# Cerebral cortex: anatomic principles cortical types

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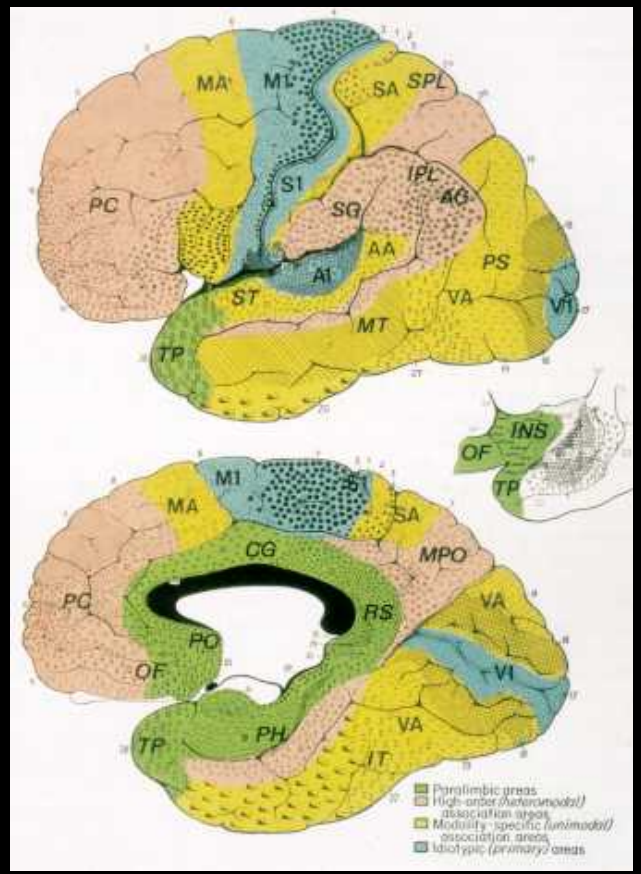
A general plan of organization for patterns of behavioral specialization and neural connectivity in cortex (Mesulam)

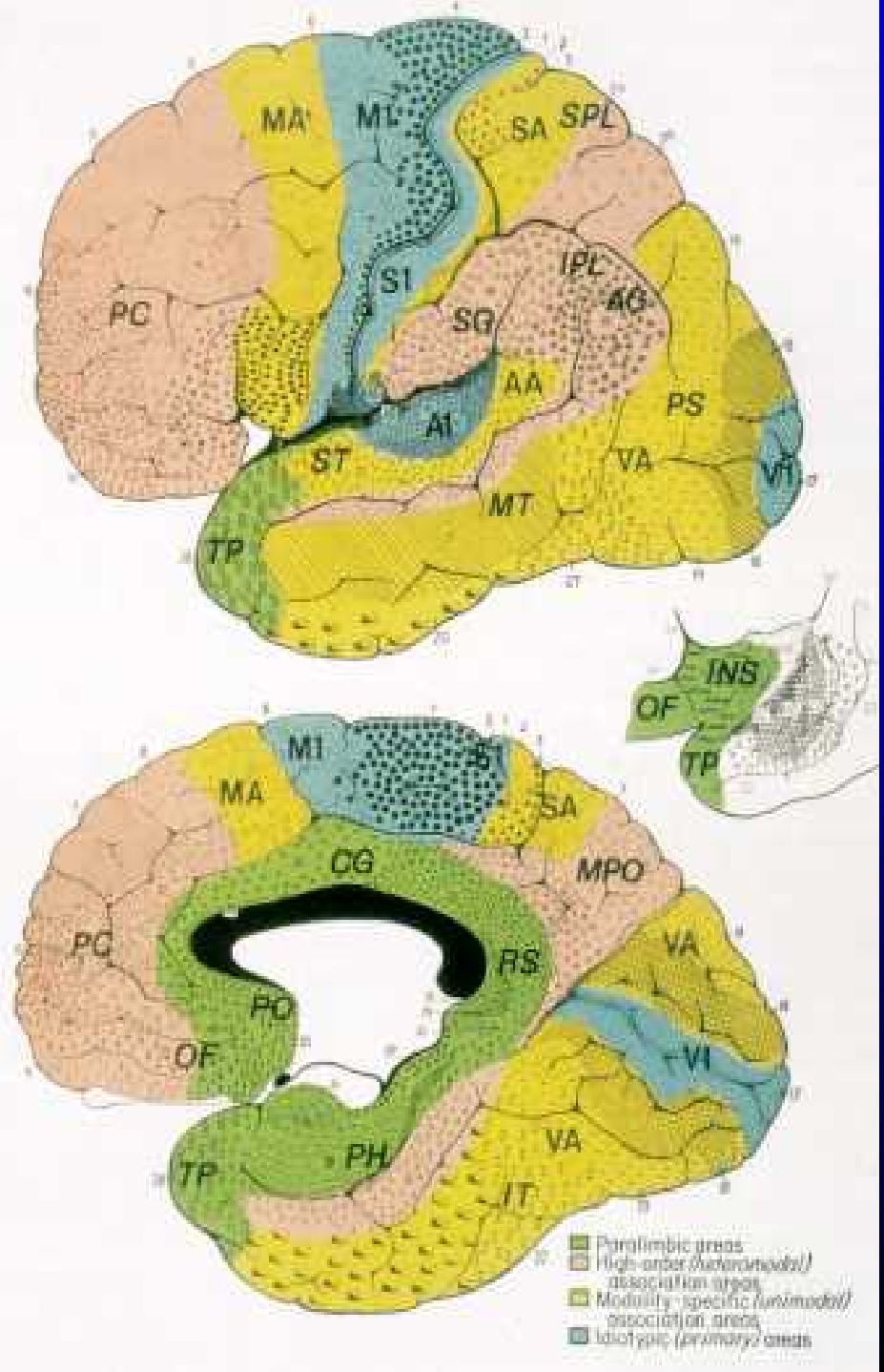
# FIVE ZONES: from the simplest to the most differentiated

1. Limbic
2. Paralimbic
3. Homotypical Unimodal (secondary areas)
4. Homotypical Heteromodal (tertiary areas)
5. Idiotypic (primary areas)

# Cortical types ("Levels")

- First level: limbic
  - Hippocampus (archicortex)
  - Pyriform olfactory (paleocortex)
- Second level: paralimbic
  - Hippocampal Division
  - Orbitofrontal Division
- Third level: homotipical (isocortex)
  - A. Unimodal
  - B. Heteromodal
- Fourth level: idiotipical
  - Koniocortex (primary sensory)
  - Macropyramidal cortex (primary motor)






Idiotypic (primary) areas

Modality specific (unimodal) association areas. Secondary areas.

High-order (heteromodal) association areas. Tertiary areas

Paralimbic areas.

# “Corticoid” or cortex-like structures

- The simplest and most undifferentiated type of cortex: basal forebrain.
  - » Rudimentary and no consistent lamination or dendritic orientation
  - » Architectonic features that are in part cortical and in part nuclear (specially the amygdala)
- Septal nuclei, substantia innominata, amigdaloid complex
- Situated directly on the ventral and medial surface of he hemispheres and are thus considered part of the cortical mantle

# 1. Allocortex (limbic cortex)

- Contains one or two principal bands of neurons arranged into moderately differentiated layers.
- Two anatomical formations:
  - Hippocampal formation (archicortex)
  - Piriform or primary olfactory cortex (paleocortex)

# 2. Paralimbic cortex

- Areas intercalated between allocortex and isocortex, so as to provide a gradual transition from one to the other.
- Allocortical cell layers often extent into the periallocortical component of paralimbic areas
  - Gradual changes in the direction of increased complexity,
- Five paralimbic regions that form an uninterrupted girdle surrounding the medial an basal aspects of the cerebral hemispheres

# The five major paralimbic formations

1. The caudal orbitofrontal cortex
2. The insula
3. The temporal pole
4. The parahippocampal gyrus
   - Includes: Entorhinal, prorhinal, perirhinal, presubicular, & parasubicular areas
5. The cingulate complex
   - Includes: Retrosplenial, cingulate, and paraolfactory areas

# SISTEMA LÍMBICO

## Componentes corticales (y número de Brodmann)

- **FORMACIONES CORTICOIDEAS** (amigdala, sustancia innominada, núcleos septales)
- **ALLOCORTEX** (hipocampo, corteza olfativa o piriforme)
- **CORTEZA PARALIMBICA** [ínsula (14, 15), corteza temporopolar (38), corteza orbitofrontal caudal (áreas caudales 11, 12, 13), complejo cingular (23, 24, 33, 31, 26, 29), región paraolfatoria (25, caudal 32), corteza parahipocampica (28, 34, 35, 30)]

# Hypothalamus

(un breve comentario)

# Hypothalamic input

- All types of cortical areas, including association isocortex, receive direct hypothalamic projections
  - This hypothalamic input is quite minor
  - Exception: The limbic structures
    - » Septal nuclei, basal nucleus of the substantia innominata, amygdaloid complex, piriform cortex, and hippocampus
    - » Paralimbic zone: other major source of connections for limbic structures

# Hypothalamus

- Corticoid & allocortical ("limbic"): The closest association with the hypothalamus.
- Neural and hormonal mechanisms: coordination...
  - Electroliyte balance, blood glucose levels, basal temperature, metabolic rate, autonomic tone, sexual phase, circadian oscillations, immunoregulation
  - Major coordinating structure for drives and instincts that promote the survival of the self and of the species

# Hypothalamus → areas of the limbic zone

- Important role in the regulation of behaviors such as...
  - Memory and learning
  - The modulation of drive
  - The emotional coloring of the experience
  - The higher control of hormonal balance and autonomic tone

Specializations related to the maintenance of the intenal milieu (homeostasis) as well as to the associated operations necessary for the preservation of the self and the species

# 3. Homotypical isocortex

- Six layered homotypical isocortex or association cortex
- Two major types:
  - (3 A). Modality specific (unimodal) isocortex
  - (3 B). High-order (heteromodal) isocortex

# 3 A. Modality specific (unimodal) isocortex: characteristics

- The constituent neurons are almost exclusively resposive to stimulation in only a single sensory input
- Predominant inputs are provided by the primary sensory cortex or by other unimodal regions in that same modality
- Damage yields modality-specific deficits confined to tasks guided by cues in that modality

# 3 B. High-order (heteromodal) isocortex: characteristics, I

- Neuronal responses are not confined to any single sensory modality
- The cortical inputs originate from unimodal areas in more than one modality and/or from other hetromodal areas, and
- Damage to this type of cortex leads to deficits that transcend any single modality

# 4-B. High-order (heteromodal) isocortex: characteristics, II

- Response to stimulation in more than one modality = multimodal convergence
- More commonly: Admixture of neurons with different preferred modalities

- HETEROMODAL CORTEX: high-order association cortex, polymodal cortex, multimodal cortex, polysensory areas, supramodal cortex, tertiary areas.

# Cortezas de asociación (número de Brodmann)

- **Unimodal visual (18, 19, 20, 21, ?37)**
- **Unimodal auditiva (22)**
- **Unimodal somatosensorial (5 y rostral 7)**
- **Unimodal motora (rostral 6, caudal 8, 44)**

- **Heteromodal prefrontal (9, 10, 11, 45, 46, 47, ? rostral 8, rostral 12, rostral 32)**
- **Heteromodal parietotemporal (39, 40, caudal 7, bordes del surco temporal superior, ? 36)**
- **Porción posterior del lóbulo temporal ventral**

# Differences between unimodal and heteromodal areas

- The unimodal areas have a more differentiated oganization, specially with respect to sublamination in layers III and V, columnarization in layer III, and more extensive granularization in layer IV, and specially in layer II

# 5. Idiotypic cortex: Primary sensory & Primary motor:

- Primary sensory: koniocortex
  - Visual: occipital pole and the banks of the calcarine fissure
  - Auditory: Heschl's gyrus on the supratemporal plane
  - Somatosensory: Postcentral gyrus
- Primary motor: macropyramidal cortex
  - Precentral gyrus

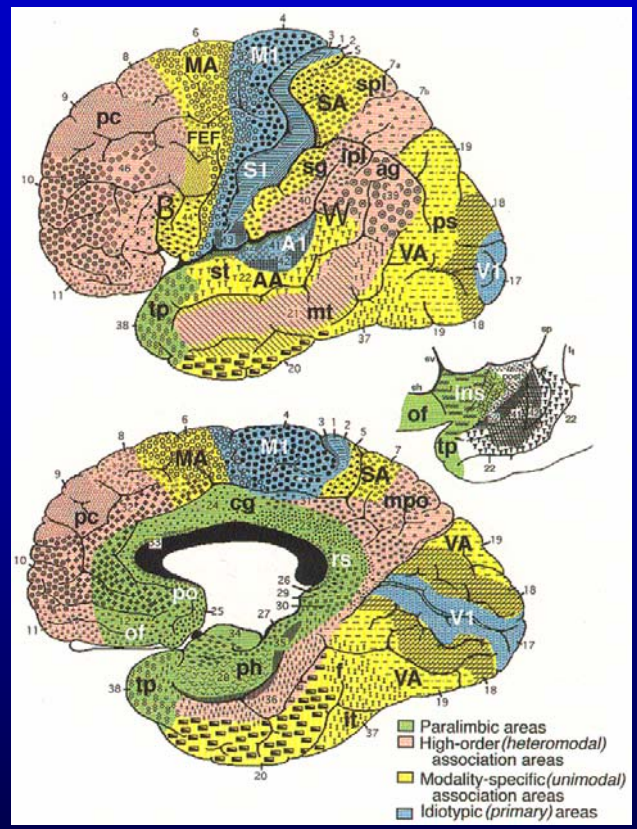
There are two divergent opinions about these primary areas:
• The most basic and elementary components of the cortex
• The most advanced and highly differentiated components of the cortex

# Idiotypic cortex

- Primaria visual (área 17)
- Primarias auditivas (áreas 41 y 42)
- Primarias somatosensoriales (áreas 3, 1, 2 pero principalmente 3b)
- Primarias motoras: (4 y porción caudal de 6)

# Patterns of connections, I

- Paralimbic areas: extensive monosynaptic connections with the limbic & the heteromodal areas
- Heteromodal areas: with paralimbic and unimodal areas
- Primary areas: from unimodal areas and major subcortical connections from the relevant thalamic relay nuclei




Primary (sensory-motor) → Secondary (unimodal) ↔ Tertiary (heteromodal) ↔ Parlimbic

# Patterns of connections, II

- The amigdala receive direct input from association isocortex
- The primary areas in the more advanced primates do not seem to receive any limbic or paralimbic cortical input
  - » This may ensure that the initial processing of sensory information is not influeced by drive or mood
  - » Emotional state does not alter the shape of an object or the pitch of a sound
- In other mamalian species as the rat this separation may be less complete: direct connectivity betwen primary and paralimbic areas has been reported

# Patterns of connections, III

- Many cotical areas have connecions with other constituents of the same functional zone. These are extermely well developed within the limbic, paralimbic, and heteromodal zones
  - The case of the frontal lobe
  - The case of the insula & the cingulate cortex
- Unimodal areas:
  - May receive extensive input from other unimodal areas in the same modality
  - There is no essentially interconnectivity between areas belonging to different modalities
- Primary areas: Except for the intimate interconnections between the primary somatosensory and motor areas, there are no neural projections among primary areas belonging to separate modalities.

# Limbic - paralimbic connections

- Amygdala from the insula
- Hippocampus from the entorhinal sector of the parahippocampal region
- The piriform cortex as well as the nucelus basalis from insular, temporopolar, and orbitofrontal paralimbic areas

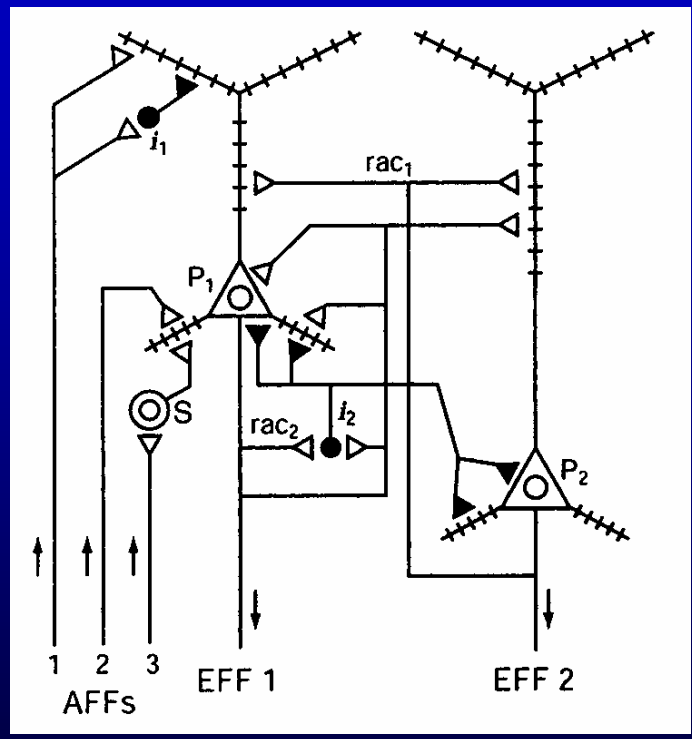
# Patterns of connections: a basic difference

- Chanel width (interconnections): within the limbic, paralimbic and heteromodal zones

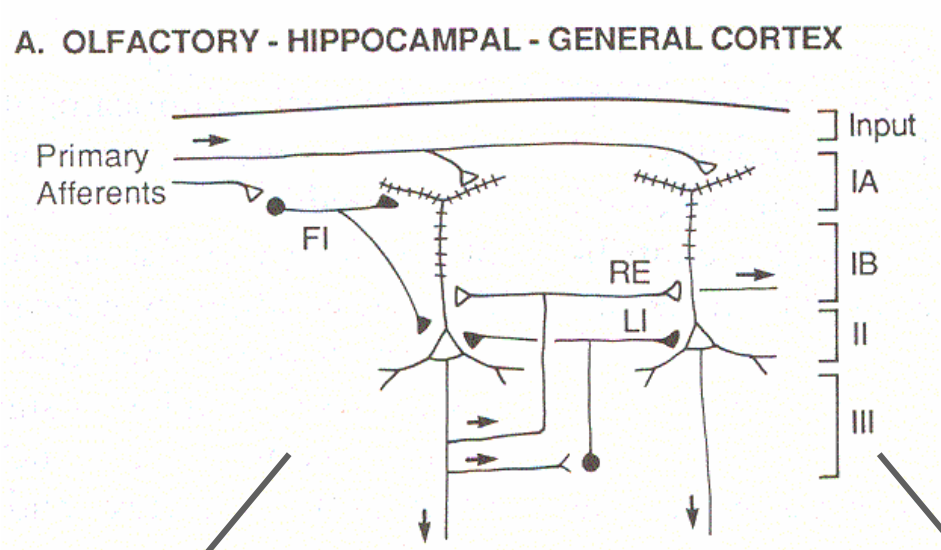
- Fidelity: unimodal and primary areas

# Cortical canonical circuits

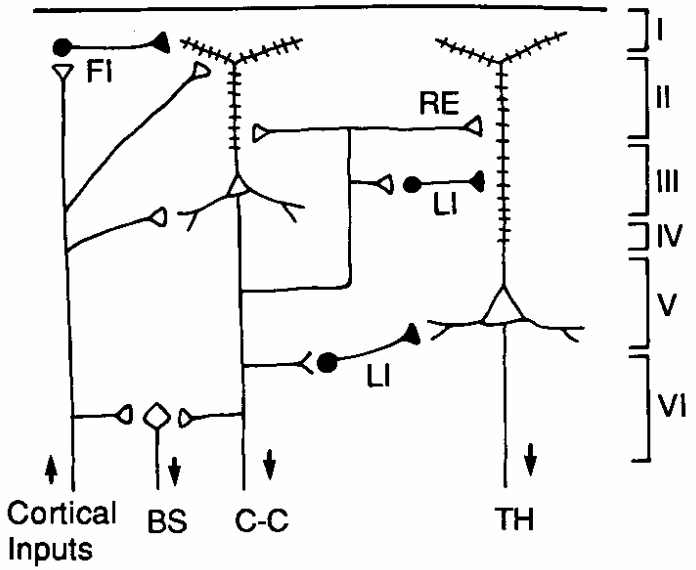
- Contribuciones tempranas de Santiago Ramón y Cajal
- Véase: Peters y Jones (1984), DeFelipe y Fariñas (2002), Silberberg et al (2002), Douglas, Markram & Marin (2004)

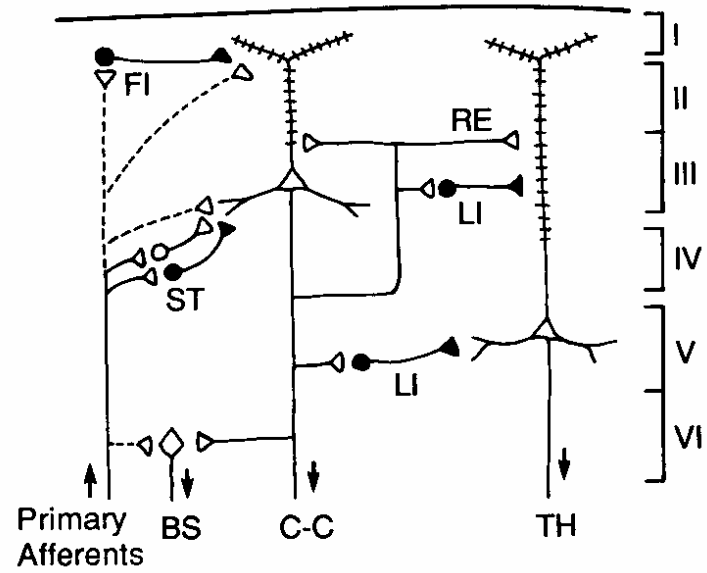


Allocortex:
Archicortex - Paleocortex



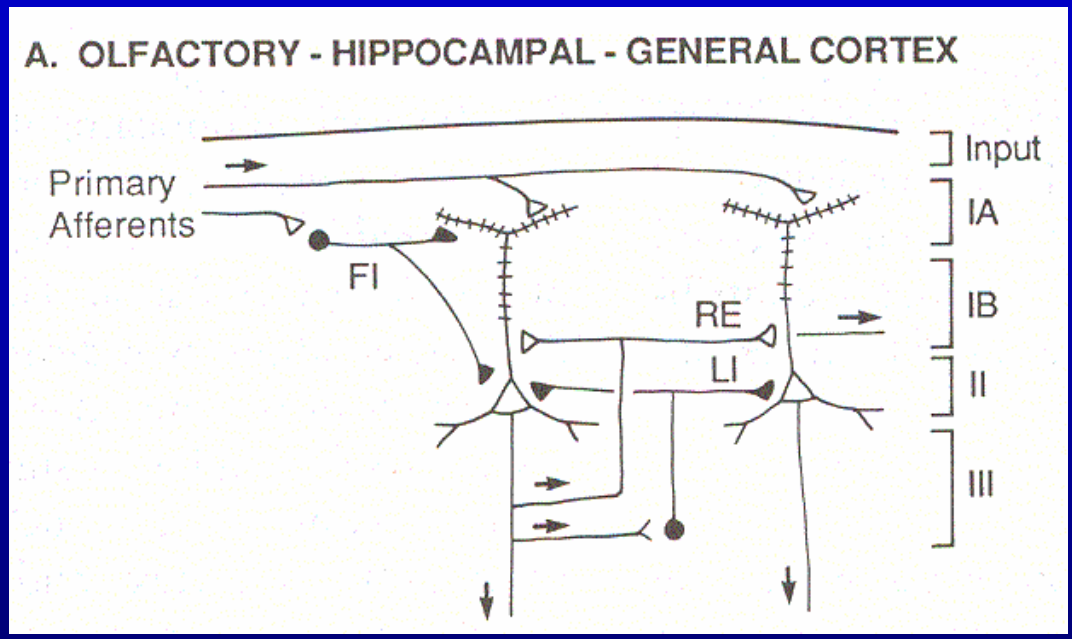

Isocortex




After Shepherd 1999

# Olfactory - hippocampal – general cortex




- FI: feedforward inhibition
- LI: Lateral Inhibition
- RE: Recurrent and lateral excitation

- Aferentes (IN): sinapsis en espinas apicales de neuronas P
- Axones intrínsecos colaterales de P que actúan como reexcitadores (RE), de las neuronas P a través de largas distancias.
- Interneuronas activadas por IN: generan inhibición anterógrada (FI)
- Interneuronas activadas por colaterales de P: generan inhibición retrógrada y lateral (LI)

# Basic six-layered structure of the neocortex

I. Molecular layer (plexiform, or tangential)

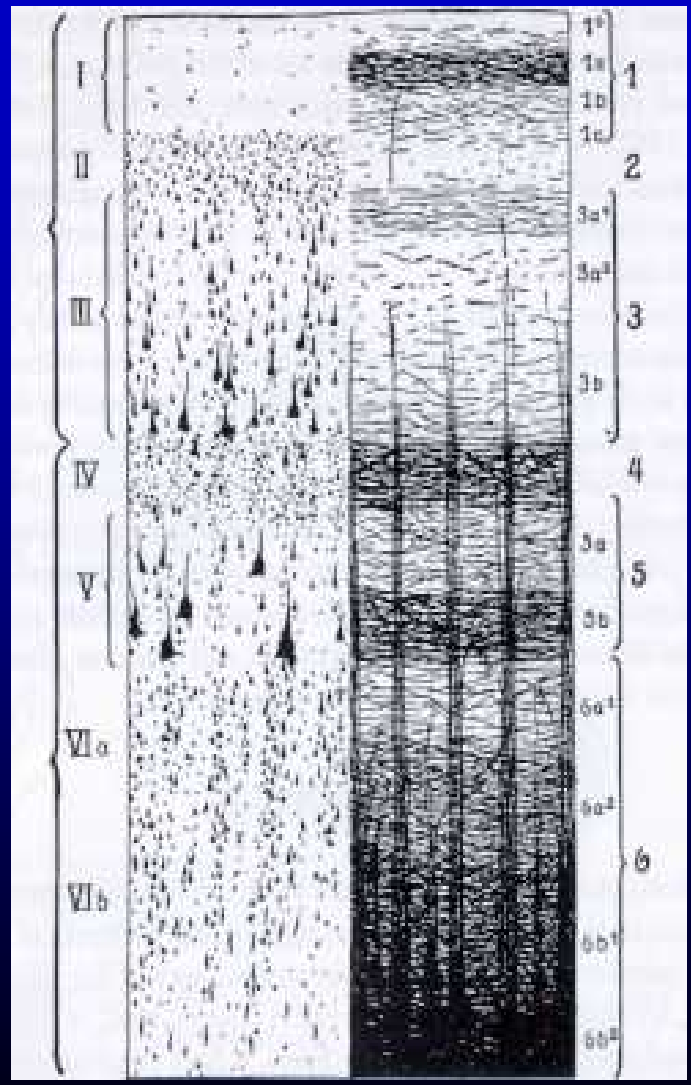
II. External granular layer

III. External pyramidal layer

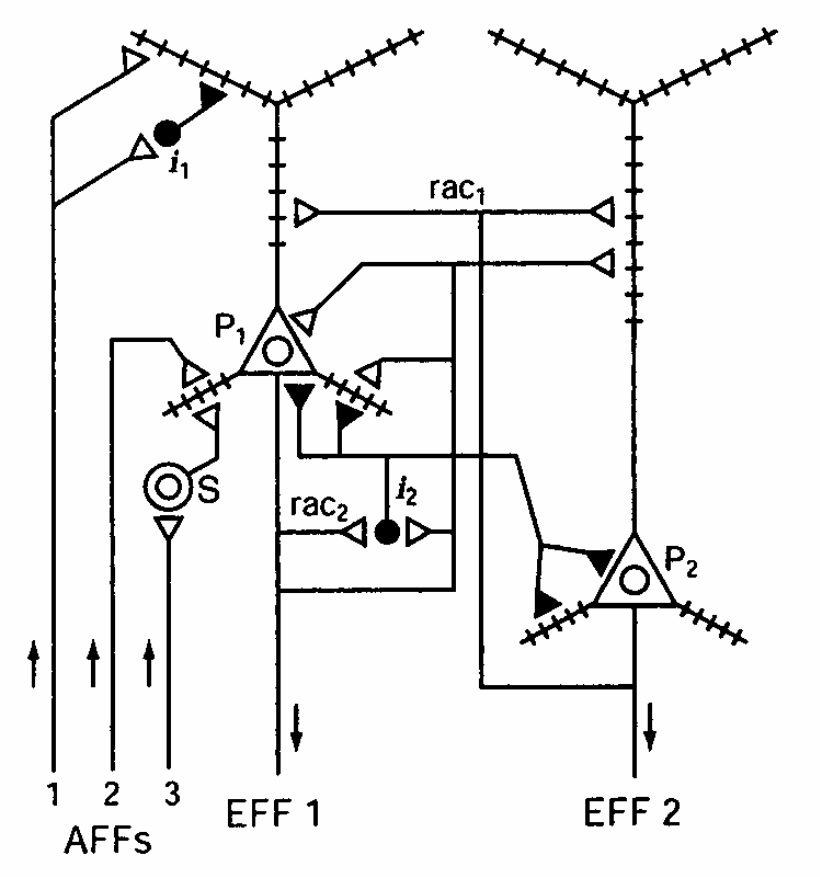
IV. Internal granular layer

V. Internal pyramidal layer

VI. Multiform layer (fusiform or polimorphic)



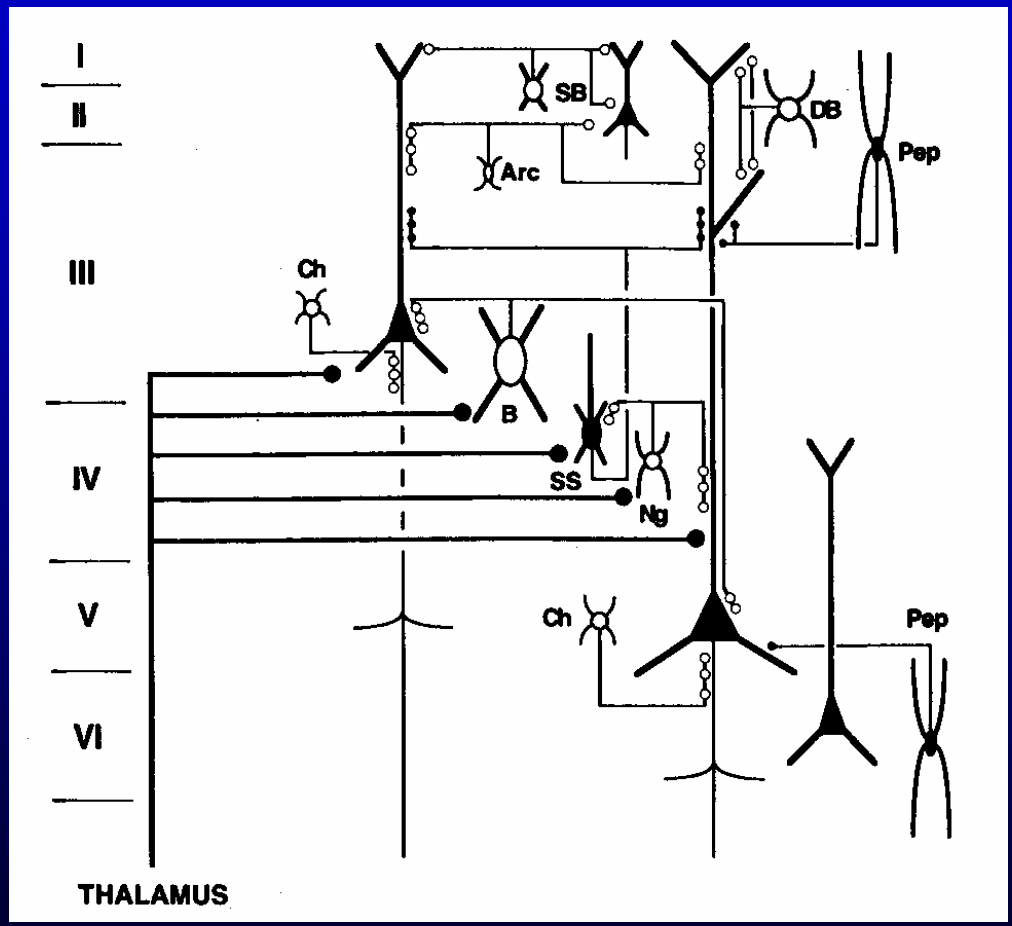
# Regional canonical circuits: neocortex




- (P1) EFF 1
- (P2) EFF 2
- rac: recurrent axon collaterals
- S: stellate cells
- i: inhibitory cells

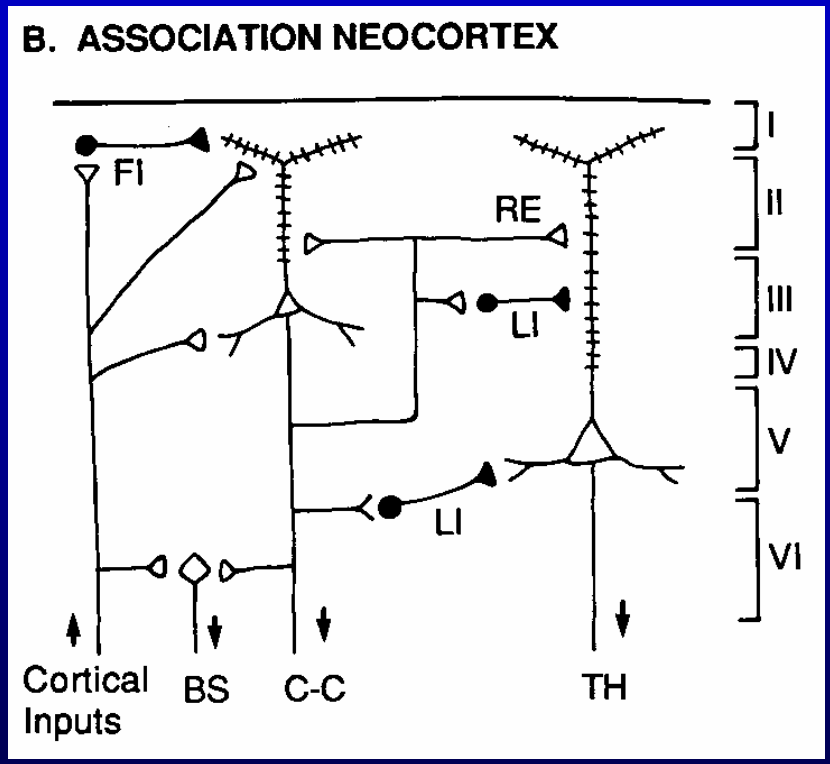
# Cortical neurons and their connections

- Arc: Arcade
- B: Large Basquet
- Ch: Chandelier
- DB: Double bouquet
- Ng: Neuroglia form
- Pep: Peptide cells
- SS: Spinny stellate
- SB: Small basquet




Open circles: inhibitory contacts; Solid cells: excitatory; Open cells: inhibitory

# Association Neocortex



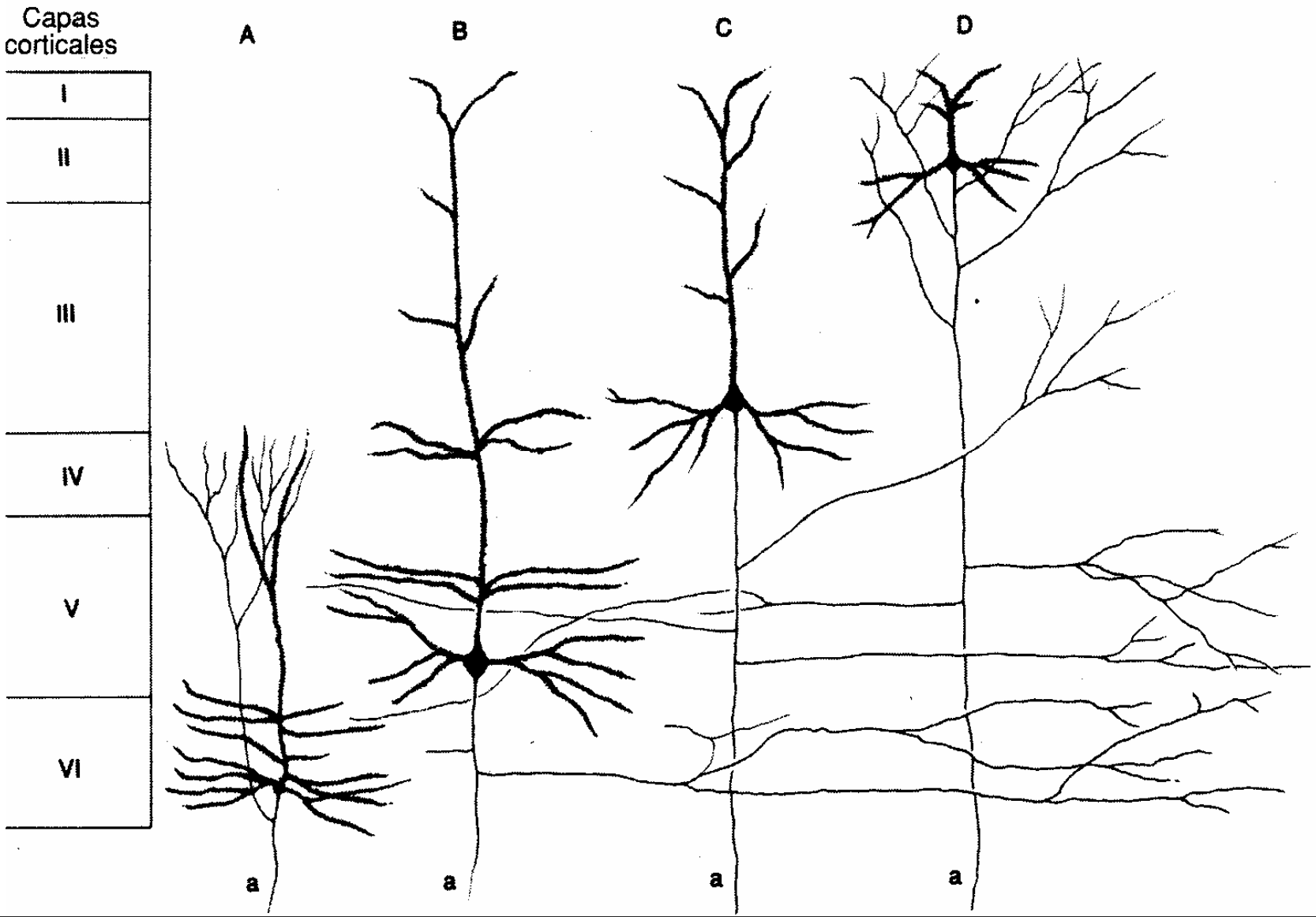

- Inputs: From cortex
- Outputs
  - BS: brainstem
  - CC: cortico-cortical
  - TH: thalamus
- Intrinsic neuron

Corteza agranular

Aferencias de otras partes de la corteza a las capas superficiales (III, I)

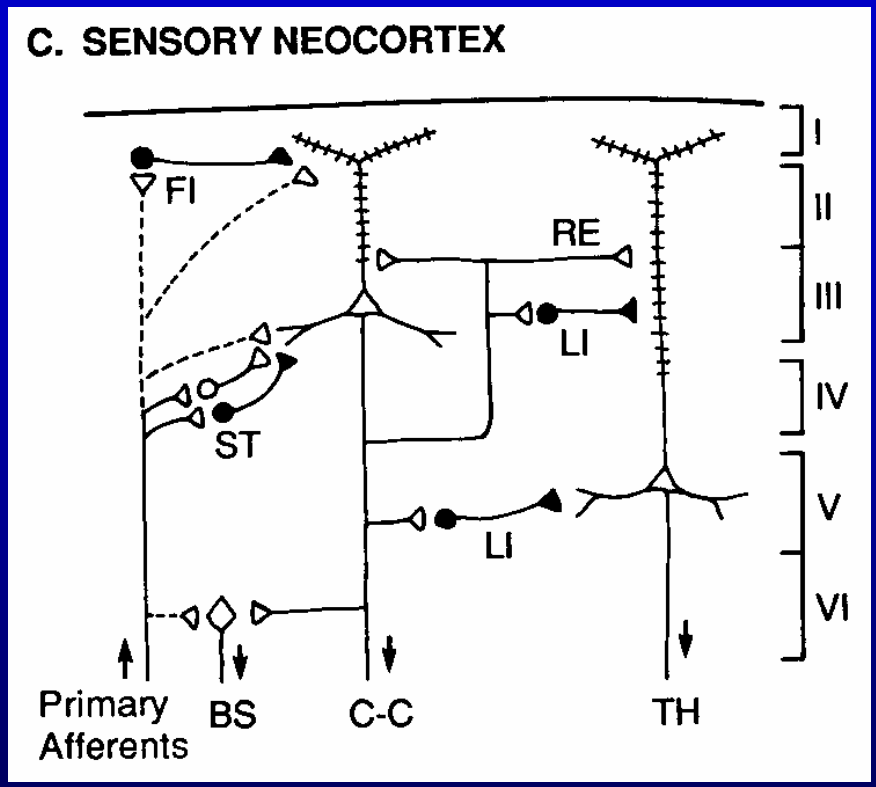
P: reexcitación (RE) de otras P a través de colaterales

Inhibición anterógrada (FI), e inhibición lateral (LI) como en corteza primitiva




| A | B | C | D |
|---|---|---|---|
| Cortico-talámica<br>Cortico-claustral | Cortico-estriada<br>Cortico-protuberancial<br>Cortico-bulbar<br>Cortico-espinal | Comisural<br>Cortico-cortical | Asociación<br>Cortico-cortical |

# Sensory Neocortex




- Predominance of afferents from the thalamus which project to an intracortical relay through stellate (ST) cells in layer IV

P1 (capa III)
P2 (capa V)
Estrelladas o granulares (capa IV)

Aferentes: a P1, directas y a través de células inhibidoras (FI)
Además: actividad RE anterógrada a través de ST (IV) = relevo intracortical
P (III): colaterales recurrentes (RE) y del inhibición lateral (LI)
Output final: en función de balances excitadores e inhibidores

CORTICOIDEAS

(1) S. Límbico

ALLOCORTEX

Amigdala, S. Innominada, Núcleos septales

ARCHICORTEX. Hipocampo

PALEOCORTEX. Corteza piriforme

PARALIMBICA
(2)

Orbitofrontal caudal, Insula, Temporopolar, Parahipocampica, Complejo cingulado

ISOCORTEX
(3, 4)

UNIMODAL
(3)

Occipital, Temporal, Parietal, Frontal

HETEROMODAL
(4)

Prefrontal, Parietal, Temporal ventral posterior

IDIOCORTEX
(5)

SENSORIAL

Occipital, Temporal, Parietal

MOTOR (Macropiramidal)

# Neurotransmisores corticales

- L-glutamato (Glu). Excitador
- Ácido γ-aminobutírico (GABA). Inhibidor.
- Acetilcolina. Rol facilitador
- Colocalizaciones de GABA
  - Somatostatina
  - Colecistokinina
  - Neuropéptido Y
  - Sustancia P
  - Polipéptido intestinal vasoactivo (VIP)
- Aferencias serotoninérgicas, colinérgicas. dopaninérgicas y noradrenérgicas.

# What makes neocortical circuits unique?

- *When the local circuits through collaterals and interneurons are added, the potential ways by which information can be integrated, stored, and recombined become enormous*

# Particularidades funcionales de la corteza[1], I

1. Recibe información de todos los sistemas sensoriales
2. No está dominada por una secuencia funcional.
   - Las interacciones funcionales laterales incrementan extraordinariamente la capacidad de almacenamiento y recombinación.

1. Shepherd, 1994

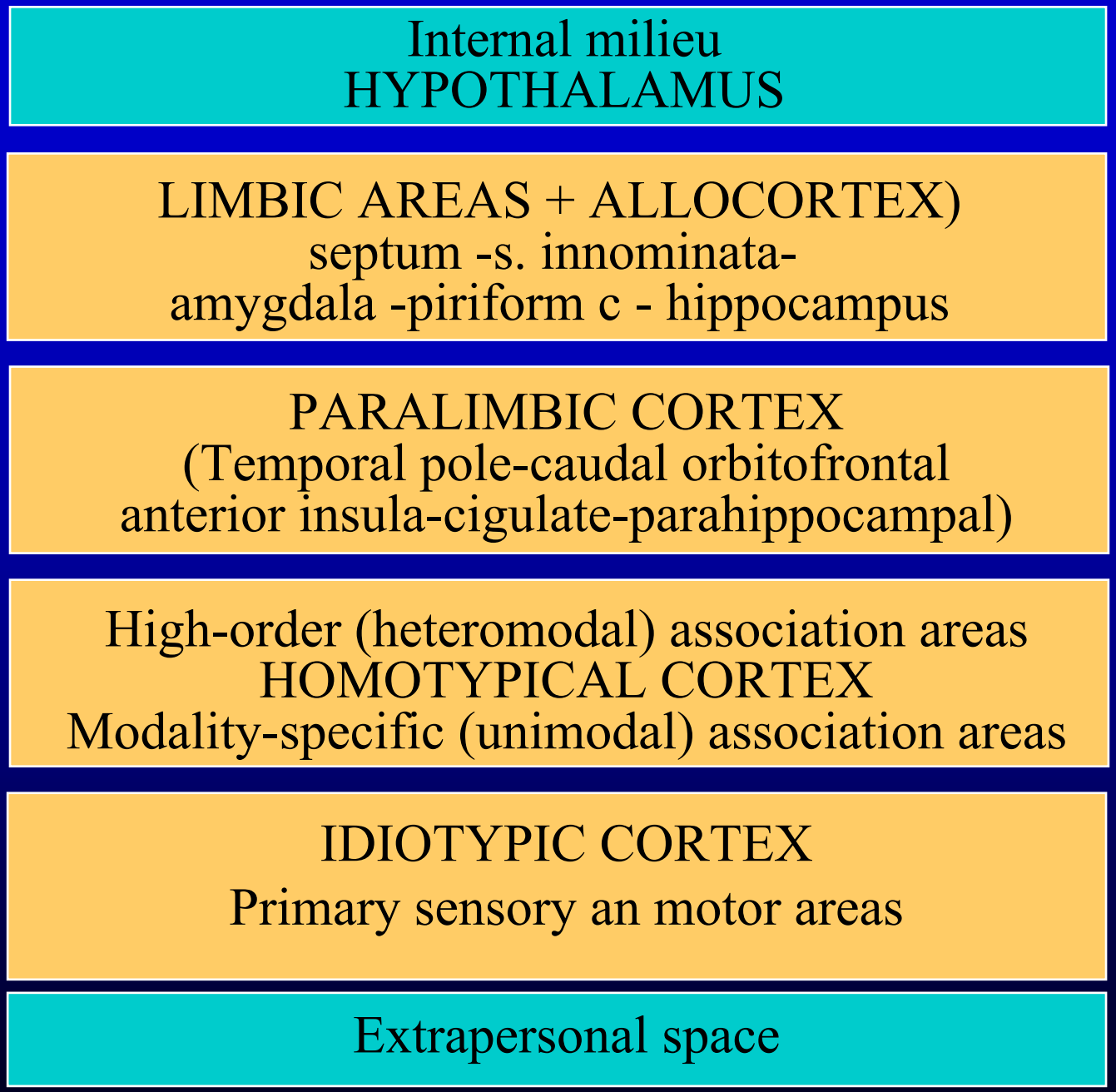
# Particularidades funcionales de la corteza, I I

3. Presenta varios tipos de eferencias. Cada capa es origen de fibras.
   - Conexiones a otras capas (p. ej I a V)
   - Conexiones distantes (II, III, V, VI)
- Cada capa puede actuar como una unidad semi-independiente con entradas, salidas, conexiones intrínsecas y a otras capas.
- Existen claros patrones de proyección anterógrada (forward), de la capa IV a la capa III, y de la capa III a la V, con sinapsis en células piramidales e interneuronas.
- Las proyecciones retrógradas de la capa V a la III, y de la capa III a la IV, únicamente se dirigen a interneuronas[1].

1. Thopson & Bannister, 2003

# Particularidades funcionales de la corteza, II

4. La interconexión entre las distintas zonas corticales –condicionada por la anatomía- permite una extraordinaria capacidad de procesamiento: combinaciones a partir de combinaciones de entradas, de patrones locales de actividad y de conexiones específicas entre zonas.
5. La función cortical está influida y modulada por estructuras subyacentes a través de circuitos que efectúan actividades reentrantes.




Adapted From Mesulam, 2000

# SISTEMAS CORTICALES DISTRIBUIDOS

## SISTEMAS FUNCIONALES COMPLEJOS (Anojin, Luria)

Most cortically mediated behavior depents on **interactions** between areas in different lobes

Cortical circuits in all the lobes must be engaged in a **coordinated manner** in order to carry out an act

# LÓBULOS Y ÁREAS CORTICALES DE LOS MAMÍFEROS

- LOBULOS
  - FRONTAL: origen de muchas vias motoras
  - TEMPORAL: input auditivo
  - PARIETAL: input somatosensorial
  - OCCIPITAL: input visual
  - LÓBULO LÍMBICO
  - ÍNSULA
- ÁREAS
  - SENSORIALES
  - MOTORAS
  - ASOCIATIVAS: Unimodales y heteromodales

# NOTA

- Es mejor referirse a estructuras anatómicas que a citoarquitectonía
  - Es mejor decir Circunvolución transversa de Heschl que área 41-42 de Brodmann (citoarquitectonía basada en criterios microscópicos