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

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Addiction involves multiple factors. 

- **Biology/Genes**
- **Environment**
- **Brain Mechanisms**
- **Addiction**

A family tree illustrates the genetic aspect, while a landscape image represents the environmental influence. The central concept, DRUG, links these factors, indicating the complex interplay in addiction.
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 that starts in adolescence and childhood.


Brain areas where volumes are smaller in adolescents than young adults:
- Subcortical
- Frontal
- Parietal
- Occipital
- Temporal


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

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

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

Novel genes identified in a high-density genome wide association study for nicotine dependence
Laura Jean Bierut1,*, 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. Hofst, Allan C. Collins, Robin P. Corley, John K. Hewitt, Christian J. Hopfer

LETTERS

A variant associated with nicotine dependence, lung cancer and peripheral arterial disease
Thorgeir E. Thorgerisson1*, Frank Geller4*, Patrick Sulem5, Thorunn Rafnar1*, Anna Wiste1,2, Kristinn P. Magnusson1, Andrén Manolescu1, Gudmar Thorleifsson1, Heiminn Stefansson1, Andres Ingason1, Simon N. Staton1, Jon T. Bergthorsson1, Steinnn Thorlacius1, Julius Gudmundsson1, Thorlakur Jonsson1, Margret Jakobsdottir1, Jona Saemundsdottir1, Ólaf Olafsdottir1, Larus J. Gudmundsson1, Gýda Björnsdóttir1, Kristjána Kristjánsson1, Halla Skuladóttir1, Helgi J. Isaksson1, Tomas Gudbjartsson1, Gregory T. Jones1, Thomas Muir6, Anders Götzsäther7, Andrea Flex1, Katja K.H. Aben7,8,9,10, Fernnie de Vogel7,11, Peter F. A. Mulders12,13,14,15, Carina Wallgren-Peterson16, Lina Gudbjartadottir1, Luisa S. Lees-Farrell17, Phillip E. Hultman18, Thorleifur Jonsson19

IMMEDIATE COMMUNICATION

α-5/α-3 nicotinic receptor subunit alleles increase risk for heavy smoking
W Berrettini1,2,3, X Yuan2,3, F Tozzé2,3, K Song2,3, C Francka2,3, H Chilcoat4, D Waterhouse2,8, P Muglia3,4, and V Moos8,9

...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 \( \Delta FosB \), which co-activates HAT leading to sustained acetylation of histones and activation of genes, such as Cdk5, involved in addiction.

Kumar et al Neuron 48: 303-314 2005
How Do Genes Influence Brain Development, Behavior and Disease?

Risk for Disease

Behavior*

BRAIN FUNCTION
- Protein expression
- Neurotransmission
- CBF
- Metabolism
- Electrophysiology

Symptoms and Disease

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

**Non-Addicted Brain**

- **Saliency**
  - Drive
  - Memory

**Control**

- **Interfere with drug’s reinforcing effects**
  - 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

**Addicted Brain**

- **Drive**
  - GO
  - STOP

- **Memory**
  - Vaccines
  - Enzymatic degradation
  - Naltrexone
  - DA D3 antagonists
  - CB1 antagonists

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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)

- Current Injectors: 13% (CI 12-15%)
- Non-Injectors: 12% (CI 9-16%)

Respondent-Driven Sampling (n=448 2004)

- Current Injectors: 15% (CI 11-19%)
- Non-Injectors: 17% (CI 12-21%)

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.

Treatment Linkage & Days Used Heroin
6 Months Post-release

Days In Treatment  Days Used Heroin

<table>
<thead>
<tr>
<th></th>
<th>Days Used Heroin</th>
<th>Days In Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>85</td>
<td>11</td>
</tr>
<tr>
<td>C+T</td>
<td>57</td>
<td>35</td>
</tr>
<tr>
<td>C+M</td>
<td>64</td>
<td>46</td>
</tr>
</tbody>
</table>

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