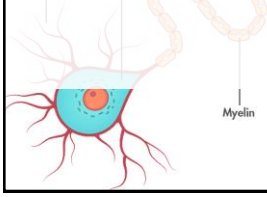
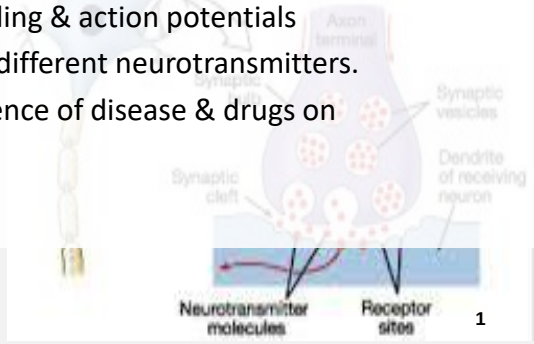
Ch 4, part 1: Neurons, Neurotransmitters, and Cell Communication.

This PowerPoint was updated 1/17/2025

Objectives:

1. Review different types of neurons and neuron anatomy.
2. Understand how neurons communicate.
   -neurotransmitter signaling & action potentials
3. Learn types & functions of different neurotransmitters.
4. Become familiar with influence of disease & drugs on neurotransmitter signaling.





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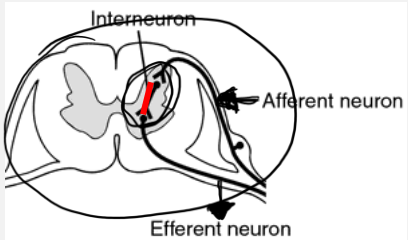
Different Types of Neurons

Anatomy REVIEW! See Pg 56, 73-74 of Wiki physiology book

1. Neurons
   a) **Sensory (afferent) neurons** = pick up sensory info & transmit to brain
   b) **Motor (efferent) neurons** = transmit motor command to muscle cells or glands, effect, movement
2. Interneurons (in CNS) =



sensory

3. Neuroglial (Glial) Cells = specialized cells

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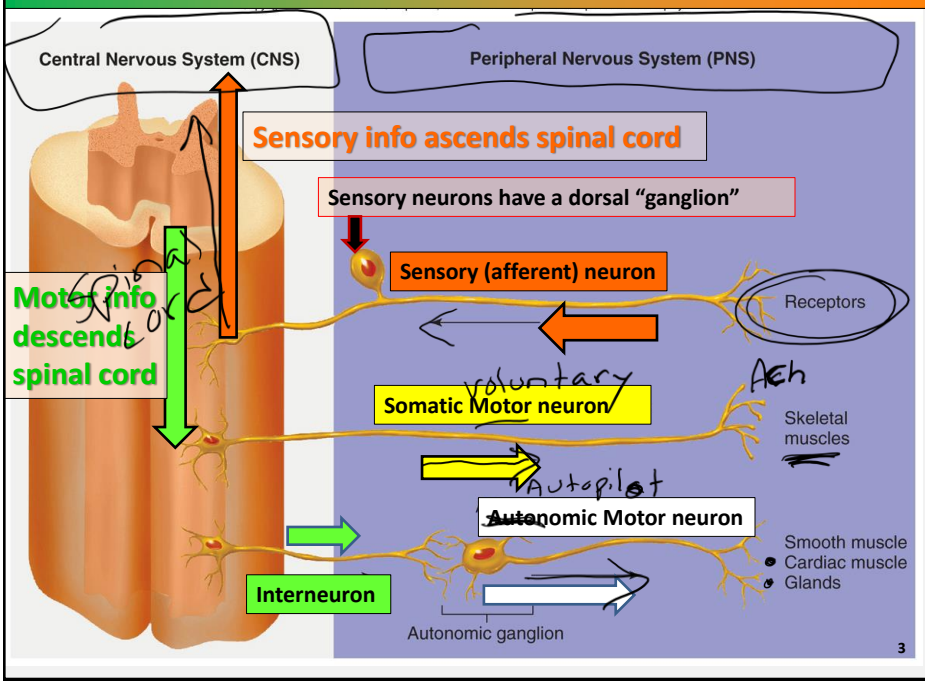
Different Types of Neurons



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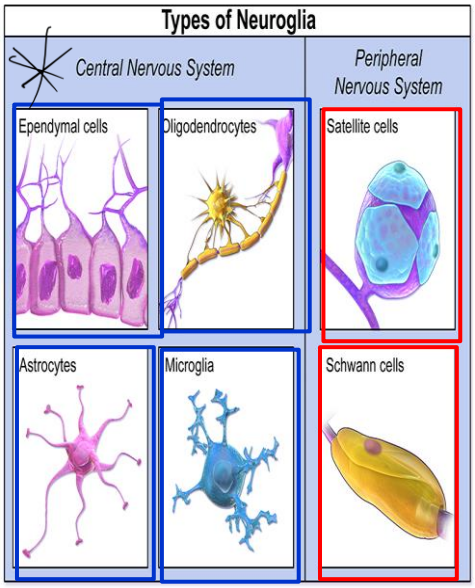
5 Types of Glial Cells (4 in CNS & 2 in PNS)



Ependymal cells = produce CSF in brain ventricles.

Astrocytes = part of blood brain barrier

Microglia = phagocytic cells that play immune function. "clean up crew"

Schwann cells (PNS) & **Oligodendrocytes (CNS)** = produce myelin sheath on neuron axons.

Satellite cells = involved in chronic pain. They ↑ in number w/ chronic paid

*Click **HERE** to read about satellite cells as future pharmacological targets for managing pain.*

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Neuron Anatomy (Anatomy Review!)

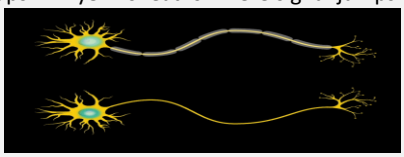
Dendrites = picks up sensory info from other neurons.

Cell body = where cell nucleus of neuron found.

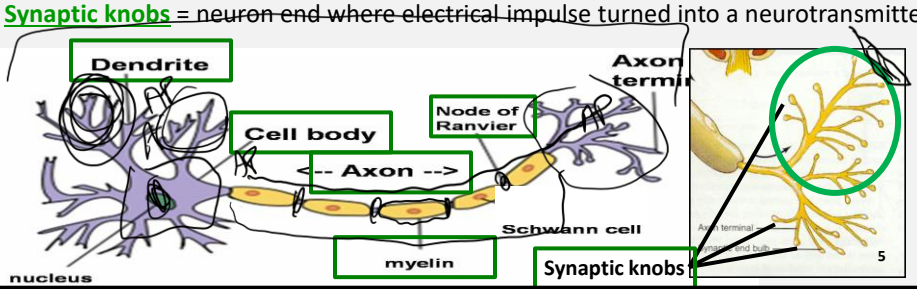
Axon = elongated tube that transmits impulse (AP) from cell body to synaptic knobs (end of neuron)

Myelin sheath = insulated wrappings around axon that keeps signal from dissipating from axon. *[unmylenated axon = **0.5 m/sec** VS mylenated axon = **100 m/sec!]***

Nodes of Ranvier = gaps in myelin sheaths where signal jumps to next node (faster conduction)



Synaptic knobs = ~~neuron end where electrical impulse~~ turned into a neurotransmitter.



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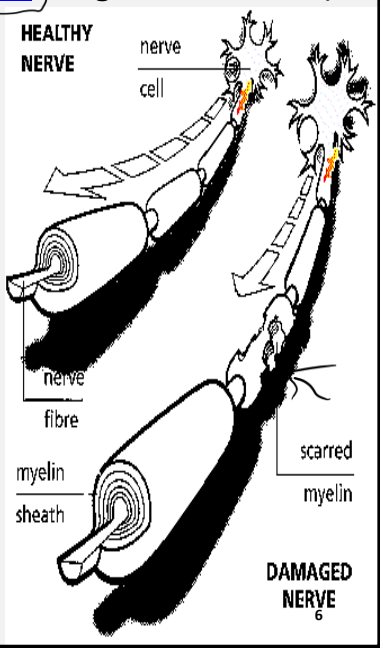
Multiple Sclerosis (Clinical App online & Pg 74 Wiki book)

= Autoimmune attack on myelin sheaths.

It slows transmission of electrical impulses, especially in motor neurons involved in movement.

Patients have motor (movement) and many other problems.



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1. Different Types of Neurons and Neuron Anatomy

Pre-synaptic neuron = neuron before synapse that secretes a neurotransmitter

Post-synaptic neuron = cell after synapse with receptor for neurotransmitter (muscle cell or gland cell)

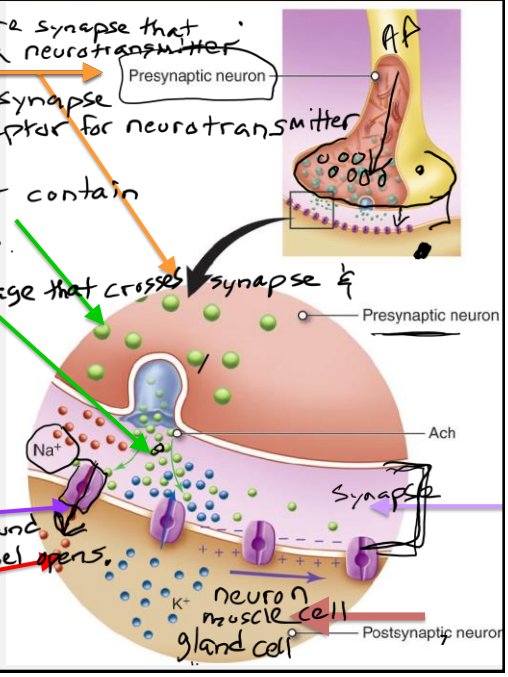
Secretory vesicles = in neurons that contain neurotransmitter.

Neurotransmitter = chemical message that crosses synapse & binds to receptor on cell.

Synapse = space between presynaptic & postsynaptic cell.

Receptor with ion channel = when bound to a neurotransmitter, ion channel opens.

*Binding of receptor opens ion channel & **ions** flood into cell, causing AP.*



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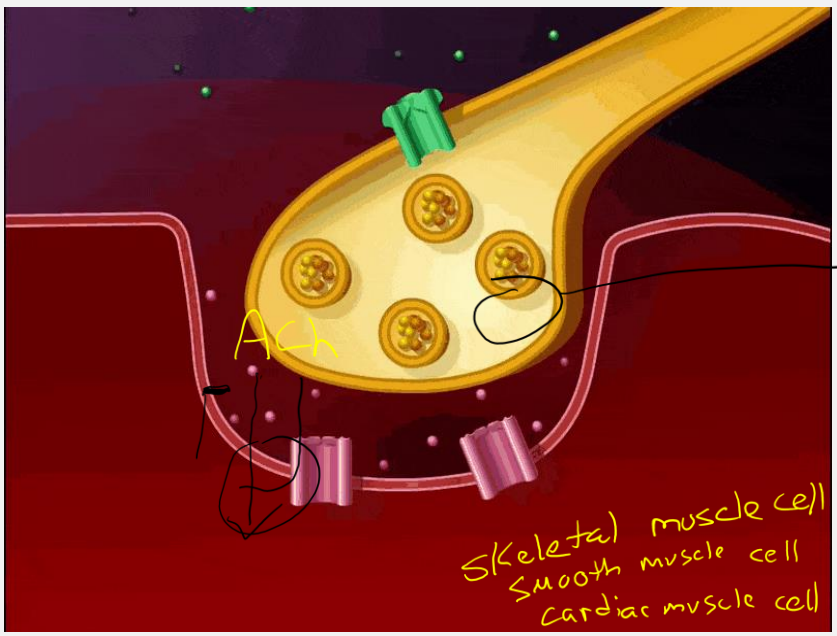

Click HERE for GIF

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Review

Types of neural tissue

- Neurons (sensory/afferent, motor/efferent, and interneurons)
- Neuroglial (Glial) cells
  - CNS – astrocytes, microglia, ependymal cells, oligodendrocytes
  - PNS – schwaan cells, satellite cells

Anatomy of a neuron

- Cell body, dendrites, axon, myelin sheath, nodes, synaptic knobs, synapse, secretory vesicles, neurotransmitters, pre-synaptic neurons, post-synaptic neurons.

Neurons communicate with post-synaptic cells by secreting neurotransmitters, which bind to receptor on post-synaptic cell and open up ion channels.

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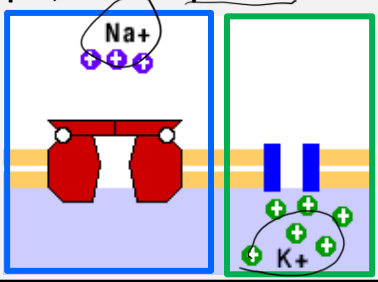
2. How Neurons Communicate with Cells

Neurotransmitter signaling = a chemical signal binds to receptor on cell membrane (ex. When acetylcholine (ACh) binds to a receptor), which:

Pg 57 in Wiki physiology textbook

① **Opens Na^+ channel or Ca^{+2} channel** in membrane, Na+ or Ca+2 floods into cell causing **action potential (AP)** or "**depolarization**", which **stimulates** a cell.

② If **K^+ channels or Cl^- open**, causes "**repolarization**" or **rest**, which inhibits cells.



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Neurotransmitter signaling:

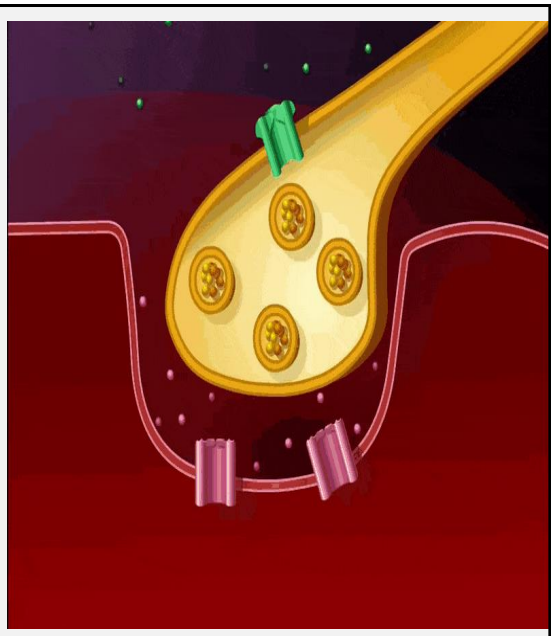
1. Pre-synaptic neuron releases neurotransmitter (like ACh) into synapse.

2. Neurotrans. binds to receptor on post-synaptic cell, opens ion (usually Na+) channels on cell membrane.

3. Na+ floods into cell, causes **action potential (AP)** to form.

4. AP travels through cell.

Click HERE for GIF



Click HERE on the PDF copy of this powerpoint for an excellent YouTube video of how neurotransmitter can either stimulates a post-synaptic cell or inhibit it.

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Ion channels and cell stimulation or inhibition

Pg 57 in Wiki Physiology textbook

IN GENERAL:

If a neurotransmitter binds to a receptor on a cell and it **opens sodium (Na+) or calcium (Ca+2) ion channels** it will

Na^+

Sodium is always **S**timulatory.
Calcium makes cells **C**razy!

Ca^{+2}

If a neurotransmitter binds to a receptor on a cell and it opens **potassium (K+) or chloride (Cl-) ion channels**, it will

potassium (**K**+) helps cells **K**ick back and relax.
Chloride helps cells stay **C**alm.

Click **HERE** for YouTube video of cell being stimulated versus inhibited, based on what ion channel opens. (~2 min)

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Neurotransmitter binding to receptor opens stimulatory ion channel:

CAN EITHER: stimulate

A) Cause an Action Potential (Excitatory post-synaptic potential or EPSP) =
IF neurotransmitter binds to receptor that opens **Na+ or Ca+2 channels**, & causes an AP to form.

- **EPSP can produce "graded potential"** = amount of neurotransmitter.
  small amt of neurotransmitter = small cell response
  a lot of neurotrans = big cell response

- **EPSP can produce "summation"** = *Repeated* (high frequency) of neurotransmitter stimulation.

Example: the increase in heart rate with epinephrine (a.k.a. adrenaline) binding to its **Beta-1 adrenergic receptor** on **heart muscle cells** is due to opening of Na+ and Ca+2 channels!

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Neurotransmitter binding to receptor opens inhibitory ion channel :

CAN EITHER:

A) Cause an Action Potential (Excitatory post-synaptic potential or EPSP) =
IF neurotransmitter binds to receptor that opens **Na+ or Ca+2 channels**, & causes an AP to form.

- **EPSP can produce "graded potential"**

- **EPSP can produce "summation"**

B) Inhibits an Action Potential (Inhibitory post-synaptic potential or IPSP) =
IF neurotransmitter binds to a receptor & opens **K+ or Cl- channels**, prevents an AP from forming.

Example: the decrease in heart rate with **acetylcholine (ACh)** binding to its **muscarinic cholinergic** receptors on heart muscle is due to opening of K+ channels!

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Regulation of Neurotransmitter Action:

The 2 R's:

1) Receptor types

- neurotransmitter effect depends on what kind of receptor it binds to.

Either:

A. Nicotinic (ion-gated) receptor – receptor found on skeletal muscles for Acetylcholine. receptors called nicotinic cholinergic receptors

You Must do it (for autonomic responses)

B. Muscarinic (G-protein coupled) receptor –

Ex. The receptor on heart muscle for ACh is a muscarinic cholinergic receptor

2) Removal systems for neurotransmitters

(4 removal systems – find on slide 23)

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1) Receptor types:

A. Nicotinic (Ion-gated) receptor on skeletal muscles

- For ACh neurotransmitter
- Binding of receptor by ACh causes Na+ ion channels to open
- **Na+** channels opening causes stimulation of a cell (muscle cells contract)

Skeletal muscle cells have nicotinic cholinergic receptors for ACh, which open Na+ channels for voluntary muscle contraction.

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1) Receptor types:

A. Nicotinic (Ion-gated) receptor

- For ACh neurotransmitter
- Binding of receptor by ACh causes Na+ ion channels to open
- **Na+** channels opening causes stimulation of a cell (muscle cells contract)

Thus, **skeletal muscle cells have nicotinic cholinergic receptors for ACh for voluntary movement.**

B. Muscarinic (G-protein coupled) receptor for cardiac muscle, smooth muscle, or gland cells:

- Neurotransmitter binding to cell receptor activates a G-protein
- then opens ion channels.

  IF **Na+ and Ca+2** channel opens = stimulates or causes EPSP

  IF **K+ or Cl-** channel opens = inhibits or causes IPSP

- For ACh, norepinephrine & epinephrine, & other neurotransmitters
- **Muscarinic receptors are for involuntary actions (heart muscle, smooth muscle, and gland cells MUST respond.**

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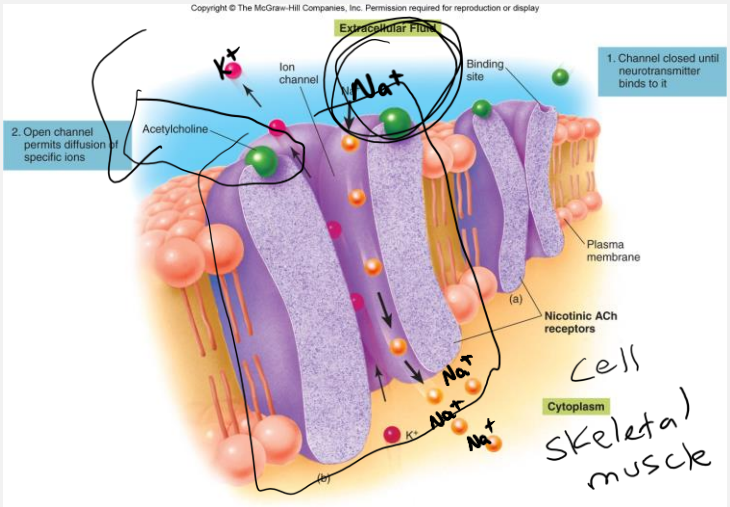
Ex. Nicotinic cholinergic (ACh) receptors



Is this neurotransmitter and receptor going to have an EPSP or IPSP response? EPSP

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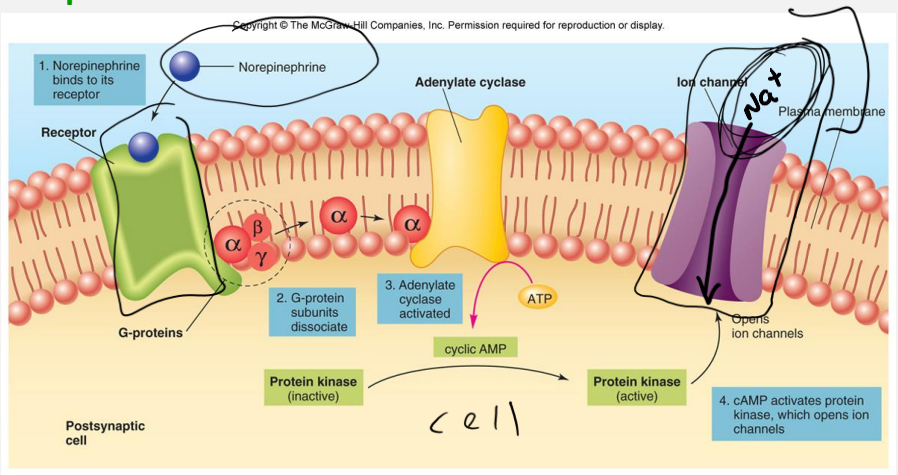
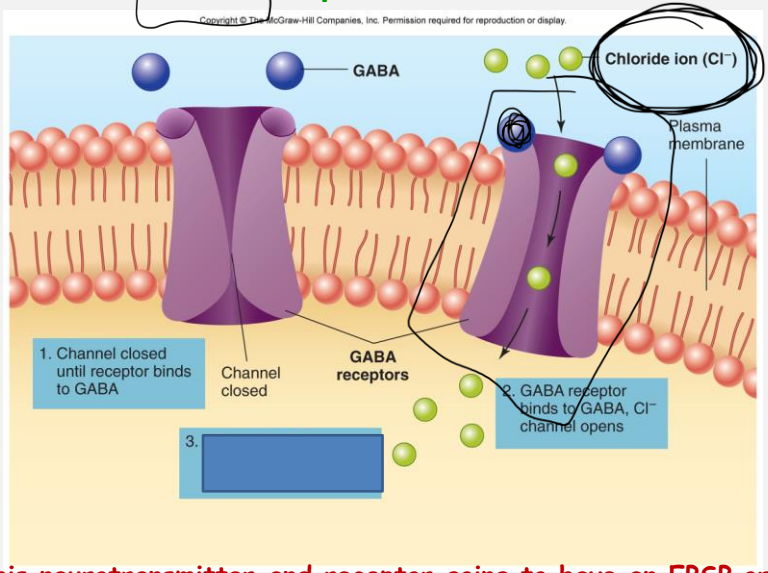
Ex. Muscarinic adrenergic (epinephrine, norepinephrine) receptors



Is this neurotransmitter and receptor going to have an EPSP or IPSP response? _____

Ex. Muscarinic GABA receptor



Is this neurotransmitter and receptor going to have an EPSP or IPSP response? _____

For ACh and its receptors:

TABLE 6.4 Effects of Acetylcholine (ACh) in the PNS

Neurons Releasing ACh	Location	Type of ACh Receptor	Response	Physiological Effect
Somatic (voluntary) motor neurons	Skeletal muscles	Nicotinic cholinergic	Depolarization, producing action potentials	Muscle contraction
Parasympathetic (involuntary) motor neurons	Smooth muscles, glands	Muscarinic cholinergic	Depolarization, producing action potentials	Contraction of smooth muscles; secretion of glands
Parasympathetic (involuntary) motor neurons	Heart	Muscarinic cholinergic	Hyperpolarization, slowing the rate of automatic production of action potentials	Slowing of heart rate

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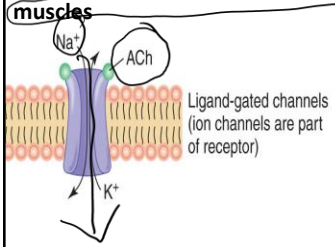
ACh & Nicotinic Cholinergic Receptors

Postsynaptic membrane of

> All autonomic ganglia from spinal cord

> For voluntary control of skeletal muscles



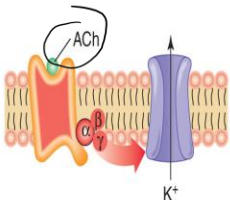
Open Na+ channels
Na+ enters cell
Cell depolarized (AP forms)

Excitation

muscle contraction

ACh & Muscarinic Cholinergic Receptors

Produces autonomic parasympathetic (rest and digest) functions in cardica muscle, smooth muscle, & glands.

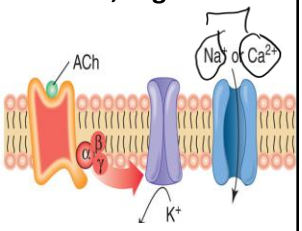


Open K+ channels
K+ leaves cell
Cell repolarized (rests)

(K+ channels opened)

Inhibition

↓ Heart rate



Open Na+ channels
Na+ enters cell
Cell depolarized (AP forms)

(K+ channels closed)

Smooth muscle

Excitation

↑ GI tract activity

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1) Receptor Types:

2) Neurotransmitter Removal Systems:

Click HERE for a YouTube video that explains neurotransmitter removal

4 Systems:

i) **Diffusion** = neurotrans diffuses out of synapse.

*** ii) **Enzyme Breakdown** = enzyme breaks down neurotrans so it's no longer active.

- Ex. **ACh-E** = Acetylcholinesterase - breaks down ACh.

MAO = monoamine oxidase - breaks down monoamine neurotransmitters like epinephrine, dopamine, and serotonin.

iii) **Glial removal** = glial cells (ex. astrocytes) remove neurotrans.

*** v) **Reuptake** = neurotrans is taken back up by neuron that secreted.

Ex. Prozac, Lexapro, Citalopram are SSRI's.

SSRI = Selective serotonin reuptake inhibitor

Pg 65 & 75 Wiki physiology text

leaves more serotonin in synapse

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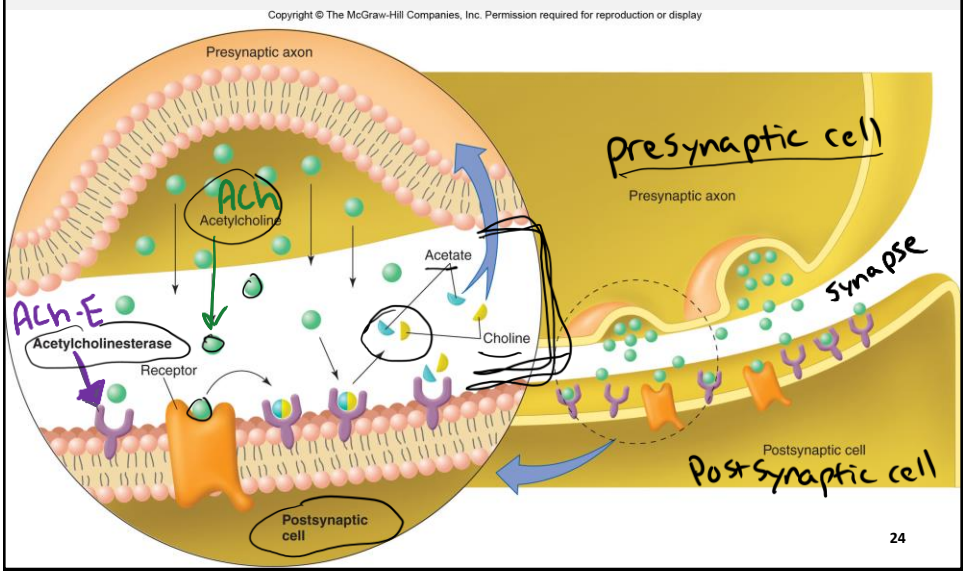
Ex. Enzyme breakdown of neurotransmitter:

Acetylcholinesterase (ACh-E) = enzyme that breaks down ACh in synapses. (Ex. Between somatic motor neurons & skeletal muscle cell)



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Click HERE on the PDF copy of the powerpoint for a YouTube video of ACh release into synapse, binding to receptor on a cell & opening Na+ channel, then breakdown of ACh by ACh-E

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Review

Neurotransmitters @ synapse

- Neurotransmitter released at synapse & binds to receptor on post-synaptic cell.
- If that receptor opens Na+ or Ca+2 channels, it causes an EPSP (cell is stimulated)
- If that receptor opens K+ or Cl- channels, it causes an IPSP (cell inhibited or rests)
- EPSPs can have: Graded potential or summation

2 Ways neurotransmitters regulated:

- Receptor types (nicotinic versus muscarinic)
- neurotransmitter removal systems

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4. Types and Functions of Neurotransmitters

+ stimulatory – inhibitory	CNS neurotransmitters	PNS neurotransmitters
I. Choline-derived:	ACh is + in CNS	ACh autonomic Parasympathetic regulation if PNS + or –
II. Mono-amine derived (catecholamines):	norepinephrine (+) dopamine + Serotonin (10% receptors in brain)	epinephrine (autonomic Sympathetic regulation of PNS) is + or – Serotonin (90% receptors in intestines)
III."Other" amino acid derived:	Glutamate (+) stimulates brain Glycine (-) GABA (-) (gamma amino butyric acid)	
IV. Soluble gas:	nitric oxide (NO)	nitric oxide (NO)

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I. Acetylcholine (ACh)

- In both CNS & PNS
- Both excitatory (EPSPs) and inhibitory (IPSPs) – depending on ion channel
- Enzyme breakdown by acetylcholinesterase (ACh-E)

- Involves 2 types cholinergic receptors: Review!

1) Nicotinic cholinergic receptor

- ACh released @ neuromuscular junction (between somatic motor neuron & skeletal muscle cells)
- excitatory only (EPSPs), opens Na+ channels on skeletal muscles.
- causes skeletal muscles to contract.

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I. Acetylcholine (ACh)

- **In both CNS & PNS**
- **Both excitatory (EPSPs) and inhibitory (IPSPs) – depending on ion channel**
- **Enzyme breakdown by acetylcholinesterase (ACh-E)**

- Involves 2 types cholinergic receptors: Review!

1) **Nicotinic cholinergic receptor**
   - ACh released @ neuromuscular junction (between somatic motor neuron & skeletal muscle cells)
   - excitatory only (EPSPs), opens Na+ channels on skeletal muscles
   - causes skeletal muscles to contract.

must For ACh

2) Muscarinic cholinergic receptor (for ACh or epinephrine)

- for **autonomic parasympathetic regulation of smooth muscles, cardiac muscle, and glands. They MUST respond.**
- **inhibitory (IPSPs)** on cardiac muscle if **K+** or **Cl-** channels open. (Ex. ↓ heart rate & contractile strength)
- **stimulatory (EPSPs)** in GI smooth muscle & glands if **Na+** or **Ca^{+2}** channels open. (↑ GI activity)

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Click **HERE** for ACh blank flow diagram, and **HERE** for KEY.

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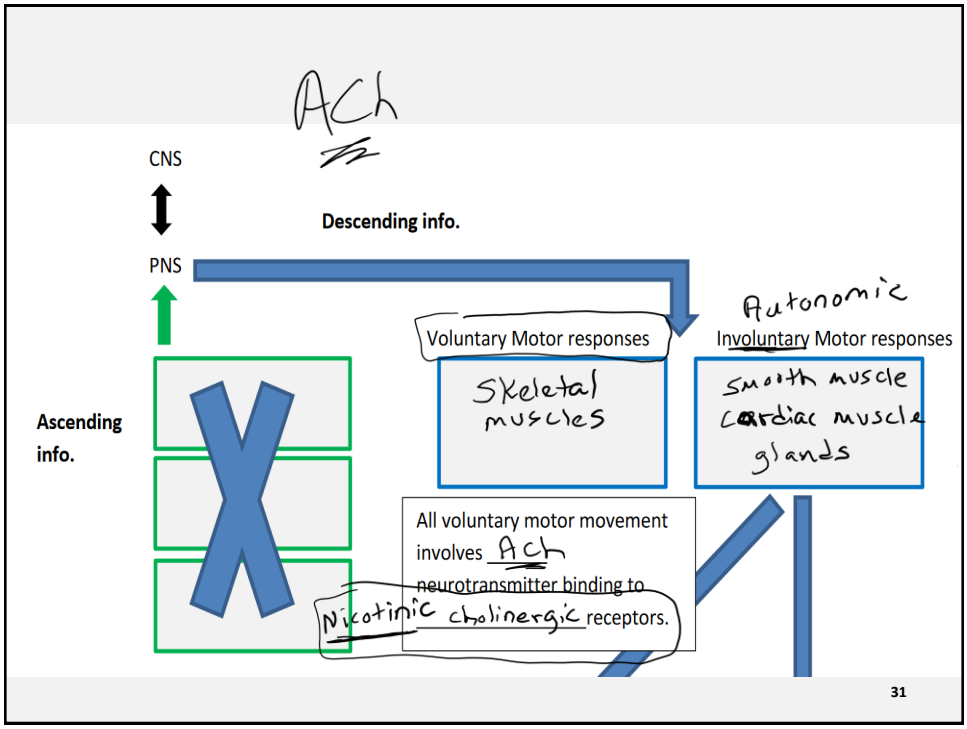
ACh
CNS
Descending info.
PNS
Autonomic
Voluntary Motor responses
Involuntary Motor responses
Skeletal muscles
smooth muscle
cardiac muscle
glands
Ascending info.
All voluntary motor movement involves ACh neurotransmitter binding to Nicotinic cholinergic receptors.
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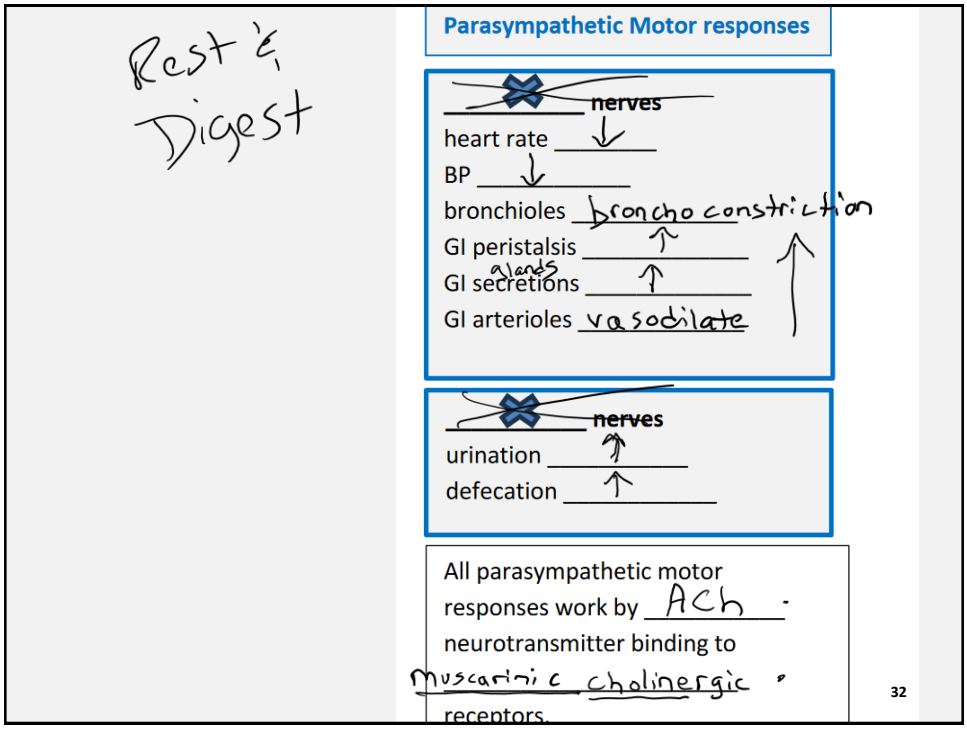
Rest & Digest
Parasympathetic Motor responses
nerves
heart rate ↓
BP ↓
bronchioles broncho constriction
GI peristalsis ↑
GI secretions (glands) ↑
GI arterioles vasodilate
nerves
urination ↑
defecation ↑
All parasympathetic motor responses work by ACh neurotransmitter binding to Muscarinic cholinergic receptors.
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Drugs/agents that influence activity of a neurotransmitter:

Agonist = drug/agent that ↑ amount of neurotrans
or stimulates its receptor.

Antagonist = drug/agent that ↓ amount of neurotrans. or stimulates its receptor directly.
Blocker

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I. Inhibition of enzyme ACh breakdown.

ACh-E = acetylcholinesterase
breaks down ACh.

A) Acetylcholinesterase inhibitor (ACh-EI)

- Stops ACh-E from breaking down ACh.
- ↑ ACh in Synapses
- causes "**cholinergic syndrome**"

Malathion fogging by truck

Question: ~~Is an ACh-EI~~
an ACh AGONIST? OR ANTAGONIST?

Ex. 1: Organophosphate pesticides are ACh-EI's

- **Malathion – mosquito control**
- **Carbamate – general insecticide**
- **Chlorpyrifos (dursban) – used in flea & tick meds**
  (banned in USA, 2001) DO NOT USE!!!

Carbamate spraying of crops

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Ex. 2: Non-organophosphate pesticide = Pyrethrins
(from *Chrysanthemum plant)*

- **Likely an ACh-EI in in cats (DO NOT USE!!!), but not dogs**

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I. Acetylcholine (ACh) - inhibition of enzyme breakdown.

Ex. 3: Sarin gas (biological weapon - nerve gas) are ACh-EI's
– Clinical App online

Sarin attack in subways:
Tokyo, Japan 1995
12 people died, 5,000 injured.

2012 – Syrian government threatening use of sarin chemical warfare against rebels.

2013 – Attack happened by rockets to surface delivery.
3,600 hospitalized patients displayed neurotoxic effects attributed to Sarin gas.

Estimated 281 – 1,729 deaths by neurotoxicity.

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"Clinical Presentation" of someone cholinergic syndrome =

Click HERE for NIH article on this. Worldwide organophosphate and carbamate exposures = 3 million / year with 200,000 fatalities. Click **HERE** for organophosphate use in US. ***Slide updated 1/31/25***

Mnemonic for cholinergic syndrome:

DUMBBELSS - stands for

D iarrhea

U rination

M iosis (constricted pupils)

B radycardia (lower HR)

B ronchoconstriction

E mesis (vomiting)

L acrimation (eyes water)

S alivation

S weating seizures

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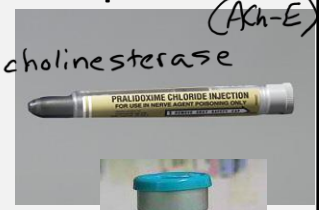
Treatment for cholinergic syndrome from ACh-EI exposure:



(ACh-E)

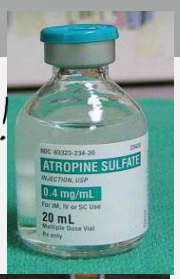
To reverse cholinergic syndrome:

Pralidoxime (2-PAM) - restore function of Acetylcholinesterase

To Treat symptoms:

Atropine (*Physiology in Health & Disease* Pg 119 and online)

is a muscarinic cholinergic receptor blocker.



Stops symptoms of DUMBBELSS

Question: is Atropine an ACh agonist or antagonist?

Valium (benzodiazepine) Clinical App Pg 114 and online

is a skeletal muscle relaxant. Stops muscle seizures

works by stimulating GABA.

Ques: is Valium a GABA agonist or antagonist?

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Toxins that are ACh Agonists:

Clinical App online

Tetanus victim

A. Tetanus = toxin produced by *Clostridium tetani*
(found on rusty metal – puncture wound)
- is an ACh agonist
- promotes muscle tetany ("**spastic paralysis**" OR **"hypertonia")**
- trismus, or lockjaw
- also a Glycine and GABA antagonist (prevents muscle relaxation).

- prevent w/booster of **tetanus vaccine** every 10 yrs
- suspect exposure, give shot of **tetanus antitoxin**

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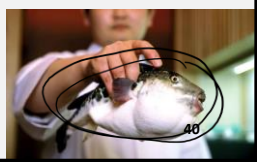
Toxins that are ACh Antagonists : *Clinical Applications* online

Clinical "presentation" of someone w/ACh insufficiency =

A. Botulism = toxin produced by *Clostridium botulinum*
> Prevents ACh from leaving presynaptic vesicles
(no ACh no skeletal muscle contractions!)
> Causes **flaccid paralysis or hypotonia** (is an ACh antagonist)

B. Paralytic shellfish poisoning (online)
> Shellfish harvested during red tide have "**saxitoxin**"
> Blocks ACh nicotinic cholinergic channels (prevent Na+ entry)
> Prevents skeletal muscle contraction
> **flaccid paralysis or hypotonia** (is an ACh antagonist)

c. Pufferfish poisoning (online)
> Fugu fish have "**tetrodotoxin**".
> Blocks ACh nicotinic cholinergic channels (prevent Na+ entry)
> Prevents skeletal muscle contraction
> **flaccid paralysis or hypotonia** (is an ACh antagonist)



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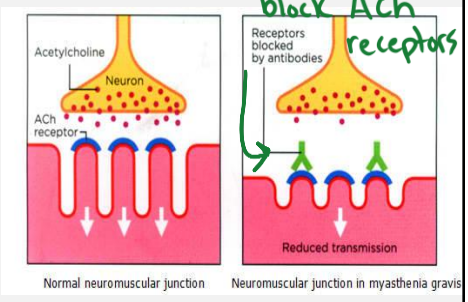
"Other Disorders" of ACh insufficiency a.k.a. ACh antagonists):

antibodies block ACh receptors

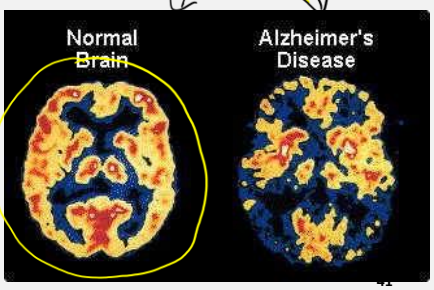
Myasthenia gravis (Clinical App online)
> Autoimmune destruction of ACh receptors.
> Reduced muscle function, weakness, pharyngeal swallowing problems.



Alzheimer's disease

+ brain & spinal cord

> loss of ACh producing neurons in brain.
> Excess glutamate production in brain (glutamate toxicity)
> memory problems.



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Question: What drug could you give a patient with low ACh (like Alzheimer's), or have a loss of ACh receptors (like Myasthenia gravis), to improve their functioning and help their symptoms?

An Acetylcholinesterase inhibitor! *No not memorize!*

Ex. For Alzheimer's: Galantamine, Rivastigmine, Donepezil

Ex. For myasthenia gravis: Neostigmine & Pyridostigmine

Although these drugs improve muscle function with these disorders, they DO have side effects from increased ACh, such as bradycardia, spastic gut, excess urination, and bronchoconstriction (part of DUMBBELLS).

What drug could you give to keep heart rate up, slow down the GI system, and to decreases the urination and bronchoconstriction??

Atropine! (blocks muscarinic cholinergic receptors.

Click HERE for a really good YouTube video explaining the problem with ACh signaling in myasthenia gravis, and the drugs used to diagnose and treat the disorder.

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Review

End of Exam 1 material

- Types of Neurotransmitters
  - ACh signaling
    - Voluntary skeletal muscle contraction
    - Involuntary actions on heart and smooth muscle
    - Removal of ACh by ACh-E
    - Cholinergic syndrome (DUMBBELLS) and its treatment
    - Chemicals & Toxins that are ACh agonists (organophosphate pesticides, Permethrin insecticides, sarin gas, and tetanus toxin)
    - Toxins that are ACh antagonists (botulism toxin, , saxitoxin, tetrodotoxin)
    - Disorders of ACh signaling in Alzheimers and Myasthenia gravis

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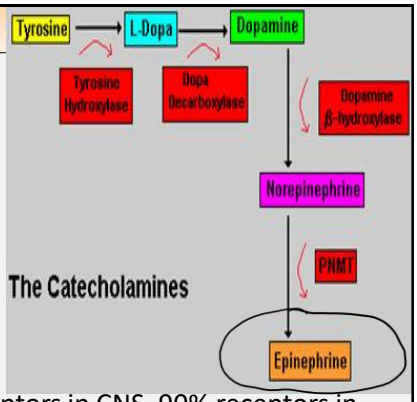
II. Monoamine Neurotransmitters

Fri Lecture

Catecholamines

> dopamine, norepinephrine & epinephrine (all made from tyrosine)



Dopamine – plays role in fine motor control And reward for pleasurable activities (also Plays role in psychological addictions)

Serotonin - made from tryptophan. 10% receptors in CNS, 90% receptors in GI system. Plays role in memory, moods, emotions.

Regulated by:

1) Reuptake – primarily with serotonin

QUES: What are SSRI's? selective serotonin reuptake inhibitor

2) Enzyme breakdown by monoamine oxidase (MAO) – breaks down dopamine, norepinephrine & epinephrine, *and some serotonin*.

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II. Monoamine Neurotransmitters – inhibiting enzyme breakdown.

If have low levels of dopamine, serotonin, or norepinephrine can treat with MAO-I's to buildup monoamines in synapse.

MAO-I = monoamine oxidase inhibitor (or a monoamine agonist)

2 types MAO-I's:

CNS

MAO-I A - agonist to norepinephrine & serotonin
*(think **A** for **A**gitation or anxiety, and **A** for **A**ppetite)*

GI

MAO-I B – agonist to dopamine
*(think **B** for Dope **B**eat)*

See supplemental reading online for MAO-I's

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II. Monoamine Neurotransmitters

Serotonin

- 10% of serotonin receptors in brain
  regulates memory, moods, emotions, behavior, & hallucinations

- 90% of serotonin receptors in intestines (regulates appetite)

- Insufficient serotonin – associated with depression & obesity

Low

QUES:
What can you give to build up serotonin in synapses?

SSRI's
MAO-I A

QUES:
WHY would there be multiple drugs to treat the same problem???

Not all people respond to meds the same.

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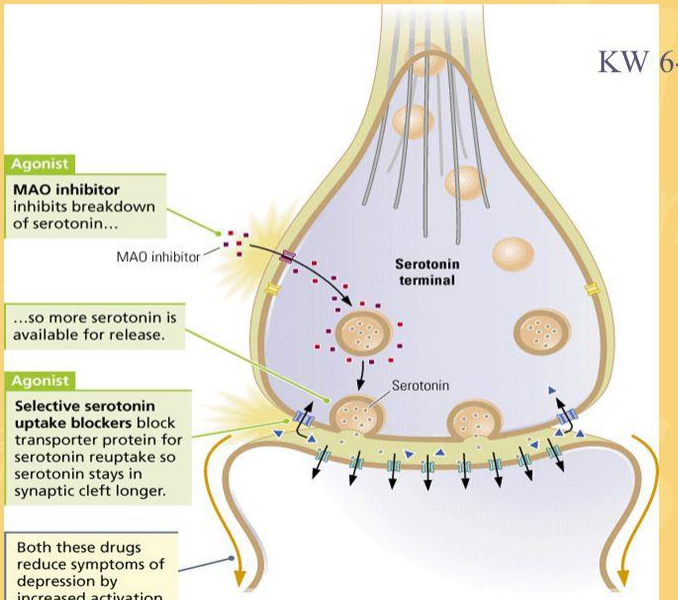
Serotonin and Depression



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II. Monoamine Neurotransmitters

Dopamine

> Produced by substantia nigra neurons in midbrain (of brainstem)

2 functions:

muscle

1) fine motor control (nigrostantial dopamine system) — muscle tremors & cognitive problems

> Insufficient dopamine - ***Parkinson's***

– Clinical App online

Treatment include dopamine agonists ex MAO-I B

> Excess dopamine - **"Schizophrenia"**

2) emotional reward system (mesolimbic dopamine system)

"addiction"

When you do something pleasurable, get a dopamine in brain reinforces you to do it again.

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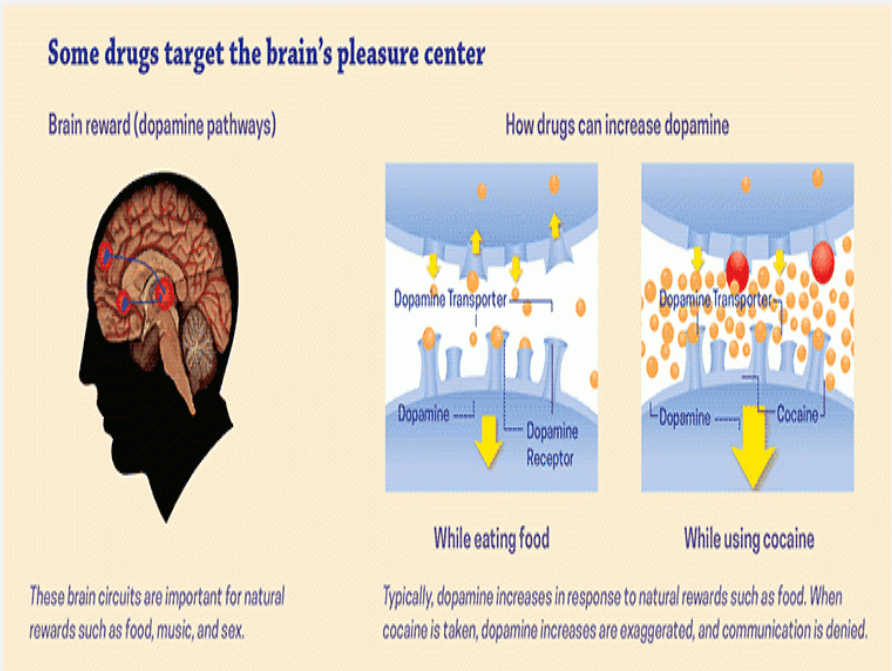

https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain

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Cocaine, Dopamine, & Addiction (Clinical App online & Pg 76 – 77 Wiki Physiology text)

Cocaine is an agonist to dopamine, serotonin, and norepinephrine (excess amount of these)

& epinephrine

Presentation reflects this:

- Hallucinations (too much serotonin)
- Muscle tremors and addiction (too much dopamine)
- High energy, fight or flight. (too much epinephrine)

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II. Monoamine Neurotransmitters

Norepinephrine/epinephrine (a.k.a noradrenaline & adrenaline)

> **Epinephrine in PNS** for autonomic sympathetic regulation (fight/flight)
↑ heart and respiratory rates, ↓ activity GI tract smooth muscles

> **Norepinephrine in CNS** for general arousal (stimulatory)

Works by 2 types G-protein coupled receptors (Table 6.3)

1) alpha adrenergic receptors (α-adrenergic)

2) beta adrenergic receptors (β-adrenergic)

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II. Monoamine Neurotransmitters

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Works by 2 types G-protein coupled receptors (Table 6.3)

1) alpha adrenergic receptors (α-adrenergic) ↓GI secretions

- slows down GI activity (↓peristalsis,
- vasoconstric of GI arterioles.

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II. Monoamine Neurotransmitters

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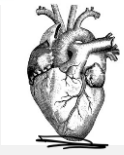
1) alpha adrenergic receptors (α-adrenergic)

- _____
- _____



2) beta adrenergic receptors (β-adrenergic)

i. β1-adrenergic receptor = ↑ HR

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II. Monoamine Neurotransmitters

Norepinephrine/epinephrine (a.k.a noradrenaline & adrenaline)

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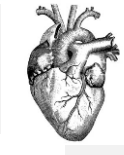
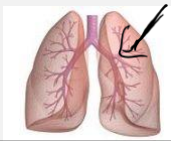


2) beta adrenergic receptors (β-adrenergic)

i. β1-adrenergic receptor = _____

ii. β2-adrenergic receptor =



- bronchodilation – max air flow
- arterial vasodilation for skeletal muscles "Best to Get away

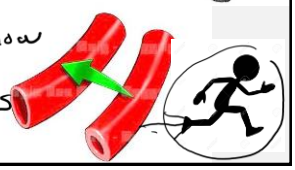


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Table 6.3 | Selected Adrenergic Effects in Different Organs

= Fight/Flight

Organ	Adrenergic Effects of Sympathoadrenal System	Adrenergic Receptor
Eye	Contraction of radial fibers of the iris dilates the pupils	α_1
Heart	Increase in heart rate and contraction strength	β_1 primarily
Skin & GI visceral vessels	Arterioles constrict due to smooth muscle contraction	α_1
Skeletal muscle vessels		
	Arterioles dilate due to hormone epinephrine	β_2
Lungs	Bronchioles (airways) dilate due to smooth muscle relaxation	β_2
Stomach and intestine	Contraction of sphincters slows passage of food ↓GI	α_1
Liver	Glycogenolysis and secretion of glucose	α_1, β_2

Source: Simplified from table 6-1, pp. 143–144, of Goodman and Gilman's *The Pharmacological Basis of Therapeutics.* Eleventh edition. J.E. Hardman et al., eds. 2006. McGraw-Hill.

See **Clinical App ONLINE**:
Beta agonists & blockers.

B1 agonist = Dobutamine
↑ HR and cardiac output
good for heart failure patients)

B1 & B2 agonist = Isoproterenol
↑ HR and cardiac output &
Bronchodilate

B2 agonist = Albuterol
Bronchodilates
good for people w/respiratory prob. asthma

B1 & B2 blocker = Propranolol
↓ HR and BP & bronchoconstrict
good for hypertension BUT not people w/respiratory prob. (it will cause bronchoconstriction!)

B1-specific blocker = Atenolol
↓ HR and BP attenuated
no effect on bronchioles
good For hypertension WITH respiratory problems (won't cause bronchoconstriction)

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III. "Other" Amino Acid (NOT monoamine) Neurotransmitters:

1. Glutamate (a.k.a glutamic acid)

- Excitatory in CNS +
- found in MSG (monosodium glutamate)
- regulated by glial cell removal (astrocytes)
- excess glutamate = **glutamate "toxicity"**, and is associated w/Alzheimer's (also influenced by ACh) & Parkinson's (also influenced by dopamine)

serene like glycine in spinal cord.

2. Glycine – inhibitory in spinal cord to inhibit skeletal muscle

3. GABA – inhibitory in brain. Inhibits skeletal muscle.
(Brain)

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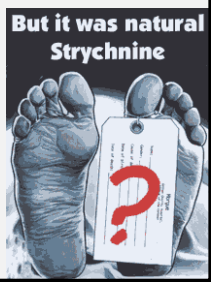
III. "Other" Amino Acid (NOT monoamine) Neurotransmitters:

Glycine

- Inhibitory (IPSPs) by opening Cl- channels

- Primarily in spinal cord

- Coordinates muscle movement by regulating antagonistic muscle contraction & relaxation (Ex. biceps brachii & triceps brachii)



Strychnine poisoning *- inhibits glycine relaxation of diaphragm. Diaphragm stays tense, can't exhale. Die from asphyxiation.*

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III. "Other" Amino Acid (NOT monoamine) Neurotransmitters:

GABA

- Inhibitory (IPSPs) by opening Cl- channels

- Found primarily in brain synapses (90%) - Coordinates muscle movement in cerebellum (fine motor control and "muscle memory" patterns)

– this is why Xanax works to calm panic attacks. Xanax is a GABA agonist in the brain.

- Insufficient GABA associated w/Huntington's disease (autosomal dominant genetic disorder.

QUESTION:
Why is benzodiazepam (Valium) a treatment for Huntington's disease or cholinergic syndrome?? → stops muscle seizures.

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IV. Gaseous Neurotransmitters:

Nitric Oxide (NO)

↓ BP in body
priapism = erection lasts longer than 3 hrs.

Sexual arousal stimulates parasympathetic response
> causes NO production – penis
> NO activates G protein, guanylate cyclase & cGMP 2nd messenger
> cGMP causes vasodilation in penile arterioles
> Corpus cavernosa fills w/blood = erection.

Stimulation wanes: enzyme breakdown by **Phosphodiesterase** (enzyme that breaks down cGMP and stop vasodilation).

ED
Erectile dysfunction drugs like Viagra, Cialis, Levitra work as **phosphodiesterase inhibitors**. So, these drugs are **cGMP agonists** ↑ cGMP ↑ blood Flow. Allows vasodilation

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Beta blocker "generations" (new slide 2/2/25) *Do NOT memorize!*
(This is just a glimpse into nursing pharmacology.)

First generation (non-specific) beta blockers -blocking B1 and B2 adrenergic receptors.
> Propranolol & Sotalol

Second generation (specific) beta blockers – blocking only B1 adrenergic receptors.
> Atenolol, metoprolol, & labetalol

Third generation – B1 blocker AND aterial vasodilators as **agonists to nitric oxide and cGMP.**
> Carvedilol & Nebivolol

Contraindications – beta blockers can lead to heart failure if patient has valve disease

Click **HERE** to read more about beta blockers, their indications for use, and contraindications.

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Review

- Other Neurotransmitters
  - Monoamines (Dopamine, serotonin, norepinephrine)
    - Their functions & disorders
    - Removal of serotonin by *reuptake
    - Low serotonin treated with SSARs
    - Removal of dopamine serotonin, norepinephrine by MAO.
    - Low dopamine or serotonin treated with MAO-I's
  - Amino acid-based (glutamate, glycine, GABA)
  - Nitric Oxide, cGMP, phosphodiesterase, and ED drugs

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