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/)

Common linking mechanisms: COME Cocaine & Meth HEMA Heroine & Marijuana, LSD & Ecstasy (S? Serotonin!)

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

III. **Addiction Medicine: Homeostasis & Overdose Story!**

G&H ch 59 pp 751-61...Additional Information as Review?

IV. **Organization of the Nervous System**

G&H ch 46 pp 582-7, LS1/2 ch 5

A. Central vs peripheral, computer analogy fig 46-4
B. Neurons, neuronal classes, neuroglia, connections

V. **Autonomic Nervous System**

G&H ch 61 pp 773-85 + LS +...

A. Sympathetic vs. parasympathetic fig 61-1,61-3
B. Neurotransmitters, receptors, actions tab 61-2, 61-1
C. Nicotine & adrenal hormonal disruption
**BI 358 Office Hr Winter 2018**

<table>
<thead>
<tr>
<th>Day &amp; Time</th>
<th>Instructor</th>
<th>Place</th>
<th>e-mail</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>W 10-11 am</td>
<td>Hannah Soukup</td>
<td>130 HUE</td>
<td>hsoukup</td>
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<tr>
<td>R 10-11 am</td>
<td>Kelsey Shultz</td>
<td>200 LISB</td>
<td>kshult7</td>
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+ and by appointment.

For Pat, please call 541-346-6055/4525 or e-mail.
For Hannah, please e-mail.
For Kelsey, 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 1-4 G&H 2016

+ FB pathological!
Venous Pooling

Electrochemical Signal

I’

Brain Stem

CV Control Center

Electrochemical Signal
e.g., Symp Acclerator N

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

Seated to Standing

NB: Corrective Change
Opposes Original Input

- FB eg

Ef

BP

HR

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

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

- NT Lack

Depression

Serotonin/Norepinephrine

Euphoria? Suicidal Ideation?

Parkinson’s

Dopamine

Schizophrenia Cocaine Addiction

Balance

Balance
Figure 45-6  Physiologic anatomy of the synapse.

NB: Pat, chemical vs electrical
Synapse Animations

http://highered.mheducation.com/sites/0072495855/student_view0/chapter14/animation_transmission_across_a_synapse.html

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>
<th></th>
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<tbody>
<tr>
<td>Acetylcholine</td>
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### Class II: The Amines
- Norepinephrine
- Epinephrine
- Dopamine
- Serotonin
- Histamine

Prominent in reward pathways & chemistry of addiction.

### Class III: Amino Acids
- Gamma-aminobutyric acid (GABA)
- Glycine
- Glutamate
- Aspartate

### Class IV
- Nitric oxide (NO)
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!

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
To cord

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

Wake up!
Back row!
Master Controller
Endocrine System
**Good Things Come in Small Packages!**

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

- 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)
**Posterior**

- Dorsomedial nucleus (GI stimulation)
- Posterior hypothalamus
  - Increased blood pressure
  - Pupillary dilation
  - Shivering
- Perifornical nucleus
  - Hunger
  - Increased blood pressure
  - Rage

**Reward**

- 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

**Midbrain**

- = Reward
- = Punishment
FIGURE 5-18
Limbic system
This partially transparent view of the brain reveals the structures composing the limbic system.

- Frontal lobe
- Cingulate gyrus
- Fornix
- Thalamus
- Hippocampus
- Temporal lobe
- Amygdala
- Hypothalamus
- Olfactory bulb
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 \( \geq 5000 \times \text{hr} \) if electrodes planted in reward center!


Figure 56–8

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

G&H 11th ed only p 735
Opiates Brain Action + Overdose Story

- **Limbic System**: Change emotions & increase feelings of pleasure.
- **Brain Stem**: Depress breathing by altering neurochemicals.
- **Spinal Cord**: Block pain message transmission.

*Source*: National Institute on Drug Abuse
Additional Background
Neuronal Physiology
Nervous System

CNS

PNS

input

output

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 → 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_iliff_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!

**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.

G&H 2011 p 546
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

- 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.

D Silverthorn 2010
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 (α₁, α₂)

= β Receptor (β₁, β₂)
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

Discussion/questions!