

Hypothalamus - pituitary - adrenal glands

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I. The Hypothalamus

A. Hypothalamic Hormones

1. The hypothalamus produces nine important hormones.
2. Seven of the nine hormones – hypophysiotropic hormones travel through the portal system and regulate the activities of the anterior pituitary; five of them are releasing hormones, and two are inhibiting hormones.
3. The other two hormones – neurohypophyseal hormones are **oxytocin (OT)** and **antidiuretic hormone (ADH)**. Neurohypophyseal hormones are produced by neurons of the hypothalamus and they are stored in the neurohypophysis in the axons of these neurons.

B. Actions of the Hypothalamic Hormones

1. The hypophysiotropic hormones
 - a. Growth hormone - releasing hormone (**GHRH**) stimulates release of growth hormone
 - b. Growth hormone – inhibitory hormone (**GHIH**, **somatostatin**) inhibits release of growth hormone. *Note that this is not the same hormone as somatostatin from pancreas.*
 - c. Gonadotropin – releasing hormone (**GnRH**) causes release of LH and FSH
 - d. Prolactin inhibitory hormone (**PIH**), **which is a dopamine** inhibits release of prolactin
 - e. Prolactin releasing factor (**PRF**) stimulates release of prolactin. It is believed to be **TRH**.
 - f. Thyrotropin – releasing hormone (**TRH**) stimulates secretion of TSH and prolactin
 - g. Corticotropin – releasing hormone (**CRH**) stimulates secretion of ACTH
2. Neurohypophyseal hormones
 - a. Antidiuretic hormone (ADH) increases water permeability in late distal tubule and collecting duct.
 - b. Oxytocin (OT) causes contraction of myoepithelial cells in the breast and contraction of the uterus.

II. The pituitary gland

A. Pituitary Hormones

1. The anterior lobe of the pituitary synthesizes and secretes six principal hormones.
 - a. Of these, follicle-stimulating hormone (**FSH**) and luteinizing hormone (**LH**) are called **gonadotropins** because they target the gonads.
 - b. Thyroid-stimulating hormone (**TSH**)
 - c. Adrenocorticotrophic hormone (**ACTH**) are considered tropins because they target other endocrine glands.
 - d. The remaining two pituitary hormones are prolactin (**PRL**) and growth hormone (**GH**).
 - e. The pars intermedia was once thought to secrete melanocyte-stimulating hormone, but is now known to give rise to anterior pituitary cells that produce pro-opiomelanocortin (**POMC**).
 - f. The posterior lobe produces no hormones of its own but stores two hormones manufactured in the hypothalamus, **OT and ADH**.

B. Actions of the Pituitary Hormones

1. Anterior Lobe Hormones
 - a. Follicle-stimulating hormone (**FSH**) stimulates follicle and egg development in the ovaries and sperm production in the testes.

- b. Luteinizing hormone (**LH**) stimulates female ovulation and growth of the corpus luteum. In males, LH stimulates the testes to secrete testosterone.
- c. Thyroid-stimulating hormone (**TSH, or thyrotropin**) stimulates the thyroid to produce and secrete its hormones.
- d. Adrenocorticotropic hormone (**ACTH**) stimulates the adrenal cortex to secrete its hormones (mostly glucocorticoids). It has MSH (melanocyte stimulating hormone) activity, so increased amounts may cause darkening of the skin.
- e. Prolactin (**PRL**) acts on the female mammary gland to promote milk synthesis. In males, it indirectly enhances the secretion of testosterone.
- f. Growth hormone (**GH**), or **somatotropin**, stimulates cellular growth, mitosis, and differentiation, promoting overall tissue and organ growth. GH inhibits ageing via many ways (eg. it inhibits formation of free radicals). GH stimulates skeletal and tissue growth via the polypeptide growth factors – **somatomedins (IGF-I, IGF-II)**, which are produced in the liver. GH also exhibits multiple metabolic effects:
 - it increases lipolysis and fat utilization for energy (anti-insulin effect of GH)
 - it promotes protein synthesis and deposition acting as a “protein sparer” (insulin-like effect of GH)
 - it decreases use of glucose for energy, increases gluconeogenesis, and thus rises blood glucose level (anti-insulin effect of GH)

Stimuli that increase GH production include: GHRH (from hypothalamus), **ghrelin** (brain-gut peptide), deficiency of energy substrate, increase in circulating certain amino acids, glucagons, going to sleep, and stress.

2. Posterior Lobe Hormones

- a. Antidiuretic hormone (**ADH**) acts on the kidneys (collecting ducts and tubules) to increase water retention and thus prevent dehydration. It has also vasoconstrictor and pressor effects.
- b. Oxytocin (**OT**) stimulates uterine labour contractions and milk release by mammary glands.

C. Control of Pituitary Secretion

1. The timing and amount of pituitary secretion is regulated by the hypothalamus, other brain centers, and feedback from the target organs.
2. Secretion by the anterior hypothalamus is controlled by hormones (hypothalamic releasing or inhibitory hormones) – see Actions of the Hypothalamic Hormones.
3. The posterior pituitary is controlled by neuroendocrine reflexes; its hormones are released when signaled by nervous impulses from the hypothalamus.
 - a. Antidiuretic hormone release is mostly controlled by:
 - osmotic regulation (via hypothalamic osmoreceptors)
 - hemodynamic regulation (via baroreceptors)
 - b. Oxytocin release is mostly controlled by:
 - suckling (stimulation of touch receptors in breast)
 - distension of uterus
 - pain
4. Neuroendocrine reflexes can be modified by emotional responses, stress, and other factors.
5. The target organs for pituitary hormones usually influence hormone release by negative feedback control.
6. Sometimes target organs are also involved in a positive feedback cycle, as is the case with oxytocin and uterine contractions.

D. Pituitary Disorders

1. A number of diseases result from hyper - or hyposecretion of pituitary hormones.

- a. Childhood hypopituitarism causes **pituitary dwarfism** due to deficient GH. Complete loss of anterior pituitary function triggers atrophy in target organs, leading to a broad range of disorders (**panhypopituitarism**). **Laron dwarfism** refers to the normal level of GH and decreased efficiency and/or quantity of IGF-I.
- b. Hyperpituitarism (excess of GH) causes **gigantism** in childhood or **acromegaly** in adulthood.
- c. **Somatopause** – age-related lowering of GH production. This event is physiological.
- d. Lack of ADH from the posterior pituitary triggers **diabetes insipidus**, leading to excessive urine output and electrolyte imbalances.

III. The Adrenal Glands.

1. The adrenal glands are located at the top of the two kidneys. They are composed of an inner core called the adrenal medulla, which is surrounded by a much thicker adrenal cortex.
 - a. The adrenal medulla is not fully formed until the age of three, and is actually a ganglion of the sympathetic nervous system made up of modified neuron somas. It secretes catecholamines (epinephrine, norepinephrine, and dopamine) in response to sympathetic stimulation. Their effects mimic those of the sympathetic nervous system but last longer because they are secreted into the blood. They also exhibit multiple metabolic effects:
 - increase in blood glucose level (\uparrow rate of glycogenolysis and gluconeogenesis)
 - increase in blood FFA (\uparrow rate of lipolysis)
 - increase in secretion of glucagons and inhibition of insulin
 - increase in metabolic rate
 - b. The adrenal cortex consists of three layers of modified epithelial cells: the outer zona glomerulosa, a middle zona fasciculata, and an inner zona reticularis. It secretes more than 25 steroid hormones (corticosteroids) that fall into three categories: sex steroids (androgens, such as DHEA), mineralocorticoids (aldosterone), and glucocorticoids (cortisol).
 - c. Glucocorticoid secretion is stimulated by ACTH. Glucocorticoids stimulate fat and protein catabolism (except proteins synthesized in the liver, which serve as an enzymes for gluconeogenesis) and increase energy supply in the bloodstream. By stimulation of gluconeogenesis and inhibition of glucose utilization, they increase blood glucose level. These hormones are secreted together with catecholamines in response to stress (permissive effects of glucocorticoids on vascular reactivity to catecholamines; they also facilitate lipolysis and other effects caused by catecholamines in response to stress).
 - d. Mineralocorticoids secretion is stimulated by **renin – angiotensin axis**. Mineralocorticoids stimulate sodium reabsorption and potassium secretion in the nephron. They increase ECF volume and blood pressure.
2. Adrenal disorders can lead to several diseases.
 - a. **Hypersecretion by the adrenal medulla** may be caused by a tumor (**pheochromocytoma**). This results in hypertension, elevated metabolic rate, hyperglycemia nervousness, sweating, and other symptoms.
 - b. **Hypersecretion by the adrenal cortex** can result from a cortical tumor, or excessive ACTH level. This causes **Cushing syndrome**, which is characterized by muscle weakness, osteoporosis and a redistribution of body fat. Since glucocorticoids exhibit slight mineralocorticoid effect 80% of patients have hypertension. Diabetes mellitus may also occur. Cushing syndrome may be also caused by prolonged treatment with glucocorticoids.
 - c. **Androgenital syndrome (AGS)** is caused by hypersecretion of the adrenal androgens. Newborn girls can be mistaken for boys due to the masculinization of their genitals. Adult women experience masculinizing effects. Other symptoms are also observed. This syndrome usually results from congenital enzymatic deficiency: 21-hydroxylase deficiency (salt loosing

form) or 11-hydroxylase deficiency (hypertensive form) – to understand see steroid synthesis see biochemistry course.

d. **Hyposecretion of glucocorticoids and mineralocorticoids** causes **Addison disease**. This is characterized by darkened skin, hypoglycemia, dehydration, hypotension, weakness, and loss of stress resistance. Addison disease usually results from a total damage of adrenal cortex.

e. **Primary hyperaldosteronism (Conn's syndrome)** results from hormonally active adrenal tumor or adrenal hyperplasia. The major effects include: ↑ ECF volume, alkalosis, hypertension, K^+ depletion. Remember: when the patient suffers from hypertension and his K^+ level is very low, always consider Conn's syndrome as a possible cause of hypertension.