
Synapses, Neurotransmitters and Receptors
 Psychology 472: Pharmacology of Psychoactive Drugs

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Synapses

- Contain three major structures
- Presynaptic Element
- Postsynaptic Element
- Synaptic Cleft

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Presynaptic Elements

- Are structures at the end of the Axon
- Contains
 - Mitochondria that provide energy for axon functions
 - Synaptic Vesicles (sacks) that contain signaling agents
 - Neurotransmitters
 - Neuropeptides
 - Cisternae (part of the Golgi apparatus that recycle vesicles)
 - Presynaptic Membrane
 - Autoreceptors
 - Other structures

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Postsynaptic Elements

- Can be part of a
 - Axon
 - Dendrite
 - Soma
- Contains
 - Postsynaptic Membrane
 - Receptors
 - Ion channels
 - Other structures

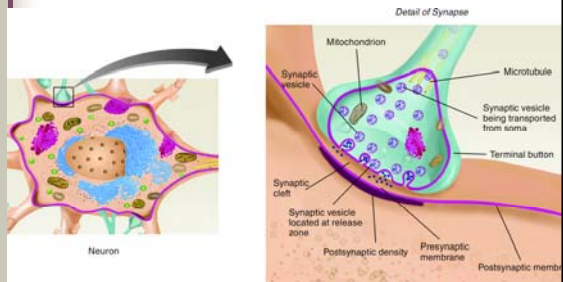
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Synaptic Cleft

- Is the physical gap between pre- and post-synaptic elements
- Is ~20-30 nM wide
- Contains enzymes from glial cells and post synaptic elements that break down signaling agents
- Neurofilaments
 - Helps keep the pre and postsynaptic elements in close proximity.
- Others

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Overview of the Synapse



The diagram illustrates the structure of a synapse. On the left, a neuron is shown with its cell body, axon, and a synapse. An arrow points to a detailed view of the synapse on the right. In this detail, a synaptic vesicle containing neurotransmitters is shown moving along a microtubule towards the synaptic cleft. A mitochondrion is also present. The synaptic cleft is the gap between the presynaptic membrane and the postsynaptic membrane. A synaptic vesicle is shown located at the release zone. Labels include: Neuron, Mitochondrion, Microtubule, Synaptic vesicle, Synaptic vesicle being transported from soma, Terminal button, Synaptic cleft, Synaptic vesicle located at release zone, Postsynaptic density, Presynaptic membrane, and Postsynaptic membrane.

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Types of Synapses

- A dendrite (axodendritic synapse)
 - Tend to be excitatory
- A cell body (axosomatic synapse)
 - Tend to be regulatory
- Another axon (axoaxonic synapse)
 - Tend to be inhibitory

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Formation of Neurotransmitters

Precursors.
 Brought to the neuron by the bloodstream.
 Taken up by cell body and/or terminal.
 Often come from substances in the diet.
 Enzymes put the ingredients together.

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Neurotransmitters

- Many types
- Most are stored in vesicles
 - Travel from the Soma
- Some are located throughout the element

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Seven Steps in Neurotransmitter Action

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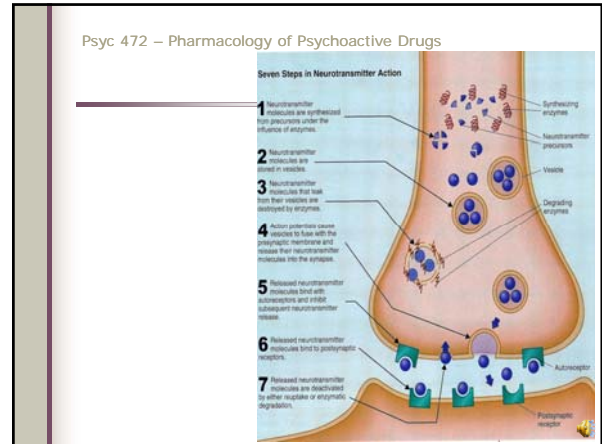
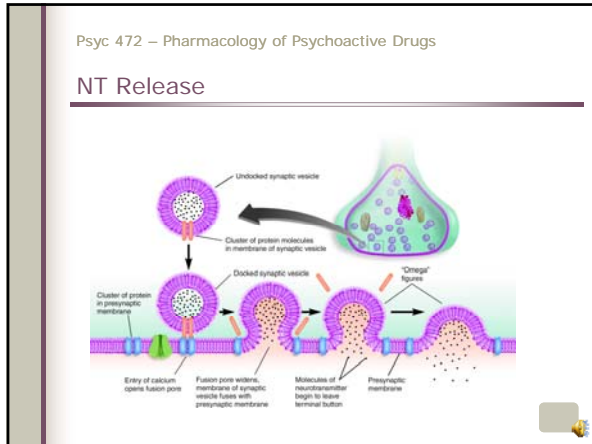
Neurotransmitter Release

- Vesicles lie near the presynaptic membrane
- The arrival of an action potential at the presynaptic element opens voltage-dependent Ca^{++} channels
 - Ca^{++} ions enter the axon via electrical and chemical concentration gradients
 - Ca^{++} ions modify the protein structure that bind the vesicles to the presynaptic membrane
 - A fusion pore is opened, which results in the merging of the vesicular and presynaptic membranes

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Vesicles

- Release their contents (exocytosis) into the synaptic cleft in packets (Called Quanta)
 - Release is called Quantal Release
- Neurotransmitter diffuses across the cleft to bind with postsynaptic membrane receptors



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Result

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Postsynaptic Potentials (PSPs)

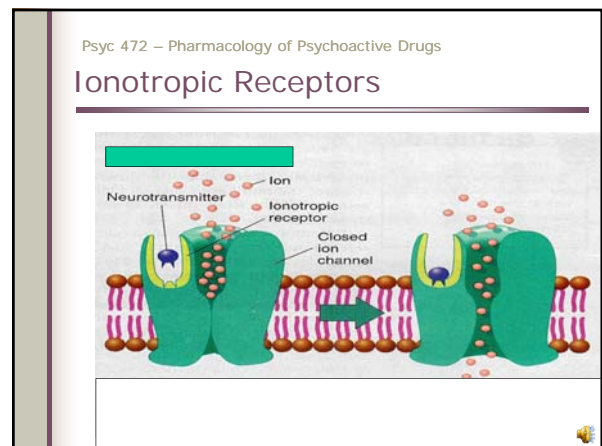
- Are either:
 1. Excitatory (EPSP)
 2. Inhibitory (IPSP)
- PSPs are conducted down the neuron membrane
- Neural integration at the Axon Hillock involves the algebraic summation of PSPs
 - More EPSPs at the Hillock will result in an action potential if depolarized 15mV

If not depolarized 15mV, no action potential
Is All or Nothing

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Receptors

- Two Major Types
 - Iontropic
 - Metabotropic



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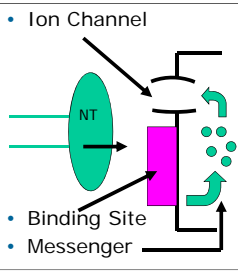
Characteristics

- Are very rapid to respond
 - Put on some NT and the channel opens
 - Take off the NT and the channel closes
- Is a simple system
- Ion channel is part of the receptor.

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Metabotropic Receptors (Metabolism)

- Ion channel and receptor sites are in different locations.
- Uses intracellular messengers from the binding site to the ion channel - Called second messengers



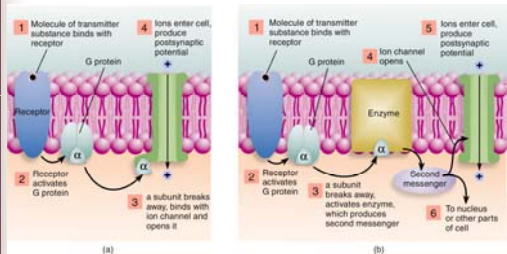
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Characteristics

- The channel is not part of the receptor
- There are intermediate steps that occur
 - Must put a phosphate group on the ion channel
 - Called Phosphorlation
- Are slow to respond compared to ionotropic receptors
- Are slow to shut down – Remove NT but have a delay to remove the phosphate groups – thus, the system still works for awhile
- Provides more regulation of the system.

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Metabotropic Receptors



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Some Second Messengers

- Calcium
- Cyclic AMP (CAMP)
- Calmodulin
- Others

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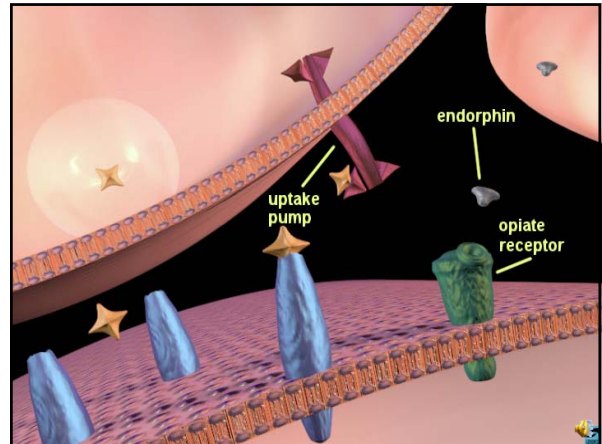
How to Shut Down the System

- Remove the NT
- Remove the phosphate group on the channel – closes the ion channel
- Remove the second messenger
 - Pump out the Ca

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How?

- Degrade
 - Simplest method
 - E.g., Acetylcholinesterase (AChE)
 - Is on the surface of the Postsynaptic Membrane
 - Degrades Ach to Choline and Acetate
 - Reabsorbed by the neuron
 - Is also in the synaptic Cleft



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How Do You Degrade and Bind on Receptors Simultaneously?

- Receptors have more affinity
- Bind tighter

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Drugs

- Can impact any part of the neuron
 - Can alter the lipid bilayer of the neuron
 - Can alter the amount of various ions entering the neuron structures
 - Can change the way the neuron processes the information
 - Can influence the speed of the action potential
 - Can influence NT release or reuptake

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Drugs

- Way the drugs alter the neuron will change the way the brain operates
 - Ultimately causes the behavioral effects
- Combinations of drugs will create multiple effects and impact multiple brain systems

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Termination of Synaptic Transmission

Seven Steps in Neurotransmitter Action

1. Degradation
2. Re-uptake
3. Re-uptake by glial cell (glutamate only)

The diagram shows a neuron with various components labeled: Synthesizing enzymes, Neurotransmitter precursors, Vesicles, Degrading enzymes, Autoreceptor, and Postsynaptic receptor. The seven steps are: 1. Neurotransmitter molecules are synthesized from precursors under the influence of enzymes. 2. Neurotransmitter molecules are stored in vesicles. 3. Neurotransmitter molecules that will bind their receptors are packaged by enzymes. 4. Action potentials cause vesicles to fuse with the presynaptic membrane and release their neurotransmitter molecules into the synapse. 5. Released neurotransmitter molecules bind with receptors and initiate subsequent neurotransmitter release. 6. Released neurotransmitter molecules bind to postsynaptic receptors. 7. Released neurotransmitter molecules are degraded in other vesicles or enzymatically degraded.

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Conclusions

- Lots of different systems operating in neurons
- Lots of systems operating in receptors
- Drugs can impact these systems at various sites or levels

