The Science of Drug Addiction: Implications for Clinical Practice

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National Institute on Drug Abuse The Science of Drug Abuse & Addiction

Scope of Substance Use in the U.S.



Source: A. T. McLellan, 2011

Shifting Landscape of Drug Abuse Over Time



Relative Shifts in Prevalence

% Students Reporting Past Month Marijuana and Cigarettes (by Grade)



Changes in Attitude Lead to Changes in Use: Marijuana Use and Perceived Risk in 12th Graders



Source: Monitoring the Future, 209817/FIT 2013

Synthetic Drugs

% of Students Reporting Synthetic Marijuana Use Annually (by Gender)



Drug Overdose Death Rates in USA More Than Tripled Since 1990 (Nearly 17,000 in 2010).



NCHS Data Brief, December, 2011, Updated with 2009 and 2010 mortality data

Motor vehicle traffic, poisoning, and drug poisoning (overdose) death rates: United States, 1980-2010

Increases in Opioid Deaths Parallel Opioid Sales and Treatment Admissions



National Vital Statistics System, DEA's Automation of Reports and Consolidated Orders System, SAMHSA's TEDS

Estimated Economic Cost to Society Due to Substance Use Disorders

Tobacco:\$193 billion/yearAlcohol:\$235 billion/yearIllegal drugs:\$181 billion/year

Total:

\$609 billion/year

CDC, 2007; Rehm et al., 2009 Lancet 373:2223-33 CRIT/FIT 2013

Advances in neuroscience have revolutionized our fundamental understanding of drug abuse and addiction





The Brain on Drugs

Front of brain

YELLOW shows places in brain where cocaine binds (Striatum)



Back of brain

Addiction is a Disease of the Brain

Decreased Brain Metabolism in SUD Patient



Sources: From the laboratories of Drs. N. Volkow and H. Schelbert

Addiction is Like Many Other Diseases

Addiction is <u>preventable</u>

Addiction is <u>treatable</u>

• <u>Recovery</u> is possible

NIDA Priority Areas

Prevention

Genetics Environment Development

Treatment

Neural mechanisms Brain circuitry

Consequences

HIV/AIDS Fetal Exposure







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



Development of Addiction Involve Multiple Factors



Susceptibility to Addiction Results from Interaction of Many Genes

- FAAH associated with drug dependence
- OPRM1 associated with opiates and alcoholism
- CYP2A6, CYP2B6 associated with smoking and smoking cessation
- ALDH2 associated with protection against alcoholism
- **DBH** (Dopamine beta-hydroxylase) cocaine-induced paranoia
- DRD2, DRD4 (Dopamine receptors) reward, craving
- NrCAM, neurexins (Cell adhesions genes) assoc with drug abuse and addiction
- **Prodynorphin gene -** associated with protection against cocaine dependence
- Nicotinic alpha 7 promoter assoc. with decreased expression of its message in different brains regions and with sensory gating defects in schizophrenics
- -- Alpha 5 and beta 3 (nicotinic receptors) assoc. with nicotine dependence
- -- **5HT1B** (serotonin receptor) associated with conduct disorder and alcoholism

Genetic Variability and Effects of Drugs



What Environmental Factors Contribute to Addiction?

Drug availability Peers who use drugs Family Problems Early physical or sexual abuse Stress in general

Effects of a Social Stressor on Brain Dopamine D2 Receptors and Propensity to Administer Drugs



Adverse Childhood Experiences (ACE) and Illicit Drug Use



ACE is associated with ½ to 2/3 of serious problems with drug use.

SR Dube, et al. PEDIATRICS 111: 564-572, 2003

Addiction Is Developmental



Source: Compton, et al. Archives of General Psychiatry 2007. NESARC Study.

What Does Science Tell Us About Effective Prevention Programs?



EXAMPLES OF RISK AND PROTECTIVE FACTORS

Risk Factors	Domain	Protective Factors
Early Aggressive Behavior	Individual	Self-Control
Poor Social Skills	Individual	Positive Relationships
Lack of Parental Supervision	Family	Parental Monitoring and Support
Substance Abuse	Peer	Academic Competence
Drug Availability	School	Anti-Drug Use Policies
Poverty	Community	Strong Neighborhood Attachment

Effective Prevention Programs





Nurse Home Visiting Program (prenatal-age 2)

0





Percent of Children with Internalizing Problems (Borderline or Clinical) 6 Child Age 12 5 -4 -3 -2 -1 -





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Neuronal Circuits Involved In Drug Abuse and Addiction



1. Reward Circuit





Drugs of Abuse Engage Systems in the Motivation Pathways of the Brain

Natural Rewards Elevate Dopamine Levels



Di Chiara et al., Neuroscience, 1999., Fiorino and CRHIII 2013

Drugs Elevate Dopamine Levels More/Longer



Source: Di Chiara and

The Neuron: How the Brain's Messaging System Works



dopamine

dopamine receptor

A PARTICULAR CONTINUE



dopamine transporters





Dopamine Receptors Lower in Addiction



Cocaine



Alcohol



Heroin



CRITÆTT 2013 CONTROL

addicted

Cutting Edge Research: Brain Changes Leading to Cocaine Addiction



Increased interaction between proteins in the nucleus accumbens may result in enhanced responsiveness (reward) to cocaine.

Bonci, et al (2013), Cell

2. Memory circuit

Amyg MEMORY/ LEARNING

Hipp

"People, places and things..."

Cocaine Craving: Population (Cocaine Users, Controls) x Film (cocaine)



Cocaine Craving:

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



Even Unconscious Cues Can Elicit Brain Responses

Activations



Brain Regions Activated by 33 millisecond cocaine cues (too fast for conscious recognition)

Childress, et al., PLoS ONE 2008 3. Motivation & Executive Control Circuits

> Dopamine is also associated with motivation and executive function via regulation of frontal activity.

EXECUTIVE

FUNCTION

INHIBITORY

CONTROL

PIC

ÓFC

MOTIVATION

DRIVE

The fine balance in connections that normally exists between brain areas active in reward, motivation, learning and memory, and inhibitory control



Becomes severely disrupted in ADDICTION



Addiction is Treatable

Partial Recovery of Brain Dopamine Transporters in Abuser After Protracted Abstinence



Behavioral Treatments

Non-Addicted Brain	Interfere with drug's reinforcing effects	Contingency Management
Contro	Executive function/ Inhibitory control	Cognitive Therapy
Saliency Drive STOP	Strengthen prefrontal- striatal communication	<i>Motivation</i> Therapies
	Interfere with conditioned memories	Biofeedback Desensitization
Memory	Teach new memories	Behavioral Therapies
CRIT/FIT 2	Counteract stress responses that lead to relapse	Relaxation Behavioral therapies

Medication Assisted Treatments

Non-Addicted Brain	Interfere with drug's reinforcing effects	Vaccines Enzymatic degradatio Naltrexone DA D3 antagonists CB ₁ antagonists
Contro	Executive function/ Inhibitory control	Biofeedback Modafinil Bupropion Stimulants
Saliency Drive STOP	Strengthen prefrontal- striatal communication	Adenosine A2 antagonists DA D3 antagonists
	Interfere with conditioned memories	Antiepileptic GVG N-acetylcysteine
Memory	Teach new memories	Cycloserine
CRIT/FIT 2	Counteract stress responses that lead to relapse	CRF antagonists Orexin antagonists

Vivitrol Significantly Increases % of Patients with Opioid-free Weeks



A Double-Blind RCT of N-Acetylcysteine in Cannabis-Dependent Adolescents

Proportion of Negative Urine Cannabinoid Tests Over Time Among Cannabis-Dependent Adolescents



Extended-Release Mixed Amphetamine Salts and Topiramate for Cocaine Dependence



Combination of MAS-ER and topiramate was superior to placebo in achieving 3 week abstinence in cocainedependent individuals Mariani et al., Biol Psychiatry 2012

Genetic Variability and Personalized Treatment



Anti- Drug Vaccine Development



Antibody holds drug in blood stream

Cutting Edge Research: Targeted Stimulation of the Pre-frontal Cortex as a Promising Treatment for Cocaine Addiction



<u>Optogenetic</u> stimulation results in: <u>- reduced</u> cocaine-seeking in addicted rats - <u>increased</u> cocaine seeking in non-addicted rats

-Evidence for a cocaine-induced deficit within a brain region involved in addictive disorders

-Rapid translation to clinical human trials via noninvasive brain stimulation

Chen, et al (2013), Nature

Translating Research into Practice



Receipt of SUD Services Lags Behind other Chronic Disorders



Low Uptake of Pharmacotherapy in Specialty Programs in 2007

	As % of all programs surveyed (N=345)	Within adopting programs, % of eligible patients receiving Rx
Psychiatric meds	54.5	70.1
<u>Opioid tx meds:</u>		
Methadone	7.8	41.3
Buprenorphine	20.9	37.3
Tablet naltrexone	22.0	10.9
Alcohol meds:		
Disulfiram	23.8	8.1
Tablet naltrexone	32.2	12.4
Acamprosate	32.5	17.5
Injectable naltrexone	15.9	(too new to report)

Knudsen et al, 2011, J Addict Med; 5:21-27

National Drug Abuse Treatment Clinical Trials Network (CTN)

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



Medications and Criminal Justice Populations

Methadone Experiment: 6 Mo Post Release (N=201)



+-- signif. diff from referral
★-- signif. diff from treatment only on release

Source: Gordon, M.S., Kinlock, T.W., Schwartz, R.P., O'Grady, K.E. (2008). Addiction. A Randomized Clinical Trial of Methadone Maintenance for Prisoners: Findings at 6-Months Post-Release.

Affordable Care Act (ACA)

- Extends coverage to more than 30 million persons, many at high risk for drug abuse
- Promotes use of electronic health records
- Fundamentally changes the ways drug abuse prevention and treatment services are financed
- Focuses on screening and prevention
- Emphasizes central role of primary care settings

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HAART as HIV Prevention



NIDA Avant Garde 2008: Dr. Julio Montaner, Univ. of British Columbia



Figure 1: Number of active HAART participants and number of new HIV diagnoses per year in British Columbia, Canada, 1996-2009 p values are for trend and were obtained from the generalised additive model. Injecting drug user (IDU) refers to individuals who have ever injected illicit drugs. HAART=highly active antiretroviral therapy. BC=British Columbia. *We* = 10 : ave ill a Me.

Montaner et al., Lancet 2008

NIDAMED

- Centers of Excellence
 - Boston University
 - Drexel/University of Pennsylvania
 - University of Massachusetts
 - Tufts University
 - University of North Dakota
 - Creigton University
- Screening tools
- CMEs on prescription drug abuse



Talking to Your Patients About Opioids CME/CNE programs from NIDA and Medscape LLC*



Managing Pain Patients Who Abuse Rx Drugs



Interactive case-based programs including video demonstrations of clinician-patient conversations.

Visit: www.drugabuse.gov/nidamed



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Drugabuse.gov