University of Idaho

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

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

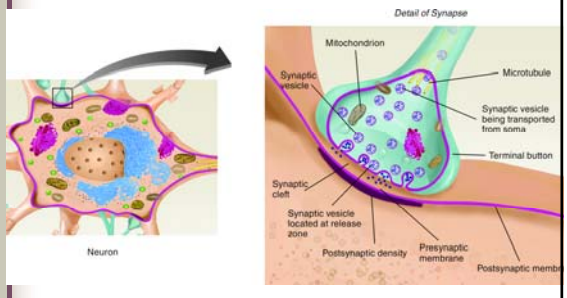
Postsynaptic Elements

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

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

Overview of the Synapse



Types of Synapses

A dendrite (axodendritic synapse)
- Tend to be excitatory

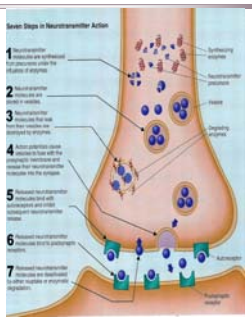
A cell body (axosomatic synapse)
- Tend to be regulatory

Another axon (axoaxonic synapse)
- Tend to be inhibitory

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.

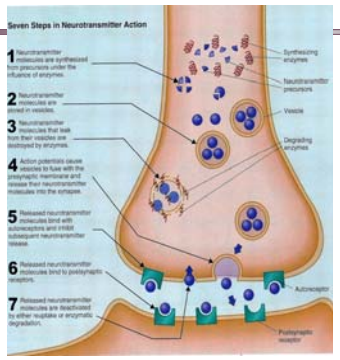


Neurotransmitters

Many types

Most are stored in vesicles
- Travel from the Soma

Some are located throughout the element



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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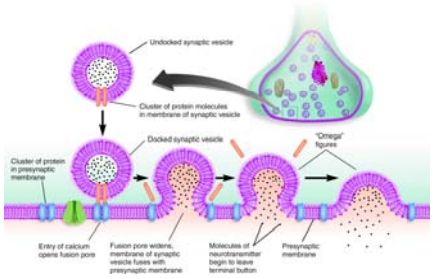
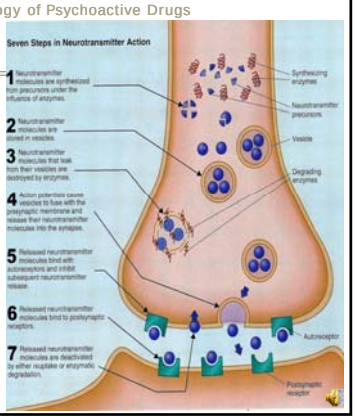
Vesicles

- 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

NT Release





Result

Postsynaptic Potentials (PSPs)

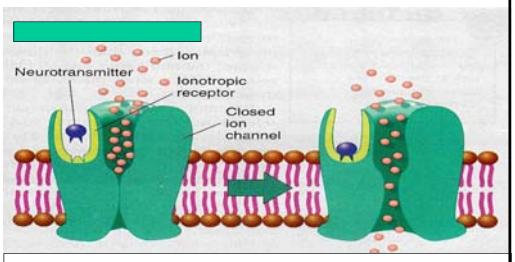
- Are either:
  1. Excitatory (EPSP)
  2. Inhibitory (IPSP)
- PSPs are conducted down the neuron membrane
- Neural integration at the Axon Hillock involves the algebraic summation of PSPs
  - More EPSPs at the Hillock will result in an action potential if depolarized 15mV

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

Receptors

- Two Major Types
  - Ionotropic
  - Metabotropic

Ionotropic Receptors

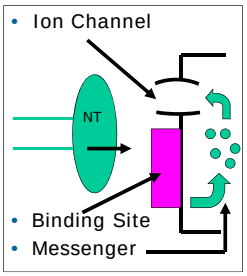


Characteristics

- 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.

Metabotropic Receptors (Metabolism)

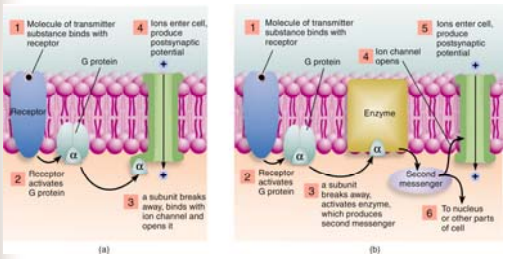
- Ion channel and receptor sites are in different locations.
- Uses intracellular messengers from the binding site to the ion channel - Called second messengers



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 ionotrophic 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.

Metabotropic Receptors



Some Second Messengers

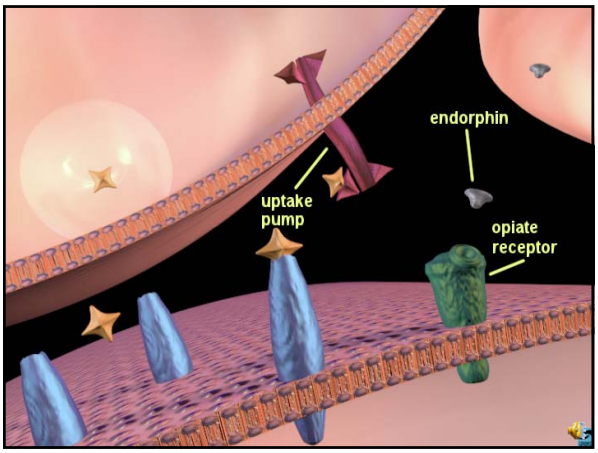
- Calcium
- Cyclic AMP (CAMP)
- Calmodulin
- Others

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

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



How Do You Degrade and Bind on Receptors Simultaneously?

- Receptors have more affinity
- Bind tighter

Drugs

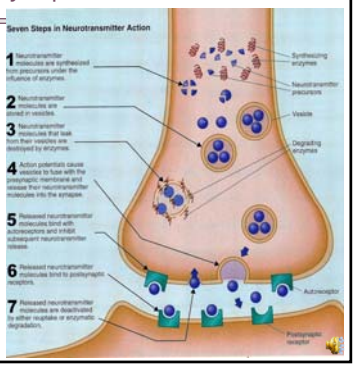
- Can impact any part of the neuron
  - Can alter the lipid bilayer of the neuron
  - Can alter the amount of various ions entering the neuron structures
  - Can change the way the neuron processes the information
  - Can influence the speed of the action potential
  - Can influence NT release or reuptake

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

Termination of Synaptic Transmission

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



Conclusions

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