Understanding the Brain: What Drugs Can Tell Us

Presented by: Dr. Rochelle D. Schwartz-Bloom

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Understanding the Brain: What Drugs Can Tell Us

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A Web Seminar to Support the NIH Curriculum Supplement: The Brain
Localization of Brain Function
Each lobe has key functions
Prefrontal lobe: matures around age 24!

- motivation
- cognition
- memory
- impulse control
- judgment
The limbic system: integrates emotions with body functions

- Attentional processing
- Mood/fear
- Memory
- Learning memory
- Sensory-motor integration
Alzheimer’s Disease: Degeneration of basal forebrain & hippocampal neurons
The basal ganglia

- movement initiation
- motivation
- pleasure euphoria
- motivation
Parkinson’s Disease: Degeneration of neurons in the basal ganglia

- Movement initiation
- Motivation

- Caudate nucleus
- Nucleus accumbens

NSTA Webinar - Understanding the Brain...
Addiction: Dysfunction in the basal ganglia & prefrontal cortex

- impulse control
- motivation
- pleasure euphoria

Caudate nucleus
Nucleus accumbens
The hypothalamus: master regulator

- body temp
- breathing
- heart rate
- feeding
- fluid volume
- circadian rhythms
- sexual activity
- hormone secretion
Test your knowledge!

In a unit on “memory”, your students learn that both alcohol and marijuana can cause problems with short-term memory.

On which area of the brain would the unit focus?

A. Brainstem  
B. Amygdala  
C. Cerebellum  
D. Hippocampus  
E. Hypothalamus
Let us Pause Two Minutes for Questions
Region to region communication
“Neuron pathways”
Neurons communicate information
The neuron...end to end
Communication happens at the synapse
Neurotransmitter pathways

- Dopamine (pleasure)
- Serotonin (mood)
- Glutamate (learning)
- Acetylcholine (memory)
- GABA (sleep)
- Norepinephrine (arousal)
The major dopamine pathway
Pleasure, motivation, movement, cognition
Dopamine is a key neurotransmitter in the reward pathway.
Test your knowledge!

Brain function is generated by the communication among neurons via pathways. Which of the following pathways is affected when neurons degenerate in Parkinson’s Disease?

A. Serotonin  
B. GABA  
C. Dopamine  
D. Glutamate  
E. Acetylcholine
Let us Pause Two Minutes for Questions
Physiology of the Neuron
(a little chemistry, physics, and biology)
Neurons communicate electrically & chemically

The impulse is initiated at the beginning of the axon
Ion distribution defines membrane potential

-70 mV
Neurons fire impulses based on the membrane potential

<table>
<thead>
<tr>
<th>Hyperpolarized</th>
<th>Resting</th>
<th>Depolarized</th>
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<tbody>
<tr>
<td>-90 mv</td>
<td>-70 mv</td>
<td>+30 mv</td>
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</table>

- Doesn’t fire | - | Will fire
Impulse generation & conduction
Sodium (Na\(^+\)) channels are key
Action potential: \( \text{Na}^+ \) in then \( \text{K}^+ \) out
Myelin speeds conduction of electrical impulse

Oligodendrocyte in CNS    Schwann cell in PNS
You’ve decided to tell your biology students that physics and chemistry play a big role in the physiology of neurons (i.e., how they work).

Which ions are major contributors to the voltage potential across a biological membrane?

<table>
<thead>
<tr>
<th>K⁺</th>
<th>Cl⁻</th>
<th>Ca²⁺</th>
<th>Na⁺</th>
<th>Mg²⁺</th>
</tr>
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</table>
Let us Pause Two Minutes for Questions
Synaptic Neurotransmission

Electrical to chemical to electrical
The synapse: Where neurons communicate
The dopamine synapse: Neuron releases dopamine
Transporters remove dopamine back into neuron
The serotonin synapse: Neuron releases serotonin
The acetylcholine synapse: Neuron releases acetylcholine
Ion channels open to produce electrical currents
Review: Steps in neurotransmission

1. Terminal membrane depolarizes
2. Neurotransmitter release
3. Receptor binding
4. Ion channels open or close
5. Change in membrane potential
6. Excitation or inhibition
7. Summation triggers action potentials
8. Inhibits action potentials

Excitation or inhibition can lead to summation, which triggers action potentials.
Test your knowledge!

Why do you think neurons need both electrical and chemical signals to communicate to each other?

A. Chemicals can’t travel down axons
B. Electrical impulses can’t jump across the synaptic space
C. Electrical currents can’t spread far enough
D. Chemicals only affect neurons locally
Let us Pause Two Minutes for Questions
How Psychoactive Drugs Work
Drugs change neurotransmission... one way or another
How do drugs work in the brain?

Drugs mimic, stimulate or reduce the actions of our neurotransmitters to change the firing rate of neurons.

....but how?
Drugs act at a target: proteins

- Receptors
- Ion channels
- Transporters
- Enzymes
Nicotine acts at acetylcholine receptor-ion channels to increase firing rate of neurons
Alcohol acts at GABA receptor-ion channels to decrease firing rate of neurons
Oxycontin™ acts at opioid receptors to decrease firing rate of neurons.
Cocaine blocks dopamine transporters (more dopamine binds receptors)
Test your knowledge!

Your students know that you took this course and want to know how marijuana works. You tell them that the THC in “pot” works similarly to morphine. It binds to a target to change the neuron firing rate.

Which is the target and what happens to the firing rate?

A. THC transporter  increases firing
B. THC ion channel  increases firing
C. THC ion channel  decreases firing
D. THC receptor  decreases firing
Let us Pause Two Minutes for Questions
Drug Addiction: A Brain Disease
Pathway in the brain for pleasure (reward)

From: SEEK about Tobacco
How do we know?

rat self-injects addicting drugs...and only into reward areas

From: SEEK about Tobacco at www.rise.duke.edu/seek
### Which drugs do rats self-inject?

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>Cocaine</td>
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<tr>
<td>Fluoxetine (Prozac™)</td>
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<tr>
<td>Morphine</td>
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<td>Alcohol</td>
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<td>Diazepam (Valium™)</td>
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<td>LSD</td>
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<tr>
<td>Amphetamines</td>
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<tr>
<td>THC</td>
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<td>Sugar</td>
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[Image: SEEK about Tobacco]
With chronic use of addictive drugs, behavioral adaptations occur

- **Tolerance**: Reduced effect…increase the dose
- **Dependence**: Function is normal with drug; withdrawal reaction without
- **Addiction**: Compulsive use, loss of control, craving
With chronic use of addictive drugs, neuronal adaptations occur:

- Receptors up- or down-regulate
- Neurotransmitter levels change
- Transporters down-regulate
- Chromatin structure changes
- Altered neurogenesis
- Dendrite spines increase or decrease
Chronic nicotine increases acetylcholine (nicotinic) receptors in the brain.
Dopamine receptors are decreased in reward pathway of drug abusers

Volkow et al., 2004
Amphetamines increase dendritic spines

normal

Meth

Robinson et al., 2001
Adaptations occur in disease

**Addiction**
- dopamine decreases
- DA receptors decrease
- dendrites change structure
- chromatin remodels
- synapses remodel
- dysfunctional prefrontal cortex

**Congestive heart failure**
- norepinephrine increases
- β-receptors decrease
- myofibrils change structure
- chromatin remodels
- muscle cells remodel
- dysfunctional ventricle
Test your knowledge!

Can nicotine change your brain? You bet!
Which of the following changes occur with repeated use of nicotine?

<table>
<thead>
<tr>
<th>More nicotinic receptors</th>
<th>More dendritic spines</th>
<th>Altered chromatin structure</th>
<th>Altered dopamine release</th>
<th>Fewer dopamine receptors</th>
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Let us Pause Two Minutes for Questions
Additional Resources for High School Teachers

Websites

The Pharmacology Education Partnership (PEP) Project  www.thepepproject.net
The Alcohol Pharmacology Education Partnership (APEP)  www.rise.duke.edu/apep
Science Education Enhances Knowledge (SEEK) About Tobacco  www.rise.duke.edu/seek
NIDA Teaching Packets  http://www.drugabuse.gov/pubs/teaching

Videos

Animated Neuroscience & The Actions of Nicotine, Cocaine & Marijuana in the Brain  (G Gross de Nunez & RD Schwartz-Bloom)  www.films.com
Additional Image Credits

**Brain Anatomy**: Slides 4-11, 19, 25-29  
From or adapted from Purves et al., (2001) Neuroscience (Sinauer, Inc.)

**The Neuron**: Slides 16, 17  
Adapted from [www.rise.duke.edu/resources.html](http://www.rise.duke.edu/resources.html) (Understanding FASD) (Illustration by Mark Williams)

**Synapses**: Slides 33-36, 43, 45, 48, 49  
Adapted from RD Schwartz-Bloom for NIDA.  

**Acetylcholine Synapses**: Slides 37, 38, 46  
From GG Gross de Nunez and RD Schwartz-Bloom.  
*[Animated Neuroscience & the Actions of Nicotine, Cocaine, & Marijuana in the Brain](http://www.films.com)*
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