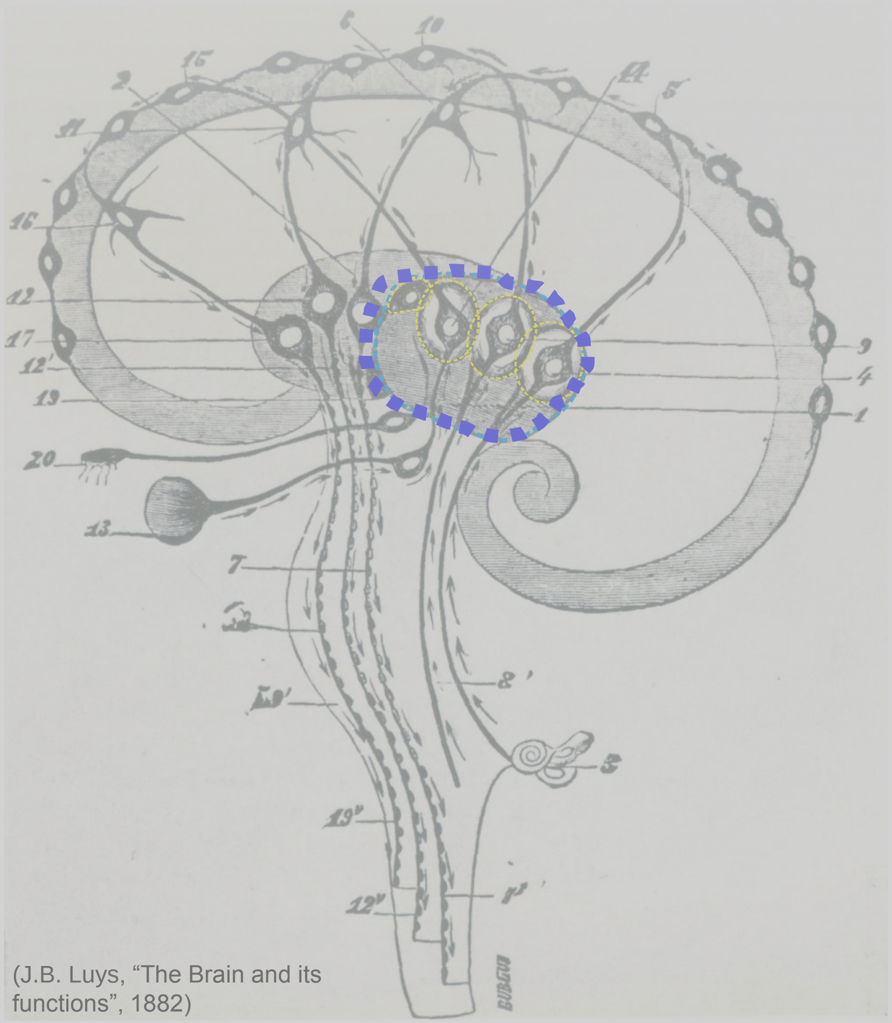
PREHISTORY OF THE THALAMUS



(J.B. Luys, "The Brain and its functions", 1882)

PART I. ADULT THALAMIC ORGANIZATION

1. General structure:

*Nuclei, what defines a thalamic nucleus, types of nuclei/classifications

2. Connectivity.

*Long-range inputs and outputs
*Intrinsic thalamic circuits

3. Thalamic physiology 101.

*Dual response modes: burst, tonic.
*Functions

4. Phylogeny

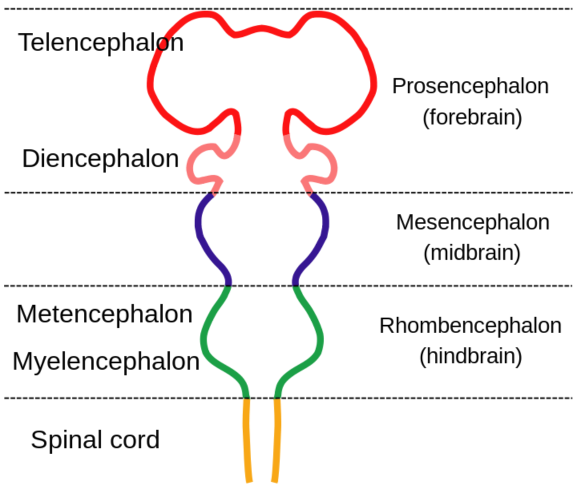
PART II. THALAMIC DEVELOPMENT

1. Thalamic specification in the neural tube

2. Molecular differentiation of thalamic nuclei

3. Development of thalamocortical circuitry

‘Loose topics’. Pulvinar, thalamic interneurons, thalamocortical motif



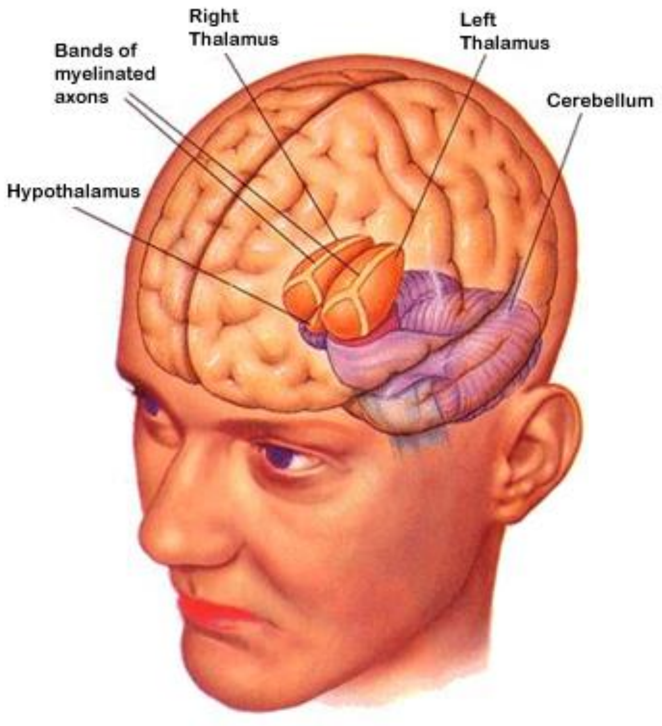
DIENCEPHALON:

- ***Thalamus***:
  - * dorsal, ventral
- ***Epithalamus***:
  - * Paraventricular nuclei?, habenula, pineal gland, stria medullaris
- ***Hypothalamus***
- ***Subthalamus***:
  - * subthalamic nucleus (basal ganglia)

Thalamus → Dorsal

Thalamus → Ventral (Thalamic reticular nucleus, zona incerta, fields of Forel, vLGN)

WHAT IS THE THALAMUS GOOD FOR?



- DURING WAKEFULNESS:
  * Relay
  * Gain control

- SLEEP: oscillations (spindles, delta)

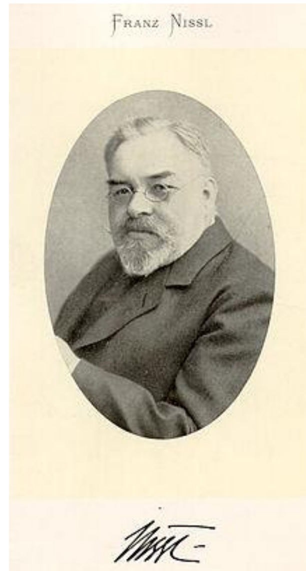
- Both WAKE & SLEEP: Binding/coordination of distributed networks e.g., perception, working memory, memory consolidation

1. THALAMIC NUCLEI

“Traditionally, a dorsal thalamic nucleus has been defined as ***a circumscribed region of cytoarchitecture receiving a particular set of afferent fibers and projecting within the borders of a particular cortical field or fields****. This is an anatomical definition derived in large part from the retrograde degeneration work of Monakow (1914) and Rose & Woolsey (1949). Although more detailed tracing techniques make it difficult to sustain this definition, it remains valid at a relatively coarse level of organization and provides a useful basis for description.”* E.G. Jones

Before Nissl:

Karl Friedich Burdach (1882): internal medullary lamina, and anterior, lat, medial groups of nuclei



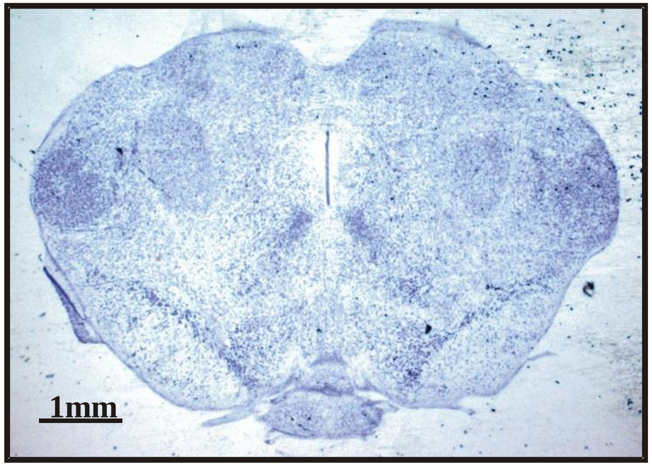
Nissl, 1889, 1913

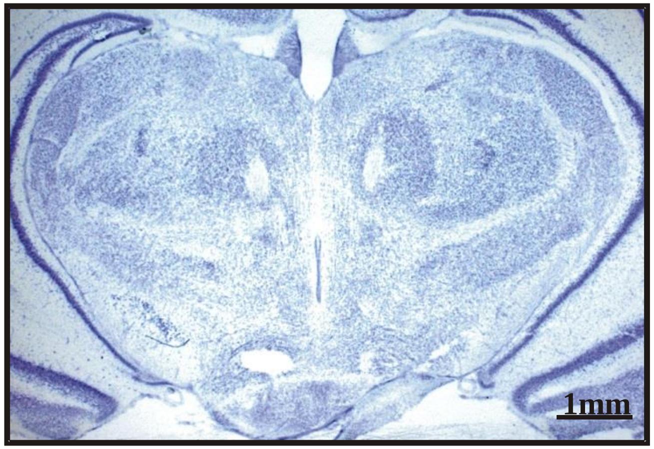
After Nissl:

development, connectivity (retrograde degeneration)
gave support to nuclei described by Nissl

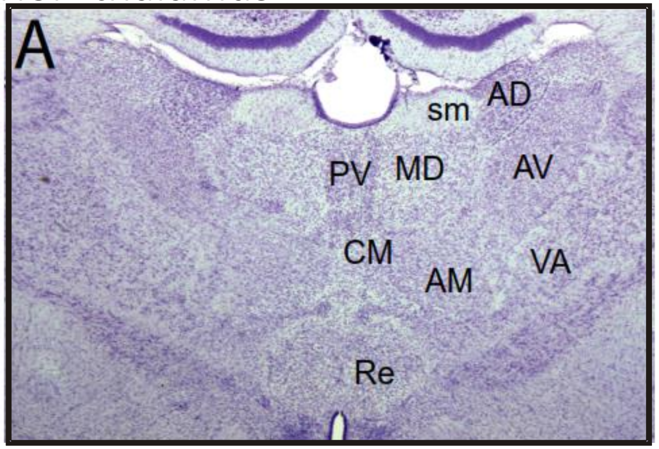
EXAMPLE OF NISSL STAINED SECTIONS, RAT

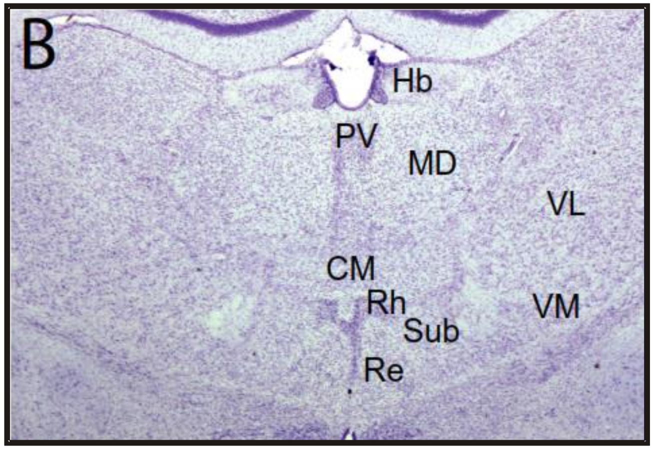
Sensory thalamus



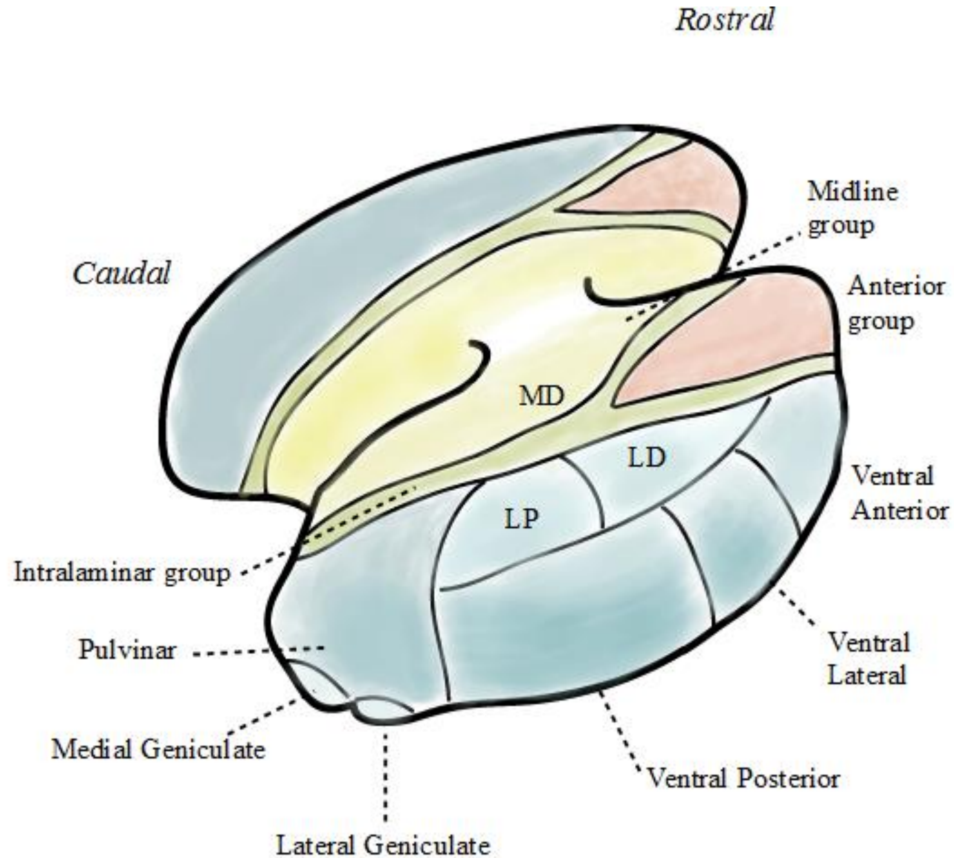


Midline/anterior thalamus





DORSAL THALAMUS (HUMAN)



LD Lateral Dorsal
LP Lateral Posterior
MD Mediodorsal

GENERAL GROUPS

-*Anterior*: dorsal, ventral, medial, LD

-*Intralaminar*:

Anterior: central medial, central lateral, paracentral

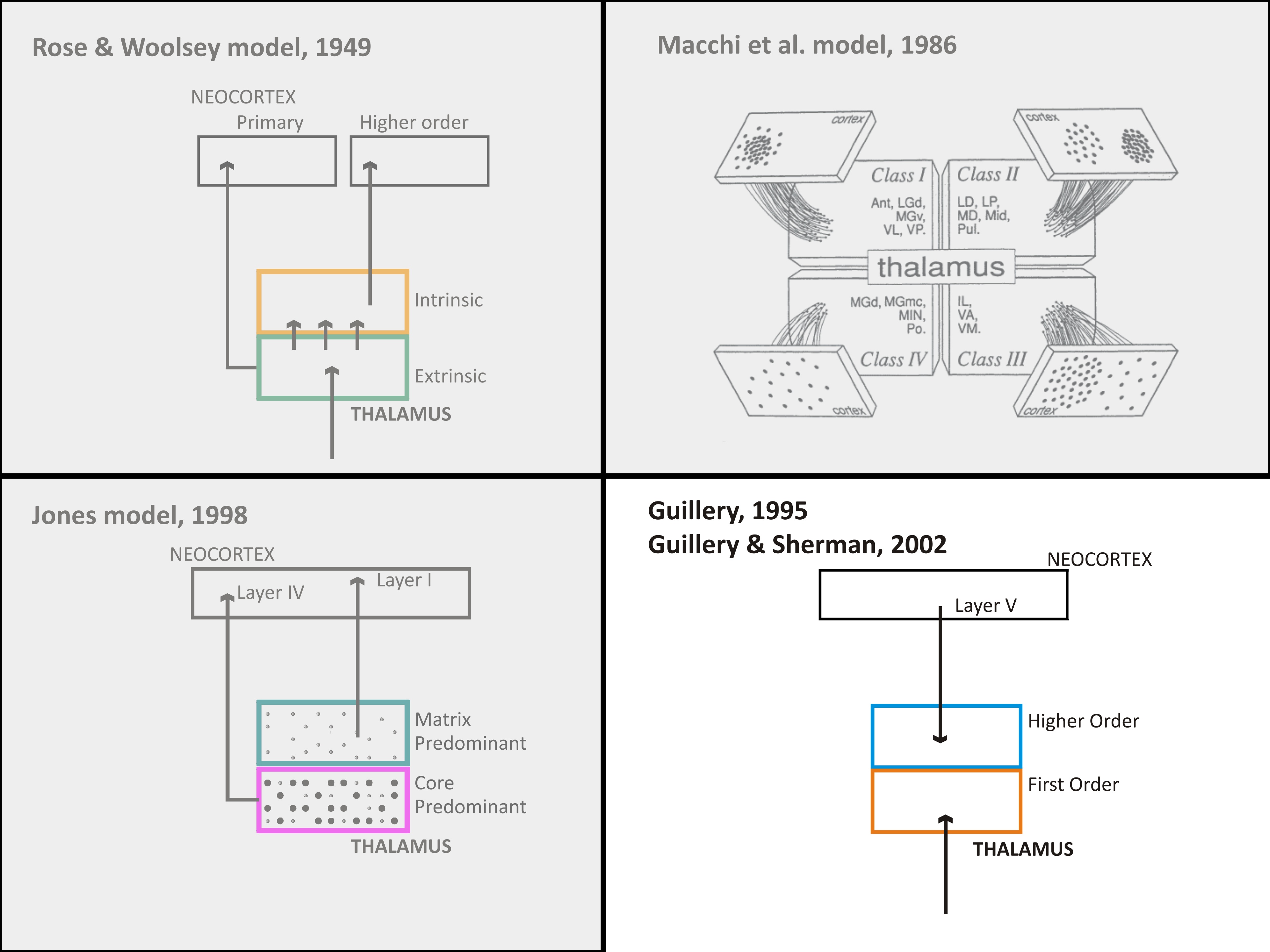
Posterior: Centermedian, parafascicular

-*Midline*: paraventricular (ant, post), paratenial, rhomboid, reuniens, mediodorsal

-Primary *sensory*: LGN, vMGB, VP

-*Association*: LP-Pulvinar, POm, dorsalMGB, LD

-*Motor*: ventral anterior, ventral lateral, ventral medial


Rose & Woolsey model, 1949
NEOCORTEX
Primary
Higher order
Intrinsic
Extrinsic
THALAMUS
Macchi et al. model, 1986
cortex
cortex
Class I
Ant, LGd, MGv, VL, VP.
Class II
LD, LP, MD, Mid, Pul.
thalamus
MGd, MGmc, MIN, Po.
IL, VA, VM.
Class IV
Class III
cortex
cortex
Jones model, 1998
NEOCORTEX
Layer IV
Layer I
Matrix Predominant
Core Predominant
THALAMUS
Guillery, 1995
Guillery & Sherman, 2002
NEOCORTEX
Layer V
Higher Order
First Order
THALAMUS

ROSE & WOOLSEY, 1949	*MACCHI, 1996*	*JONES, 1998*	*SHERMAN & GUILLERY, 1995, 2001*
dLGN	**dLGN**	**dLGN laminae**	**LGN**
MGB	**vMGB**	**vMGB**	**vMGB**
VA			
VL	**VL**	**VLp**	
VP	**VP**	**VP**	**VP**
Anterior group	**Anterior group**		**Anterior group**
Post Intralaminar (Centromedian)		**Post intralaminar**	
MD	**MD**		**MD**
PO		**POm**	**POm**
Pulvinar	**LP-Pulvinar**	**Pulvinar**	**LP-Pulvinar**
	LD		**LD**
	Midline (PV, PT, Re)		**Re**
Midline	**VA**	**VA**	**VA /VL**
Intralaminar (except centromedian)	**Intralaminar**	**Ant Intralaminar**	**Post Intralaminar**
	VM	**VM**	
	Medial interlaminar nucleus		
	C1-C3 laminae in cat; interlaminar cells in monkey; magno and dorsal divisions of MGB; suprageniculate; Pom; limitans in monkeys	**LGN interlaminar cells in monkey; magno and dorsal divisions of MGB**	

overlap across studies

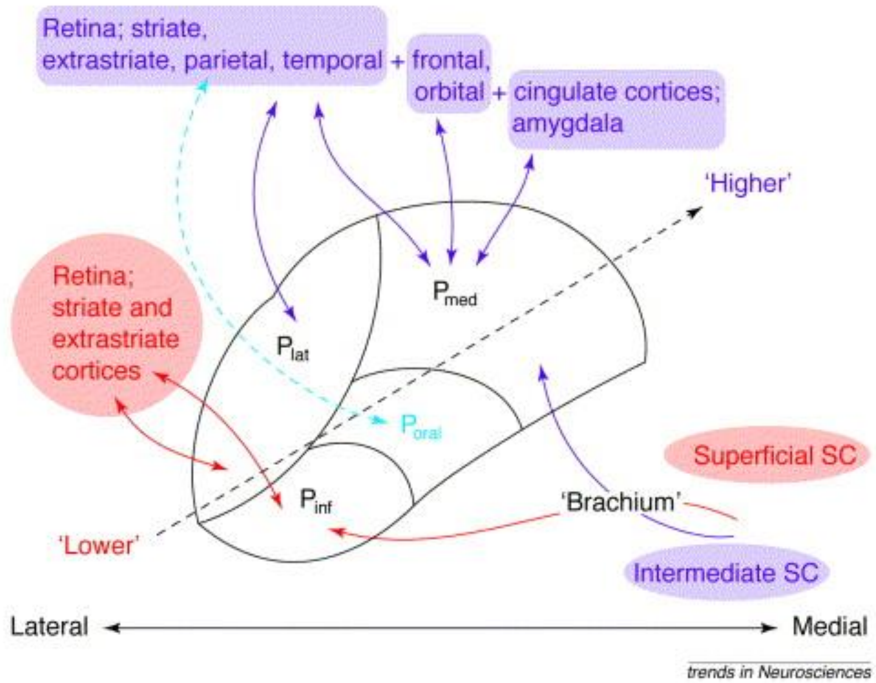
dLGN
vMGB
VL
VP
Anterior group
MD
POm
LP-Pulvinar
LD
Midline (PV, PT, Re)
Intralaminar
VM

-Evolutionary 'stable' (Rose & Woolsey)
-Specific projections to primary sensory areas (Macchi, Jones)
-Primary/driver input from non-cortical areas (Sherman & Guillery)

-Evolutionary 'variable' (Rose & Woolsey)
-Non-specific projections to higher order regions (Macchi, Jones)
-Primary/driver input from cortical areas (Sherman & Guillery)

-VA/VL
-Intralaminar (post)

PULVINAR



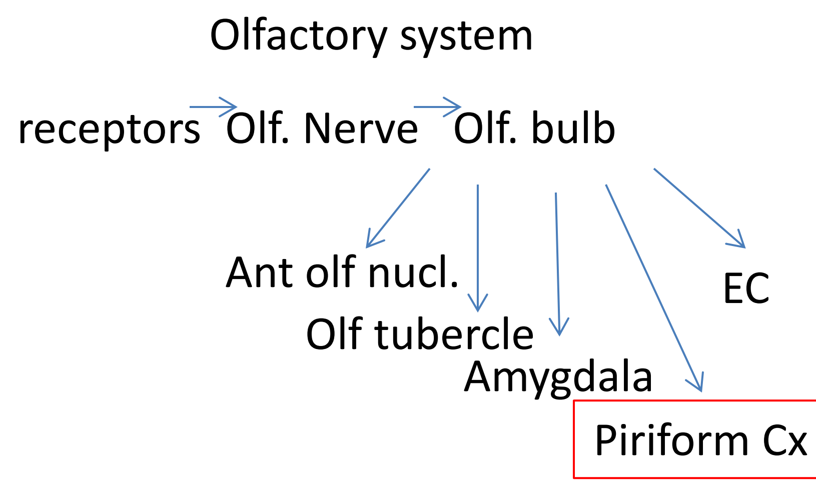
Grieve et al 2000

2. THALAMIC LONG-RANGE CONNECTIVITY.

2.1 Afferents

THALAMIC AFFERENTS

First Order	
visual	**dLGN**
auditory	**vMGB**
Cerebellar/basal ganglia	**VL**
Somatosensory, vestibular	**VP**
Mamillothalamic tract	**Anterior group**
Higher Order	
PFC, piriform	**MD**
somatosensory HO	**POm**
Visual HO	**LP-Pulvinar**
Ant group HO	**LD**
mPFC	**Midline (PV, PT, Re)**
Cingulate, FEF, parietal, etc	**Intralaminar**
Cerebellar/basal ganglia	**VM**

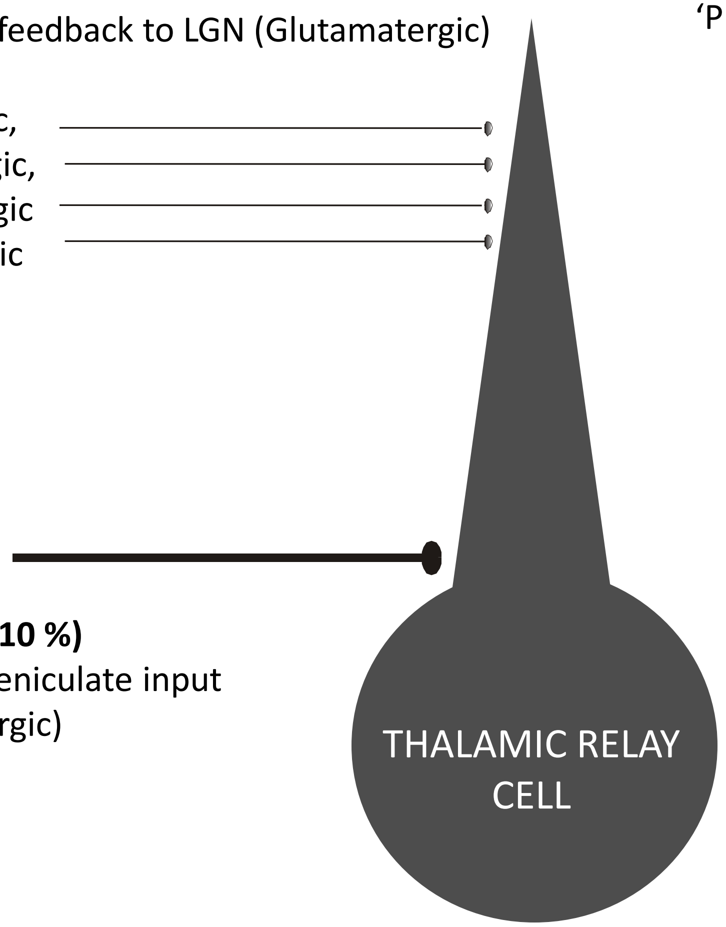


(Kay & Sherman TINS 2007)

THALAMIC AFFERENTS

MODULATORS
Ex. Layer VI feedback to LGN (Glutamatergic)
Cholinergic,
Serotonergic,
Dopaminergic,
Noradrenergic
Histaminergic

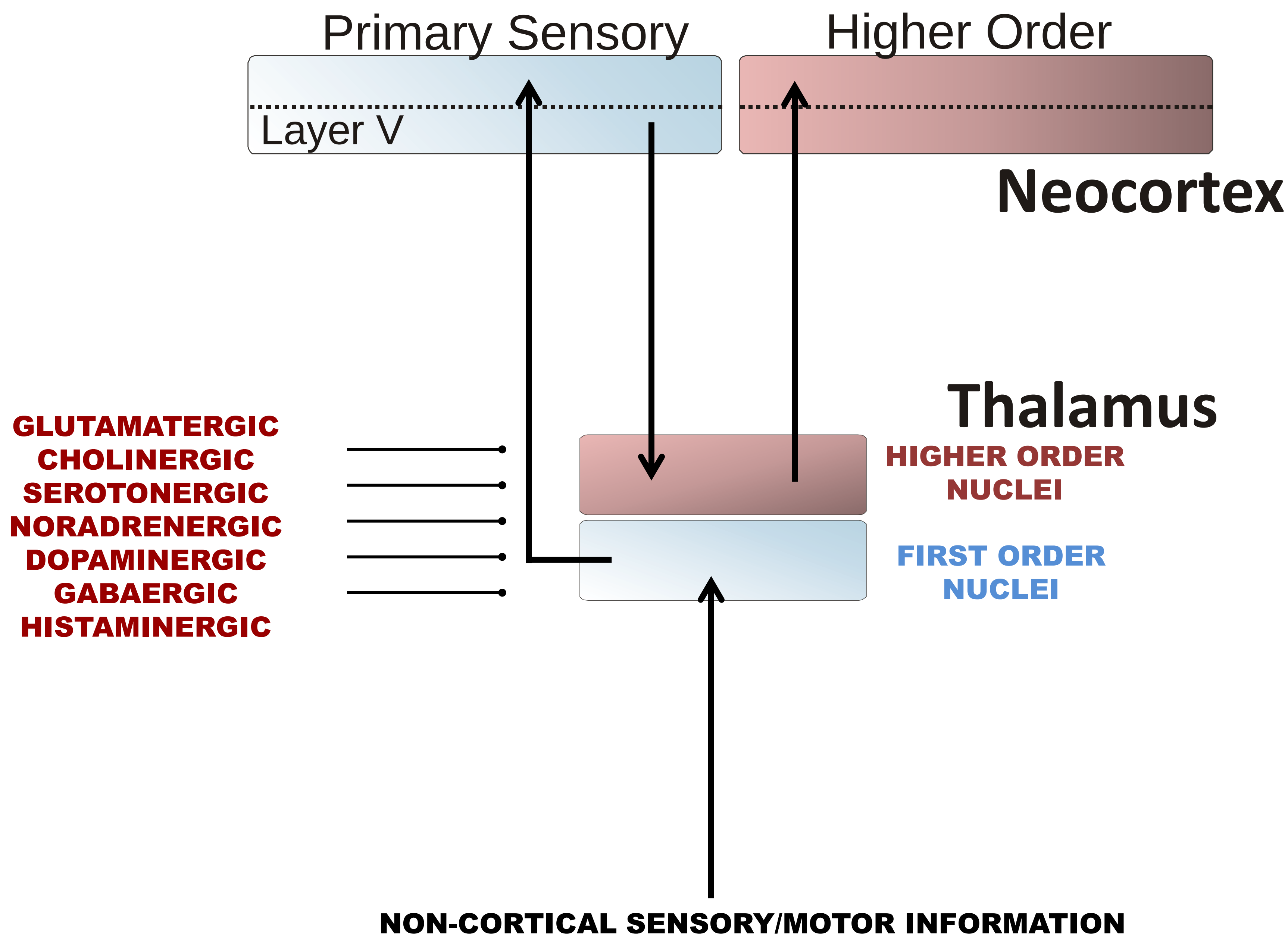
MODULATORS----- e.g. SWITCH RESPONSE MODE, 'PROBABILITY OF TRANSMISSION'

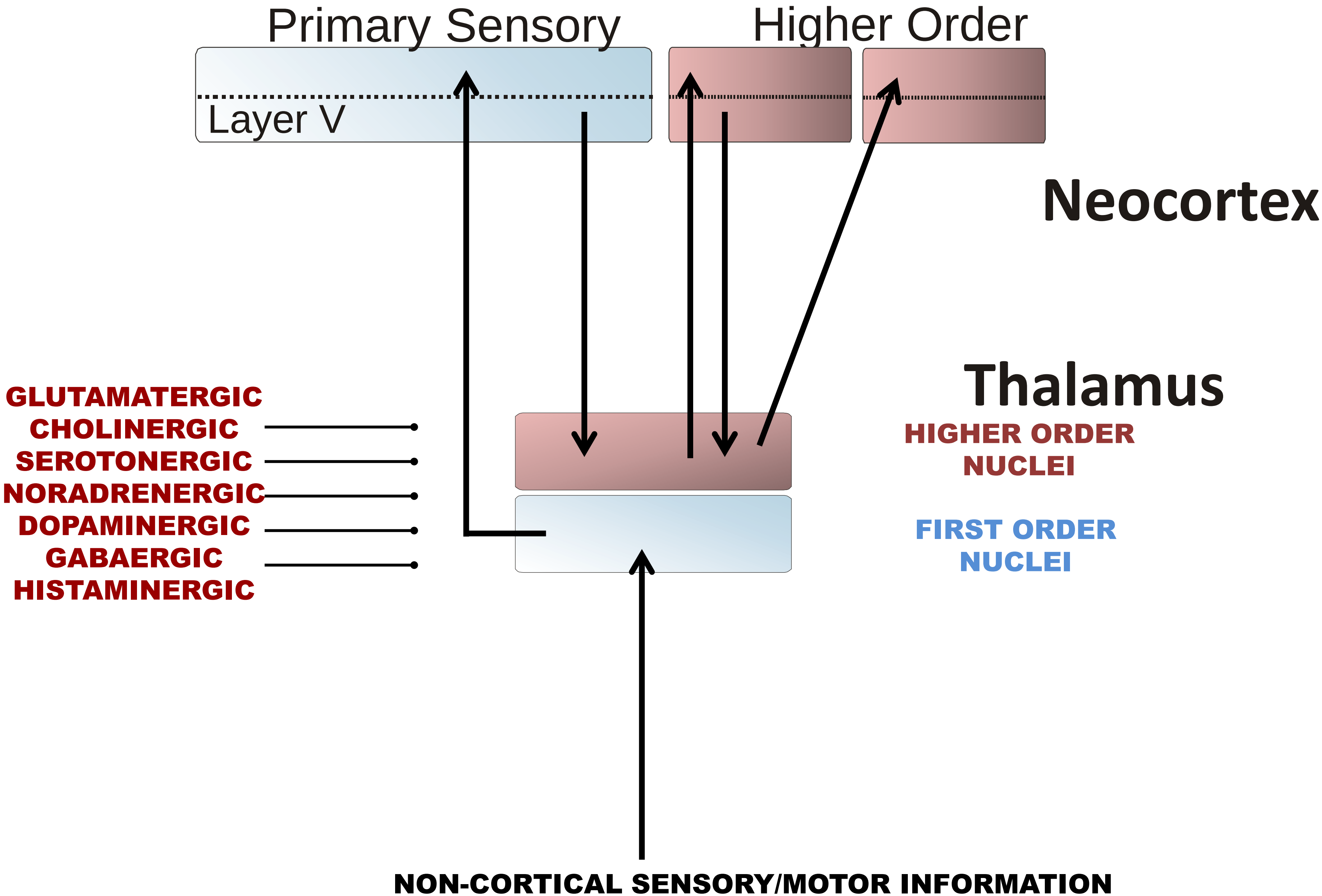


DRIVERS (~10 %)
Ex. Retinogeniculate input
(Glutamatergic)

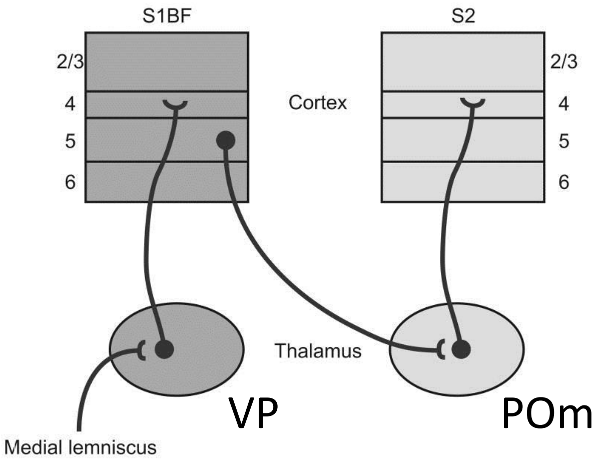
DRIVERS----- RECEPTIVE FIELD, 'MESSAGE'

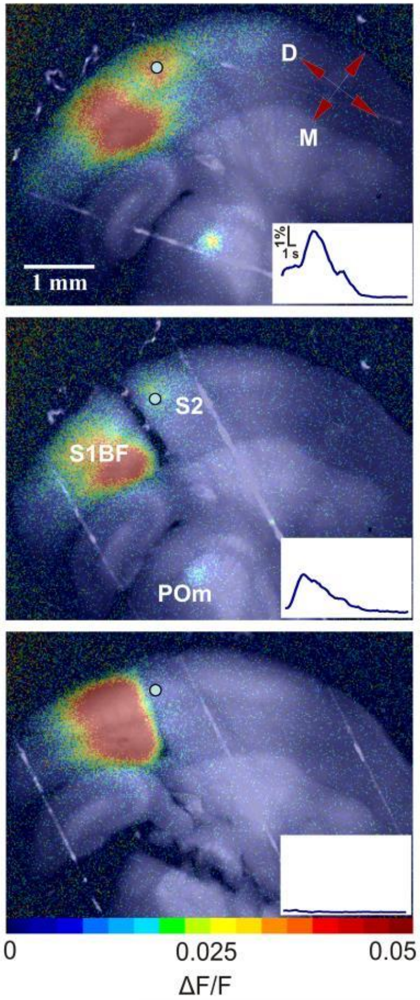
Based on: Guillery, 1995; Guillery & Sherman, 2002


Primary Sensory
Higher Order
Layer V
Neocortex
Thalamus
GLUTAMATERGIC
CHOLINERGIC
SEROTONERGIC
NORADRENERGIC
DOPAMINERGIC
GABAERGIC
HISTAMINERGIC
HIGHER ORDER NUCLEI
FIRST ORDER NUCLEI
NON-CORTICAL SENSORY/MOTOR INFORMATION


Primary Sensory
Higher Order
Layer V
Neocortex
Thalamus
GLUTAMATERGIC
CHOLINERGIC
SEROTONERGIC
NORADRENERGIC
DOPAMINERGIC
GABAERGIC
HISTAMINERGIC
HIGHER ORDER NUCLEI
FIRST ORDER NUCLEI
NON-CORTICAL SENSORY/MOTOR INFORMATION

EVIDENCE FOR CORTICO-CORTICAL COMMUNICATION THROUGH THALAMUS

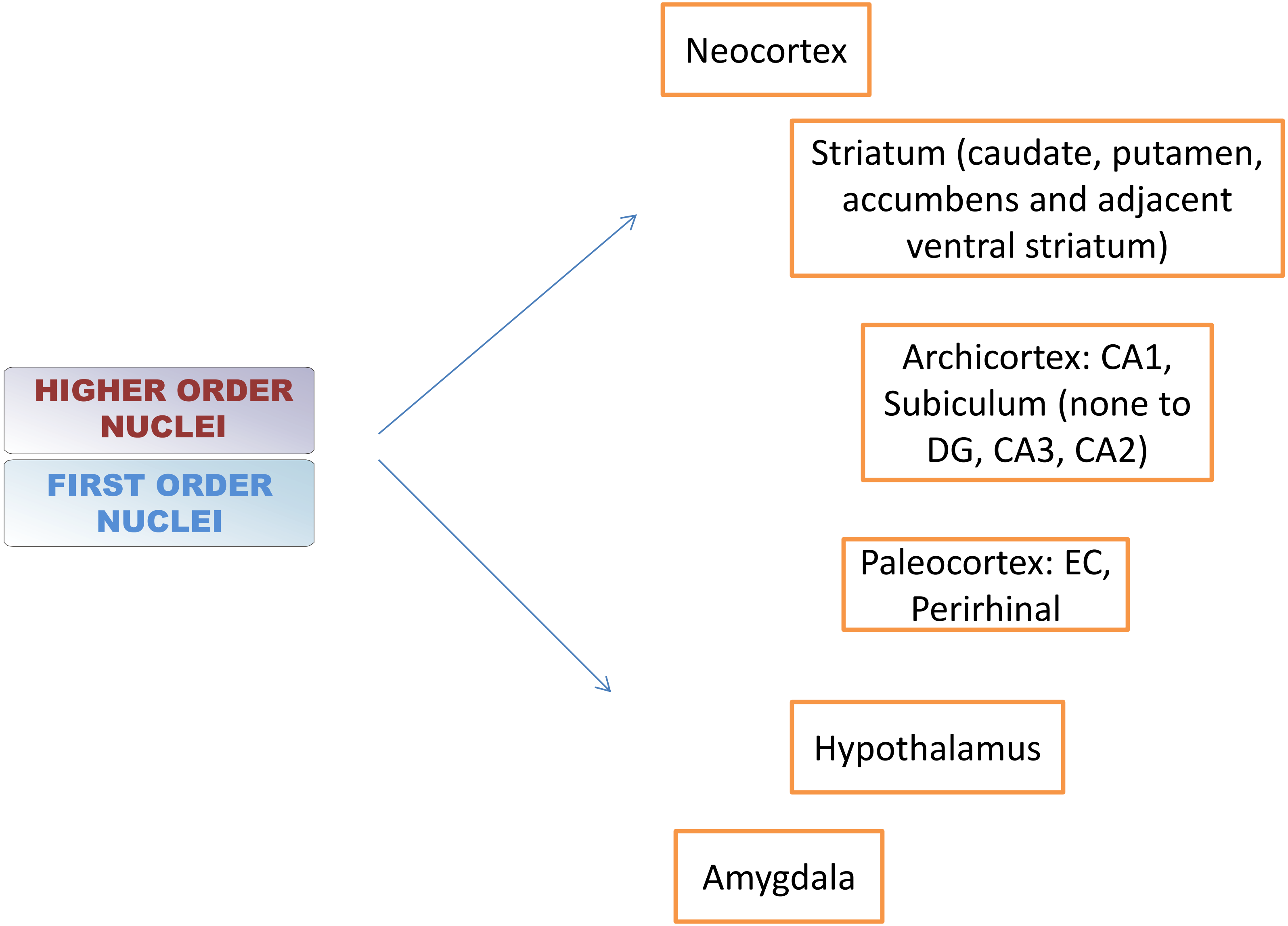




Theyel, Llano & Sherman, NNS 2010

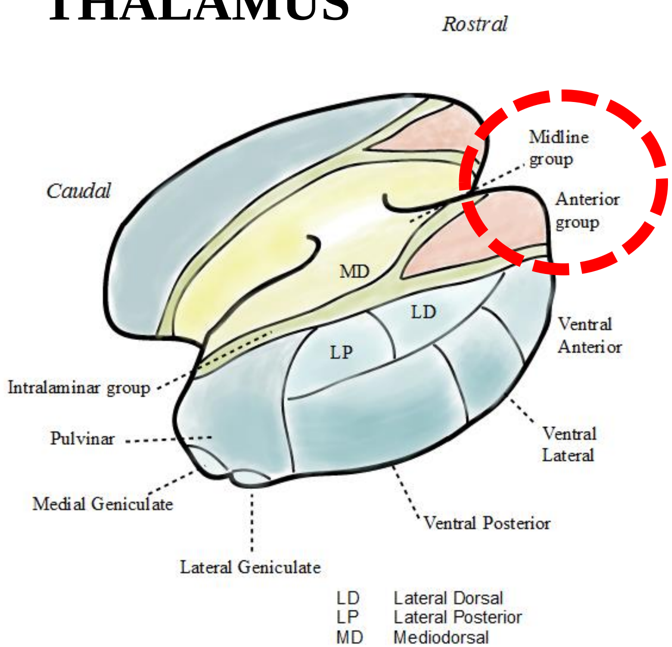
2. THALAMIC LONG-RANGE CONNECTIVITY.

2.2 Efferents


HIGHER ORDER NUCLEI
FIRST ORDER NUCLEI
Neocortex
Striatum (caudate, putamen, accumbens and adjacent ventral striatum)
Archicortex: CA1, Subiculum (none to DG, CA3, CA2)
Paleocortex: EC, Perirhinal
Hypothalamus
Amygdala

THALAMO-HIPPOCAMPAL PROJECTIONS

THALAMUS



Reuniens
Paraventricular
Paratenial

Reuniens
Rhomboid

Reuniens
Paraventricular
Paratenial

Anterior group

EC

CA1

Subicular Region

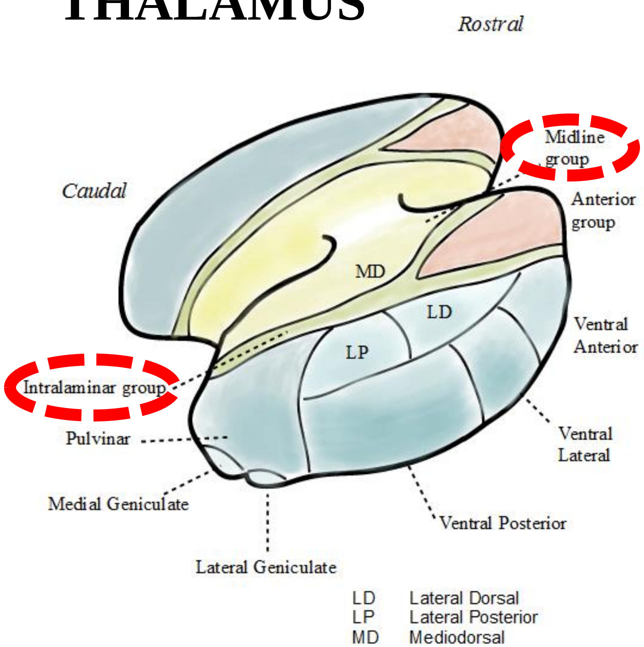
HIPPOCAMPUS

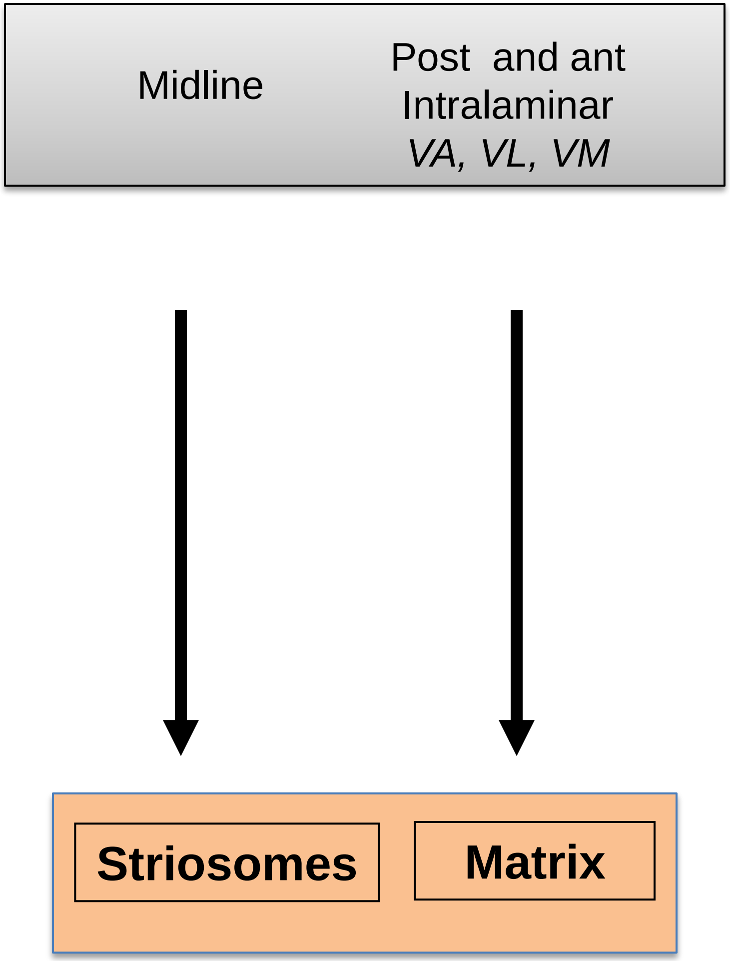
(No projections to DG, CA3, CA2)

Based on: Herkenham, 1978; Wouterlood et al., 1990; Dolleman-Van der Weel & Witter, 2000; Vertes 2000; Van der Werf et al., 2002, etc

THALAMO-STRIATAL PROJECTIONS

THALAMUS

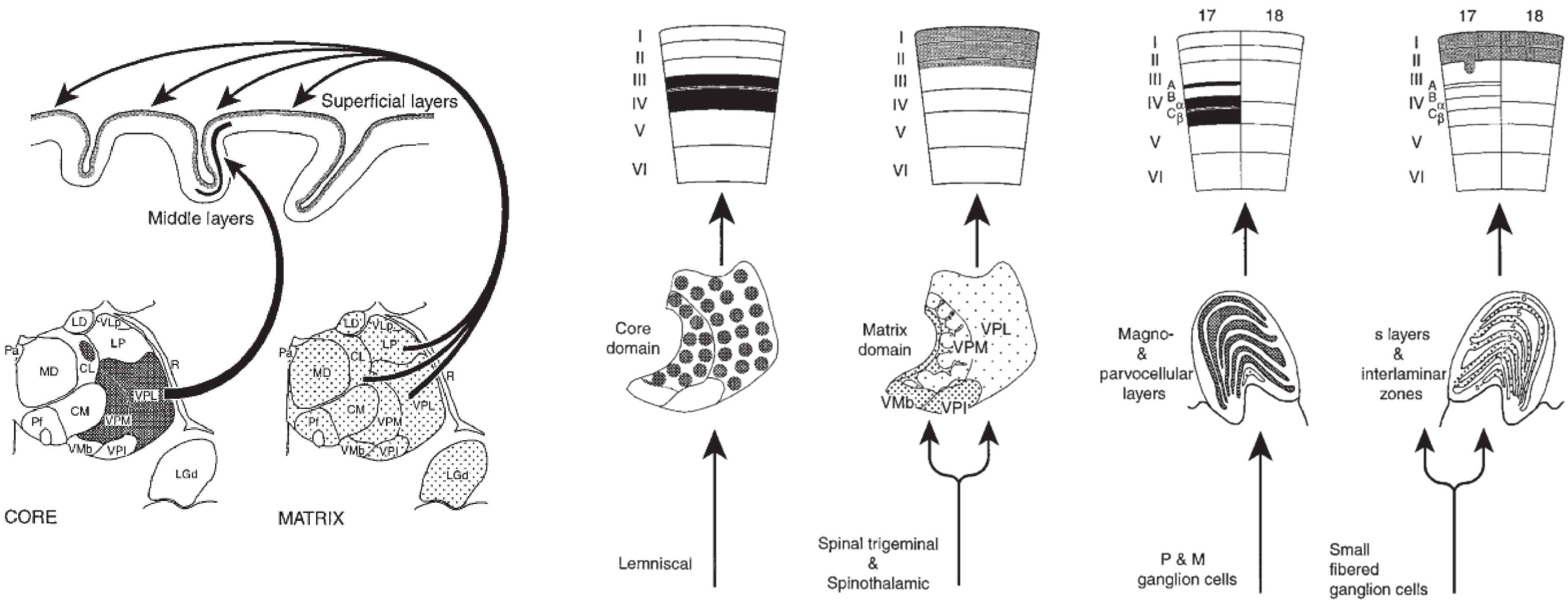




STRIATUM

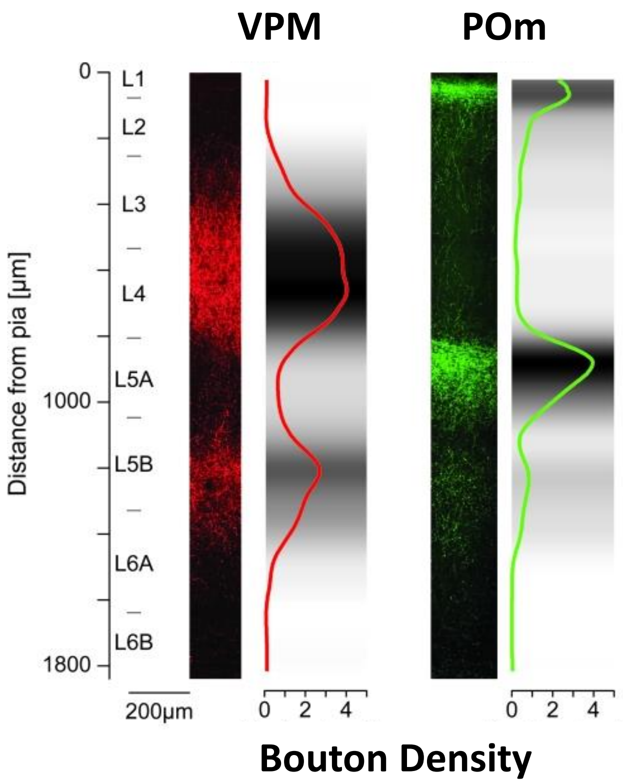
Based on: Raggsdale & Graybiel, 1991; Jones, 1998

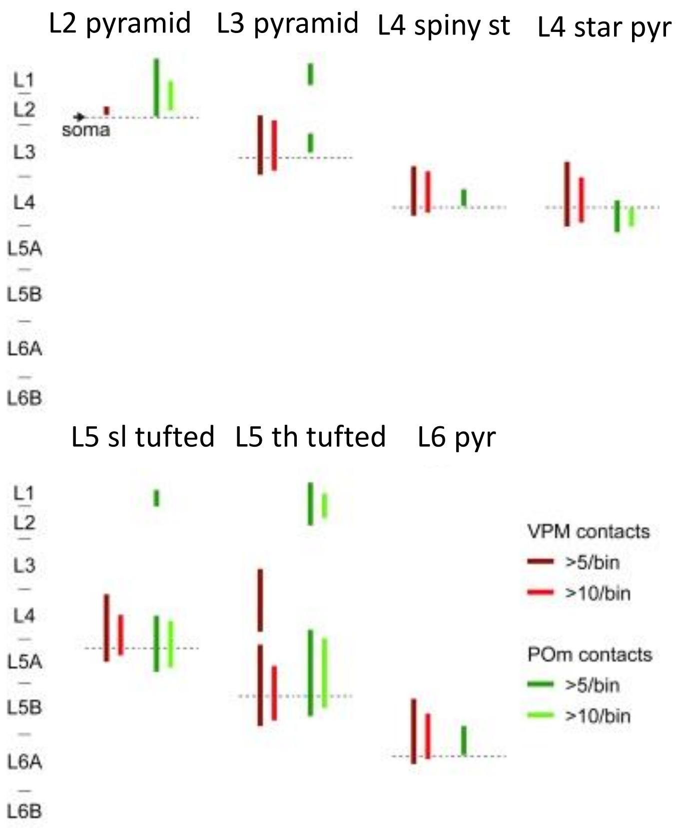
NEOCORTICAL LAYERS OF TERMINATION. CORE & MATRIX



Jones 1998

NEOCORTICAL LAYERS OF TERMINATION





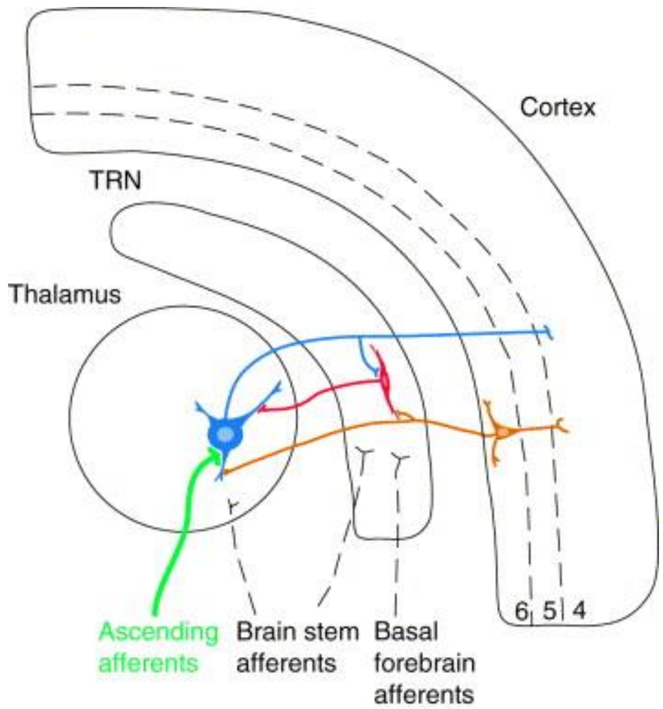
Meyer et al, Cereb Cortex. 2010

2. THALAMIC CONNECTIVITY.

2.3 Intrinsic circuitry

‘SIMPLE’ INTRINSIC CIRCUITRY

-Excitatory relay cells
-‘No intrathalamic connections’ in dorsal thalamus (reuniens,…)
-GABAergic cells in ventral thalamus in rodents, bats. ~20% in dorsal thal.

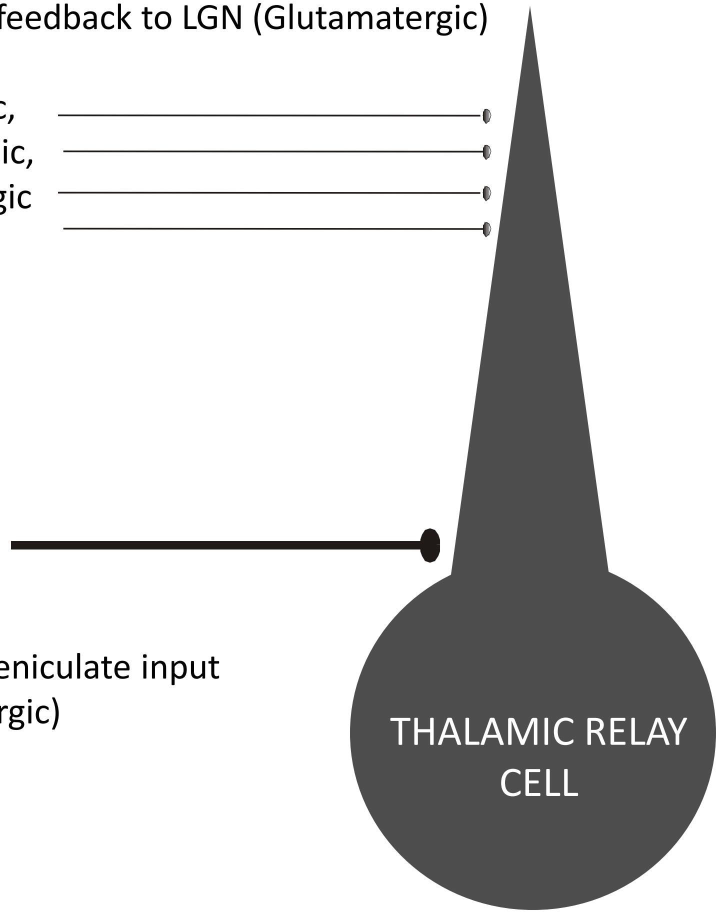


3. THALAMIC PHYSIOLOGY 101

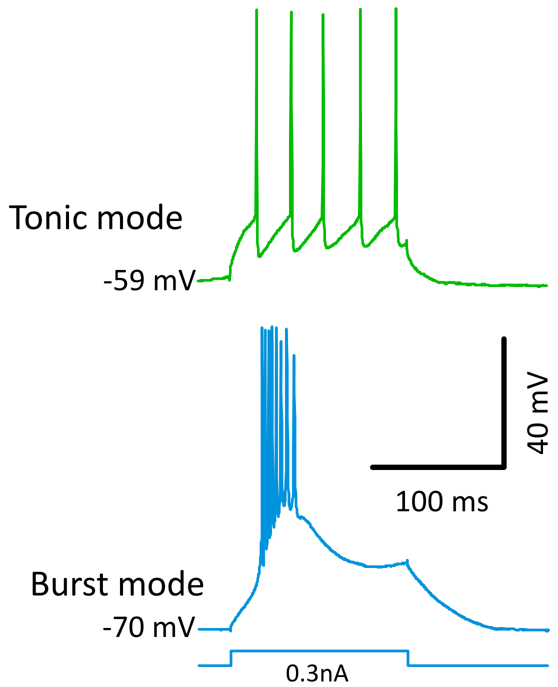
DUAL RESPONSE MODE: BURST – TONIC. T current

MODULATORS
Ex. Layer VI feedback to LGN (Glutamatergic)
Cholinergic,
Serotonergic,
Dopaminergic,
Noradrenergic
Gabaergic

DRIVERS
Ex. Retinogeniculate input
(Glutamatergic)

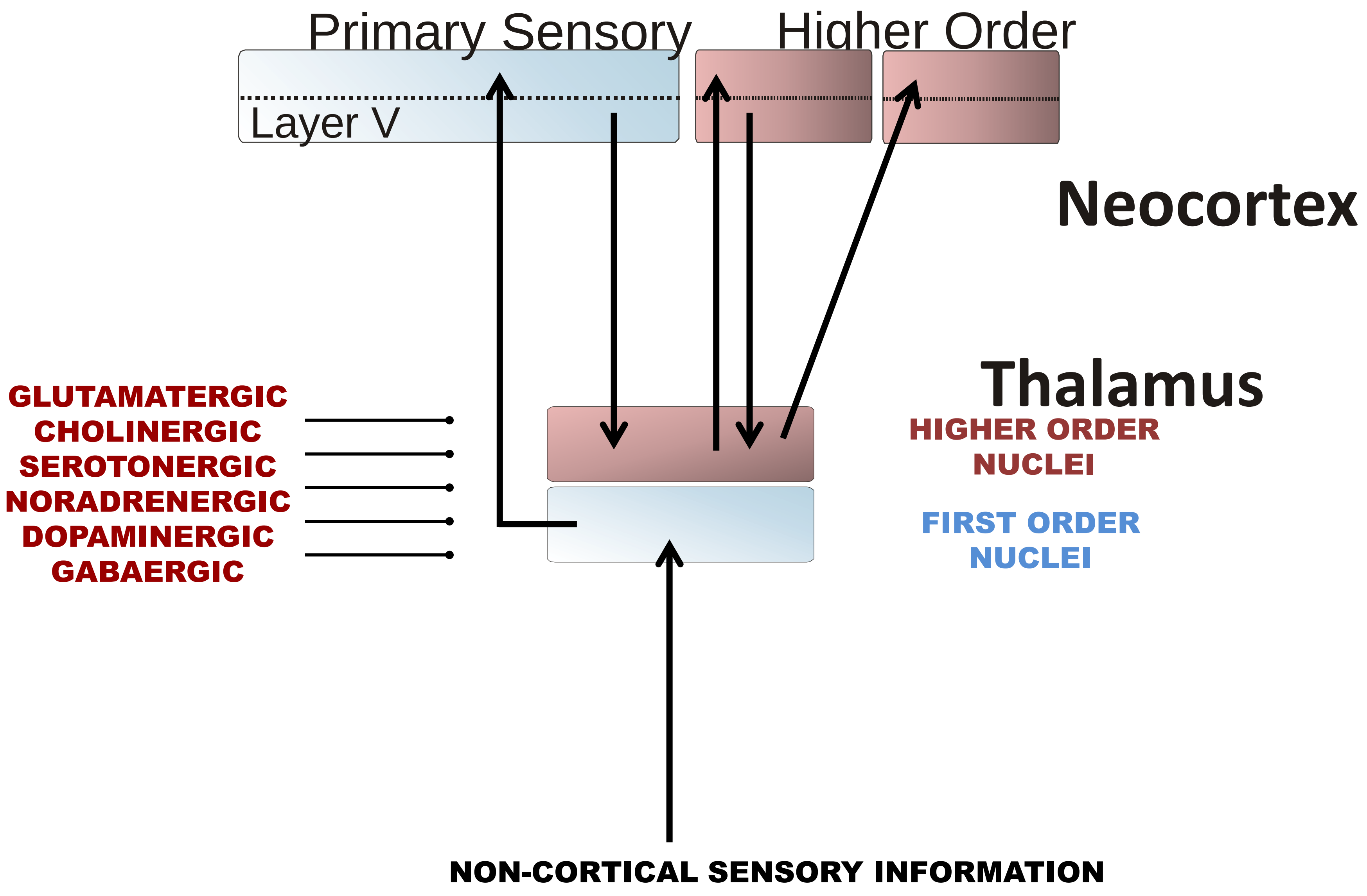


MODULATORS----- e.g. SWITCH RESPONSE MODE



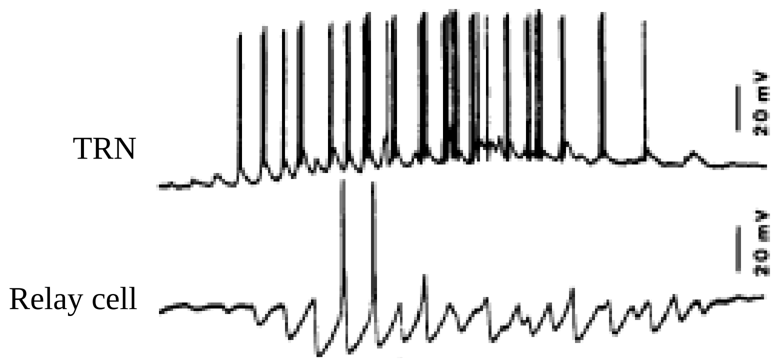
DRIVERS----- RECEPTIVE FIELD

AWAKE THALAMUS: RELAY

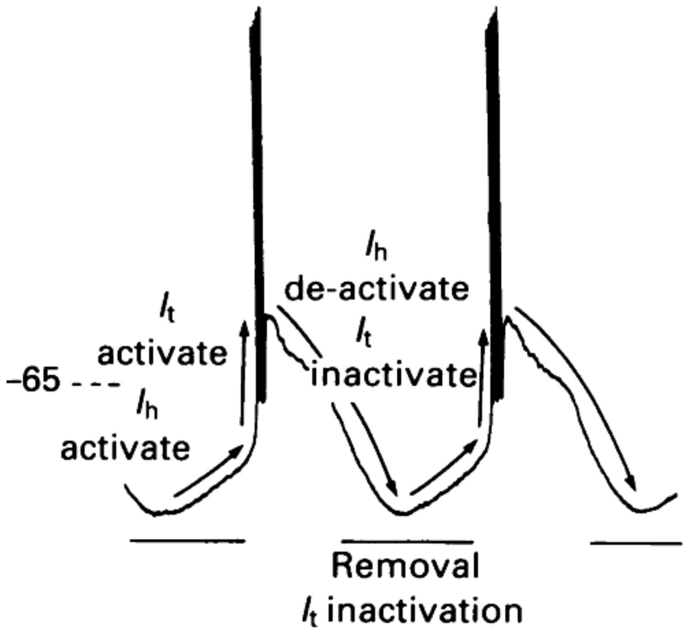


THALAMUS DURING SLEEP: OSCILLATIONS (spindles, delta)

Spindle



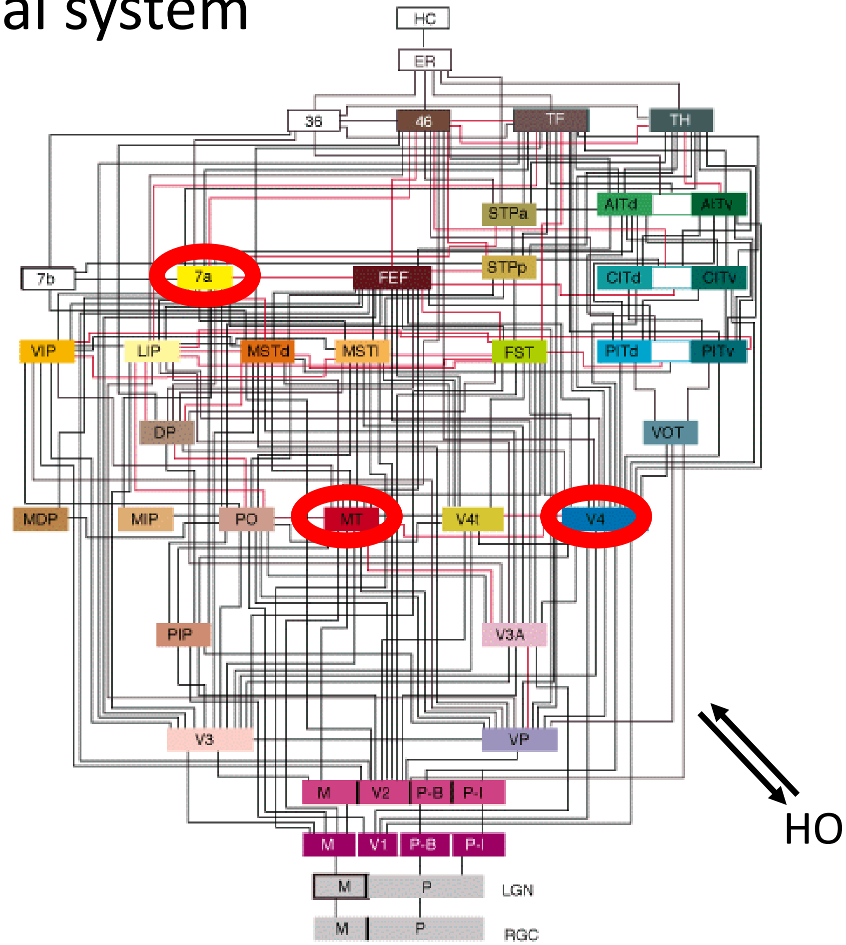
Steriade, 1994

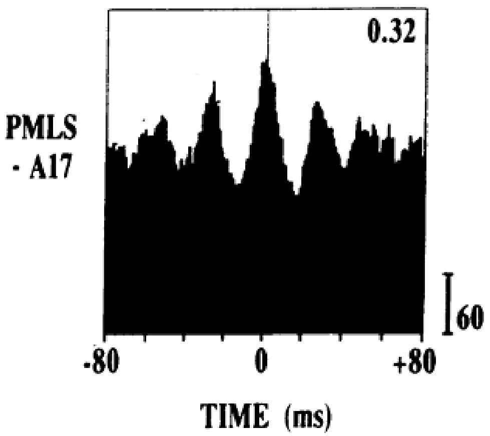


McCormick & Pape, 1990

THALAMUS: COORDINATOR OF DISTRIBUTED NETWORKS?

Visual system

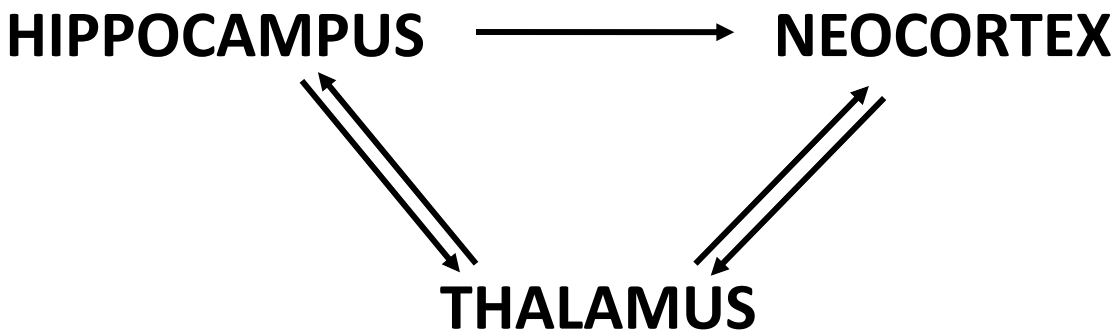




Felleman & Van Essen, Cereb. Cx. 1991

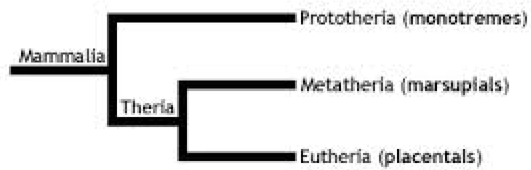
Engel et al 1991 ; Gray et al 1989, Crick & Koch 1998, etc

THALAMUS: COORDINATOR OF DISTRIBUTED NETWORKS?

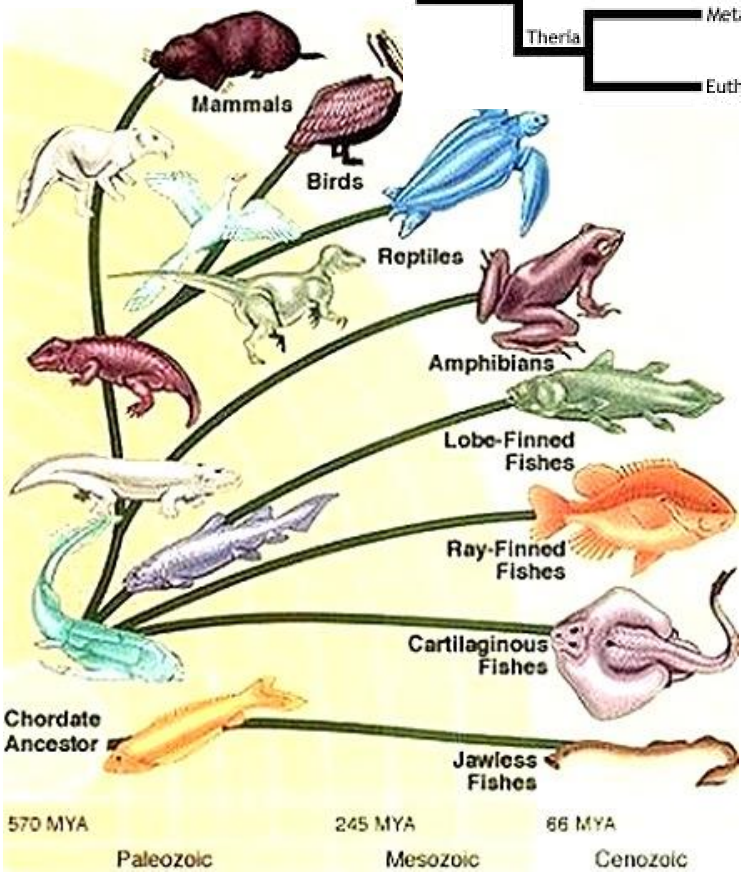


WORKING
MEMORY

4. THALAMIC PHYLOGENY

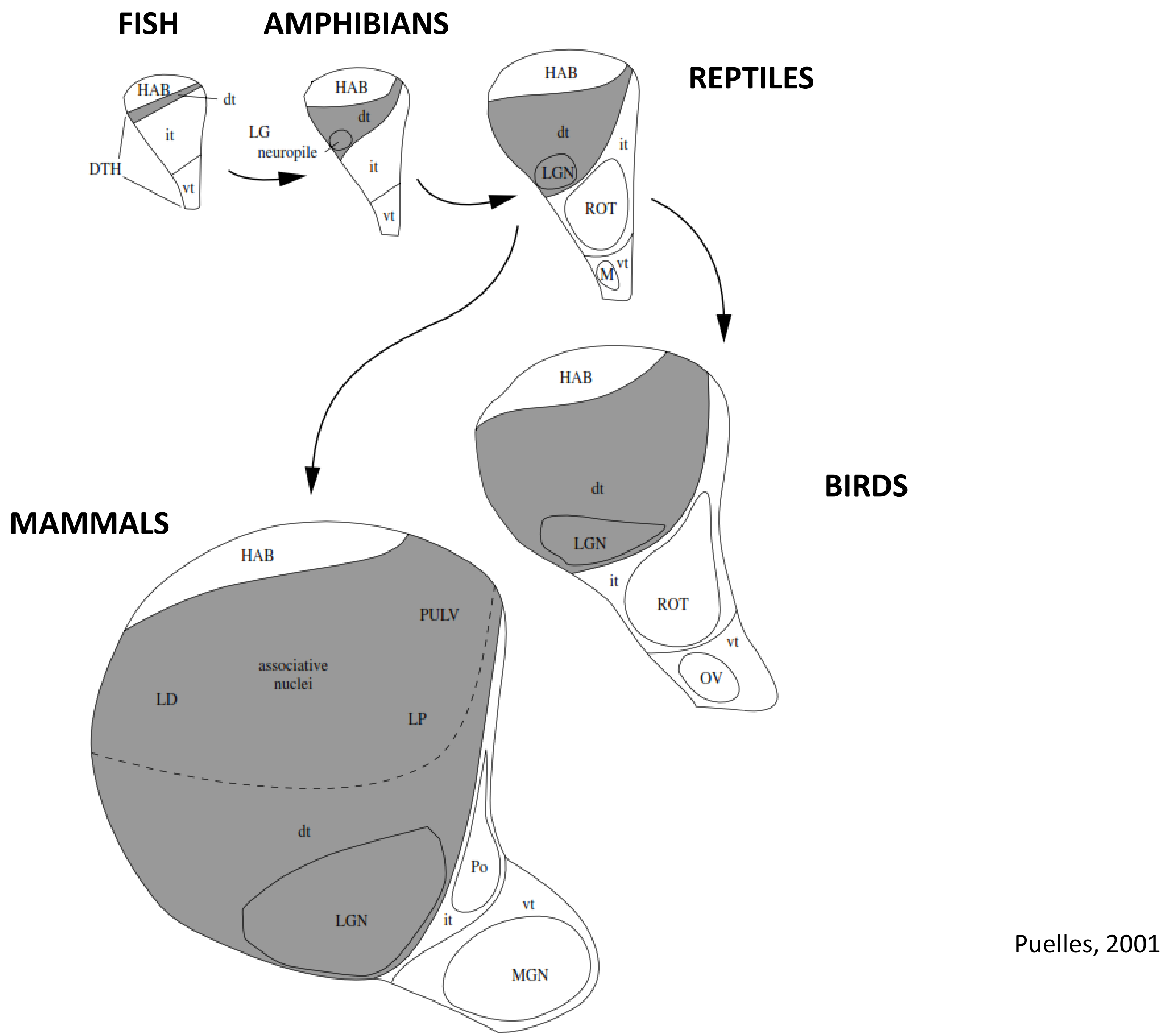


Mammalian thalamic plan ‘in place’ by the time of emergence of the monotremes



-‘Periventricular’ thalamus; progressive nuclei differentiation in representatives within same class
-Modulatory input from brainstem (all vertebrates)

‘The Thalamus’ book, EG Jones, Chapter 17



Puelles, 2001

VERTEBRATES. NON-MAMMALS

-**Fish**. Little nuclear differentiation

Cyclostomes: lamprey: diencephalon is tubular, only habenular nuclei clearly distinct. No nuclei within dorsal thal. (hagfish a few nuclei). GABA cells in dorsal thalamus

-**Amphibian**. Little nuclear differentiation in anuran compared to urodeles. Parallel tectal and sensory afferents (at least from amphibians). From amphibians, GABA cells primarily restricted to ventral thal. (except for optical regions –LGN-)

-**Reptiles**. From reptiles, projections to circumscribed areas of the pallium.

-**Birds**. Projection to striatum.. Maybe starts in reptiles?

VERTEBRATES. MAMMALS

-**Monotremes (echidna, platypus)**.

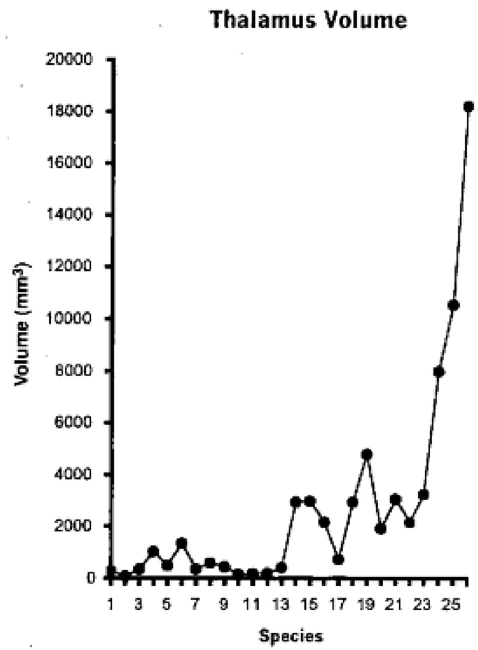
* No internal medulary lamina (dispersion of fibers entering thalamus) nor equivalents of intralaminar nuclei (maybe rudimentary parafascicular)
* Ventral posterior nucleus is the most distinct; no MGB, fibers forming brachium of inf colliculus dissappear into the post pole of the VP.
*GABAergic cells in ventral and dorsal thalamus

-**Marsupials**.

* No corpus callosum, enlarged ant. commissure. Thalamus similar to rodents.

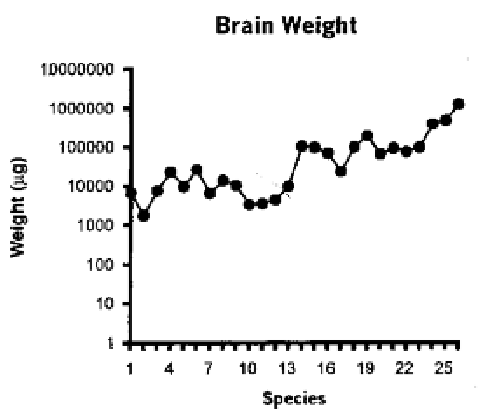
VERTEBRATES. MAMMALS-PRIMATES

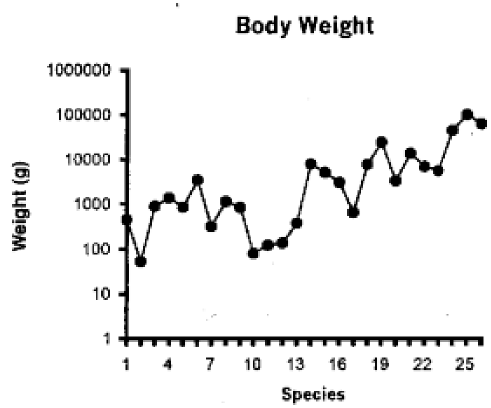
Number	Species	Family
1	*Cheirogaleus major*	Prosimians
2	*Microcebus murinus*	
3	*Lepilemur ruficaudatus*	
4	*Lemur fulvus*	
5	*Avahi l. occidentalis*	
6	*Propithecus verreauxi*	
7	*Loris tardigradus*	
8	*Periodicticus potto*	
9	*Galago crassicaudatus*	
10	*Galago demidovii*	
11	*Tarsius* sp.	
12	*Cebuella pygmaea*	New World monkeys
13	*Saguinus oedipus*	
14	*Ateles geoffroyi*	
15	*Lagothrix lagotricha*	
16	*Cebus* sp.	
17	*Saimiri sciureus*	
18	*Cercocebus albigena*	Old World monkeys
19	*Papio anubis*	
20	*Cercopithecus ascanius*	
21	*Nasalis larvatus*	
22	*Colobus badius*	
23	*Hylobates lar*	Apes
24	*Pan troglodytes*	
25	*Gorilla gorilla*	
26	*Homo sapiens sapiens*	Humans



In humans:

Enlargement of pulvinar, also VL





Jones 1998