1. **The Neuroendocrine System**: Sum of the glands, hormones, and target tissues/organs involved in the control of bodily functions (including behavior)

**Glands**: __________________________________________________________

______________________________________________________________

______________________________

**Two types:**

_____________________: secrete their chemicals into “ducts”, which are carried to the surface of the body (ex., sweat and tear glands)

_____________________: ductless glands that secrete “hormones” into the general circulation (ex., pituitary and gonadal glands)
Hormones:

I. Amino acid derivatives (ex., adrenaline)
II. Short peptides and proteins (ACTH)
III. Steroids (lipid soluble - synthesized from ________ - ex., cortisol, estrogen, testosterone)
Examples of hormones released by the different glands:
Pineal: **Melatonin**
Hypothalamus: _______________________________
Pituitary: _______________________
Thyroid: ______________________
Thymus: ___________________________________
Adrenals:_________ _________
Pancreas: ________
Testes: _________________________
Ovaries: _________________________

Melatonin
Thyroxin hormone (T3, T4)
Lymphokines (involved in immunity - IL -1)
Testosterone, estradiol
Hierarchical control of hormones

The ________________ ultimately controls many of the hormones found in the body.

This is usually regulated through “multi-step” signaling mechanisms (__________) all the way to the various glands in the body that synthesize hormones.

In turn, many hormones reach back to the brain and influence various cognitive and behavioral functions.

(A) In response to sensory stimuli and cognitive activity, the hypothalamus produces neurohormones that enter the anterior pituitary through veins and the posterior pituitary through axons.

(B) On instructions from these releasing hormones, the pituitary sends hormones into the bloodstream to target endocrine glands.

(C) In response to pituitary hormones, the endocrine glands release their own hormones that stimulate target organs, including the brain. In response, the hypothalamus and the pituitary decrease hormone production.
Neural control of the ANTERIOR pituitary gland

- neurons of several hypothalamic nuclei (see yellow, pink and green neurons below) produce and release hormones (“_________________”) from their axons in the median eminence;
- the median eminence is highly vascularised by the hypophyseal artery, which transport the released hormones into the anterior pituitary via portal veins;
- anterior pituitary cells respond to hypothalamic hormones by producing and releasing their hormones into the hypophyseal vein, which bring hormones into the general blood circulation (goes everywhere in the body).
- Ex., Gonadotropin-releasing hormone (GnRH) from the hypothalamus produces the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary, which target the gonads.
- neurons from different hypothalamic nuclei also control the posterior pituitary gland;
- hormone containing neurons of the hypothalamus (see blue and red neurons below) release their hormones directly in the ___________________; 
- the released hormones then enter the _____________ and reach the ________ __________.

- Example: oxytocin is released from neurons of the supraoptic nucleus of the hypothalamus directly into the posterior pituitary and is involved in uterine contraction during childbirth and milk ejection during suckling.
Example: Release of GONADAL HORMONES

- Neurons of different hypothalamic nuclei produce and release gonadotropin-releasing hormone (GnRH) in the anterior pituitary gland;
- GnRH induces the production and release of follicle-stimulating and luteinizing hormones (FSH & LH) from anterior pituitary cells, which reach the general circulation;
- FSH and LH eventually reach the gonads, inducing the production and release of estrogens, progesterone, and androgens (testosterone) from cells in the gonads.
Regulation of Hormone Levels

- **Concept of Homeostasis**: A state of internal metabolic balance, which keeps body functions within a narrow range.

- This is achieved via 1. Feedback loops; 2. Neural controls; and 3. Experience or learning.

1. **Feedback in the Neuroendocrine System**: Most of the feedback in the neuroendocrine system is ________________________________

    **Negative feedback**: ________________________________

    **Example of negative feedback**: heating system in your house or apartment
2. Neural control:
Neurons from other brain regions send their axons to hypothalamic nuclei and can regulate the activity of hypothalamic releasing-hormone neurons (see (B) above);
- this can increase or decrease hormone release and overall levels in bloodstream.

3. Experience/learning:
Repeated experience (learning) with a specific situation can lead to increased or decreased hormone levels;
- often regulated by brain regions that send axons to hypothalamus.
MOTIVATED BEHAVIORS

There are 2 general classes of motivated behaviors:

**Regulatory Behaviors:**

- Examples: temperature regulation, eating (energy) and drinking, salt appetite, waste elimination

**Non-regulatory Behaviors:** behaviors that are not controlled by homeostatic mechanisms - all behaviors excluding those regulated by homeostatic processes

- Examples: sexual behavior, parental behavior, aggression, playing sports, watching TV, etc

The hypothalamus is particularly important for the control of regulatory and non-regulatory behaviors.
Example of Non-regulatory behavior: Sexual Behavior

Gonadal (sex) hormones have various actions on the brain and behavior; these actions are both developmental (__________________) and in adulthood (________________);

1. Organizational effects of sex steroids on the brain and body: Process whereby gonadal hormones act on the brain to produce distinctly female or male brains;
   - some brain areas are referred to as ________________;
   - the suprachiasmatic and parts of the preoptic nuclei are generally larger in males; additional differences in spinal cord, amygdala, and frontal cortex.

During fetal development, higher testosterone levels produce these changes in the brain, but . . . estradiol masculinizes the brain!

How?
2. Activational effects of gonadal hormones:
Female reproductive cycle: While males have daily fluctuations in sex steroid levels, females display “cycling” gonadal steroid levels, called the menstrual cycle in primates (including humans) and estrous cycle in other mammals;
- the levels of the different sex steroid hormones change significantly over the cycle period in women (on average, 28 days).

In animals, adult female behavior varies across estrous cycle;
- high estrogen levels are associated with sexual receptivity;
- high estrogen levels are also associated with increased numbers of dendritic spines in the hippocampus (next page).

In adult males, high testosterone levels are associated with increased motivation to seek sexual and copulatory behaviors.
Brain Regions and Sexual Behaviors

Known from animal studies - not clear if this applies to humans!

________________________ controls the sexual receptivity posture (mating posture - lordosis) in females;

_____________________________ controls copulatory behavior (thrusting) in males, but not sexual motivation;

___________________________ in males (and possibly in females) controls sexual motivation (the trap door experiment!!!);

Cortex, especially frontal lobes?
Example of Regulatory Behavior: EATING

Eating is partly controlled by the digestive tract, the hypothalamus, and cognitive factors.

- The digestive tract (below): functions as a reservoir where a variety of chemicals and enzymes released (hydrochloric acid, pepsin, etc) help ____________________ essential nutrients and energy molecules.

Three classes: __________

____________________

____________________

Lipids provide approximately 85% of stored energy, whereas amino acids (14.5%) and glycogens (0.5%) provide the rest.
Early work indicating role of ventromedial hypothalamus

**EXPERIMENT 11-1**

**Question:** Does the hypothalamus play a role in eating?

**Procedure**
- The ventromedial hypothalamus (VMH) of the rat on the right was damaged, and her body weight was monitored for a year. Her sister on the left is normal.

**Intact brain of sister rat**

**Rat brain with lesion**

**Results:**
- The VMH-lesioned rat showed a dramatic increase in food intake and body weight.

**Graph:**
- Lesioned rat vs Control rat
  - Lesioned rat: Body weight (gm) increases dramatically over 12 months.
  - Control rat: Body weight remains relatively stable.

**Conclusion**
- The VMH plays a role in controlling the cessation of eating. Damage to the VMH results in prolonged and dramatic weight gain.
Multiple peripheral signals contribute to the Regulation of feeding:

**Hunger signals**
- **Sight of food and thinking about food**: raises activity of autonomic nervous system, which activates pancreas to release insulin in blood circulation - produces _____________________ that initiates response in nucleus of the solitary tract (see below)

- **Hypoglycemia**: a drop in blood glucose levels which is sensed by specialized receptors onto neurons of the area postrema (no blood-brain-barrier), and peripherally in the liver, via the ____________ (neurons in the nucleus of the solitary tract in the medulla)

- **Lipoprivation**: a drop in fatty acid levels (leptin) available to cells, detected __________________________. Information provided to brain via vagus nerve
Regulation of feeding (continued):

Satiety signals

- **Gastric distension**: somatosensory receptors located in gastrointestinal tract and enteric nervous system sense ________________, and provide this information to nucleus of the solitary tract via the vagus nerve.

- **Cholecystokinin (CCK)**: peptide released from ________________
  - responds to both volume and caloric content of food being absorbed - acts on vagal somatosensory receptors and synergises with gastric distension signals from gastrointestinal tract.

- High levels of **Insulin** (released from β-cells of pancreas) and **glucose** in blood serve as a satiety signal at the level of the hypothalamus (________ ________).
Some brain control of feeding: 3 hypothalamic nuclei critically control feeding and metabolism:

1. ____________________ : involved in the release of ACTH and thyrotropin from the anterior pituitary (involved in metabolism);

2. ____________________ : coordinates motor responses involved in feeding behaviors;

3. _________________ : receives signals from leptin & insulin, and project to paraventricular nucleus and lateral hypothalamus to • or • feeding.
The Control of Drinking: Water Balance

The human body is made out of approximately 70% water; there is a significant need to keep intracellular and extracellular levels of water at a relatively constant level, via two mechanisms

1. Osmotic thirst (cellular dehydration): _______

- bar peanuts and chips!!!
2. Hypovolemic thirst: decrease in overall blood volume
- increases water retention via two mechanisms:

a) reduced blood flow in renal system produces release of ________________ which is sensed by hypothalamic neurons.
- these neurons activates paraventricular ADH neurons to release vasopressin from posterior pituitary.

b) mechanoreceptors (baroreceptors) in wall of ________________ signal loss of blood to the hypothalamus via vagus nerve and nucleus of the solitary tract (NTS).
- NTS also projects to paraventricular nucleus and synergizes with effects of angiotensin and activate sympathetic nervous system to help correct the reduction in blood pressure

- NTS also projects to lateral hypothalamus to stimulate drinking behaviors.