Pharmacology

- The study of drugs
Psychopharmacology

- The study of psychoactive drugs
Psychoactive drugs

- Drugs that influence psychological processes
  - mood
  - emotion
  - perception
  - cognition
  - behavior

- Psychoactive drugs exert direct action on the brain
History of drug use and abuse

- Early drug use
- The Soldier’s disease: morphine addiction
- Cocaine in the 1890’s
Was Prohibition Effective?

- Enormous growth in organized crime and government corruption
- Millions became criminals
- Beer consumption dropped—little change in hard liquor
- Saloon to Speak easy—more women drinkers
- Industrial liquor produced neuropathies
- Decrease in cirrhosis of the liver
The Evolution of Drug Laws

- 1906 Pure Food and Drug Act
- 1914 Harrison Act
- 1920 Prohibition Amendment
- 1965 Drug Abuse Control Amendment
1965 law controls:

• “Any substance having potential for abuse because of stimulant, depressant or hallucinogenic effects”
The Evolution of Drug Laws

- 1906 Pure Food and Drug Act
- 1914 Harrison Act
- 1920 Prohibition Amendment
- 1965 Drug Abuse Control Amendment
- 1970 Controlled Substances Act
# 1970 Schedule System

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Medical</th>
<th>Abuse Potential</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>NO</td>
<td>High</td>
<td>Heroin, LSD</td>
</tr>
<tr>
<td>II</td>
<td>YES</td>
<td>High</td>
<td>Morphine, Cocaine, Barbs</td>
</tr>
<tr>
<td>III</td>
<td>YES</td>
<td>Some</td>
<td>Barbs</td>
</tr>
<tr>
<td>IV</td>
<td>YES</td>
<td>Low</td>
<td>Valium, Xanax, Cough meds</td>
</tr>
<tr>
<td>V</td>
<td>YES</td>
<td>Very Low</td>
<td></td>
</tr>
</tbody>
</table>
The Evolution of Drug Laws

- 1986 Analogue Act
- 2009 Family Smoking Prevention and Tobacco Control Act
- 2012 Synthetic Drug Abuse Prevention Act
- 2013 Marijuana in CO and WA
What is drug abuse?

- Physical harm to oneself
- Physical harm to others
- Psychological harm to oneself
- Psychological harm to others
Drug Addiction

- Is addiction abuse?
- Physical addiction vs. Psychological dependence
- WHO definition: Drug dependence is specified by the occurrence of withdrawal symptoms = abstinence syndrome
Rebound effect:

withdrawal symptoms are opposite the drug effect
DSM IV
- Substance Dependence
- Substance Abuse

DSM V
- Substance Use Disorder
Substance use disorder is a problematic pattern of substance use leading to a clinically significant impairment or distress as manifested by at least two of the following within a 12-month period:

- Tolerance
Tolerance

- After regular use, a larger dose is required to produce a given effect
- A given dose of the drug has less effect upon repetition
DSM-V: Substance Use Disorder

- Tolerance
- Withdrawal
- Taking more than intended
- Unable to cut down or control
- Excessive time spent re drug
- Important activities given up
- Continuing use despite persistent social or interpersonal problems
DSM-V: Substance Use Disorder (New)

- Failure to fulfill major role obligations at work, school or home
- Physically dangerous situations
- Persistent Social/Psychological problems
- Cravings or a strong desire to use the substance (Rinaldi’s psychological dependence)
DSM-V: Substance Use Disorder
(11 total symptom criteria)

- Mild = 2-3 total symptoms present
- Moderate = 4-5 symptoms
- Severe = 6 or more
Mechanisms of Tolerance

- Dispositional (metabolic)
- Functional
- Behavioral (learned)
- Acute vs protracted tolerance
- Cross-tolerance
- Cross-dependence
Nervous System

- Central N.S.
  - Brain
  - Spinal Cord

- Peripheral N.S.
  - Sensory Nerves
  - Motor Nerves
  - Autonomic N. S.
  - Sympathetic
  - Parasympathetic
The Neuron

- 1. Cell body
- 2. Nucleus
- 3. Dendrites
- 4. Myelin
- 5. Axon
- 6. Axon Terminals
The Synapse
Drug Action

- **Agonist:** Activates receptor
- **Antagonist:** Blocks receptor
Two Types of Receptor:

- **Ionotropic receptors**: Close or open ion channels
- **Metabotropic receptors**: Act through “second” messenger chemicals
Ionotropic receptor
Metabotropic Receptor

1. Transmitter molecule attaches to receptor

2. Receptor releasing

3. G protein activates a “second messenger” such as cyclic AMP, which alters a metabolic pathway, turns on a gene in the nucleus, or opens or closes an ion channel.
Drug Action

- **Agonist**: Activates receptor
- **Antagonist**: Blocks receptor
- **Indirect action**
  - Alters enzyme activity
  - Blocks reuptake
Chronic Effects

- Depletion of transmitters
- Alter transmitter production
- Alter receptor density
- Affect neurogenesis
Neurotransmitters

- **Acetylcholine**
  - Motor control: muscular dystrophy, myasthenia gravis
  - Thirst
  - Memory: Alzheimer’s disease
Monoamines

- Norepinephrine-hunger
- Dopamine-Parkinson’s disease
Parkinson’s Disease

- Parkinson’s disease, dopamine and the substantia nigra
Monoamines

- Dopamine
- Norepinephrine
- Serotonin
- All three affect mood
The Monoamine Theory of Mood:

- Depression
  - Reserpine
  - Antidepressants
  - Stimulant drugs
Monoamine Oxidase: MAO
-ase = enzyme

-ergic = transmitter as adjective
- Monoamine Oxidase: MAO
- The first antidepressants: MAO-inhibitors
The Monoamine Theory of Mood:

- Schizophrenia
  - Antipsychotic drugs
  - Thorazine (chlorpromazine)
  - Parkinsonian side effects
  - Dopamine hypothesis
  - Stimulant drugs
Neurotransmitters

- Acetylcholine
- Dopamine
- Norepinephrine
- Serotonin
- Endorphins
- GABA-inhibitory neurotransmission
Mesolimbic Dopaminergic Pathway--Pleasure center: James Olds
Drug Development

- Discovery of compound-in vitro tests
- Animal studies
Institutional Animal Care & Use Committee

- Includes Veterinarian and Ethics expert
- Evaluates all proposals
- Weigh medical/scientific benefits against risk to animals
- May refuse protocol or require changes
- Unannounced site inspections (2/yr)
Drug Development

- Discovery of compound-in vitro tests
- Preclinical trials: animal studies--toxicity, efficacy, abuse potential, at least 2 species
DOSE-EFFECT CURVE

GRAPHS A MEASURABLE EFFECT OF A DRUG AS A FUNCTION OF THE DRUG DOSE
POTENCY

THE DOSE OF A DRUG REQUIRED TO PRODUCE A GIVEN EFFECT (LOWER VALUE = MORE POTENT)
**ED50**

- THE DOSE OF A DRUG REQUIRED TO PRODUCE A 1/2 MAXIMAL EFFECT
- THE DOSE OF A DRUG REQUIRED TO PRODUCE A GIVEN EFFECT IN 50% OF THE INDIVIDUALS TESTED
LD50

- THE DOSE OF A DRUG REQUIRED TO PRODUCE LETHALITY IN 50% OF THE INDIVIDUALS TESTED
**THERAPEUTIC INDEX**

- THE RATIO OF THE LD50 OF A DRUG AND THE ED50 OF A PARTICULAR EFFECT

LD50/ED50
Drug Interactions

- Antagonism
- Synergy/Potentiation
Animal Research Methods

- Self-administration
Animal Research Methods

- Self-administration
- Drug discrimination
- Conflict
Drug Development

- Discovery of compound-in vitro tests
- Preclinical trials:
  - Animal studies--toxicity, efficacy, abuse potential, at least 2 species
- Clinical trials
Clinical Trials

- Phase 1—Laboratory studies of safety: Normal volunteers (small N—20-40)
- Phase 2—Patients (N = 200-400)—highly controlled studies of safety and efficacy
- Phase 3—Patients—large scale—thousands: efficacy and safety in actual practice setting
- FDA approval (5-18 years from discovery)
Institutional Review Board

- Must include physician and lawyer
- Must review all protocols involving human participants
- Evaluate Risks/Benefits
- Voluntary, informed consent
Non-Specific drug effects (placebo):

Effects NOT based on specific pharmacological actions of the drug.
Placebo Effect

- Sir Henry K. Beecher—WWII Studies
- 35% + in many disorders
- Pain, anxiety, depression, etc.
- Side effects/withdrawal
Double-Blind

Neither the subject nor the experimenter knows which condition (drug or placebo) the subject is in.