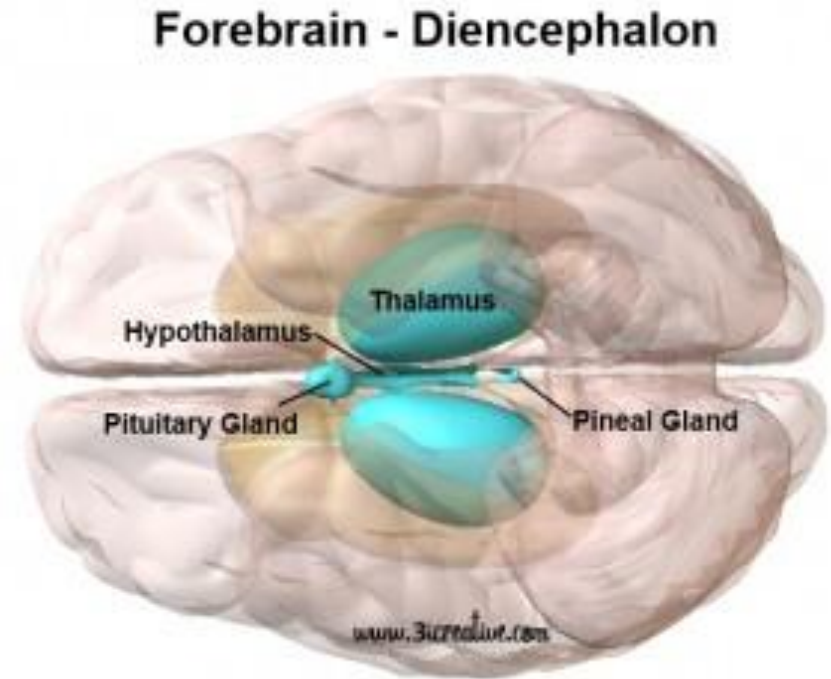


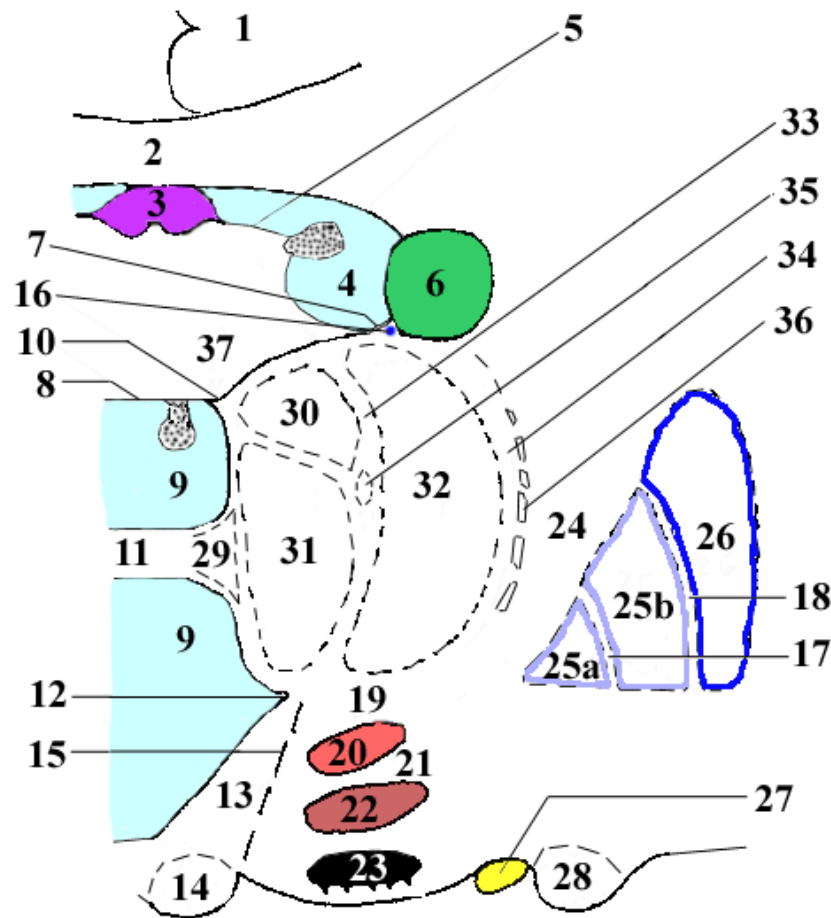
# DIENCEPHALON

# diencephalon

- epithalamus
- subthalamus
- thalamus
- metathalamus
- hypothalamus
- thalamus opticus



# FRONTÁLNÍ ŘEZ DIENCEPHALEM



- 1 - gyrus cinguli
- 2 - corpus callosum
- 3 - corpus fornix cerebri
- 4 - ventriculus lateralis
- 5 - tela choroidea ventriculi lateralis
- 6 - caput nuclei caudati
- 7 - lamina affixa thalami
- 8 - tela choroidea ventriculi tertii
- 9 - ventriculus tertius
- 10 - stria medullaris thalami
- 11 - adhesio interthalamica
- 12 - sulcus hypothalamicus
- 13 - hypothalamus
- 14 - corpus mamillare
- 15 - hranice hypo- a subthalamu
- 16 - vena thalamostriata superior
- 17 - lamina medullaris med. nuclei lentiformis
- 18 - lamina medullaris lat. nuclei lentiformis
- 19 - *Forelovo poličko* H1  
(fasciculus thalamicus + nucleus campi dorsalis)
- 20 - zona incerta
- 21 - *Forelovo poličko* H2  
(fasciculus lenticularis + nucleus campi ventralis)
- 22 - nucleus subthalamicus /*Luys*/
- 23 - substantia nigra
- 24 - capsula interna
- 25a - globus pallidus medialis
- 25b - globus pallidus lateralis
- 26 - putamen
- 27 - tractus opticus
- 28 - corpus geniculatum laterale
- 29 - nuclei mediani thalami
- 30 - nuclei anteriores thalami
- 31 - nuclei mediales thalami
- 32 - nuclei ventrales, dorsales et posteriores thalami
- 33 - lamina medullaris medialis thalami
- 34 - lamina medullaris lateralis thalami
- 35 - nuclei intralaminare thalami
- 36 - nucleus reticularis thalami
- 37 - fissura telodiencephalica

# diencephalon - development

Alar plate → thalamus, subthalamus

Bazal plate → hypothalamus

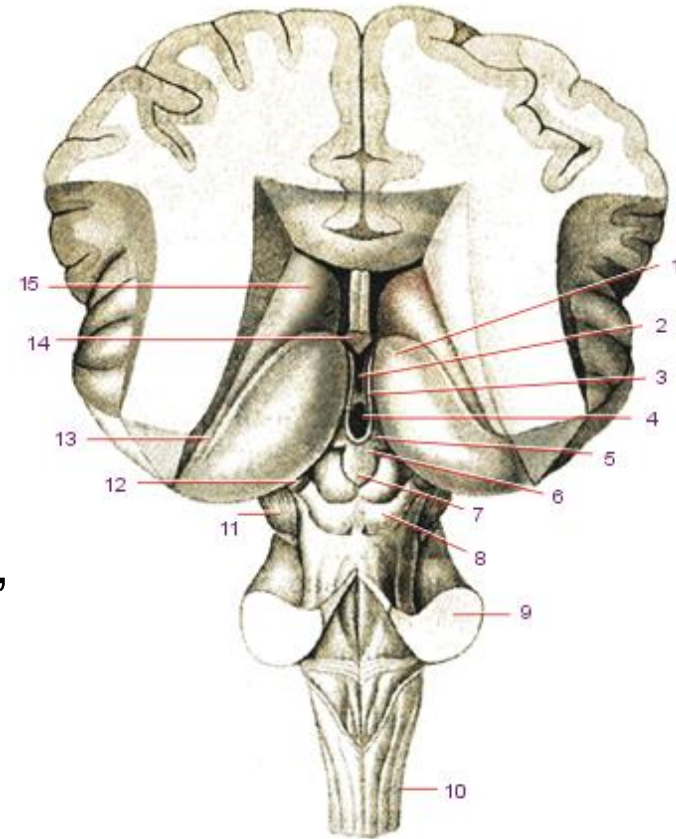
canalis centralis → 3rd ventricle

*fissura telodiencephalica*

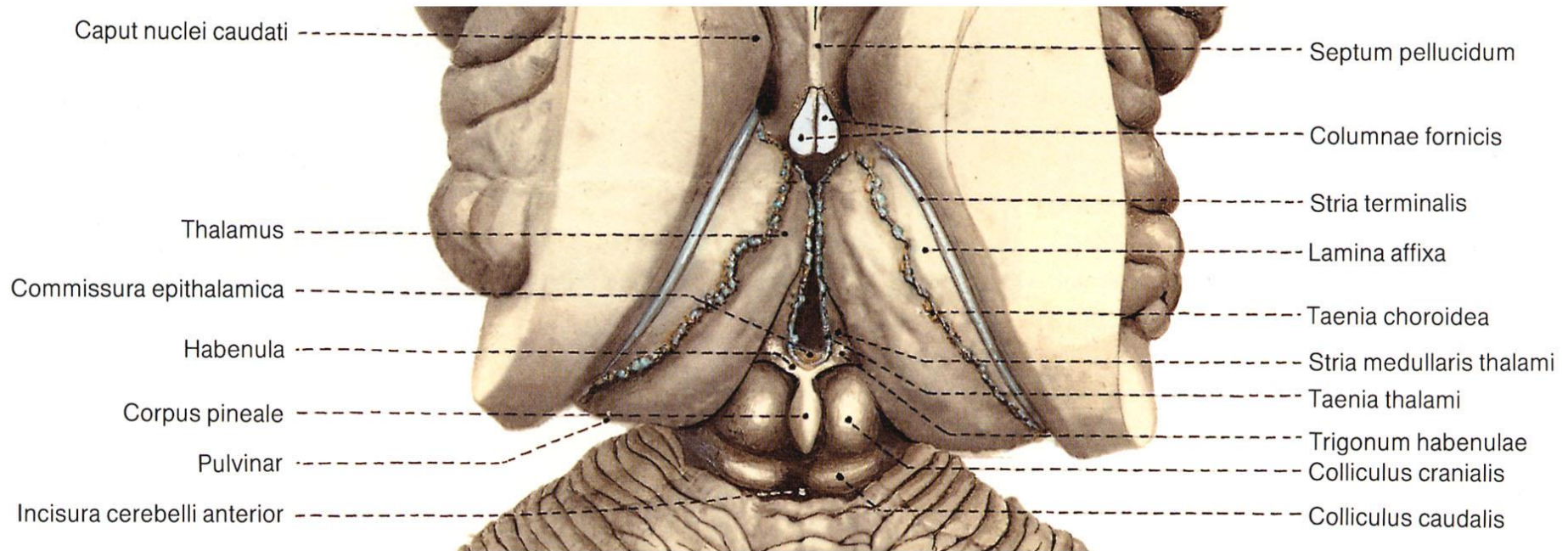
*sulcus hypothalamicus*

# Epithalamus

- **habenula (trigonum habenulare)**
  - ncl. habenularis med. + lat.
- **commissura habenularum**
- **commissura posterior**
  - Commissural fibers
    - Posterior thalamic nuclei, colliculi sup., ncl. preectales
  - Non commissural fibers
    - ncl. interstitialis *Cajali* + ncl. commissurae posterioris *Darkschewitzi*  
→ fasciculus longitudinalis medialis from other side

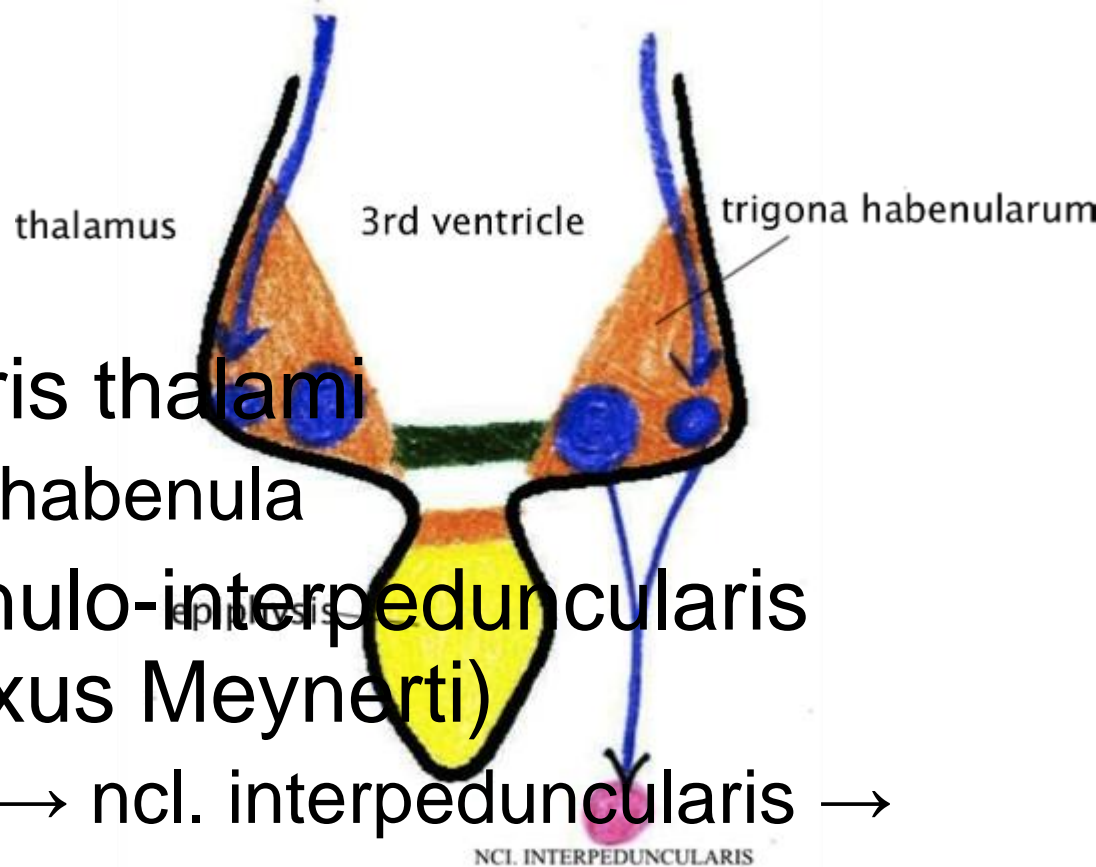


# Epithalamus



# Epithalamus

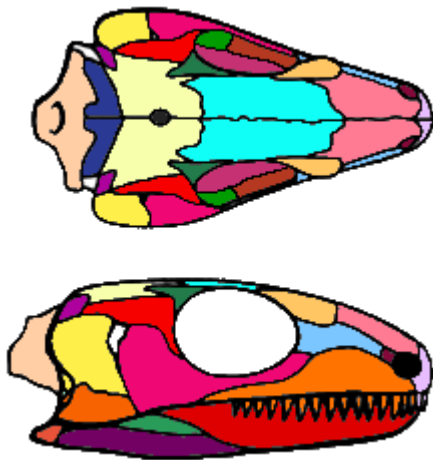
- AF: stria medullaris thalami
  - septum verum → habenula
- EF: tractus habenulo-interpeduncularis (fasciculus retroflexus Meynerti)
  - ncl. habenulares → ncl. interpeduncularis → stem



## commissura habenularum

# *Glandula pinealis; Corpus pineale* „Epiphysis;“

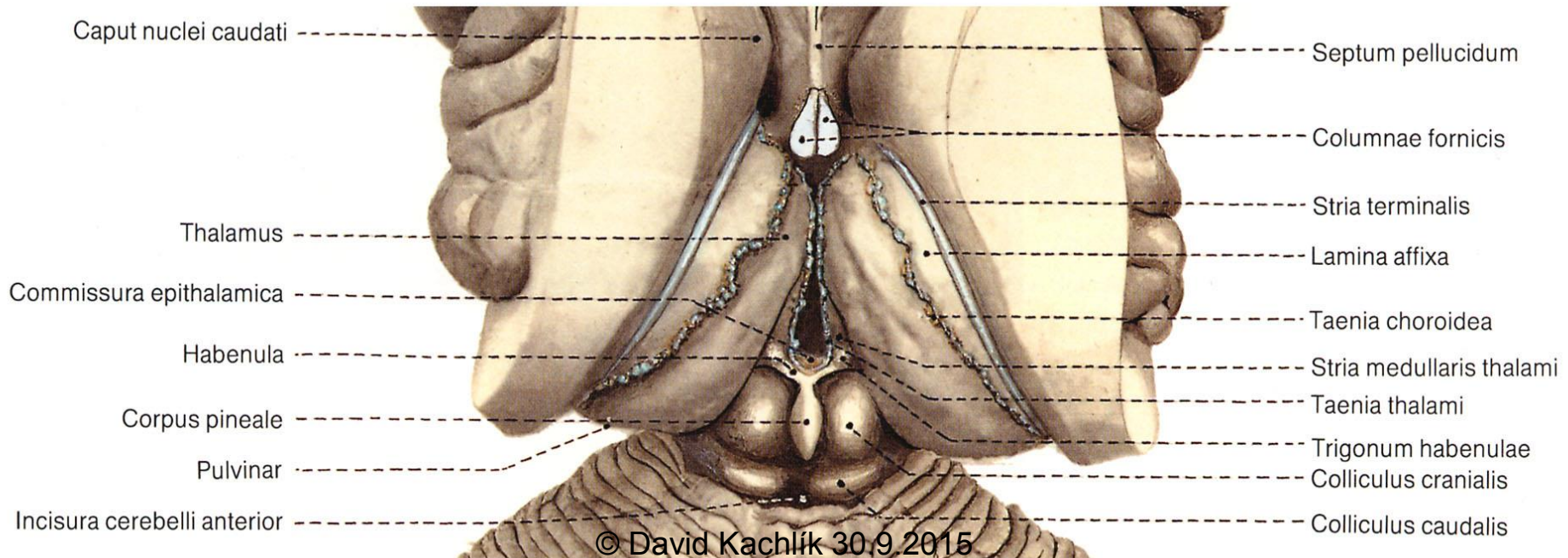
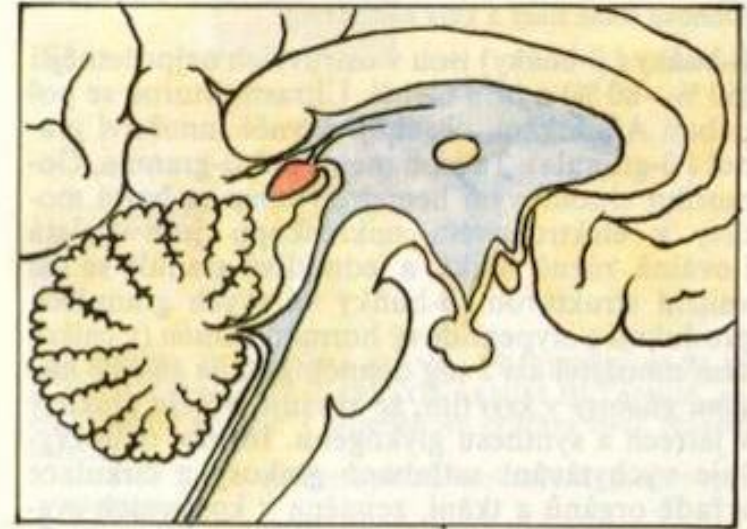
- Developmental relation to parietal eye
- Hateria New Zealand (*Sphenodon punctatus*)
- Reaction to polarized light (monthly biorhythms)

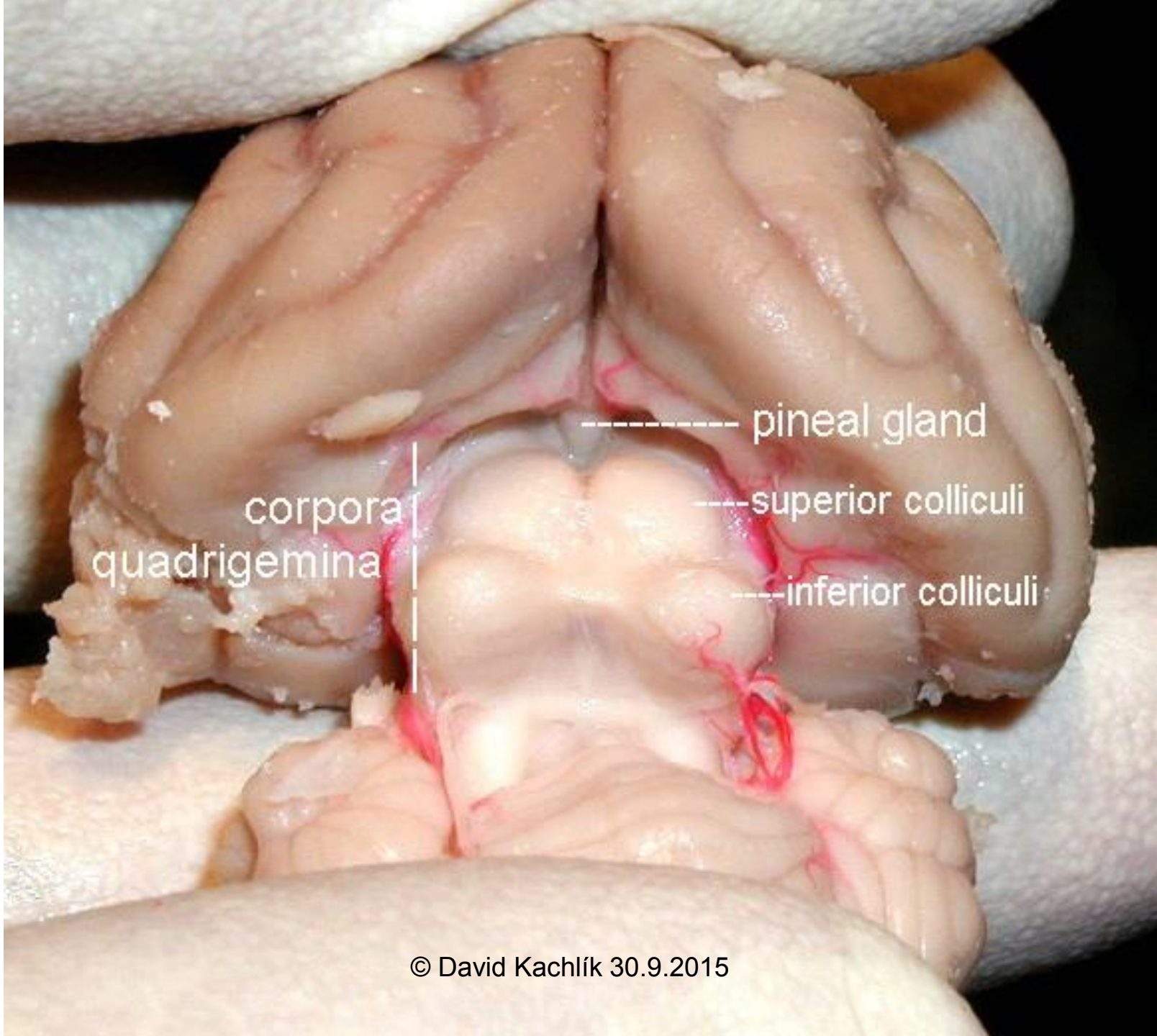




# Epiphysis

- Behind upper posterior end of
- Part of epithalamus
- Rudimentary endocrine gland on sexual glands → pubertas p
- Dorsally extends above brain



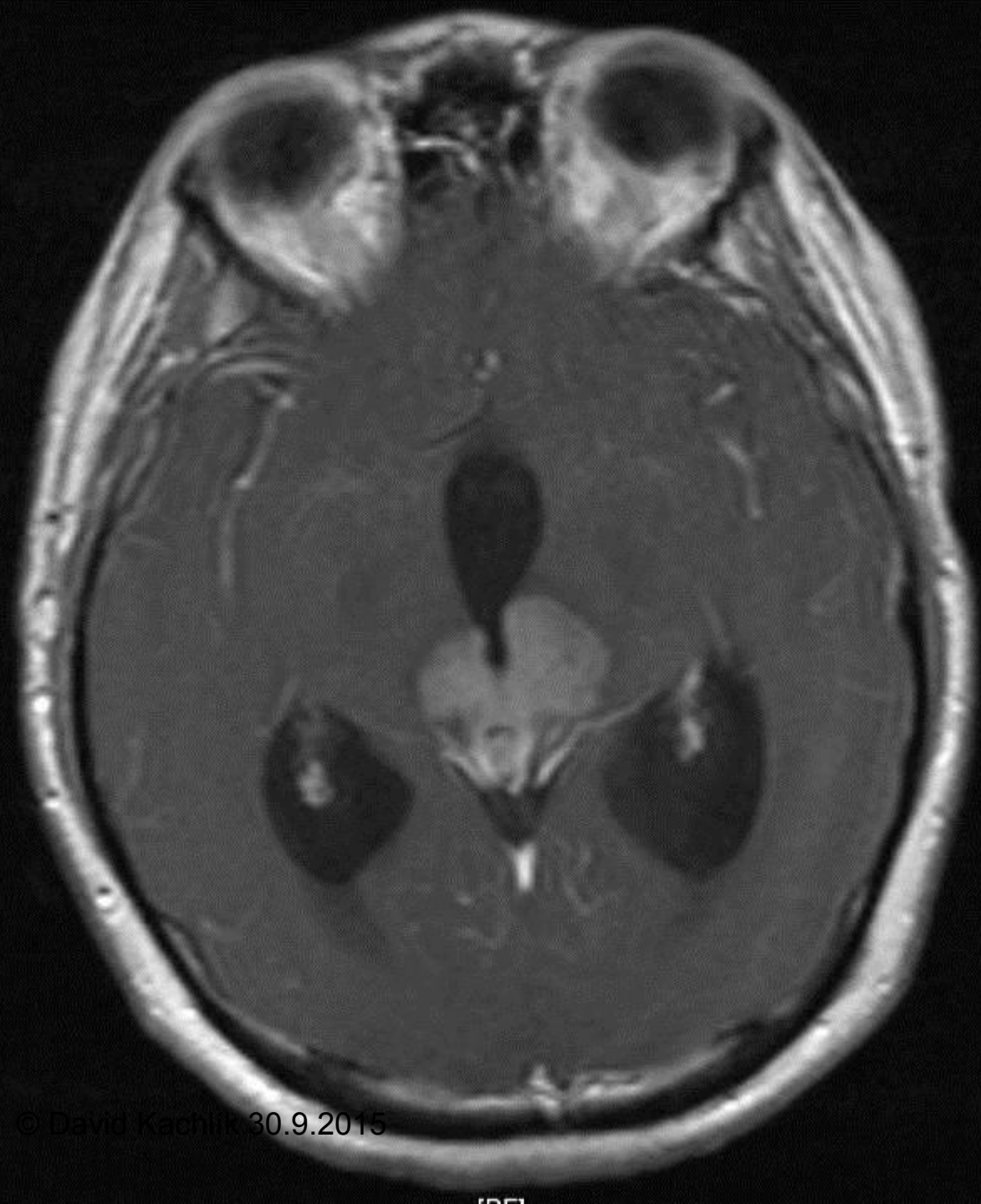


corpora  
quadrigemina

pineal gland

superior colliculi

inferior colliculi



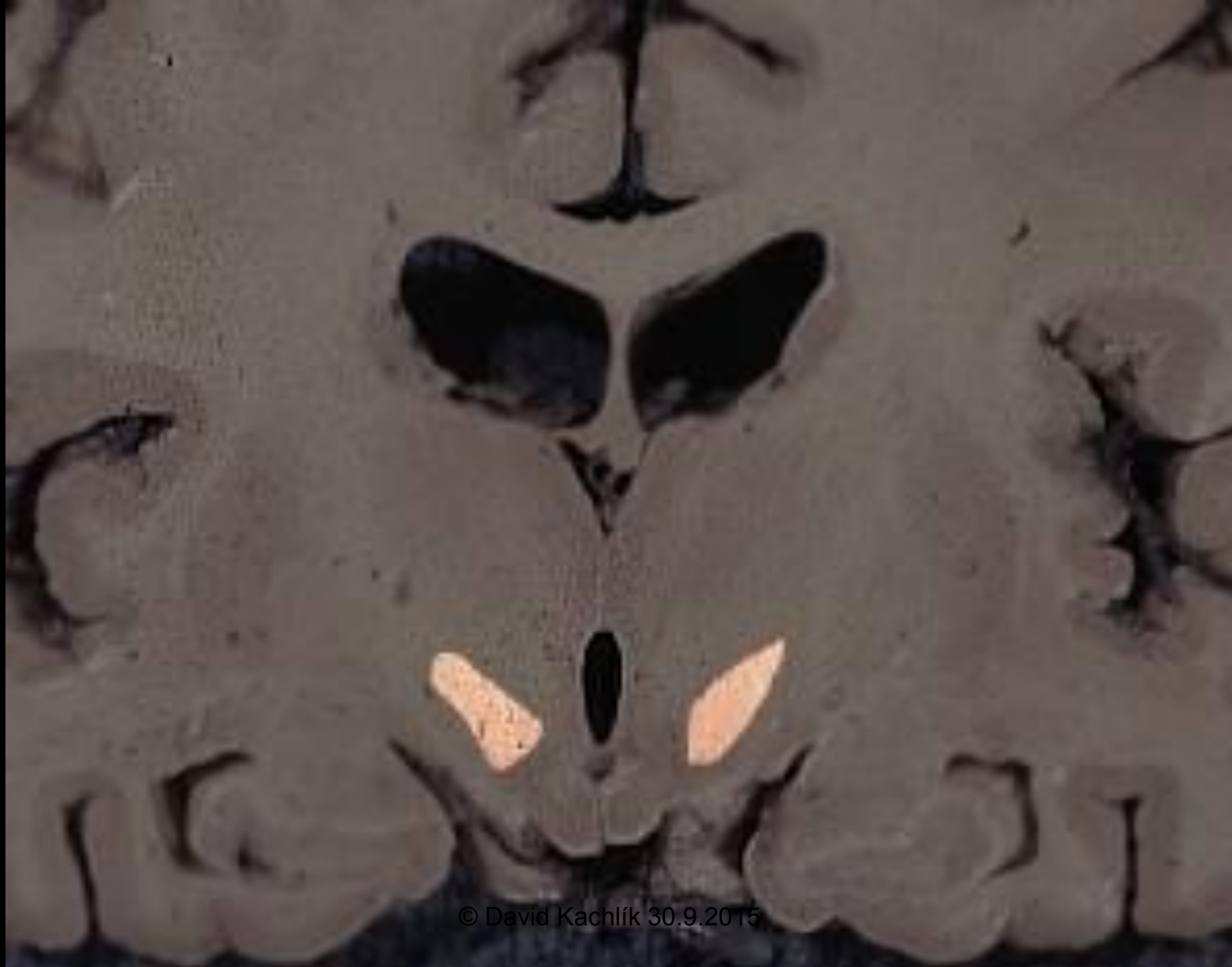
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# Subthalamus

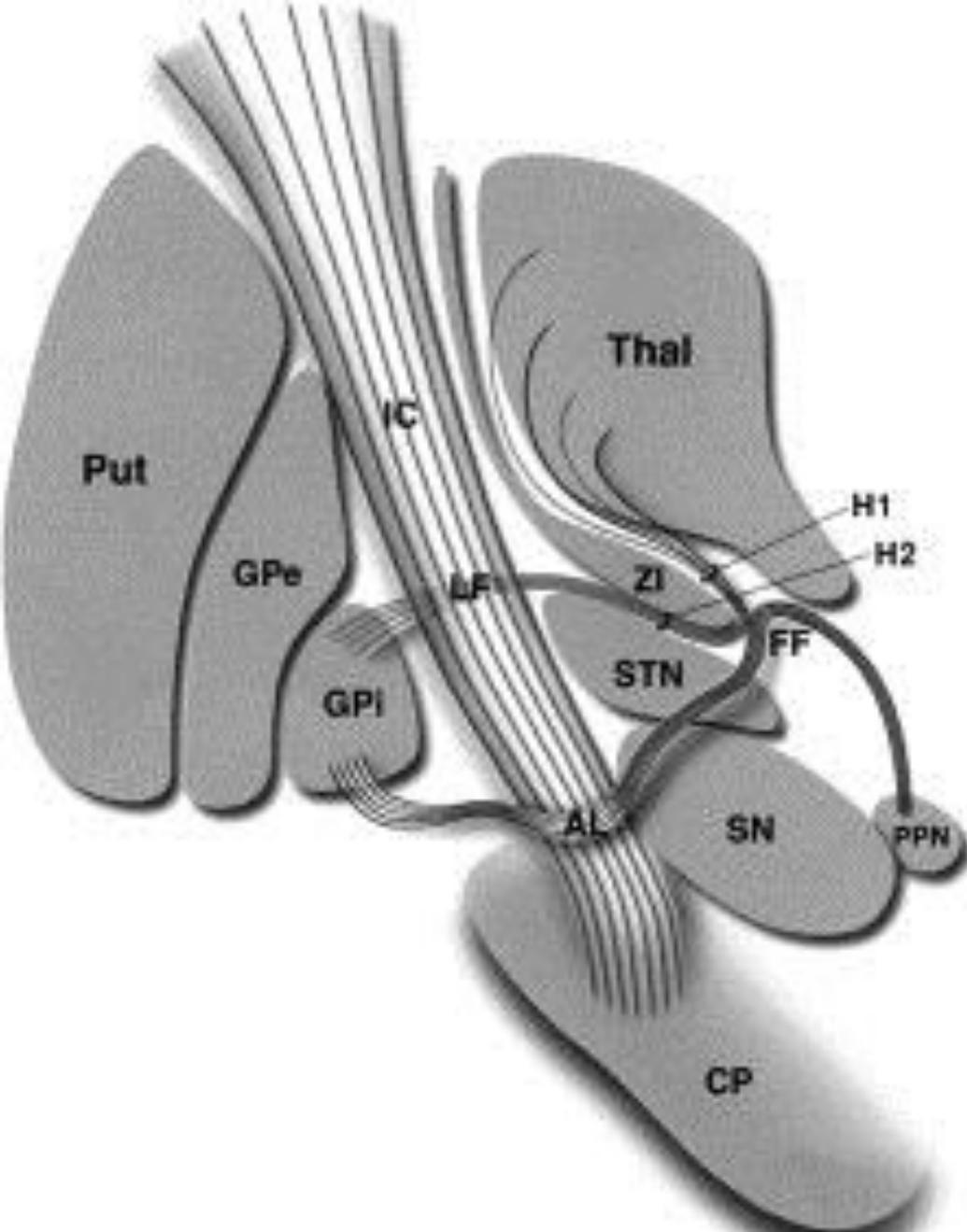
- Positioned below thalamus – separated by *Forels field* H1
- Externally to hypothalamus – w/o visible border
- **zona incerta**
- **nucleus subthalamicus (= corpus Luysi)**
- Forels fields = campi perizonales  
= H zone (Haubenfelder)

# Subthalamus

- **zona incerta**
  - Composition resembles RF
  - Integration of inputs from cortex and stem
  - GABA inhibits ncll. intralaminares and association nuclei of thalamus (similarly to ncll. reticulares thalami)
- **nucleus subthalamicus (= corpus Luysi)**
  - Connected to basal ganglia system (Glu into globus pallidus)
  - *lesion: hemiballismus (rough non coordinated movements of contralateral cingulum muscles) after CMP, non ketonic hyperglycemia*
- **Forels fields = campi perizonales**
  - = H zones (Haubenfelder)
  - H = ansa lenticularis
    - H1 = fasciculus thalamicus
    - H2 = fasciculus lenticularis



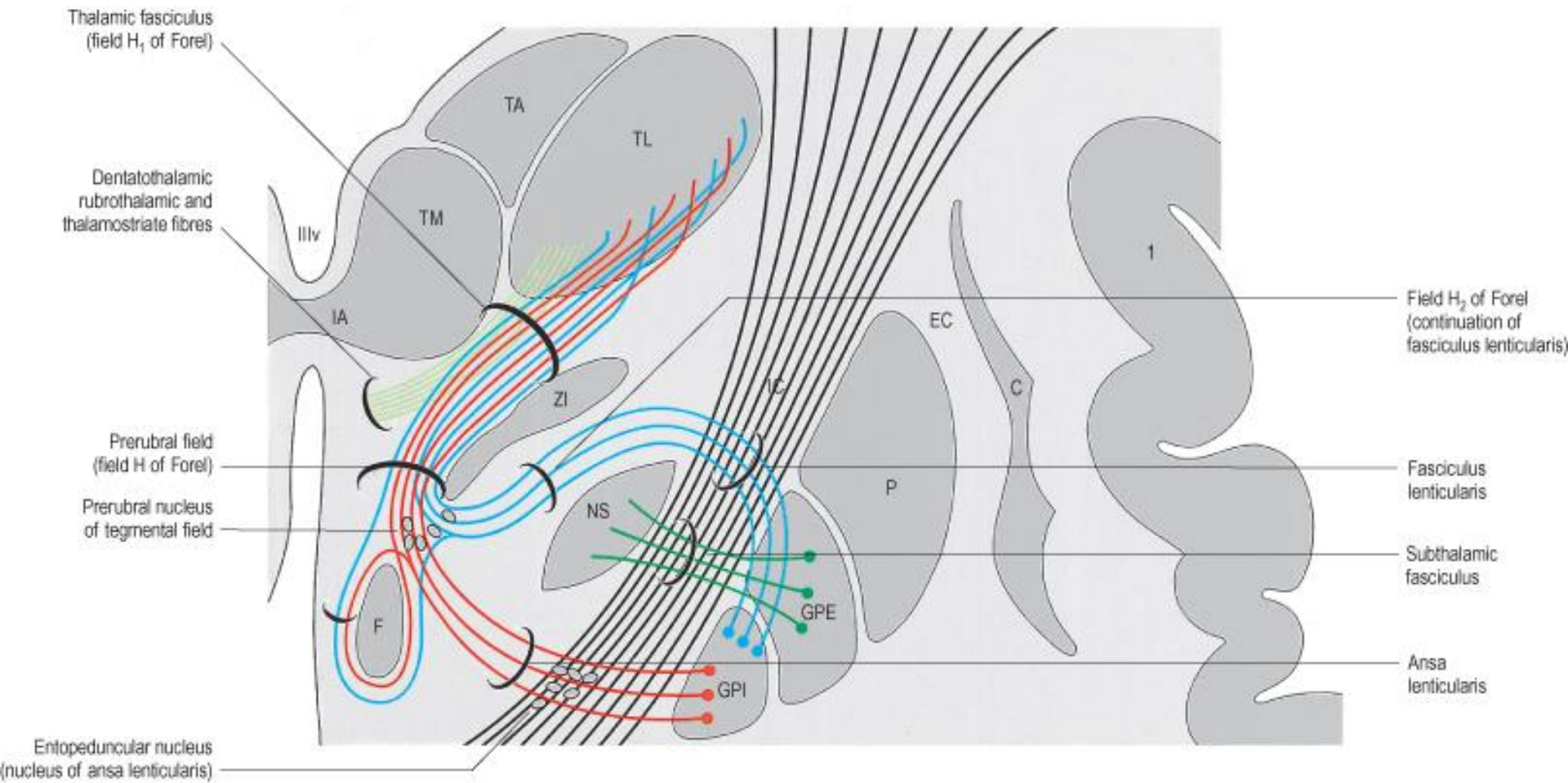
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**Nuclear groups and fiber tracts associated with the subthalamus include the subthalamic nucleus, zonal incerta, and the fields of Forel and their associated fiber bundles.**

**AL, ansa lenticularis;  
 CP, cerebral peduncle;  
 FF, fields of Forel;  
 GPe, globus pallidus externus;  
 GPi, globus pallidus internus;  
 H1, H1 field of Forel (thalamic fasciculus); IC, internal capsule;  
 LF, lenticular fasciculus (H2);  
 PPN, pedunculopontine nucleus;  
 Put, putamen; SN, substantia nigra;  
 STN, subthalamic nucleus; Thal, thalamus; ZI, zona incerta. H, corresponding to the nucleus of the medial field is not shown.**

**Used with permission from Hamani et al., Brain 127:4-20, 2004.**

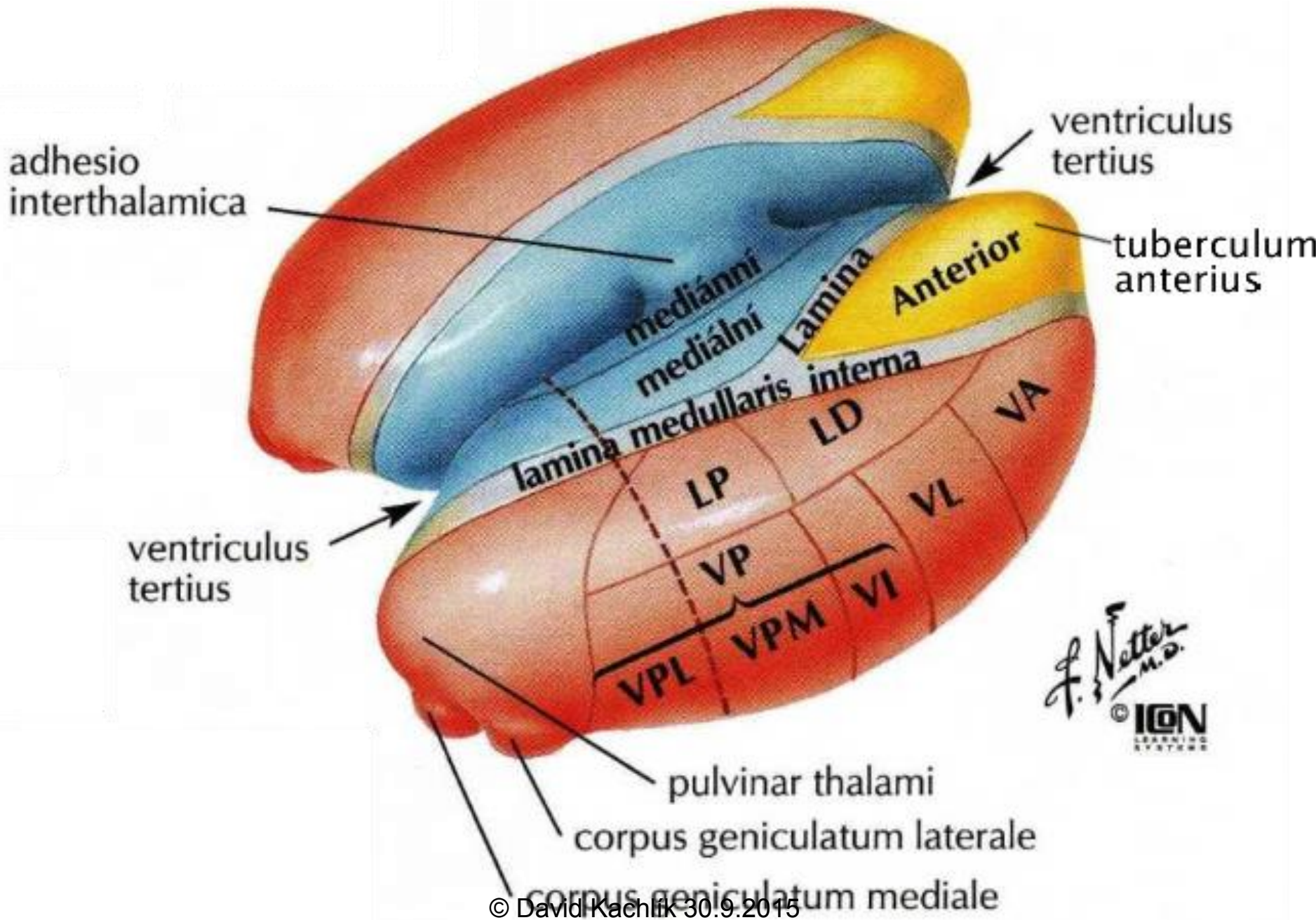


© Elsevier Ltd 2005. Standing: Gray's Anatomy 39e - [www.graysanatomyonline.com](http://www.graysanatomyonline.com)



# Thalamus (thalamus dorsalis)

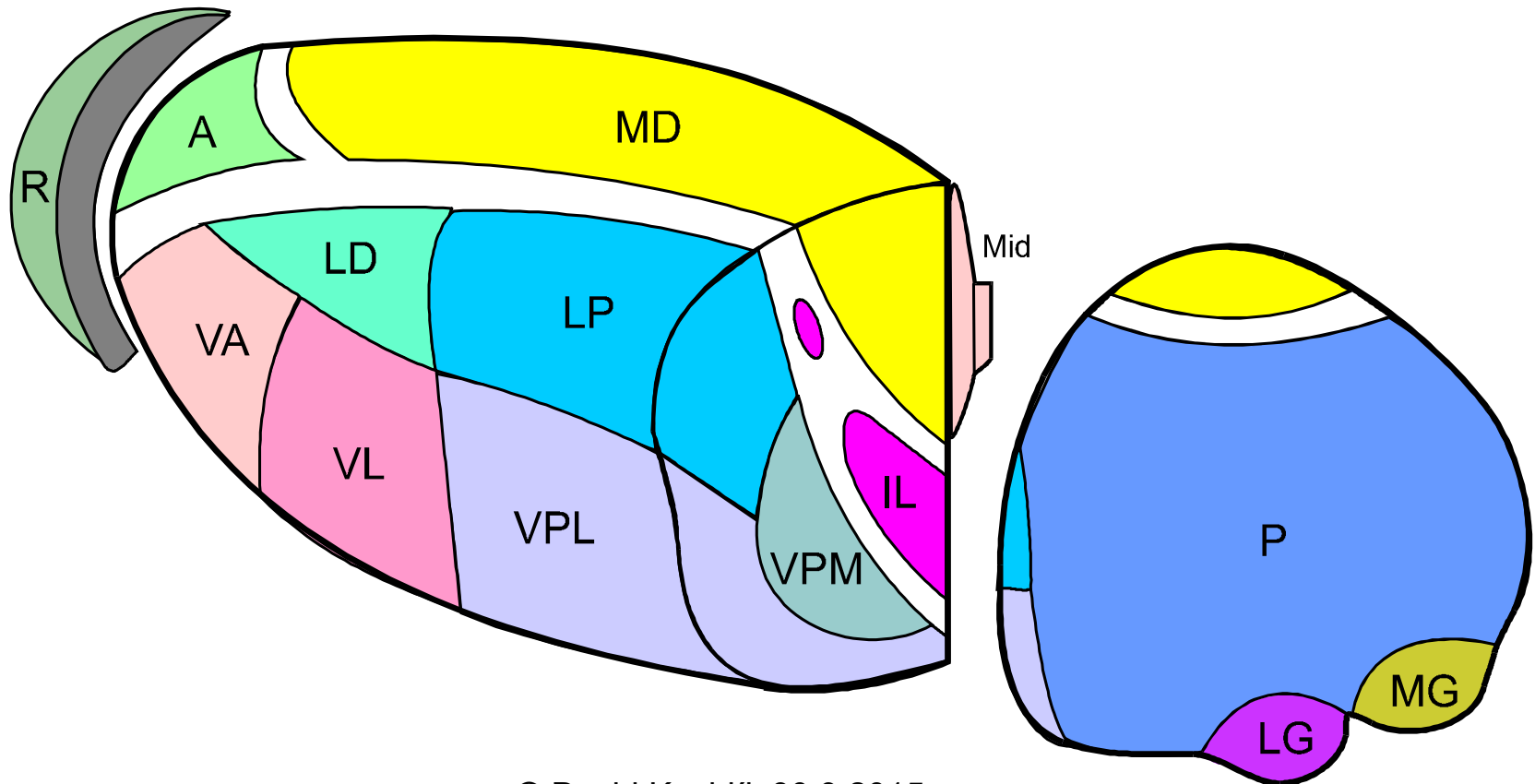
- „secretary of brain“ ← all except for smell
- pulvinar (dorsally)
- tuberculum anterius (ventrally)
- lamina medullaris medialis + lateralis thalami
- adhesio interthalamica (80 %) – *w/o notion*
- **Nuclei parcellated according to position or connection**
  - nuclei anteriores, dorsales, intralaminares, mediani, mediales, posteriores, ventrales, reticularis
  - specific sensory nuclei
  - specific non sensory nuclei
  - Non specific nuclei
  - Association nuclei



*F. Netter M.D.*  
 © IGM  
 LEARNING SYSTEMS

# Parcellation of thalamic nuclei acc to position

**nuclei anteriores, dorsales, intralaminares, mediani, mediales, posteriores, ventrales, reticularis**



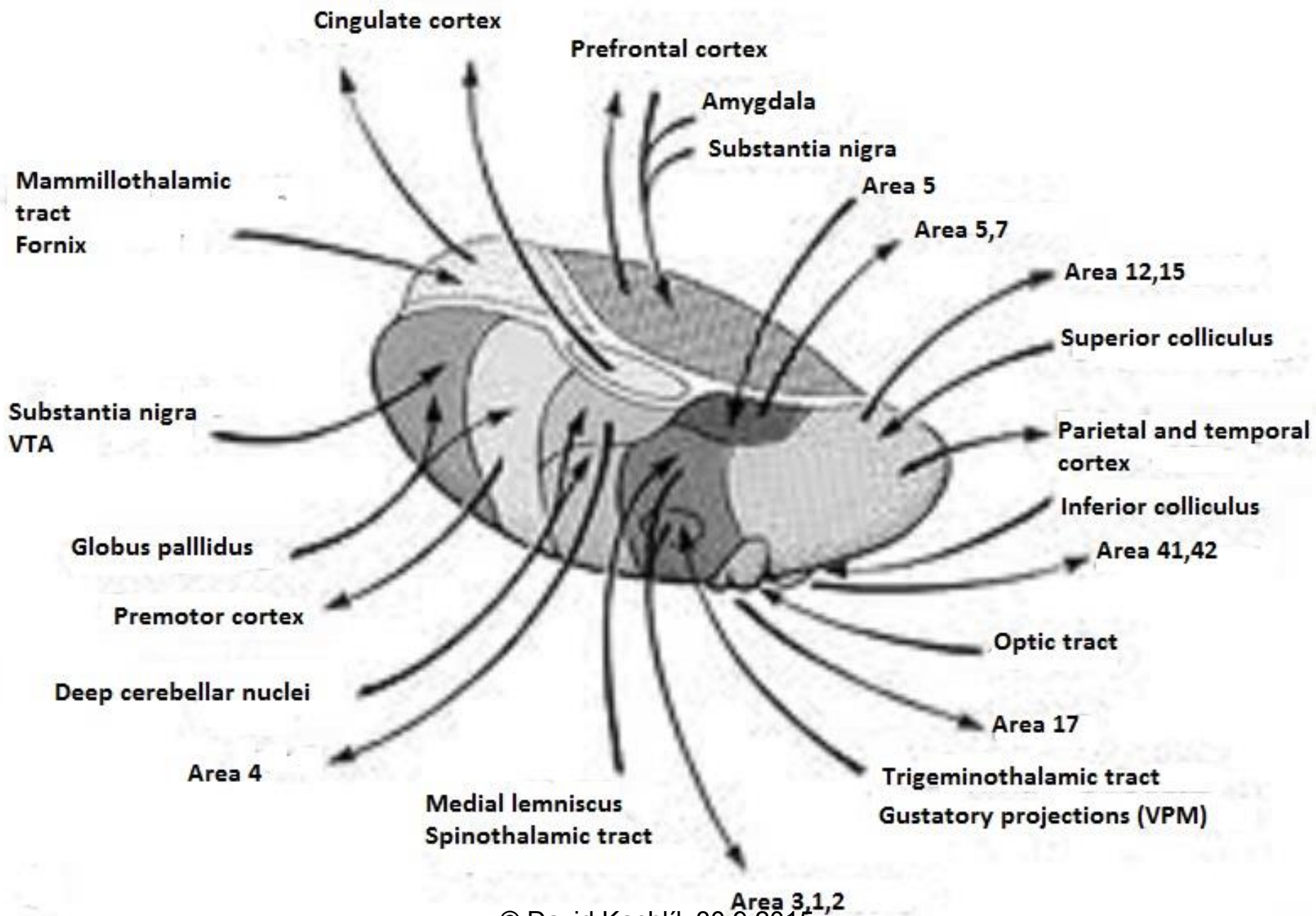
# Thalamic connections

## **AF:**

- sensitive and sensory
  - Pain, proprioception, touch, taste, balance, hearing, vision
- motoric
  - cerebellum, BG
- RF - ARAS
- limbic system
  - corpus mammillare, hippocampus

**EF:** cortex + hypothalamus

**Reciprocal connections:** BG, RF, cortex, stem, cerebellum, spine



# Specific nuclei

- tractus mamillothalamicus → **ncl. anterior** → gyrus cinguli
  - *reverberation enforces emotions*
- globus pallidus → **ncl. VA** → prefrontal cortex
- globus pallidus → **ncl. VL** → supplementary motoric cortex
- nucleus dentatus cerebelli → **ncl. VL** → motoric cortex
- lemniscus medialis et spinalis → **ncl. VPL** → senz. cortex
- lemniscus trigeminalis → **ncl. VPM** → sensitive cortex

# Association nuclei

- **ncl. LD (lat. dors.)** → area cingularis posterior
- Olfactory and limbic brain → **ncl. MD (mediodors.)**  
→ prefrontal cortex (*thinking, reasoning, mood, mind state – integration with sensory inputs*)
- colliculus superior → **ncl. LP (lat. post.) + pulvinar**  
→ visual and parietal association cortex  
(*draws attention to objects on the periphery of visual field*)
- **ncl. P (pulvinar)** → frontal, temporal, parietal and occipital association cortex  
(*integration of visual, auditory, tactile and proprioceptive inputs*)

# Non specific nuclei

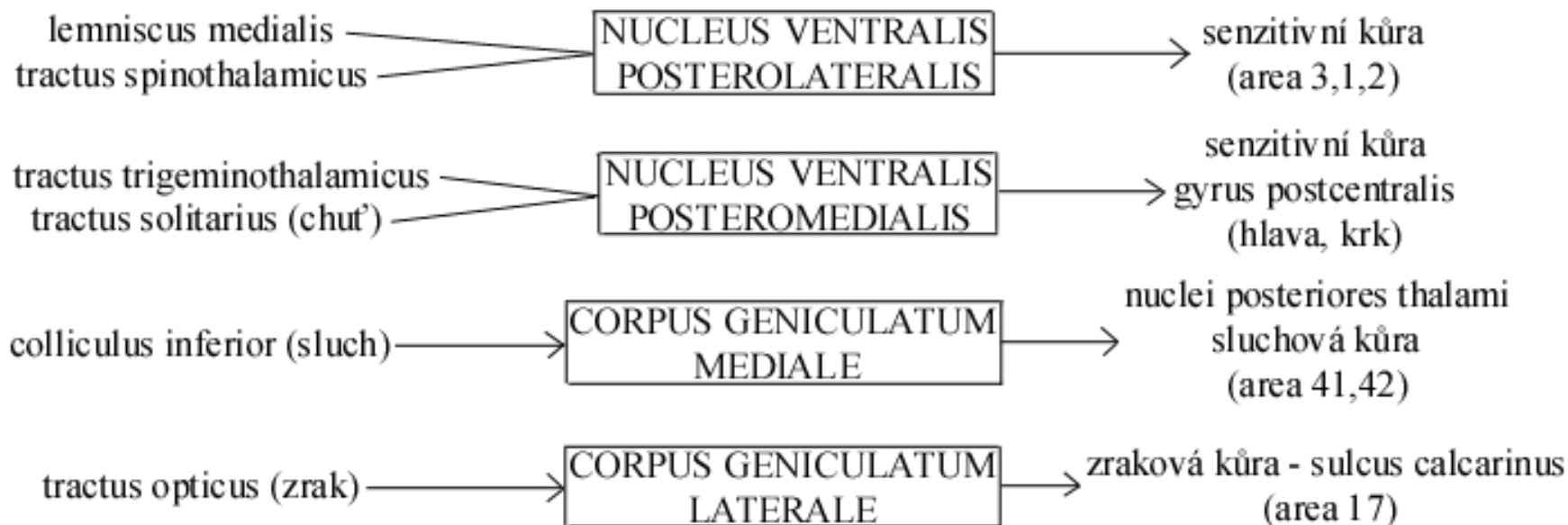
- ***ncll. intralaminares***
  - Slow pain
  - ARAS
- ***ncll. mediani***
  - Limbic system (according to efferentation)



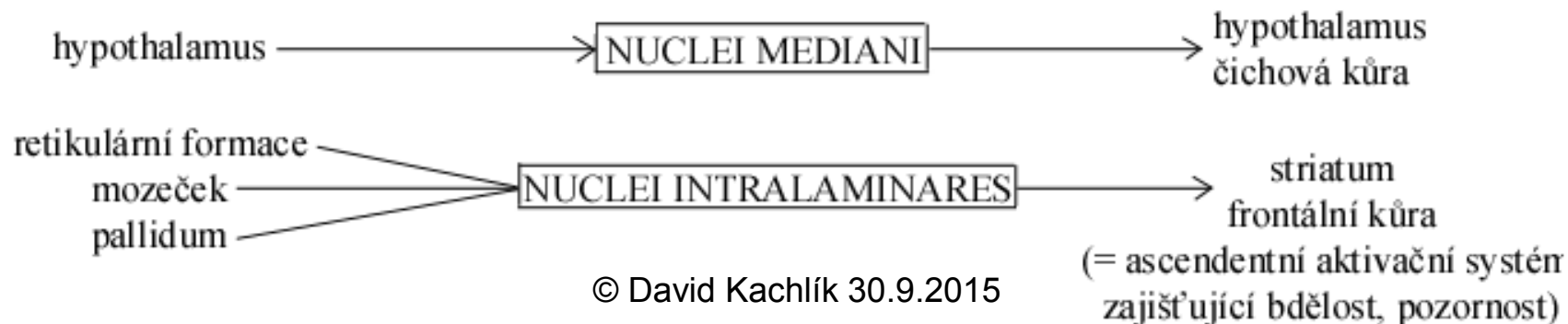
# Ncll. reticulares

- GABA
- Excitatory collaterals from all specific nuclei of thalamus and cortex
- Inhibitory efferentation back to thalamus
- Similarly as zona incerta
- *Function: labels new inputs and differentiates them from regular inputs from environment*

## SPECIFICKÁ SENZORICKÁ JÁDRA



## NESPECIFICKÁ JÁDRA



## SPECIFICKÁ NESENZORICKÁ JÁDRA



## ASOCIAČNÍ JÁDRA



# Thalamic connection

## Cortex

tractus thalamocorticalis ↑

↓ **tractus corticothalamicus – strong tract  
inhibiting thalamus**

*„cleaning further incoming informations“*

# Thalamic connection

- **sensitive + sensory inputs**
  - sensitivity (pain, proprioception, touch)
  - Special sensory (taste, balance, hearing, vision)
- **motoric inputs**
  - Cerebellum, basal ganglia
- **Reticular formation**
- **limbic system**
  - corpus mammillare
  - Hippocampal formation
- ncll. reticulares only do not have efferentation to other thalamic nuclei

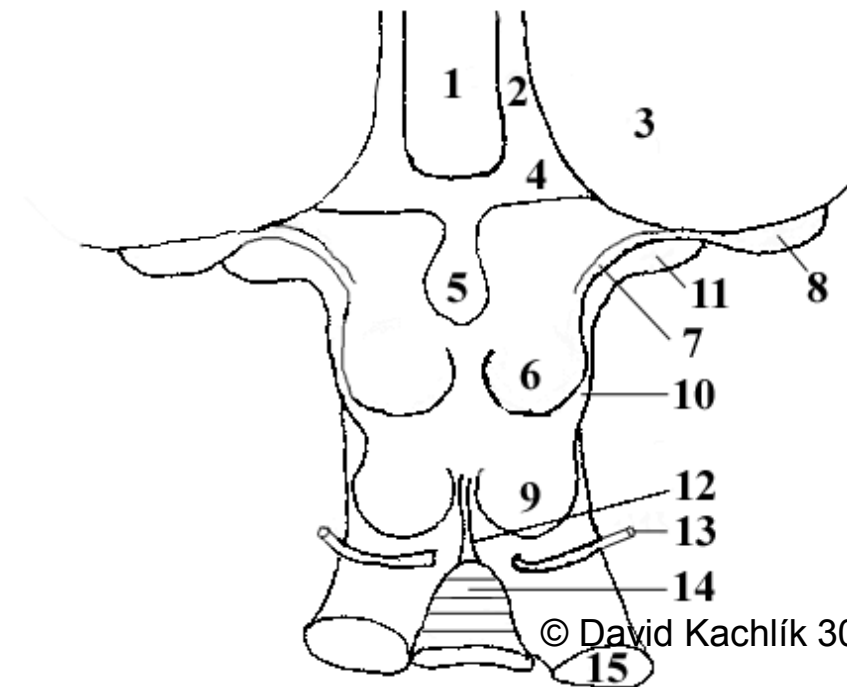
# Pain – *processing in thalamus*

- fast – acute
  - ncl. VPL + VPM
  
- slow – chronic
  - nuclei intralaminares
    - for example:
      - ncl. centromedianus (CM)
      - ncl. parafascicularis (PF)

# Metathalamus

- corpus geniculatum laterale – *visual center*
- corpus geniculatum mediale – *auditory center*

## DORSAL VIEW OF MESENCEPHALON



- 1 - third ventricle
- 2 - stria medullaris of thalamus
- 3 - pulvinar
- 4 - habenular trigone
- 5 - pineal gland
- 6 - superior colliculus
- 7 - brachium of inferior colliculus
- 8 - lateral geniculate body
- 9 - inferior colliculus
- 10 - brachium of superior colliculus
- 11 - medial geniculate body
- 12 - frenulum of superior medullary velum
- 13 - trochlear nerve
- 14 - lingula
- 15 - superior cerebellar peduncle

# Corpus geniculatum laterale

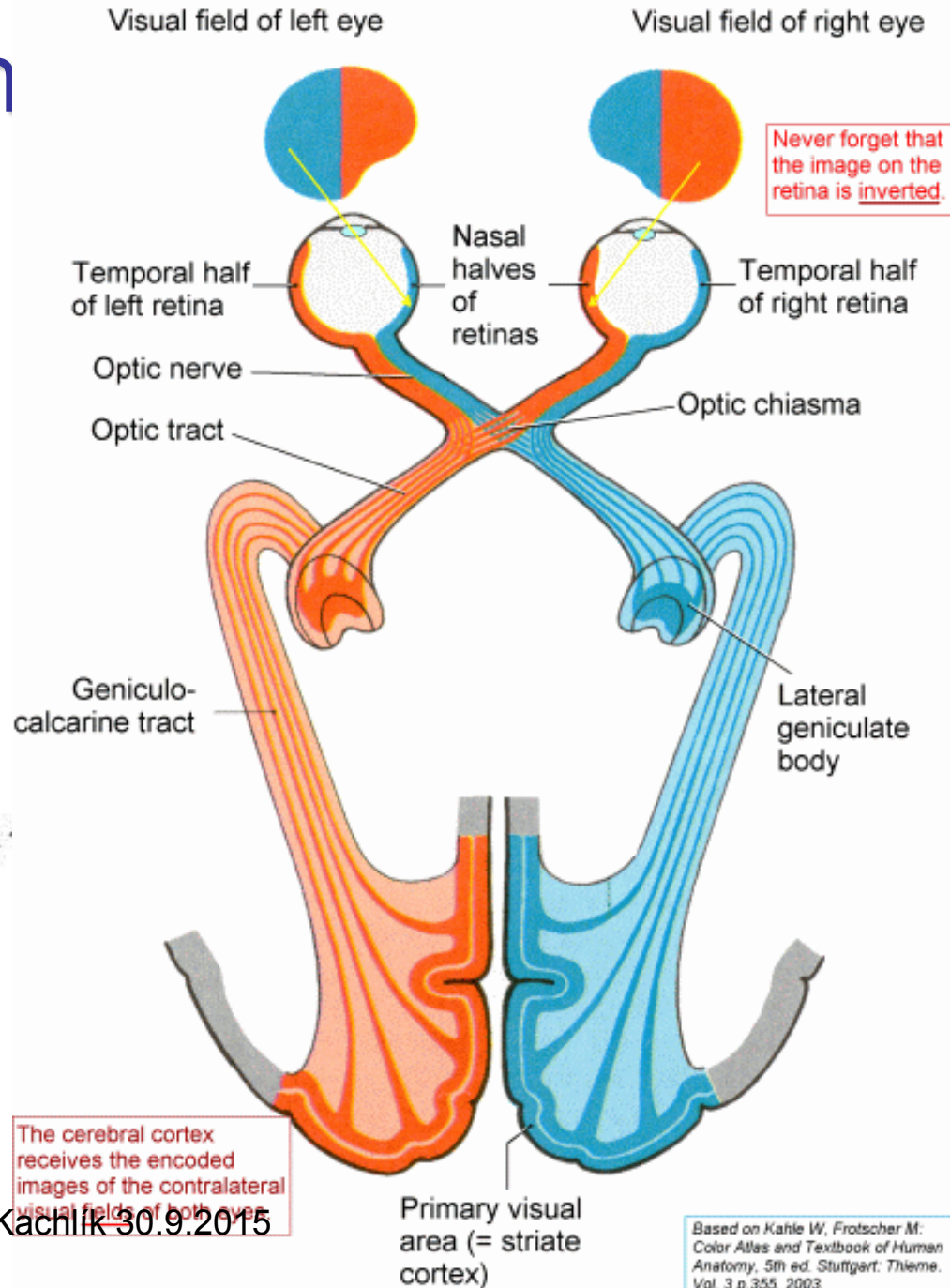
## Visual center

- *pars magnocellularis: movement, depth and perspective*
- *pars parvocellularis: diameters, volume, shape and colors*



# Thalam

1. nervus opticus
2. chiasma opticum
3. tractus opticus
4. corpus geniculatum laterale
5. radiatio optica
6. Visual cortex



# Thalamic syndrom

## „6 hemi“

- **hemihypestezia /hemianestezia**
- **hemiataxia (+ hemiapraxia)**
- **hemiparesis**
- **hemialgia (+ hemipathia)**
- **hyperkinesis choreatic and athetoid**
- **hemianopsia homonymous  
contralateral**
- **Consciousness problems / epilepsy /  
cataplexy**

# Clinical thalamic syndromes

## posterolateral thalamic syndromes

- sensitive and sensoric lesions
- thalamic syndrom =  
*Dejerine-Roussy syndrome*
  - ncl. VPL, VPM
  - thalamic pain



Joseph  
Jules  
Dejerine  
(1849-  
1917)



Gustave  
Roussy  
(1874-  
1948)

# Clinical thalamic syndromes

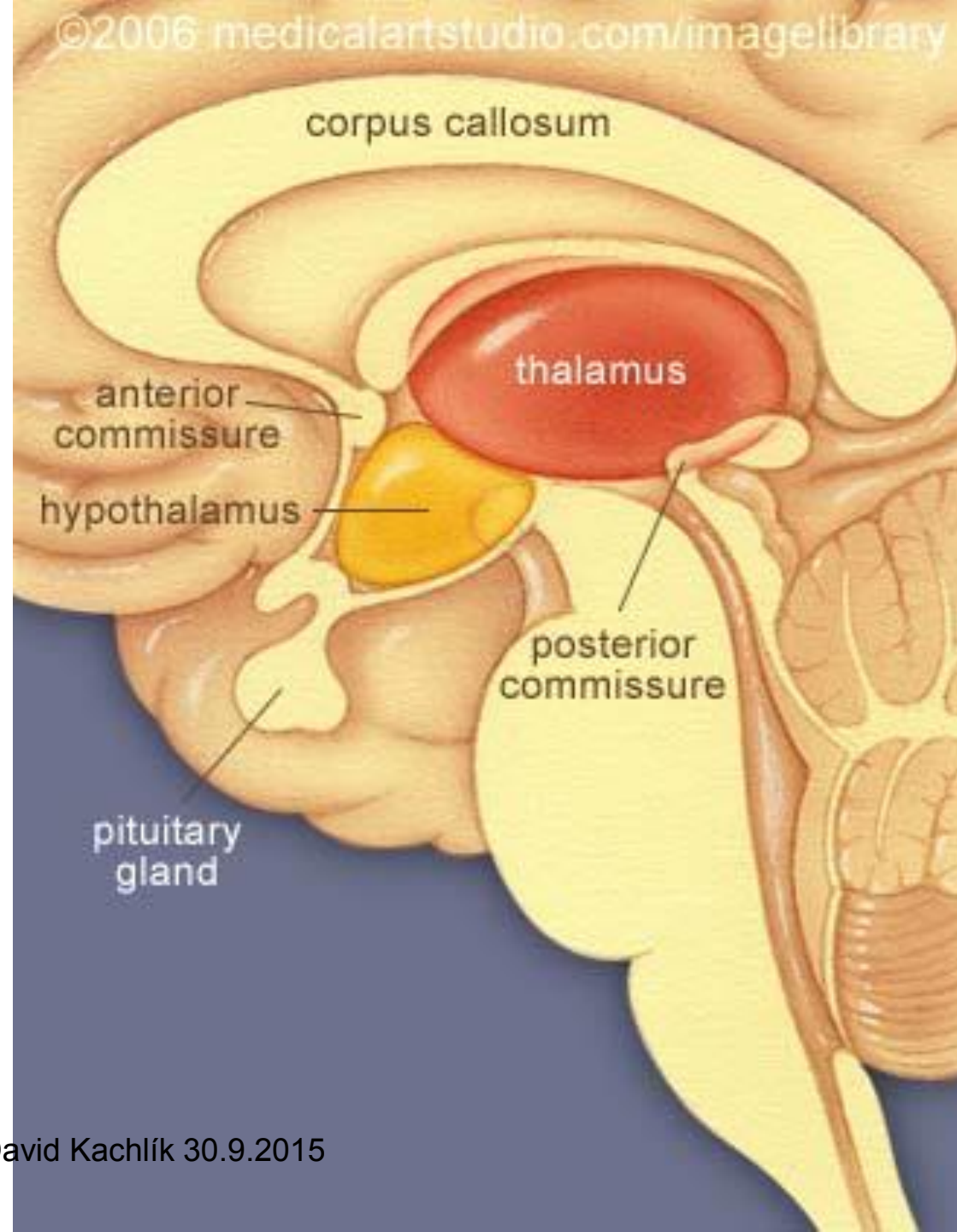
## medial thalamic syndromes

- Consciousness lesions
- „thalamic neglect“, thalamic amnesia, akinetic mutism

## anterolateral thalamic syndromes

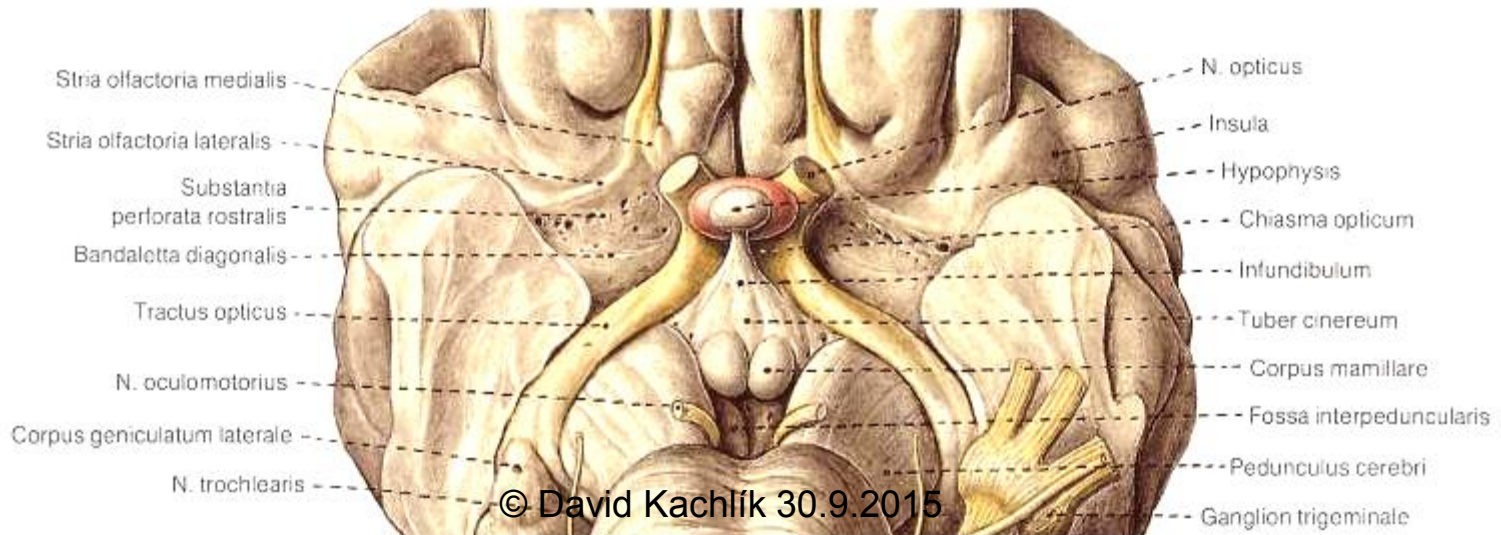
- Motoric lesions
- palsy, ataxia, motoric non coordination, dysphagia

# Hypothalamus



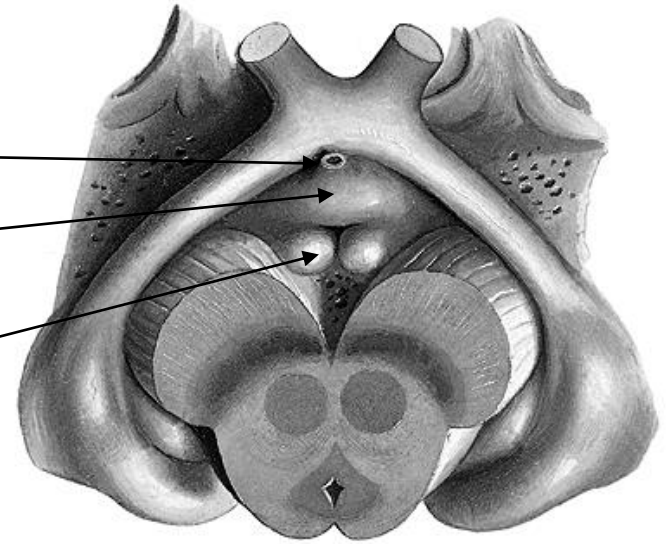
# Hypothalamus

- Is derivative of visceromotor zone of basal plate
- Highest autonomous center
- **infundibulum + hypophysis**
- **tuber cinereum (eminentia mediana) + corpus mamillare**
- **area preoptica + chiasma et tractus opticus**

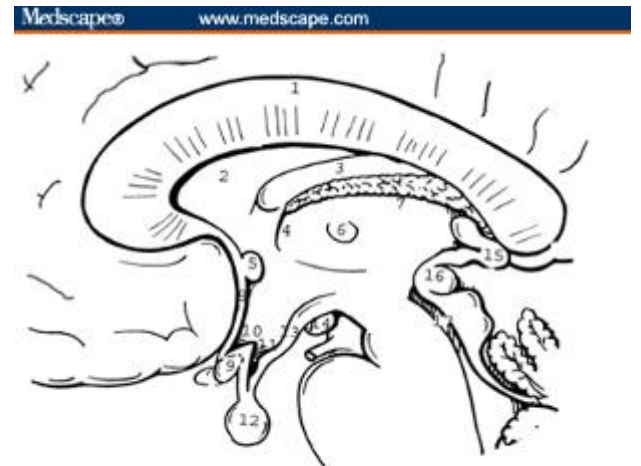


# Hypothalamus

- infundibulum
- tuber cinereum
- corpora mammillaria



- *recessus infundibuli*
- *recessus opticus*



# Hypothalamus – *borders*

- up: sulcus hypothalamicus
- down: base of brain
- front: lamina terminalis
- back: continues into tegmentum mesencephali
- Medially: 3rd ventricle
- laterally: capsula interna



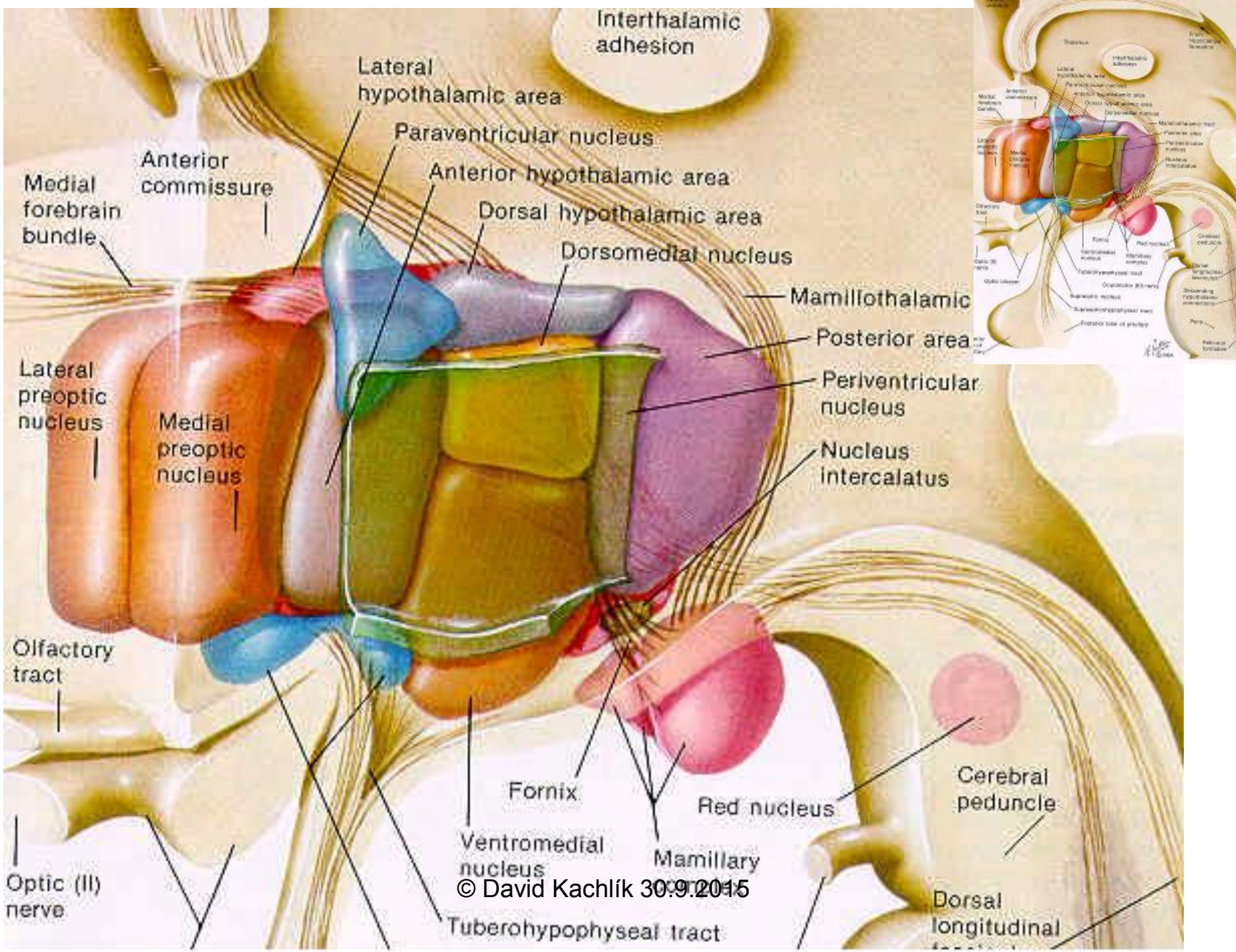
# Hypothalamus

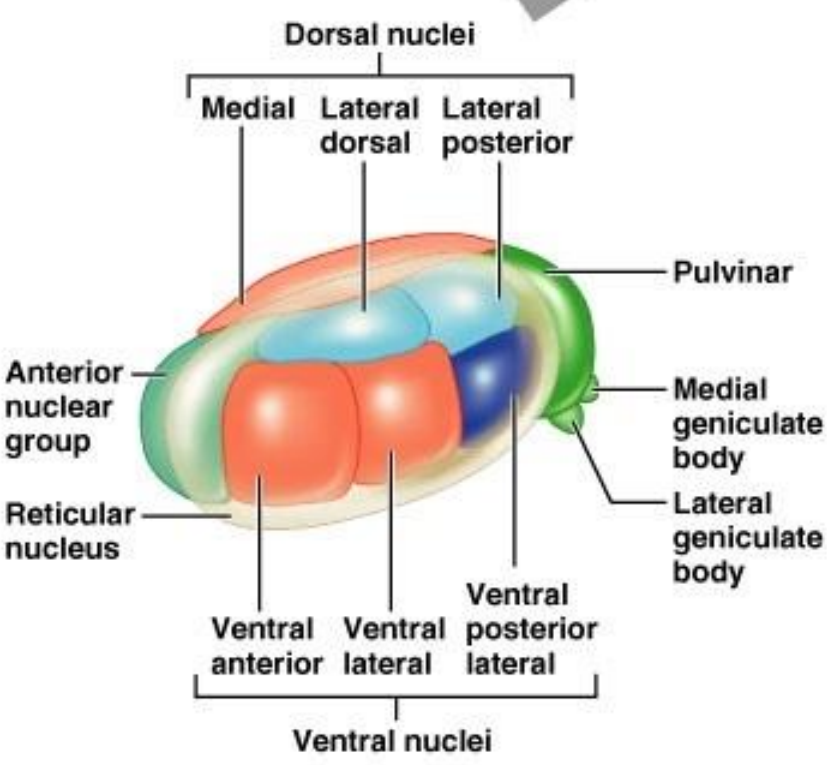
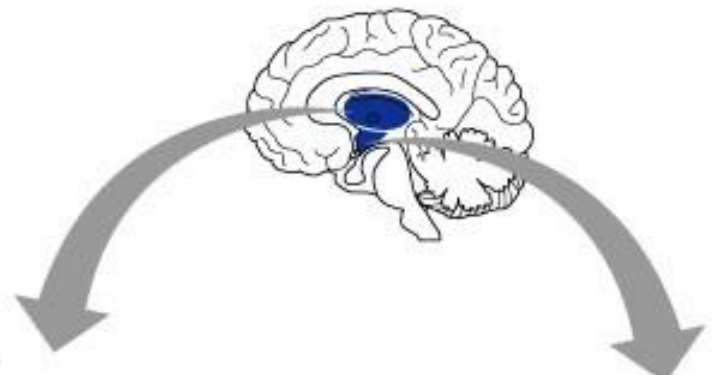
3 longitudinal zones: periventricular, medial, lateral zones

3 horizontal zones: anterior, middle, posterior hypothalamus

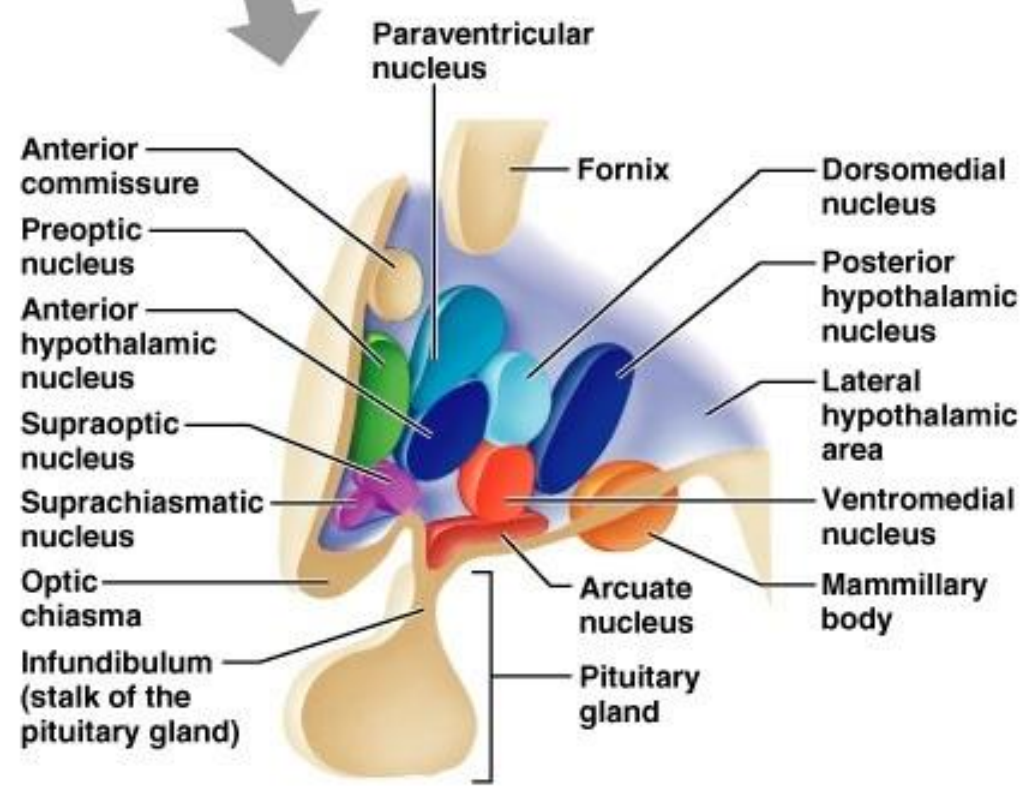
## Nuclei

- **ventral hypothalamus** (area hypothalamica rostralis) - **nucleus paraventricularis, supraopticus, suprachiasmaticus**
- **middle hypothalamus** (area hypothalamica intermedia et dorsalis) **nuclei tuberales laterales et ventromediales**
- **posterior hypothalamus** (area hypothalamica posterior) - **nuclei mammillares, nucleus h. posterior, nucleus tuberomammillaris**

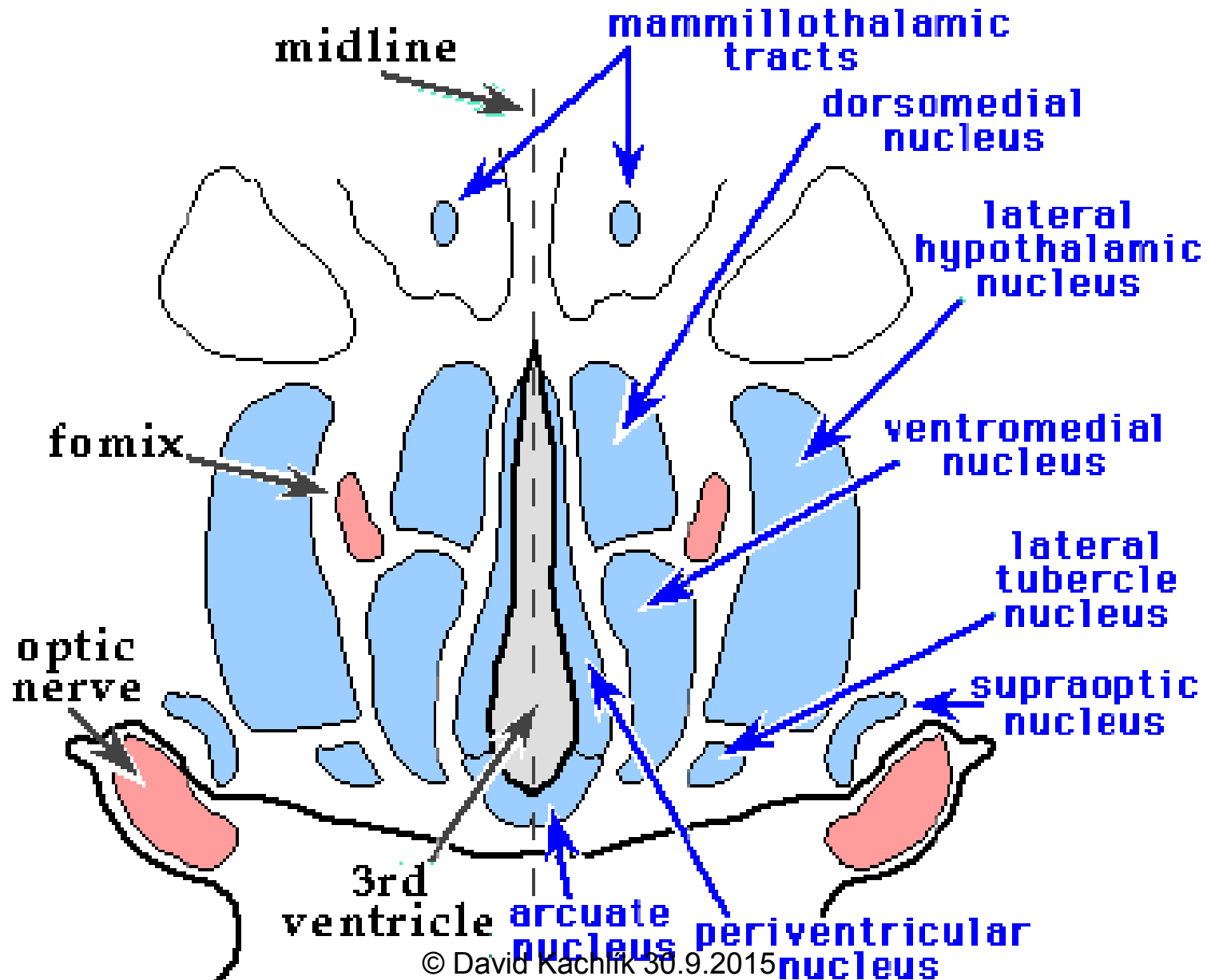




**(a)**



**(b)**



# Hypothalamus – function

Receives inputs from almost all receptors – especially from **RF, prefrontal cortex and hippocampus**

## *former hypothesis:*

- **anterior** hypothalamus - **parasympaticus**
- **Middle** hypothalamus - **sympaticus**
- **posterior** hypothalamus – **limbic system**

# Hypothalamus – *fyziology*

Hormones (blood), nerves, CSF



**HYPOTHALAMUS**

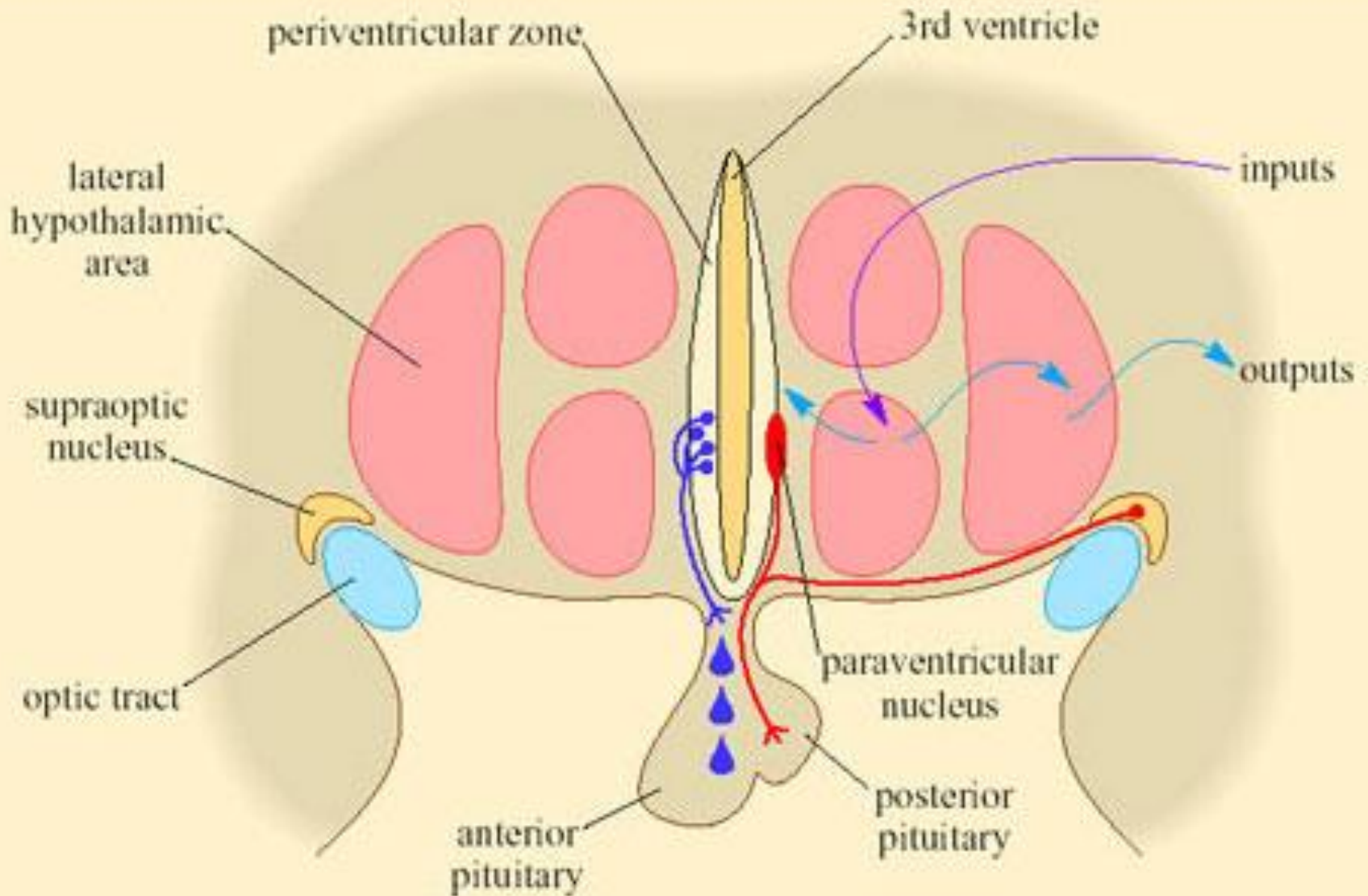


Endocrine + autonomic system



***HOMEOSTASIS***

***emotions*** (= LIMBIC SYSTEM)



# Hypothalamus – *function*

- termoregulation
  - center **hyperthermia** – anterior h.
  - center **cold** – posterior h.
- lateral h.: center **hunger, thirst and anger**
- medial h.: center **satiety** and **passivity**
- anterior h.: center **sleep and wake**
- **sex**
  - ♂ *nucleus preopticus*
  - ♀ *nucleus ventromedialis*



# Hypothalamus – *function*

- *ncl. suprachiasmaticus*
  - center of circadian rhythms
- *ncl. supraopticus + paraventricularis*  
(*magnocellular neurons*)
  - ADH (vazopresin) + oxytocin
- *ncl. arcuatus (infundibularis) and around*  
(*parvocellular neurons*)
  - statins and liberins
- *ncl. tuberomamillaris*
  - histamine to brain and spine („arousal“)
    - Activated by *orexin from lat. hypothalamus*
    - Lack in narcolepsia

# Anterior hypothalamus

- ncl. paraventricularis - *oxytocin, ADH*
- ncl. supraopticus – *oxytocin, ADH*
- ncl. preopticus medialis – *blood pressure down, puls too*
- ncl. hypothalamicus anterior – *termoregulation, sweating, inhibition of TSH*
- ncl. suprachiasmaticus – *circadian rhythm*

# Sexually dimorphic areas of anterior hypothalamus

- SDN (sexually dimorphic nucleus) – in area preoptica bigger in males comp to females (?testosterone effect)
- INAH3 in humans, oSDN in sheeps, SDN-POA in rats, AHdc in macaques, POM in quails
- Affects sexual behavior in animals

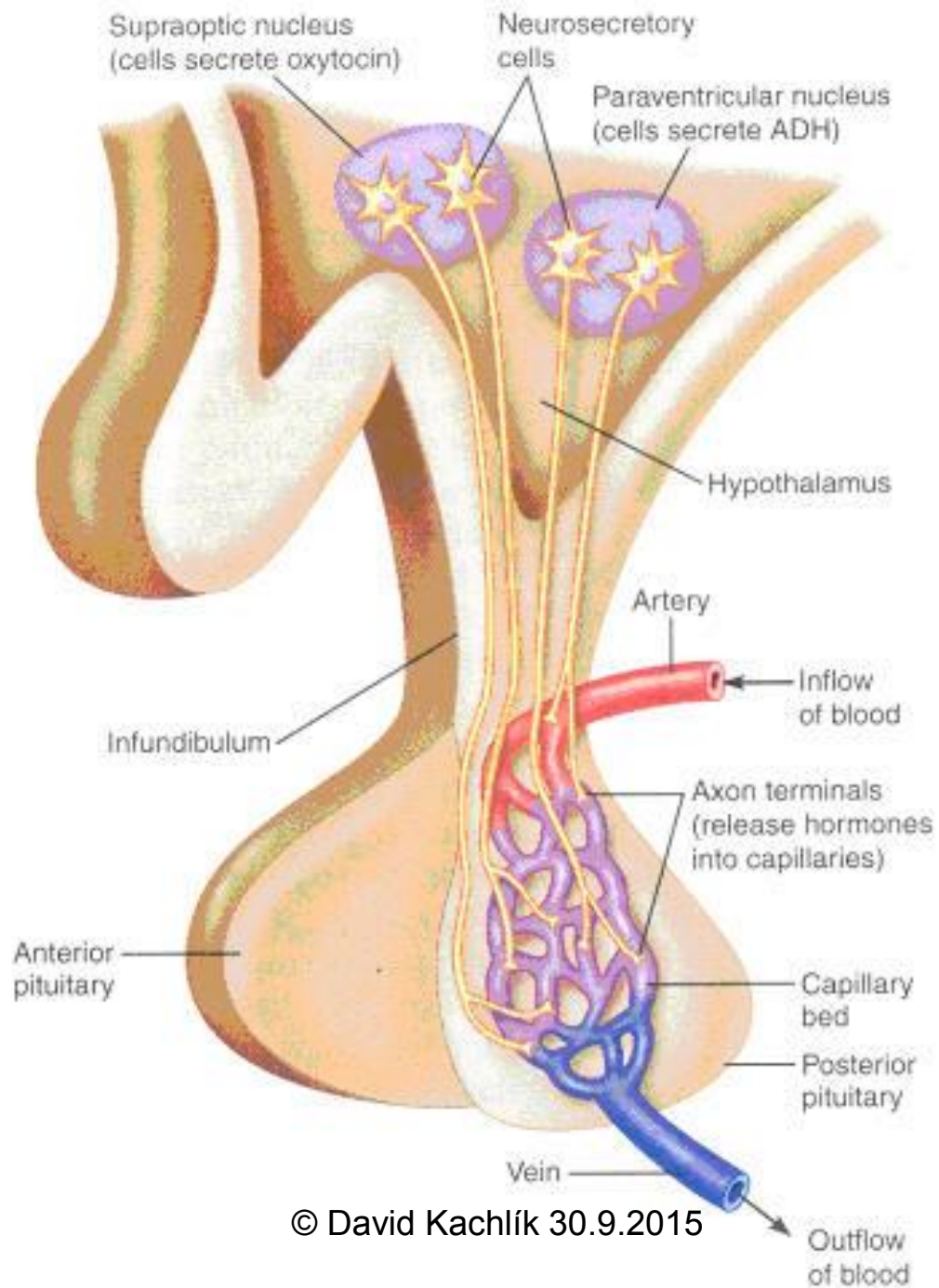
# Middle hypothalamus

= tuberal hypothalamus (tuber cinereum)

- ncl. infundibularis = ncl. arcuatus – *statins and liberins*
- ncl. tuberales – *hunger and thirst*
- ncl. hypothalamicus ventromedialis - *hunger*
- ncl. hypothalamicus dorsomedialis – *increase of blood pressure and puls*

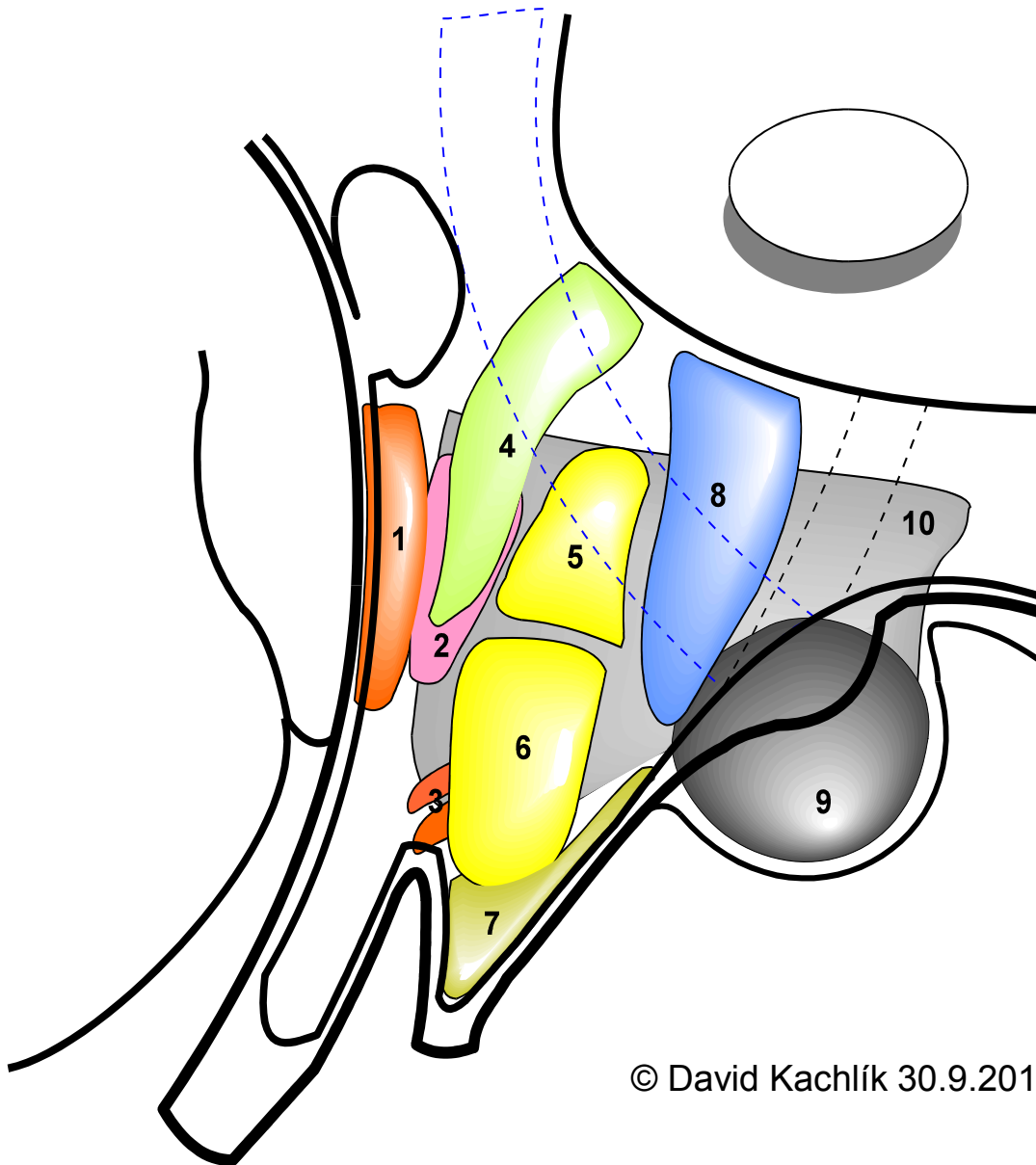
# Posterior hypothalamus

- ncl. mammillares
  - *memory, connection to limbic system*  
(ncl. anterior thalami)
  
- ncl. hypothalamicus posterior
  - *increase of blood pressure, mydriasis, tremor*



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# Hypothalamus



## MEDIAL ZONE

### Preoptic Region

1. Preoptic Nucleus

### Anterior (Supraoptic) Region

2. Anterior Nucleus
3. Supraoptic Nucleus
4. Paraventricular Nucleus

### Intermediate (Tuberal) Region

5. Dorsomedial Nucleus
6. Ventromedial Nucleus
7. Infundibular or Arcuate Nucleus

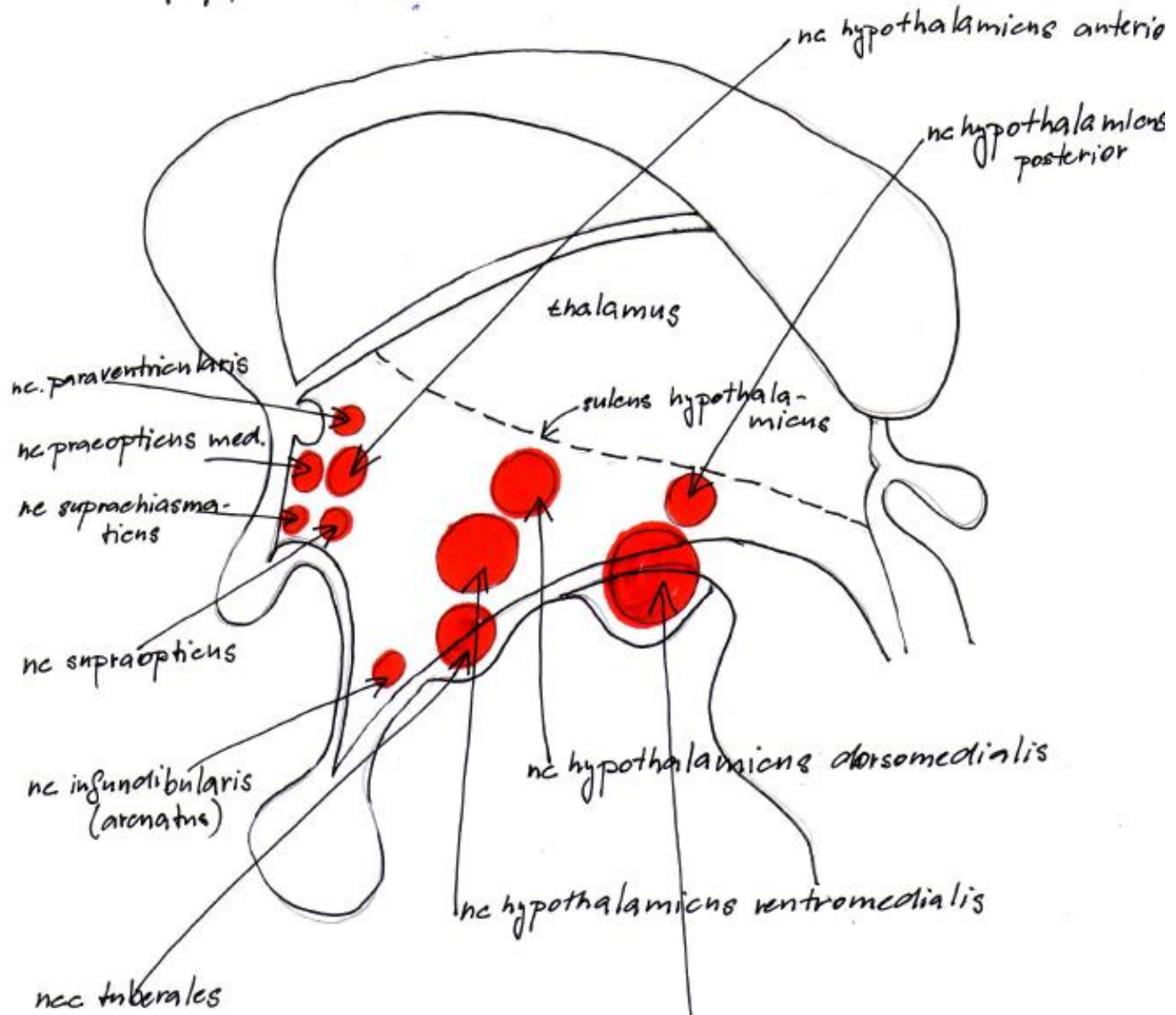
### Posterior Region

8. Posterior Nucleus
9. Mammillary Nucleus

## LATERAL ZONE

10. Lateral Hypothalamic Nucleus

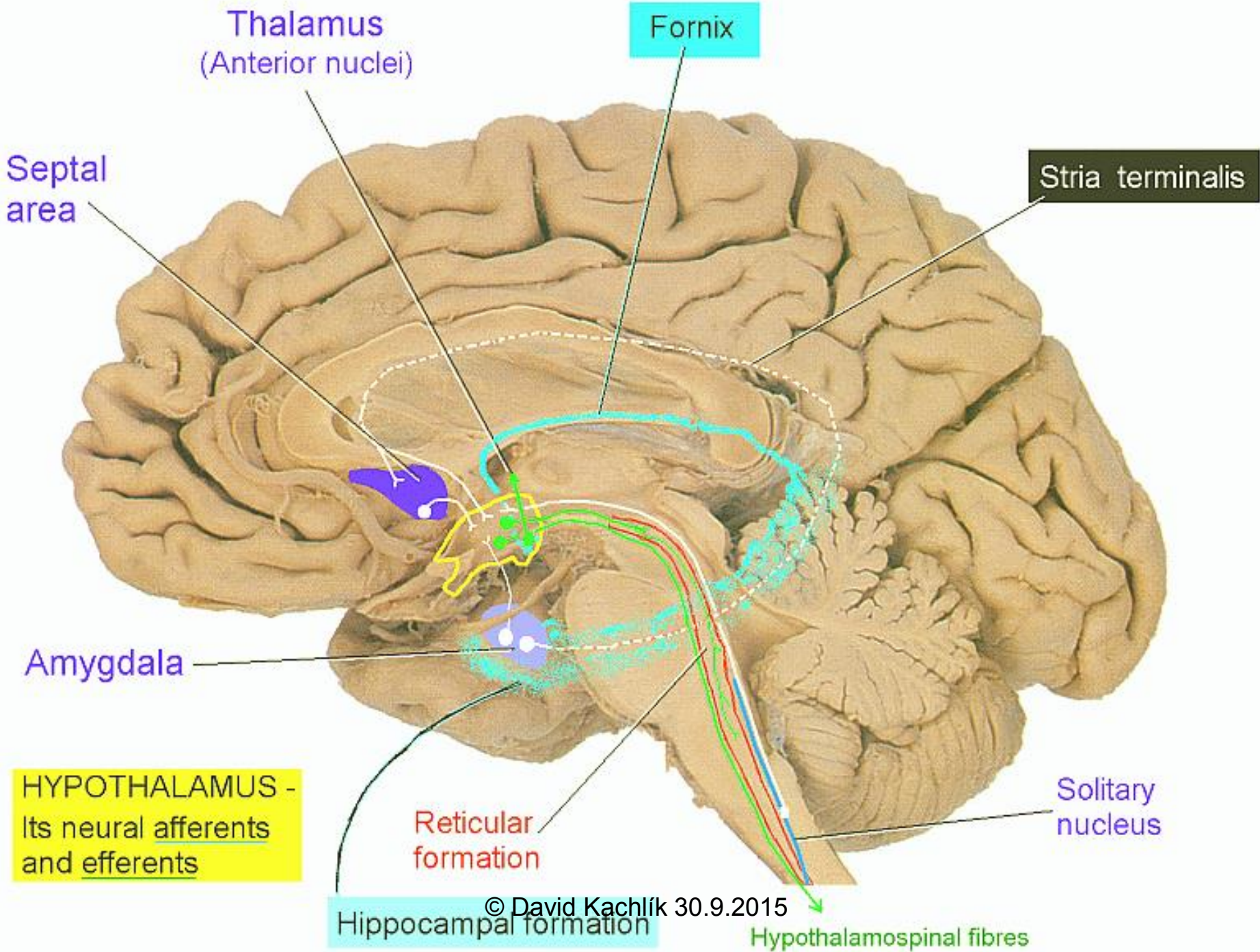
# HYPOTHALAMUS





# Hypothalamus – *white matter*

- **fornix** → corpus mammillare (nuclei corporis mammillaris) → tractus mammillaris princeps /splits into/
  - tractus mamillothalamicus → ncl. anteriores thalami
  - tractus mamillo tegmentalis → RF of stem (ncl. *Guddeni*)
- **stria terminalis**
  - corpus amygdaloideum → hypothalamus
- **stria medullaris thalami**
  - hypothalamus → habenula



# Hypothalamus – *white matter*

- **fasciculus medialis telencephali**
  - = fasciculus prosencephalicus medialis = medial forebrain bundle (**MFB**)
  - between medial and lateral zone of nuclei – connects hypothalamus with cortical limbic system + limbic system of brain stem (+ RF)
- **pedunculus mammillaris**
  - connects corpora mammillaria and nucleus dorsalis tegmenti *Guddeni* (in RF of mid brain) and **fasciculus longitudinalis posterior Schützi**
  - ncl. in medial zone of hypothalamus → autonomic nuclei, nuclei of cranial nerves (eventually into spine)

# Hypophysis (pituitary gland)

- **adenohypophysis (= lobus anterior)**
  - Development from *Rathke pouch* from roof of pharynx
  - hormones (**ACTH, TSH, FSH, LH, STH, MSH**)
  - Influenced by hypothalamic **releasing and inhibiting hormones**
  - transport from ncl. arcuatus via tractus tuberoinfundibularis (= neurokrinie) → *hypotalamo-hypofyzoportal system*
  - *Sheehan syndrome*
- **neurohypophysis (= lobus posterior)**
  - Development as diencephalic pouch
  - nucleus supraopticus (vazopressin = ADH)
  - ncl. paraventricularis (oxytocin)
  - axonal transport from **hypothalamus**
  - Reacts to changes of osmolality via *organum subfornicale*

# Hypothalamus – *summary*

- Part of limbic system = preserve of species and individual
  - reproduction
  - Growth and metabolism
  - Intake of food and water
  - Attack and defense
  - thermoregulation
  - Cycle of wake - sleep
  - memory

# Optional reading

## Neuroanatomy of sleep cycle

# Why sleep?

- You need almost as much sleep after a day of sitting around the house as after a day of intense physical or mental activity (Horne and Minard, 1985, Shapiro et al., 1981).
- You feel tired at the end of the day because inhibitory processes in your brain force you to become less aroused and less alert.

# Functions of sleep

- Rest our muscles
- Decrease metabolism
- Rebuild proteins in the brain
- Reorganize synapses
- Strengthen memories



# Why sleep?

- You need almost as much sleep after a day of sitting around the house as after a day of intense physical or mental activity (Horne and Minard, 1985, Shapiro et al., 1981).
- You feel tired at the end of the day because inhibitory processes in your brain force you to become less aroused and less alert.

# Why sleep?

- You need almost as much sleep after a day of sitting around the house as after a day of intense physical or mental activity (Horne and Minard, 1985, Shapiro et al., 1981).
- You feel tired at the end of the day because inhibitory processes in your brain force you to become less aroused and less alert.

# Search for primary reason

- All species sleep, not just vertebrates with big brain and complex memories
- Bacteria have circadian rhythms
- Conservation theory:
  - -Simple way of conserving energy
- NASA's Rover built to explore Mars had mechanisms to make it „sleep“ at night to conserve its batteries.

# Conservation theory

- We might not guess original function for which it was evolved.
- Consider computer analogy:
- Important functions today include writing papers, sending e-mail, searching Internet, playing games, storing photographs, playing movies etc.
- Previously served for mathematical operations

# Search for primary reason

- Sleep conserves energy during the inefficient time
- Mammal's body temperature is decreased by 1°C or 2°C during sleep
- Animals increase sleep duration during food shortages
- **Sleep** is therefore analogous to **hibernation**

# Hibernation

- Hibernating animals decrease their body temperature to that of the environment (but do not let it drop to freeze 😊)
- Hamsters sometimes hibernate, if you let your favorite pet during winter in cold place, make sure it is not hibernating before you bury it 😊
- Hibernating animals come out of hibernation for few hours every few days, raising temperature to normal

# Hibernation

- Hibernating retards the ageing process
- Hibernation is also a period of relative invulnerability to infection and trauma. Procedures that would ordinarily damage brain, such as inserting a needle into it, produce little if any harm (Zhou et al.,2001)
- Na-K dependent ATPase on cell membrane

# Hibernation

- Herbivores graze many hours per day – sleep is briefer and often interrupted
- Dolphins and other aquatic mammals have asleep one hemisphere at time, other is awake and control swimming and breathing
- Birds during migration decrease need for sleep – in primates drugs exciting glutamate receptor can decrease sleep need
- Even if you keep migratory bird in cage during migratory period, it does not sleep



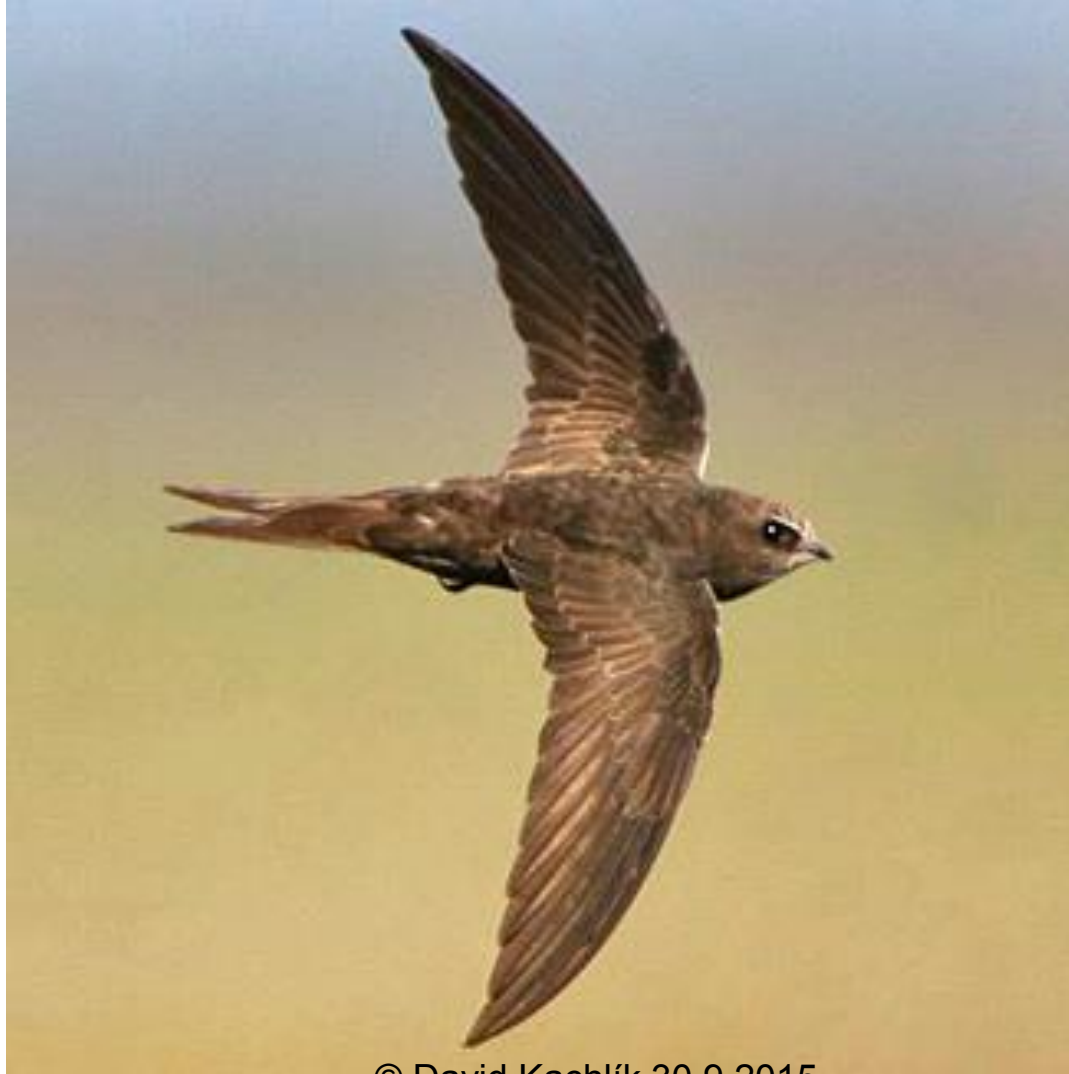
# Hibernation

- The fact that it is possible to decrease the need for sleep argues that sleep is not necessary for repair and restoration, or at least that sleep usually last longer than required for repair and restoration



Hazel dormouse  
hibernating

# Swift example



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# Swift example

- Question: when a baby swift first takes off from its nest, how long would you guess its first flight lasts, until it lands again?
- Answer: up to 2 years!
- It spends both night and days in the air, except huge storms
- Perhaps it switches brain hemispheres, but we do not know – EEG during flight is problem

# Other functions of sleep

- Restorative functions
- Sleep and memory
- 600 hrs of REM per year
- REM – eyeball movement for cornea to get enough oxygen by shaking eyeballs
- Strengthening consolidation of different type of memory

# Biology of dreaming

- Activation-synthesis hypothesis – dreams begin with periodic bursts of spontaneous activity in the pons – the PGO waves, which partly activates many but not all parts of the cortex. Cortex combines this haphazard input with whatever other activity was already occurring and does its best to synthesize a story that makes sense of all this information

# Biology of dreaming

- Because activity is suppressed in the primary visual cortex and somatosensory cortex, normal sensory information cannot compete with the self-generated stimulation and hallucinations result
- Input from pons usually activates amygdala – emotional processing
- Prefrontal cortex is inactive during PGO waves, memory is weak

# Biology of dreaming

- Patients with pons lesion still have dreams, even though they do not move eyeballs and other features of REM
- Paradox: brain produces dreams, but do not perceive them as self-produced. Some people can tickle themselves and actually feel it as a tickling sensation, at least slightly

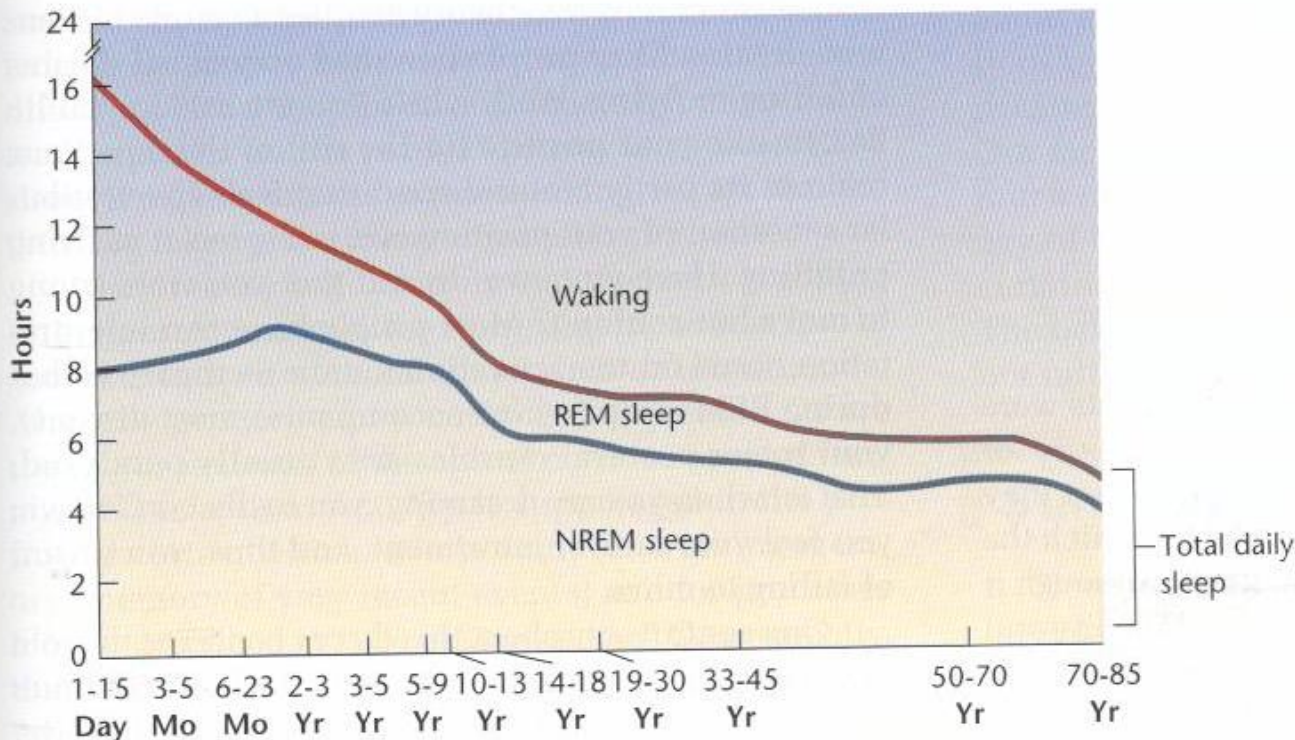
# Biology of dreaming

- Clinico-anatomical hypothesis
- Similar to activation-synthesis theory
- Inferior part of parietal cortex is active during dreaming – patients with damage have no dreams
  
- [www.dreamresearch.net](http://www.dreamresearch.net)



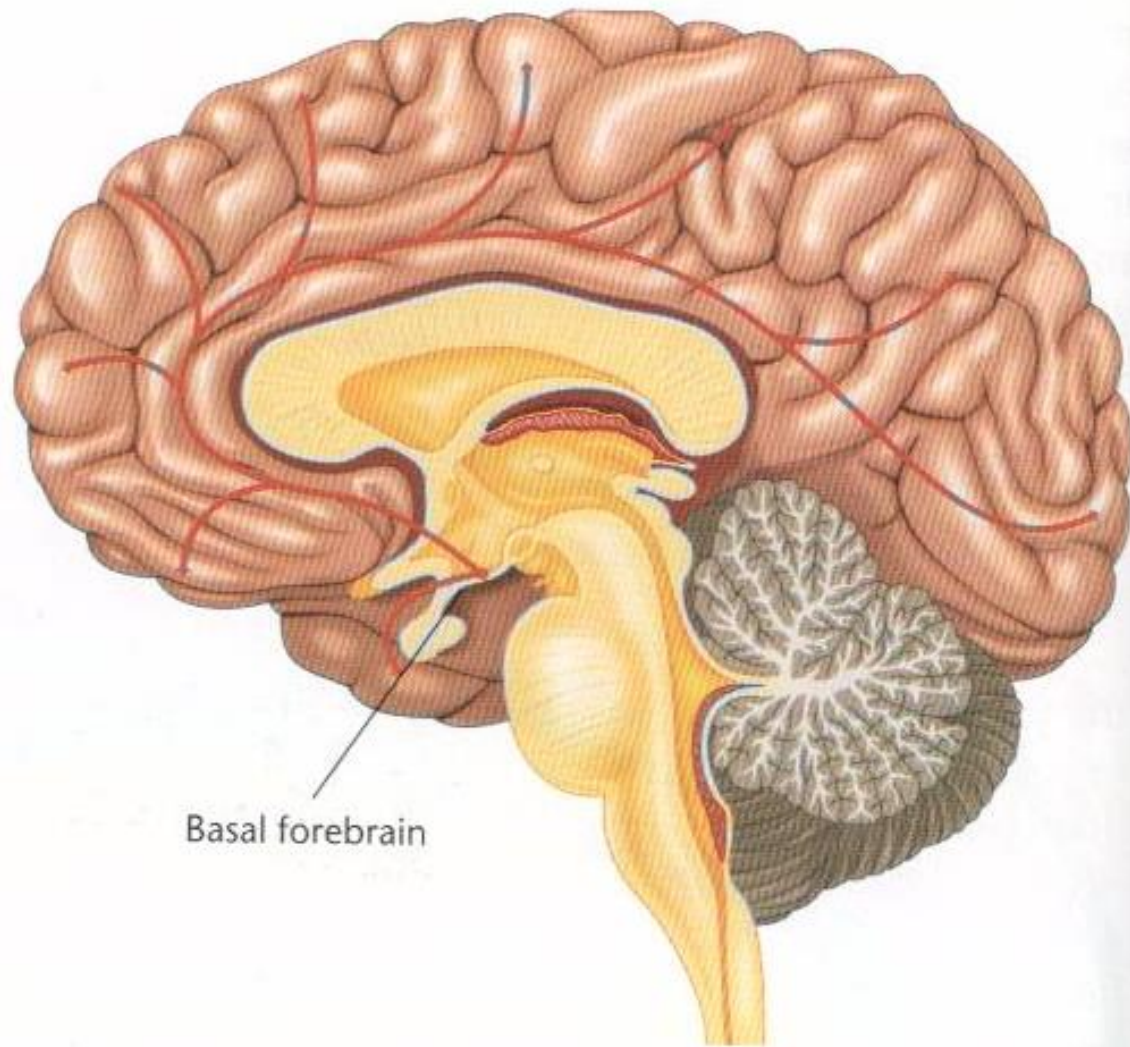
# Variation in sleep

- Cats and bats eat rich food and face little threat – they sleep many hours per day



**Figure 9.18** Time spent by people of different ages in waking, REM sleep, and NREM sleep

REM sleep occupies about 8 hours a day in newborns but less than 2 hours in most adults. The sleep of infants is not quite like that of adults, however, and the criteria for identifying REM sleep are not the same. (Source: From "Ontogenetic development of human sleep-dream cycle," by H. P. Roffwarg, J. N. Muzio, and W. C. Dement, *Science*, 152, 1966, 604–609. Copyright 1966 AAAS. Reprinted by permission.)

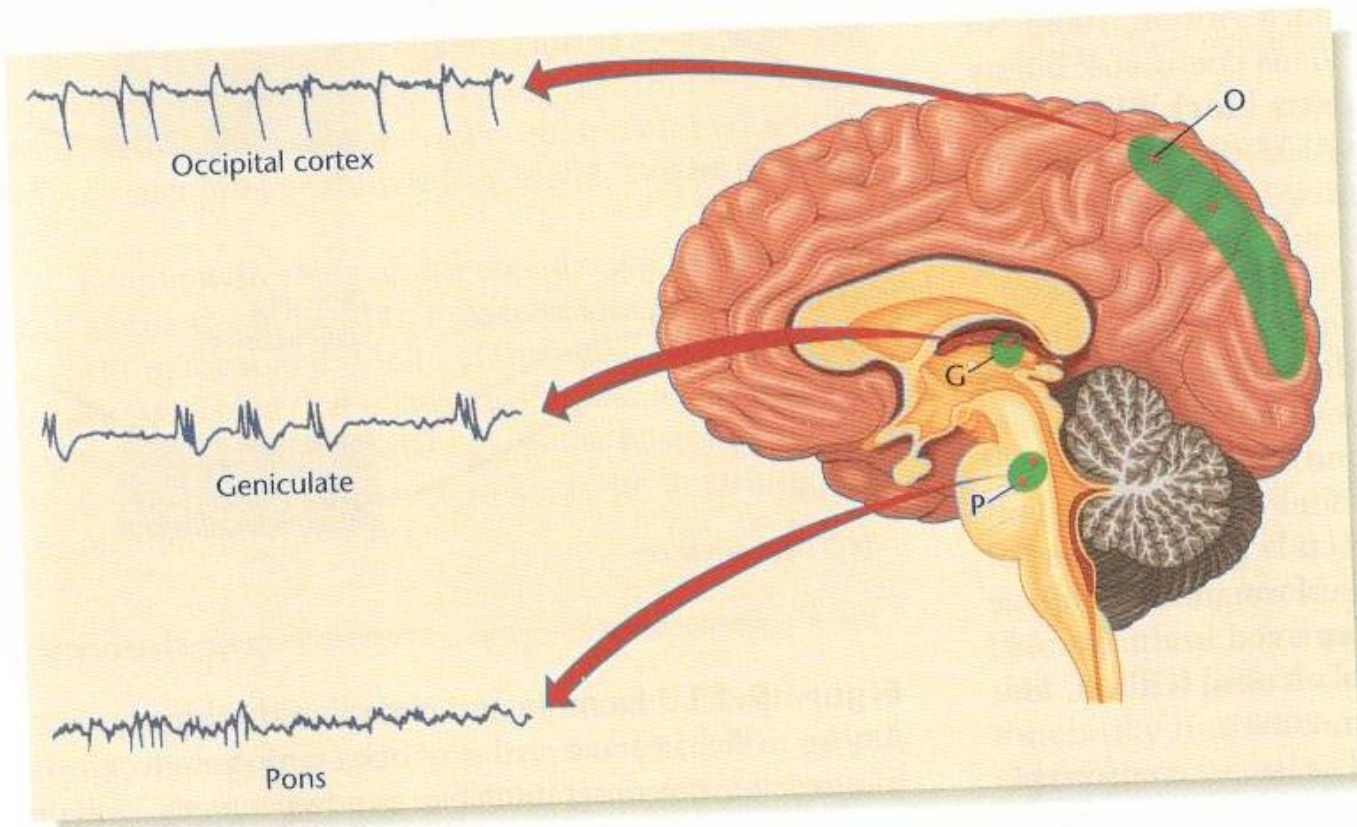


### Figure 9.12 Basal forebrain

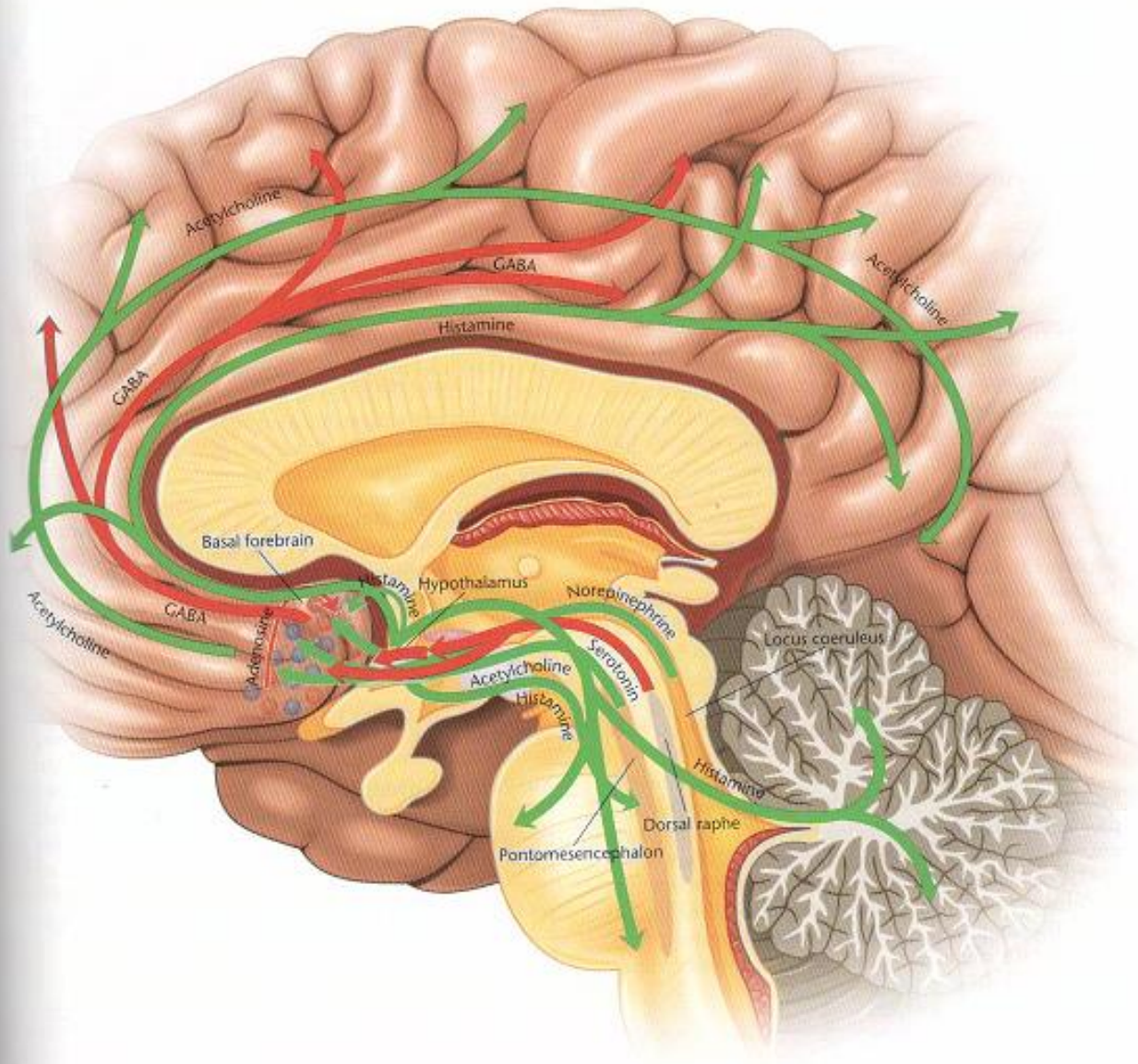
The basal forebrain is the source of many excitatory axons (releasing acetylcholine) and inhibitory axons (releasing GABA) that regulate the activity of the cerebral cortex.

**Table 9.1 Brain Structures for Arousal and Sleep**

Structure	Neurotransmitter(s) It Releases	Effects on Behavior
Pontomesencephalon	Acetylcholine, glutamate	Increases cortical arousal
Locus coeruleus	Norepinephrine	Increases information storage during wakefulness; suppresses REM sleep
Basal forebrain		
Excitatory cells	Acetylcholine	Excites thalamus and cortex; increases learning, attention; shifts sleep from NREM to REM
Inhibitory cells	GABA	Inhibits thalamus and cortex
Hypothalamus (parts)	Histamine	Increases arousal
	Orexin	Maintains wakefulness
Dorsal raphe and pons	Serotonin	Interrupts REM sleep



**Figure 9.13** PGO waves start in the pons (P) and then show up in the lateral geniculate (G) and the occipital cortex (O). Each PGO wave is synchronized with an eye movement in REM sleep.



**Figure 9.11** Brain mechanisms of sleeping and waking

Green arrows indicate excitatory connections; red arrows indicate inhibitory connections.

Neurotransmitters are indicated where they are released by axons. © David Kachlík 30.9.2015

(Source: Based on Lin, Hou, Sakai, & Jouvet, 1996; Robbins & Everitt, 1995; and Szymusiak, 1995)

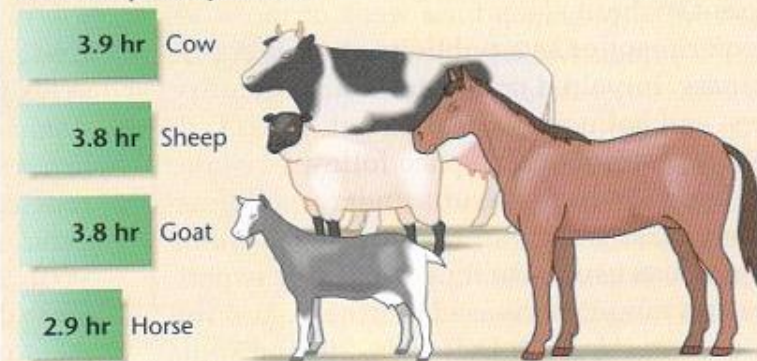
### Much sleep per day



### Moderate amount of sleep per day



### Little sleep, easily aroused



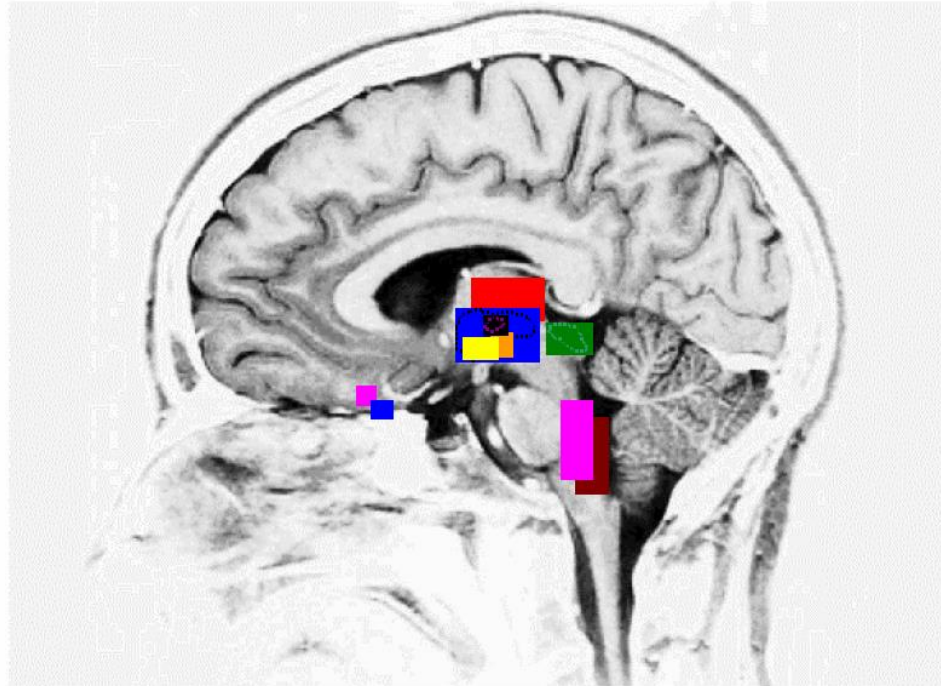
**Figure 9.17** Hours of sleep per day for various animal species. Generally, predators and others that are safe when they sleep tend to sleep a great deal; animals in danger of being attacked while they sleep spend less time asleep.











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# Biological clock

- Richter 1967 introduced idea that the brain generates its own rhythms
- Disruption of BC occurs after damage to hypothalamic area – **suprachiasmatic nucleus**
- After disruption rhythms are less consistent and no longer synchronized to light and dark pattern

Figure 2

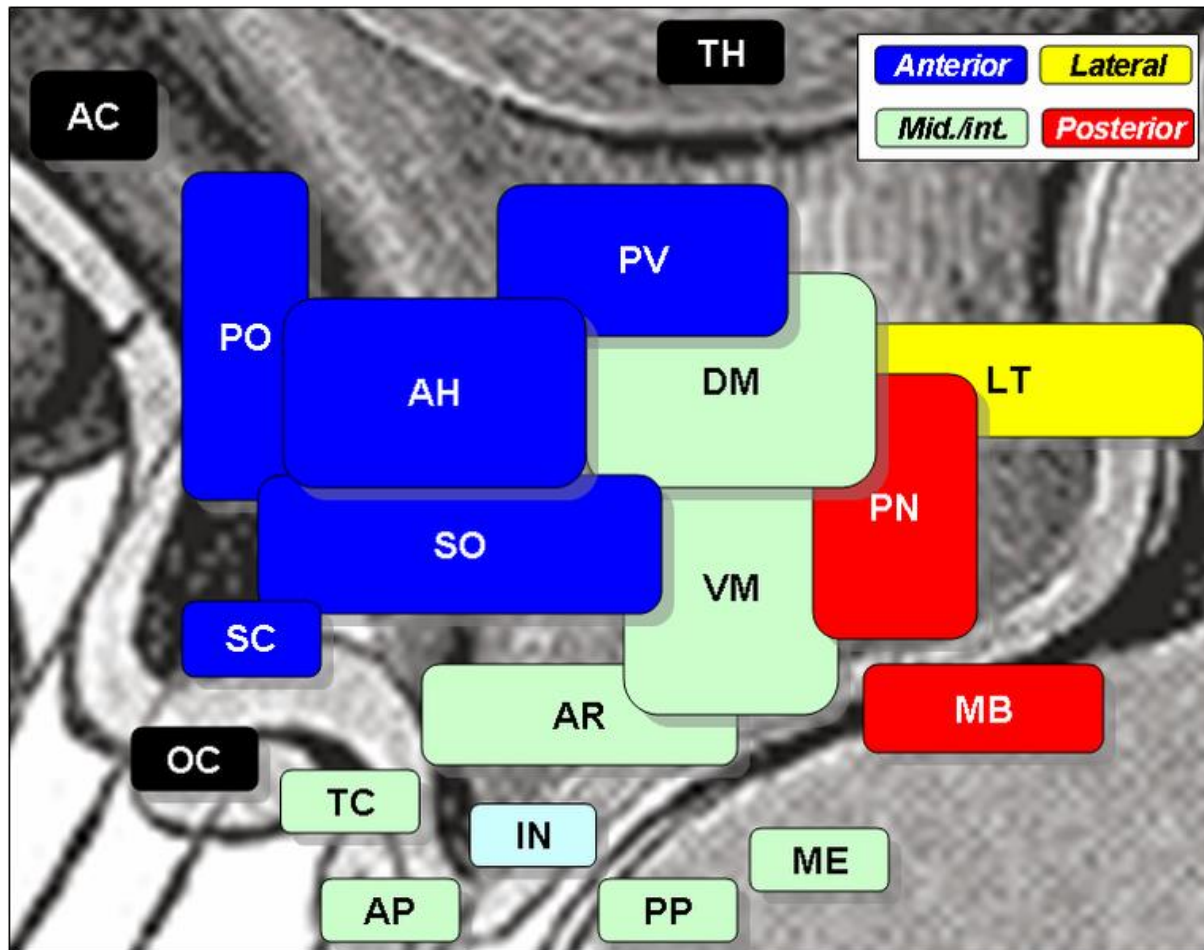


	Suprachiasmatic Nucleus		Locus Coeruleus
	Thalamus		Perifornical Lateral Hypothalamus
	Hypothalamus		Ventrolateral Pre-optic Nucleus
	Tuberomammillary Nucleus		Median Pre-optic Nucleus
	Raphé Nucleus		Pineal Gland

Sleep-related structures in the brain as discussed in the neural mechanism section. Notice that some structures like the Tuberomammillary Nucleus are located within another structure, the hypothalamus. The positions in the brain are only meant to be relative and will vary from one organism to another.



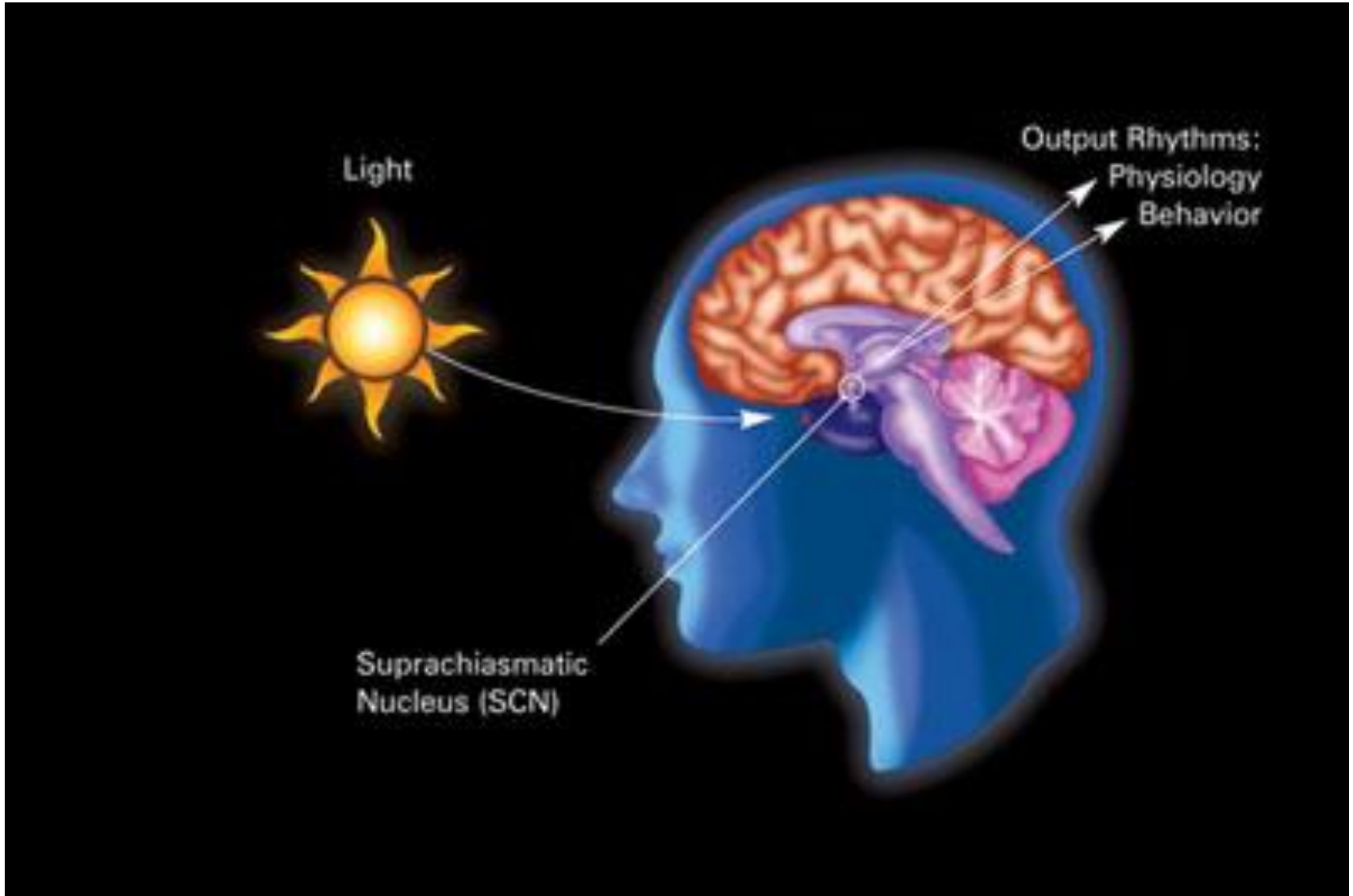
# Suprachiasmatic nucleus



# Suprachiasmatic nucleus

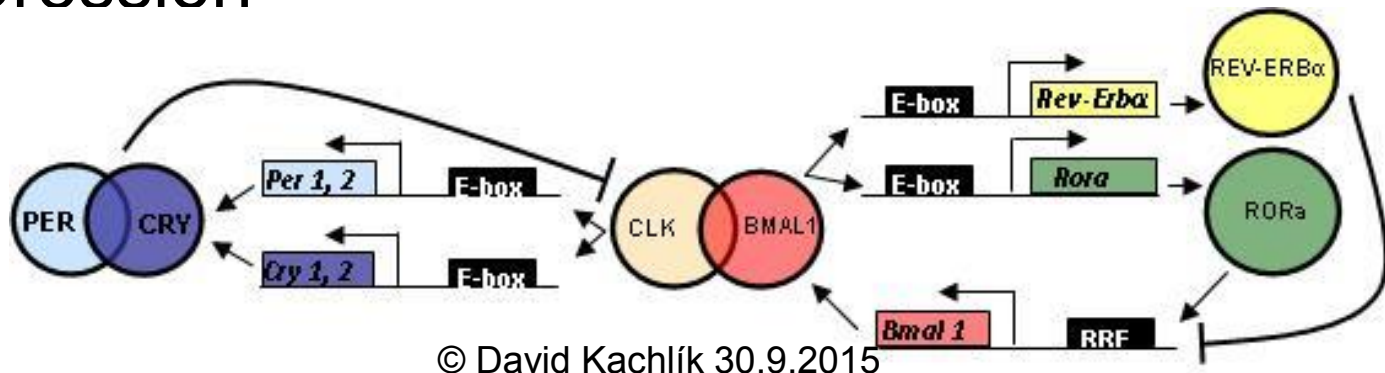
- It generates rhythm in a genetically controlled, unlearned manner
- From *Drosophilla* – isolated genes *period* (*per*) and *timeless* (*tim*), producing proteins Per and Tim
- In the morning their levels are low, in the evening high
- Interact with protein Clock to induce sleepiness

# SCN




# Suprachiasmatic nucleus

- Pulse of light during night inactivates protein Tim, so extra light during evening resets biological clock
- People having mutation in *per* gene have odd circadian rhythms: run faster
- Mutation in *per* is closely linked to clinical depression



# Dorsal raphe nucleus (DRN)

- Sleep antagonist
- Extra DRN path (DRN SC nucleus)
- Intra DRN path  (medial and lateral DRN nc.)

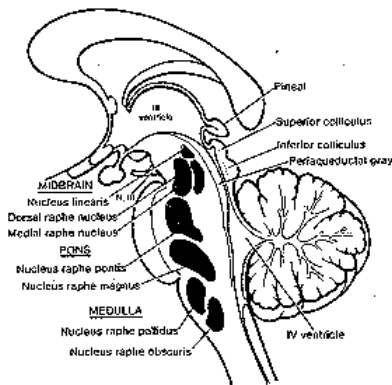
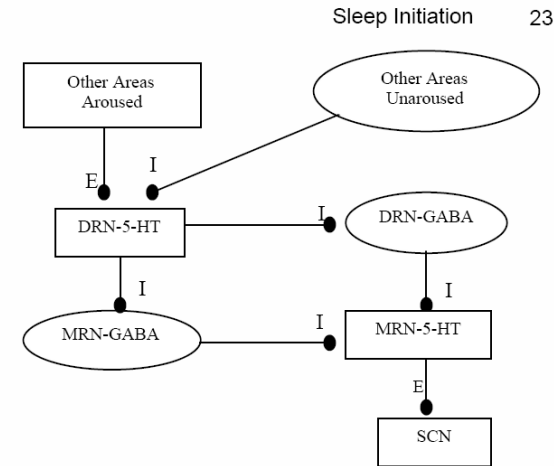
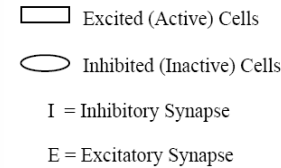


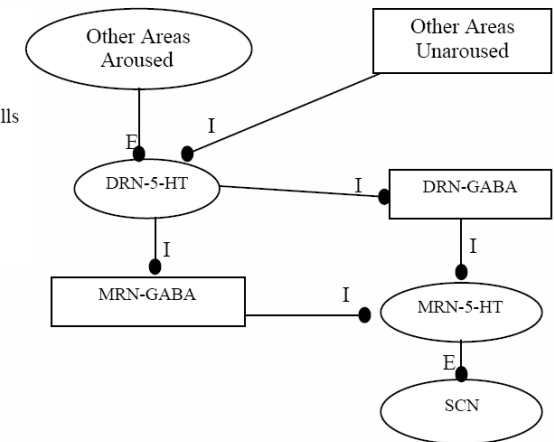
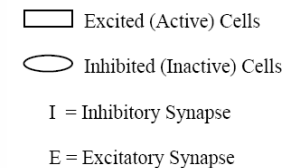
Fig. 5. The midsagittal section of the brain stem indicating the position of the raphe nuclei.

Figure 3

If RN is excited:



If RN is inhibited:



The intra-Raphé nucleus pathway as described in the neural mechanism works as a switch. Notice that if the RN is excited by other brain structures, an output to the SCN is observed by inhibiting (I) the MRN- and DRN-GABA cells. When the RN is inhibited by other brain structures, the MRN-GABA and DRN-GABA cells are allowed to fire tonically, thereby suppressing the output of the RN to the SCN.

# Locus coeruleus (LC)

- Does not communicate with SC nc. as DRN, but through *dorsal medial hypothalamus*
- The only adrenergic nucleus involved in sleep
- Arousal function, but according to some also most decreased firing rate during REM phase sleep

# Tuberomammillary nucleus (TMN)

- Histamine neurotransmission (the only place in brain, where histamine is produced)
- Maximum firing rate during waking state

# Perifornical lateral hypothalamus

- Source of Hypocretin (Orexin)
- Hypocretin causes arousal
- Hypocretin has effect on LC and TMN, but not with SCN



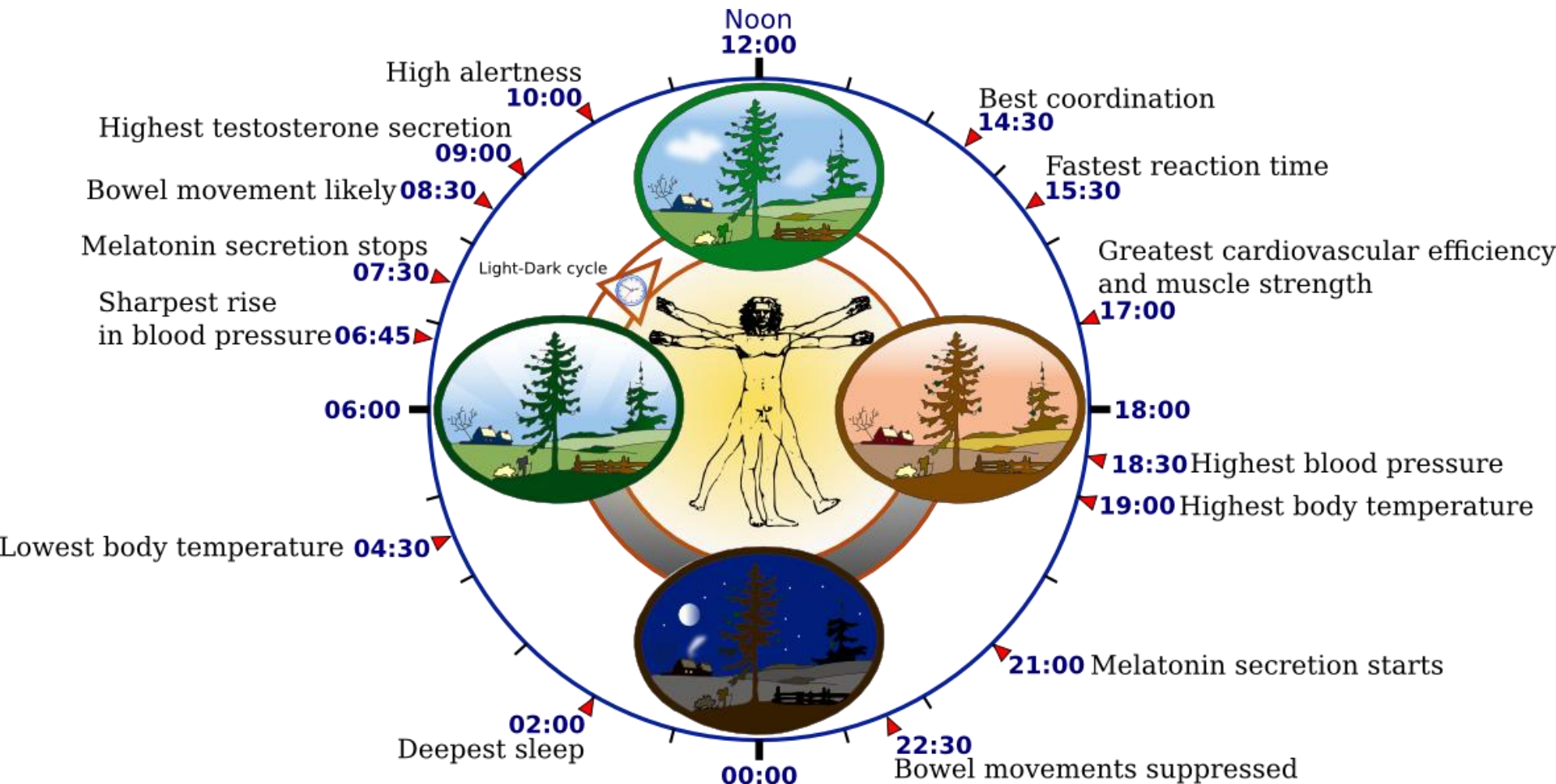
# Melatonin

- Melatonin is produced by pineal gland (*is outside blood barrier*) and increases sleepiness
- Tumor of pineal gland – sleepiness
- Melatonin secretion starts usually 2-3 hours prior to bedtime
- Moderate dose of melatonin in the afternoon phase-advances the clock
- Single dose in the morning has little effect

# Melatonin

- Dim-Light Melatonin Onset (DLMO)
- Anti Alzheimer disease
- Anti ageing factor
- Prolonging REM phase of sleep
- Its level with ageing decreases
- Scavenger function
- Drowsiness and hypothermia = circadian r.

# Biological clock



# Triggers

- Light is dominant „zeitgeber“ for land animals
- Retinohypothalamic path – from special population of retinal ganglion cells, having its own photopigment – melanopsin, unlike the ones found in rods and cones
- These cells respond directly to light and do not require any input from rods and cones

# Jet lag

- Disruption of circadian rhythms due to crossing time zones
- Going west we stay awake later at night – phase-delay
- Going east we have to go to sleep earlier and awake earlier – phase-advance
- Adjusting to jet lag - ↑ cortisol levels – hippocampal shrinkage

# Jet lag memory loss

- Female flight attendants – 5 years on Chicago-Italy route with less than 6 days interval – smaller hippocampal volume and memory impairments (Cho, 2001)
- To treat the jet lag, the recommended dose of melatonin is 0.3–0.5 mg, to be taken the first day of traveling

# Sleep disorders

- Dyssomnias (insomnia, hypersomnia, narcolepsia...)
- Parasomnias (Bruxism, sleep sex, sleep enuresis, pavor nocturnus, somnambulism, exploding head syndrome...)