Drugs of Abuse: Stimulants, Marijuana, and Opiates

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Learning Objectives

1. List the common drugs of abuse and their mechanisms of action.
2. Review how drugs affect the brain and the body.
Classes of Drugs of Abuse

- Stimulants
- Caffeine
- Nicotine
- Cannabis
- Opioids
- Sedative-hypnotics
- Hallucinogens
- Dissociative Drugs
- “Club drugs”
- Anabolic Steroids
- Inhalants
Stimulants

- Examples:
  - Amphetamine (prototype)
  - Cocaine (most common, includes “crack”)
  - Methamphetamine (“crank,” “ice”)
  - Methylphenidate
  - Ephedrine
  - Khat

Stimulants

- All have sympathomimetic activity and cause euphoria
- Routes of administration: Oral, IN, IV, smoked
- Reinforcing effects are predominantly related to dopaminergic effects in the nucleus accumbens
- Tolerance and cross-tolerance occur
Stimulants

- Medical uses
  - Attention deficit disorder
  - Narcolepsy
  - Treatment resistant depression
  - Obesity (YIKES!)
  - Local anesthesia (cocaine)

Stimulant Intoxication and Withdrawal

- Intoxication:
  - Euphoria
  - Agitation and violence
  - Insomnia
  - Anorexia
  - Decreased dreaming
  - Tachycardia, arrhythmia
  - Hypertension
  - Dilated pupils
  - Paranoia, hallucinations
  - Hyperthermia
  - Seizure, stroke

- Withdrawal
  - Dysphoria
  - Lethargy
  - Hypersomnia
  - Hyperphagia
  - Increased dreaming
  - Bradycardia
  - Intense craving
Cocaine
Cocaine

- Tends to be used in a “binge/crash” pattern
- Medical complications:
  - Nasal congestion
  - Perforated nasal septum
  - Cardiac arrhythmias
  - Seizure, stroke
  - Psychosis
  - Cellulitis, endocarditis (IV use)
  - Hepatitis B and C, HIV infection
  - Suicide
  - Homicide

Cocaine

- Different forms and routes of administration
  - Cocaine HCL: snorted or injected
  - “Crack” or freebase: smoked
  - Coca leaf: chewed
  - Smoking produces high within seconds that lasts 20-30 minutes
  - Intense “crash” as effects of the drug wear off
Methamphetamine

Mechanism of action

- Four percent of the US population has tried Methamphetamine
- Use formerly restricted to certain areas of the country (San Diego, Hawaii, Texas)
- Increasing use in rural areas, including Southern Ohio
- Easily synthesized using OTC pills and other readily available reagents
Methamphetamine

- Used in “binge/crash” pattern
- Rapid onset of action when smoked.
- High lasts 12-14 hours
- Can cause long-lasting psychosis
- Can cause substantial damage to dopaminergic neurons with prolonged use, even in relatively low doses
- Severe “crash” after use

Treatment of Stimulant Withdrawal

- Stimulant withdrawal alone is psychologically uncomfortable, but not life threatening
- Pharmacological treatment of stimulant withdrawal is at best moderately helpful
- BUT, many individuals addicted to stimulants are also addicted to other drugs
- It may be necessary to treat withdrawal from other drugs in individuals who are stimulant dependent
Bath Salts: A New Epidemic

They are not really bath salts, they are just marketed that way—may also be marketed as plant fertilizer

They are labeled "not for human consumption," which helps them skirt the federal Analog Act, under which any substance "substantially similar" to a banned drug is deemed illegal if it is intended for consumption

Head shops/convenience stores/gas stations sell them

Bath salts swept Britain, which banned them in April 2010

Imported into United States through the Port of New Orleans via ships from India and China
Bath Salts A New Epidemic

- Earlier this year, the Drug Enforcement Agency listed MDPV as a "drug of concern."
- As of Sept 7, 2011, the DEA used it’s emergency authority to temporarily control MDPV and mephedrone.
- DEA and US Dept. of HHS deciding on whether permanently control these substances

Bath Salts A New Epidemic

- States that added synthetic cathinones to the controlled substances list as Schedule I drugs:
  - Alabama
  - Arkansas
  - Florida
  - Hawaii
  - Idaho
  - Illinois
  - Kentucky
  - Mississippi
  - North Dakota
  - Ohio (July 2011)
  - Oregon
  - Utah
  - Virginia
  - Washington
  - Wisconsin
  - Wyoming
**Bath Salts in Ohio**

- ELYRIA, Ohio - The first person in northeast Ohio has been charged under a new state law that makes it a crime to sell or possess a drug known as bath salts, as well as synthetic marijuana.
- House Bill 64 was signed in July 2011, making it a crime to sell or have bath salts.
  - It went into effect on Monday October 17, 2011.
- Allison Hughes, 30, became the first person arrested in Elyria under the bath salts law. Police said she was pulled over for a traffic stop and was caught with the salts.
- Elyria police said bath salts are becoming a growing problem.
  - "People jumping out of second story windows, just acting very irrational," said Lt. Eichenlaub.

**Bath Salts in Ohio (cont.)**

- The Kettering Medical Center in Dayton blamed five deaths on the substance already.
- "If you take PCP, cocaine, methamphetamines, and kind of wrap 'em up altogether, you have bath salts," said Pam Lamb with the Kettering Medical Center.
  - "They are paranoid, delusional. They have very extreme hallucinations. May see werewolves, may believe hospital staff is trying to harm them," said Lamb.
Methylenedioxypyrovalerone:

- Developed in the 60’s which was used for the treatment of chronic fatigue and as an anorectic
- Caused problems with dependency and abuse.
- MDPV, which is the most widely known ingredient in bath salts, acts as a stimulant with effects reportedly similar to cocaine

Methylenedioxypyrovalerone:

- These products can contain stimulant compounds such as 3,4-Methylenedioxypyrovalerone (MDPV) or 4-methylmethcathinone (mephedrone).
- Both drugs are related to khat, an organic stimulant found in Arab and East African countries that is illegal in the United States
Methylenedioxypyrovalerone:

- Methylenedioxypyrovalerone is a stimulant chemically related to methylphenidate (Ritalin) & methylenedioxymethamphetamine (Ecstasy).

- Acts as a norepinephrine and dopamine re-uptake inhibitor and has been compared with methylphenidate at low doses and cocaine at high doses.
Caffeine
Intoxication and Withdrawal

- Intoxication
  - Anxiety
  - Agitation
  - Motor restlessness
  - Insomnia
  - Tachycardia
  - Flushed face
  - Diuresis

- Withdrawal*
  - Dysphoria
  - Headache
  - Fatigue
  - Hypersomnia
  - Muscle tension
  - Nausea

*Not described in DSM-IV

Nicotine Intoxication and Withdrawal

- Intoxication*
  - Arousal
  - “Calm”
  - Appetite suppression
  - Tachycardia
  - Salivation
  - Dizziness

- Withdrawal
  - Insomnia
  - Anxiety
  - Irritability
  - Hyperphagia
  - Bradycardia
  - Difficulty concentrating

*Not described in DSM-IV
“I’m on too much medicine”

**Tobacco Use**

Interferes with metabolism of Rx

Need higher doses to get therapeutic effect

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Fact: Tobacco use interferes with the metabolism of many medications.

Psychotropics
- Haloperidol (Haldol)
- Olanzapine (Zyprexa)
- Chlorpromazine (Thorazine)
- Clozapine (Clozaril)
- Fluphenazine (Prolixin)
- Clomipramine (Anafranil)
- Imipramine (Tofranil)

- Desipramine (Norpramin)
- Nortriptyline (Pamelor/Aventil)
- Doxepin (Sinequan)
- Carbamazepine (Tegretol)
- Desmethyl Diazepam (Benzodiazapine)
- Oxazepam (Serax - Benzo)
**Fact:** Tobacco use interferes with the metabolism of many medications.

- Heparin (Blood Thinner)
- Acetaminophen (Tylenol)
- Insulin
- Caffeine (Your coffee)
- Theophylline

- Propranolol (Inderal – Beta blocker)
- Tacrine (Cognex)
- Warfarin (Cumadin)
- Others...ipramine

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**Tobacco use**

<table>
<thead>
<tr>
<th>Increased insulin resistance</th>
<th>Interferes w/ metabolism of Rx</th>
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<tr>
<td></td>
<td>Need higher dose of Rx</td>
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<td>Rx related to onset diabetes</td>
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<td>Weight gain</td>
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**Diabetes**
### Obesity

#### Tobacco Use
- Interferes with metabolism of Rx
- Higher dose of psychotropics needed
- Weight gain potential side effect of meds
- Sedation side effect of meds leads to inactivity

### Premature Death

#### Tobacco use
- Cardiovascular Disease / Respiratory Illnesses / Diabetes / Cancer / Accidents
- Death
Perceived “Positives” of Tobacco in SMI?

- Nicotine improves sensory gating and cognitive symptoms in schizophrenia acutely (short term)
- Nicotine acts as a monoamine oxidase inhibitor and COULD have antidepressant effects
- Implications for reduction/cessation

Williams and Ziedonis, 2006, Snyder, 2006

“Positives” of Tobacco in SMI?

- Tobacco itself is untested for all of these effects and its lethality is unquestionable. Much safer treatments are available.
- Long-term smoking causes appreciable cognitive decline, with decrease in memory, problem solving ability, thinking speed and even IQ
- Alcoholics who smoke have more cerebral atrophy than alcoholics who do not smoke

Marijuana

- Most widely used illicit drug in the U.S
- At least 30% of the population has tried marijuana (80 million people)
- Effects are often situation dependent
- Route of administration: Smoked, oral
- Active ingredient: delta-9-tetrahydrocannabinol (THC)
- Endogenous cannabinoid receptors have been identified
- Mild tolerance may develop, with some cross tolerance to alcohol
Cannabis Intoxication and Withdrawal

- Intoxication:
  - Euphoria
  - Sedation
  - Antiemetic
  - Hyperphagia
  - Memory deficits
  - Conjunctival injection
  - Ptosis
  - Tachycardia
  - Psychosis

- Withdrawal*:
  - Dysphoria
  - Anxiety
  - Insomnia
  - Nausea
  - Anorexia
  - Headache

*Not described in DSM-IV
Marijuana Withdrawal

Abstinence Elicits Aggressive Behavior in Long-Term Marijuana Smokers

Number of Aggressive Responses per Session

Marijuana
Potential Medical Uses

- Treatment of:
  - Nausea in chemotherapy patients
  - Wasting due to AIDS
  - Spasticity
  - Glaucoma
  - Pain syndromes
MARIJUANA IS NOT A HARMLESS DRUG!!!

- Can cause toxic psychosis
- Heavy users are more likely to develop schizophrenia
- Panic reactions
- Accidents: found in 10% of fatal accident victims
- Hastens age-related loss of hippocampal neurons
- Impairs immune function
- Increased risk of heart attack within an hour of smoking

MARIJUANA IS NOT A HARMLESS DRUG!!!

- Contains more carcinogens than tobacco (and marijuana smokers inhale deeper and hold longer)
- Bronchitis
- Increased risk of lung, head and neck cancers
- Substantial motivational and cognitive deficits
Overview: Synthetic Cannabinoids

- K2/Spice

“Spice” first appeared in Europe in 2004

- March 2011→ DEA bans 5 chemicals most commonly found in K2/Spice
  - JWH-018, JWH-073, CP-47,497, JWH-200, and cannabicyclohexanol

- DEA reports that increased use of synthetic marijuana has lead to a surge in ER visits and poison-control centers calls.

- Adverse health effects: seizures, hallucinations, paranoid behavior, agitation, anxiety, nausea, vomiting, racing heartbeat and elevated blood pressure
Opioids

- Opioid agonists:
  - Morphine
  - Heroin
  - Meperidine
  - Methadone
  - Propoxyphene
  - Oxycodone (including Oxycontin)
  - Hydrocodone
  - Hydromorphone
  - Diphenoxylate

- Opioid antagonists
  - Naloxone
  - Naltrexone

- Mixed Agonist/antagonist:
  - Buprenorphine

Opioids

- Opioid medications are invaluable in the treatment of acute, severe pain
- Opioid abuse and dependence have been problematic for centuries
- Main classes of opioid abusers:
  - Street (usually heroin) abusers
  - Medical abusers
  - Methadone patients
- Routes of administration: Oral, IV, IM, SC, IN, Smoking, PR
Opioids

- Effects are mediated through endogenous opioid receptors:
  - Mu: Analgesia, euphoria, respiratory depression, dependence
  - Kappa: Sedation, diuresis
  - Sigma: Dysphoria, hallucinations
  - Delta: Cardiovascular effects, analgesia
- Tolerance and cross-tolerance exist
Opioid Intoxication and Withdrawal

- **Intoxication**
  - Euphoria
  - Sedation
  - Slurred speech
  - Constipation
  - Analgesia
  - Decreased respirations
  - Attentional deficits

- **Withdrawal**
  - Dysphoria, anxiety
  - Insomnia
  - Diarrhea, nausea, vomiting
  - Muscle and joint pain
  - Diaphoresis
  - Chills
  - Piloerection
  - Tearing
  - Yawning

Treatment of Opioid Withdrawal

- Withdrawal is exceedingly uncomfortable, but not life-threatening
- **Clonidine:**
  - 0.1-0.3 mg tid to qid on day one, up to 1 mg/day
  - Up to 1.2 mg/day on day two
  - Maintain 5-10 days depending on drug half-life
  - Taper by 0.2 mg/day
  - Beware of hypotension, bradycardia, sedation
Treatment of Opioid Withdrawal

- Adjunctive medications for symptom relief:
  - NSAIDS for pain
  - Kaopectate or immodium for diarrhea
  - Hydroxyzine for anxiety or insomnia
  - Benzodiazepines can be used, if needed
  - Decongestants for rhinorhea
  - Phenergan for nausea and vomiting
  - Avoid using needles

Treatment of Opioid Withdrawal

- Methadone (requires special license)
  - Give enough methadone on day one to make the patient comfortable (rarely >30-40 mg)
  - Give test dose of 5-10 mg
  - If symptoms remain after 60 minutes, repeat dose
  - If necessary, give another dose 12 hrs later
  - Taper by 10 mg every 1-2 days
  - 40 mg of oral methadone can be fatal
  - Can also be used for maintenance through licensed clinics (dosage usually >60 mg daily)
Treatment of Opioid Withdrawal

- Buprenorphine
  - Approved for office-based treatment of opioid dependence in 2002
  - Form usually used in addiction treatment is combination of buprenorphine and naloxone (Suboxone)
    - Limits risk of abuse and toxicity in overdose
    - Requires certification of prescribing physician

Treatment of Opioid Withdrawal

- Buprenorphine protocol:
  - Patient should be in mild withdrawal and negative for methadone, then give:
    - Day 1: TWO 2mg/0.5mg Suboxone* tablet SL
    - Day 2: ONE 8mg/2mg Suboxone
    - Day 3: TWO 8mg/2mg Suboxone
    - Then decrease by 2mg of Suboxone every one-to two days until the patient is off the medication
  - Can also be used for maintenance, usually at a dose of 16mg/4mg daily

*First number reflects buprenorphine dose, second naloxone dose
Contact Information

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