

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

Timothy P. Condon, Ph.D.  
Deputy Director  
National Institute on Drug Abuse  
National Institutes of Health  
Department of Health and Human Services

California Society of Addiction Medicine  
Addiction Medicine Review Course 2006  
San Francisco, California  
October 6, 2006

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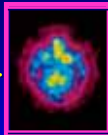
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## *NIDA Research*

*From Molecules...*



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



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**Advances in Science Are Bringing Us New  
Understanding of Drug Abuse & Addiction**



**AND...**

**This Knowledge Is Allowing  
Us To Develop More  
Targeted Strategies for Its  
Prevention and Treatment**



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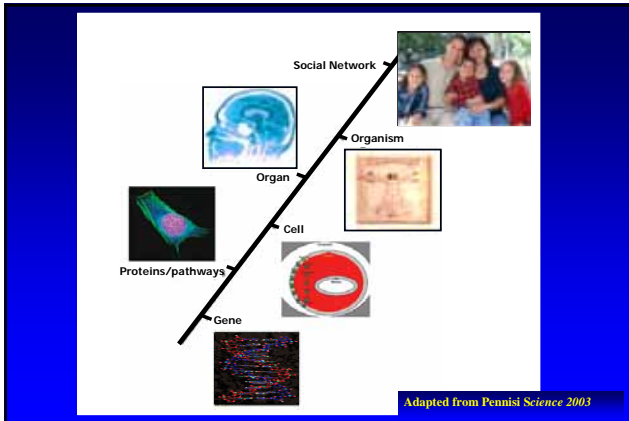
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## Priority Areas for NIDA

- Prevention Research (Children and Adolescents)
  - genetics
  - development
  - environment
  - co-morbidity
- Treatment Interventions (New Targets)
- HIV/AIDS Research
- Training Researchers




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## What have we learned?

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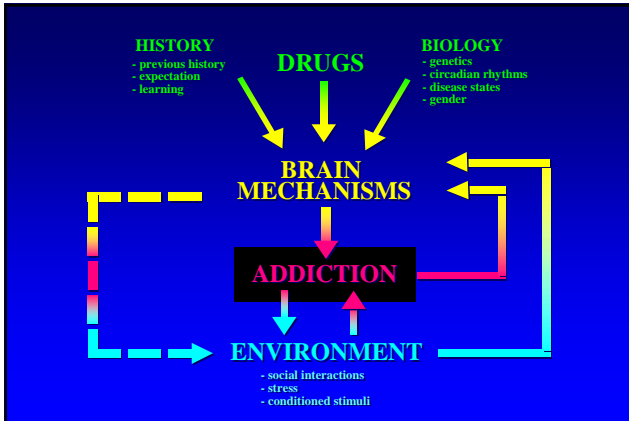
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**What have we learned about Vulnerability?**

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Why do some people become addicted while others do not?

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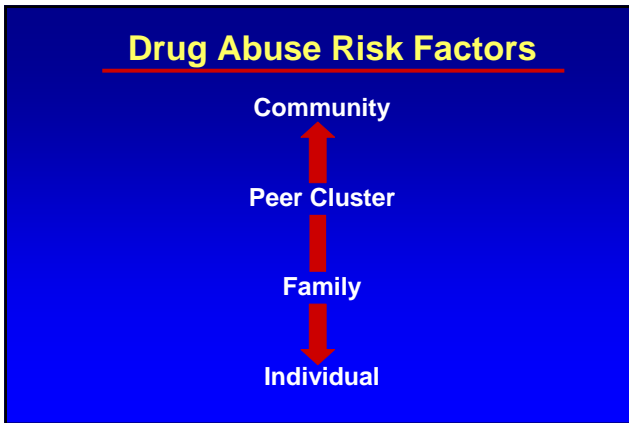
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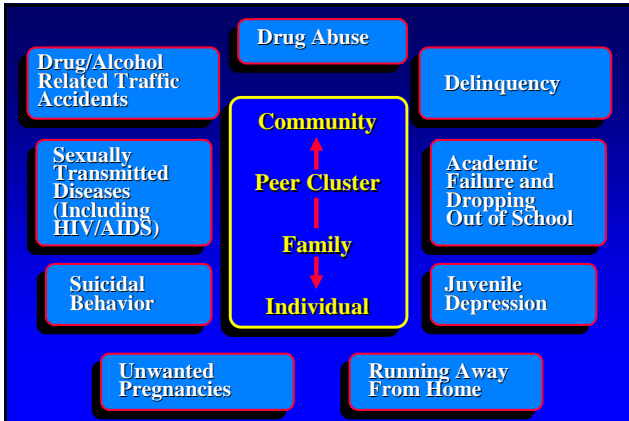
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**We Know There's A  
 Big Genetic Contribution To  
 Drug Abuse and Addiction...**  
**And the Nature of this Contribution  
 Is Extremely Complex**

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**Genetic component of  
common traits**

Trait	Heritability
Type II (adult-onset) diabetes	0.3 <sup>1</sup>
Type I (insulin-dependent) diabetes	0.7 <sup>2</sup>
Hypertension	0.3 - 0.5 <sup>3</sup>
Peanut allergy	0.8 <sup>4</sup>
Cataract (age-related)	0.5 <sup>5</sup>
Alcoholism	0.6 <sup>6</sup>
Nicotine	0.5 - 0.6 <sup>7</sup>
Cocaine and stimulants	0.4 - 0.8 <sup>8</sup>
Heroin and opiates	0.5 <sup>9</sup>
Marijuana	0.3 - 0.8 <sup>10</sup>

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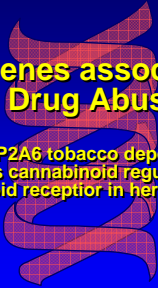
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## Some Genes associated with Drug Abuse:

CYP2A6 tobacco dependence  
FAAH (endogenous cannabinoid regulator) problem drug use  
Mu-opioid receptor in heroin addiction



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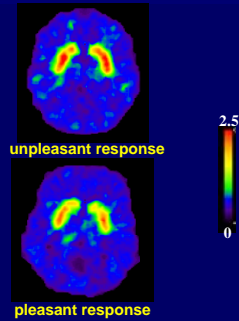
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## DA Receptor Levels and Response to MP



Subjects with low receptor levels found MP pleasant while those with high levels found MP unpleasant

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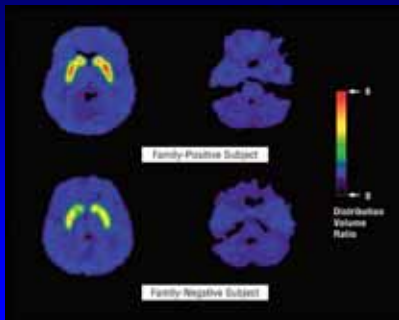
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## High Levels of Dopamine D2 Receptors May Provide Protection Against Alcoholism in Unaffected Members of Alcoholic Families



Researchers also found that increased D2 receptors in the family positive subjects correlated with metabolism in the frontal regions and with positive emotionality

Volkow, N. D. et al. Arch Gen Psychiatry 2006;63:999-1008.

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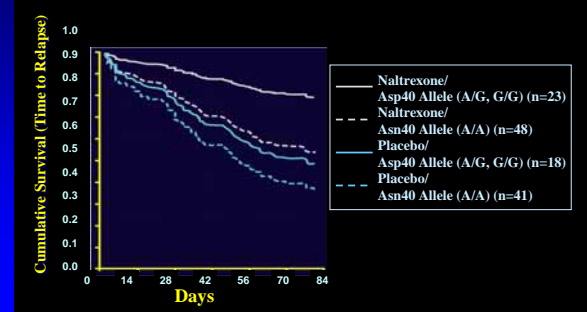
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## Genetic Variation Predicts Naltrexone Treatment Response for Alcohol Dependence



Source: Oslin DW et al., Neuropsychopharmacology 28, 1546-1552, 2003.

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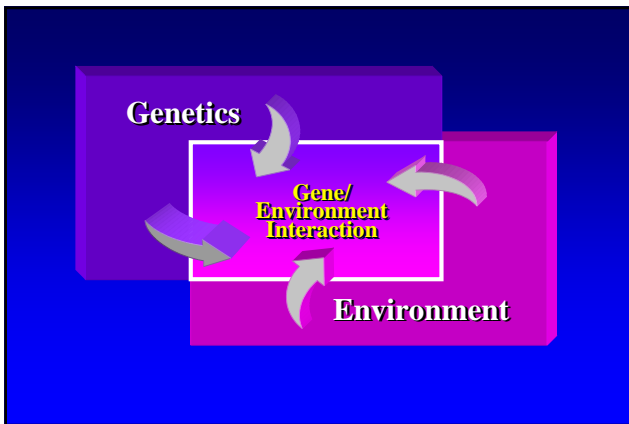
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**What have we learned about other aspects of vulnerability?**

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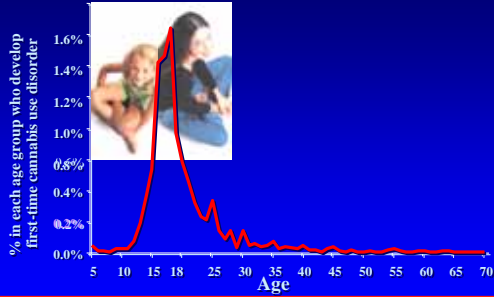
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**Drug Addiction is a Developmental Disease that Starts in Adolescence and Childhood**



Age at cannabis use disorder as per DSM IV  
 NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003

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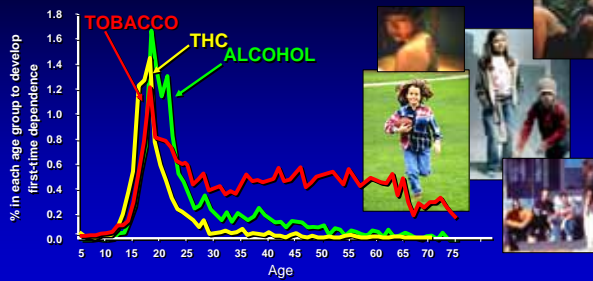
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**Addiction Is a Developmental Disease starts in childhood and adolescence**



Age at tobacco, at alcohol and at cannabis dependence, as per DSM IV  
 National Epidemiologic Survey on Alcohol and Related Conditions, 2003

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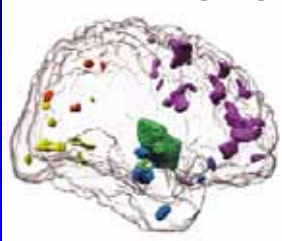
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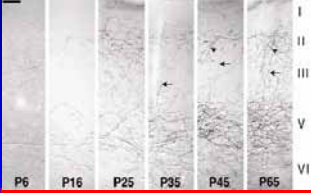
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**The Adolescent Brain Is Still Undergoing Development**



Brain areas where volumes are smaller in adolescents than young adults

**Amygdalo-cortical Sprouting Continues Into Early Adulthood**



During Adolescence the COGNITION-EMOTION Connection is Still Forming

Source: Sowell, E.R. et al., Nature Neuroscience, 2(10), pp. 859-861, 1999.

Source: Cunningham, M et al., J Comp Neurol 453, pp 116-130, 2002.

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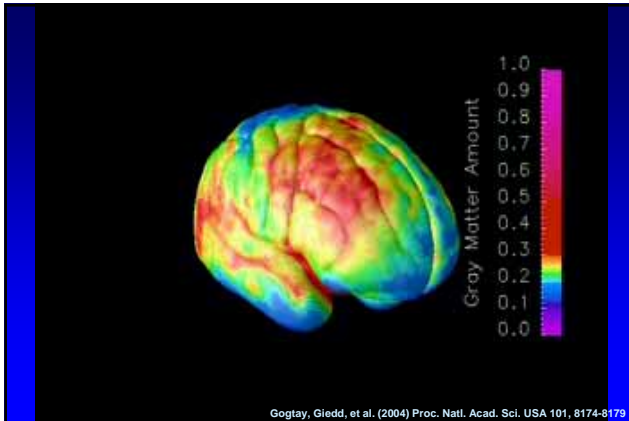
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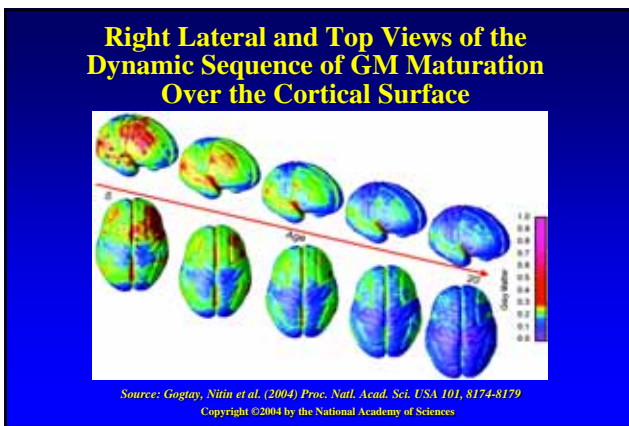
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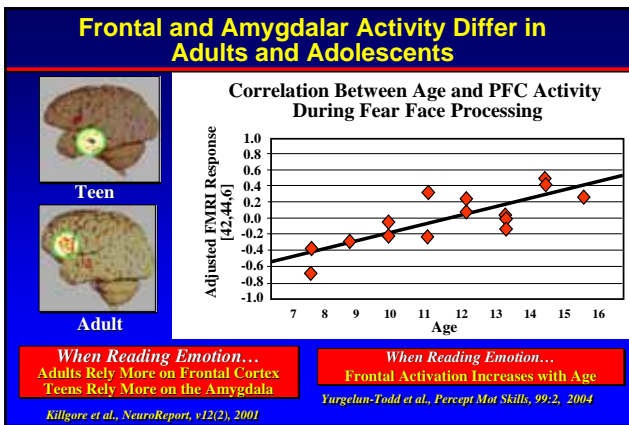
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- Exposure to drugs of abuse during adolescence could have profound effects on **Brain Development & Brain Plasticity**



- Understanding drug abuse and addiction from a **Development Perspective** has important implications for their **Prevention & Treatment**

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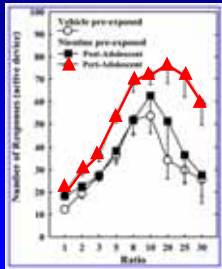
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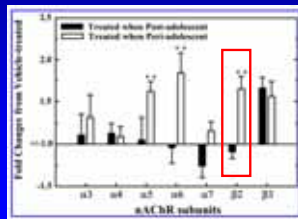
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### The Adolescent Brain Responds to Drugs Differently than the Adult Brain

Treatment of adolescent rats (but not young adults) with Nicotine leads to Increases in Nicotine Self Administration



#### Increases in Nicotine Receptors



Source: Adriana, W. et al., *J of Neurosci*, 23(11), pp. 4712-4716, June 1, 2003.

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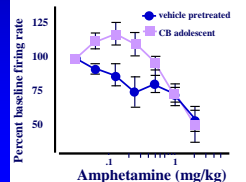
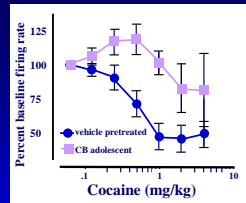
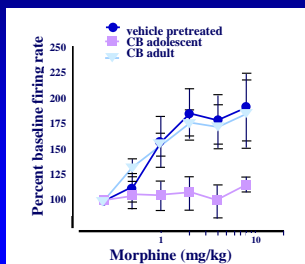
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### Adolescent Exposure to Cannabinoids Alters the Response of VTA Dopamine Neurons to Drugs of Abuse



Source: Pistis, M. et al., *Biol Psychiatry*, 56: 86-94, 2004.

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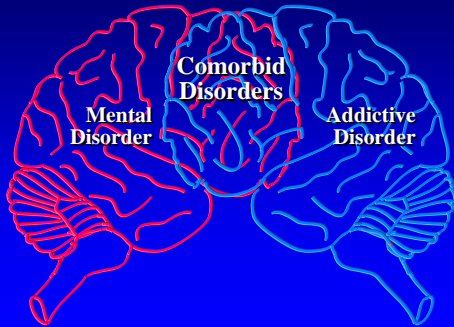
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**ADDICTIVE DISORDERS OFTEN CO-EXIST WITH MENTAL DISORDERS**




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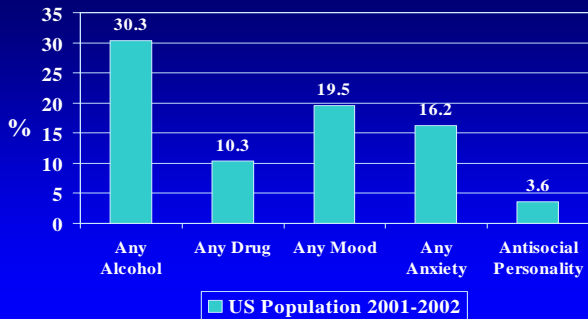
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**Results: Lifetime Disorders**



*Source: Results from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)*

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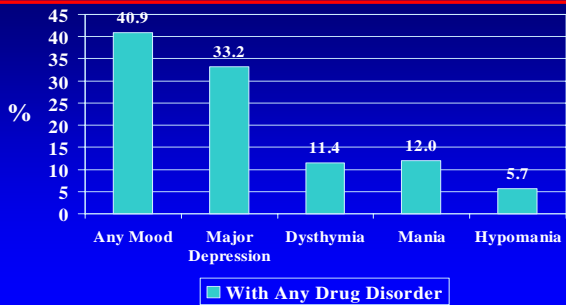
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**Lifetime Mood Disorders Among Those with Drug Disorders**



*Source: Results from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)*

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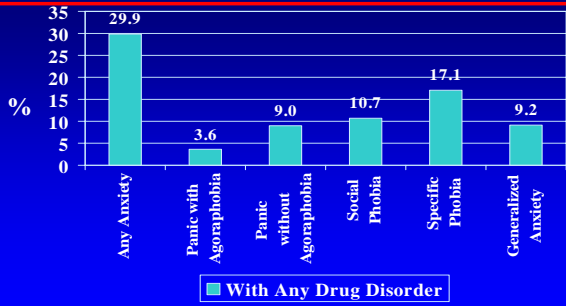
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### Lifetime Anxiety Disorders Among Those with Drug Disorders



Source: Results from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

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### COMORBIDITY

#### Smoking and Mental Illness



- 44% of all cigarettes consumed in the US are by individuals with a current psychiatric disorder
- 75% of patients in addiction and mental health treatment programs smoke cigarettes

Source: Lasser, K et al., JAMA 284(20), November 22/29, 2000.

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### Comorbidity is a Reality

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## What have learned about how drugs work?

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### Activation of the reward pathway by addictive drugs




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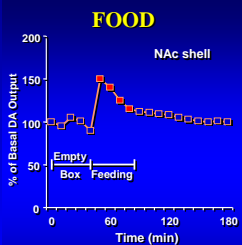
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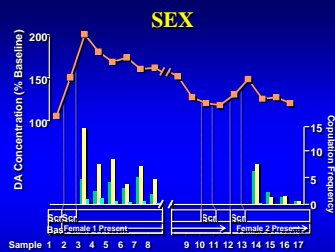
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### Natural Rewards Elevate Dopamine Levels



Source: Di Ciano et al.



Source: Fiorino and Phillips

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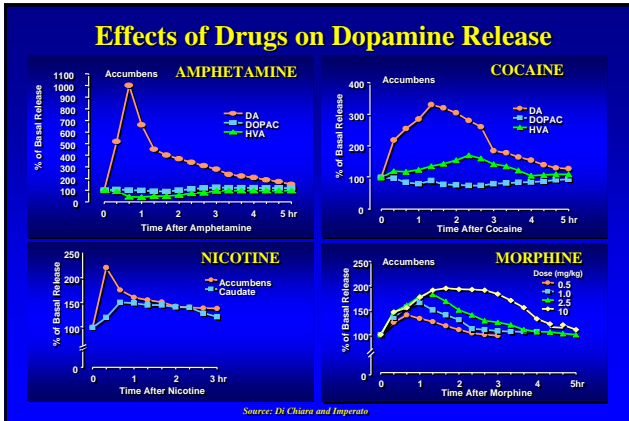
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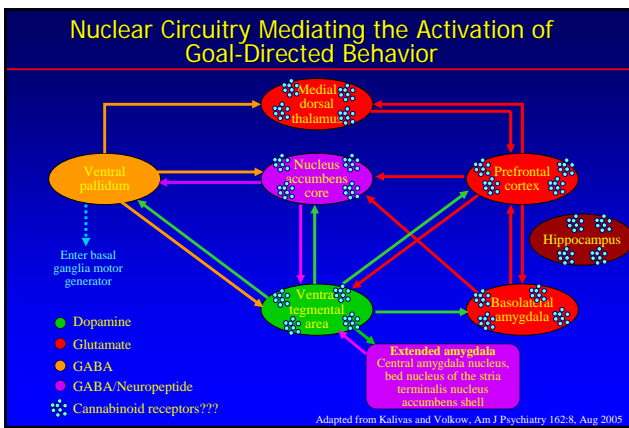
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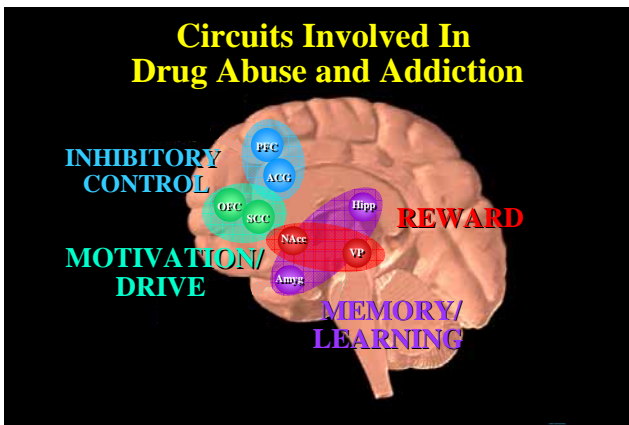
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**Prolonged Drug Use Changes  
The Brain In Fundamental and  
Long-Lasting Ways**

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**AND...**

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

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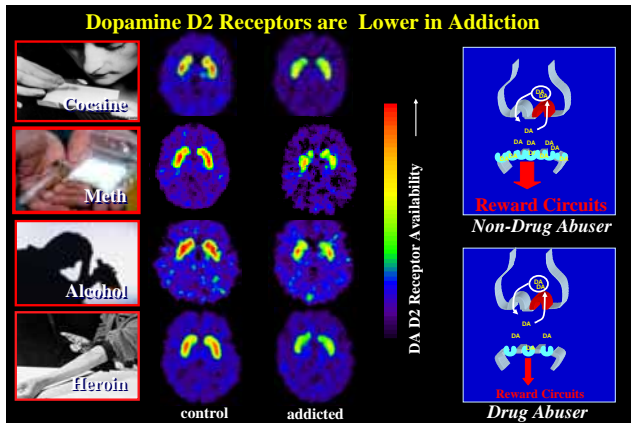
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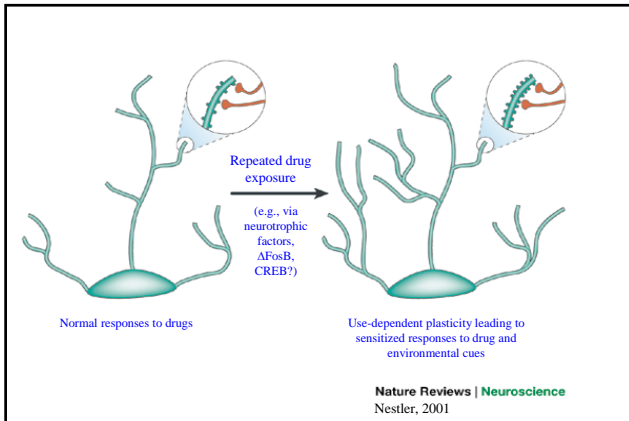
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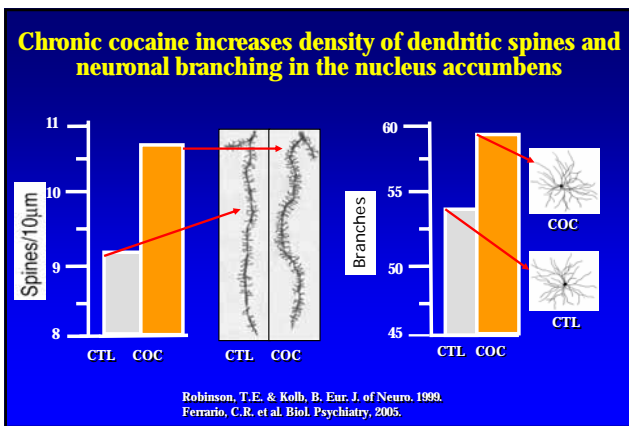
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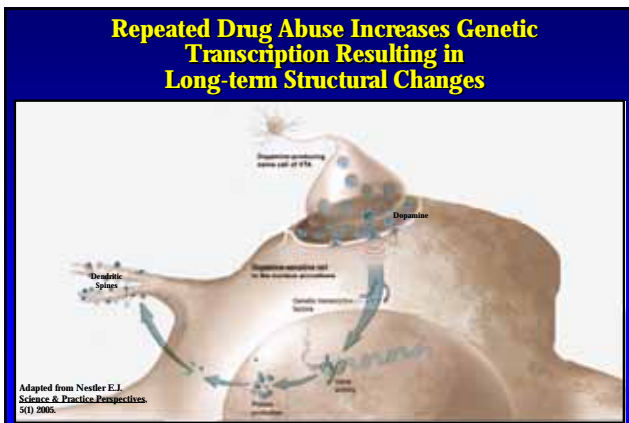
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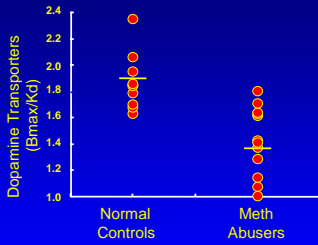
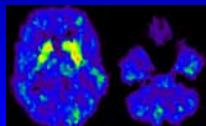
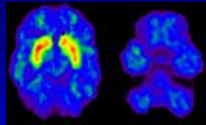
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### Dopamine Transporters in Methamphetamine Abusers



Methamphetamine abusers have significant reductions in dopamine transporters.

BNL - UCLA - SUNY  
NIDA - ONDCP - DOE

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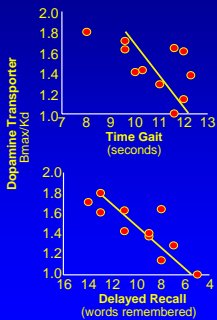
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### Dopamine Transporters in Methamphetamine Abusers



#### Motor Task

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

#### Memory Task

Loss of dopamine transporters in the meth abusers may result in memory impairment.

BNL - UCLA - SUNY  
NIDA - ONDCP - DOE

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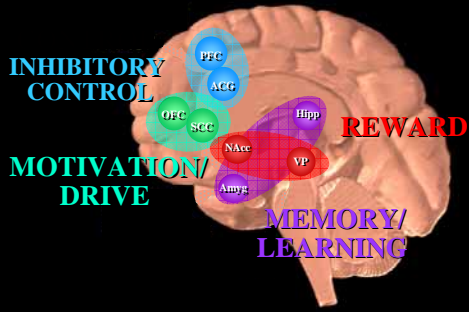
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## Circuits Involved In Drug Abuse and Addiction




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

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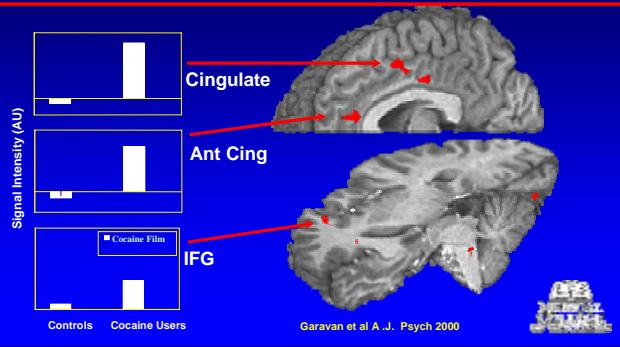
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## Cocaine Craving:

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




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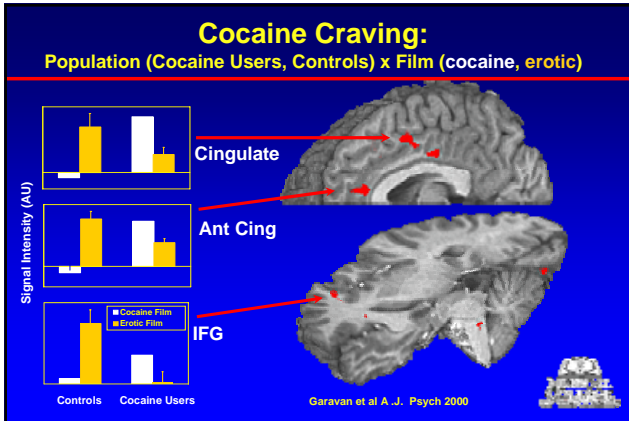
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**This Results in  
“Motivational Toxicity”  
and Compulsive Drug  
Use (Addiction)**

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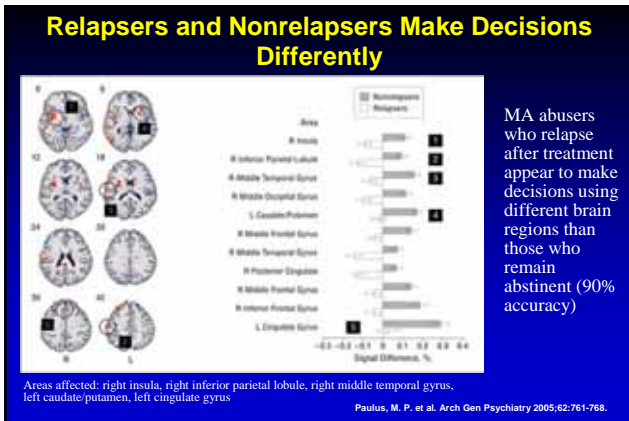
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MA abusers who relapse after treatment appear to make decisions using different brain regions than those who remain abstinent (90% accuracy)

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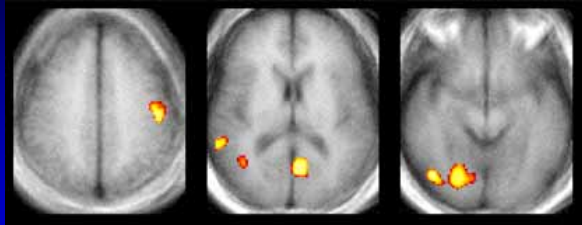
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### Cue-Induced Brain Activity Changes Better Predictor of Relapse in Cocaine-Dependent Patients than Subjective Reports of Craving



left precentral cortex      left posterior cingulate & right superior temporal cortices      right lingual & inferior occipital cortices

Kosten et al. *Neuropsychopharmacology* (2006) 31, 644-650

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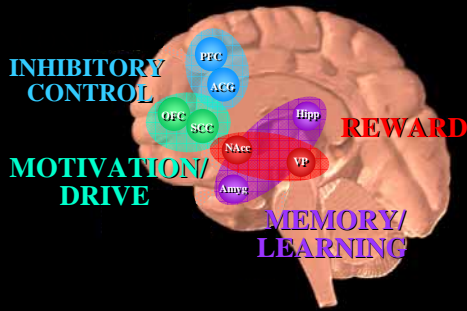
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### Circuits Involved In Drug Abuse and Addiction




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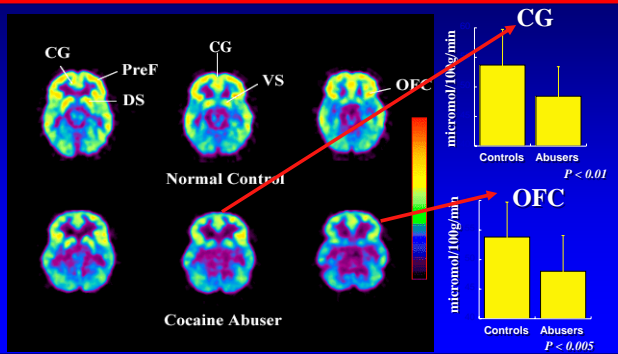
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### Brain Glucose Metabolism in Cocaine Abusers (n = 20) and Controls (n = 23)




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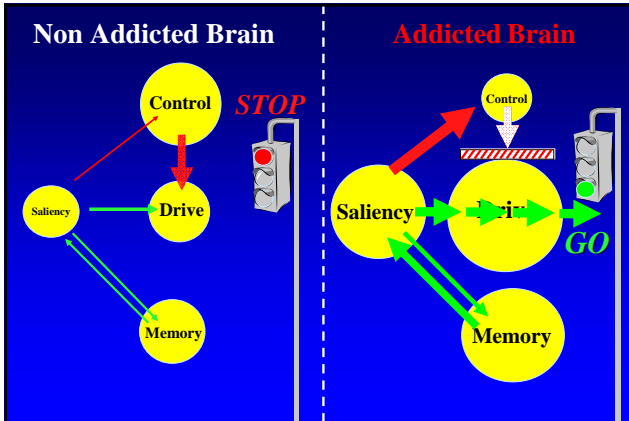
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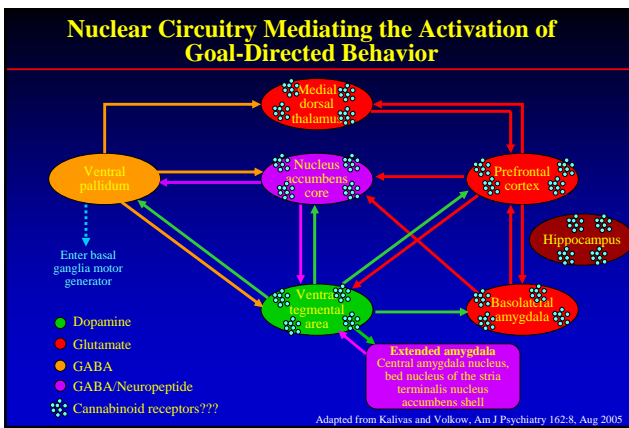
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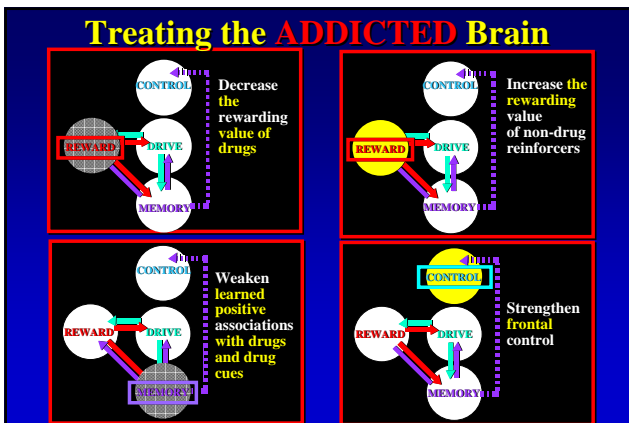
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**Implication:**

**Brain changes resulting from prolonged use of drugs may be reflected in compromised cognitive functioning**

*Is there recovery?*

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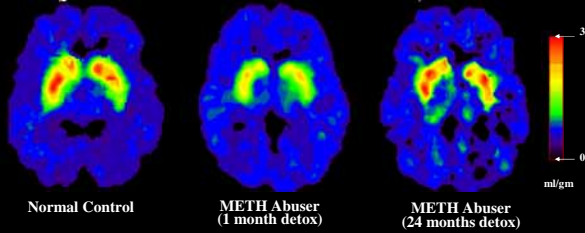
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**ADDICTION CAN BE TREATED**

**Partial Recovery of Brain Dopamine Transporters in Methamphetamine (METH) Abuser After Protracted Abstinence**



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

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

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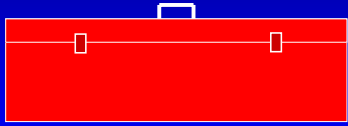
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**We Have A Variety Of Effective Treatment Options In The Clinical Toolbox**



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**Some Behavioral Treatments with a Strong Science Base**

- Behavioral Treatments for MJ Abuse
- Behavioral Treatments for Smoking Cessation
- Cognitive-Behavioral Treatment
- Combined Pharmacotherapies and Behavioral Therapies
- Multisystemic Therapy
- Contingency Management Treatments\*
- Dialectical Behavioral Therapy
- Drug Counseling
- Family Treatments
- Group Behavior Therapy
- HIV Risk Reduction
- Motivational Interviewing/Enhancement\*
- Seeking Safety (PTSD)
- Work Therapy

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**Medications Development**

- Methadone
- Naltrexone
- Clonidine
- *Buprenorphine*
- *Bupropion*
- *NRT*

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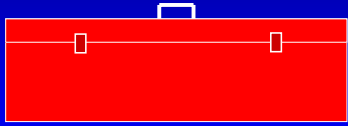
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**We Have A Variety Of Effective  
Treatment Options In The  
Clinical Toolbox**



**...But We Need To And  
Can Do Better**

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**Interventions targeting:  
Reward/Saliency  
Motivation  
Relapse (stress, craving,  
conditioned-cues, other?)  
Inhibitory Control**

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**HIV/AIDS**



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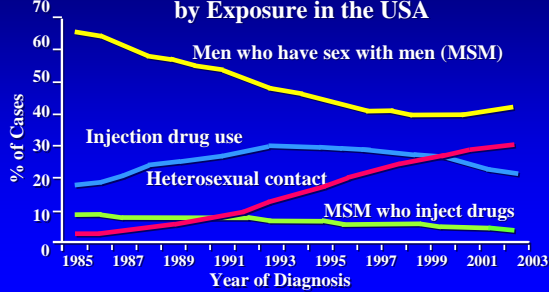
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## Drugs of Abuse Have Had A Major Impact on the HIV/AIDS Epidemic

Proportions of AIDS Cases in Adults & Adolescents by Exposure in the USA



Source: Centers for Disease Control and Prevention (CDC)

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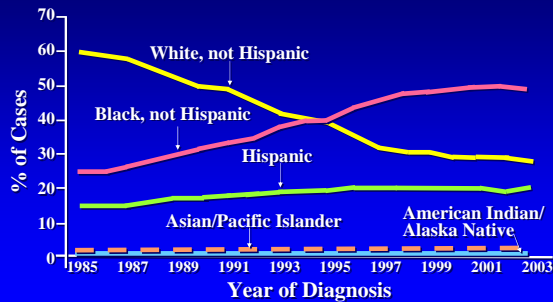
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## Proportions of AIDS Cases in Adults and Adolescents by Race/Ethnicity in the USA



Source: Centers for Disease Control and Prevention (CDC)

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Drug Addiction Treatment is HIV Prevention




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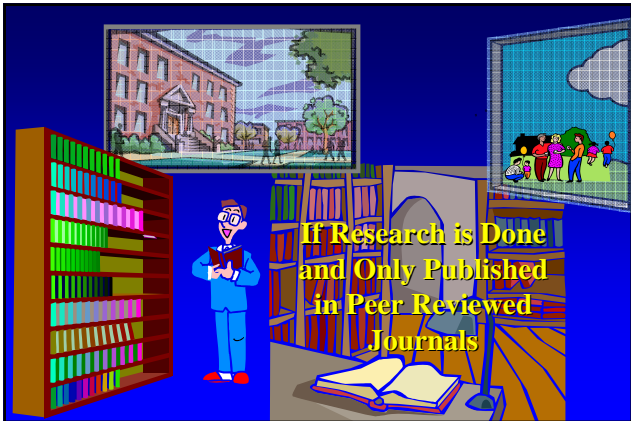
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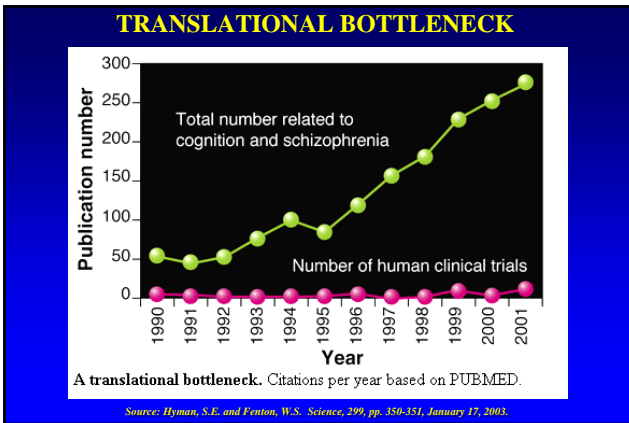
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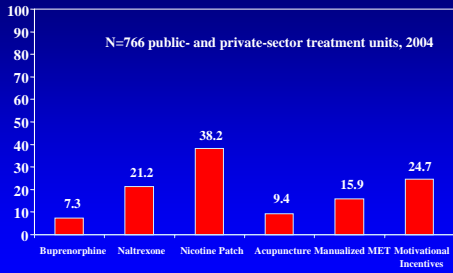


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### Few Treatment Programs Use Treatment Innovations



Source: Roman et al., National Treatment Center Study, 2004

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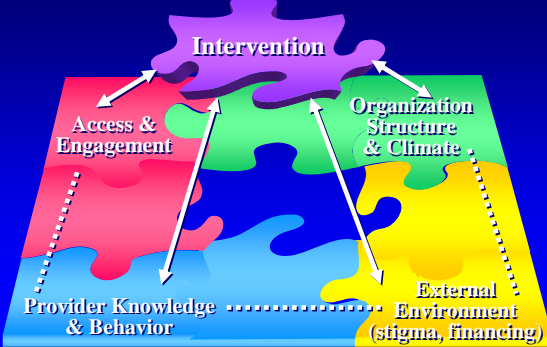
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### Developing an Evidence-Based-Practice is Only One Piece of the Translation Puzzle




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**NIDA**  
*What Are We Doing About All of This?*

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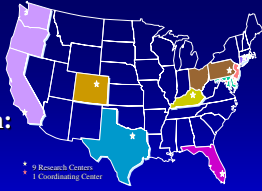
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## CJ-DATS Update

Criminal Justice Drug Abuse Treatment Studies



- 6 studies in the field focused on:
  - ❖ Reducing HIV risk behavior
  - ❖ Screening for mental illness
  - ❖ Transitioning from prison to community
- 2 juvenile justice studies being developed
  - ❖ Community re-entry and HIV risk behaviors
- 2 HIV studies being developed:
  - ❖ Men
  - ❖ Women

[www.cjdats.org](http://www.cjdats.org)

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**Partnerships Are Essential In  
Advancing the Science of Addiction  
and in Translating Promising  
Strategies into Practice**





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## Blending Research and Practice “Science to Services Initiative”

<p style="color: yellow; font-weight: bold;">SAMHSA</p> <p style="color: white;">CSAT CSAP CMHS</p>	<p style="color: yellow; font-weight: bold;">NIH</p> <p style="color: white;">NIDA NIAAA NIMH</p>
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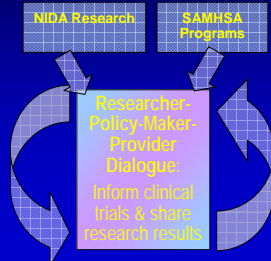
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## NIDA/SAMHSA Blending Initiative

The Blending Initiative encompasses three primary components:

- Blending Conferences
- Blending Teams
- State Agency Partnerships




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## Research Dissemination & Application: A "Recipe" for Success

- One part CSAT
- One part NIDA
- A pinch of \$\$
- Ok...a few more \$\$\$
- Some TLC
- A dash of luck
- Shake vigorously and....




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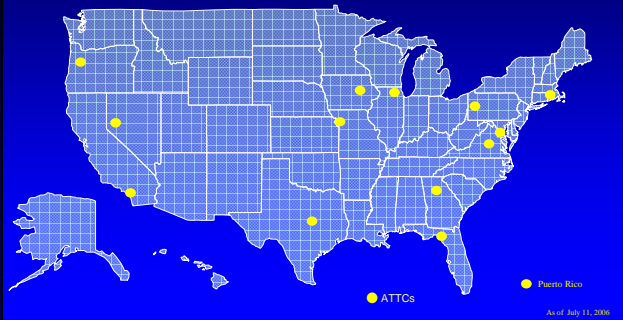
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## SAMHSA/CSAT Addiction Technology Transfer Centers (ATTCs)




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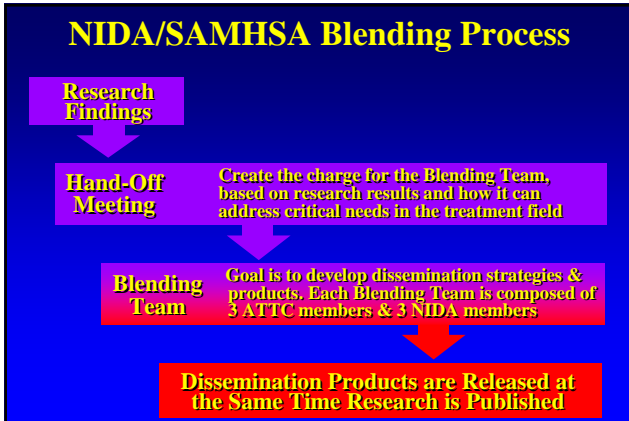
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- ### Five Blending Teams
- 1) Buprenorphine Treatment: A Training for Multidisciplinary Addiction Professionals
  - 2) Short-Term Opioid Withdrawal Using Buprenorphine
  - 3) Utilizing the Addiction Severity Index (ASI)
  - 4) Motivational Interviewing Assessment: Supervisory Tools for Enhancing Proficiency (MIA-STEP)
  - 5) Promoting Awareness of Motivational Incentives (PAMI)
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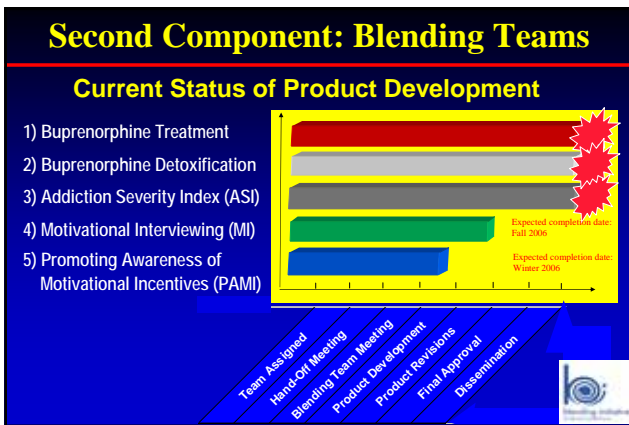
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**NIDA**  
NATIONAL INSTITUTE  
ON DRUG ABUSE

U.S. Department of Health  
& Human Services  
**SAMHSA**

**Partnerships Are Essential In  
Advancing the Science of Addiction  
and in Translating Promising  
Strategies into Practice**



attc addiction technology transfer centers  
LEARNING INITIATIVE

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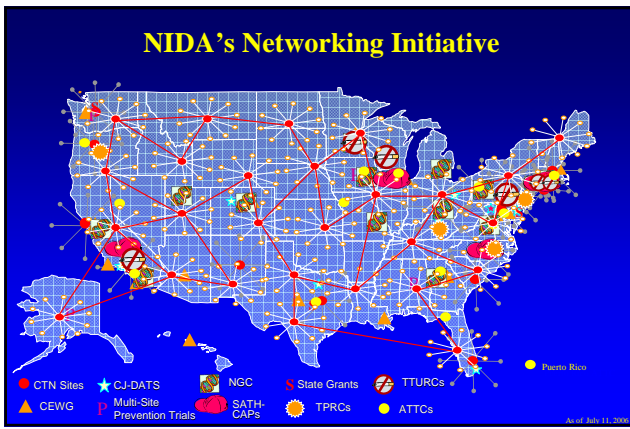
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**Priority Areas for NIDA**



- **Prevention Research (Children and Adolescents)**  
genetics  
development  
environment  
co-morbidity
- **Treatment Interventions (New Targets)**
- **HIV/AIDS Research**
- **Translating Research into Practice**

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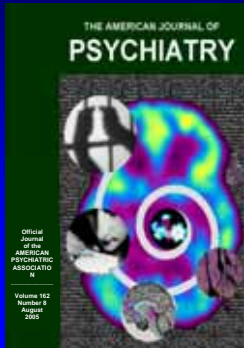
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*We Need Addiction Medicine to...*

**Continue to Study  
Drug Abuse & Addiction  
at All Levels and to Help  
Ensure that Promising  
Strategies Are Adopted  
in Clinical Practice**



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*Where Do We Need  
to Go From Here?*

**We Need to Work  
TOGETHER to...**

**Advance the SCIENCE**  
*and to...*  
**Erase the STIGMA**



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*Visit Our Website @*



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**Addiction is the  
Quintessential  
Biobehavioral Disorder**

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