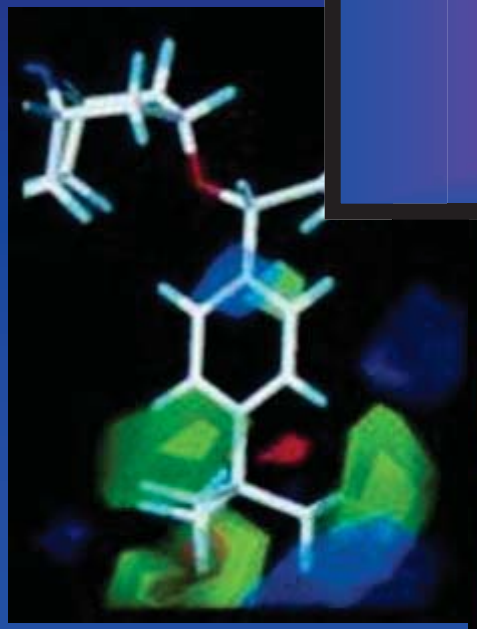
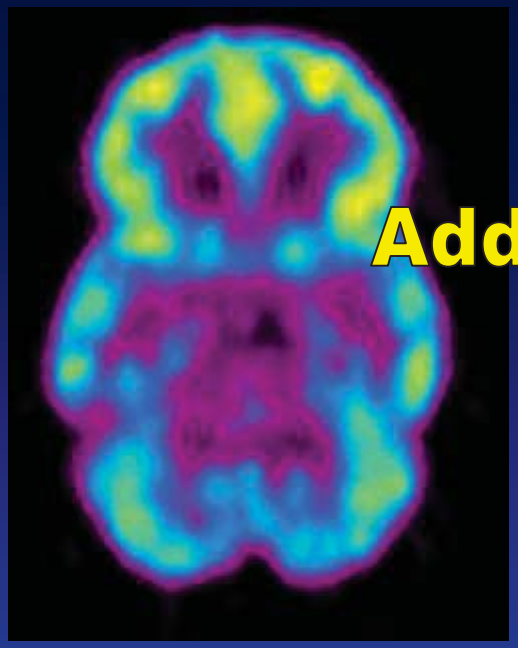
NIDA

NATIONAL INSTITUTE ON DRUG ABUSE

Bringing the Full Power of Science to Bear on

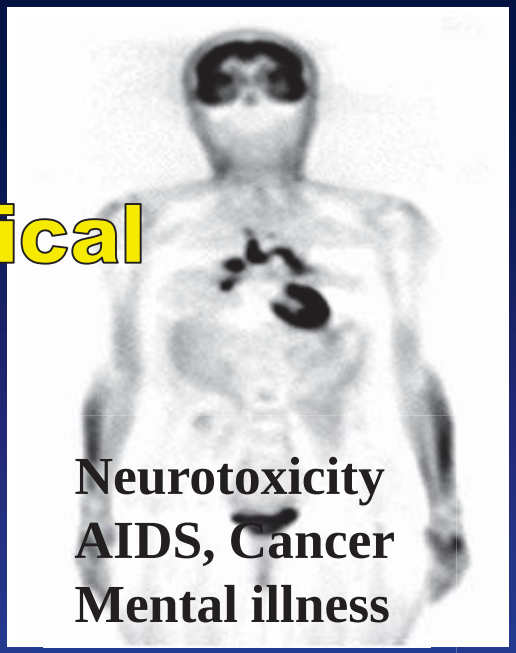
Drug Abuse & Addiction





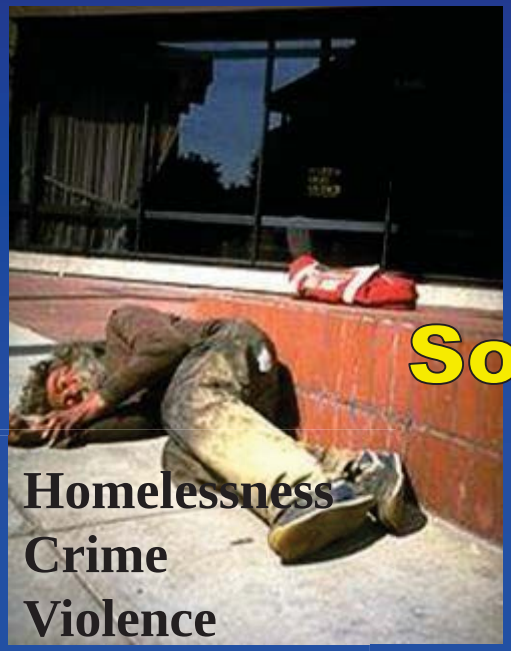
Addiction

Medical



Neurotoxicity
AIDS, Cancer
Mental illness

DRUGS



Social

Homelessness
Crime
Violence

Economic

Health care
Productivity
Accidents

4 Out of 10 U.S. AIDS Deaths Are Related to Drug Abuse

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Estimated Economic Cost to Society Due to Substance Abuse and Addiction:

Illegal drugs:	**$181 billion/year**
Alcohol:	**$185 billion/year**
Tobacco:	**$158 billion/year**
Total:	**$524 billion/year**

Surgeon General's Report, 2004; ONDCP, 2004; Harwood, 2000.

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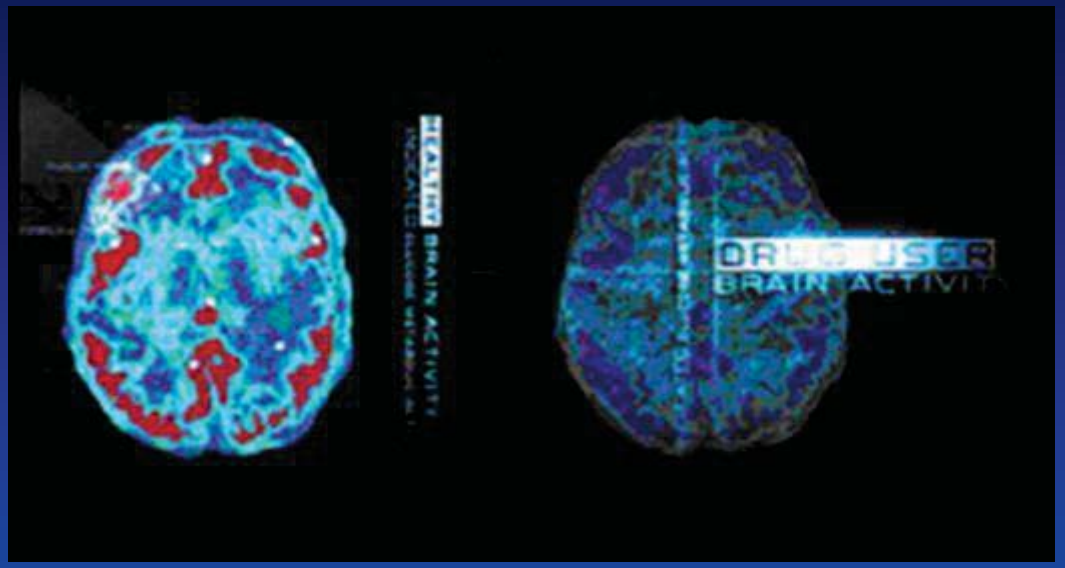
What is Addiction?
Addiction is A Brain Disease



- Characterized by:
  - Compulsive Behavior
  - Continued abuse of drugs despite negative consequences
  - Persistent changes in the brain's structure and function

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Advances in science have revolutionized our fundamental views of drug abuse and addiction.

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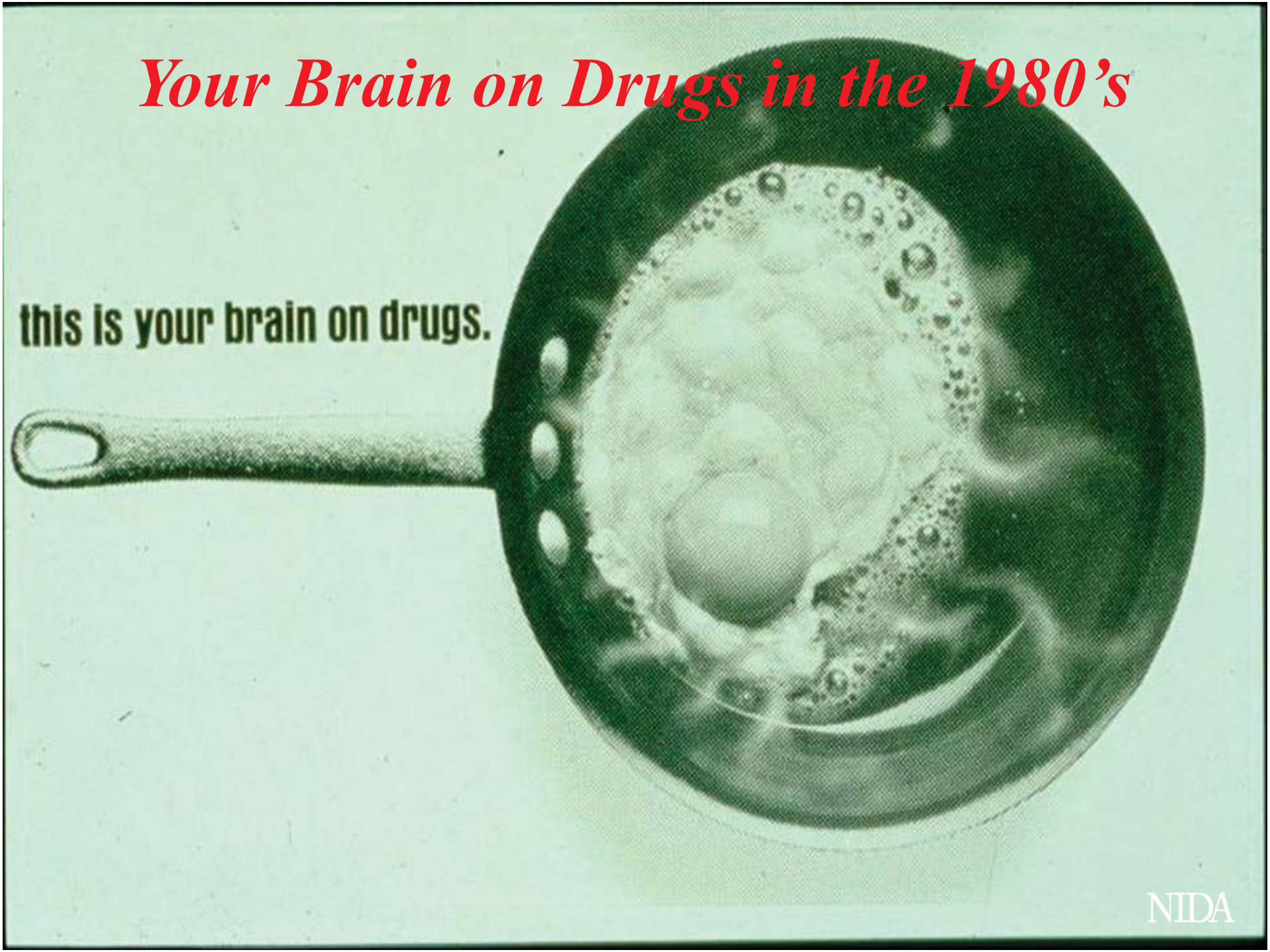
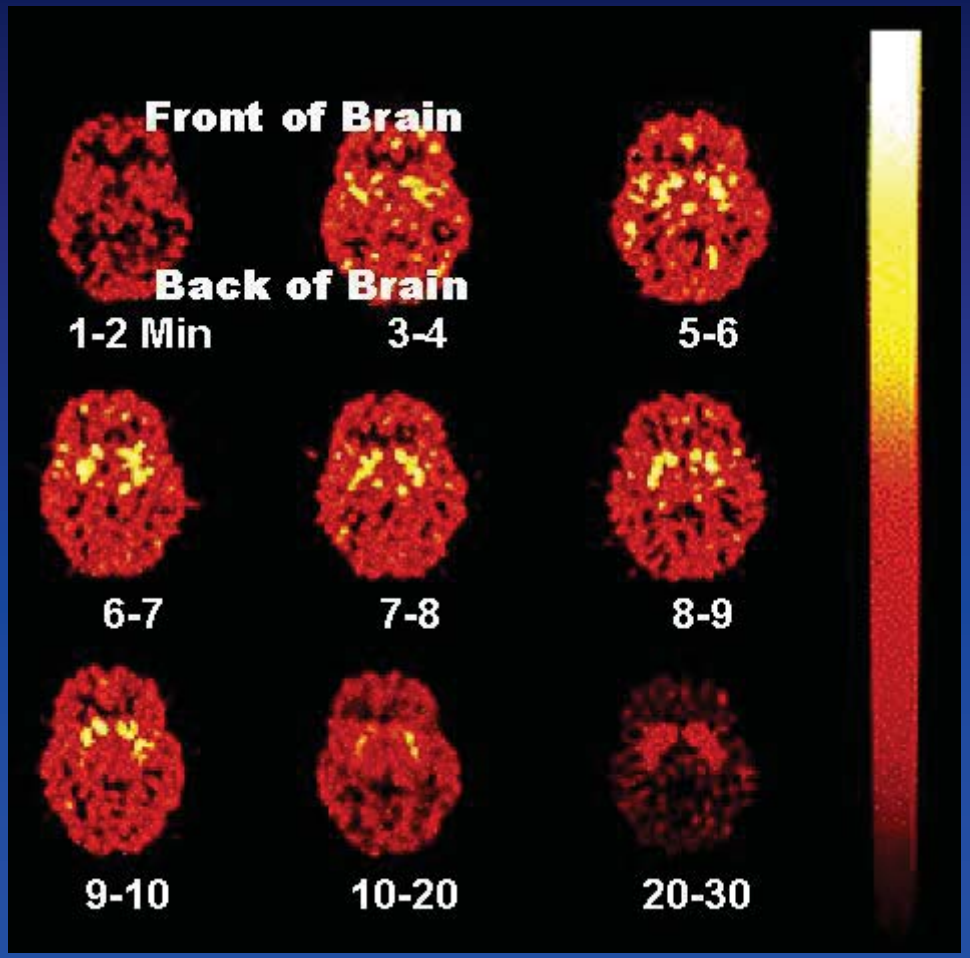
Your Brain on Drugs in the 1980's



Your Brain on Drugs Today



YELLOW shows places in brain where cocaine binds (e.g., striatum)

Fowler et al., Synapse, 1989.

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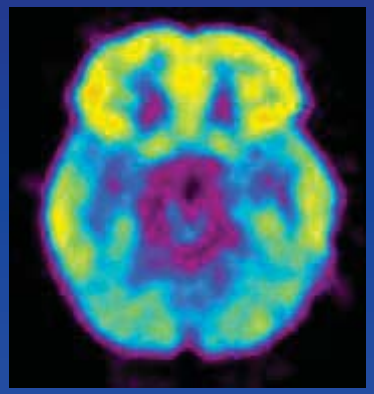
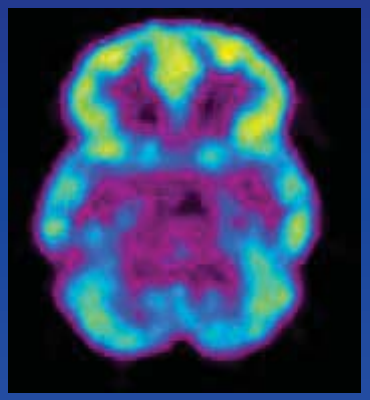
Addiction is Like Other Diseases…

- It is preventable
- It is treatable
- It changes biology
- If untreated, it can last a lifetime

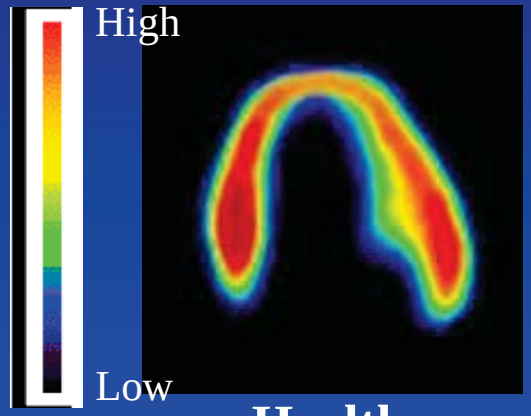
Decreased Brain Metabolism in *Drug Abuser*



Healthy Brain

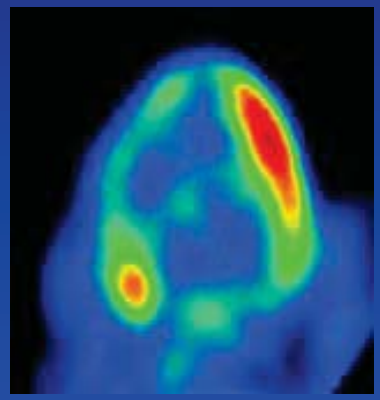


Diseased Brain/ Cocaine Abuser



Decreased Heart Metabolism in *Heart Disease Patient*

Healthy Heart



Diseased Heart

Research supported by NIDA addresses all of these components of addiction.

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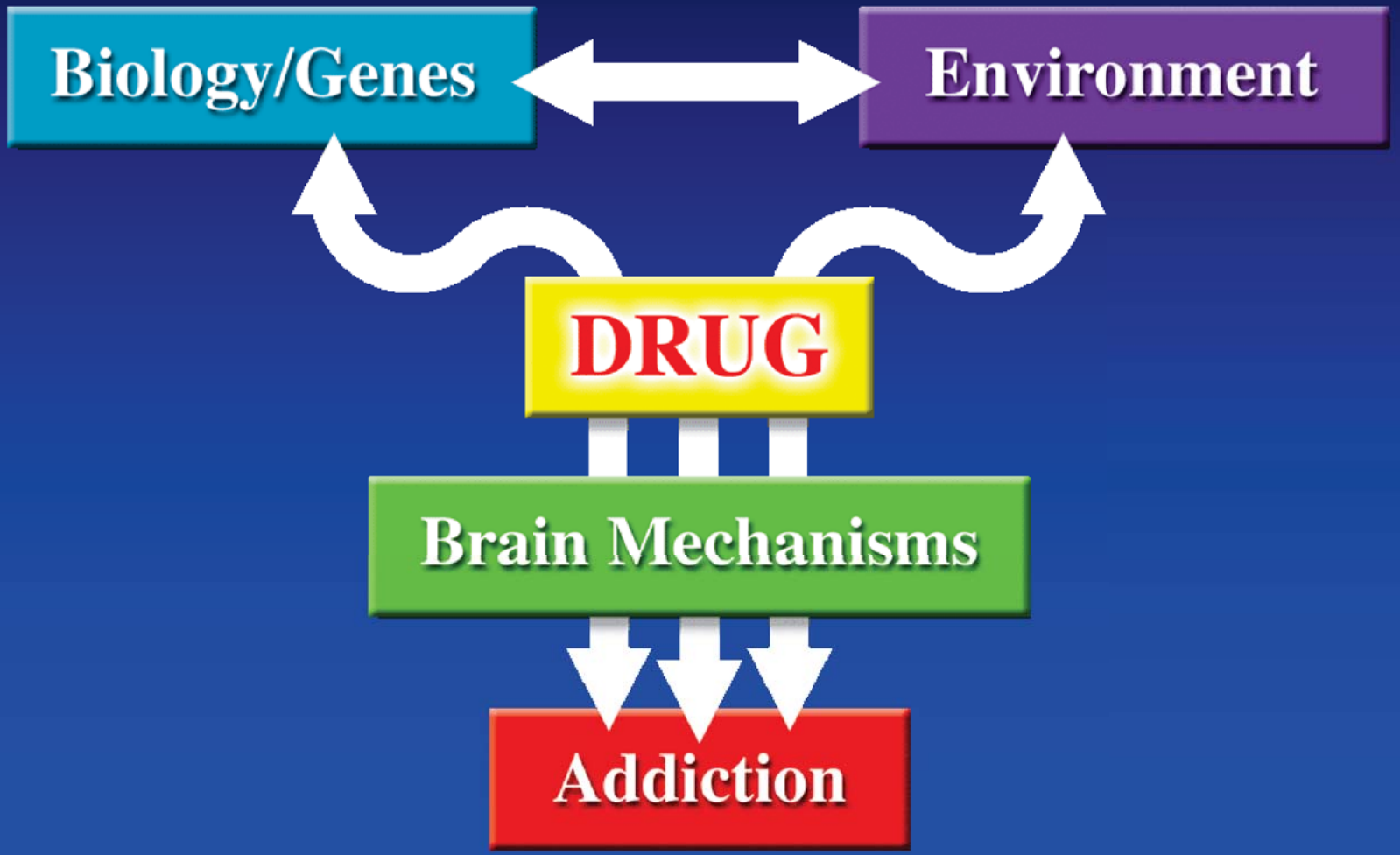
Addiction Involves Multiple Factors



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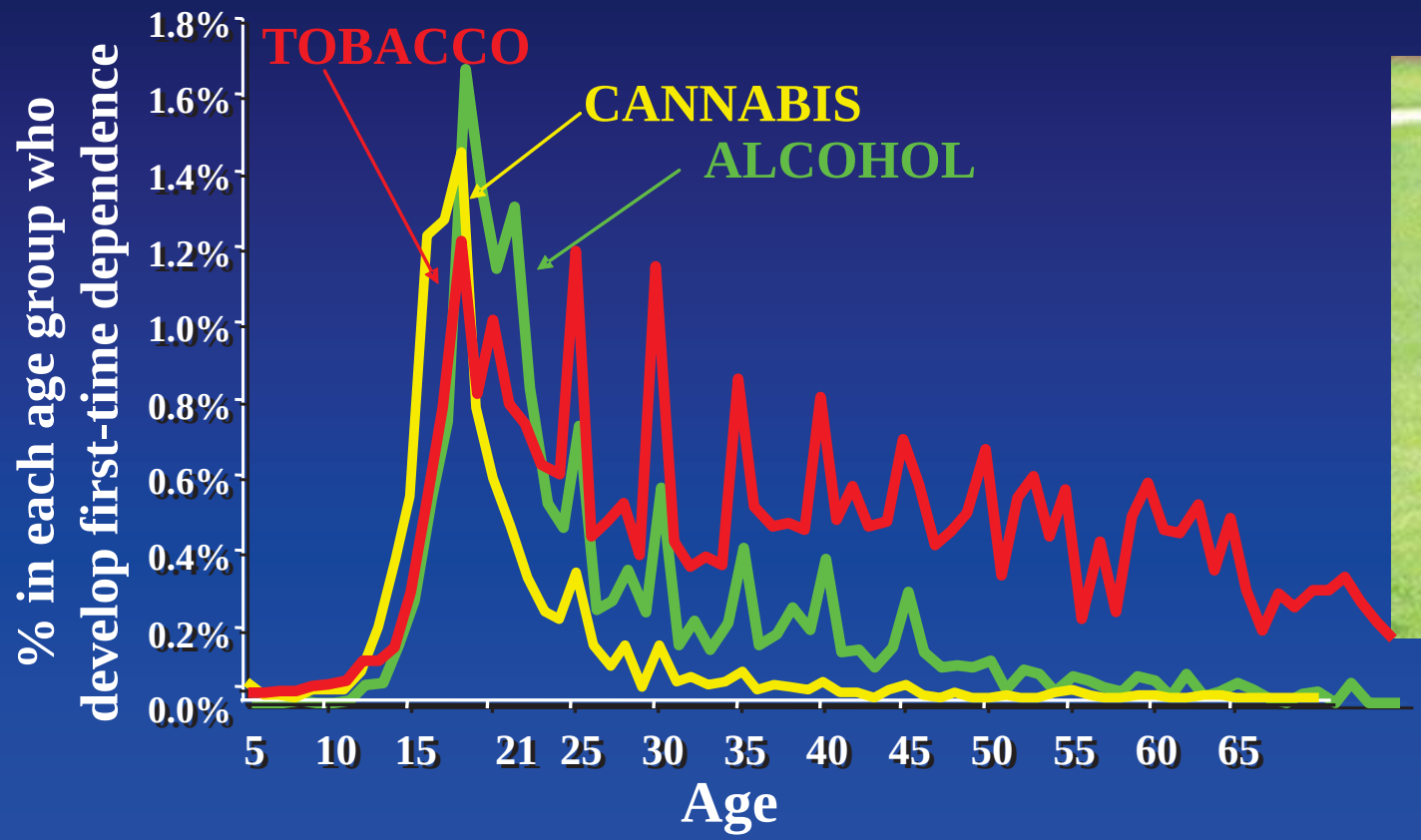
Addiction Is A Developmental Disease that starts in adolescence and childhood



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

National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

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Why Do People Take Drugs in The First Place?

To Feel Good

To have novel:

feelings

sensations

experiences

AND

to share them

To Feel Better

To lessen:

anxiety

worries

fears

depression

hopelessness

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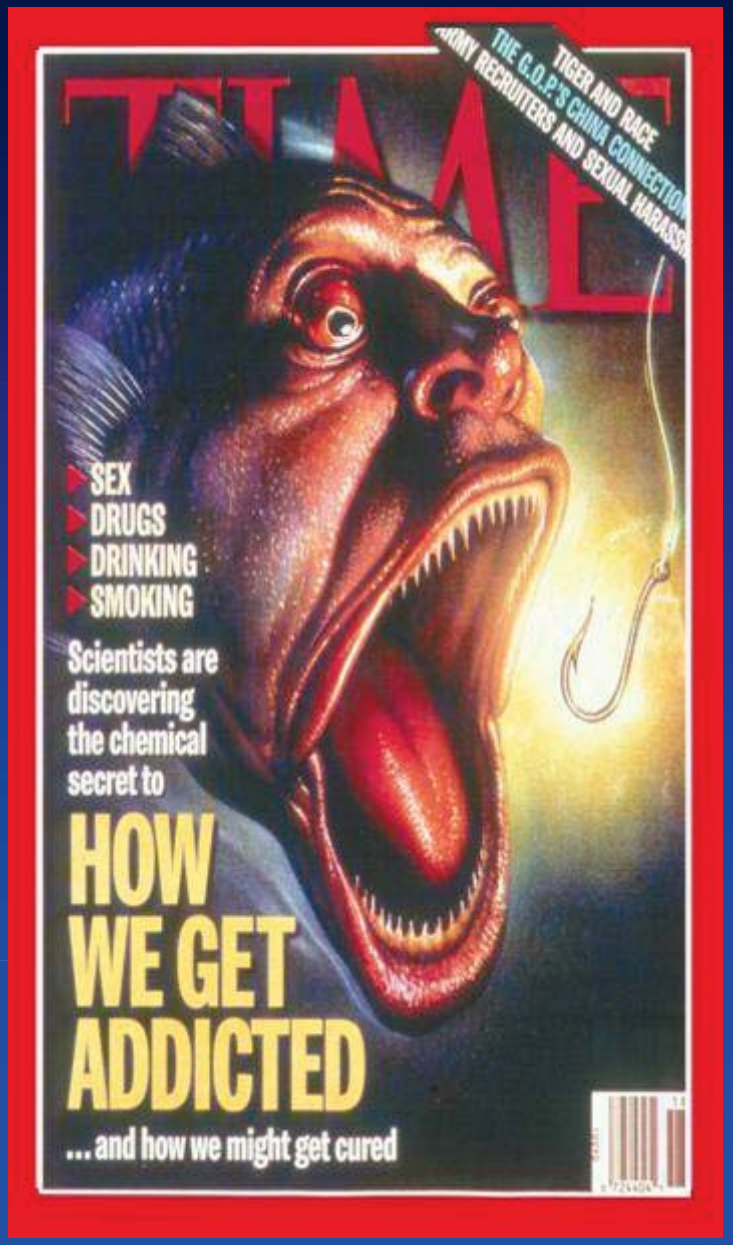
Why Do People Abuse Drugs?

Drugs of Abuse Engage *Motivation* and *Pleasure Pathways of the Brain*



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Drugs can be "Imposters" of Brain Messages

Brain's Chemical

Anandamide

Drug

THC

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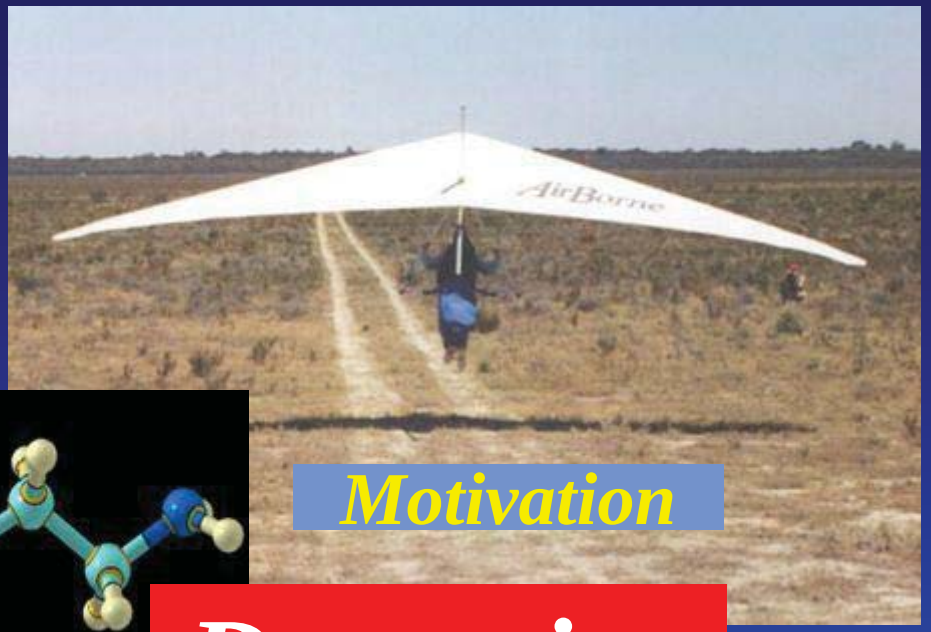
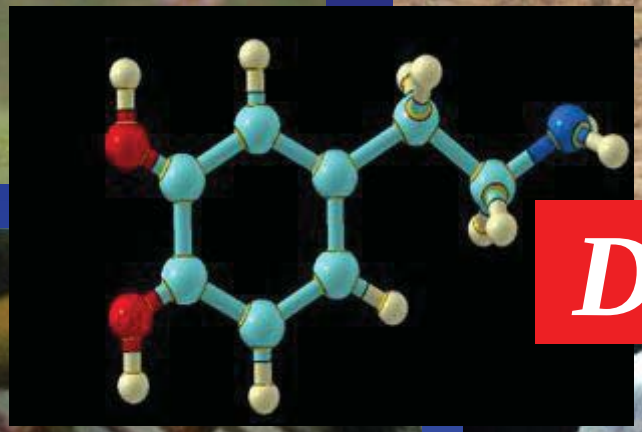
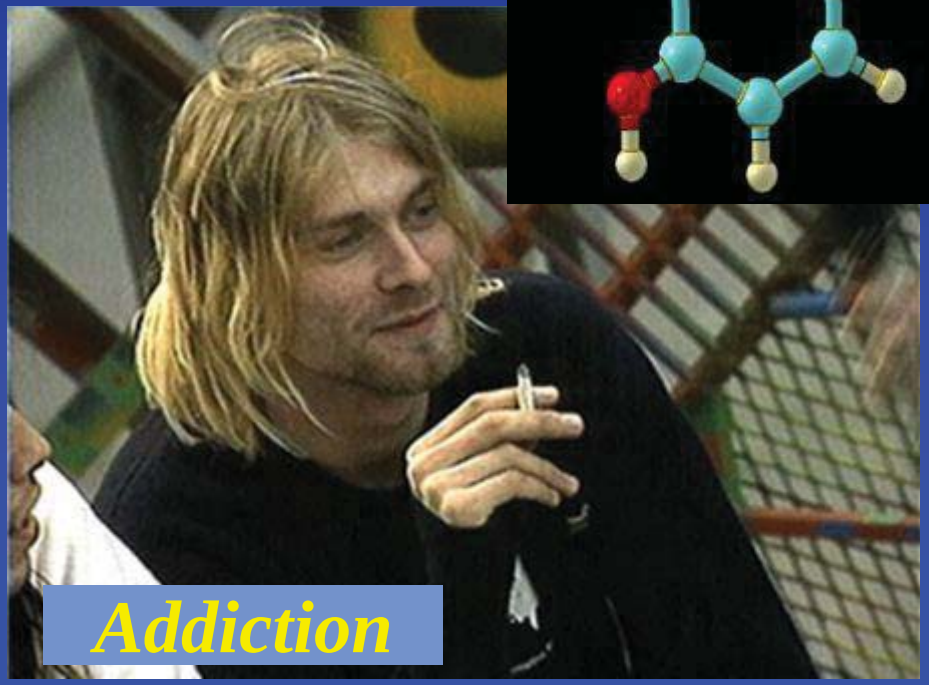
Movement



Motivation



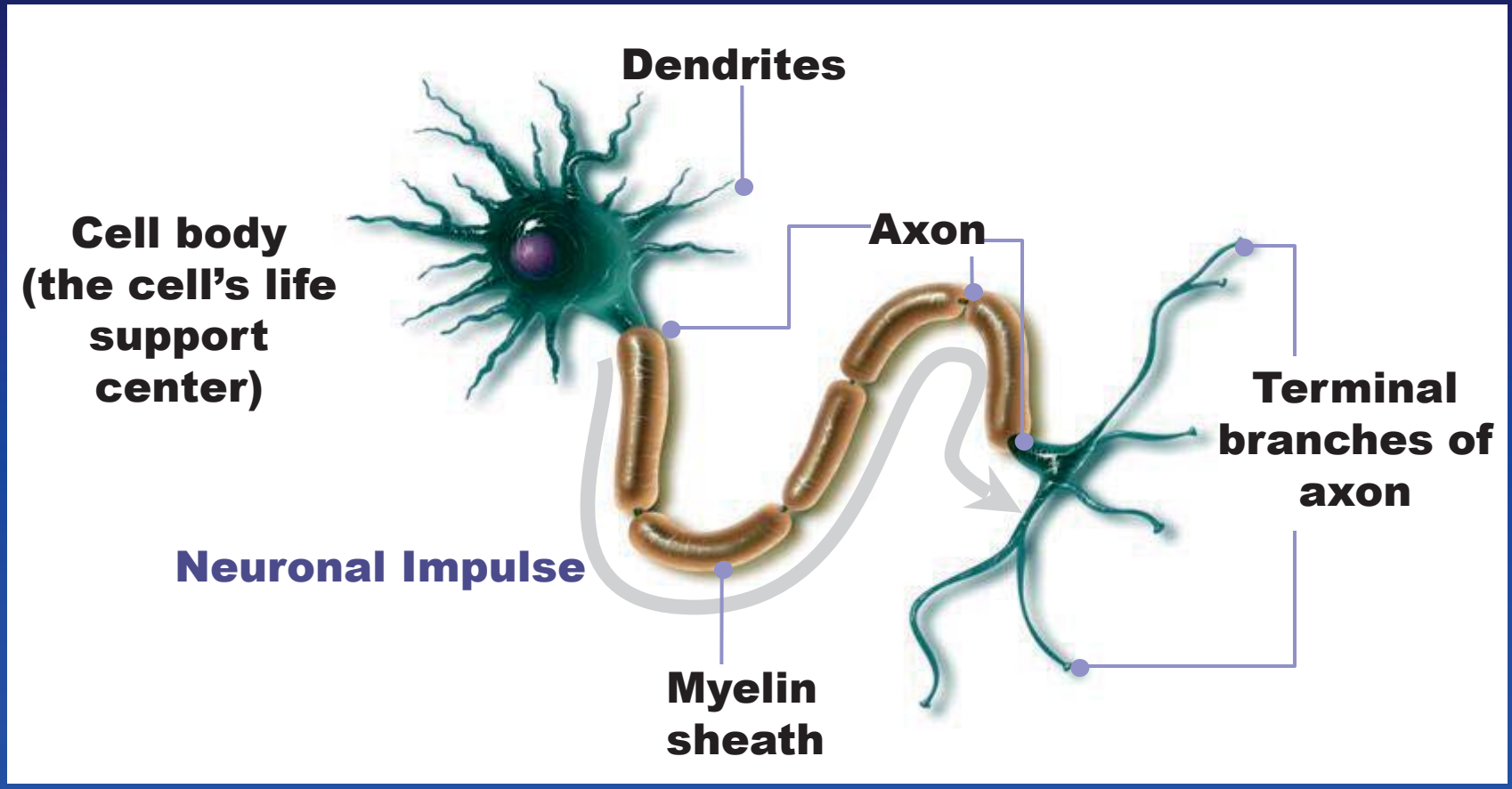
Dopamine



Addiction

Reward & well-being

The Neuron: How the Brain's Messaging System Works



Donald Bliss, MAPB, Medical Illustration

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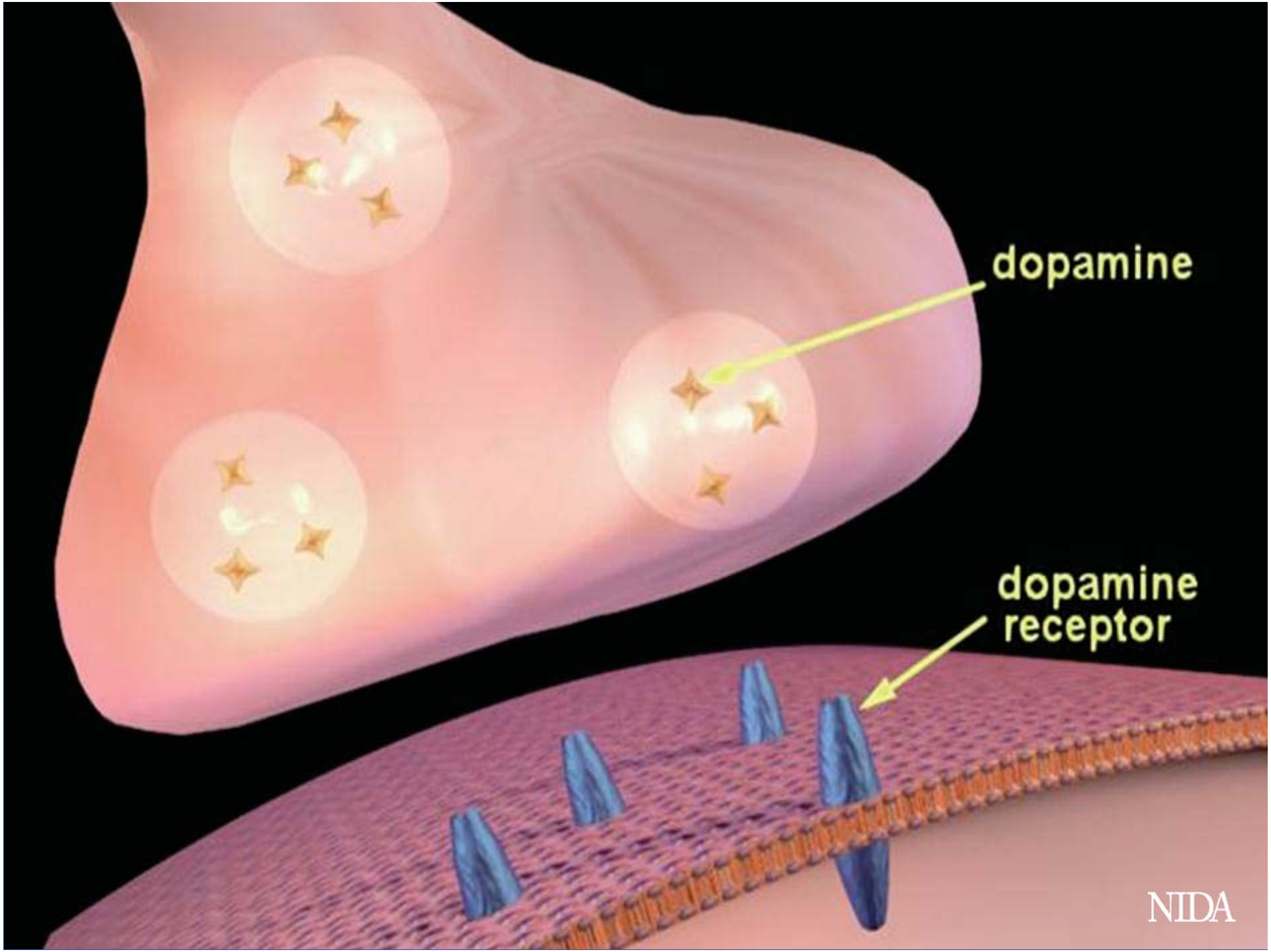
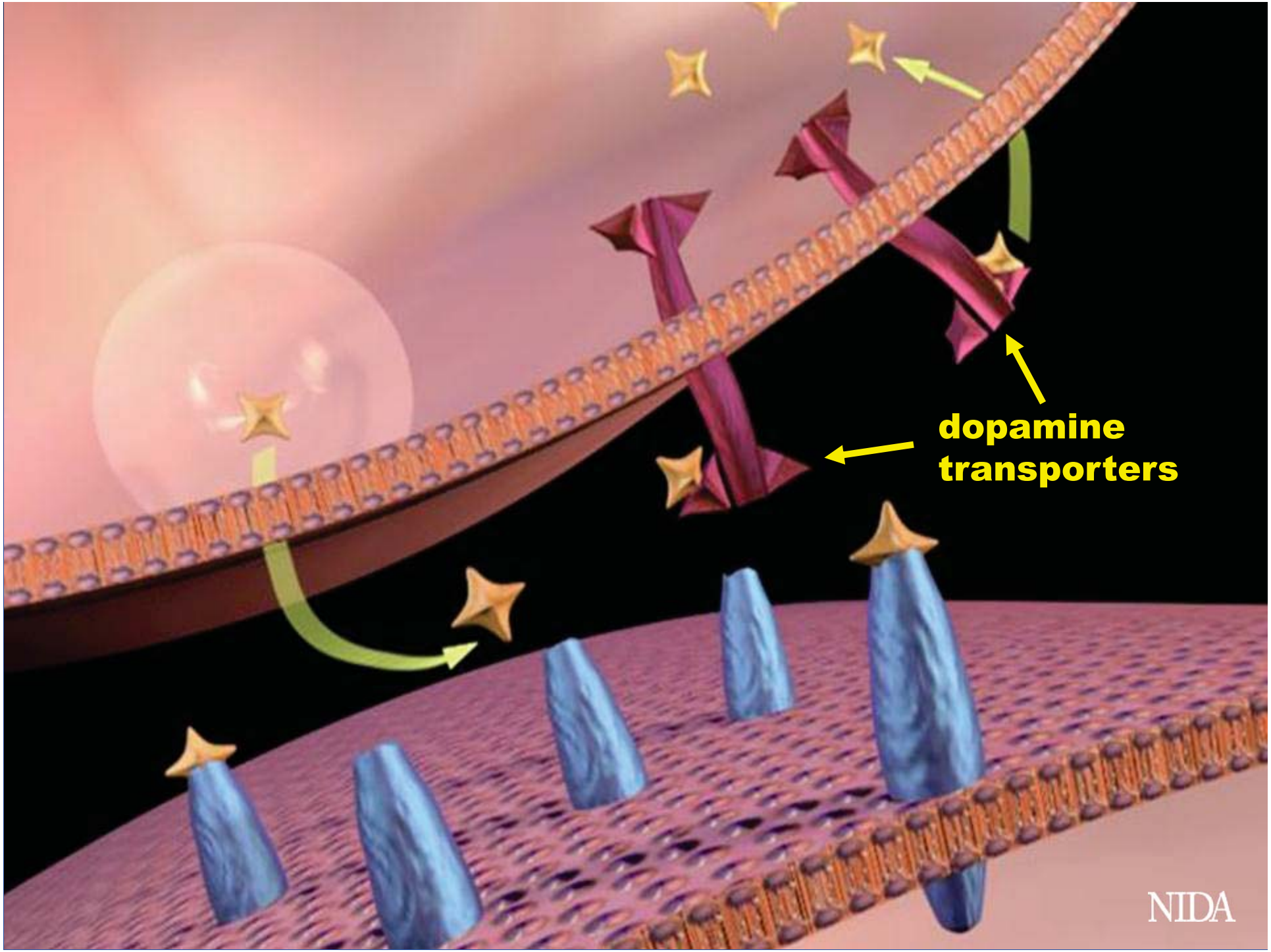
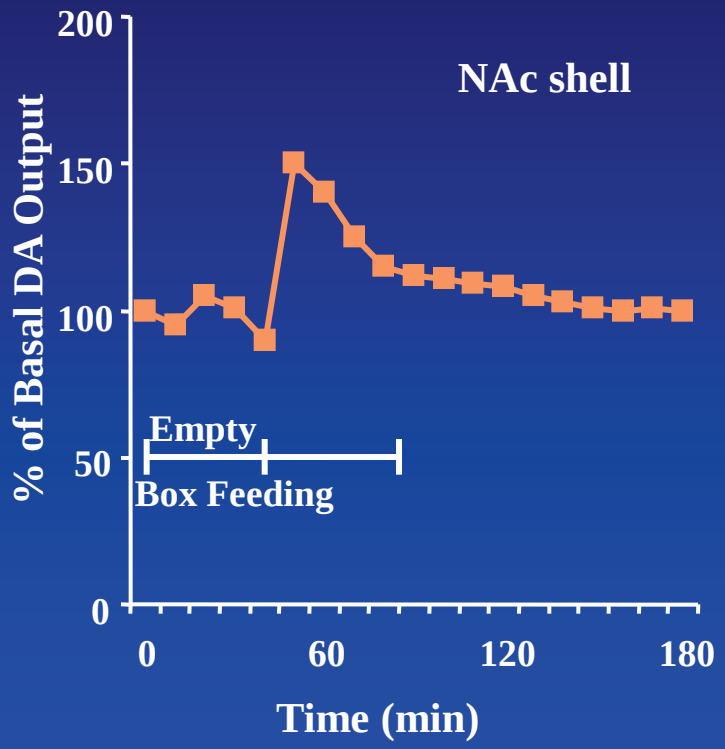

dopamine
dopamine receptor
NIDA

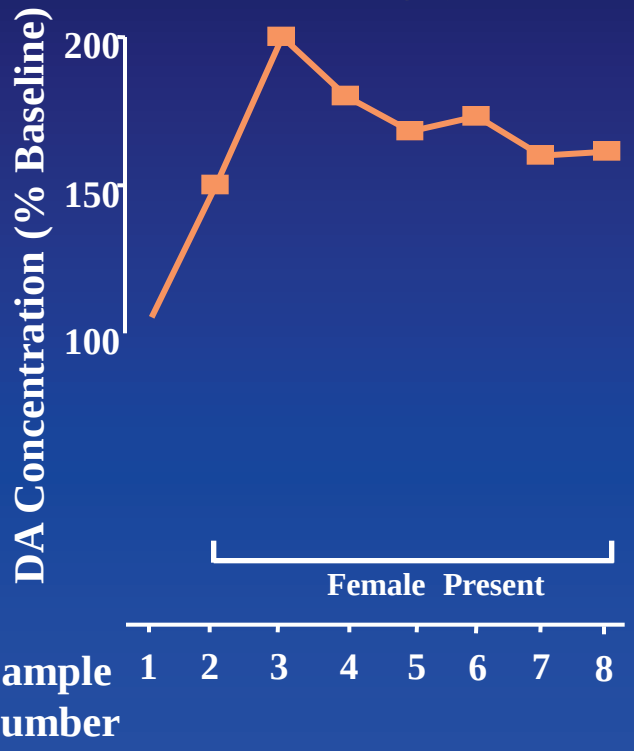

dopamine
transporters
NIDA

Natural Rewards Elevate Dopamine Levels

Food

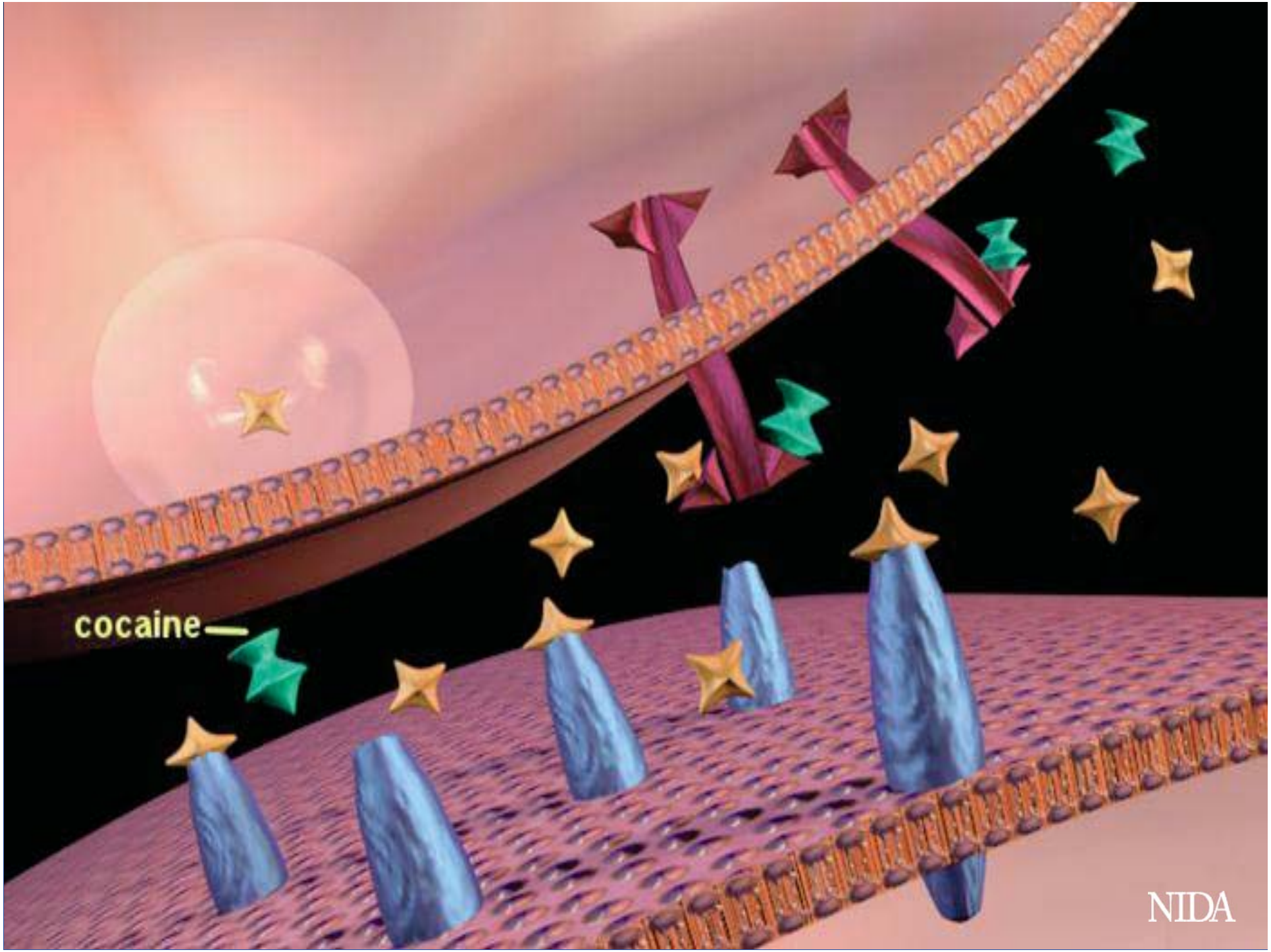


Sex



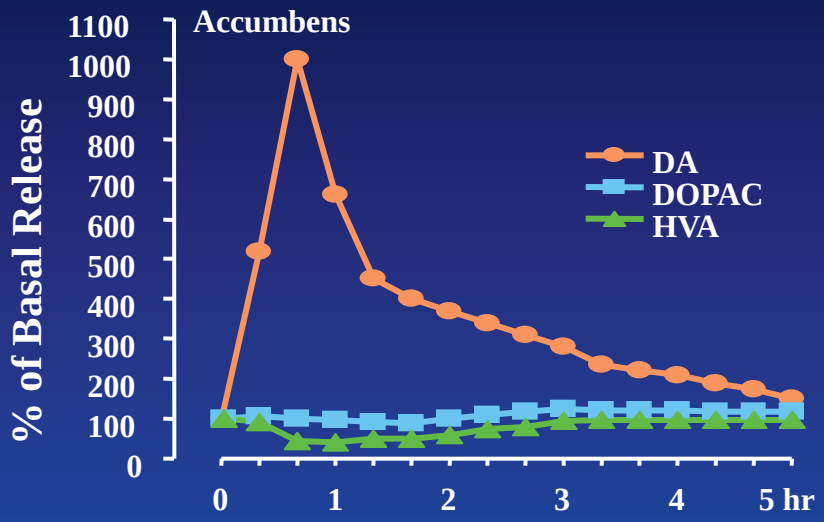
Di Chiara et al., Neuroscience, 1999.,Fiorino and Phillips, J. Neuroscience, 1997.

NIDA

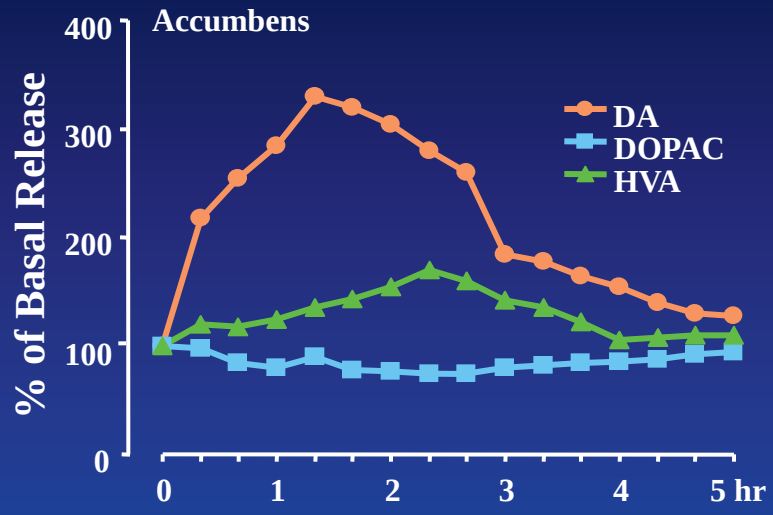

cocaine
NIDA

Effects of Drugs on Dopamine Release

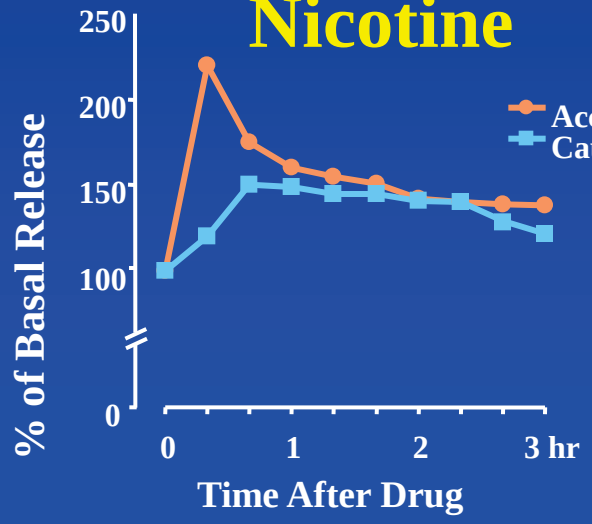
Amphetamine



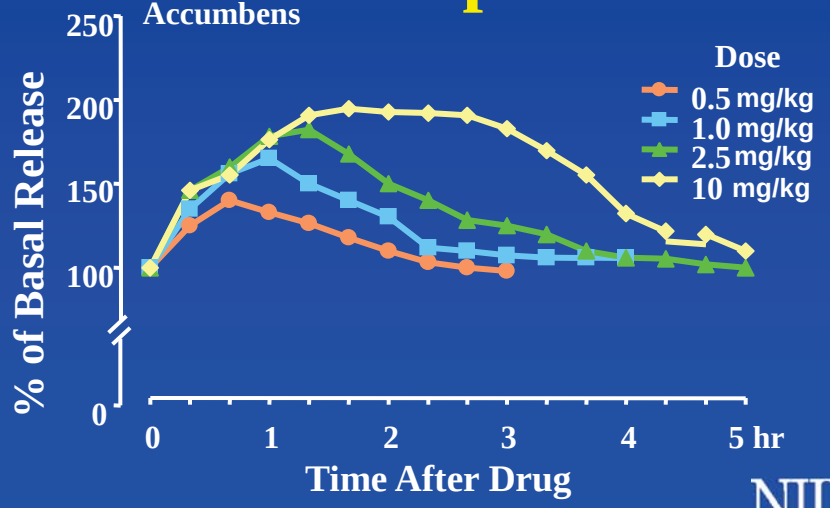
Cocaine



Nicotine



Morphine



Di Chiara and Imperato, PNAS, 1988

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But Dopamine is only Part of the Story

- Scientific research has shown that other neurotransmitter systems are also affected:
  - Serotonin
    - Regulates mood, sleep, etc.
  - Glutamate
    - Regulates learning and memory, etc.

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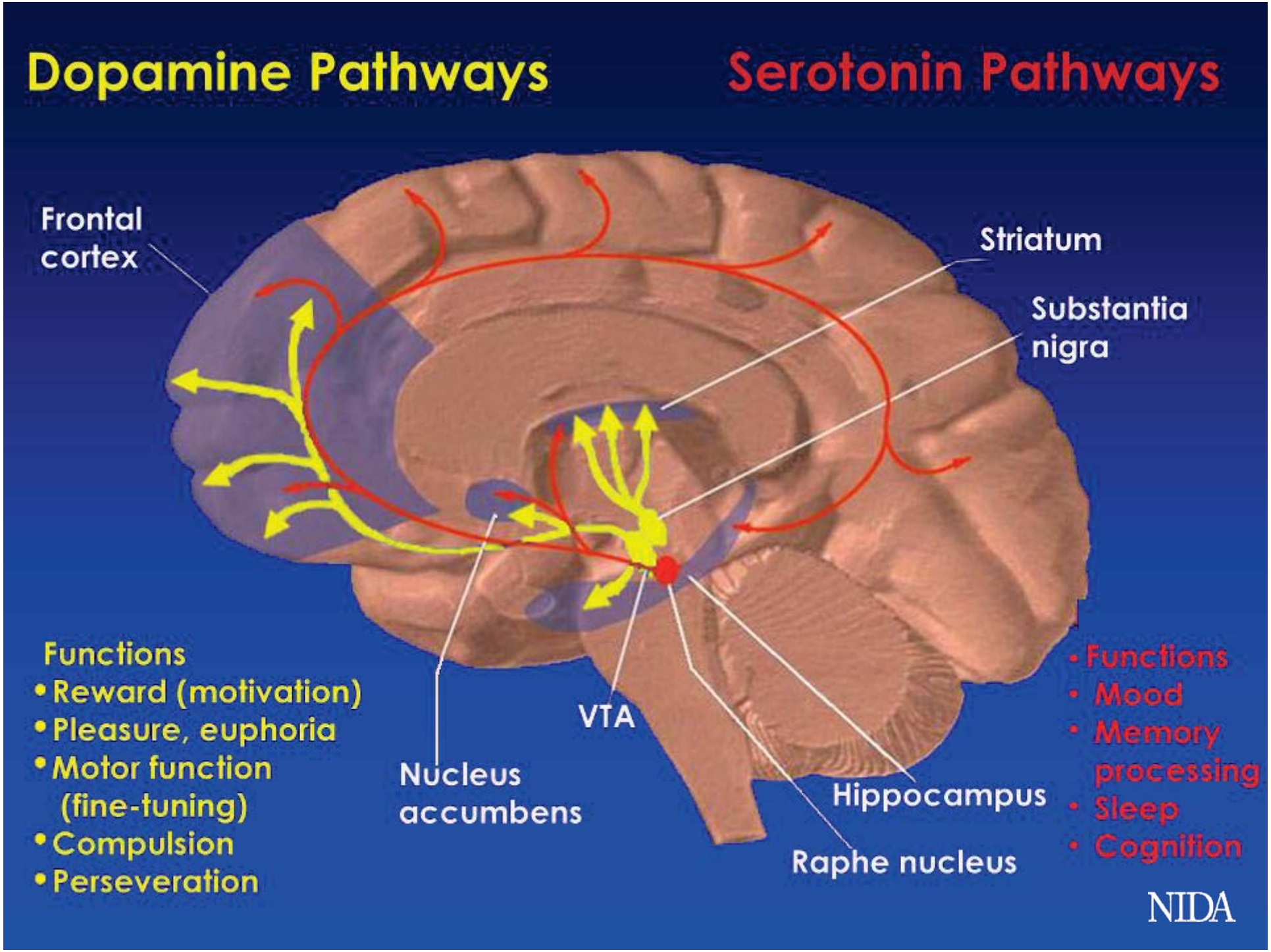
Dopamine Pathways
Serotonin Pathways
Frontal cortex
Striatum
Substantia nigra
Functions
• Reward (motivation)
• Pleasure, euphoria
• Motor function (fine-tuning)
• Compulsion
• Perseveration
VTA
Nucleus accumbens
Hippocampus
Raphe nucleus
• Functions
• Mood
• Memory processing
• Sleep
• Cognition
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Science Has Generated Much Evidence Showing That…

Prolonged Drug Use Changes the Brain In Fundamental and Long-Lasting Ways

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AND…

We Have Evidence That These Changes Can Be Both *Structural* and *Functional*

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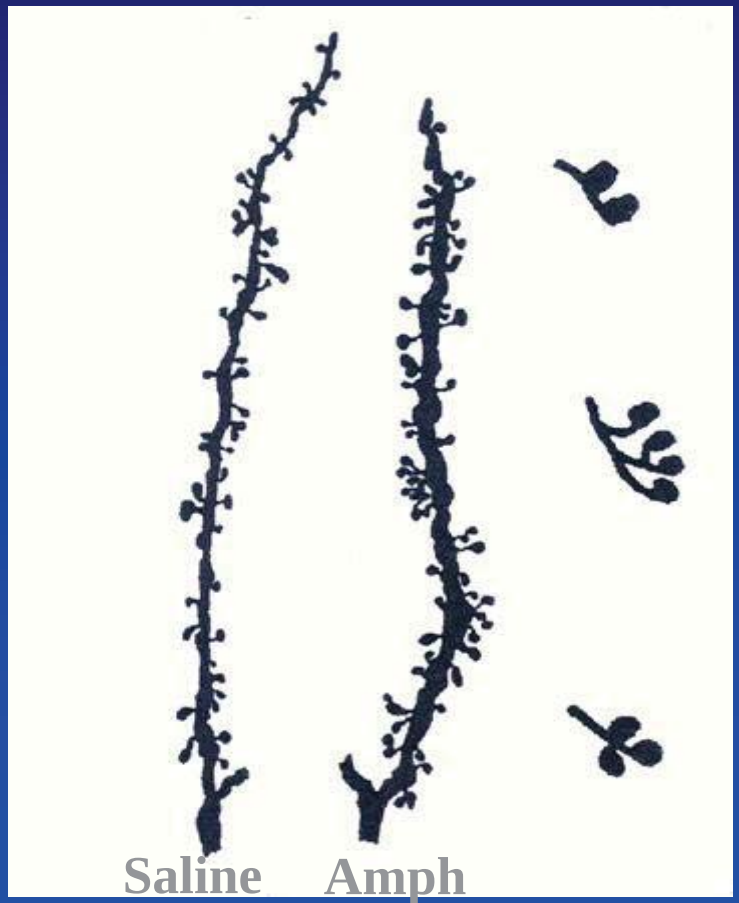
Structurally…

Neuronal Dendrites in the Nucleus Accumbens



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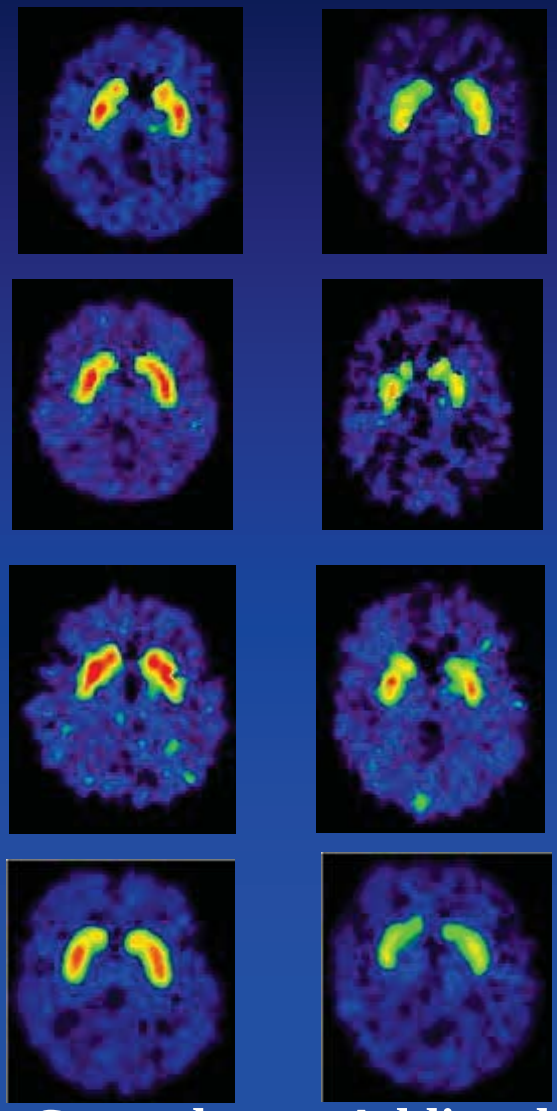
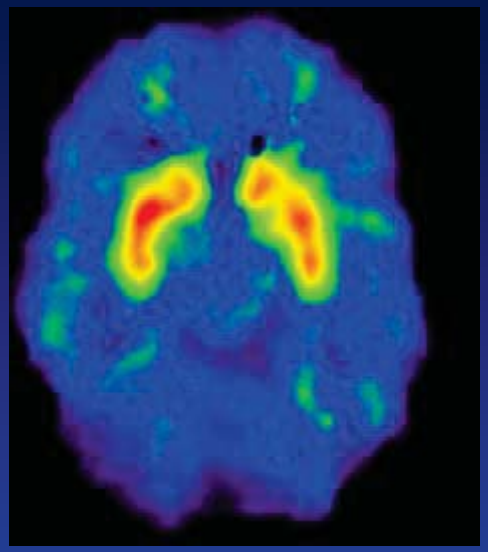
Robinson & Kolb, Journal of Neuroscience, Volume: 1997

Functionally…

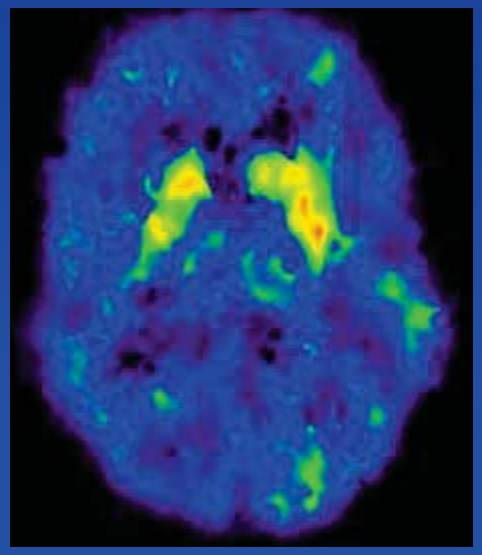
Dopamine D2 Receptors are Decreased by Addiction



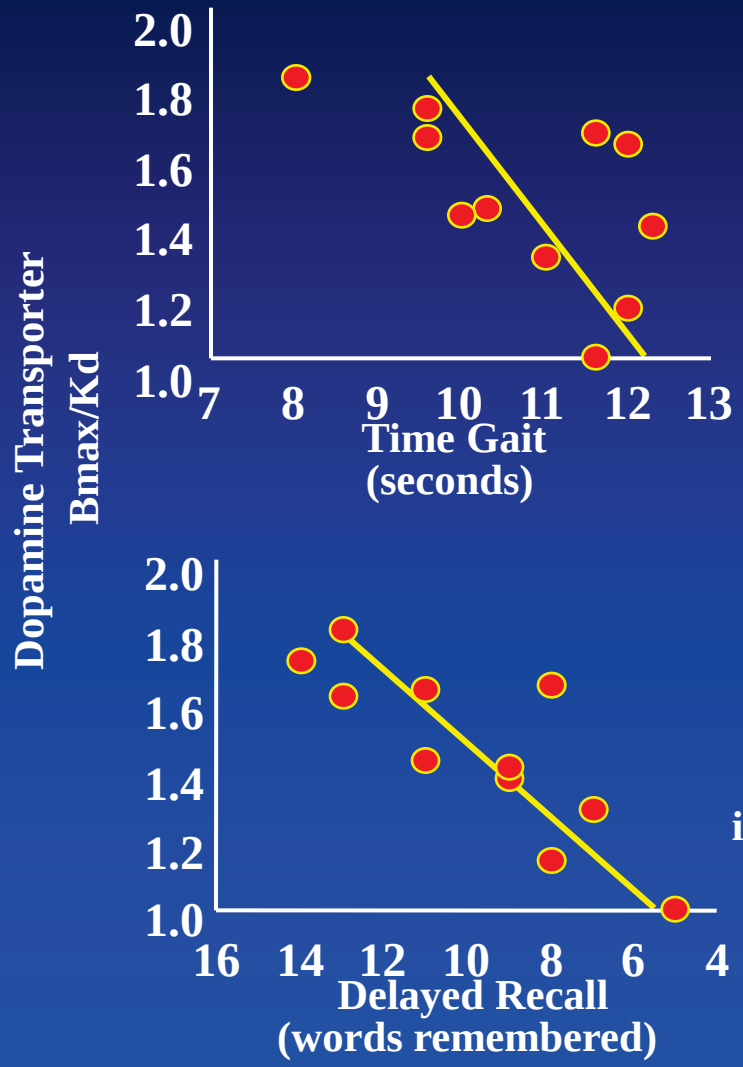
Dopamine Transporters in Methamphetamine Abusers



Normal Control



Methamphetamine Abuser



Motor Task

Loss of dopamine transporters in methamphetamine abusers may result in slowing of motor reactions.

Memory Task

Loss of dopamine transporters in methamphetamine abusers may result in memory impairment.

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Volkow et al., Am. J. Psychiatry, 2001.

Implication?

Brain changes resulting from prolonged use of drugs

may compromise

mental AND motor function.

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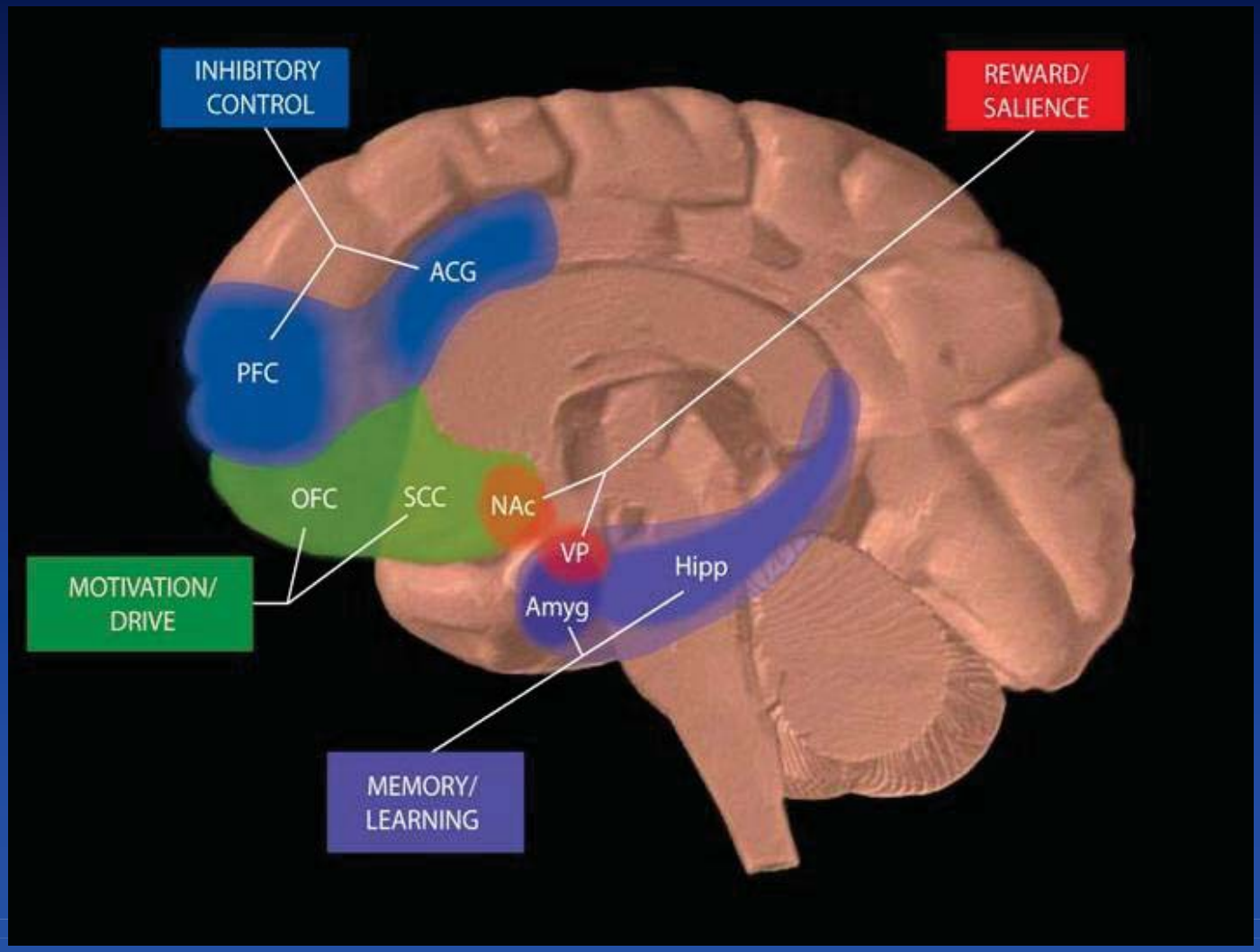
Circuits Involved In Drug Abuse and Addiction



All of these brain regions must be considered in developing strategies to effectively treat addiction

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Priority Areas for NIDA

Prevention Research (Children & Adolescents)

- **genetics**
- **environment**
- **development**
- **co-morbidity**

Treatment Research

(New Targets & New Strategies)

HIV/AIDS Research

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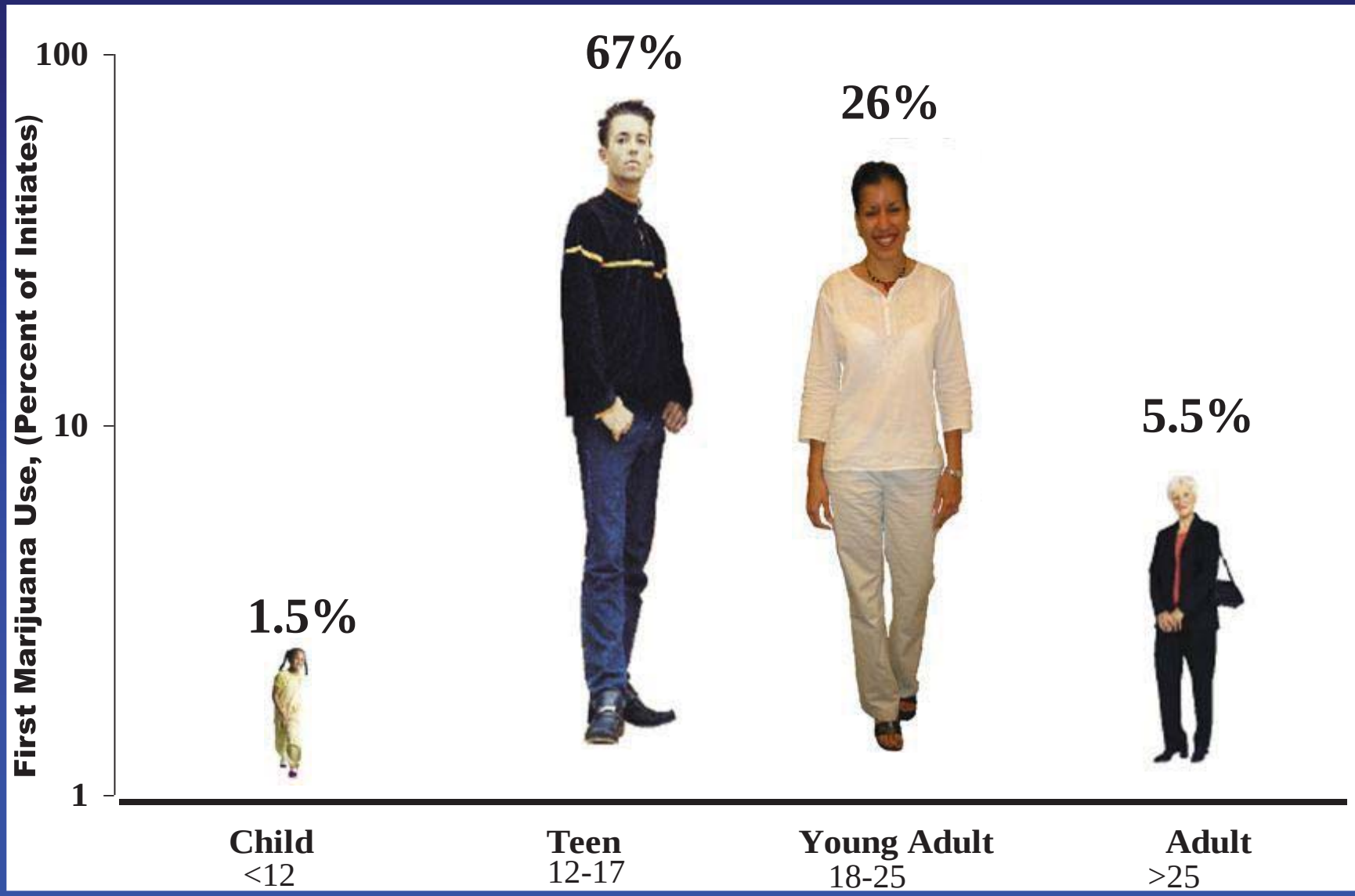
Addiction is a Developmental Disease:
It Starts Early



Basic Science Tells Us that Adolescents' Brains Are Still Developing…

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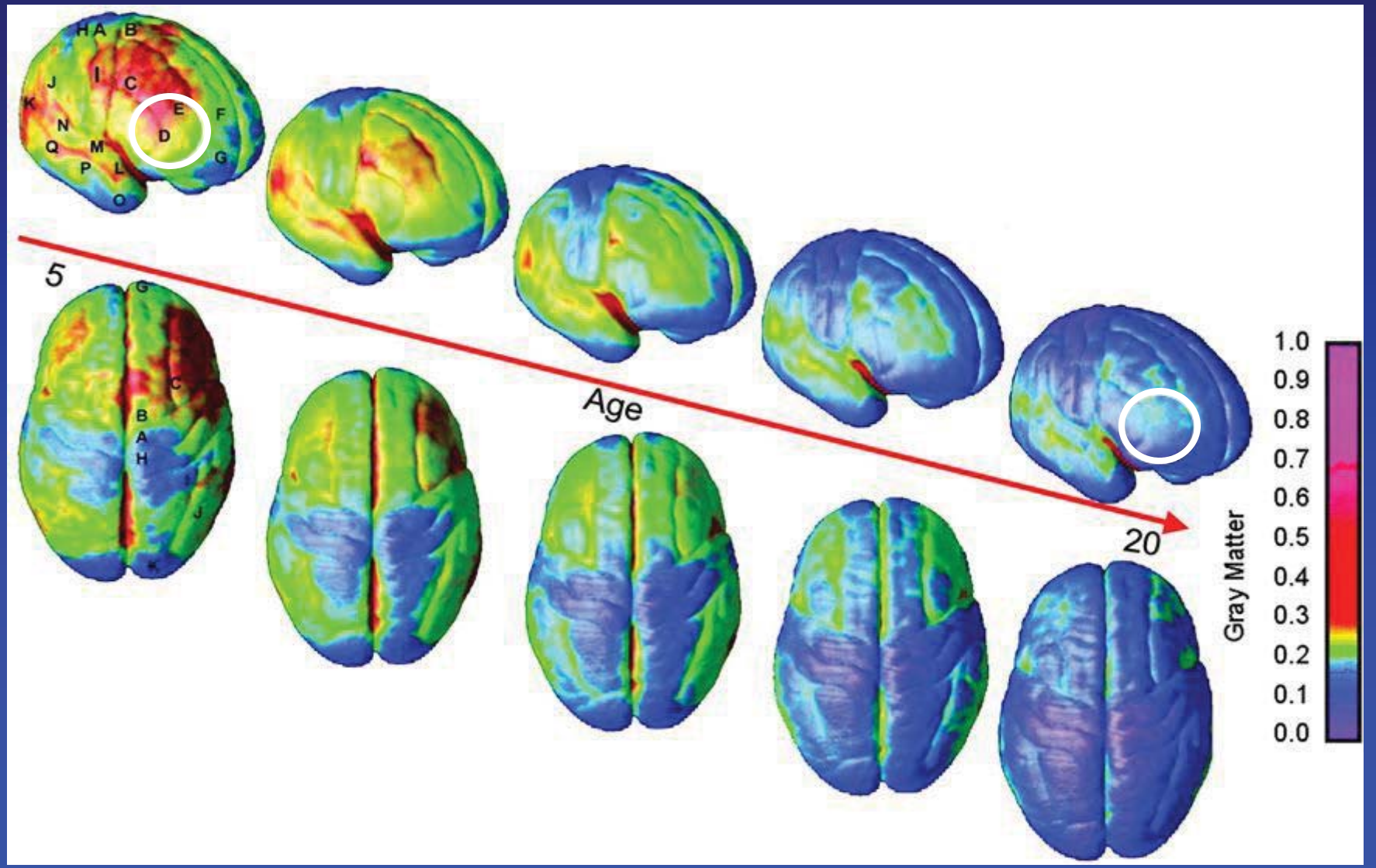
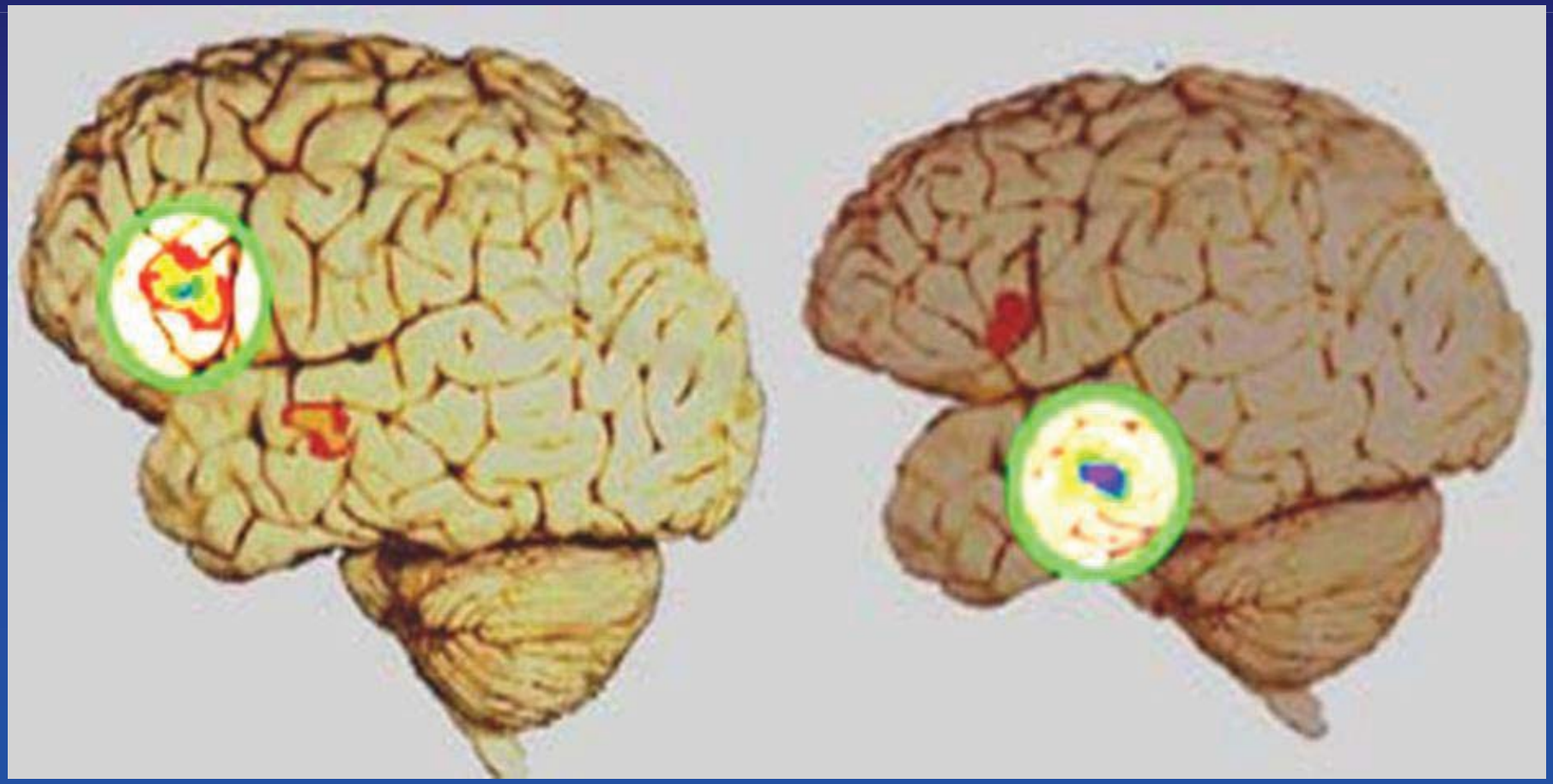
MRI Scans of Healthy Children and Teens Over Time



Gogtay, Giedd, et al. Proc. Natl. Acad. Sci., 2004

When Reading Emotion…
Adults Rely More on the Frontal Cortex While Teens Rely More on the Amygdala



Deborah Yurgelon-Todd 2000.

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Do Adolescents React Differently than Adults to Substances of Abuse?

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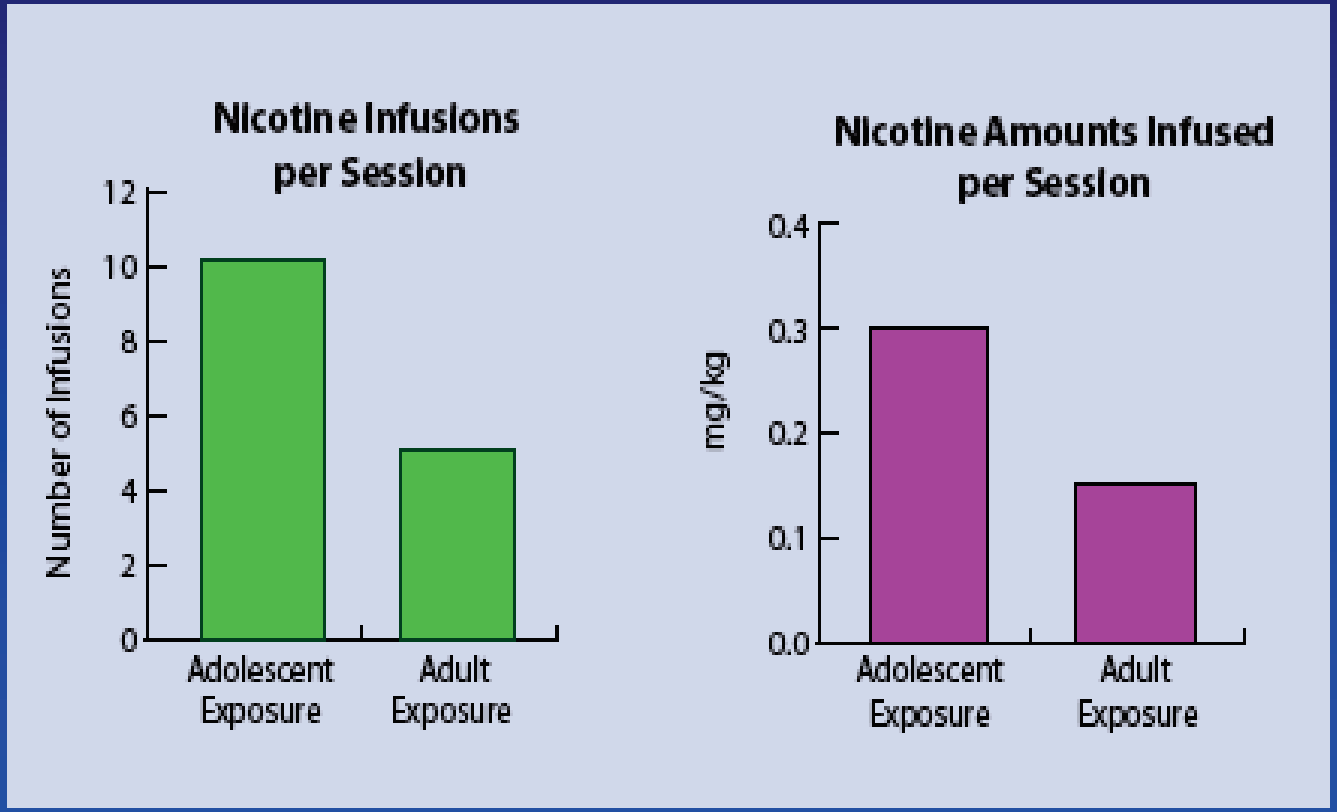
Rats Exposed to Nicotine in Adolescence Self-Administer More Nicotine Than Rats First Exposed as Adults



Collins et al, Neuropharmacology, 2004, Levin et al, Psychopharmacology, 2003

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Do We Need Fundamentally Different Strategies At Different Stages of Adolescence?

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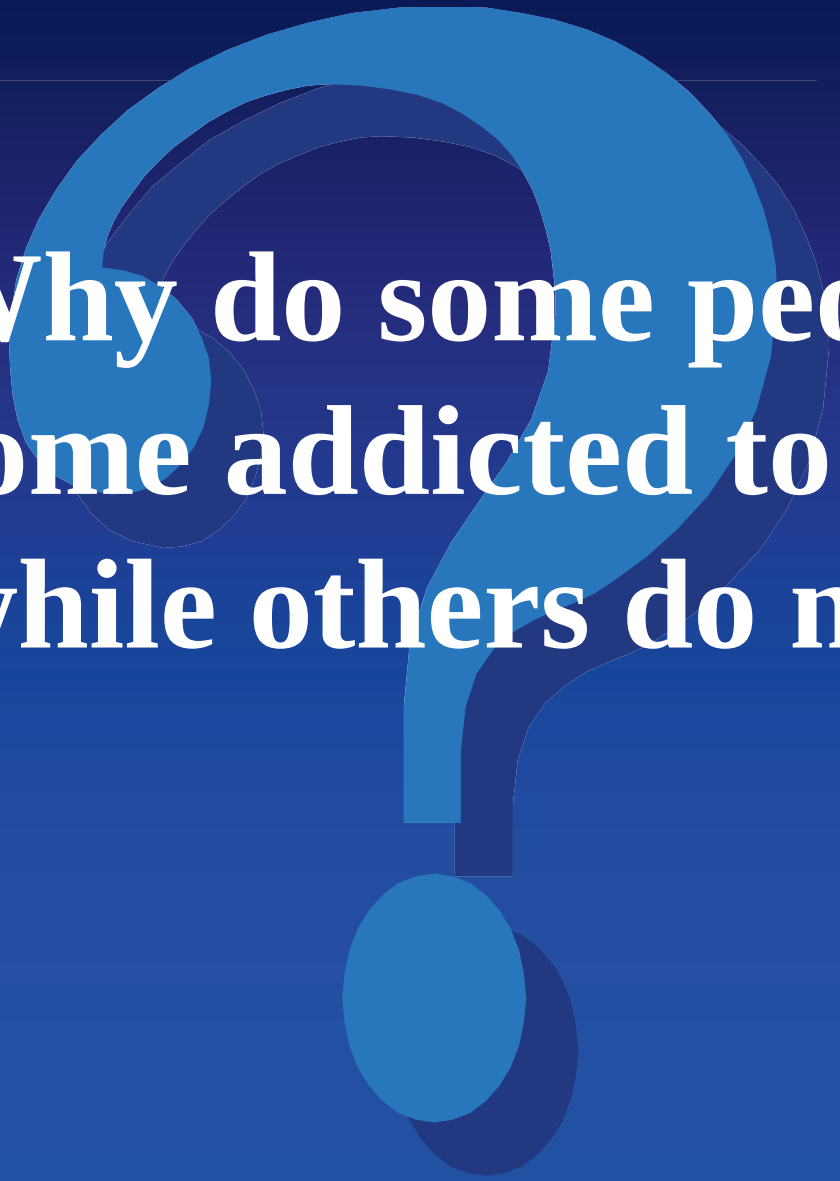
Vulnerability



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

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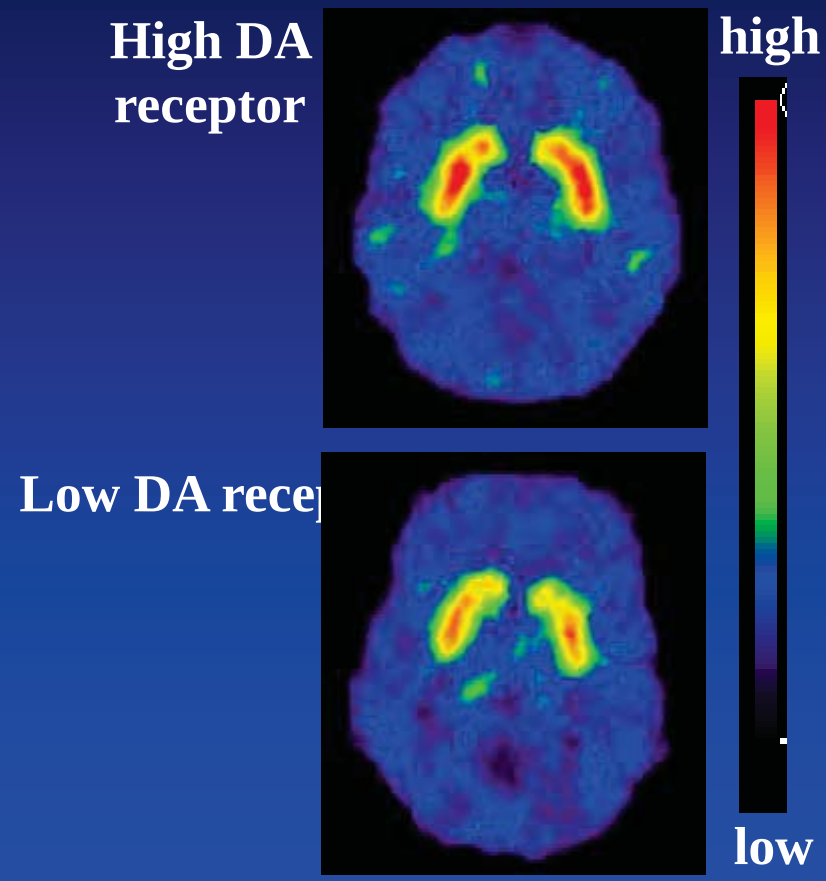
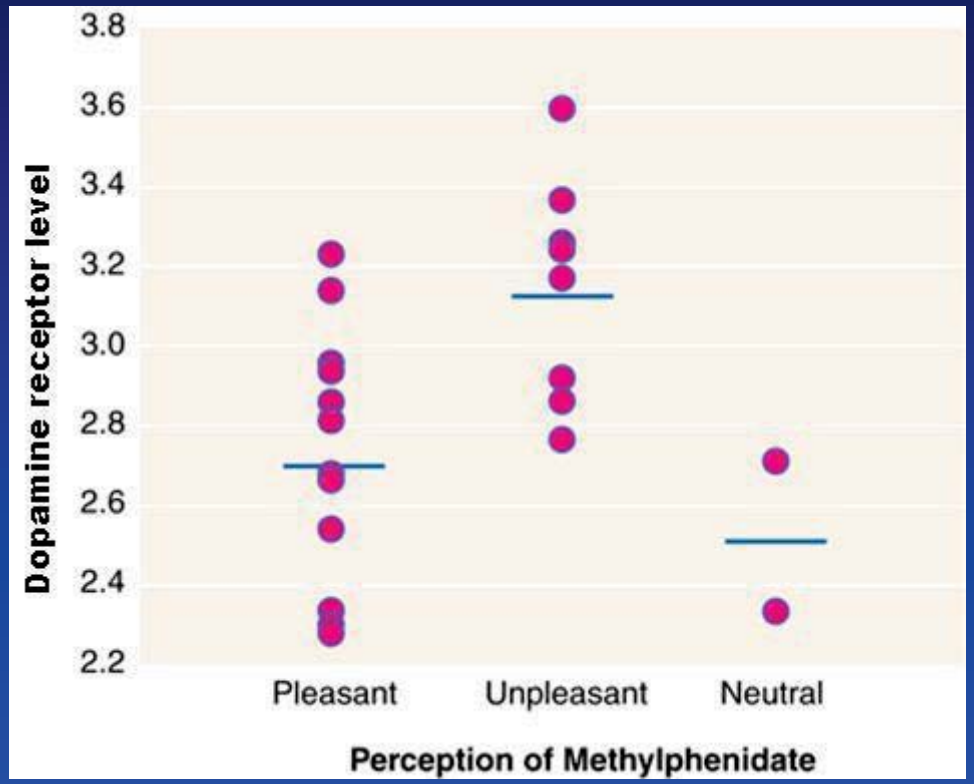
Individual Differences in Response to Drugs: DA Receptors influence drug liking





As a group, subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant

Adapted from Volkow et al., Am. J. Psychiatry, 1999.

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Genetics is a Big Contributor to the Risk of Addiction…

And…

The Nature of this Contribution Is Extremely Complex

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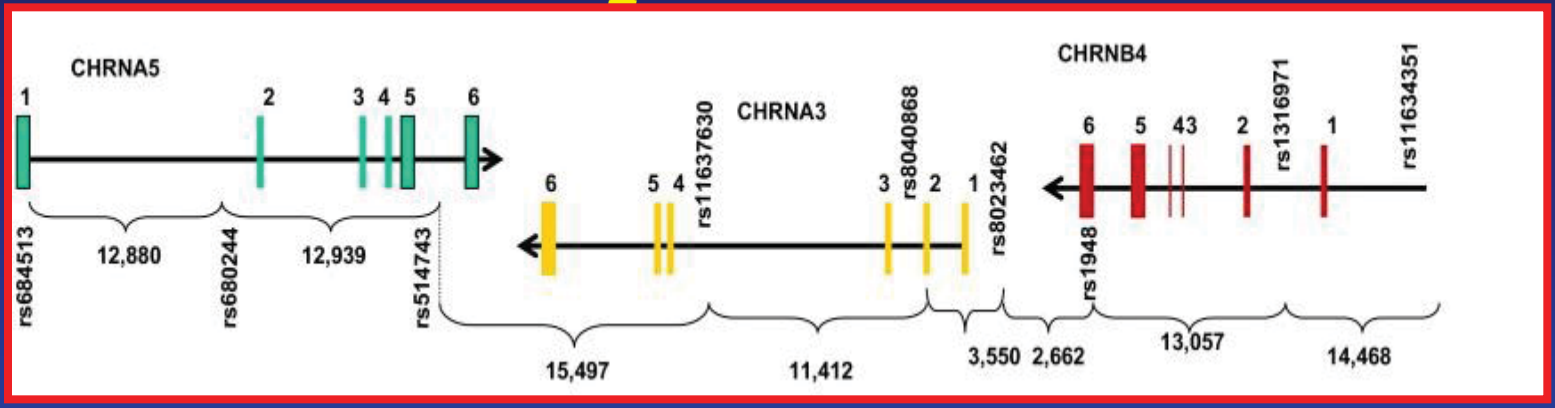
Gene Cluster is Associated with Nicotine Dependence



Human Molecular Genetics, 2007, Vol. 16, No. 1 24-
doi:10.1093/hmg/ddl441
Advance Access published on December 7, 2006

Novel genes identified in a high-density genome wide association study for nicotine dependence

Laura Jean Bierut[1,*], Pamela A.F. Madden[1], Naomi Breslau[2], Eric O. Johnson[3],
Dorothy Ha
Louis Fox[1]
Nicholas G
Jen C. War

Molecular Psychiatry (2008), 1–6

www.nature.com/mp

IMMEDIATE COMMUNICATION

α-5/α-3 nicotinic receptor subunit alleles increase risk for heavy smoking

W Berrettini[1,2,3], X Yuan[2,3], F Tozzi[2,3], K Song[2,3], C Francks[2,3], H Chilcoat[4], D Waterworth[2,3], P Muglia[2,3,5] and V Mooser[2,3]

ARTICLE IN PRESS

The CHRNA5/A3/B4 Gene Cluster Variability as an Important Determinant of Early Alcohol and Tobacco Initiation in Young Adults

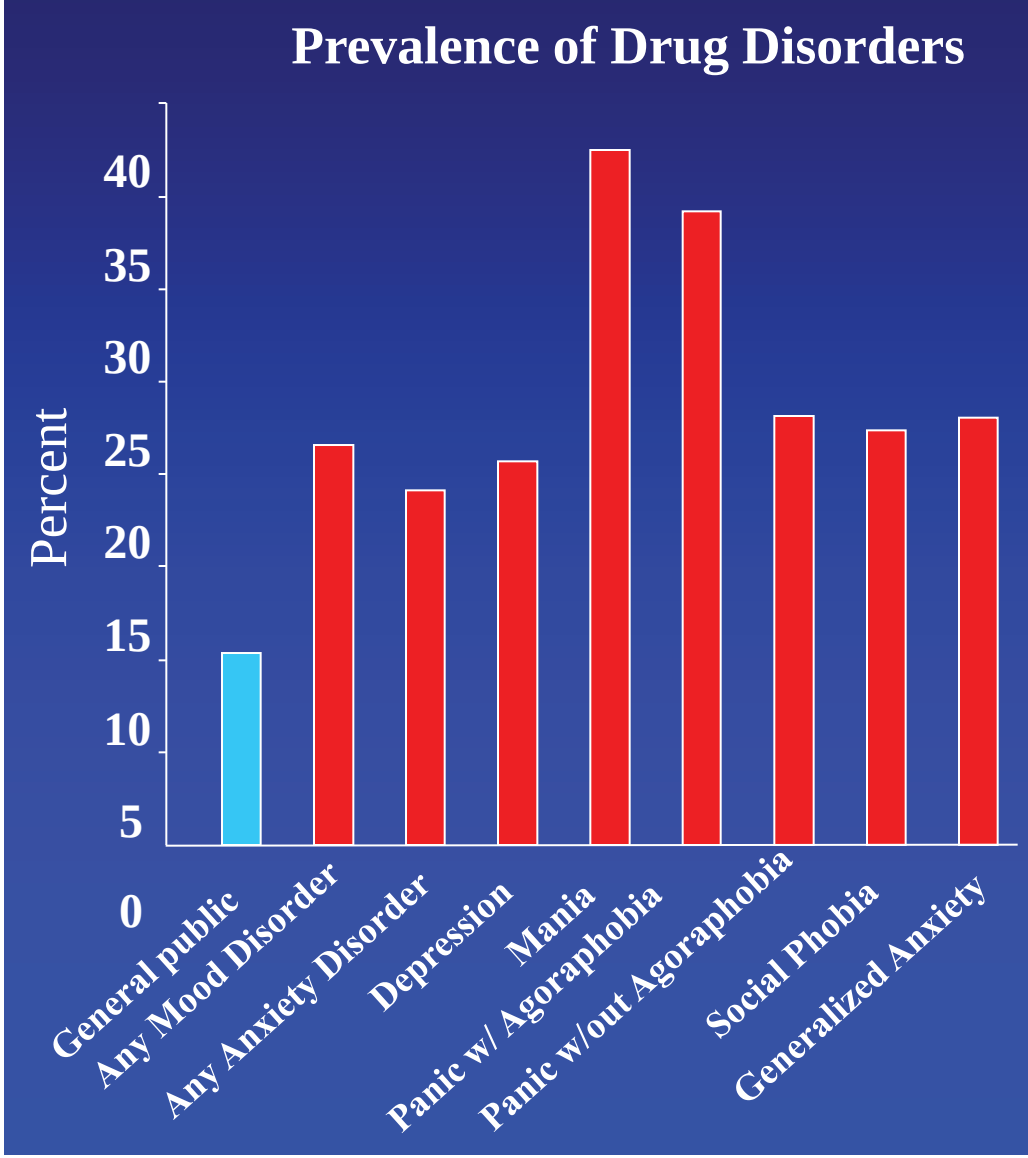
Isabel R. Schlaepfer, Nicole R. Hoft, Allan C. Collins, Robin P. Corley, John K. Hewitt, Christian J. Hopfer, Jeffrey M. Lessem, Matthew B. McQueen, Soo Hyun Rhee, and Marissa A. Ehringer

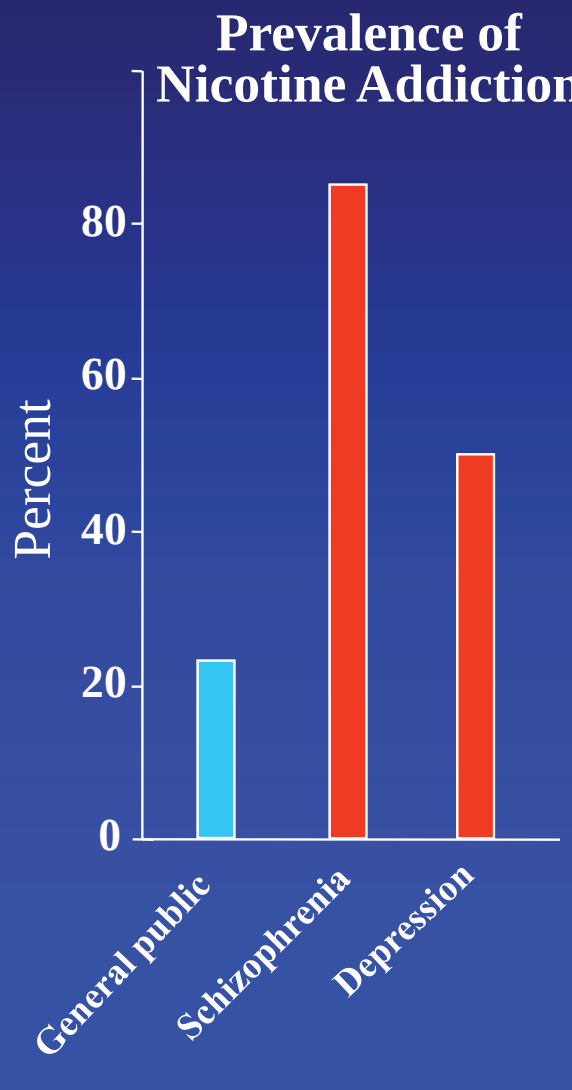
Vol 452|3 April 2008|doi:10.1038/nature06846

A variant associated with nicotine dependence, lung cancer and peripheral arterial disease

Thorgeir E. Thorgeirsson[1]*, Frank Geller[1]*, Patrick Sulem[1]*, Thorunn Rafnar[1]*, Anna Wiste[1,2], Kristinn P. Magnusson[1], Andrei Manolescu[1], Gudmar Thorleifsson[1], Hreinn Stefansson[1], Andres Ingason[1],

What Other Biological Factors Contribute to Addiction--Comorbidity





COMORBIDITY

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Why do Mental Illnesses and Substance Abuse Co-occur?

- **Self-medication**
  - substance abuse begins as a means to alleviate symptoms of mental illness
- **Causal effects**
  - Substance abuse may increase vulnerability to mental illness
- **Common or correlated causes**
  - the risk factors that give rise to mental illness and substance abuse may be related or overlap

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What Environmental Factors Contribute to Addiction?

- Stress
- Early physical or sexual abuse
- Witnessing violence
- Peers who use drugs
- Drug availability

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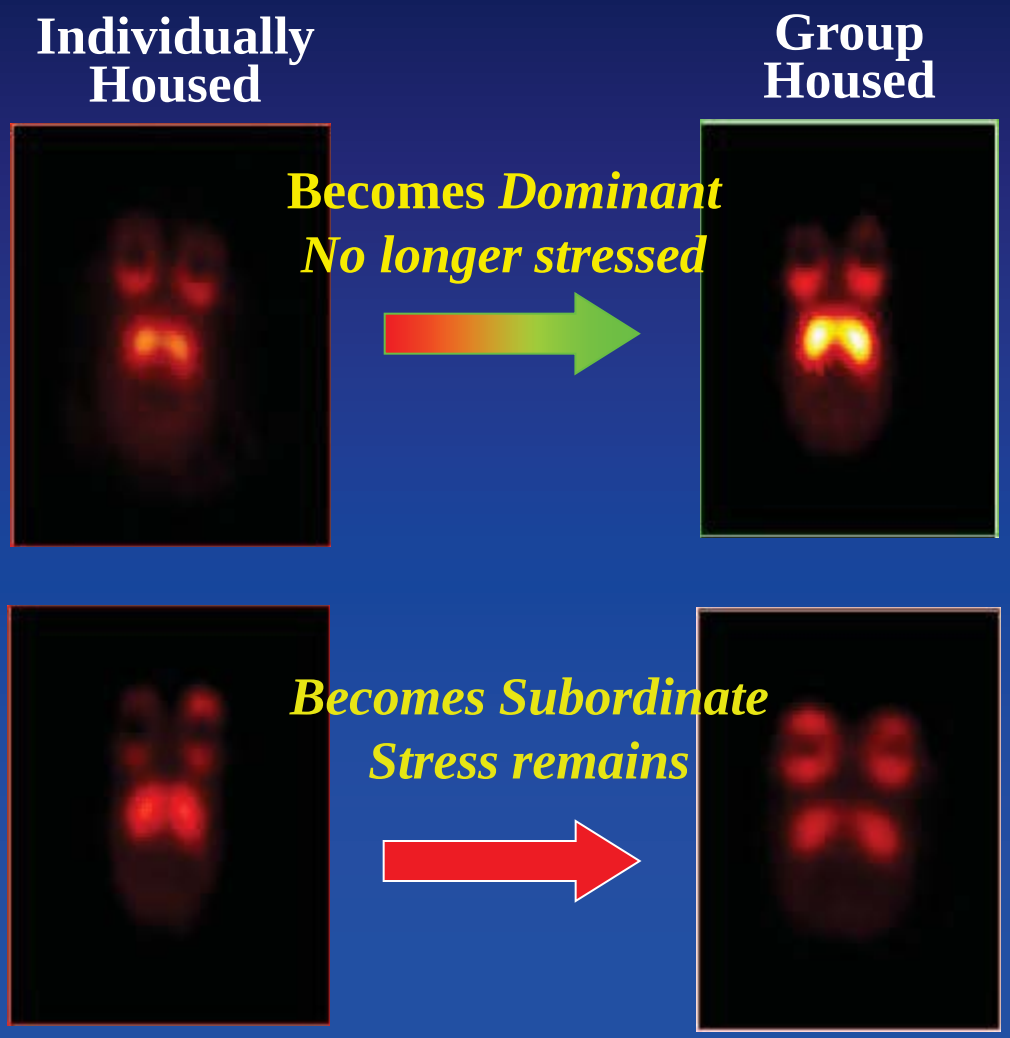
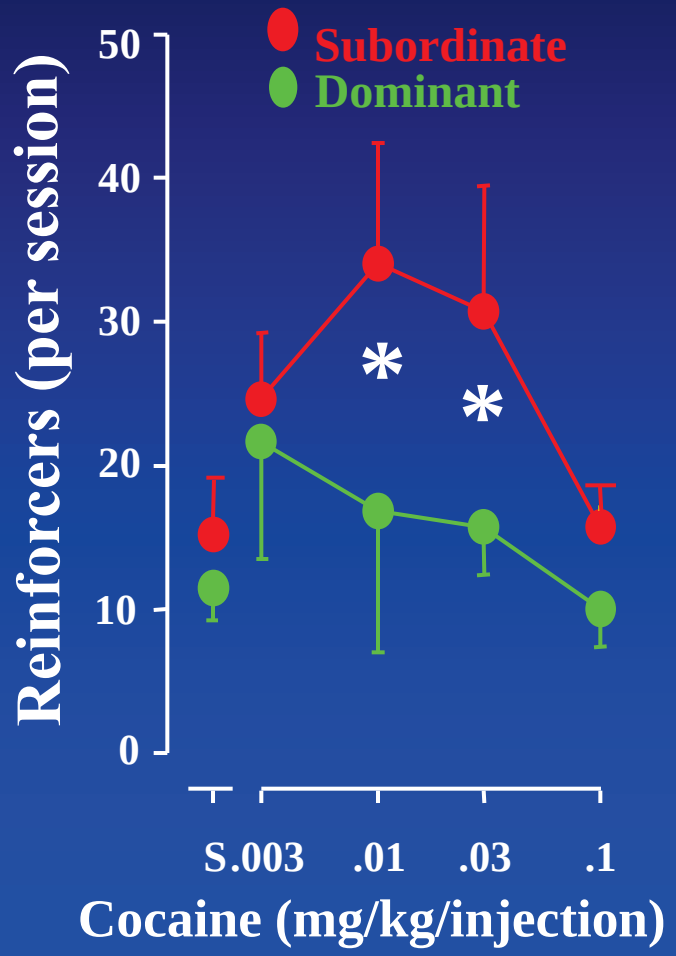
Social Stressor Affects Brain DA D2 Receptors and Drug Self-Administration





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

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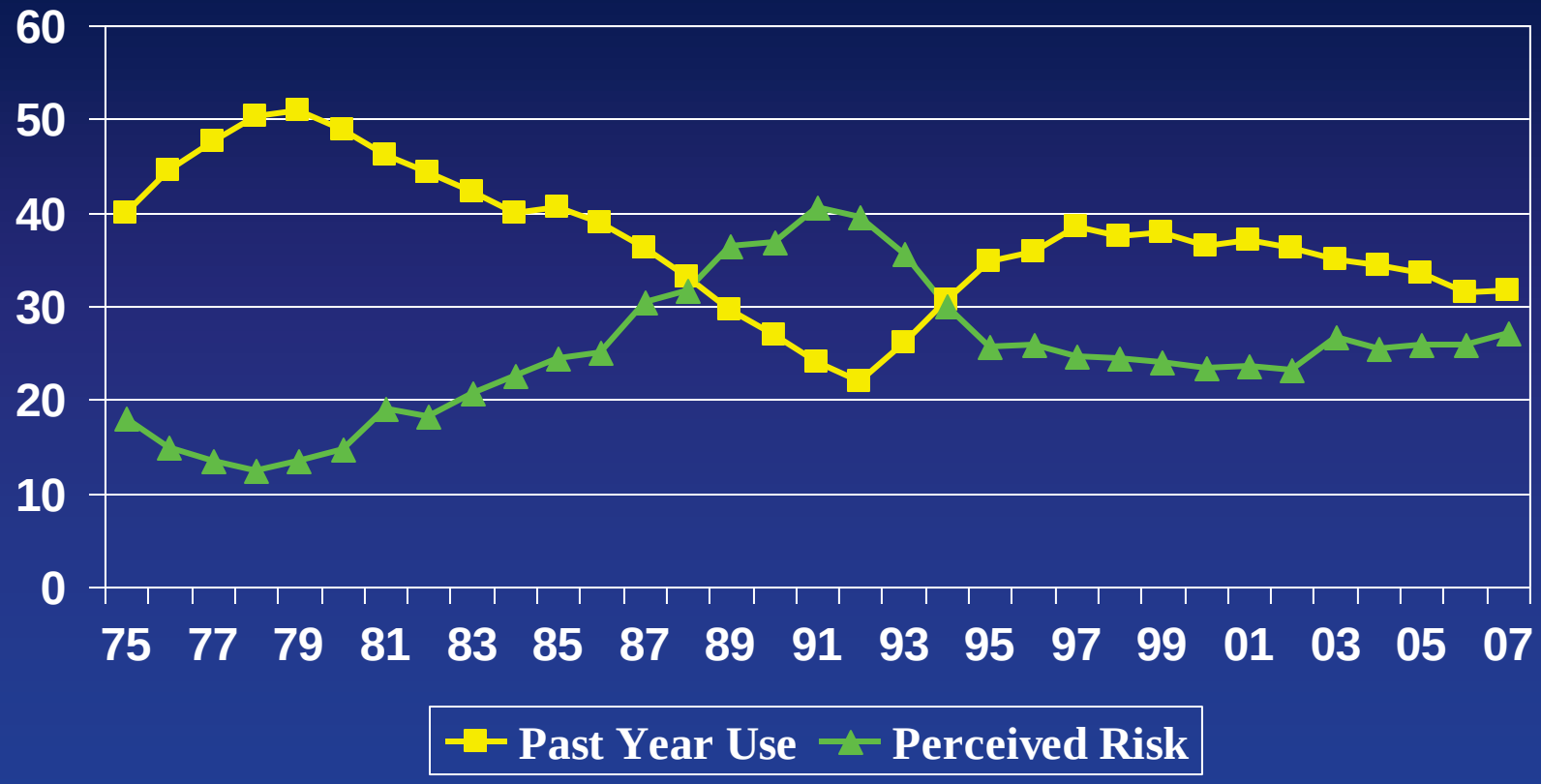
Prevention Works:

Knowledge of Risk and Protective Factors Has Led to the Development of Effective Prevention Strategies

NIDA

Changes in Attitudes Lead to Changes in Use



Monitoring the Future Study, 2007.

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Priority Areas for NIDA

Prevention Research (Children & Adolescents)

- genetics
- environment
- development
- co-morbidity

Treatment Research

(New Targets & New Strategies)

HIV/AIDS Research

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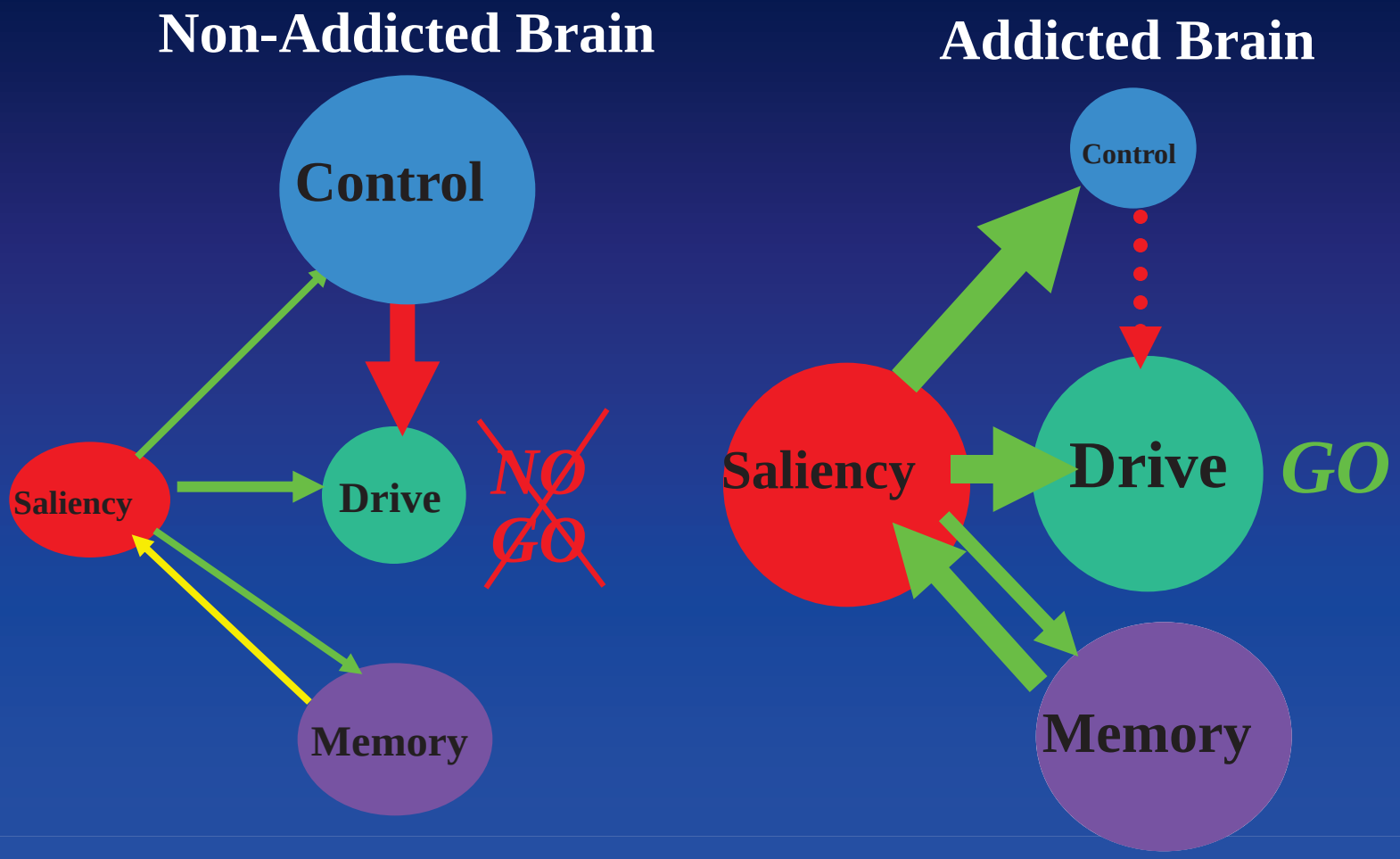
Why Can't Addicts Just Quit?



Because Addiction Changes Brain Circuits

Adapted from Volkow et al., Neuropharmacology, 2004.

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This is why addicts can't just quit.

and…

This is why treatment is essential.

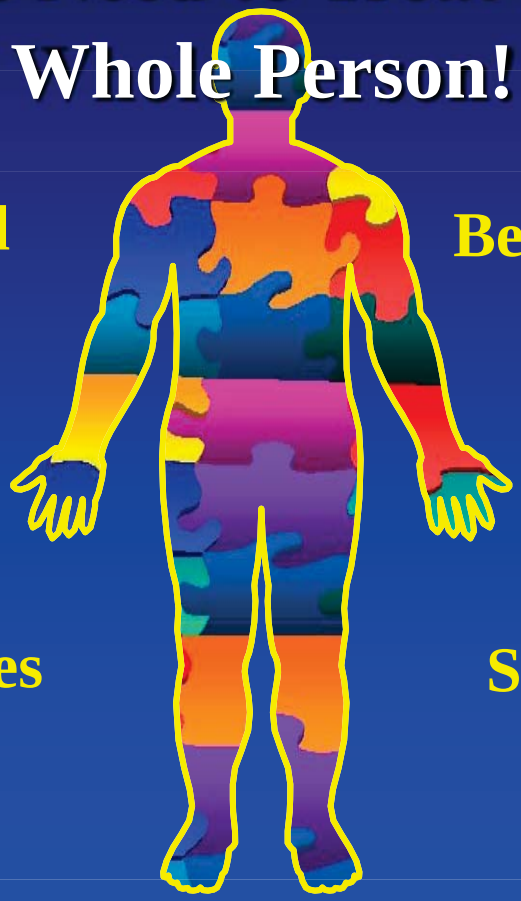
NIDA

Treating a Biobehavioral Disorder Must Go Beyond Just Fixing the Chemistry

We Need to Treat the Whole Person!

Pharmacological Treatments (Medications)

Behavioral Therapies



Medical Services

Social Services

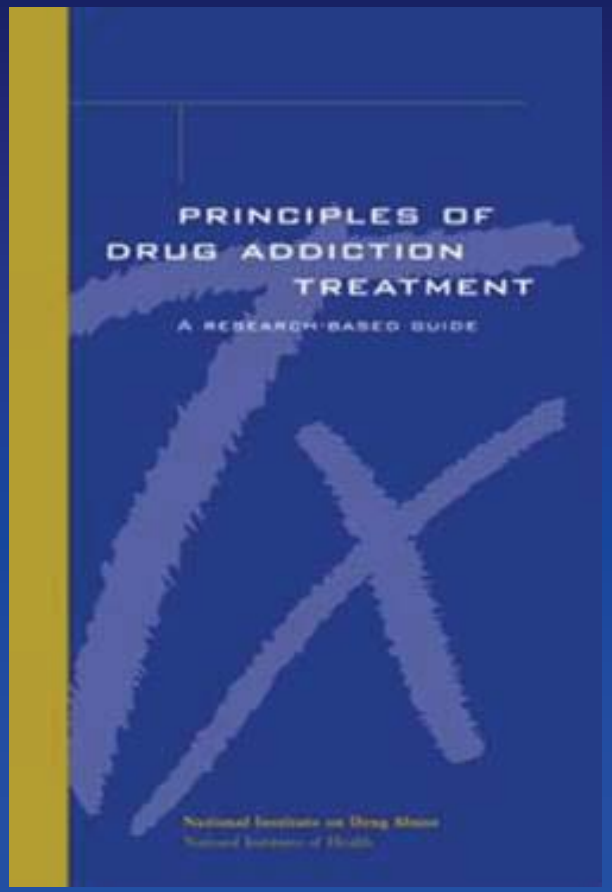
In Social Context

NIDA

Treatment Can Work!

NIDA's Principles of Treatment

- **No single treatment is appropriate for all individuals.**
- **Treatment needs to be readily available.**
- **Treatment must attend to multiple needs of the individual, not just drug use.**
- **Multiple courses of treatment may be required for success.**
- **Remaining in treatment for an adequate period of time is critical for treatment effectiveness.**



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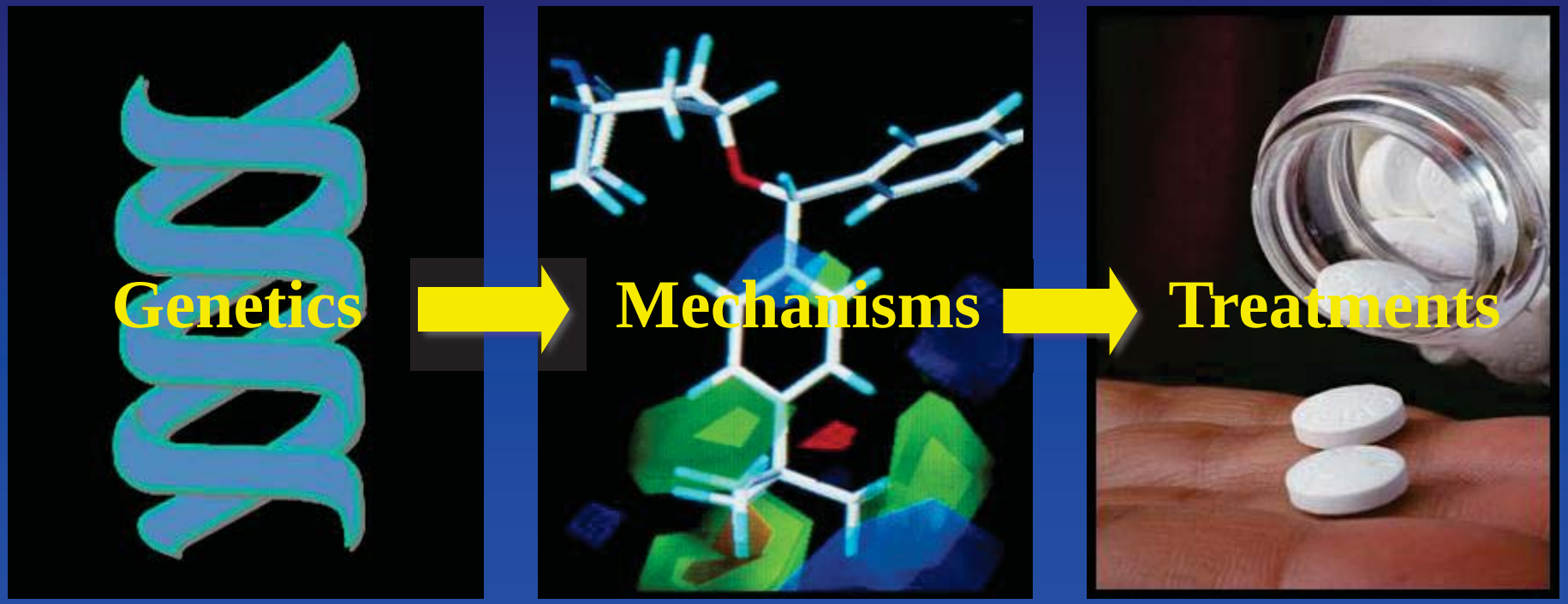
We Are Using Science to Develop Even Better Treatments



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Basic Research → *Medication*

Opiate agonists stabilize brain function in heroin addicts	**Agonist Therapy** Methadone Buprenorphine
CB1 KO mice have decreased responses to multiple drugs of abuse	**CB1 Antagonists**
Smokers who are poor nicotine metabolizers smoke less	**Inhibitors of metabolizing enzymes**
Stress triggers relapse in animal models of addiction and CRF antagonists interfere with the response to stress	**CRF Antagonists**

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But, drug addiction is a chronic illness with relapse rates similar to those of hypertension, diabetes, and asthma.

McLellan et al., JAMA, 2000.

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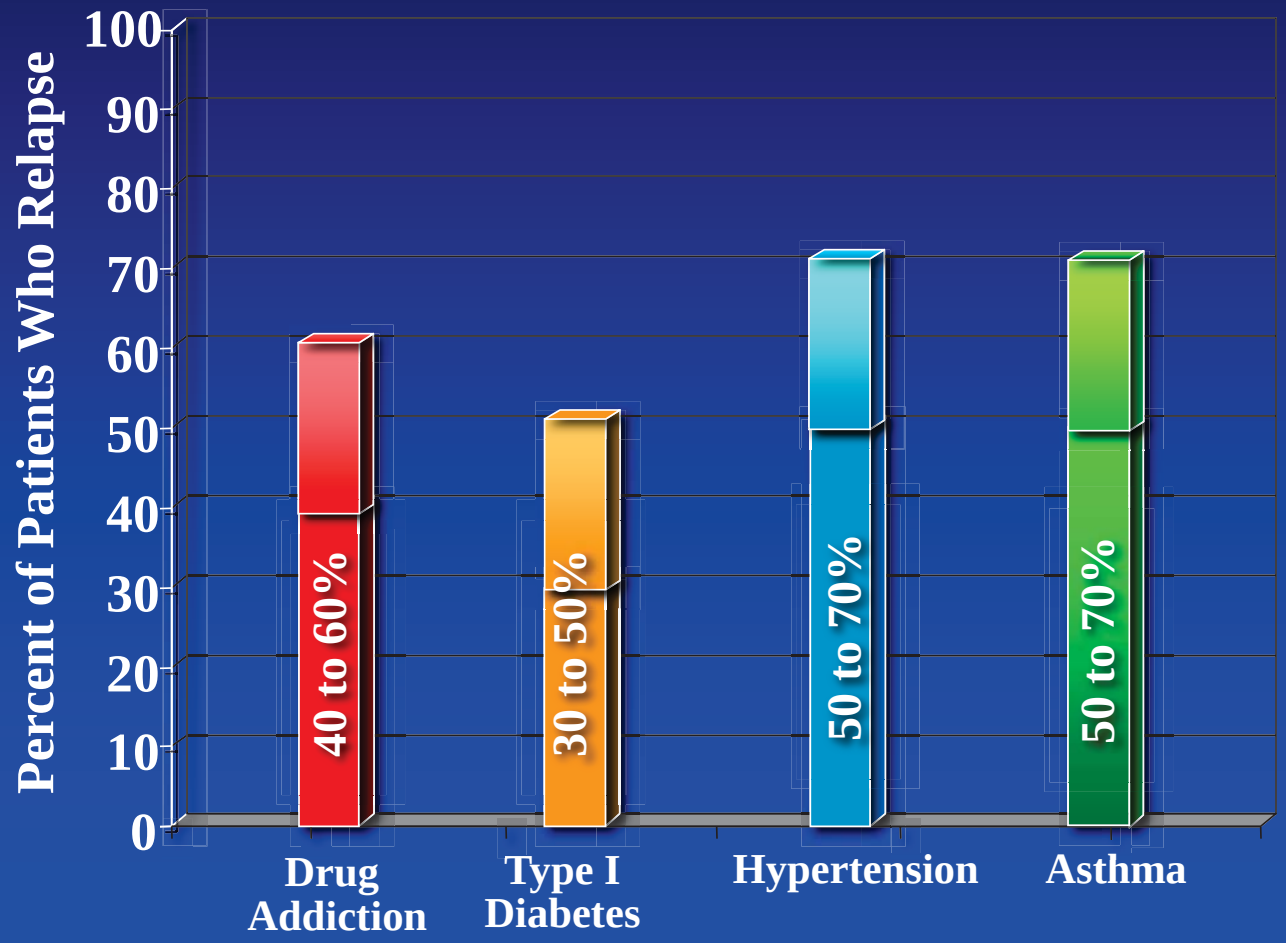
Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses



McLellan et al., JAMA, 2000.

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Addiction is Similar to Other Chronic Illnesses Because:

- **It has biological and behavioral components, both of which must be addressed during treatment.**
- **Recovery from it--protracted abstinence and restored functioning--is often a long-term process requiring repeated episodes of treatment.**
- **Relapses can occur during or after treatment, and signal a need for treatment adjustment or reinstatement.**
- **Participation in support programs during and following treatment can be helpful in sustaining long-term recovery**

Therefore…

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Full recovery is a challenge but it is possible …

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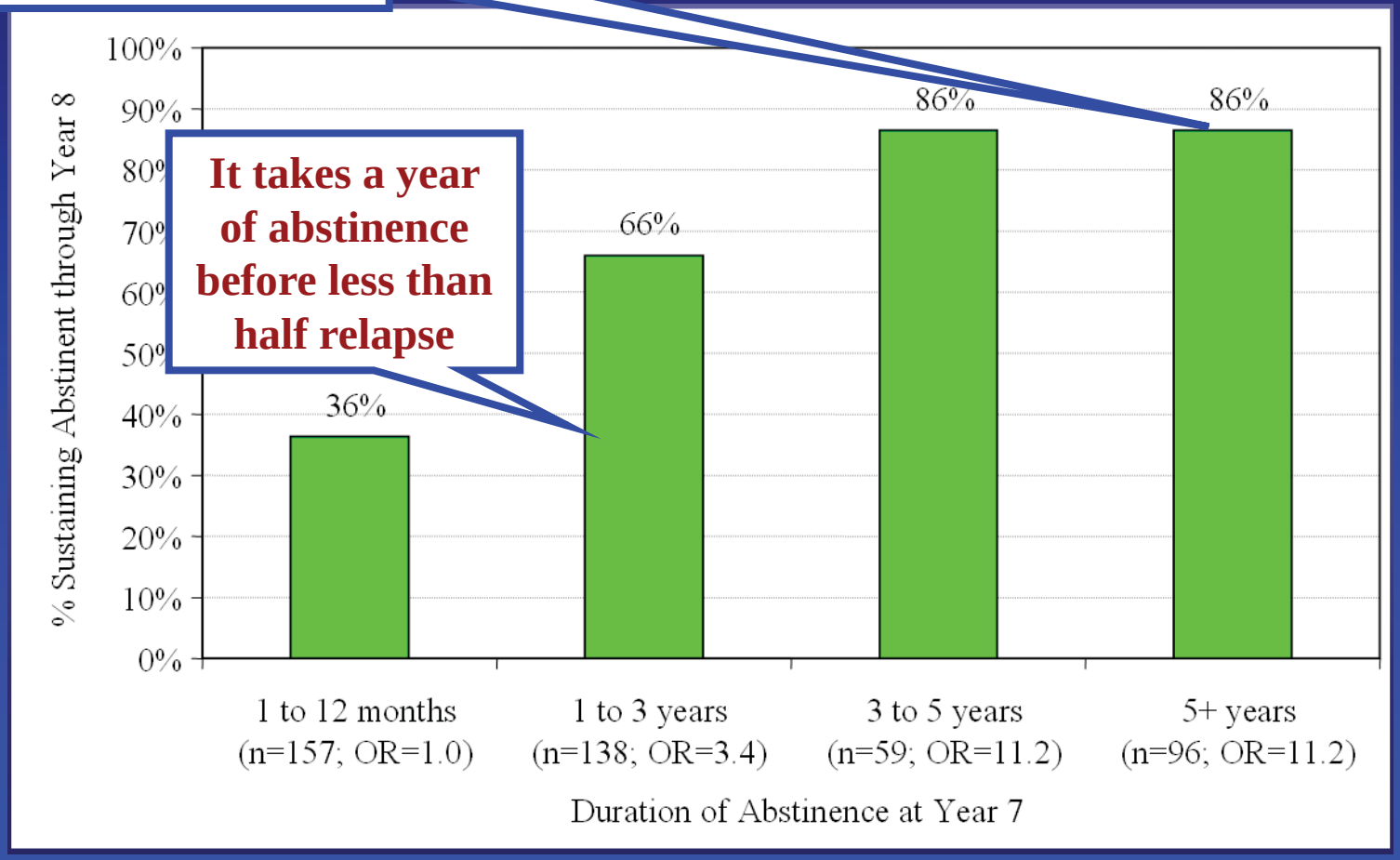
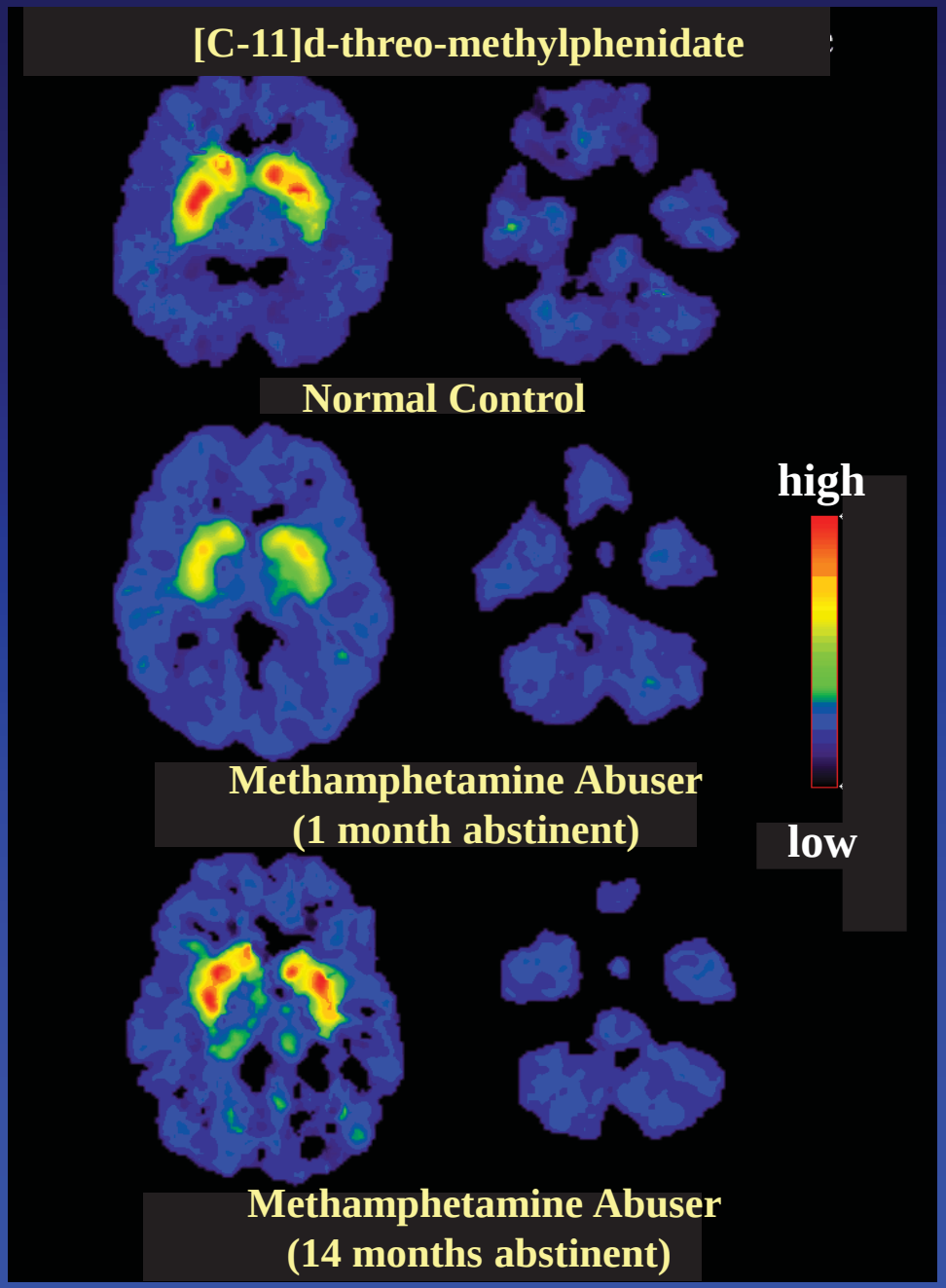
Extended Abstinence is Predictive of Sustained Recovery

After 5 years – if you are sober, you probably will stay that way.



Dennis et al, Eval Rev, 2007

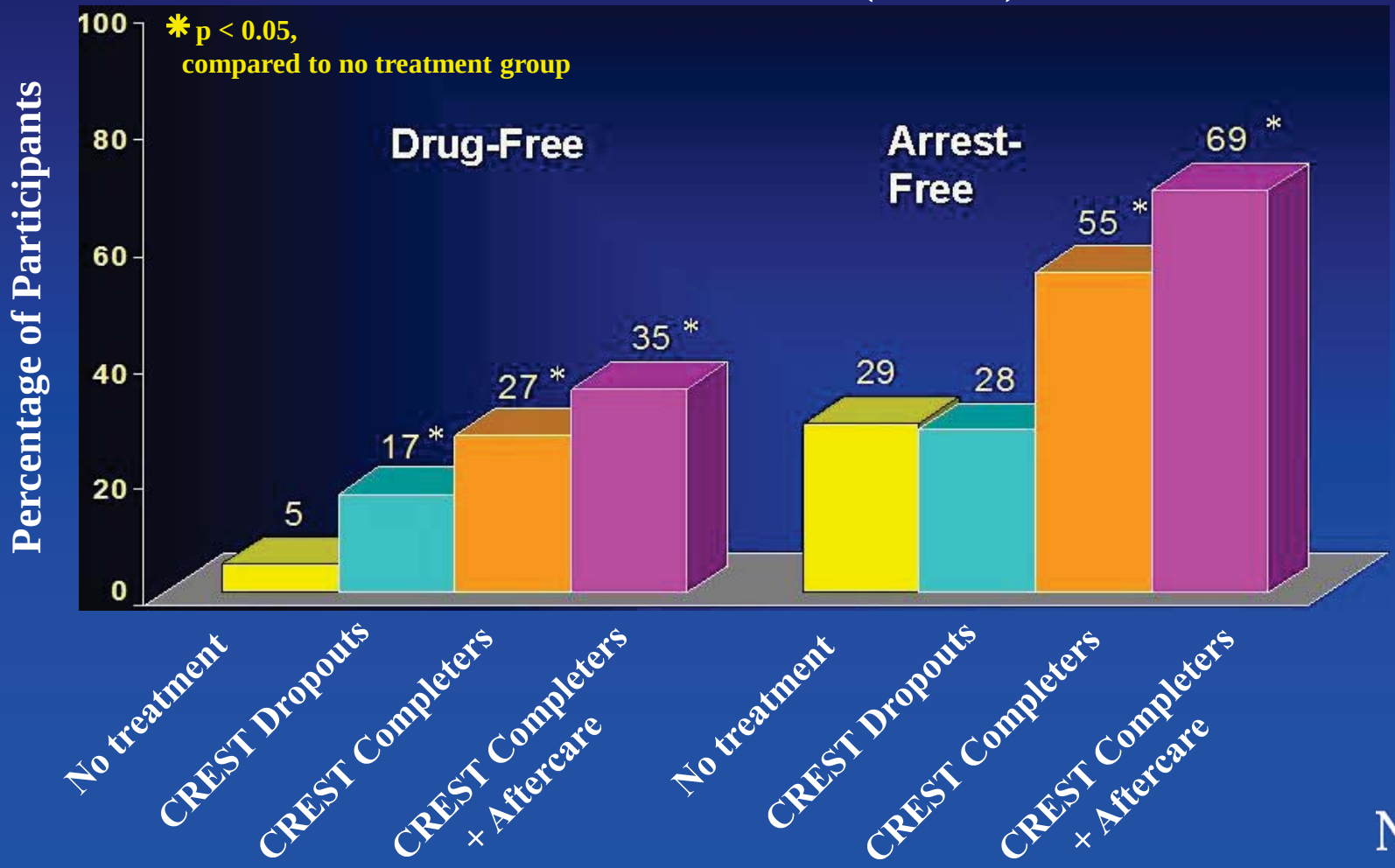
DAT Recovery with prolonged abstinence from methamphetamine



Volkow et al., J. Neuroscience, 2001.

Treatment Reduces Drug Use and Recidivism

Delaware Work Release Therapeutic Community (CREST) + Aftercare
3 Years After Release (N=448)



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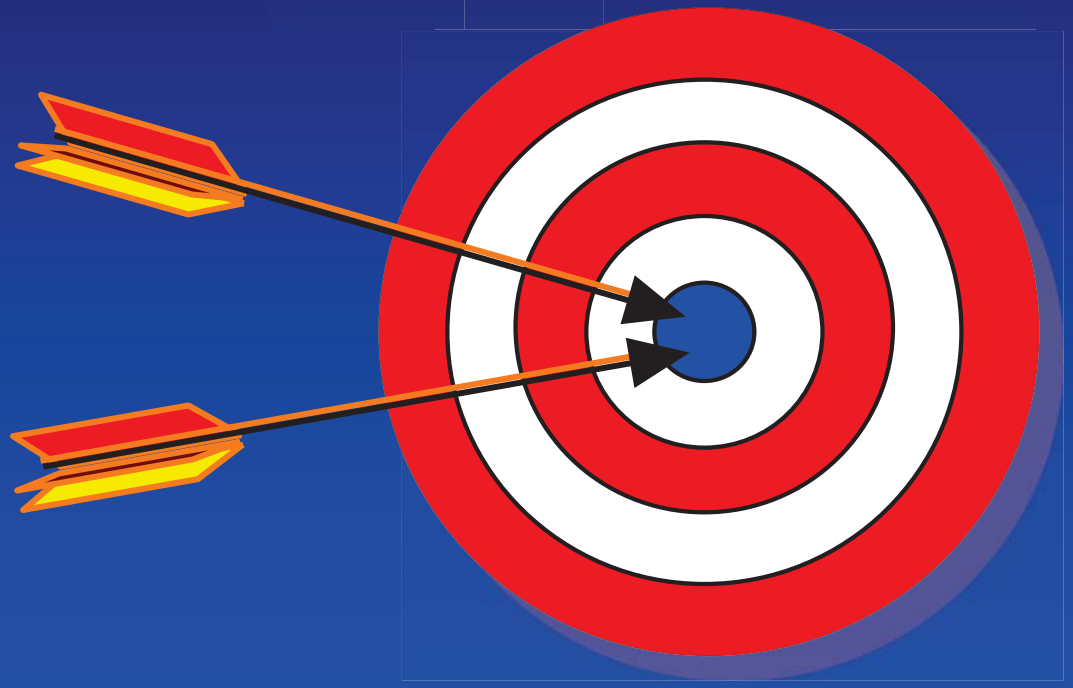
In Treating Addiction…

We Need to Keep Our Eye on the Real Targets!

Abstinence



Functionality in Family, Work and Community

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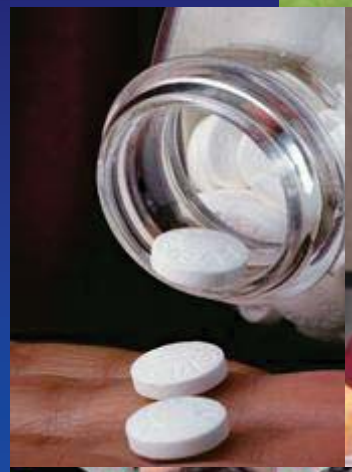
Priority Areas for NIDA

Prevention Research (Children & Adolescents)

- genetics
- environment
- development
- co-morbidity



Treatment Research

(New Targets & New Strategies)

HIV/AIDS Research

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Drug Use Has Played a Prominent Role in the HIV/AIDS Epidemic In Several Ways

- **Disease Transmission**
  - **IV Drug Use—Needle sharing**
  - **Drug Intoxication: Impaired judgment, disinhibition, leading to risky sexual behaviors**
- **Disease Progression**
- **Neurological Complications**

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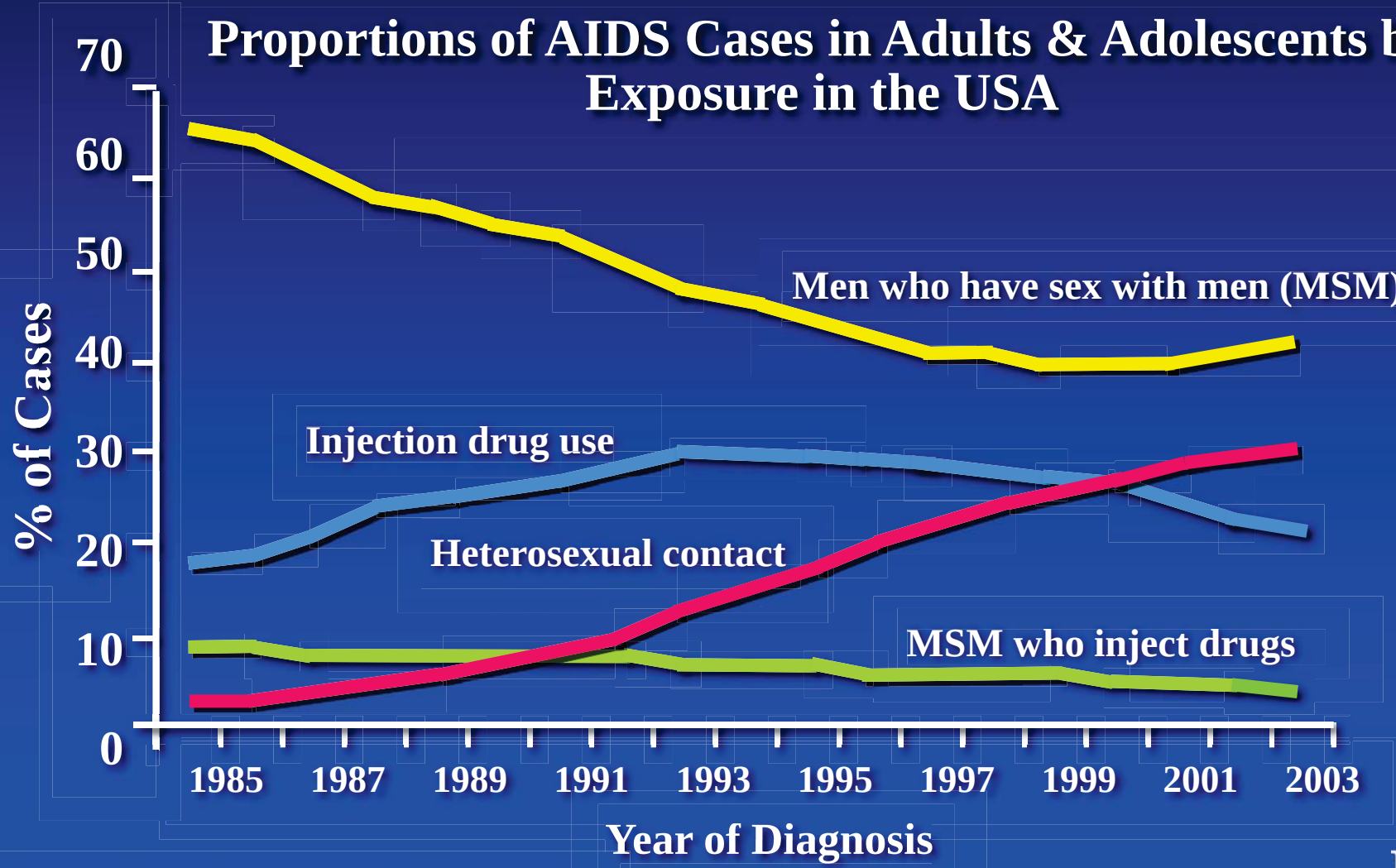
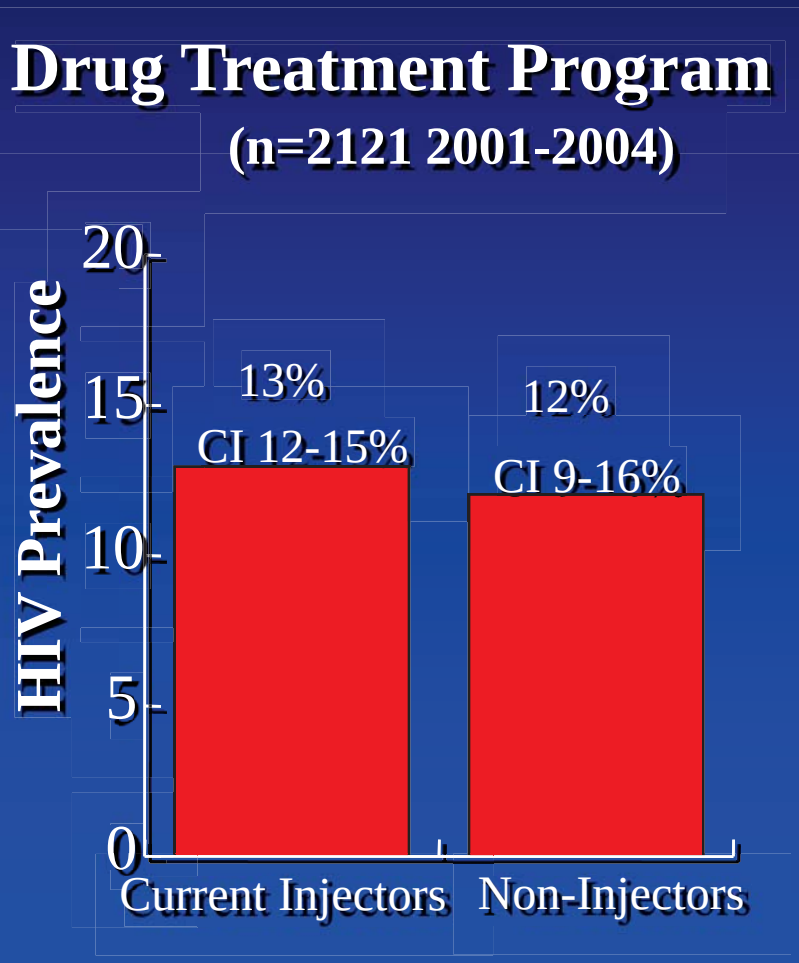
Drugs of Abuse Have Had A Major Impact on the HIV/AIDS Epidemic

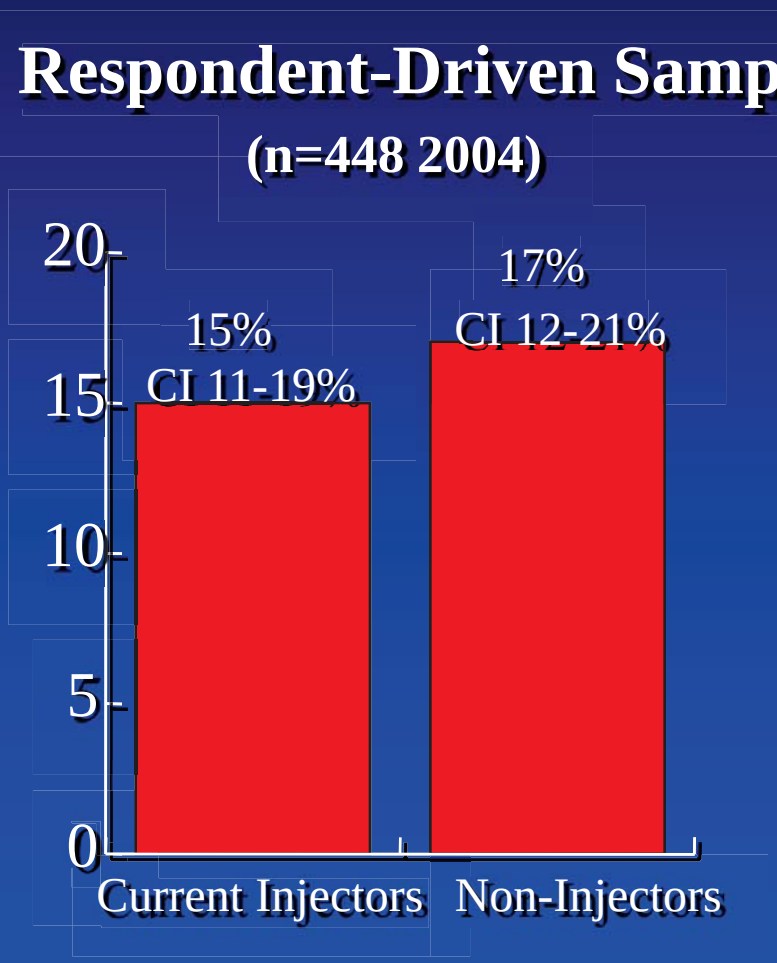


Centers for Disease Control and Prevention (CDC)

NIDA

Convergence of HIV Seroprevalence Among Injecting and Non-injecting Drug Users





Source: Des Jarlais et al AIDS, 21: 231-235, 2007.

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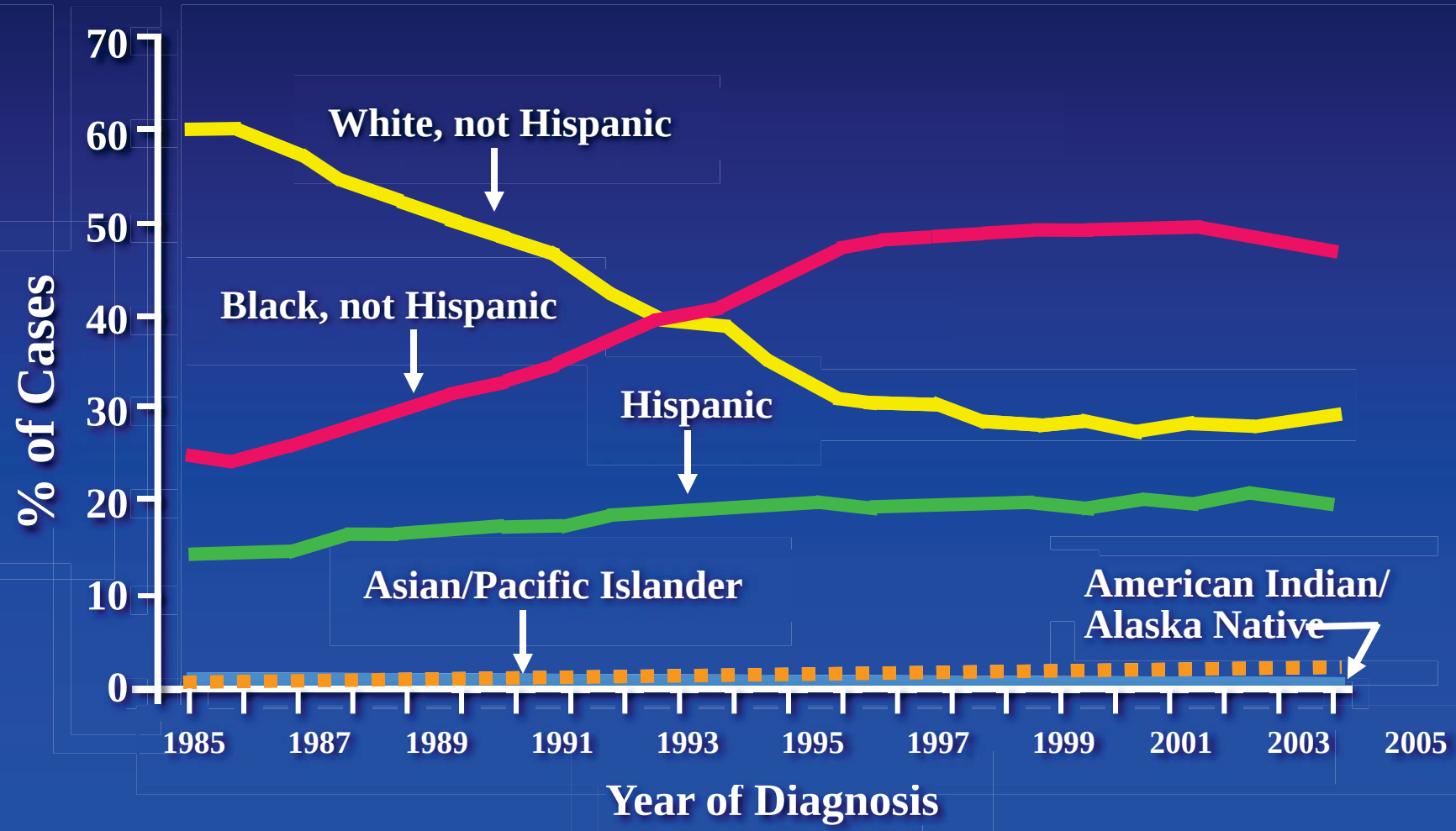
The AIDS Epidemic Disproportionately Affects Minority Populations



Centers for Disease Control and Prevention (CDC)

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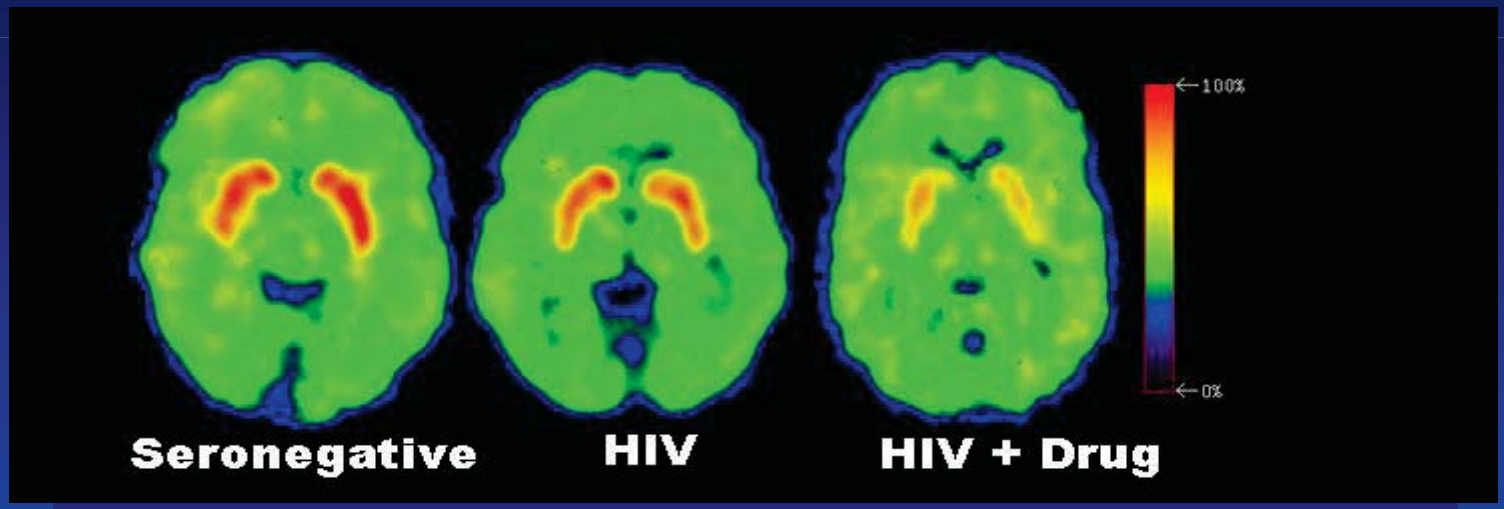
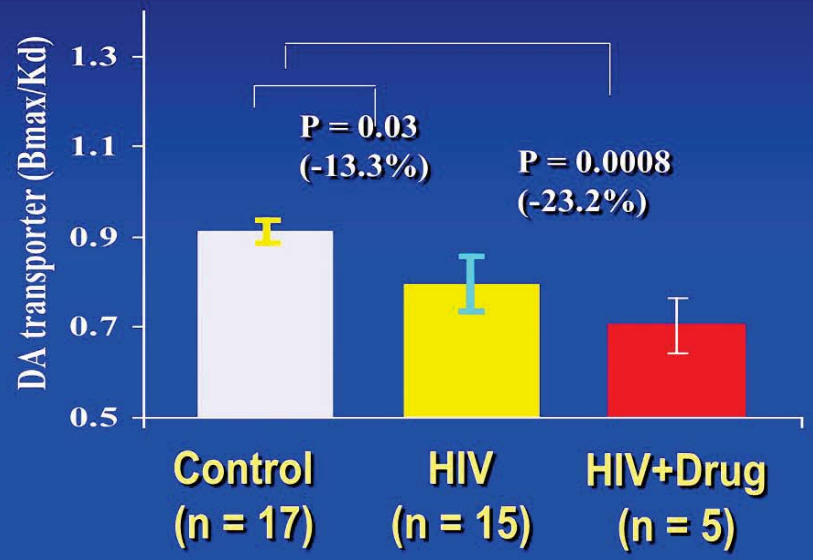
Acceleration of HIV Degeneration of Dopamine Cells With Cocaine





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NIDA International Program Components

Post-Doctoral Research Fellowship

Technical Consultation

International Research Collaboration

Scientific Exchange

Information Dissemination

NIDA

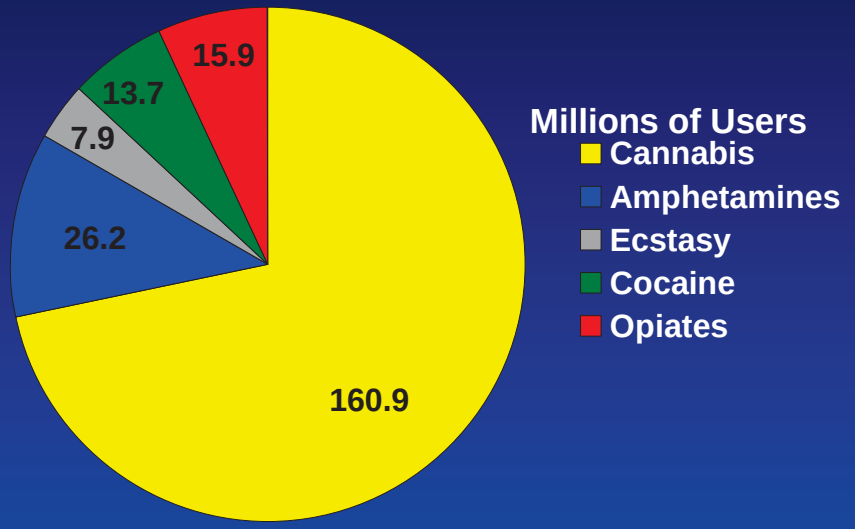
Why focus on drug abuse internationally?

I. Drug abuse is a global phenomenon

- **5 % of people aged 15-64**

II. Intertwined dual-epidemics of drug addiction & HIV/AIDS

- **HIV Infections Attributed to Injection Drug Use and Risky Sexual Behaviors Related to Drug Abuse**



UNODC *2005 World Drug Report*

III. Take advantage of unique opportunities to advance scientific knowledge through research

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NIDA Supports International Drug Abuse Research In Numerous Ways

- **Fund international research**
- **Provide training and exchange opportunities**
- **Set international research priorities**
- **Organize & sponsor conferences and meetings**
- **Binational agreements**
- **Dissemination of information**

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Where Do We Need to Go From Here?

We Need to…

Advance the SCIENCE

and…

Erase the STIGMA

NIDA

For More Information

NIDA Public Information:

www.nida.nih.gov

www.drugabuse.gov

NIDA International Program:

www.international.drugabuse.gov