Drugs, The Brain, and Behavior

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What is a drug?

Difficult to define

Know it when you see it

Neuroactive vs Non-Neuroactive drugs

Two major categories of neuroactive drugs:

- Therapeutic Drugs
- Recreational Drugs (Drugs of Abuse)

Both types of neuroactive drugs affect neural functioning and behavior
How does a drug affect behavior

Neural Circuits Altered

Neuroactive Drug
(Antidepressant)

Behavioral Outcome
(Capable of positive emotions)

Different Levels at which drug effects in the brain can be studied

Molecular events → Cellular Events → Intercellular Events → Organismal Events
“Good” Therapeutic Drugs vs “Bad” Addictive drugs

No clear boundary!

All “good” drugs have undesirable side effects

Many “good” drugs are addictive (i.e. “bad”) and deadly under the right circumstances (e.g. prescription opiates, amphetamine, valium)

Two US Federal Agencies decide if a drug is good or bad

Food and Drug Administration (FDA) decides if drug is therapeutic (i.e. good)

Drug Enforcement Administration (DEA) decides whether a drug is illegal (i.e. bad).

A “bad” drug in the US can be a “good” drug in other countries
Epidemic of Opioid Abuse

2010: Over twice as many overdose deaths from prescription opiates than heroin and cocaine combined.

Drug overdose deaths involving opioids, by type of opioid, United States, 2000-2014

How Societally Serious are Drug-Overdose Deaths?

Drug-Induced Deaths Second Only to Motor Vehicle Fatalities, 1999–2007

What about now?

2015, drug-induced deaths surpassed motor vehicle fatalities!!

An incredibly serious problem!!!
Neuroactive Drugs Work by Altering Chemical Signaling in the Brain

Two Classes of Chemical Signals in the brain
  Neurotransmitters
  Neurohormones

Two Ways a Drug Affects Neural Signaling
  Agonist for chemical signal
  Antagonist for chemical signal

In order to understand drug action must have a good understanding of chemical signaling in brain
Neuronal communication

Three Ways that information is transmitted in a Neuron:
- Graded Potential
- Action Potential
- Neurotransmitter

Most neuroactive drugs act by altering synaptic transmission.
Generalized Synapse (Major Drug Events)

Most neurotransmitters are either AA, modified AA, or peptides

Neurotransmitter Agonists
1. serve as precursors
2. block degradative enzymes in cytoplasm
3. facilitate release (reverse transporter)
4. activate receptors directly
5. Block reuptake
6. Autoreceptor blocker
7. deactivate degradative enzymes in synapse

Neurotransmitter Antagonists
1. block synthetic enzymes
2. Block neurotransmitter pumps in vesicles
3. Block release (docking proteins)
4. Postsynaptic receptor blockers
5. Ion Channel blockers
Why are Some Neuroactive Drugs Addictive?

Hallmark of addiction is compulsive drug use

Older Model of Addiction

- Tolerance and Withdrawal
- Problem With Older Model

Newer Model of Addiction

Final Common Reward Circuitry

- Nucleus Accumbens
- Ventral Tegmental Area
- Tegmentostriatal branch of Mesolimbic/Mesocortical Pathway
## Effects of Different Drugs of Abuse

<table>
<thead>
<tr>
<th>Type of Drug</th>
<th>Major Synaptic Effects</th>
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</thead>
<tbody>
<tr>
<td>Amphetamine, Methamphetamine</td>
<td>Promote DA release</td>
</tr>
<tr>
<td></td>
<td>Inhibit Dopamine and NE Reuptake</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Reverses Dopamine Reuptake Transporter</td>
</tr>
<tr>
<td>Heroin, Morphine, Codeine</td>
<td>Activate endogenous opiate receptors</td>
</tr>
<tr>
<td>Alcohol, Benzodiazepines &amp; Barbiturates</td>
<td>GABA$_A$ agonist (allosteric modulators)</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Blocks adenosine receptors</td>
</tr>
<tr>
<td>Nicotine</td>
<td>Activates Acetylcholine nicotinic receptors</td>
</tr>
<tr>
<td>Marijuana (THC)</td>
<td>Activates endogenous cannabinoid receptors</td>
</tr>
</tbody>
</table>

All Drugs of Abuse cause dopamine release in the nucleus accumbens!! (either directly or indirectly)
Some diseases treated with therapeutic drugs

Diseases are mainly diseases of **regional** modulatory neurotransmitters, defects in Glutamic Acid or GABA often fatal

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Neurotransmitter Malfunction</th>
<th>Problem</th>
<th>Drug Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>Dopamine</td>
<td>Receptor Hypersensitivity</td>
<td>Dopamine antagonists</td>
</tr>
<tr>
<td>ADHD or ADD</td>
<td>Dopamine</td>
<td>Receptor insensitivity</td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td>Dopamine</td>
<td>Neuron Degeneration</td>
<td>Dopamine agonists</td>
</tr>
<tr>
<td>Depression</td>
<td>Serotonin/Norepinephrine</td>
<td>Receptor insensitivity</td>
<td>Serotonin/Norepinephrine agonists</td>
</tr>
<tr>
<td>Obsessive/Compulsive Disorder</td>
<td>Serotonin</td>
<td>Receptor insensitivity</td>
<td>Serotonin agonists</td>
</tr>
<tr>
<td>Manic/Depressive Disorder</td>
<td>Serotonin?</td>
<td>Receptor hypersensitivity?</td>
<td>Lithium</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td>Acetylcholine</td>
<td>Neuron Degeneration</td>
<td>Acetylcholine agonists</td>
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</table>
Learning more about Drug Effects in the Brain at Lehigh

Must first learn how Brain works

Bios 120: Biology Core III: Integrative and Comparative

Bios 276: Central Nervous System and Behavior

Bios 315: Neuropharmacology

Bios 366: Diseases of the Nervous System

Most students taking these courses major in BNS, Biology, Molecular Biology, or Biochemistry
Any Questions?