

Come see us during office hr!



Dr. Bovee next session, Tuesday!
No more Pat 'til Thursday! Hooray!



BI 358 Lecture 2

- I. Announcements Douglas Bovee, MD, Addiction & Internal Medicine Specialist next session! **NB**: Sign-in + e-feedback < 24-48 hr. Quiz 1 + Outline due next Tues. Q? Great drug overview for Quiz. U Utah Addiction website!

<http://learn.genetics.utah.edu/content/addiction/mouse/>

Common linking mechanisms: COME Cocaine & Meth
HEMA Heroin & Marijuana, LSD & Ecstasy (S? Serotonin!)

- II. Homeostasis Connections Model, BP e.g. Q? Gain? G&H p 8

III. Addiction Medicine: Homeostasis & Overdose Story!

G&H ch 59 pp 751-61...Additional Information as Review? →

IV. Organization of the Nervous System

G&H ch 46 pp 582-7, LS1/2 ch 5

- A. Central vs peripheral, computer analogy fig 46-4
- B. Neurons, neuronal classes, neuroglia, connections

V. Autonomic Nervous System G&H ch 61 pp 773-85 + LS +...

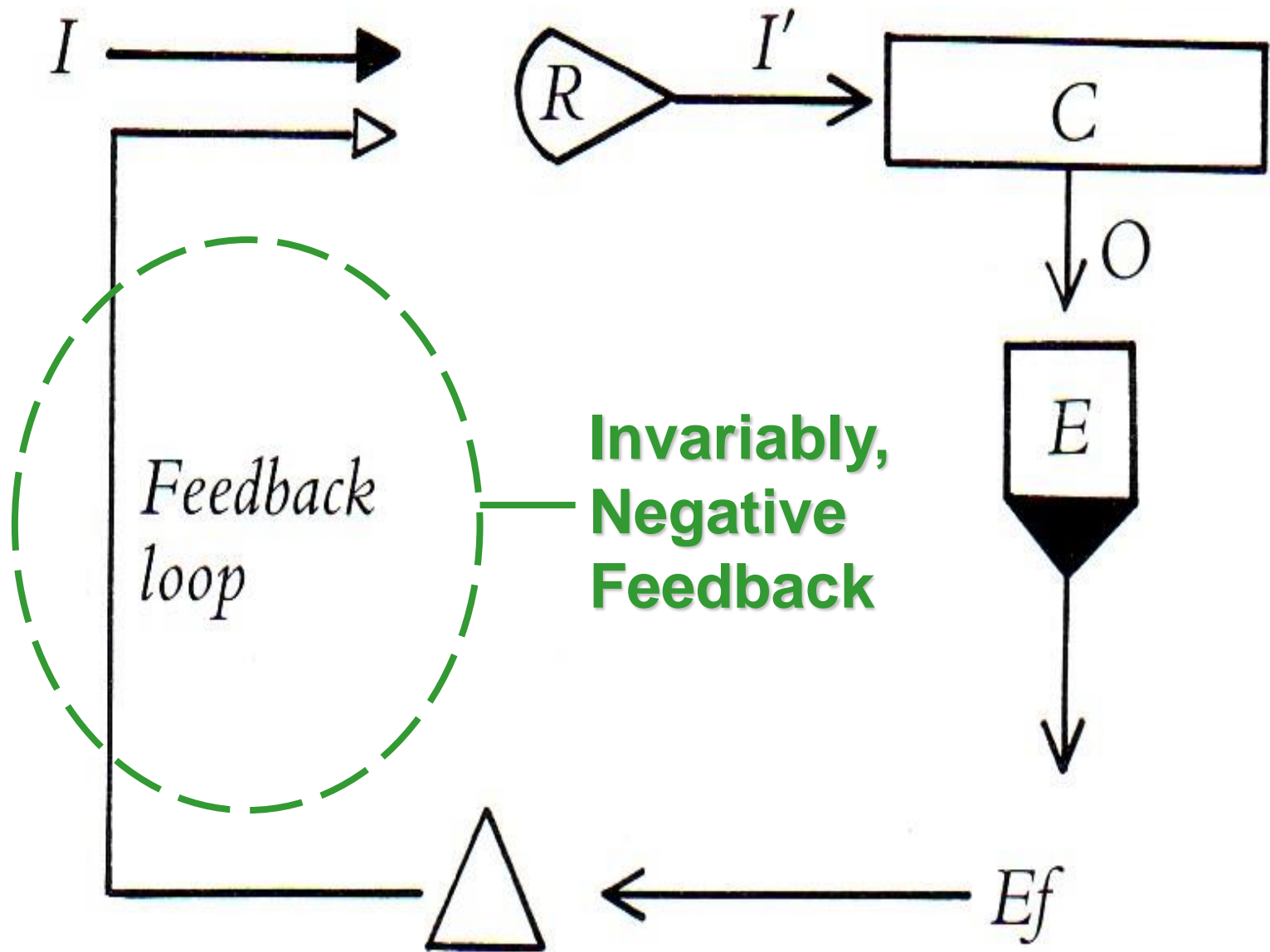
- A. Sympathetic vs. parasympathetic fig 61-1,61-3
- B. Neurotransmitters, receptors, actions tab 61-2, 61-1
- C. Nicotine & adrenal hormonal disruption

Methamphetamine, the “mother of all highs”!



<https://www.pbs.org/wgbh/pages/frontline/meth/body/>

<https://www.pbs.org/wgbh/pages/frontline/meth/body/methbrainflash.html>



NB: Though most often **negative** feedback, there are exceptions:

Selected +FB e.g.:

LH Surge → Ovulation

Oxytocin → Uterine Contraction

Blood Clotting Cascade

cAMP Cascade

Na⁺ influx during AP

Nonpathological! Temporarily amplifies,
but ultimately turned off by - FB!



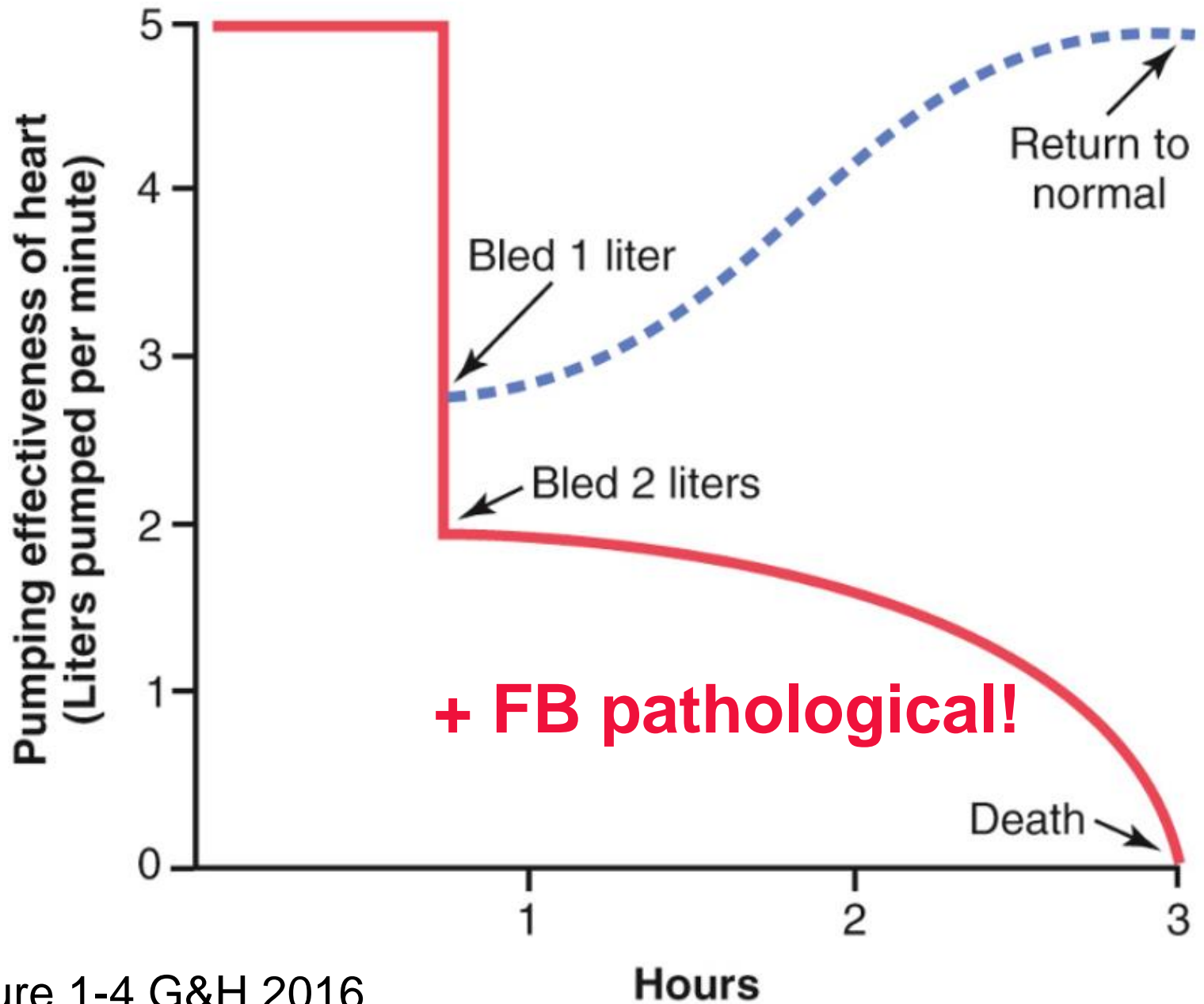
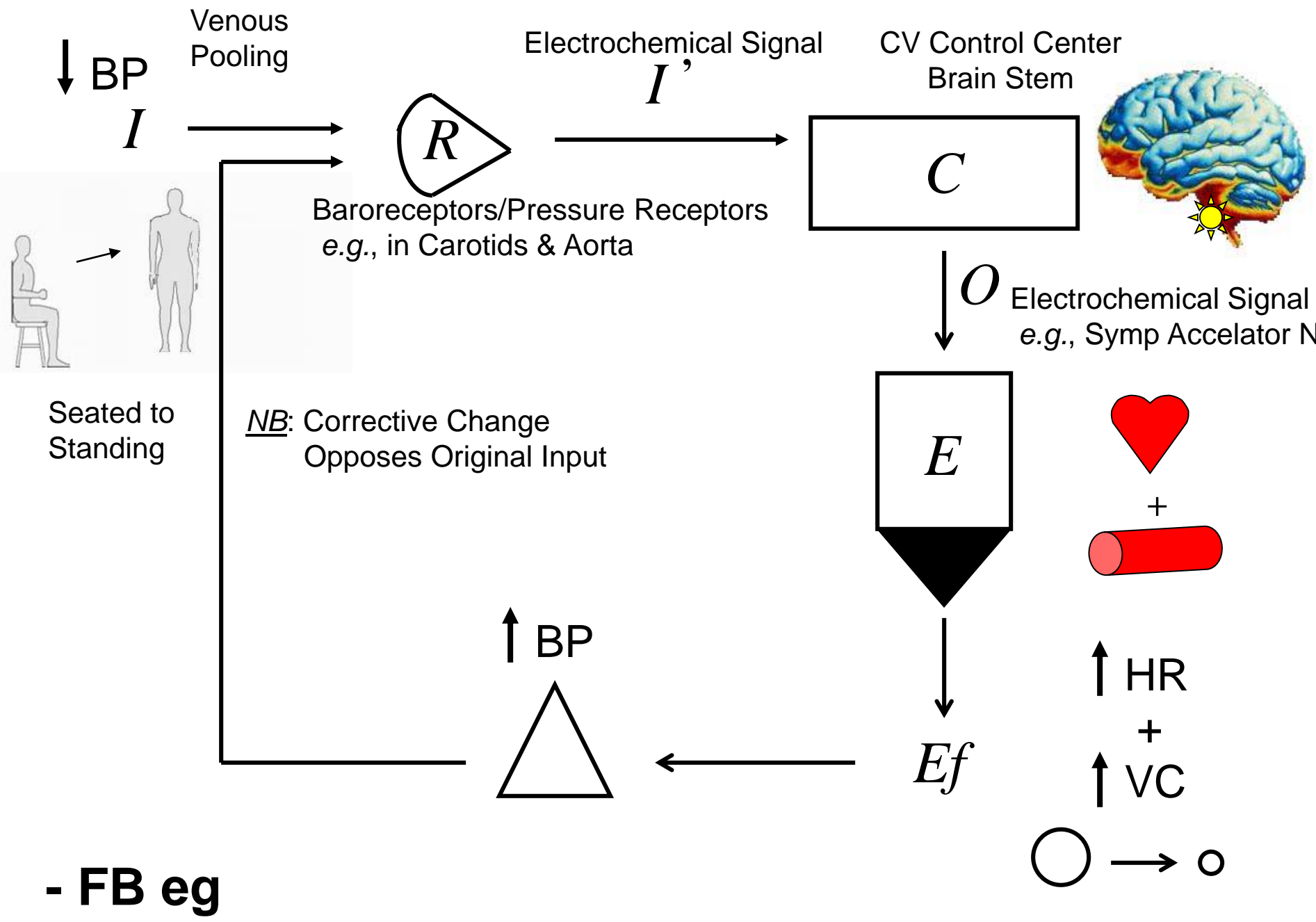


Figure 1-4 G&H 2016



How Effective is a System at Maintaining Relative Constancy? Feedback Gain?

$$\text{Gain} = \frac{\text{Correction}}{\text{Error}}$$

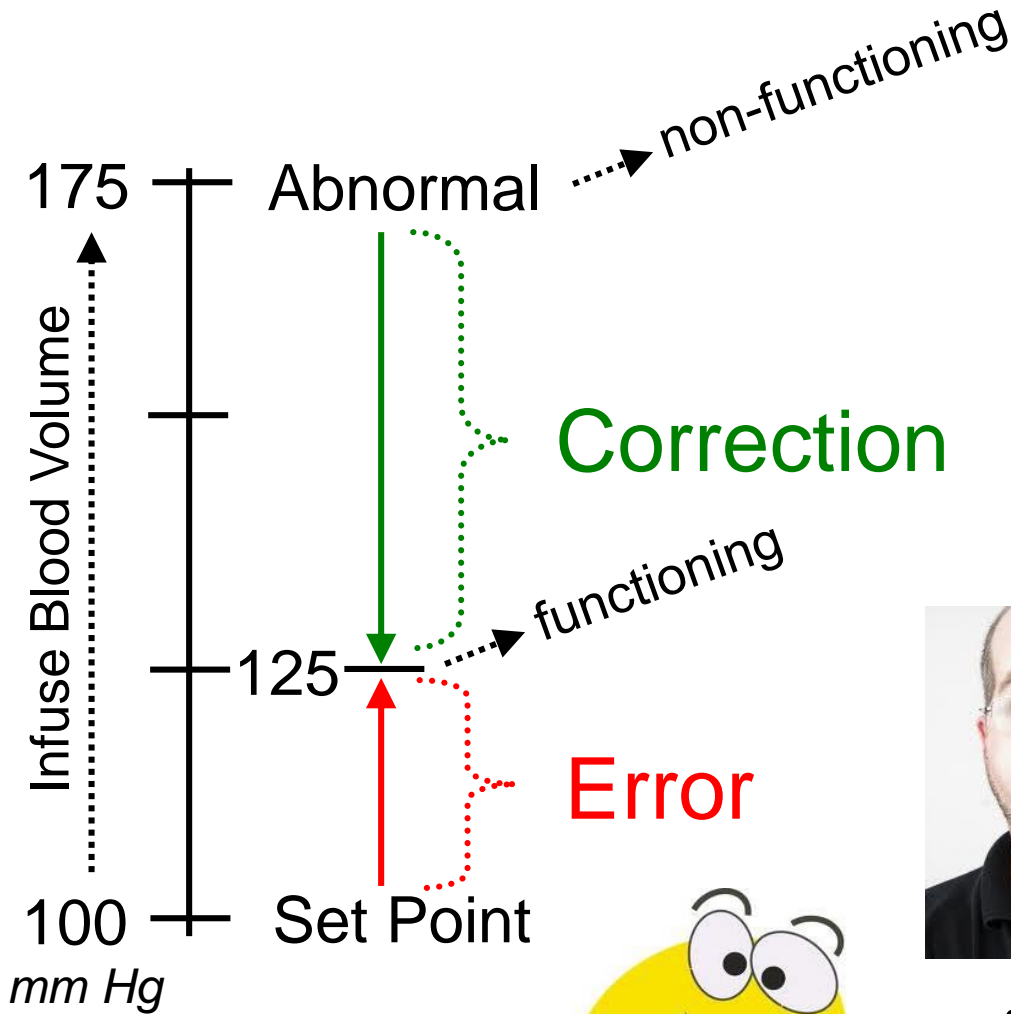
e.g., Transfuse large volume of blood into person with non-functioning Baroreceptor system

BP: 100 mm Hg → 175 mm Hg

...into person with functioning system

BP: 100 mm Hg → 125 mm Hg

Gain for Human Baroreceptor System?

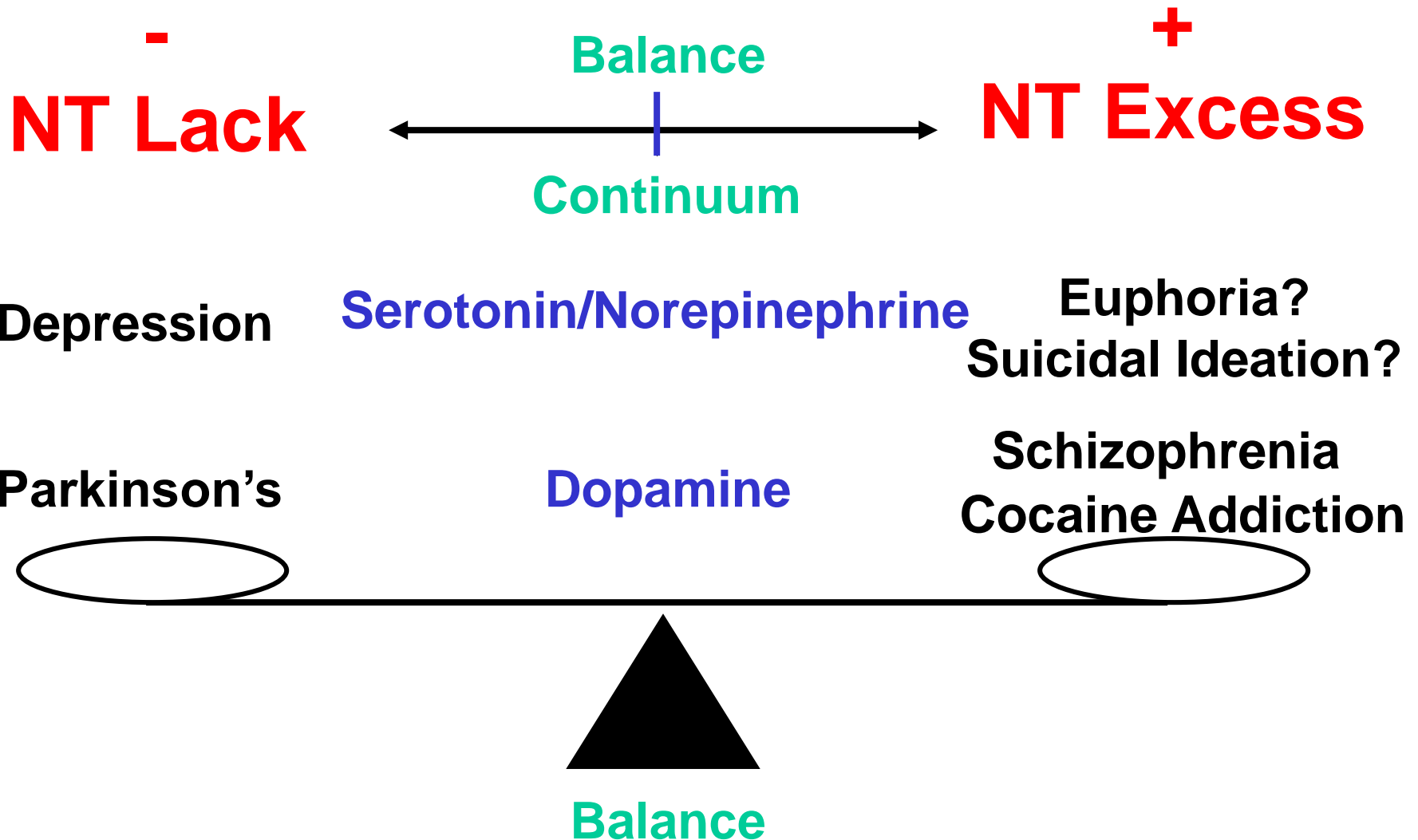


$$\text{Gain} = \frac{-50 \text{ mm Hg}}{+25 \text{ mm Hg}} = -2$$

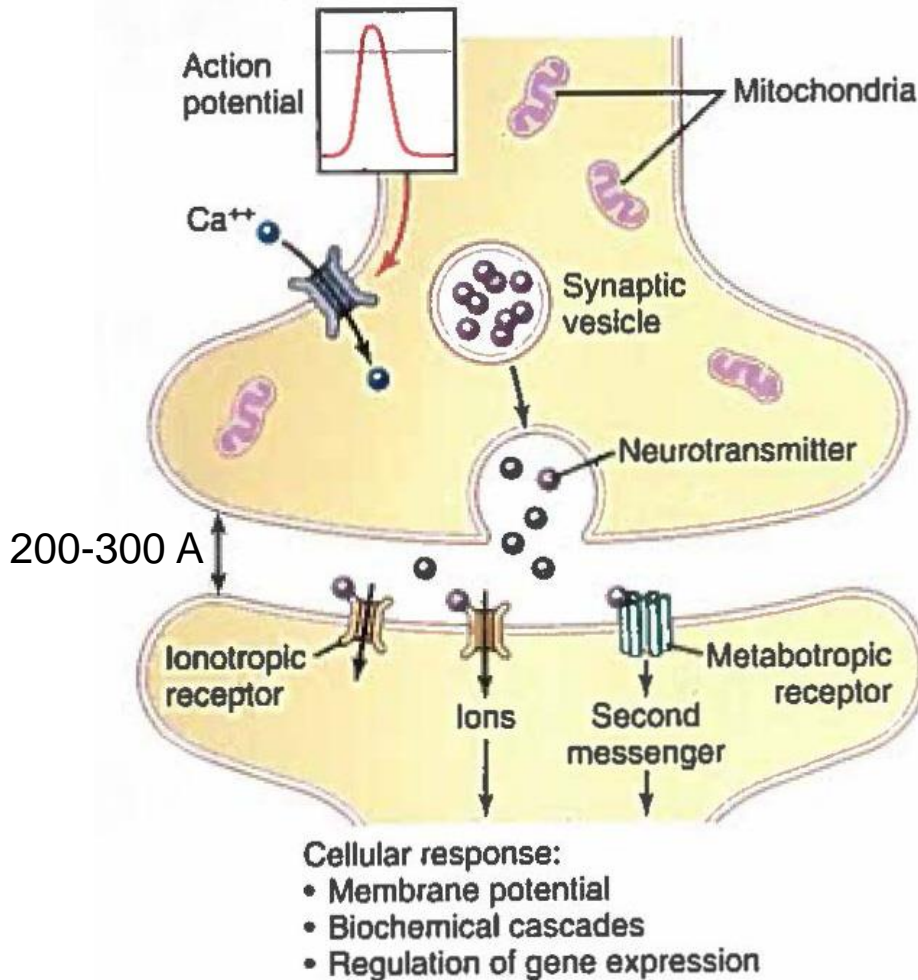


cf. Gain for Human Body Temperature = -33

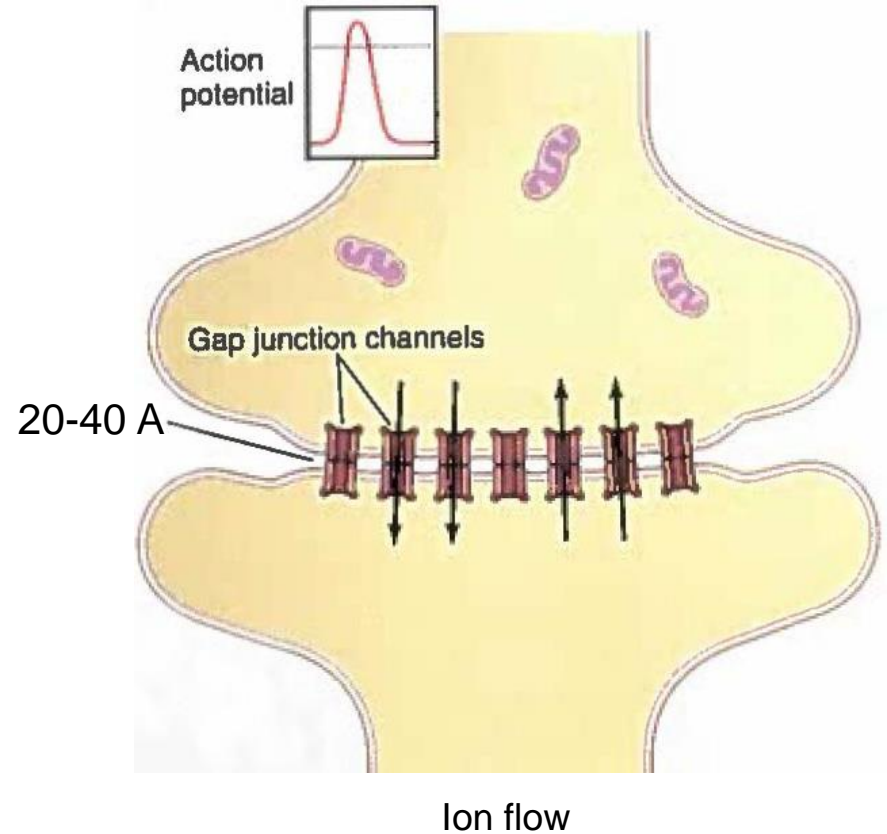
Neurotransmitter (NT) Balance: Diseases/Addictions/Moods?



Chemical vs. Electrical Synapse



1-way

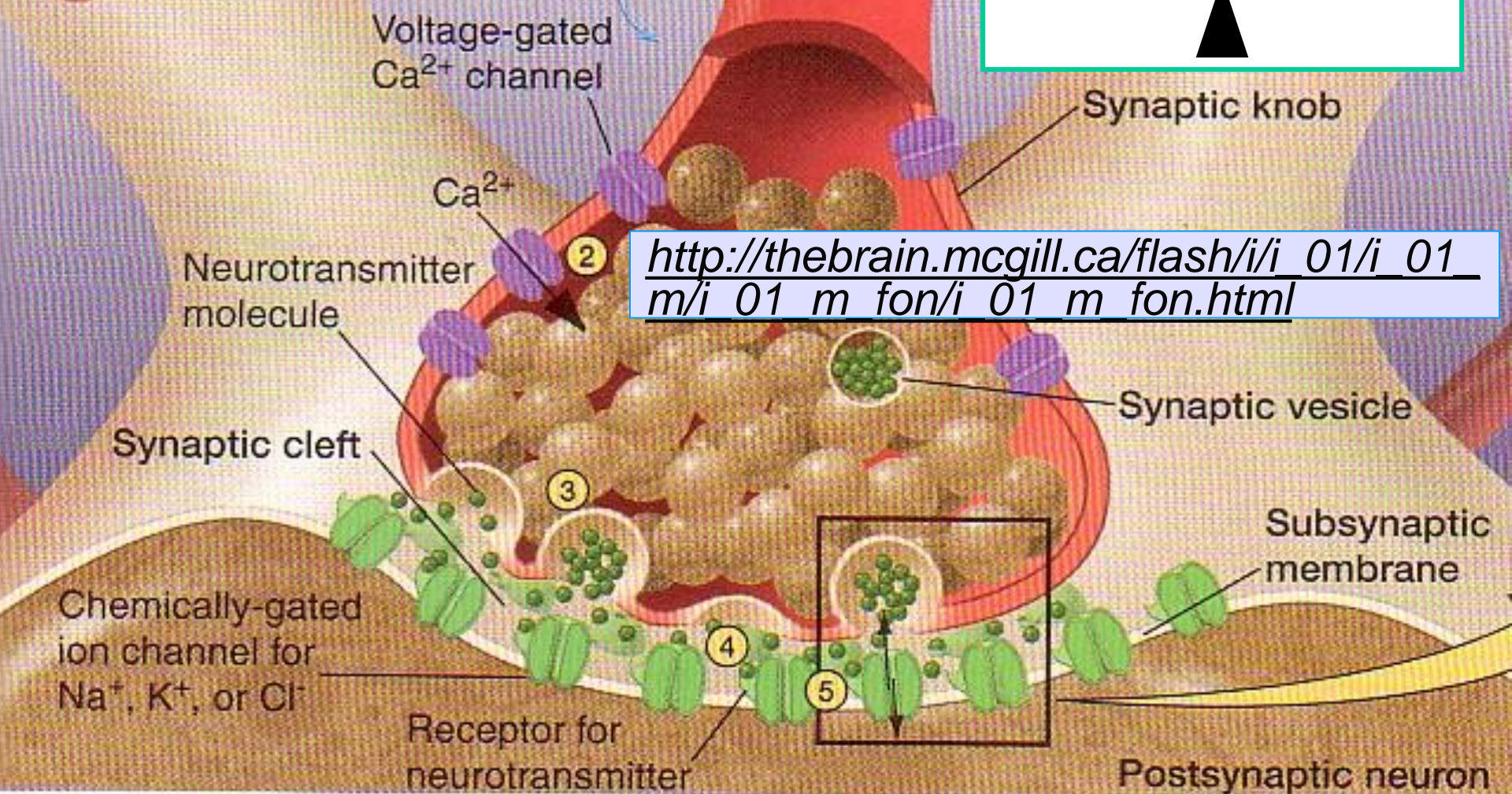
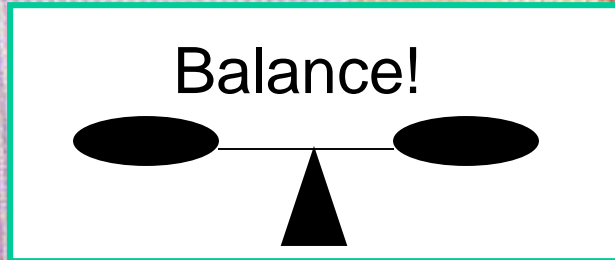


2-way

Chemical Synapse Animations

http://highered.mheducation.com/sites/0072495855/student_view0/chapter14/animation_transmission_across_a_synapse.html

Presynaptic axon terminal




http://thebrain.mcgill.ca/flash/i/i_01/i_01_m/i_01_m_fon/i_01_m_fon.html

Table 45-1 Small-Molecule, Rapidly Acting Transmitters

Class I

Acetylcholine


Class II: The Amines


 Norepinephrine

Epinephrine



Prominent in reward pathways
& chemistry of addiction.

 Dopamine

 Serotonin

Histamine

Class III: Amino Acids

Gamma-aminobutyric acid (GABA)

Glycine

Glutamate

Aspartate

Class IV

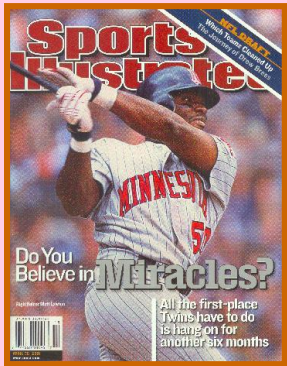
Nitric oxide (NO)



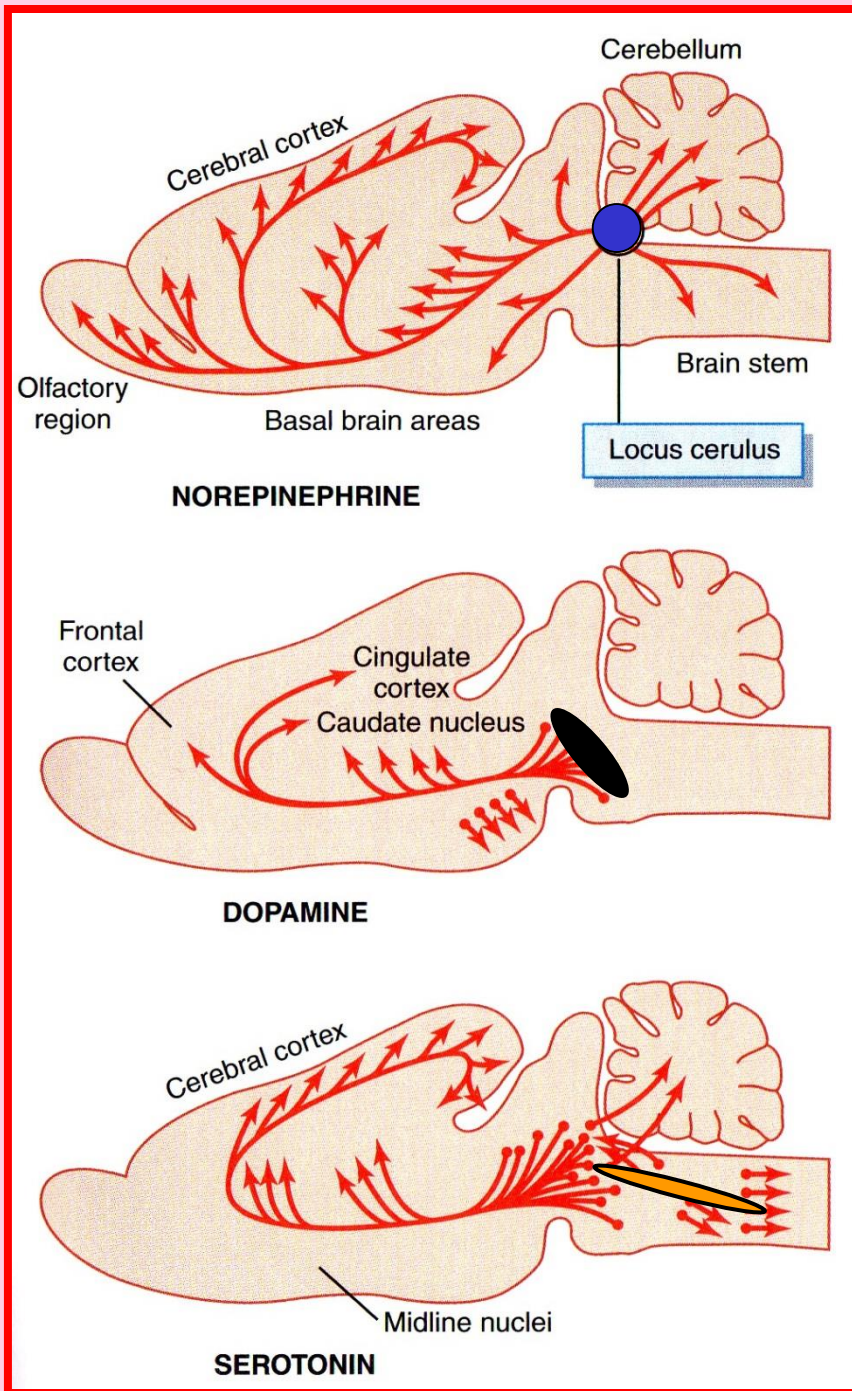
Norepinephrine
= NE



Dopamine = D?



Serotonin = SI



Locus ceruleus =
“Blue/azur spot”

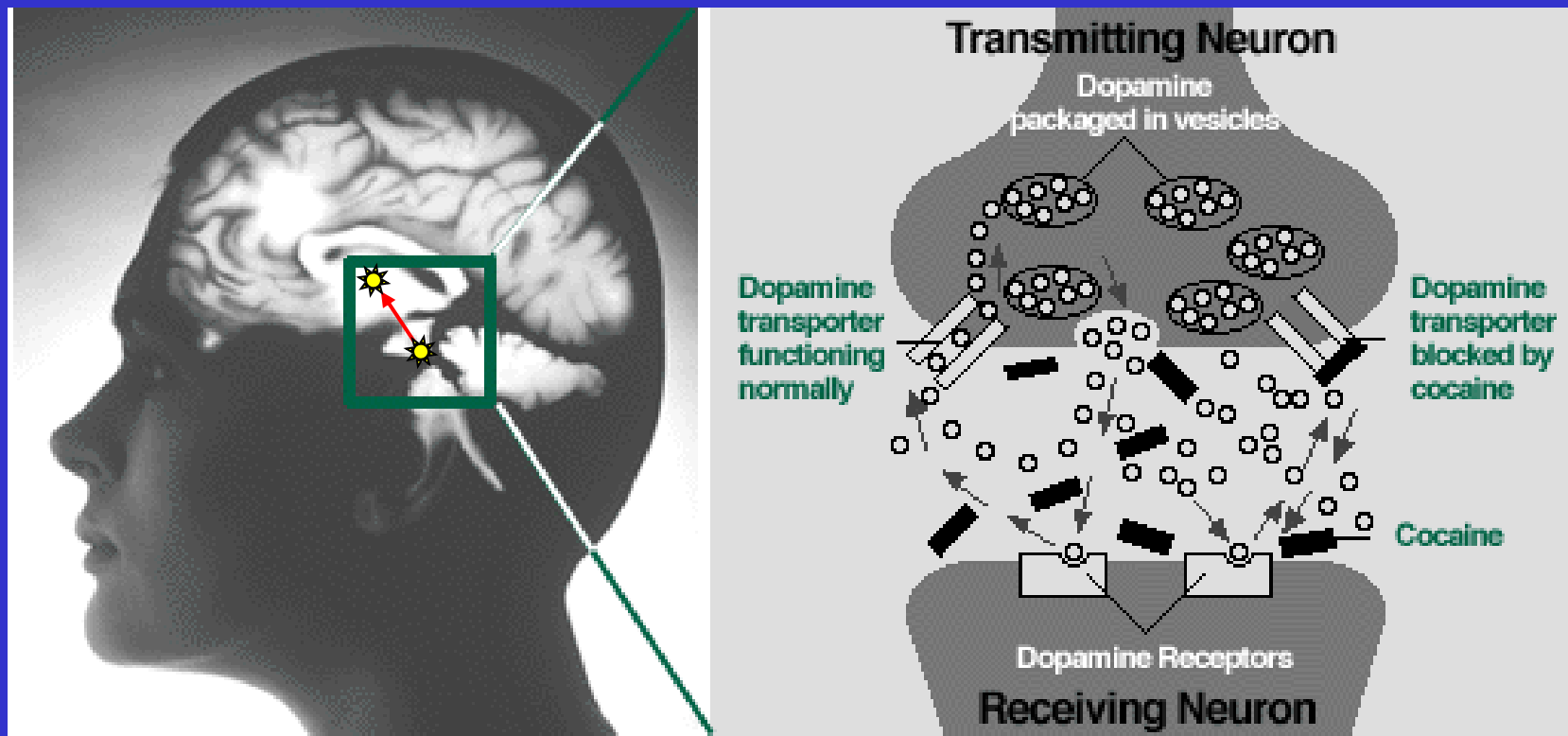
Substantia nigra =
“Black substance”

Raphe nuclei =
“Nut seam/line”

G&H 2011 p 713;
G&H 2016 p 753

Cocaine prevents re-uptake of Dopamine (1st discovery),
Norepinephrine (2nd...) & Serotonin (3rd...) & alters the
plasticity of all 3 pathways!!!

<http://www.ncbi.nlm.nih.gov/pubmed/18624911>

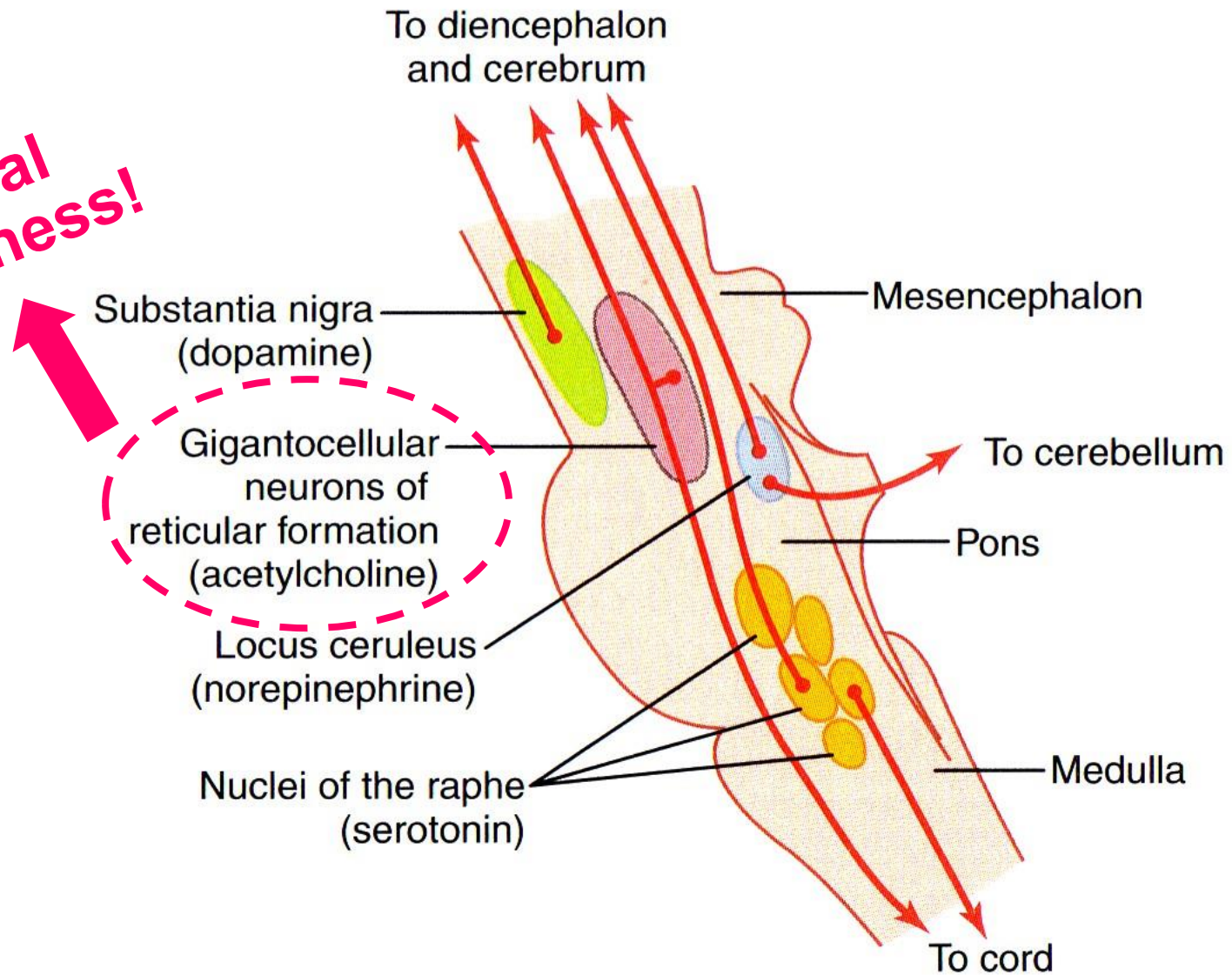


Nerve cells eg: Ventral Tegmentum (Substantia Nigra)
to Nucleus Accumbens (Limbic System)

<http://learn.genetics.utah.edu/content/addiction/>

4th Pathway Releases Acetylcholine!

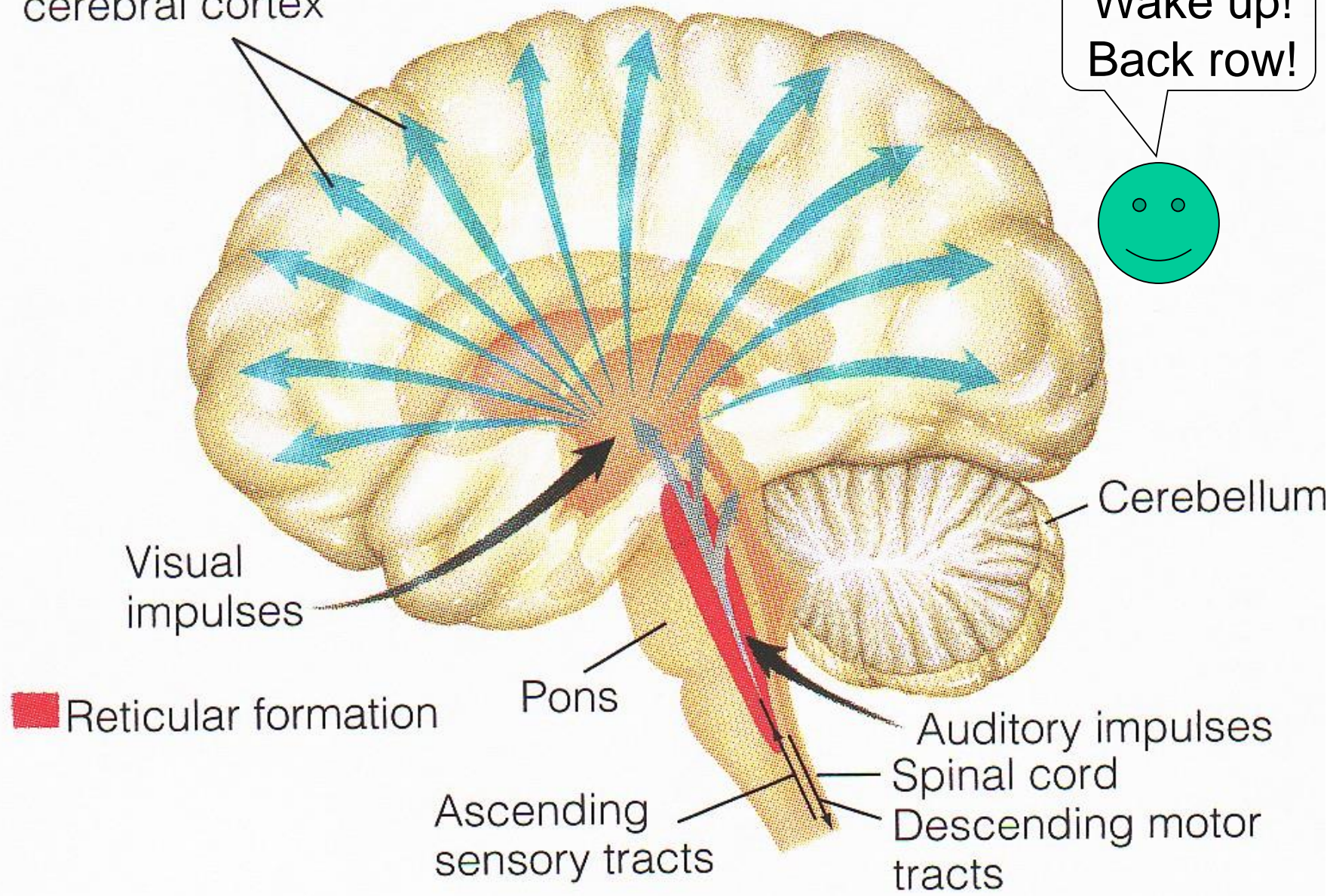
Cortical Alertness!

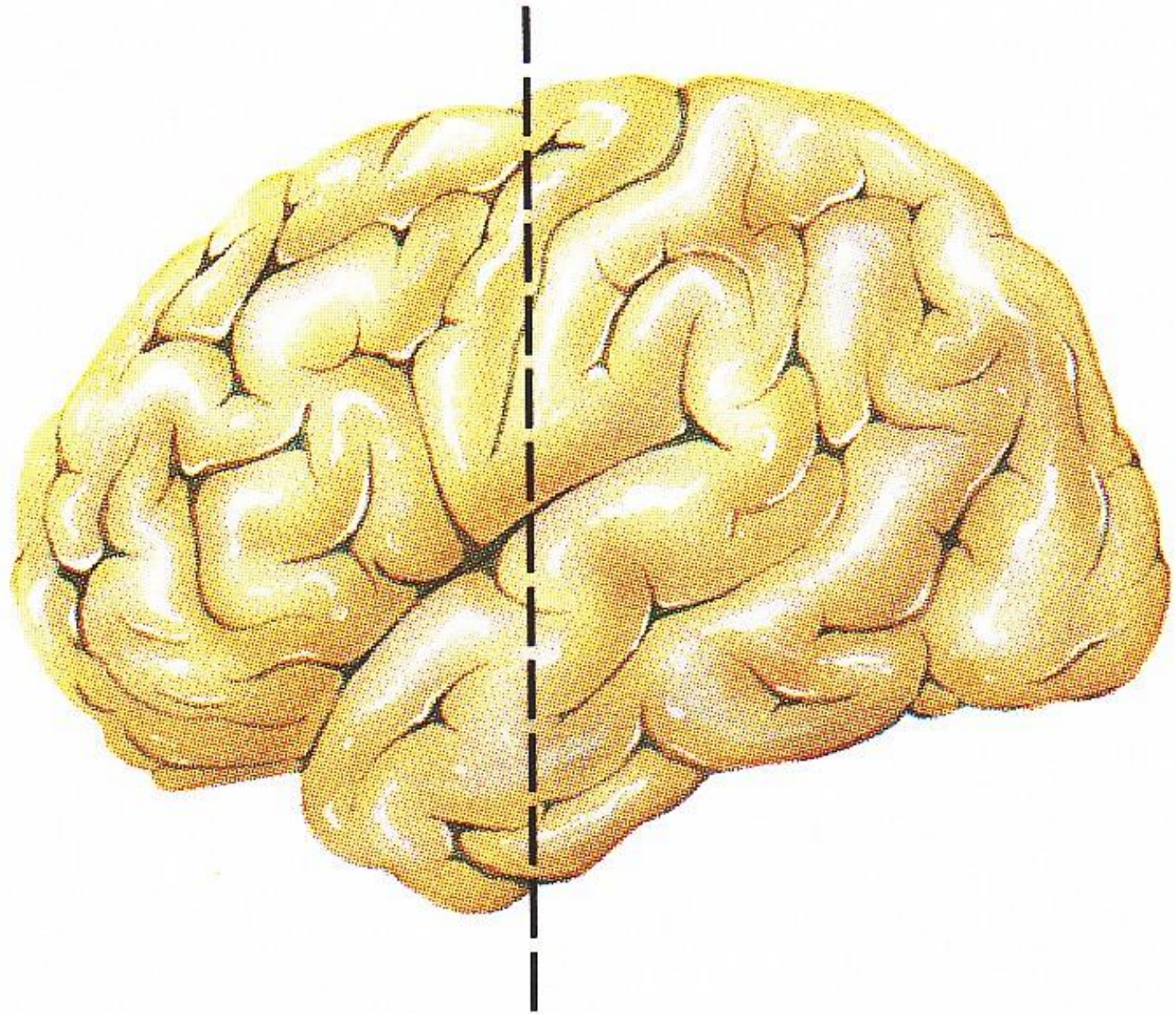


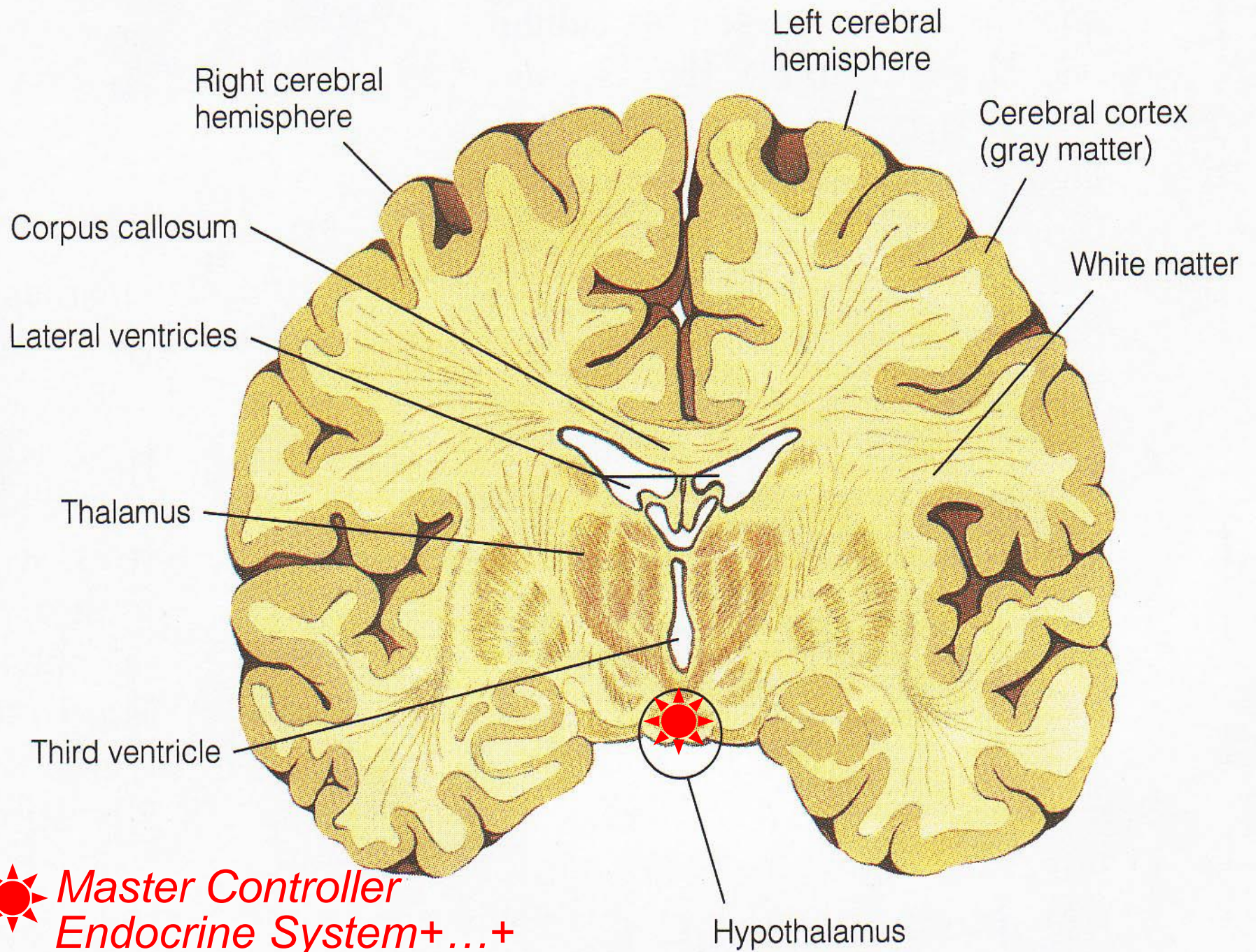
Reticular Activating System (RAS)

Radiations to **Overall Cortical Alertness!**
cerebral cortex

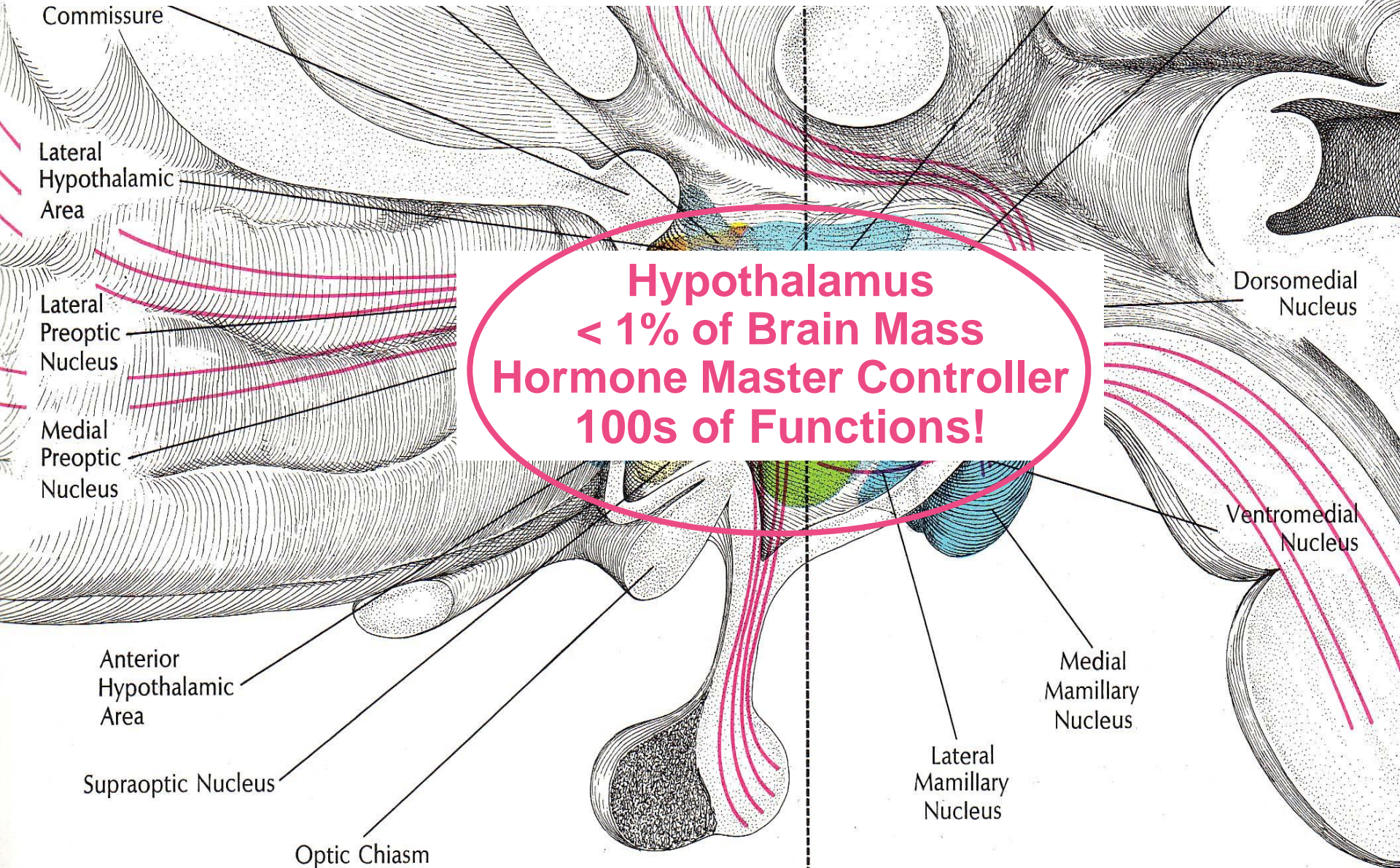
Wake up!
Back row!







Good Things Come in Small Packages!




POSTERIOR

ANTERIOR

Dorsomedial nucleus
(GI stimulation)


Posterior hypothalamus
(Increased blood pressure)
(Pupillary dilation)
(Shivering)

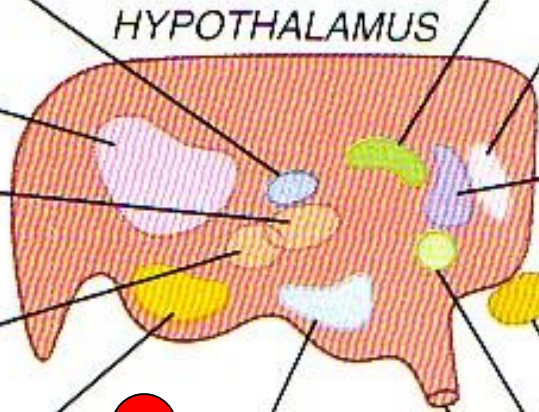
Perifornical nucleus
(Hunger)
(Increased blood pressure)
(Rage)

 Ventromedial nucleus
(Satiety)
(Neuroendocrine control)

Mamillary body
(Feeding reflexes)

Arcuate nucleus and periventricular zone
(Neuroendocrine control)

 Lateral hypothalamic area (not shown)
(Thirst and hunger)



midbrain

Paraventricular nucleus
(Oxytocin release)
(Water conservation)

Medial preoptic area
(Bladder contraction)
(Decreased heart rate)
(Decreased blood pressure)

Posterior preoptic and
anterior hypothalamic areas
(Body temperature regulation)
(Panting)
(Sweating)
(Thyrotropin inhibition)

Optic chiasm (Optic nerve)

Supraoptic nucleus
(Vasopressin release)

Infundibulum

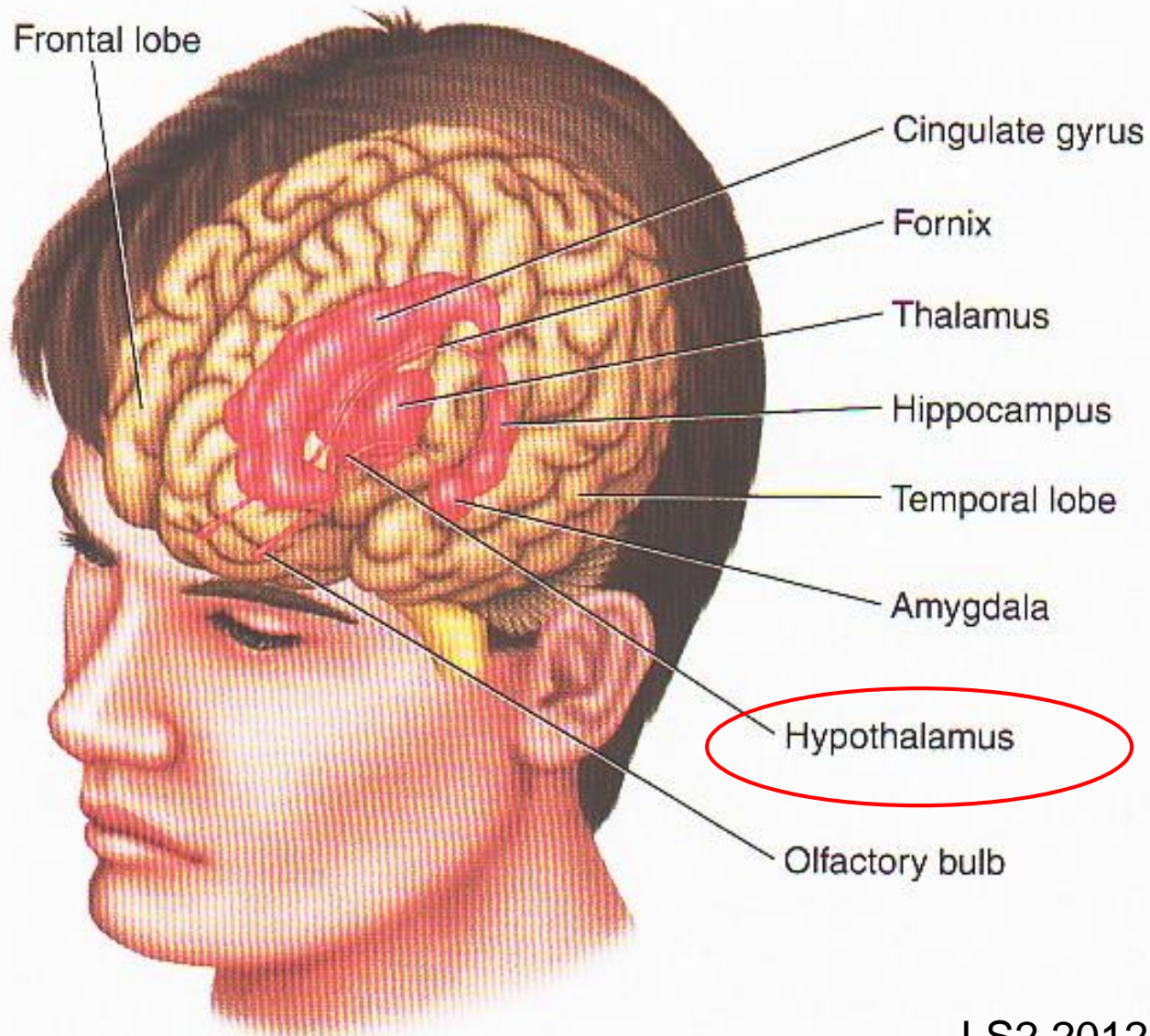
 = Reward

 = Punishment

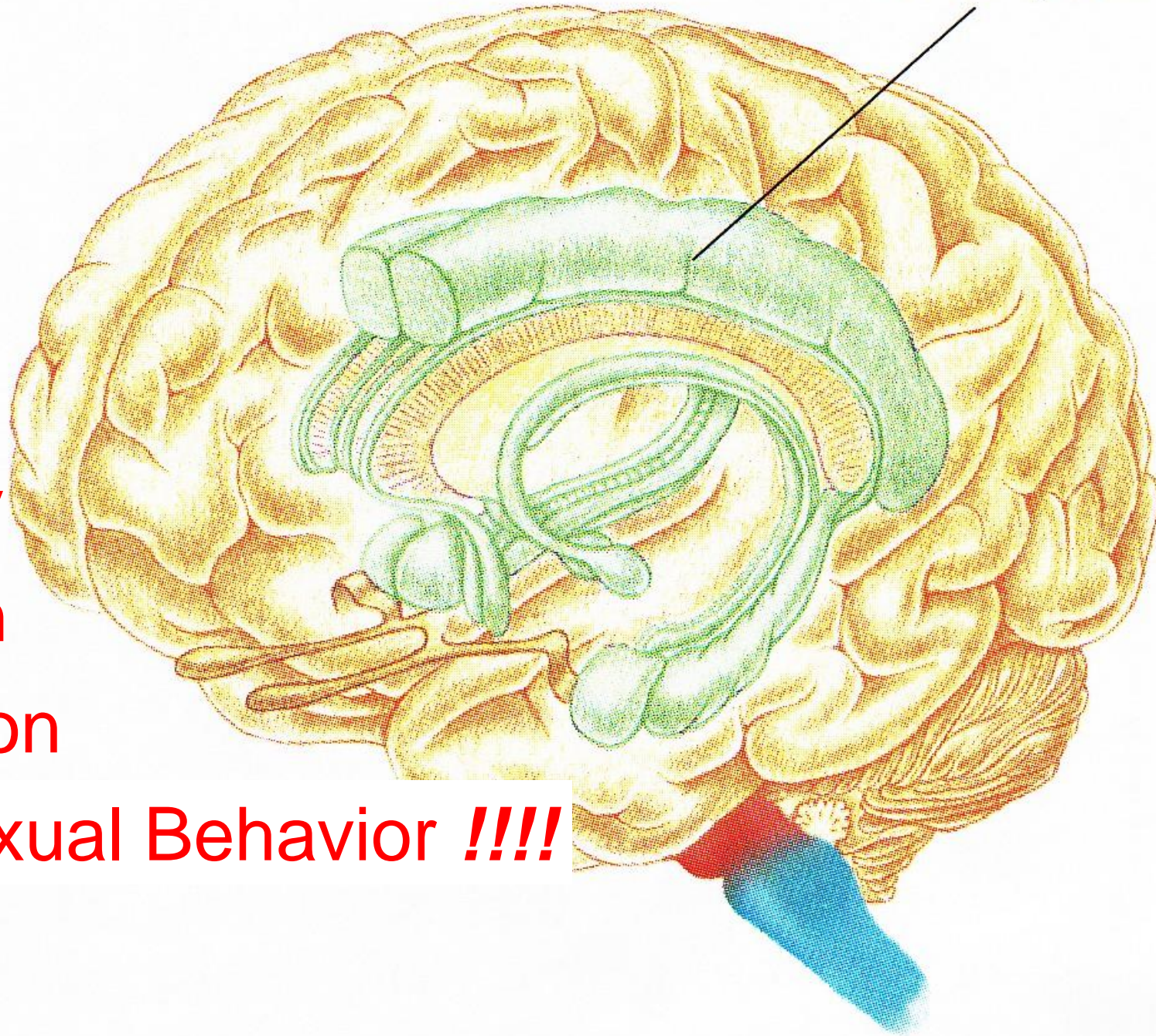
● **FIGURE 5-18**

Limbic system

This partially transparent view of the brain reveals the structures composing the limbic system.



Limbic system

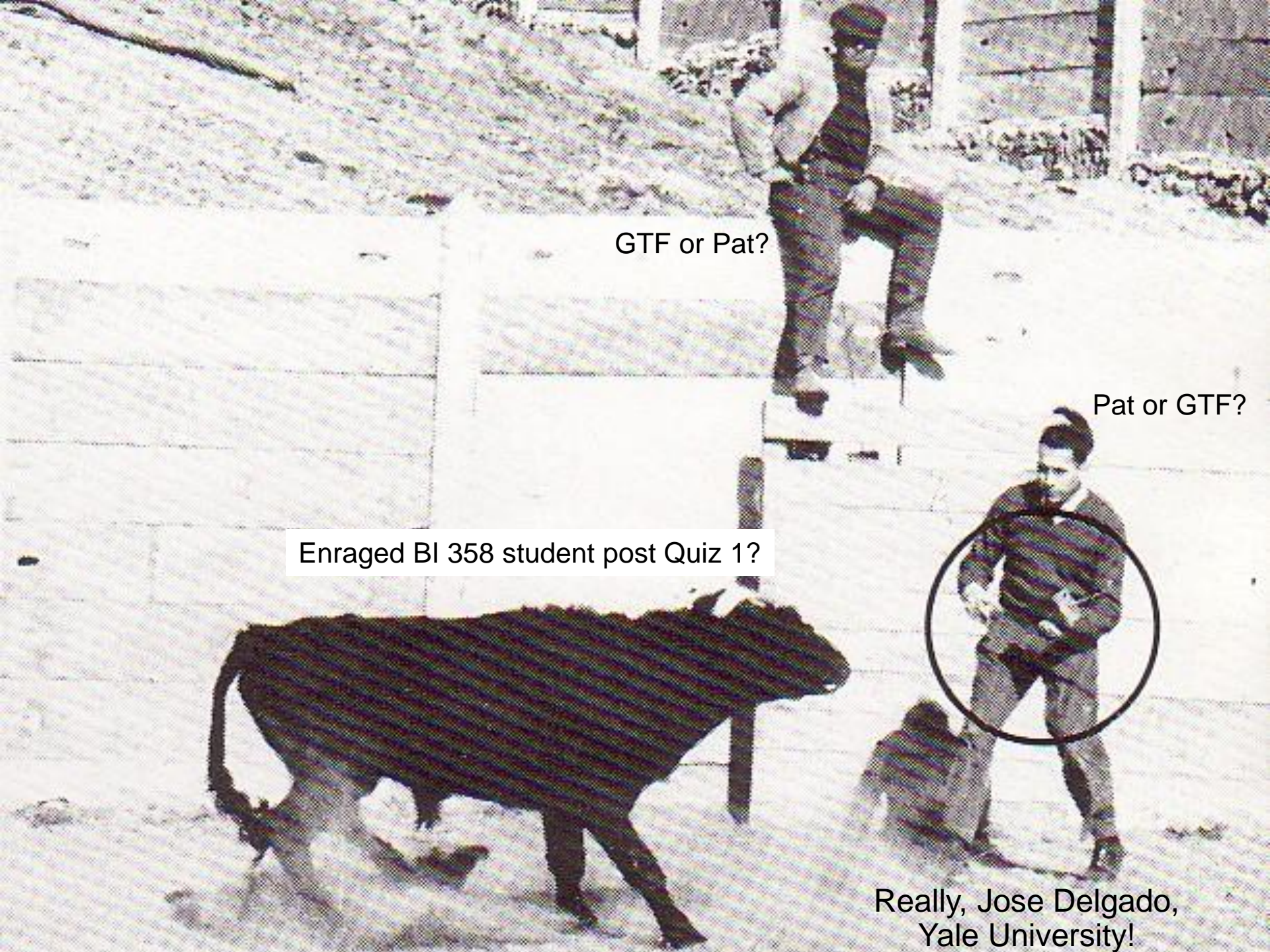


Memory

Emotion

Motivation

Sociosexual Behavior !!!!

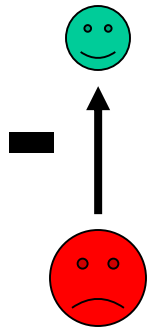


GTF or Pat?

Pat or GTF?

Enraged BI 358 student post Quiz 1?

Really, Jose Delgado,
Yale University!



Reward Centers = Hypothalamus, lateral & ventromedial n.

Punishment Centers = Mesencephalon, central gray area, Hypothalamus & Thalamus, periventricular zones

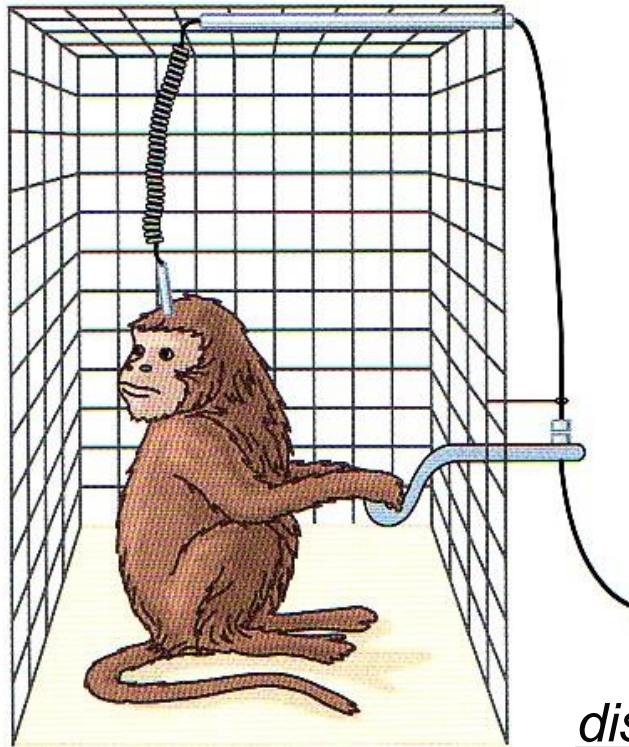


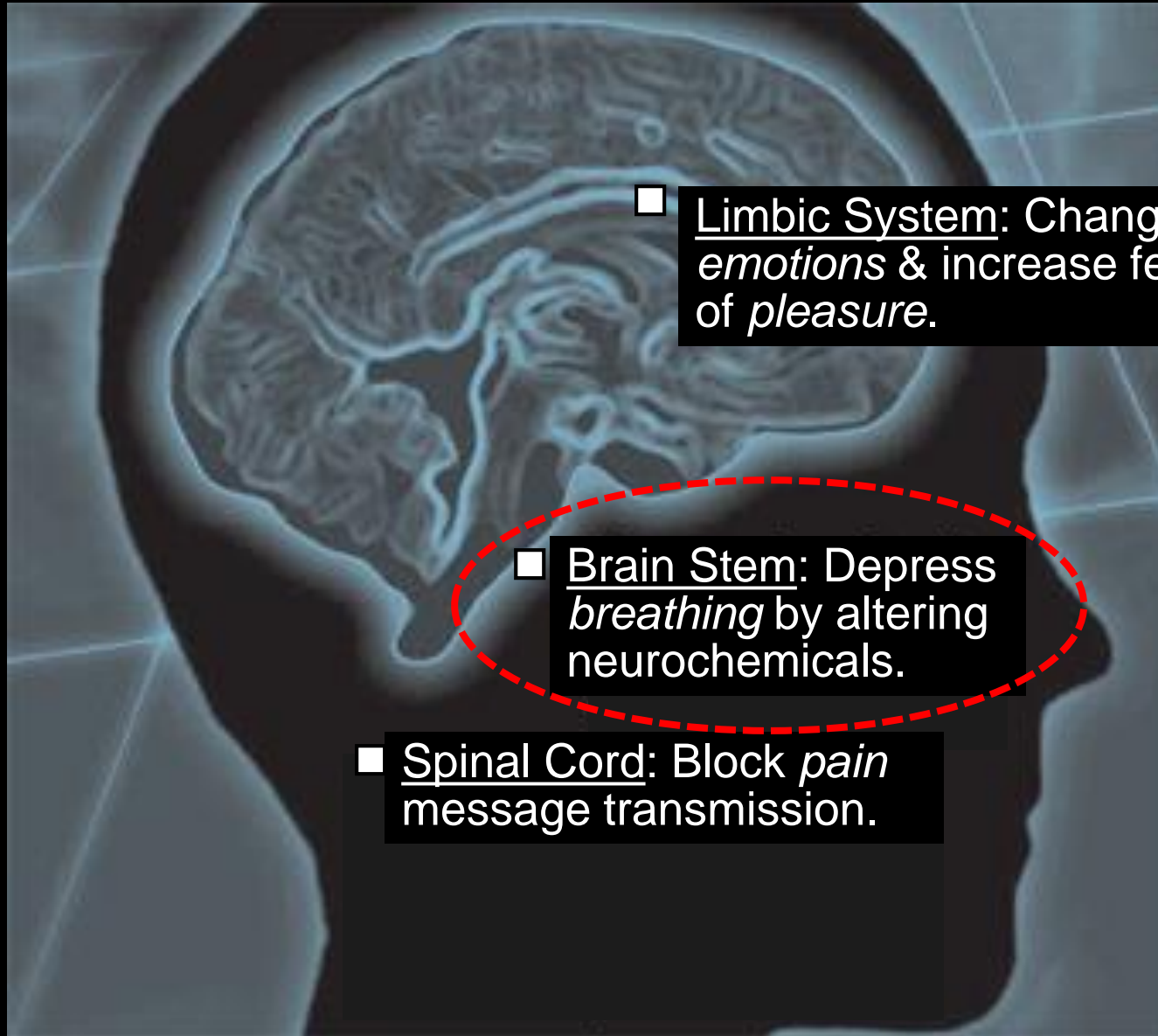
Figure 58-8

Technique for localizing reward and punishment centers in the brain of a monkey.

Animal will self-stimulate $\geq 5000x/hr$ if electrodes planted in reward center!

<http://www.brainfacts.org/diseases-disorders/addiction/articles/2010/reward-and-punishment/>

Opiates Brain Action + Overdose Story

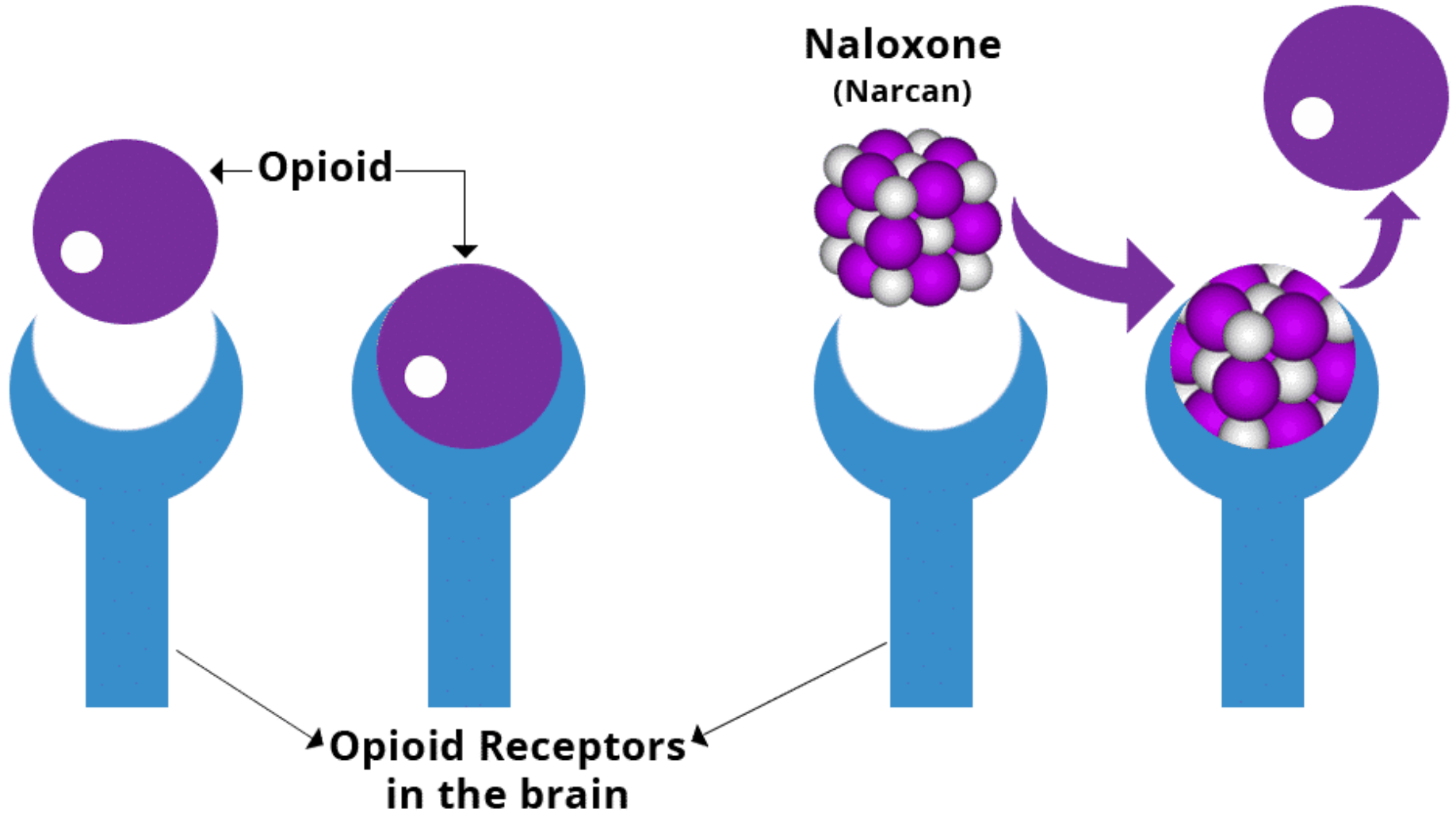


■ Limbic System: Change *emotions* & increase feelings of *pleasure*.

■ Brain Stem: Depress *breathing* by altering neurochemicals.

■ Spinal Cord: Block *pain* message transmission.

Naloxone/Narcan has much higher affinity for opioid receptors & thus restores breathing within minutes!



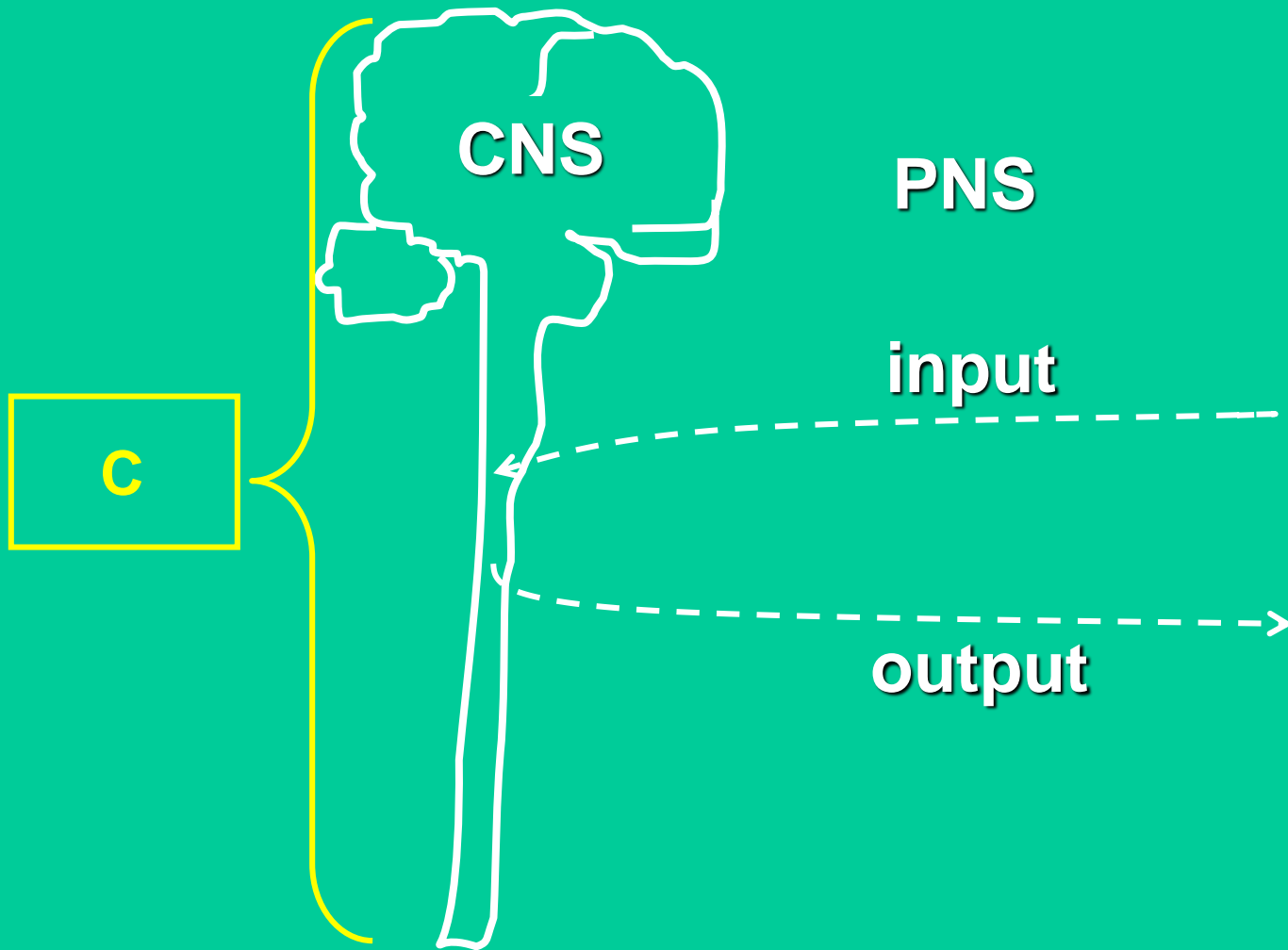
SOURCE: <https://www.detoxes.net/narcan-work-secret-life-miracle-drug/>

Active Learning Group Work



**Additional
Background
Neuronal
Physiology**

Nervous System



Systems Level

~ 90% of Cells w/in CNS are Glial Cells/Neuroglia!

1. Neuron spatial relationships.
2. Scaffolding during fetal development.
3. Induce capillary changes to establish Blood-Brain Barrier.
4. Transfer nutrients from blood to neurons.
5. Repair brain injuries & form neural scars.
6. Uptake & degrade neurotransmitters.
7. Soak up excess K^+ to sustain normal neural excitability.
8. Communicate with neurons & each other electrochemically.

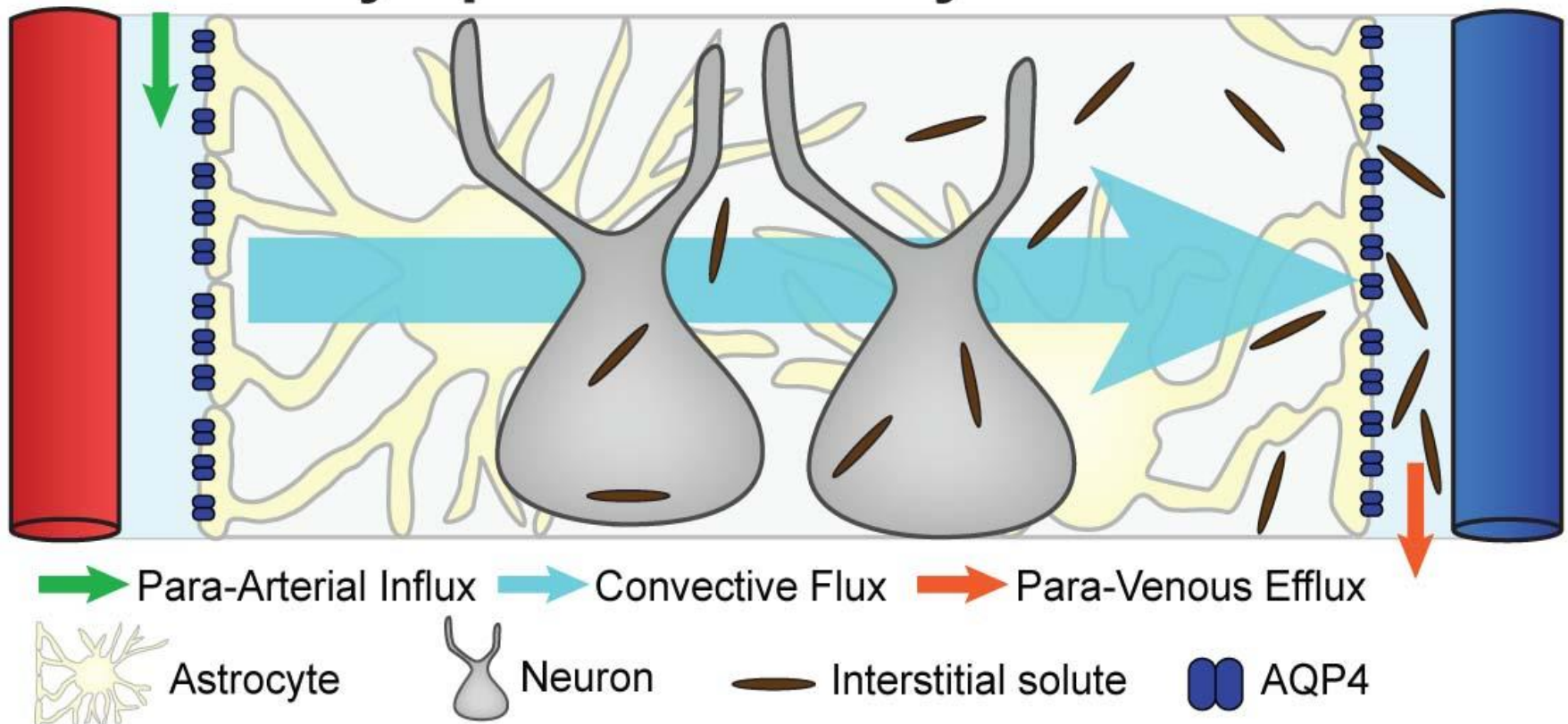
100 Billion Neurons →
900 Billion Glial Cells!

Astrocytes

A fluorescence micrograph showing a network of astrocytes. The cells are stained with red and green dyes, highlighting their complex, branching morphology. Several nuclei are stained blue. Two white arrows point from the word 'Astrocytes' to specific cells in the network.

What the Heck is the Glymphatic System? CNS Functional Waste Clearance Pathway!

Glymphatic Pathway Function

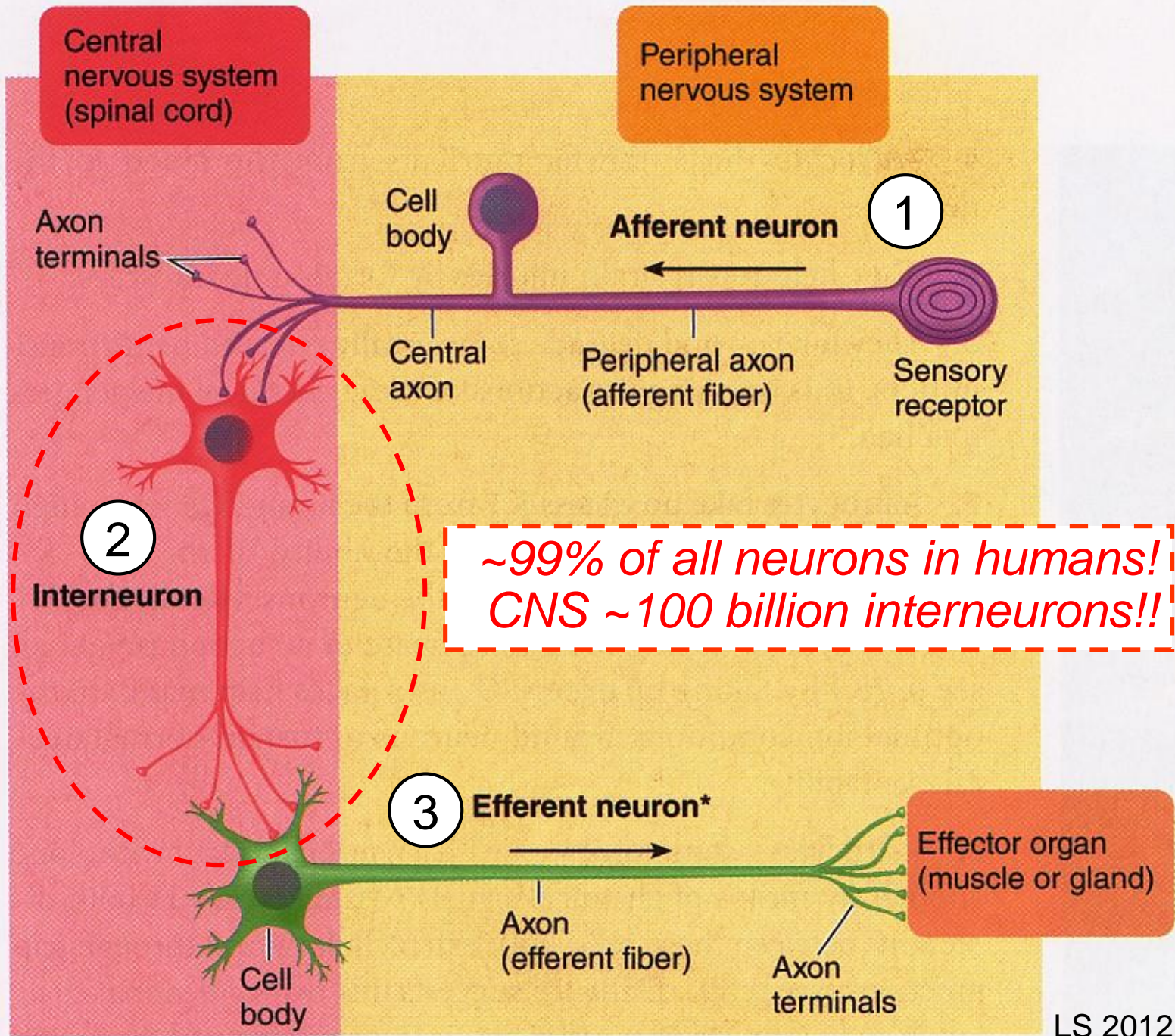


<http://www.sciencedaily.com/releases/2012/08/120815142042.htm>

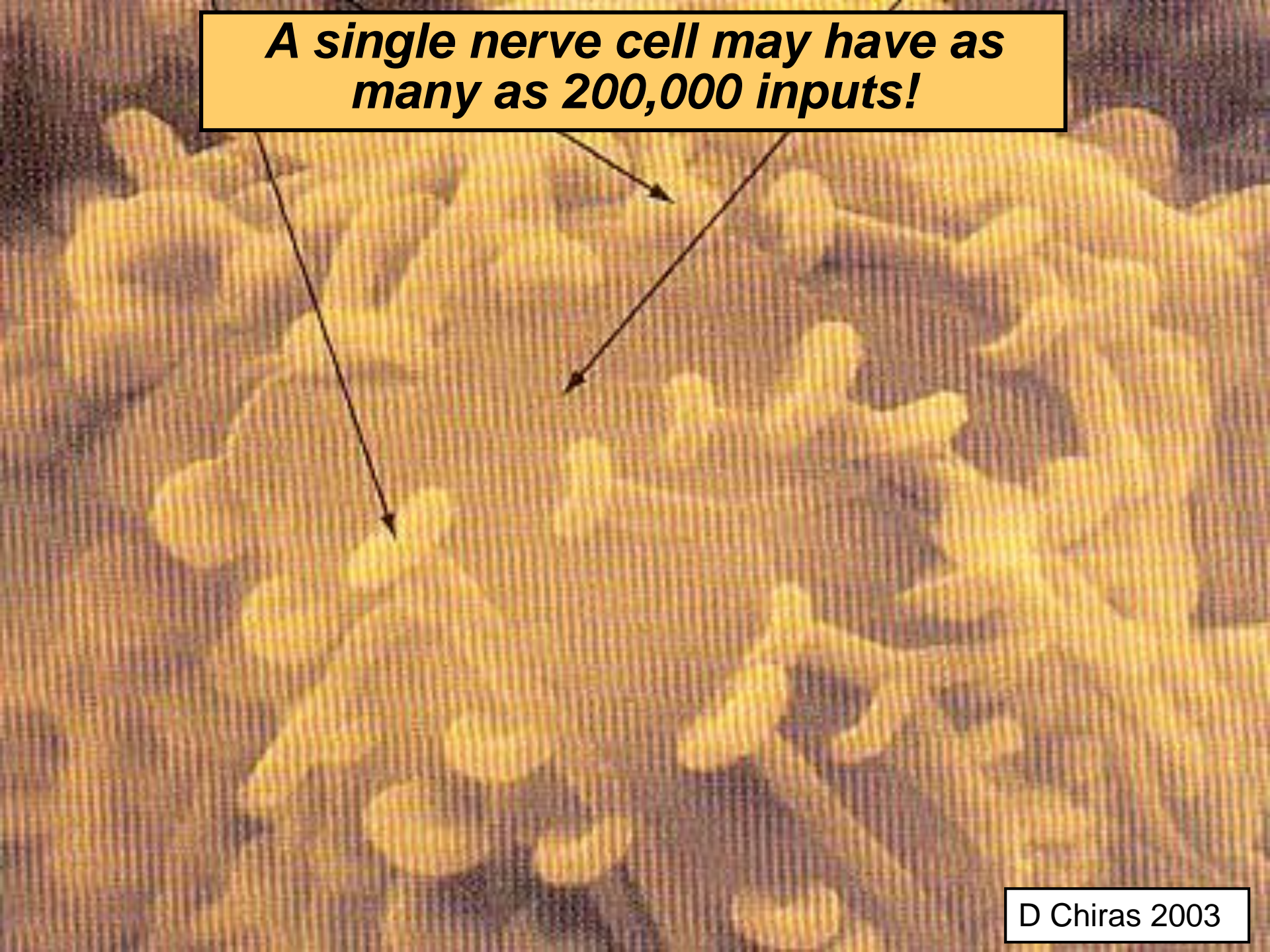
<https://www.urmc.rochester.edu/news/story/3584/scientists-discover-previously-unknown-cleansing-system-in-brain.aspx>

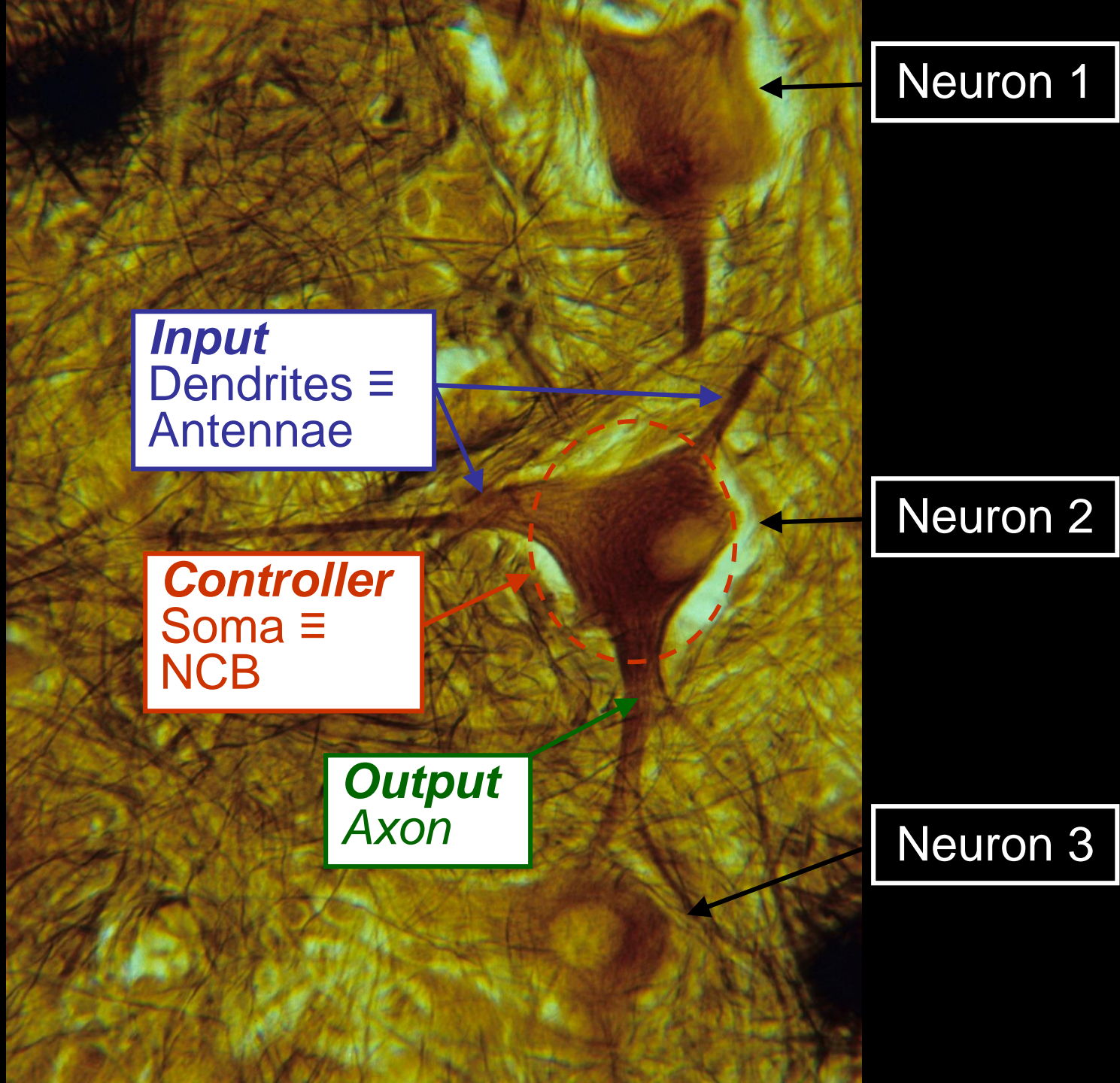
https://www.ted.com/talks/jeff_iliff_one_more_reason_to_get_a_good_night_s_sleep

Organ/Tissue Level



A single nerve cell may have as many as 200,000 inputs!





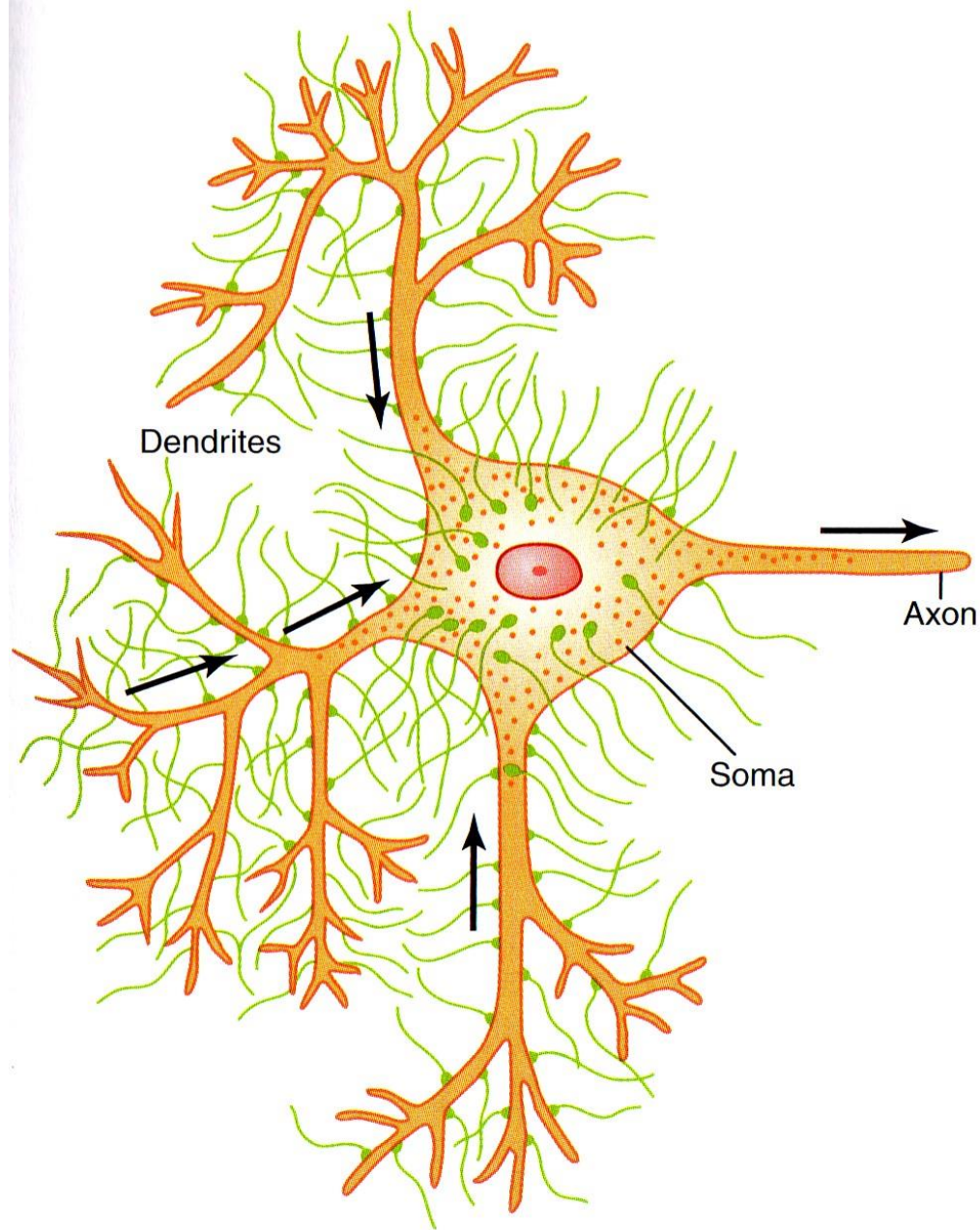


Figure 45-5 Typical anterior motor neuron, showing presynaptic terminals on the neuronal soma and dendrites. Note also the single axon.

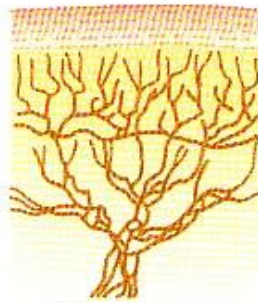
G&H 2011 p 547;
G&H 2016 p 582

***Nerve cell with multiple axons grown by adding
a mitogen/neurogen \equiv nerve growth factor!***



Courtesy Fengquan Zhou
UNC Chapel Hill

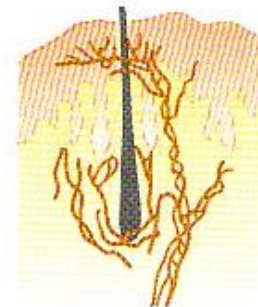
**Sensory
nerves
especially,
come in all
shapes &
sizes!**



Free nerve endings



Expanded tip receptor



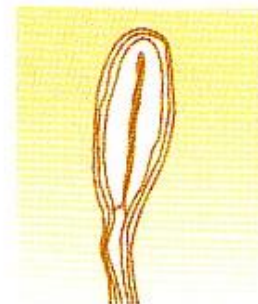
Tactile hair



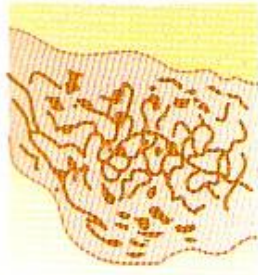
Pacinian corpuscle



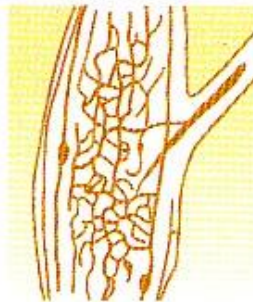
Meissner's corpuscle



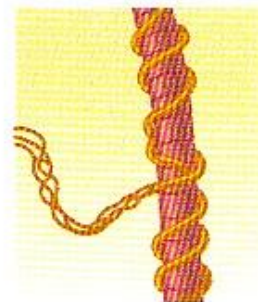
Krause's corpuscle



Ruffini's end-organ



Golgi tendon apparatus



Muscle spindle

Figure 46-1

Several types of somatic sensory nerve endings.

G&H 2011 p 547;
G&H 2016 p 596

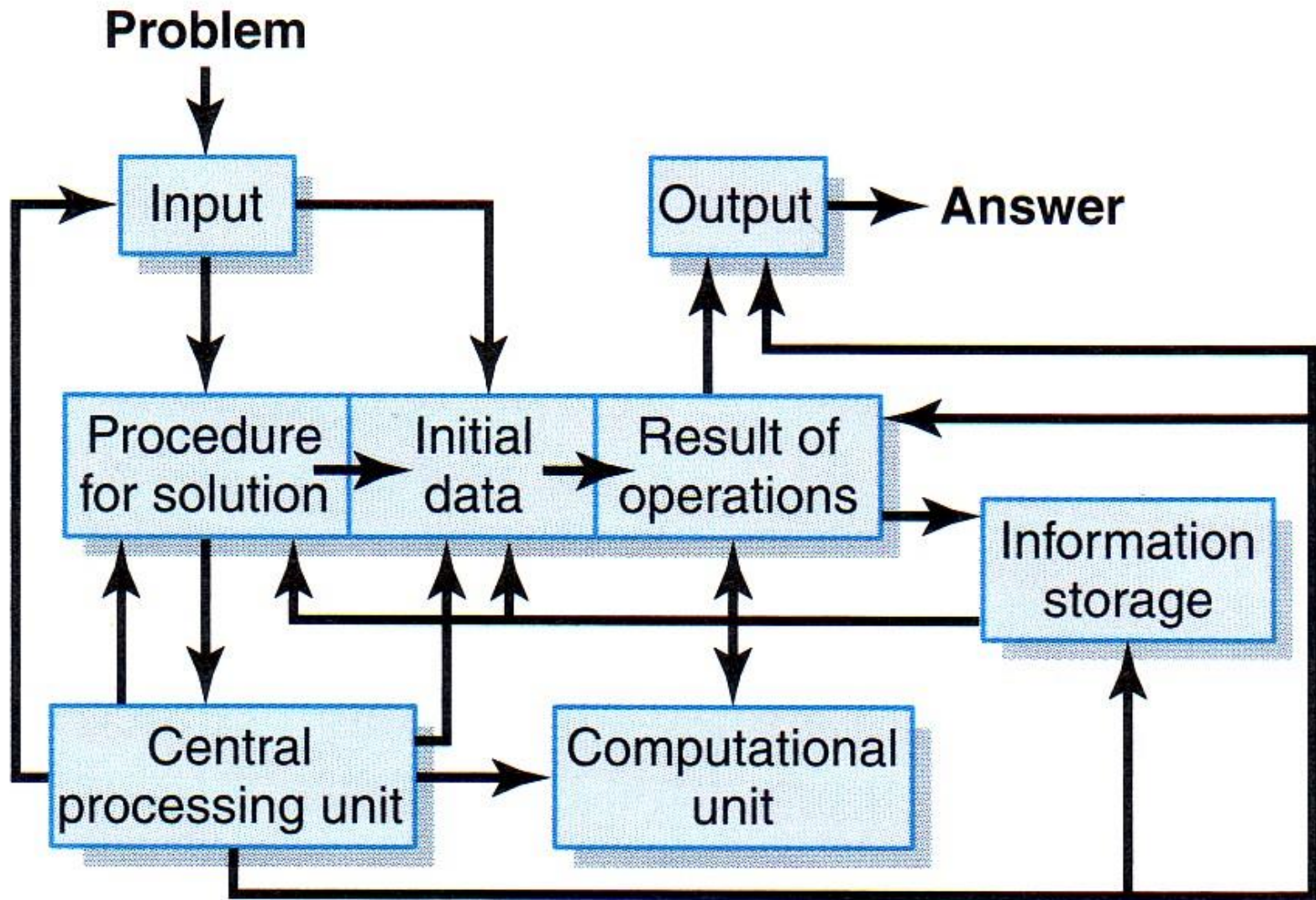
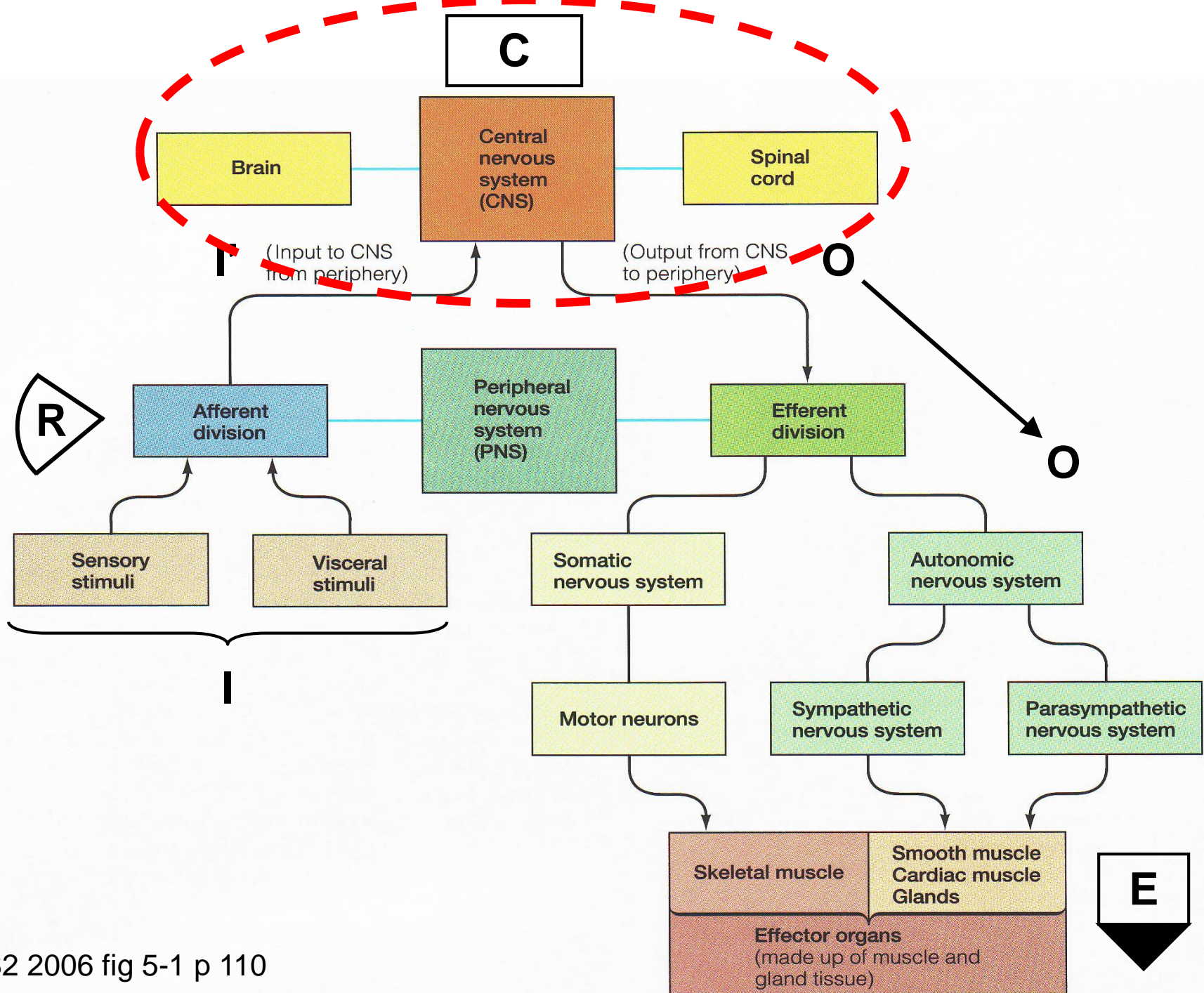


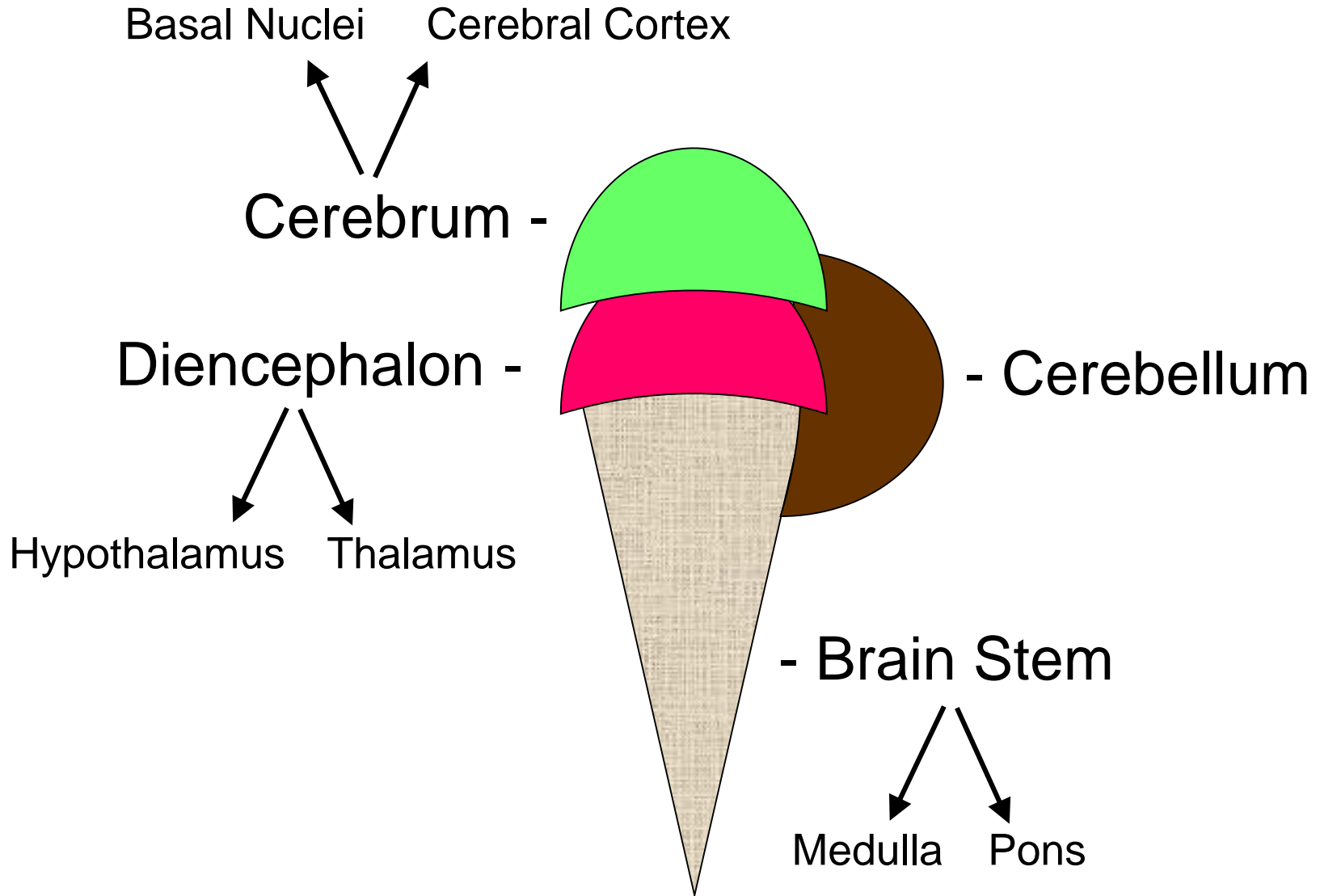
Figure 45-4 Block diagram of a general-purpose computer, showing the basic components and their interrelations. G&H 2011 p 546; G&H 2016 p 580

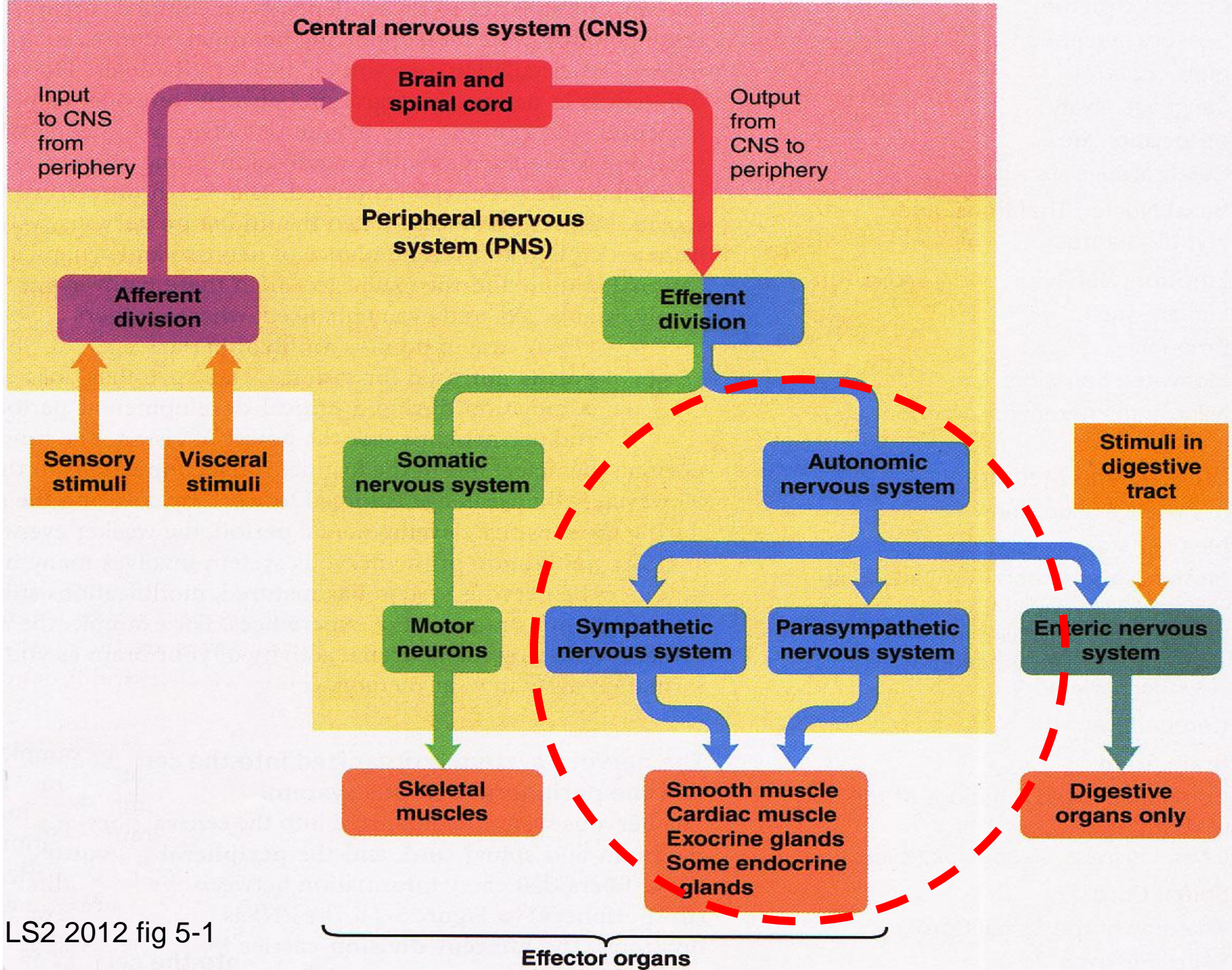


CNS Connections: The Central 7!

- Fore- {
1. Cerebrum
 2. Diencephalon – Hypothalamus + Thalamus
- Mid- {
3. Midbrain
- Hind- {
4. Cerebellum
 5. Pons
 6. Medulla
 7. Spinal Cord
- } – Brain Stem

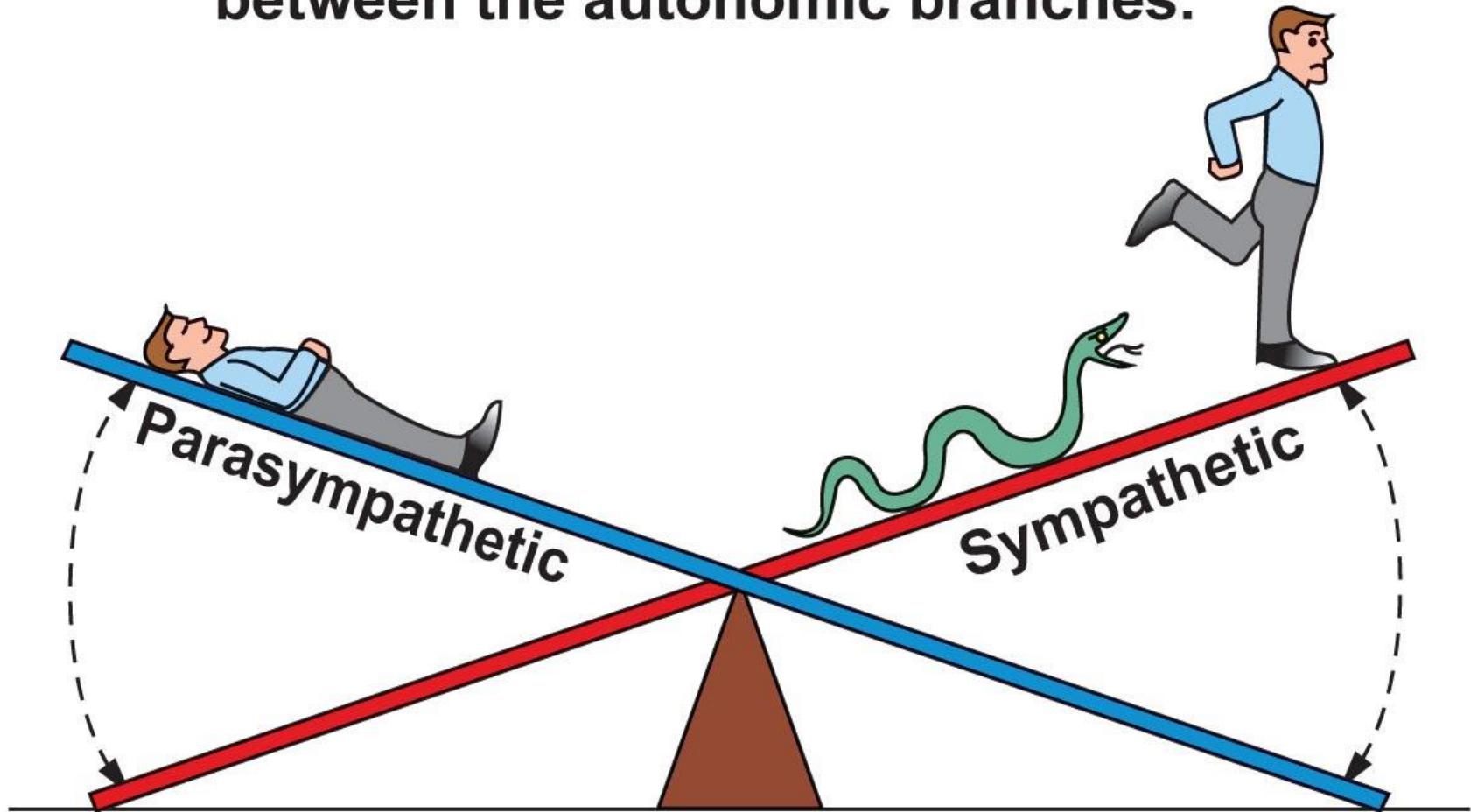
Ice Cream Cone Evolution Analogy





LS2 2012 fig 5-1

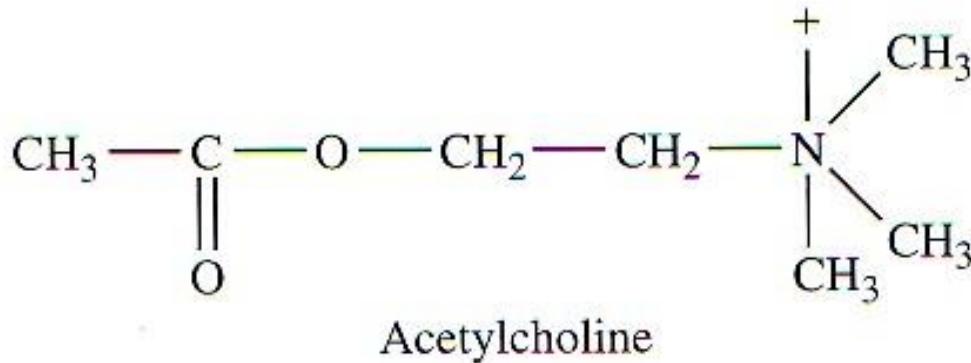
Homeostasis is a dynamic balance between the autonomic branches.



**Rest-and-digest:
Parasympathetic
activity dominates.**

**Fight-or-flight:
Sympathetic activity
dominates.**

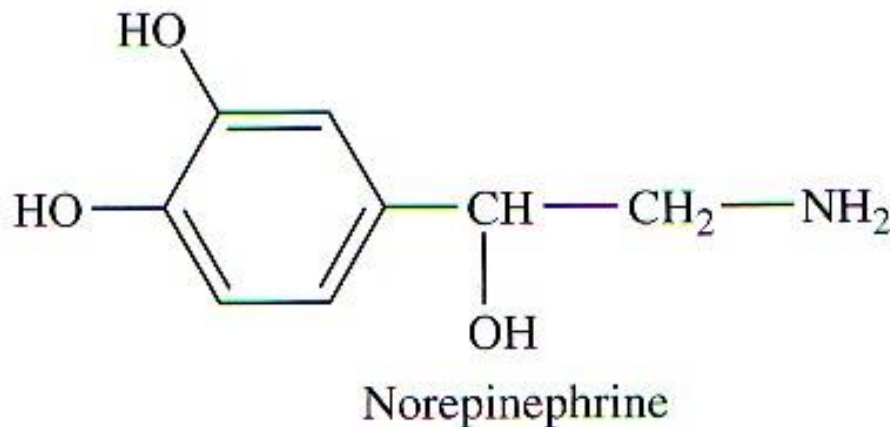
Autonomic Neurotransmitters & Receptors



Cholinergic

Nicotinic

Muscarinic

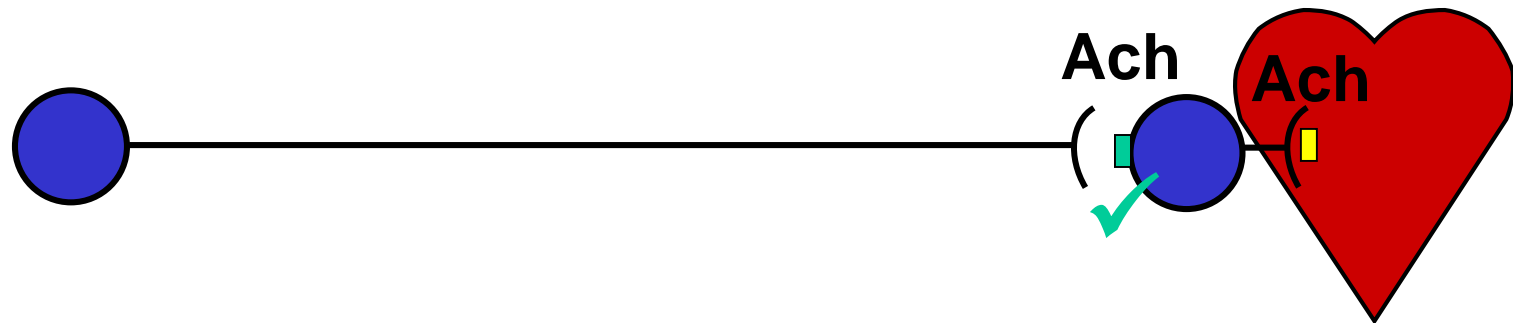


Adrenergic

α = Alpha

β = Beta

Parasympathetic

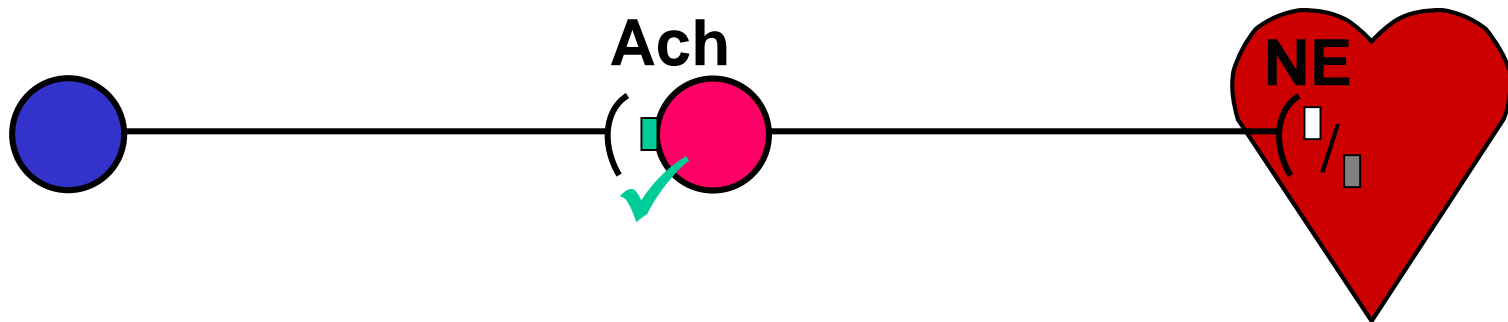


Ach = Acetylcholine

■ = Nicotinic Receptor

■ = Muscarinic Receptor

Sympathetic



NE = Norepinephrine

□ = α Receptor (α_1 , α_2)

■ = β Receptor (β_1 , β_2)

Nicotine activates both Sympathetic & Parasympathetic post-ganglionic neurons!

Problem?



Like hammering the gas pedal & brake at the same time!!



Nicotine also triggers the release of adrenalin & cortical hormones & causes generalized adrenal disruption!

80% Epinephrine/Adrenaline (E)

20% Norepinephrine (NE)

Output ↑ *to blood*

Adrenals = Paired organs above kidneys

