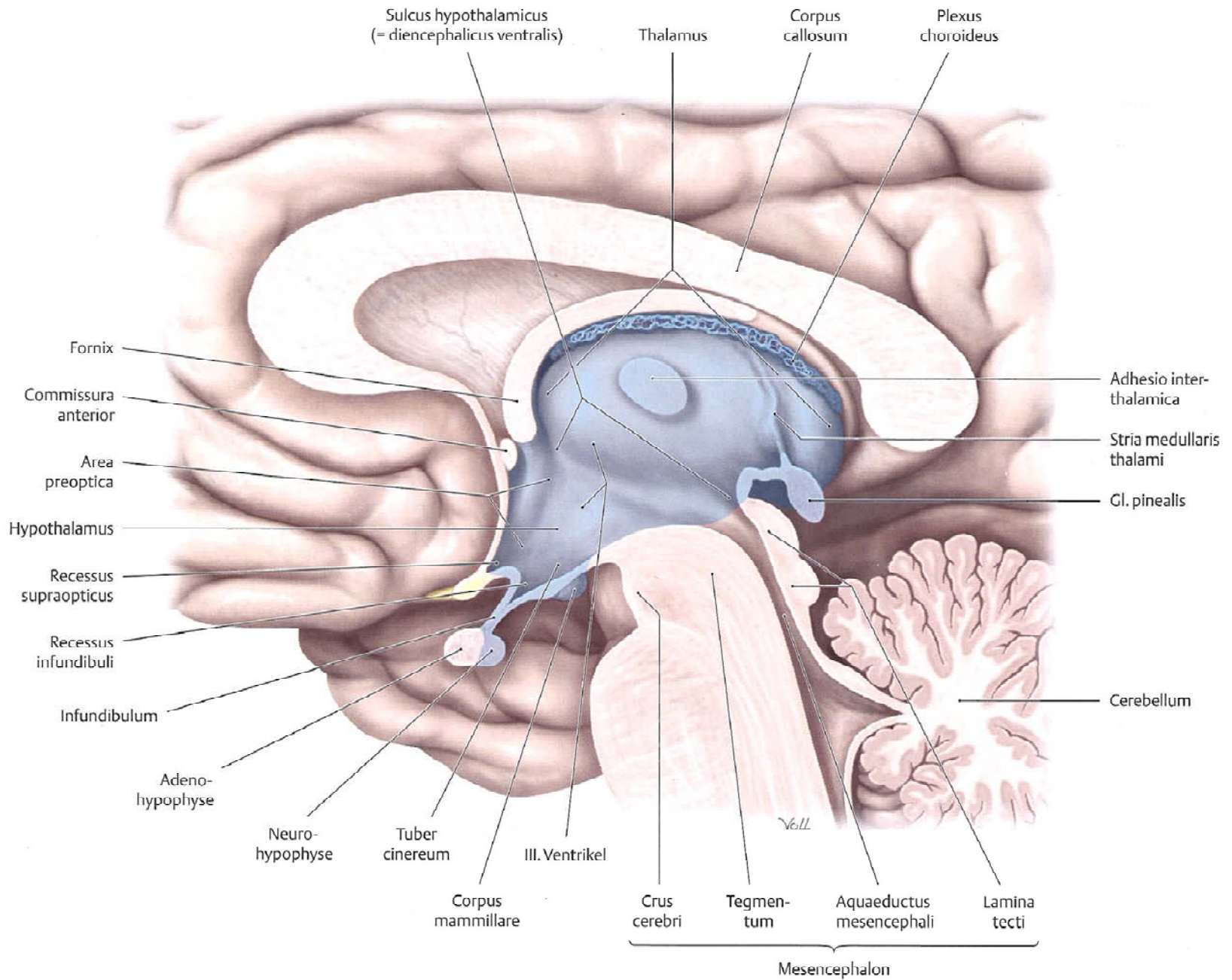


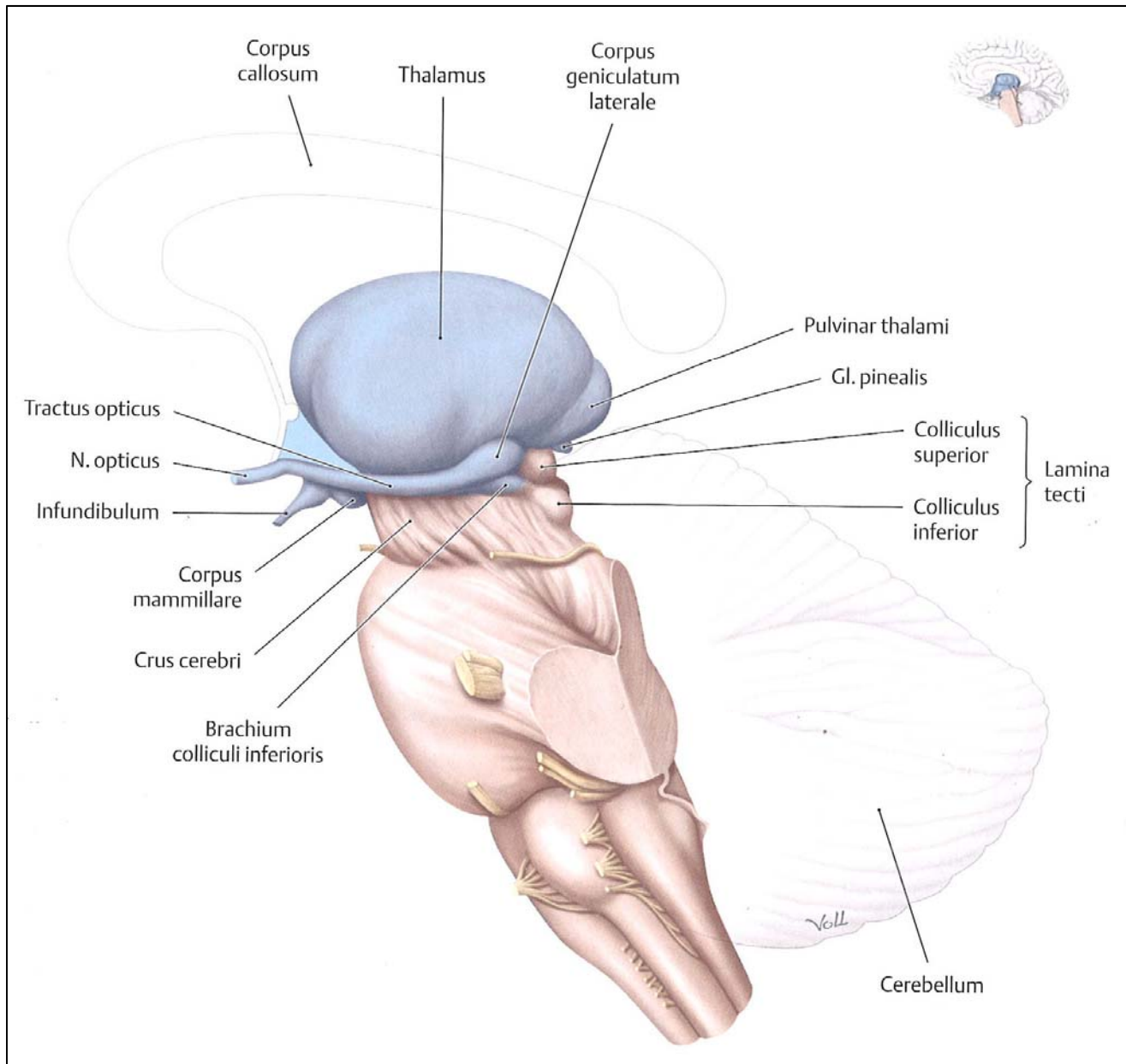
# ORGANIZATION OF THE CNS

## - DIENCEPHALON -

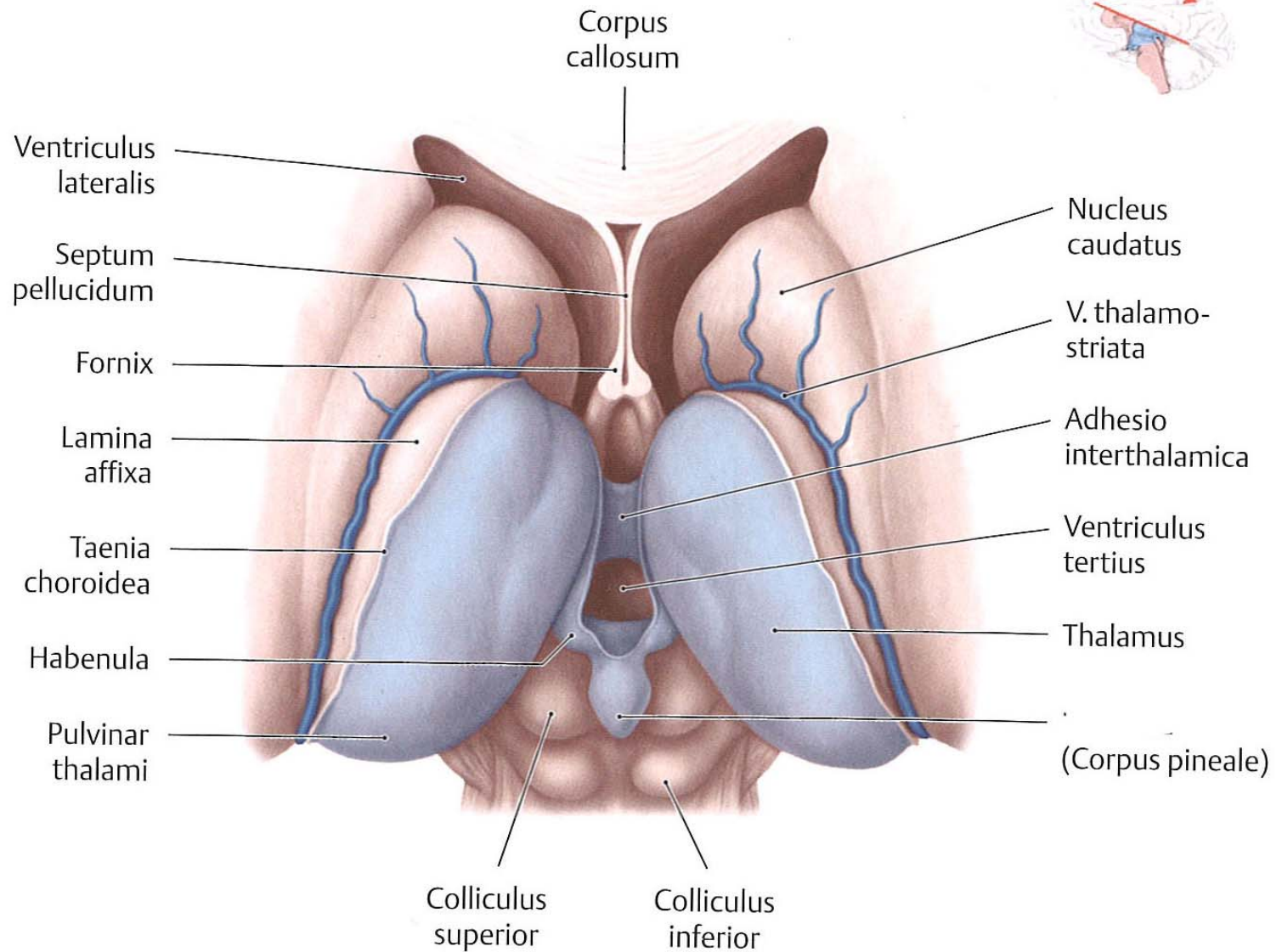
Prof. Maja Valić, M.D., Ph.D.





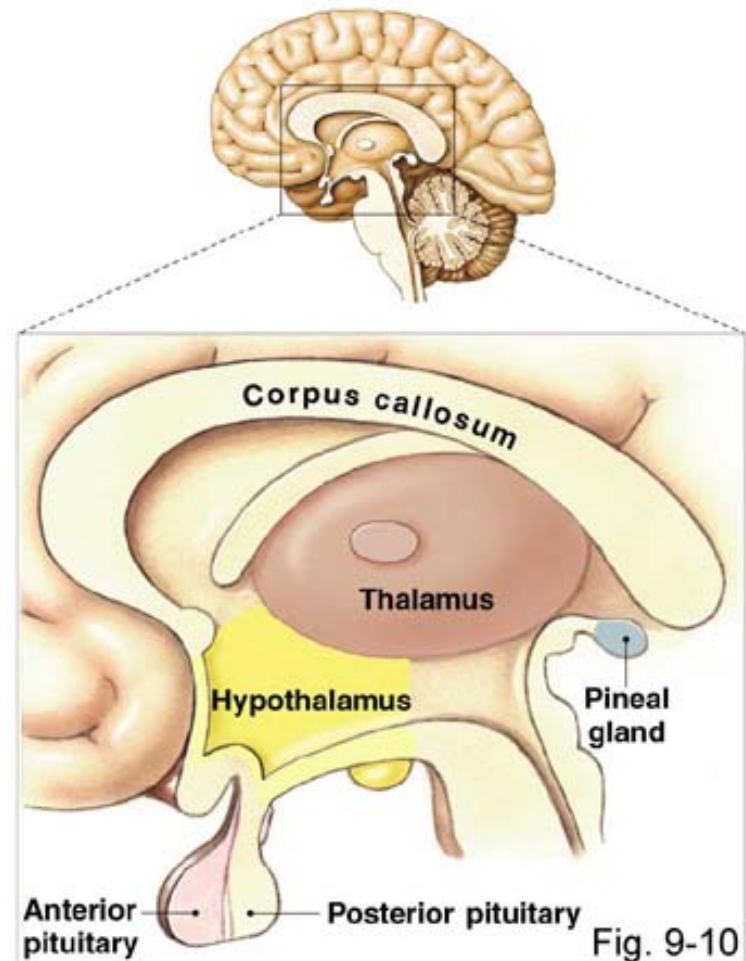






# Diencephalon

- Hypothalamus
- Epithalamus
- Thalamus
- Metathalamus
- Subthalamus



# Hypothalamus

- Is central regulator of **homeostasis**
- Nicknamed “**homeostatic head ganglion**”
- It participates in:
- **H**omeostatic control of hunger, sexuality, thirst, sleep-wake cycle etc
- **E**ndocrine control via pituitary gland
- **A**utonomic control
- **L**imbic mechanisms

# Hypothalamus

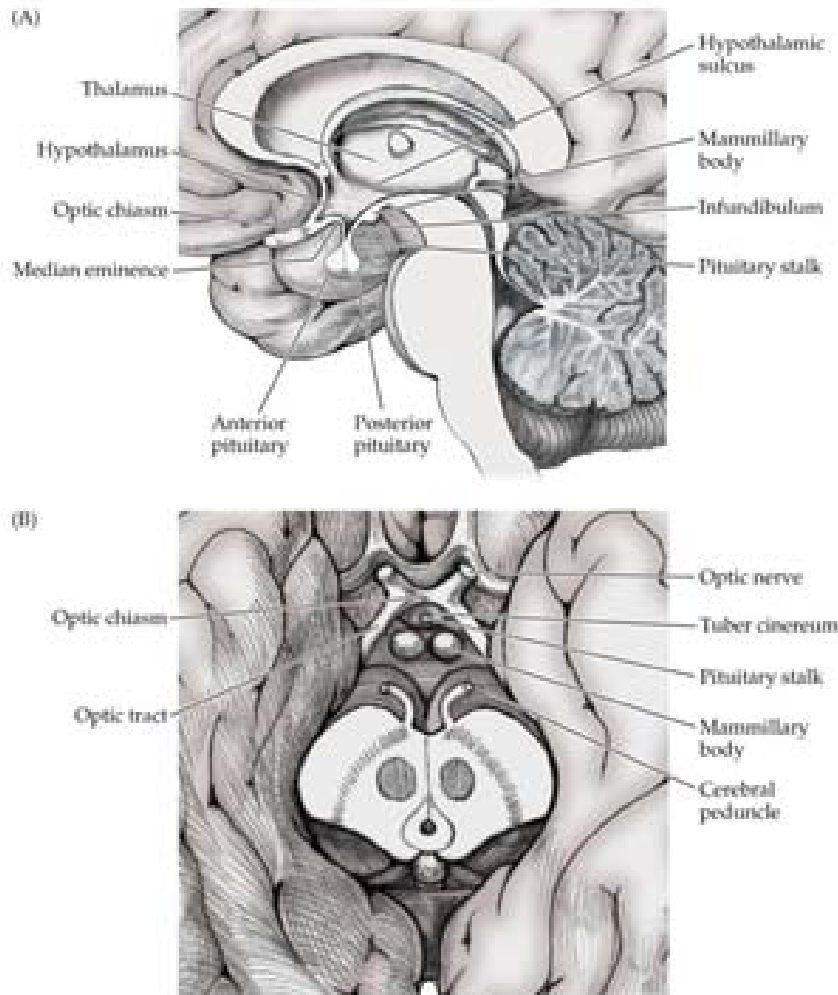
- is part of the diencephalon, and it is named for its location underneath the thalamus
- forms the walls and floor of the inferior portion of the third ventricle
- is separated from the thalamus by a shallow groove on the wall of the third ventricle called the **hypothalamic sulcus**



# Hypothalamus

- At the ventral surface of the brain the hypothalamus can be seen just posterior to the optic chiasm, (tuber cinereum and mammillary bodies) although portions of the hypothalamus are located dorsal to the optic chiasm as well

# Hypothalamus



The **tuber cinereum**, meaning “gray protuberance,” is a bulge located between the optic chiasm and the mammillary bodies.

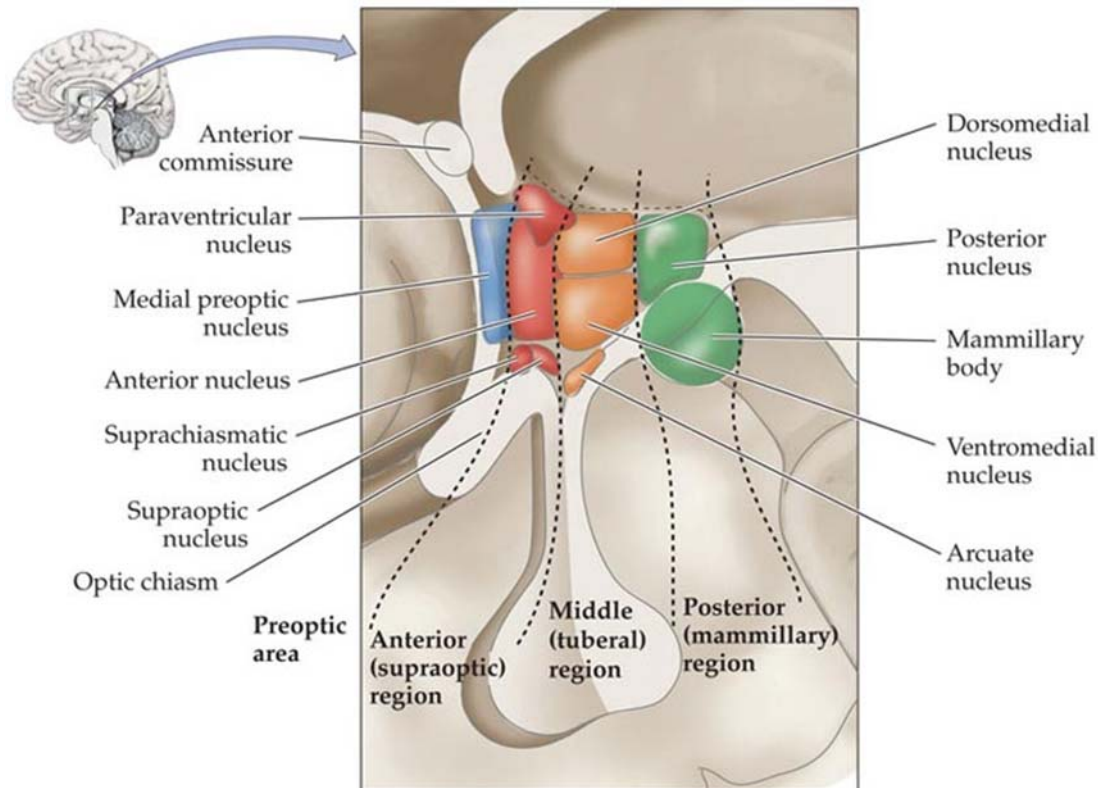
The **mammillary bodies** are paired structures that form the posterior portion of the hypothalamus.

The **infundibulum**, meaning “funnel,” arises from the tuber cinereum and continues inferiorly as the **pituitary stalk**.

The anterior portion of the infundibulum is slightly elevated and is called the **median eminence**. The **median eminence** is the region where hypothalamic neurons release regulating factors that are carried by portal vessels to the anterior pituitary.

# Major Hypothalamic Nuclei

- The hypothalamic nuclei can be divided into **four major regions** from anterior to posterior and into **three areas** from medial to lateral



## **TABLE 17.1 Some Important Hypothalamic Nuclei**

### **PERIVENTRICULAR AREA**

Periventricular nucleus

### **MEDIAL HYPOTHALAMIC AREA**

Preoptic area

Medial preoptic nucleus

Anterior (supraoptic) region

Anterior hypothalamic nucleus

Supraoptic nucleus

Paraventricular nucleus

Suprachiasmatic nucleus

Middle (tuberal) region

Arcuate nucleus

Ventromedial nucleus

Dorsomedial nucleus

Posterior (mammillary) region

Medial mammillary nucleus

Intermediate mammillary nucleus

Lateral mammillary nucleus

Posterior hypothalamic nucleus

### **LATERAL HYPOTHALAMIC AREA**

Lateral preoptic nucleus

Lateral hypothalamic nucleus

# Periventricular area

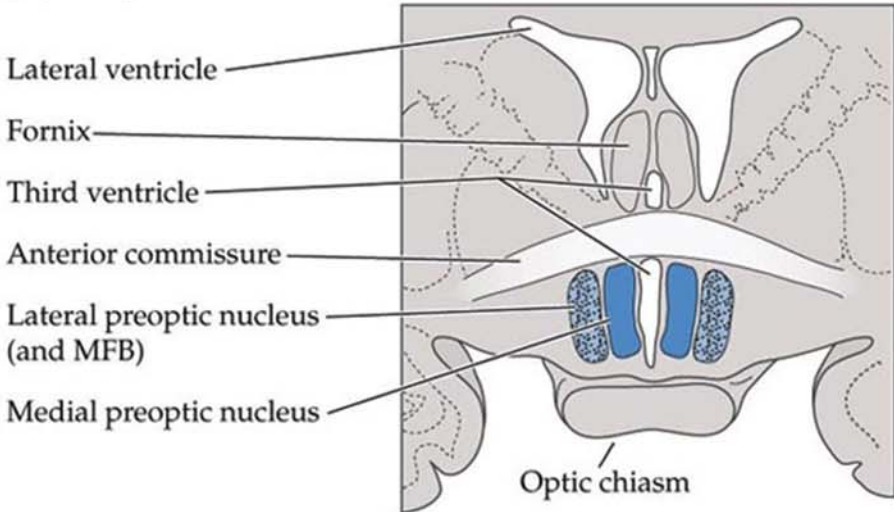
- Most medially, the **periventricular nucleus** is a thin layer of cells that lies closest to the third ventricle.
- The fibers of the fornix pass through the hypothalamus on the way to the mammillary body, dividing the major portions of the hypothalamus into a **medial hypothalamic area** and a **lateral hypothalamic area**



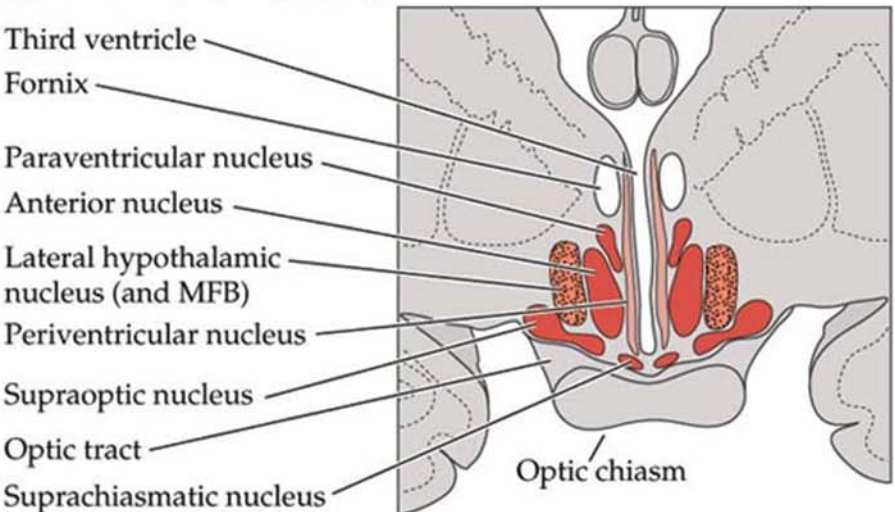
# Lateral hypothalamic area

- The lateral hypothalamic area consists of the **lateral hypothalamic nucleus** and several smaller nuclei.
- Running through the lateral hypothalamic area in the rostrocaudal direction is a diffuse group of fibers called the **medial forebrain bundle (MFB)** which carries many connections to and from the hypothalamus, and between other regions. **Note that the *medial* forebrain bundle runs through the *lateral* hypothalamus.**

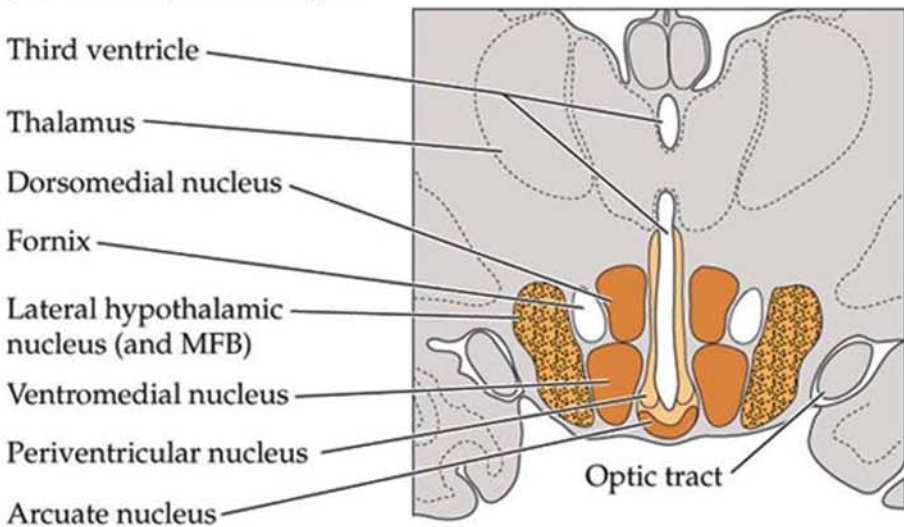
(A) Preoptic area



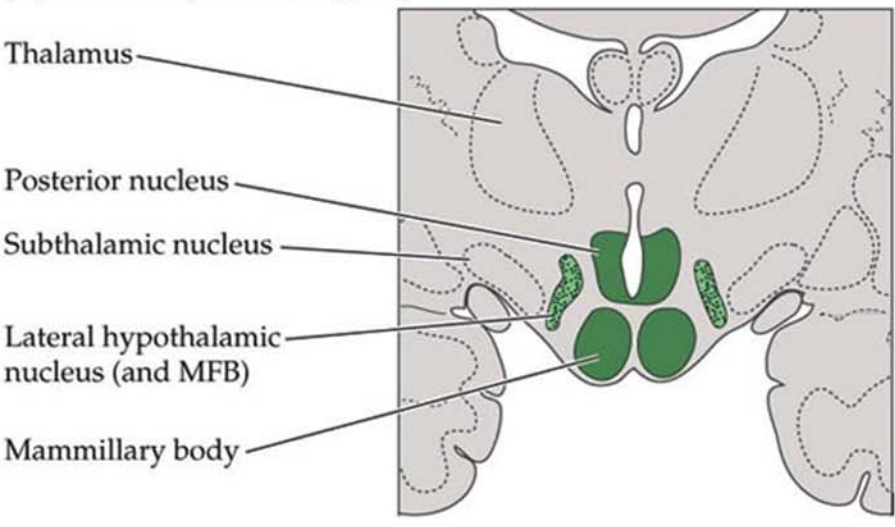
(B) Anterior (supraoptic) region



(C) Middle (tuberal) region



(D) Posterior (mammillary) region

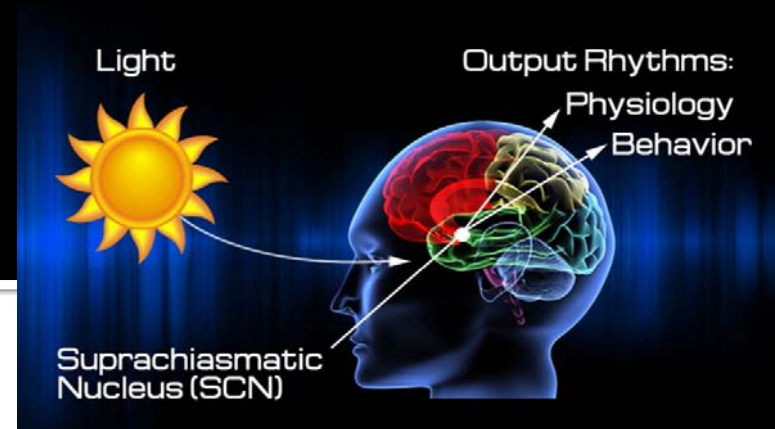


# Medial hypothalamic area

- consists of several different nuclei, which divide into four regions from anterior to posterior.
- Most anteriorly, the **preoptic area** is derived embryologically from the telencephalon, while the hypothalamus is derived from the diencephalon. Nevertheless, the preoptic area is functionally part of the hypothalamus.
- The **lateral preoptic nucleus** and **medial preoptic nucleus** are the rostral continuations of the lateral and medial hypothalamic areas, respectively.
- The remaining medial hypothalamic area can be divided into three regions from anterior to posterior

# Anterior hypothalamic area

- or **supraoptic region**, includes the **anterior hypothalamic nucleus, supraoptic nucleus, paraventricular nucleus, and suprachiasmatic nucleus**
- Some neurons located in both the supraoptic and the paraventricular nuclei contain oxytocin or vasopressin and project to the posterior pituitary



- The **suprachiasmatic nucleus** is the “master clock” for circadian rhythms. It receives inputs from specialized **retinal ganglion cells** containing the photopigment melanopsin, which convey information about day–night cycles directly to the suprachiasmatic nucleus via the **retinohypothalamic tract** arising from the optic chiasm



# Middle hypothalamic region

- or **tuberal region**, includes the **arcuate nucleus**, **ventromedial nucleus**, and **dorsomedial nucleus**.
- The arcuate nucleus is one of the hypothalamic nuclei projecting to the median eminence to control the anterior pituitary

# Posterior hypothalamic region

- or mammillary region, includes the medial mammillary nucleus, intermediate mammillary nucleus, lateral mammillary nucleus, and posterior hypothalamic nucleus

# Hypothalamic Control of the Autonomic Nervous System

- The hypothalamus has important descending projections that influence both the sympathetic and the parasympathetic divisions of the autonomic nervous system.
- Descending autonomic fibers originate mainly from the **paraventricular nucleus** but also from the **dorsomedial** hypothalamic nucleus and from the **lateral and posterior** hypothalamus.

- Ultimately they synapse onto preganglionic parasympathetic nuclei in the brainstem and intermediate zone of the sacral spinal cord, and onto preganglionic sympathetic neurons in the intermediolateral cell column of the thoracolumbar spinal cord
- autonomic pathways also descend from several brainstem nuclei, including the nucleus solitarius, noradrenergic nuclei, raphe nucleus, and pontomedullary reticular formation.
- Many of these nuclei also receive inputs from the hypothalamus.

# Hypothalamic-Limbic pathways



- Functions:
- Control of emotional influences on autonomic pathways (palms get wet, stomach churns when you are anxious)
- Control of emotional influences on immune system (depressed individuals are more susceptible to infection)



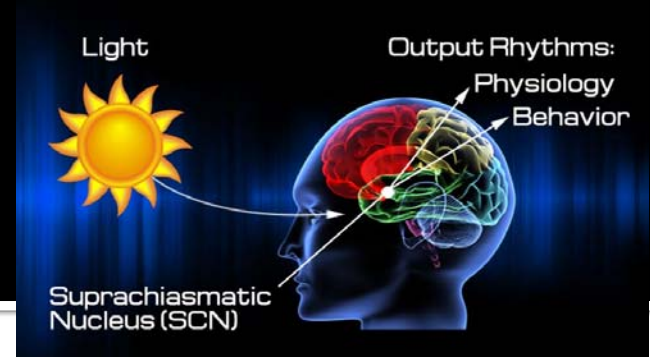
# Hypothalamic-Limbic pathways

- The **subiculum of hippocampal formation** projects to the **mammillary bodies** via the **fornix**
- Mammillary bodies project **via mammillothalamic tract** to the **anterior thalamic nucleus**, which in turn project to the **limbic cortex in the cingulate gyrus**

- **Amygdala** has reciprocal connections with the hypothalamus via **two pathways**:
- **1. stria terminalis**
- **2. ventral amigdalofugal pathway**

# Other Regionalized Functions of the Hypothalamus

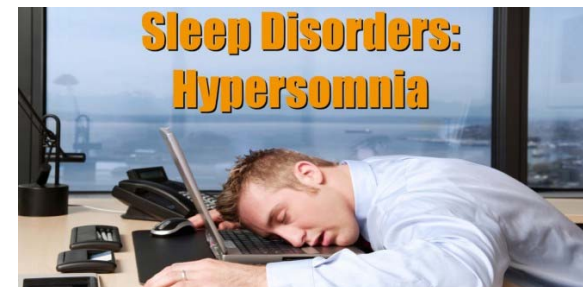
- hypothalamus is important in regulating a variety of appetitive, homeostatic, and other behaviors that are often essential to survival of the organism



- the **suprachiasmatic nucleus** in the anterior hypothalamus is an important regulator of circadian rhythms.
- **GABAergic neurons** in the ventral lateral preoptic area (**VLPO**) contribute to nonREM sleep by inhibiting the arousal systems including:
  - **histaminergic** neurons in the tuberomammillary nucleus (TMN)
  - **orexin**-containing neurons in the posterior lateral hypothalamus, as well as
  - brainstem **serotonergic**, **noradrenergic**, **dopaminergic** and **cholinergic** nuclei.



- Therefore, **lesions of the anterior hypothalamus** including the VLPO tend to cause **insomnia**.
- Conversely, **lesions of the posterior hypothalamus**, which destroy the histaminergic neurons in the TMN and orexin-containing neurons, tend to cause **hypersomnia**

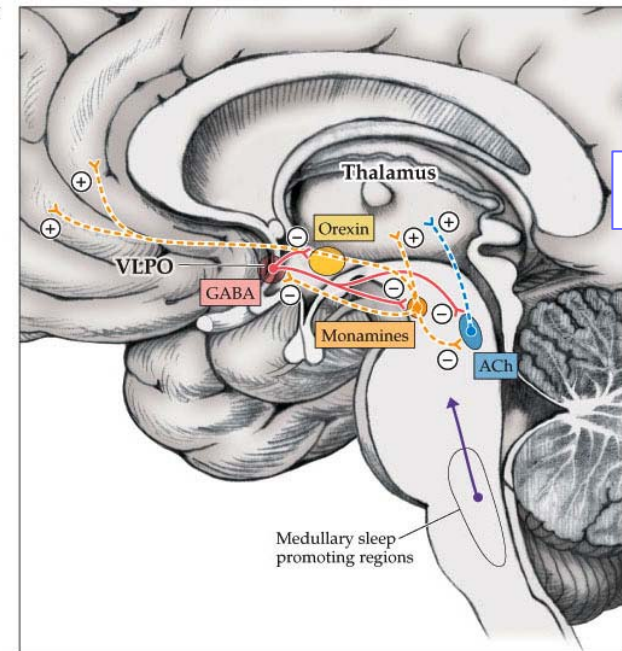




(A) During nonREM sleep, **GABAergic** (and **galanin**) neurons in the ventral lateral preoptic area of the anterior hypothalamus **inhibit** neurons in the ascending activating systems, including posterior hypothalamic **orexin** neurons, monamines such as **histamine** (in the tuberomammillary nucleus, not shown), **serotonin**, **noradrenalin**, and **dopamine**, as well as brainstem **cholinergics** (ACh). Certain regions of the medulla may also play a role in promoting nonREM sleep.

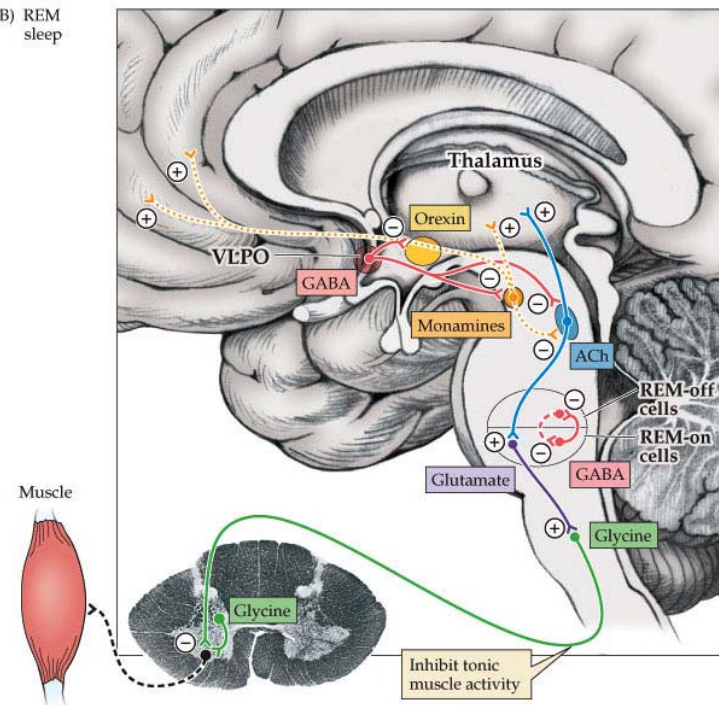
(B) During REM sleep, monoamine transmitters, particularly noradrenalin and serotonin, are further reduced. This contributes to **increased cholinergic inputs** to the thalamus and EEG appearance of arousal. Pontine circuits include mutually inhibitory REM-on and REM-off cells, as well as neurons that inhibit tonic muscle activity during REM dream states. (Spinal cord section modified from DeArmond SJ, Fusco MM, Maynard MD. 1989. Structure of the Human Brain: A Photographic Atlas. 3rd Ed. Oxford, New York.)

(A) NonREM sleep



ARAS

(B) REM sleep





- The **lateral hypothalamus** is important in **appetite**, and lateral hypothalamic **lesions** cause a **decrease in body weight**.
- Conversely, the **medial hypothalamus**, especially the ventromedial nucleus, appears to be important in **inhibiting appetite**, and medial hypothalamic lesions can cause obesity.

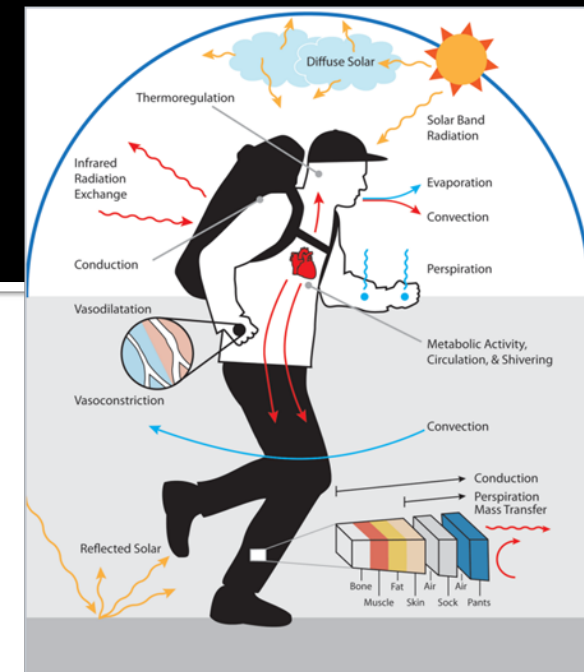


- Recently, **leptin**, a hormone that is produced by adipose tissue, was discovered. Leptin binds to **Ob receptors** in the hypothalamus and plays an important role in feedback regulation of food intake, **reducing appetite** and obesity.
- **Ghrelin**—the opposing hormone—is elaborated by gastric mucosal cells, binds in the hypothalamus, and **stimulates appetite**.

- **Thirst** appears to result from the activation of osmoreceptors in the anterior regions of the hypothalamus. Hypovolemia or elevated body temperature can also activate thirst. Lesions of the lateral hypothalamus decrease water intake.



- **Thermoregulation** involves the control of multiple systems, including sweat production; smooth muscles that affect core and surface blood flow; skeletal muscles involved in shivering, panting, and other motor activity; and endocrine systems that control the metabolic rate.



- The **anterior hypothalamus** appears to **detect increased body temperature** and activates mechanisms of **heat dissipation**. Anterior hypothalamic lesions can cause hyperthermia.
- In contrast, the **posterior hypothalamus** functions to **conserve heat**.



- Bilateral lesions of the posterior hypothalamus usually cause poikilothermia, in which the body temperature varies with the environment because these lesions destroy both heat conservation mechanisms of the posterior hypothalamus and descending pathways for heat dissipation arising from the anterior hypothalamus.

# Endocrine functions of the pituitary and hypothalamus

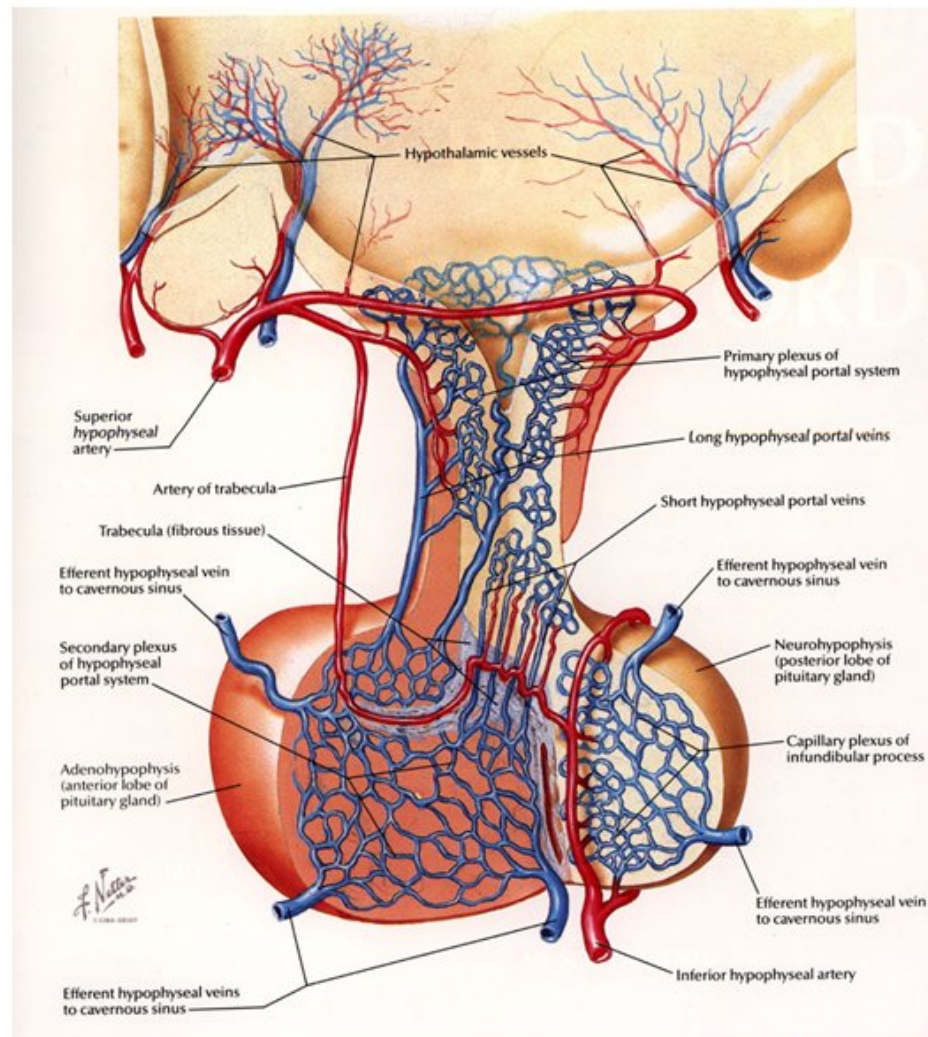
- The anterior pituitary produces six important hormones, many of which regulate endocrine systems in other parts of the body, such as the adrenal cortex, thyroid, and gonads. These anterior pituitary hormones are
  - **adrenocorticotrophormone (ACTH),**
  - **growth hormone (GH),**
  - **prolactin, thyroid-stimulating hormone (TSH),**
  - **luteinizing hormone (LH),**
  - **and follicle-stimulating hormone (FSH)**

- The intermediate lobe is rudimentary in humans, produces pro-opiomelanocortin (POMC) and melanocyte-stimulating hormone (MSH), and has little known clinical significance.
- Two hormones are released in the posterior pituitary: (1) **oxytocin** and (2) **vasopressin**, which is also called **arginine vasopressin (AVP)** or **antidiuretic hormone (ADH)**.

**TABLE 17.2 Anterior Pituitary Hormones and Hypothalamic Releasing and Inhibitory Factors**

PITUITARY HORMONE	HYPOTHALAMIC RELEASING FACTORS	HYPOTHALAMIC INHIBITORY FACTORS
Adrenocorticotrophic hormone (ACTH)	Corticotropin-releasing hormone (CRH), vasopressin, and other peptides	—
Thyroid-stimulating hormone (TSH)	Thyrotropin-releasing hormone (TRH)	Growth hormone-inhibiting hormone (GIH, somatostatin)
Growth hormone (GH)	Growth hormone-releasing hormone (GHRH)	Growth hormone-inhibiting hormone (GIH, somatostatin)
Prolactin	Prolactin-releasing factor (PRF) and thyrotropin-releasing hormone (TRH)	Prolactin release-inhibiting factor (PIF, dopamine)
Luteinizing hormone (LH)	Luteinizing hormone-releasing hormone (LHRH)	—
Follicle-stimulating hormone (FSH)	Luteinizing hormone-releasing hormone (LHRH)	—

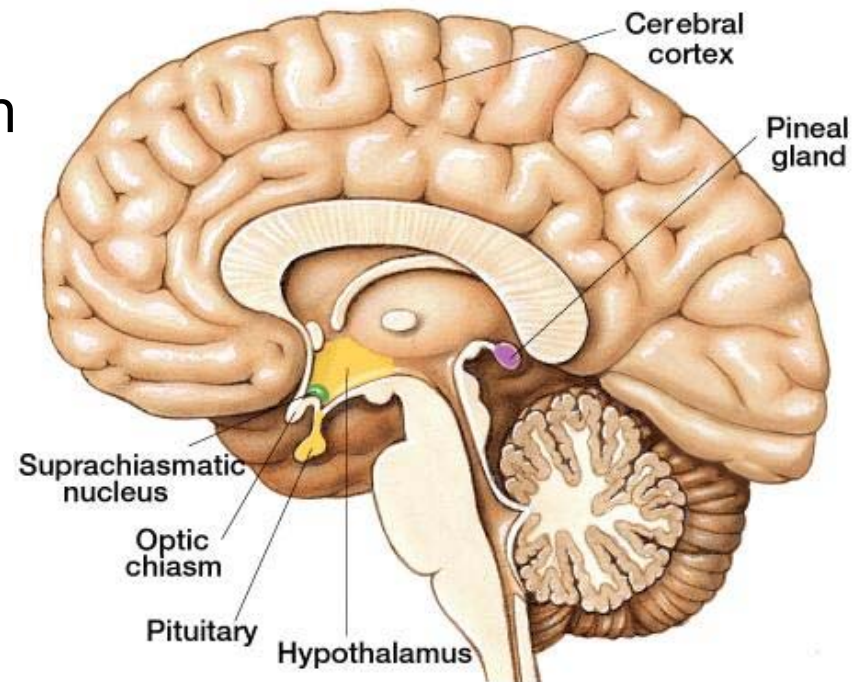
# Hypophyseal Vessels



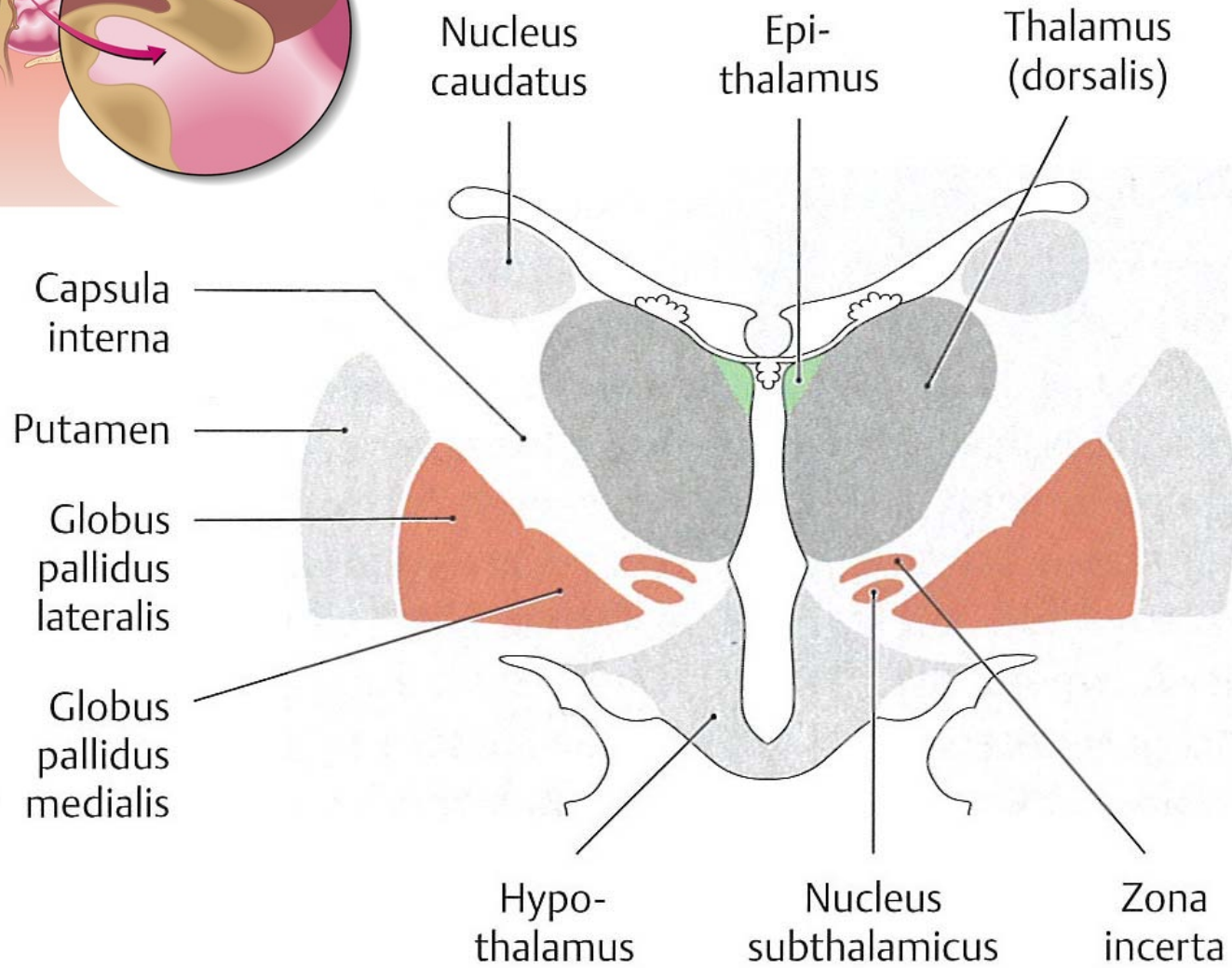
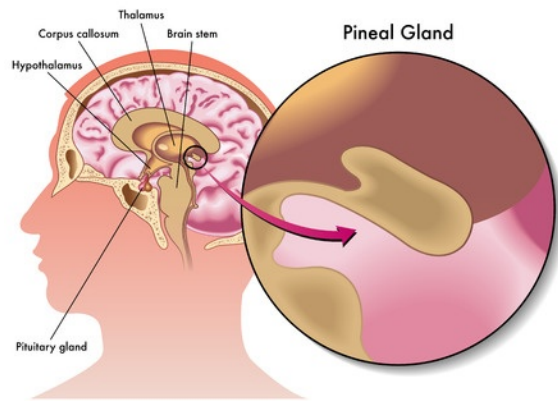
From F. Netter Atlas of Human anatomy. Ciba Geigy 1989

# Epithalamus

- Smallest part of the diencephalon
  - ❖ Corpus pineale (epiphysis cerebri) – pineal gland
  - ❖ Habenular complex:
    - ❖ Commissura habenularum
    - ❖ Habenulae
  - ❖ Stria medullaris







# Habenular complex

- Habenulopeduncular tract (fasciculus retroflexus)- unknown function
- Stria medullaris – afferent and efferent habenular fibers

Possible relay by which limbic system and hypothalamus influence midbrain structures



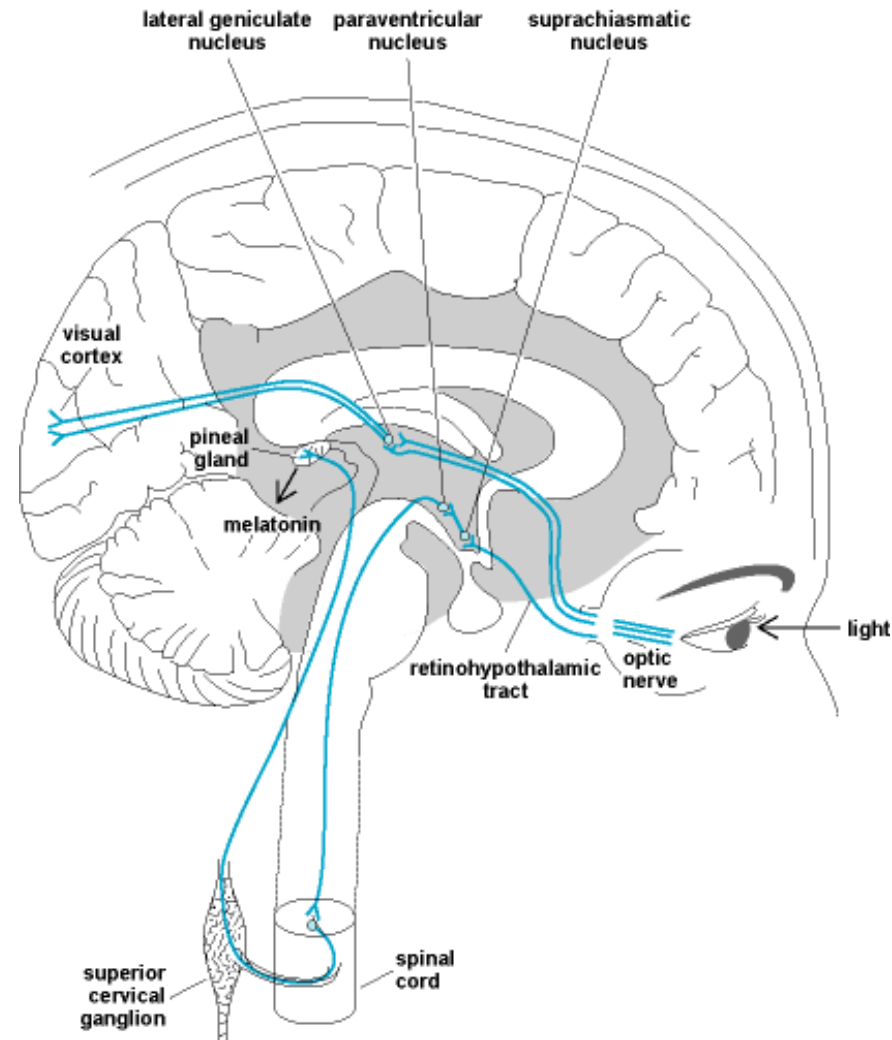
# Pineal gland

- No direct connections with CNS
- Inputs from sympathetic NS via superior cervical ganglia
- Pinealocytes – melatonin, serotonin, norepinephrine, hypothalamic-releasing hormones (during childhood)



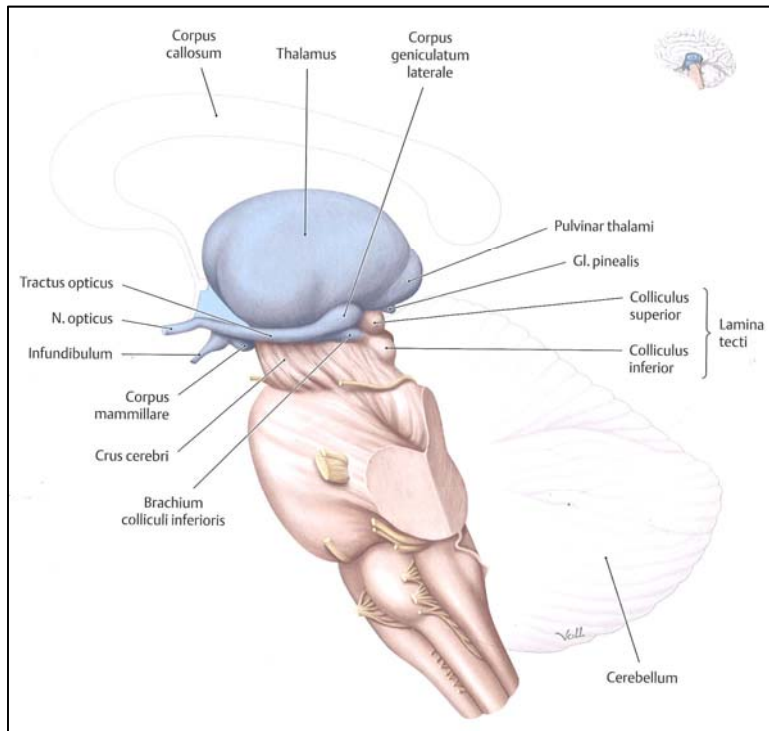
# Pineal gland

- Circadian rhythm  
(retina - suprachiasmatic  
nucl - thoracic cord -  
sup.cervical ganglia)
- Melatonin secretion



# Thalamus

- Meaning (in Greek): “inner chamber” or “bedroom”
- Located in the center of the brain

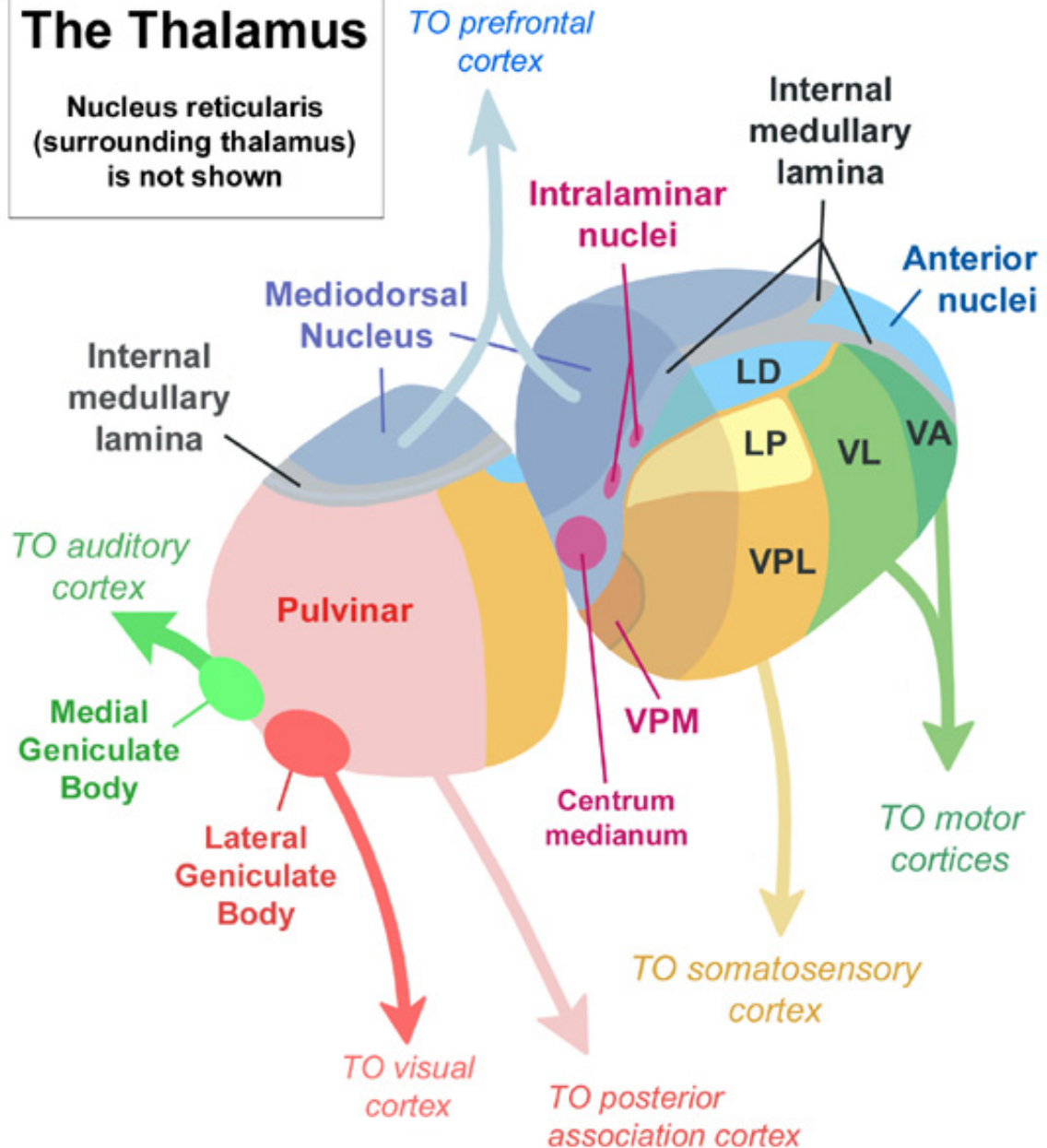


# Thalamus

- Oval shaped
- Largest component of the diencephalon
- the major sensory relay station (CNS to cortex)

## The Thalamus

Nucleus reticularis (surrounding thalamus) is not shown



# Thalamus

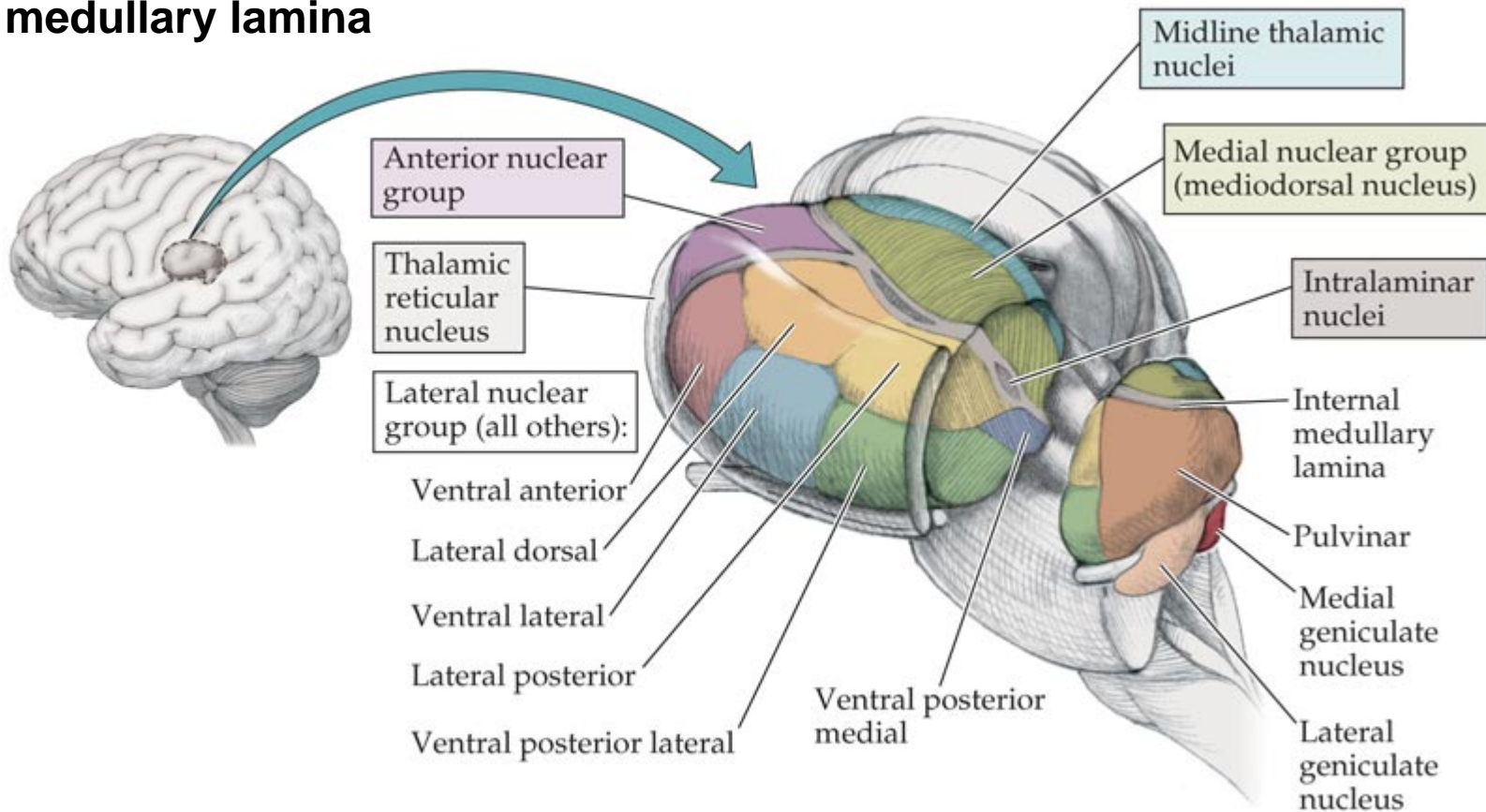
- also conveys nearly all other inputs to the cortex including:
- **motor inputs** from the **cerebellum** and **basal ganglia**
- **limbic inputs**
- widespread modulatory inputs involved in **behavioral arousal** and **sleep–wake cycles**
- and other inputs.

# Thalamus

- Some thalamic nuclei have specific topographical projections to restricted cortical areas,
- others project more diffusely.
- Thalamic nuclei typically receive dense reciprocal feedback connections from the cortical areas to which they project.
- In fact, **corticothalamic** projections outnumber **thalamocortical** projections.

# Thalamus

The thalamus is divided into a **medial nuclear group**, **lateral nuclear group**, and **anterior nuclear group** by a Y-shaped white matter structure called the **internal medullary lamina**



# Thalamus – three main categories of the nuclei

- Relay nuclei
- Intralaminar nuclei
- Reticular nucleus



# Thalamus – Relay Nuclei

- **relay nuclei** receive inputs from numerous pathways and then project to the cortex.
- receive massive reciprocal connections back from the cortex.
- **SPECIFIC THALAMIC RELAY NUCLEI**
- **WIDELY PROJECTING (NONSPECIFIC) THALAMIC RELAY NUCLEI**

# SPECIFIC THALAMIC RELAY NUCLEI

- Projections to the primary sensory and motor areas
- These specific relay nuclei lie mainly in the lateral thalamus
- **Somatosensory pathways** from the spinal cord and cranial nerves relay in the **ventral posterior lateral (VPL)** and **ventral posterior medial (VPM)** nuclei, respectively. The VPL and VPM in turn project to the primary somatosensory cortex

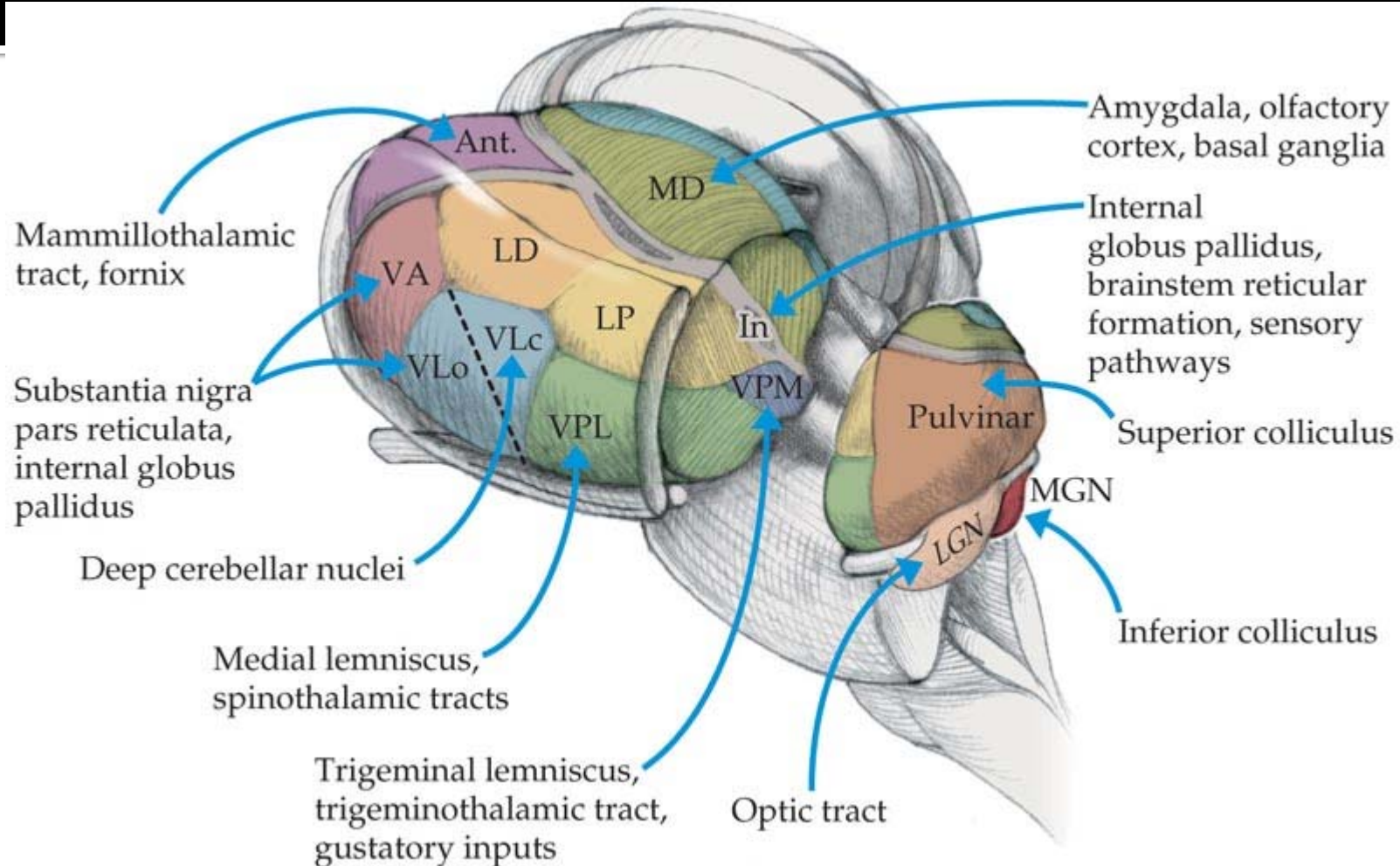
# SPECIFIC THALAMIC RELAY NUCLEI

- **Visual information** is relayed in the **lateral geniculate nucleus (LGN)**
- **Auditory information** is relayed in the **medial geniculate nucleus (MGN)**.
- A useful **mnemonic** for these two nuclei is **lateral light** (vision), **medial music** (audition).

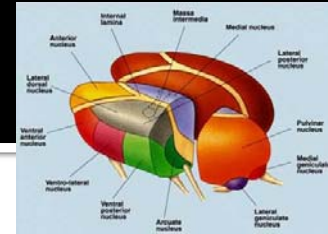
# SPECIFIC THALAMIC RELAY NUCLEI

- **Motor pathways** leaving the cerebellum and basal ganglia also have specific thalamic relays in the **ventral lateral nucleus (VL)** en route to the **motor, premotor, and supplementary motor cortex**
- Some **limbic pathways** have cortical projections: from **anterior nuclear group** to the **anterior cingulate cortex**.

# Noncortical Inputs to the Thalamus



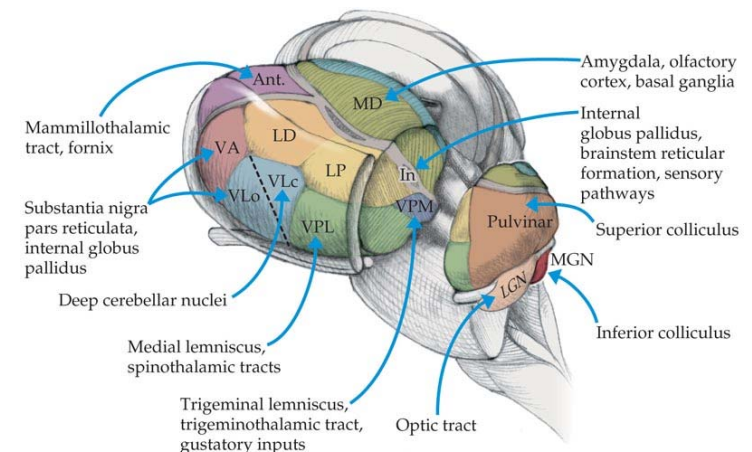
# WIDELY PROJECTING (NONSPECIFIC) THALAMIC RELAY NUCLEI



- Many thalamic nuclei have more widespread cortical projections
- **Visual** and other **sensory inputs** to the **pulvinar** are relayed to large regions of the **parietal, temporal, and occipital association cortex** involved in behavioral orientation toward relevant stimuli.
- The pulvinar (“couch” or “cushion” in Latin) is a large, pillow-shaped nucleus that occupies most of the posterior thalamus.

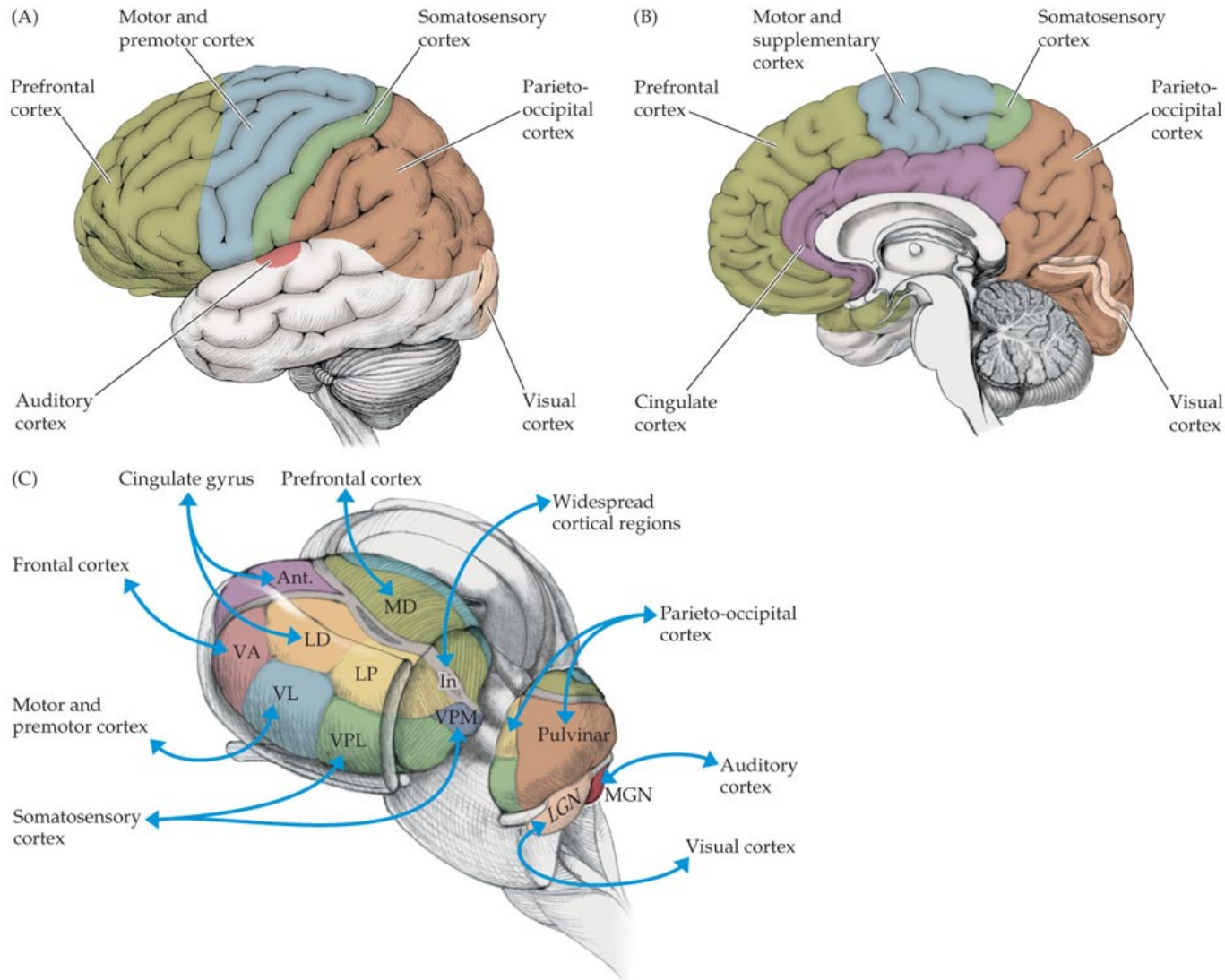
# WIDELY PROJECTING (NONSPECIFIC) THALAMIC RELAY NUCLEI

- Diffuse relays of **limbic inputs** and other information involved in cognitive functions occur in the **mediodorsal nucleus (MD)**, as well as in the **midline** and **intralaminar thalamic nuclei**.
- MD nucleus forms a large bulge lying medial to the internal medullary lamina, best seen in coronal sections.
- The MD serves as the major thalamic relay for information traveling **to the frontal association cortex**.



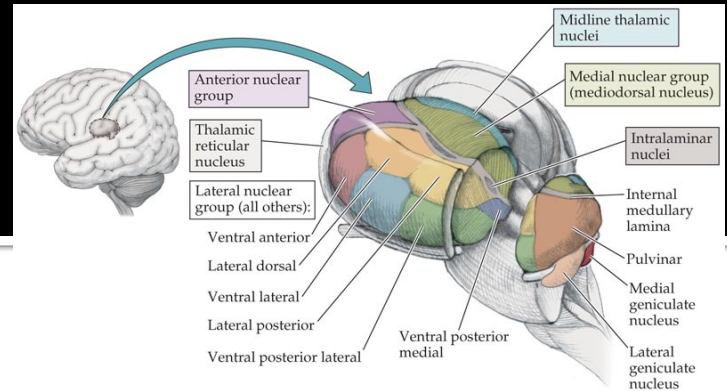


# Reciprocal Connections between Thalamus and Cortex





# Intralaminar Nuclei



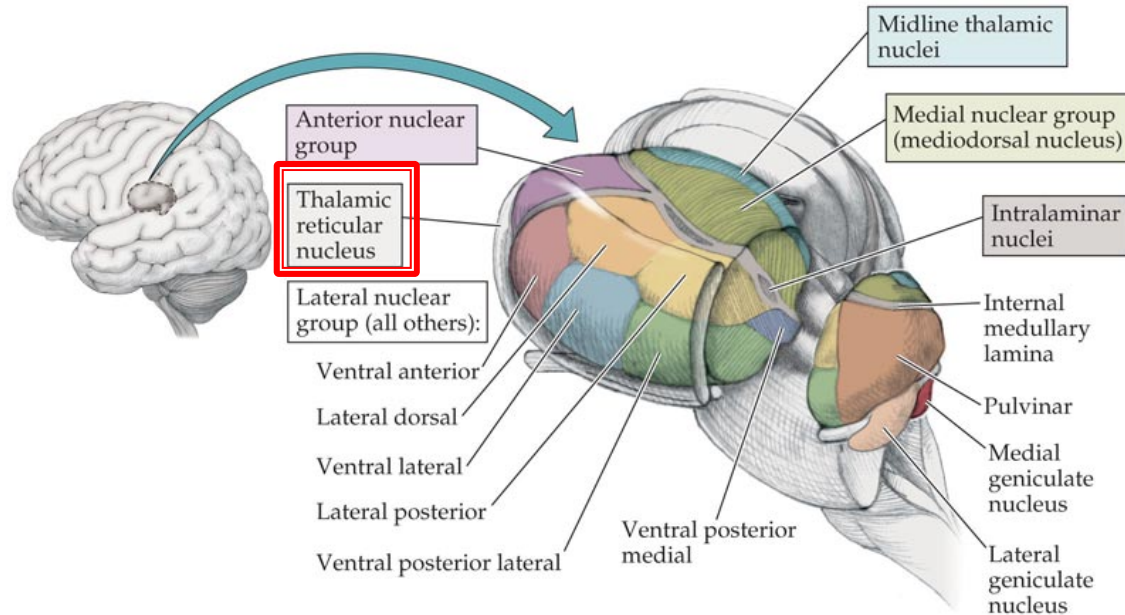
- The **intralaminar nuclei** lie within the internal medullary lamina
- They receive inputs from numerous pathways and have reciprocal connections with the **cortex**.
- Unlike relay nuclei, their main inputs and outputs are from the **basal ganglia**.

# Intralaminar Nuclei

- Can be divided into two functional regions:
  1. The **caudal intralaminar nuclei** include the large **centromedian nucleus** and are involved mainly in **basal ganglia circuitry**
  2. The **rostral intralaminar nuclei** also have input and output connections with the basal ganglia. In addition, they relay inputs from the **ascending reticular activating systems (ARAS)** to the cortex, maintaining the alert, conscious state.

# Reticular nucleus

- forms a thin sheet located just lateral to the rest of the thalamus and just medial to the internal capsule



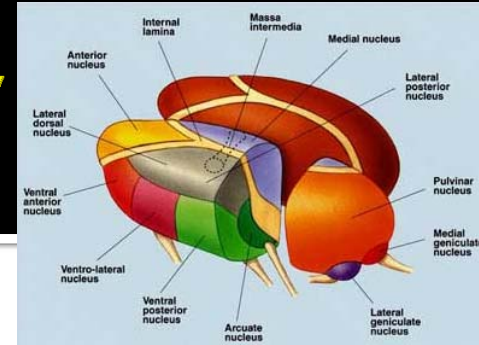
# Reticular nucleus

- The reticular nucleus is the only nucleus of the thalamus that **does not project to the cortex**.
- Instead, it receives inputs mainly from other thalamic nuclei and the cortex and then projects back to the thalamus.

# Reticular nucleus

- It consists of inhibitory **GABAergic** neurons. This composition, together with its connections with the entire thalamus, make it well suited to **regulate thalamic activity**.
- In addition to cortical and thalamic inputs, other inputs to the reticular nucleus arising from the brainstem reticular activating systems and the basal forebrain may participate in modulating the state of **alertness and attention**.

# Thalamus - summary



- In summary, the thalamus has major reciprocal connections with all regions of the cerebral cortex.
- It contains many different nuclei with different functions.
- These nuclei convey information from other parts of the nervous system, as well as from the periphery to the cortex.

# Major Thalamic Nuclei

**TABLE 7.3** Major Thalamic Nuclei

NUCLEI <sup>a</sup>	MAIN INPUTS <sup>b</sup>	MAIN OUTPUTS	DIFFUSENESS OF PROJECTIONS TO CORTEX <sup>c</sup>	PROPOSED FUNCTIONS
<b>RELAY NUCLEI</b>				
Lateral nuclear group				
<b>Ventral posterior lateral nucleus (VPL)</b>	Medial lemniscus, spinothalamic tract	Somatosensory cortex	+	Relays somatosensory spinal inputs to cortex
<b>Ventral posteromedial nucleus (VPM)</b>	Trigeminal lemniscus, trigeminothalamic tract, taste inputs	Somatosensory and taste cortex	+	Relays somatosensory cranial nerve inputs and taste to cortex
<b>Lateral geniculate nucleus (LGN)</b>	Retina	Primary visual cortex	+	Relays visual inputs to cortex
<b>Medial geniculate nucleus (MGN)</b>	Inferior colliculus	Primary auditory cortex	+	Relays auditory inputs to cortex
<b>Ventral lateral nucleus (VL)</b>	Internal globus pallidus, deep cerebellar nuclei, substantia nigra pars reticulata	Motor, premotor, and supplementary motor cortex	+	Relays basal ganglia and cerebellar inputs to cortex
<b>Ventral anterior nucleus (VA)</b>	Substantia nigra pars reticulata, internal globus pallidus, deep cerebellar nuclei	Widespread to frontal lobe, including prefrontal, premotor, motor, and supplementary motor cortex	+++	Relays basal ganglia and cerebellar inputs to cortex
<b>Pulvinar</b>	Tectum (extrageniculate visual pathway), other sensory inputs	Parietotemporo-occipital association	++	Behavioral orientation toward relevant visual and other stimuli
Lateral dorsal nucleus	See anterior nucleus	—	++	Functions with anterior nuclei
Lateral posterior nucleus	See pulvinar	—	++	Functions with pulvinar
Ventral medial nucleus	Midbrain reticular formation	Widespread to cortex	+++	May help maintain alert, conscious state
Medial nuclear group				
<b>Mediodorsal nucleus (MD)</b>	Amygdala, olfactory cortex, limbic basal ganglia	Frontal cortex	++	Limbic pathways, major relay to frontal cortex
Anterior nuclear group				
<b>Anterior nucleus</b>	Mammillary body, hippocampal formation	Cingulate gyrus	+	Limbic pathways
Midline thalamic nuclei				
Paraventricular, parataenia, interanteromedial, intermediodorsal, rhomboid, reuniens (medial ventral)	Hypothalamus, basal forebrain, amygdala, hippocampus	Amygdala, hippocampus, limbic cortex	++	Limbic pathways
<b>INTRALAMINAR NUCLEI</b>				
Rostral intralaminar nuclei	Deep cerebellar nuclei, globus pallidus, brainstem ascending reticular activating systems (ARAS), sensory pathways	Cerebral cortex, striatum	+++	Maintain alert consciousness; motor relay for basal ganglia and cerebellum
Central medial nucleus				
Paracentral nucleus				
Central lateral nucleus				
Caudal intralaminar nuclei				
<b>Centromedian nucleus</b>	Globus pallidus, ARAS, sensory pathways	Striatum, cerebral cortex	+++	Motor relay for basal ganglia
Parafascicular nucleus				
<b>RETICULAR NUCLEUS</b>				
	Cerebral cortex, thalamic relay and intralaminar nuclei, ARAS	Thalamic relay and intralaminar nuclei, ARAS	None	Regulates state of other thalamic nuclei

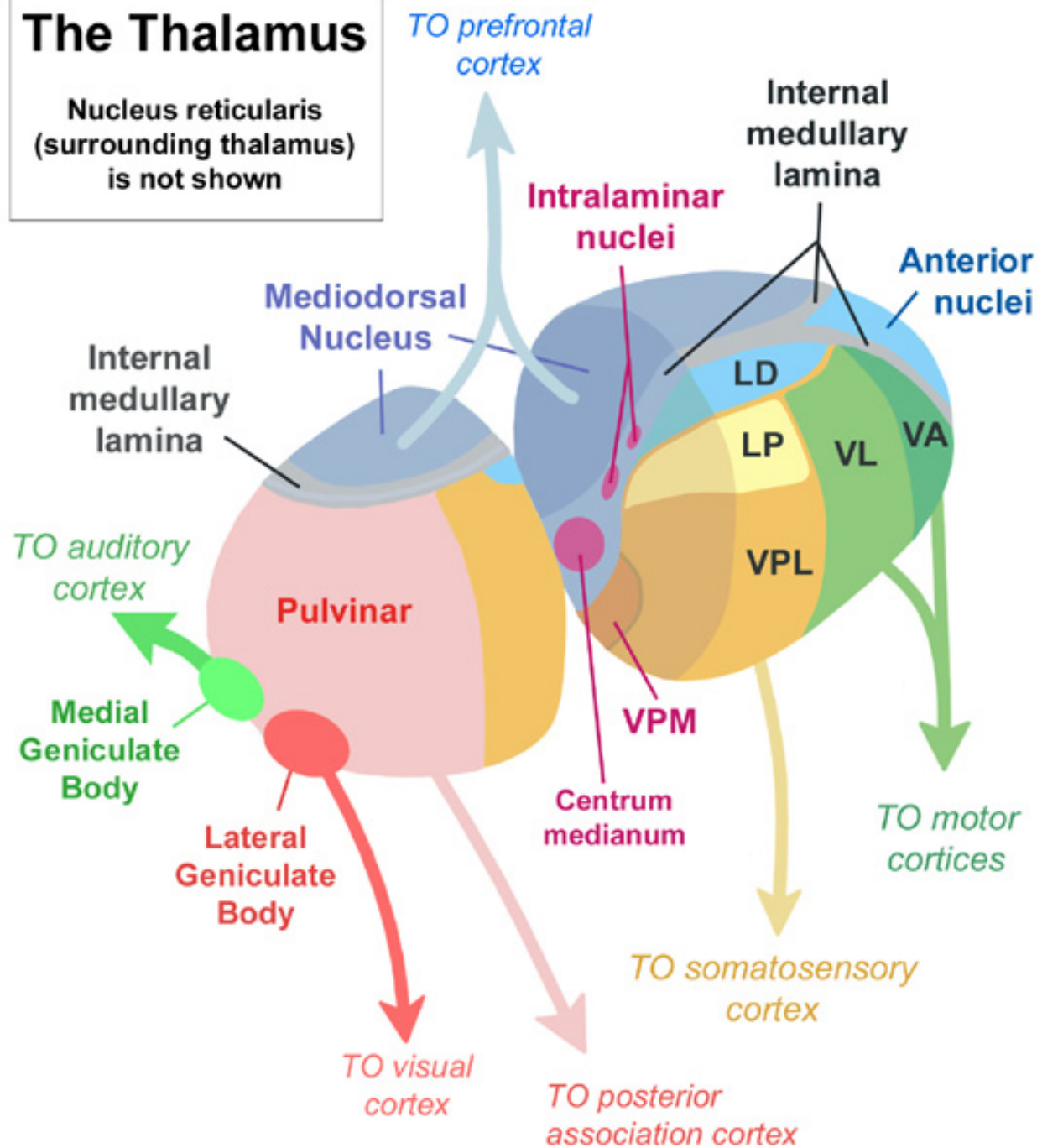
<sup>a</sup>The most well known and clinically relevant nuclei are shown in **bold**. Some additional, smaller nuclei have not been included.

<sup>b</sup>In addition to the inputs listed, all thalamic nuclei receive reciprocal inputs from the cortex and from the thalamic reticular nucleus. Modulatory cholinergic, noradrenergic, serotonergic, and histaminergic inputs also reach most thalamic nuclei (see Chapter 14).

<sup>c</sup>+ represents least diffuse (specific thalamic relay nuclei); ++ represents moderately diffuse; +++ represents most diffuse.

# The Thalamus

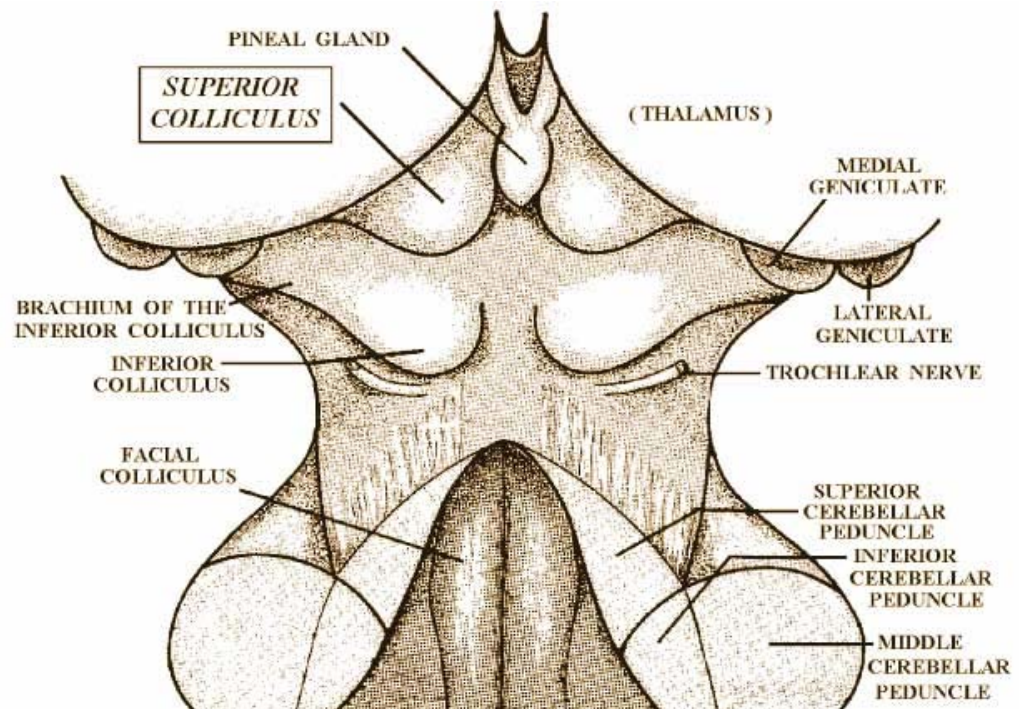
Nucleus reticularis  
(surrounding thalamus)  
is not shown



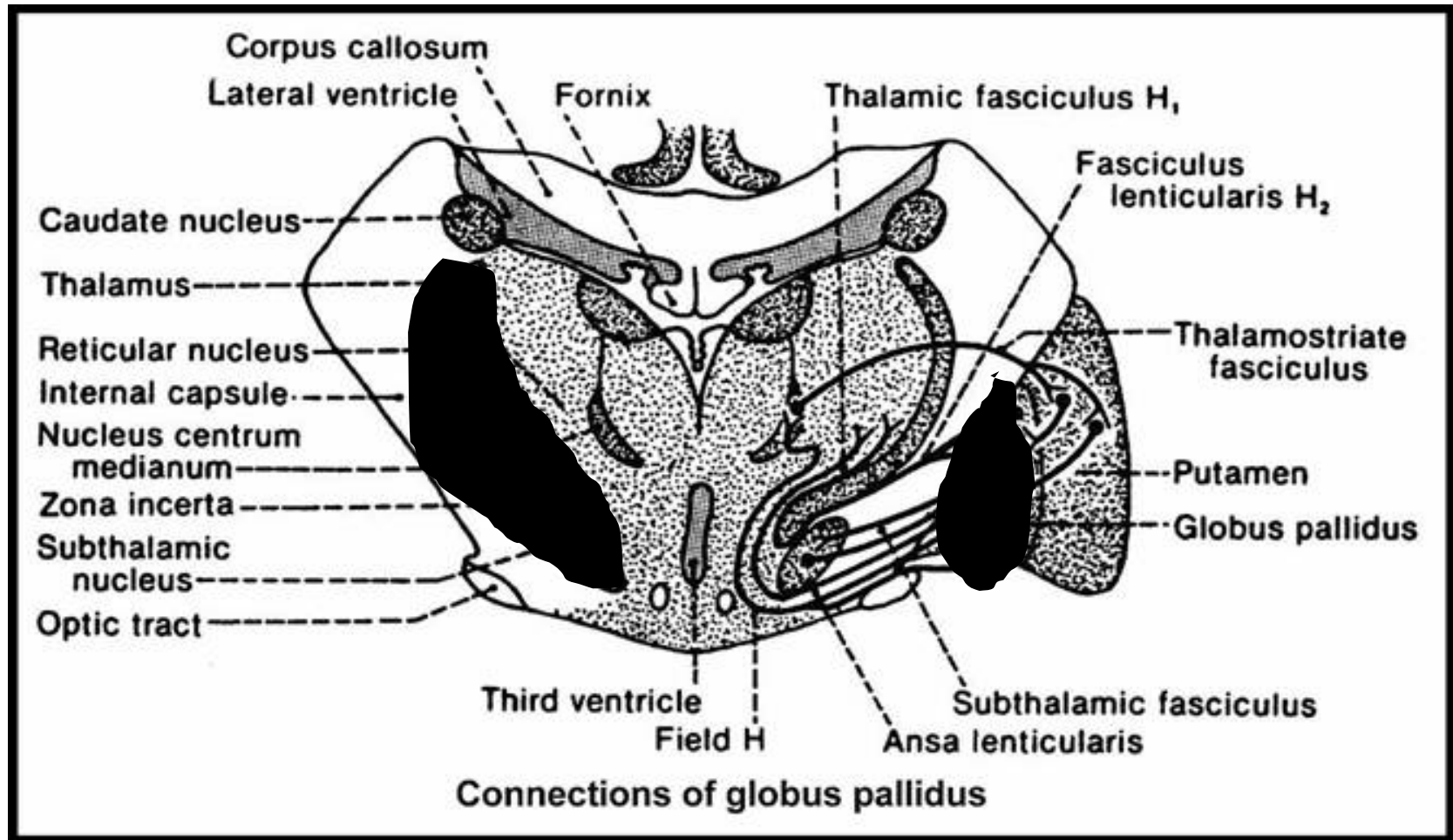


# Metathalamus

- ***Corpus geniculatum laterale*** – relay of visual impulses to the visual cortex from retina
- ***Corpus geniculatum mediale*** – relay for auditory system

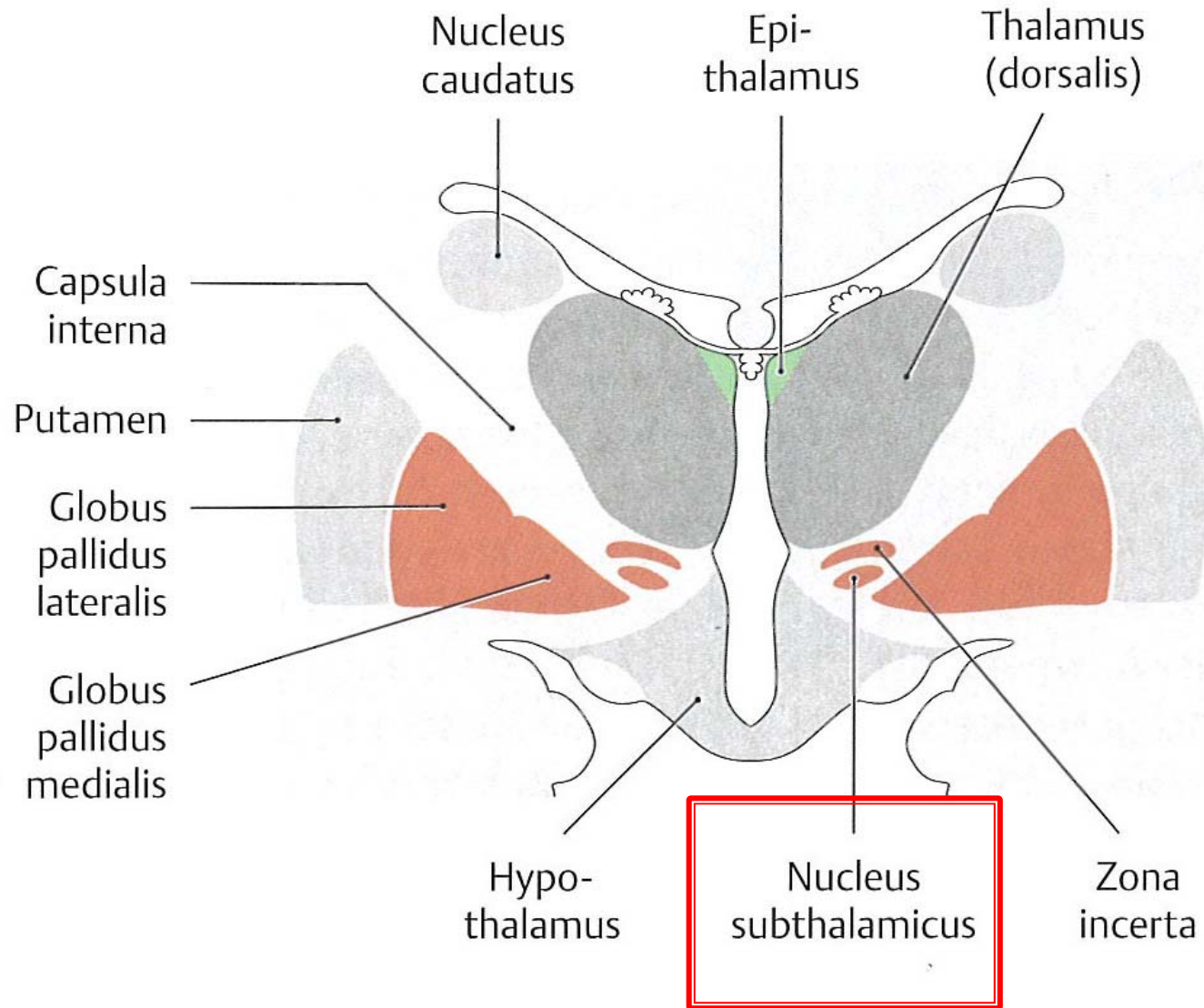


# Subthalamus



# Subthalamus

- Zona incerta (DA, tractus incerto-hypothalamicus)
- Nucl. subthalamicus (corpus subthalamicum Luysi)
  - reciprocal connections with the globus palidus –  
**motor functions!**
- **Motor functions associated with the basal ganglia.**



# Subthalamic fibers

- Ansa lenticularis
  - Fasciculus lenticularis
  - Fasciculus thalamicus
  - FLM
  - Spinothalamic and trigeminothalamic fibers
- *"thalamic gatekeeper"*
- Nigrostriatal dopaminergic fibers
  - Strionigral GABA-ergic fibers

Basal ganglia outputs