Course Administration

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Internal Regulation

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Biologically, what is necessary for life is a coordinated set of chemical reactions. These reactions take place in water at a rate dependent on the temperature of the solution, concentration of the solutes and availability of energy.

Homeostasis refers to biological processes that keep body variables within a fixed range. If the range is very narrow, then it is referred to as a set point.

The process of homeostasis includes:
- sensory transduction of a variable and signaling changes from the optimal range
- integrated response (visceromotor, humoral and somatic) to restore parameter back to optimal (called negative feedback)

The hypothalamus plays a key role in the regulation of body temperature, fluid balance, and energy balance.
Hypothalamus and Homeostasis

The hypothalamus orchestrates an integrated response to maintain the homeostasis of body parameters. The response generally has three components:

- **visceromotor (fast physiological):** adjusting the balance of sympathetic and parasympathetic outputs of the autonomic nervous system (ANS)
- **humoral (slow physiological):** releasing hormones
- **somatic motor (behavioral):** motivating appropriate behaviors by the somatic motor system

The **paraventricular nucleus (PVN)** initiates the visceromotor and humoral responses:

- dorsal and ventral parvocellular cells control the ANS
- medial parvocellular cells release hormones that affect the release of other hormones from the anterior pituitary; and
- magnocellular cells release directly hormones from the posterior pituitary

The **lateral hypothalamic area (LHA)** motivates the somatic motor response via release of orexin in the dorsolateral prefrontal cortex (and ventral tegmental area – reward circuit).
The autonomic nervous system influences the function of internal organs. The sympathetic nervous system is often considered the “flight or fight” system, while the parasympathetic nervous system is often considered the "rest and digest" system. These systems differ in many ways: outflow path; location of second-order neurons; neurotransmitter used by second-order neurons (nor/epinephrine vs acetylcholine) and physiological effect.
The endocrine system consists of a variety of organs (shown) whose primary function is to release hormones directly into the circulatory system. All endocrine glands are regulated directly by the hypothalamus and pituitary.

The pituitary gland (about the size of a pea) is a protrusion off the bottom of the hypothalamus. It is composed of two lobes: anterior and posterior.

- anterior pituitary synthesizes and secretes hormones in response to hormones released by the hypothalamus.
- posterior pituitary develops as an extension of the hypothalamus: it stores and secretes (but does not synthesize) hormones.
Body temperature is a measure of an organism’s ability to generate and to eliminate heat. It is tightly regulated.

Heat is generated within the body as a byproduct of many chemical reactions, including cellular respiration (the conversion of nutrients into ATP).

Amphibians, reptiles and fish are ectothermic (cold-blooded) (their body temperature matches that of the environment). Mammals/birds are endothermic (warm-blooded).

Adult humans expend about 2/3rds of their daily caloric energy input to maintain a nearly-constant high body temperature. Benefits: mobile all year long; protects against infection.
Endothermic animals use both physiological and behavioral mechanisms to control changes in body temperature.

Physiological mechanisms if hot or cold:
- sweat (pant or lick) or shiver
- increase or decrease blood flow to the skin
- decrease or increase metabolism

Behavioral mechanisms if hot or cold:
- find a cool or hot place
- become less or more active
- sleek or fluff fur (human: less or more clothes)
- stand alone or together
Sensors: in medial preoptic and anterior nuclei. These areas receive input from the anterolateral tract and respond to changes in local body temperature.

Responses:
- PVN (visceromotor – sweat glands, skin arterioles; humoral – thyroxine)
- dorsal medial nucleus (shivering)
- LHA: somatic
Thirst

Water constitutes about 70% of the mammalian body. Because the rate of chemical reactions depends on the concentration of chemicals, and the body needs enough fluid in the body to maintain normal blood pressure, water is regulated within very narrow limits.

Mechanisms of regulation:
- drink plenty of water, eat moist foods, excrete dilute urine (default role of kidney)
- drink little water, decrease sweat, constrict blood vessels, excrete concentrated urine
Two Types of Thirst

Thirst is divided into two types: osmotic and hypovolemic.

Osmotic thirst is caused by eating salty foods, which increases the concentration of solutes (e.g., sodium ions) in the extracellular space.

Hypovolemic thirst is caused by losing fluid volume, such as by bleeding or vomiting.
The combined concentration of all solutes (molecules in solution) in mammalian body fluids (inside and outside of cells) is held nearly constant (0.15 mol/liter).

Osmotic pressure for water to flow occurs when solutes are more concentrated in one area than another.

If something salty is eaten, then sodium ions spread throughout the fluid outside of cells but cannot cross into cells. This draws water out of the cells (to equalize total concentrations) with the result that cells shrink.

Cells in the organum vasculosum (OVLT; rostral to the hypothalamus) and the subfornical organ (SFO; superior to the thalamus) detect their own water loss.
Osmotic Thirst Mechanisms

Osmoreceptors activate various nuclei in the hypothalamus to conserve water (paraventricular and supraoptic) and to generate the desire to drink (LHA).

Water conservation is controlled by the release of antiduretic hormone (ADH) from the posterior pituitary. ADH enables the kidneys to reabsorb water and thus excrete a concentrated urine.
Hypovolemic Thirst Receptors

Blood volume (blood pressure) is controlled on a minute-by-minute basis by inputs from baroreceptors, which are found in the walls of arteries, veins and the heart.

Baroreceptors are a type of mechano-receptor sensory neuron that is excited by stretch and inhibited by relaxation of the blood vessel.
Hypovolemic Thirst Mechanisms

Hypovolemia causes suppression of baroreceptor activity, which stimulates the vasomotor center in the medulla to activate various nuclei in the hypothalamus to conserve water and to generate the desire to drink.

Unlike osmotic thirst, hypovolemic thirst is best quenched with a salty drink (not pure water). In addition to its effects in the hypothalamus, hypovolemia causes the kidneys to release renin, which leads to the synthesis of angiotensin II and the release of aldosterone. These hormones alter the properties of the gustatory system to produce a craving for sodium tastes.
The brain’s requirement for energy, in the form of glucose, is urgent: even a few minutes of deprivation will lead to loss of consciousness and death.

The body’s energy stores are replenished during and immediately after consuming food. During the parandial state, glucose is stored (via anabolism) in the form of two macromolecules: glycogen (in liver and skeletal muscles) and triglycerides (in fat). During the fasting state, stored glycogen and triglycerides are broken down (via catabolism) to provide nutrients to the body.

Homeostatic mechanisms aim to reach an equilibrium between energy intake and energy expenditure. Current theory suggests that body weight drifts around a natural settling point (a balance between hunger and satiety factors) as opposed to a particular set point.
The function of the digestive system is to break food down into smaller molecules that cells can use. Digestion takes place in the mouth, stomach and small intestines. Material is absorbed in the small and large intestines.

The digestive system influences food intake in multiple ways:
- lactose intolerance
- conditioned taste aversion
Long-Term Regulation of Feeding

Homeostatic long- and short-term mechanisms regulate energy reserves and feeding. Body weight is usually very stable in the long-term. Weight lost during a period of starvation is gained rapidly when food is available. Similarly, if an animal is force fed, it will gain weight, but the weight is lost if the animal can regulate its own food intake.

➔ Lipostatic hypothesis (Kennedy 1953): the brain monitors the level of body fat and “defends” this source against perturbation. Thus, long-term regulation of body weight is asymmetric (more sensitive to weight loss than weight gain).

Evidence suggests that fat cells release the hormone leptin to communicate the level of fat to the brain. In particular, mice lacking both copies of the ob gene (which codes for leptin) are obese, whereas deficient mice which receive daily doses of leptin are normal in size.

Leptin deficiency is rare in humans; rather obesity may be caused in part by decreased penetration through the blood-brain barrier; reduced receptors; altered CNS response.
In addition to the long-term regulation of feeding behavior by leptin, the motivation to eat depends on short-term factors such as the length of time since the last meal and how much was consumed at that time.

Hunger/satiety is regulated by a variety of short-term factors including signals from the stomach, intestines, and the composition of chemicals in the blood.

**Stomach:**
- hormone ghrelin (hunger)
- distention (vagus nerve) (satiety)

**Intestines:**
- hormone cholecystokinin CCK (satiety) (also closes the exit of the stomach causing its distention → activation of the vagus nerve)

**Blood:**
- hormone insulin (pancreas) low = hunger; high = satiety
Neural Regulation of Appetite

The arcuate nucleus (or infundibulum) of the hypothalamus is considered to be the “master area” for control of appetite.

It has two sets of neurons: one set sensitive to hunger signals (purple) and one set sensitive to satiety signals (green).

When activated, hunger-sensitive neurons release AgRP and NPY onto their targets (PVN and LHA), whereas satiety-sensitive neurons release αMSH and CART into the same targets.

Hunger/satiety produces the following effects:

• **(visceromotor)** activate parasympathetic or sympathetic nervous system
• **(humoral)** decrease/increase release of thyroxine to affect metabolic rate
• **(somatic)** stimulate-suppress feeding
Obesity and Eating Disorders

Obesity is a medical condition in which excess body fat has accumulated, with adverse health effects (e.g., heart disease and diabetes). It is often caused by a mix of excessive food intake, lack of physical activity, and genetic susceptibility. Dieting and exercising are the main treatments. If these do not work, then weight-loss drugs or surgery may be effective.

Common eating disorders include anorexia nervosa and bulimia nervosa.

- Anorexia nervosa is a condition in which people refuse to eat or fear to eat as much as they need. Its causes are not yet understood.
- Bulimia nervosa is characterized by alternation between undereating and overeating. It has been compared to addictive behaviors.