Pharmacokinetics
Administration, Travel, Metabolism and Elimination of Psychoactive Drugs

Pharmacology of Psychoactive Drugs

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Neuropharmacology
- Is the scientific study of drug effects on the nervous system.
- Is an all encompassing term
- Is applied to ALL drugs that influence the nervous system
- Includes
  - Sensory systems
  - Motor systems
  - Cognitive functioning
  - Others

Psychoactive Drugs

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Psychoactive Drugs

Some Terms and Definitions
- Psychopharmacology
  - Usually used to describe drug effects on psychological parameters such as emotion and cognition (Nestler)
- Psychotropics
  - Drugs that influence behavior
- Pharmacokinetics
  - Is the study of how drugs enter, are distributed, metabolized, and removed (excreted) from the body
- Pharmacodynamics
  - Is the study of what drugs do various structures in the body.

Pharmacokinetics
- Four variables to examine (ADME)
  - How drugs enter or are Absorbed into the system
  - How drugs are Distributed throughout the system
  - How drugs are Metabolized in the system
  - How drugs are Eliminated from the system.

1: How Drugs Enter or are Absorbed

- Influences
  - How fast a drug reaches its target organ
  - Which structure(s) the drug influences
  - Risk of acquiring BBPs

Oral
- Has a slow onset of action
  - Minutes
  - Can take longer if time release or has special coatings
- Advantage
  - Easy to take
  - Low risk for BBPs
Drug must be soluble and stable in stomach fluid.
Drug is absorbed through upper intestine through passive diffusion.
Drugs must generally be somewhat lipid soluble.
Disadvantages:
- Vomiting and stomach distress
- Hard to know how much of drug will be absorbed due to genetic differences.
- Stomach acid destroys some drugs.

Blood goes from the gastrointestinal (GI) tract to the liver before the body.
Some amount of the drug will be inactivated or metabolized as it goes through the liver.
- Important for steroid use
- Reason for other routes of ingestion

Rectal
- Used if a person is vomiting, unconscious, or unable to swallow.
- Absorption is often irregular, unpredictable, and incomplete.
- Rarely used for illicit drugs
  - Takes too long
  - Other issues

Faster routes (Seconds)
- Respiratory (Nasal/Oral) Nicotine Cocaine
- Intravenous (Venous system) Meth. Opiates
- Intraarteral (Arterial system) Meth. Opiates
- Problem – Risk of BBPs

Slower routes (Minutes)
- Intramuscular (muscle groups) Steroids
- Mucus Membranes Cocaine
- Subcutaneous (under the skin) Some Halluc.
- Cutaneous (Dermal) ACh. Nerve Agents, Nicotine Patches

Absorbed through membranes in mouth or nose.
Examples:
- Nitroglycerine, cocaine, nicotine gum.

Popular for recreational drugs (e.g., tobacco, marijuana, cocaine, heroin).
Lung tissues’ large surface area allows for rapid absorption into blood.
Pulmonary capillaries carry drug directly into left side of heart and then directly into the aorta and arteries going to the brain.
Even faster onset than injection.
Transdermal
- Provides continuous, controlled release.
- Allows for slow continuous absorption
- Decreases side effects.
- **Examples:**
  - Nicotine patches
  - Birth control medications
  - Pain medications
  - Not usually used for illicit drugs
  - Can be dangerous if used with combinations of other drugs
  - Opiates for pain plus injection or oral = overdose

Injection
- **Intravenous - IV**
  - Drug is introduced directly into bloodstream.
  - Dosage can be extremely precise.
  - (most dangerous route).
- **Intramuscular - IM**
  - Drugs injected into skeletal muscle.
  - More rapid than absorption from stomach
  - Slower than intravenous.
- **Subcutaneous – Sub Q**
  - Injected under the skin.
  - Slower than IV or IM

Additional Medical/Scientific Routes
- Intraperitoneal (peritoneal-abdominal cavity)
- Intracerebroventricular (cerebral ventricular)
- Intracerebral (brain parenchyma)
- Takes seconds or minutes
- Can be dangerous
- Minimal risk of BBPs due to sterile techniques used.

**2: How Drugs are Distributed in the Body**
- Circulatory system
- Blood goes from the Heart to the
- Lungs to
- Heart to
- Body structures via arteries
- Arteries to smaller blood vessels
- Small blood vessels to Heart via veins
- Repeat

Distribution Methods
- Plasma–more likely with water soluble drugs
- Platelets–more likely with lipid soluble drugs
- Attached to proteins (e.g., albumin)–bound vs. free

Capillaries
- Tiny cylindrical blood vessels
- Have small pores (between 90 and 150 angstroms), which are larger than most drugs.
- Allow transport of drugs regardless of lipid-solubility.
- Blood and protein are too big for pores; drugs that bind to plasma proteins cannot pass through.
Bioavailability

- Determines how much of a drug that actually reaches a target.
- Effects can depend on:
  - Gastrointestinal loading (decreases absorption)
  - Liver metabolism (First Pass)
  - Binding to plasma proteins that makes the drug unavailable to the target
  - Cannot penetrate the Blood-Brain Barrier
  - Cannot penetrate other cell membranes

Cell Membranes

- Membranes made of a phospholipid layer.
- The membrane is only permeable to small, lipid-soluble molecules.
- Important as barriers to absorption and distribution of drugs.

Effects on Target Binding Site

- All drugs bind on some receptor site
- Causes some effect on the target site
- Creates some behavioral effect
  - Called Main Effect
- Also has other unintended effects
  - Called Side Effect
  - Called Pharmacodynamics

Pharmacodynamics

- Generally is defined as effects of drugs on neurological systems.
- Can be associated with any system: Heart, Liver, Endocrine System, etc.
- Lots of issues influence pharmacodynamics
  - Amt. of drug available
  - Past drug use - Tolerance
  - Drug Stability
  - How long a drug lasts in the body before it is metabolized
  - Drug Consistency
  - Does it need metabolized before it can be used
    - L-Dopa vs. Dopamine

3: Metabolism and Elimination of Drugs

- Drugs can be removed many ways:
  - Breathing
  - sweating
  - Feces
- Liver metabolism
  - Have specific enzymes that break down drugs to inactive compounds
  - Can be influenced by:
    - Liver disease
    - Other compounds that are present: Multiple drugs, Fluid levels, Other health effects

Breathing, Sweat, Feces

- Removes trace amounts of some drugs
- Alcohol
  - Is removed multiple ways
  - Reason for breathalyzer
Liver
- Protects the body from toxic substances.
- Uses enzymes/proteins to change from toxic to non-toxic states
  - Physically located in liver cells.
  - Most are nonspecific.
  - Referred to as the microsomal enzymes (main category = cytochrome P450).

Factors influencing P45O Activity
1. Disease, especially of the liver
2. Species
3. Age, changes in young and old
4. Genetics
5. Environment
6. Past experience with drugs

Kidneys
- Also metabolizes some drugs (Ibuprofen)
- Removes other waste products from the blood
- Can be influenced by fluid levels and other compounds (salt)
- Also removes other drugs and products
  - BCPs, Lithium, some hallucinogens, metabolites
  - Can cause problems in other organisms

Other issues
- Genetics and Age
  - Have major influences in how the body absorbs and eliminates drugs
- Additive and Synergistic Effects
  - Different drugs can combine to create a greater effect than before
  - Alcohol and Barbiturates vs Alcohol and Benzodiazepines

Drug Half-Life
- Definition
  - Time it takes for the body to eliminate half of a given blood level of a drug.
- Varies by type of drug
- Influences potential for overdose

Blood Brain Barrier
- Designed to protect neurons from toxins.
- Brain capillaries do not allow drugs to pass as easily as capillaries in rest of body.
Steady State Dynamics

- Is the balance point at which the rate of drug administration approximates the rate of excretion.
- Used when providing drugs to achieve some effect
- Important for medicine
- Also important for withdrawal issues

Conclusions

- Many variables can influence drugs in the body
- Is important for the clinician to be aware of them
  - Reason psychopharmacology is important
  - Reason medical exams are an important component for drug/alcohol treatment