

Anatomy and functional organization of the thalamus

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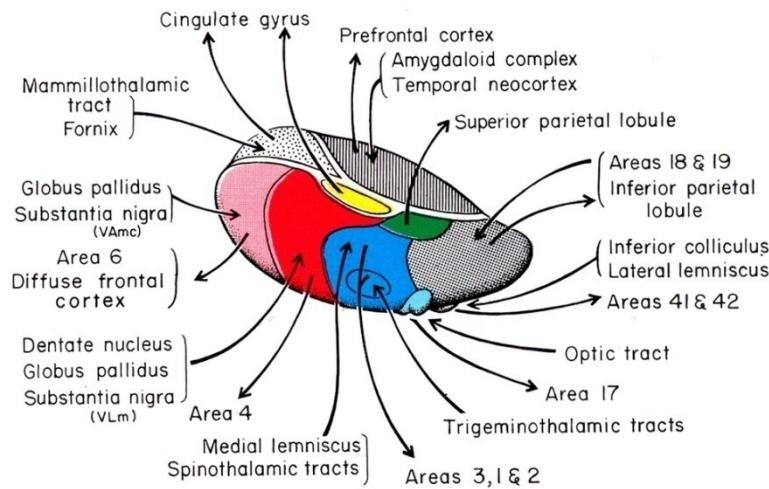
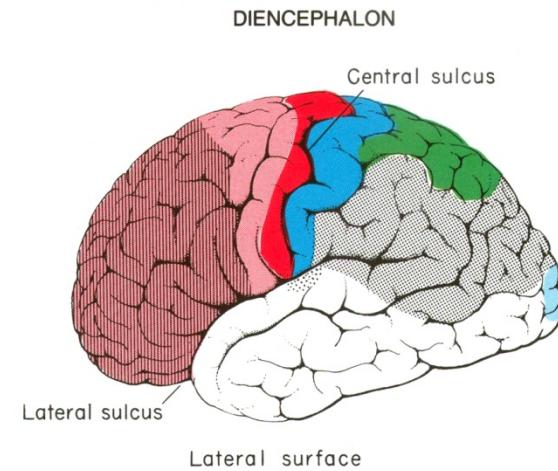
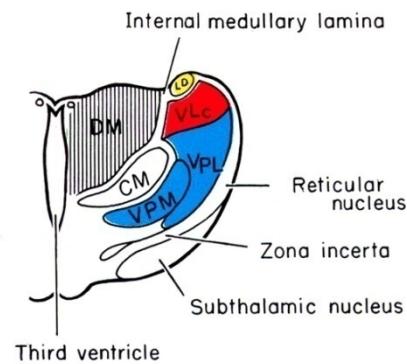
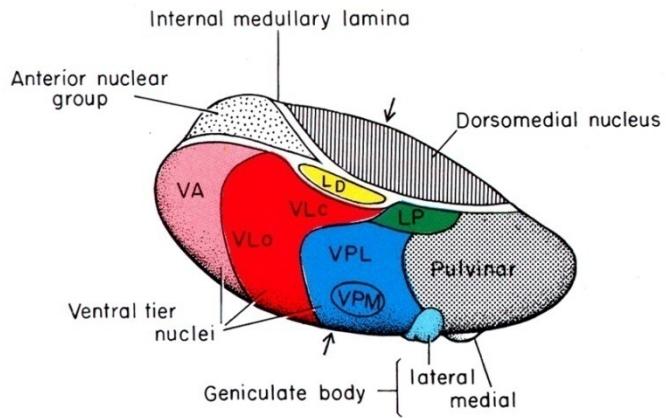
Overview

- The thalamus is part of the diencephalon; it is a bilateral structure, subdivided into multiple nuclei, which receive afferents from either sensory systems or associative cortex
- The thalamus is a relay center, through which all information about the outside world, except olfaction, passes before reaching the neocortex, striatum, and amygdala
- Thalamo-cortical projections are reciprocal and established with specific areas of the ipsilateral neocortex
- Thalamocortical neurons have two fundamental modes of operation (tonic firing, bursting mode), which occur mainly during wakefulness and sleep.
- The thalamus plays an essential role in the generation of oscillatory activities, which are fundamental to higher cortical functions

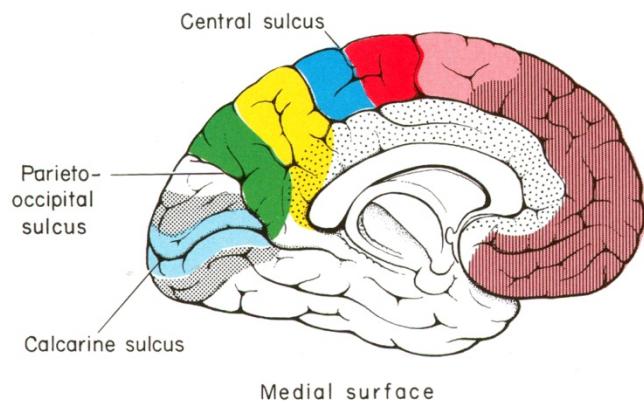
Main subdivisions of the thalamus

- Dorsal thalamus
 - Five main divisions (anterior, dorsal-medial, ventral, lateral, posterior) + intralaminar nuclei
- Ventral thalamus
 - Reticular nucleus
 - Ventral geniculate nucleus
 - Zona incerta
- Epithalamus
 - Habenula
 - Pineal gland

Major thalamic nuclei (human)

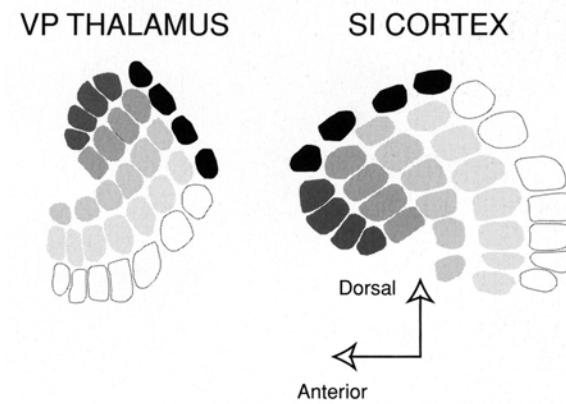
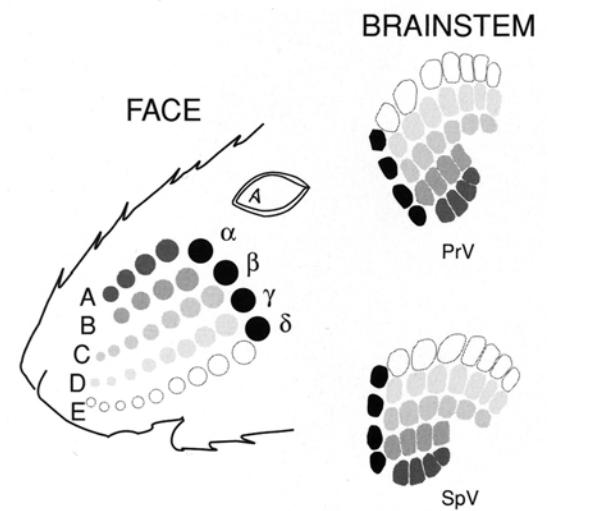


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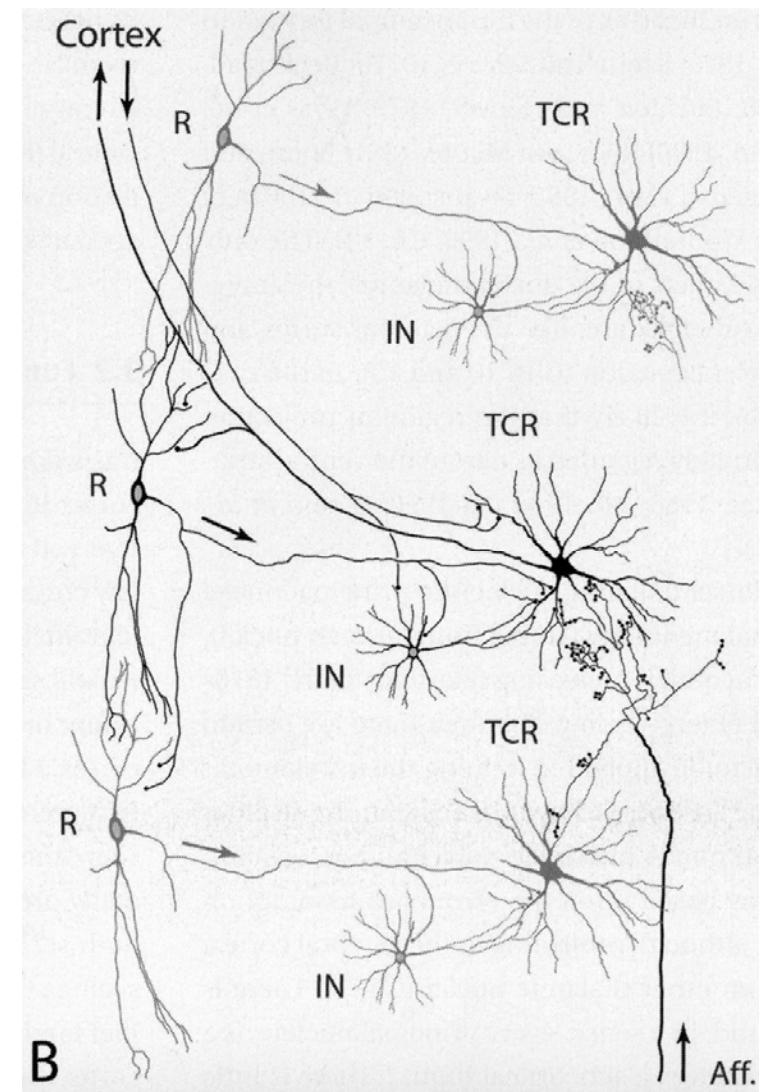
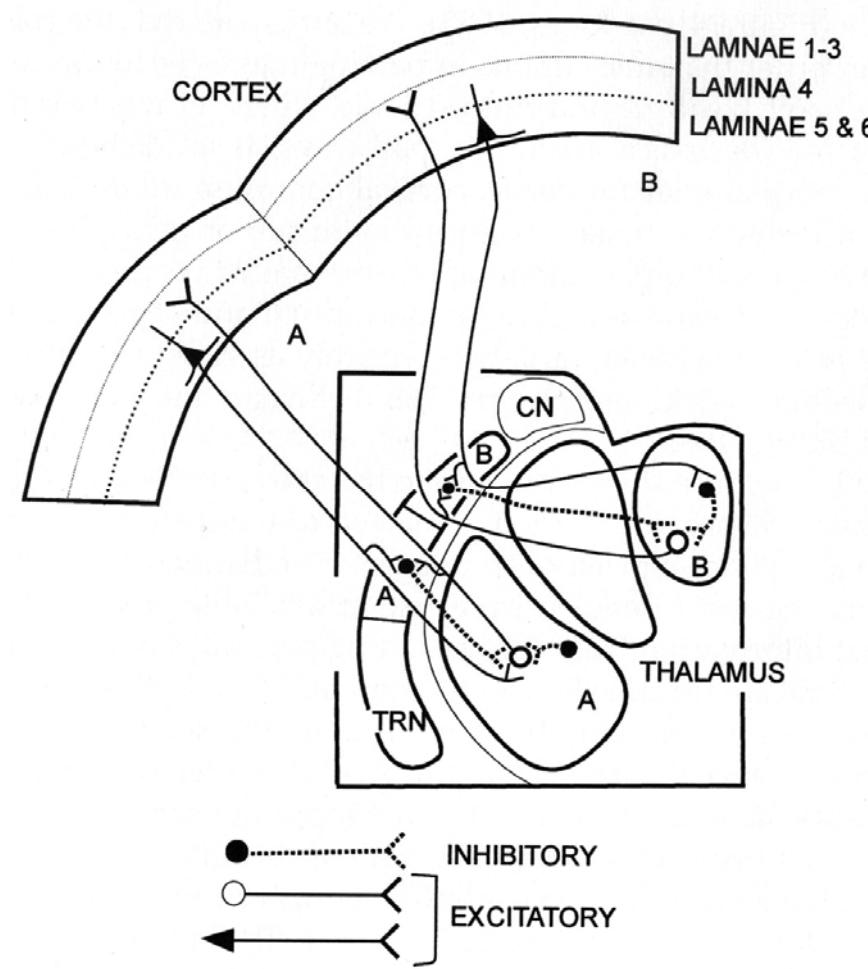


Topography in the thalamocortical system

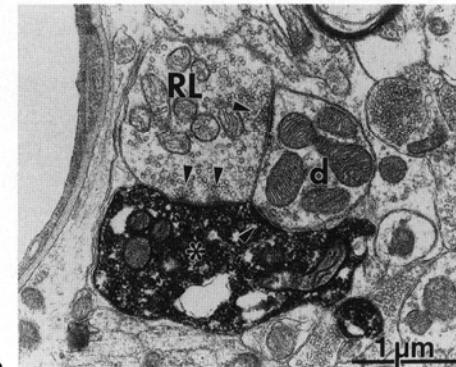
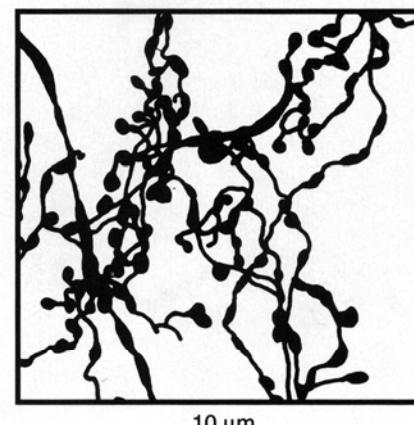
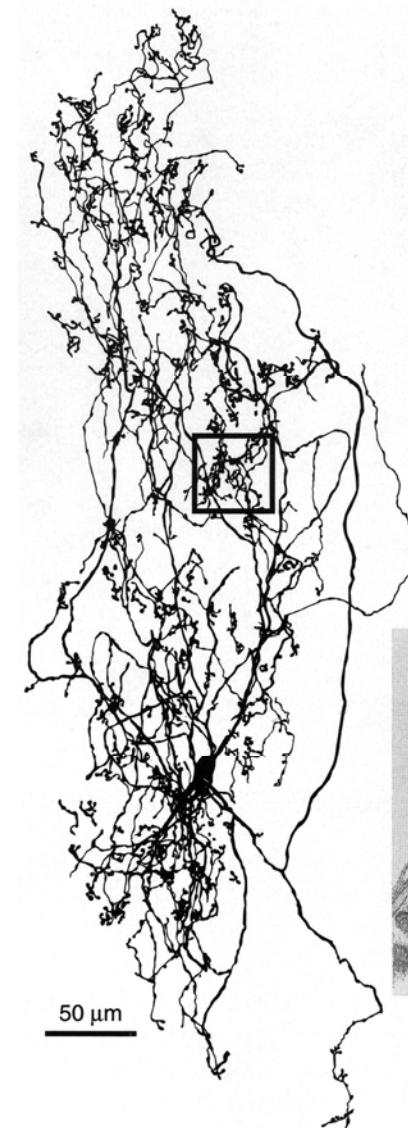
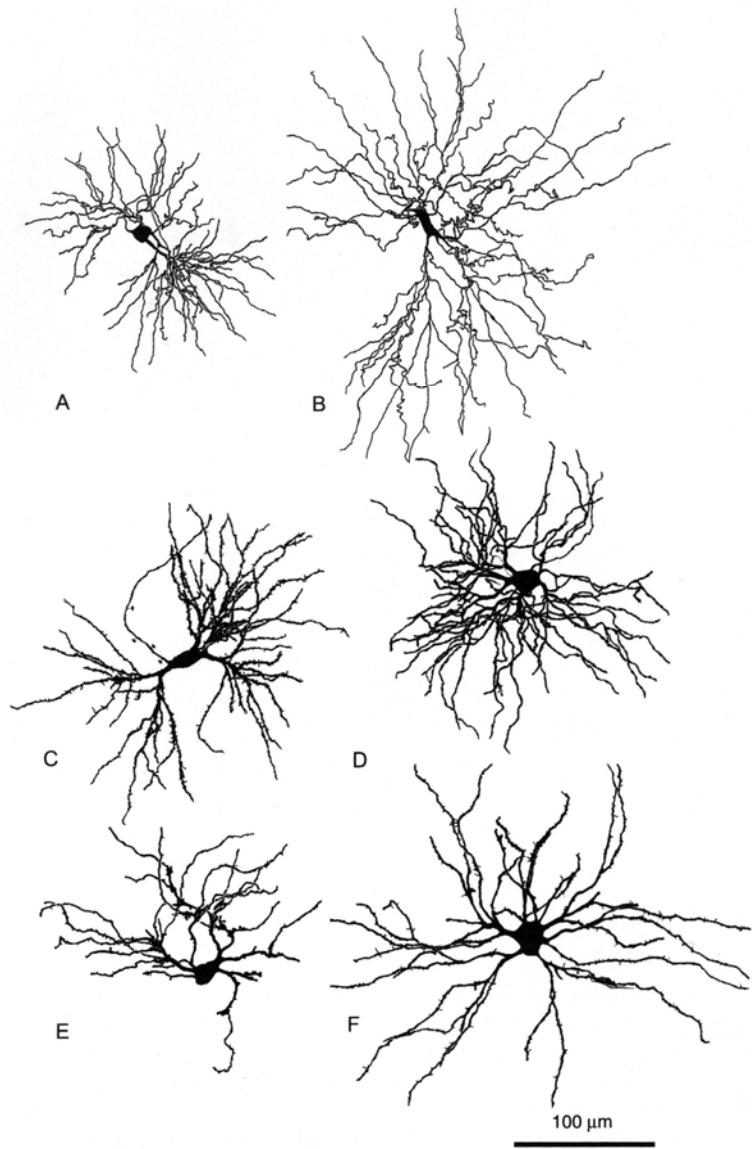
- Sensory (somatotopic, retinotopic, tonotopic, etc) and motor maps are present at all relay stations of ascending and descending systems.
- First order relay nuclei in the thalamus contain precise maps of the system they belong to



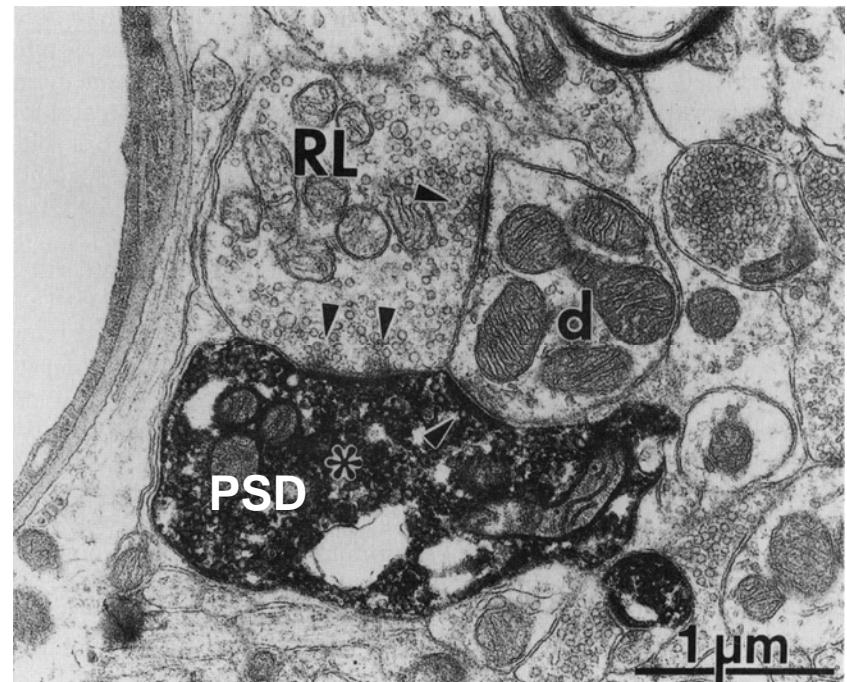
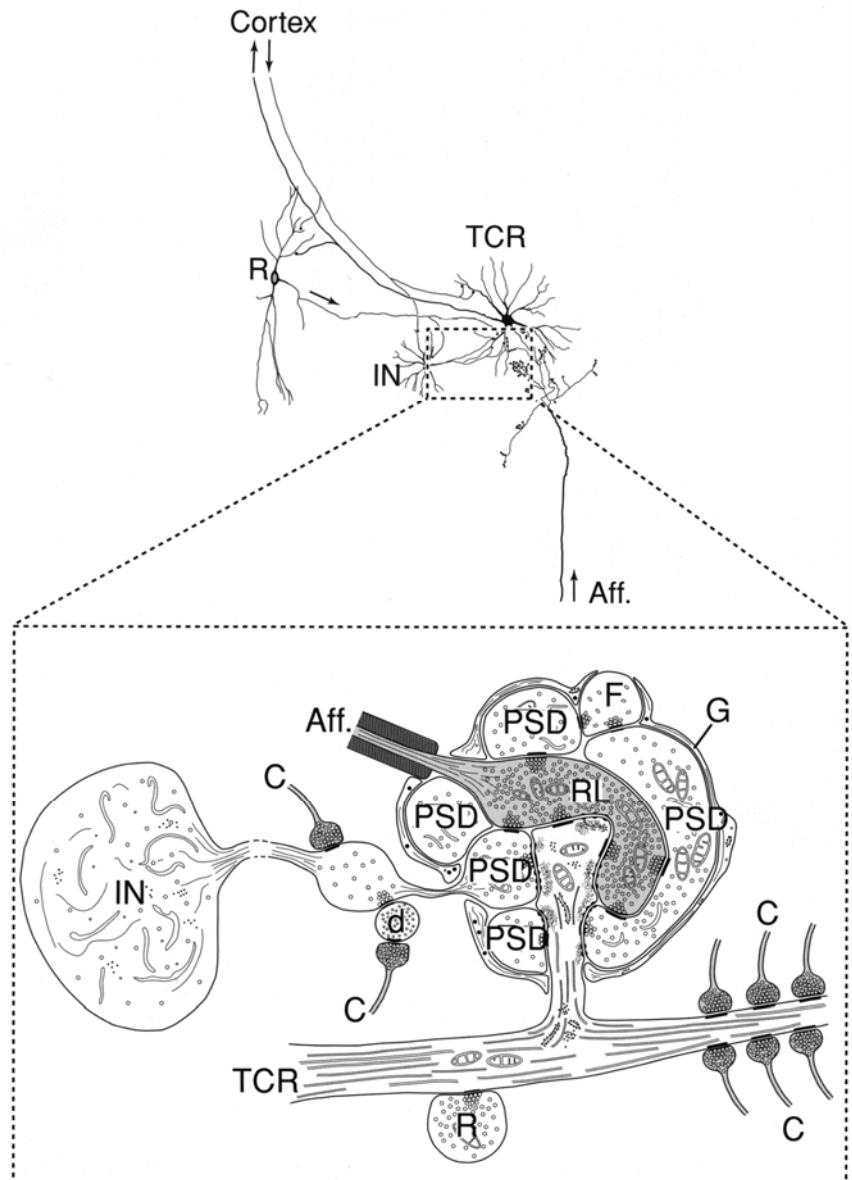
The thalamo-cortical loop



Relay cells and interneurons



Synaptic connections

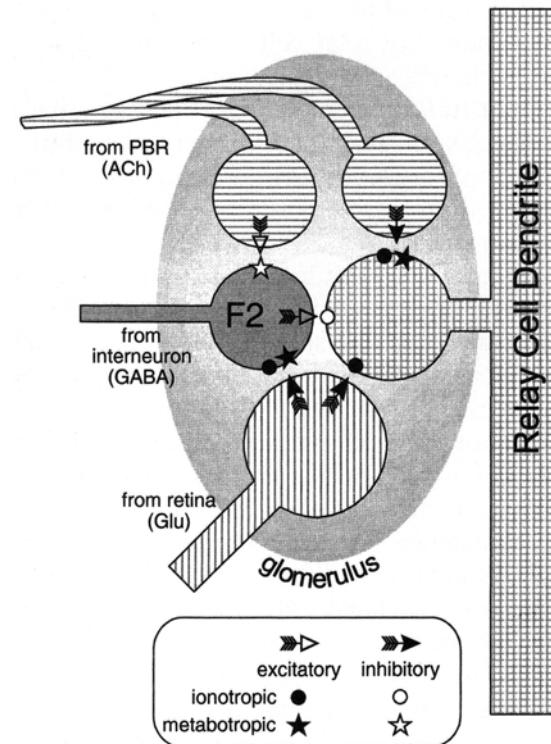


Arrowheads: presynaptic site

TCR: relay cell; RL: subcortical afferent;
PSD: presynaptic dendrite (interneuron, IN);
F: terminal from reticular nucleus;
c: cortico-thalamic terminal; G, astrocyte

Brainstem afferents

- Cholinergic
 - Parabrachial region
- Serotonergic
 - Dorsal and median raphe nuclei
- Noradrenergic
 - Locus coeruleus
- GABAergic
 - Pretectal area

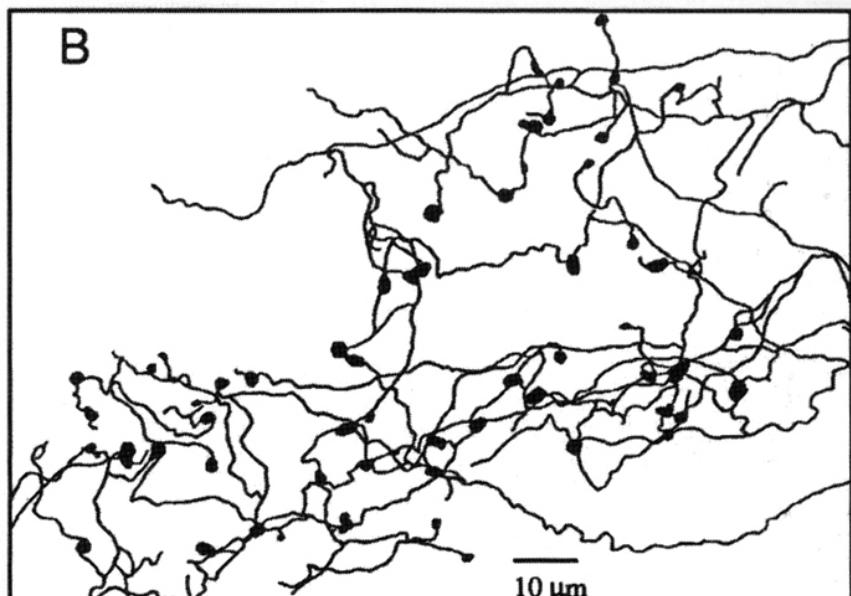


Cholinergic and monoaminergic afferents exert a facilitating action by activating relay cells and inhibiting interneurons

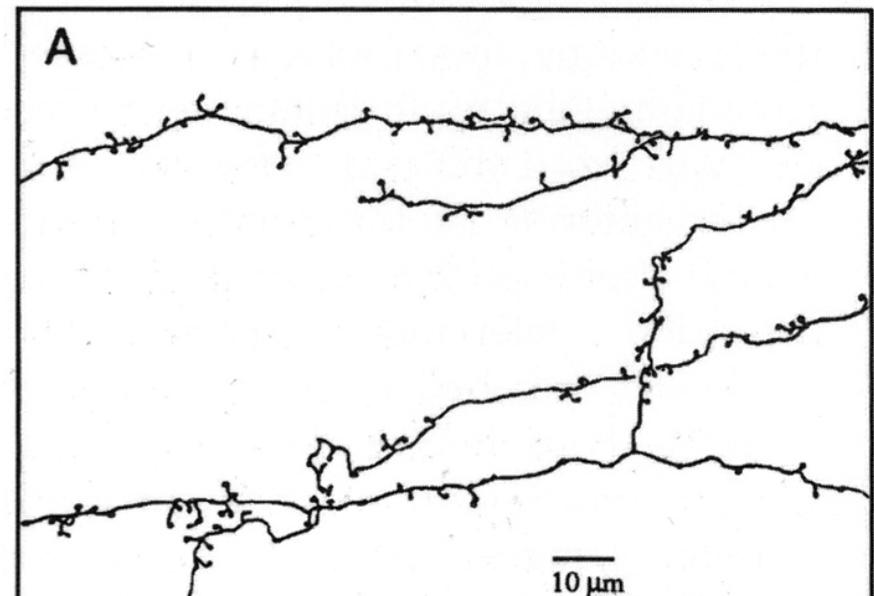
Drivers and modulators

- Sensory afferent inputs to first order thalamic nuclei (LGN, VP, MGN) are characterized by richly branching axons, forming large, type 2, terminals, which exert a strong excitatory influence of thalamocortical cells (“drivers”)
- Afferents from “motor systems” to VA and VL, as well as mamillary bodies to the anterior thalamus have a similar morphology and properties, and are also considered “drivers”
- In contrast, cortical afferents from layer VI form poorly branched axons, with small terminals, innervating distal dendrites of thalamocortical cells, and are considered “modulators”. These axons typically have collaterals innervating the RT
- “Modulators” also arise from multiple subcortical origins and from the brainstem and are characterized by rather diffuse projection
- Afferents from layer V are morphologically similar to “drivers” and do not connect the RT, suggesting that also cortical afferents are functionally “drivers” of specific cortico-thalamic neurons (e.g. in Po)

Morphology of drivers and modulators

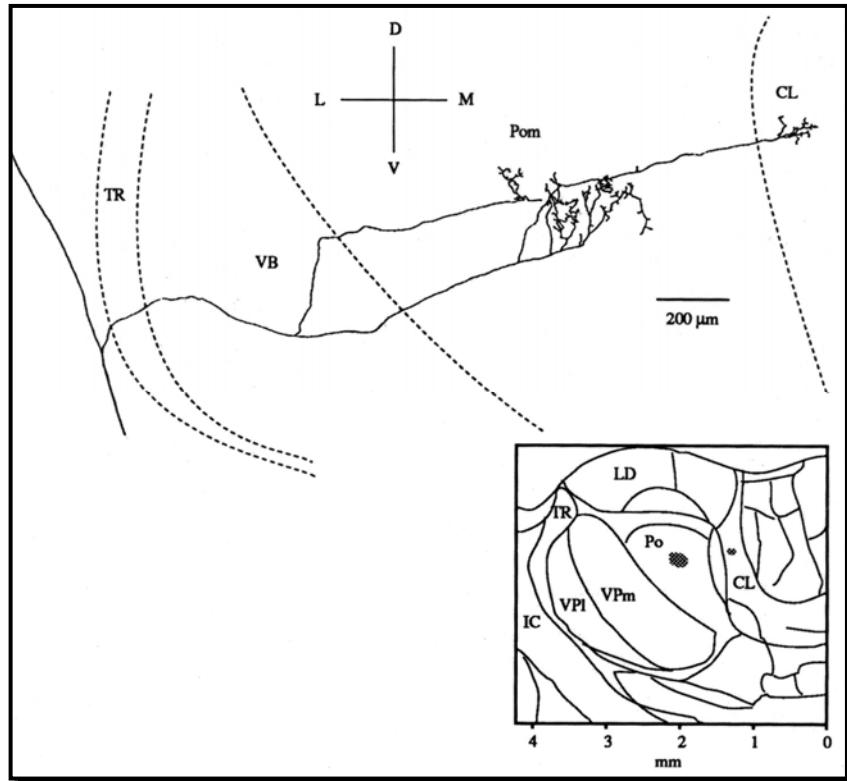


driver

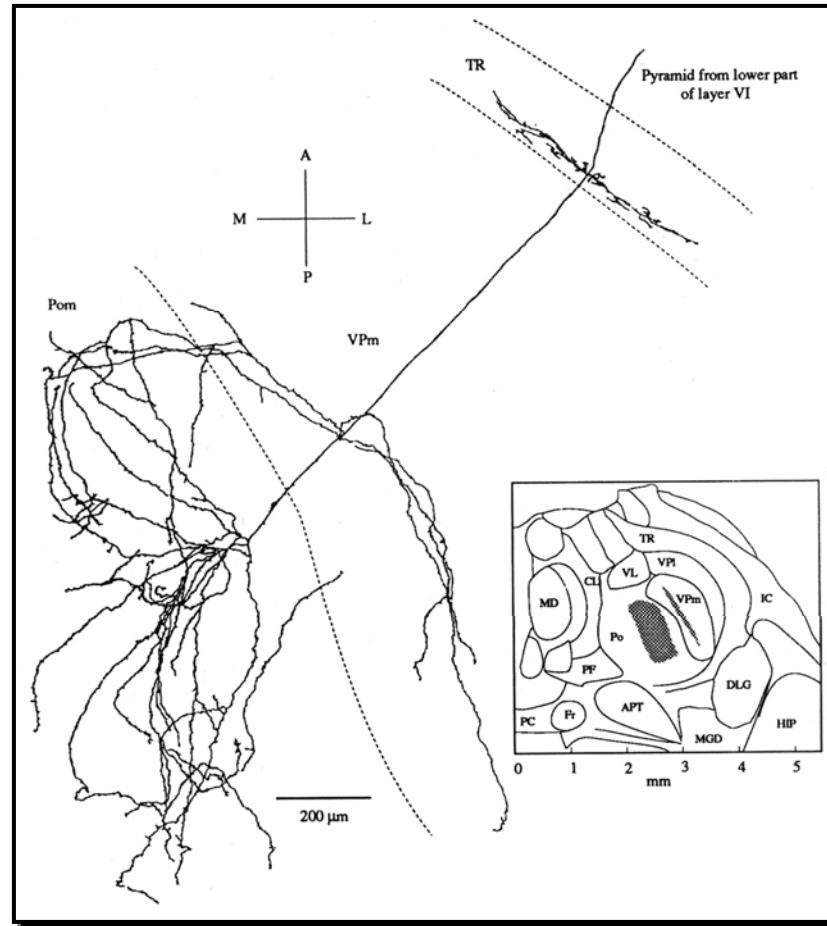


modulator

Distinction between terminal fields of cortical drivers and modulators



Axon of a layer V pyramidal cell (S1)
driver



Axon of a layer VI pyramidal cell (S1)
modulator

First and higher order relay nuclei

- First order relay nuclei are innervated by drivers of subcortical origin (sensory and motor modalities)
- They include AV, AM, AD, VA, VL, VP, LGN, MG
- Higher order relay nuclei (e.g., Po, MD, LD, LP) are innervated by drivers originating in layer V neurons (also collaterals of layer V cortico-striatal neurons); the presence of some subcortical drivers in higher order relay nuclei suggests a “mixed” organization
- Both receive cortico-thalamic input from layer 6 pyramidal cells (modulators)

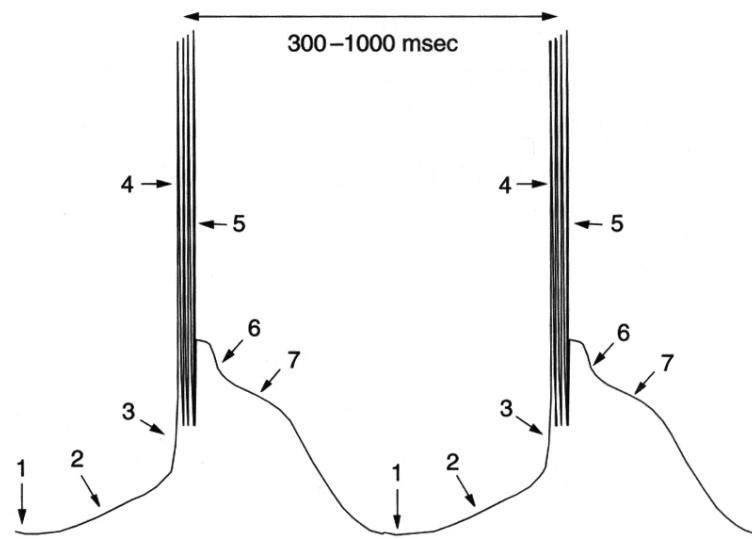
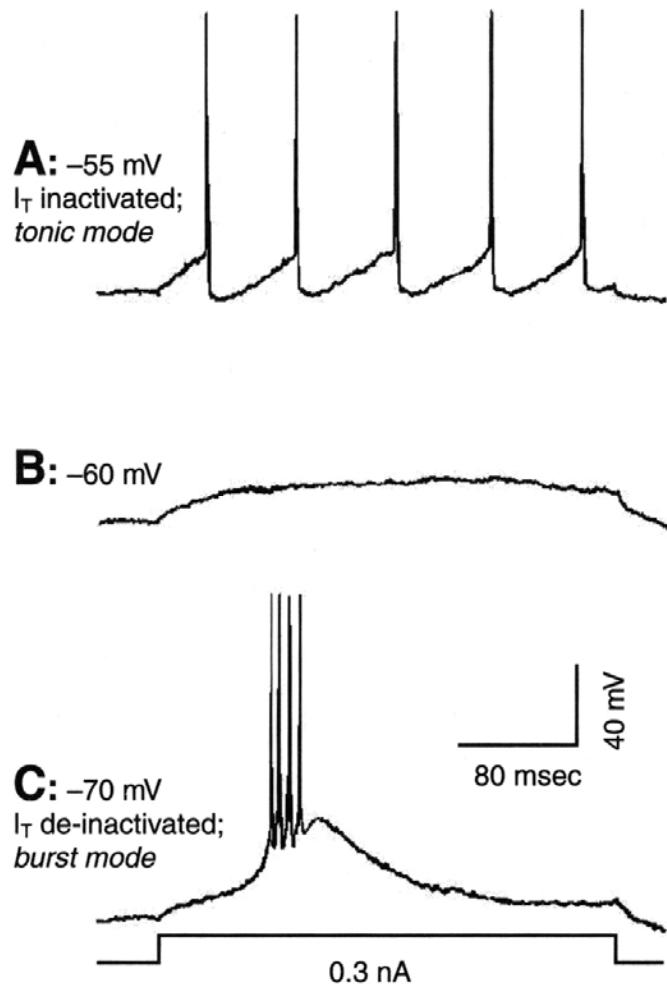
The thalamic reticular nucleus (RT)

- Part of the ventral thalamus (surrounds the thalamus laterally and posteriorly like a shell)
- Comprises exclusively GABAergic neurons (interconnected) that innervate the dorsal thalamus (no cortical projections)
- Receives a topographically organized “point-to-point” copy (axon collaterals) of thalamo-cortical and of cortico-thalamic input
- Plays a key role in the generation of sleep-related slow rhythms and in the modulation of relay cell hyperpolarization
- Contributes to absence epilepsy

White matter tracts in the thalamus

- Stria terminalis
 - Output of the amygdala towards the septum and hypothalamus; runs along the ventricular border of the thalamus
- Stria medullaris
 - Input of the habenula (from the septum, preoptic area, anterior thalamic nuclei); runs horizontally along the lateral border of the thalamus
- Fasciculus retroflexus
 - output of the habenula towards the interpeduncular nucleus
- Fornix
 - output of the hippocampus towards the mamillary bodies

Firing modes of relay neurons



Control of response mode

Brainstem

- Cholinergic neurons (parabrachial region) activate relay neurons via ligand-gated and metabotropic receptors (M1) and switch their firing mode from bursting to tonic
- Cholinergic innervation of interneurons and RT neurons is inhibitory (M2 receptors)
- Noradrenergic neurons also activate relay cells
- Serotonergic neurons inhibit relay cells and promote burst firing
- How regional selectivity is achieved is not clear

Neocortex

- Role of cortico-thalamic projections difficult to establish experimentally; stimulation of layer 6 pyramidal cells promotes tonic firing

Thalamus and sleep

Table 1 Functional states of thalamocortical circuits

Behavioral state	Drowsiness and non-REM (slow wave) sleep	Wakefulness and REM sleep
TC neuron activity	Rhythmic burst firing	Tonic firing
Membrane potential of TC neuron	Hyperpolarized (≈ 75 mV)	Depolarized (≈ 55 mV)
Calcium channel involved	T-type	P/Q type
GABAergic influence from ReT neurons	Strong	Weak
Cholinergic influence from Neurons of the PPT/LDT	Weak	Strong
Cortical (EEG) activity	High amplitude, slow (0.5–1.5 Hz), with superimposed spindles	High frequency (30–50 Hz, gamma band)
Functional implications	Memory consolidation?	Temporal binding for perceptual awareness and cognition

TC = thalamocortical; GABA = γ -aminobutyric acid; ReT = reticular thalamic nucleus; PPT = pedunculopontine tegmental nucleus; LDT = laterodorsal tegmental nucleus.

Dorsal thalamic nuclei

Name	Subcortical input	Cortical target
Ventral group		
VA	Substantia nigra	Prefrontal and cingulate
VL	GPi, deep cerebellar nuclei, vestibular nuclei	Premotor and motor
VM	Substantia nigra, taste, vagal, spinal	Frontal, cingulate
VPL, VPM	Medial lemniscus, spinothalamic tract	S1, S2, insula
MG	Inferior colliculus	A1
LGN	Retina	V1
Lateral group	Superior colliculus and pretectum	Parietal, parietotemporal, superior temporal, prestriate
Posterior group	Superior colliculus, spinothalamic	Insula

Dorsal thalamic nuclei (2)

Name	Subcortical input	Cortical target
Medial group MD, MV	Spinal, sup. colliculus, olfactory cortex, amygdala	Orbitofrontal, lateral frontal, olfactory structures, hippocampus
Pt	Hypothalamus, basal forebrain	Same + striatum
Anterior group AV, AM, AD LD	Mamillary nuclei Hypothalamus	Cingulate, retrosplenial, subiculum, presubiculum
Intralaminar complex		
CL ant	Spinothalamic	Striatum, S1, parietal
CL post	Cerebellar nu, s.nigra	Parietal, frontal
CM	Gpi	Frontal, motor
Pf	Periaqueductal gray	Lateral frontal

LGN

- Dorsal LGN (dLGN)

Only first-order relay nucleus in rodents that contains a substantial number of interneurons

- Afferents: retina (mainly contralateral temporal+nasal; restricted ipsilateral); RT; brainstem (sup. colliculus, pretectal areas, monoamines); V1 (layer 6; numerically the most important)
- Efferents: V1 (layer 4, 1, 6); some to V2; RT

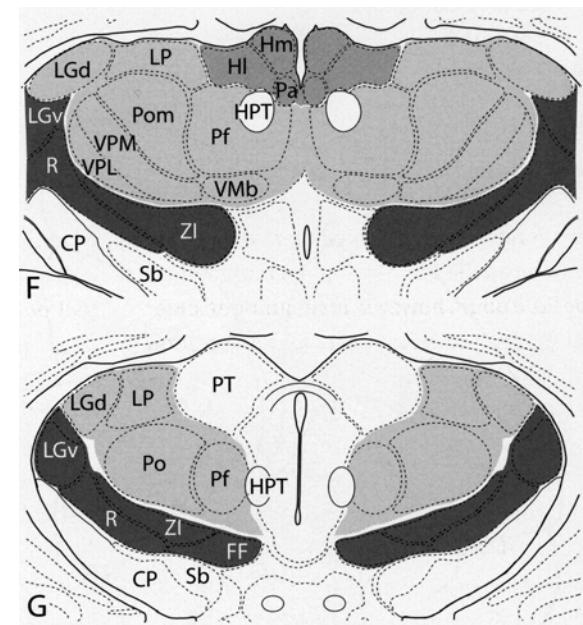
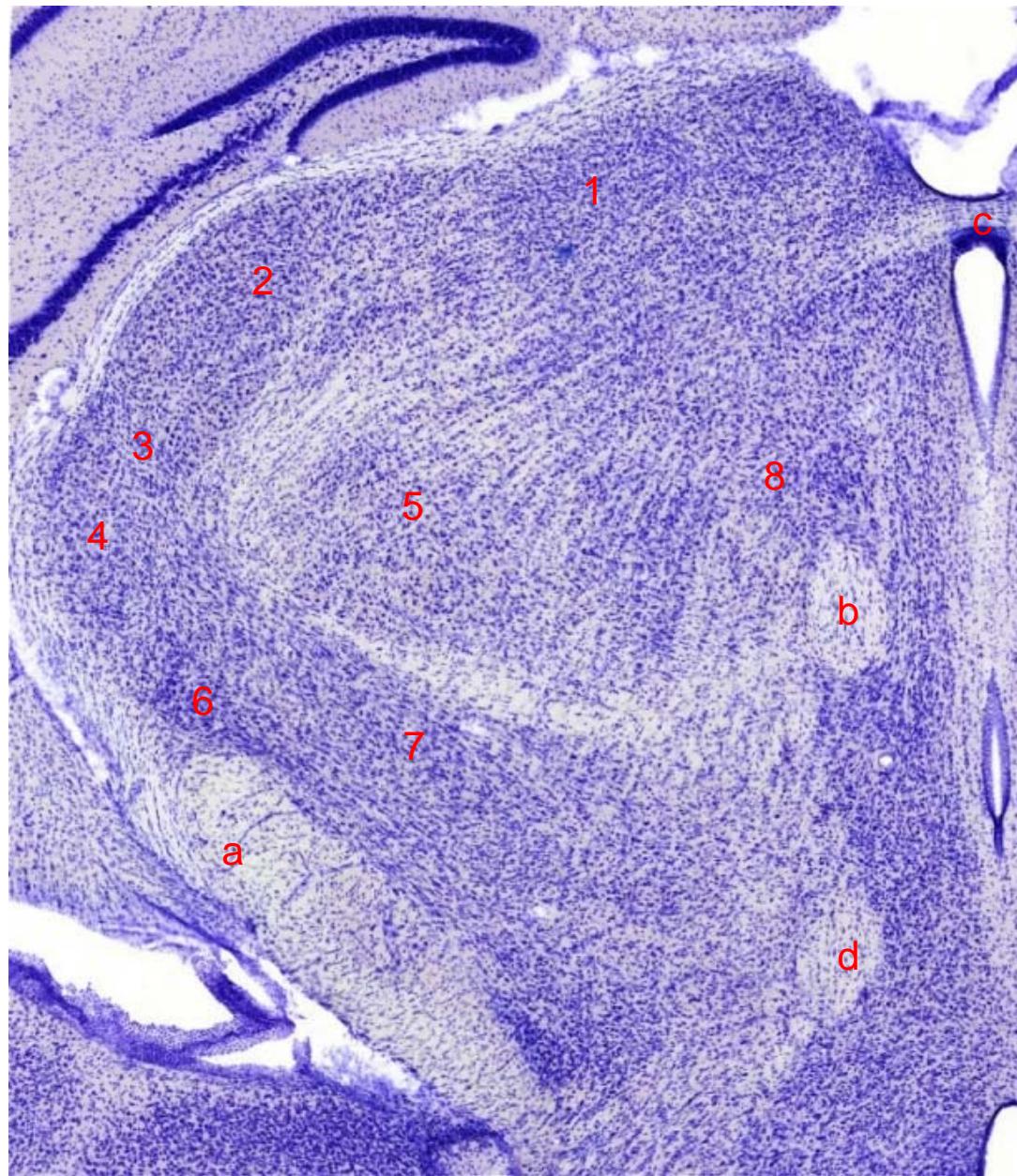
Function

The dLGN is a relay nucleus for the visual system; it contains about 18'000 relay neurons and receives input from about 25'000 ganglion cells (all ganglion cells project also to the superior colliculus)

LGN (2)

- Ventral LGN (vLGN; part of ventral thalamus)
 - Afferents: medial: brainstem (reticular formation, PAG, Sup. Colliculus, substantia nigra, cerebellar nuclei, monoamines). Lateral: retina and layer 5 of V1
 - Efferents: thalamic nuclei (dLGN, Po, intralaminar); hypothalamus, zona incerta, sup. Colliculus, PAG
- Intergeniculate leaflet
 - Afferents: retina, suprachiasmatic nucleus, post. hypothalamus, brainstem
 - Efferents: suprachiasmatic nucleus, ant. hypothalamus, pineal gland

Function: Control of visuo-motor responses and circadian rhythms

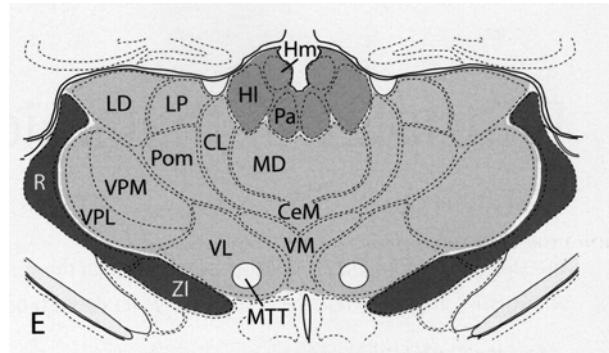
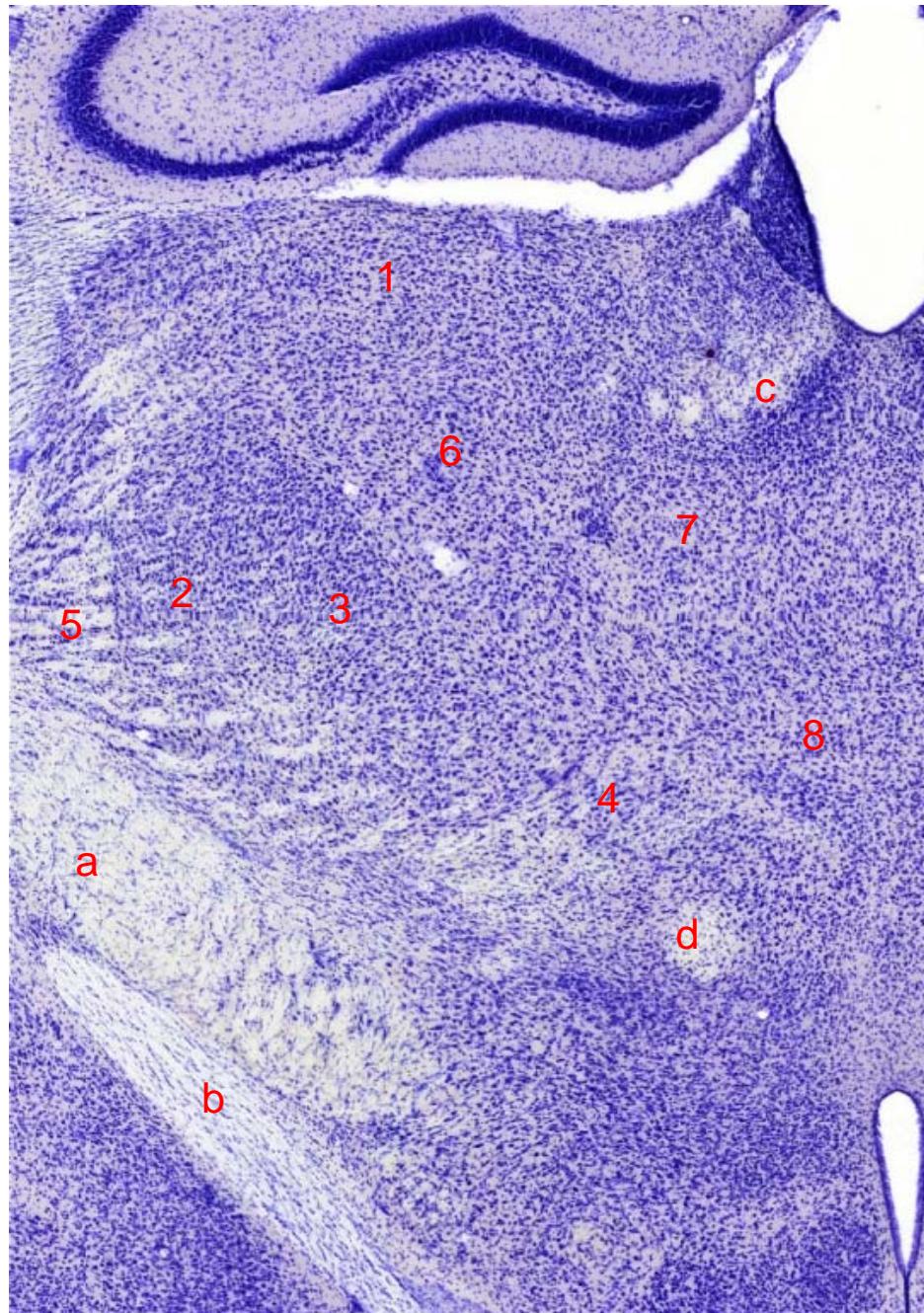


- a. Cerebral peduncle
- b. Fasciculus retroflexus
- c. Posterior commissure
- d. Mamillothalamic tract
- 1. Preoptic nucleus
- 2. Lateral geniculate nucleus, dorsal
- 3. Intergeniculate leaflet
- 4. Lateral geniculate nucleus, ventral
- 5. Posterior nucleus
- 6. Reticular nucleus
- 7. Zona incerta
- 8. Parafascicular nucleus

Ventral posterior complex

Main relay for somatosensory information

- VPL: spinal cord, dorsal column nuclei; VPM, trigeminal
 - Afferents: spino-thalamic neurons, reticular formation, dorsal column nuclei, trigeminal complex (these afferents also innervate the posterior nucleus and intralaminar nuclei); RT, brainstem; cortico-thalamic: layer 6 of S1 (collaterals in RT)
 - Efferents: layer 4 of S1 (also layers 1 and 6)
 - Gustatory and visceral nuclei (VPPC; ventromedial part of VPL and VPM)
 - Afferents: parabrachial nucleus, solitary tract, monoaminergic nuclei, posterior insula
 - Efferents: Amygdala (central and lateral), posterior insula
- Note: some parabrachial projections bypass the thalamus and go directly to the amygdala



- a. Cerebral peduncle
- b. Optic tract
- c. Fasciculus retroflexus
- d. Mamillo-thalamic tract
- 1. Lateral posterior nucleus
- 2. Ventral, posterolateral nucl
- 3. Ventral posteromedial nucl
- 4. Gustatory thalamic nucl (VPPC)
- 5. Reticular nucleus
- 6. Posterior nucleus
- 7. Mediodorsal nucleus
- 8. Ventromedial nucleus

Posterior nucleus

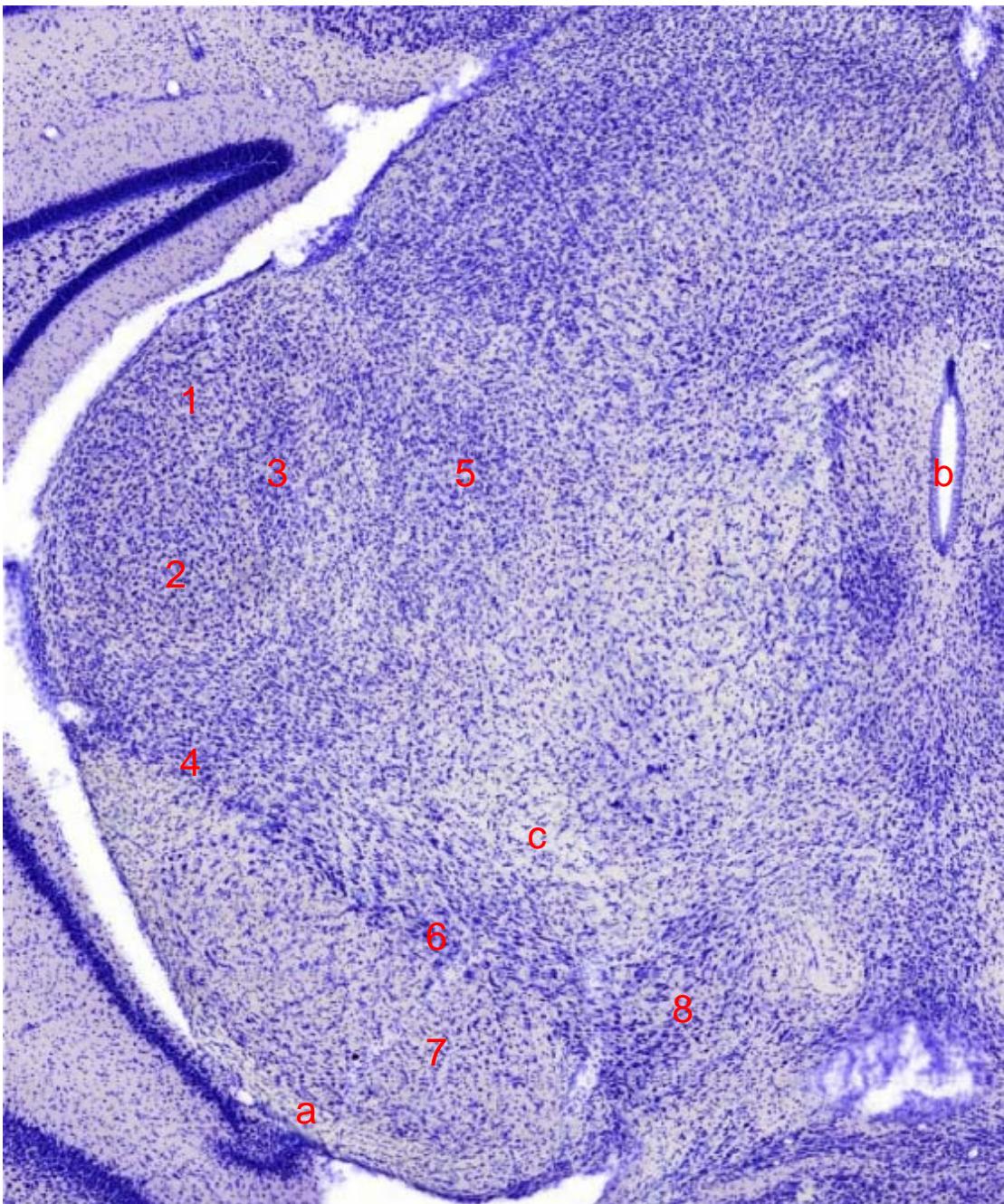
- Afferents: spino-thalamic and principal trigeminal nucleus, brainstem; topographically-organized but more diffuse than VPL/VPM; neocortex layer 5 (collaterals of cortico-striatal and cortico-brainstem projections); visual, vestibular, auditory afferents; red nucleus
- Efferents: S1-S2, insula, motor cortex, frontal areas; red nucleus

Functions: interface between sensory and motor function in whisker-to-barrel system

Medial geniculate nucleus

- Relay nucleus of the auditory system
- Most caudal thalamic structure; subdivided into multiple nuclei (MGD, MGM, MGV, and several more medial structures, related to intralaminar nuclei)
 - Afferents: inferior colliculus (central nucleus to MGV, focal, tonotopically organized projection); RT, auditory cortex
 - Efferents: MGV mainly to A1; MGD and MGM also to additional parts of temporal cortex, amygdala; MGM to striatum

Afferent fibers from inf. colliculus and auditory cortex are morphologically highly heterogeneous, suggesting multiple functions

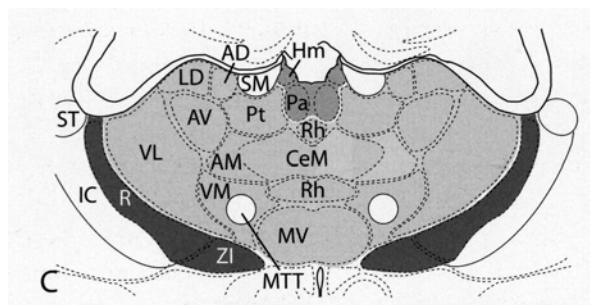
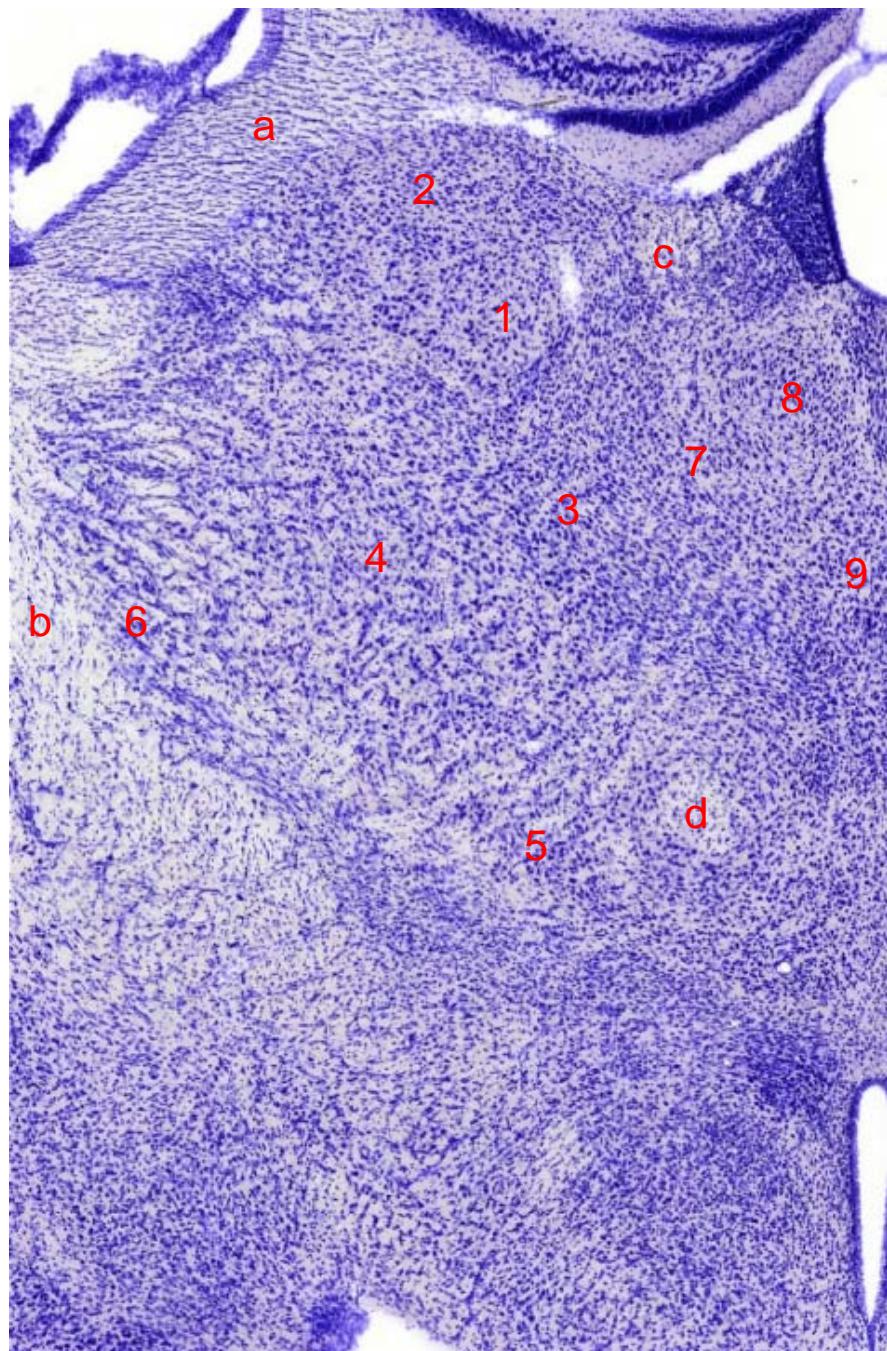


- a. Cerebral peduncle
- b. aqueduct
- c. Medial lemniscus
- 1. MGN dorsal
- 2. MGN ventral
- 3. MGN medial
- 4. Reticular nucleus
- 5. Pretectal nucleus
- 6. Subst. Nigra compacta
- 7. Subst. Nigra reticulata
- 8. VTA

Motor nuclei

- VL/VA complex
 - Afferents: cerebellum (deep nuclei, mainly to VL), basal ganglia (entopeduncular nucleus, subst. nigra, mainly to VA), somatomotor, premotor cortical areas, RT
 - Efferents: VL somatomotor cortex (mainly layers III-V); VA premotor cortex (frontal cortex)
- VM
 - Afferents: entopeduncular nucleus, substantia nigra reticulata, numerous brainstem nuclei (medullary reticular formation, superior colliculus, PAG, monoaminergic nuclei), cerebellum
 - Efferent: layer 1 of most of the neocortex (!)

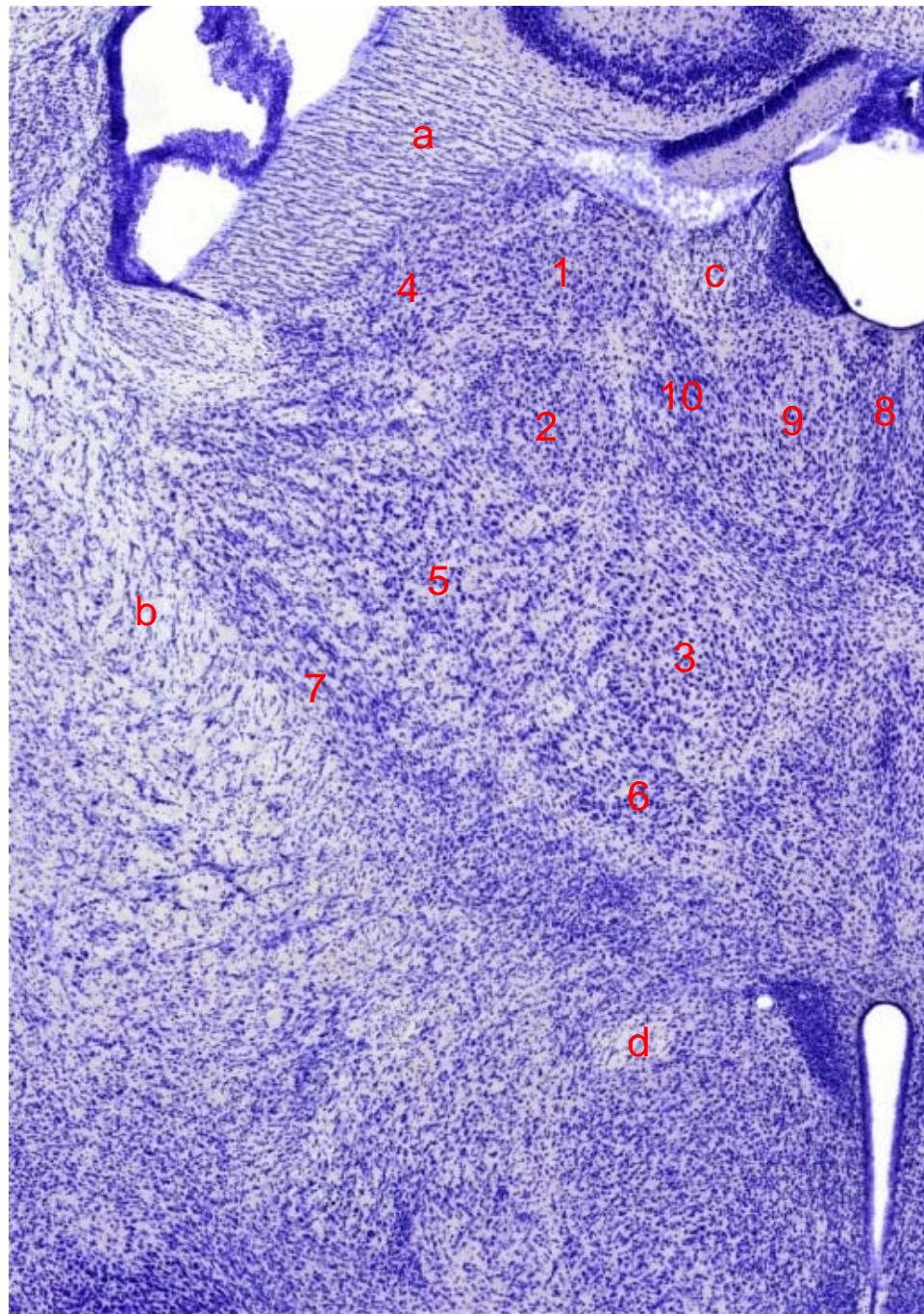
Function: Attentional role; perhaps integration of nociceptive inputs



- a. Fornix
- b. Internal capsule
- c. Stria medullaris
- d. Mamillothalamic tract
- 1. Anteroventral nucleus
- 2. Laterodorsal nucleus
- 3. Anteromedial nucleus
- 4. Ventral lateral nucleus
- 5. Ventral medial nucleus
- 6. Reticular nucleus
- 7. Central lateral nucleus
- 8. Mediodorsal nucleus
- 9. Central medial nucleus

Mediodorsal nucleus

- Subdivided into several subnuclei and reciprocally connected with the “prefrontal cortex”
 - Afferents: several thalamic nuclei (AM, LD, VM, intralaminar nuclei; RT); cortical input (layer 5) is bilateral; amygdala, basal forebrain, ventral pallidum, substantia nigra, VTA, brainstem nuclei
 - Efferents: cingulate cortex, prefrontal cortex (pre- and infralimbic, agranular cortex); note: many other thalamic nuclei project to these regions
- Functional considerations: The MD is embedded in multiple distinct circuits implicated in “limbic-emotional” and visceral functions, learning and memory, control of epileptic activity



- a. Fornix
- b. Internal capsule
- c. Stria medullaris
- d. fornix
- 1. Anteromedial nucleus
- 2. Anteroventral nucleus
- 3. Anteromedial nucleus
- 4. Laterodorsal nucleus
- 5. Ventral anterior nucleus
- 6. Ventral medial nucleus
- 7. Reticular nucleus
- 8. Paraventricular nucleus
- 9. Mediodorsal nucleus
- 10. Central lateral nucleus

Anterior nuclei

- Three nuclei of the anterior thalamic pole (AM, AD, AV) and the laterodorsal (LD) nucleus have common input-output connectivity
 - Afferents: mammillary nuclei, limbic cortices, hippocampal formation (subiculum, pre- and parasubiculum), monoaminergic and cholinergic nuclei, RT
 - Efferents: medial prefrontal and cingulate cortex, entorhinal, perirhinal
- Functional considerations: “Extended” hippocampal system; spatial learning and memory; attentional processes; head direction

Lateral nuclei

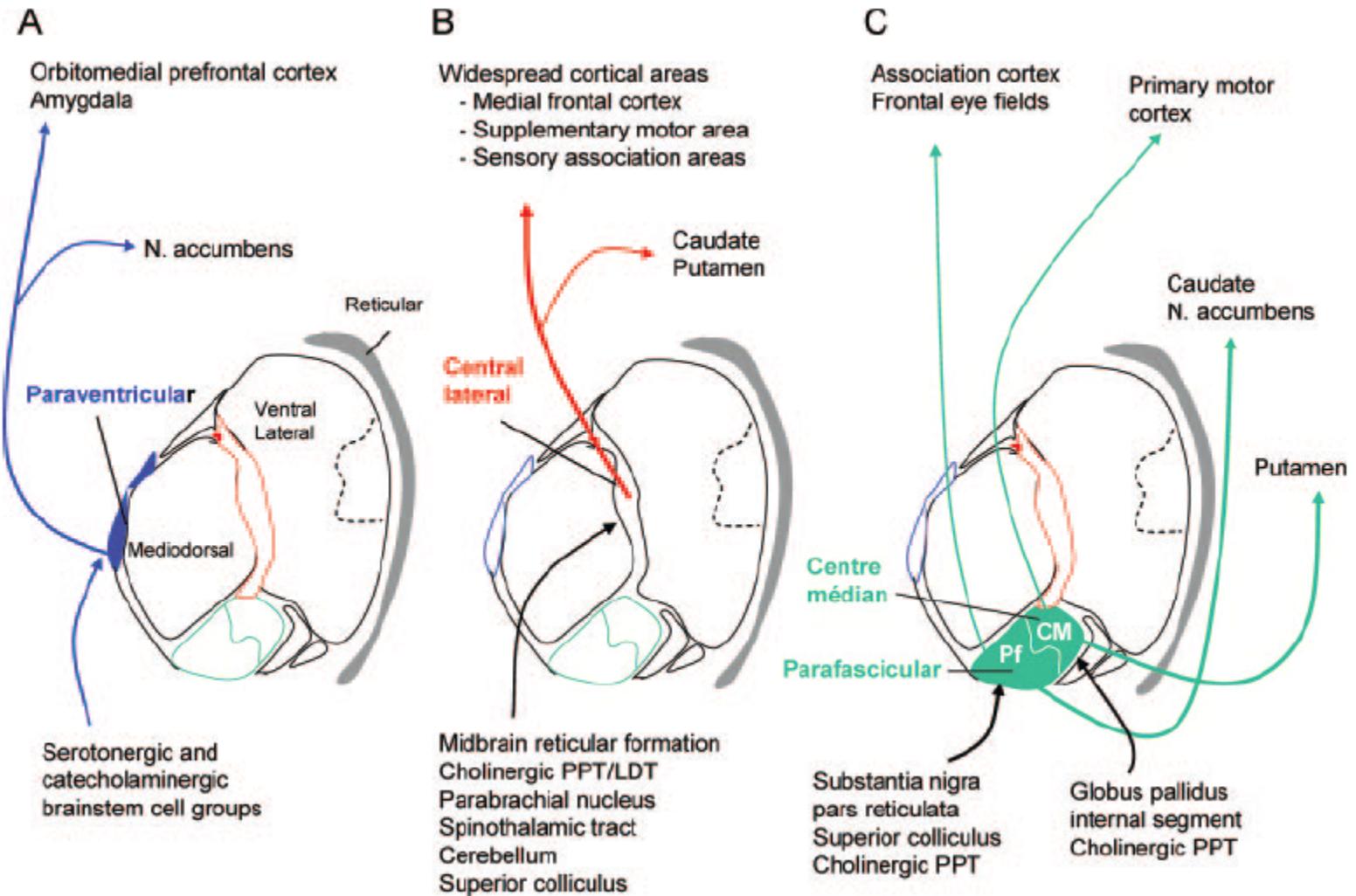
- LD and LP occupy a large dorsolateral territory of the thalamus; they are neurochemically heterogeneous
- Afferents:
 - LD: retrosplenial cortex (layers 5 and 6), area 17-18, subiculum, RT, pretectum, vLGN
 - LP: Association cortices, primary sensory cortices (collaterals of layer 5 pyramidal cells)
- Efferents:
 - LD: limbic cortex (cingulate, retrosplenial, entorhinal)

Functions

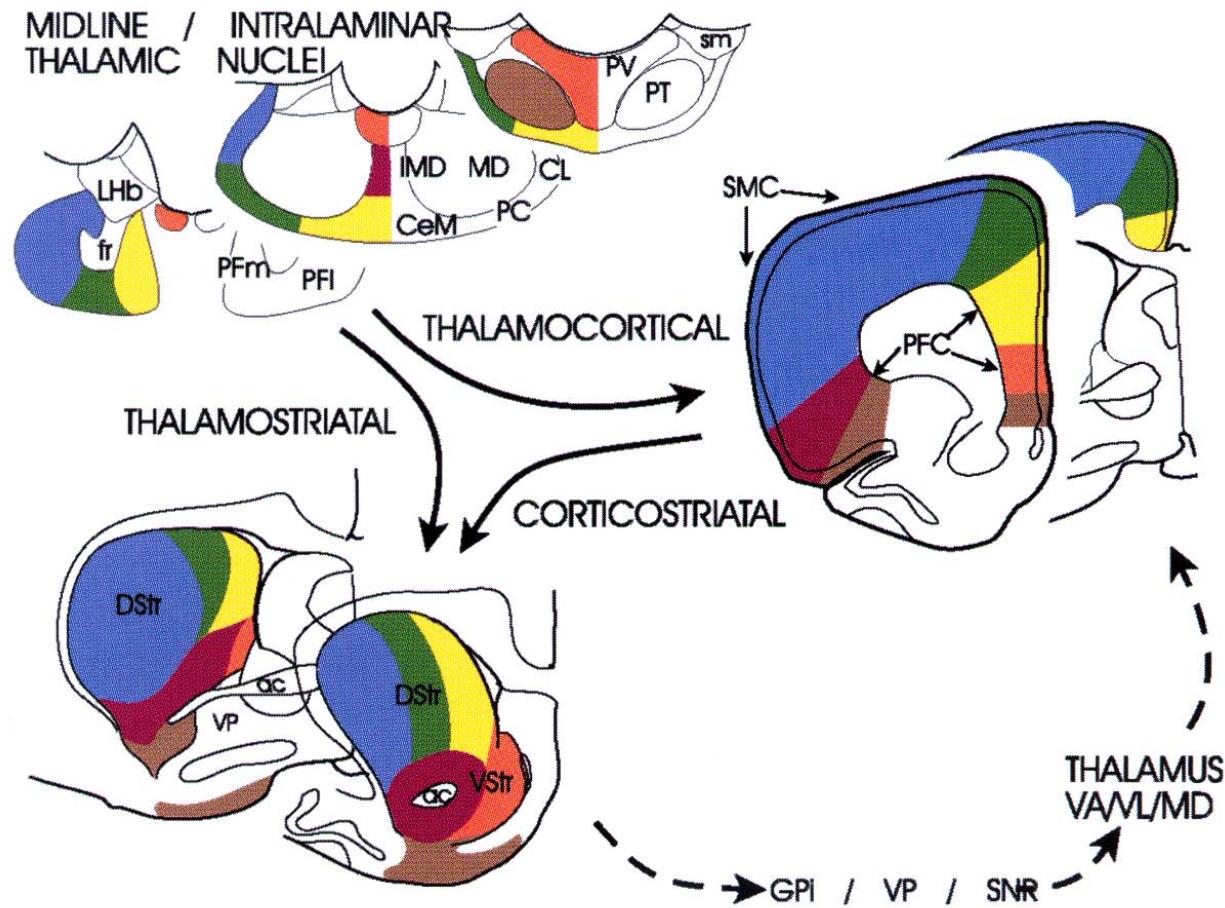
- LD: related to anterior thalamus, head direction, spatial learning;
- LP: visual association cortex (similar to pulvinar in primates)

Midline and intralaminar nuclei

Afferent and efferent connections



Thalamo-striatal and thalamo-cortical projections



Functions:

Arousal and attention; cognitive awareness; motor responses to salient stimuli; visceral systems; control of sexual behavior