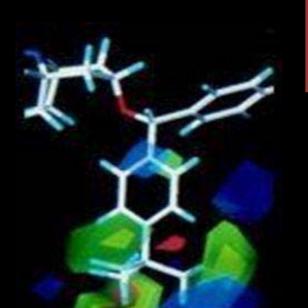
Advances in Drug Abuse and Addiction Research from NIDA: Implications for Treatment

Gaya J. Dowling, Ph.D.
Acting Chief, Science Policy Branch
Office of Science Policy and Communications
National Institute on Drug Abuse
National Institutes of Health
Department of Health and Human Services

Addiction Medicine: Improving Clinical and Teaching Skills for Generalists
2011 Chief Resident Immersion Training (CRIT) Program
Cape Cod, Massachusetts
May 2011

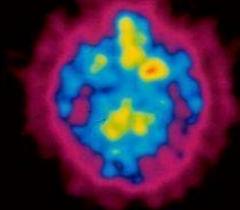
NATIONAL INSTITUTE **ON DRUG ABUSE**

Rringing the Full Power of Science to Bear on



Drug Abuse & Addiction





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

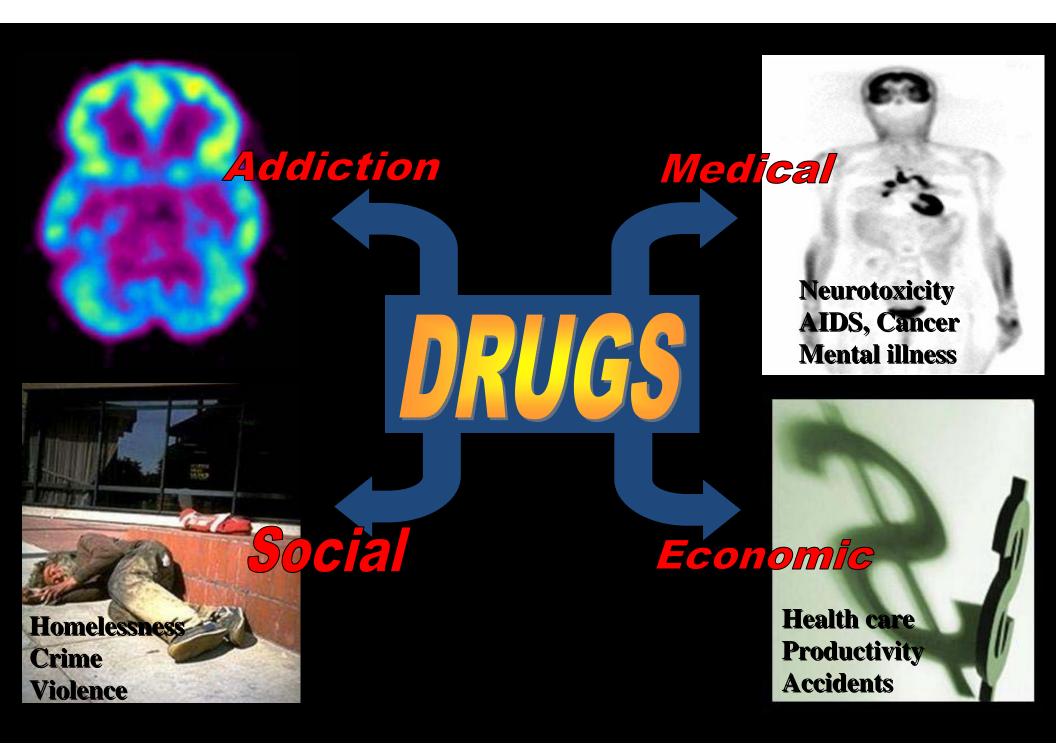
Tobacco: \$193 billion/year

Alcohol: \$235 billion/year

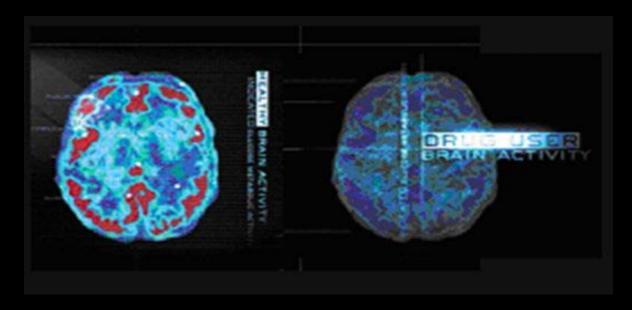
Illegal drugs: \$181 billion/year

Total: \$609 billion/year





What is Addiction? Addiction is A Brain Disease

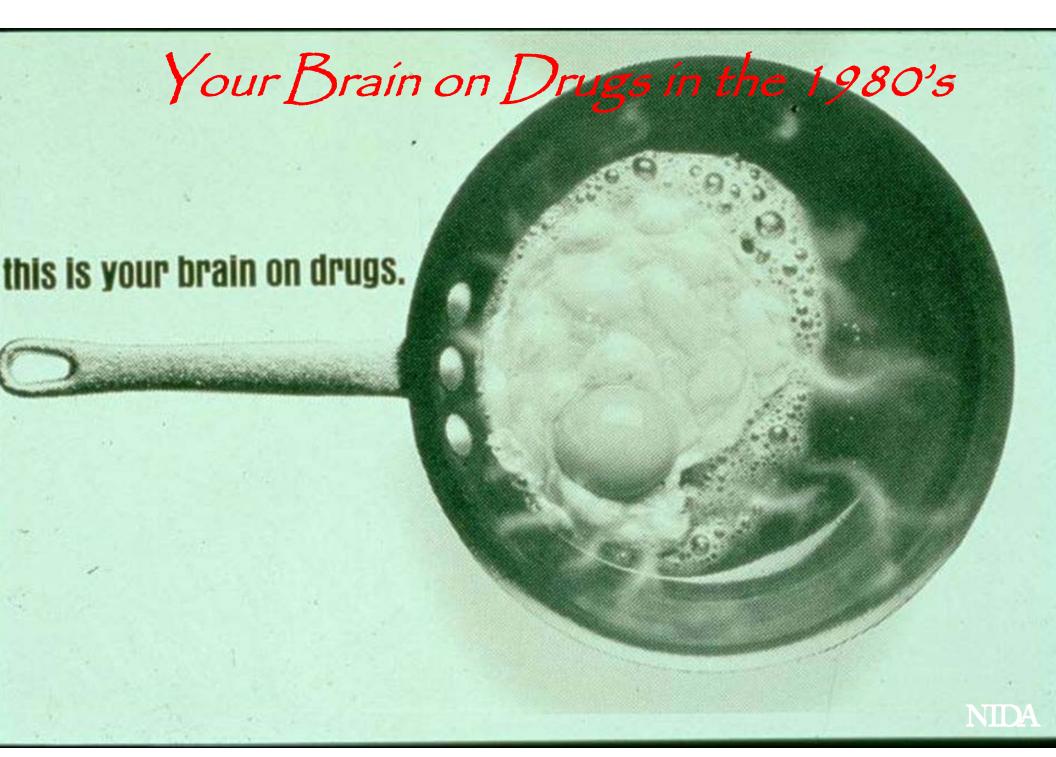


- Characterized by:
 - Compulsive Behavior
 - Continued abuse of drugs despite negative consequences
 - Persistent changes in the brain's structure and function

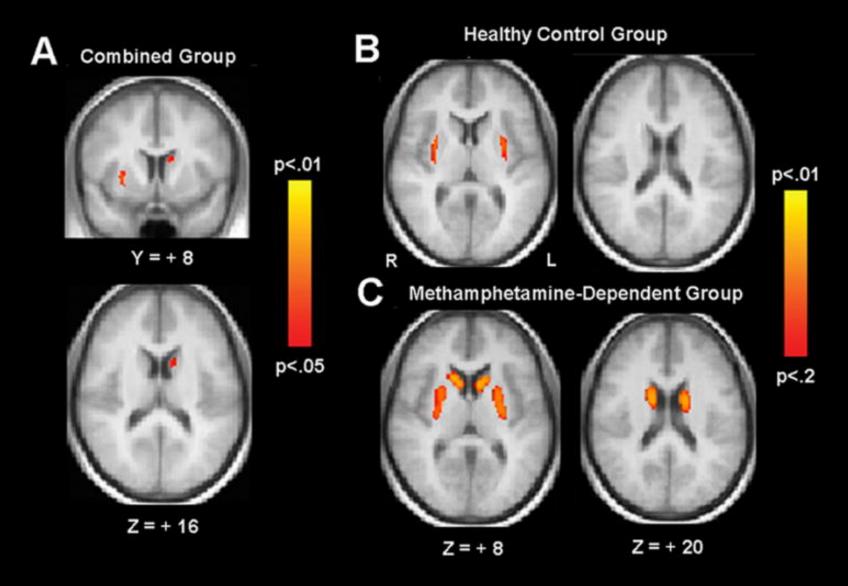


Advances in science have revolutionized our fundamental views of drug abuse and addiction.





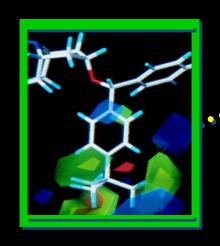
Your Brain on Drugs - Now



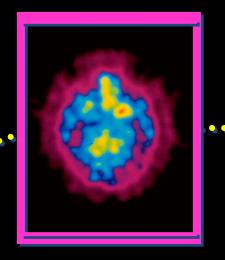
Source: Lee et al., 2009 J Neurosci 29:14734-40.

NIDA Research

From Molecules...









...To Managed Care
...Drug Courts
...Community Coalitions

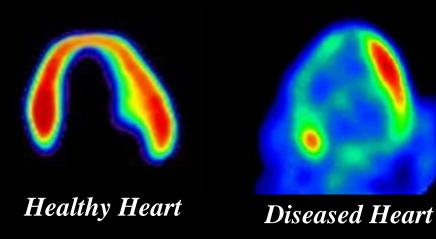


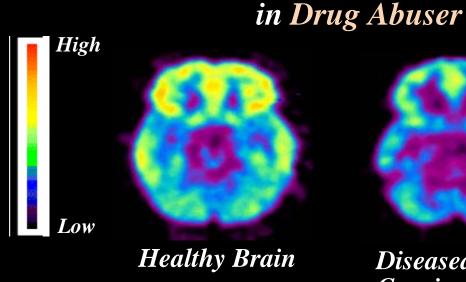
What have we learned?

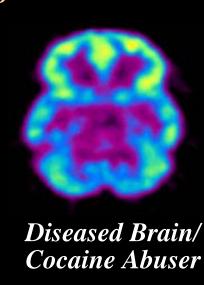
Addiction is Like Other Diseases...

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

Decreased Heart Metabolism in Heart Disease Patient





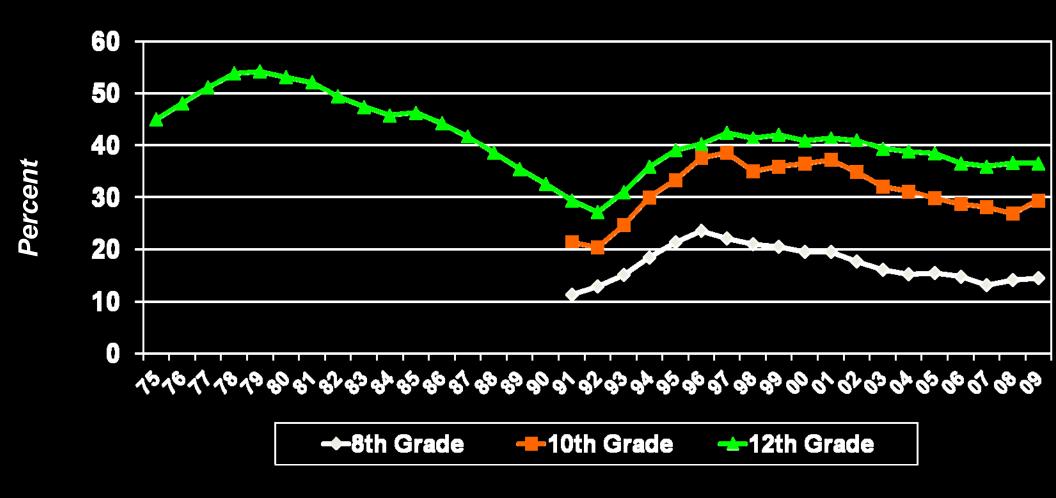


Decreased Brain Metabolism

In 2009, an estimated 21.8 million Americans, or 8.7 percent of the population aged 12 or older, were current illicit drug users.

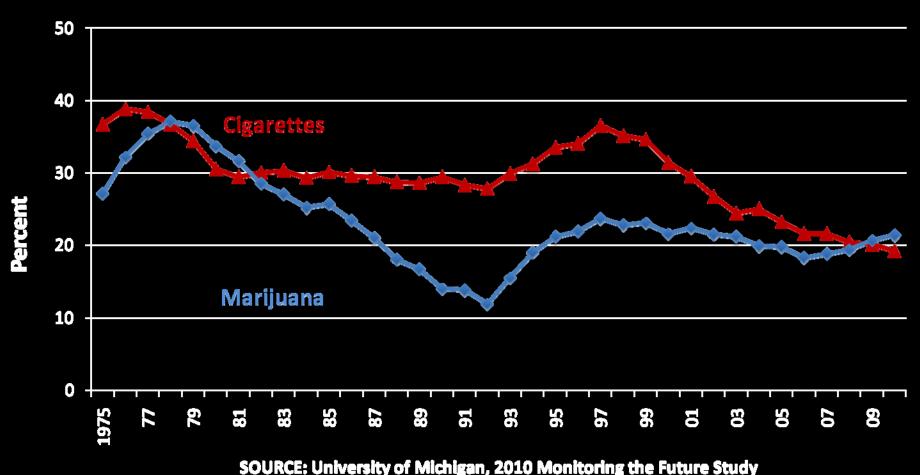
Source: National Survey on Drug Use and Health (NSDUH), SAMHSA, 2010

Percent of Students Reporting Any Illicit Drug Use in Past Year, by Grade

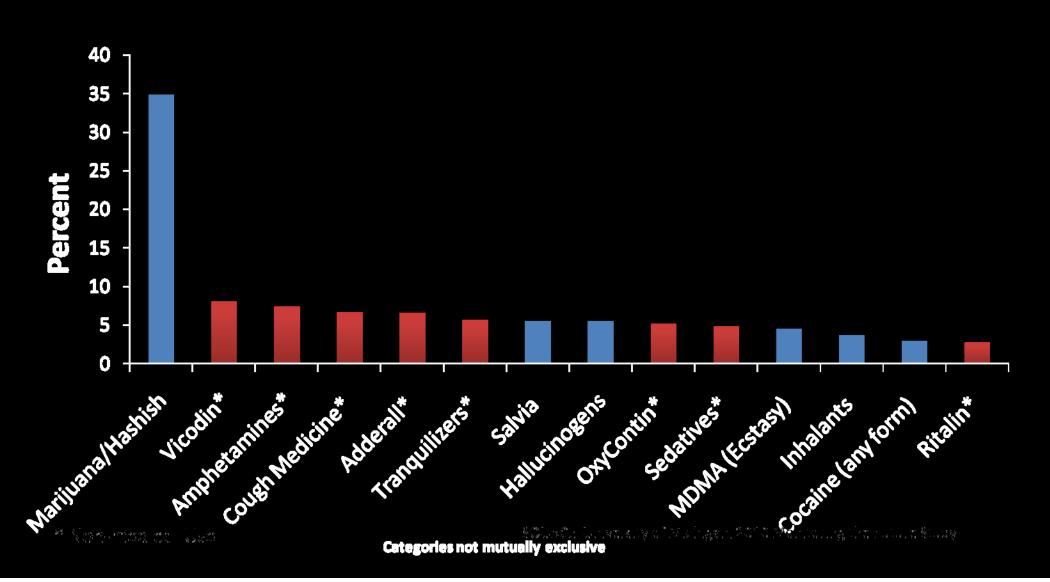


SOURCE: University of Michigan, 2009 Monitoring the Future Study

Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes and Marijuana, 1975 to 2010



After Marijuana, Prescription and Over-the-Counter Medications Account for Most of the Commonly Abused Drugs Prevalence of Past Year Drug Use Among 12th Graders



Why Do People Take Drugs in The First Place?

To Feel Good

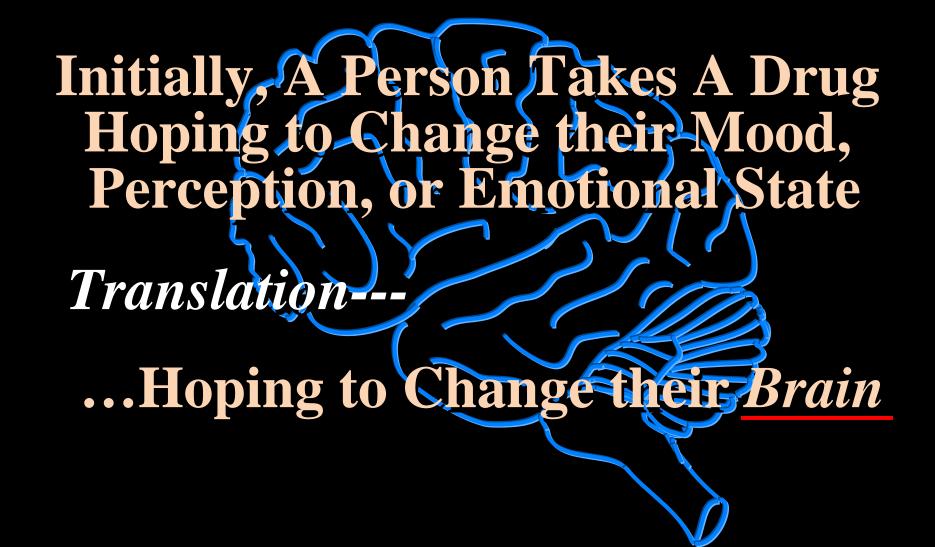
To have novel:
feelings
sensations
experiences
AND
to share them



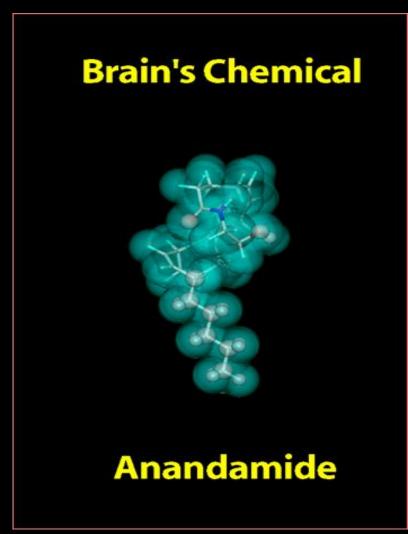
To Feel Better

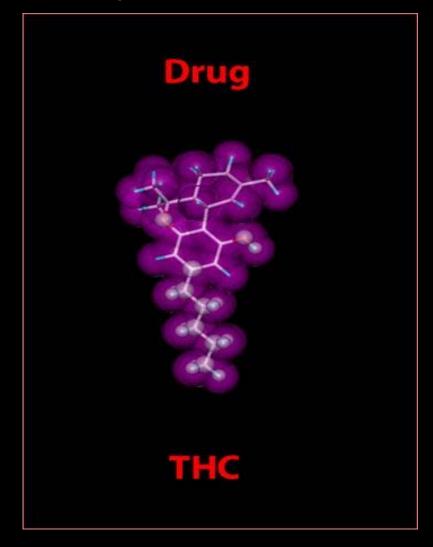
To lessen:
anxiety
worries
fears
depression
hopelessness





Drugs can be "Imposters" of Brain Messages

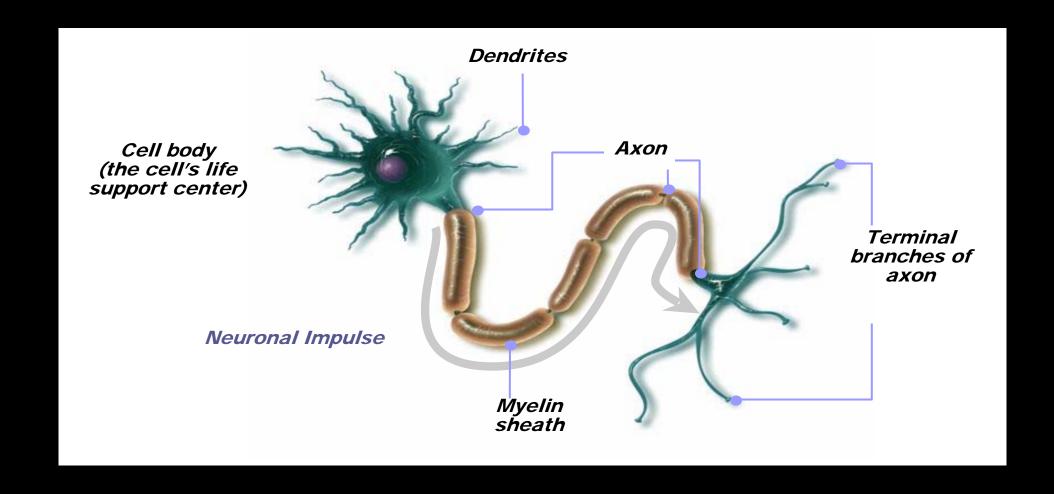




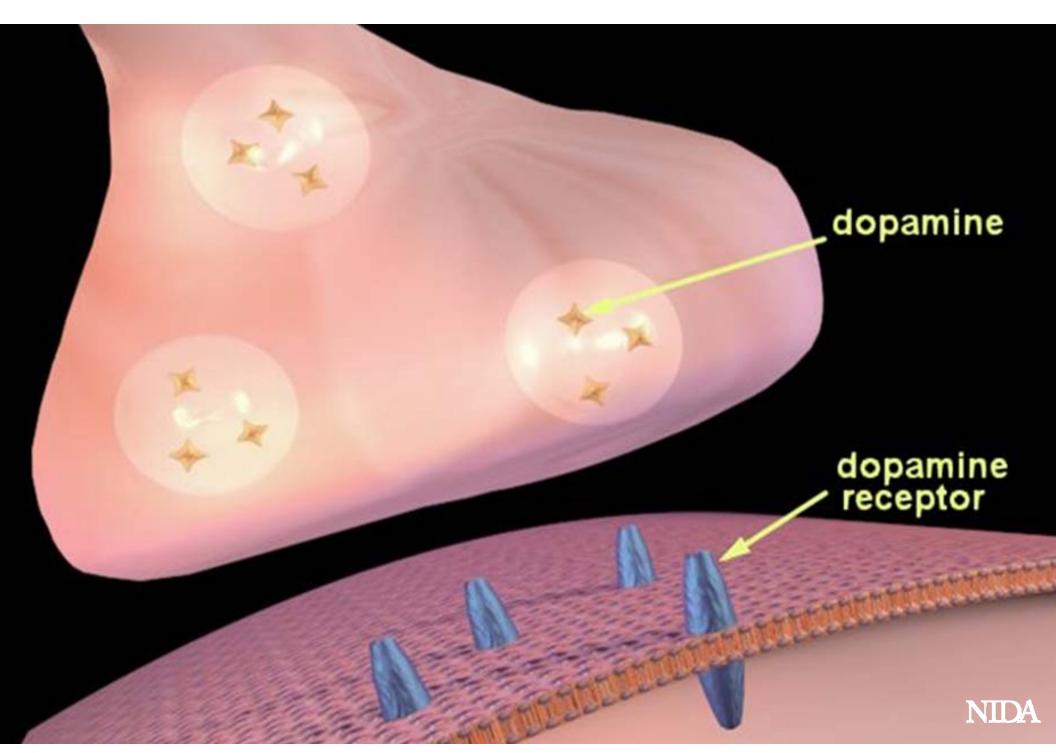


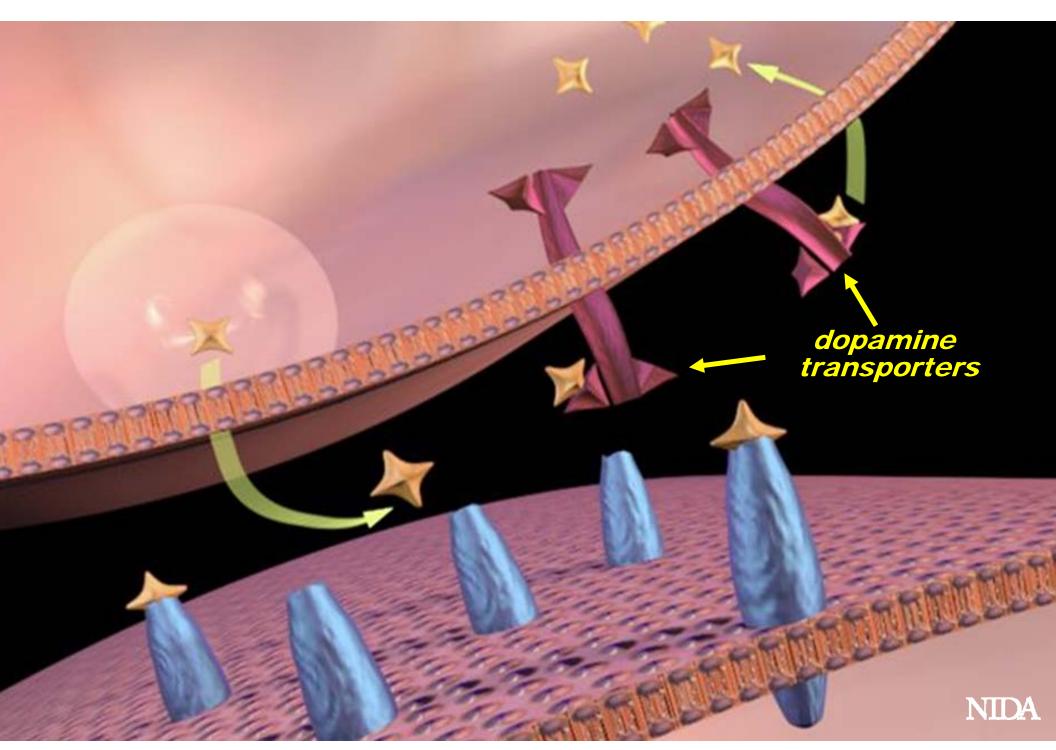


The Neuron: How the Brain's Messaging System Works

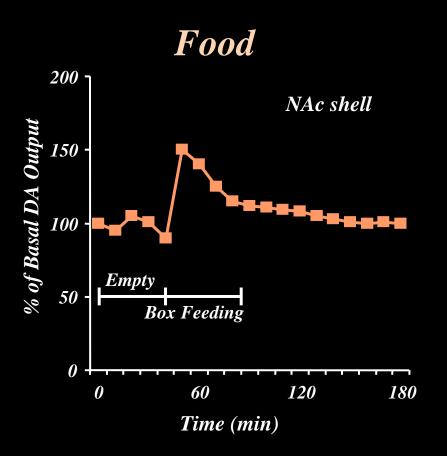


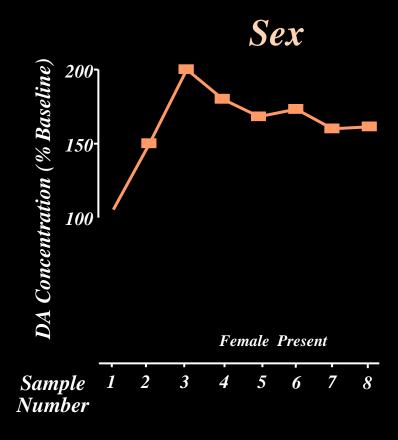




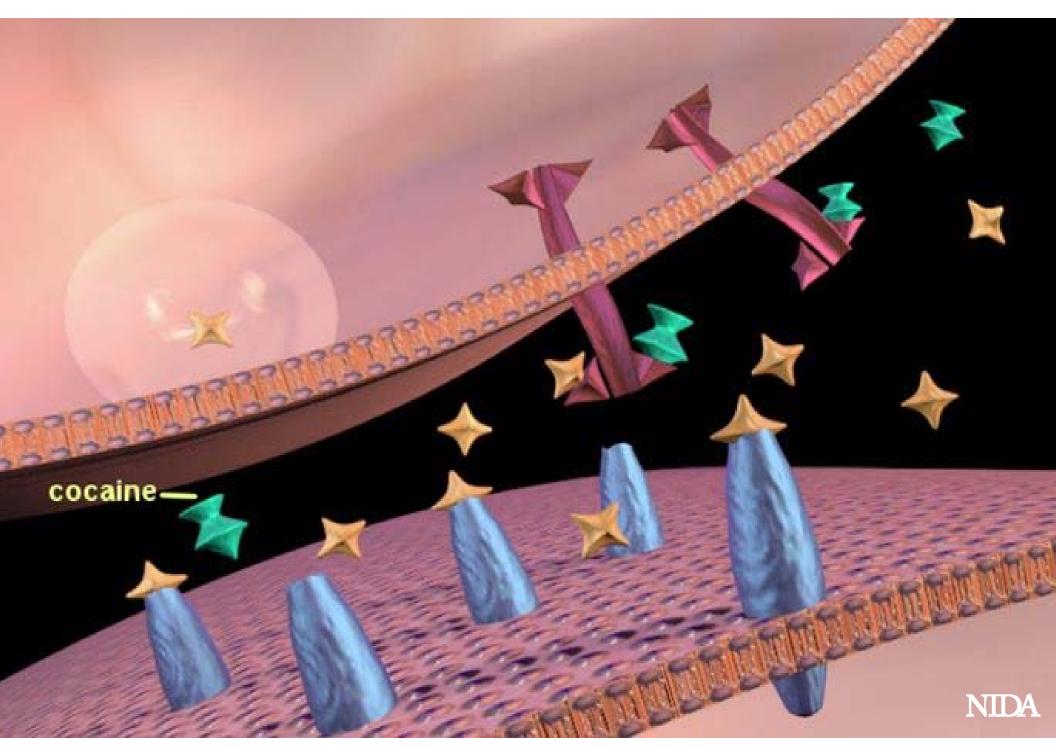


Natural Rewards Elevate Dopamine Levels

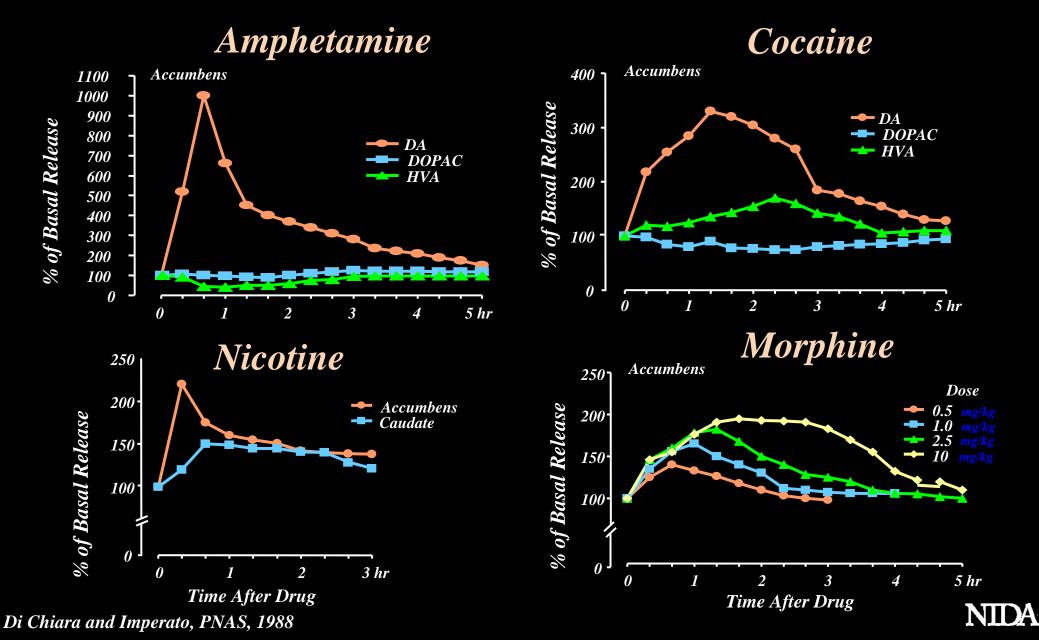








Effects of Drugs on Dopamine Release

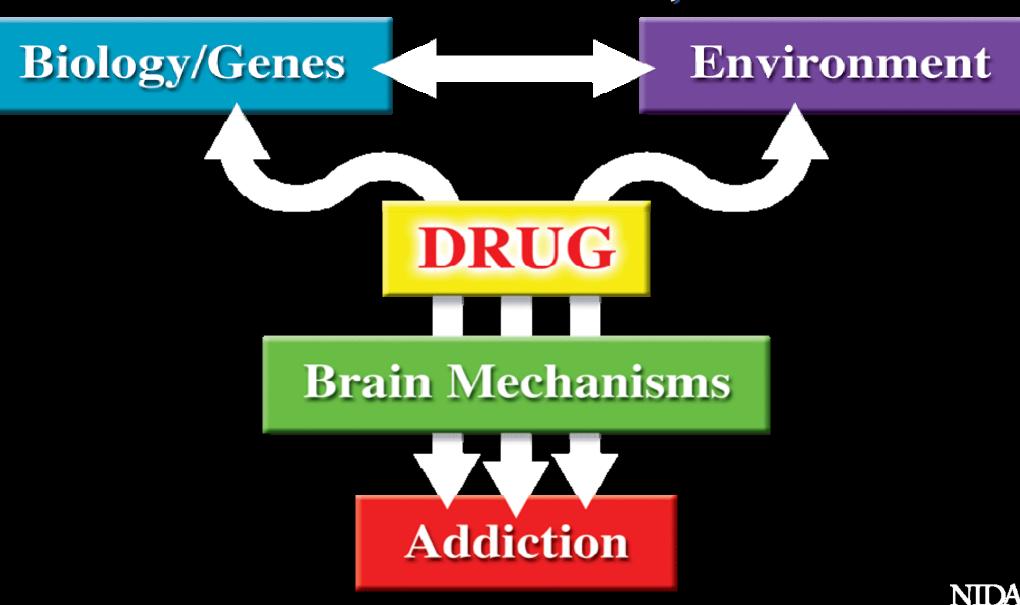


Vulnerability

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



Addiction Involves Multiple Factors

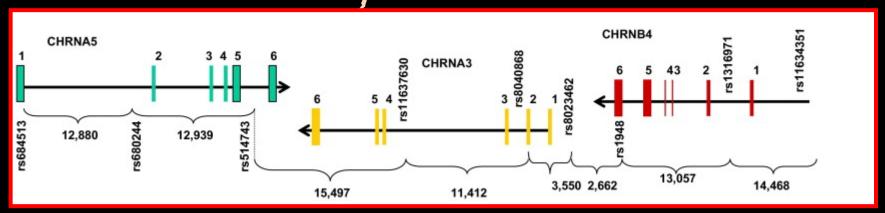




The Nature of this Contribution Is Extremely Complex

NIDA

Gene Cluster is Associated with Nicotine Dependence



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

Molecular Psychiatry (2008), 1-6 o 2008 Nature Publishing Group All rights reserved 1359-4184/08 \$30.00 www.nature.com/mp

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

Laura Jean Bierut^{1,*}, Pamela A.F. Madden¹, Naomi Breslau², Eric O. Johnson³,

Dorothy Ha Louis Fox¹ Nicholas G Jen C. War

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

IMMEDIATE COMMUNICATION

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

W Berrettini^{1,2,3}, X Yuan^{2,3}, F Tozzi^{2,3}, K Song^{2,3}, C Francks^{2,3}, H Chilcoat⁴, D Waterworth^{2,3}, P Muglia^{2,3,5} and V Mooser^{2,3}

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

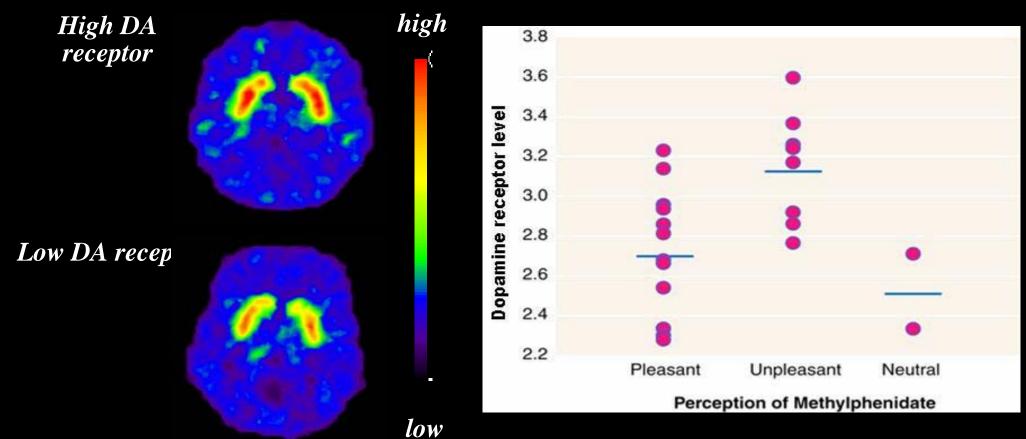
A variant associated with nicotine dependence, lung cancer and peripheral arterial disease

Thorgeir E. Thorgeirsson¹*, Frank Geller¹*, Patrick Sulem¹*, Thorunn Rafnar¹*, Anna Wista^{1,2}, Kristinn P. Magnusson¹, Andrei Manolescu¹, Gudmar Thorleifsson¹, Hreinn Stefansson¹, Andres Ingason¹, Simon N. Stagou¹, Ind. T. Borrethorgeon¹, Stagou¹, Ind. T. Borrethorgeon¹, Stagou¹, Ind. Gudmandoson¹, Thorleign Longeon¹, Thorleign Longeon¹,

Some Gene Variants Implicated in Addiction

- 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

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

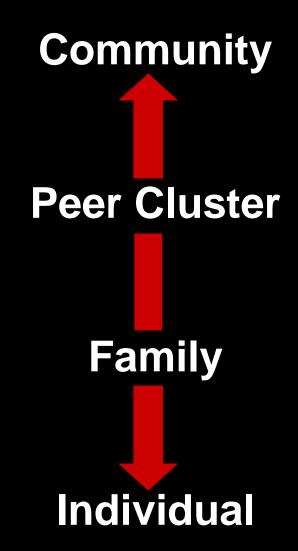


As a group, subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant



But it isn't all genetics

Drug Abuse Risk Factors

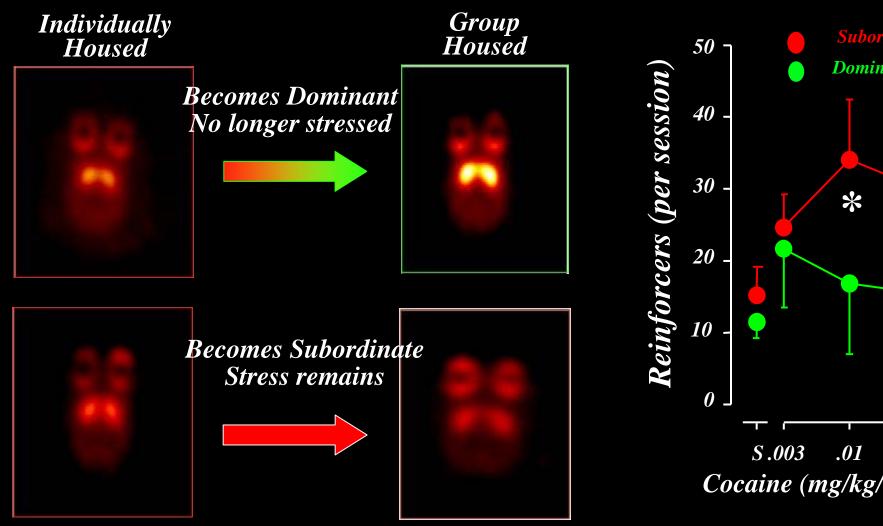


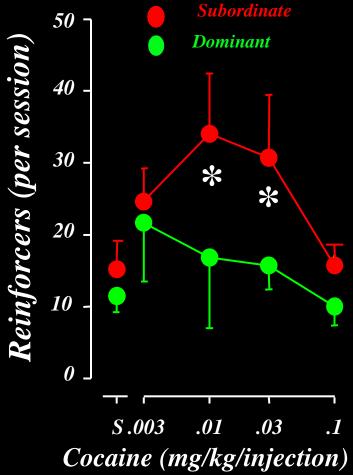
What Environmental Factors Contribute to Addiction?

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

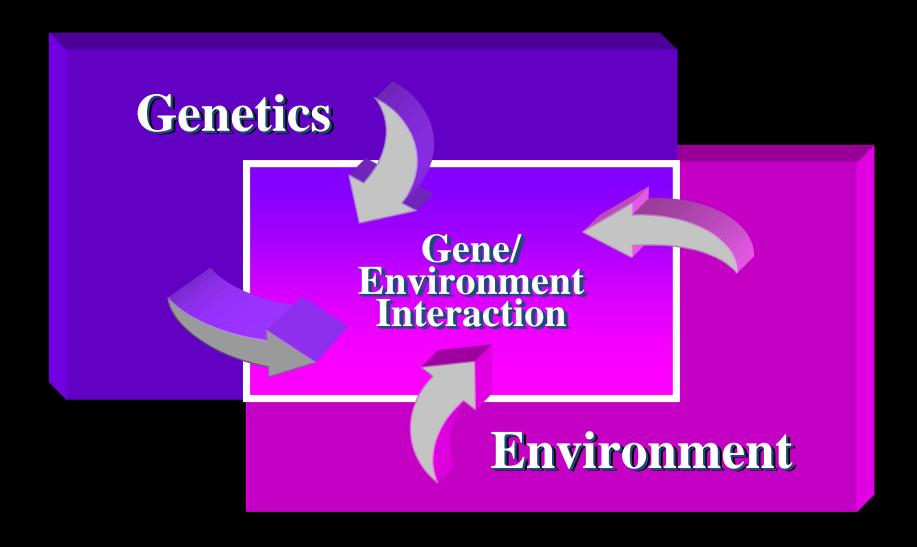


Social Stressor Affects Brain DAD2 Receptors and Drug Self-Administration



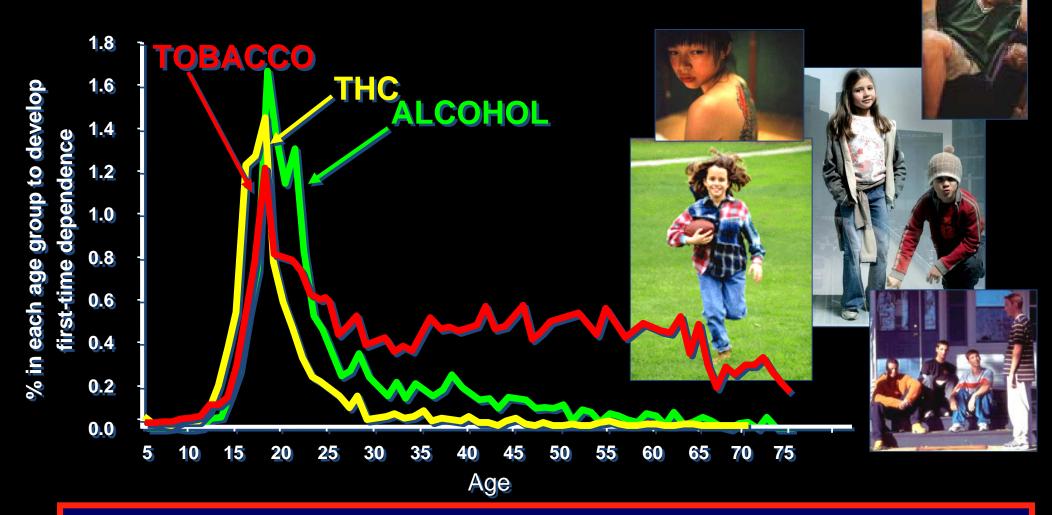






What have we learned about other aspects of vulnerability?

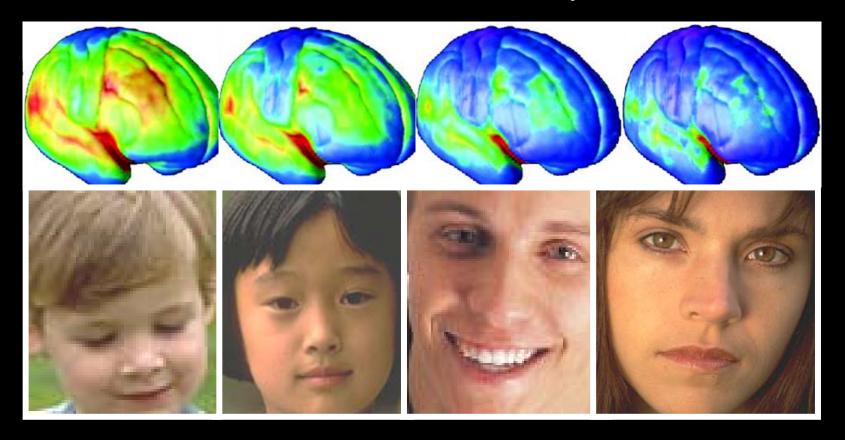
Addiction Is a Developmental Disease starts in childhood and adolescence



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

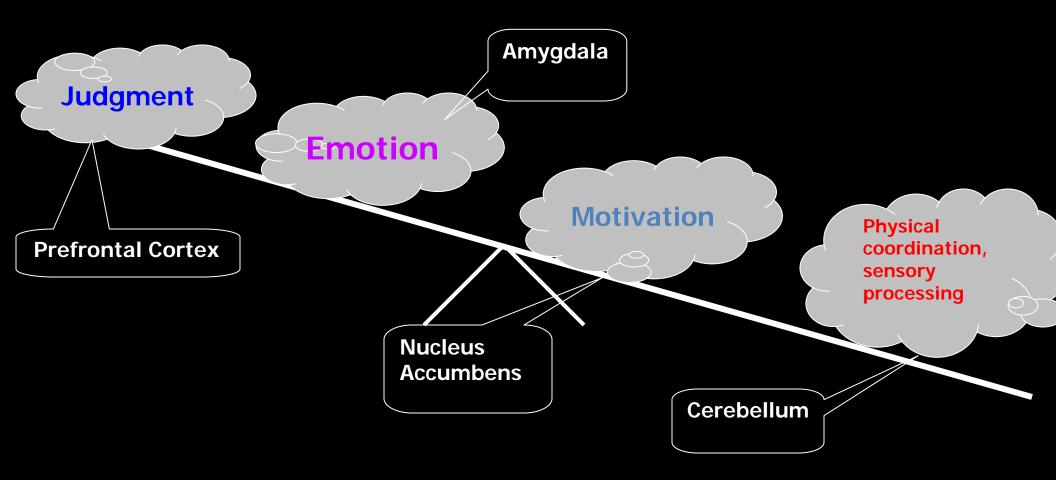
National Epidemiologic Survey on Alcohol and Related Conditions, 2003

Adolescents' Brains Are Still Developing...



Implications for prevention and Treatment?

Maturation starts at the back of the brain ... and moves to the front



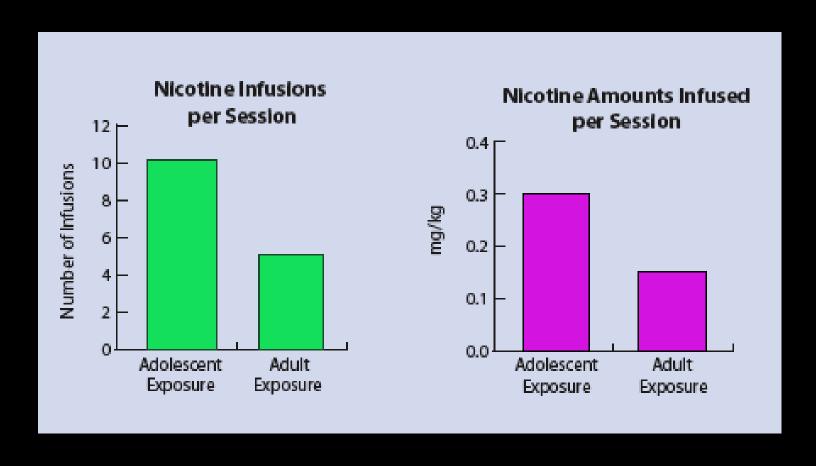
Notice: Judgment is last to develop!

Source: K. Winters

Do Adolescents React Differently than Adults to Substances of Abuse?



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







Do We Need Fundamentally Different Strategies For Adolescents?

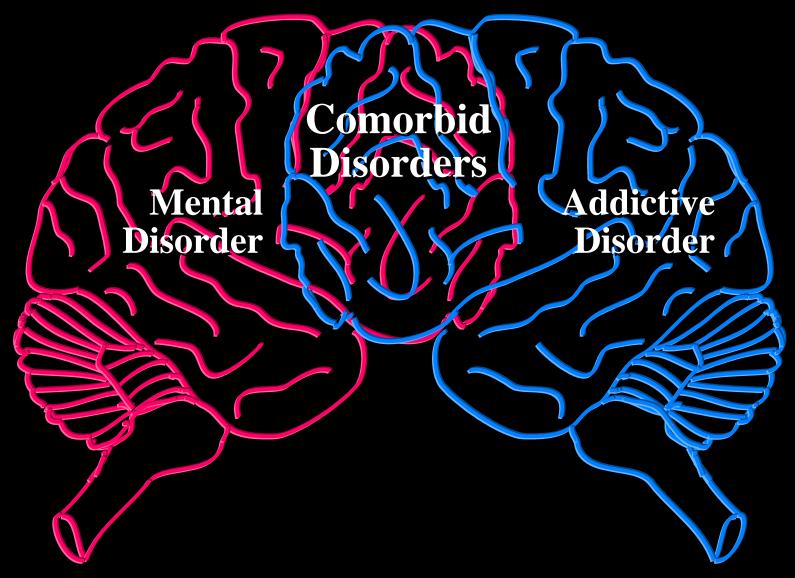




NIDA

What Else Have We Learned?

Addictive Disorders Often Co-Exist With Mental Disorders



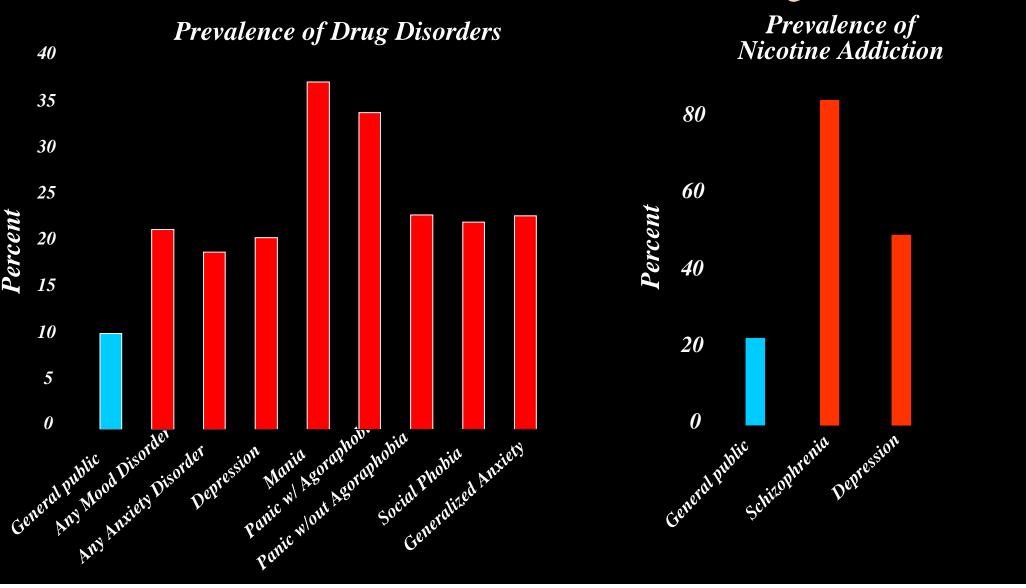
Addictive Disorders Often Co-Exist With Mental Disorders

Comorbid Serious Substance Disorders Psychological Use Disorder Distress 24.3 million 15 million Co-Occurrence of Serious Psychological Distress and Substance Use Disorder in the Past Year

SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 2007

among Adults Aged 18 or Older: 2007

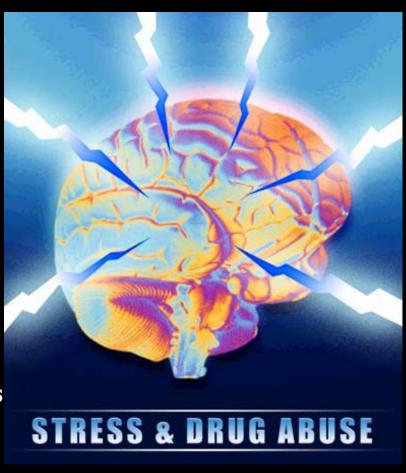
What Other Biological Factors Contribute to Addiction—Comorbidity



Many Common Factors Are Involved in Addiction and Mental Illness

Addiction:

- •Early Physical or Sexual Abuse
- •Stress
- •Family History
- •Mental Illness
- •Peers who use Drugs



Mental Illness:

- •Early Physical or Sexual Abuse
- •Stress
- •Family History
- Drug and Alcohol Abuse

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



NIDA

These may contribute to vulnerability to initial drug use

But what happens to the brain over time?

Science Has Generated Much Evidence Showing That...

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



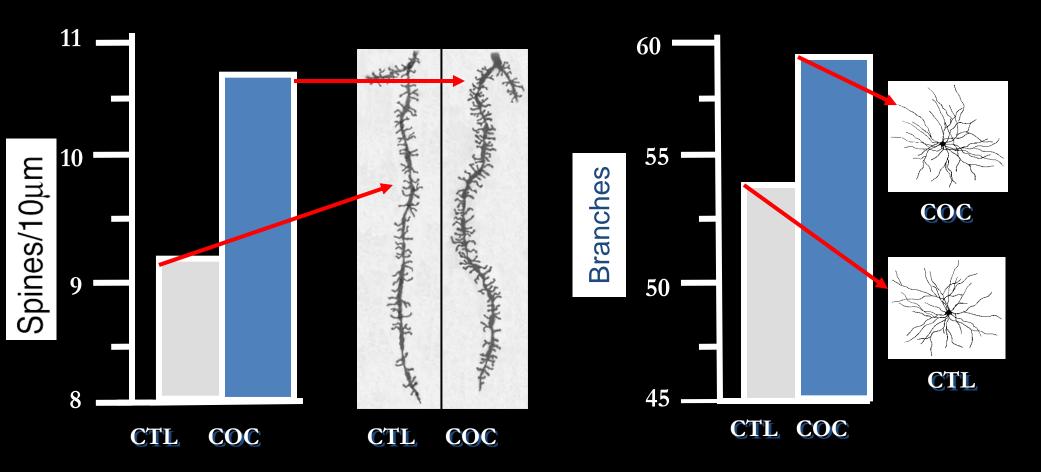
AND...

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



Structurally...

Chronic cocaine increases density of dendritic spines and neuronal branching in the nucleus accumbens



Robinson, T.E. & Kolb, B. Eur. J. of Neuro. 1999. Ferrario, C.R. et al. Biol. Psychiatry, 2005.

Functionally...

Dopamine D2 Receptors are Decreased by Addiction

Cocaine



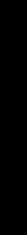
Meth



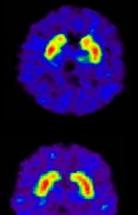
Alcohol

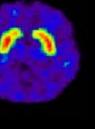
Heroin

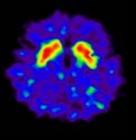




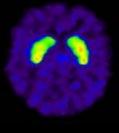


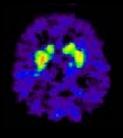


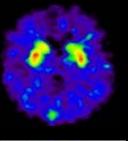










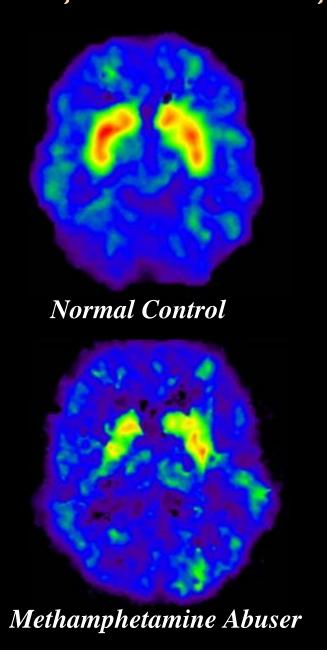


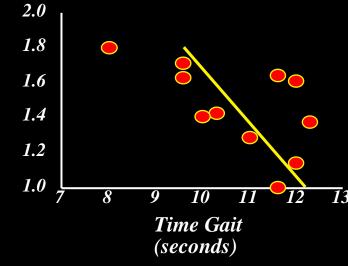


DA D2 Receptor Availability

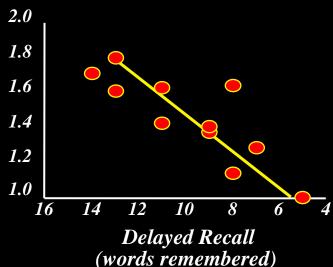
Dopamine Transporters in Methamphetamine Abusers

Dopamine Transporten





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.



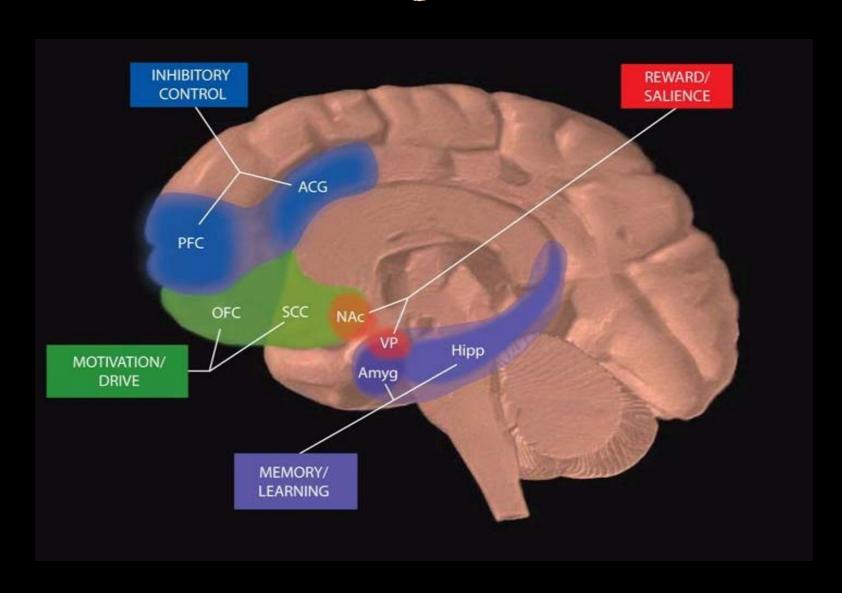
Volkow et al., Am. J. Psychiatry, 2001.

But Dopamine is only <u>Part</u> 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.



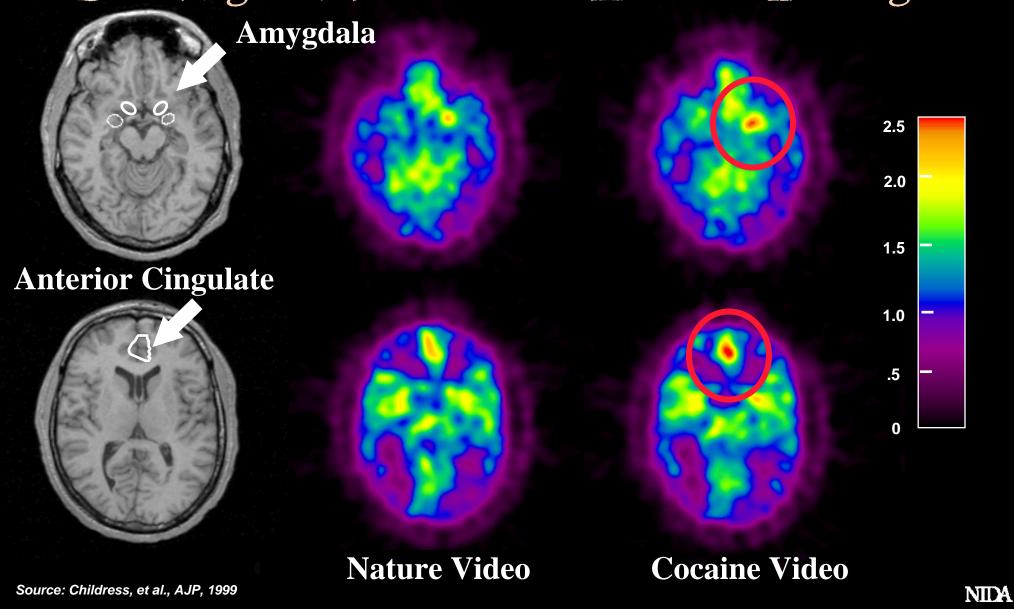
Circuits Involved In Drug Abuse and Addiction



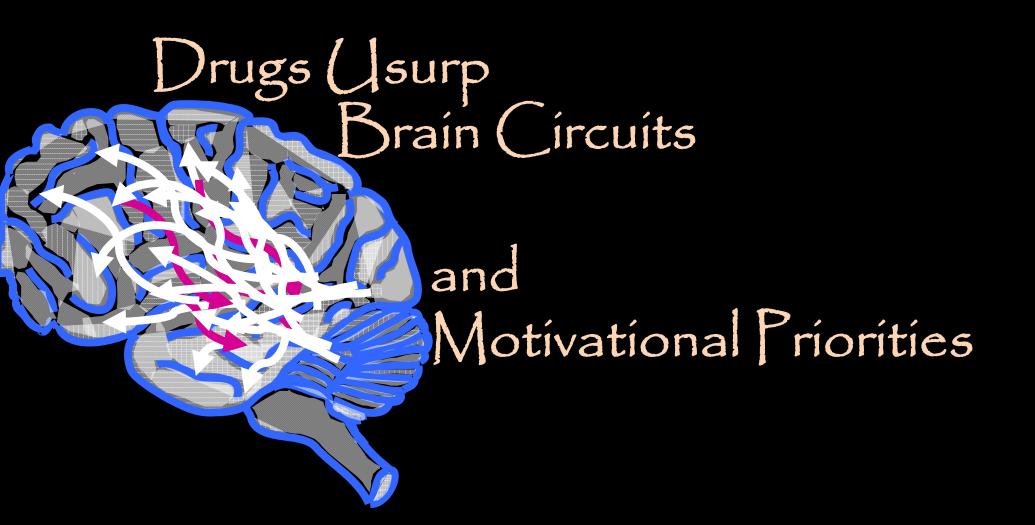


Memories Appear to Be A Critical Part of Addiction

Cocaine Abusers Have Increased Activation in Brain Regions Associated with Emotional Learning



But lt's Not Just Memories...

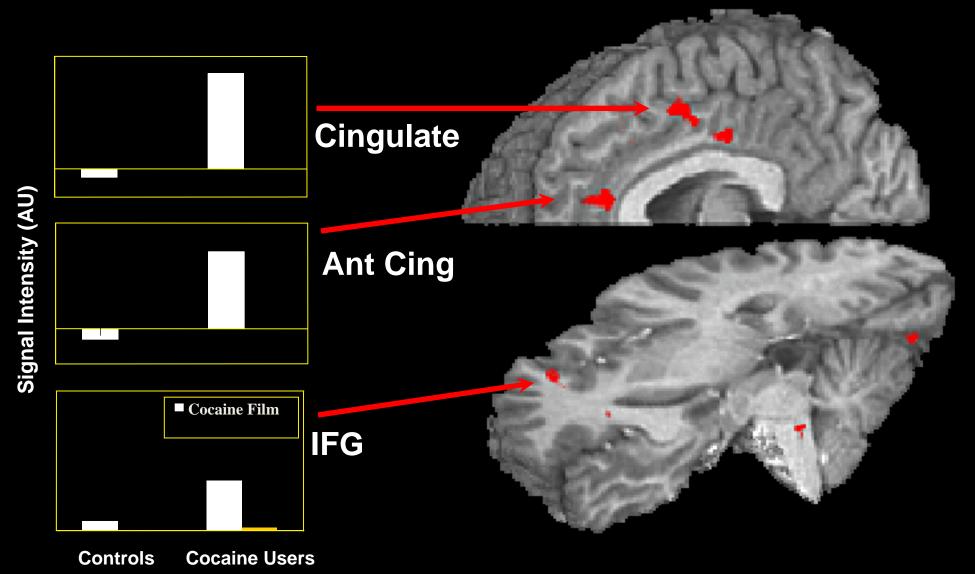


We Don't Know the Exact Switch

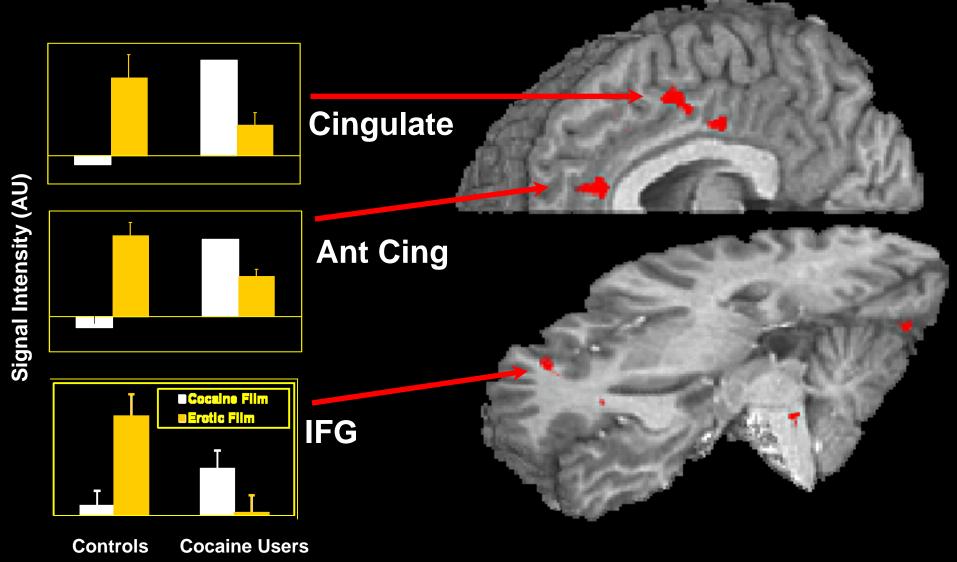
BUT...

We Do Know that the Brain Circuitry Involved in Addiction Has Similarities to that of Other Motivational Systems

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



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

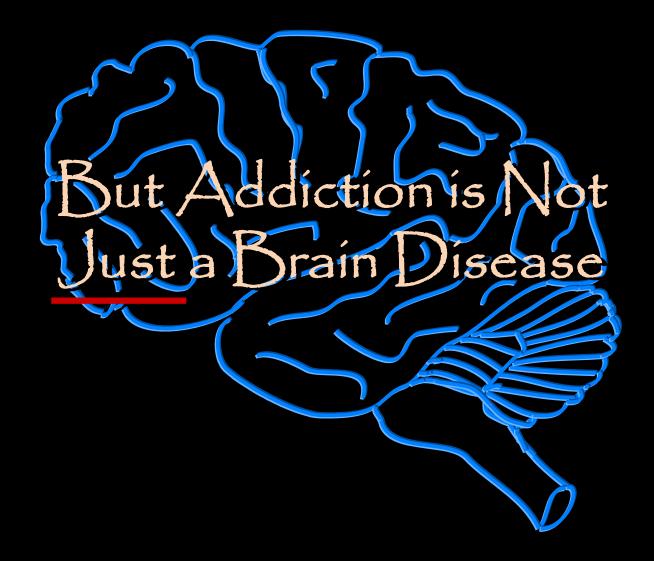


This Results in "Motivational Toxicity" and Compulsive Drug (Jse (Addiction)



The Brains of Addicts Are Different From the Brains of Non-Addicts

...And Those Differences
Are An Essential Element
of Addiction



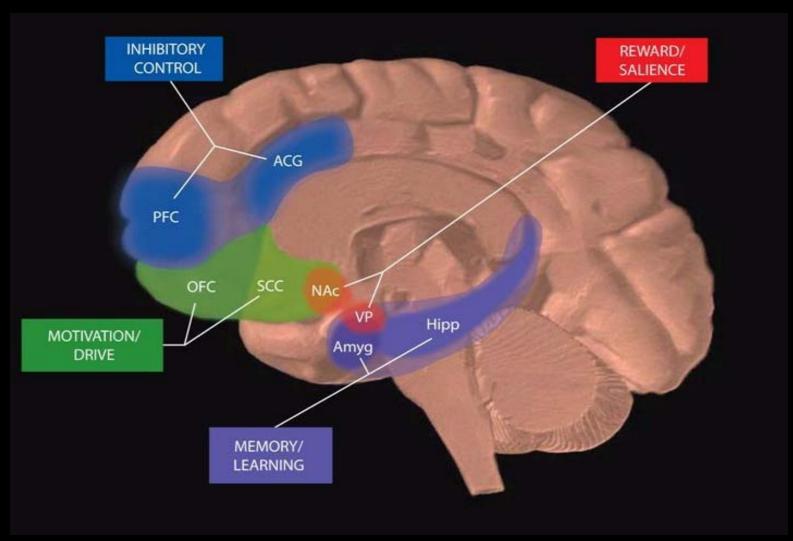
Addiction | S A Brain Disease Expressed As Compulsive Behavior

It is the Quintessential Biobehavioral Disorder

50....

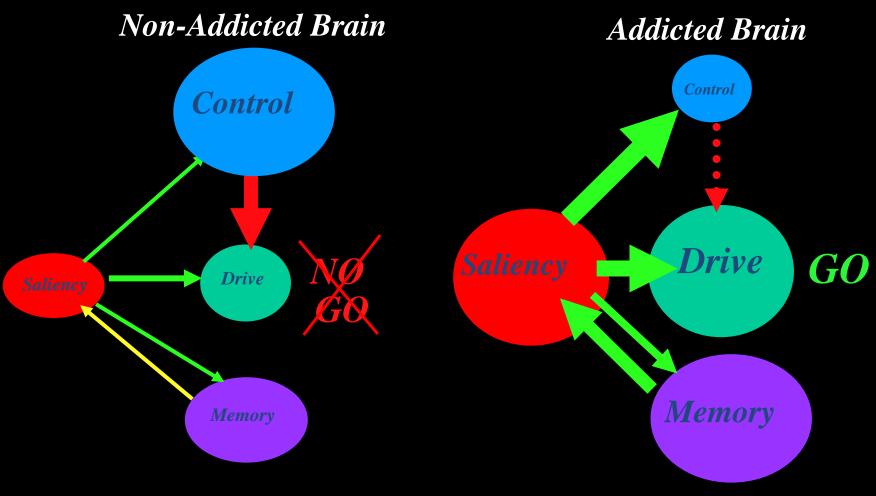
....What Does This Mean For Treatment?

Circuits Involved In Drug Abuse and Addiction



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

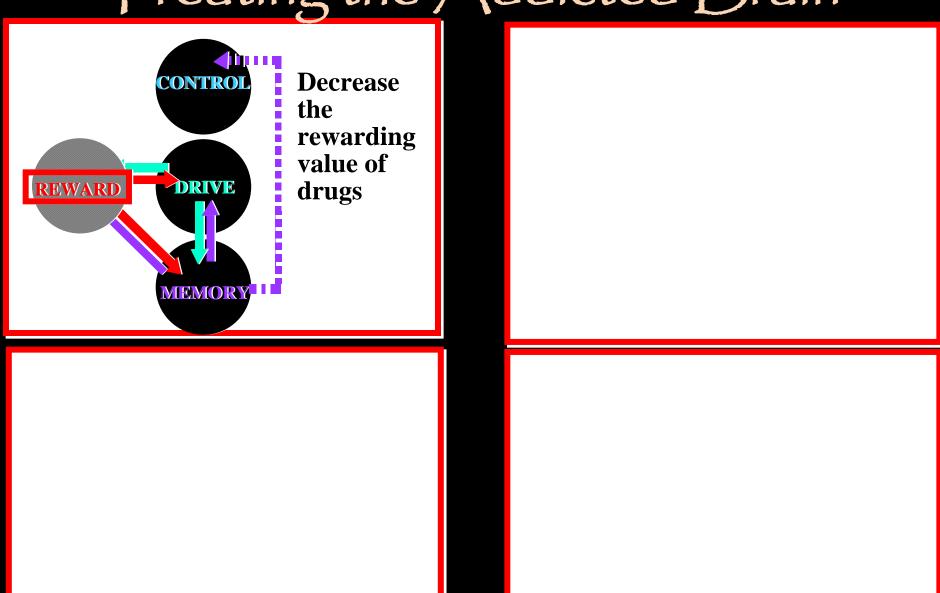
Why Can't Addicts Just Quit?



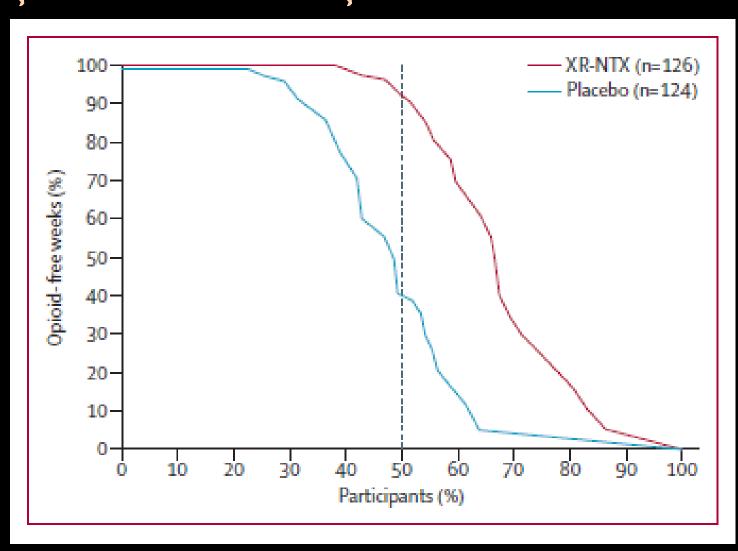
Because Addiction Changes Brain Circuits



Treating the Addicted Brain



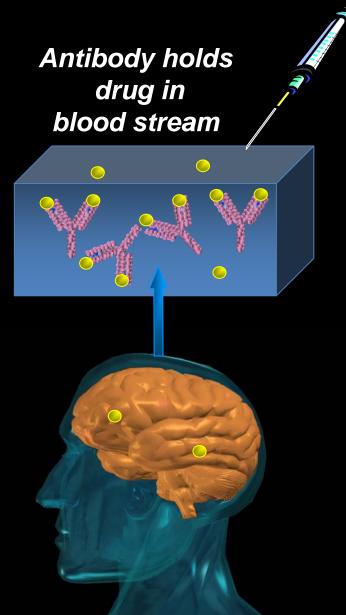
Vivitrol significantly increases percentage of patients with opioid-free weeks



Antibodies can reduce brain concentrations

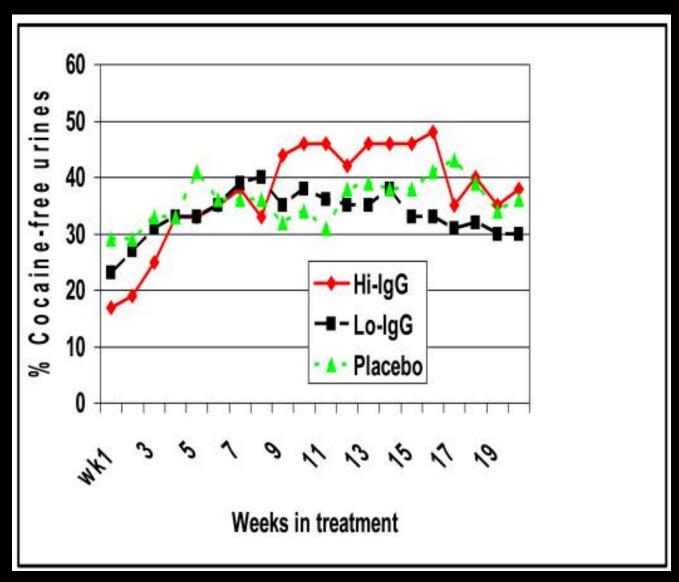
Blood Flow Brain

Capillary



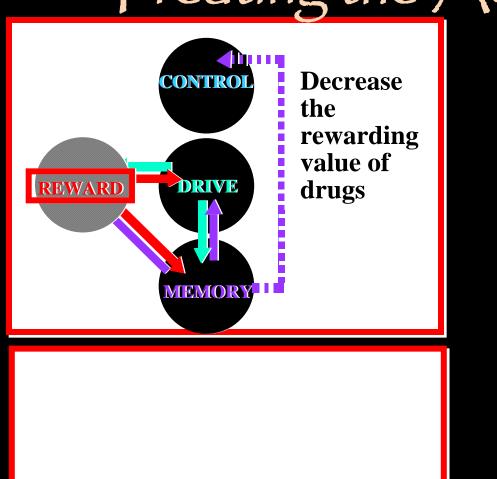


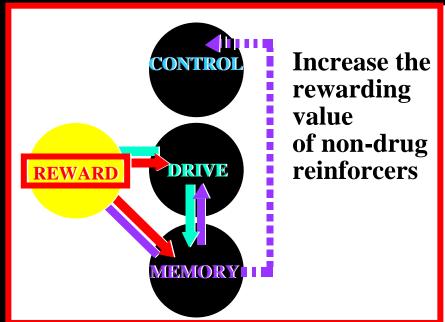
Fewer cocaine urines at higher vaccine dose



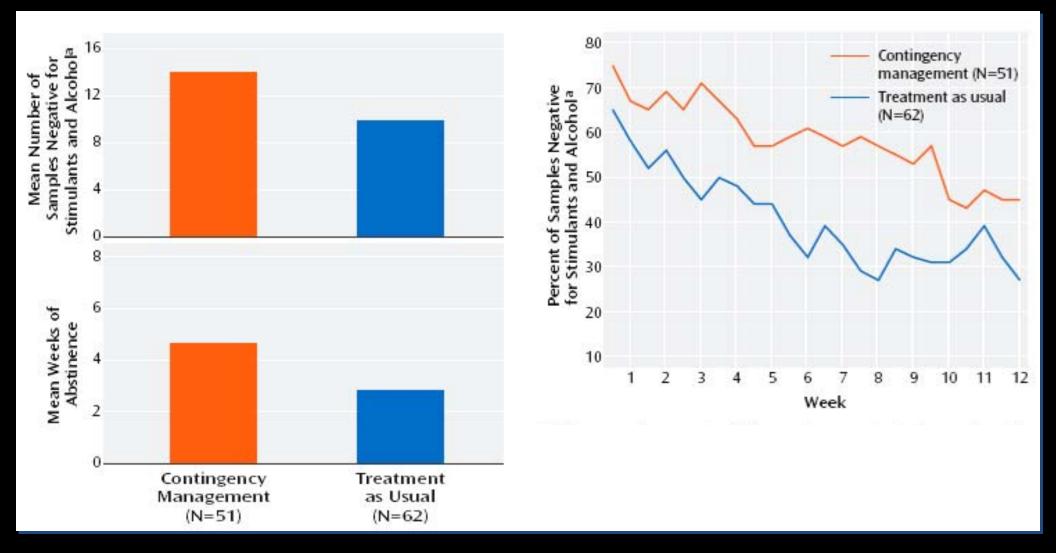
Kosten, et al, 2010 Arch Gen Psych

Treating the Addicted Brain



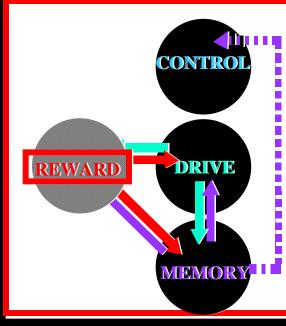


Contingency Management for the Treatment of Methamphetamine Use Disorders

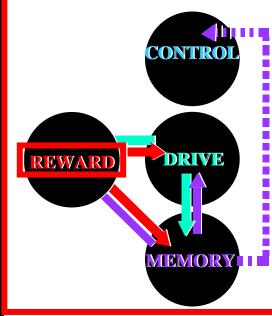


Roll, J.M. et al., AJP 163(11) pp. 1993-1999, November 2006.

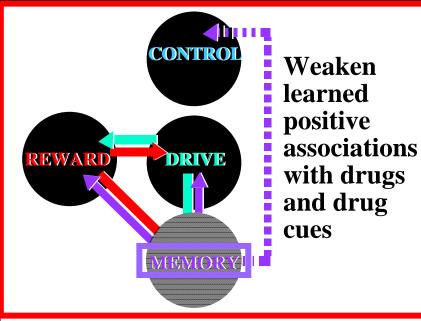
Treating the Addicted Brain

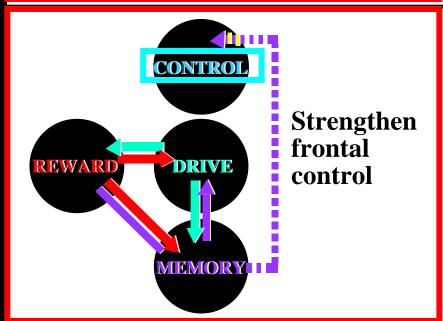


Decrease the rewarding value of drugs



Increase the rewarding value of non-drug reinforcers





Behavioral Interventions Medications Biofeedback

Treating A Biobehavioral Disorder Must Go Beyond Just Fixing The Chemistry

The Most Effective Intervention Strategies Will Attend to All Aspects of Addiction:

- Biology
- Behavior
- Social Context

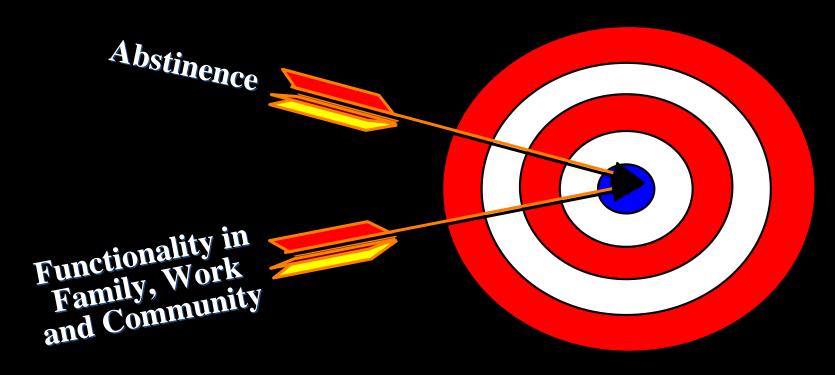
Drug Abuse Treatment Core Components and Comprehensive Services Medical Mental **Financial** Health **Group/Individual** Core Counseling Housing & **Urine** Vocational **Monitoring Treatment Transportation Abstinence** Intake Case **Based Assessment Management Pharmacotherapy Treatment Continuing Child Care Educational Plans** Care Self-Help (AA/NA) **Family** Legal AIDS / HIV

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

Risks

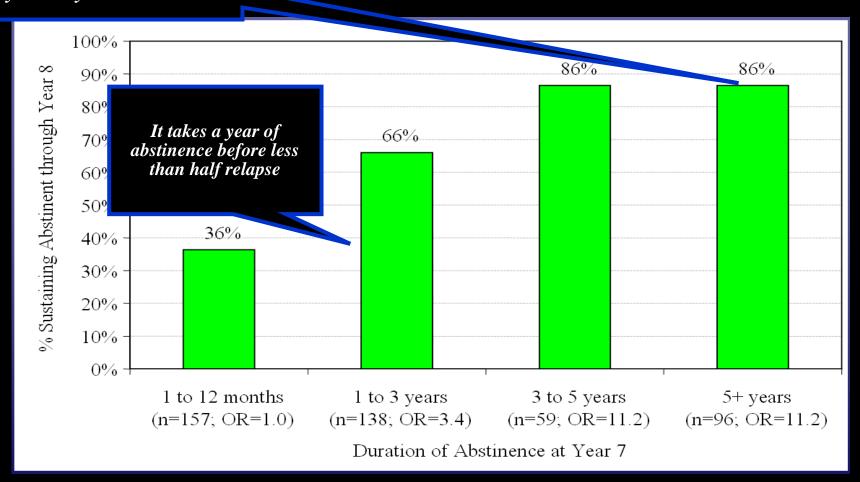
In Treating Addiction...

We Need to Keep Our Eye on the Real Target

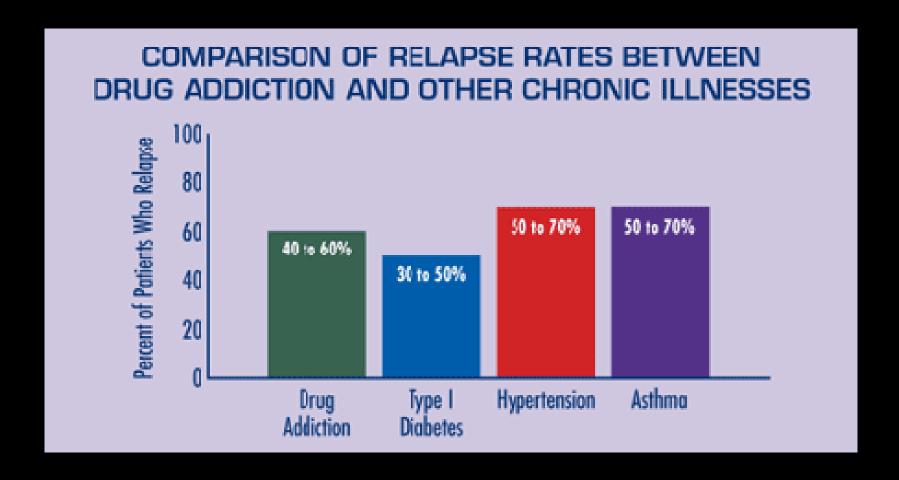


Extended Abstinence is Predictive of Sustained Recovery

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

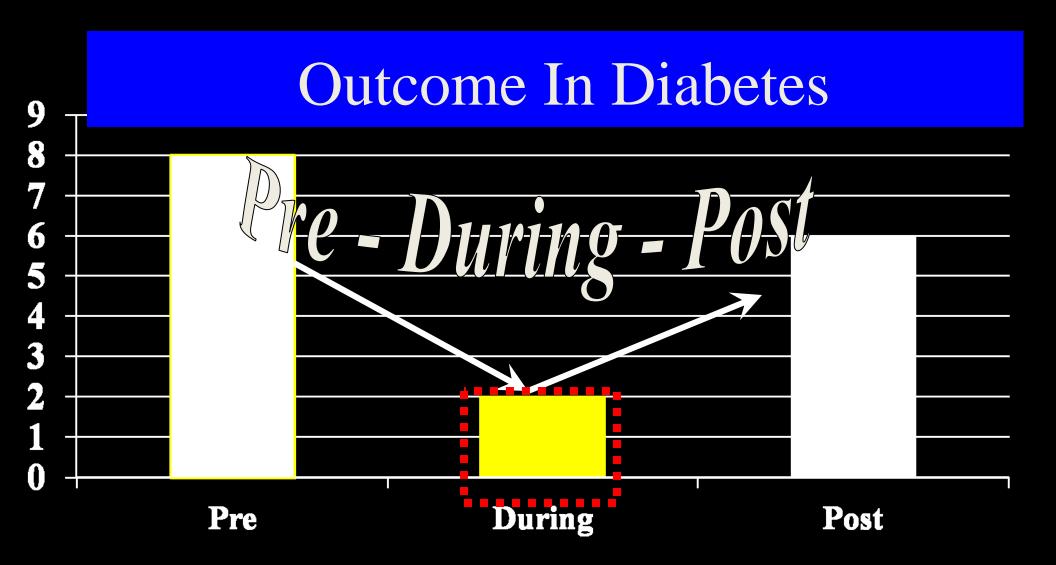


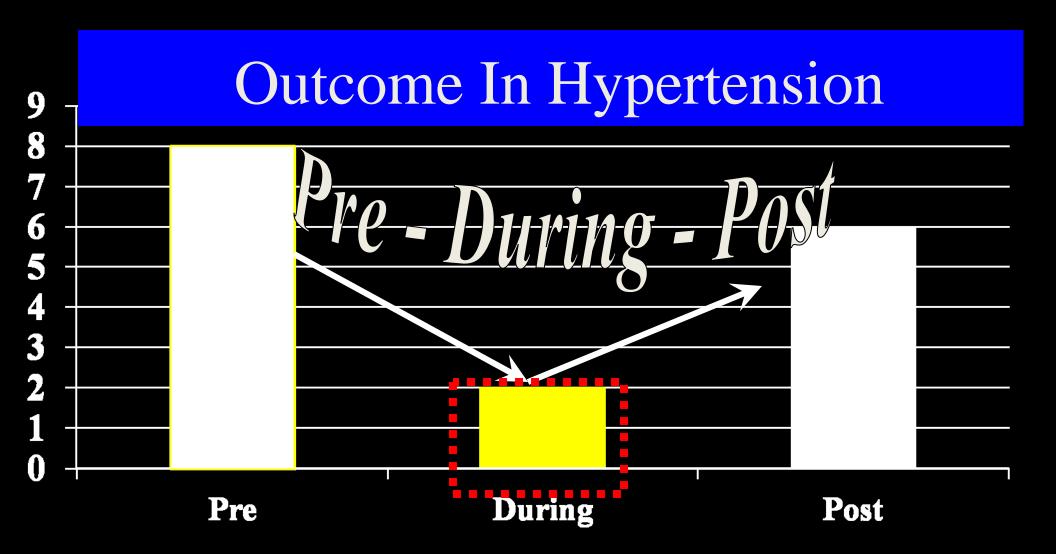
But, drug addiction is a chronic disease with relapse rates similar to those of other chronic illnesses

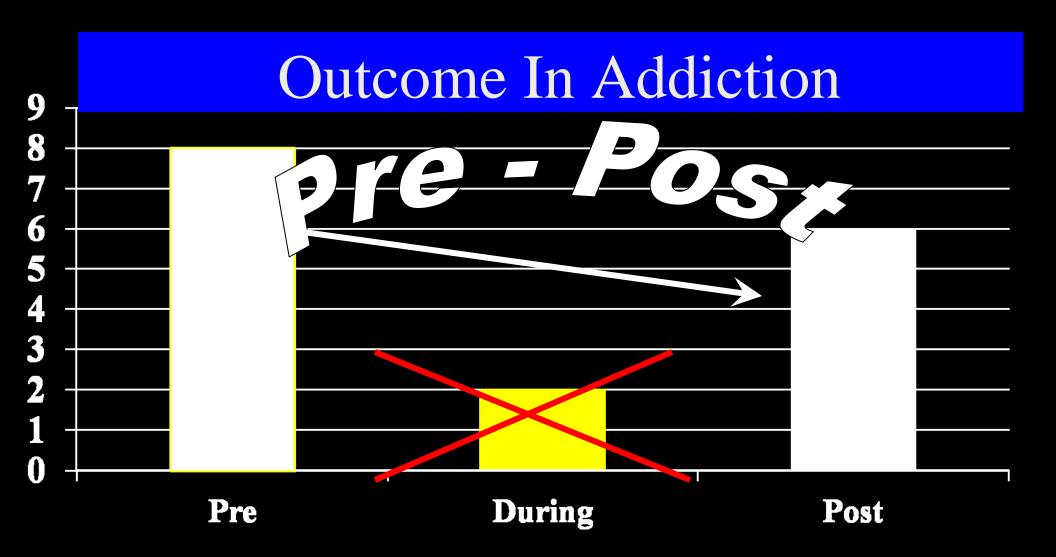


Source: McLellan, A.T. et al., JAMA, Vol 284(13), October 4, 2000.

We Need to View and Treat Addiction As A Chronic, Relapsing Illness







If we treat a diabetic and symptoms don't subside....what do we do?

Would we increase the dose?
Would we change medications?
Would we change treatment approaches?

Would we fail to provide ongoing treatment for a diabetic?

Addiction is Similar to Other Chronic Ilnesses 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

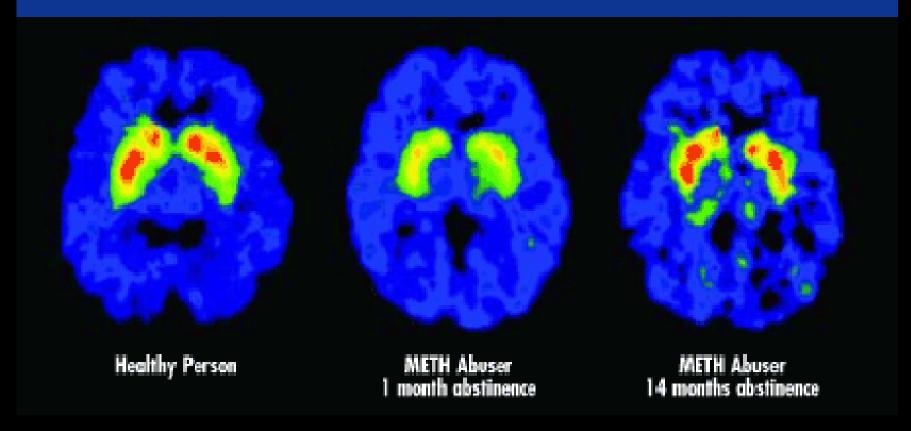
Therefore...



Full recovery is a challenge but it is possible ...

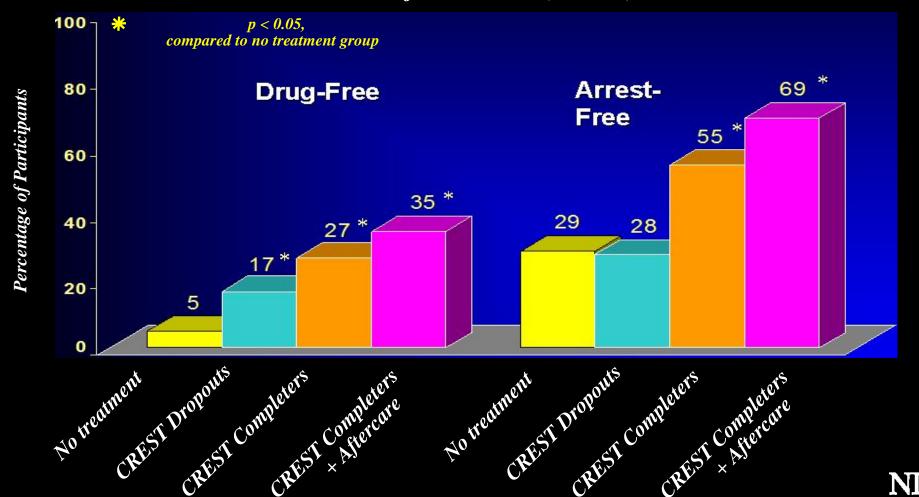


BRAIN RECOVERY WITH PROLONGED ABSTINENCE



Treatment Reduces Drug Use and Recidivism

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



Research

Practice

NIDA Physician Outreach

low is substance abuse relevant to primary care?

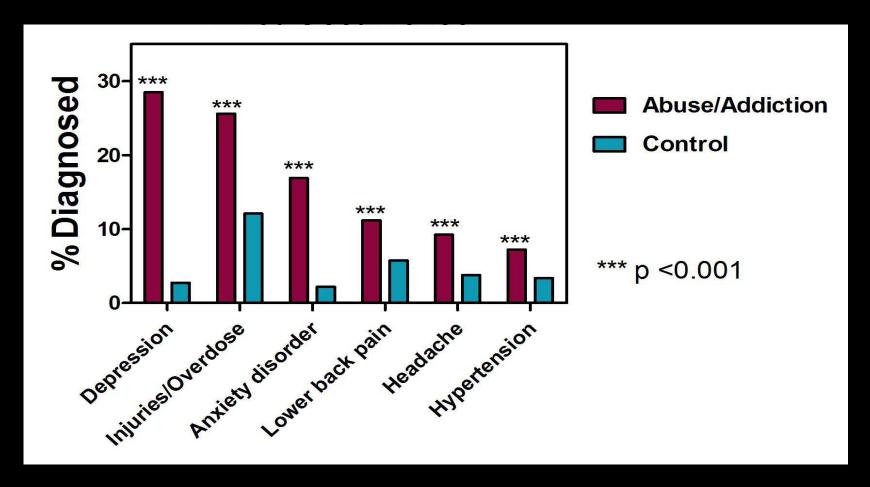
Substance abuse can:

- Lead to unintentional injuries
- Exacerbate medical conditions
- Exacerbate psychiatric problems (anxiety, depression)
- Induce medical diseases (stroke, cancer, dementia, hypertension)

- Induce infectious diseases (HIV, HCV)
- Affect the efficacy of prescribed medications
- Be associated with abuse of Rx medications
- Result in low birth weight, premature deliveries, developmental delays
- Result in addiction

low is substance abuse relevant to primary care?

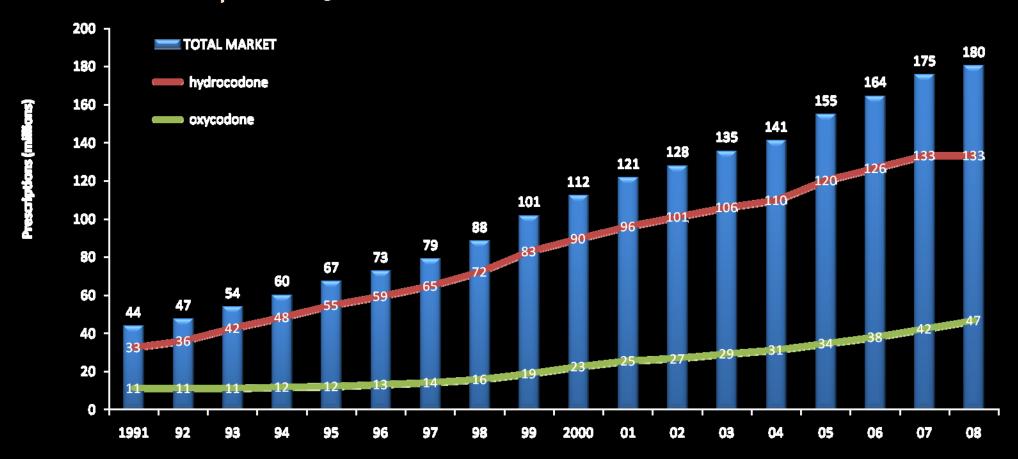
Higher Prevalence of Medical Conditions in Substance Abusers vs. Controls



Source: Mertens JR et al, Arch Intern Med 163: 2511-2517, 2003

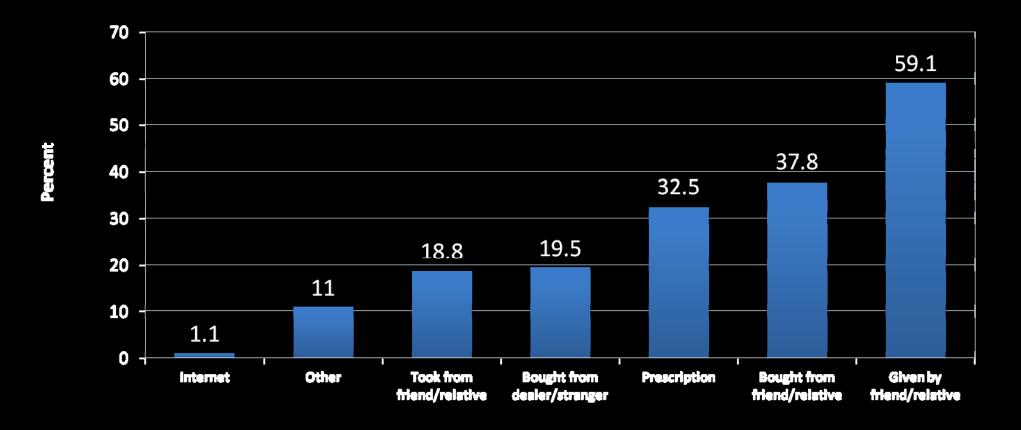
Physicians Can Play a Role in Both Prevention and Treatment

Projected Prescriptions for Hydrocodone and Oxycodone Products Dispensed by US Retail Pharmacies, Years 1991–2008



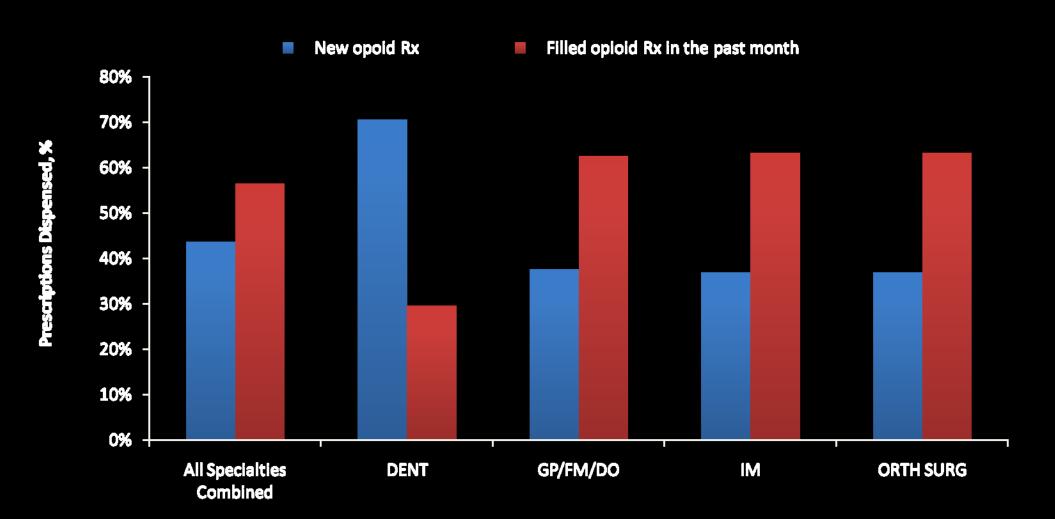
Source: SDI Health Vector One® National (VONA)

Source of Prescription Narcotics among Those Who Used in the Past Year, 12th Grade*

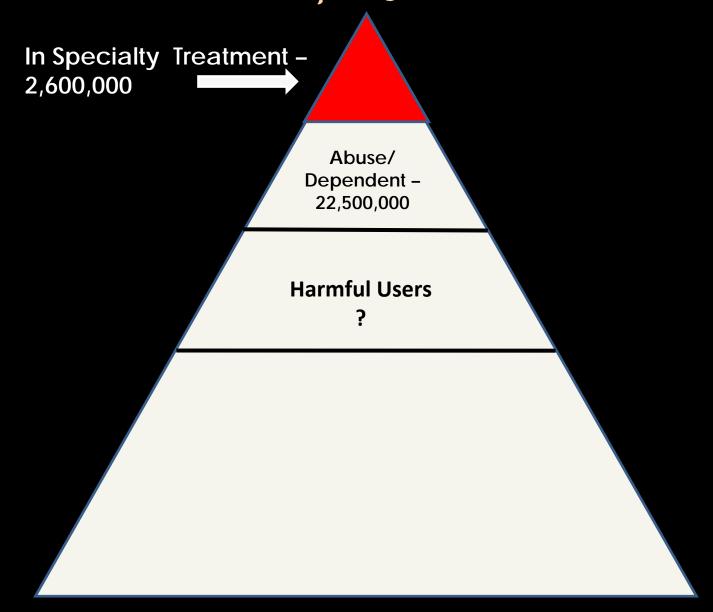


SOURCE: University of Michigan, 2010 Monitoring the Future Study

New vs. Continuing or Switch/Add-on Opioid Prescriptions Dispensed by US Retail Pharmacies as a Function of Specialty, 2009

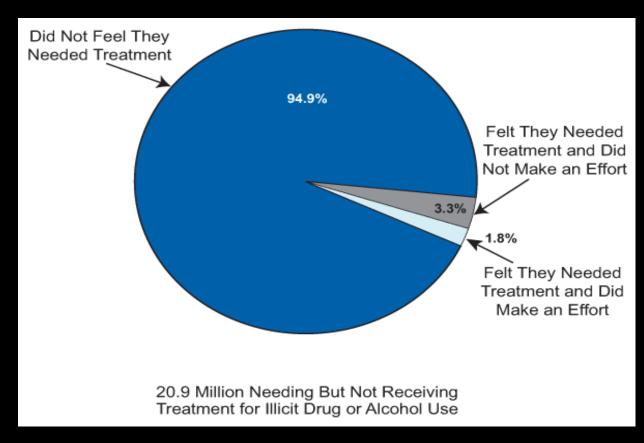


Physicians can also play a role in Treatment



Physicians Can Play a Role in Treatment

 Most substance abusing patients don't feel they need treatment and therefore won't seek it on their own.



Treatment Referral Sources

	1990	2004
Criminal Justice	38%	59%
Employers/EAP	10%	6%
Welfare	8%	16%
Hosp/Phys	4%	3%

Evidence for SBIRT in primary care

- Using screening and brief intervention (SBI) procedures in general medical settings can make a difference in drug use behaviors
 - Research has demonstrated that SBI can reduce alcohol and tobacco use.

Tobacco - USPSTF Grade A (strongly recommended)

http://www.uspreventiveser vicestaskforce.org/uspstf/us pstbac.htm

Alcohol - USPSTF Grade B (recommended)

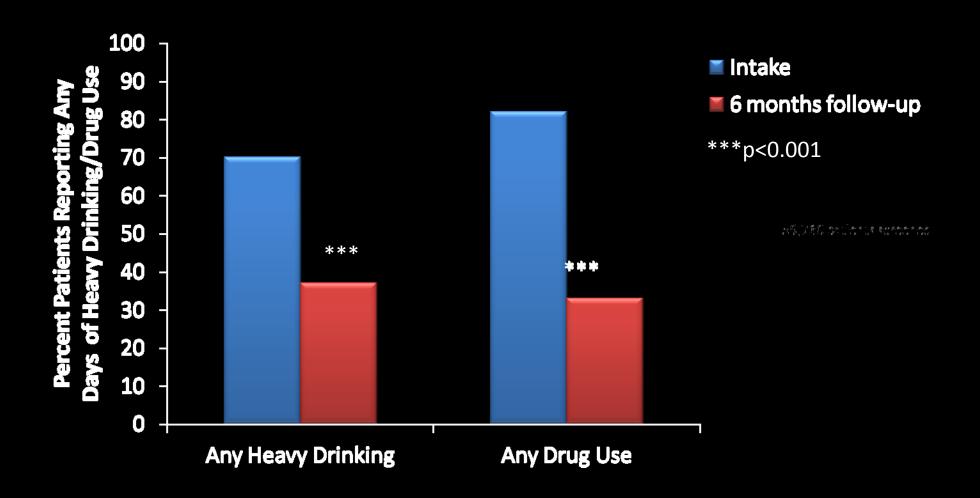
http://www.uspreventiveser vicestaskforce.org/uspstf/us psdrin.htm

Evidence for SBIRT in primary care

Illicit Drugs: Promising and Proliferating

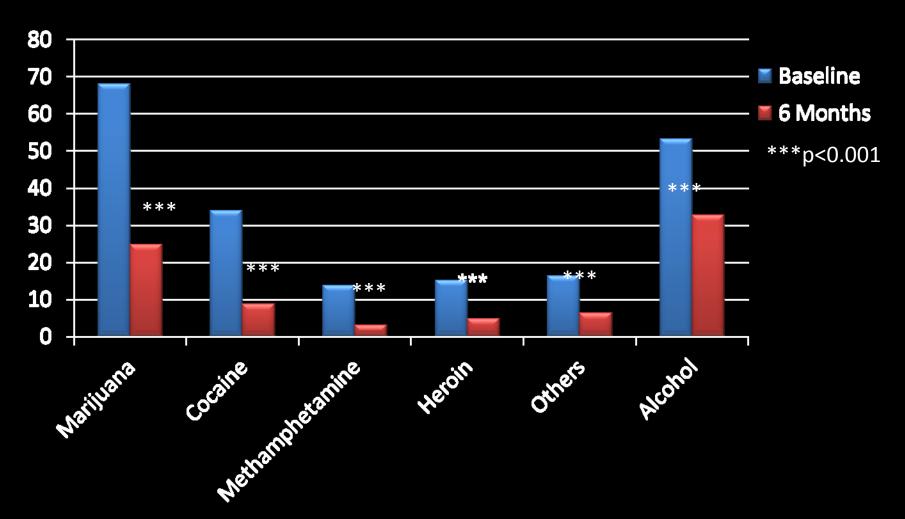
- Bernstein, et al. 2005: Randomized Controlled Trial (RCT)
- WHO study, 2008: Randomized Controlled Trial (RCT) in Multiple Sites Internationally
- InSight Project Research Group 2009
- Madras, et al. 2009: SAMHSA program evaluation of (SBIRT) for illicit drug and alcohol use at multiple sites

SBIRT Reduces Heavy Alcohol and Drug Use in a Hospital District-Based Program (N=1,278)

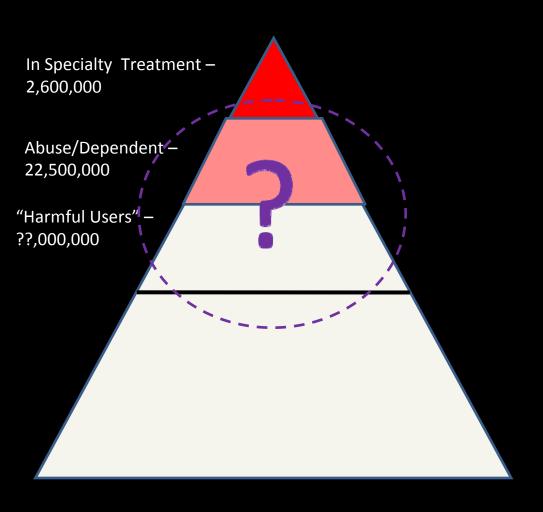


Source: The InSight Project Research Group, 2009. Alcoholism: Clinical and Experimental Research

SAMHSA SBIRT Service Program - Reductions in Substance Use at 6 Month Follow-up



Substance Abuse Pyramid



Physicians can:

- Identify patients at high risk for a substance use disorder and refer for specialty assessment and treatment, if necessary.
- Identify those at lower or moderate risk to intervene early and prevent the escalation to abuse and addiction.

Physicians Don't Routinely Screen for Substance Abuse - Why?

- Don't believe it is a medical problem
- Don't believe there is effective treatment
- Can't be reimbursed
- Don't know what to do
- Not enough time

Physicians Say They Don't Know What To Do

- National surveys of medical schools suggest dramatic variability in training in this area.
 - More than 55 percent of medical students had 9 hours or less of formal instruction on substance abuse (n=1340)
- Residency training
 - Only about half of residency programs required a curriculum in substance use disorders
 - 65 percent of residents had 9 hours or less of formal instruction on substance abuse (n=246)

Source: Yoast et al., 2008. Journal of Addictive Diseases; NIDA CoE Formative Assessment

Centers of Excellence for Physician Information

NIDA has partnered with the American Medical Association and eight medical schools across the country to develop curriculum resources that contain scientifically accurate information about substance abuse and addiction.

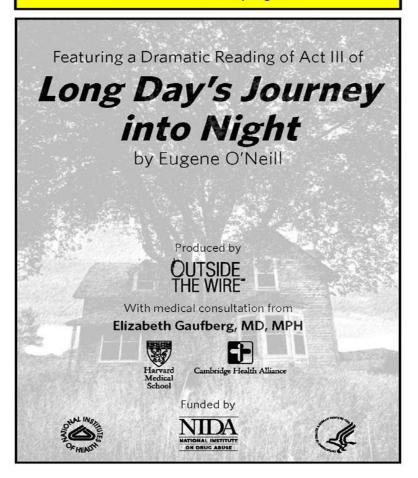
These curriculum resources address pressing issues facing physicians today, in particular recognizing risk factors for as well as identifying prescription drug abuse in their patients.



Innovative Continuing Medical Education Program

Addiction Performance Project

A NIDAMED CME program



The Addiction Performance Project offers healthcare providers the opportunity to help break down the stigma associated with addiction and promote a healthy dialogue that fosters compassion, cooperation, and understanding for patients living with this disease.

Dramatic reading by award-winning professional actors followed by a brief expert panel reaction and facilitated audience discussion of:

- the challenges and opportunities in caring for drug-addicted patients in primary care settings,
- physician biases, and
- how best to incorporate screening, brief intervention, and referral to treatment into primary care settings.

NIDAMED

NIDAMED Online Screening Tool

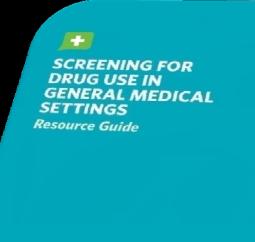
- NIDA Quick Screen
- •NMASSIST Based on the WHO ASSIST
- Screens for tobacco, alcohol, illicit, and non-medical prescription drug use
- •Based on patients' responses, automatically:
 - Leads to next appropriate question
 - Determines substance involvement score (i.e., risk level not a diagnosis)
 - Links to additional resources

Website and Online Tool



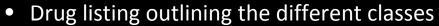
Online Resource Guide

- Rationale
- •Instructions on how to implement screening
- The five A's of intervention Ask,
 Advise, Assess, Assist, Arrange
- Scripts on how to discuss drug use with patients
- Additional Resources

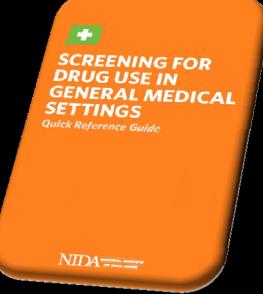




Quick Reference Guide



- Screening questions
- Point value for each response
- Brief summary of the recommended intervention for each risk level





C PCSSmentor.org

Physician Clinical Support System - Primary Care
An Educational Resource for Those Addressing Substance Abuse in Primary Care

- A free, nationwide service to help primary care providers seeking to identify and advise their patients regarding alcohol and drug abuse before they evolve into lifethreatening conditions.
- PCSS-P provides physicians with easy access to clinical tools (e.g., NIDA Screening Tool), information, and resources to help them incorporate screening, brief intervention, and referral to substance abuse treatment into their practices.
- PCSS-P also links physicians to trained clinical advisors that can provide telephone or email responses to specific questions, and offer support on how to use and integrate PCSS-related clinical resources as a regular part of patient care.
- For more information, please visit PCSS-P at www.PCSSmentor.org, email PCSSproject@asam.org or call 1-877-630-8812.

Encouraging Patients to Talk About Drug Use



WITHOUT THE WHOLE PICTURE, YOU MIGHT NOT GET THE WHOLE TREATMENT.

To give you the best possible care, your doctor needs to know about any and all drugs you are taking, including tobacco, alcohol, illicit drugs, over-the-counter and prescription medications—even those not

Tell Your Doctor About ALL the Drugs You Use.

www.drugabuse.gov/nidamed

email: information@nida.nih.gov. To order free copies of this card, call 1-800-729-6686

Your right to privacy is protected by law. For more information on privacy rights, visit http://www.hhs.gov/ocr/ hipaa or call 1-866-627-7748

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES AND HUMAN SERVICES
National Institutes of Health
NIDAMED



Encouraging Patients to Talk About Drug Use



The Ultimate Goal – Addressing substance abuse becomes a part of routine medical care.

- Practicing physicians need to implement
- •It must become a routine part of medical education.

NATIONAL INSTITUTE ON DRUG ABUSE



www.drugabuse.gov

www.drugabuse.gov/nidamed/

www.drugabuse.gov/coe

www.PCSSmentor.org

