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/](http://learn.genetics.utah.edu/content/addiction/mouse/)

II. **Medical Physiology in the News** Your brain…in love?
OHSU Brain Institute
[http://www.ohsu.edu/blogs/brain/2014/02/14/your-brain-in-love/](http://www.ohsu.edu/blogs/brain/2014/02/14/your-brain-in-love/)

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

IV. **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

V. **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

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

Come see us during office hr! Dr. Bovee next session, Tuesday! No more Pat 'til Thursday! Hooray!
<table>
<thead>
<tr>
<th>Day &amp; Time</th>
<th>Instructor</th>
<th>Place</th>
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<tbody>
<tr>
<td>M 11 am-12n</td>
<td>Pat Lombardi(^+)</td>
<td>65A Klamath</td>
<td>lombardi</td>
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<tr>
<td>T 10-11 am</td>
<td>Precious deVerteuil</td>
<td>273 Onyx</td>
<td>precious</td>
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<tr>
<td>T 2-3 pm</td>
<td>Aleesa Schlientz</td>
<td>360 Onyx</td>
<td>aleeesas</td>
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\(^+\) and by appointment.

For Aleesa, please e-mail.
For Precious, please e-mail.
For Pat, please call 541-346-6055/4525 or e-mail.
Balance is the Key to Life
Invariably, Negative Feedback
Venous Pooling

Baroreceptors/Pressure Receptors e.g., in Carotids & Aorta

NB: Corrective Change Opposes Original Input

Seated to Standing

Electrochemical Signal

CV Control Center Brain Stem

Electrochemical Signal e.g., Symp Accelerator N

FB eg

HR +

VC +
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

\[ \text{BP: } 100 \text{ mm Hg} \rightarrow 175 \text{ mm Hg} \]

...into person with \textbf{functioning} system

\[ \text{BP: } 100 \text{ mm Hg} \rightarrow 125 \text{ mm Hg} \]

G&H pp 7-8
Gain for Human Baroreceptor System?

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

cf: Gain for Human Body Temperature = -33
Nervous System

CNS

PNS

input

output

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

Glymphatic Pathway Function

http://www.sciencedaily.com/releases/2012/08/120815142042.htm
http://www.urmc.rochester.edu/labs/nedergaard-lab/projects/glymphatic_system
~99% of all neurons in humans! CNS ~100 billion interneurons!!
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.
Nerve cell with multiple axons grown by adding a mitogen/neurogen ≡ nerve growth factor!
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.
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 – Brain Stem
7. Spinal Cord
Ice Cream Cone Evolution Analogy

- Basal Nuclei
- Cerebral Cortex
- Diencephalon
- Hypothalamus
- Thalamus
- Cerebrum
- Cerebellum
- Brain Stem
- Medulla
- Pons
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

G&H 2011 p 731-3
**Parasympathetic**

Ach = Acetylcholine

- = Nicotinic Receptor
- = Muscarinic Receptor

**Sympathetic**

NE = Norepinephrine

= α Receptor ($\alpha_1$, $\alpha_2$)
= β 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)

Adrenals = Paired organs above kidneys

Output to blood

Break for discussion/questions!
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; 11ed fig 58-8 p 735
Neurotransmitter (NT) Balance: Diseases/Addictions/Moods?

- NT Lack

Balance

Continuum

NT Excess

Depression  Serotonin/Norepinephrine  Euphoria? Suicidal Ideation?

Parkinson’s  Dopamine  Schizophrenia Cocaine Addiction

Balance
Figure 45-6 Physiologic anatomy of the synapse.

G&H 2011 p 547

NB: Pat, chemical vs electrical
Synapse Animations

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

Balance!

http://thebrain.mcgill.ca/flash/i/i_08/i_08_m/i_08_m_dep/i_08_m_dep_isrs.html#3
Table 45-1  Small-Molecule, Rapidly Acting Transmitters

<table>
<thead>
<tr>
<th>Class I</th>
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<tbody>
<tr>
<td>Acetylcholine</td>
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<tr>
<th>Class II: The Amines</th>
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<tbody>
<tr>
<td>Norepinephrine</td>
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<tr>
<td>Epinephrine</td>
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<tr>
<td>Dopamine</td>
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<td>Serotonin</td>
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<td>Histamine</td>
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<tr>
<th>Class III: Amino Acids</th>
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<tbody>
<tr>
<td>Gamma-aminobutyric acid (GABA)</td>
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</tr>
<tr>
<td>Glycine</td>
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<td>Glutamate</td>
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<tr>
<td>Aspartate</td>
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<thead>
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<tr>
<td>Nitric oxide (NO)</td>
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Prominent in reward pathways & chemistry of addiction.
Locus ceruleus = “Blue/azur spot”

Substantia nigra = “Black substance”

Norepinephrine = NE

Dopamine = D?

Serotonin = SI

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!!!


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

http://learn.genetics.utah.edu/content/addiction/
4th Pathway Releases Acetylcholine!

- To diencephalon and cerebrum
- Substantia nigra (dopamine)
- Gigantocellular neurons of reticular formation (acetylcholine)
- Locus ceruleus (norepinephrine)
- Nuclei of the raphe (serotonin)

Cortical Alertness!

G&H 2011 p 713
Reticular Activating System (RAS)
Overall Cortical Alertness!

Radiations to cerebral cortex

Visual impulses

Reticular formation

Pons

Ascending sensory tracts

Auditory impulses

Spinal cord

Descending motor tracts

Cerebellum

Wake up! Back row!
Master Controller
Endocrine System

- Right cerebral hemisphere
- Cerebral cortex (gray matter)
- White matter
- Corpus callosum
- Lateral ventricles
- Thalamus
- Third ventricle
- Hypothalamus
Good Things Come in Small Packages!

Hypothalamus
< 1% of Brain Mass
Hormone Master Controller
100s of Functions!

An anterior hypothalamic area
Optic chiasm
Supraoptic nucleus
Lateral hypothalamic area
Lateral preoptic nucleus
Medial preoptic nucleus
Dorsomedial nucleus
Ventromedial nucleus
Medial mamillary nucleus
Lateral mamillary nucleus
Plane of frontal section (page 6)
Reward

- 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)

Punishment

- 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
Limbic system
This partially transparent view of the brain reveals the structures composing the limbic system.
Memory
Emotion
Motivation
Sociosexual Behavior
GTF or Pat?

Enraged BI 358 student post Quiz 1?

Really, Jose Delgado,
Yale University!

Pat or GTF?
Reward Centers = Hypothalamus, lateral & ventromedial n.

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

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


G&H 11th ed only p 735