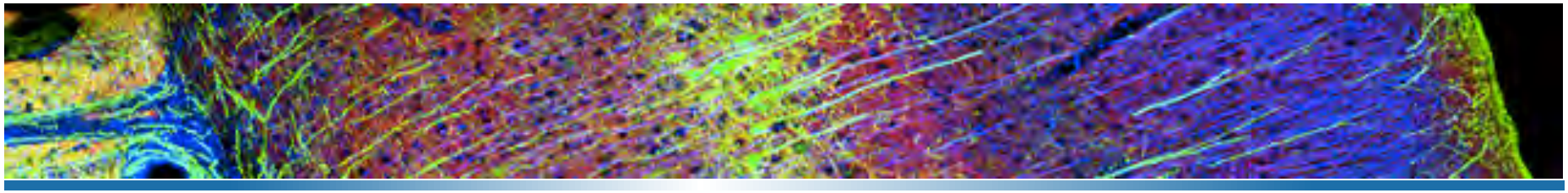
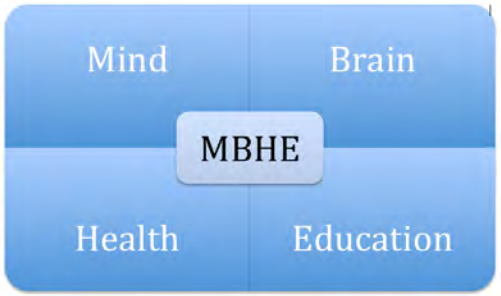
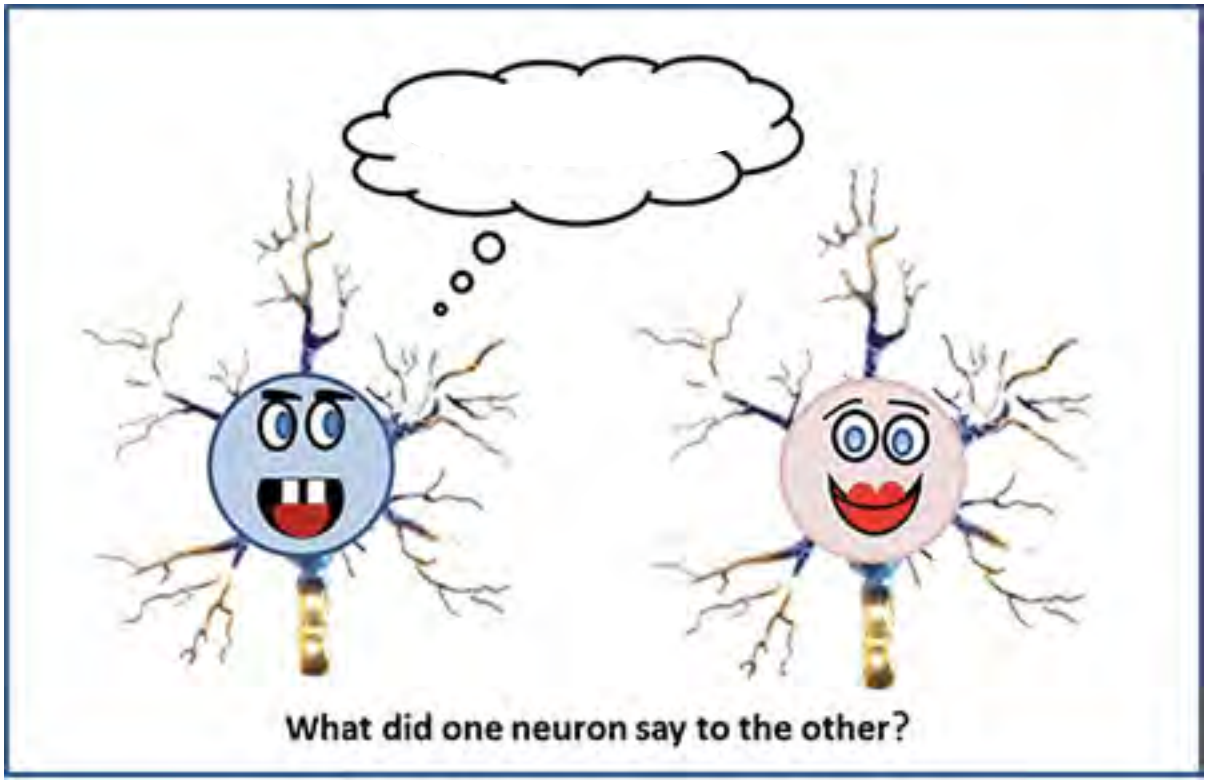


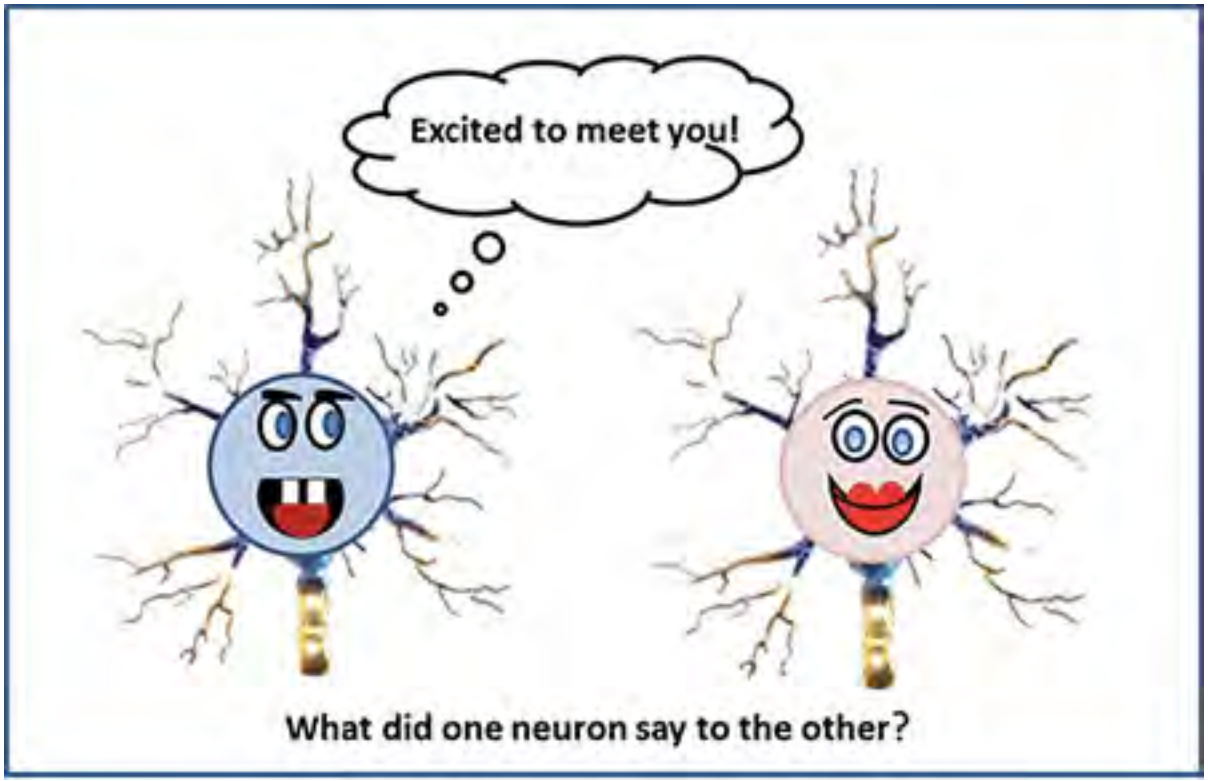
Neuroscience of Learning
An Introduction to
Mind, Brain, Health, and Education

Section: Neurotransmitters

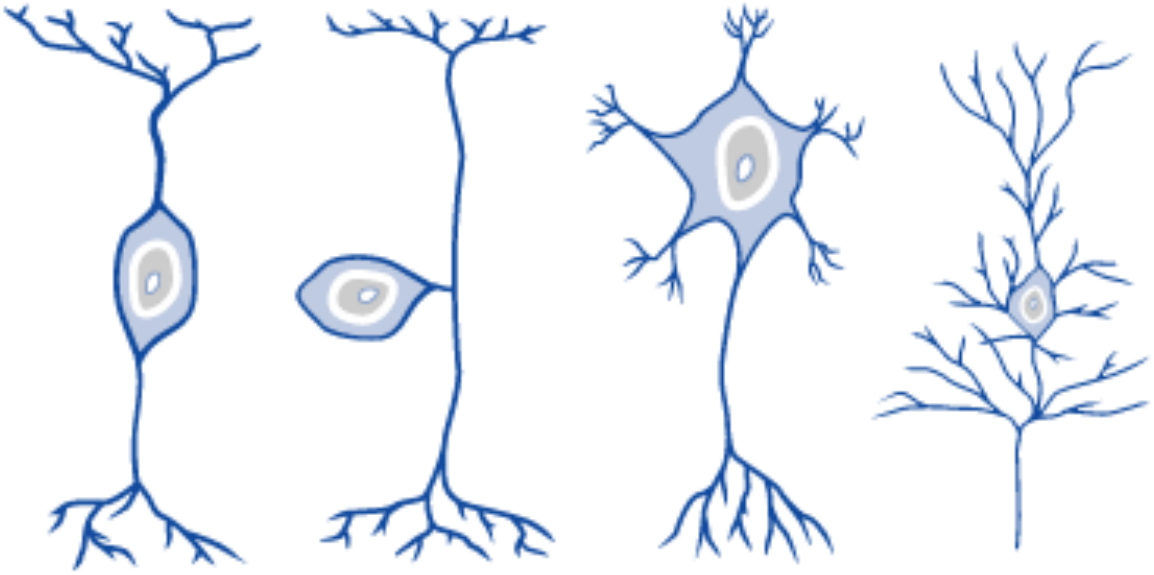
Harvard University Extension School (PSYCE-1609)
February 2, 2016




What did one neuron say to the other?

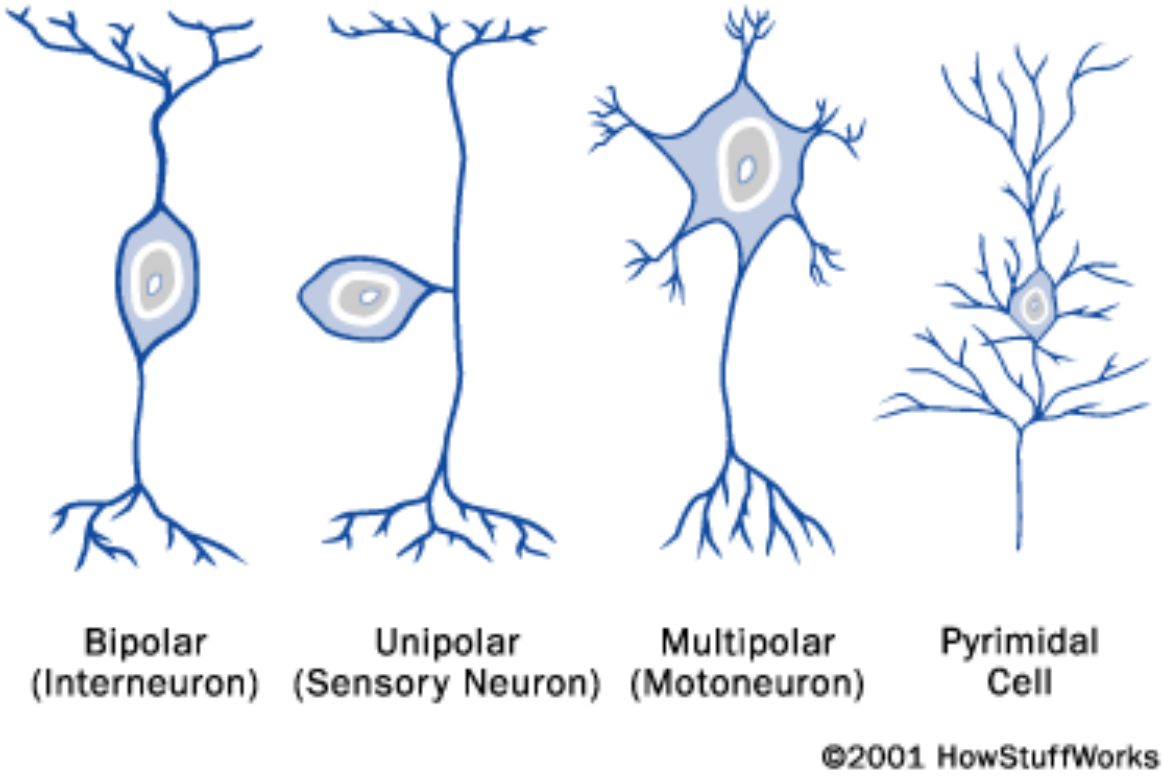

Excited to meet you!
What did one neuron say to the other?

Which of these is a neuron?



Which of these is a neuron?

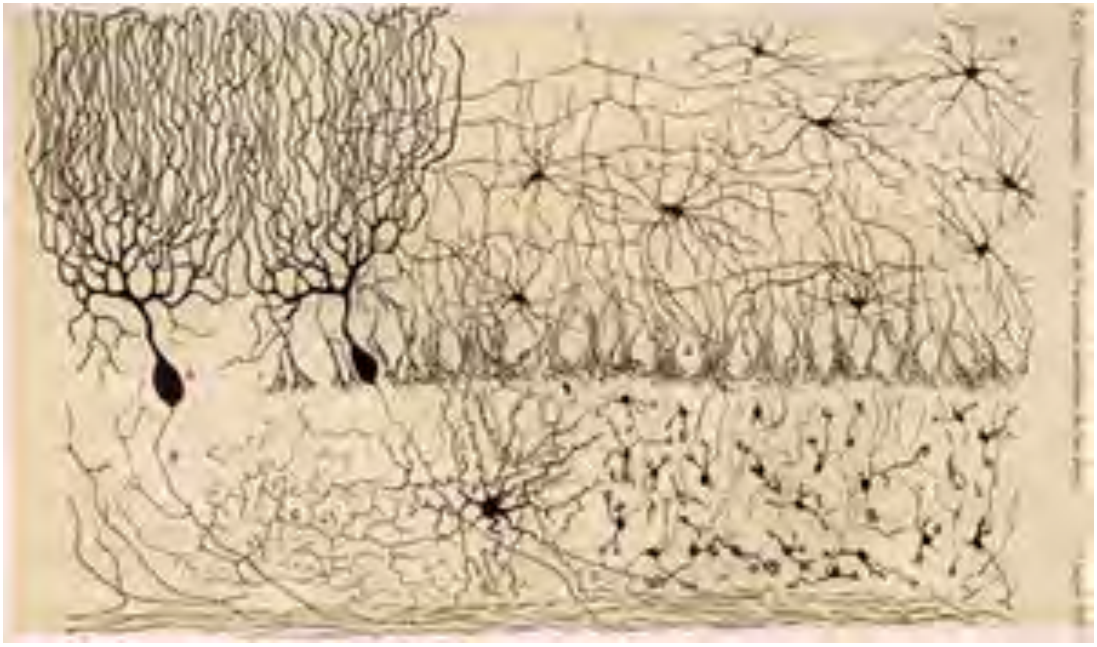
All of them!



What is the neuron doctrine?

The Neuron Doctrine

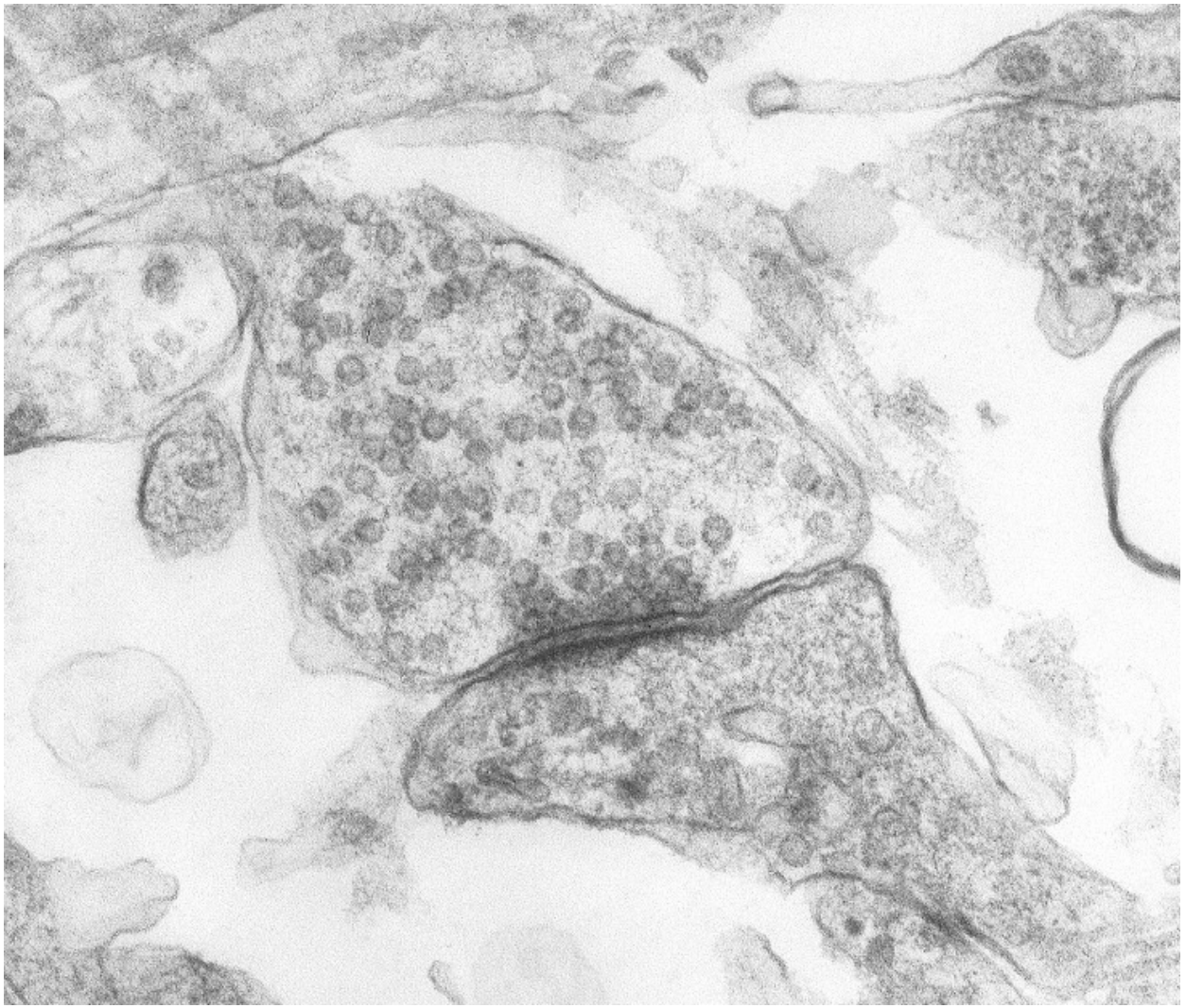
Santiago Ramon y Cajal



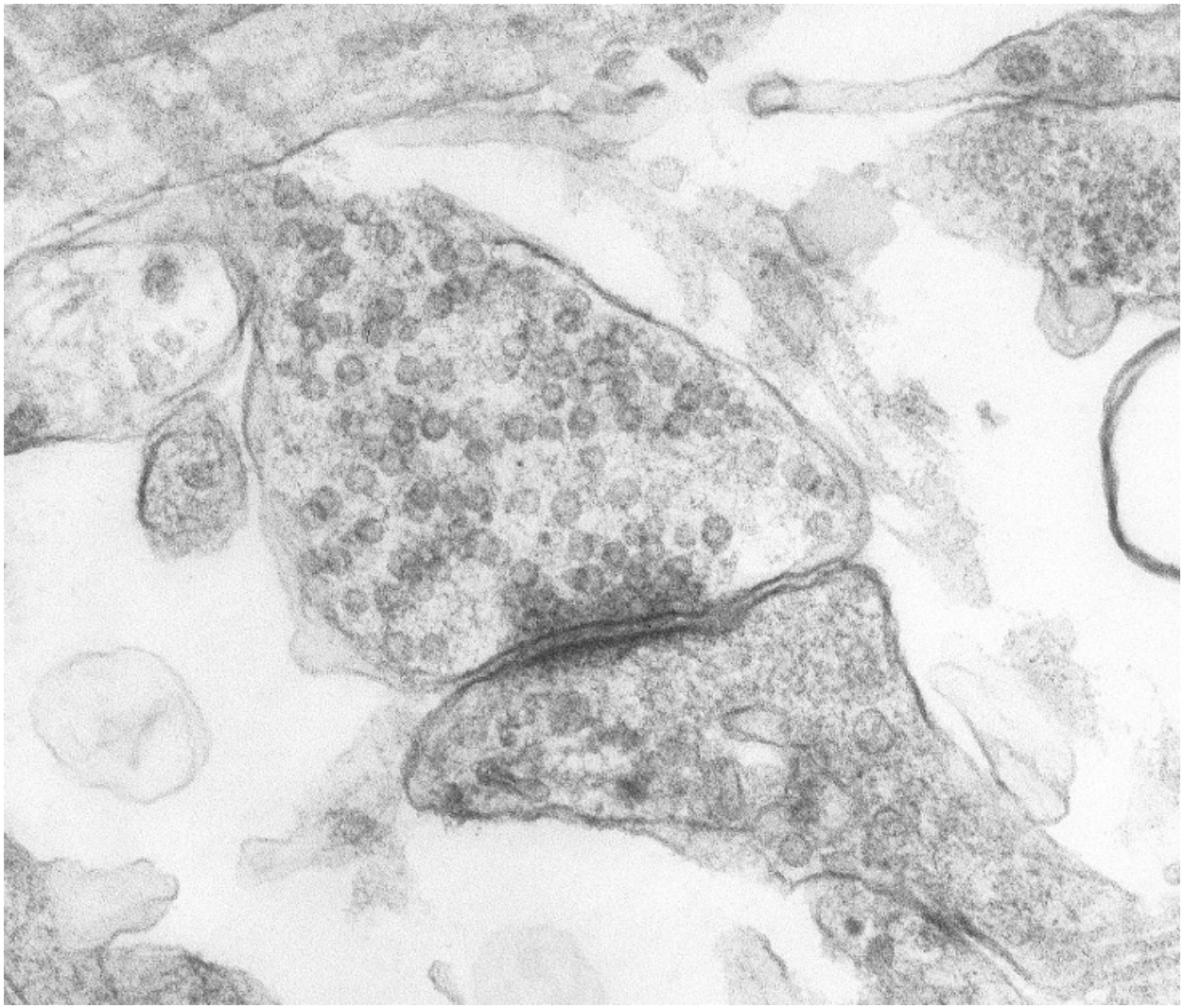
Chick cerebellum neurons drawing by Ramon y Cajal (1905)

Key tenet: Neurons are specialized brain cells that are not continuous, but contiguous (e.g., there is a gap/transmission barrier between neurons)

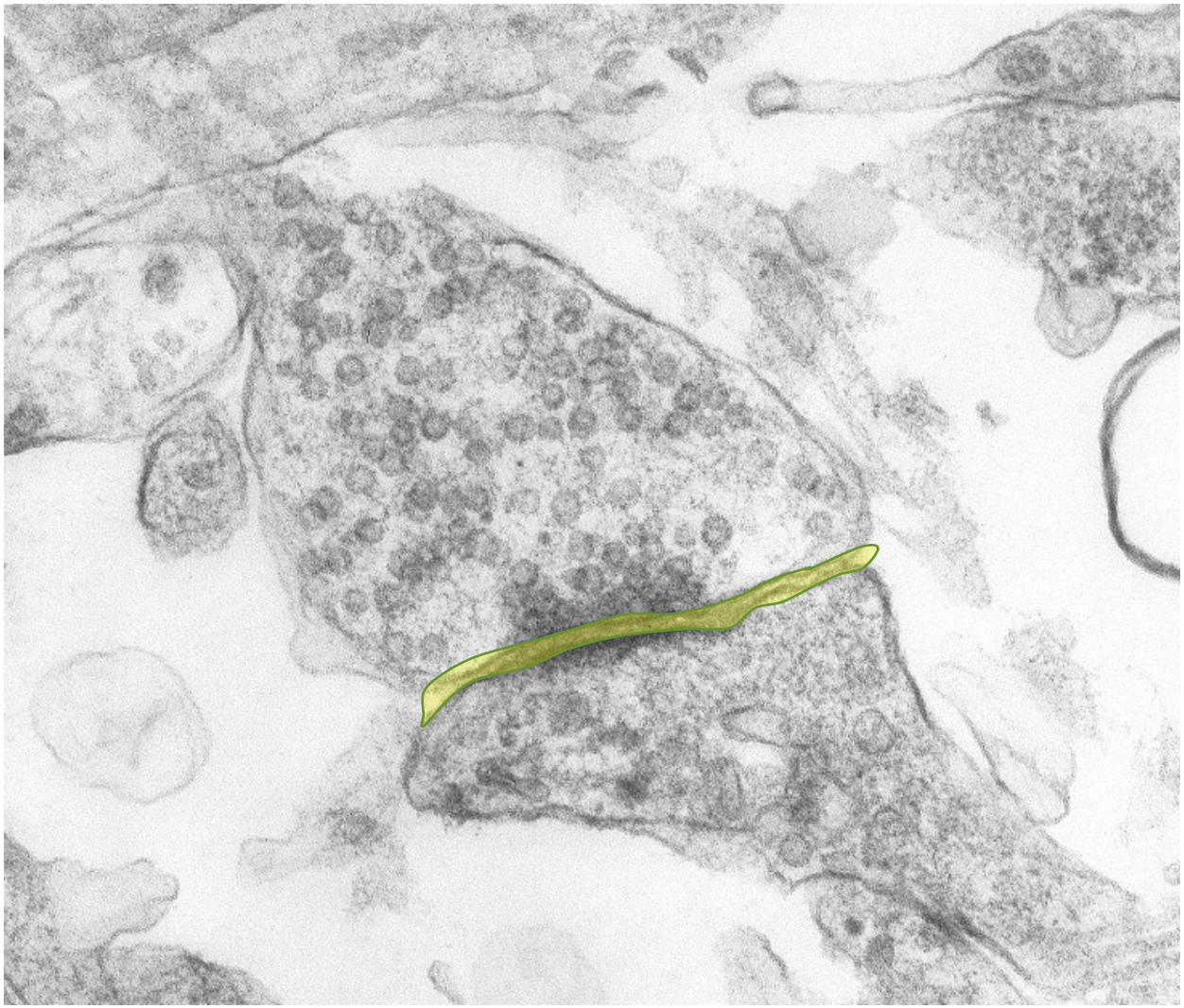
Neurons connect via a synapse



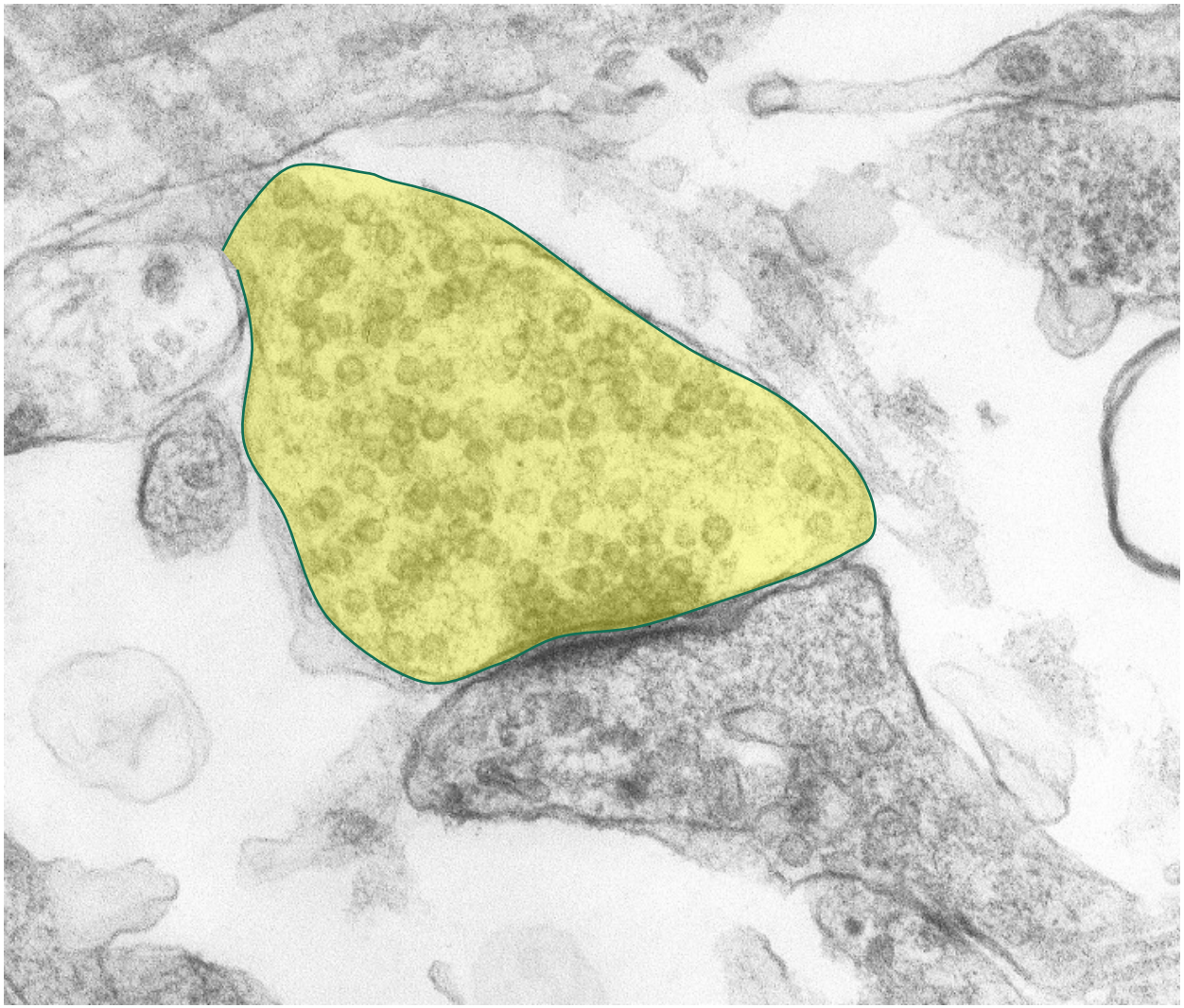
Where’s the synapse?



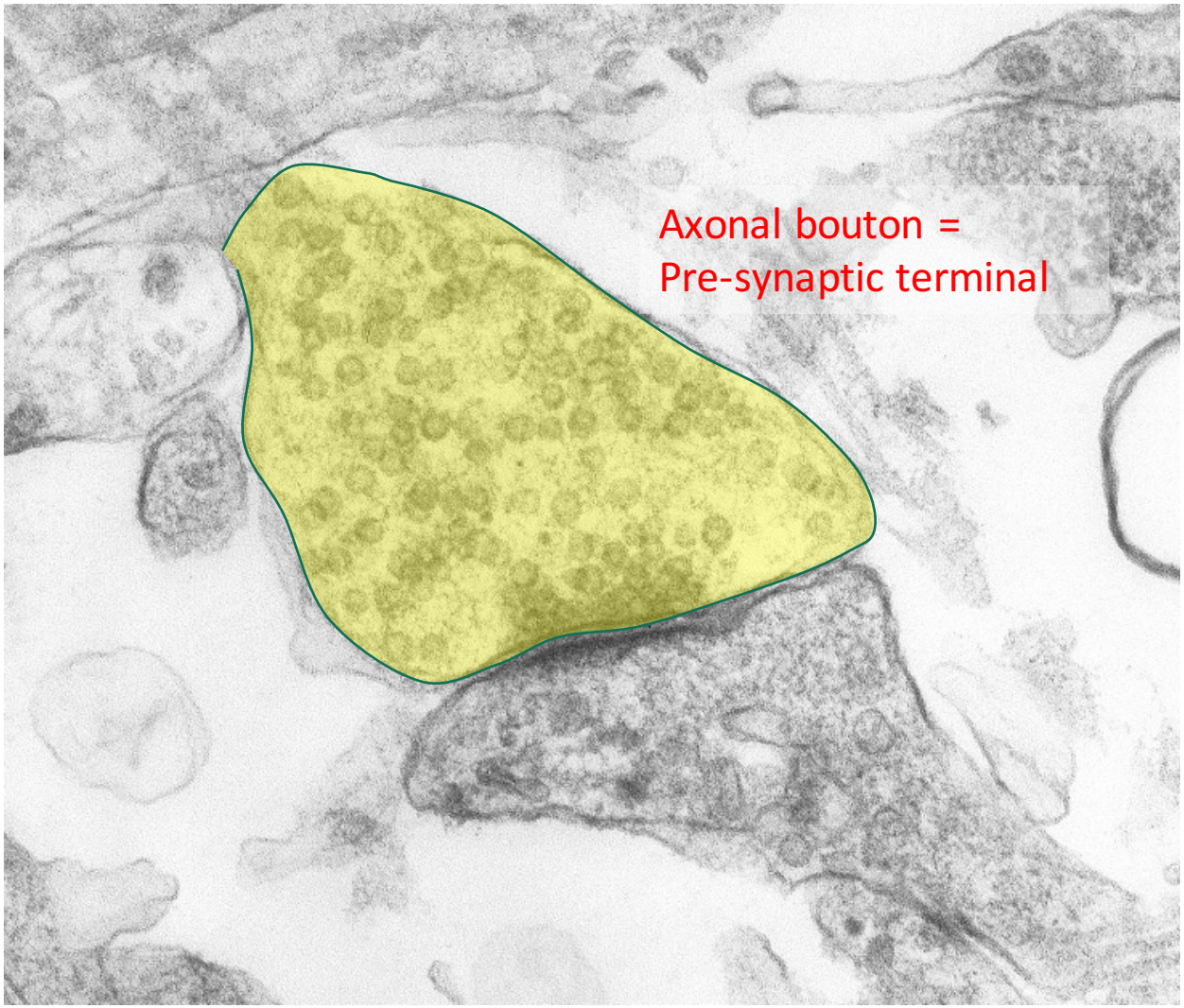
Where’s the synapse?



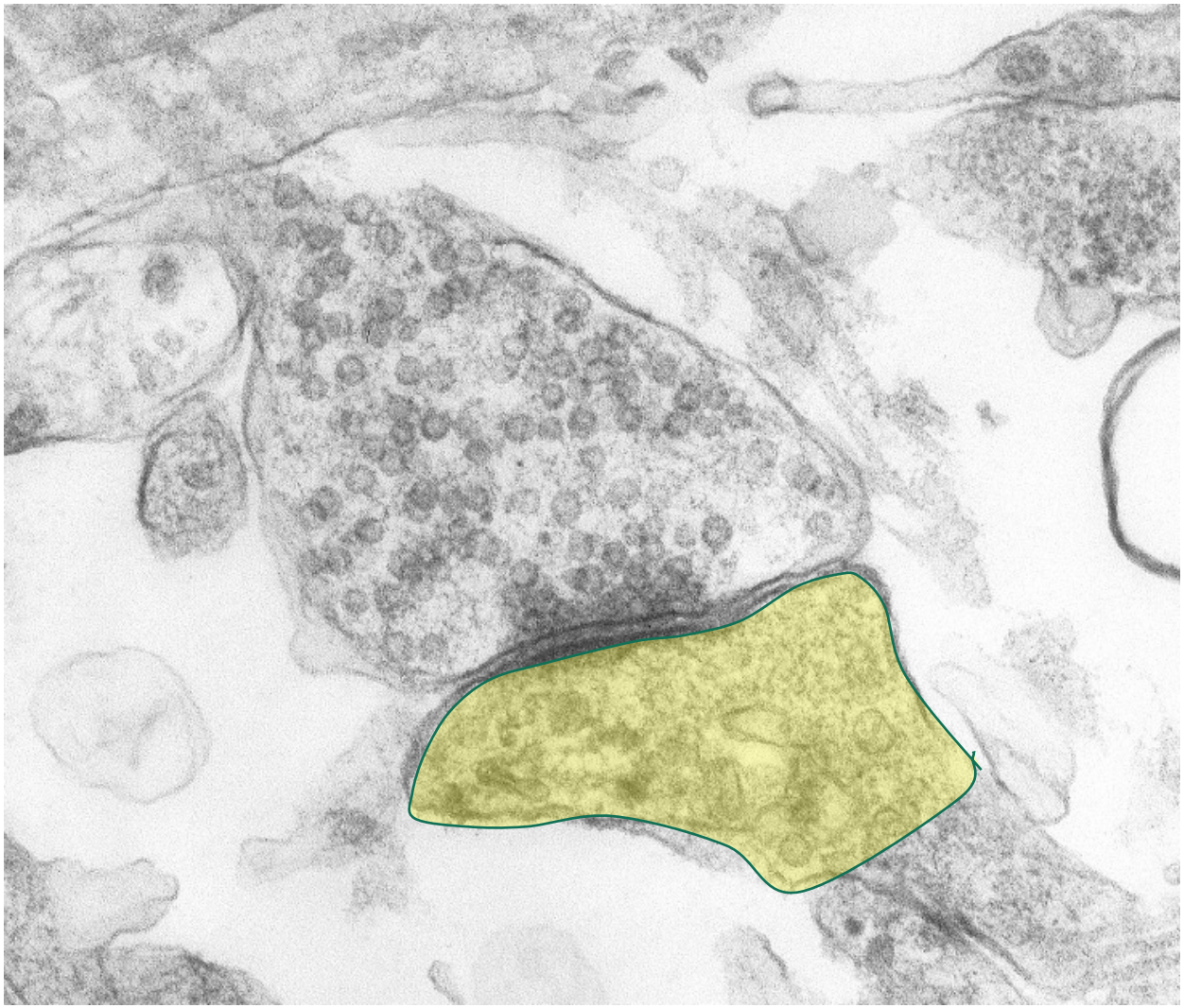
Name that anatomy…



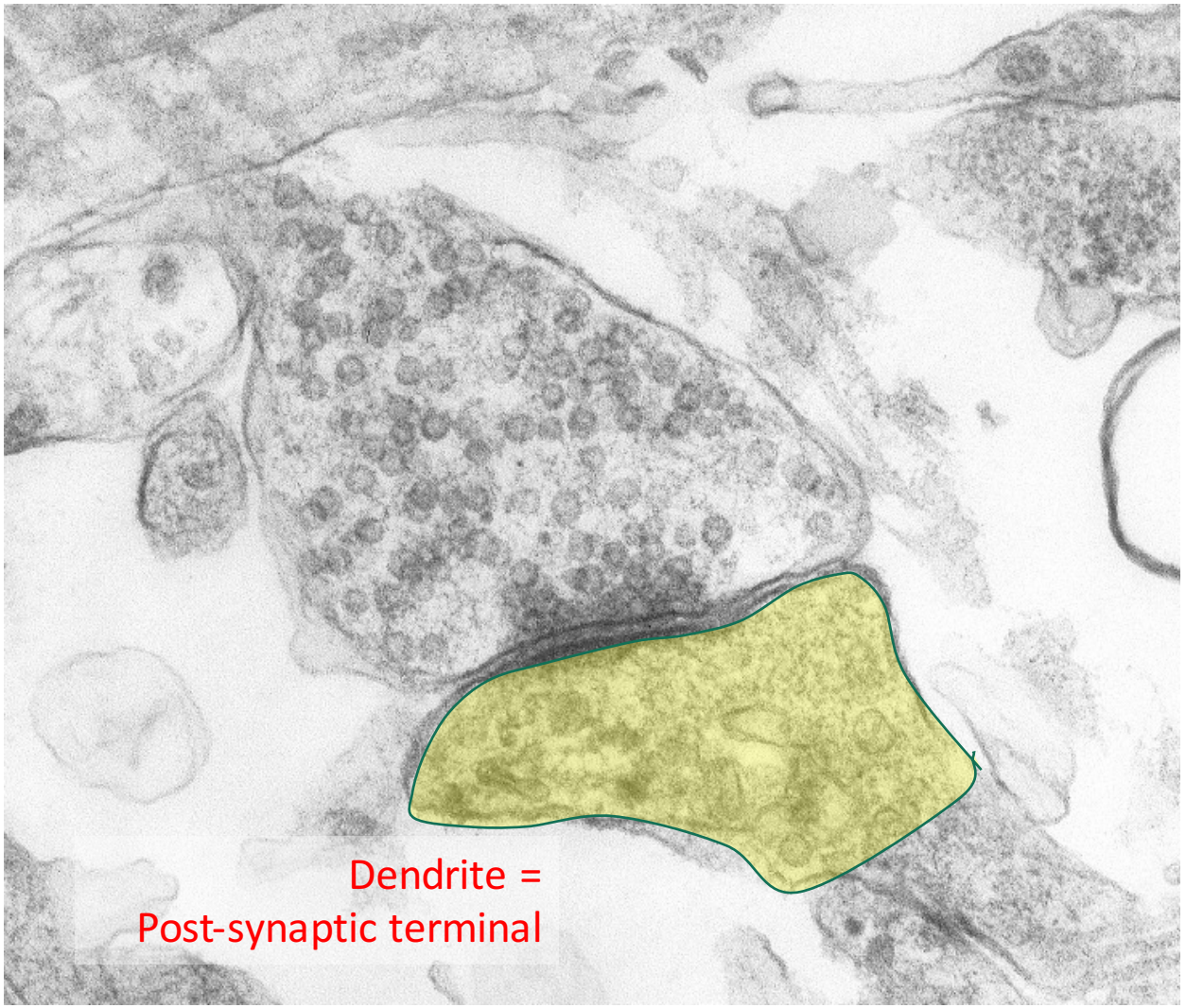
Name that anatomy…



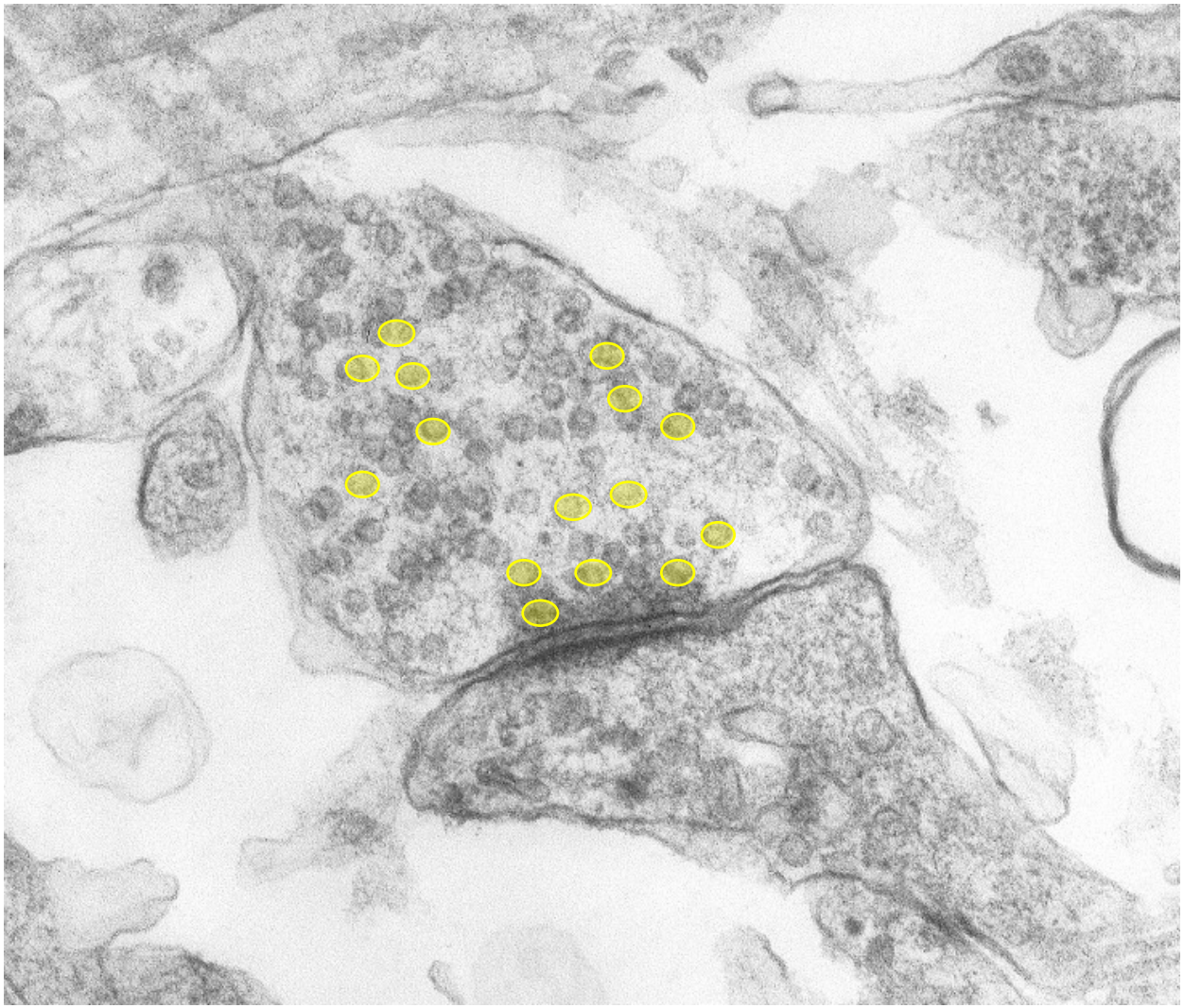
Name that anatomy…



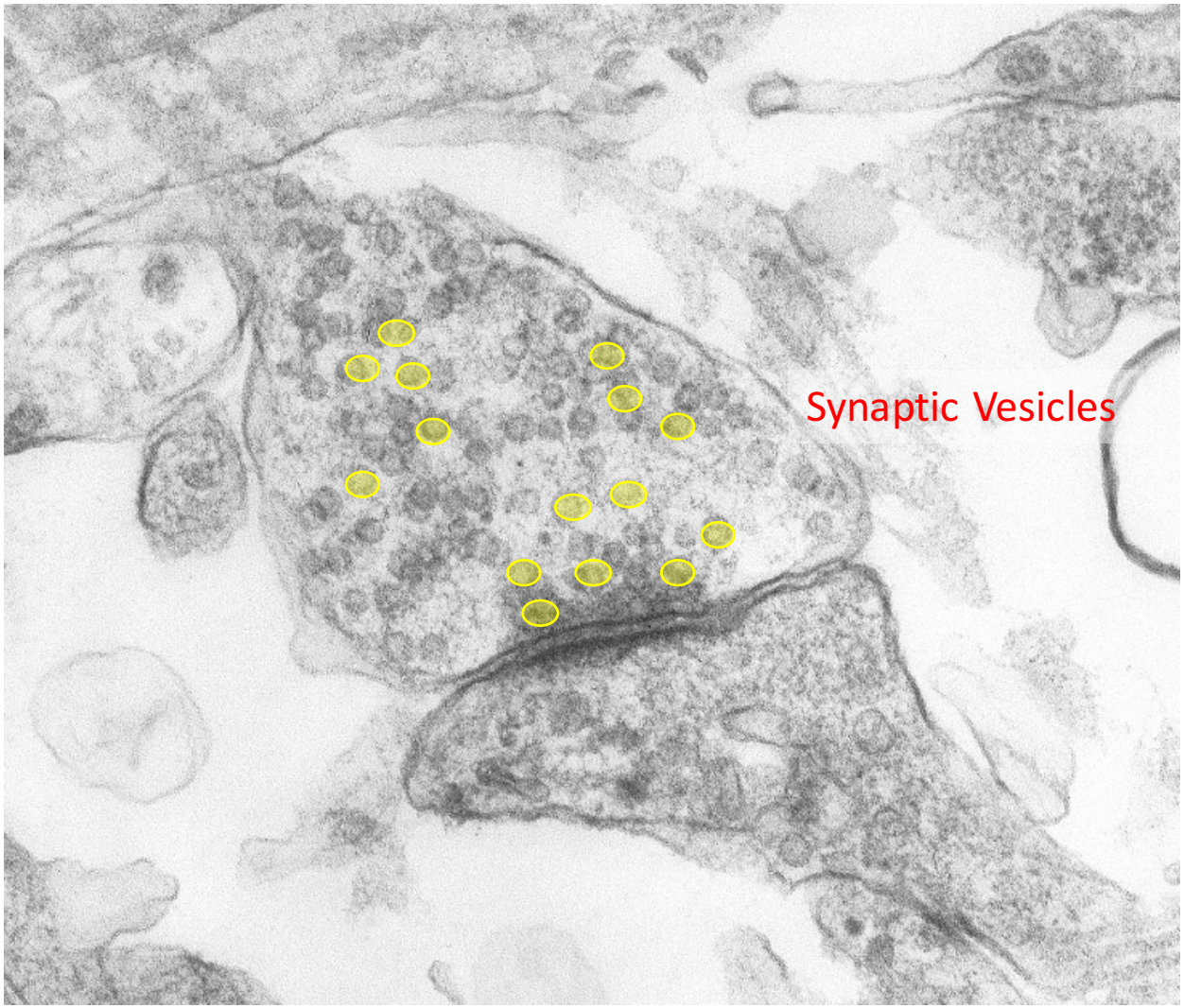
Name that anatomy…



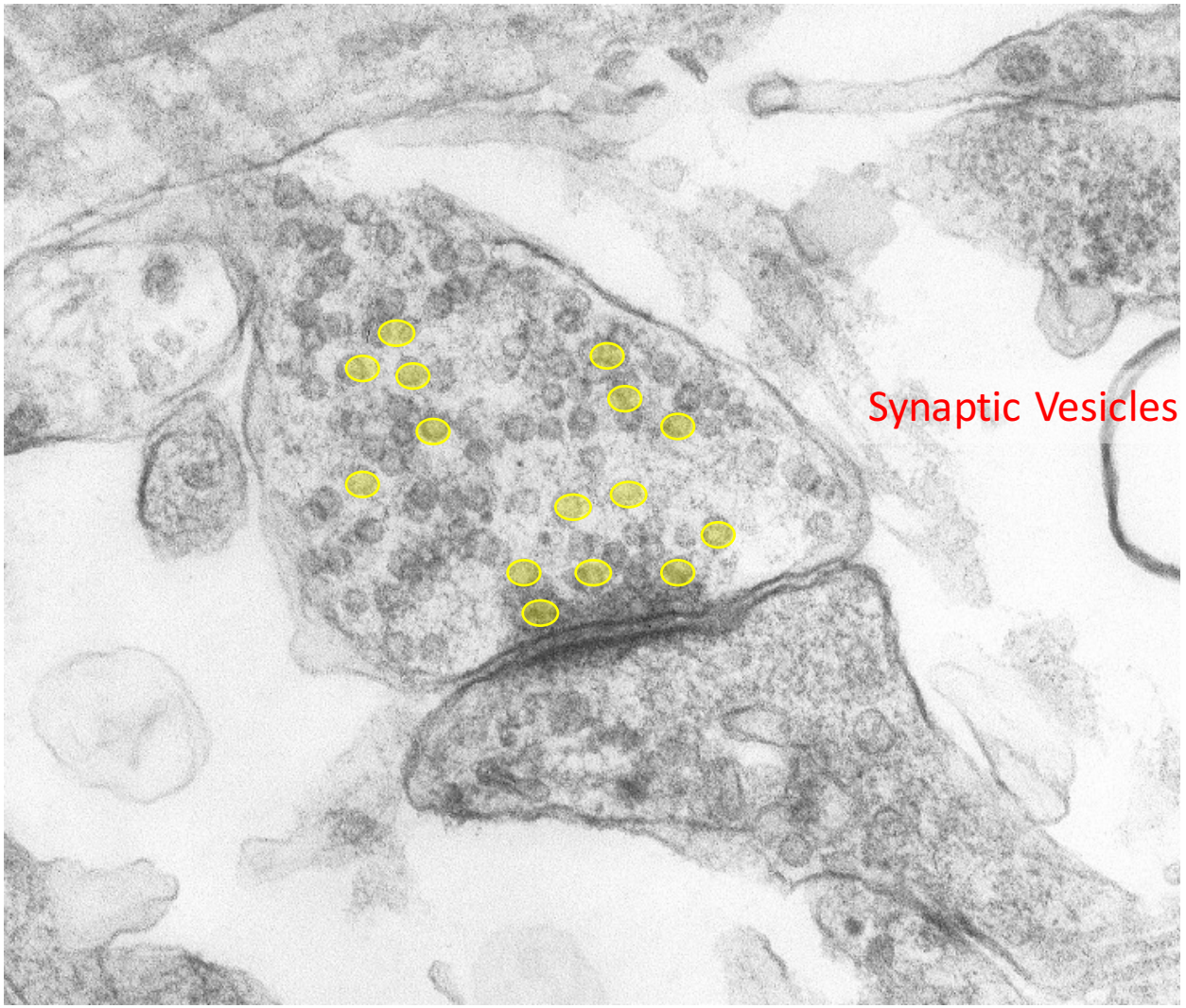
Name that anatomy…



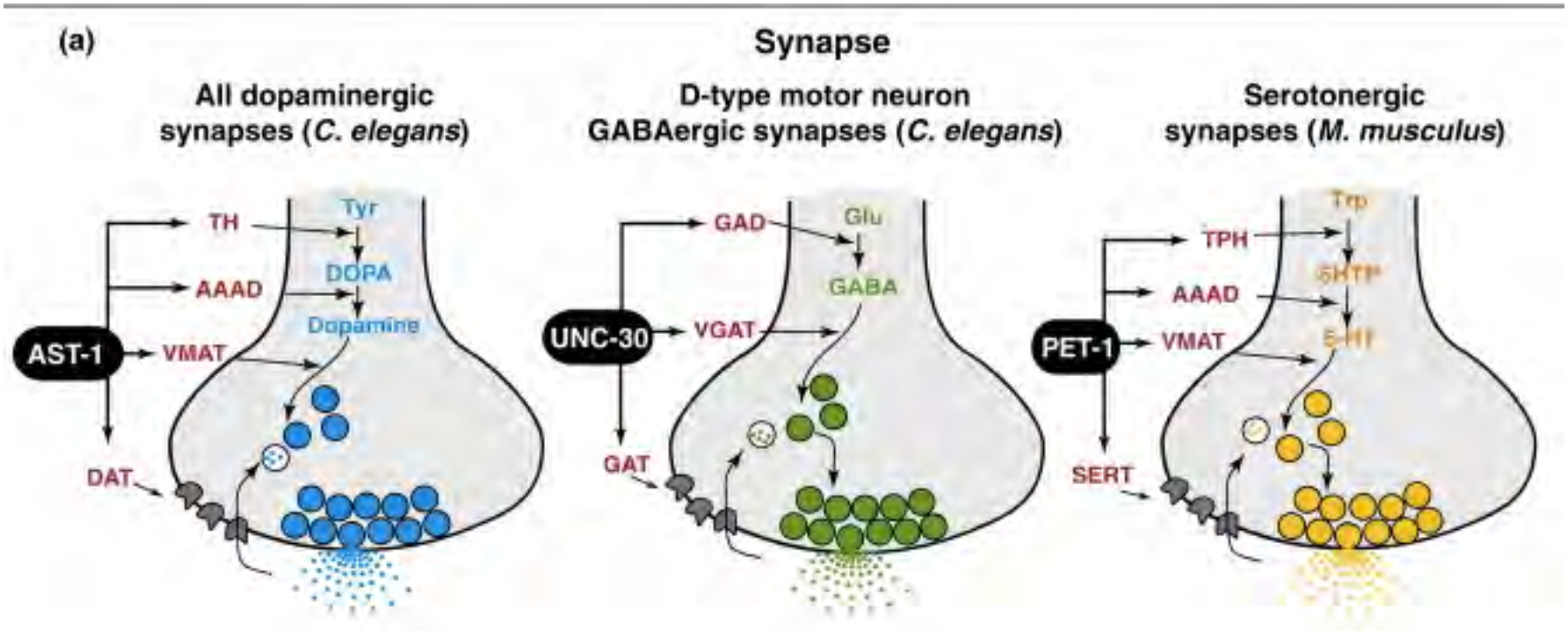
Name that anatomy…



What's inside synaptic vesicles?

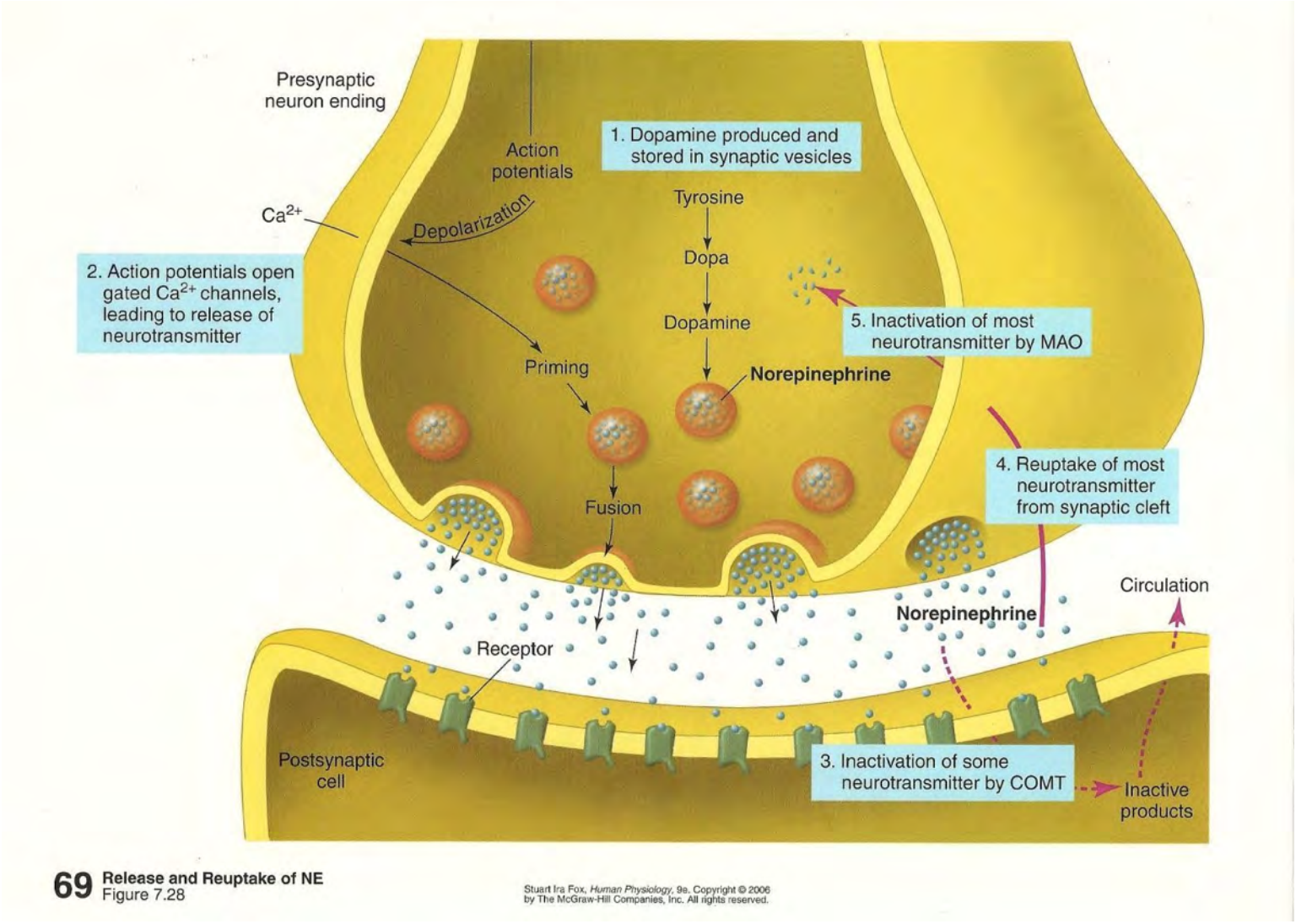


Neurotransmitters



Are we making new vesicles all the time?

Synaptic vesicles are constantly emptied, recycled, and refilled



69 **Release and Reuptake of NE**
Figure 7.28

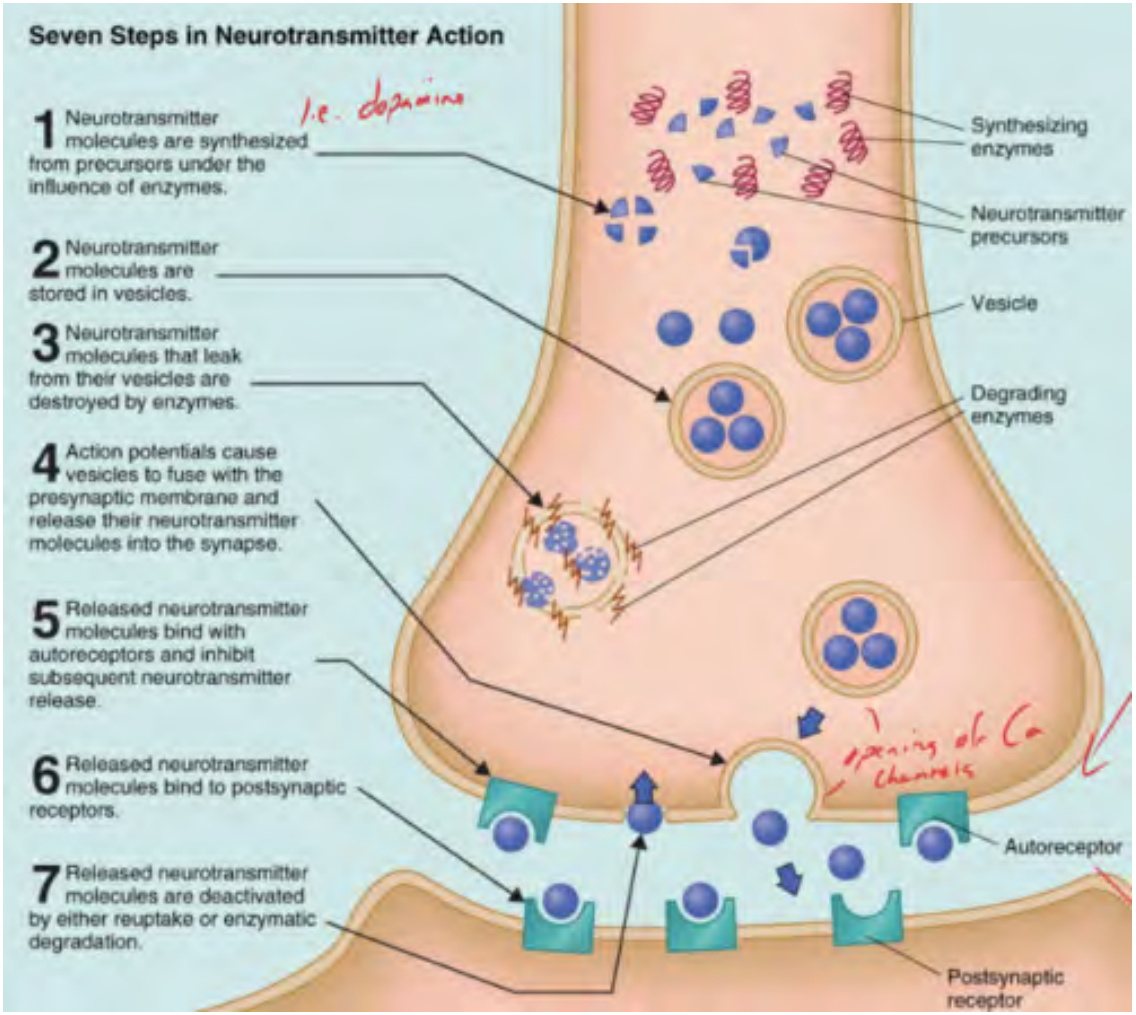
Where does all the NT go?

Reuptake, Diffusion, Metabolism

A lot of NTs are taken back into the vesicles for reuse

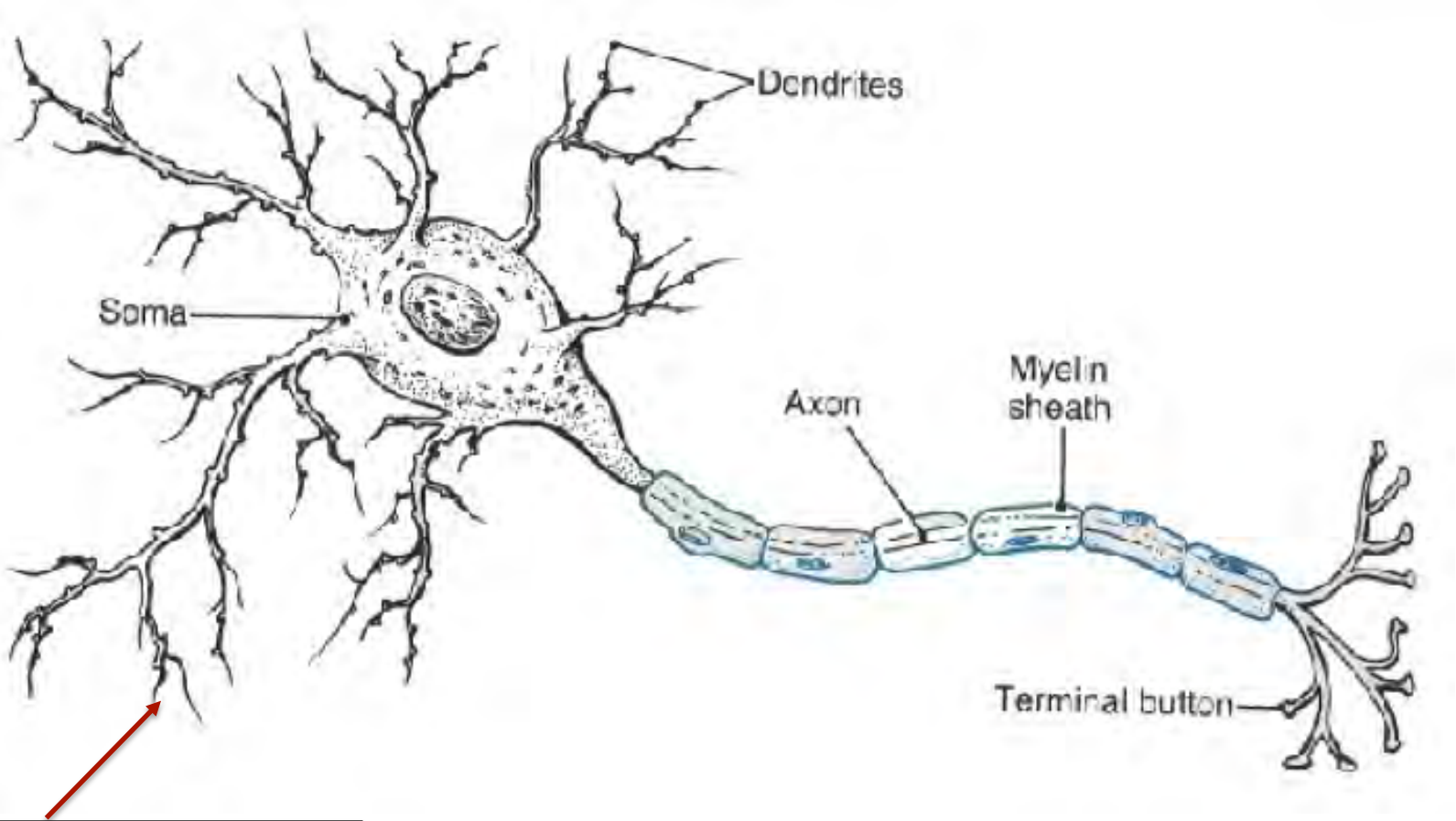
Some breakdown

Some diffuse

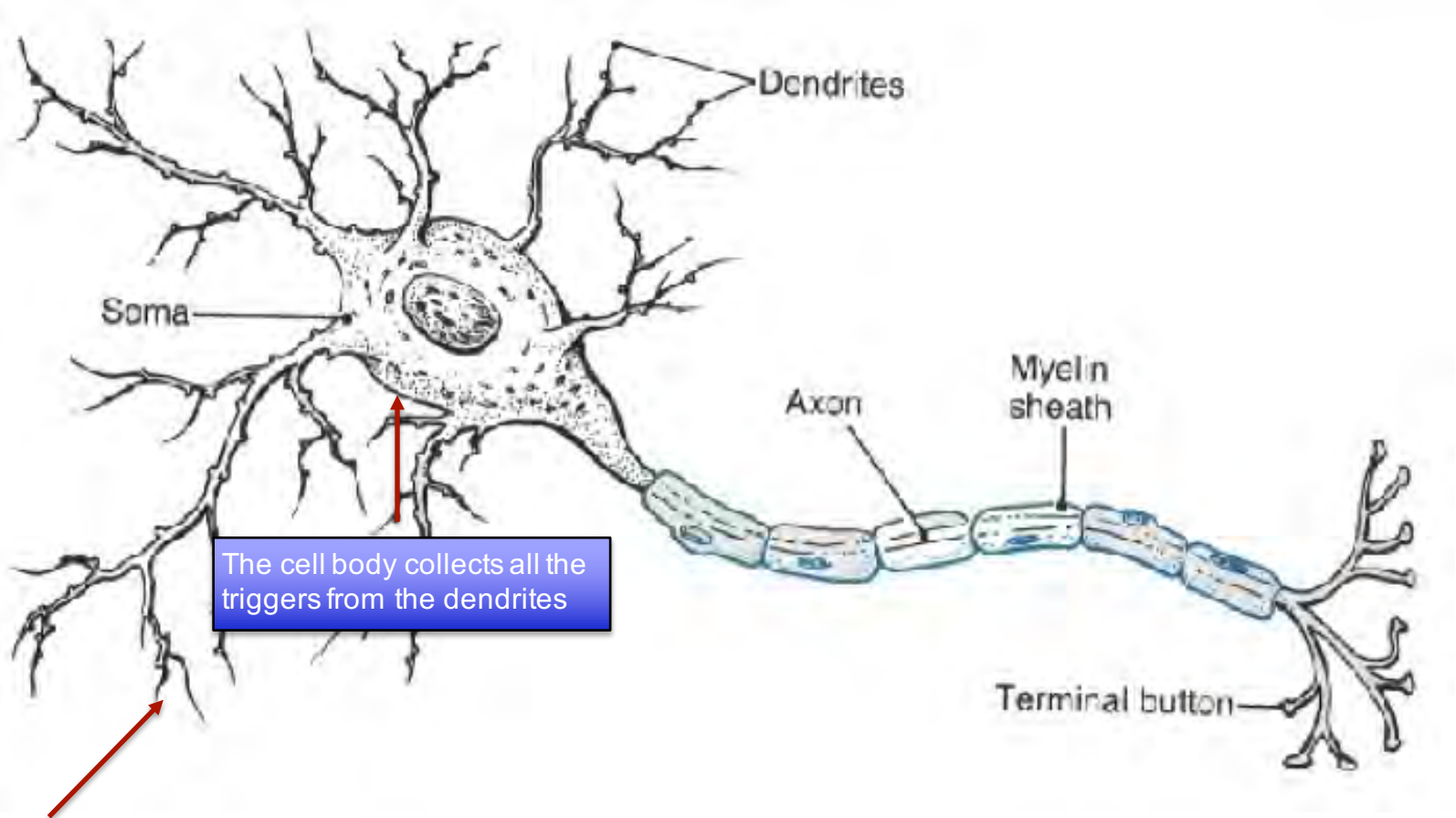


How do neurons “fire?”

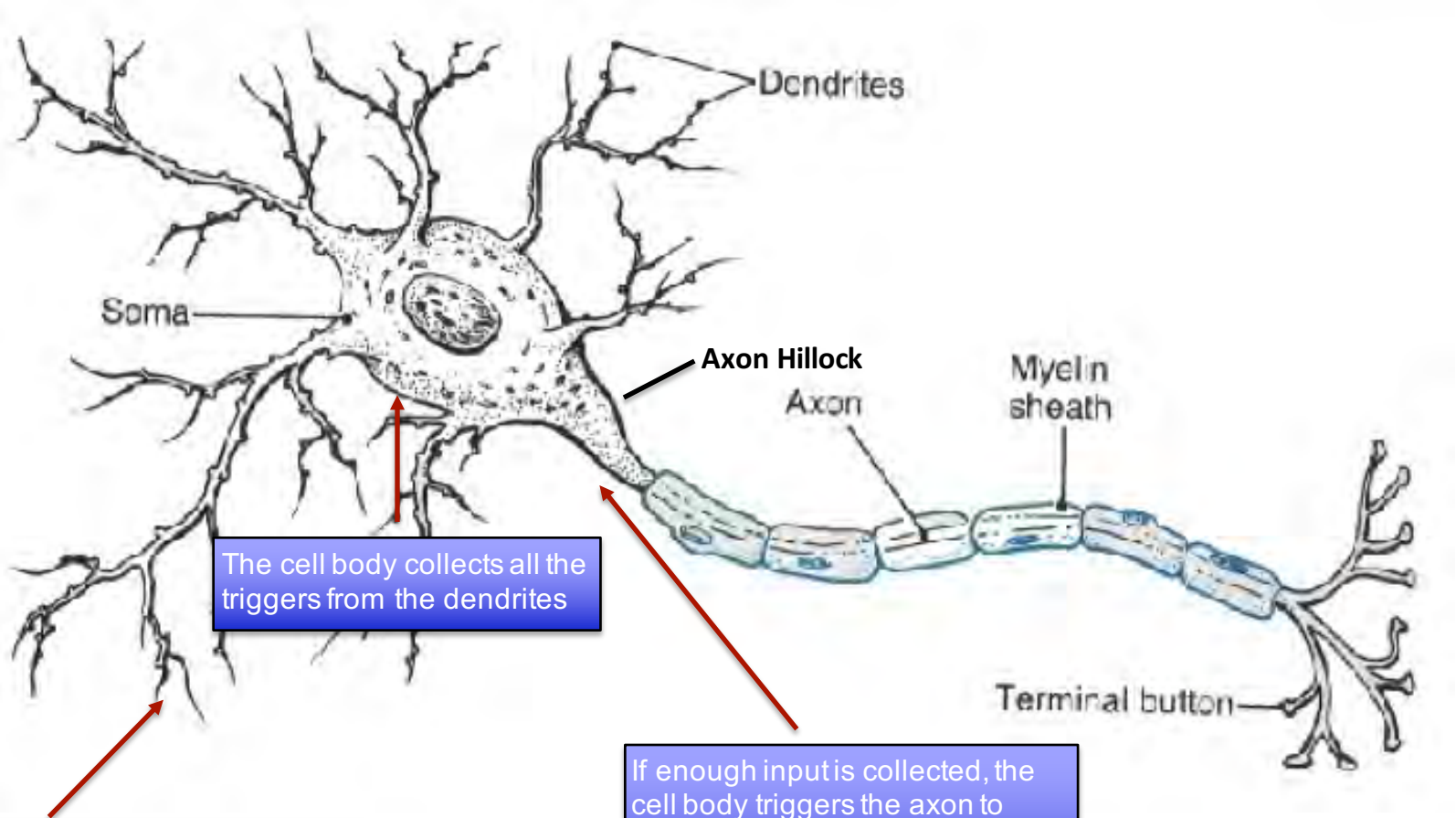
Triggering an Action Potential = Firing



Triggering an Action Potential = Firing

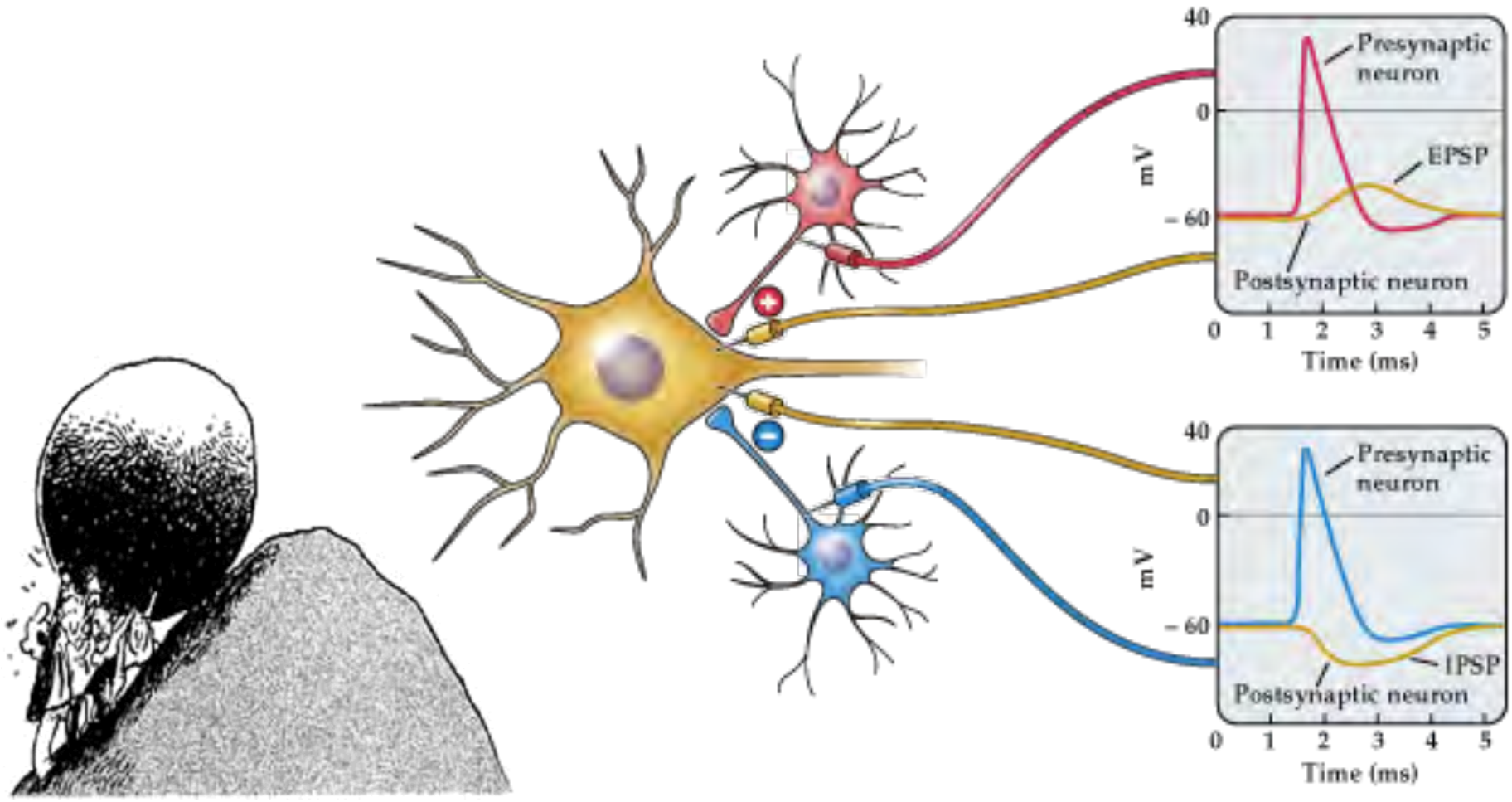


Triggering an Action Potential = Firing



How does summation happen? Why does it need to?

Because neurons receive both excitatory *and* inhibitory input



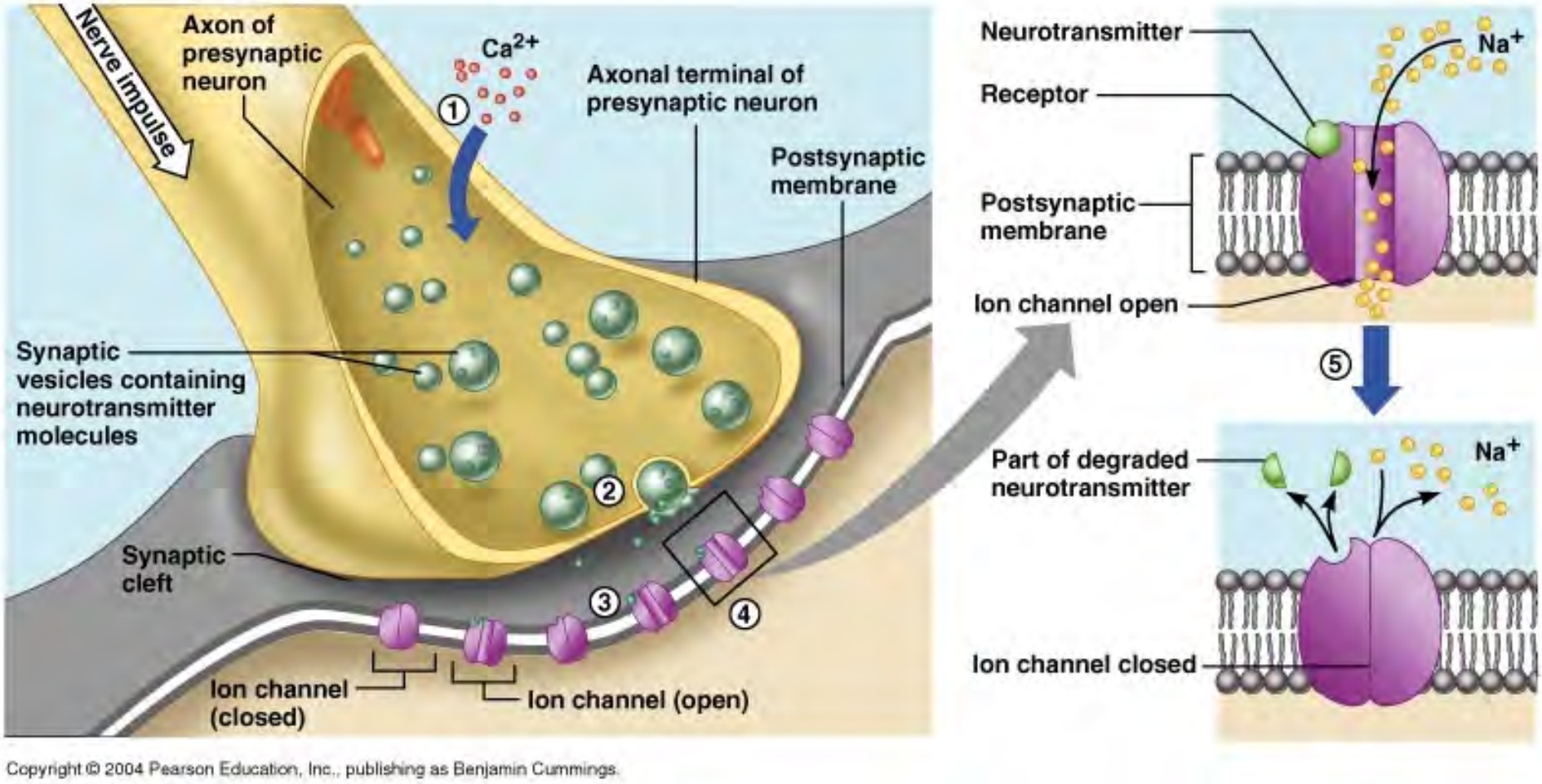
http://antranik.org/actions-of-excitatory-and-inhibitory-neurotransmitters/;
http://7e.biopsychology.com/vs03.html

What is the end result of a neuron firing?

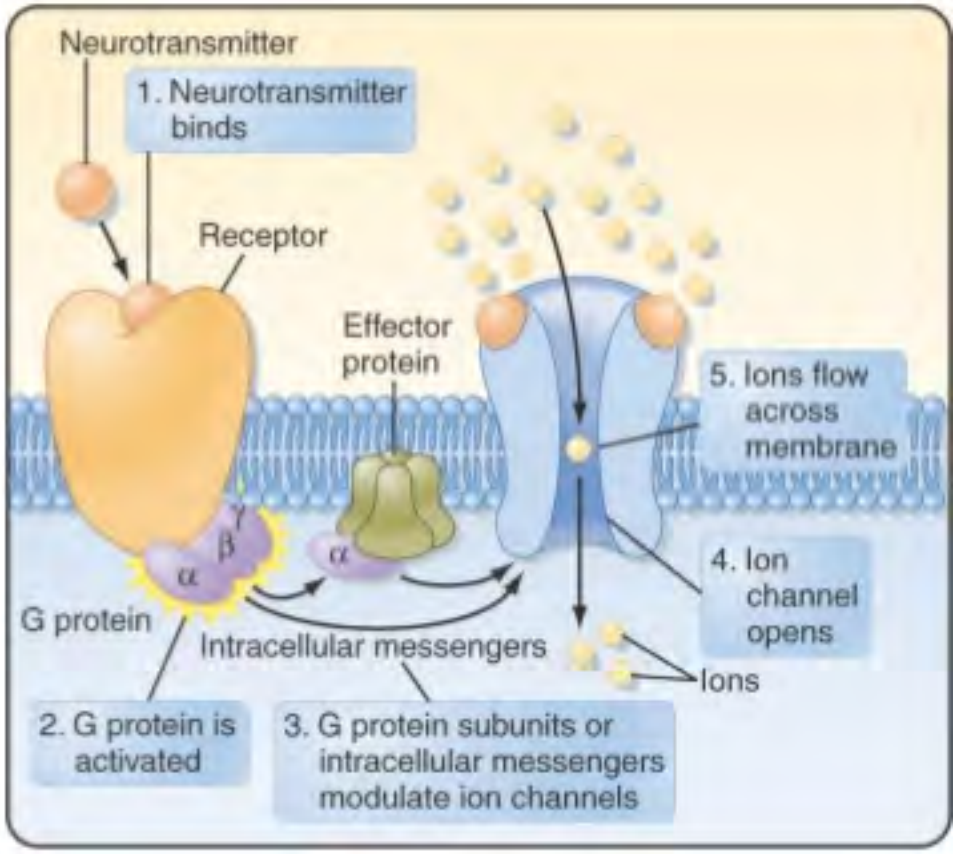
What is the end result of a neuron firing?

Neurotransmitter release

Ionotropic: NT binds to the ion channel



Metabotropic: NT binding opens ion channels

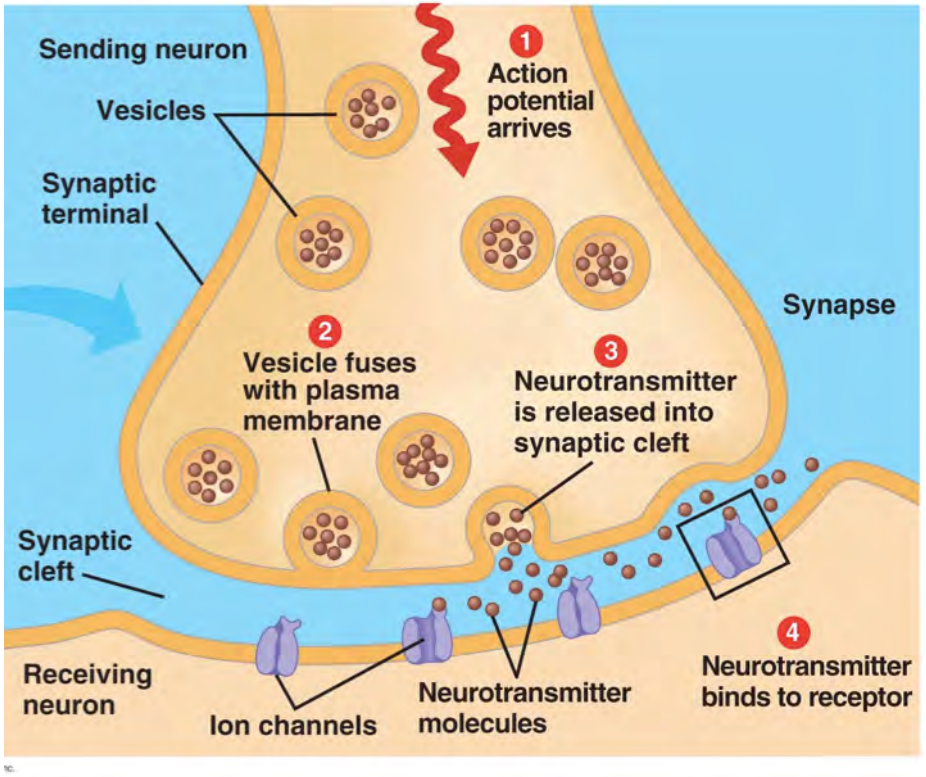


How much is being released?

- All of the vesicles within a neuron contain about the same amount of NT

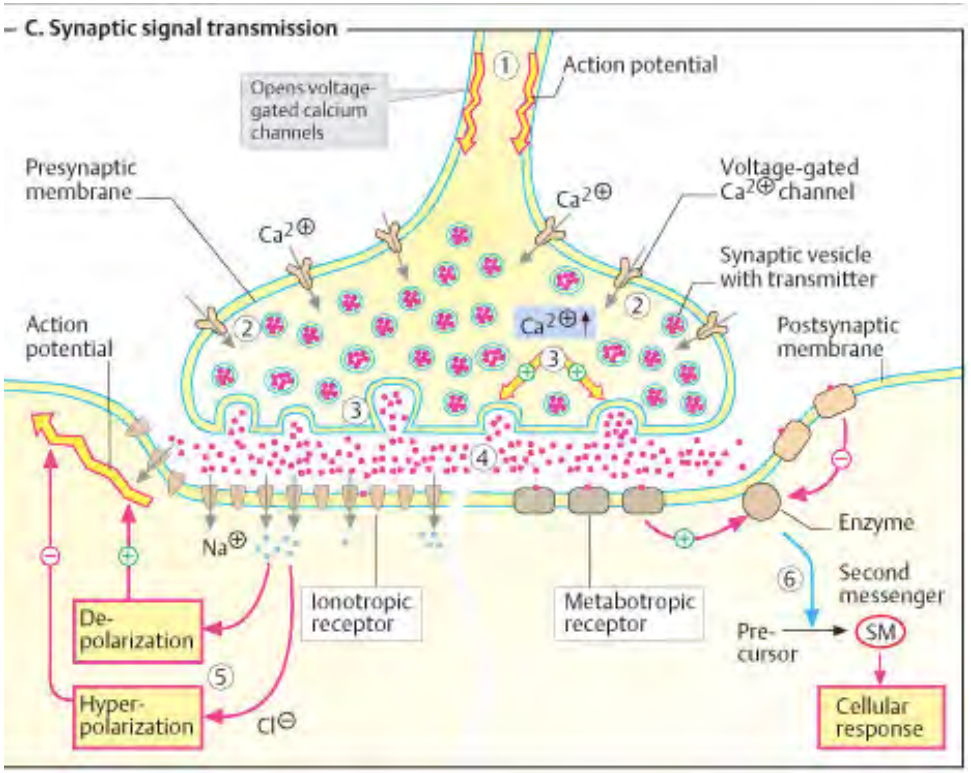
How much is being released?

- All of the vesicles within a neuron contain about the same amount of NT
- CNS synapses typically release one vesicle per action potential



How much is being released?

- All of the vesicles within a neuron contain about the same amount of NT
- CNS synapses typically release one vesicle per action potential
- Neuromuscular synapses release about 200 vesicles per action potential



How much is being released?

Why do muscles get more?

How much is being released?

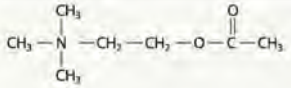
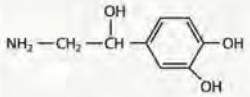
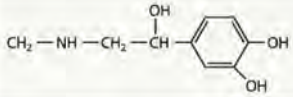
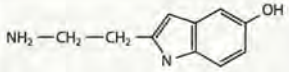
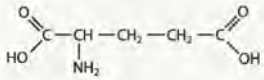
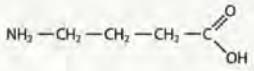
Why do muscles get more?

As a fail-safe to make sure muscles can contract

Poll: What influences NT levels?

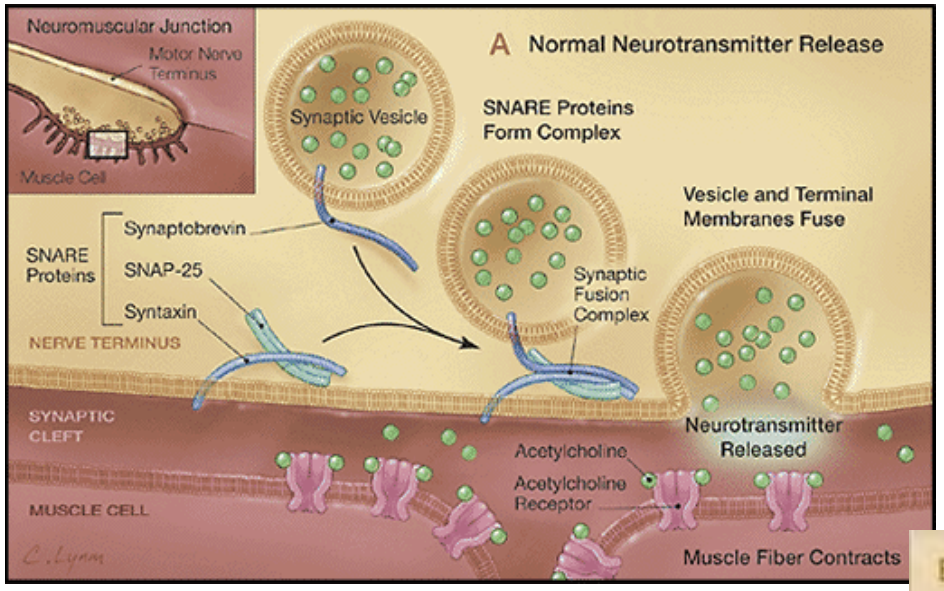
Neurotransmitters have different jobs

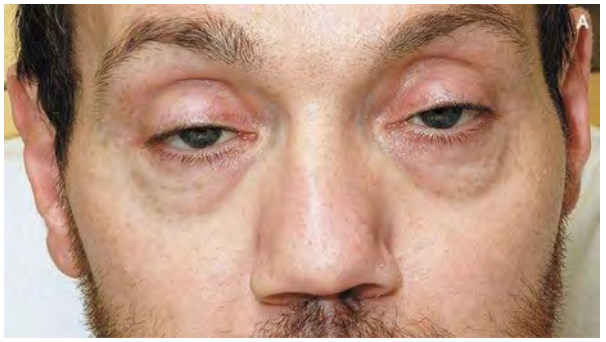
Selected Neurotransmitters

Neurotransmitter	Chemical Structure	Mechanism of Action	Location(s)	Comments
Acetylcholine (ACh)		Primarily direct, through binding to chemically gated channels	CNS: Synapses throughout brain and spinal cord PNS: Neuromuscular junctions, neuroglandular junctions, and synapses in autonomic ganglia	Widespread in CNS and PNS; best known and most studied of the neurotransmitters
Norepinephrine (NE)		Indirect, through G proteins and second messengers	CNS: Cerebral cortex, hypothalamus, brain stem, cerebellum, and spinal cord PNS: Most neuromuscular and neuroglandular junctions of sympathetic division of ANS	Involved in attention and consciousness, control of body temperature, and regulation of pituitary gland secretion
Epinephrine (E)		Indirect: G proteins and second messengers	CNS: Thalamus, hypothalamus, midbrain, and spinal cord	Generally excitatory effect along autonomic pathways
Serotonin		Primarily indirect: G proteins and second messengers	CNS: Hypothalamus, limbic system, cerebellum, spinal cord, and retina	Important in emotional states, moods, and body temperature; several illicit hallucinogenic drugs, such as Ecstasy, target serotonin receptors
Glutamate		Indirect: G proteins and second messengers Direct: opens calcium/ sodium channels	CNS: Cerebral cortex and brain stem	Important in memory and learning; most important excitatory neurotransmitter in the brain
Gamma-aminobutyric acid (GABA)		Direct or indirect (G proteins), depending on type of receptor	CNS: Cerebral cortex, cerebellum, interneurons throughout brain and spinal cord	Direct inhibitory effects: opens Cl^- channels; indirect effects: opens K^+ channels and blocks entry of Ca^{2+}

What if blocking a certain neurotransmitter caused muscle paralysis? What would you guess about it's function?

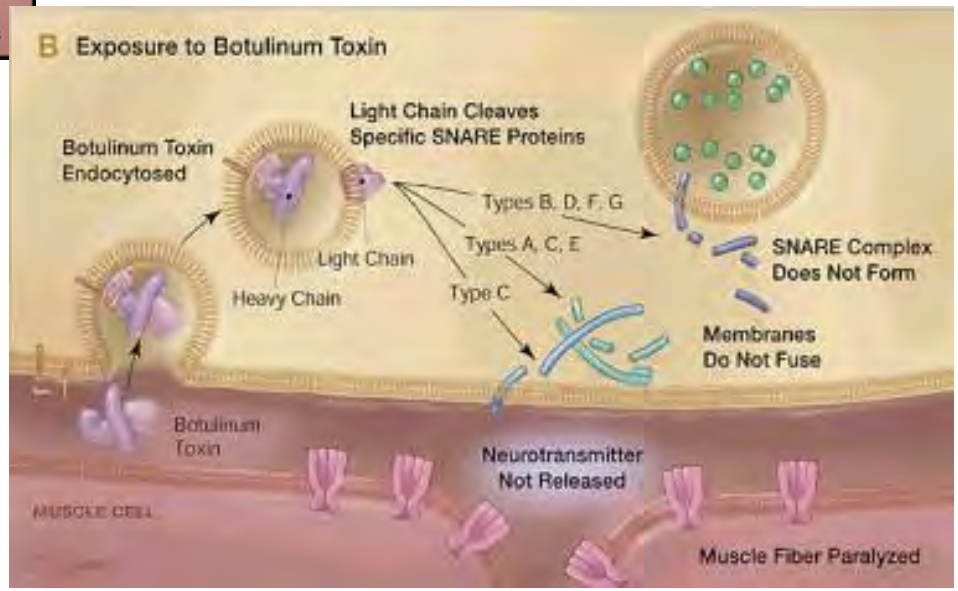
Botulism: Acetylcholine vesicles can't release





http://www.247wellness.org/botulism/

Botulism causes paralysis because it prevents the release of acetylcholine (necessary for muscle contraction)



Acetylcholine (excitatory)

- Stimulates muscle contraction
- Stimulates release of some hormones
- Helps regulate lots of things including:
  - Wakefulness
  - Attention/vigilance
  - Anger
  - Aggression
  - Sexual drive
  - Thirst
  - Learning/memory

Acetylcholine (excitatory)

- Alcohol decreases acetylcholine transmission

What if blocking a certain neurotransmitter caused muscle spasms? What would you guess about it's function?

Tetanus: GABA vesicles can't release

Tetanus causes muscle spasm because it prevents the release of GABA which inhibits muscular contraction…the muscles never stop contracting

Muscle spasms in a person with tetanus. Painting by Sir Charles Bell, 1809. Retrieved from https://en.wikipedia.org/wiki/Tetanus

GABA (inhibitory)

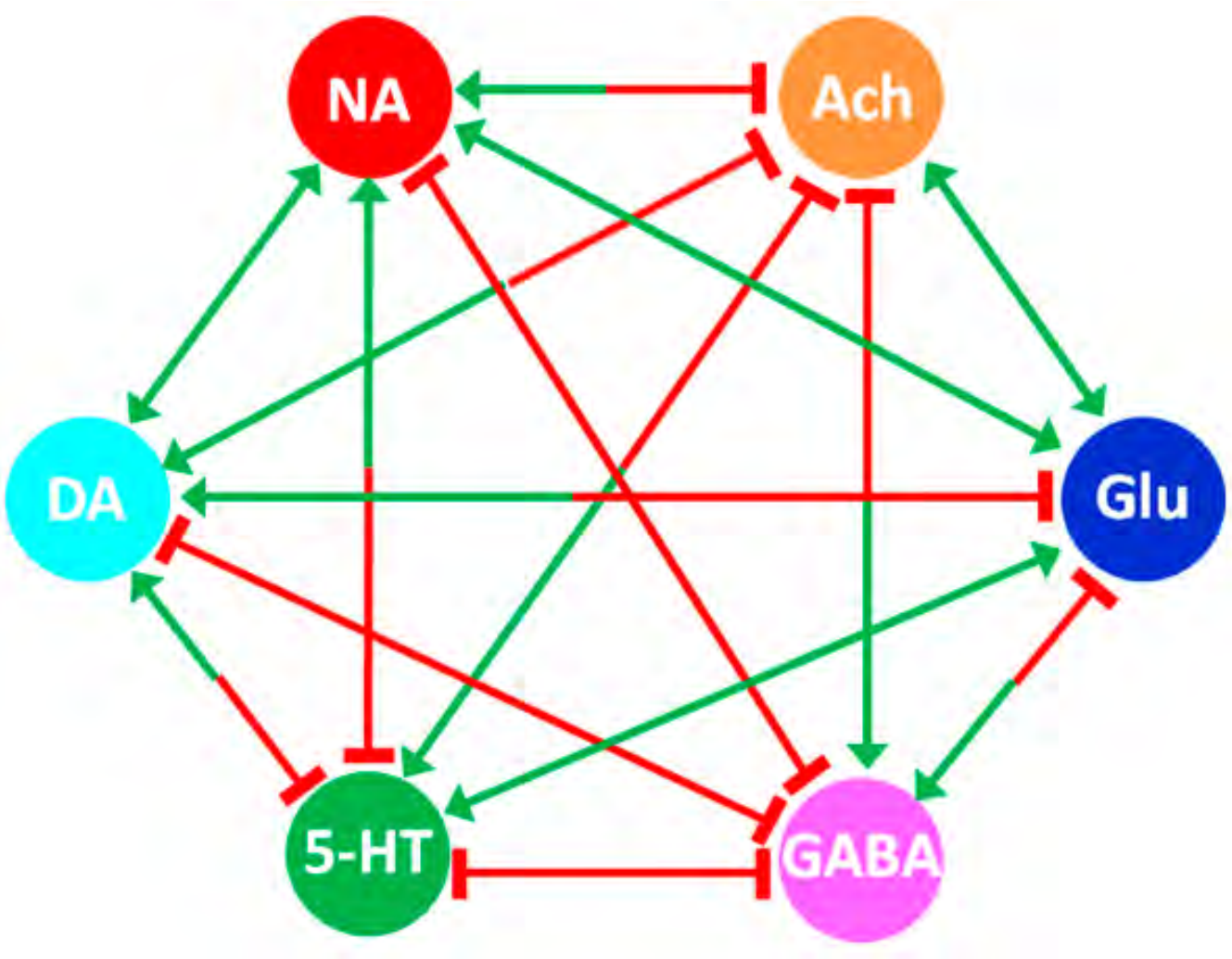
- Works throughout the brain to balance excitatory NTs
  - About 40% of neurons have GABA receptors
  - Most active inhibitory NT
- Synthesized from glutamate (the major excitatory NT)
- Essential for:
  - Motor control (refines movement)
  - Vision
  - Anxiety regulation

What would happen to GABA levels if glutamate levels decreased?

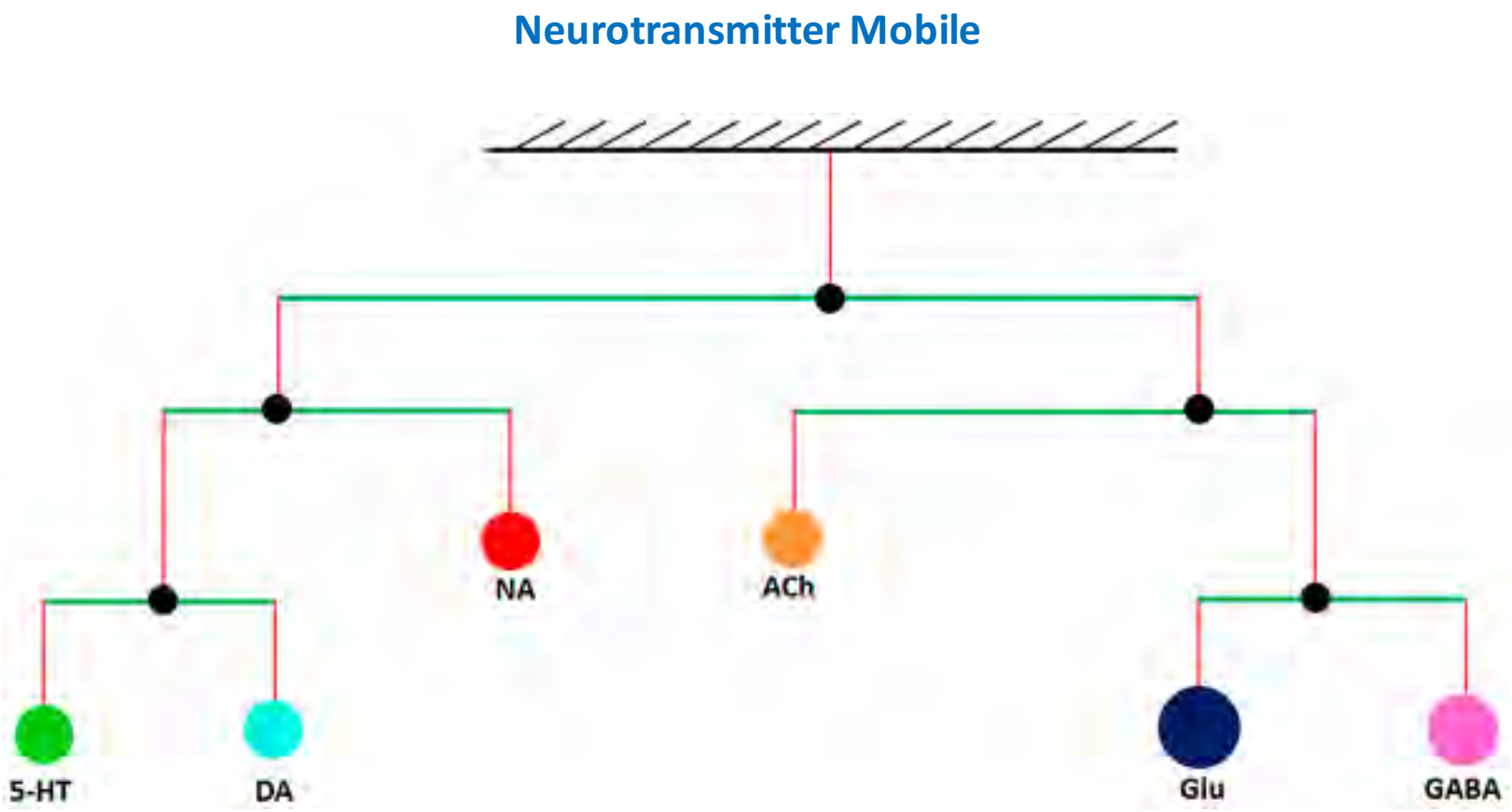
What would happen to GABA levels if glutamate levels decreased?

They would decrease

Neurotransmitters influence each other



If you alter the levels of one, the others will adjust in response



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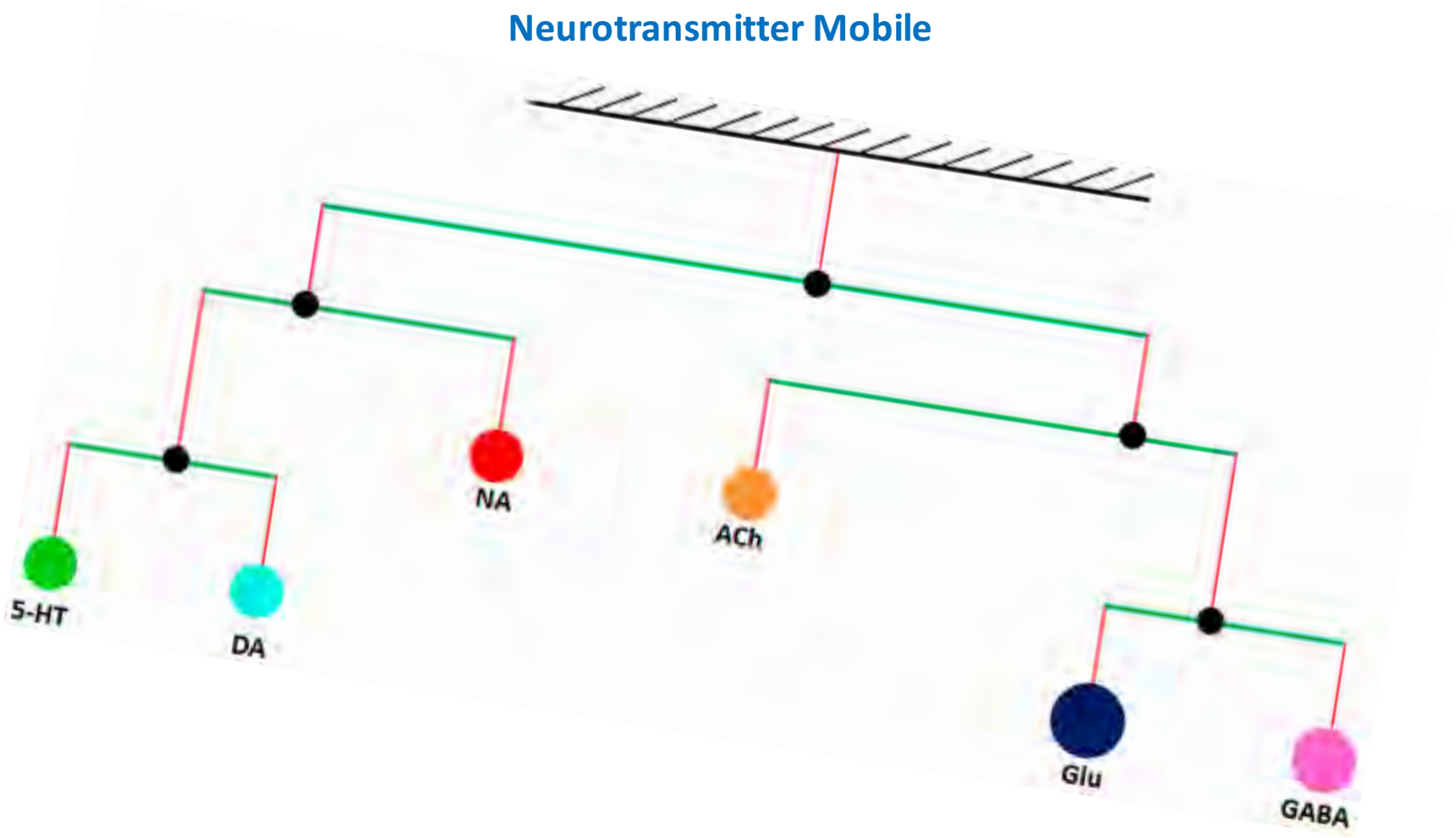

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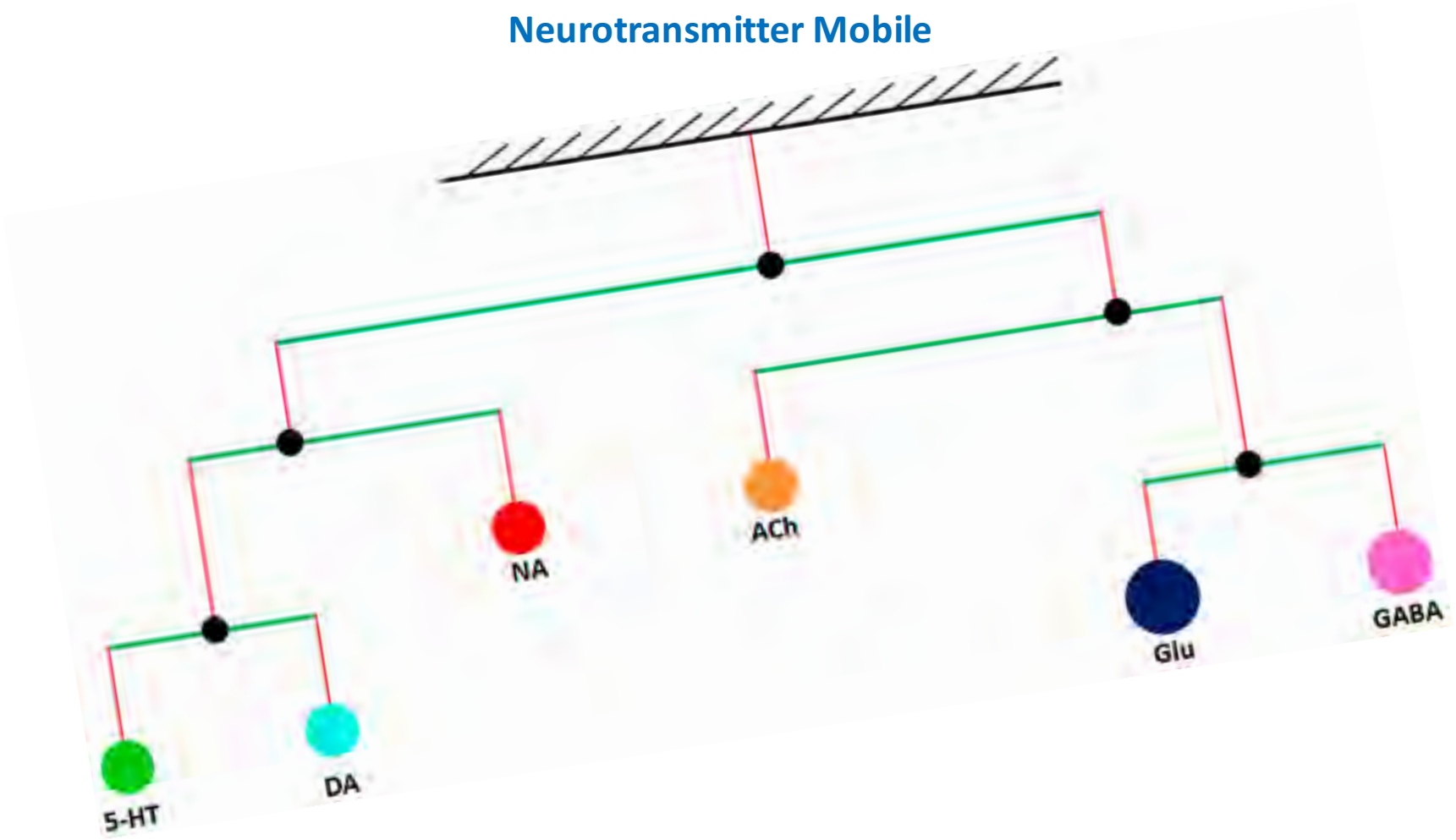
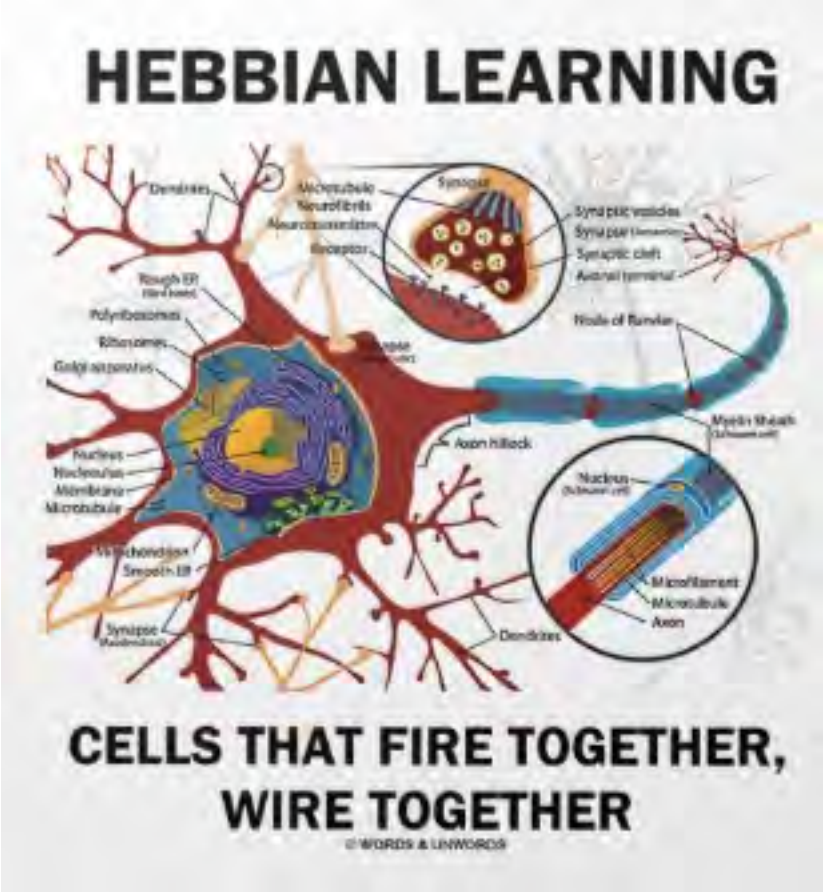


Glutamate (excitatory)

- Works throughout the brain
- Involved in most cognitive functions, especially learning and memory
- Critical agent for long-term potentiation (Hebbian learning)



Vance (2014)

Glutamate (excitatory)

- Actions (at NMDA glutaminergic receptors) can be blocked by alcohol

Glutamate (excitatory)

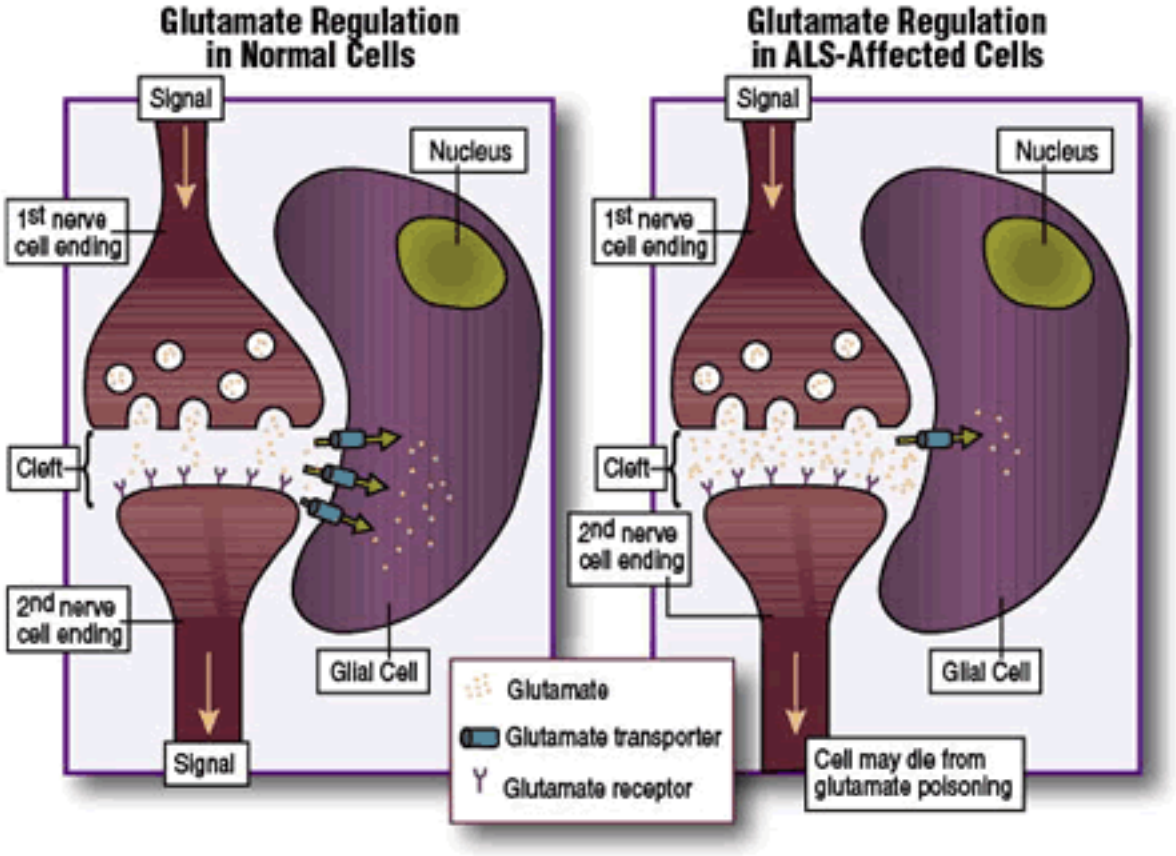
- Actions (at NMDA glutaminergic receptors) can be blocked by alcohol

- St. John's Wort can increase release

Vance (2014)

If you want to learn better, should you take lots of St. John's Wort so you increase your glutamate levels?

Too much glutamate is a bad thing



https://www.studyblue.com/notes/note/n/l3-degenerative-disease-and-dementia/deck/14274590

Do genes influence NT levels?

Genes can influence NT levels/processing

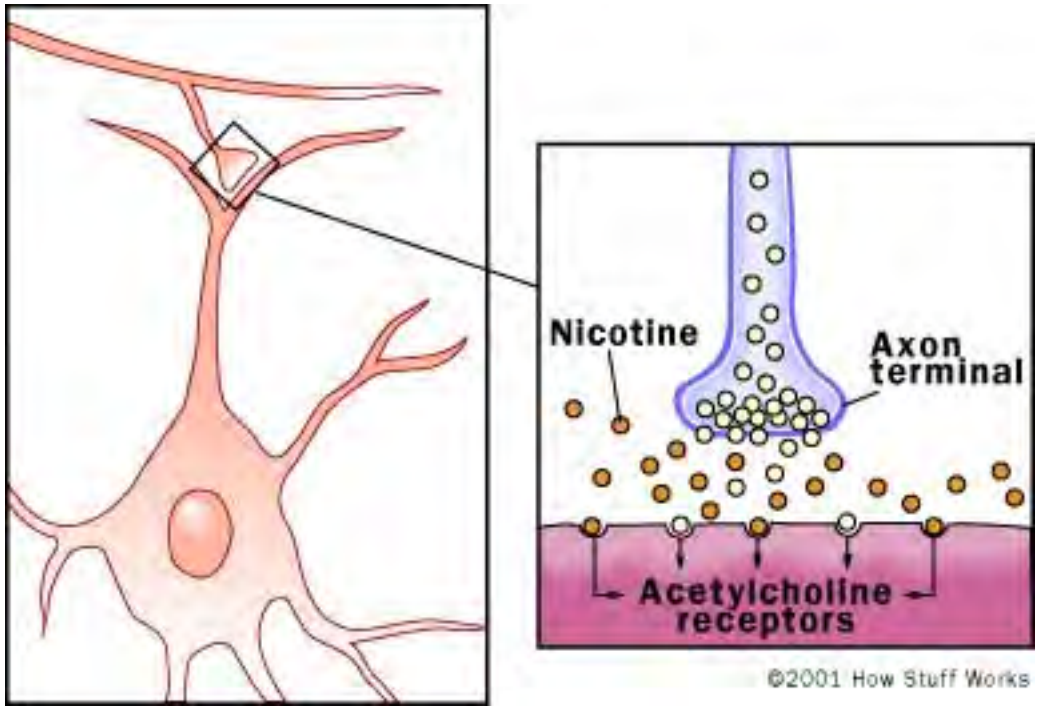
- ADHD gene reduces dopamine release in dorsal striatum
- Gene associated with depression and suicide decreases noradrenergic transmission
- Adolescent binge drinking alters adult gene expression resulting in decreased cholinergic neuron density

Coleman (2011), Kim (2014), Sanchez-Mora (2013)

Do lifestyle choices influence NT levels?

Lifestyle factors can influence NT levels

Nicotine blocks cholinergic receptors



Lifestyle factors can influence NT levels

- Exercise:
  - Attenuated dopamine depletion
  - Increased serotonin and Ach levels
- Enriched environment
  - Upregulates genes that balance NT activity
- Diet:
  - One-week of high-fat/low-carb diet decreased serotonin levels in the hypothalamus
  - Consuming fat/sugar combinations reduced dopamine signaling
  - Long-term consumption of low-protein/high-carb diet decreased dopaminergic receptor density

Kramer (2006), Lee (2013), Lopresti (2013)

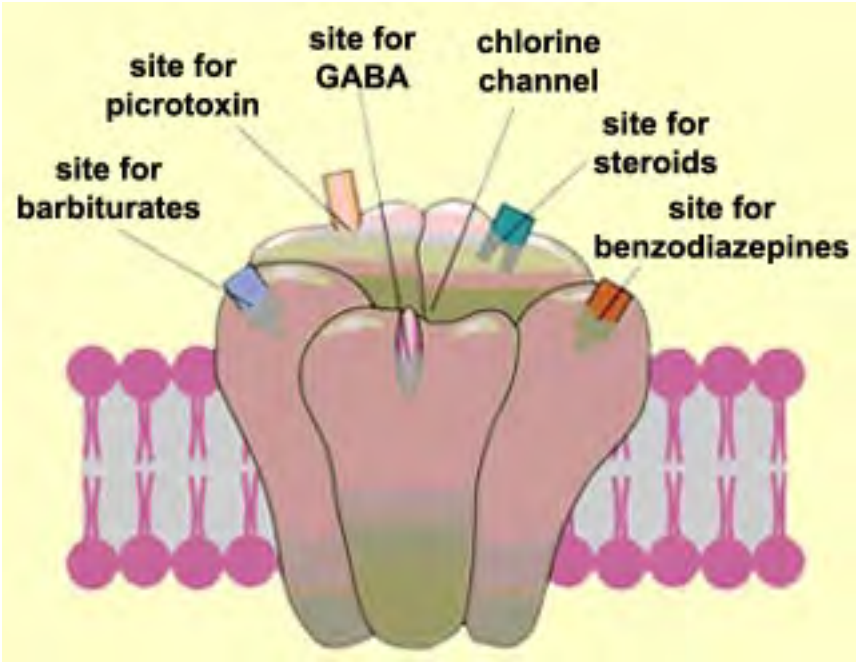
Valium? Inhibitory or Excitatory?

Valium? Inhibitory or Excitatory?

Inhibitory

GABA (inhibitory)

- Nature's "valium-like" substance
- Drugs like valium, Ambien, Lunesta work by increasing the activation of GABA-ergic receptor sites

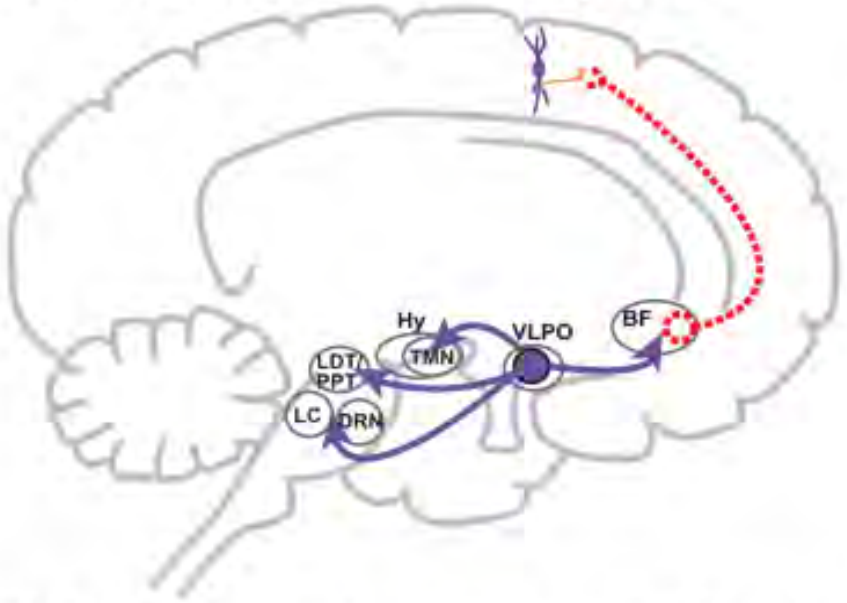


Benzodiazepines (like valium) are effective in treating anxiety

How might GABA influence sleep? ADHD?

GABA promotes sleep

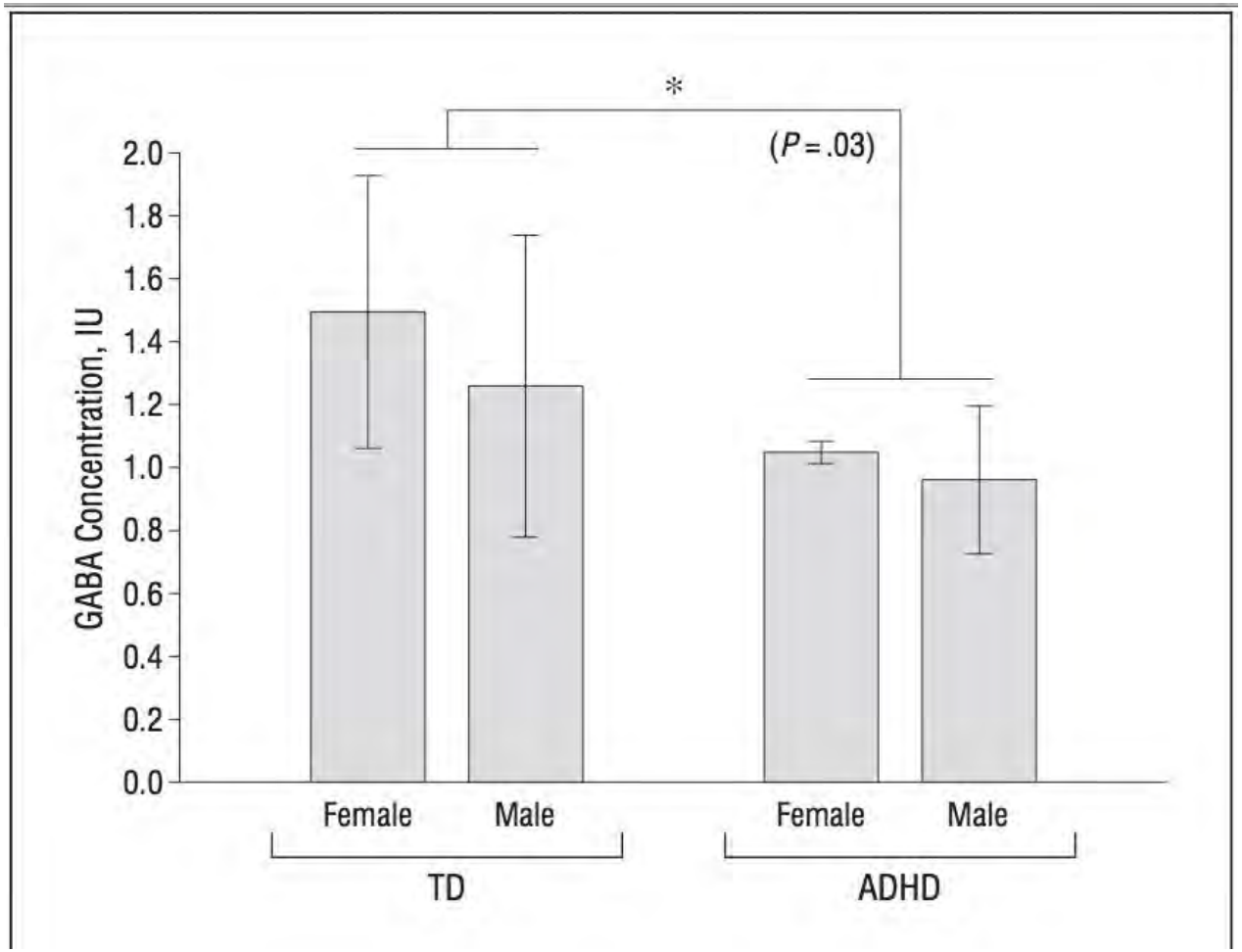
FIGURE 2.
Sleep-promoting GABA system



GABA=□-aminobutyric acid; Hy=hypothalamus; BF=basal forebrain; LDT=laterodorsal tegmental; PPT=peduncolopontine tegmental; TMN=tuberomamillary nucleus; VLPO=ventrolateral preoptic nucleus; LC=locus coeruleus; DRN=dorsal raphe nucleus.

Stahl SM. *CNS Spectr.* Vol 13, No 12. 2008.

GABA levels decreased in ADHD

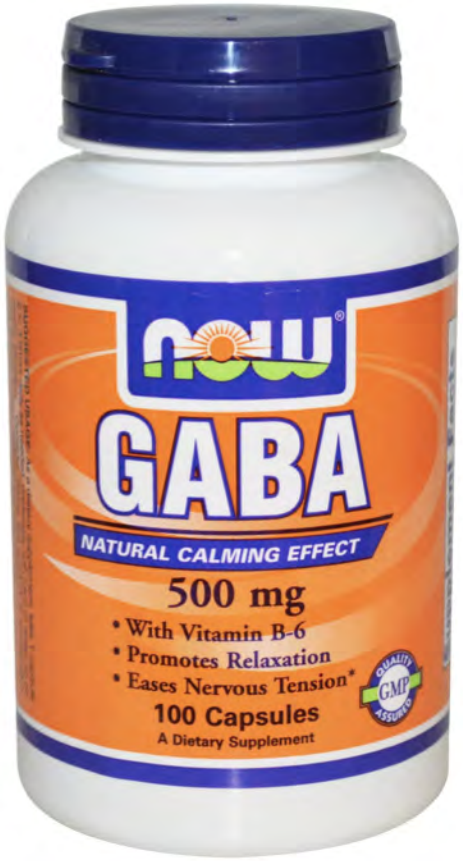


Edden, Crocetti, Zhu, Gilbert & Mostofsky (2012)

Do we have any way to influence our GABA levels?

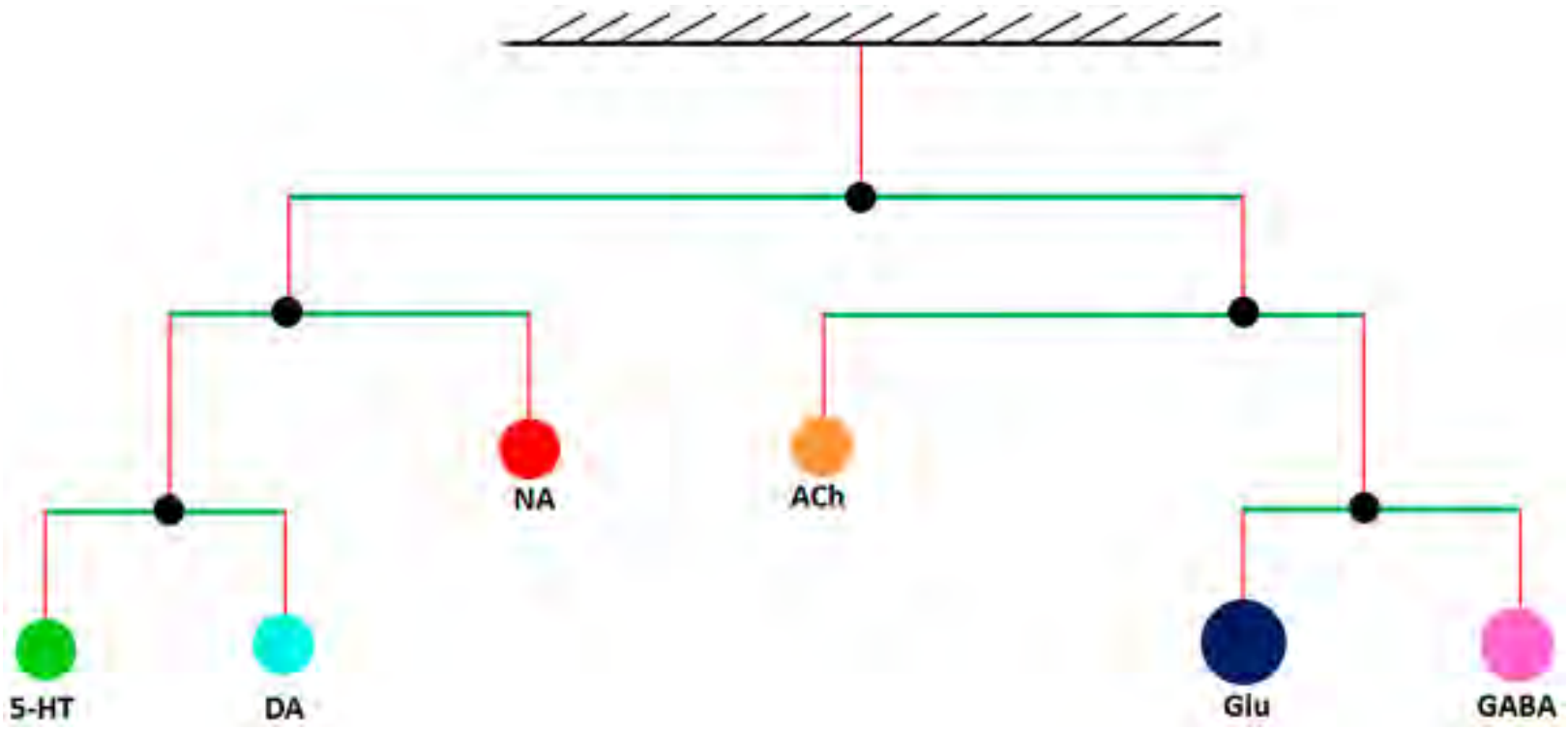
Increasing GABA

- Supplements not thought to cross BBB but may enter through enteric routes
- Animal data shows some benefits in sleep



Boonstra et al., (2015); Mabunga, et al., (2015)

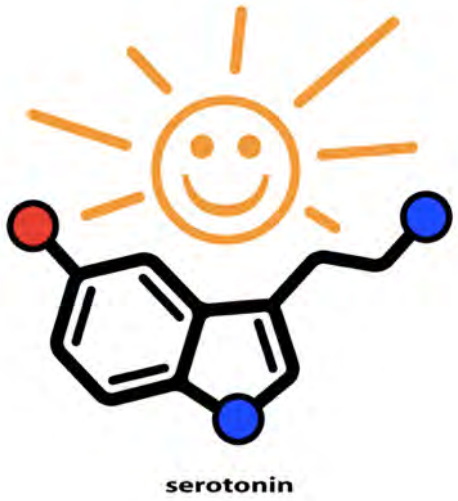
What might happen if you increase GABA?

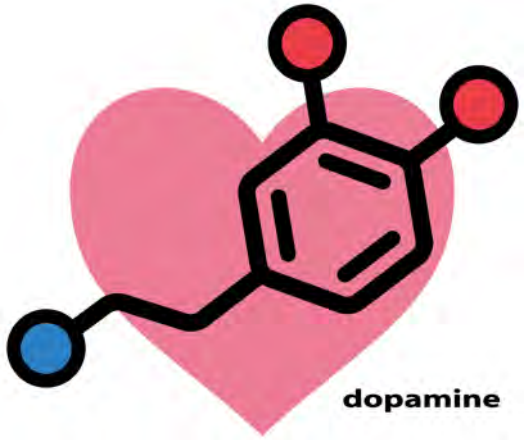


Why is Calvin mad?

http://www.achievetruehealth.com/winter-blues-low-serotonin-may-be-the-culprit/

Why is Calvin mad? He needs happy juice?





http://www.achievetruehealth.com/winter-blues-low-serotonin-may-be-the-culprit/


The first date:
Do it better with dopamine!

Dopamine (excitatory & inhibitory)

- Involved in:
  - Reward center/positive reinforcement

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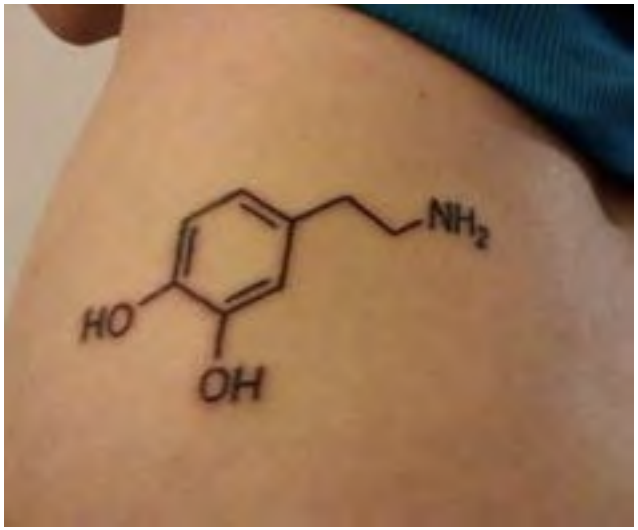


Dopamine (excitatory & inhibitory)

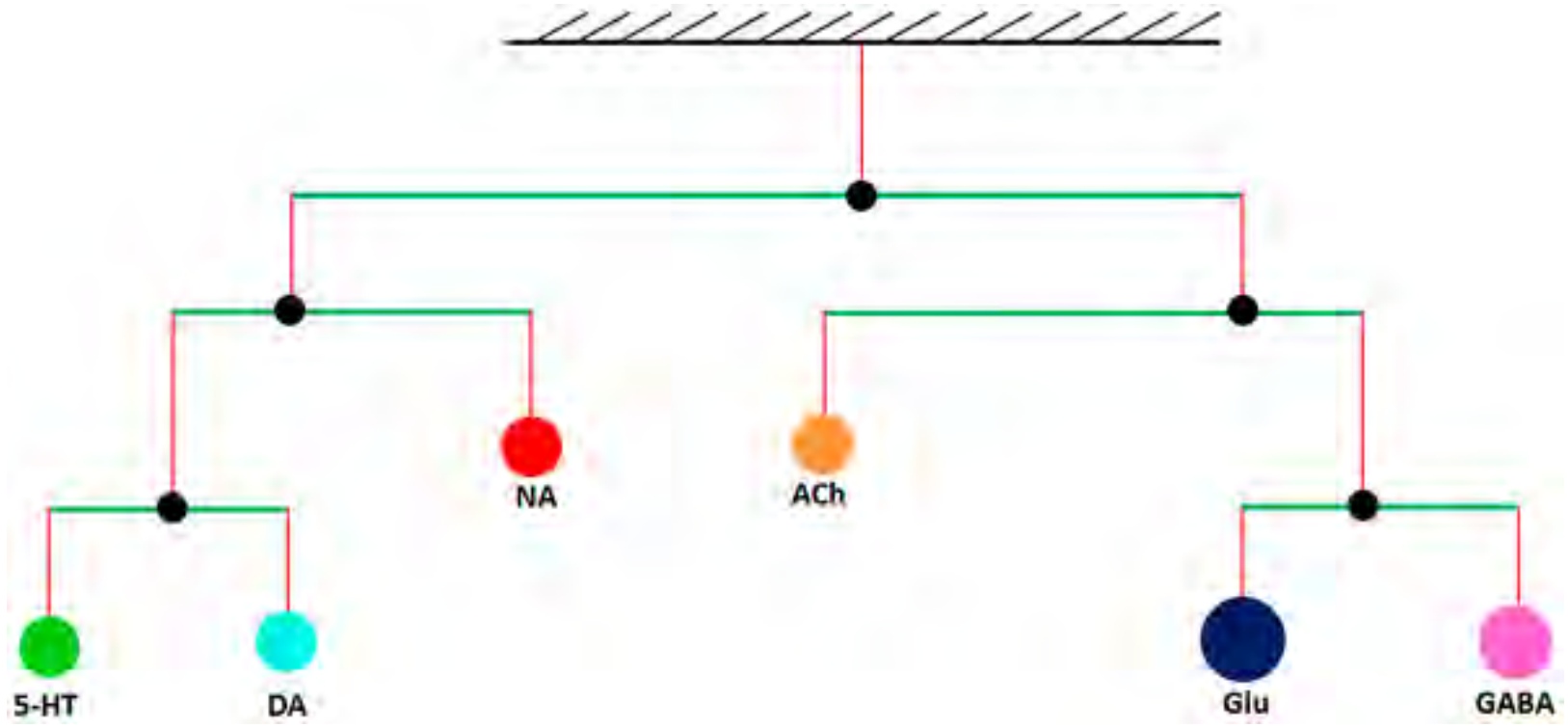
- Involved in:
  - Reward center/positive reinforcement
  - Ability to experience pleasure/pain
  - Motivation
  - Emotional response (altered levels seen in depression)
  - Maintaining focus
    - Stimulants/caffeine push dopamine into the synapse…result is increased focus (long-term, causes dopamine depletion)
  - Movement control

Dopamine errors

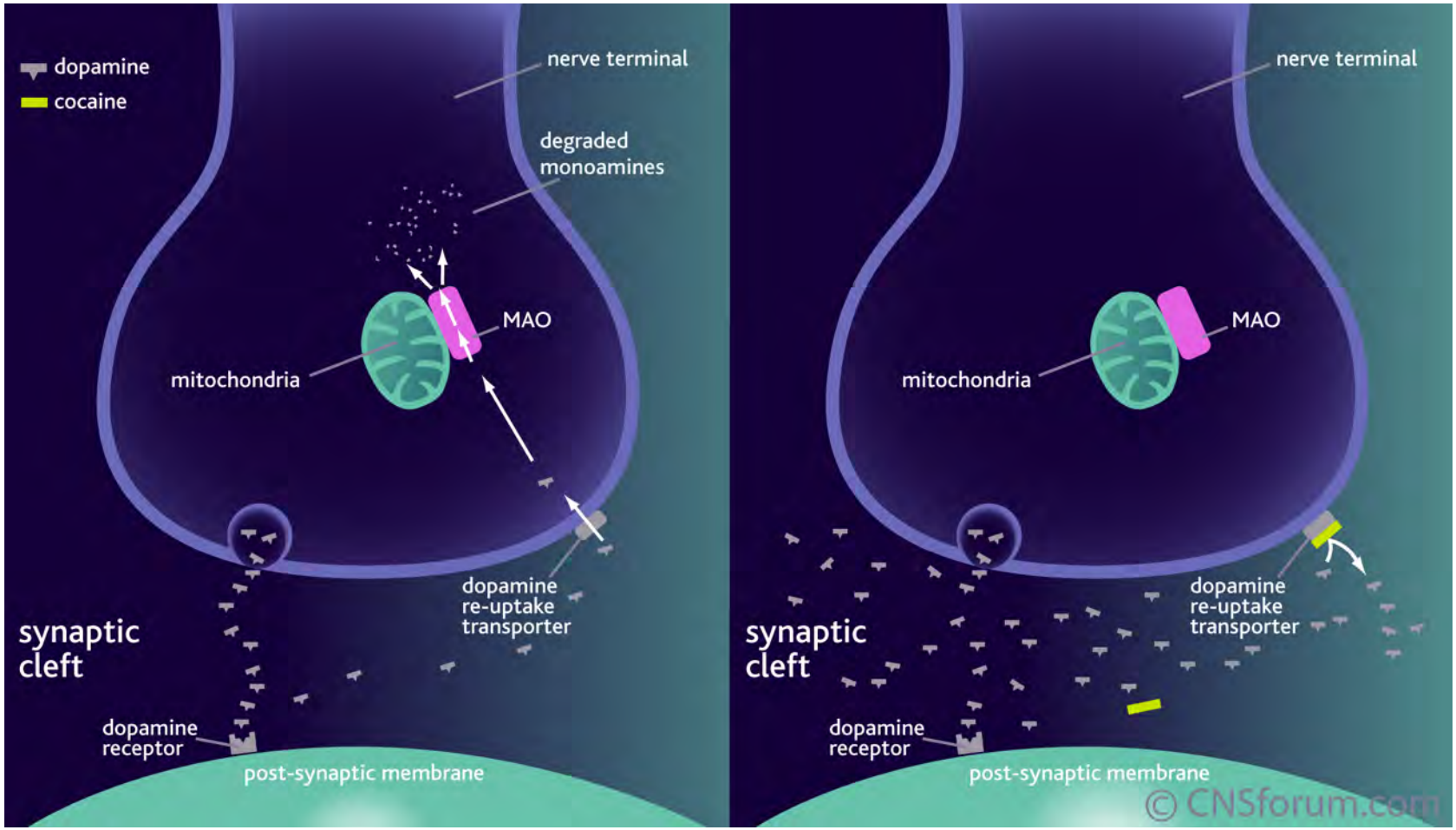
- Motor/movement disorders
- ADHD (low levels)
- Addictions (mild elevations)
- Paranoia (high levels)
- Schizophrenia (very high levels)

Do we want to increase dopamine levels?

Neurotransmitter Mobile



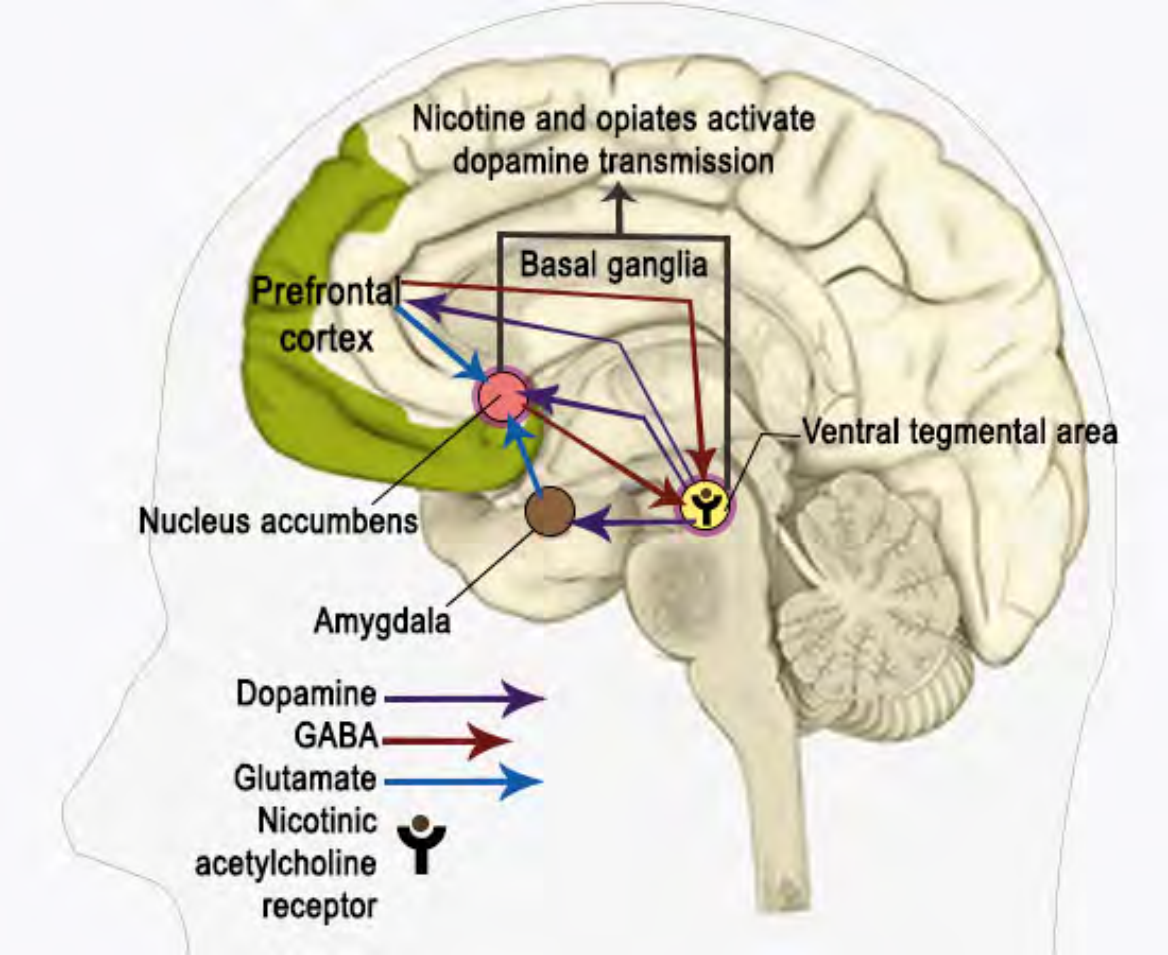
Cocaine increases dopamine levels



https://www.cnsforum.com/educationalresources/imagebank/substance_abuse/mao_cocaine

Cocaine causes short-term improvements but long-term deficits in cognition (attention, flexible thinking) … why?

Long-term cocaine use induces plastic changes in the reward circuit (nucleus accumbens)

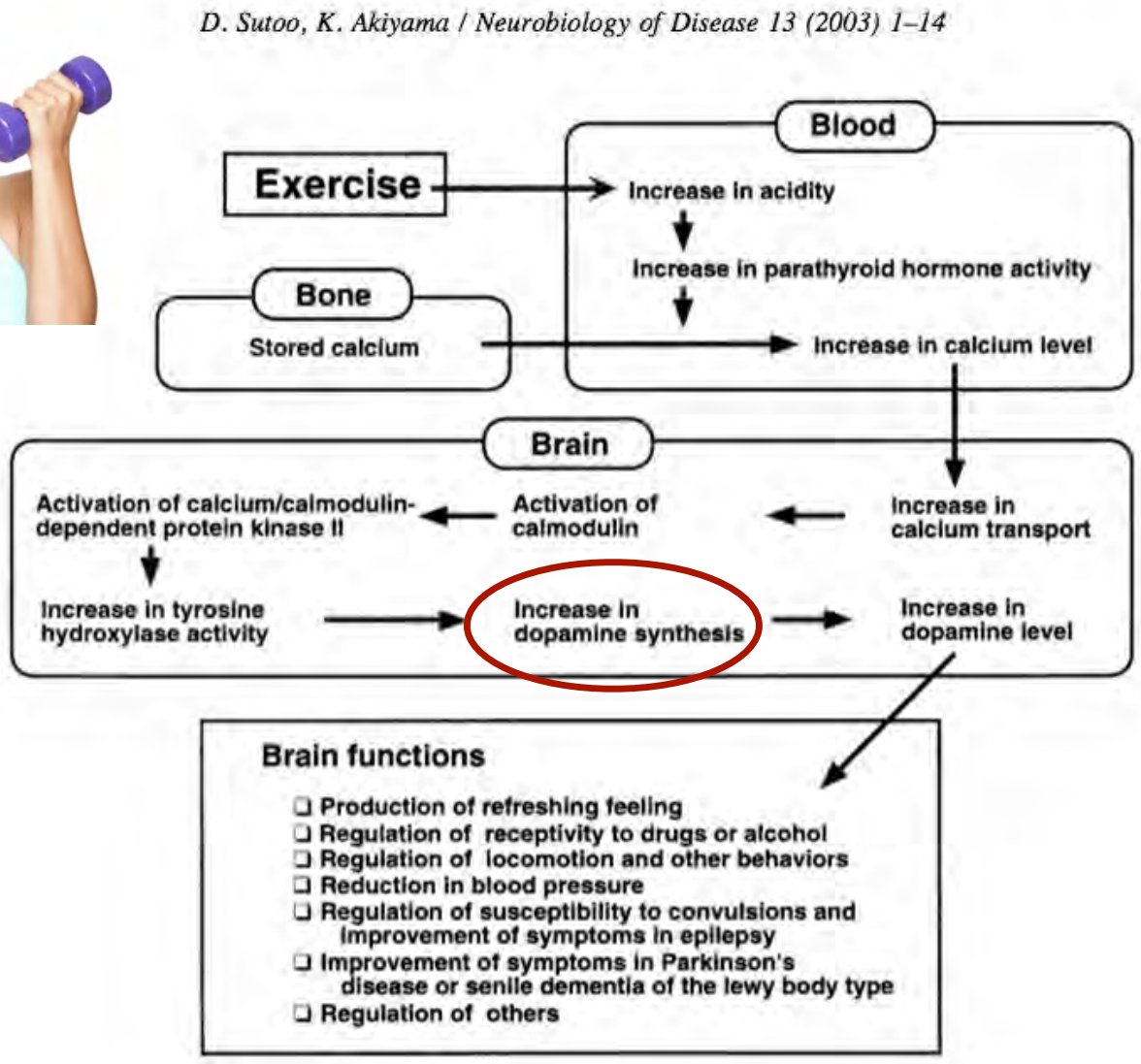


http://www.buzzle.com/articles/structure-and-function-of-the-nucleus-accumbens.html

Can we legally influence our dopamine levels?

Can we legally influence our dopamine levels?

Exercise increases dopamine synthesis



Serotonin (inhibitory)

- Helps regulate:
  - Mood (balances excitatory NTs to create stable mood)
  - Hostility/aggression, arousal
  - Sleep (inhibits wakefulness)

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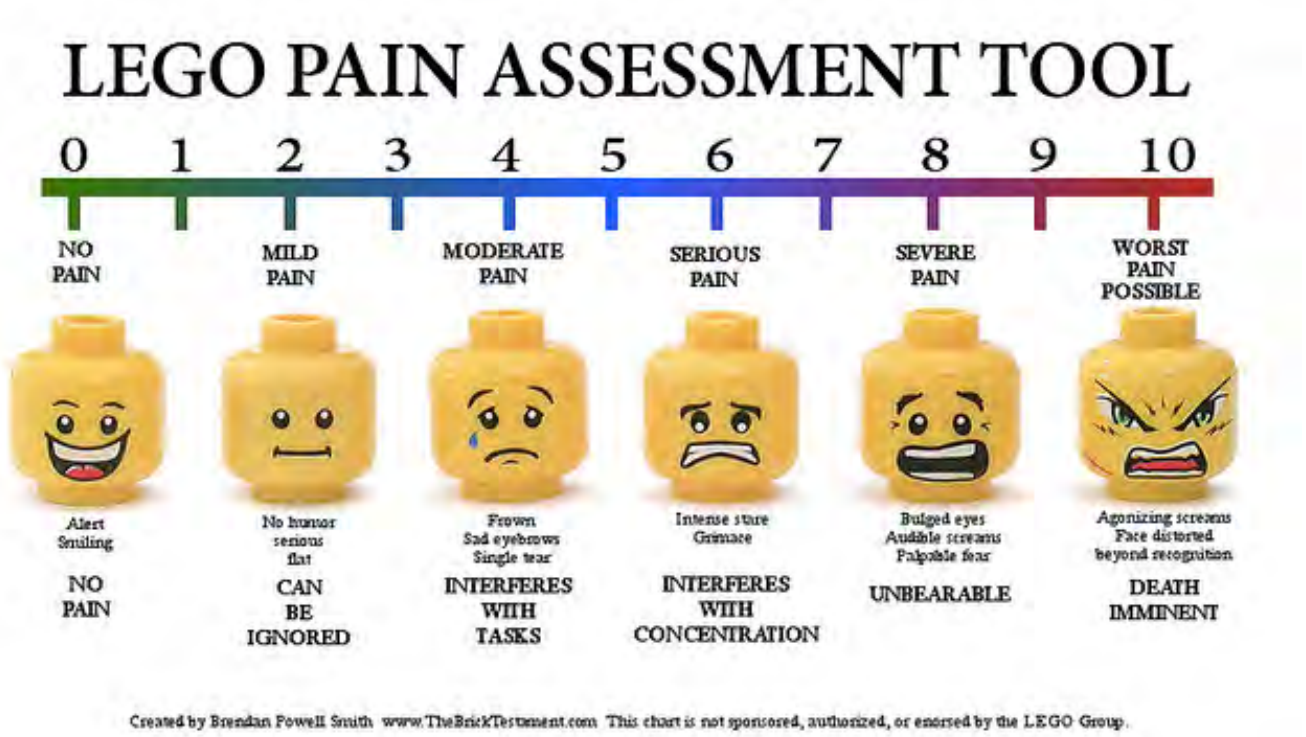


Serotonin (inhibitory)

- Helps regulate:
  - Mood (balances excitatory NTs to create stable mood)
  - Hostility/aggression, arousal
  - Sleep (inhibits wakefulness)
  - Pain control
  - Digestion
  - Sensory perception
  - Higher cognitive function

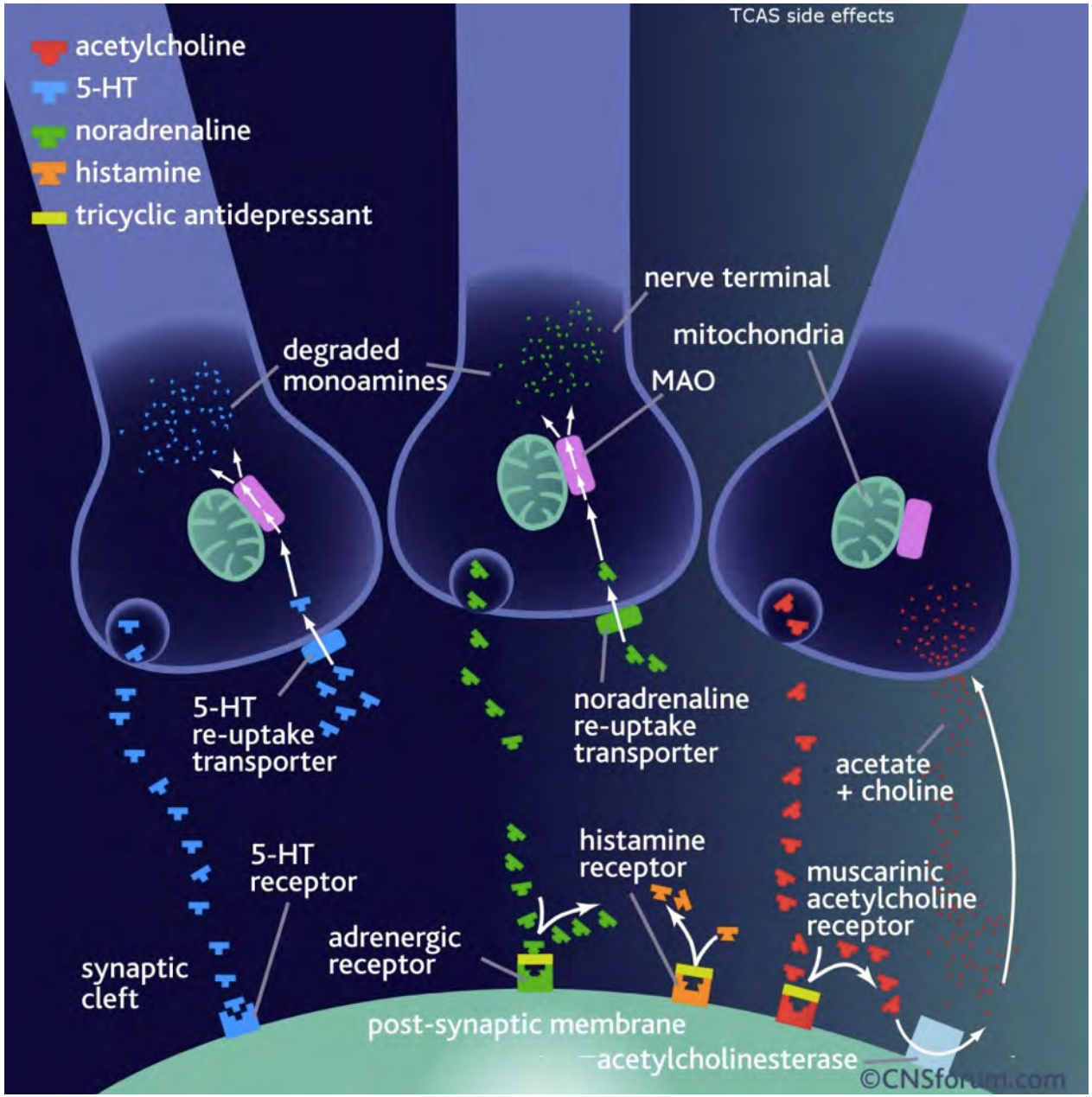
What happens if we don’t have the right serotonin level?

Serotonin (inhibitory)

- Imbalance can cause:
  - Depression
  - Insomnia
  - Decreased immune function
  - Carbohydrate cravings

Can we influence our serotonin levels?

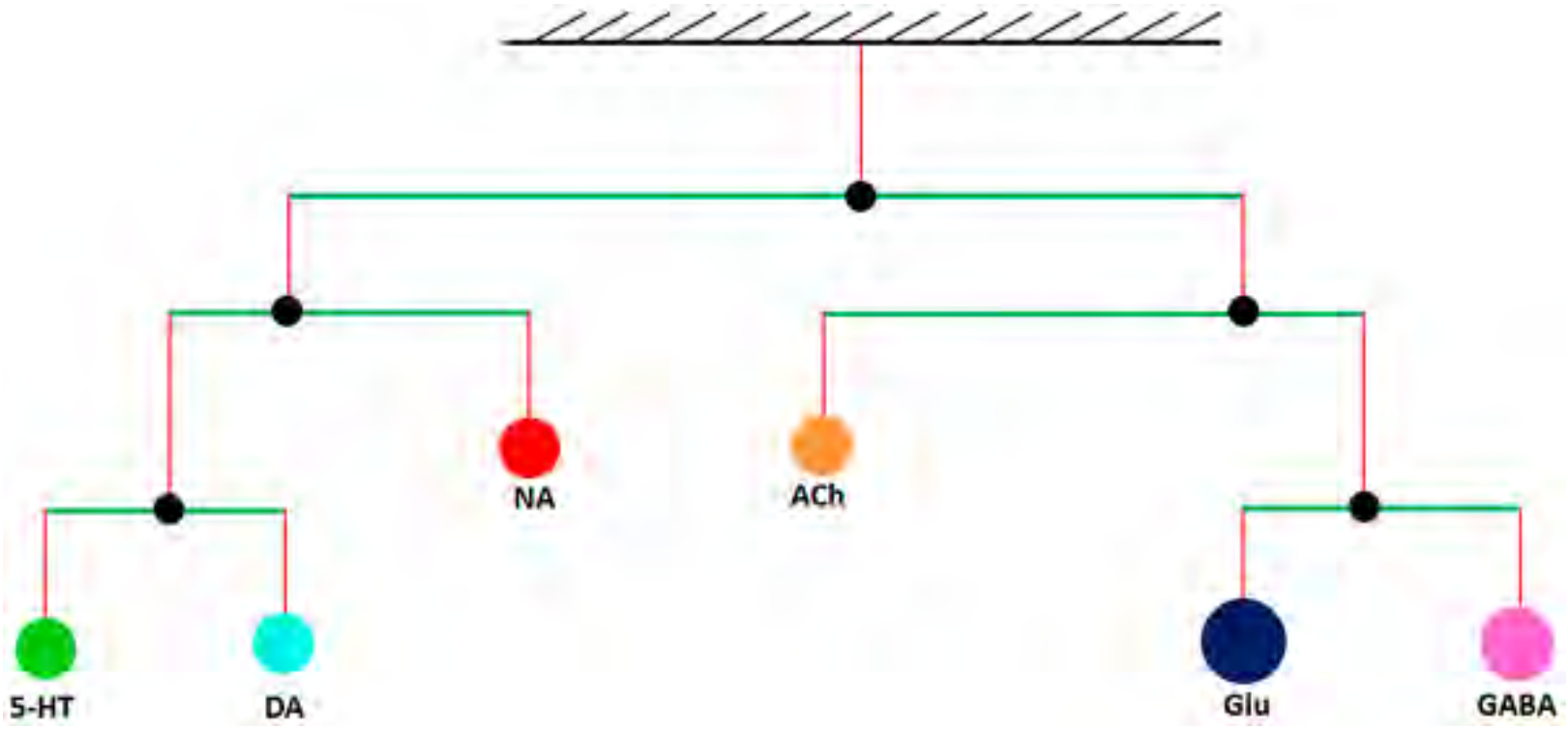
Medications alter NT levels by interrupting neurotransmission



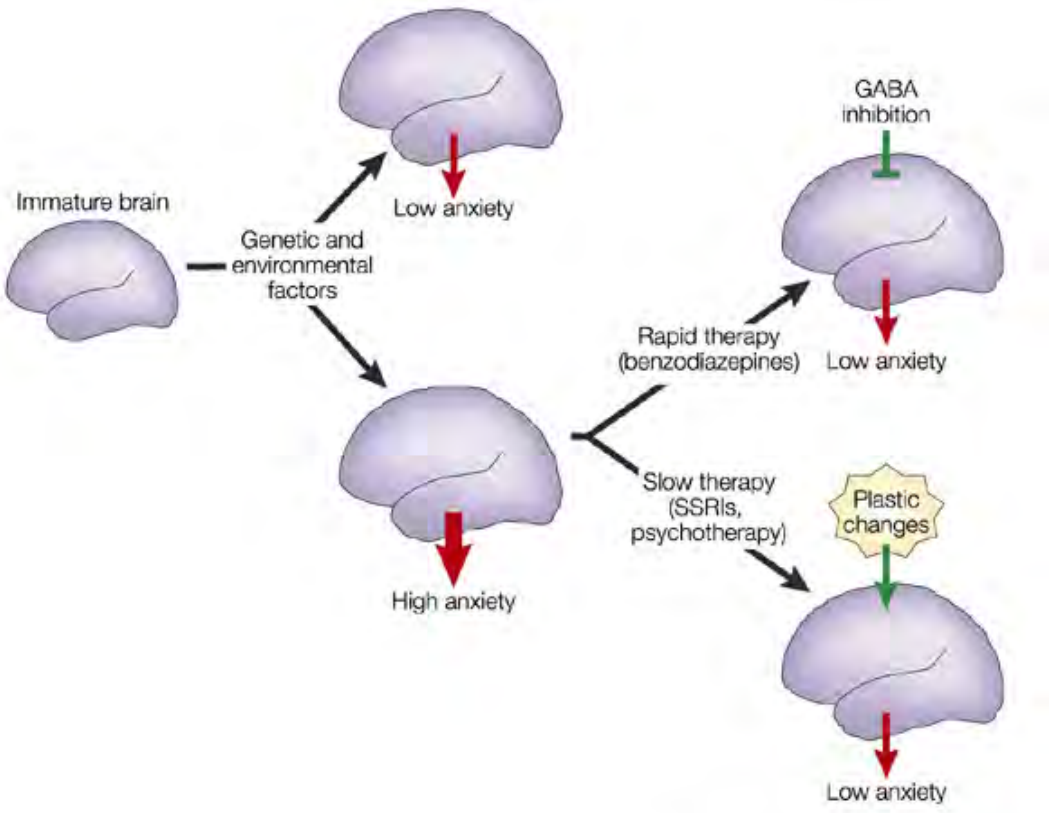
http://pharmacologycorner.com/differences-between-tricyclic-antidepressants-and-selective-serotonin-norepinephrine-reuptake-inhibitors-mechanism-of-action/

Why are SSRIs preferred over valium for anxiety?

Neurotransmitter Mobile



Valium is temporary; SSRIs induce plastic changes



- Benzodiazepines cause immediate GABA-like actions
- SSRIs cause plastic changes to change overall NT balance

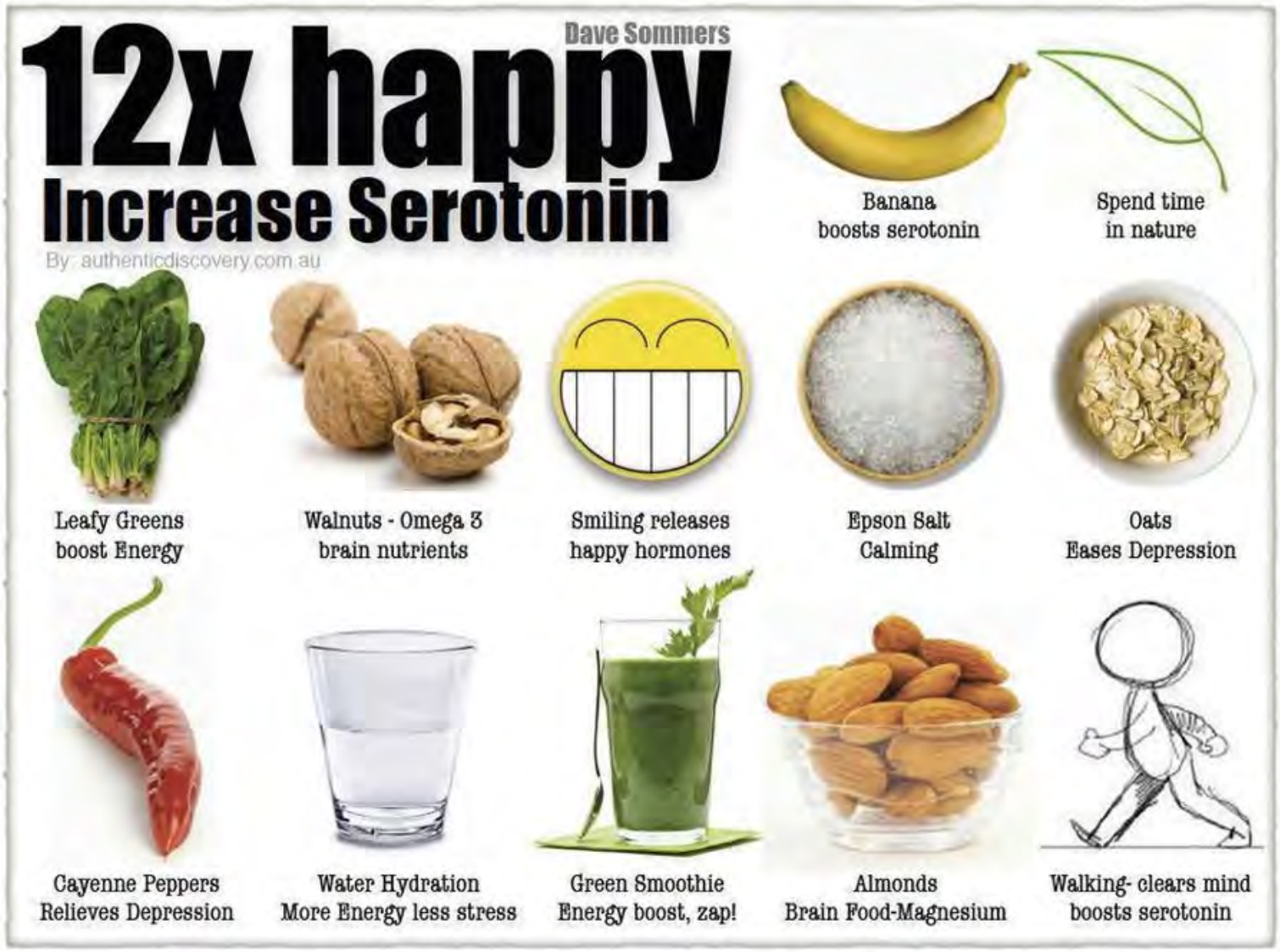
Gross (2004)

Can supplements help?

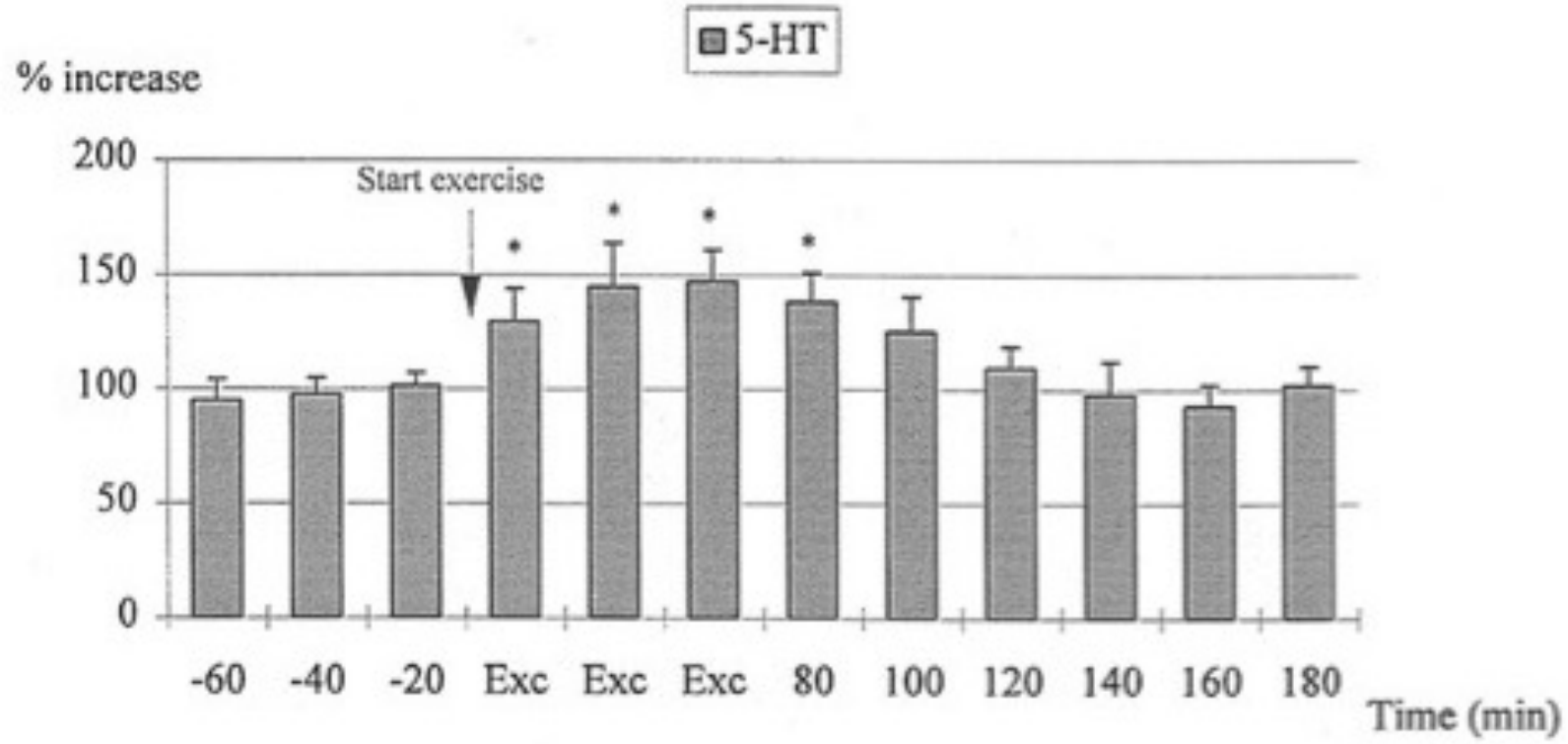
- Tryptophan supplement (serotonin precursor) altered serotonin levels and behavior in mice
- Vitamin D and omega-3s may modulate serotonin synthesis

Patrick & Ames (2015); Zhang et al., (2015)

Eat nuts, be happy?



Animal data shows an increase in serotonin levels with exercise



Melancon (2014)

Take a Quiz: Excitatory vs. Inhibitory

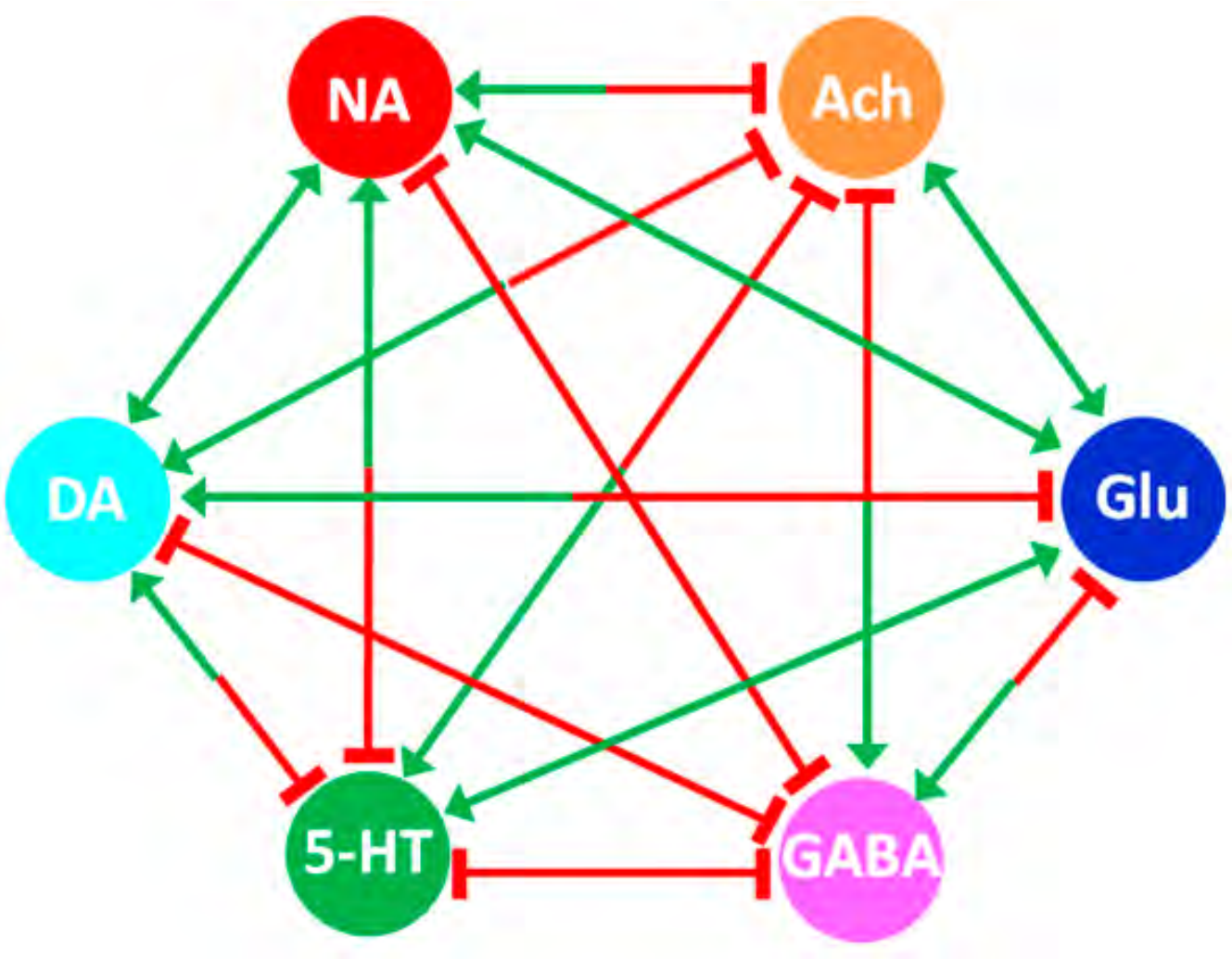
- Excitatory
  - Glutamate
  - Acetylcholine
  - Norepinephrine (noradrenaline)
  - Epinephrine (adrenaline)
  - Dopamine

- Inhibitory
  - GABA (gamma-aminobutyric acid)
  - Serotonin
  - Dopamine

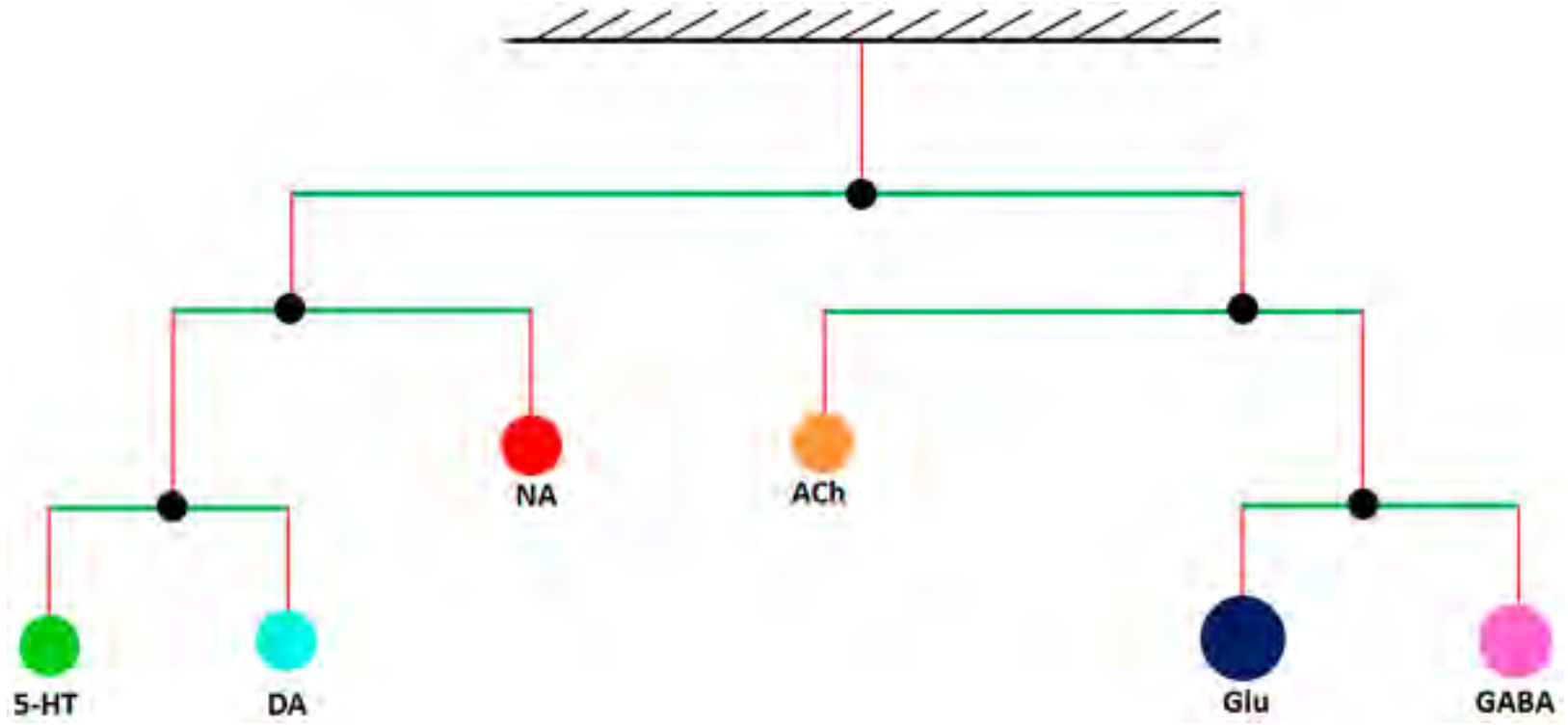
Neurotransmitters—the big picture

- Neurotransmitters (NTs) communicate information throughout the brain & body
- NTs tell your heart to beat, lungs to breath, stomach to digest
- NTs regulate mood, sleep, hunger, concentration, and more…lack of balance can cause adverse symptoms
- Genetic and lifestyle factors influence NT balance/levels/function
- NT levels are inter-related; you can't alter one without altering the others

Neurotransmitters influence each other



Balance is key…remember the mobile



Questions?

juliav@maitrilearning.com

Complete the 3-2-1

https://canvas.harvard.edu/courses/8447/discussion_topics/90505

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