BI 358 Lecture 2

I. **Announcements**
   Douglas Bovee, MD, Addiction & Internal Medicine Specialist next session! *NB:* Sign-in + e-feedback < 24-48 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 & Ecstacy (S? Serotonin!)

II. **Homeostasis Connections**
   Model, 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

Come see us during office hr!   Dr. Bovee next session, Tuesday!
No more Pat 'til Thursday! Hooray!
Methamphetamine, the “mother of all highs”!

https://www.pbs.org/wgbh/pages/frontline/meth/body/
https://www.pbs.org/wgbh/pages/frontline/meth/body/methbrainflash.html
Invariably, Negative Feedback
**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'

CV Control Center
Brain Stem

C

Electrochemical Signal
e.g., Symp Accelator N

O

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

Seated to Standing

NB: Corrective Change
Opposes Original Input

FB eg

BP

HR

VC

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

Gain = \frac{Correction}{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

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
  - Parkinson’s

Balance Continuum

+ NT Excess
  - Serotonin/Norepinephrine
    - Euphoria?
    - Suicidal Ideation?
  - Dopamine
    - Schizophrenia
    - Cocaine Addiction

Balance
Chemical vs. Electrical Synapse

1-way

- Action potential
- Ca++
- Synaptic vesicle
- Neurotransmitter
- Ionotropic receptor
- Ions
- Metabotropic receptor
- Second messenger
- Cellular response:
  - Membrane potential
  - Biochemical cascades
  - Regulation of gene expression

2-way

- Action potential
- Gap junction channels
- Ion flow

G&H 2016 fig 46-5
Chemical 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>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td></td>
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</tbody>
</table>

**Class II: The Amines**

- Norepinephrine
- Epinephrine
- Dopamine
- Serotonin
- Histamine

**Class III: Amino Acids**

- Gamma-aminobutyric acid (GABA)
- Glycine
- Glutamate
- Aspartate

**Class IV**

- Nitric oxide (NO)

Prominent in reward pathways & chemistry of addiction.

G&H 2011 p 550; G&H 2016 p 585
**Locus ceruleus** = "Blue/azur spot"

**Substantia nigra** = "Black substance"

**Raphe nuclei** = "Nut seam/line"

**Norepinephrine** = NE

**Dopamine** = D?

**Serotonin** = SI
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
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

Cerebellum

Auditory impulses

Spinal cord

Ascending sensory tracts

Descending motor tracts

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!
**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)

**ARCULATE 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

**HYPOTHALAMUS**

- 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
- Olfactory bulb

*Hypothalamus*
Memory
Emotion
Motivation
Sociosexual Behavior !!!!
Enraged BI 358 student post Quiz 1?

GTF or Pat?

Really, Jose Delgado, Yale University!

Pat or GTF?
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.

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
Naloxone/Narcan has much higher affinity for opioid receptors & thus restores breathing within minutes!

SOURCE: [https://www.detoxes.net/narcan-work-secret-life-miracle-drug/](https://www.detoxes.net/narcan-work-secret-life-miracle-drug/)
Active Learning Group Work
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!
Neuron 1

Input
Dendrites ≡ Antennae

Controller
Soma ≡ NCB

Output
Axon

Neuron 2

Neuron 3

H. Howard 1980
Figure 45-5  Typical anterior motor neuron, showing presynaptic terminals on the neuronal soma and dendrites. Note also the single axon.

G&H 2011 p 547; G&H 2016 p 582
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.

G&H 2011 p 547; G&H 2016 p 596
Figure 45-4  Block diagram of a general-purpose computer, showing the basic components and their interrelations. G&H 2011 p 546; G&H 2016 p 580
CNS Connections: The Central 7!

Fore-

1. Cerebrum

2. Diencephalon – Hypothalamus + Thalamus

Mid-

3. Midbrain

4. Cerebellum

Hind-

5. Pons

6. Medulla – Brain Stem

7. Spinal Cord
Ice Cream Cone Evolution Analogy

- Brain Stem
  - Medulla
  - Pons

- Cerebellum

- Diencephalon
  - Hypothalamus
  - Thalamus

- Cerebrum
  - Basal Nuclei
  - Cerebral Cortex
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 pp 731-3; G&H 2016 pp 775-8
**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!

Adrenals = Paired organs above kidneys

Output to blood

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