Thalamus

A) Basic functions of different thalamic nuclei

B) Cellular level: basic functions of typical thalamic neurons

C) Thalamic neurons role in sleep and Absence epilepsy

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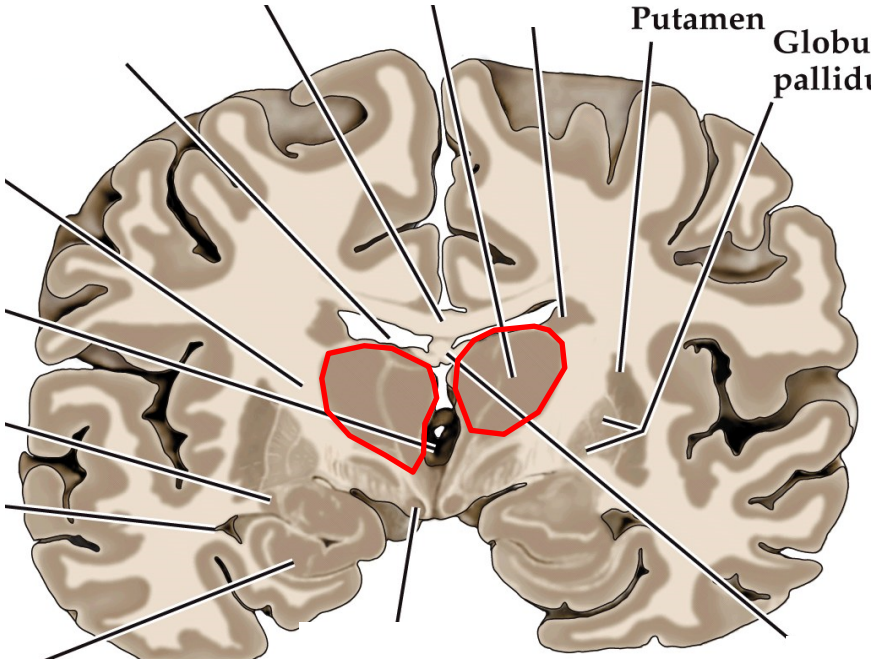
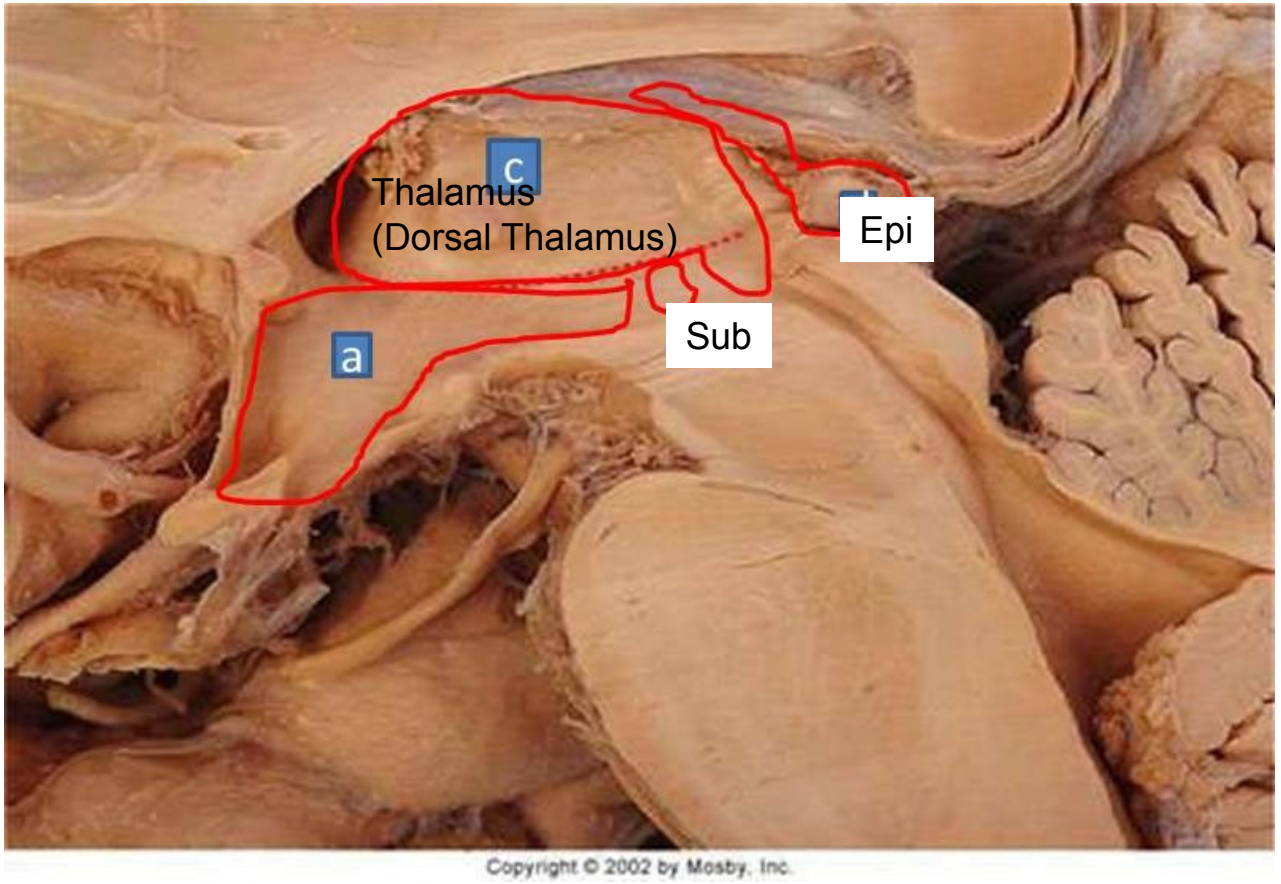
Thalamic location in sections



The thalamus is medial to the putamen and ventral to the somatosensory cortex

Thalamic aspects of the Diencephalon



Epi Thalamus – pineal gland attached + habenular nucleus – limbic system, circadian rhythms

THALAMUS = Dorsal Thalamus

Sub Thalamus – motor functions – (connected to basal ganglia and substantia nigra - target for Parkinson's surgery)

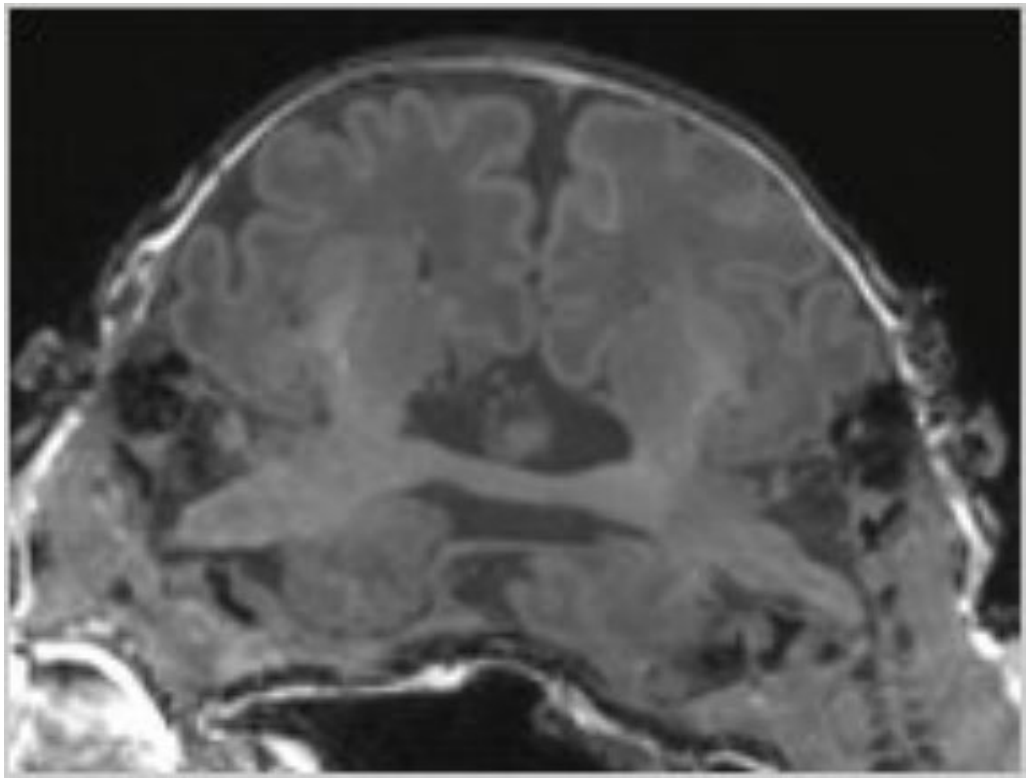
This is a video of conjoined twins. The first twin, Krista has her eyes covered. A toy is shown to the second twin, Tatiana. Then their mother asks Krista with her eyes covered what is the toy? Krista knows what the toy is despite the fact that she didn't see it with HER eyes.

How does she know?

http://video.nytimes.com/video/2011/05/13/magazine/100000000814707/two-united-as-one.html

Start – then 1:56

Conjoined twins connected at thalamus

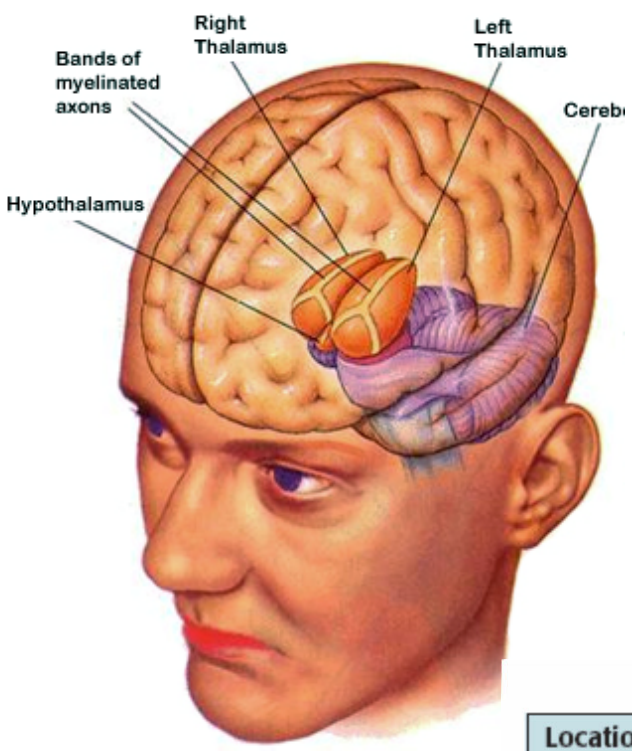


http://video.nytimes.com/video/2011/05/13/magazine/100000000814707/two-united-as-one.html

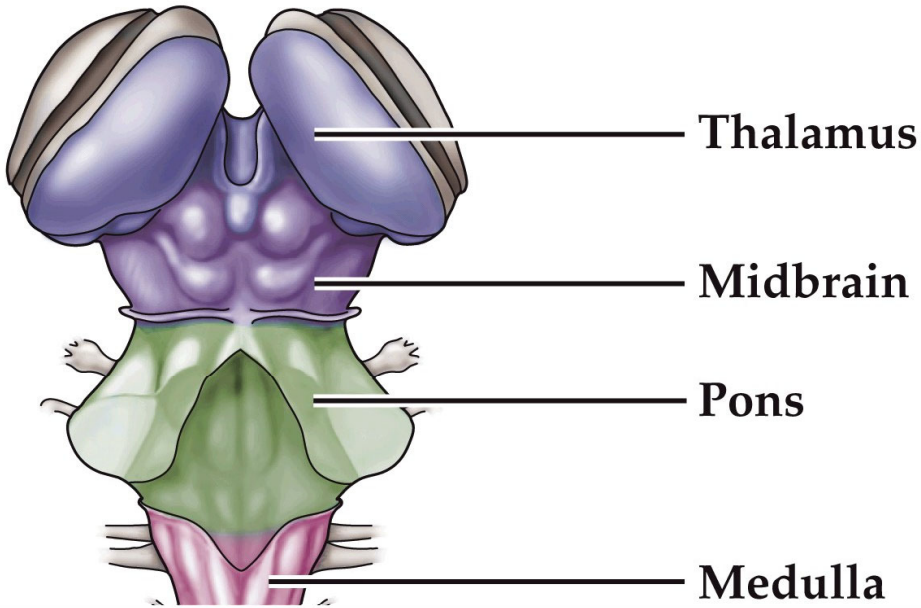
One twin can transfer information from her fingers or eyes to the consciousness of the other twin because they share the thalamus. They both have inputs to that thalamus and it projects to both of their cortices.

An important function of the thalamus is transferring sensory information from the periphery to consciousness (cortex)

Thalamus – Sensory Gateway to the Cortex



Dorsal Surface



Location	Paired, medially placed, deep egg-shaped nuclear structures that form part of the lateral wall of the 3rd ventricle
Architecture	Composed of multiple nuclei, which receive input from many cortical and subcortical structures
Function	Functions as the "gateway to the cortex." Sensory input, other than olfaction, relays through the thalamus before reaching the cortex. All output to the cortex from the cerebellum and basal ganglia relays through the thalamus. The thalamus also relays limbic input to the cortex
Clinical Significance	Due to its multiple functions, damage to the thalamus can cause many problems, including sensory abnormalities, visual-field deficits, and behavioral changes Lesions to the sensory area can cause numbness on the contralateral body and face

Thalamic Structure: 3 Main Groups of Nuclei

Anterior: *attention, memory and learning*
anterior nuclei

Medial: *sensory integration for abstract thinking and long-term, goal oriented behavior*
dorsomedial (DM) nucleus also called Mediodorsal(MD)

Lateral: *motor and sensory relay*

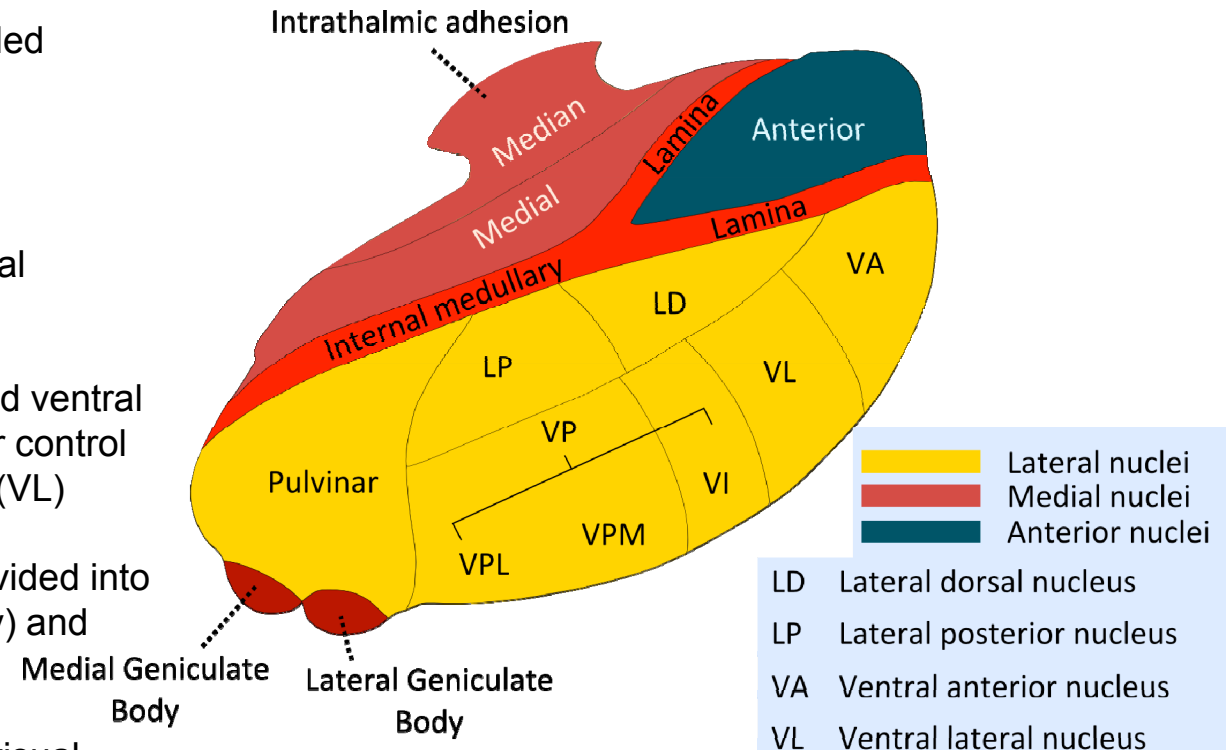
dorsal tier: lateral dorsal (LD); lateral posterior (LP), pulvinar (P) nuclei

ventral tier: ventral anterior (VA) and ventral lateral (VL) nuclei involved in motor control with cerebellum and basal ganglia (VL)

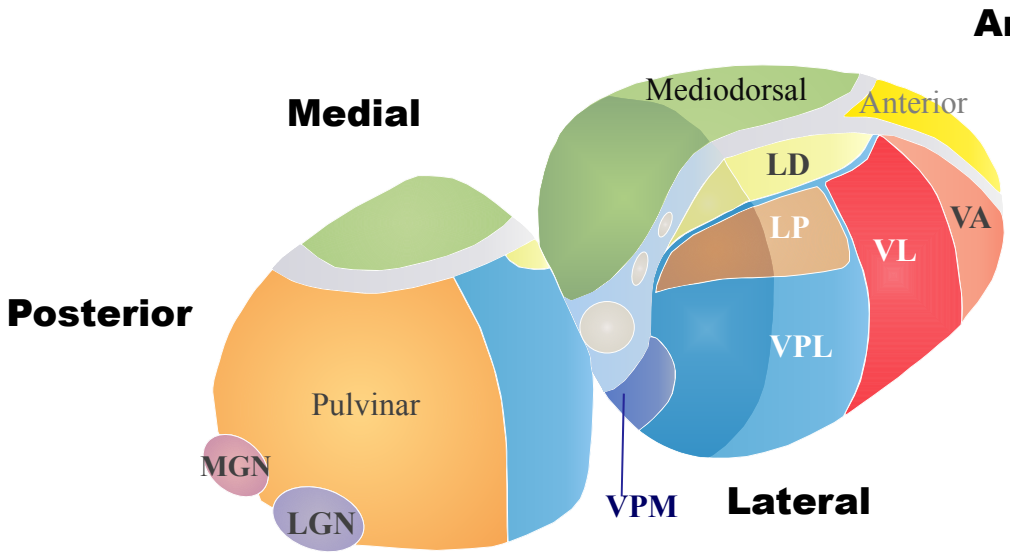
ventral posterior nucleus (VP) is divided into VPL (somatosensory relay for body) and VPM (somatosensory for head)

Posterior to ventral tier is LGN (visual relay) and MGN (auditory relay)

The internal medullary lamina divides the thalamus into anterior, medial and lateral nuclear groups. The lateral nuclear groups are subdivided into dorsal and ventral tiers



Visual Thalamus: Lateral Geniculate Nucleus (LGN)



VA = Ventral Anterior

VL = Ventral Lateral

LD = Lateral Dorsal

LP = Lateral Posterior

VPL = Ventral Posterior Lateral

VPM = Ventral Posterior Medial

LGN = Lateral Geniculate Nucleus

MGN = Medial Geniculate Nucleus

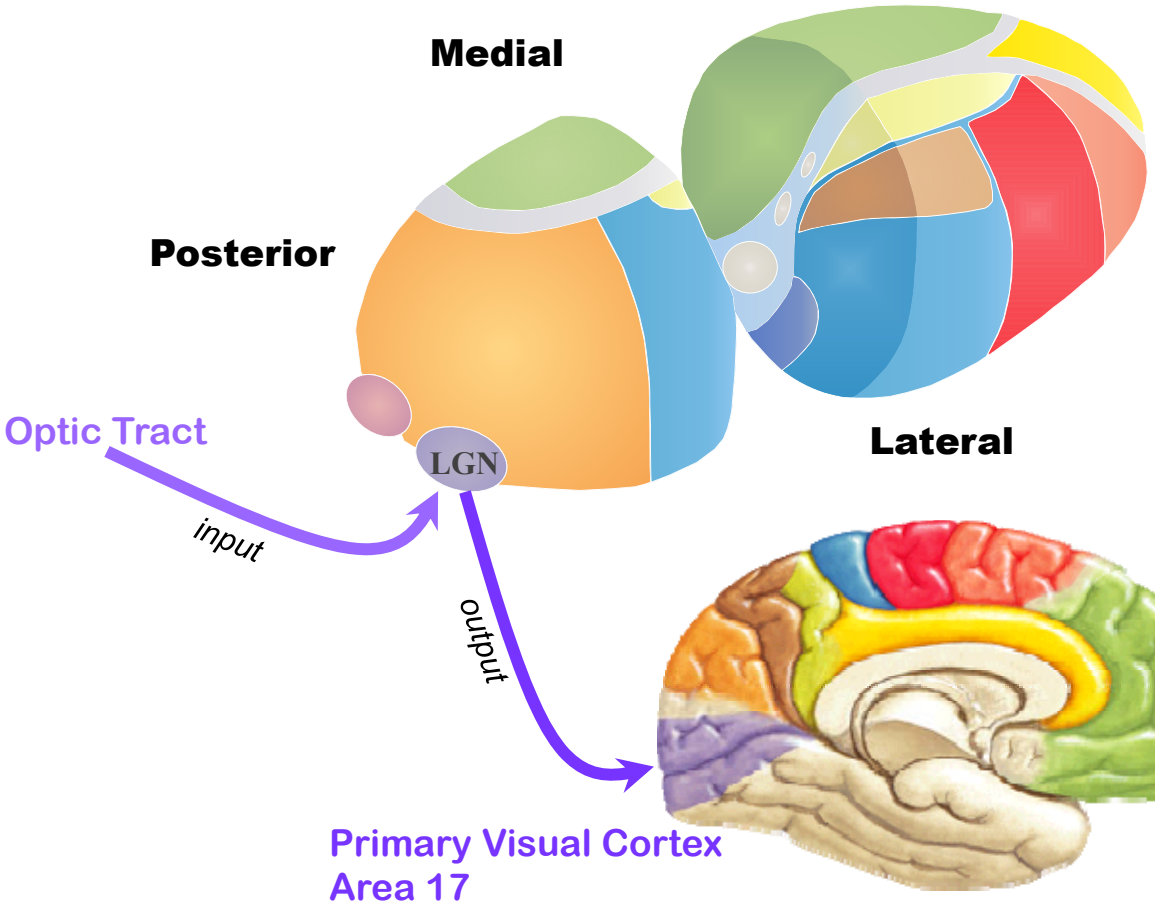
Thalamus: Lateral Geniculate Nucleus (LGN)

Function

LGN: Vision

Thalamic LESION: in LGN: contralateral homonymous hemianopsia
- same hemifield in both eyes lost

Lesion on right side produces loss on left side



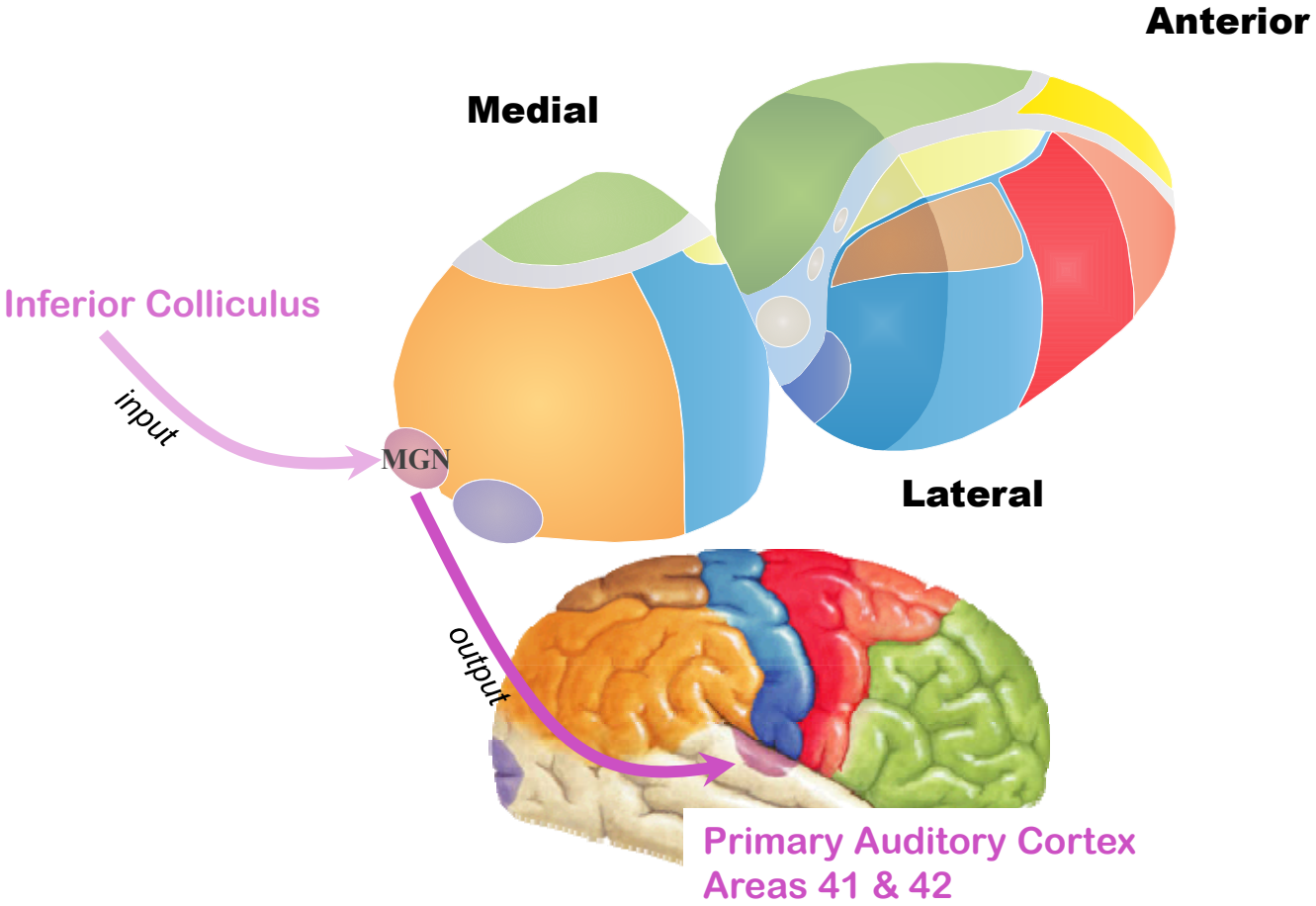
LGN = Lateral Geniculate Nucleus

Thalamus: Medial Geniculate Nucleus (MGN)

Function

MGN: Audition

Thalamic LESION: in MGN unilateral lesions have little effect on hearing, because auditory information from each ear ascends bilaterally. But bilateral lesions will cause auditory deficits.



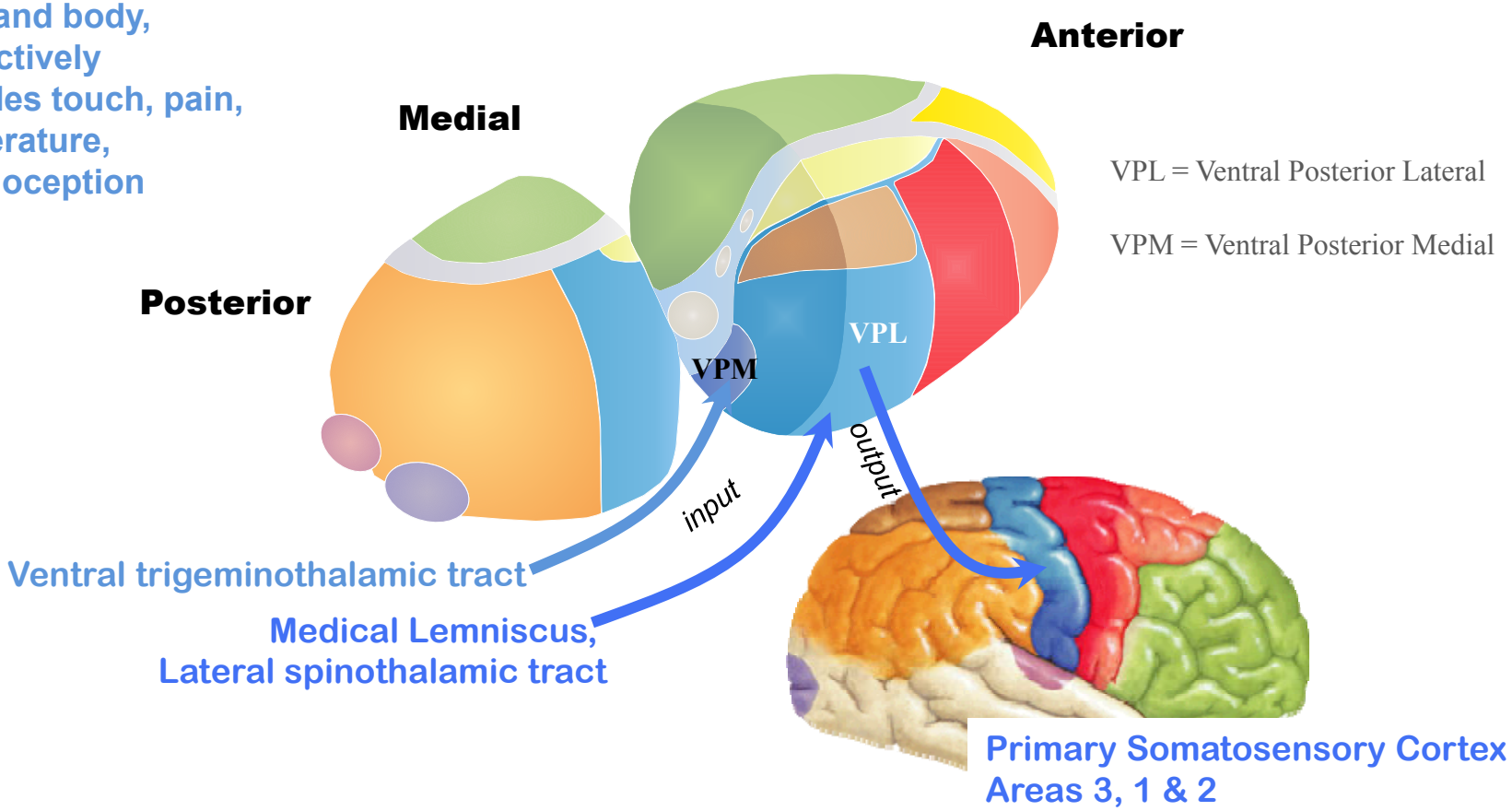
MGN = Medial Geniculate Nucleus

Thalamus: Ventral Posterior Medial and Lateral (VPM, VPL)

Thalamic LESION: In VPL - Loss of touch, pain, temperature and conscious proprioception, in the contralateral body; for VPM: same modalities, contralateral (to lesion) head and face.

Function

VPM, VPL:
Somatosensation of head and body, respectively
Includes touch, pain, temperature, proprioception



VPL = Ventral Posterior Lateral

VPM = Ventral Posterior Medial

Thalamic Pain or Central Pain Syndrome

Interrupting pain tracts can cause pain sensation

Paradoxically, some patients experience abnormally painful sensations (Athalamic pain) on the anesthetic side.

After a stroke, a person may experience thalamic pain or "**central pain syndrome**" due to damage to the spinal tracts that carry pain and temperature sensation from the periphery to the thalamus.

Damage to the spinothalamic or trigeminothalamic tract result in severe, spontaneous pain in the parts of the body connected to the damaged tracts.

Thalamic pain starts several weeks after the stroke and presents as an intense burning pain on the side of the body affected by the stroke and is often worsened by cutaneous stimulation.

If interested – treatment involving temperature changes in good limb combined with mirror therapy: https://www.youtube.com/watch?v=eRKCla2JIL4

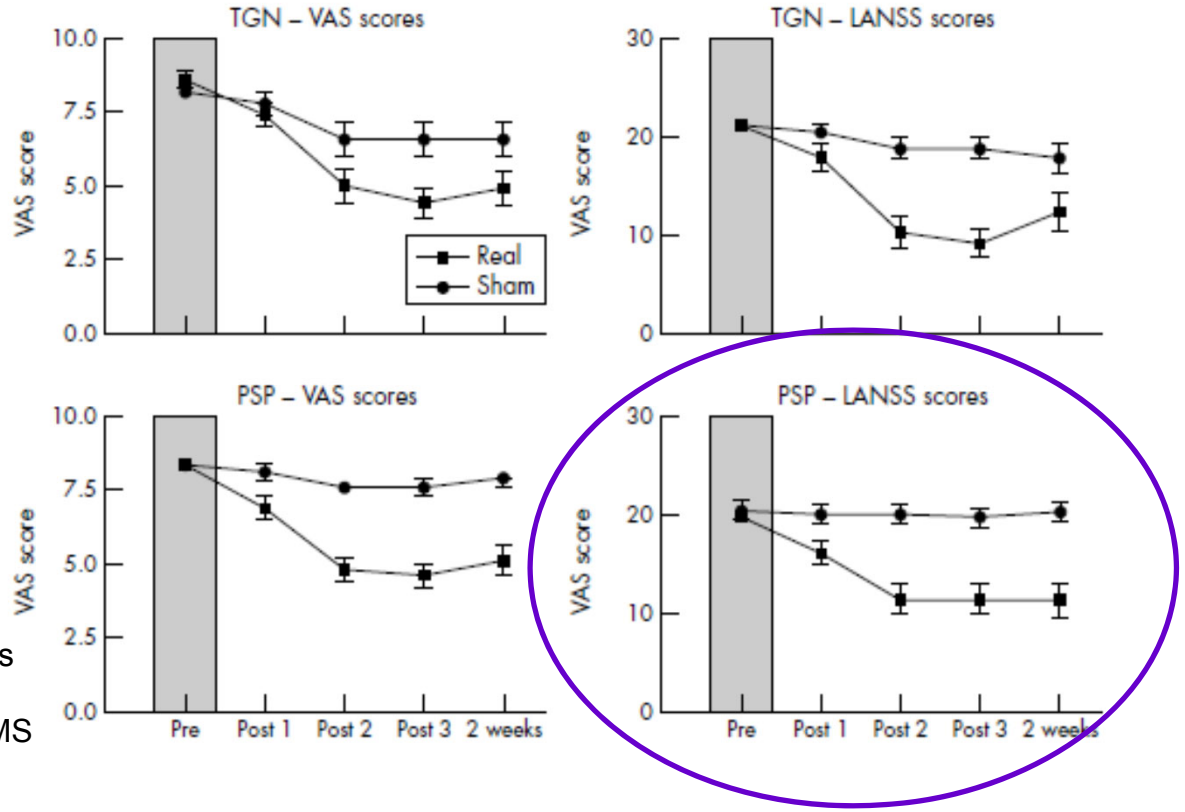
Repetitive TMS helps alleviate Central Pain Syndrome

Longlasting antalgic effects of daily sessions of repetitive transcranial magnetic stimulation in central and peripheral neuropathic pain

Khedr et al 2005 J Neurol Neurosurg Psychiatry, 76: 833.

Real vs sham TMS

10 min rTMS over hand area of motor cortex at 80% of motor threshold every day for 5 days



TGN = trigeminal neuralgia
PSP = post stroke pain

VAS = visual analogue scale

LANSS = Leeds assessment of neuropathic symptoms and signs

Post 1 is after first session of TMS
Post 2 is after 4th session
Post 3 is after 5th session
Last point is 2 weeks later.

2017 Meta-analysis: “Use of rTMS improves the efficacy of conventional medical treatment in chronic pain patients. This treatment is not associated with any direct adverse effects. However, the duration and frequency of rTMS therapy is presently highly variable and needs standardization.” *Anesth Essays Res, 11: 751.*

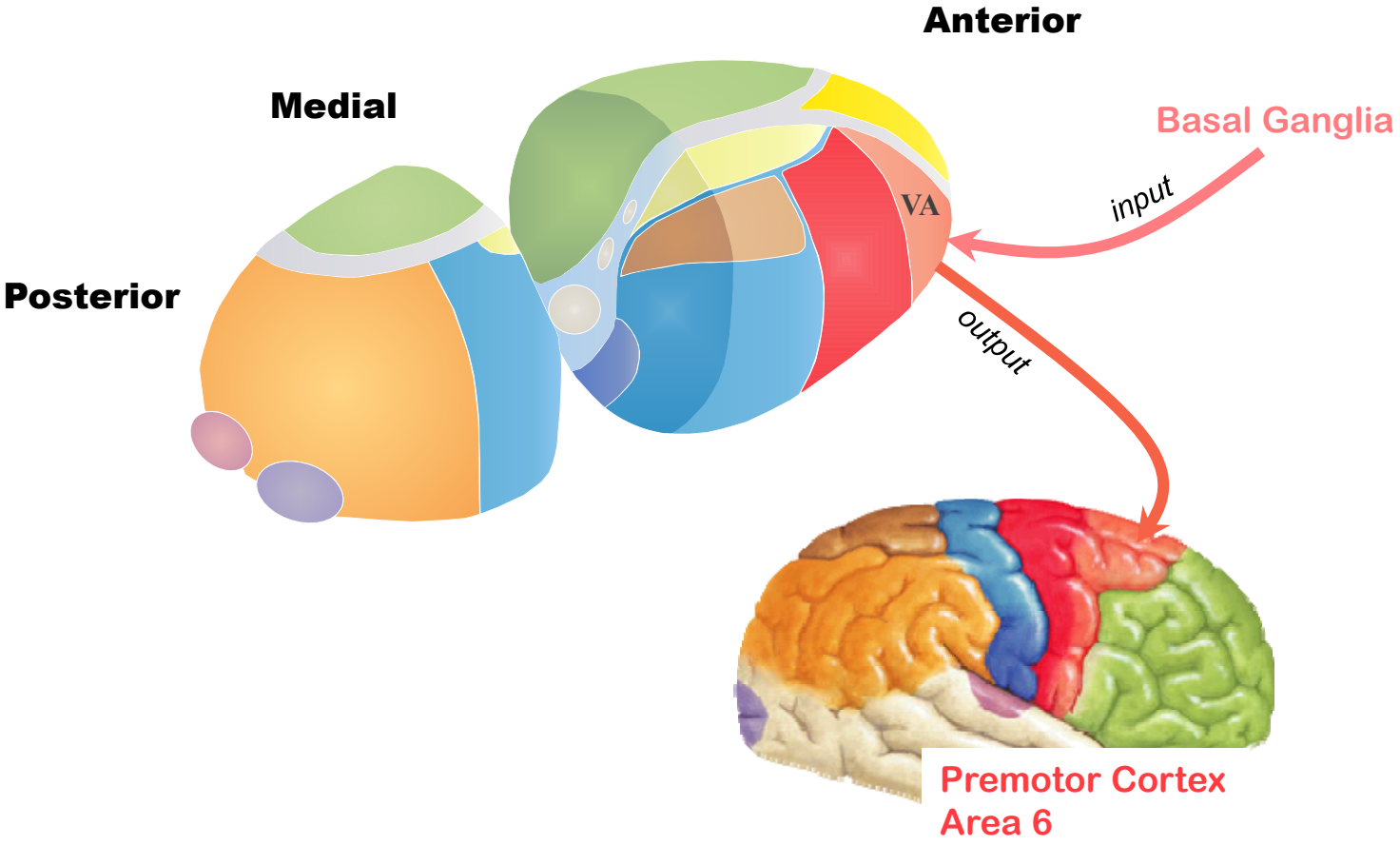
Thalamus: Ventral Anterior (VA)

Thalamic LESION: In VA interruption of basal ganglia input may result in akinesia (loss of voluntary movement).

Function

VA: Initiation and planning of movement

VA = Ventral Anterior



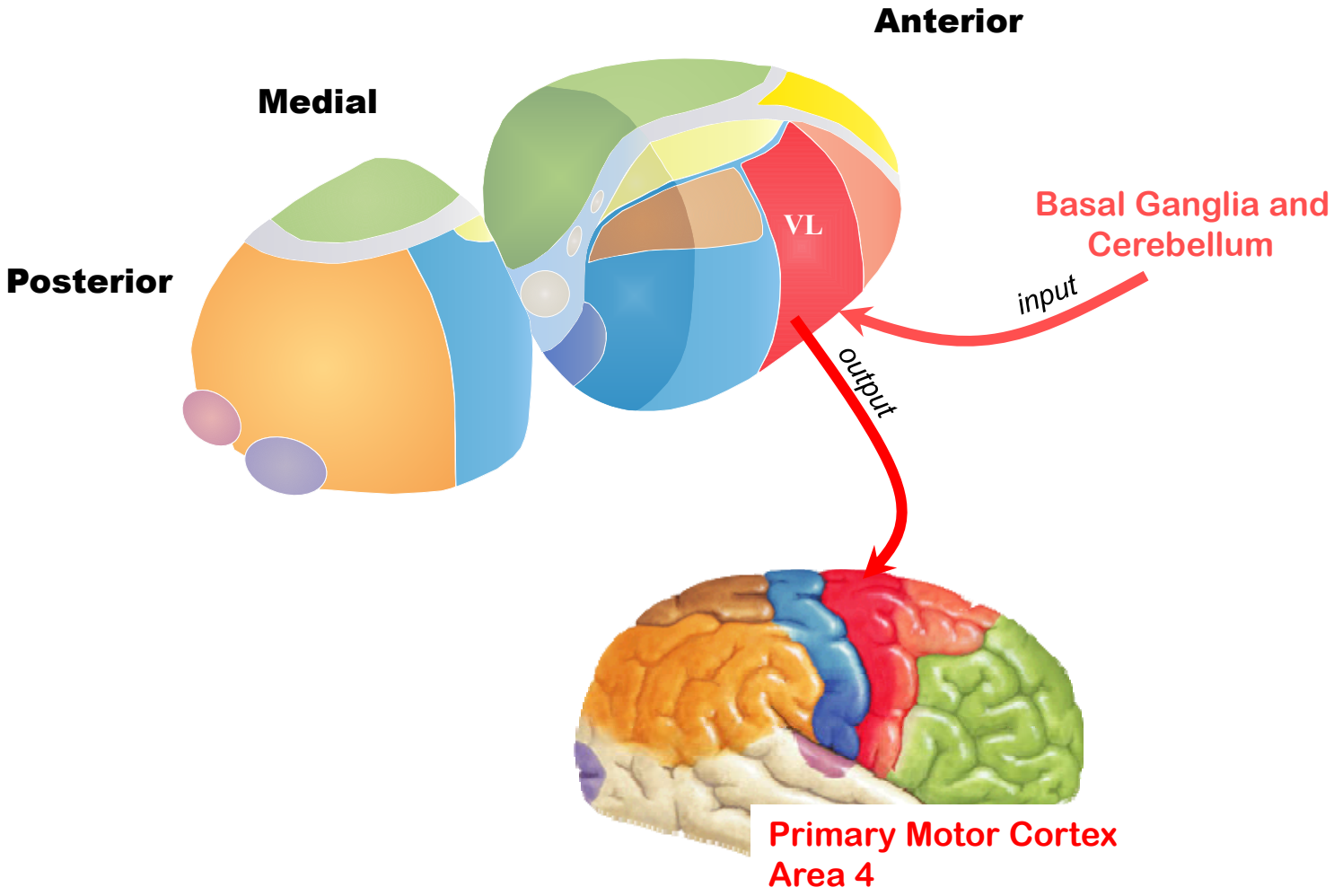
Thalamus: Ventral Lateral (VL)

Thalamic LESION: In VL interruption of basal ganglia input may result in akinesia (loss of voluntary movement).

Function

VL: Modulation and Coordination of movement

VL = Ventral Lateral

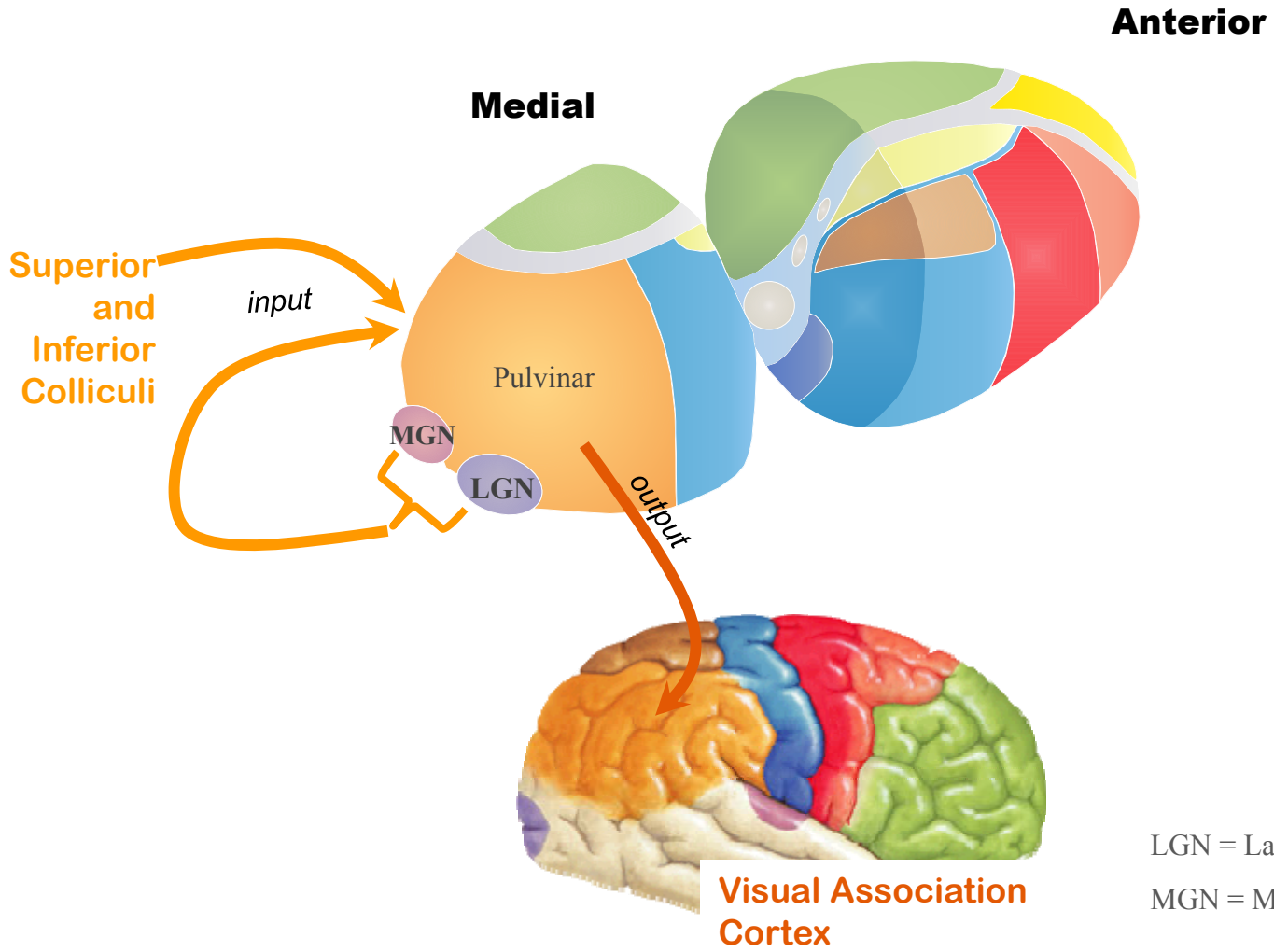


Thalamus: Pulvinar

Thalamic LESION: Lesion of the pulvinar can produce neglect or attentional deficit syndromes.

Function

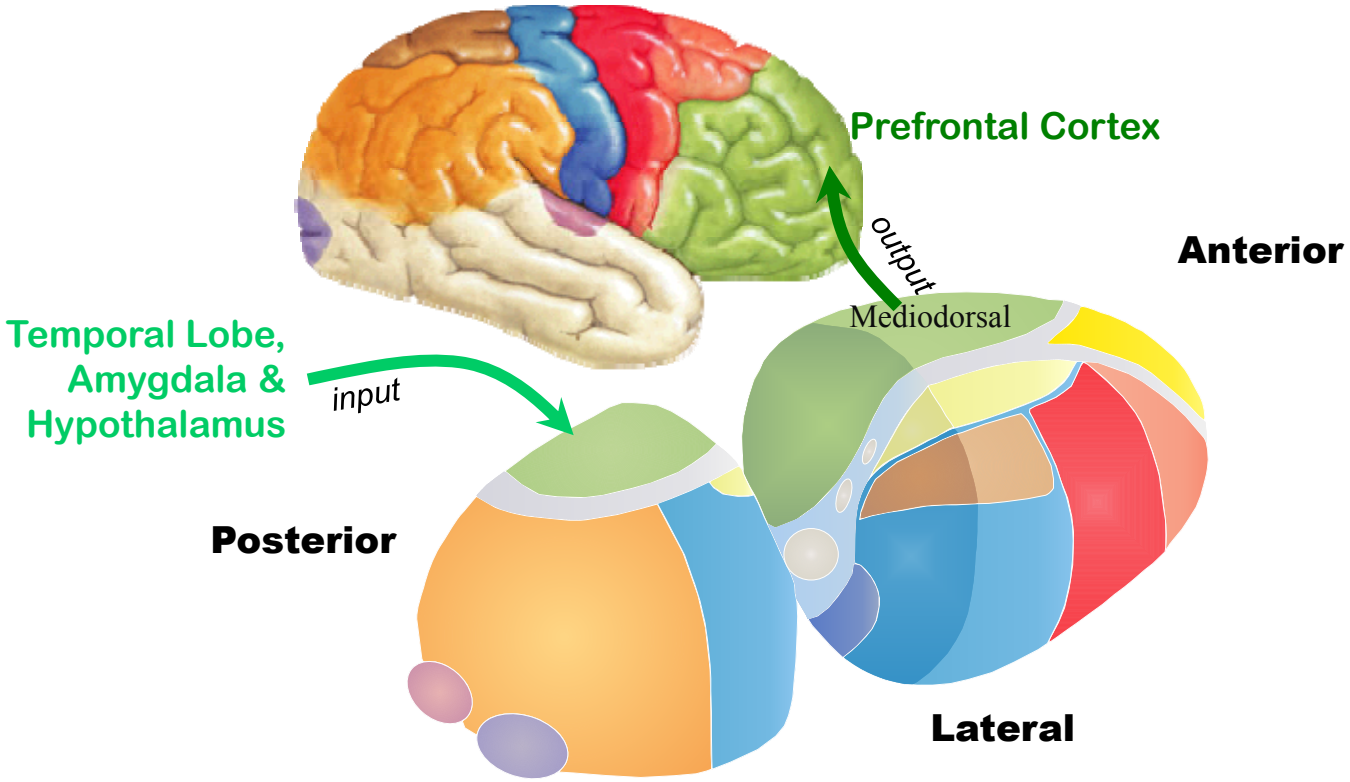
Pulvinar: Higher order visual function



LGN = Lateral Geniculate Nucleus

MGN = Medial Geniculate Nucleus

Thalamus: Mediodorsal Nucleus (MD)



Function

Mediodorsal: motivation, drive, emotion – sensory integration for abstract thinking and goal-directed behavior, may play a role in personality

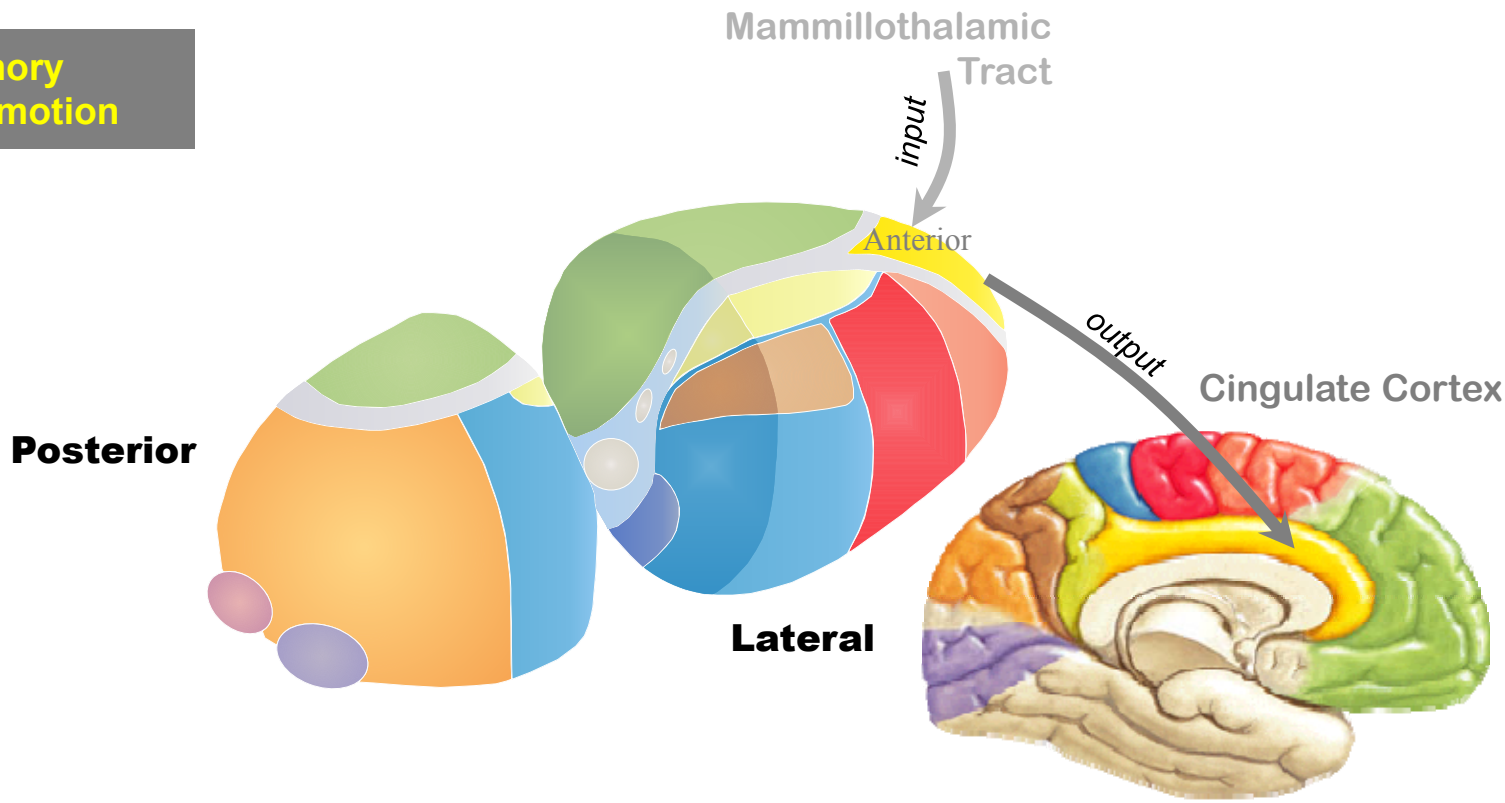
Thalamic LESION:

In MD can cause memory deficits, particularly when involving temporal lobe inputs

Thalamus: Anterior Nucleus

Function

Anterior: Memory storage and emotion



Thalamic LESION:

In Anterior Nucleus can cause memory deficits – significant amnesia

Additional Effect of Thalamic Lesions

Cognitive function:
Arousal: bilateral lesions affecting the intralaminar thalamic nuclei, which can be considered extensions of the brainstem reticular formation, can cause unresponsiveness, but the eyes remain open. This has been called coma vigil or akinetic mutism.

Memory: Lesions affecting medial thalamic structures (the confluence of mammillothalamic and amygdalofugal tracts, dorsomedial and possibly anterior nuclei) can cause profound amnesia.

Other cognitive functions: aphasia, neglect and visuospatial dysfunction have been described with thalamic lesions, and presumably relate to interruption of reciprocal thalamic connections with the cerebral cortex.

Thalamus: Internal Capsule

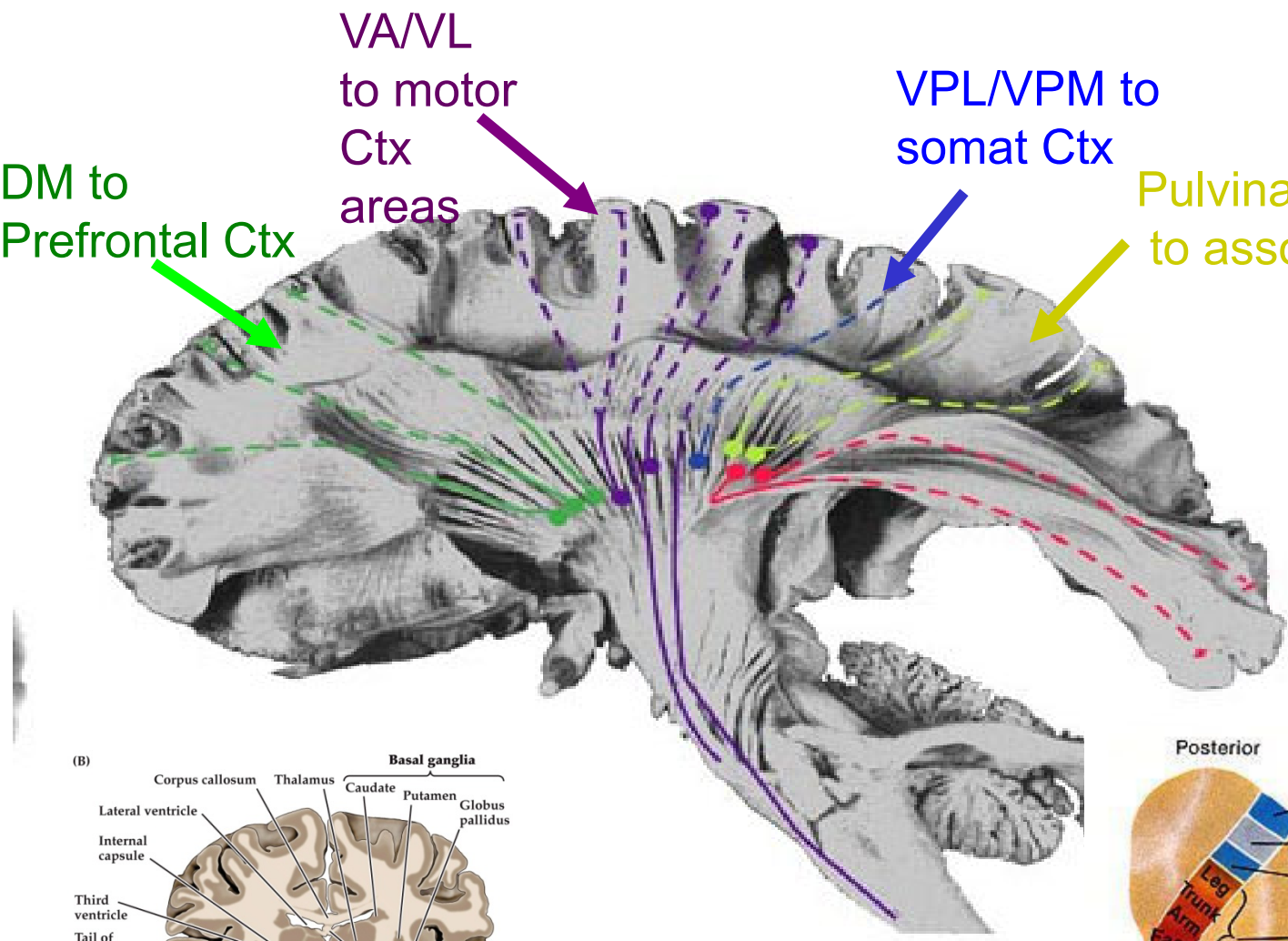
VA/VL to motor Ctx areas

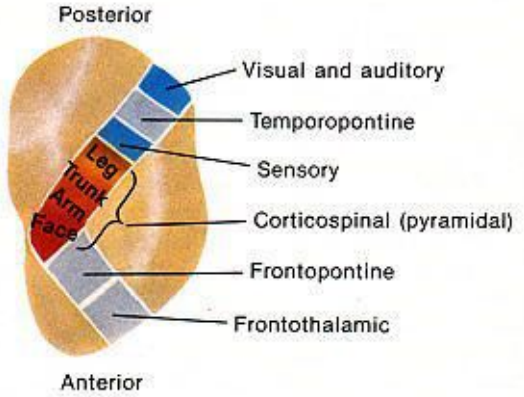
VPL/VPM to somat Ctx

DM to Prefrontal Ctx

Pulvinar/LP to association Ctx

LGN to Visual Ctx





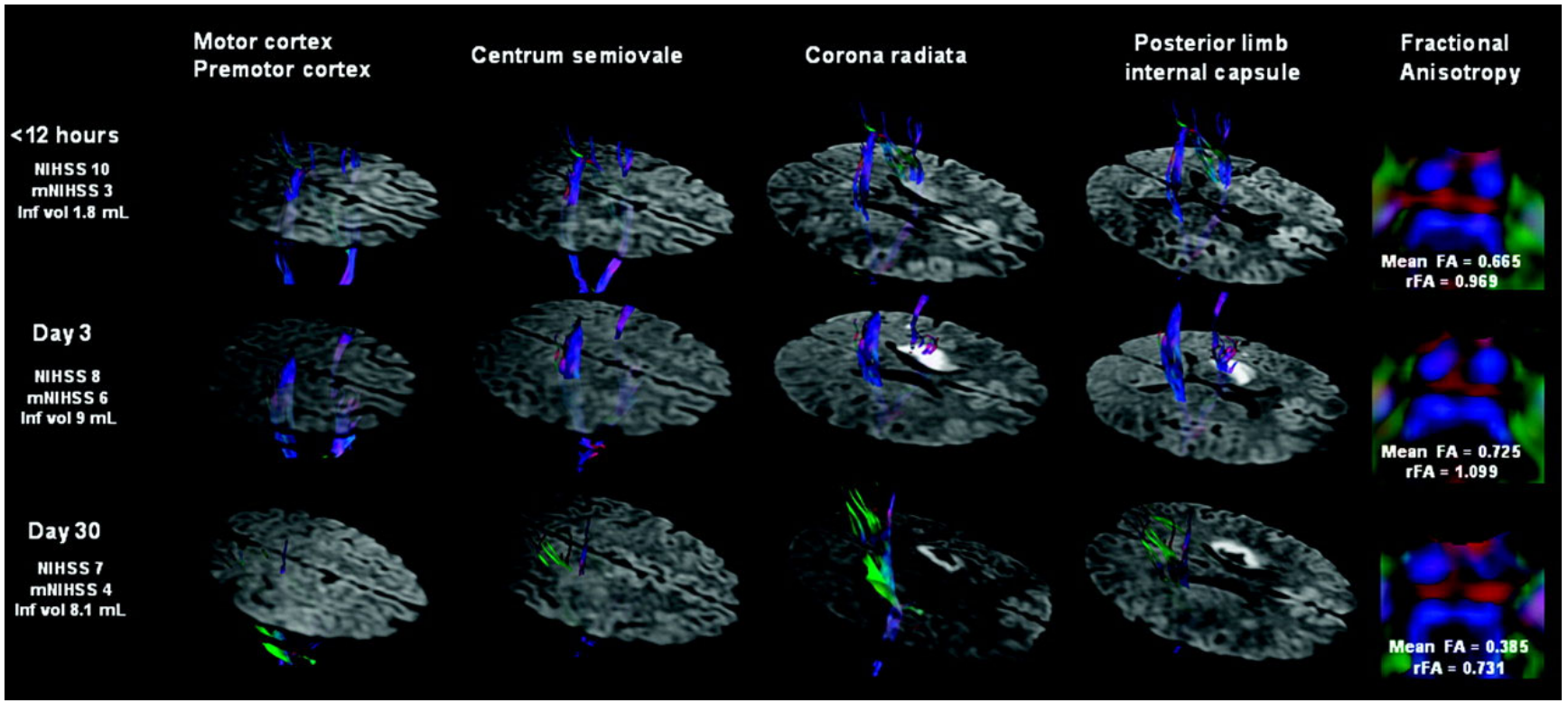
Horizontal section through internal capsule to show location of principal pathways

Acute Damage to the Posterior Limb of the Internal Capsule on Diffusion Tensor Tractography as an Early Imaging Predictor of Motor Outcome after Stroke

J. Puig, S. Pedraza, G. Blasco, J. Daunis-i-Estadella, F. Prados, S. Remollo, A. Prats-Galino, G. Soria, I. Boada, M. Castellanos and J. Serena

American Journal of Neuroradiology May 2011, 32 (5) 857-863; DOI: https://doi.org/10.3174/ajnr.A2400

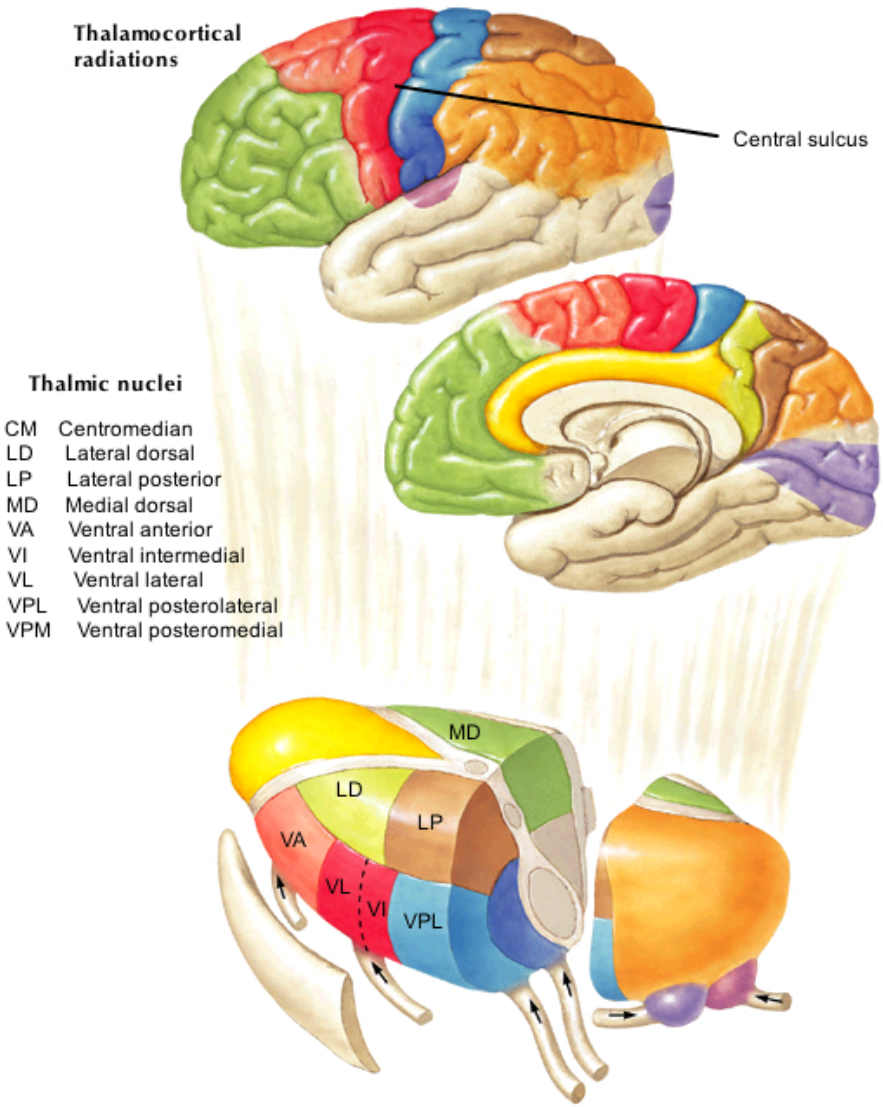
"CONCLUSIONS: In the acute setting, DTT *[Diffusion Tensor Tractography]* is promising for stroke mapping to predict motor outcome. Acute CST *[Cortical Spinal Tract]* damage at the level of the PLIC *[Posterior Limb of the Internal Capsule]* is a significant predictor of unfavorable motor outcome."



"Damage to the PLIC in the first 12 hours and at day 3 after stroke correlated with clinical severity, axonal damage expressed as decreased FA and rFA values, and motor outcome at day 30 and day 90 ($P < .001$) better than damage to any other CST region." No sig correlation btw acute infract volume and motor outcome!

Associations between specific thalamic and specific cortical regions

Thalamic Anatomy and Interconnections With the Cerebral Cortex



NUCLEUS	INPUT(S)	OUTPUT(S)	FUNCTION
Sensory Nuclei			
Ventroposterolateral (VPL)	Spinothalamic tract Medial lemniscus	Primary sensory cortex	Somatic sensation for contralateral body
Ventroposteromedial (VPM)	Trigeminothalamic tract, pontine taste area	Primary sensory cortex	Somatic sensation for contralateral face, taste
Medial geniculate (MGN)	Brachium of the inferior colliculus	Primary auditory cortex	Hearing
Lateral geniculate (LGN)	Optic tract	Primary visual cortex	Vision
Pulvinar	Lateral geniculate body (LGB), medial geniculate body (MGB), superior and inferior colliculi	Visual association cortex	Visual processing
Motor Nuclei			
Ventrolateral (VL)	Cerebellum and basal ganglia	Primary motor cortex	Modulation and coordination of movement
Ventroanterior (VA)	Basal ganglia	Premotor cortex	Initiation and planning of movement
Ventrointermedial (VI)	Cerebellum	Primary motor cortex	Coordination of movement
Limbic and Nonspecific Projection Nuclei			
Anterior (Ant)	Mammillothalamic tract	Cingulate cortex	Memory storage and emotion
Mediodorsal (MD)	Temporal lobe, amygdala, hypothalamus	Prefrontal cortex	Motivation, drive, emotion
Centromedian (CM)	Slow pain pathways	Nonspecific cortical projections	Emotional content of pain

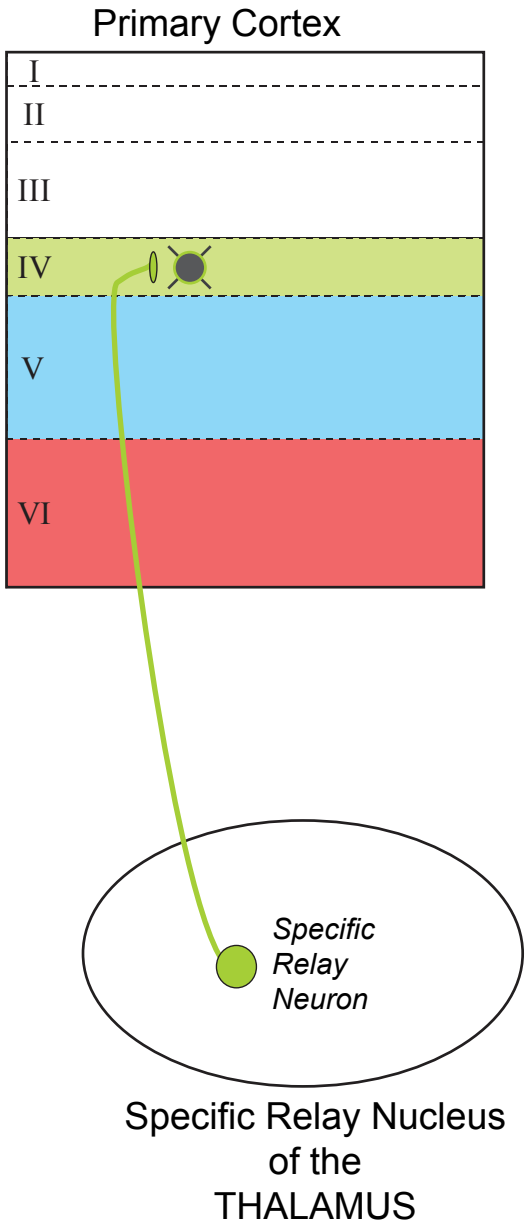
B) Cellular level: basic functions of typical thalamic neurons

A) Basic functions of different thalamic nuclei

B) Cellular level: basic functions of typical thalamic neurons

C) Thalamic neurons role in sleep and Absence epilepsy

Specific Relay Nuclei have Specific Relay Neurons that provide the focal high resolution input to Primary Cortical Areas



Examples:

<u>Specific Relay Nucleus</u> → <u>Primary Cortical Region</u>

VL → Primary Motor Cortex

VPM/VPL → Primary Somatosensory Cortex

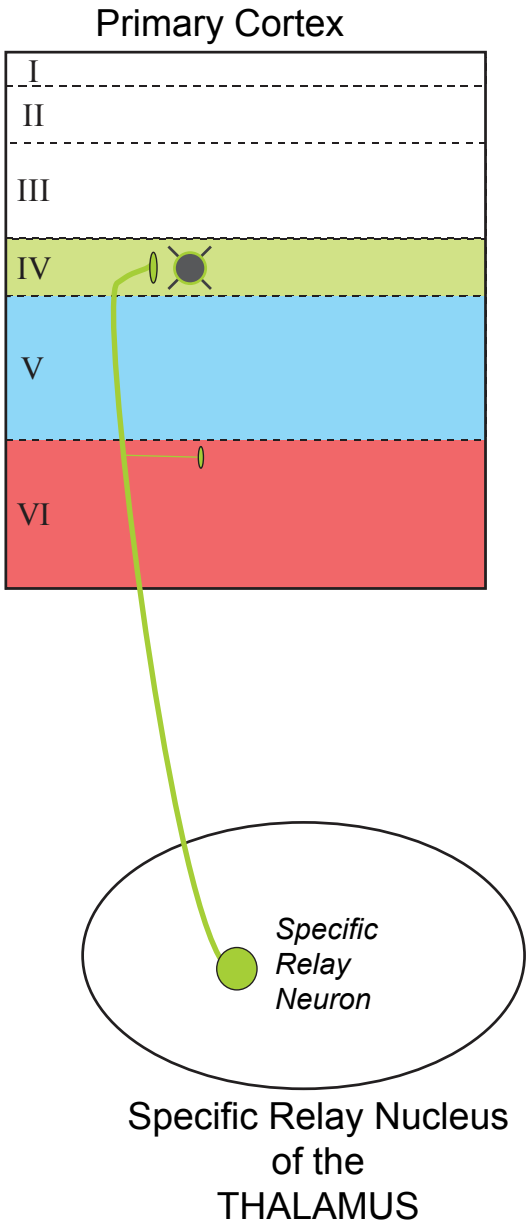
MGN → Primary Auditory Cortex

LGN → Primary Visual Cortex

Not for testing:
taste area is medial VPM → Primary Gustatory Cortex

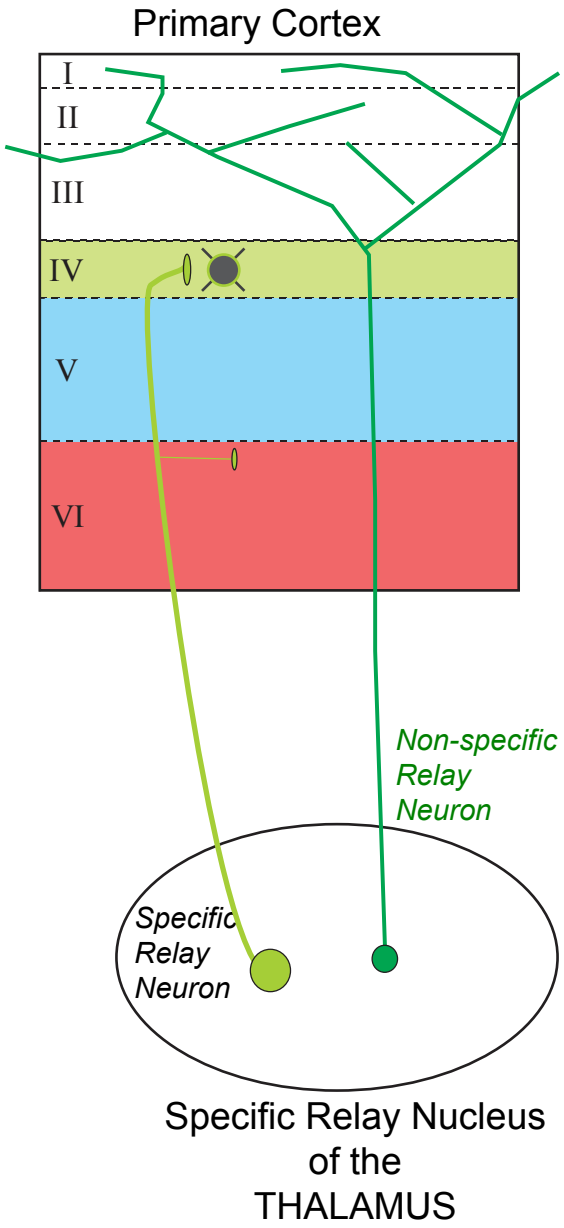
Olfaction goes directly to cortex – so no specific olfactory thalamic nucleus but thalamic lesions can modify whether things smell good and what you think the smell is – suggesting that olfactory cortex provides some inputs to thalamus.

Thalamic input to cortex



Although the main large input from thalamus is to layer IV, there is also a small input to superficial layer VI from the same cells

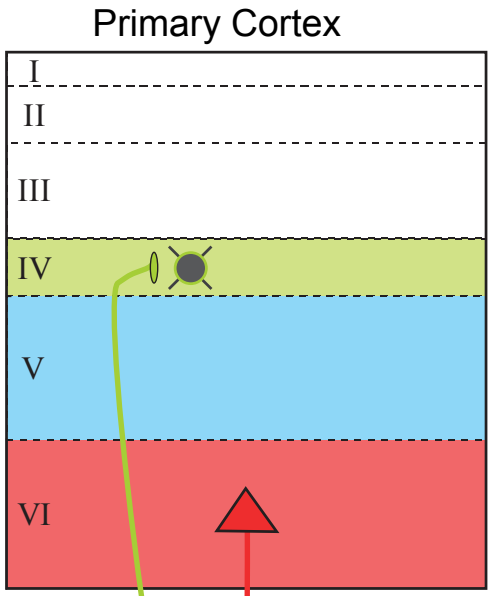
Thalamic input to cortex



Within specific thalamic nuclei, there are 2 types of thalamic cells. Specific relay cells and nonspecific cells. The nonspecific cells project diffusely to superficial layers of the cortex.

That is all you need to know about the nonspecific cells. They likely provide attentional cues – for the specific input conveyed by the specific relay neurons. We can stain for instance for calcium binding proteins and differentiate these two cell types. *If interested, see:* ***Thalamic*** *circuitry and thalamocortical* ***synchrony.*** ***Jones EG.*** *Philos Trans R Soc Lond B Biol Sci.* ***2002*** *Dec 29;357(1428):1659-73.*

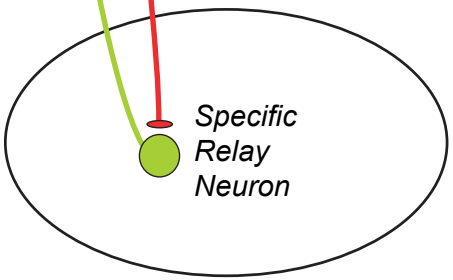
Cortex Provides Feedback to the Thalamus



Layer IV = input to cortex

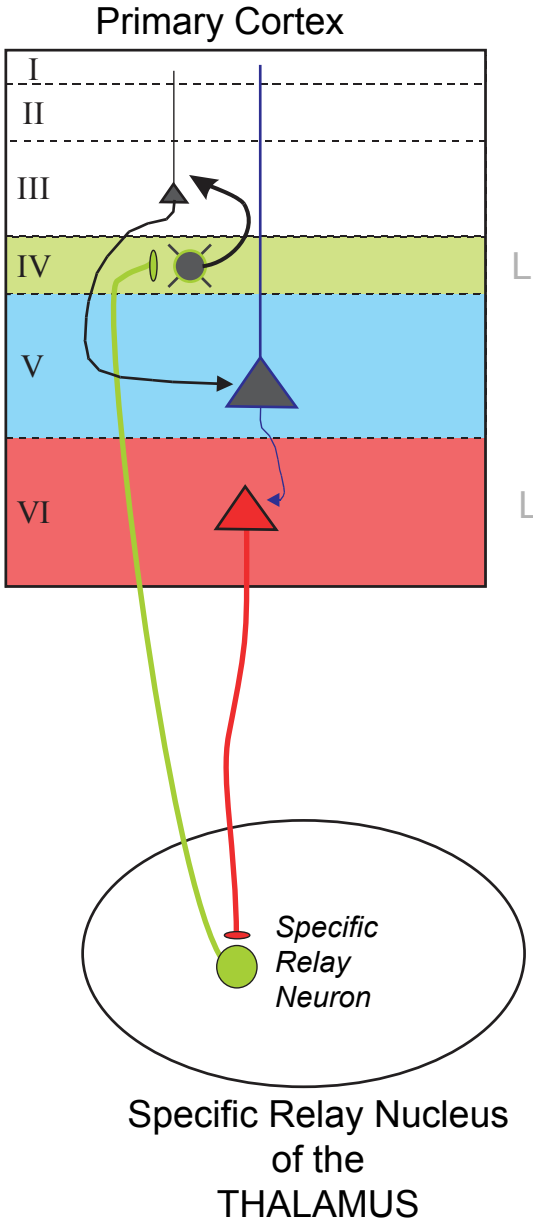
Layer VI = output back to the specific relay nucleus that innervates layer IV directly above the layer VI cells

Cortico-thalamic fibers (from cortex to thalamus)



Specific Relay Nucleus of the THALAMUS

How does the information get down to cortical layer VI?



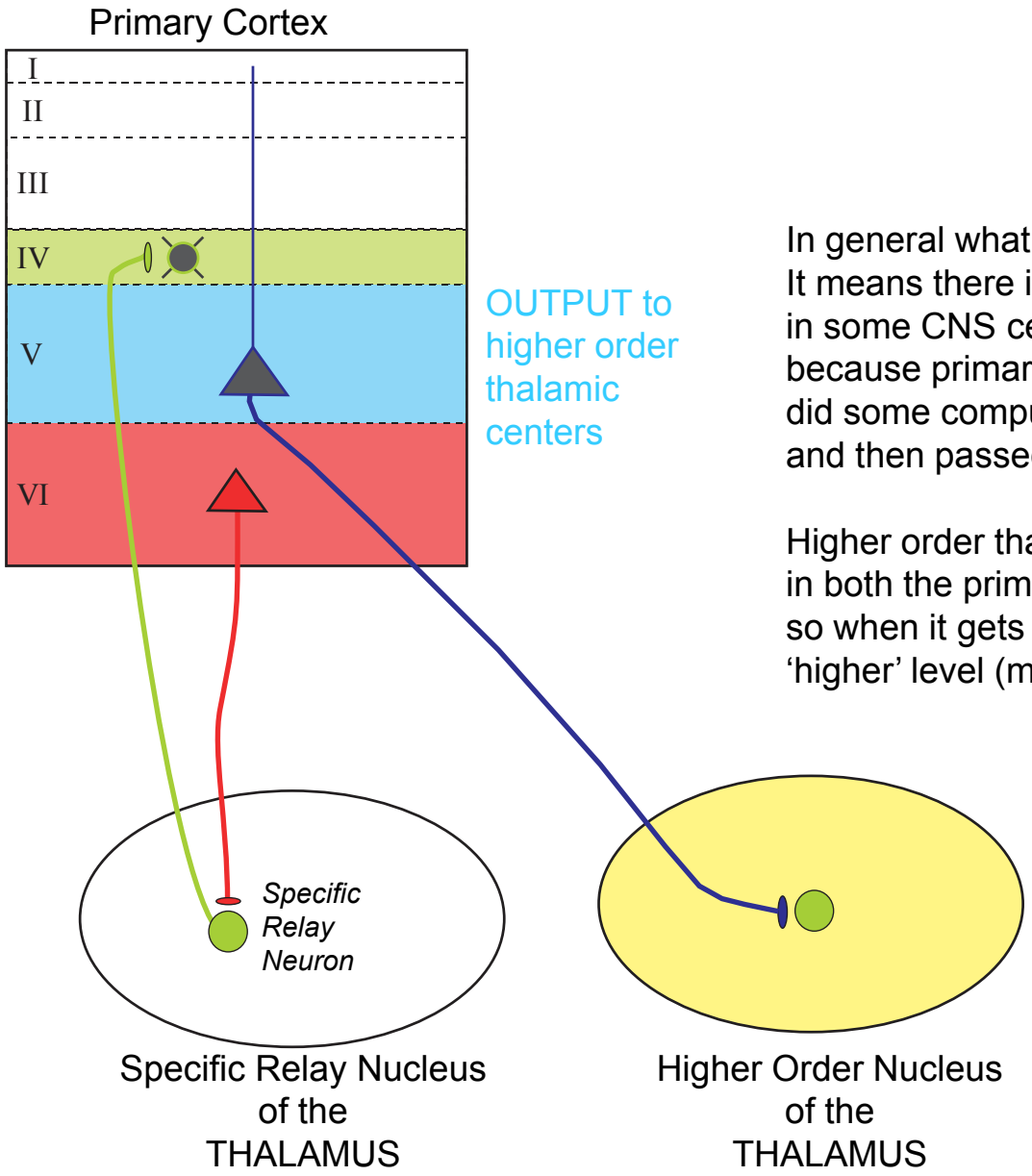
Intracortical connections transfer the information (after processing) down to layer VI

Layer IV = input to cortex

Layer VI = output back to the specific relay nucleus that innervates layer IV directly above the layer VI cells

The projection from layer V pyramidal neurons to layer VI are axonal collaterals,
as you will see – these cells also have other projections

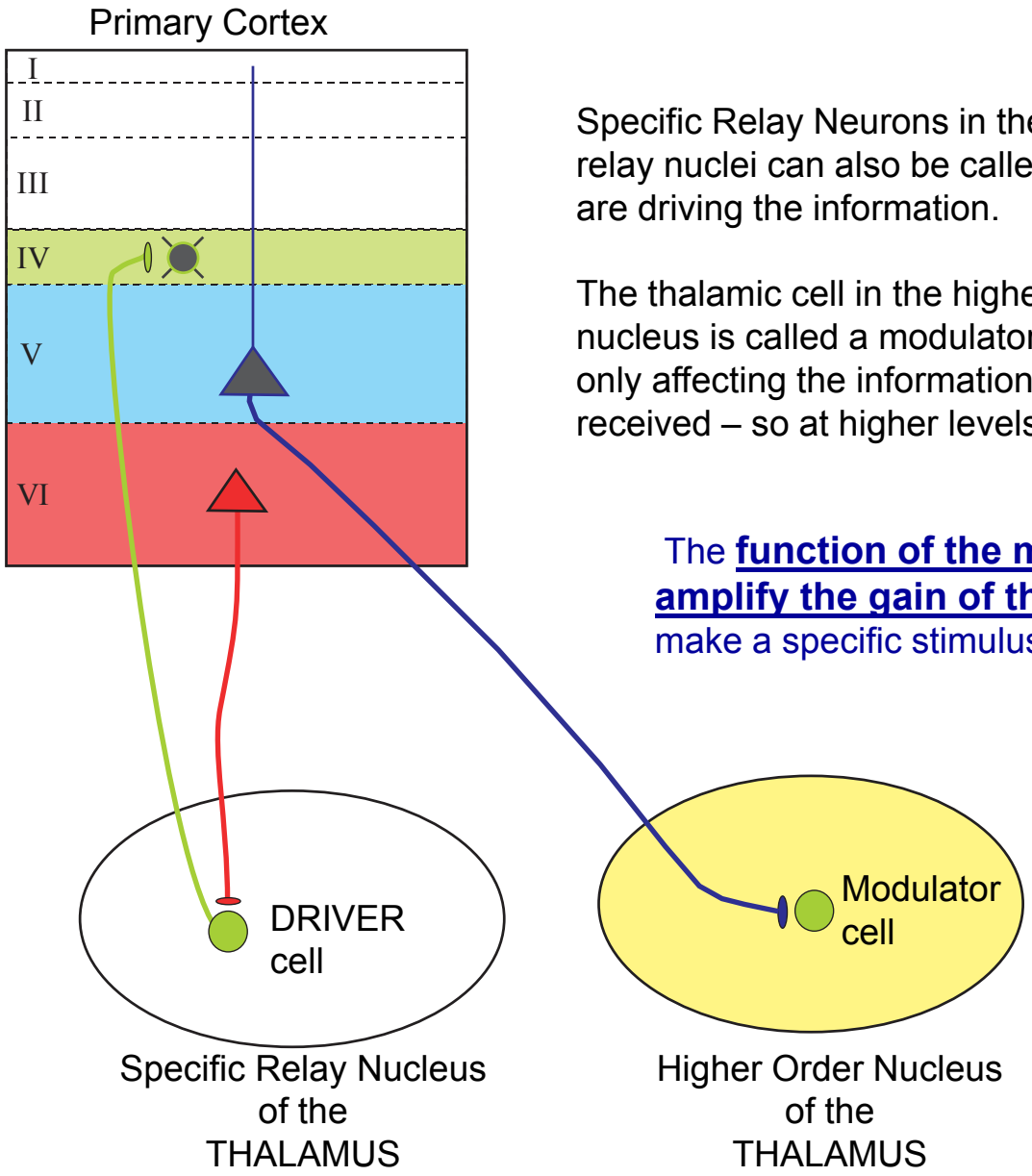
Primary Cortex Provides a Connection to Higher Order Thalamus



In general what does higher order mean?
It means there is additional processing that has gone on in some CNS center. Secondary Cortex is higher order because primary cortex already received that information did some computation through intracortical connectivity and then passed it to secondary cortex.

Higher order thalamus – processing has already occurred in both the primary thalamic nucleus and within the cortex so when it gets to higher order thalamic nucleus – it is 'higher' level (more processed) information.

Primary Cortex Provides a Connection to Higher Order Thalamus



Specific Relay Neurons in the primary or specific relay nuclei can also be called DRIVERS – they are driving the information.

The thalamic cell in the higher order thalamic nucleus is called a modulator cell – because it is only affecting the information after it is already received – so at higher levels modulation occurs.

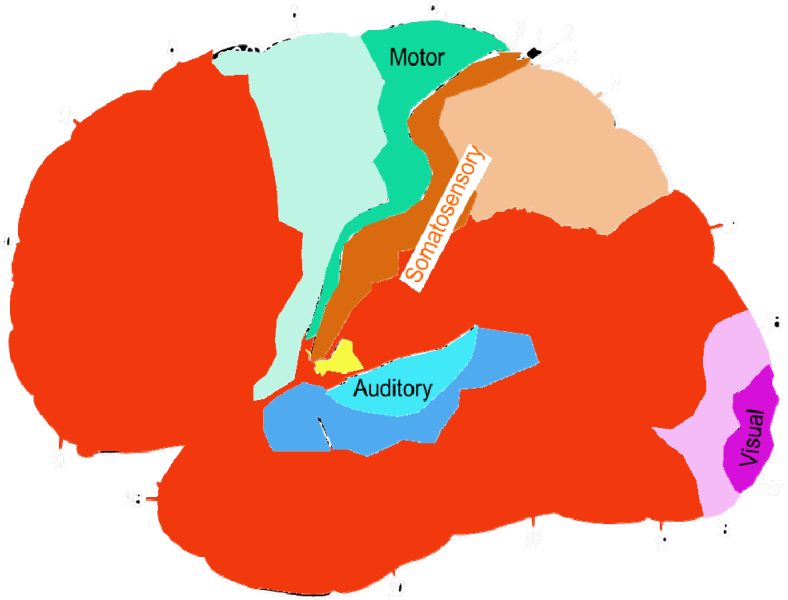
The **function of the modulator neurons is to amplify the gain of the signal**, that is they can make a specific stimulus become more important.

Secondary cortical areas surround primary areas. Much of what is left is Association cortex where senses are integrated

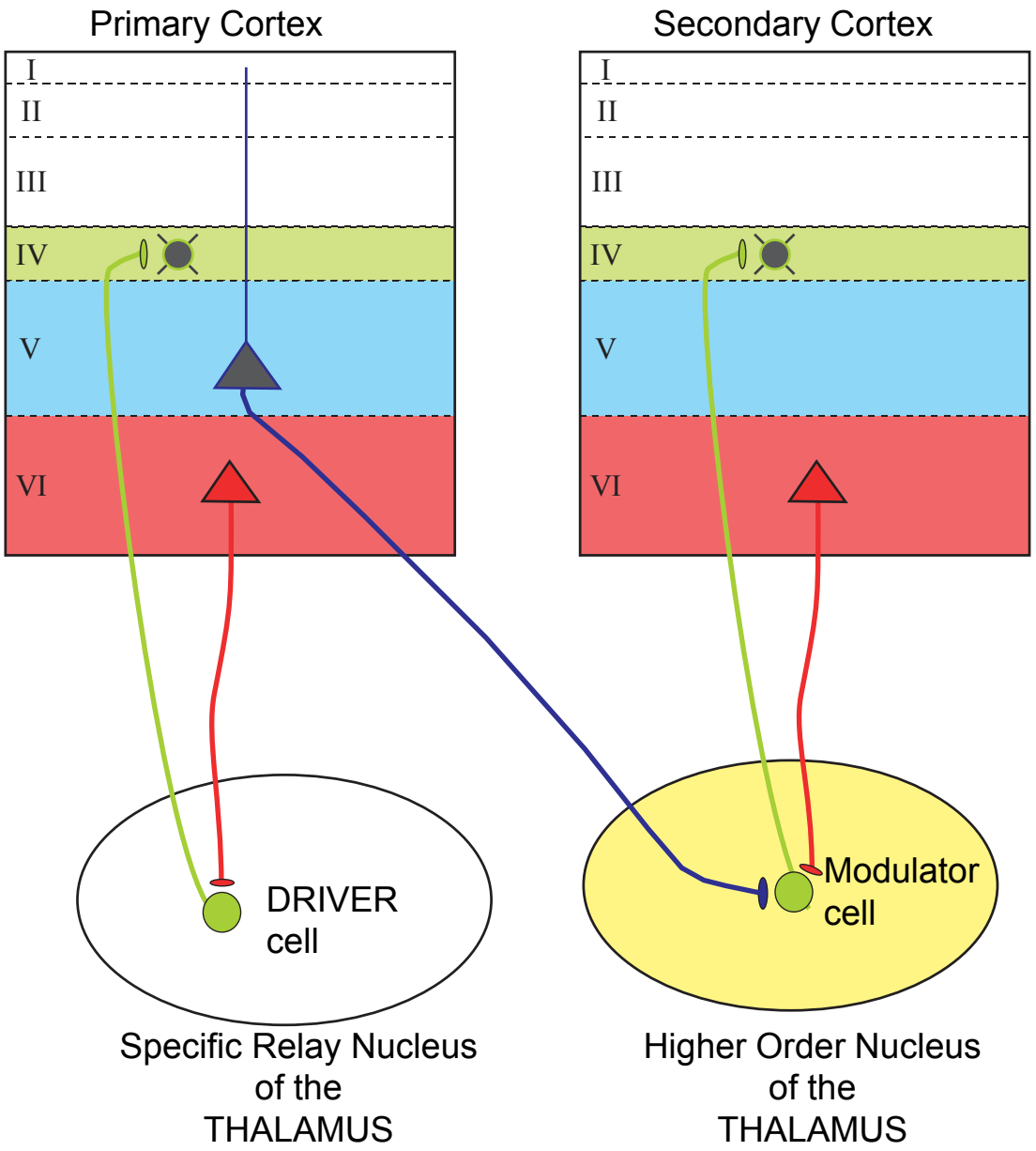
Primary Areas Identified

Secondary Areas Added

Core Field (primary)
Belt - Less Specialized (secondary)
Association areas

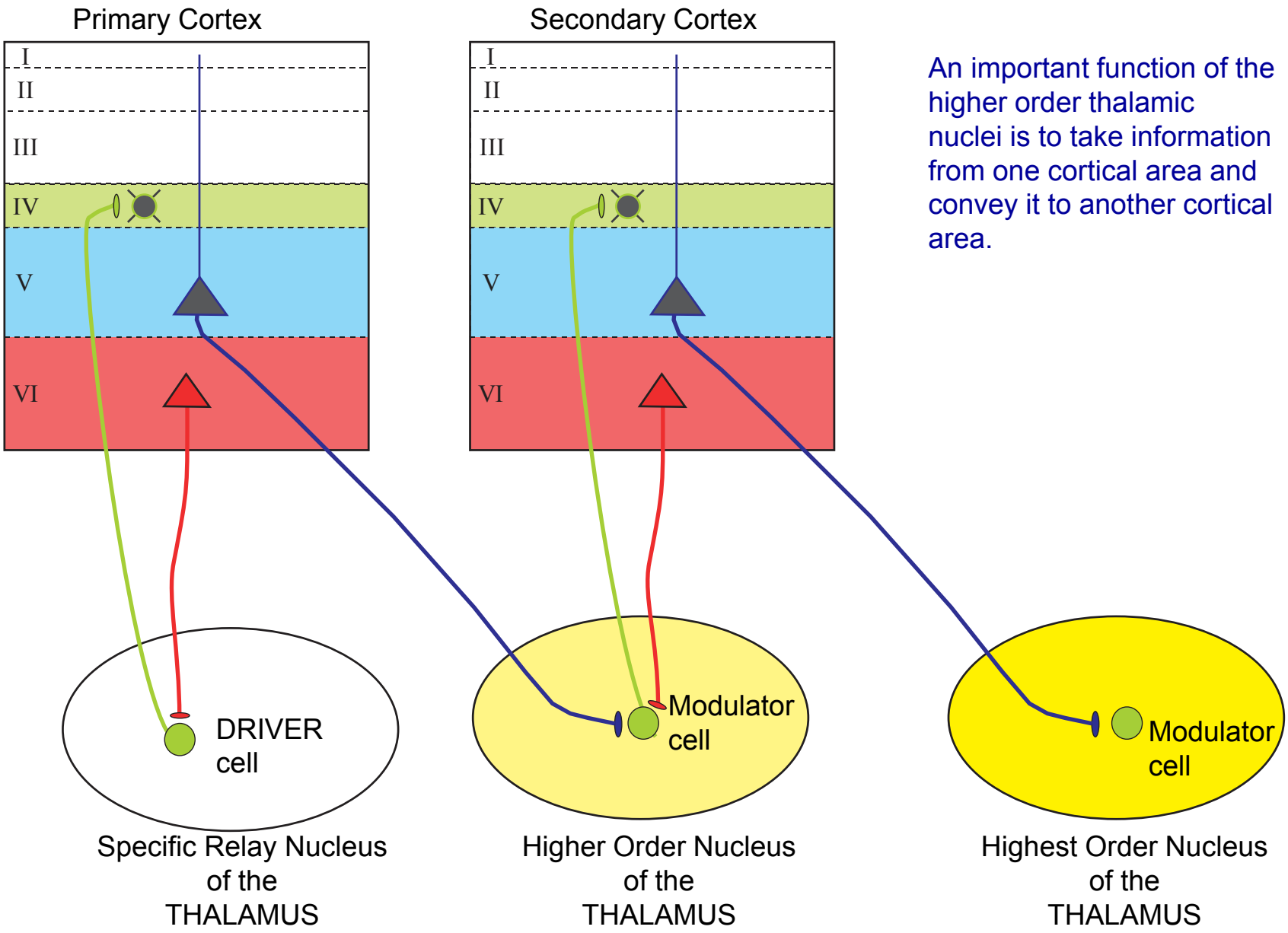


Thalamic cells project mainly to layer IV and receive back from layer VI



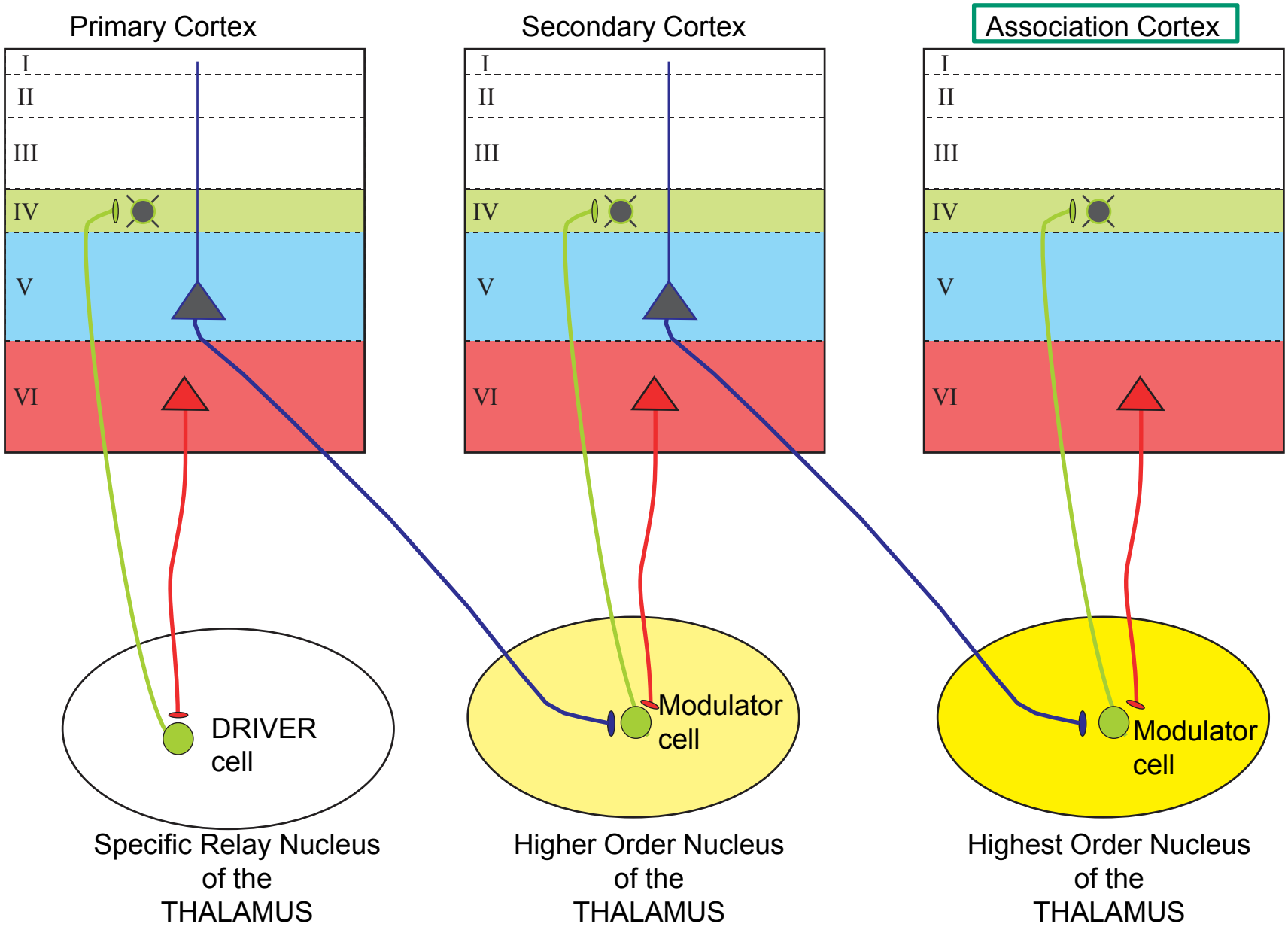
Higher order thalamic nucleus projects to layer IV of SECONDARY Cortex

There are three (known) levels of this hierarchy – the pattern is the same

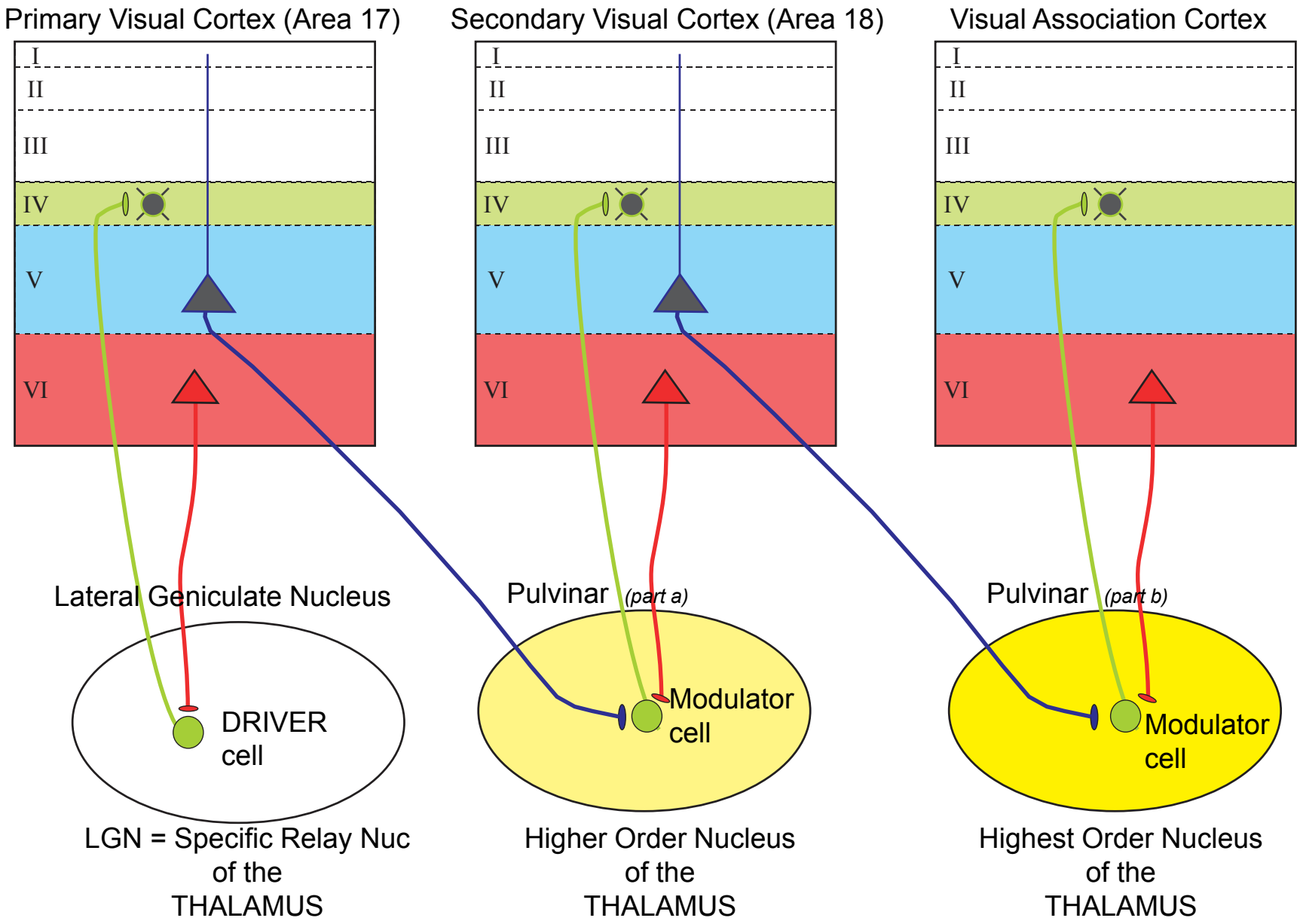


An important function of the higher order thalamic nuclei is to take information from one cortical area and convey it to another cortical area.

There are three (known) levels of this hierarchy– the pattern is the same



EXAMPLE FOR VISION



C) Thalamic neurons role in sleep and Absence epilepsy

A) Basic functions of different thalamic nuclei

B) Cellular level: basic functions of typical thalamic neurons

C) Thalamic neurons role in sleep and Absence epilepsy

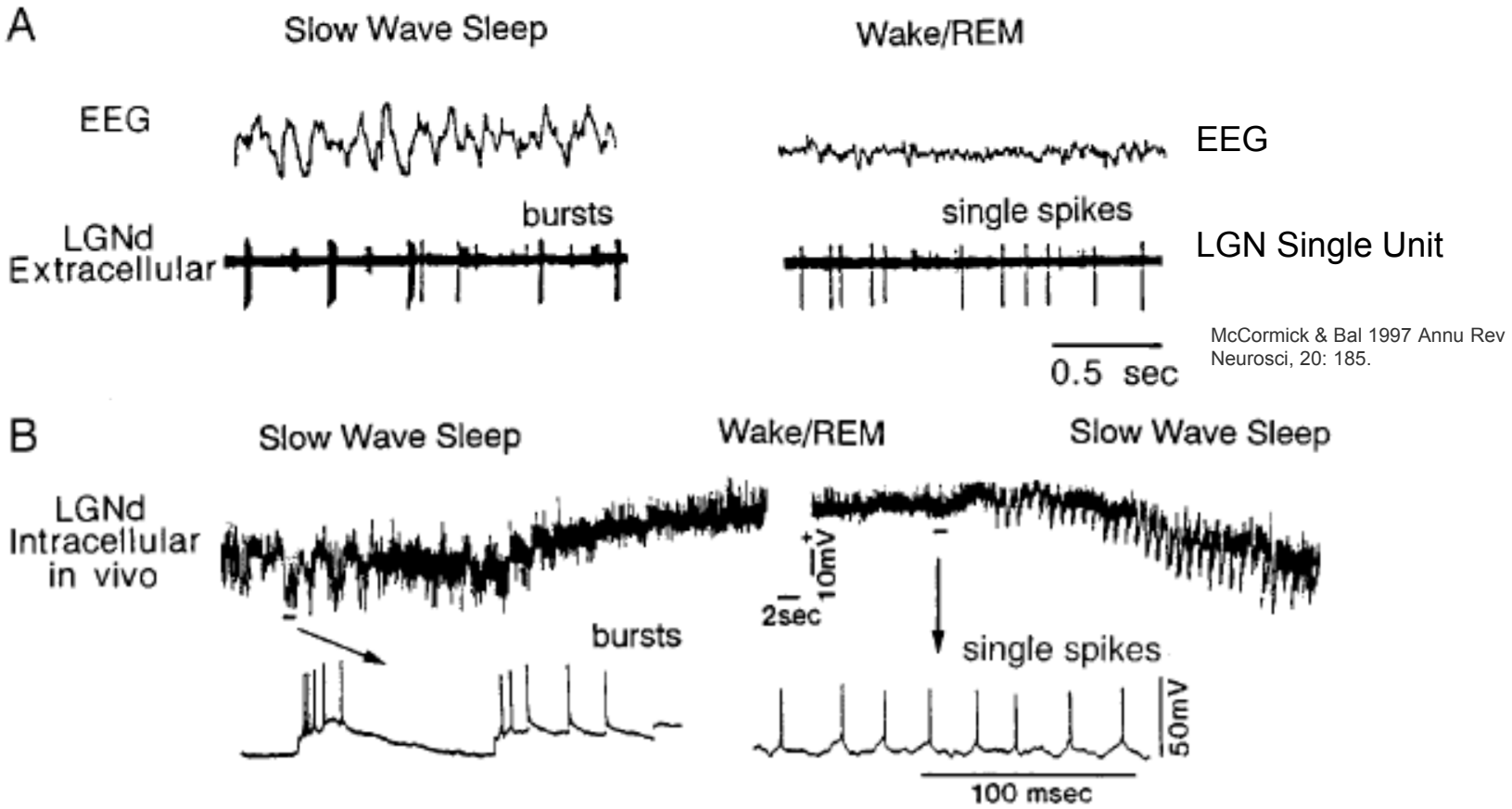
Thalamic Neurons have 2 firing modes: Bursting and Single Spike Firing

Where do these oscillations come from? The bursting ability of thalamic neurons

rly_osc.mpeg

rly_exp.mpeg

Thalamic Neurons have two firing Modes: Single Spike and Burst-firing



McCormick & Bal 1997 Annu Rev Neurosci, 20: 185.

During burst-firing – thalamic neurons can no longer faithfully transmit information from the periphery to the consciousness (cortex) because they cannot do frequency following.

Relay neurons transmit burst-firing to cortex – large numbers of thalamic and cortical neurons firing synchronously means large amplitude EEG waves.

Connections between nRt and Relay Neurons control whether spindling occurs (and the amount of synchronization within the Relay Nuclei)

How is the thalamus involved in Epilepsy?

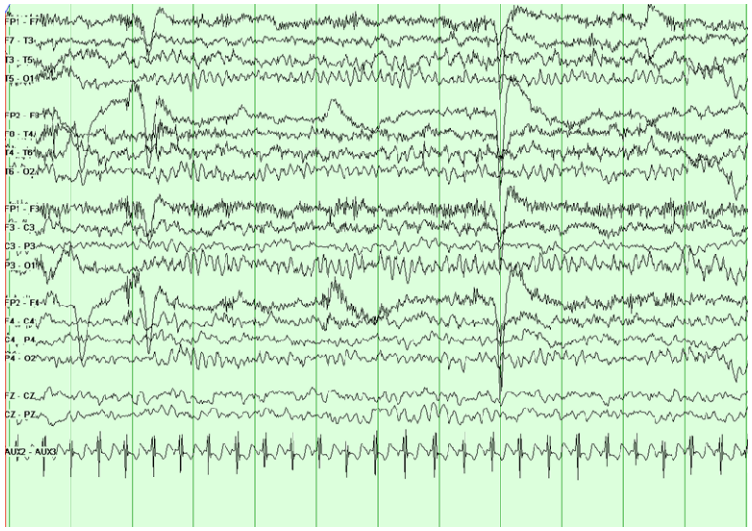
Nucleus reticularis (nRT) contains inhibitory interneurons and is an initiator of sleep spindles – initiating the bursting pattern of thalamic neurons.

In Angelman's syndrome, there is a mutation of GABA receptors specifically within nRT.

These receptors occurring at nRT -> nRT synapses, normally act to desynchronize the nucleus. Without these receptors – once the bursting starts in one part of the nucleus, it spreads to the whole nucleus and intiates a seizure.

Patients with this syndrome have Absence seizures. This is treated with the drug Ethosuximide, which blocks a T-type Calcium channel in the thalamic neurons, and thereby reduces their ability to burst.

Normal EEG



Angelman's 3 Hz Spike and Wave

Graph lines are 1 sec divisions

https://www.angelman.org/what-is-as/medical-information/epilepsy-and-its-treatment-for-providers/

Questions

The VA nucleus of the thalamus receives input from _____ and sends output to _____ .

A) Basal Ganglia, Premotor Cortex Answer = A

B) Trigeminothalamic tract, Primary Somatosensory Cortex

C) Motor Cortex, Cerebellum

D) Spinothalamic and Medial Lemniscus tracts, Facial Nucleus

E) Mammillothalamic tract, Cingulate Cortex

The Anterior nucleus of the thalamus receives input from _____ and sends output to _____ .

A) Basal Ganglia, Premotor Cortex

B) Trigeminothalamic tract, Primary Somatosensory Cortex

C) Motor Cortex, Cerebellum

D) Spinothalamic and Medial Lemniscus tracts, Facial Nucleus

E) Mammillothalamic tract, Cingulate Cortex Answer = E

Questions

The MGN and VL thalamic nuclei have roles in _____ and _____.

A) Vision, Preparation of Movement

B) Audition, Coordination of Movement Answer = B

C) Somatosensation, Memory

D) Motivation, Emotion

E) Higher order visual function, Initiation of Movement

Specific Relay Nuclei of the thalamus send projections to what layer of the cortex and receive projections back to the same nucleus from what layer of the cortex?

A) Layer V, Layer III

B) Layer II, Layer IV

C) Layer VI, Layer IV

D) Layer IV, Layer VI Answer = D

E) Layer III, Layer V

Questions

A major role of specific thalamic relay neurons is:

A) Provide nonspecific general attentional information for a specific sense

B) Drive high resolution focused sensory information to perception (the cortex) Answer = B

C) Connect thalamic reticular and specific thalamic relay nuclei

D) Amplify the gain of the signal

E) Provide connections between senses within the thalamus

A major role of modulatory neurons within higher order thalamic nuclei is to:

A) Provide nonspecific general attentional information for a specific sense

B) Drive high resolution focused sensory information to perception (the cortex)

C) Connect thalamic reticular and specific thalamic relay nuclei

D) Amplify the gain of the signal Answer = D

E) Provide connections between senses within the thalamus