  
**Synapses, Neurotransmitters,  
and Receptors**  
**Neurochemical Influences on  
Postsynaptic Elements**  
 Psychology 372  
 Physiological Psychology  
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**Synapses**

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

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**Presynaptic Elements**

- Presynaptic Elements are 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
  - Others

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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.

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**Neurotransmitter Release**

- Occurs when action potential causes voltage-gated  $Ca^{++}$  channels to open.
  - Ions enter due to electrical and chemical gradients
  - $Ca^{++}$  alters proteins that bind the vesicles to the presynaptic membrane.
- A fusion pore is opened,
  - Merges the vesicular and presynaptic membranes
- Vesicles release their contents (exocytosis) into the
  - synaptic cleft in packets (**Called Quanta**)
    - Release is called Quantal Release
- NT diffuses across the synaptic cleft
- Binds with postsynaptic membrane receptors

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### Result

- Postsynaptic Potential (PSPs)
- Are either:
  - Excitatory (EPSP) (depolarization)
  - Inhibitory (IPSP) (hyperpolarization)
- PSPs are conducted down the neuron membrane
- PSPs get to the Hillock
- Summate all of PSPs that arrive
  - If depolarized more than 15mV, get an action potential
  - If not depolarized 15mV, no action potential
  - Is All or Nothing

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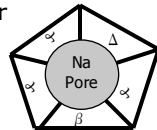
### Receptors

- Two Major Types
  - Ionotropic
  - Metabotropic

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### Ionotropic Receptors

- Receptor and ion channel are one Unit
- e.g., Nicotinic receptor



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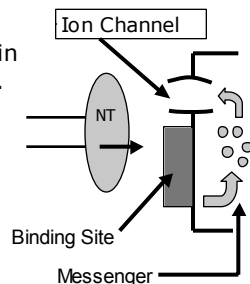
### Characteristics

- Are very rapid to respond
- – Put on some NT and the channel opens
  - Take of the NT and the channel closes
- Is a simple system
- Ion channel is part of the receptor. Most are not

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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 there is a delay to remove the phosphate groups – thus, the system still works for awhile
- Provides more regulation in the system.

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### Some Second Messengers

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

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### How to Shut Down the System

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

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### How to Remove NT?

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- Degrade
  - Simplest method
  - E.g., Acetylcholinesterase (AChE)
    - Is on the surface of the Postsynaptic Membrane
  - Degrades ACh.
    - Breaks into Choline and Acetate
  - Is also in the synaptic Cleft

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### Second Way

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- Reuptake
  - Reabsorb NT into the Presynaptic Element
- Lashachle Theorm
  - At equilibrium, NT bound on the receptor is the same concentration as the NT that is not bound.
  - Remove NT from the deft and the NT on the receptors comes off
    - Based on concentration gradients

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### How Do You Degrade and Bind on Receptors Simultaneously?

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- Receptors have more affinity
- Bind tighter

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### Receptors and Their Neurotransmitters

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### Acetylcholine (ACh)

- Is the primary NT secreted by efferent CNS cells
- In the periphery ACh neurons are found in:
  - Autonomic ganglia (e.g. the heart)
  - The neuromuscular junction (activation of muscle movement)
- In the brain: ACh neurons are found in:
  - Dorsolateral pons
  - Medial septum
  - Basal forebrain
  - Causes stimulatory effects

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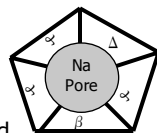
### ACh Receptors

- Two Types
- Nicotinic receptors
  - are found in skeletal muscle (ionotropic effect)
  - Agonists: ACh, nicotine
  - Antagonists: d-tubocurarine and curare
- Muscarinic receptors
  - are found in heart and smooth muscle (have metabotropic effects)
  - Agonists: ACh, muscarine
  - Antagonists: Atropine and scopolamine

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### Nicotinic Receptor

- Receptor and ion channel are one unit
- ACh binds to alpha subunit
- Beta and Delta subunits are concerned with regulatory functioning



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### Nicotinic Receptor

- If you put a phosphate group on Beta or Delta subunits – causes endocytosis. Receptor enters post synaptic element and is destroyed –
- Decreases sensitivity

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### Muscarinic Receptors

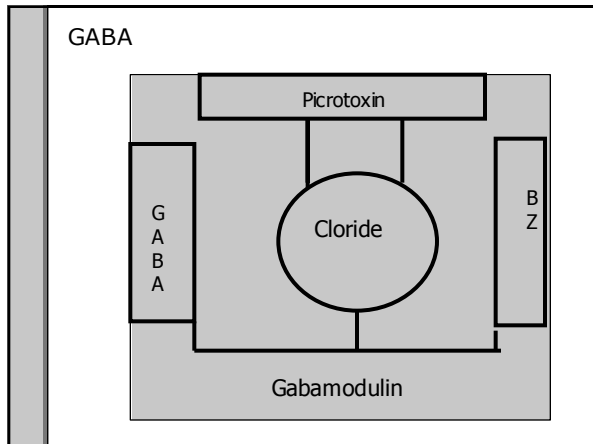
- Uses a GP second messenger system
- |  |                         |     |
|--|-------------------------|-----|
|  | ACh                     |     |
|  | Muscarinic Ach Receptor |     |
|  | Gp                      | PLC |
|  | IP-3                    | DA  |
|  | Ca Release              | PKC |

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### GABA

- Is synthesized from glutamic acid
- GABA induces IPSPs on post synaptic elements
- GABA acts via 2 receptors
  - GABA<sub>A</sub>: ionotropic receptor (controls a chloride channel)
  - Contain 5 distinct binding sites
    - GABA site
    - Benzodiazepine site
    - Barbiturates
    - Steroid binding site
    - Picrotoxin binding site
  - GABA<sub>B</sub>: metabotropic receptor (controls a K<sup>+</sup> channel)

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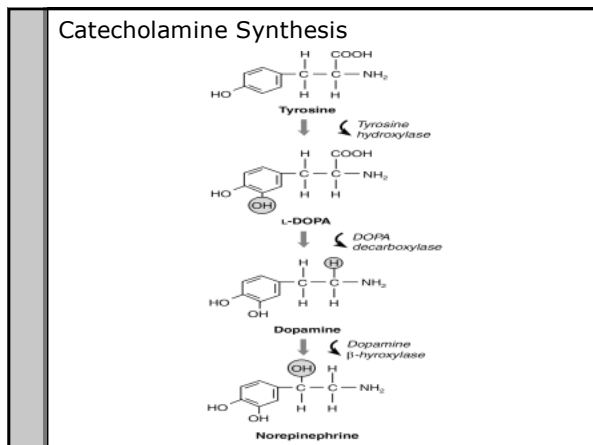


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### Biogenic Amine Transmitters

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### Dopamine

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- Is used by several systems
- Examples:
  - **Nigrostriatal** system projects from the substantia nigra to the caudate nucleus and putamen
  - **Mesolimbic** system projects from ventral tegmental area to the limbic system (including the nucleus accumbens, amygdala, and hippocampus)
  - **Mesocortical** system projects from the ventral tegmental area to the cortex
- Receptors are metabotropic
- D1 receptors are postsynaptic, whereas D2 receptors are pre- and postsynaptic

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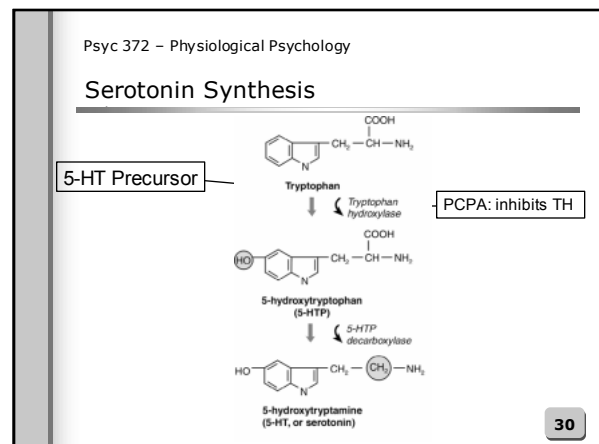
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### Norepinephrine

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- Is synthesized from dopamine within vesicles
- The locus coeruleus gives rise to NE fiber systems
  - NE is secreted from varicosities along fibers
- Interacts with four receptor types in brain
  - $\alpha$ -adrenergic (subtypes 1 and 2)
  - $\beta$ -adrenergic (subtypes 1 and 2)
- Adrenergic receptors are metabotropic

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### Serotonin

- Receptors are mostly located in the gut (98%)
- Only 2% of serotonin cells are in brain
- Serotonin cell bodies are located in brainstem raphe nuclei and project to cortex
- Serotonin systems:
  - D system originates in the dorsal raphe nucleus, but does not form synapses (used as a neuromodulator)
  - M system originates from the median raphe nucleus and ultimately forms synapses

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### Release and Termination

- Serotonin release:
  - 8-OHDPAT is an autoreceptor agonist that reduces 5-HT release
  - No selective release blocker
  - Fenfluramine is a 5-HT releasing drug
- Serotonin termination:
  - Reuptake is blocked by SSRI's (elevates 5HT)
  - Degradation: MAO converts serotonin to 5-HIAA

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### Serotonin Receptors

- There are at least 9 types of 5-HT receptors
  - 5-HT<sub>1</sub> : 1A, 1B, 1D, 1E, and 1F
  - 5-HT<sub>2</sub> : 2A, 2B, and 2C
  - 5-HT<sub>3</sub>
- 5-HT<sub>3</sub> receptors are ionotropic, the remainder are metabotropic
- 5-HT<sub>1B</sub> and 5-HT<sub>1D</sub> are presynaptic autoreceptors

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### Glutamate (Glutamic acid)

- Is an excitatory neurotransmitter
- Glutamate interacts with four receptor types
  - NMDA receptor:
    - Controls a Ca<sup>++</sup> channel
    - Activation requires glycine binding and displacement of magnesium ions
  - AMPA receptor: controls sodium channels
  - Kainate receptor: controls sodium channels
  - Metabotropic glutamate receptor

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### Peptides

- Are small proteins
- Usually consist of 30-40 amino acids
- Have more than 100 types
- Are synthesized in the soma and transported to axon terminal in vesicles
- Are released from the presynaptic element
- After release are degraded (no reuptake)
- Can be co-released with other NTs
  - Peptide can serve as neuromodulator

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