Addiction is a Brain Disease and It *Still* Matters

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Addiction Is a Brain Disease, and It Matters

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Scientific advances over the past 20 years have shown that drug addiction is a chronic, relapsing disease that results from the prolonged effects of drugs on the brain. As with many other brain diseases, addiction has embedded behavioral and social-context aspects that are important parts of the disorder itself. Therefore, the most effective treatment approaches will include biological, behavioral, and social-context components. Recognizing addiction as a chronic, relapsing brain disorder characterized by compulsive drug seeking and use can impact society’s overall health and policy strategies and help diminish the health and social costs associated with drug abuse and addiction.

Dramatic advances over the past two decades in both the neurosciences and the behavioral sciences have revolutionized our understanding of drug abuse and addiction. Scientists have identified neural circuits that subserve the actions of every known drug of abuse, and they have specified the mechanisms that are affected by almost all such drugs. Researchers have also identified and cloned the major receptors for virtually every available drug, as well as the natural ligands for most of those receptors. In addition, they have elaborated many of the biochemical cascades within the cell that follow receptor activation by drugs. Research has also begun to reveal major differences between the brains of addicted and nonaddicted individuals and to indicate some common elements of addiction, regardless of the substance.

That is the good news. The bad news is the dramatic lag between these advances in science and their application by the general public or their adoption in either practice or public policy settings. There is a wide gap between the scientific facts and public perceptions about drug abuse and addiction. For example, many, perhaps most, people see drug abuse and addiction as a social problem, to be handled only by social solutions, particularly by the criminal justice system. On the other hand, science has taught us that drug abuse and addiction are as much health problems as they are social problems. The consequence of this gap is a significant delay in gaining control over the drug abuse problem.

Drug and Addiction as Public Health Problems

At the most general level, research has shown that drug abuse is a dual-ended health issue, as well as a social issue. It affects both the health of the individual and the health of the public. The use of drugs has well-known and severe health consequences for the individual, both mental and physical. But drug abuse and addiction also have tremendous implications for the health of the public, because drug use, directly or indirectly, is now a major vector for the transmission of many serious infectious diseases—particularly acquired immunodeficiency syndrome (AIDS), hepatitis, and tuberculosis—as well as violence. Because addiction is such a complex and pervasive health issue, we must include in our overall strategy a committed public health approach, including extensive education and prevention efforts, treatment, and research. Science is providing the basis for such public health approaches. For example, two large sets of studies (1) have demonstrated the effectiveness of well-designed outreach strategies in modifying the behaviors of addicted individuals that put them at risk for acquiring the human immunodeficiency virus (HIV), even if they continue to use drugs and do not want to enter treatment. This approach runs counter to the broadly held view that addicts are so incapacitated by drugs that they are unable to modify any of their behaviors. It also suggests a base for improved strategies for reducing the negative health consequences of injection drug use for the individual and for society.

What Matters in Addiction

Scientific research and clinical experience have taught us much about what really matters in addiction and where we need to concentrate our clinical and policy efforts. However, too often the focus is on the wrong aspects of addiction, and efforts to deal with this difficult issue can be badly misguided.

Any discussion about psychoactive drugs inevitably turns to the question of whether a particular drug is physically or psychologically addictive. In essence, this issue revolves around whether or not a drug’s physical withdrawal symptoms occur when an individual stops taking a drug, what is typically called physical dependence by professionals in the field. The assumption that often follows is that the more dramatic the physical withdrawal symptoms, the more serious or dangerous the drug must be. This thinking is outdated. From both clinical and policy perspectives, it does not...
Addiction is a brain disease, and that has implications for how we deal with the issue.
Advances in science over the past 50 years have changed some fundamental concepts

- How the brain and mind work normally
- Brain dysfunction and its tie to disease
- What to do about brain disorders
  - Clinically
  - Public policy
Your Brain on Drugs!
Why do people take drugs in the first place?
Risk and Protective Factors

Community

Peer Cluster

Family

Individual

Drug Abuse

Drug/Alcohol Related Traffic Accidents

Sexually Transmitted Diseases (Including HIV/AIDS)

Suicidal Behavior

Unwanted Pregnancies

Running Away From Home

Delinquency

Academic Failure and Dropping Out of School

Juvenile Depression

Unwanted Pregnancies

Drug Abuse
Immediate (proximal) reasons people take drugs

- To feel good
  - Sensation seeking
- To feel better
  - Self-medicating
People take drugs to change their mood, perception or emotional state

Hoping to change their brains
Your Brain on Drugs

YELLOW shows places in brain where cocaine goes (Striatum)
Acute Effects of Cocaine (0.6 mg/kg, iv)

Transient activation correlates with euphoria

Sustained activation correlates with craving

Neuron 19:591-611, 1997
MGH NMR Center and Department of Psychiatry
Acute Effects of Cocaine (0.5 mg/kg, iv)

Transient activation correlates with euphoria

Sustained activation correlates with craving

AC

NAcStC

Signal Change

Time (minutes)

Hippocampus

MRI

Image from: Bluhm et al. 1997, MGH NDE Center and Department of Psychiatry.
How do drugs work in the brain?

Despite Their Many Differences, most Abused Substances Enhance the Dopamine and Serotonin Pathways
Dopamine Pathways

- Functions
  - reward (motivation)
  - pleasure, euphoria
  - motor function (fine tuning)
  - compulsion
  - perserveration

Serotonin Pathways

- Functions
  - mood
  - memory processing
  - sleep
  - cognition

Regions:
- frontal cortex
- striatum
- hippocampus
- nucleus accumbens
- substantia nigra/VTA
- raphe
Circuits Involved In Drug Abuse and Addiction

All of These Must Be Considered In Developing Strategies to Most Effectively Treat Addiction
A Major Reason People Take a Drug is They Like What It Does to Their Brains
Activation of the reward pathway by addictive drugs
Effects of Drugs on Dopamine Levels

**AMPHETAMINE**
- % of Basal Release vs. Time After Amphetamine
- Axes: % of Basal Release vs. Time (0-5 hr)
- Graphs show DA, DOPAC, HVA levels over time.

**COCAIN**
- % of Basal Release vs. Time After Cocaine
- Axes: % of Basal Release vs. Time (0-5 hr)
- Graphs show DA, DOPAC, HVA levels over time.

**NICOTINE**
- % of Basal Release vs. Time After Nicotine
- Axes: % of Basal Release vs. Time (0-3 hr)
- Graphs show Accumbens and Caudate levels over time.

**MORPHINE**
- % of Basal Release vs. Time After Morphine
- Axes: % of Basal Release vs. Time (0-5 hr)
- Graphs show different dose levels (0.5, 1.0, 2.5, 10 mg/kg) over time.

Source: Di Chiara and Imperato
Another Critical Question...

Why Do Some People Get Into Trouble With Drugs And Others Don’t?
Genetics

Gene/Environment Interaction

Environment
# Heritabilities Derived From Twin Studies

<table>
<thead>
<tr>
<th>DRUG</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>44% (Tsuang et al., 1996)</td>
<td>81% (Kendler et al., 1999)</td>
</tr>
<tr>
<td>Heroin (opiates)</td>
<td>54% (Tsuang et al., 1996)</td>
<td>54% (Kendler et al., 2000)</td>
</tr>
<tr>
<td>Sedatives</td>
<td>87% (Kendler, et al., 2000)</td>
<td>79% (Kendler &amp; Prescott, 1998)</td>
</tr>
<tr>
<td>Marijuana</td>
<td>33% (Tsuang et al., 1996)</td>
<td>79% (Kendler &amp; Prescott, 1998)</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>79% (Kendler, et al., 2000)</td>
<td>79% (Kendler &amp; Prescott, 1998)</td>
</tr>
<tr>
<td>Nicotine</td>
<td>53% (Carmelli et al., 1990)</td>
<td>72% (Kendler et al., 1999)</td>
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</tbody>
</table>
After a person uses drugs for a while, why can’t they just stop?
Prolonged drug use changes the brain in fundamental and long-lasting way
Effect of Cocaine Abuse on Dopamine D2 Receptors

- Normal subject
- Cocaine abuser (1 month post)
- Cocaine abuser (4 months post)
Dopamine Transporter Loss After Heavy Methamphetamine Use

Comparison Subject       METH Abuser

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

...And Those Differences Are An Essential Element of Addiction
Voluntary Drug Use

Compulsive Drug Use (Addiction)
We don’t know the exact switch

But we know the circuits involved in addiction are similar to other motivations
Effects of Drugs on Dopamine Levels

**AMPHETAMINE**

Time After Amphetamine

**COCAINE**

Time After Cocaine

**NICOTINE**

Time After Nicotine

**MORPHINE**

Time After Morphine

Source: Di Chiara and Imperato
Natural Rewards Elevate Dopamine Levels

**FOOD**

- % of Basal DA Output
- NAc shell
- Time (min)
- Source: Di Chiara et al.

**SEX**

- DA Concentration (% Baseline)
- Copulation Frequency
- Sample Number
- Source: Fiorino and Phillips
Does the Brain Recover?
DAT Recovery with prolonged abstinence from methamphetamine
Addiction is, Fundamentally, a Brain Disease
Addiction Is A Brain Disease
Expressed As Compulsive Behavior

Both Developing and Recovering From It Depend on Behavior and Social Context
Drug Addiction:  
A Complex Behavioral and Neurobiological Disorder
As with all complex scientific issues, people only hear the sound bite

Addiction is a Brain Disease
Back then, more than half of people hated the claim

- Too simplistic
- Let addicts “off the hook”
- Some thought it stigmatizing
  - Or destigmatizing
Why does society care about that?

- We can’t just will addiction away
- Addiction requires comprehensive treatment and rehabilitation approaches
- Policy questions:
  - How to deal with addicted individuals
  - Particularly if they commit crimes
The complexity of addictive disorders requires strategies for dealing with them that equal their complexity.
Treatment strategies are also very complex

Must attend to biological, behavioral and social aspects
Treatment Process and Outcomes Model

Induction

Detoxification

Motiv

Patient Attributes at Intake

Counselor Attributes & Skills

Program Characteristics

Behavioral Therapies /Counseling

Early Engagement

Program Participation

Therapeutic Relationship

Medications

Social Skills Training

Family & Friends

Early Recovery

Behavioral Change

Psycho-Social Change

Sufficient Retention

Personal Health Services

Supportive Networks

Drug Use

Crime

Social Relations

Posttreatment

Modified from: Simpson, 2001 (Addiction)
Drug abuse and addiction are more than just health issues

- Drugs are illegal
- Some addicts commit crimes other than drug use
- Addiction often leads to family disruption
- Addicts can be a drain on societal resources
We need societal strategies that are as complex as the phenomenon(a)
No More "War on Drugs"
We need to stop polarizing drug abuse related issues

- Controlling supply *versus* reducing demand
- Failure of will *versus* chronic relapsing illness
- Punishment *versus* treatment
We need blended criminal justice/public health strategies
We make a big mistake not treating people while they are under criminal justice control

Could argue it’s unethical
  Denying needed medical care

At a minimum, it’s dumb!
Percent Offenders Arrest-Free 3 Years After Release CREST Work-Release Therapeutic Community and Aftercare

Martin, Butzin, Saum, & Inciardi, 1999, *The Prison Journal*

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**No. at Risk**

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<thead>
<tr>
<th></th>
<th>Extended-release naltrexone</th>
<th>Usual treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week</td>
<td>153 144 139 129 121 117 112 110 104 100 92 87 87</td>
<td>155 116 104 96 84 76 72 67 65 61 59 56 56</td>
</tr>
</tbody>
</table>

**Probability of Relapse-free Survival**

- Extended-release naltrexone
- Usual treatment
One does not need to want treatment!
Legal Pressure and 90-Day Retention Rates

% Retained 90 Days

<table>
<thead>
<tr>
<th>Program A</th>
<th>Program B</th>
<th>Program C</th>
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<tbody>
<tr>
<td>(42%)</td>
<td>(69%)</td>
<td>(88%)</td>
</tr>
<tr>
<td>28</td>
<td>39</td>
<td>25</td>
</tr>
</tbody>
</table>

Three Programs (with % of Caseload CJ Supervised)

Source: Hiller, et al., Legal Pressure and Treatment Retention in DATOS (ASC Meeting, San Diego, Nov 1997)
How far have we come since 1997?
In spite of the evidence

- Only 20% of individuals with opioid use disorder receive treatment in any year
- Only 5% of people in prison who have OUD receive treatment
- Only 36% of formal treatment programs offer medication
  (As of 2016; up from 20% in 2007)
National Academies of Science, Engineering and Medicine

Committee on Medication-Assisted Treatment for Opioid Use Disorder
Making the case for using medications based on

- Evidence base about their effectiveness
- Rationale based on understanding addiction as a brain disease
Also looking at barriers to use of medications – and to concept of addiction as a brain disease

- Misunderstanding about addiction and about medications
- Ideology
- Stigma
- Search for simple solutions
- Everyone’s an expert
Science must replace ideology, stigma and misunderstanding as the basis for how we approach this issue

- Clinically
- From a policy perspective