RAJA NARENDRALAL KHAN WOMEN'S COLLEGE (AUTONOMOUS)

HUMAN PHYSIOLOGY

PG 2ND SEMESTER

NEUROENDOCRINOLOGY

Paper-PHY-203/UNIT-18/Module-IV

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HYPOTHALAMUS : A NEUROENDOCRINE ORGAN

- The hypothalamus, located at the most rostral region of the brain stem in the diencephalon,
- The hypothalamus contains several groups of cells that are defined as neuroendocrine, meaning that they have both neuronal and endocrine features. Neuroendocrine cells in the central nervous system have a neuronal phenotype, and release a peptide or neurotransmitter in response to a depolarizing stimulus.
- These neuroendocrine cells in the brain are true endocrine organs in the sense that their targets are a vascular system. Although the substances released by most neuroendocrine cells are peptides and neurotransmitters, they are also appropriately referred to as hormones because they are released into blood vessels to act remotely at a target organ.

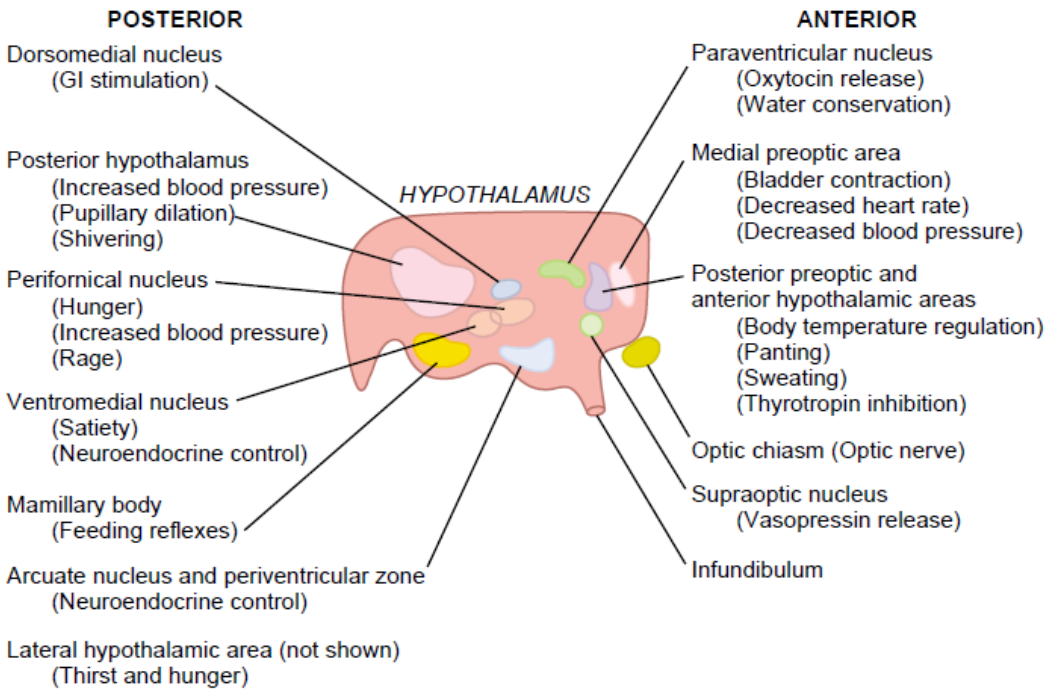


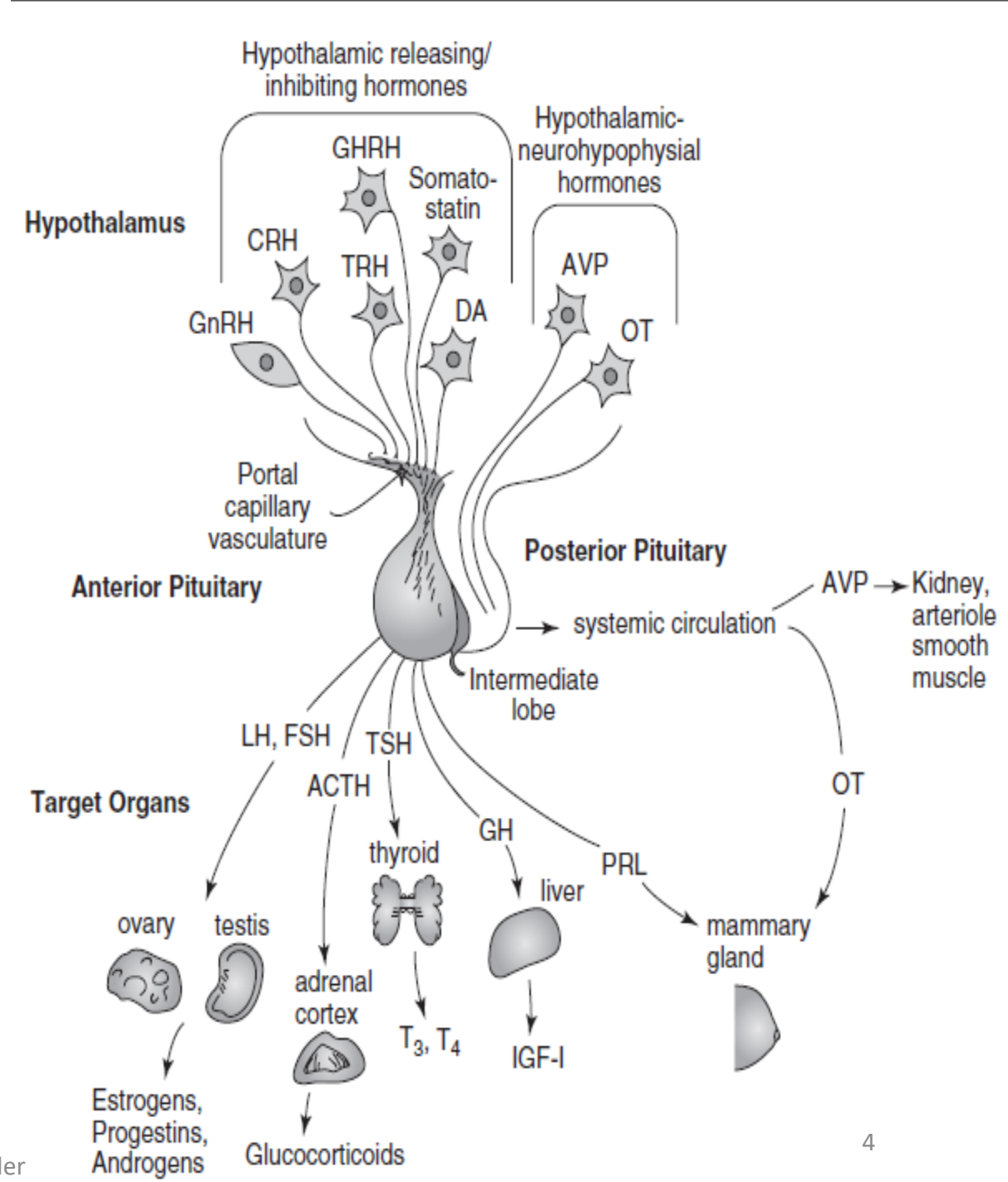
Fig: Control centers of the hypothalamus (sagittal view).

- The primary target of hypothalamic neuroendocrine cells is the pituitary gland. The pituitary gland comprises the anterior pituitary (adenohypophysis) and the posterior pituitary (neurohypophysis). Some species also possess an intermediate pituitary lobe.
- The hypothalamic cells that regulate the anterior pituitary are referred to as hypothalamic releasing or inhibiting cells. These neurons have their cell somata in the hypothalamus, and they have a nerve process that extends to the median eminence at the base of the hypothalamus.
- The median eminence is highly vascularized by a blood system called the portal capillary plexus. Hypothalamic releasing/inhibiting hormones are released into the portal capillary vasculature, which then transports these neurohormones to the anterior pituitary gland.

- For the five hypothalamic releasing/inhibiting hormonal systems that control reproduction, stress, metabolism, growth, and lactation, each system has a hypothalamic neurosecretory cell, a corresponding pituitary hormone, and a target organ and/or hormone.

- The hypothalamic-neurohypophysial hormones, AVP and OT, are shown at the right.

[ACTH, adrenocorticotrophic hormone; AVP, arginine vasopressin; CRH, corticotropin-releasing hormone; DA, dopamine; FSH, follicle-stimulating hormone; GHRH, growth hormone-releasing hormone; GnRH, gonadotropin-releasing hormone; IGF-I, insulin-like, growth factor I; LH, luteinizing hormone; OT, oxytocin; PRL, prolactin; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating, hormone; T3, triiodothyronine; T4, thyroxine.]



Characteristics of Neuro-hormone Release: Ultradian, Circadian/ Diurnal, an Seasonal Rhythms

- In considering the release of a hypothalamic hormone and its resulting effect on downstream targets, it is important to note the rhythmicity of this release.
- Hypothalamic hormones are released in a pulsatile manner, characterized by brief bursts of release, usually at intervals of 1–2 hour. This rhythmic pattern also is referred to as ultradian (i.e., shorter than daily rhythms) or circhoral (approximately hourly intervals of release).
- The corresponding anterior pituitary cells respond to each pulse of a hypothalamic hormone with a corresponding pulse of its pituitary hormone shortly thereafter (Fig).
- It has been speculated that the pulsatile release of hypothalamic hormones is necessary to prevent the desensitization of their receptors in the anterior pituitary gland. Indeed, infusion of exogenous hypothalamic hormone analogs in a continuous manner may result in an initial activation of pituitary hormone release, but subsequent refractoriness of the pituitary cell and overall decreases in release.
- In contrast, infusion of exogenous hypothalamic hormones in a pulsatile manner maintains the maximal pituitary sensitivity to its corresponding hypothalamic hormone.

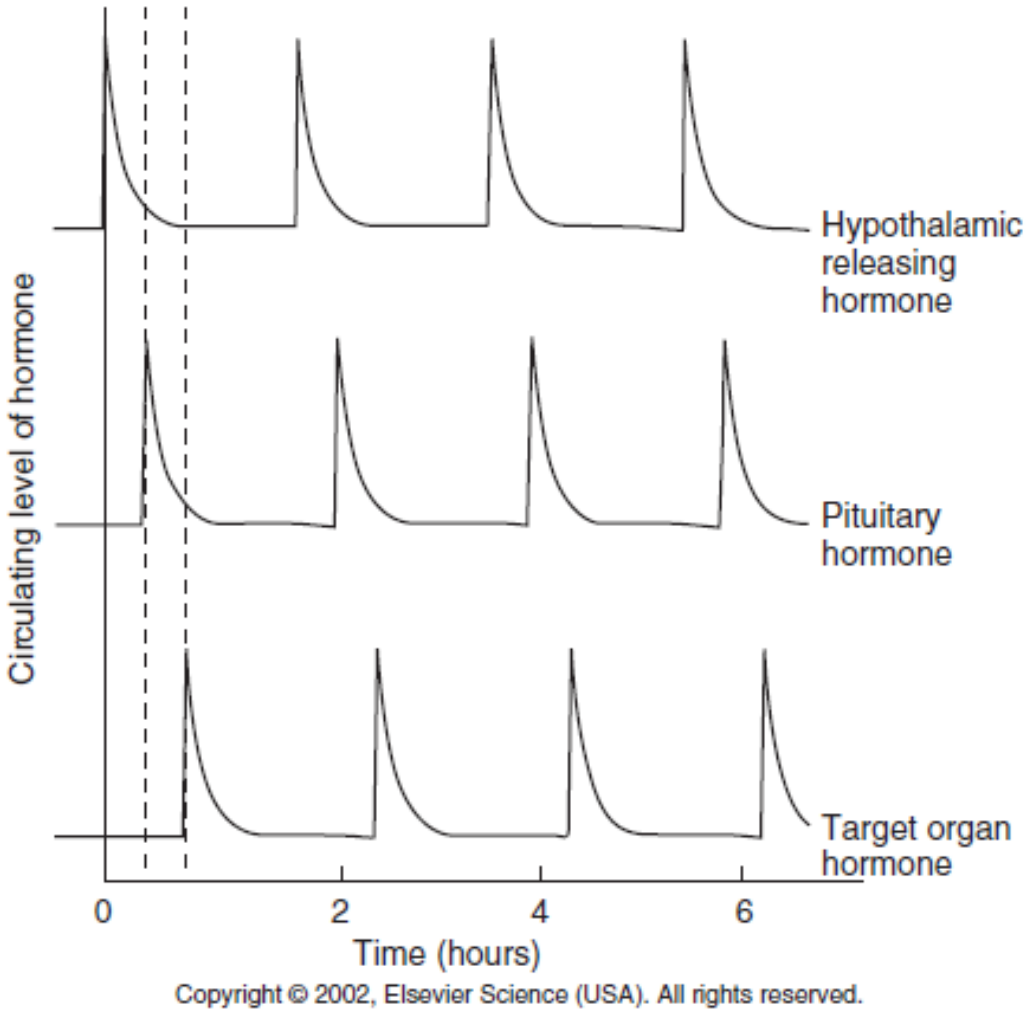


Fig: Representation of pulsatile hormone release in a neuroendocrine system.

Neurosecretion: Biosynthesis, transport, release.

- The term **neurosecretion** was originally coined to describe the secretion of hormones by neurons.
- There are neural connections between the hypothalamus and the posterior lobe of the pituitary gland.
- Embryologically, the posterior pituitary arises as an evagination of the floor of the third ventricle. It is made up in large part of the endings of axons that arise from cell bodies in the supraoptic and paraventricular nuclei and pass to the posterior pituitary (Fig) via the **hypothalamohypophysial tract.** Most of the supraoptic fibers end in the posterior lobe itself, whereas some of the paraventricular fibers end in the median eminence.

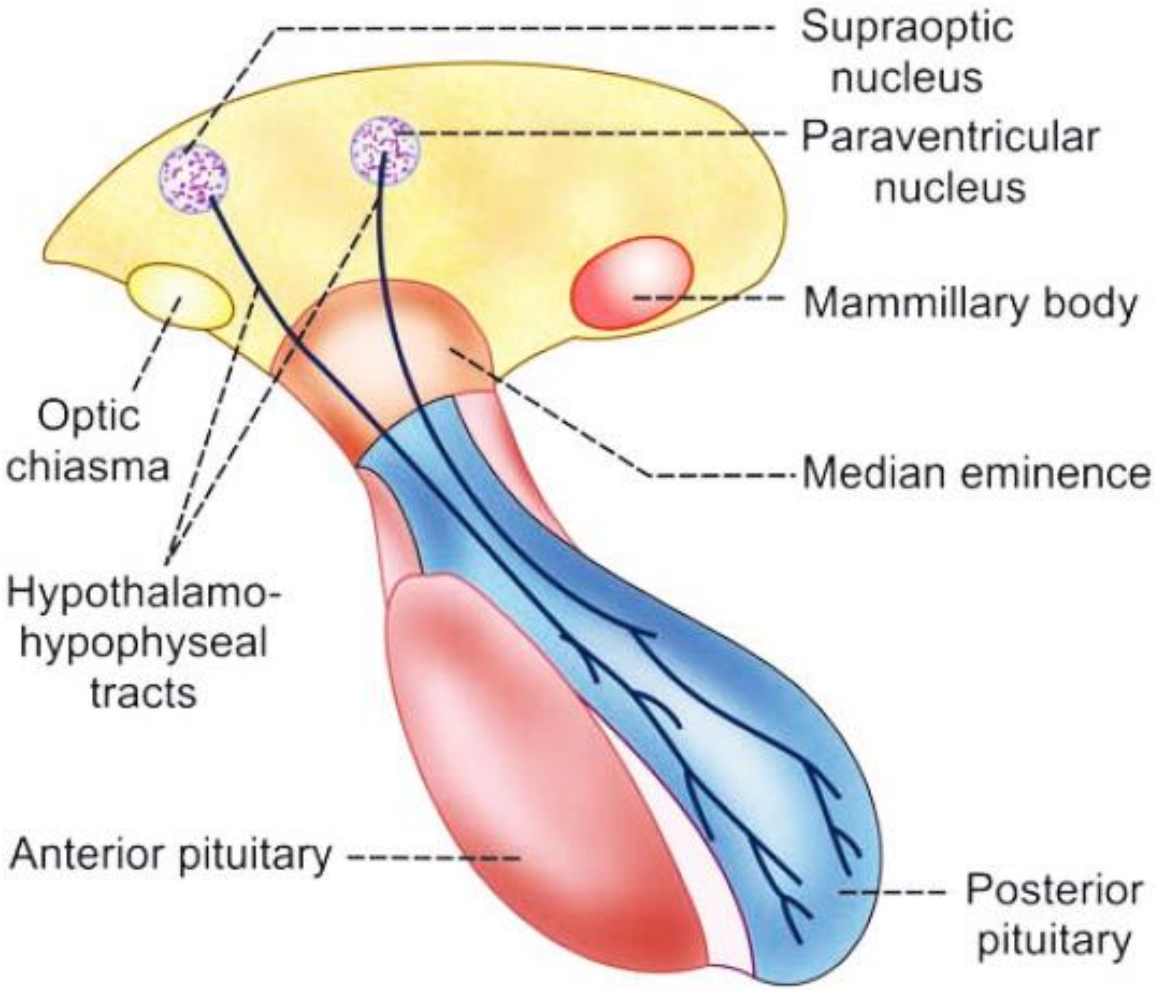


Fig: **Hypothalamo- hypophysial tract**

- The hormones of the posterior pituitary gland are synthesized in the cell bodies of the magnocellular neurons in the supraoptic and paraventricular nuclei and transported down the axons of these neurons to their endings in the posterior lobe, where they are secreted in response to electrical activity in the endings.
- Some of the neurons make oxytocin and others make vasopressin, and oxytocin-containing and vasopressin-containing cells are found in both nuclei. Oxytocin and vasopressin are typical **neural hormones,** that is, hormones secreted into the circulation by nerve cells.
- 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 (Figure). **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 (**Herring bodies)** in the Golgi apparatus, and are transported down the axons by axoplasmic flow to the endings in the posterior pituitary.

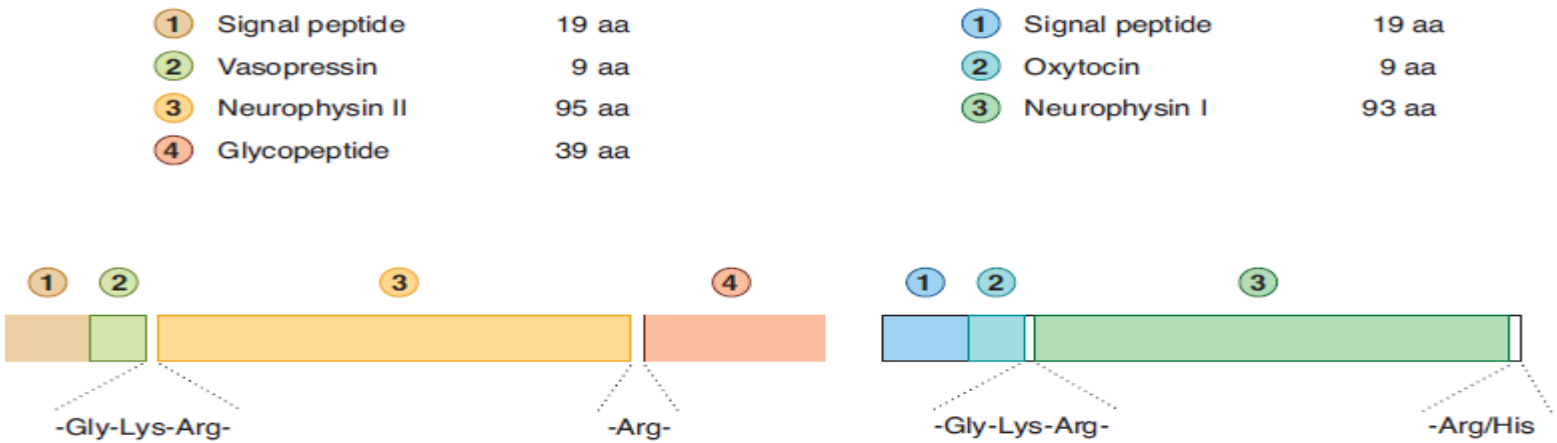


Fig: **Structure of bovine prepropressophysin (left) and prepro-oxyphysin (right).**

Effects of Vasopressin

- Because one of its principal physiologic effects is the retention of water by the kidney, vasopressin is often called the **antidiuretic hormone (ADH).**
- It increases the permeability of the collecting ducts of the kidney so that water enters the hypertonic interstitium of the renal pyramid.
- The urine becomes concentrated and its volume decreases.
- The overall effect is therefore retention of water in excess of solute; consequently, the effective osmotic pressure of the body fluids is decreased.
- In the absence of vasopressin, the urine is hypotonic to plasma, urine volume is increased, and there is a net water loss. Consequently, the osmolality of the body fluid rises.

Effects of Oxytocin

- In humans, oxytocin acts primarily on the breasts and uterus, though it appears to be involved in luteolysis as well.
- A G protein-coupled serpentine oxytocin receptor has been identified in human myometrium, and a similar or identical receptor is found in mammary tissue and the ovary. It triggers increases in intracellular Ca^{2+} levels.
- Oxytocin causes contraction of the **myoepithelial cells,** smoothmuscle- like cells that line the ducts of the breast. This squeezes the milk out of the alveoli of the lactating breast into the large ducts (sinuses) and thence out of the nipple **(milk ejection).**
- Oxytocin may also act on the nonpregnant uterus to facilitate sperm transport. The passage of sperm up the female genital tract to the uterine tubes, where fertilization normally takes place, depends not only on the motile powers of the sperm but also, at least in some species, on uterine contractions.

Probable questions:

1. Why hypothalamus is considered as a neurosecretary organ?
2. What are neuro-hormones?
3. What are the biological functions of neurosecretary materials, oxytocin and vasopressin?
4. Discuss the process of biosynthesis and secretion of any neurosecretoary material.