Substance Related Disorders
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Objectives. At the end of this talk you will be able to:
- Identify the diagnostic criteria for substance-related disorders
- Describe the epidemiology of substance-related disorders
- Describe treatment options
- Discern intoxication/withdrawal of different substances
- Apply the information above to clinical cases

Substance Classes
- Alcohol
- Caffeine
- Cannabis
- Hallucinogens
  - PCP
  - others
- Inhalants
- Opioids
- Sedatives, hypnotics, and anxiolytics
- Stimulants
- Tobacco
- Other
- Gambling

Substance-Related Disorders
- 2 Groups:
  - Substance Use Disorders
    - Previously split into abuse or dependence
    - Involves: impaired control, social impairment, risky use, and pharmacological criteria
    - Substance-Induced Disorders
- Substance Use Disorder
  - Using larger amounts or for longer time than intended
  - Persistent desire or unsuccessful attempts to cut down or control use
  - Great deal of time obtaining, using, or recovering
  - Craving
  - Fail to fulfill major roles (work, school, home)
  - Persistent social or interpersonal problems caused by substance use

Substance Use Disorder
- Important social, occupational, recreational activities given up or reduced
- Use in physically hazardous situations
- Use despite physical or psychological problems caused by use
- Tolerance
- Withdrawal (not documented after repeated use of PCP, inhalants, hallucinogens)
Severity

-Severity
  - Depends on # of symptom criteria endorsed
  - Mild: 2-3 symptoms
  - Moderate: 4-5 symptoms
  - Severe: 6 or more symptoms

Specifiers

- Specifiers
  - In early remission: no criteria for > 3 months but < 12 months (except craving)
  - In sustained remission: no criteria for > 12 months (except craving)
  - In a controlled environment: access to substance restricted (ex. Jail)

Substance-Induced

- Intoxication
- Withdrawal
- Psychotic Disorder
- Bipolar Disorder
- Depressive Disorder
- Anxiety Disorder
- Sleep Disorder
- Delirium
- Neurocognitive
- Sexual Dysfunction

Intoxication

- Reversible substance-specific syndrome due to recent ingestion of a substance
- Behavioral/psychological changes due to effects on CNS developing after ingestion:
  - ex. Disturbances of perception, wakefulness, attention, thinking, judgement, psychomotor behavior and interpersonal behavior
- Not due to another medical condition or mental disorder
- Does not apply to tobacco

Clinical picture of intoxication depends on:

- Substance
- Dose
- Route of Administration
- Duration/chronicity
- Individual degree of tolerance
- Time since last dose
- Person’s expectations of substance effect
- Contextual variables

Withdrawal

- Substance-specific syndrome problematic behavioral change due to stopping or reducing prolonged use
- Physiological & cognitive components
- Significant distress in social, occupational or other important areas of functioning
- Not due to another medical condition or mental disorder
- No withdrawal: PCP; other hallucinogens; inhalants
**Substance-Induced Mental Disorder**

- Potentially severe, usually temporary, but sometimes persisting CNS syndromes
- Context of substances of abuse, medications, or toxins
- Can be any of the 10 classes of substances

**Substance-Induced Mental Disorder**

- Clinically significant presentation of a mental disorder
- Evidence (Hx, PE, labs)
  - During or within 1 month of use
  - Capable of producing mental disorder seen
- Not an independent mental disorder
  - Preceded onset of use
  - Persists for substantial time after use (which would not expect)

**Neuroadaptation:**

- Refers to underlying CNS changes that occur following repeated use such that person develops tolerance and/or withdrawal
  - Pharmacokinetic – adaptation of metabolizing system
  - Pharmacodynamic – ability of CNS to function despite high blood levels

**Tolerance**

- Need to use an increased amount of a substance in order to achieve the desired effect
- OR
- Markedly diminished effect with continued use of the same amount of the substance

**Epidemiology: Prevalence**

- NIDA ’04: 22.5M > 12yo – substance-related d/o 15M – Alcohol Dependence or Abuse
- Start at earlier age (<15yo), more likely to become addicted – ex. alcohol: 18% vs. 4% (if start at 18yo or older)
- Rates of abuse vary by age: 1% (12yo) - 25% (21yo) - 1% (65yo)
- Men; American Indian; whites; unemployed; large metro areas; parolees

**Epidemiology (cont.)**

- ETOH - $300 billion/year
- 13 million require treatment for alcohol
- 5.5 million require treatment for drug use
- 2.5% population reported using Rx meds nonmedically within past month
Epidemiology (cont.)

- 40% of hospital admission have alcohol or drugs associated
- 25% of all hospital deaths
- 100,000 deaths/year
- Intoxication is associated with 50% of all MVAs, 50% of all DV cases and 50% of all murders

ER Visits (NIDA ’09)

- 1.2M: non-medical use of pharmaceuticals
- 660K: alcohol
- 425K: cocaine
- 380K: marijuana
- 210K: heroin
- 93K: stimulants

Etiology

- Multiple interacting factors influence using behavior and loss of decisional flexibility
- Not all who become dependent experience it same way or motivated by same factors
- Different factors may be more or less important at different stages (drug availability, social acceptance, peer pressure VS personality and biology)

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Etiology

- “Brain Disease” – changes in structure and neurochemistry transform voluntary drug-using compulsive
- Changes proven but necessary/sufficient? (drug-dependent person changes behavior in response to positive reinforcers)
- Psychodynamic: disturbed ego function (inability to deal with reality)

Etiology

- Self-medication
  - EtOH - panic; opioids -anger; amphetamine - depression
- Genetic (well-established with alcohol)
- Conditioning: behavior maintained by its consequences
  - Terminate aversive state (pain, anxiety, w/d)
  - Special status
  - Euphoria
  - Secondary reinforcers (ex. Paraphernalia)

Etiology

- Receptors
  - Too little endogenous opioid activity (ie low endorphins) or too much endogenous opioid antagonist activity = increased risk of dependence.
  - Normal endogenous receptor but long-term use modulates, so need exogenous substance to maintain homeostasis.
- Neurotransmitters
  - Opioid
  - Catecholamines
  - GABA
  - Serotonin
- Pathways
Learning and Physiological Basis for Dependence

- After using drugs or when stop – leads to a depleted state resulting in dysphoria and/or cravings to use, reinforcing the use of more drug.
- Response of brain cells is to downregulate receptors and/or decrease production of neurotransmitters that are in excess of normal levels.

Comorbidity

- Up to 50% of addicts have comorbid psychiatric disorder
  - Antisocial PD
  - Depression
  - Suicide

Typical Presentation and Course:

- Present in acute intoxication, acute/chronic withdrawal or substance induced mood, cognitive disorder or medical complications
- Abstinence depends on several factors: social, environmental, internal factors (presence of other comorbid psychiatric illnesses)
- Remission and relapses are the rule (just like any other chronic medical illness)
- Frequency, intensity and duration of treatment predicts outcome
- 70% eventually able to abstain or decrease use to not meet criteria

Options for where to treat

- Hospitalization:
  - Due to drug OD, risk of severe withdrawal, medical comorbidities, requires restricted access to drugs, psychiatric illness with suicidal ideation
- Residential treatment unit:
  - No intensive medical/psychiatric monitoring needs
  - Require a restricted environment
  - Partial hospitalization
- Outpatient Program:
  - No risk of med/psych morbidity and highly motivated patient

Treatment

**Manage Intoxication & Withdrawal**

- Intoxication
  - Ranges: euphoria to life-threatening emergency
- Detoxification
  - outpatient: "social detox" program
  - inpatient: close medical care
  - preparation for ongoing treatment

**Behavioral Interventions (target internal and external reinforcers)**

- Motivation to change (MI)
- Group Therapy
- Individual Therapy
- Contingency Management
- Self-Help Recovery Groups (AA)
- Therapeutic Communities
- Aversion Therapies
- Family Involvement/Therapy
- Twelve-Step Facilitation
- Relapse Prevention
Treatment

- Pharmacologic Intervention
- Treat Co-Occurring Psychiatric Disorders
  - 50% will have another psychiatric disorder
- Treat Associated Medical Conditions
  - cardiovascular, cancer, endocrine, hepatic, hematologic, infectious, neurologic, nutritional, GI, pulmonary, renal, musculoskeletal

ALCOHOL- CNS depressant

- Intoxication
  - Blood Alcohol Level - 0.08g/dl
  - Progress from mood lability, impaired judgment, and poor coordination to increasing level of neurologic impairment (severe dysarthria, amnesia, ataxia, obtundation)
- Can be fatal (loss of airway protective reflexes, pulmonary aspiration, profound CNS depression)

Alcohol

Alcohol Withdrawal

- Early
  - anxiety, irritability, tremor, HA, insomnia, nausea, tachycardia, HTN, hyperthermia, hyperactive reflexes
- Seizures
  - generally seen 24-48 hours
  - most often Grand mal
- Withdrawal Delirium (DTs)
  - generally between 48-72 hours
  - altered mental status, hallucinations, marked autonomic instability
  - life-threatening

Alcohol Withdrawal (cont.)

- CIWA (Clinical Institute Withdrawal Assessment for Alcohol)
  - Assigns numerical values to orientation, N/V, tremor, sweating, anxiety, agitation, tactile/auditory/visual disturbances and HA. VS checked but not recorded. Total score of > 10 indicates more severe withdrawal
  - Based on severity of withdrawal or history of previous withdrawal seizures or DTs, med therapy can be scheduled or symptom-triggered

Alcohol Withdrawal (cont.)

- Benzodiazepines
  - GABA agonist - cross-tolerant with alcohol
  - reduce risk of SZ; provide comfort/sedation
- Anticonvulsants
  - reduce risk of SZ and may reduce kindling
  - helpful for protracted withdrawal
  - Carbamazepine or Valproic acid
- Thiamine supplementation
  - Risk thiamine deficiency (Wernicke/Korsakoff)
Alcohol treatment

➢ Outpatient CD treatment:
  • support, education, skills training, psychiatric and psychological treatment, AA

➢ Medications:
  • Disulfiram
  • Naltrexone
  • Acamprosate

Medications - ETOH Use Disorder

➢ Disulfiram (antabuse) 250mg-500mg po daily
  • Inhibits aldehyde dehydrogenase and dopamine beta hydroxylase
  • Aversive reaction when alcohol ingested - vasodilatation, flushing, NV, hypotension/HTN, coma / death
  • Hepatotoxicity - check LFT's and no hep C
  • Neurologic with polyneuropathy / paresthesias that slowly increase over time and increased risk with higher doses
  • Psychiatric side effects - psychosis, depression, confusion, anxiety
  • Dermatologic rashes and itching
  • Watch out for disguised forms of alcohol - cologne, sauces, mouth wash, OTC cough meds, alcohol based hand sanitizers, etc

➢ Naltrexone 50mg po daily
  • Opioid antagonist thought to block mu receptors reducing intoxication euphoria and cravings
  • Hepatotoxicity at high doses so check LFT's

➢ Acamprosate(Campral) 666mg po tid
  • Unknown MOA but thought to stabilize neuron excitation and inhibition - may interact with GABA and Glutamate receptor - cleared renally (check kidney function)

Medications - ETOH Use Disorder

Benzodiazepine (BZD)/ Barbiturates

➢ Intoxication
  • similar to alcohol but less cognitive/motor impairment
  • variable rate of absorption (lipophilia) and onset of action and duration in CNS
  • the more lipophilic and shorter the duration of action, the more "addicting" they can be
  • all can by addicting

➢ Withdrawal
  • Similar to alcohol with anxiety, irritability, insomnia, fatigue, HA, tremor, sweating, poor concentration - time frame depends on half life
  • Common detox mistake is tapering too fast; symptoms worse at end of taper
  • Convert short elimination BZD to longer elimination half life drug and then slowly taper
  • Outpatient taper - decrease dose every 1-2 weeks and not more than 5 mg Diazepam dose equivalent
    • 5 diazepam = 0.5 alprazolam = 25 clonazepam = 0.25 lorazepam = 1 lorazepam
  • May consider carbamazepine or valproic acid especially if doing rapid taper

Benzodiazepine

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Benzodiazepines

- Alprazolam (Xanax) t1/2 6-20 hrs
- Oxazepam (Serax) t1/2 8-12 hrs
- Temazepam (Restoril) t1/2 8-20 hrs
- Clonazepam (Klonopin) t1/2 18-50 hrs
- Lorazepam (Ativan) t1/2 10-20 hrs
- Chlordiazepoxide (Librium) t1/2 30-100 hrs (less lipophilic)
- Diazepam (Valium) t1/2 30-100 hrs (more lipophilic)

*Oxazepam, Temazepam & Lorazepam- metabolized through only glucuronidation in liver and not affected by age/hepatic insufficiency.

Opioids

- Bind to the mu receptors in the CNS to modulate pain
- Intoxication - pinpoint pupils, sedation, constipation, bradycardia, hypotension and decreased respiratory rate
- Withdrawal - not life threatening unless severe medical illness but extremely uncomfortable. s/s dilated pupils, lacrimation, goosebumps, n/v, diarrhea, myalgias, arthralgias, dysphoria or agitation
- Rx: symptomatically with antiemetic, antacid, antidiarrheal, muscle relaxant (methocarbamol), NSAIDS, clonidine and maybe BZDs
- Neuroadaptation: increased DA and decreased NE

Treatment - Opiate Use Disorder

- CD treatment
  - support, education, skills building, psychiatric and psychological treatment, NA
- Medications
  - Methadone (opioid substitution)
  - Naltrexone
  - Buprenorphine (opioid substitution)

Naltrexone
- Opioid blocker, mu antagonist
- 50mg po daily

Methadone
- Mu agonist
- Start at 20-40mg and titrate up until not craving or using illicit opioids
- Average dose 80-100mg daily
- Needs to be enrolled in a certified opiate substitution program

Buprenorphine
- Partial mu partial agonist with a ceiling effect
- Any physician can Rx after taking certified ASAM course
- Helpful for highly motivated people who do not need high doses

Stimulants
STIMULANTS

- Intoxication (acute)
  - Psychological and physical signs
  - Euphoria, enhanced vigor, gregariousness, hyperactivity, restlessness, interpersonal sensitivity, anxiety, tension, anger, impaired judgment, paranoia
  - Tachycardia, papillary dilation, HTN, N/V, diaphoresis, chills, weight loss, chest pain, cardiac arrhythmias, confusion, seizures, coma

- Chronic intoxication
  - Affective blunting, fatigue, sadness, social withdrawal, hypotension, bradycardia, muscle weakness

- Withdrawal
  - Not severe but have exhaustion with sleep (crash)
  - Treat with rest and support

Cocaine

- Route: nasal, IV or smoked
- Has vasoconstrictive effects that may outlast use and increase risk for CVA and MI (obtain EKG)
- Can get rhabdomyolysis with compartment syndrome from hypermetabolic state
- Can see psychosis associated with intoxication that resolves
- Neuroadaptation: cocaine mainly prevents reuptake of DA

Treatment - Stimulant Use Disorder (cocaine)

- CD treatment including support, education, skills, CA
- Pharmacotherapy
  - No medications FDA-approved for treatment
  - If medication used, also need a psychosocial treatment component

Amphetamines

- Similar intoxication syndrome to cocaine but usually longer
- Route - oral, IV, nasally, smoked
- No vasoconstrictive effect
- Chronic use results in neurotoxicity possibly from glutamate and axonal degeneration
- Can see permanent amphetamine psychosis with continued use
- Treatment similar as for cocaine but no known substances to reduce cravings
- Neuroadaptation
  - Inhibit reuptake of DA, NE, SE - greatest effect on DA

Treatment – Stimulant Use Disorder (amphetamine)

- CD treatment: including support, education, skills, CA
- No specific medications have been found helpful in treatment although some early promising research using atypical antipsychotics (methamphetamine)
Tobacco

- Most important preventable cause of death / disease in USA
- 25% current smokers, 25% ex smokers
- 20% of all US deaths
- 45% of smokers die of tobacco induced disorder
- Second hand smoke causes death / morbidity
- Psychiatric pts at risk for Nicotine dependence - 75%-90% of Schizophrenia pts smoke

Tobacco (cont.)

- Drug Interactions
  - induces CYP1A2 - watch for interactions when start or stop (ex. Olanzapine)
- No intoxication diagnosis
  - initial use associated with dizziness, HA, nausea
- Neuroadaptation
  - nicotine acetylcholine receptors on DA neurons in ventral tegmental area release DA in nucleus accumbens
- Tolerance
  - rapid
- Withdrawal
  - dysphoria, irritability, anxiety, decreased concentration, insomnia, increased appetite

Treatment – Tobacco Use Disorder

- Cognitive Behavioral Therapy
- Agonist substitution therapy
  - nicotine gum or lozenge, transdermal patch, nasal spray
- Medication
  - bupropion (Zyban) 150mg po bid,
  - varenicline (Chantix) 1mg po bid

Hallucinogens

- Naturally occurring - Peyote cactus (mescaline); magic mushroom (Psilocybin) - oral
- Synthetic agents – LSD (lysergic acid diethylamide) - oral
- DMT (dimethyltryptamine) - smoked, snuffed, IV
- STP (2,5-dimethoxy-4-methylamphetamine) – oral
- MDMA (3,4-methyl-enedioxymethamphetamine) ecstasy – oral

HALLUCINOGENS
MDMA (XTC or Ecstasy)

- Designer club drug
- Enhanced empathy, personal insight, euphoria, increased energy
- 3-6 hour duration
- Intoxication - illusions, hyperacusis, sensitivity of touch, taste/smell altered, "oneness with the world", tearfulness, euphoria, panic, paranoia, impairment judgment
- Tolerance develops quickly and unpleasant side effects with continued use (teeth grinding) so dependence less likely

MDMA (XTC or Ecstasy) cont.

- Neuroadaptation - affects serotonin (5HT), DA, NE but predominantly 5HT2 receptor agonists
- Psychosis
  - Hallucinations generally mild
  - Paranoid psychosis associated with chronic use
  - Serotonin neural injury associated with panic, anxiety, depression, flashbacks, psychosis, cognitive changes.
- Withdrawal – unclear syndrome (maybe similar to mild stimulants-sleepiness and depression due to 5HT depletion)

Cannabis

- Most commonly used illicit drug in America
- THC levels reach peak 10-30 min, lipid soluble; long half life of 50 hours
- Intoxication - Appetite and thirst increase
  Colors/ sounds/ tastes are clearer
  Increased confidence and euphoria
  Relaxation
  Increased libido
  Transient depression, anxiety, paranoia
  Tachycardia, dry mouth, conjunctival injection
  Impaired cognition
  Psychosis

Cannabis (cont.)

- Neuroadaptation
  - CB1, CB2 cannabinoid receptors in brain/body
  - Coupled with G proteins and adenylyl cyclase to CA channel inhibiting calcium influx
  - Neuromodulator effect; decrease uptake of GABA and DA
- Withdrawal - insomnia, irritability, anxiety, poor appetite, depression, physical discomfort

Cannabis (cont.)

- Treatment
  - Detox and rehab
  - Behavioral model
  - No pharmacological treatment but may treat other psychiatric symptoms
PCP

**PHENACYCLIDINE (PCP)**

"Angel Dust"

- Dissociative anesthetic
- Similar to Ketamine used in anesthesia
- **Intoxication**: severe dissociative reactions – paranoid delusions, hallucinations, can become very agitatedviolent with decreased awareness of pain.
- Cerebellar symptoms - ataxia, dysarthria, nystagmus (vertical and horizontal)
- With severe OD - mute, catatonic, muscle rigidity, HTN, hyperthermia, rhabdomyolysis, seizures, coma and death

**PCP cont.**

- **Treatment**
  - antipsychotic drugs or BZD if required
  - Low stimulation environment
  - acidify urine if severe toxicity/coma
- **Neuroadaptation**
  - opioid receptor effects
  - allosteric modulator of glutamate NMDA receptor
- **No tolerance or withdrawal**

**Websites**

- SAMHSA – [www.samhsa.gov](http://www.samhsa.gov)
  - Substance Abuse and Mental Health Services Administration
- NIDA – [www.drugabuse.gov](http://www.drugabuse.gov)
  - National Institute on Drug Abuse
- AAAP – [www.aaap.org](http://www.aaap.org)
  - American Academy of Addiction Psychiatry
- ASAM – [www.asam.org](http://www.asam.org)
  - American Society of Addiction Medicine