



NIDA

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buse

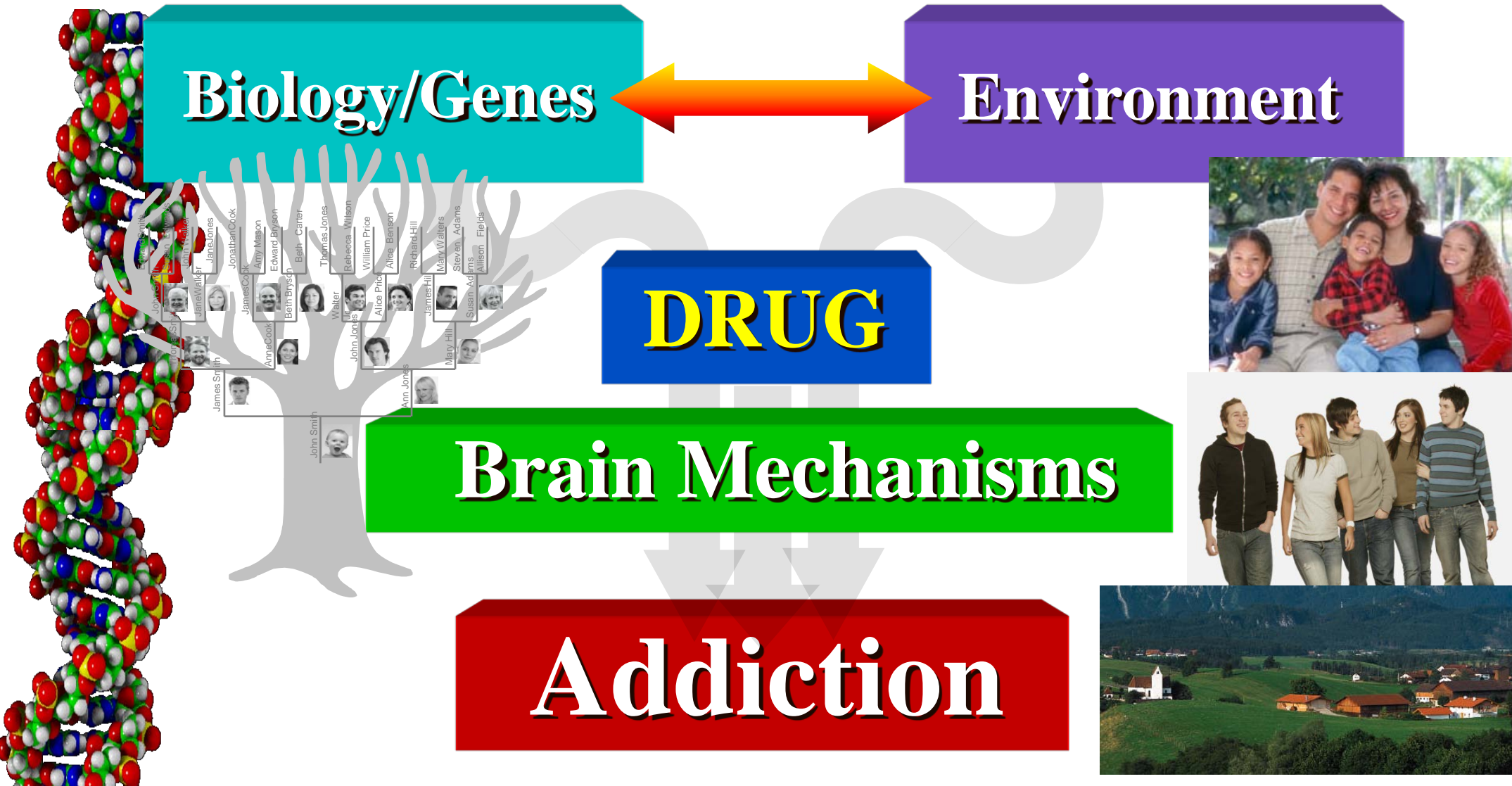
*... Bringing the full power
of science to bear on*
Drug Abuse & Addiction



Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

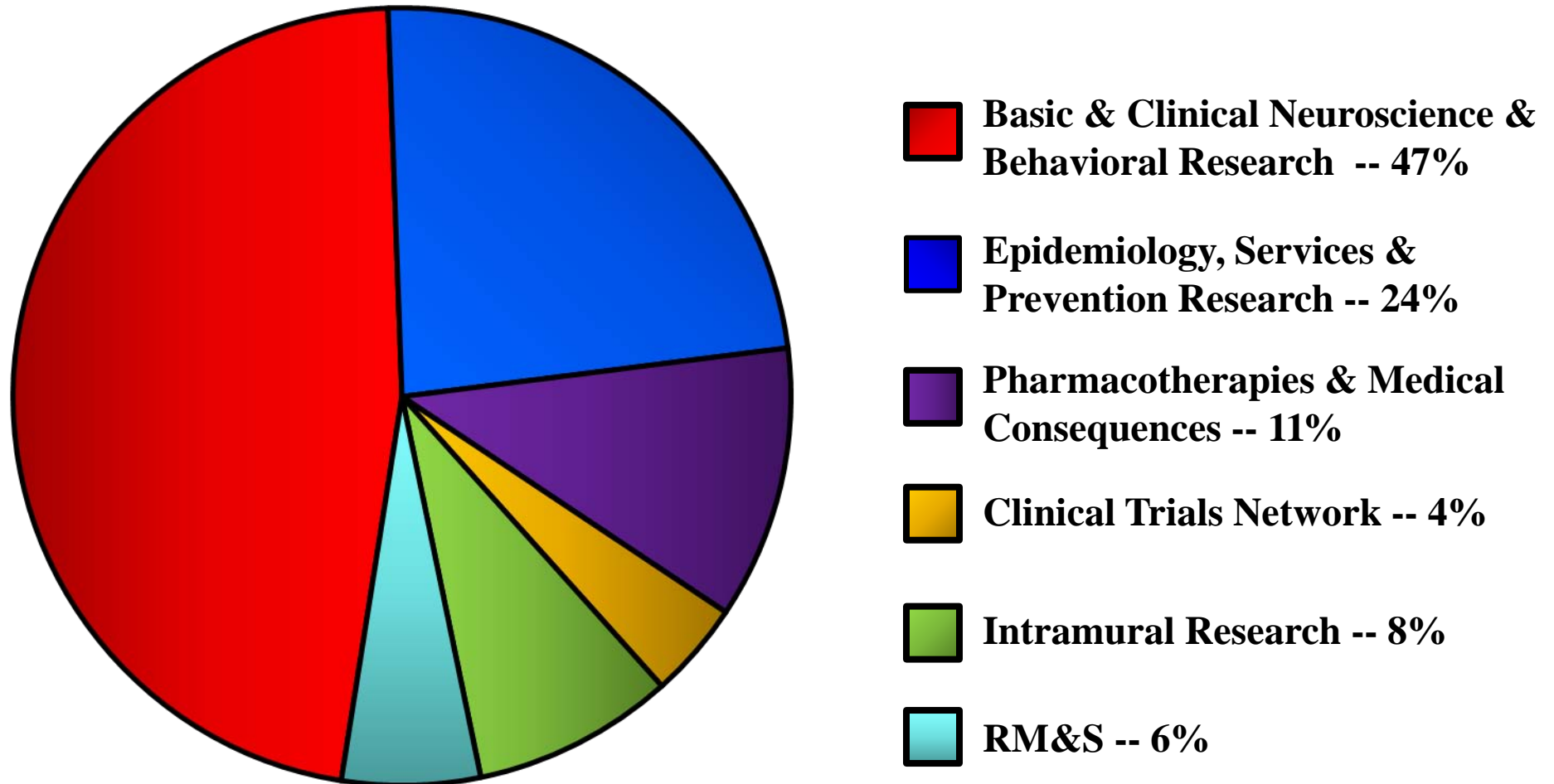


ADDICTION INVOLVES *MULTIPLE FACTORS*



National Institute on Drug Abuse Portfolio

FY 2008 Actual



Priority Areas for NIDA

Prevention Research

(Children & Adolescents)

genetics/epigenetics

development

environment

co-morbidity



Treatment Interventions

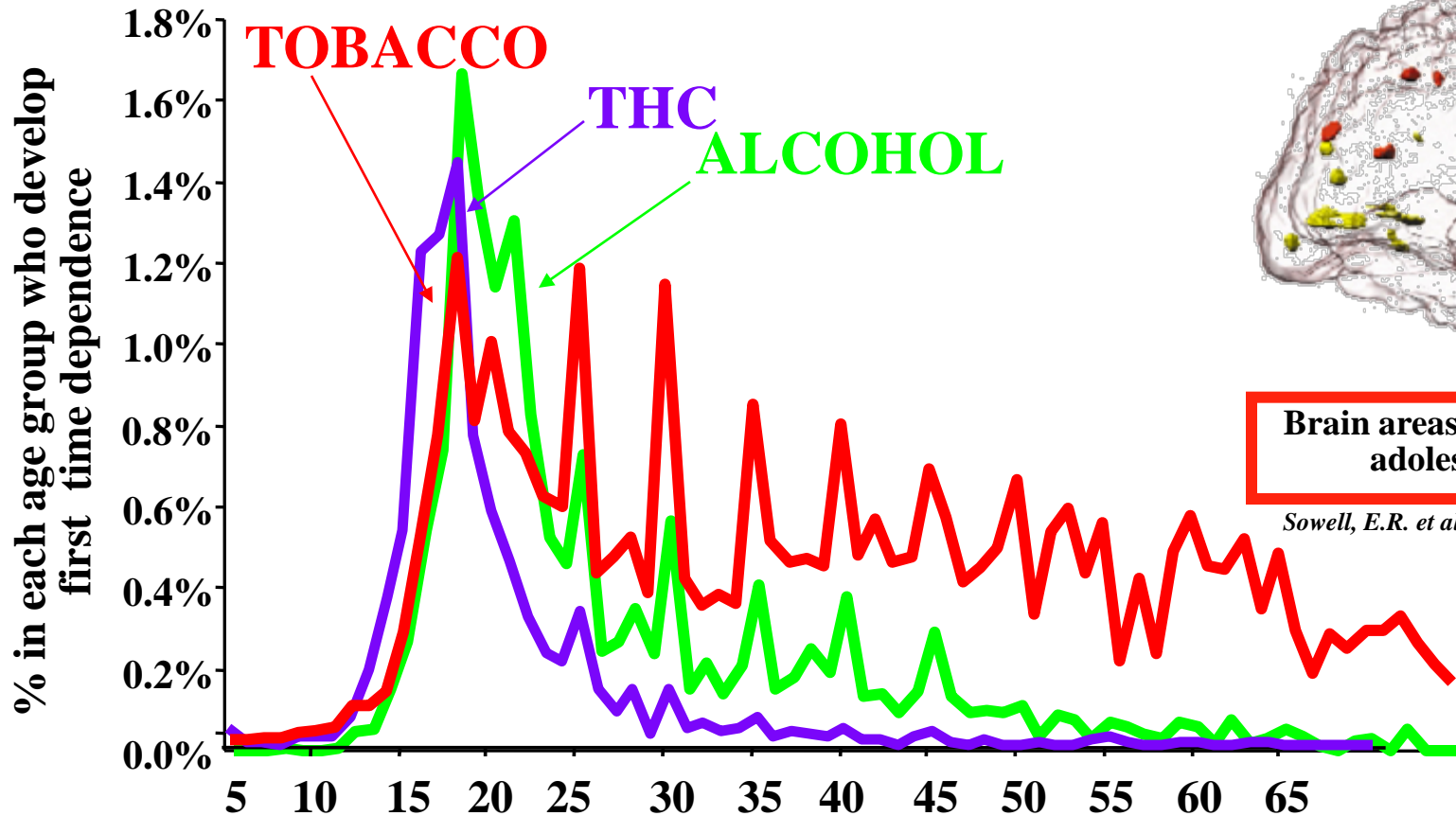
(New Targets & New Strategies)



HIV/AIDS Research



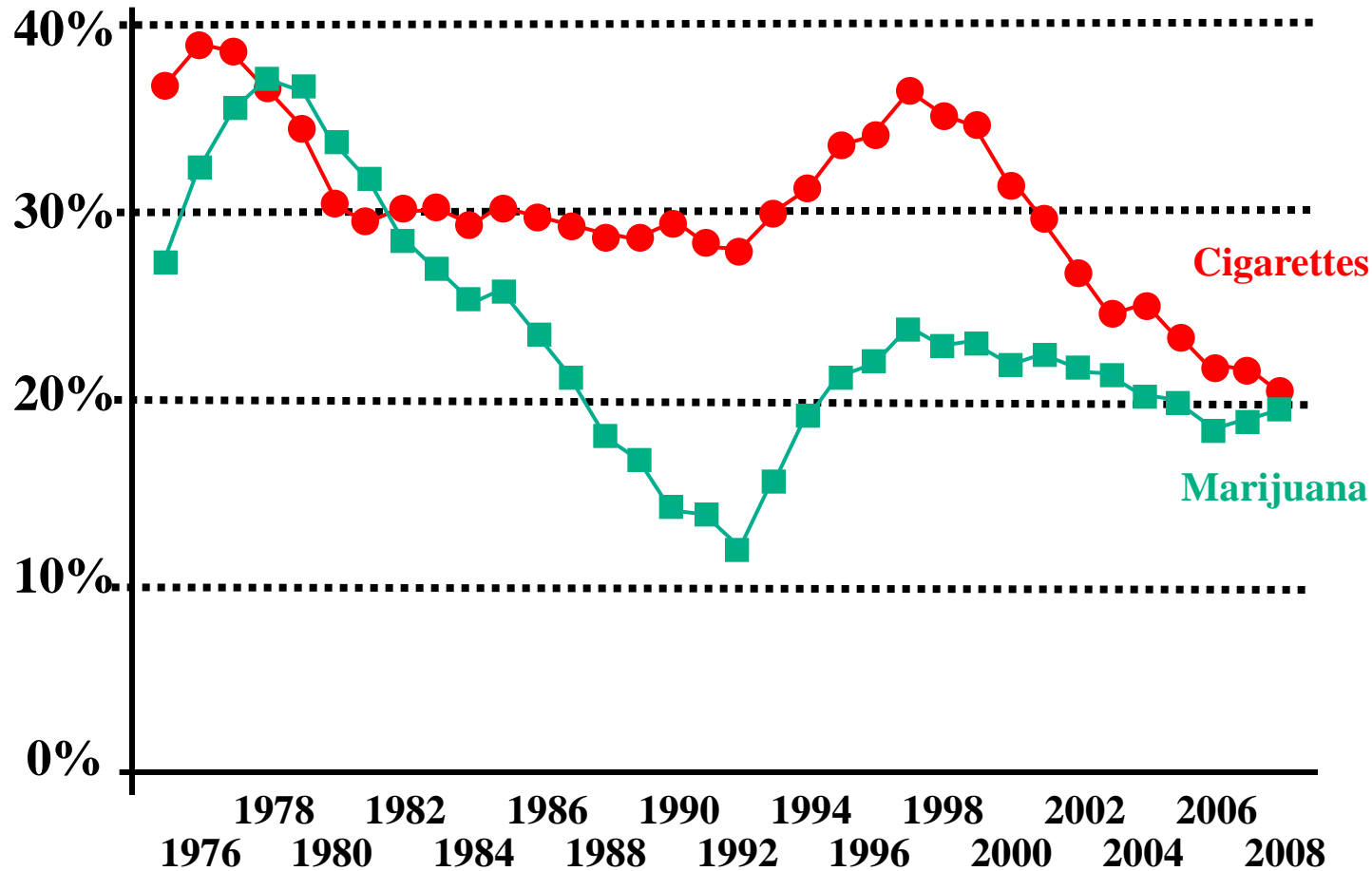
ADDICTION IS A *DEVELOPMENTAL* DISEASE *starts in adolescence and childhood*



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

NIAAA National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

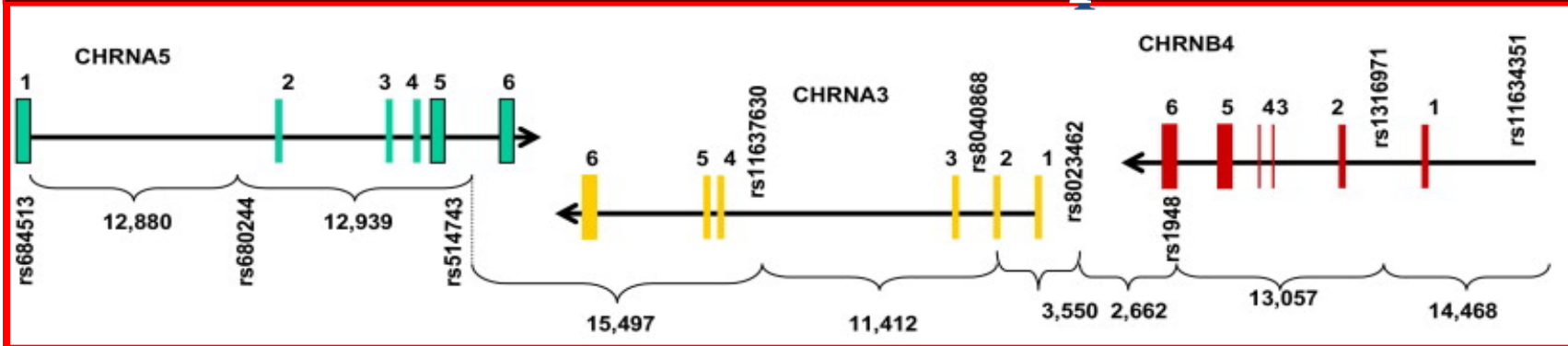
Percentage of U.S. 12th Grade Students Reporting Past Month Use of Cigarettes and Marijuana, 1975 to 2008



CESAR FAX January 19, 2009, Vol. 18, Issue 2.

Adapted by CESAR from University of Michigan, "Trends in 30-Day Prevalence of Use of Various Drugs in Grades 8, 10, and 12," Monitoring the Future study, 2008.

Convergent Results Support CHRNA5/A3/B4 Gene Cluster Association with Nicotine Dependence



Human Molecular Genetics, 2007, Vol. 16, No. 1 24–35
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. Madden¹, Naomi Breslau², Eric O. Johnson³,

Biological Psychiatry

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,

Molecular Psychiatry (2008), 1–6
© 2008 Nature Publishing Group All rights reserved 1359-4184/08 \$30.00
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 Chilcoat⁴, D Waterworth^{2,3}, P Muglia^{2,3,5} and V Mooser^{2,3}

nature

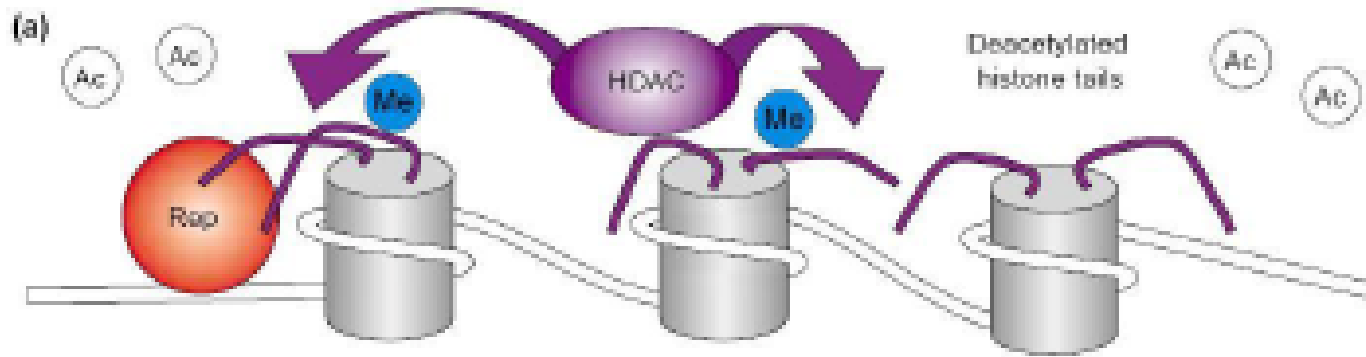
LETTERS

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

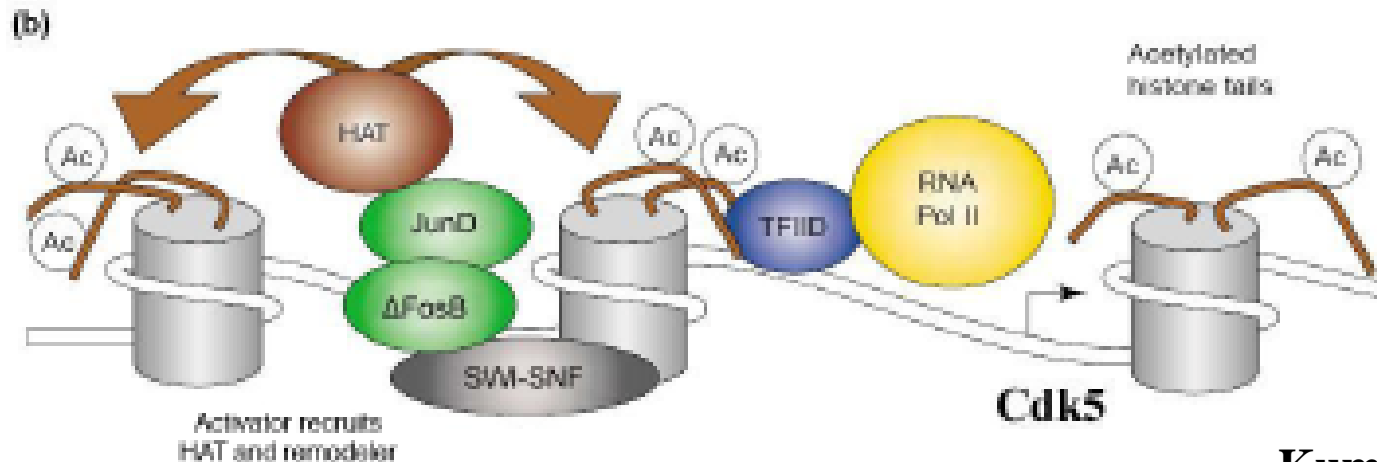
Thorgeir E. Thorgeirsson^{1*}, Frank Geller^{1*}, Patrick Sulem^{1*}, Thorunn Rafnar^{1*}, Anna Wiste^{1,2}, Kristinn P. Magnusson¹, Andrei Manolescu¹, Gudmar Thorleifsson¹, Hreinn Stefansson¹, Andres Ingason¹, Simon N. Stacey¹, Jon T. Bergthorsson¹, Steinunn Thorlacius¹, Julius Gudmundsson¹, Thorlukur Jonsson¹, Margret Jakobsdottir¹, Jona Saemundsdottir¹, Olof Olafsdottir¹, Larus J. Gudmundsson¹, Gyda Bjornsdottir¹, Kristleifur Kristjansson¹, Halla Skuladottir³, Helgi J. Isaksson⁴, Tomas Gudbjartsson⁵, Gregory T. Jones⁶, Thomas Mueller⁷, Anders Gottsäter¹⁰, Andrea Flex¹¹, Katja K. H. Aben^{12,13}, Femmie de Vegt¹², Peter F. A. Mulders¹⁴, Dolores Irla¹⁵, Maria J. Vidali¹⁵, Laura Acin¹⁶, Berta Saez¹⁷, Laura Murillo¹⁸, Thorsteinn Blondal¹⁹

...and with the risk of such smoking-related diseases as lung cancer and peripheral arterial disease

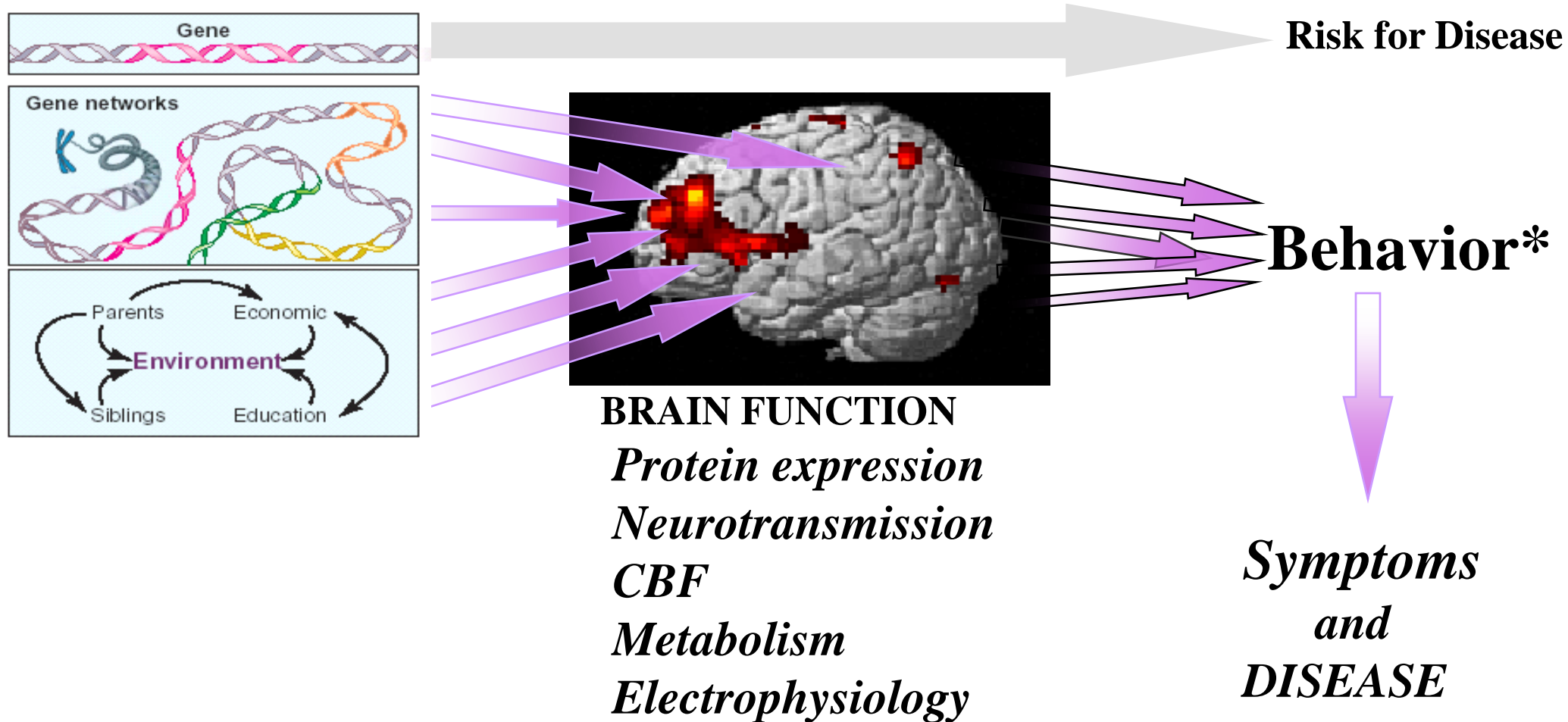
Epigenetic Marks Are Altered by Repeated Exposure to Drugs of Abuse



Cocaine induces the transcription factor • FosB, which co-activates HAT leading to sustained acetylation of histones and activation of genes, such as Cdk5, involved in addiction



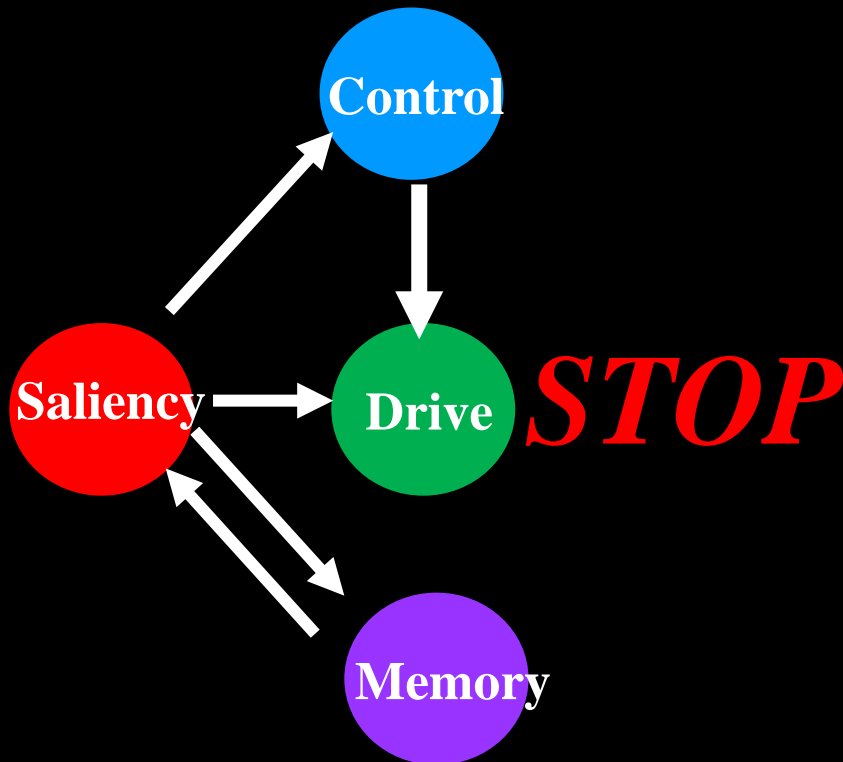
How Do Genes Influence Brain Development, Behavior and Disease?



*Adapted from Hamer, *Science*, 2002; MAO A genotype studies from Caspi et al., *Science*, 2002.

Medications for Relapse Prevention

Non-Addicted Brain



Interfere with drug's reinforcing effects

Vaccines
Enzymatic degradation
Naltrexone
DA D3 antagonists
CB₁ antagonists

Executive function/
 Inhibitory control

Biofeedback
Modafinil
Bupropion
Stimulants

Strengthen prefrontal-striatal communication

Adenosine
A2 antagonists
DA D3 antagonists

Interfere with conditioned memories (craving)

Antiepileptic GVG
N-acetylcysteine

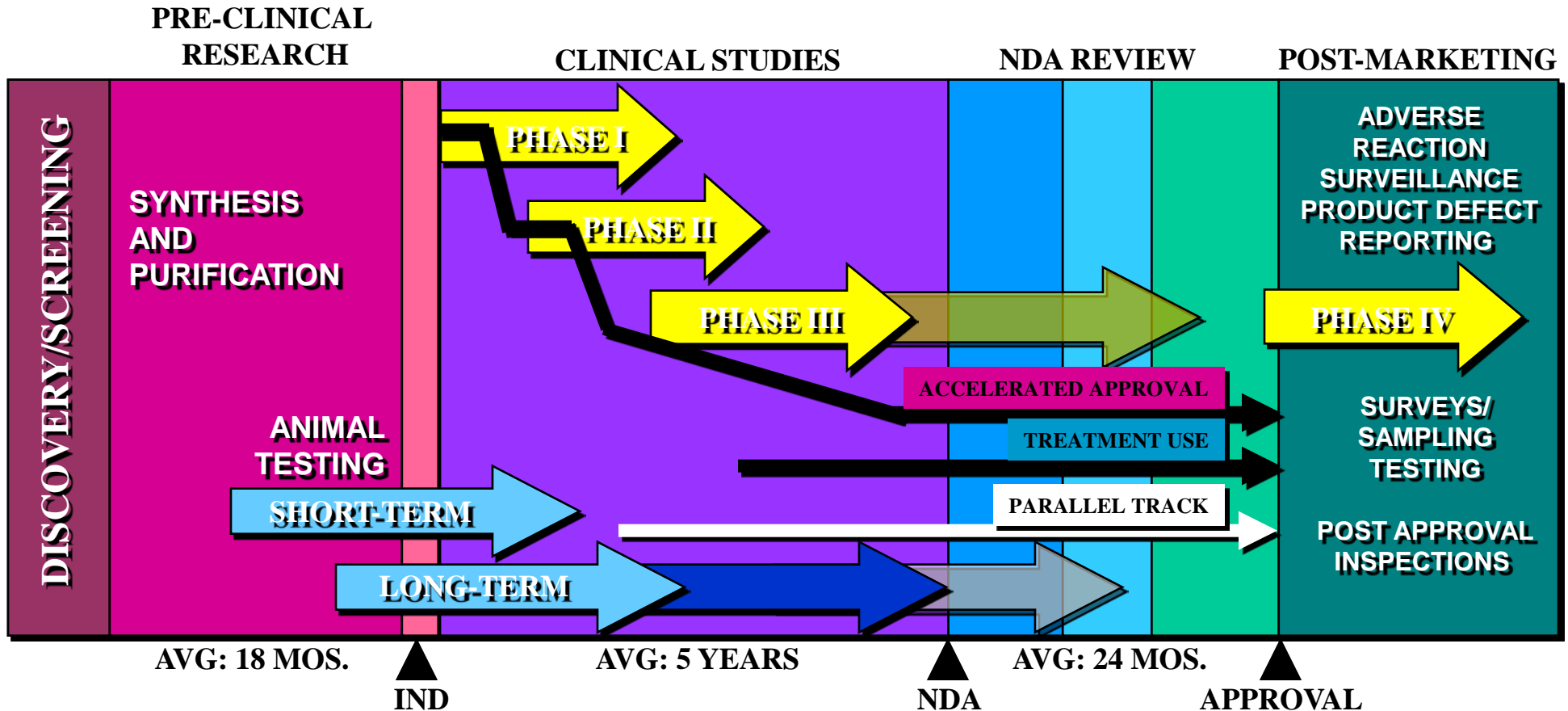
Teach new memories

Cycloserine

Counteract stress responses that lead to relapse

CRF antagonists
Orexin antagonists

ROADBLOCK #1: Lack of Pharmaceutical Industry Interest in Developing Medications to Treat Addiction



**The Process of NEW DRUG DEVELOPMENT
Is Long...and Expensive**

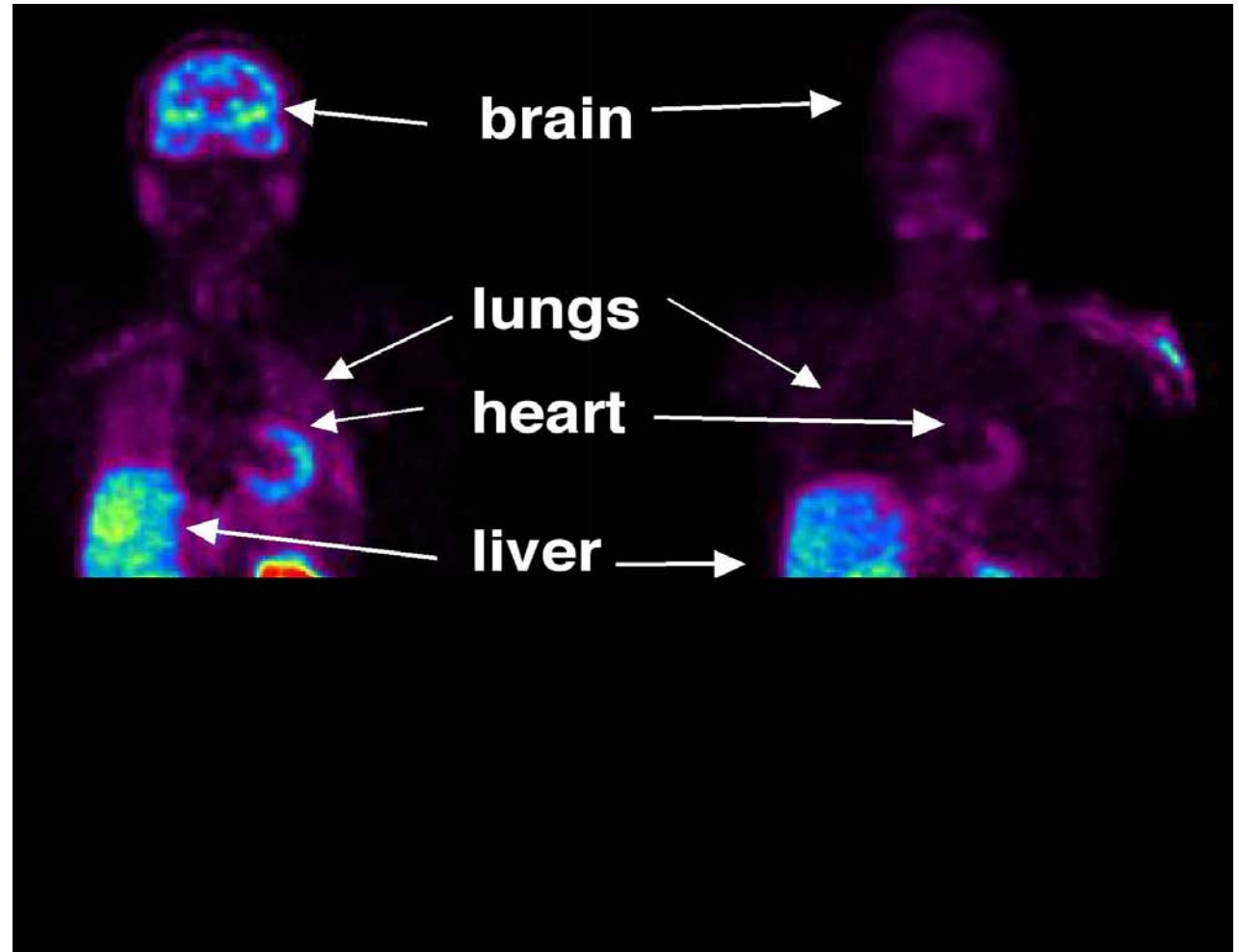
ROADBLOCK #2: Erosion of the Medical Community's Involvement in Preventing and Treating Drug Abuse and Addiction

Primary Care Physicians Are Often Reluctant To Treat Substance Abuse or Fail to Link This With Their Patients' Other Medical Conditions



ADDICTION CONTRIBUTES TO MANY SERIOUS *MEDICAL CONSEQUENCES*

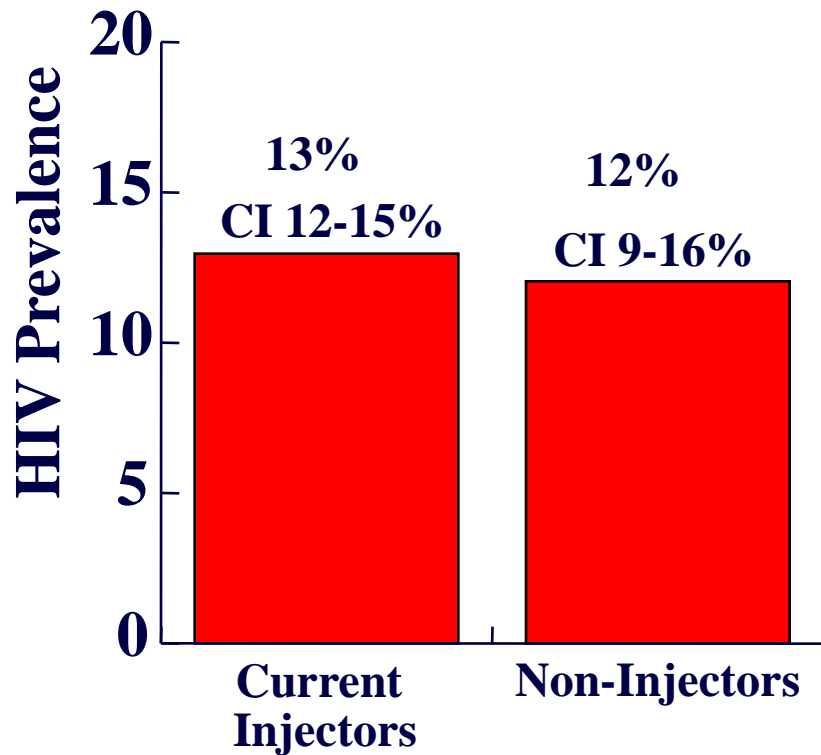
- **Mental Illness**
- **Cancer**
- **Infectious Diseases**
(HIV/HCV)
- **Cardiac**
- **Pulmonary**
- **Learning Disorders**
- **Obesity**
- **Cerebrovascular**
(strokes)
- **Trauma**
(accidents)



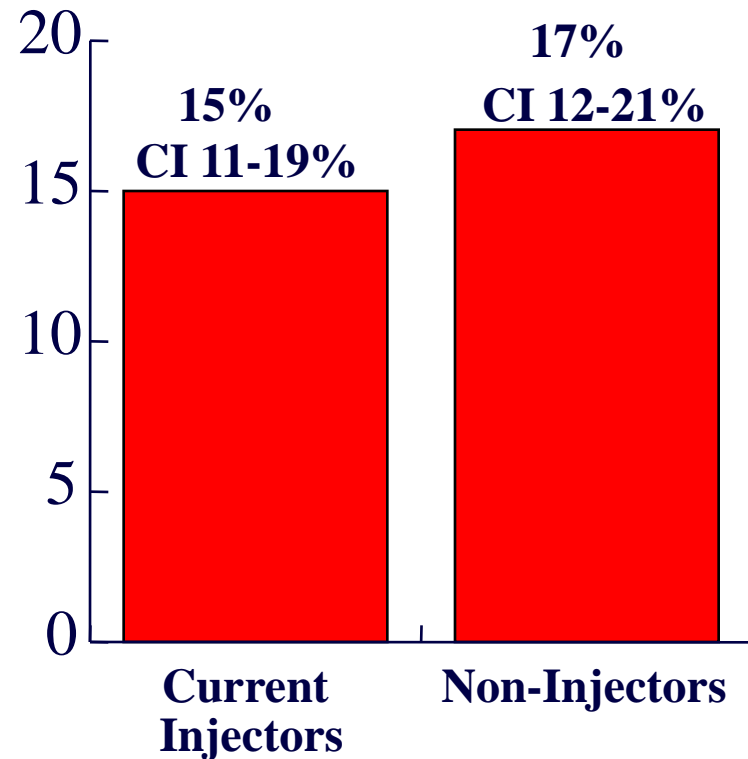
Source: Fowler JS et al., PNAS. 2003;100(20):11600-5.

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

**Drug Treatment Program
(n=2121 2001-2004)**



**Respondent-Driven Sampling
(n=448 2004)**

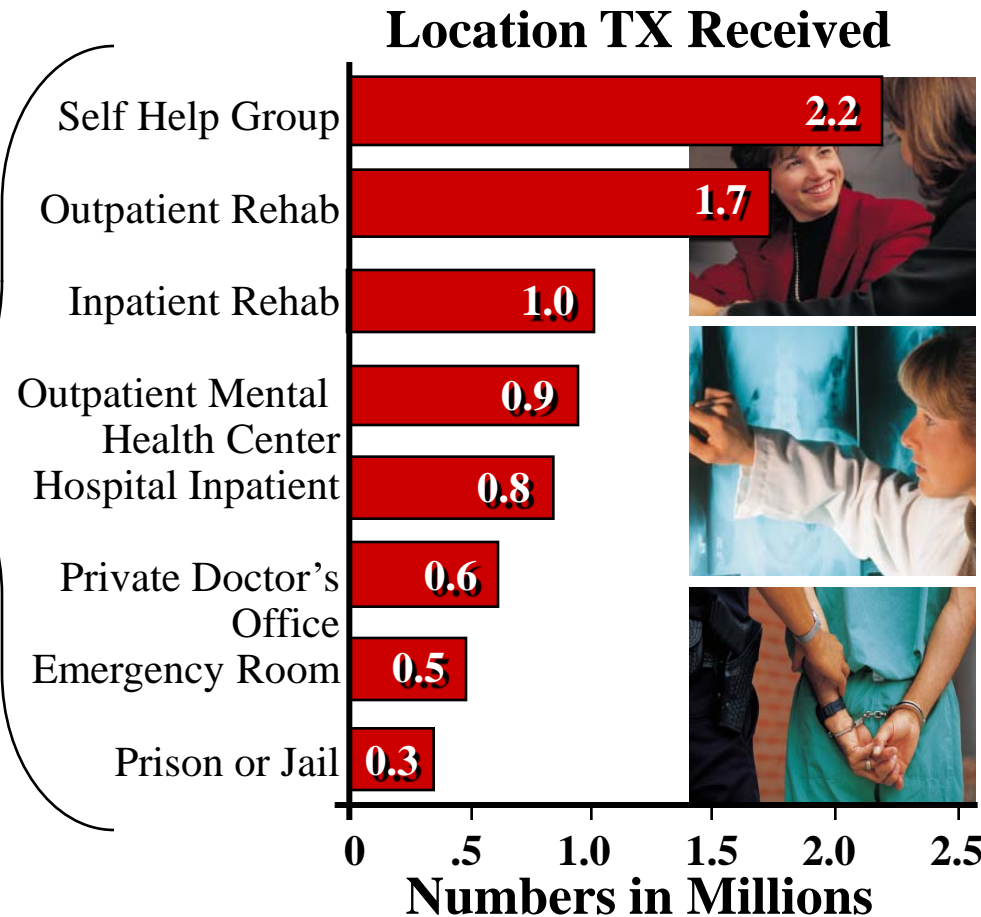


Source: Des Jarlais et al AIDS, 21: 231-235, 2007.

ROADBLOCK #3: Although Treatments For Addiction Are Available, They Are Not Being Widely Used By Those Who Need Them

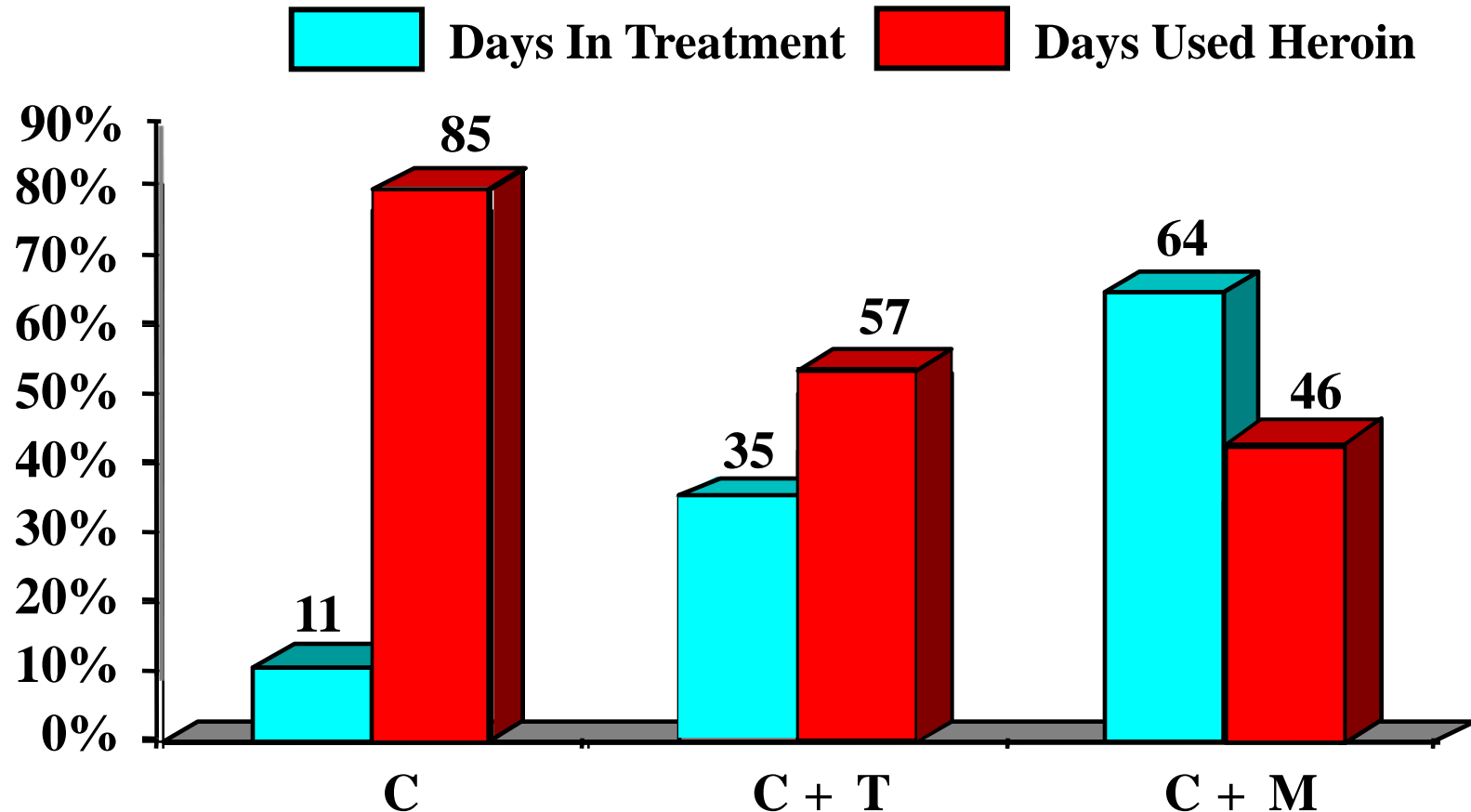
In 2007 An Estimated 22.3 Million Americans Were Dependent On or Abused Any Illicit Drugs or Alcohol

But...Only 3.9 Million (17%) of These Individuals Had Received Some Type of Treatment In the Past Year



Source: 2007 NSDUH, National Findings, SAMHSA, OAS, 2008.

Treatment Linkage & Days Used Heroin 6 Months Post-release



C = Counseling Only
C+T = Counseling & Treatment Referral
C+M = Counseling & Methadone Started in Prison

Blending Research and Practice

National Drug Abuse Treatment Clinical Trials Network (CTN)



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

Research Centers & CJ Partner Sites

