The Science of Drug Addiction: Implications for Clinical Practice

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NIH National Institute on Drug Abuse
The Science of Drug Abuse & Addiction

The Many Faces of Addiction

NIH National Institute on Drug Abuse

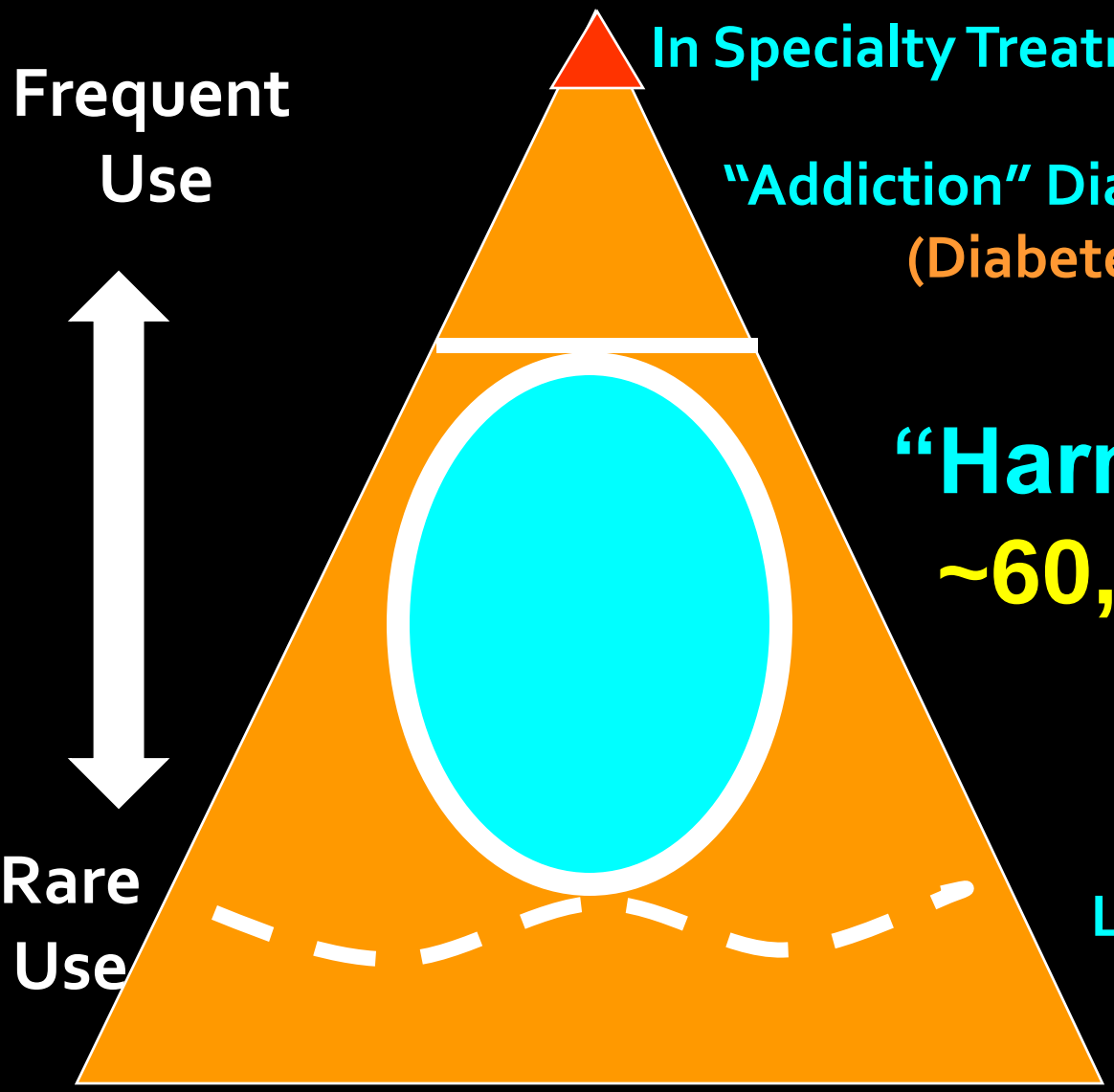
The Science of Drug Abuse & Addiction

Today's Topics

- Trends in Substance Use
- Understanding Addiction
- NIDA Priority Areas
  - Prevention
  - Treatment
  - Health Consequences
- Resources

Trends in Substance Use

Scope of Substance Use in the U.S.



Source: A. T. McLellan, 2011

Question:

What is the most widely used drug by teens?

Drugs Frequently Abused by U.S. Teens

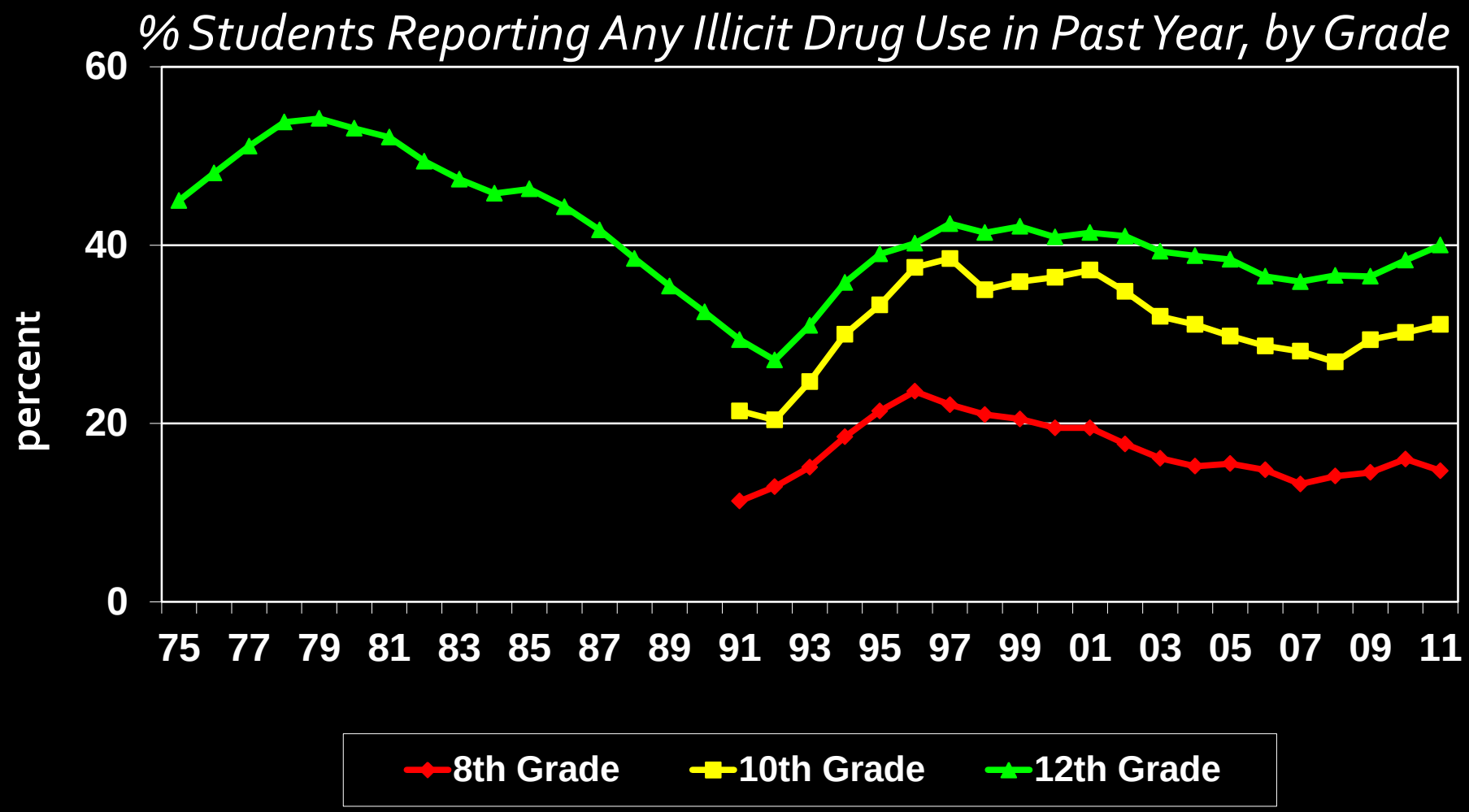
Alcohol	63.5%	Tranquilizers	5.3%
Marijuana/Hashish	36.4%	Cough Medicine	5.6%
Small Cigars	19.9%	Hallucinogens	4.8%
Hookah	18.3%	Sedatives*	4.5%
Synthetic Marijuana	11.3%	Salvia	4.4%
Snus (tobacco)	7.9%	MDMA (Ecstasy)	3.8%
Prescription Opioids	7.9%	Inhalants	2.9%
Amphetamines*	7.9%	Cocaine (any form)	2.7%

Monitoring the Future study, 2011

Question:

What's Molly?

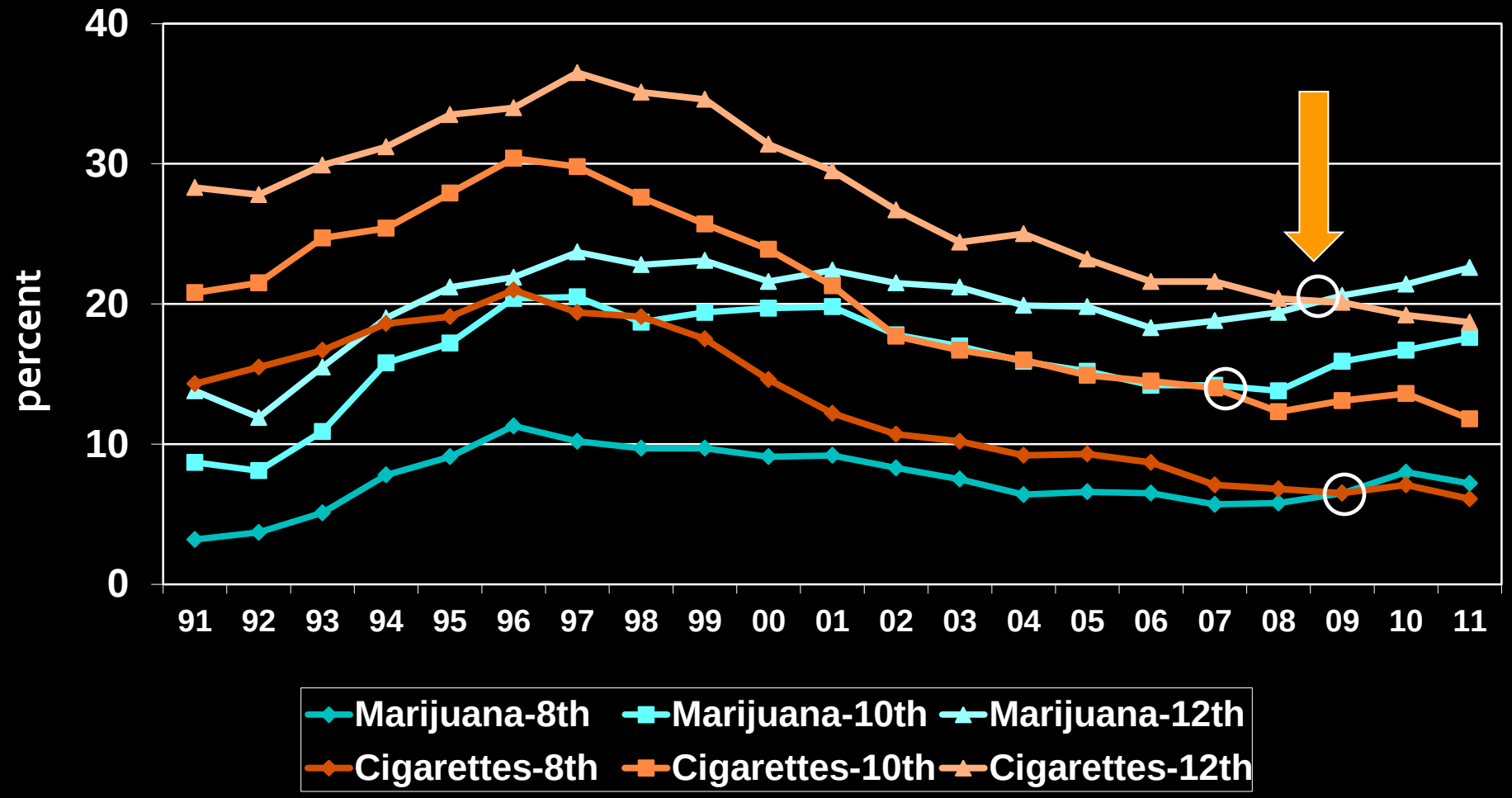
Shifting Landscape of Drug Abuse Over Time



SOURCE: University of Michigan, 2011 Monitoring the Future Study

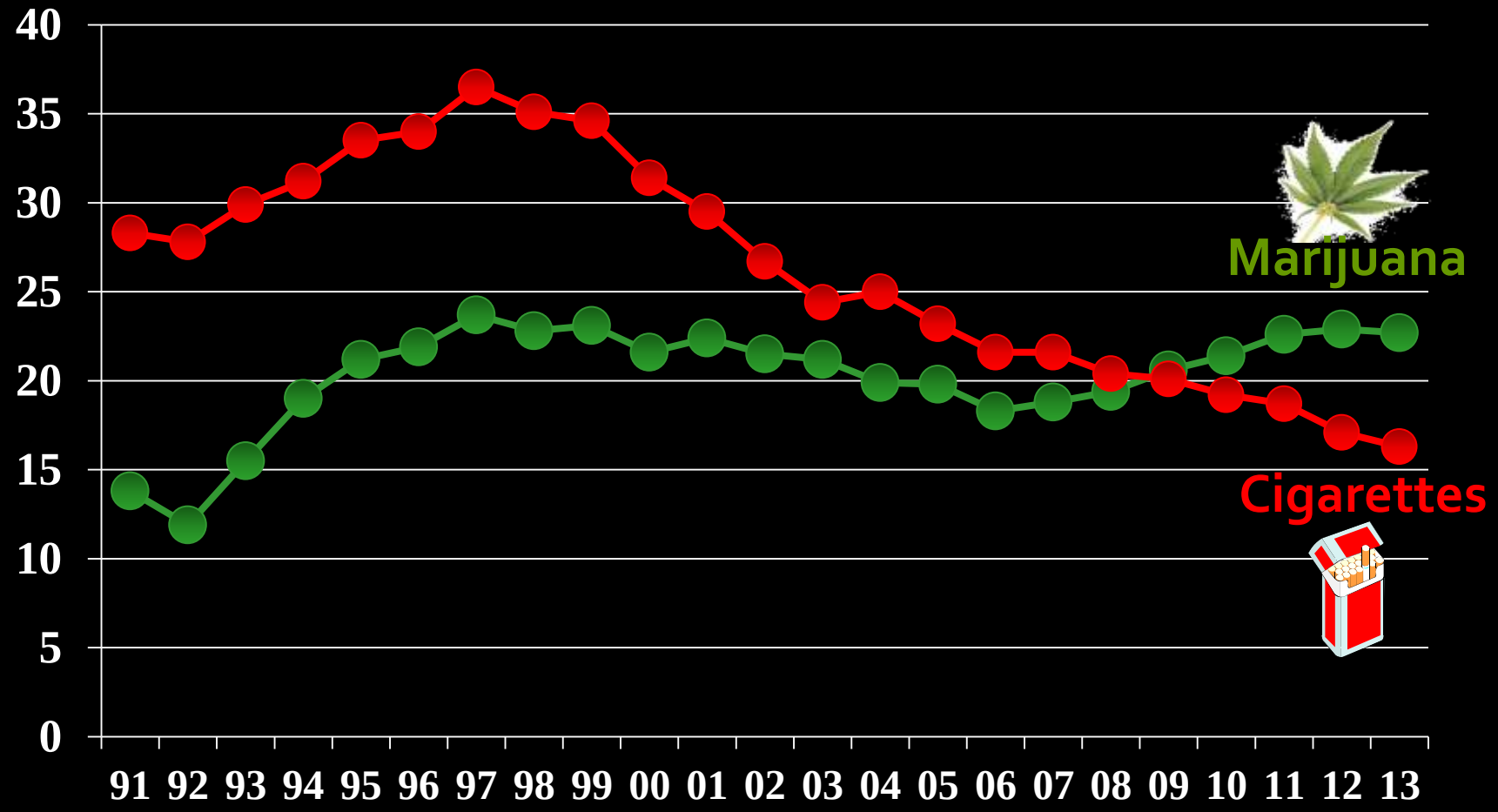
Relative Shifts in Prevalence

% Students Reporting Past Month Marijuana and Cigarettes (by Grade)



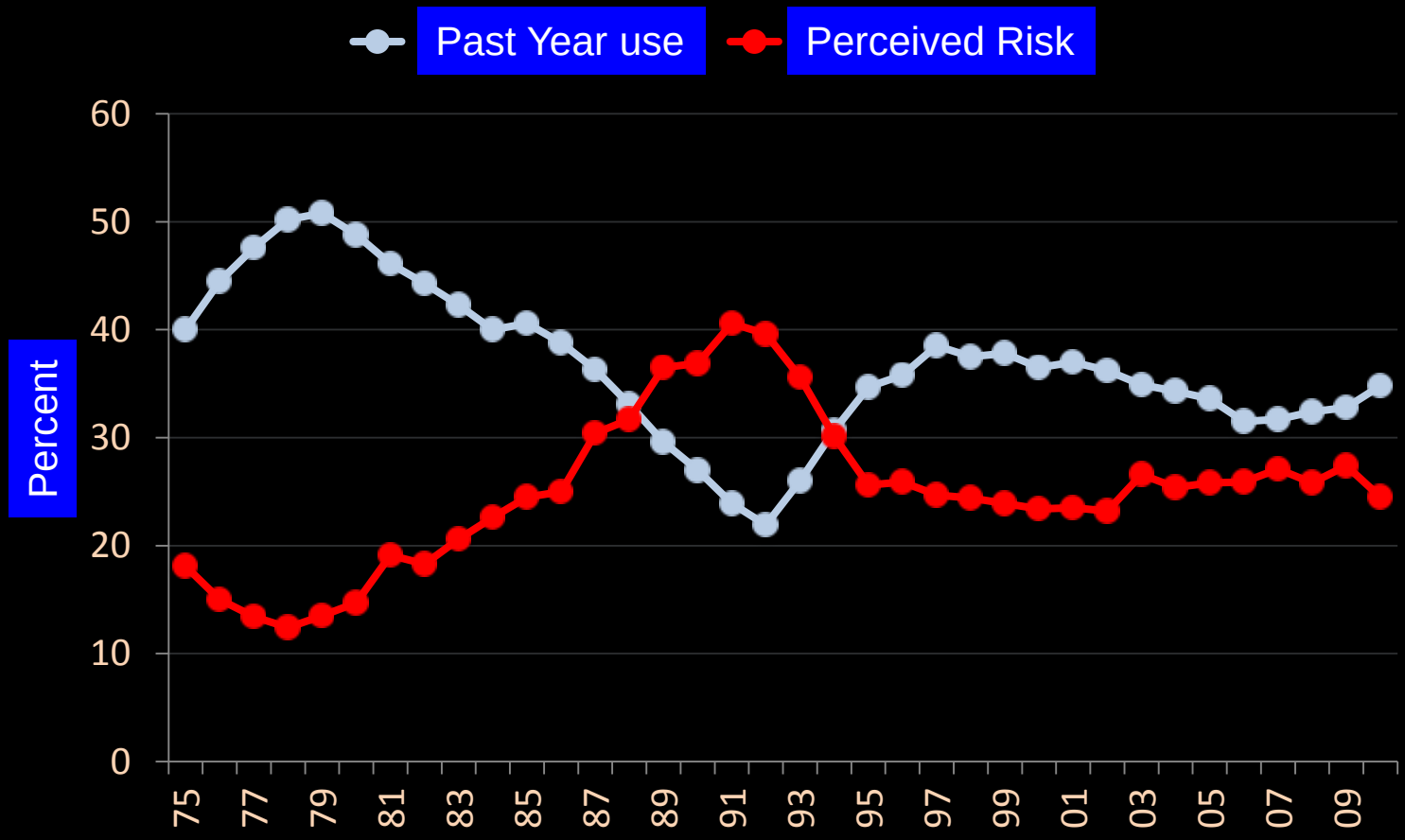
SOURCE: University of Michigan, 2011 Monitoring the Future Study

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



SOURCE:2013 Monitoring the Future Study

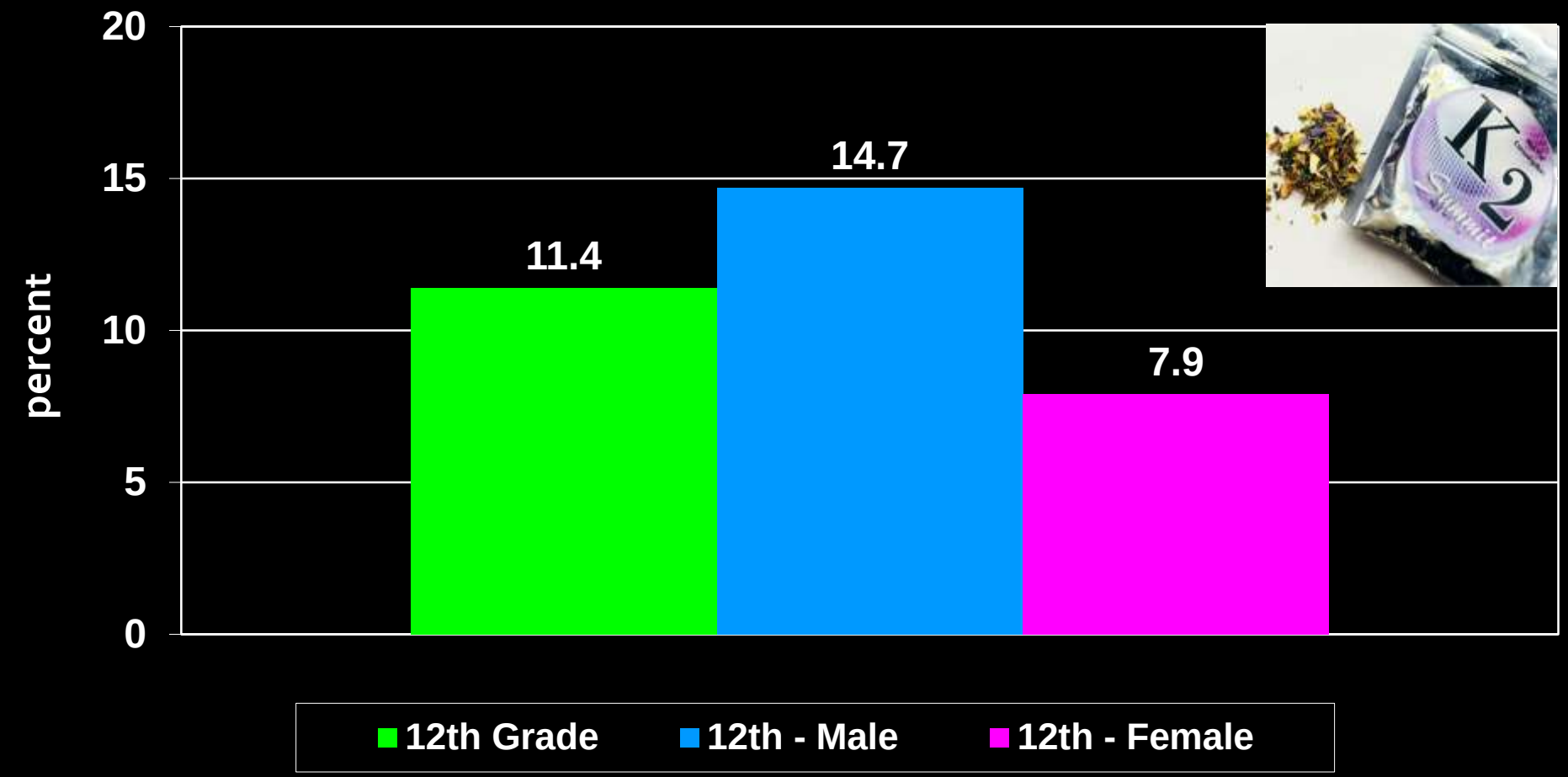
Changes in Attitude Lead to Changes in Use: Marijuana Use and Perceived Risk in 12th Graders



Source: Monitoring the Future, 2011

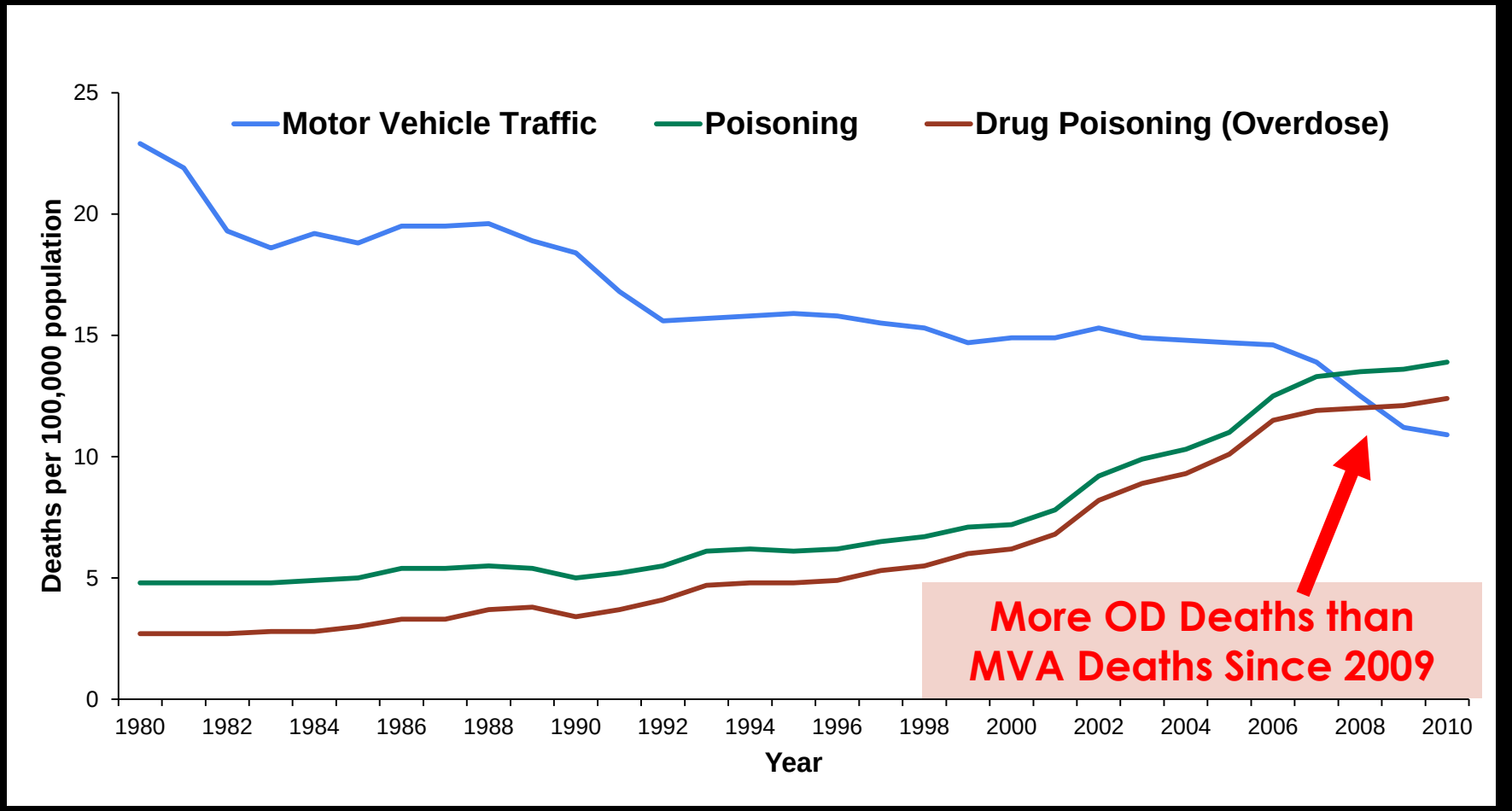
Synthetic Drugs

% of Students Reporting Synthetic Marijuana Use Annually (by Gender)



SOURCE: University of Michigan, 2011 Monitoring the Future Study

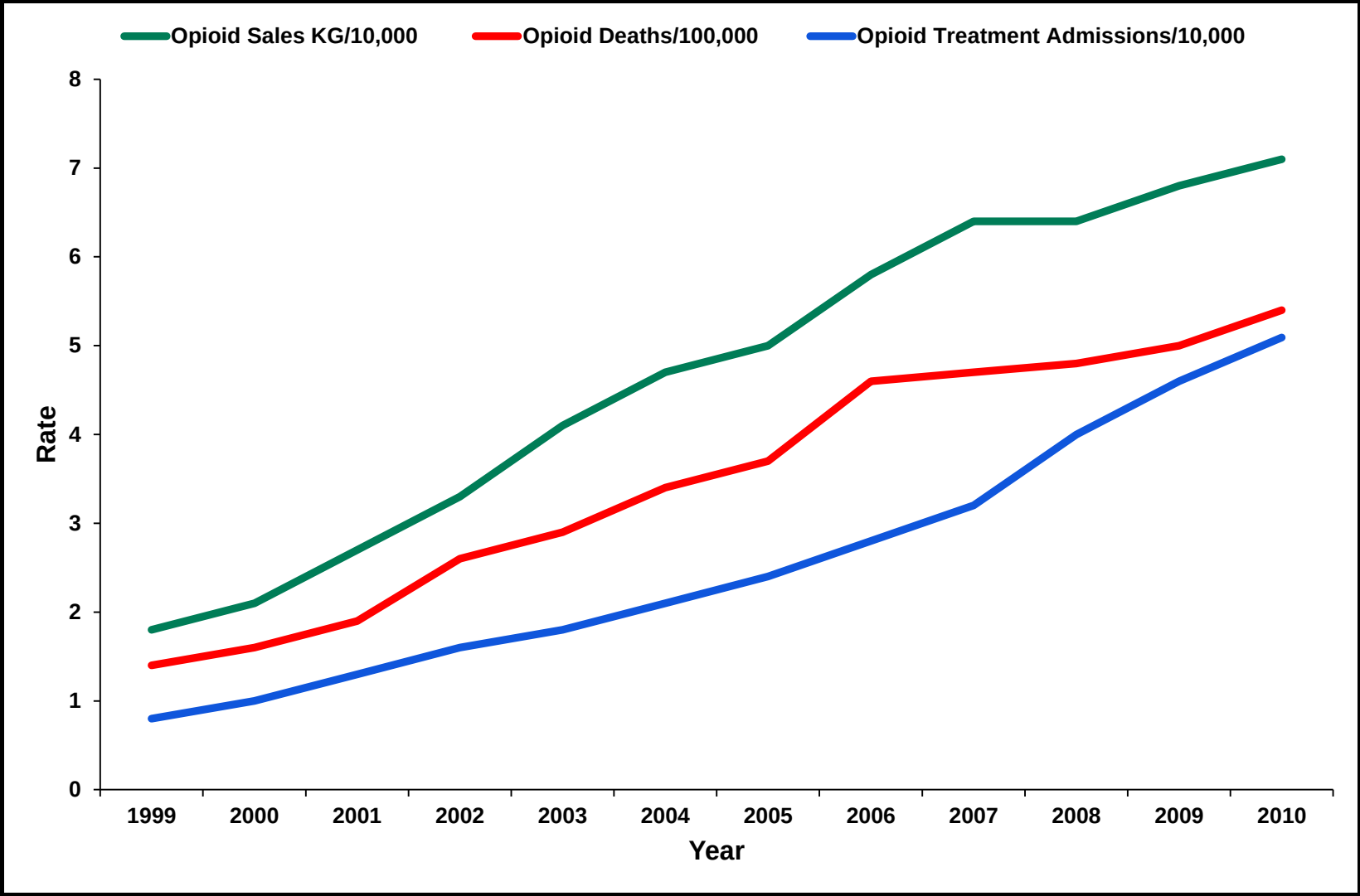
Drug Overdose Death Rates in USA More Than Tripled Since 1990 (Nearly 17,000 in 2010).



NCHS Data Brief, December, 2011, Updated with 2009 and 2010 mortality data

Motor vehicle traffic, poisoning, and drug poisoning (overdose) death rates: United States, 1980-2010

Increases in Opioid Deaths Parallel Opioid Sales and Treatment Admissions

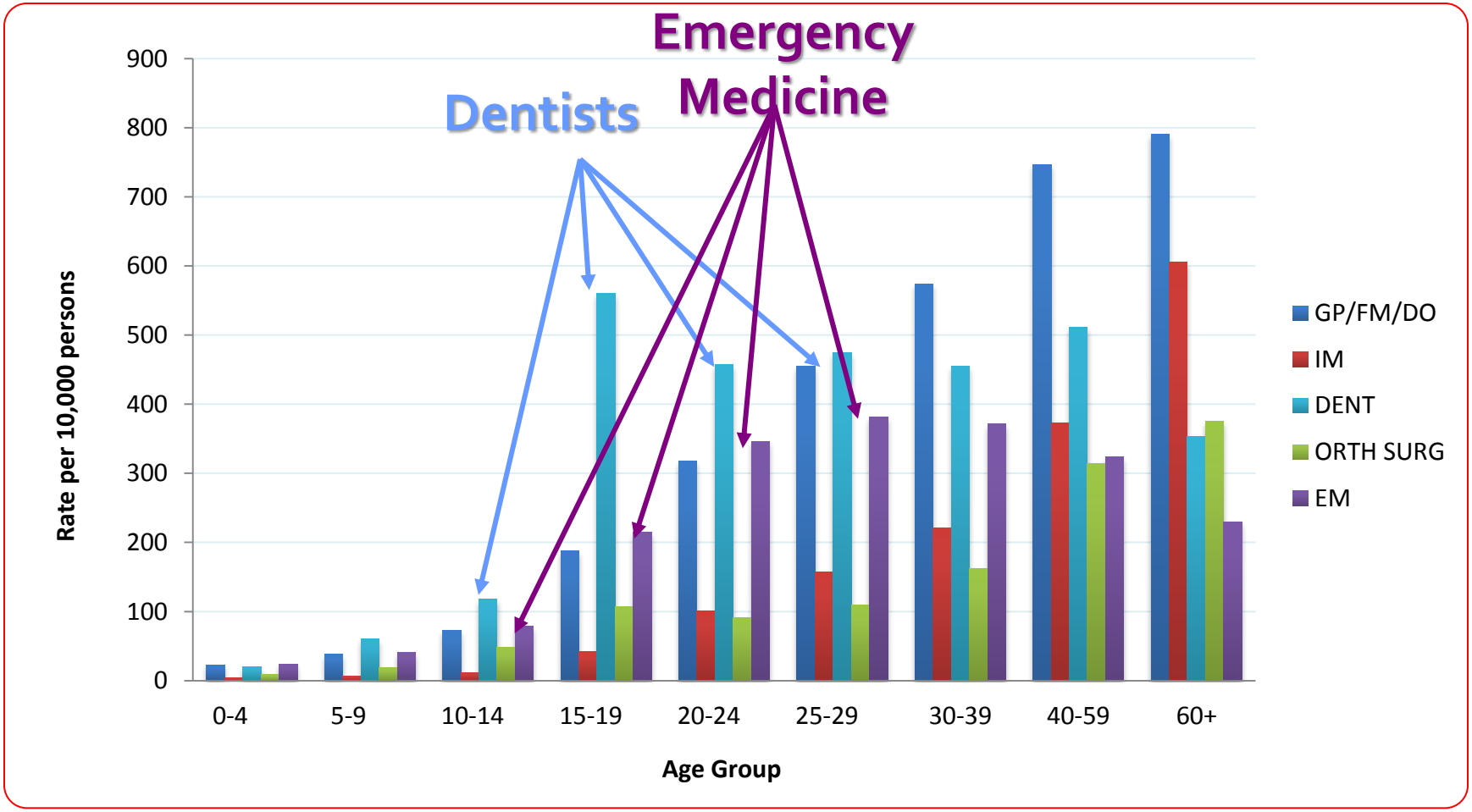


National Vital Statistics System, DEA's Automation of Reports and Consolidated Orders System, SAMHSA's TEDS

Question:

What medical specialties prescribe the most opioid medications to youth?

Opioid Medication Prescribers by Specialty



Source: IMS Vector ®One National, TPT 06-30-10 Opioids Rate 2009

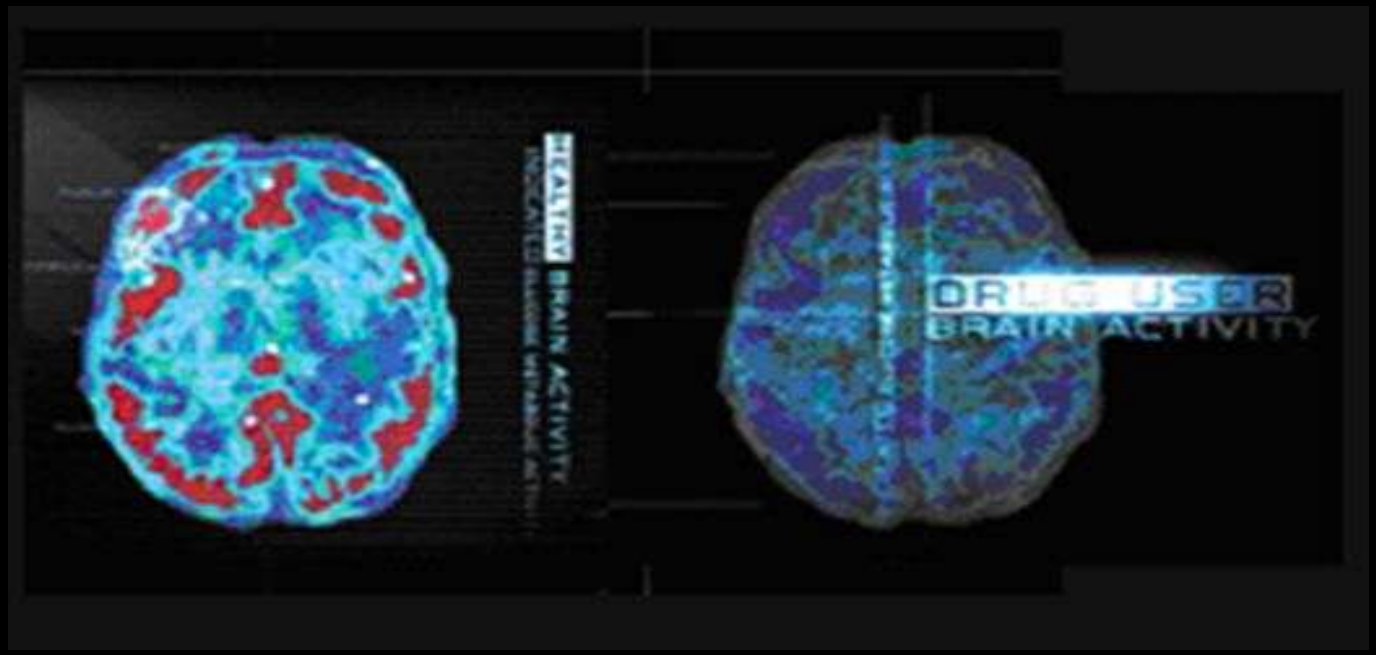
Estimated Economic Cost to Society Due to Substance Use Disorders

Tobacco:	$193 billion/year
Alcohol:	$235 billion/year
Illegal drugs:	$181 billion/year
Total:	$609 billion/year

CDC, 2007; Rehm et al., 2009 Lancet 373:2223-33

Understanding Addiction

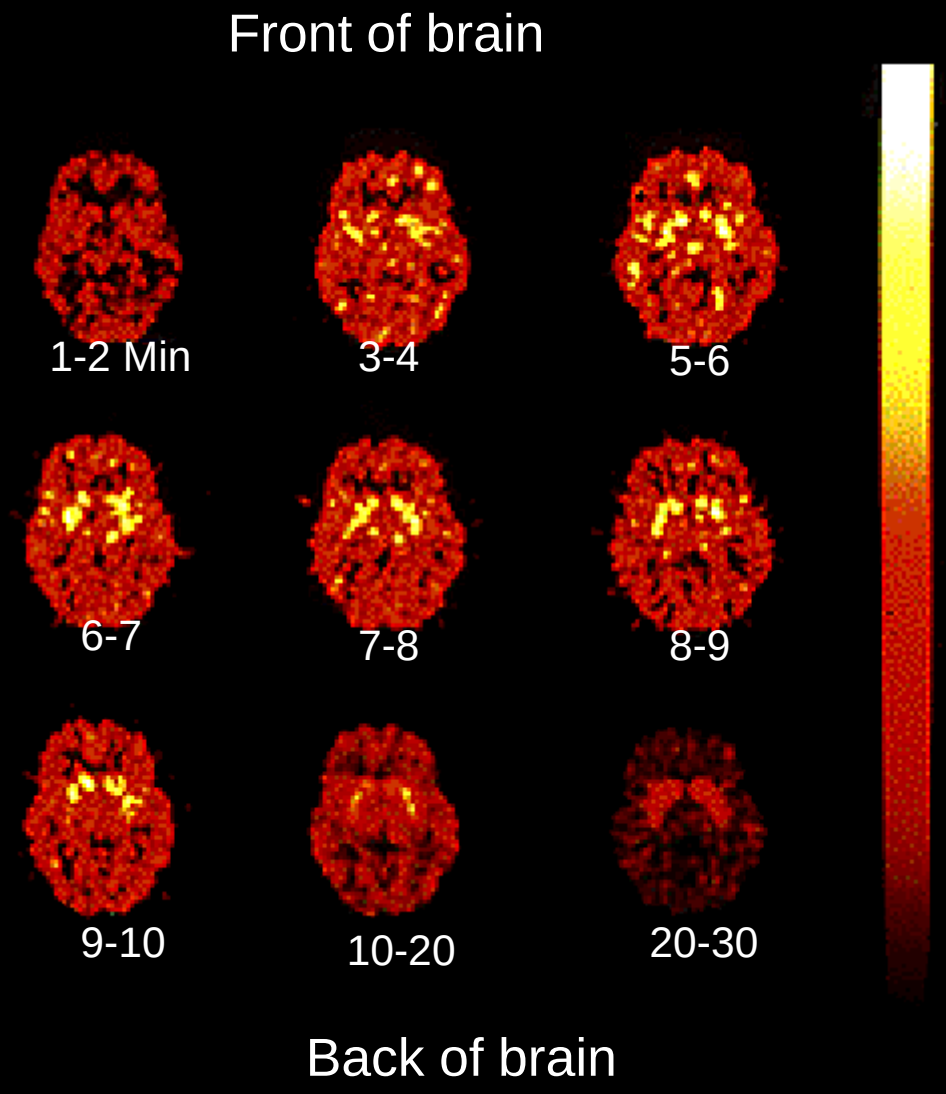
Advances in neuroscience have revolutionized our fundamental understanding of drug abuse and addiction



this is your brain on drugs.

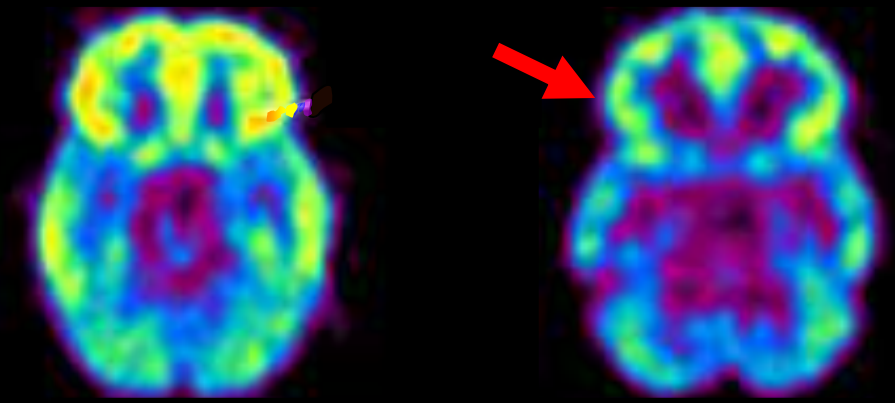
The Brain on Drugs

YELLOW shows places in brain where cocaine binds (Striatum)



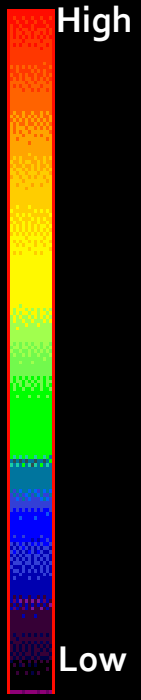
Addiction is a Disease of the Brain

Decreased Brain Metabolism in *SUD Patient*

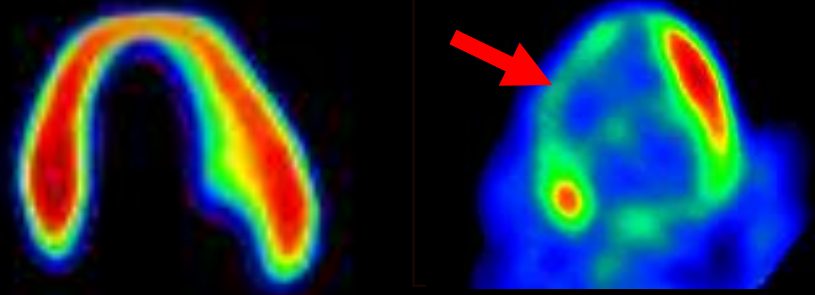


Control

Cocaine Abuser



Decreased Heart Metabolism in *Heart Disease Patient*



Healthy Heart

Diseased Heart

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

Addiction is Like Many Other Diseases

- Addiction is preventable
- Addiction is treatable
- Recovery is possible

NIDA Priority Areas

Prevention

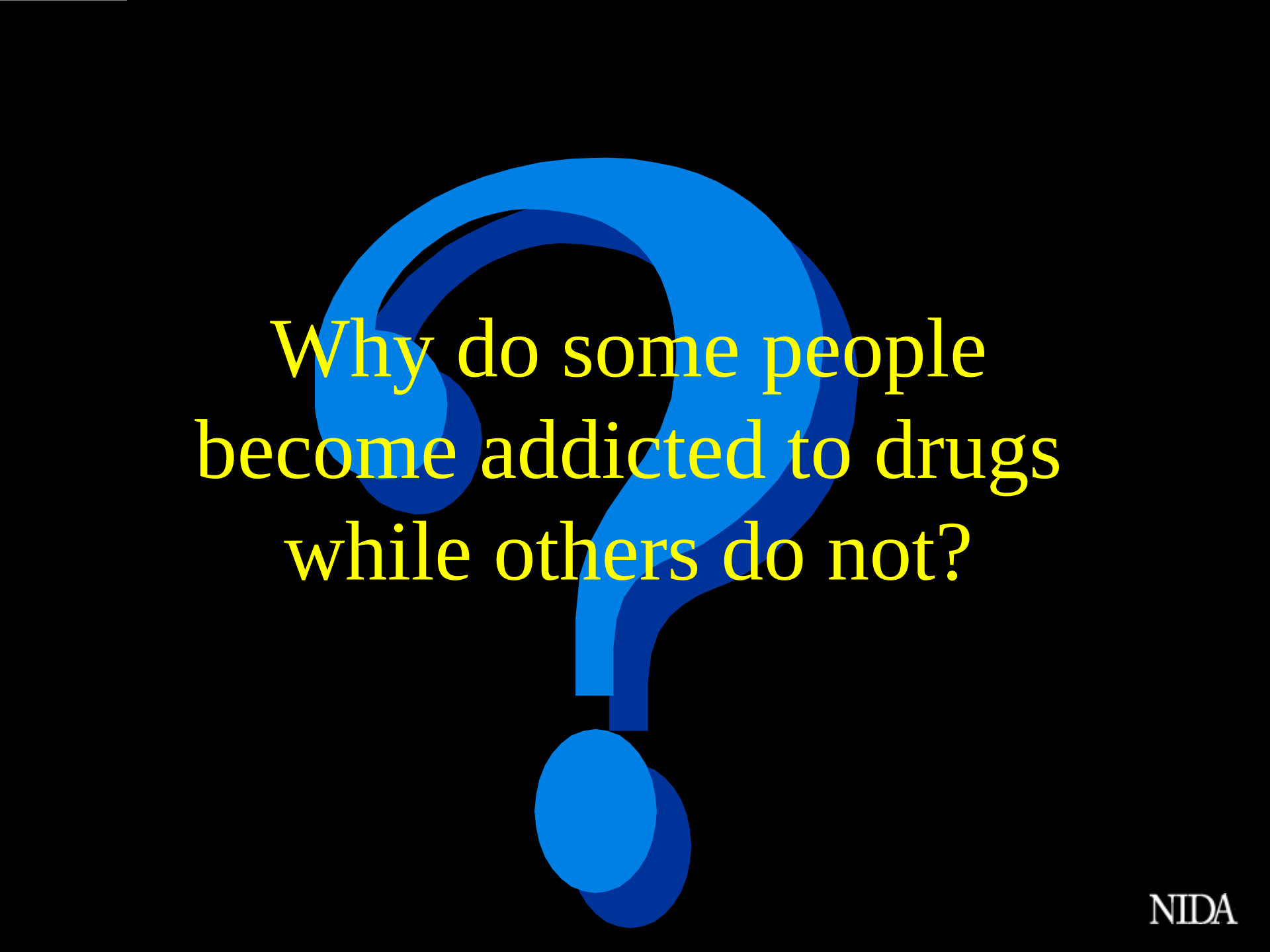
Genetics
Environment
Development

Treatment

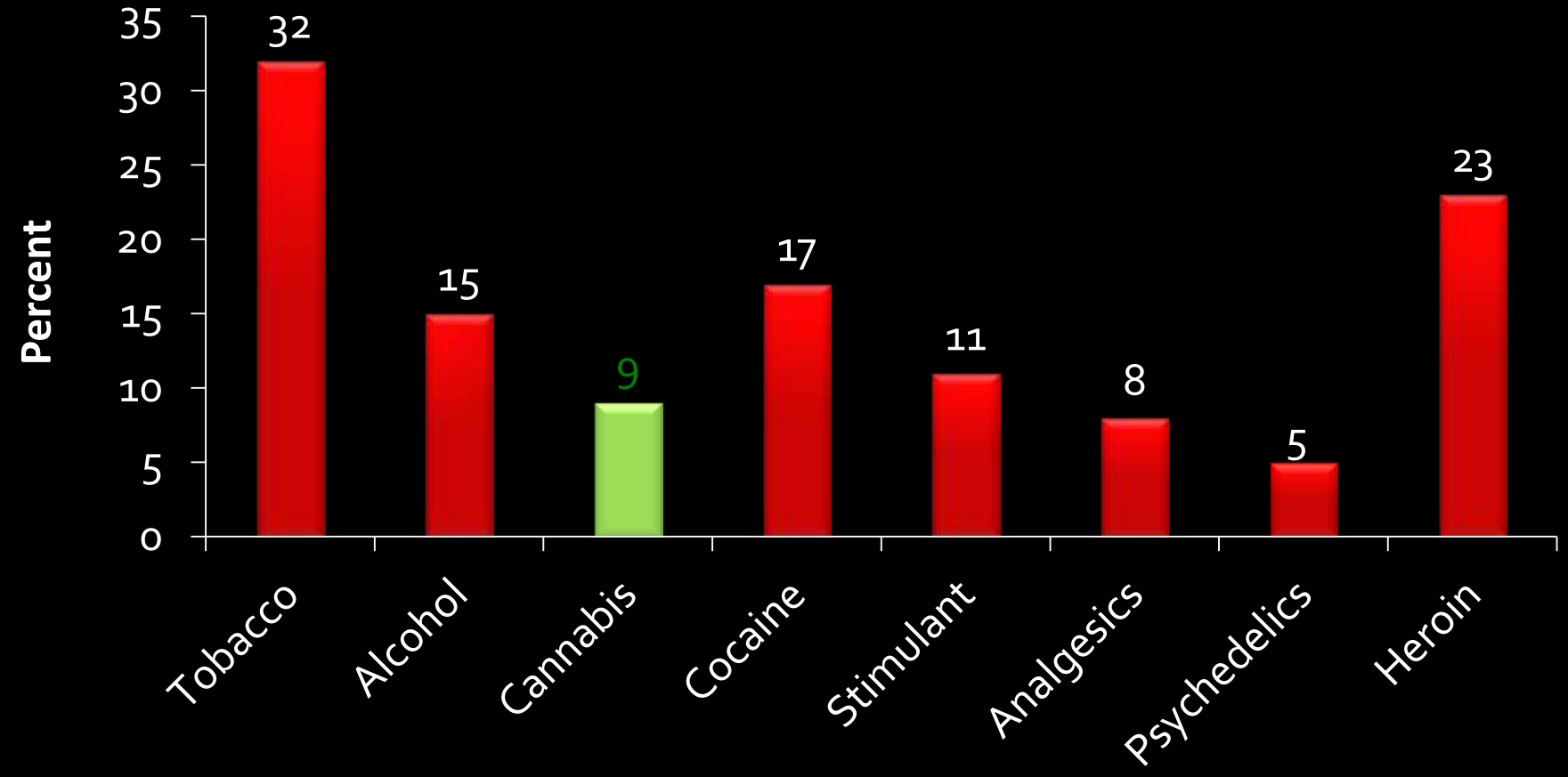
Neural mechanisms
Brain circuitry

Consequences

HIV/AIDS
Fetal Exposure


Why do some people become addicted to drugs while others do not?
NIDA

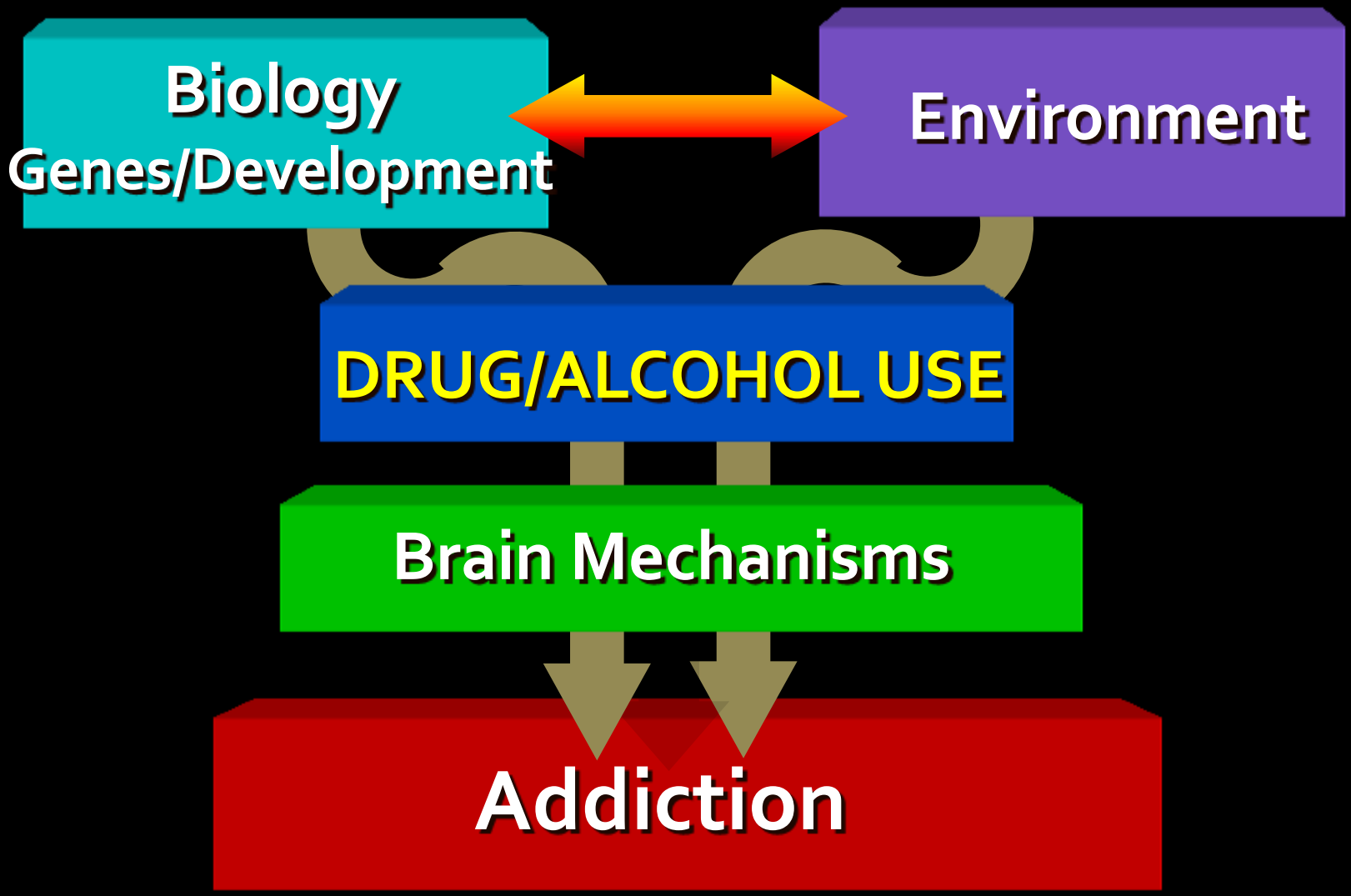
Addiction Prevalence Varies by Drug



Estimated Prevalence of Dependence Among Users

Source: Anthony JC et al., 1994

Development of Addiction Involve Multiple Factors



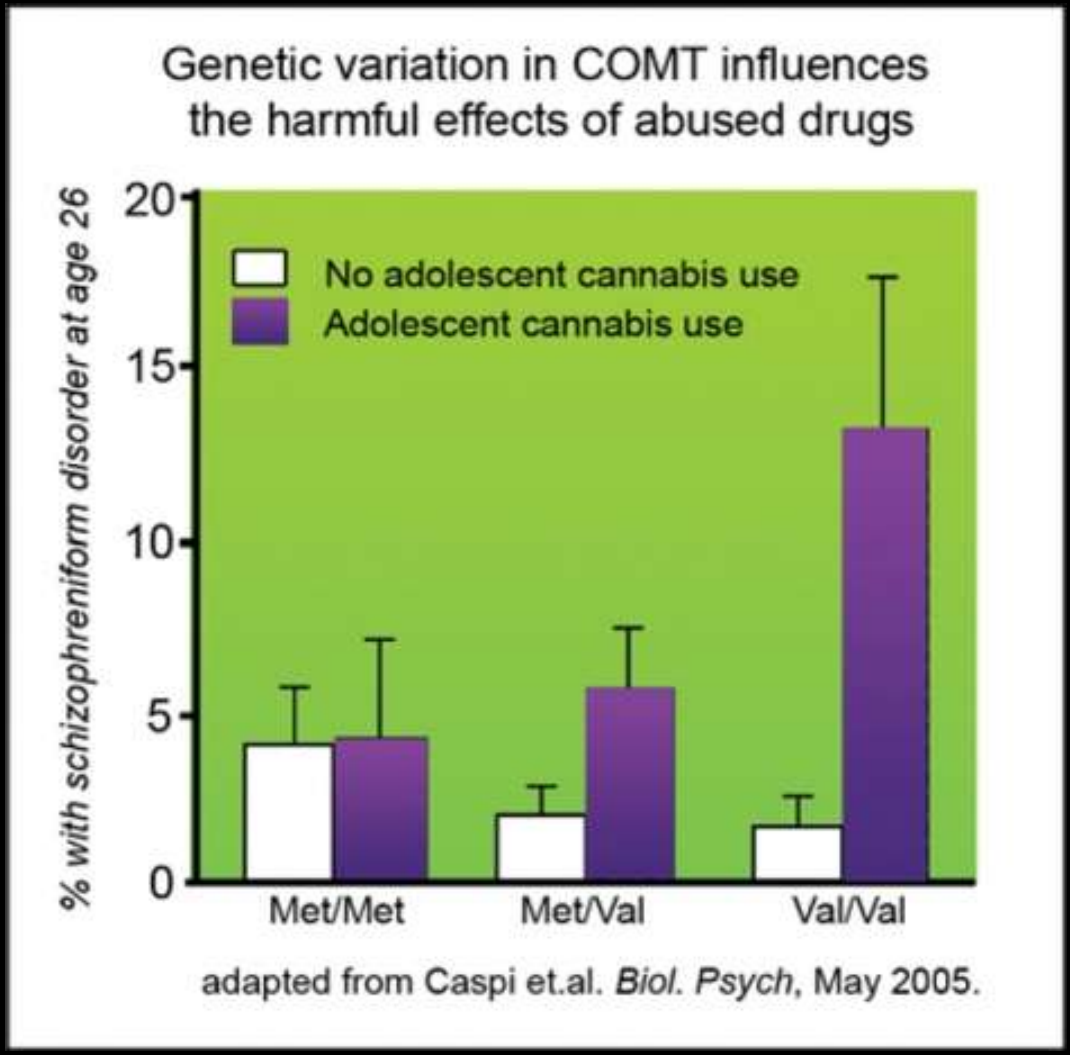
Susceptibility to Addiction Results from Interaction of Many Genes

- **FAAH -** associated with drug dependence
- **OPRM1** - associated with opiates and alcoholism
- **CYP2A6, CYP2B6** - associated with smoking and smoking cessation
- **ALDH2** - associated with protection against alcoholism
- **DBH** (Dopamine beta-hydroxylase) – cocaine-induced paranoia
- **DRD2, DRD4** (Dopamine receptors) - reward, craving
- **NrCAM, neurexins** (Cell adhesions genes) - assoc with drug abuse and addiction
- **Prodynorphin gene -** associated with protection against cocaine dependence
- **Nicotinic alpha 7 promoter –** assoc. with decreased expression of its message in different brains regions and with sensory gating defects in schizophrenics

-- **Alpha 5 and beta 3** (nicotinic receptors) – assoc. with nicotine dependence

-- **5HT1B** (serotonin receptor) - associated with conduct disorder and alcoholism

Genetic Variability and Effects of Drugs



What Environmental Factors Contribute to Addiction?

Drug availability

Peers who use drugs

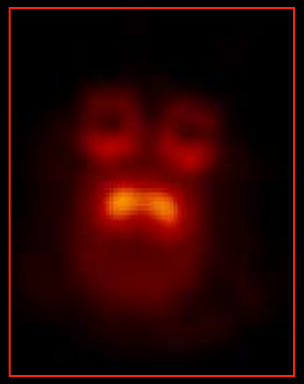
Family Problems

Early physical or sexual abuse

Stress in general

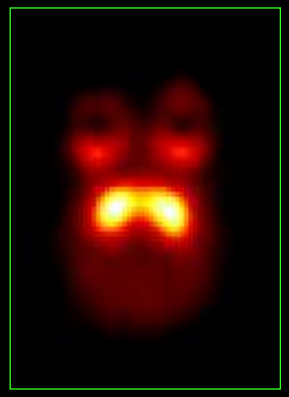
Effects of a Social Stressor on Brain Dopamine D2 Receptors and Propensity to Administer Drugs

Individually Housed



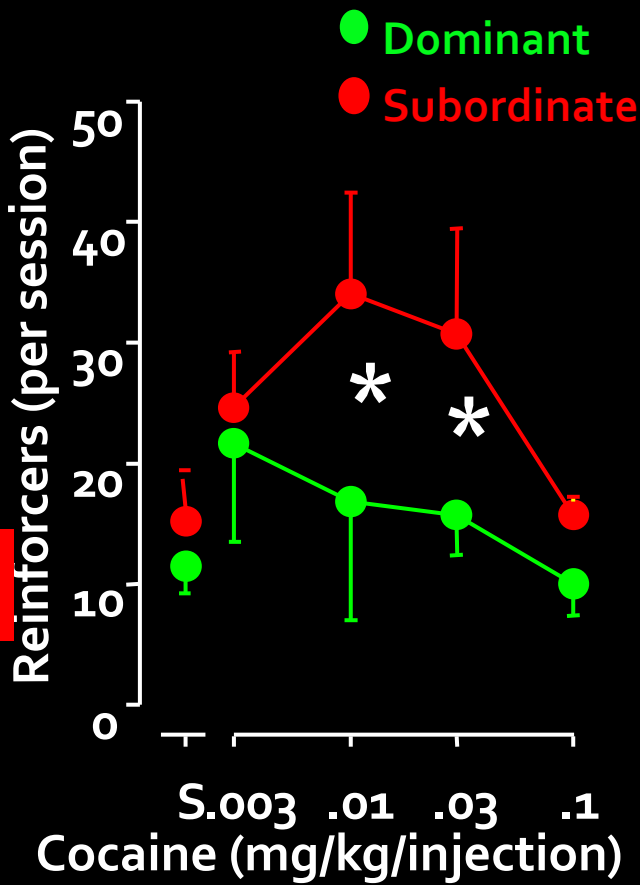
Becomes Dominant
No longer stressed

Group Housed



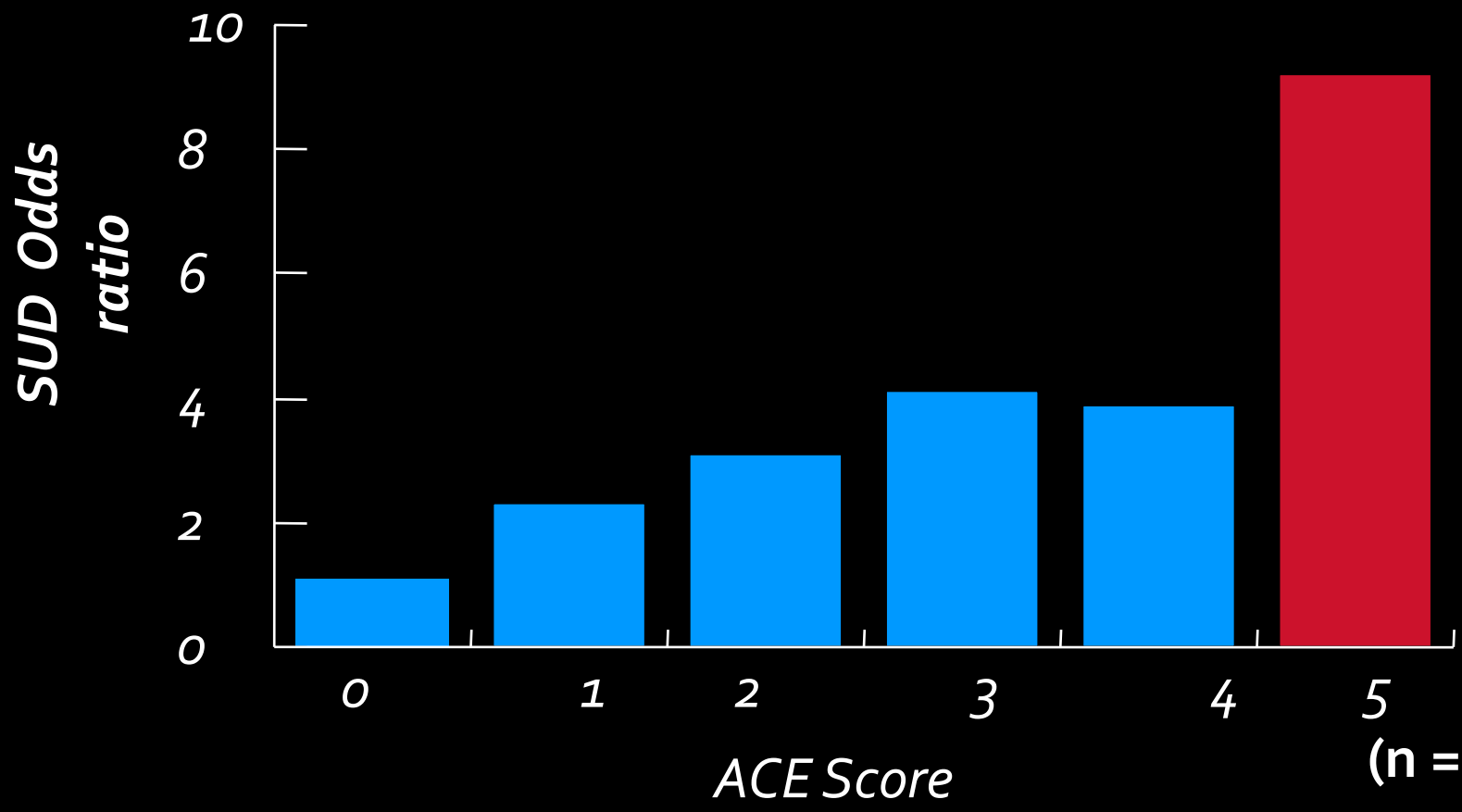
Social Setting Can Change Neurobiology

Becomes Subordinate
Stress remains



Morgan, D. et al. *Nature Neuroscience*, 2002.

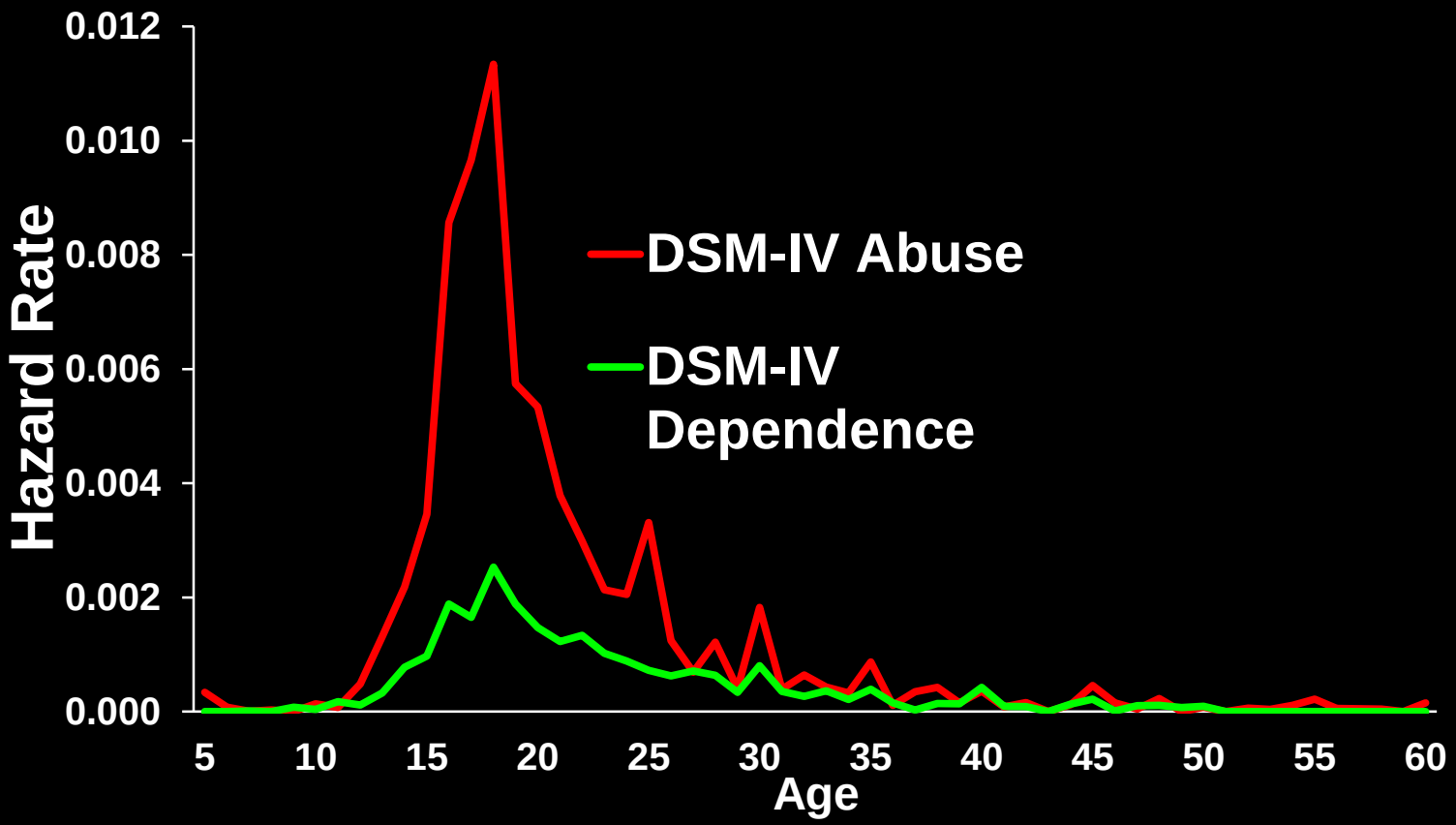
Adverse Childhood Experiences (ACE) and Illicit Drug Use



ACE is associated with ½ to 2/3 of serious problems with drug use.

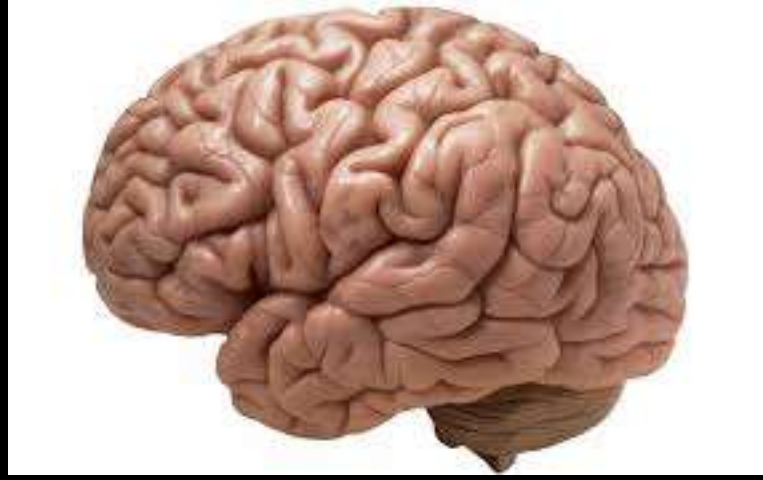
SR Dube, et al. PEDIATRICS 111: 564-572, 2003

Addiction Is Developmental



Age of Onset of Drug Abuse and Dependence

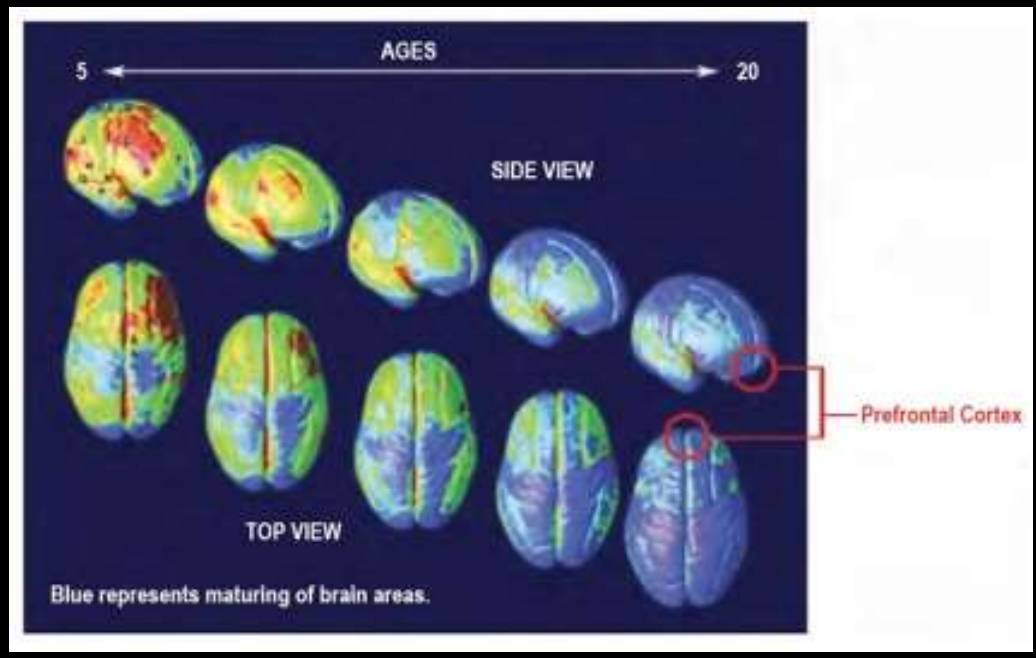
Source: Compton, et al. *Archives of General Psychiatry* 2007. NESARC Study.



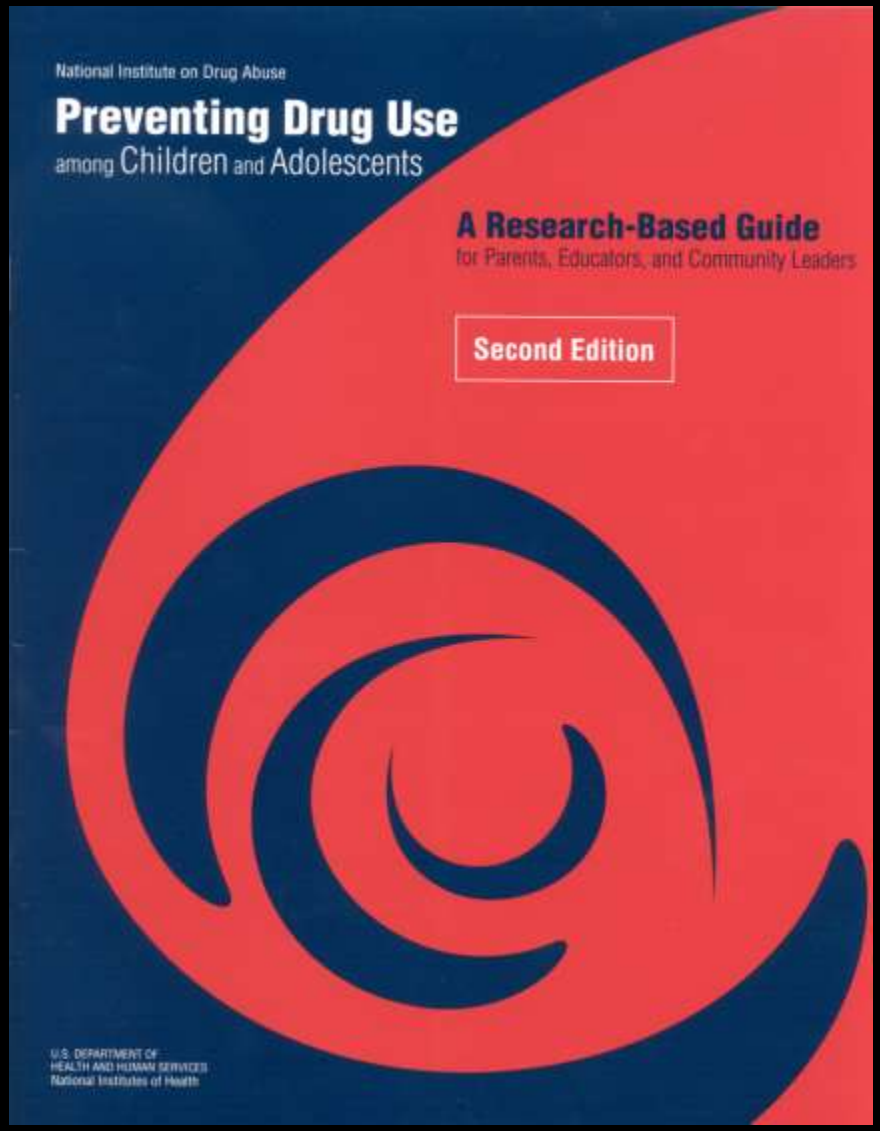
The brain continues to develops until what age?

The Adolescent Brain

- Brain develops till mid/late 20s!
- Pre-frontal cortex last to develop
- Age of drug use onset is predictor of later life drug problems
- 15% of those who start drinking by age 14 develop problems as adults (vs 2% who wait till age 21)



What Does Science Tell Us About Effective Prevention Programs?



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

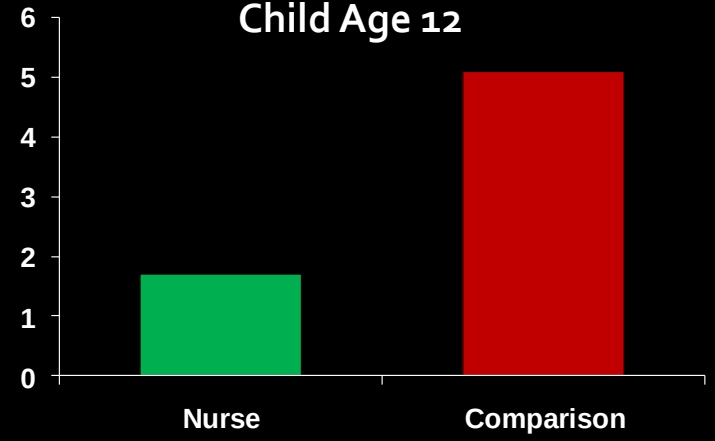
Effective Prevention Programs

Reduce these

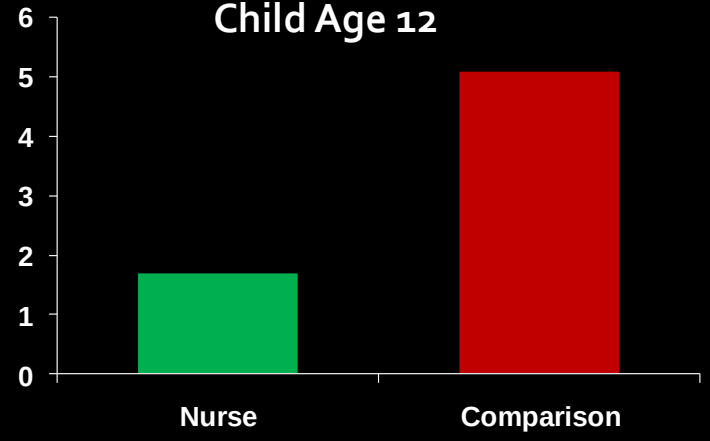
Elevate these

Nurse Home Visiting Program (prenatal-age 2)

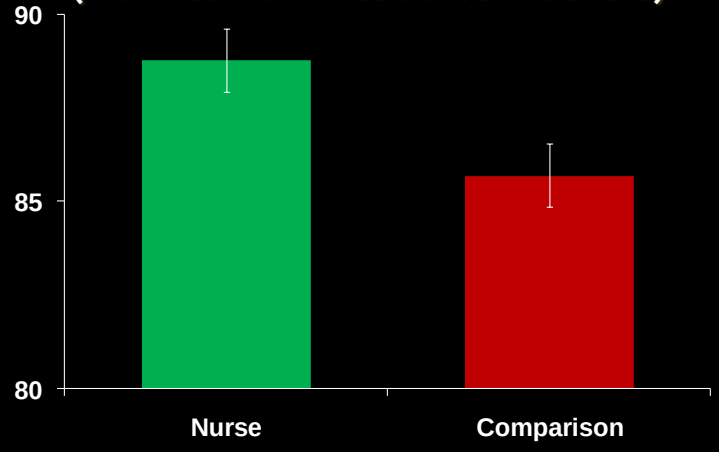
Percent of Children Who Used Tobacco, Alcohol, or Marijuana (Last 30 Days) Child Age 12



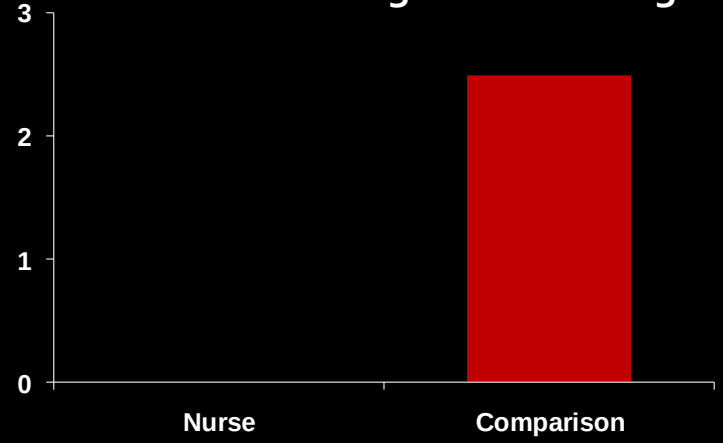
Percent of Children with Internalizing Problems (Borderline or Clinical) Child Age 12



PIAT Scores - Reading & Math – Age 12 (Born to Low-Resource Mothers)



Percent of Mothers with Role Impairment due to Alcohol or Drug Use – Child Age 12



Arch Pediatr Adoles Med, 164(5) 412-418, 2010

NIDA Priority Areas

Prevention

Genetics
Environment
Development

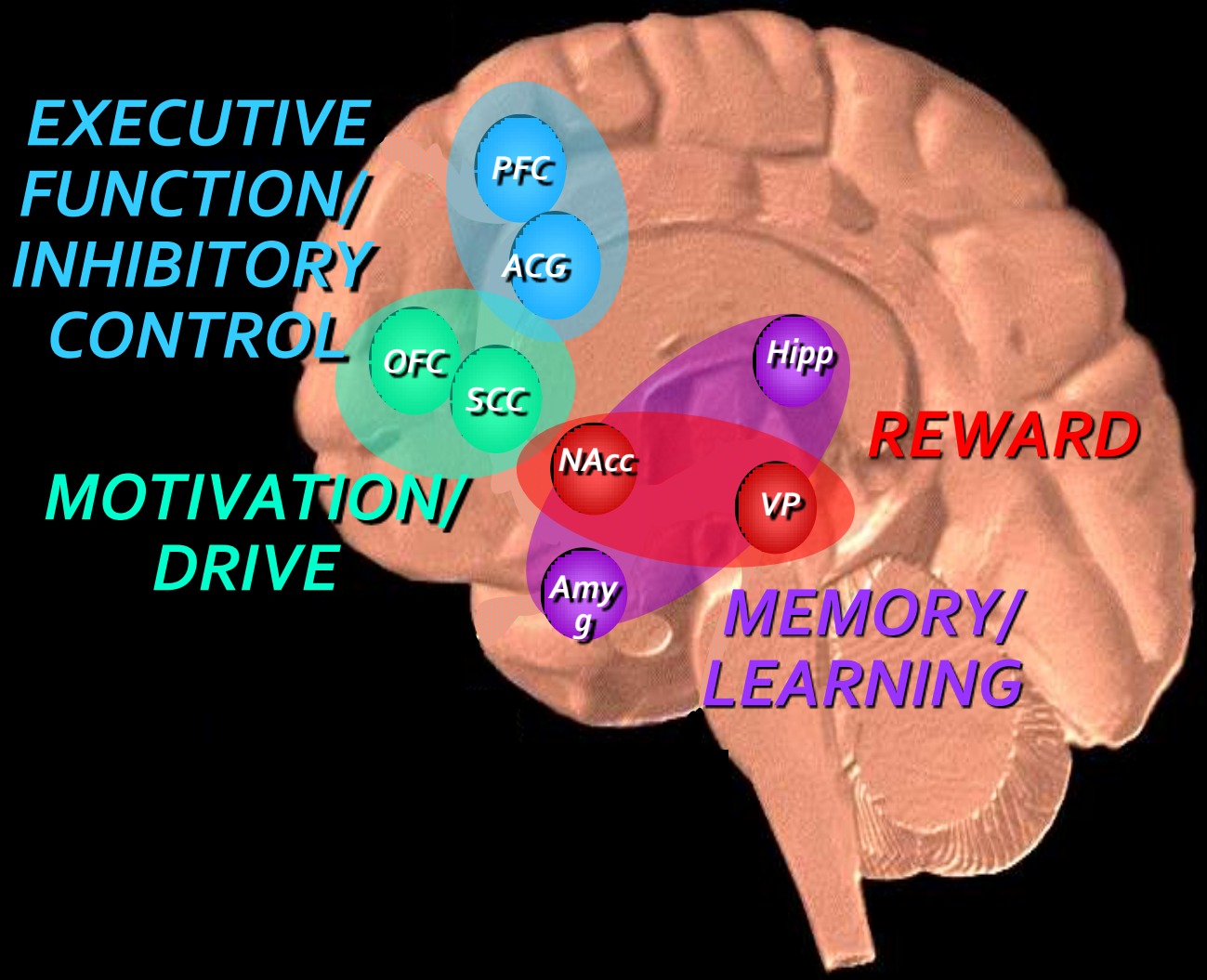
Treatment

Neural mechanisms
Brain circuitry

Consequences

HIV/AIDS
Fetal Exposure

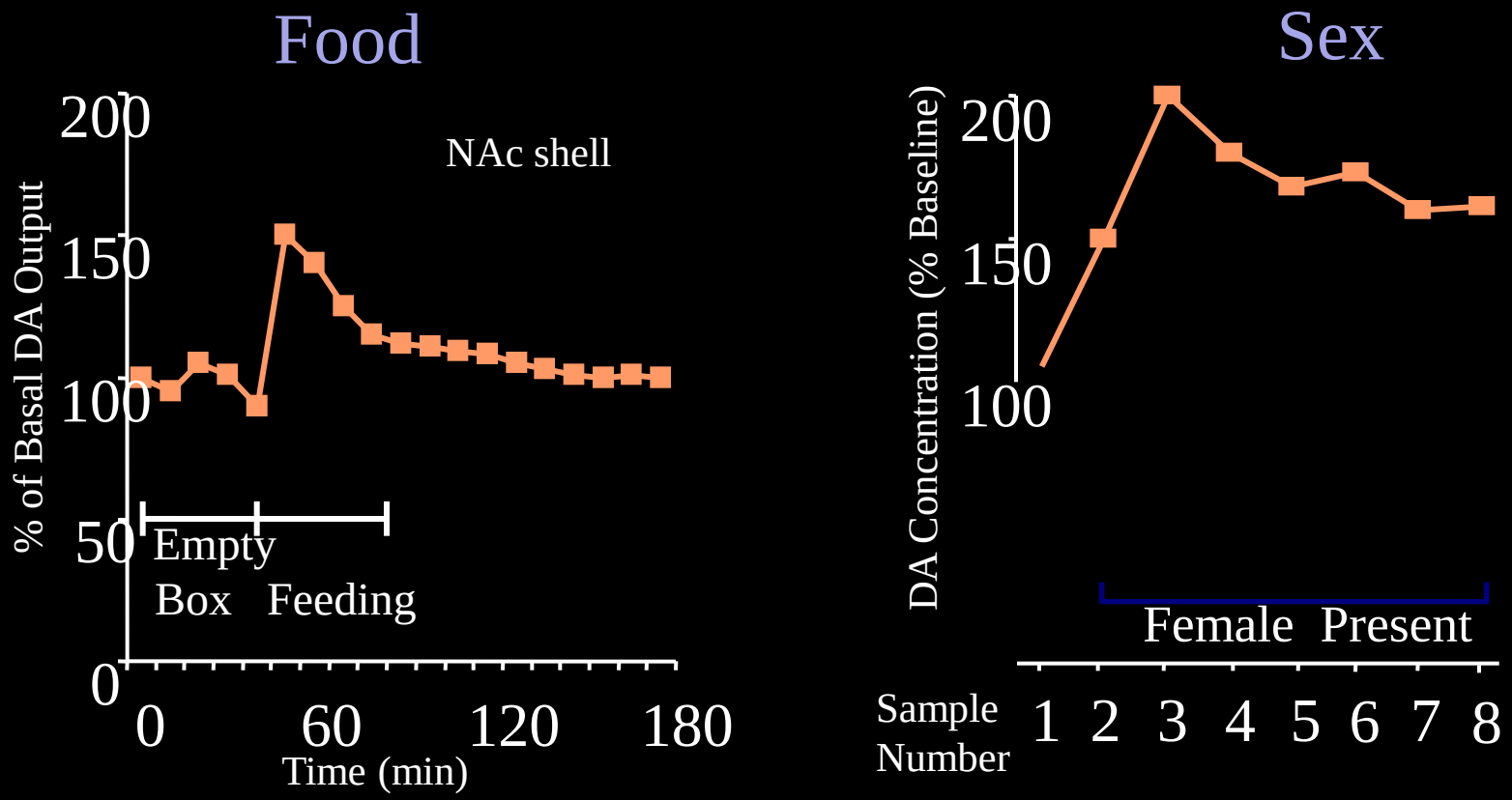
Neuronal Circuits Involved In Drug Abuse and Addiction



1. Reward Circuit

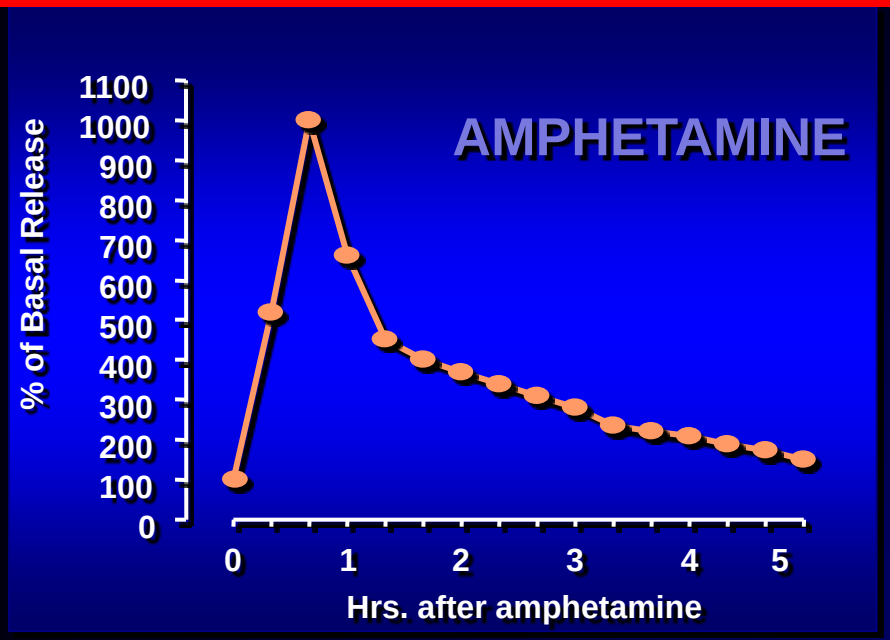
Drugs of Abuse Engage Systems in the Motivation Pathways of the Brain

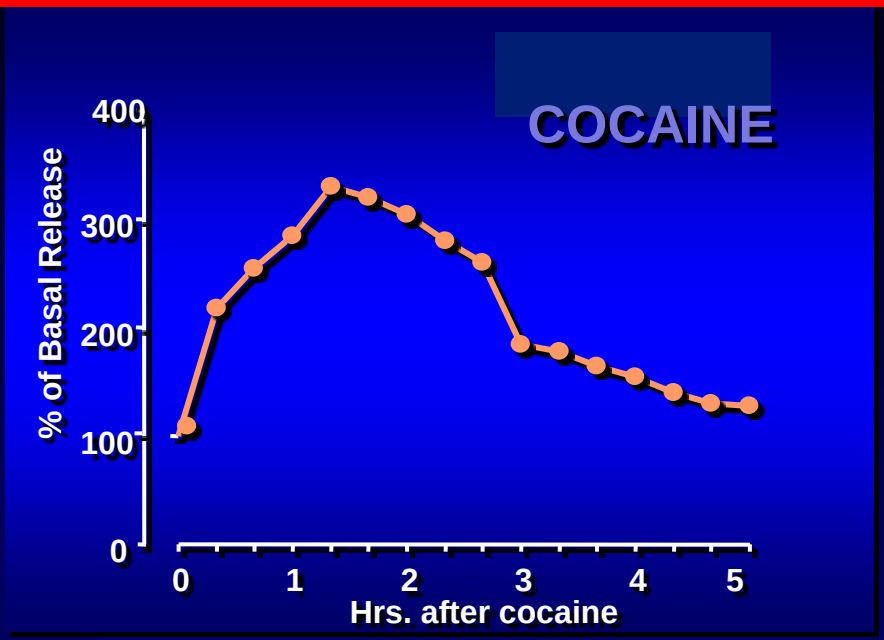
Natural Rewards Elevate Dopamine Levels

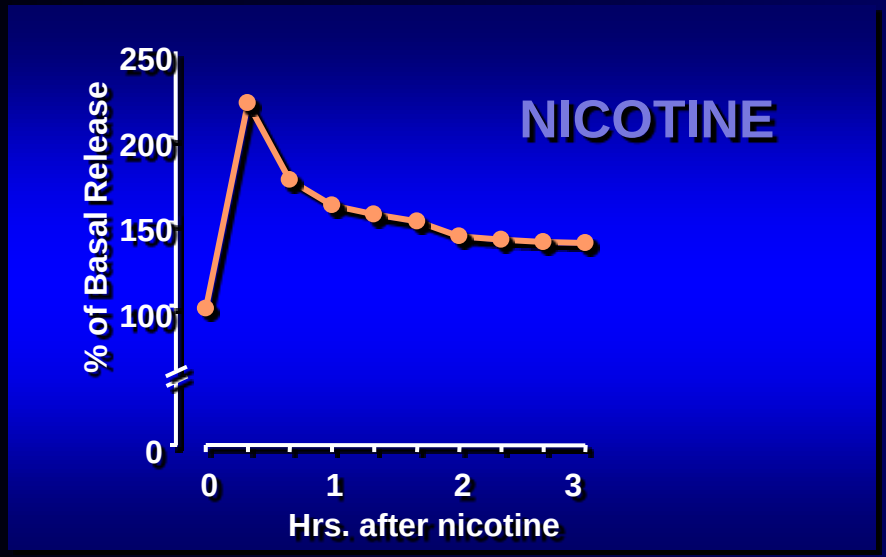


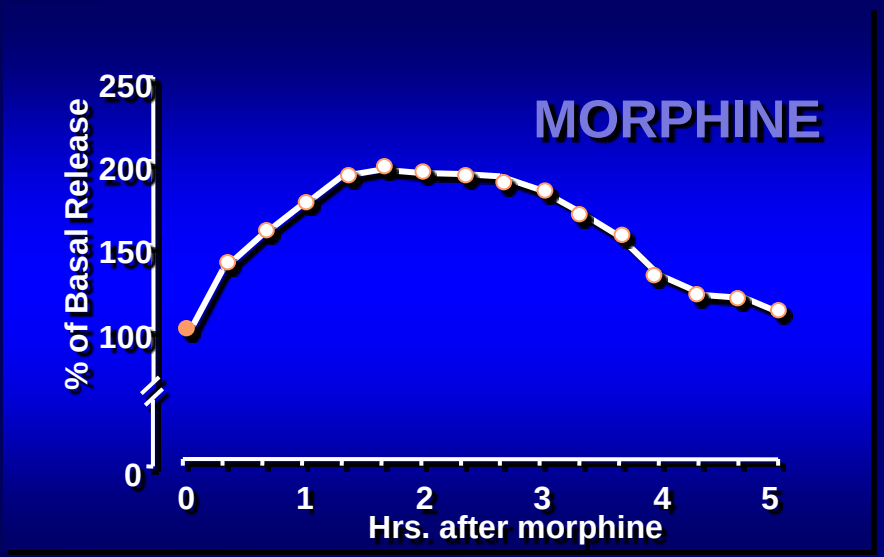
Di Chiara et al., Neuroscience, 1999.,Fiorino and Phillips, J. Neuroscience, 1997.

Drugs Elevate Dopamine Levels More/Longer



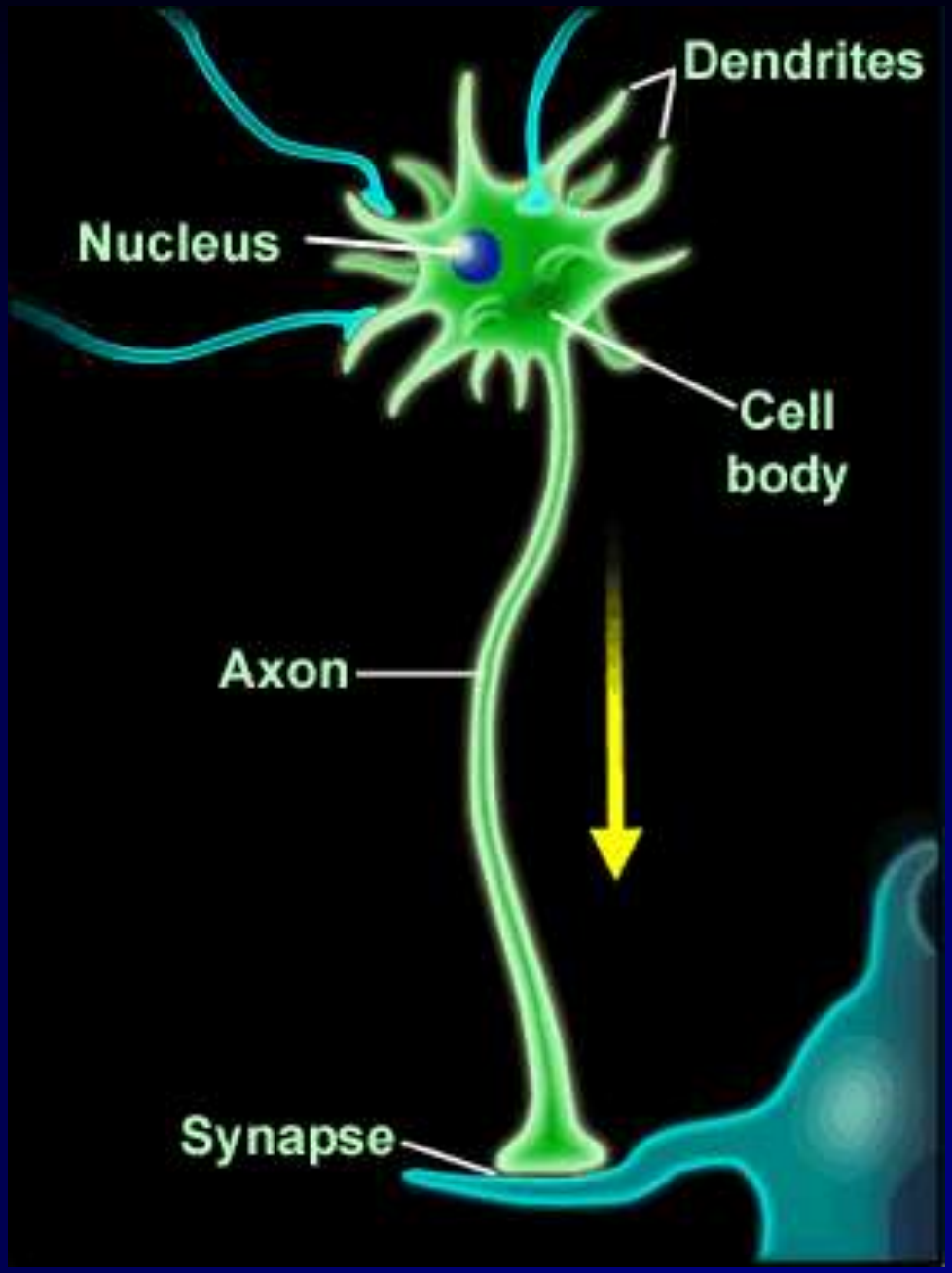


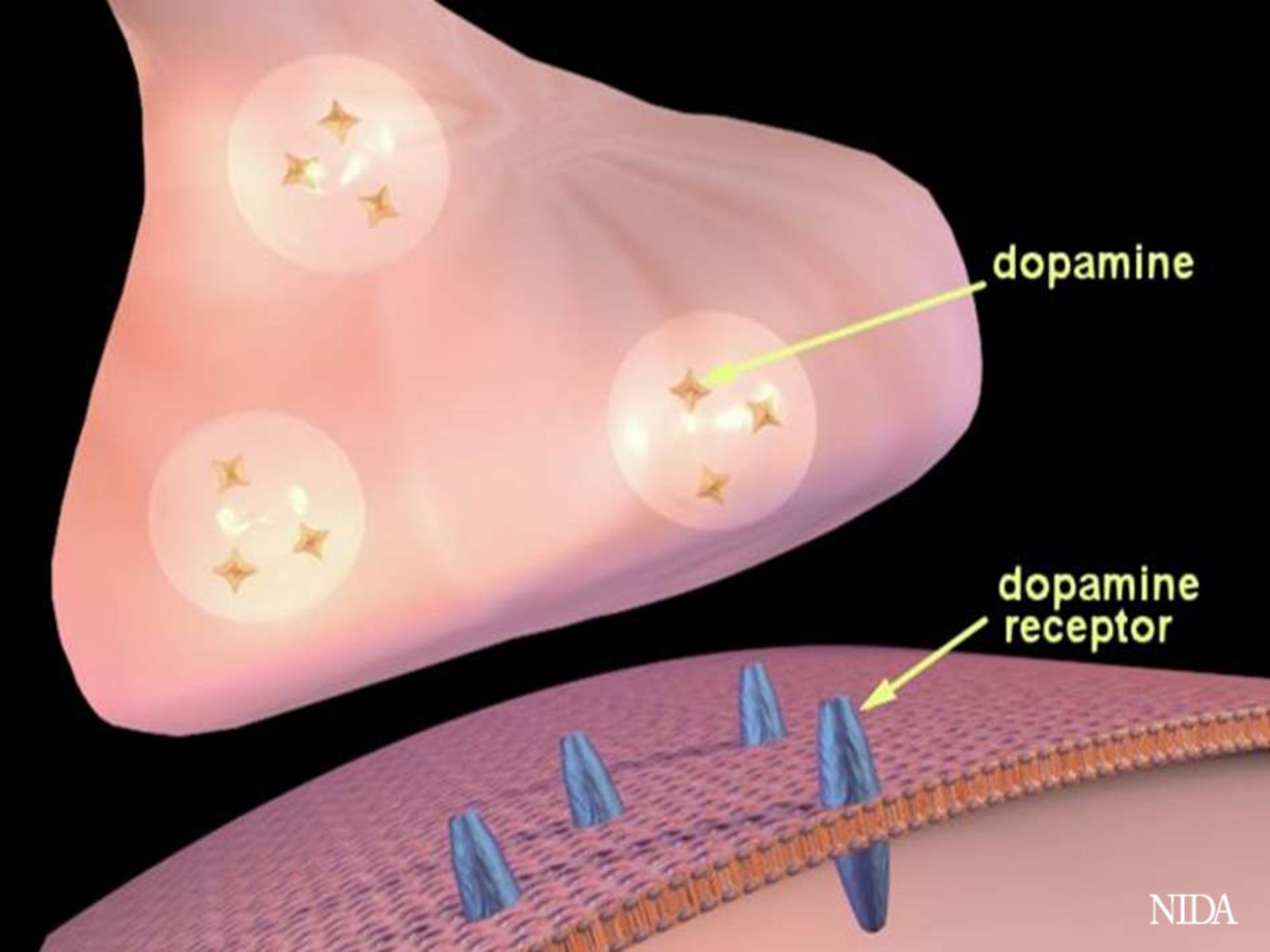


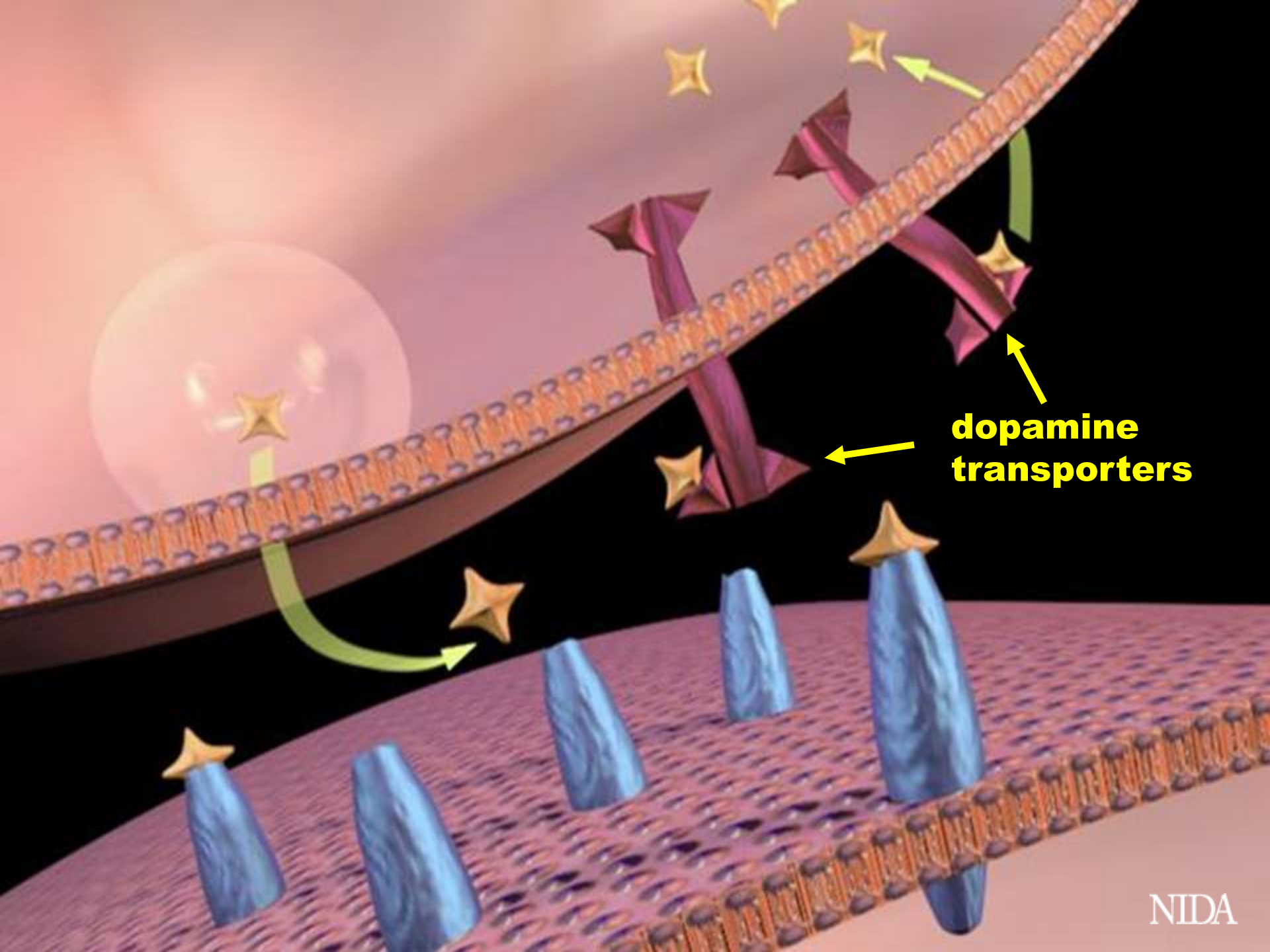


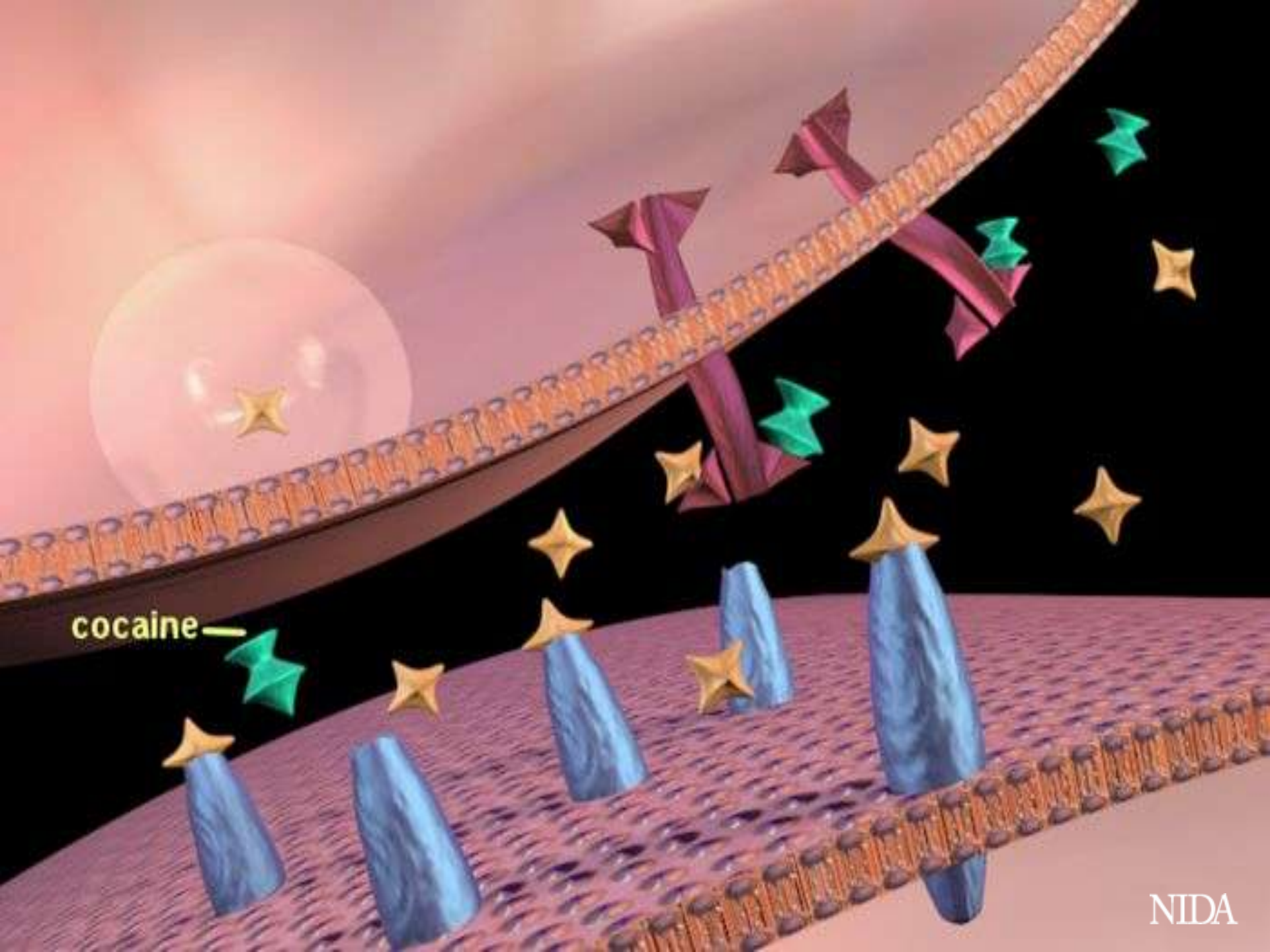
Source: Di Chiara and Imperato

The Neuron: How the Brain's Messaging System Works




dopamine
dopamine receptor
NIDA


dopamine
transporters
NIDA

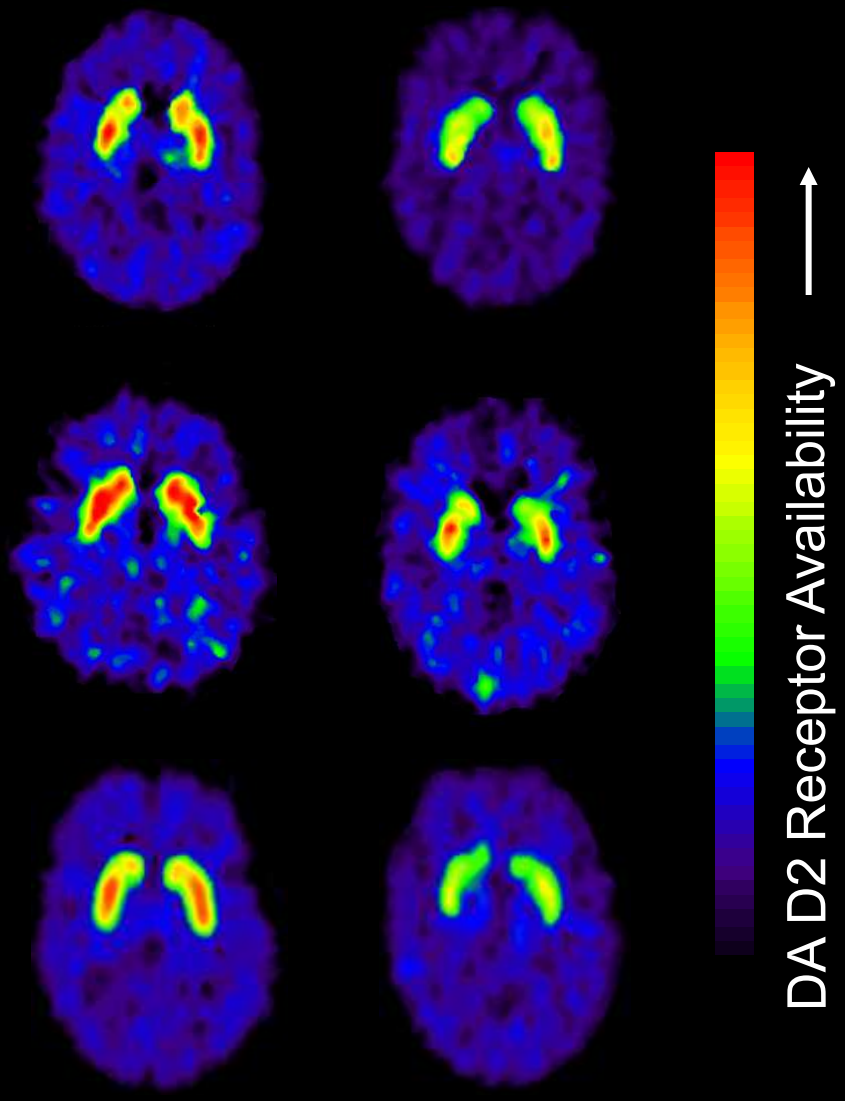

cocaine
NIDA

Dopamine Receptors Lower in Addiction

Cocaine

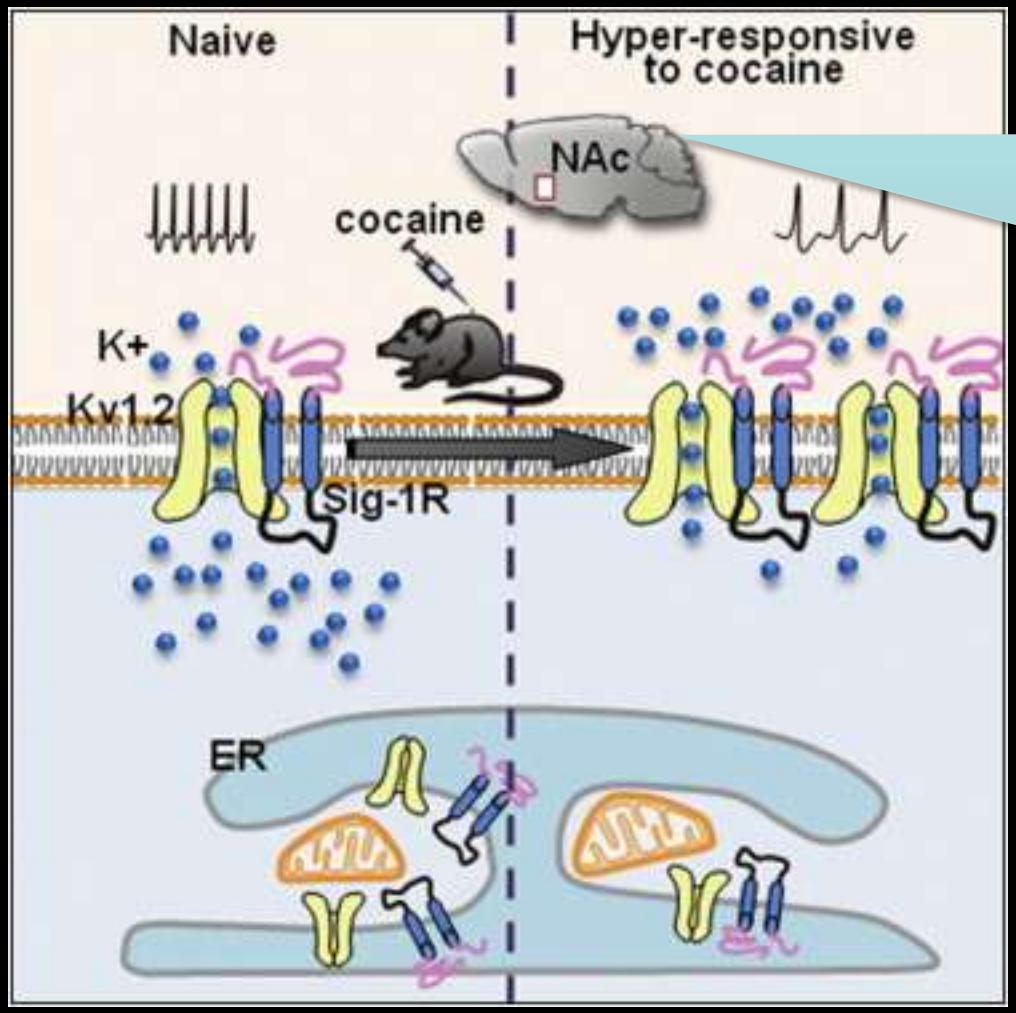
Alcohol

Heroin



control addicted

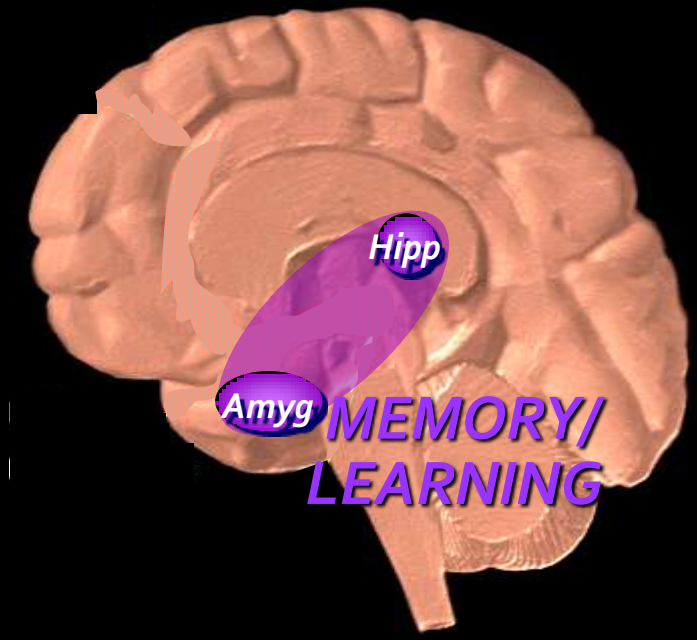
Cutting Edge Research: Brain Changes Leading to Cocaine Addiction



Increased interaction between proteins in the nucleus accumbens may result in enhanced responsiveness (reward) to cocaine.

Bonci, et al (2013), *Cell*

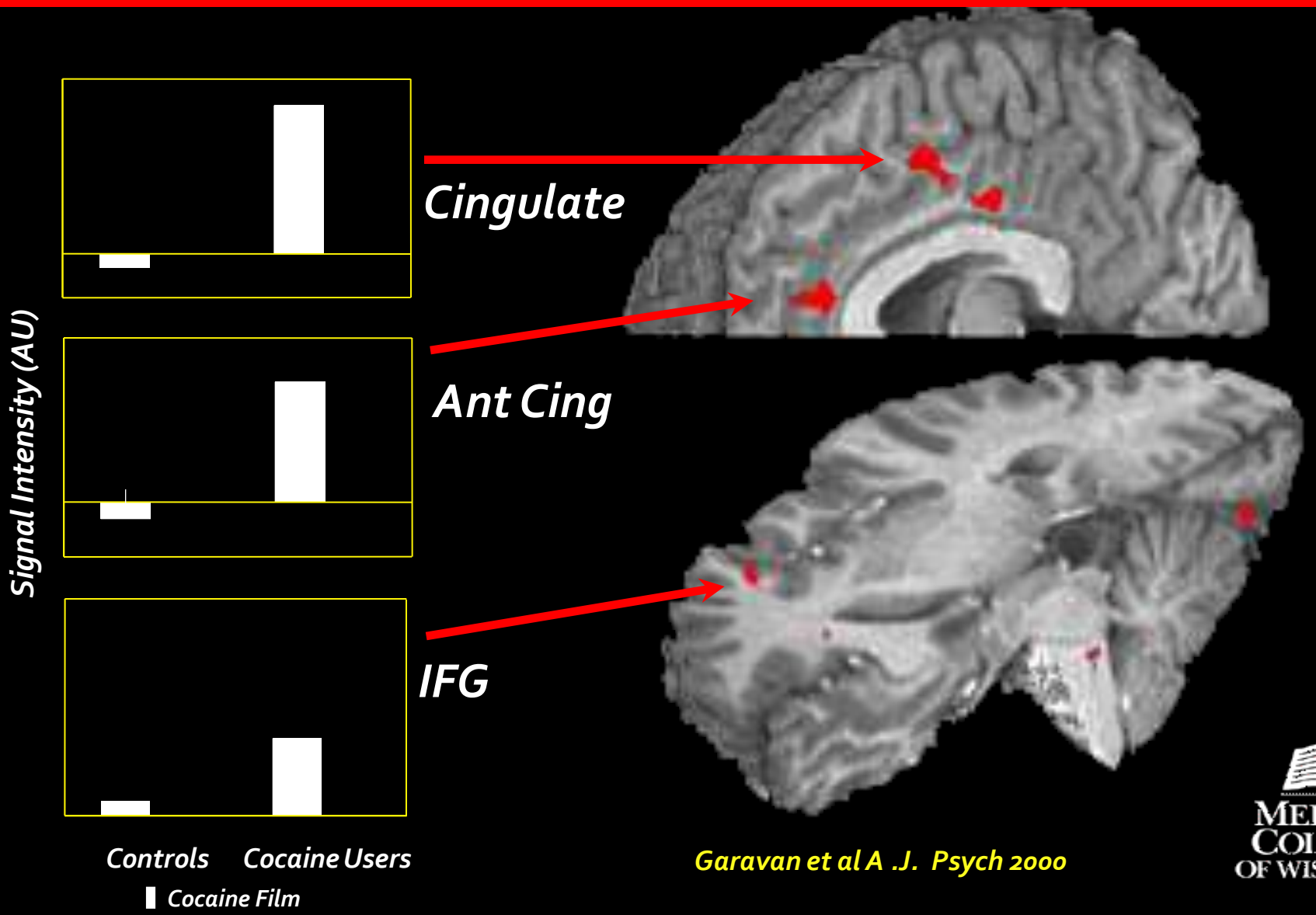
2. Memory circuit



"People, places and things..."

Cocaine Craving:

Population (Cocaine Users, Controls) x Film (cocaine)

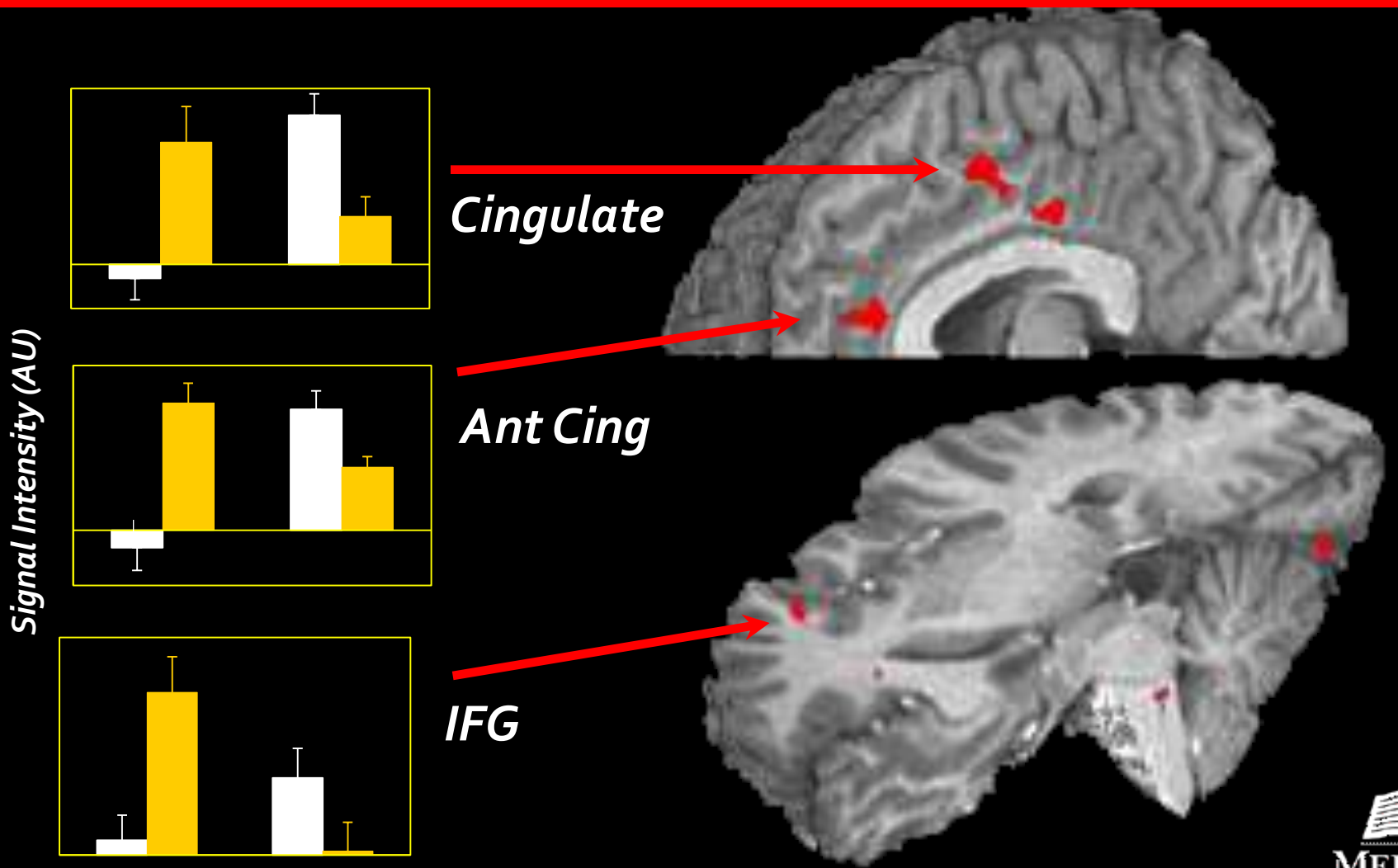


Garavan et al A .J. Psych 2000

MEDICAL COLLEGE OF WISCONSIN

Cocaine Craving:

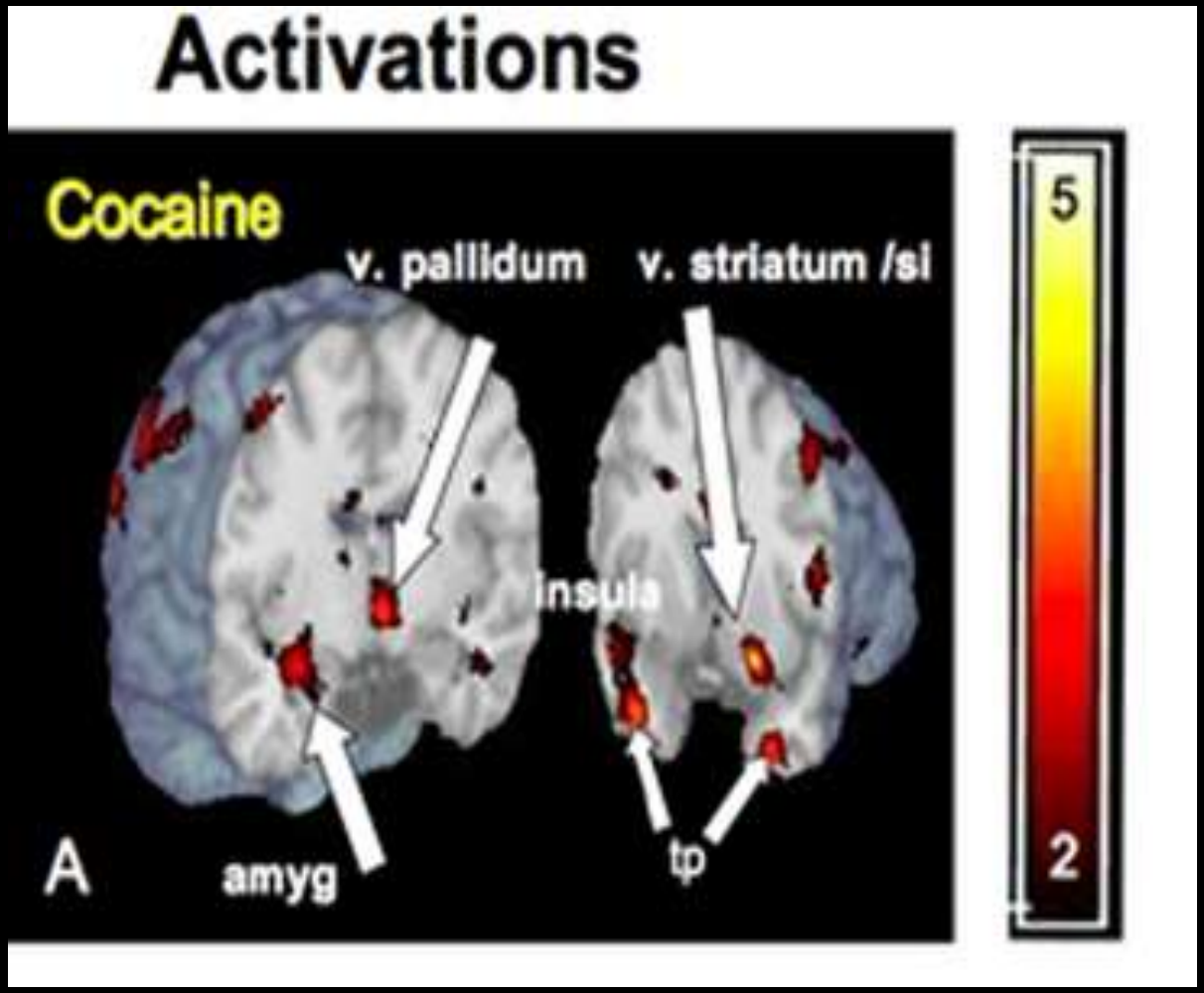
Population (Cocaine Users, Controls) x Film (cocaine, erotic)



Garavan et al A .J. Psych 2000

MEDICAL COLLEGE OF WISCONSIN

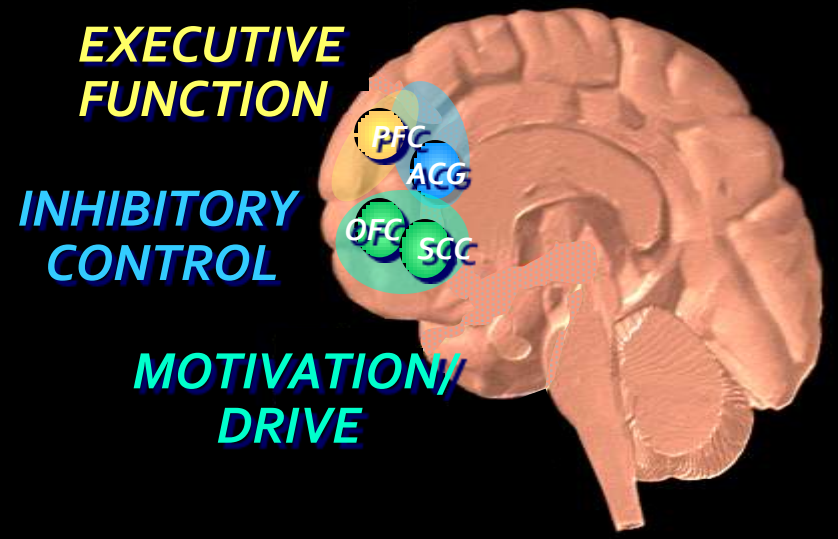
Even Unconscious Cues Can Elicit Brain Responses



Brain Regions Activated by 33 millisecond cocaine cues (too fast for conscious recognition)

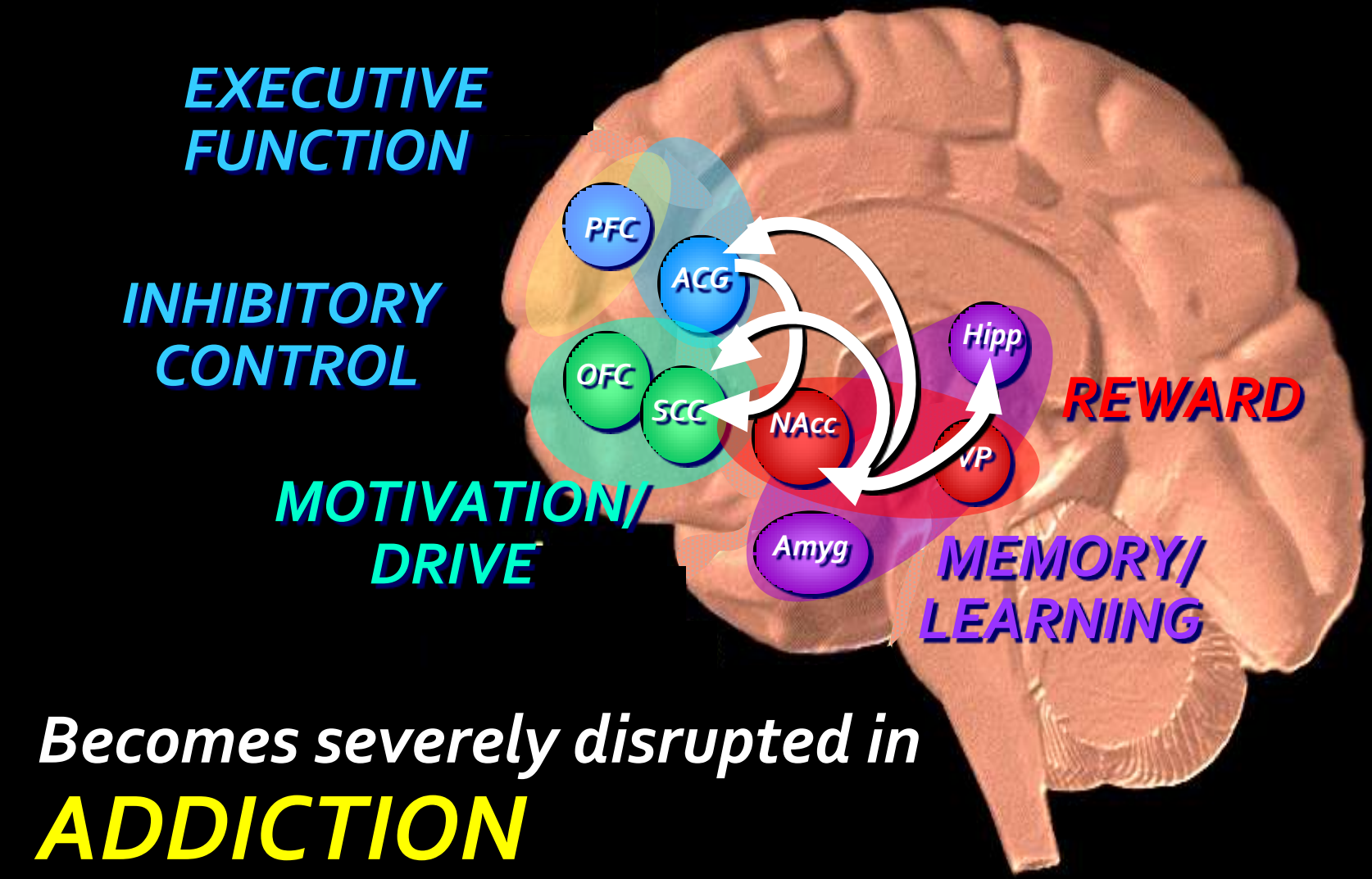
Childress, et al., PLoS ONE 2008

3. Motivation & Executive Control Circuits



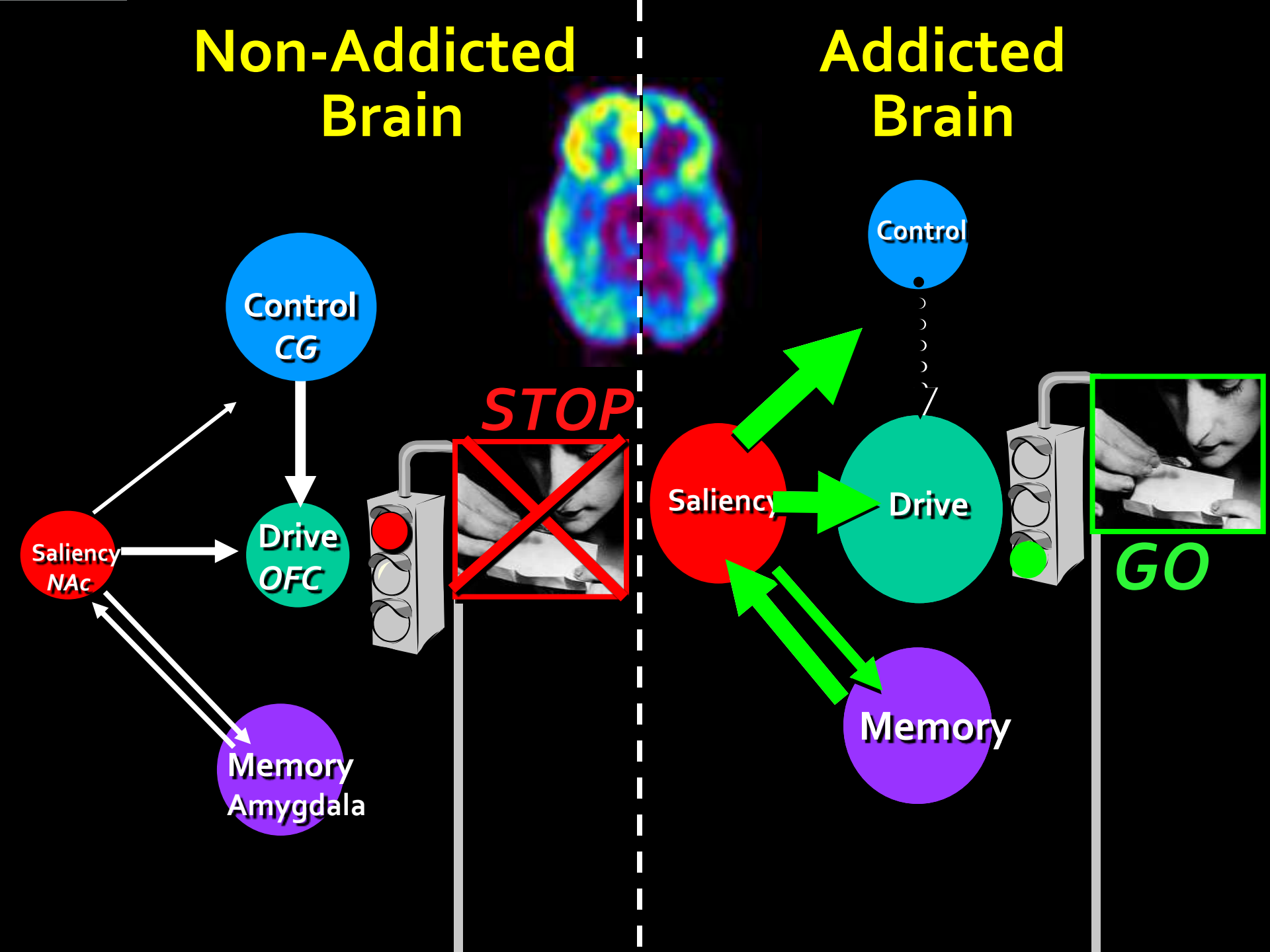
Dopamine is also associated with motivation and executive function via regulation of frontal activity.

The fine balance in connections that normally exists between brain areas active in reward, motivation, learning and memory, and inhibitory control



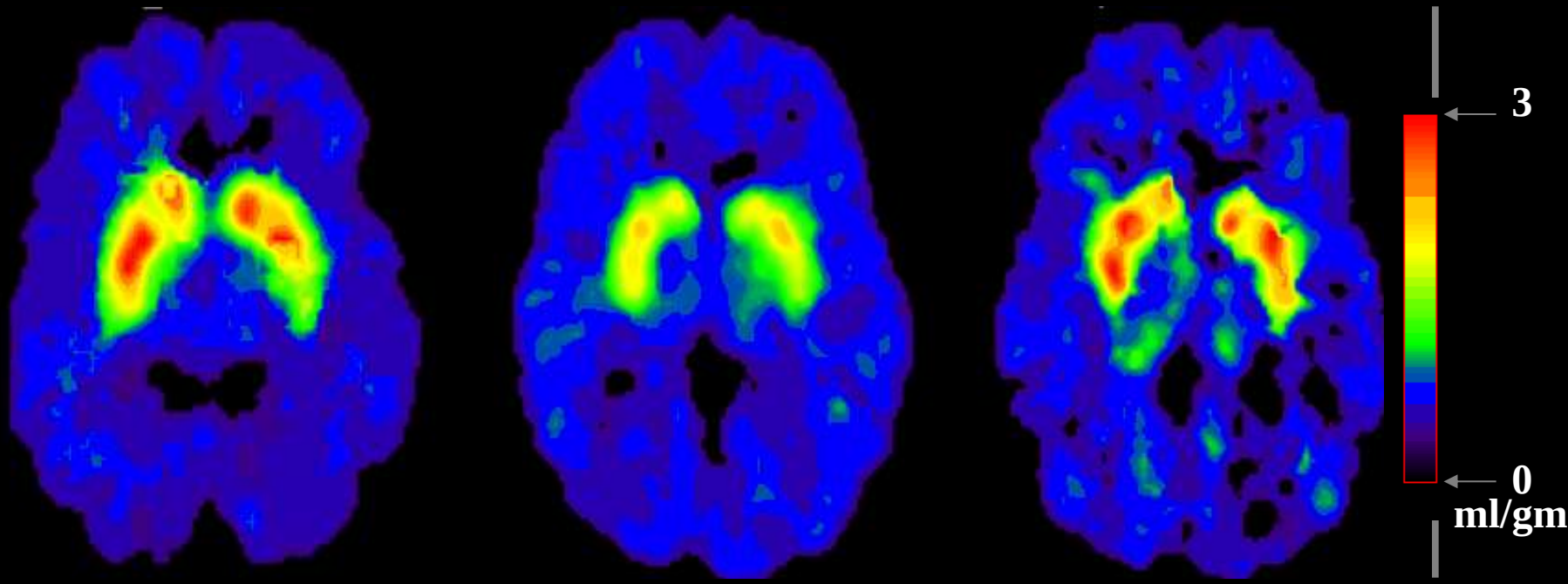
Becomes severely disrupted in

ADDICTION


Non-Addicted Brain
Addicted Brain
Control
CG
Saliency
NAc
Drive
OFC
Memory
Amygdala
STOP
Control
Saliency
Drive
Memory
GO

Addiction is Treatable

Partial Recovery of Brain Dopamine Transporters in Abuser After Protracted Abstinence



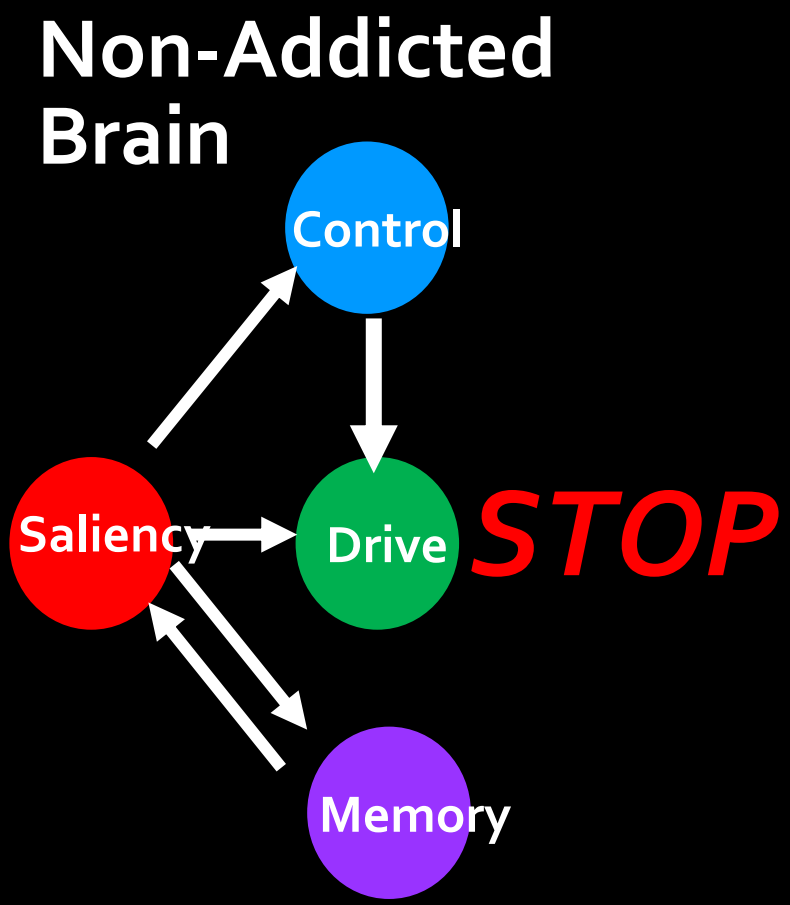
Normal Control

METH Abuser (1 month detox)

METH Abuser (14 months detox)

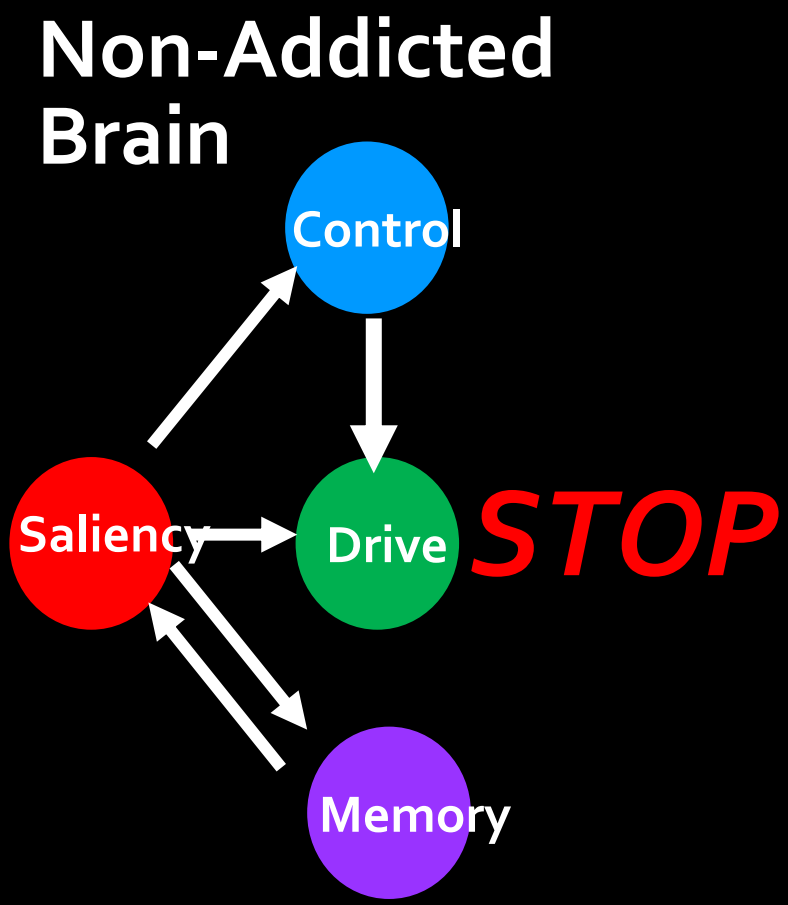
Source: Volkow, ND et al., Journal of Neuroscience 21, 9414-9418, 2001.

Behavioral Treatments



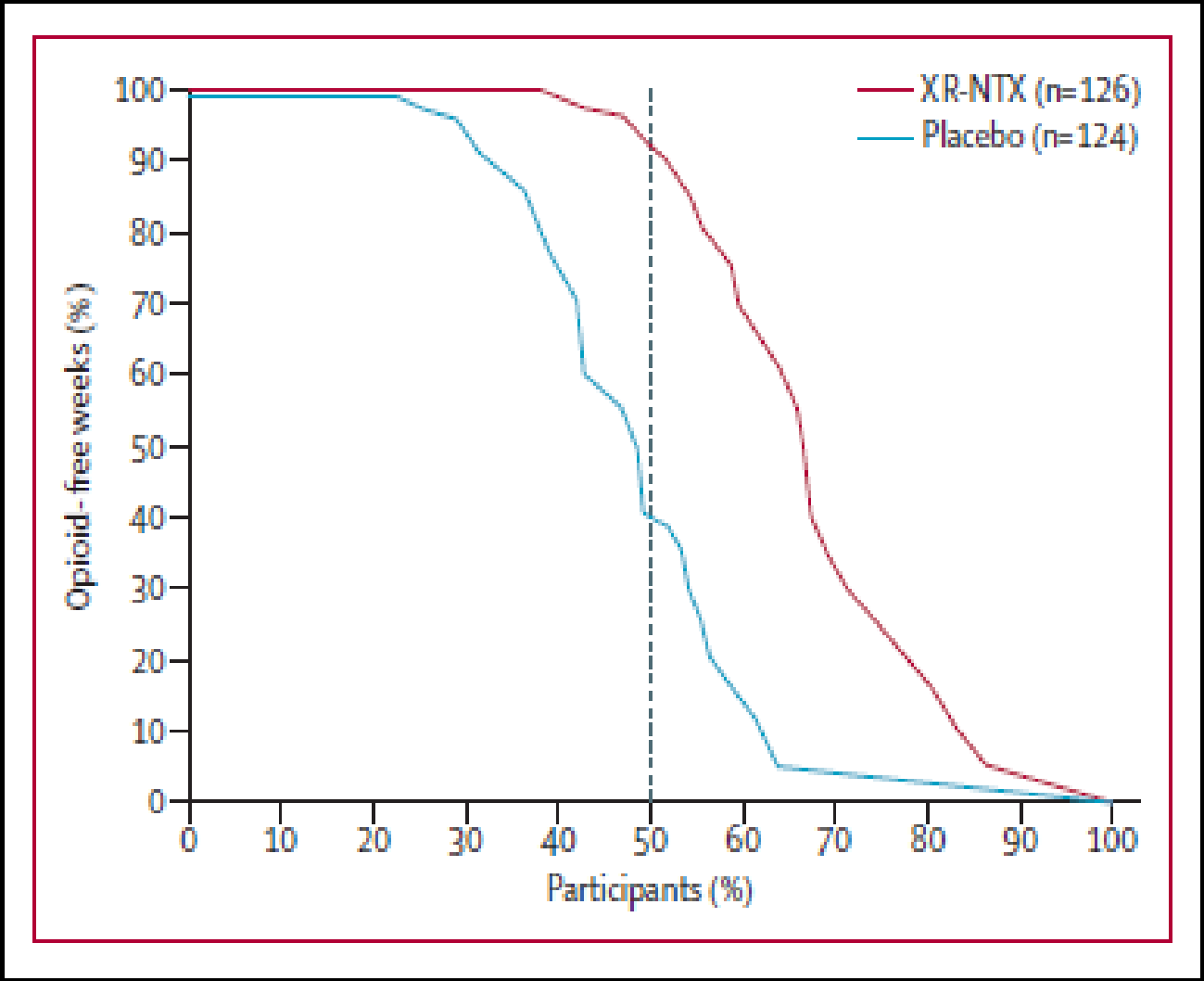
Interfere with drug's reinforcing effects	*Contingency Management*
Executive function/ Inhibitory control	*Cognitive Therapy*
Strengthen prefrontal-striatal communication	*Motivation Therapies*
Interfere with conditioned memories	*Biofeedback Desensitization*
Teach new memories	*Behavioral Therapies*
Counteract stress responses that lead to relapse	*Relaxation Behavioral therapies*

Medication Assisted Treatments



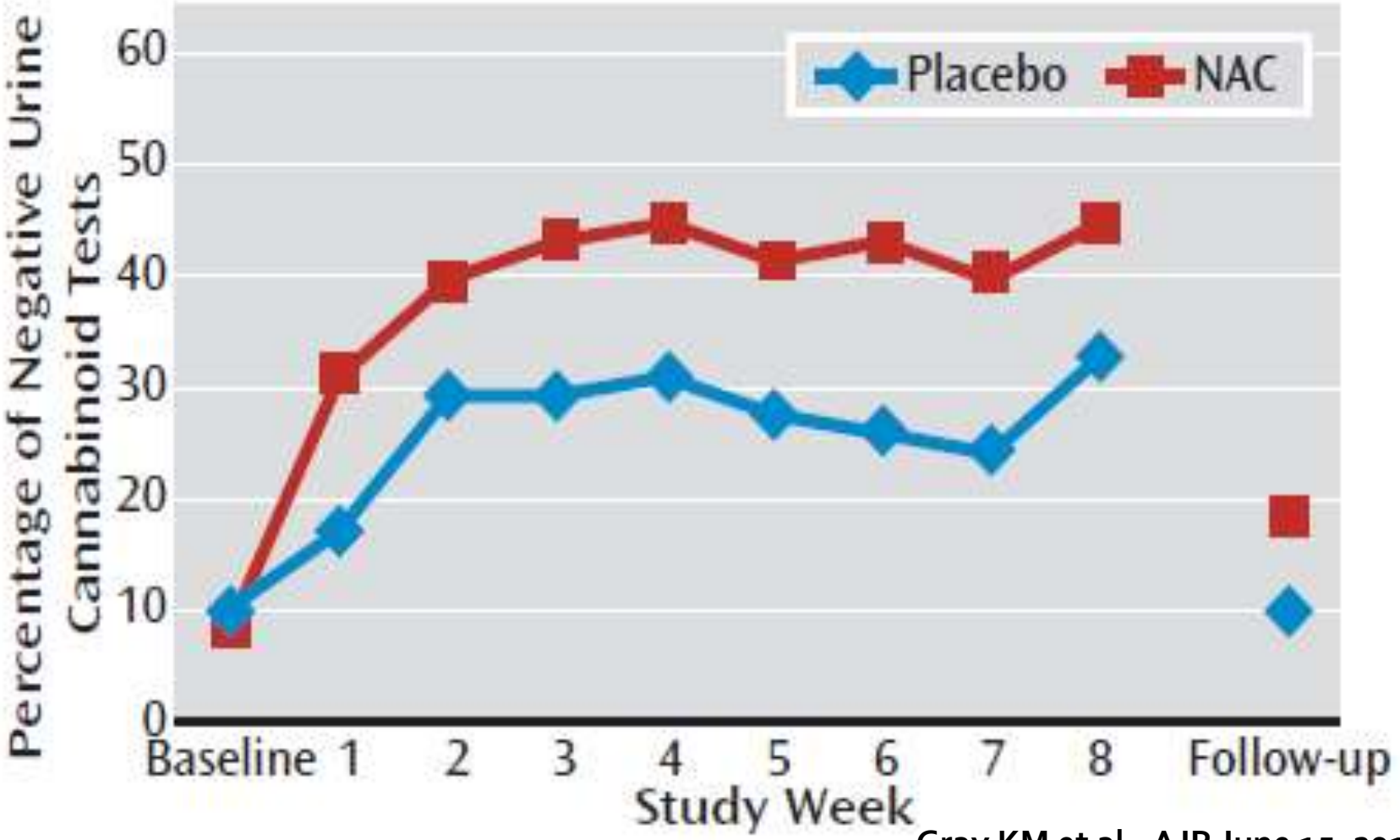
Interfere with drug's reinforcing effects	*Vaccines* *Enzymatic degradation* *Naltrexone* *DA D3 antagonists* *CB_1 antagonists*
Executive function/ Inhibitory control	*Biofeedback* *Modafinil* *Bupropion* *Stimulants*
Strengthen prefrontal-striatal communication	*Adenosine* *A2 antagonists* *DA D3 antagonists*
Interfere with conditioned memories	*Antiepileptic GVG* *N-acetylcysteine*
Teach new memories	*Cycloserine*
Counteract stress responses that lead to relapse	*CRF antagonists* *Orexin antagonists*

Vivitrol Significantly Increases % of Patients with Opioid-free Weeks



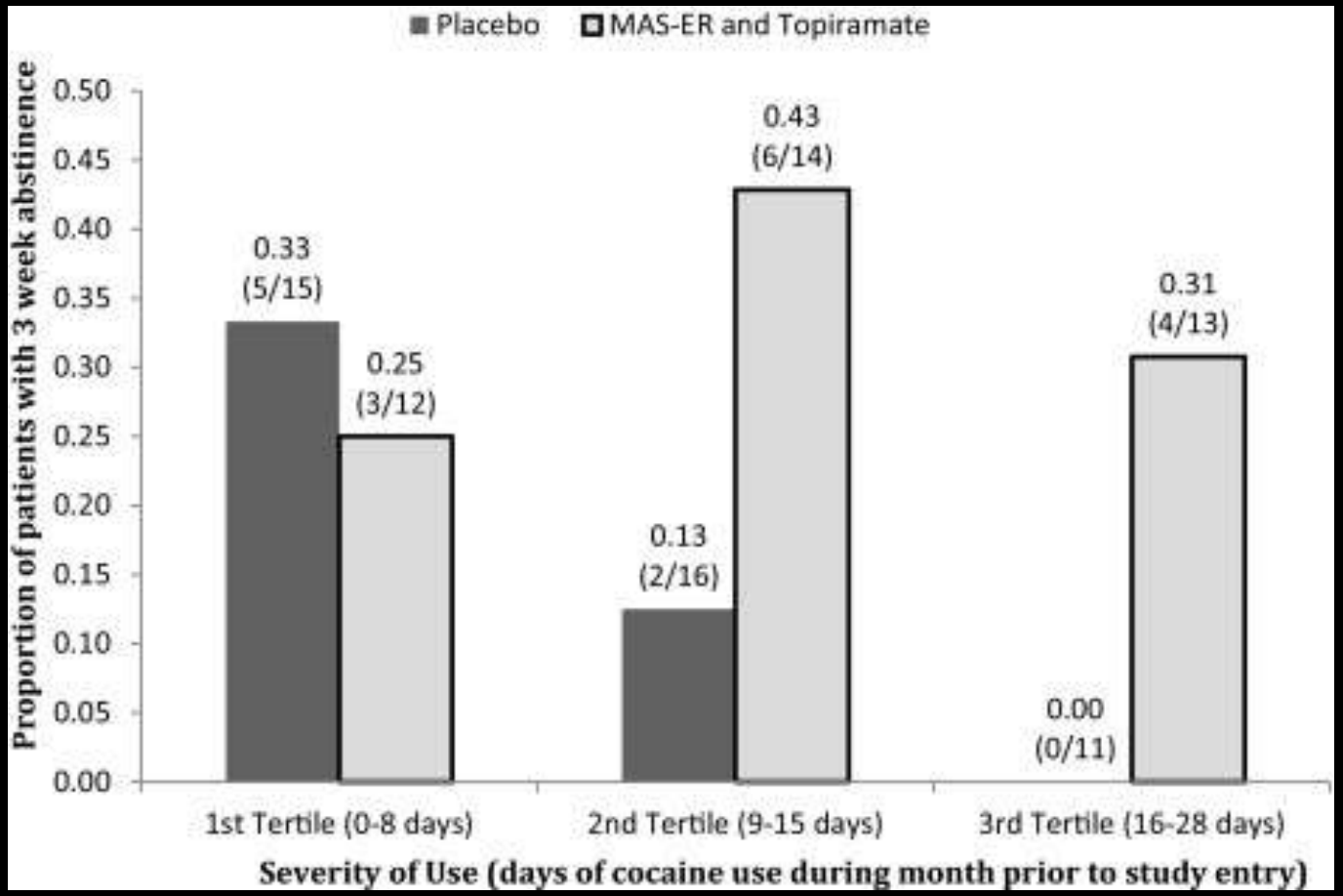
A Double-Blind RCT of N-Acetylcysteine in Cannabis-Dependent Adolescents

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



Gray KM et al., AJP June 15, 2012

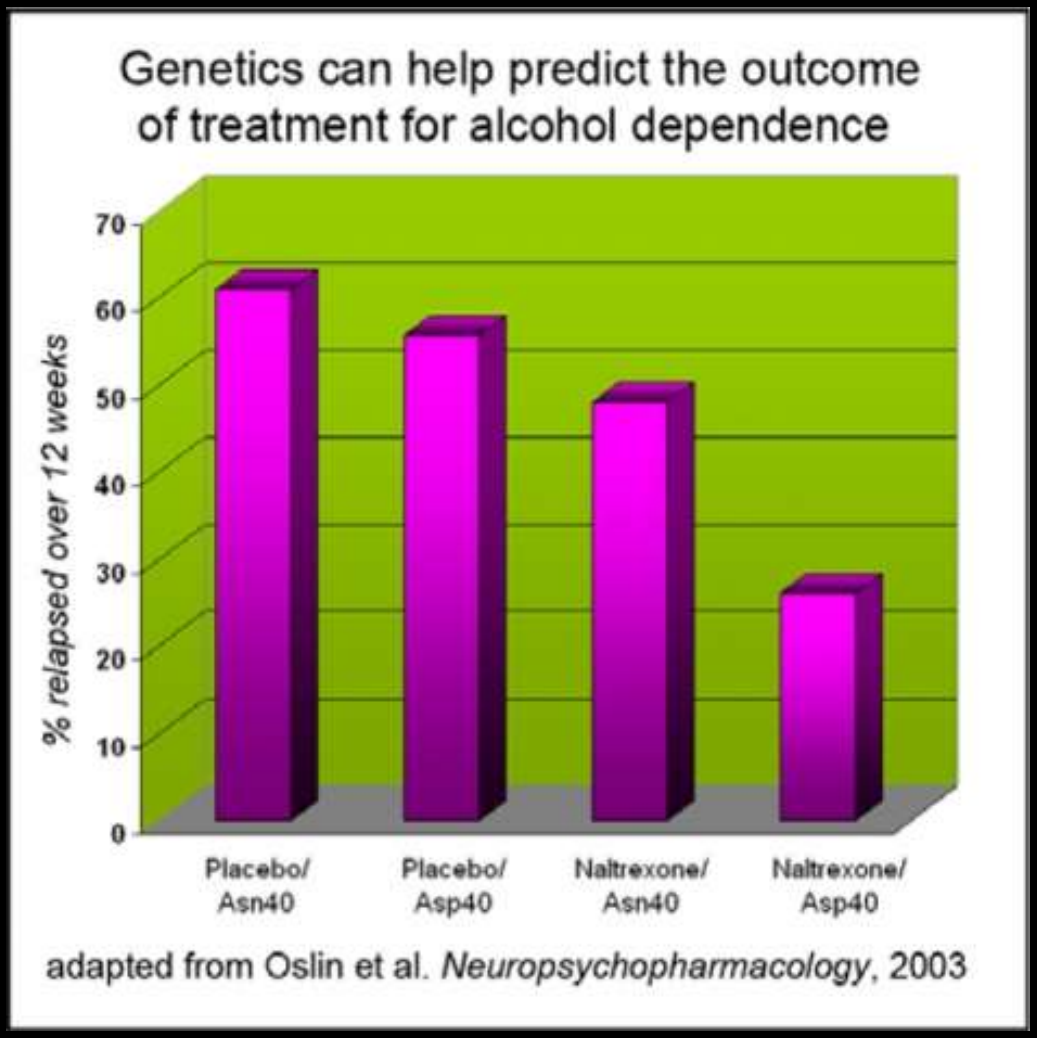
Extended-Release Mixed Amphetamine Salts and Topiramate for Cocaine Dependence



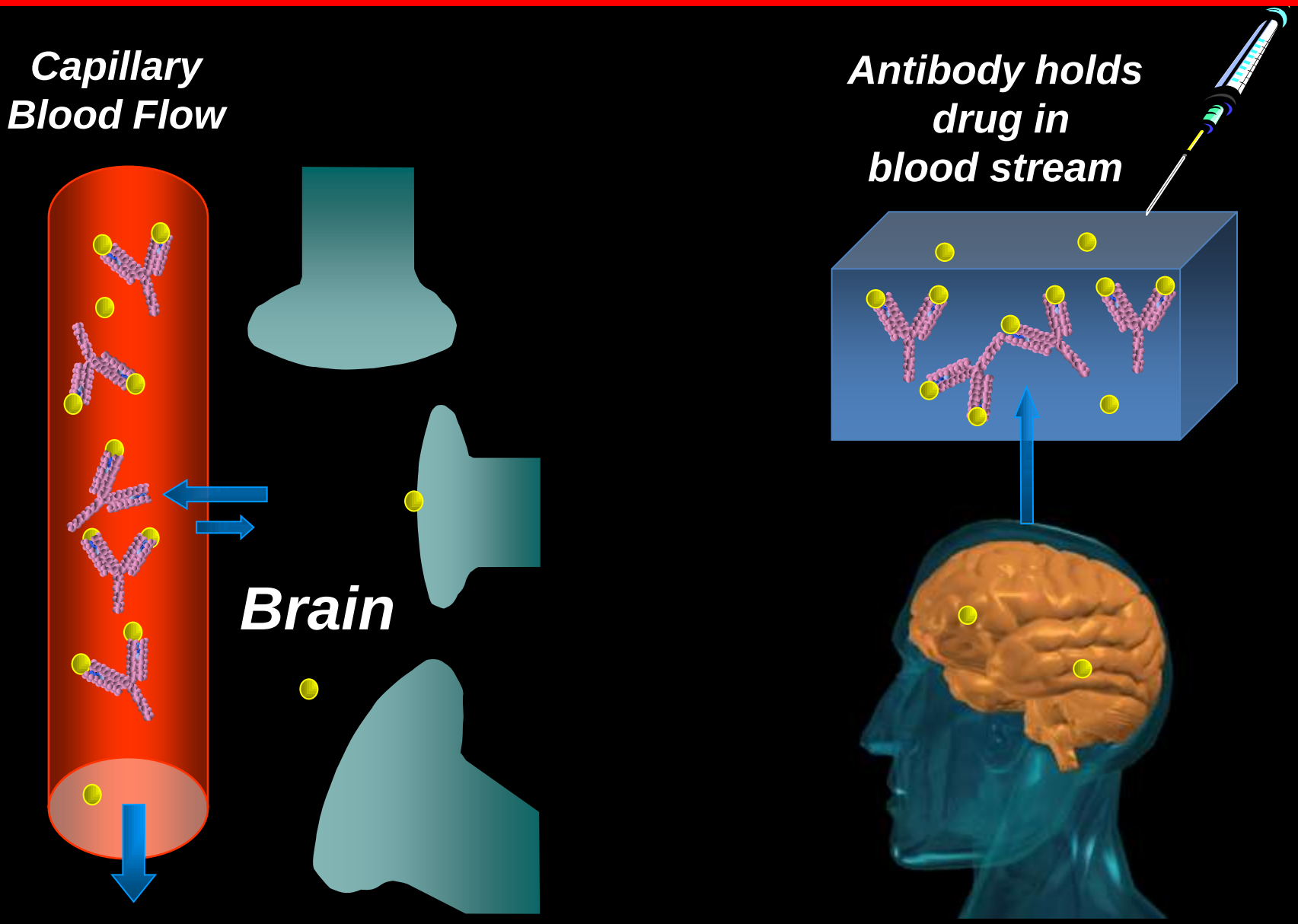
Combination of MAS-ER and topiramate was superior to placebo in achieving 3 week abstinence in cocaine-dependent individuals

Mariani et al., Biol Psychiatry 2012

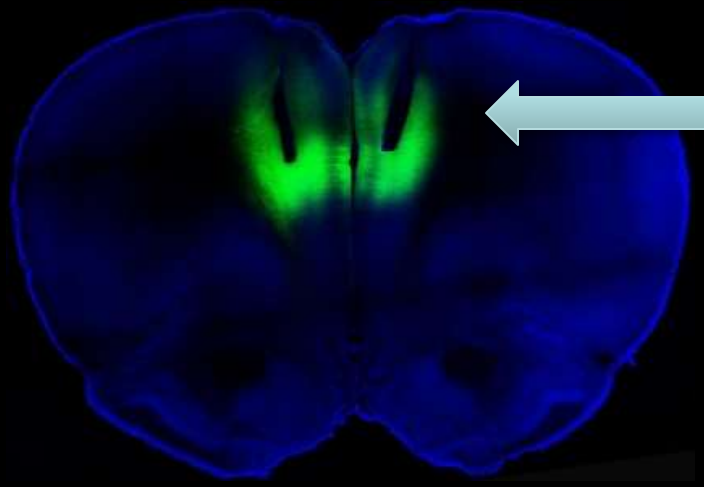
Genetic Variability and Personalized Treatment



Anti- Drug Vaccine Development



Cutting Edge Research:
Targeted Stimulation of the Pre-frontal Cortex as a Promising Treatment for Cocaine Addiction



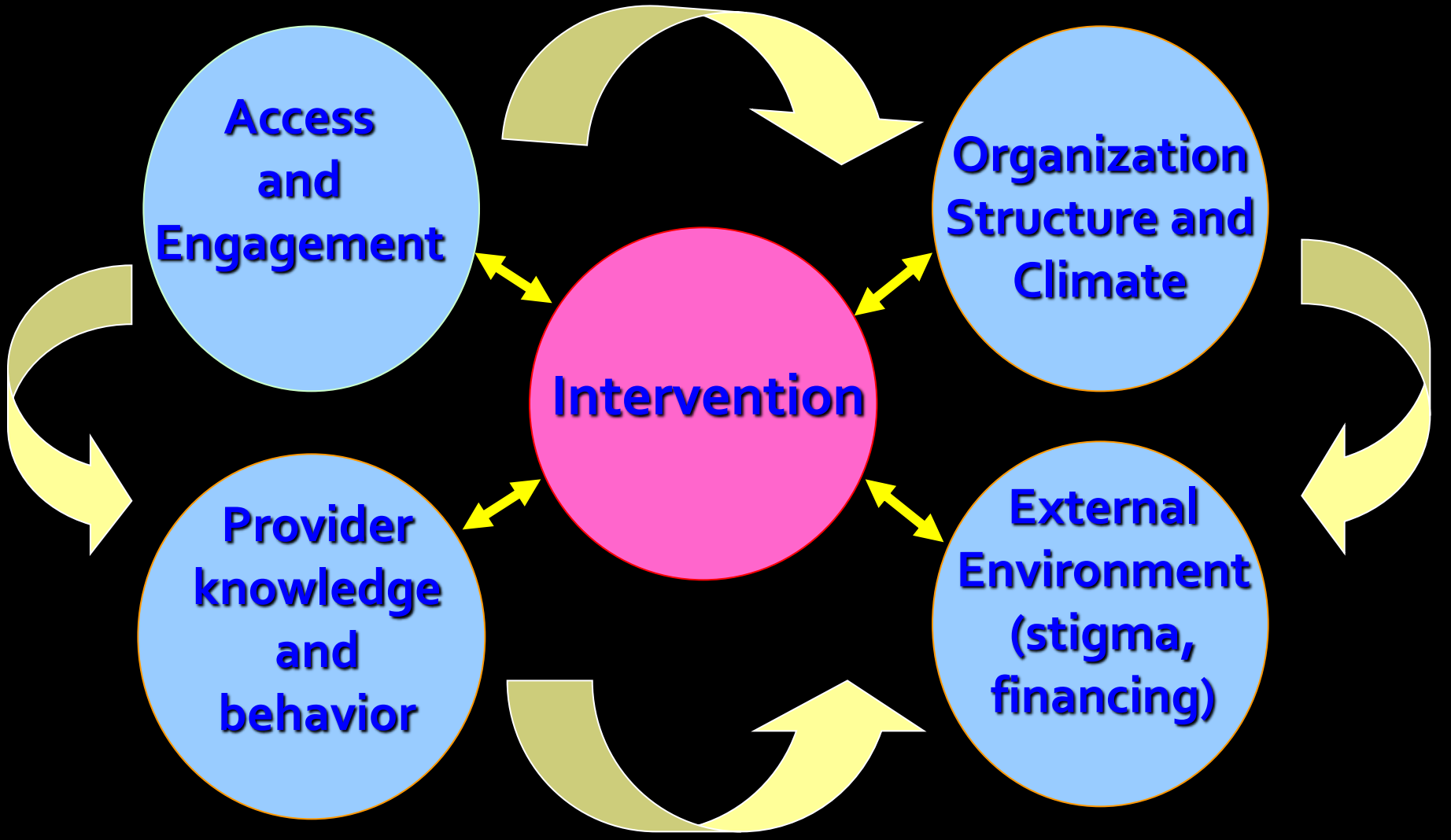
Optogenetic stimulation results in:
- reduced cocaine-seeking in addicted rats
- increased cocaine seeking in non-addicted rats

-Evidence for a cocaine-induced deficit within a brain region involved in addictive disorders

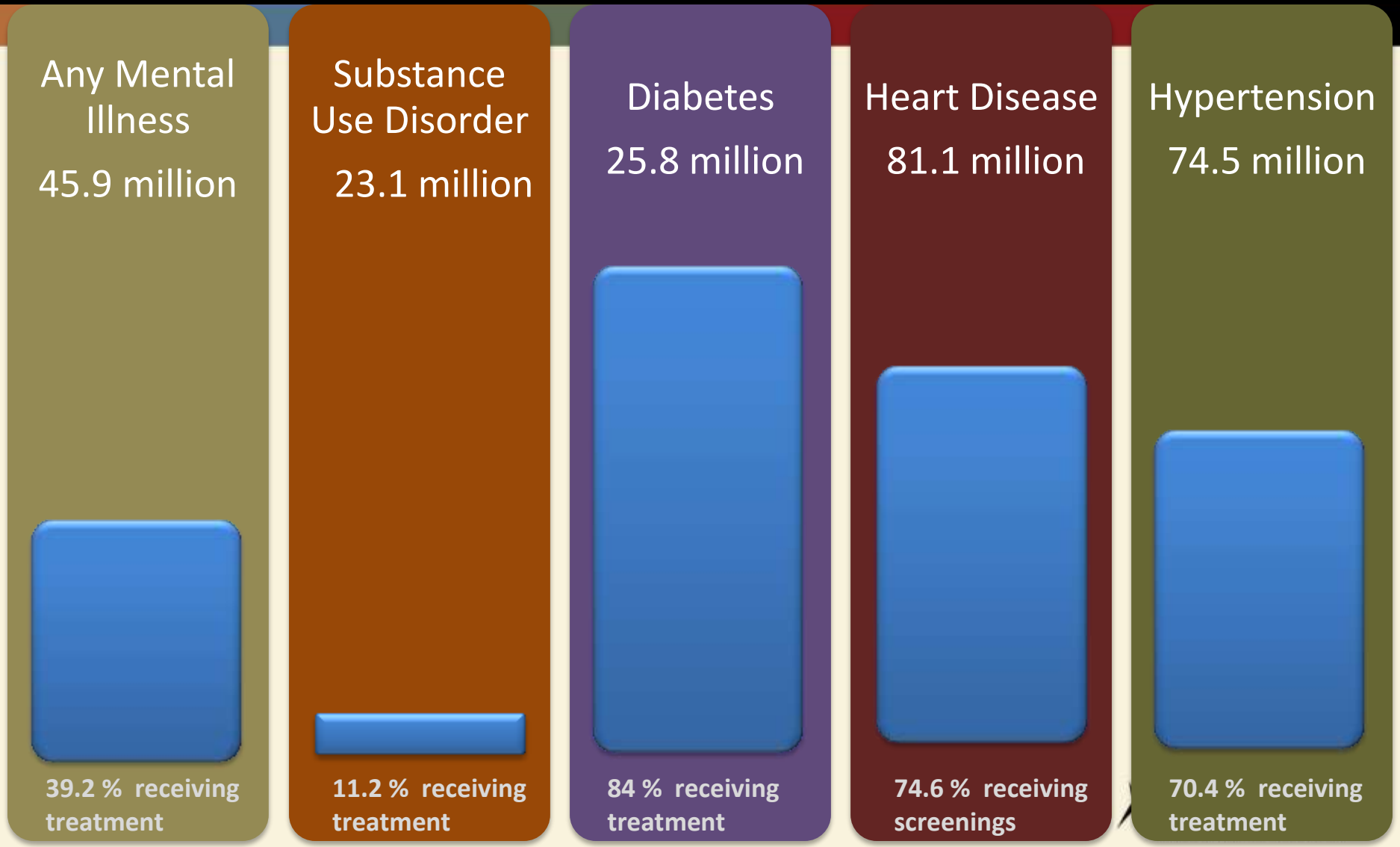
-Rapid translation to clinical human trials via non-invasive brain stimulation

Chen, et al (2013), *Nature*

Translating Research into Practice



Receipt of SUD Services Lags Behind other Chronic Disorders

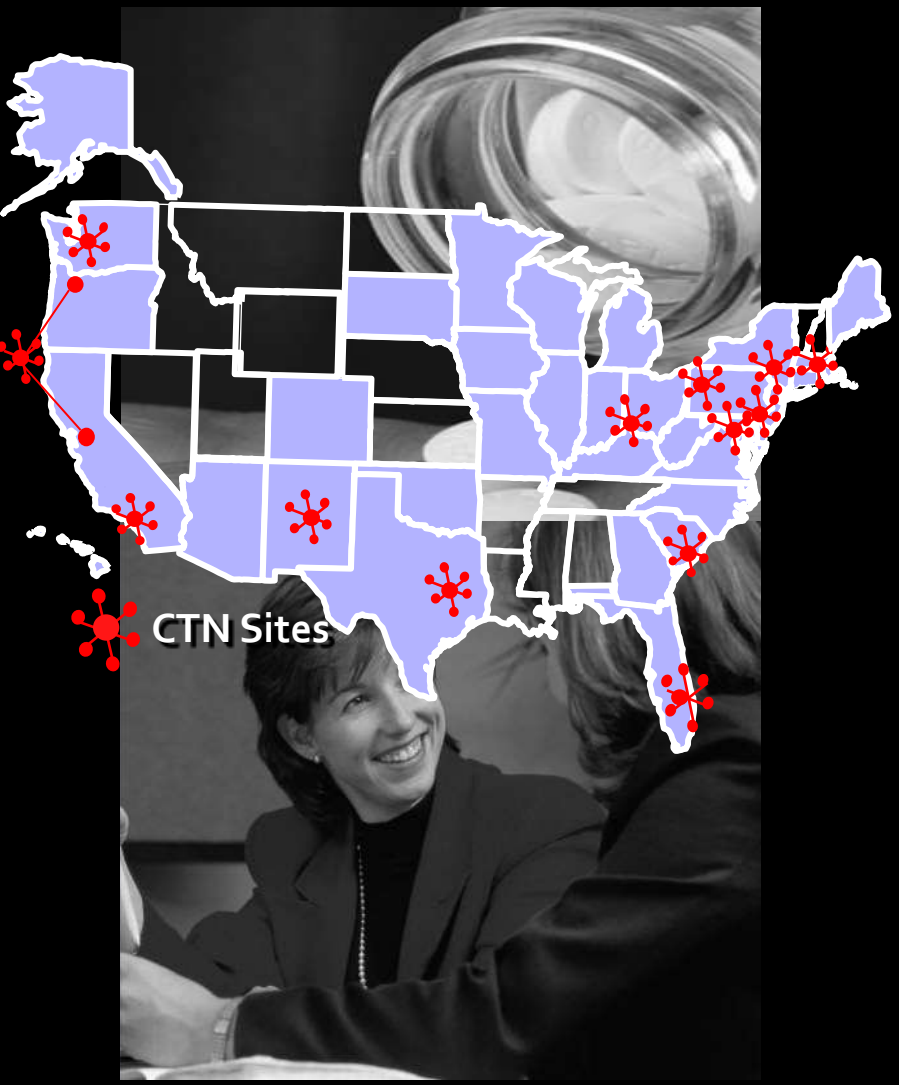


Low Uptake of Pharmacotherapy in Specialty Programs in 2007

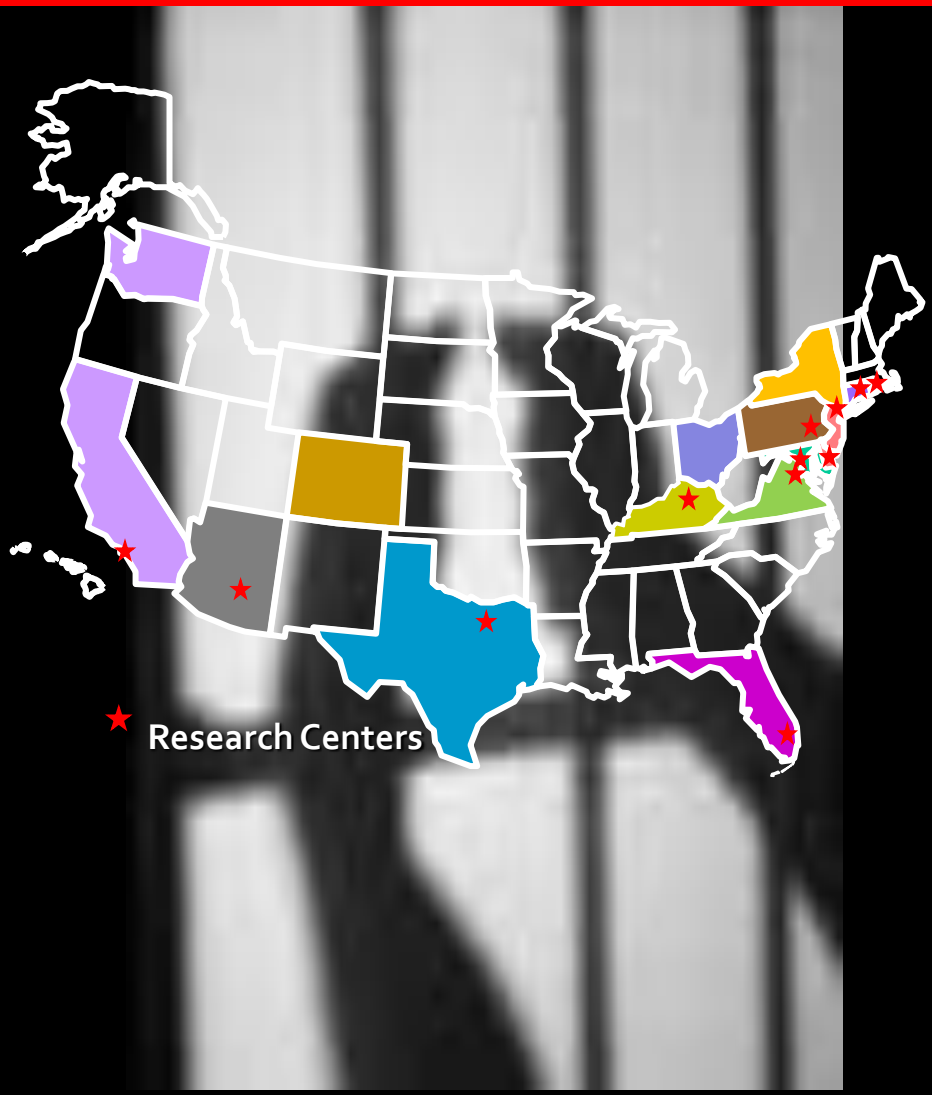
	As % of all programs surveyed (N=345)	Within adopting programs, % of eligible patients receiving Rx
Psychiatric meds	54.5	70.1
Opioid tx meds:		
Methadone	7.8	41.3
Buprenorphine	20.9	37.3
Tablet naltrexone	22.0	10.9
Alcohol meds:		
Disulfiram	23.8	8.1
Tablet naltrexone	32.2	12.4
Acamprosate	32.5	17.5
Injectable naltrexone	15.9	(too new to report)

Knudsen et al, 2011, J Addict Med; 5:21-27

National Drug Abuse Treatment Clinical Trials Network (CTN)

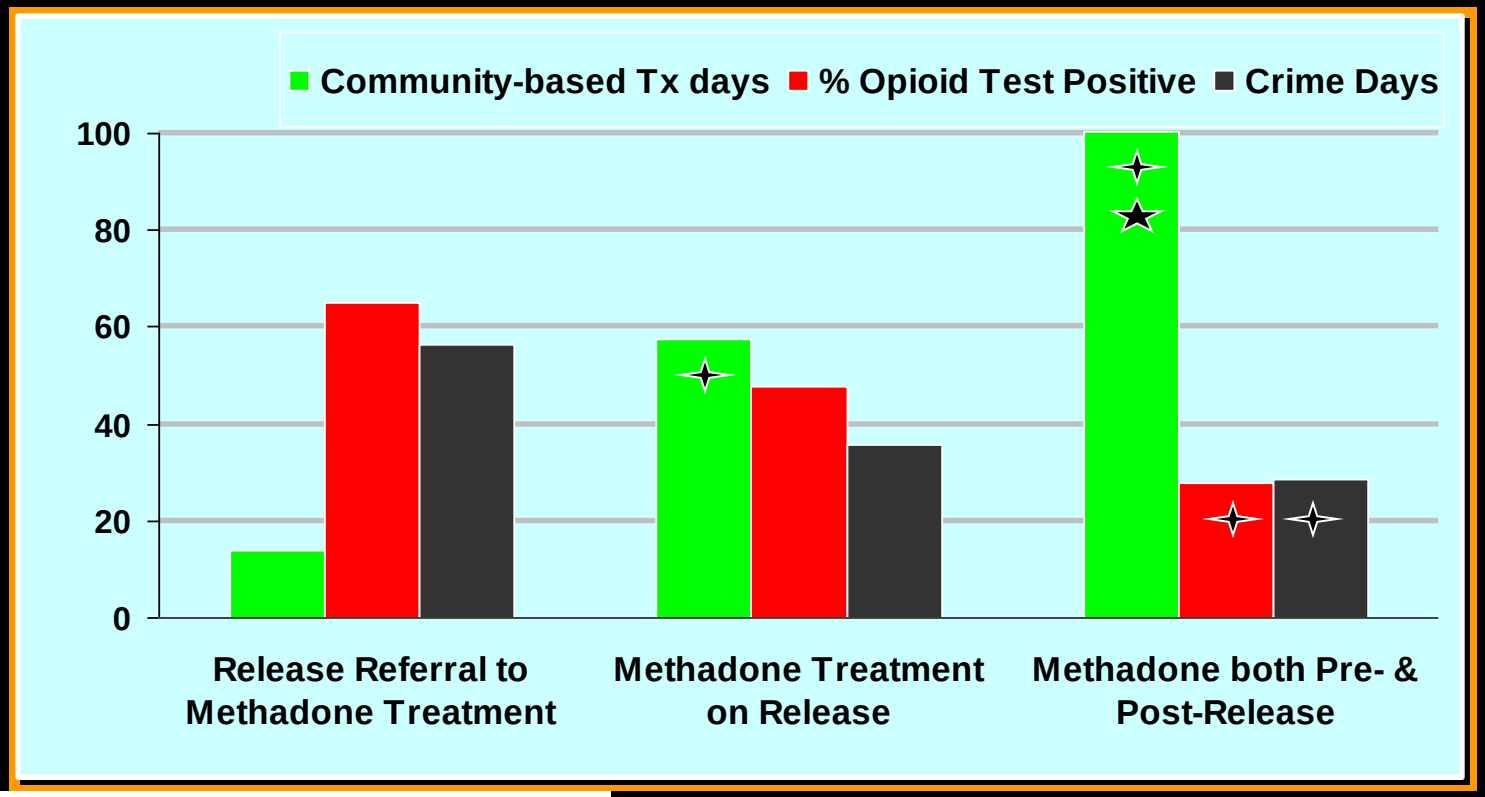


NIDA Criminal Justice Drug Abuse Treatment Studies (CJ-DATS)



Medications and Criminal Justice Populations

Methadone Experiment: 6 Mo Post Release (N=201)



✦-- *signif. diff from referral*
★-- *signif. diff from treatment only on release*

Source: Gordon, M.S., Kinlock, T.W., Schwartz, R.P., O'Grady, K.E. (2008). Addiction. A Randomized Clinical Trial of Methadone Maintenance for Prisoners: Findings at 6-Months Post-Release.

Affordable Care Act (ACA)

- Extends coverage to more than 30 million persons, many at high risk for drug abuse
- Promotes use of electronic health records
- Fundamentally changes the ways drug abuse prevention and treatment services are financed
- Focuses on screening and prevention
- Emphasizes central role of primary care settings

NIDA Priority Areas

Prevention

Genetics
Environment
Development

Treatment

Neural mechanisms
Brain circuitry

Consequences

HIV/AIDS
Fetal Exposure

HAART as HIV Prevention

NIDA Avant Garde 2008: Dr. Julio Montaner, Univ. of British Columbia

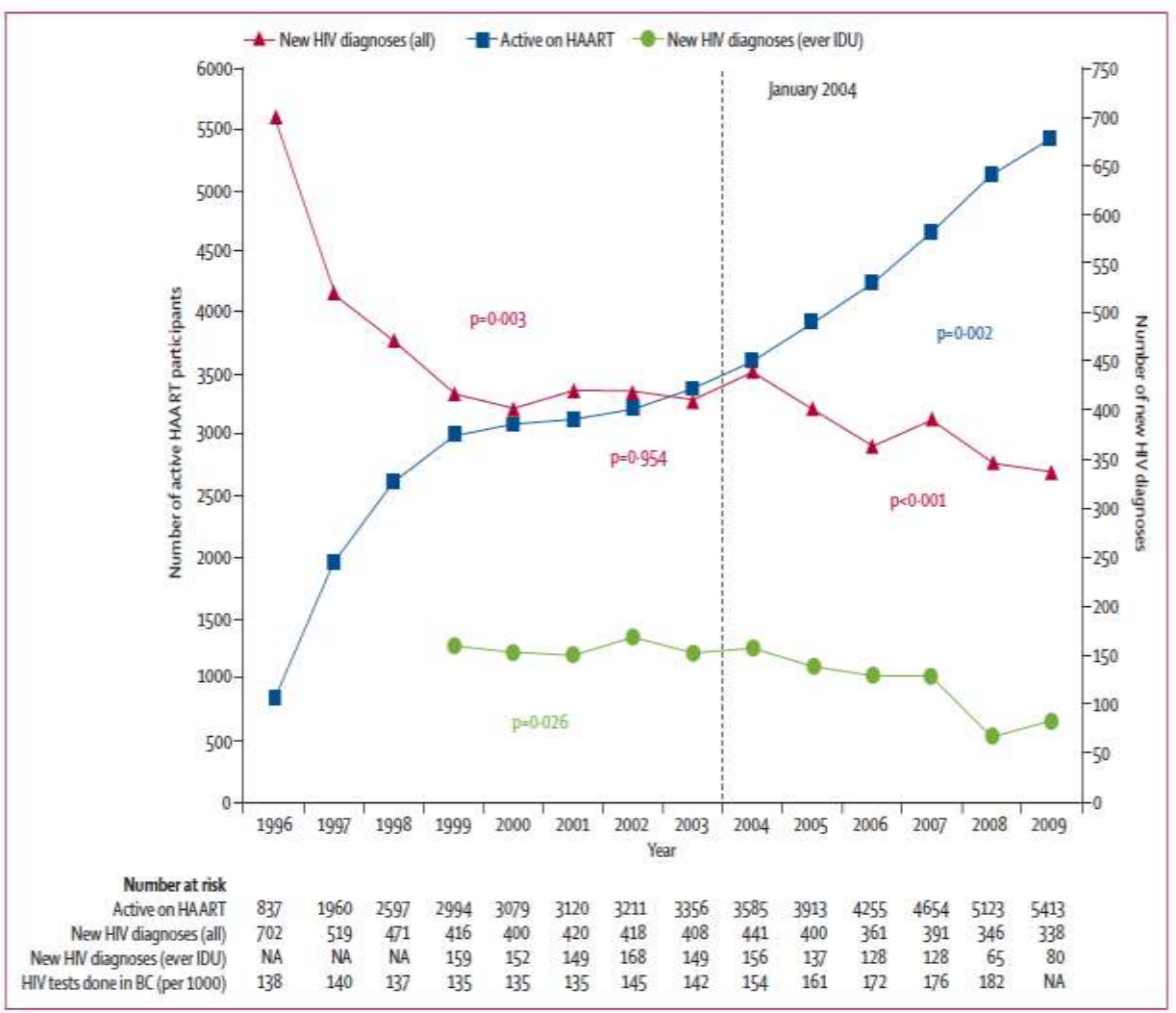


Figure 1: Number of active HAART participants and number of new HIV diagnoses per year in British Columbia, Canada, 1996–2009
p values are for trend and were obtained from the generalised additive model. Injecting drug user (IDU) refers to individuals who have ever injected illicit drugs. HAART=highly active antiretroviral therapy. BC=British Columbia. NA=not available.

Montaner et al., Lancet 2008

Resources

NIDAMED

- Centers of Excellence
  - Boston University
  - Drexel/University of Pennsylvania
  - University of Massachusetts
  - Tufts University
  - University of North Dakota
  - Creigton University
- Screening tools
- CMEs on prescription drug abuse

NIDAMED

doc.com

Innovative E-Learning Rx Drug Abuse CME:

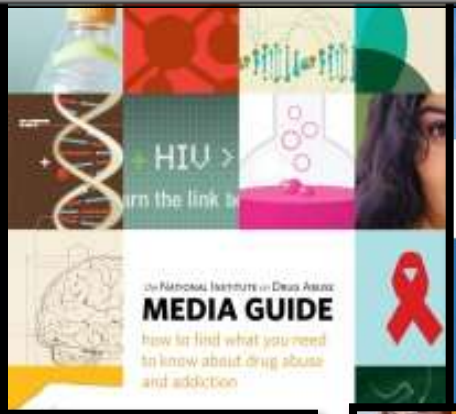
NIDA and Medscape, Funded by ONDCP, October 2012

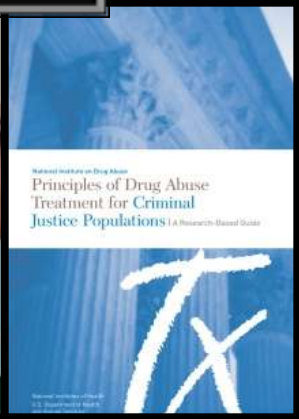
Safe Prescribing for Pain

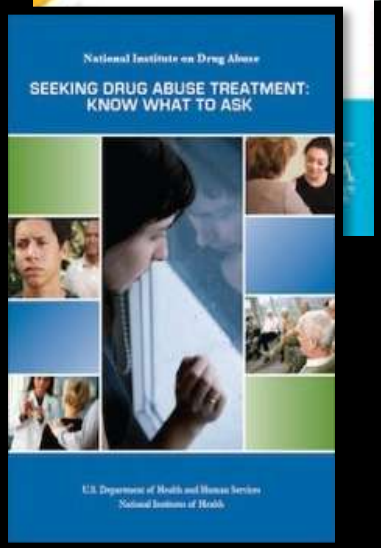
Managing Pain Patients Who Abuse Rx Drugs

NIDAMED

www.drugabuse.gov







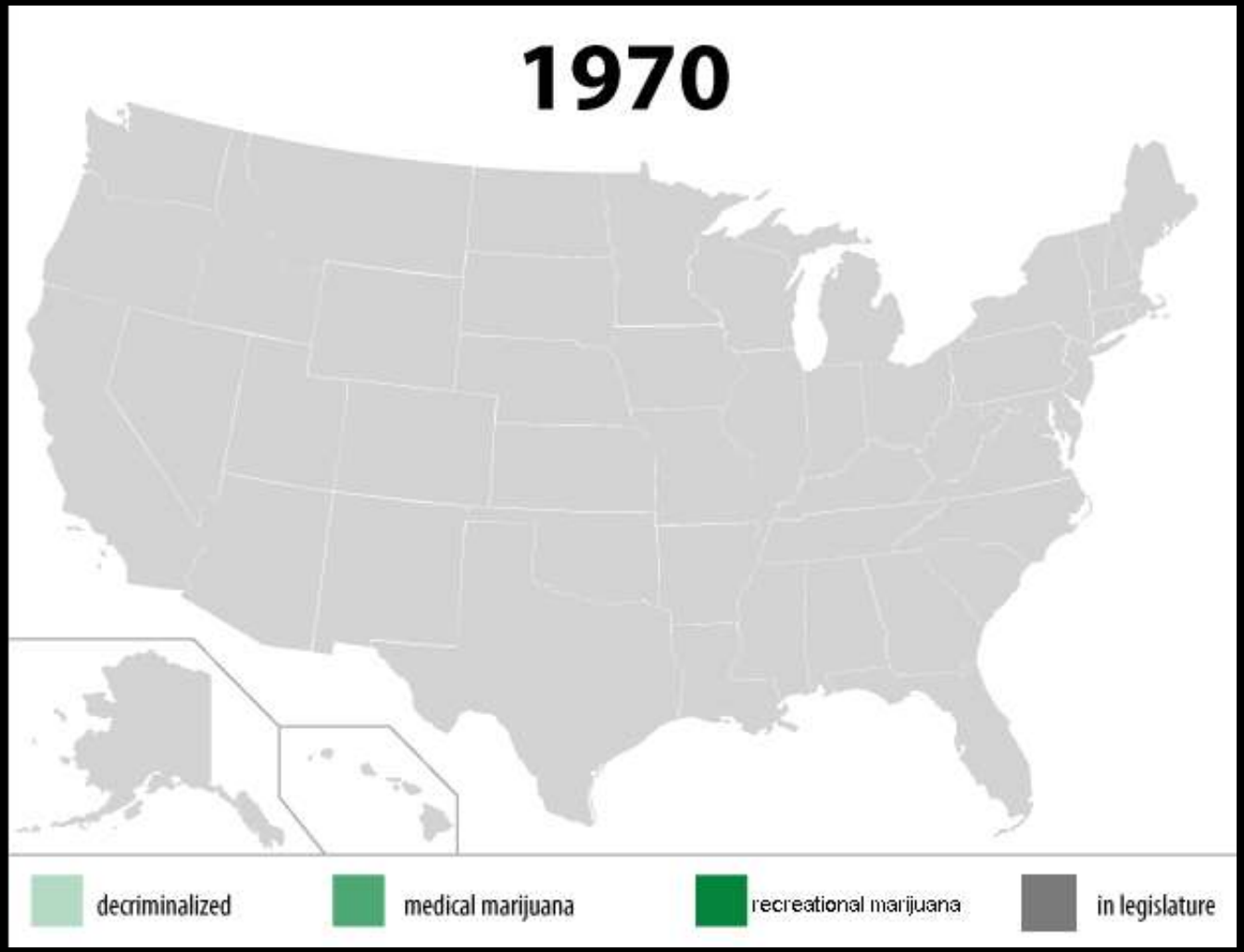
NIDAMED

Any Questions?

- Jack.stein@nih.gov

So, what's going on with Marijuana??

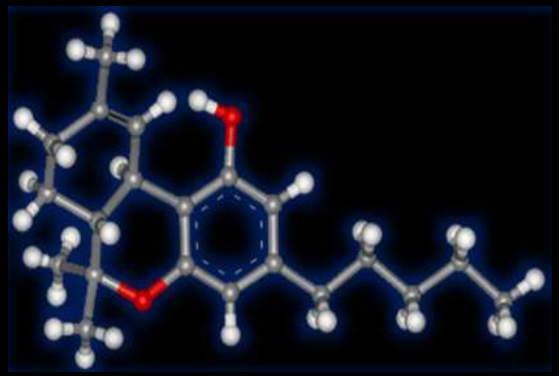
Shifting policy landscape



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

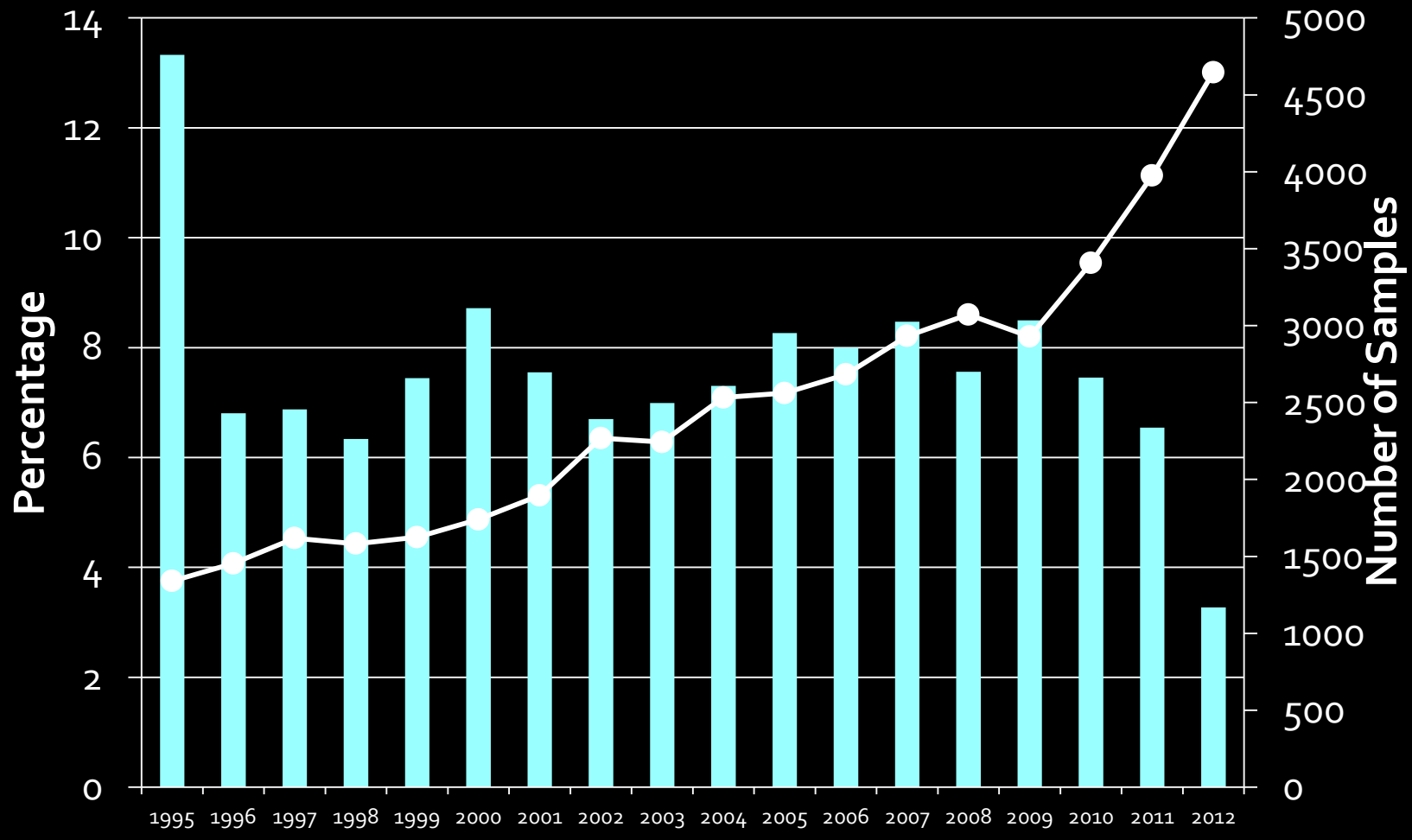
- Over 111 million Americans have tried it at ….least
- An estimated 2.4 million Americans used it for the first time in 2012

Tetrahydrocannabinol (THC) = Active Ingredient in Marijuana



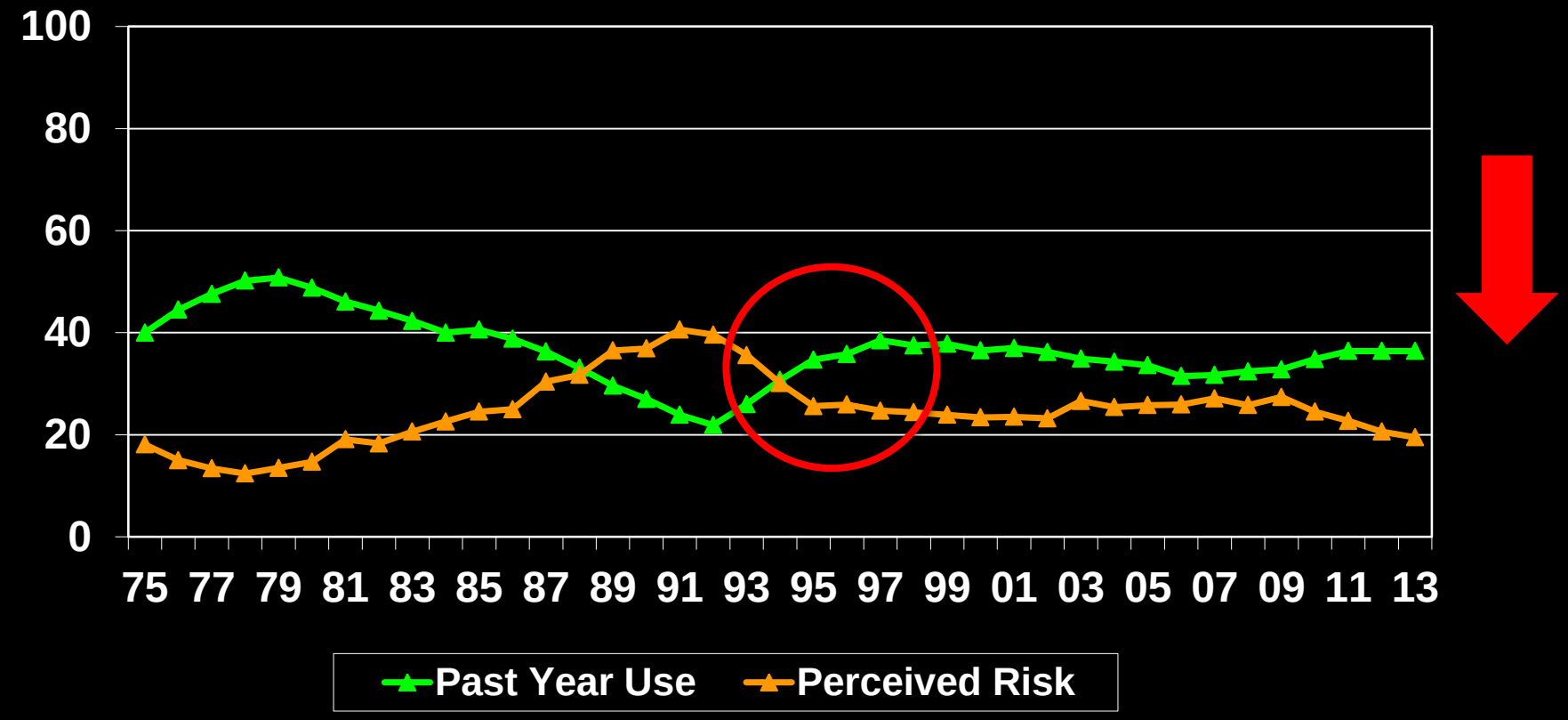
Source: 2012 National Survey on Drug Use and Health, SAMHSA

Average Delta-9 THC Concentration Per Year



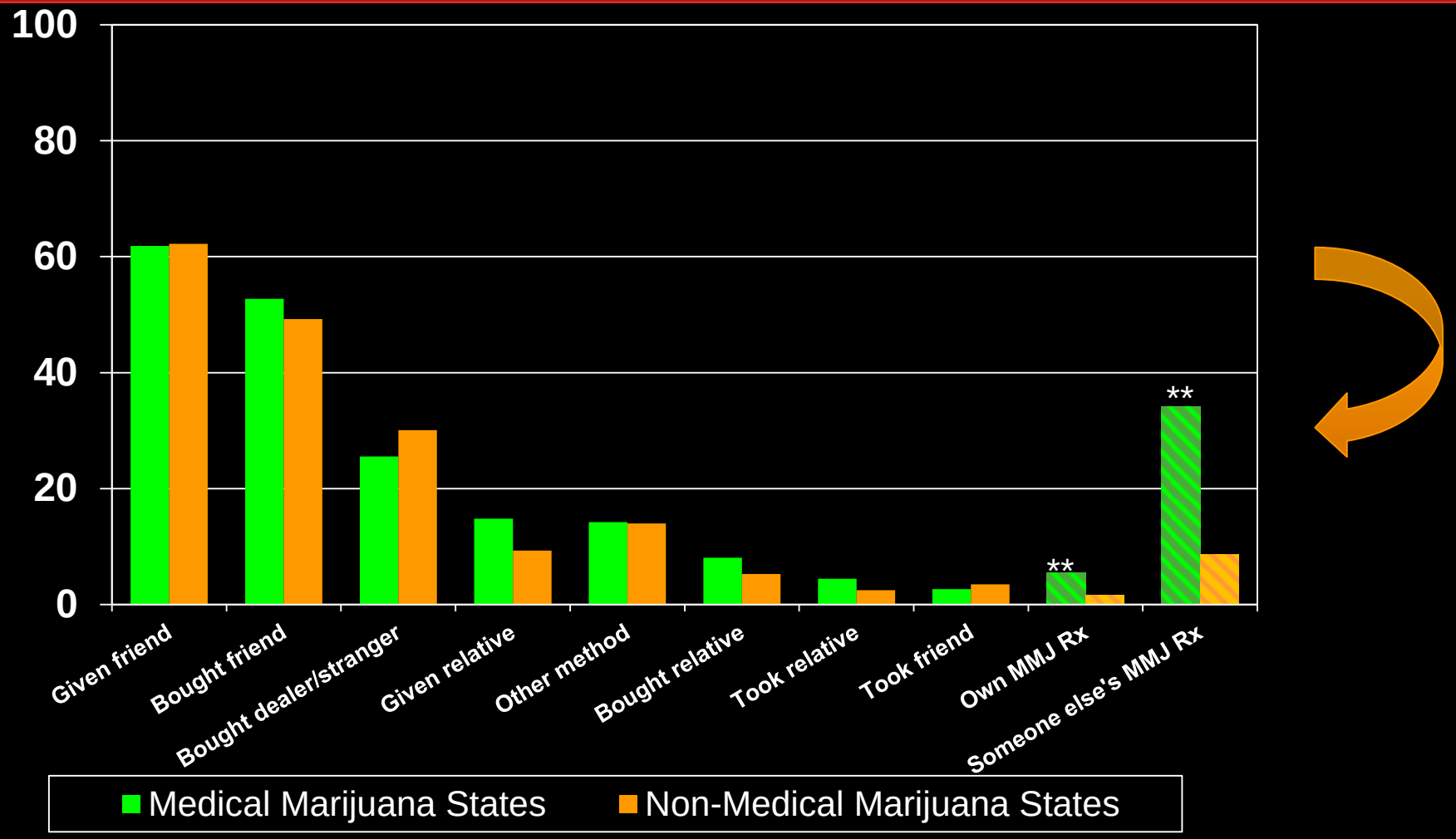
The Marijuana Farm: University of Mississippi

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



SOURCE: University of Michigan, 2013 Monitoring the

Source of Marijuana* among 12th Graders in 2012 and 2013, by State Policy

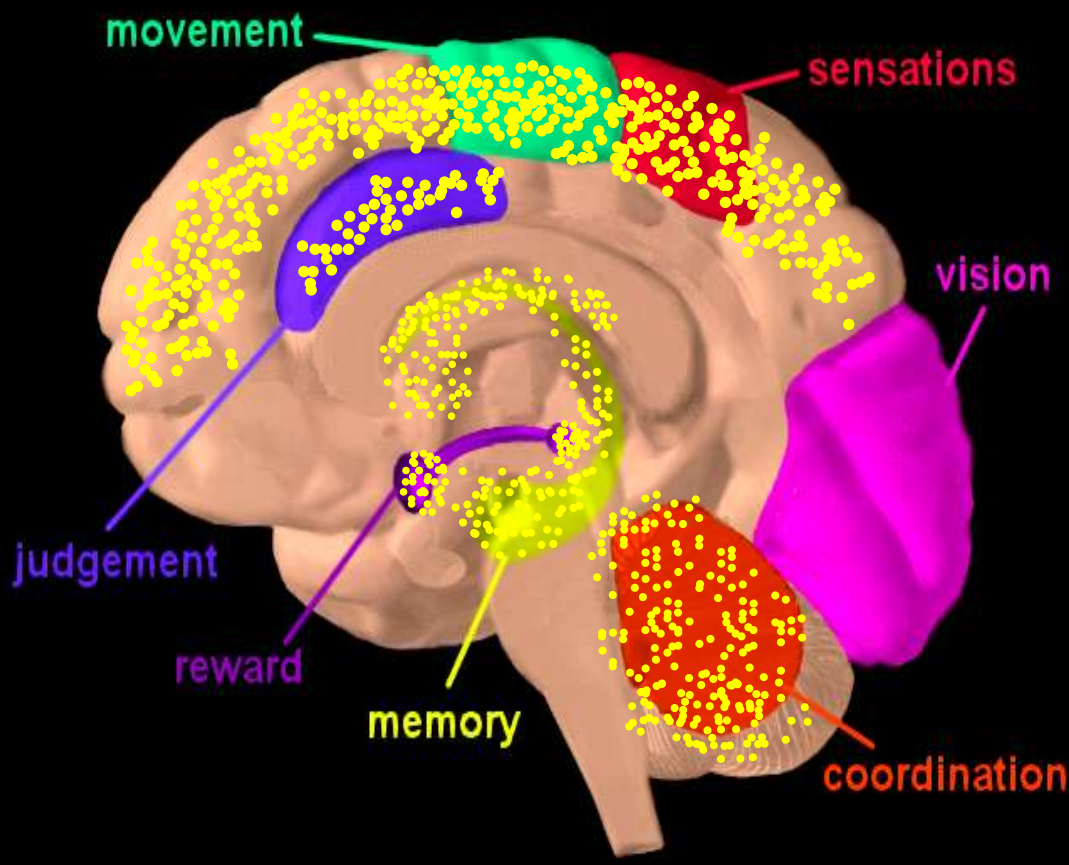


*Categories not mutually exclusive
** Statistically significant difference

SOURCE: University of Michigan, 2013 Monitoring the

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



Marijuana: What's the harm?

- Addiction
- Motor Vehicle Accidents
- Motivation, Mood, Paranoia, Psychosis

Marijuana addiction is also linked to a withdrawal syndrome that can make it hard to quit. Symptoms include:

- irritability,
- sleeping difficulties,
- craving,
- anxiety, and
- increased aggression.

Marijuana withdrawal is now recognized in DSM-5