STUDY MATERIALS

On

REGULATION OF HYPOTHALAMIC HORMONE SECRETION

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The hypothalamus is involved in many functions of the autonomic nervous system, as it receives information from nearly all parts of the nervous system. As such, it is considered the link between the nervous system and the endocrine system.

Anatomy of the Hypothalamus

The hypothalamus is located below the thalamus (a part of the brain that relays sensory information) and above the pituitary gland and brain stem. It is about the size of an almond.

Hormones of the Hypothalamus

The hypothalamus is highly involved in pituitary gland function. When it receives a signal from the nervous system, the hypothalamus secretes substances known as neurohormones that start and stop the secretion of pituitary hormones.

Primary hormones secreted by the hypothalamus include:

Anti-diuretic hormone (ADH): This hormone increases water absorption into the blood by the kidneys.

Corticotropin-releasing hormone (CRH): CRH sends a message to the anterior pituitary gland to stimulate the adrenal glands to release corticosteroids, which help regulate metabolism and immune response.

Gonadotropin-releasing hormone (GnRH): GnRH stimulates the anterior pituitary to release follicle stimulating hormone (FSH) and luteinizing hormone (LH), which work together to ensure normal functioning of the ovaries and testes.

Growth hormone-releasing hormone (GHRH) or growth hormone-inhibiting hormone (GHIH) (also known as somatostain): GHRH prompts the anterior pituitary to release growth hormone (GH); GHIH has the opposite effect. In children, GH is essential to maintaining a healthy body composition. In adults, it aids healthy bone and muscle mass and affects fat distribution.

Oxytocin: Oxytocin is involved in a variety of processes, such as orgasm, the ability to trust, body temperature, sleep cycles, and the release of breast milk.

Prolactin-releasing hormone (PRH) or prolactin-inhibiting hormone (PIH) (also known as dopamine): PRH prompts the anterior pituitary to stimulate breast milk production through the production of prolactin. Conversely, PIH inhibits prolactin, and thereby, milk production. Thyrotropin releasing hormone (TRH): TRH triggers the release of thyroid stimulating hormone (TSH), which stimulates release of thyroid hormones, which regulate metabolism, energy, and growth and development.

Hypothalamic regulation in secretion of hormones from posterior pituitary or neurohypophysis-

In most mammals, the hormones secreted by the posterior pituitary gland are arginine vasopressin (AVP) and oxytocin. In hippopotami and most pigs, arginine in the vasopressin molecule is replaced by lysine to form lysine vasopressin. Oxytocin and vasopressin are typical neural hormones, that is, hormones secreted into the circulation by nerve cells. This type of neural regulation is compared with other types in figure below.

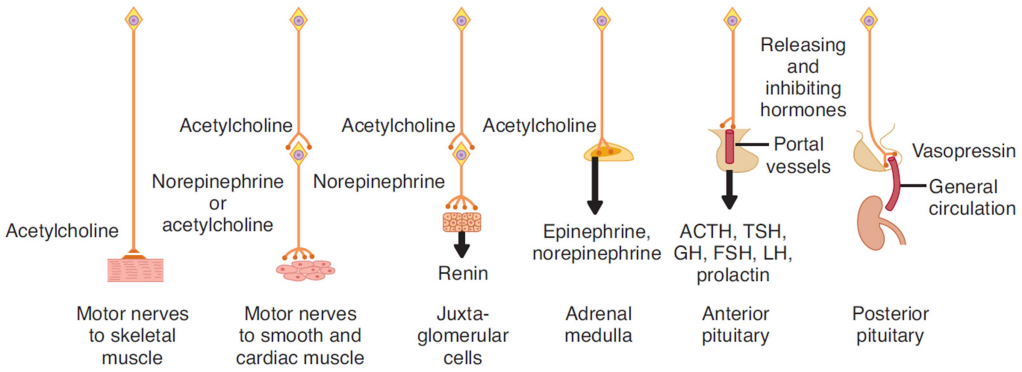

FIGURE 18–6 **Neural control mechanisms.** In the two situations on the left, neurotransmitters act at nerve endings on muscle; in the two in the middle, neurotransmitters regulate the secretion of endocrine glands; and in the two on the right, neurons secrete hormones into the hypophysial portal or general circulation.

The term neurosecretion was originally coined to describe the secretion of hormones by neurons, but the term is somewhat misleading because it appears that all neurons secrete chemical messengers. Like other peptide hormones, the posterior lobe hormones are synthesized as part of larger precursor molecules. Vasopressin and oxytocin each have a characteristic neurophysin associated with them in the granules in the neurons that secrete them—neurophysin I in the case of oxytocin and neurophysin II in the case of vasopressin. The neurophysins were originally thought to be binding polypeptides, but it now appears that they are simply parts of the precursor molecules. The precursor for arginine vasopressin, prepropressophysin, contains a 19-amino-acid residue leader sequence followed by arginine vasopressin, neurophysin II, and a glycopeptide Prepro-oxyphysin, the precursor for oxytocin, is a similar but smaller molecule that lacks the glycopeptide. The precursor molecules are synthesized in the ribosomes of the cell bodies of the neurons. They have their leader sequences removed in the endoplasmic reticulum, are packaged into secretory granules in the Golgi apparatus, and are transported down the axons by axoplasmic flow to the endings in the posterior pituitary.

Hypothalamic regulation in secretion of hormones from anterior pituitary or adenohypophysis-

The anterior pituitary secretes six hormones: adrenocorticotropic hormone (corticotropin, ACTH), thyroid-stimulating hormone (thyrotropin, TSH), growth hormone, folliclestimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL). An additional polypeptide, β –lipotropin (β -LPH), is secreted with ACTH, but its physiologic role is unknown. Anterior pituitary secretion is controlled by chemical agents carried in the portal hypophysial vessels from the hypothalamus to the pituitary. These substances used to be called releasing and inhibiting factors, but now they are commonly called hypophysiotropic hormones. The latter term seems appropriate since they are secreted into the bloodstream and act at a distance from their site of origin.

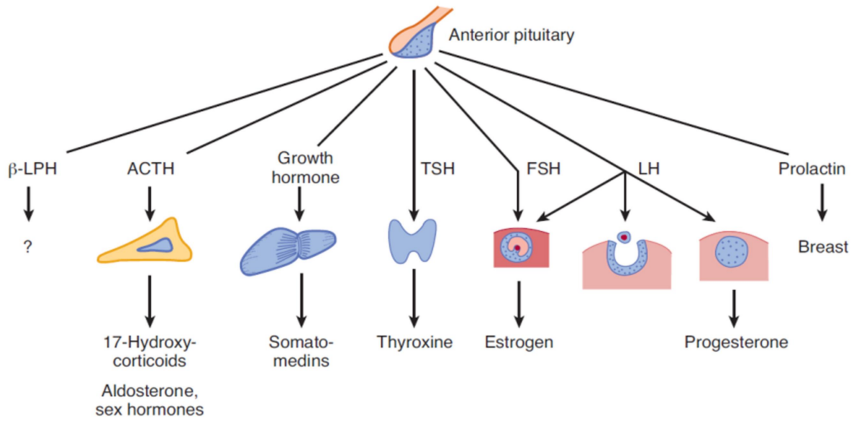

FIGURE 18–9 **Anterior pituitary hormones.** In women, FSH and LH act in sequence on the ovary to produce growth of the ovarian follicle, ovulation, and formation and maintenance of the corpus luteum. Prolactin stimulates lactation. In men, FSH and LH control the functions of the testes.

Small amounts escape into the general circulation, but they are in high concentration in portal hypophysial blood. There are six established hypothalamic releasing and inhibiting hormones, corticotropin-releasing hormone (CRH); thyrotropin-releasing hormone (TRH); growth hormone-releasing hormone (GRH); growth hormone-inhibiting hormone (GIH), now generally called somatostatin; luteinizing hormone-releasing hormone (LHRH), now generally known as gonadotropin-releasing hormone (GnRH); and prolactin-inhibiting hormone (PIH). In addition, hypothalamic extracts contain prolactin-releasing activity, and a prolactin- releasing hormone (PRH) has been postulated to exist. TRH, VIP, and several other polypeptides found in the hypothalamus stimulate prolactin secretion, but it is uncertain whether one or more of these peptides is the physiologic PRH. Recently, an orphan receptor was isolated from the anterior pituitary, and the search for its ligand led to the isolation of a 31-amino-acid polypeptide from the human hypothalamus. This polypeptide stimulated prolactin secretion by an action on the anterior pituitary receptor, but additional research is needed to determine if it is the physiologic PRH. GnRH stimulates the secretion of FSH as well as that of LH, and it seems unlikely that a separate follicle stimulating hormone-releasing hormone exists. The structures of the six established hypophysiotropic hormones are shown in. The structures of the genes and preprohormones for TRH, GnRH, somatostatin, CRH,

and GRH are known. PreproTRH contains six copies of TRH. Several other preprohormones may contain other hormonally active peptides in addition to the hypophysiotropic hormones.

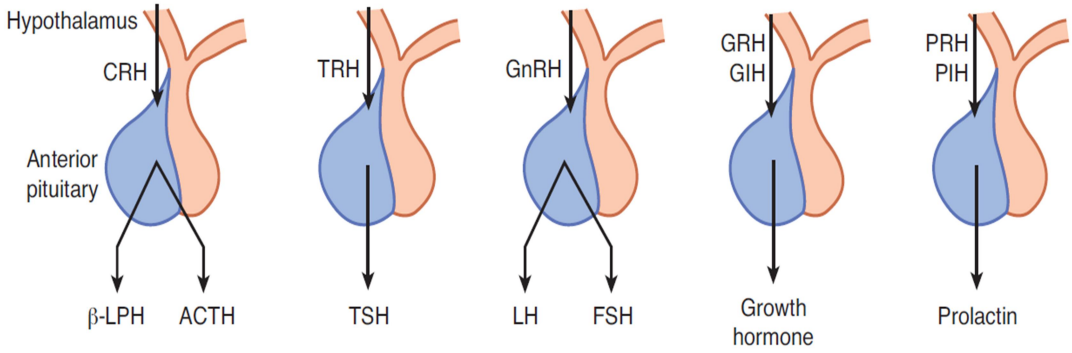

FIGURE 18–10 **Effects of hypophysiotropic hormones on the secretion of anterior pituitary hormones.**

The area from which the hypothalamic releasing and inhibiting hormones are secreted is the median eminence of the hypothalamus. This region contains few nerve cell bodies, but many nerve endings are in close proximity to the capillary loops from which the portal vessels originate. The locations of the cell bodies of the neurons that project to the external layer of the median eminence and secrete the hypophysiotropic hormones are shown in, which also shows the location of the neurons secreting oxytocin and vasopressin. The GnRH-secreting neurons are primarily in the medial preoptic area, the somatostatin-secreting neurons are in the periventricular nuclei, the TRH-secreting and CRH-secreting neurons are in the medial parts of the paraventricular nuclei, and the GRH-secreting and dopamine- secreting neurons are in the arcuate nuclei. Most, if not all, of the hypophysiotropic hormones affect the secretion of more than one anterior pituitary hormone. TRH stimulates the secretion of prolactin as well as TSH. Somatostatin inhibits the secretion of TSH as well as growth hormone. It does not normally inhibit the secretion of the other anterior pituitary hormones, but it inhibits the abnormally elevated secretion of ACTH in patients with Nelson's syndrome. CRH stimulates the secretion of ACTH and β-LPH. Hypophysiotropic hormones function as neurotransmitters in other parts of the brain, the retina, and the autonomic nervous system. In addition, somatostatin is found in the pancreatic islets, GRH is secreted by pancreatic tumors, and somatostatin and TRH are found in the gastrointestinal tract. Receptors for most of the hypophysiotropic hormones are serpentine and coupled to G proteins. There are two human CRH receptors: hCRH-RI, and hCRH-RII. The latter differs from the former in having a 29-amino-acid insert in its first cytoplasmic loop. The physiologic role of hCRH-RII is unsettled, though it is found in many parts of the brain. In addition, a CRH-binding protein in the peripheral circulation inactivates CRH. It is also found in the cytoplasm of corticotropes in the anterior pituitary, and in this location it might play a role in receptor internalization. However, the exact physiologic role of this protein is unknown.

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