Introduction to Addictions: 
Substances of Misuse, Mechanisms of Action, and Implications for the Legal Community

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Acknowledgments & Disclosures

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- Dr. Suzanne Thomas, Ph.D.
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Goals and Objectives

• Review genetics of addiction

• Understand basic neurobiological principles of addiction

• Discuss common substances of misuse

• Highlight basic mechanisms of addiction related to each specific substance

• Discuss implications of addiction to society, treatment options, and implications for the legal community
Genetics Review 101

- DNA
- Genes
- Variability
- Heritability

The body is made of cells. Cells contain DNA. Genes are made of DNA, and they make proteins.

https://www.cincinnatichildrens.org/service/d/diagnostic-labs/molecular-genetics/whole-exome-sequencing/families
Genetic Mechanisms: Cystic Fibrosis

Health Problems with Cystic Fibrosis

- Sinus Problems
- Nose Polyps (growths)
- Frequent lung infections
- Salty sweat
- Enlarged heart
- Trouble breathing

Genetic Mechanisms: Cystic Fibrosis

Inheritance of Cystic Fibrosis

Parents

Father: a carrier of CF gene
Mother: a carrier of CF gene

Children

Child healthy
Child a carrier of CF gene
Child a carrier of CF gene
Child with Cystic Fibrosis

Genetic Mechanisms of Addiction

- Altered Metabolism of a drug
  - Alcohol, Nicotine
- Altered function of a drug receptor
  - Nicotine
- General Mechanisms of Addiction
  - Stress Response, Emotion, Behavioral Control
Epigenetics

- Functional and inherited changes
- Expression does not depend on gene sequence
- Histones

Genetics and Addiction

- Major forms of substance dependence are heritable
  - Alcohol
  - Nicotine
  - Opioid
  - Cocaine

- Genes influencing heritable traits can be identified

- Gene-by-environment interaction is an important area of research
Neurobiology of Addiction
Neurobiology of Addiction: Dopamine Transmission
Neurobiology of Addiction

Neurobiology of Addiction

The Limbic System

The **Limbic System** is a doughnut-shaped system of neural structures at the border of the brainstem and cerebrum, associated with emotions such as fear, aggression and drives for food and sex. It includes the hippocampus, amygdala, and hypothalamus.

https://www.google.com/search?q=hijacking+of+limbic+system&source=lnms&tbm=isch&sa=X&ved=2ahUKEwj797RjtZ9hA沃尔VoTbKHckaCBoQ_AUIDigB&biw=1920&bih=934#imgrc=-V6hjWyvzC_zUM
Neurobiology of Addiction: Hijacking of Limbic System
Neurobiology of Addiction

- Liking
- Wanting
- Needing

Repeated use over time
Substances of Misuse

- Alcohol
- Cannabis
- Cocaine
- Methamphetamine
- Opioids
- Fentanyl
- Carfentany
- Heroin
- Kratom
- Inhalants
- MDMDA
- Tobacco
- E-Cigarettes
- Bath Salts
- Flakka
- Hallucinogens
Alcohol

- In 2016, 6.6% of the US adult population reported heavy alcohol use.
- In 2010, alcohol-related costs in the US were 249 billion.
- Leading cause of alcohol-associated deaths are cardiovascular disease and diabetes.
Alcohol

- Nearly 50% of Alcohol Use Disorder (AUD) is heritable with other 50% contributed by environmental factors

- Environmental Factors
  - Physical, Verbal, Sexual Abuse
  - Household Instability
    - Physical violence towards mother
    - Parental psychiatric illness
    - Incarceration of household members

- Environmental factors can further exacerbate a biological predisposition for AUD
Alcohol

- Rewarding aspects of alcohol are mediated through mesolimbic dopamine system
- GABA
- Glutamate
- Endogenous Opioids
- Cannabinoids
- Norepinephrine
- Hypothalamic-Pituitary-Adrenal Axis
Alcohol Use: What is Typical?

- National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines alcohol use based on a “standard drink.”
  - Men: no more than four drinks in one day AND no more than 14 drinks per week
  - Women: no more than three drinks in one day and no more than seven drinks per week
- Note this recommendation is also for all men and women over the age of 65.

Reference: niaaa.nih.gov
Alcohol: What is a Standard Drink?

Reference: niaaa.nih.gov
What is Binge Drinking?

- National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines binge drinking as “a pattern of drinking that brings blood alcohol concentration (BAC) levels to 0.08 g/dL.
  - Typically after four standard drinks in women or five standard drinks in men within a two hour timeframe.

- SAMHSA defines binge drinking as five or more alcohol drinks for males or four or more alcoholic drinks for females on the same occasion (i.e., at the same time or within two hours) on at least one day in the past month.

Reference: niaaa.nih.gov
Alcohol and Health

- Detox from alcohol can result in medical complications
  - Seizures
  - Delirium Tremens

Reference: niaaa.nih.gov

http://americanaddictioncenters.org/withdrawal-timelines-treatments/alcohol/
Cannabis

- Most commonly used illicit substance in the United States

- Estimated that 4.3 million people have used marijuana at levels consistent with alcohol use disorder over the past year

- Estimated 188 million recreational users in 2017 (worldwide)

- More than two-fold increase in potency of cannabis over the past decade

- Highest prevalence among young adults and males
Cannabis

- **Cannabis Sativa**
  - Dried flowers

- **Joints**
  - Hand-rolled cigarette

- **Bongs**
  - Water pipe

- **Blunts**
  - Marijuana rolled into cigar wrap

- **Edibles**
  - Brownies, cookies, candies
Cannabis

- Delta-9-Tetrahydrocannabinol (THC)
  - Main psychoactive chemical

- 500 other chemicals

- 100 compounds chemically related to THC
  - Cannabinoids
Cannabis

- THC binds to endocannabinoid 1 (CB1) receptor
- Abnormal functioning of CB1 rich brain areas is linked to increased use
- Impairment in memory, concentration, motivation, self-esteem, interpersonal relationships, health, employment, or finances
  - 2011, 456,000 ER visits
When marijuana is smoked, its active ingredient, THC, travels throughout the body, including the brain, to produce its many effects. THC attaches to sites called cannabinoid receptors on nerve cells in the brain, affecting the way those cells work. Cannabinoid receptors are abundant in parts of the brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgment, and pleasure.
Genetic Variations in COMT Influences the Harmful Effects of Abused Drugs

Percent with schizophreniform disorder at age 26

- No adolescent marijuana use
- Adolescent marijuana use

COMT genotype

<table>
<thead>
<tr>
<th>Genotype</th>
<th>No adolescent marijuana use</th>
<th>Adolescent marijuana use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Met/Met</td>
<td>4 (151)</td>
<td>3 (48)</td>
</tr>
<tr>
<td>Val/Met</td>
<td>2 (311)</td>
<td>1 (91)</td>
</tr>
<tr>
<td>Val/Val</td>
<td>4 (148)</td>
<td>3 (54)</td>
</tr>
</tbody>
</table>
Cocaine

- Blow, Coke, Crack, Rock, Snow
- Coca Plant
- Mixed with amphetamine or synthetic opioids
- Cornstarch, Talcum Powder, Flour
Cocaine

- Intranasal use of powder cocaine or rubbed into gums
- Inject into bloodstream
- Smoke rock crystal cocaine
  - Freebase Cocaine
Cocaine increased dopamine in reward circuitry of the brain

- Extreme happiness and energy
- Mental alertness
- Hypersensitivity to sight, sound, and touch
- Irritability
- Paranoia
# Cocaine

**National Survey on Drug Use and Health: Trends in Prevalence of Various Drugs for Ages 12 or Older, Ages 12 to 17, Ages 18 to 25, and Ages 26 or Older; 2018 (in percent)***

<table>
<thead>
<tr>
<th>Drug</th>
<th>Time Period</th>
<th>Ages 12 or Older</th>
<th>Ages 12 to 17</th>
<th>Ages 18 to 25</th>
<th>Ages 26 or Older</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocaine</td>
<td>Lifetime</td>
<td>14.70</td>
<td>0.70</td>
<td>11.40</td>
<td>16.80</td>
</tr>
<tr>
<td></td>
<td>Past Year</td>
<td>2.00</td>
<td>0.40</td>
<td>5.80</td>
<td>1.60</td>
</tr>
<tr>
<td></td>
<td>Past Month</td>
<td>0.70</td>
<td>0.00</td>
<td>1.50</td>
<td>0.70</td>
</tr>
<tr>
<td>Crack Cocaine</td>
<td>Lifetime</td>
<td>3.40</td>
<td>0.10</td>
<td>1.00</td>
<td>4.10</td>
</tr>
<tr>
<td></td>
<td>Past Year</td>
<td>0.30</td>
<td>0.00</td>
<td>0.30</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>Past Month</td>
<td>0.20</td>
<td>^</td>
<td>0.10</td>
<td>0.20</td>
</tr>
</tbody>
</table>

* indicate low precision; no estimate reported.
Methamphetamine

• **Stimulant**
  • Commonly referred to as blue, crystal, ice, meth, and speed

• **Methods of Use:**
  • Smoking
  • Swallowing
  • Snorting
  • Injecting
Methamphetamine (green) fools the cell into dumping dopamine (red) into the synapse, causing a surge of exhilaration.
Methamphetamine

• **Short-Term Effects:**
  - Increased wakefulness
  - Decreased appetite
  - Faster breathing
  - Rapid heartbeat
  - Increased blood pressure

• **Long-Term Effects:**
  - Dental issues
  - Itching
  - Violent behavior
  - Paranoia, Psychosis
Opioids

- Naturally found in opium poppy plant
- Prescription Opioids:
  - Hydrocodone, Oxycodone, Oxymorphone, Codeine, Fentanyl
- Opioids bind to the opioid receptors located in the brain, spinal cord, and other parts of the body
# Opioids

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug name</th>
<th>Brand names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural opiates</td>
<td>Morphine</td>
<td>AVINza, Kadian, MS-Contin, Ora-morph</td>
</tr>
<tr>
<td>Alkaloids in the opium poppy plant</td>
<td>Codeine, Thebaine (also called paramorphine)</td>
<td></td>
</tr>
<tr>
<td>Semi-synthetic opioids</td>
<td>Hydrocodone</td>
<td>Lortab and Vicodin (with acetaminophen)</td>
</tr>
<tr>
<td>Created from natural opiates</td>
<td>Hydromorphone, Oxycodone</td>
<td>Dilaudid, Exalgo, OxyContin, Roxicodone, Percocet and Tylox (with acetaminophen), Percodan (with aspirin), Opana, Butrans</td>
</tr>
<tr>
<td>Fully synthetic opioids</td>
<td>Fentanyl</td>
<td>Duragesic, Fentora, Onsolis, Demerol, Diskets, Dolophine, Methadose, ConZip, Rybix ODT, Ryzolt, Ultrim</td>
</tr>
<tr>
<td>Chemically made</td>
<td>Meperidine, Methadone, Tramadol</td>
<td></td>
</tr>
</tbody>
</table>
Opioids

**MORPHINE**
Opioid
Opiate
(Occurs naturally)

**HEROIN**
Opioid
Opiate
(Synthetic)

**FENTANYL**
Opioid
(Synthetic)

**TRAMADOL**
Opioid
(Synthetic)
Fentanyl

- Powerful synthetic opioid
- 50-100x more potent than morphine
- Prescription Forms:
  - Actiq, Duragesic, Sublimaze
- Street Names:
  - Apache, China Girl, China White, Dance Fever, Friend, Goodfella, Jackpot, Murder 8, TNT, Tango, Cash
Carfentanyln: “Elephant Tranquilizer”

- Analog of Fentanyl
  - Carfentanyl, Carfentanil
  - Wildnil

- Potency 10,000x stronger than Morphine and 100x stronger than Fentanyl

- Large Animal Tranquilizer
Carfentanylin the News

https://youtu.be/9pGZLx9_Fnc

September 22, 2016
Contact: National Media Affairs Office
Phone Number: (202) 307-7977

FOR IMMEDIATE RELEASE

DEA Issues Carfentanil Warning To Police And Public

Dangerous opioid 10,000 times more potent than morphine and 100 times more potent than fentanyl

WASHINGTON - DEA has issued a public warning to the public and law enforcement nationwide about the health and safety risks of carfentanil. Carfentanil is a synthetic opioid that is 10,000 times more potent than morphine and 100 times more potent than fentanyl.
Carfentanyln in the News

What is ‘gray death’ and is it in Horry County?

By Stephanie Pedersen

spedersen@thesunnews.com

JULY 21, 2017 12:01 PM
Heroin

- Made from morphine
- Inject, Sniff, Snort, Smoke heroin
- Heroin binds to opioid receptors and can produce euphoria, sedation, respiratory depression, and cognitive dulling
Kratom

- Tropical tree with leaves from Southeast Asia
  - Mitragynine
  - 7-a-hydroxymitragynine

- Not currently illegal in the US

- Green powder, extract, or gum

- Most use as a pill, extract, or capsule
Kratom

- Produces similar effect to opioids and stimulants
- Nausea, itching, sweating, dry mouth, constipation, increased urination, loss of appetite, seizures, hallucinations
Inhalants

- Solvents
- Aerosol Sprays
- Gases
- Nitrites
Inhalants

- Approximately 21.7 million American 12 and older have used inhalants at least once in their life
- Spray paints, markers, glues, cleaning fluids
- Sniffing, snorting, bagging, or huffing
- Inhalants act on the central nervous system and can produce symptoms similar to alcohol intoxication
  - Slurred speech
  - Poor coordination
  - Euphoria
  - Dizziness
MDMA

- Ecstasy, Molly

- Produces increased energy, pleasure, emotional warmth, and distorted sensory and time perception

- Usually taken as capsule or tablet
MDMA

- Dopamine
  - Reward System

- Norepinephrine
  - Increased heart rate, BP

- Serotonin
  - Mood, appetite, sleep, sexual arousal, trust
Tobacco

- Nicotine is absorbed into the bloodstream
- Stimulates adrenal glands to produce epinephrine
- Nicotine also activates dopamine in the brain
E-Cigarettes

- Electronic Nicotine Delivery Systems

- Elements of an E-Cigarette:
  - Cartridge
  - Heating Element
  - Power Source
  - Mouthpiece

- Most commonly used form of tobacco among US youth
E-Cigarettes

- Absorbed from the lungs into the bloodstream
- Similar to cigarettes
- Exposure of the lungs to various chemicals
- Recent outbreak
Bath Salts

- Synthetic cathinones
- Khat plant
  - Grown in East Africa and southern Arabia
- White or brown crystal powder
- Common Names:
  - Bliss, Cloud nine, Lunar Wave, Vanilla Sky, White Lightning
Bath Salts

- **Methods of Delivery:**
  - Swallow
  - Snort
  - Smoke
  - Inject

- Chemically similar to MDMA and cocaine
  - Increased levels of dopamine

- **Health Effects:**
  - Paranoia
  - Hallucinations
  - Panic Attacks
  - Excited Delirium
Bath Salts in the News

- https://www.youtube.com/watch?v=bXo-oIFj8Ys&oref=https%3A%2F%2Fwww.youtube.com%2Fwatch%3Fv%3DbXo-oIFj8Ys&has_verified=1
Flakka

- Form of bath salt
  - Synthetic Cathinone
  - Alpha-Pyrrolidinopentiophenone (Alpha-PVP)

- Inexpensive
  - One dose may cost as little as $5

- Health Effects:
  - Excited delirium
  - Agitation
  - Elevated heart rate
  - Hallucinations
  - Paranoia
Flakka in the News

Live 5 Investigates: Flakka in Colleton County

By Karina Bolster | November 18, 2015 at 12:15 AM EST - Updated July 25 at 2:50 PM
Hallucinogens

- Classic Hallucinogens
  - LSD
  - Psilocybin

- Dissociative Drugs
  - PCP
  - Ketamine
  - Dextromethorphan
# Hallucinogens

<table>
<thead>
<tr>
<th>Method</th>
<th>DMT</th>
<th>LSD</th>
<th>Peyote</th>
<th>Psilocybin</th>
<th>DXM</th>
<th>Ketamine</th>
<th>PCP</th>
<th>Salvia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swallowing as tablets or pills</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Swallowing as liquid</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Consuming raw or dried</td>
<td></td>
<td></td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Brewing into tea</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Snorting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Injecting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Inhaling, vaporizing, or smoking</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Absorbing through the lining in the mouth using drug-soaked paper pieces</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>
Hallucinogens

- Disruption of communication between brain and spinal cord
- Hallucinogens interfere with the action of serotonin
  - Mood
  - Sensory Perception
  - Sleep
  - Hunger
  - Body Temperature
  - Sexual Behavior
  - Intestinal Muscle Control
- Health Effects:
  - Increased heart rate
  - Nausea
  - Intense feelings and sensory experiences
  - Changes in sense of time
Diagnostic and Statistical Manual of Mental Disorders (DSM)
DSM-5 Substance Use Disorders

- Substance-related disorders encompass 10 separate classes of drugs:
  - Alcohol
  - Caffeine
  - Cannabis
  - Hallucinogens
  - Inhalants
  - Opioids
  - Sedatives, hypnotics, and anxiolytics
  - Stimulants (amphetamine-type substances, cocaine, and other stimulants)
  - Tobacco
  - Other (or unknown) substances.
Substance-Related Disorders

Two Categories:
- Substance Use Disorders
  - Formerly known as “abuse” or “dependence” diagnoses
  - Criteria involve the following groupings: impaired control, social impairment, risky use, and pharmacological criteria
  - Must have two or more criteria
- Substance-Induced Disorders
  - Intoxication
  - Withdrawal
  - Substance/Medication-induced Mental Disorders
Treatment of Substance Use Disorders

- Medication
  - Naltrexone, Antabuse
  - Suboxone, Methadone
- Therapy
  - Cognitive Behavioral Therapy
  - Motivational Interviewing
- 12-Step Community Treatment
Treatment: When to Get Help?

- Impairment
  - Work
  - Home
  - Interpersonal relationships

- Tolerance and Withdrawal
  - Using to feel “normal”

- Health-related consequences
  - Cirrhosis
  - Hypertension
Selected References

• National Institute on Drug Abuse (NIDA)

• Substance Abuse and Mental Health Services Administration (SAMHSA)

• Textbook of Substance Abuse Treatment, DSM-5 Edition

• DSM-5, American Psychiatric Association
Questions?

Contact: Lewiset@musc.edu