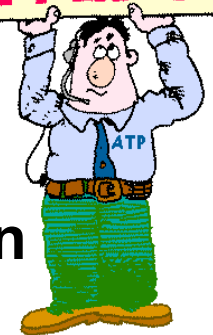


Come see us during office hr!



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

**APPLAUSE!**



## 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/>
- II. Medical Physiology in the News *Glymphatic System?*
- III. Homeostasis Connections BP e.g. Q? + Gain? G&H pp 7- 8
- IV. Discussion Follow-up Addiction Medicine  
Cigarette smoking, nicotine & PADDs!
- V. 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
- VI. 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
- VII. Addiction Medicine: Homeostasis & Applications

**Come see us!**



All @uoregon.edu

**BI 358 Office Hr Winter 2014**

<b><u>Day &amp; Time</u></b>	<b><u>Instructor</u></b>	<b><u>Place</u></b>	<b><u>e-mail</u></b>
<b>M 11 am-12n</b>	<b>Pat Lombardi<sup>+</sup></b>	<b>73A Klamath</b>	<b><u><i>lombardi</i></u></b>
<b>W 11:30-12:30 am-pm</b>	<b>Tony Yang</b>	<b>15E Klamath</b>	<b><u><i>anthonyy</i></u></b>
<b>R 10-11 am</b>	<b>Conor O'Sullivan<sup>+</sup></b>	<b>206 LISB</b>	<b><u><i>conoro</i></u></b>
<b>F 2-3 pm</b>	<b>Emile Rutherford<sup>+</sup></b>	<b>360 ONYX</b>	<b><u><i>srutherf</i></u></b>

**<sup>+</sup> and by appointment.**

**For Emile, please e-mail or call 541-346-4536.**

**For Conor, please e-mail or call 541-346-4536.**

**For Pat, please call 541-346-4536 or 541-346-6055.**

# ~ 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.

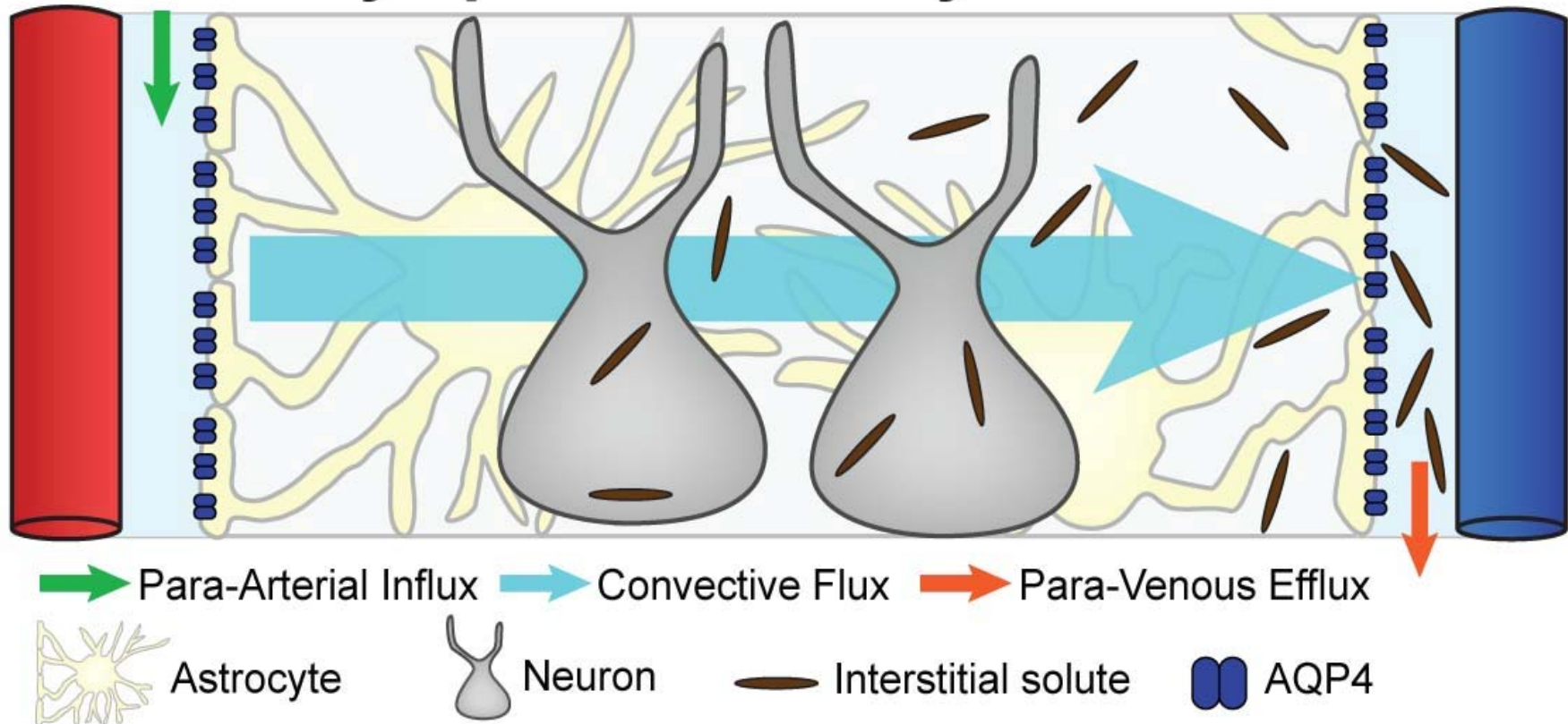
100 Billion Neurons →  
900 Billion Glial Cells!

Astrocytes

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

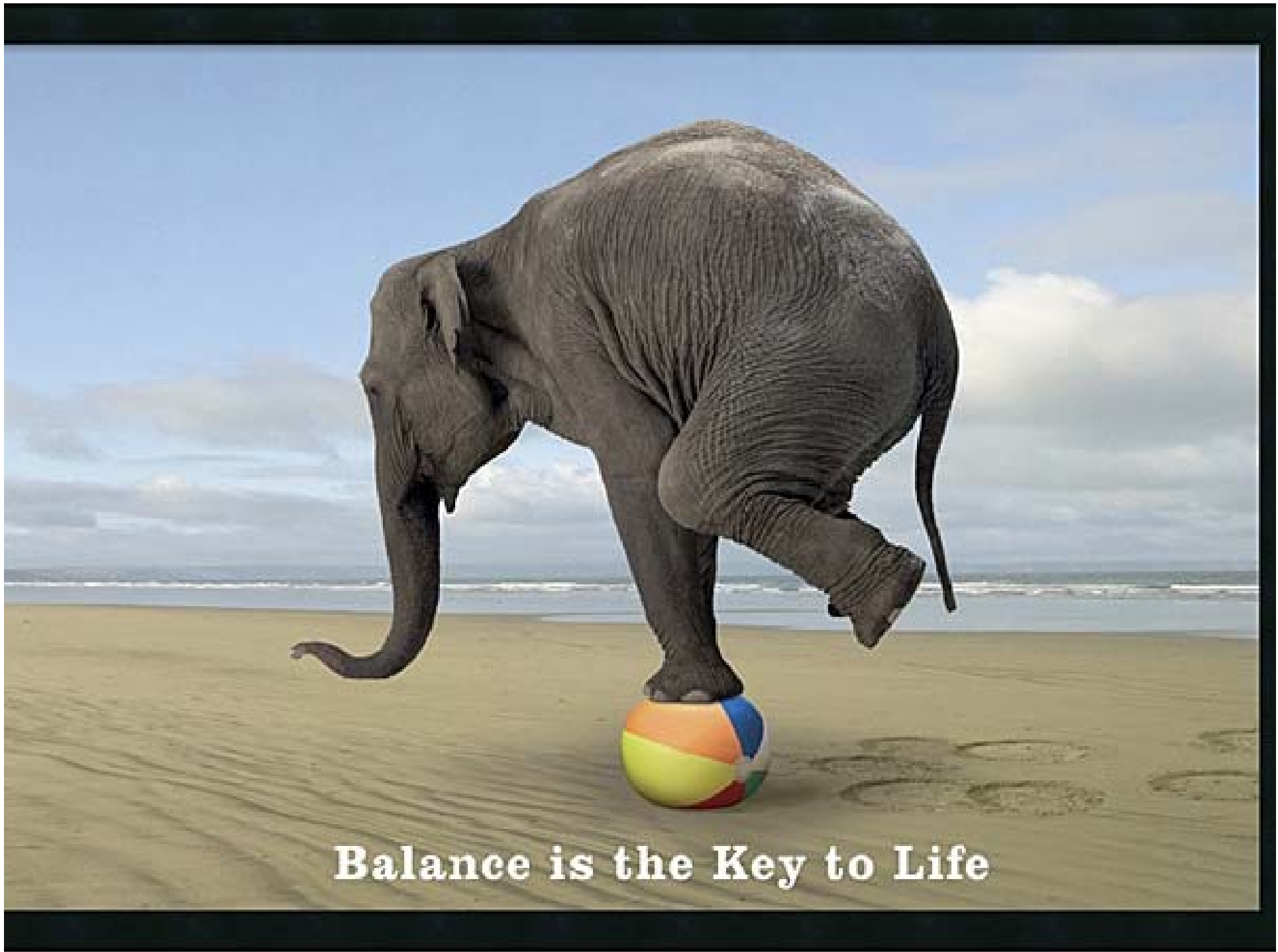
# *What the Heck is the Glymphatic System? CNS Functional Waste Clearance Pathway!*

## **Glymphatic Pathway Function**

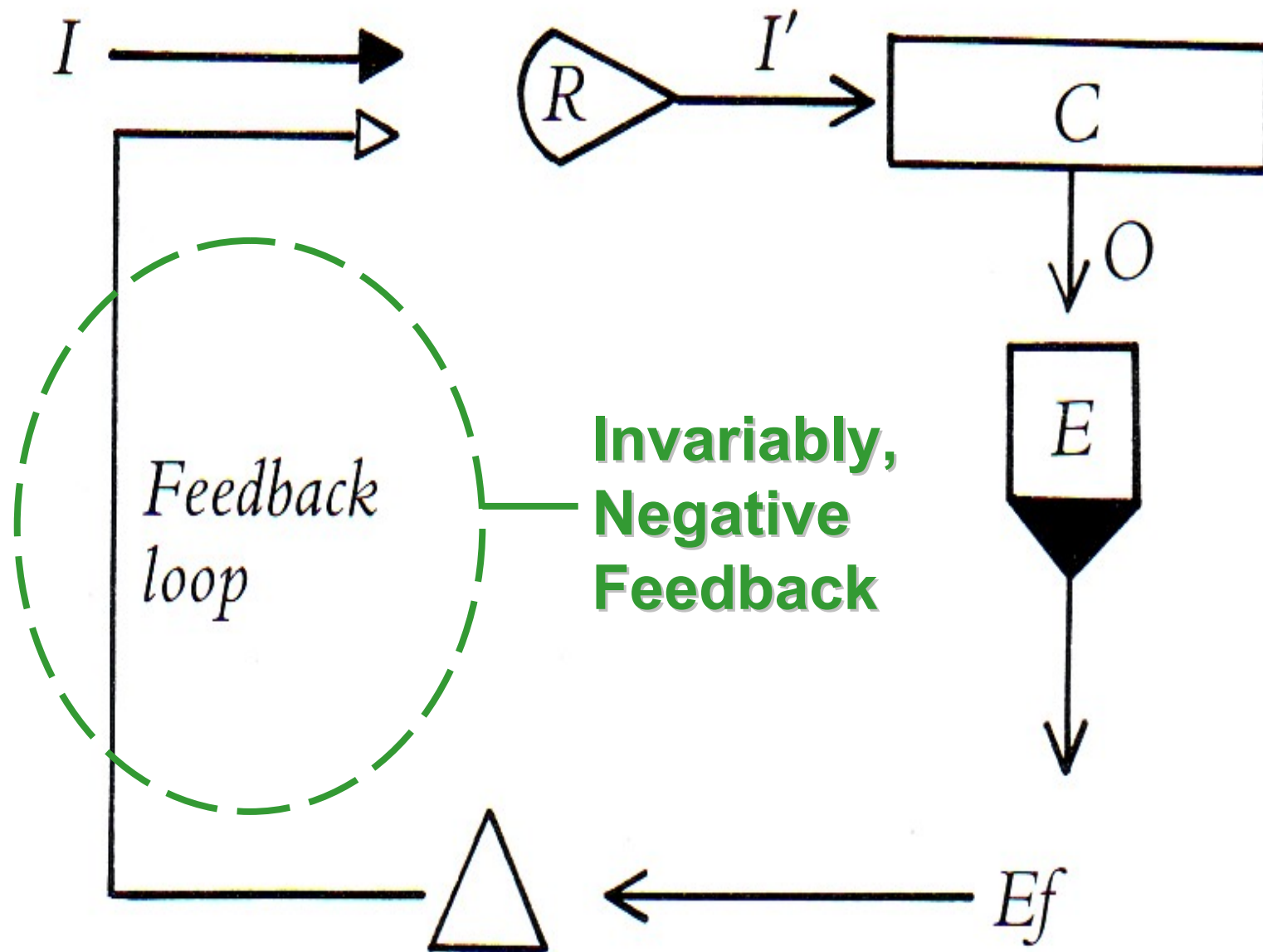


<http://www.sciencedaily.com/releases/2012/08/120815142042.htm>

[https://www.urmc.rochester.edu/labs/nedergaard-lab/projects/glymphatic\\_system](https://www.urmc.rochester.edu/labs/nedergaard-lab/projects/glymphatic_system)

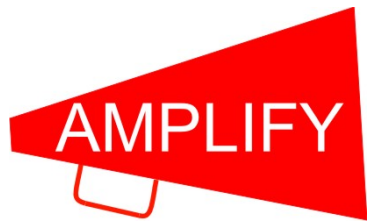


**Balance is the Key to Life**



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

**Selected +FB e.g.:**



**LH Surge → Ovulation**

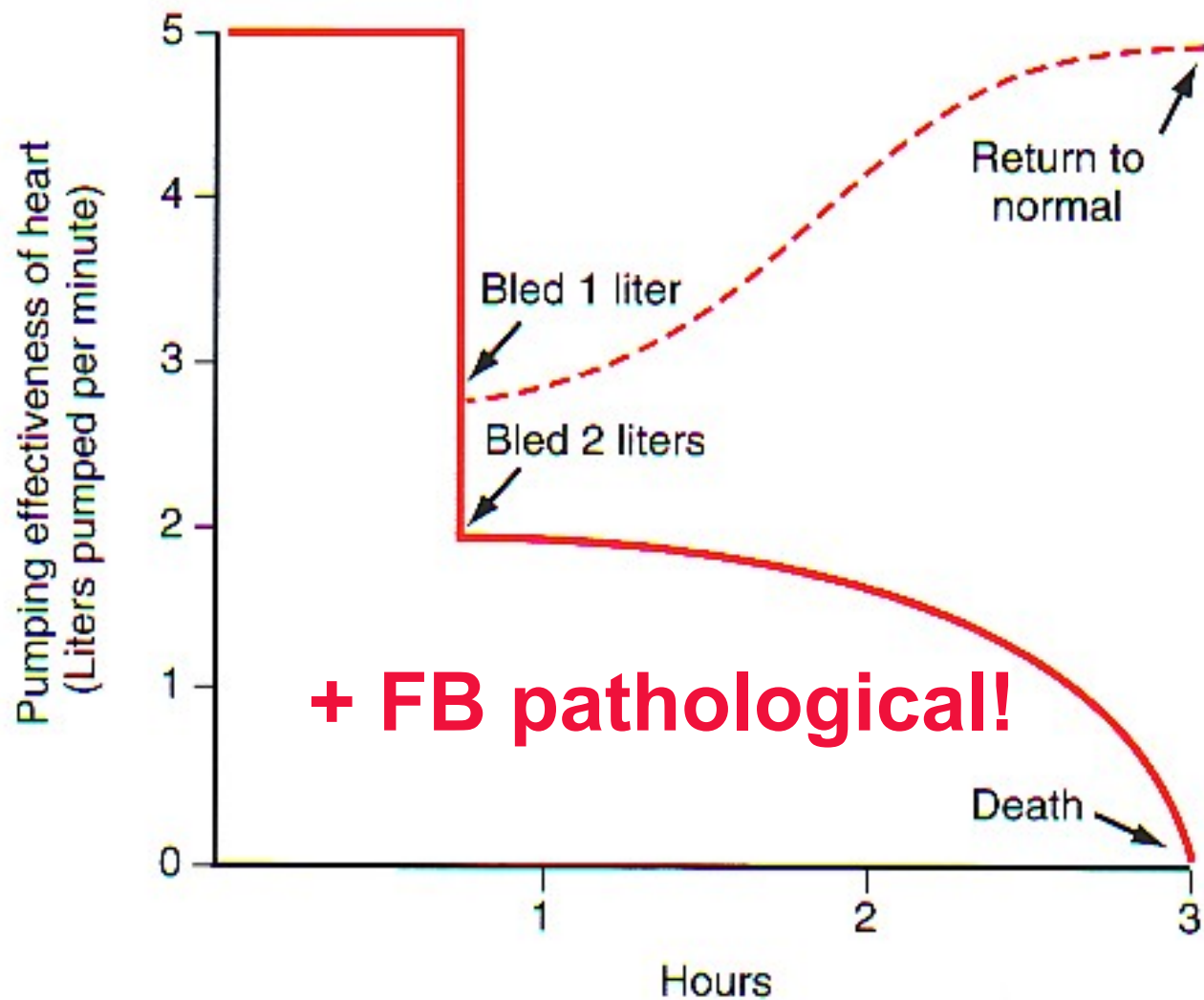
**Oxytocin → Uterine Contraction**

**Blood Clotting Cascade**

**cAMP Cascade**

**Na<sup>+</sup> influx during AP**

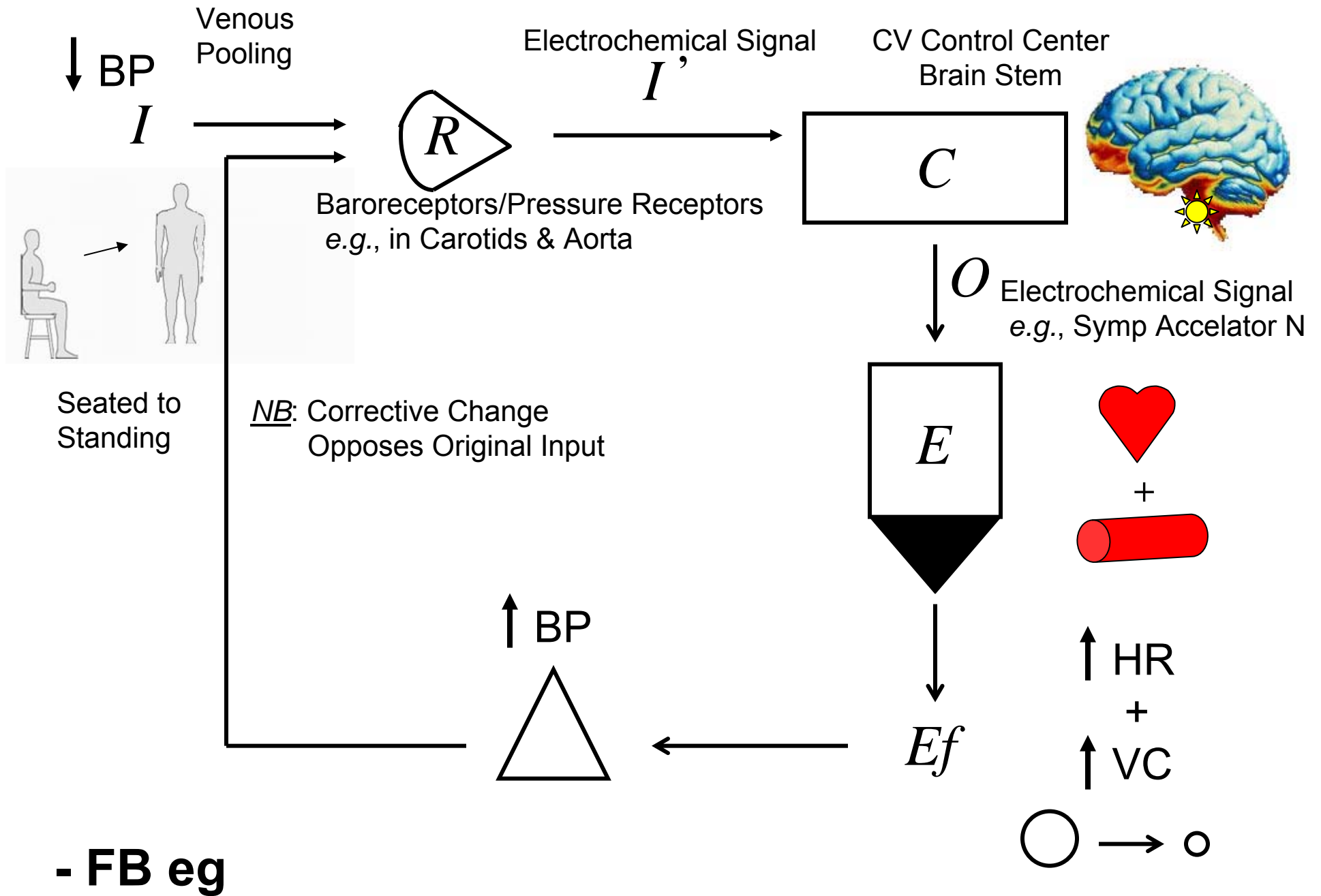
Nonpathological! Temporarily amplifies,  
but ultimately turned off by - FB!



**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.





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

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

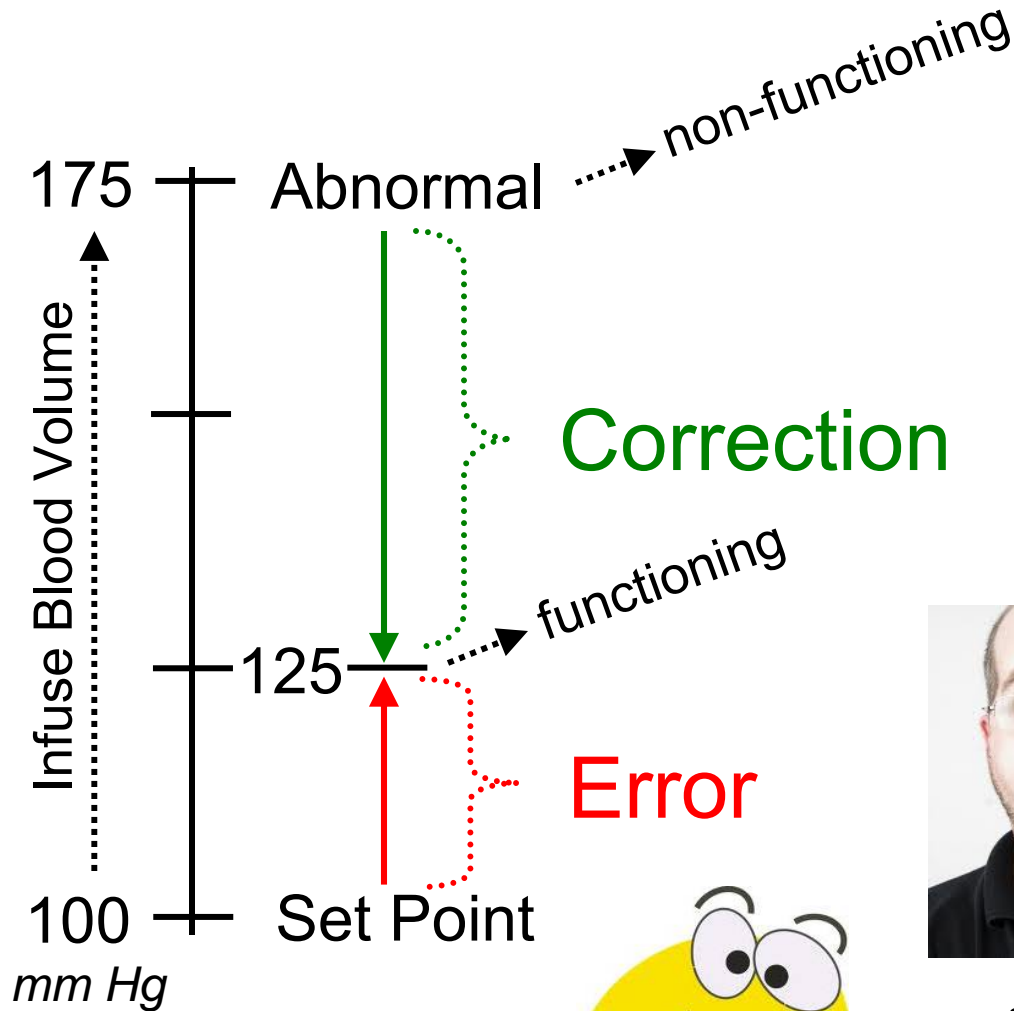
e.g., Transfuse large volume of blood into person with non-functioning Baroreceptor system

BP: 100 mm Hg → 175 mm Hg

...into person with functioning system

BP: 100 mm Hg → 125 mm Hg

# Gain for Human Baroreceptor System?



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

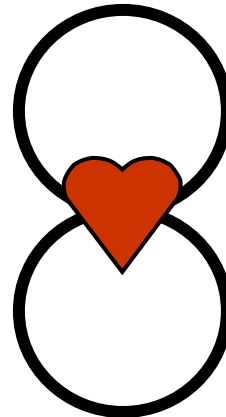


cf. Gain for Human Body Temperature = -33

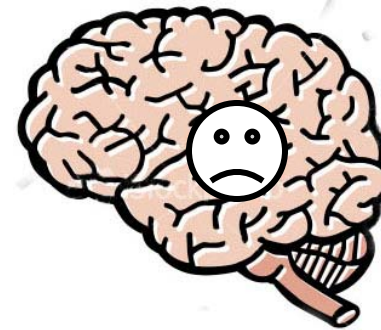
***Cigarettes ≡ Patient-Assisted Drug-Delivery System  
Inhaling Bypasses the Systemic Circulation  
& Is Powerfully Reinforcing!***



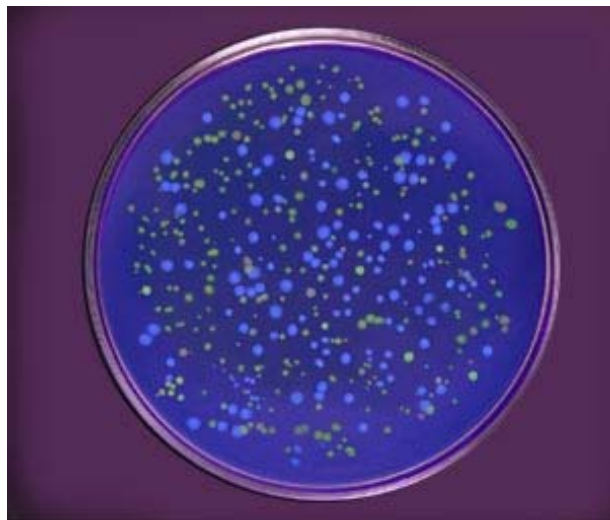
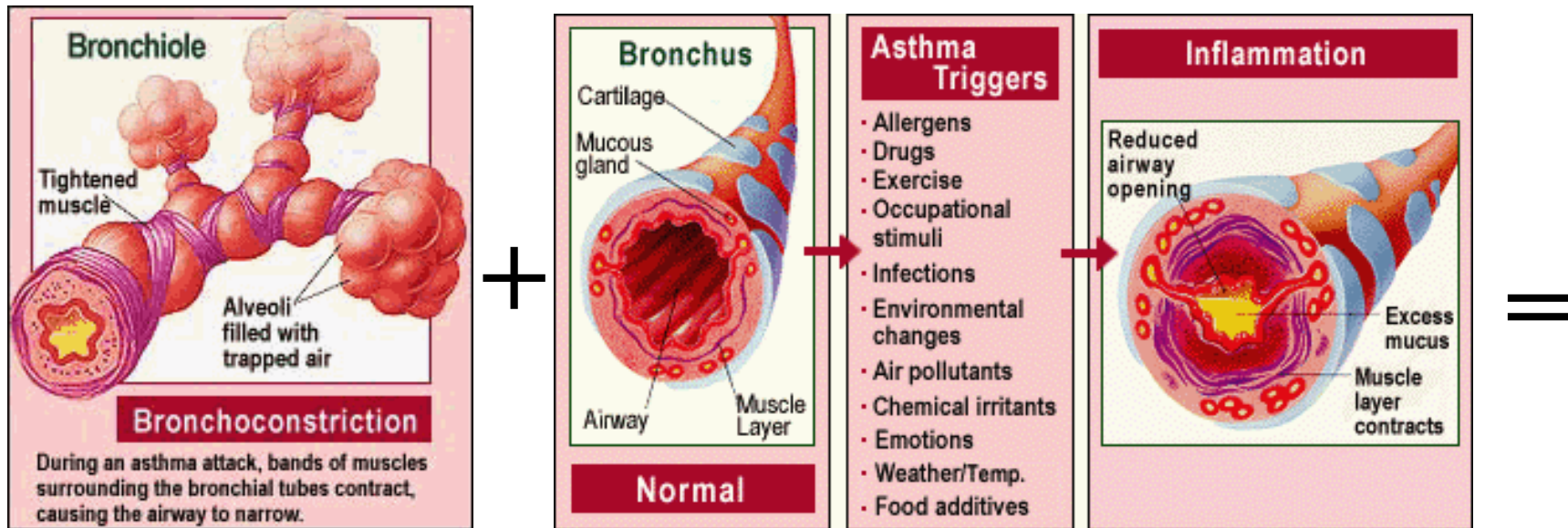
Pulmonary



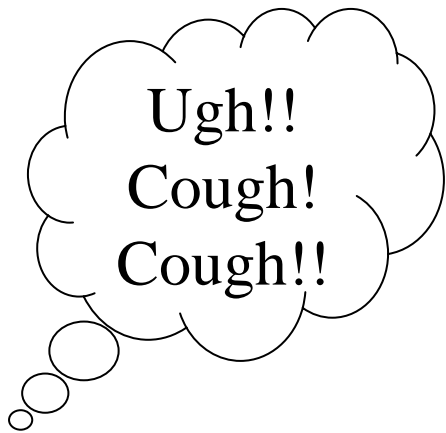
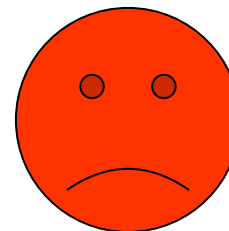
Systemic



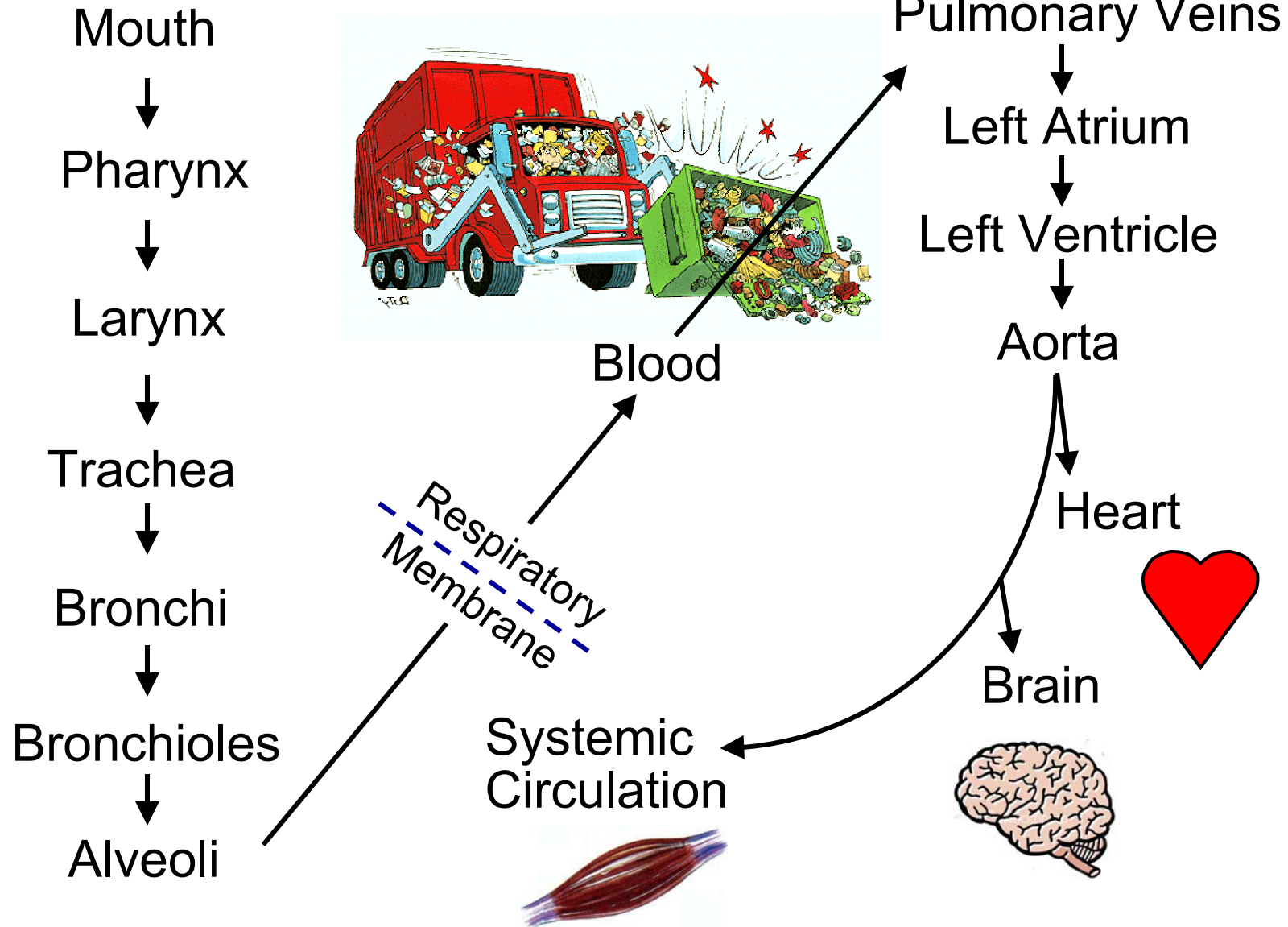
# SMOKING ≡ ASTHMA?



**Petri-dish  
Effect**



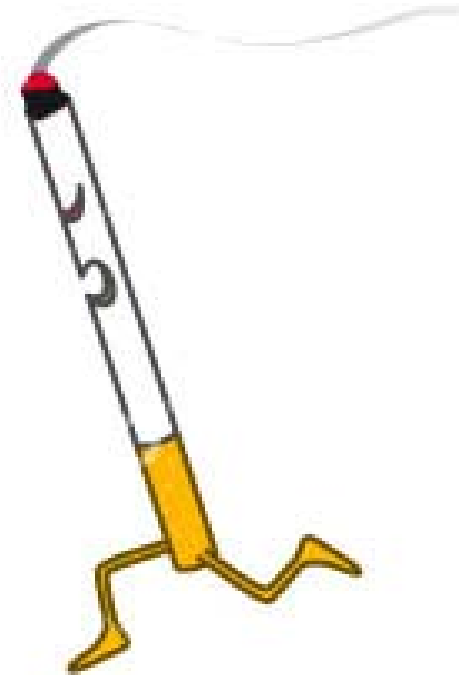
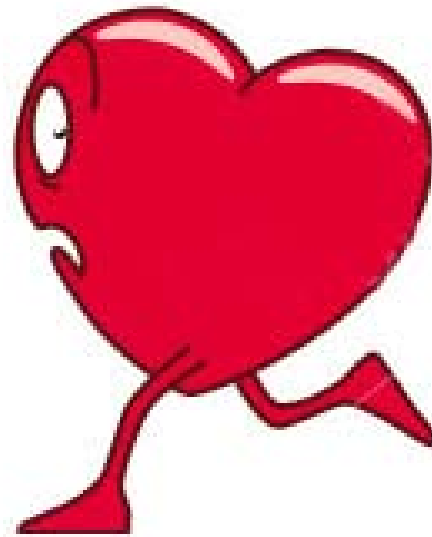
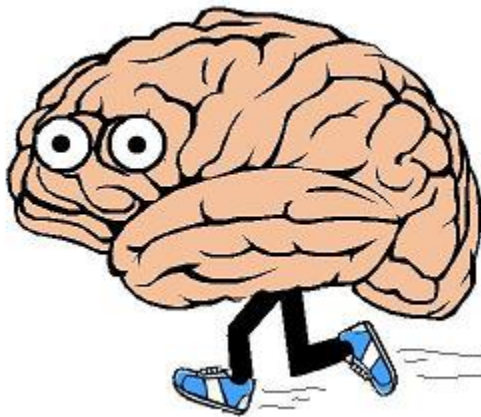
# Tracing the Route of Cigarette Smoke Puff to Brain Time 5 to 8 seconds!!



***Not only the Lungs, Heart & Brain, but 100s of Other Tissues & Organs are Adversely Affected!***



So sorry I was forced to deliver!



**Cigarette + Smoke: > 7000 Chemicals; ~600 Tobacco Company Additives  
Atherogenic, Carcinogenic (C), Tumor Initiating, Tumor Promoting (TP),  
Toxic (T) Cornucoppia of Unknowns, Synergistic, Reactive...?**

4-aminobiphenyl	C	140 ng <u>per cigarette</u> ...
benz(a)anthracene	C	40-200 ng
benzene	C	400 µg
benz(o)pyrene	C	40-70 ng
carbon monoxide	T	26.8-61 mg
formaldehyde	C	1500 µg
hydrazine	C	90 ng
hydrogen cyanide	T	14-110 µg
2-naphthylamine	C	70 ng
nitrogen oxides	T	500-2000 µg
N-nitrosodimethylamine	C	200-1040 ng
N-nitrosodiethanolamine	C	43 ng
N-nitrospyrrolide	C	30-390 ng
phenol	TP	70-250 µg
polonium 210	C	0.5-1.6 pCi
quinoline	C	15-20 µg
O-toluidine	C	3 µg

**SOURCES: US Surgeon General's Office, American Cancer Society, American Heart Association.**



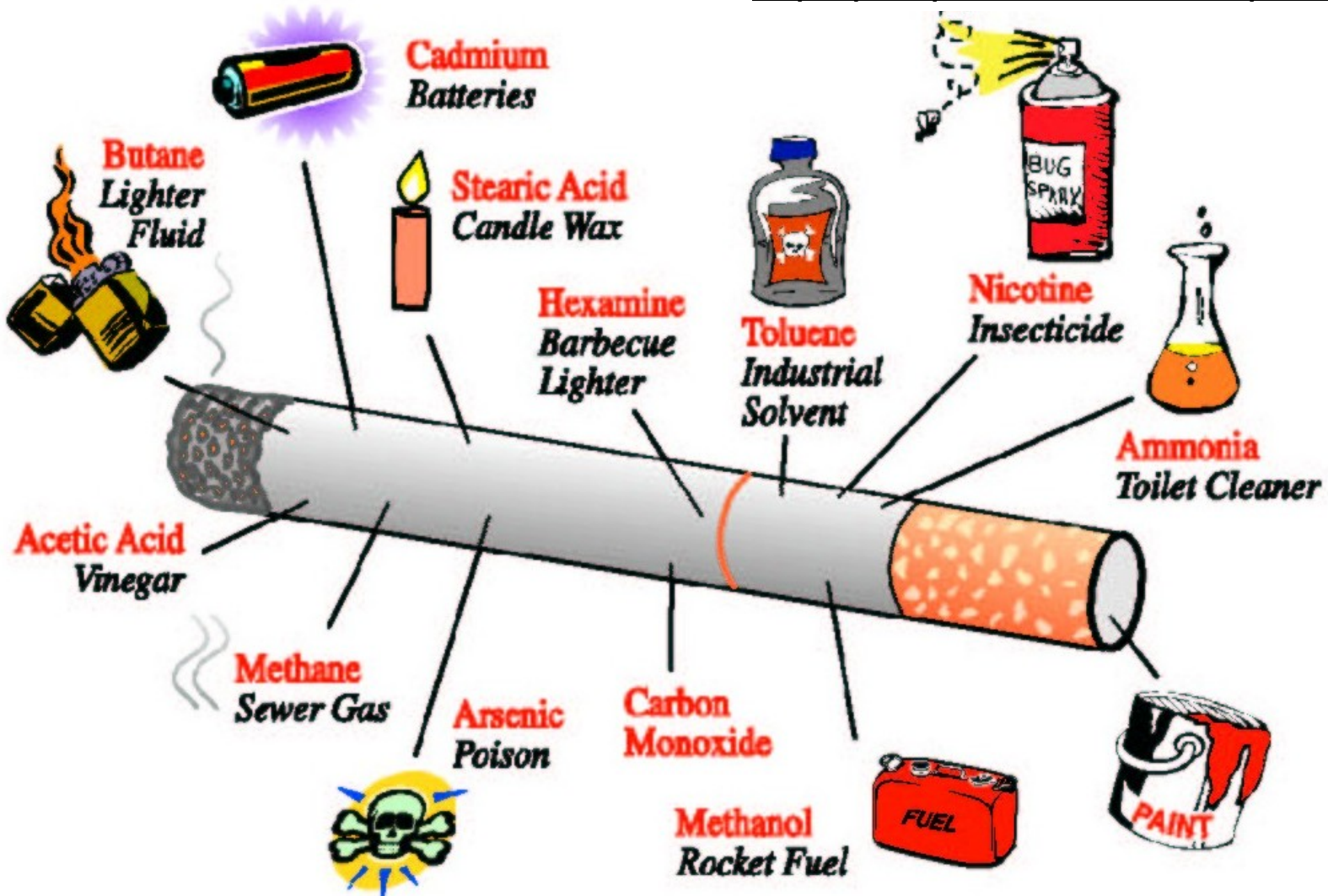
...propyl acetate, 2-Propylpropanoate, 2-(2-Propylpropanoate), Phosphoric Acid, Pimenta Leaf Oil, Pine Needle Oil, Pine Oil, Scotch, Pineapple  
...trate, alpha-Pinene, beta-Pinene, D-Piperitone, Piperonal, Pipsissewa L  
... Potassium Sorbate, 1-Proline, Propenylguaethol, Propionic Acid, Propyl  
...hydroxybenzoate, Propylene Glycol, 3-Propylideneephthalide, Prune Juice  
...e, Pyroligneous Acid And Extract, Pyrrole, Pyruvic Acid, Raisin Juice Co  
...nol, Rose Abs... l, Rum, Rum Ether, Rye Extract,  
...age Oleoresin...ood Oil, Yellow, Sclareolide, Ska  
...; Snakeroot C...n Benzoate, Sodium Bicarbonate  
...nate, Sodium... Sodium Hydroxide, Solanone, Spe  
...t, Gum and Oil, Sucrose Octaacetate, Sugar Alcohols, Sugars, Tagetes  
...ic Acid, Tea Leaf and Absolute, alpha-Terpineol, Terpinolene, Terpinyl Ac  
...3-Tetrahydroquinoxaline, 1,5,5,9-Tetramethyl-13-Oxatricyclo(8.3.0.0(4,9))  
...5, and 3,4,5,6-Tetramethylethyl-Cyclohexanone, 2,3,5,6-Tetramethylpyraz  
...chloride, Thiazole, 1-Threonine, Thyme Oil, White and Red, Thymol, Tob  
...pherols (mixed). Tolu Balsam Gum and Extract Toluvaldehydes para-Tol

Absorbs H<sub>2</sub>O  
Preserves tobacco  
Antifreeze & de-icing  
Polyester compounds  
Artificial smoke in  
Theater & electric cigarettes

**American Cancer Society**  
**What's in tobacco?**

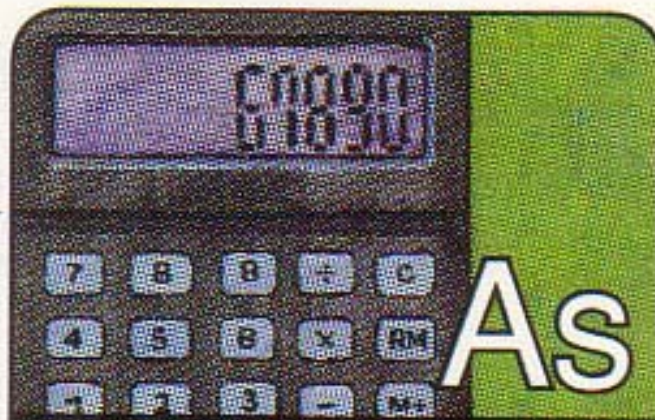
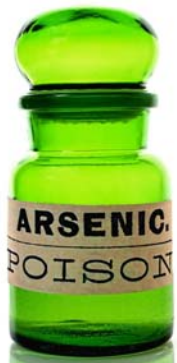
**US Food & Drug Administration**  
**Constituents in tobacco?**

<http://pmep.cce.cornell.edu/profiles/>



<http://livealittlelonger.wordpress.com/tobacco/whats-inside-that-cigarette/>


<http://www.smokefree.gov/>



**As**

**Arsenic 33**

- o Shotgun pellets
- + Metal for mirrors
- v Glass, lasers
- v **Light emitting diodes=LED**
- x 74.9216



**Po**

**Polonium 84**

- o **Nuclear batteries**
- o Neutron source
- o Antistatic agents
- o Film cleaner
- x (209)

**RODENT POISON**  
in your  
**SMOKES?**



## TOBACCO ADDITIVES

The tobacco industry has acknowledged that nearly 600 chemicals are added to cigarettes. It is not clear, however, how much of the various additives are used or which combinations appear together. Some of the chemicals among cigarette additives most questioned by tobacco opponents include:

■ **Megastigmatrienone:** A flavoring that tobacco companies contend is found naturally in grapefruit juice.

■ **Dehydromenthofuro lactone:** A flavoring that tobacco companies say is found in peppermint.

■ **Ethyl furoate:** Found naturally in coffee, kiwi and peanuts.

■ **Maltitol:** A sweetener used in chewing gum and diabetic candy.

■ **Sclareolide:** A synthetic form of a naturally occurring tobacco element.

■ **Ammonia:** A processing aid.

■ **Methoprene:** An insecticide that toxicologists say is biodegradable.

■ **Other additives:** Yeast, wine, caffeine, beeswax, beta carotene, chocolate, coconut oil.



## freebase nicotine!!

Ammonia converts nicotine, the addictive agent in tobacco, into a more volatile form, Pan-kow said. “Ammonia is the thing that helps tobacco companies hook the smoker by providing a means of delivering the nicotine.”

Last October a former tobacco industry employee revealed that secret industry documents indicated that ammonia was added to tobacco to double the impact of nicotine. The Oregon Graduate Institute study confirms the contention that

# Tobacco-free Campus

For better health,  
smoking and use of  
tobacco products are  
prohibited everywhere  
on our property.



UO's Josh Buehler

U.S. Surgeon General  
Regina Benjamin

## SMOKE AND TOBACCO-FREE UNIVERSITY



**September 1, 2012**

For a healthier community and cleaner  
environment, the University of Oregon  
will be smoke and tobacco free



**Ready to Quit Tobacco?**

Visit [tobaccofree.uoregon.edu](http://tobaccofree.uoregon.edu) for free and low cost resources



UNIVERSITY OF OREGON

[tobaccofree.uoregon.edu](http://tobaccofree.uoregon.edu)

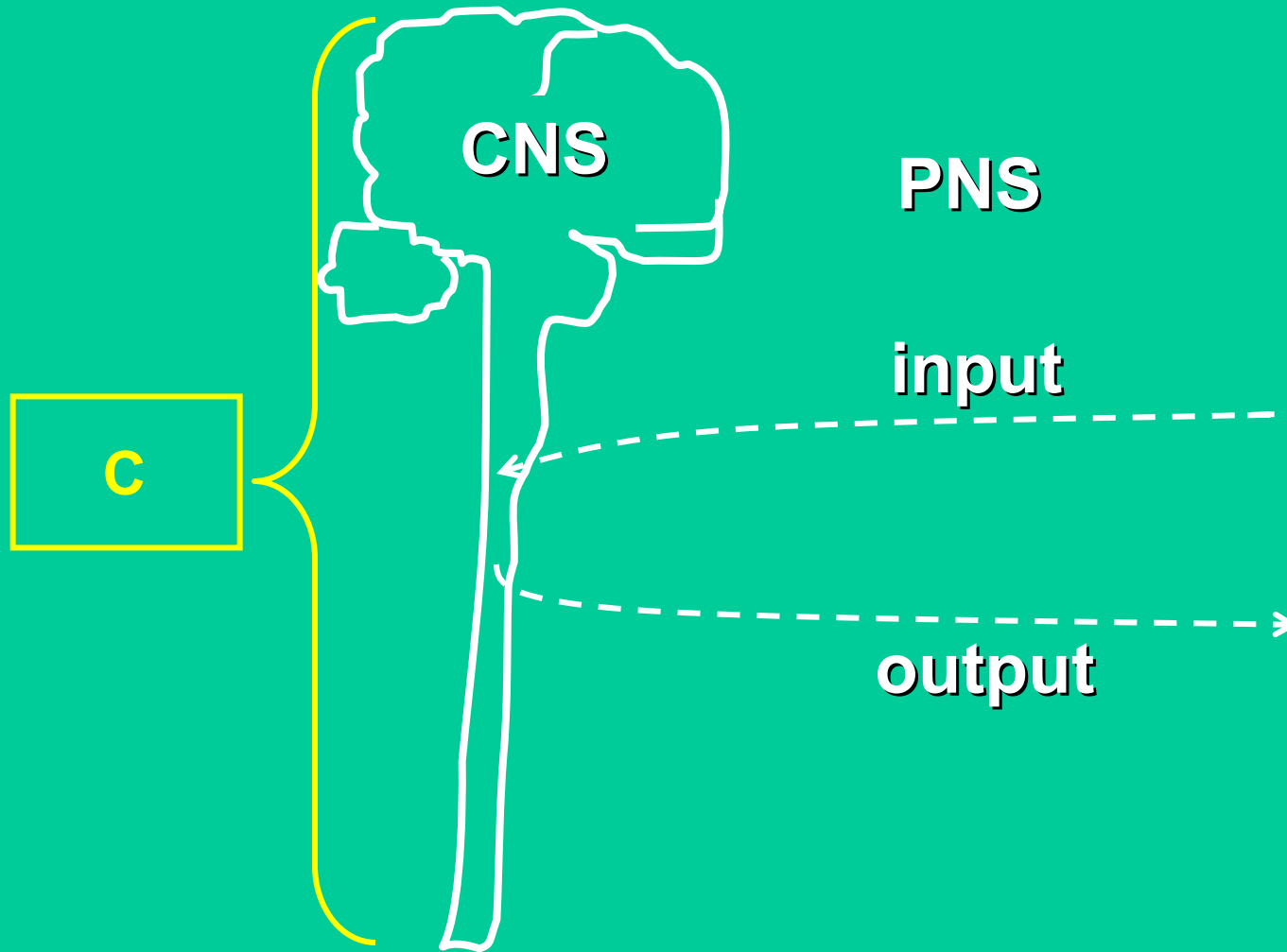


For a healthier community and cleaner  
environment, the University of Oregon  
is smoke and tobacco-free.

*Discussion/Questions?*



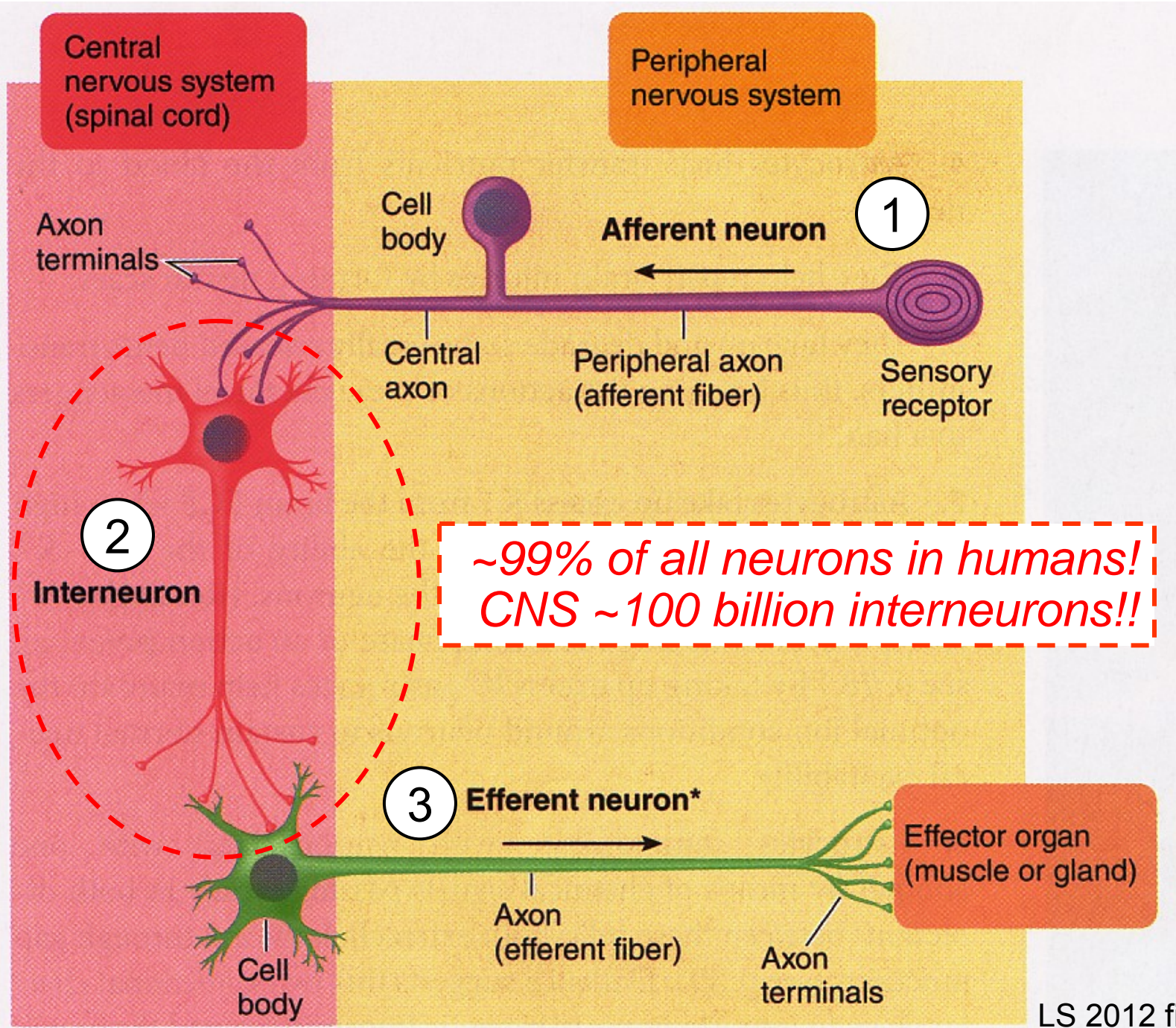
# Nervous System



*Systems Level*

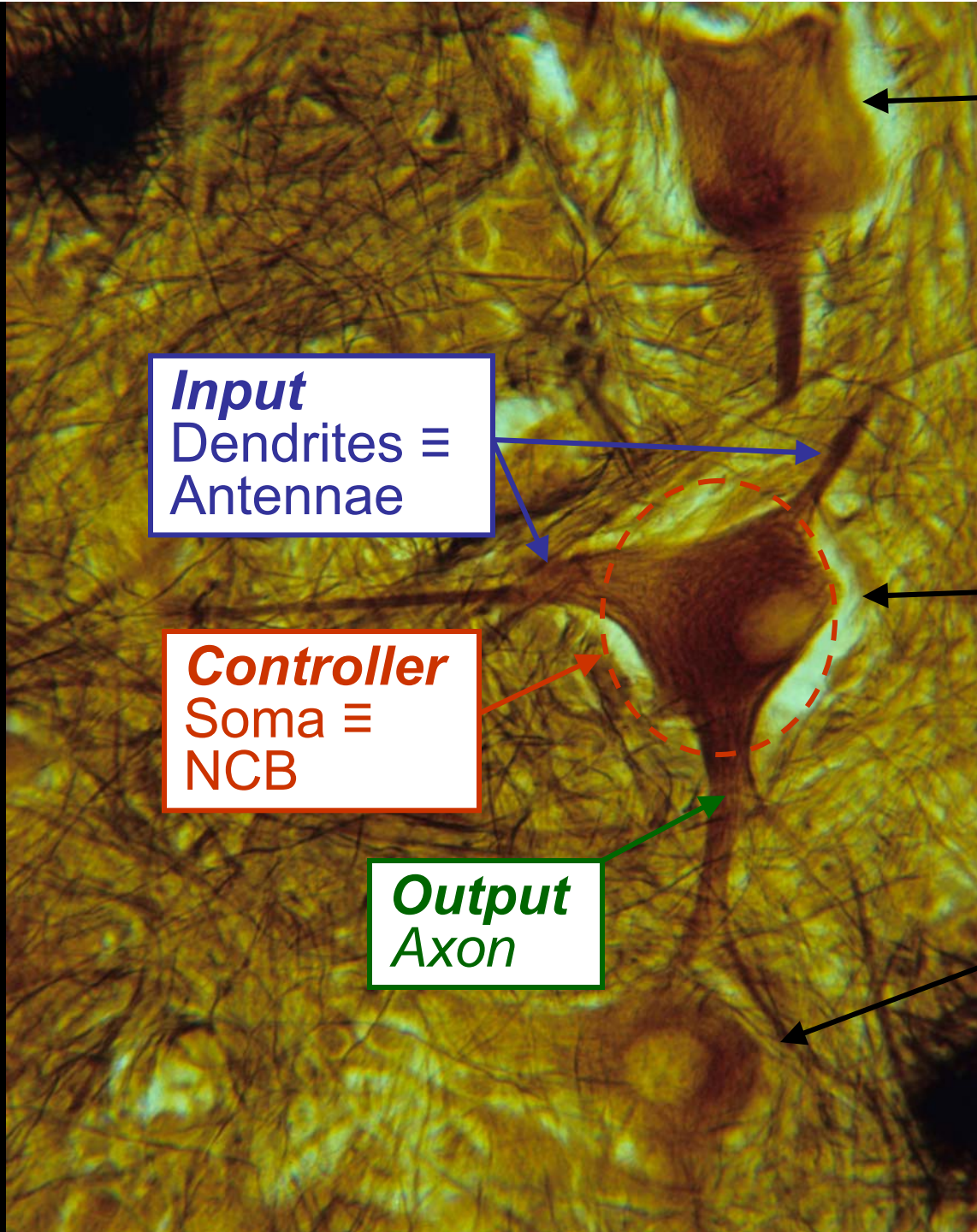


Organ/Tissue Level



LS 2012 fig 5-2

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



Neuron 1

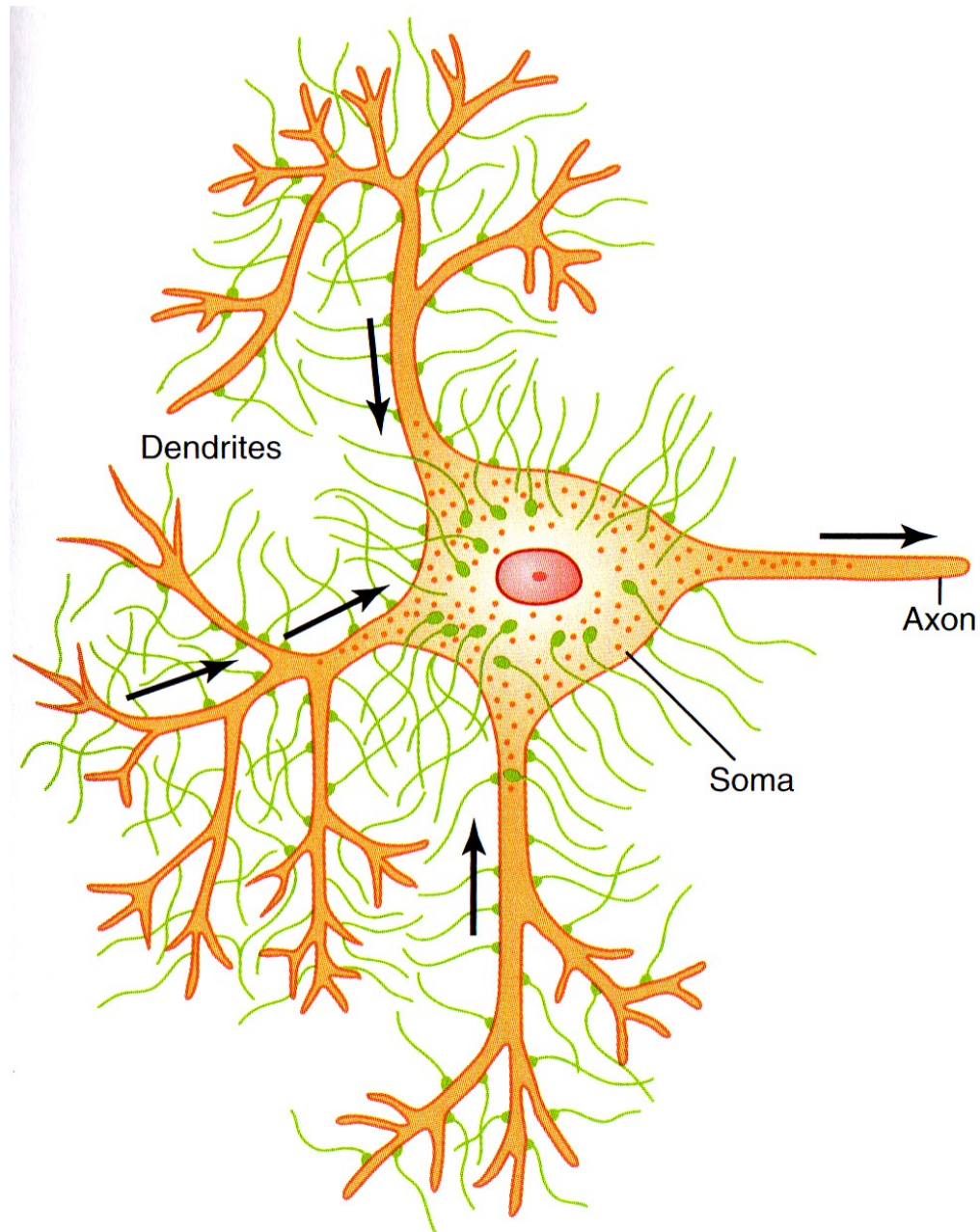
**Input**  
Dendrites ≡  
Antennae

Neuron 2

**Controller**  
Soma ≡  
NCB

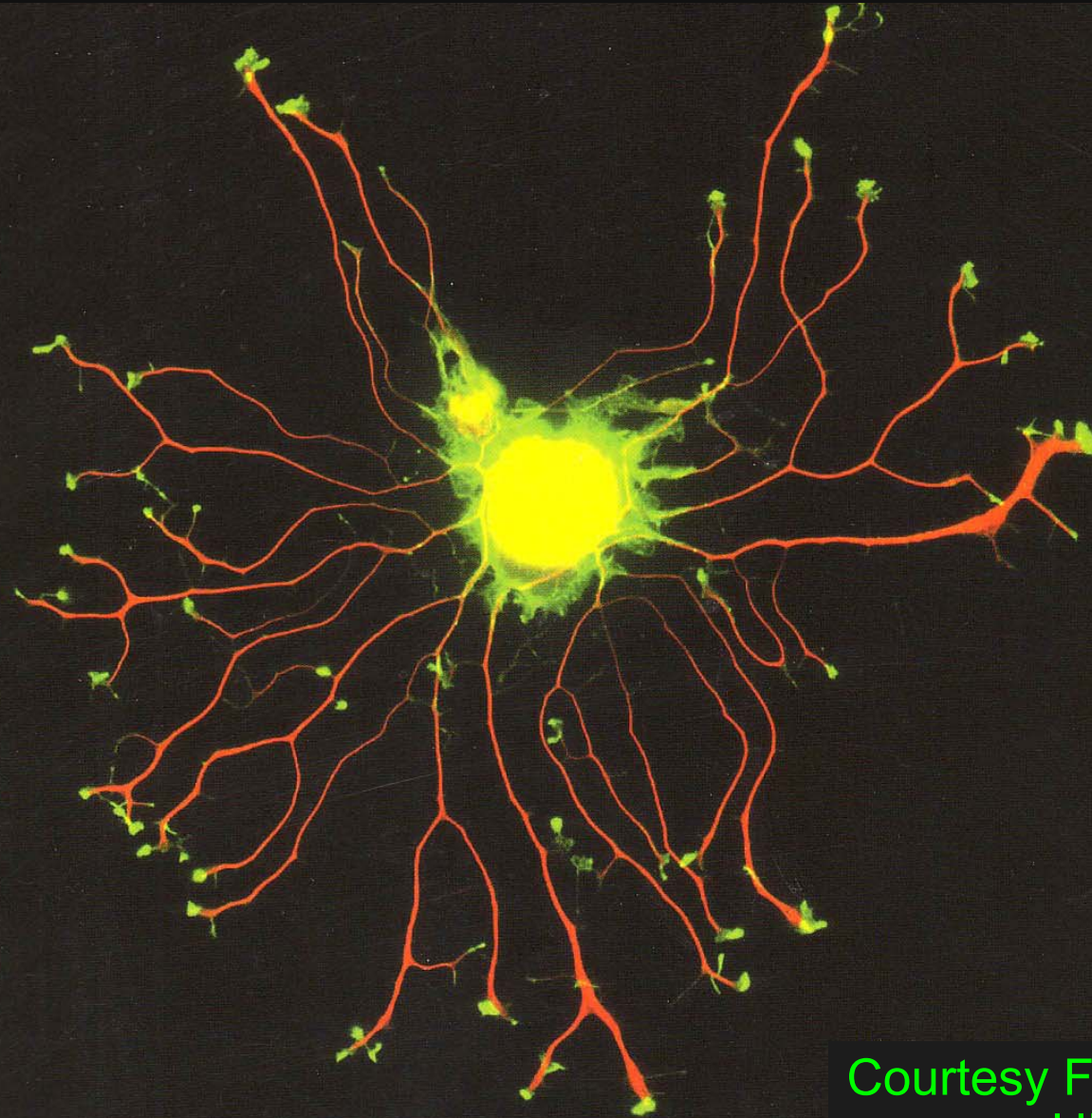
**Output**  
Axon

Neuron 3



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

***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



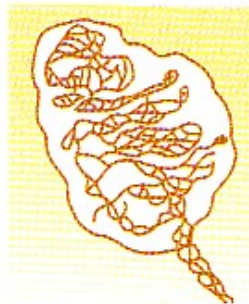
Expanded tip receptor



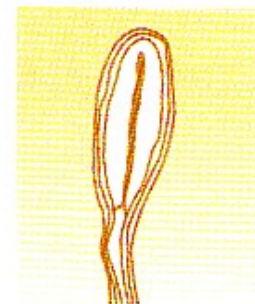
Tactile hair



Pacinian corpuscle



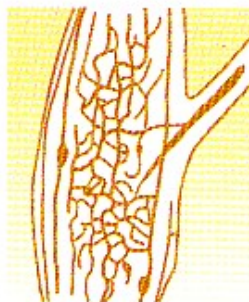
Meissner's corpuscle



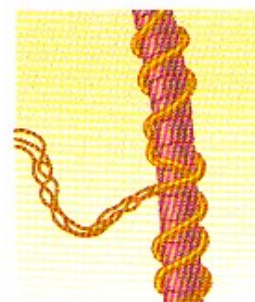
Krause's corpuscle



Ruffini's end-organ



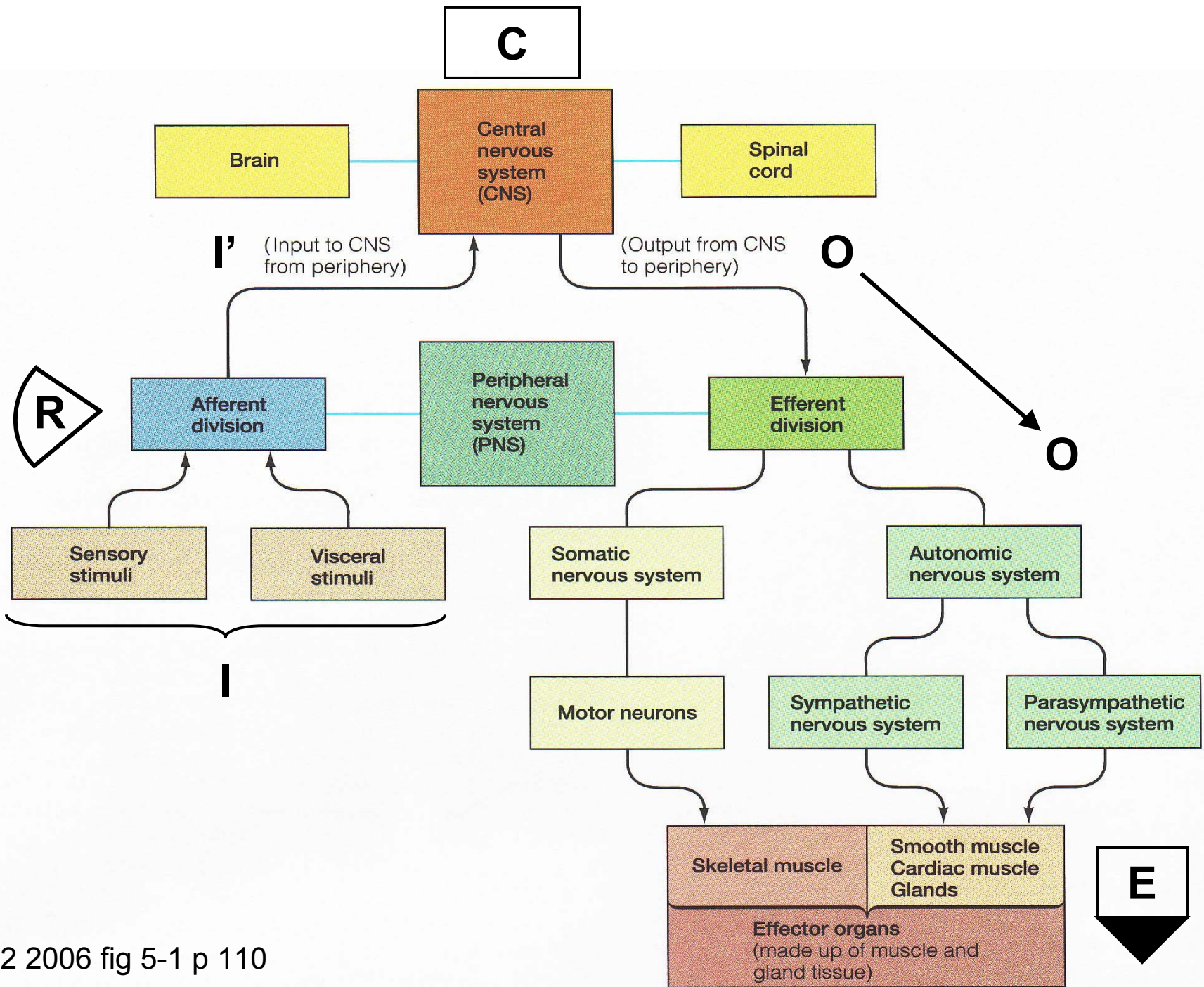
Golgi tendon apparatus



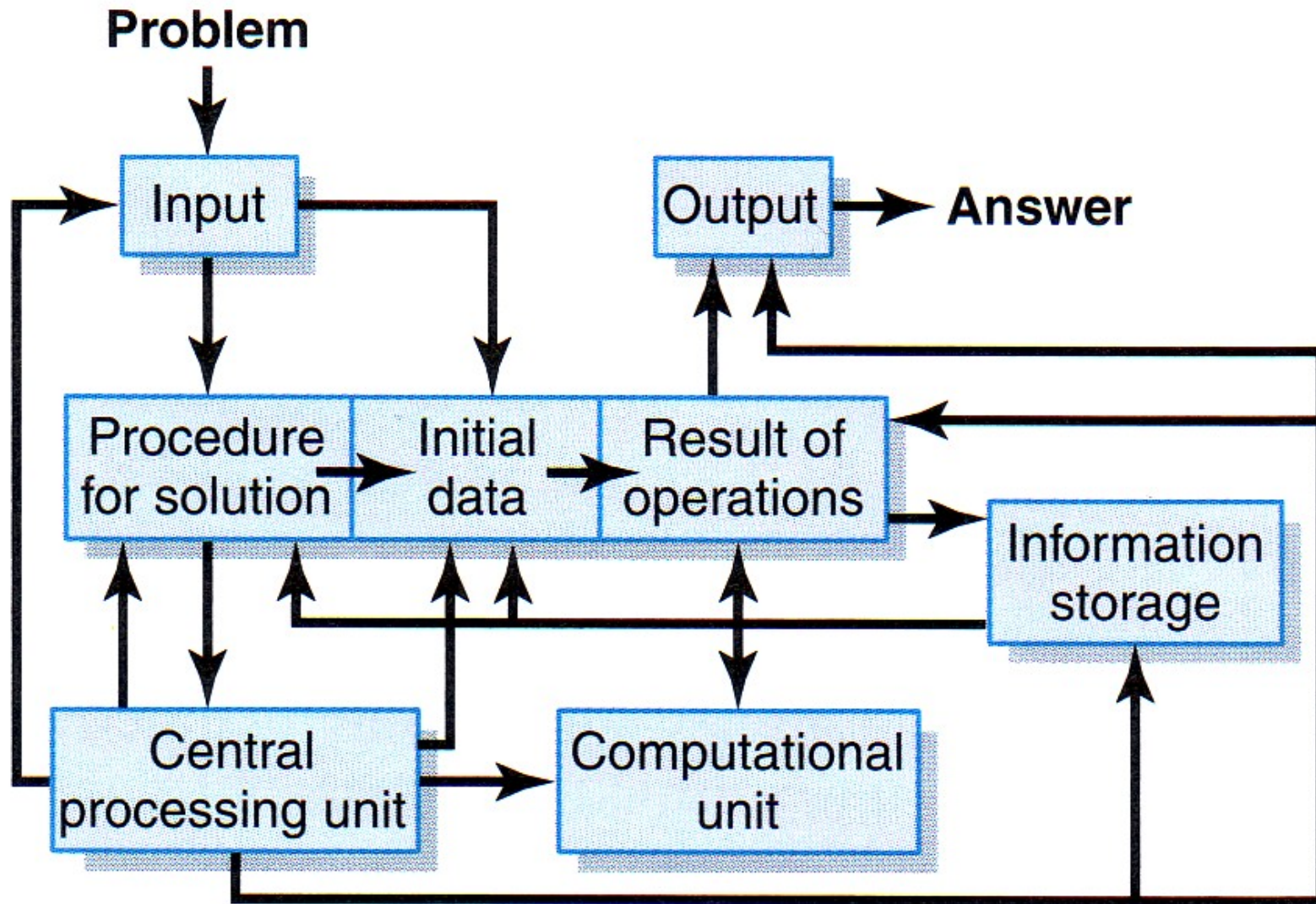
Muscle spindle

**Figure 46-1**

Several types of somatic sensory nerve endings.



LS2 2006 fig 5-1 p 110



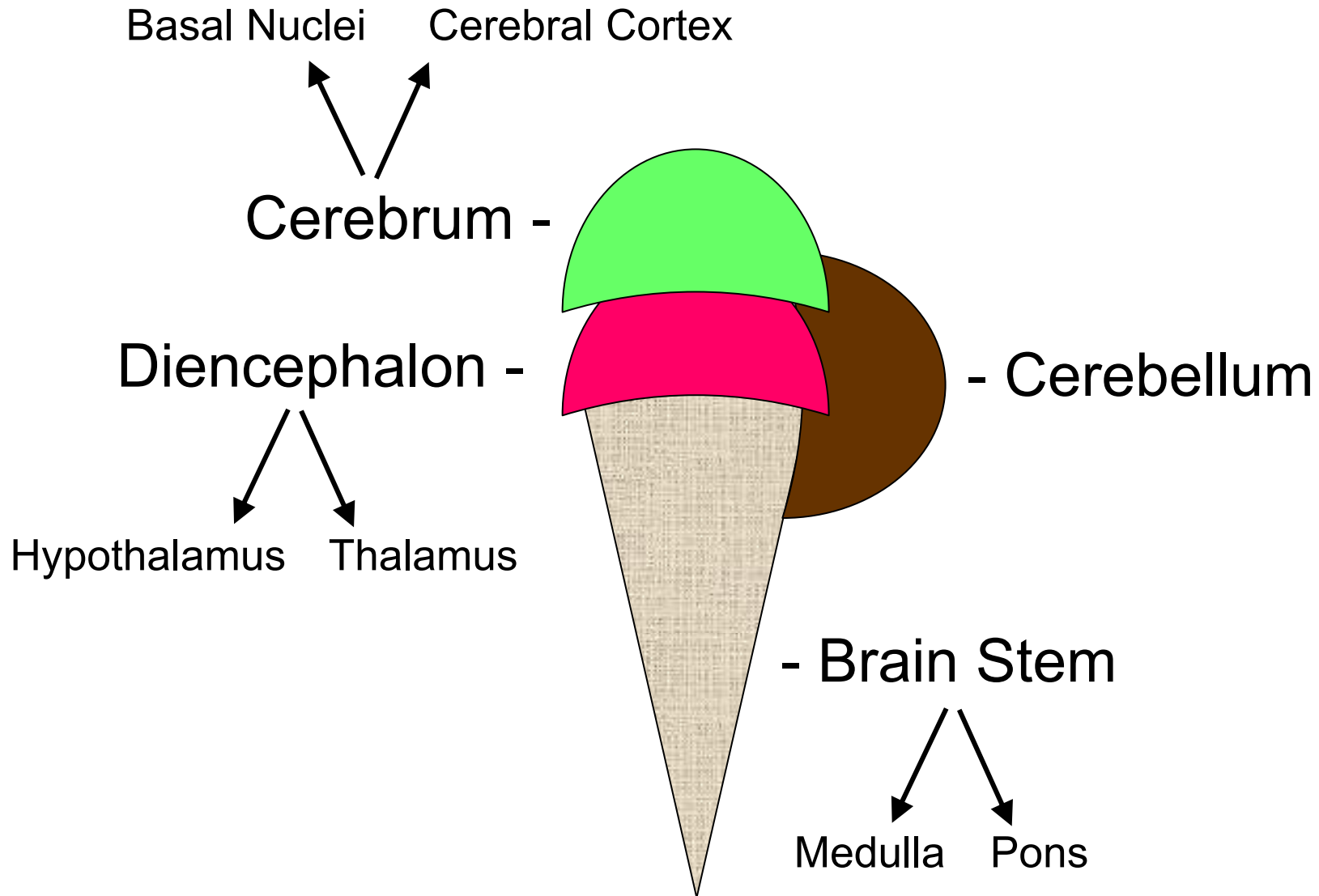
**Figure 45-4** Block diagram of a general-purpose computer, showing the basic components and their interrelations.

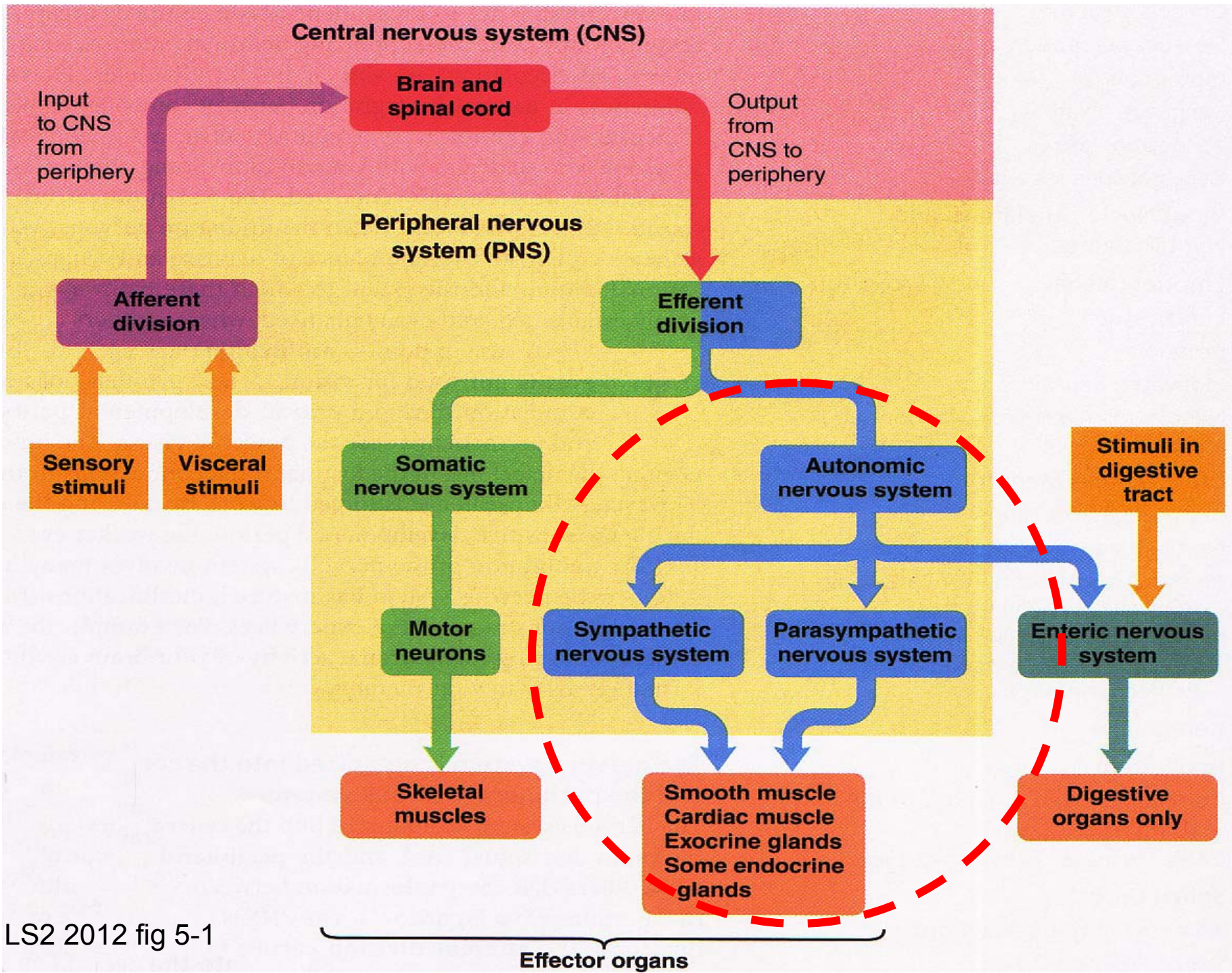


# ***CNS Connections: The Central 7!***

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

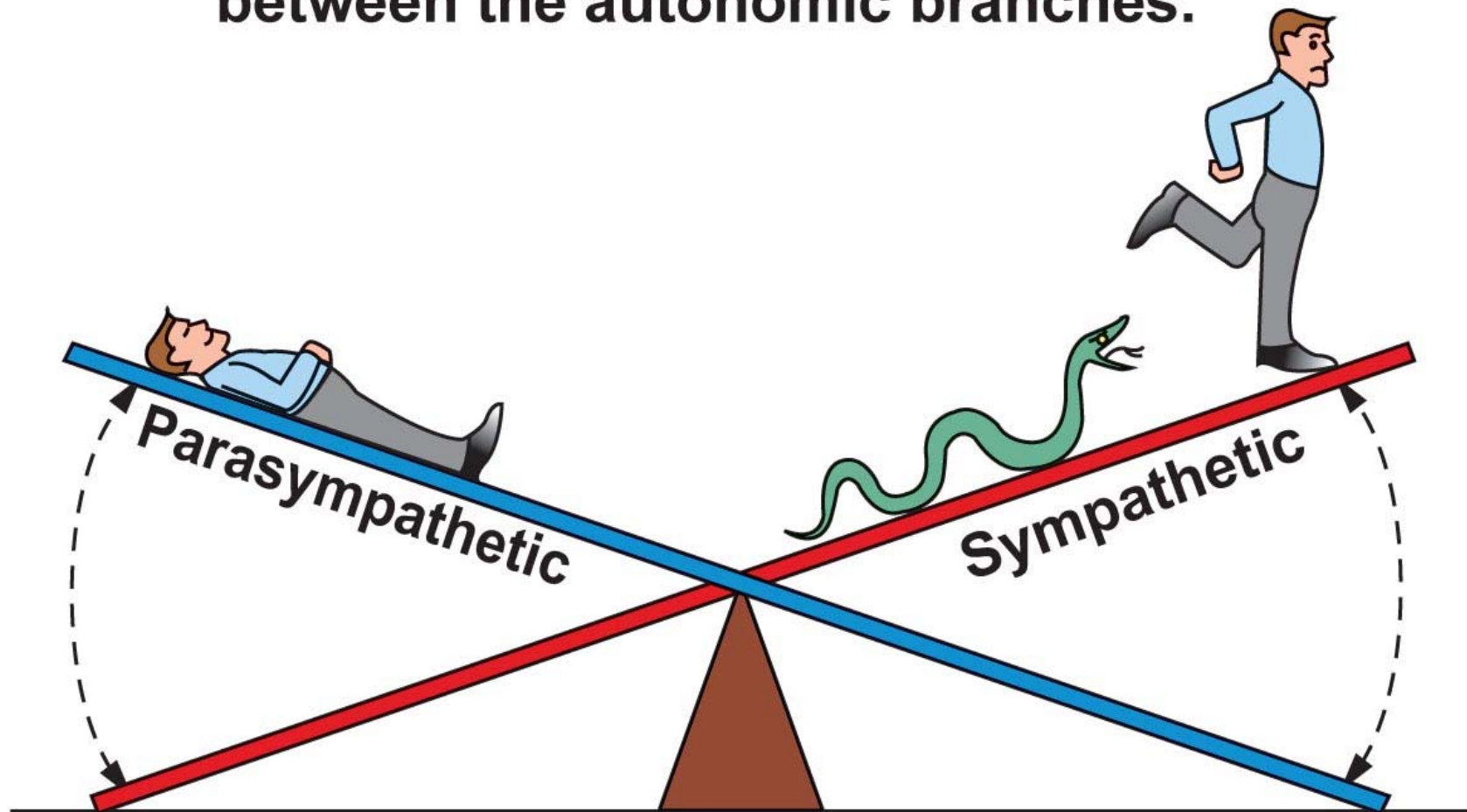
# *Ice Cream Cone Evolution Analogy*





LS2 2012 fig 5-1

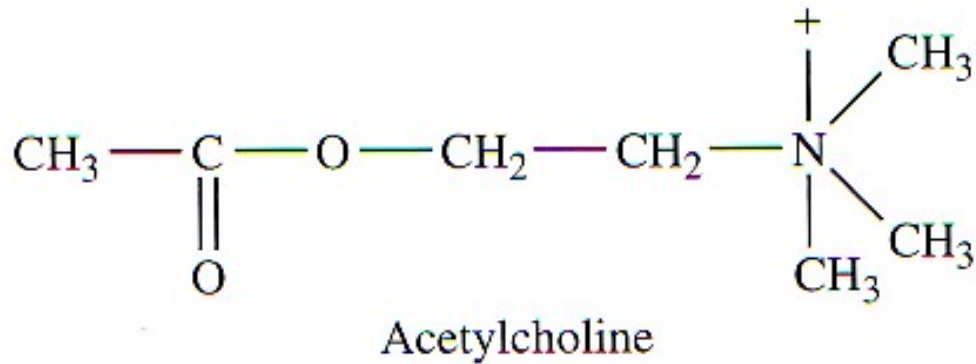
**Homeostasis is a dynamic balance between the autonomic branches.**



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

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

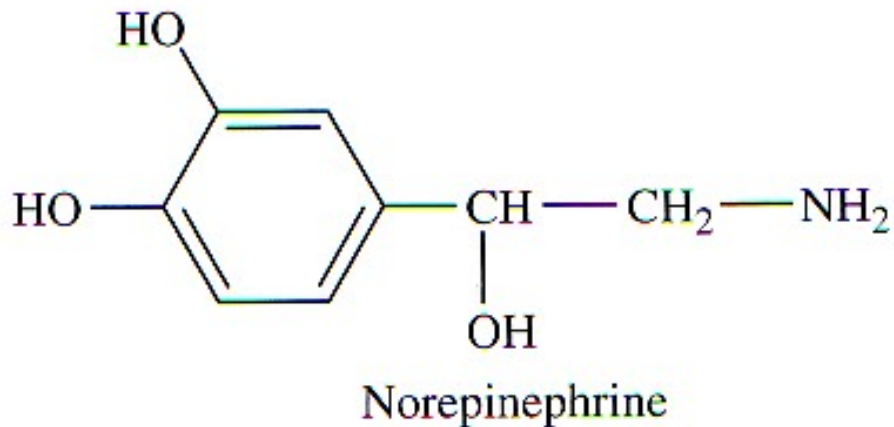
# Autonomic Neurotransmitters & Receptors



## Cholinergic

Nicotinic

Muscarinic

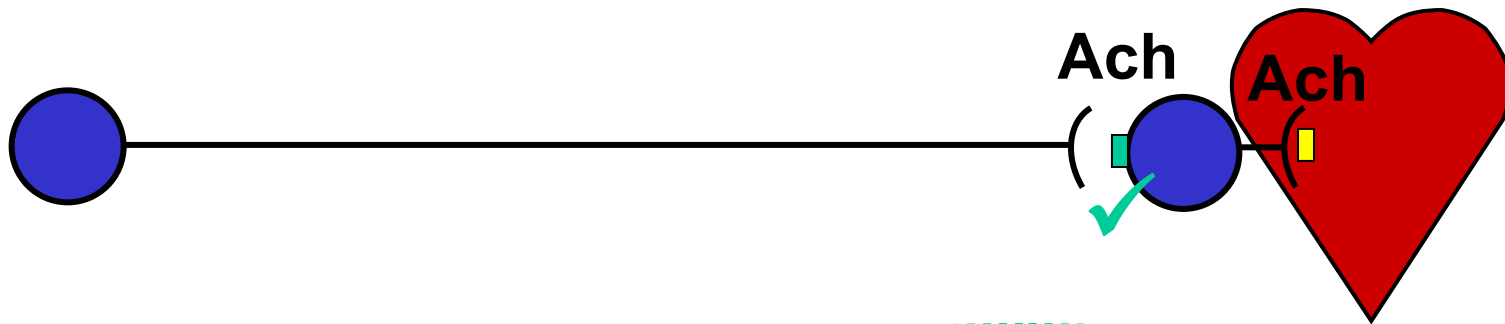


## Adrenergic

α = Alpha

β = Beta

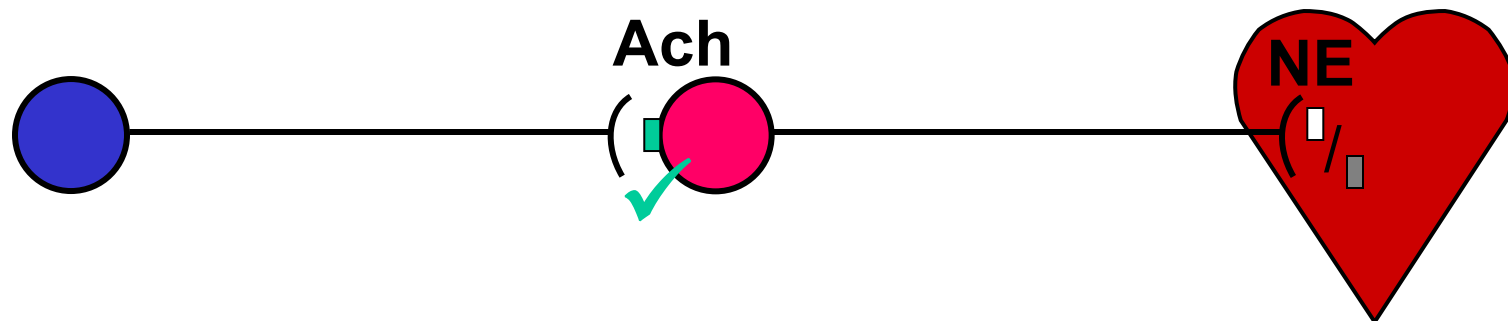
## Parasympathetic



Ach = Acetylcholine

- = Nicotinic Receptor
- = Muscarinic Receptor

## Sympathetic



NE = Norepinephrine

- =  $\alpha$  Receptor ( $\alpha_1$ ,  $\alpha_2$ )
- =  $\beta$  Receptor ( $\beta_1$ ,  $\beta_2$ )

**Nicotine activates both Sympathetic & Parasympathetic post-ganglionic neurons!**

**Problem?**



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

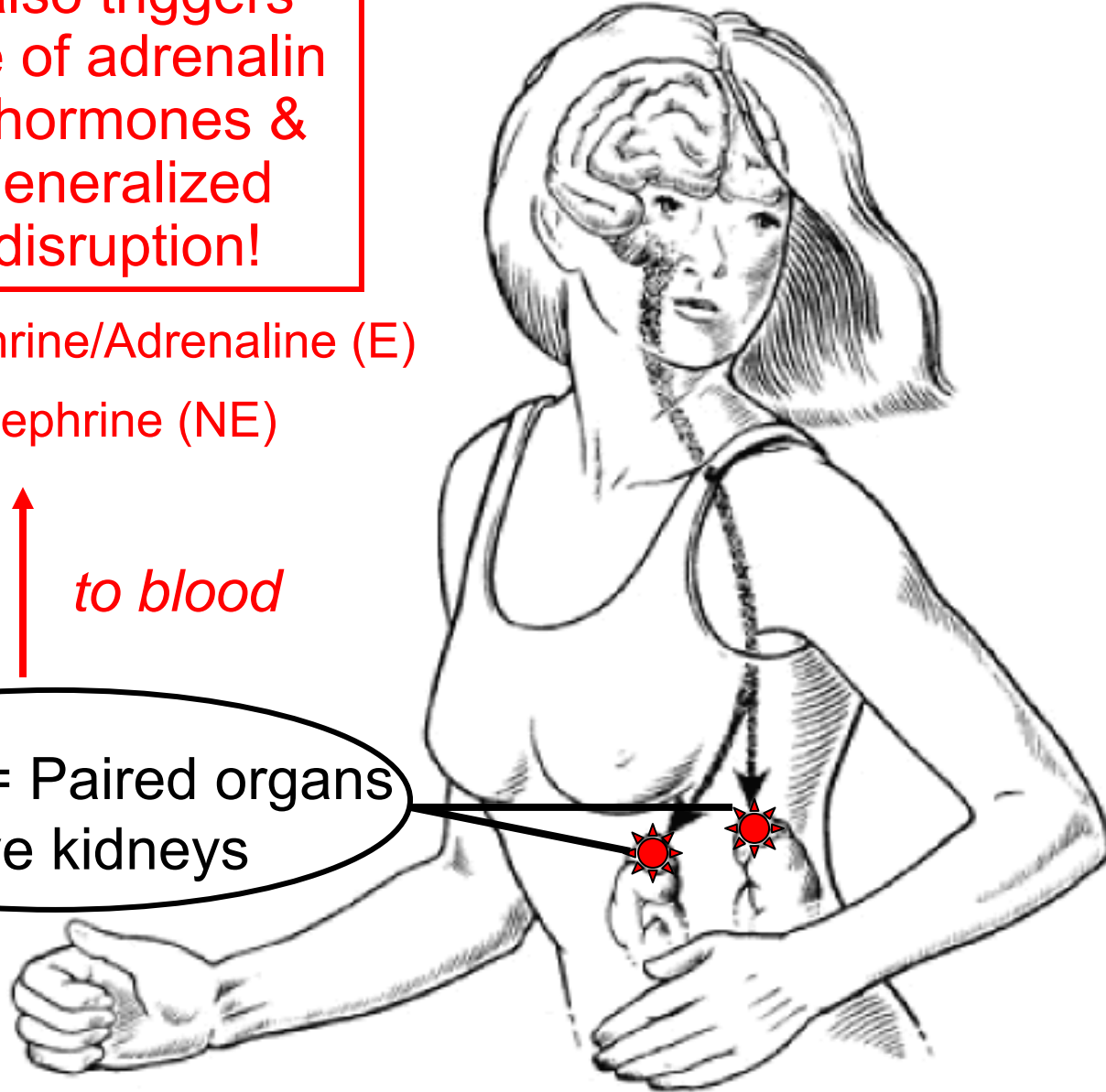


Nicotine also triggers the release of adrenalin & cortical hormones & causes generalized adrenal disruption!

80% Epinephrine/Adrenaline (E)  
20% Norepinephrine (NE)

*Output* ↑ *to blood*

Adrenals = Paired organs above kidneys





***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**

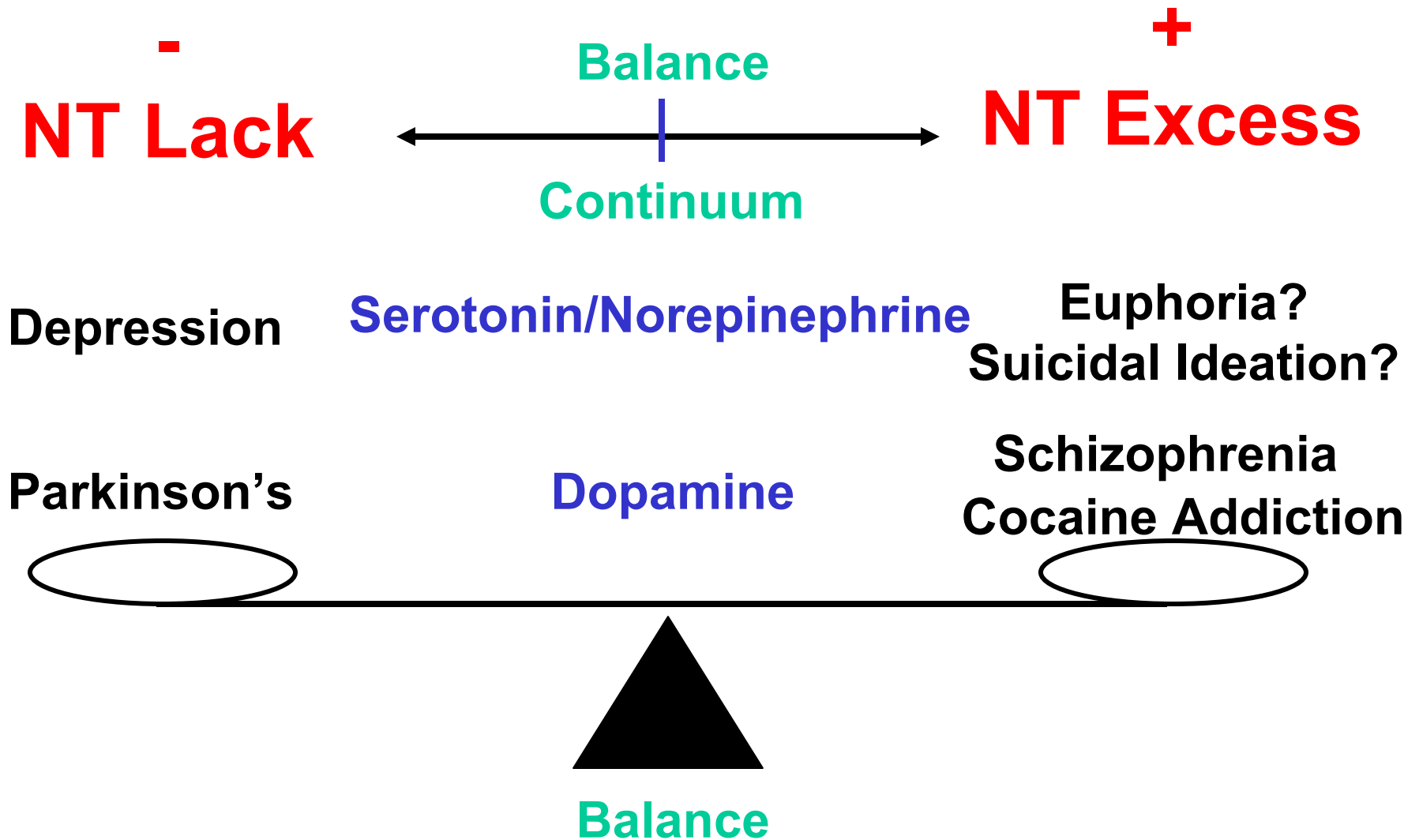
**nuclei (SI-) large cells of RAS (Ach+) + cocaine**

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

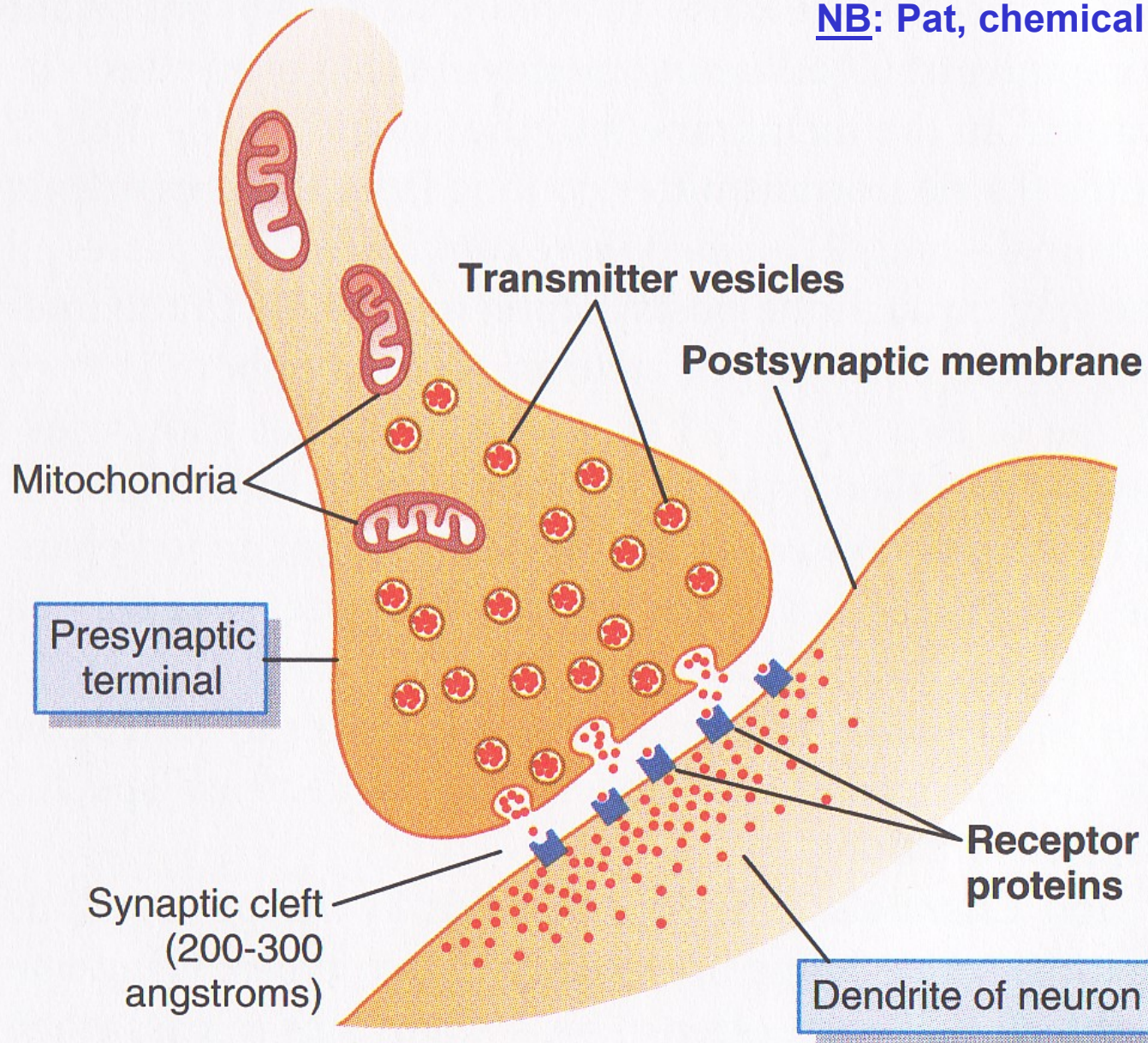
**1. Hypothalamus headquarters, reward & punishment**

**G&H fig 58-5, fig 58-6 pp 714-6; 11<sup>ed</sup> fig 58-8 p 735**

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



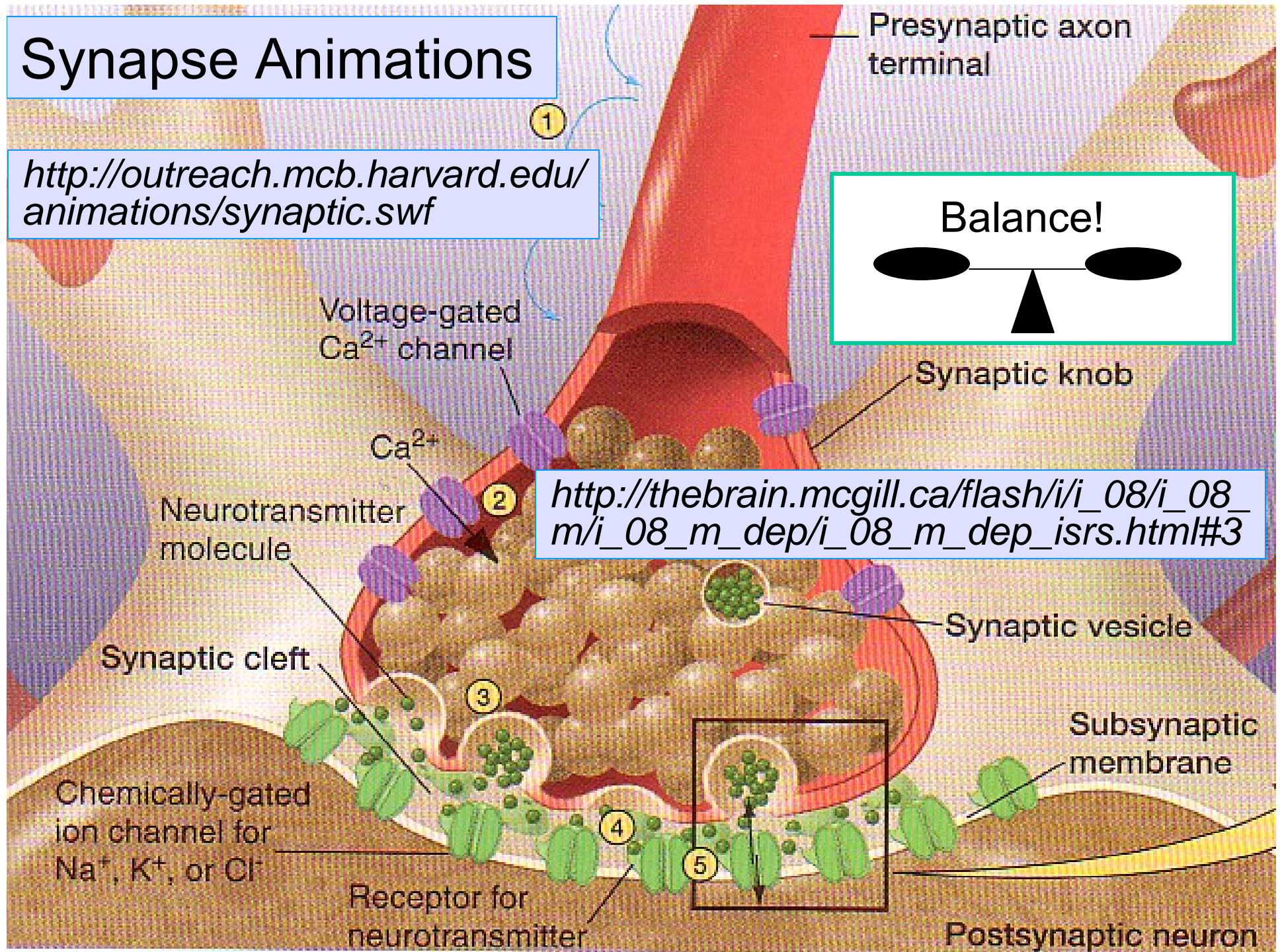
NB: Pat, chemical vs electrical



**Figure 45-6** Physiologic anatomy of the synapse.

# Synapse Animations

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




**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)



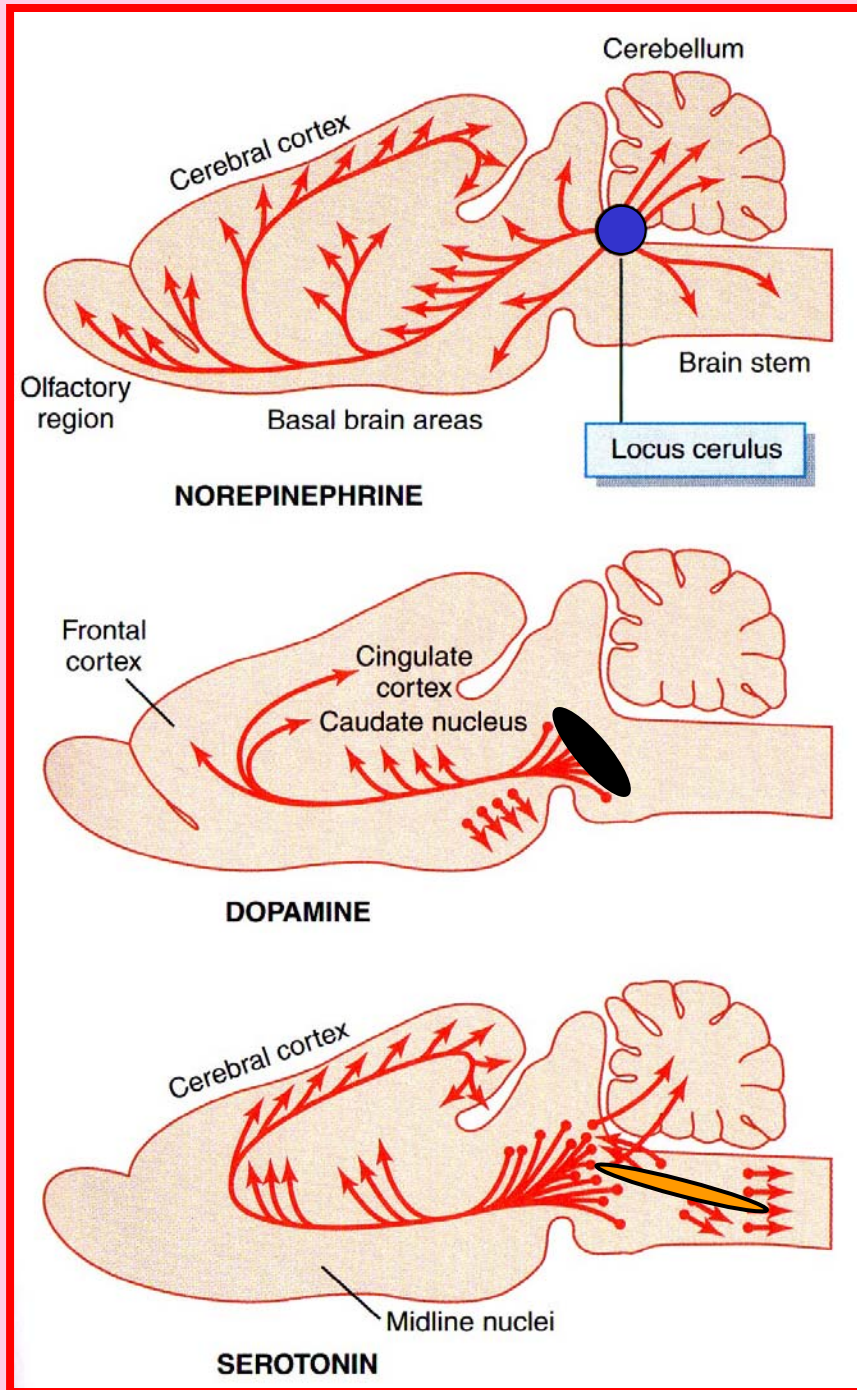
**Norepinephrine**  
**= NE**



**Dopamine** = D?



**Serotonin** = SI



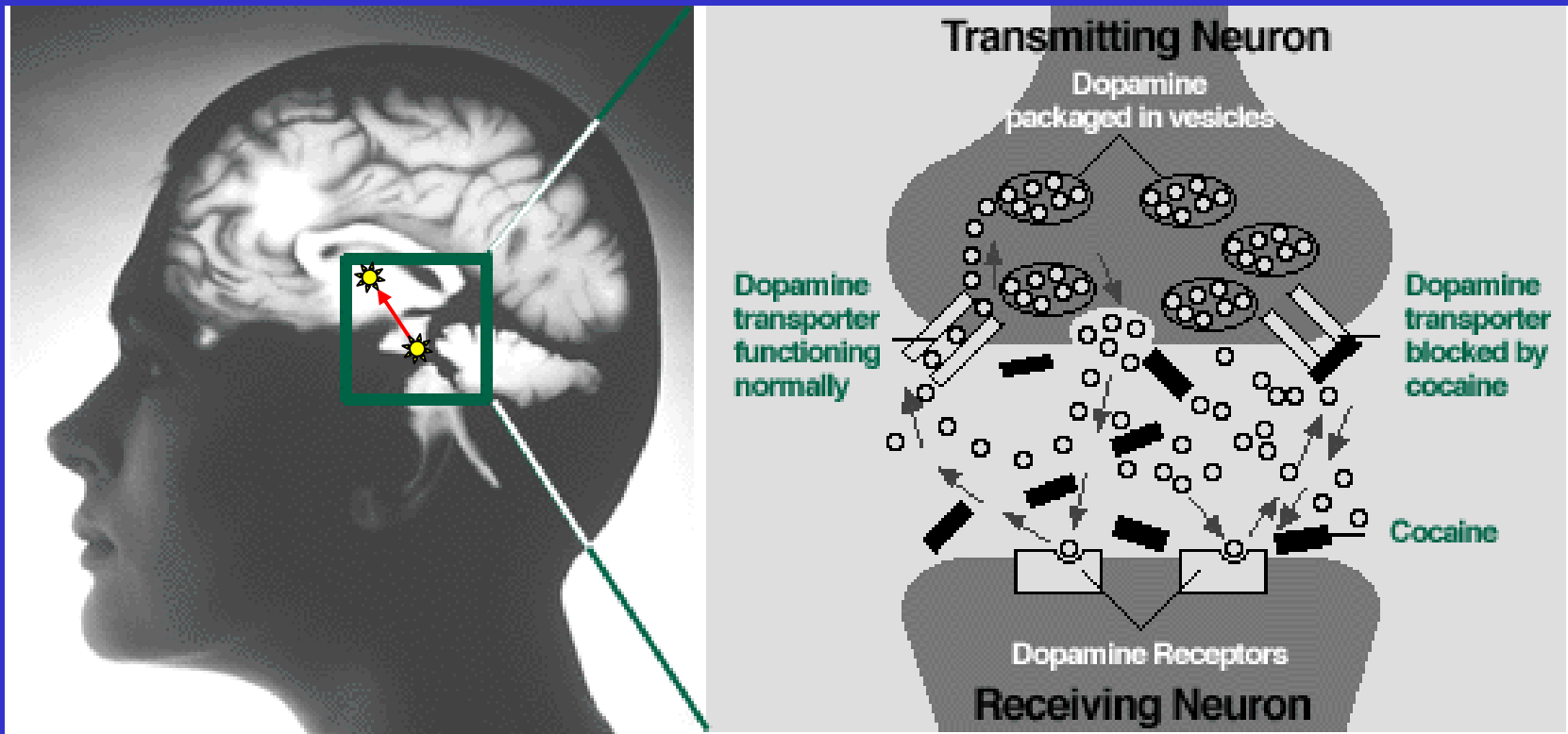
**Locus ceruleus =**  
**“Blue/azur spot”**

**Substantia nigra =**  
**“Black substance”**

**Raphe nuclei =**  
**“Nut seam/line”**

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

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

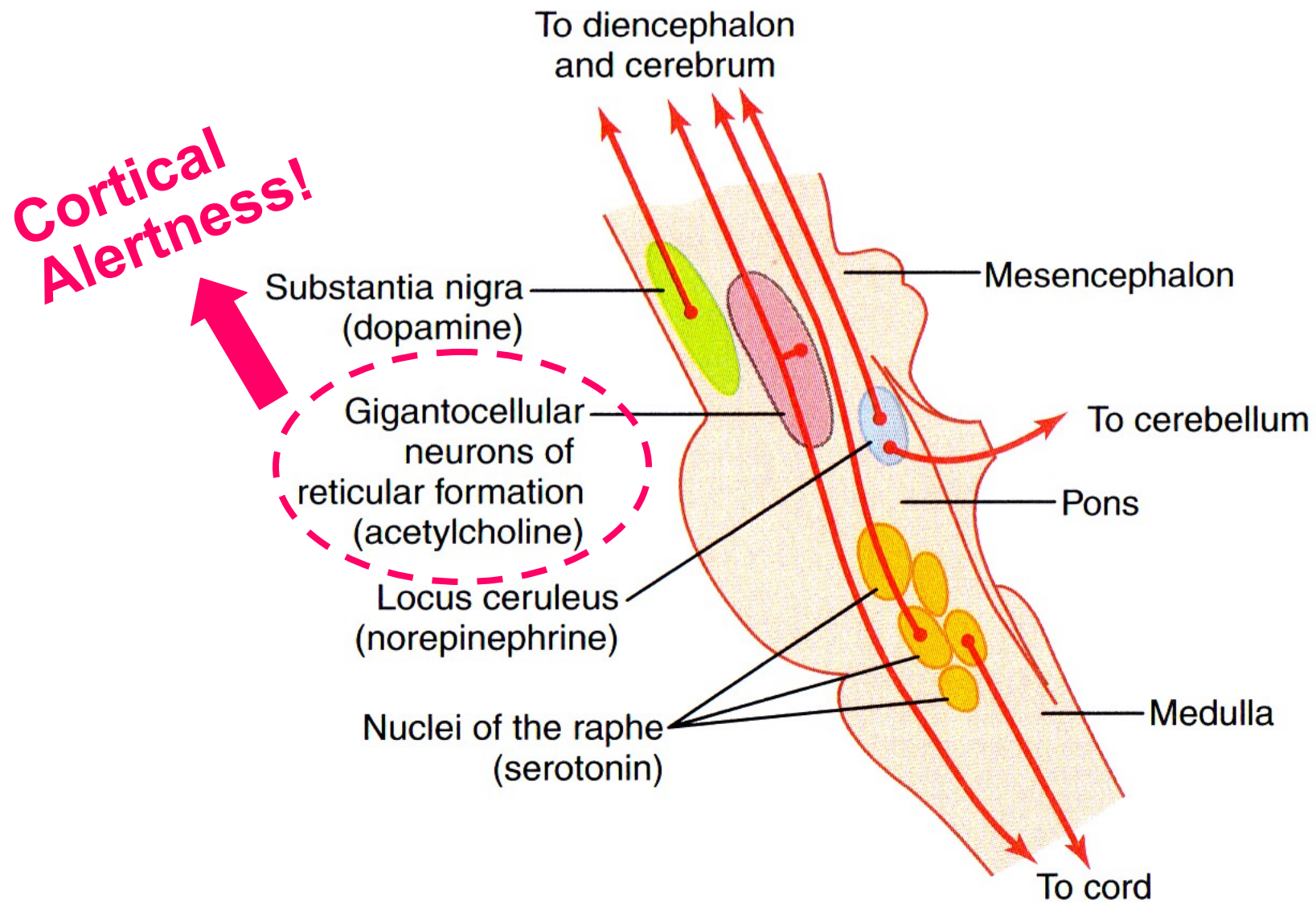


Nerve cells eg: Ventral Tegmentum (Substantia Nigra)  
to Nucleus Accumbens (Limbic System)

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



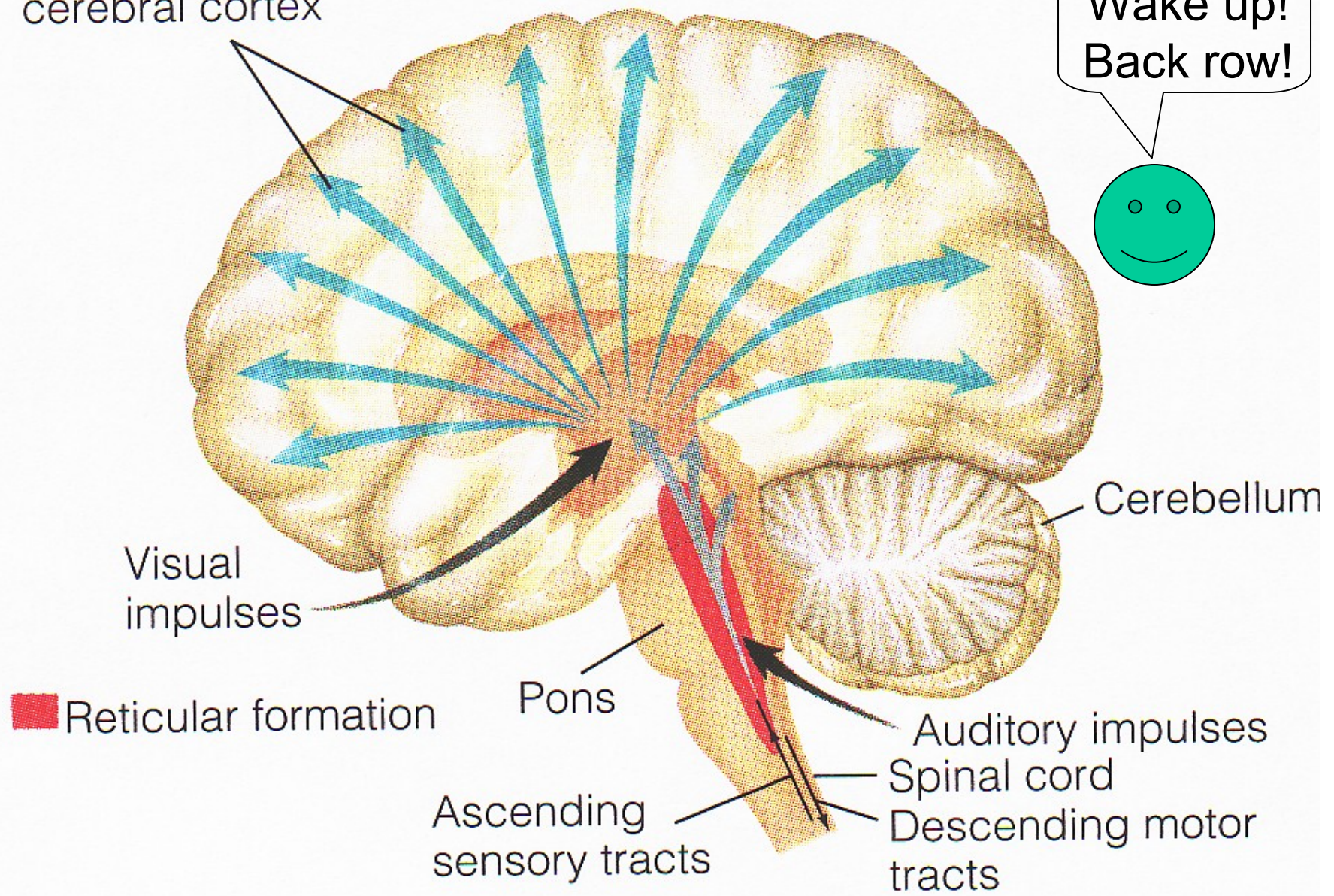
# 4<sup>th</sup> Pathway Releases Acetylcholine!

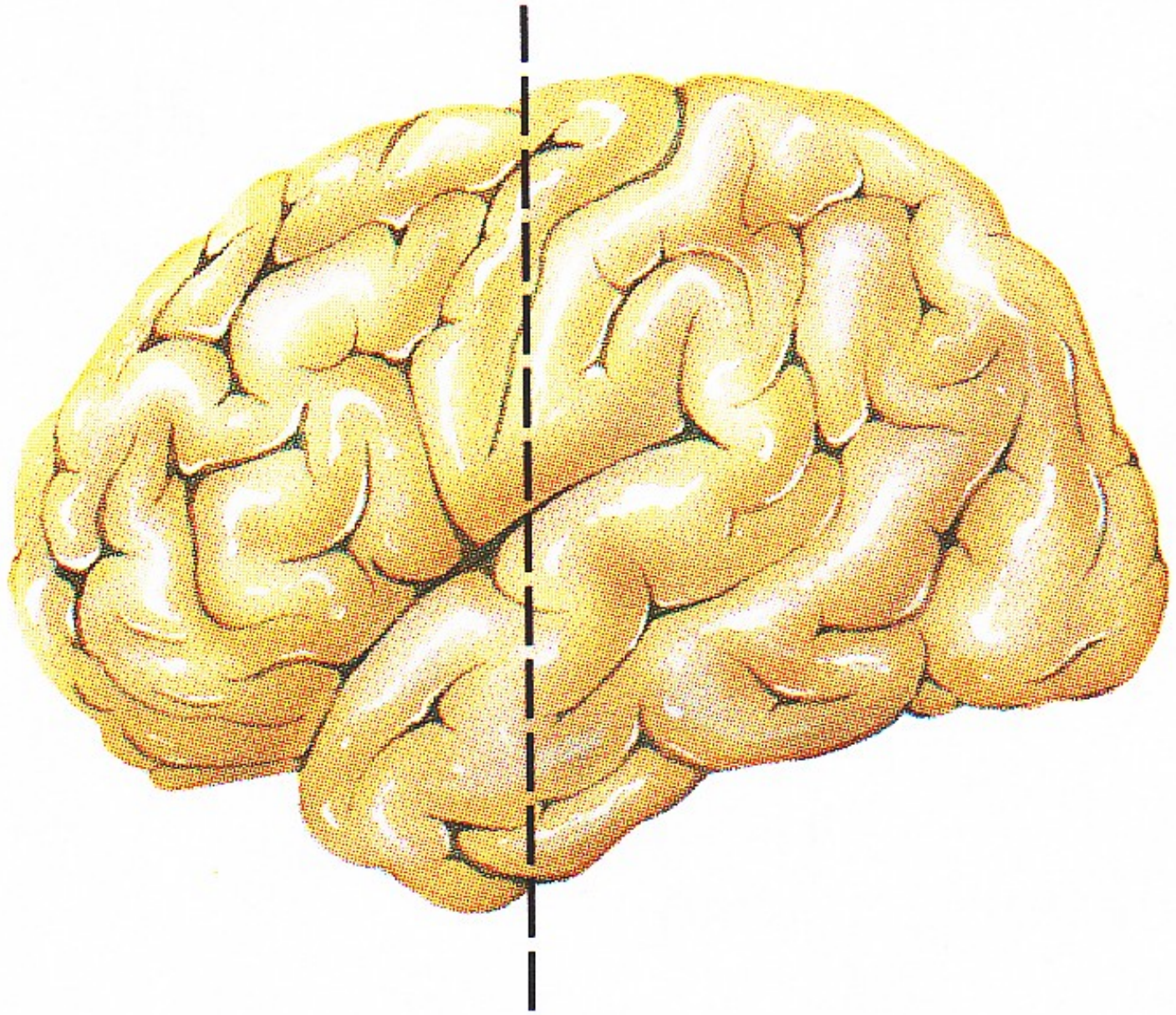


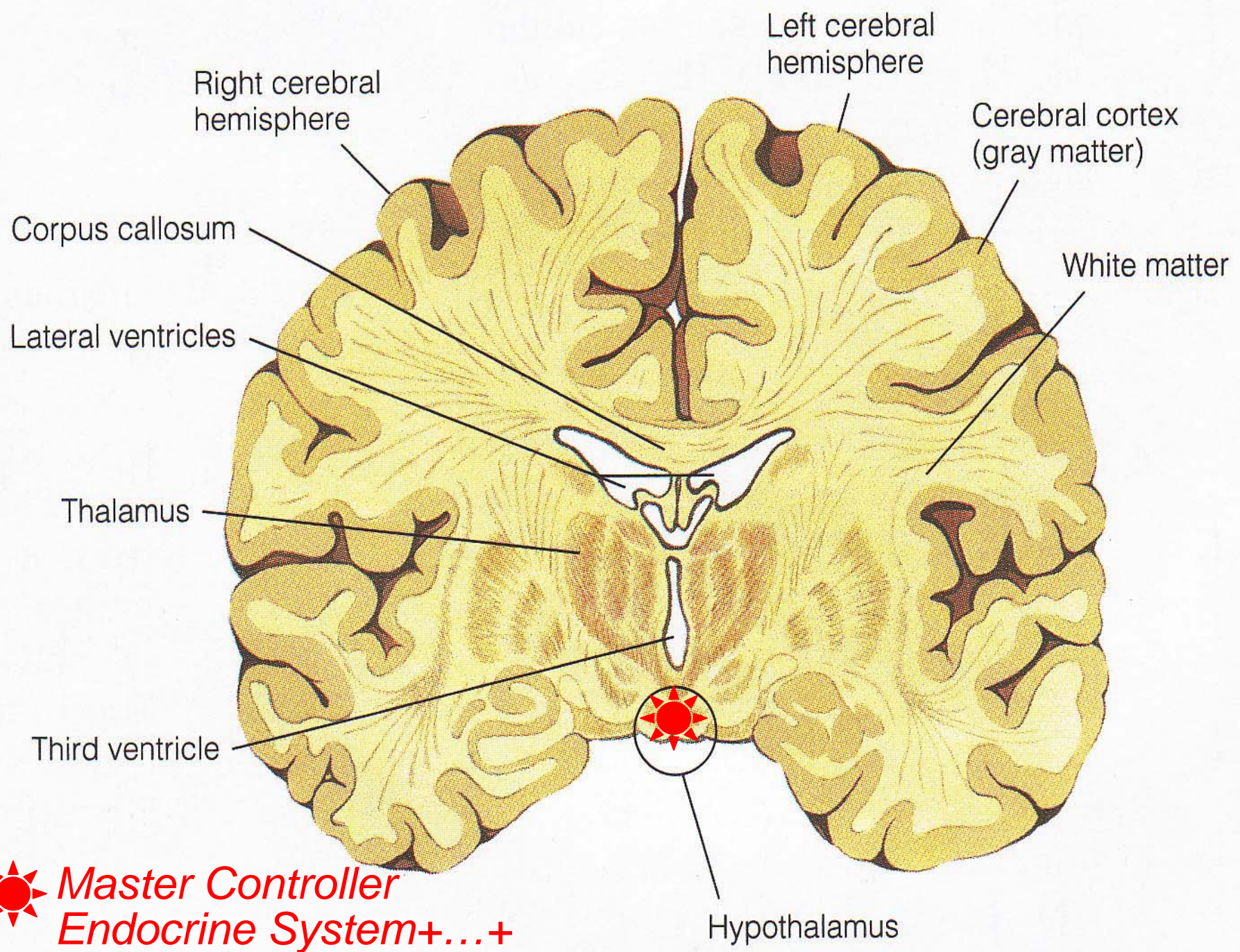
# Reticular Activating System (RAS)

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

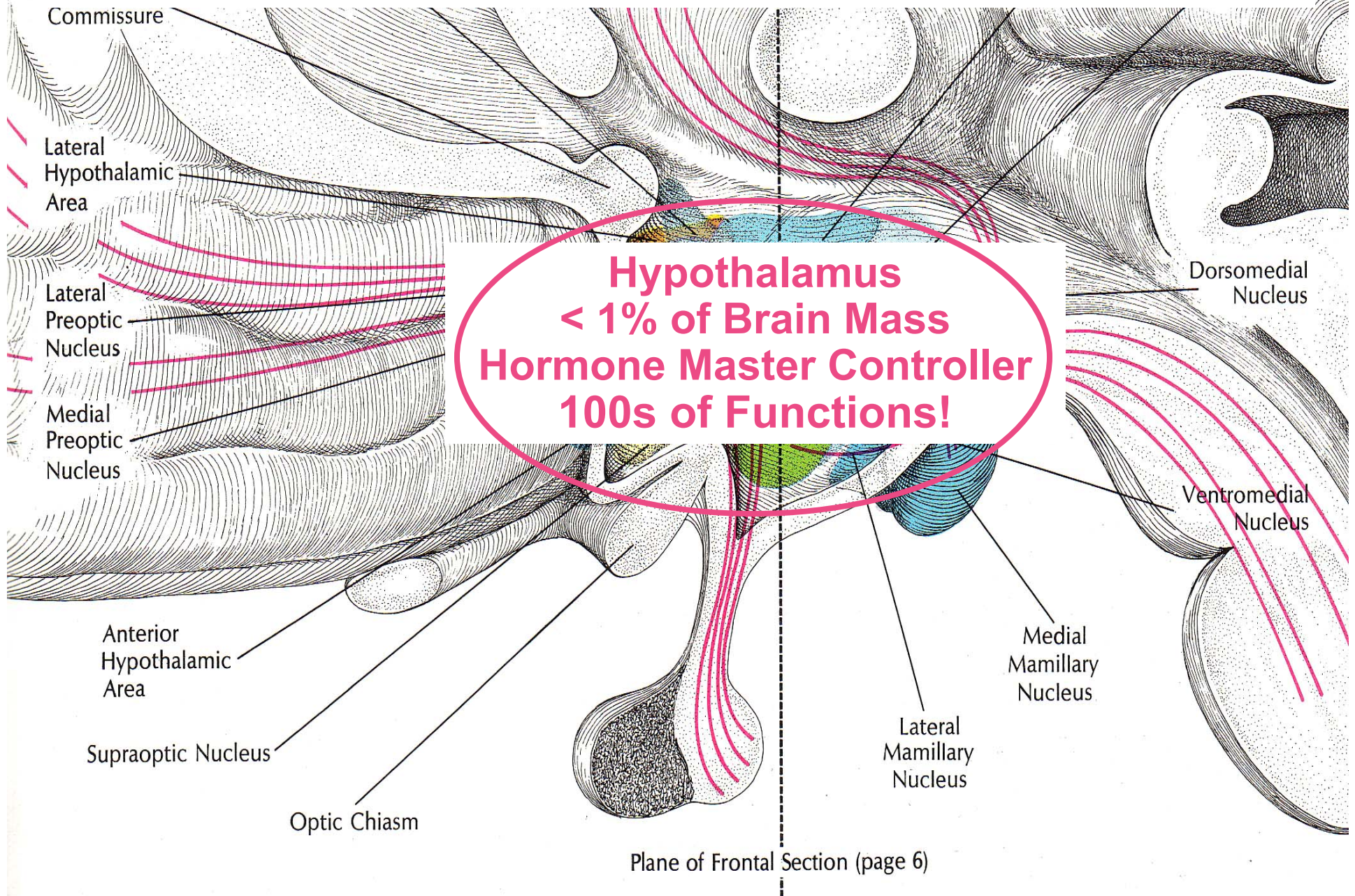
Wake up!  
Back row!

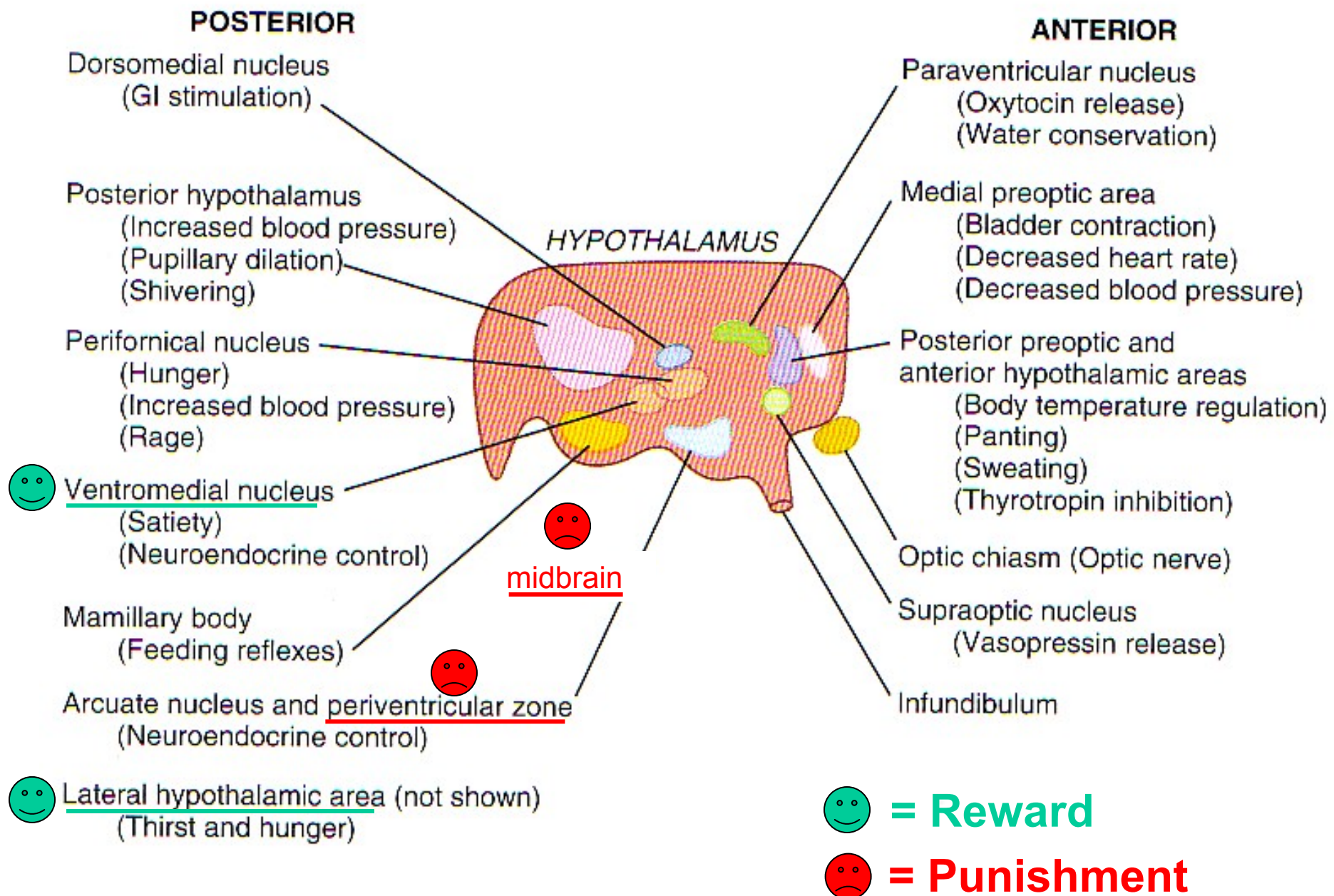






# Good Things Come in Small Packages!

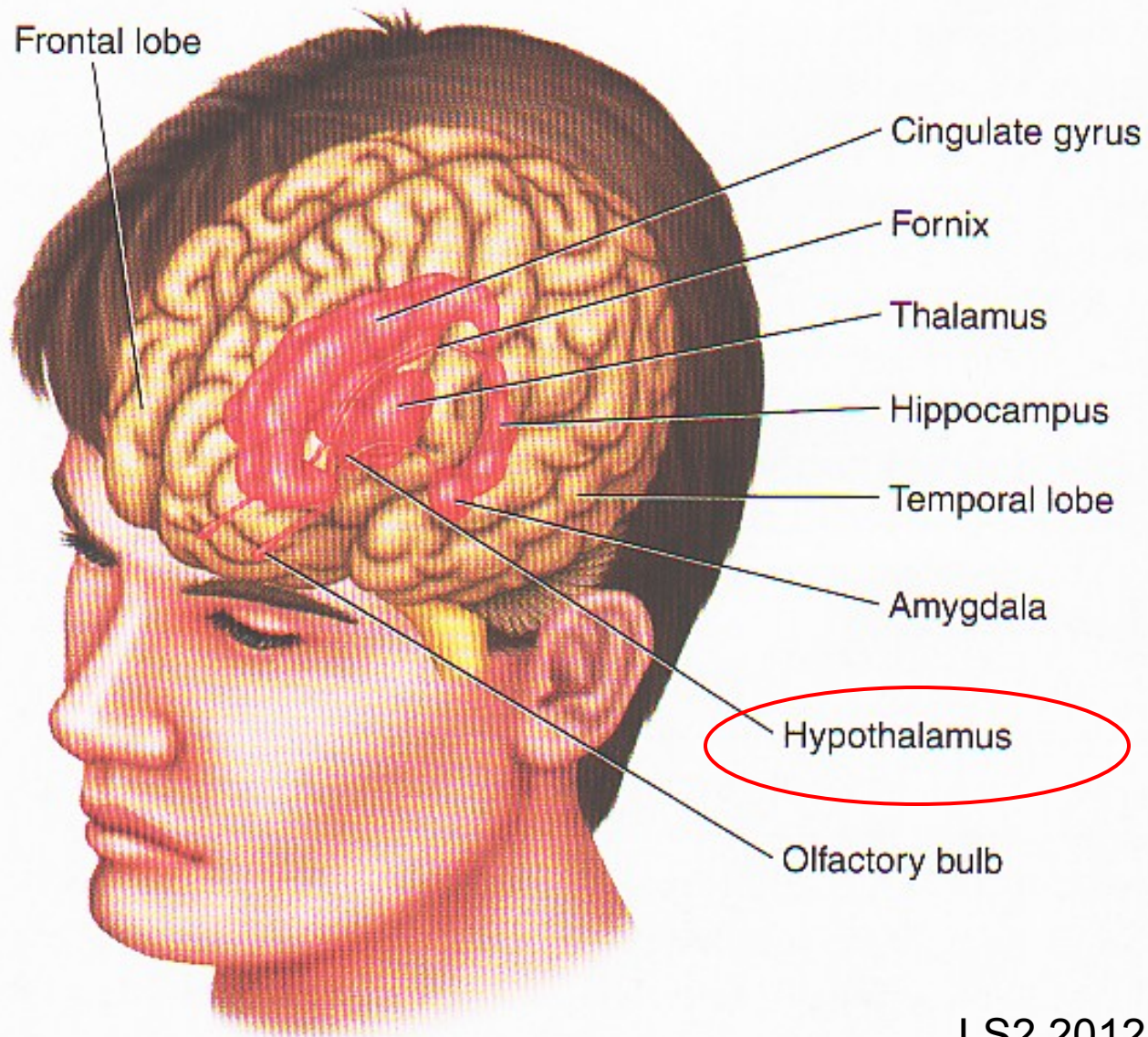




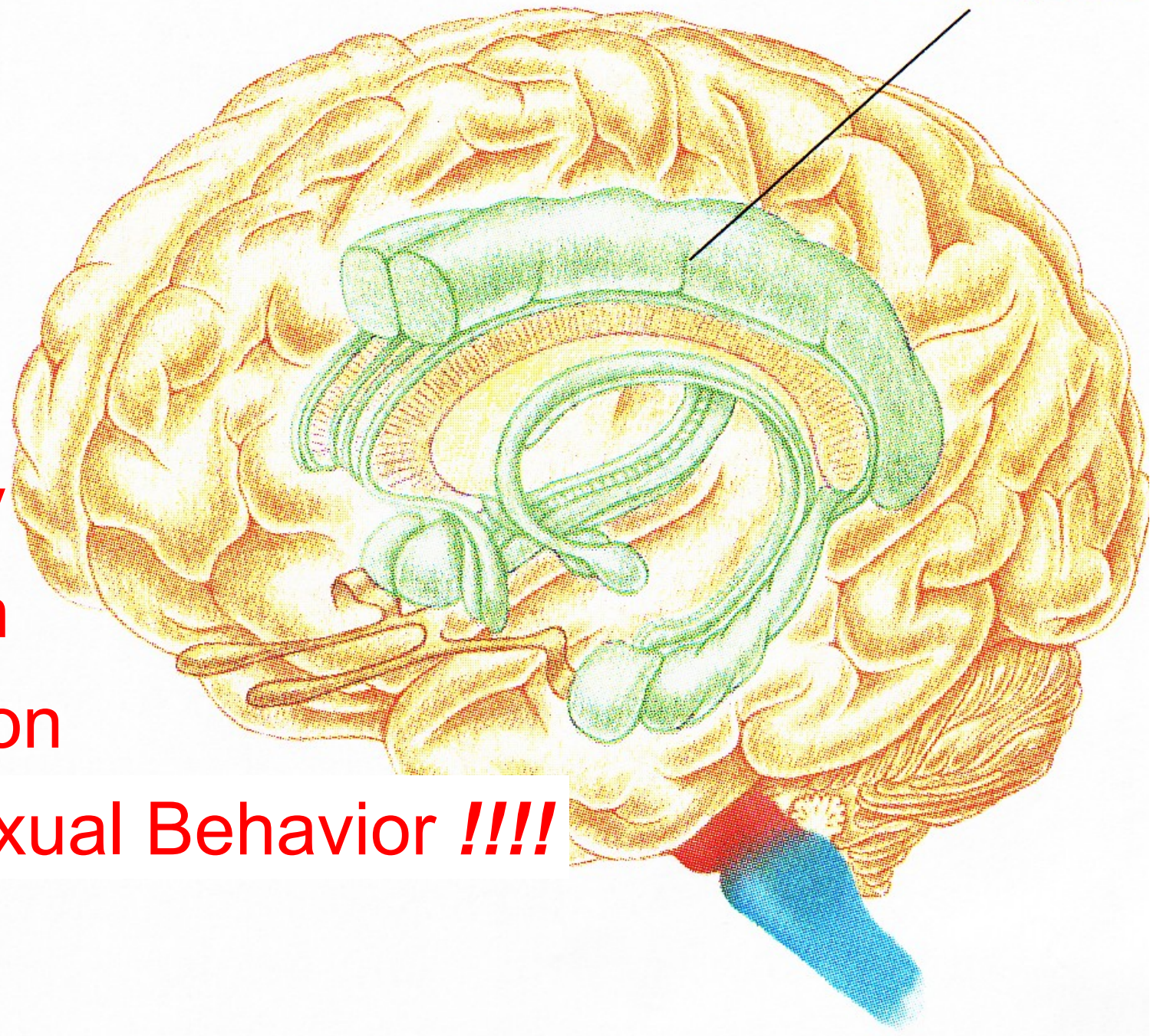
● **FIGURE 5-18**

**Limbic system**

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



Limbic system



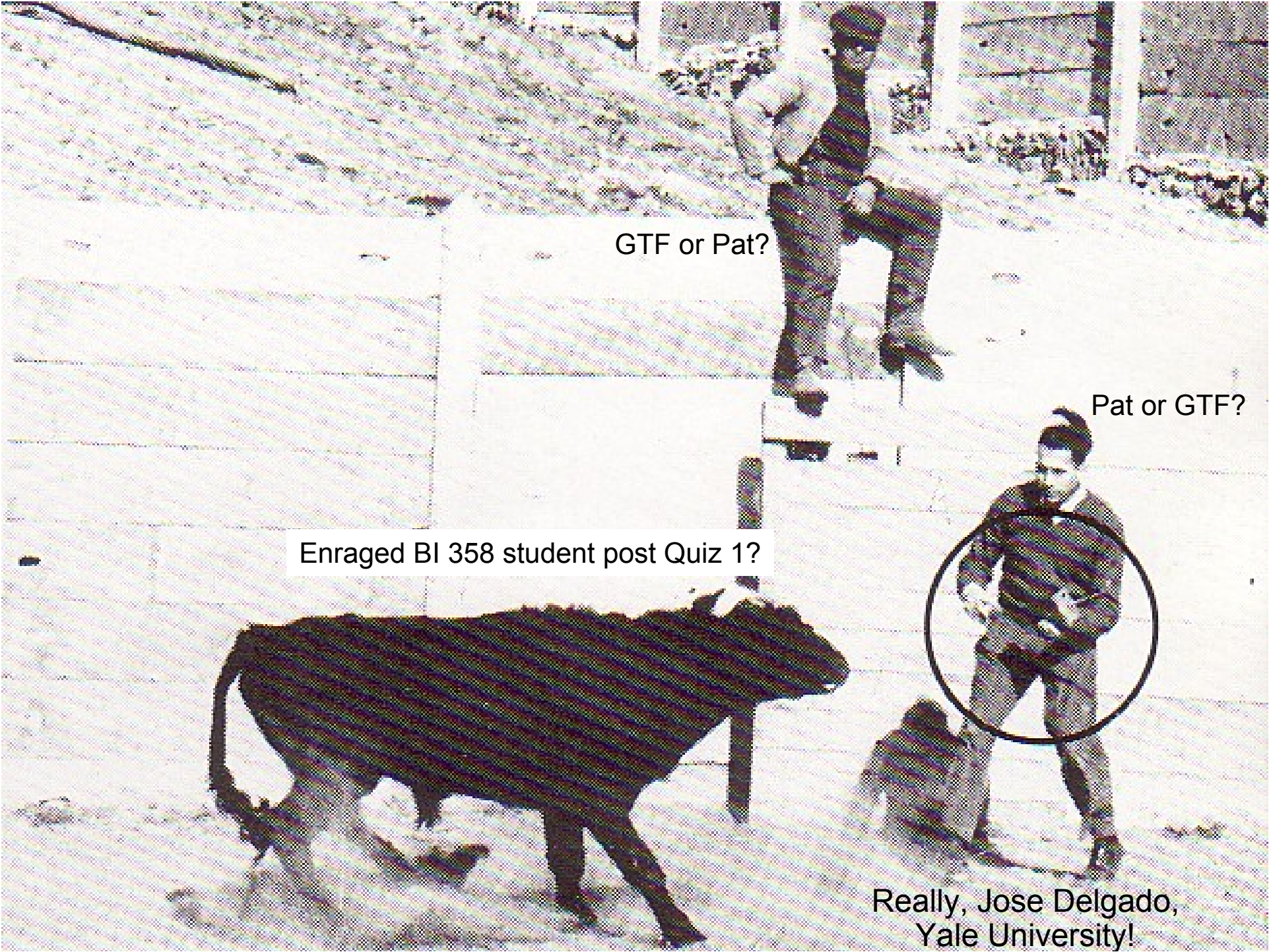
***Memory***

***Emotion***

***Motivation***

***Sociosexual Behavior !!!!***



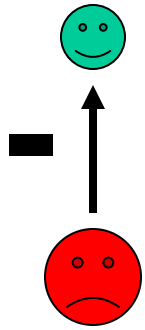


GTF or Pat?

Pat or GTF?

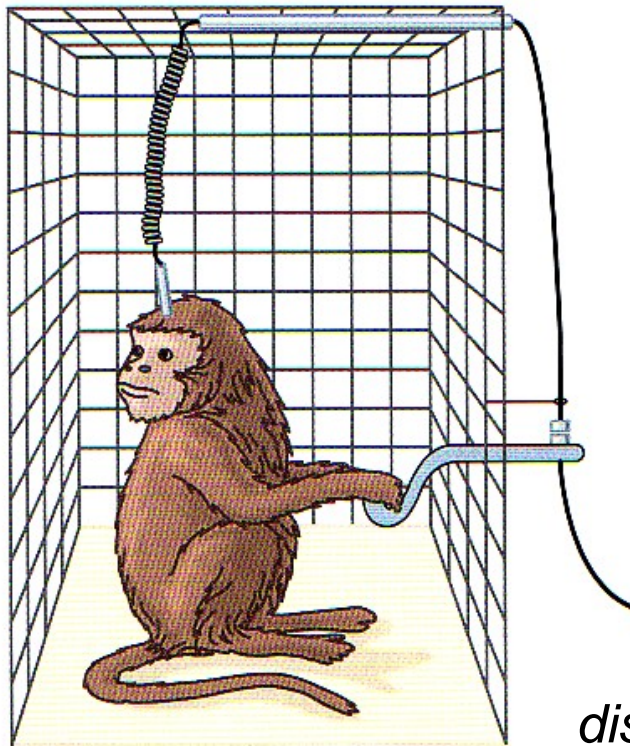
Enraged BI 358 student post Quiz 1?

Really, Jose Delgado,  
Yale University!



**Reward Centers = Hypothalamus, lateral & ventromedial n.**

**Punishment Centers = Mesencephalon, central gray area, Hypothalamus & Thalamus, peri-ventricular zones**



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

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

**Figure 58-8**

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