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HYPOTHALMO-HYPOPHYSIAL AXIS

BY DR. LUNA PHUKAN

The hypothalamus **is a portion of the brain that contains a number of small nuclei with a variety of functions. One of the most important functions of the hypothalamus is to link the nervous system to the endocrine system via the pituitary gland. The hypothalamus is located below the thalamus and is part of the limbic system In the terminology of neuroanatomy, it forms the ventral part of the diencephalon. All vertebrate brains contain a hypothalamus. In humans, it is the size of an almond.**

The hypothalamus is responsible for the regulation of certain metabolic processes and other activities of the autonomic nervous system. It synthesizes and secretes certain neurohormones, called releasing hormones or hypothalamic hormones, and these in turn stimulate or inhibit the secretion of hormones from the pituitary gland. The hypothalamus controls body temperature, hunger, important aspects of parenting and attachment behaviours, thirst, fatigue, sleep, and circadian rhythms.

Hypothalamo-hypophysal axis means the connecting portion between hypothelamas and both anterior and posterior pituitary which consists of nerve fibers, blood vessels , neurons .This portion or axis control and release of various hormones which controls all metabolic and physiological activity of body.

Hypothelamo- hypophysal axis is divided into 4 parts

1. **The hypothalamic-pituitary-adrenal axis**
2. **The hypothalamic–pituitary–gonadal axis (HPG axis)**
3. **hypothalamic–pituitary–thyroid axis (HPT), and the**
4. **hypothalamic–neurohypophyseal system are the four major neuro endocrine system**

Hypothalamo-Hypophyseal System

A collection of NEURONS, tracts of NERVE FIBERS, endocrine tissue, and blood vessels in the HYPOTHALAMUS and the PITUITARY GLAND. This hypothalamo-hypophyseal portal circulation provides the mechanism for hypothalamic neuroendocrine (HYPOTHALAMIC HORMONES) regulation of pituitary function and the release of various PITUITARY HORMONES into the systemic circulation to maintain HOMEOSTASIS

1.The hypothalamic–pituitary–adrenal axis (HPA axis or HTPA axis) is a complex set of direct influences and feedback interactions among three components: the hypothalamus, the pituitary gland (a pea-shaped structure located below the thalamus), and the adrenal (also called "suprarenal") glands (small, conical organs on top of the kidney

These organs and their interactions constitute the HPA axis, a major neuroendocrine system that controls reactions to stress and regulates many body processes, including digestion, the immune system, mood and emotions, sexuality, and energy storage and expenditure. It is the common mechanism for interactions among glands, hormones, and parts of the midbrain that mediate the general adaptation syndrome While steroid hormones are produced mainly in vertebrates, the physiological role of the HPA axis and corticosteroids in stress response is so fundamental that analogous systems can be found in invertebrates and monocellular organisms as well

Anatomy

The key elements of the HPA axis are:

The paraventricular nucleus of the hypothalamus, which contains neuroendocrine neurons which synthesize and secrete vasopressin and corticotropin-releasing hormone (CRH). These two peptides regulate:

The anterior lobe of the pituitary gland. In particular, CRH and vasopressin stimulate the secretion of adrenocorticotropic hormone (ACTH), once known as corticotropin. ACTH in turn acts on:

the adrenal cortex, which produces glucocorticoid hormones (mainly cortisol in humans) in response to stimulation by ACTH. Glucocorticoids in turn act back on the hypothalamus and pituitary (to suppress CRH and ACTH production) in a negative feedback cycle.

CRH and vasopressin are released from neurosecretory nerve terminals at the median eminence. CRH is transported to the anterior pituitary through the portal blood vessel system of the hypophyseal stalk and vasopressin is transported by axonal transport to the posterior pituitary gland. There, CRH and vasopressin act synergistically to stimulate the secretion of stored ACTH from corticotrope cells. ACTH is transported by the blood to the adrenal cortex of the adrenal gland, where it rapidly stimulates biosynthesis of corticosteroids such as cortisol from cholesterol.

Cortisol is a major stress hormone and has effects on many tissues in the body, including the brain. In the brain, cortisol acts on two types of receptor – mineralocorticoid receptors and glucocorticoid receptors, and these are expressed by many different types of neurons. One important target of glucocorticoids is the hypothalamus, which is a major controlling centre of the HPA axis.

Vasopressin can be thought of as "water conservation hormone" and is also known as "antidiuretic hormone." It is released when the body is dehydrated and has potent water-conserving effects on the kidney. It is also a potent vasoconstrictor.

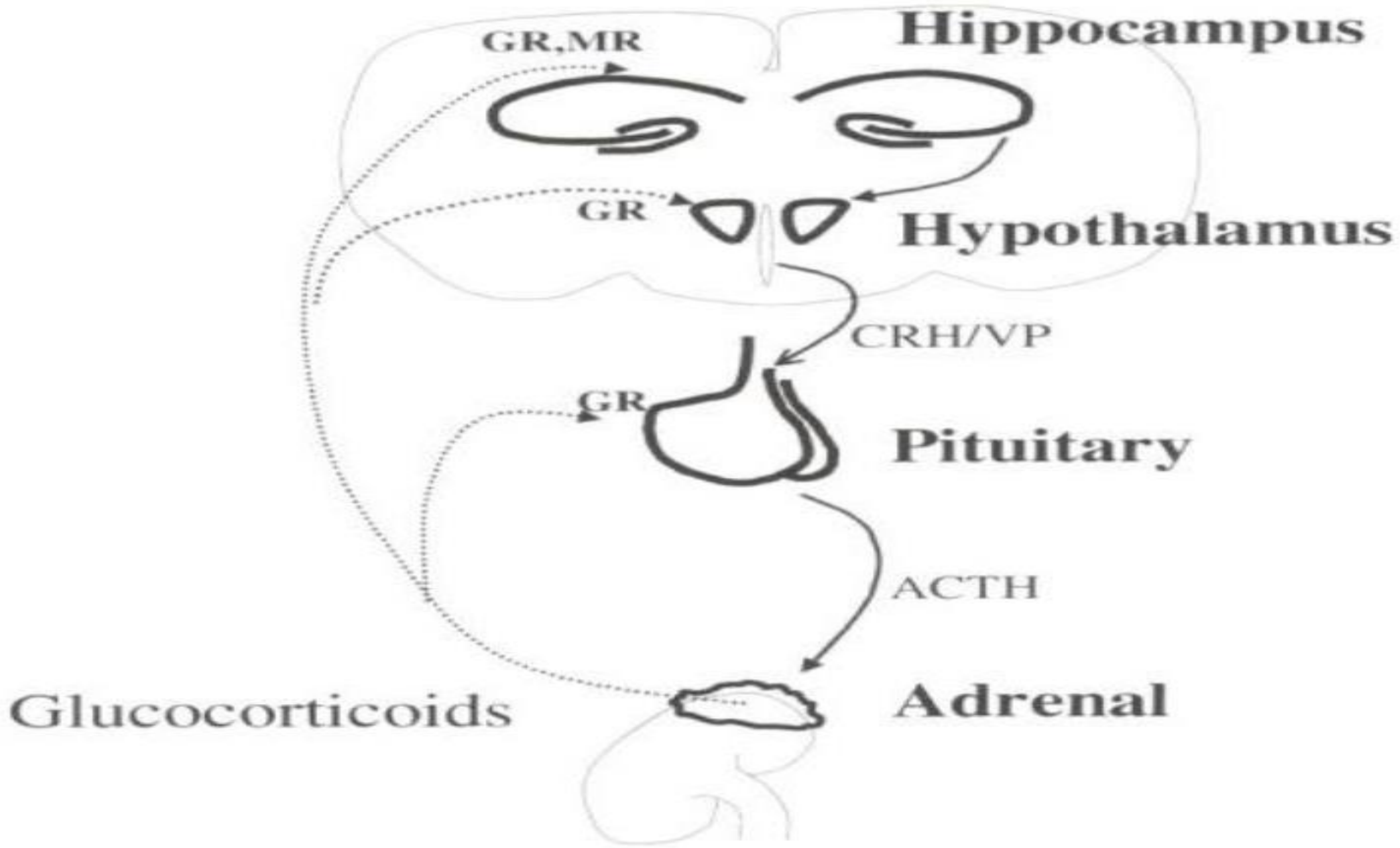
Important to the function of the HPA axis are some of the feedback loops: Cortisol produced in the adrenal cortex will negatively feedback to inhibit both the hypothalamus and the pituitary gland. This reduces the secretion of CRH and vasopressin, and also directly reduces the cleavage of proopiomelanocortin (POMC) into ACTH and β-endorphins.

Epinephrine and norepinephrine (E/NE) are produced by the adrenal medulla through sympathetic stimulation and the local effects of cortisol (upregulation enzymes to make E/NE). E/NE will positively feedback to the pituitary and increase the breakdown of POMCs into ACTH and β-endorphins.

Function

Release of corticotropin-releasing hormone (CRH) from the hypothalamus is influenced by stress, physical activity, illness, by blood levels of cortisol and by the sleep/wake cycle (circadian rhythm). In healthy individuals, cortisol rises rapidly after wakening,

The HPA axis has a central role in regulating many homeostatic systems in the body, including the metabolic system, cardiovascular system, immune system, reproductive system and central nervous systemAnatomical connections between brain areas such as the amygdala, hippocampus, prefrontal cortex and hypothalamus facilitate activation of the HPA axis.Sensory information arriving at the lateral aspect of the amygdala is processed and conveyed to the amygdala's central nucleus, which then projects out to several parts of the brain involved in responses to fear. At the hypothalamus, fear-signaling impulses activate both the sympathetic nervous system and the modulating systems of the HPA axis.



GR,MR
Hippocampus
GR
Hypothalamus
CRH/VP
GR
Pituitary
ACTH
Glucocorticoids
Adrenal

Almost all secretion by the pituitary is controlled by either hormonal or nervous signals from the hypothalamus. Indeed, when the pituitary gland is removed from its normal position beneath the hypothalamus and transplanted to some other part of the body, its rates of secretion of the different hormones (except for prolactin) fall to very low levels.Secretion from the posterior pituitary is controlled by nerve signals that originate in the hypothalamus and terminate in the posterior pituitary. In contrast, secretion by the anterior pituitary is controlled by hormones called

hypothalamic releasing and hypothalamic inhibitory hormones (or factors) secreted within the hypothalamus and then conducted, as shown in Figure to the anterior pituitary through minute blood vessels called hypothalamic-hypophysial portal vessels. In the anterior pituitary, these releasing and inhibitory hormones act on the glandular cells to control their secretion

The hypothalamus receives signals from many sources in the nervous system. Thus, when a person is exposed to pain, a portion of the pain signal is transmitted into the hypothalamus.

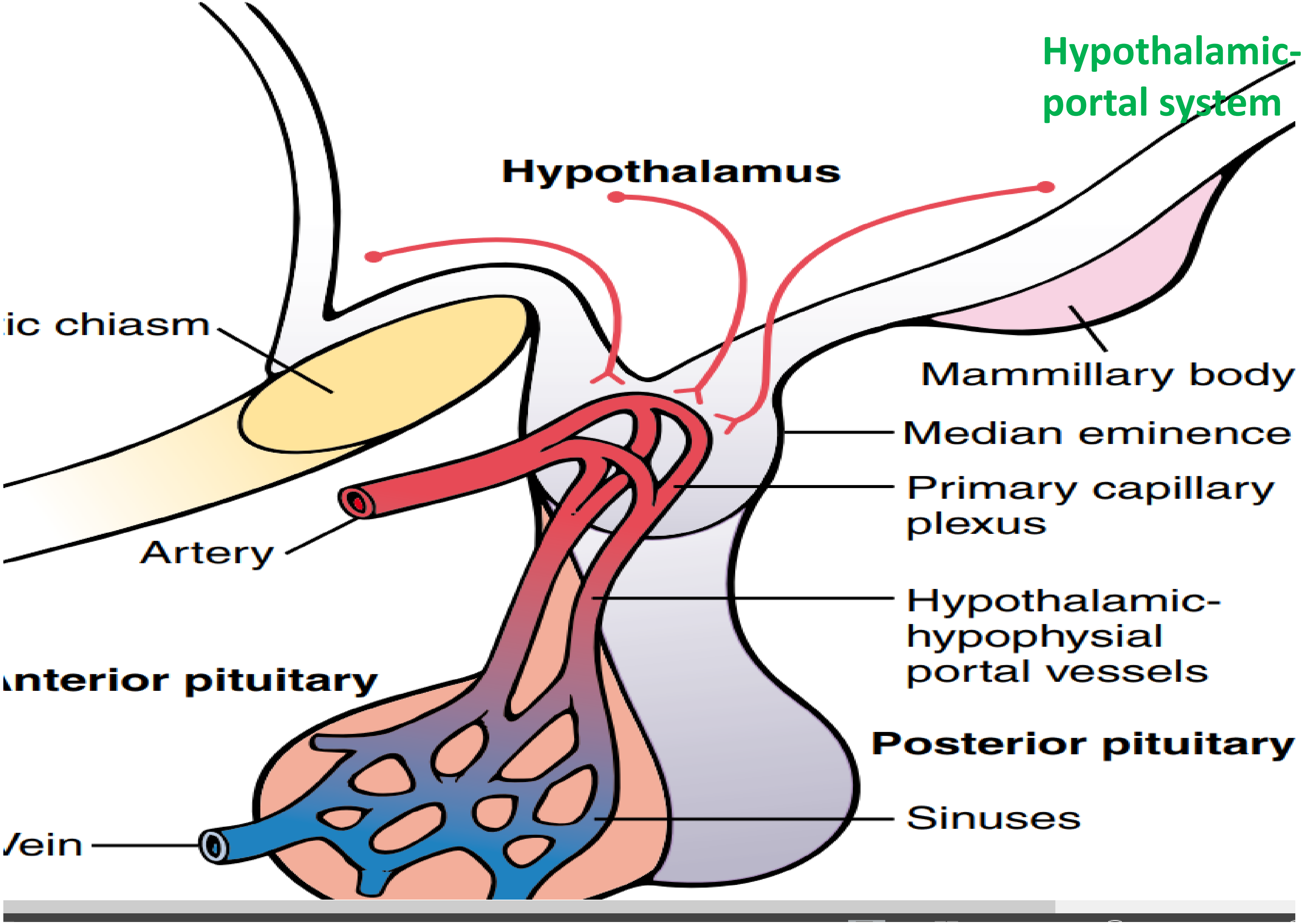
Hypothalamic-Hypophysial Portal Blood Vessels of the Anterior Pituitary Gland

The anterior pituitary is a highly vascular gland with extensive capillary sinuses among the glandular cells.

Almost all the blood that enters these sinuses passes first through another capillary bed in the lower hypothalamus. The blood then flows through small hypothalamichypophysial portal blood vessels into the anterior pituitary sinuses. Figure shows the lowermost portion of the hypothalamus, called the median eminence, which connects inferiorly with the pituitary stalk.

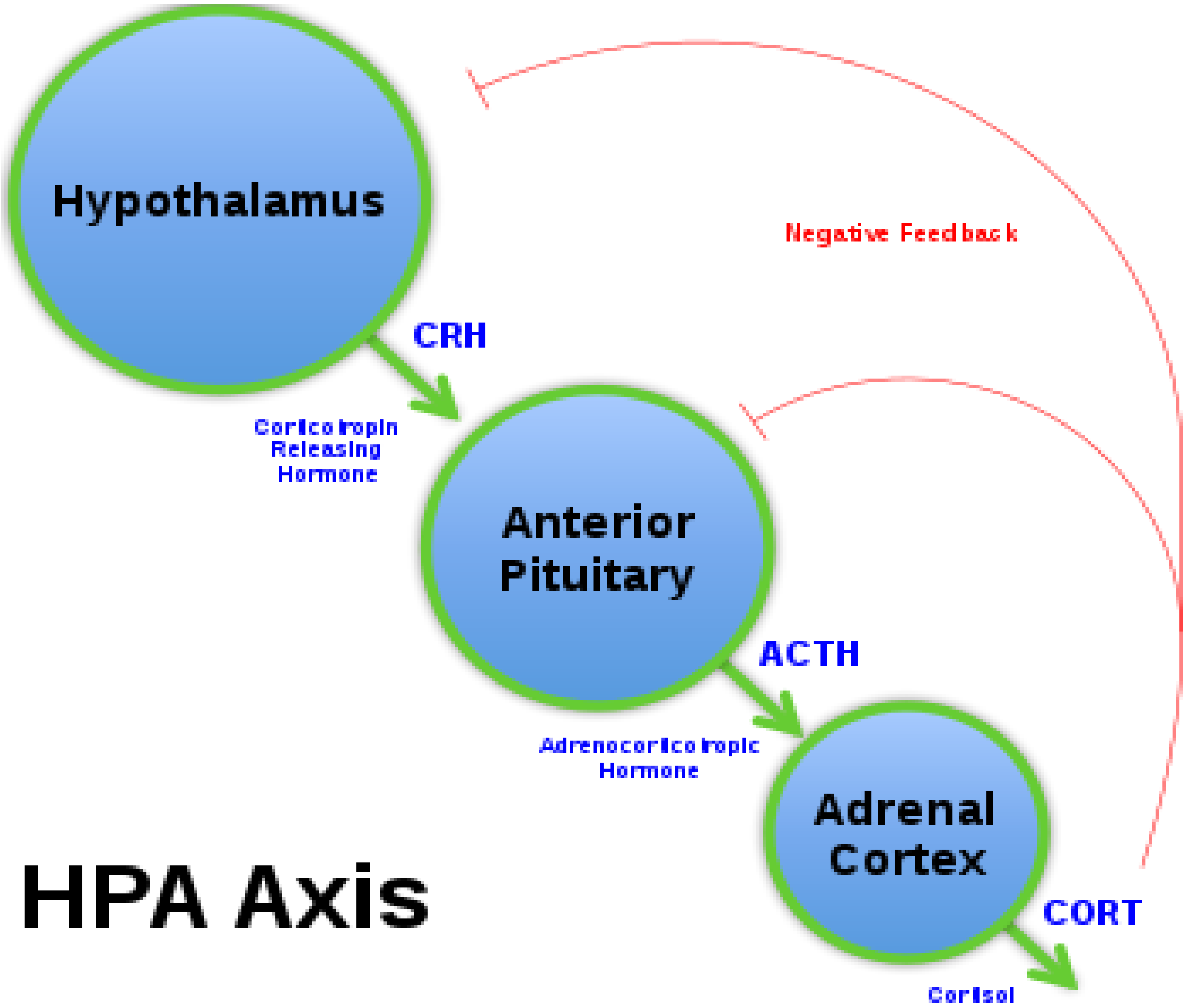
Small arteries penetrate into the median eminence and then additional small vessels return to its surface, coalescing to form the hypothalamic-hypophysial portal blood vessels. These pass downward along the pituitary stalk to supply blood to the anterior pituitary sinuses.

Hypothalamic-hypophysial portal system



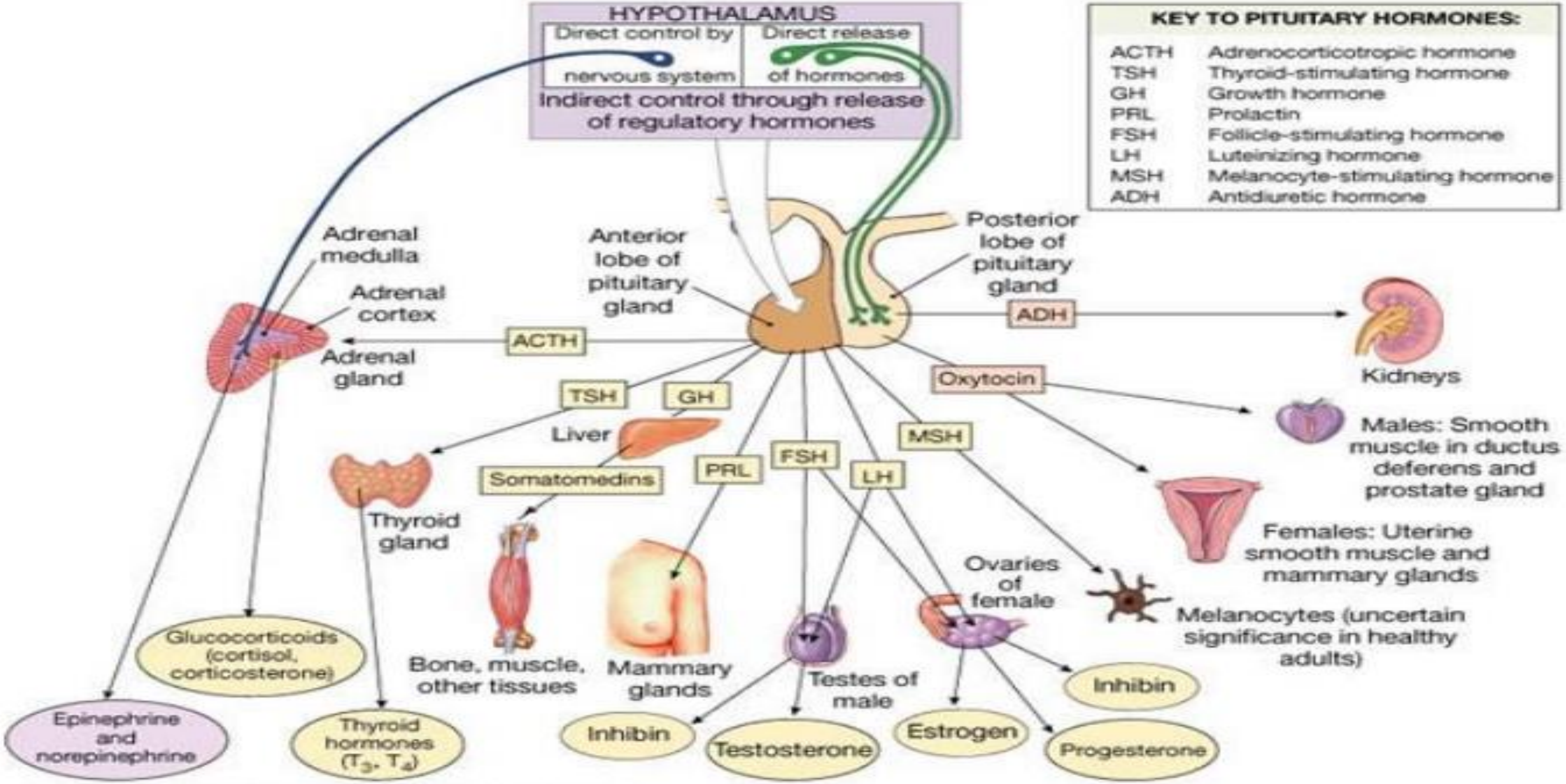
Hypothalamic Releasing and Inhibitory Hormones Are Secreted into the Median Eminence.

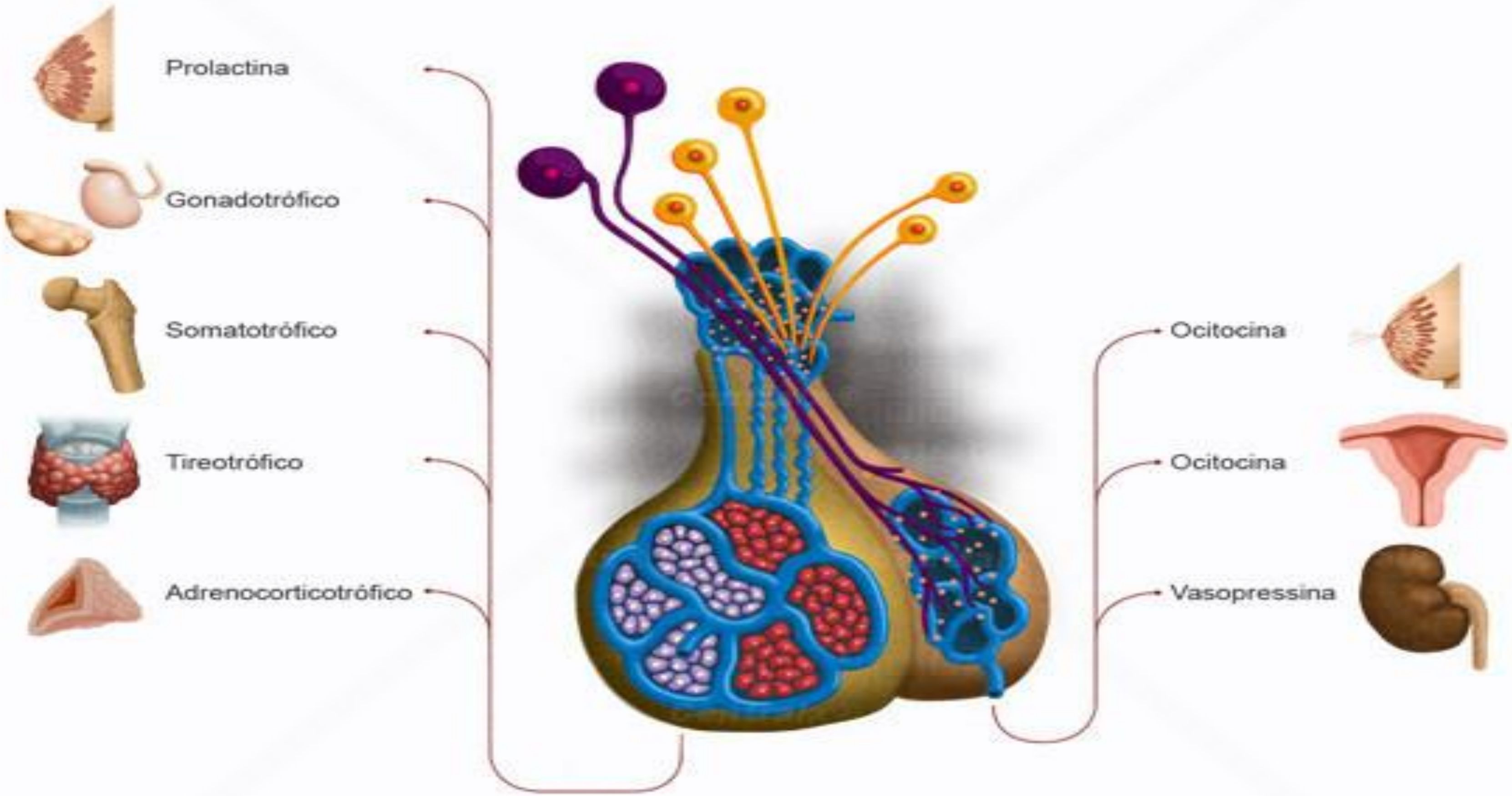
Special neurons in the hypothalamus synthesize and secrete the hypothalamic releasing and inhibitory hormones that control secretion of the anterior pituitary hormones. These neurons originate in various parts of the hypothalamus and send their nerve fibers to the median eminence and tuber cinereum, an extension of hypothalamic tissue into the pituitary stalk

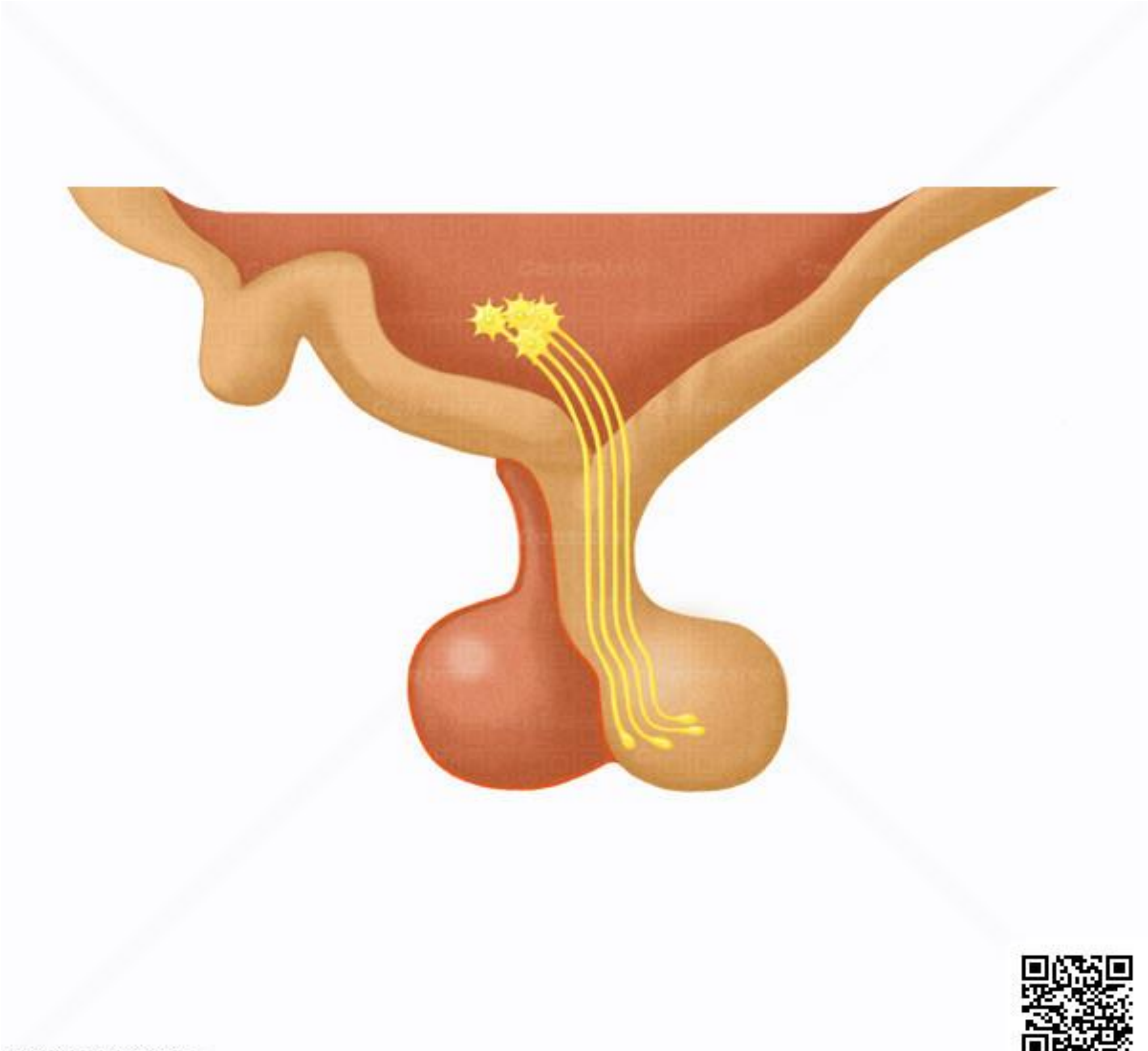

Hypothalamus
Negative Feedback
CRH
Corticotropin Releasing Hormone
Anterior Pituitary
ACTH
Adrenocorticotropic Hormone
Adrenal Cortex
CORT
Cortisol

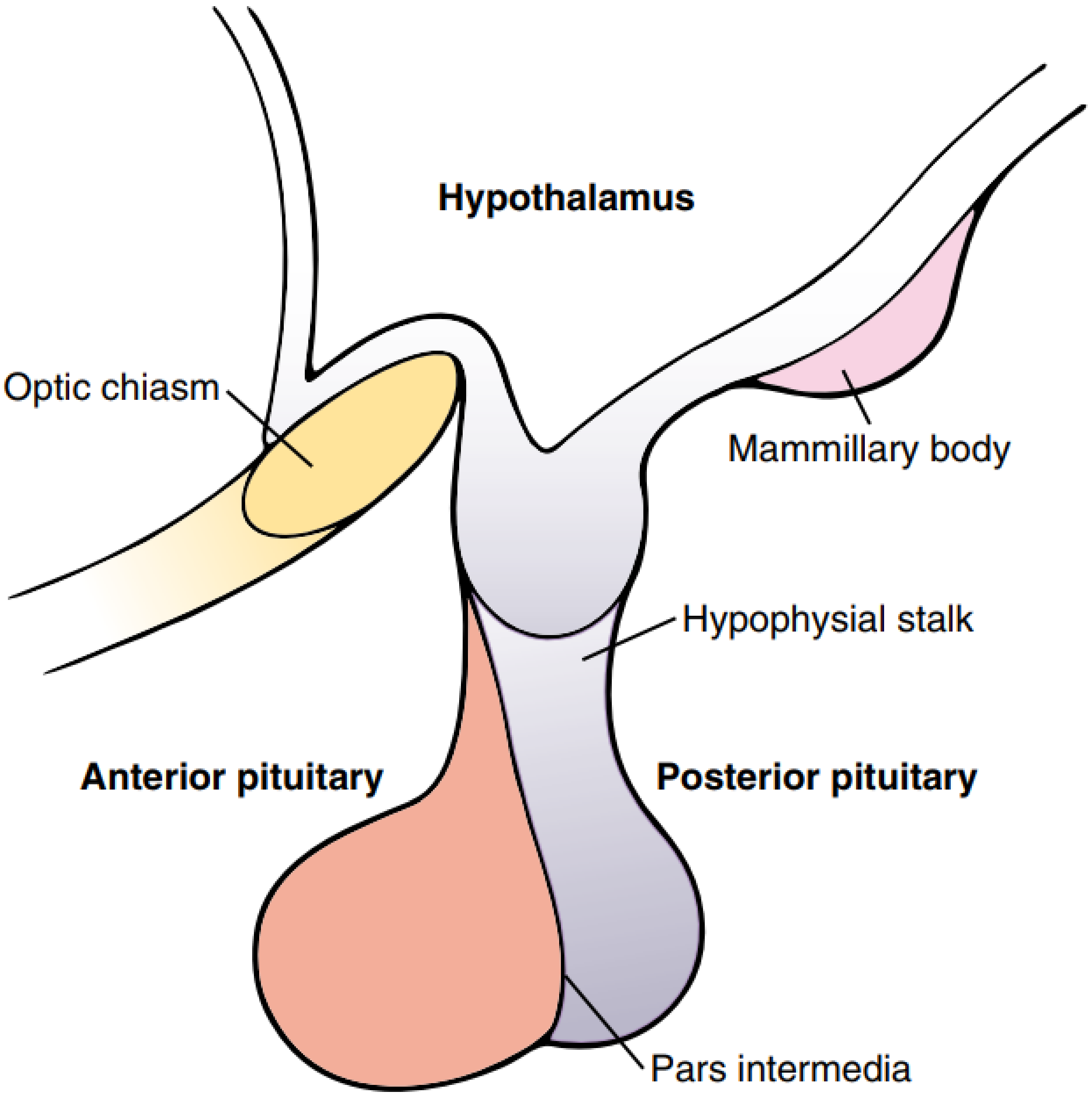
HPA Axis

The hypothalamo-hypophyseal system-neuroendocrine system




Prolactina
Gonadotrófico
Somatotrófico
Tireotrófico
Adrenocorticotrófico
Ocitocina
Ocitocina
Vasopressina




Hypothalamus
Optic chiasm
Mammillary body
Hypophysial stalk
Anterior pituitary
Posterior pituitary
Pars intermedia

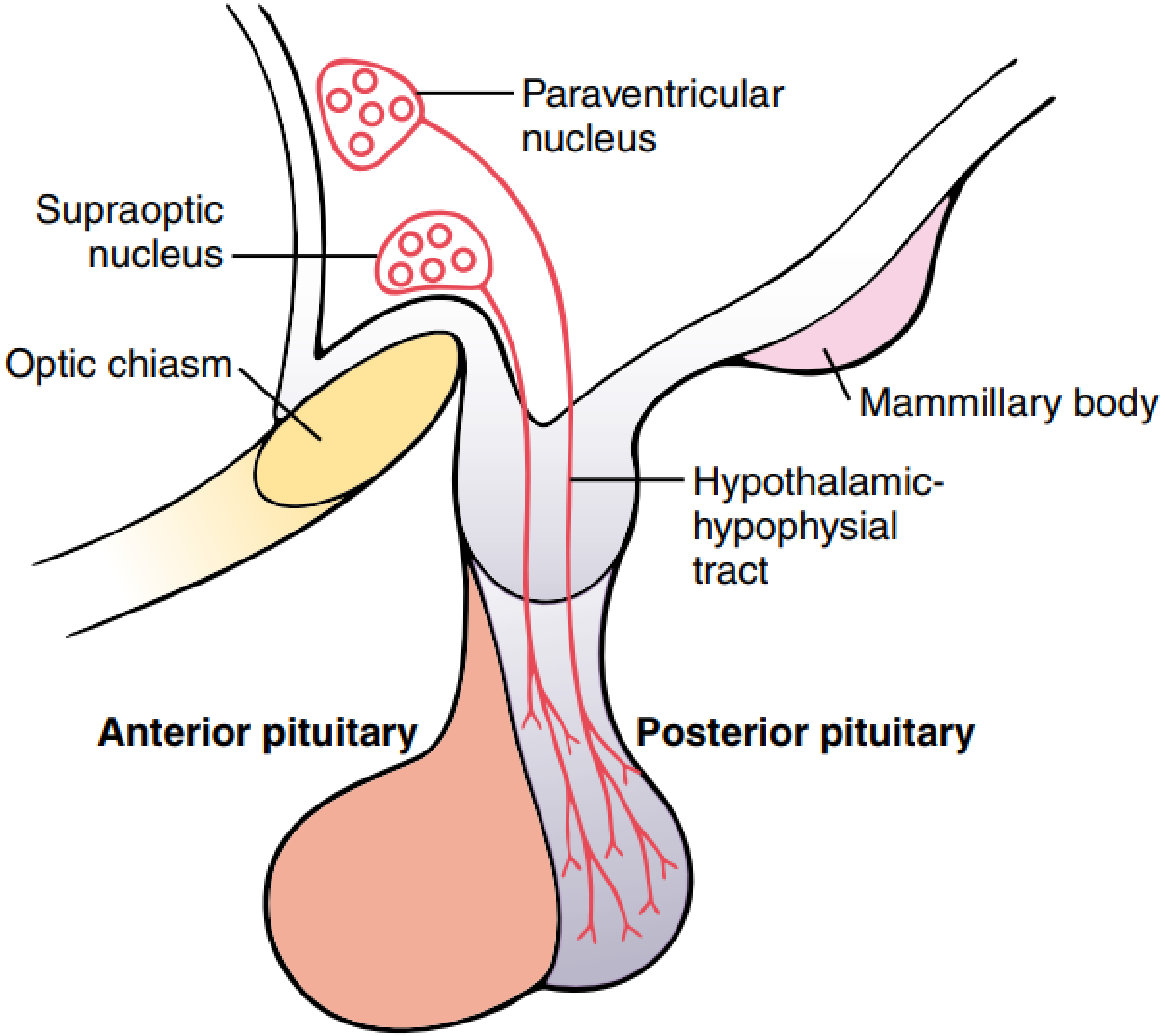
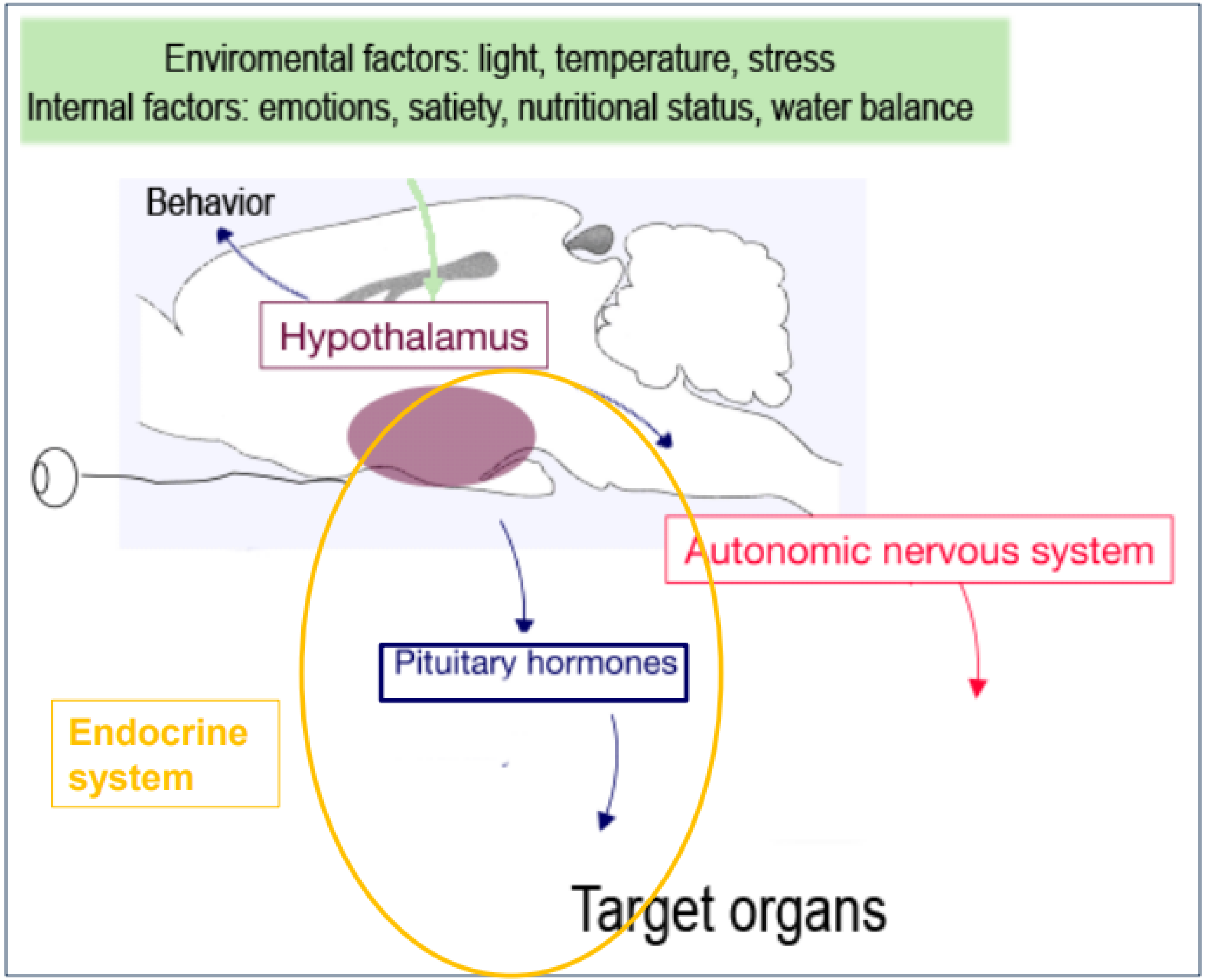


Figure 75-9 Hypothalamic control of the posterior pituitary.

Homeostatic integration within the hypothalamus



Hypothalamic nuclei and areas

Anterior region

- n. anterior
- n. preopticus med. and lat.
- n. paraventricularis
- n. supraopticus
- n. suprachiasmaticus

Medial region

- **Periventricular zone**

Medial zone

n. ventro- and dorsomedialis

- n. infundibularis (arcuatus)

Lateral zone

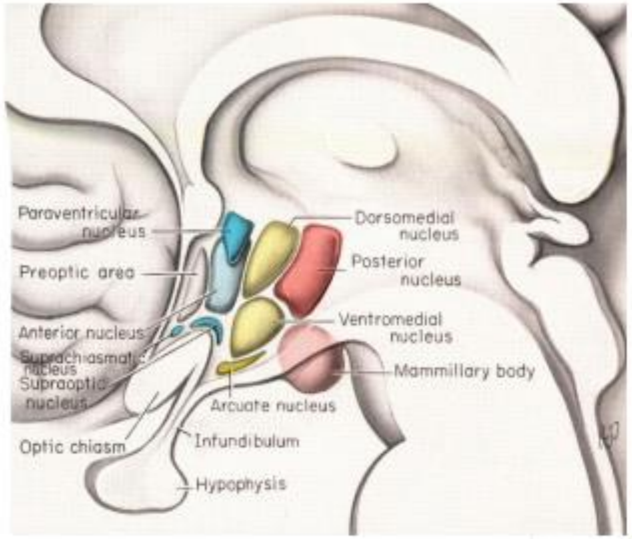
dorsolateral hypothalamic area

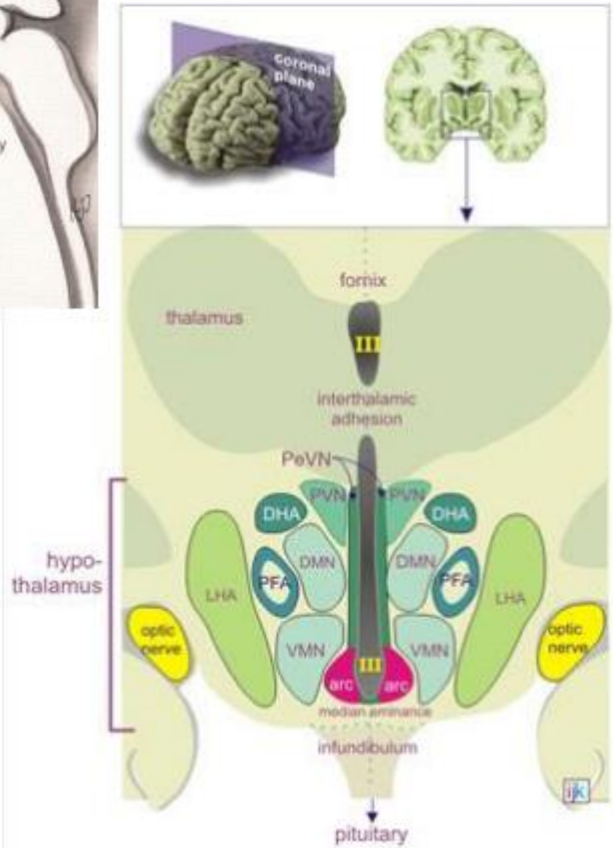
medial forebrain bundle

Posterior region

n. hypothalamicus posterior

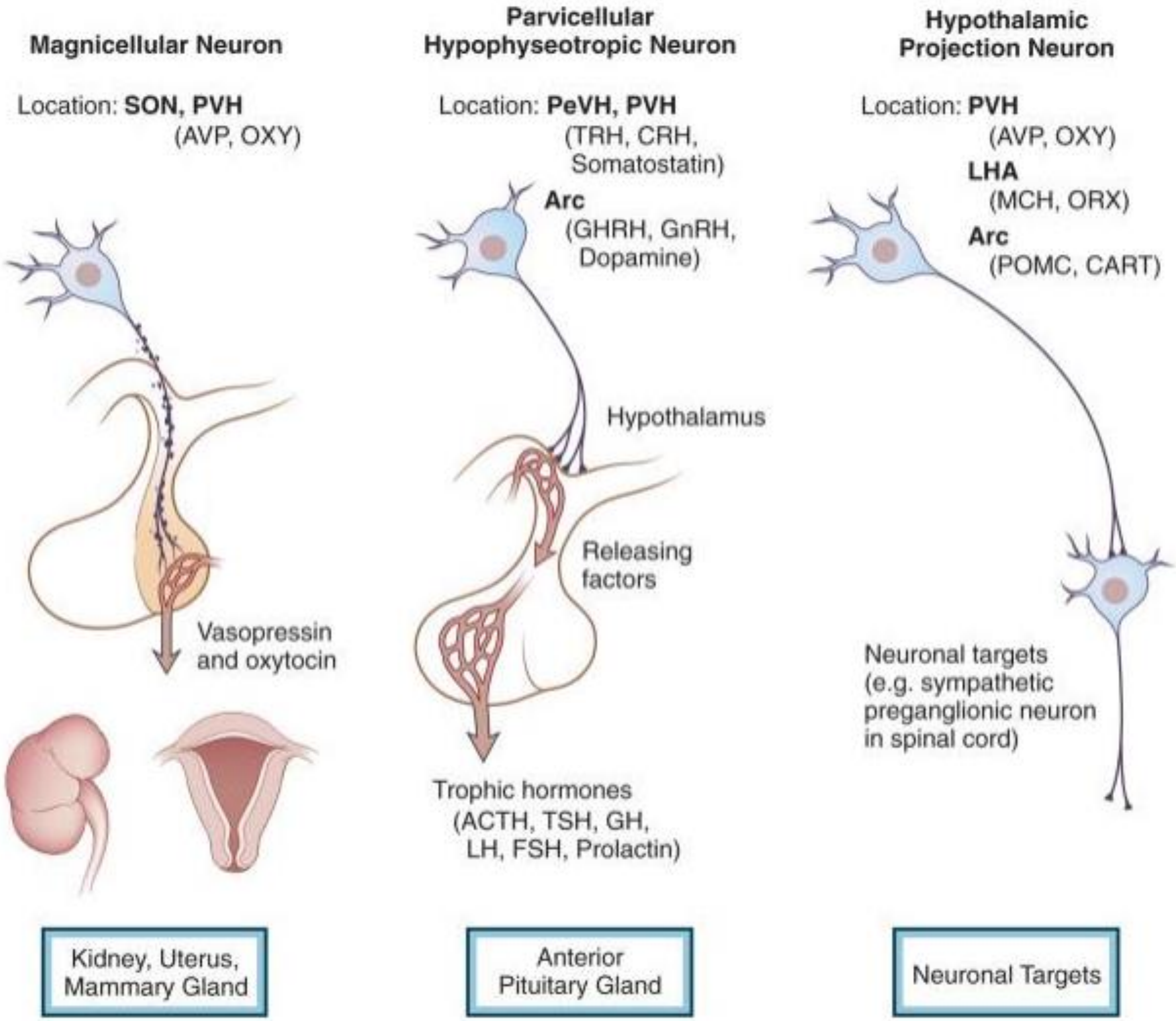
corpus mamillare



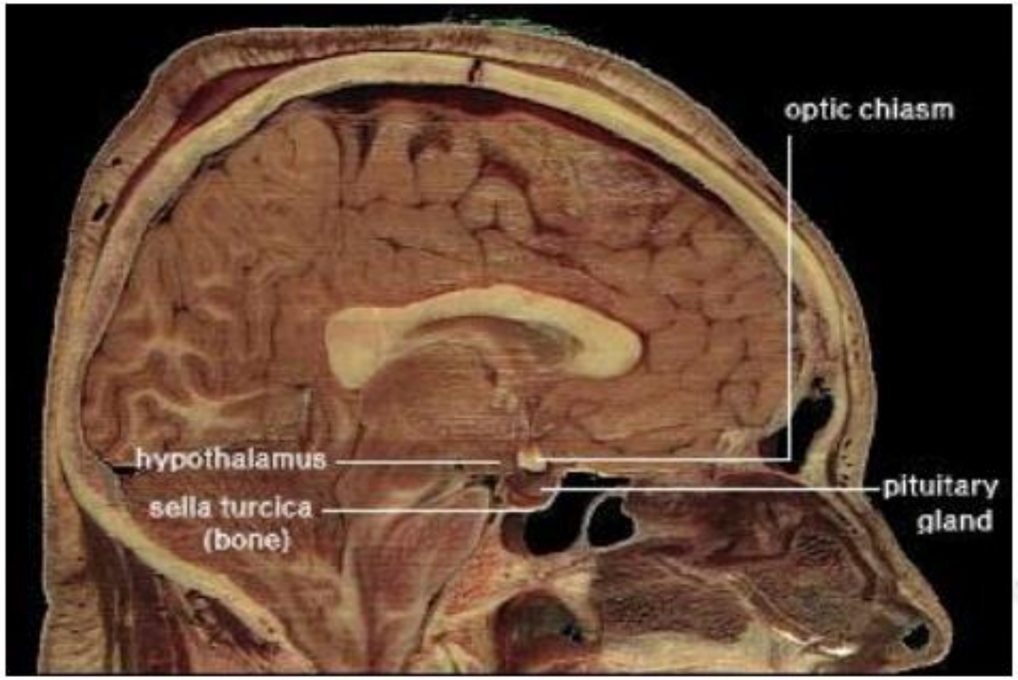


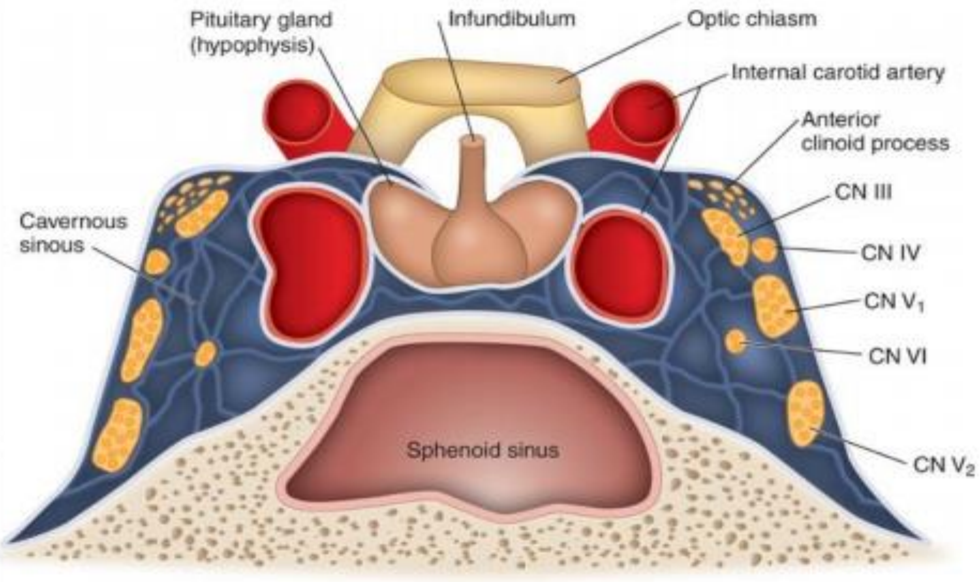
contributes to the HTH system

Neurosecretory cells are the magno- and parvocellular neurons in the hypothalamus



The pituitary is connected with the hypothalamus via the infundibulum





Blood supply:

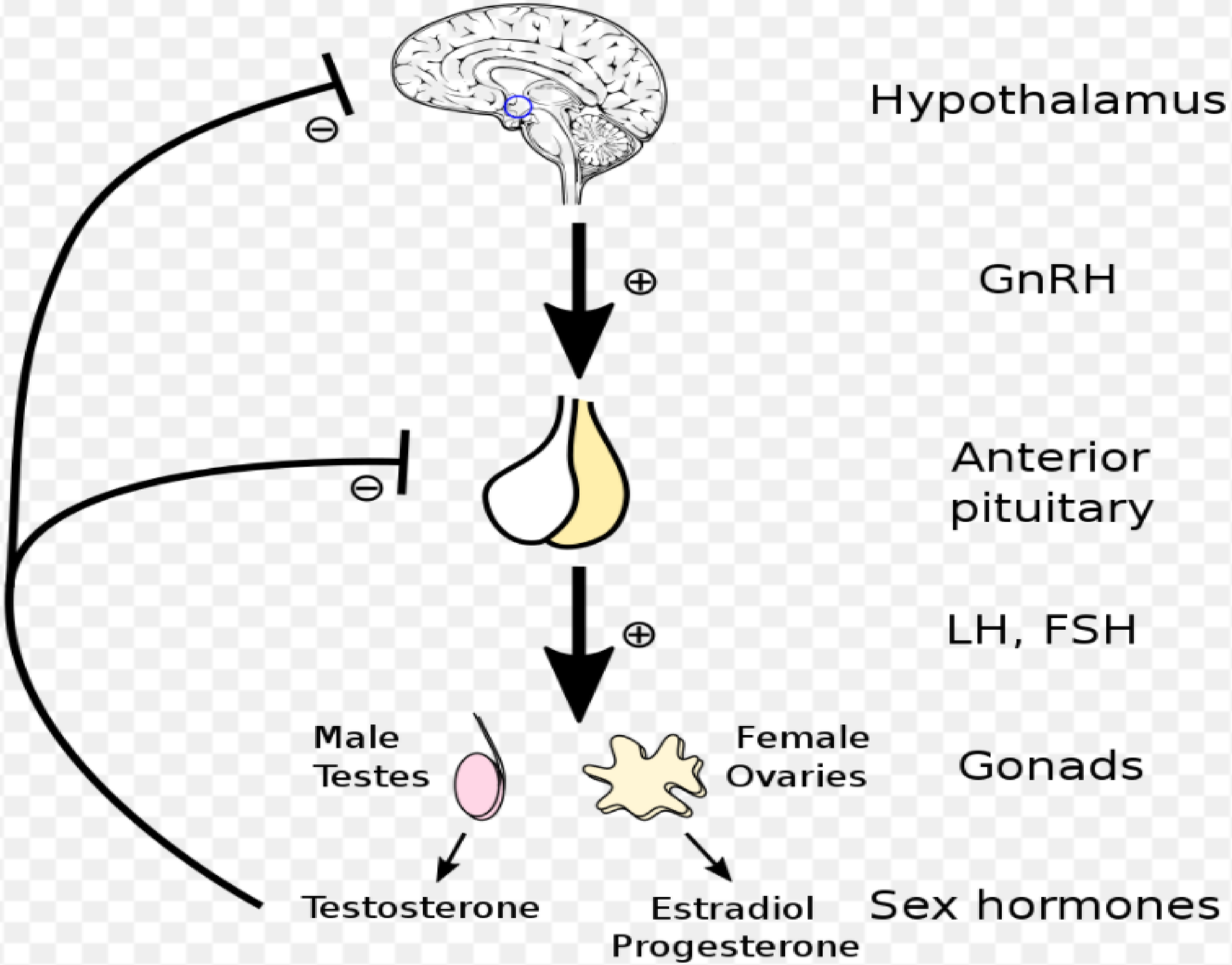
Superior hypophyseal artery – internal carotid artery

Inferior hypophyseal artery - circulus arteriosus

2.The hypothalamic–pituitary–gonadal axis (HPG axis)

refers to the hypothalamus, pituitary gland, and gonadal glands as if these individual endocrine glands were a single entity. Because these glands often act in concert, physiologists and endocrinologists find it convenient and descriptive to speak of them as a single system.

The axis controls development, reproduction, and aging in animals. Gonadotropin-releasing hormone (GnRH) is secreted from the hypothalamus by GnRH-expressing neurons. The anterior portion of the pituitary gland produces luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and the gonads produce estrogen and testosterone.

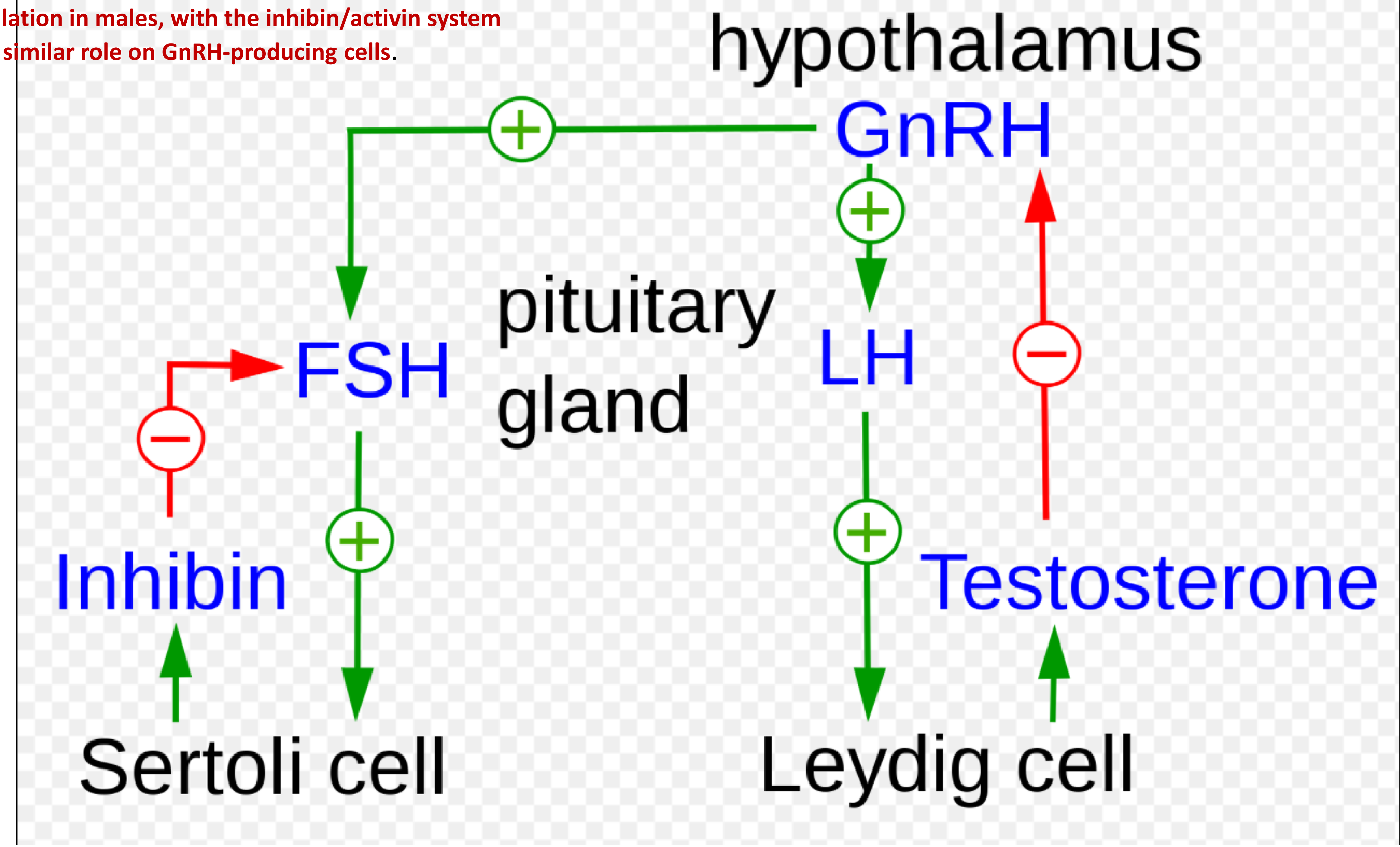


Hypothalamus
GnRH
Anterior
pituitary
LH, FSH
Male
Testes
Female
Ovaries
Gonads
Testosterone
Estradiol
Progesterone
Sex hormones

In oviparous organisms (e.g. fish, reptiles, amphibians, birds), the HPG axis is commonly referred to as the hypothalamus-pituitary-gonadal-liver axis (HPGL-axis) in females. Many egg-yolk and chorionic proteins are synthesized heterologously in the liver, which are necessary for ovocyte growth and development. Examples of such necessary liver proteins are vitellogenin and choriogenin.

The HPA, HPG, and HPT axes are three pathways in which the hypothalamus and pituitary direct neuroendocrine function.

HPG regulation in males, with the inhibin/activin system playing a similar role on GnRH-producing cells.



Location and regulation

HPG regulation in males, with the inhibin/activin system playing a similar role on GnRH-producing cells.

The hypothalamus is located in the brain and secretes GnRH.GnRH travels down the anterior portion of the pituitary via the hypophyseal portal system and binds to receptors on the secretory cells of the adenohypophysis. In response to GnRH stimulation these cells produce LH and FSH, which travel into the blood stream.

These two hormones play an important role in communicating to the gonads. In females FSH and LH act primarily to activate the ovaries to produce estrogen and inhibin and to regulate the menstrual cycle and ovarian cycle. Estrogen forms a negative feedback loop by inhibiting the production of GnRH in the hypothalamus.

Function :Reproduction

One of the most important functions of the HPG axis is to regulate reproduction by controlling the uterine and ovarian cycles. In females, the positive feedback loop between estrogen and luteinizing hormone help to prepare the follicle in the ovary and the uterus for ovulation and implantation. When the egg is released, the empty follicle sac begins to produce progesterone to inhibit the hypothalamus and the anterior pituitary thus stopping the estrogen-LH positive feedback loop. If conception occurs, the placenta will take over the secretion of progesterone; therefore the mother cannot ovulate again.

If conception does not occur, decreasing excretion of progesterone will allow the hypothalamus to restart secretion of GnRH. These hormone levels also control the uterine (menstrual) cycle causing the proliferation phase in preparation for ovulation, the secretory phase after ovulation, and menstruation when conception does not occur. The activation of the HPG axis in both males and females during puberty also causes individuals to acquire secondary sex characteristics.

3.The hypothalamic–pituitary–thyroid axis

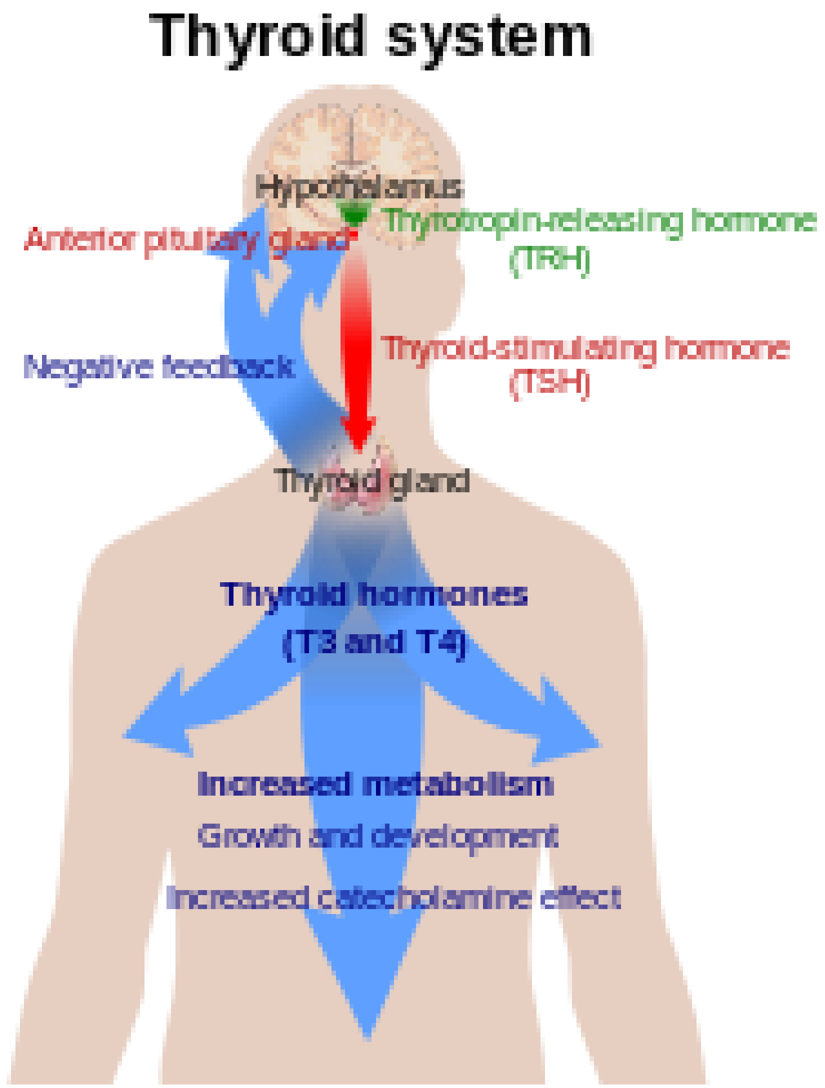
(HPT axis for short, a.k.a. thyroid homeostasis or thyrotropic feedback control) is part of the neuroendocrine system responsible for the regulation of metabolism and also responds to stress.

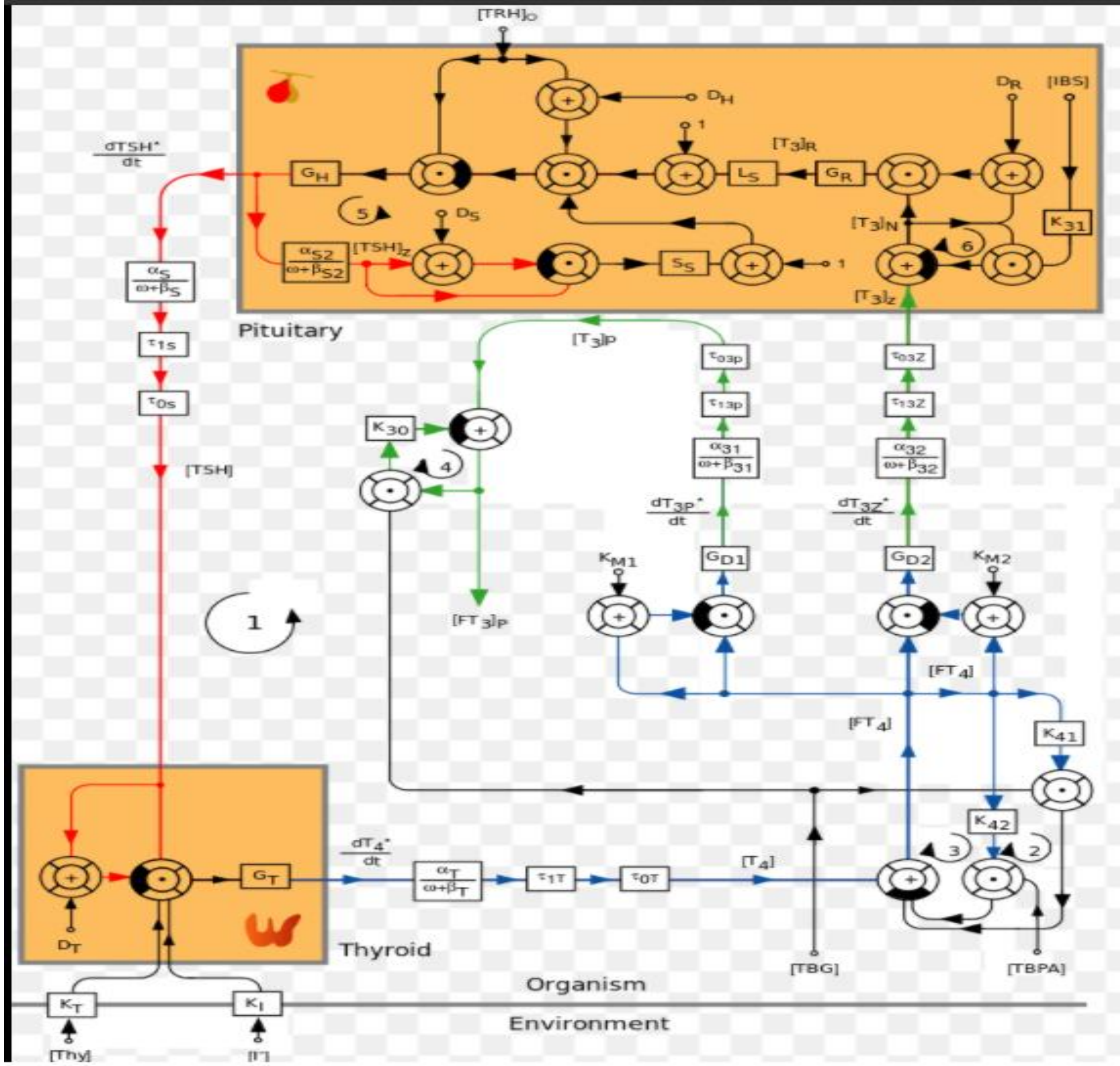
As its name suggests, it depends upon the hypothalamus, the pituitary gland, and the thyroid gland.

The hypothalamus senses low circulating levels of thyroid hormone (Triiodothyronine (T3) and Thyroxine (T4)) and responds by releasing thyrotropin-releasing hormone (TRH). The TRH stimulates the anterior pituitary to produce thyroid-stimulating hormone (TSH).

The TSH, in turn, stimulates the thyroid to produce thyroid hormone until levels in the blood return to normal. Thyroid hormone exerts negative feedback control over the hypothalamus as well as anterior pituitary, thus controlling the release of both TRH from hypothalamus and TSH from anterior pituitary gland.

The HPA, HPG, and HPT axes are three pathways in which the hypothalamus and pituitary direct neuroendocrine function.


Thyroid system
Hypothalamus
Anterior pituitary gland
Thyrotropin-releasing hormone
(TRH)
Negative feedback
Thyroid-stimulating hormone
(TSH)
Thyroid gland
Thyroid hormones
(T3 and T4)
Increased metabolism
Growth and development
Increased catecholamine effect


Pituitary
Thyroid
Organism
Environment
[TSH]
[TBG]
[TBPA]
[FT4]
[T4]

The pituitary gland secretes thyrotropin (TSH; Thyroid Stimulating Hormone) that stimulates the thyroid to secrete thyroxine (T4) and, to a lesser degree, triiodothyronine (T3).

The major portion of T3, however, is produced in peripheral organs, e.g. liver, adipose tissue, glia and skeletal muscle by deiodination from circulating T4. Deiodination is controlled by numerous hormones and nerval signals including TSH, vasopressin and catecholamines.

Both peripheral thyroid hormones (iodothyronines) inhibit thyrotropin secretion from the pituitary (negative feedback). Consequently, equilibrium concentrations for all hormones are attained.

Thank you