Fundamentals of Psychopharmacology

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Distribution of Receptors Influences Safety

- Opioid Receptors
- Cannabinoid Receptors
Brief History of Drug Advances

- 1200s - first record of alcohol distillation
- Early 1800s – isolation of morphine
- Mid 1800s – invention of hypodermic syringe
- Late 1800s – cocaine isolated
- 1900s molecular chemistry accelerates discovery and invention of novel pharmaceuticals

Brief History of Drug Policy in US

- 1906 – Pure Food and Drug Act
  - Drug labels
  - Over the counter/Rx distinction
- 1909 – Opium Smoking exclusion act
- 1914 - Harrison Act gave Treasury dept. ability to regulate drugs through taxation
- 1970 - Controlled Substances Act
- 1986 – Synthetic Analog Act
Neurotransmitters of Interest

**Amino Acids**
- Glutamate (Glu)
- GABA

**Biogenic Amines**
- Quaternary Amines
- Acetylcholine (Ach)
- Monoamines
- Catecholamines
  - Dopamine (DA)
  - Norepinephrine (NE)
- Indolamines
  - Serotonin (5-HT)

**Neuropeptides**
- Opioid Peptides
- Enkephalins
- Endorphins
- Dynorphins
- Endomorphins

(Others: lipids & soluble gases)

Drugs of Interest

- Psycho Stimulants
- Hallucinogens
  - LSD
  - MDMA
  - PCP
- Antipsychotics
- Dementia
- Novel Compounds
  - DIPT

- Catecholamines
- Varies
  - Serotonin like
  - Catecholamine like
  - Dissociative/anesthetic
- Biogenic Amines
Psychomotor Stimulants

- Cocaine
- Methylphenidate (ritalin)
- Amphetamine (adderall)
  - Methamphetamine
Psychomotor stimulant kinetics

- Absorption
  - Nasal membrane
  - stomach/intestinal
  - Lungs
  - Bloodstream

- Half Lives
  - Cocaine: 50-90 min
  - Methylphenidate: 3-4 hrs
  - Amphetamines: 6-8 hrs
  - Methamphetamine < 12 hr
Hallucinogens

- Self Administration?
- Psychedelics
- Entheogens
- Psychotomimetics
Hallucinogens

- **3 Classes**
  - Serotonin-like
    - DMT
    - LSD
    - Psilocybin/psilocyn
  - Catecholamine-like
    - Mescaline/peyote
    - MDMA
  - Dissociative / Anesthetics
    - DXM
    - Ketamine
    - PCP
    - Tropane alkaloids
LSD Kinetics

- Absorption
  - Oral
  - Sublingual
  - Injection & insufflation also work
- Peak Plasma Concentration
  20-60 minutes
- Half-life about 2 hours (but effects for 4-12)
- Eliminated primarily in feces

LSD – the 'dirty' hallucinogen

- Dissociation Constant (Ki) for receptors LSD binds to
  - the lower the Ki, the greater the affinity (ex 5-HT2a has one of the highest binding affinities)
MDMA - Ecstasy

- Structure resembles Catecholamines & Indolamines
- Exerts stimulant and hallucinogenic effects
  - Sometimes unbalanced mixture due to impurities
Methods of Ingestion & Time to Peak Plasma Concentration

<table>
<thead>
<tr>
<th>Method</th>
<th>Time to Peak Plasma Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orally</td>
<td>20 to 40 minutes</td>
</tr>
<tr>
<td>Snorted (Powder)</td>
<td>5 to 10 minutes</td>
</tr>
<tr>
<td>Smoked</td>
<td>20 to 30 seconds</td>
</tr>
<tr>
<td>Injected</td>
<td>10 to 20 seconds</td>
</tr>
</tbody>
</table>

Effect lasts 3-6 hrs
Average dose is 1-2 tablets (60-120 mg)

MDMA - Pharmacodynamics

- Affinity for Monoamine transporters
- Blocks reuptake
- Reverses transporters?
Dissociative Hallucinogens

- PCP, Ketamine, DXM
- Effects are dose dependant
  - Low doses induce perceptual changes
  - High doses can cause unconsciousness

PCP

- NMDA receptor antagonist
- Pharmacokinetics
  - Absorption & peak [ ]
    - Oral: 2 hours
    - Smoked: 15 minutes
  - Half-life 18 hours
  - Excreted in urine
  - Metabolites detectable for 1 week
Antipsychotics

- Early use of Antihistamines
- DA hypothesis of schizophrenia
- Atypical antipsychotics
  - Indiscriminate binding profiles:
  - Treats greater variety of symptoms
  - More indiscriminate side effects
Dementia Pharmacotherapy

- No known mechanism to reverse damage
- Strategies to preserve functioning/minimize loss
- Treatment for Alzheimer’s focuses on:
  - Choline-esterase (moderate)
  - NMDA antagonism (moderate - severe)

Acetylcholine

- 1st Neurotransmitter discovered
- 2 Receptors
  - Nicotonic
  - Muscarinic
- Associated Functions
  - Memory
  - Attention
  - Muscles
- Acetylcholine esterase
Compounds Affecting Ach

- Nicotine
- Amanita Muscaria
- Crotoxin
- Latrotoxin
- Botulism

DIPT
'Novel Hallucinogen'

- Indole ring
- At low doses affects exclusively auditory perception
  - Dropped pitch
- At higher doses synesthetic affects with sounds
- Lasts 4-8 hours

- Synthesized by Alexander Shulgin in 'Tihkal'