Fourth Semester UG Zoology, Core -8, Unit -2
Hypothalmo- Hypophysial Portal System

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The pituitary is closely applied to the floor of the brain and remain attached to it by means of delicate stalk. The functional capacity of the anterior pituitary depends upon its neural and vascular connection with the hypothalamus. In this way the pituitary present itself as an essential link between the two vital system of the vertebrate physiology viz nervous system and endocrine system. Thus, making possible establishment of a neuroendocrine system.

In other words, the hypothalamus and hypophysis function so closely together that they are often studied as a single integrated unit called the hypothalamo-hypophyseal system. This system, also referred to as the hypophyseal portal system, consists of a specialized network of blood vessels that carries signals from the hypothalamus in the brain to the anterior pituitary (adenohypophysis), thereby connecting and coordinating their activities.

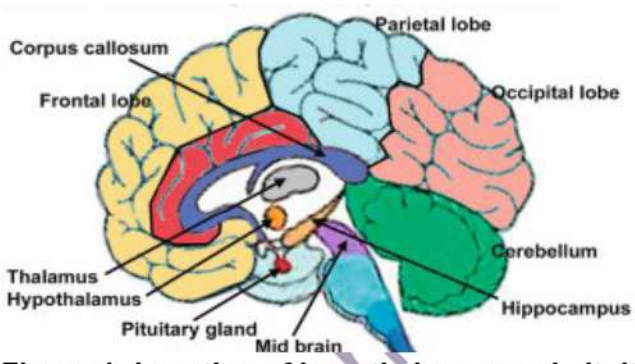

Figure 1: Location of hypothalamus and pituitary

Hypothalamus

The diencephalon is a small posterior region of the forebrain. Its walls become thickened to form two important structures: the thalamus in the upper part and the hypothalamus in the lower part.

The hypothalamus plays a vital role in regulating many visceral functions, as numerous internal sensory nerve fibres terminate here. It helps control several essential body processes such as body temperature, sleep, water balance, feeding, drinking, emotions, and reproductive behaviour.

In addition to these functions, the hypothalamus is also an important centre for neurosecretion. Through this function, it exerts a significant influence on the pituitary gland and other endocrine glands of the body. It also regulates various physiological activities including heart rate, respiration, and gastrointestinal motility through its control over the autonomic nervous system and the endocrine system.

Origin of Hypothalamus:

The hypothalamus develops from the ectodermal layer of the embryo during early development.

Location and Structure of Hypothalamus:

The hypothalamus is situated below (inferior to) the thalamus in the brain. It forms an important link between the nervous system and the endocrine system, mainly through its connection with the hypophysis or pituitary gland.

The hypothalamus communicates with the anterior lobe of the pituitary gland through the hypophyseal portal veins. In contrast, it is connected to the posterior lobe of the pituitary gland primarily by the axons of neurosecretory cells.

Hormones produced by the hypothalamus regulate and influence the activity of the pituitary gland. Because of this key regulatory role, the hypothalamus is often regarded as the **major control centre** of endocrine regulation.

Hormones of Hypothalamus:

Cells in the hypothalamus synthesize at least (09) nine different hormones. The neurosecretory cells (neurons) of hypothalamus secrete hormones called neurohormones (= releasing factors) which
are summarised below.

Releasing and Inhibiting Hormones

Hypothalamic Releasing Hormones:

- CRH (Corticotropin Releasing Hormone) – Stimulates the release of ACTH
- TRH (Thyrotropin-Releasing Hormone) – Stimulates the release of TSH
- GnRH (Gonadotropin-Releasing Hormone) – Stimulates the release of FSH and LH
- GHRH (Growth Hormone Releasing Hormone) – Stimulates the release of GH

Hypothalamic Inhibiting Hormones:

Growth Hormone-Inhibitory Hormone (GHIH):This hormone is also called somatostatin (SS). It inhibits the secretion of growth hormone from the anterior lobe of the pituitary gland.

Prolactin Inhibitory Hormone (PIH): Inhibits the secretion of prolactin from the anterior lobe of pituitary gland.

- MIH (Melanotropin-Inhibiting Hormone) – Inhibits the secretion of MSH

Control, secretion, regulation of anterior pituitary by the hypothalamus: The neurosecretory cells of the hypothalamus are specialized neurons that produce hypothalamic releasing and inhibiting hormones. These hormones are synthesized in the cell bodies of the neurons and are packed into small vesicles. The vesicles move along the axons through fast axonal transport and are stored at the axon terminals.

When these hypothalamic neurosecretory cells are stimulated, nerve impulses cause the vesicles to undergo exocytosis, releasing the hormones. The released hypothalamic hormones enter the blood of the primary capillary plexus of the hypophyseal portal system. From there, they are rapidly carried through the hypophyseal portal veins to the secondary capillary plexus in the anterior pituitary.

This specialized portal circulation allows hypothalamic hormones to reach the anterior pituitary cells quickly and directly, preventing them from being diluted or destroyed in the general bloodstream. In the secondary plexus, the hypothalamic hormones leave the blood and interact with the cells of the anterior pituitary.

When stimulated by the appropriate releasing hormones, the anterior pituitary cells release their hormones into the secondary plexus capillaries. These hormones then pass into the hypophyseal veins and enter the general circulation, from where they travel to their target tissues throughout the body.

Some anterior pituitary hormones act on other endocrine glands and are therefore called tropic hormones (tropins). The secretion of anterior pituitary hormones is controlled not only by the hypothalamus but also through negative feedback mechanisms. For example,

when the levels of hormones produced by target glands increase in the blood, the activity of certain anterior pituitary cells—thyrotrophs, corticotrophs, and gonadotrophs—is reduced, thereby decreasing further hormone secretion.

Example: Thyrotropin-Releasing Hormone (TRH) from the hypothalamus stimulates the anterior pituitary. The anterior pituitary releases Thyroid-Stimulating Hormone (TSH).
TSH acts on the Thyroid Gland to produce thyroid hormones. When the level of thyroid hormone increases it suppresses the activity of TRH.

Adrenocorticotropic hormone (ACTH) stimulates the cortex of the adrenal gland to secrete glucocorticoids, mainly cortisol. In turn, an elevated blood level of cortisol decreases secretion of both ACTH (corticotropin) and corticotropin-releasing hormone (CRH) by suppressing the activity of the anterior pituitary corticotrophs and hypothalamic neurosecretory cells.

HYPOPHYSIS : Pituitary gland is located in the Sell turcica, a concavity in the sphenoid bone. The gland is encapsulated by the dura matter and a shelf like fold of the later forms the diaphrogena sellae and extend around the infundibular stalk. Pituitary is derived from the epithelial and neural components. It is divisible into two parts i.e. Adenohypophysis and Neurohypophysis.

Adenohypophysis (anterior lobe) consists of 1. Pars Intermedia 2. Pars tuberalis 3. Pars Distalis

Neurohypophysis (posterior lobe) consists of 1. Pars nervosa 2. Infundibulum

The embryonic development of the lobes of the pituitary gland is completely distinct. The anterior lobe is derived from an inward invagination of the primitive mouth cavity (oral ectoderm) known as Rathke's pouch while the neural lobe arises from the neural ectoderm of the floor of the developing forebrain, the infundibulum of diencephalon. Cells of the anterior wall of Rathke's pouch develop into the pars distalis, containing most of the hormone producing cells of the adenohypophysis.

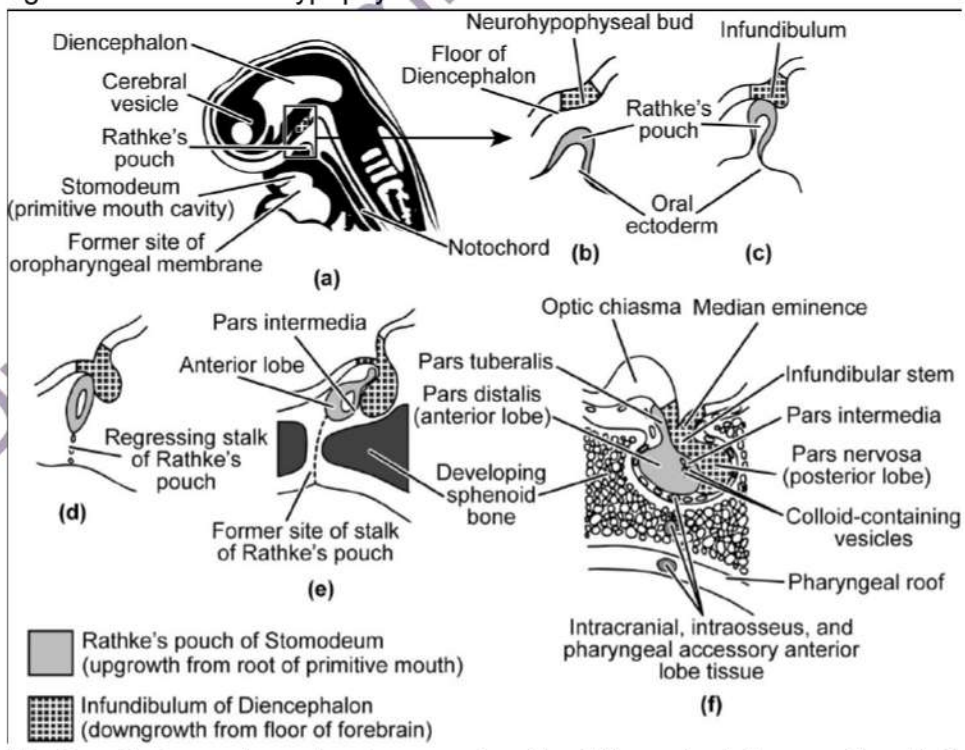

Fig.2: Embryonic development of different lobes of pituitary gland (Source:egyankosh)

Pars-intermedia : The pars intermedia is a zone of cells that is separated from the pars distalis by the hypophyseal cleft, which is the remnant of the embryonic Rathke's pouch that extended up from the roof of the oral cavity Pars intermedia is the boundary between the anterior and posterior lobes of the pituitary. It contains colloid-filled cysts and two types of cells - basophils and chromophobes. The cysts are the remainder of Rathke's pouch. The pars intermedia is closely associated with pars nervosa and separated from the pars distalis by the hypophyseal cleft. This lobe of the pituitary shows considerable variation in size among species. It is small in man, but much larger in species such as amphibians. The pars intermedia contains large pale cells that often surround follicles filled with ill-defined "colloid". Melanocyte-stimulating hormone is the predominant hormone secreted by the pars intermedia.

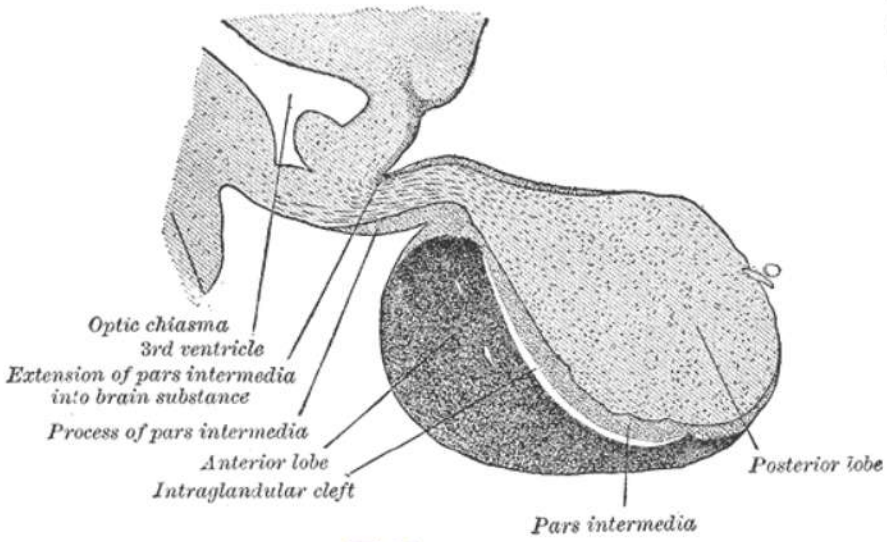

Figure 3: Location of three lobes of pituitary

Pars intermedia is present in young human being only merges into the neural lobe in adults. This lobe is absent in the birds and in certain mammals such as whales, Indian elephants. Hormones are produced in the pars intermedia are-Dopamine, Adrenocorticotropic Hormone, Proopiomelanocortin, Thyrotropin-Releasing Hormone & Cortisol.

Pars tuberalis : - The pars tuberalis is part of the anterior lobe of the pituitary gland which wraps the pituitary stalk in a highly vascularized sheath. The pars tuberalis is constituted of the adenohypophysis which is a thin epithelial plate of cells that is formed by the fusion of two outgrowth from the embryonic pars distalis. Pars tuberalis is constituted of the adenohypophysis which is a thin epithelial plate of cells that is formed by the fusion of two outgrowth from the embryonic pars distalis.

Pars Distalis: This is the portion in which the majority of the hormone production occurs. It is the distal part of the pituitary and forms the majority of adenohypophysis.The pars distalis have two general cell types chromophils (50%) and chromophobes (50%). The chromophils can be further subdivided into acidophils (40%) and basophils (10%).The acidophils secrete GH (somatotropes) and prolactin (mammotropes). These cells all together produce hormones of the anterior pituitary and release them into the blood stream. The pars distalis produces GH, PRL, GTHs, (FSH, LH), ACTH, TSH and endorphins (EOPs). The

posterior portion of the adenohypophysis is the pars intermedia, which is responsible for synthesis of α-MSH and endorphins. The pars tuberalis contains some stainable cell types and secretes tuberalin that stimulates PRL release.

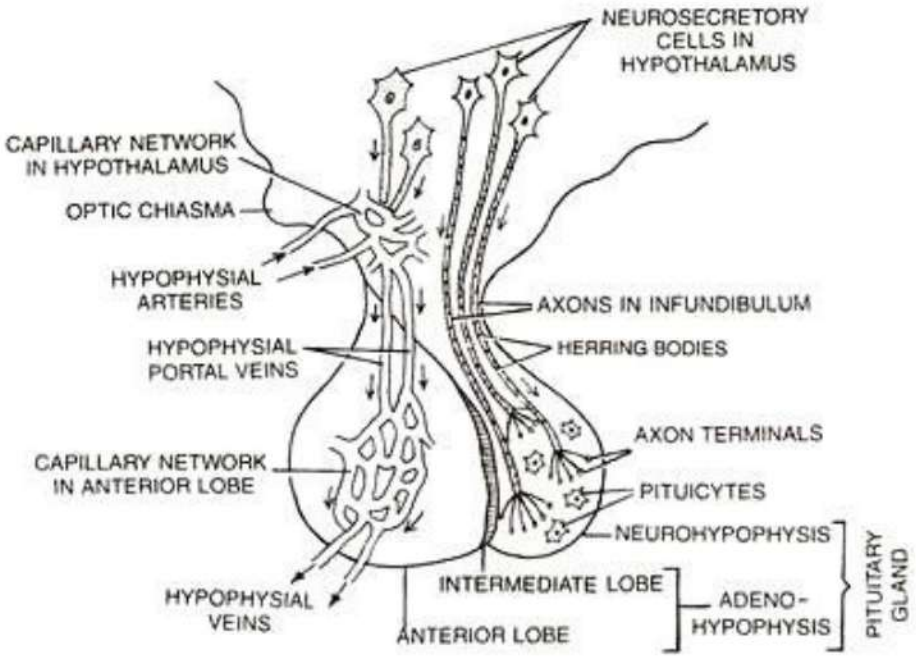

Figure 4: Neurosecretory cells of hypothalamus discharging neurohormones into hypophyseal portal vein and into neurohypophysis of pituitary gland

Hypophyseal portal system allows endocrine communication between the hypothalamus and the anterior pituitary gland. The anterior pituitary receives releasing and inhibitory hormones in the blood. Using these the anterior pituitary is able to fulfill its function of regulating the other endocrine glands.

The anterior pituitary (adenohypophysis) is derived from embryonic ectoderm. The anterior pituitary (adenohypophysis) secretes five endocrine hormones from five different types of epithelial endocrine cells. The release of anterior pituitary hormones is regulated by hypothalamic hormones (releasing or inhibitory), which are synthesized in the cell bodies of neurons located in several nuclei that surround the third ventricle. These include the arcuate, the para ventricular and ventromedial nuclei and the medial preoptic and para ventricular regions.

In response to neural activity, the hypothalamic hormones are released from the nerve endings into the hypophyseal portal blood and are then carried down to the anterior pituitary. Hypothalamic hormones that releases or inhibit anterior pituitary hormones reach the anterior pituitary through a hypothalamic hypophyseal portal system. Usually, blood passes from the heart through an artery to a capillary to a vein and back to the heart.

In a portal system, blood flows from one capillary network into a portal vein and then into a second capillary network before returning to the heart. The name of the portal system indicates the location of the second capillary network. In the hypophyseal portal system, blood flows from capillaries in the hypothalamus into portal veins that carry blood to capillaries of the anterior pituitary. In other words, the hormones carried by the hypothalamo-hypophyseal portal system allow communication between the hypothalamus and anterior pituitary and establish an important link between the nervous system and the endocrine system. The superior hypophyseal arteries, branches from the medial aspect of the internal carotid artery just after

leaving the cavernous sinus, bring blood into the hypothalamus. The superior hypophyseal arteries emerge 5-mm distal to the origin of the ophthalmic artery and then will go on to form the primary capillary network found in the median eminence. At the junction of the median eminence of the hypothalamus and the infundibulum, these arteries divide into a capillary network called the primary plexus of the hypophyseal portal system. This capillary plexus supplies blood to the pars distalis.

From the primary plexus, blood drains into the anterior and posterior hypophyseal portal veins that pass down the outside of the infundibulum. It is via this system that peptides that are released at the median eminence enter the primary plexus. From that point, the peptides would be transmitted to the adenohypophysis via the hypophyseal portal veins to the secondary plexus. The portal system has fenestrated capillaries which would allow for exchange between the hypothalamus and the pituitary. The cells of the adenohypophysis express G-protein coupled receptors that bind to the peptides allowing the release of hormones from the anterior pituitary. In the anterior pituitary, the hypophyseal portal veins divide again and form another capillary network called the secondary plexus of the hypophyseal portal system. Hypophyseal veins drain blood from the anterior pituitary. The primary and secondary capillary plexuses in the pituitary gland, plus the intervening hypophyseal portal veins, constitute the hypophyseal portal system. Short veins from the pituitary gland drain into the neighbouring dural venous sinuses. As stated previously, the release of hormones from the anterior pituitary gland is generally controlled by hormones from the hypothalamus. The hypothalamus exerts its control by secreting peptide hormones called releasing hormones (releasing factors), which then prompt the cells in the anterior lobe to release their hormones. Similarly, inhibiting hormones, which turns off the secretion of hormones by the anterior lobe when necessary.

Releasing hormones made in hypothalamic neurons are secreted like neurotransmitters from the axon terminals of these neurons. In this case, neurons are serving as endocrine cells. The secreted releasing hormones enter a primary capillary plexus in the median eminence of the hypothalamus and then travel inferiorly in hypophyseal portal veins to a secondary capillary plexus in the anterior lobe. The releasing hormones leave the bloodstream and attach to the anterior lobe cells and stimulate these cells to secrete hormones (GH, LH, TSH, PRL, and ACTH). The hormones secreted from the anterior lobe cells enter the secondary plexus. From there the newly secreted anterior lobe hormones proceed into the general circulation and travel to their target organs throughout the body.

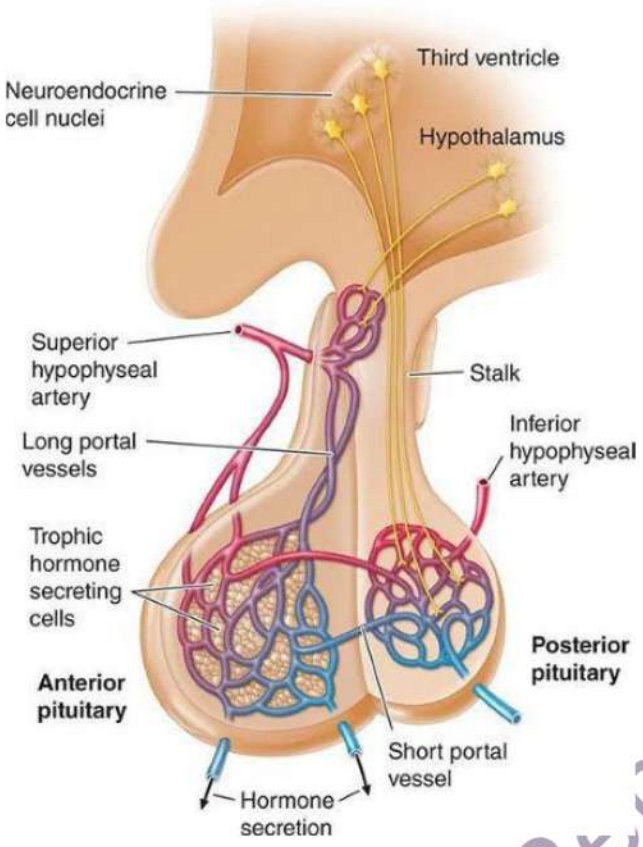

Figure 5: Hypophyseal portal system

Hypophyseal portal circulation:

The hypophyseal portal circulation receives signals from the hypothalamus by releasing/inhibiting hormones. Then, it carries the stimulating/inhibitory message to the anterior pituitary system, which releases the hormone for the target organ. The hypothalamic nuclei produce multiple releasing or inhibiting hormones which stimulate or inhibit the secretion of the responsible hormones from the adenohypophysis through a **feedback mechanism**.

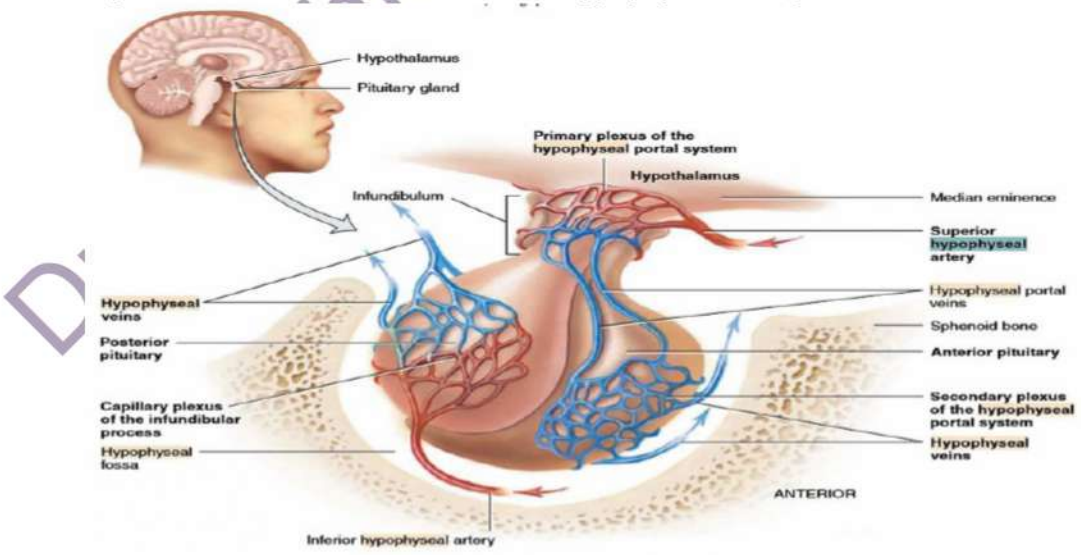

Figure 6: Relationship of hypothalamus to pituitary gland

Clinical significance of the hypothalamic nuclei and hypophyseal portal system :

- The hypothalamus moderates food intake using the satiety centre as a mechanism to counter obesity.
- It induces an acute-phase immune response to destroy pathogens incubating in the body (fever).
- It controls dopamine-prolactin balance in lactating women.
- It induces natural growth, development and maturity through the proper functioning of the hypothalamic nuclei.
- It balances blood sugar levels and ADH secretion to prevent diabetes development.

The role of hypothalamic nuclei in the body:

The hypothalamus coordinates all neural signals using autonomic, somatic and endocrine mechanisms makes it a seamless control centre. The hypothalamic nuclei functions as a moderator in the human body. This includes:

- Internal homeostasis (maintaining body temperature)
- Balancing blood pressure ϖ Managing hunger and thirst (satiety)
- Emotional mood and psychological well-being
- Inducing or suppressing the sex drive
- Monitoring the sleep cycle
- Breathing rate
- Heartbeat
- Regulation of the endocrine system (periventricular zone nuclei)
- Regulates autonomic functions (medial nuclei)
- Regulates somatic functions (lateral nuclei)

It maintains connectivity with the following organelles:

- Amygdala (via the stria terminalis)
- The brain stem (via the dorsal longitudinal fasciculus)
- The cerebral cortex (via the median forebrain bundle)
- Hippocampus (via the formix)
- Pituitary gland (via the median eminence).
- Retina (via the retinohypothalamic tract)
- Thalamus (via the mammillothalamic tract)