

بنام خداوند جان و خرد



Connectome for Neuroimaging

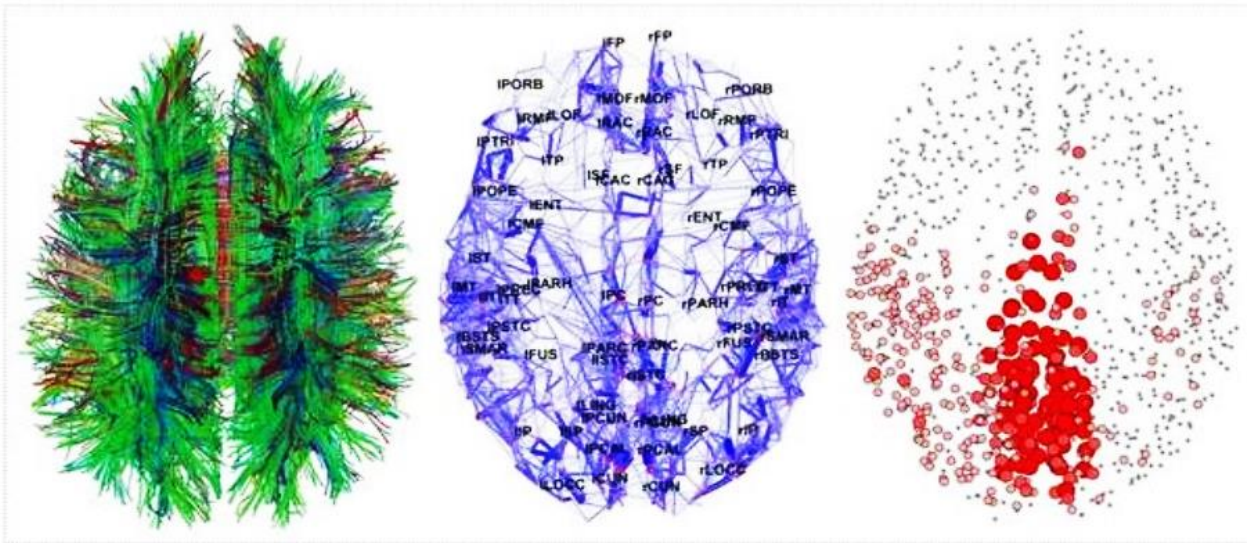
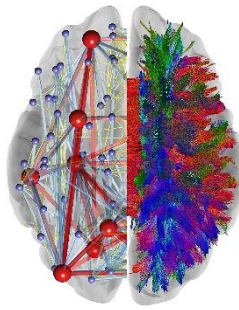
Presenter:

Dr. Auob Rustamzadeh

(Assistant Professor of Anatomical Sciences
Qazvin University of Medical Sciences)

CONNECTOME:

A NEW PARADIGM FOR UNDERSTANDING BRAIN FUNCTION

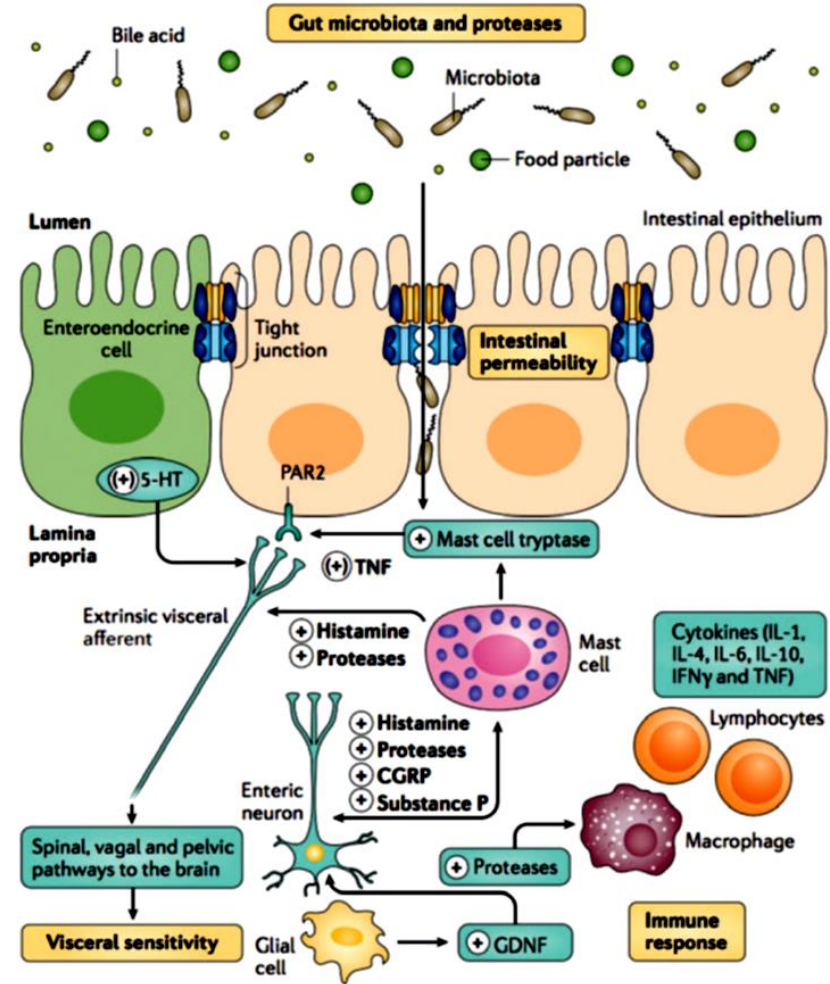
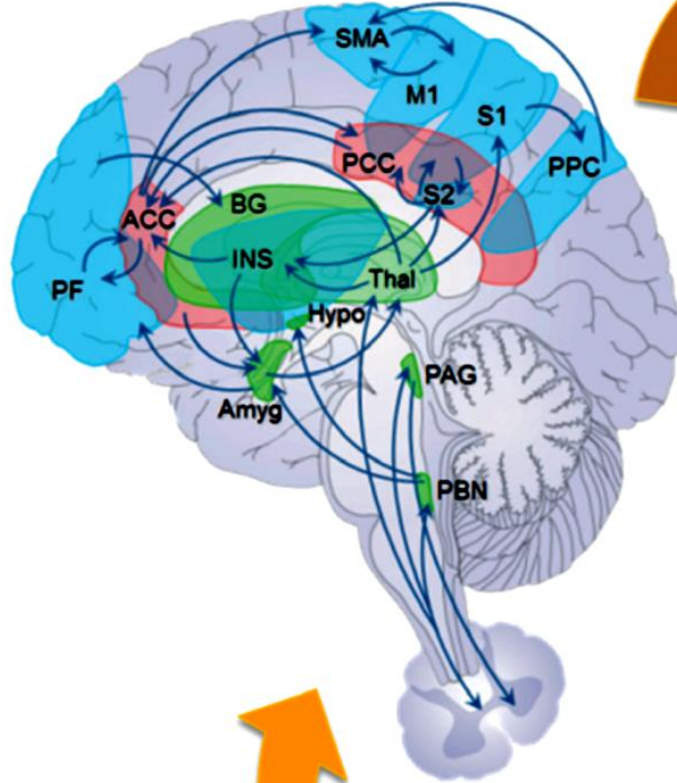


The term **connectome**, proposed roughly 10 years ago, describes a comprehensive network map of extrinsic connections between functionally specialized brain regions.

the **principle barriers** presently preventing application of connectomic imaging in brain surgery are:

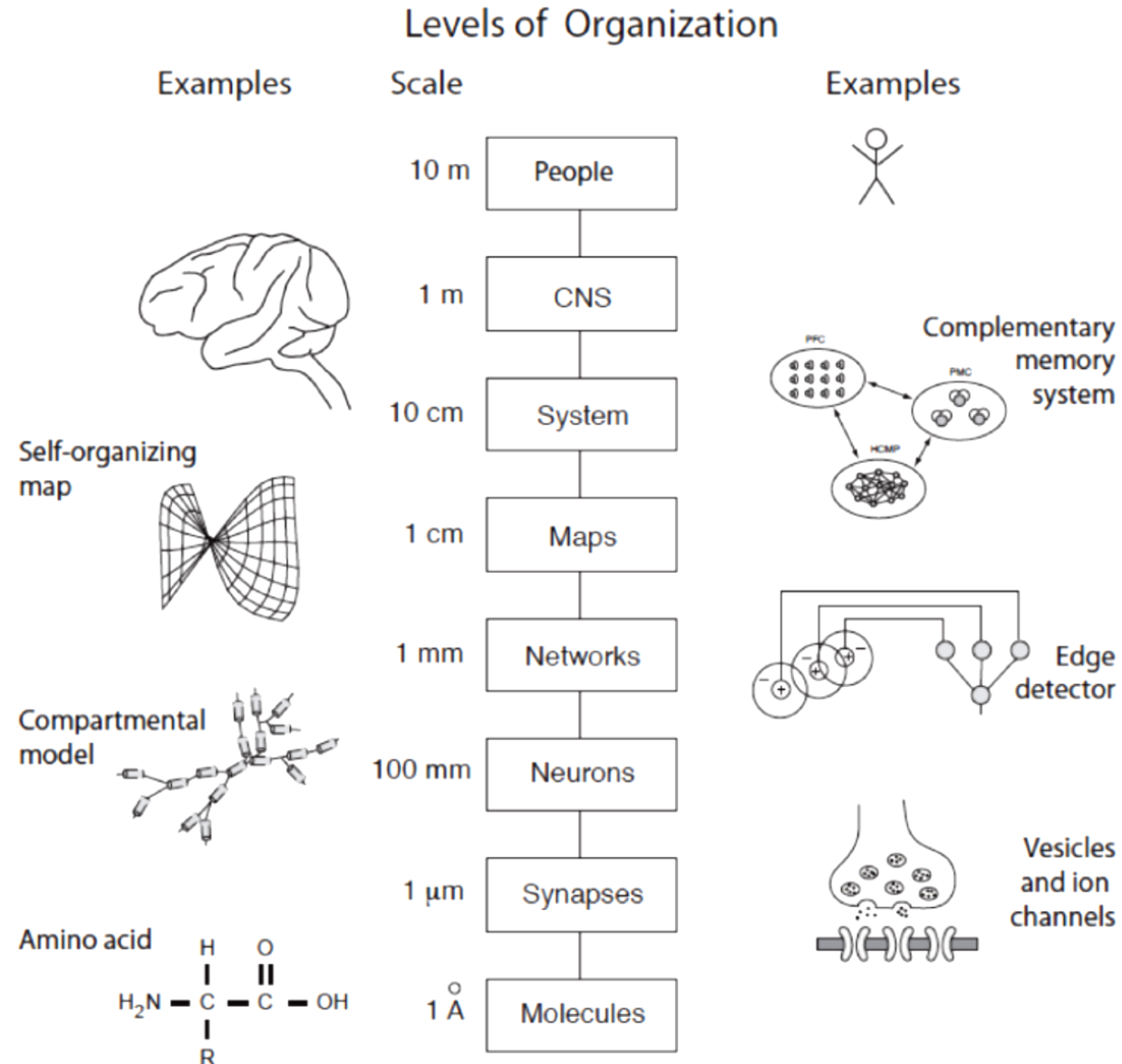
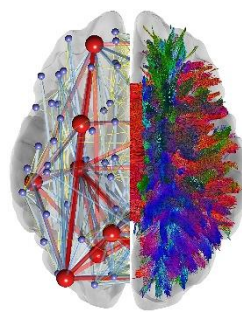
- (1) the relative difficulty of **postprocessing** MRI images to provide clinically useful data that can be used for intraoperative navigation and planning,
- (2) a relative lack of knowledge about the anatomy of **brain networks and tracts**,
- (3) difficulty **linking connectomic anatomy to clinical phenotypes** and functional significance.

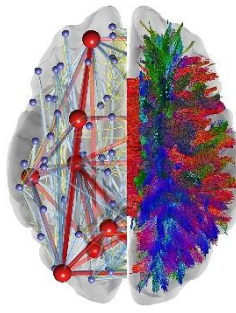
Brain Connectome



Gut Connectome

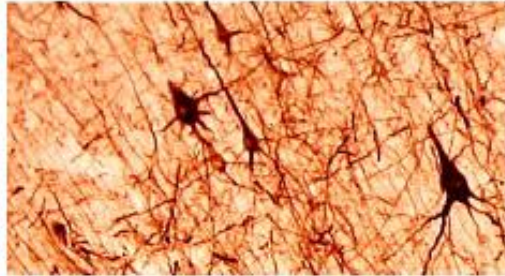
Levels of organizations in the nervous system



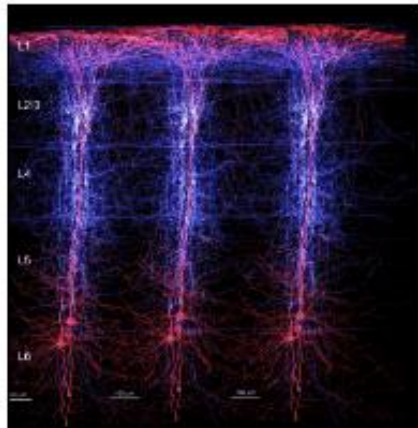


What are neural connectome and networks?

Levels of connectivity



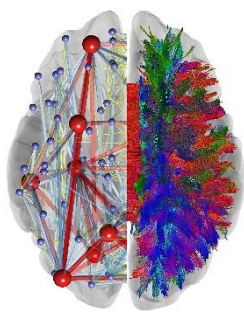
Axons between neurons



Links between cortical columns

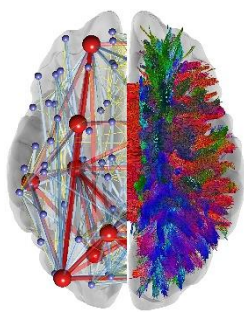
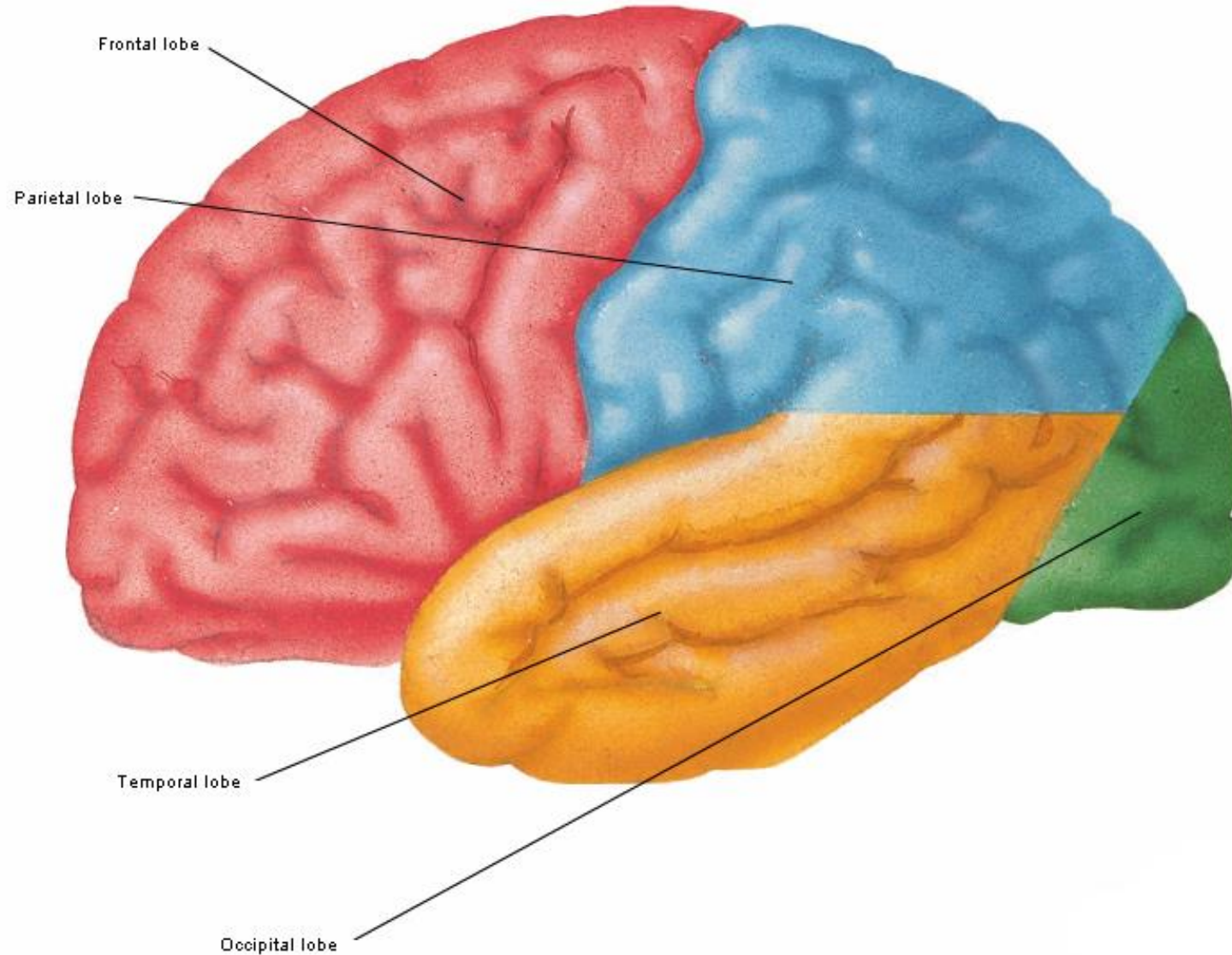


Fibre tracts between brain areas



Anatomo-physiological perspective versus Neuroimaging perspective?!

Grey matter

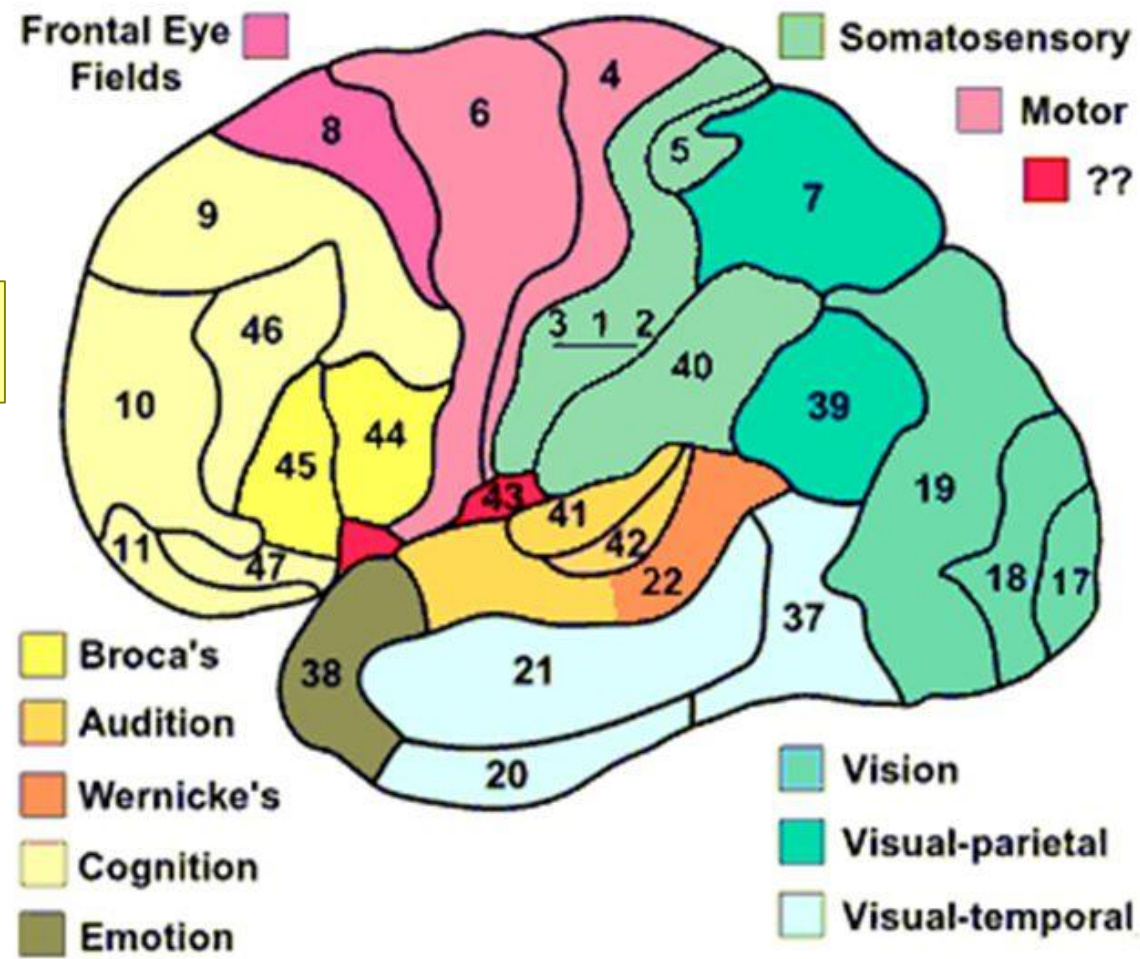


Grey matter

Brodmann's Functional Map

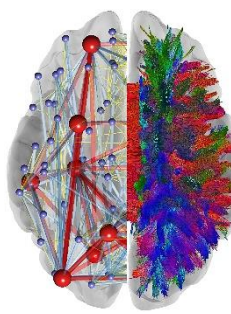
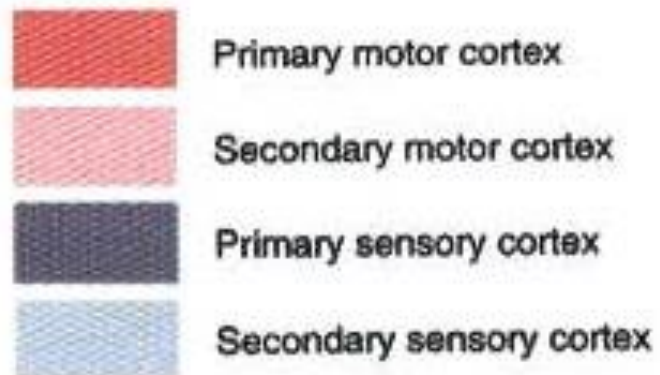
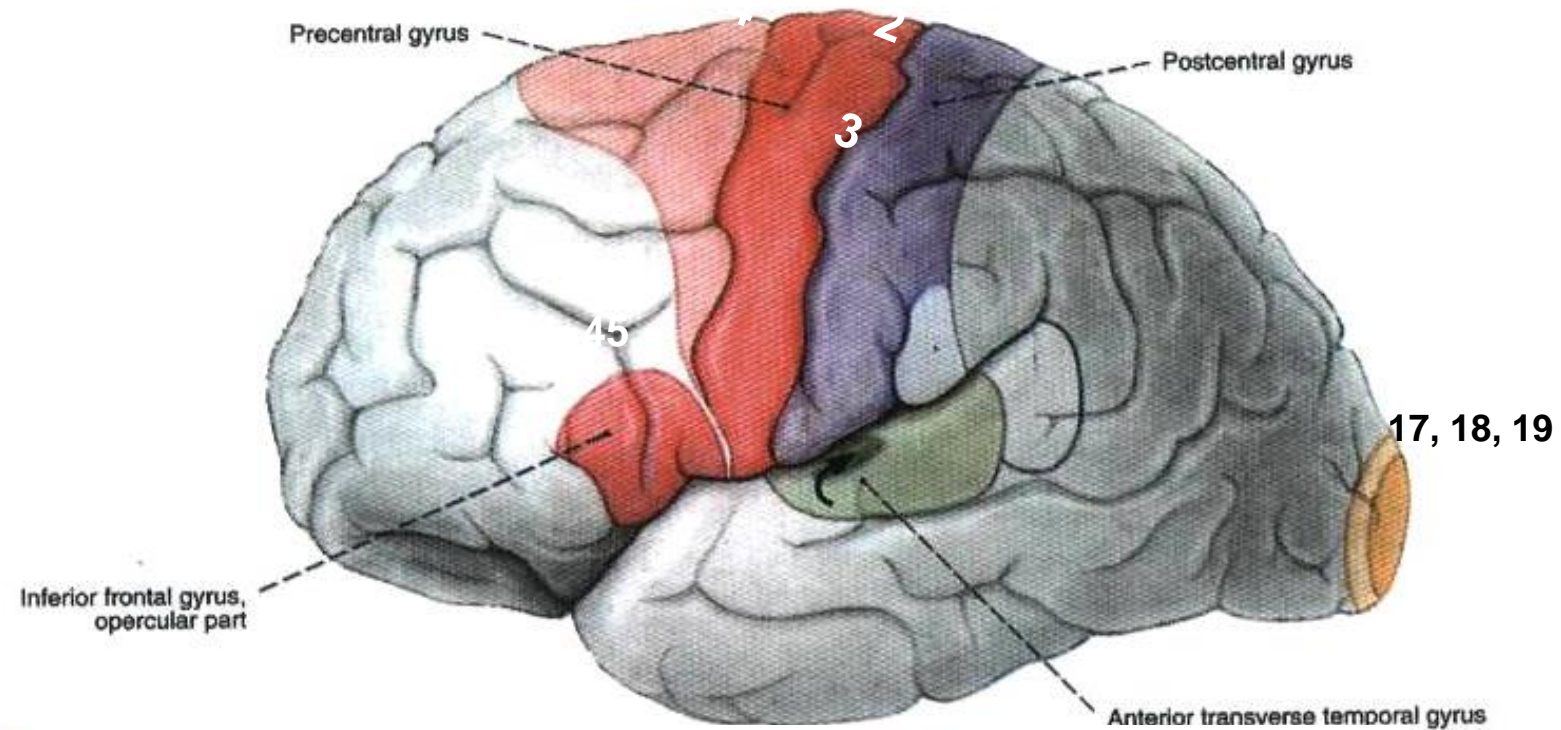
Brodmann [1909]

German neurologist Korbinian Brodmann based on the [cytoarchitecture](#) organization of [neurons](#)



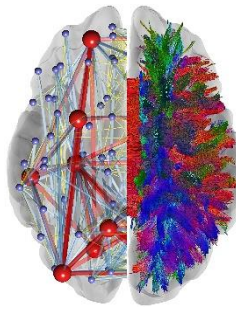
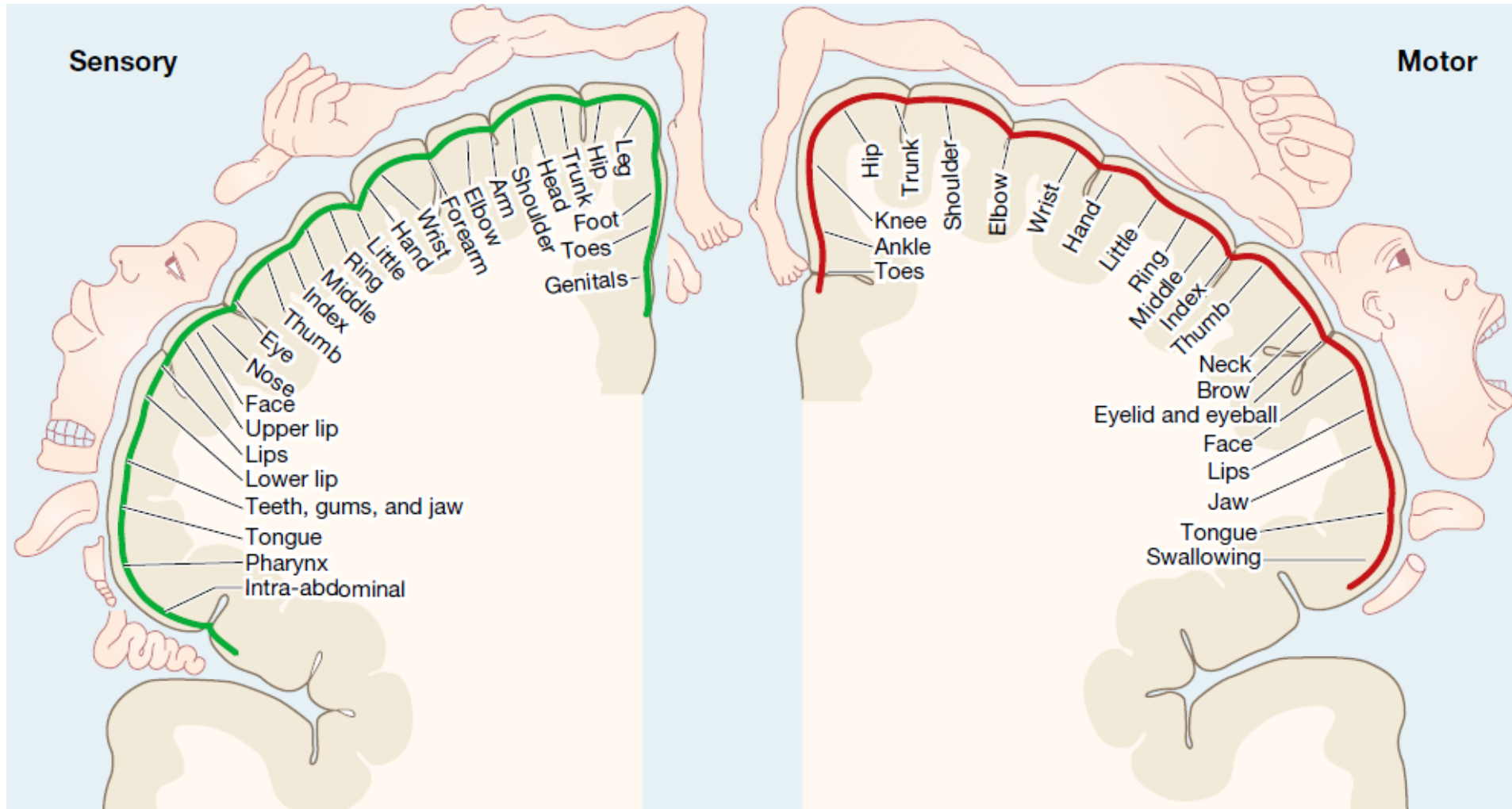
An example of Anatomo-physiological perspective

Grey matter



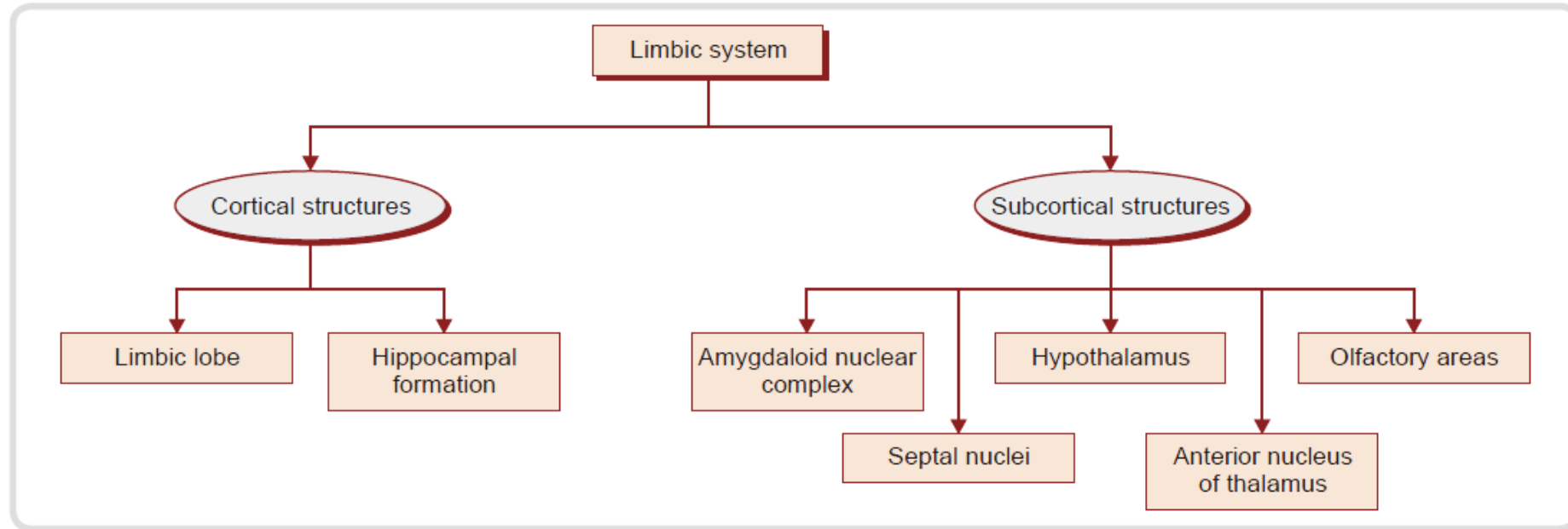
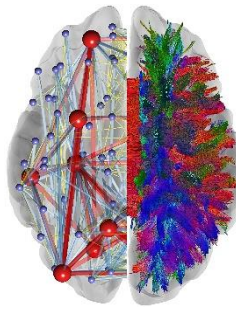
An example of Anatomo-physiological perspective

Grey matter



An example of Anatomo-physiological perspective

Grey matter



Grey matter

An example of Anatomo-physiological perspective

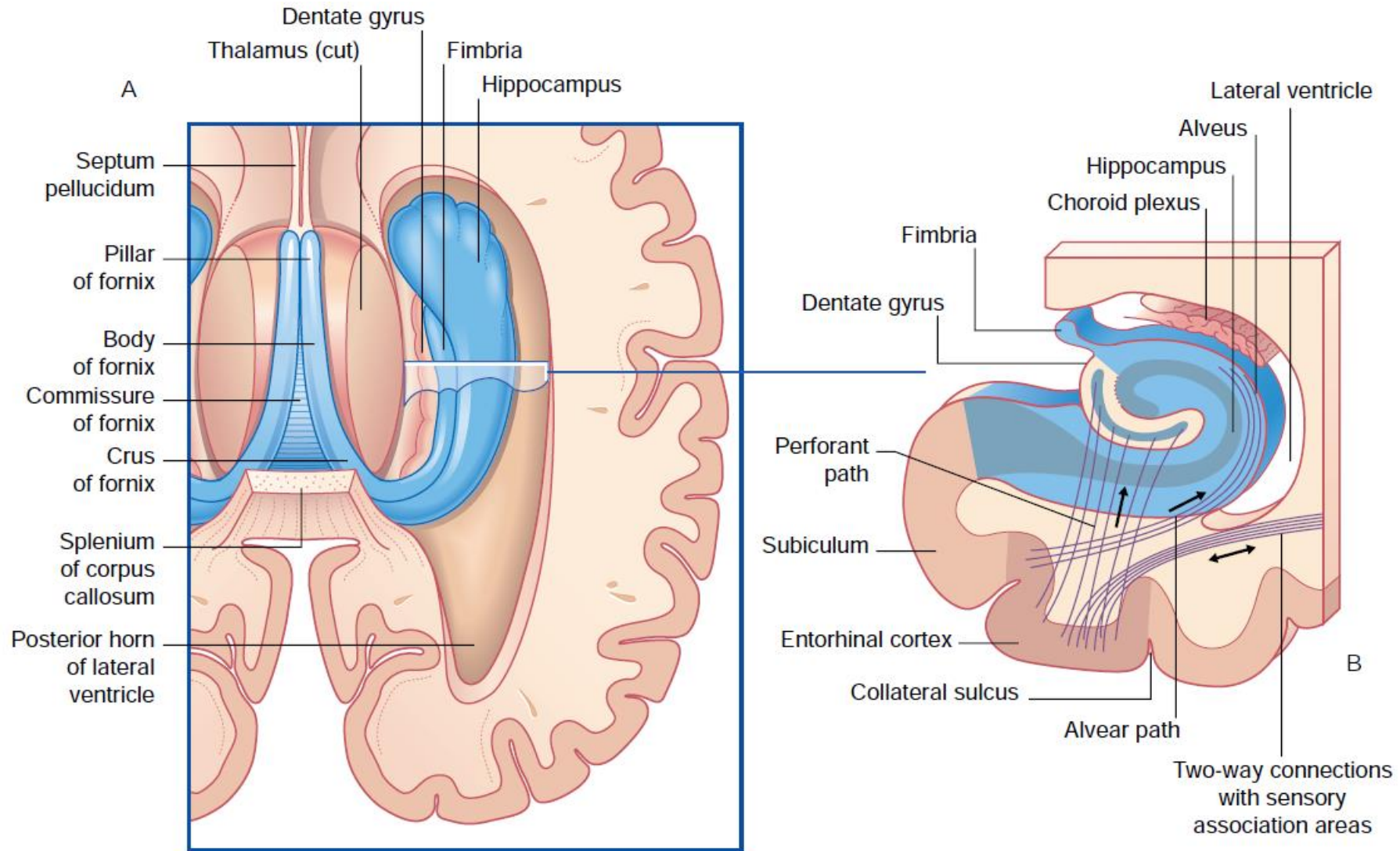
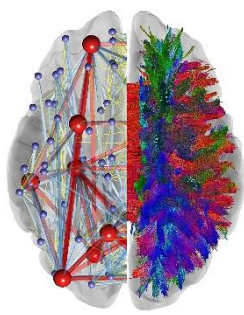


Figure 34.5 Hippocampal formation. **(A)** View from above. **(B)** Enlargement from (A) showing the entorhinal cortex and the three component parts of the hippocampal formation.



Grey matter

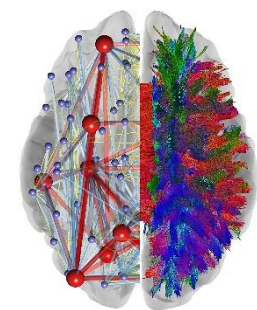
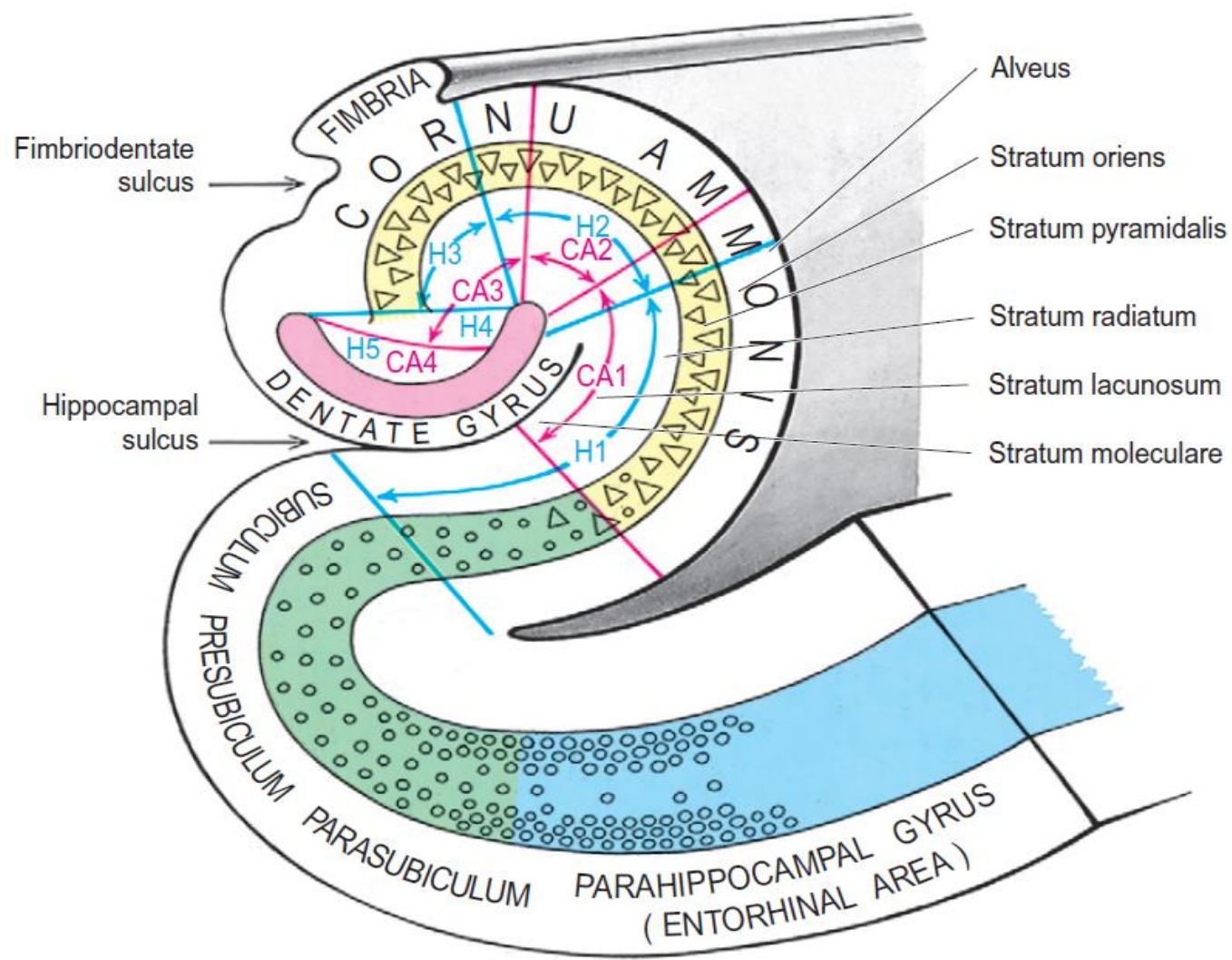
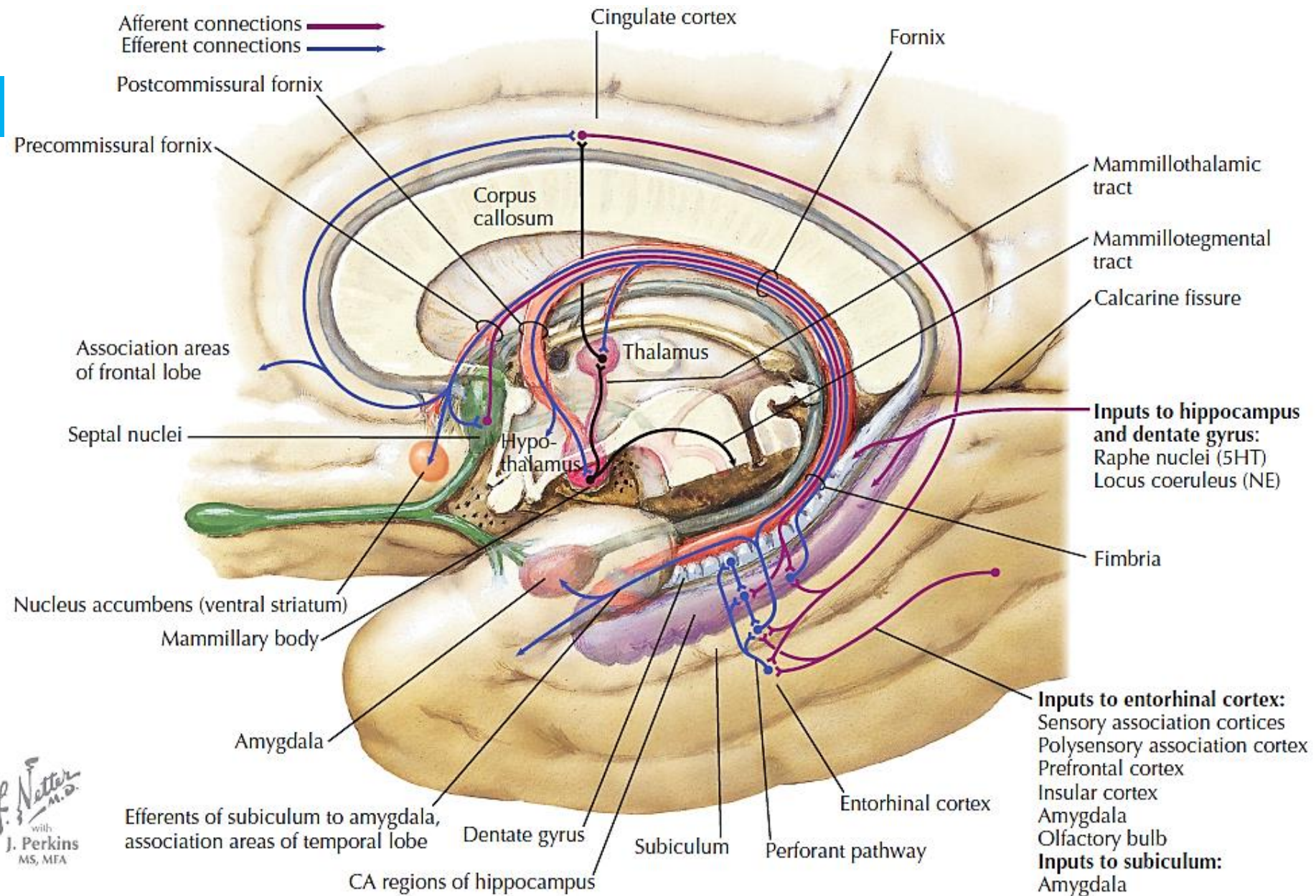
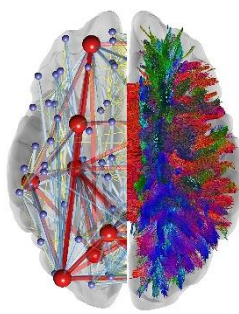
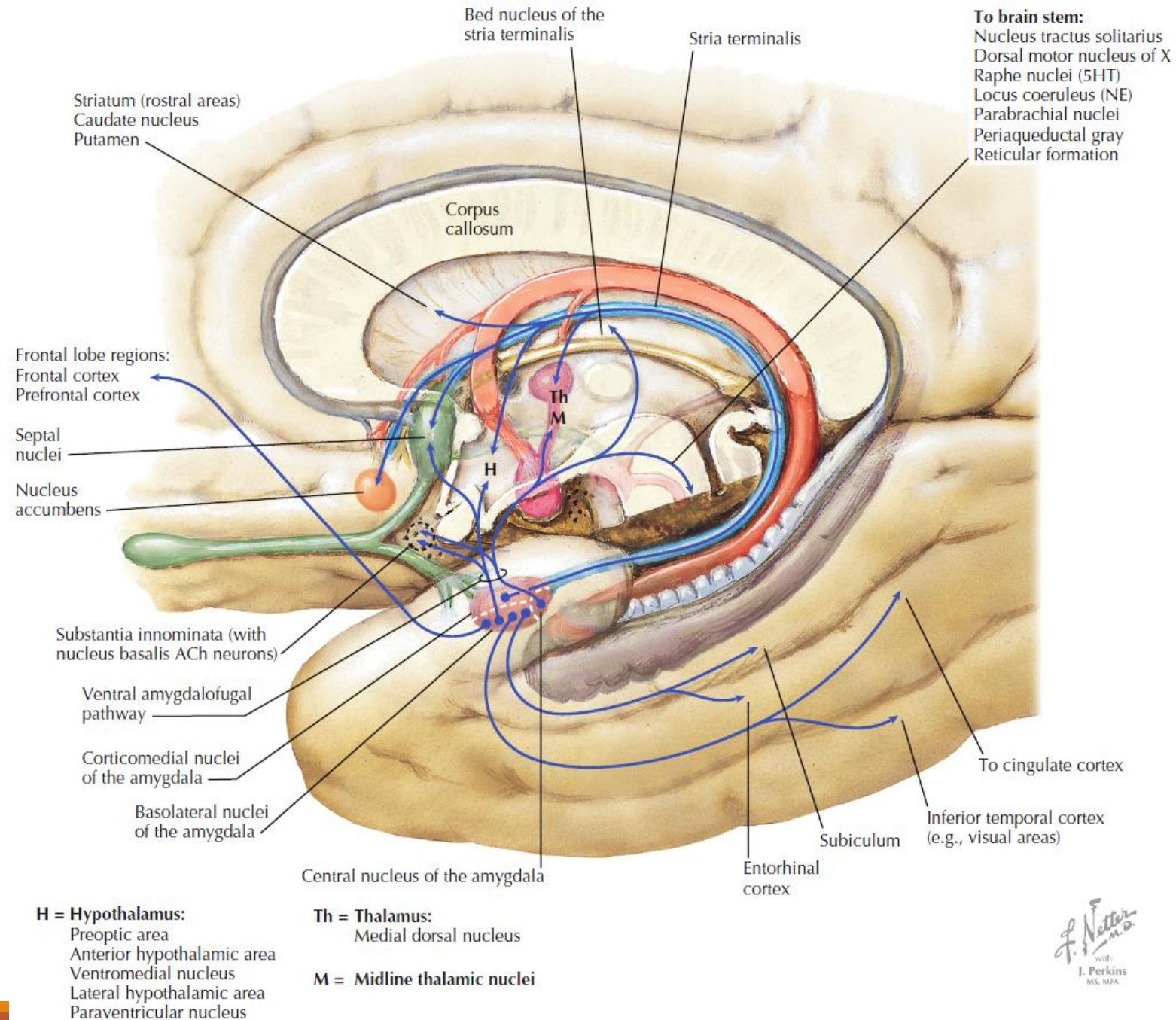


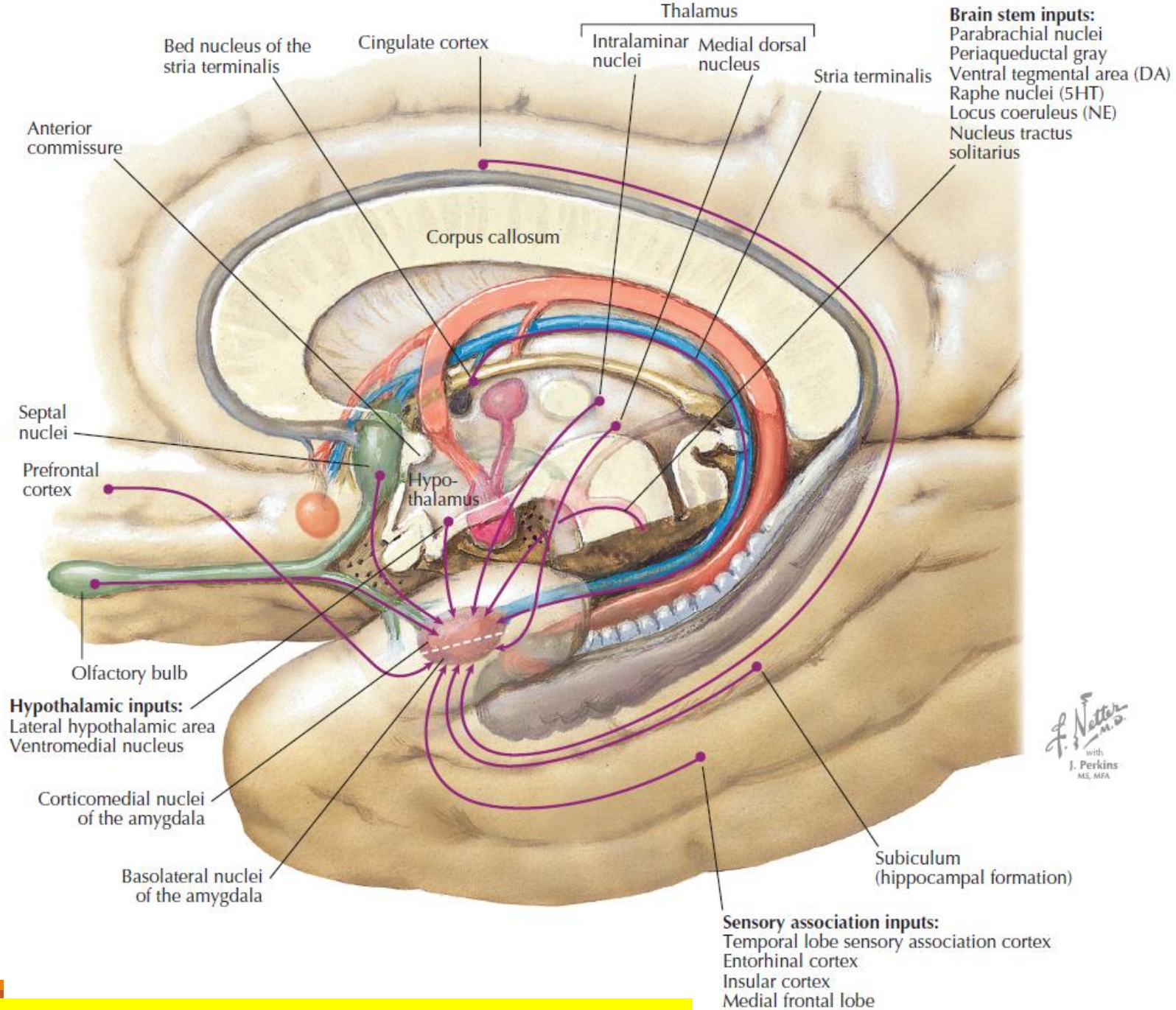
Fig. 16.29 Hippocampal formation, showing the disposition of the various cell fields. Dentate gyrus, pink; hippocampus proper (cornu ammonis), yellow; areas of the subicular complex, green; entorhinal cortex, blue. CA1–CA3, hippocampal cell fields.

Grey matter



Major afferent and efferent connections of the hippocampal formation





Major afferent connections of the amygdala

An example of Anato-mo-physiological perspective

White matter

Association Fibers

Short arcus

Connects 2 gyrus

Long arcus

Uncinate fasciculus

Superior longitudinal Fasciculus

Inferior longitudinal Fasciculus

Cingulate fasciculus

Commissural Fibers

Corpus callosum

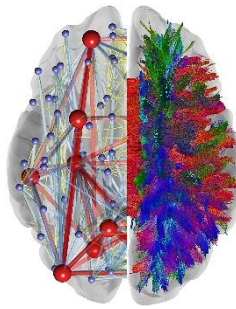
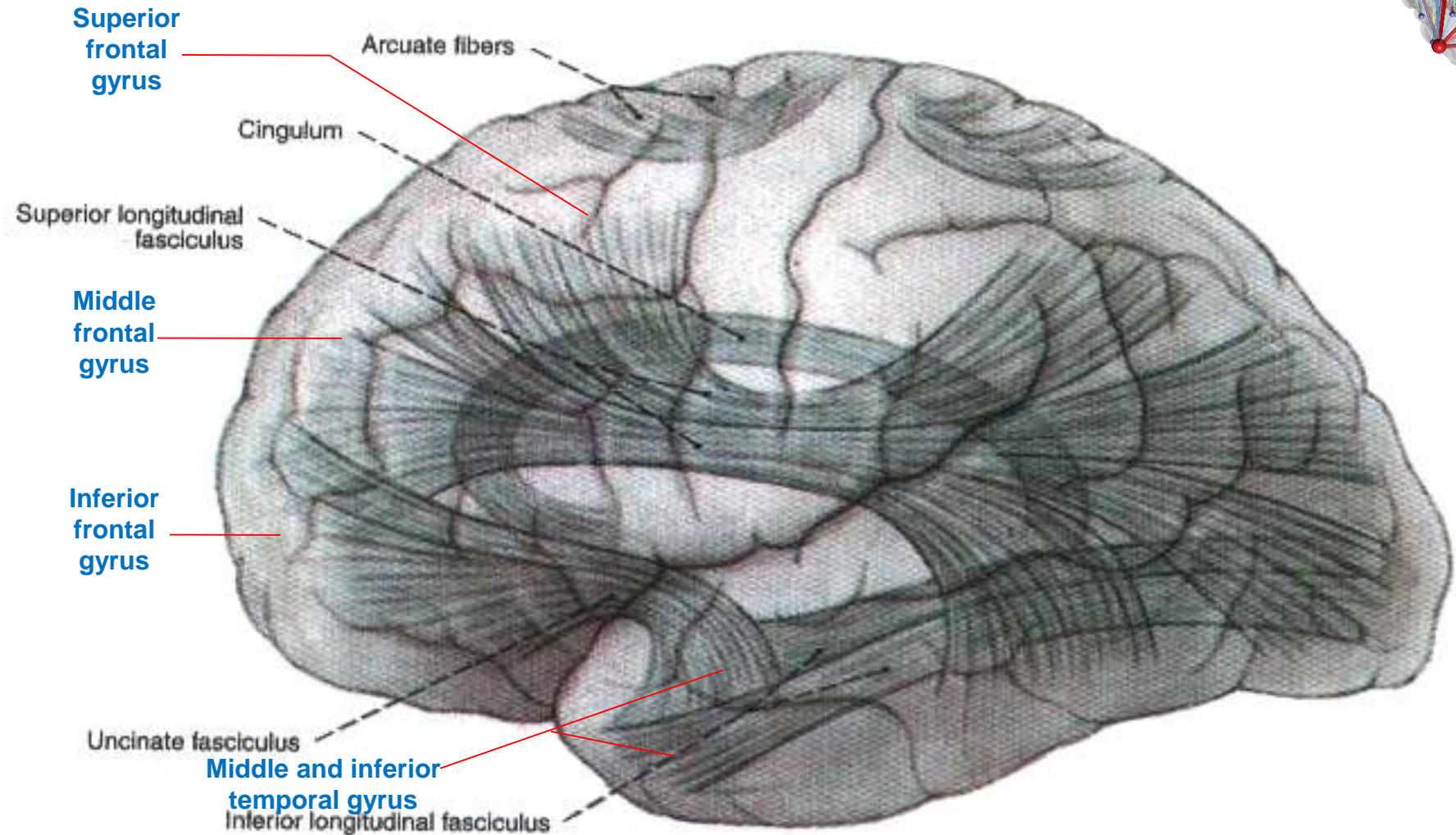
Fornix

Anterior commissure

Posterior commissure

Habenular commissure

Projectional Fibers



White matter

Association Fibers

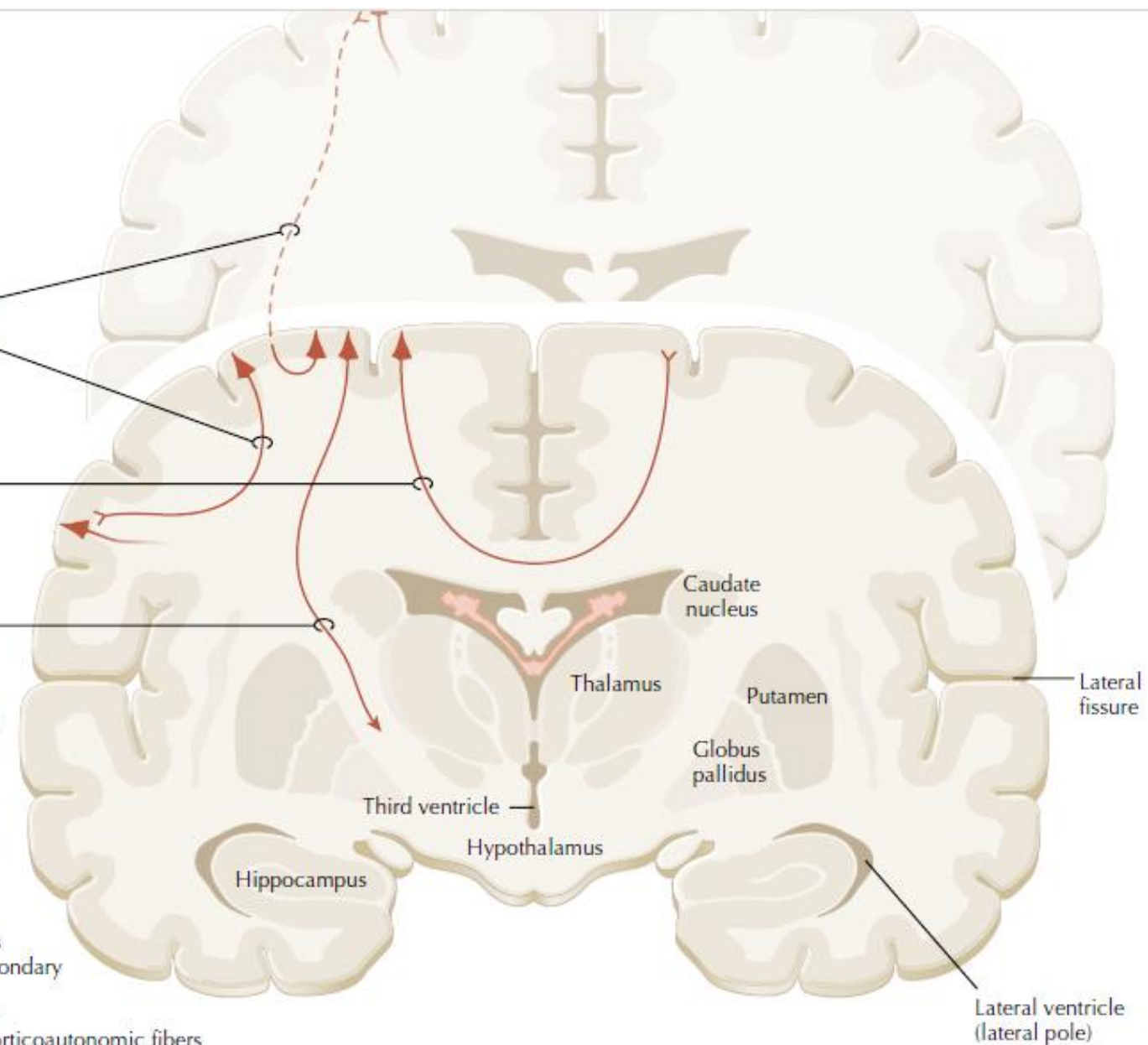
Long - to distant regions of ipsilateral hemisphere
Short - to nearby regions of ipsilateral hemisphere

Commissural Fibers

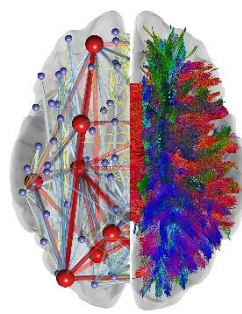
To cortical regions of contralateral hemisphere

Projection Fibers

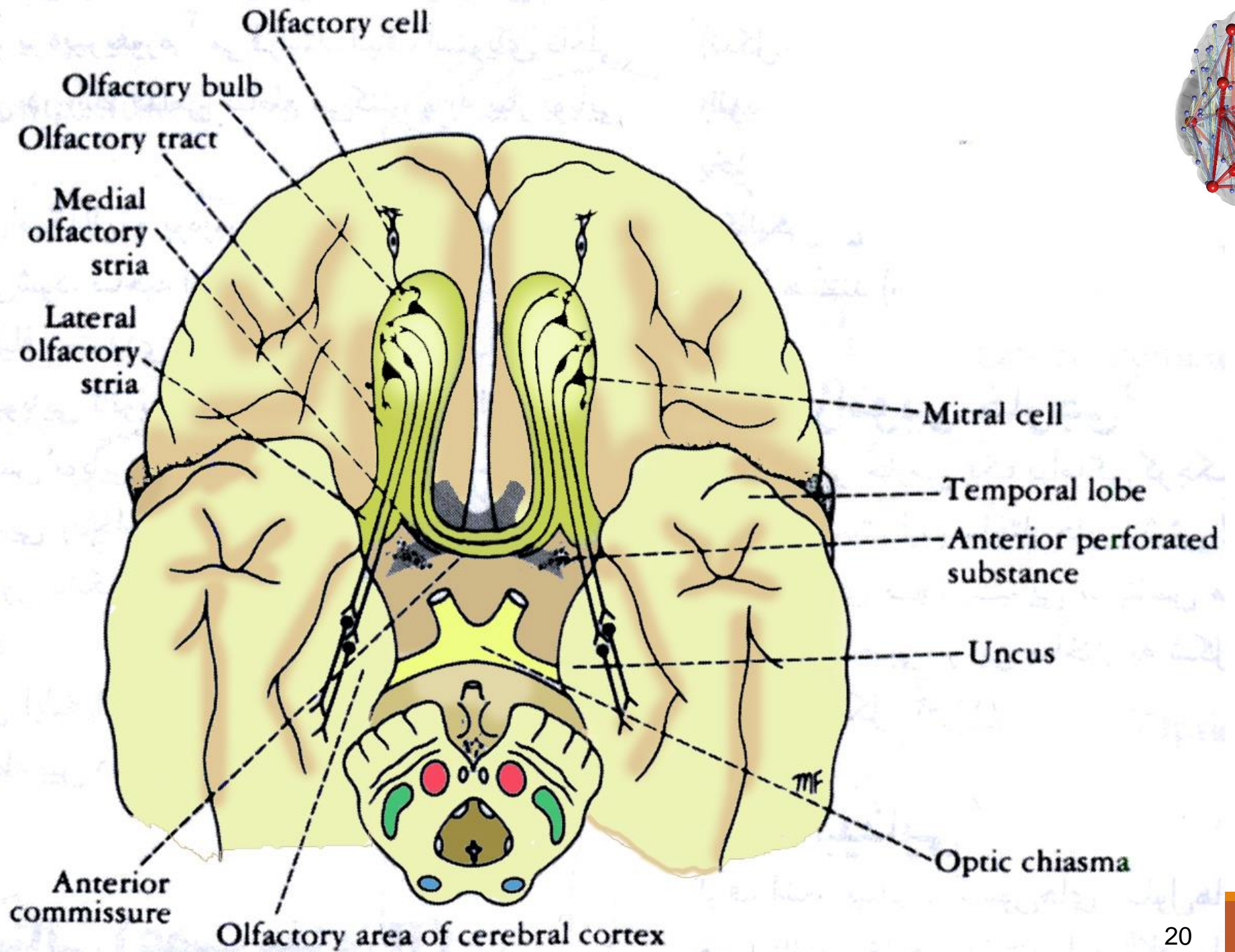
Corticospinal tract
Corticobulbar tract
Corticorubrospinal system
Corticoreticulospinal system
Corticobulbospinal system (polysynaptic)
Corticotectal fibers
Corticopontine fibers (to cerebellum)
Corticostriate fibers (to basal ganglia)
Corticonigral and corticosubthalamic fibers
Corticonuclear fibers (to secondary sensory nuclei)
Corticothalamic projections
Corticohypothalamic and corticoautonomic fibers
Cortico-olivary fibers
Corticolimbic fibers (in subcortical forebrain)



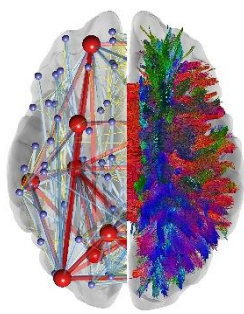
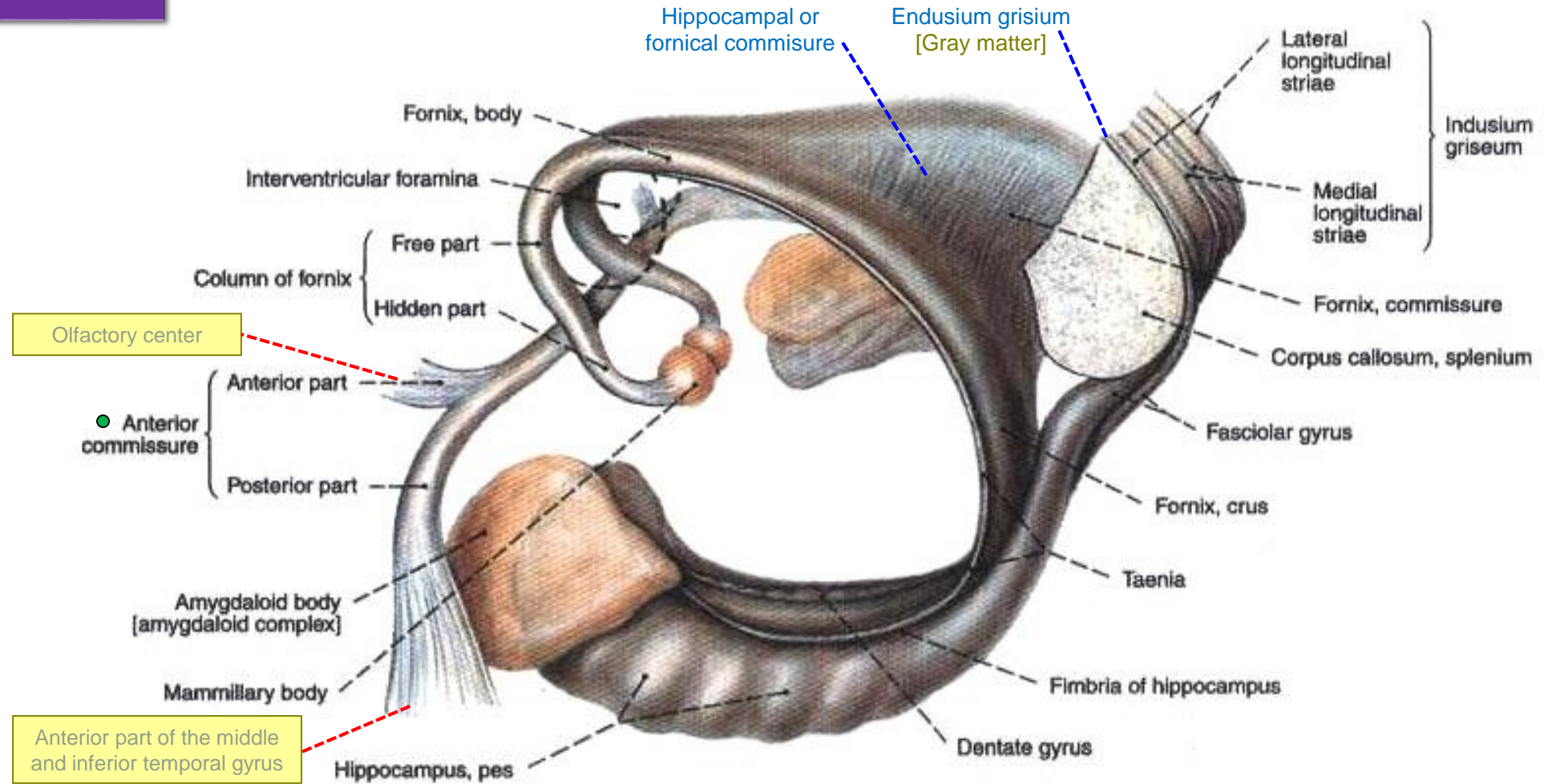
I. Perkins



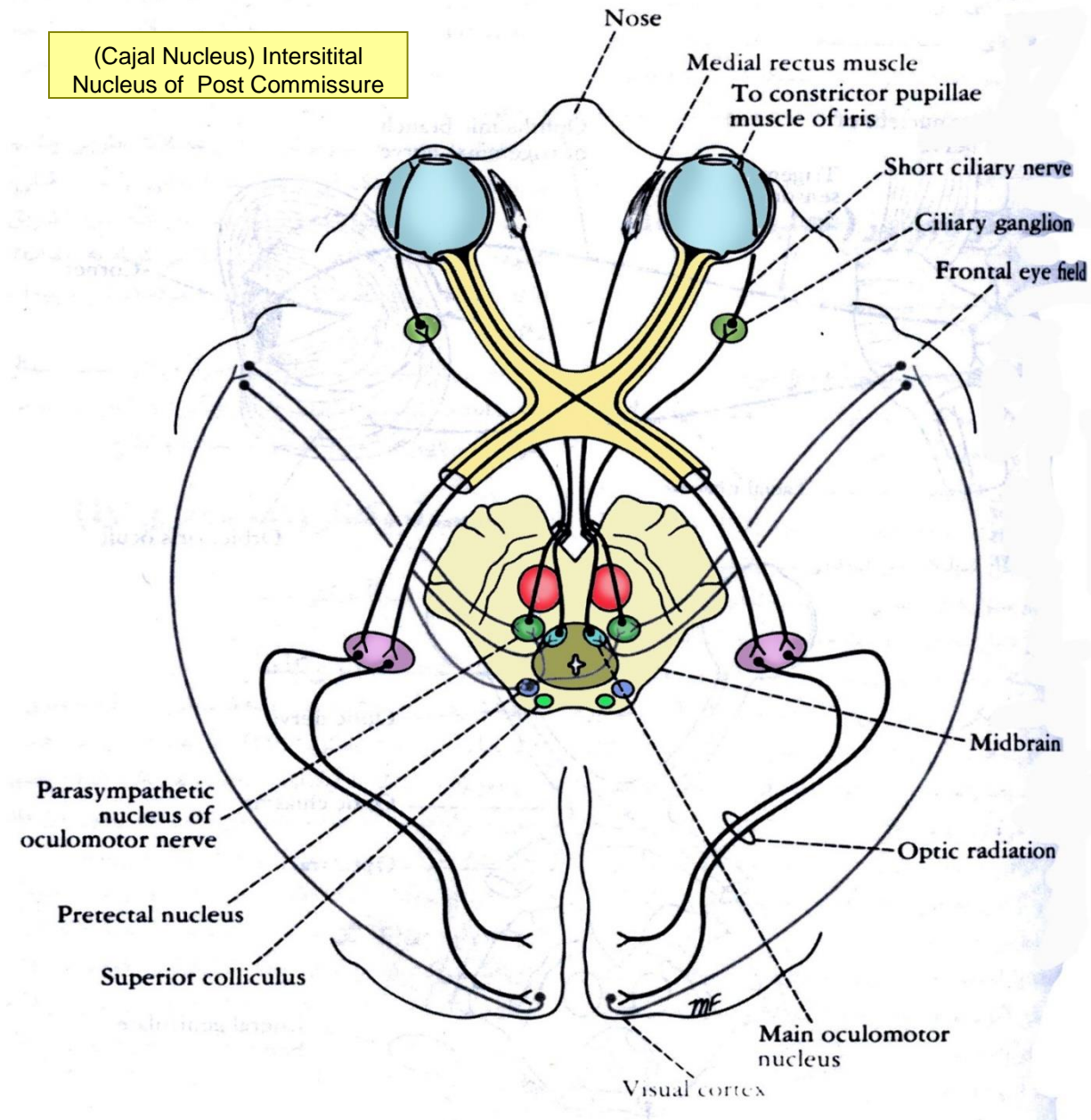
White matter



White matter



White matter



White matter

Association Fibers

Short arcus

Connects 2 gyri

Long arcus

Uncinate fasciculus

Superior longitudinal Fasciculus

Inferior longitudinal Fasciculus

Cingulate fasciculus

Commissural Fibers

Corpus callosum

Fornix

Anterior commissure

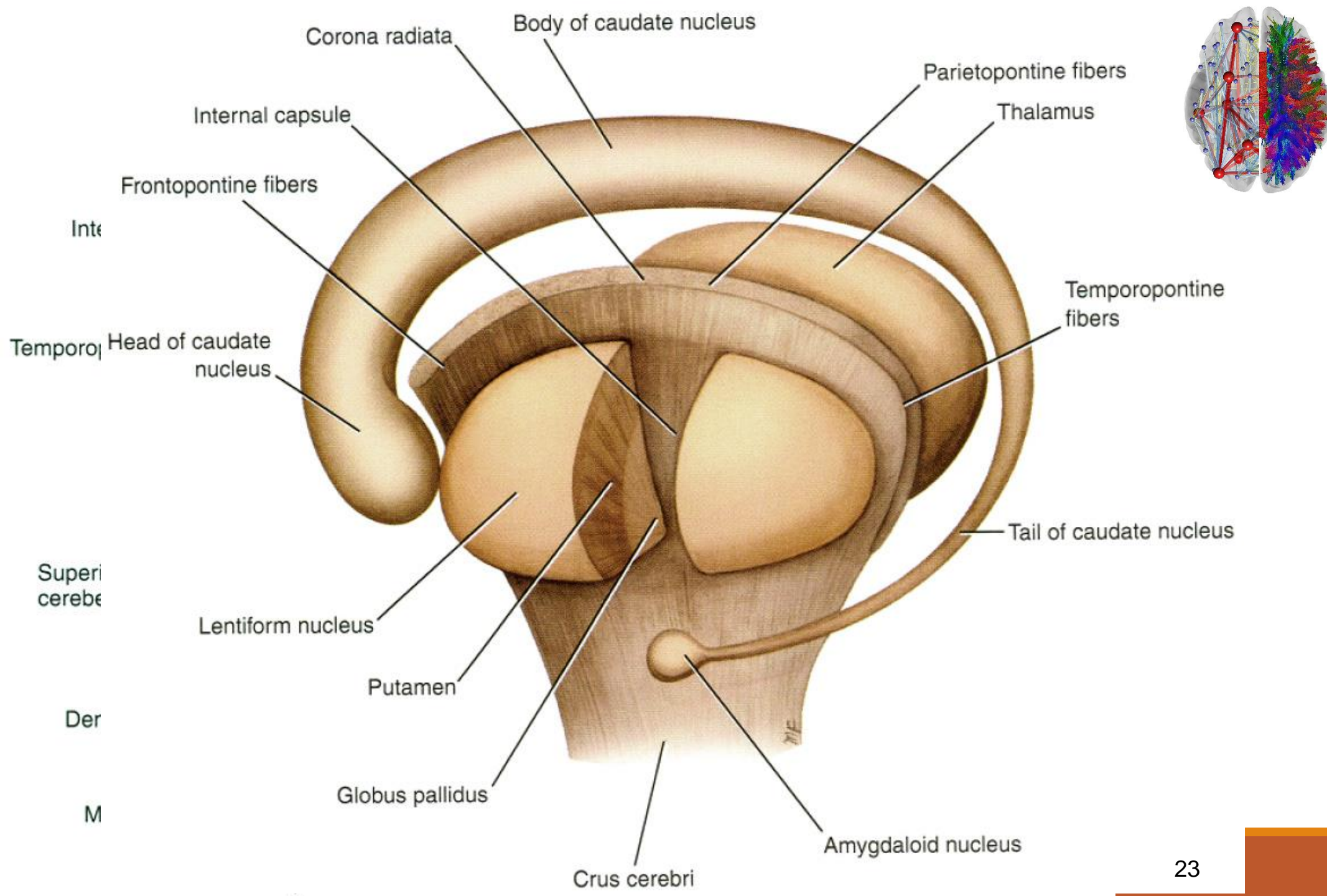
Posterior commissure

Habenular commissure

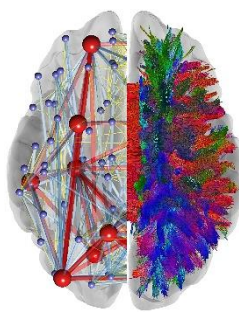
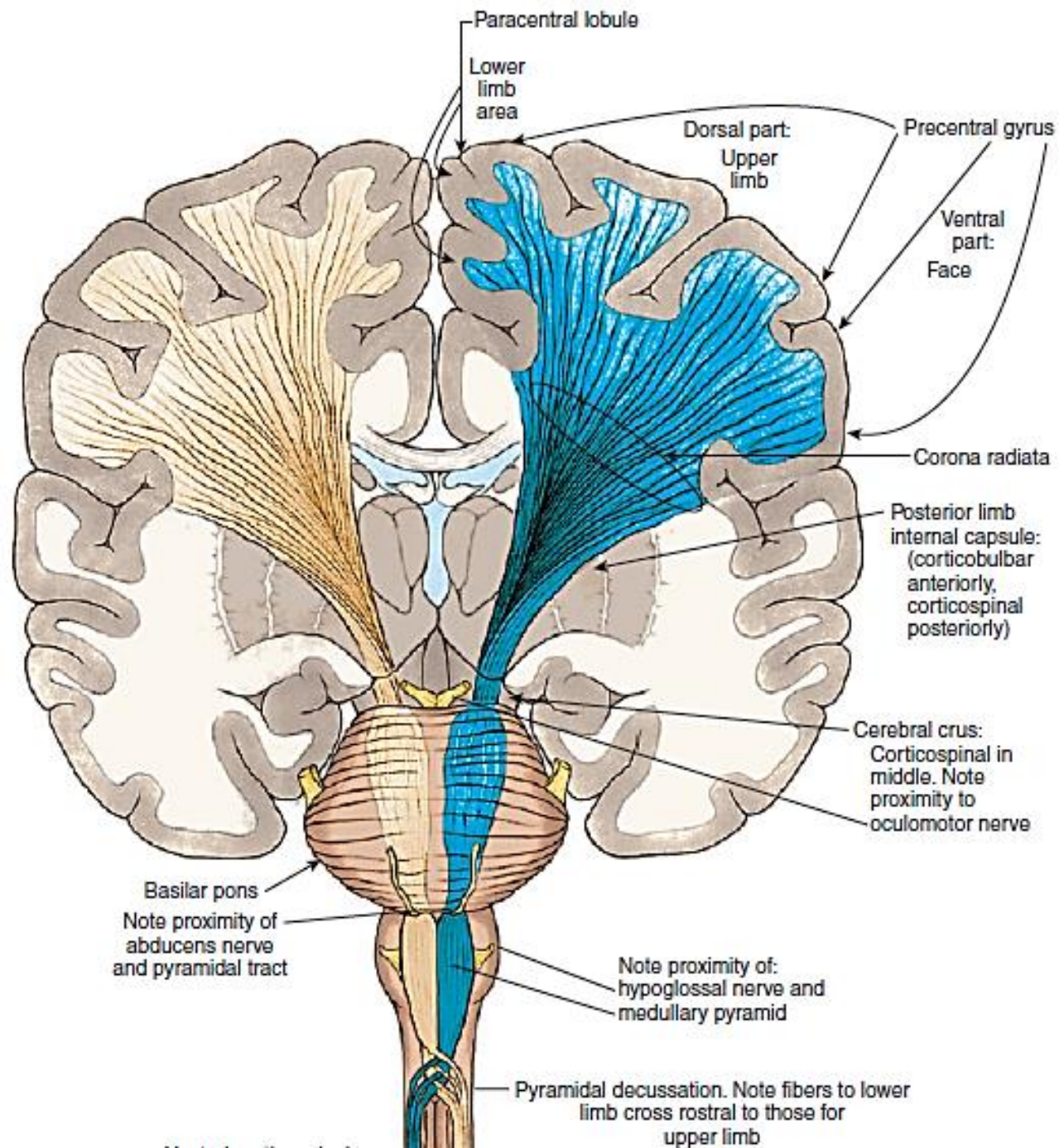
Projectional Fibers

Afferent fibers

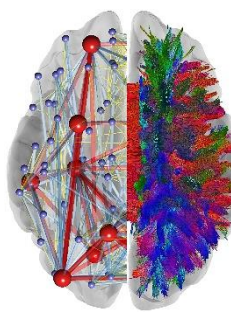
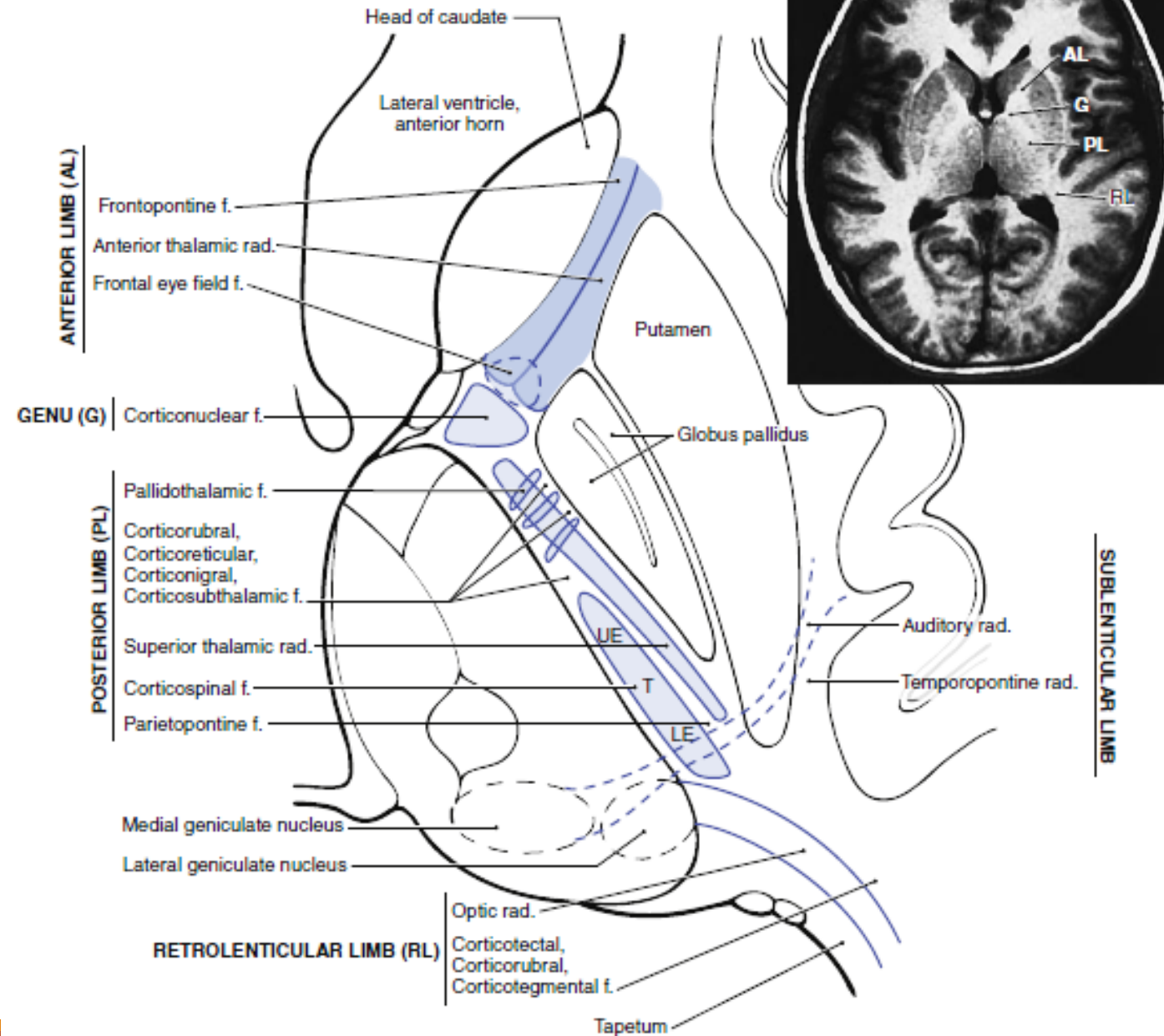
Efferent fibers



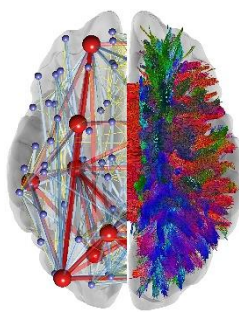
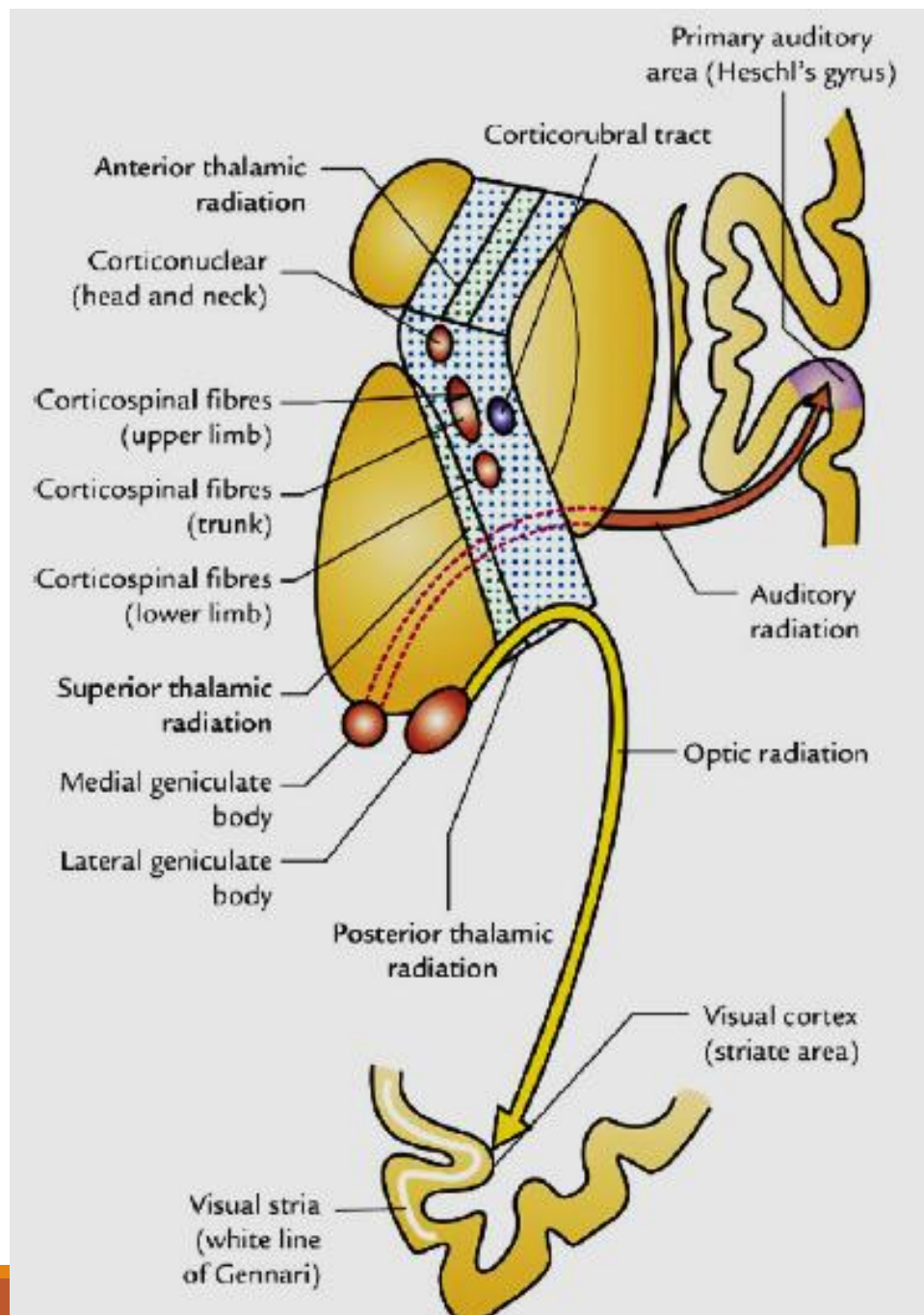
White matter

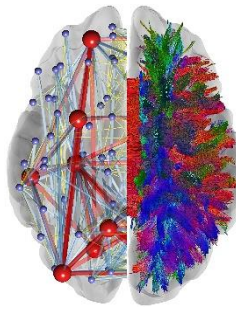


White matter



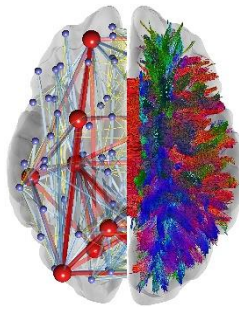
White matter





New concept and theory in neural system Network and connectome

Applications of medical imaging techniques in Anatomical domains



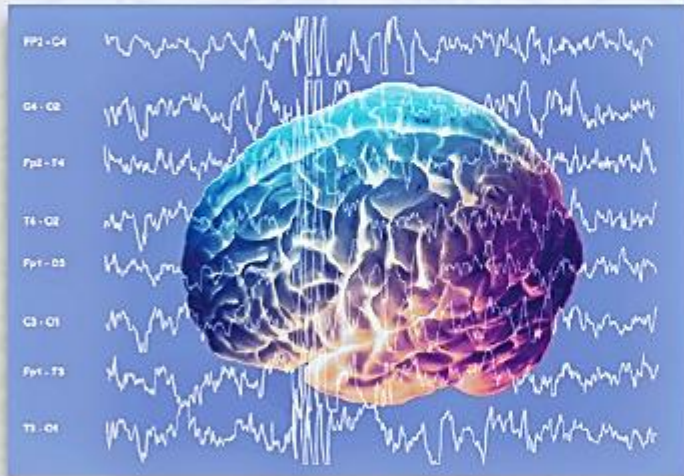
- 1) **Clinical anatomy** (Radiography, Ultrasound, MRI, CT, PET and SPECT);
- 2) **Sectional anatomy** (Ultrasound, MRI, CT);
- 3) **Surface anatomy** (Ultrasound, MRI, CT)
- 4) **Anthropometry and morphometry** (Radiography, MRI, CT);
- 5) **Neuroimaging** (MRI, CT and PET).

MRI techniques used for Neuroimaging to achieve a brain connectome include:

- 1) **Contrast**: for Vascularity (structural level).
- 2) **Diffusion** and SWI: for Microarchitecture (structural level).
- 3) **Perfusion**: for Neo-angiogenesis (functional & structural level).
- 4) **Spectroscopy**: for chemistry substance and metabolites (biochemical level).
- 5) **fMRI**: for function and spatial localization (functional level).

Obtaining a functional brain network in three steps:

STEP 1



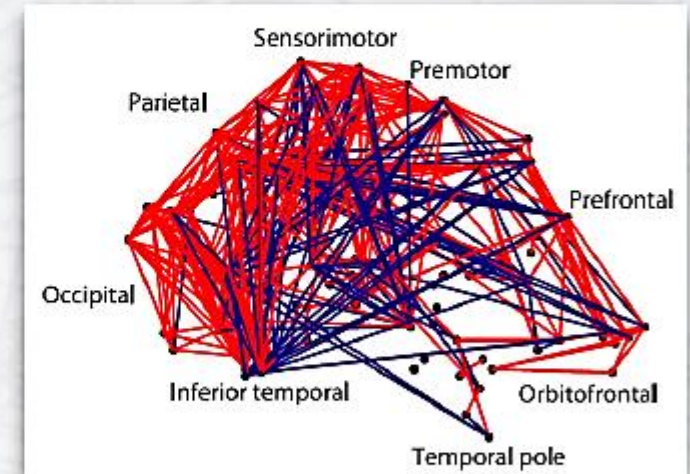
Measuring Brain Activity

STEP 2



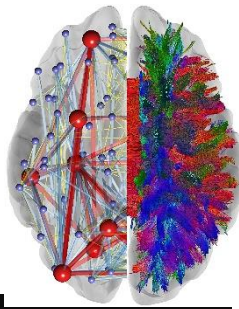
Time Series Analysis &
Network Construction

STEP 3



Network Analysis

Methods for Measuring Brain Activity to Draw the Brain Connectome



- 1) Electroencephalography (EEG)**
- 2) Patch Clamp Electrophysiology (PCE)**
- 3) Magnetoencephalography (MEG)**
- 4) Photobiomodulation (PBM)**
- 5) Magnetic Resonance Imaging (MRI) include Structural, Metabolical and Functional Techniques (DTI, DTT, ASL, MRS, fMRI, etc.)**
- 6) Positron Emission Tomography (PET)**

Imaging modality	Description
Positron emission tomography	Measures regional glucose utilisation, cerebral blood flow (both measures of regional brain activity) and receptor occupancy.
Arterial spin labelling	Cerebral blood flow.
Electroencephalogram	Cerebral electrical activity.
Magnetoencephalography	Measures magnetic fields produced by electrical activity of the brain.
Magnetic resonance spectroscopy	Measures brain concentration of brain metabolites and neurotransmitters.
Structural MRI	Provides high spatial resolution and soft tissue contrasts to measure brain morphometry.
Functional MRI	Measures brain activity by detecting changes in blood oxygenation and flow during rest or an evoked task.
Diffusion tensor imaging	Assesses the microstructure of white matter and anatomical connectivity and integrity.

❖ THE HUMAN CONNECTOME PROJECT

- ❑ Launched in 2012, with an NIH-sponsored budget of approximately \$ 40 million, the Human Connectome Project aims to create a wiring diagram of the human brain.
- ❑ Currently, the Human Connectome Project is gathering data on 1200 individuals using a combination of MRI modalities from high resolution 3T and 7T magnetic resonance scanners.
- ❑ Despite being in its early stages, this project has already yielded some interesting insights that point to the potential impact of this dataset on our understanding of the human brain and behavior.
- ❑ demonstrated that certain connectivity patterns such as cognition, memory, years of education, substance use and aggression (Smith et al. 2015).
- ❑ HCP data provided a revised map of cortical regions which reclassified the traditional Brodmann's areas based on functional connectivity, degree of myelination, cortical thickness, and cross-correlations with previously published cortical parcellation schemes.
- ❑ This landmark effort increased the number of cortical regions from Brodmann's 47 areas to 180 distinct cortical parcellations.

❑ Connectome has since come to reflect a more global systematic account of connections, from local circuits to networks forming entire nervous systems (Bota et al. 2015).

❑ Connectomes are connection matrices that can be directed or undirected, **binary** or **weighted** (Bota et al. 2015).

Binary connections only report the absence or presence of a connection.

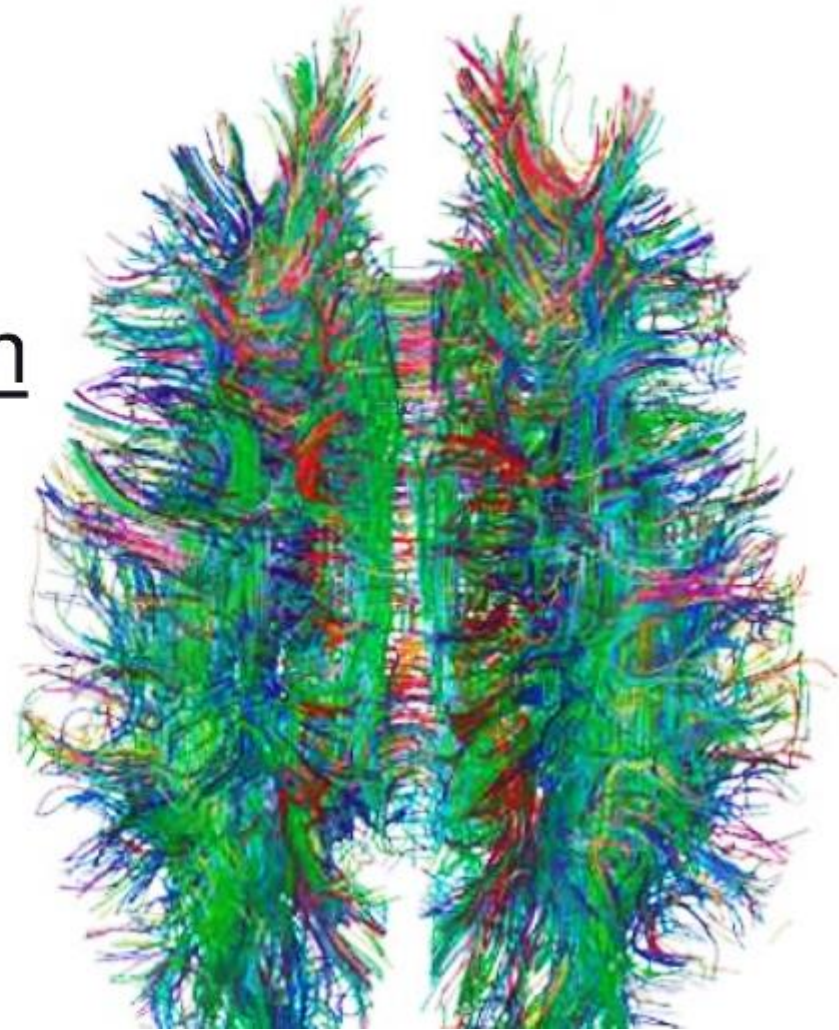
Weighted links can also show the strength of a connection.

❑ Perturbations and distortion of the normal human connectome have been named ***connectopathies*** (Lichtman and Sanes 2008).

The Brain - A complex network

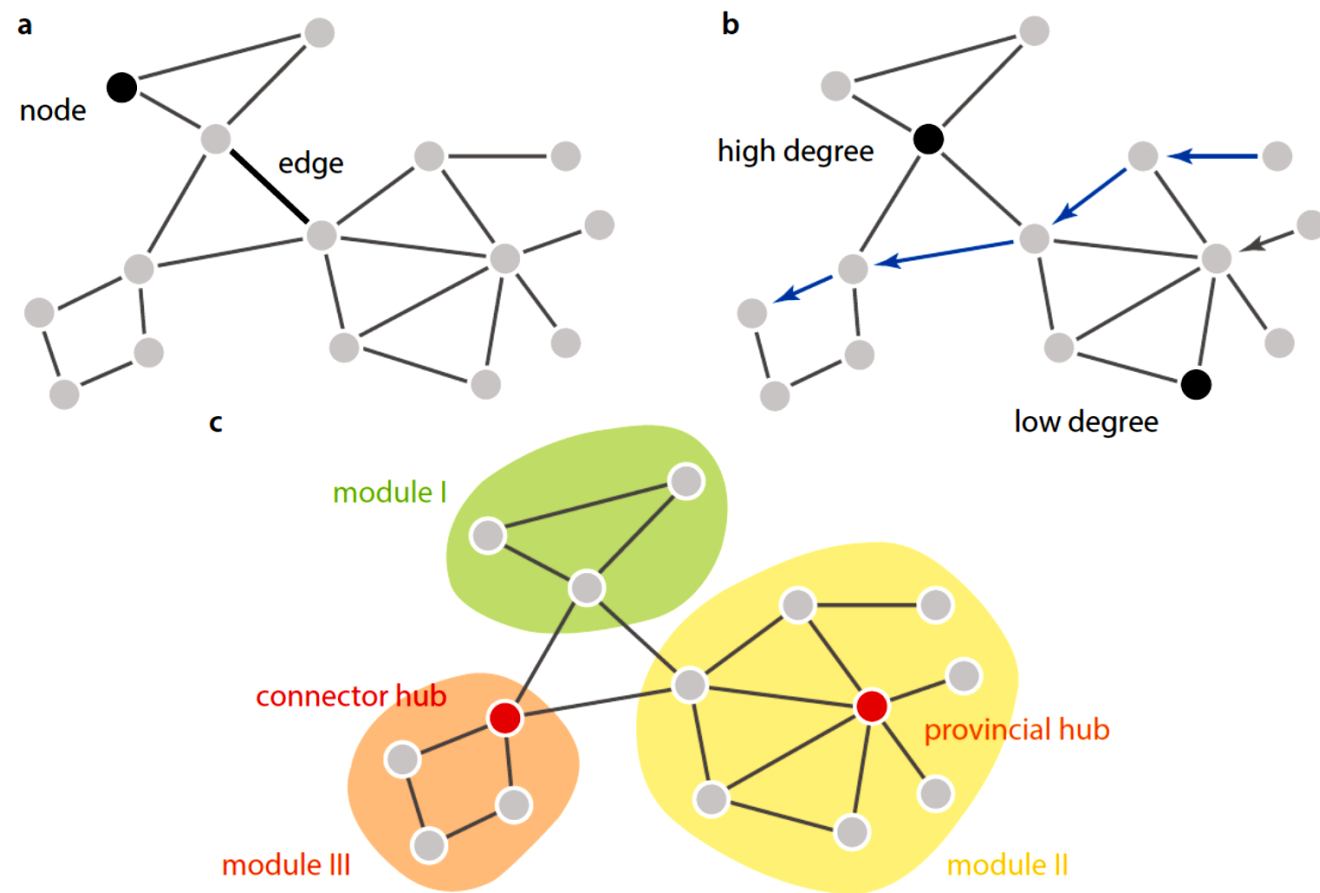
Brain organization :
segregation and integration

There is segregation and integration
in the brain at the same time.



The brain's anatomical and functional organization can be approached mathematically in terms of graphs or networks comprising:

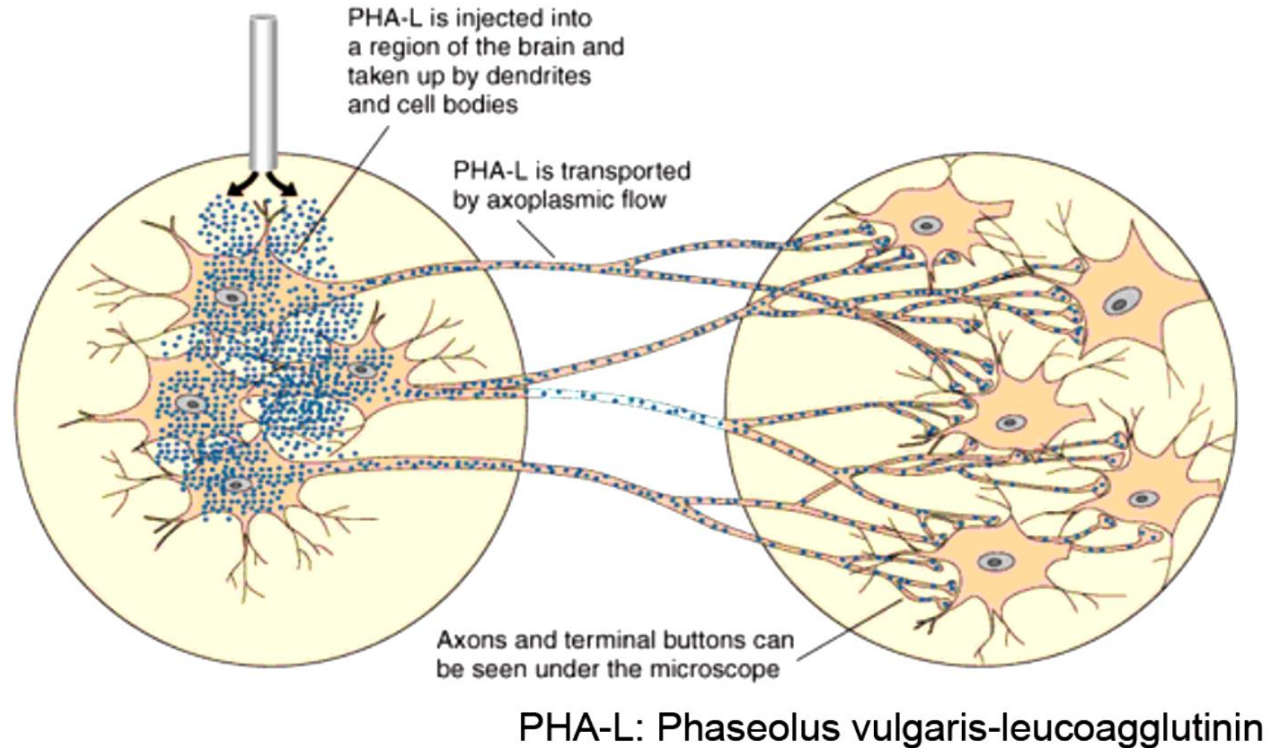
- 1) nodes** (neurons and/or brain regions) and;
- 2) edges** (synaptic connections or interregional pathways).



Basic network attributes. **a** Brain networks can be described as graphs comprising a collection of nodes (describing neurons/brain regions) and a collection of edges (describing structural connections or functional relationships). A module includes a subset of nodes of the network that show a relatively high level of within-module connectivity and a relatively low level of intermodule connectivity. “Provincial hubs” are high-degree nodes that primarily connect to nodes in the same module. “Connector hubs” are high-degree nodes that show a diverse connectivity profile by connecting to several different modules within the network.

How can the fiber tract network structure be examined?

Tract tracing with dyes*



Invasive approaches to map brain connections have existed for many decades using techniques such as:

1- **At the microscale:**

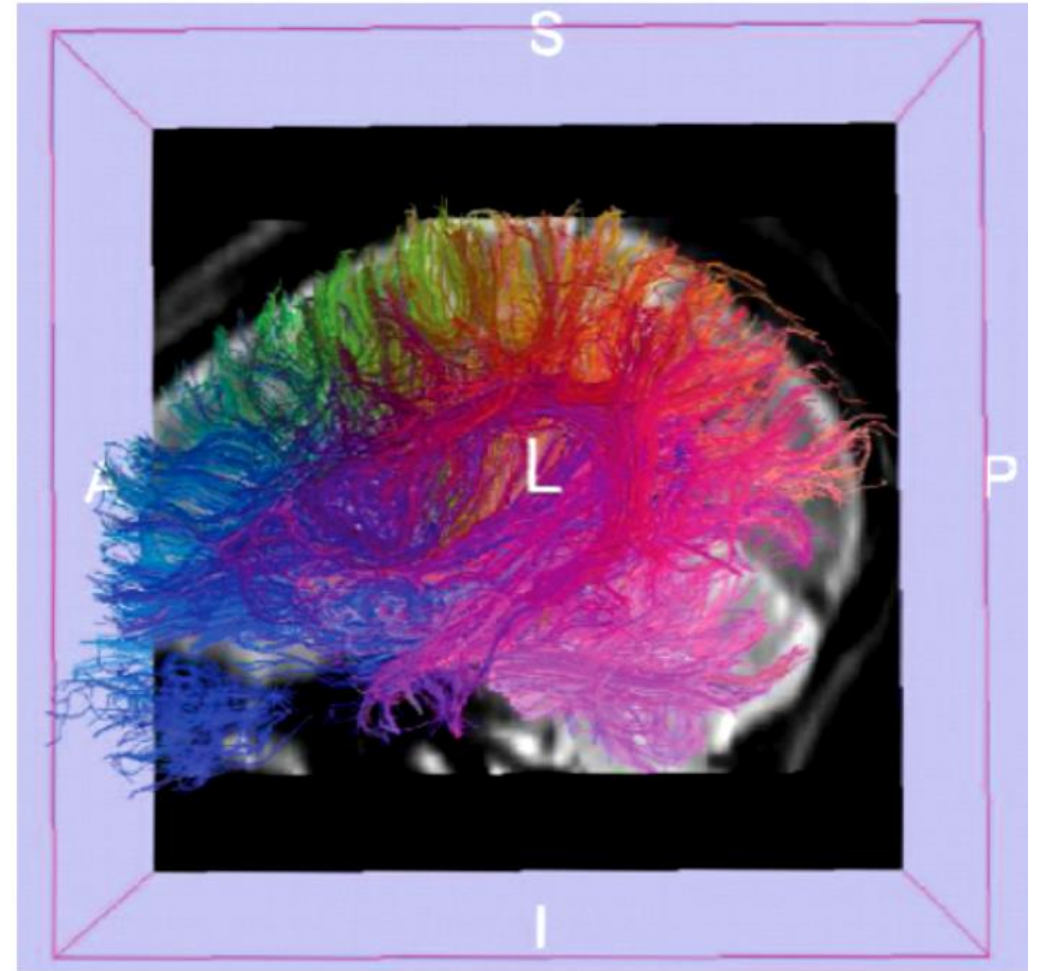
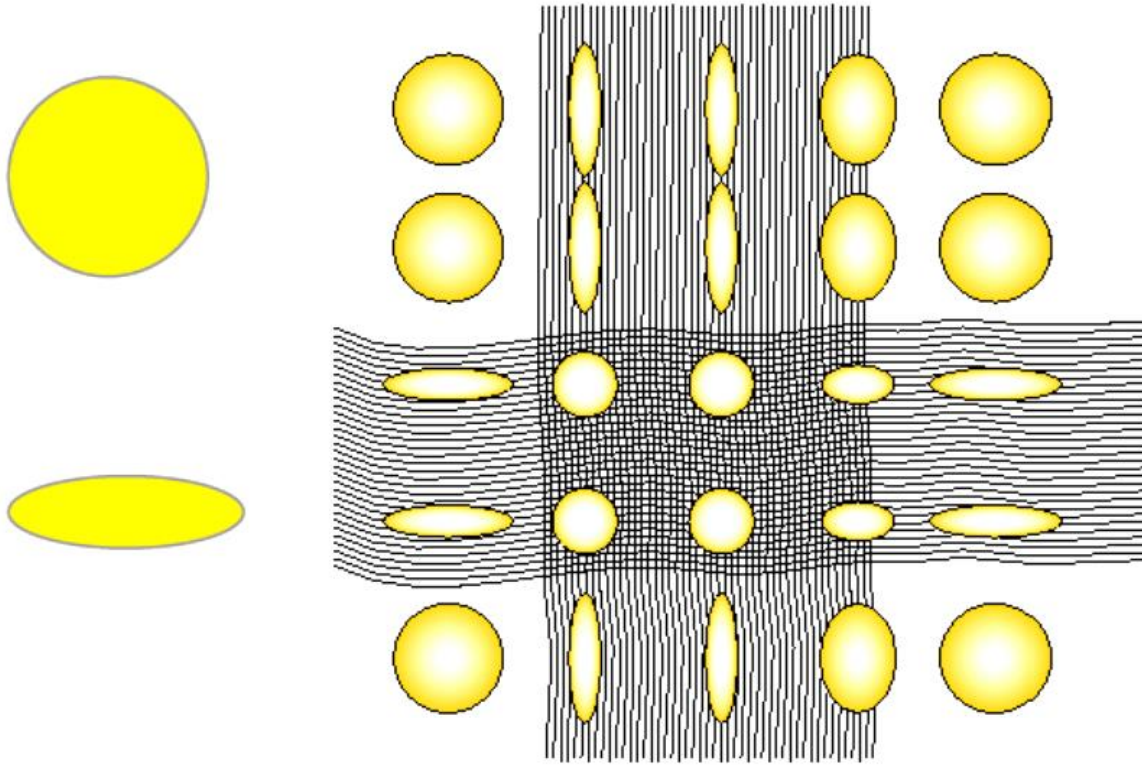
- a) histological staining;
- b) serial electron microscopy;
- c) 3D fluorescence imaging.

2- **At the mesoscale**, chemical tracers for mapping longer-range white matter connections: fluorochromes, enzymes, metals, particles, and radioisotopes.

Anterograde: soma → synapse
Retrograde: soma ← synapse

* Horseradish peroxidase (HRP) method; fluorescent microspheres; Phaseolus vulgaris-leucoagglutinin (PHA-L) method; Fluoro-Gold; Cholera B-toxin; Dil; tritiated amino acids

Diffusion Tensor Imaging (DTI)

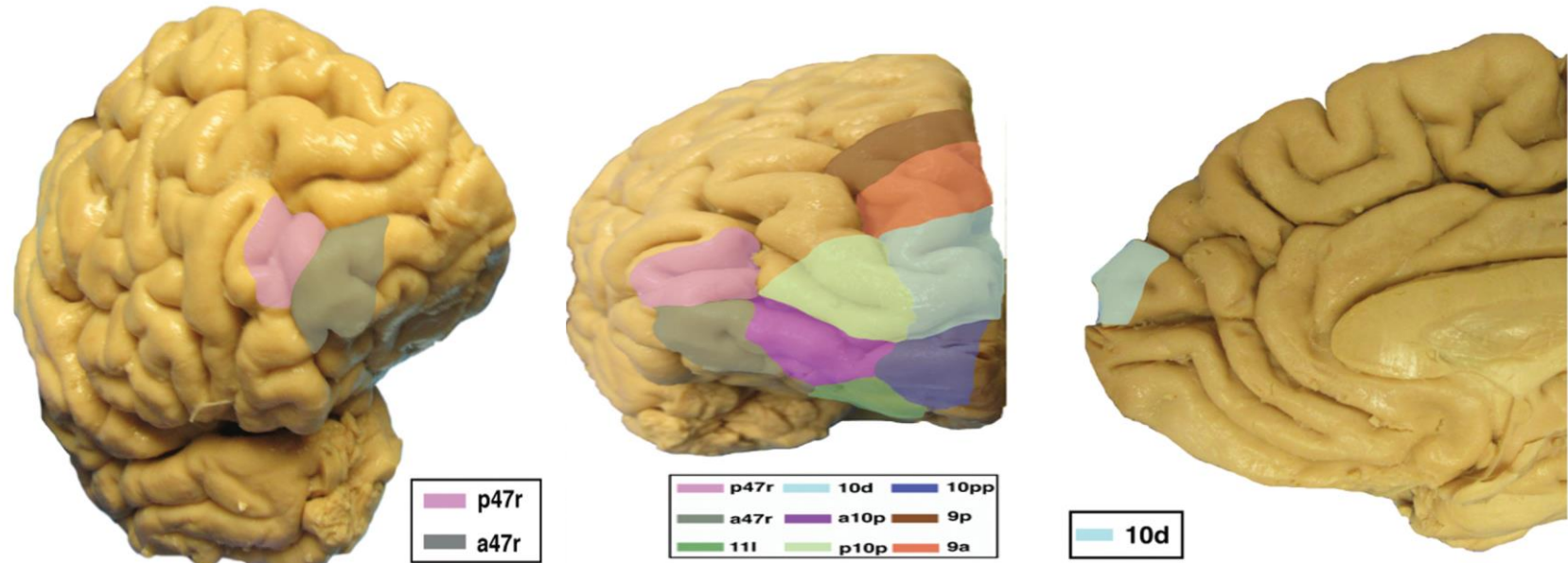


Reorganize of Brodmann's area in neuroimaging classification

- Frontal pole: area 10 subregions
- Superior frontal gyrus (SFG): anterior: area 9 subregions, posterior: area 8 subregions
- Middle frontal gyrus (MFG): anterior: areas 46 and 9-46 hybrid subregions, posterior: area 8 subregions
- Inferior frontal sulcus: IFS subregions
- inferior frontal gyrus (IFG): anterior: area 47 subregions, posterior: areas 44 and 45

FRONTAL POLAR REGION

- ✓ The four subregions of polar area 10 are located on the more anterior and medial parts of the pole.
- ✓ The rostral parts of area 47 make up the anterior parts of the IFG and form the anterior boundary of the IFS.



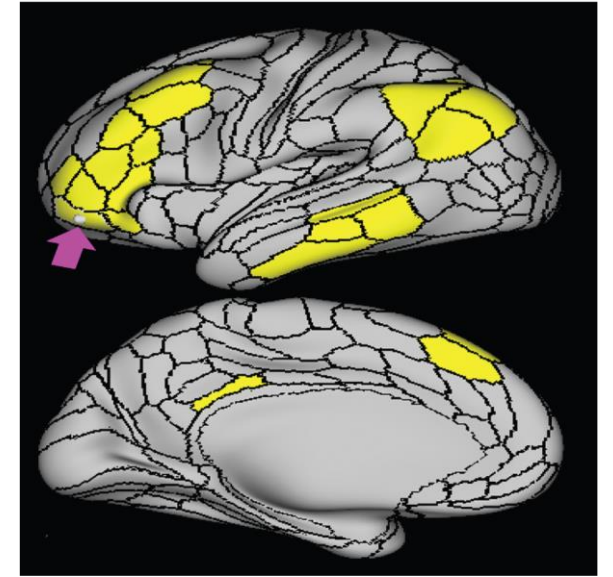
The parcellations that comprise the frontal polar region include 10pp, 10d, p10p, a10p, p47r, and a47r.

Area a47r:

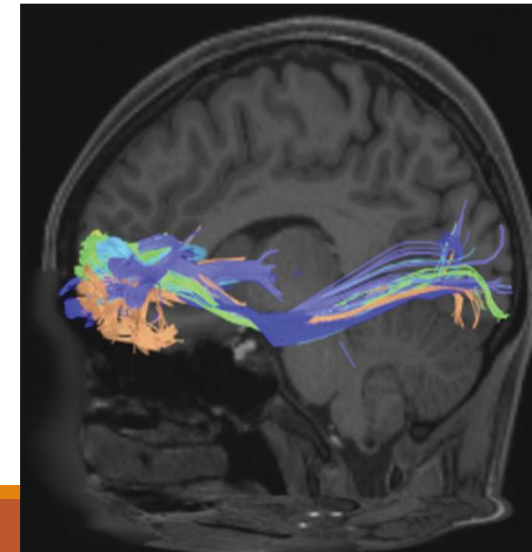
Area a47r (anterior 47 rostral) is a j-shaped area located at the anterior inferior portion of the pars orbitalis of the IFG.

What is its Functional Connectivity?

Area a47r demonstrates functional connectivity to areas p47r, 8C, 8av 8BL, 8BM, i6-8, a9-46v, and p9-46v in the dorsolateral frontal lobe, areas IFSa, IFSp, 47l, and 45 in the IFG regions, areas IP1, IP2, PGi, PGs, and PFm in the **inferior parietal lobule**, areas TE1m, TE1p, TE2a, and STSv in the **lateral temporal lobe**, and area d23ab in the **posterior cingulate region**.



Tracks include 10pp (dark blue), 10d (light blue), a10p (pink), p10p (yellow), a47r (gray), and p47r (light pink).



Medial Frontal Lobe and Cingulate Gyrus

medial frontal and anterior cingulate regions with the orbitofrontal cortices not only due to their **anatomic** proximity, but also due to the common **functional** association of many of these areas with limbic and emotional function.

ANTERIOR CINGULATE REGIONS

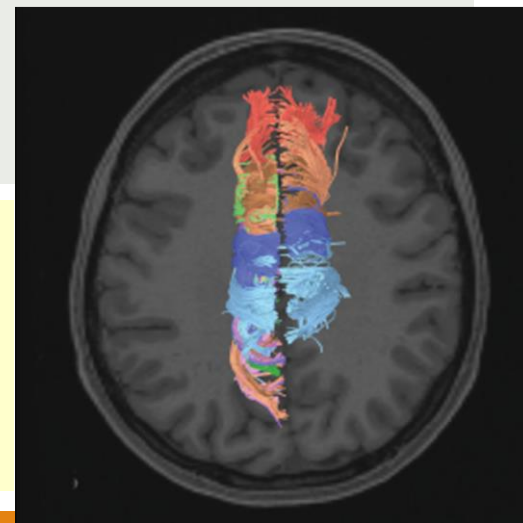
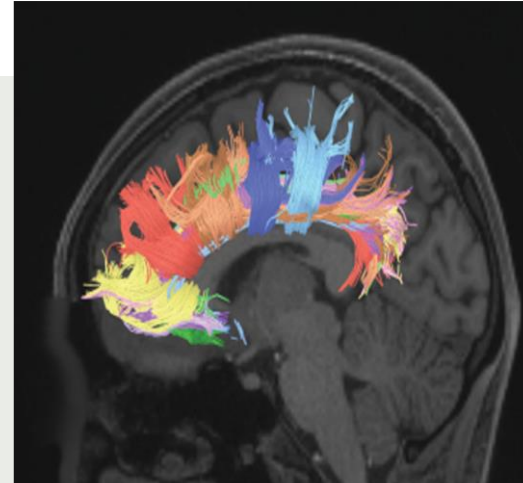
Brodmann divided it into 6 areas (areas 23 24, 25, 31, 32, and 33), but currently cingulate gyrus divides into 21 distinct regions:

The anterior portion contains 13 of these:

- ❑ 6 regions as part of area 24,
- ❑ 5 regions as part of area 32,
- ❑ 1 region each for areas 25 and 33.

structural connectivity of anterior cingulate parcellations.

Tracks include 33pr (pink), 24dd (light blue), 24dv (dark blue), p24pr (gray), a24pr (light green), p24 (pink), a24 (dark green), p32pr (orange), a32pr (green), d32 (red), p32 (yellow), s32 (gray), and 25 (light blue).



Whole of cingulate gyrus (Ant. & Post.) have essentially **3 parallel, C-shaped rows** of areas which follow the shape of the anterior cingulate from posterior to anterior, bending inferiorly to reach the subcallosal region:

- 1) Immediately adjacent to the corpus callosum, in the depths of the callosal sulcus, is area 33prime, which represents the **inner row**.
- 2) The **middle row** comprises area 24 subregions which extend superiorly in their posterior aspect into the paracentral lobule.
- 3) The **outer row** comprises area 32 subregions which make up the superior border of the anterior cingulate gyrus and portions of the cingulate sulcus.

Middle Cingulate Gyrus and the Cingulum Bundle

The cingulum bundle is the white matter pathway linking the anterior and posterior cingulate components of the DMN.

The main 3 components of the DMN are:

- 1) the anterior cingulate gyrus and adjacent frontal lobe,
- 2) the PCC and retrosplenial cortex (RSC),
- 3) the lateral parietal lobes.

Functional members of the DMN include the following parcellations:

Anterior cingulate regions: a24, p24, d32, 9M, 10r, 10v

Posterior cingulate regions: 31a, 31pv, 31pd, v23ab, d23ab, 23d, RSC, 7m, POS1, POS2

Lateral parietal lobe regions: PFm, PGs, PGi

The middle cingulate is primarily comprised of the “prime regions,” ie, a24pr, p24pr, a32pr, and p32pr. Our analysis suggests that these middle cingulate areas are physically highly interconnected with areas of the PCC.

Functional Segregation Within the DMN of posterior cingulate regions

dorsal PCC: coordinates visuospatial body orientation.

ventral PCC: is involved in self-reflection, self-monitoring, and other internally motivated states.

Dorsal PCC (31a, 23c, 23d, d23ab):

These regions connect to other PCC members and to the middle cingulate parcellations. They **do not connect to the anterior DMN** members.

Ventral PCC (31pv, 31pd, v23ab, RSC):

These regions **connect to the anterior DMN members** (involve in sense of motion), the PCC members and also to the middle cingulate parcellations, making them more densely interconnected.