

#### NATIONAL INSTITUTE ON DRUG ABUSE

Bringing the Full Power of Science to Begron

# Drug Abuse & Addiction







Homelessness

Crime

Violence

#### Medical

Neurotoxicity AIDS, Cancer Mental illness

Social

#### **Economic**

Health care Productivity Accidents

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



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

> Illegal drugs: Alcohol: Tobacco:

\$181 billion/year
\$185 billion/year
\$158 billion/year

**Total:** 

**\$524 billion/year** 

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



# 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 in the 1980's

#### this is your brain on drugs.

# Your Brain on Drugs Today



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



## 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* 

#### Decreased Heart Metabolism in *Heart Disease Patient*



**Healthy Brain** 



Diseased Brain/ Cocaine Abuser



Healthy Heart



**Diseased Heart** 

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



# **Addiction Involves Multiple Factors**





## Addiction Is A Developmental Disease that starts in adolescence and childhood



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

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National Epidemiologic Survey on Alcohol and Related Conditions, 2003.

# 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



# Why Do People Abuse Drugs?

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





# Drugs can be "Imposters" of Brain Messages







Addiction

#### Reward & well-being

# The Neuron: How the Brain's Messaging System Works



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#### dopamine

#### dopamine receptor

A PARTY CLARKER



#### dopamine transporters

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## Natural Rewards Elevate Dopamine Levels



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



## Effects of Drugs on Dopamine Release



## 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.



#### **Dopamine Pathways**

#### **Serotonin Pathways**

Frontal cortex

Substantia nigra

Striatum

Functions • Reward (motivation) • Pleasure, euphoria • Motor function (fine-tuning) • Compulsion

Perseveration

Nucleus accumbens

VTA

Hippocampus

Raphe nucleus

- Functions
- Mood
- Memory processing
- Sleep
- Cognition



Science Has Generated Much Evidence Showing That...

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



## **AND...**

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





#### Neuronal Dendrites in the Nucleus Accumbens





Robinson & Kolb, Journal of Neuroscience, Volume: 1997

## **Functionally...** Dopamine D2 Receptors are Decreased by Addiction











Control

Addicted

# **DA D2 Receptor Availability**

#### **Dopamine Transporters in Methamphetamine Abusers**



**Normal Control** 



**Methamphetamine Abuser** 



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

#### 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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## Implication?

# Brain changes resulting from prolonged use of drugs may compromise mental AND motor function.



#### **Circuits Involved In Drug Abuse and Addiction**



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

# **Priority Areas for NIDA**

## **Prevention Research** (Children & Adolescents)

genetics environment development co-morbidity

**Treatment Research** (New Targets & New Strategies)

**HIV/AIDS Research** 





## Addiction is a Developmental Disease: It Starts Early



**Basic Science Tells Us that** Adolescents' Brains Are Still Developing...





## 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.

Do Adolescents React Differently than Adults to Substances of Abuse?


# Rats Exposed to Nicotine in Adolescence Self-Administer <u>More</u> Nicotine Than Rats First Exposed as Adults



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



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









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



# 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.

# Genetics is a Big Contributor to the Risk of Addiction...





# 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

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

Laura Jean Bierut<sup>1,\*</sup>, Pamela A.F. Madden<sup>1</sup>, Naomi Breslau<sup>2</sup>, Eric O. Johnson<sup>3</sup>,

Dorothy Ha Louis Fox<sup>1</sup> Nicholas G Jen C. War

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#### 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

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

#### IMMEDIATE COMMUNICATION

#### $\alpha\text{-}5/\alpha\text{-}3$ nicotinic receptor subunit alleles increase risk for heavy smoking

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

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

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

Thorgeir E. Thorgeirsson<sup>1</sup>\*, Frank Geller<sup>1</sup>\*, Patrick Sulem<sup>1</sup>\*, Thorunn Rafnar<sup>1</sup>\*, Anna Wiste<sup>1,2</sup>, Kristinn P. Magnusson<sup>1</sup>, Andrei Manolescu<sup>1</sup>, Gudmar Thorleifsson<sup>1</sup>, Hreinn Stefansson<sup>1</sup>, Andres Ingason<sup>1</sup>, Simon N. Steory<sup>1</sup>, Len T. Bergtherscon<sup>1</sup>, Steinung Thorlacius<sup>1</sup>, Iulius Gudmundeen<sup>1</sup>, Thorlakur, Joneson<sup>1</sup>

### What Other Biological Factors Contribute to Addiction--Comorbidity



## **COMORBIDITY**

#### Drug Users have a Higher Risk of Developing Mental Disorders

Psychosis

- Depression
- Anxiety
- Panic attacks



# 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





What Environmental Factors Contribute to Addiction?

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



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



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

### **Prevention Works:**

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





### Changes in Attitudes Lead to Changes in Use



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Monitoring the Future Study, 2007.

# **Priority Areas for NIDA**

Prevention Research (Children & Adolescents) genetics environment development co-morbidity

**Treatment Research** 

(New Targets & New Strategies)

**HIV/AIDS Research** 









#### **Because Addiction Changes Brain Circuits**

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Adapted from Volkow et al., Neuropharmacology, 2004.

# This is why addicts can't just quit. and...

This is why treatment is essential.





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# **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.





### We Are Using Science to Develop Even Better Treatments





# **Basic Research**

**Opiate agonists stabilize brain function in heroin addicts** 

**CB1 KO mice have decreased responses to multiple drugs of abuse** 

Smokers who are poor nicotine metabolizers smoke less

Stress triggers relapse in animal models of addiction and CRF antagonists interfere with the response to stress Agonist Therapy Methadone Buprenorphine

Medication

**CB1** Antagonists

Inhibitors of metabolizing enzymes

**CRF Antagonists** 

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





# **Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses**



McLellan et al., JAMA, 2000.



# 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





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



### **Extended Abstinence** is Predictive of Sustained Recovery

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



DAT Recovery with prolonged abstinence from methamphetamine



# Treatment Reduces Drug Use and Recidivism

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









# **Priority Areas for NIDA**

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#### Treatment Research (New Targets & New Strategies)

**HIV/AIDS Research** 







# 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

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



Centers for Disease Control and Prevention (CDC)

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

Drug Treatment Program (n=2121 2001-2004)



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





### The AIDS Epidemic Disproportionately Affects Minority Populations



ΝΠ

**Centers for Disease Control and Prevention (CDC)** 

### Acceleration of HIV Degeneration of Dopamine Cells With Cocaine



(n = 15)

(n = 5)

(n = 17)

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# NIDA International Program Components

**Post-Doctoral Research Fellowship** 

#### **Technical Consultation**

International Research Collaboration

Scientific Exchange

**Information Dissemination** 



# Why focus on drug abuse internationally?

#### I. Drug abuse is a global phenomenon

S 5 % of people aged 15-64

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

> S HIV Infections Attributed to Injection Drug Use and Risky Sexual Behaviors Related to Drug Abuse



III. Take advantage of unique opportunities to advance scientific knowledge through research
NIDA Supports International Drug Abuse Research In Numerous Ways

- S Fund international research
- S Provide training and exchange opportunities
- Set international research priorities
- Organize & sponsor conferences and meetings
- Sinational agreements
- Solution States Stat



## Where Do We Need to Go From Here?

## We Need to...

## Advance the STIGMA



## **For More Information**

NIDA Public Information: www.nida.nih.gov www.drugabuse.gov

NIDA International Program: www.international.drugabuse.gov

www.drugabuse.gov

