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. **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 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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<tr>
<td>M 11 am-12n</td>
<td>Pat Lombardi+</td>
<td>65A Klamath</td>
<td>lombardi</td>
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<tr>
<td>W 10-11am</td>
<td>Stacy Levichev-Connolly</td>
<td>203 LISB</td>
<td>aleviche</td>
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<tr>
<td>W 11 am-12n</td>
<td>Connor O’Sullivan</td>
<td>206 LISB</td>
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* 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 $\rightarrow$ Ovulation
- Oxytocin $\rightarrow$ 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.
Venous Pooling

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

NB: Corrective Change Opposes Original Input

- 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 non-functioning Baroreceptor system

BP: 100 mm Hg \(\rightarrow\) 175 mm Hg

...into person with functioning system

BP: 100 mm Hg \(\rightarrow\) 125 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

C

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 $\rightarrow$ 900 Billion **Glial Cells**!
What the Heck is the Glymphatic System? CNS Functional Waste Clearance Pathway!

Glymphatic Pathway Function

- Para-Arterial Influx
- Convective Flux
- Para-Venous Efflux

Astrocyte, Neuron, Interstitial solute, AQP4

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


https://www.ted.com/talks/jeff_iliiff_one_more_reason_to_get_a_good_night_s_sleep
~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

- Brain Stem
  - Medulla
  - Pons

- Cerebellum
- Cerebrum
  - Basal Nuclei
  - Cerebral Cortex
- Diencephalon
  - Hypothalamus
  - Thalamus
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**
- $\alpha = \text{Alpha}$
- $\beta = \text{Beta}$

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!

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!
VI. Addiction Medicine: Homeostasis & Applications

A. Neurotransmitter balance: Mood/Diseases/Addiction?
   G&H fig 45-5, 45-6 pp 546-48

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 - NT Excess

Depression
Serotonin/Norepinephrine
Euphoria? Suicidal Ideation?

Parkinson’s
Dopamine
Schizophrenia Cocaine Addiction

Balance
Balance Continuum
Figure 45-6 Physiologic anatomy of the synapse.
Synapse Animations

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

Balance!

http://thebrain.mcgill.ca/flash/i/i_01/i_01m/i_01_m_fon/i_01_m_fon.html
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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<thead>
<tr>
<th>Class II: The Amines</th>
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<tbody>
<tr>
<td>Norepinephrine</td>
<td>Prominent in reward pathways &amp; chemistry of addiction.</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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<th>Class III: Amino Acids</th>
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<tbody>
<tr>
<td>Gamma-aminobutyric acid (GABA)</td>
<td></td>
</tr>
<tr>
<td>Glycine</td>
<td></td>
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<tr>
<td>Glutamate</td>
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<td>Aspartate</td>
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<td>Nitric oxide (NO)</td>
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Locus ceruleus = “Blue/azur spot”

Substantia nigra = “Black substance”

Raphe nuclei = “Nut seam/line”

Norepinephrine = NE

Dopamine = D?

Serotonin = SI

G&H 2011 p 713
Cocaine prevents re-uptake of Dopamine (1\textsuperscript{st} discovery), Norepinephrine (2\textsuperscript{nd}...) & Serotonin (3\textsuperscript{rd}...) & alters the plasticity of all 3 pathways!!!
"4th Pathway Releases Acetylcholine!

Cortical Alertness!

To diencephalon and cerebrum

Substantia nigra (dopamine)

Gigantocellular neurons of reticular formation (acetylcholine)

Locus ceruleus (norepinephrine)

Nuclei of the raphe (serotonin)

Mesencephalon

To cerebellum

Pons

Medulla

To cord

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

Radiations to cerebral cortex

Visual impulses

Reticular formation

Pons

Auditory impulses

Spinal cord

Ascending sensory tracts

Descending motor tracts

Cerebellum

Wake up!
Back row!
Master Controller
Endocrine System
Hypothalamus
< 1% of Brain Mass
Hormone Master Controller
100s of Functions!

Good Things Come in Small Packages!

Commissure
Lateral Hypothalamic Area
Lateral Preoptic Nucleus
Medial Preoptic Nucleus
Anterior Hypothalamic Area
Supraoptic Nucleus
Optic Chiasm
Dorsomedial Nucleus
Ventromedial Nucleus
Medial Mamillary Nucleus
Lateral Mamillary Nucleus

Plane of Frontal Section (page 6)
midbrain

**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)

**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.
Memory
Emotion
Motivation
Sociosexual Behavior
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 ≥ 5000x/hr if electrodes planted in reward center!


Figure 56-8
Technique for localizing reward and punishment centers in the brain of a monkey.