Corso Video EEG LICE, Catania 2021

Anatomia funzionale del lobo frontale

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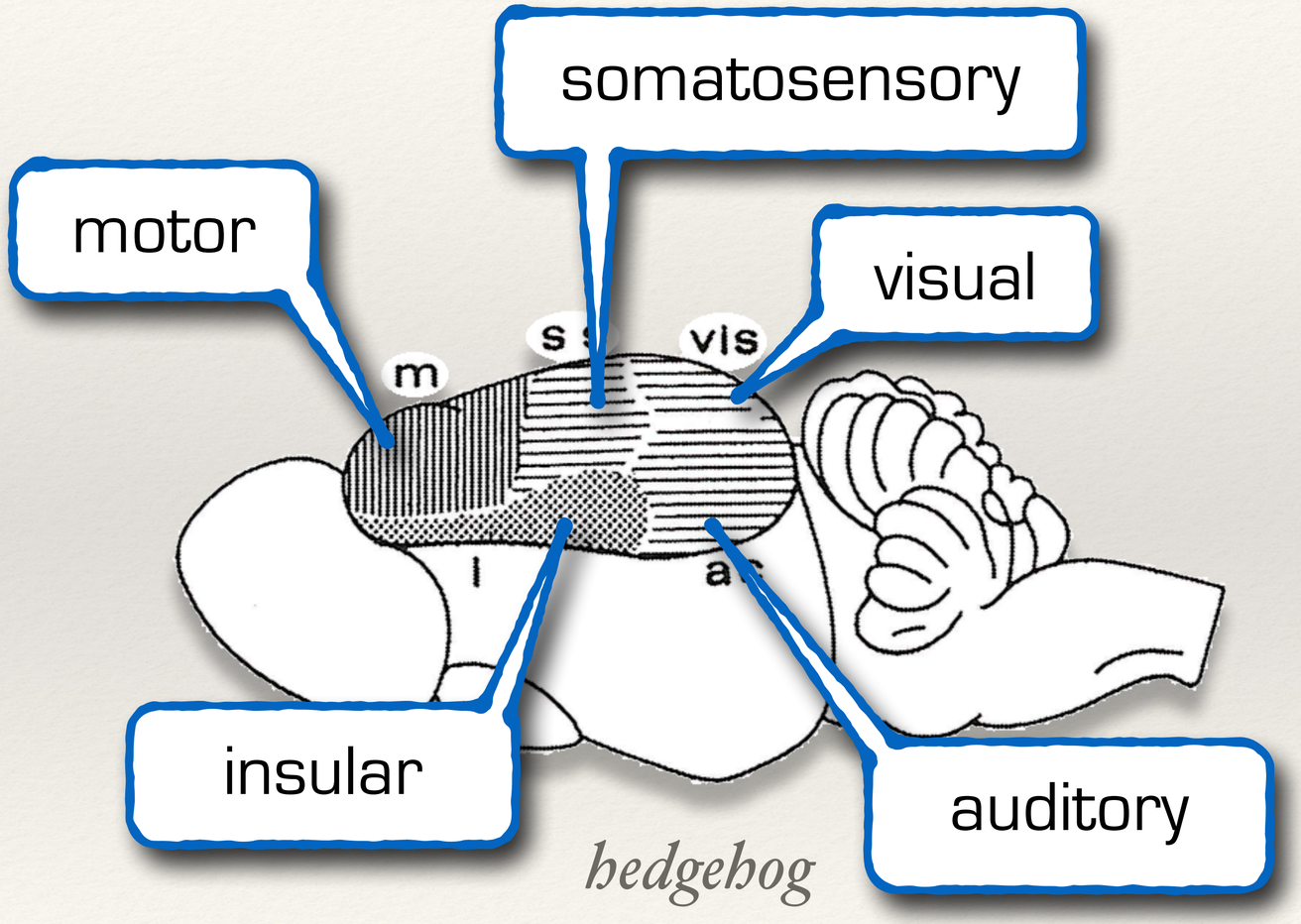
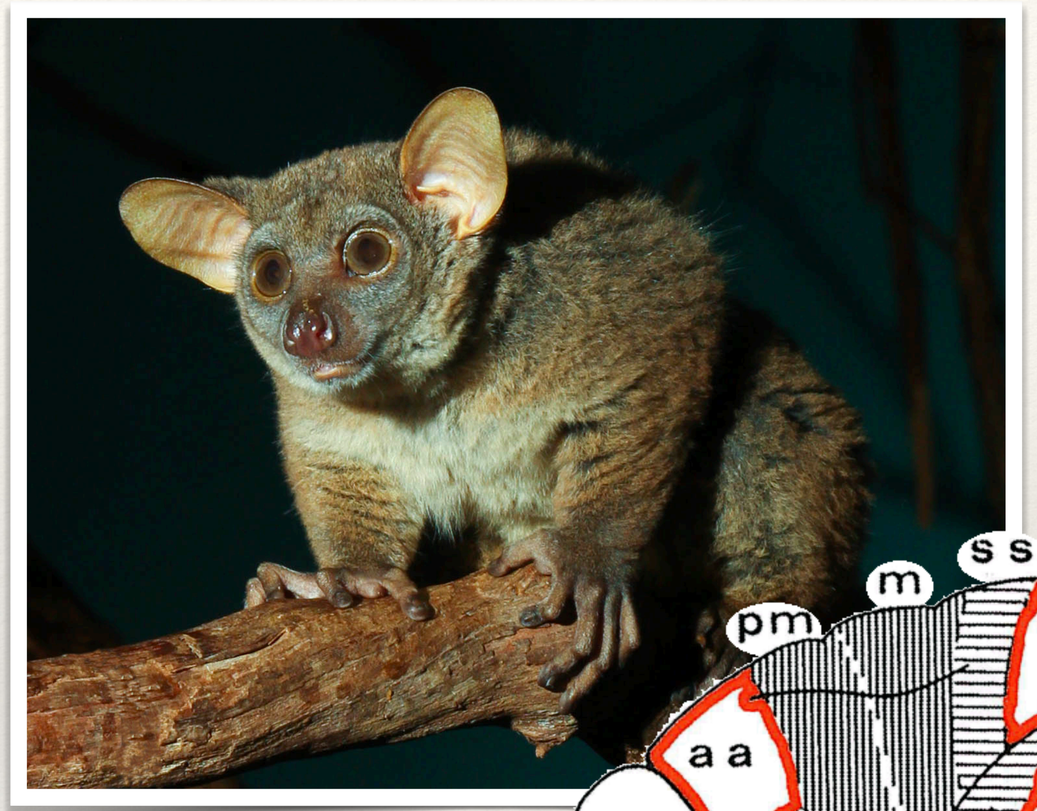
il lobo frontale

il roditore: una “macchina” sensori-motoria

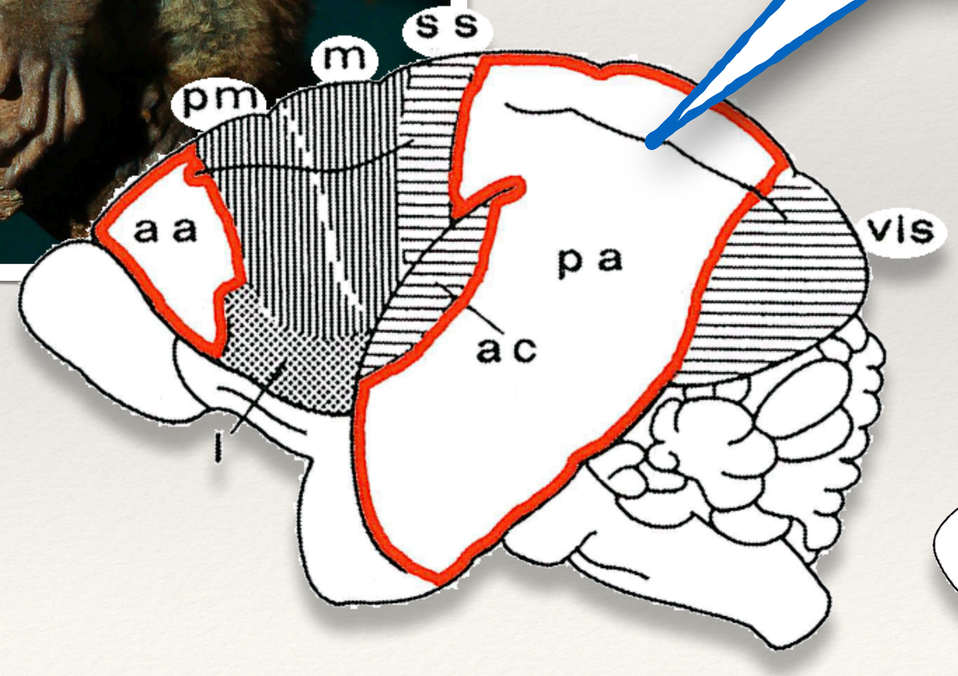


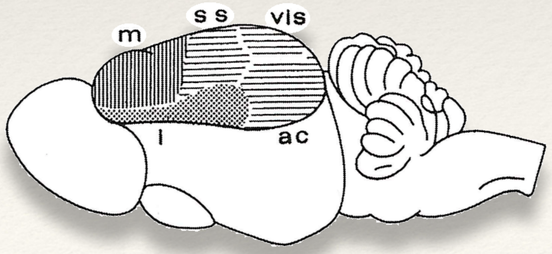
espansione delle cortecce associative



Galago

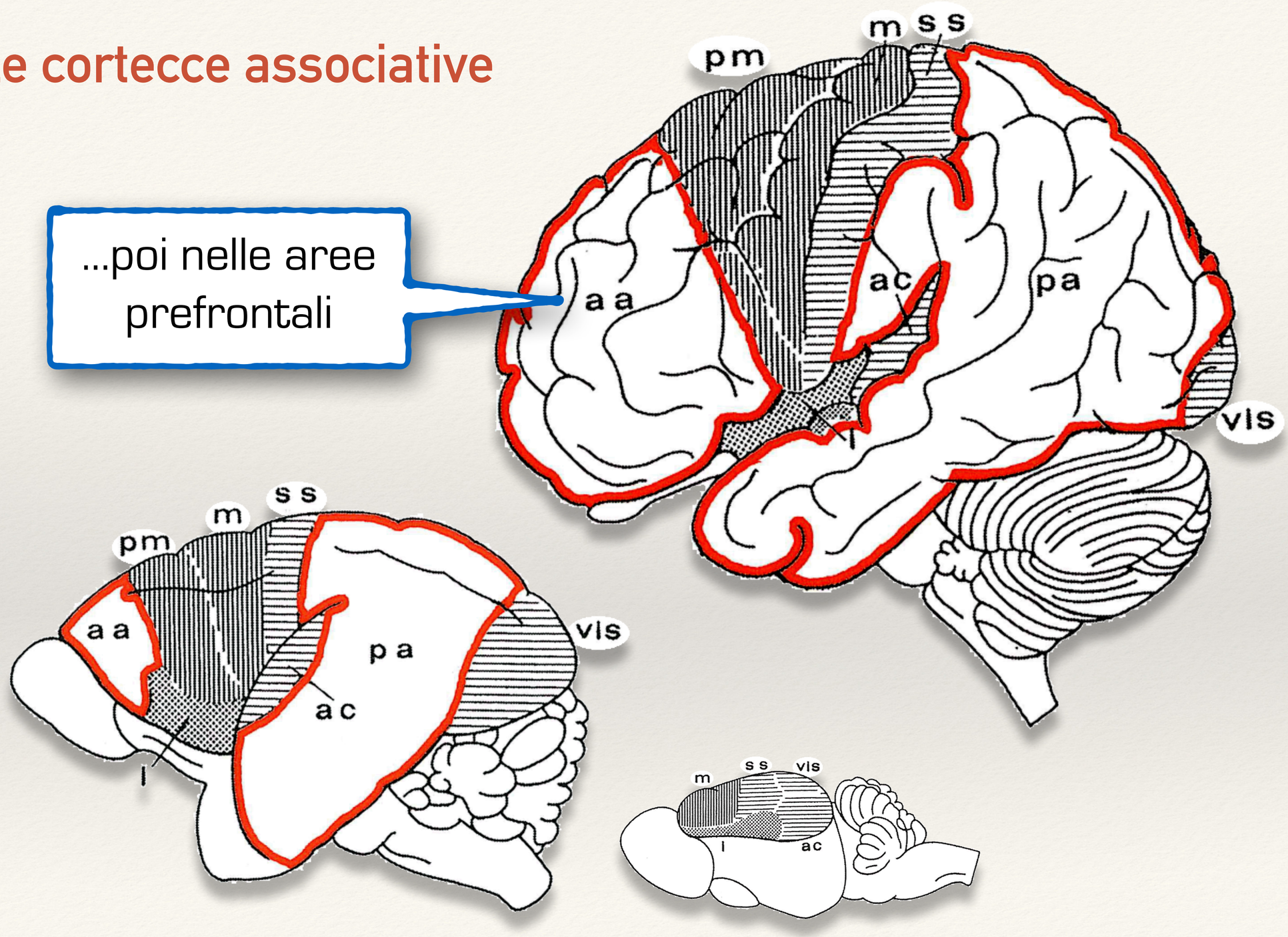
prima a carico delle aree parietali e temporali...





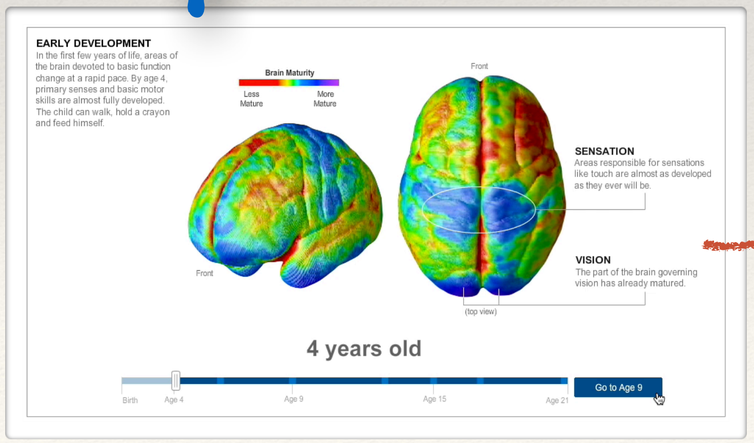
espansione delle cortecce associative

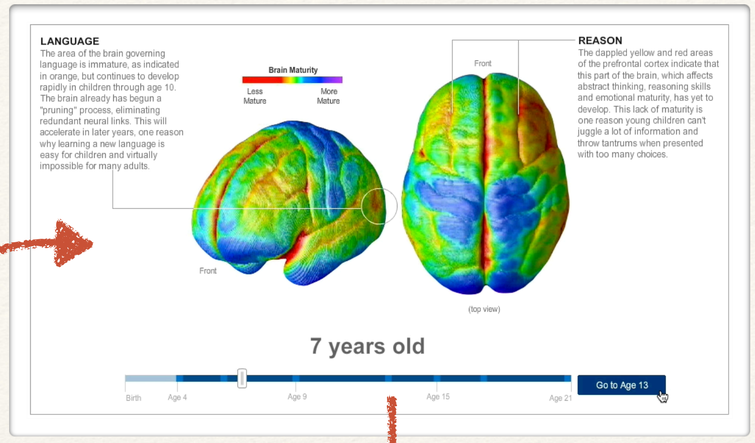
...poi nelle aree prefrontali

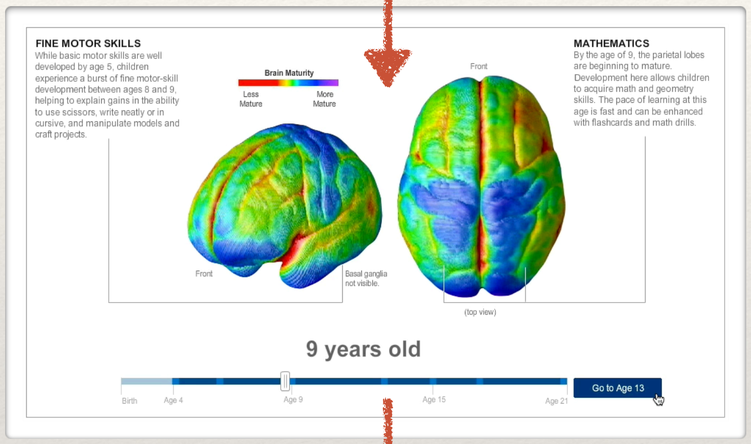


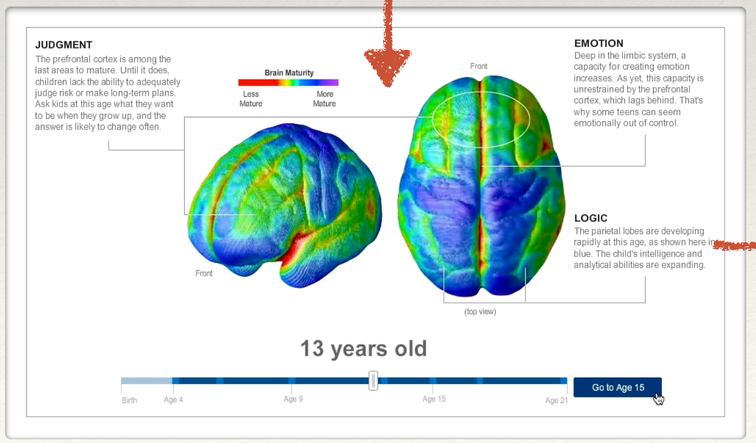
“l’ontogenesi ricapitola la filogenesi”

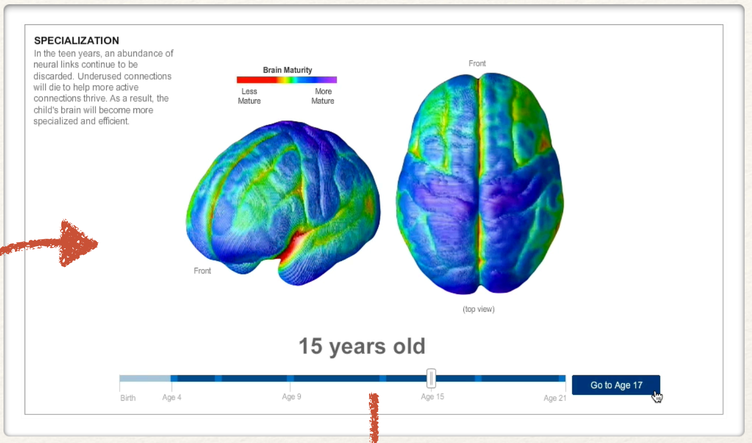
la maturazione della corteccia è precoce a carico delle aree primarie, molto più tardiva nelle cortecce associative, specialmente prefrontali

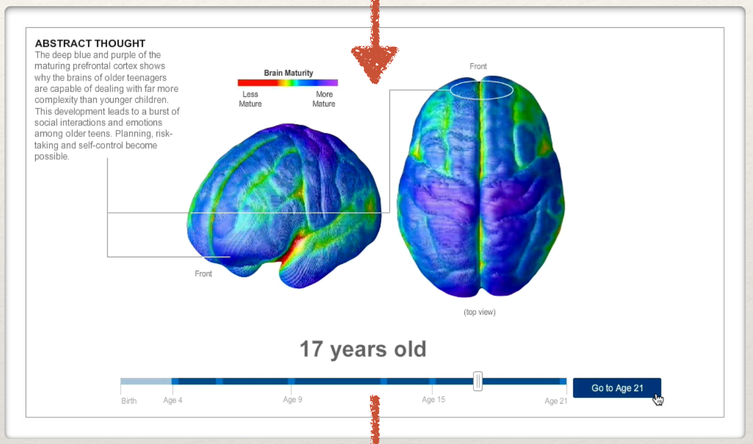


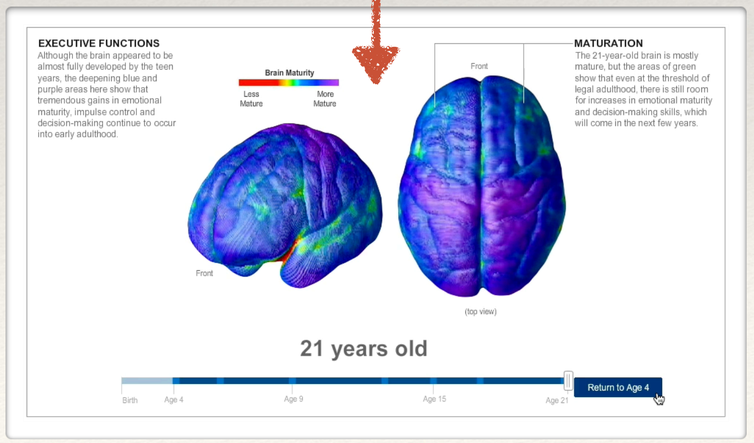




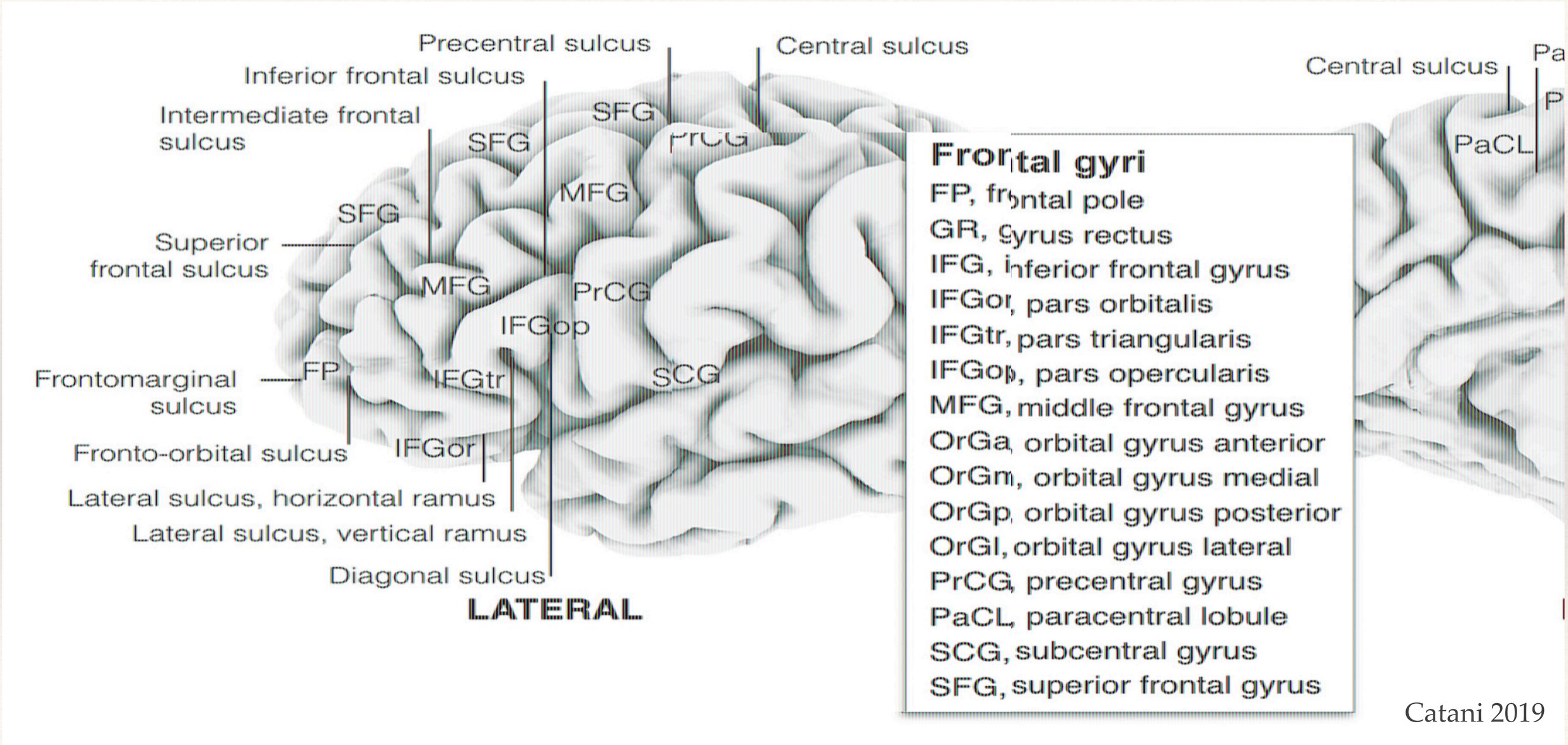




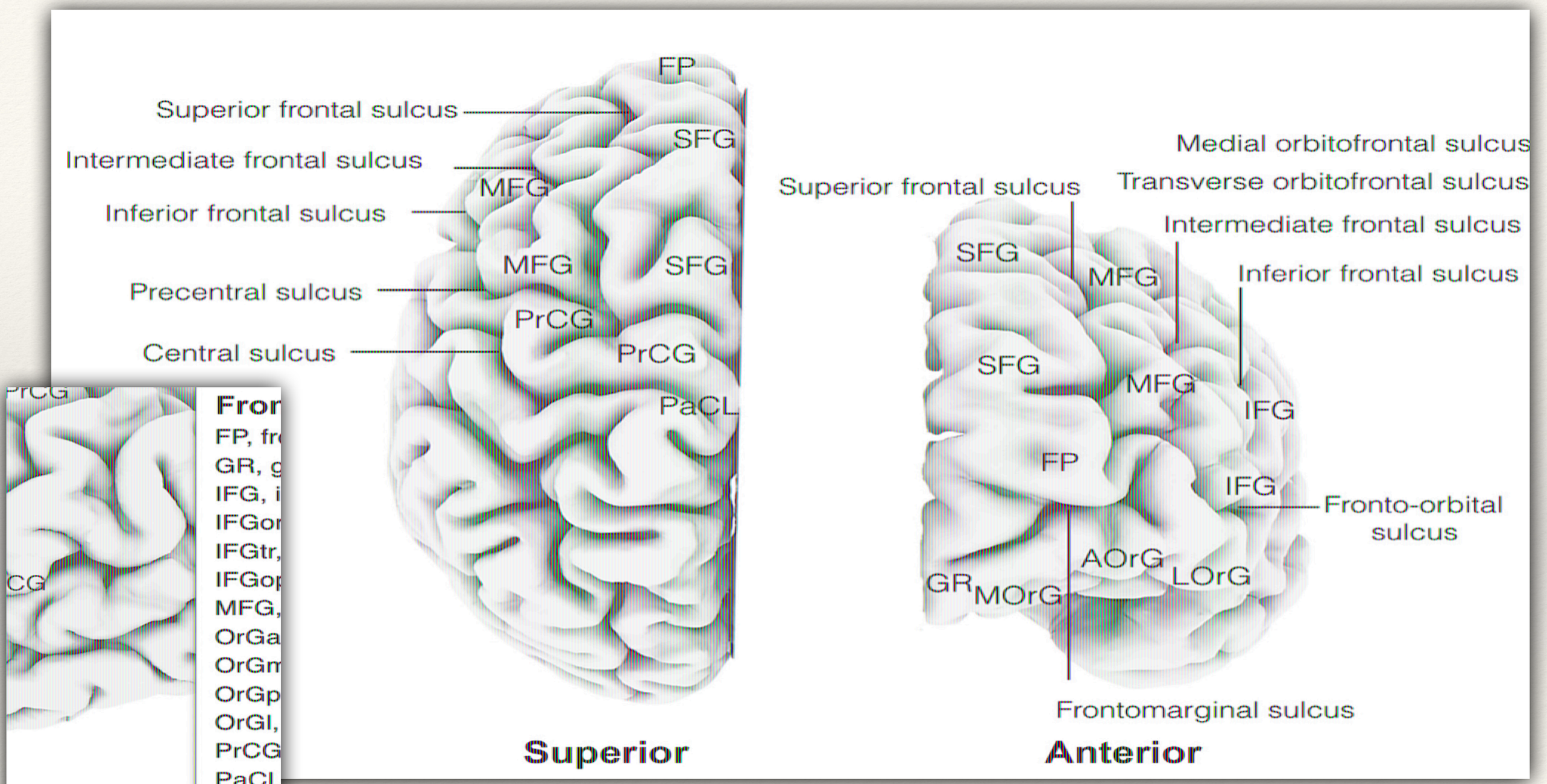




aspetto esteriore del lobo frontale

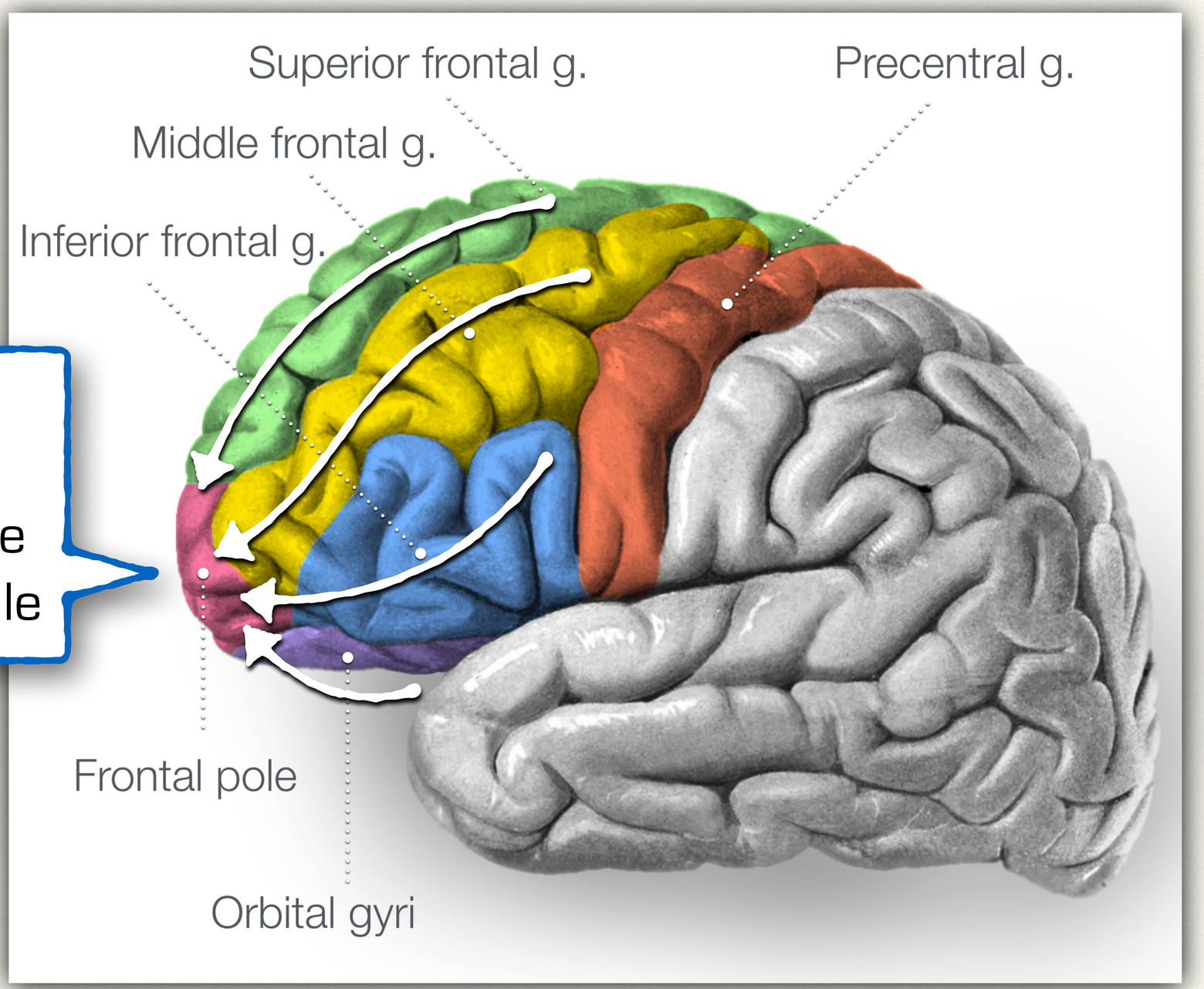


Catani 2019


FP
Superior frontal sulcus
SFG
Intermediate frontal sulcus
MFG
Inferior frontal sulcus
MFG
SFG
Precentral sulcus
PrCG
Central sulcus
PrCG
PaCL
Superior
Medial orbitofrontal sulcus
Superior frontal sulcus
Transverse orbitofrontal sulcus
Intermediate frontal sulcus
SFG
MFG
Inferior frontal sulcus
SFG
MFG
IFG
FP
IFG
Fronto-orbital sulcus
AOrG
LOrG
GR
MOrG
Frontomarginal sulcus
Anterior

Catani 2019

i giri frontali
convergono
anteriormente
sul polo frontale



Frank Gaillard
Radiopedia.org

Table 1.1 Prefrontal (PF) areas in human and macaque monkey brains. Area numbers in parentheses

Type	Area	Humans	Monkeys
Granular PF cortex	Caudal PF	Caudal lateral (8)	Prearcuate (8)
	Dorsomedial PF	Superior frontal gyrus and medial PF (9)	Superior frontal gyrus and medial PF (9)
	Lateral area 9	Superior frontal gyrus (9)	Superior frontal gyrus (9)
	Mid-lateral PF	Middle frontal gyrus (46)	Principal sulcus (46)
	Postero-lateral PF	Caudal middle frontal gyrus (9/46)	Caudal principal sulcus (9/46)
	Ventral PF	Inferior frontal gyrus (45, 47)	Inferior convexity (45, 12)
	Granular orbital PF	Orbital surface (11, rostral 13, rostral 14)	Orbital surface (11, rostral 13, rostral 14)
	Polar PF	Frontal pole (10)	Frontal pole (10)
Agranular PF cortex	Medial agranular PF	Anterior cingulate (24), infralimbic (25), prelimbic (32)	Anterior cingulate (24), infralimbic (25), prelimbic (32)
	Lateral agranular PF	Caudal areas 13 and 14 and agranular insular cortex	Caudal areas 13 and 14 and agranular insular cortex

la ~~confusione~~ articolazione nella nomenclatura rivela la complessità del tema

Passingham & Wise 2012

Table 1.2 Terms for groups of frontal areas

Region	Components
Caudal PF	Area 8, including frontal eye field (FEF),?postero-lateral PF (area 9/46)?
Dorsal PF	Mid-lateral PF (area 46), lateral area 9,?postero-lateral PF (area 9/46)?
Medial PF	Infralimbic (area 25), prelimbic (area 32), anterior cingulate (area 24), medial area 9, and polar PF (area 10)[a]
Orbital PF, OFC	Granular & agranular orbital cortex (11, 13, 14), agranular insular cortex
Ventral PF	Area 12/47 and area 45,? area 44?
Lateral premotor	Dorsal and ventral premotor areas
Medial premotor	Presupplementary motor area (preSMA), supplementary motor area (SMA), cingulate motor areas (CMAs)
Premotor cortex	Lateral and medial premotor areas

[a] Medial parts of the polar PF cortex in humans.

? An area that might be included in a group.

Passingham & Wise 2012

cosa fa?

- “Frontal lobe functions are conditional on the development of an intricate set of connections that guarantee access to sensory information, memories, and internal states for the online control of cognitive activities and movement”

  (Marco Catani, 2019)

cosa fa?

JM Fuster 2008

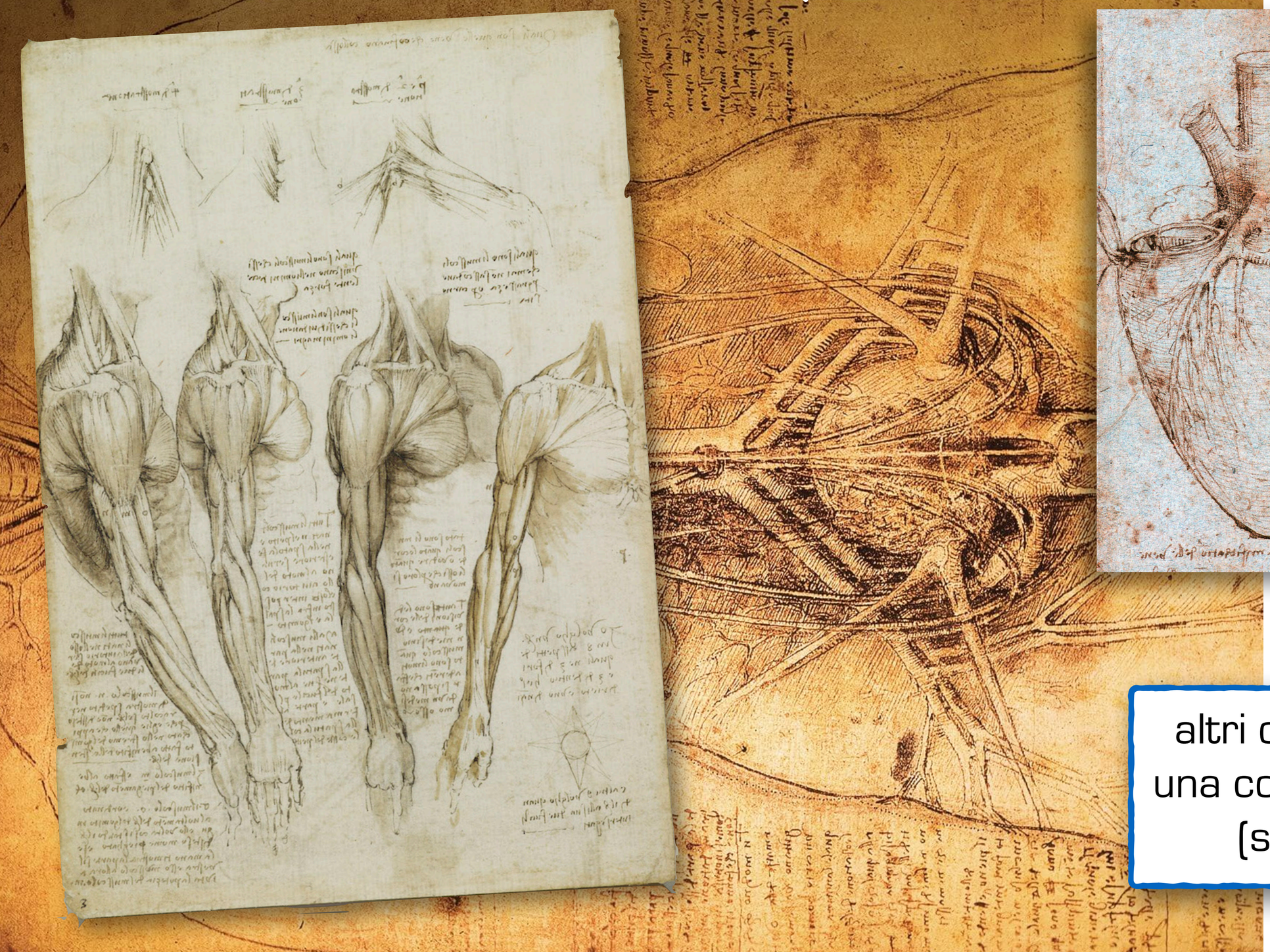
- **store of long-term executive memory (representational)**
  - vast array of widely distributed, intersecting and overlapping networks representing long-term memory of actions upon the environment
  - networks formed over repeated interactions of the organism with the environment, probably by Hebbian plasticity
  - **medial** and **orbital**: patterns of emotional, social, visceral action
    lateral: structured actions in the behavioral, linguistic, cognitive domains
    (all three regions are heavily interconnected)
- **goal-directed behavior (operational)**

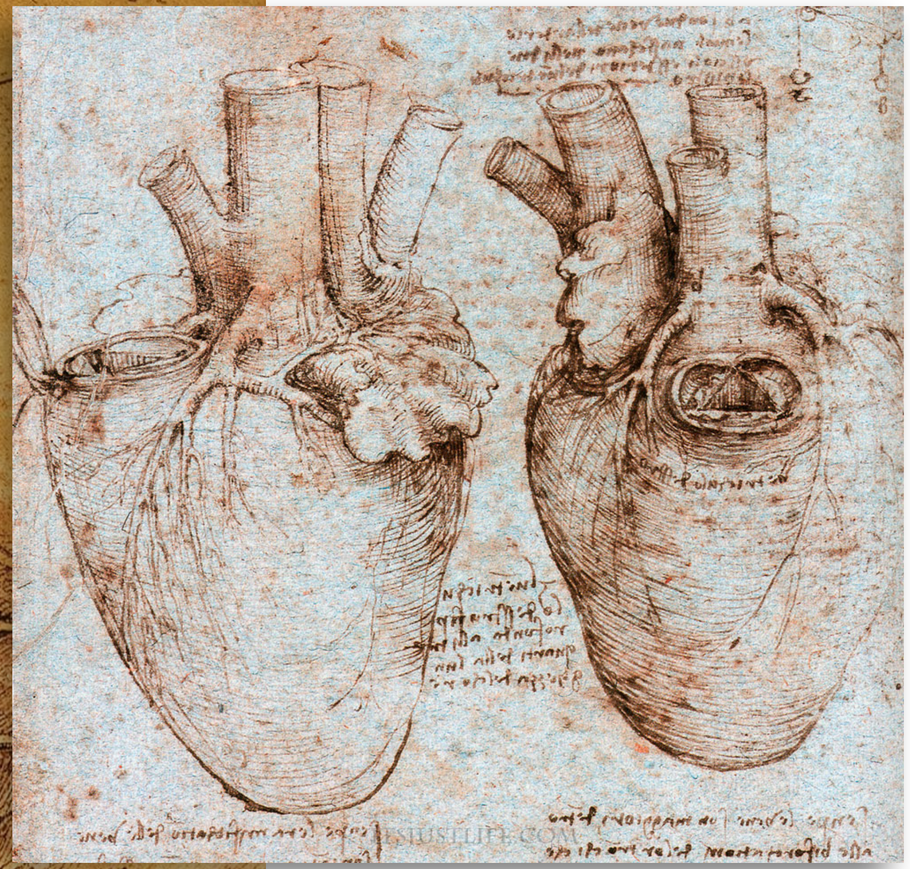
cosa fa?

Passingham & Wise 2012

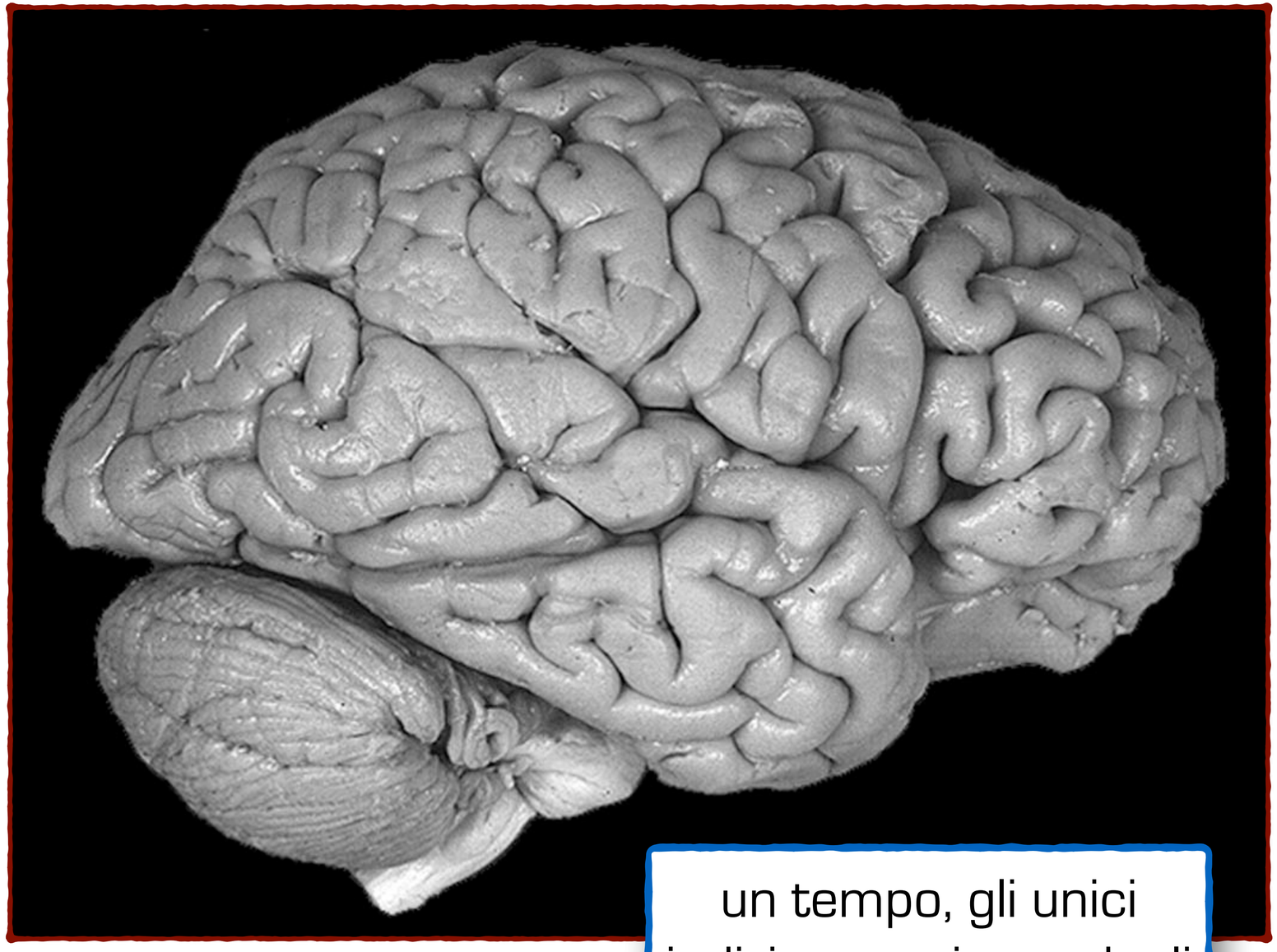
- the prefrontal cortex performs a simple fundamental function: it uses information about the current behavioral context to generate goals according to current biological needs, and it can do so on the basis of single events

in effetti, capire
“cosa fa” il cervello è
tutt’altro che semplice:
l’aspetto morfologico
non offre indizi sulla
sua funzione

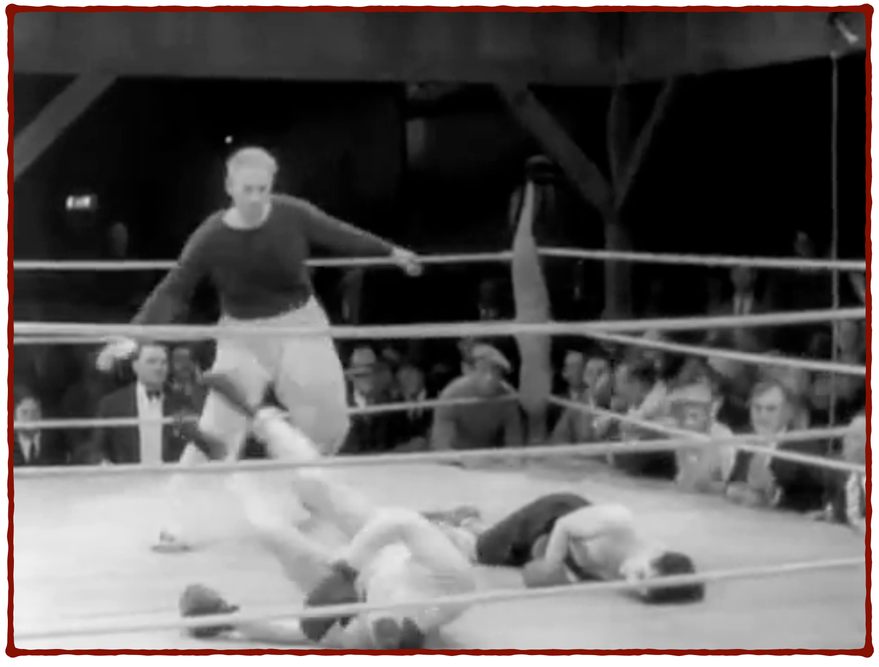




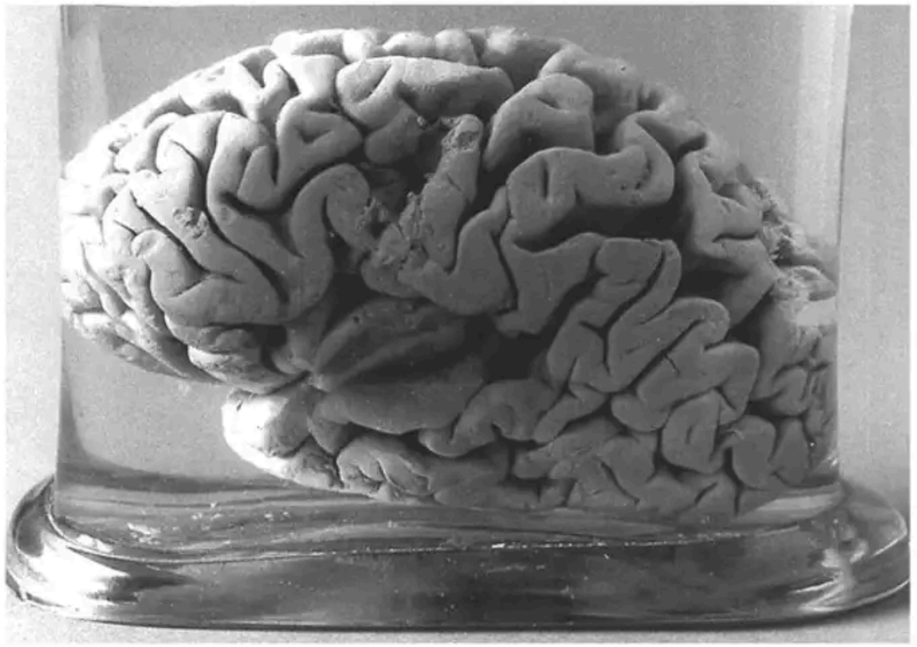
altri organi si prestano a una comprensione intuitiva (sia pure parziale)

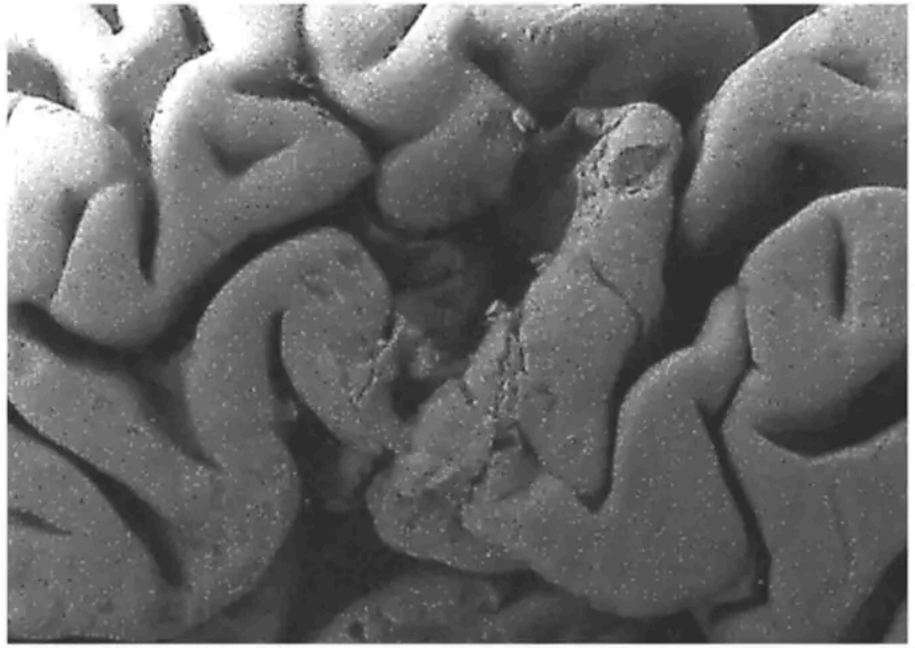


un tempo, gli unici indizi provenivano dagli effetti delle lesioni

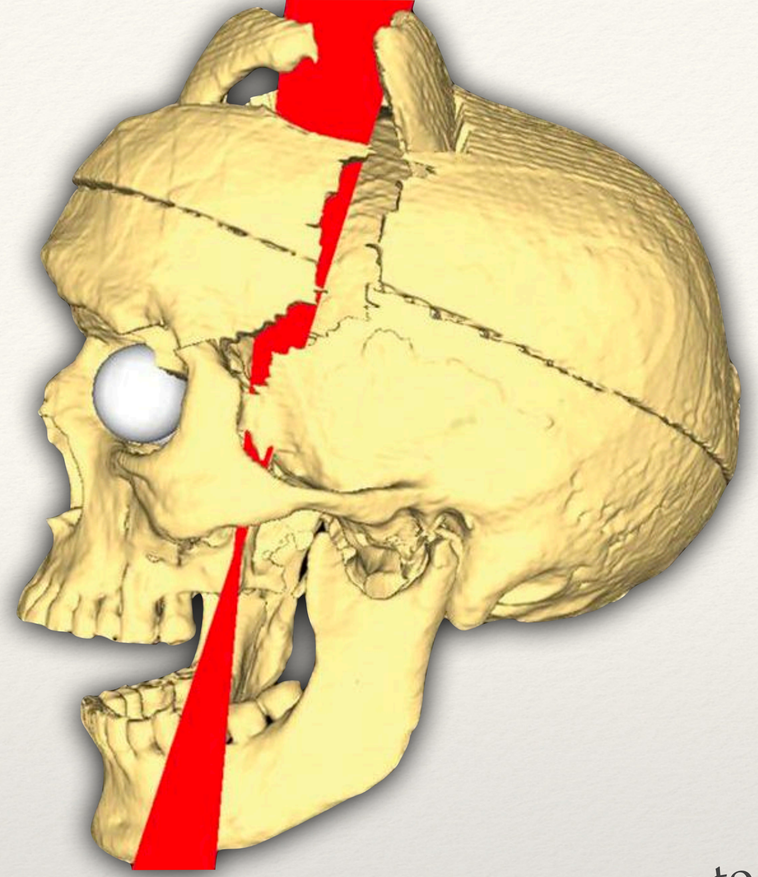


Broca's patients

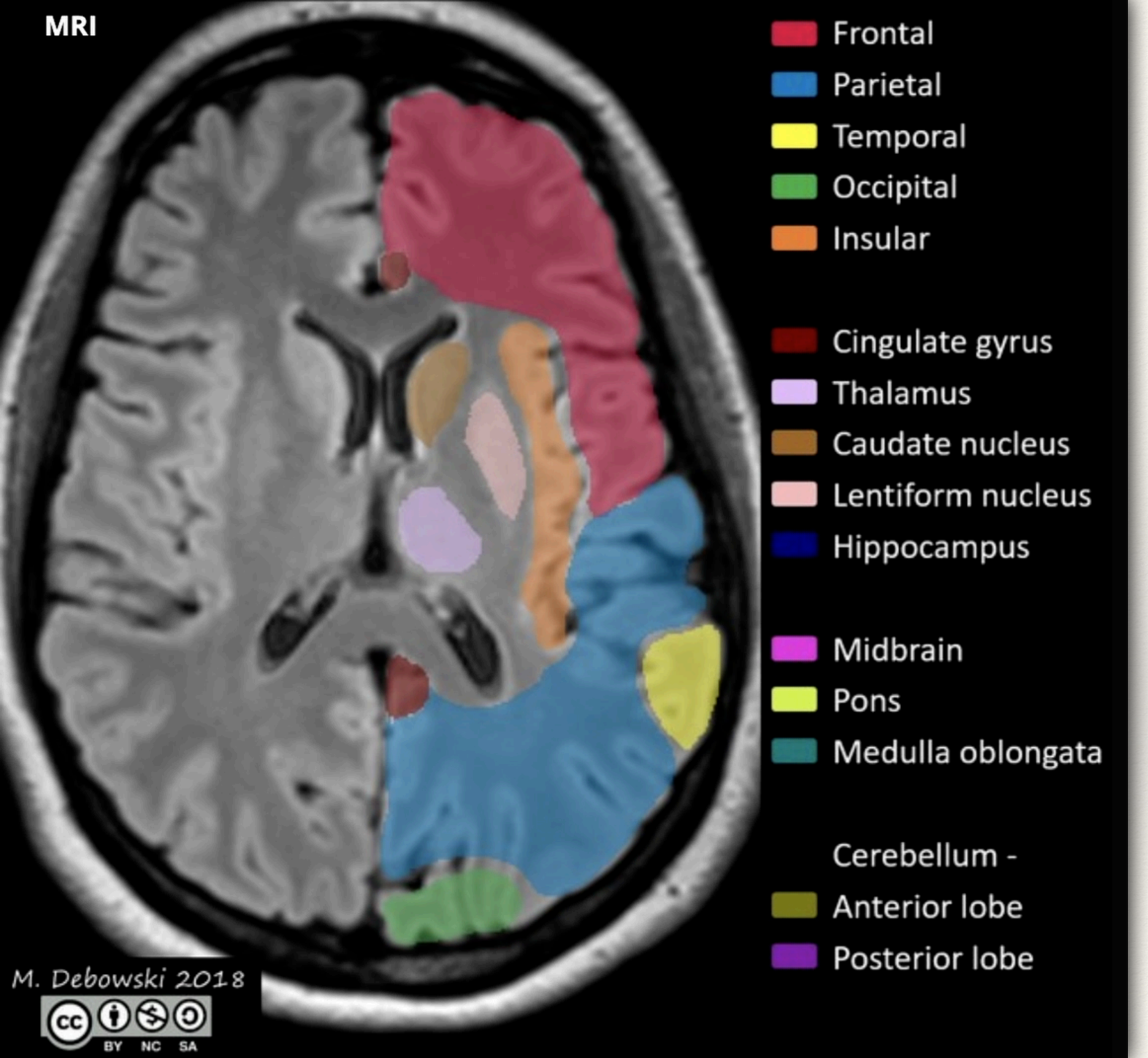




Phineas P. Gage (1823–1860)



"The equilibrium or balance, so to speak, between his intellectual faculties and animal propensities, seems to have been destroyed. He is fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operations, which are no sooner arranged than they are abandoned in turn for others

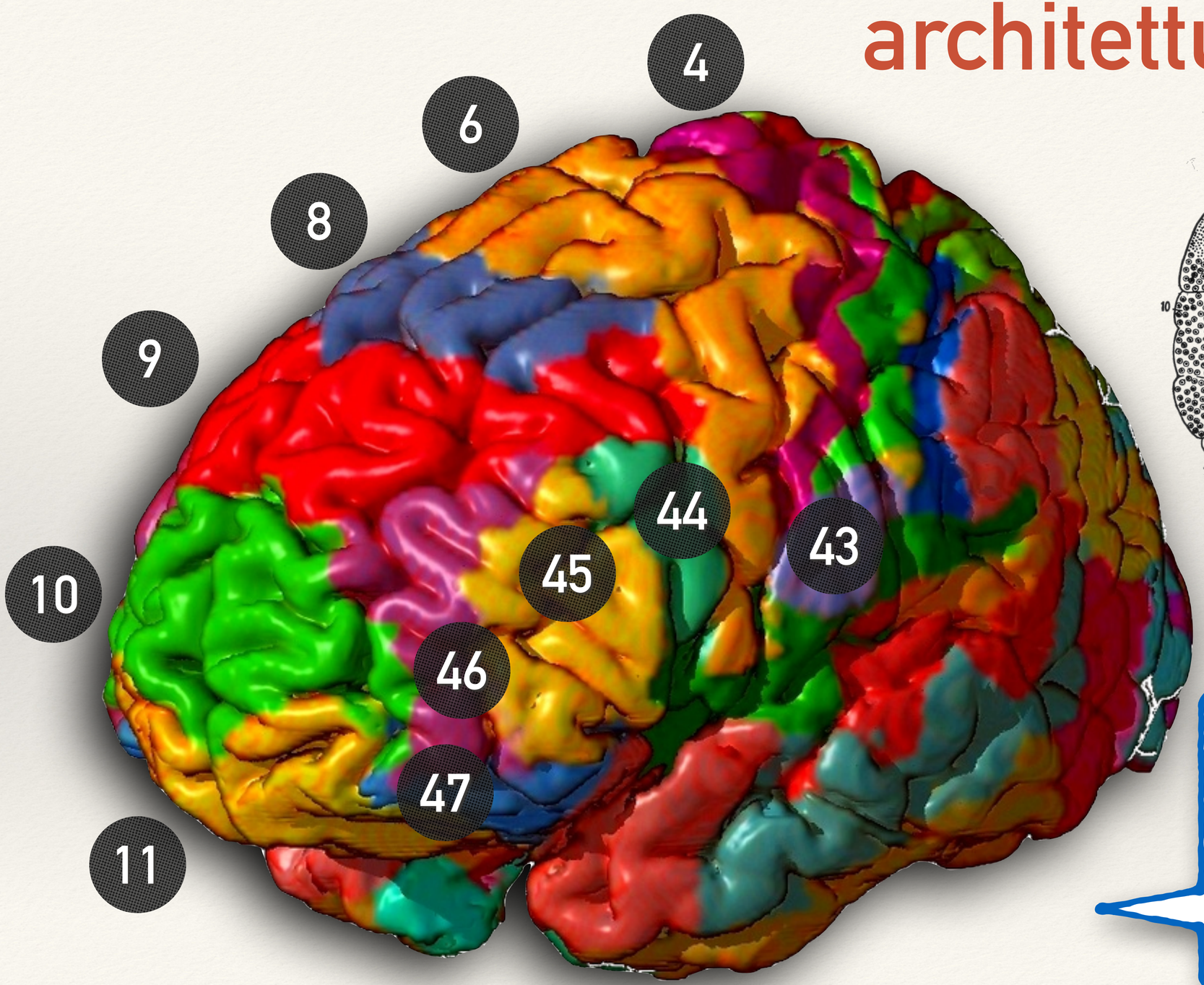


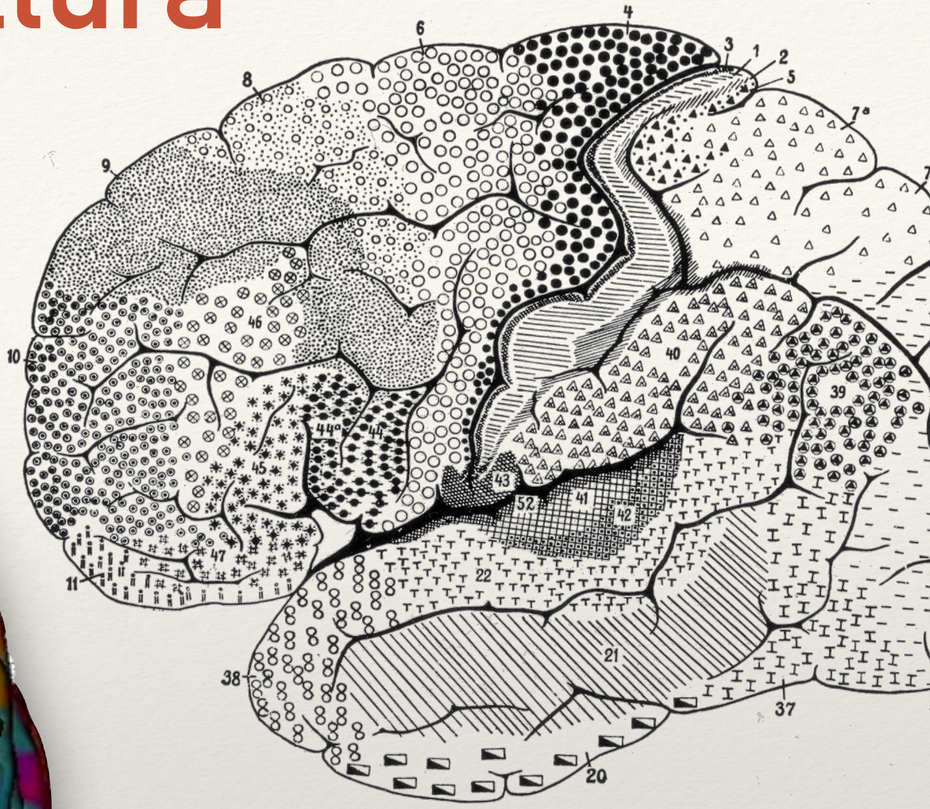
dalla neuroanatomia puramente descrittiva…

…ai primi passi verso una neuroanatomia funzionale

Brodmann:
aree identificate e numerate in base a sistematiche differenze di architettura istologica

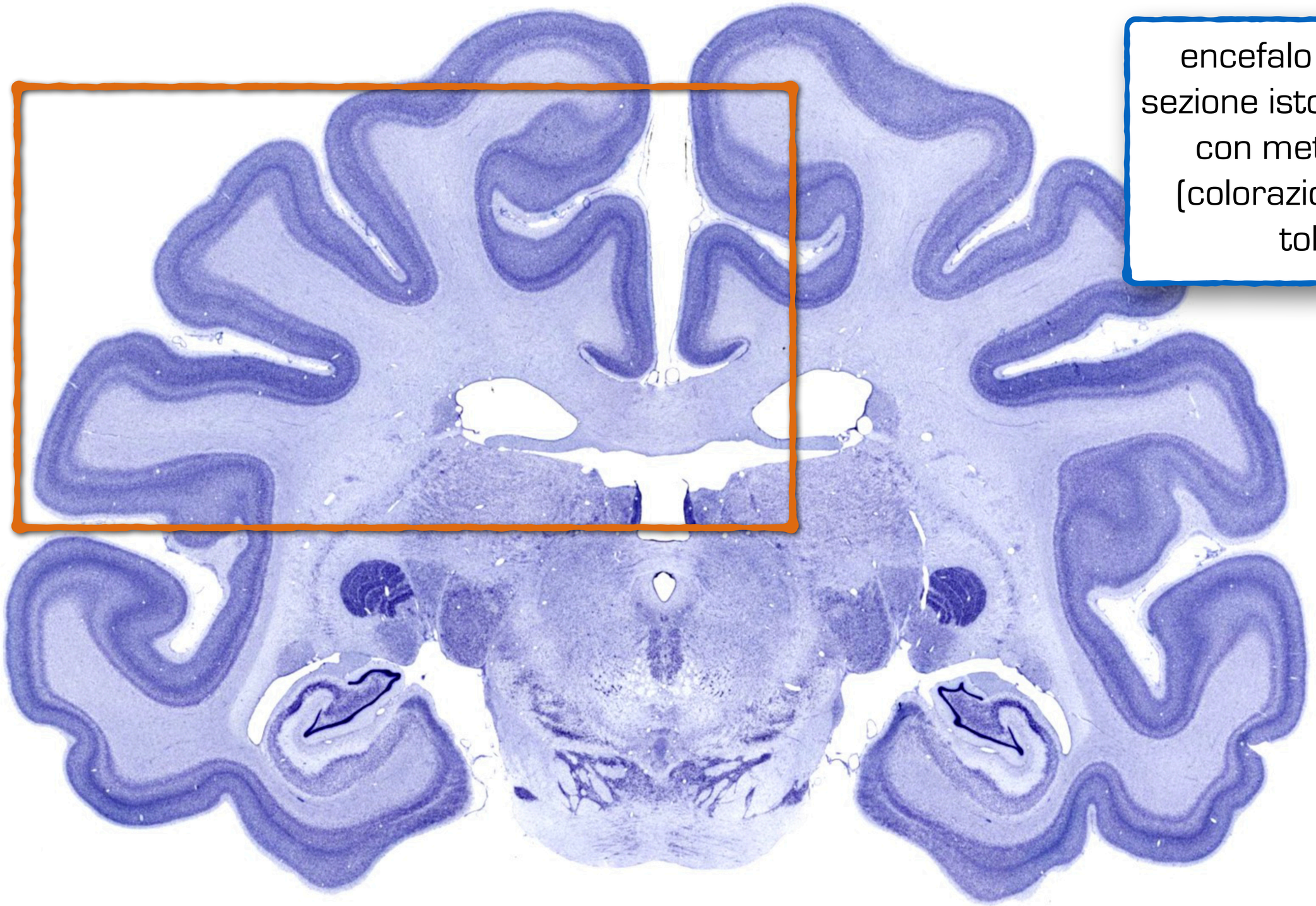
architettura



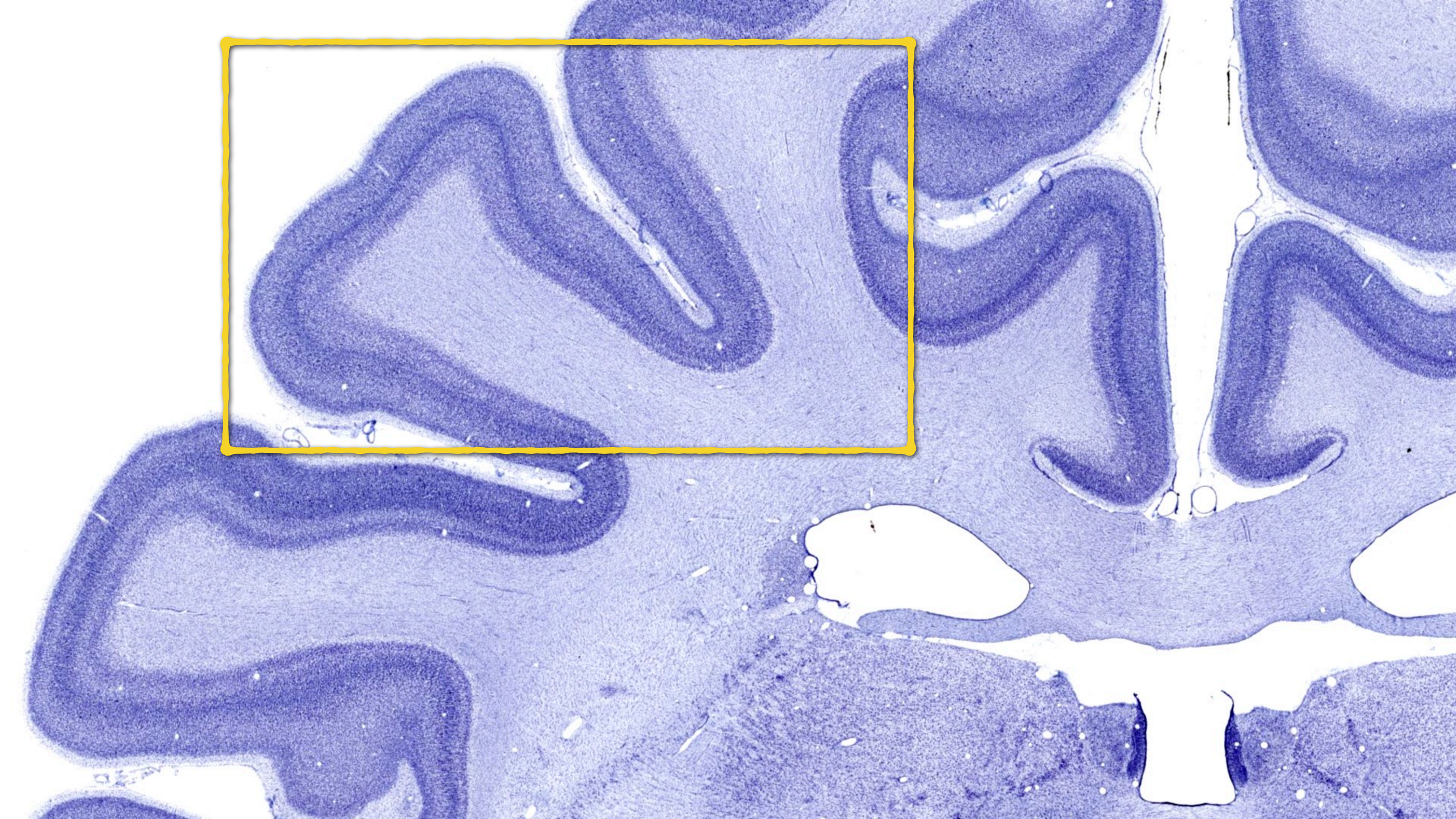


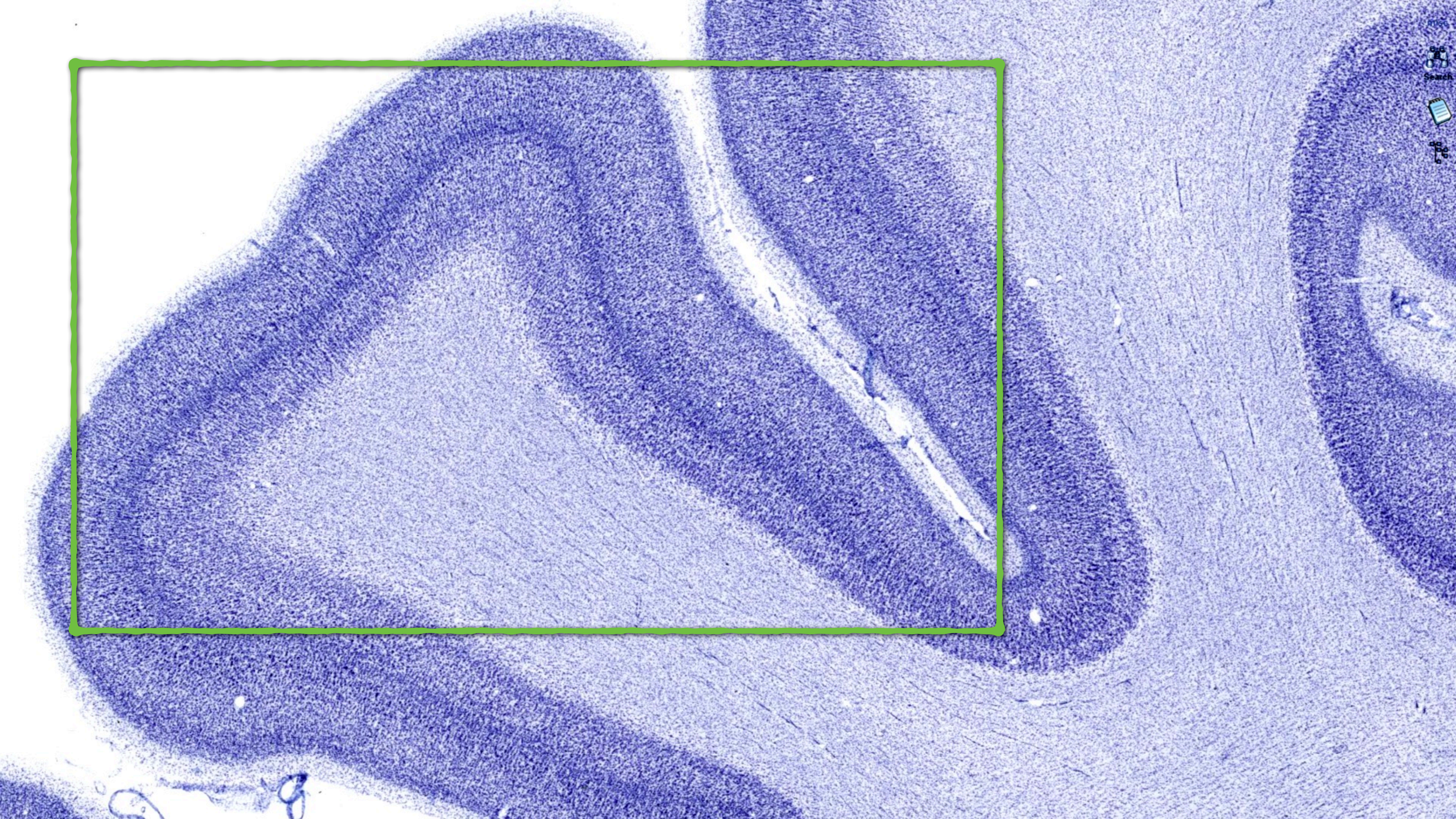
sorprendenti paralleli tra intima architettura della corteccia e funzione delle aree corrispondenti

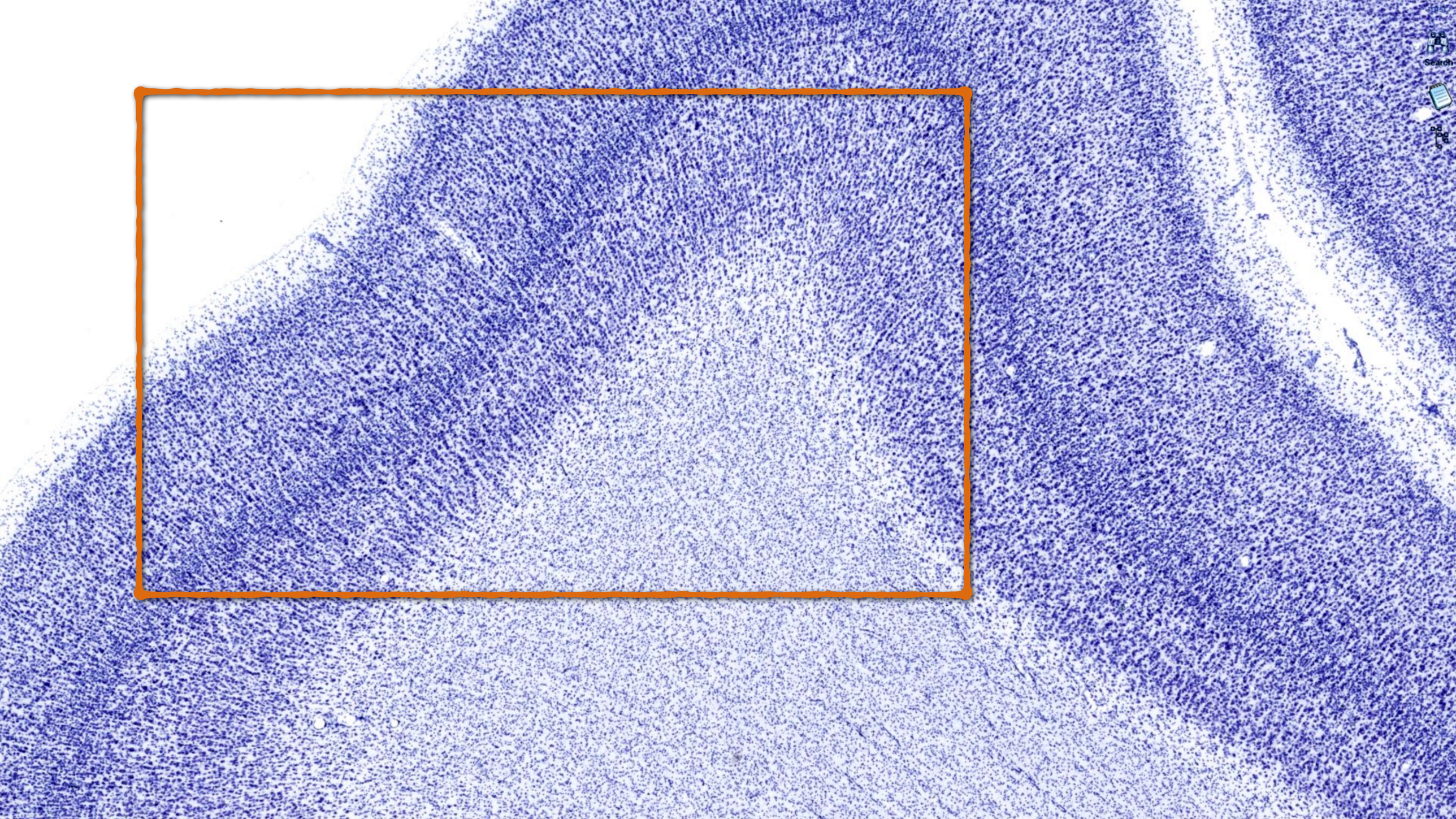
esercizio importante:
colmare il solco tra strutture nervose (visibili a occhio nudo e attraverso le comuni metodiche di imaging) e architettura microscopica del tessuto nervoso

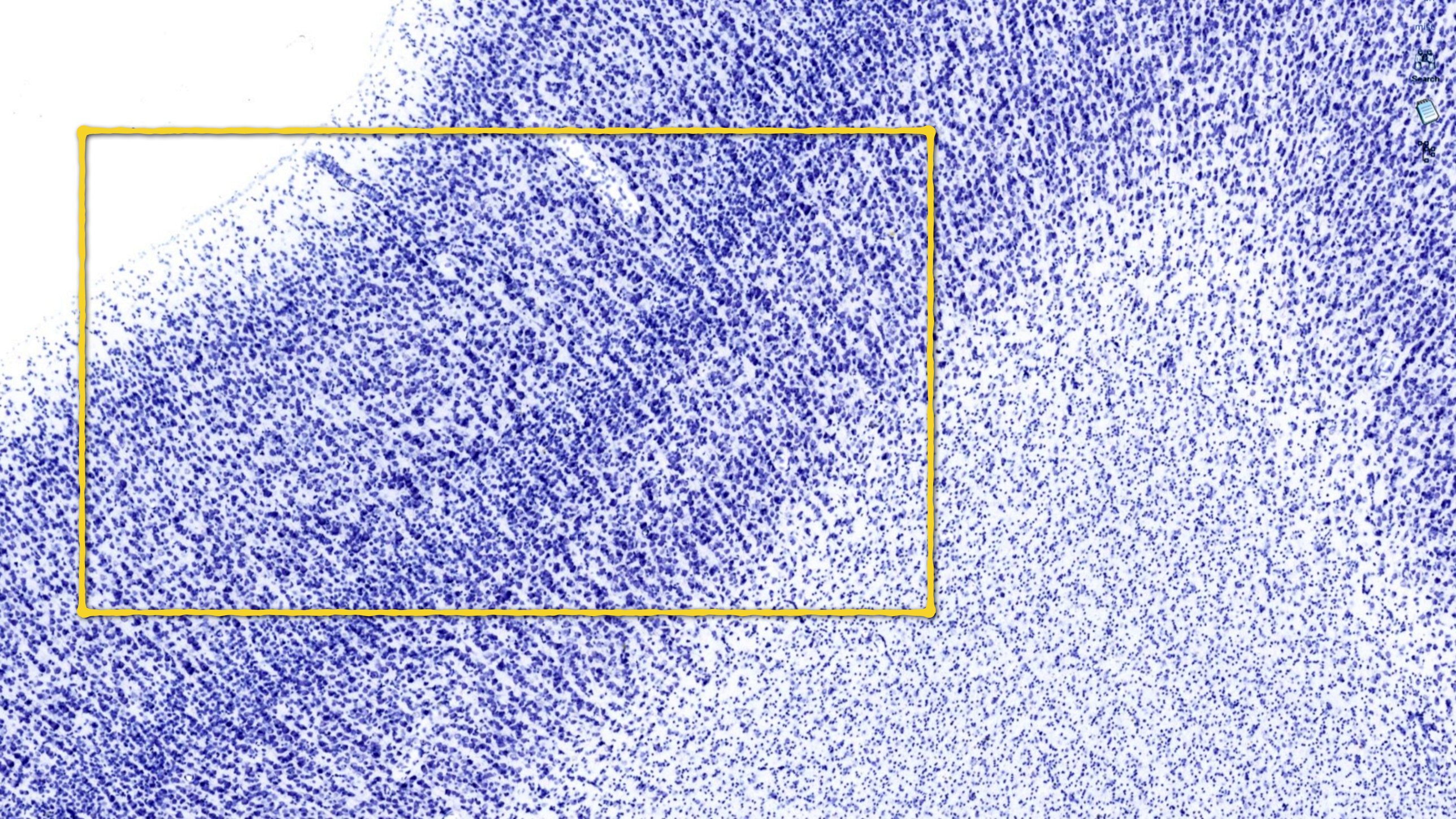


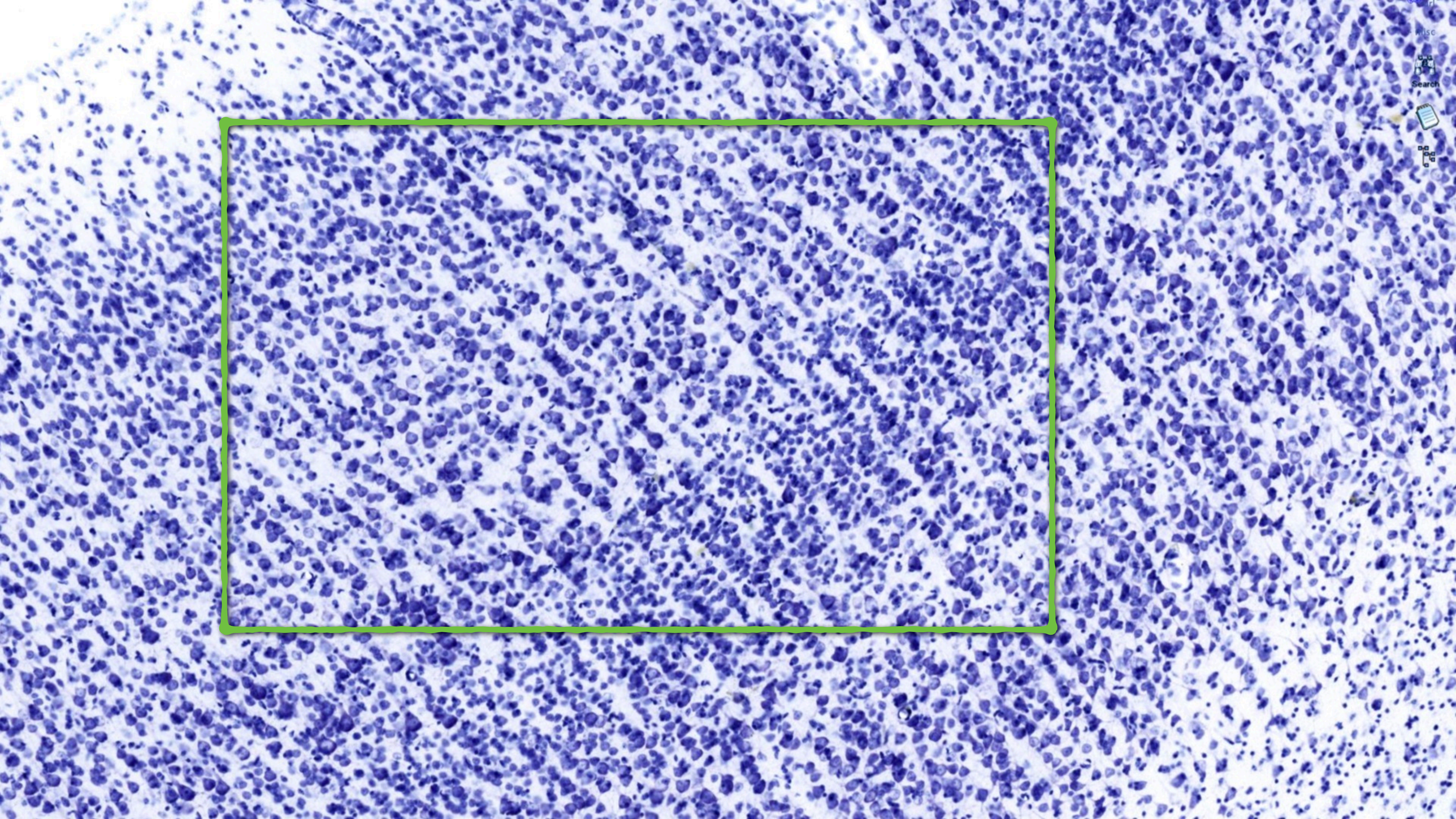
encefalo di macaco in sezione istologica ottenuta con metodo di Nissl (colorazione con blu di toluidina)

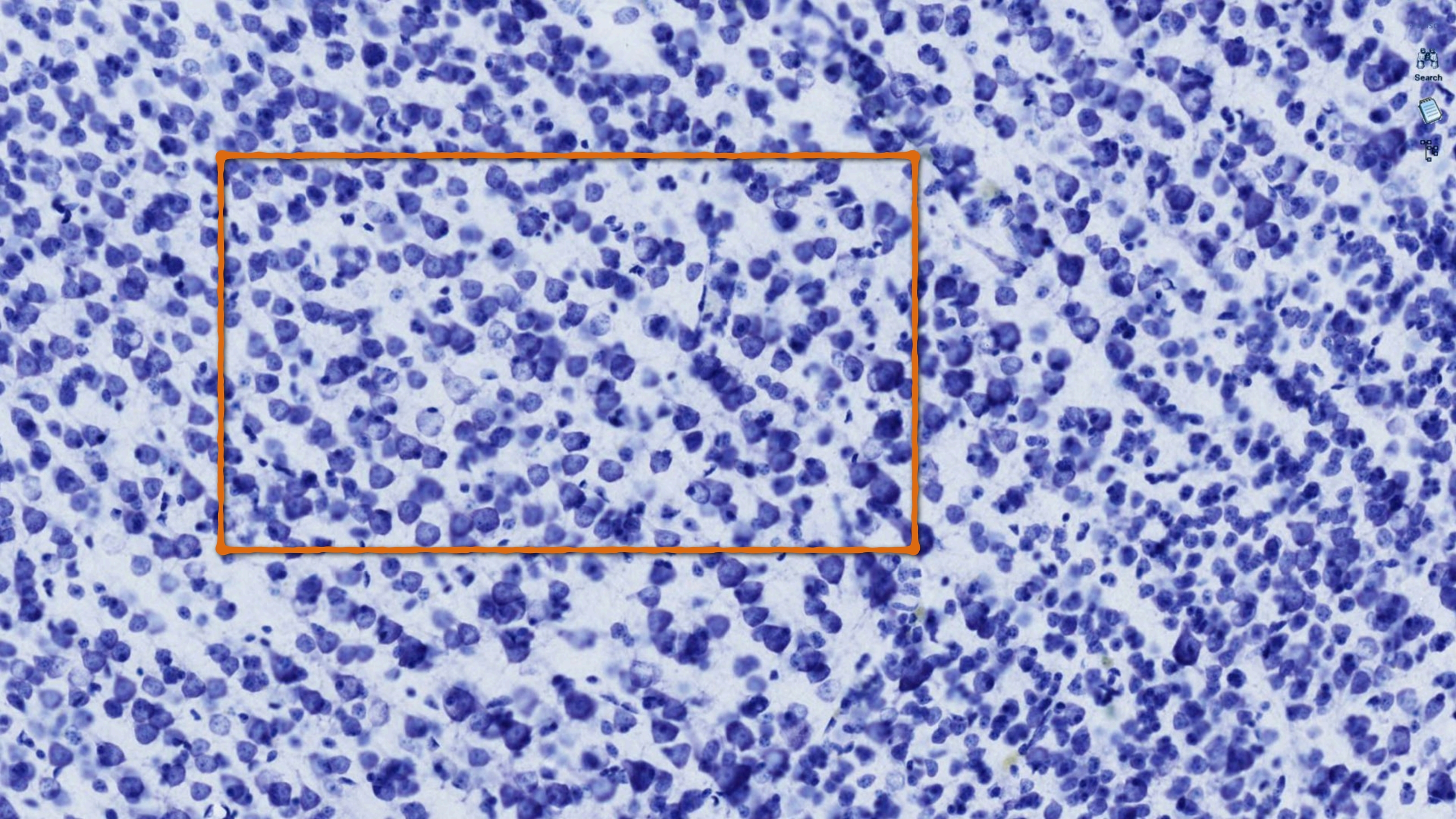




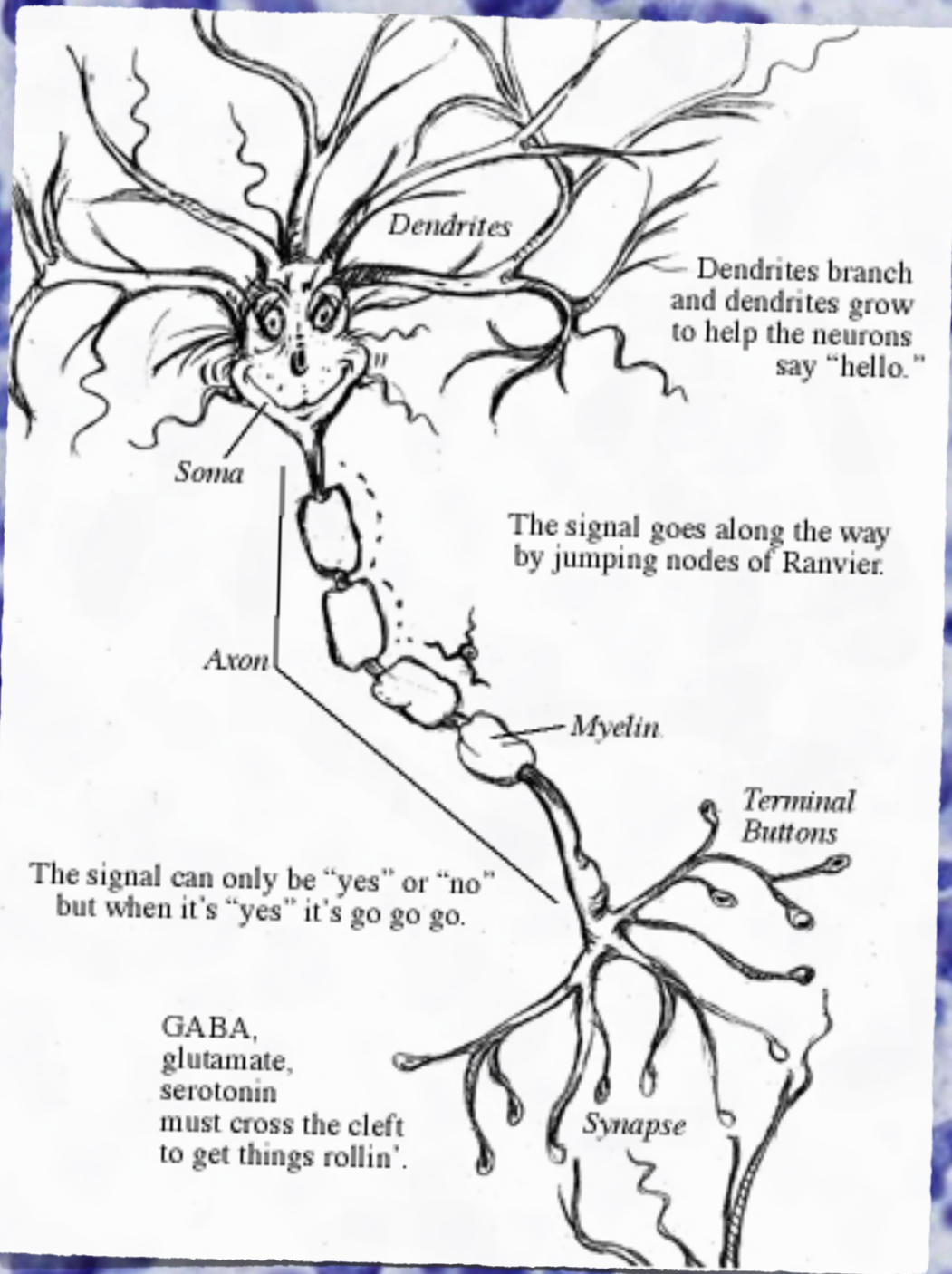




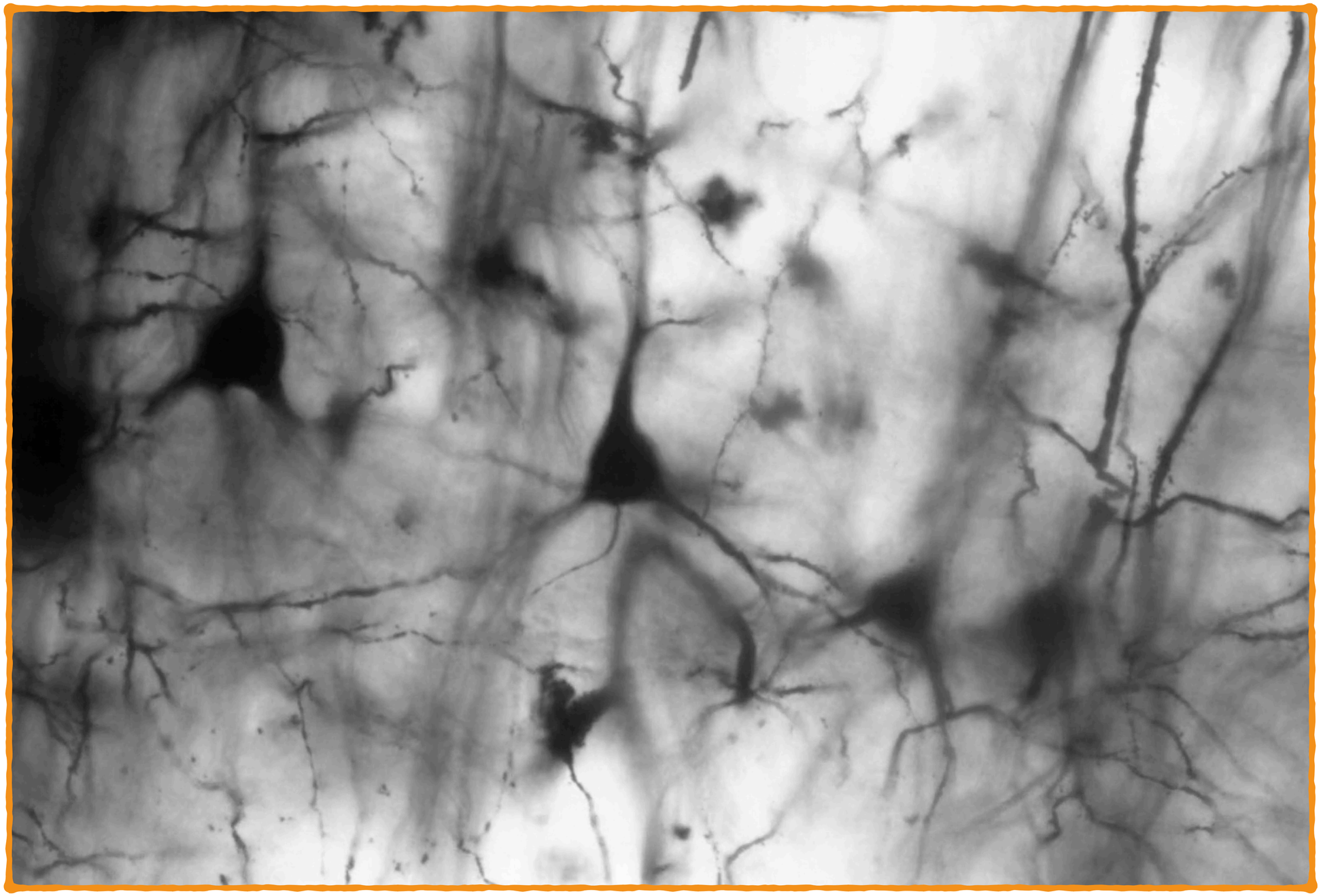




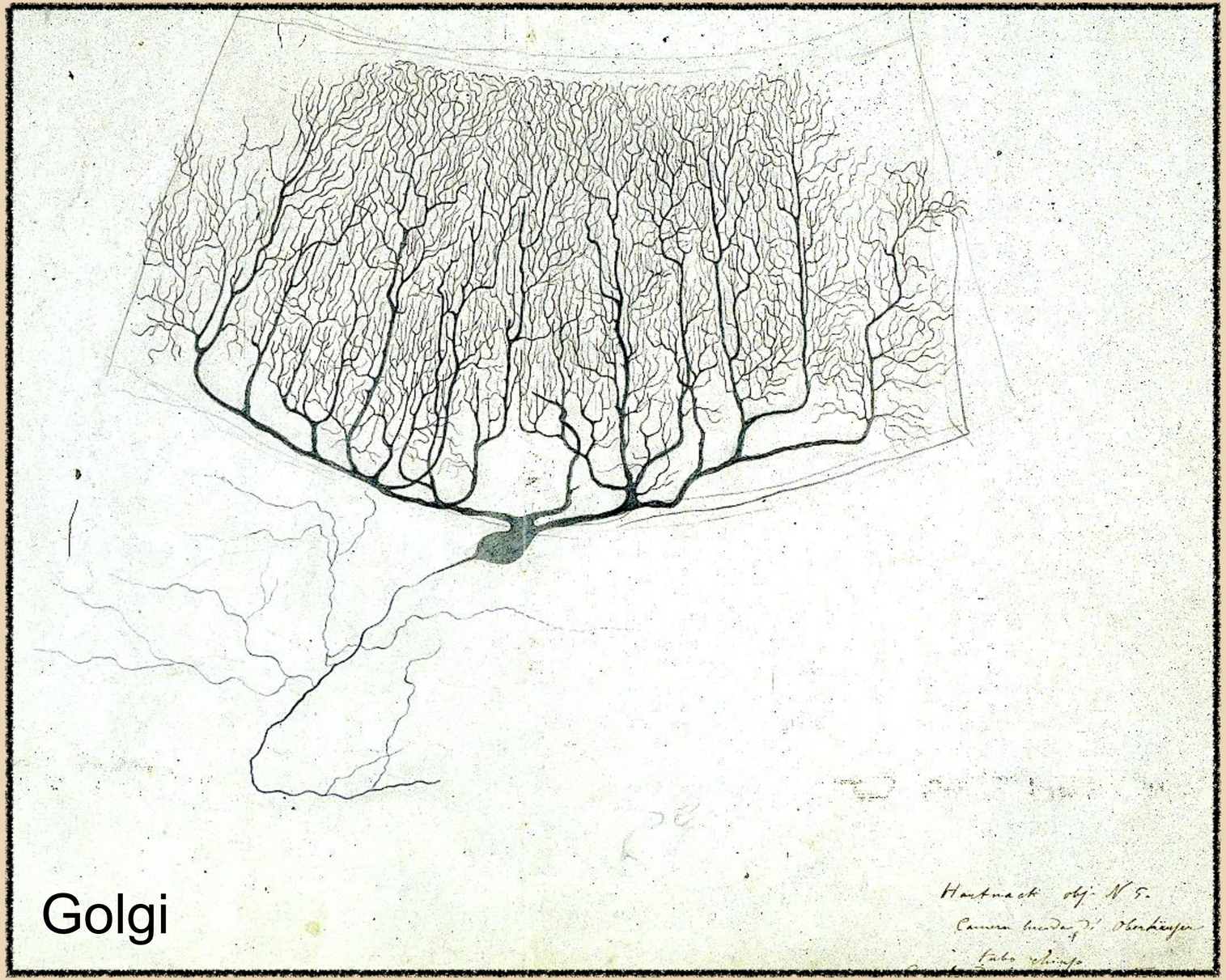
la colorazione di Nissl mostra solo il corpo cellulare e una breve porzione iniziale di grossi dendriti delle cellule nervose



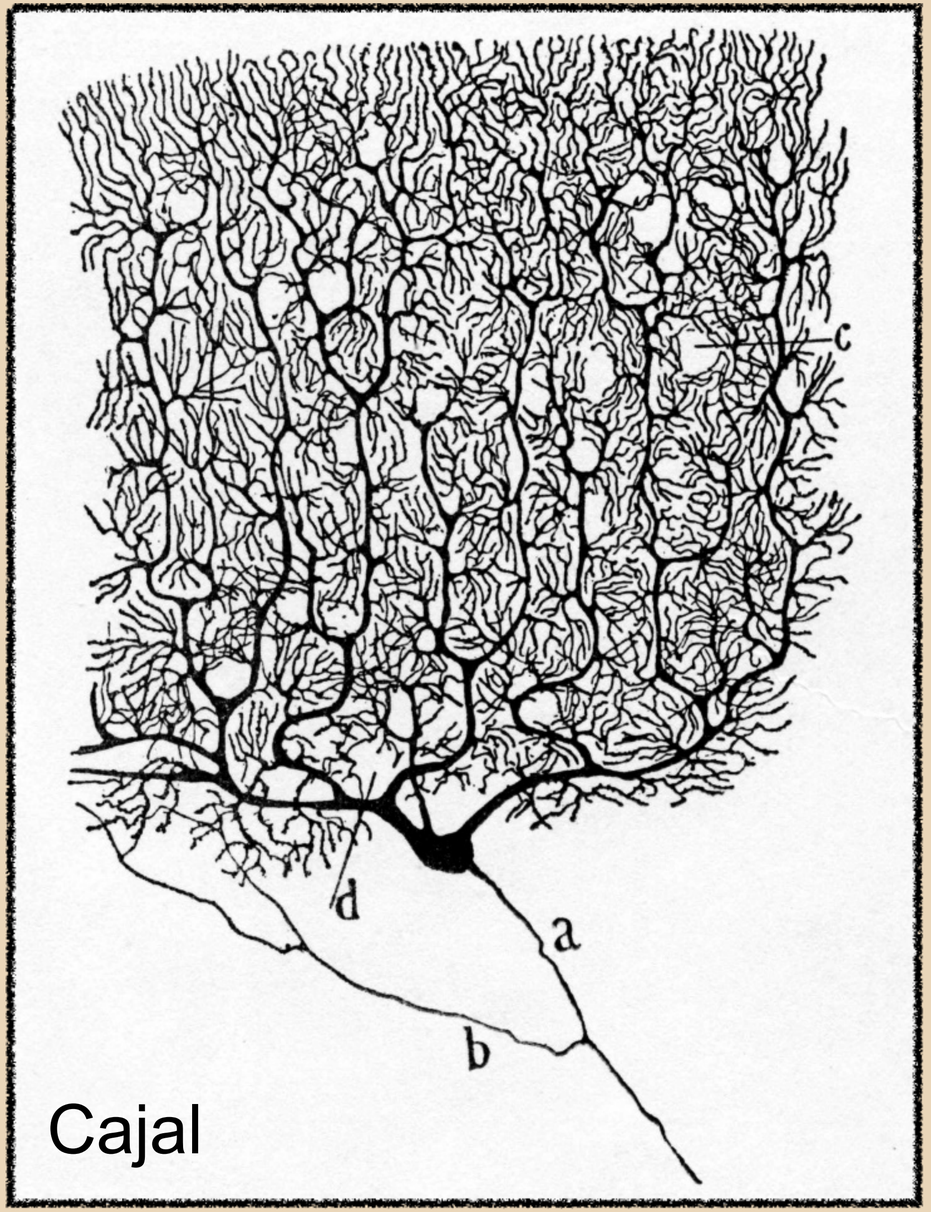
la “reazione nera” di Golgi rivela la vera, completa morfologia dei neuroni



Camillo Golgi, corteccia cerebrale di coniglio

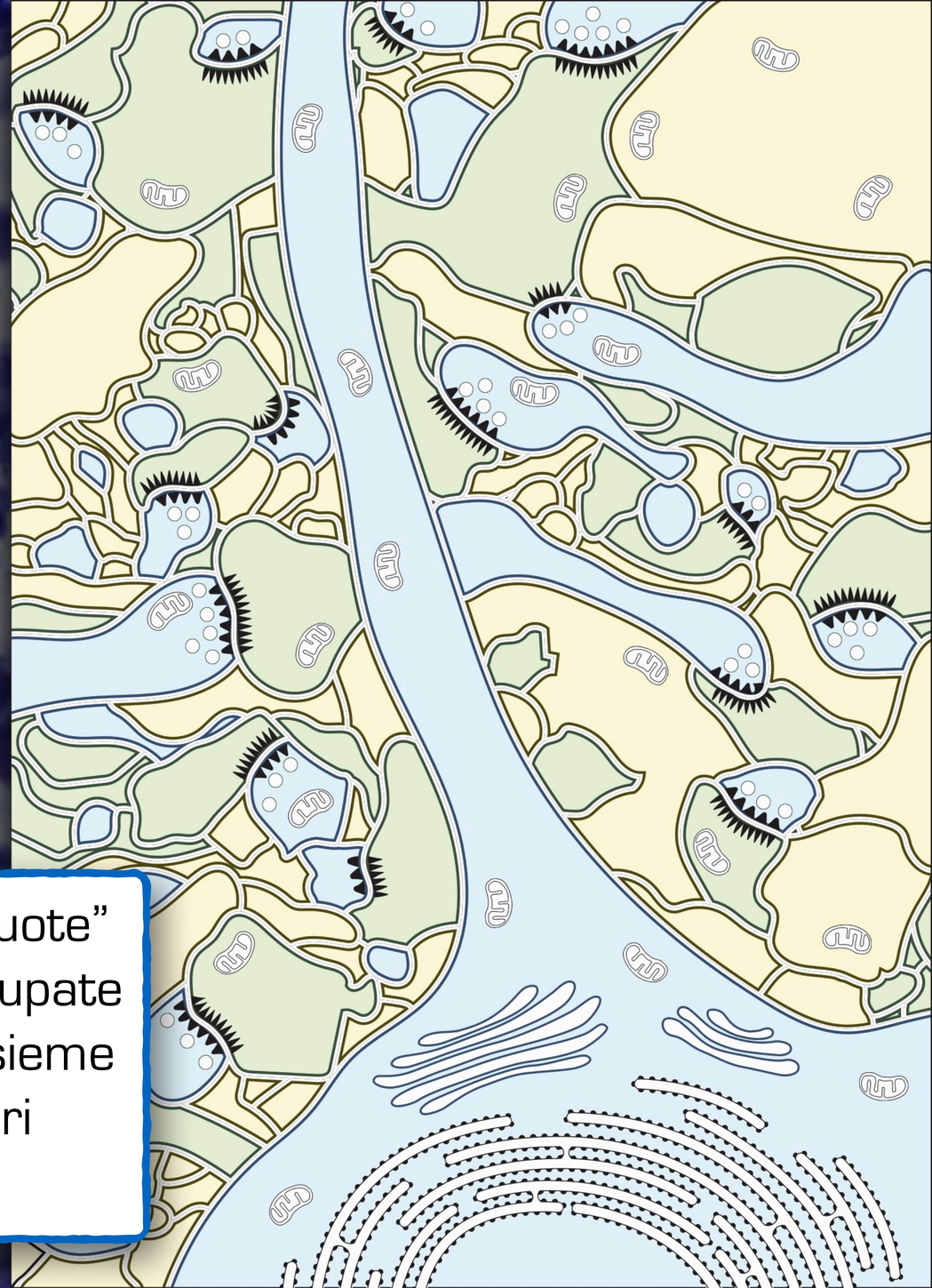


Golgi



Cajal

cellula di Purkinje



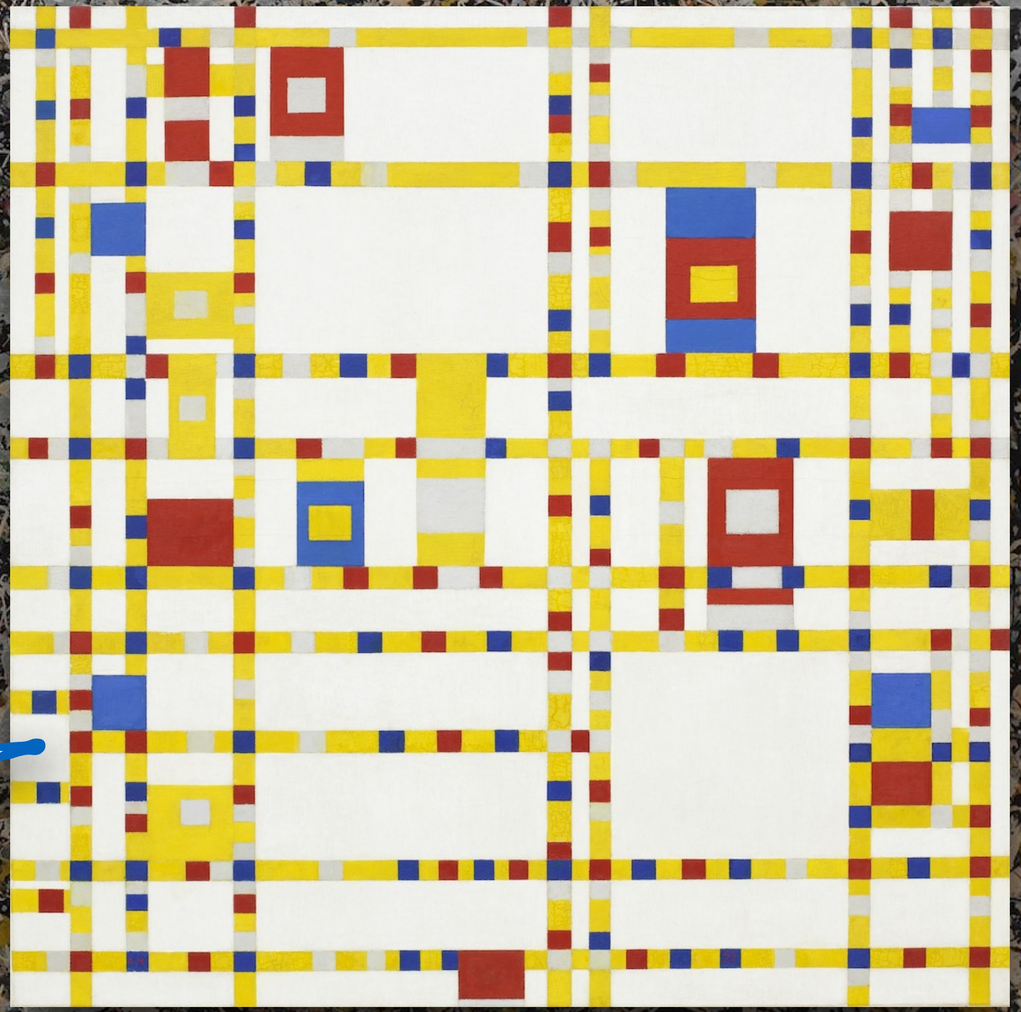
le zone apparentemente “vuote” tra i corpi cellulari sono occupate da “neuropilo”, l’intricato insieme di prolungamenti cellulari neuronali e gliali

Cortex by numbers

Cortical surface:	2600 cm^2
Number of neurons:	27.4 x 10^9
Synapses per mm^3	440 x 10^6

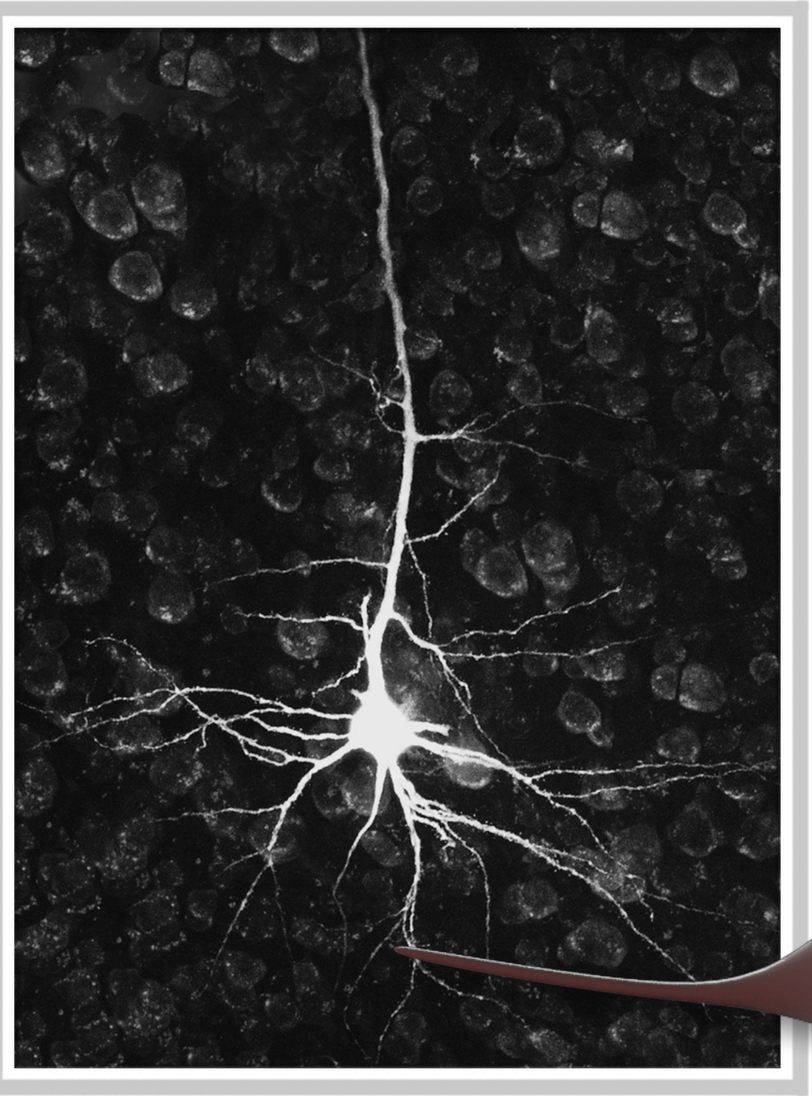
il numero di cellule nervose e la complessità del neuropilo rendono futili i tentativi di comprensione della funzione nervosa su base cellulare?

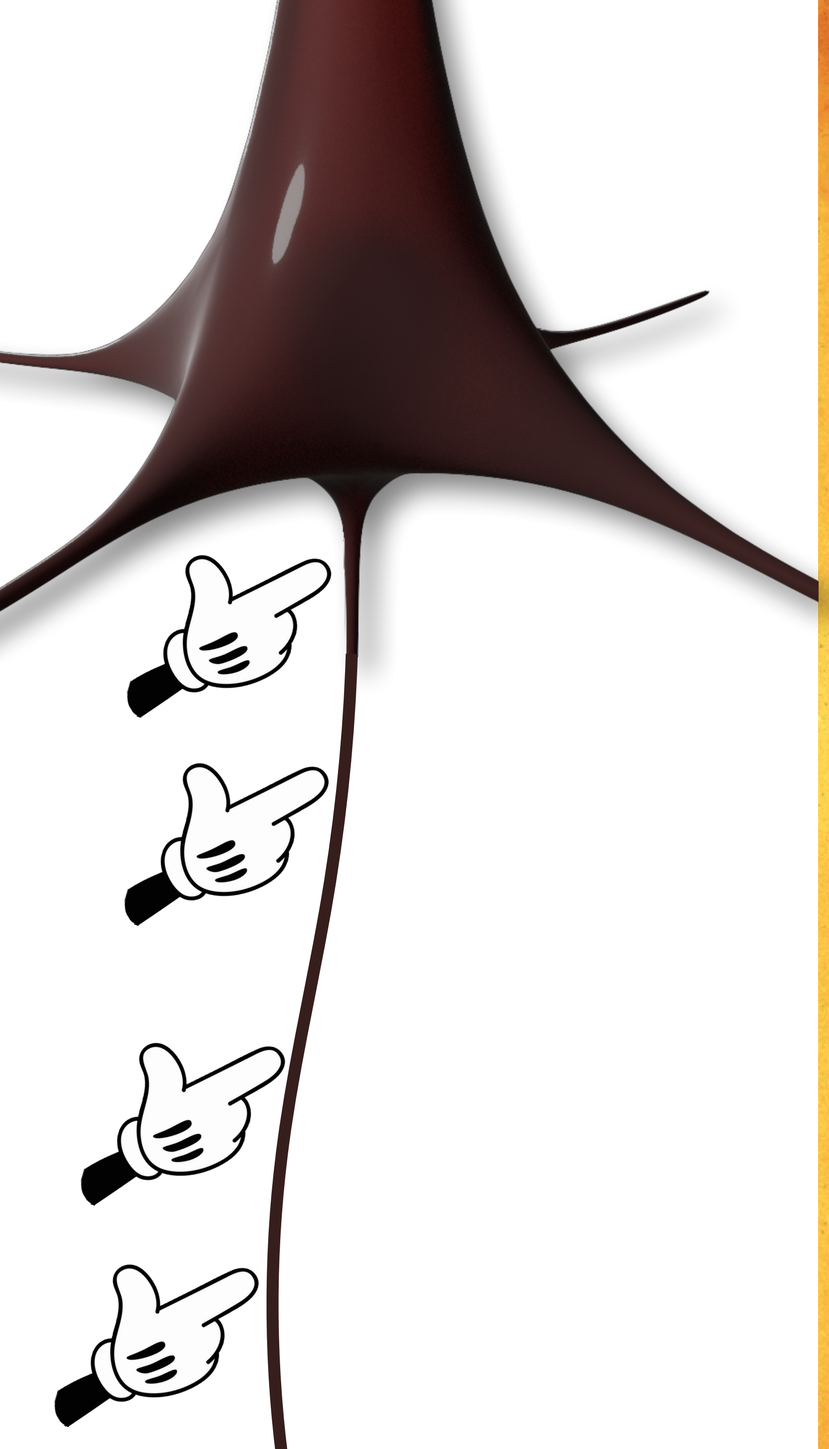
la corteccia è stratificata



è possibile individuale regole di organizzazione in grado di ridurre la complessità dell'immagine d'insieme?

neuroni piramidali

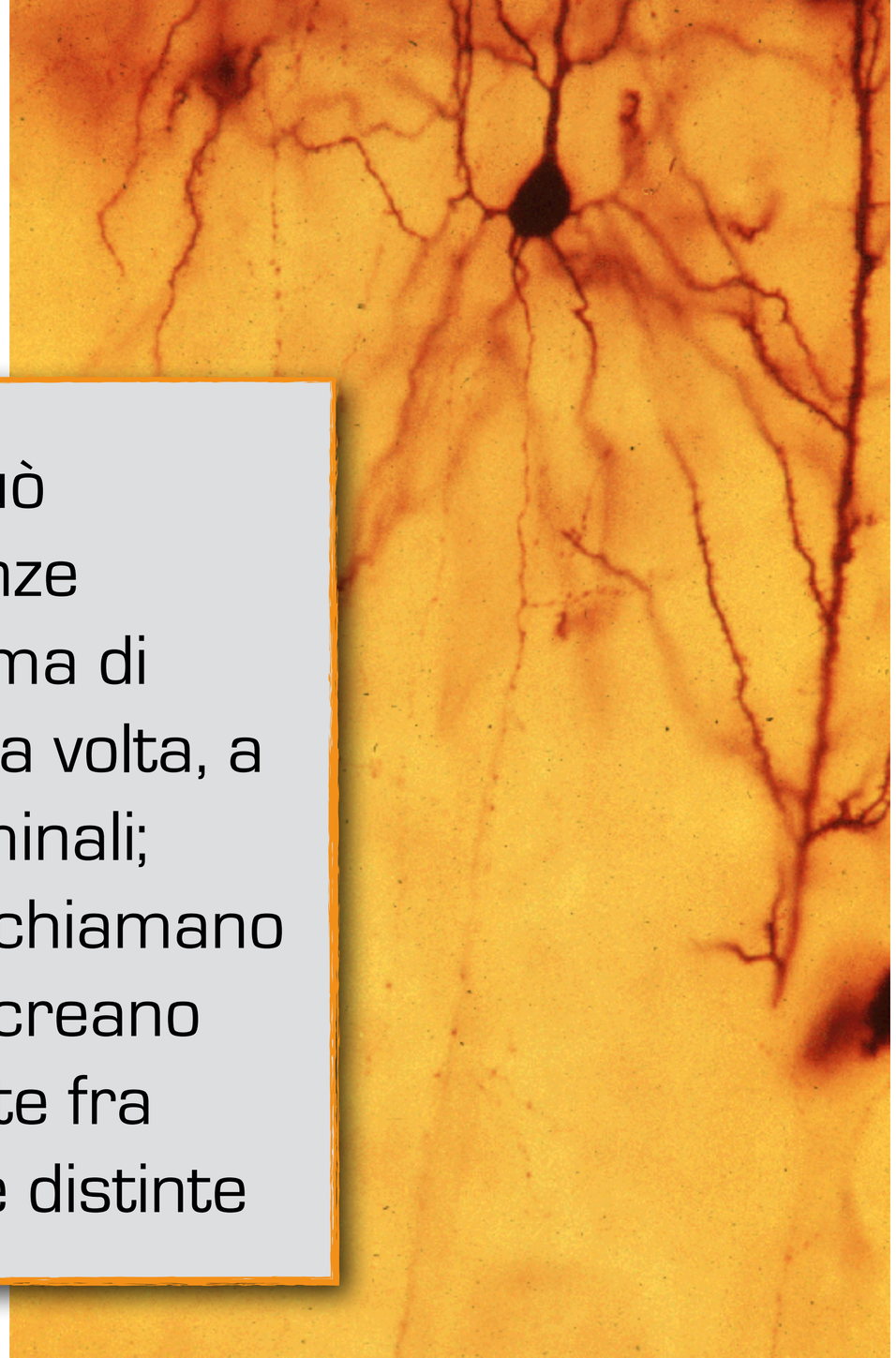




neuroni di proiezione

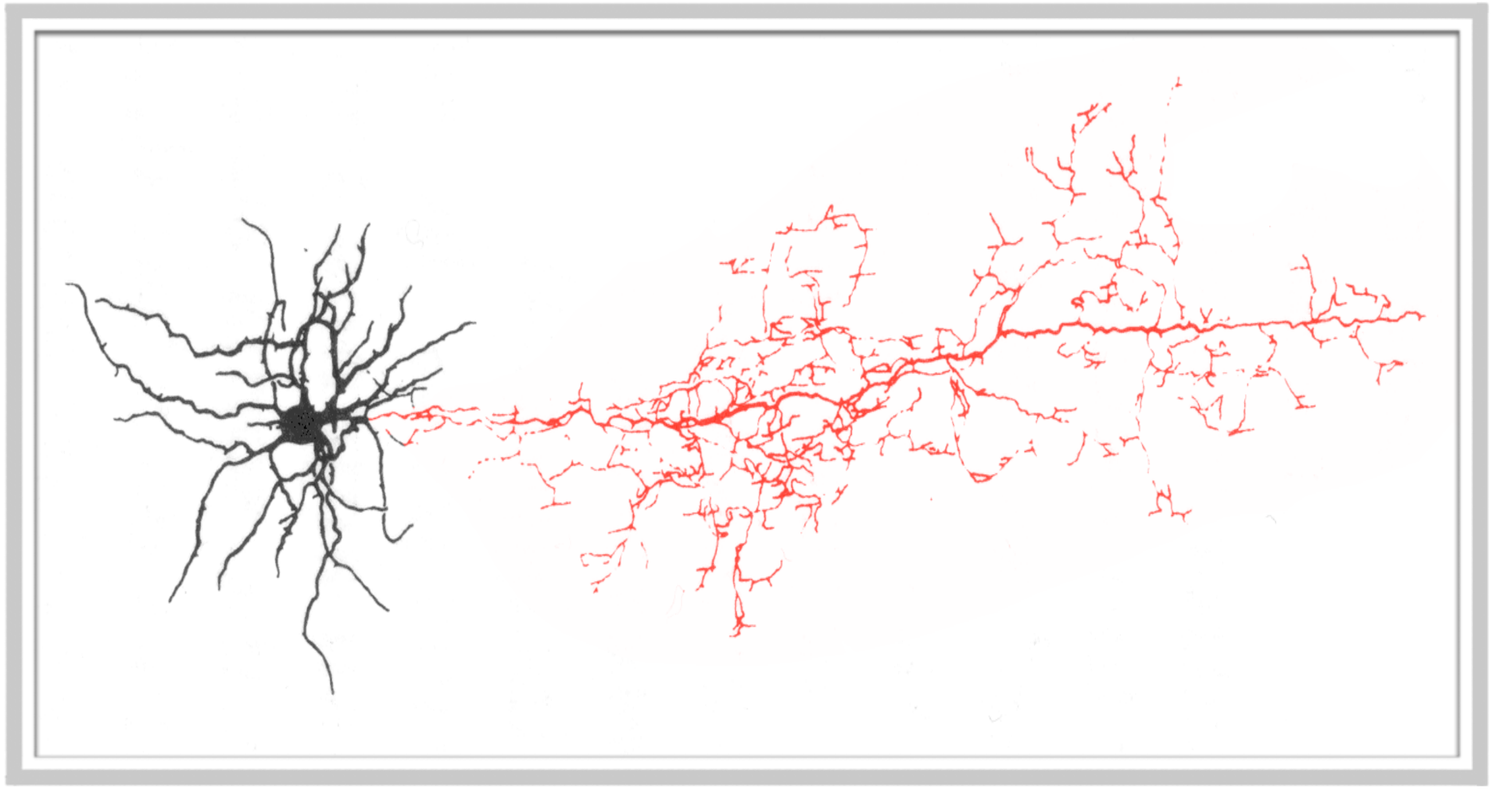
questo assone può percorrere distanze notevolissime prima di dare origine, a sua volta, a ramificazioni terminali; questi neuroni si chiamano “**di proiezione**” e creano connessioni dirette fra strutture nervose distinte

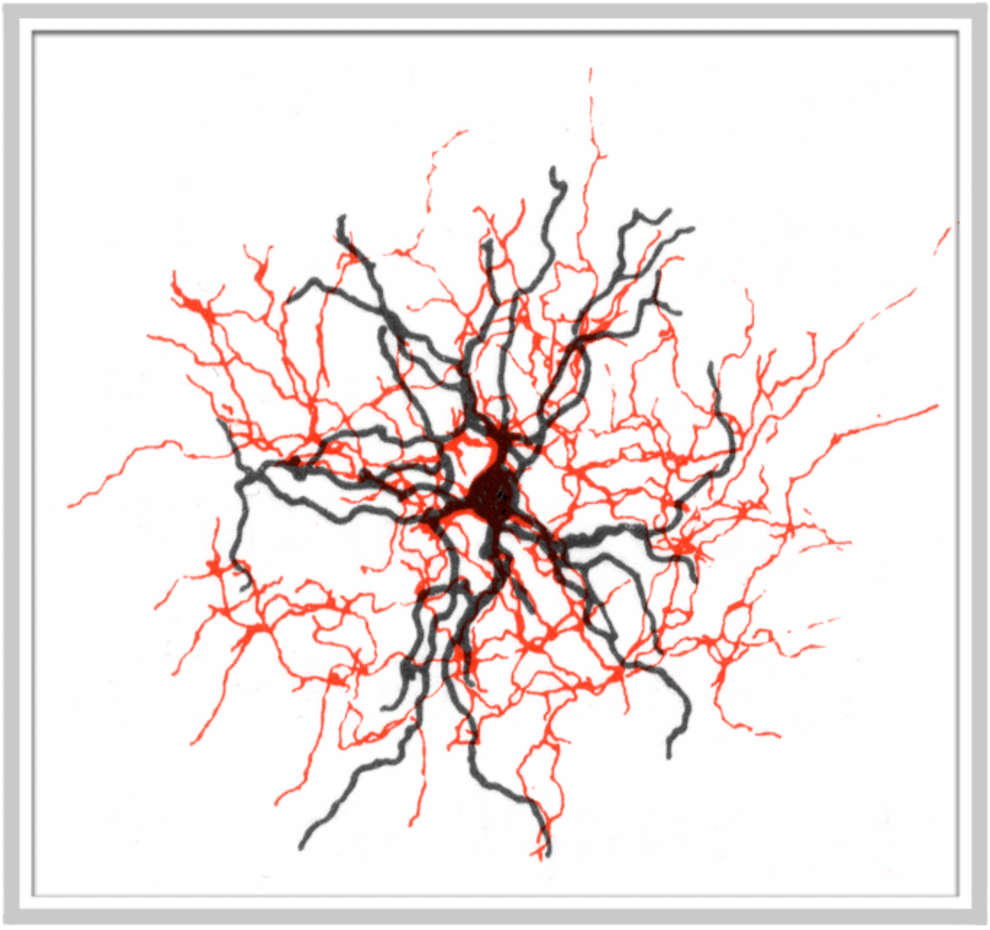
questo assone è “lungo”



questo assone può percorrere distanze notevolissime prima di dare origine, a sua volta, a ramificazioni terminali; questi neuroni si chiamano “**di proiezione**” e creano connessioni dirette fra strutture nervose distinte

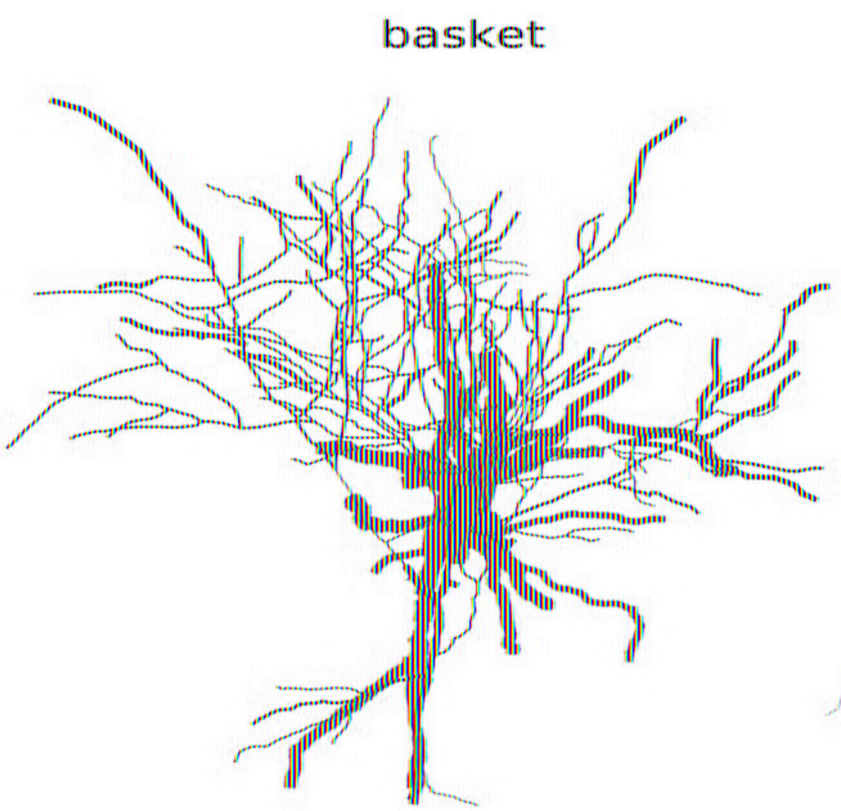
neuroni ad assone “corto”

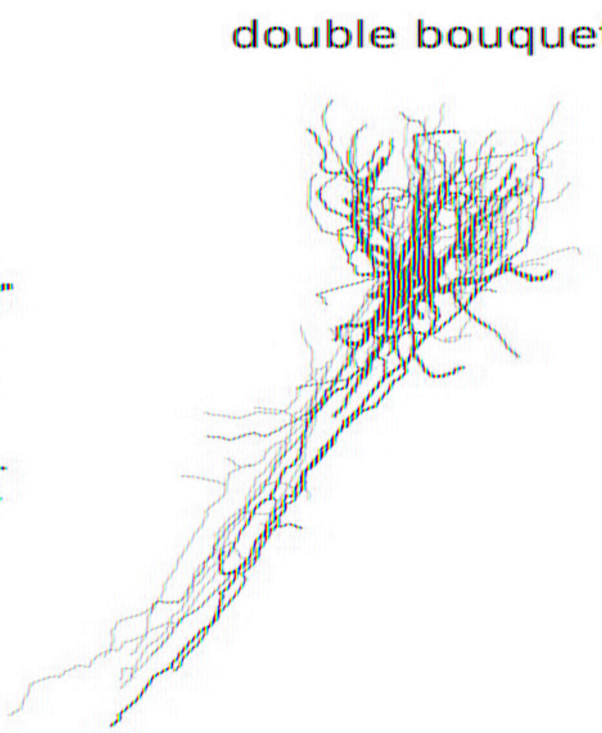


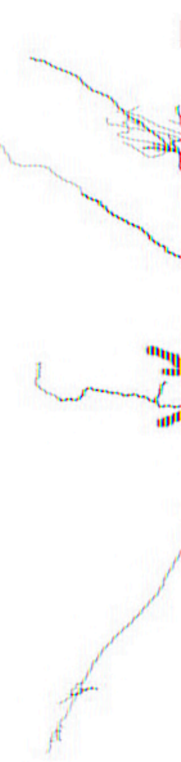


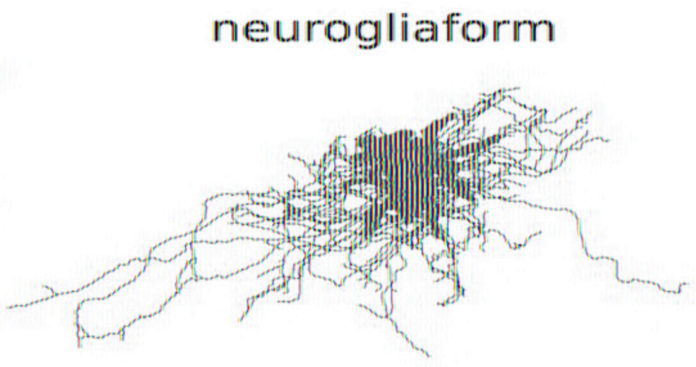
soma e dendriti

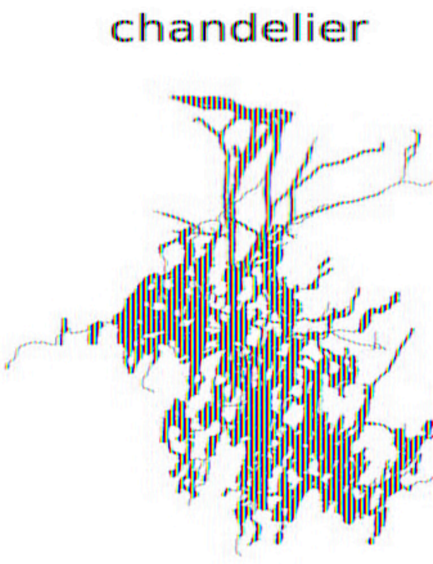
assone e terminazioni







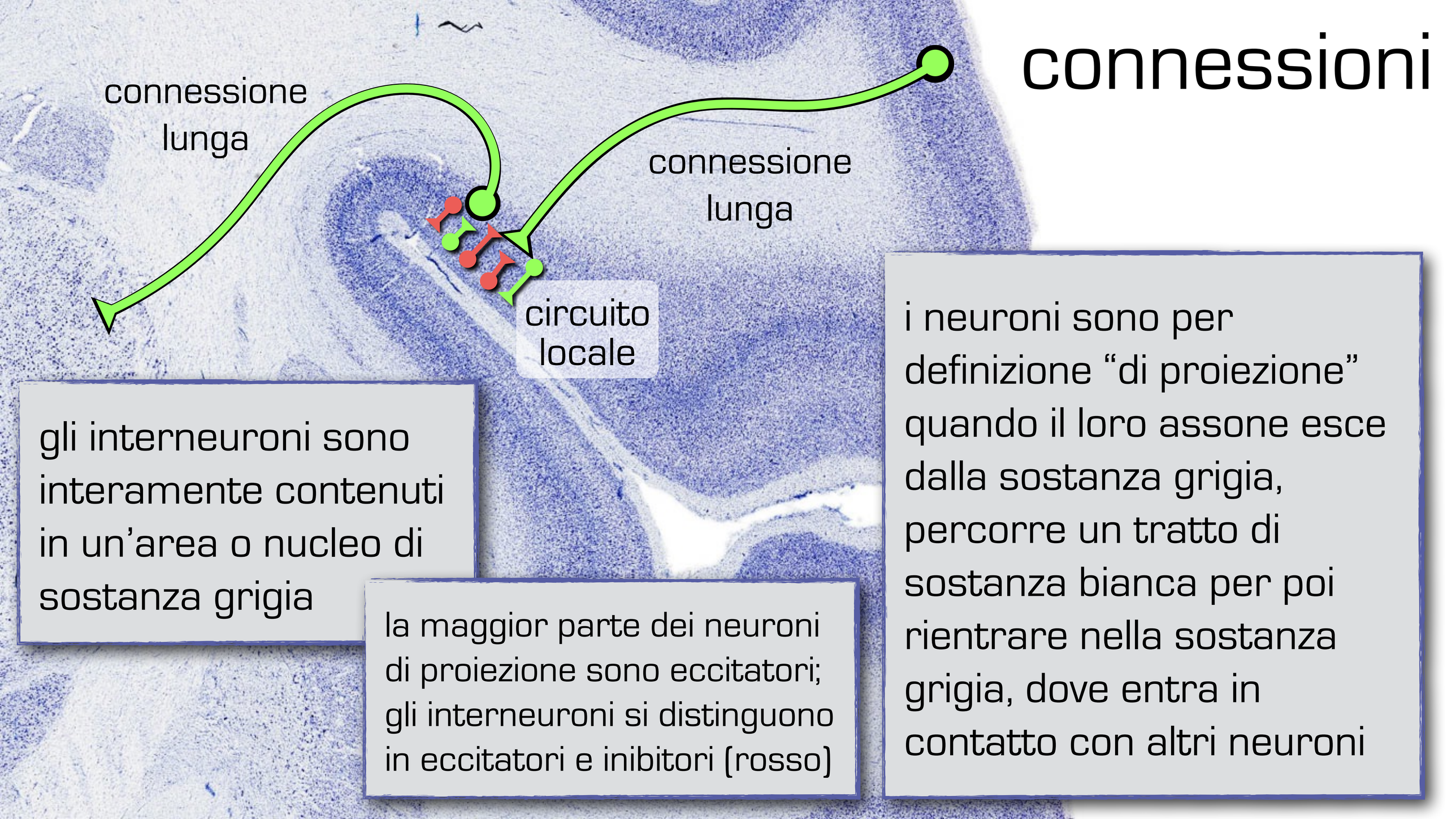




neuroni a circuito locale

interneuroni

connessioni

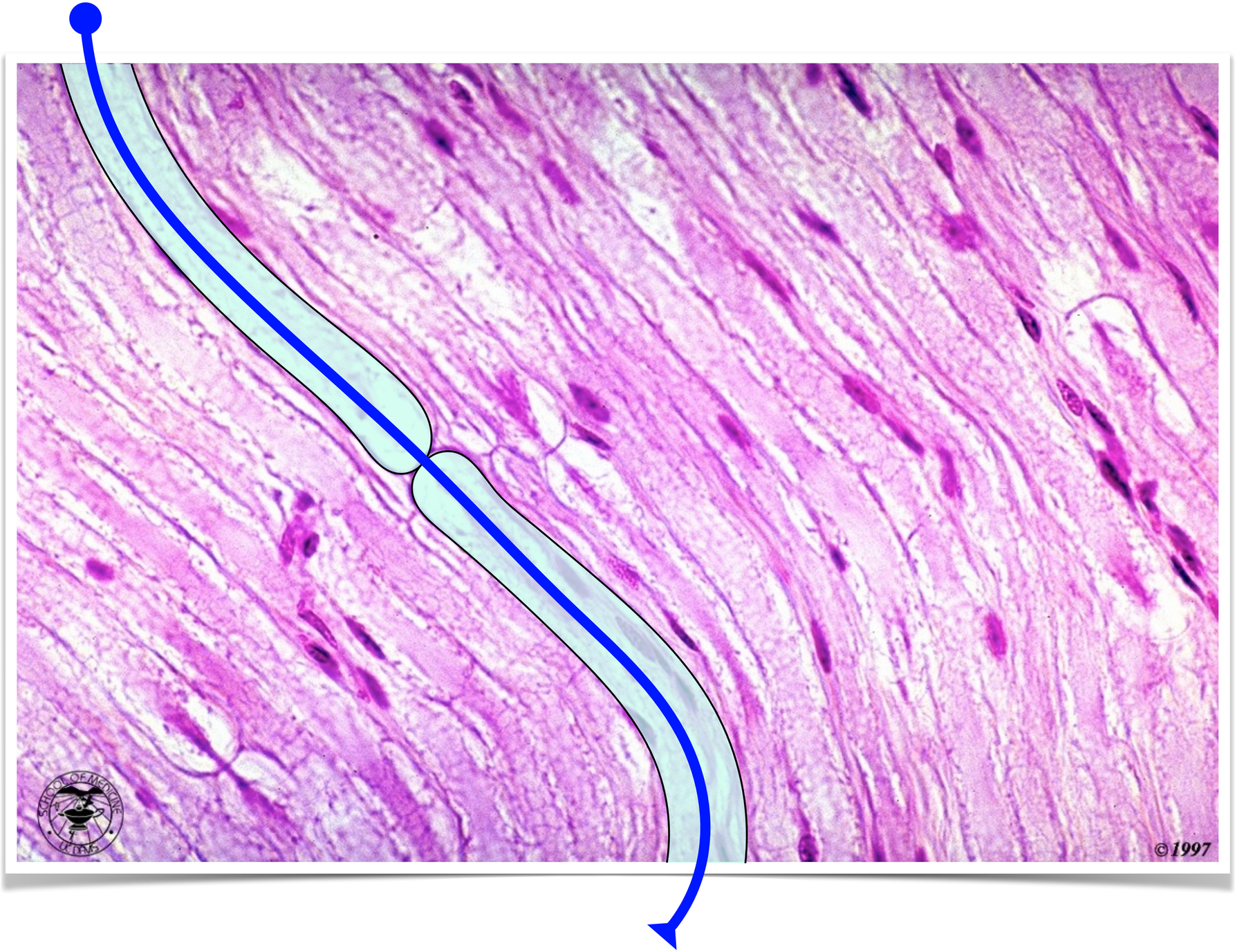


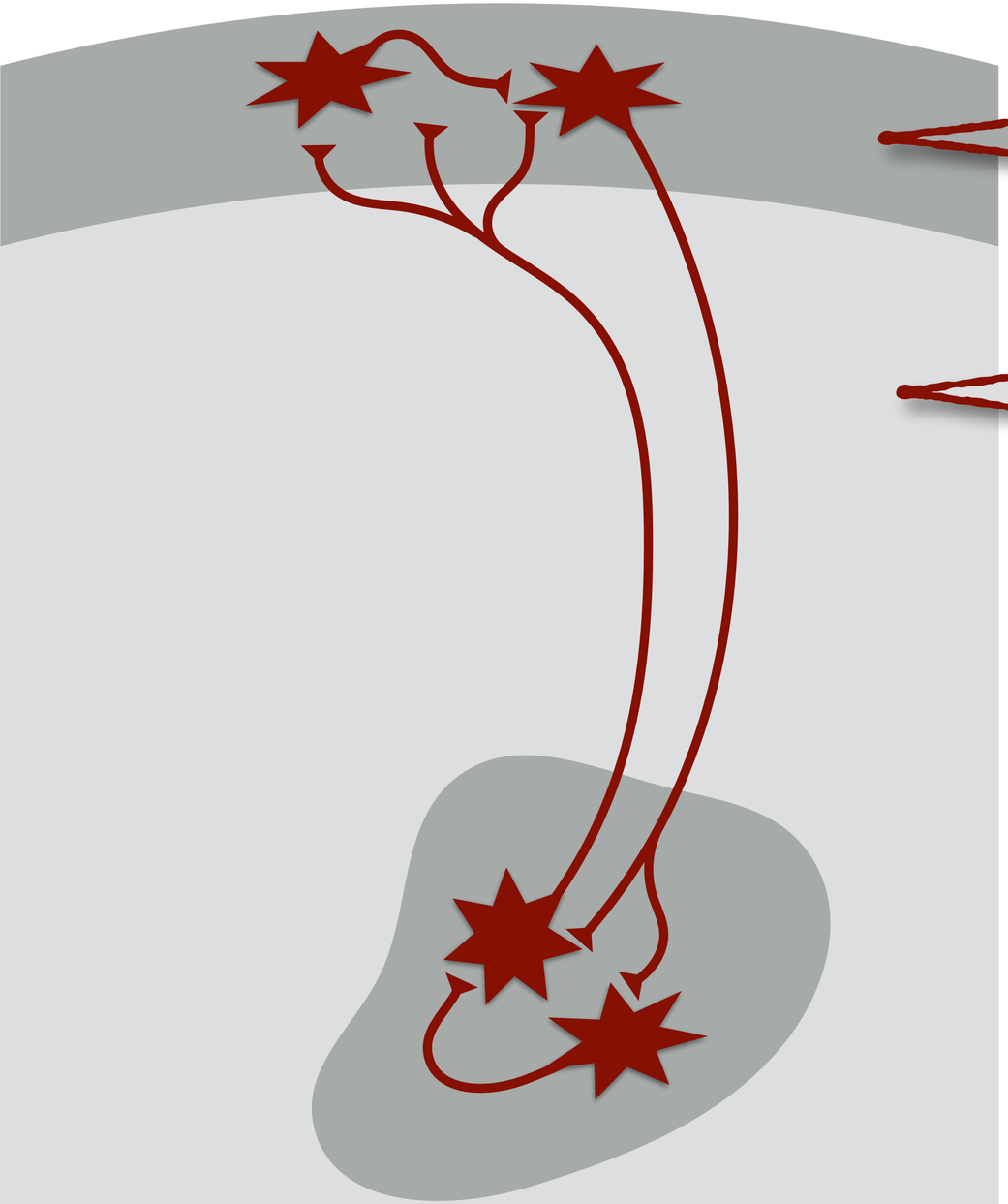
gli interneuroni sono interamente contenuti in un'area o nucleo di sostanza grigia

la maggior parte dei neuroni di proiezione sono eccitatori; gli interneuroni si distinguono in eccitatori e inibitori (rosso)

i neuroni sono per definizione "di proiezione" quando il loro assone esce dalla sostanza grigia, percorre un tratto di sostanza bianca per poi rientrare nella sostanza grigia, dove entra in contatto con altri neuroni

mielina



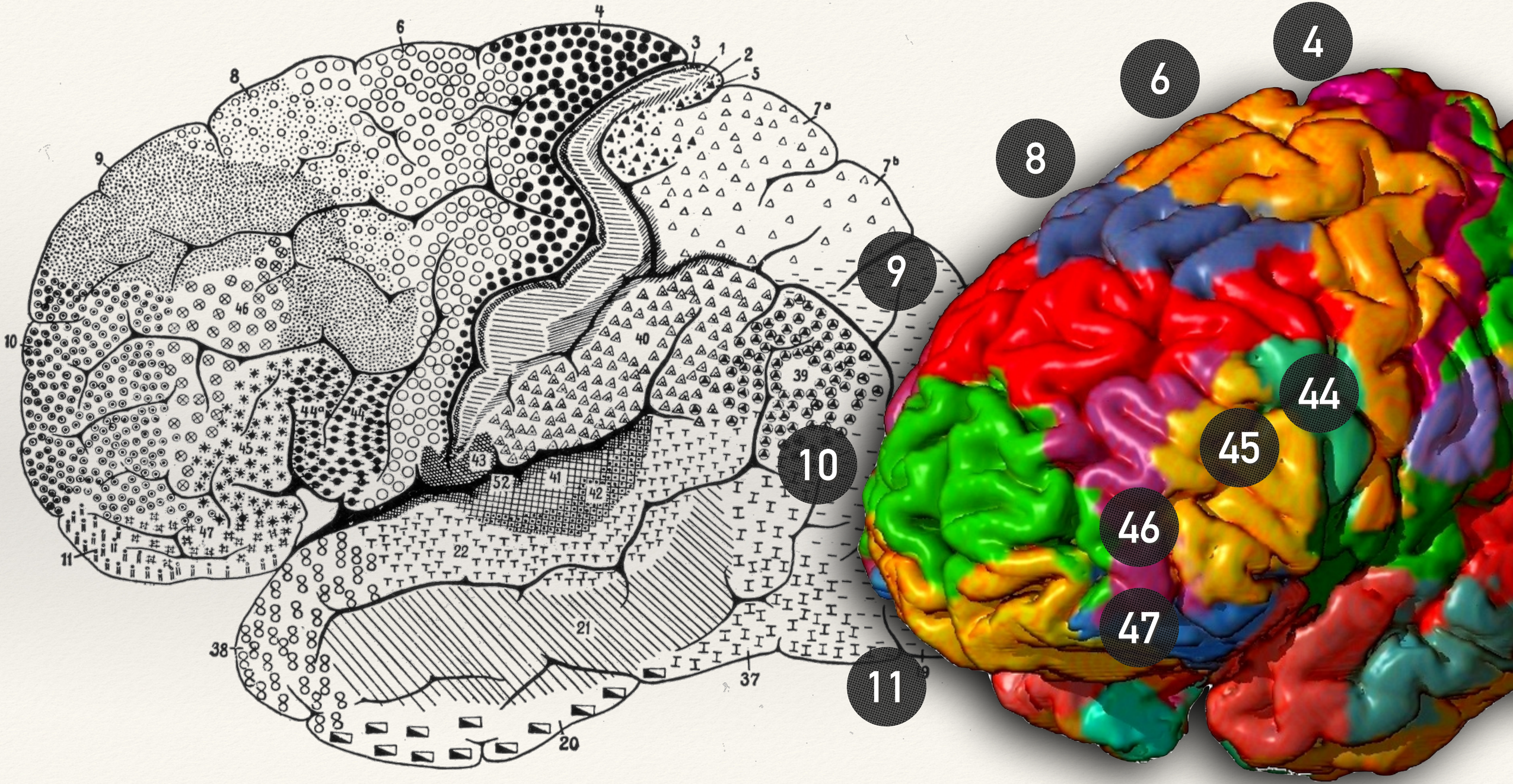


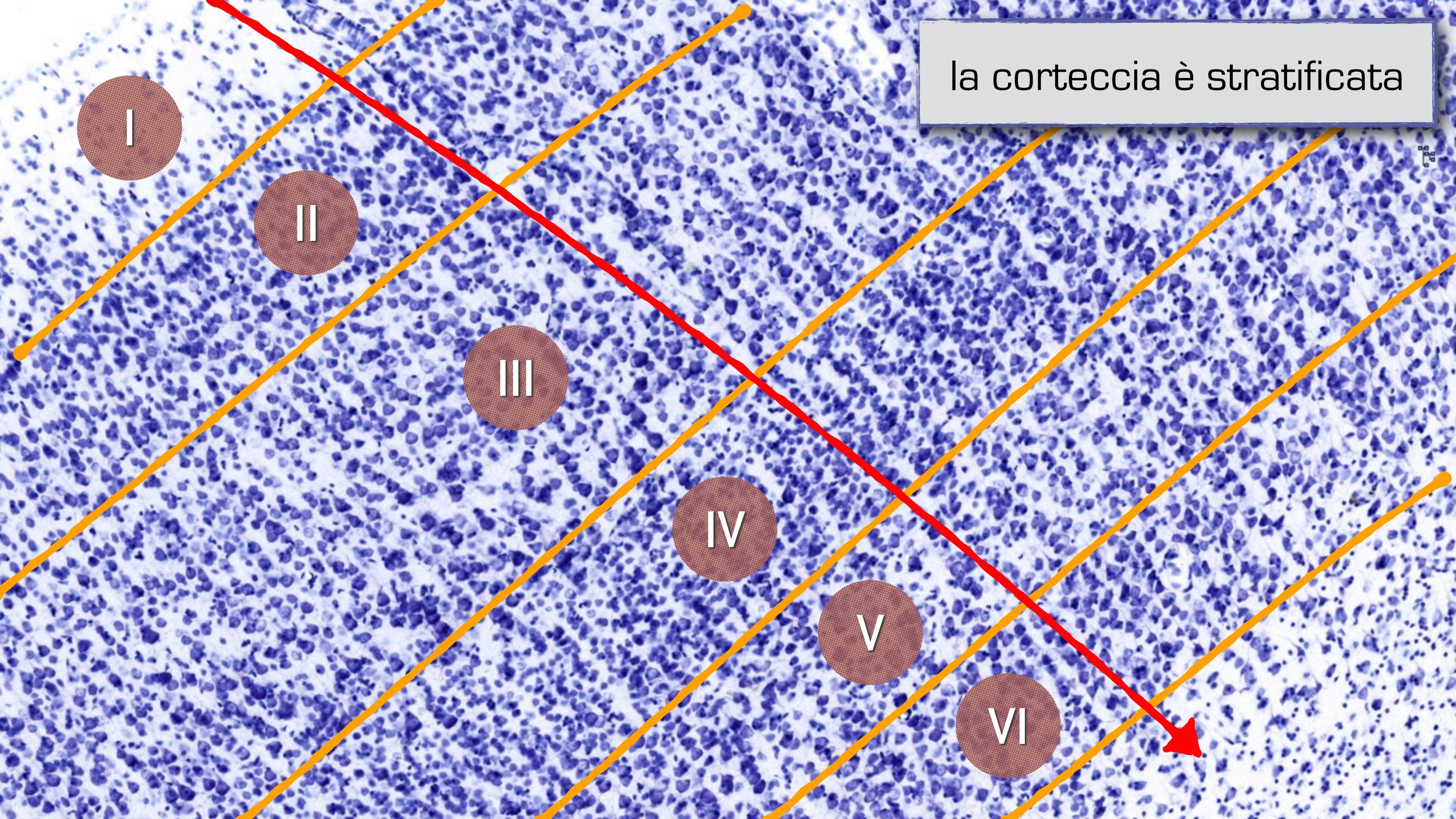
corpi cellulari, dendriti, assoni corti, terminazioni assoniche

assoni lunghi mielinizzati

il contenuto delle sostanze grigia e bianca

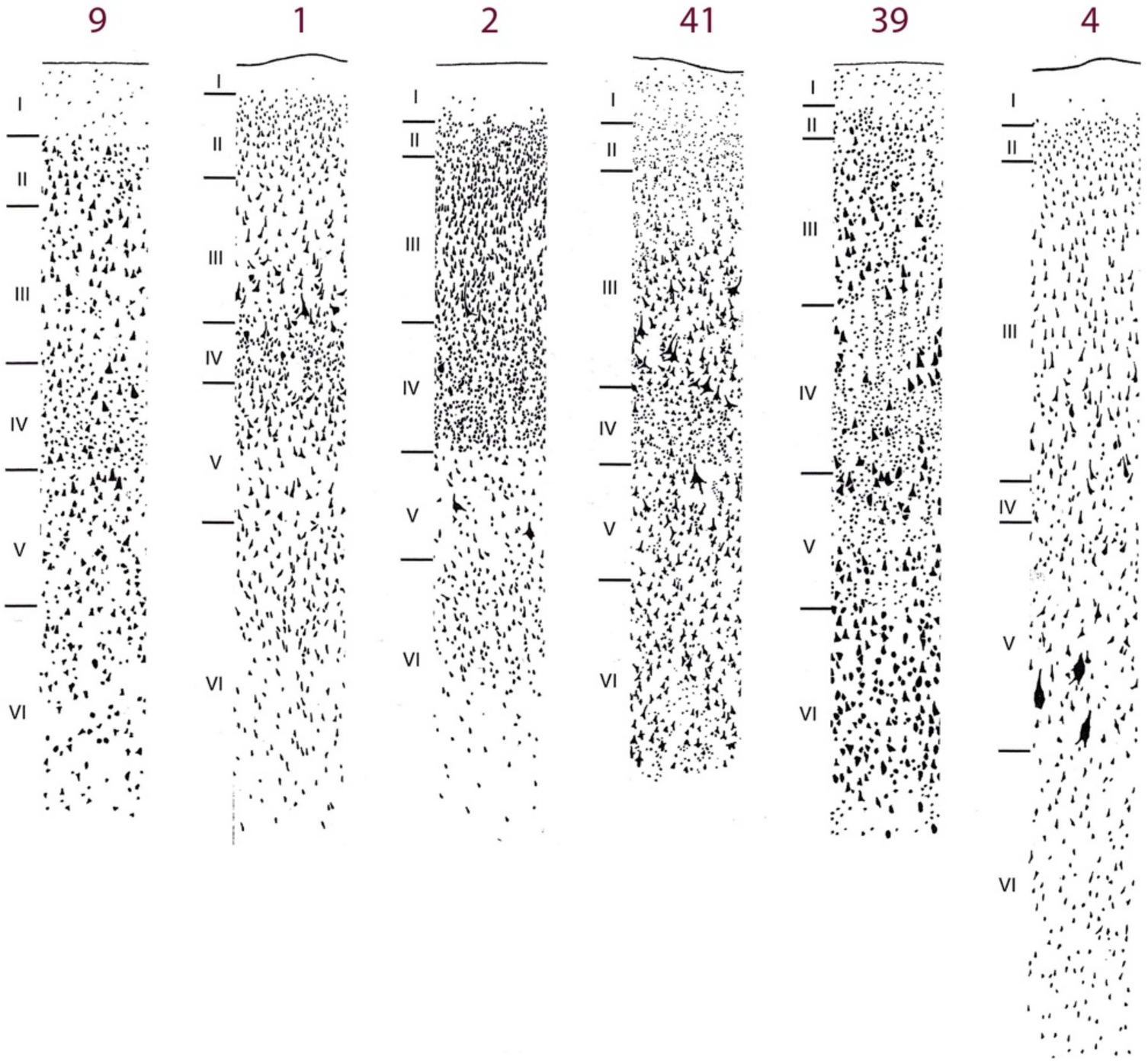
su cosa si basa lo studio dell'architettura del tessuto nervoso?



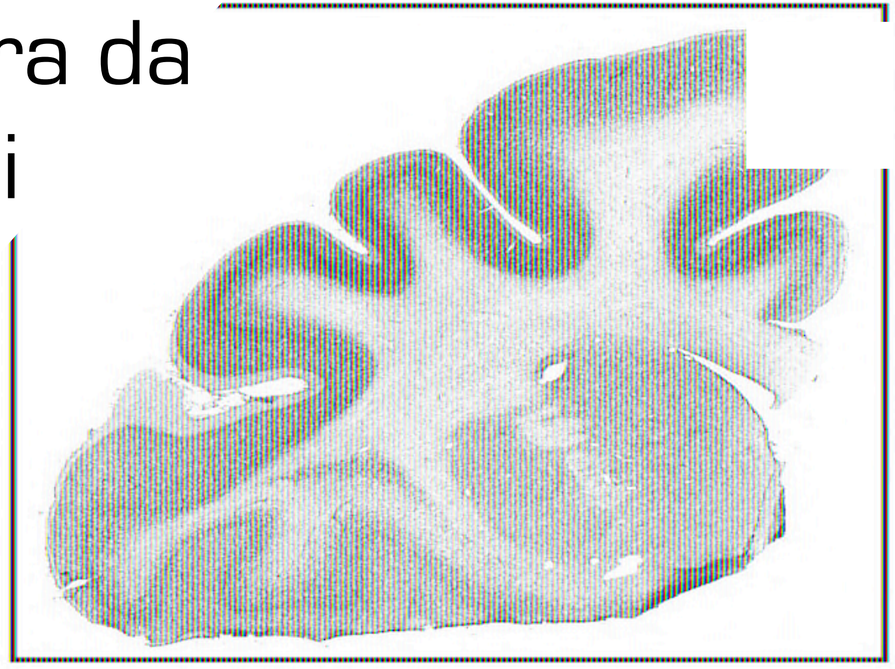

la corteccia è stratificata
I
II
III
IV
V
VI

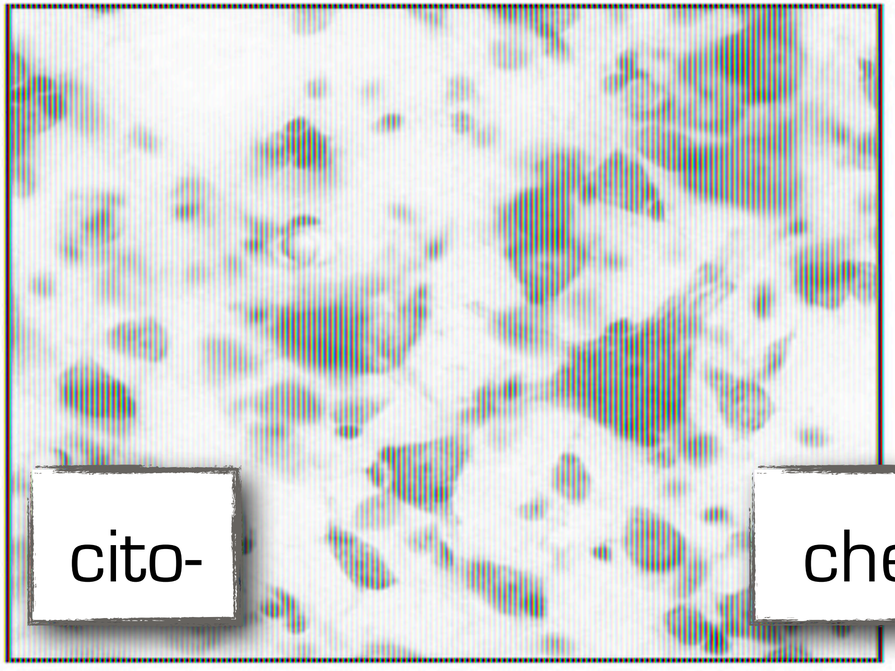
Brodmann

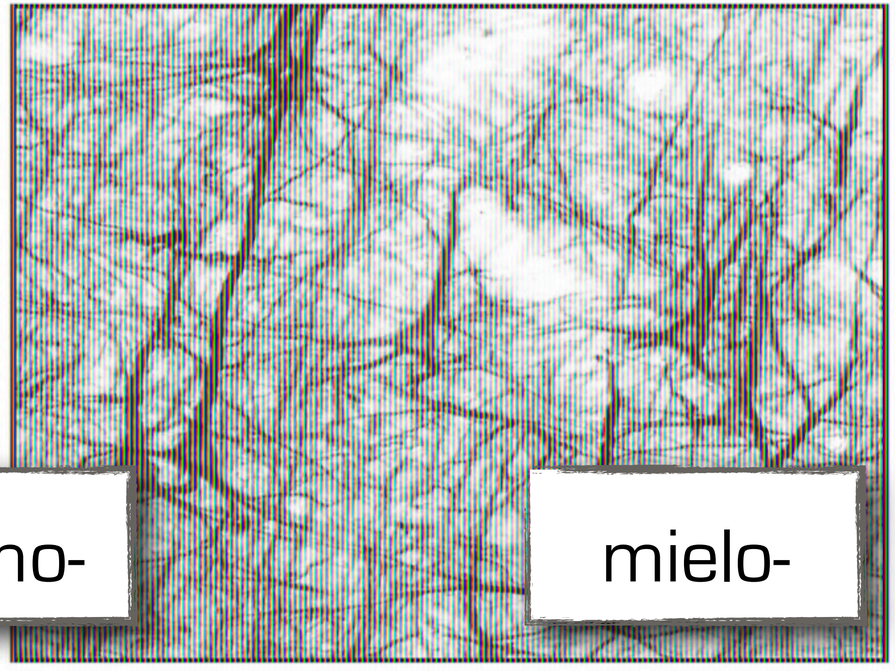
aree corticali numerate in base allo spessore e organizzazione degli strati



architettura da più punti di vista... 👀



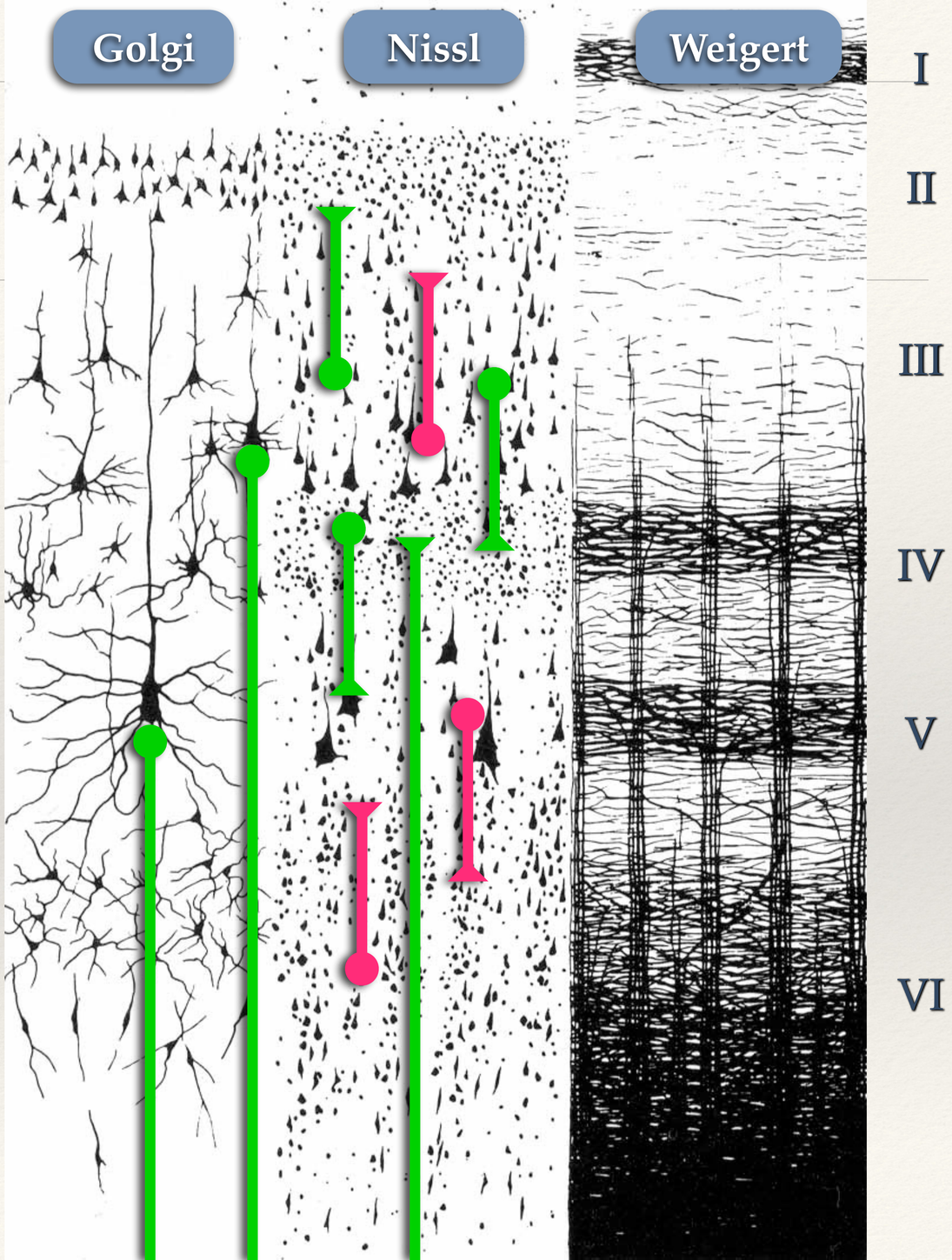




altre “semplificazioni”

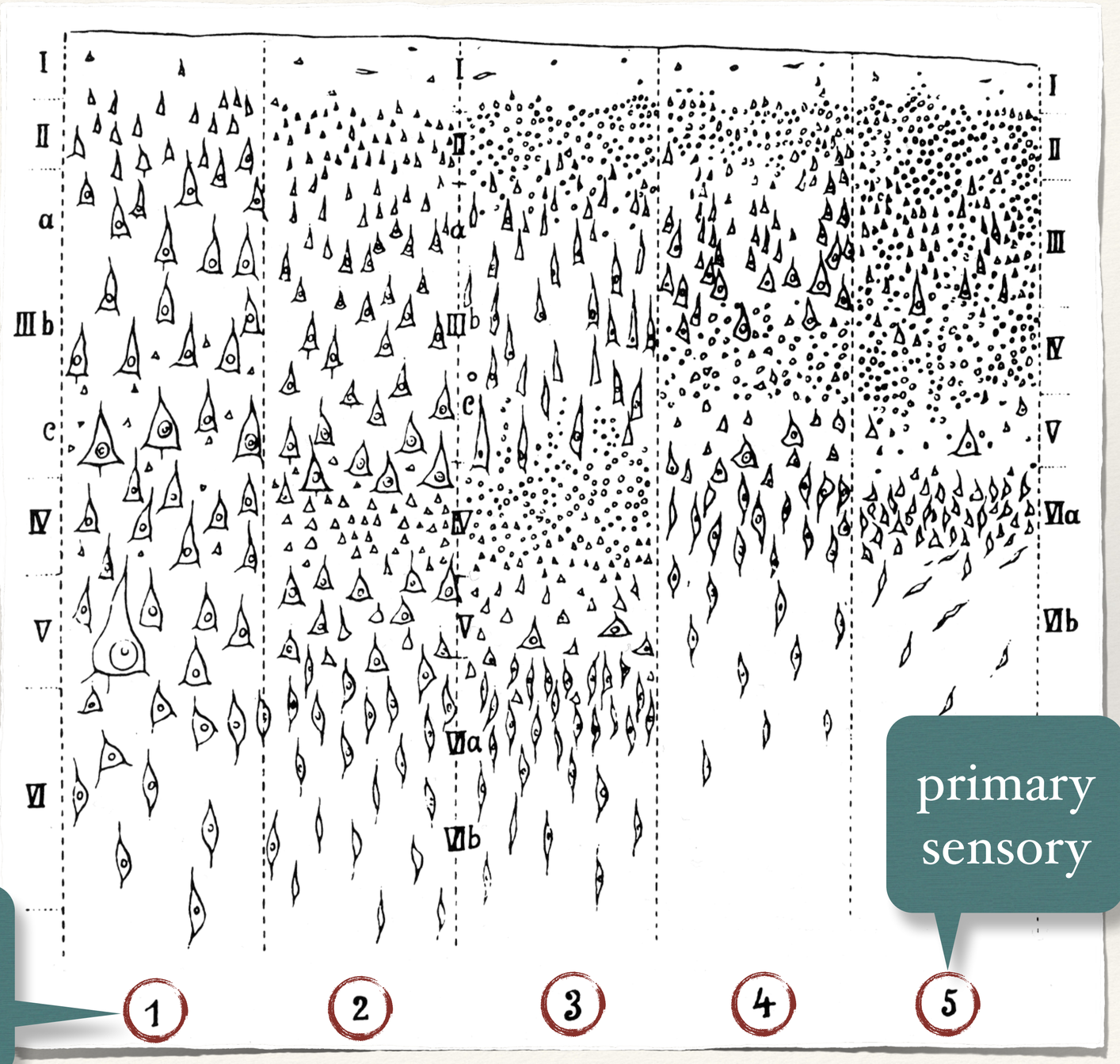
cortical I/O

- **input**
  most of the cortical afferents end on layer IV interneurons
- **integration**
  local circuit neurons (both excitatory and inhibitory) process information
- **output**
  layer III & V pyramidal (projection) neurons carry signals away



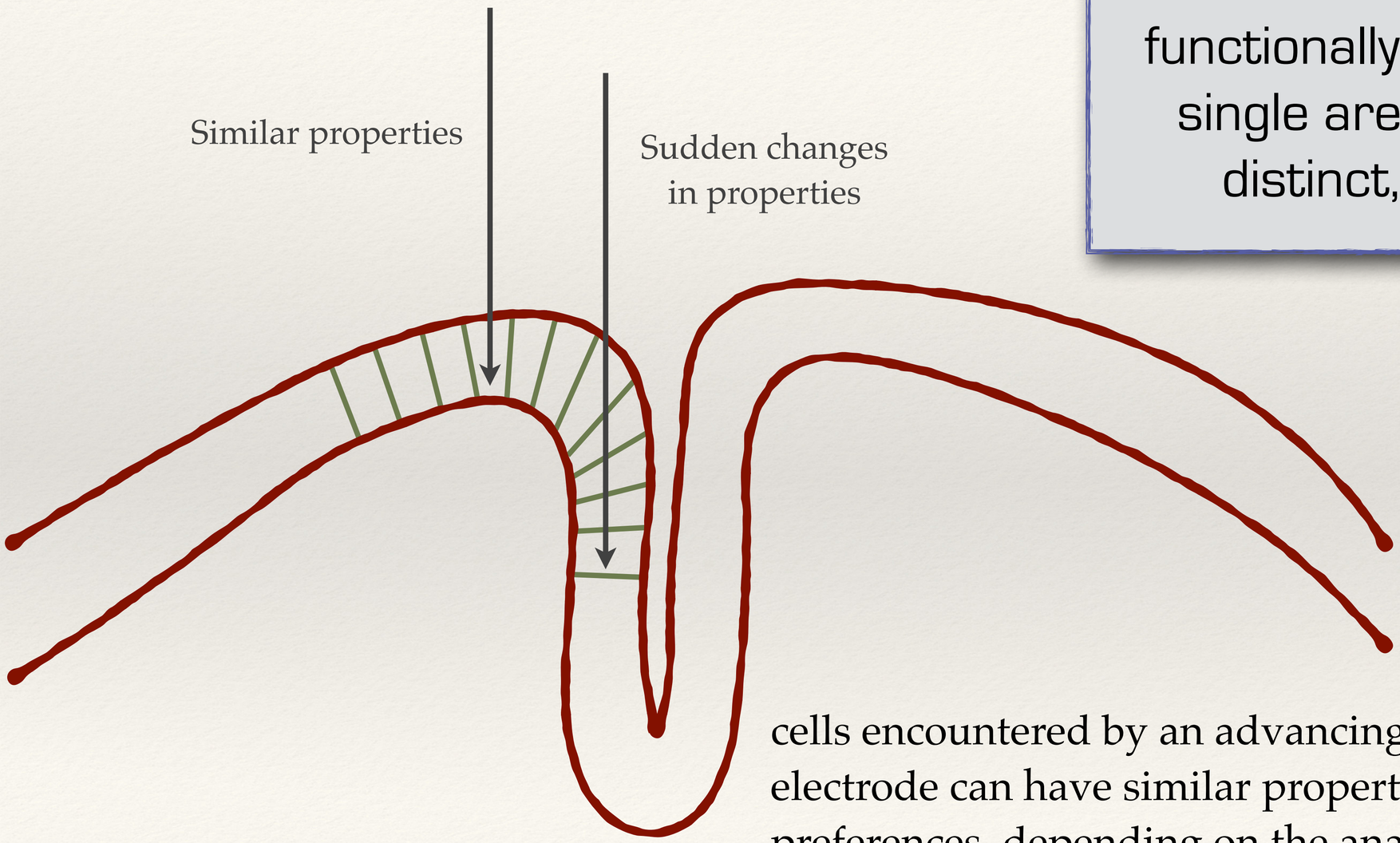
Von Economo

1. heterotypical, agranular
2. homotypical, frontal
3. homotypical, parietal
4. homotypical polar
5. heterotypical, granular



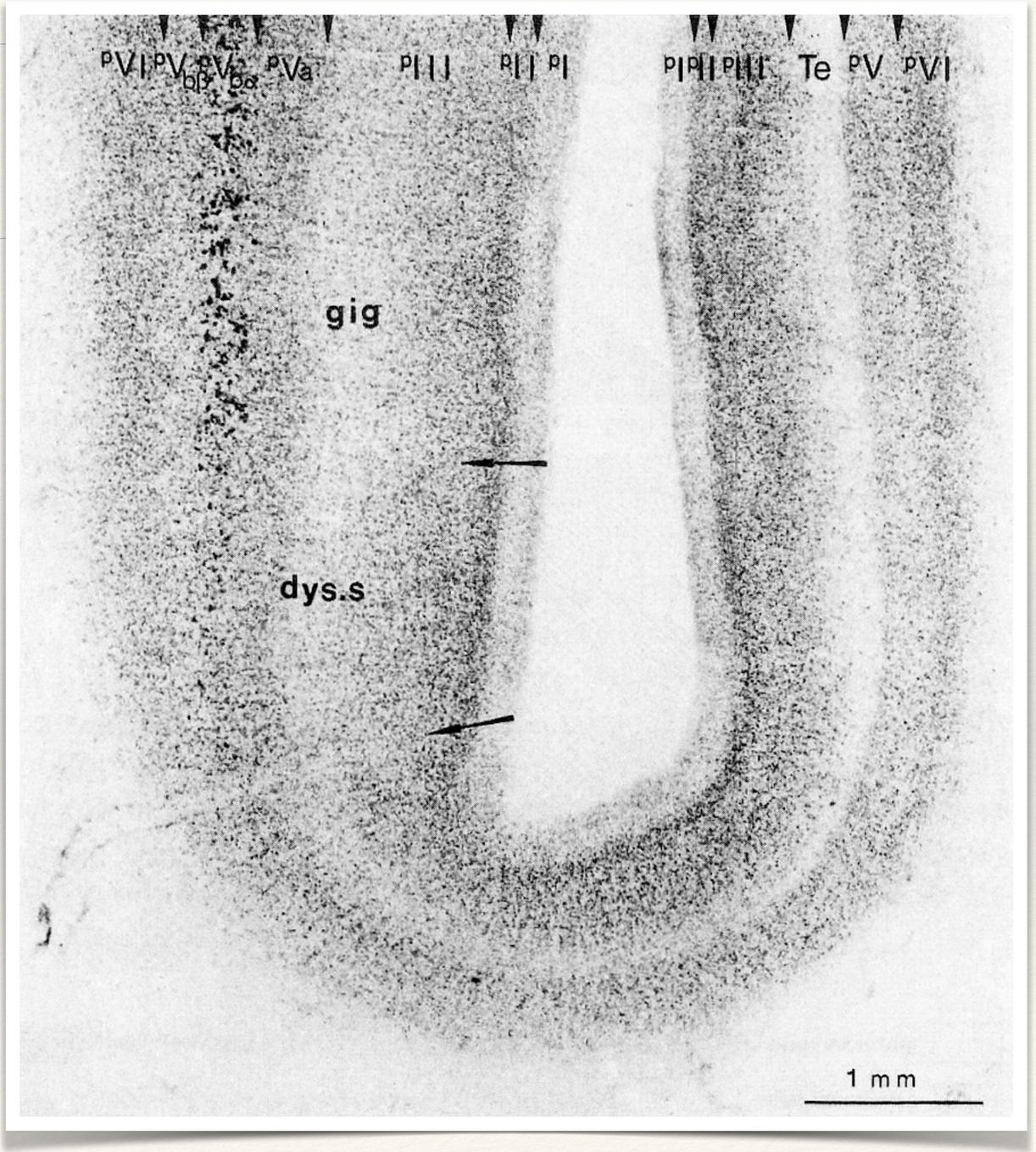
la corteccia è modulare

cortical areas are often, and perhaps typically, further divided into two or more sets of modules or columns of functionally related neurons, so that single areas can mediate several distinct, but related functions

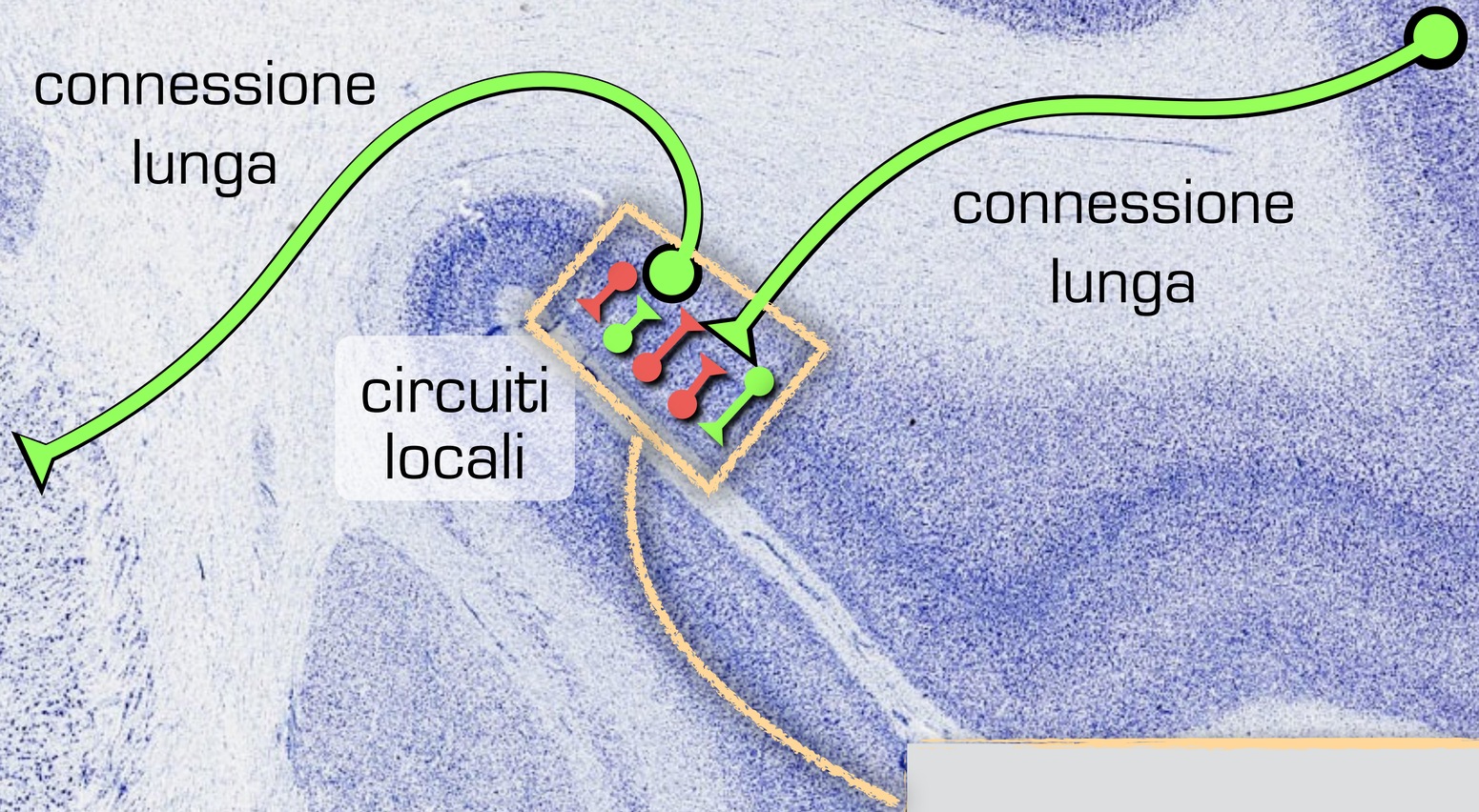


cells encountered by an advancing (recording or stimulating) electrode can have similar properties, or can regularly shift in preferences, depending on the anatomical location of the penetration

M1-S1 transition



definizione di area corticale



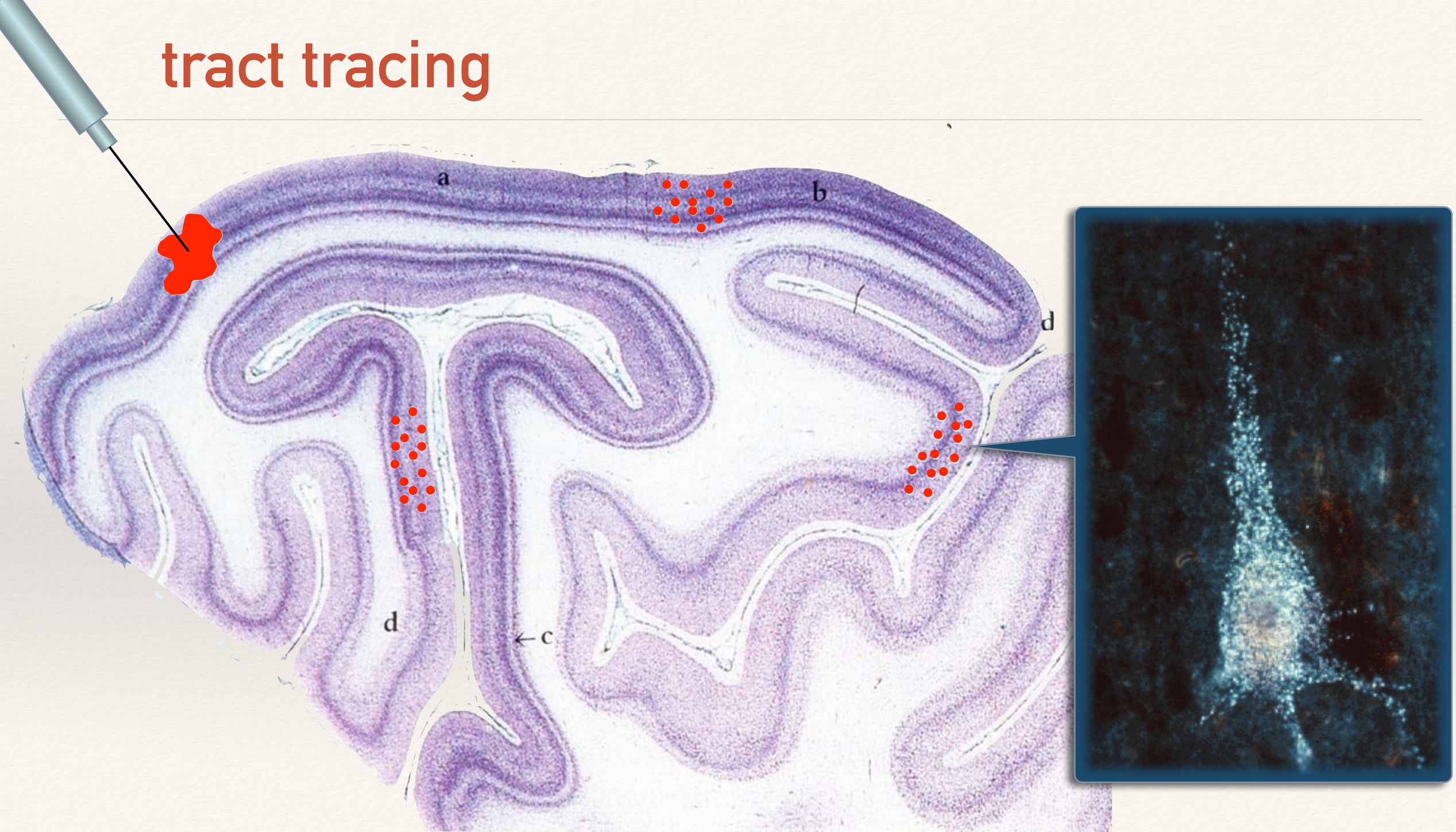
un’area corticale è una porzione di corteccia caratterizzata da una particolare architettura, da un pattern di connessioni assonali con altri centri nervosi e da specifiche proprietà elettrofisiologiche dei suoi neuroni

un grande debito di riconoscenza verso le specie animali su cui è basata la ricostruzione dell'organizzazione morfologica e funzionale della corteccia e delle altre strutture nervose

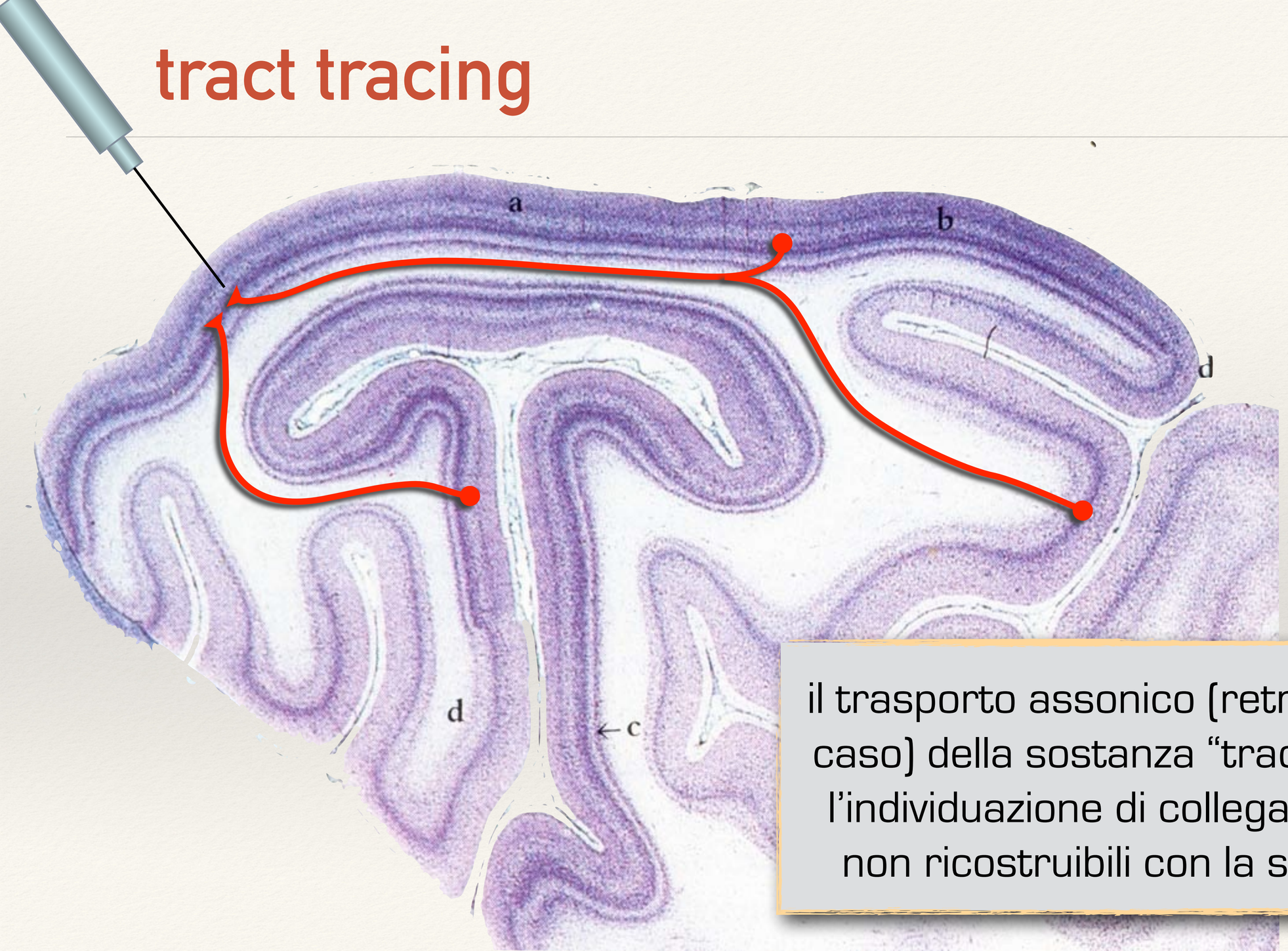
nei modelli animali:

- **aree corticali (e nuclei sottocorticali)**
  - architettura (istologia, immunoistochimica)
  - proprietà funzionali delle cellule (elettrofisiologia)
- **connessioni**
  - identificazione dei punti di partenza e di arrivo (tract tracing)

tract tracing



tract tracing



il trasporto assonico (retrogrado, in questo caso) della sostanza “tracciante” consente l’individuazione di collegamenti a distanza non ricostruibili con la sola microscopia

la caratterizzazione istologica/elettrofisiologica delle aree e la identificazione delle principali connessioni lunghe ha consentito di ricostruire l'organizzazione di interi sistemi funzionali

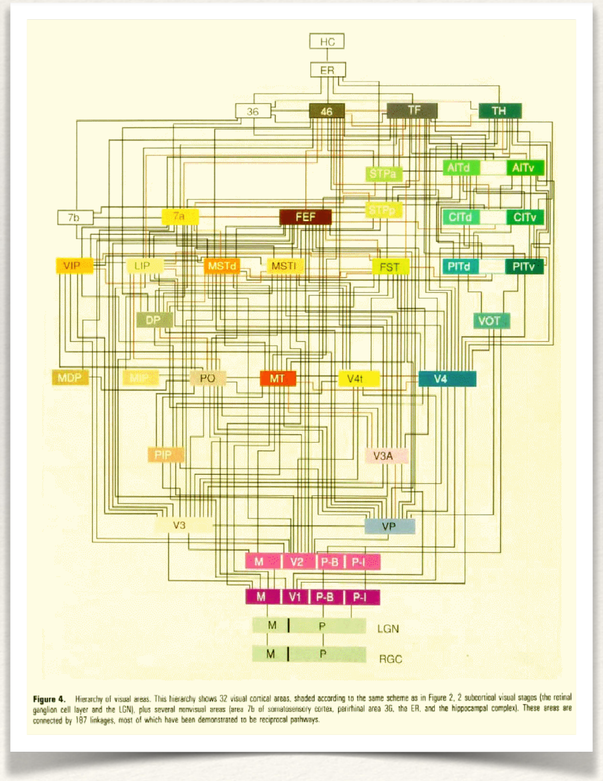
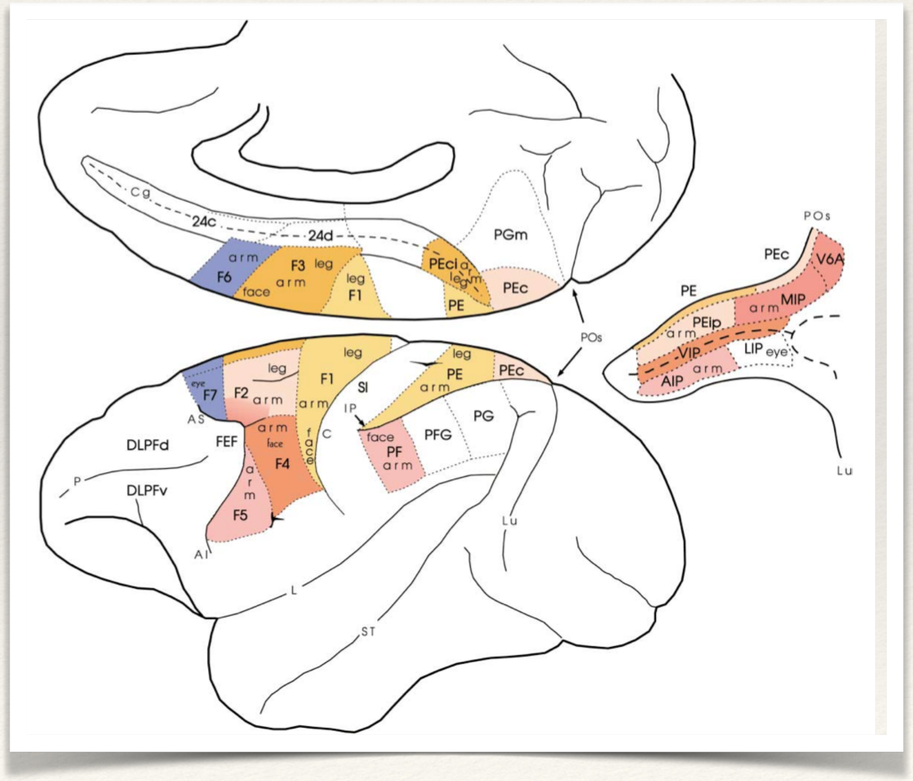
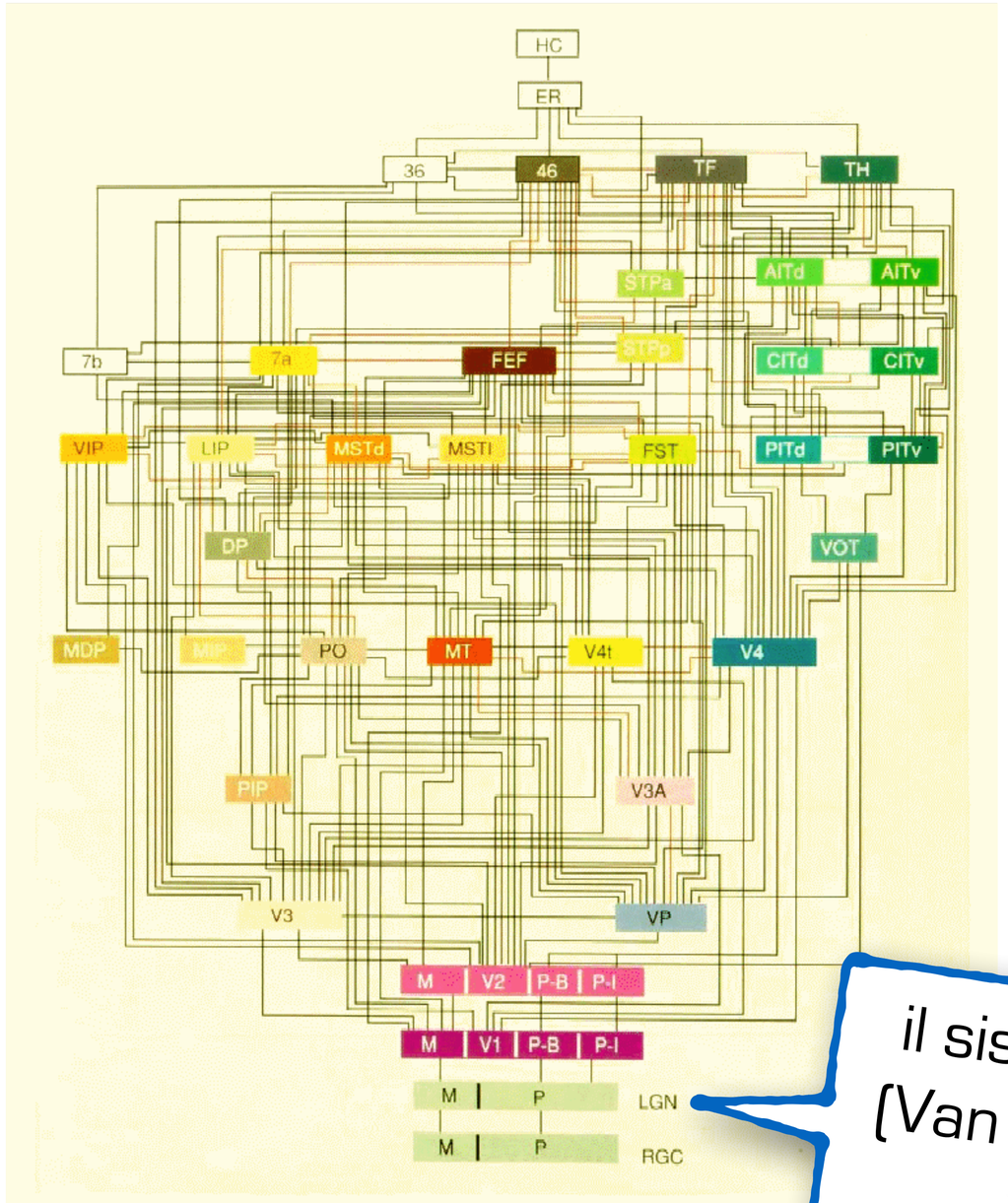


Figure 4. Hierarchy of visual areas. This hierarchy shows 32 visual cortical areas, shaded according to the same scheme as in Figure 2, 2 subcortical visual stages (the retinal ganglion cell layer and the LGN), plus several nonvisual areas (area 7b of somatosensory cortex, parahippocampal area 36, the ER, and the hippocampal complex). These areas are connected by 187 linkages, most of which have been demonstrated to be reciprocal pathways.





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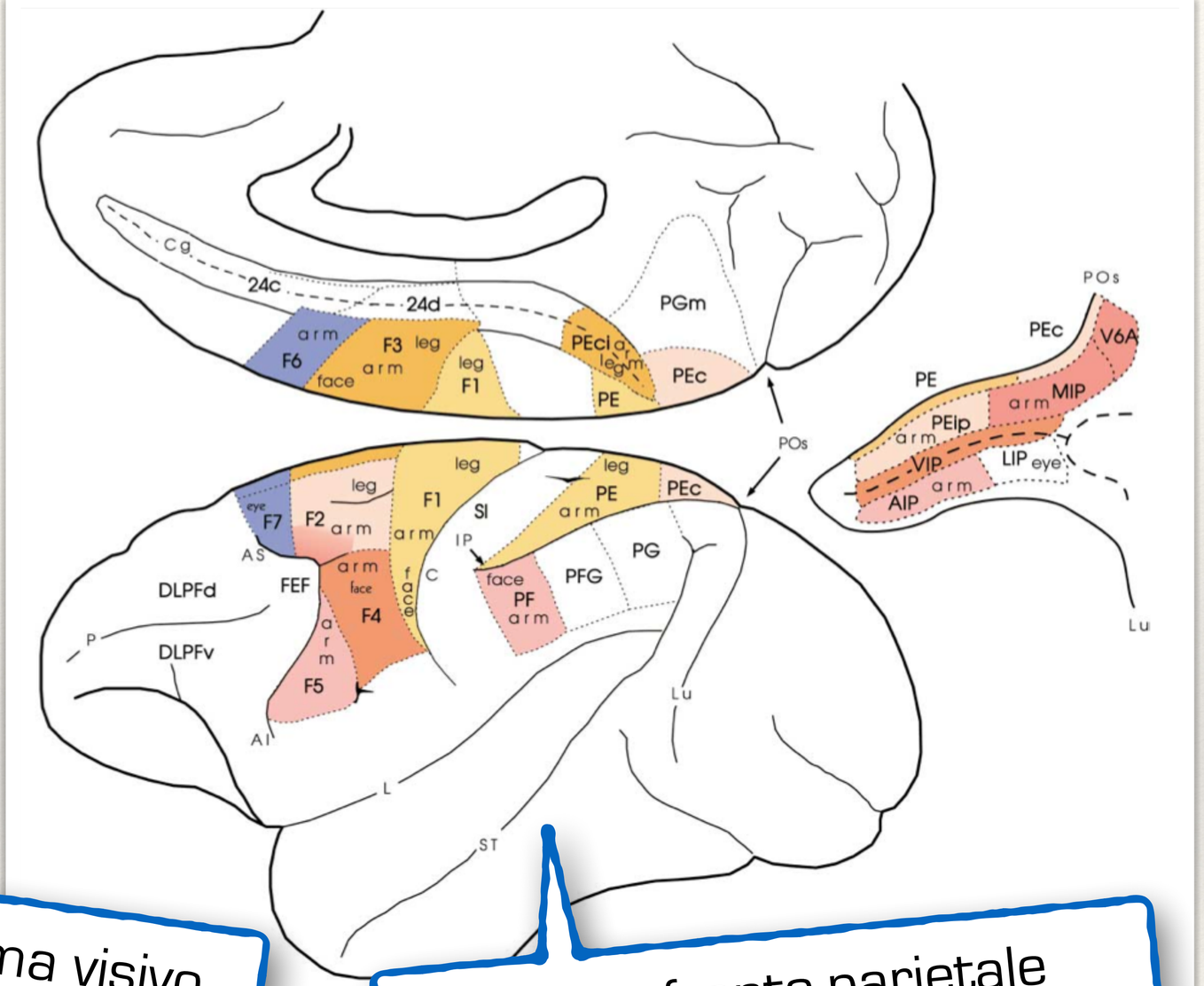


il sistema visivo (Van Essen et al. 1991)

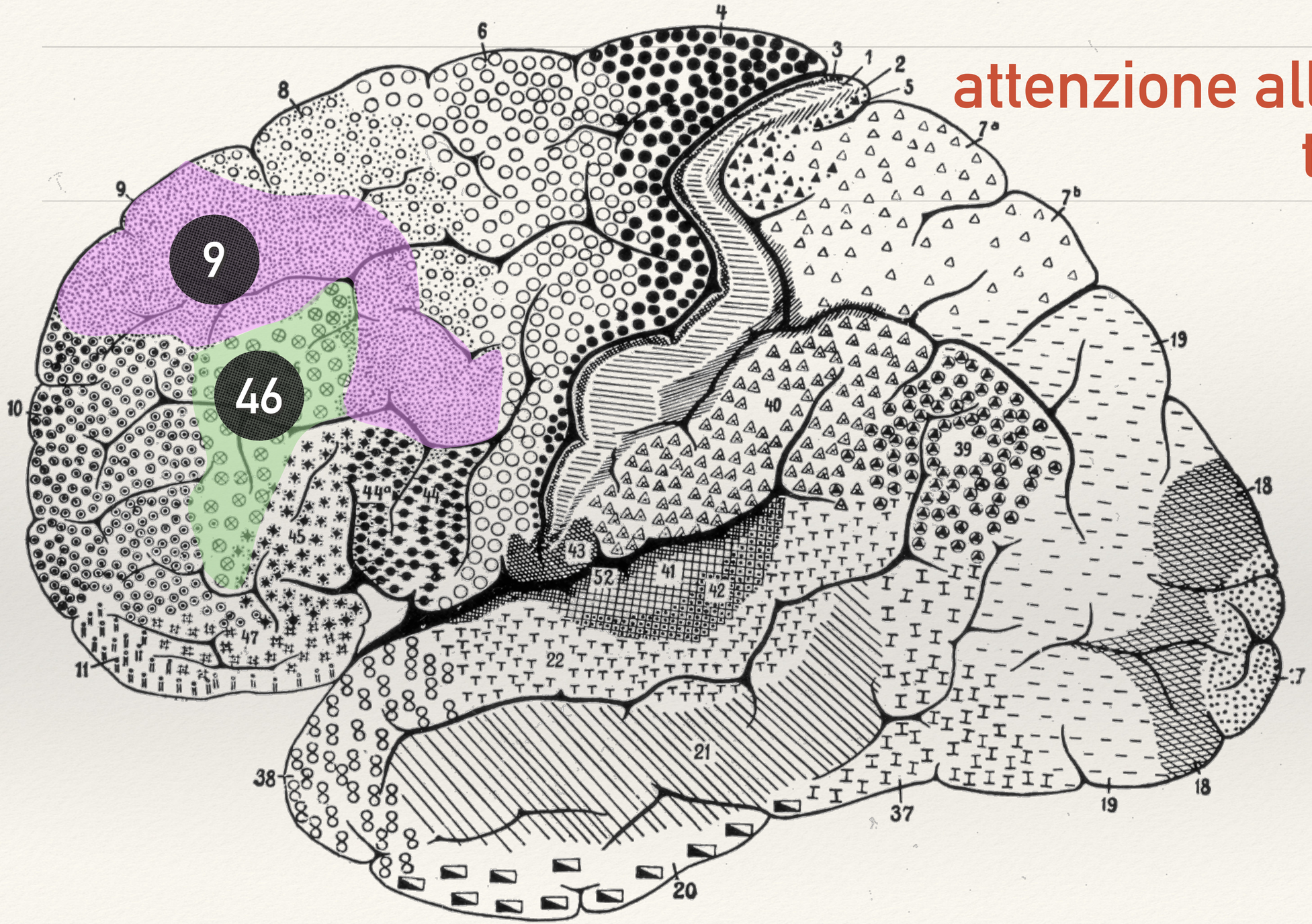
la rete franto-parietale (Rizzolatti & Luppino 2001)

modelli animali

cervello umano

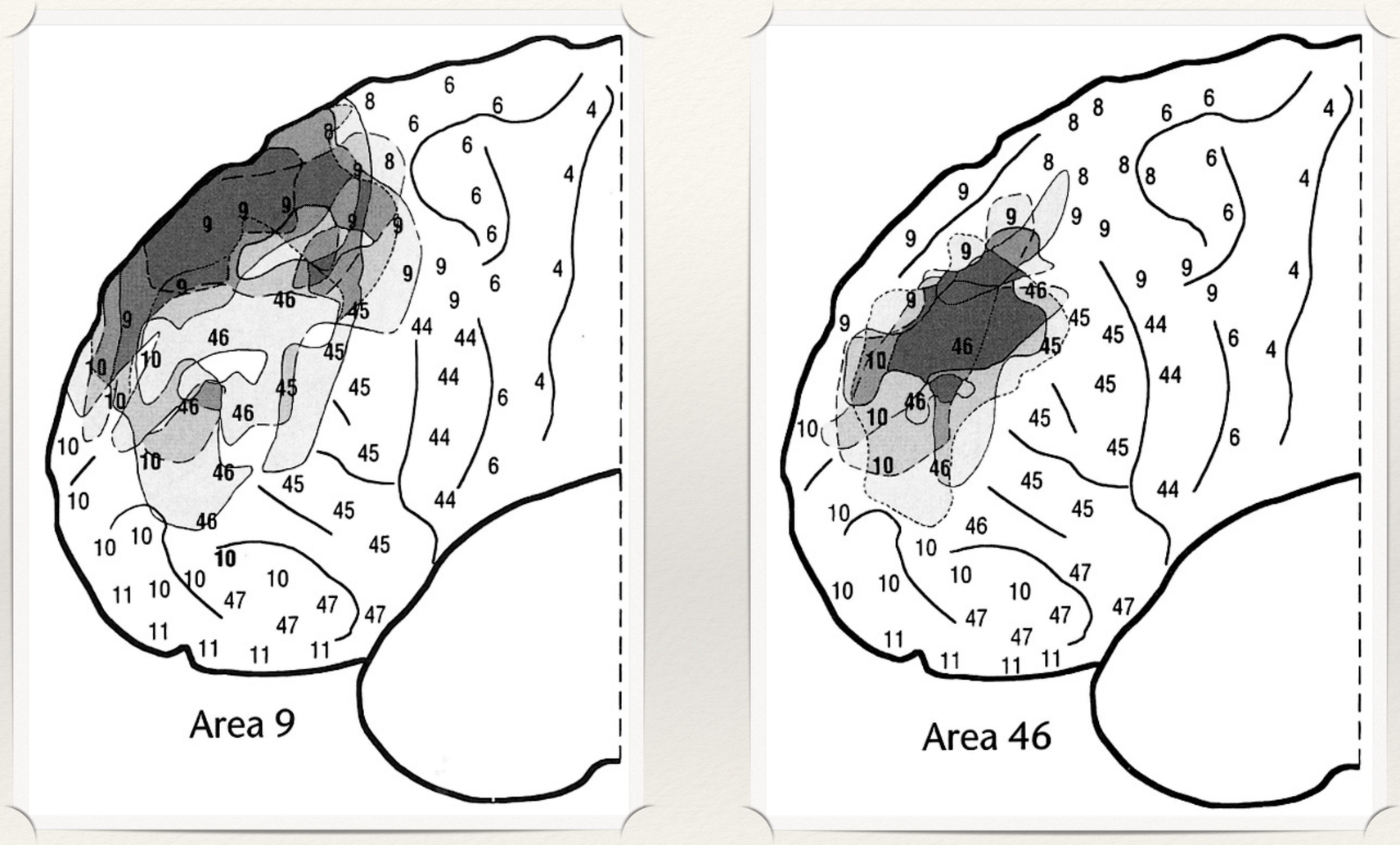
- **aree corticali (e nuclei sottocorticali)**
  - architettura (istologia, immunoistochimica)
  - proprietà funzionali delle cellule (elettrofisiologia)
- **connessioni**
  - identificazione dei punti di partenza e di arrivo (tract tracing)

- **aree cor… …icali)**
  - archi…ttur… immu…ist…
  - proprietà fu… …e cellule (elettrofisiologi…
- **connessioni**
  - identificazion… …ti di partenza e di arrivo (…



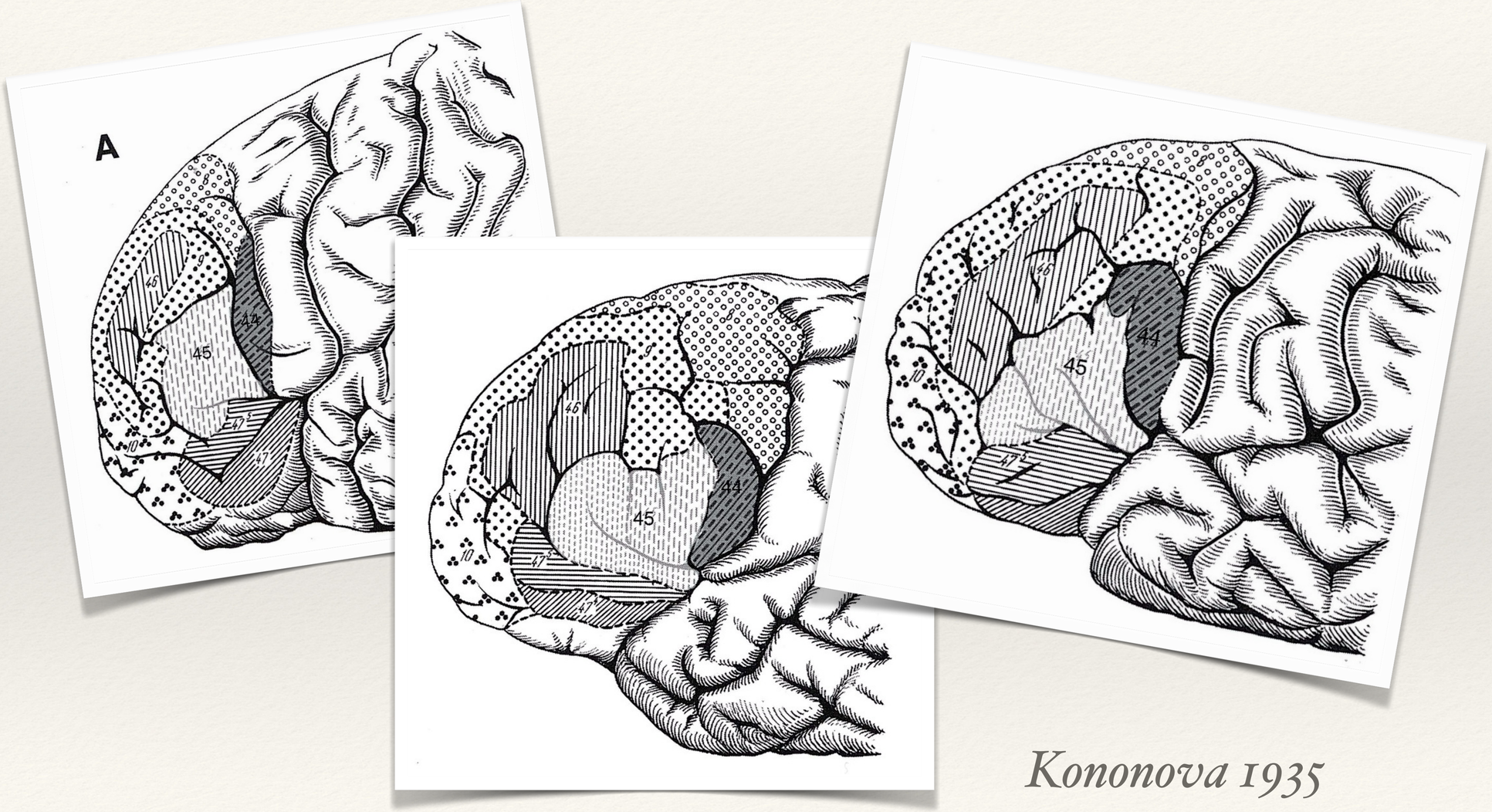
attenzione alla variabilità tra individui!

variabilità tra individui



Rajkowska and Goldman-Rakic 1995

variabilità tra individui



Kononova 1935

“frenologia” (circa 1800)

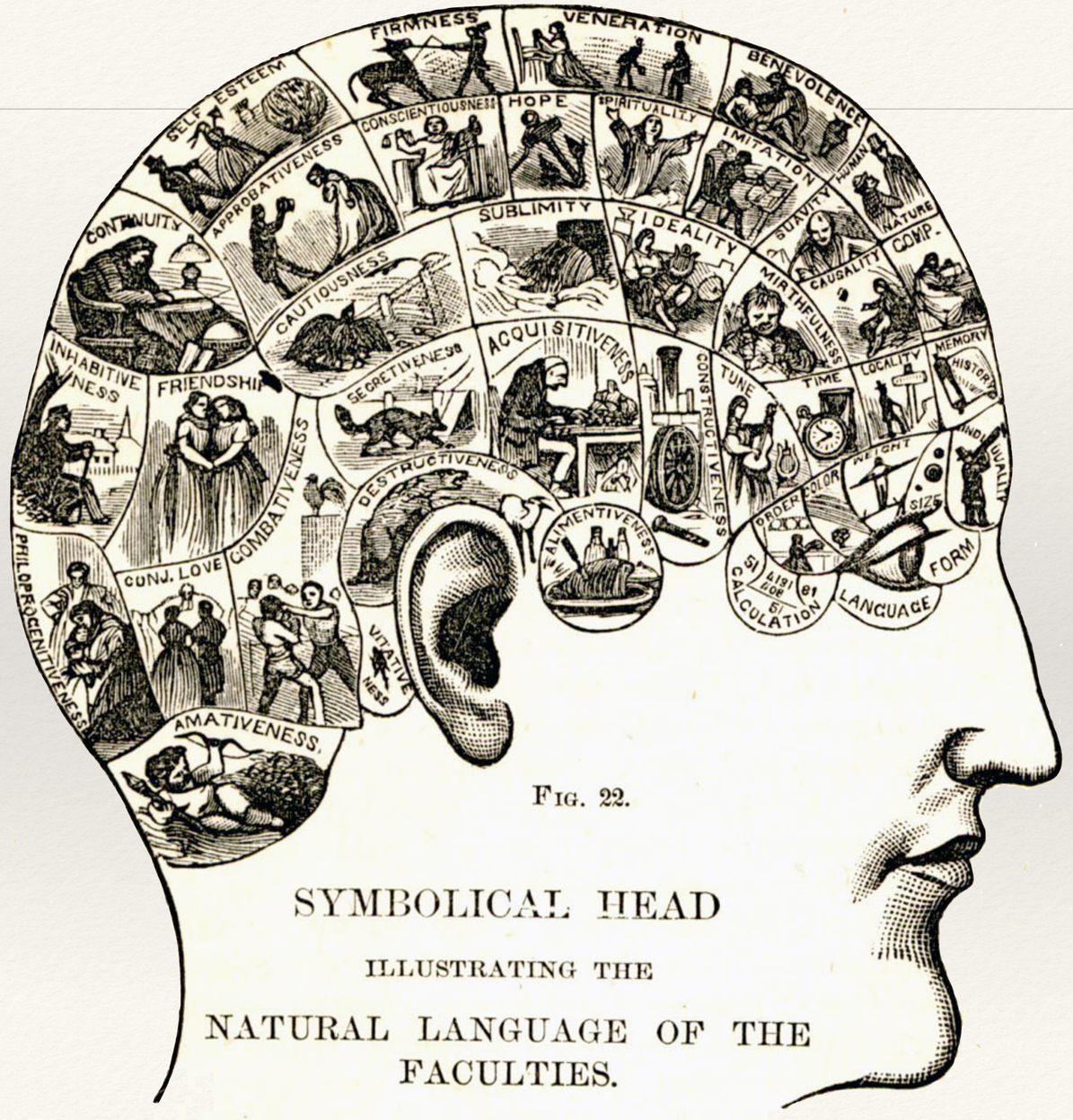


Fig. 22.

SYMBOLICAL HEAD

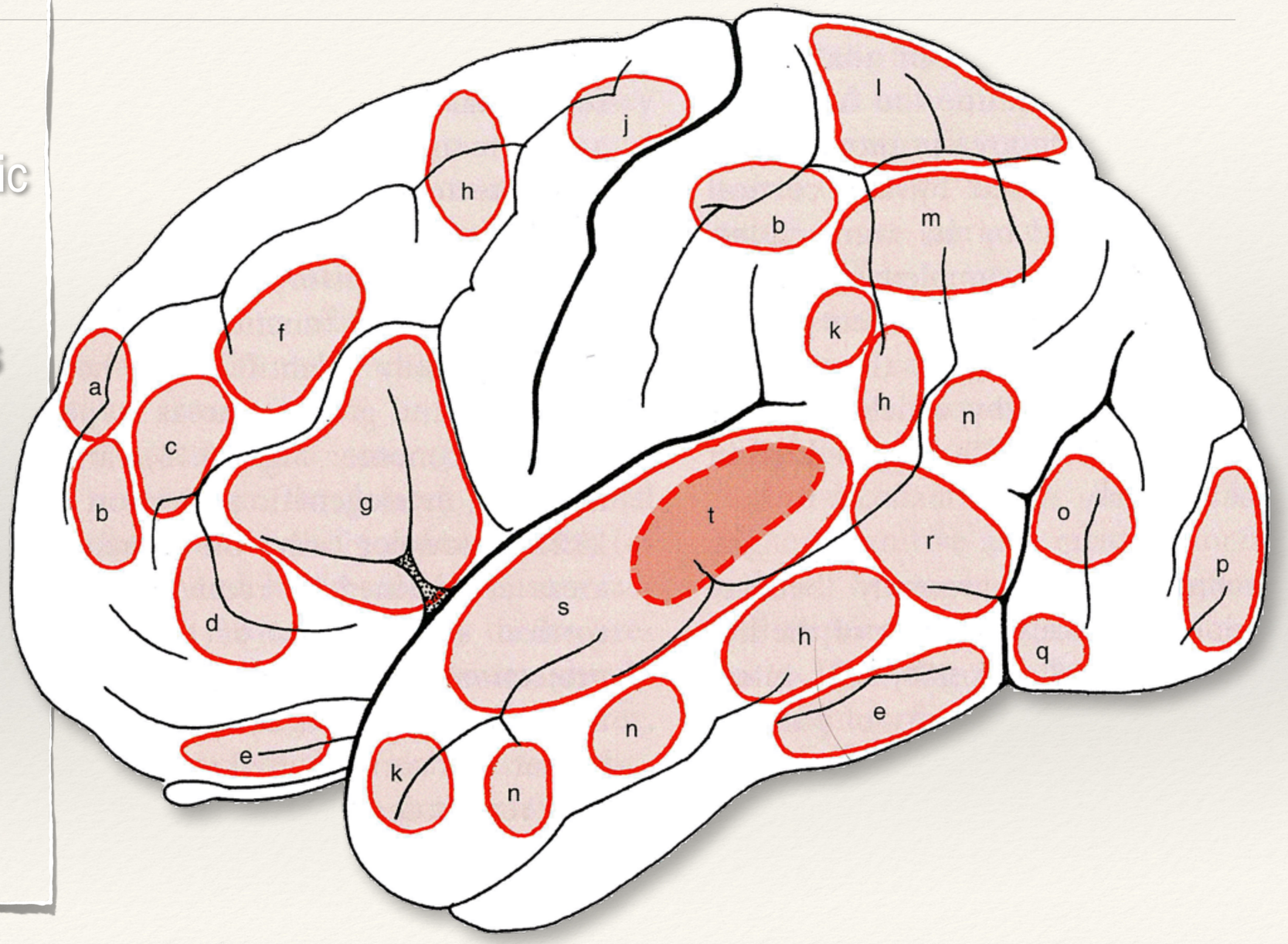
ILLUSTRATING THE

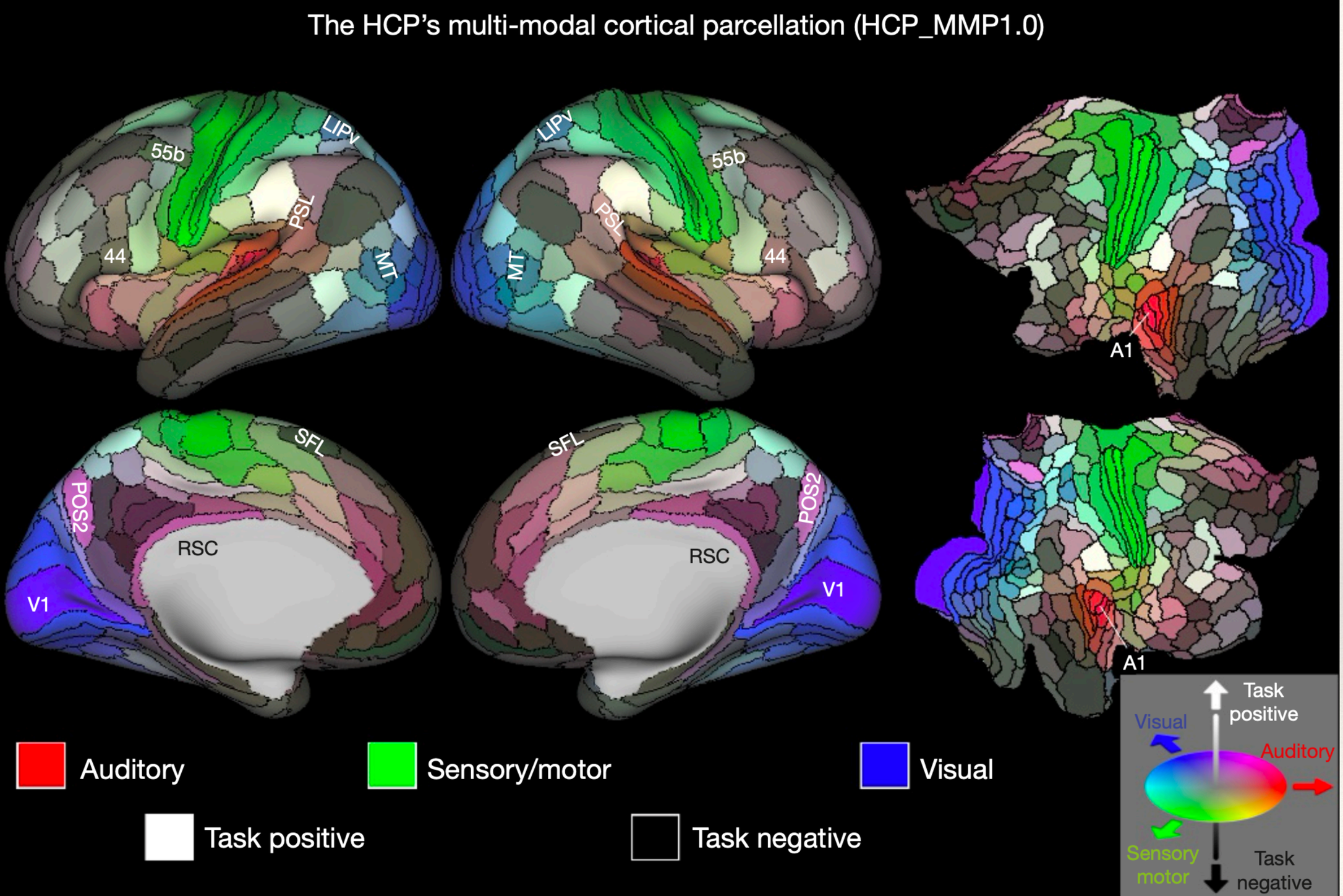
NATURAL LANGUAGE OF THE FACULTIES.

Franz Joseph Gall

una neofrenologia?

- attention
- calculation
- working memory task
- processing incorrect arithmetic equations
- maternal love
- reading aloud irregular words
- meditative state
- finger opposition task
- visual-spatial orienting
- language comprehension
- embarrassment
- verb comprehension
- evaluation of unpleasant, arousing words

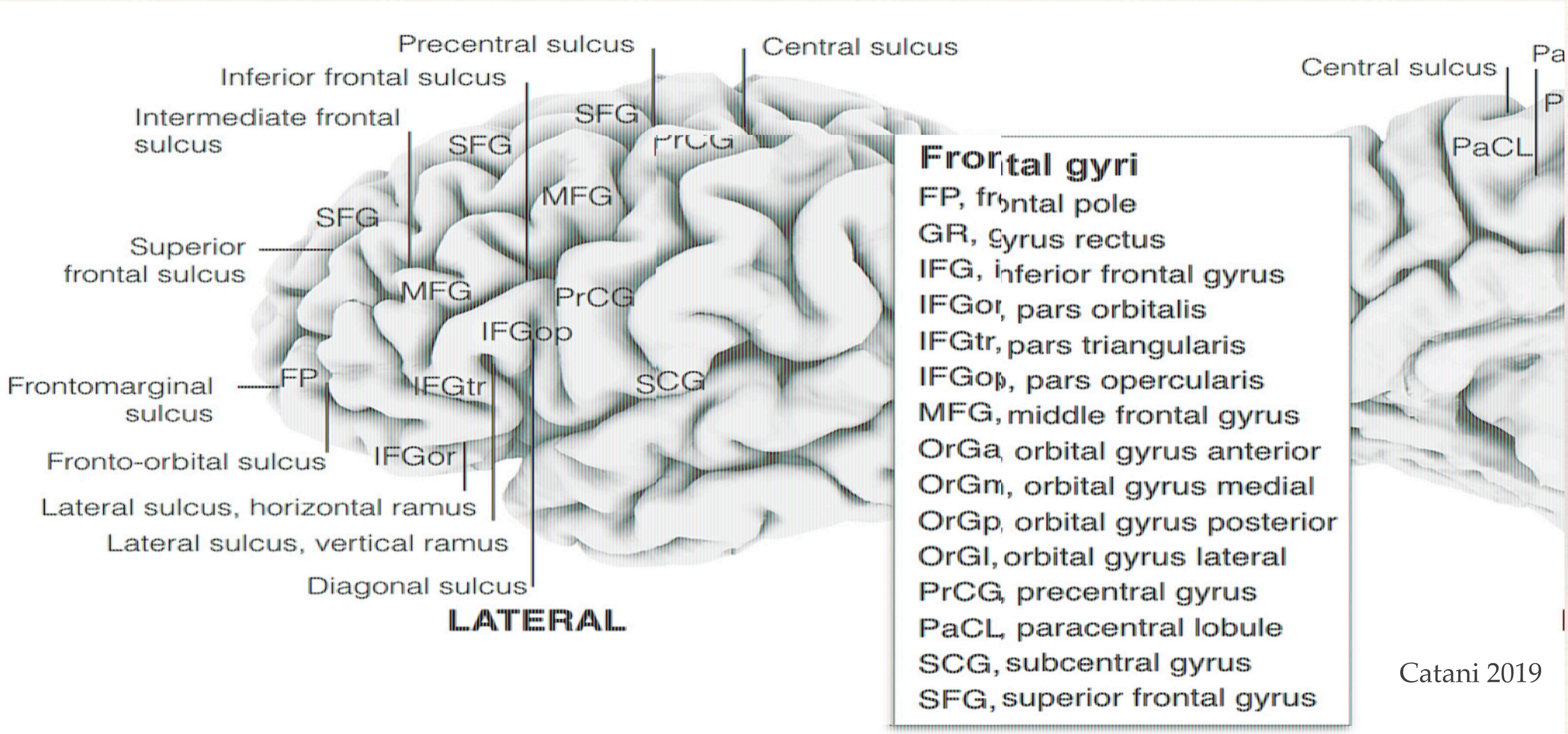




180 aree!

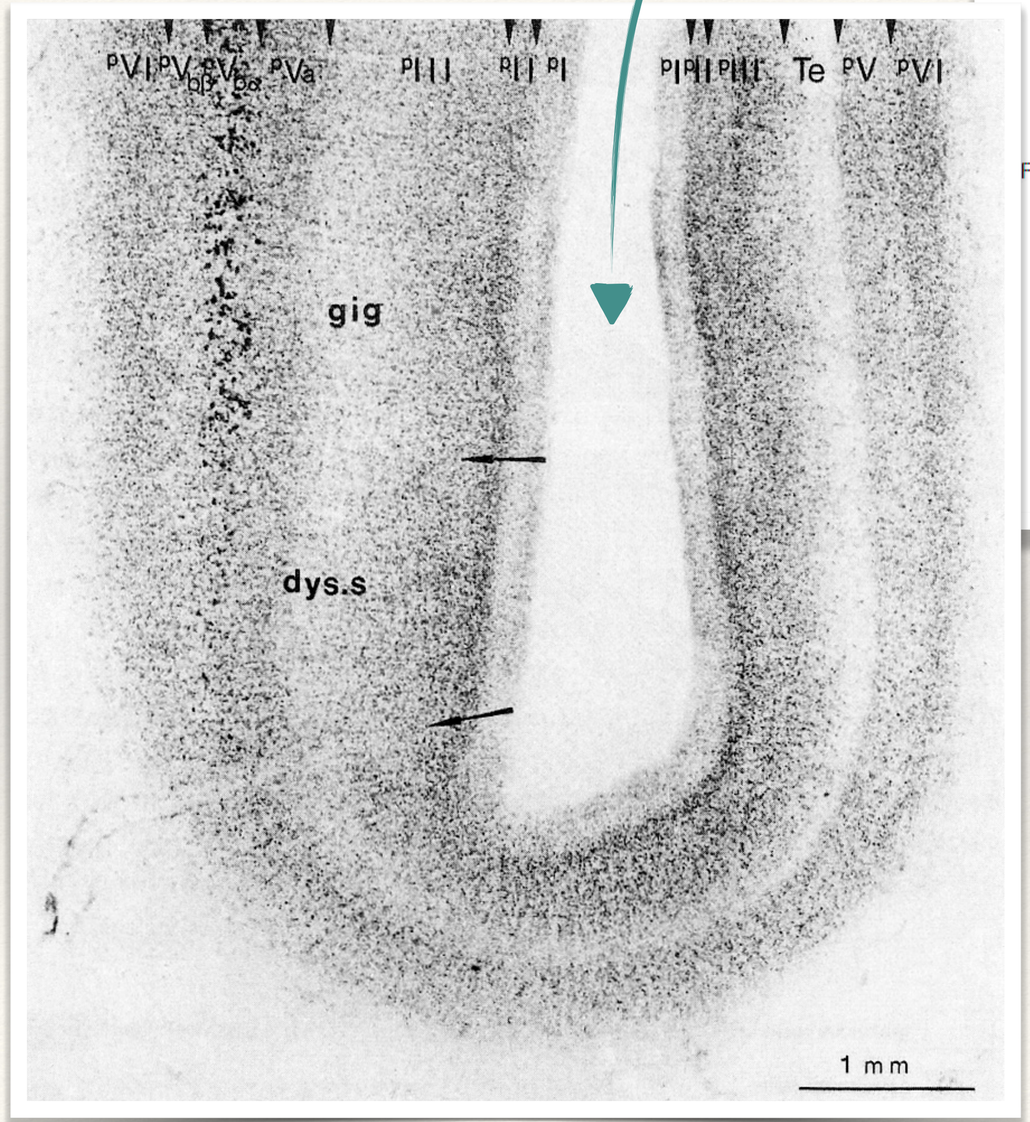
Glasser et al, 2016

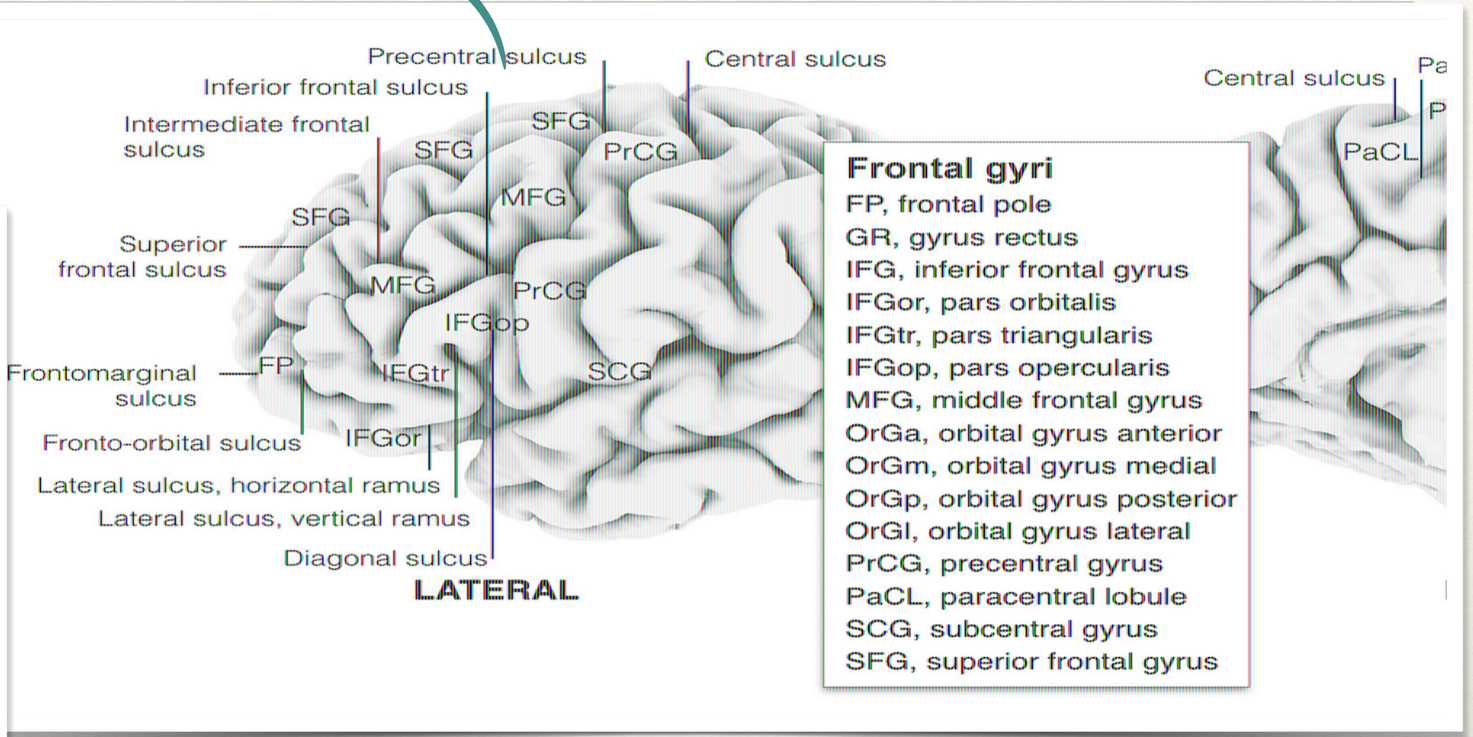
le aree frontali “più famose”



Catani 2019

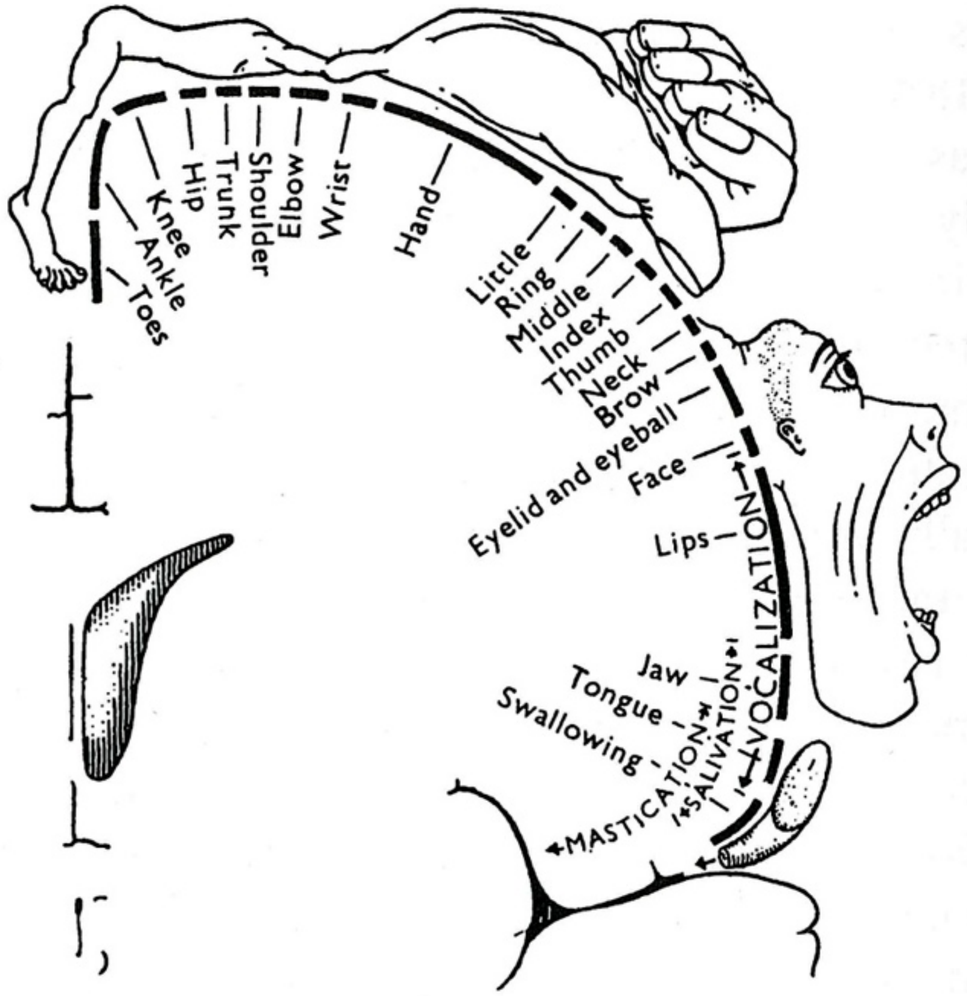
Area 4



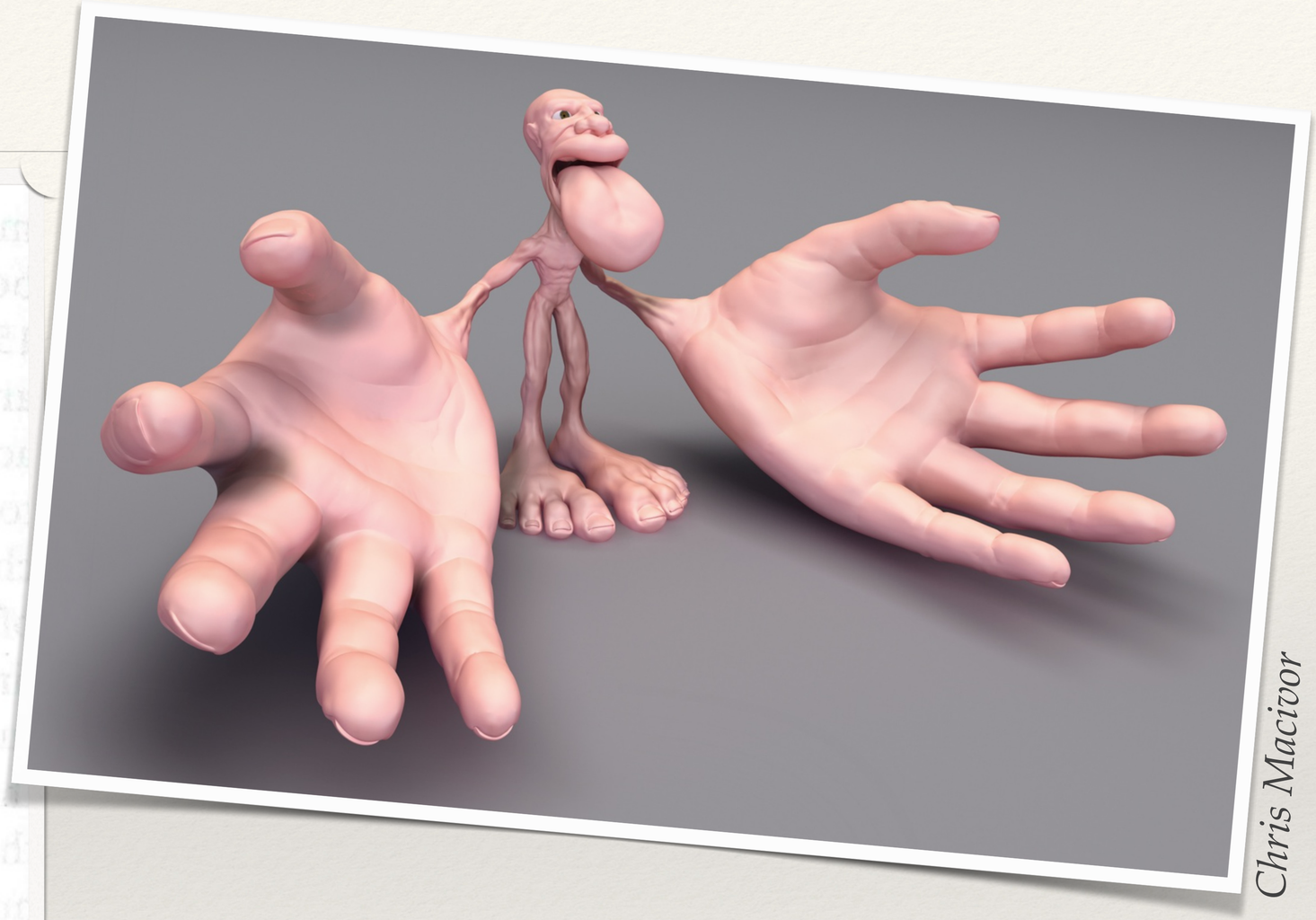


- la corteccia motoria primaria
- “caratterizzata dalla soglia di stimolazione elettrica più bassa per evocare una contrazione muscolare controlaterale”

homunculus



Penfield & Rasmussen

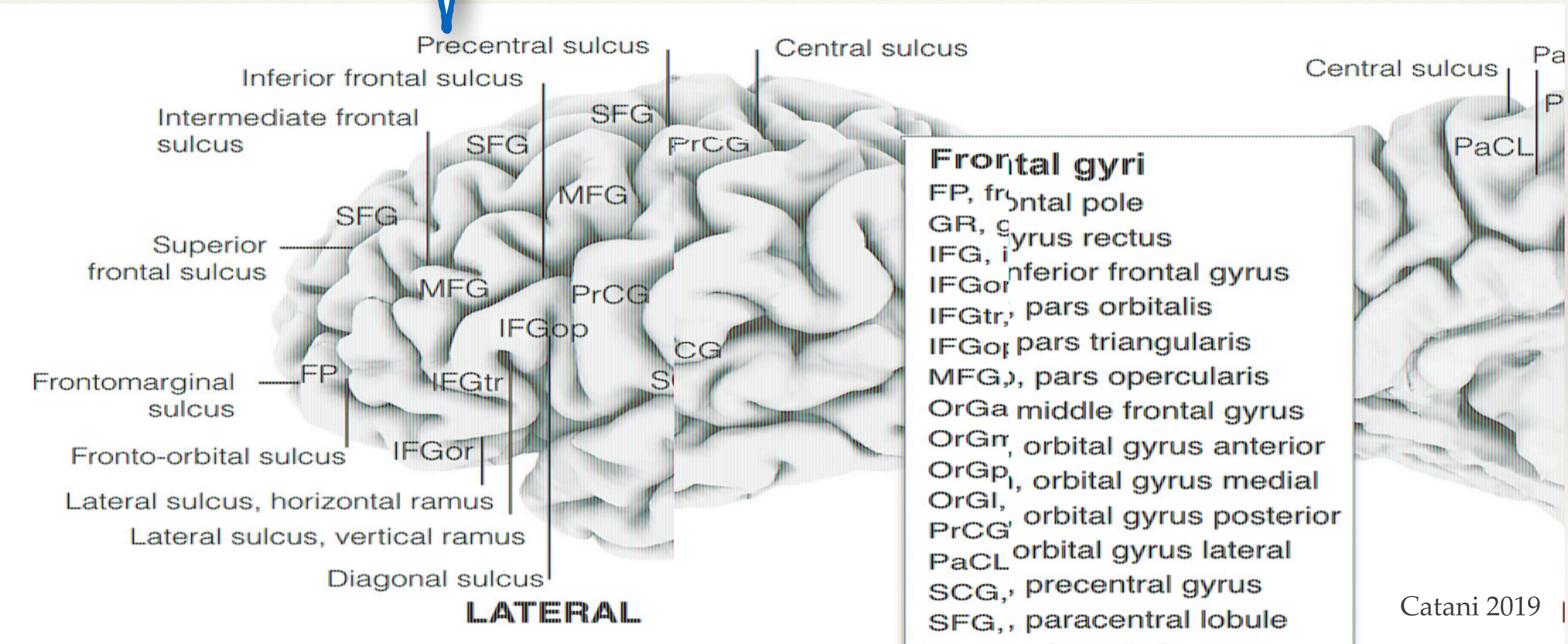


Chris Macivor

- 4a: anteriore, più ampia
- 4b: nascosta nel solco

Area 6

il resto del giro precentrale e la porzione posteriore dei giri frontali superiore e medio



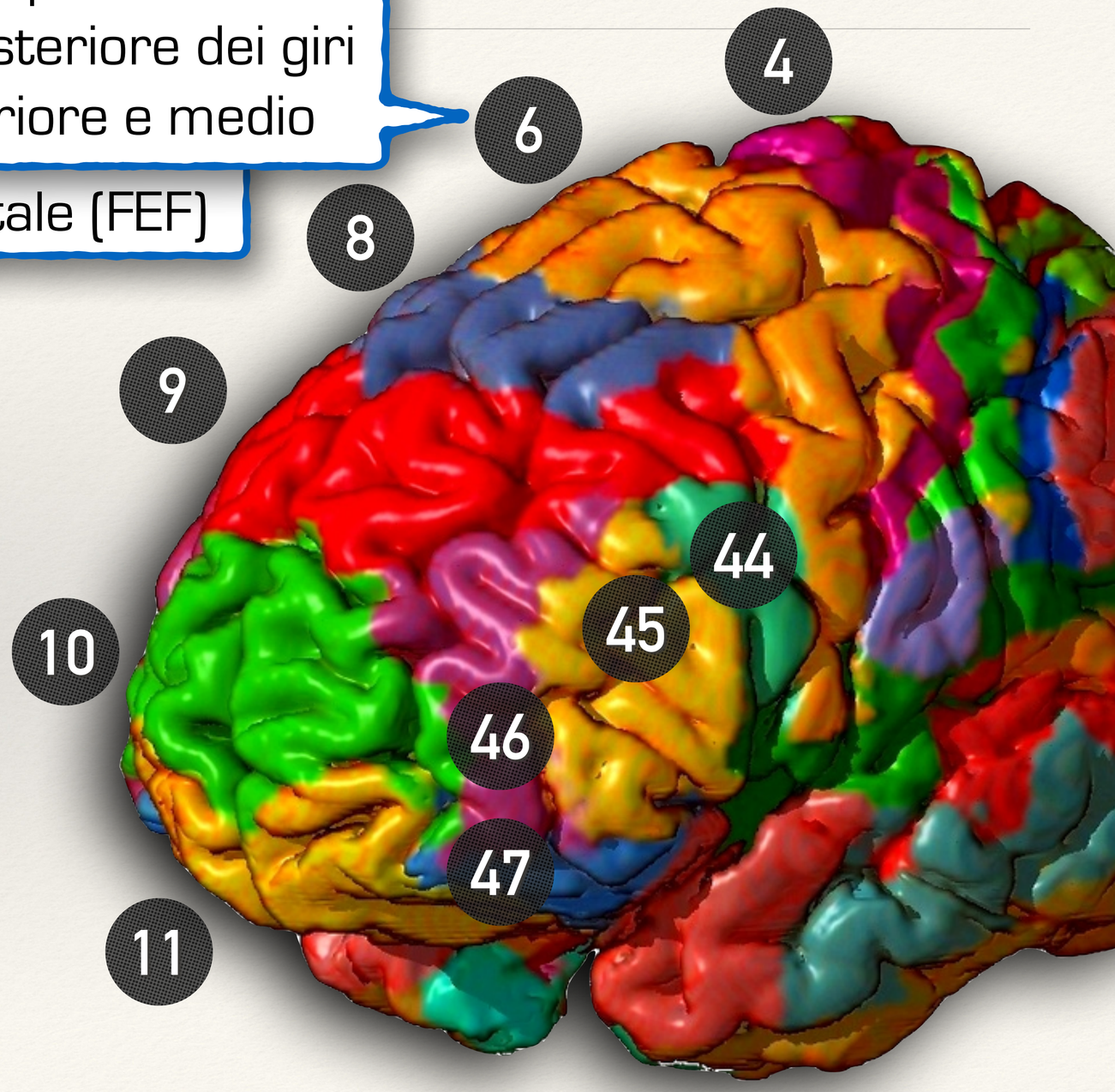
Catani 2019

Area 6

il resto del giro precentrale e la porzione posteriore dei giri frontali superiore e medio

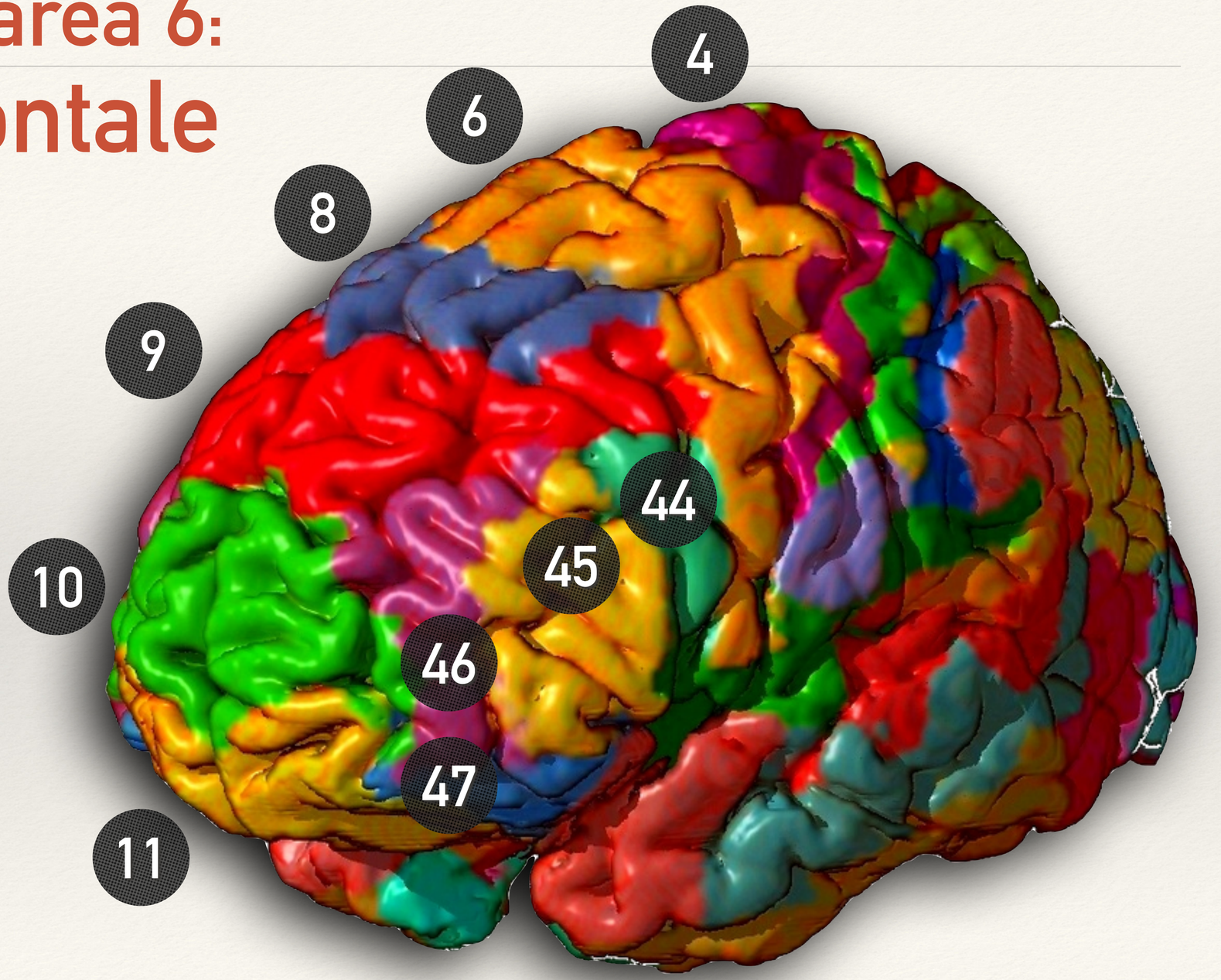
incluso il campo oculare frontale (FEF)

- supplementary motor area (SMA)
- pre-supplementary motor area (pre-SMA)



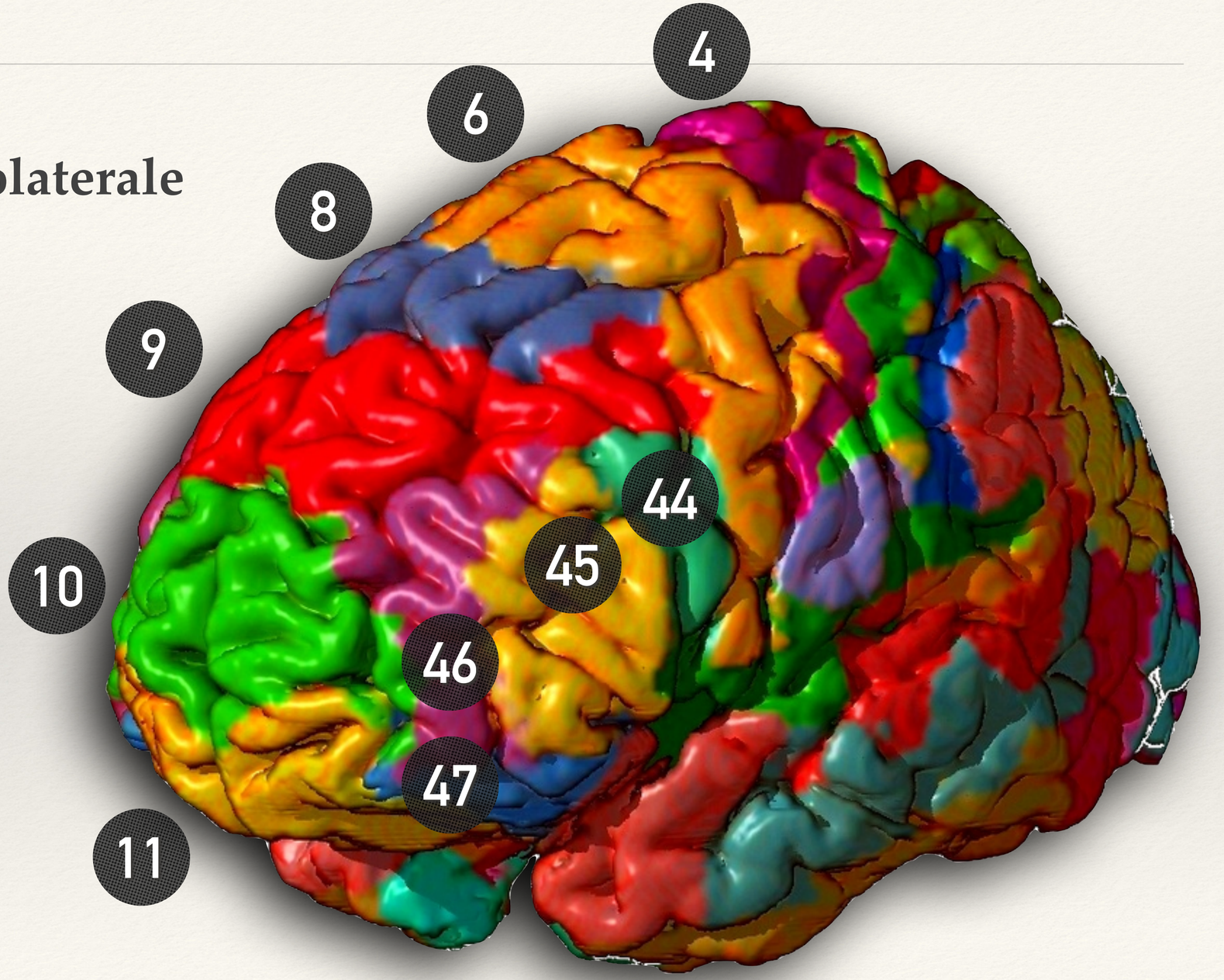
anteriormente all'area 6:
corteccia prefrontale

- mediale
- dorsolaterale
- ventrolaterale
- polare



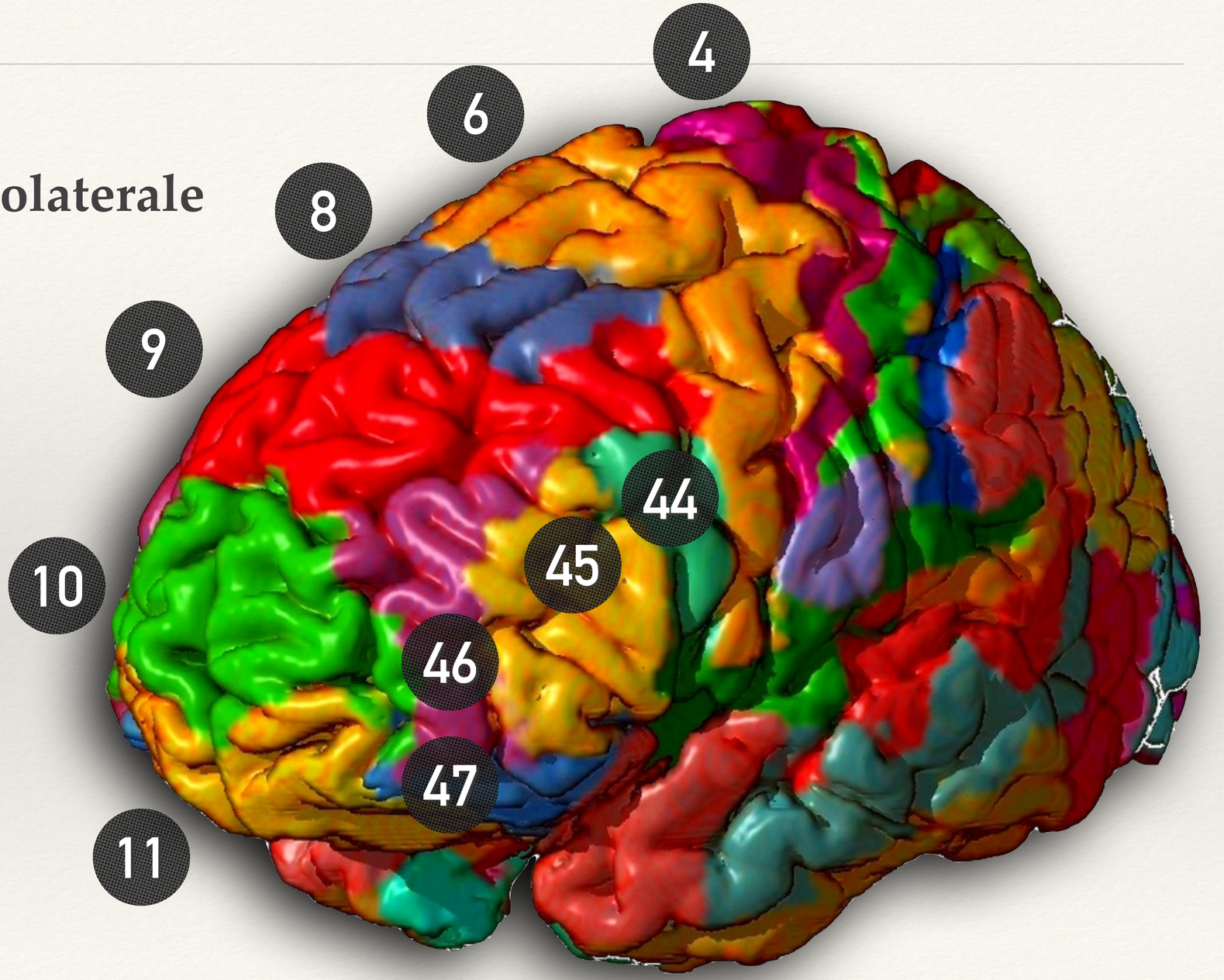
area 8, 9, 46

- corteccia **prefrontale dorsolaterale**
- **lesioni** → problemi di memoria e di controllo esecutivo



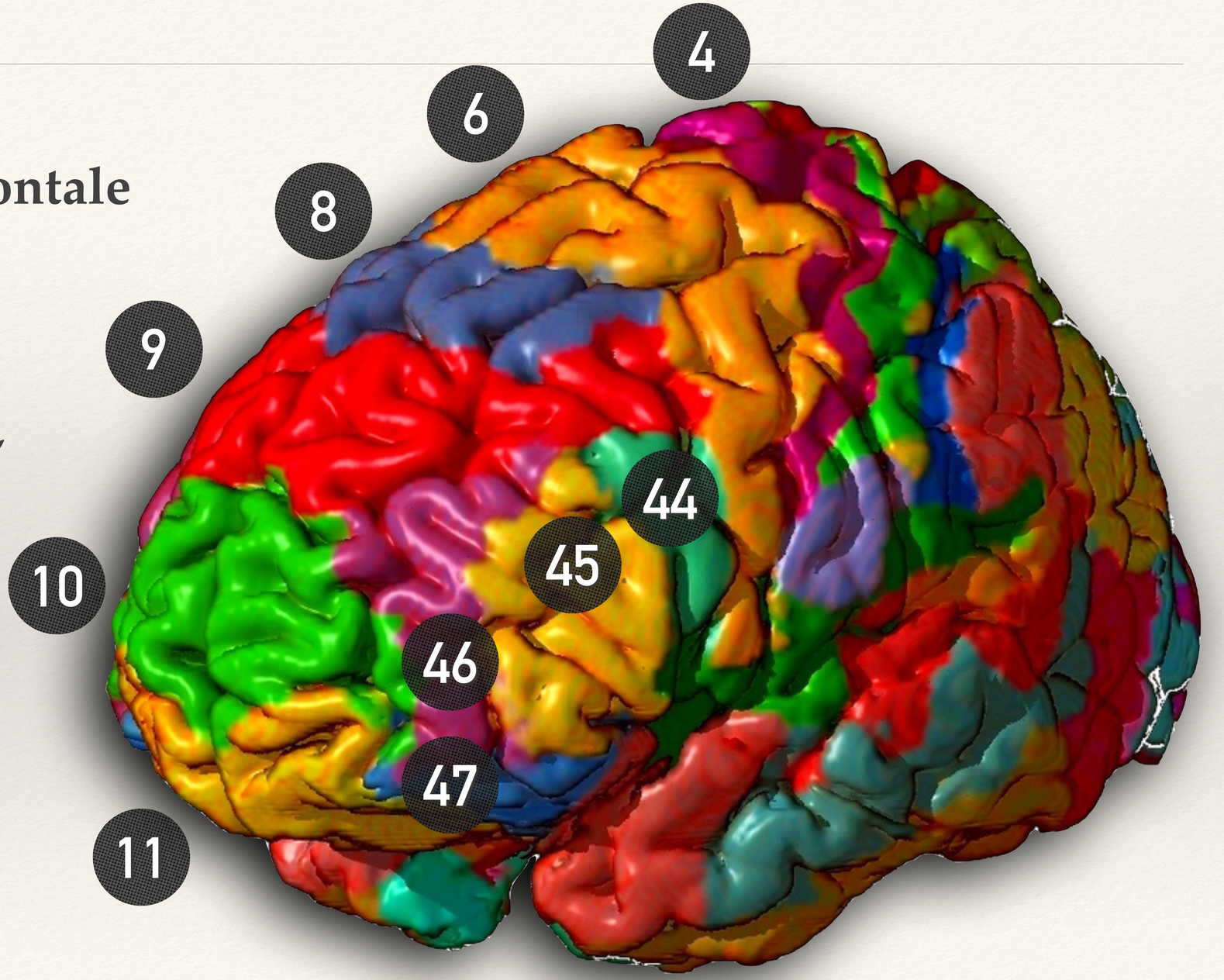
area 44, 45, 47

- corteccia **prefrontale ventrolaterale**
- **lesioni** → afasia di Broca, altre sindromi motorie



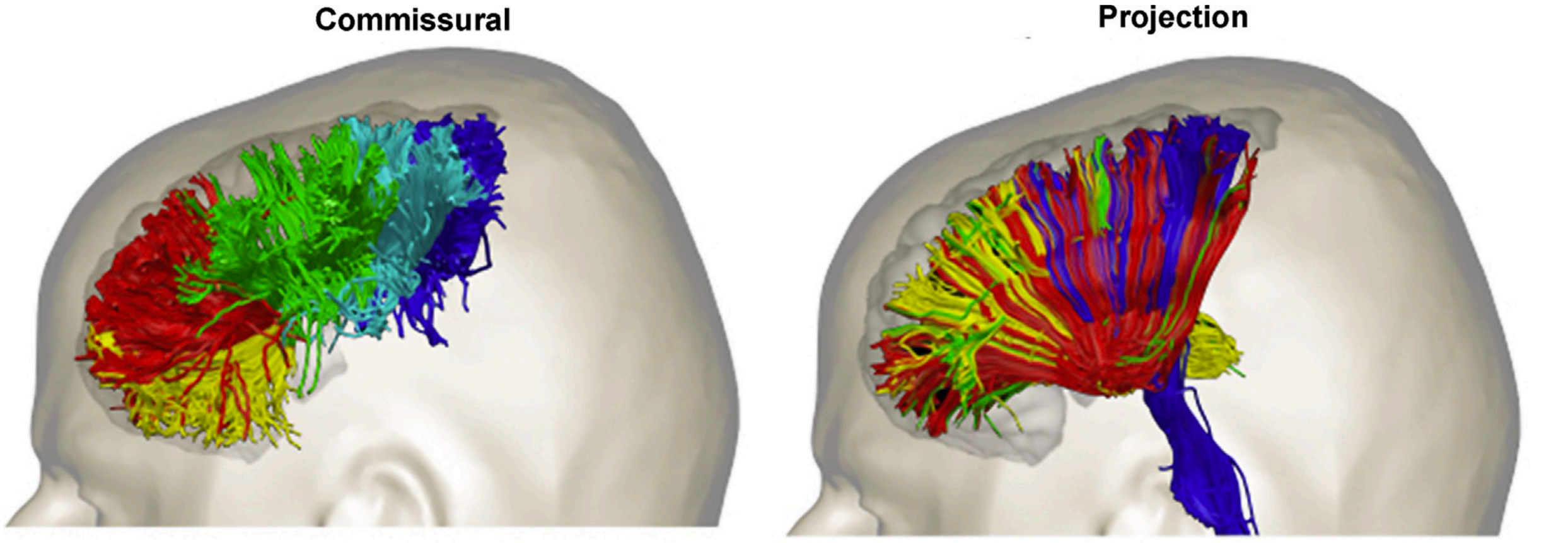
area 10, 11

- corteccia **polare e orbitofrontale**
- **lesioni** → disturbi del comportamento: abulia, *reversal learning impairment*, disinibizione, labilità emozionale, ecc.

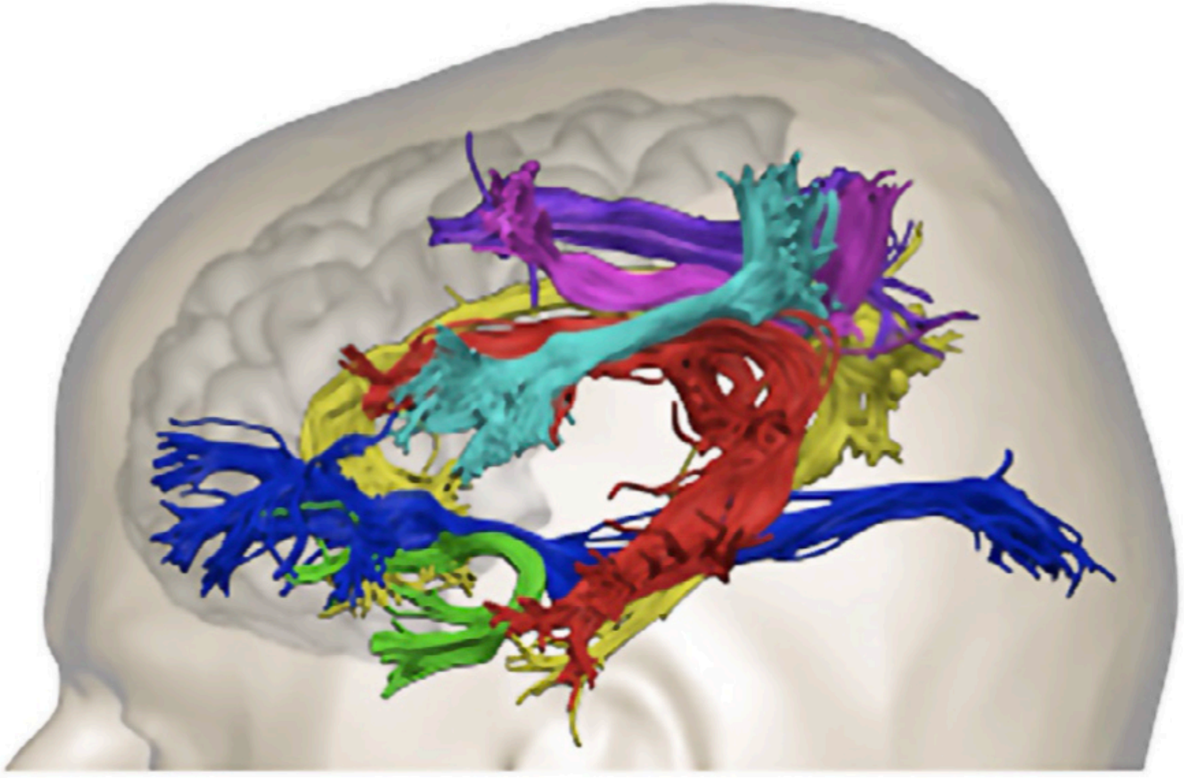


connettività nel cervello umano:

trattografia


Commissural
Projection
Genu
Rostral body
Posterior midbody
A
Rostrum
Anterior midbody
Fronto-striatal (putamen)
Fronto-striatal (caudate)
B
Corticofugal pathways
Fronto-thalamic projections

Interlobar association



Superior longitudinal fasciculus (SLF I)

Superior longitudinal fasciculus (SLF II)

Arcuate (anterior segment)/(SLF III)

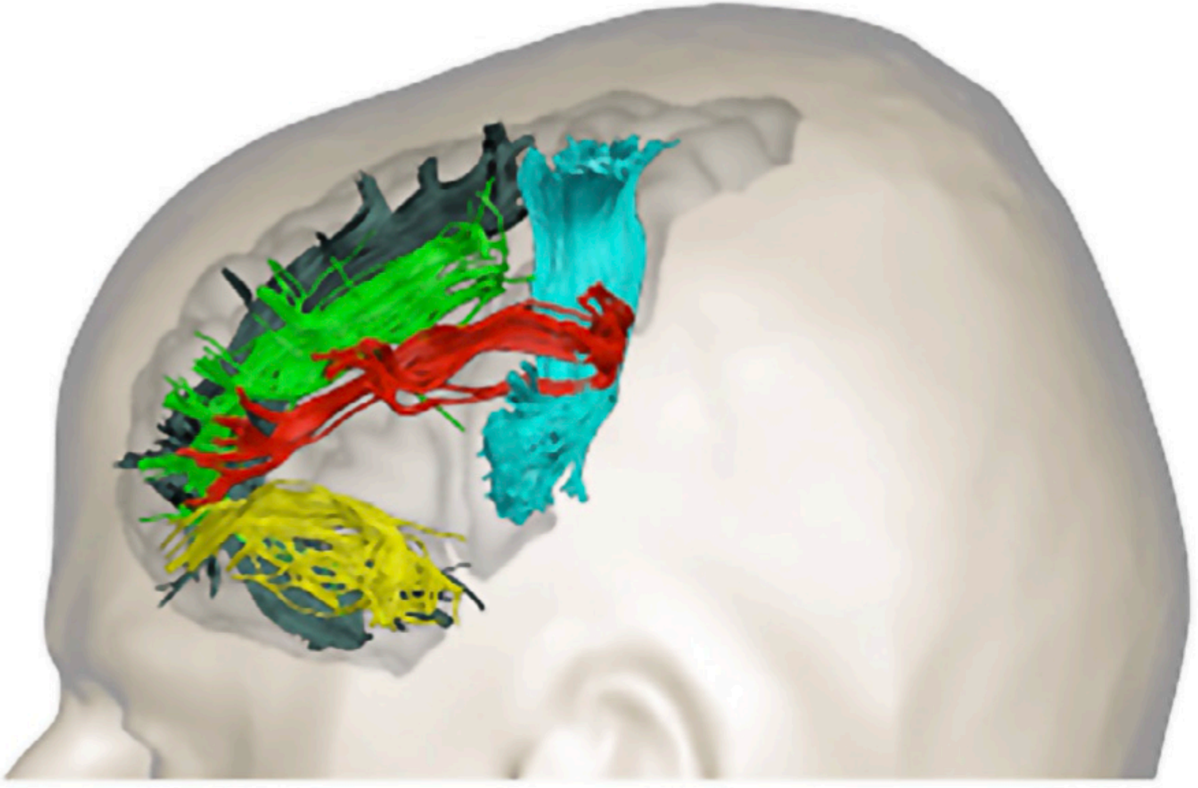
Arcuate (long segment)

Uncinate

IFOF

Cingulum

Intralobar association



Fronto-orbitopolar tract

Frontal paracingulate tract

Frontal aslant tract

Frontal superior longitudinal tract

Frontal inferior longitudinal tract

B

Short U-shaped fibers

Perirolandic U-fibers

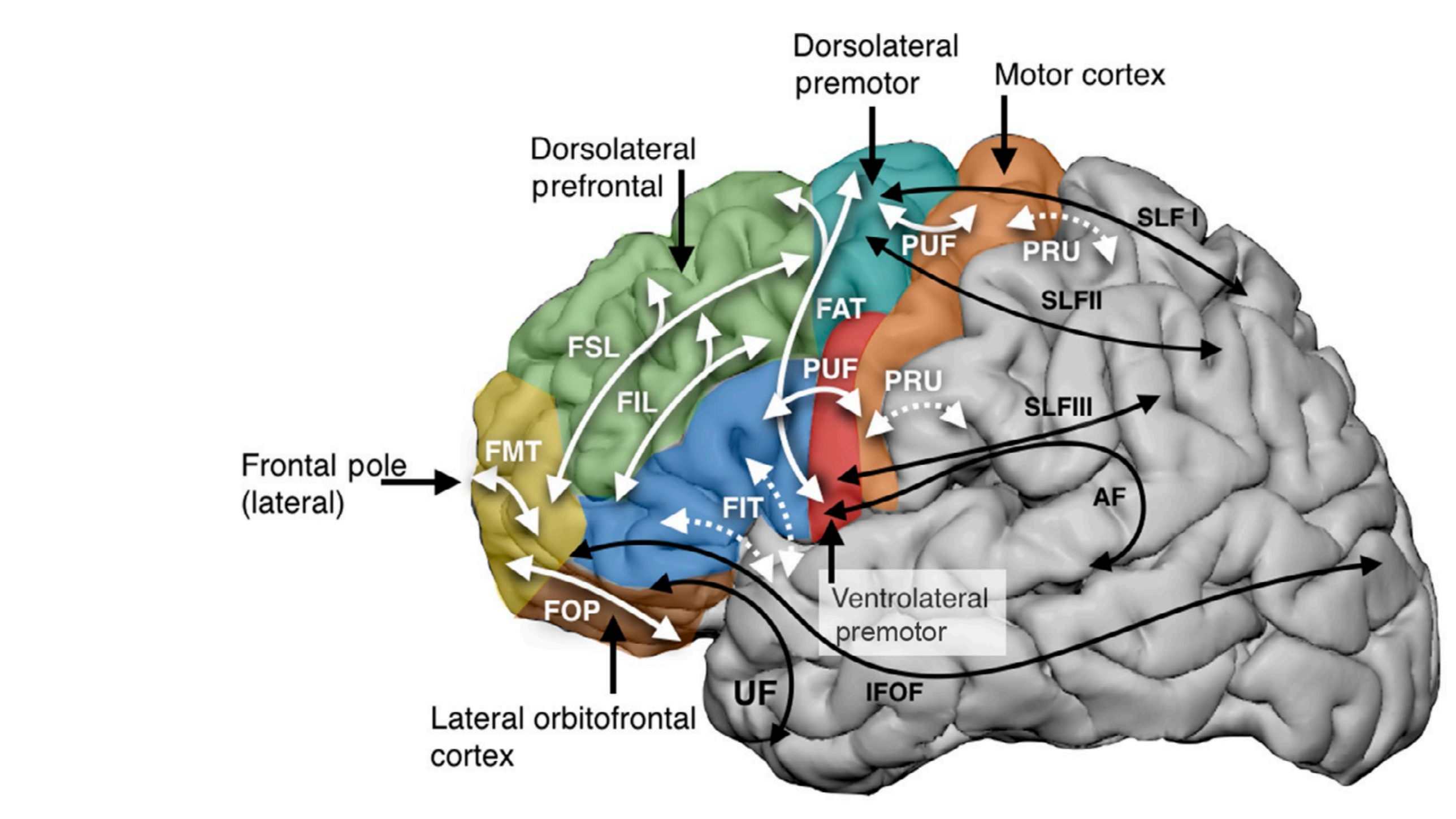
Precentral sulcus U-fibers

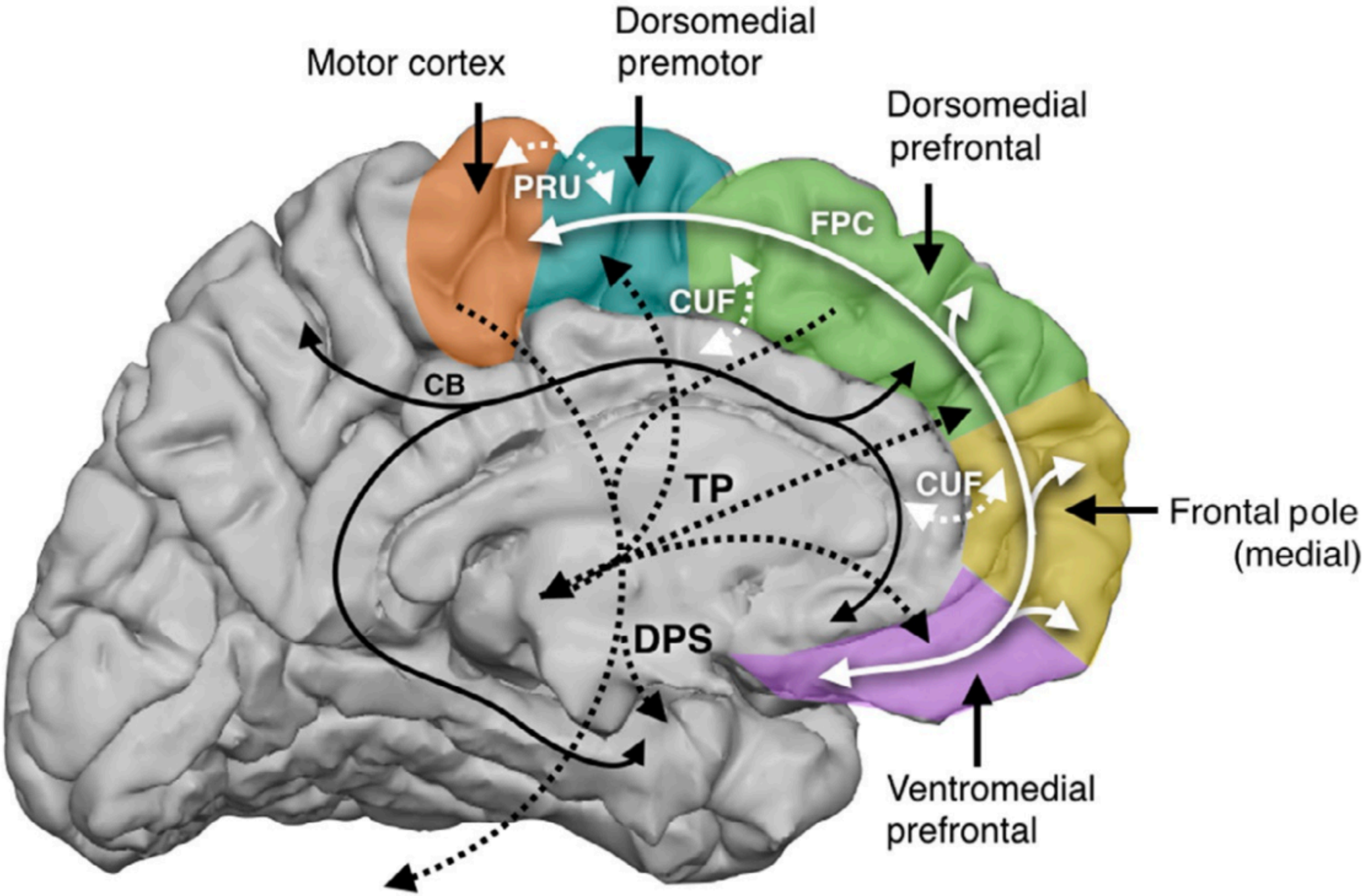
Fronto-insular tracts

Inferior frontal sulcus U-fibers

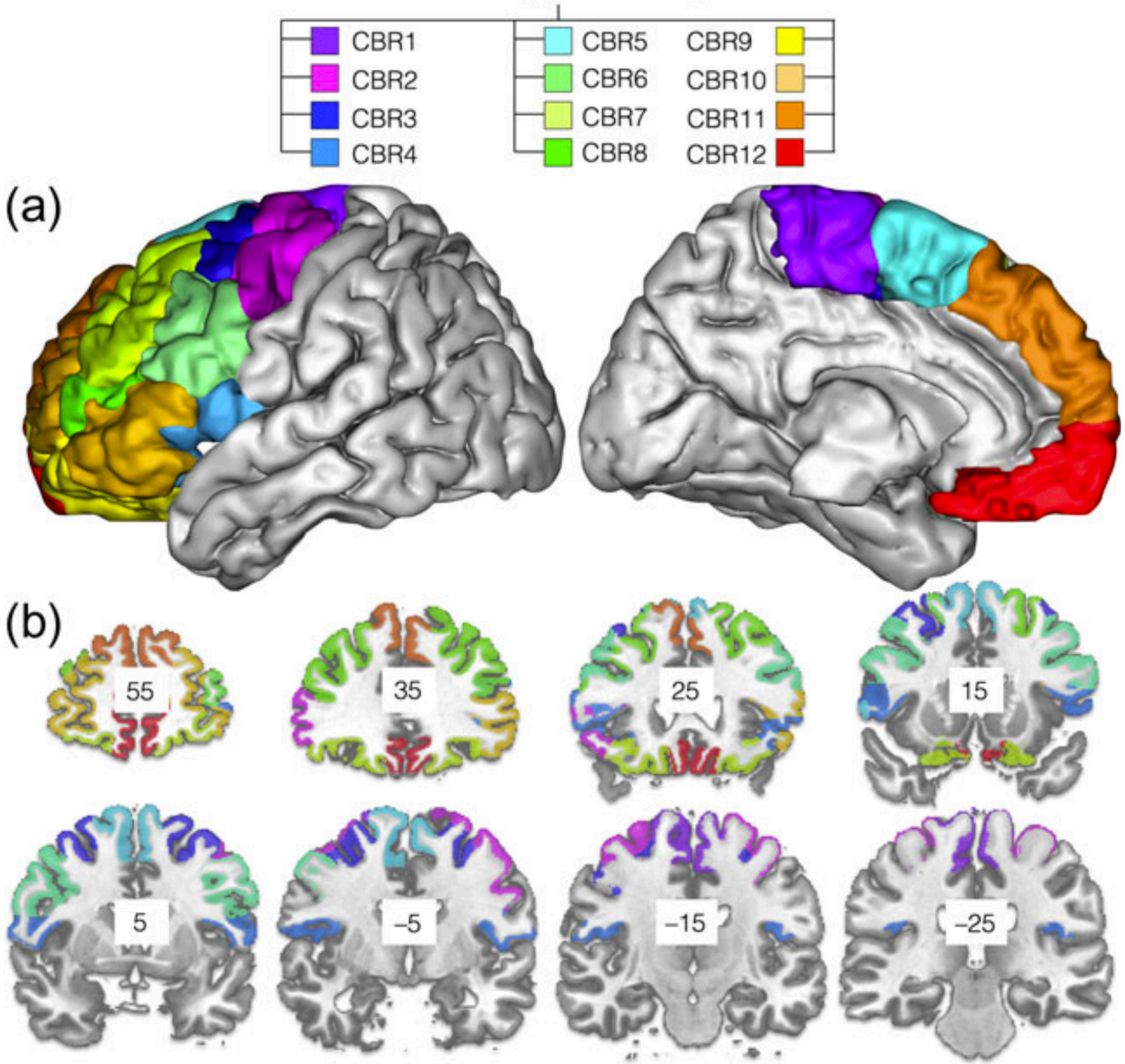
Fronto-marginal tract

Superior frontal sulcus U-fibers


Dorsolateral premotor
Motor cortex
Dorsolateral prefrontal
SLF I
PUF
PRU
SLFII
FAT
FSL
PUF
PRU
FIL
SLFIII
FMT
Frontal pole (lateral)
AF
FIT
Ventrolateral premotor
FOP
UF
IFOF
Lateral orbitofrontal cortex


Motor cortex
Dorsomedial premotor
Dorsomedial prefrontal
PRU
FPC
CUF
CB
TP
CUF
Frontal pole (medial)
DPS
Ventromedial prefrontal

connectivity-based frontal regions



Thiebaut de Schotten et al, 2017