Drugs 101: Behavioral Pharmacology

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Drug Facts

• Drug effects are dose-dependent
• Drugs effects are time-dependent
• Drugs are toxic at high enough doses
• Drugs have multiple effects
Pharmacology

- Drugs – chemicals that affect living tissue
- Drug naming conventions
  - Trade name – Ritalin, Risperdal, Mellaril, Thorazine
  - Generic name – methylphenidate, risperidone, thioridazine, chlorpromazine
  - Chemical name - C_{23}H_{27}FN_{4}O_{2}
  - Manufacturer code – Ro15-4513

Pharmacology

- Drug Classification Schemes
  - Therapeutic usage – antipsychotics, antianxiety, anticonvulsants
  - Behavioral effects – stimulants, sedatives, sleep aids
  - Chemical classes – Benzodiazepines such as Valium, Librium, Xanax
Fate of a Drug

- Administration/Absorption:
  - Oral (PO)
  - Intravenous (IV)
  - Intramuscular (IM)
  - Intraperitoneal (IP)
  - Subcutaneous (SC)
  - Inhalation
  - Topical

Drug effects are time-dependent and depend on route of admin

Figure 1-11: The time courses for blood levels of a drug given by different routes of administration.
Fate of a Drug

- **Distribution to site of action**
  - Bloodstream → capillaries → intracellular fluids → neuron receptors in brain/spinal cord/periphery
  - Some to bone and fat cells

- **Biotransformation**
  - Liver
  - GI Tract

- **Excretion**
  - Kidneys
  - Lungs

Site of action: Neuron
Site of action: Neuron

Site of action: Synapse
Neurotransmitters

- Dopamine (DA)
  - Mediates reinforcers
  - Movement
  - Psychosis
- Serotonin (SE & 5-HTP)
  - Depression

- Norepinephrine (NE)
  - Arousal
- GABA
  - Inhibition
- Acetylcholine (ACh)
  - Movement
Drug effects on NT actions

**Summary of the Ways Drugs Affect the Synaptic Transmission**

1. Drug serves as precursor AGO (e.g., l-DOPA—dopamine)
2. Drug activates synaptic enzyme; inhibits synthesis of T.S. ANT (e.g., PCPA—serotonin)
3. Drug stimulates uptake of T.S. ADO (e.g., chlorpromazine—acetylcholine)
4. Drug stimulates release of T.S. ADO (e.g., lidocaine—acetylcholine)
5. Drug inhibits release of T.S. ANT (e.g., bleomycin—catecholamines)
6. Drug stimulates postsynaptic receptors ADO (e.g., nicotine, muscarine—acetylcholine)
7. Drug blocks postsynaptic receptors ANT (e.g., cocaine, atropine—acetylcholine)
8. Drug blocks autoreceptors; increases synthesis/release of T.S. ADO (e.g., clonidine—noradrenaline)
9. Drug blocks autoreceptors; inhibits synthesis/release of T.S. ADO (e.g., clonidine—noradrenaline)
10. Drug blocks reuptake ADO (e.g., cocaine—dopamine)
11. Drug increases acetylcholinesterase ADO (e.g., physostigmine—acetylcholine)

AGO = agonist
ANT = antagonist
T.S. = transmitter substance

Drug effects on NT actions

**Before Drug**
- Natural chemical
- Receptor site
- Normal cellular activity

**Agonist Drug**
- Natural chemical
- Receptor site
- Enhanced cellular activity

**Antagonist Drug**
- Natural chemical
- Receptor site
- Blocked cellular activity
Drug effects on NT actions

Drug Processes
• Tolerance - decrease effect over repeated admin
  • Metabolic –
    • Alcohol produces enzymes that breaks it down
  • Cellular –
    • Cells become less responsive to drug
• Behavioral –
  • Organism learns to respond while under the influence of drug
• Cross Tolerance
Drug Processes

• Sensitization
  • Drug effects increase with repeated administrations
    • High dose
    • Liver problems

Drug Processes

- Withdrawal syndrome

<table>
<thead>
<tr>
<th>Caffeine</th>
<th>W/D</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effects</strong></td>
<td></td>
</tr>
<tr>
<td>Increase HR</td>
<td>Decrease HR</td>
</tr>
<tr>
<td>Increase alertness</td>
<td>Decrease alertness</td>
</tr>
<tr>
<td>Decrease sleep</td>
<td>Increase sleep</td>
</tr>
<tr>
<td>Decrease headache</td>
<td>Headaches!</td>
</tr>
</tbody>
</table>
Drug Processes

- **Withdrawal syndrome**
  - Physiological changes after termination of drug administrations or decrease in dose.

**Morphine**

**Effects**

<table>
<thead>
<tr>
<th>Effect</th>
<th>W/D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesia</td>
<td>Pain sensitivity</td>
</tr>
<tr>
<td>HR decrease</td>
<td>HR increase</td>
</tr>
<tr>
<td>Euphoria</td>
<td>Depression</td>
</tr>
<tr>
<td>Resp decrease</td>
<td>Resp increase</td>
</tr>
<tr>
<td>Constipation</td>
<td>Explosive diarrhea</td>
</tr>
</tbody>
</table>

- **Physical Dependence**
  - A condition in which termination of drug will produce withdrawal syndrome.
  - Is a function of reinforcing value of drug, dose, time of exposure.

- **Psychological Dependence**
  - A condition in which termination of drug will evoke drug seeking, cravings, etc.
  - Is a function of reinforcing value of drug, dose, time of exposure.
Drug Processes

- **Potency**
  - To get a given effect, which drug (Drug A or Drug B) requires less MG?
    - Risperdal requires 6 mg
    - Thorazine requires 800 mg

- **Peak efficacy**
  - What is the maximum effect of Drug A vs Drug B
    - Risperdal decreases aggression by 50%
    - Thorazine decreases aggression by 50%

Drug Processes

- **Metabolic Factors**
  - 0-Order Kinetics (non-linear)
    - Fixed mg of drug is metabolized per time period
    - Alcohol: 10 ml/hour
  - 1st Order Kinetics (linear)
    - Fixed % of drug is metabolized per time period
    - Expressed in $T_{1/2}$
    - $T_{1/2}$ of 6 hours = $1/2$ of drug is metabolized every 6 hours
    - Drug is eliminated in 5-6 half lives
**Drug Processes**

0 Order Kinetics: 10mg/hour

<table>
<thead>
<tr>
<th>Injestion</th>
<th>4 hours</th>
<th>8 hours</th>
<th>12 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 mg</td>
<td>760 mg</td>
<td>720 mg</td>
<td>680 mg</td>
</tr>
</tbody>
</table>

1st Order Kinetics: $T \frac{1}{2} = 4$ hours

<table>
<thead>
<tr>
<th>Injestion</th>
<th>4 hours</th>
<th>8 hours</th>
<th>12 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 mg</td>
<td>400 mg</td>
<td>200 mg</td>
<td>100 mg</td>
</tr>
</tbody>
</table>

**Drug Class Profile Antipsychotics**

- **Classes**
  - Typical (older drugs with more side effects)
    - Thorazine, Mellaril
  - Atypical (new drugs with fewer side effects)
    - Risperdal, Zyprexa, Seroquel
Antipsychotics

Fate

Administration/Absorption
- Oral – GI → bloodstream
- IM – muscles → bloodstream

Distribution
- Brain and entire body
- Collects in fat cells

Antipsychotics

Fate

Metabolism
- Drug metabolized in liver
- Almost all molecules are transformed

Excretion
- Kidneys
- T½ = 11 – 58 hours
Antipsychotics

**Effects**
- Prescribed for schizophrenia and bipolar disorder
- Decreases psychotic behavior
- Decreases disruptive/dangerous behavior

**Side effects: Extrapyramidal symptoms**
- Tardive dyskinesia (TD) → [Video](#)
- Dystonia → [Video](#)
- Parkinson-like symptoms → [Video](#)
- Akathesia → [Video](#)
- Neuroleptic Malignant Syndrome
  - Low grade fever
  - Rigidity of limbs
  - Unstable BP
  - Stupor

**Side effects: Diabetes**
Antipsychotics

- **Mechanism of Action**
  - Dopamine antagonist
  - Blocks D receptors but does not operate
  - **Antagonist**

- **Withdrawal?**
  - None
  - Drug resides in fat cells and is slowly released over time after termination

- **Reinforcer?**
  - No
  - EO? – yes, for food

Antidepressants

<table>
<thead>
<tr>
<th>Class</th>
<th>Names</th>
<th>Admin</th>
<th>T/1/2</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st generation</td>
<td>1. MAOI: Parnate</td>
<td>Oral</td>
<td>1. 3 hours</td>
<td>1. Decrease HR, orthostatic hypotension</td>
</tr>
<tr>
<td></td>
<td>2. Tricyclics: Tofranil, Elavil</td>
<td></td>
<td>2. 24 hours</td>
<td>2. Dry mouth, constipation, increase appetite, sexual impairment</td>
</tr>
<tr>
<td>2nd generation</td>
<td>SSRI: Prozac, Luvox, Zoloft, Paxil</td>
<td>Oral</td>
<td>15-20 hours</td>
<td>Nausea, headache, insomnia, weight gain, Serotonin syndrome</td>
</tr>
</tbody>
</table>
## Antianxiety and sleep aids

<table>
<thead>
<tr>
<th>Class</th>
<th>Names</th>
<th>Admin</th>
<th>T/1/2</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antianxiety</td>
<td>Valium, Librium, Xanax, Ativan</td>
<td>Oral, IV, IM</td>
<td>11-48 hrs</td>
<td>Decrease anxiety, decrease muscle tension, driving impairment, decrease in effects of aversive stimuli, decrease seizures</td>
</tr>
<tr>
<td>Sleep</td>
<td>1. Halcion, Restoril 2. Z drugs: Ambien, Lunesta</td>
<td>Oral</td>
<td>1. 3.5-8 hrs 2. 1-3 hrs</td>
<td>Increase sleep, memory loss</td>
</tr>
</tbody>
</table>

## ADHD

<table>
<thead>
<tr>
<th>Class</th>
<th>Names</th>
<th>Admin</th>
<th>T/1/2</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulants</td>
<td>Ritalin, Concerta, Focalin, Adderal</td>
<td>Oral, Oral</td>
<td>3-6 hours</td>
<td>Decrease sleep &amp; appetite, small increase in HR/BP</td>
</tr>
<tr>
<td>Non-stimulants</td>
<td>Tenex, Catapres</td>
<td>Oral</td>
<td>12-17 hrs</td>
<td>Dry mouth, sleep, fatigue, constipation</td>
</tr>
</tbody>
</table>
Pharmacology

**Drug classes:**

- Therapeutic Use

**Behavioral Functions of Drugs**

- Drugs as reinforcers
  - Anti-psychotics
  - Anti-depressants
  - ADHD drugs
  - Anti-convulsants

- Drugs as EOs/Aos
  - Anti-psychotics
  - Anti-depressants
  - ADHD drugs
  - Anti-convulsants
Interfacing with Psychiatry

- Psychiatry role
- BCBA role
  - Learn from psych
  - Collect data on main and side effect
  - Influence when appropriate
- Developing professional relationship
  - Behavioral view
  - Pairing
  - Positive reinforcement
  - Shaping

Prescribing Drugs

- Prescribing drugs to special populations in need of protection should involve safeguards.
  - Goals are clear with specific targets and in P interests
  - Tx decisions made on basis of drug effects
  - Flexible and integrated with beh Tx.
Prescribing Drugs

- Manage the psychiatrist!
  - Attend appointments
  - Collect data
  - Report side effects
  - Learn about drugs!

Drug Evals

- Essential features of a drug evaluation?
  - Objective measure of behavior
  - Meds given according to protocol
  - Design
  - Data analysis must be adequate
  - Placebo control
  - Blind study?
    - Single
    - Double
    - Triple
  - Informed consent
Effects of Drug on Aggression

Drug Tx of SIB

- Hypothesis: SIB causes body to release endorphins
  - Endorphins: Body’s natural reaction to pain
  - “Endogenous morphine-like substance”
  - Effects: reduced pain + effects that mimic “runners high”
Special Topics

Drug Tx of SIB

- **Mechanism**
  - If SIB releases endorphins, then we need a way to block this
  - Morphine antagonist = Naltrexone
Drug Abuse Theories

- Drug taking is sinful
  - Should be punished
  - Was a factor in passage of 18th Prohibition Amendment
- Drug taking is a disease
  - Person is sick
  - Needs treatment
  - A factor in AA

SIB – Naltrexone effects

![Graph showing the effects of naltrexone on self-injurious behavior.](image-url)
Drug Abuse Theories

- Behavioral view
  - Drugs are reinforcers
  - Drug taking produces social reinforcers
  - Drug taking produces escape/avoidance of withdrawal

<table>
<thead>
<tr>
<th>Phase</th>
<th>Years</th>
<th>Population</th>
<th>Purpose</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PreClinical</td>
<td>3.5</td>
<td>Lab and animals</td>
<td>Safety and bioactivity</td>
<td>5000 tested</td>
</tr>
<tr>
<td>Phase 1</td>
<td>1</td>
<td>20-80 Healthy Volunteers</td>
<td>Safety and dose</td>
<td>5 enter</td>
</tr>
<tr>
<td>Phase 2</td>
<td>2</td>
<td>100-300 patient volunteers</td>
<td>Efficacy and side effects</td>
<td>5 enter</td>
</tr>
<tr>
<td>Phase 3</td>
<td>3</td>
<td>1000-3000</td>
<td>Efficacy &amp; adverse reactions to longer term use</td>
<td>5 enter</td>
</tr>
<tr>
<td>FDA</td>
<td>2.5</td>
<td>Review and approval</td>
<td></td>
<td>1 approved</td>
</tr>
<tr>
<td>Phase 4</td>
<td></td>
<td>Additional post marketing study</td>
<td>required by FDA</td>
<td></td>
</tr>
</tbody>
</table>