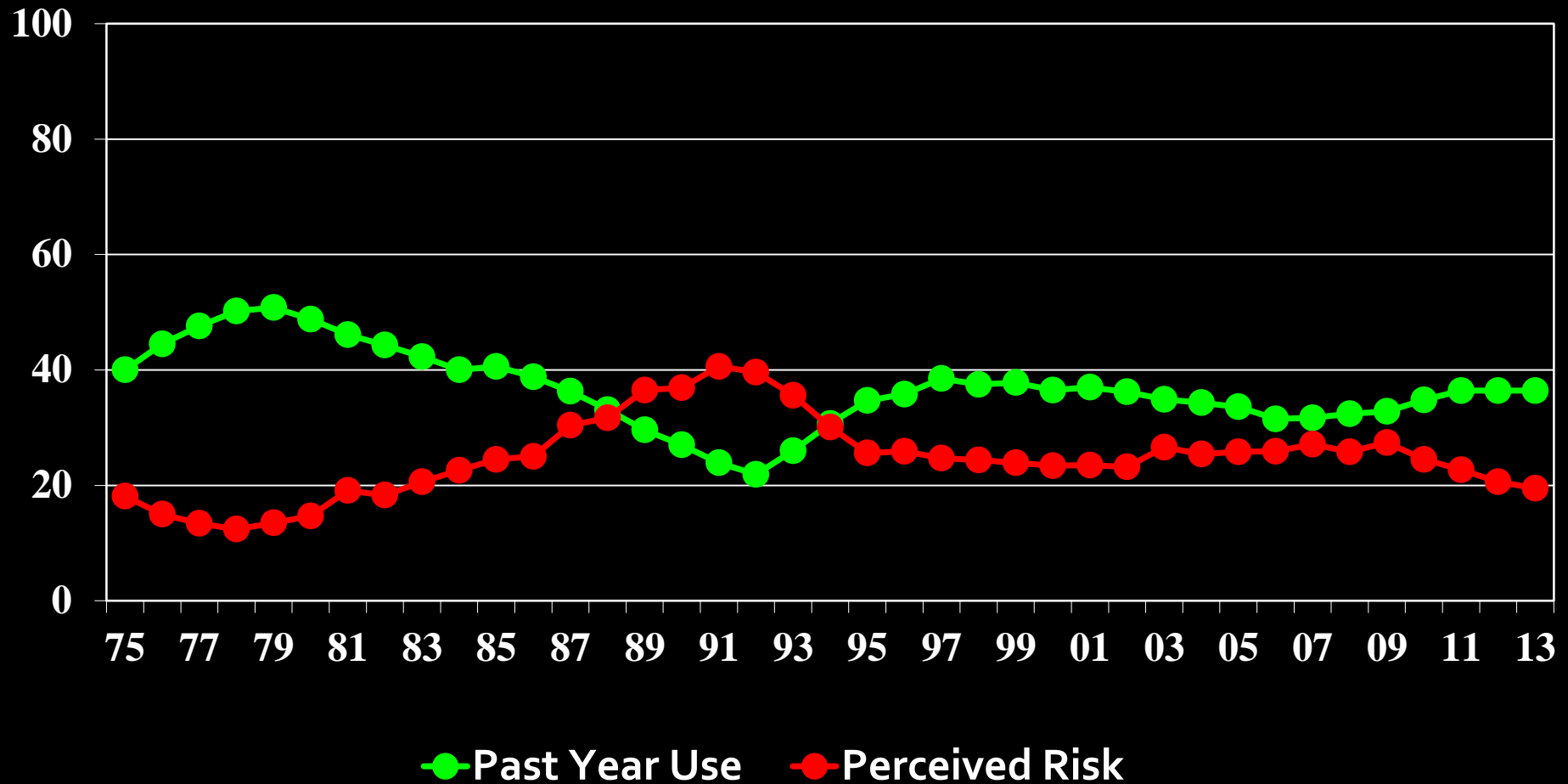


Denotes significant difference  
between 2012 and 2013

SOURCE: University of Michigan, 2013 Monitoring the Future Study

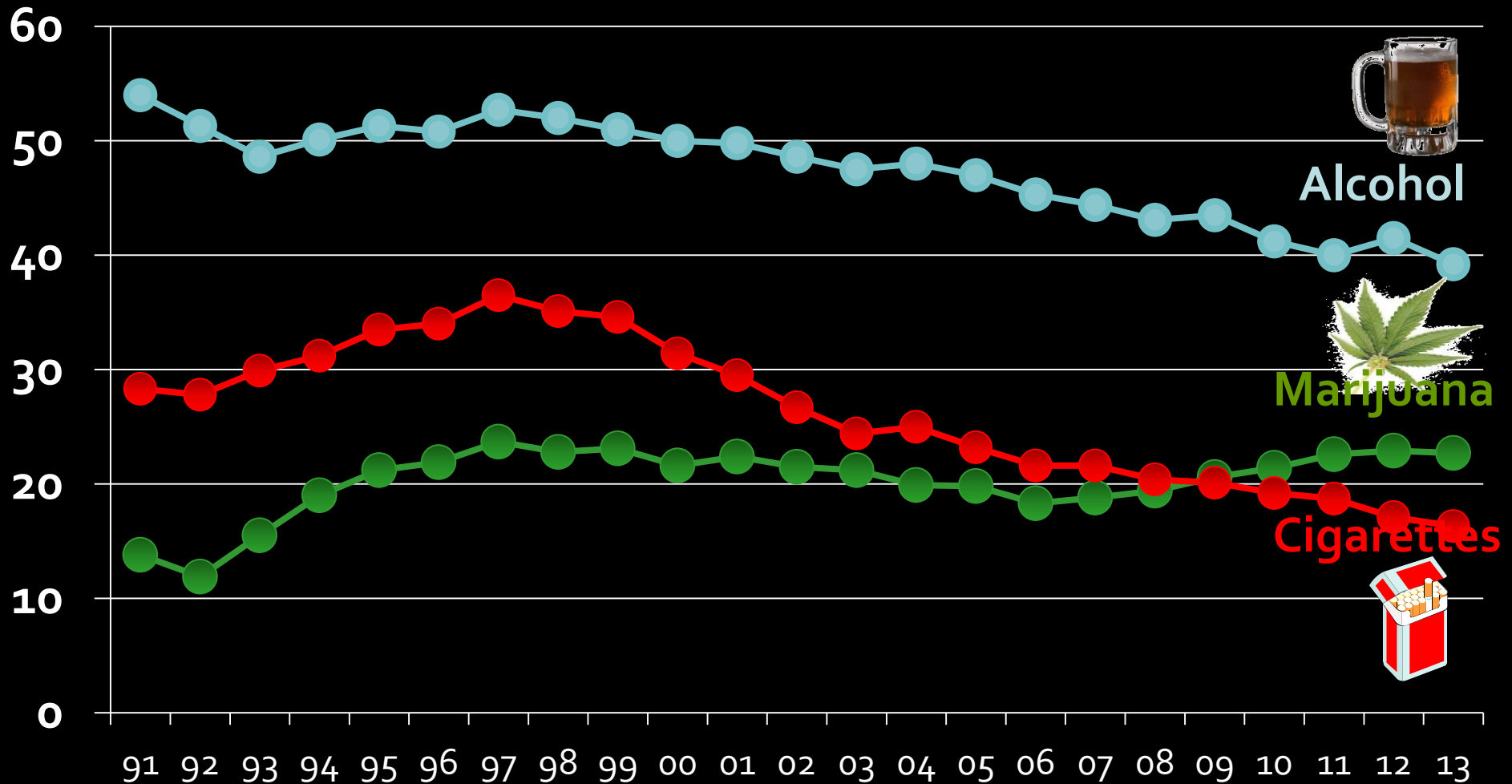
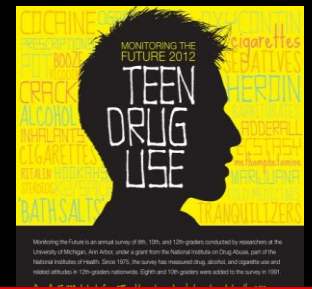


# 12<sup>th</sup> Graders' Past Year Marijuana Use vs. Perceived Risk of Occasional Marijuana Use



SOURCE: University of Michigan, 2013 Monitoring the Future Study

# Percentage of U.S. 12<sup>th</sup> Grade Students Reporting Past Month Use of Cigarettes, Marijuana and Alcohol



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

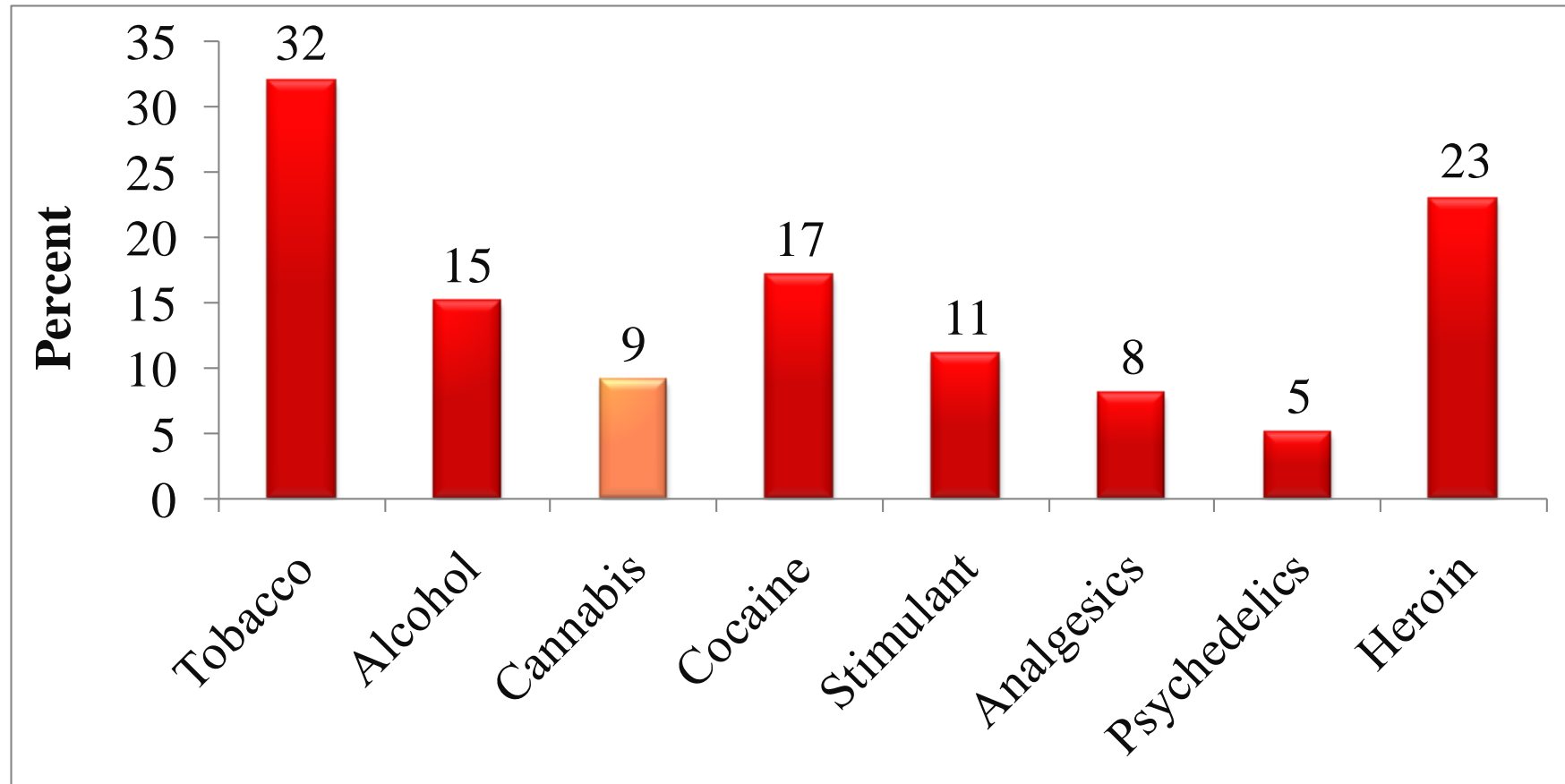
***Is marijuana  
addictive?***



# Marijuana is Addictive:

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



Sources: Anthony JC et al., 1994 and Lopez-Quintero M et al., 2011

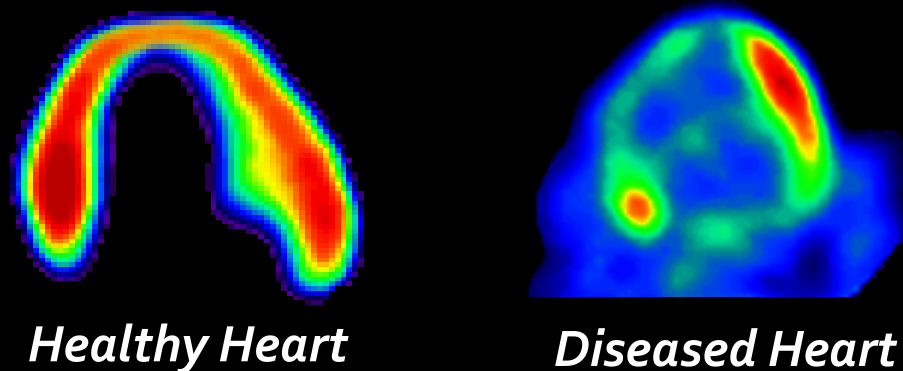
# *ADDICTION IS A **DISEASE OF THE BRAIN** as other diseases it affects the tissue function*

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## *Decreased Brain Metabolism in **Drug Abuse***

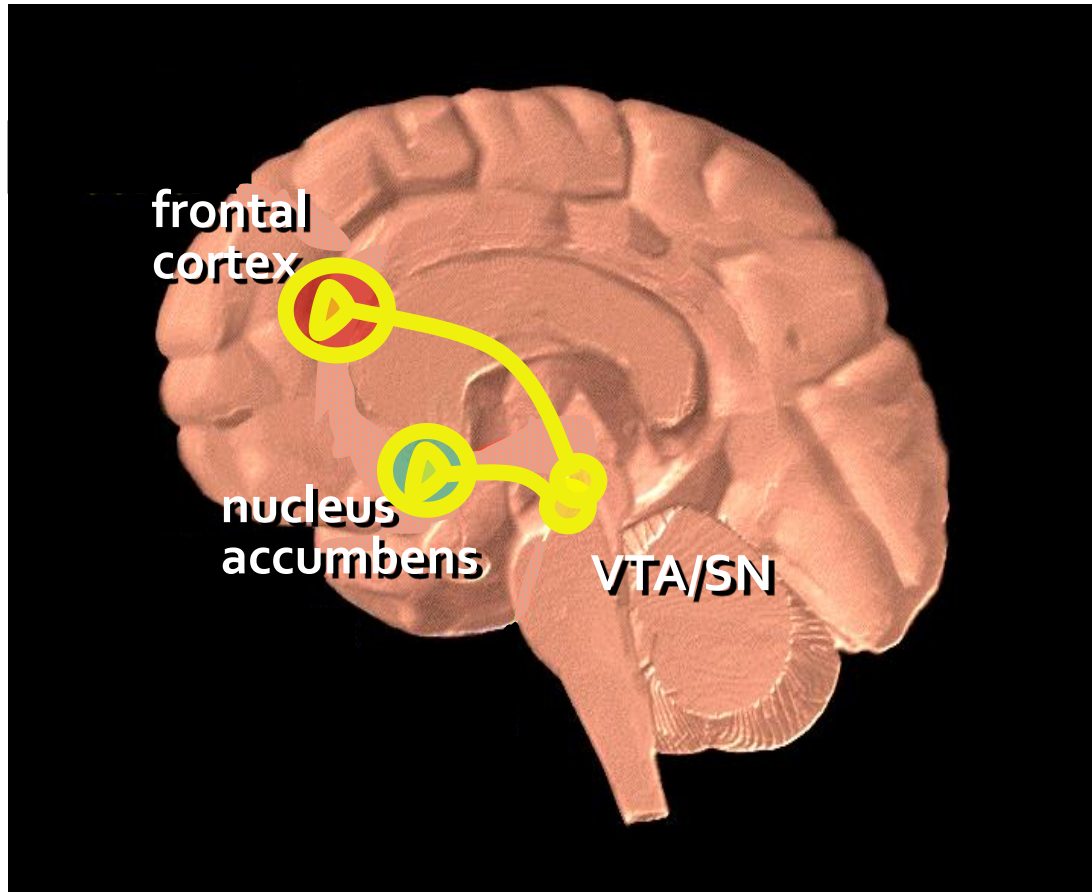


## *Decreased Heart Metabolism in **Heart Disease***

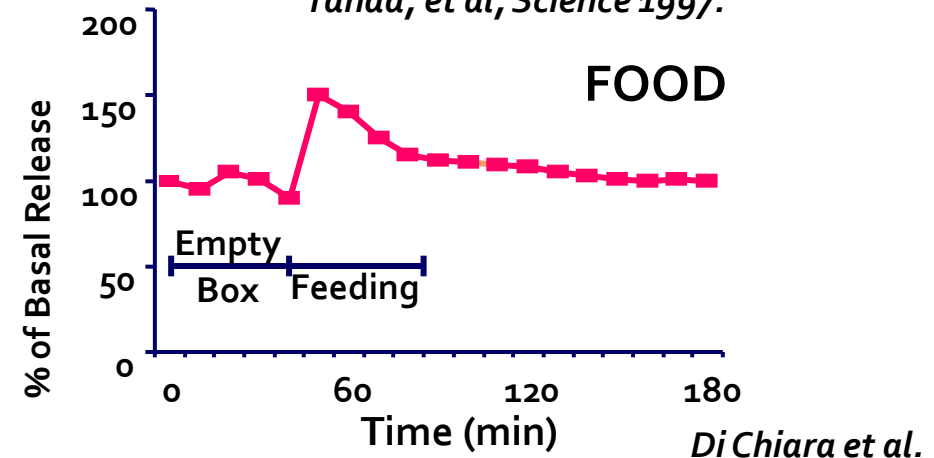
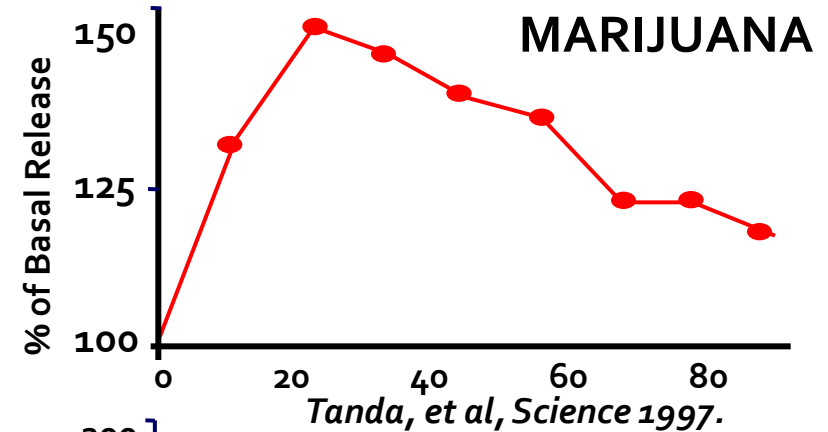
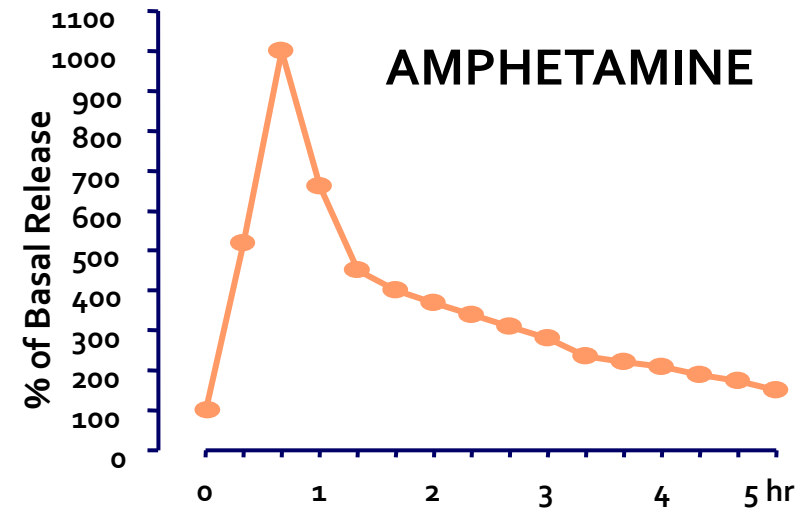


*Sources: From the laboratories of Drs. N. Volkow and H. Schelbert*

# Natural and Drug Reinforcers Increase Dopamine in NAc



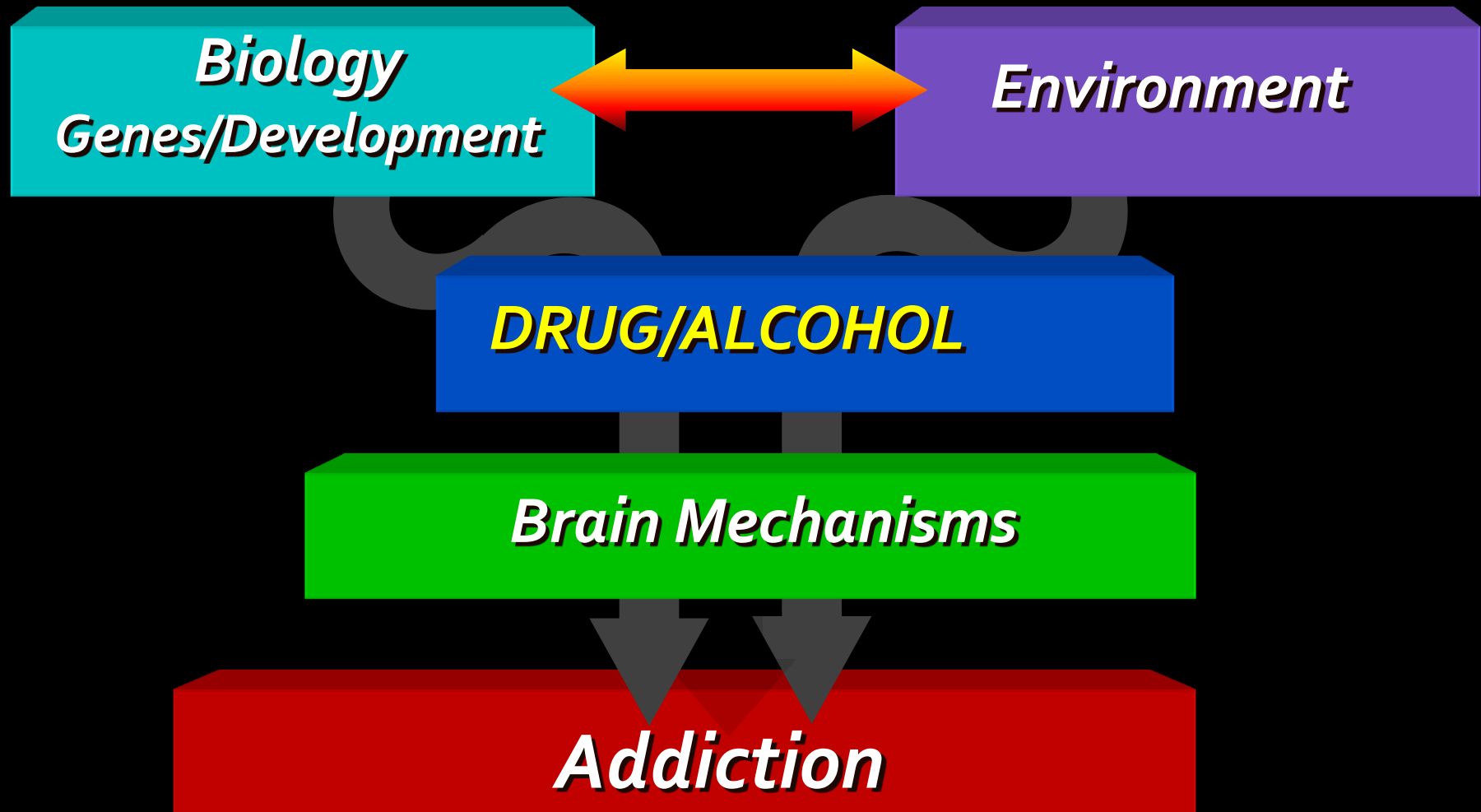
Drugs of abuse increase DA in the Nucleus Accumbens, which is believed to trigger the neuroadaptations that result in addiction





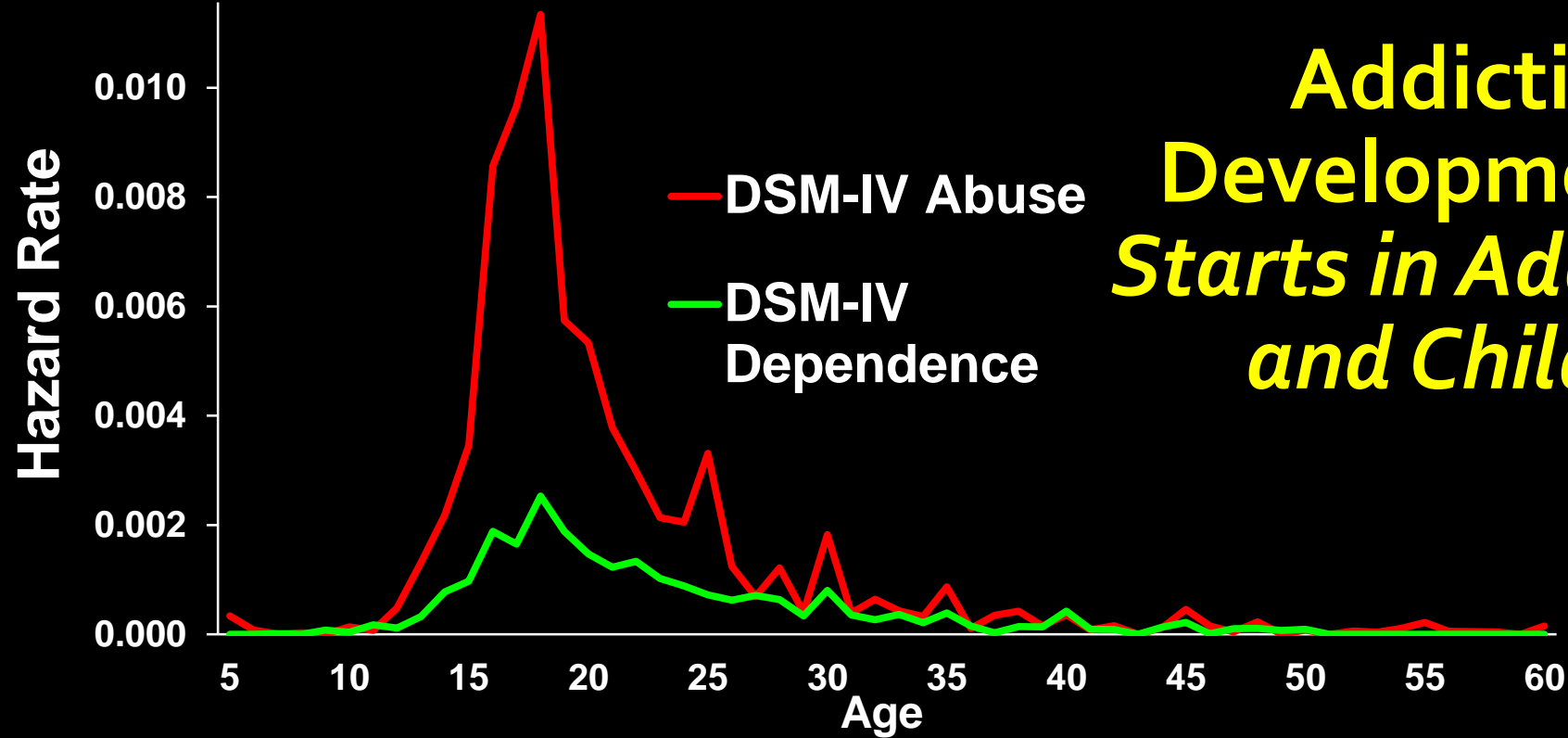
# **ADDICTIONS** as diseases of **Gene-Environment-Development**

*Addictions are common, developmental brain diseases expressed as compulsive behavior through continued use of a drug despite negative consequences: Onset depends on many intrinsic and extrinsic factors.*



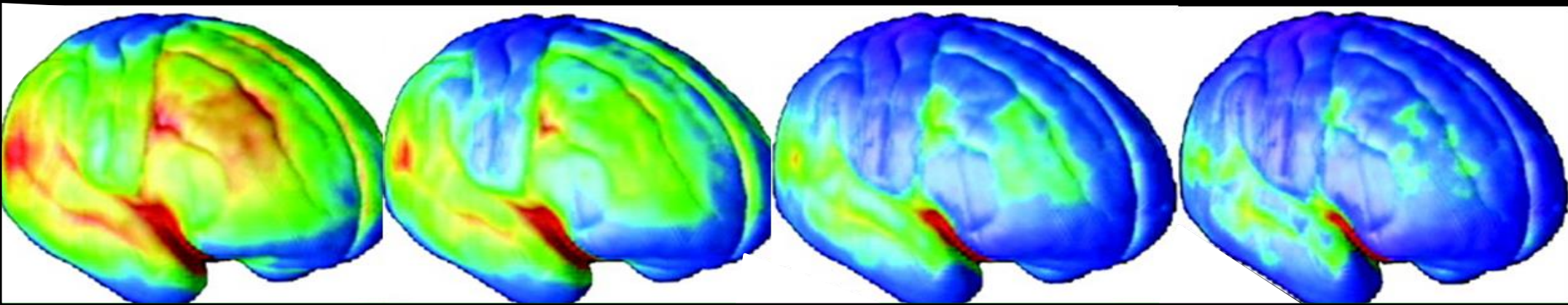


# Addiction Is Developmental: *It Starts in Adolescence and Childhood*



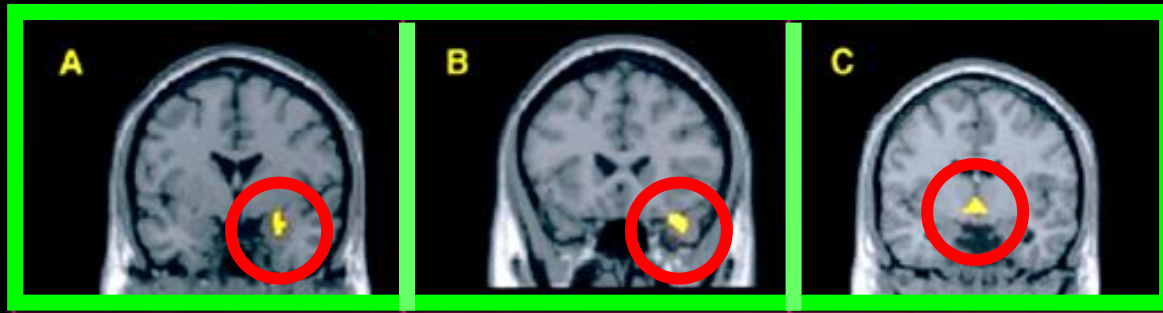
## *Age of Onset of Drug Abuse and Dependence*

Source: Compton, et al. Archives of General Psychiatry 2007. NESARC Study.

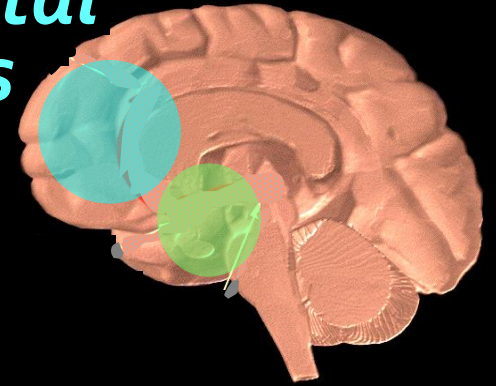


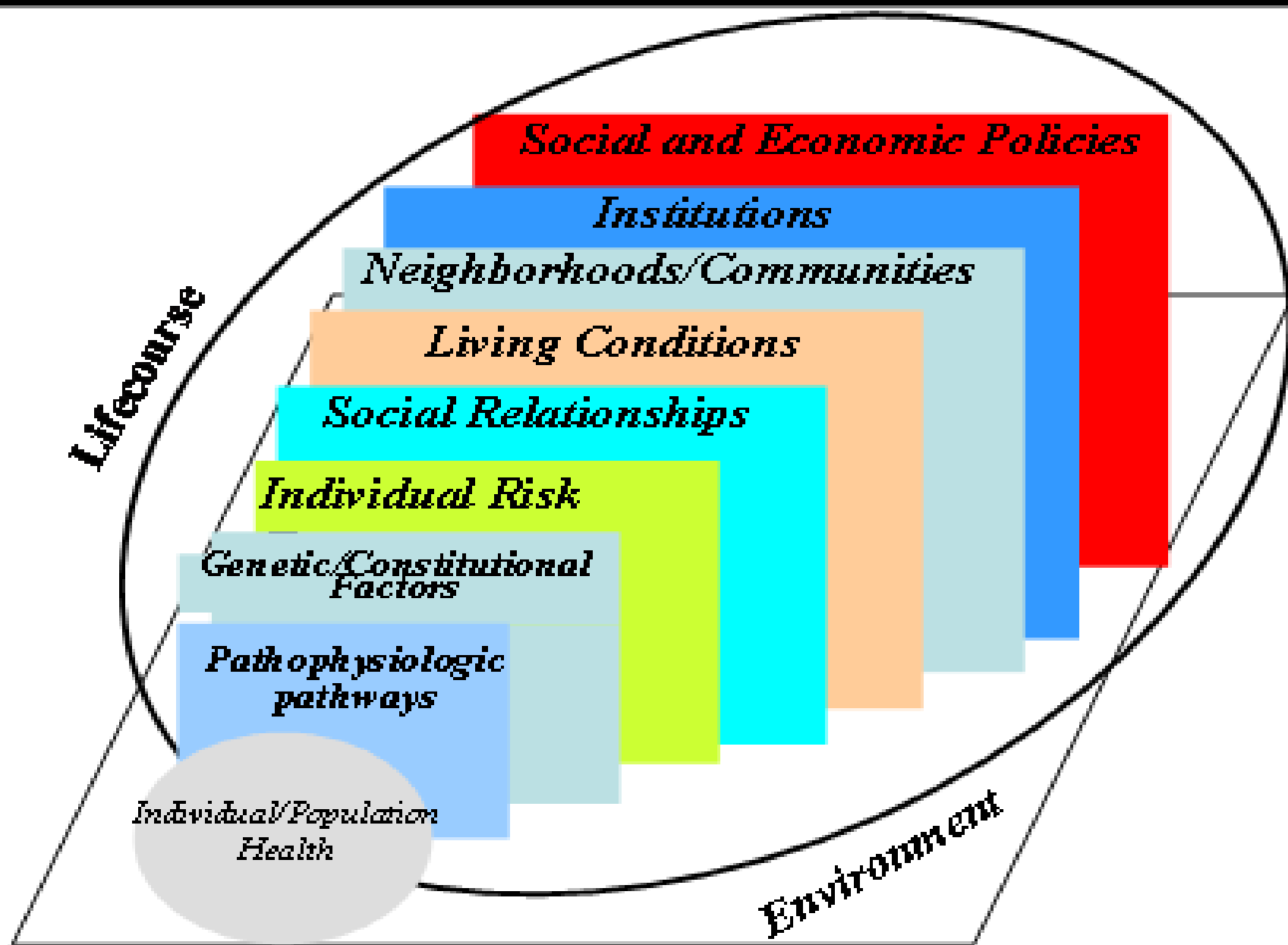
# *In Adults, Emotional Self Regulation Normally Implemented By A Neural Circuit Comprising Various Subcortical Limbic Structures...*

*Sexual Arousal Condition*



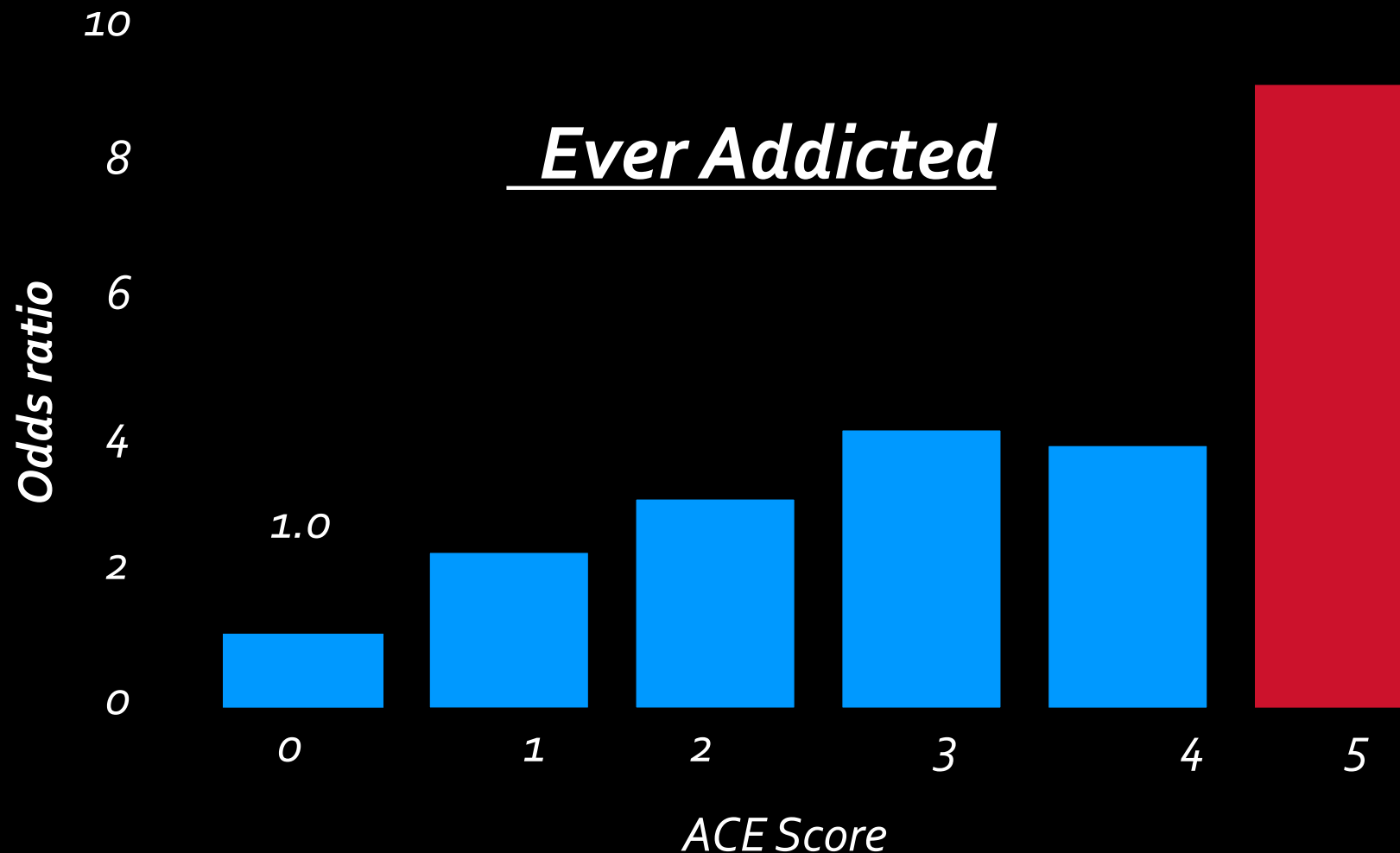
*& Prefrontal Regions*





(Kaplan, 2000)

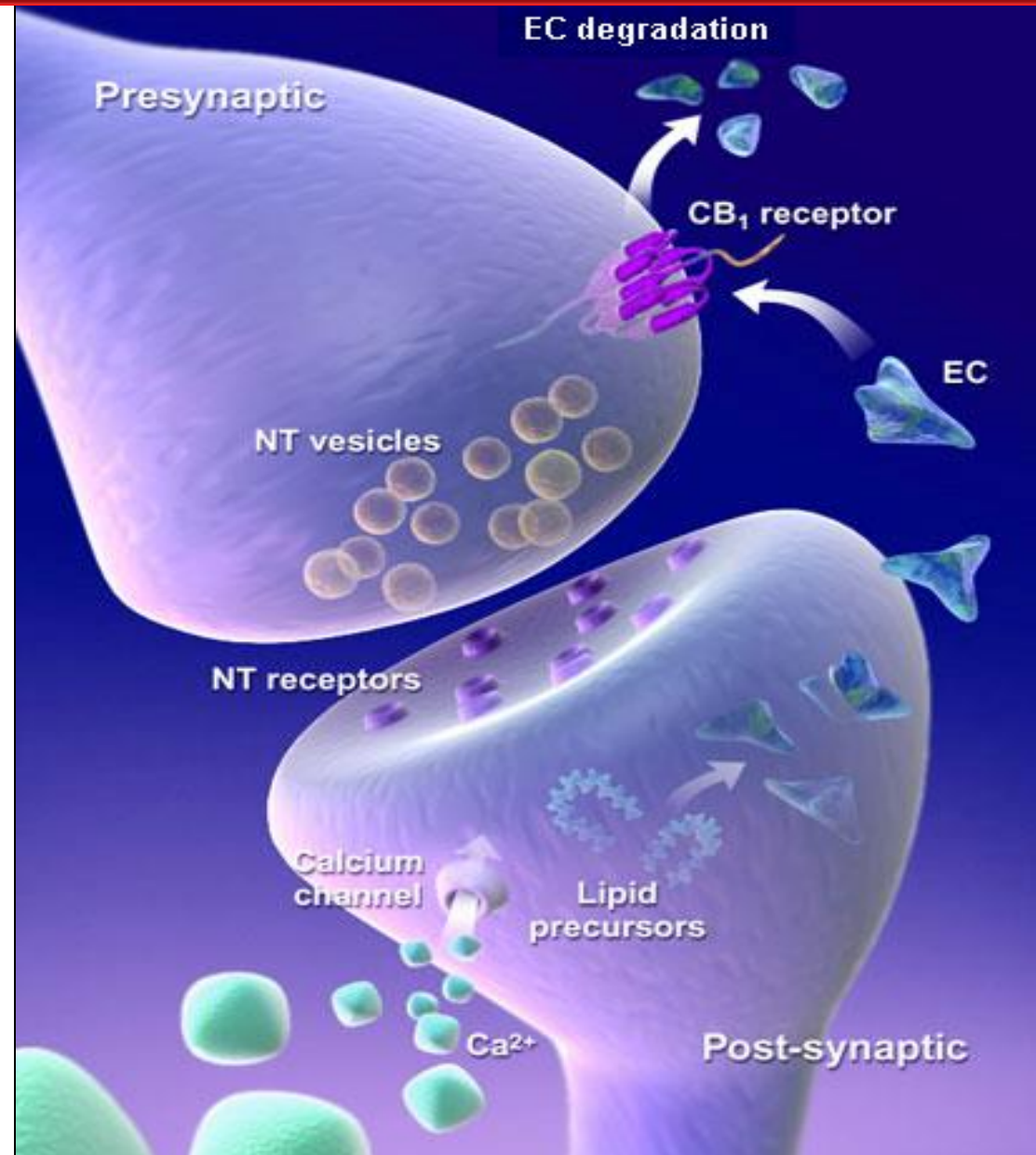
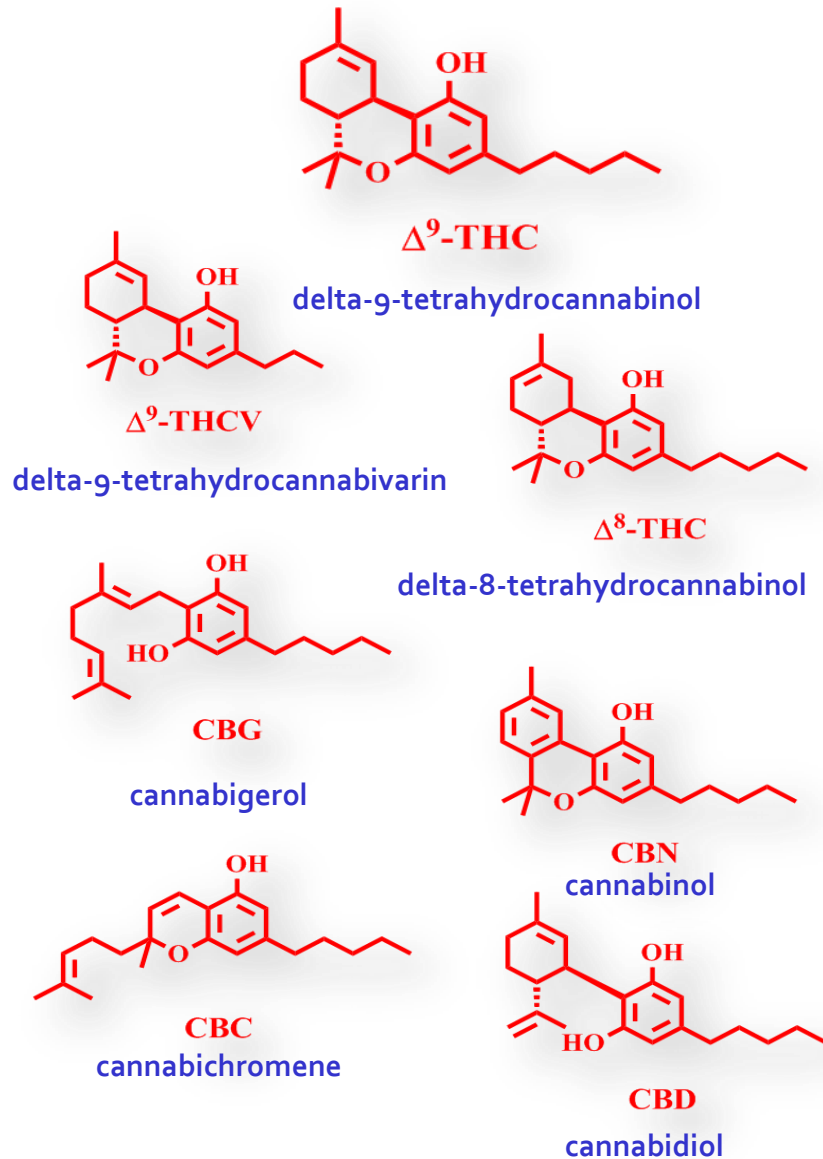
# Adverse Childhood Experiences (ACE) and Illicit Drug Use (n = 8603)



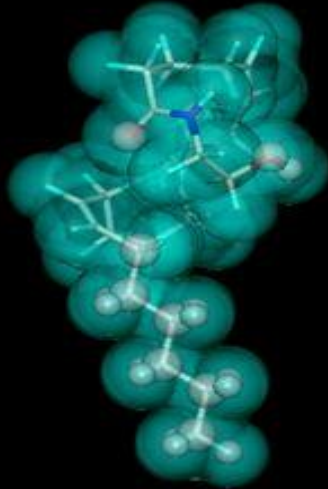
***Does marijuana use  
negatively affect the  
brain?***



# Constituents of MJ and the Cannabinoid System

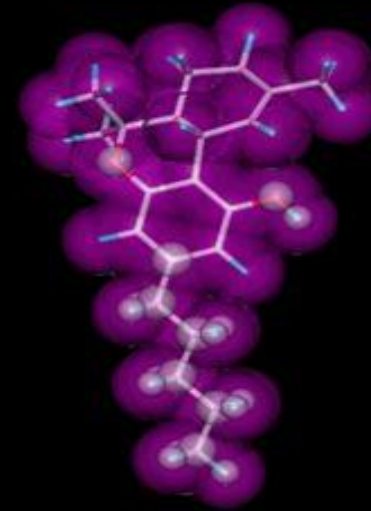


**Brain's Chemical**



**Anandamide**

**Drug**



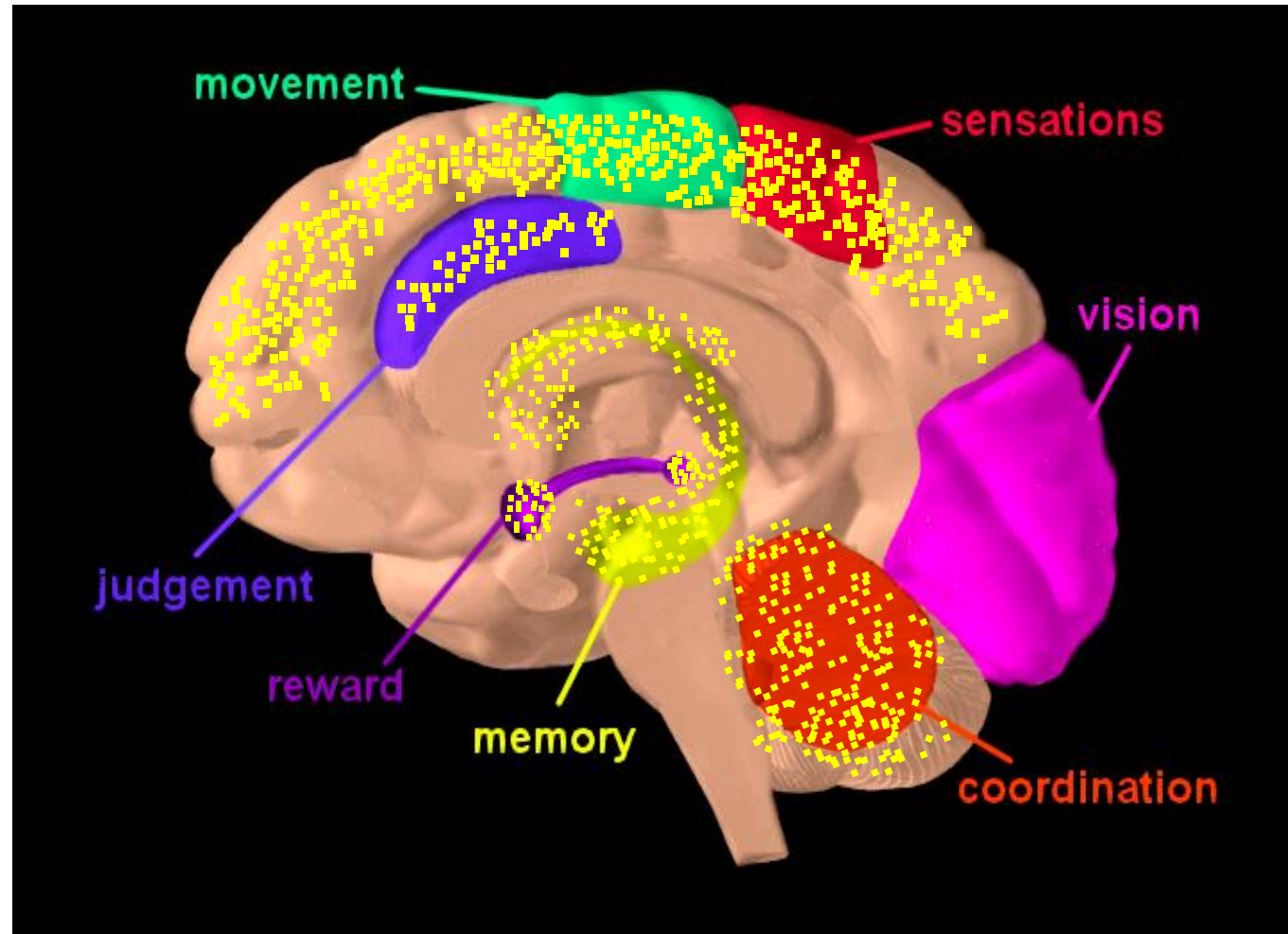
**THC**

***Drugs Can be Chemical Imposters***



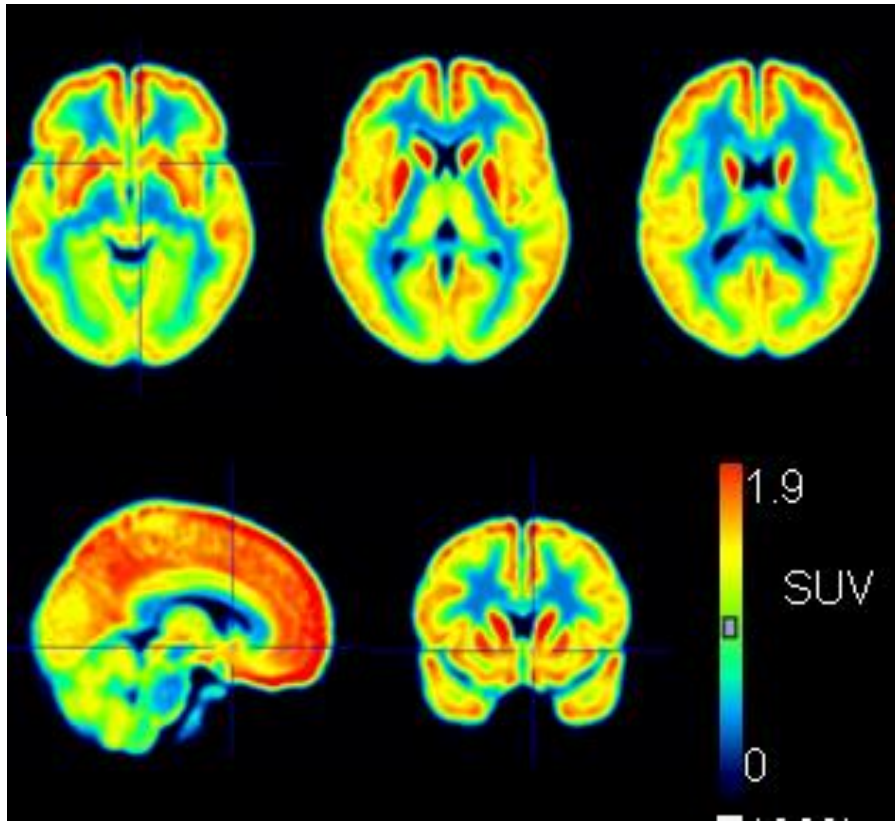
# Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

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

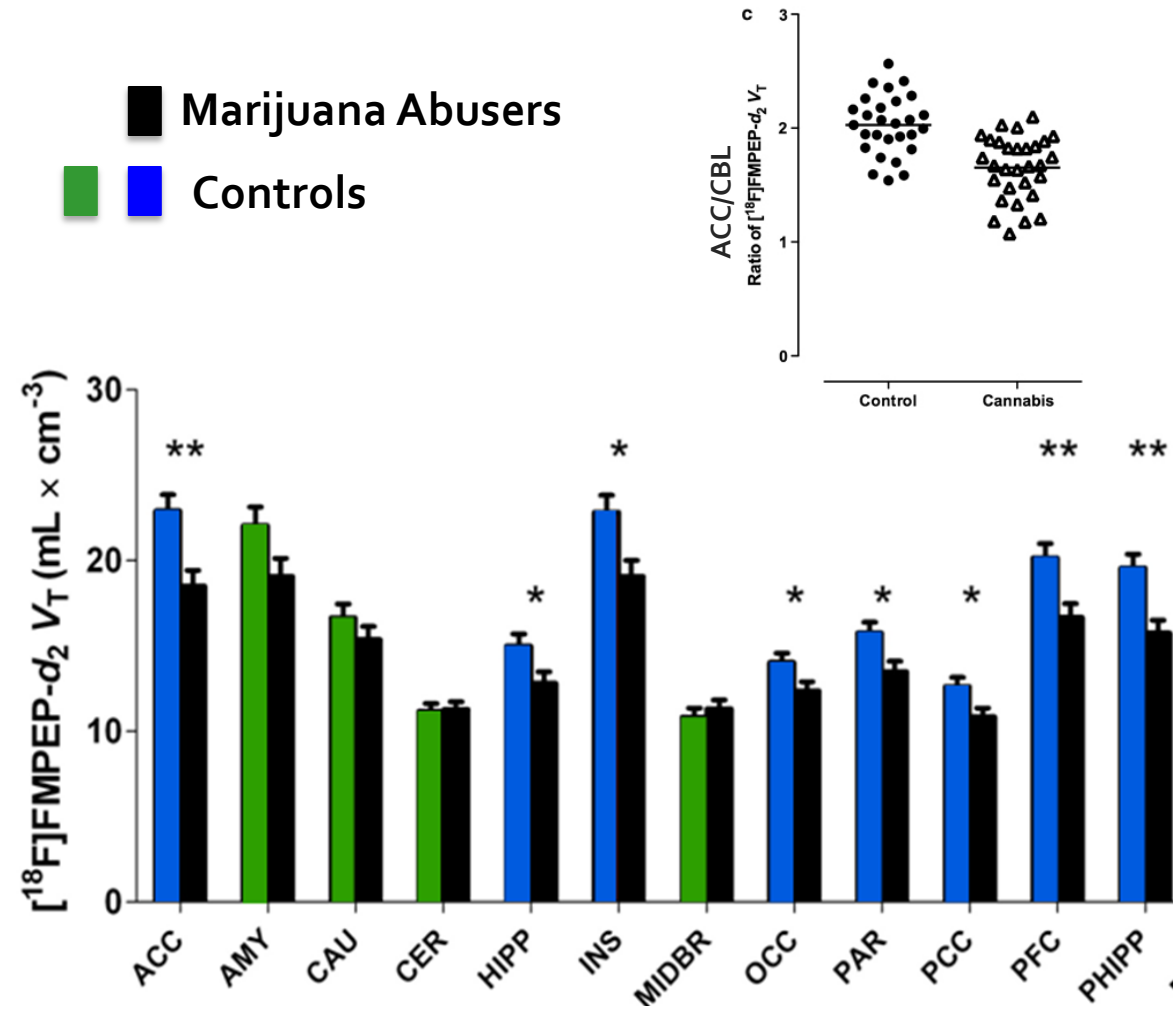




# Cannabinoid CB<sub>1</sub> Receptors in Human Brain are Downregulated in Marijuana Abusers



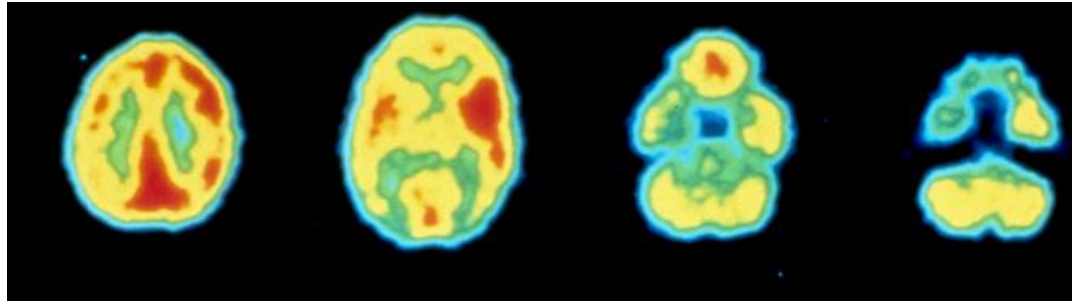
Van Loere et al., 2007.



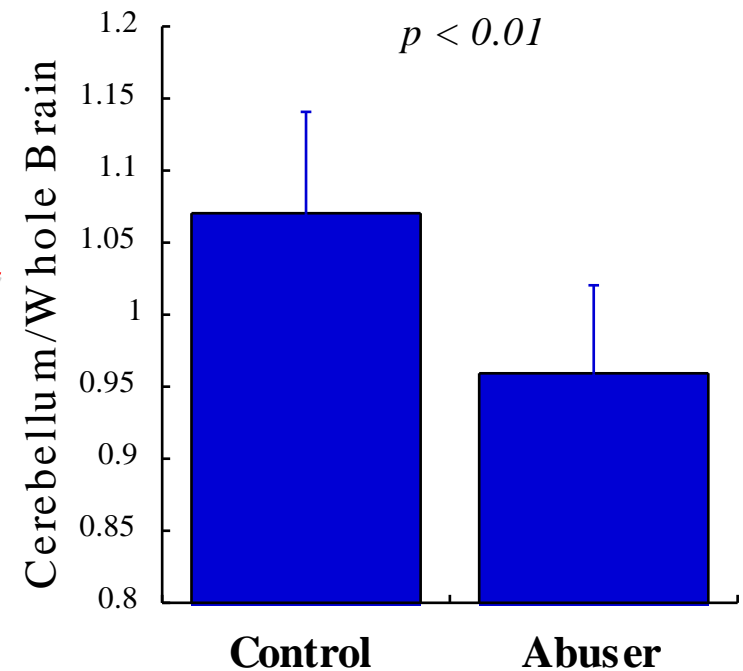
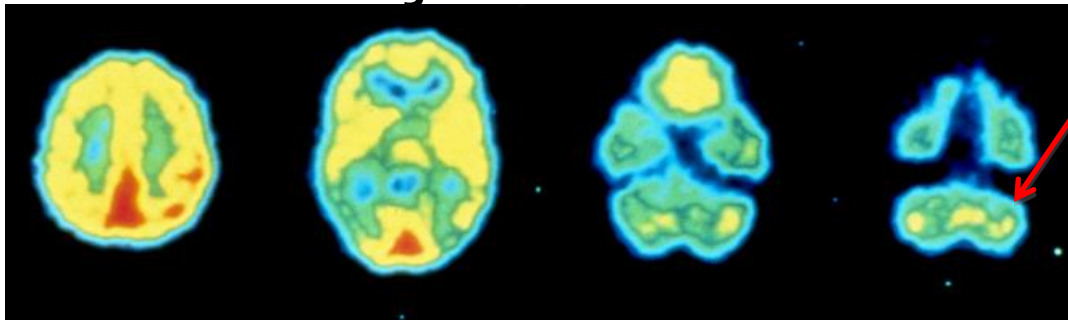
Hirvonen et al., Mol Psychiatry 2013

# Brain Glucose Metabolism in Controls and Marijuana Abusers

Control

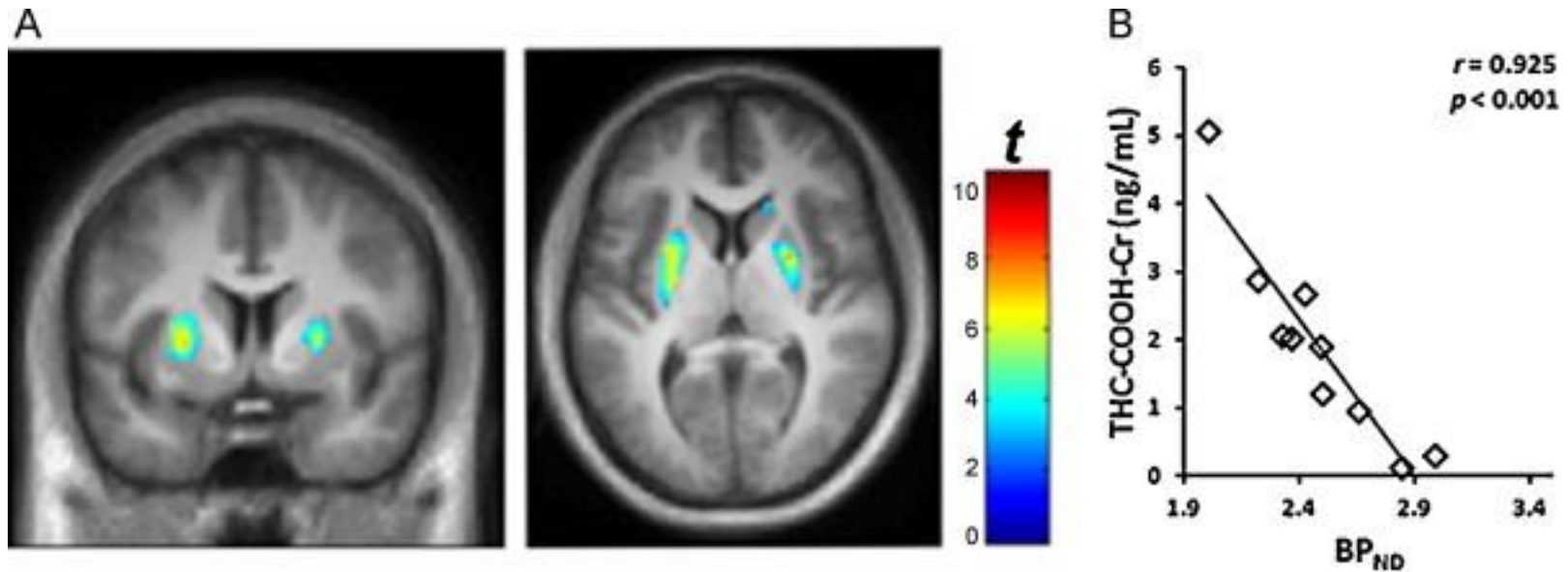


Marijuana Abuser



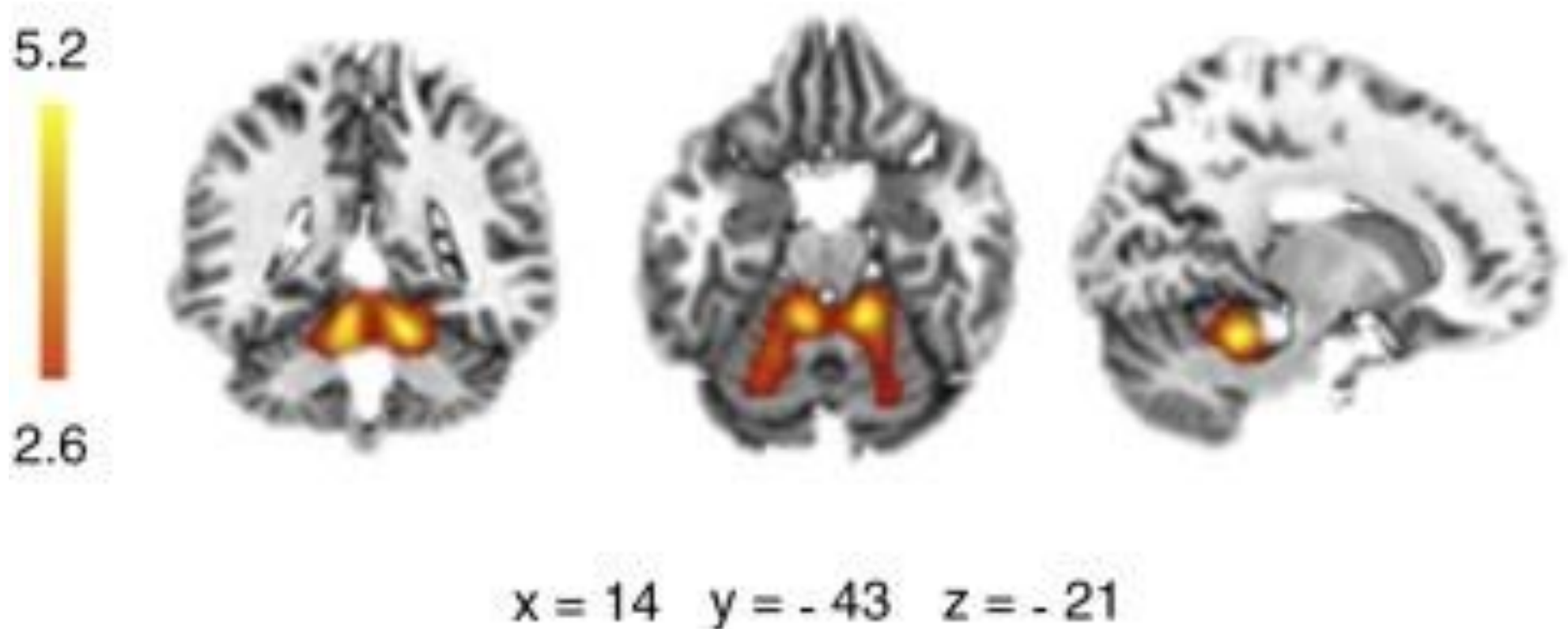
***Cerebellar metabolism is decreased in Marijuana Abusers***

# Correlations between Urine Concentration of THC and D<sub>2</sub>R availability (RAC BP<sub>ND</sub>) in Marijuana Users (n = 10)



Marijuana abusers with heavier consumption  
had lower Striatal D<sub>2</sub>R

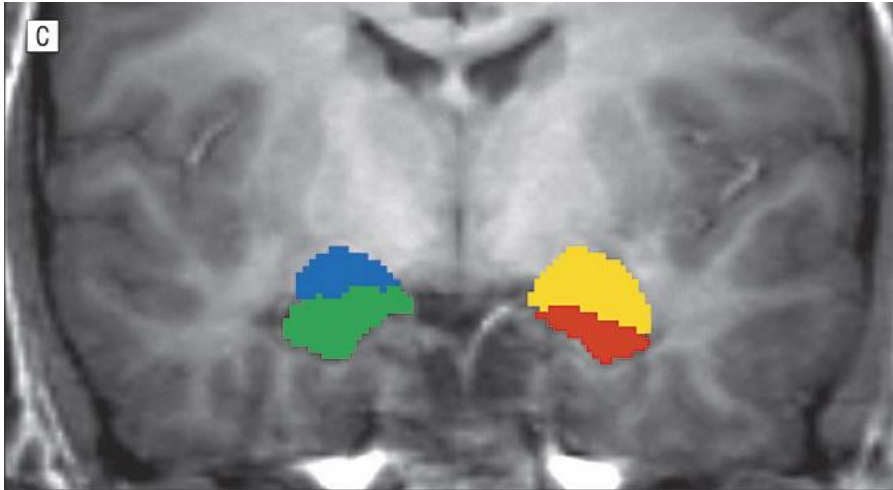
# Heavy Marijuana Users (N=33) Show Increases In Cerebellar Volumes Compared To Controls (N=42)



Source: Cousijn et al., Neuroimage, 59 (4), pp. 3845-3851 (2012).

***Medina et al 2010 associated larger cerebellar volume with decreased executive function***

# Brain abnormalities associated with long-term heavy marijuana use

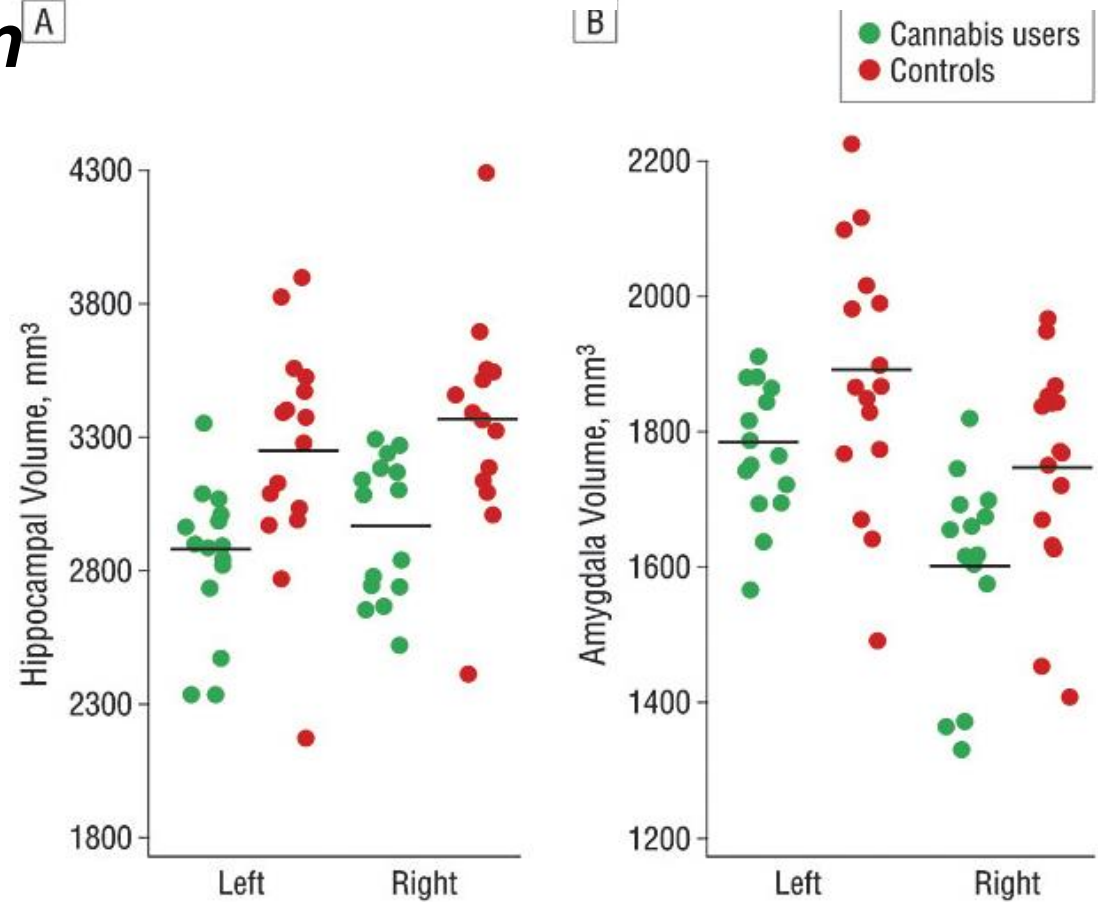


L (yellow) and R (blue) amygdala  
L (red) and R (green) hippocampus

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

*Hippocampus*

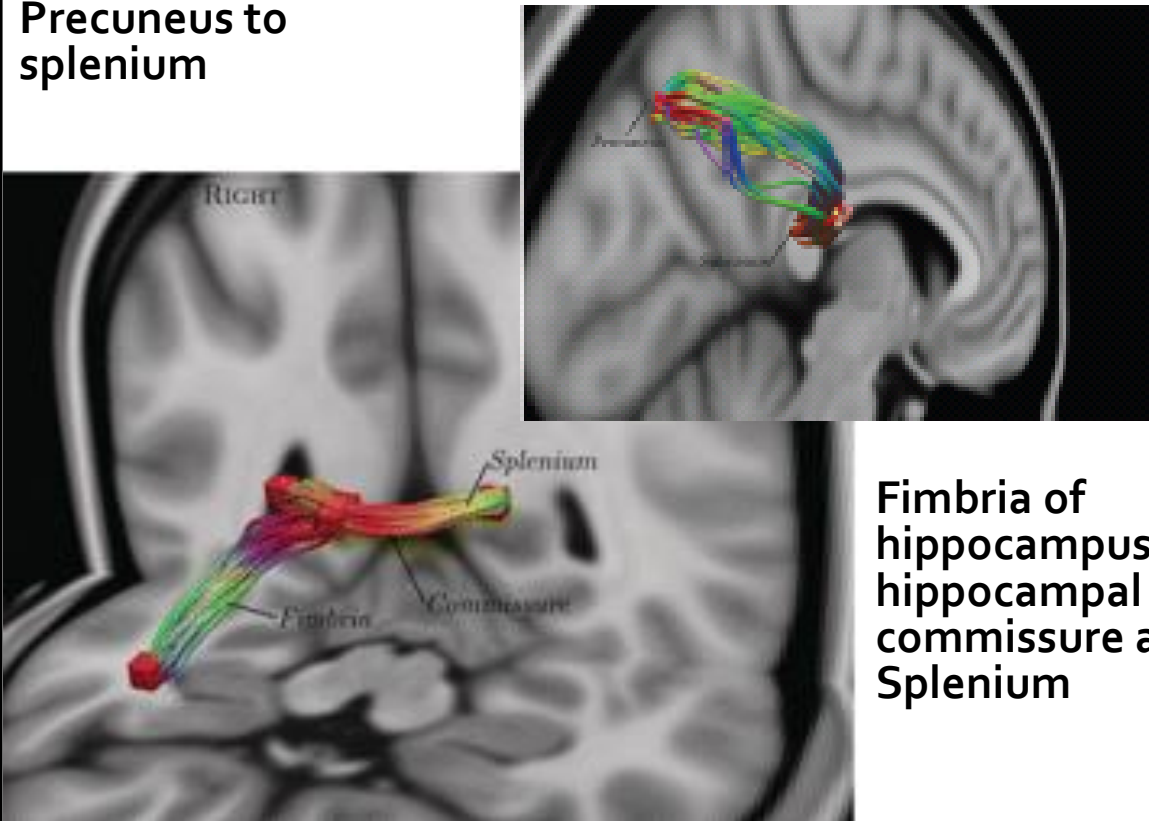
*Amygdala*



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

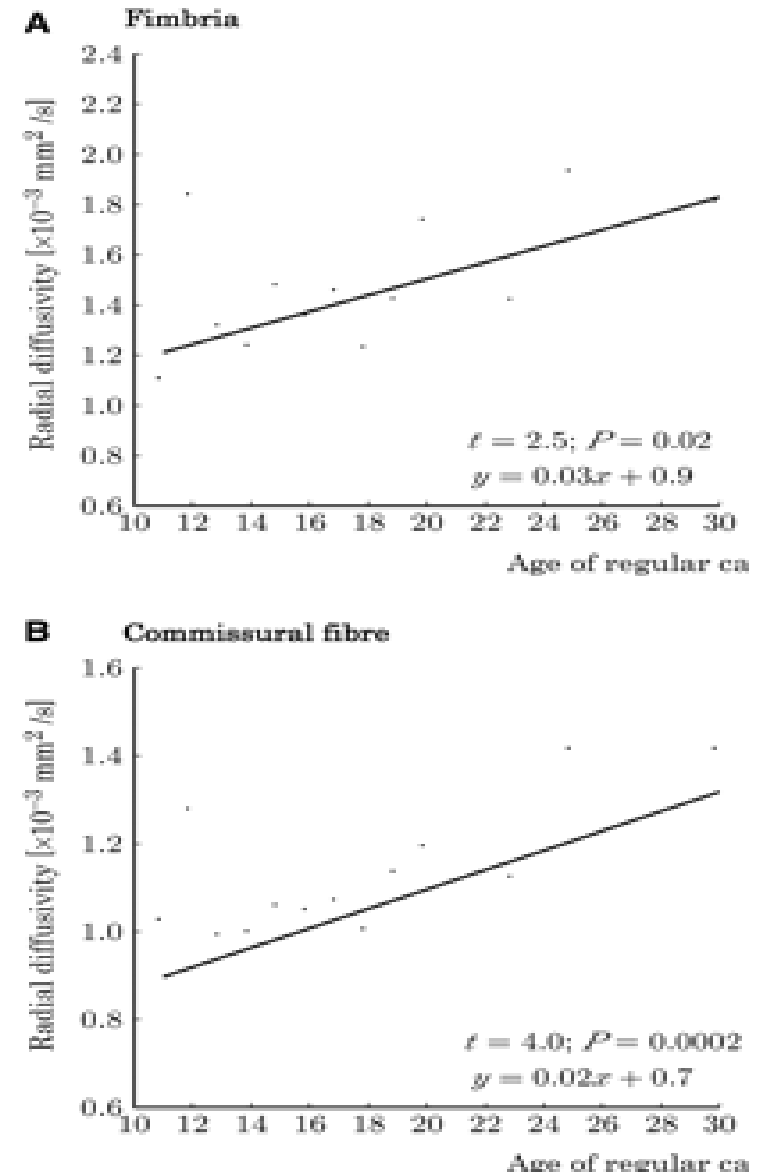
# Early (<18y) Long-Term Marijuana Use Decreases Axonal Fiber Connectivity

Precuneus to splenium



Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33).

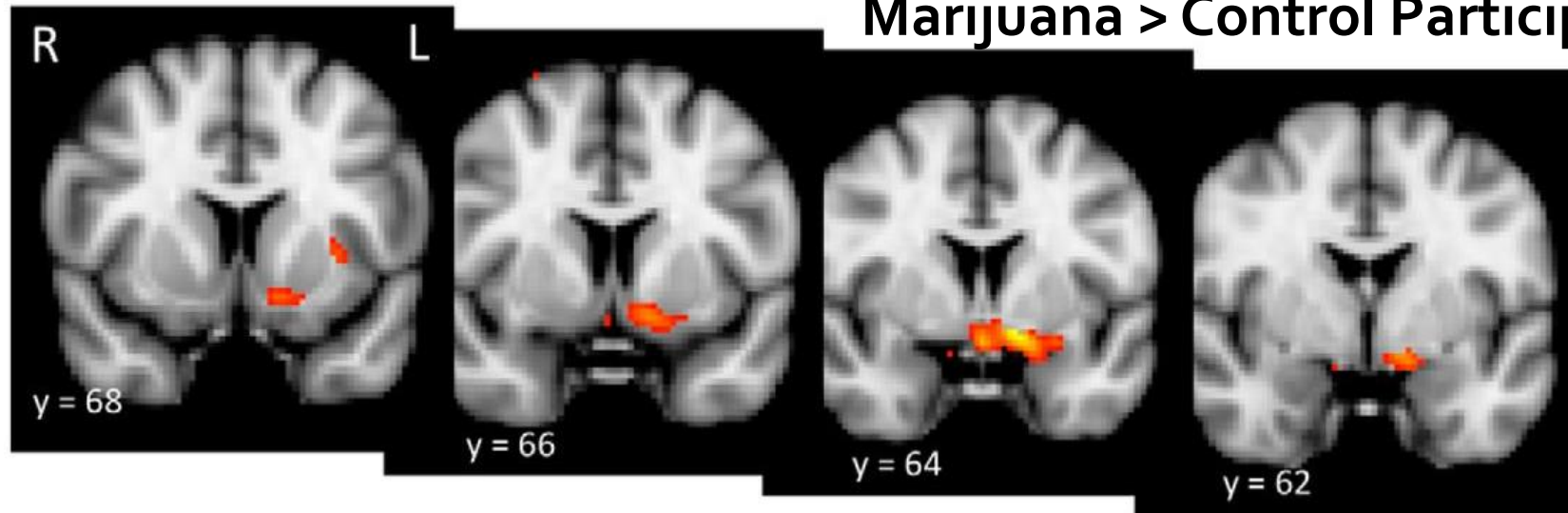
*Zalesky et al Brain 2012.*



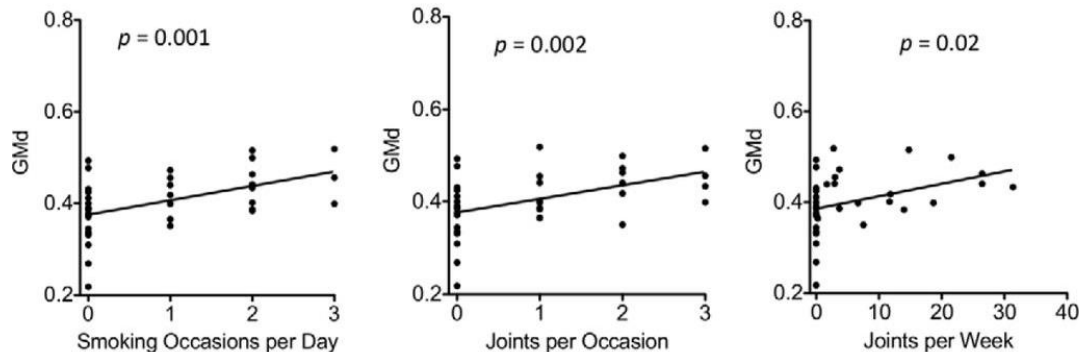


# Marijuana Use may be Associated with Brain Abnormalities in Young Adult Recreational Users

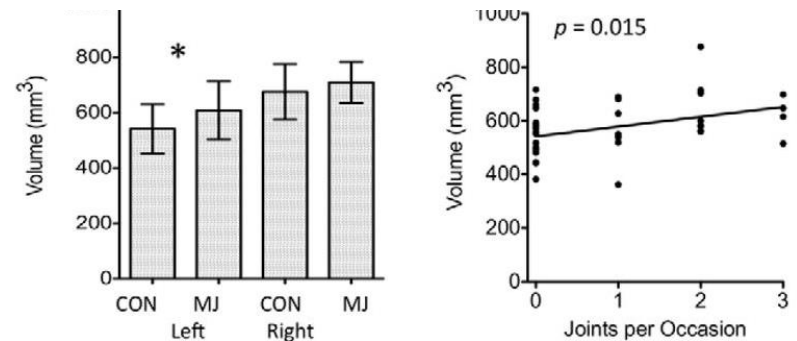
Gray Matter Density:  
Marijuana > Control Participants



Associations Drug Use Behavior & Gray Matter Density in Left Nucleus Accumbens

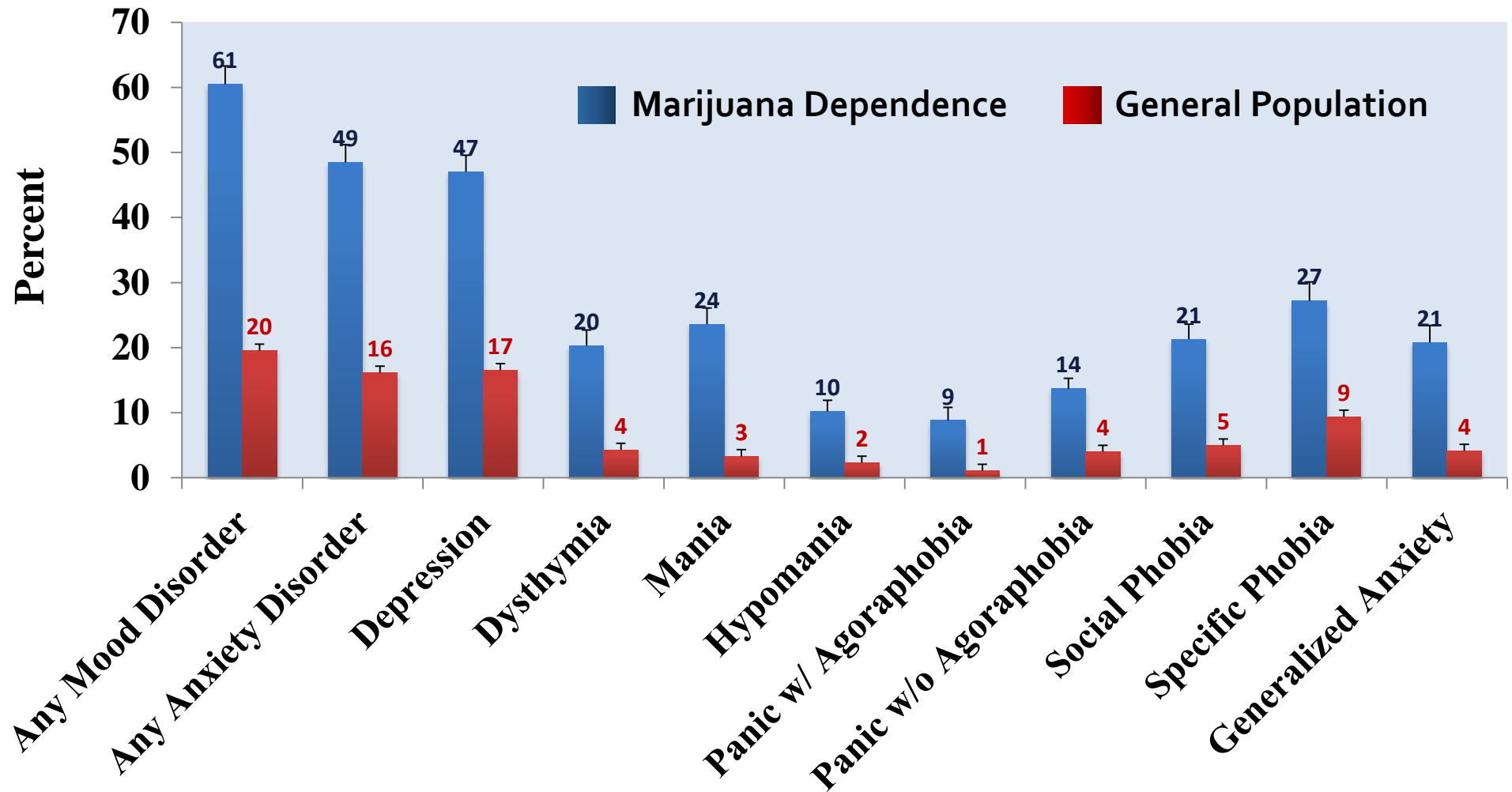


Volume & Associations with Drug Use in Left Nucleus Accumbens



*Gilman J M et al. J. Neurosci. 2014;34:5529-5538.*

# High Rates of Comorbid Mood & Anxiety Disorders Among Respondents with Marijuana Dependence (NESARC)



Conway KP et al., *J Clin Psychiatry* 2006; 67(2): 247-257.



***What harms does  
marijuana cause?***

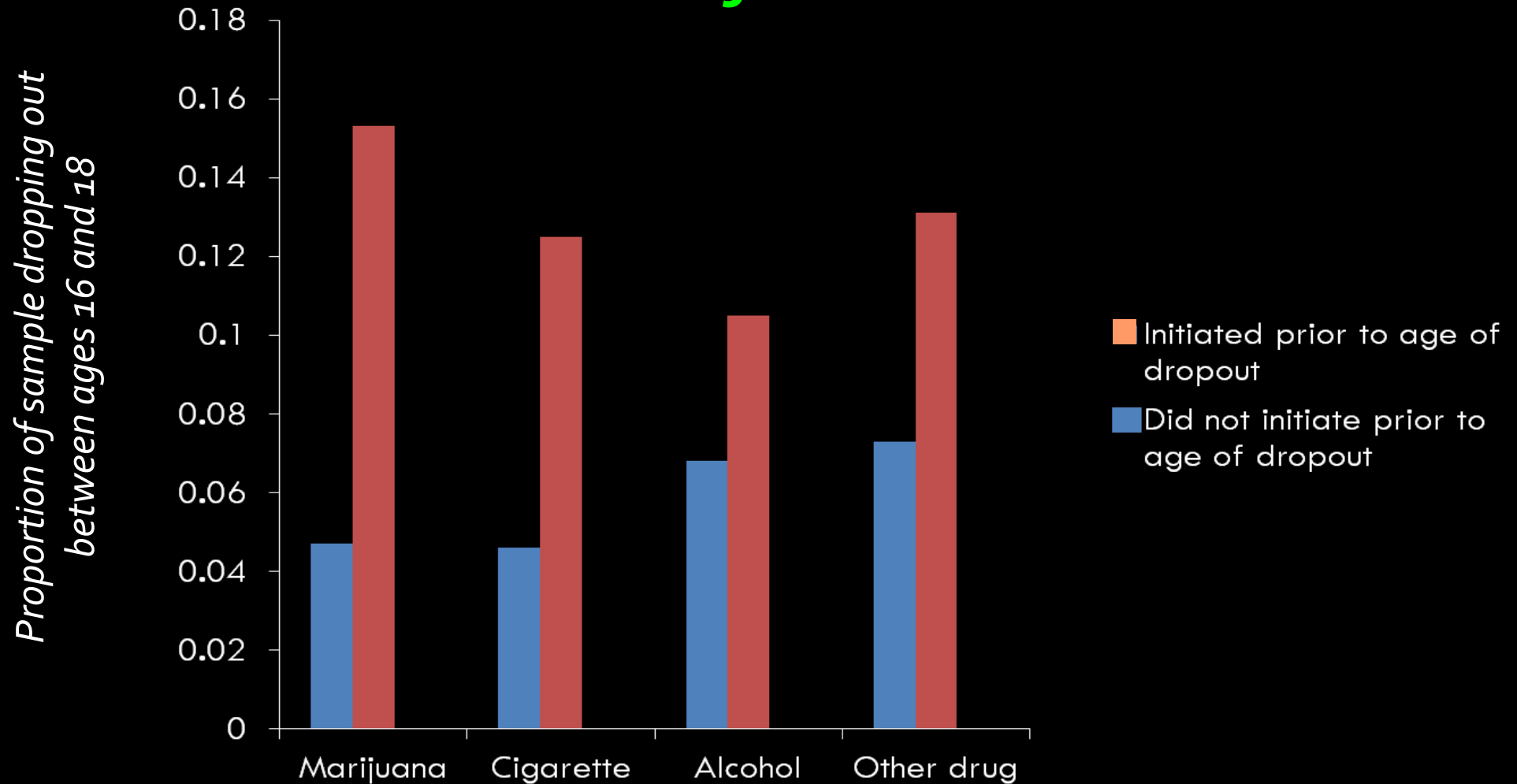




*Especially with  
Heavy/Chronic Use*

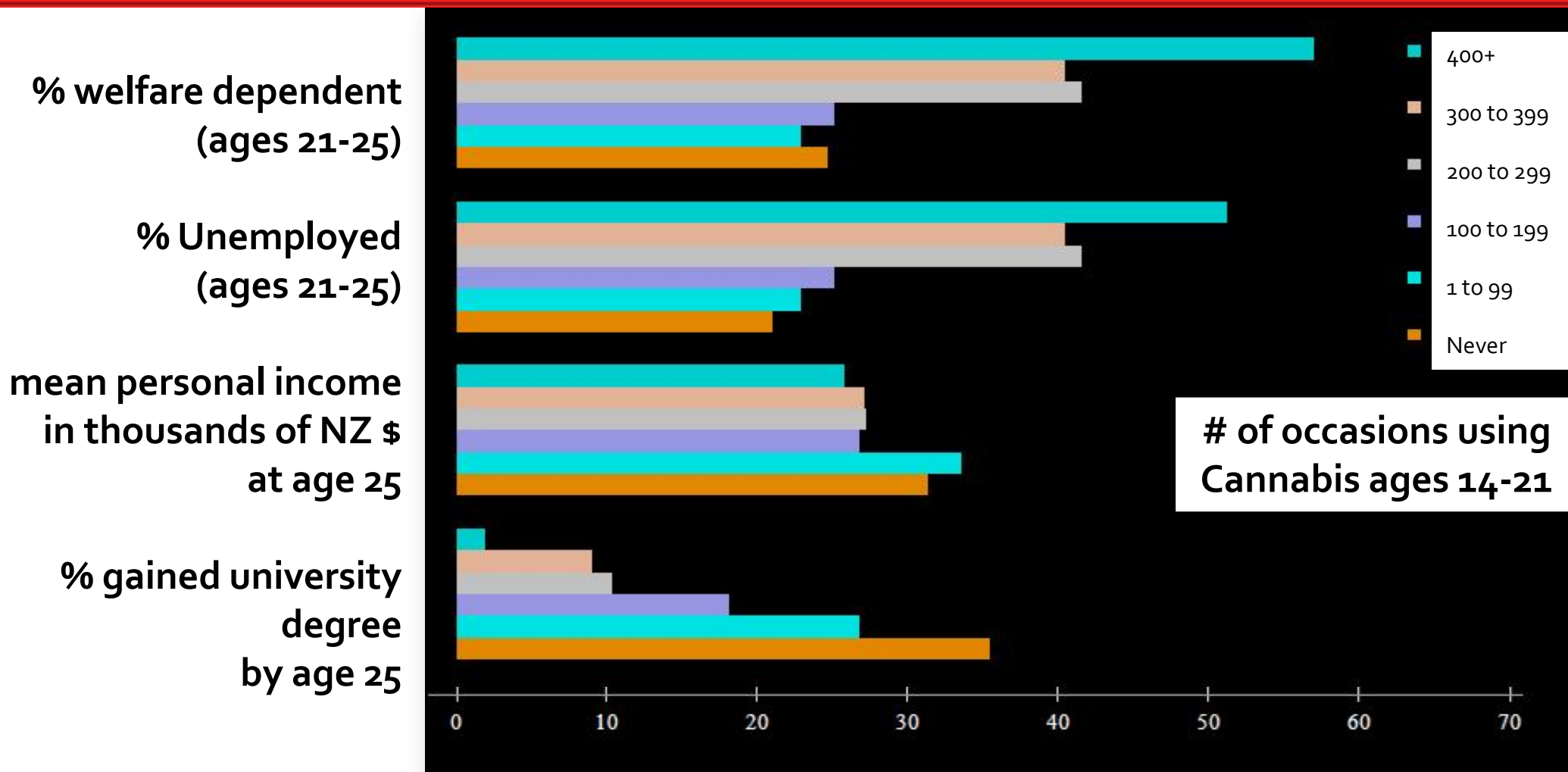
- Social problems: *School dropout*
- Accidents: *Double risk of motor vehicle accidents*
- Brain: *Impairs motivation and mood; causes addiction and paranoia; may cause schizophrenia and cognitive decline*
- Lung: *Cough and bronchitis*

# *Early Marijuana (and other drug) Use Linked to Dropping Out of School*



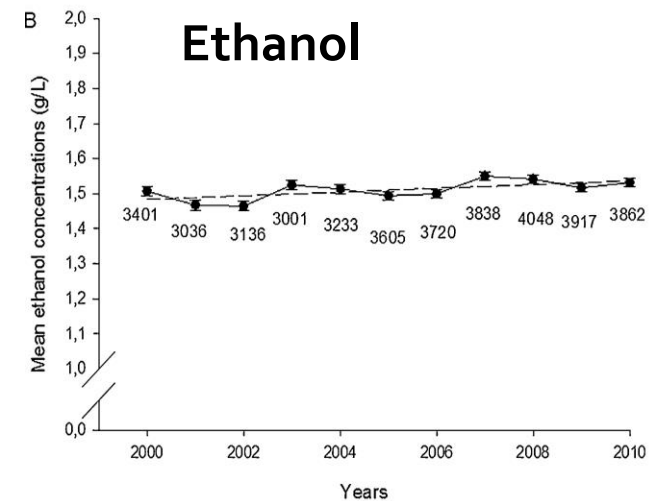
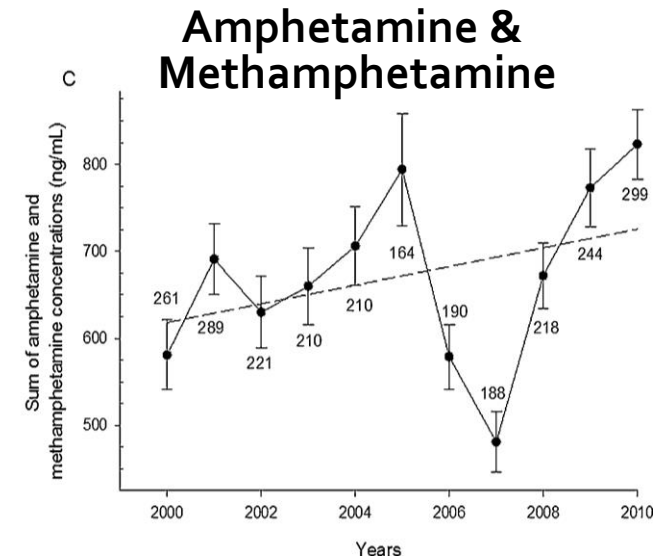
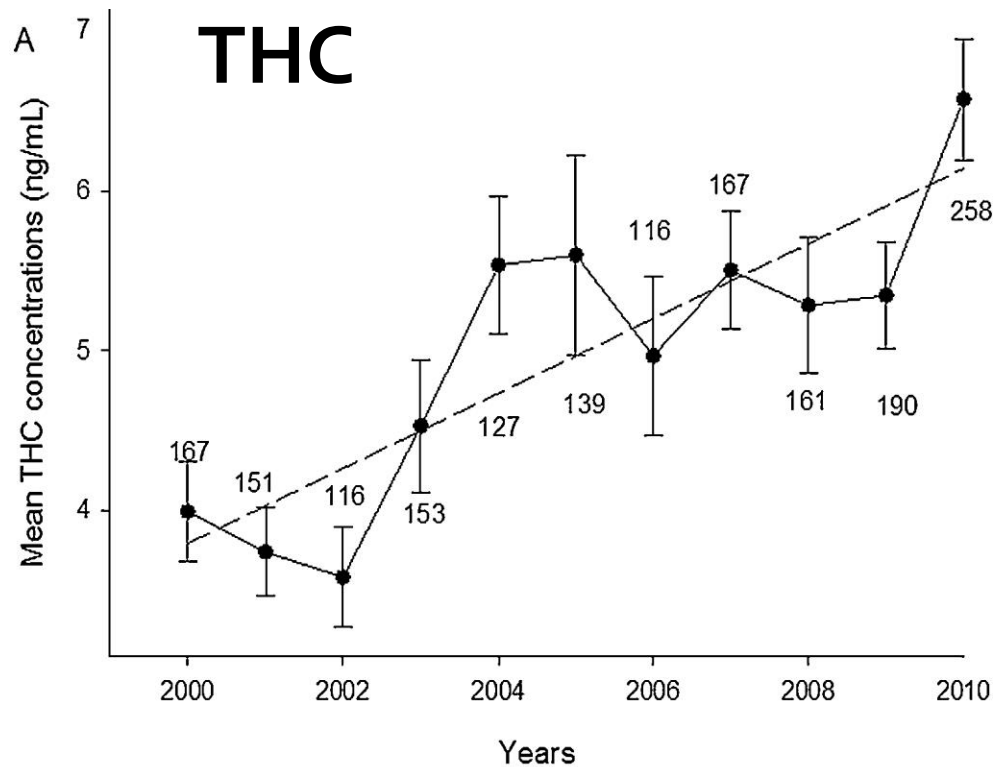
Source: Bray et al. *Health Economics*, 9(1), pp. 9-18, 2000.

# Marijuana Use and Later Life Outcomes Are Dose Dependent

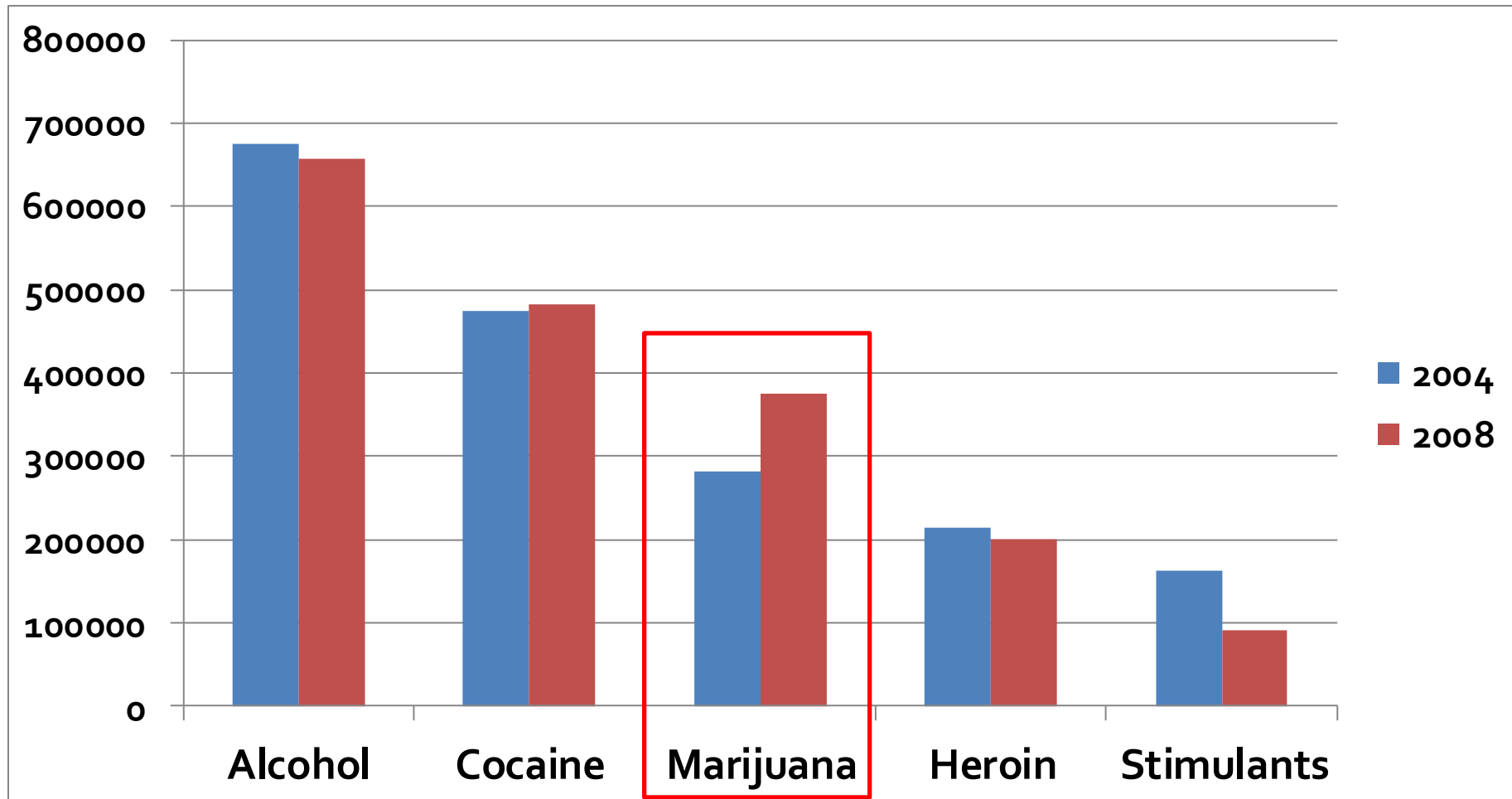


Source: Fergusson and Boden. *Addiction*, 103, pp. 969-976, 2008.

# Increasing Concentrations of THC In Whole Blood Samples From Drivers Apprehended By The Police Suspected Of Driving Under the Influence in Norway

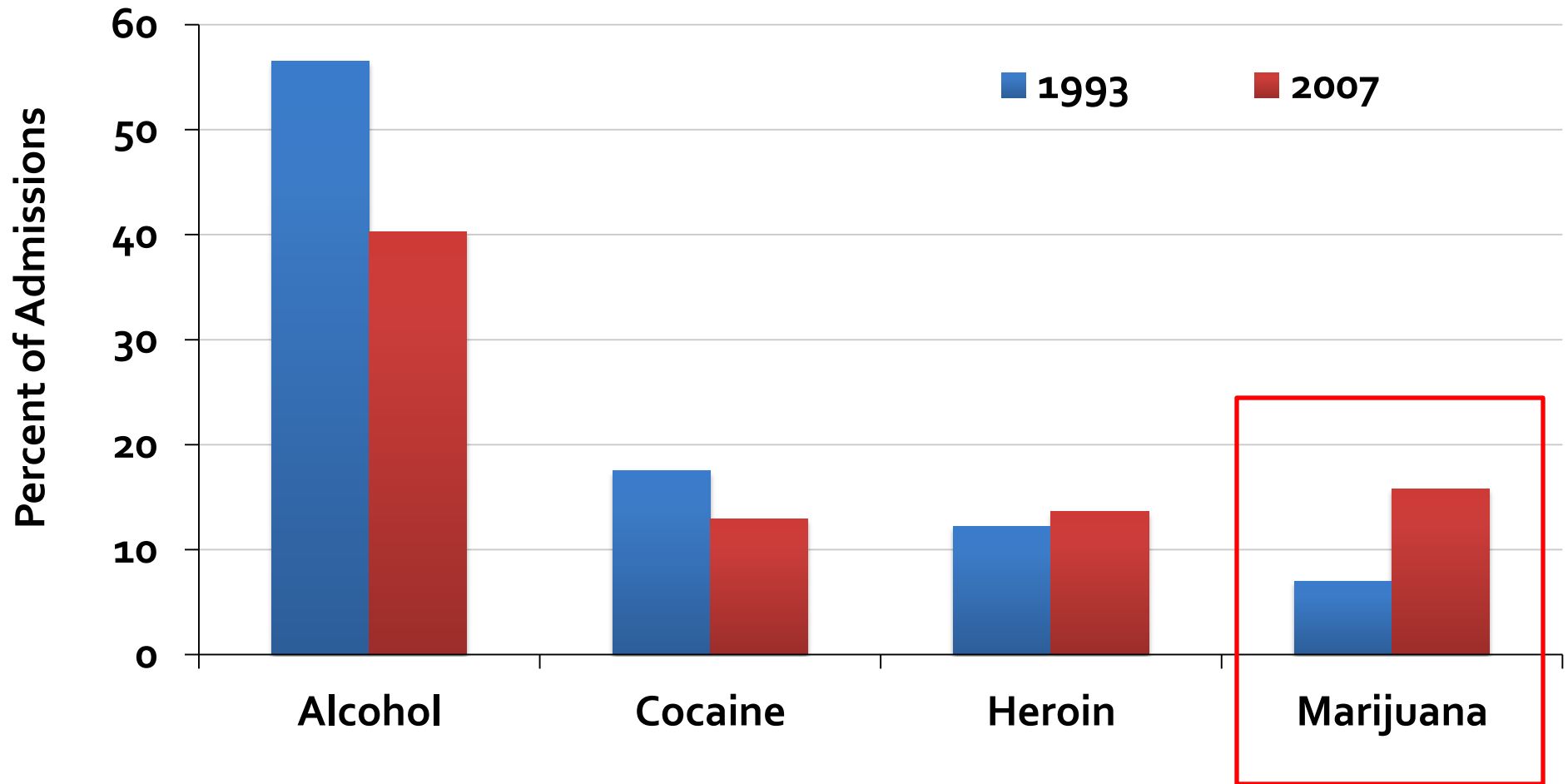


# Emergency Department Visits Involving Selected Drugs: 2008



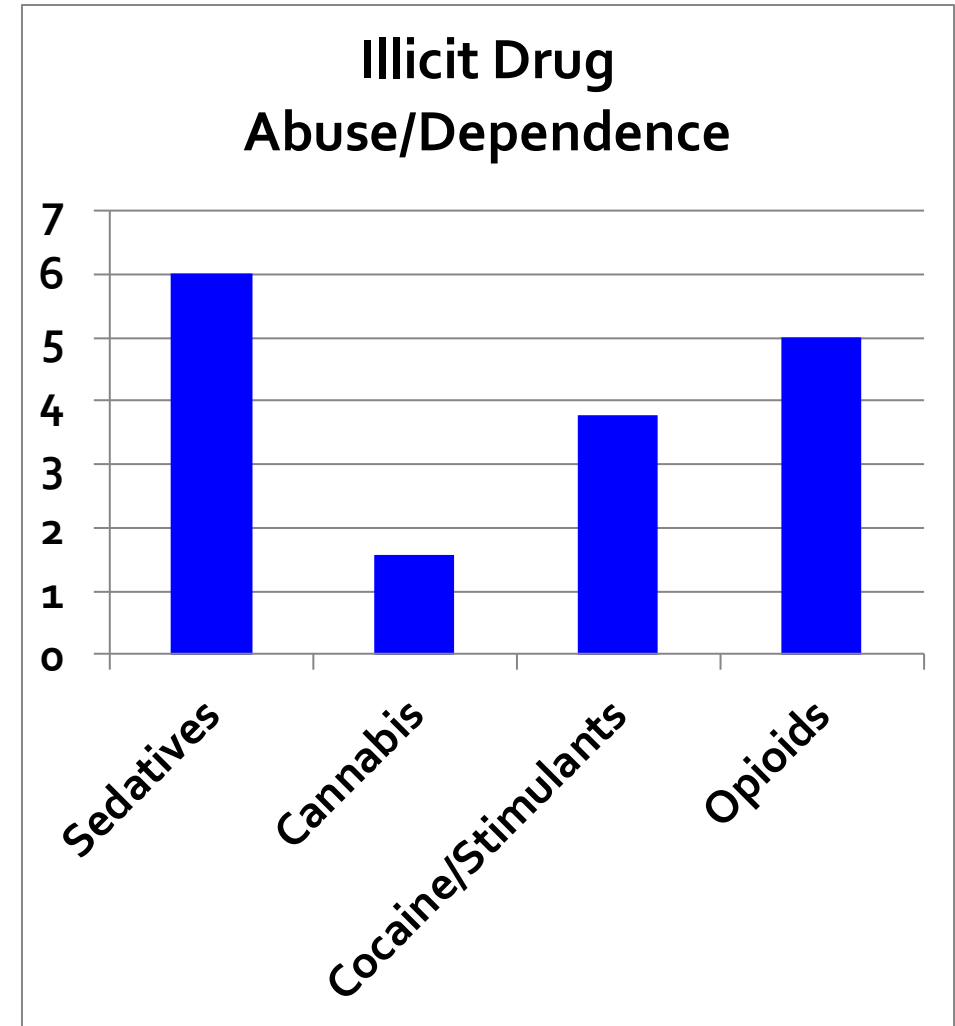
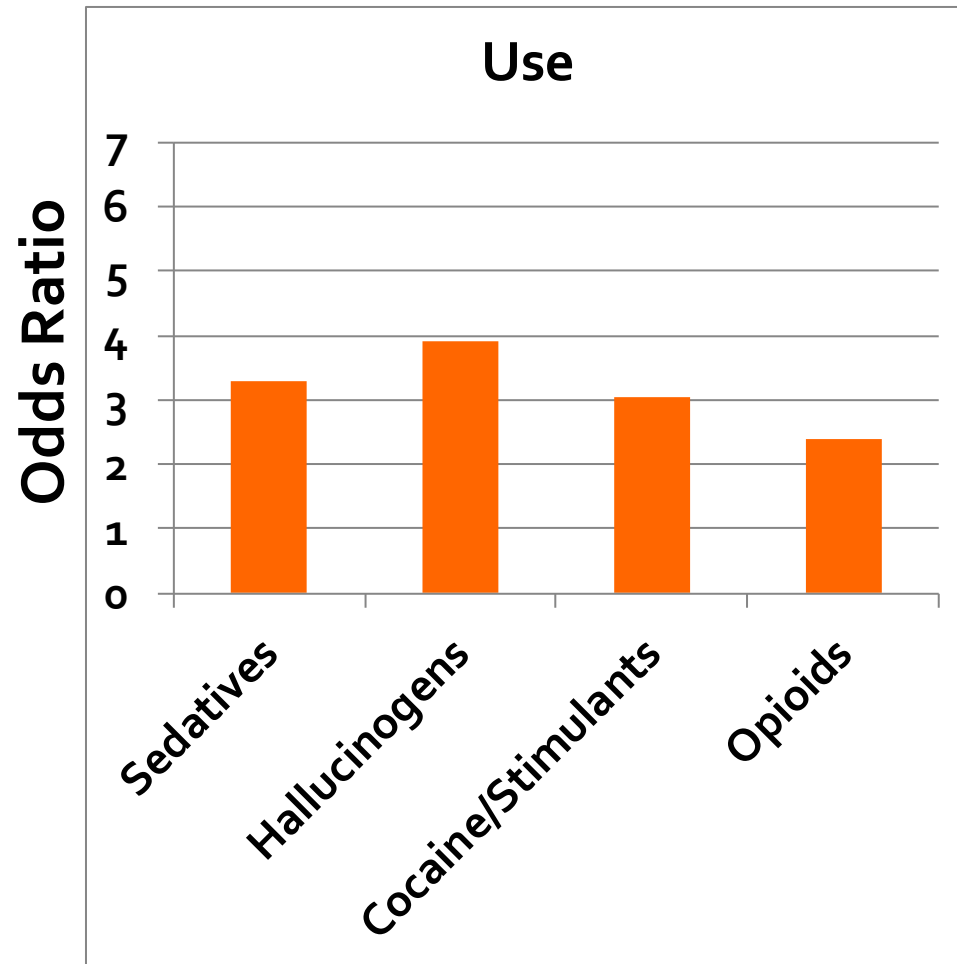
Source: SAMHSA, 2008 DAWN.

# Increased Marijuana Treatment Admissions 1993 and 2007



Source: SAMHSA, TEDS 1993 & 2007

# Marijuana Users More Likely to Have Other Drug Disorders: *Drug Use Outcomes in Twin Pairs (n =234) Discordant for Cannabis Use Before Age 17*

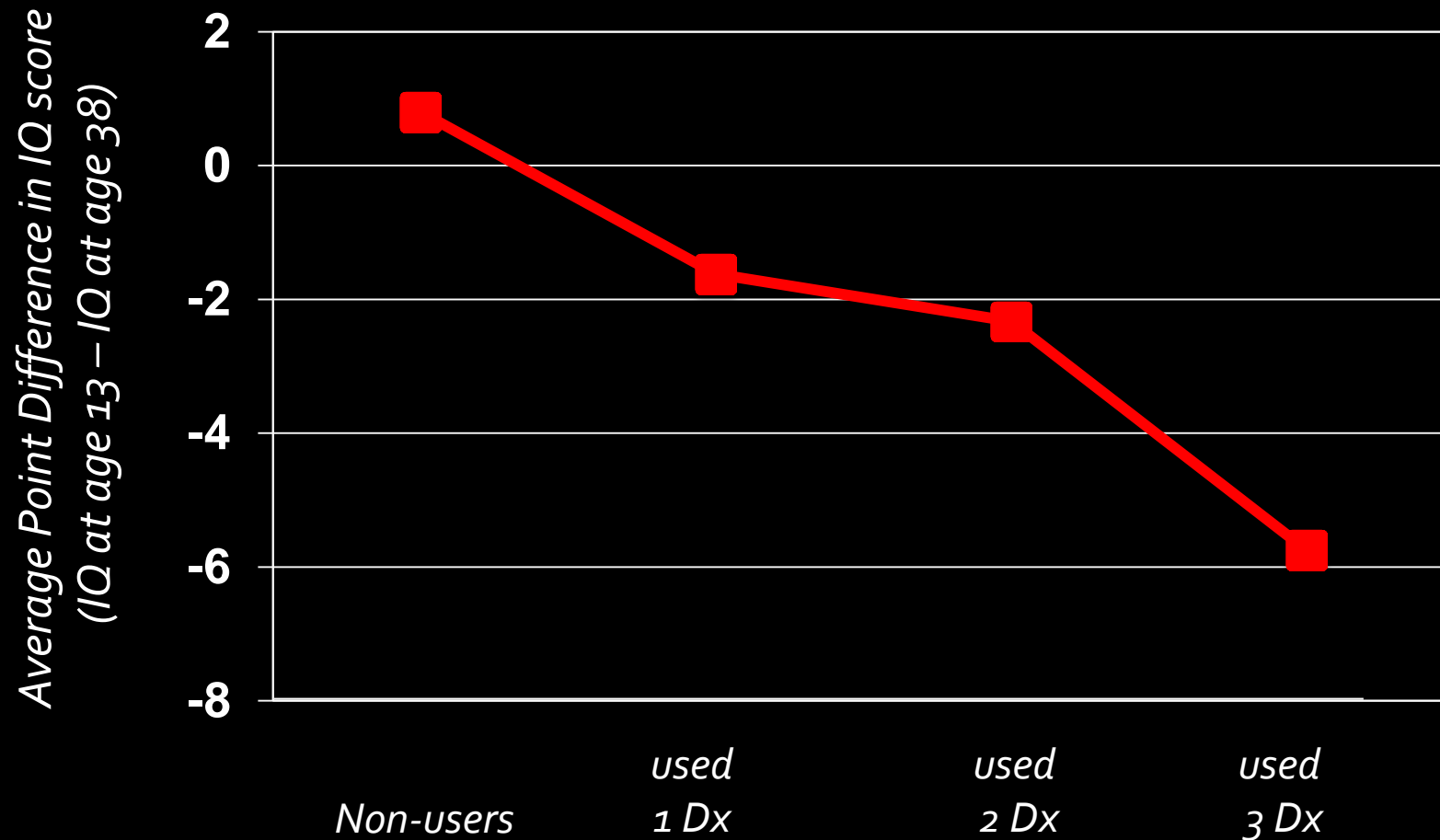


Source: Lynskey, MT et al., JAMA, 289, pp. 427-433, 2003.



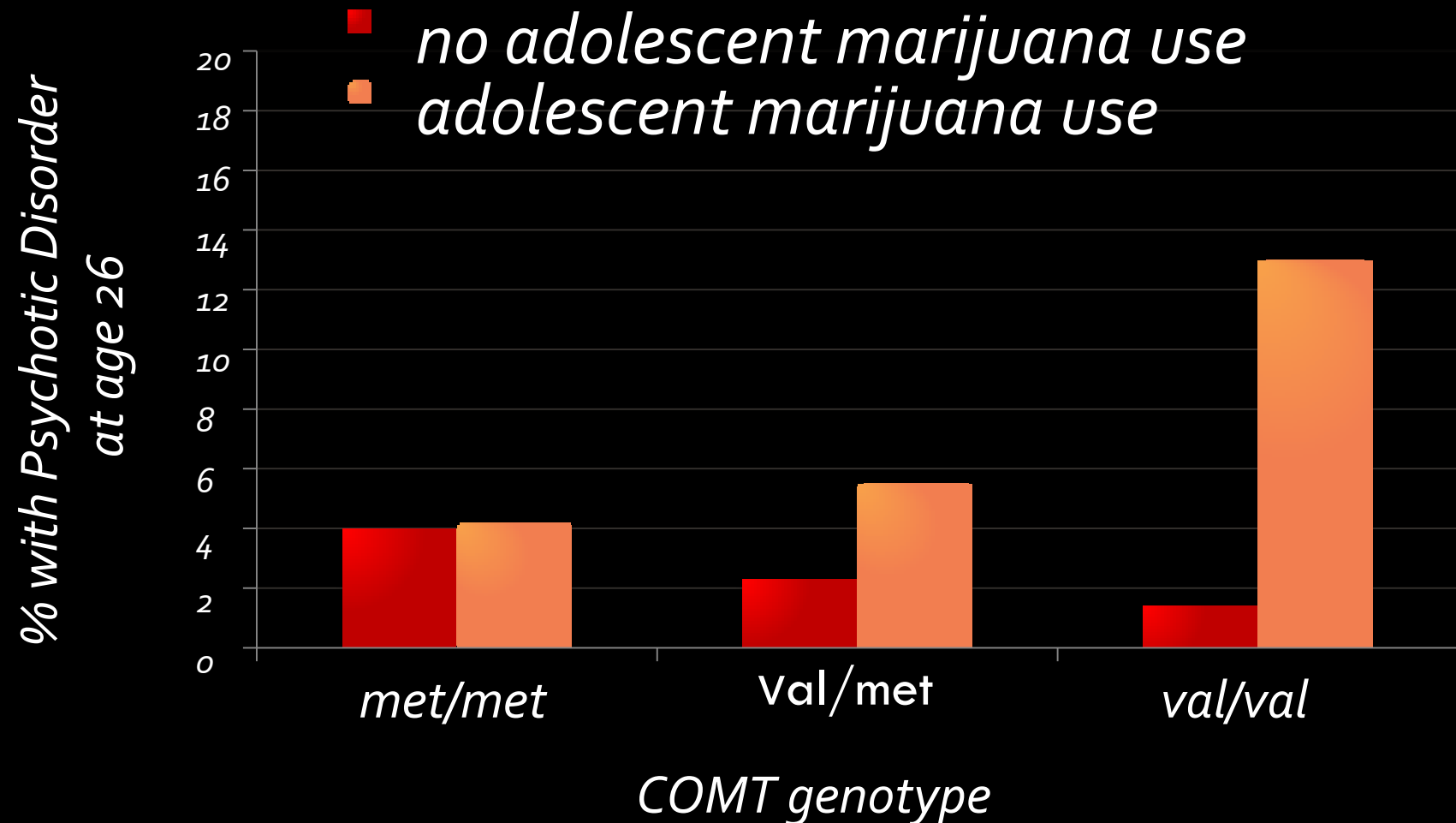
# ***Persistent Marijuana Users Show A Significant IQ Drop between Childhood and Midlife***

***Followed 1,037 individuals from birth to age 38. Tested marijuana use at 18, 21, 26, 32 and 38. Tested for IQ at ages 13 and 38***



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

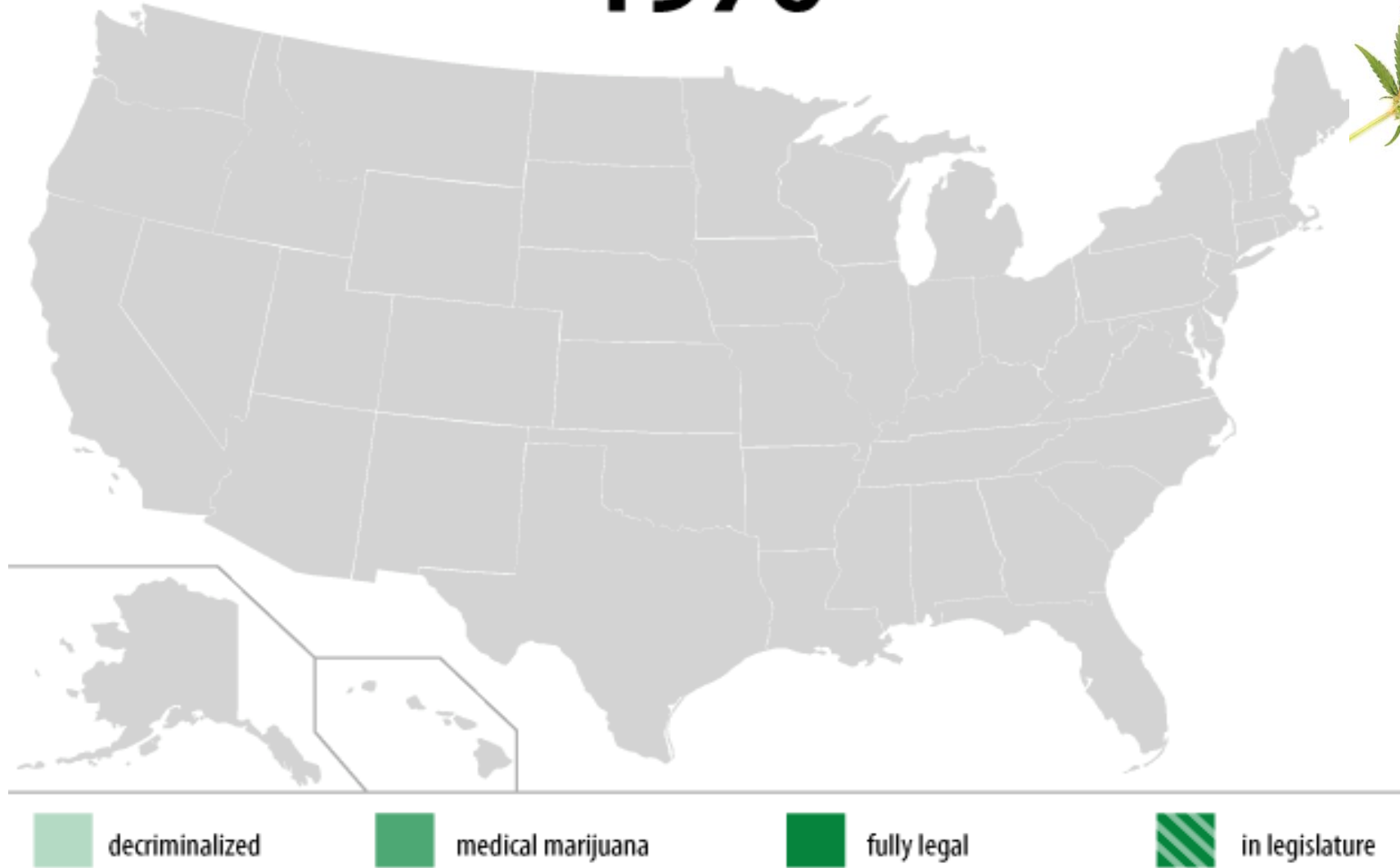
# *Adolescent Marijuana Use Increases the Risk for Adult Psychosis in Genetically Vulnerable Individuals*



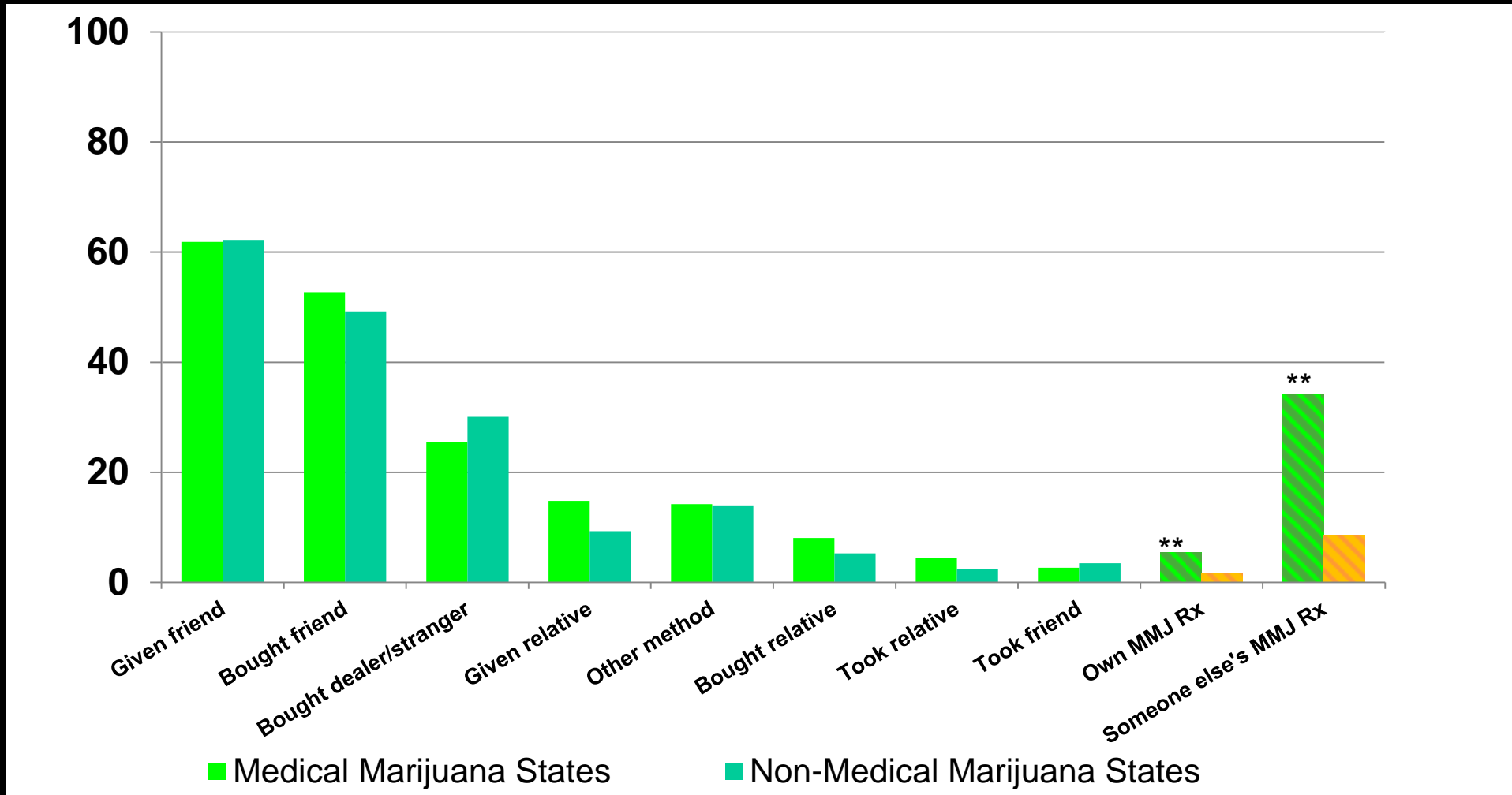
Source: Caspi, A. et al., *Biol. Psychiatry*, 57: 1117-1127; 2005.

# Changes in Marijuana Policy in the USA

## 1970



# Source of Marijuana\* among 12<sup>th</sup> Graders in 2012 and 2013, by State Policy



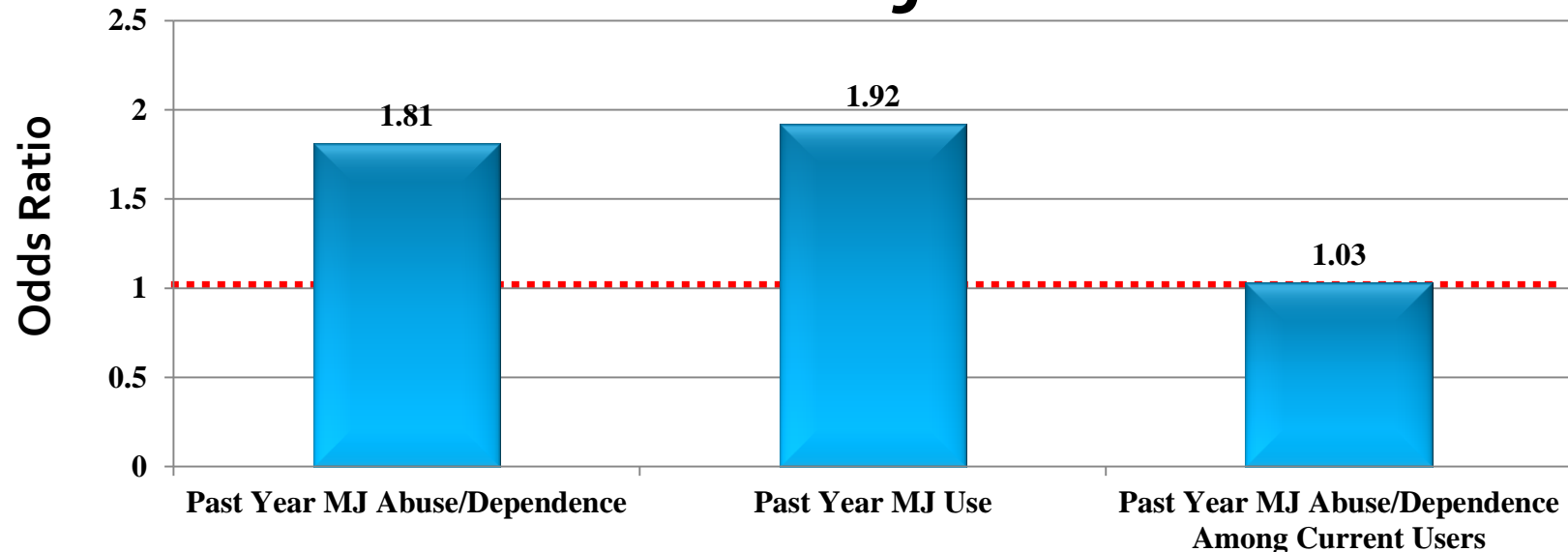
\*Categories not mutually exclusive  
\*\* Statistically significant difference

SOURCE: University of Michigan, 2013 Monitoring the Future Study

# Map Of States That Legalized Marijuana By 2004



## *Outcomes of Interest*



NESARC: National Epidemiologic Survey on Alcohol and Related Conditions

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

# Marijuana as Medicine?

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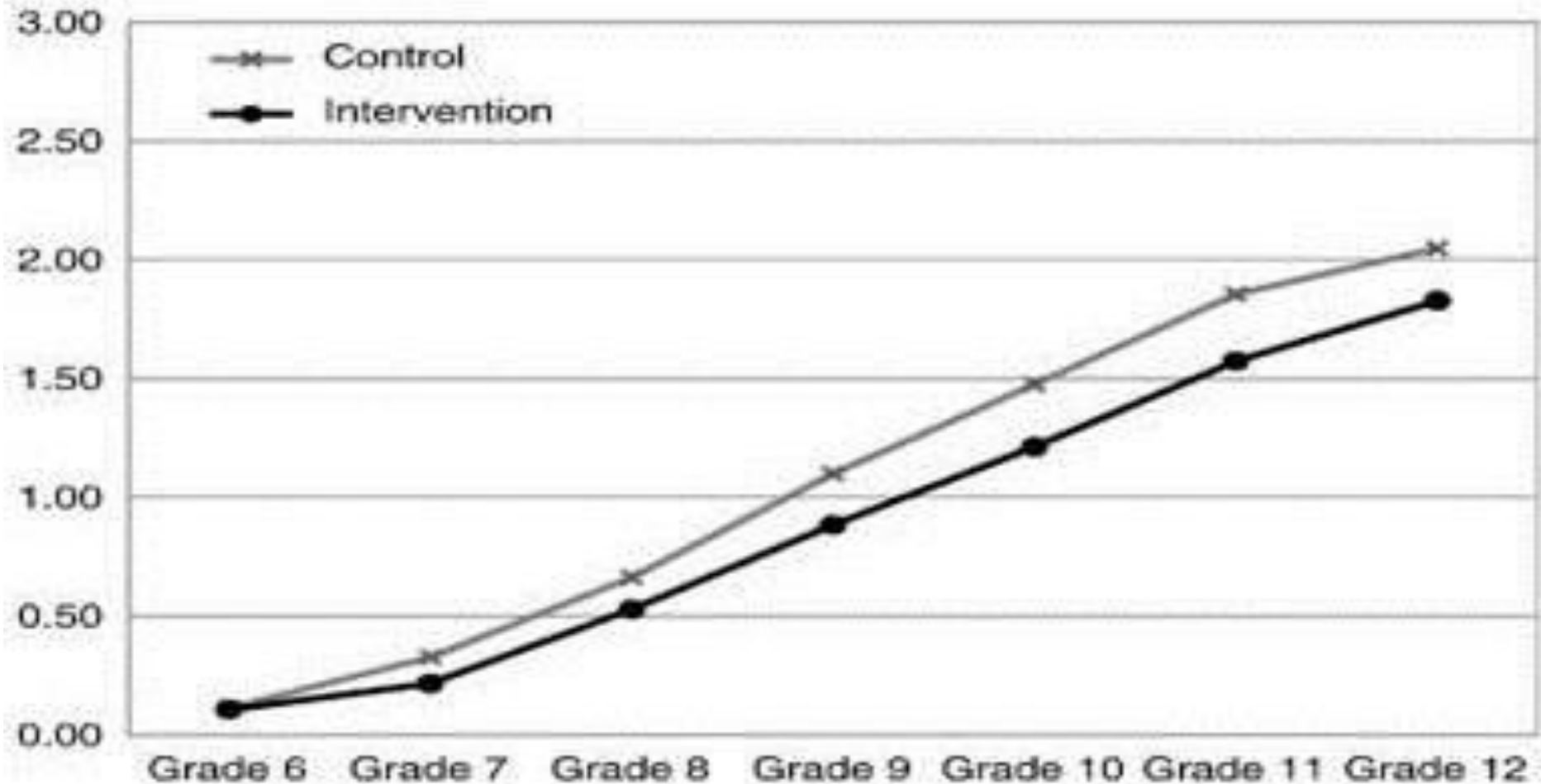
- Promise lies in purified ingredients or synthetic compounds with more selectivity, less adverse effects
- Applications: pain, nausea, wasting, obesity, muscle spasticity, addiction, inflammatory conditions, HIV

**NIDA research focuses on THC, CBD, and compounds that alter the function of the endocannabinoid system**

***What can be done?***



# *Universal Prevention:* Reduced Onset of Marijuana Use in PROSPER over 6.5 Years



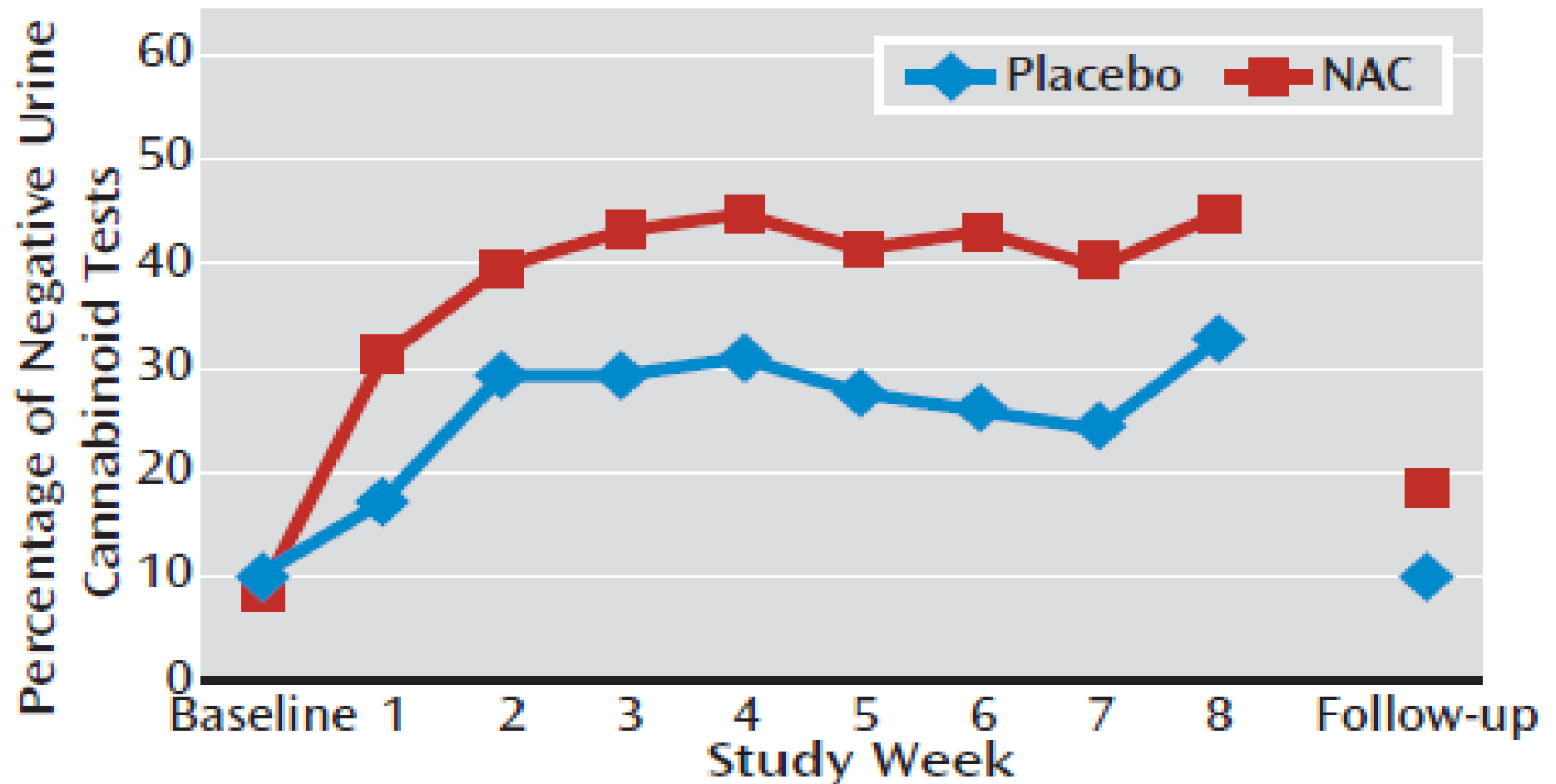
Frequency of marijuana use through 6.5 years past baseline. Frequency of marijuana use was scored on a 7-point scale, ranging from 0 (never) to 7 (more than weekly).

*Spoth, et al. Preventive Medicine (2013) 56, 190-196.*



# ***A Double-Blind RCT of N-Acetylcysteine in Marijuana-Dependent Adolescents***

*Proportion of Negative Urine Cannabinoid Tests Over Time Among Cannabis-Dependent Adolescents*



- ***RFA-DA-11-008 Medical Marijuana Policy Research: Exploring Trends And Impacts (R01)***
  - *Awarded 3 grants to inform social, behavioral, and public health impacts of medical marijuana use and policies ; 6 grants awarded outside RFA on this topic*
- ***PA-13-138 Research on Marijuana Legalization in the US (Admin Supp)***
- ***PAS-14-020 Public Health Impact of the Changing Policy/Legal Environment for Marijuana (R01)***

# Summary

- Marijuana is the *most commonly used* illicit drug in the U.S.
- Marijuana use generally *begins in adolescence*
- Use of marijuana can have a *wide range of effects on an individual's brain, body and behavior* including short and long term effects on such functions as:
  - ✓ *Brain development*
  - ✓ *Memory and cognition*
  - ✓ *Motivational systems and reward*
  - ✓ *Addiction*
  - ✓ *Lung health*
- In recent years there has been an *increase in both treatment admissions* for marijuana abuse and in *Emergency Department visits* involving marijuana



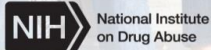
# New Online Resources

*For teens and those that care about them*

## Treatment Publication Principles of Adolescent Substance Use Disorder Treatment: A Research Based Guide

*Outlines thirteen principles and evidence-based approaches for treating adolescent substance use disorders (SUD).*

**Principles of Adolescent  
Substance Use Disorder Treatment:  
A Research-Based Guide**

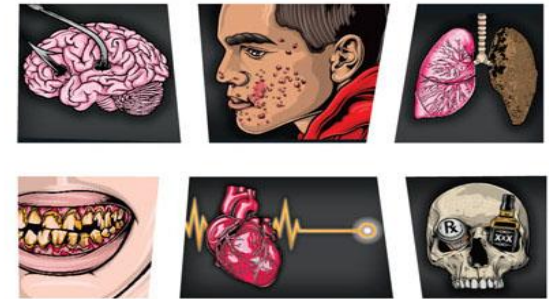


## Medical School Curriculum The Substance Use Disorder in Adolescents: Screening and Engagement in Primary Care Settings

*Provides a series of videos demonstrating effective screening techniques.*

## **DRUGS + YOUR BODY:** **It Isn't Pretty**

- **Web Interactive**
- **[scholastic.com/drugsandyourbody\\_web](http://scholastic.com/drugsandyourbody_web)**



## **Web interactive Drugs + Your Body: It Isn't Pretty**

*Includes graphics, videos, quizzes and much more on harmful effects of drugs on the brain and body.*