The diencephalon of the brain consists of four components. These are the thalamus, the epithalamus, the hypothalamus and the subthalamus. Overall, the diencephalon co-ordinates unconscious vegetative and sensomotoric functions.

Embryological Development of the Diencephalon

Throughout the embryological development, the brain, the medulla and the central nervous system arise from the neural tube, which itself stemmed from the dorsal surface ectoderm. Three primary brain vesicles develop from the cranial segment of the neural tube.
One of these brain vesicles grows into the **prosencephalon** (forebrain). The other two brain vesicles form the **rhombencephalon** (hindbrain) and the **mesencephalon** (midbrain). The diencephalon and telencephalon proceed to grow from the prosencephalon.

**Structure of the Diencephalon (Interbrain)**

The **thalamus**, **the epithalamus**, **the hypothalamus** and the **subthalamus** develop from the diencephalon, which grew from the prosencephalon.

**Structure of the thalamus**

The halved structure of the thalamus makes up the majority of the diencephalon and has been dubbed the “gate to the conscience”, as a **large amount of sensitive information passes** through it before it is further processed in the **cortex** to make it to the conscience.
Topography of the thalamus

The thalamus is not visible as such from the outside, as it is surrounded by the telencephalon. The corpus callosum of the telencephalon, as well as the two lateral ventricles, borders the thalamus on the cranial side. The hypo- and subthalamus are located on the caudal side of the thalamus.

![Image: “Thalamus image” by Life Science Databases. License: CC BY-SA 2.1 JP]

The separation of the thalamus and hypothalamus is called the sulcus hypothalamicus.

Medially, the thalamus is bordered by the outer wall of the 3rd ventricle. This is also the location of the adhesio interthalamica, which connects the two thalami together. However, they do not share any function, i.e. there are no commissural fibres between the two thalami.

Laterally, the v. thalamostriata forms the border between the di- and telencephalon, whereby the capsula interna of the telencephalon is located here.

Function of the thalamus

The switch of sensory and motoric information occurs in the thalamus before it passes into the telencephalon, and thus into the conscience (radiatio thalami). On the way there, this information is filtered in the thalamus to prevent too much information from passing into the telencephalon. This is why the thalamus is called the “gate to the conscience”.

If the thalamus is harmed, e.g. during a stroke, there may be disruptions in sensory perception. The sense of smell is an exception to the sensory system, as the information from the olfactory tract is not carried over into the thalamus.

Nuclei of the thalamus and their projections

With regard to its nuclei and their connections, the thalamus can be divided into a specific and a non-specific area. The specific area (= palliothalamus) is connected to certain areas of the cerebral cortex, whereas the non-specific area (= truncothalamus) primarily communicates with the brain stem. The thalamus consists of a total of 120...
There are four different core groups in the area of the palliothalamus named for their topographic location and which each project into different areas of the brain.

The anterior group (nuclei anteriores) chiefly transmits information into the limbic system, the medial group (nuclei mediales) projects to the frontal lobe, and the dorsal group (nuclei dorsales) to the visual cortex.

The ventral group (nuclei ventrolaterales) does not project solely into one area, but rather can be divided into different nuclei; each connected to specific regions of the brain. Among the nuclei of the ventral group are the nucleus ventralis anterior (NVA), the nucleus ventralis lateralis (NVL) and the nucleus ventralis posterior (NVP). The projection to the NVA serves the premotor cortex, the NVL the motor cortex and the NVP which is the sensitive area of the cortex.

Located in the most lateral location are the nucleus reticularis thalami, which is externally complexed with the other nuclei. Its impulses can be deviated in the EFG.

The corpus geniculatum laterale and mediale also number among the thalamus nuclei of the palliothalamus, whereby the corpus geniculatum laterale (CGL) is projected to the visual cortex, and the corpus geniculatum mediale (CGM) to the auditory pathway. Together, both are called the metathalamus.

Located above the CGL and the CGM is the pulvinar thalami, which is also allocated to the specific thalamus nucleus (lateral group). The pulvinar thalami receive afferents via the CGL and the colliculi superiores. Its efferents primarily move into the cortex area of the temporal, occipital and parietal lobes. A portion of the efferents also moves into the
frontal lobe – yet solely to the frontal eye field.

Together, the fibers that move from the specific thalamus nucleus to the cerebral cortex are called radiatio thalami, and these can be further divided by projection area.

The radiatio thalami anterior moves through the nuclei mediales to the frontal lobe, the radiatio thalamica posterior to the occipital lobe, the radiatio thalami centralis through the nuclei ventrales to the parietal lobe, and the radiatio thalami inferior to the temporal lobe, meaning that all areas of the brain are reached.

A portion of the radiatio thalami inferior is the radiatio acustica, whereas the radiatio optica is part of the radiatio thalami posterior.

Thalamus nuclei of the truncothalamus

The non-specific thalamus nuclei are connected to the basal ganglia, the formatio reticularis (primarily the ARAS) and the cerebellum via afferents from these areas. The efferents from the truncothalamus lead to the specific thalamus nuclei – whereby these stimulate the respective nuclei – to other nuclei of the diencephalon, to the brain stem and to the corpus striatum.

Contrary to the specific nuclei, these do not have any direct connection to the cerebral cortex and thus only have a non-specific influence on the cortex. Among the non-specific nuclei are, among others, the nuclei mediani and the nuclei intralaminares. The nucleus centromedianus is the largest nucleus of the intralaminar group.

Clinical symptoms upon damage to the thalamus nuclei

Damage to the specific thalamus nuclei results in paresis on the contralateral side (hemiparesis) and disruptions in the area of sensitivity. Sensitivity disruptions may lead to burning; stinging neuropathic pains which arise with no recognisable pain stimulus, and which are called “thalamus pain”.

Damage to the non-specific thalamus nuclei, however, may result in reduced alertness and apathy.

Structure of the epithalamus

The epithalamus is, as the name suggests (epi = top), located above the thalamus. It includes the epiphysis, the stria medullaris thalami, and the habenuelae with their nuclei habenuelares, the area praetectalis and the commissura posterior (epithalamica).

The epiphysis (glandula pinealis) is responsible for the production of melatonin, which is primarily distributed at night and has a soothing effect on the function of the central nervous system. The information concerning the brightness and darkness of the individual’s surroundings, and thus the circadian rhythm, is received by the epiphysis via the nucleus suprachiasmaticus of the hypothalamus.

The olfactory system is connected to the epithalamus through the stria medullaris. This fibre pathway begins in the area of the substantia perforata anterior and ends dorsal of the thalamus in the form of the habenulae, which forms a thickening in the fibre pathway.

The nuclei habenuelares are located in the area of the habenuelae. These are the changeover area for the information of the olfactory system. From here, the information
is forwarded to the **motoric and salivatory nuclei**, where the secretion of saliva is triggered by the scent of food, for instance. The two habenulae are connected through the **commissura habenularum**.

The **area praetectalis** is located on the border of the mesencephalon and diencephalon, and is involved in the formation of the **pupillary light reflex**. To this end, it receives information (afferents) via the tractus opticus and the colliculi superiores. From the area praetectalis, its efferents are transmitted to the **nucleus accessorius nervi oculomotorii** (Edinger-Westphal nucleus) on the ipsilateral and contralateral side. **Consensual light reaction** – i.e. upon illumination of an eye, the ipsilateral and contralateral pupils narrow – occurs through the **Edinger-Westphal nucleus**. Areas of the formatio reticularis, the quadrigeminal bodies and the area praetectalis on both sides are connected through the **commissura posterior**.

**Structure of the subthalamus**

The subthalamus consists of the **nucleus subthalamicus** and the **globus pallidus**. Both are components of the **basal ganglia loop**, which is responsible for the coordination of specific, voluntary and fine-motor processes.

**Structure of the hypothalamus**

The hypothalamus comprises the **corpora mammillaria**, the **tuber cinerum**, the **infundibulum**, the **neurohypophysis** and the **eminencia mediana**.

**Function of the hypothalamus**

An integration of **vegetative functions** occurs through the hypothalamus, so that the majority of the nuclei of the hypothalamus are connected with vegetative centres in the area of the brain stem and the medulla. One example of a vegetative function transmitted through the hypothalamus is the feeling of thirst.

**Nuclei of the hypothalamus**

The nuclei of the hypothalamus are the **anterior, intermediate and posterior core group**.

The **anterior core group** includes the nuclei preoptici, the nucleus suprachiasmaticus, the nucleus supraopticus and the nucleus paraventricularis.

The **nuclei preoptici** regulate body temperature and sexual behaviour. Topographically, they are located beneath the **chiasma opticum**.

The **nucleus suprachiasmaticus** regulates circadian rhythm. Processes subordinate to this regulation include body temperature, the sleep-wake cycle and the distribution of hormones. The nucleus suprachiasmaticus draws afferents from the retina of the eye and projects into the epiphysis through its efferents.

Located above the tractus opticus is the **nucleus supraopticus**, which produces the antidiuretic hormone (**ADH**) – also called **vasopressin**, as it causes arterial vasoconstriction. The name “antidiuretic hormone” stems from the fact that ADH promotes the re-absorption of water in the collecting ducts of the kidney.

The production of **oxytocin**, which triggers both uterus contractions during birth and
lacrimation of the mammary glands, occurs within the **nucleus paraventricularis**. Before being released, oxytocin passes through the **tractus hypothalamohypophysialis to the neurohypophysis**, where it is passed into, and stored, by the blood. The same process also applies to ADH, which is likewise stored in the area of the neurohypophysis and secreted as necessary.

The **intermediate core group** includes the **nuclei tuberales** and the nucleus arcuatus. The nuclei tuberales are located within the **tuber cinerum** and release the releasing hormone (**liberine**) and release-inhibiting hormone (**statine**), which regulate the hormone secretion of the adenohypophysis.

The aforementioned steering hormones are also released by the **nucleus arcuatus**, which is located in the area of the **eminentia mediana**.

The nuclei of the posterior **core group** are made up by the **nuclei mamillares**, which are part of the limbic system.

**Afferents of the hypothalamus**

The hypothalamus also includes afferents from the **hippocampus, the olfactory system, the amygdala, visceral areas and erogenous zones**, such as the nipples.

The hippocampus is connected to the hypothalamus via the fornix, and to the olfactory system via the **medial forebrain bundle**. Starting from the amygdala, the hypothalamus is connected with this via the **striae terminales**, and there also exists a connection to the visceral and erogenous zones via the **pedunculus corporis mammillaris**.

**Efferents of the hypothalamus**

The efferents of the hypothalamus move through the **tractus mammillotegementalis** to the tegmentum of the mesencephalon, and from there they continue to the formatio reticularis. An additional efferent from the hypothalamus is moved through the **fasciculus longitudinalis dorsalis** to the parasympathetic nuclei of the brain stem.

As part of the limbic system, the fibres of the **fasciculus mammillothalamicus (bundle of Vicq d’Azyr)** begin in the hypothalamus and reach the nucleus anterior thalami.

Furthermore, efferents to the hypophysis (see below) exist via the **tractus supraoptichypophysialis** and the **tractus tuberohypophysialis**. Together, the two are referred to as the **tractus hypothalamohypophysialis**.

**Structure of the hypophysis**

The hypophysis is divided into an **anterior and posterior lobe**, both of which have different origins. The anterior lobe (**adenohypophysis**) stems from the epithelium of **Rathke’s pouch** (roof of the throat), whereas the posterior lobe (**neurohypophysis**) forms an eversion of the diencephalon and is allocated to the hypothalamus.

The two sections also differ in function. The adenohypophysis is a production site for various hormones (see below), whereas the area of the neurohypophysis merely stores and secretes the hormones produced in the hypothalamus (ADH and oxytocin).

The **pars tuberalis** and the **pars intermedia** are located between the neurohypophysis and the adenohypophysis. The two parts of the hypophysis are connected to the hypothalamus via the **infundibulum**.
In terms of a topographical location, the hypophysis is located within the **sella turcica** and above the **sinus sphenoidalis** (sphenoidal sinus). The sinus sphenoidalis also serves as an operative pathway to tumours in the area of the epiphysis.

**Histological structure of the hypophysis**

The different developmental origins of the two sections of the hypophysis can also be determined by the histological structure.

The adenohypophysis consists of epithelial cells, which can be divided into three groups. These are the acidophilic, basophilic and chromophobic cells. The acidophilic and basophilic cells number among the hormone-forming cells, whereas the chromophobic cells are not dyeable and are presumably inactive cells.

Prolactic (PRL) and somatotropin (STH) are the hormones of the acidophilic cells. Lutropin (LH), follitropin (FSH), thyrotropin (TSH), melanotropin (MSH) and the adrenocorticotropic hormone (ACTH) are formed by the basophilic cells.

In contrast, the neurohypophysis consists of nerve tissue. This is where the axons from the hormone-producing nuclei of the hypothalamus (nucleus supraopticus, nucleus paraventricularis) end.

**Hormones of the adenohypophysis and their effects**

The aforementioned hormones of the acidophilic and basophilic cells are the hormones of the adenohypophysis.

**Somatotropin**, which is also referred to as a growth hormone, promotes length growth. Increased STH production results in symptoms of **acromegaly**. These symptoms differ in their clinical presentation depending on whether the physes have already sealed or not.

If the physes have not yet sealed, the result is excessive growth. Already sealed physes result in, among other things, enlargement of organs and body parts, such as the hands or tongue (**macroglossia**).

Along with the promotion of growth, **STH** also affects carbohydrate and lipid metabolism.

The mammary gland is stimulated to secrete milk (**lacrimation**) by the hormone prolactin. Higher values of a prolactinoma can lead to secondary **amenorrhoea** in women. Increased prolactin values may cause a loss of lipids in both women and men. Physiologically increased values are exhibited during pregnancy and the nursing period.

The function of the **FSH** is the stimulation of spermatogenesis, follicular maturation and the formation of oestrogen.

Thyrotropin, or thyroid-stimulating hormone (**TSH**), has a stimulating effect on the thyroid’s production of thyroid hormones (T3 and T4). The hypofunctions and hyperfunctions, among others, of the thyroid (hypo- and hyperthyreosis) can thus be determined with the TSH value.

**ACTH** affects the adrenal cortex and also leads to increased production of the hormones
formed there, i.e. the mineralocorticoid **aldosterone**, the glucocorticoid **cortisol**, and **androgens**. An increased ACTH value due to an adenoma of the adenohypophysis is referred to as **Cushing’s disease**.

The **MSH** formed in the adenohypophysis promotes the formation of melanin in the skin, thereby leading to increased pigmentation and thus **protection against UV radiation**.

**Hormones of the neurohypophysis and their effects**

The hormones of the neurohypophysis are the hormones vasopressin (**ADH**) and **oxytocin** (see above), formed in the hypothalamus. These are transported to the neurohypophysis via **axonal transport**, stored there and released into the blood circulation as needed.

The two hormones are stored in vesicles, which are also referred to as **Herring bodies**. The effects of the two hormones can be found in the section “Nuclei of the hypothalamus” (see above).

**Note:** The hormones of the adeno- and neurohypophysis are popular exam topics. You should thus memorise them well.

**Hormonal regulatory circuit of the hypophysis**

The hormonal regulatory circuit of the hypophysis / the hypothalamus-hypophysis system can be divided into different levels. Located on the first level is the **hypothalamus**, which affects the **release of the hormones** of the adenohypophysis with its steering hormone-producing nuclei (intermediate core group, see above), and thus has an indirect effect on the endocrine system.
One example of a steering hormone would be TRH (thyrotropin-releasing hormone), which belongs to the liberine group (see above) and stimulates the release of TSH.

The hypothalamus has a direct influence on specific organ areas, e.g. the water reabsorption in the kidney by means of ADH, due to its effector hormone-producing nuclei (ncl. paraventricularis and ncl. supraopticus).

The peripheral endocrine system, which is affected by the hormones of the adenohypophysis, is formed by the respective effector organs. These include the kidneys, the adrenal glands, the thyroid, the parathyroid, the ovaries, the testicles and the pancreas.

**Portal venous system of the hypophysis**

Similar to the liver, the adenohypophysis also possesses a second venous circulation referred to as "portal circulation" of the adenohypophysis. Through this portal circulation, the steering hormones of the hypothalamus reach the adenohypophysis in order to either stimulate (liberine) or inhibit (statin) the distribution of hormones.

The two arteriae hypophysiales superiores, within the infundibulum, form a net of capillaries, where the axons of the hypothalamic nuclei end. This area of the infundibulum is called the eminentia mediana. Starting from the capillaries of the eminentia mediana, the blood enters the venous portal vessels of the adenohypophysis.
Review Questions

The solutions are below the references.

1. Which of these statements about the hypophysis is not true?

   A. It consists of an anterior and posterior lobe.
   B. The anterior lobe (adenohypophysis) consists of hormone-producing epithelial cells.
   C. The posterior lobe (neurohypophysis) consists of nerve tissue.
   D. The chiasma opticum is located above the anterior lobe of the hypophysis.
   E. The hormones of the anterior lobe of the hypophysis are released in the eminentia mediana.

2. Which of these statements about the hormones of the adenohypophysis is not true?

   A. Prolactin is formed by the acidophilic cells.
   B. Somatotropin promotes length growth.
   C. Cushing’s disease refers to increased ACTH values due to adenoma of the adenohypophysis.
   D. ACTH affects the adrenal cortex.
   E. TSH has an inhibiting effect on the production of thyroid hormones.

3. Which of these statements on the hormones of the neurohypophysis is true?

   A. Oxytocin and ADH are formed by the neurohypophysis.
   B. The transportation of hormones to the neurohypophysis starts in the epithalamus.
   C. The hormones are stored in vesicles within the neurohypophysis.
   D. Oxytocin inhibits labour pains during birth.
   E. More urine is excreted through the kidneys upon higher ADH values.

References


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Correct Answers: 1E, 2E, 3C

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Notes