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. 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/

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
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<thead>
<tr>
<th>Day &amp; Time</th>
<th>Instructor</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>Anna Lakunina</td>
<td>212 Huestis</td>
<td>alakuni3</td>
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<td>R 11 am-12n</td>
<td>Connor O’Sullivan</td>
<td>203 LISB</td>
<td>conoro</td>
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† and by appointment.

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

Electrochemical Signal $I'\rightarrow CV$ Control Center
Brain Stem

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

Seated to Standing

$NB$: Corrective Change
Opposes Original Input

$E$: Feedback eg

$- FB$ 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 → 175 mm Hg

...into person with functioning system

BP: 100 mm Hg → 125 mm Hg
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
Astrocytes

~ 90% of Cells w/in CNS are **Glial Cells/Nuroglia**

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 $\rightarrow$ 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

[Links]
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!

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!

1. Cerebrum
2. Diencephalon – Hypothalamus + Thalamus
3. Midbrain
4. Cerebellum
5. Pons
6. Medulla
7. Spinal Cord
Ice Cream Cone Evolution Analogy

- Brain Stem
  - Medulla
  - Pons

- Cerebrum
  - Basal Nuclei
  - Cerebral Cortex

- Diencephalon
  - Hypothalamus
  - Thalamus

- Cerebellum
Central nervous system (CNS)

Input to CNS from periphery

Brain and spinal cord

Output from CNS to periphery

Peripheral nervous system (PNS)

Afferent division

Sensory stimuli

Visceral stimuli

Efferent division

Stimuli in digestive tract

Effector organs

Motor neurons

Skeletal muscles

Smooth muscle
Cardiac muscle
Exocrine glands
Some endocrine glands

Enteric nervous system

Digestive organs only

Somatic nervous system

Sympathetic nervous system

Parasympathetic nervous system

Autonomic nervous system
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
Ach = Acetylcholine

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

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; 11\textsuperscript{ed} fig 58-8 p 735
Neurotransmitter (NT) Balance: Diseases/Addictions/Moods?

- NT Lack
  - Depression
  - Parkinson’s

Balance

NT Excess
  +
  - Euphoria?
  - Suicidal Ideation?
  - Schizophrenia
  - Cocaine Addiction

Continuum

Dopamine

Serotonin/Norepinephrine

Balance
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_01_m/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>
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<tr>
<td>Epinephrine</td>
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<tr>
<td>Dopamine</td>
<td></td>
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<tr>
<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>
<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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Prominent in reward pathways & chemistry of addiction.
Norepinephrine = NE

Dopamine = D?

Serotonin = 5HT

Locus ceruleus = “Blue/azur spot”

Substantia nigra = “Black substance”

Raphe nuclei = “Nut seam/line”
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!!!


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!

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

To diencephalon and cerebrum
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

Ascending sensory tracts

Auditory impulses

Spinal cord

Descending motor tracts

Cerebellum

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

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)

**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

- Midbrain

**Emoticons**

- 😊 = 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 !!!!
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 ≥ 5000x/hr if electrodes planted in reward center!


G&H 11th ed only p 735