Chemical Signals in Animals

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An Introduction to Regulatory Systems

- **Hormone** ("excite" in Gr.) is a chemical signal that is secreted directly into body fluid, and communicates regulatory messages within the body.
  - Hormones can act at very low concentrations.

The endocrine system and the nervous system are structurally, chemically, and functional related

1. Structural relationships:
   A. Many endocrine glands contain specialized nerve cells, **neurosecretory cell**s, which secrete hormones: hypothalamus, and posterior pituitary.
   B. Endocrine glands that are not nervous tissue have evolved from the nervous system: the adrenal medulla is derived from a modified ganglion.
2. Chemical relationships: several vertebrate hormones are used as signals by the nervous system as well as by the endocrine system, e.g., epinephrine.
3. Functional relationships:
   A. The coordinating system controlling physiological processes, e.g., the release of milk by a mother during nursing: Suckling stimulates sensory cells in the nipples, and nervous signals to the hypothalamus trigger release of oxytocin from the posterior pituitary.
   B. Each system affects the output of the other: the endocrine system affects both the development of the nervous system and its output, behavior.

- Feedback is common to both the endocrine and nervous systems:

Invertebrate regulatory systems clearly illustrate endocrine and nervous system interactions

- *Aplysia*:
  - A hormone stimulates the laying of thousands of eggs and also inhibits feeding and locomotion: Such activities interfere with reproduction.

- Arthropods
  - **Ecdysone** (molting hormone) is secreted from prothoracic gland.
  - **Brain hormone** produced by neurosecretory cells in the brain promotes development by stimulating the prothoracic gland to secrete ecdysone.
  - **Juvenile hormone** (JH): retention of larval stage.
    - Brain hormone and ecdysone are balanced by juvenile hormone.
    - Synthetic JH are used as insecticides to prevent insects from maturation.

Chemical Signals and Their Modes of action

A variety of local regulators affect neighboring target cells

- Local regulators: **autocrine**, or **paracrine**
  - Neurotransmitters, histamine, interleukin:
    - In addition on body's defense, histamine also promotes the secretion of hydrochloric acid and pepsin by the cells of stomach.
  - **Nitric oxide** (NO) secretes by neurons as neurotransmitter, secretes by WBCs to kill cancer cells and bacteria, secretes by endothelial cells to dilate blood vessels.
  - **Growth factor**s: nerve growth factor (NGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF)

- **Prostaglandin**s (**PG**s): modified fatty acids derived from lipids of the plasma membrane.
  - Prostaglandin E and prostaglandin F have antagonistic effects: PGE causes the muscles to relax, and PGF signals the muscles to contract.
  - PGs induce fever and inflammation and intensify the sensation of pain.
    - **Aspirin**: inhibit the synthesis of prostaglandins.
  - PGs secreted by cells of the placenta cause chemical changes in the uterus muscles, making them more excitable and helping to induce labor.

Chemical signals bind to specific receptor proteins within target cells or on their surface

- A given hormone can affect different target cells in an animal differently.

- A given hormone can vary the effects in different species of animals, e.g., thyroxine: metabolic regulation in mammals, and metamorphosis in frog.

Most chemical signals bind to plasma-membrane proteins, initiating signal-transduction pathways

- The chemical signals (**ligand**s) like most neurotransmitters, growth factors, and most hormones are unable to pass through the plasma membrane of their target cells: The receptors are components of **signal-transduction pathways** that convert the extracellular signals to a specific intracellular response.

- **Melanocyte-stimulating hormone** (**MSH**): direct microinjection of MSH into individual melanocytes does not induce melanosome dispersion

Steroid hormones, thyroid hormones and some local regulators enter target cells and bind with intracellular receptors

- **Steroid hormones** derived from cholesterol is fat-soluble, e.g., sex hormones.
  - Steroids such as estrogen and progesterone diffuse through the target cell membrane, and bind to a receptor protein. This hormone-receptor complex enters the nucleus, then bind to specific regions of the chromatin to initiate the transcription of specific genes.
  - Two types of cells respond differently to a same chemical signal: In female bird, estrogen induces cells in the reproductive system to synthesize ovalbumin, but different proteins in liver cells.
  - The same hormone may have different effects in different species: human thyroxine – metabolic regulation; frog thyroxine – metamorphosis.

The Vertebrate Endocrine System

- The functions of a hormone are often countered by another hormone: **antagonistic effect**.
- **Tropic hormone**s: hormones have other endocrine glands as their targets.

The hypothalamus and the pituitary integrate many functions of the vertebrate endocrine system

- **Hypothalamus** receives information from peripheral nerves and from other parts of the brain, and then initiates endocrine signals.
  - Two sets of neurosecretory cells; one produces the hormones of the posterior pituitary, and the other secret **releasing factor**s or **inhibiting hormone**s to regulate the anterior pituitary.

- **Pituitary** is a small appendage at the base of the hypothalamus, and has two lobes, each with a different function.
  - The anterior pituitary, **adenohypophysis**, produces its own hormones.
  - The posterior pituitary, **neurohypophysis**, is an extension of the brain, which develops from a small bulge of the hypothalamus and remains attached to the hypothalamus

Posterior Pituitary Hormones:

- The two posterior pituitary hormones made by the hypothalamus are peptide hormones.
- **Oxytocin** induces contraction of the uterine muscles during birth and causes the mammary glands to eject milk during nursing.

- **ADH** (**antidiuretic hormone**) acts on the kidneys to increase water reabsorption that helps regulate the osmolarity of the blood, which is monitored by a group of nerve cells that function as osmoreceptors in the hypothalamus: negative feedback on osmotic regulation:
  1. The blood osmolarity increasing stimulates hypothalamus to release ADH.
  2. ADH bound with ADH receptors on the lining cells of the collecting ducts increase the cAMP concentration to enhance the permeability of H_2O in the collecting ducts, which make the blood osmolarity decreasing.
  3. The hypothalamus senses the lower blood osmolarity and then stops to release ADH.

Anterior Pituitary Hormones: Four tropic hormones

- **Growth hormone** (**GH**): a protein of almost 200 a.a.
  - GH signaling the liver to produce growth factor called **insulin-like growth factors** (**IGF**s), which stimulate bone and cartilage growth.
  - **Gigantism** and **acromegaly**:
  - Hypopituitary dwarfism: Genetic engineering to produce human GH.

- **Prolactin** (**PRL**): protein structure is similar to GH
  - PRL is an **ancient hormone** whose functions have diversified during the evolution of the various vertebrate classes: PRL stimulates mammary gland growth and milk synthesis in mammals, regulates fat metabolism and reproduction in bird, delays metamorphosis in amphibians, and regulates salt and water balance in freshwater fish.

- **Follicle-stimulating hormones** (FSH) and l**uteinizing hormone** (LH) are called **gonadotropin**s, because they stimulate the activities of the male and female gonads, the testis and ovaries.
- **Thyroid-stimulating hormone** (**TSH**) regulates release of thyroid hormones.

- **Pro-opiomelanocortin** (**POMC**) can be cleaved into ACTH, MSH, endorphin, and enkephalin.
  - **Adrenocorticotropin** (**ACTH**) stimulates the production and secretion of steroid hormones by the adrenal cortex.
  - **Endorphin** and **enkephalin** mimic the actions of morphine on the nervous system and appear to inhibit **pain reception**: the body's natural opiates.

The Pineal gland is involved in biorhythms

- Pineal gland is a small mass of tissue near the center of the mammalian brain or closer to the brain surface in some other vertebrates.
  - The pineal contains light-sensitive cells or has nervous connections from the eyes: light period might regulate biological rhythms associated with reproduction.

- **Malatonin**, a modified a.a., secretes by the pineal at night: the main target cells of malatonin are in the part of the brain, **superchiasmatic nucleus** (SCN), which functions as a biological clock.

Thymus

- **Thymus** is quite large during childhood. At puberty, it begins to decline quickly and disappears by adulthood.
  - **Thymosin** stimulates the development and differentiation of T lymphocytes.

Thyroid hormones function in development, bioenergetics, and homeostasis

- The thyroid gland produces two very similar hormones derived from tyrosine, **triiodothyronine** (T3) and **thyroxine** (T4).

- **Hypothyroidism** can cause **cretinism** in infants and produce symptoms such as weight gain, lethargy and intolerance to cold in adults.
  - **Cretinism** results in retarded skeletal growth and poor mental development.
  - **Goiter**: enlargement of thyroid often caused by **iodine** deficiency in the diet.
- **Hyperthyroidism** produces such symptoms as high body temperature, profuse

sweating, weight loss, irritability, and high blood pressure.

- The secretion of thyroid hormones is controlled by the hypothalamus and pituitary in a negative feedback loop.

- The thyroid gland also secret **calcitonin**, which lowers calcium, levels in the blood as part of calcium homeostasis.

Parathyroid hormone and calcitonin balance blood calcium

- **Parathyroid hormone** (PTH) has an effect opposite to calcitonin.
  - PTH elevates blood Ca^{++} by stimulating Ca^{++} absorption in the intestine and Ca^{++} reabsorption in the kidney, and by inducing **osteoclast**s (special bone cells) to decompose the matrix of bone and release Ca^{++} to the blood.

- Vitamin D is essential to PTH function:

- **Tetany** is fatal: leading to convulsive contractions of the skeletal muscles.

Endocrine tissues of the pancreas secrete insulin and glucagon, antagonistic hormones that regulate blood glucose

- **Islets of Langerhans**: Each islet has a population of **α cell**s, which secrete the peptide hormone **glucagon**, and a population of **β cell**s which secrete the protein hormone **insulin**.
- The liver, skeletal muscles, and adipose tissues store large amounts of fuel molecules:
  - **Insulin** lowers blood sugar by increasing glucose uptake from the blood to

form **glycogen** in the muscle and liver, by slowing glycogen breakdown, by inhibiting the conversion of a.a. or fatty acid to sugar: Insulin is the only hormone can reduce blood sugar levels.

- **Glucagon** counters insulin action: antagonistic hormone
  - Only liver cells are sensitive to glucagon: glycogen hydrolysis

- **Diabetes mellitus**: human normal blood glucose level: 90mg/100ml
  - As more glucose concentrates in the urine, more water is excreted with it, resulting in excessive volumes of urine and persistent thirst.
  - Because glucose is unavailable, fat serves as major fuel source: acidic metabolites formed by fat breakdown accumulate in blood to threaten life.
  - **Type I diabetes mellitus**:
    - **Insulin-dependent** or juvenile-onset diabetes: an autoimmune disorder
    - Treatment: genetic engineering insulin injections.
  - **Type II diabetes mellitus**:
    - **Insulin-independent** or adult-onset diabetes: a deficiency of insulin or changes of insulin receptors to reduce responsiveness in target cells.
    - More than 90% of diabetes is type II occurred after about age 40, and heredity is a major factor.
    - Most cases can manage their blood sugar by exercise and dietary control.

The adrenal medulla and adrenal cortex help the body manage stress

- Adrenal gland is made up of two glands with different cell types, functions, and embryonic origins: Adrenal medulla has close developmental and functional ties with nervous system.
- Adrenal medulla:

- **Fight-or-flight syndrome**: **Epinephrine** is secreted in response to stress.
  - Response to stress: **Acetylcholine** is secreted from the stressed nerve cells in the adrenal medulla, and the epinephrine releasing cells have acetylcholine receptor on their cell surfaces.
  - Epinephrine and **norepinephrine** synthesized from **tyrosine** are members of **catecholamine**.
  - Epinephrine and **norepinephrine** mobilize glucose from skeletal muscle and liver cells, stimulate the release of fatty acids from fat cells, increase the rate and stroke volume of the heartbeat, contract the blood vessels to shunt blood away from the skin, gut, and kidney, but relax blood vessels to increase the blood supply to heart, brain, and skeletal muscle.

- Adrenal cortex
  - The adrenal cortex also reacts to stress, but it responds to endocrine signals.
    1. Stress stimulates hypothalamus to secrete releasing factor, which cause anterior pituitary to release ACTH.
    2. Adrenal cortex received the signal of ACTH can secrete corticosteroid.
    3. The increasing corticosteroid causes negative feedback to anterior pituitary.
  - **Corticosteroid**: **glucocorticoid**s, **mineralocorticoid**s, and **sex hormone**s.
    - **Mineralocorticoid**s have their major effects on salt and water balance.
      - **Aldosterone** stimulates kidney cells to reabsorb sodium ions from the filtrate, which also causes water reabsorption and raises blood pressure.

- **Glucocorticoid**s promote the synthesis of glucose from non-carbohydrate substrates making more glucose available as fuel in response to a stressful situation: This effect is slower but longer than epinephrine.
- **Immune suppressor**: **Cortisone**, a miracle drug can cure arthritis.

Gonadal steroids regulate growth, development, reproductive cycles, and sexual behavior

- All three gonadal steroids are found in both males and females:
  - **Androgen**s: also secret by adrenal cortex.
    - **Testosterone**, the main hormone synthesizes in testes.
    - At embryo, androgens produce and determine the fetus to develop as a male rather than a female.

  - **Estrogen**s: the most important is **estradiol**, which mainly maintain the female reproductive system, and develop of female secondary sex characteristics.

  - **Progestin**s are primarily involved with preparing and maintaining the uterus.

- Synthesis of both estrogens and androgens is controlled by **gonadotropin**s, FSH and LH which releasing is controlled by one hypothalamic releasing factor, **gonadotropin-releasing hormone** (**GnRH**).