A Brief Course in Functional Neuroanatomy: Part I

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Acknowledgement:

- *Serge Campeau, PhD, U of Colorado; W. Lee, PhD,*
- *Frank H. Netter, MD, Paul Malloy, PhD*

Charlie Vella in a nutshell

- Born on Malta; immigrated age 5
- 10 years in Roman Catholic Seminary (Franciscan)
- BA in Philosophy; (MA) in Theology; PhD in Counseling Psychology (UCB) 1977
- 34 years at Kaiser Psychiatry (til 2009): Chief Psychologist, Director Neuropsychology
- Married 42 years, Marilyn; daughters: Lea, 4th year in PhD in NP, UCSD; Maya, UCSF Med 2nd year
- Rabid genealogist, hominid evolution enthusiast, mineral collector, cook & baker
- New grandfather of Noelle Rivka Byrd

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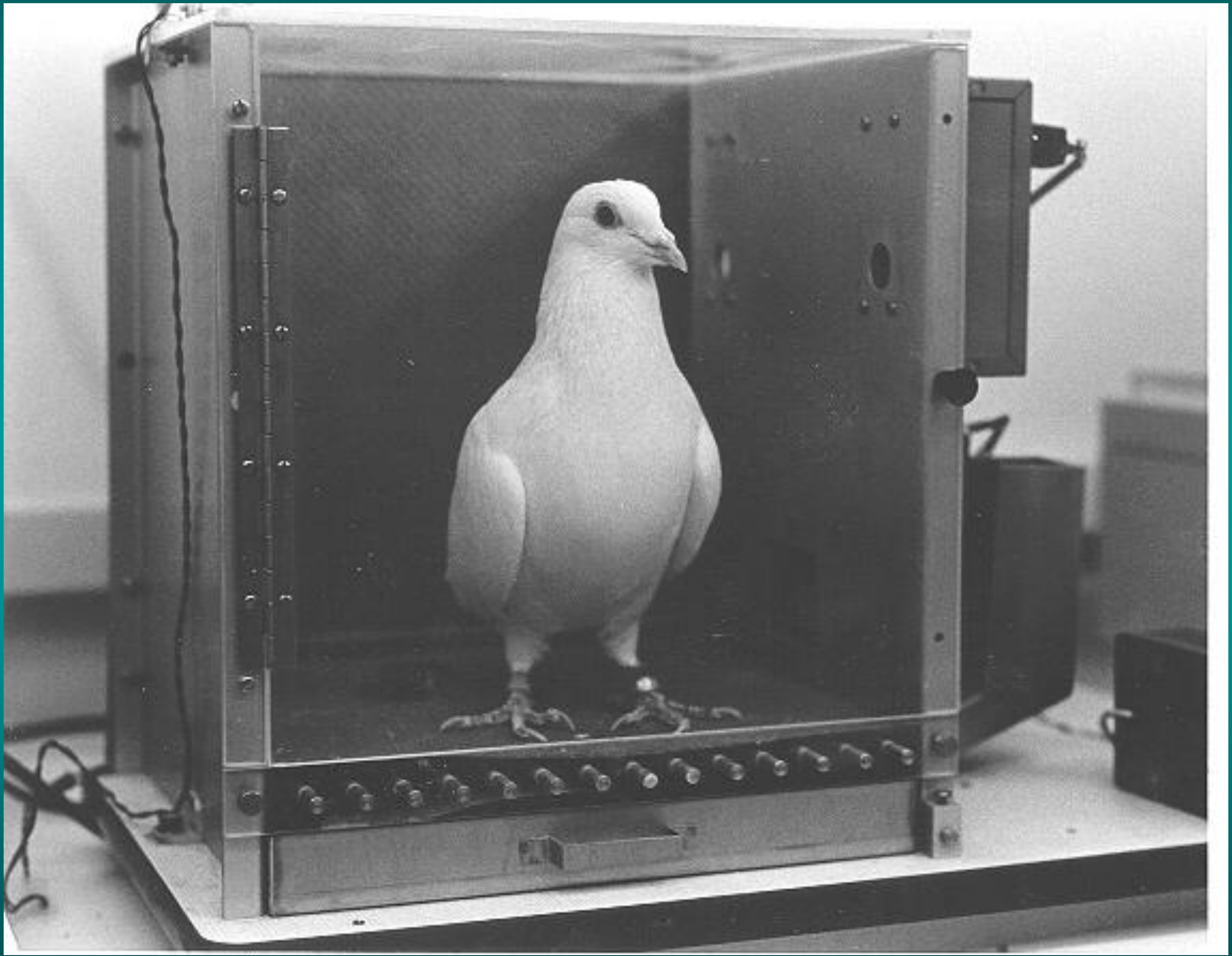
- All of my lectures in PDF files
- Go to “Neuropsychology Seminar Talks”
- Logon: Kaiser
- Password: Kaiser

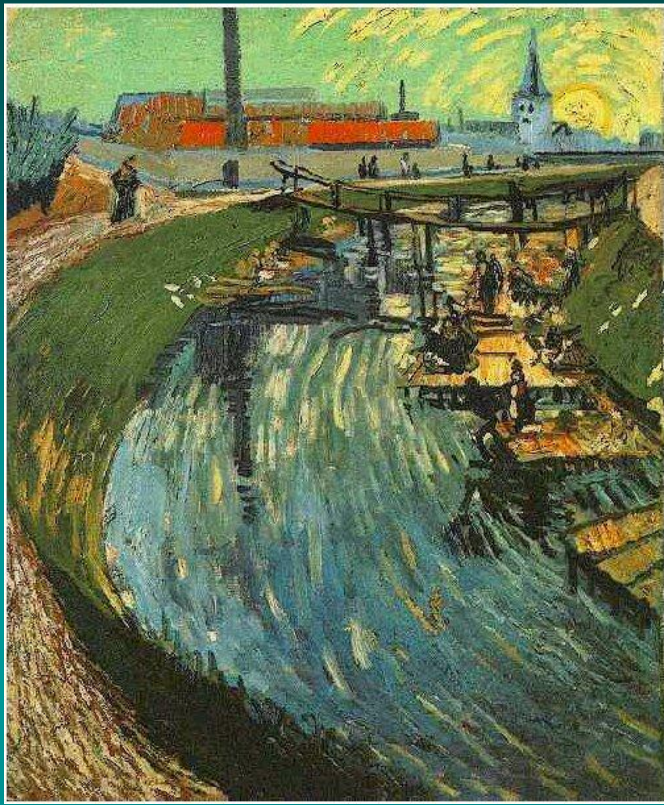
The major brain study methods

- Lesion studies
- 1960s - Single-unit recording
- Neurosurgery-related methods
  - Direct cortical stimulation
  - Split-brain
  - WADA
- Functional imaging
  - 1970s - Electromagnetic: EEG, MEG
  - Hemodynamic: PET, fMRI
- Transcranial magnetic stimulation (TMS)

Pigeons: A Cautionary Tale



Watanabe, Sakamoto and Wakita, 1995



Van Gogh

Chagall

Pigeons were <u>able to discriminate between Van Gogh and Chagall with 95% accuracy</u> (for trained on pictures); Discrimination still <u>85% </u>successful <u>for previously unseen paintings of the artists</u>

Convergent Evolution of Intelligence

Aesop was right! A crow drops in pebbles to raise the water level.
University of Cambridge

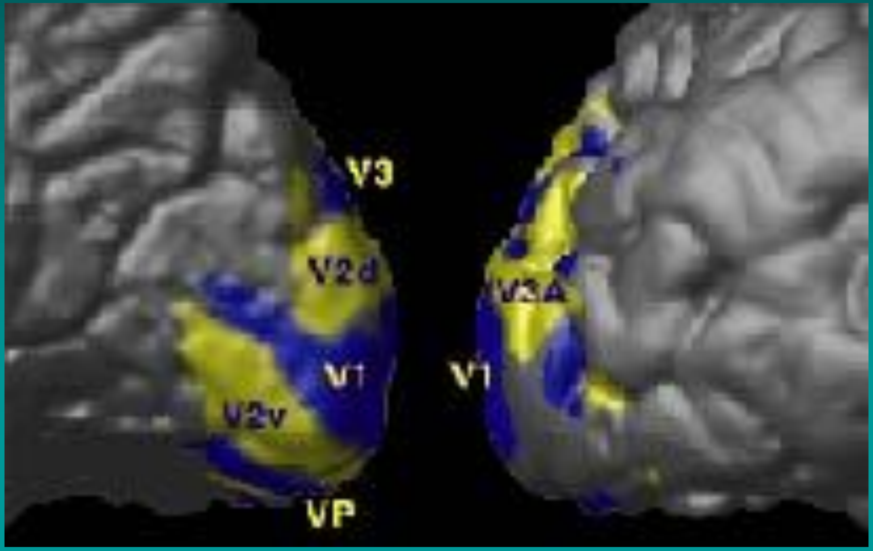
Advanced Neuroimaging circa 1905:
Phrenology "MRI"

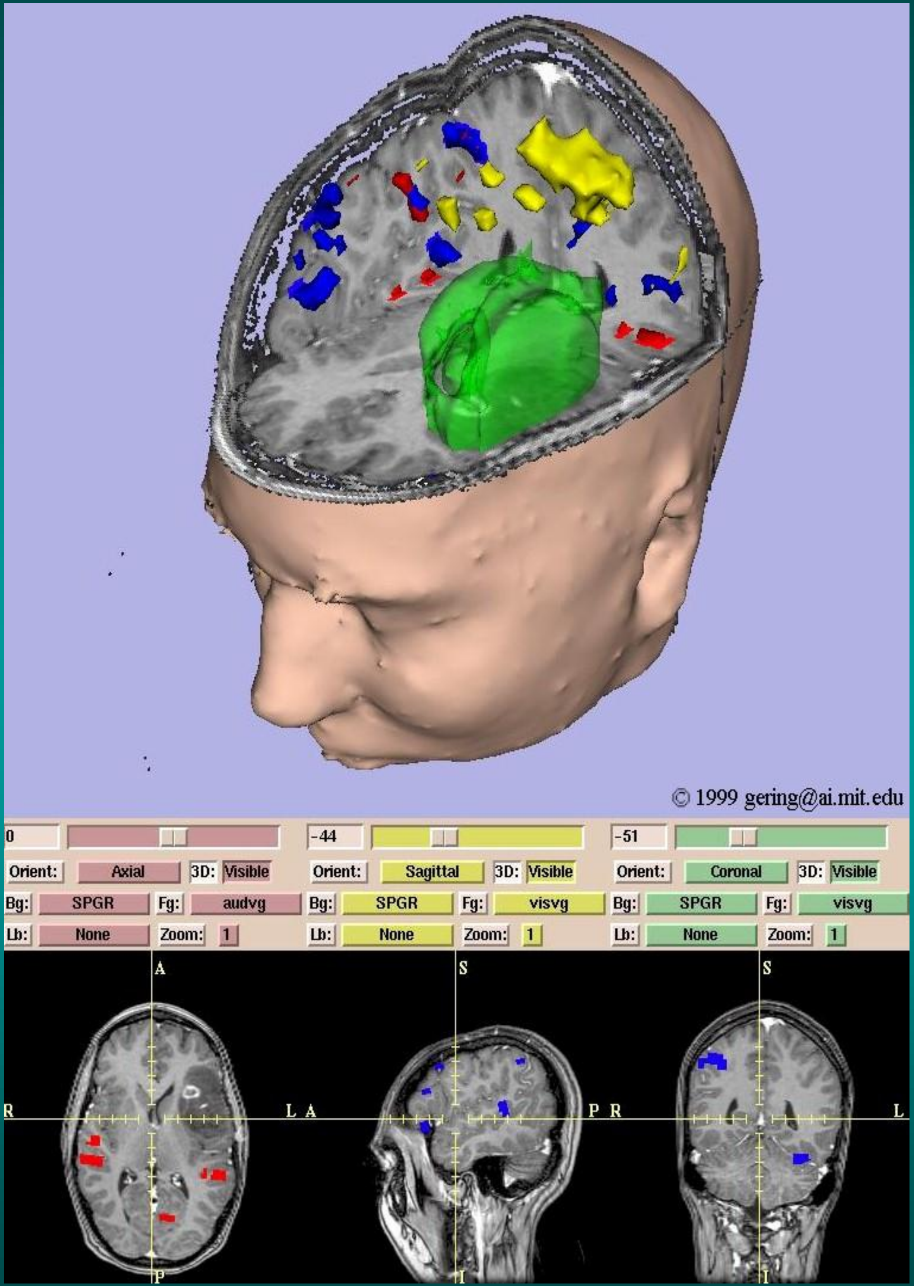
Cautionary Tale: Many "current" theories are eventually discredited

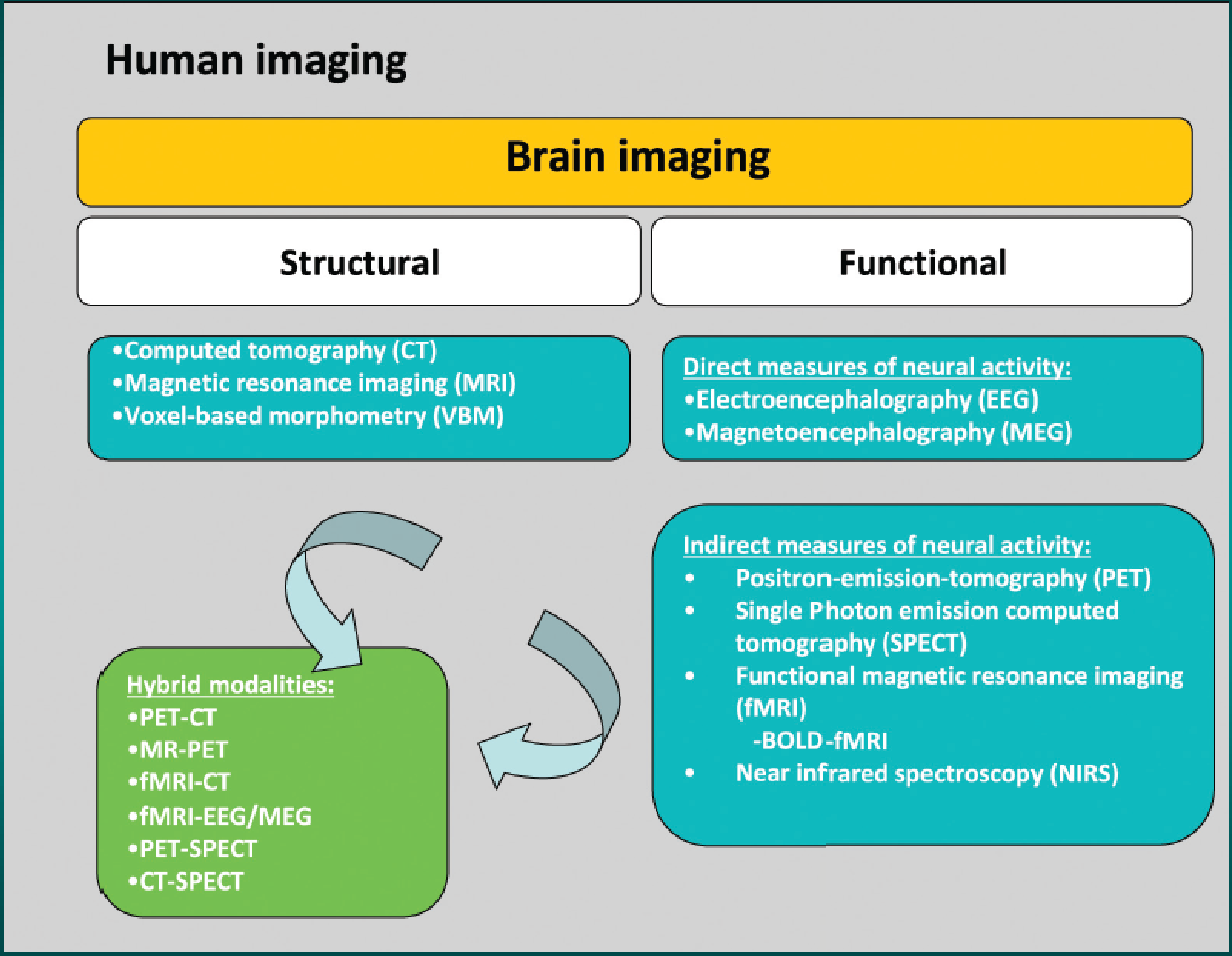
Psychoanalysis Device, 1931

A demonstration of a new "psychoanalyzing apparatus" in 1931

Modern Phrenology







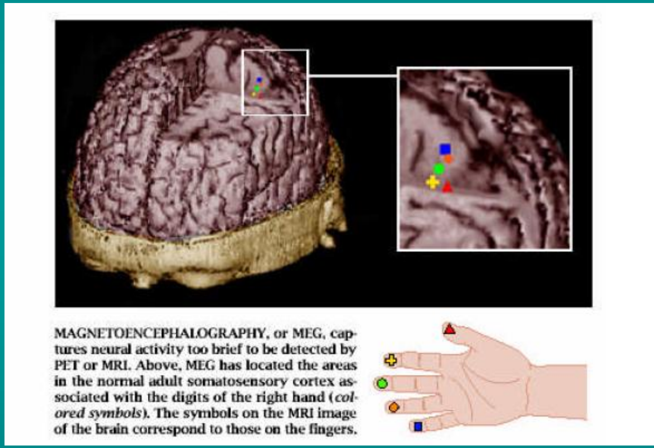
Human imaging
Brain imaging
Structural
Functional
•Computed tomography (CT)
•Magnetic resonance imaging (MRI)
•Voxel-based morphometry (VBM)
Direct measures of neural activity:
•Electroencephalography (EEG)
•Magnetoencephalography (MEG)
Indirect measures of neural activity:
• Positron-emission-tomography (PET)
• Single Photon emission computed tomography (SPECT)
• Functional magnetic resonance imaging (fMRI)
-BOLD-fMRI
• Near infrared spectroscopy (NIRS)
Hybrid modalities:
•PET-CT
•MR-PET
•fMRI-CT
•fMRI-EEG/MEG
•PET-SPECT
•CT-SPECT

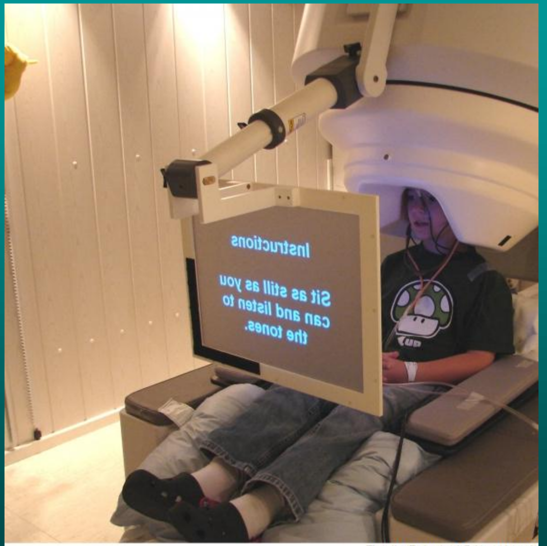
Imaging The Living Brain

- Computed Tomography (CT)
- Magnetic Resonance Imaging (MRI)
- Positron Emission Tomography (PET)
- Functional MRI (fMRI)
- Electroencephalography (EEG)
- Diffuse Tensor Imaging (DTI)
- Magnetoencephalography (MEG)

MEG: Magnetoencephalography
"Hairdresser from Mars"

Temporospatial resolution of MEG surpasses that of all other neuroimaging techniques, in real time; direct measure of neuronal activity; magnetic equivalent of EEG.



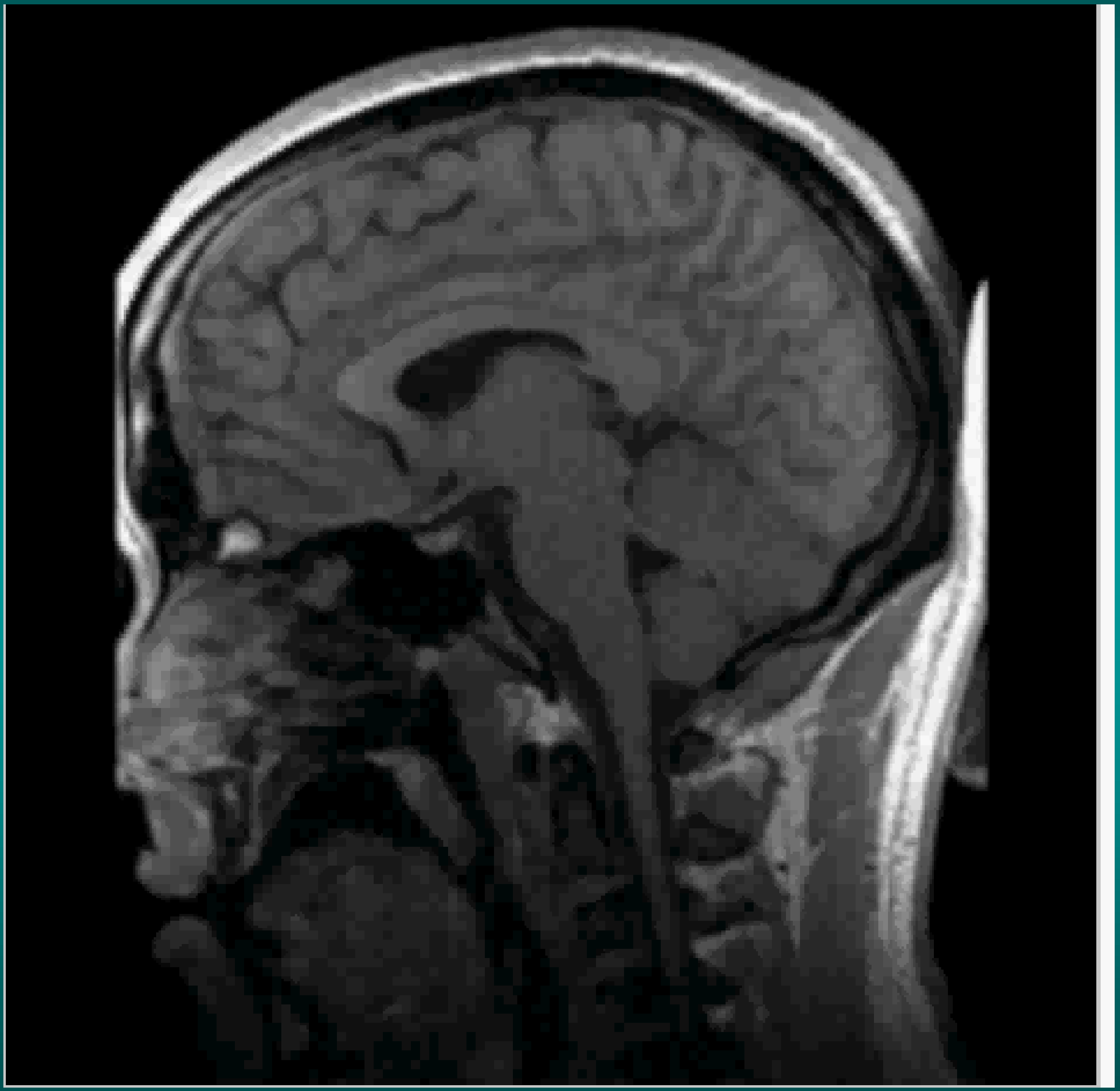


Timothy Roberts, 4-D Neuroimagin

MRI & fMRI

A la Rembrandt's The Anatomy Lesson of Dr. Nicolaes Tulp

MRI



New Couples fMRI Machine: Brain Areas sync when we interact

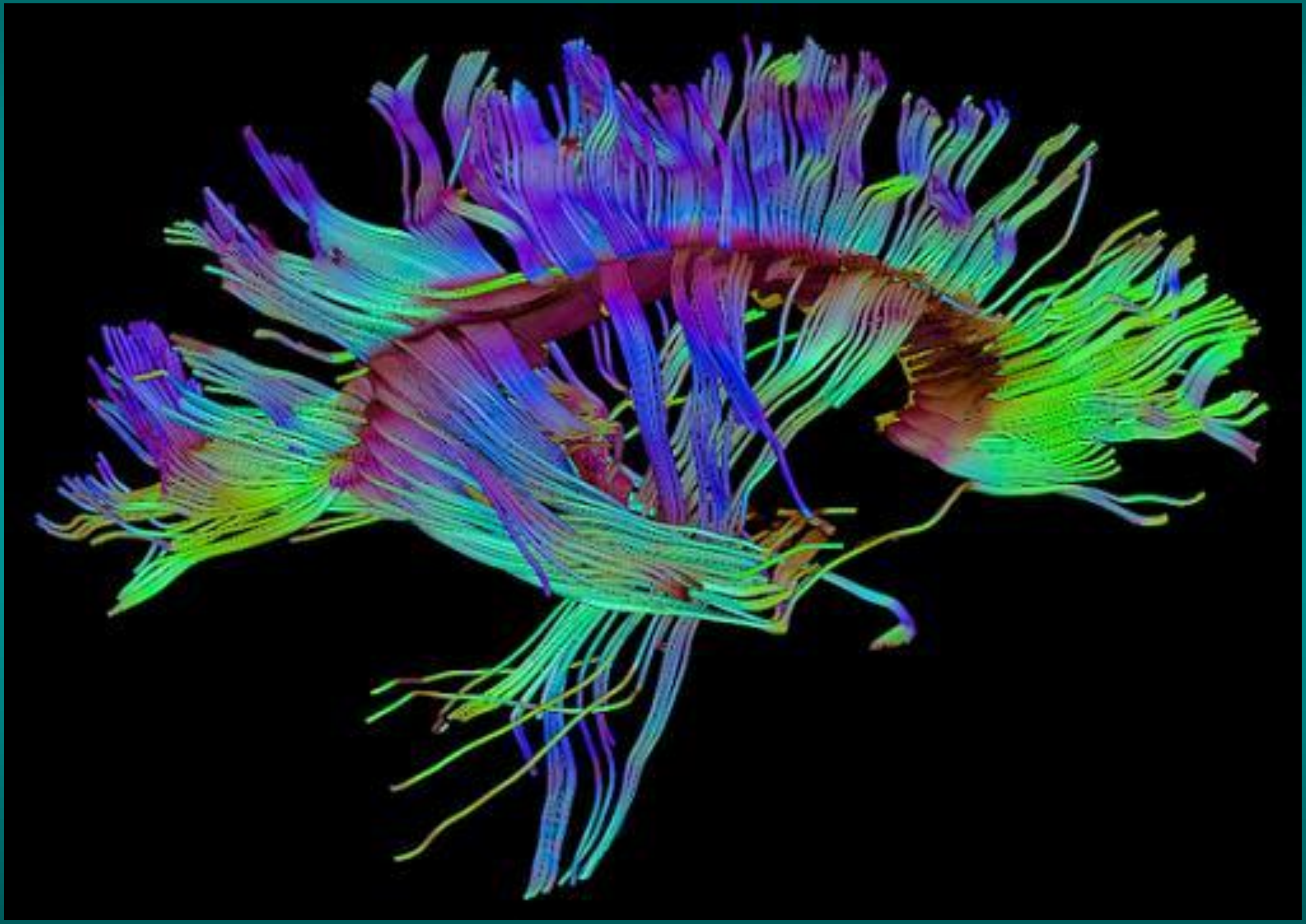
Friends: basal ganglia
Lovers: pCC

When touched: toucher's motor and somatosensory cortex couples to the other person's STS and somatosensory cortex.

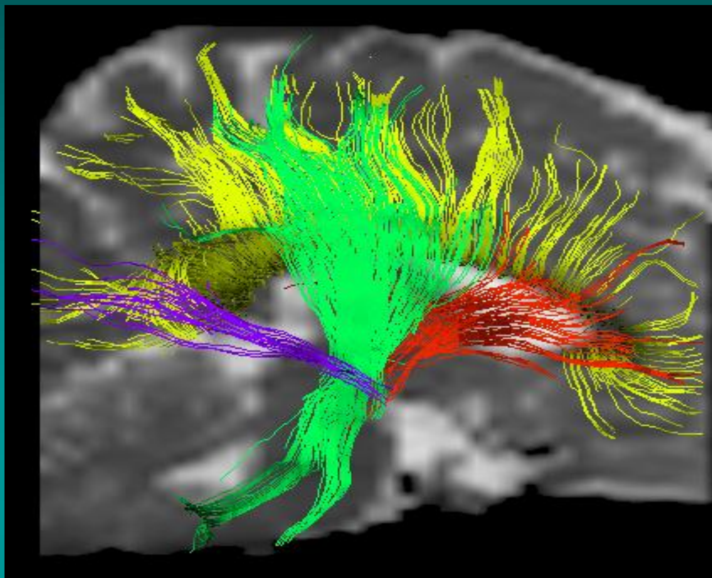
When people communicate: activates mPFC, TPJ, ACC

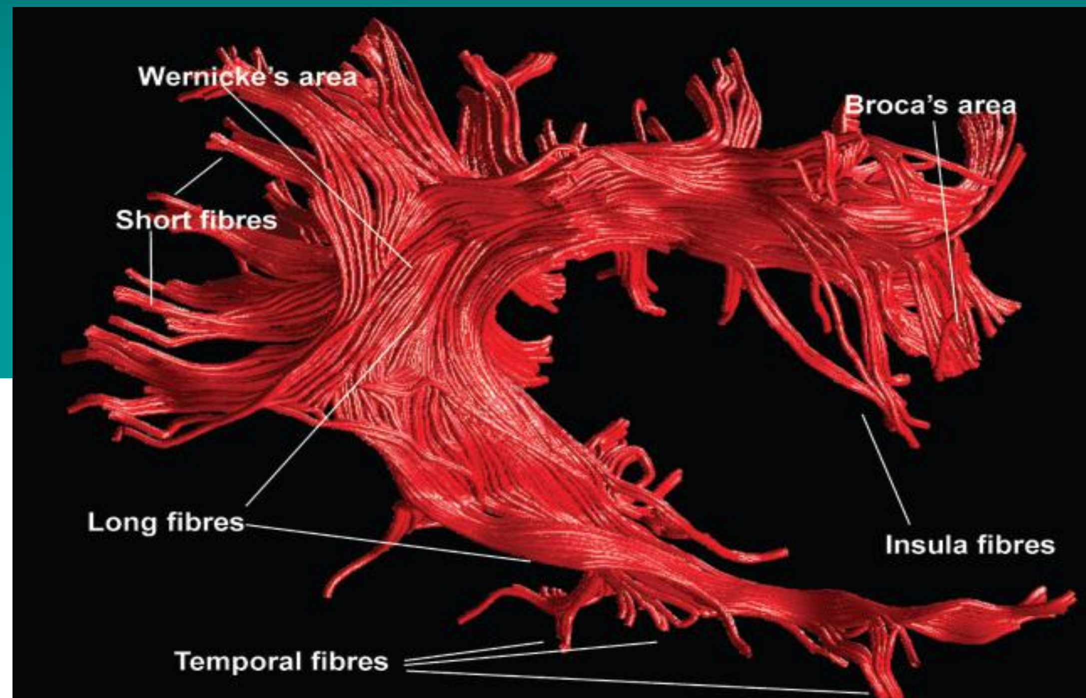
Ray Lee at Princeton University

DTI: Diffusion Tensor Imaging - Direction of water molecules



DTI – Tractography

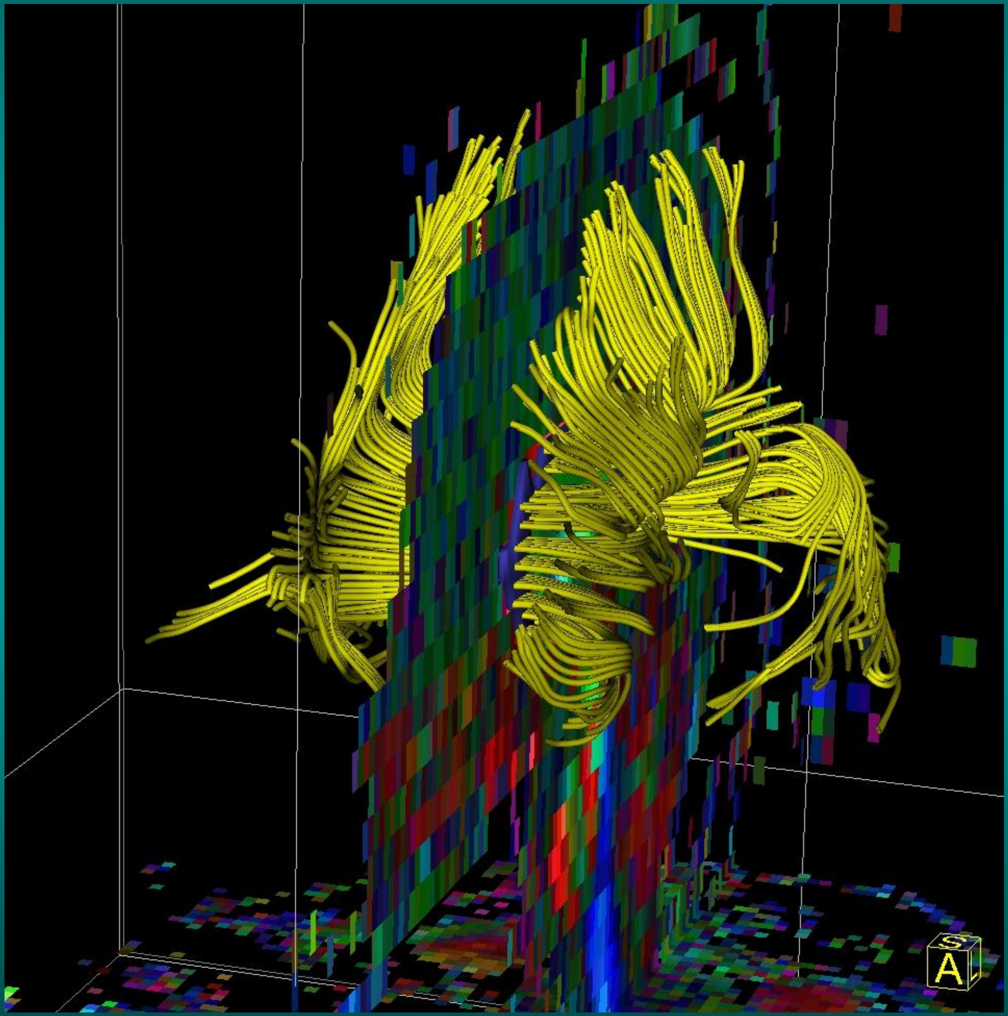


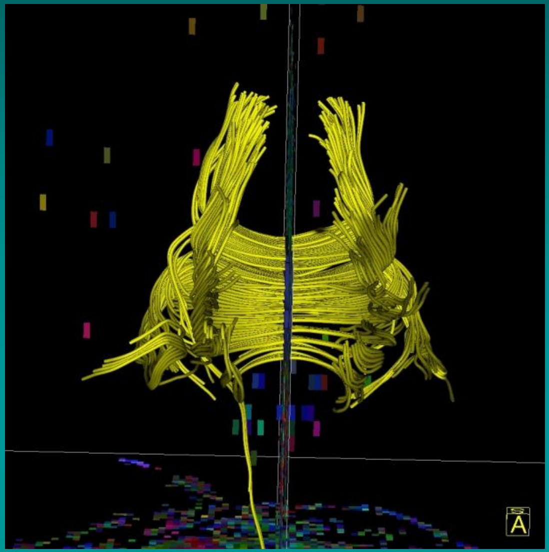


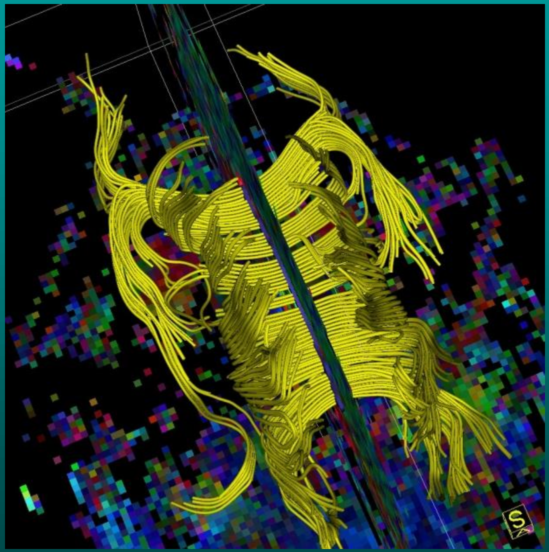
D. Jones – U Nottingham, UK

S. Mori - JHU

DTI-Tractography: Corpus Callosum

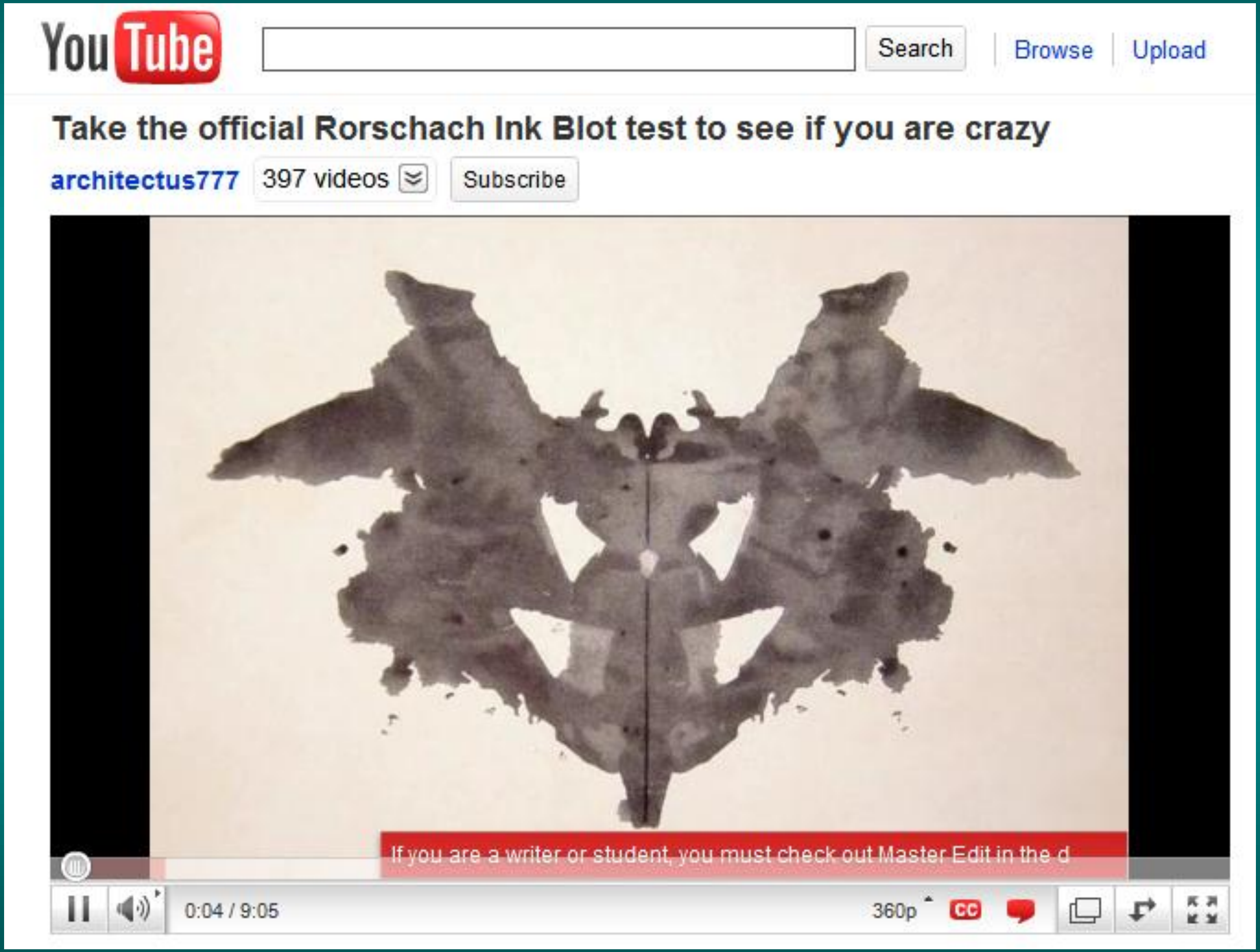






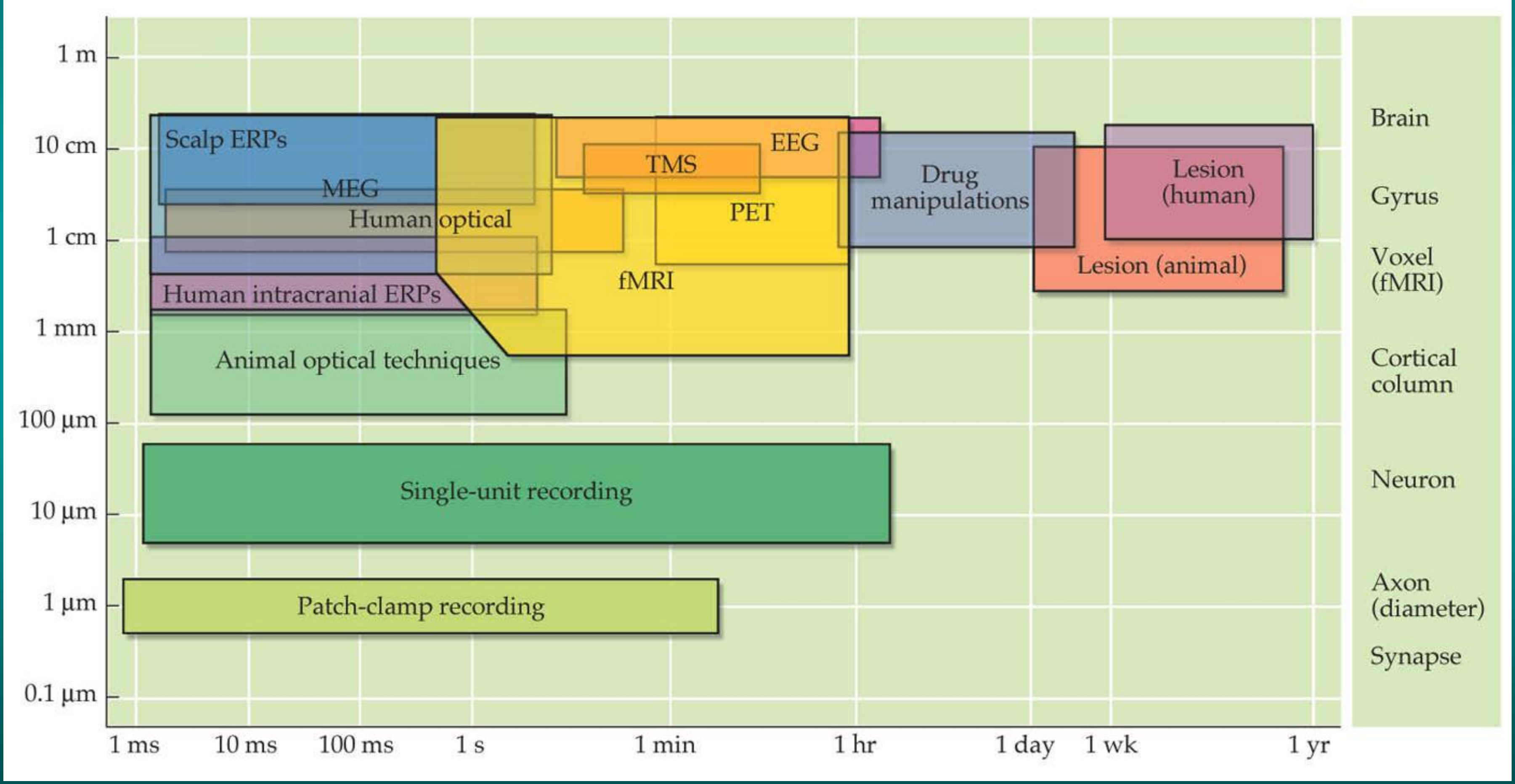
W.Zhan et. al.

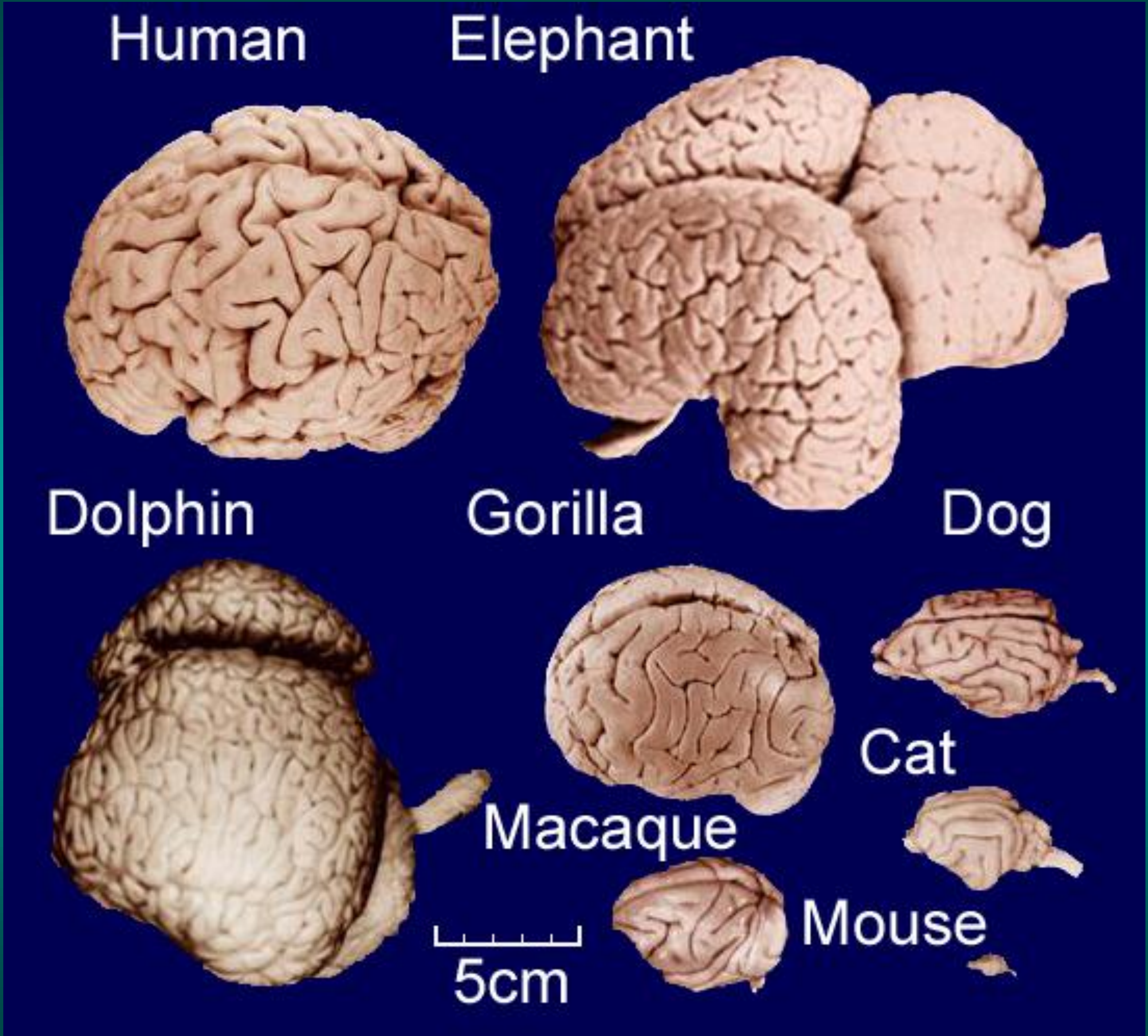
Older method, but Alas, alas…



New: Rorschach Performance Assessment System

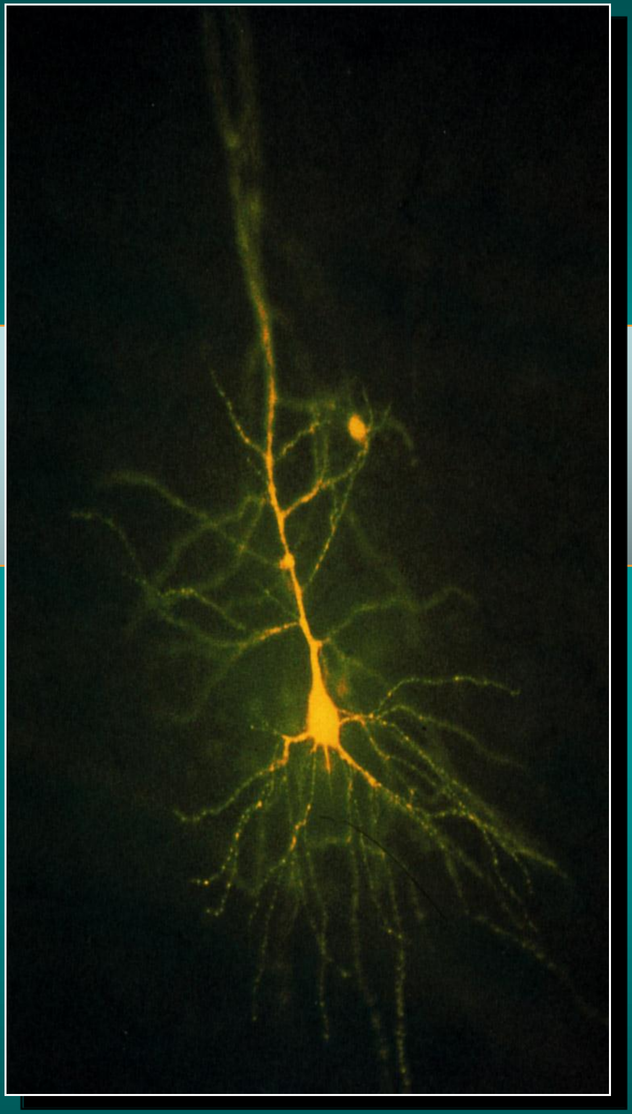
Scale in studying the nervous system




Human
Elephant
Dolphin
Gorilla
Dog
Cat
Macaque
Mouse
5cm

Chimpanzees and Human Genomes

- 1.8 % Exon Difference: of 3 billion DNA letters, only 1.5 million are different
- Most change sequences: HAR1 (brain development), FOXP2 (speech), ASPM (brain size), HAR2 (hand and wrist development), AMY1 (digestion of starch), LC (digestion of milk)
- Deficits in HAR1: lissencephally (no folds); in ASPM: microcephaly
- 4% Intron “noncoding area” differences



Cerebral Cortex

Numerical Data

❖ ***Number of neuronal cells in cerebral cortex***

neurons ----------- 100 billion (in both cortex & cerebellum)

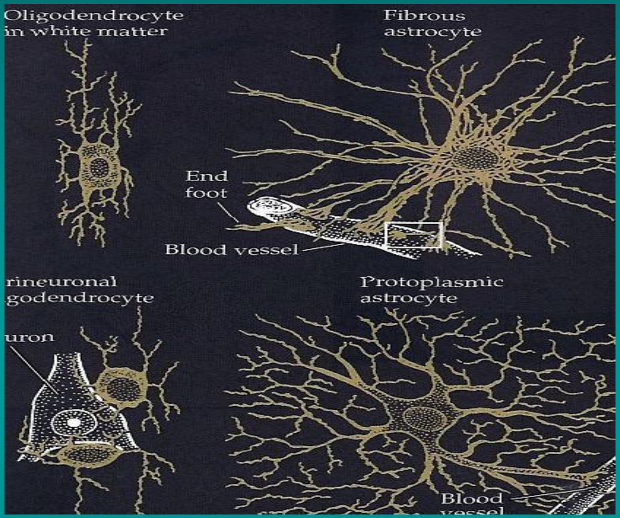
glial cells ---------- 300 billion

❖ ***Estimation of number of cortical neurons***

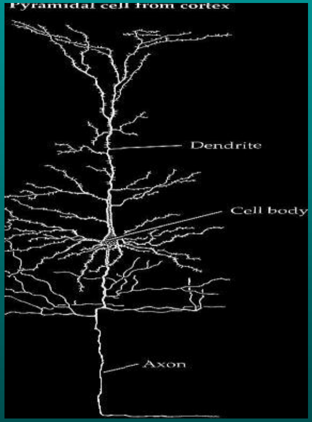
von Economo and Koskinas (1925)	**14.0 billion**
Shariff (1953)	**6.9 billion**
Sholl (1956)	**5.0 billion**
Pakkenberg (1966)	**2.6 billion**

Brain: Cellular Organization

- Glia:

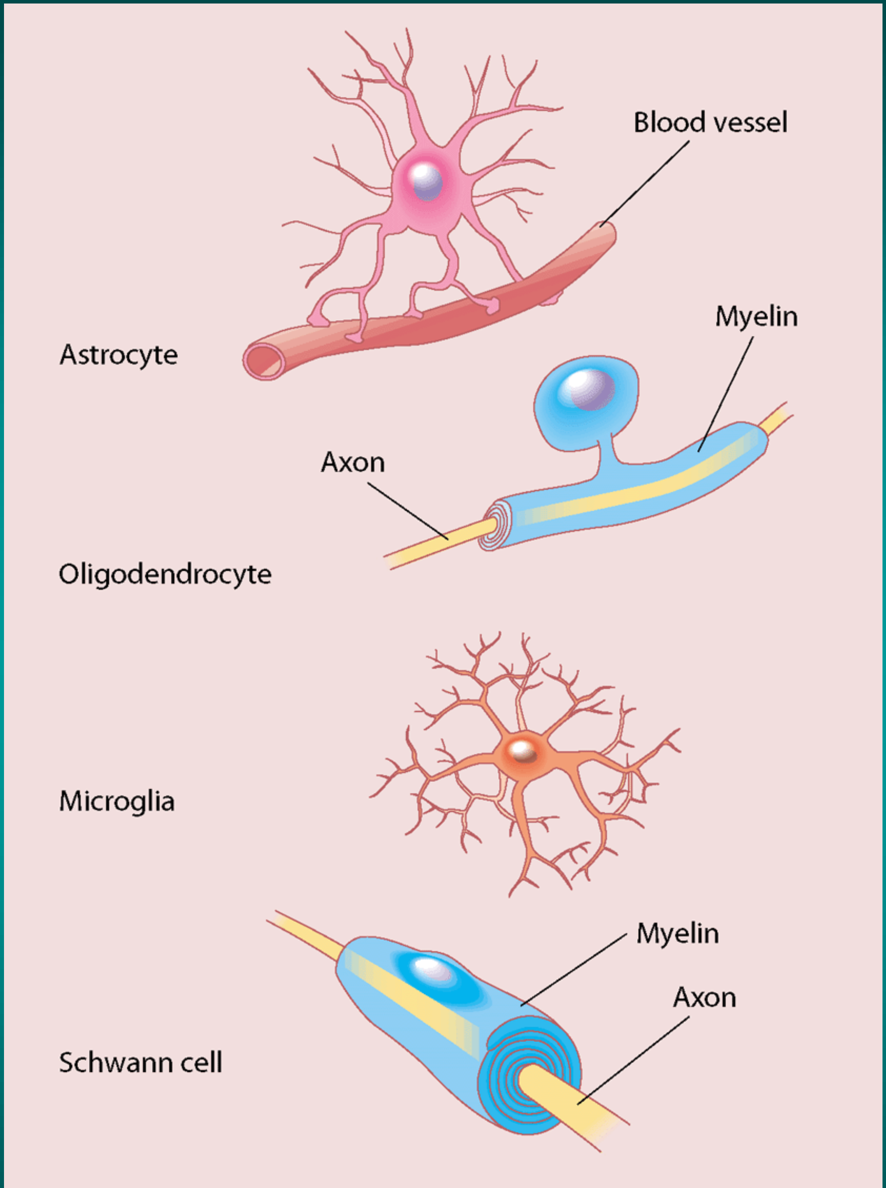


- Neurons:



Glia (Glue)

- 3 glia to 1 neuron
- Myelin sheath
- Form blood-brain barrier
- Removing debris and excess neurochemicals
- Structural support for neurons
- Critical role in brain development
- Enhances neuronal performance: overall moderator, regulating which messages are sent on and when



Neuroglia – the supporting cells

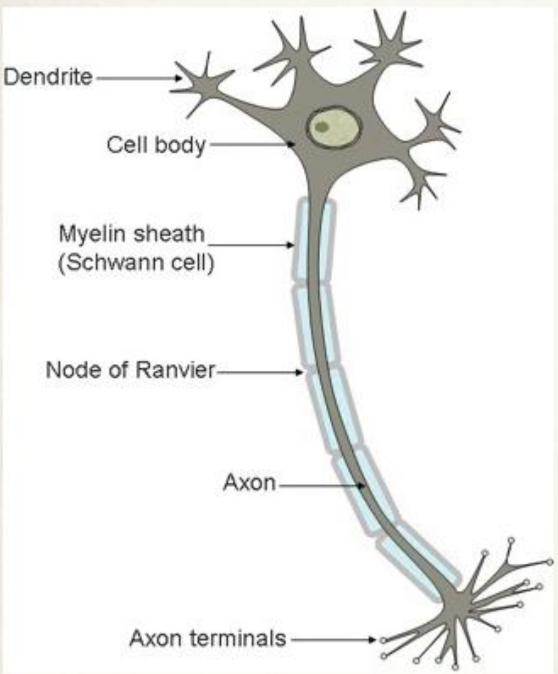
- Oligodendrocytes – Myelination in CNS
- Schwann cells – Myelination in PNS
- ____
- Astrocytes – Blood brain barrier & regulates extracellular environment
- Microglia – Phagocytic function (kill microbes) to protect brain from micro-organisms
- ____
- Radial glia – Guides neuronal development
- Satellite cells – Nourish & support neurons of PNS, especially in ganglia.

Neurons

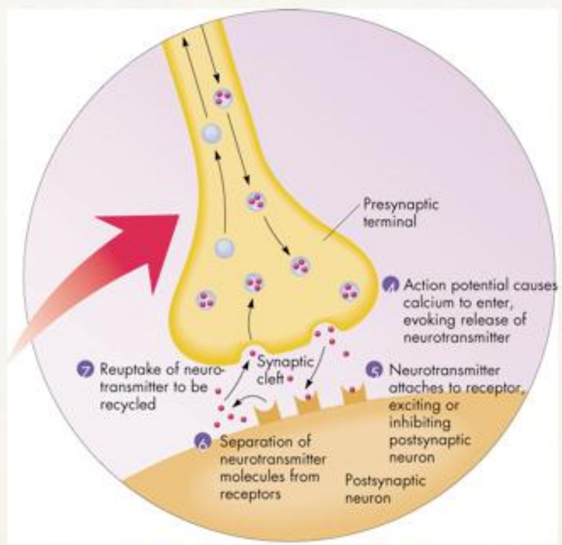
- Anatomy
- Physiology

The Least Brain Anatomy You Need to Know

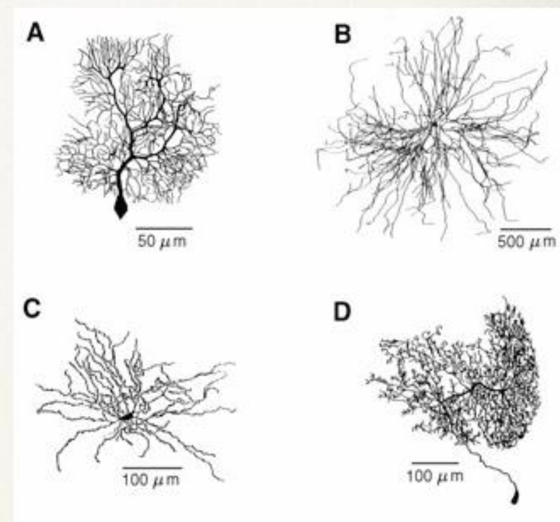
A ***neuron*** is a specialized brain cell



Neurons connect at ***synapses***

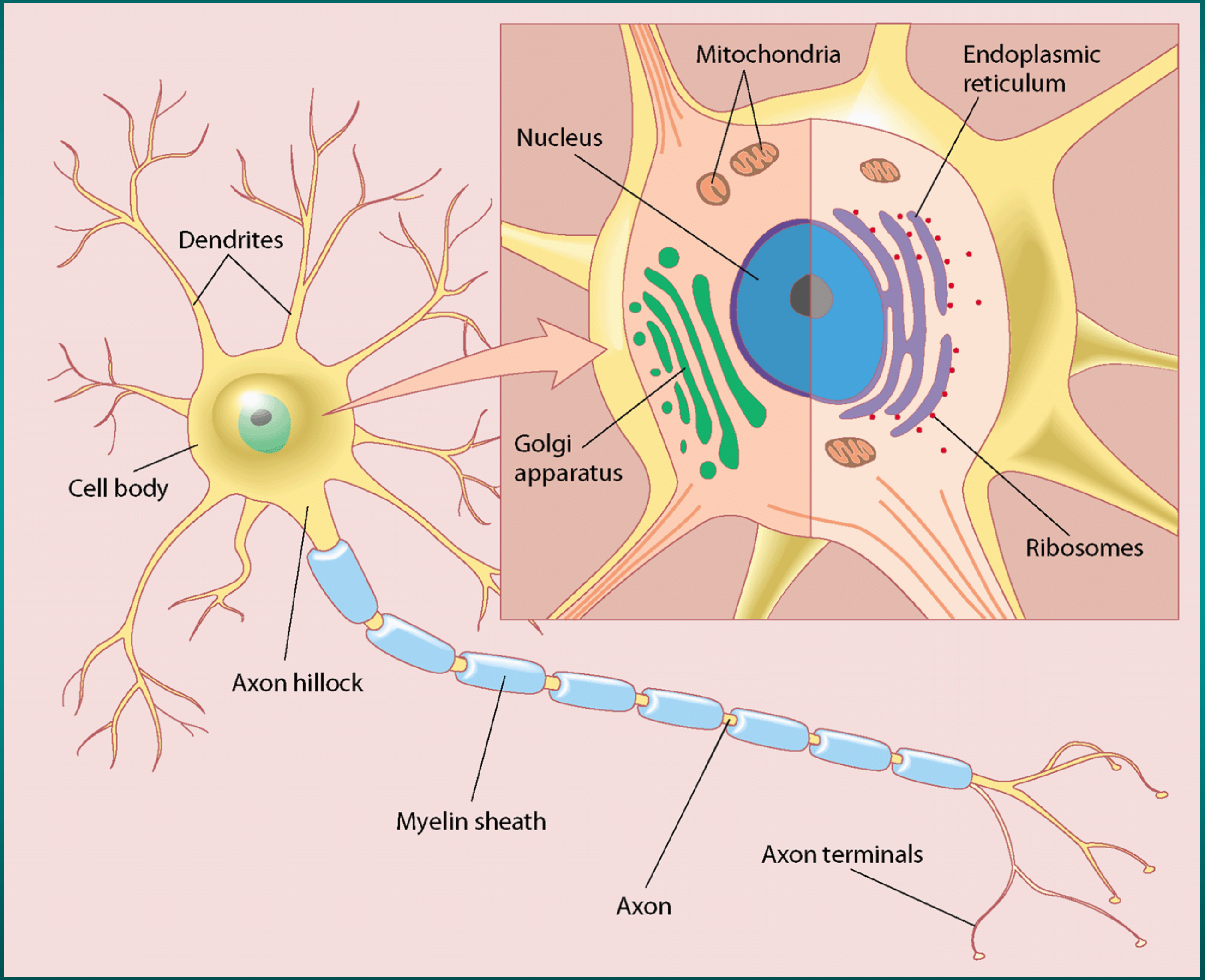


Neurons come in many ***varieties***

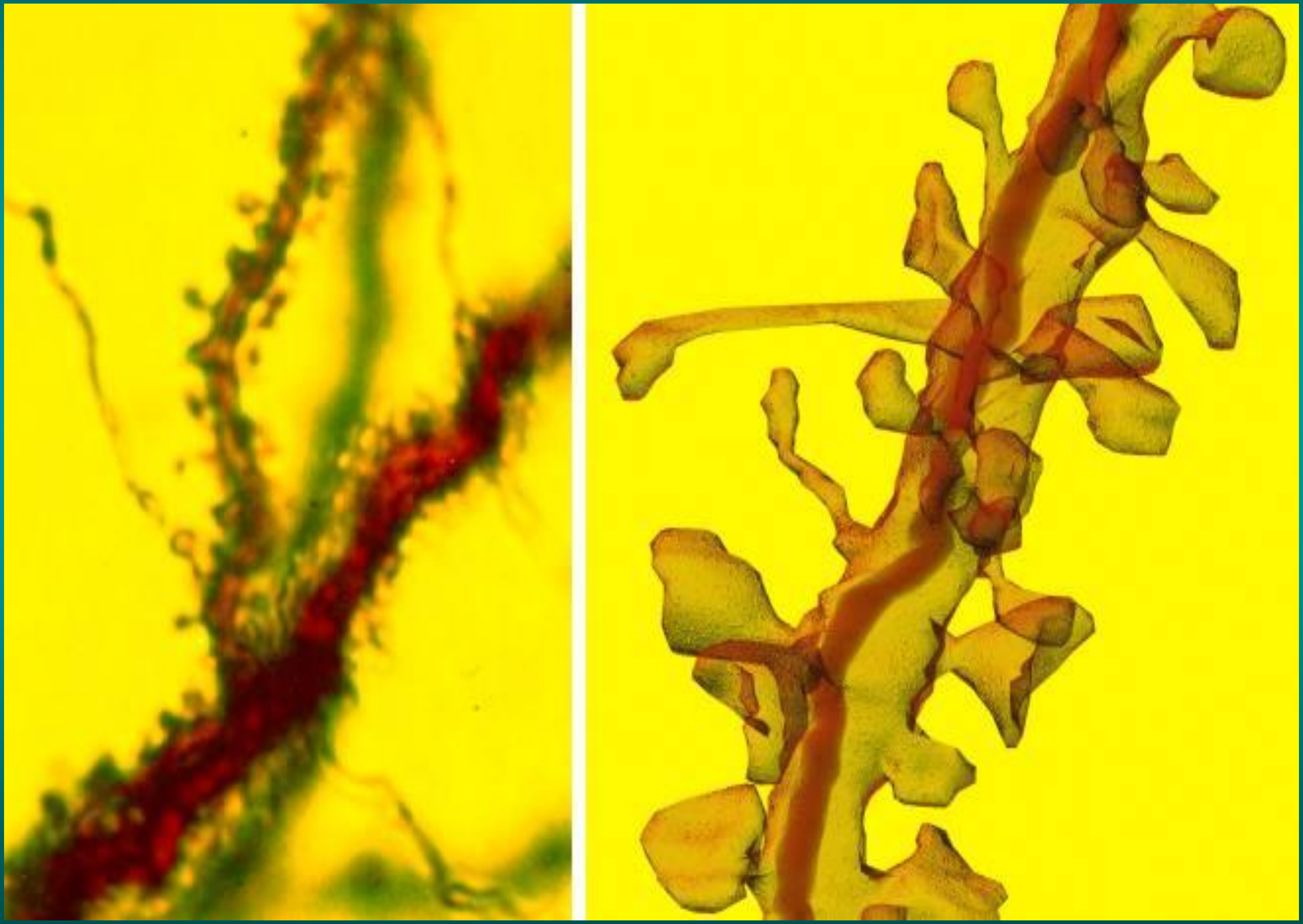


Anatomy of a Neuron 1

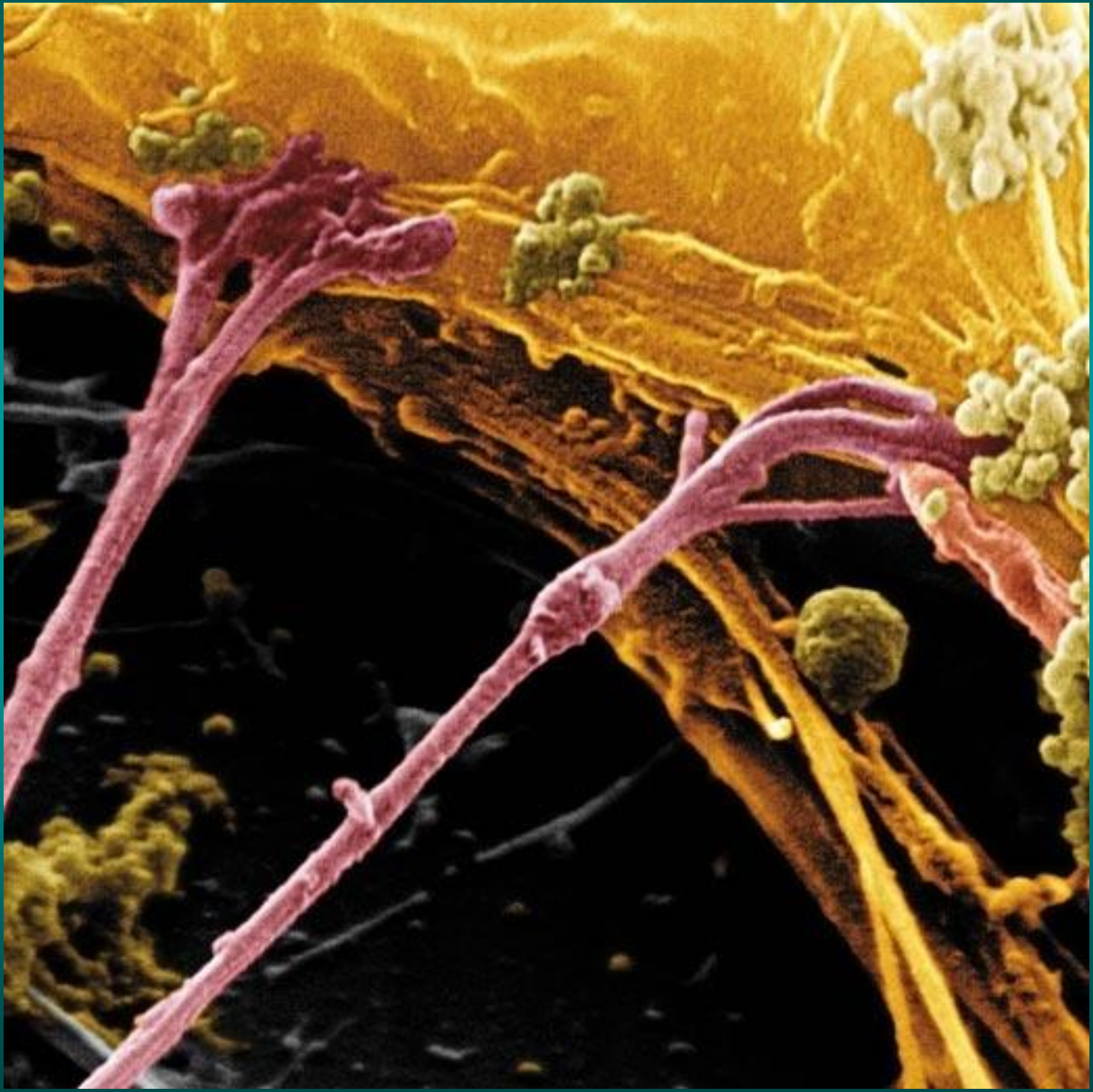
- Cell body (or soma),
- Dendrites
- Axon



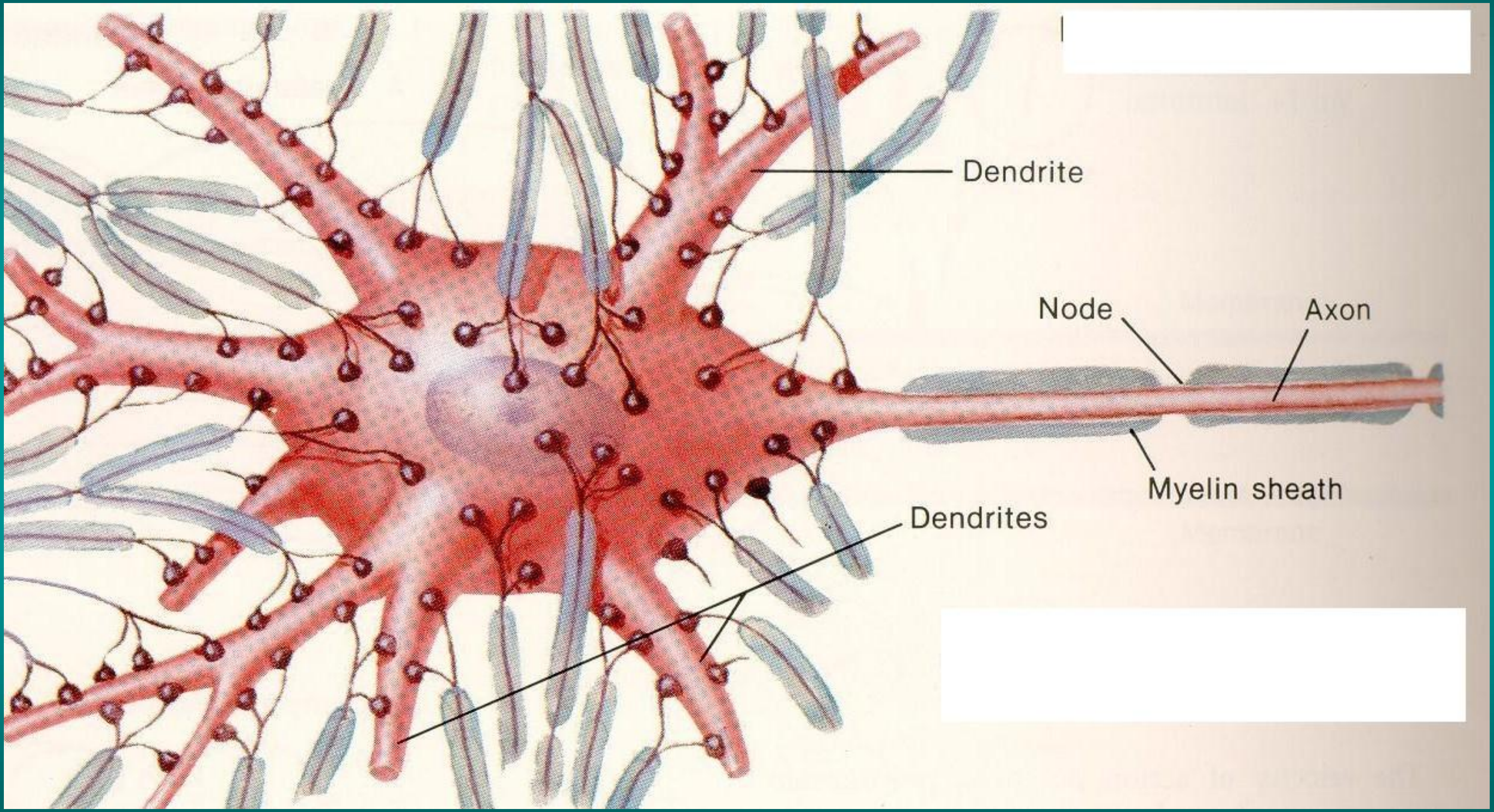
Dendrites: Electron Microscope



Dendrites



1000s of Synapses



Data Estimate: 100-1000 terabytes of information

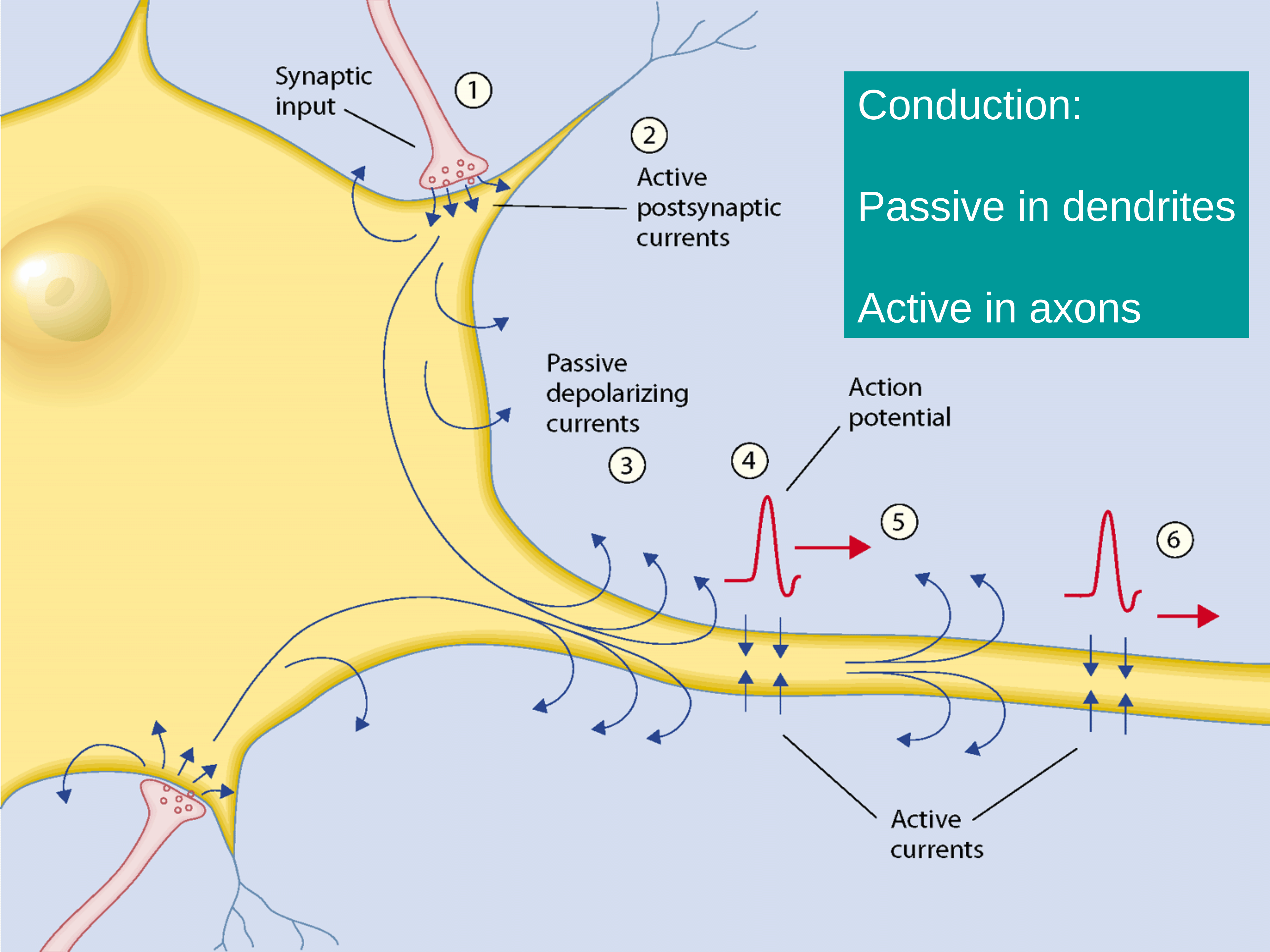
Neuron Physiology

- Neurons perform computations;
  they transform information.
- The functional components of a neuron.
  - input = (dendrites)
  - integration = (axon hillock)
  - transmission = (axon)
  - output = (synapse)
- Passive vs. active conductance
- Electrical vs. chemical transmission

Conduction:

Passive in dendrites

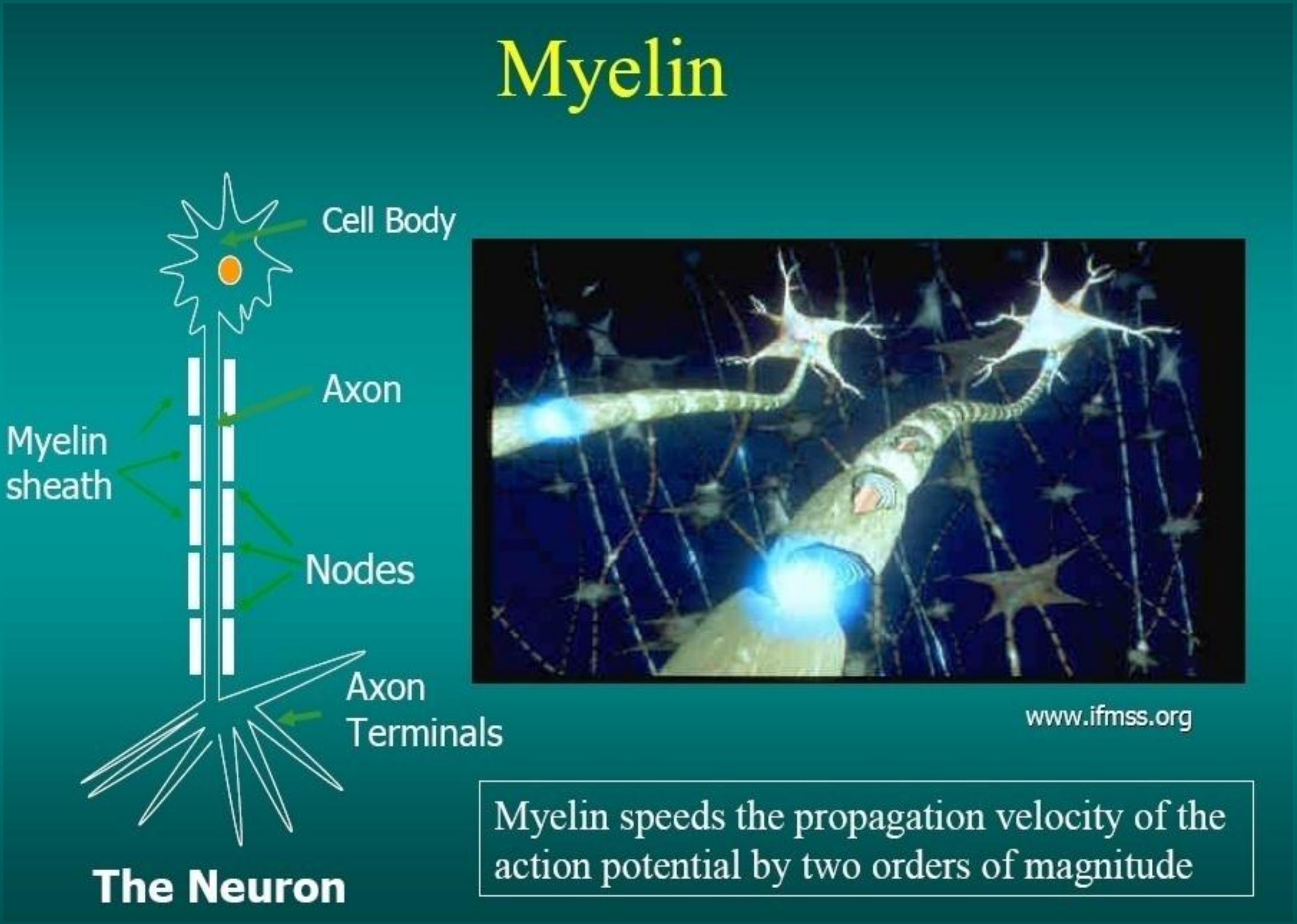
Active in axons



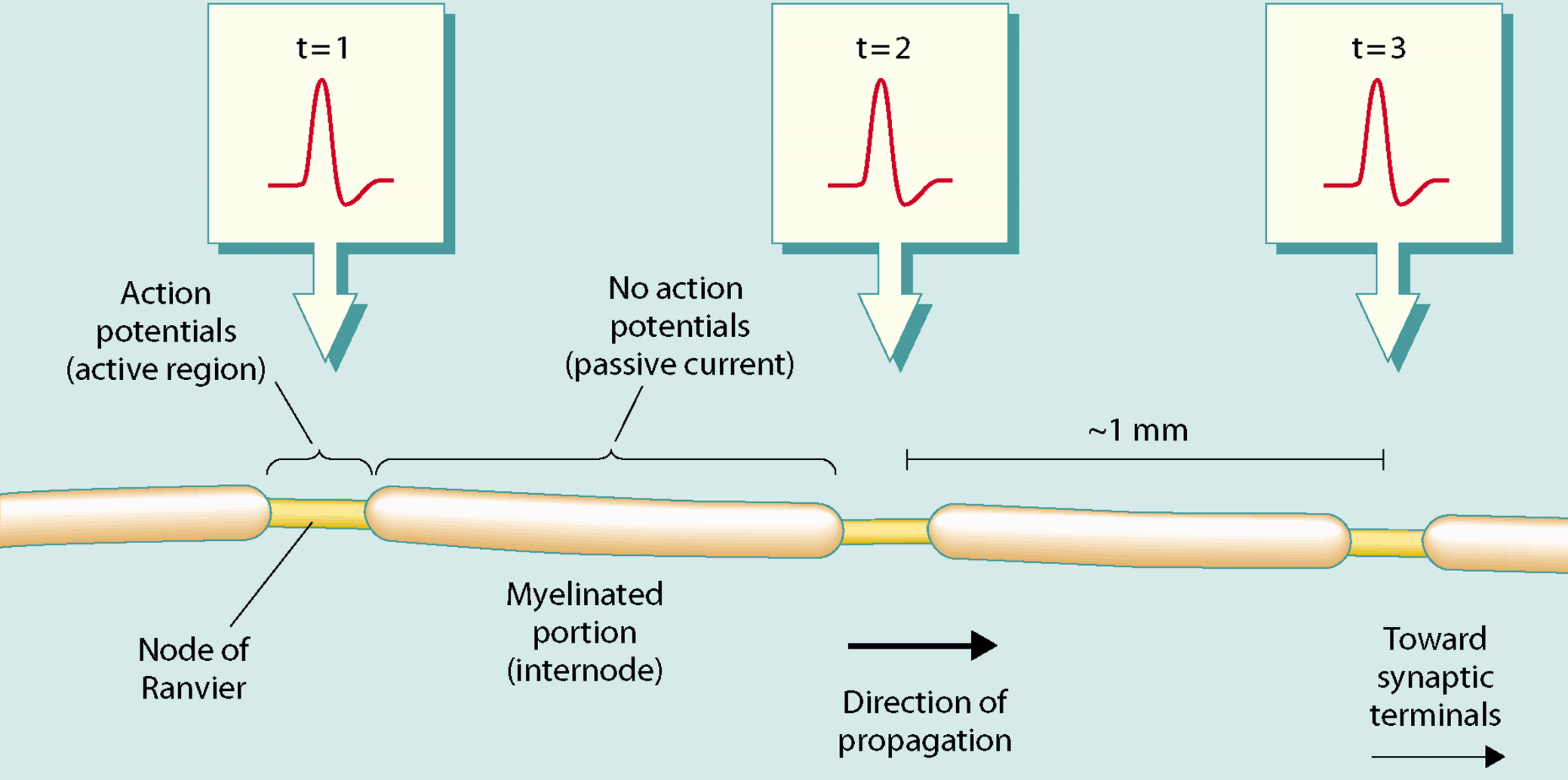
Neurotransmitters

- Acetylcholine: diffuse; memory; major projection areas: nucleus basalis of Meynert
- Glutamate: slow excitatory; diffuse; LTP
- GABA: fast inhibitory; diffuse
- Dopamine: neuromodulatory; alertness, reward: projections from sub. nigra, ventral tegmental, hypothalamus
- Norepinephrine: neuromodulatory; alertness, reward from locus coeruleus & lateral tegmental
- Serotonin: neuromodulatory: from raphe nuclei

Myelin: 136,000 KM of Myelinated Axons

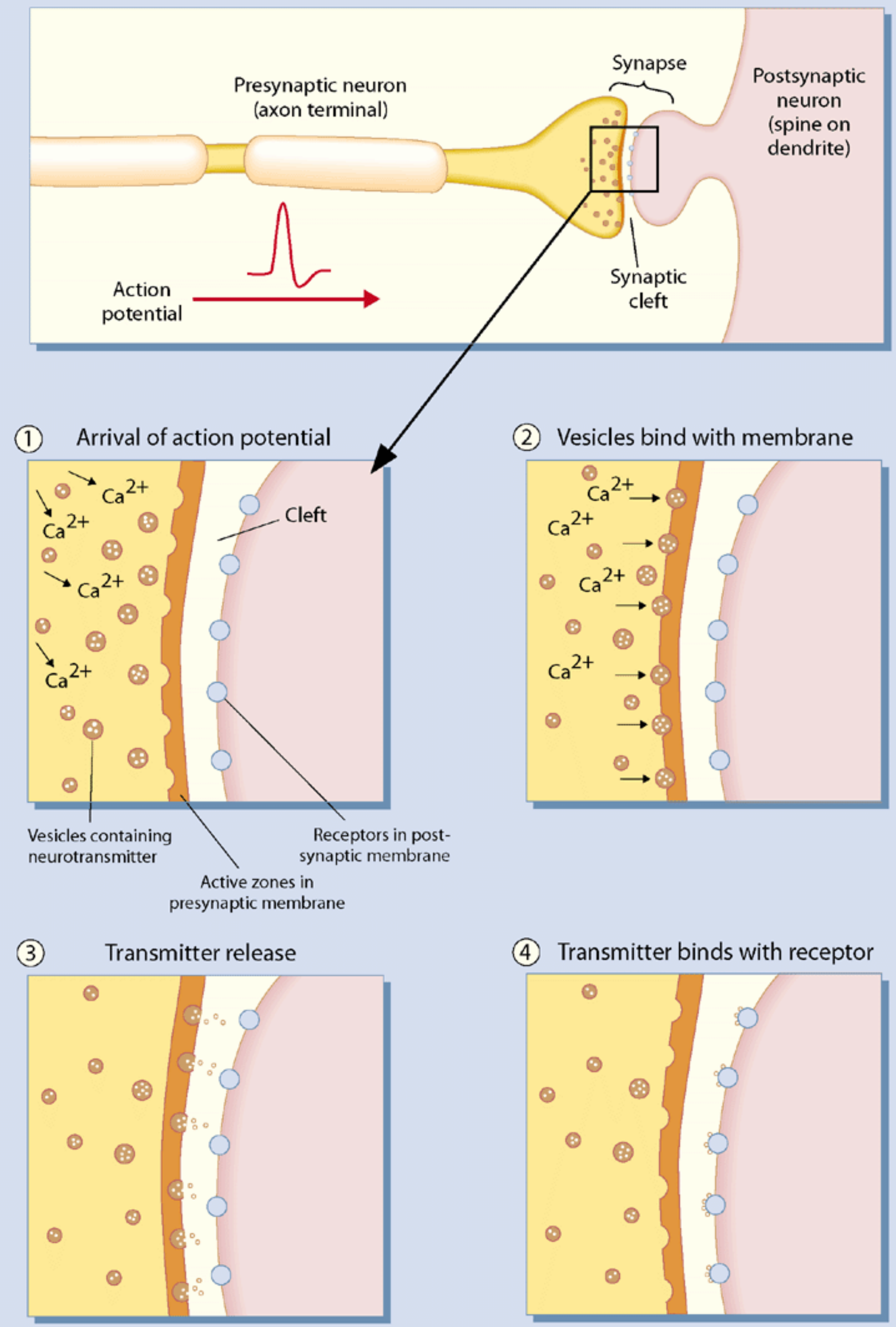


Electrical Conduction in Myelinated Axons



Chemical transmission across the synapse

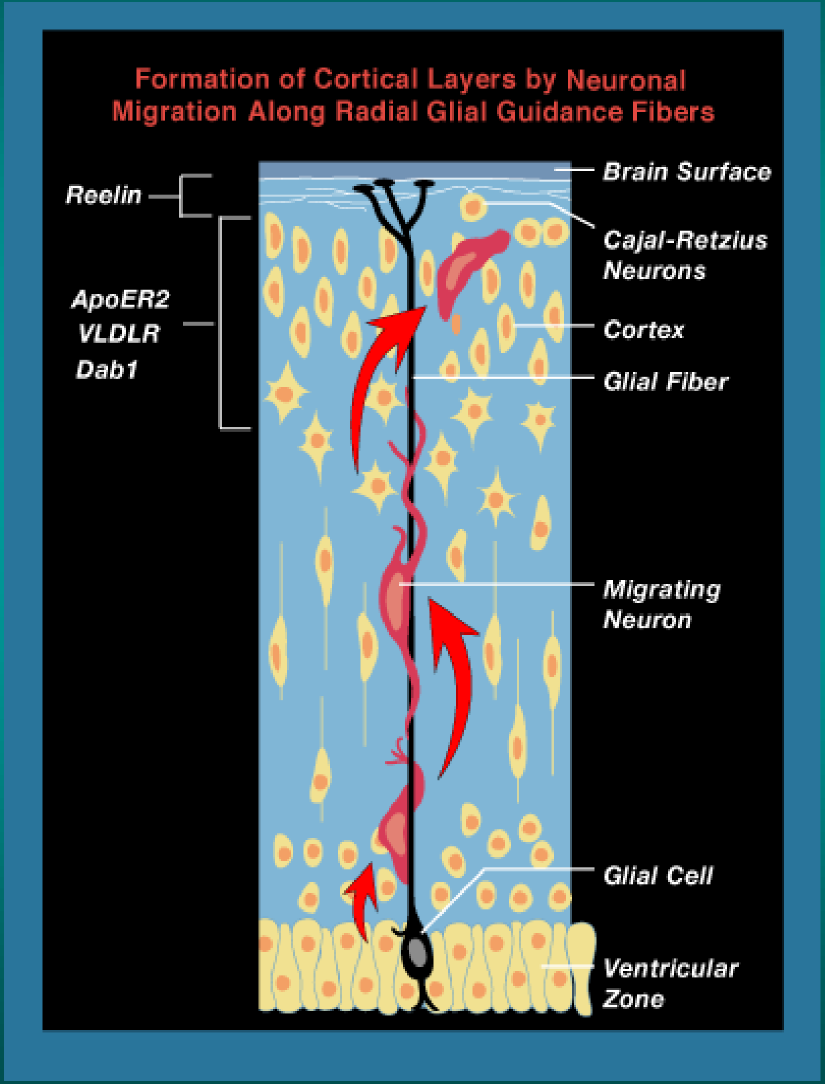
Axon to Dendrite



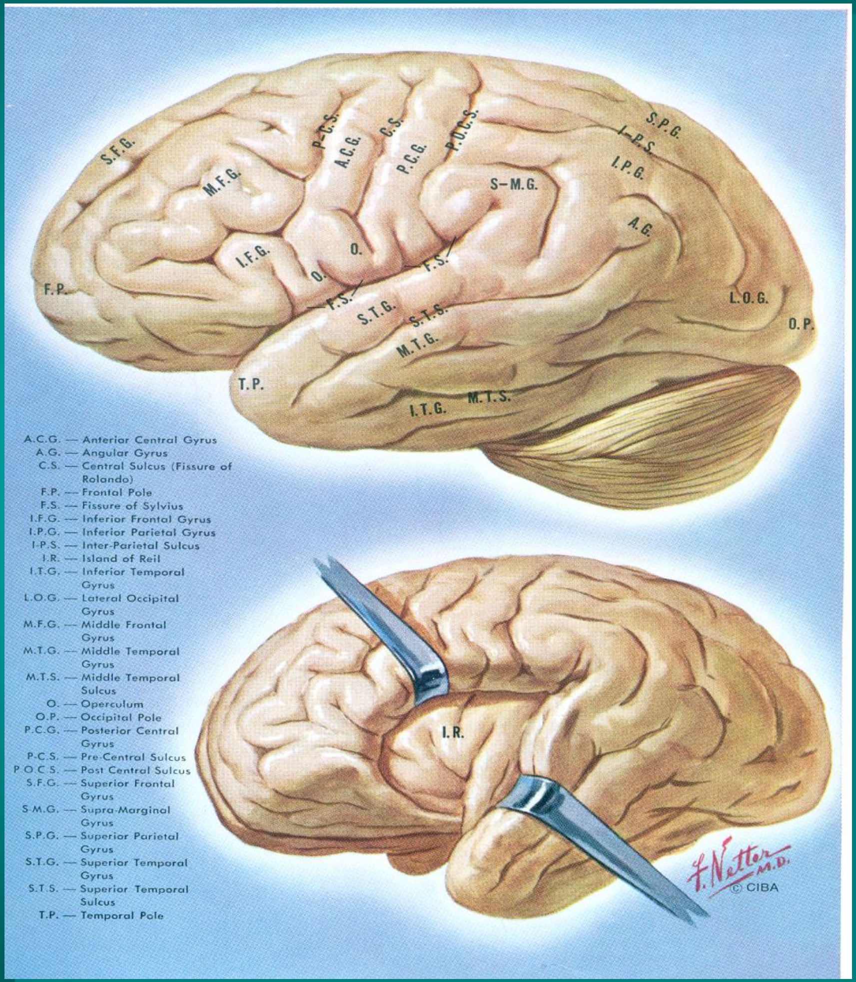
Cortex: 2 types of cells

- In humans, 90% of the cerebral cortex is neocortex.
- Neocortex contains two primary types of neurons, excitatory pyramidal neurons (~80% of neocortical neurons) and inhibitory interneurons(~20%).
- Pyramidal neurons are the primary excitation units of the mammalian prefrontal cortex and the corticospinal tract.

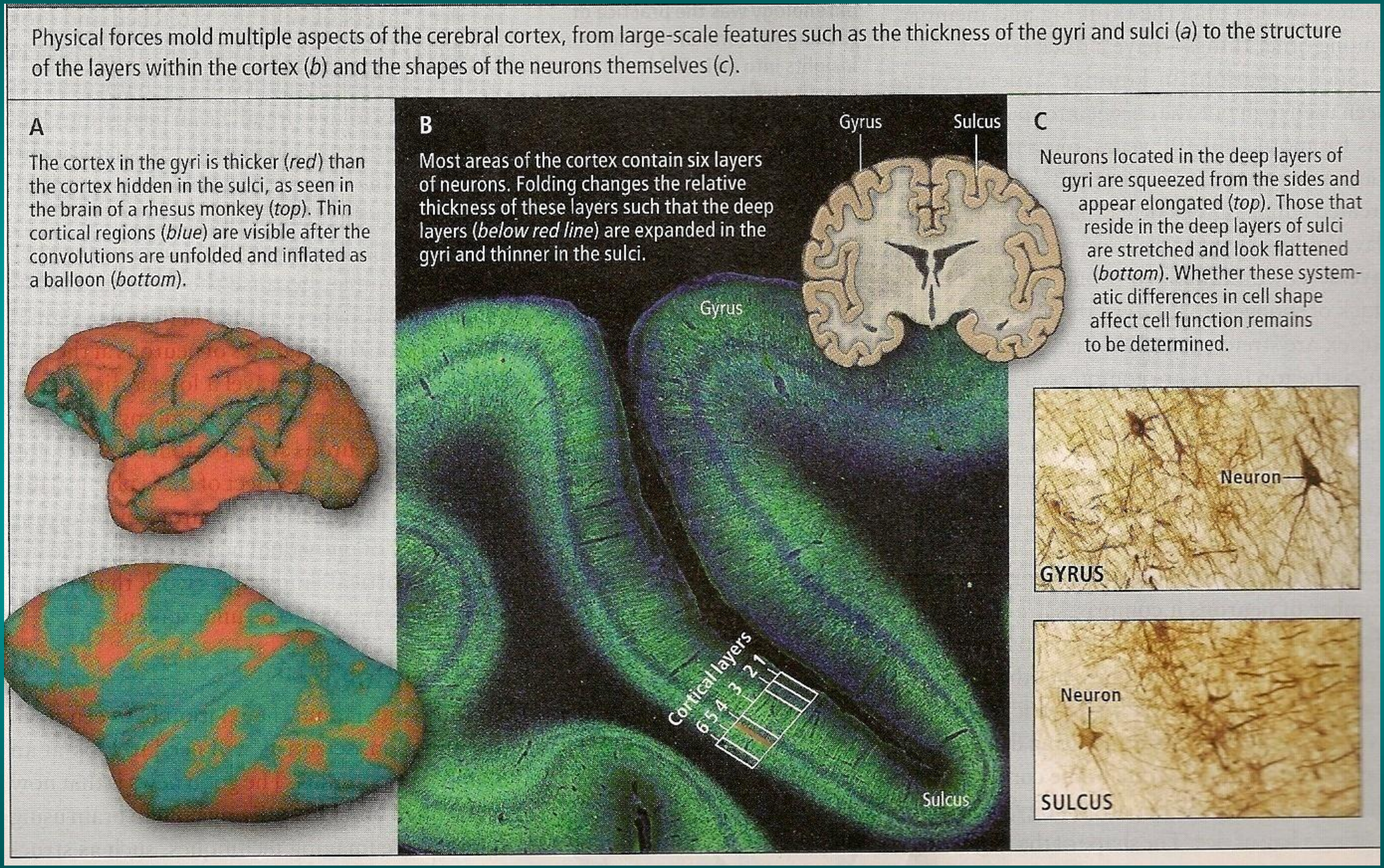
Neuronal Migration: Follow that Glial Cell



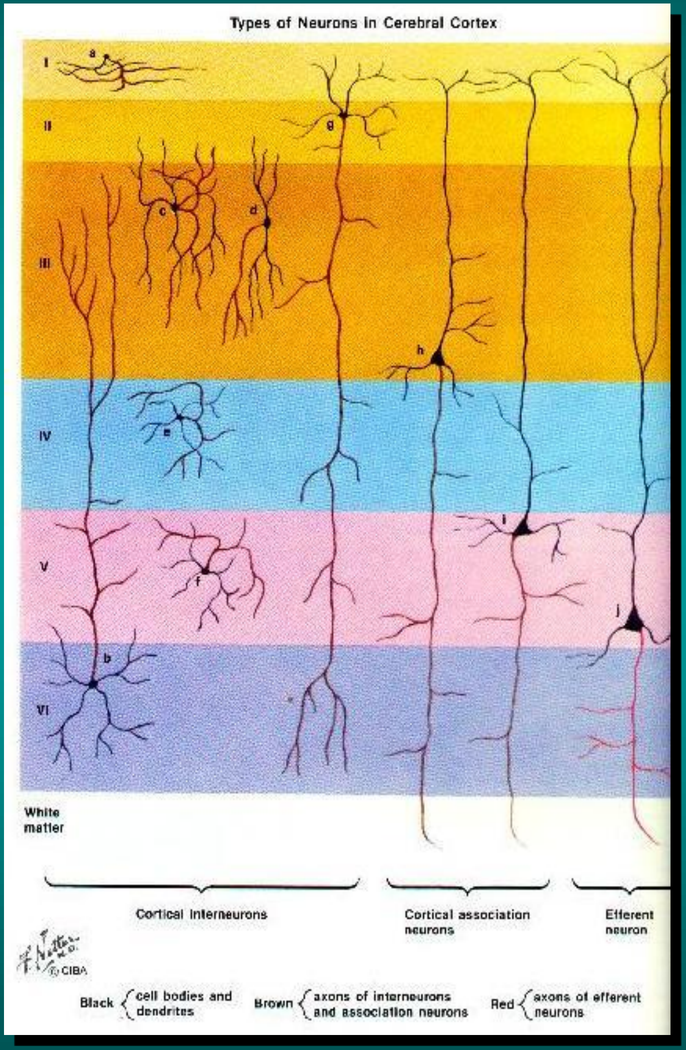
Gyri and Sulci: Hills & Valleys



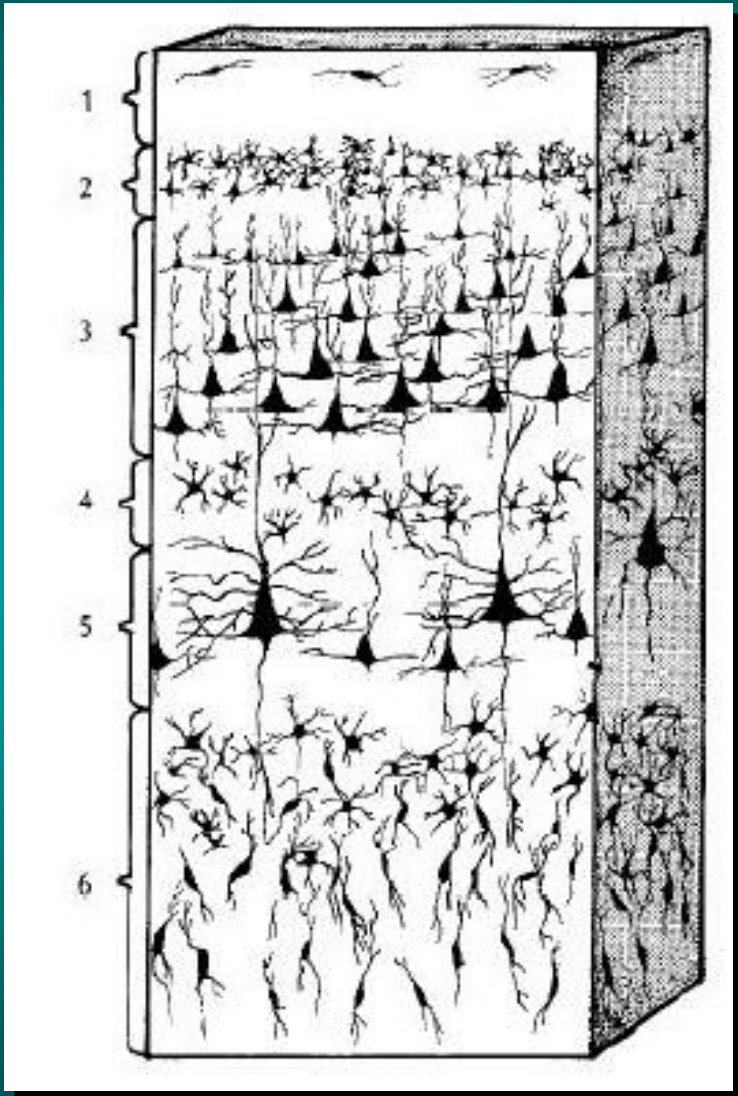
Gyrus & Sulcus: Thinner in Sulcus (valleys)



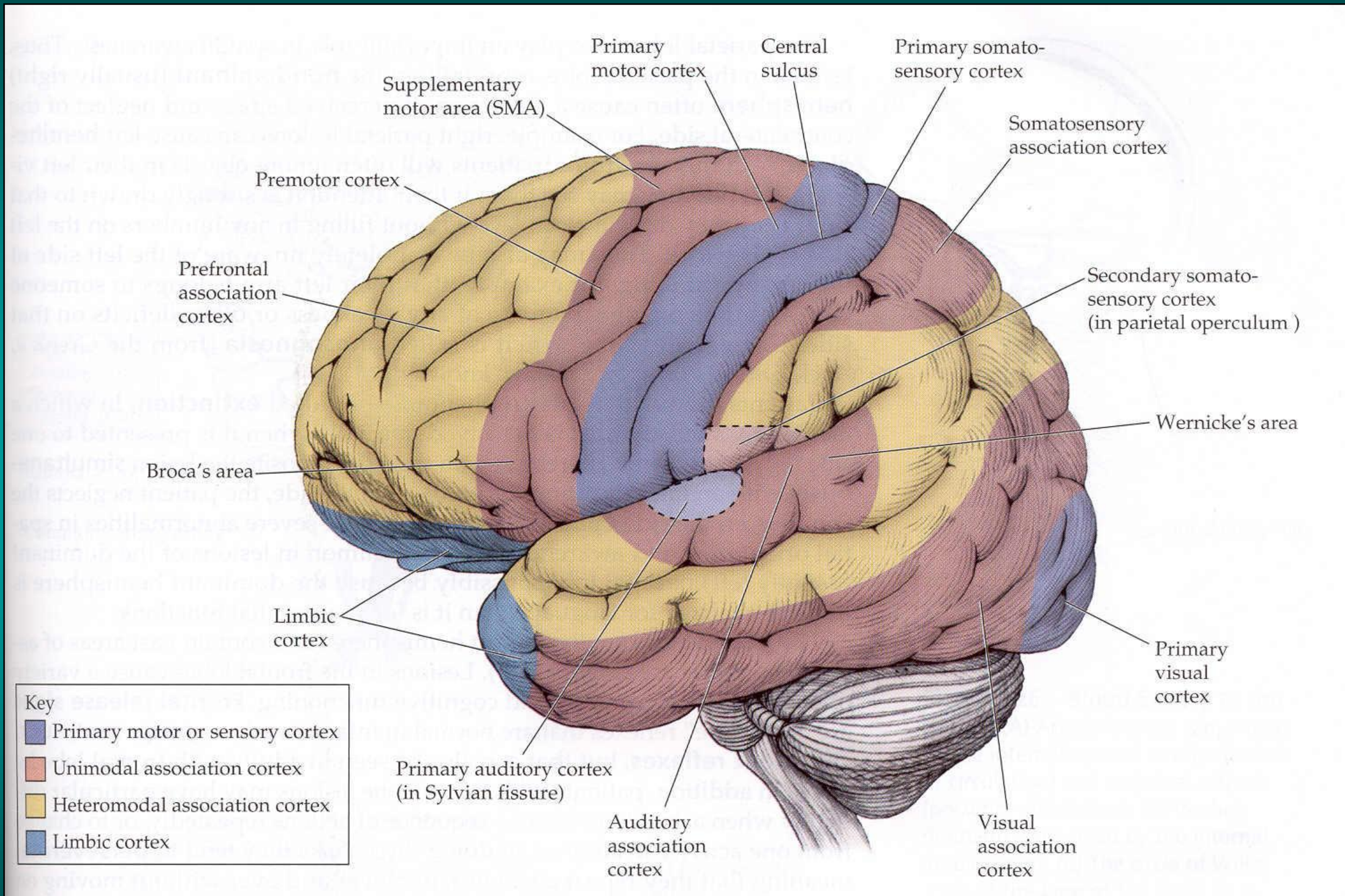
Cortical Layerization: 6 layers



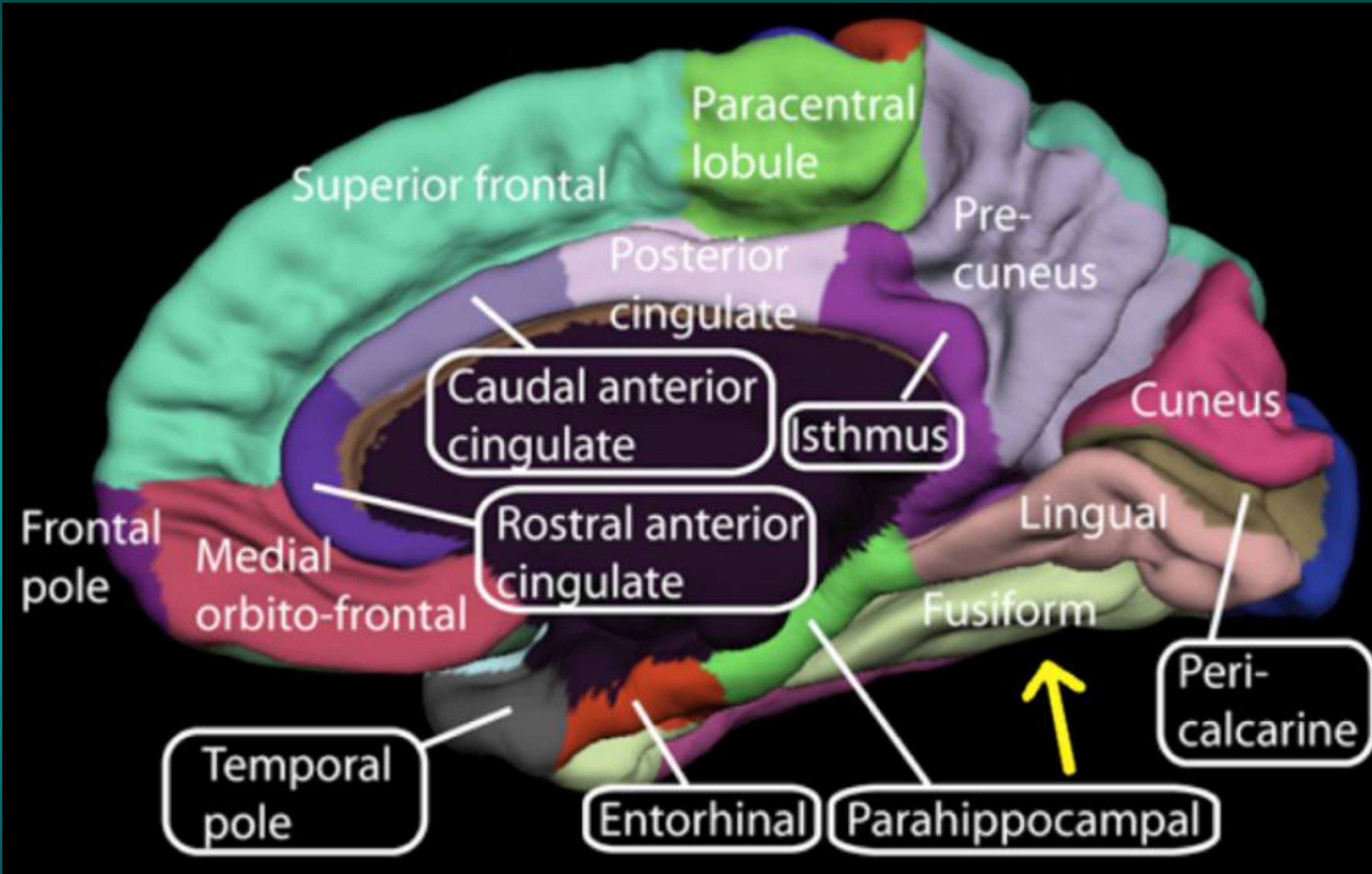
Cortical Layer Organization

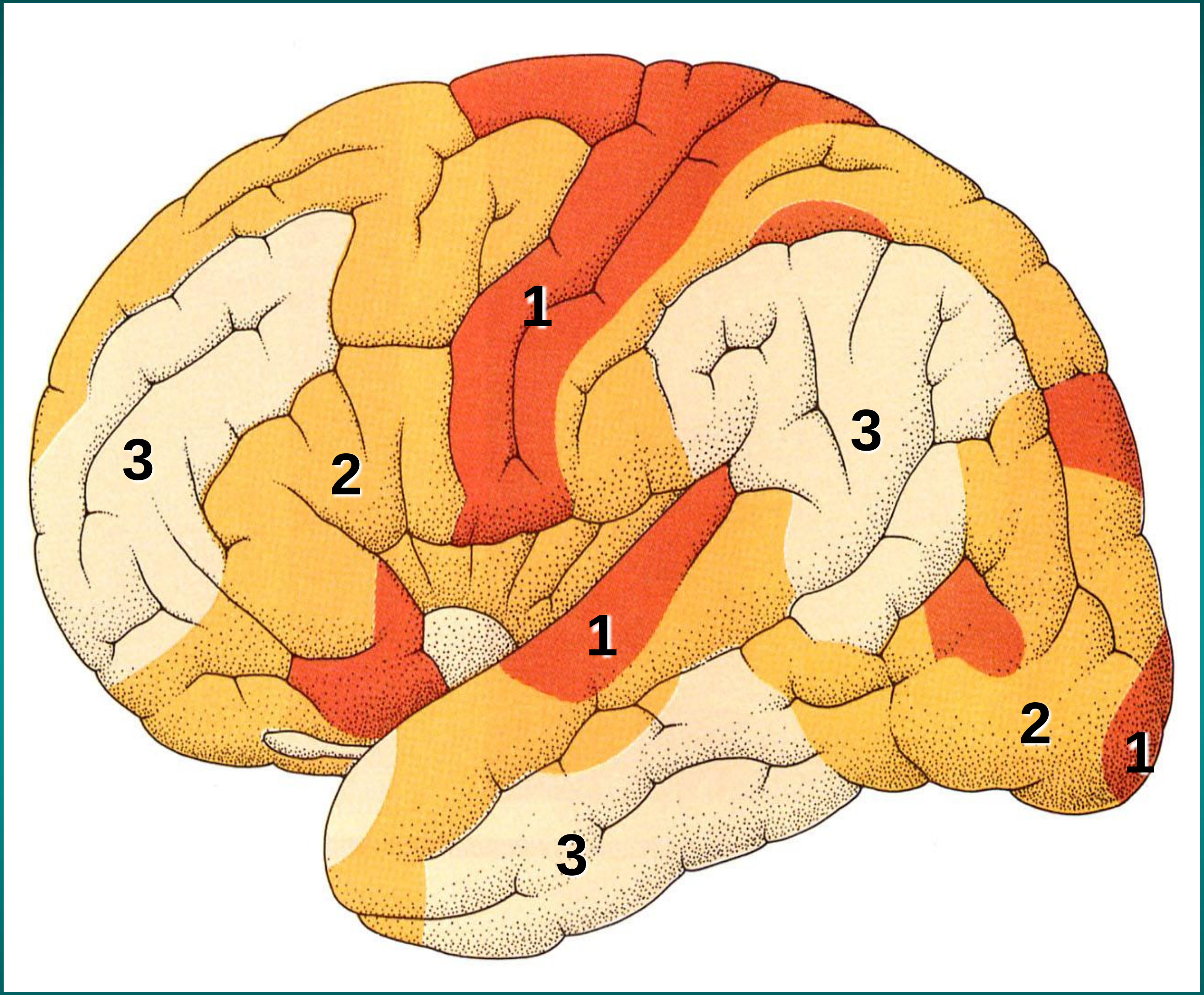


- Layer I: Input dendrites & axons from lower levels
- Layer II: Input from CC & Association areas
- Layer III: Output to association areas (thought)
- Layer IV: Input from thalamus (outside cortex: senses)
- Layer V: Outputs to other subcortical: motor (voluntary movement)
- Layer VI: Outputs to thalamus



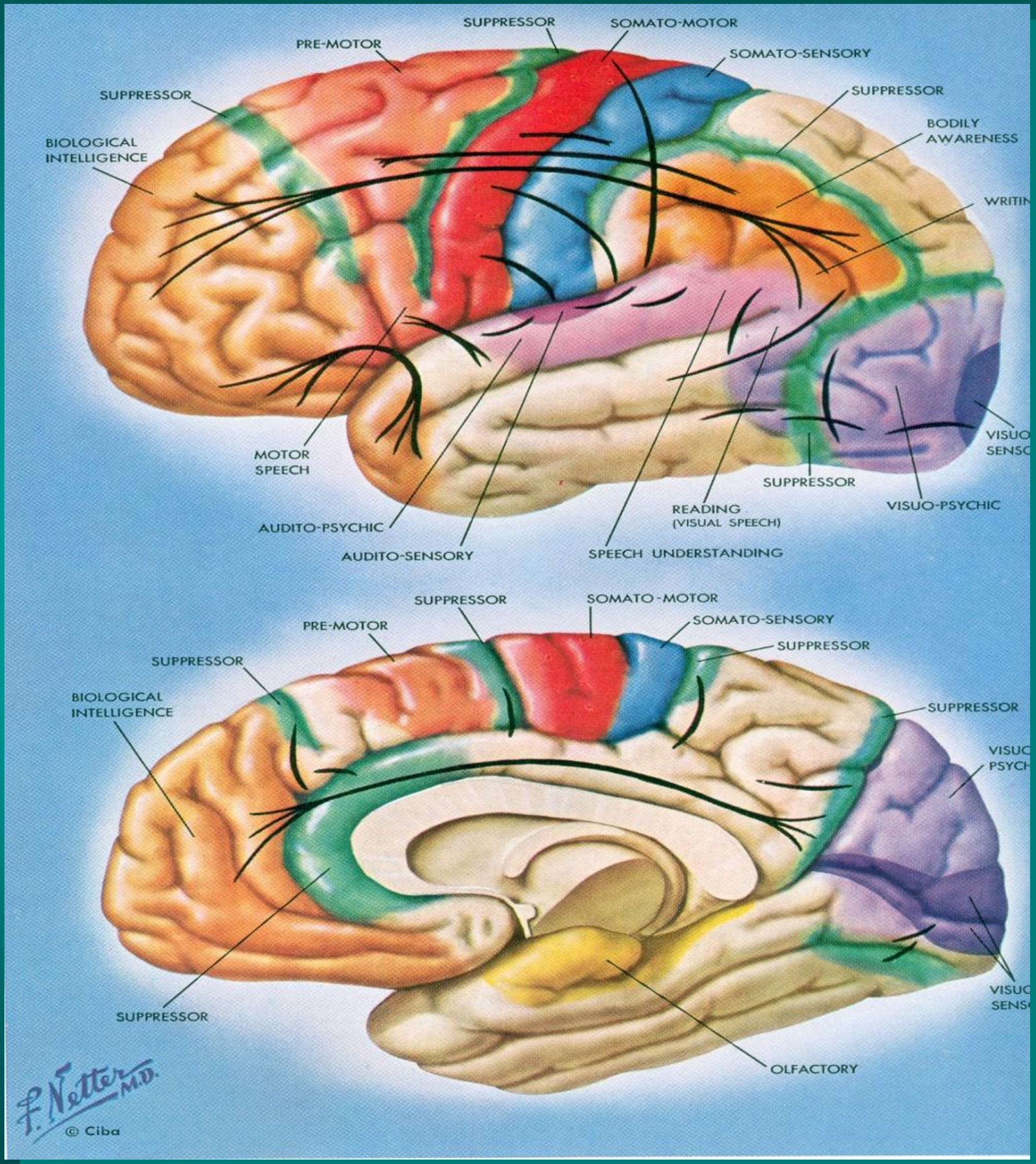
Blumenfeld, 2002


Paracentral lobule
Superior frontal
Pre-cuneus
Posterior cingulate
Caudal anterior cingulate
Isthmus
Cuneus
Rostral anterior cingulate
Lingual
Frontal pole
Medial orbito-frontal
Fusiform
Peri-calcarine
Temporal pole
Entorhinal
Parahippocampal

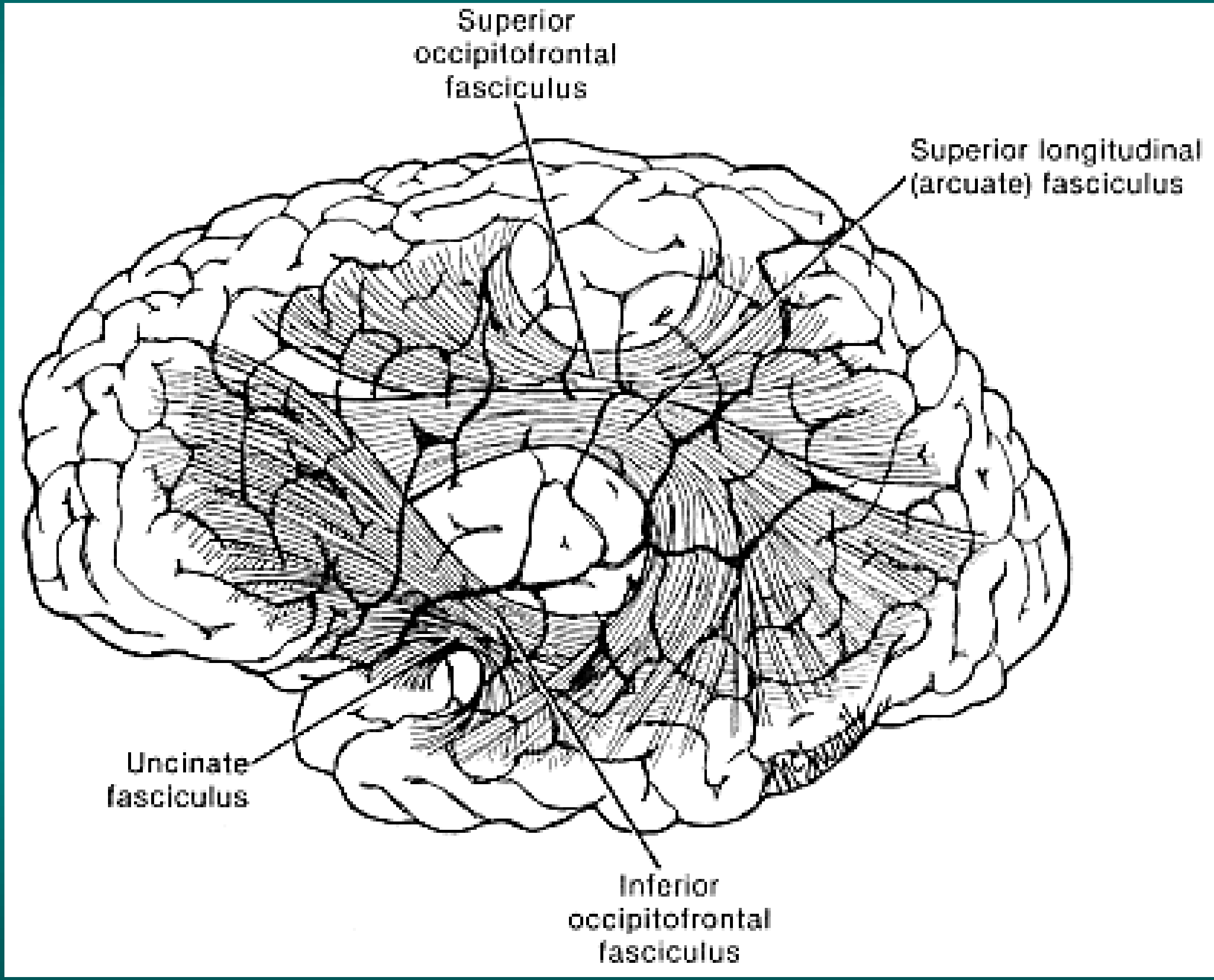


Order of Cortical Maturation

Cerebral fasciculi (long range axon connections)

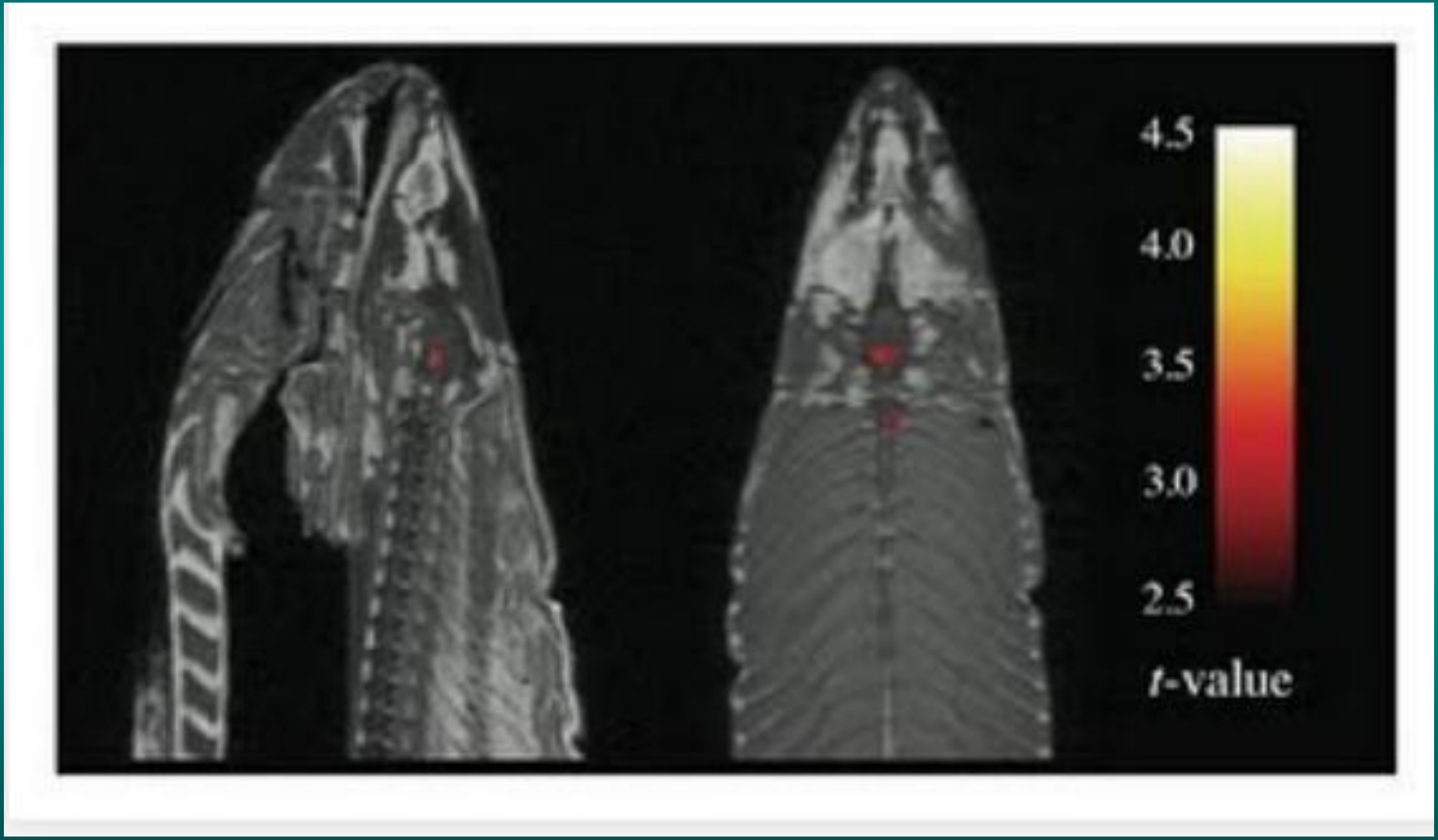


Fasciculi: Major axon tracts



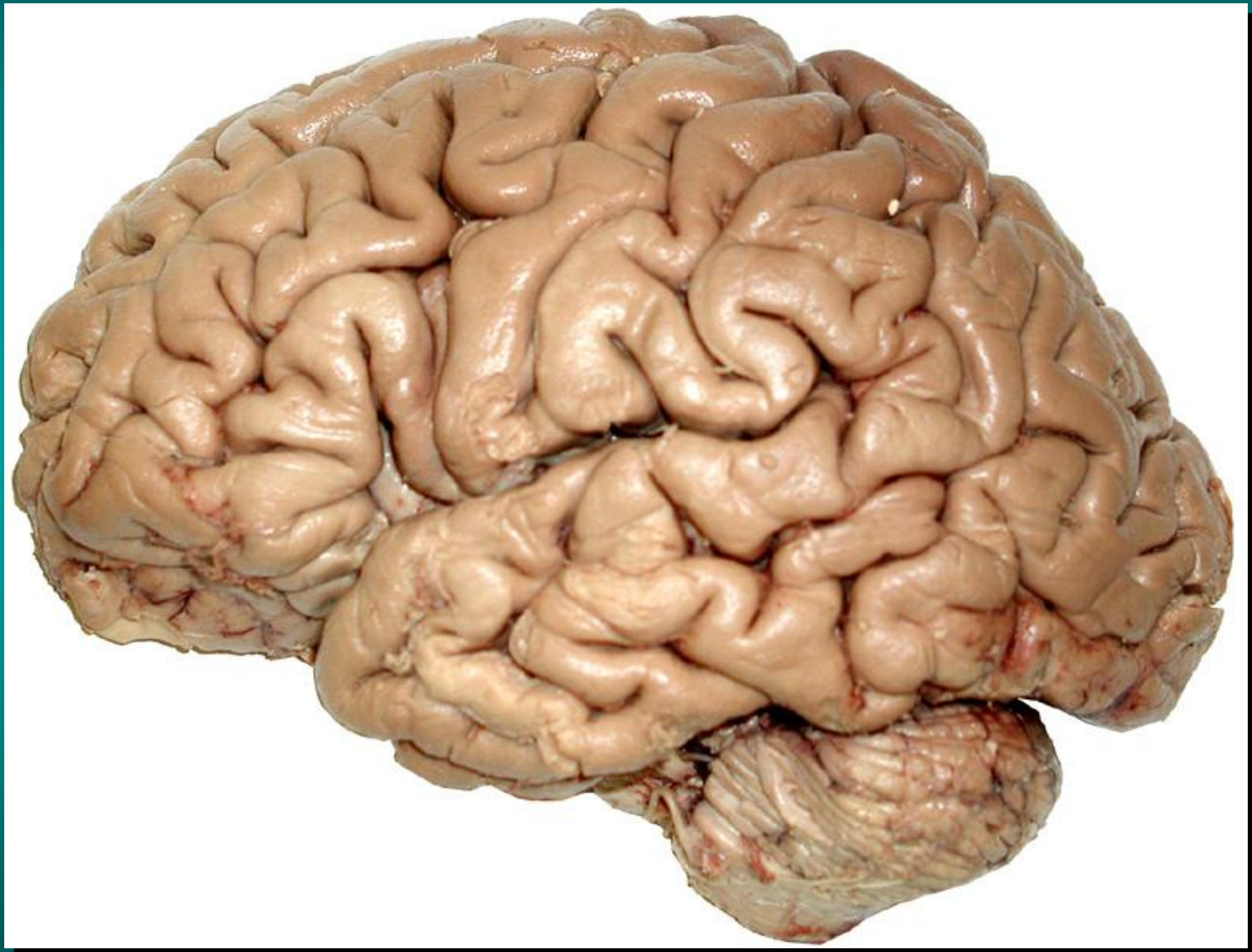
Cautionary Tale:

Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction



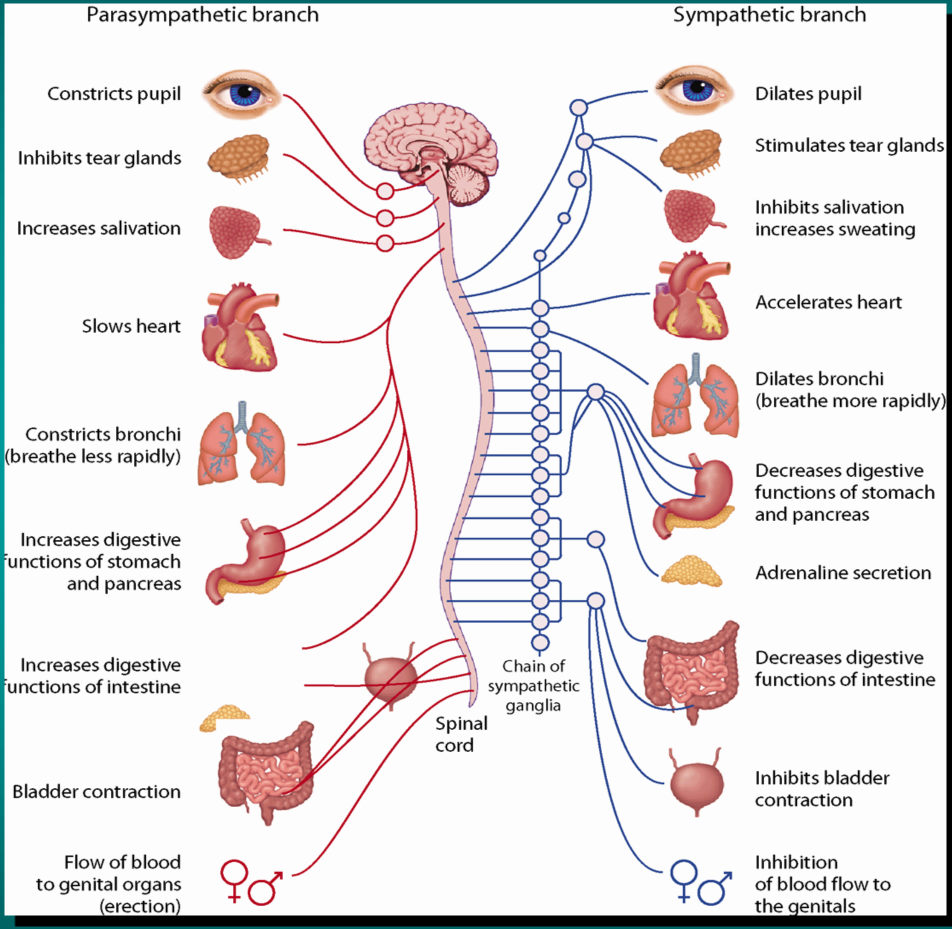
Bennett, 2009

Human Brain



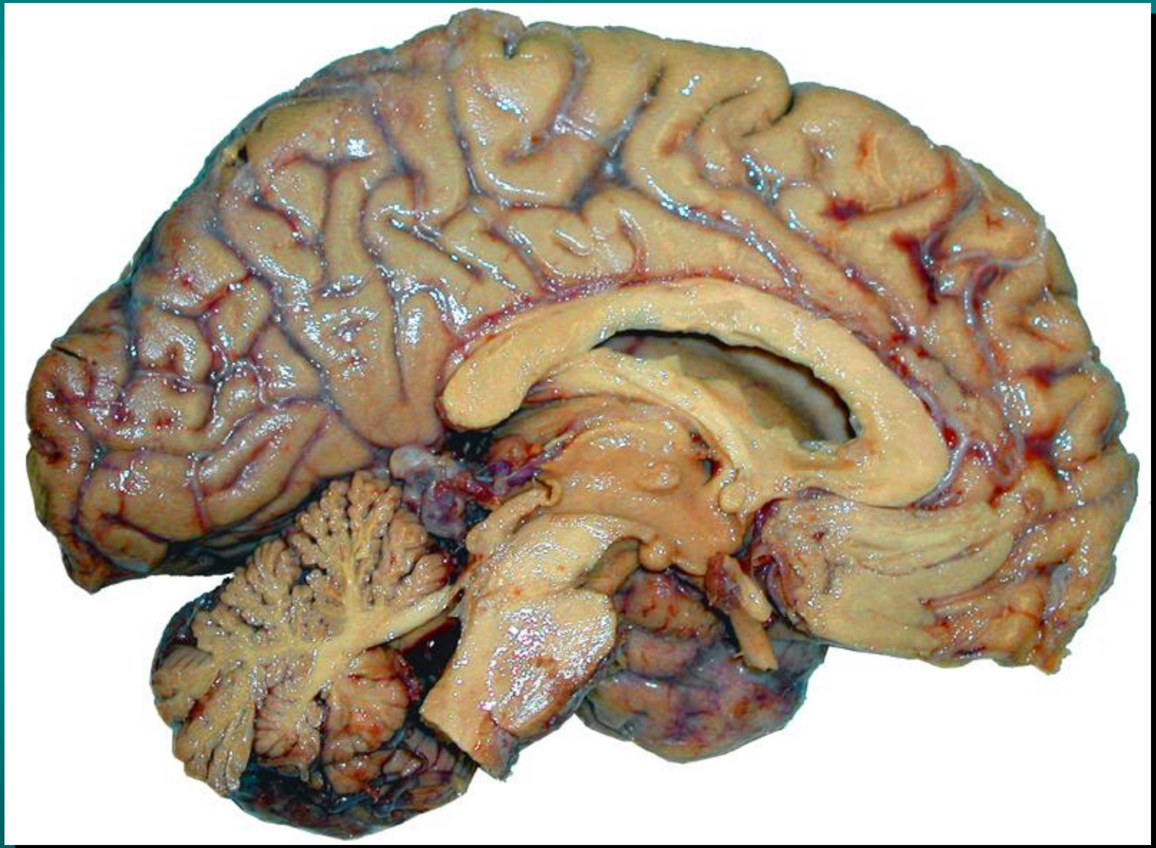
CNS and PNS

- Central nervous system (CNS)
- Peripheral nervous system (PNS)



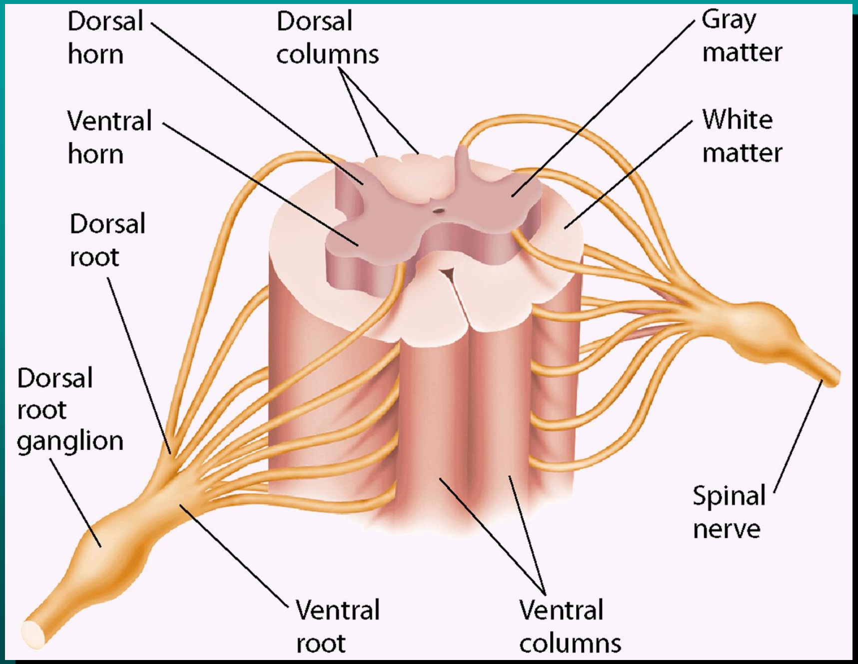
Central Nervous System: CNS

- Brain
- Spinal Cord

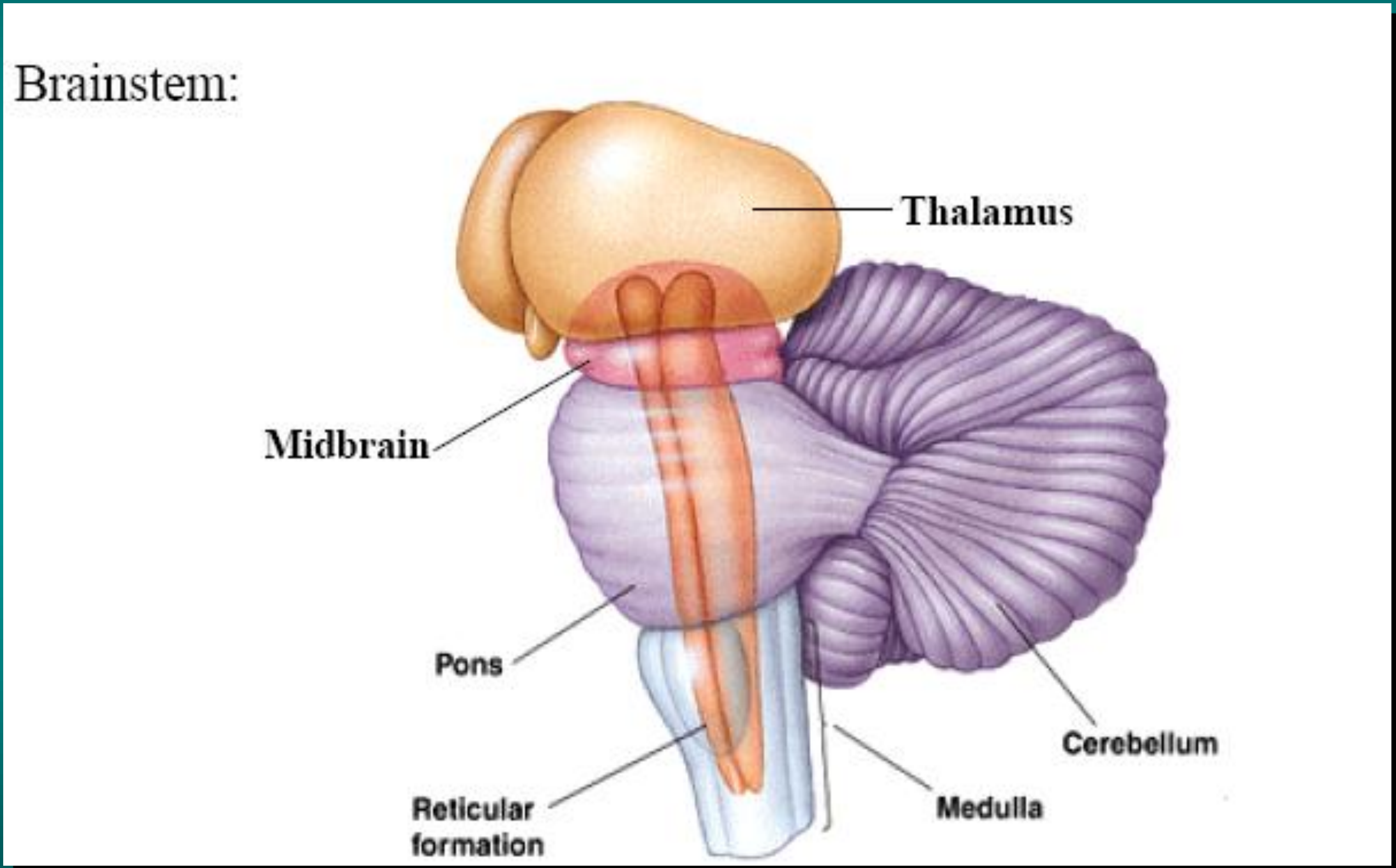


Spinal Cord

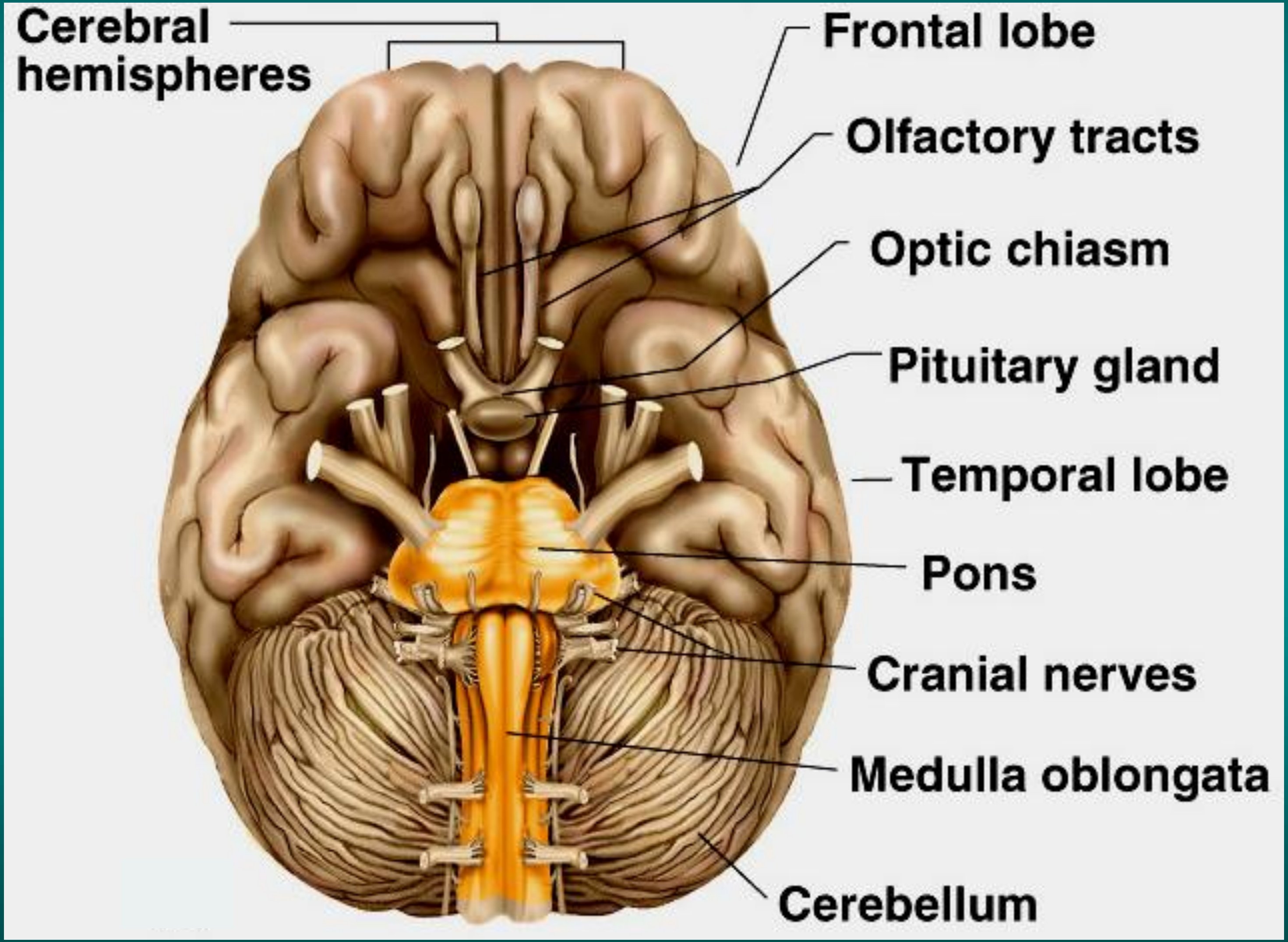
- Two major classes of nerve fibers
  - <u>motor descending</u> fibers (ventral portion)
  - <u>sensory ascending</u> fibers (dorsal portion)
- spinal reflexes
- gray matter vs.
  white matter



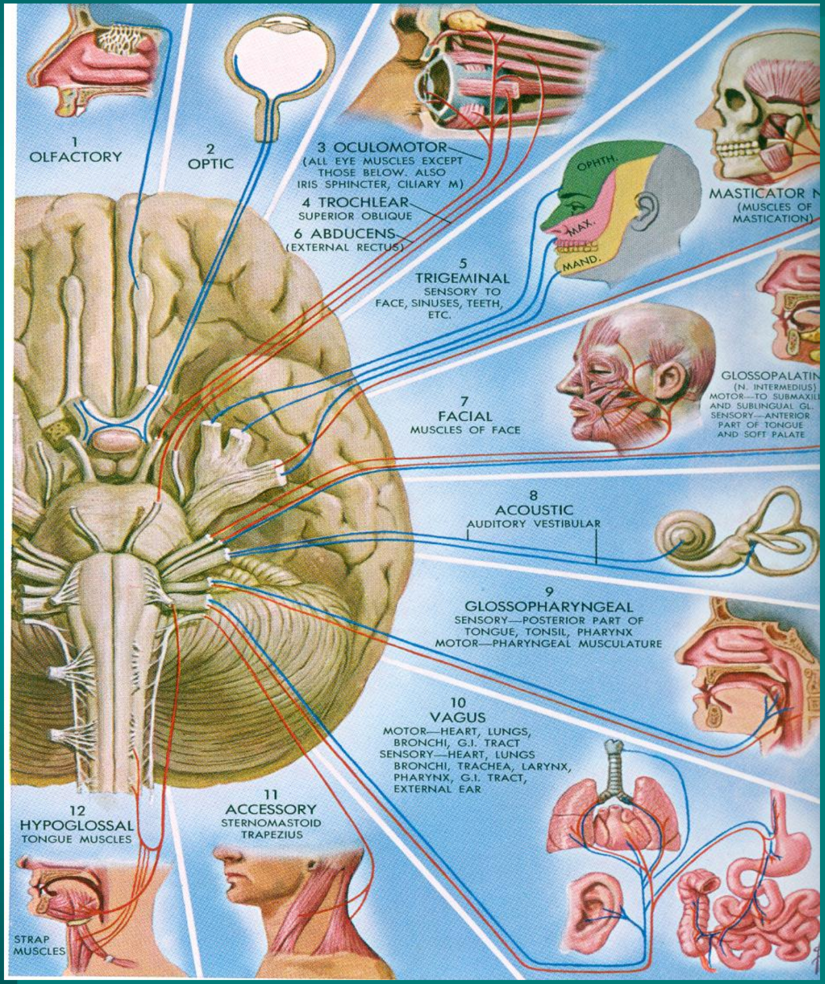
Brainstem: Life Support; Damage = death



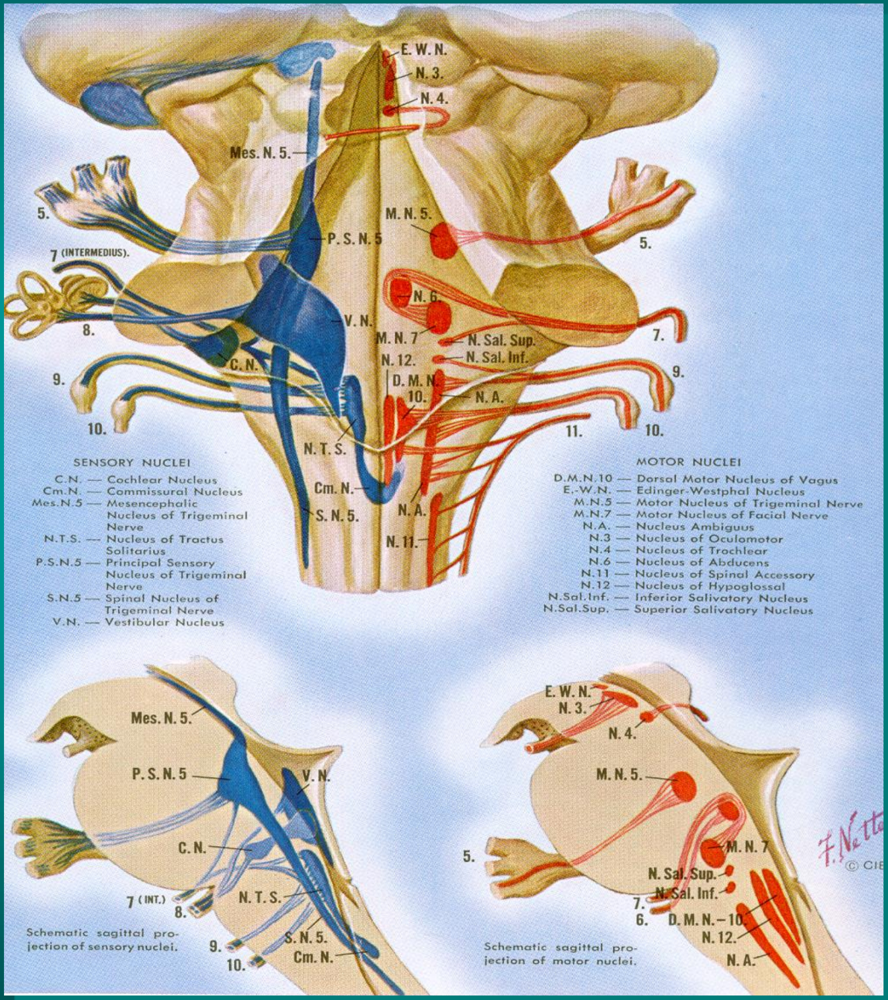
Inferior View of the Brain



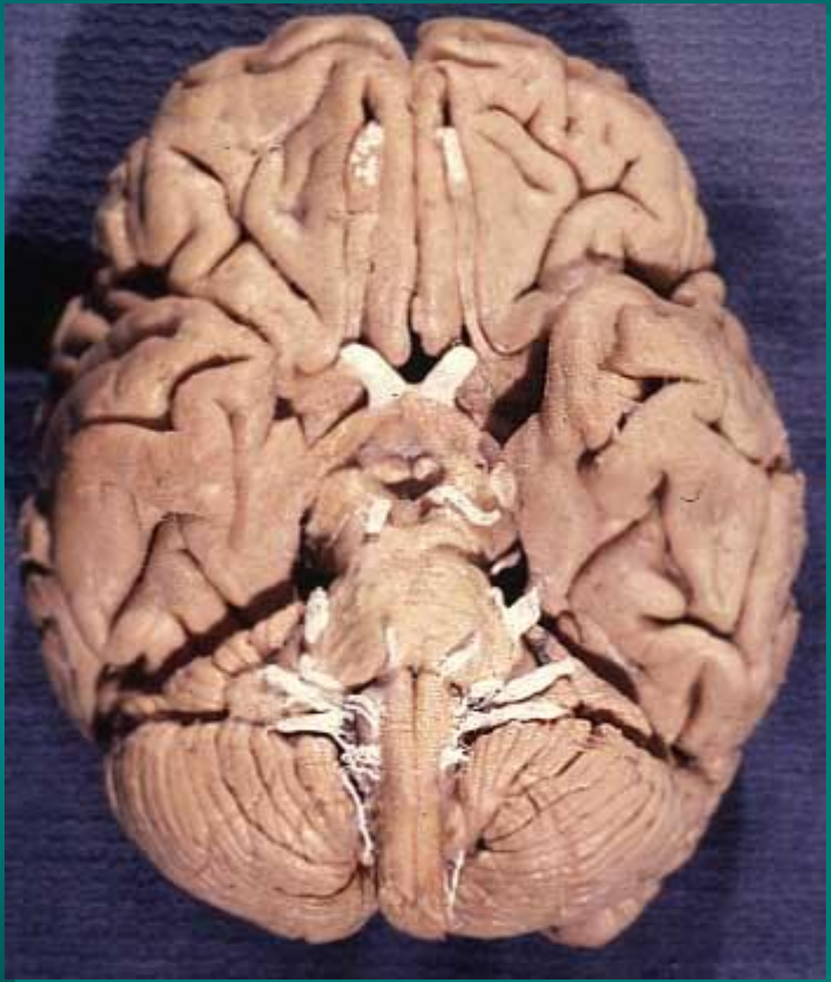
Cranial Nerves: domain of Neurology



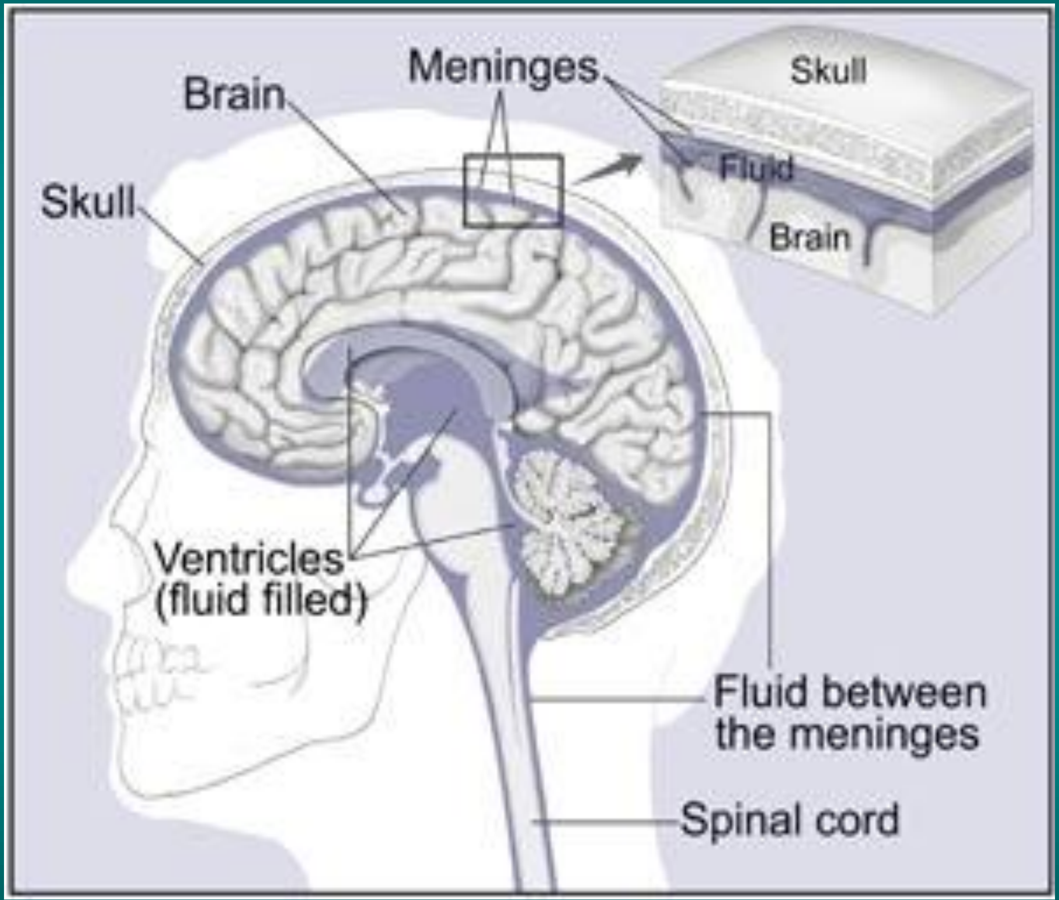
Cranial Nerves 2



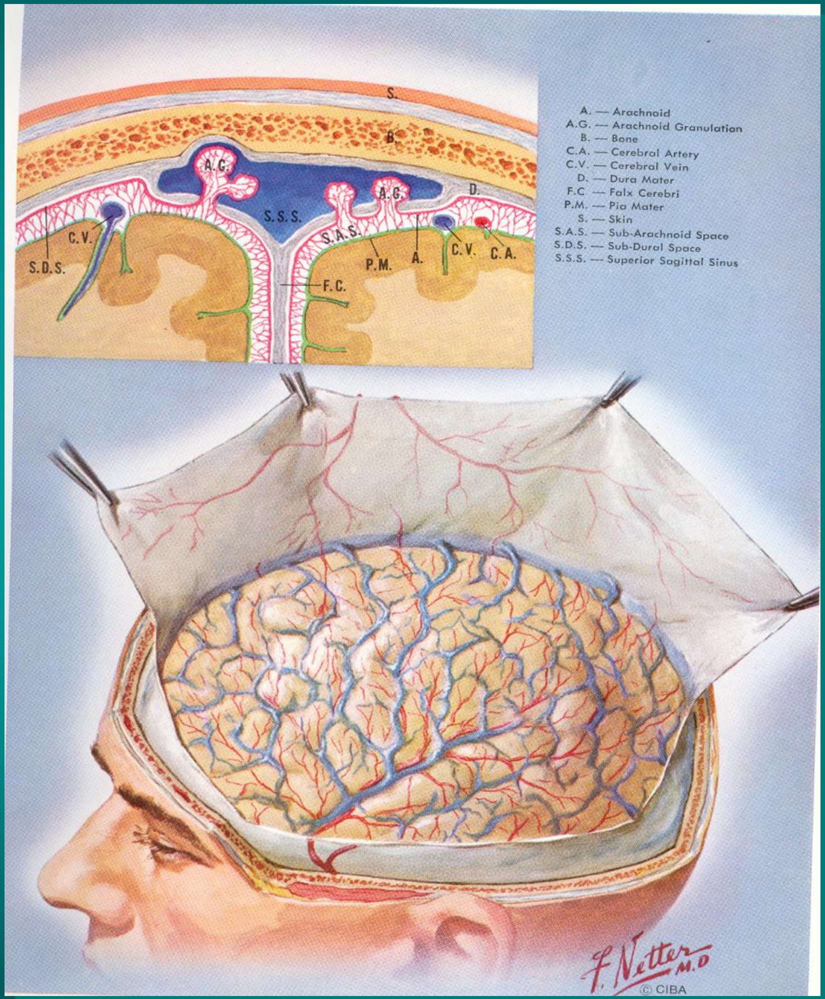
Cranial Nerves 3



Meninges

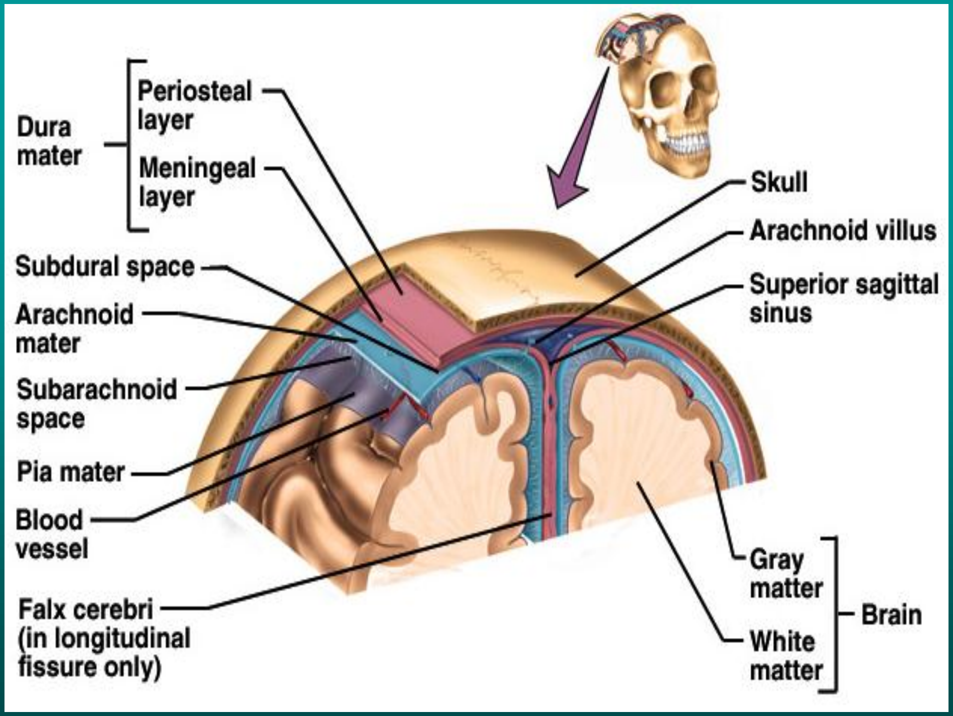

Brain
Meninges
Skull
Skull
Fluid
Brain
Ventricles
(fluid filled)
Fluid between
the meninges
Spinal cord

Meninges: Dura, Arachnoid, Pia

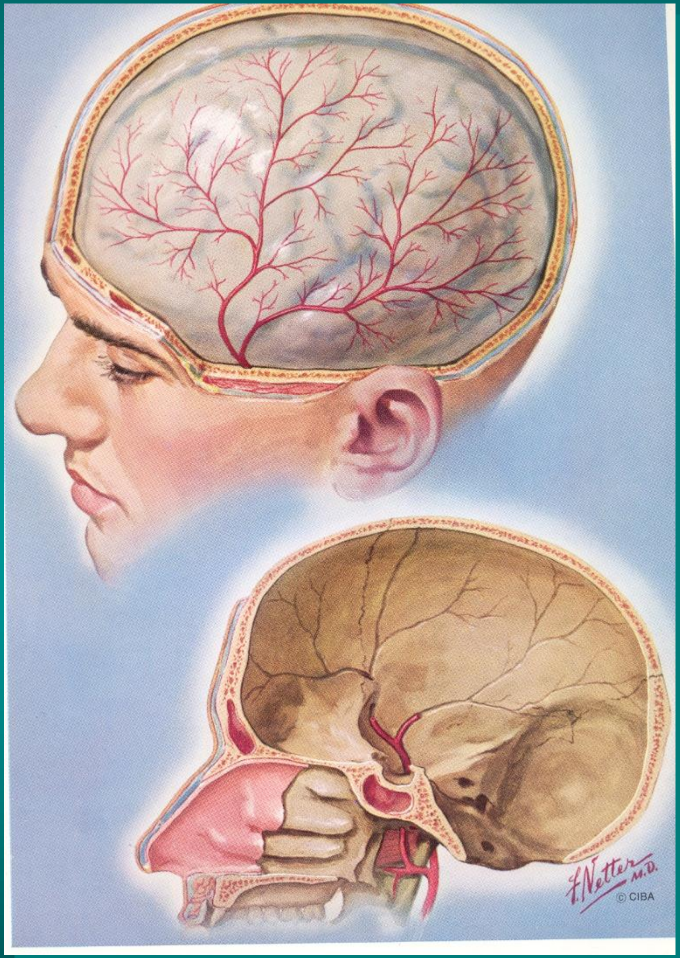


Meninges: Brain cover

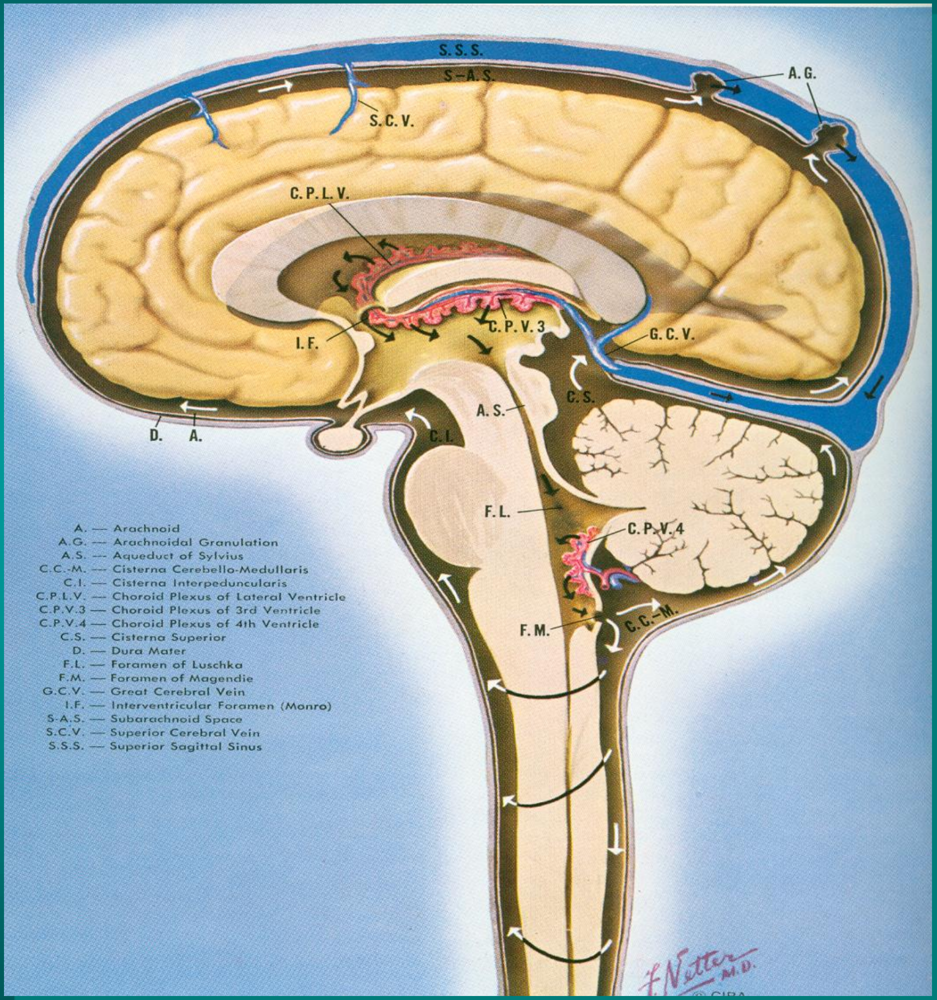
- Dura mater -- outermost, tough membrane
  - Closest to bone
- Arachnoid mater is spider web filamentous layer
- Pia mater is a thin vascular layer adherent to contours of brain



Dura



Cerebral Spinal Fluid



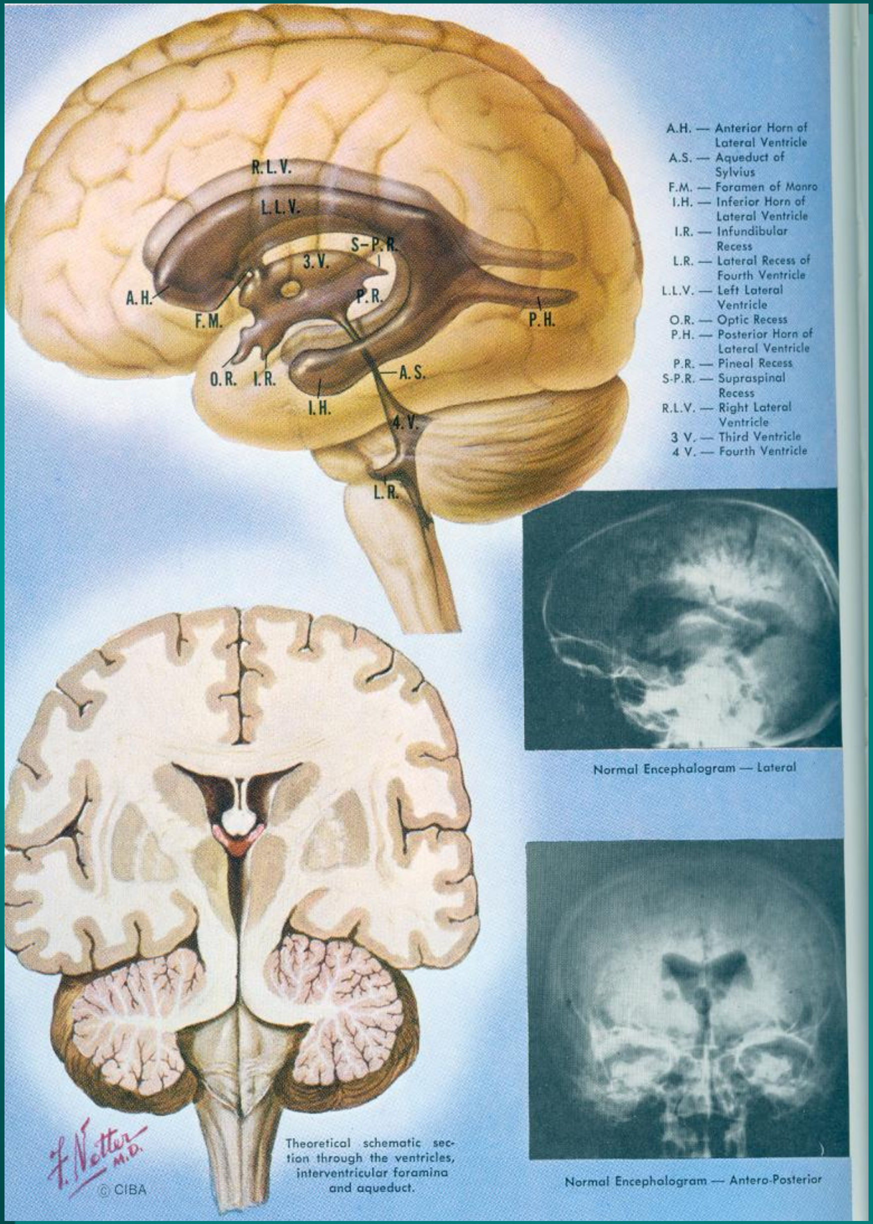
Produced by choroid lexus

20 ml per hour

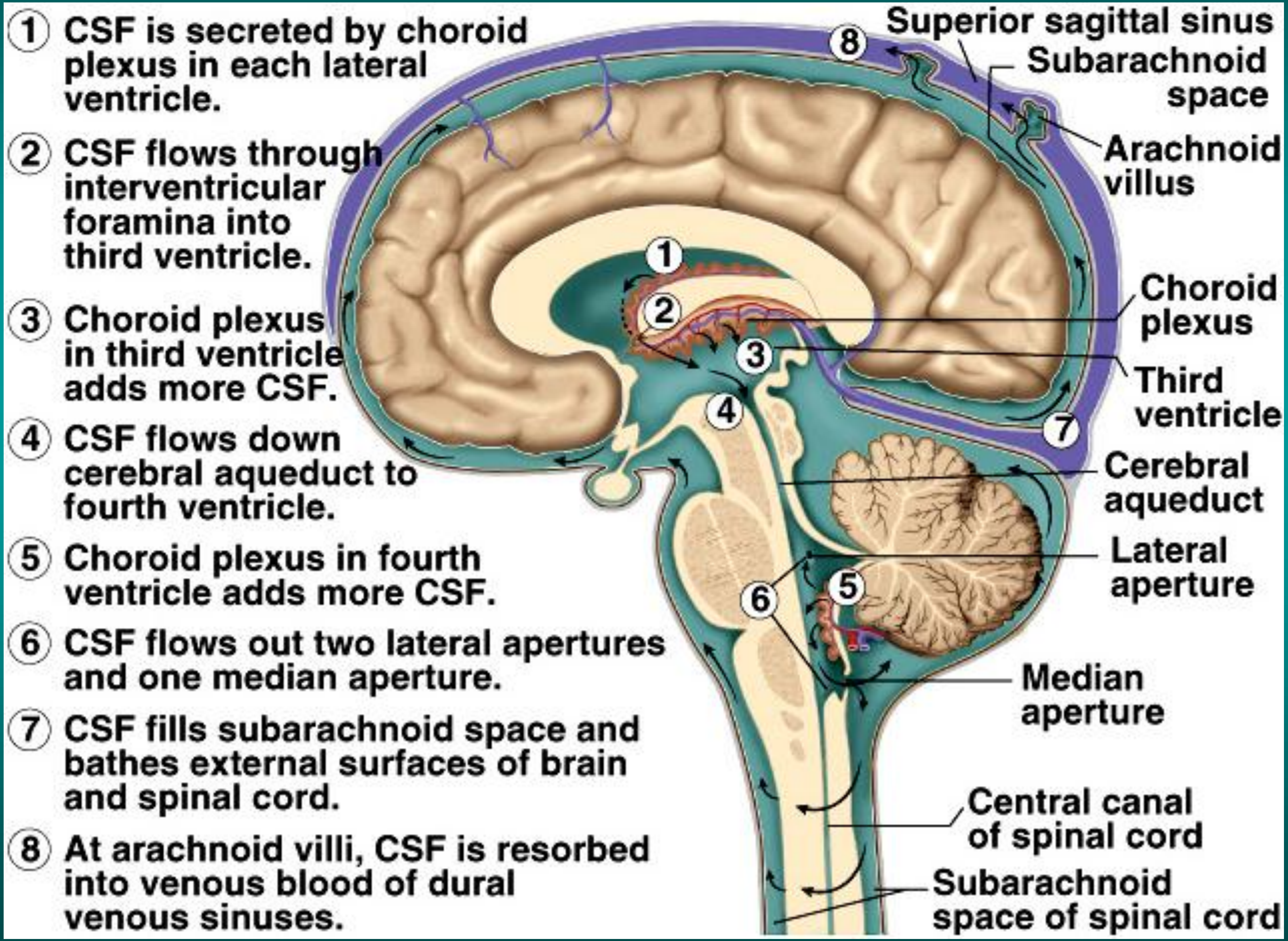
Total Volume: 125-150 ml

Provides buoyancy to brain

Ventricles: Lateral, 3rd, 4th



Flow of Cerebrospinal Fluid

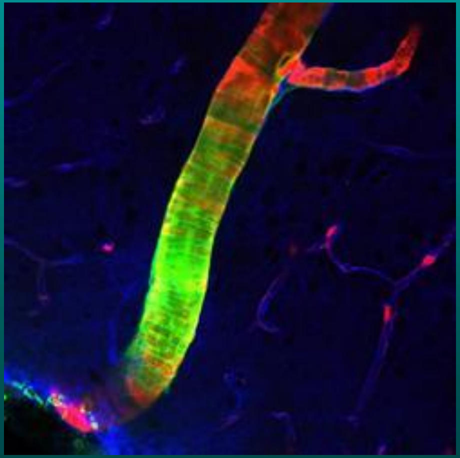


Cerebrospinal Fluid

- <u>Clear liquid fills ventricles</u> and canals & <u>bathes its external surface</u> (in subarachnoid space)
- Brain produces & absorbs about <u>500 ml/day</u>
  - produced by ependymal cells lining the ventricles
  - filtration of blood through choroid plexus
- Functions
  - <u>buoyancy</u> -- floats brain so it neutrally buoyant
  - <u>protection</u> -- cushions from hitting inside of skull
  - <u>chemical stability -- rinses away wastes</u>

Glymphatic System: 2nd garbage system

- Garbage disposal system; under pressure, pushes large volumes of CSF through the brain each day to carry waste away more forcefully.
- Acts much like the lymphatic system but is managed by brain cells known as glial cells.
- Astrocytes use projections known as “end feet” to form a network of conduits around the outsides of arteries and veins; removes 50% of beta amyloid

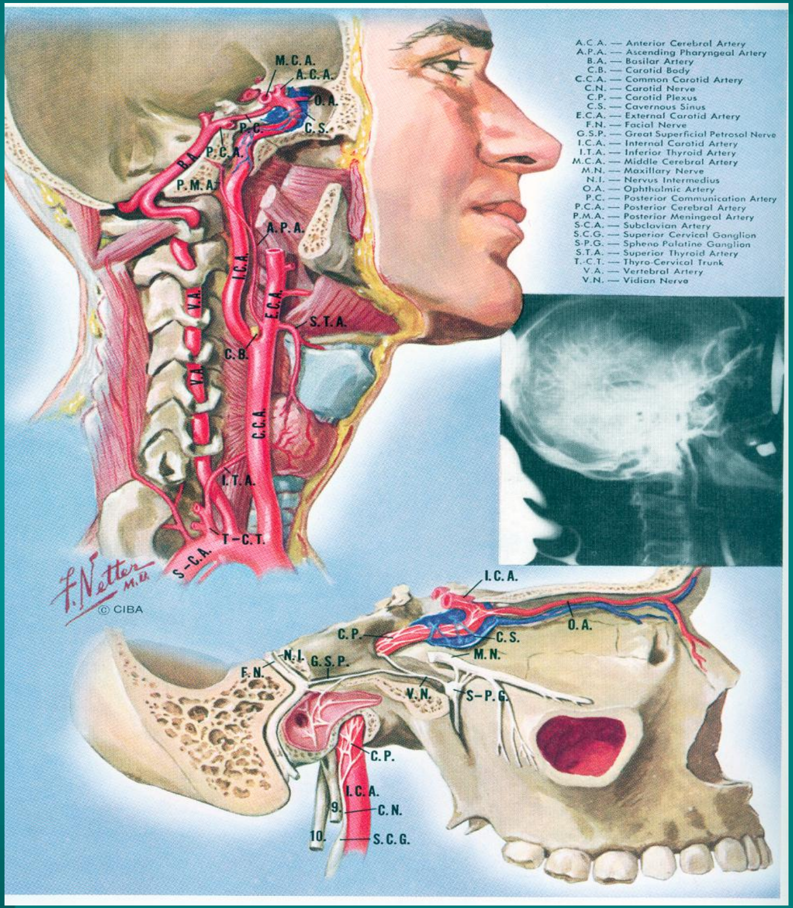


Blood-Brain and Blood-CSF Barriers

- Blood-brain barrier is tightly joined endothelium (thin layer of glial cells that lines the interior surface of blood vessels)

  - permeable to lipid-soluble materials (alcohol, O2, CO2, nicotine and anesthetics)

Blood Supply:
Internal Carotid, Basilar, Carotid, Vertebral Arteries



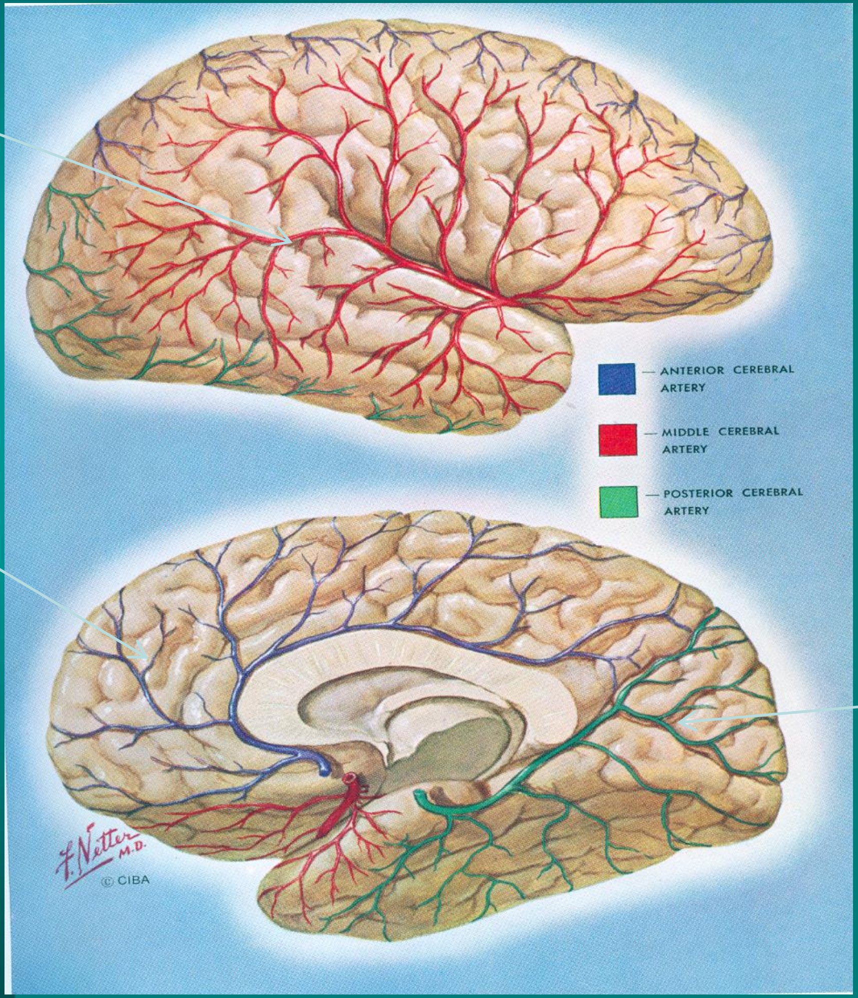
<u>Never let chiropractor do a neck adjustment</u>: basilar stroke

Blood Supply 2: ACA, MCA, PCA

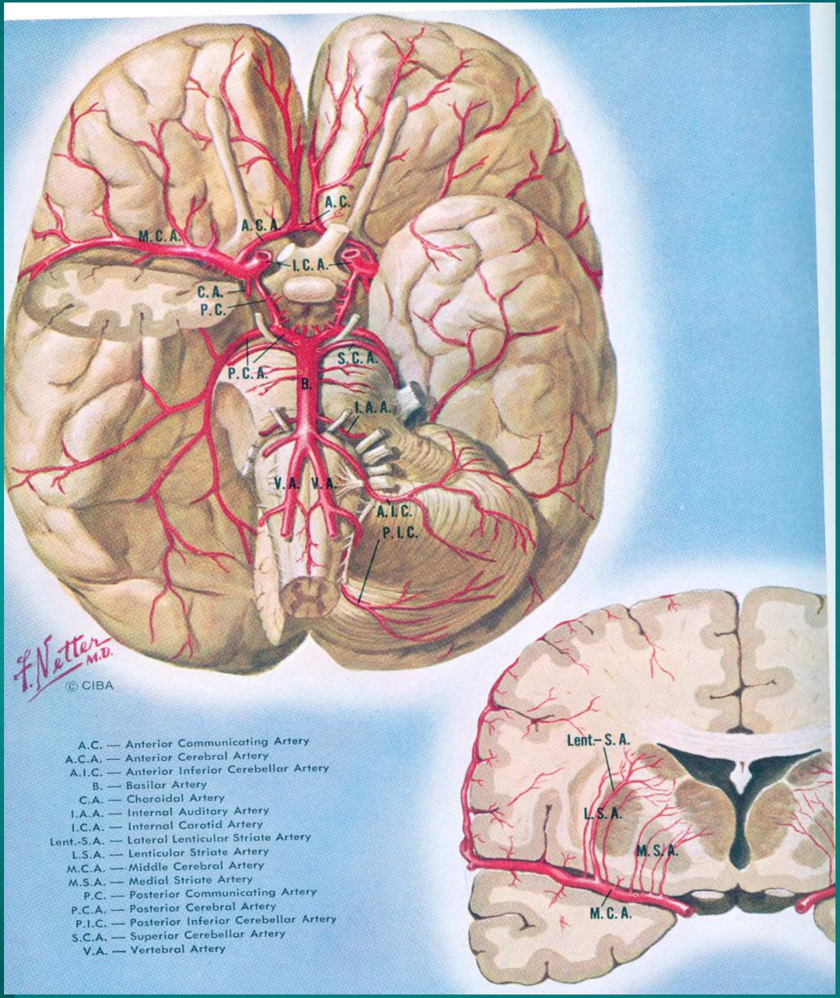
MCA

ACA

PCA

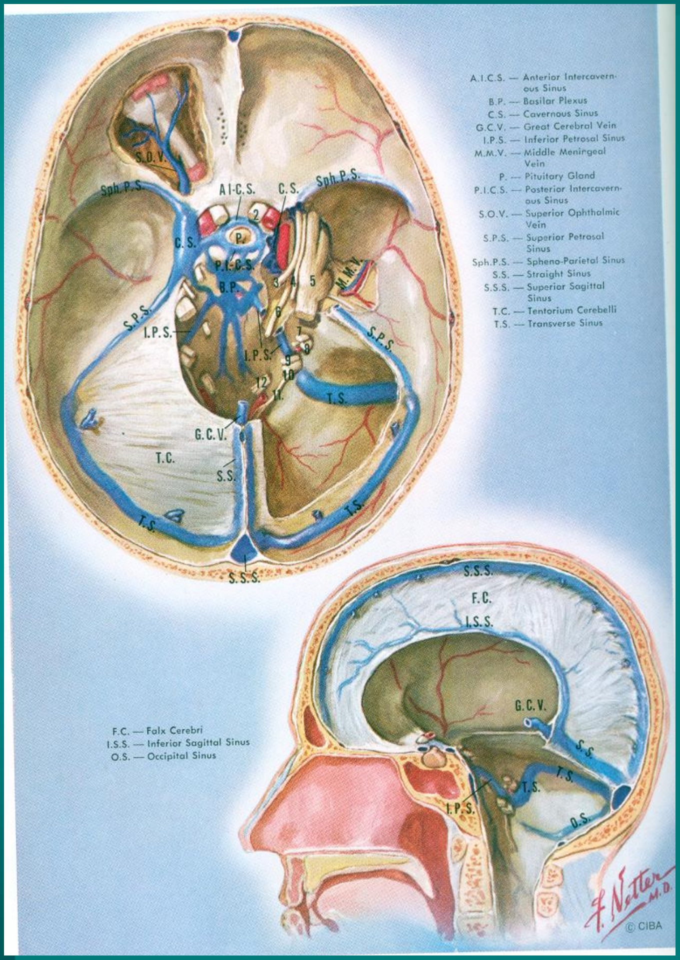


Circle of Willis



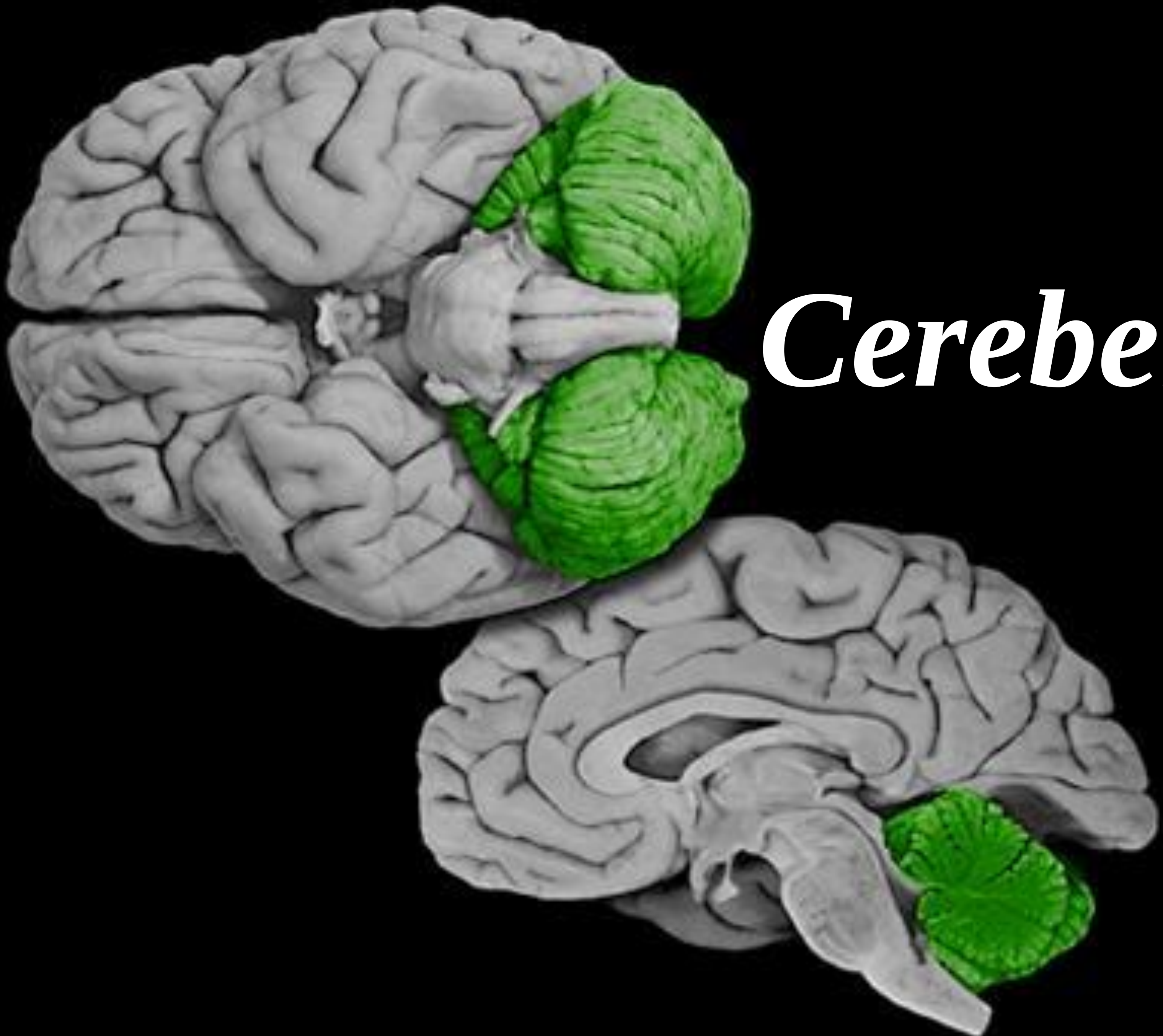
Venous Sinuses, Falx, Tentorium

Tentorium

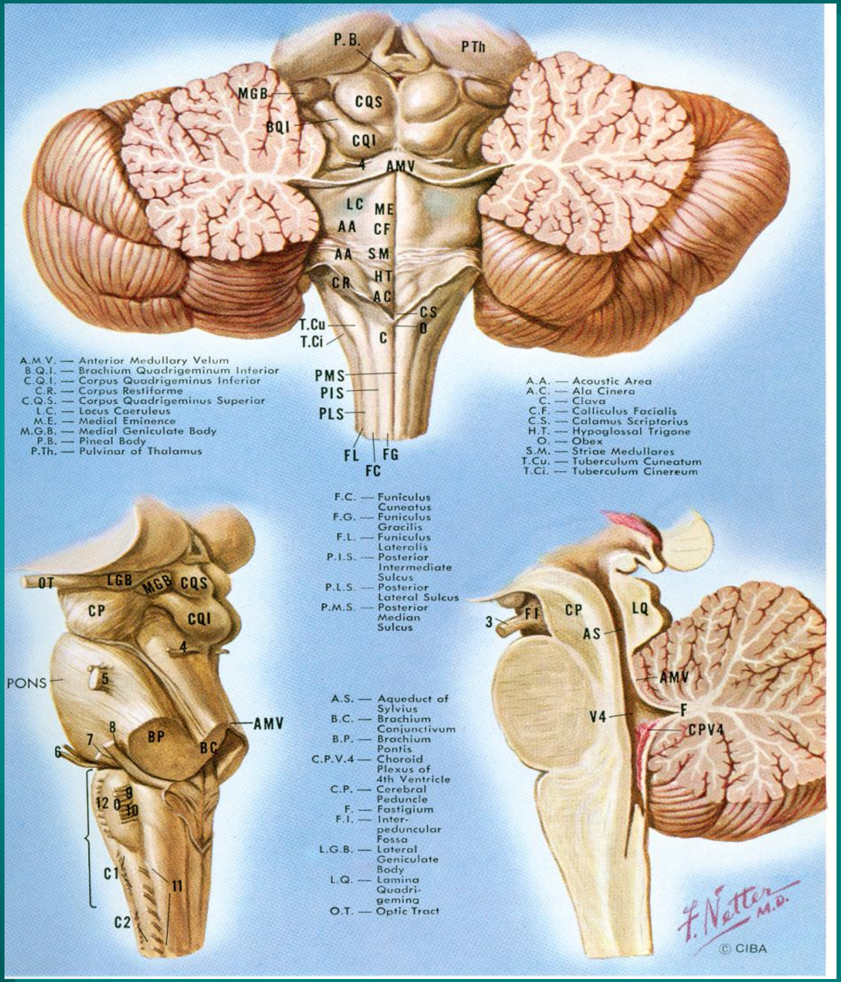


Falx

Cerebellum

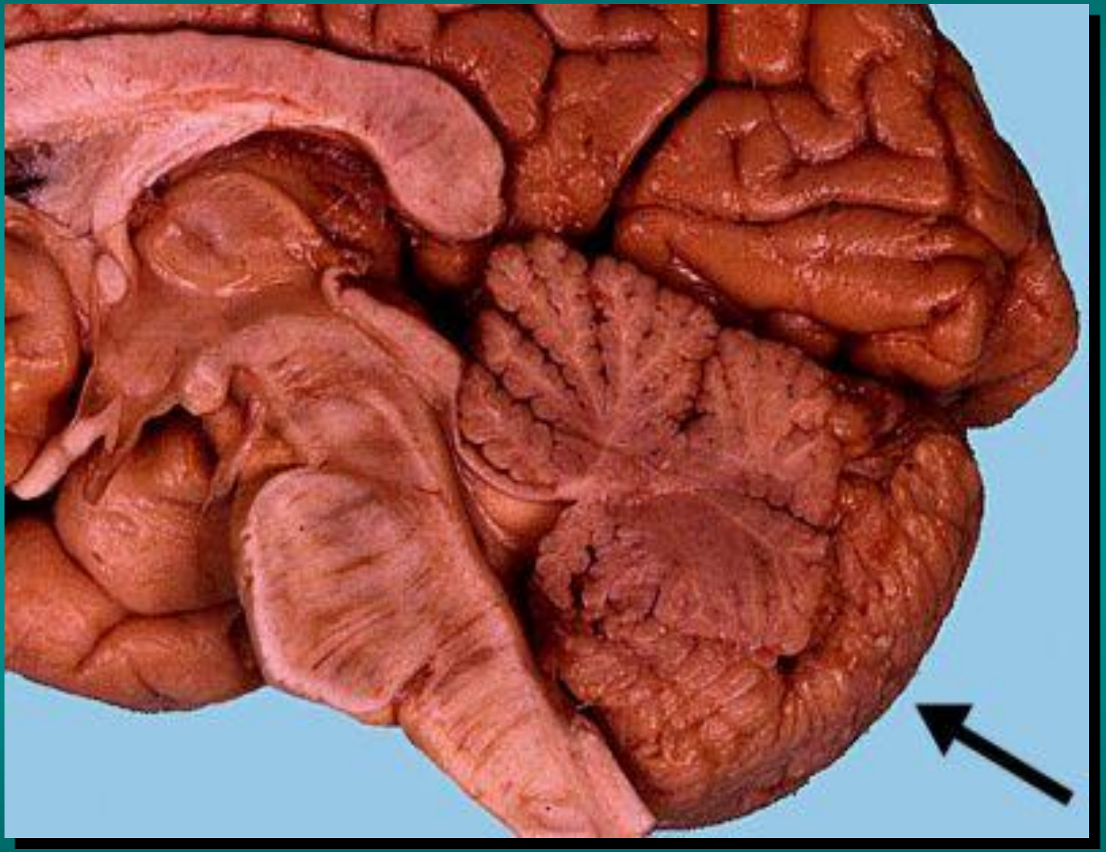


Cerebellum



P.B.
PTh
MGB
CQS
BQI
CQI
4
AMV
LC
ME
AA
CF
AA
SM
HT
CR
AC
CS
O
T.Cu
T.Ci
C
PMS
PIS
PLS
FL
FG
FC
A.M.V. — Anterior Medullary Velum
B.Q.I. — Brachium Quadrigeminum Inferior
C.Q.I. — Corpus Quadrigeminus Inferior
C.R. — Corpus Restiforme
C.Q.S. — Corpus Quadrigeminus Superior
L.C. — Locus Caeruleus
M.E. — Medial Eminence
M.G.B. — Medial Geniculate Body
P.B. — Pineal Body
P.Th. — Pulvinar of Thalamus
A.A. — Acoustic Area
A.C. — Ala Cinera
C. — Clava
C.F. — Colliculus Facialis
C.S. — Calamus Scriptorius
H.T. — Hypoglossal Trigone
O. — Obex
S.M. — Striae Medullares
T.Cu. — Tuberculum Cuneatum
T.Ci. — Tuberculum Cinereum
F.C. — Funiculus Cuneatus
F.G. — Funiculus Gracilis
F.L. — Funiculus Lateralis
P.I.S. — Posterior Intermediate Sulcus
P.L.S. — Posterior Lateral Sulcus
P.M.S. — Posterior Median Sulcus
OT
LGB
MGB
CQS
CP
CQI
4
PONS
5
AMV
8
7
BP
BC
6
12
9
10
C1
11
C2
A.S. — Aqueduct of Sylvius
B.C. — Brachium Conjunctivum
B.P. — Brachium Pontis
C.P.V.4 — Choroid Plexus of 4th Ventricle
C.P. — Cerebral Peduncle
F. — Fastigium
F.I. — Interpeduncular Fossa
L.G.B. — Lateral Geniculate Body
L.Q. — Lamina Quadrigemina
O.T. — Optic Tract
3
FI
CP
LQ
AS
AMV
F
V4
CPV4
F. Netter M.D.
© CIBA

Cerebellum 2



Classical Functions of cerebellum

- Equilibrium and balance.

- Learned movement patterns, is involved with fine motor movement.

- It compares intended movement coming from the motor cortex with actual movement sensation coming from the joints and muscles.

Newer ideas about Cerebellum

- Cerebral association areas are linked with the lateral hemispheres of the cerebellar posterior lobe
- Cerebellar cognitive affective syndrome (CCAS): Neurobehavioral deficits in the absence of the cerebellar motor syndrome: impairments in executive, spatial cognition and linguistic processing (agrammatism and dysprosodia)
- Patients with CCAS experience dysregulation of affect
- Connections to all cerebral networks, i.e. DMN

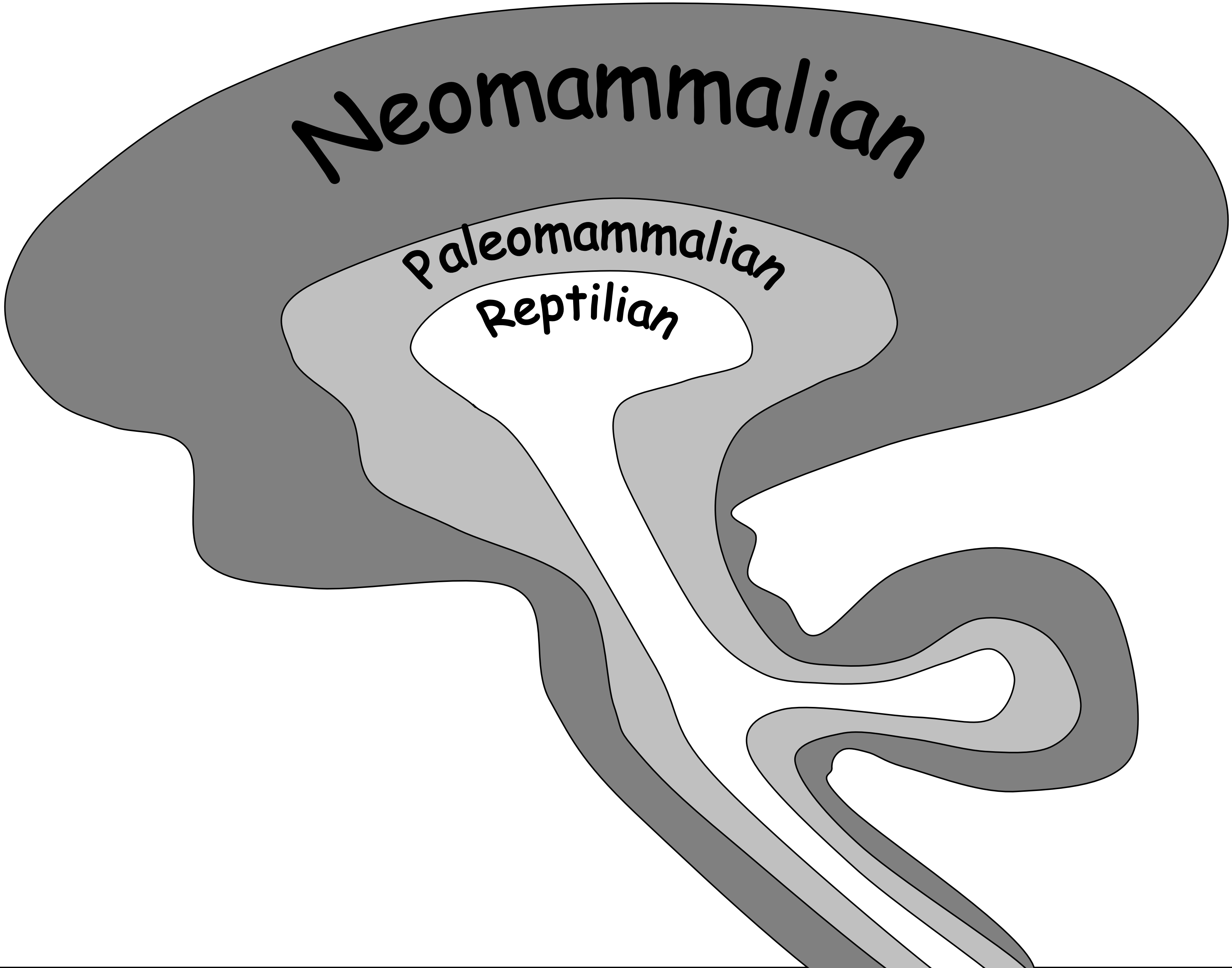
Clinical abnormalities of cerebellum

- Hypotonia (decrease of normal muscle tone)
- Dysmetria (past pointing)
- Ataxia
- Dysdiadochokinesia (no rapid alternating moves)
- Dysarthria
- Intention tremor
- Cerebellar nystagmus

Patient with cerebellar rigidity (attitude) with unilateral cerebellar lesion

Evolutionary Development

- If you examine the brain in an evolutionary perspective, this can help to understand the interlinks between form and function. The brain can be divided anatomically and functionally into three basic components.


Neomammalian
Paleomammalian
Reptilian

Reptilian Brain: Brainstem

- <u>Medulla, pons, midbrain and basal ganglia</u>
- <u>Medulla</u>: life-support functions (heart rate, blood pressure, gag reflex)
- <u>Pons</u>: life-support (sleep, breathing, heart rate), arousal (RAS)
- <u>Midbrain</u>: sensory/motor pathways, motor control, eye movements, pleasure
- <u>Behaviors directed towards individual preservation and propagation</u> such as feeding, drinking and sexual aggression.
- Serious damage = death

Just a brain stem!

The "Headless Wonder Chicken" lived for 18 months without a head

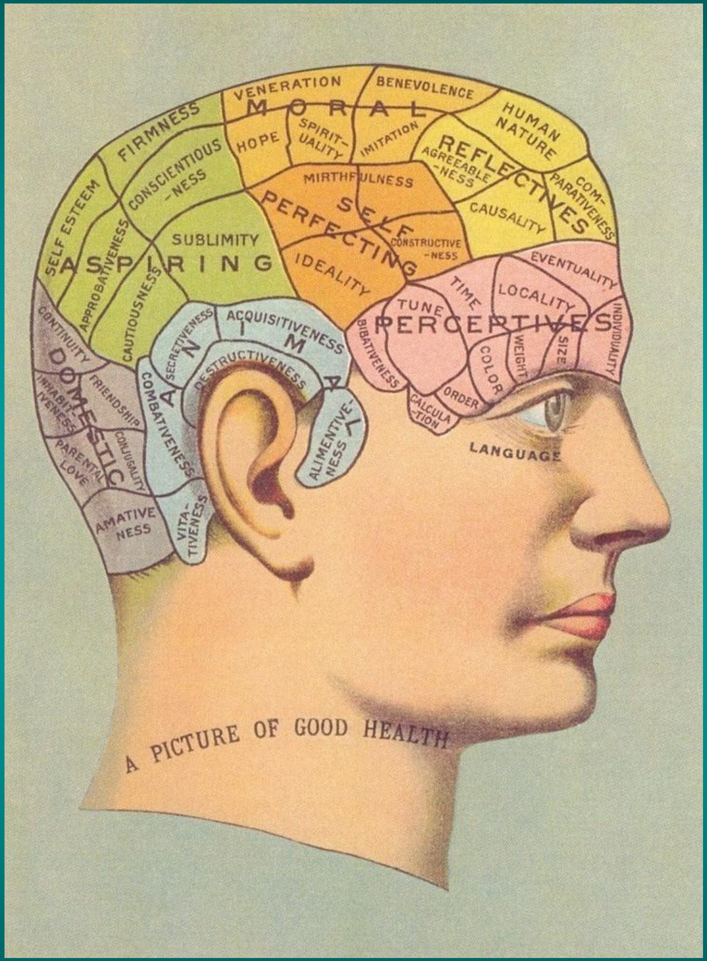
Paleomammalian Brain

- The primitive cortex of the limbic lobe
- Hypothalamus, Septal Nuclei, Amygdala, Hippocampus
- Subserves primitive (but distinctly mammalian behaviors) such as hoarding and parental care of offspring.

Neomammalian Brain

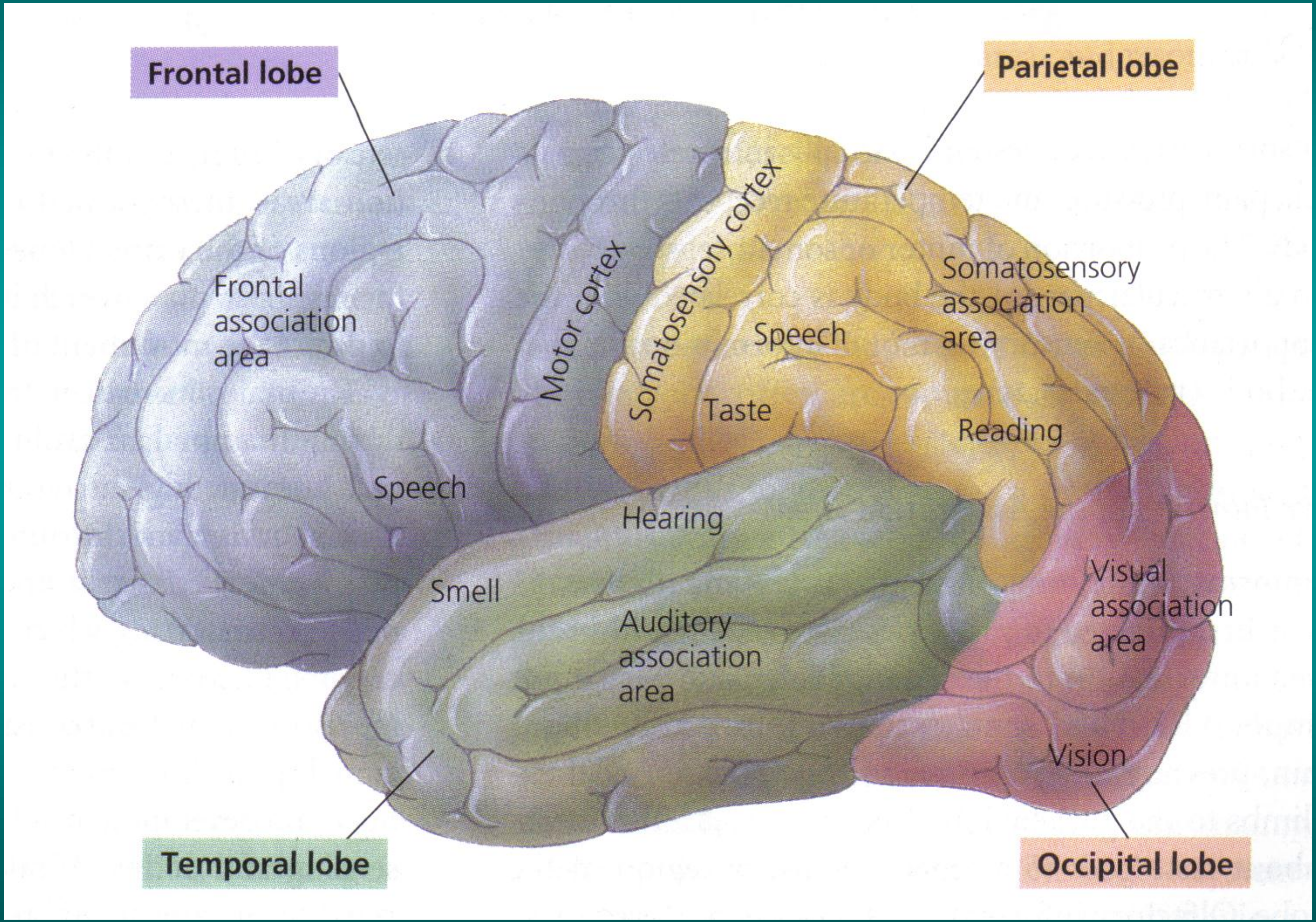
- The <u>neocortex</u>
- Subserves <u>higher cognitive functioning and speech which facilitate social behavior.</u>
- <u>Controls prior brains.</u>

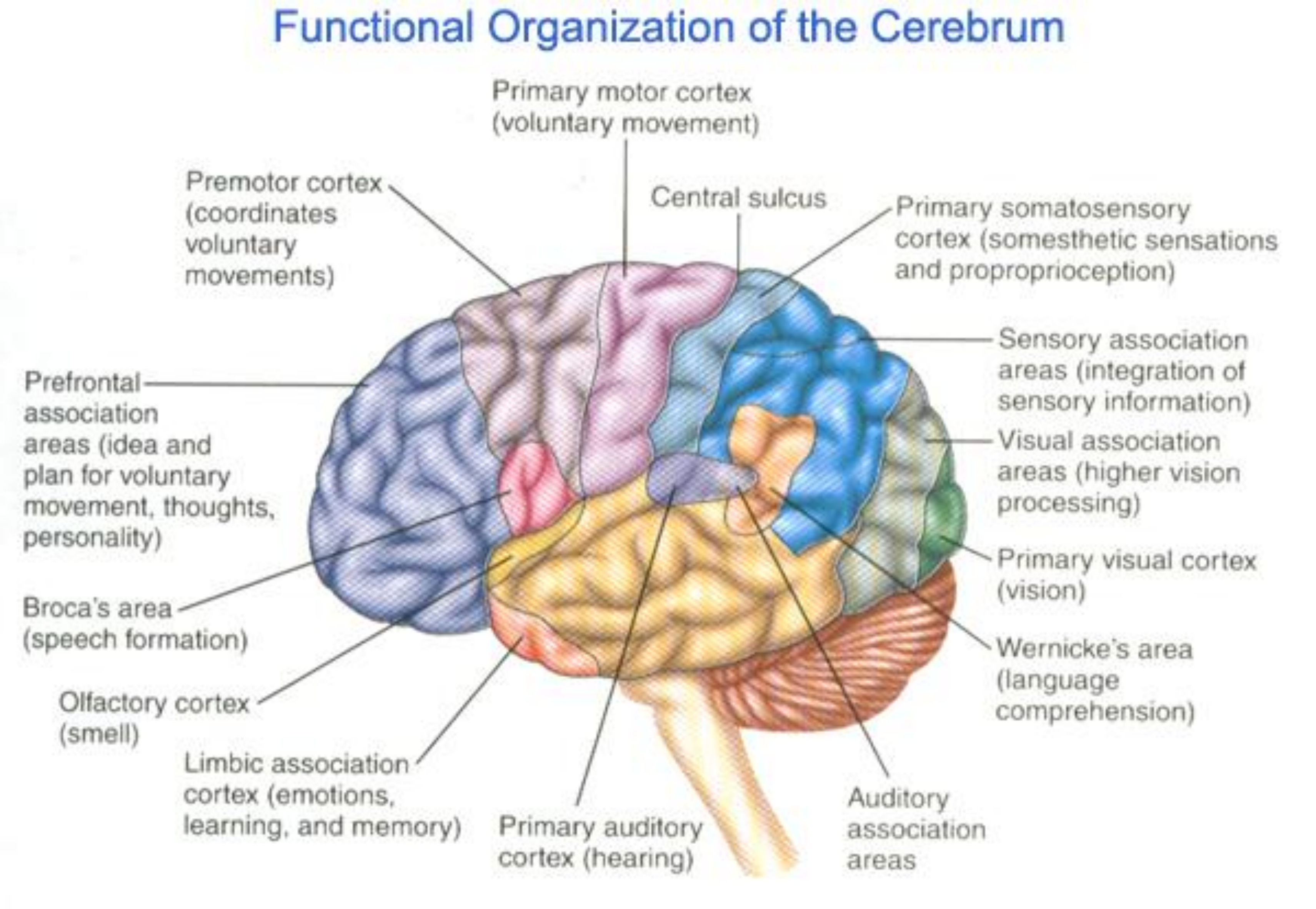
Phrenological Model of Brain circa 1870



Phrenology had right idea: brain is functionally divided

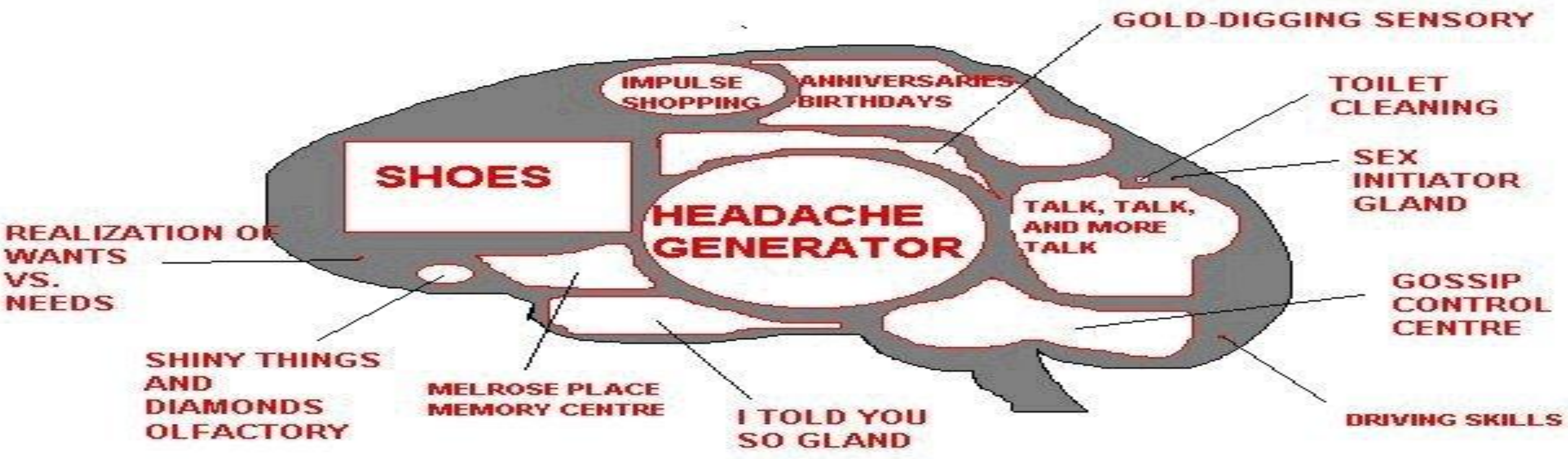
Regions of the cerebrum are specialized for different functions





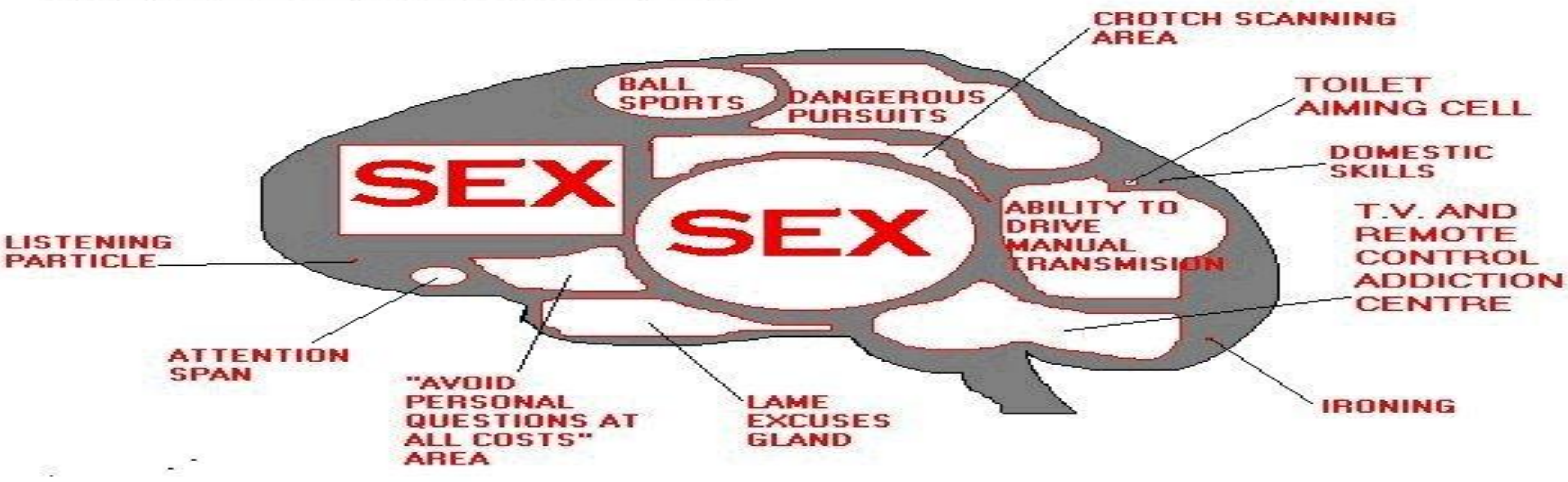
While the back brain produces instinctive stimulus-response reactions (perception), the front brain facilitates decisions based on association and analysis (conception).

THE FEMALE BRAIN

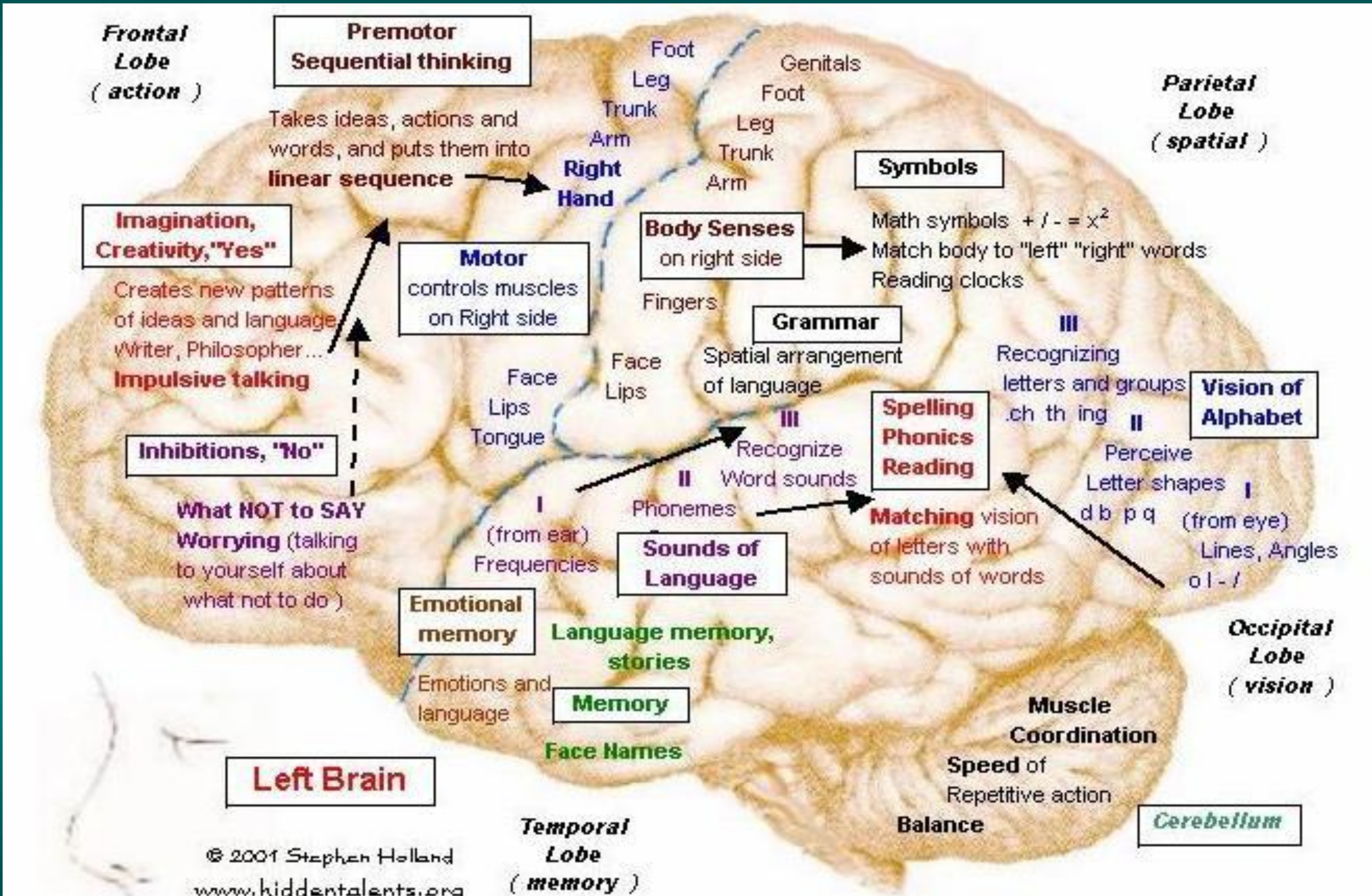


FOOTNOTE: The "Put Oil into the Car" and "Be Quite During the Game" glands are active only when the "SHINY THINGS AND DIAMONDS" OLFactory has been satisfied or when there is a shoe sale.

THE MALE BRAIN



FOOTNOTE: the "Listening to children cry in the middle of the night" gland is not shown due to it's small and underdeveloped nature. Best viewed under a microscope.


Frontal Lobe (action)
Premotor Sequential thinking
Takes ideas, actions and words, and puts them into linear sequence
Foot
Leg
Trunk
Arm
Right Hand
Genitals
Foot
Leg
Trunk
Arm
Parietal Lobe (spatial)
Symbols
Imagination, Creativity,"Yes"
Creates new patterns of ideas and language Writer, Philosopher...
Impulsive talking
Motor controls muscles on Right side
Body Senses on right side
Math symbols + / - = x²
Match body to "left" "right" words
Reading clocks
Fingers
Grammar
Spatial arrangement of language
Face
Lips
Face
Lips
Tongue
III
Recognizing letters and groups .ch th ing
Vision of Alphabet
Inhibitions, "No"
Spelling Phonics Reading
III
Recognize Word sounds
II
II
Perceive Letter shapes
d b p q
I
What NOT to SAY
Worrying (talking to yourself about what not to do)
I
(from ear)
Frequencies
Phonemes
Sounds of Language
Matching vision of letters with sounds of words
(from eye)
Lines, Angles
o l - /
Emotional memory
Language memory, stories
Occipital Lobe (vision)
Emotions and language
Memory
Face Names
Muscle Coordination
Speed of Repetitive action
Balance
Cerebellum
Left Brain
Temporal Lobe (memory)
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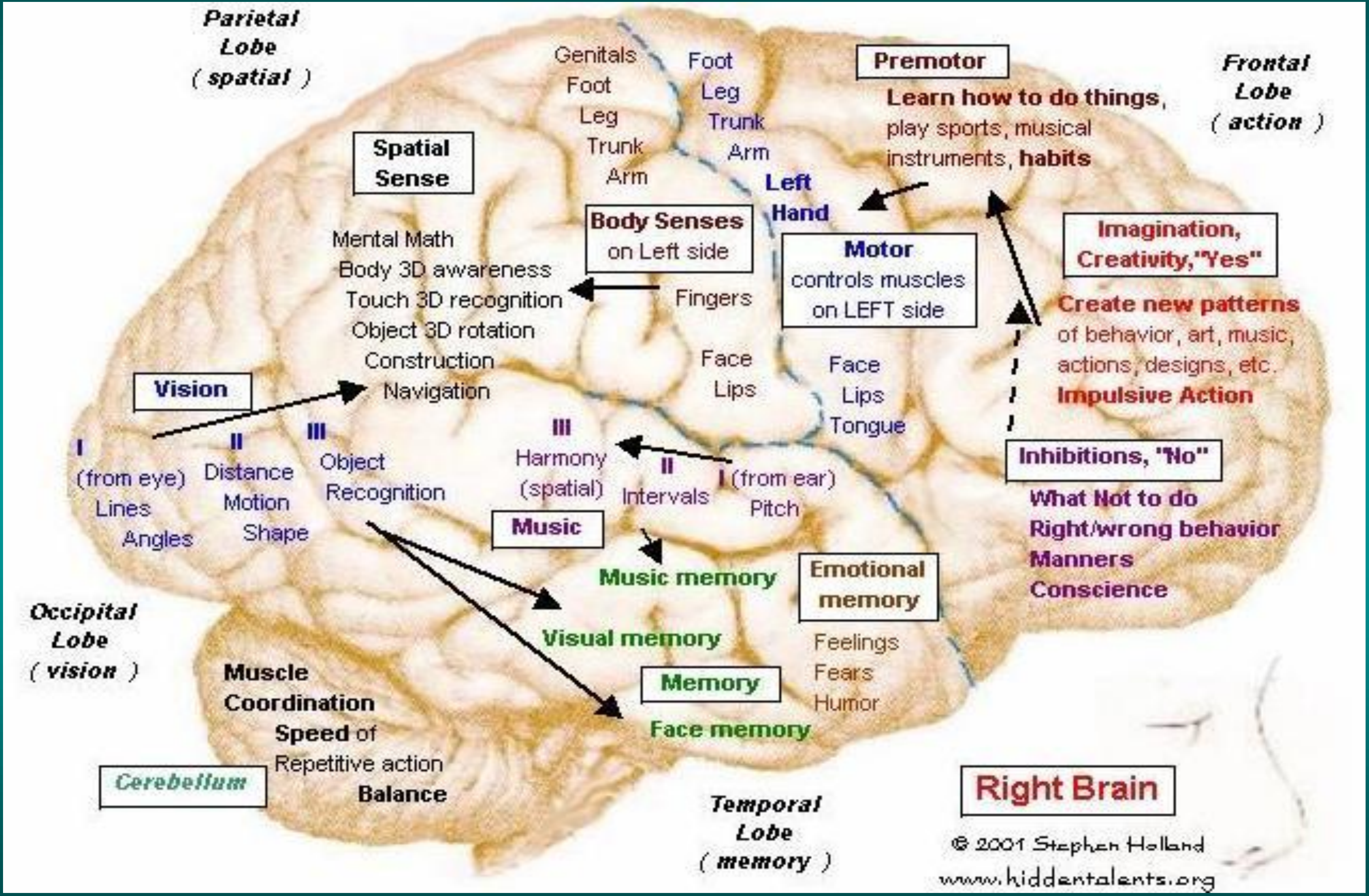

Parietal Lobe (spatial)
Genitals
Foot
Leg
Trunk
Arm
Foot
Leg
Trunk
Arm
Left Hand
Premotor
Learn how to do things, play sports, musical instruments, habits
Frontal Lobe (action)
Spatial Sense
Body Senses on Left side
Mental Math
Body 3D awareness
Touch 3D recognition
Object 3D rotation
Construction
Navigation
Fingers
Motor controls muscles on LEFT side
Imagination, Creativity,"Yes"
Create new patterns of behavior, art, music, actions, designs, etc.
Impulsive Action
Face
Lips
Face
Lips
Tongue
Vision
I (from eye)
Lines
Angles
II Distance
Motion
Shape
III Object Recognition
III Harmony (spatial)
II Intervals
I (from ear)
Pitch
Inhibitions, "No"
What Not to do
Right/wrong behavior
Manners
Conscience
Music
Music memory
Emotional memory
Visual memory
Feelings
Fears
Humor
Occipital Lobe (vision)
Muscle Coordination
Speed of Repetitive action
Balance
Cerebellum
Memory
Face memory
Temporal Lobe (memory)
Right Brain
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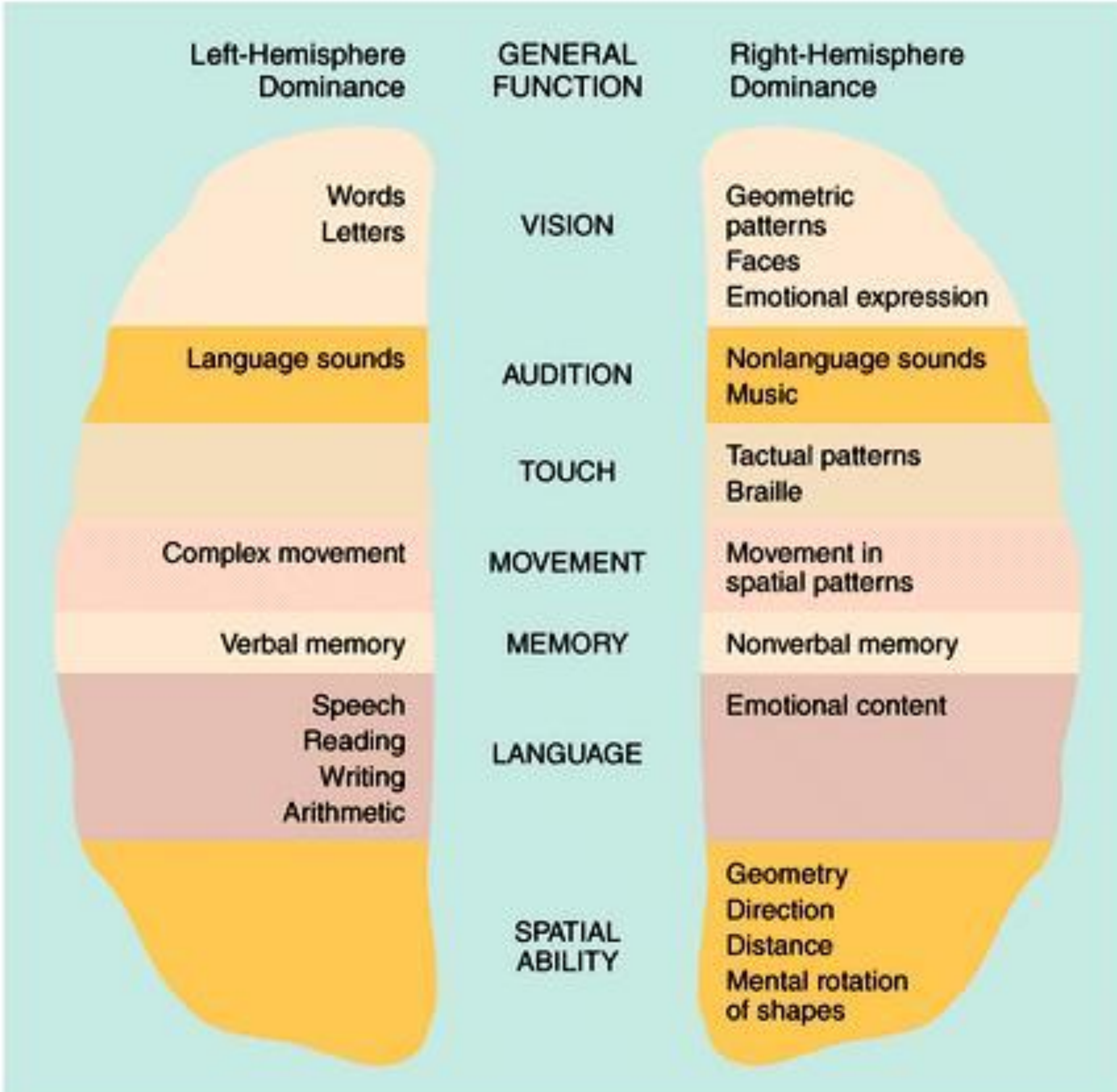
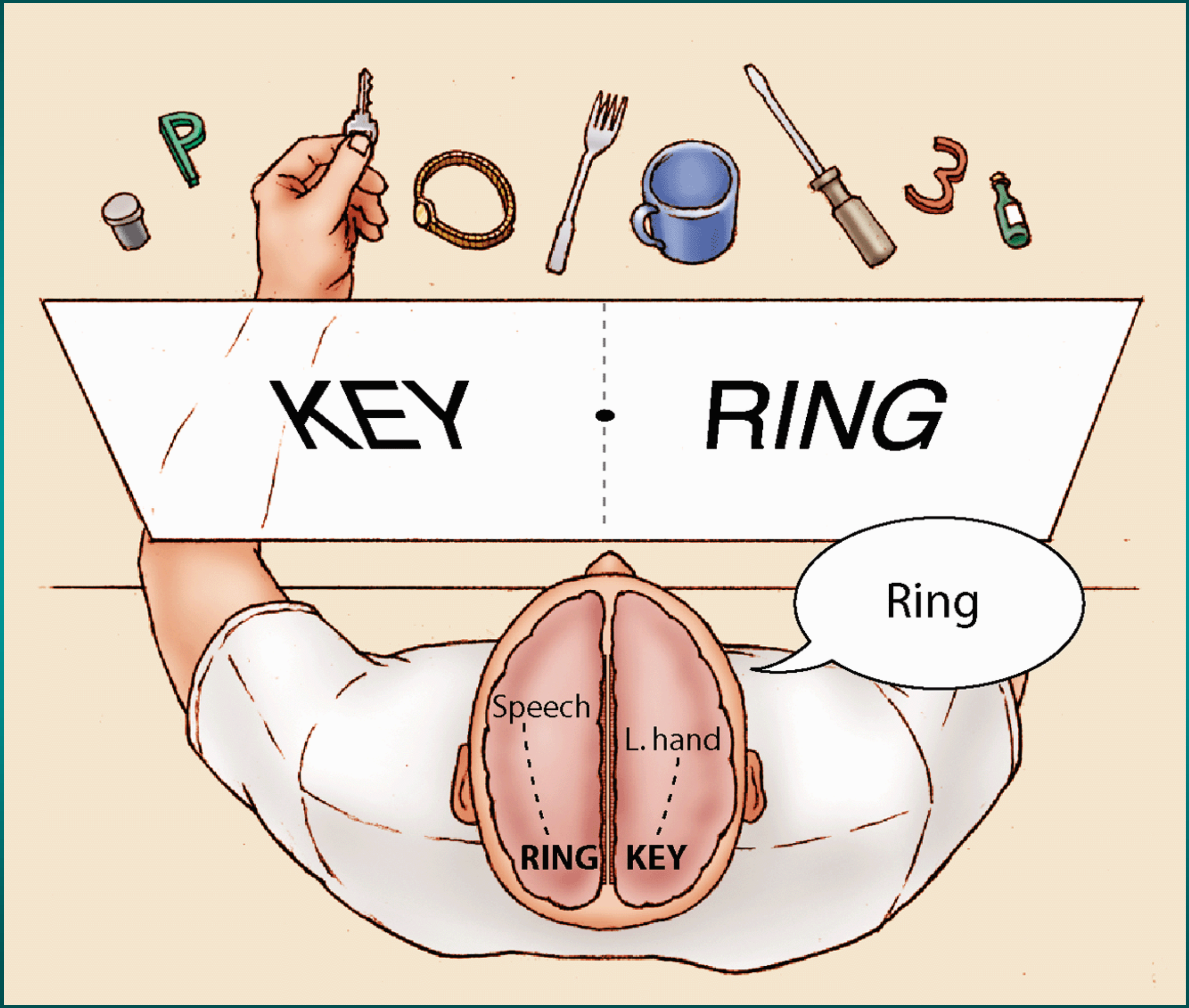
► Abilities That Display Cerebral Lateralization of Function



Cerebral Lateralization

- Left hemisphere is categorical hemisphere
  - specialized for spoken & written language, sequential & analytical reasoning (math & science), analyze data in linear way; templates of learned behaviors
- Right hemisphere is representational hemisphere
  - perceives information more holistically, perception of spatial relationships, pattern analysis, imagination & insight, music and artistic skill, attention; reality analysis
- Lateralization develops with age
  - trauma creates more problems in males since females have more communication between hemisphere (corpus callosum is thicker posteriorly in women)

Split brain effects



W. W. Norton

Brain Asymmetries

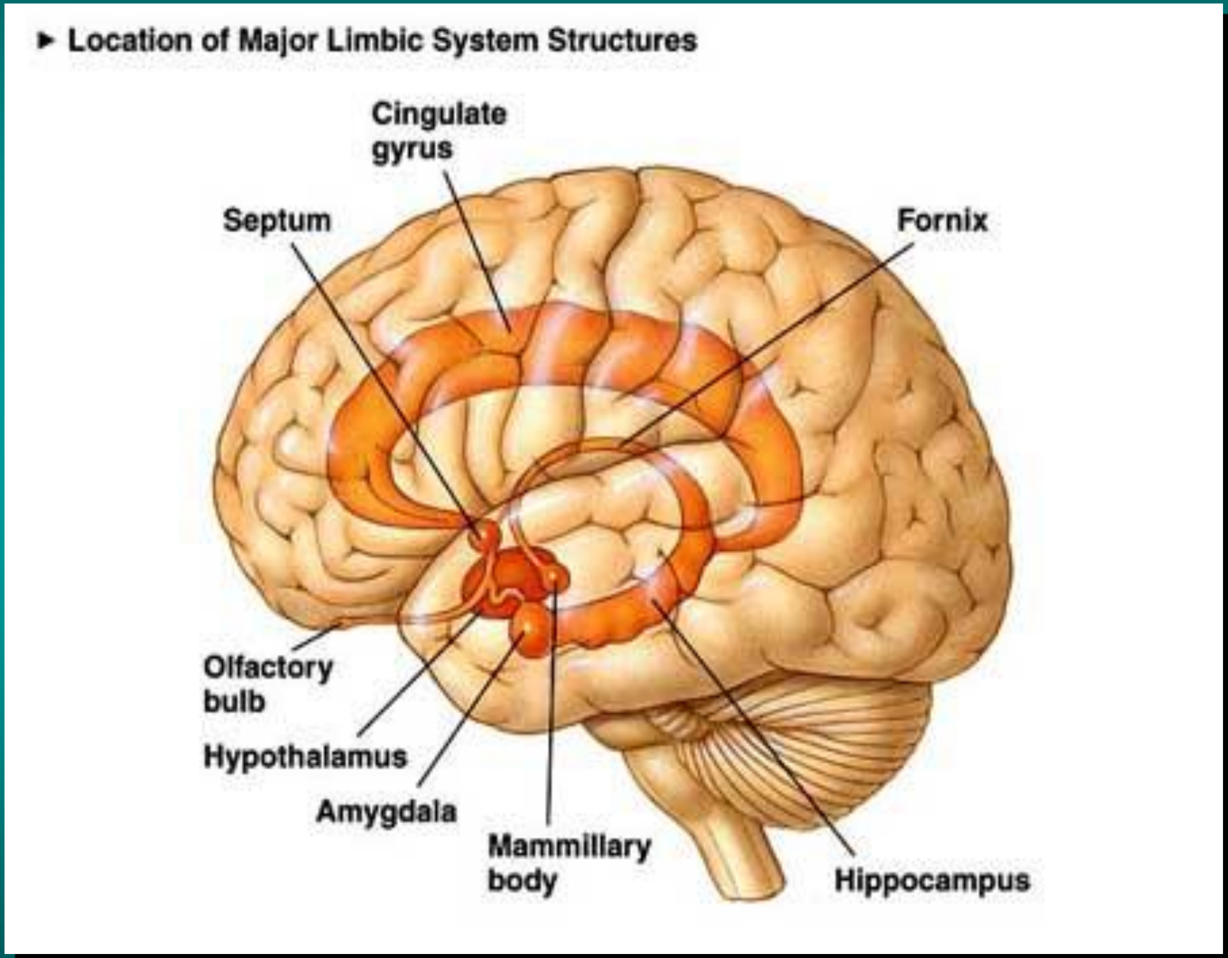
- <u>90% of people are right-handed</u>
- 95% of right-handers are <u>left hemisphere dominant for speech</u>
- 5% of right-handers are either right-lateralized for language or have their language areas distributed between their two hemispheres;
- <u>80% of left handers are left dominant for language</u>
- <u>Larger protrusions of the right frontal lobe and the left occipital lobe.</u>
- Structures involved in <u>language processing are larger in the left hemisphere</u> than in the right.
  - Broca’s area in the left frontal lobe is larger
  - Greatest asymmetries are found mainly in the posterior language areas, such as the temporal planum and the angular gyrus.

Left handers

- Approach motivation is computed mainly in the left hemisphere of the brain, and withdraw motivation in the right hemisphere.
- This is reversed in left-handers.
-

Brookshire and Casasanto, 2012

Cingulate Gyrus



Conflict Resolution circuit; Salience network

Cingulate Gyrus: Truth or Consequence

- Location: Collar around Corpus Callosum

- Functions:
  - Flags response conflict (incongruent trial on Stroop)
  - error detection (Stroop; error + 1 slower RT)
  - anticipation of tasks
  - motivation
  - modulation of emotional responses
  - Social cognition
  - Bravery

- Executive (anterior), evaluative (posterior), cognitive (dorsal), and emotional (ventral)

- Coactivation with DLPFC (which then corrects behavior)

Cingulate

- Receives information about a stimulus, selects an appropriate response, monitors the action, and adapts behavior if there is a violation of expectancy
- Self-monitoring: such as noticing bodily sensations of pain and hunger or recognizing that one has made a mistake.
- Damage: OCD, akinetic mutism, ADHD, depression, psychopathy

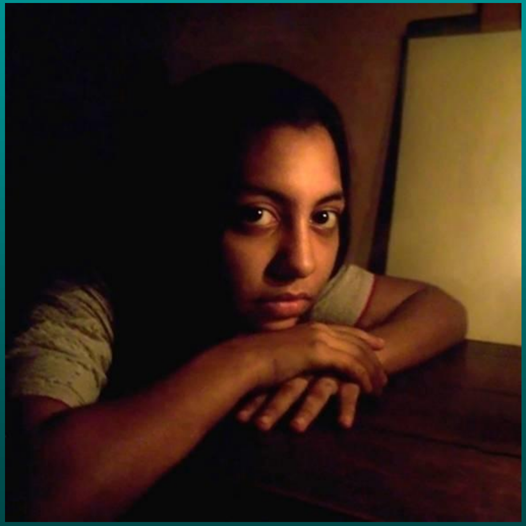
Area 25 in depression

- Extremely rich in serotonin transporters and is considered a governor for a vast network involving areas like hypothalamus and brain stem, the amygdala and insula, the hippocampus, and some parts of the frontal cortex.
- Subcallosal cingulate gyrus has been the target of deep brain stimulation to treat that severe depression
- BA25 is overactive in treatment-resistant depression.

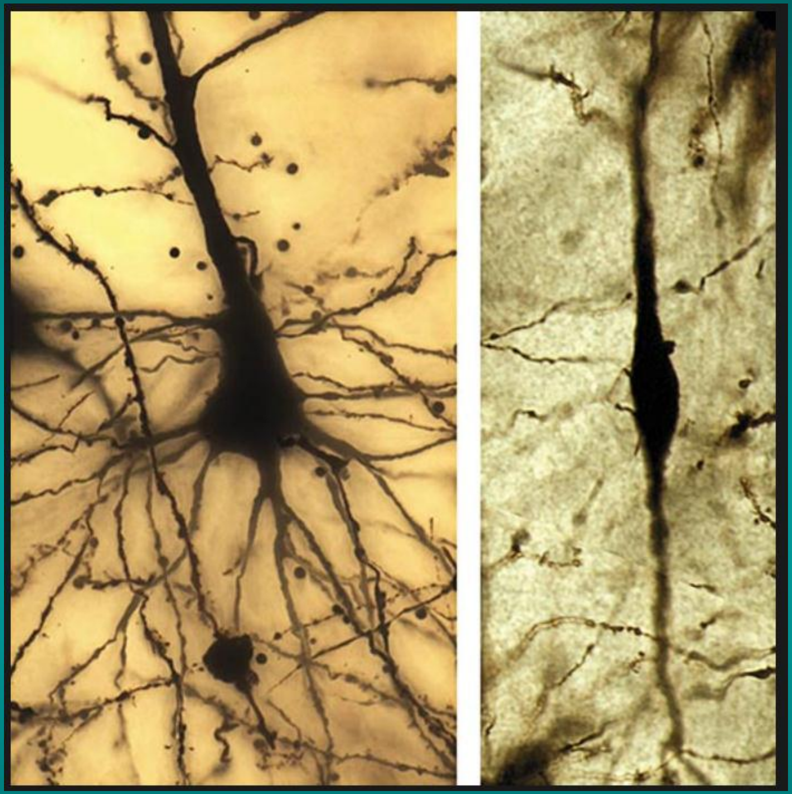
GAD & DTI of Uncinate fasciculus

- Reduced integrity of the uncinate fasciculus (bilaterally reduced FA values), a crucial white matter pathway linking ventral PFC and ACC to limbic regions, in patients with GAD.
- Neural pathway involved in both normative emotion regulation and fear extinction processes may contribute to atypical emotional processing in GAD.
- Suggest weak top-down control of amygdala reactivity.
- Worry, the hallmark feature of GAD, its presumed function in avoiding negative emotional experiences may actually sensitize amygdala activity, resulting in a generalized state of heightened anxiety

What is the neuronal commonality in social animals with large brains?



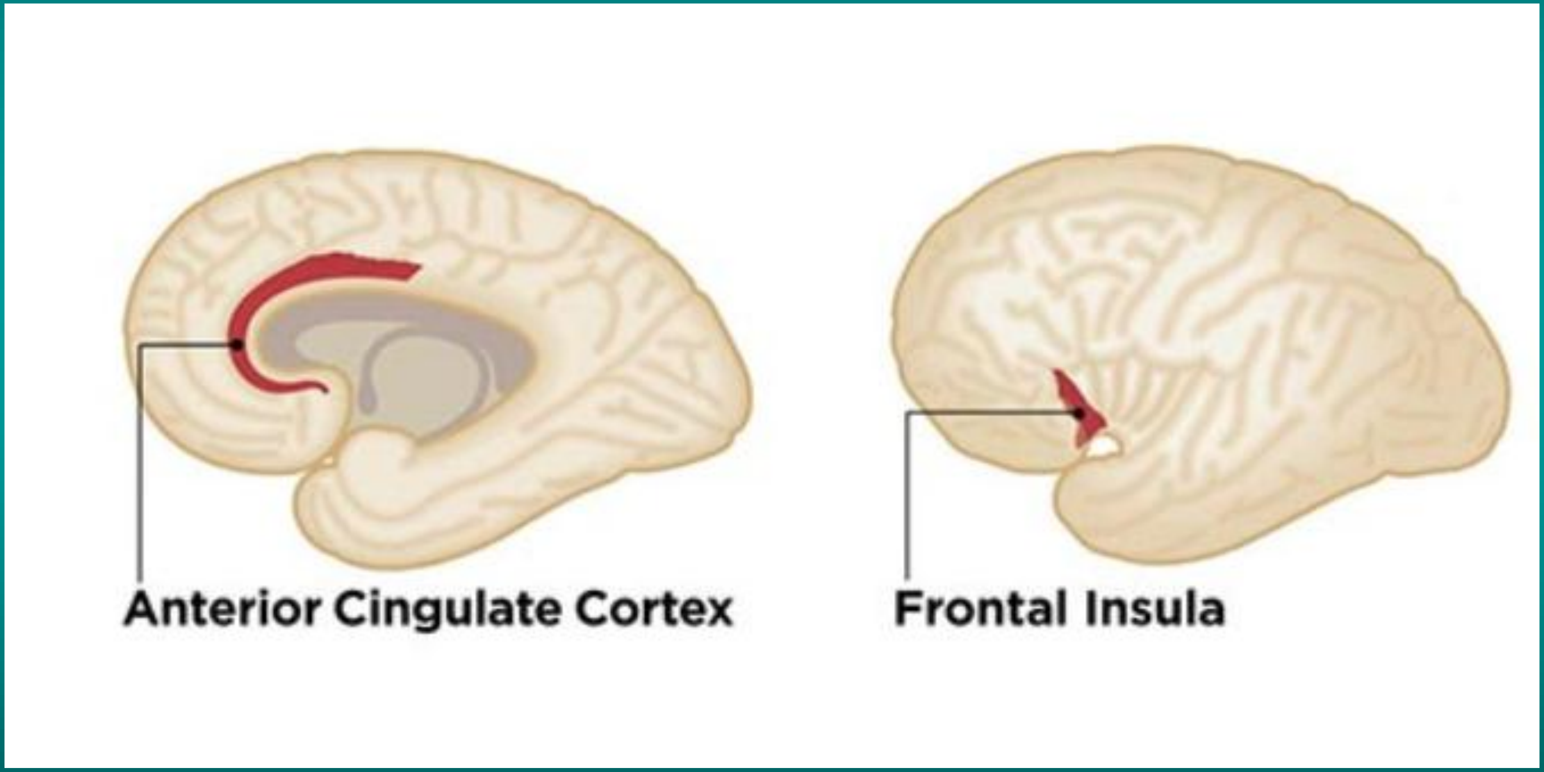
Brain Cells for Socializing?



A focal concentration of VENs in ACC and FI distinguishes large-brained, highly social mammals from other mammalian species.

(Allman et al., 2010; Hakeem et al., 2009; Hof and Van der Gucht 2007; Nimchinsky et al., 1999; Rose 1928)

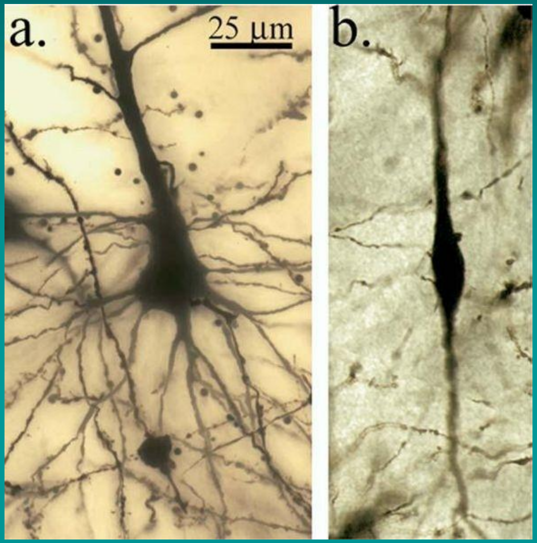
Location of VENS: ACC & FI

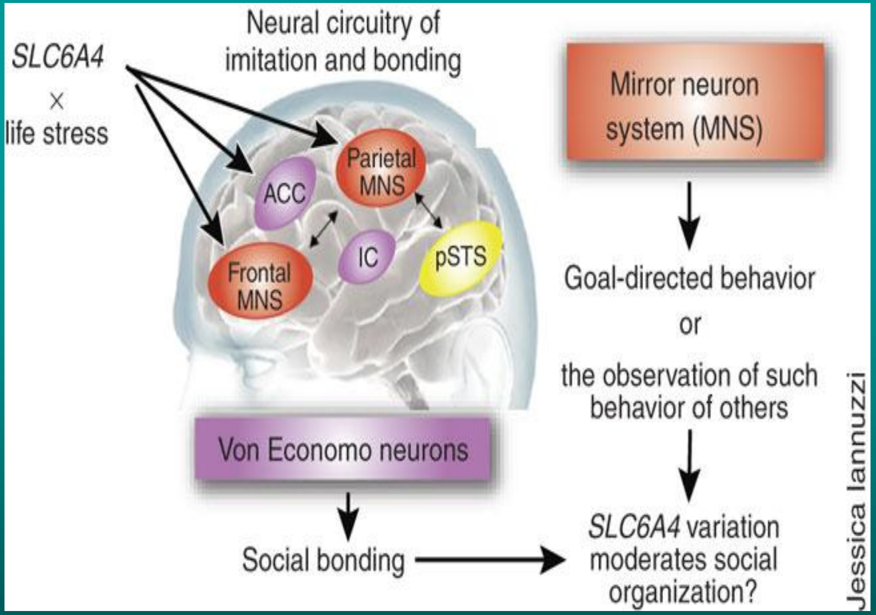


The FI features the other layer 5 neuron, the fork cell, which is scarcely seen in ACC.

Von Economo Cells:
ACC/Insula/DLPFC & Serotonin Transport

Layer Vb in Brodmann's subareas
 24a, 24b, and 24c and are most abundant in the cortex forming the medial wall of the cingulate gyrus
 (area 24b).





Von Economo Cells

- Von Economo neurons are fastest, large, bipolar neurons located only in the anterior cingulate and insula (layer Vb), & DLPFC.
- Only 4 animals: primates, certain cetacians, elephants and humans. More of them in chimps and human (2x more than chimps).
- The volume of Von Economo neurons is correlated with increased encephalization.
- Evolved to speed information around a big brain
- Start to work at age 4; peak at 8 y

Von Economo Cells

- Co-opted by the demands of social interactions: rapid regulation of behavior within a complex social environment.

- Ability to recognize oneself in a mirror

- FTD targets ACC and Insula: 70 percent of VENs destroyed
- Abnormally located in autistic brains

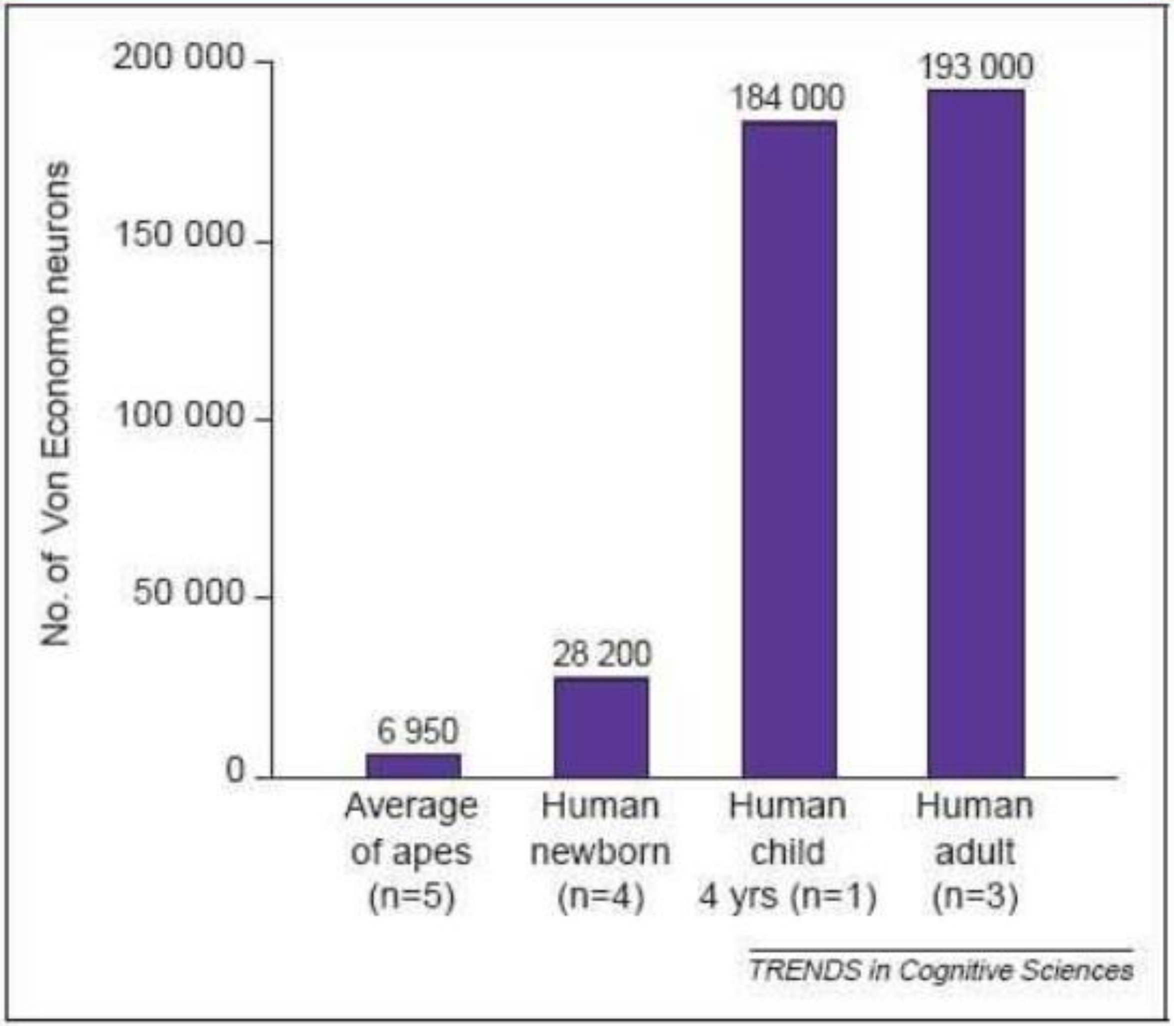


Figure 2. Comparison of Von Economo neuron numbers. Total number of VENs in FI (total of right and left hemispheres) is shown for apes, human neonates, a four-year-old child, and an adult human. The number of subjects is given in parentheses. The data are stereological counts by the authors on brains in the Yakovlev Collection at the National Museum of Health and Science and the Semendeferi Collection at the University of California, San Diego.

Next 4 slides: 2011 NIMH Development Study

- 1989-2011: 6000 scans from 2000 subjects, incl. normal, ADHD, ASD, SZ, and twins) from age 3 to 30
- Child Psychiatry Branch of NIMH

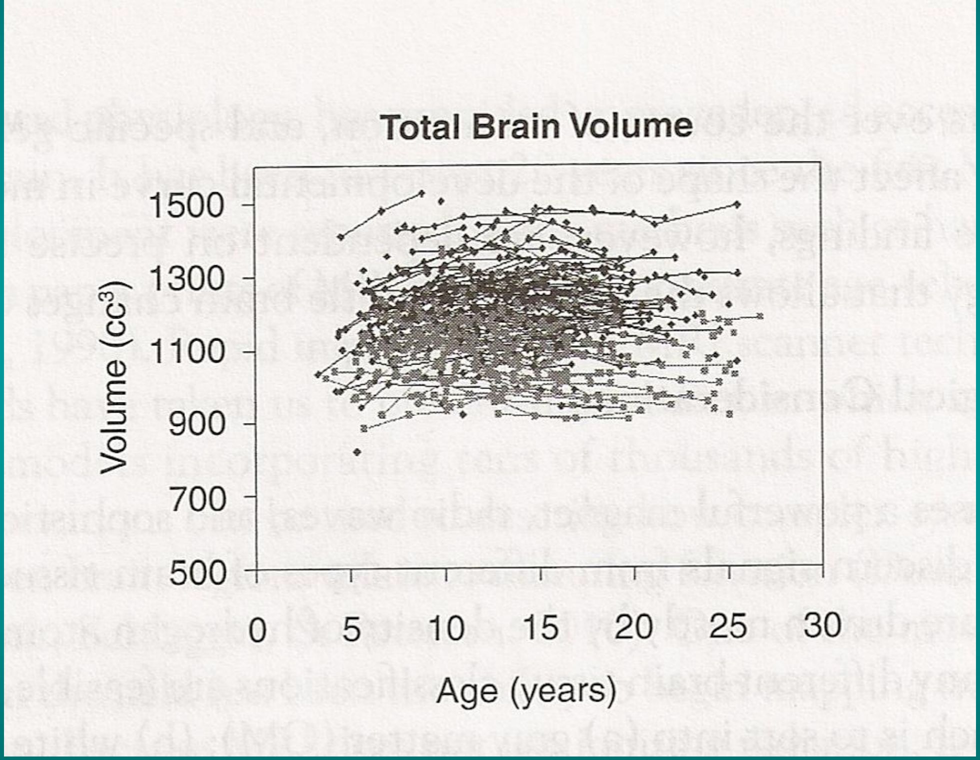
J. Giedd, et al., 2011

Total Brain Volume and Age

Inverted-U peak:
10.5 in girls
14.5 in boys

95% peak by age 6

High Variability:
2 10yo boys can be 2x different



Brain size not linked to body size:
Group ave size for males = 10% larger (in adults, on MRI & post mortem)

Boy's bodies not larger until after puberty; girls taller from 10-13

<u>Variability range from 900 to 1500 cc</u>

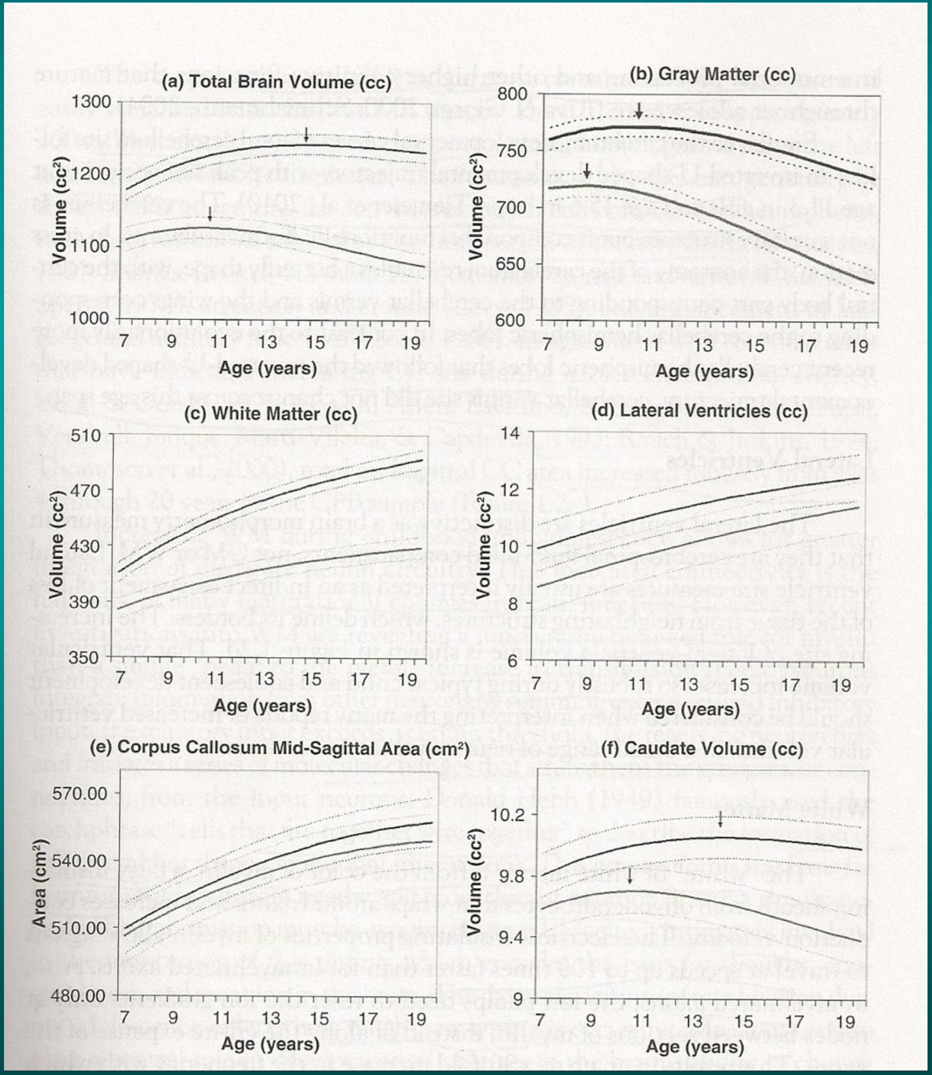
R. K. Lenroot, et al. 2007

Brain Component Development

Brain Volume

<u>White Matter & CC increase</u>: <u>Increased processing speed</u> (3000-fold increase in info transmission per sec)

<u>Correlation with</u> improved language, reading, inhibition, & memory functions



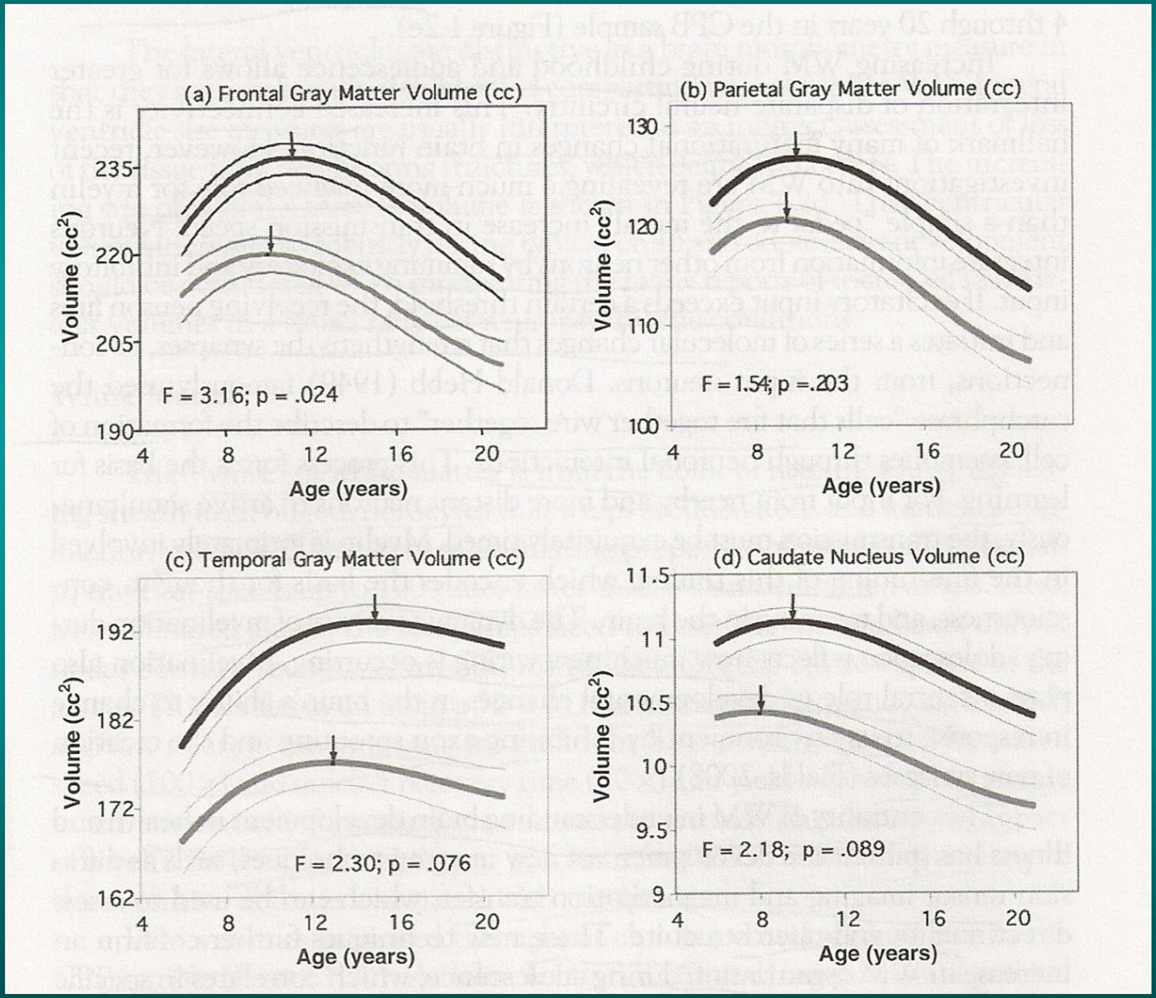
<u>GM decrease</u>

<u>Ventricle increase</u>

The Great Pruning: Inverted U: GM changes related to synaptic reduction

Frontal Peaks:
9.5 y in girls
10.5 in boys
peaks latest
In prefrontal

Temporal Peaks:
10 in girls
11 in boys

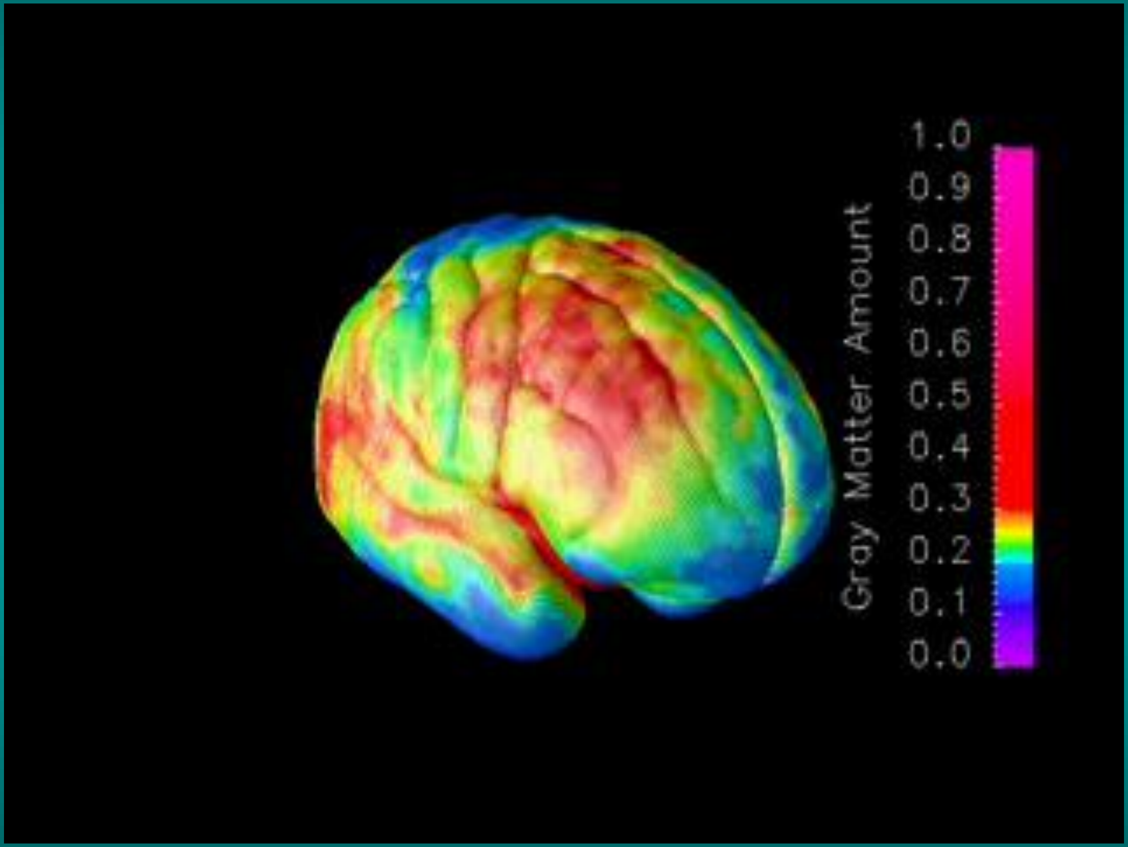


Parietal Peaks:
7.5 in girls
9 in boys

Caudate Peaks:
10.5 in girls
14 in boys

R. K. Lenroot, et al. 2007

Teen Brain: age 5 to 21



Lose 50% of all synaptic connections.

Other findings

- Robust sex differences in development, with females peaking earlier (related to puberty)
- Rate of cortical thinning more rapid in males; protracted maturity of frontal lobes (testosterone related)
- Amygdala volume increased only in males (higher androgen receptors in Amygdala)
- Hippocampus volume increased only in females (higher number of estrogen receptors in hippocampus)

J. Giedd, et al., 2011; Clark, MacLusky, & Goldman-Rakic, 1988; Morse, Scheff, & DeKosky, 1986

Major Adolescent Brain Changes

- Major synaptic pruning (loss of 50% of synaptic connections in the brain)
- Maturation of frontal and limbic regions
- Increased integration of brain circuitry
- Increase in mylenization, particularly in frontal region: increase in impulse control
  - In boys, self report of behavioral impulse control
  - In girls, increase in ability to inhibit incorrect answers
- Dopamine distribution changes (risk taking↑↑, reward seeking)

Adolescent Brain Changes 2

- Frontal brain circuits, which control attention, grew fastest from ages three to six.
- Just before puberty, children lose up to 50 percent of their brain tissue in their deep motor nuclei. These systems control motor skills such as writing and sports.
- Language systems underwent a rapid growth spurt around the age of 11 to 15, and then drastically shut off in the early teen years (end of a period when we are thought to be most efficient at learning foreign languages)
- As abstract reasoning increases, so does social anxiety

Myelin Sheets on Axons Mature Slowly in Frontal Lobes; may increase into 60s.

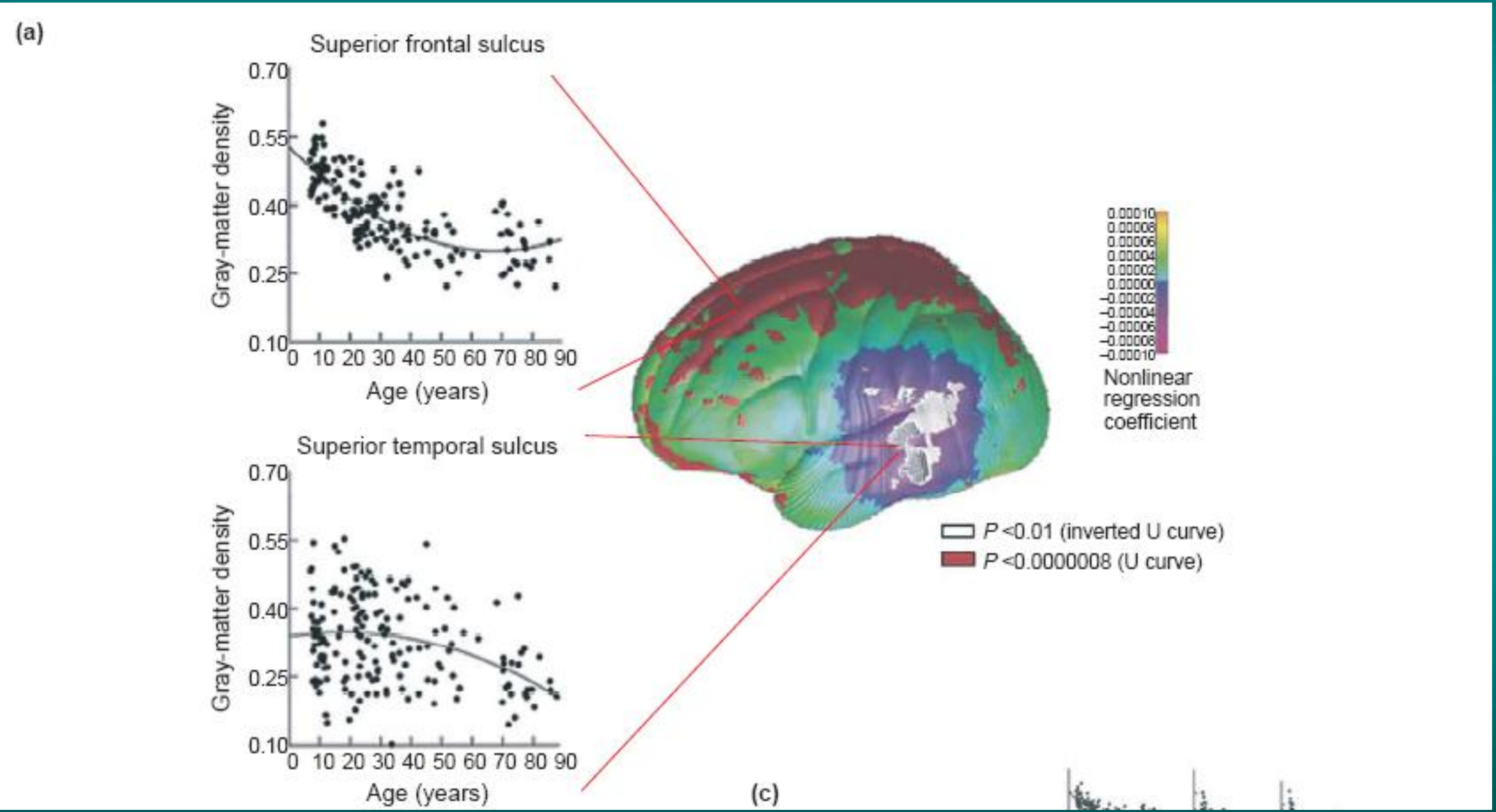
Regional Maturation: Myelogenetic Cycles

Taken from Yakovlev & Lecours, The Myelogenetic Cycles

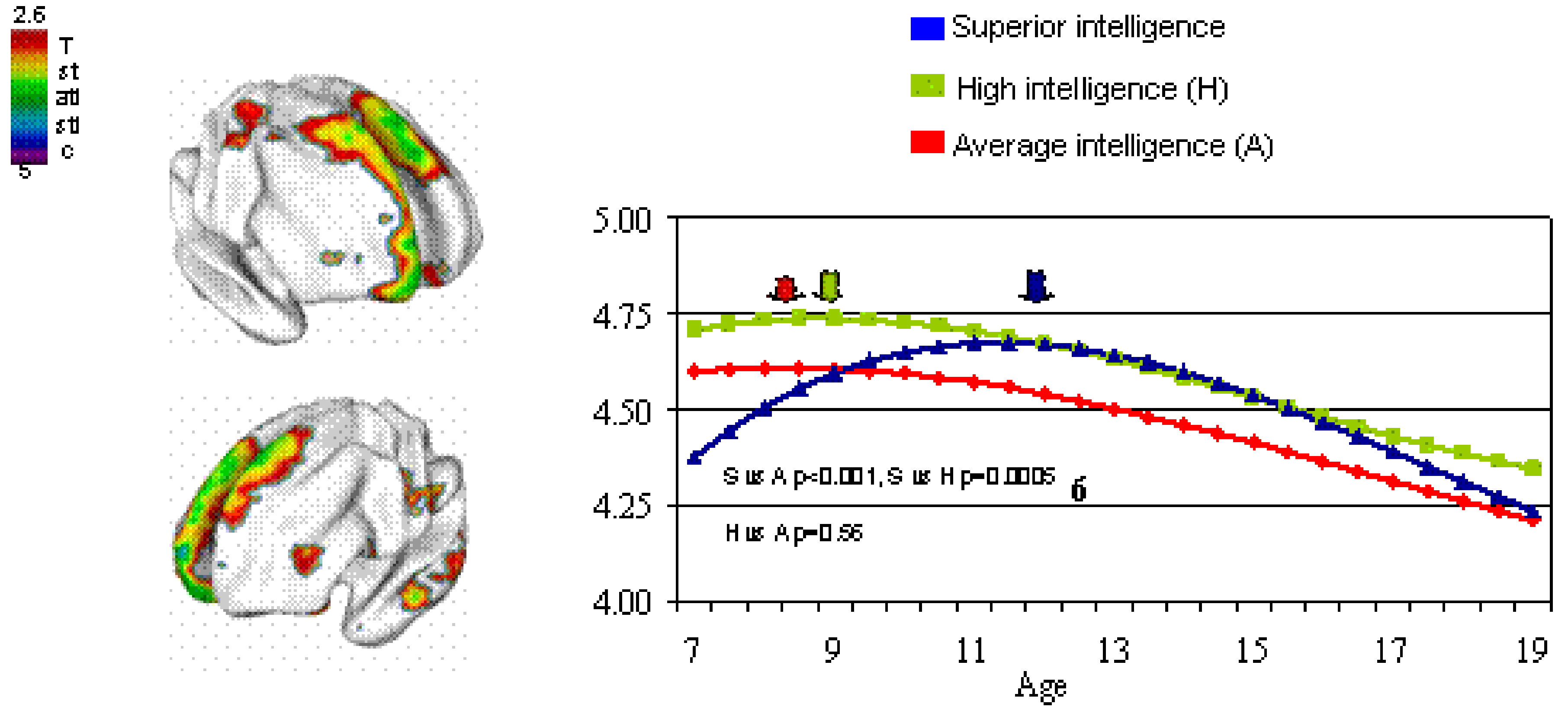
<u>Amount of white matter (axon interconnections) distinguishes us from primates, not size of prefrontal lobes. Creates "greater bandwidth" and processing speed. Einstein had more white matter, not neurons.</u>

Yakovlev & Lecours 1967

Grey matter density and age:
Rapid decrease in frontal grey in adolescence;
Steady decrease in temporal through lifespan



IQ and Brain Development:
IQs of 100, 120, 140



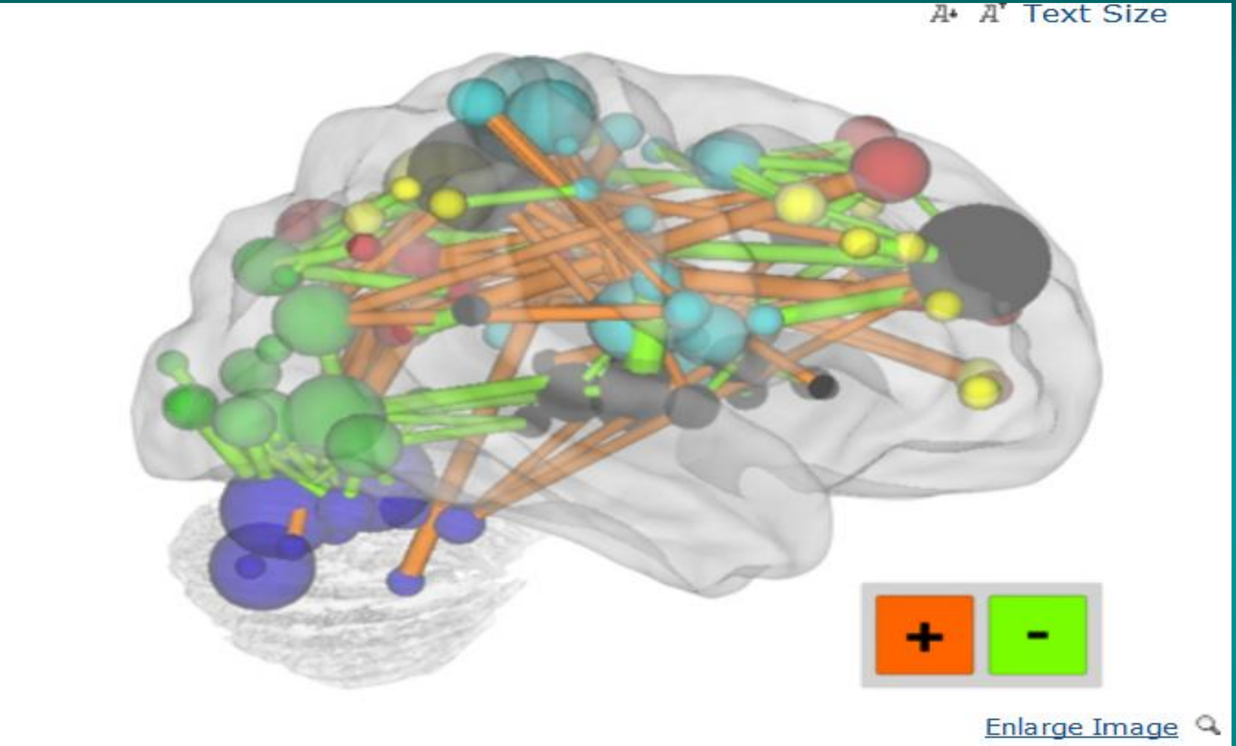
Superior IQ peaks latest before pruning

Neurobiology of Risk in Adolescence: A Tale of Two Systems

- Risk taking related to a) earlier maturation of subcortical limbic region, b) later maturation of top-down prefrontal control region, and c) context.
- Improved cognitive control with maturation of prefrontal cortex.
- Context of behavior increases in importance (presence of other teens, alcohol & drugs, sex, etc.)
- Larger dopamine release in adolescence leads to hypersensitivity to reward which leads to risker behavior

A. Galvan, 2011

Connectivity growth curve for the brain



As the brain matures, some connections get stronger (orange) while others weaken (green). The sizes of the brain regions shown indicate their relative importance in predicting maturity.

13,000 functional brain connections and selected the best 200 produce a single index of the maturity of each subject.

Growth Curve: a brain maturity test

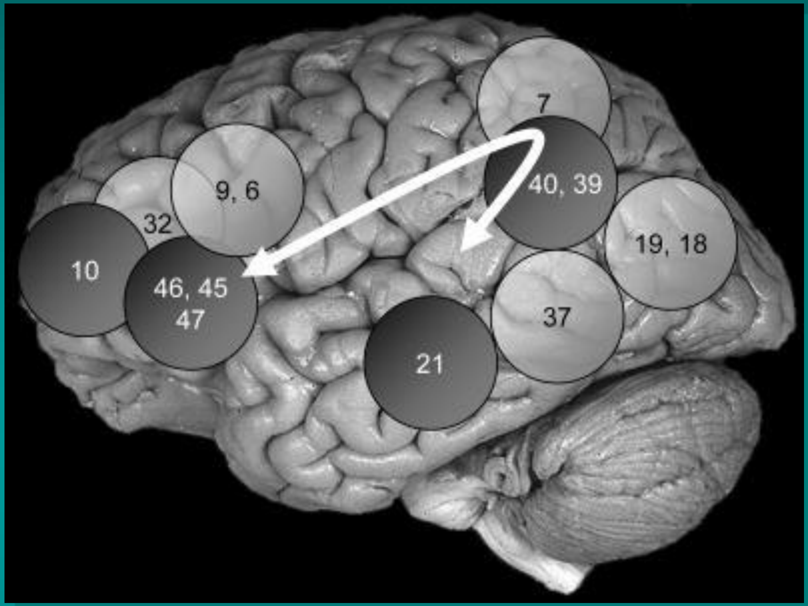
- Links between brain regions that are physically close to each other get weaker with age, while specific long-range connections tend to get stronger.
- Child: networks involving regions physically close to each other,
- Adult: networks that connect distant regions
- Connections between the right anterior prefrontal cortex and the precuneus were the best predictors for overall brain maturity

Parietal-frontal integration theory (P-FIT)

- The most empirically-based neuroscience model of human intelligence
- In a review of 37 imaging studies related to intelligence, a distinct neurobiology of human intelligence
- High intelligence probably requires *undisrupted information transfer among the involved brain regions along white matter fibers*

Jung, Haeir, Colom et al.. (Colom et al., 2009; Jung & Haier, 2007; Deary et al. (2010)

P-FIT: Parieto-Frontal Integration Theory: Biological basis of IQ



Dark Grey: Left Hem

Light Grey: Right Hem

Arcuate Fasiculus: connector

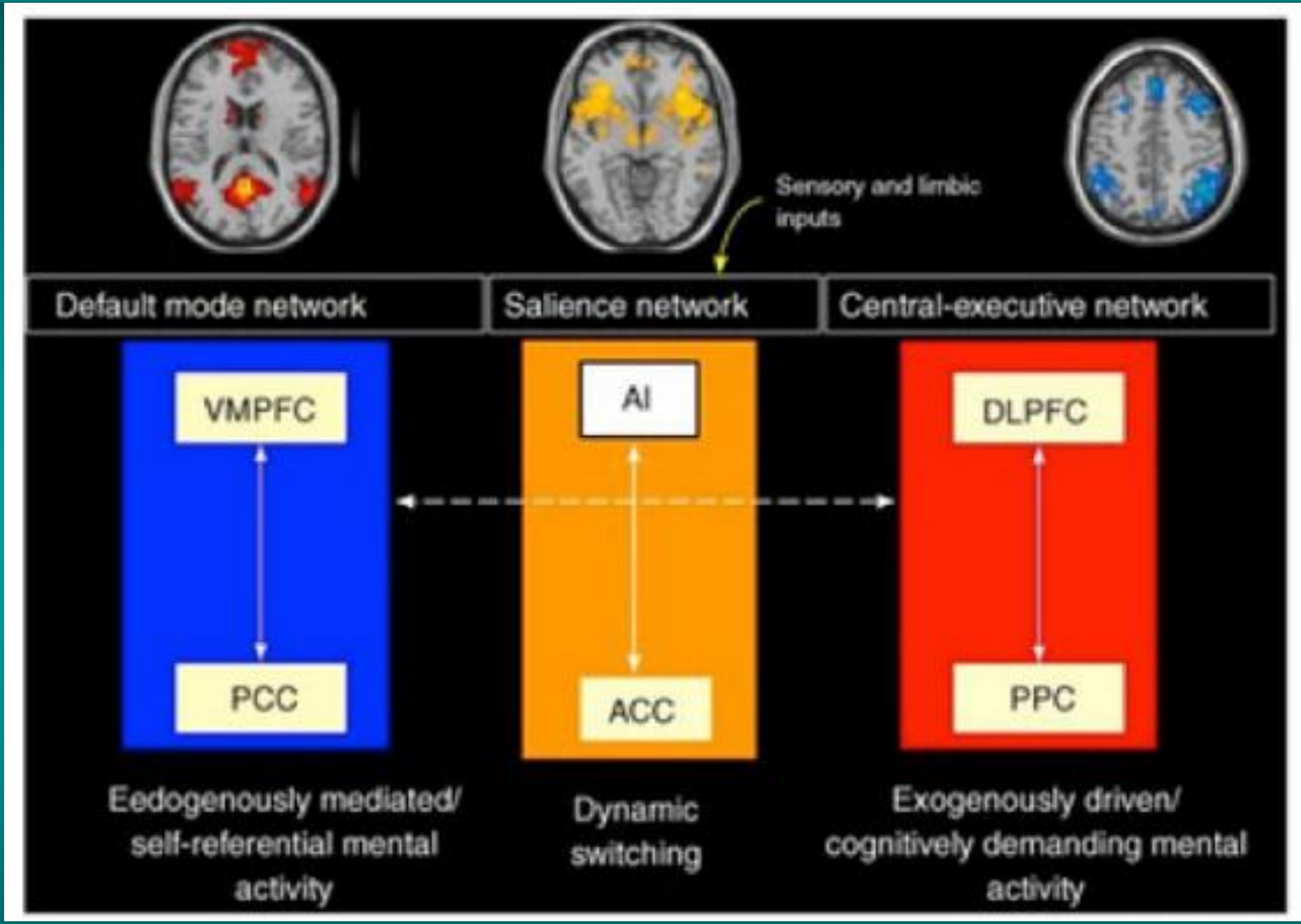
Their Parieto-Frontal Integration Theory (P-FIT) identifies a brain network related to intelligence, one that primarily <u>involves areas in the frontal and the parietal lobes:</u> *correlations between individual differences in general intelligence (g; and also the CHC domains of Gf, Gc and Gv) and certain core brain networks;* a function of the efficient flow of information between the dorsolateral prefrontal cortex, parietal lobe, anterior cingulate cortex and specific regions in the temporal and occipital cortices.

Variance in Fluid Intelligence

- 1. Overall brain size accounts for 6.7% of individual variation in intelligence.
- 2.Prefrontal cortex is a critical hub for high-level mental processing, 5%.
- 3. Strength of neural pathways connecting the left prefrontal cortex to the rest of the brain, 10%
- It is the left prefrontal cortex that helps coordinate these processes and maintain focus on the task at hand

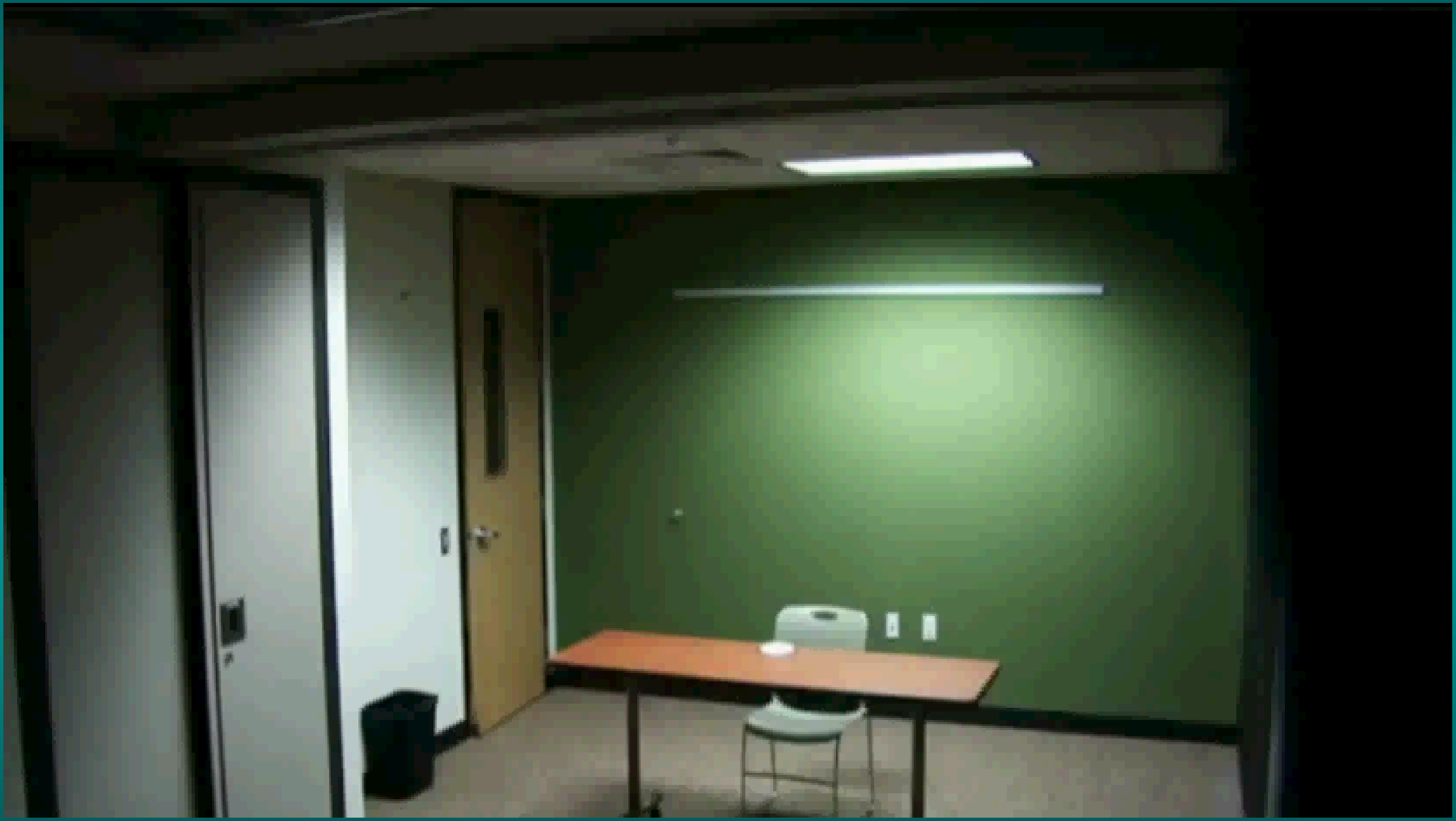
Michael W. Cole, et al., 2012

Major Networks



- Three major networks: Default, Salience, Executive; the central executive network "*is engaged in higher-order cognitive and attentional control*."

Marshmallow Test



Marshmallow at 4: Self control

- Walter Meschel, 1968, 4 year olds, get 2 marshmallows if wait 15 minutes; ring bell and get to eat, but no 2nds; 2 minute wait was average; 25% made it to 15 min.

- Children who rang the bell within a minute were much more likely to have behavioral problems, both in school and at home. They struggled in stressful situations, often had trouble paying attention in class and had serious problems with their temper.

- At age 4, ability to wait 15 minutes before eating a marshmallow predicts SAT scores 210 points higher at age 18.

Marshmallows & Frontal Lobe

- They were better adjusted, were less likely to abuse drugs, had higher self-esteem, had better relationships, were better at handling stress, obtained higher degrees and earned more money.

- At age 45, delayers better at go/nogo task; increased activity in the inferior frontal gyrus and low ventral striatum activation.

- Practice or innate neural structures?

Type of experience: Pre 4 Language & SES

- Quantity:
  - Low SES: 600 words spoken to child per day
  - High SES: 2100 words spoken to child per day

The Bilingual Advantage

- Brain activates both languages when speaking one (more EF choice, cope with constant interference):
- Children: Increased levels of self-control and better at learning abstract rules and ignoring irrelevant information.
- Better decision making in second language
- Less impact of emotion on thinking
- Dementia 4 years later than monolingual

- Tourette's also have better self control

Neurobiology of Childhood Abuse

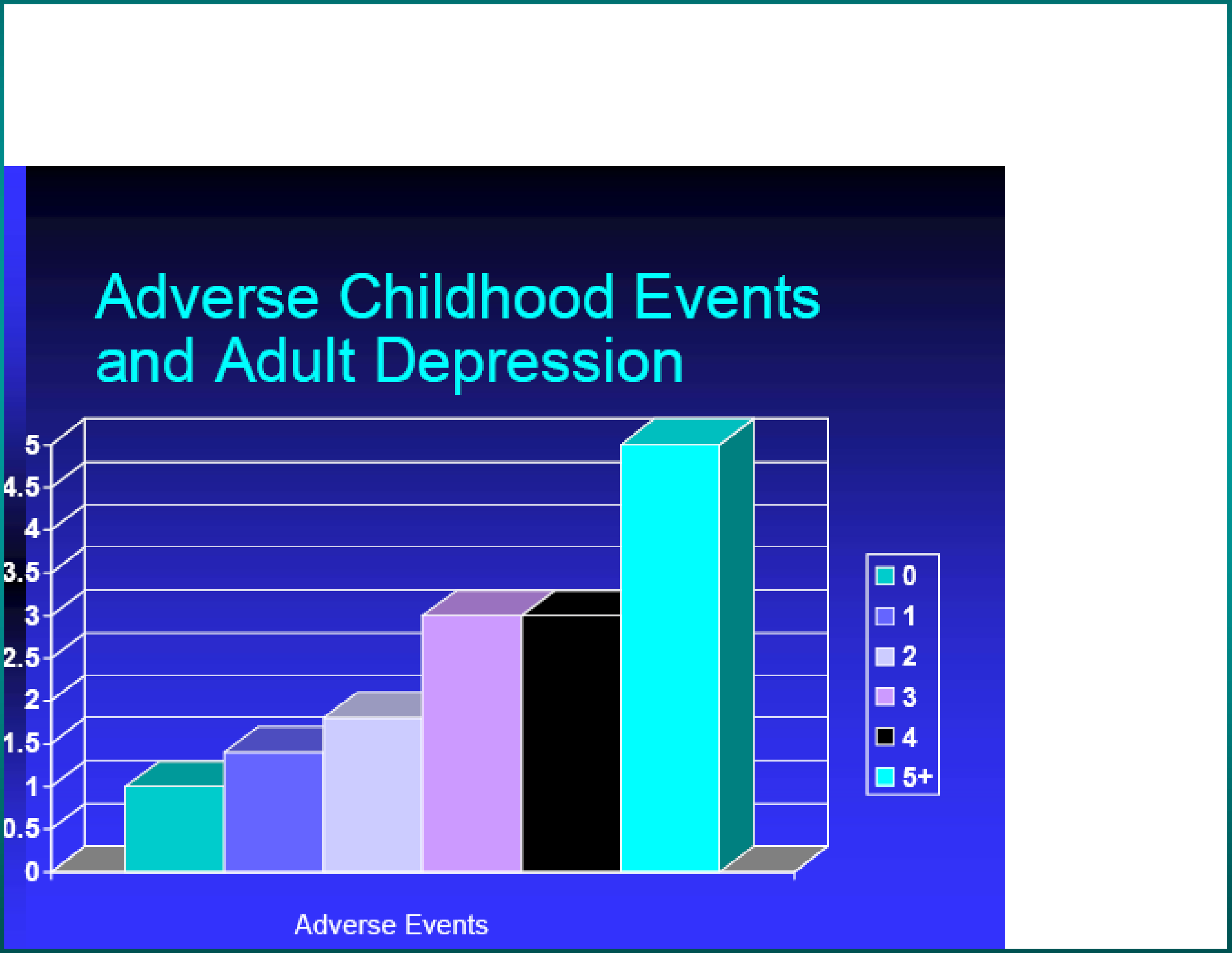
- Long term effects of early trauma/stress
- Effects Limbic circuits:
  - Amygdala = emotional reactivity (50 ms vs. 600ms for csness = 12 x faster),
  - Hippocampus = higher cortisol levels & stress sensitivity
- Chronic Stress =Smaller hippocampus, more reactive amygdala (GABA↓= less inhibition), greater R Hemisphere Activation
- Adverse Childhood Experience (ACEs) predict adult health and longevity

Adverse Childhood Experiences: Felitti and Anda

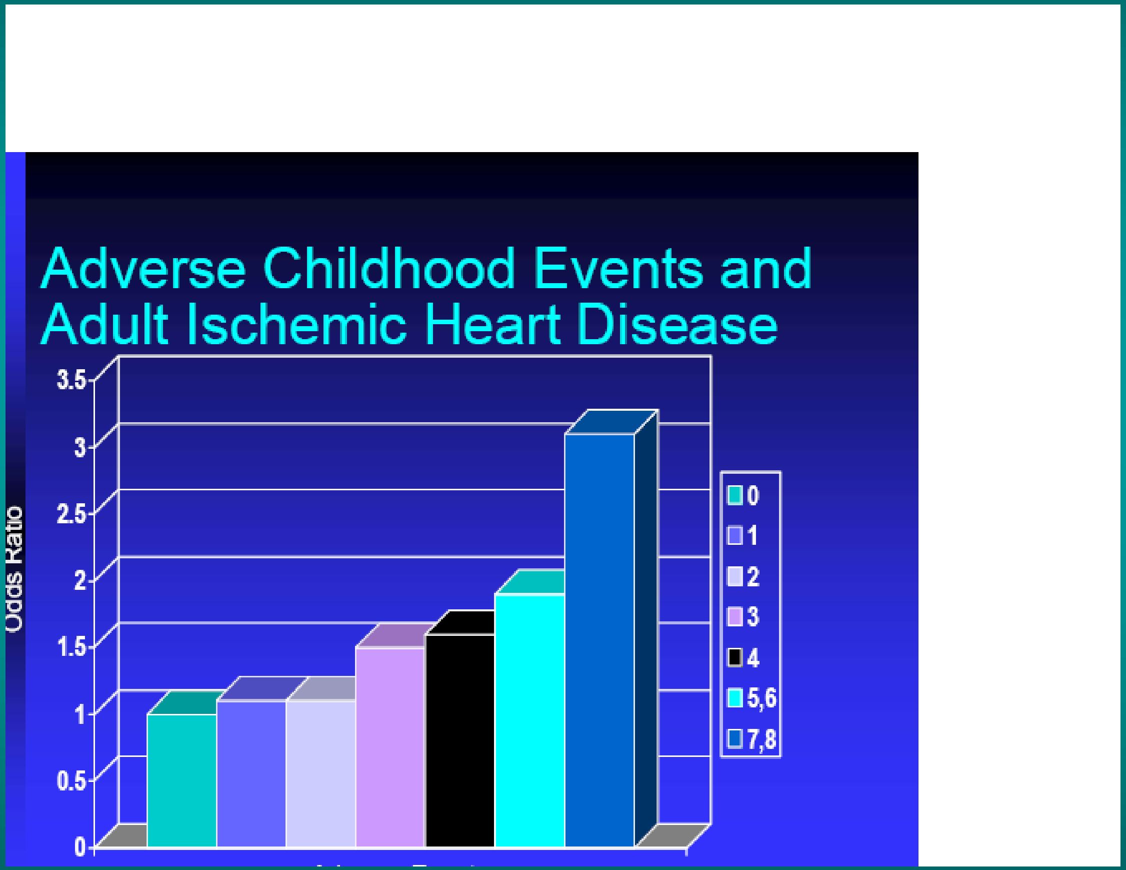
Growing up (prior to age 18) in a household with:

- Recurrent physical abuse.
- Recurrent emotional abuse.
- Sexual abuse.
- An alcohol or drug abuser.
- An incarcerated household member.
- Someone who is chronically depressed, suicidal, institutionalized or mentally ill.
- Mother being treated violently.
- One or no parents.
- Emotional or physical neglect.

Adverse Childhood Events 1: Adult Depression

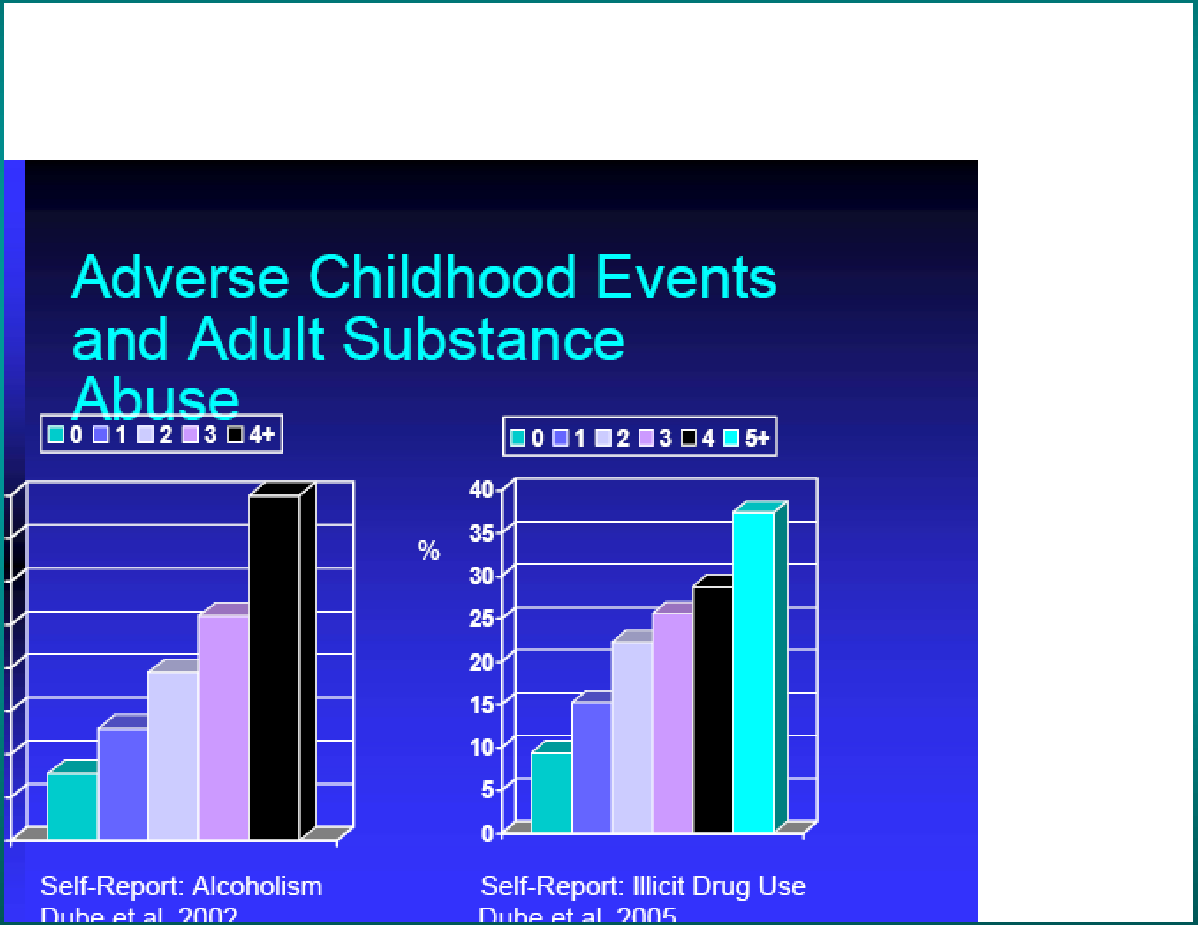


Adverse Childhood Events 2:
Adult Heart Disease



Having 6 or more ACES reduces life expectancy down to age 60.

Adverse Childhood Events 3: Substance Abuse



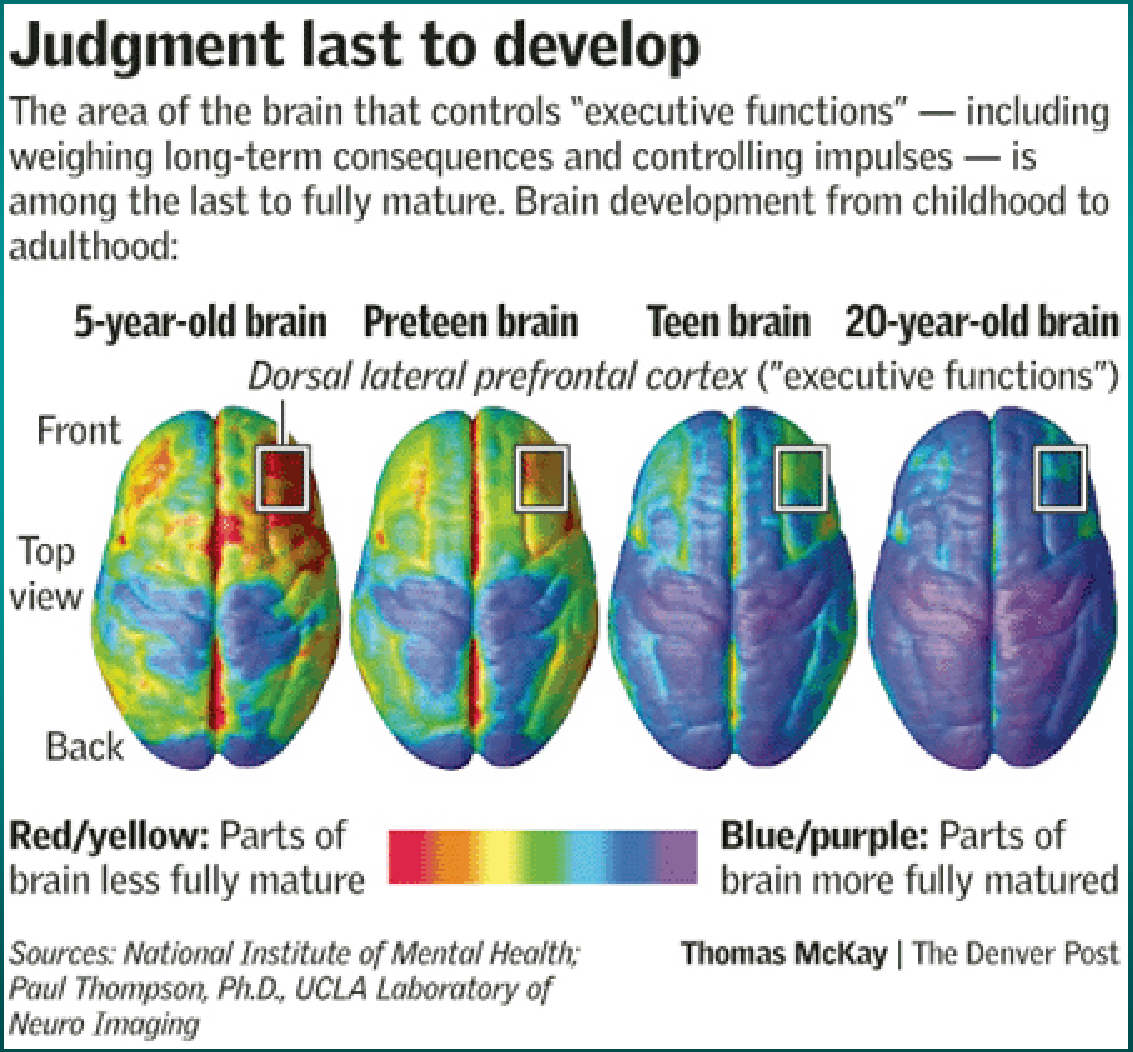
Trauma and Brain Response

- Evocation of traumatic memory:
  - Right Hemisphere increased activation of limbic, amygdala, and visual centers
  - Decreased Left Broca’s area

Development of Executive Functioning: Sorting

- Age 3: can sort object by 1 criterion (red car), but not a 2nd criterion (yellow flower)
- Age 4: can do 2 categories

Executive Functioning: Last to develop fully



Use it or lose it theory

- People who use their brain cells protect these cells from wear and tear
- <u>Without use, neuron is signaled that it is no longer needed</u>
  - <u>Dendrites atrophy</u>
  - <u>Synaptic connections weaken</u>
- With no new input, brain synapses begin to weaken.

Hardware vs. Software

- Brain = Your hardware
- Experience = Your software
- Experience produces constant neurological changes: new synapses, new dendrites

Neuroplasticity:

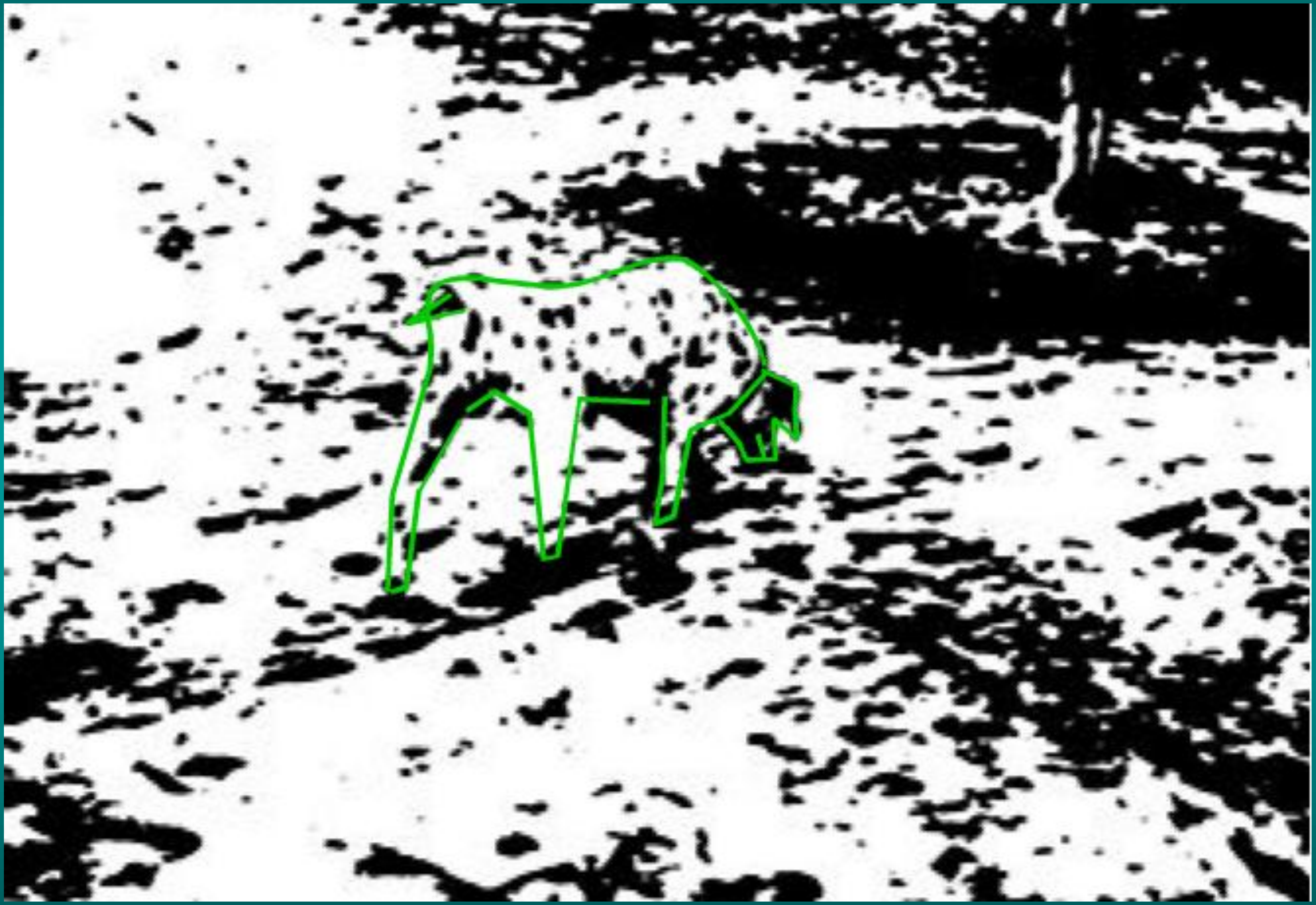
We all have the power to change one another’s brain.

On the next slide I will forever change your brain.

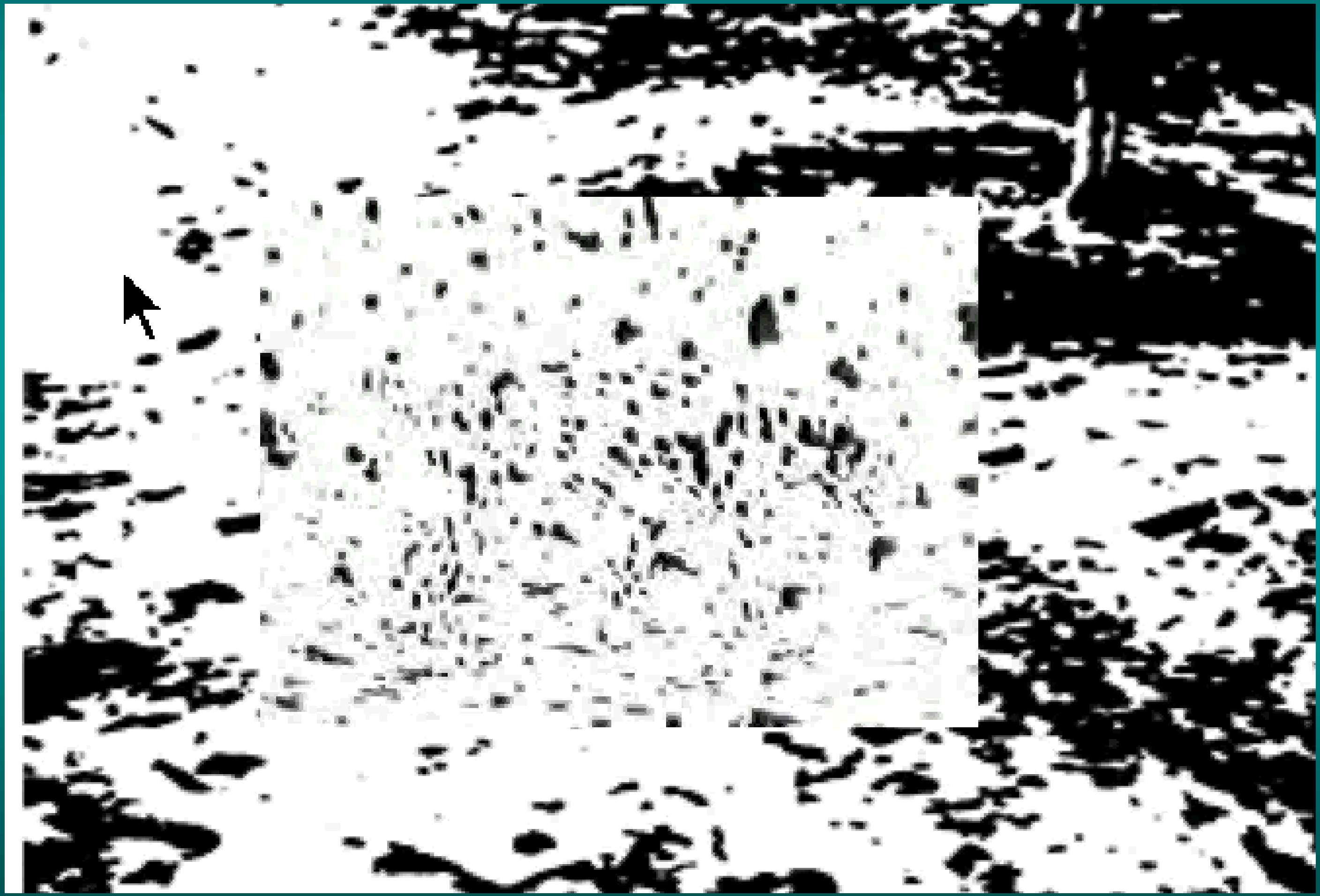
R.C. James's Camouflaged Dalmatian

Your brain (perception and memory processes) is permanently changed by each experience

Dalmatian Revealed



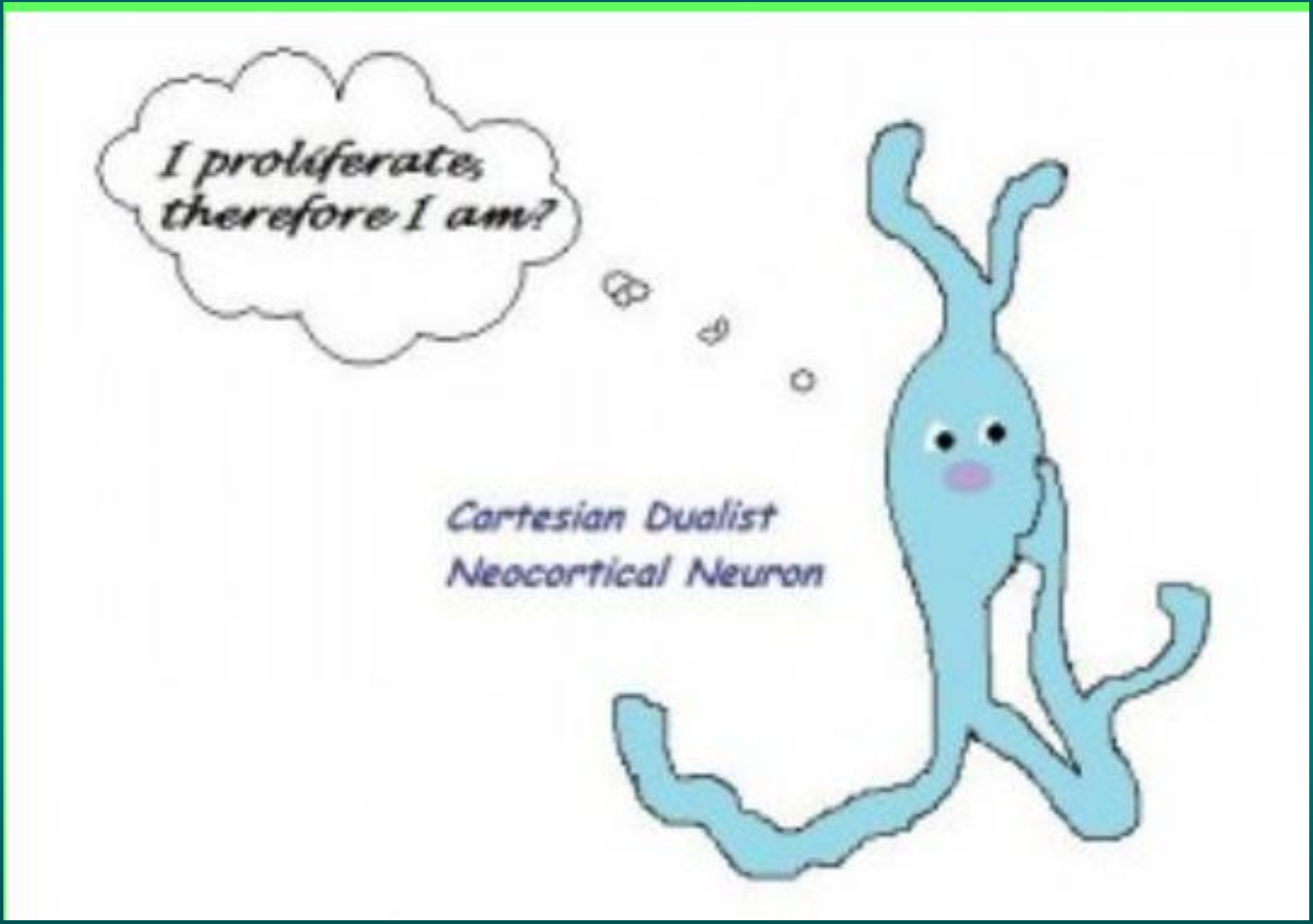
Or moving….



Neuroplasticity

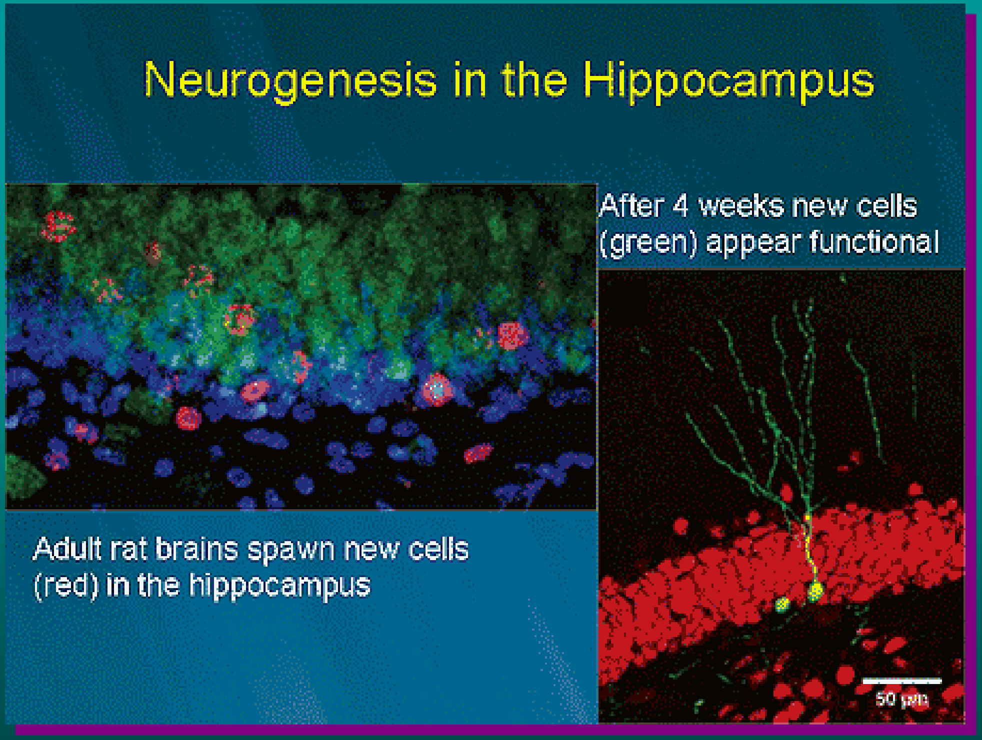
- Brain’ capacity to rewire itself due to experience
- Some areas don’t rewire
- There are critical periods for experiential exposure in some areas i.e. language
- Areas unused from birth are rewired for other use i.e. born deaf (Heschel’s area rewired for vision & touch)

Is there adult neuronal proliferation ?

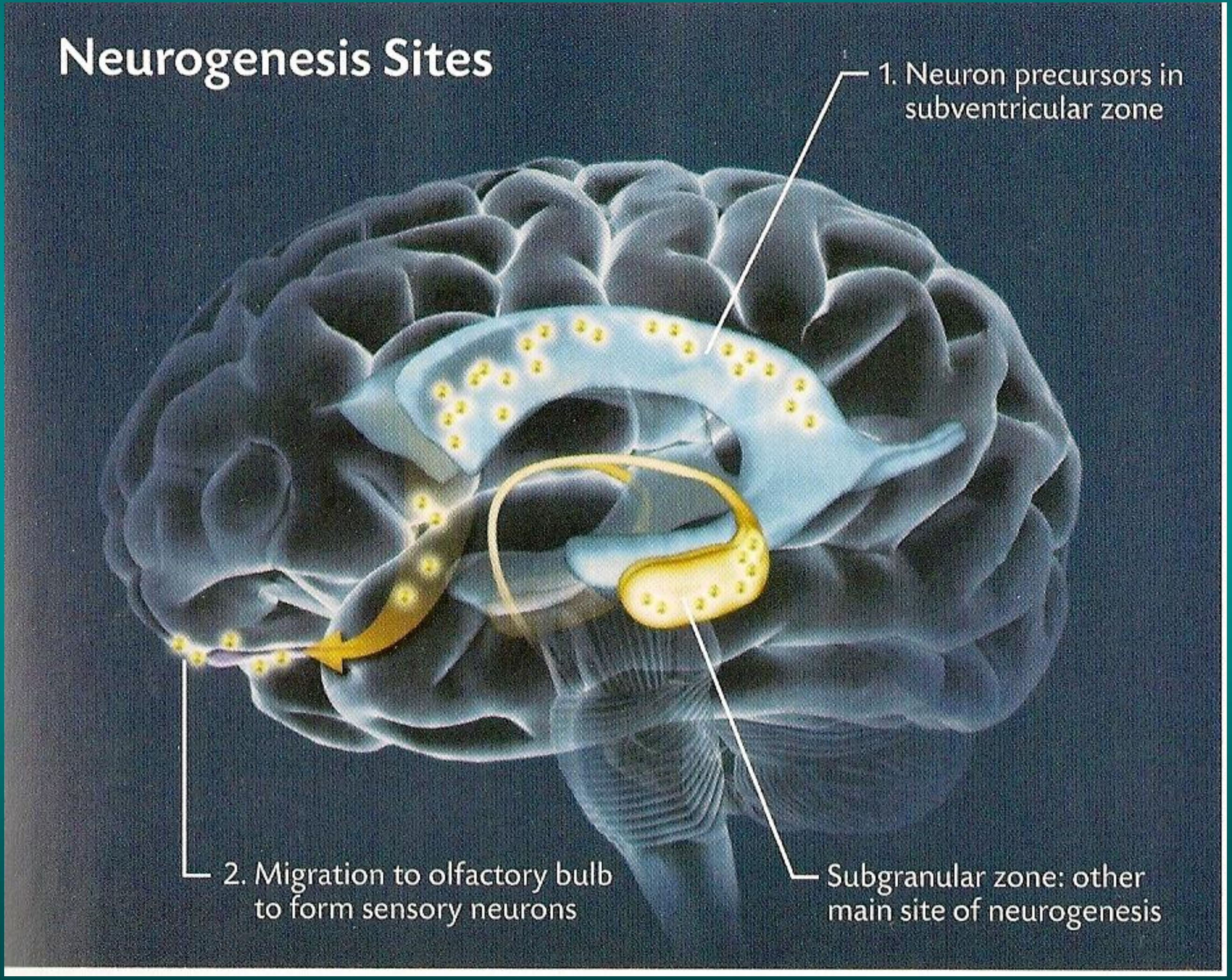


Neurogenesis

- Neurogenesis: growth of new neurons in the adult brain; Stem cells become new adult neurons



Neurogenesis: 2 major sites



Neurogenesis: Who & Where

- Mice
- Rats
- Birds
- Cats
- Guinea Pigs
- Tree shrews
- Marmosets
- Primates
- Humans

Definitely:

- Hippocampus
- Olfactory Bulb

Maybe:

- Amygdala
- Striatum
- Damaged tissue from stroke & TBI

Function of Neurogenesis

- Most stem cells die
- Those involved in new learning survive
- Decreased by:
  - Stress (Cortisol)
  - Depression
  - Aging
  - Alzheimer's
  -

Increased by:

Environmental enrichment

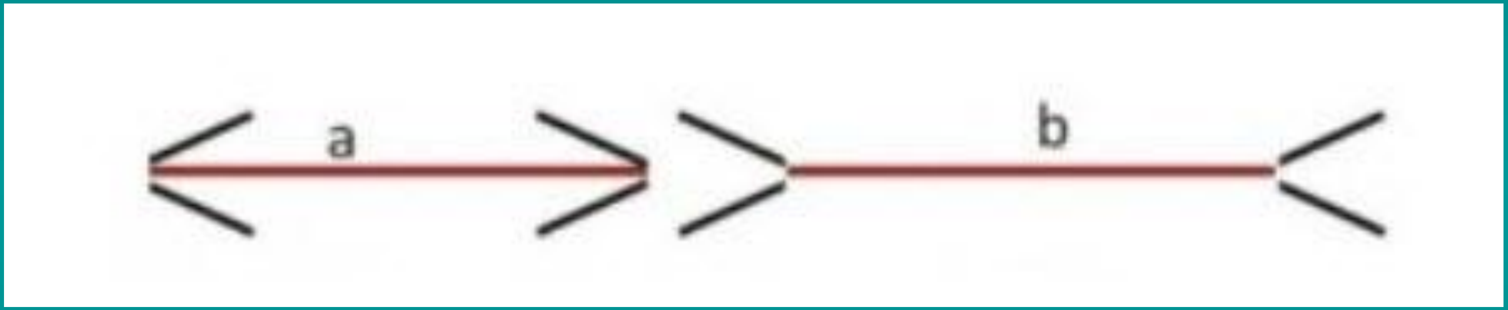
Exercise

Antidepressants

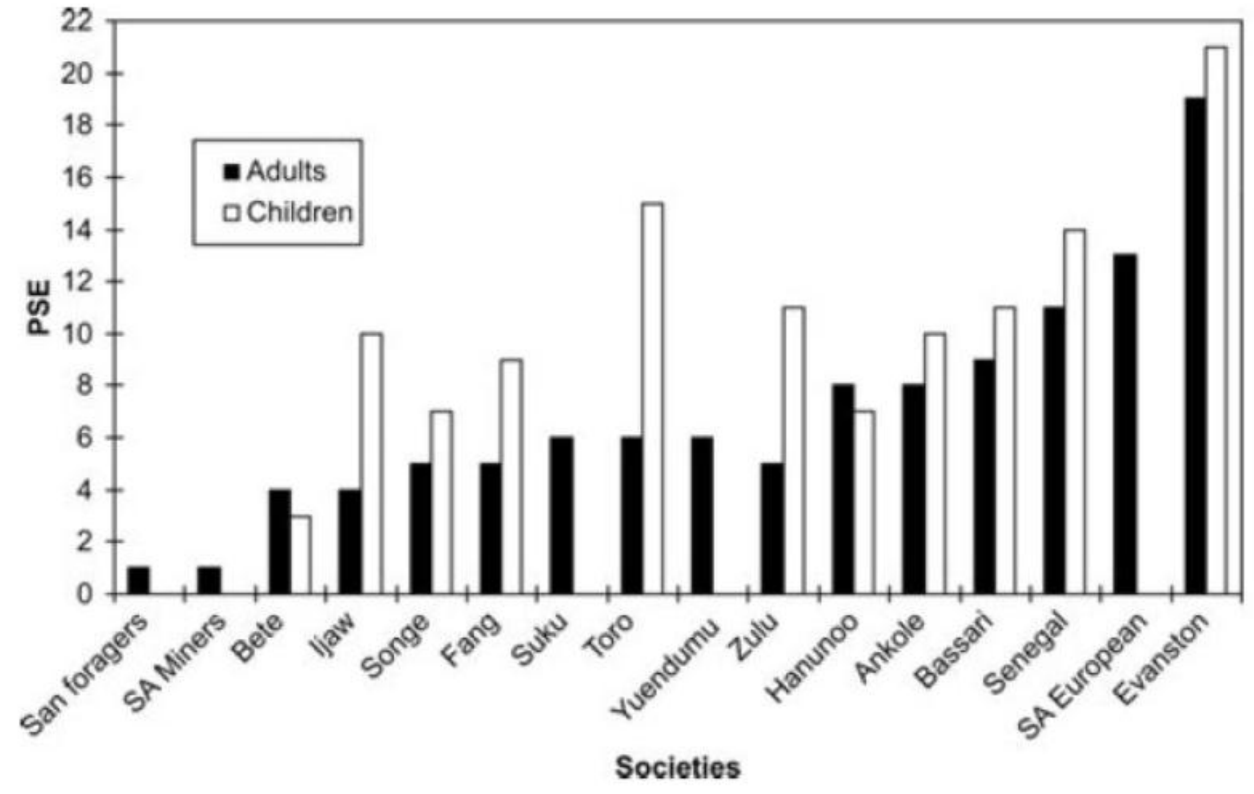
Alzheimer's

Seizures

Which is longer, a or b



Americans choose B

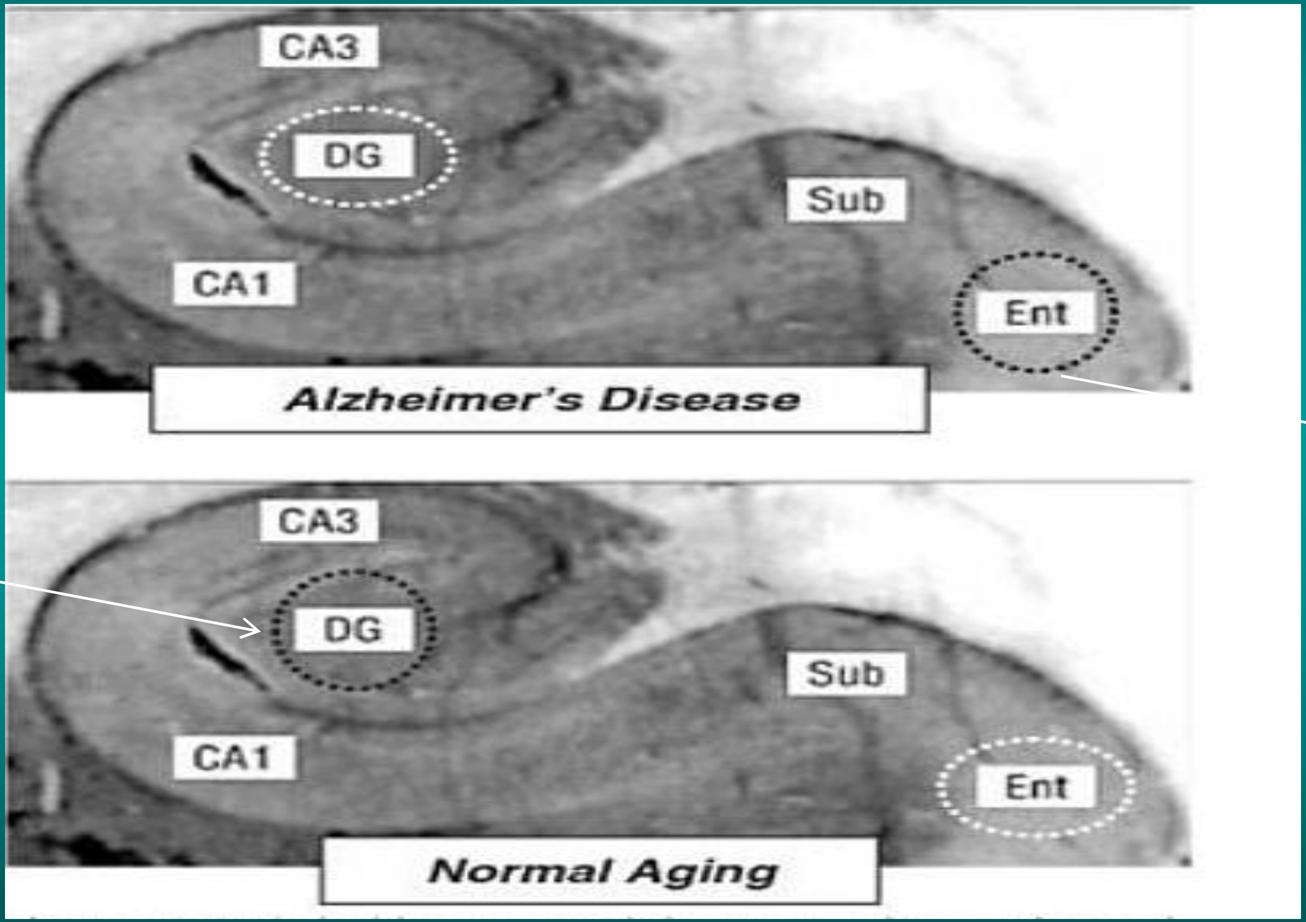


The strength of the Müller-Lyer Illusion in 16 separate societies. Reproduced from Henrich et al. (2010)

Cultural evolution due to environment: Americans most fooled by illusion; used to horizontal lines and sharp corners

Hippocampus:
Normal aging & Dentate Gyrus (high glucose↓↓)
(vs. AD and Entorhinal Gyrus)

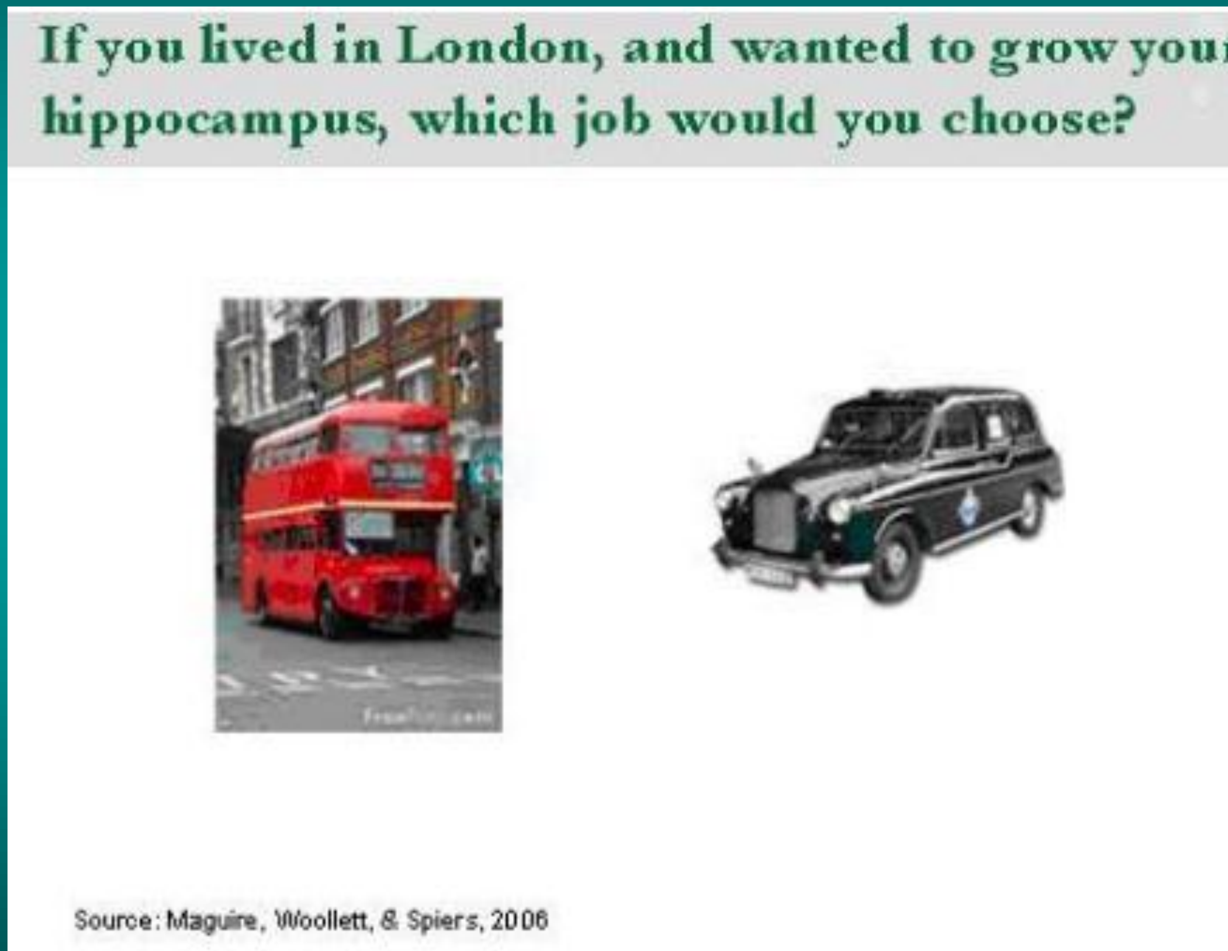
Normals



AD

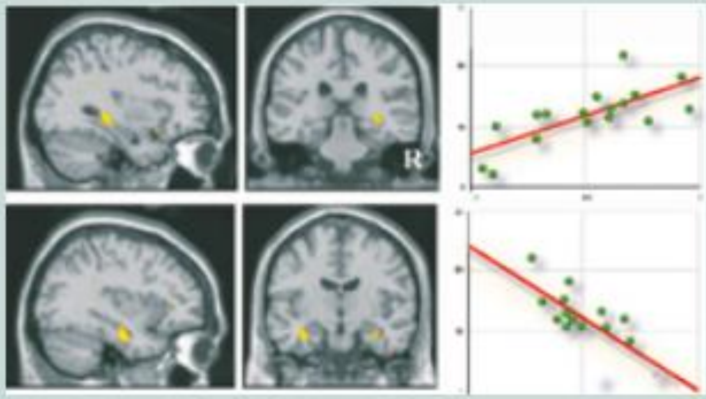
Dentate Gyrus is area of greatest neurogenesis

Role of experience in neuroplasticity.



Study of London Taxi cab drivers (vs. bus drivers)

Larger Right Hippocampus in London Taxi Drivers



Christoph Schneider, based on an original from: Maguire EA, Woollett K, Spiers HJ. 2006. London taxi drivers and bus drivers: A structural MRI and neuropsychological analysis. Hippocampus 16:1091-1101.

London taxi drivers: posterior portion of the hippocampus was larger in experienced taxi drivers than in other subjects.

Factors that affect neurogenesis

Experience

The following affect the number of newly generated neurons:

-enriched environment increases neuron number

-hippocampally mediated learning tasks increases neuron number

-exercise increases neuron number

-stress and depression inhibit new neurons reduced neuron number

Neurochemicals

-neurotrophic factors increase neuron number

-serotonin increases neuron number (antidepressants)

-estrogen increases neuron number

-glucocorticoids (stress hormones) reduce neuron number

Factors that affect neurogenesis 2

Age: lower

Genetic and epigenetic factors also play a role.

Some types of brain damage can induce neurogenesis, but it is not known if this has a beneficial effect on the brain or not.

- <u>epileptic seizures (abnormal neurogenetic cells)</u>
- <u>Schizophrenia</u>
- <u>stroke</u>

<u>Drugs</u>:

- extended exposure to antidepressant drugs (& ECT)