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 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/***

II. ***Homeostasis Connections*** **BP *e.g.* Q? + Gain? G&H pp 7- 8**

III. ***Organization of the Nervous System***
G&H ch 45 pp 543-8, LS1/2 ch 5
- **A. Central vs peripheral, computer analogy fig 45-4 p 546**
- **B. Neurons, neuronal classes, neuroglia, connections**

IV. ***Autonomic Nervous System*** **G&H ch 60 pp 729-41 + LS +...**
- **A. Sympathetic *vs.* parasympathetic fig 60-1,60-3 pp730-1**
- **B. Neurotransmitters, receptors, actions tab 60-1 pp 731-7**
- **C. Nicotine & adrenal hormonal disruption**

V. ***Addiction Medicine: Homeostasis & Applications***

Come see us!

All @*uoregon.edu*

BI 358 Office Hr Winter 2016

Day & Time	Instructor	Place	e-mail
M 11 am-12n	Pat Lombardi[+]	65A Klamath	*lombardi*
W 10-11am	Stacy Levichev-Connolly	203 LISB	*aleviche*
W 11 am-12n	Connor O'Sullivan	206 LISB	*conoro*

[+] and by appointment.

For Pat, please call 541-346-6055/4525 or *e-mail*.

For Stacy, please *e-mail*.

For Conor, please *e-mail*.

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!

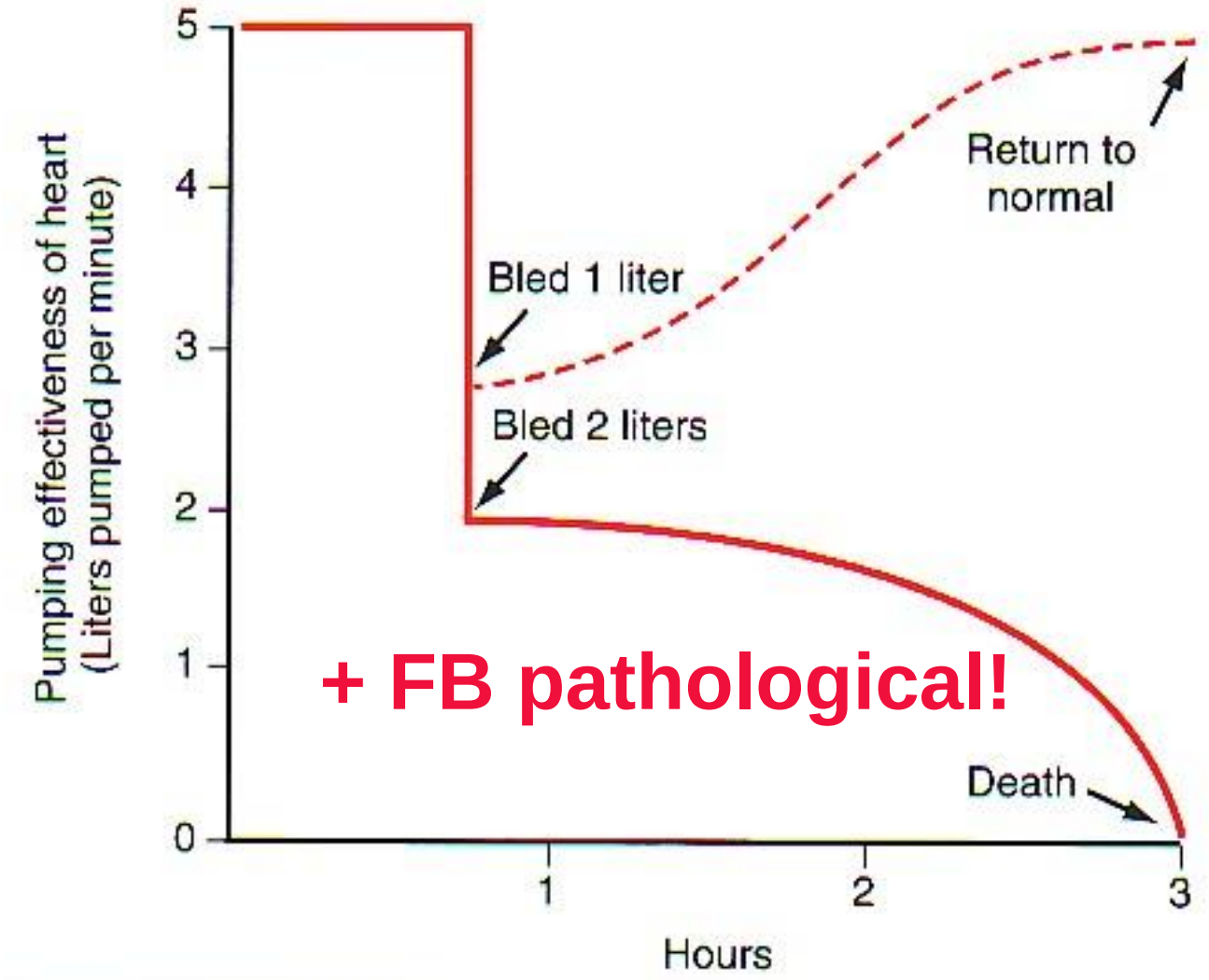
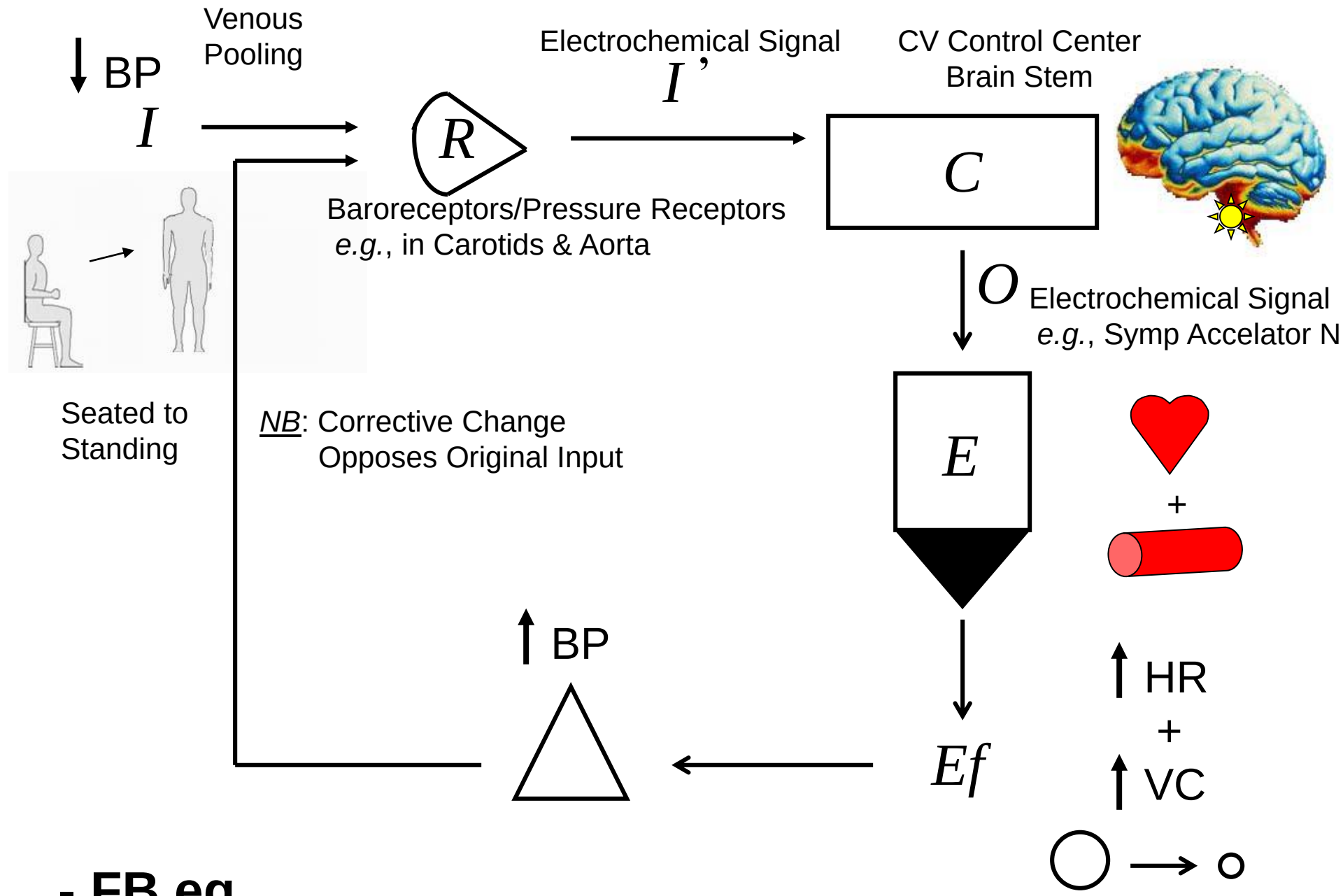


FIGURE 1–3

Recovery of heart pumping caused by *negative feedback* after 1 liter of blood is removed from the circulation. Death caused by positive feedback when 2 liters of blood are removed.


BP
I
Venous Pooling
R
Electrochemical Signal
I'
CV Control Center
Brain Stem
C
Baroreceptors/Pressure Receptors
e.g., in Carotids & Aorta
O
Electrochemical Signal
e.g., Symp Accelator N
Seated to Standing
NB: Corrective Change
Opposes Original Input
E
+
BP
HR
+
VC
Ef

- FB eg

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 <u>non-functioning</u> Baroreceptor system

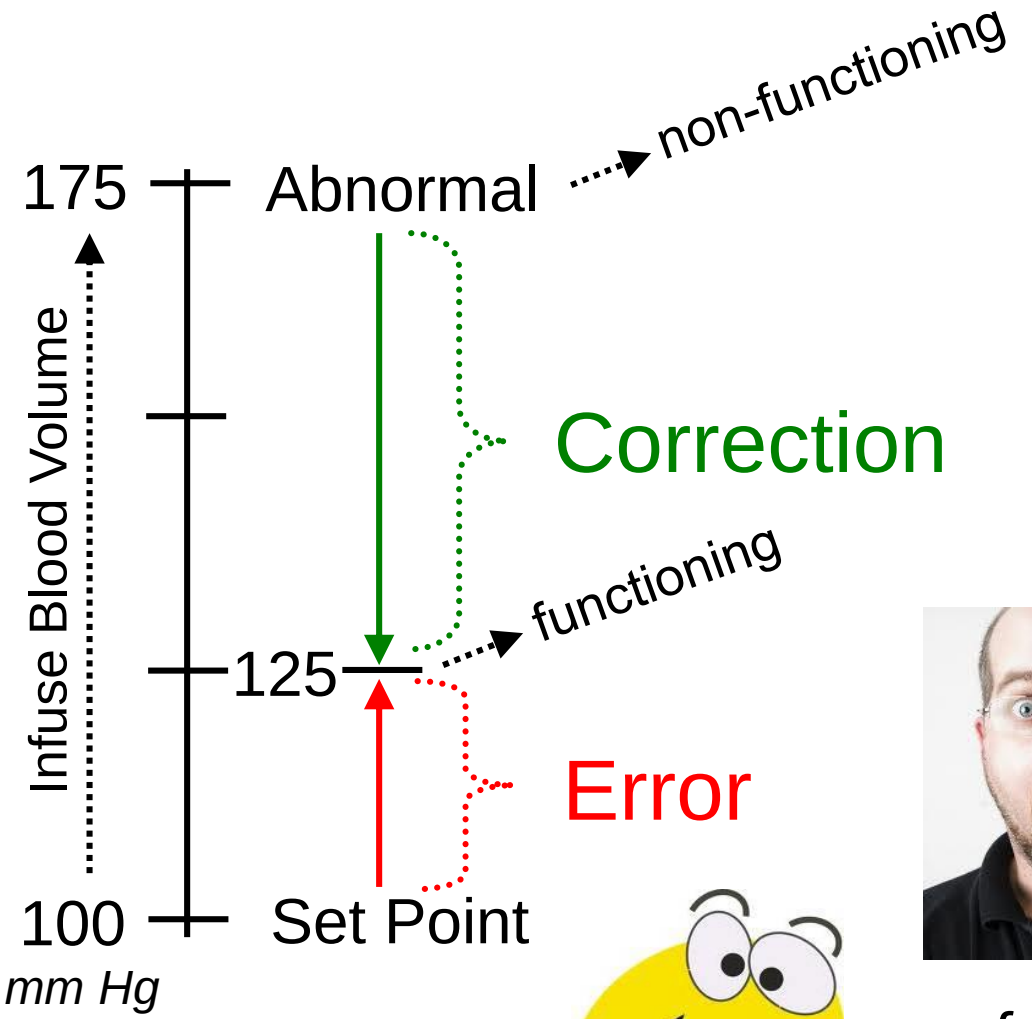
BP: 100 mm Hg → 175 mm Hg

...into person with <u>functioning</u> system

BP: 100 mm Hg → 125 mm Hg

G&H pp 7-8

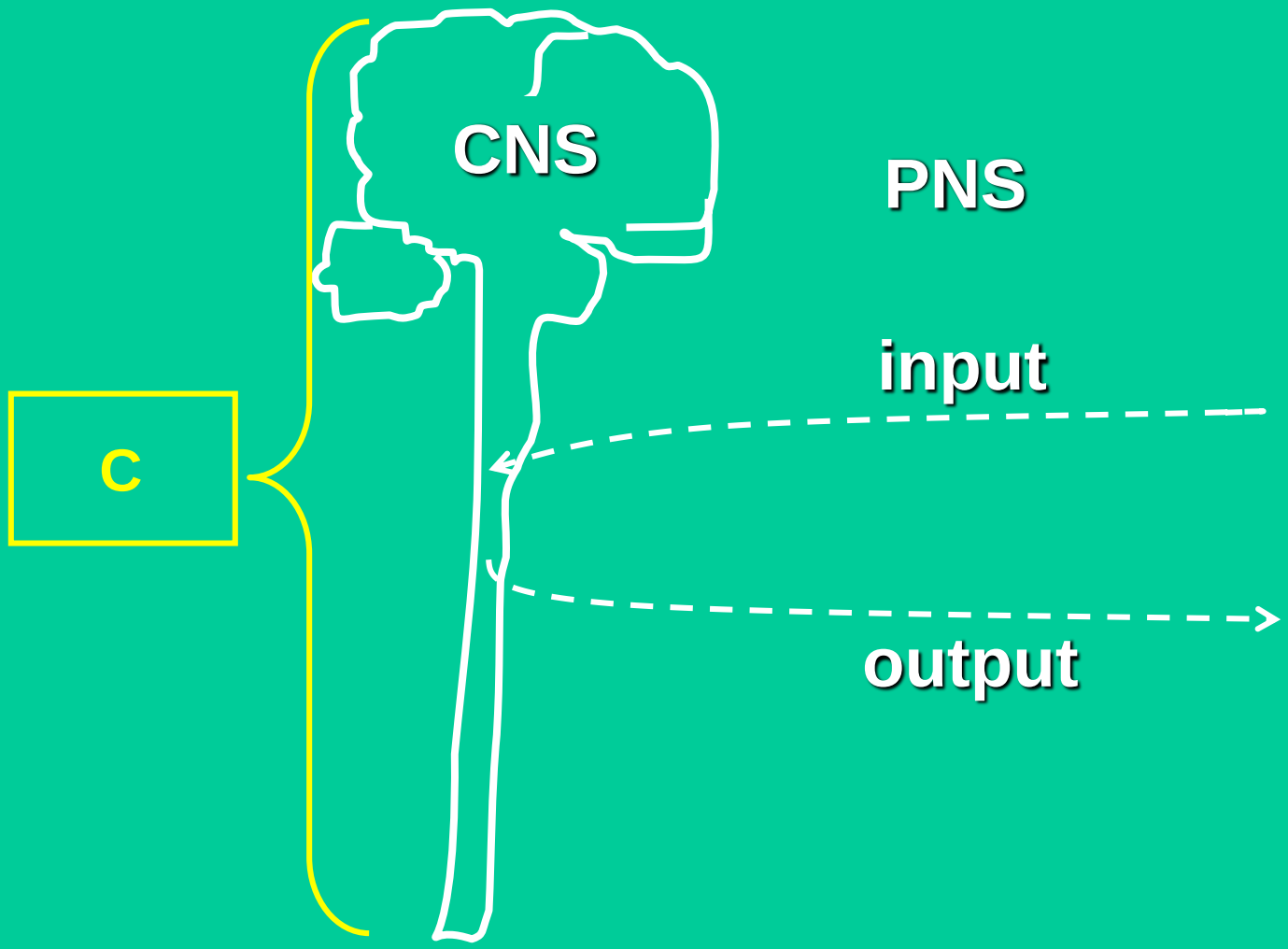
Gain *for Human Baroreceptor System?*



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

cf: Gain for Human Body Temperature = -33

Nervous System



Systems Level

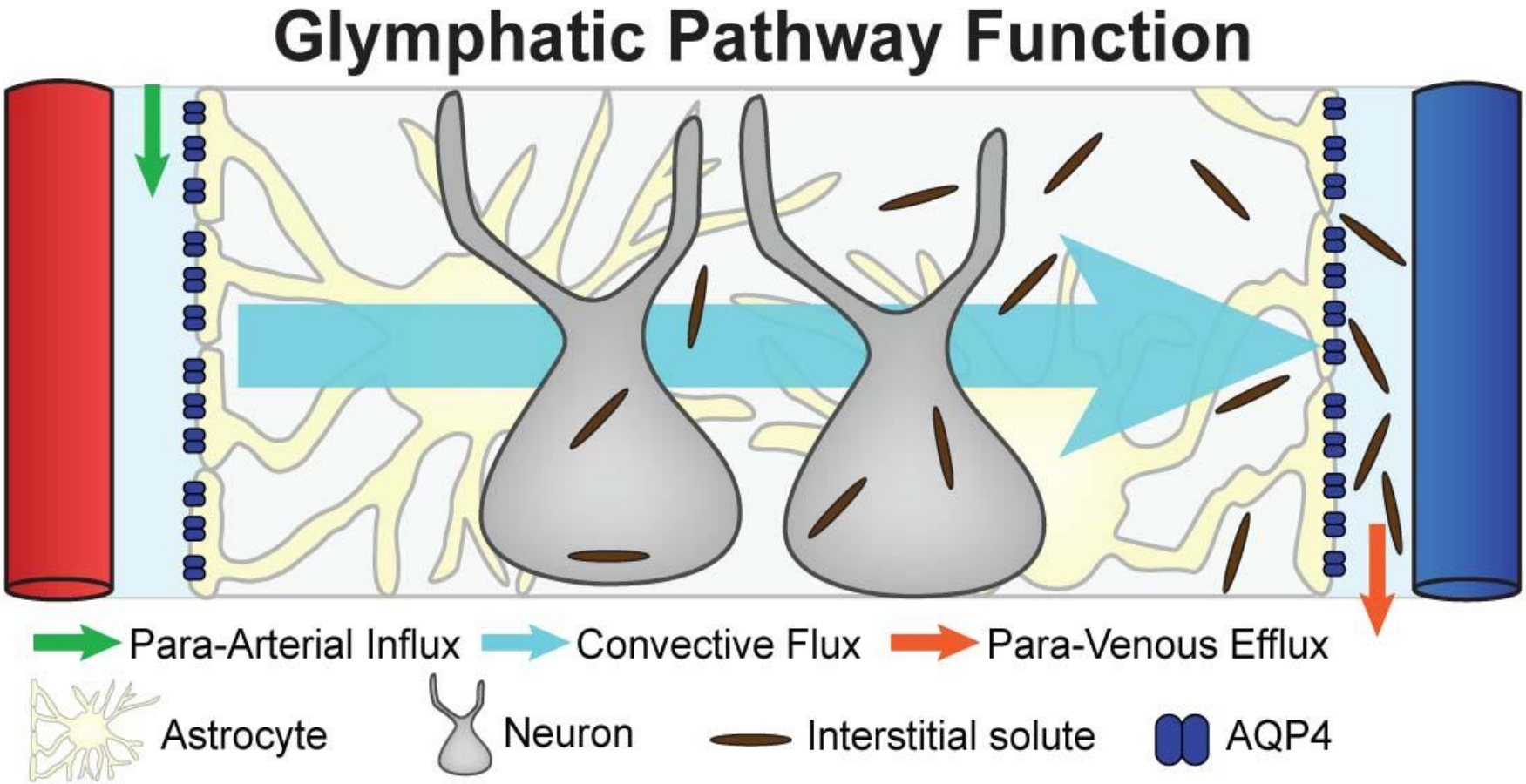
~ 90% of Cells w/in CNS are Glial Cells/Neuroglia!

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 neuro-transmitters.
7. Soak up excess K+ to sustain normal neural excitability.
8. Communicate with neurons & each other electrochemically.

100 Billion Neurons →
900 Billion Glial Cells!

LS2 2012 fig 5-4 p 110

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

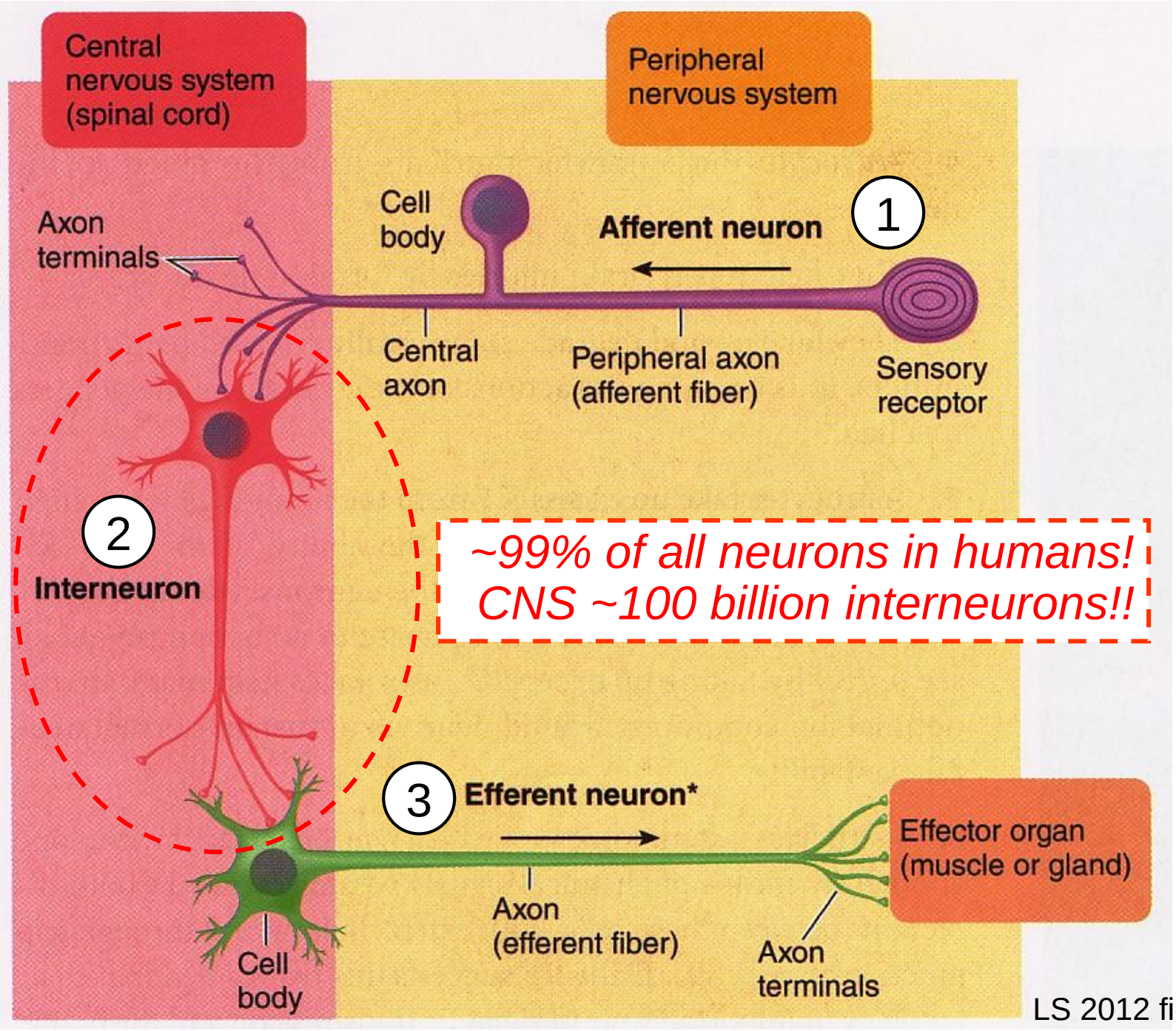


http://www.sciencedaily.com/releases/2012/08/120815142042.htm

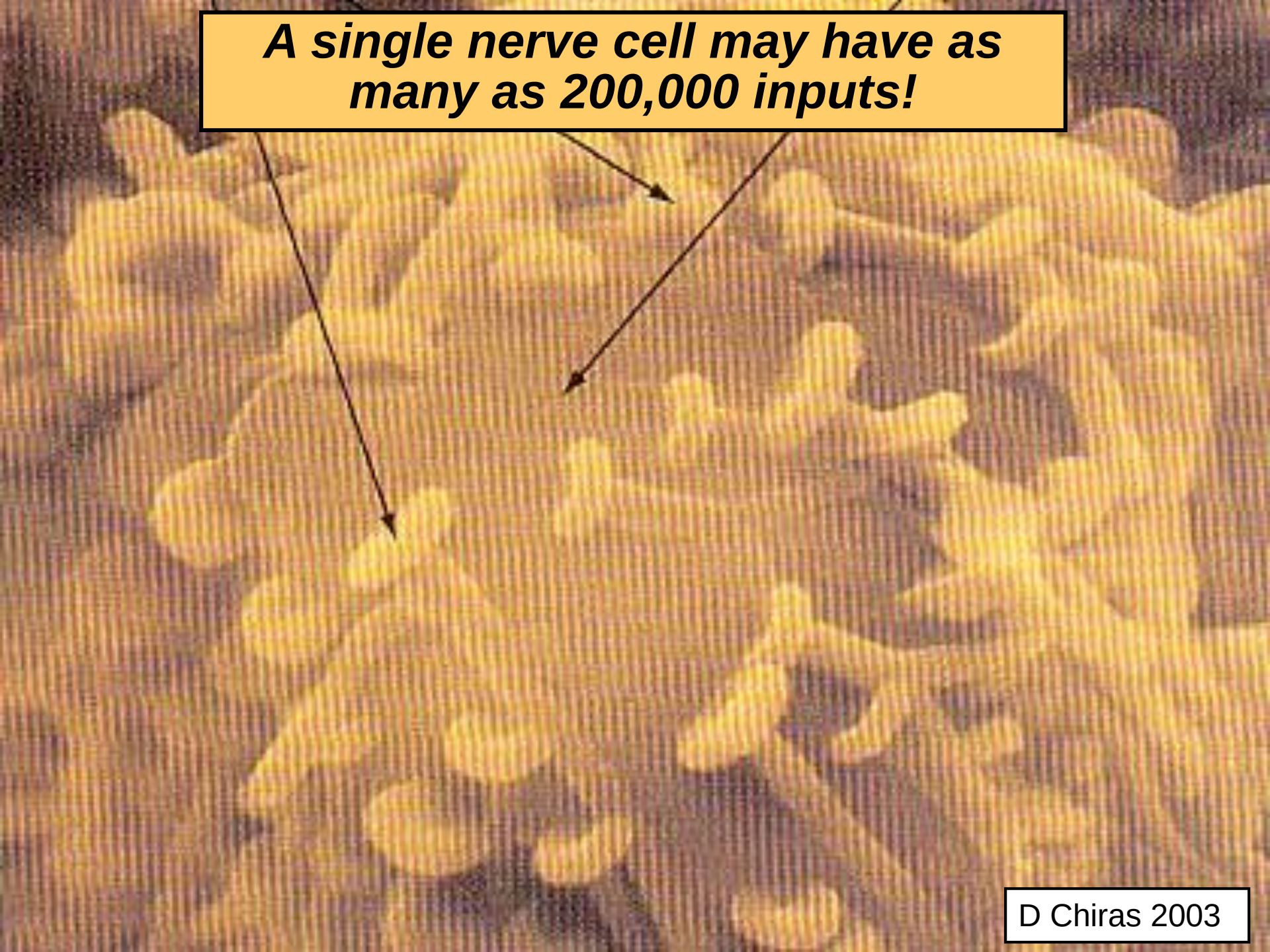
https://www.urmc.rochester.edu/news/story/3584/scientists-discover-previously-unknown-cleansing-system-in-brain.aspx

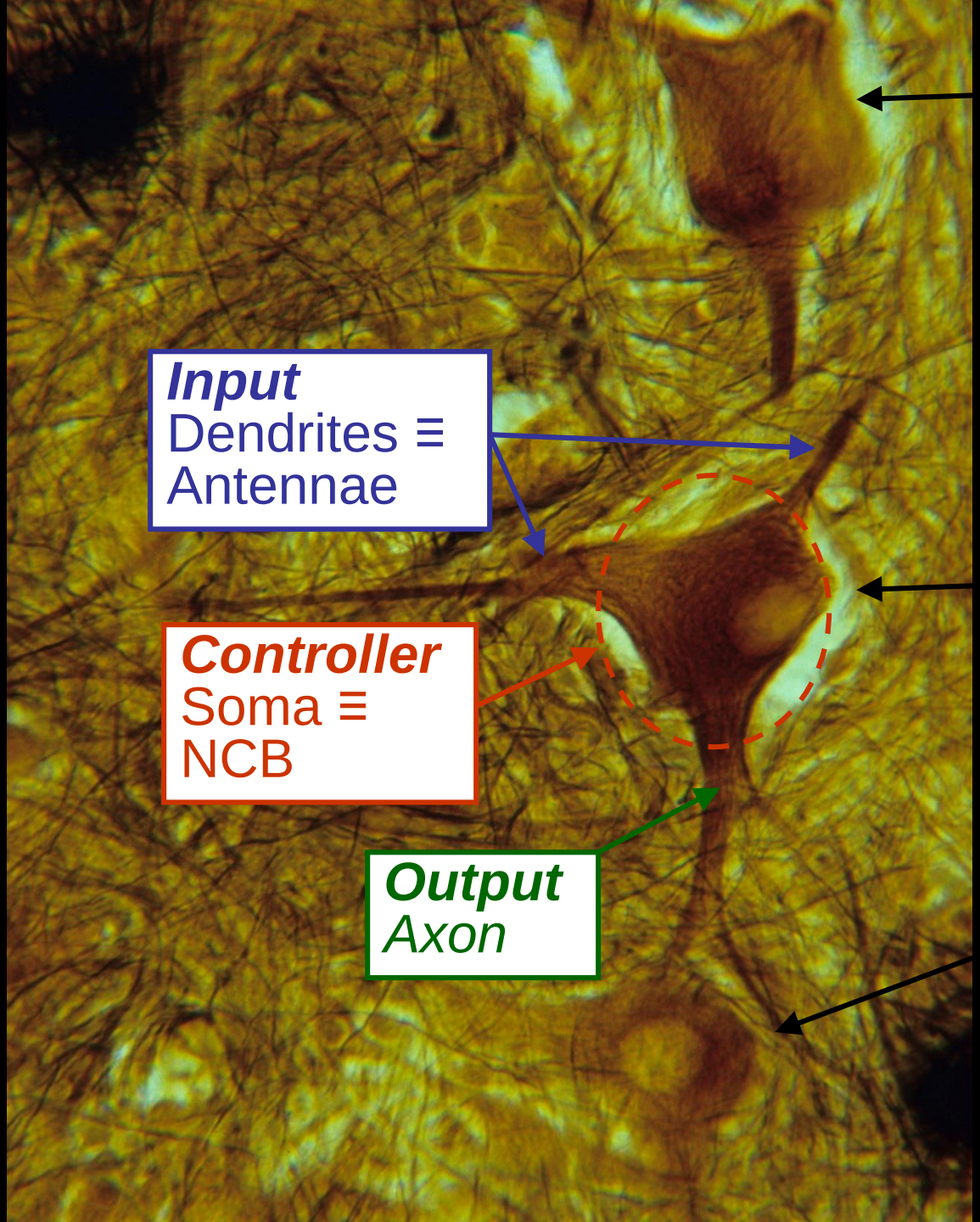
https://www.ted.com/talks/jeff_iliff_one_more_reason_to_get_a_good_night_s_sleep

Organ/Tissue Level



LS 2012 fig 5-2


A single nerve cell may have as many as 200,000 inputs!
D Chiras 2003



H. Howard 1980

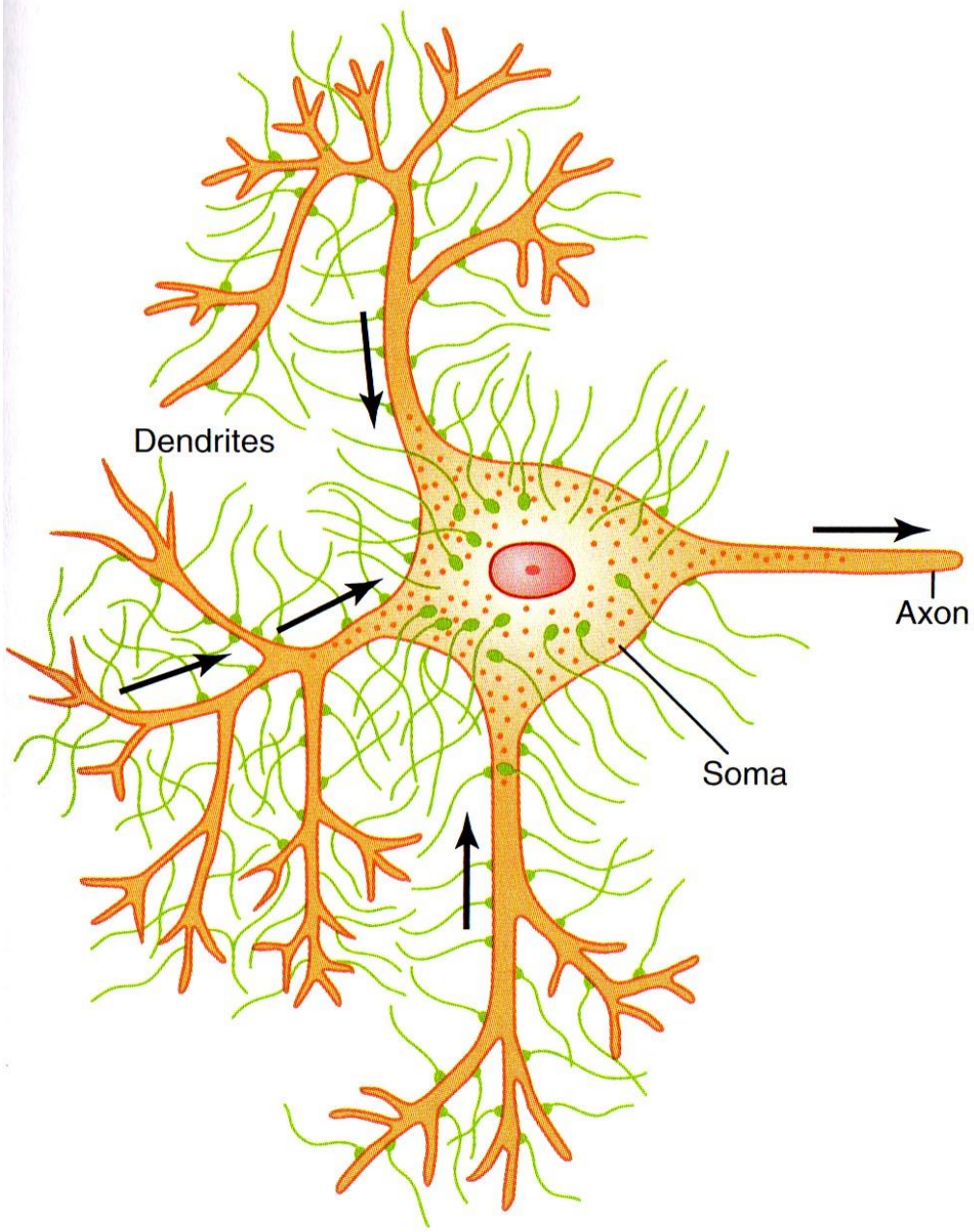
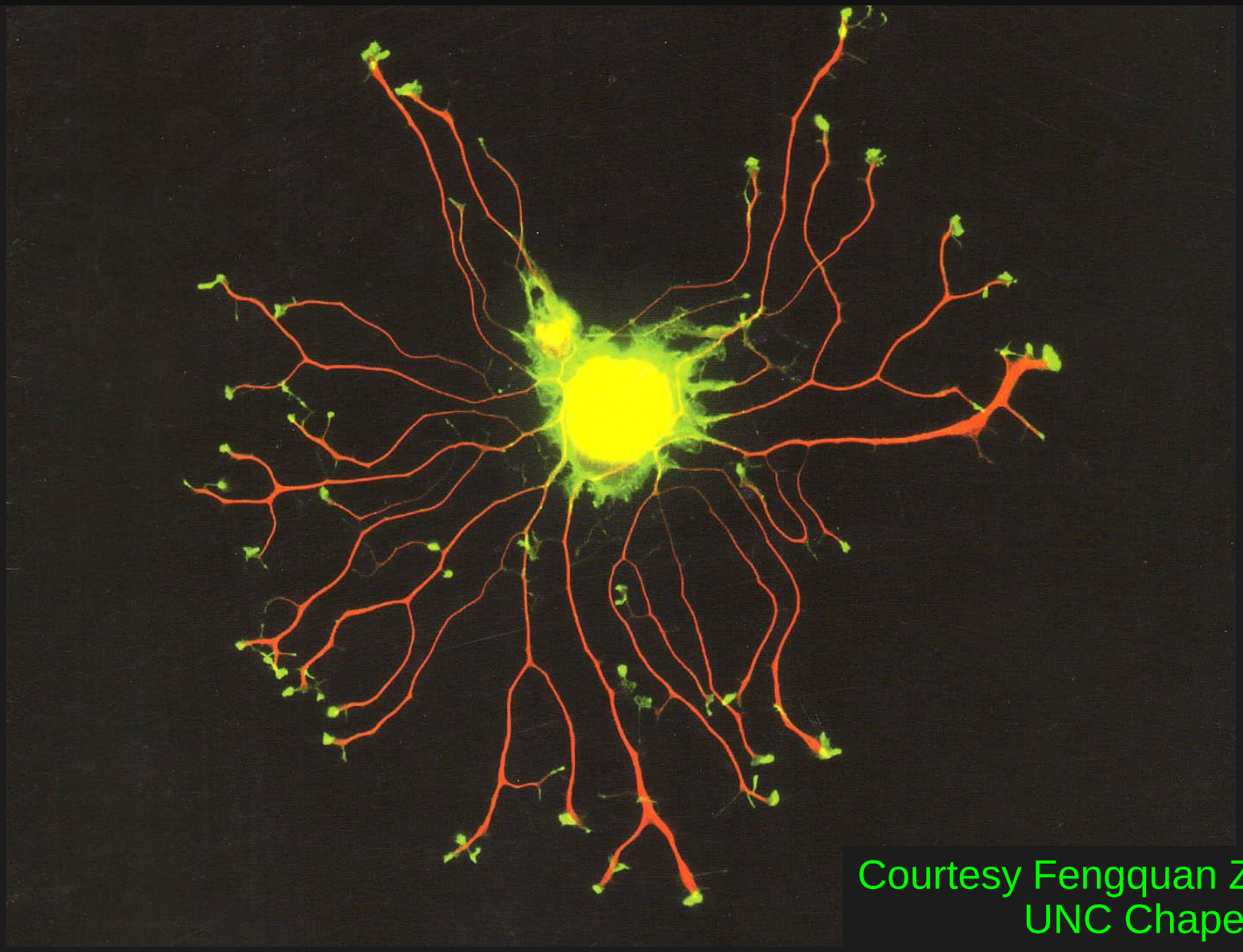


Figure 45-5 Typical anterior motor neuron, showing presynaptic terminals on the neuronal soma and dendrites. Note also the single axon.

G&H 2011 p 547

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



Courtesy Fengquan Zhou
UNC Chapel Hill

Sensory nerves especially, come in all shapes & sizes!

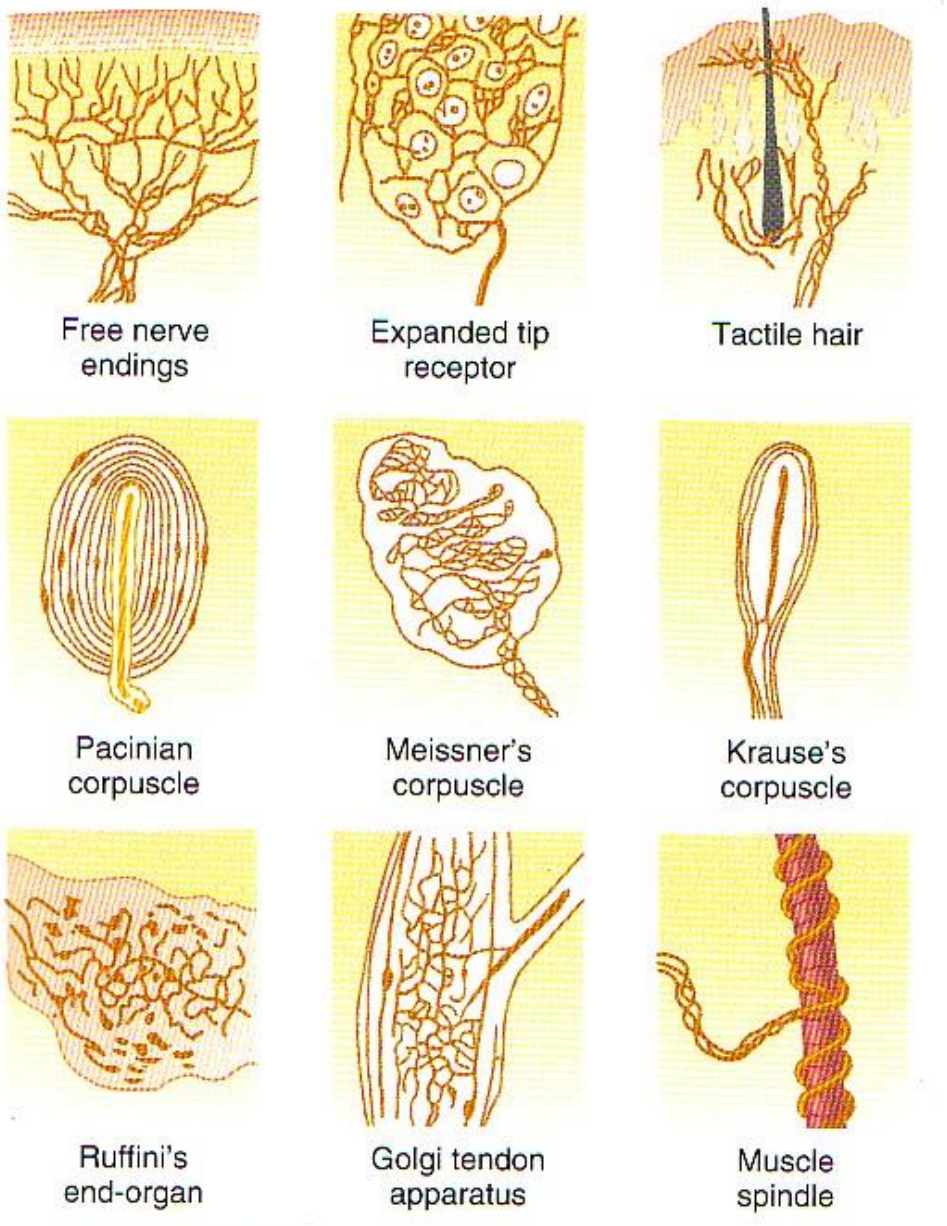


Figure 46–1

Several types of somatic sensory nerve endings.

Guyton & Hall 2011

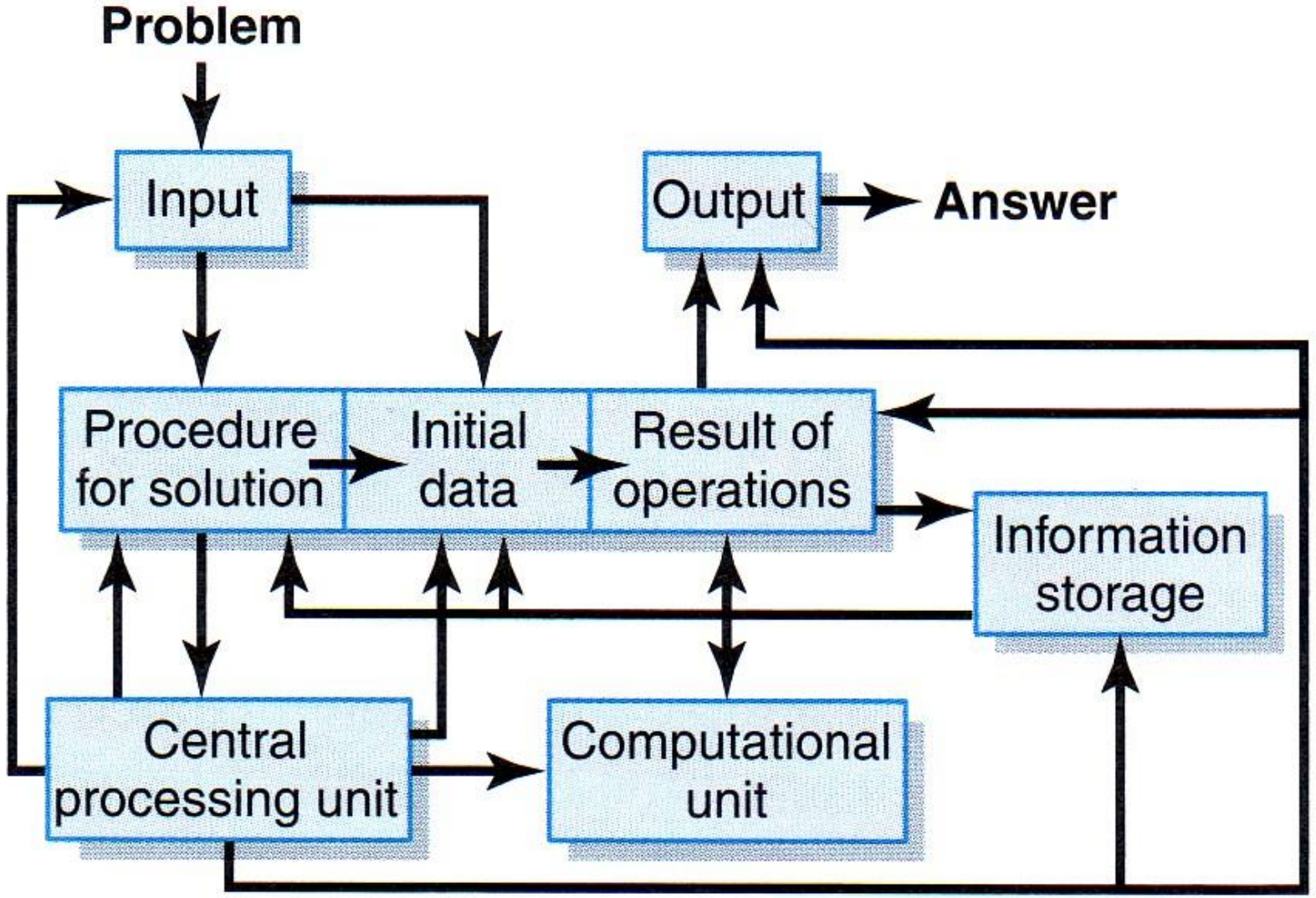
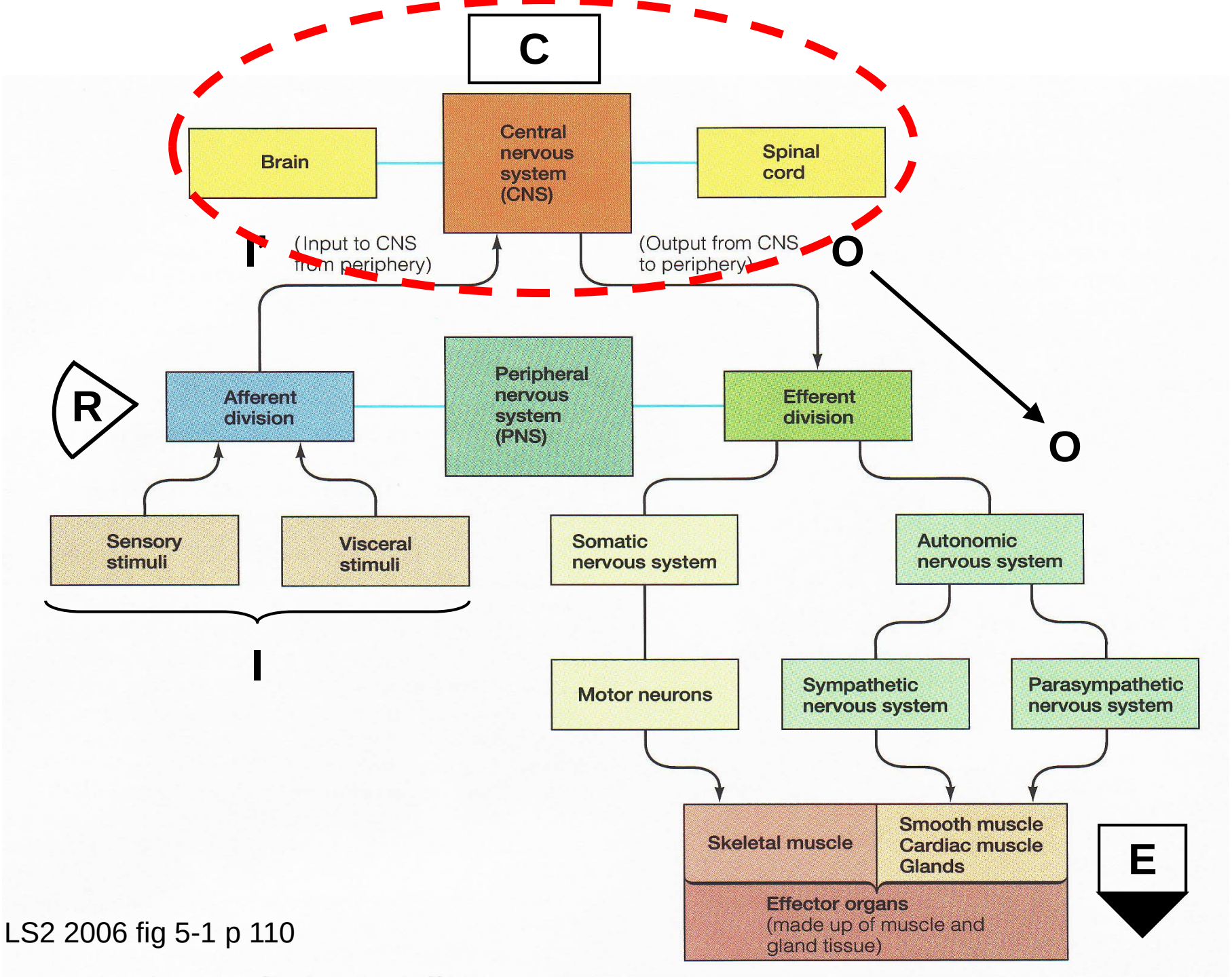


Figure 45-4 Block diagram of a general-purpose computer, showing the basic components and their interrelations.

G&H 2011 p 546



LS2 2006 fig 5-1 p 110

CNS Connections: The Central 7!

Fore-
- 1. Cerebrum
- 2. Diencephalon – Hypothalamus + Thalamus

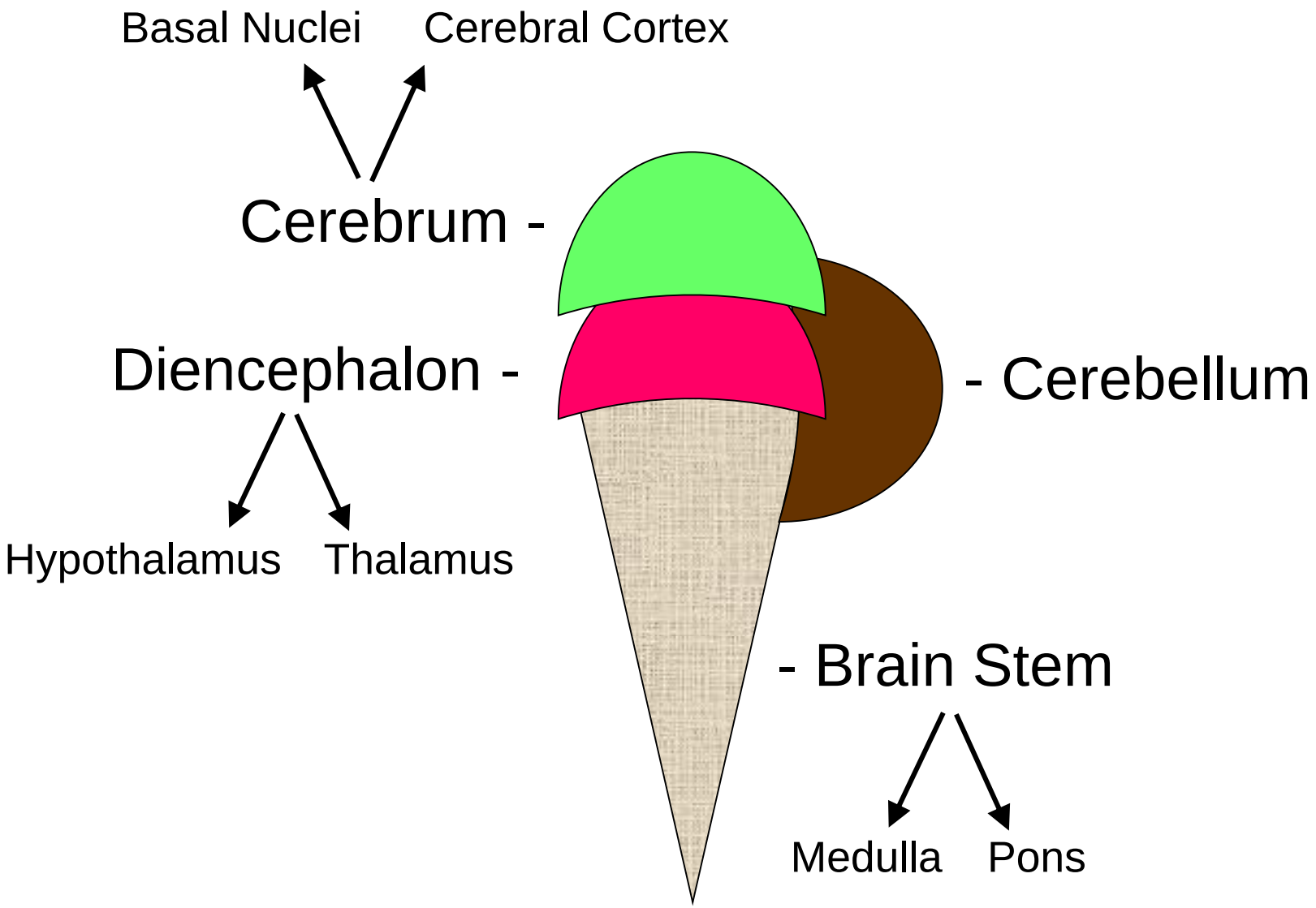
Mid-
- 3. Midbrain

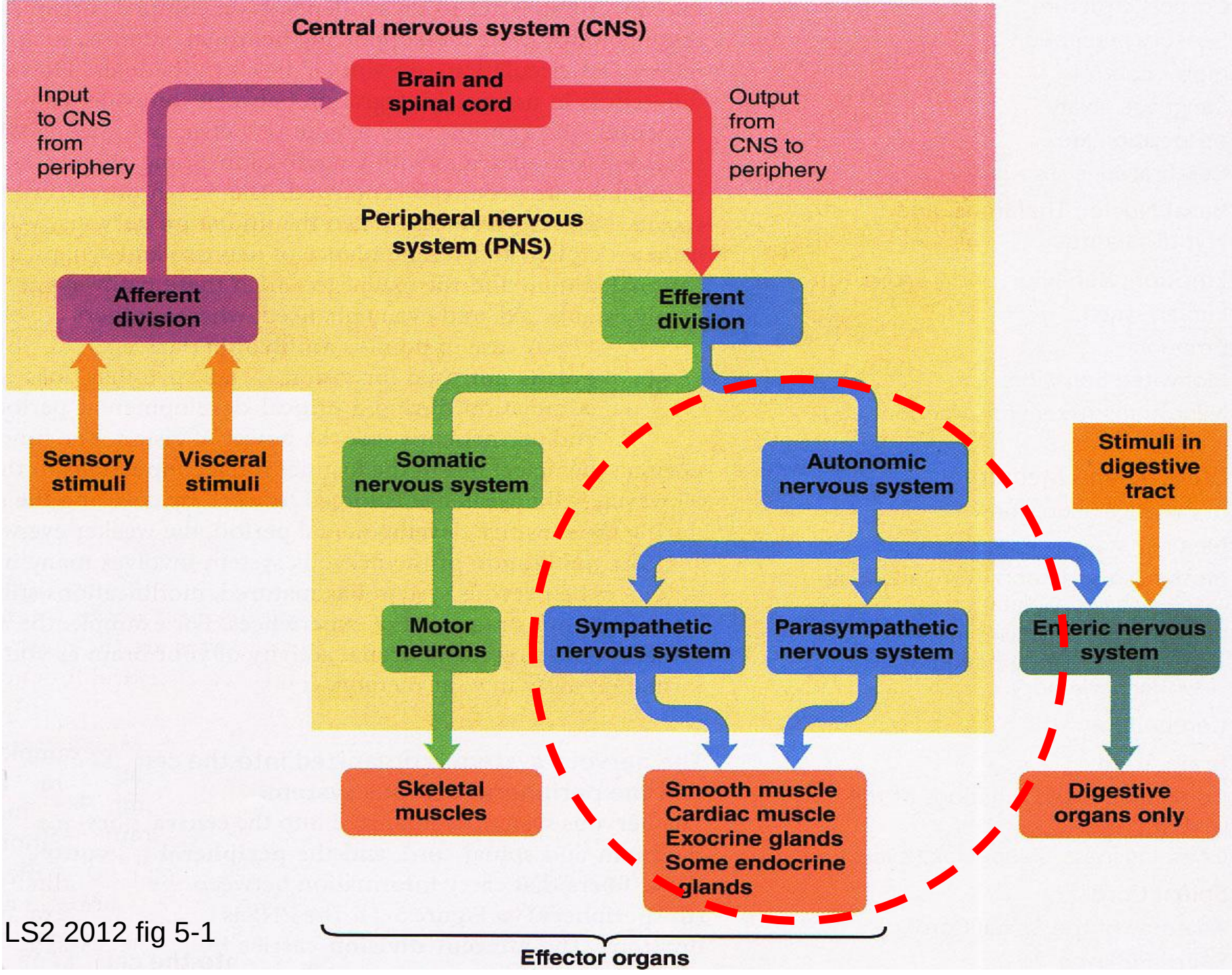
Hind-
- 4. Cerebellum
- 5. Pons
- 6. Medulla

(5. Pons, 6. Medulla) – Brain Stem

- 7. Spinal Cord

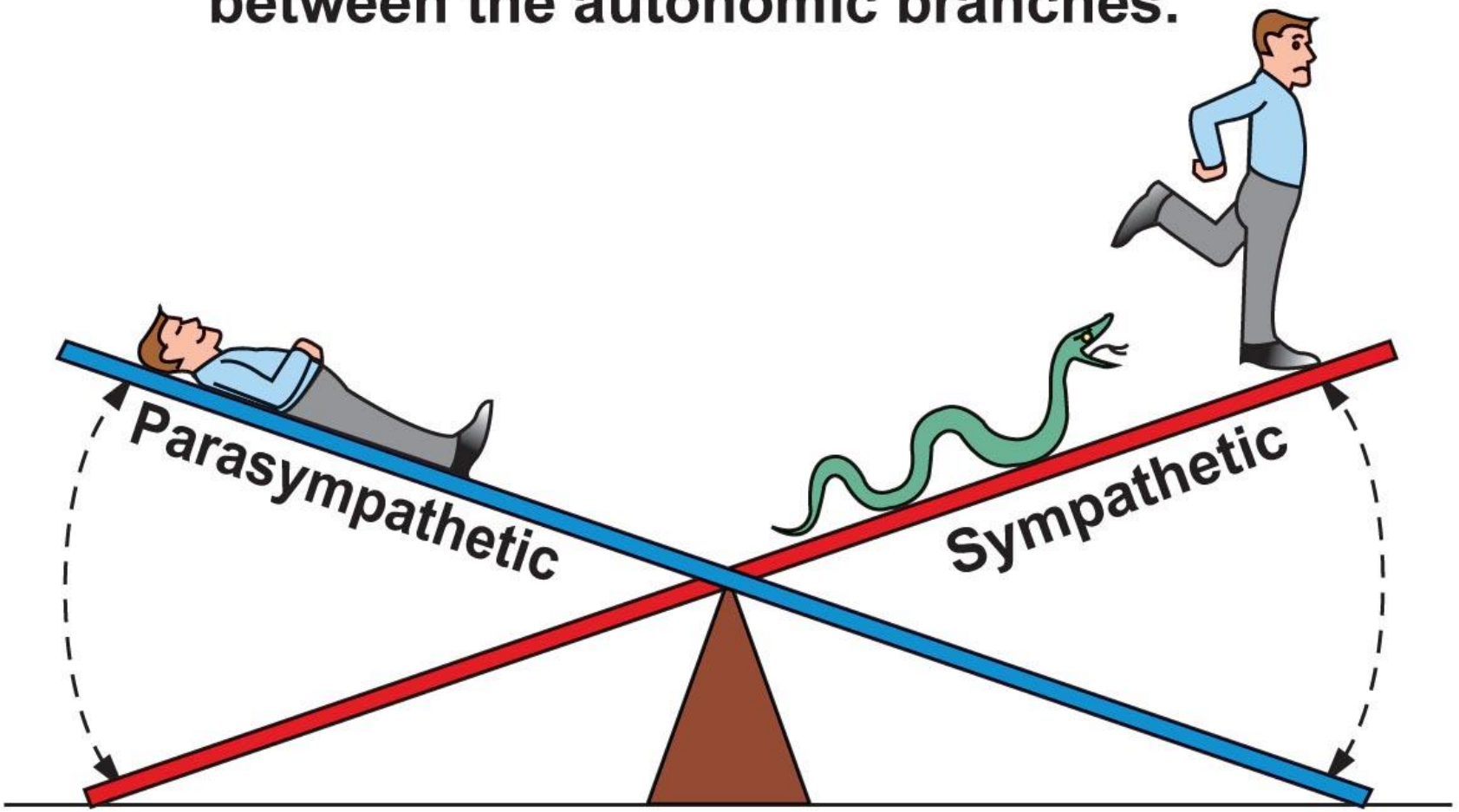
Ice Cream Cone Evolution Analogy





LS2 2012 fig 5-1

Homeostasis is a dynamic balance between the autonomic branches.

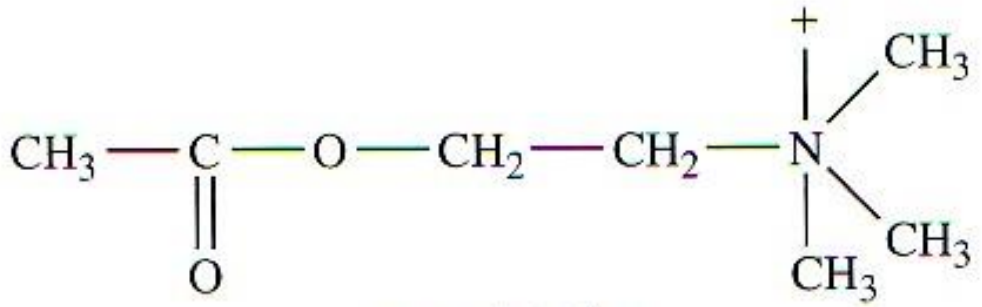


Rest-and-digest: Parasympathetic activity dominates.

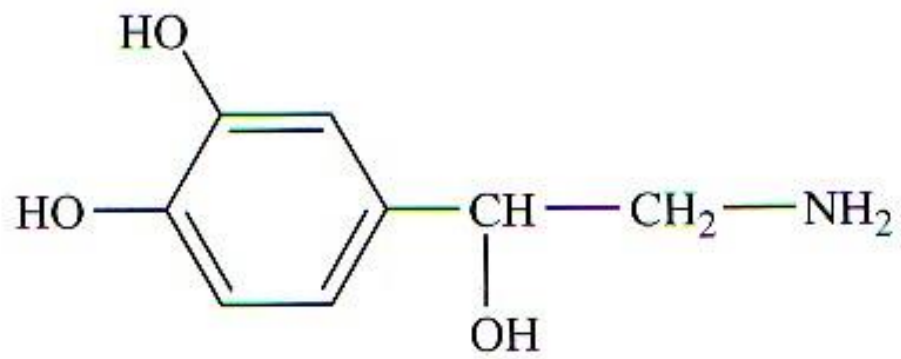
Fight-or-flight: Sympathetic activity dominates.

D Silverthorn 2010

Autonomic Neurotransmitters & Receptors



Acetylcholine



Norepinephrine

<u>Cholinergic</u>

Nicotinic

Muscarinic

<u>Adrenergic</u>

α = Alpha

β = Beta

G&H 2011 p 731-3

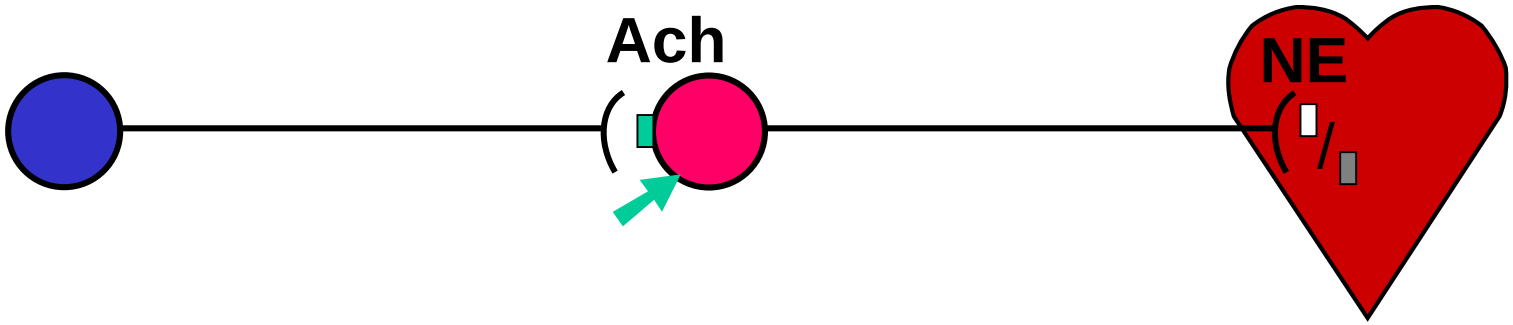
Parasympathetic

Ach = Acetylcholine

= Nicotinic Receptor

= Muscarinic Receptor

Sympathetic



NE = Norepinephrine

= α Receptor (α_1 , α_2)

= β Receptor (β_1 , β_2)

Nicotine activates <u>both</u> Sympathetic & Parasympathetic post-ganglionic neurons!

Problem?

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

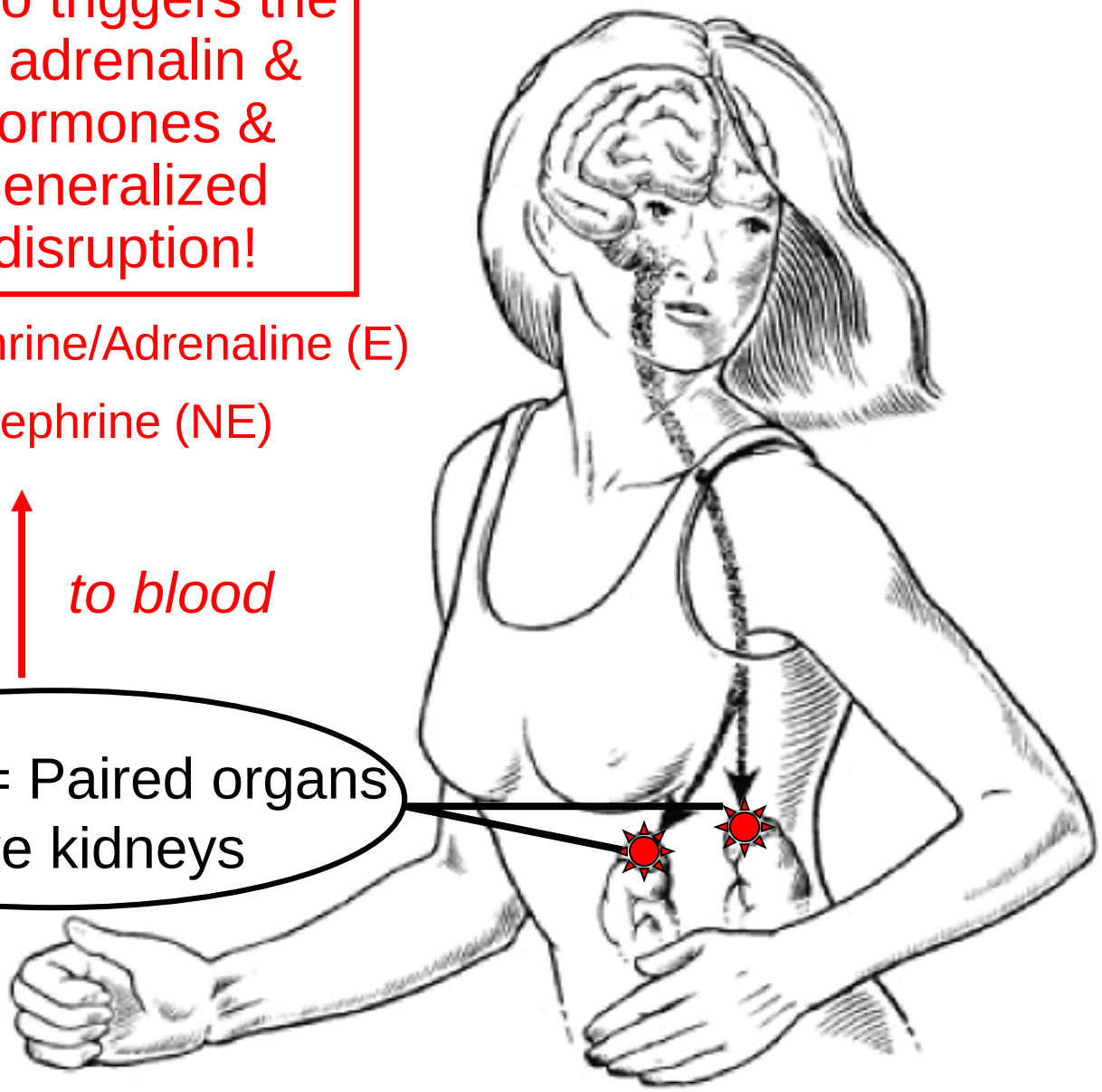
Nicotine also triggers the release of adrenalin & cortical hormones & causes generalized adrenal disruption!

80% Epinephrine/Adrenaline (E)

20% Norepinephrine (NE)

Output *to blood*

Adrenals = Paired organs above kidneys



http://www.medscape.com/viewarticle/496223_4

Break for discussion/questions!

BI 358 Lecture 2 (continued)

VI. Addiction Medicine: Homeostasis & Applications

G&H ch 45, 58 & 60 + DLN section B

A. Neurotransmitter balance: Mood/Diseases/Addiction?

B. Synapses, classes, NT release, homeostasis?
G&H fig 45-5, 45-6 pp 546-48

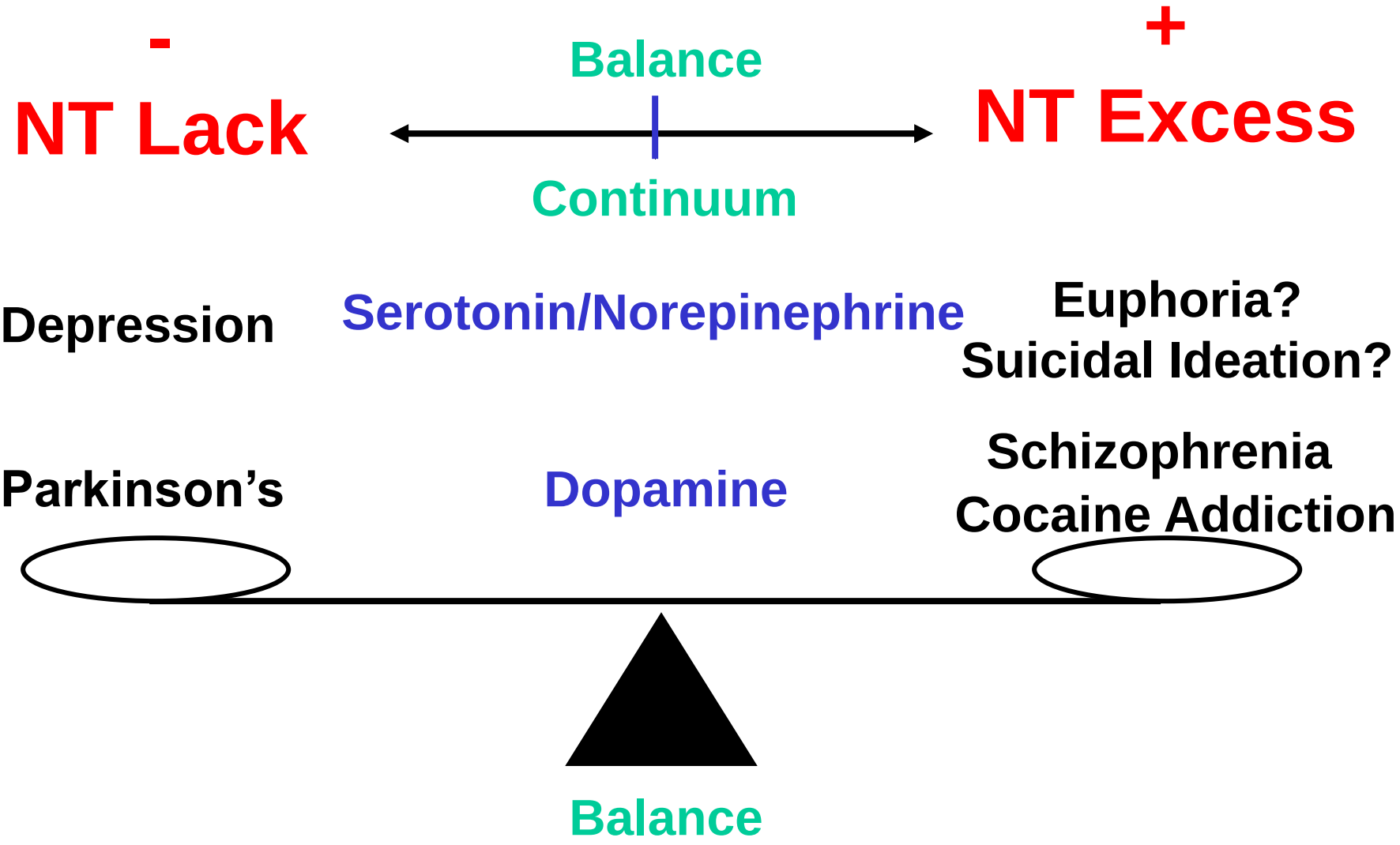
C. Neurotransmitters prominent in addiction medicine
G&H tab 45-1 p 550, LS2 2006 fig 4-15

D. Brain neurohumoral systems fig 58-2, 58-3 pp 712-13
locus ceruleus (NE+), substantia nigra (D-/+),raphe nuclei (SI-) large cells of RAS (Ach+) + cocaine

E. Limbic system G&H ch 58 p 714-20 fig 58-4 + LS1 & LS2

1. Hypothalamus headquarters, reward & punishment
G&H fig 58-5, fig 58-6 pp 714-6; 11^{ed} fig 58-8 p 735

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



NB: Pat, chemical vs electrical

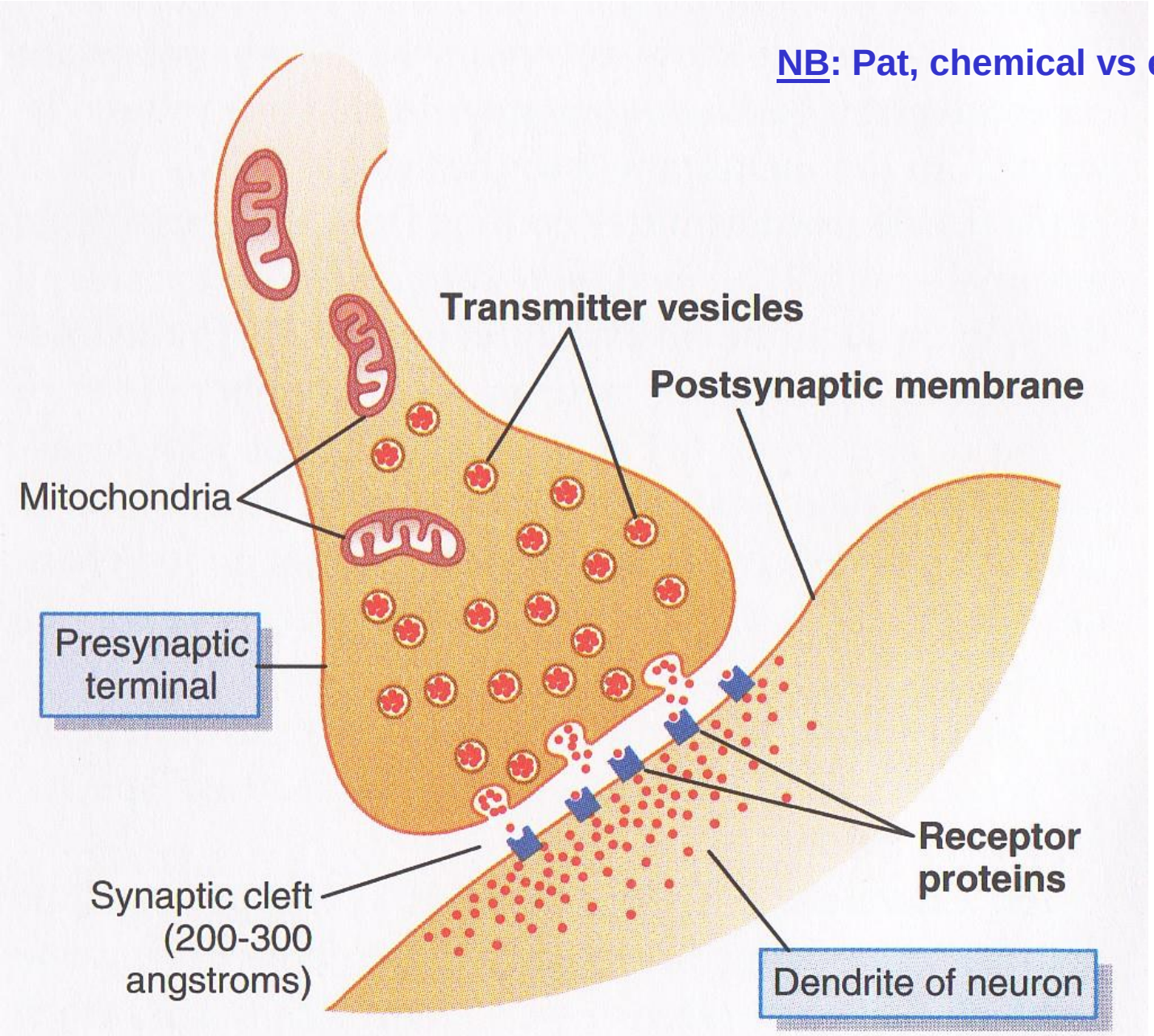
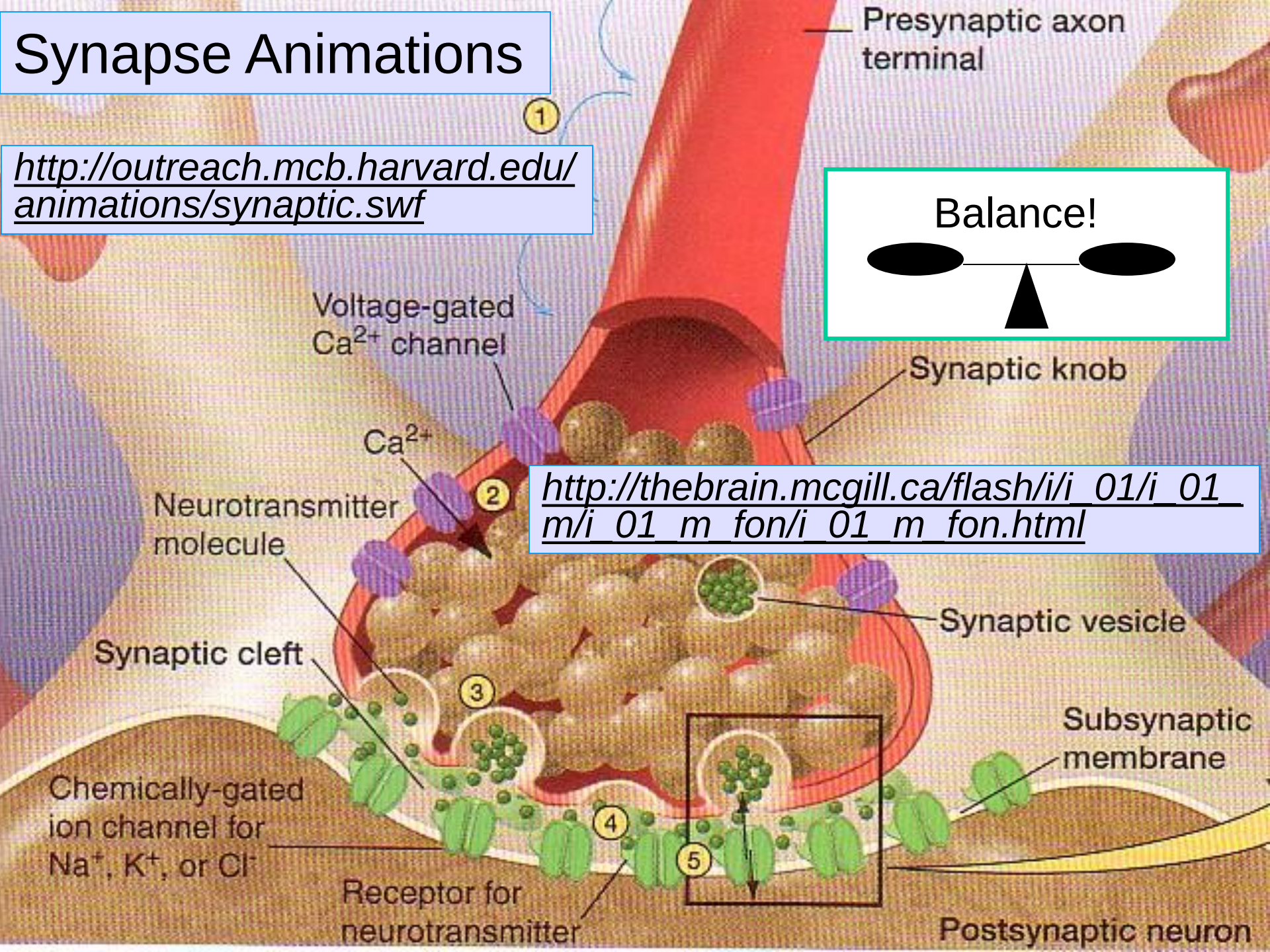


Figure 45-6 Physiologic anatomy of the synapse.

G&H 2011 p 547

Synapse Animations

http://outreach.mcb.harvard.edu/animations/synaptic.swf



Balance!

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
Dopamine
Serotonin
Histamine
Class III: Amino Acids
Gamma-aminobutyric acid (GABA)
Glycine
Glutamate
Aspartate
Class IV
Nitric oxide (NO)

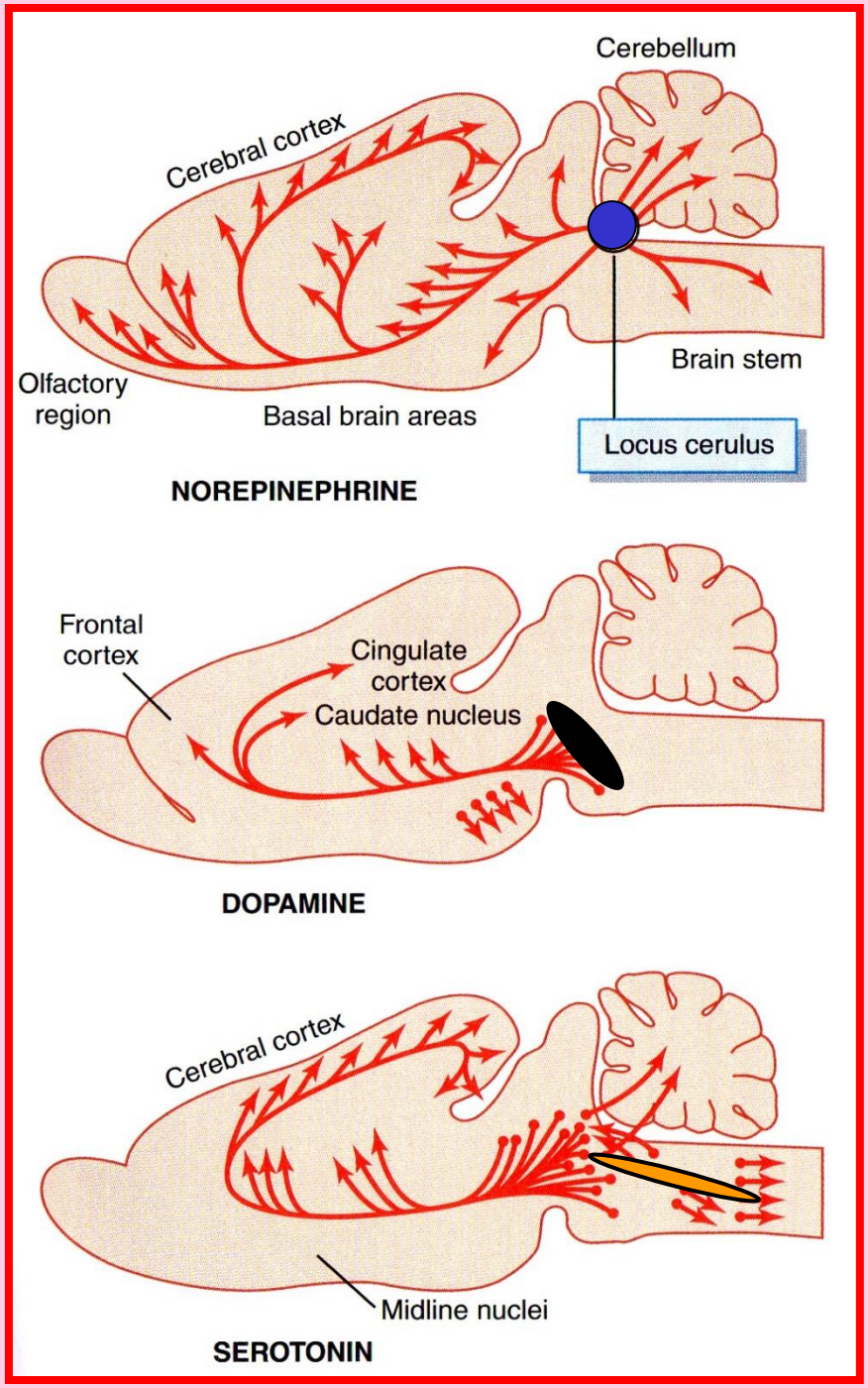
Prominent in reward pathways & chemistry of addiction.

G&H 2011 p 550

Norepinephrine = NE

Dopamine = D?

Serotonin = SI



Locus ceruleus = "Blue/azur spot"

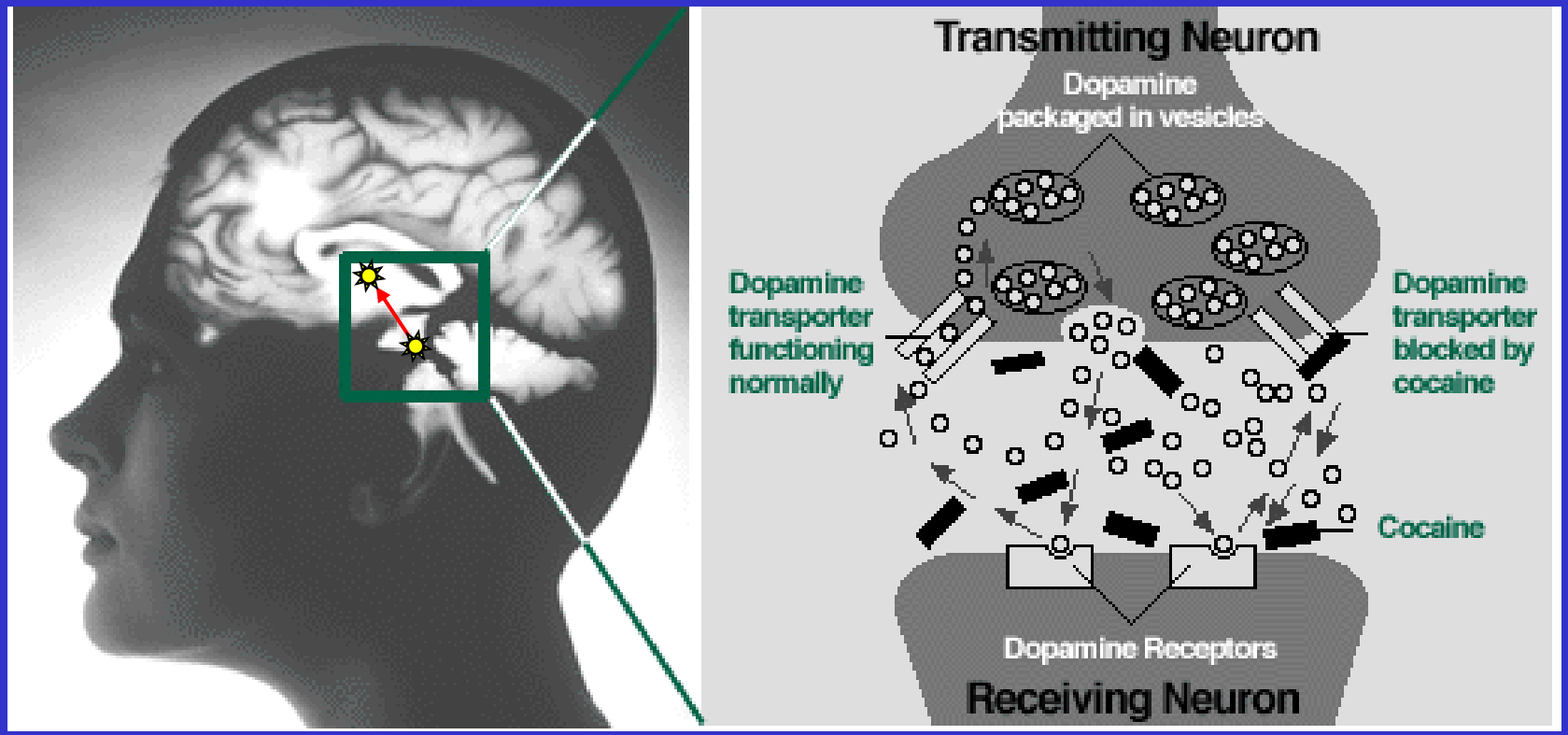
Substantia nigra = "Black substance"

Raphe nuclei = "Nut seam/line"

G&H 2011 p 713

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

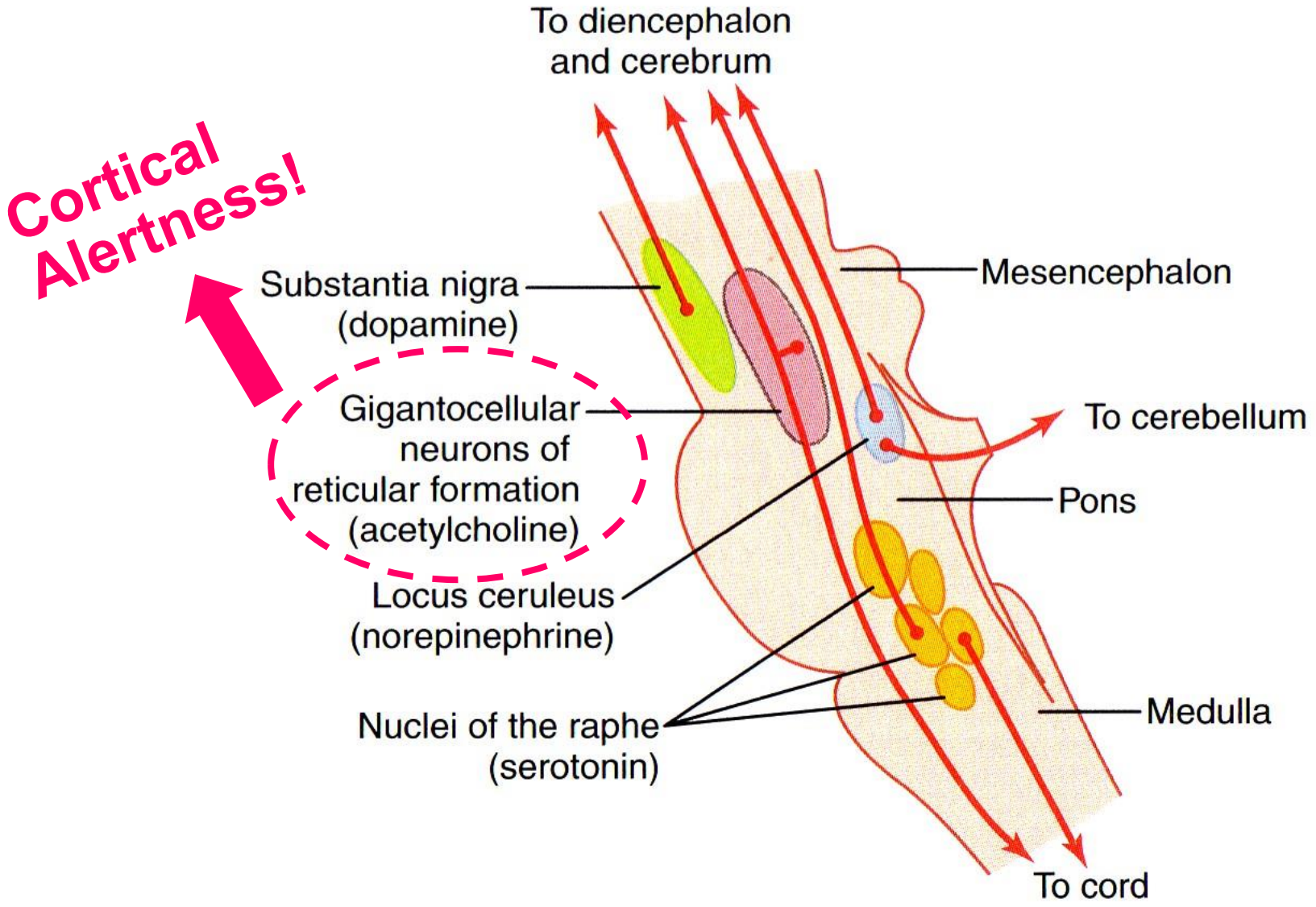
http://www.ncbi.nlm.nih.gov/pubmed/18624911



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

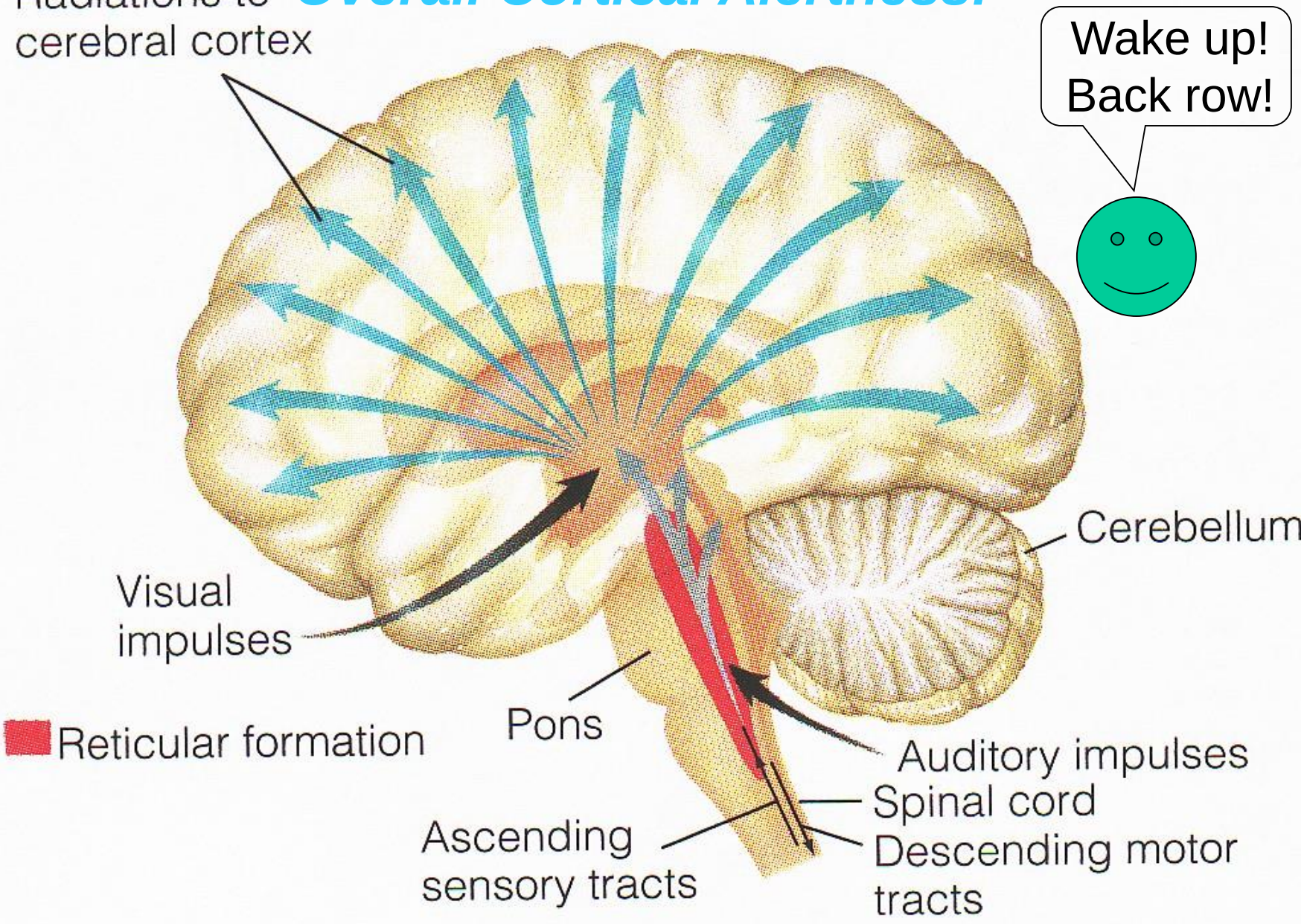
http://learn.genetics.utah.edu/content/addiction/

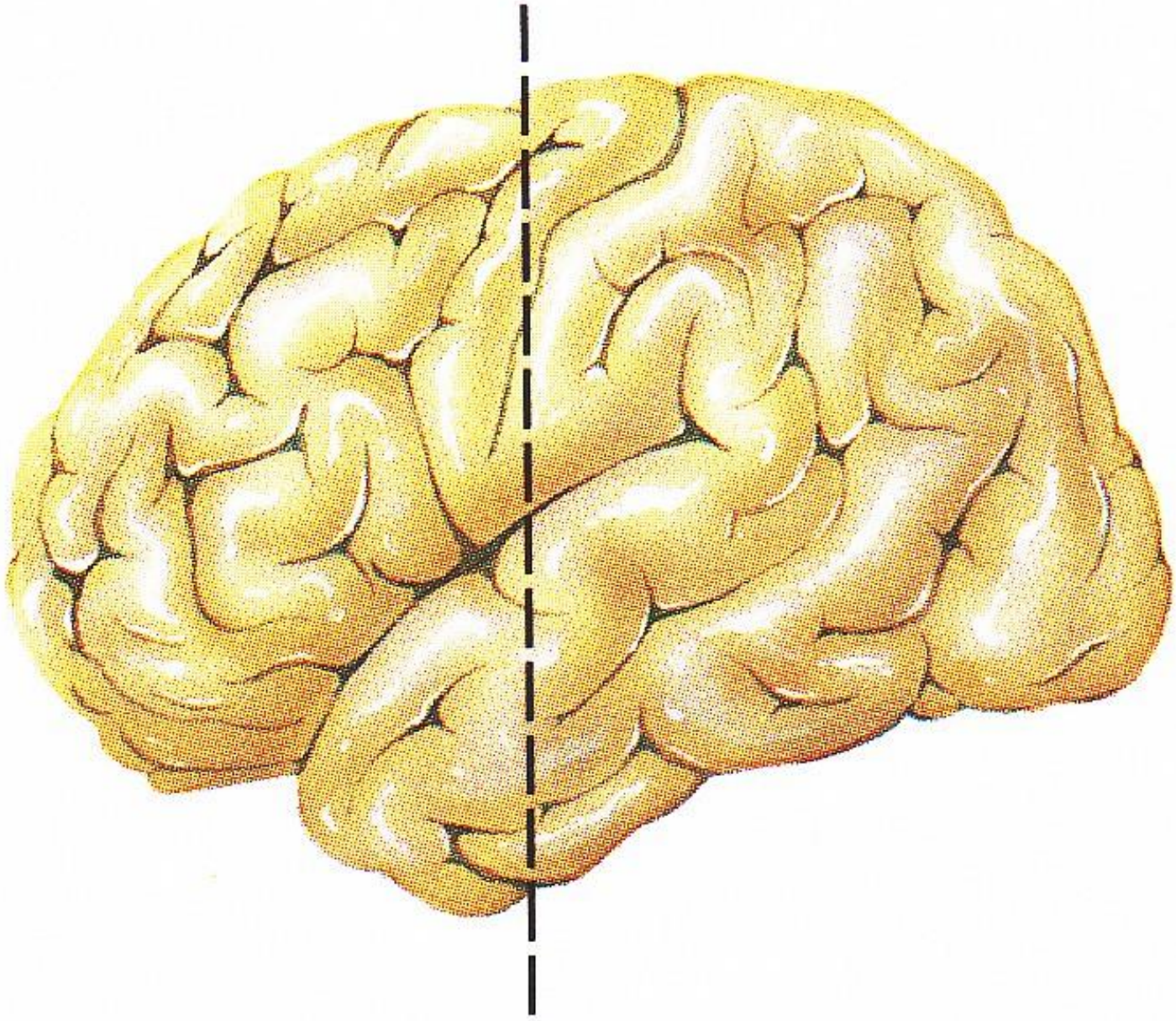
4th Pathway Releases Acetylcholine!

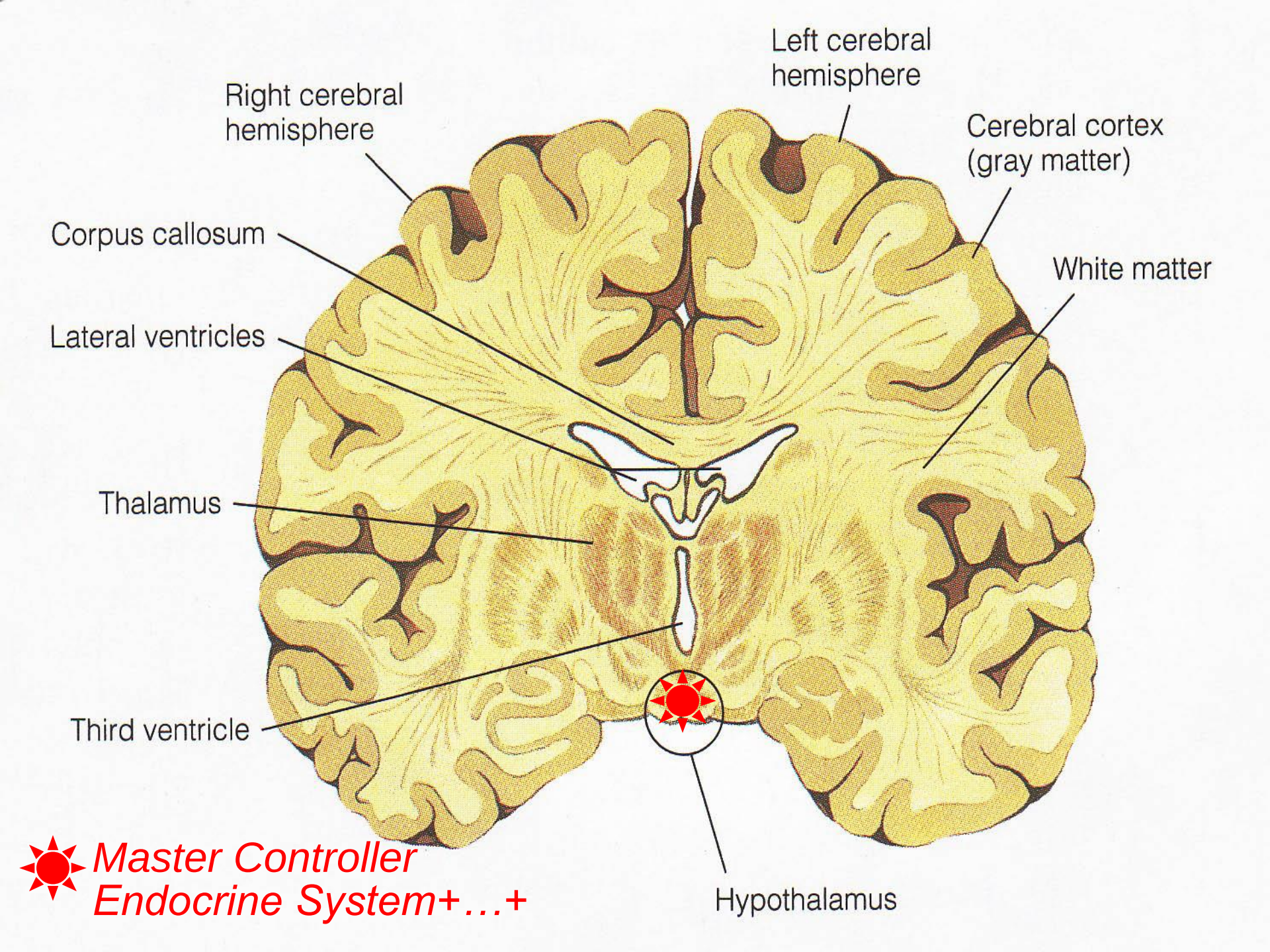


G&H 2011 p 713

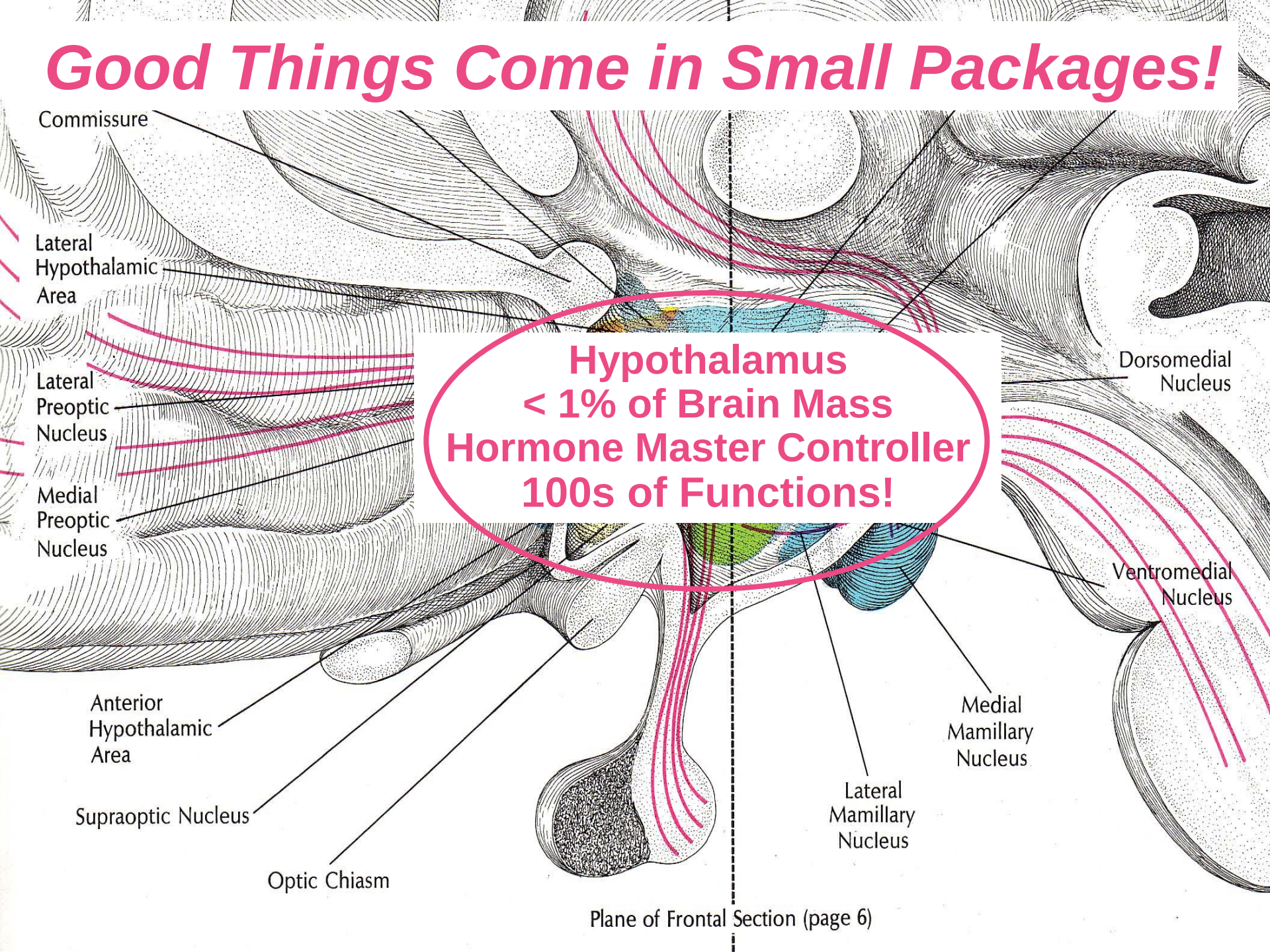
Reticular Activating System (RAS)
Overall Cortical Alertness!

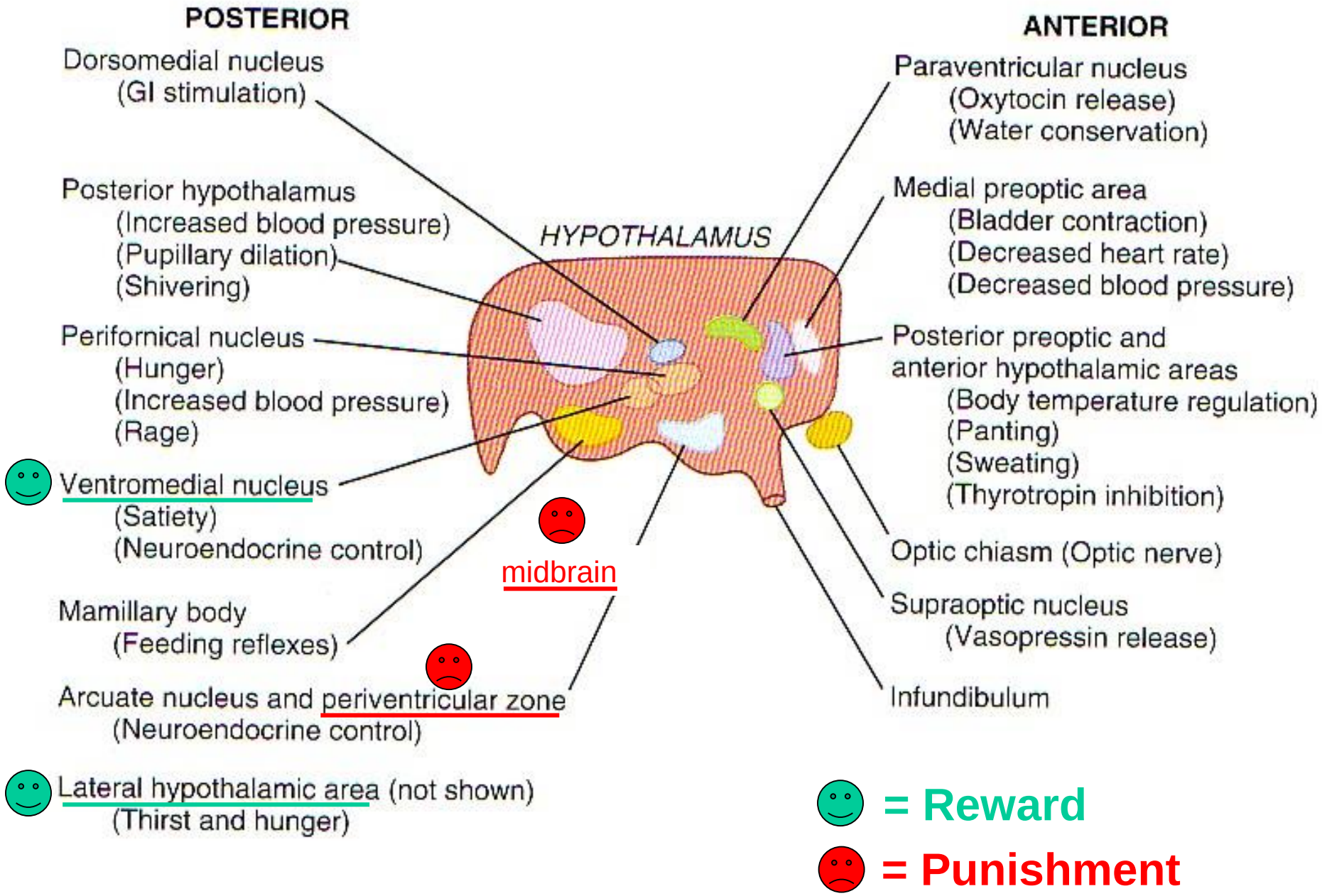





Left cerebral hemisphere
Right cerebral hemisphere
Cerebral cortex (gray matter)
Corpus callosum
White matter
Lateral ventricles
Thalamus
Third ventricle
Hypothalamus
Master Controller
Endocrine System+…+

Good Things Come in Small Packages!

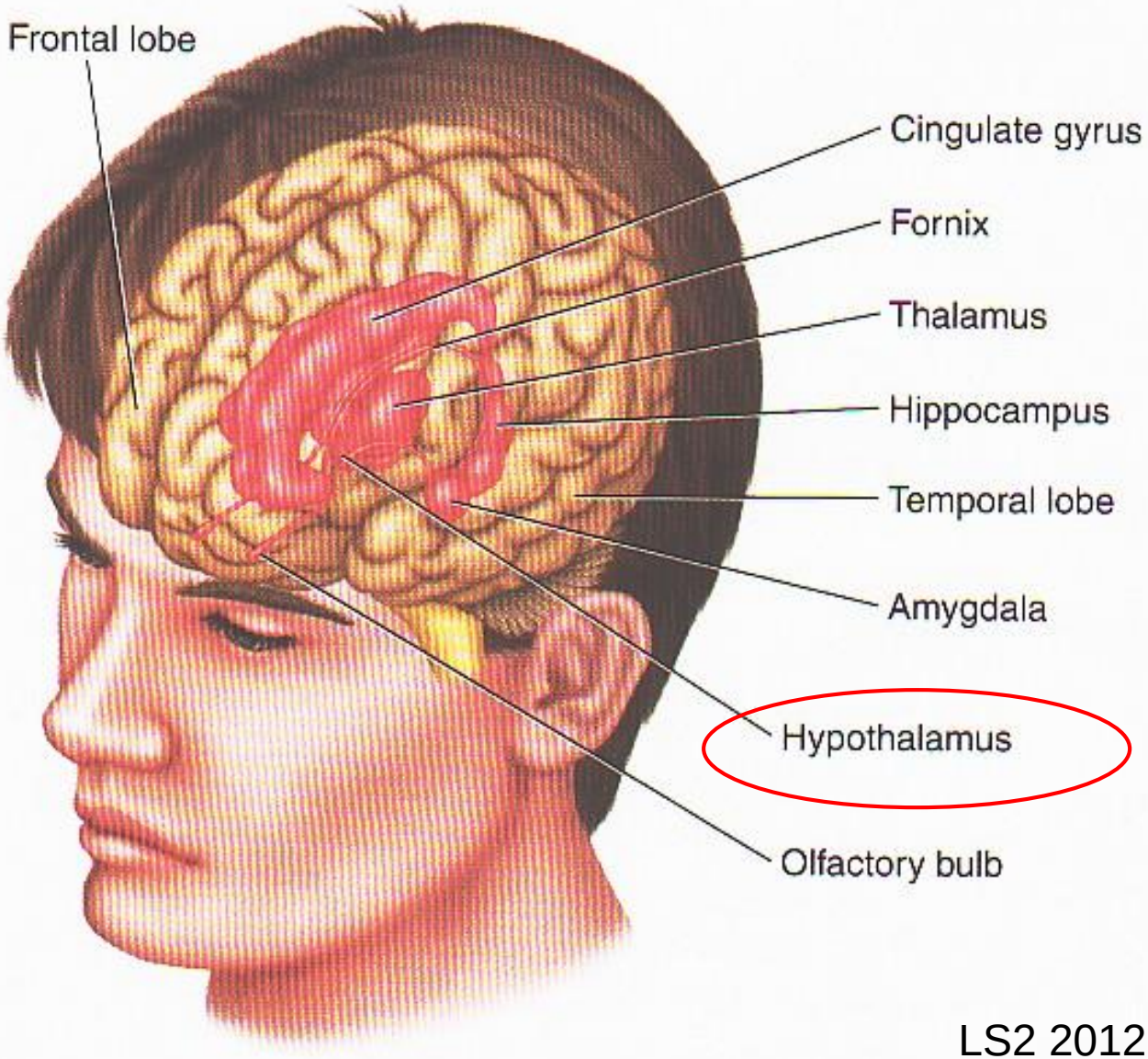



POSTERIOR
Dorsomedial nucleus
(GI stimulation)
Posterior hypothalamus
(Increased blood pressure)
(Pupillary dilation)
(Shivering)
Perifornical nucleus
(Hunger)
(Increased blood pressure)
(Rage)
Ventromedial nucleus
(Satiety)
(Neuroendocrine control)
Mamillary body
(Feeding reflexes)
Arcuate nucleus and periventricular zone
(Neuroendocrine control)
Lateral hypothalamic area (not shown)
(Thirst and hunger)
HYPOTHALAMUS
midbrain
ANTERIOR
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

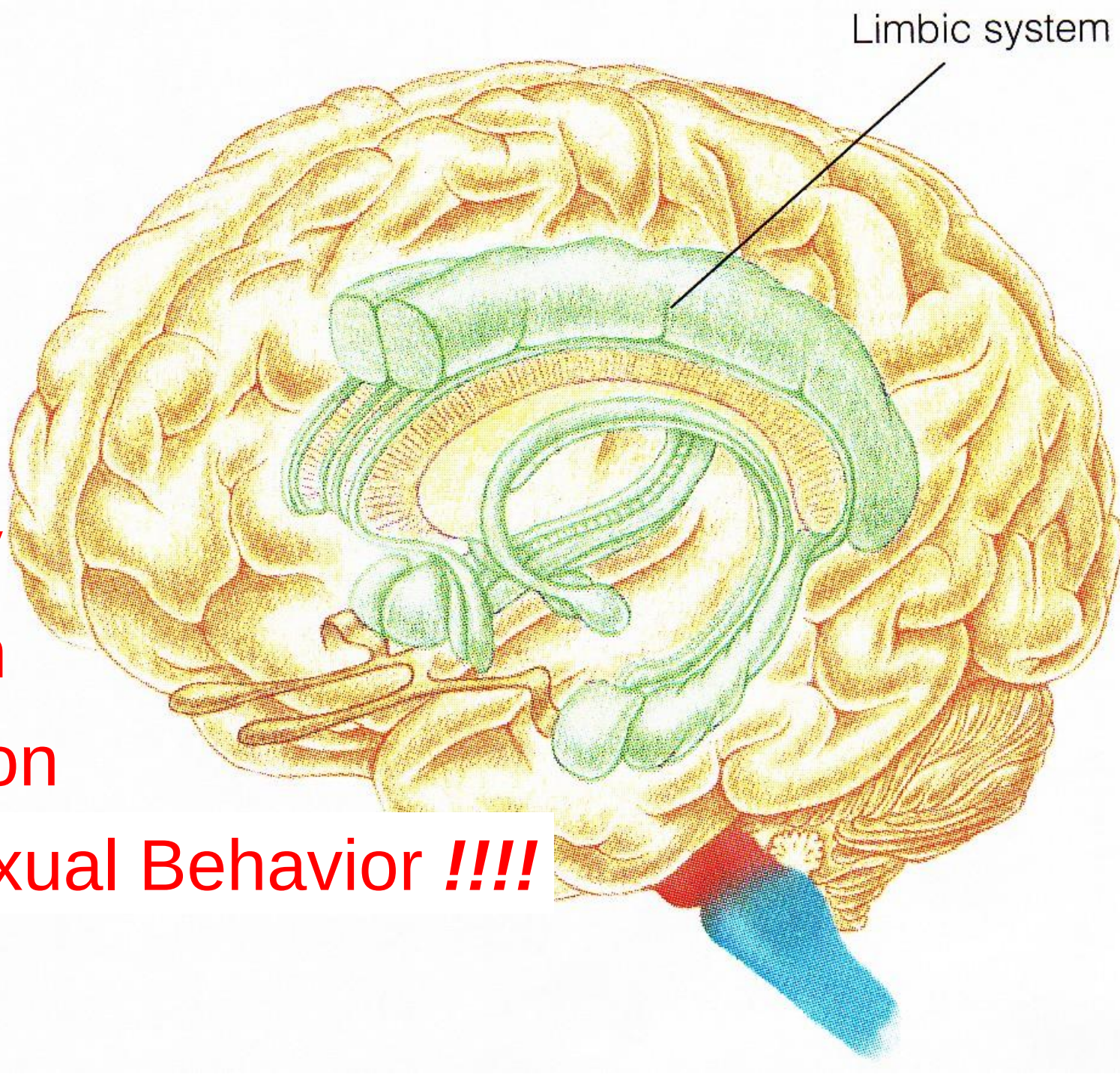
● FIGURE 5-18

Limbic system

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



LS2 2012 4th ed p 124

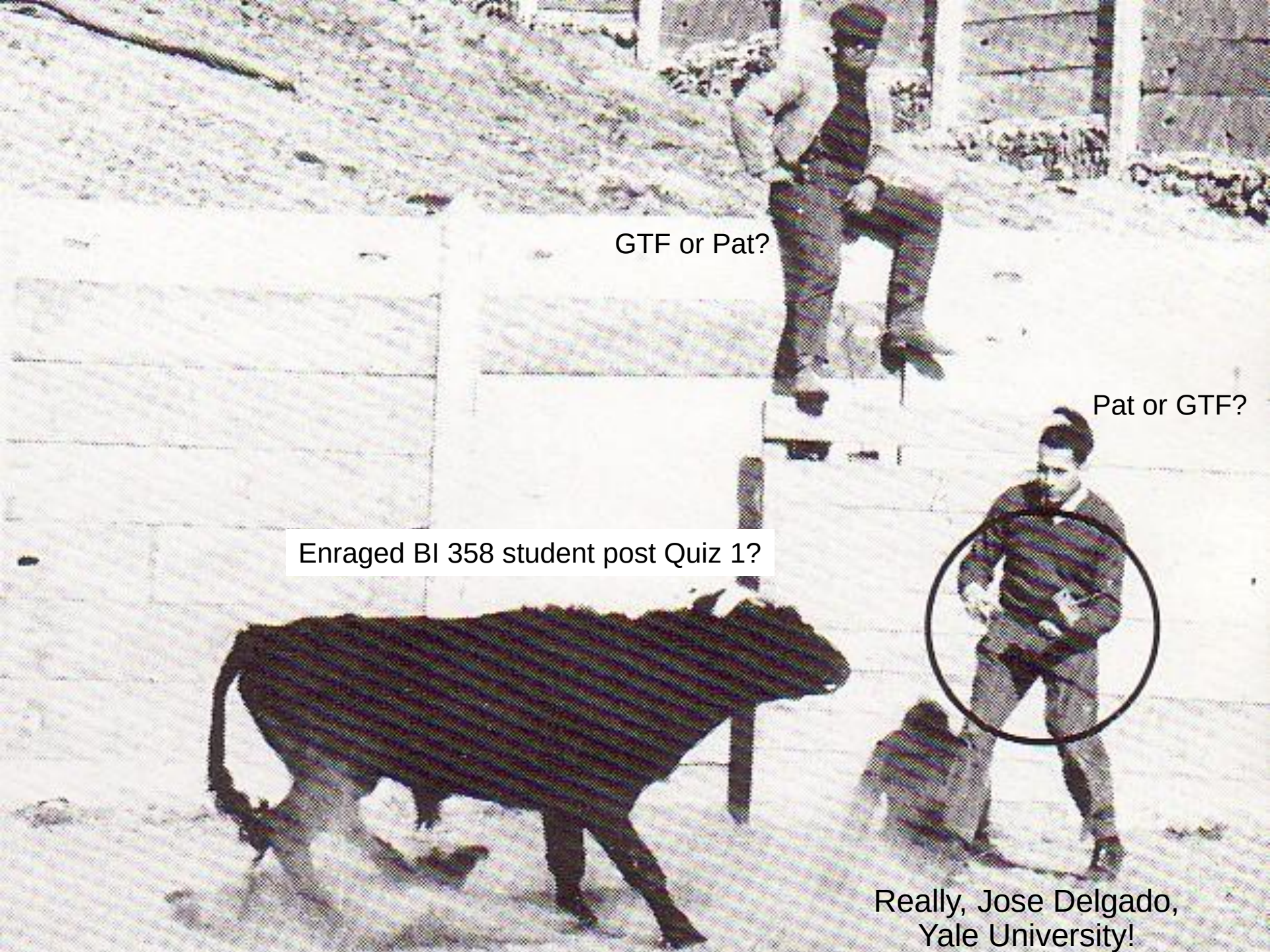


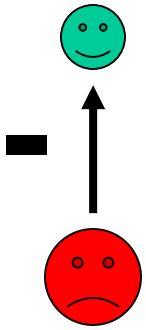
Memory

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, peri-ventricular zones

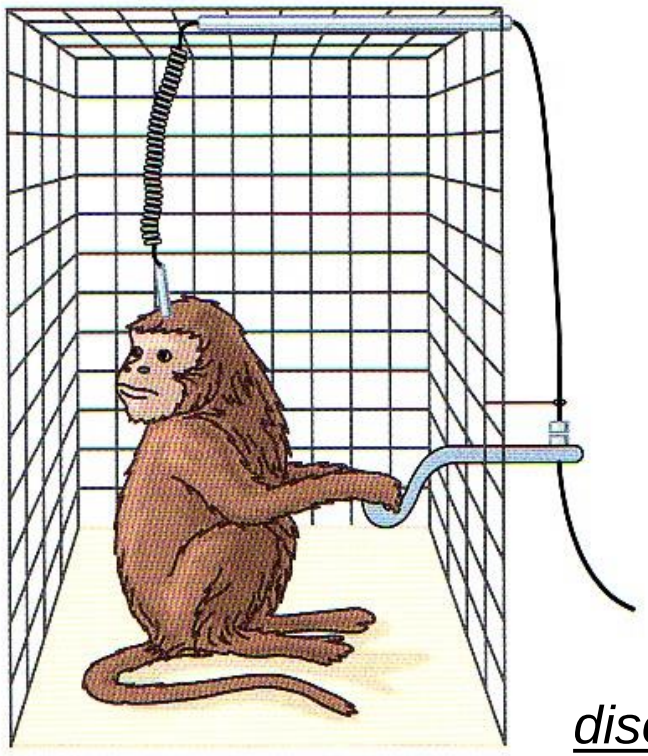


Figure 58–8

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

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

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

G&H 11th ed only p 735