The Science of Addiction

Immersion Training in Addiction Medicine Program 2018

April 23, 2018

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Boston Medical Center EXCEPTIONAL CARE. WITHOUT EXCEPTION.

Grayken Center for Addiction Boston Medical Center

Agenda

- Definitions
- Epidemiology and Trends
- Understanding Substance Use and Addiction (Use Disorders)
- And more…

Substance Use Disorder

Substance Use Disorder a diagnostic term in DSM-5 recurrent use of alcohol or other drugs causing significant impairment, such as health problems, disability and failure to meet major responsibilities

It combines the DSM-IV categories of **substance abuse** and **dependence** into a single disorder measured on a continuum from **mild, moderate,** or **severe**

American Psychiatric Association DSM-5 (2013)

Addiction

Addiction indicates the most severe, chronic stage of Substance Use Disorder (synonymous with "**severe Substance Use Disorder**")

It is a primary, chronic disease of the brain reward, motivation, memory and related circuitry

Volkow ND et al. *N Engl J Med*. 2016

Some Important Organizations (Acronyms)

- **NIDA** (National Institute on Drug Abuse)
  - supports and conducts biomedical and behavioral research on the causes, consequences, treatment, and prevention research on drug use and addiction

- **NIAAA** (National Institute on Alcohol Abuse and Alcoholism)
  - supports and conducts biomedical and behavioral research on the causes, consequences, treatment, and prevention of alcoholism and alcohol-related problems

Some Important Organizations (Acronyms)

- **SAMHSA** (Substance Abuse and Mental Health Services Administration)
  - a branch of the U.S. Department of Health and Human Services charged with improving the quality and availability of prevention, treatment, and rehabilitative services for substance use and mental illnesses

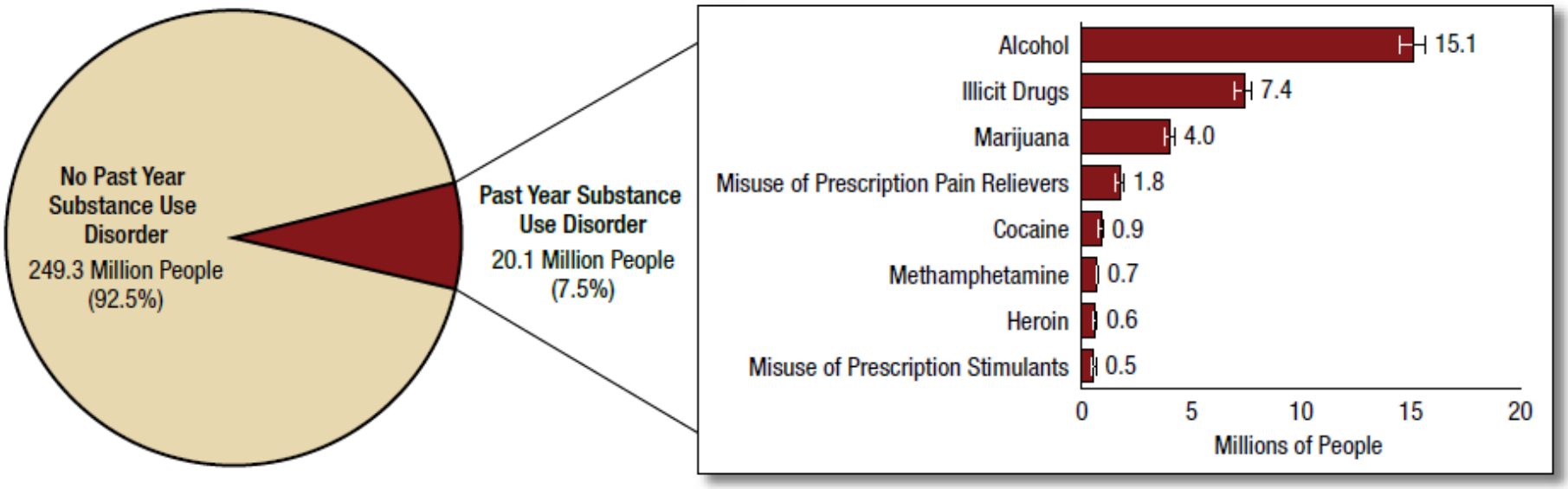
- **ONDCP** (Office of National Drug Control Policy)
  - establishes policies, priorities, and objectives to eradicate illicit drug use, manufacturing, and trafficking, drug-related crime and violence, and drug-related health consequences

Trends: Sources of Data

- **National Survey on Drug Use and Health (NSDUH)**
  - annual since 1971, SAMHSA survey on use of illicit drugs, alcohol, and tobacco in the US civilian, noninstitutionalized population aged ≥12 years. Face-to-face interviews at their place of residence obtained from approximately **67,500 individuals**

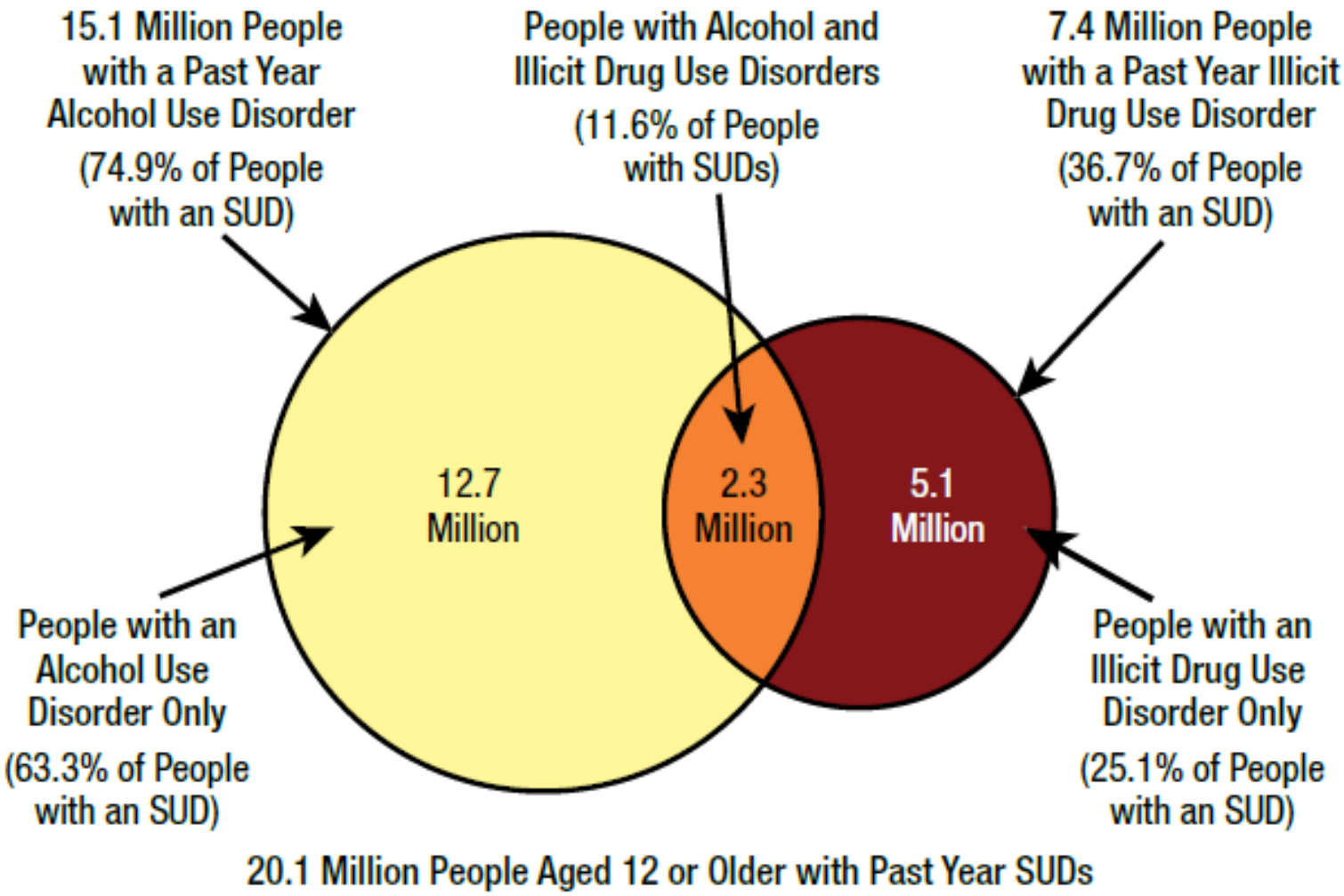
- **Monitoring the Future (MTF)**
  - annual since 1975, NIDA funded survey of 8th, 10th, and 12th graders measuring drug, alcohol, and cigarette use by the University of Michigan. About **44,000 students from 360 public and private schools** are surveyed

Past Year Substance Use Disorder



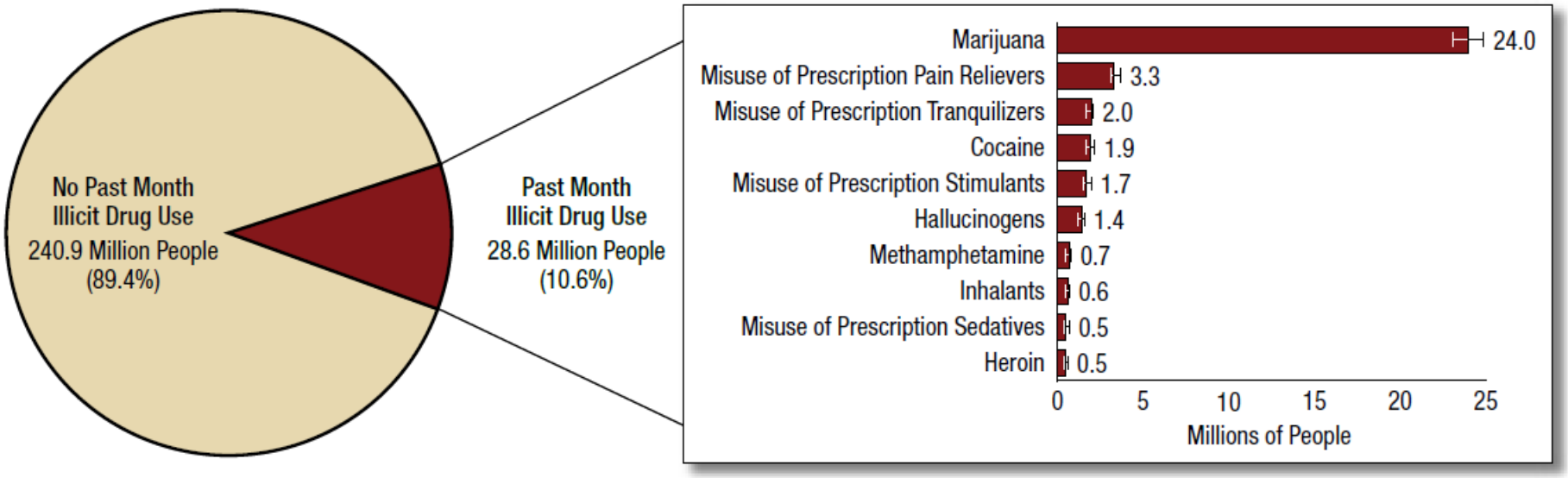
SAMHSA. (2017). Results from the 2016 National Survey on Drug Use and Health

Past Year Substance Use Disorder



SAMHSA. (2017). Results from the 2016 National Survey on Drug Use and Health

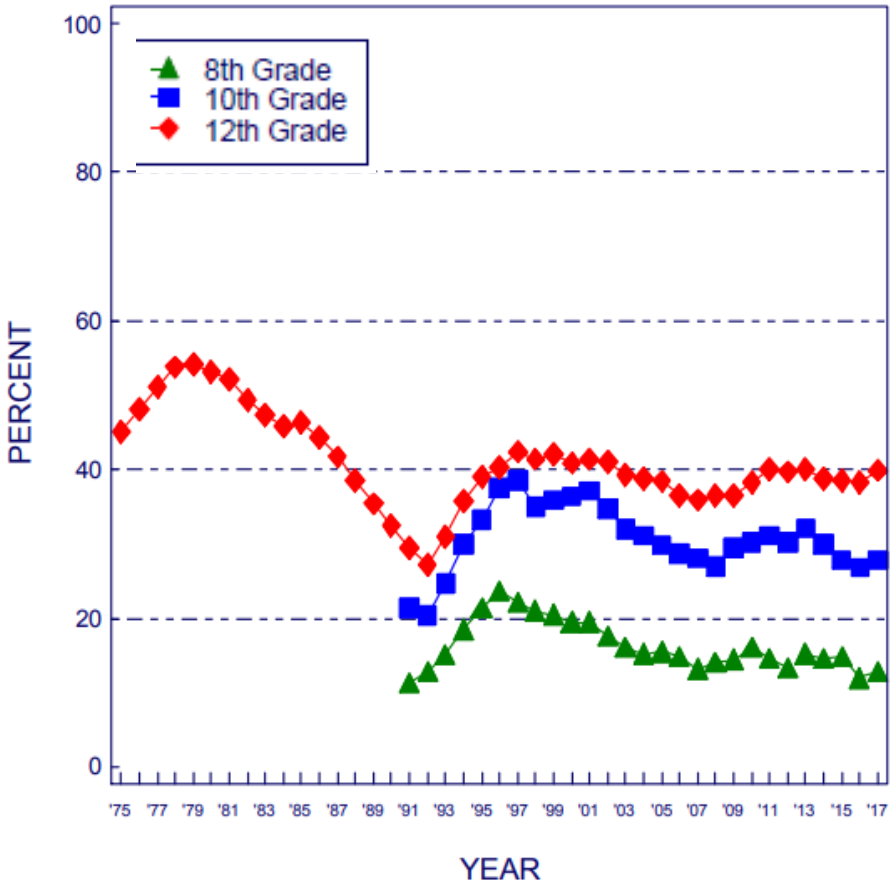
Past Month Illicit Drug Use



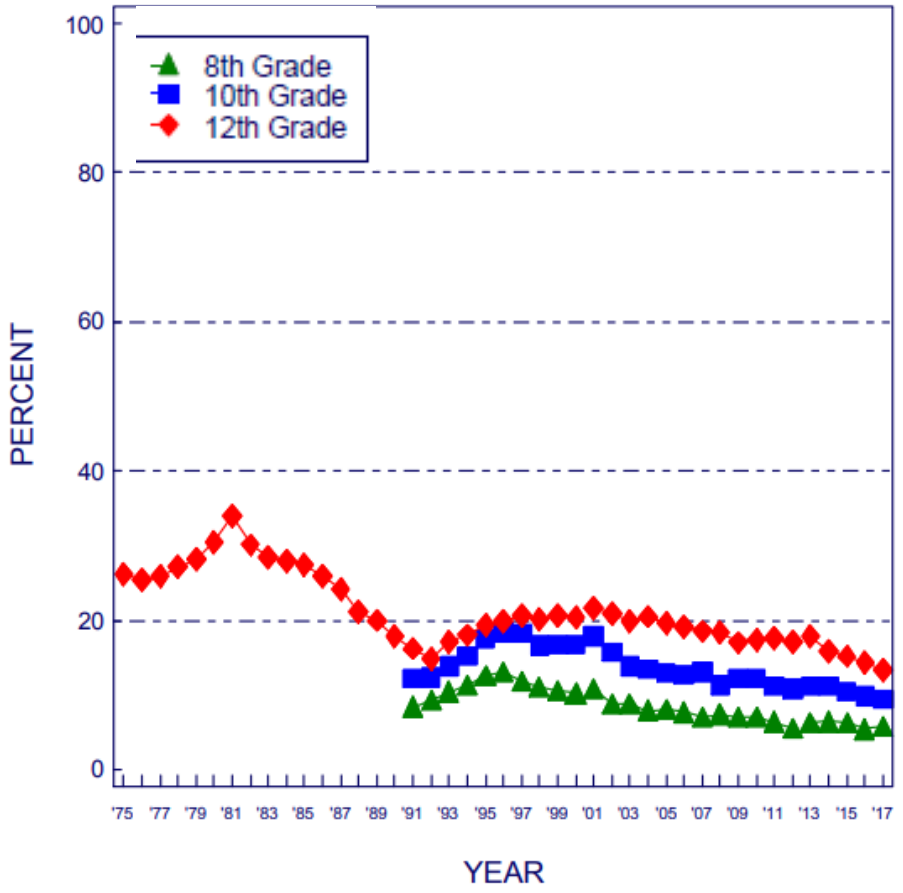
SAMHSA. (2017). Results from the 2016 National Survey on Drug Use and Health

Trends in Annual Illicit Drug Use by Teens

Illicit Drug Use

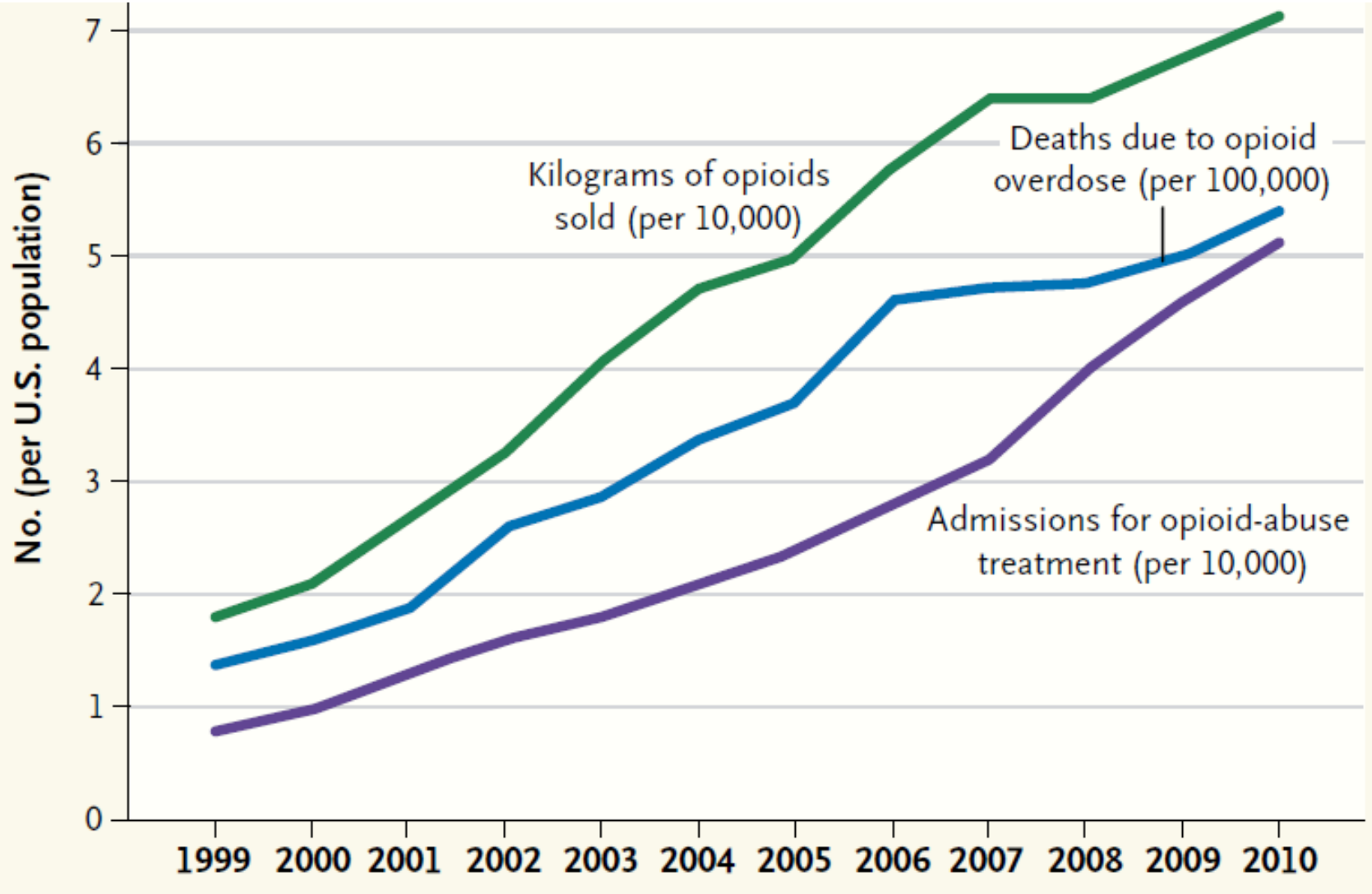


Illicit Drug Use *excluding* Cannabis



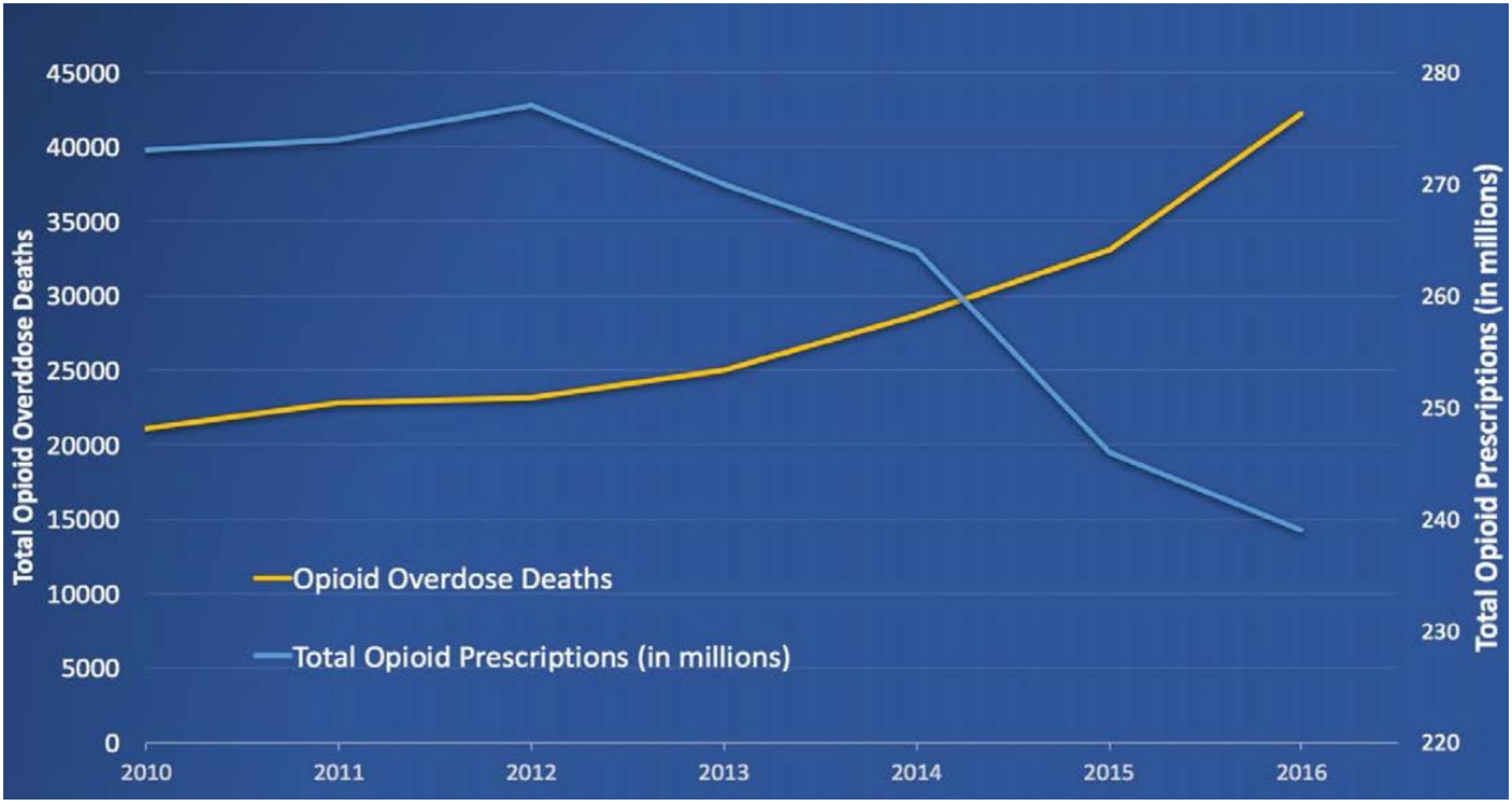
Johnston LD et al. (2018). Monitoring the Future Study

Prescription Opioid Trends 1999-2010



Volkow ND et al. *N Engl J Med*. 2014

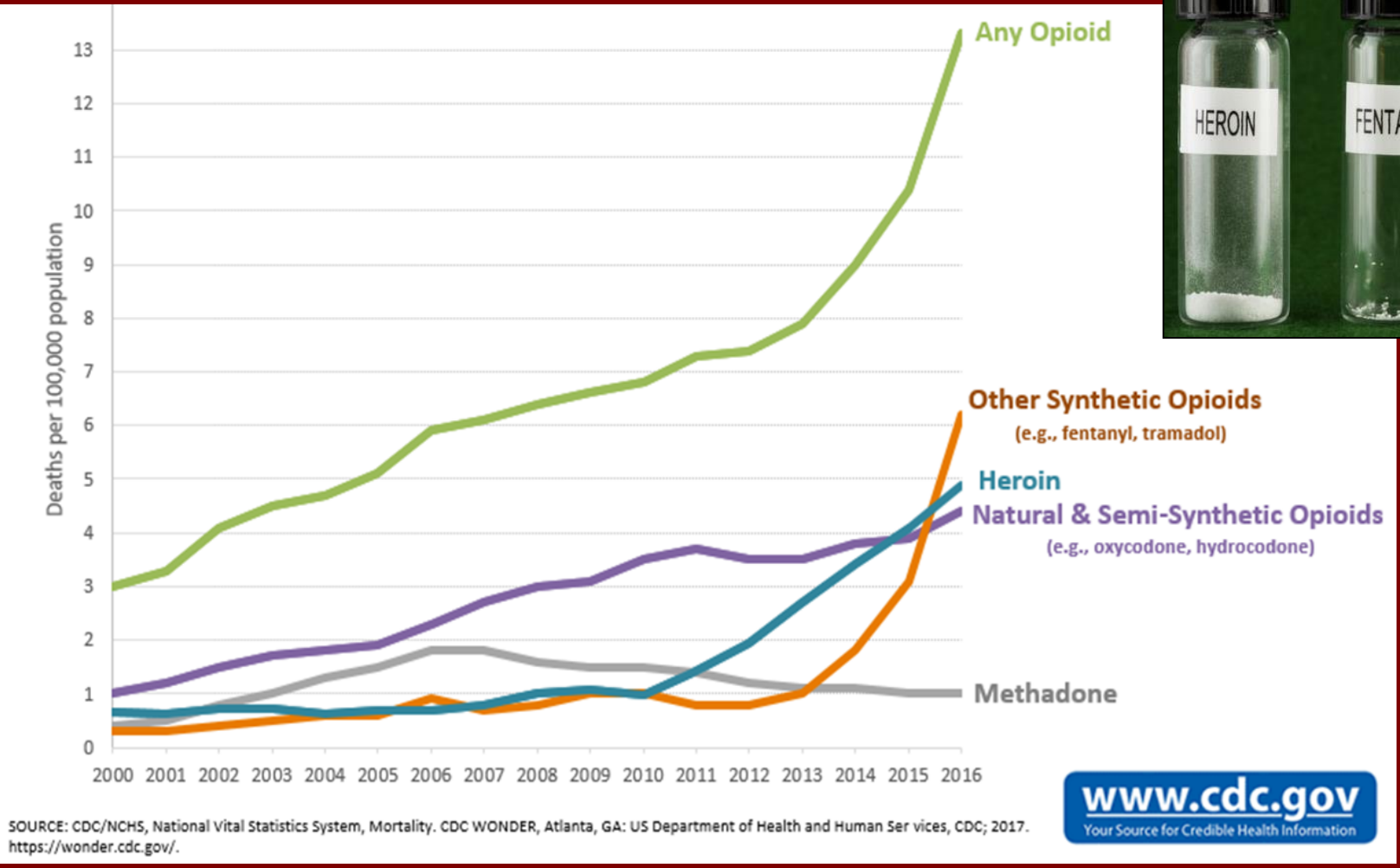
Prescription Opioid Trends since 2010



CDC 2018, Pezalla et al. 2017.

Graph prepared by Stefan Kertesz, MD

Overdoses by Specific Opioid

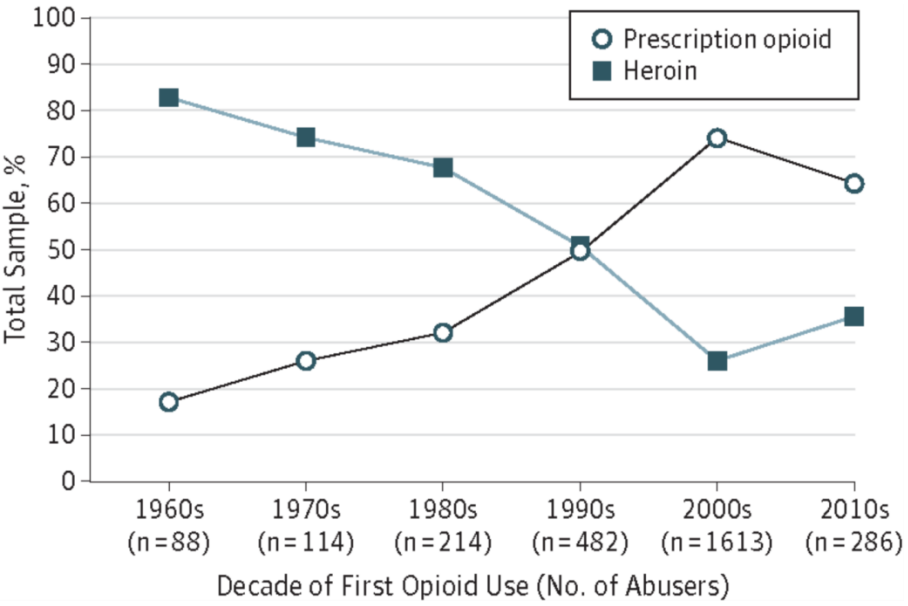


SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Ser vices, CDC; 2017. https://wonder.cdc.gov/.

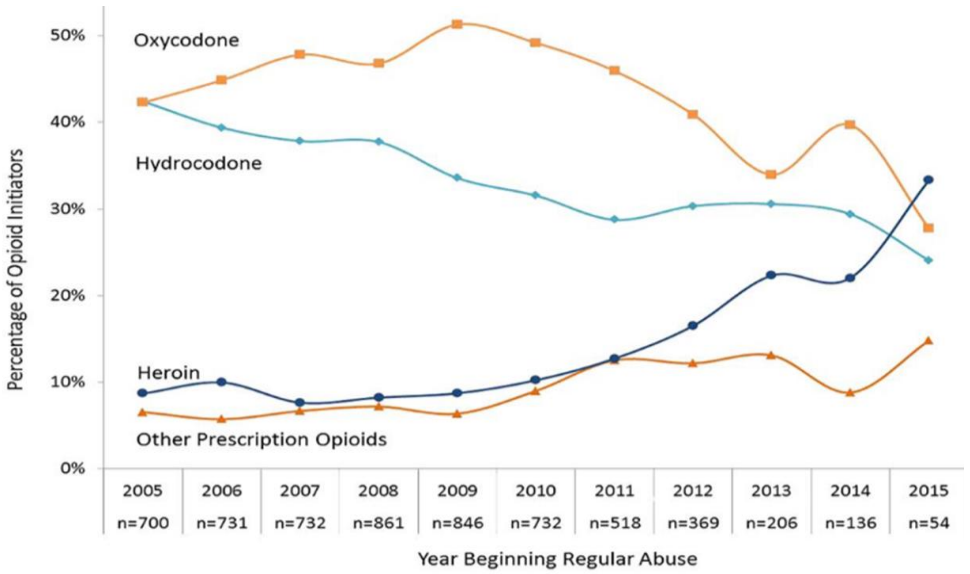
www.cdc.gov
Your Source for Credible Health Information

Shifting Patterns of First Opioid Used

Percentage of Heroin-Addicted Treatment Admissions



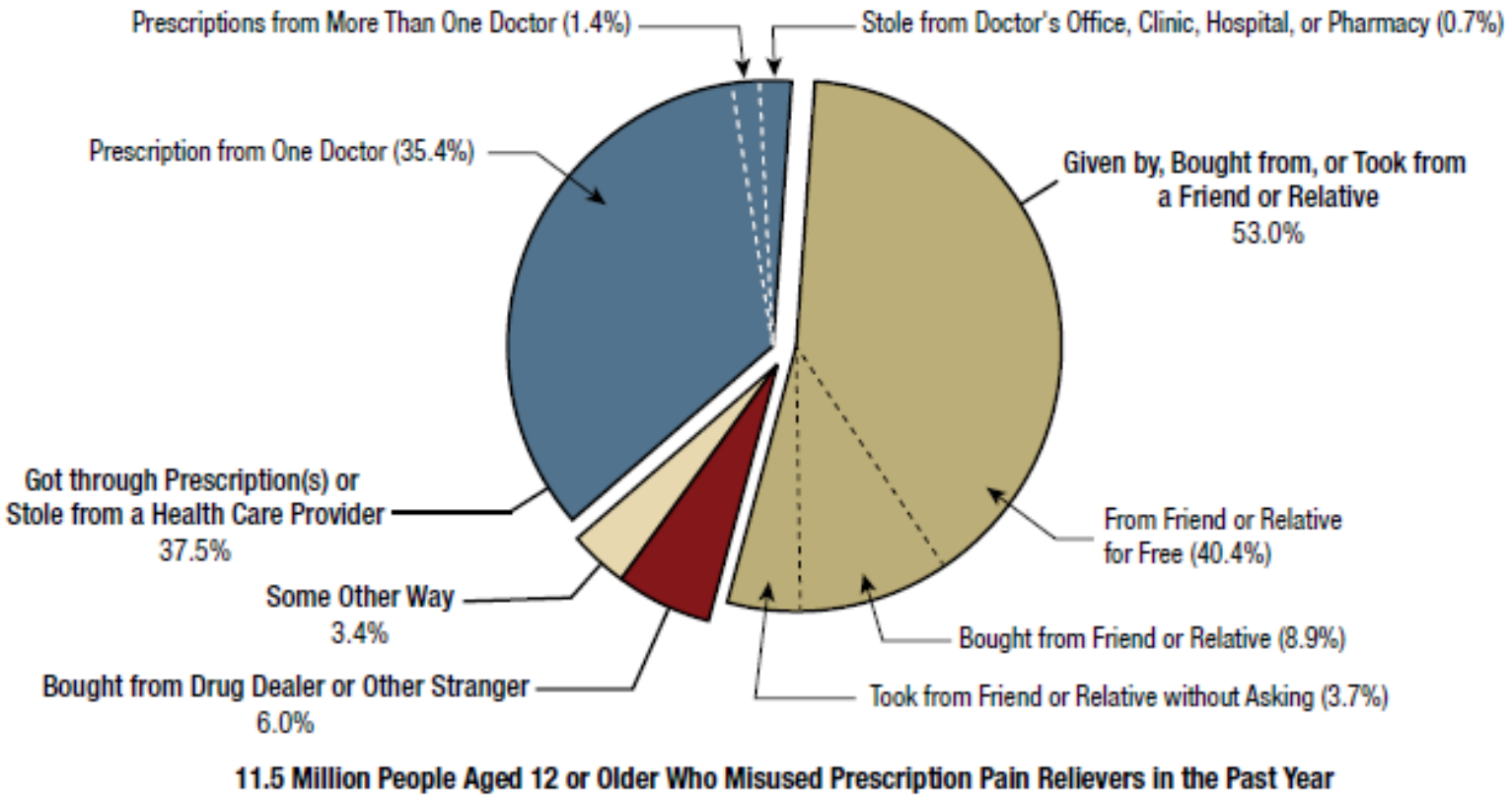
Cicero T et al. JAMA Psychiatry. 2014



Cicero T et al. Addictive Behaviors. 2017

- **1960s**: >80% started with heroin
- **2000s**: >75% started with prescription opioids
- **2010-2015**: Increasing initiation with heroin

Source of Prescription Opioid Misused

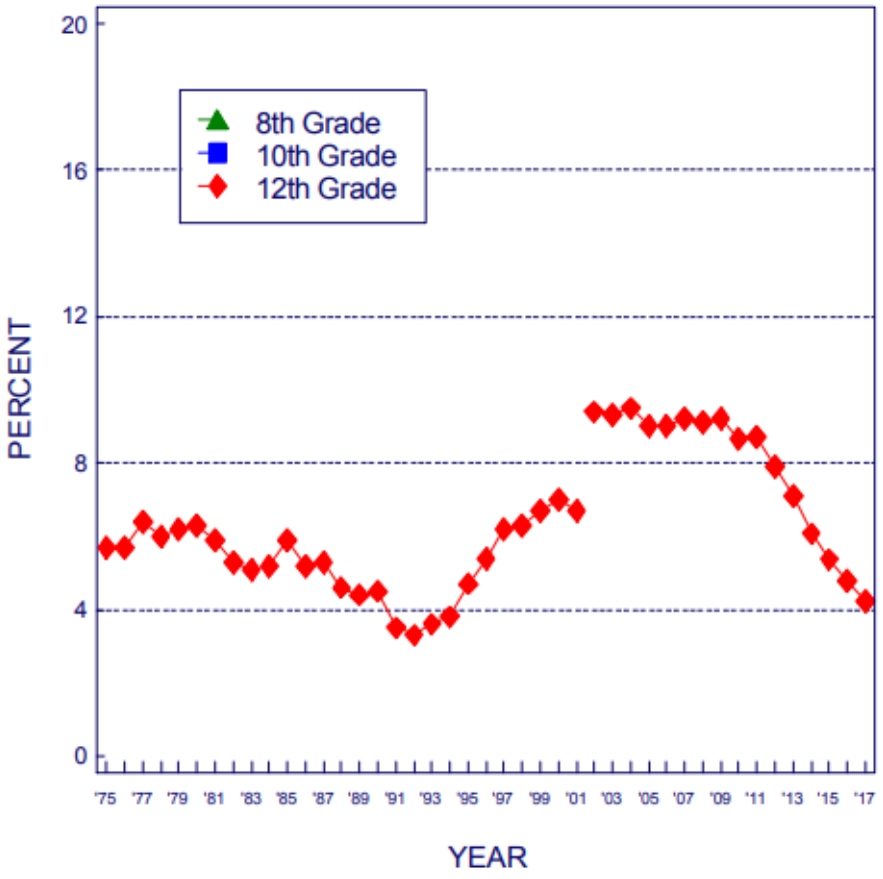


Over ½ from family or friend

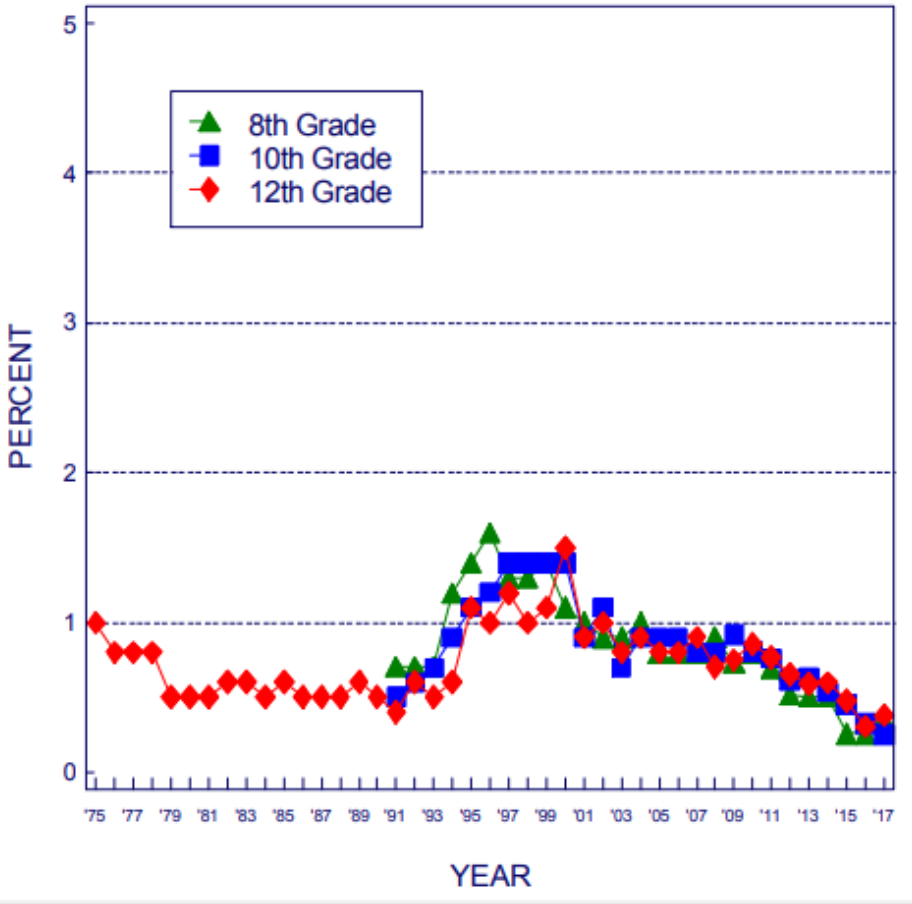
SAMHSA. (2017). Results from the 2016 National Survey on Drug Use and Health

Teens and Opioid Use in Past Year

Prescription Opioids



Heroin

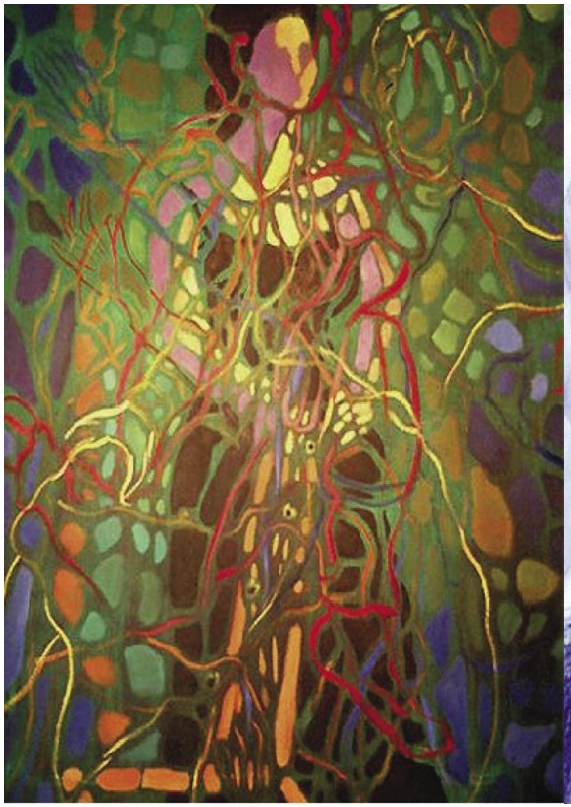


Johnston LD et al. (2018). Monitoring the Future Study

Why do people take drugs?

To feel good

To have novel:
Feelings
Sensations
Experiences
AND
To share them

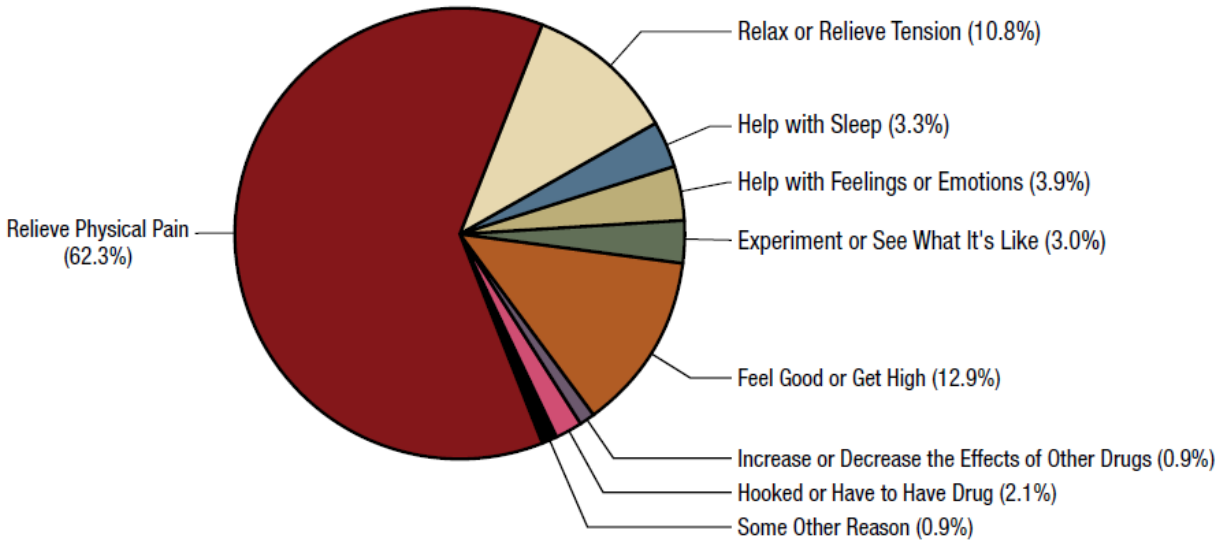


To feel better

To lessen:
Anxiety
Worries
Fears
Depression
Hopelessness
Withdrawal

Drawings courtesy of Vivian Felsen

Reasons for Prescription Opioid Misuse



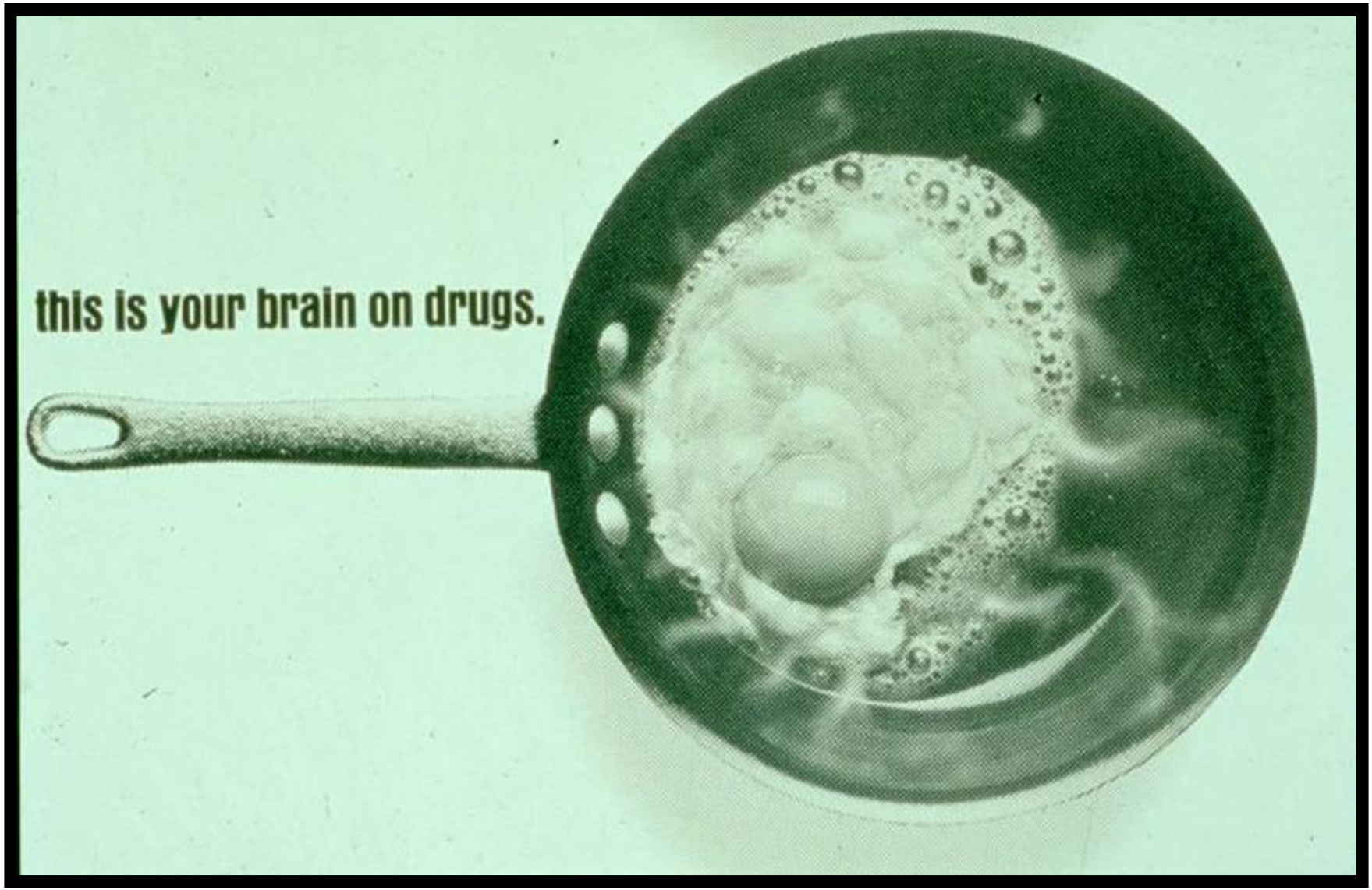
SAMHSA. (2017). 2016 NSDUH

Pain and Substance Use

589 patients who screened positive for drug use, in an urban, hospital-based primary care practice

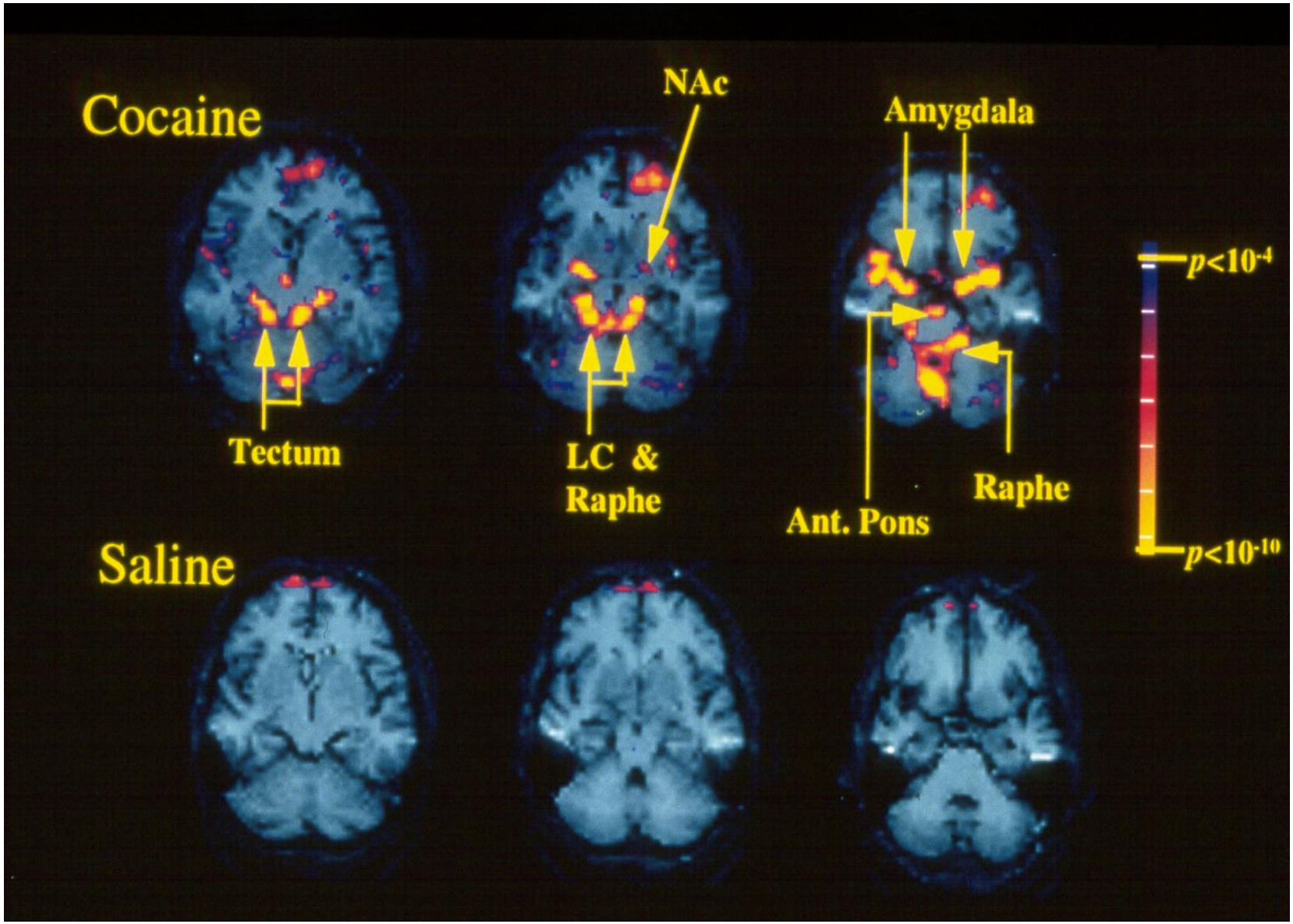
Substance Use	% Used to Self-Treat Chronic Pain
Any illicit drug	**51%**
Marijuana use only	43%
Cocaine use only	42%
Heroin use only	71%
Prescription drug misuse	**81%**

Alford DP et al. *J Gen Intern Med*. 2016



Campaign by Partnership for a Drug-Free America launched in 1987

Your Brain on Drugs



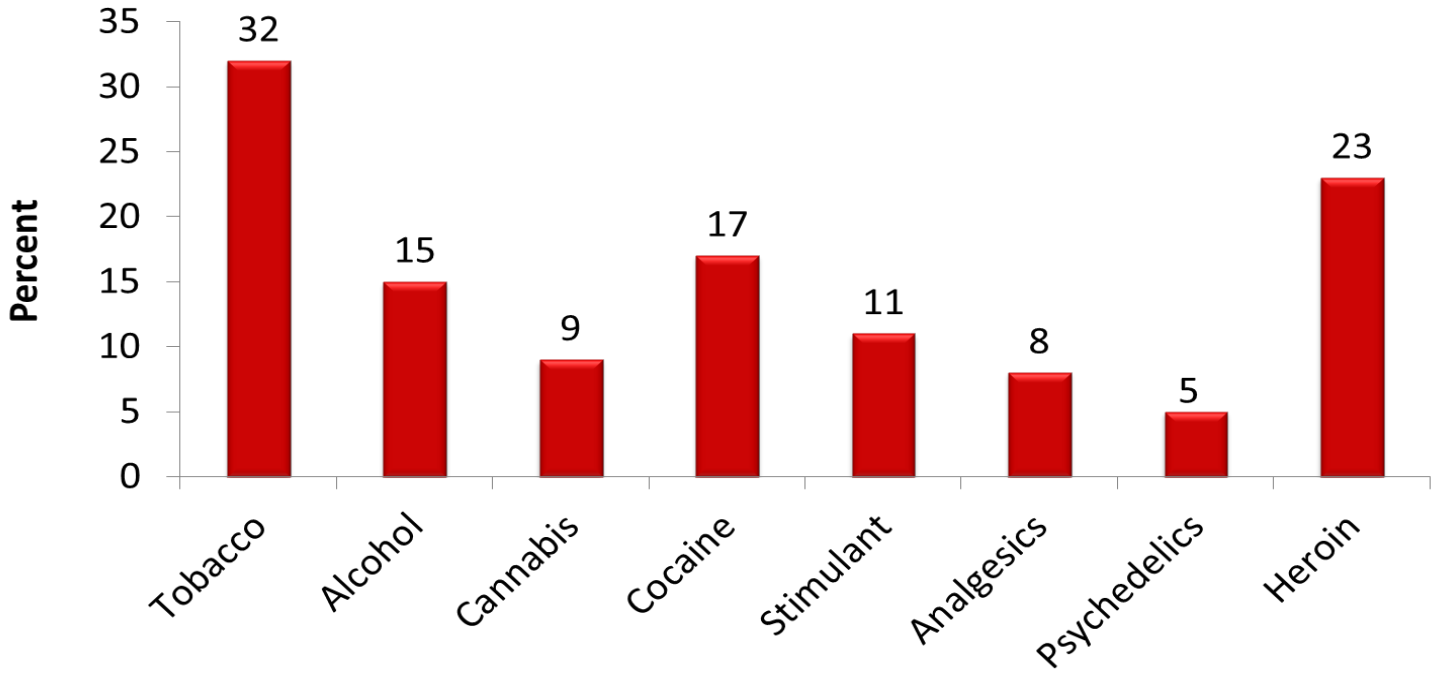
Breiter & Rosen, Ann N Y Acad Sci 1999

What have we learned about vulnerability?

Why do some people become addicted while others do not?

Addiction Prevalence Varies by Substance

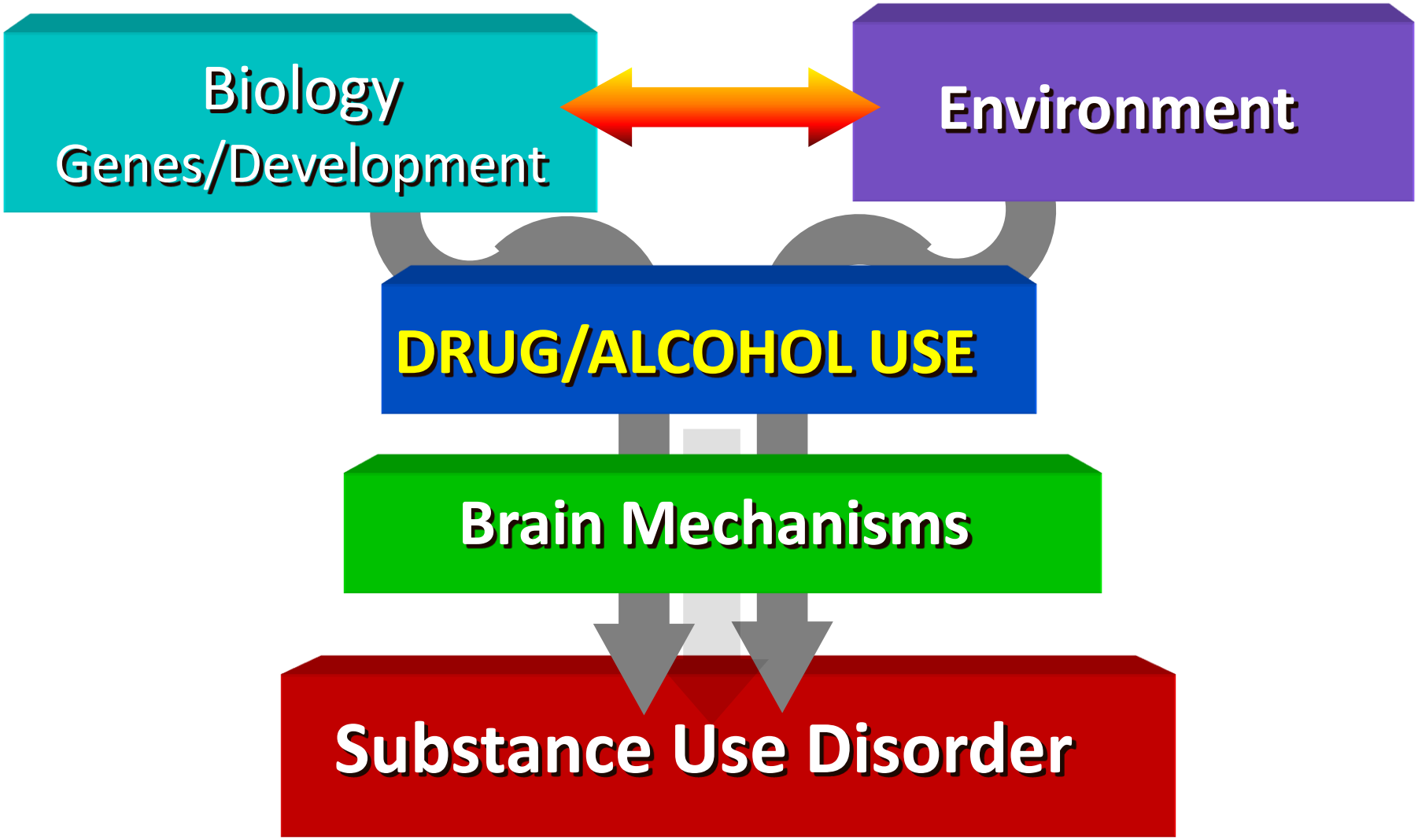
Weighted estimates from the National Comorbidity Survey data using DSM-III-R, collected in 1990-1992 from noninstitutionalized civilian population aged 15-54 years old (n=8,098)



Estimated Prevalence of Dependence (Use Disorder) **among Users**

Anthony JC et al., *Exp Clin Psychopharm* 1994

Development of Substance Use Disorders Involves Multiple Factors



Heritability

Trait	Heritability
Type II DM	0.3[1]
Type I DM	0.7[2]
Hypertension	0.3 - 0.5[3]
Peanut allergy	0.8[4]
Cataract (age-related)	0.5[5]
Alcoholism	**0.6[6]**
Nicotine	**0.5 – 0.6[7]**
Cocaine and stimulants	**0.4 – 0.8[8]**
Heroin and opioids	**0.5[9]**
Cannabis	**0.3 – 0.8[10]**

[1]Poulsen et al., Diabetologia 1999

[2]Kyvik et al., BMJ 1995

[3]Corvol & Jeunemaitre, Endocrine Rev 1997

[4]Sicherer et al., J Allergy Clin Immunol 2000

[5]Hammond et al., N Engl J Med 2000

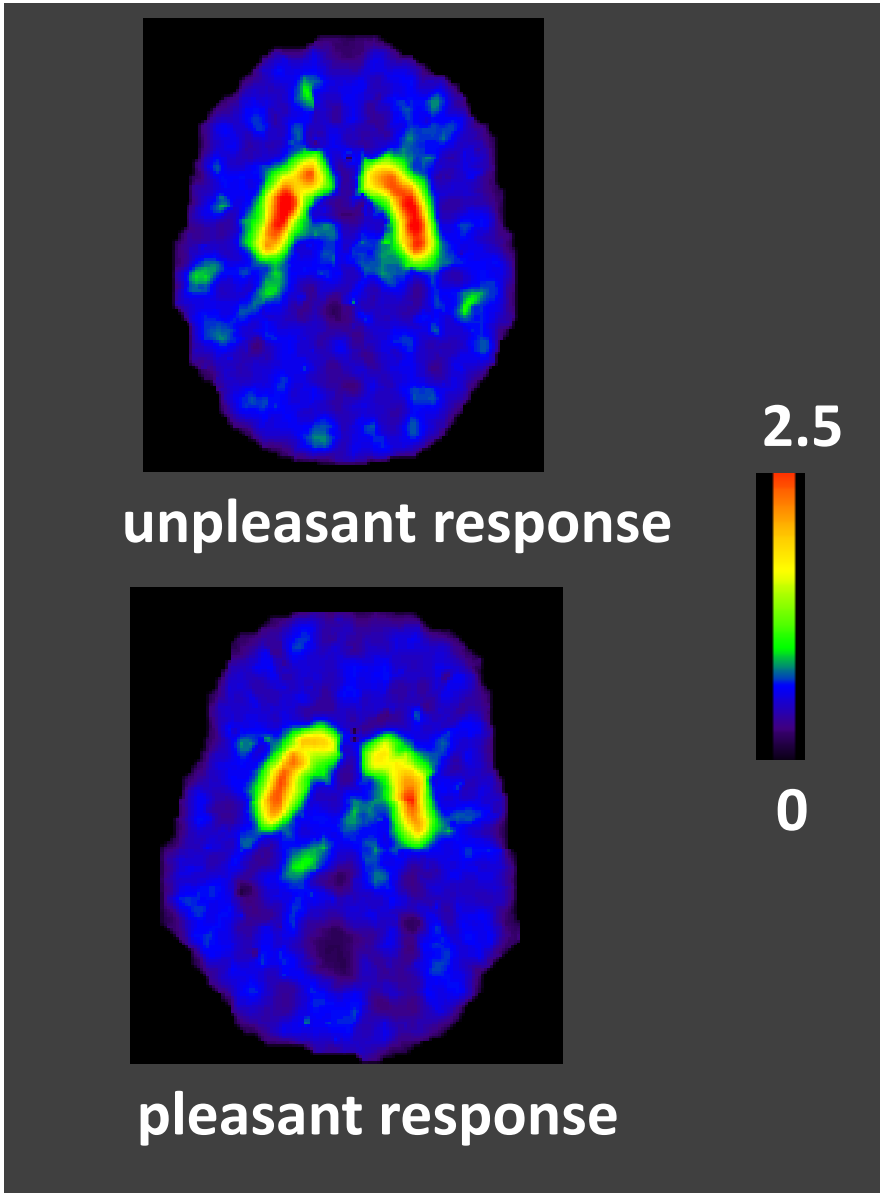
[6]Goate & Edenberg, Curr Opin Genet Dev.1998

[7]Sabol et al., Health Psych. 1999

[8-10]Tsuang et al. 1996; Am J Med Genet. 1996

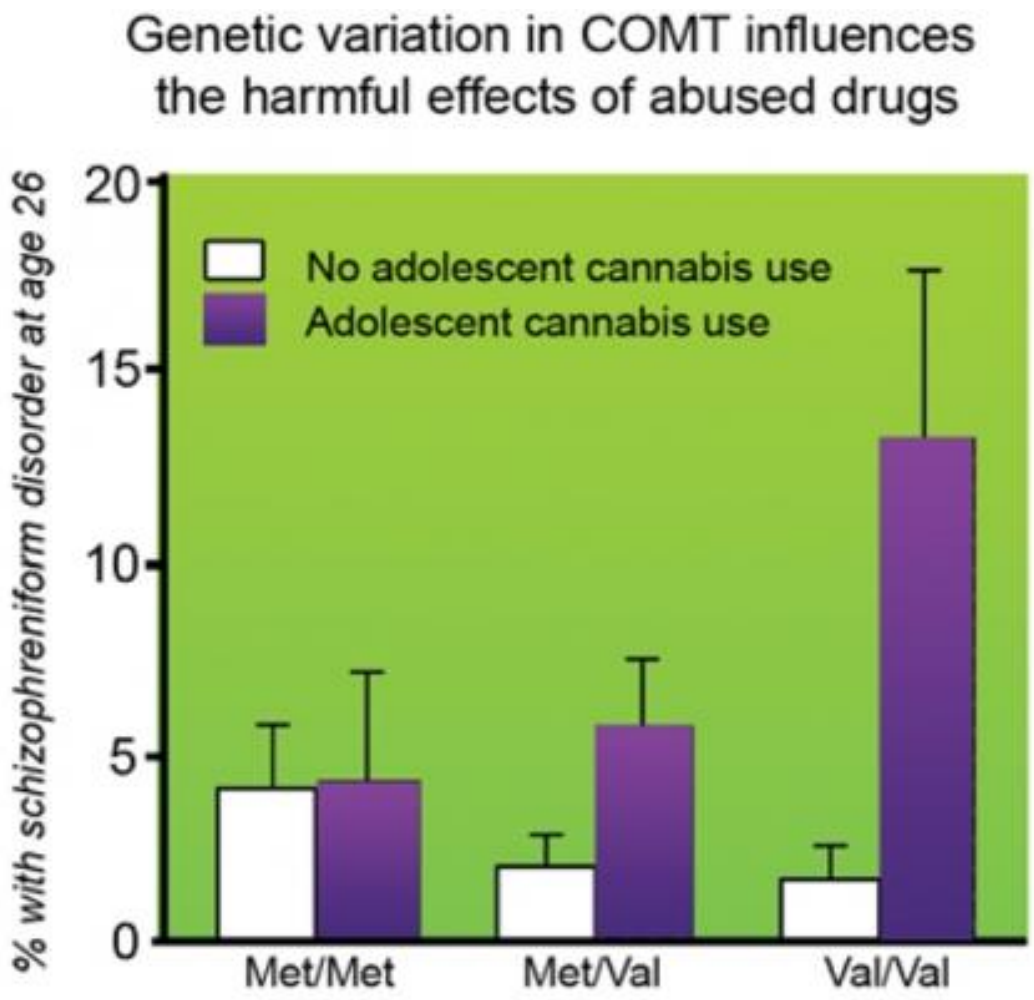
DA Receptor Levels and Response to MP

- Striatal **Dopamine D2 receptors (D2R)** levels predicted reinforcing responses to the psychostimulant methylphenidate (MP) in nondrug-using subjects (n=7)
- Subjects with **low D2R** found **MP pleasant** while those with **high D2R** found **MP unpleasant**
- Low D2R = **"reward deficiency syndrome"**
- Striatal D2R modulate reinforcing responses to stimulants in humans and may underlie predisposition for drug self-administration



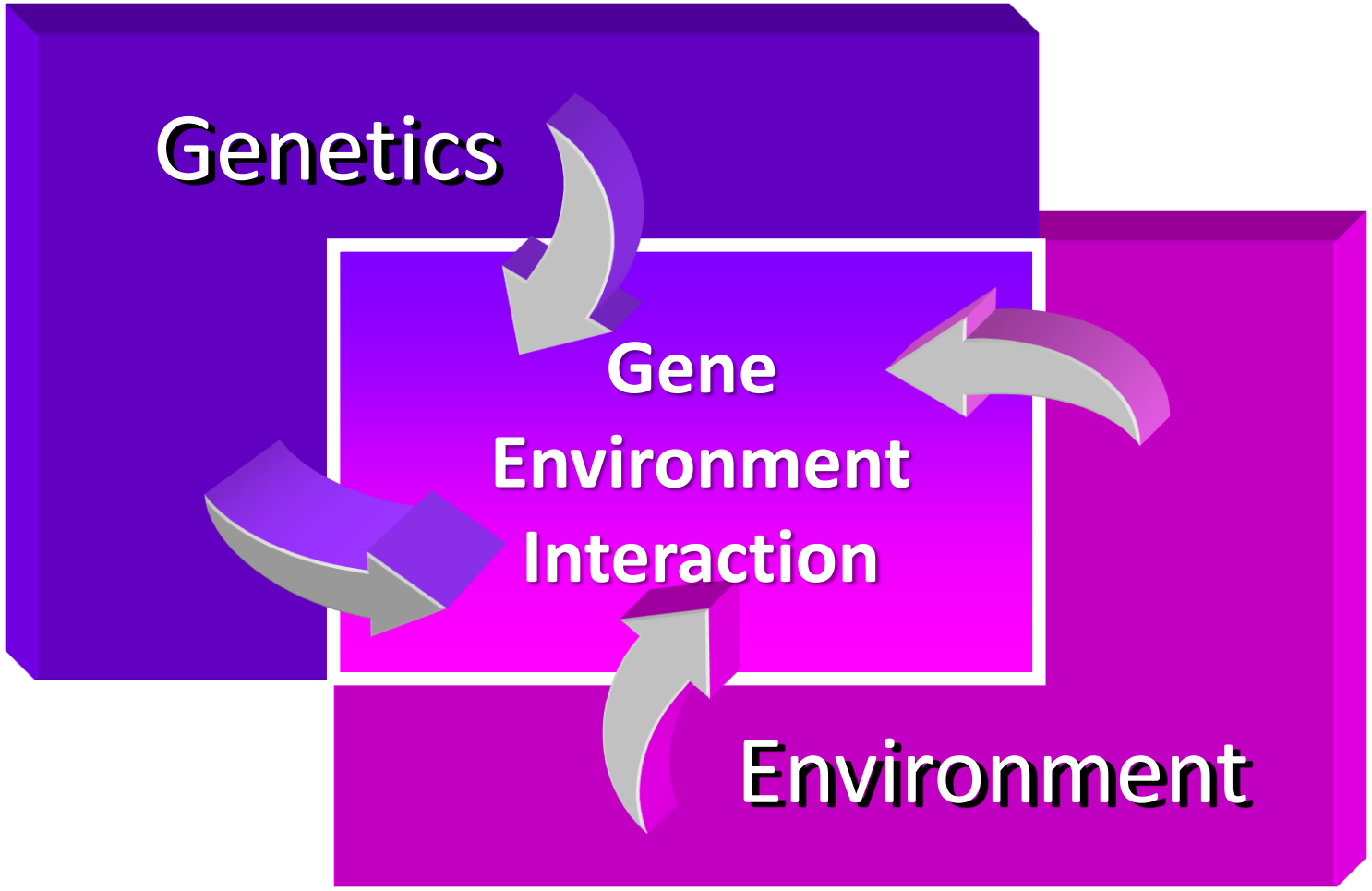
Volkow ND et al. *Synapse*. 2002

Genetic Variability and Drug Effects



- Longitudinal birth cohort n=1,037 followed from 3y to adulthood
- Functional polymorphism in catechol-O-methyl-transferase (COMT) gene
- COMT valine allele more likely to develop psychotic symptoms and schizophreniform disorder if used cannabis

Caspi A et al. *Biol Psych* 2005


Genetics
Gene
Environment
Interaction
Environment

What Environmental Factors Contribute to Addiction?

Drug availability

Peers who use drugs

Family problems

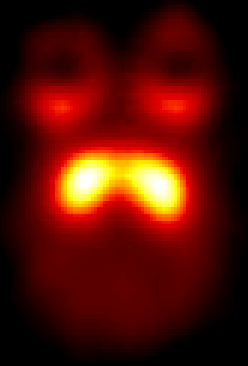
Early physical or sexual abuse

Chronic stress

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

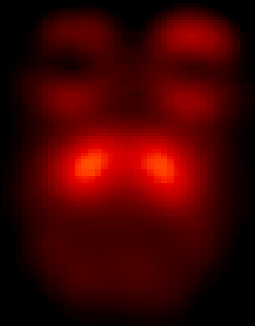
Individually Housed

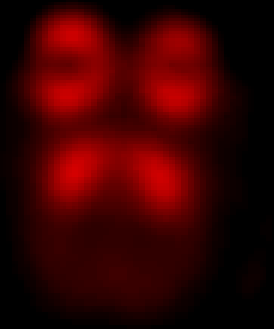
Group Housed



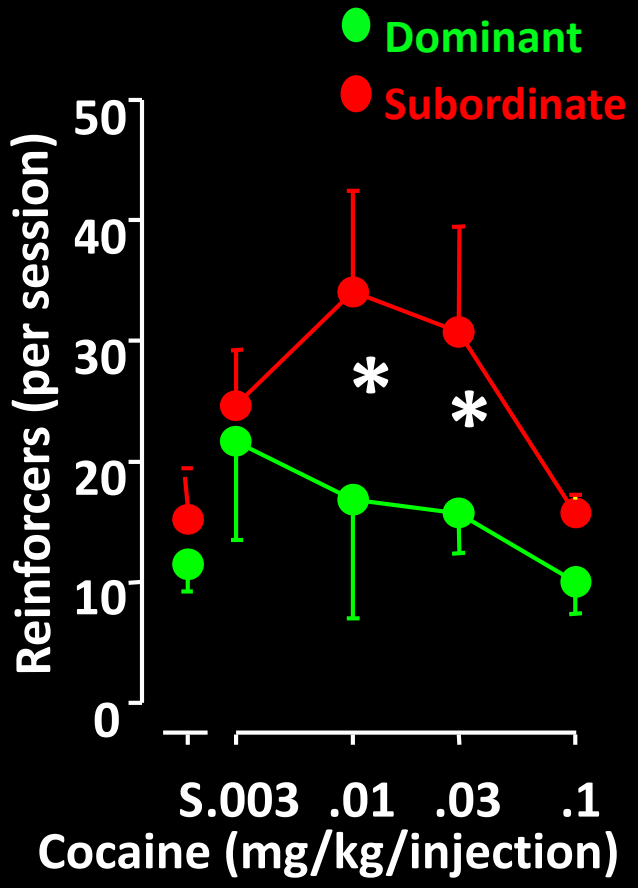
Becomes Dominant
No longer stressed

Social Setting Can Change Neurobiology





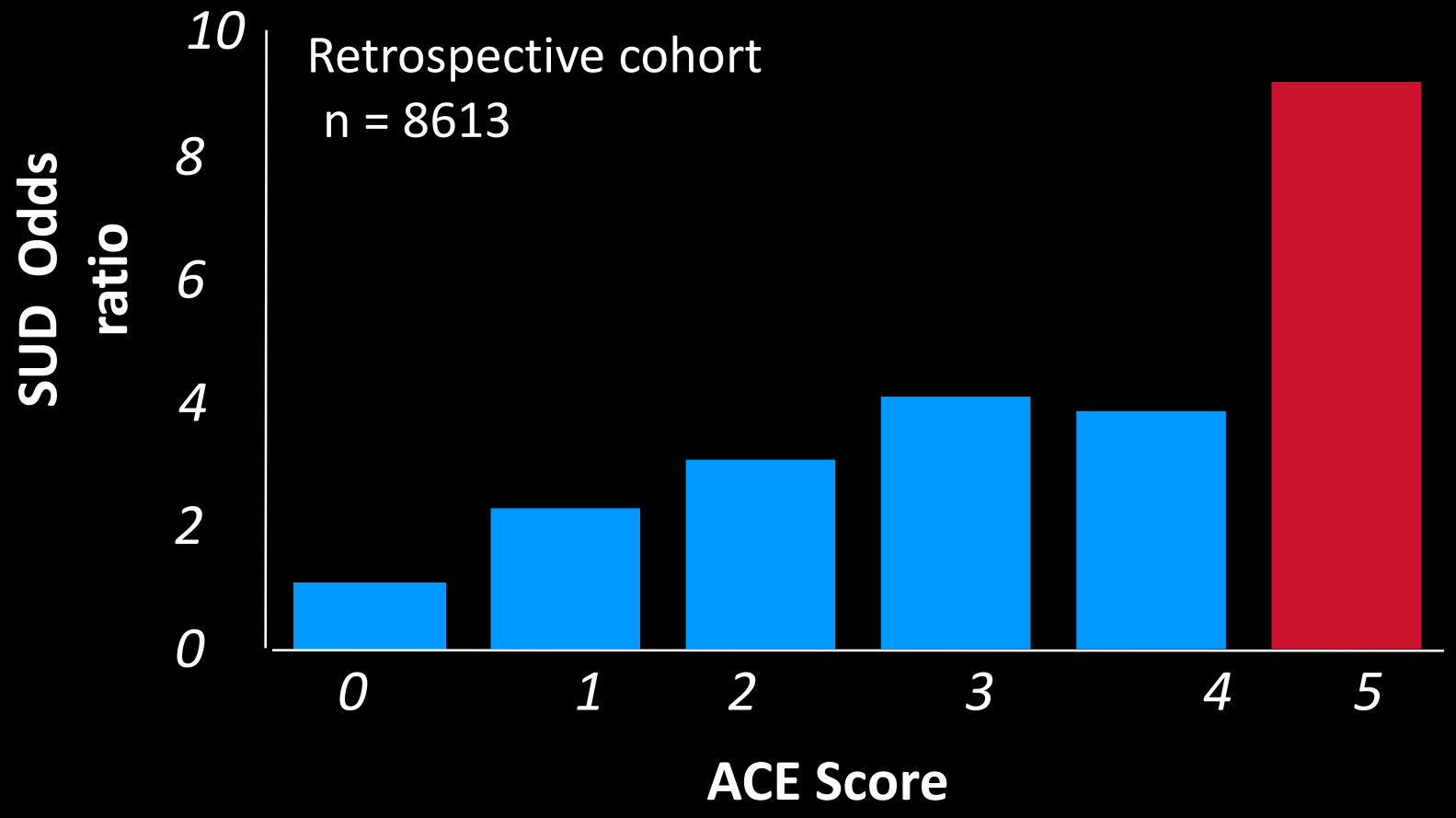
Becomes Subordinate
Stress remains



N=20 monkeys

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

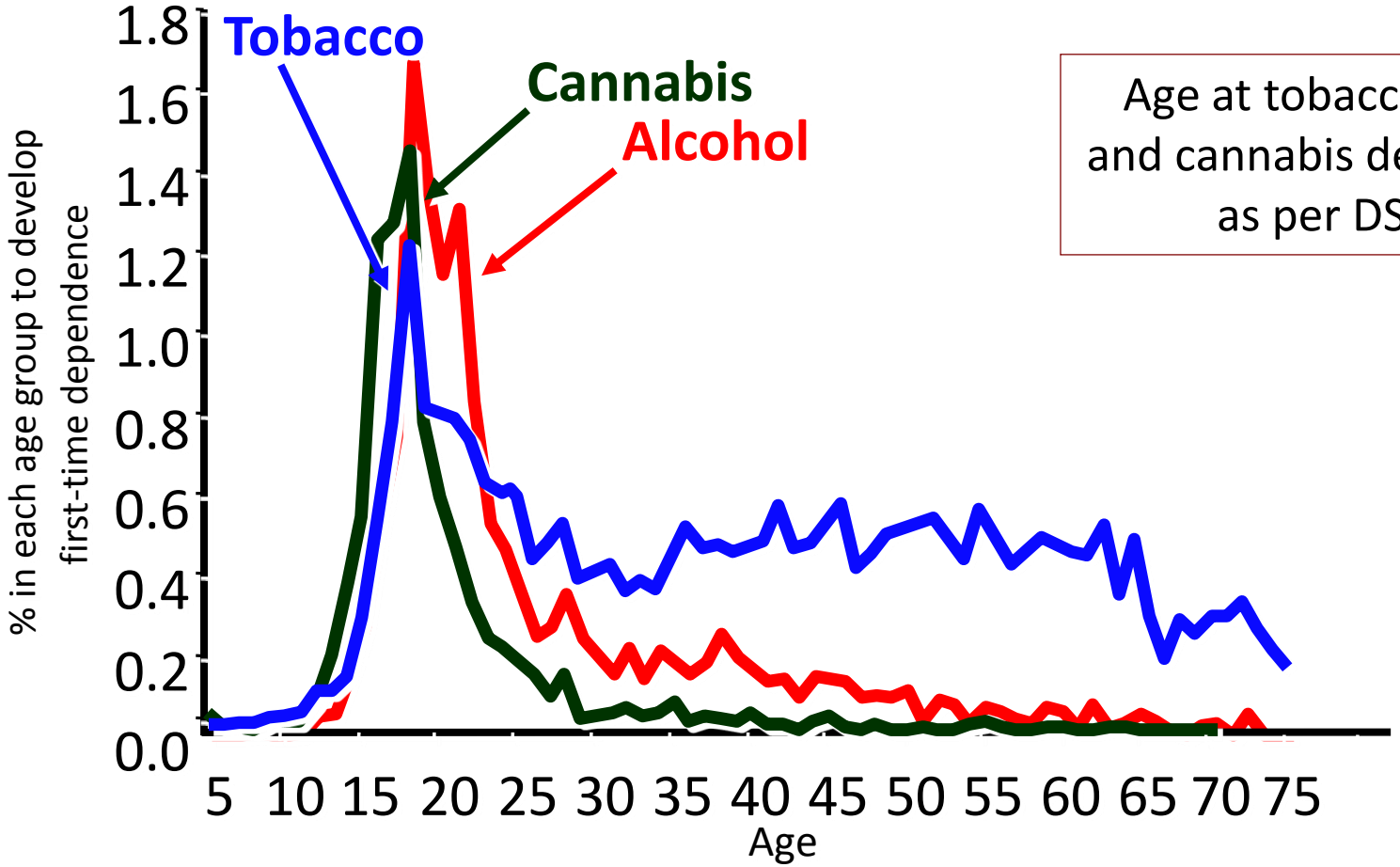
Adverse Childhood Experiences (ACE) and Illicit Drug Use



- Each ACE increased likelihood of early drug use by 2- to 4-fold
- ≥ 5 ACEs were 7- to 10-fold more likely to report illicit drug use problems

Dube SR et al. Pediatrics 2003

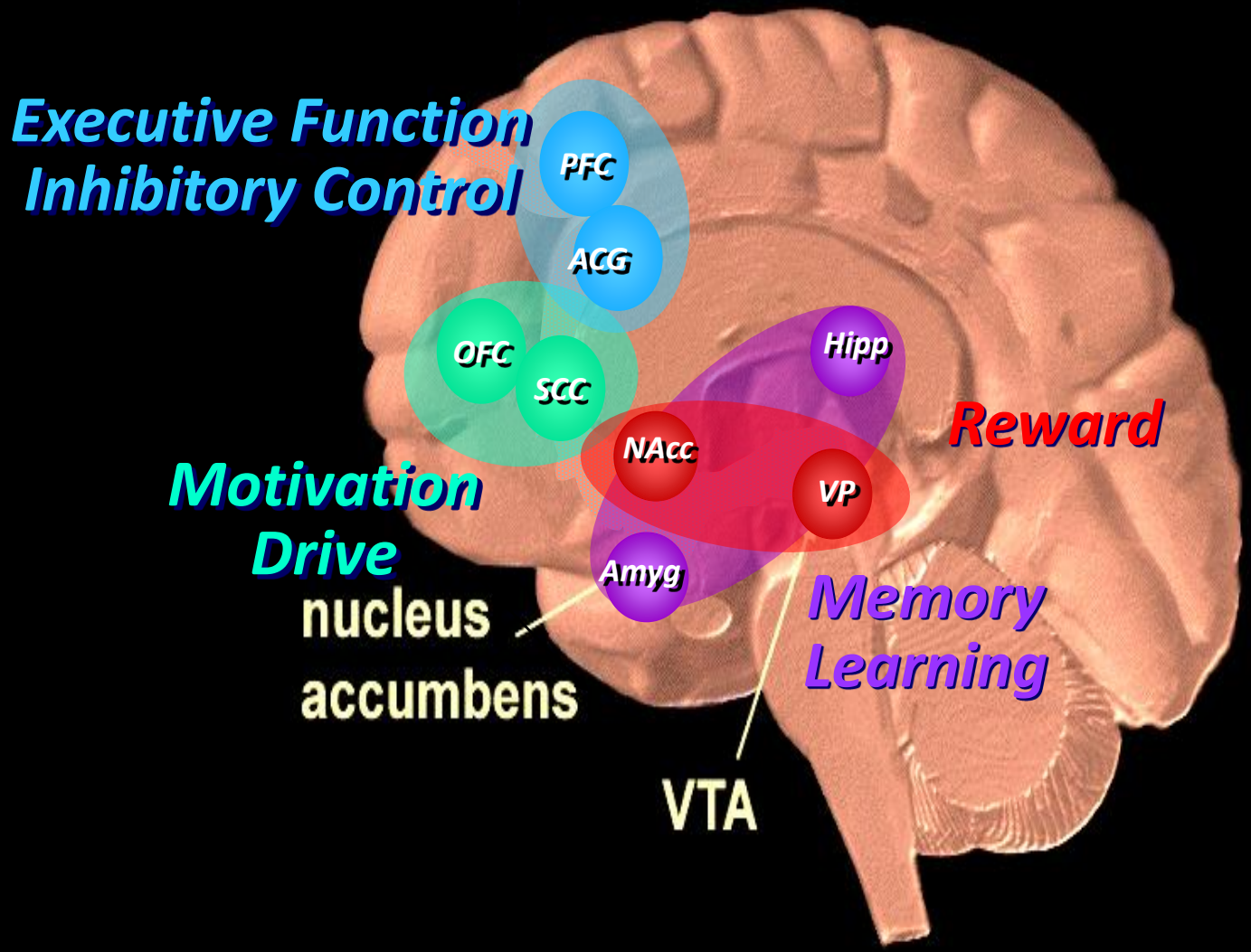
Addiction Is a Developmental Disease starts in Childhood and Adolescence



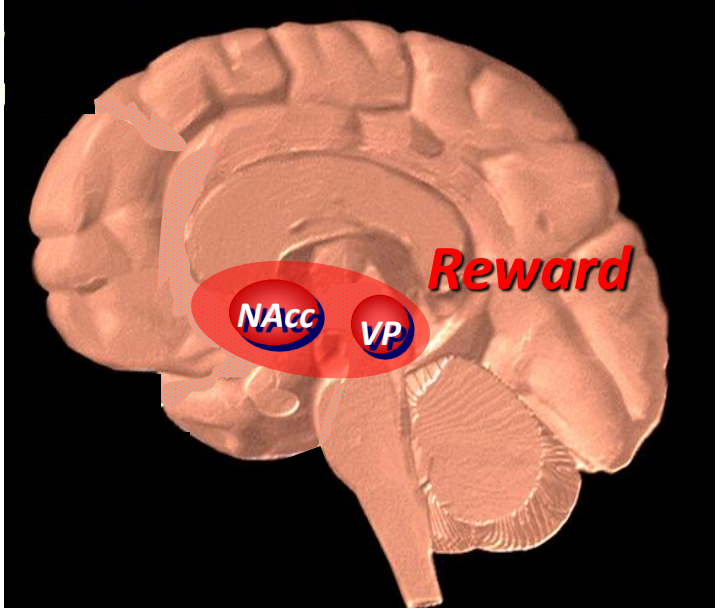
Age at tobacco, alcohol and cannabis dependence, as per DSM IV

National Epidemiologic Survey on Alcohol and Related Conditions, 2003

Neuronal Circuits Involved In Substance Use and Addiction

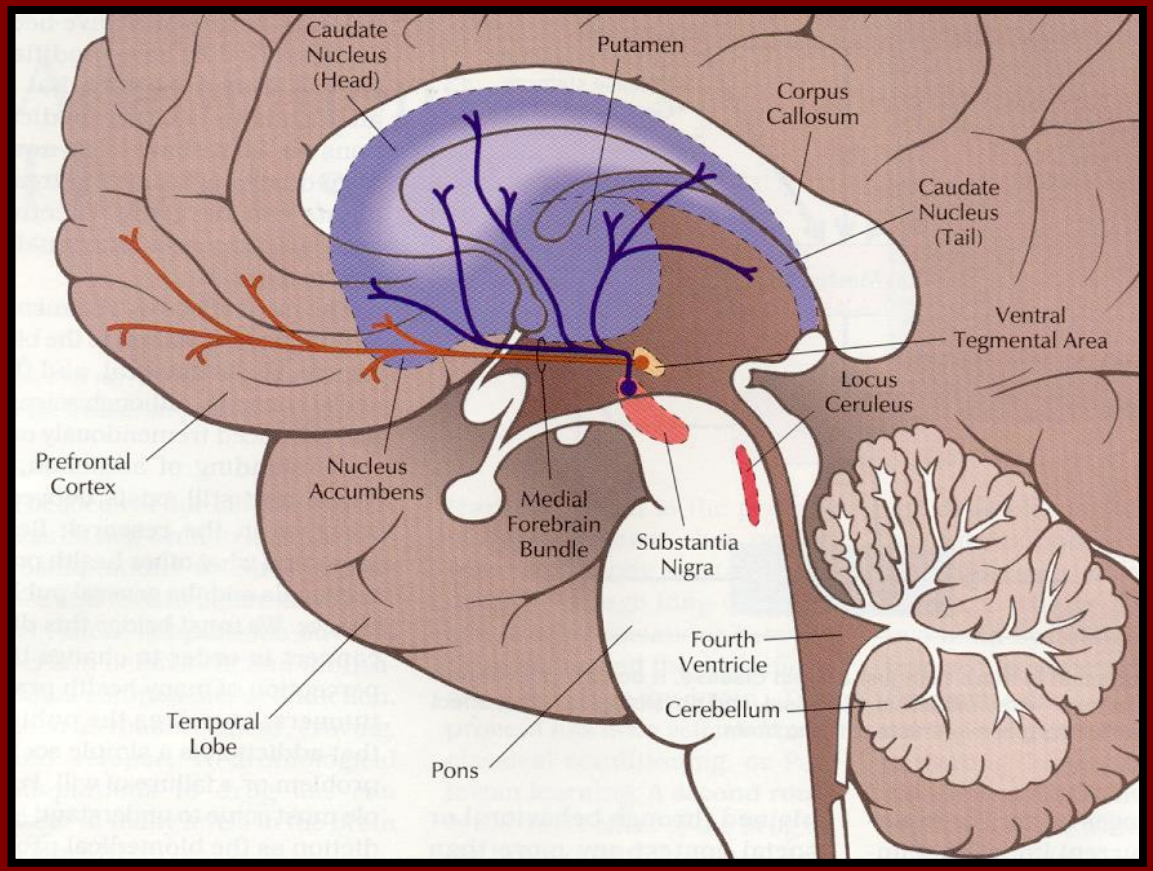


1. Reward Circuit



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

The Reward Pathway

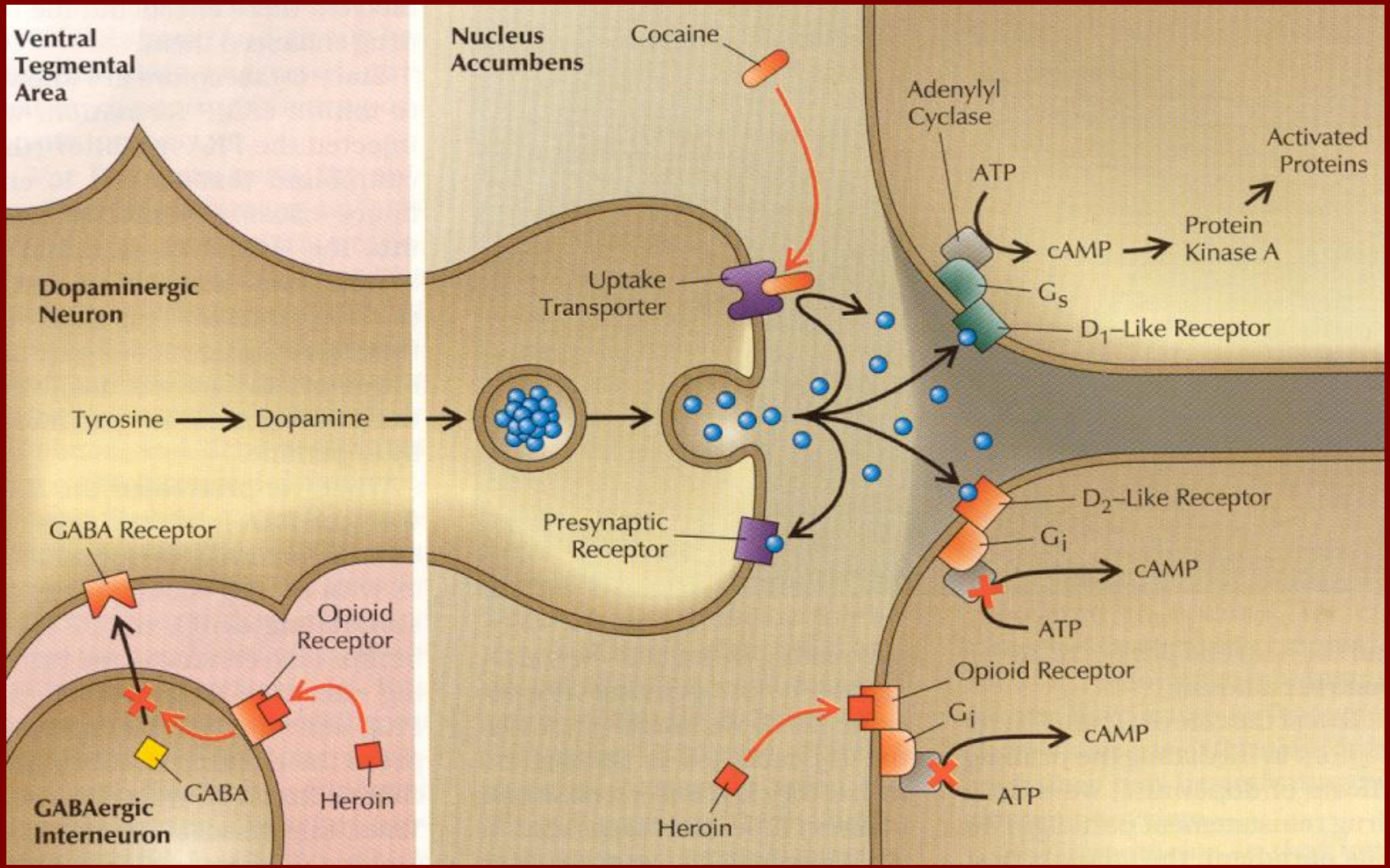


Reward and reinforcement is in part controlled by mu-opioid receptors in the <u>Reward Pathway</u>:

- Ventral Tegmental Area (VTA)
- Nucleus Accumbens with projections to Prefrontal Cortex
- Dopaminergic system

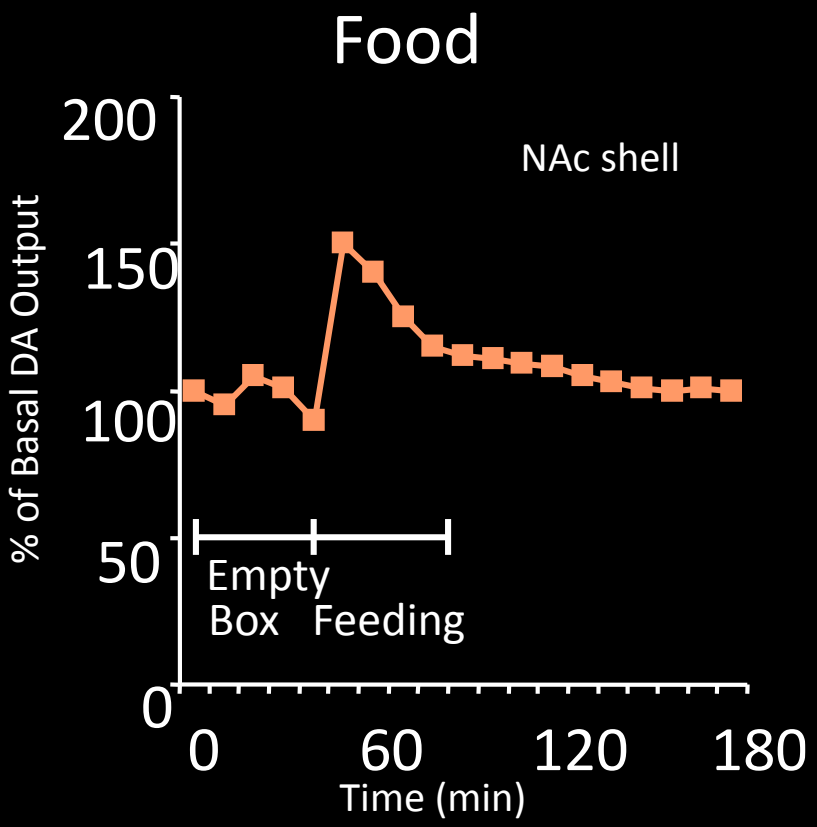
Leshner A. *Hospital Practice.* 1996

The Reward Pathway



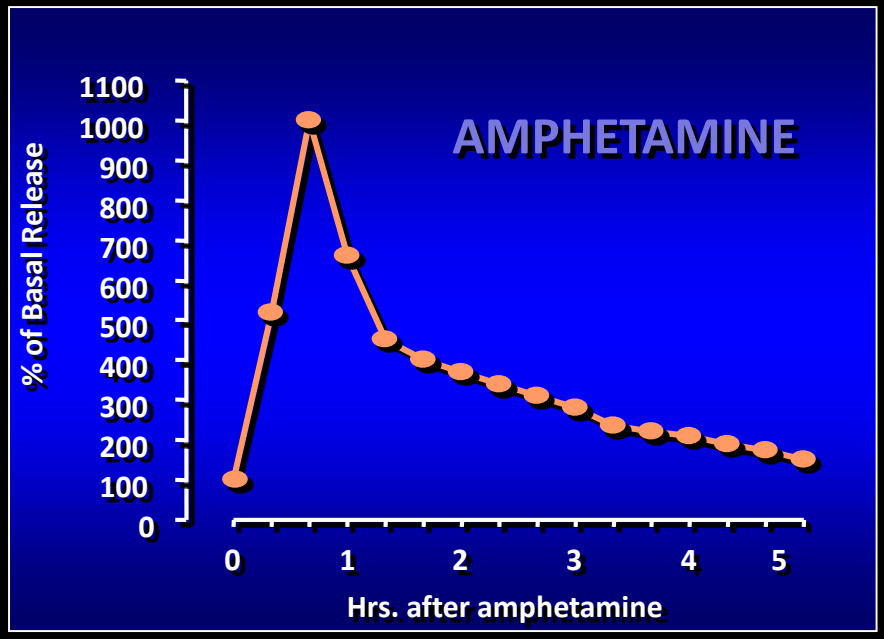
Leshner A. *Hospital Practice.* 1996

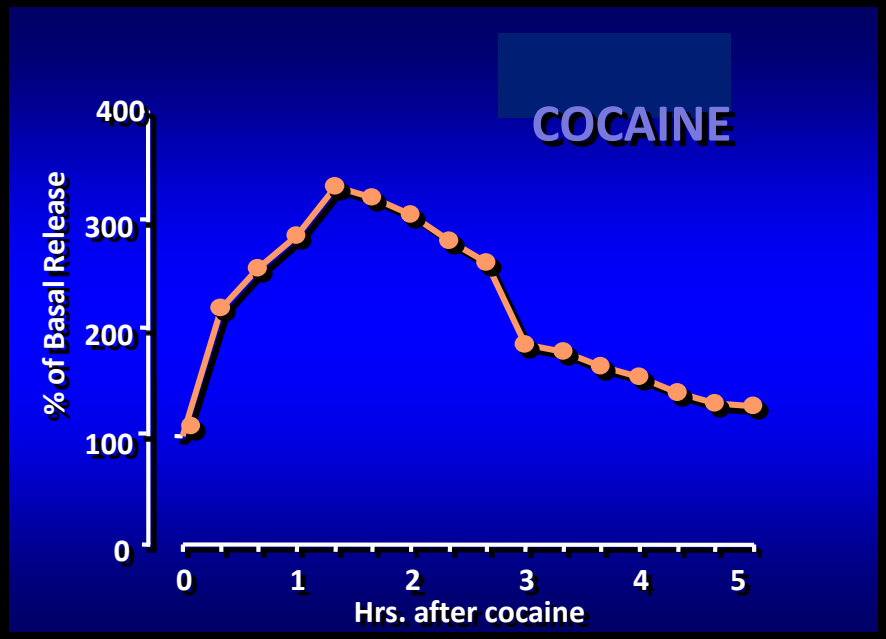
Natural Rewards Elevate Dopamine Levels

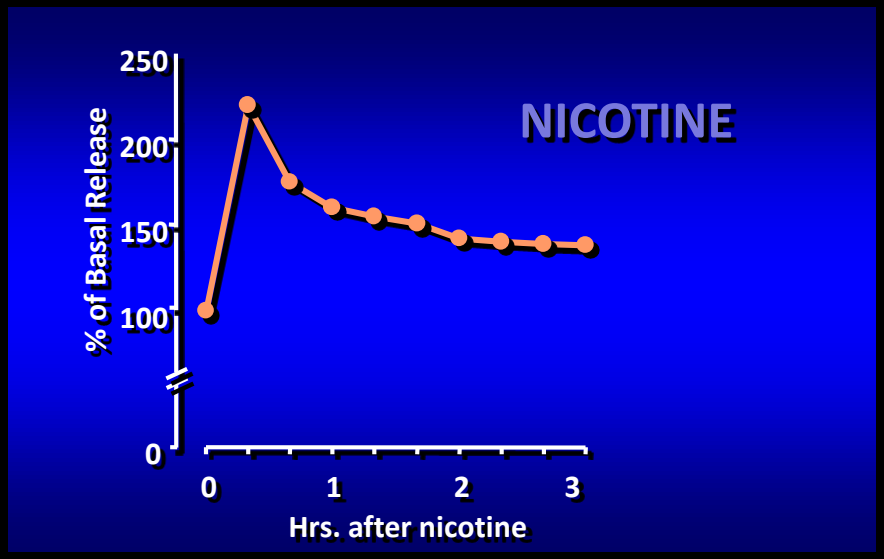


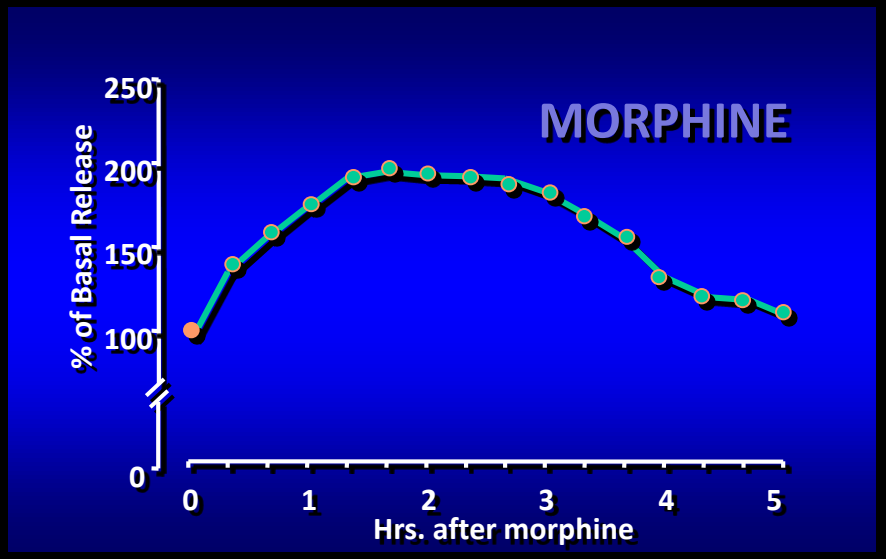
Di Chiara et al., *Neuroscience*, 1999
Fiorino and Phillips, *J. Neuroscience*, 1997

Drugs Elevate Dopamine More/Longer









Di Chiara G, Imperato A. *Proc Natl Sci*. 1988

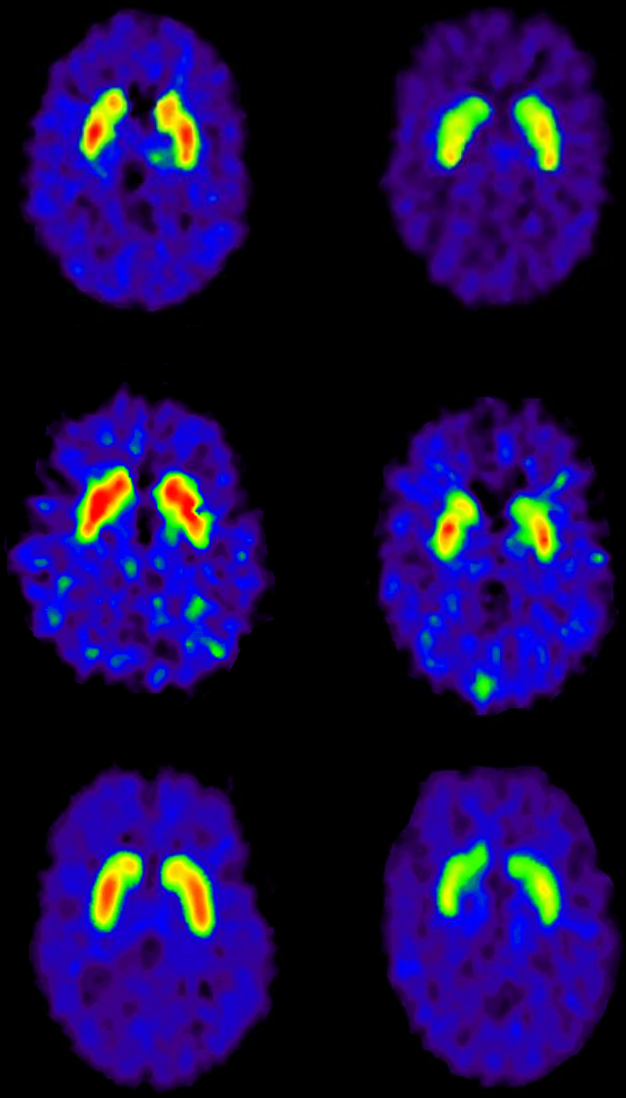
Dopamine D2 Receptors Lower in Individuals with Addiction

Volkow et al., *Neuro Learn Mem* 2002

Cocaine

Alcohol

Heroin

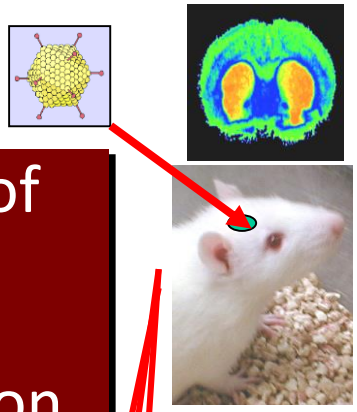


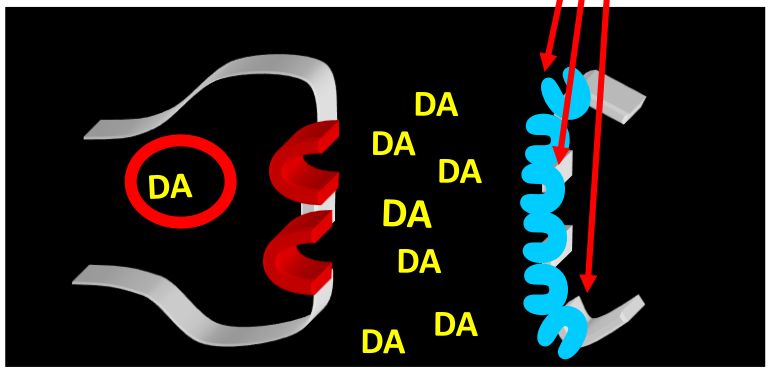
DA D2 Receptor Availability

Control **Addicted**

Effects of an Adenovirus Vector Carrying a DA D2 Receptor Gene into NAc

Overexpression of DA D2 receptors reduces alcohol self-administration

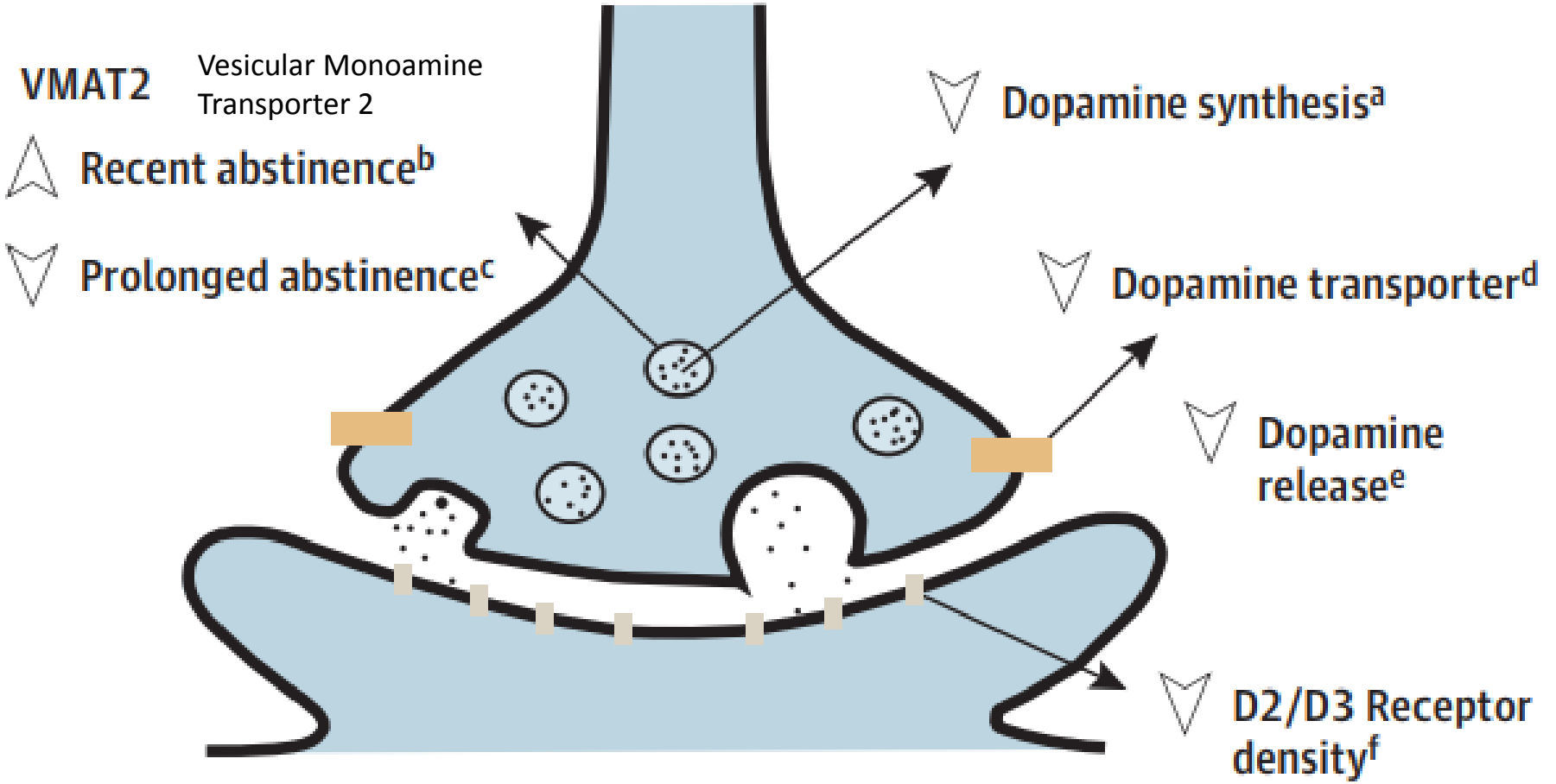




Thanos, PK et al., *J Neurochem*, 2001.

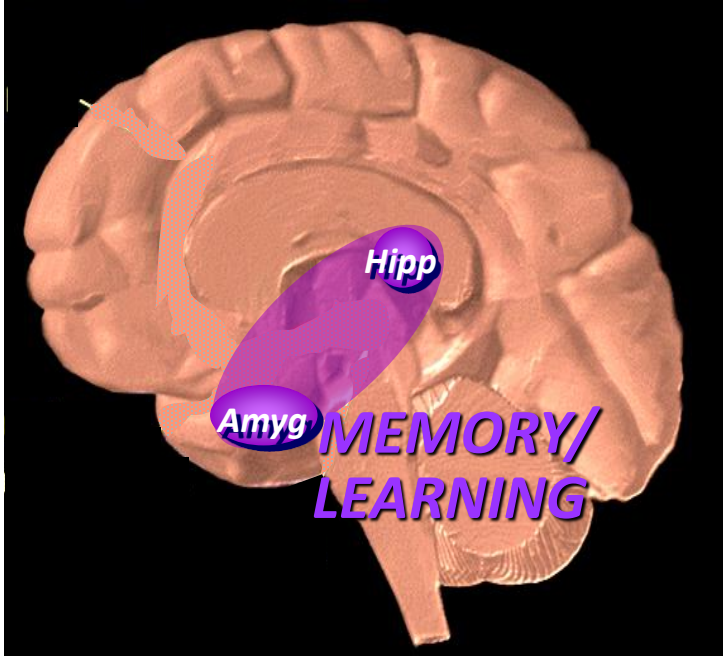
Stimulant Use and Dopaminergic Dysfunction

Figure 4. Summary of Dopaminergic Alterations in Stimulant Users



Ashok AH et al. *JAMA Psych* 2017

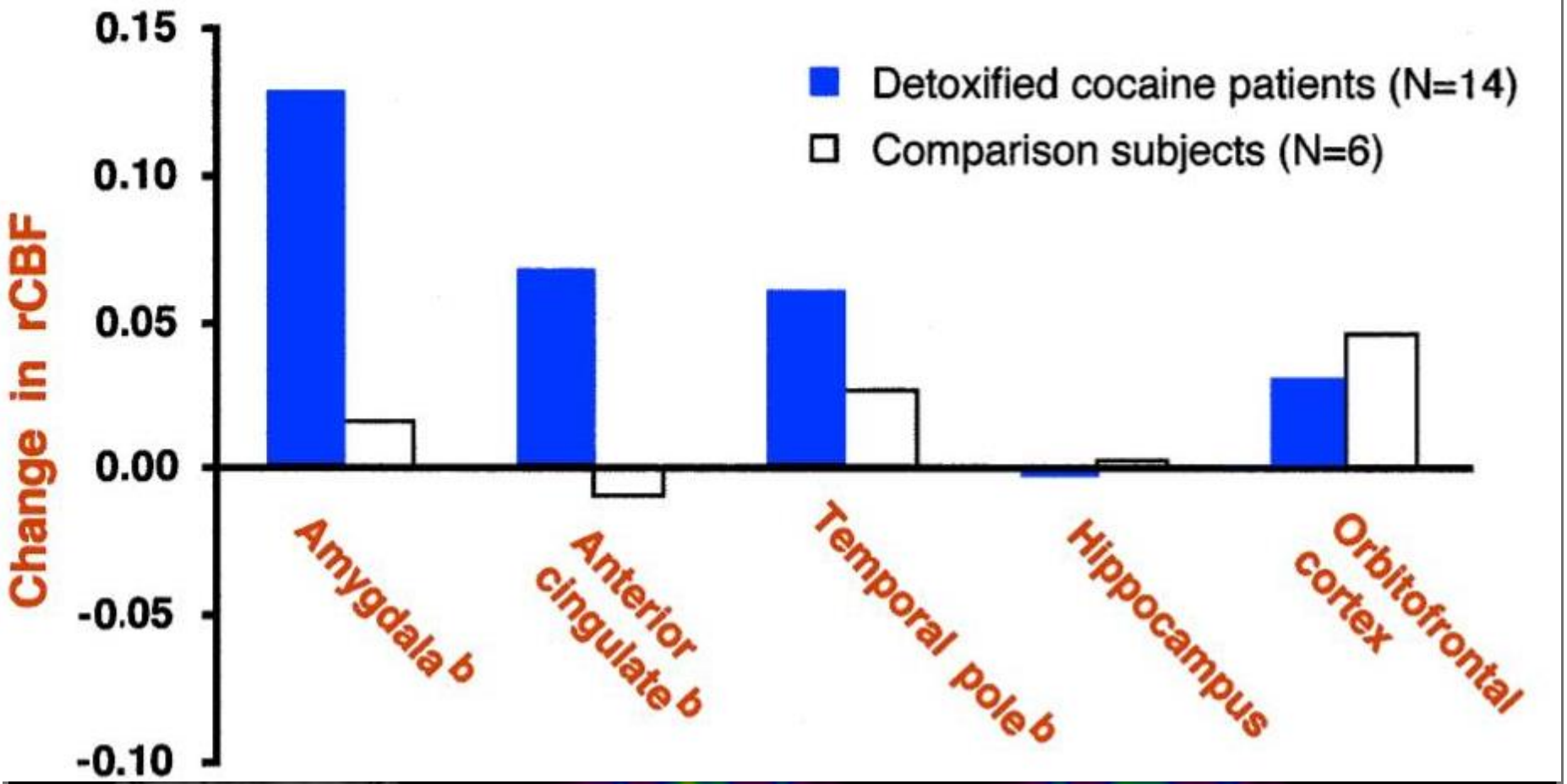
2. *Memory circuit*



People, places and things…”

Conditioned

Amygdala



Nature Video

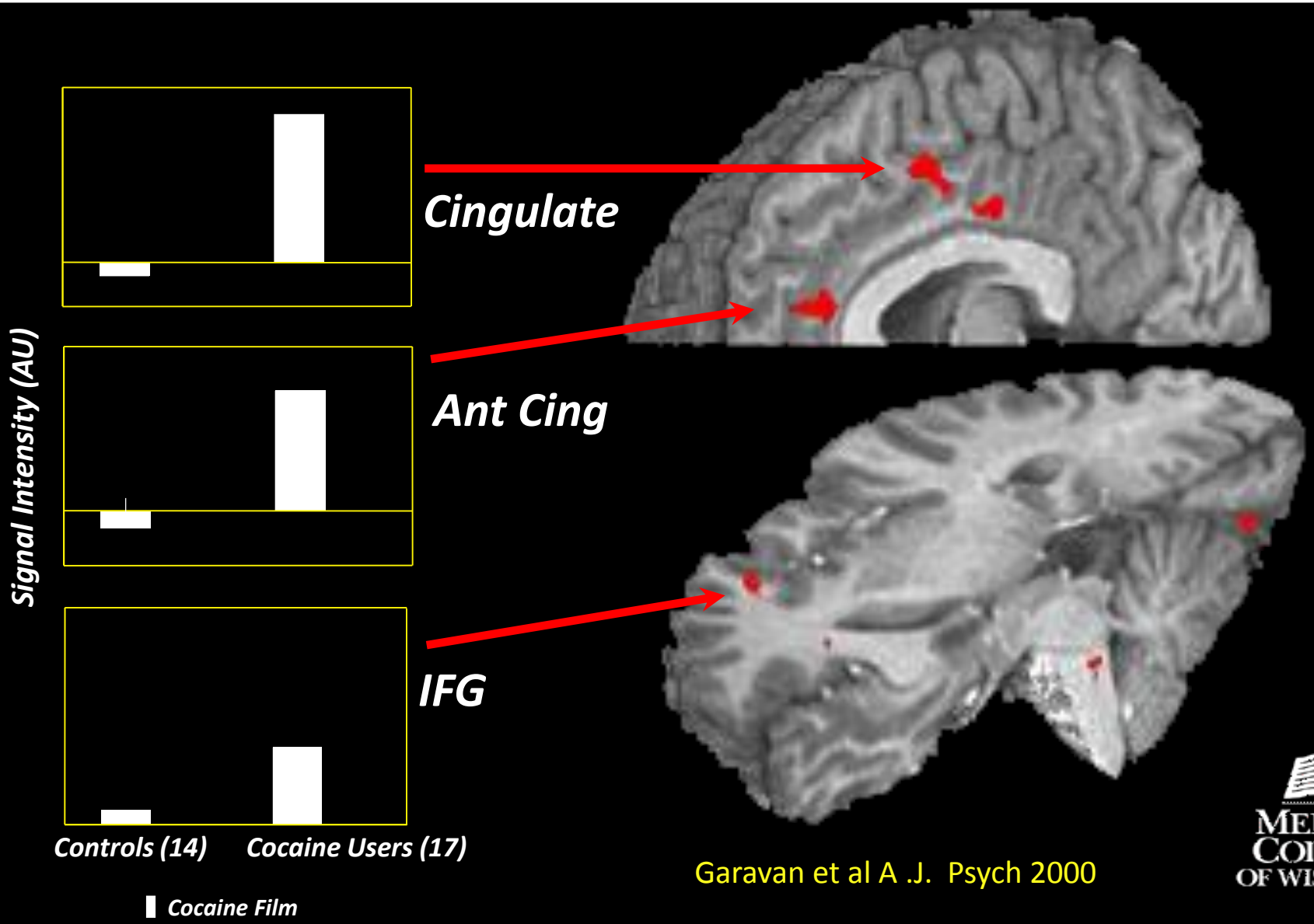
Cocaine Video

Childress, et al., AJP, 1999

NIDA

Cocaine Craving:

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

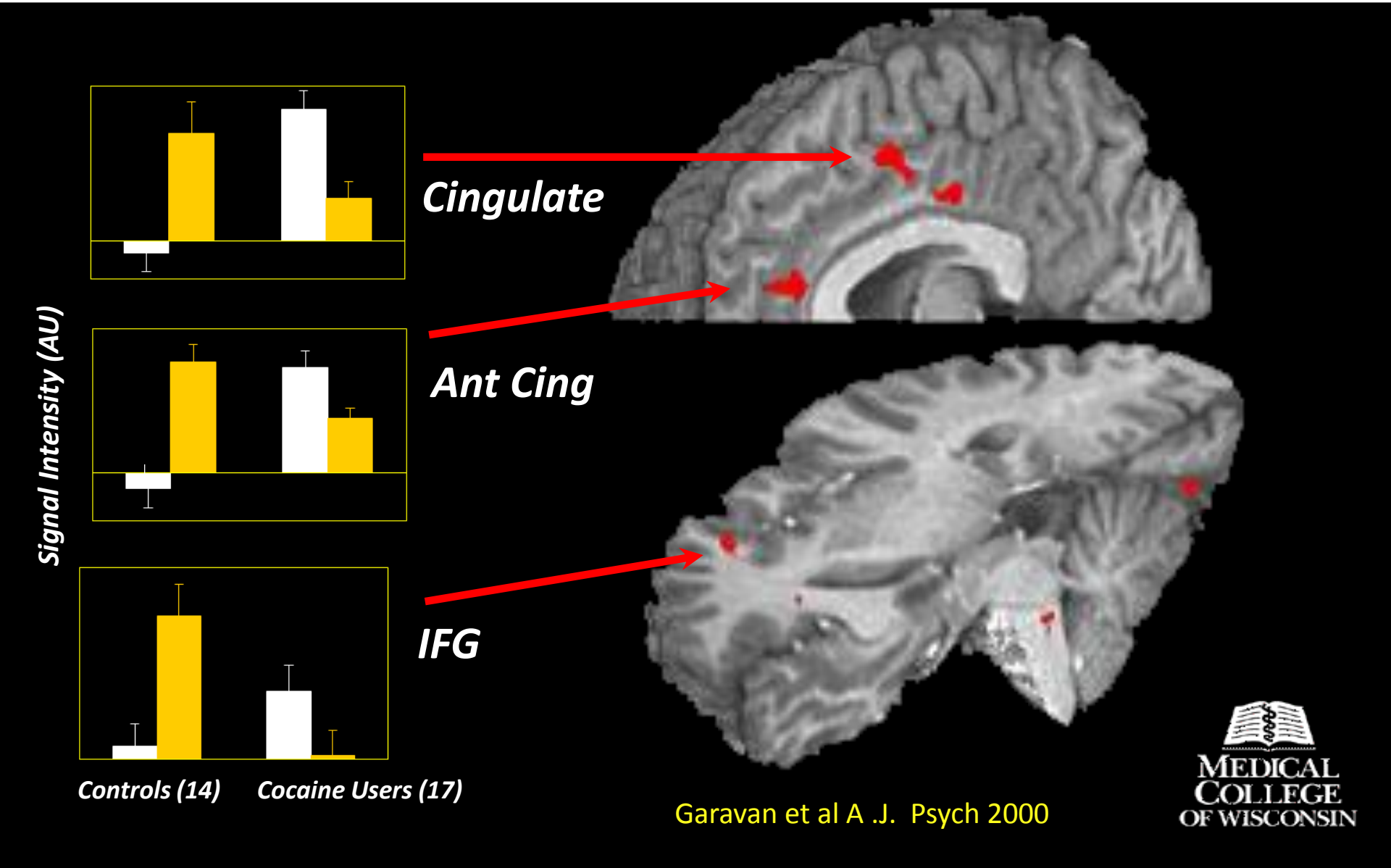


Garavan et al A .J. Psych 2000

MEDICAL COLLEGE OF WISCONSIN

Cocaine Craving:

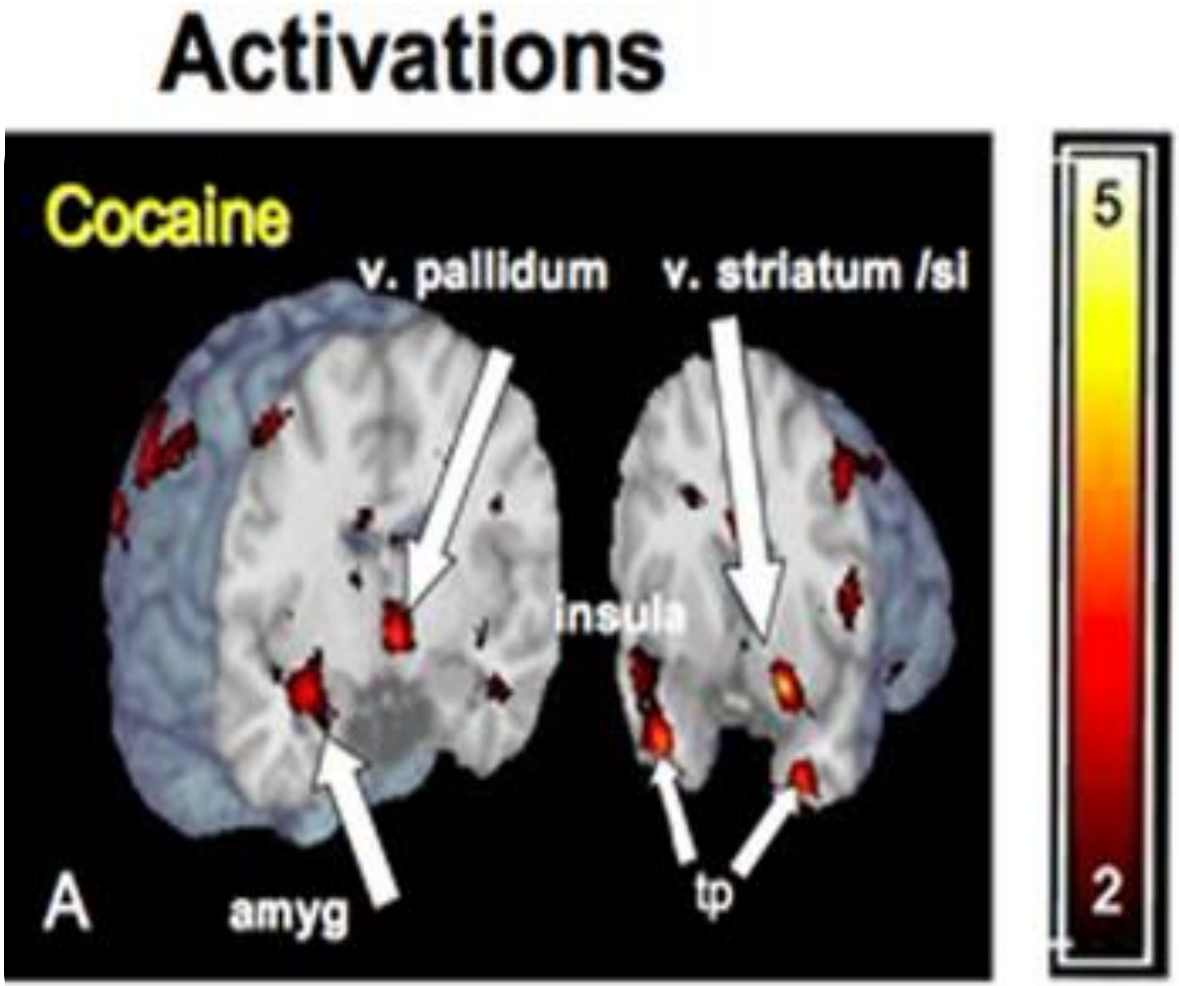
Population (Cocaine Users, Controls) x Film (cocaine, erotic)



Garavan et al A .J. Psych 2000

MEDICAL COLLEGE OF WISCONSIN

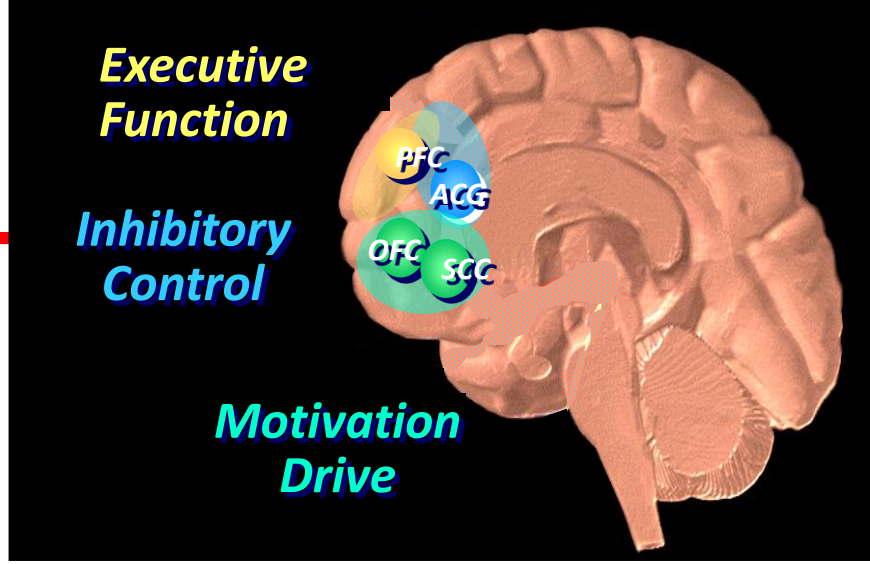
Even Unconscious Cues Can Elicit Brain Responses



Brain Regions Activated by 33 millisecond Cocaine Cues *(too fast for conscious recognition)*

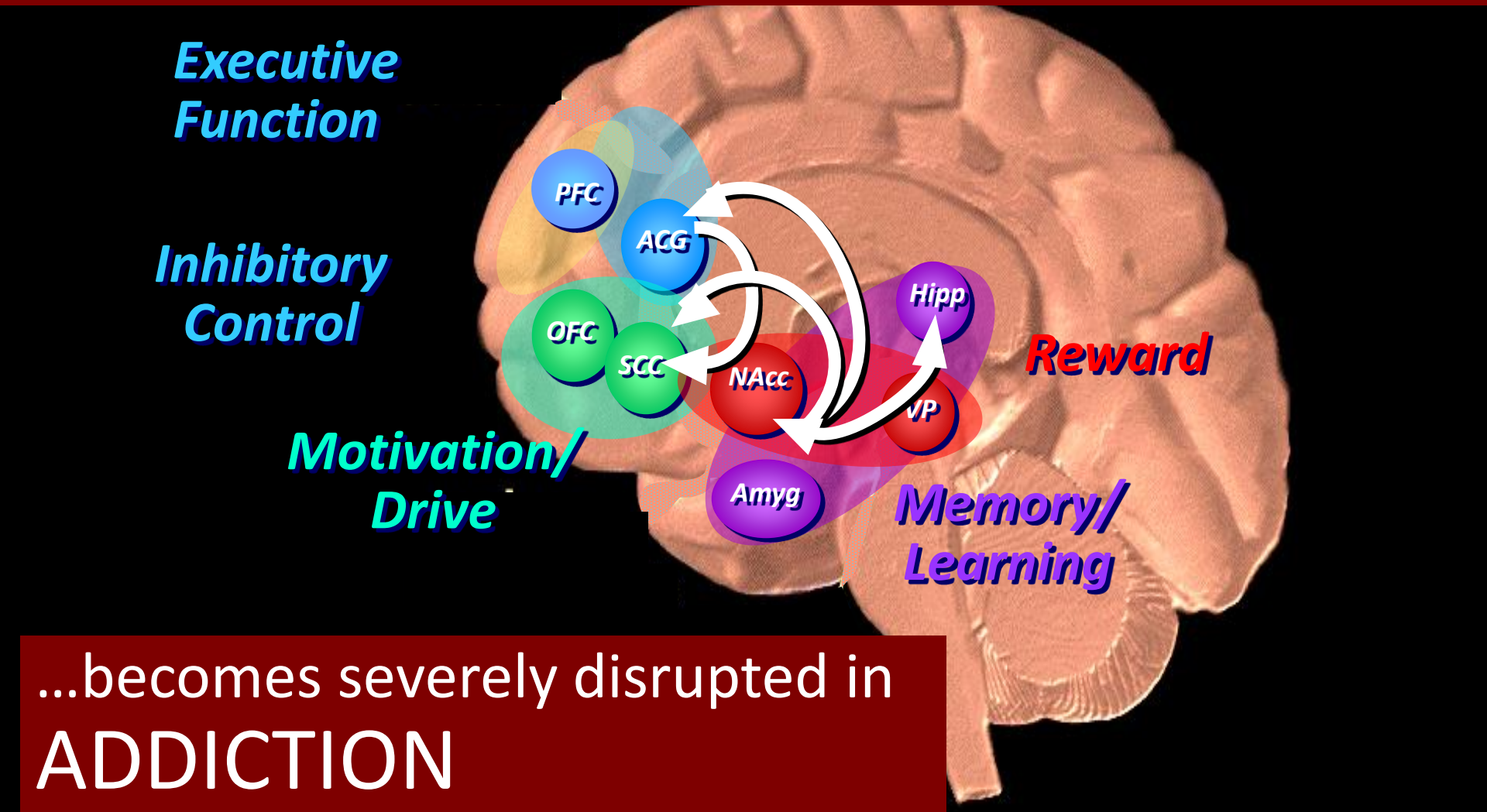
Childress, et al., PLoS ONE 2008

3. Motivation & Executive Control Circuits

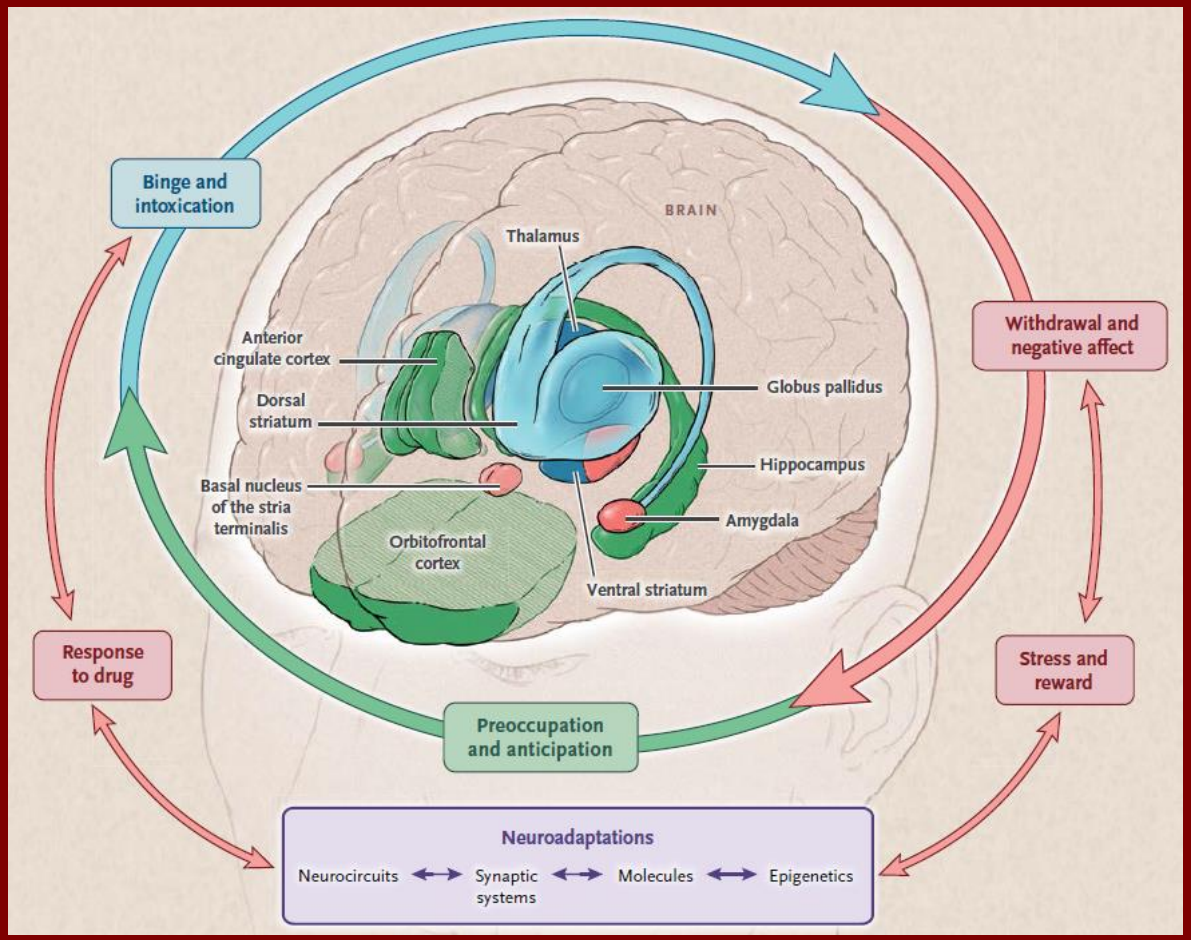


Dopamine is also associated with motivation and executive function via regulation of frontal activity.

Fine balance in connections that normally exists between **reward**, **motivation/drive**, **learning/memory** and **inhibitory control**…



…becomes severely disrupted in ADDICTION

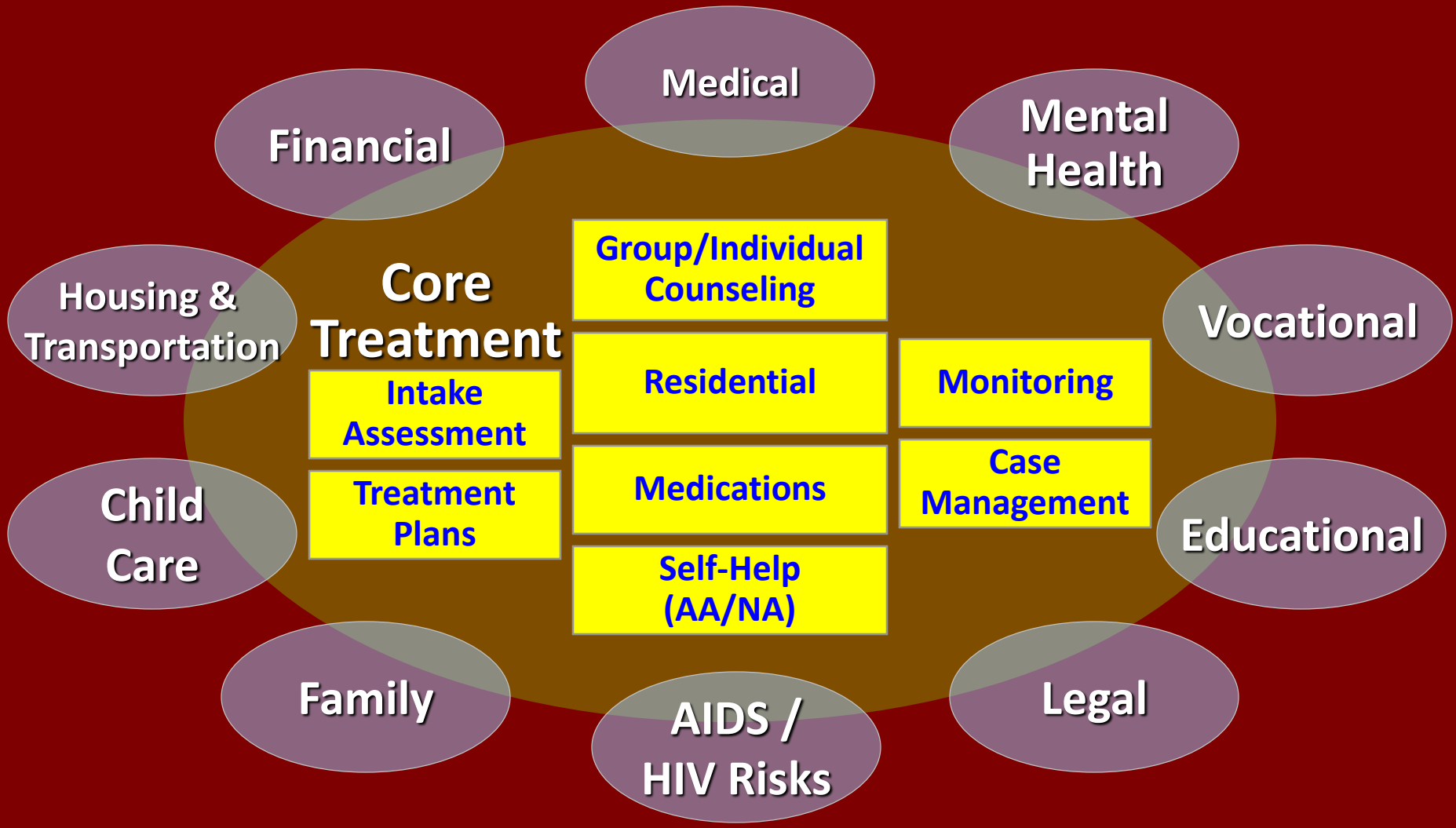


- Desensitized reward circuits → dampened pleasure
- Conditioned responses & stress reactivity → cravings and negative emotions
- Weakened executive function decision making, inhibitory control & self regulation → relapse

Stage of Addiction	Shifting Drivers Resulting from Neuroadaptations		
Binge and intoxication	Feeling euphoric	Feeling good	Escaping dysphoria
Withdrawal and negative affect	Feeling reduced energy	Feeling reduced excitement	Feeling depressed, anxious, restless
Preoccupation and anticipation	Looking forward	Desiring drug	Obsessing and planning to get drug

Volkow ND et al. N Engl J Med. 2016

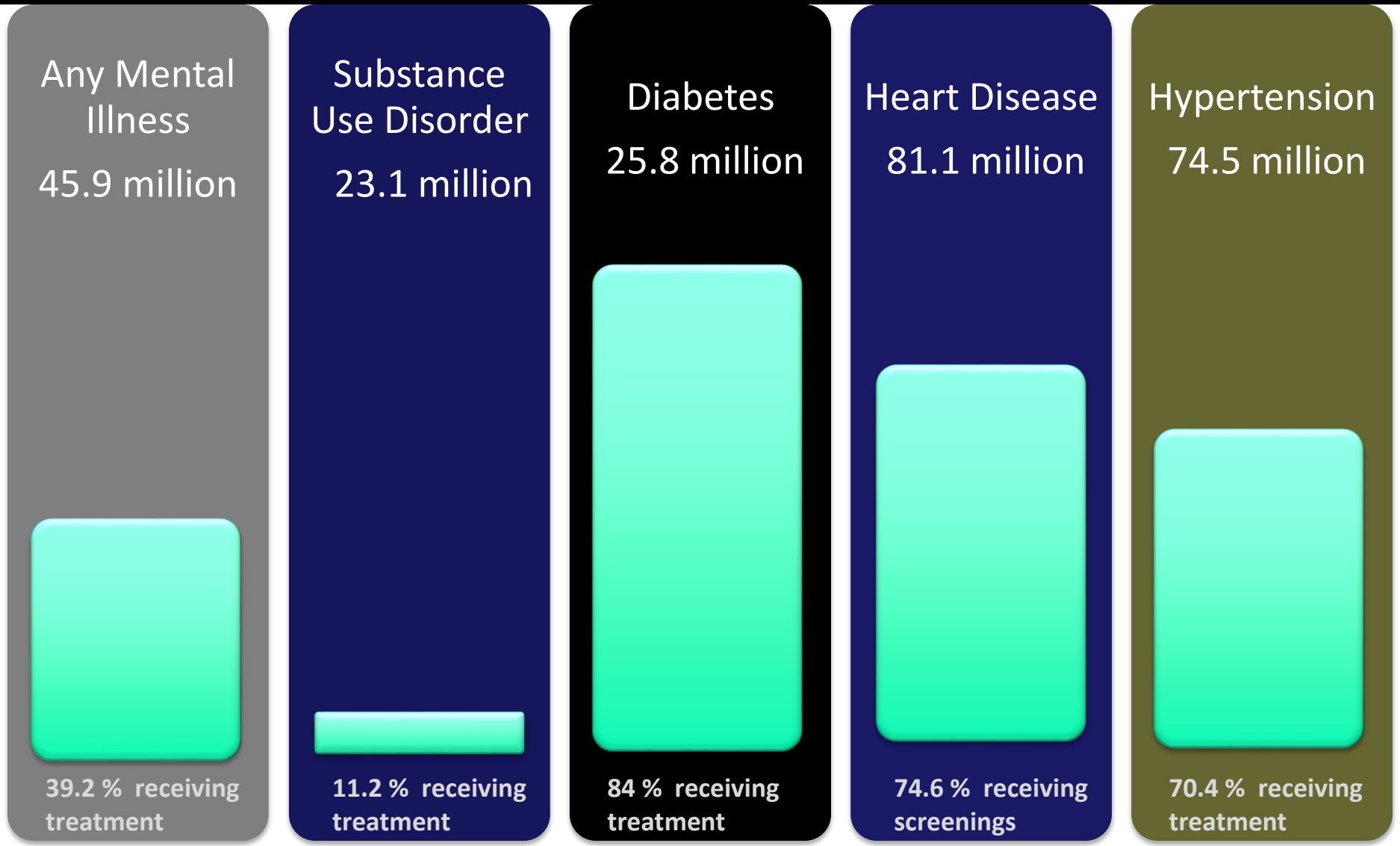
Addiction Treatment



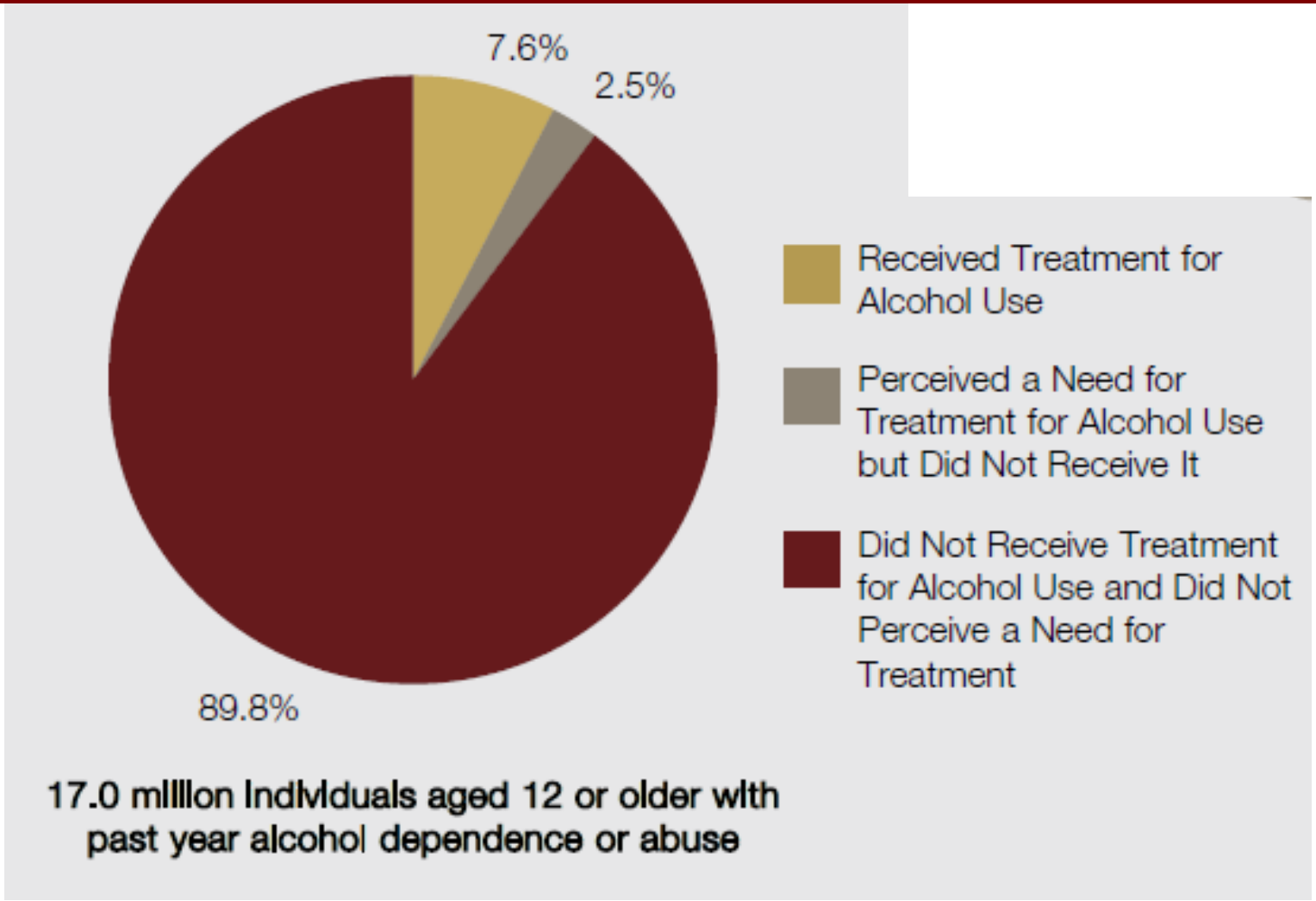
Etheridge, Hubbard, Anderson, Craddock, & Flynn, 1997 (PAB)

NIDA

Receipt of SUD Services Lags Behind other Chronic Disorders

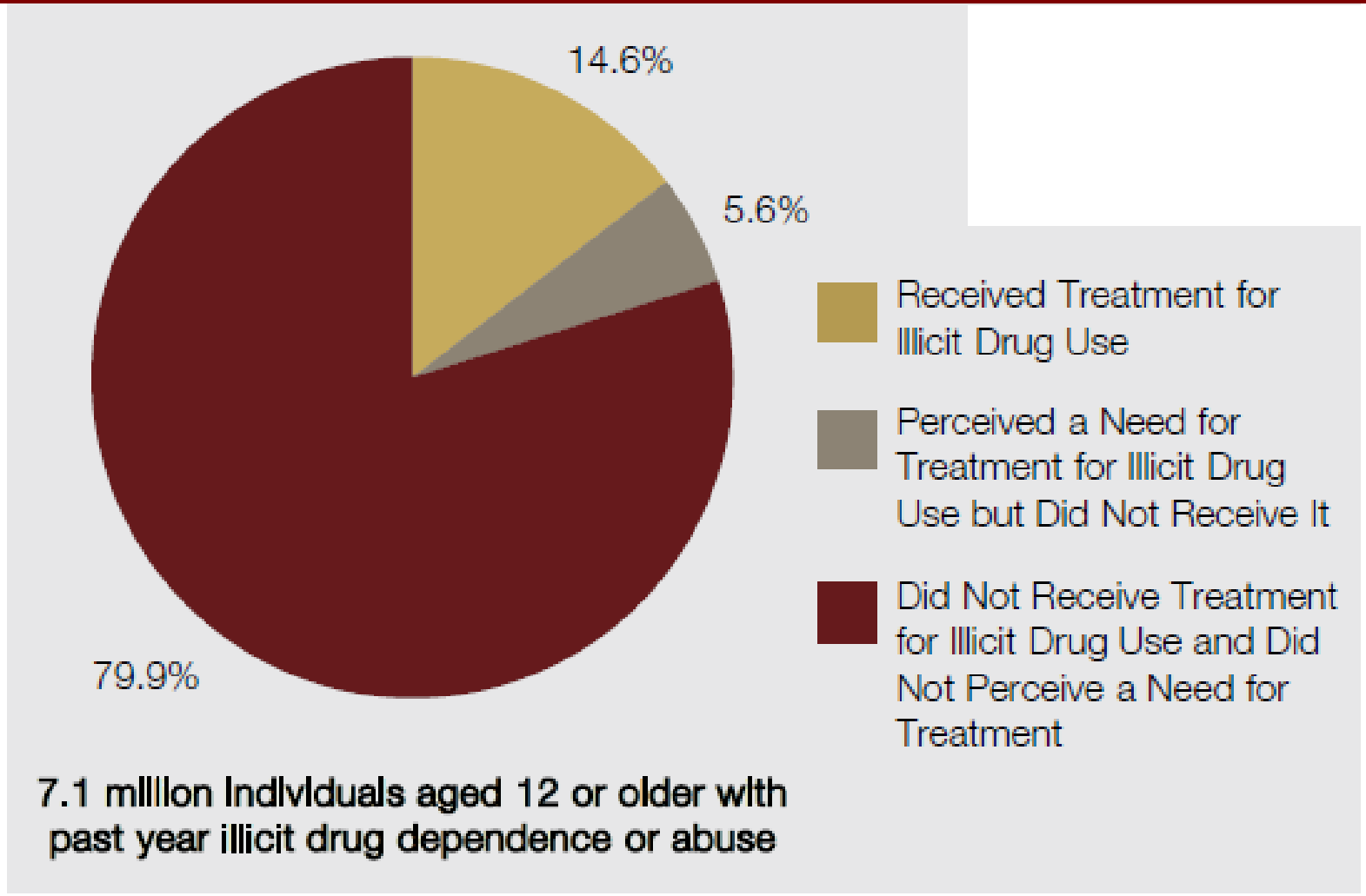


Perception of Treatment Need Among Adults with Alcohol Use Disorders



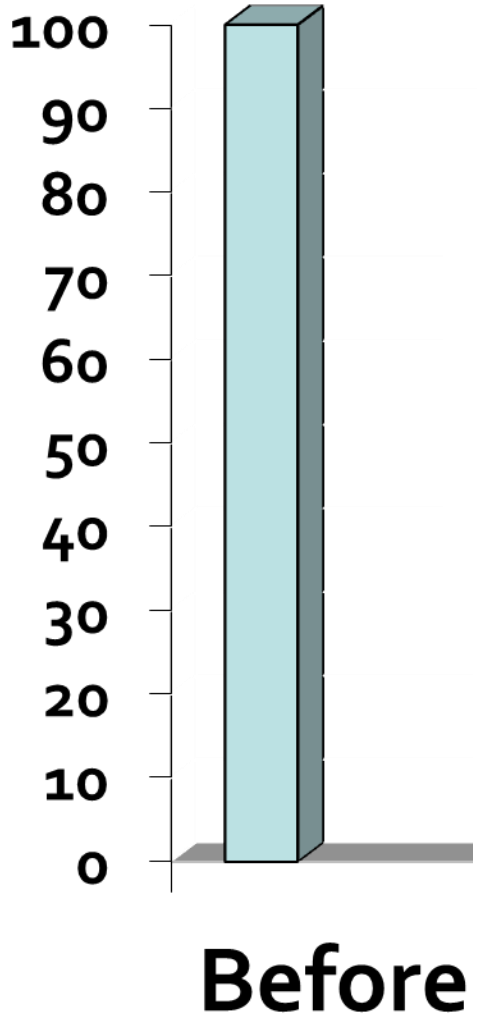
SAMHSA 2015 NSDUH

Perception of Treatment Need Among Adults with Drug Use Disorders



SAMHSA 2015 NSDUH

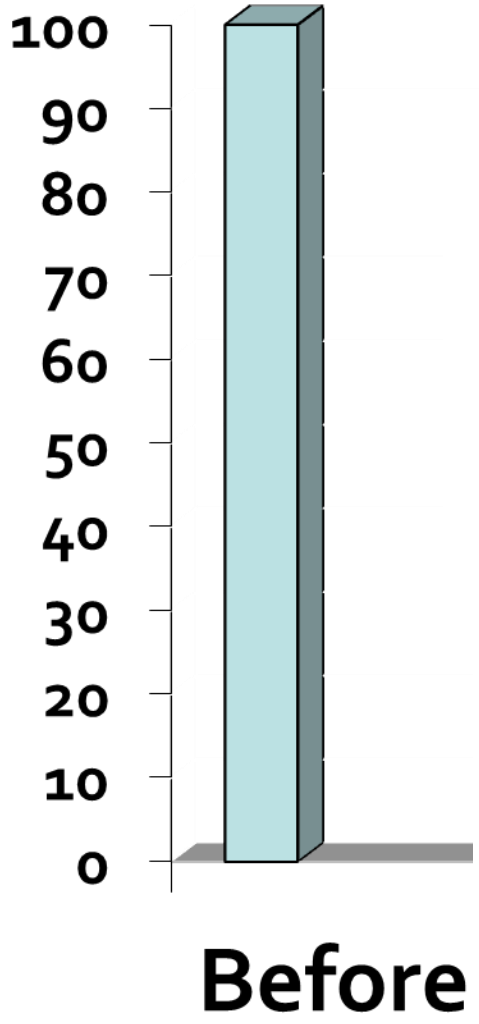
Evaluating Hypertension Treatment



It Works!

McLellan AT et al. JAMA 2000

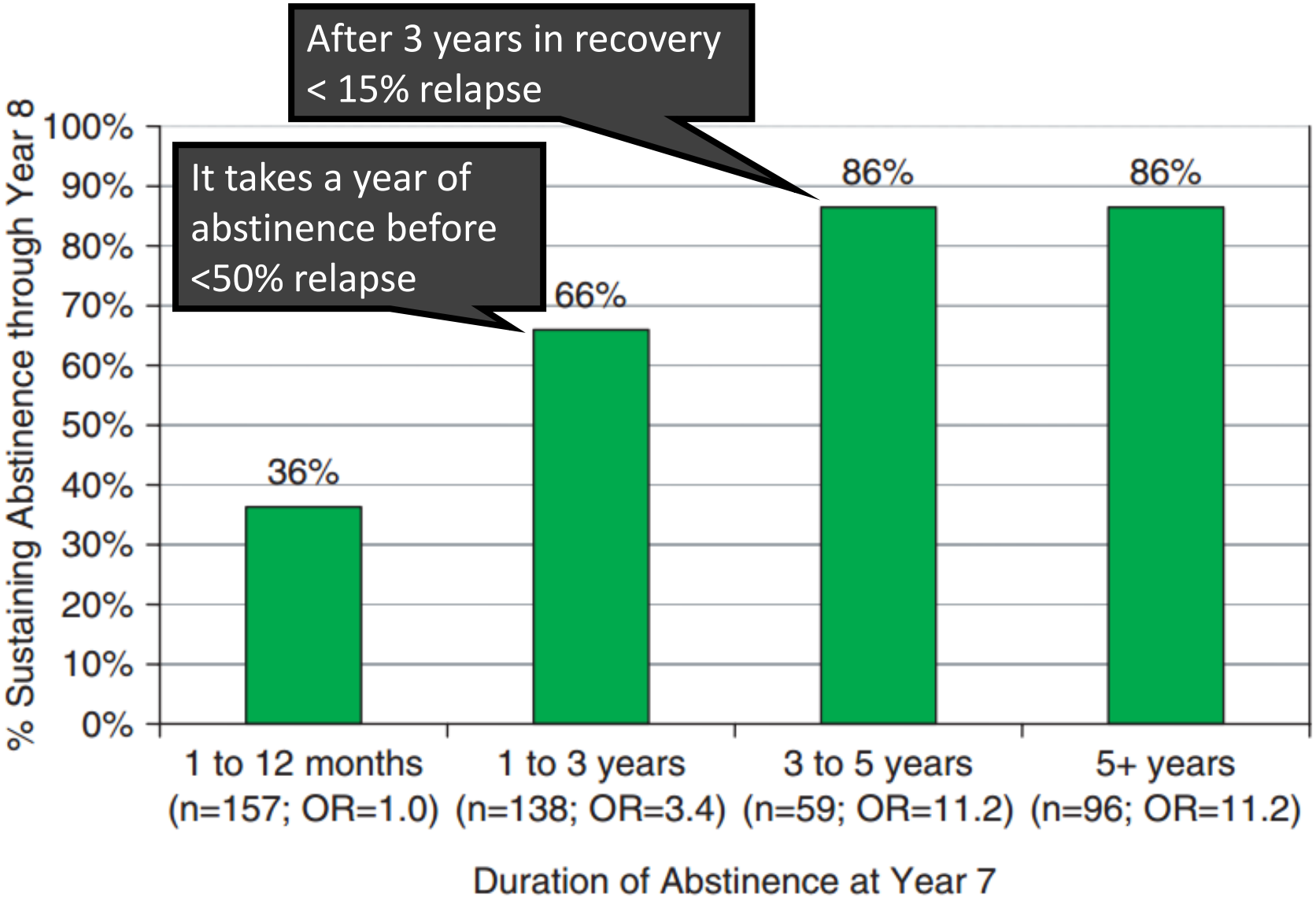
Evaluating Addiction Treatment



It Doesn't Work!?

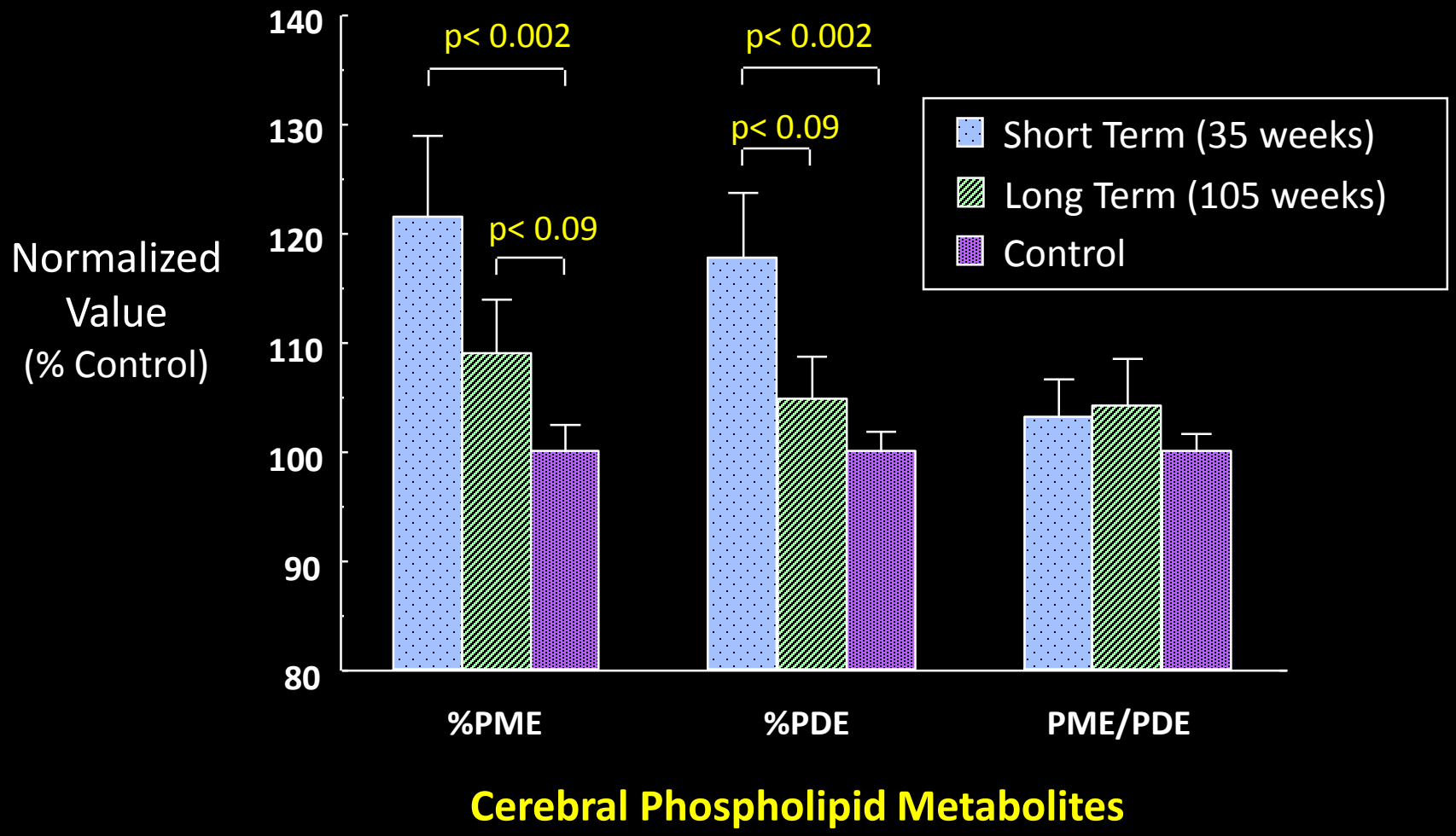
McLellan AT et al. JAMA 2000

Longitudinal Trends in Recovery



Dennis ML et al. Eval. Rev. 2007

Methadone Maintenance Improved Brain Neurochemistry



Kaufman MJ et al. Psychiatry Res 1999

The Language We Use…

Medications For Addiction Treatment: Changing Language to Improve Care

Sarah E. Wakeman, MD, FASAM

The term medication-assisted treatment has been widely adopted in reference to the use of opioid agonist therapy. Although it is arguably better than the older terms of replacement or substitution therapy, medication-assisted treatment implies that medications are a corollary to whatever the main part of treatment is. No other medication for other health conditions is referred to this way. It has finally been recognized that to improve care and reduce stigma, we must use medically accurate and person-first language, describing those with the disease of addiction as people with substance use disorder. However, to truly change outcomes, we must also alter the language of treatment.

Key Words: language, medication-assisted treatment, opioid agonist therapy, stigma

(*J Addict Med* 2017;11: 1–2)

person-first language, describing those with the disease of addiction as people with substance use disorder. However, to truly change outcomes, we must also alter the language of treatment.

The stigma surrounding the use of pharmacotherap… particular opioid agonist therapy, is arguably more potent … harmful than the general stigma about addiction. The … widely held and stigmatizing belief is the notion that … cation is simply a "replacement addiction," "substituting … drug for another," or even "liquid handcuffs." Not only … this false notion of replacement or substitution misunderst… the definition of addiction, but it is quite literally killing pe… Recent statistics demonstrate that although starting op… agonist therapy after an overdose is associated with a … reduction in subsequent death, less than 5% of those … survive an overdose receive pharmacotherapy (Massachus… Department of Public Health, 2016) The term "medicat…

Friedmann and Schwartz *Addiction Science & Clinical Practice* 2012, **7**:10
http://www.ascpjournal.org/content/7/1/10

ADDICTION SCIENCE & CLINICAL PRACTICE

COMMENTARY **Open Access**

Just call it "treatment"

Peter D Friedmann[1*] and Robert P Schwartz[2]

ELSEVIER

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Editorial

Stop Talking 'Dirty': Clinicians, Language, and Quality of Care for the Leading Cause of Preventable Death in the United States

John F. Kelly, PhD[a], Sarah E. Wakeman, MD[b], Richard Saitz, MD[c]

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EDITORIAL

Confronting Inadvertent Stigma and Pejorative Language in Addiction Scholarship: A Recognition and Response

Lauren M. Broyles, PhD, RN,[1,2,3] Ingrid A. Binswanger, MD, MPH,[4,5] Jennif… Deborah S. Finnell, DNS, PMHNP,[6] Babalola Faseru, MD, MPH,[7,8,9] Alan… Marianne Pugatch, MSW,[11,12,13,14] and Adam J. Gordon, MD, M…

VIEWPOINT

Changing the Language of Addiction

JAMA 2016

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White House Office of National Drug Control Policy, Washington, DC.

Howard K. Koh, MD, MPH
Harvard T.H. Chan School of Public Health, Boston, Massachusetts; and Harvard Kennedy School, Cambridge, Massachusetts.

Words matter. In the scientific arena, the routine vocabulary of health care professionals and researchers frames illness[1] and shapes medical judgments. When these terms then enter the public arena, they convey social norms and attitudes. As part of their professional duty, clinicians strive to use language that accurately reflects science, promotes evidence-based treatment, and demonstrates respect for patients.

However, history has also demonstrated how language can cloud understanding and perpetuate societal bias. For example, in the past, people with mental illness were derided as "lunatics" and segregated to

Stigma isolates people, discourages people from coming forward for treatment, and leads some clinicians, knowingly or unknowingly, to resist delivering evidence-based treatment services. The 2014 National Survey on Drug Use and Health[4] estimates that of the 22.5 million people (aged ≥12 years) who need specialty treatment for a problem with alcohol or illicit drug use, only an estimated 2.6 million received treatment in the past year; of the 7.9 million specifically needing specialty treatment for illicit drug use, only 1.6 million received treatment. The survey noted that reasons for not seeking treatment included fears that