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 types of neuroactive drugs:
- Psychotherapeutic Drugs
- Drugs of Abuse

Both types of drugs affect behavior
How does a drug affect behavior

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

Molecular events → Cellular Events → Organismal Events

Drug (Antidepressant) → Behavioral Outcome (Capable of positive emotions)
“Good” Therapeutic Drugs vs “Bad” Addictive drugs

No clear boundary!

All “good” drugs have undesirable side effects

Many “good” drugs can be addictive (i.e. “bad”) under the right circumstances (i.e. Rush Limbaugh and oxycontin)

How does Drug Enforcement Administration (DEA) decide whether a drug is a “good” therapeutic drug or a “bad” illegal drug.

A “bad” drug in the US can be a good drug in other countries
Psychoactive Drugs Work by Altering Chemical Signaling in the Brain

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

**Neurotransmitter Agonists**
1. serve as precursors
2. block degradative enzymes in cytoplasm
3. facilitate release
4. activate receptors directly
5. Block reuptake
6. Autoreceptor blocker
7. deactivate degradative enzymes in synapse
8. activate $G_S$ or inhibit $G_I$ proteins
9. Open postsynaptic ion channels

**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
6. Activate $G_I$ or inactivate $G_S$

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**Diagram Notes**
- Peptide in vesicle
- NT in synapse
- Opening ion channel
- Reuptake
- Autoreceptor
- Neurotransmitter pump or transporter
- Diffusion
- Postsynaptic receptor binding
- EPSP or IPSP
Why are Some Neuroactive Drugs addictive?

Older Model of Addiction
Tolerance and Withdrawal
Problem With Older Model
Newer Model of Addiction

Final Common Reward Circuitry

Tegmentostriatal branch of Mesolimbic/Mesocortical Pathway

Nucleus Accumbens
Ventral Tegmental Area
### Effects of Different Drugs of Abuse

<table>
<thead>
<tr>
<th>Type of Drug</th>
<th>Major Synaptic Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine, Methamphetamine</td>
<td>Promote DA release, 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&lt;sub&gt;A&lt;/sub&gt; agonist (allosteric modulators)</td>
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<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>
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</table>
Some diseases that are malfunctions in neurosecretion in the brain

Diseases are mainly diseases of modulatory neurotransmitters, defects in GA 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>
</tr>
</tbody>
</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 390: Neuropharmacology

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