Neurobiology of Addiction

JeanAnne Johnson Talbert,
DHA, APRN-BC, FNP, CARN-AP
FPMHNP(s)

Disclosures

• None
Objectives

• Define drug addiction
• Identify the neurotransmitter systems that mediate the reinforcing effects of drugs
• Explain the fundamental changes that occur in the brain with addiction

What is Addiction?

• Narcissistic? Antisocial? Poor decision makers?

• Changes in the DSM
  • IV-TR differentiated between abuse and dependence
  • 5 clusters it as Substance Use Disorder

• The term “Addiction” is sloppy
  • Chocolate
  • TV shows
  • Exercise
Degrees of Use

- Occasional, controlled
  - “Social”
- Abuse or harmful use
- Addiction

- A person may fluctuate or “get stuck” in one of these categories

Why do we use?

- To *Feel Good* and/or To *Feel Better*
  - Fit in
  - Escape, Relax
  - Relieve boredom
  - Rebel
  - Experiment
  - “Spiritual” or “Intellectual” Reason
  - Self-Medication
Disease Progression

• Does abuse evolve into addiction? “Pre-Addiction?”
  • Some people are “instantly addicted”
  • Some people become addicted during the first year of use
  • Some abusers never become addicted
• Estimated lifetime prevalence risk
  • Nicotine 32%
  • Heroin 23%
  • Cocaine 17–20%
  • Alcohol 15%
  • Cannabis 9%
  • Analgesic opioids 9%

Contributions to Addiction

• Genetic Factors

• Environmental Factors

• Age of Onset

• Protective Factors
Abuse/ Addiction in the U.S.

- >22 million Americans have abuse/addiction problem
  - No discrimination as to race, gender, socioeconomic status, age
- Tobacco, Alcohol and Illegal drugs
  - $524 billion a year spent
- 15- 20% of patients have alcohol/ drug abuse and addiction disorders
- 20% of Medicaid hospital costs and 25% of Medicare hospital costs are associated with substance abuse
- Economic burden is twice as much as any other disease affecting the brain

Addiction/ Brain Disease
(Substance Use Disorder per DSM 5)

- Compulsion to seek and take a drug/ substance
- Loss of control in limiting the intake of the substance
- Negative emotional and/or physiological state if access to the substance is prevented
- Progressive disease with chronic relapses
- Shifts from an impulse control disorder involving positive reinforcement to a compulsive disorder involving negative reinforcement
What are we really talking about today? (Neurobiology)

• What happens in the brain to cause an addicted person to lose control? Especially when there is serious drug related consequences?

• Why are relapses in drug use so common, even in people who have years of abstinence?

Movie Clip

• Losing Isaiah
Brain Basics

- The Brain…
  - Tells us who we are, what we are doing, what we have done
  - Controls basic and critical body functions
    - HR, B/P, breathing
  - Extremely complex
    - Thousands of different kinds of nerve cells
- **Plasticity**
  - Changes in response to experience
  - Excitatory and Inhibitory influences

Brain Function

- Neurons
  - Information is stored
  - Feelings are sensed
  - Actions are initiated
  - Held together by cell membrane (lipids and proteins)
  - Action potentials = action
- Synapse
  - Presynaptic region
  - Postsynaptic region
  - Neurotransmitters
- Drugs
  - Act at presynaptic terminal or postsynaptic membrane on the neurotransmitter receptor
Your Brain on Drugs in the 1980’s
Neuroimaging and Neurobiology

- PET, SPECT, MRI, EEG
- Useful in drug investigation
  - Determine the drug distribution in the body
  - Measure local concentration of drug at binding sites
  - Estimate receptor occupancy based on competitive binding assays
  - Evaluate the effects of drugs on neurotransmitters
  - Investigate activity of enzymes that metabolize drugs

Your Brain on Drugs Today

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

Powier et al., Synapse, 1989
Brain of the Typical Male

The Female Brain

FOOTNOTE: The "Put Oil into the Car" and "Be Quite During the Game" glands are active only when the "Shiny Things and Diamonds" olfactory has been satisfied or when there is a shoe sale.
Neurobiology of Addiction

• Most progress derived from study of animal models of addiction
  • Focused on specific drugs
    • Opiates
    • Psychostimulants
    • Alcohol
  • Synaptic sites and transductive mechanisms in nervous system
    • Positive effects
    • Negative effects
    • Craving stage
Impulsivity and Compulsivity

- **Impulsivity**
  - Increase in sense of tension or arousal before committing an impulsive act
  - Pleasure, gratification or relief at the time of committing the act
  - Regret, self-reproach, or guilt following the act
- **Compulsivity**
  - Anxiety or stress before committing a compulsive, repetitive behavior
  - Relief from stress by performing the behavior

Stages of Addiction

- Progresses from impulsivity to compulsivity in a 3 stage cycle:
  - Binge/ intoxication
  - Withdrawal/ negative affect
  - Preoccupation/ anticipation
  - Drive shifts from positive to negative reinforcement
  - Impulsivity and Compulsivity coexist in different stages of addiction cycle
Binge/Intoxication Stage

- Positive Reinforcing Effects
- Activation of Reward Systems
- Basal Forebrain Interaction
- Neurotransmitters/neuromodulators
  - Dopamine, opioid peptides, GABA, serotonin, endocannabinoids
Nucleus Accumbens

- Critical to learning, reward and motivation
- Everyday activities produce increases in the Nucleus Accumbens
  - Food
  - Relationships
  - Sex

- Pleasurable feelings reinforce the behavior so it will be repeated
Natural Rewards Elevate Dopamine Levels

Effects of Drugs on Dopamine Release

Amphetamine

Cocaine

Nicotine

Morphine
Other Neurotransmitters Involved

- Serotonin
  - Mood, sleep
- Opioid Peptides
  - Pain, GI system, Mood
- Cannabinoids
  - Mediation of synaptic traffic
- Norepinephrine
  - Arousal, dreaming, moods, blood pressure, heart rate
- Acetylcholine
  - Muscle contraction
- Glutamate and GABA
  - Learning and memory
- Corticotropin Releasing Factor (CRF)
  - Stress
Thus, drugs are associated with neurotransmitters

- Assume that genetics + drug use = dysregulations of neurotransmitter systems
- As people use, the drugs “connect” to specific dysregulated neurotransmitter system
  - May be why people have “drugs of choice”
- Multiple dysregulations could explain co-dependence on several drugs
Drugs of Choice and Neurotransmitters

- Amphetamines, cocaine, ETOH
  - Dopamine, Serotonin
- Opioids, ETOH
  - Endorphins
- Nicotine, ETOH
  - Acetylcholine
- Benzos, ETOH
  - GABA
- Marijuana, ETOH
  - Endocannabinoids

- Don't judge
Stage 2: Withdrawal/ Negative Affect

- Integration of arousal-stress systems with reward pathway
- Extended Amygdala
- Nucleus Accumbens

Anti-Reward System

- Within-system adaptation
  - Adaptation to the cellular response following drug intake
    - Decreases in dopaminergic transmission
    - Increased sensitivity of opioid receptor transductions
    - Decreased GABA transmission
- Between-system adaptation
  - Chronic activation of the reward system results in dysregulation of other neurochemical systems
    - Recruitment of the brain stress system (CRF)
    - Synaptic plasticity
Functionally...

Dopamine D2 Receptors are Decreased by Addiction

Dopamine Transporters in Methamphetamine Abusers

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.

NIDA

What does Stage 2 look like?

• Tolerance develops
  • Rewarding capacity decreases
  • Consumption of larger amounts of drugs does not increase reward
  • Motivation for the use increases
• Withdrawal Symptoms
  • Anxiety
  • Pain
  • Sleep disturbance
  • Loss of motivation for natural rewards
  • Malaise
  • Dysphoria
  • Irritability
• Compromised social, occupational or recreational activities
• Craving

Stage 3: Preoccupation/ Anticipation

• Where does the loss of control come from?
  • Orbitofrontal cortex changes
  • Anterior cingulate gyrus changes
  • Cognitive impairment / Prefrontal Cortex changes
  • Stress

• Craving

• Relapse
Pickles

- Once a cucumber becomes a pickle, it is no longer a cucumber

- Some cucumbers never become pickles
  - Why do some people become addicted to drugs while others do not?
    - Vulnerability
      - Interaction of the person’s biology, environment and age
Genetics

- 40% - 60% of the predisposition to addiction is genetic

- Increases when combined with exposure, environmental factors and exposure to stress
But....

- Substance abusers experience higher rates of other comorbid mental illness compared to the general population
  - Psychosis
  - Depression
  - Anxiety
  - Panic Attacks
Environmental Factors

• Stress
• Early abuse (physical or sexual)
• Witnessing violence
• Peers who use drugs
• Drug availability

Addiction is a **Chronic Disease**…

• Biological *and* behavioral components

• Recovery is *long term*
  • Often requires repeated episodes of treatment

• *Relapses occur*
  • During or after treatment
  • Treatment may need to be reinstated or adjusted
Continued Treatment is Critical

Normal Control  Meth user (1 month abstinent)  Meth user (36 months abstinent)

Relapse Rates Are Similar for Drug Addiction & Other Chronic Illnesses

Percent of Patients Who Relapse

- Drug Addiction: 40-60%
- Type I Diabetes: 50-70%
- Hypertension: 20-70%
- Asthma: 20-70%

McCallan et al., JAMA, 2000
Where do we go from here?

- Research
  - Continue to advance science for prevention and treatment

- Education
  - Erase the stigma of addiction as a poor choice, narcissistic, antisocial behavior
  - Understand the severity and chronicity of the brain disease

Thank You!
References


Post Presentation Questions

1. Define drug addiction.

2. Addiction is a relapsing disorder with roots in __________________ and __________________.

3. Name the 3 stages of addiction.

4. What neurotransmitter is associated with the Reward Pathway?
1. Define drug addiction. Compulsion to seek and take drugs despite negative consequences; loss of control in limiting intake; if access is prevented, negative emotional and physical state occur.

2. Addiction is a relapsing disorder with roots in Impulsivity and Compulsivity.

3. Name the 3 stages of addiction. Binge/Intoxication; Withdrawal; Preoccupation/Anticipation.

4. What neurotransmitter is associated with the Reward Pathway? Dopamine.