Functional Neuroanatomy

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Acknowledgement:

- Serge Campeau, PhD, W. Lee, PhD, Frank H. Netter, MD, Paul Malloy, PhD, Hal Blumenfeld, MD

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- All of my lectures in PDF files
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Disclosures

- I am a clinical neuropsychologist.
- I am a CAS docent; evolution group
- I am not a neuroanatomist
- I am not a neuroscientist
- I have a passionate interest in brain studies

Disclosures

- What follows is my personal compilation of what I have found interesting in the research literature
- Lots of material: Lots of research conclusions without discussing methodology
- I present a lot of conclusions: current state of hypotheses about brain functioning

Plan for classes

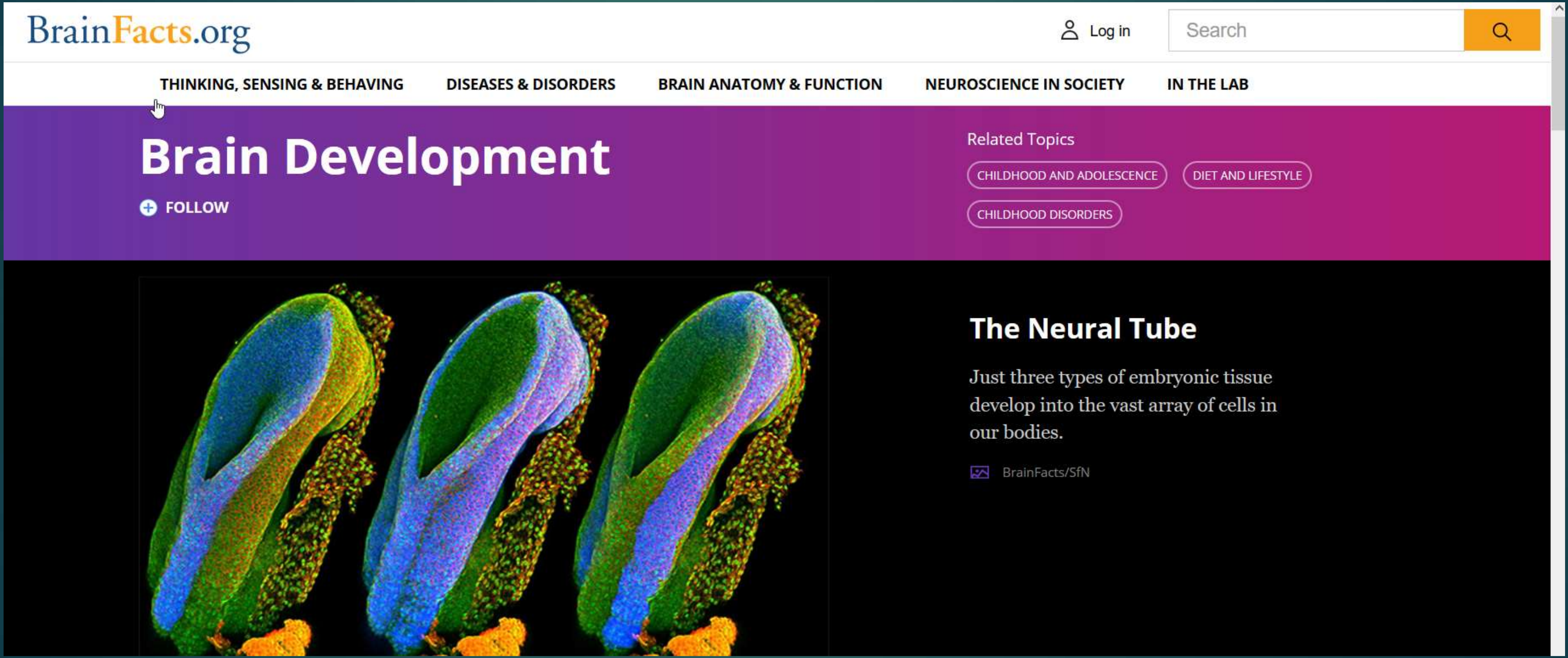
- I always have too many slides; for 1st talk, please reserve questions to end; lots of material to cover
- Entire talk is available in pdf format
- I usually make 1 or 2 comments for most slides
- Some slides that I will skip are for your later perusal: things you may want to know, but too much detail for this talk, i.e. complex neuronal pathways

Neuroanatomy Books

- * *Neuroanatomy Through Clinical Cases* by Blumenfeld
- *Neuroanatomy - Fix*
- *Neuroanatomy: An Atlas of Structures, Sections, and Systems* by Haines
- *The Human Brain: An Introduction to Its Functional Anatomy* by Nolte
- *Atlas of Morphology and Functional Anatomy of the Brain* by Scarabino, Salvolini, Salle, Duvernoy, Rabischong
- *Netter's Concise Neuroanatomy* by Rubin and Safdieh
- *Atlas of Neuroanatomy and Neurophysiology (Sections from the Netter Collection of Medical Illustrations),* text by Hansen and Koeppen, illustrations by Netter, Craig, Perkins
- *Neuroanatomy: Draw It to Know It* by Fisch
- *Atlas of the Human Brain* by Mai, Paxinos, Voss
- *Clinical Neuroanatomy* by Waxman
- *Neuroanatomy for the Neuroscientist* by Jacobson and Marcus

BrainFacts.Org

- Society for Neuroscience website

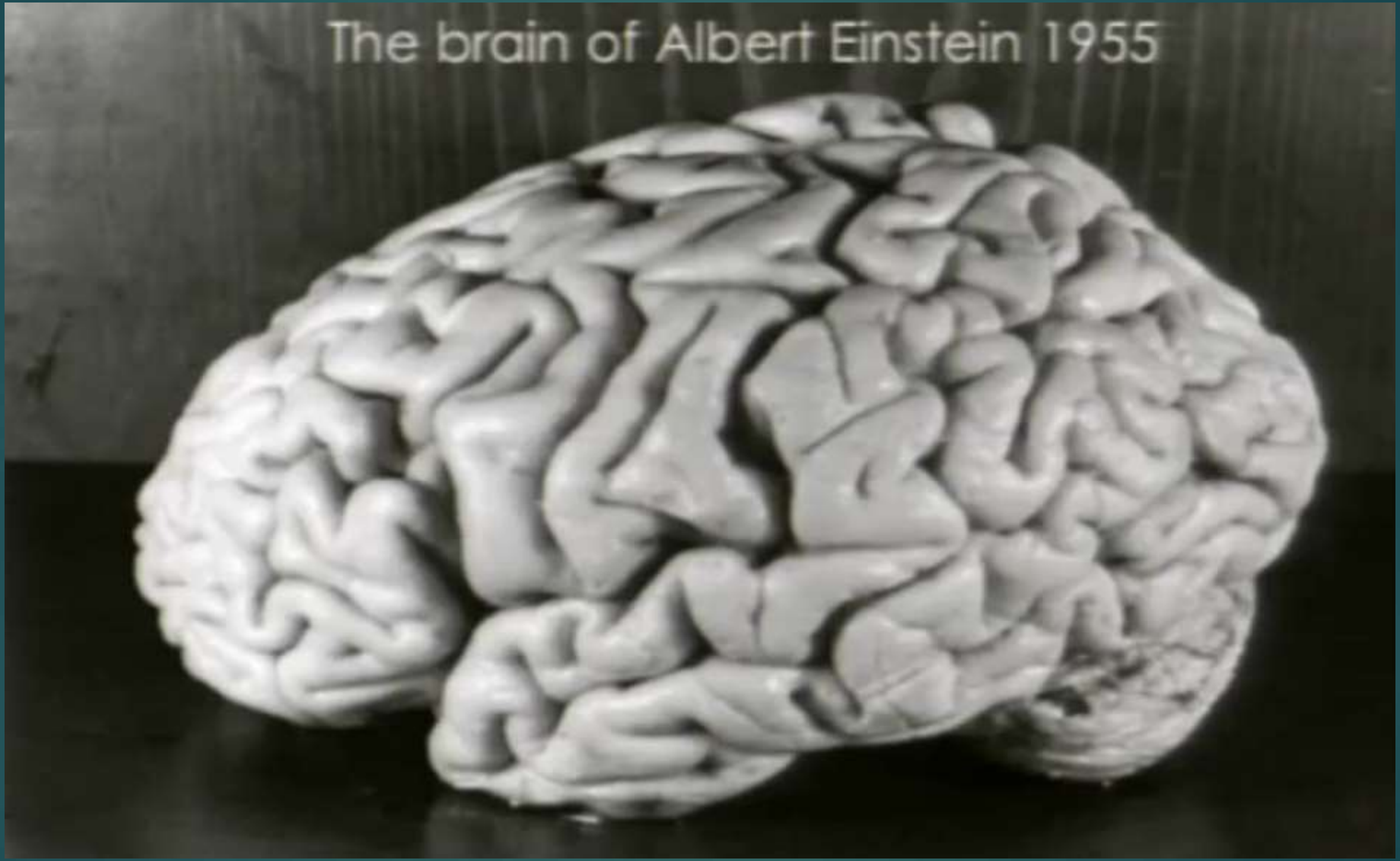


Teach me anatomy site

- http://teachmeanatomy.info/the-basics/

The Human Brain

Very good brain



Driving Mr. Albert: A Trip Across America with Einstein's Brain Paperback – 2001
by Michael Paterniti

A not so good brain:
Agyria – lack of gyri and sulci

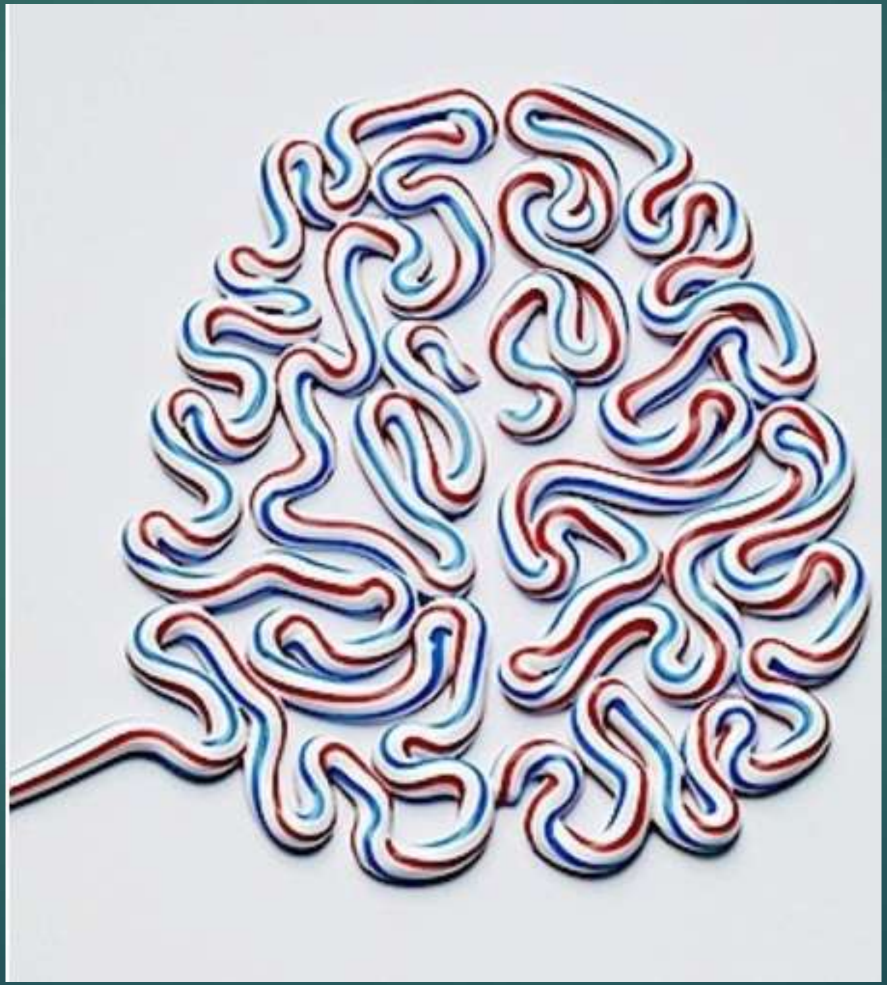
Phrenology

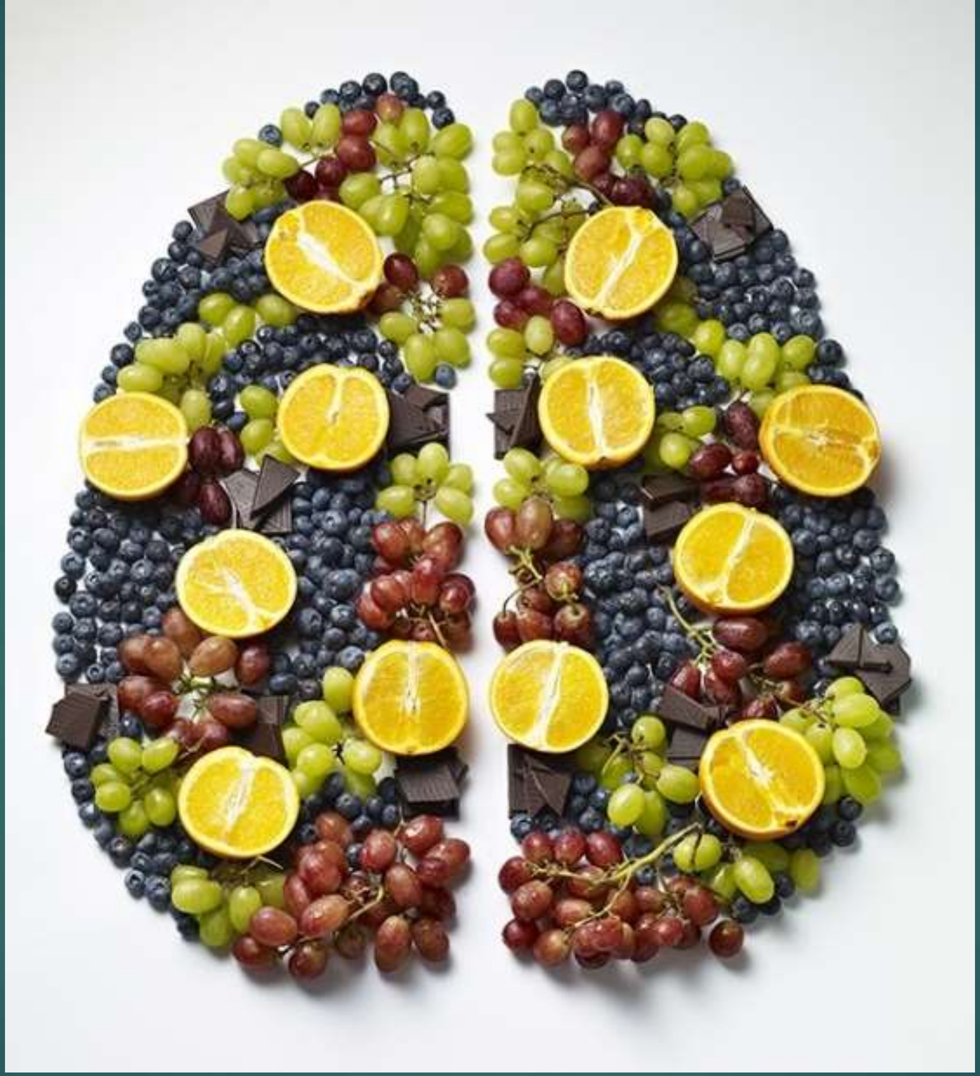
Sublimity
Cautiousness
Perfection
Refinement
Prudence
Solicitude
Timidity
Wit
Constructiveness
Acquisitiveness
Secretiveness
Repose
Contrivance
Ingenuity
Dexterity
Acquiring
Saving
Hoarding
Reserve
Policy
Evasion
Tune
Modulation
Destructiveness
Executiveness
Extermination
Courage
Combativeness
Defence
Order
Calculation
Figures
Estimates
Desire for Liquids
Alimentiveness
Desire for Solids
Mastoid Process
Vitativeness

Dance company Capacitor & photo by RJ Muna

Out of Clay

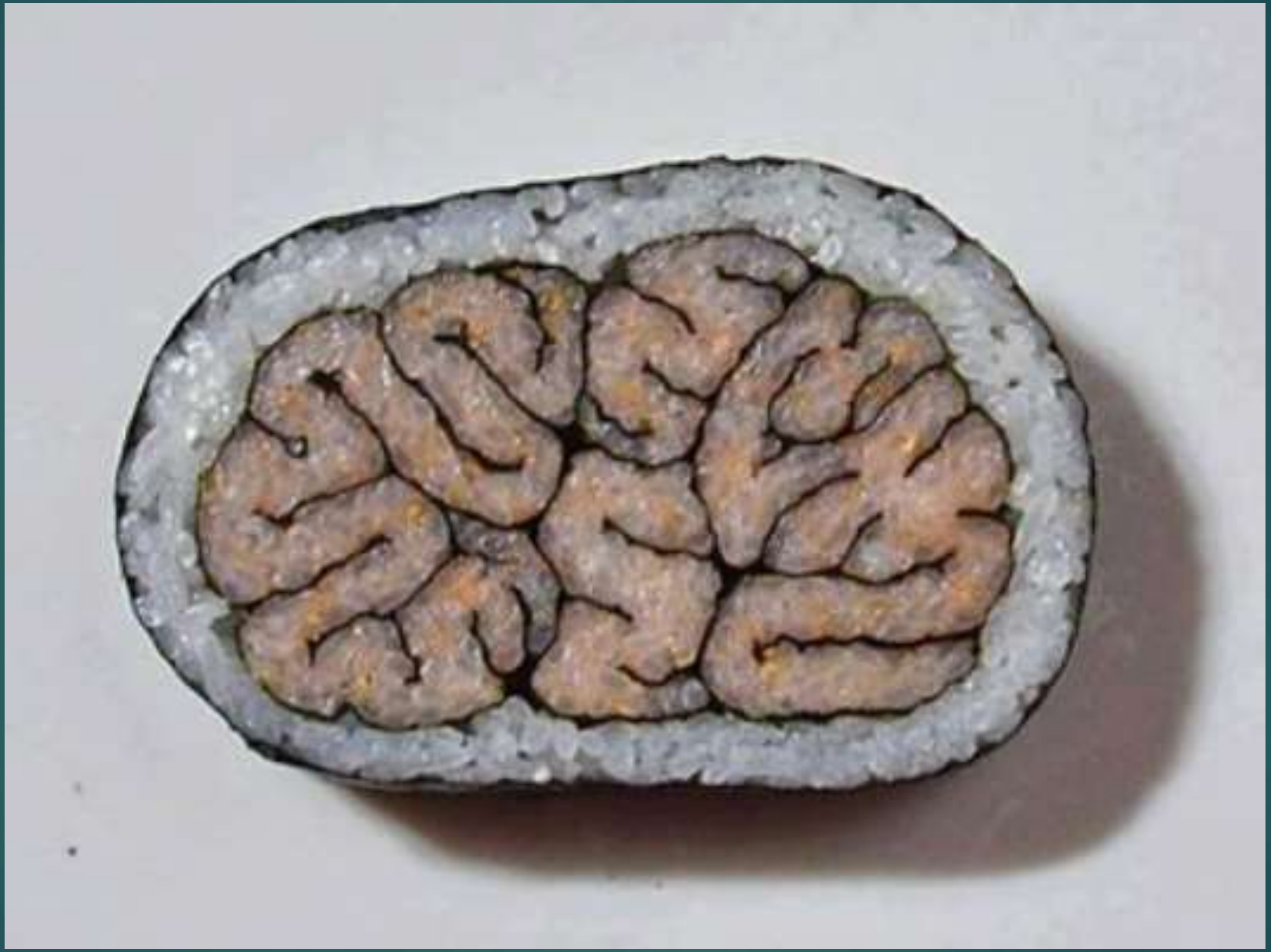
Toothpaste by Kyle Bean



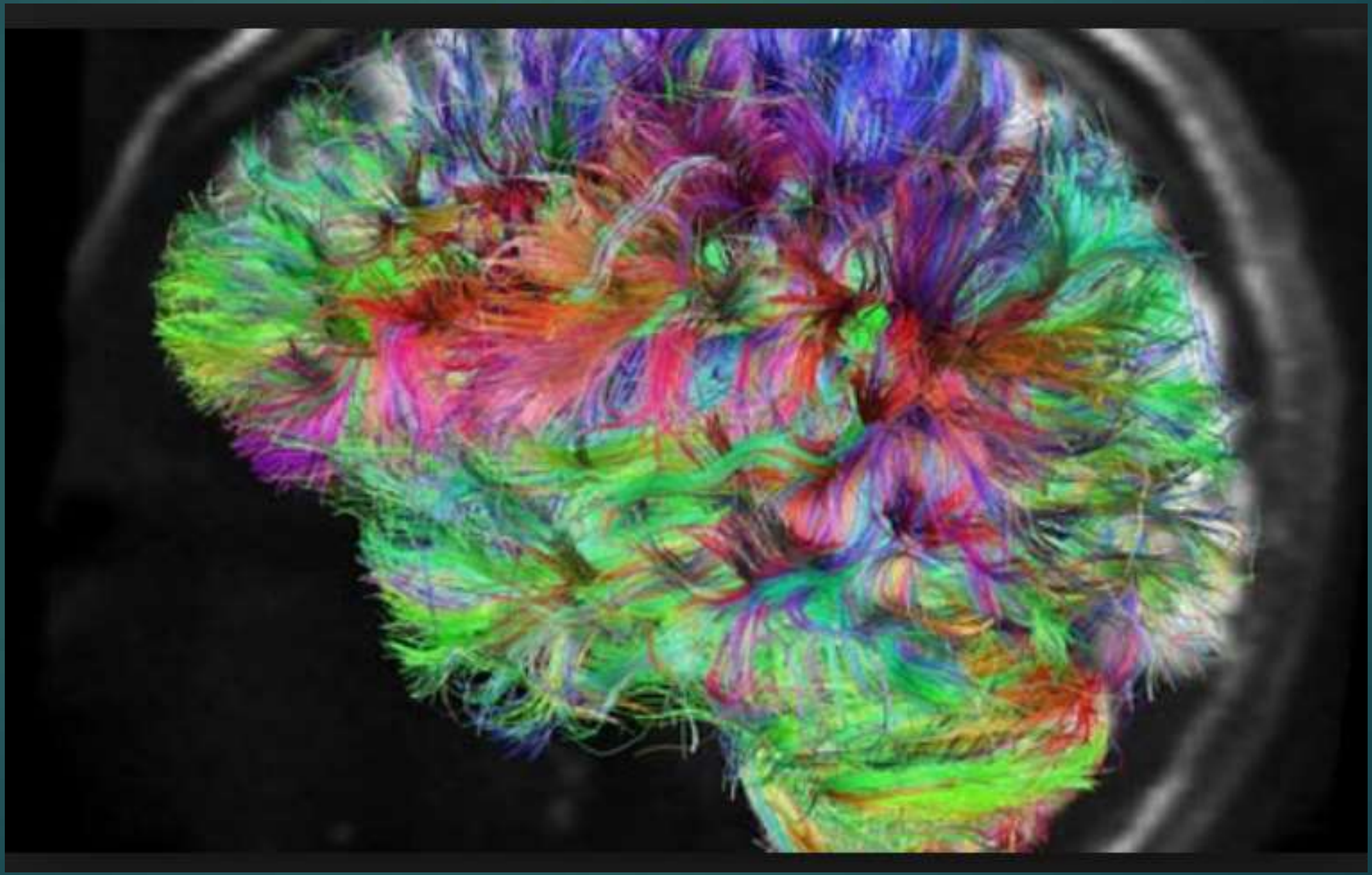


Lisa Nilsson - Quilted Paper

Sushi as Brain

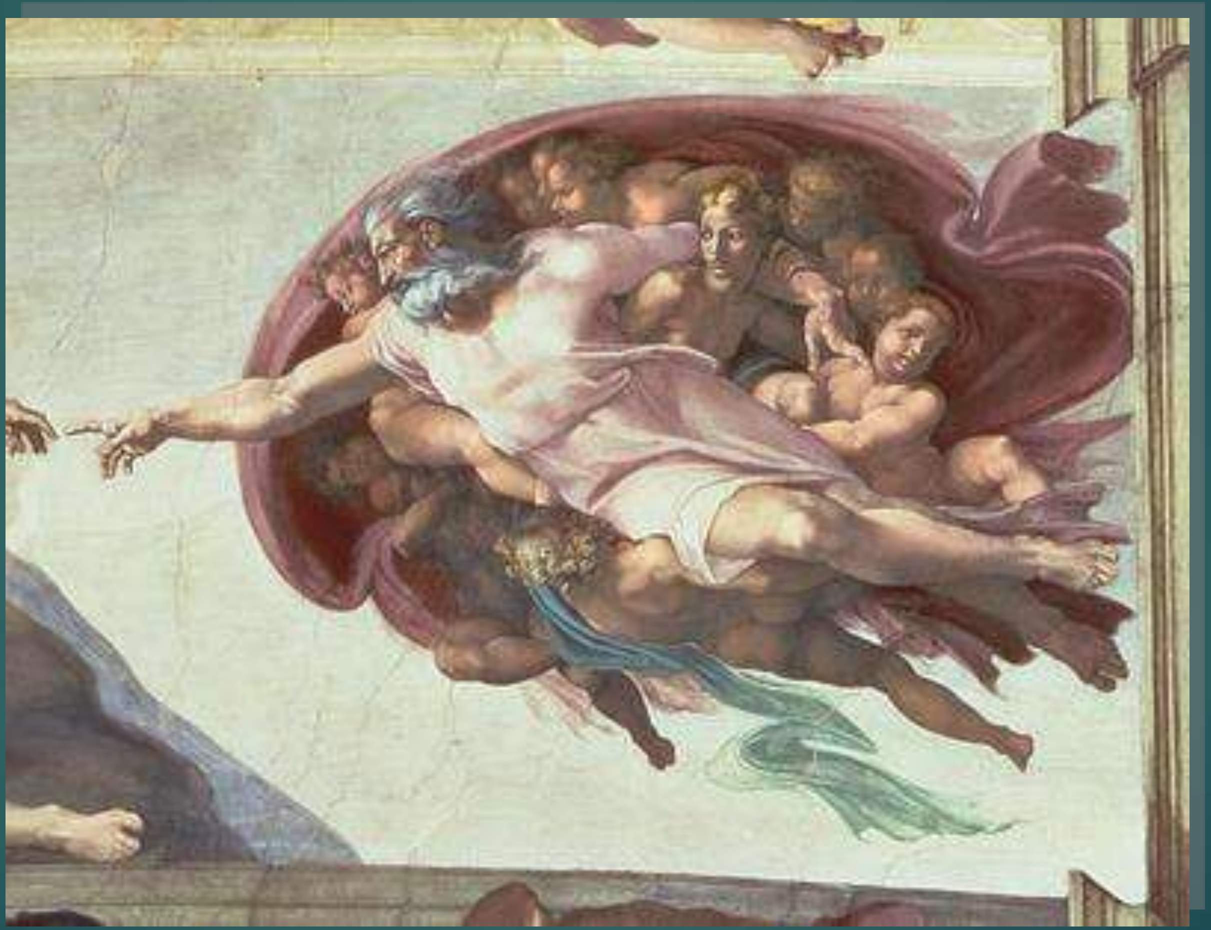


Real: Diffuse Tensor Imaging

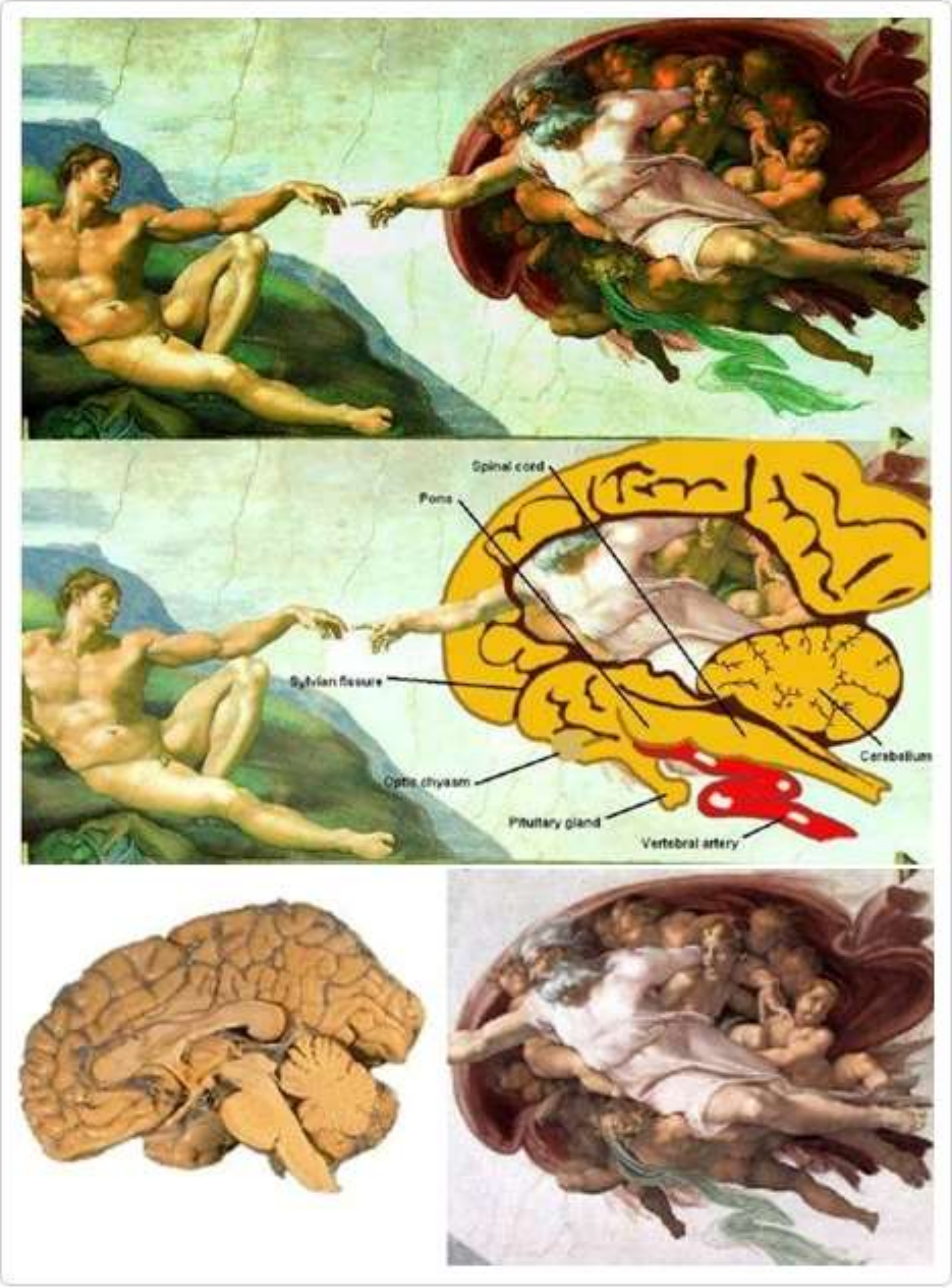


Creation of Adam, 1508: Michelangelo's Theory of creative brain?

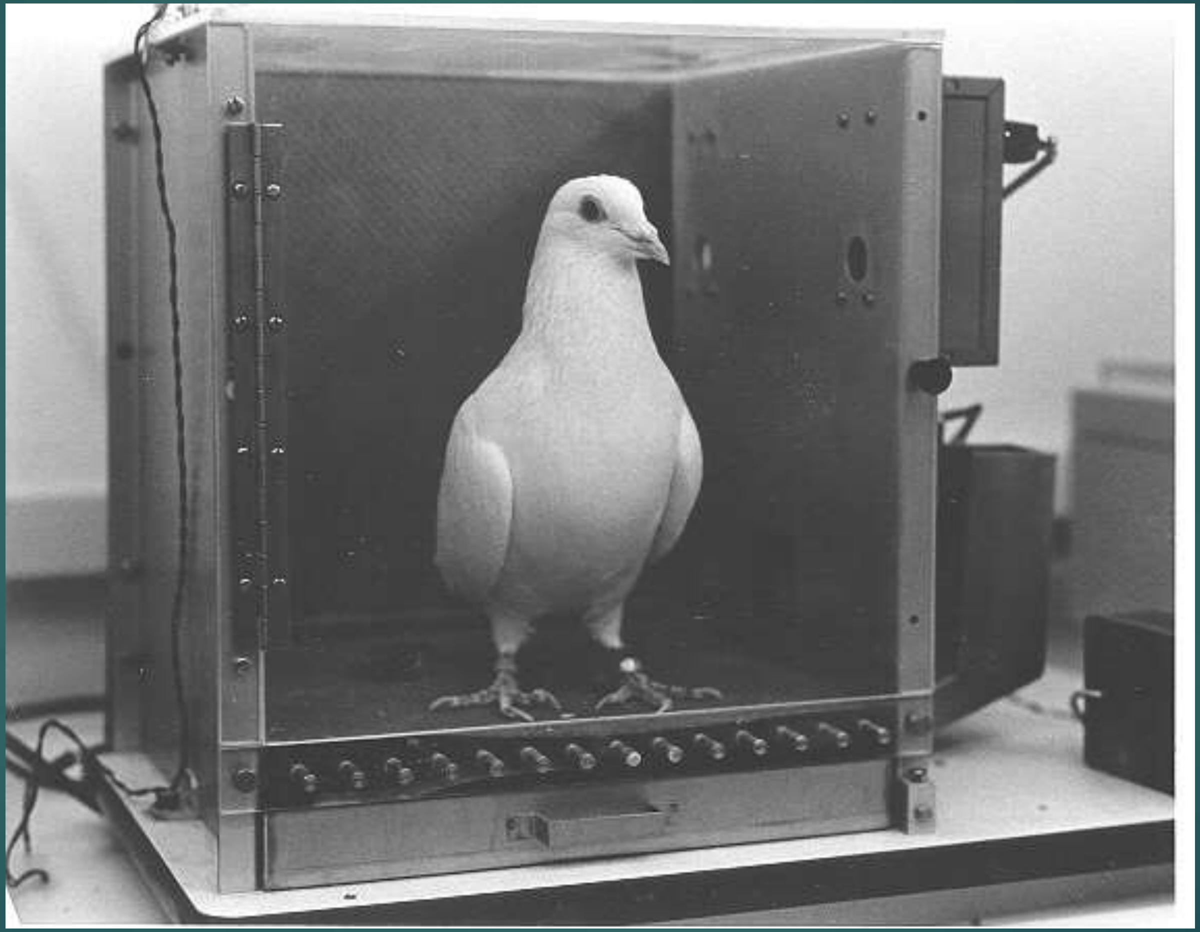
Frank Meshberger: *Mid-sagittal cross-section of a human brain.*



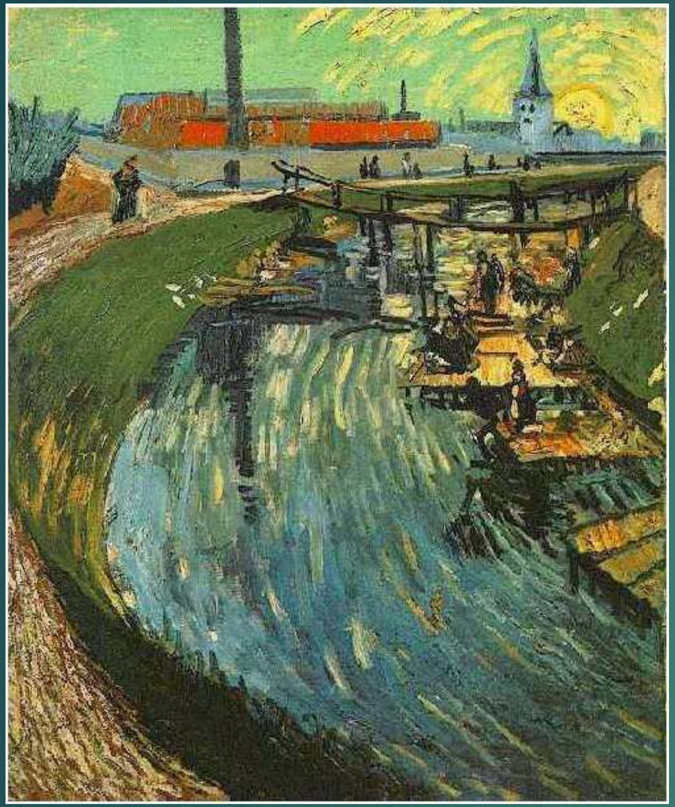
Concealed Neuroanatomy in Michelangelo's Separation of Light and Darkness in the Sistine Chapel, 2010, Ian Suk and Rafael J. Tamargo in Neurosurgery, *Vol. 66, No. 5, pp. 851-861.*


Spinal cord
Pons
Sylvian fissure
Optic chyasm
Pituitary gland
Vertebral artery
Cerebellum

Pigeons: A Cautionary Brain Tale – you can do a lot with a small brain



Watanabe, Sakamoto and Wakita, 1995

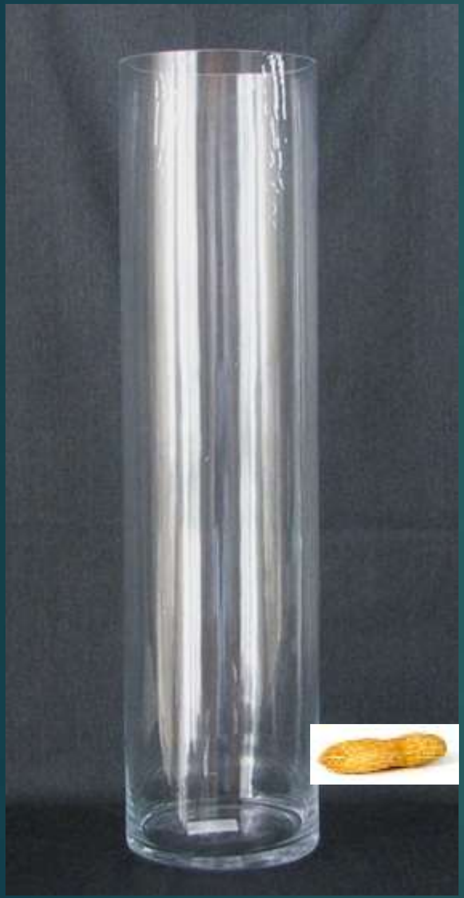


Van Gogh

Chagall

Pigeons were trained to discriminate between Van Gogh and Chagall with 95% accuracy (for those trained on specific paintings);
Discrimination still 85% successful for previously unseen paintings of the artists

Bird Brains: See Nova special Convergent Evolution of Intelligence



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

Crows can:
Problem solve

Remember where they hide food and who saw

Have theory of mine

Are socially conscious:
6 generations of crow remembered a man in a face mask who mistreated some crows 7 yrs earlier

Show social emotions (grief, sadness)

Historical metaphors for brain based on current technology

- Body's coolant system,
- a hydraulic pump for "animal fluids."
- self-winding springs or an "enchanted loom,"
- a clock,
- an electromagnet,
- a telephone switchboard,
- a hologram
- and, most recently, a biological supercomputer.

What we do not know about the human brain

- How brain generates consciousness
- How memory works
- How neurons use electrical and chemical messaging
- Roles of glial cells
- Number of glial cells (10 x number of neurons?)
- Number of neurons (until recently 100 billion?)
- Why we sleep or dream
- Biological causes of mental illnesses

Myths

- Brain is half android and half artist, with a left hemisphere dedicated to logic and analytical thinking and a right hemisphere for intuition and creativity
- We use only 10% of our brain (misquote of William James by Dale Carnegie)
- Primitive reptilian brain tucked inside your more sophisticated mammalian tissues (MacLean's triune brain).
- Karl Lashley: scoop out portions and still able to learn maze (mass action vs localization)
- Glial cells are passive garbage collectors
- Many mental abilities once regarded as uniquely human — toolmaking, problem-solving, sophisticated communication, self-awareness, theory of mind — turn out to be far more widespread among animals than previously thought.

Methods of Studying the Brain: Neuroimaging

Another cautionary tale: None of modern imaging technology (& research klg based on it) existed 40 years ago when I received my PhD in 1977 from UC Berkeley.

Advanced Neuroimaging circa 1905: Phrenology “MRI”

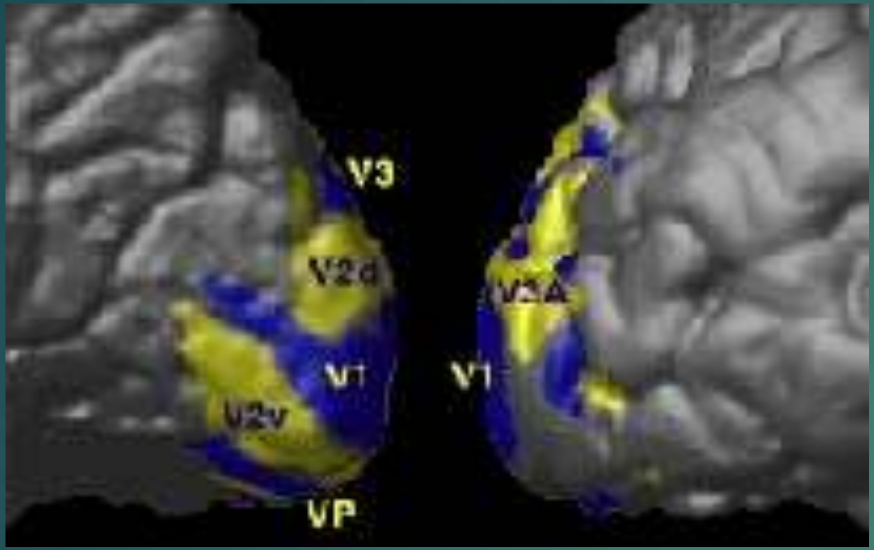
Measured head at 32 points per a five-point scale ranging from “Deficient” to “Very Superior.”
It produced a printed tape that evaluated the character of the person whose head had been poked at.

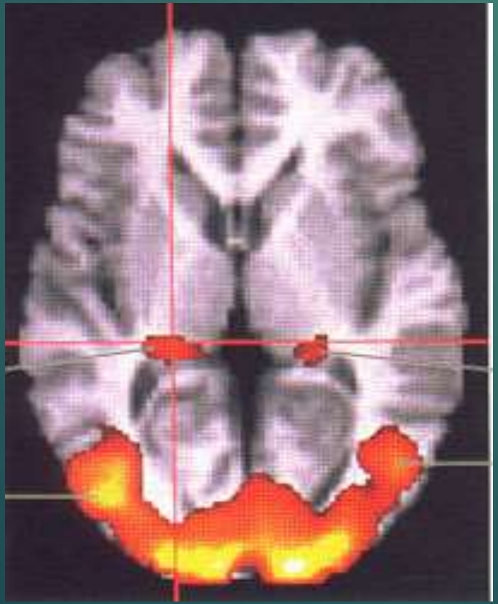
Cautionary Tale: Many “current” theories are eventually discredited

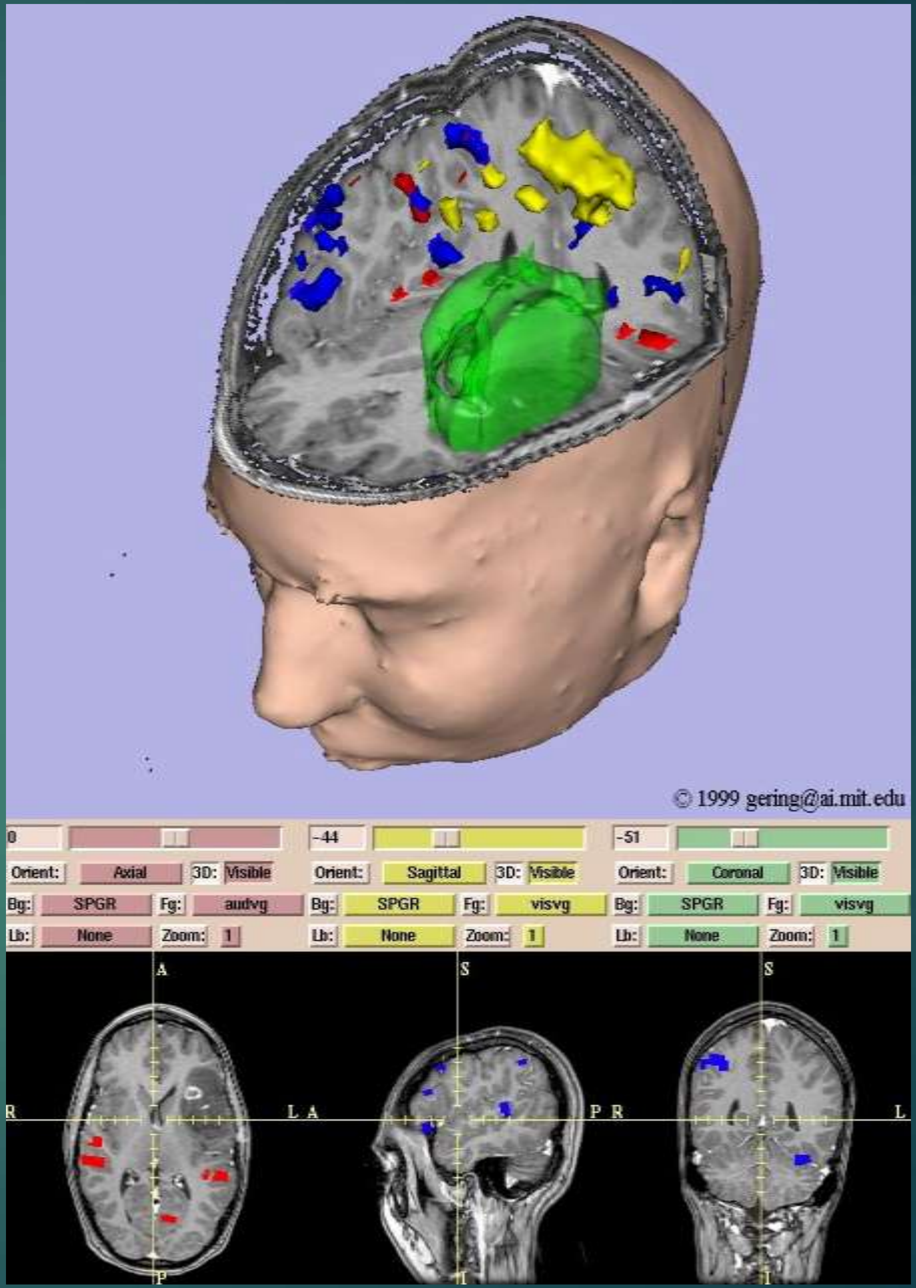
Psychoanalysis Device, 1931

A demonstration of a new “psychoanalyzing apparatus” in 1931

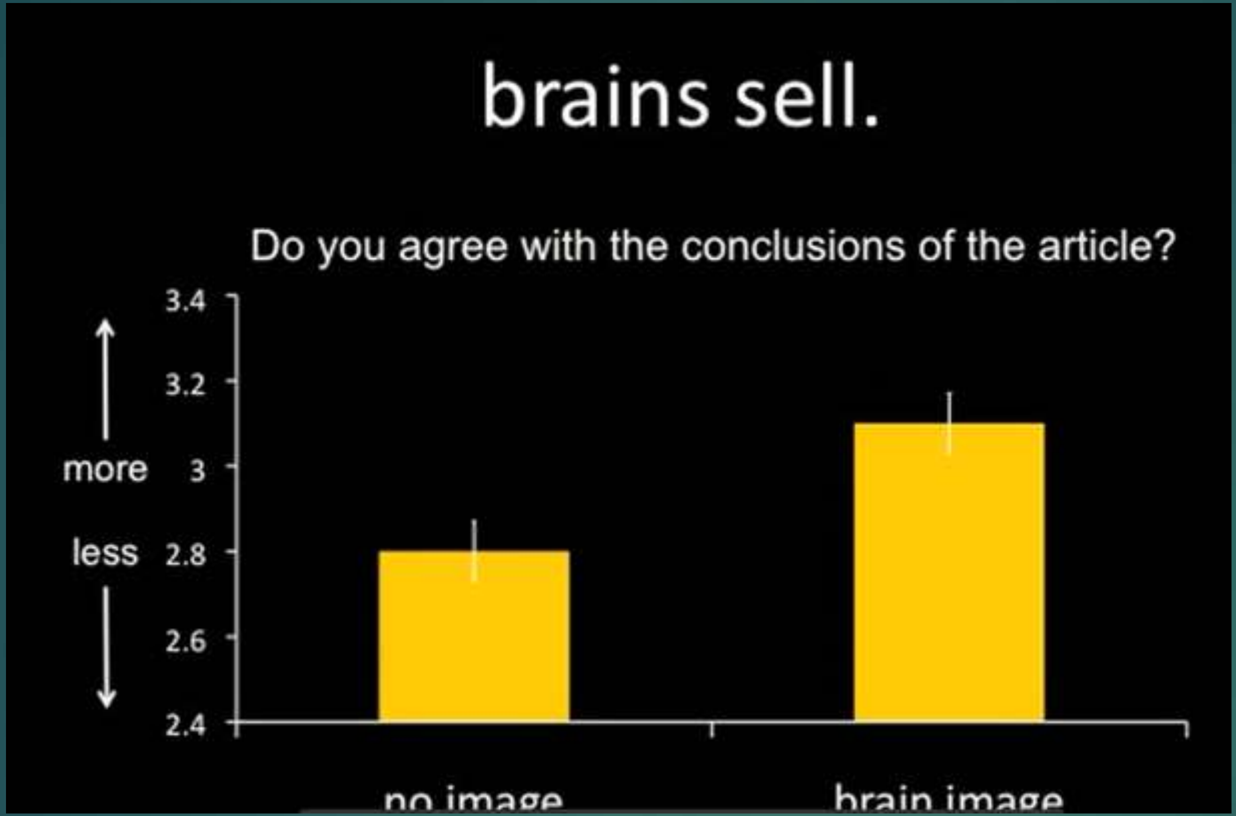
Modern Phrenology ?

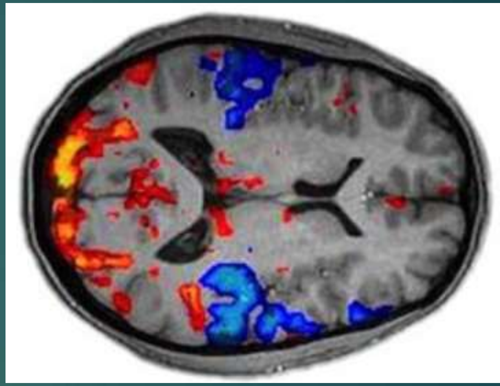






Neurobunk: brain images trigger belief





People perceive articles with images of brains that summarizing cognitive neuroscience research more scientifically credible than articles with no images or images other than brains.

McCabe, D. P., & Castel, A. D. (2008).

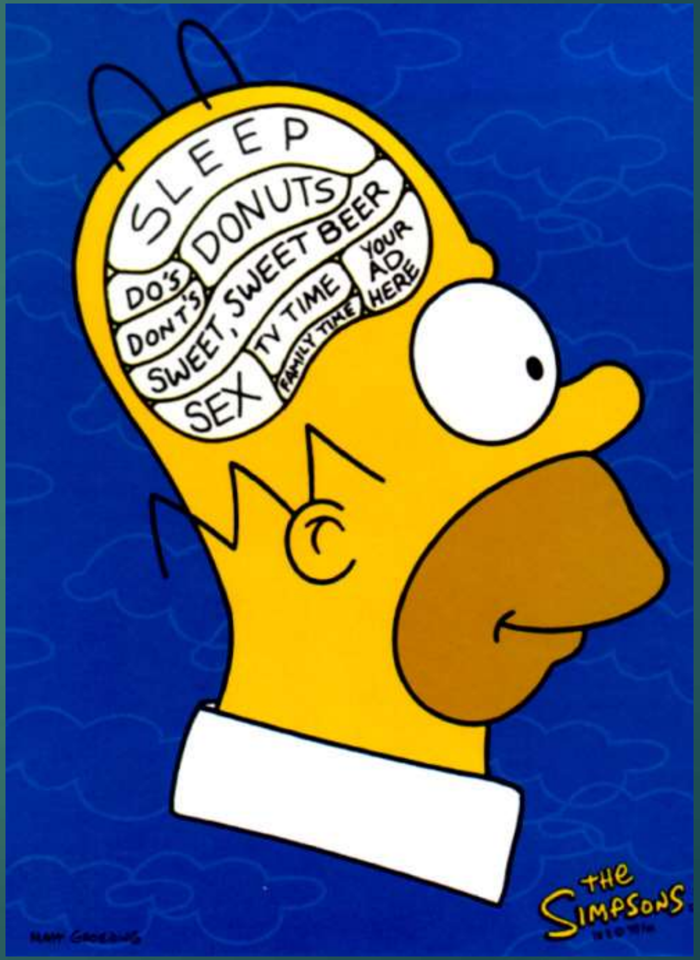
The major brain study methods

- Lesion studies
- 1960s - Single-unit neuron recording
- Neurosurgery-related methods
  - Direct cortical stimulation
  - Split-brain
  - WADA - now MRI
- Functional imaging
  - 1970s - Electromagnetic: EEG, MEG
  - Hemodynamic: PET, fMRI
- Transcranial magnetic stimulation (TMS- 1 tesla jolt)
- Optogenetics (turn on a neuron using light)

MRI vs. fMRI

MRI studies brain anatomy.

FMRI studies brain function.



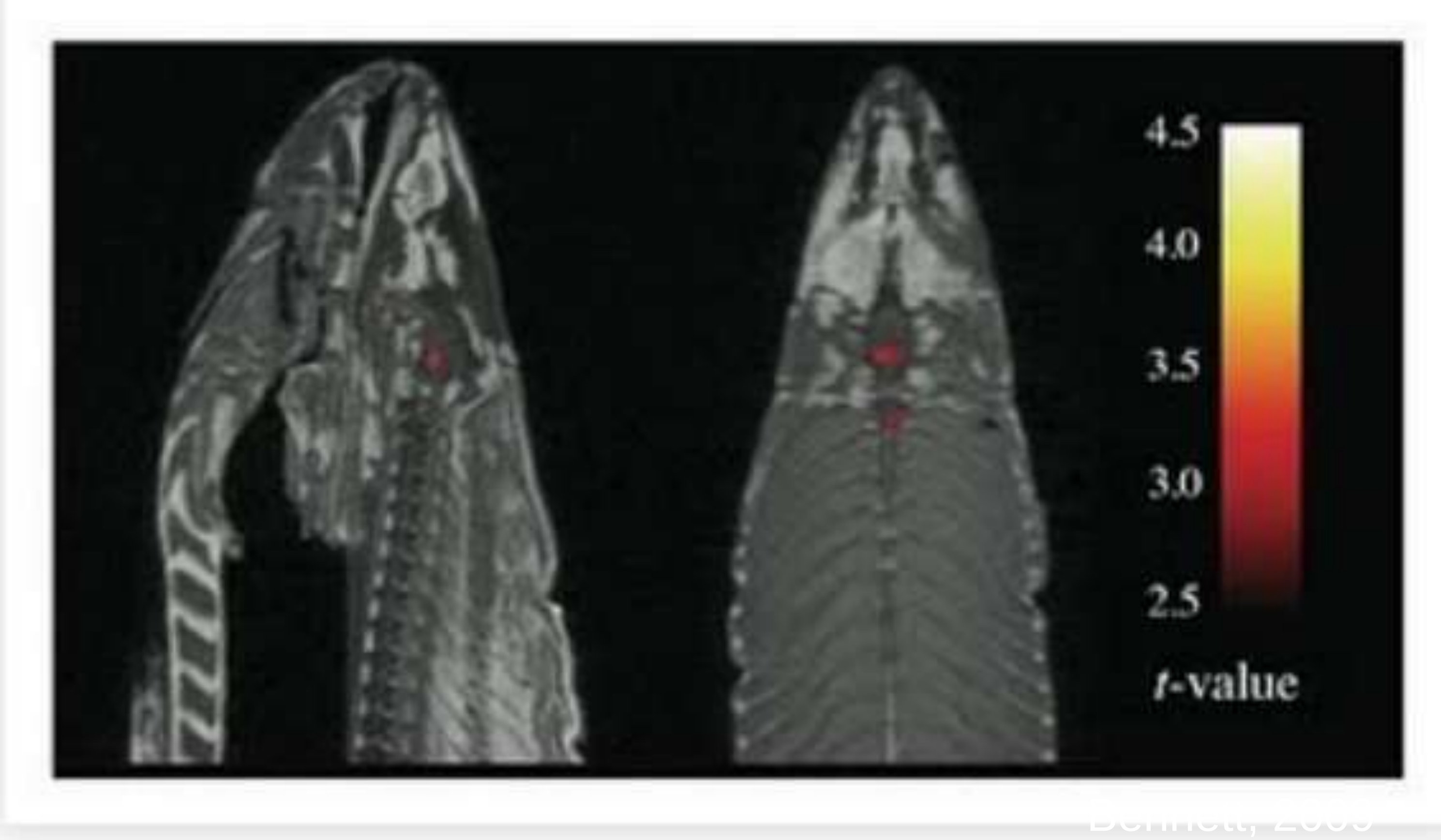
Source: Jody Culham's fMRI for Dummies web site

Brain Imaging

Structural	Functional
	Direct measures of neural activity:
CT - Computed tomography	EEG - Electroencephalography
MRI - Magnetic resonance imaging	MEG - Magnetoencephalography
VBM - Vox-based morphometry	
DTI - Diffuse Tensor Imaging	Indirect measures of neural activity:
Hybrid modalities:	PET - Positron-emission-tomography
PET-CT	SPECT - Single Photon emission computed tomography
MRI-PET	fMRI - Functional magnetic resonance imaging
fMRI-EEG/MEG	NIRS - Near infrared spectroscopy
PET-SPECT	
CT-SPECT	

Cautionary Tale: Post-Mortem Atlantic Salmon: false positives in MRI phantom data

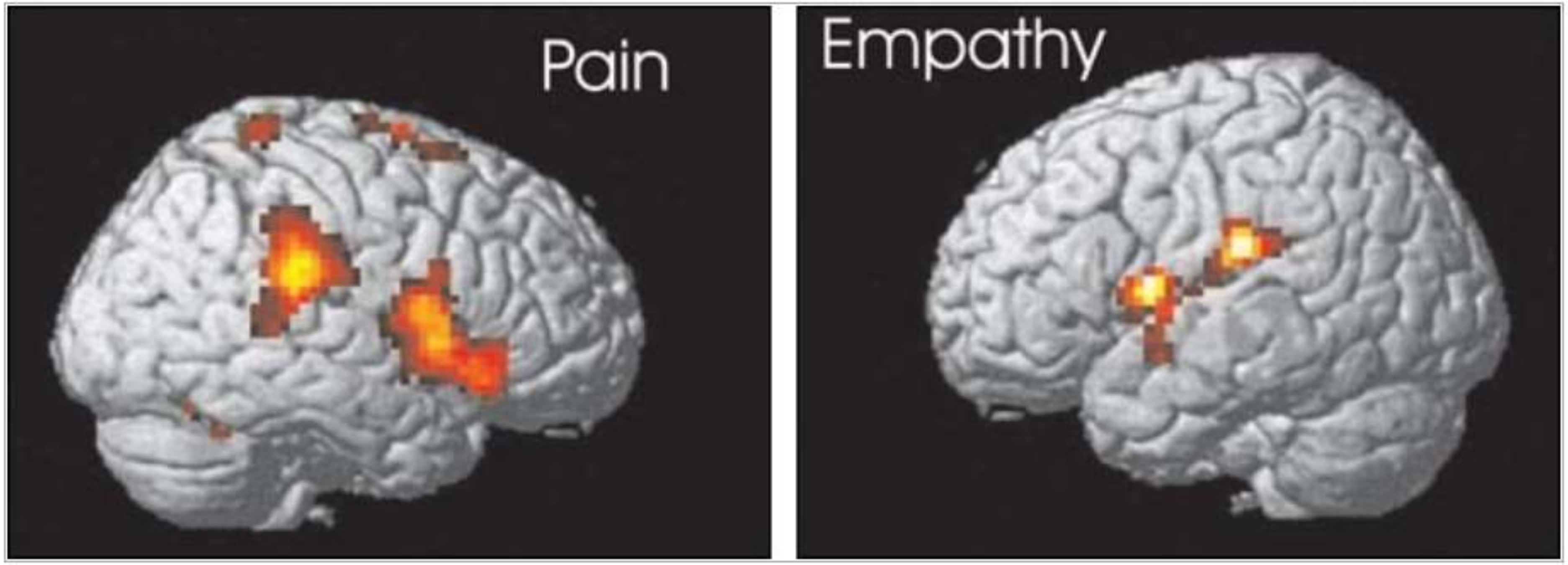
Neural correlates of interspecies perspective taking in the post-mortem Atlantic Salmon: An argument for multiple comparisons correction



Bennett, 2009

This is a lesson in statistics, not in fMRI. Which is why this was never published in a peer-reviewed journal. It is a lesson about how probability indicates that you certainly can get activation in a dead salmon by chance, and that if you only have one salmon and no corrected threshold in 2 million samples, you will get about 100000 false positives.

Example of fMRI image of location of pain and empathy areas in the human brain



Tania Singer / University College London

Functional brain imaging shows that some of the same regions of the brain are activated by personal pain, at left, and by empathy over the pain of a loved one, at right. But other areas are not activated by empathy.

Pain area lights up for: pain that is physical, social, or existential – take Tylenol for all

Images are hemodynamic & statistical creations

- fMRI is a technique that measures changes in levels of oxygen in the blood flowing inside the neuron.
  - Signals that the scanner receives are noisy because of the subject's respiration and heartbeat.
  - Anatomical and physical details can also vary greatly from person to person.
  - Imaging studies usually statistically average their results from the scans of many people to uncover meaningful information about how brains work.

Caution about fMRI results

- Pretty Images are statistically derived; colors are imaginary

- Neuroimaging reveals only correlations between image & function.

- Little evidence of a direct causal relationship

- Brain imaging can't tell you if the region is necessary for anything.

- You cannot test causality of an area without disrupting it. Area's necessity for a function can only be established through the use of disruption techniques (TMS, lesion studies).

Caution

- fMRI measure hemodynamics, not exact neuronal activity
- *Voxel equals* 1 cubic mm in size = 1 million neurons
- Best DTI of 1 fiber bundle = 200T axons
- Studies often tend to be underpowered (n=15-20): fMRI analysis detects only a small minority of true effects while producing a high rate of false positives.
- Replication always needed!!

2015 study of statistical errors fMRI studies:

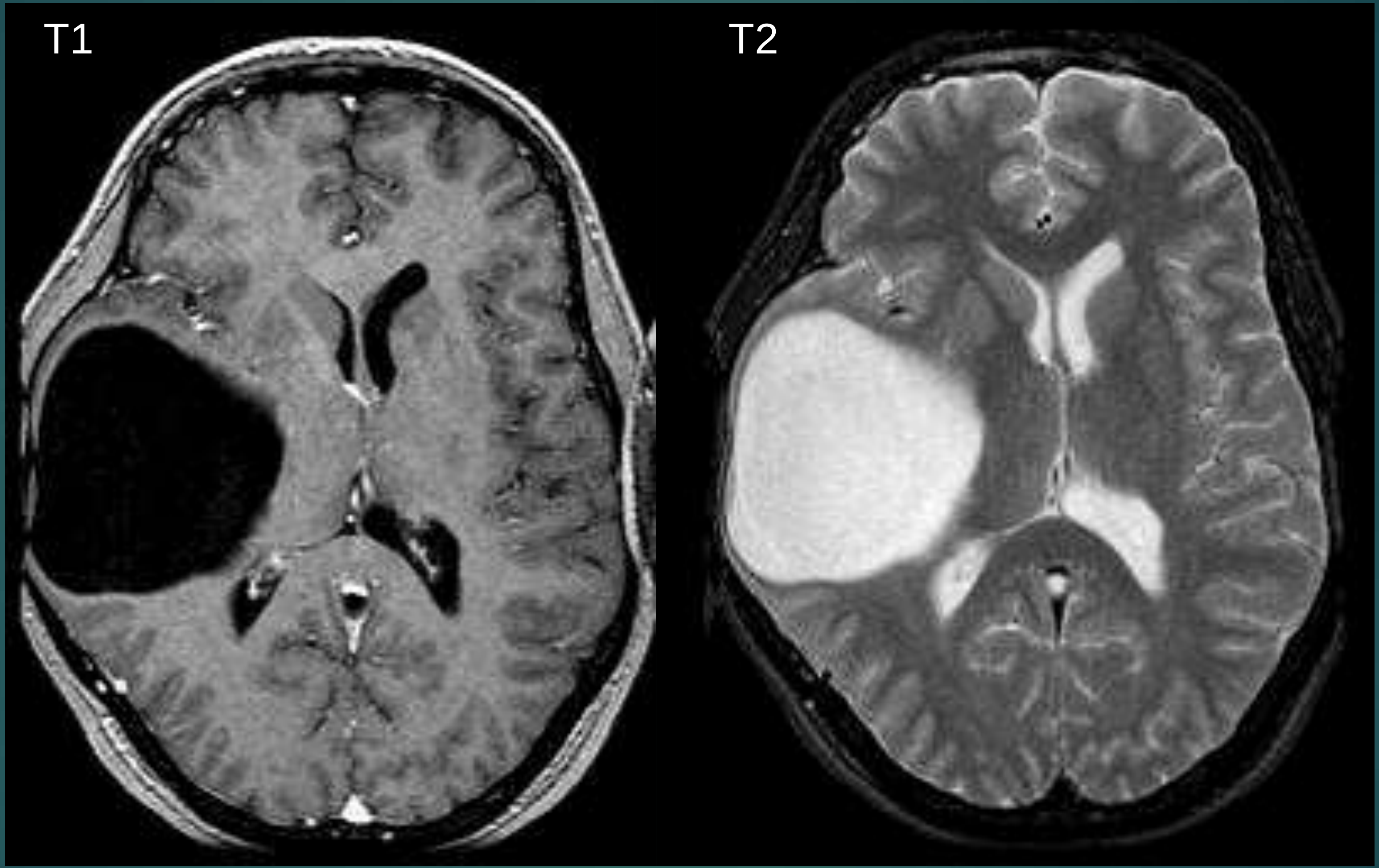
- Parametric statistical methods used for group fMRI analysis can produce p-values that are erroneous, being spuriously low and inflating statistical significance.

- This calls into question the validity of countless published fMRI studies based on parametric cluster-wise inference.

- 40% of a sample of 241 recent fMRI papers did not report correcting for multiple comparisons, meaning that many group results in the fMRI literature suffer even worse false positive rates

Anders Eklun, et al., 2015

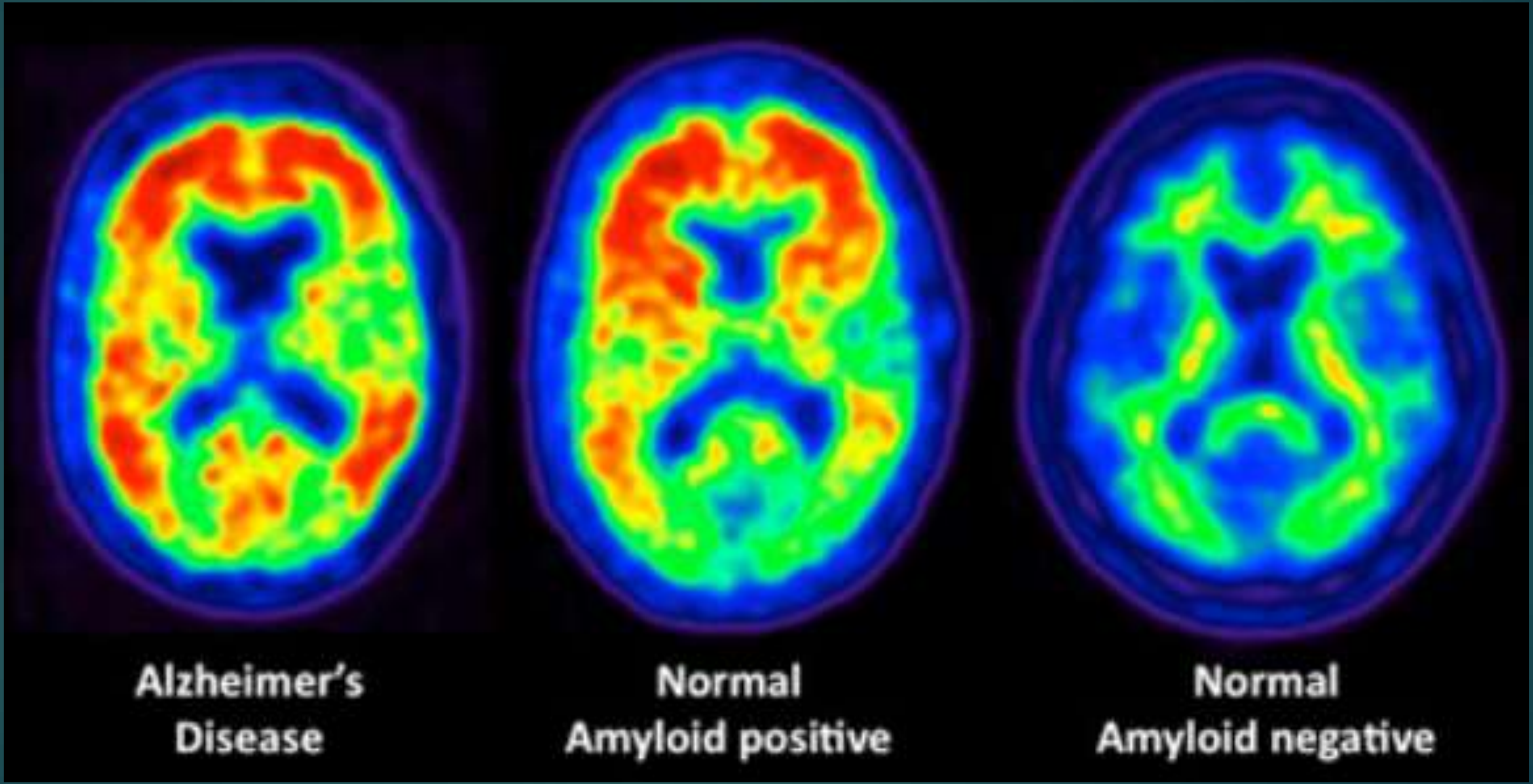
Magnetic Resonance



Arachnoid Cyst: water is bright on T2

MRI film

PET: beta amyloid binding – Alzheimer’s?



New Couples fMRI Machine:
Brain areas sync when we interact

Friends: basal ganglia
Lovers: pCC

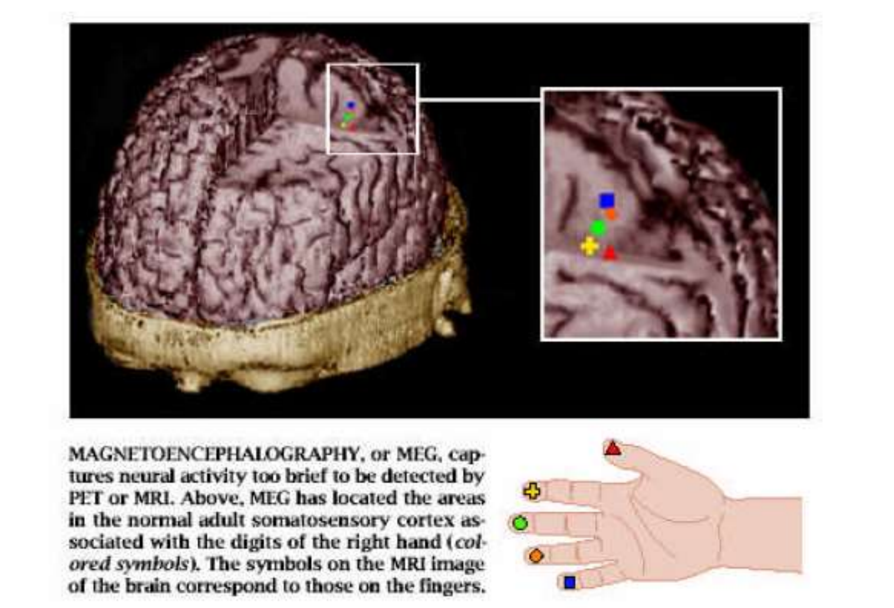
When touched:
toucher's motor and somatosensory cortex couples to the other person's STS and somatosensory cortex.

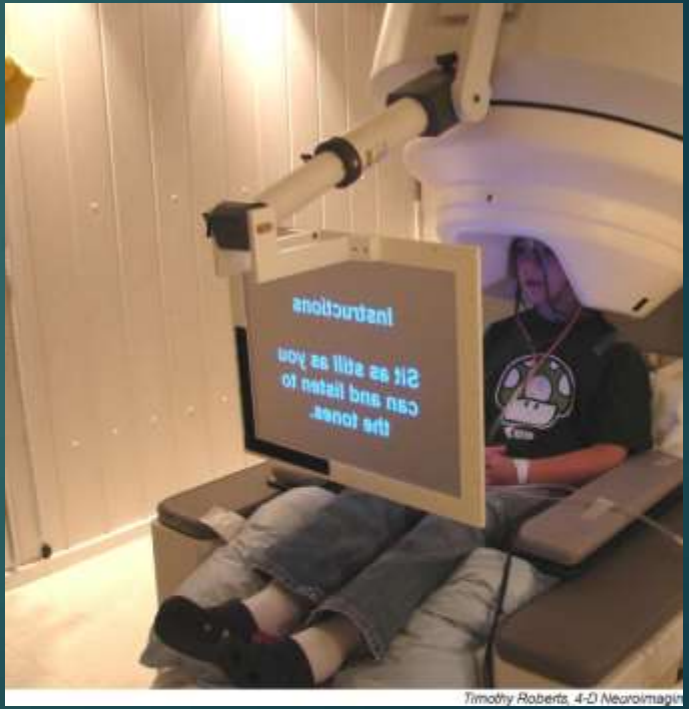
When people communicate: activates mPFC, TPJ, ACC

Ray Lee at Princeton University

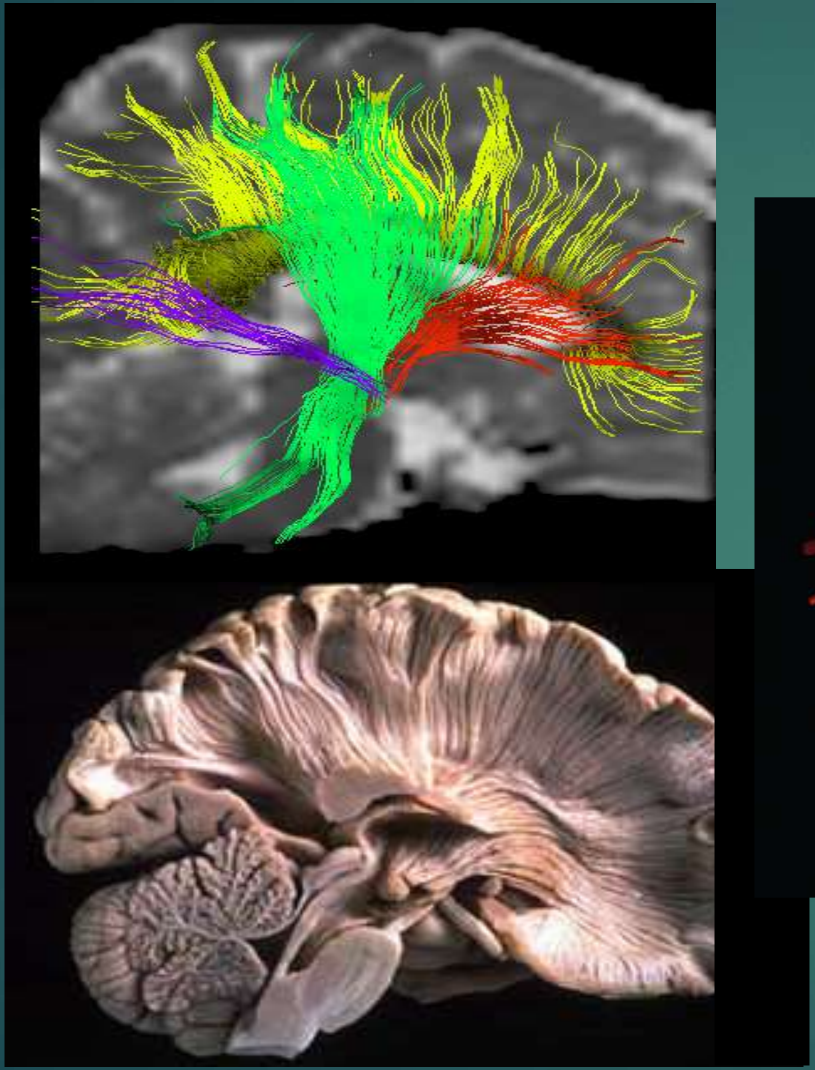
MEG: Magnetoencephalography: “Hairdresser from Mars”

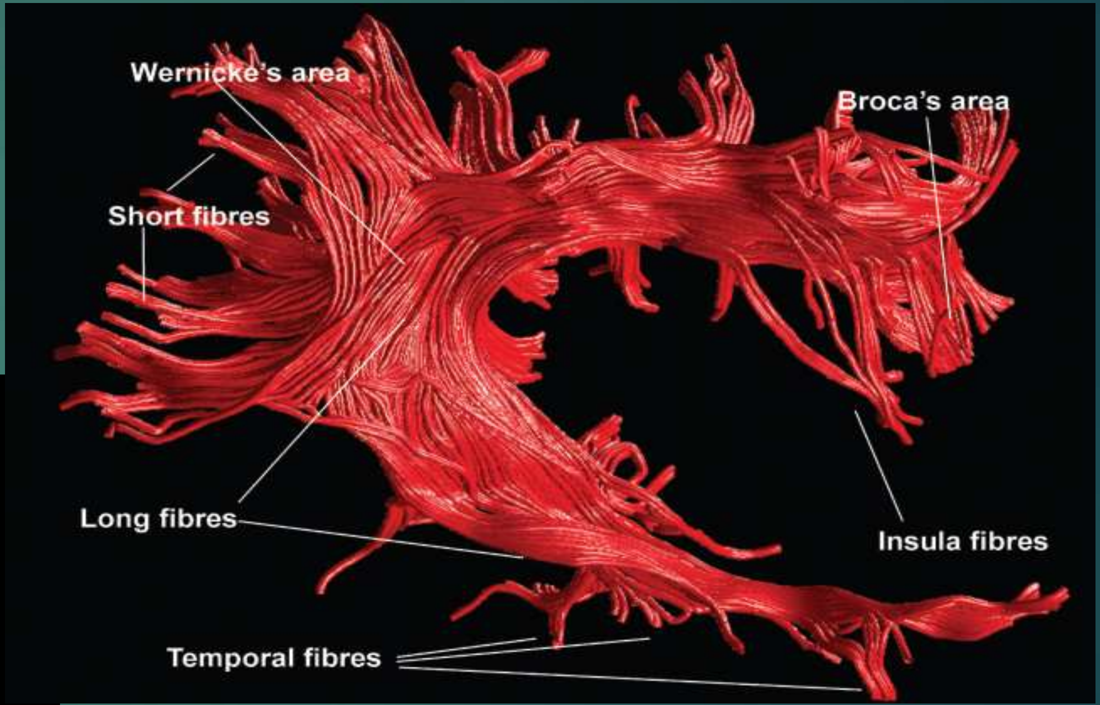
Temporospatial resolution of MEG surpasses that of all other neuroimaging techniques, in real time; direct measure of neuronal activity; magnetic equivalent of EEG.





Diffuse Tensor Imaging – Tractography of axons



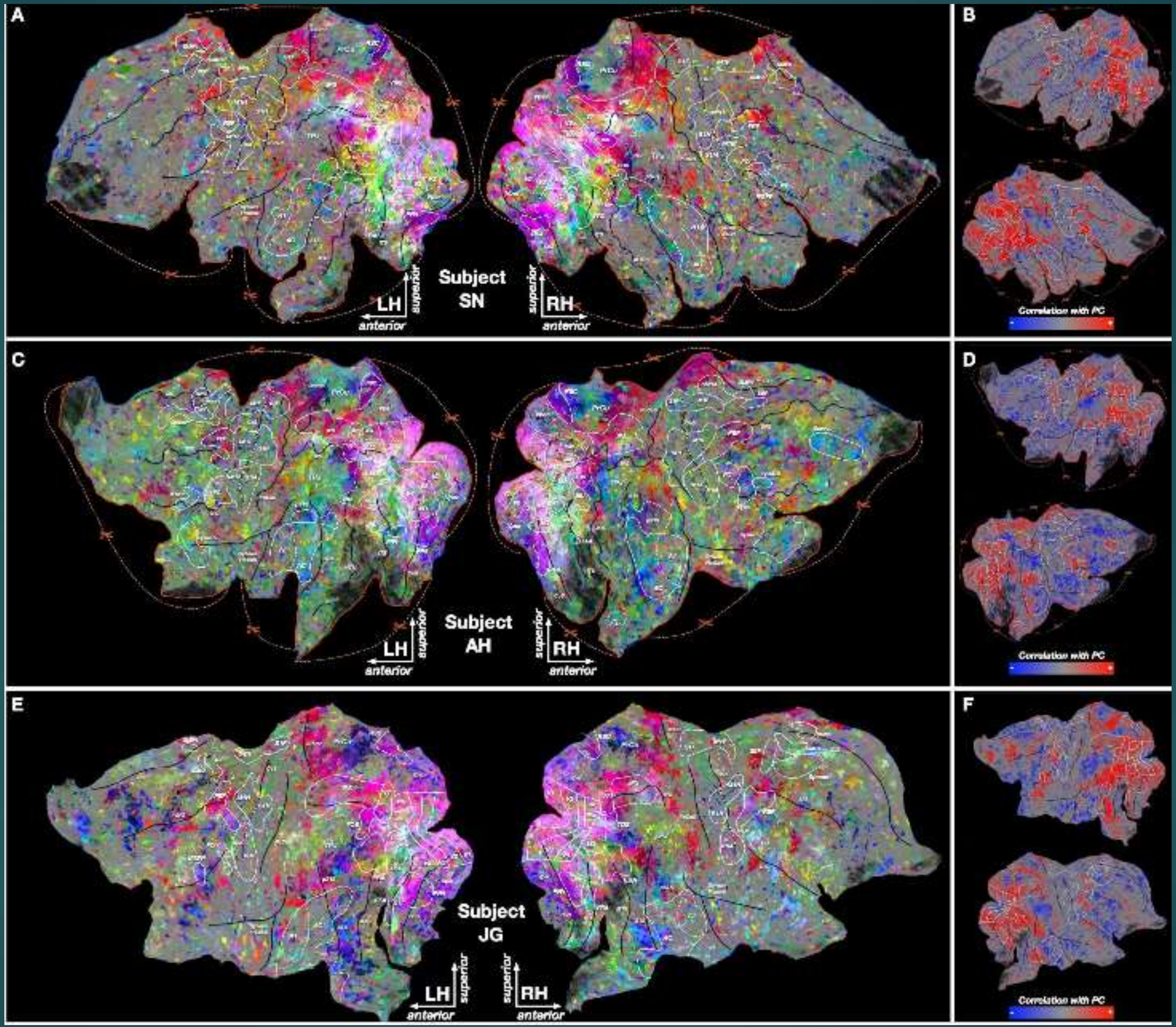


D. Jones – U Nottingham, UK

S. Mori - JHU

Decoding Brains

- J. L. Gallant, UCB (http://gallantlab.org/): Predictive models of brain activity are the gold standard of computational neuroscience
- Using EEG, fMRI for voxel analysis & statistical analysis: how each element of the visual system encodes information
- Models can be inverted in order to *decode* brain activity, providing a direct way to do "brain reading", and to build brain-machine interfaces (BMI) and neural prosthetics.
- Lab has been able to make videos of what people see, what people are semantically thinking about



Cortical maps of semantic representation

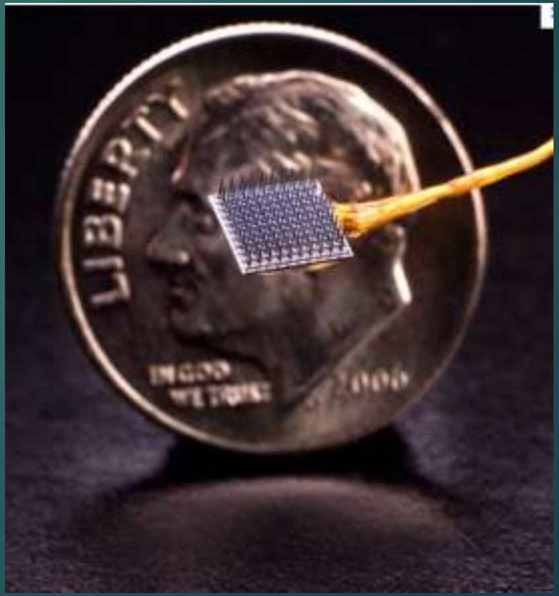
Physics in the brain

- Thinking about physics prompts common brain-activation patterns (rhythm processing and sentence structure processing)
- Study: 30 physics concepts in fMRI - machine learning could identify which of 2 types of physics concepts individual was thinking
- All participants used same brain areas for same concepts; same brain regions repurposed for specific types of concepts
- Brain responses for scientific concepts of “frequency” or “wavelength” occurred in regions that active “periodicity” region which handles watching dancers, music listening, hearing rhythmic patterns
- Brain responses for mathematical equations trigger areas that process sentences

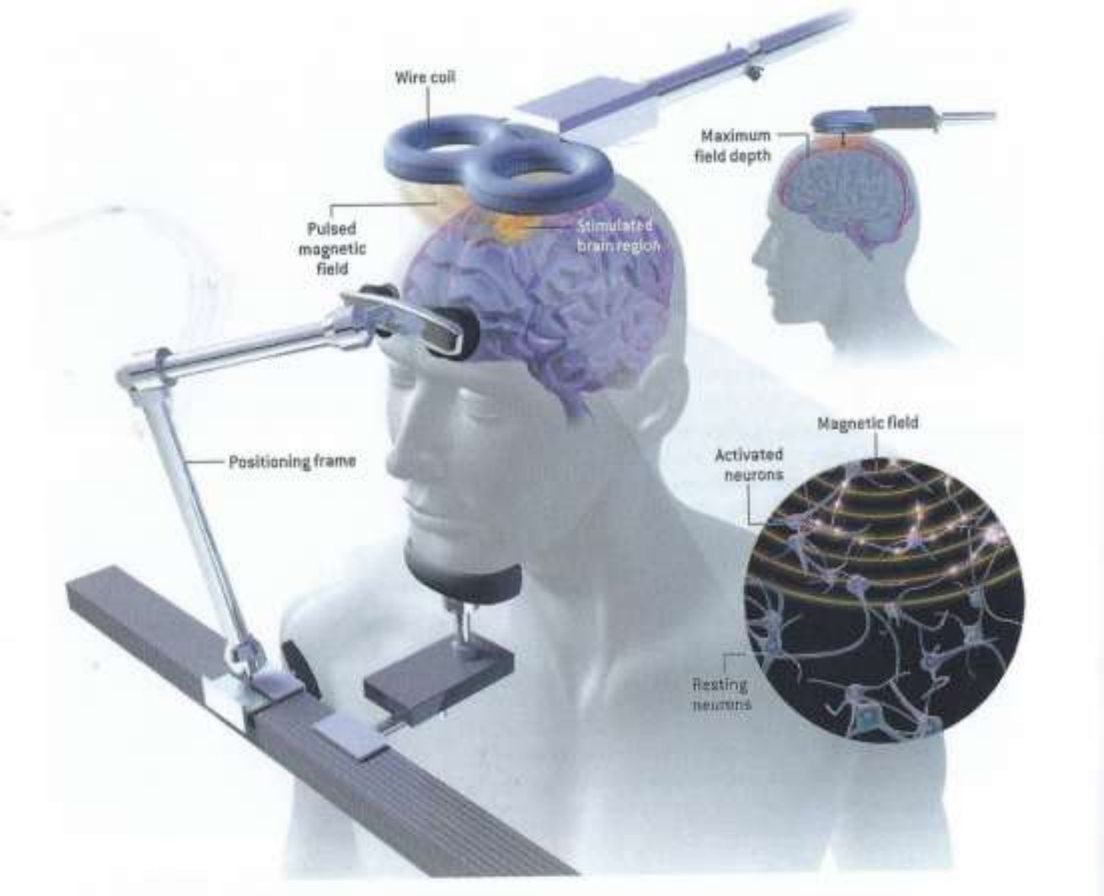
Just and Mason, 2016

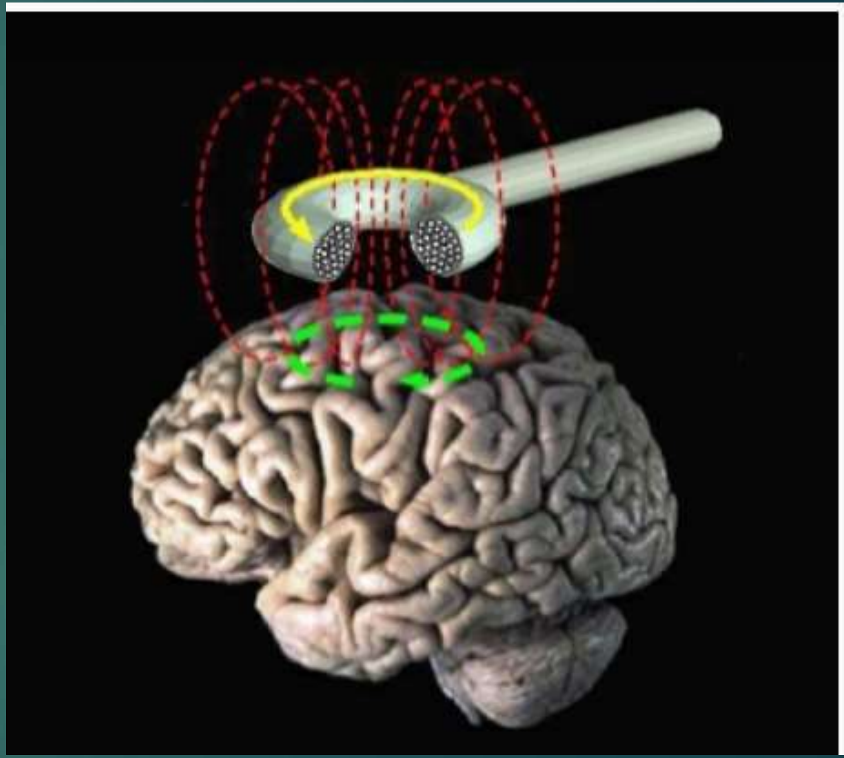
Robotic Connections: brain-machine interfaces (BMI) and neural prosthetics.

She is able to move external robot arm just by thinking; (2012: BrainGate system)



Neuronal disruption: Transcranial Magnetic Stimulation (TMs)





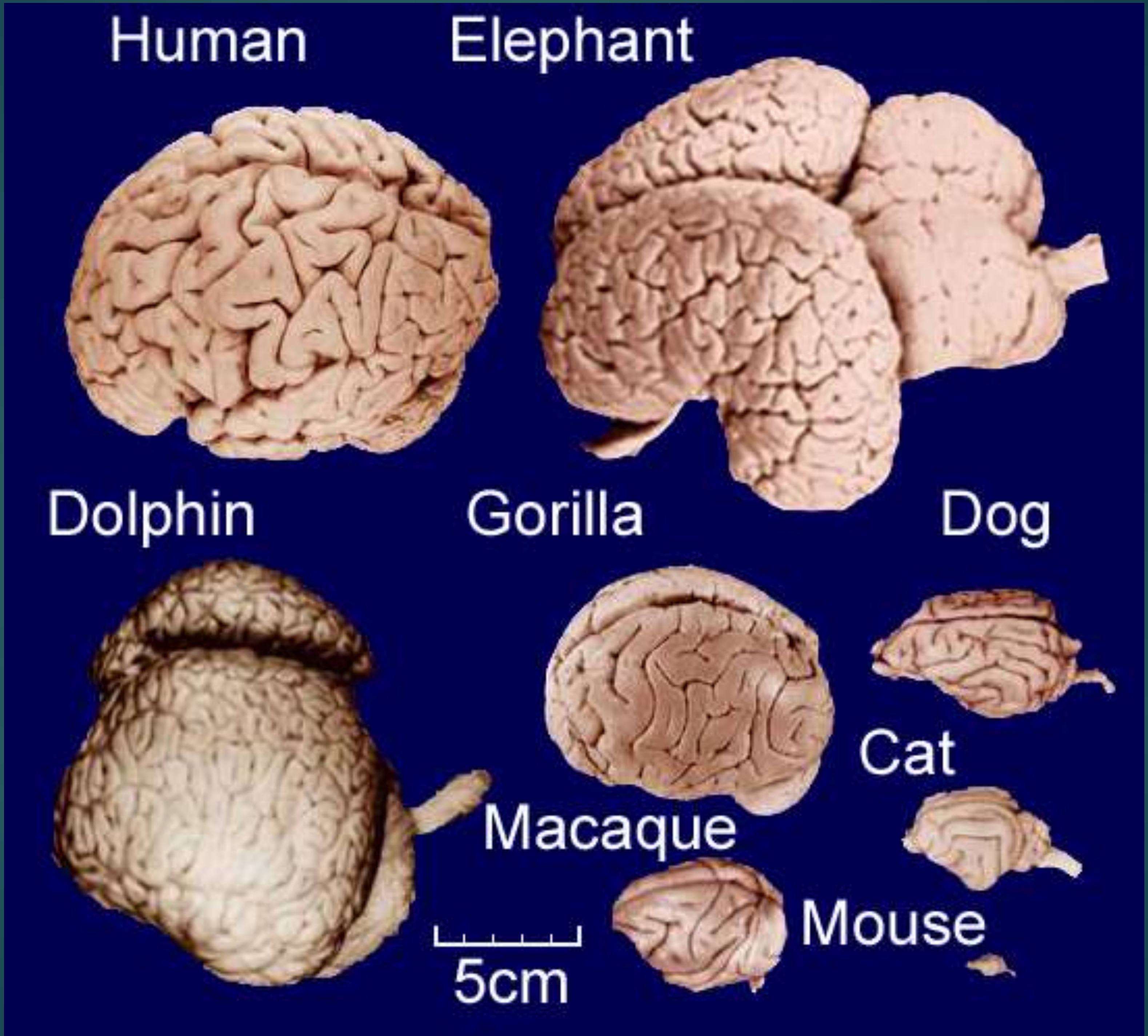
Can momentarily render a brain area dysfunctional

Up to 2.5 tesla
(strength of a magnetic field)

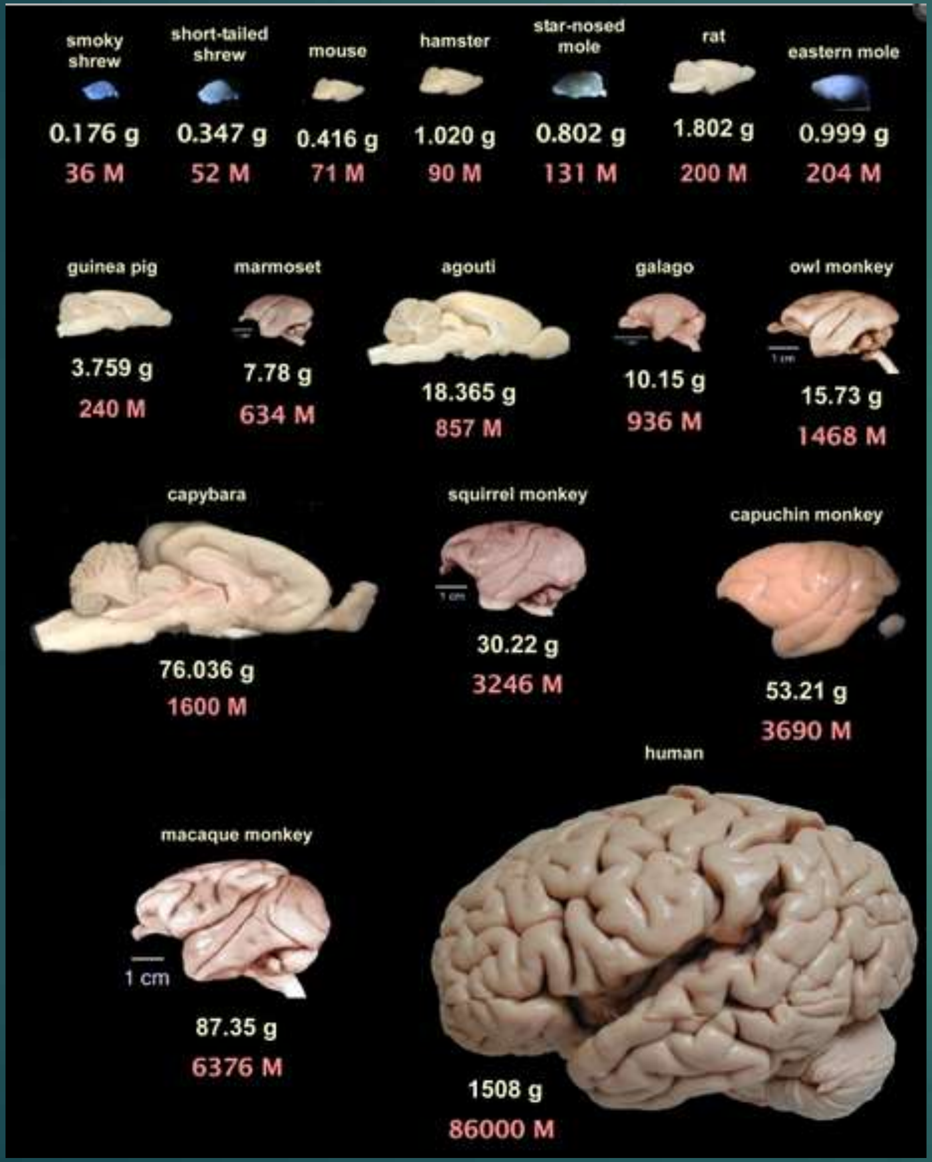
A Cautionary note

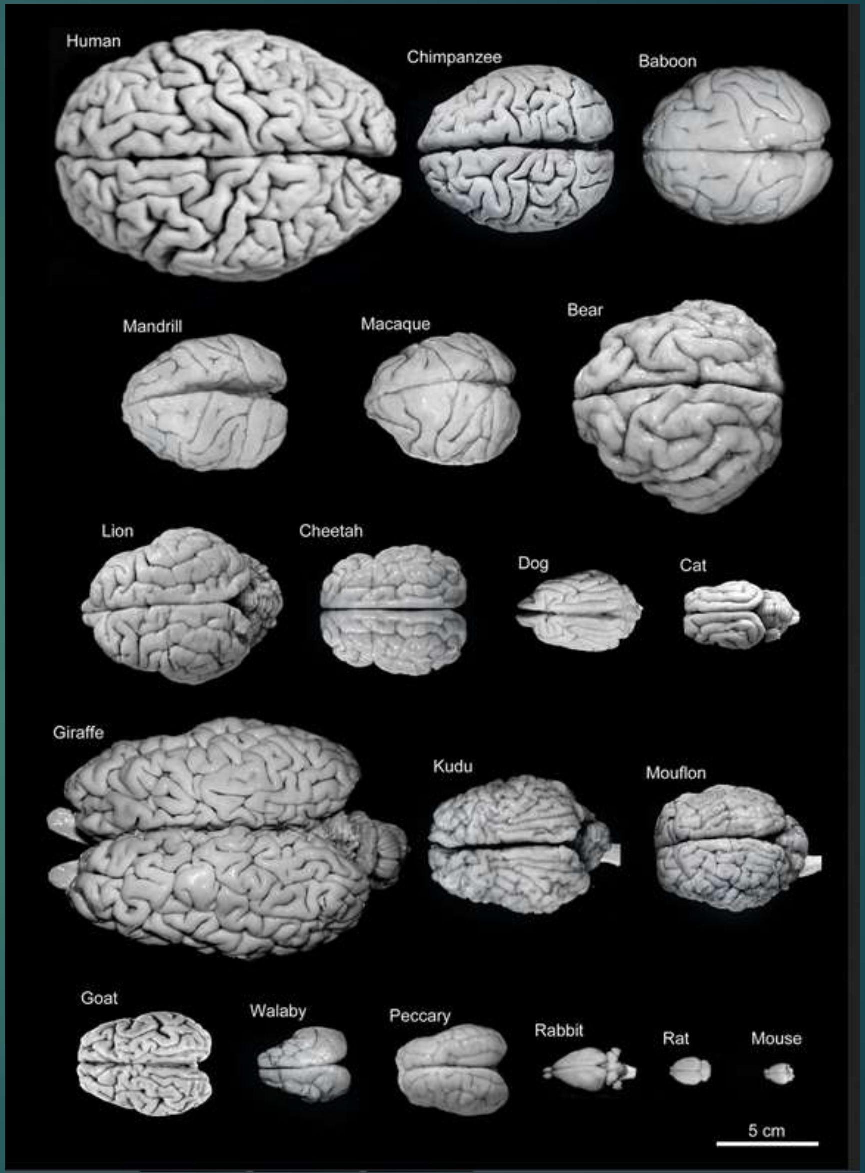
- Brain is one of nature’s great unknown black boxes
- Neuroscientist have discovered major facts about the human brain
- But there is a massive amount of information about the human brain that is yet unknown
- Chimpanzees have recently been put on the excluded list except for essential medical research.

Brain Sizes



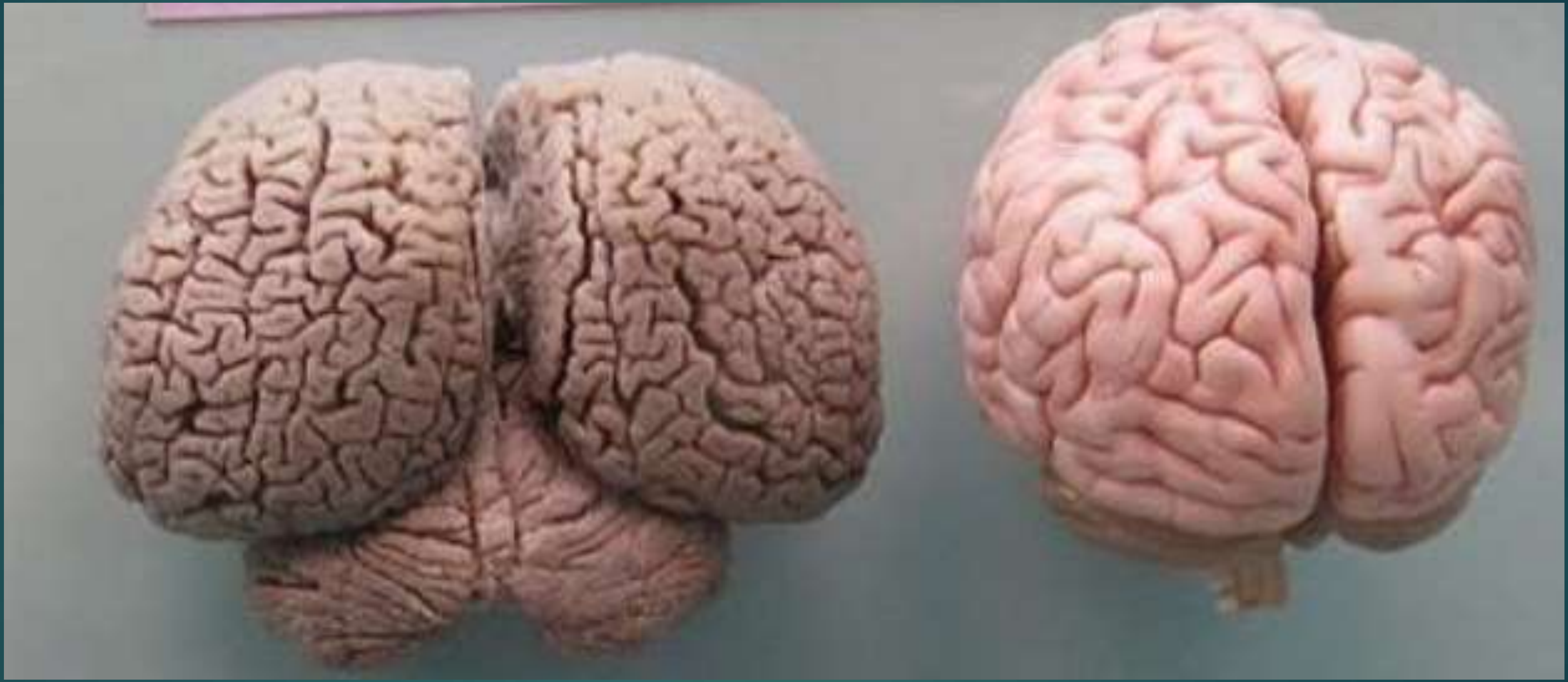
Relative Brain Size: Brain size depends on body size





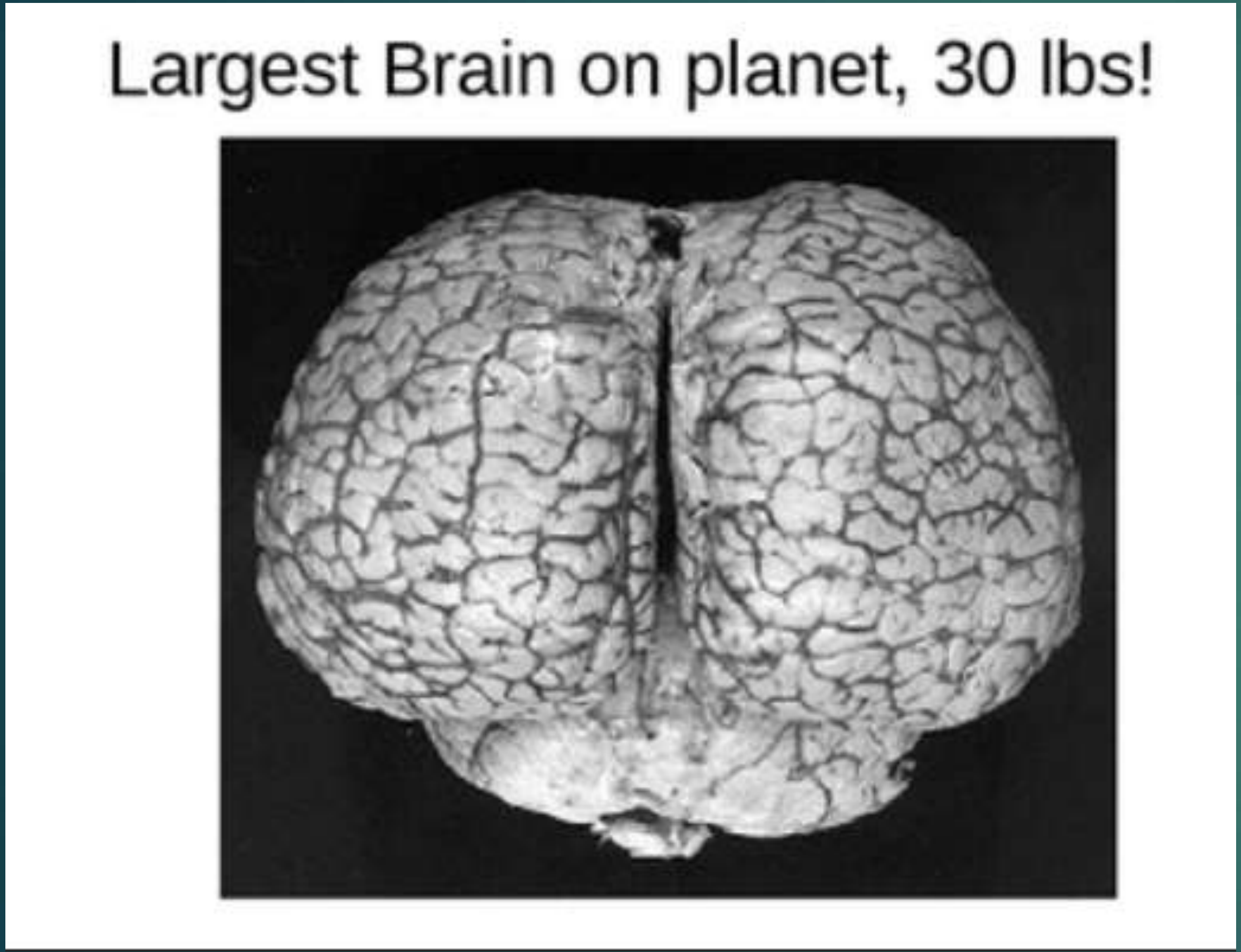
Neandertal brain = 1450 cc average; H. sapiens = 1350

Dolphin & Human: equally smart??

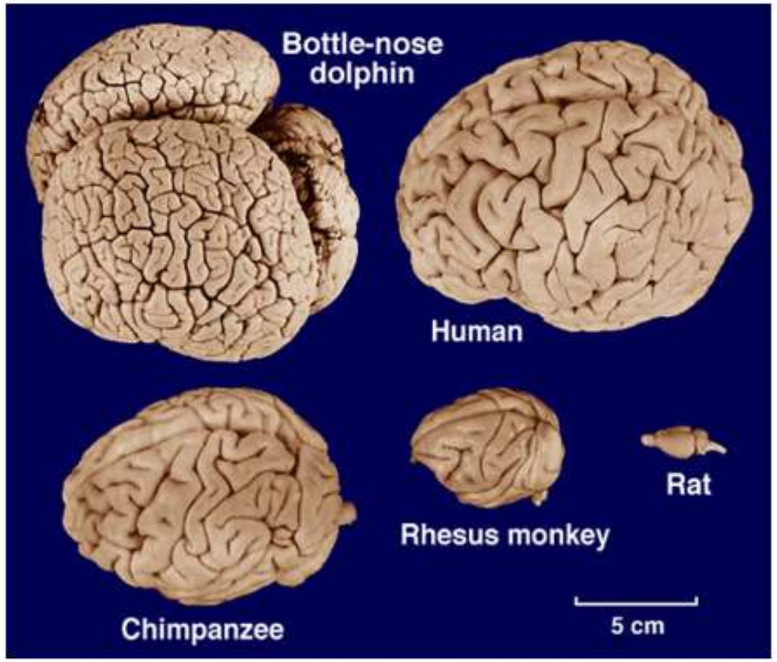


Dolphin has more folds, but less hippocampus

Largest Brain on Planet: Sperm Whale



Brain Size relative to Body Size



Species	Adult Brain Weight (grams)
Chimpanzee	450
Human	1,350
Bottlenosed dolphin	1,600
African elephant	6,075
Fin whale	7,200
Sperm Whale	9,200

Relative Brain Weight

Of all animals, man has the largest brain in proportion to his size" - Aristotle

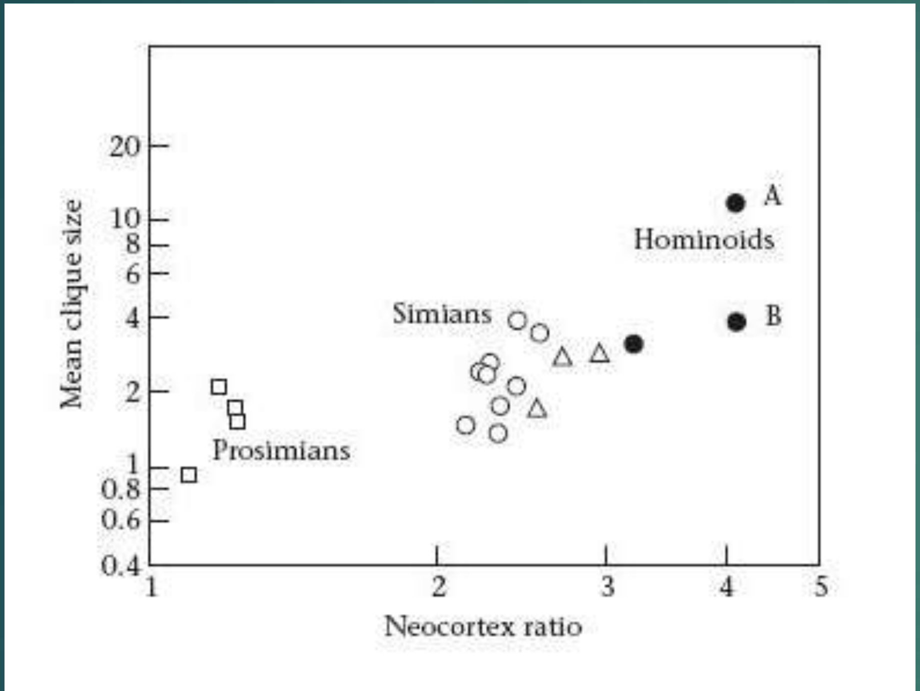
Species	Brain to Body Weight
Human	2.1 %
Bottlenosed dolphin	1.2 %
Chimpanzee	0.70 %
African elephant	0.50 %
Killer whale	0.10 %
Cow	0.08 %
Sperm Whale	0.02 %

Brain size comparison: 400cc vs. 1400 cc

98% identical genetically

Social Brain Hypothesis:

As social group size goes up, so does neocortical brain size



Mean clique size in primates

Average group size

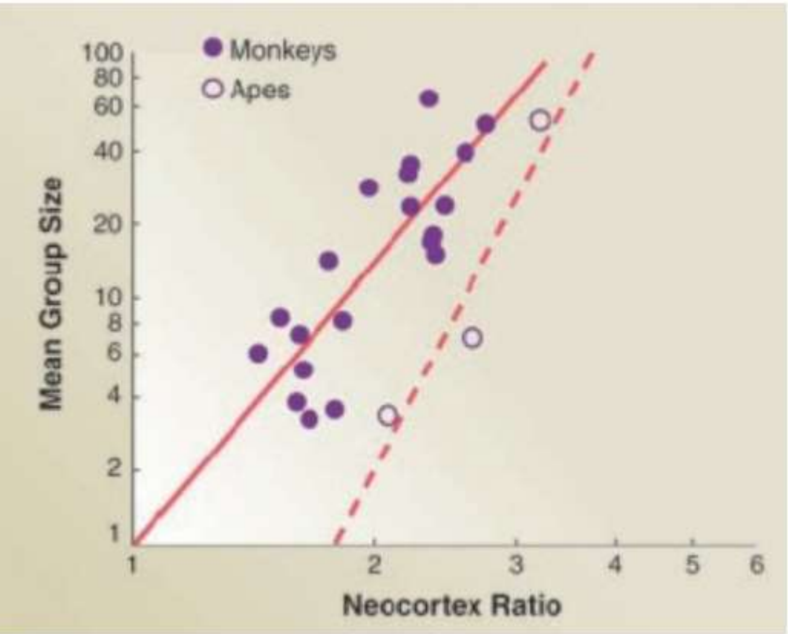
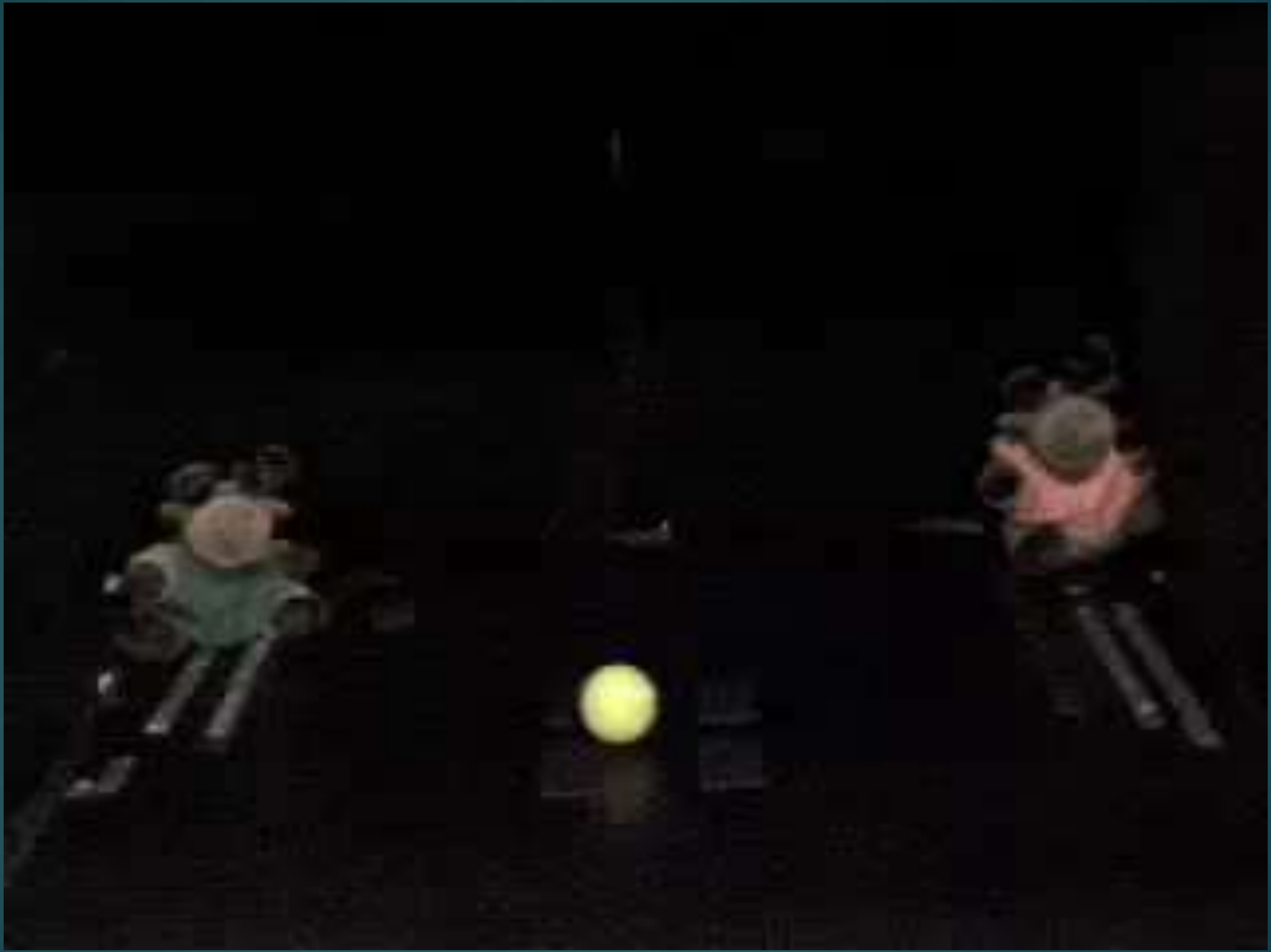


Figure 1. As average group size increases in monkeys and apes, so does neocortex ratio. Reproduced from Dunbar and Shultz (2007).

It takes a lot of brain abilities to be social

- Visual face recognition
- Emotional recognition: visual and auditory
- Memory for faces
- Memory for relationships
- Ability to manipulate information about a set of relationships
- Eye gaze and hand intent recognition
- Empathy
- Desire to be in social group
- Appropriate social responding
- Ability to inhibit behavior
- Language: Ability to listen and to talk
- Fast processing of all of these functions

Taking



Rejecting the selfish orange moose puppet:

5 & 9 month old infants prefer prosocial to antisocial others

8 m old toddlers direct positive behaviors toward prosocial others & negative behaviors toward antisocial others.

Hamlin, J.K., & Wynn, K. (2011).

Cerebral Cortex

Reason why we have a brain: Movement

Number of Brain Cells: 170 Billion: First Official Count in 2009 by Suzana Herculano-Houzel: “Dissolve the brain, yes! But don’t count DNA. Count nuclei!

- Adult male human brain contains on average 170 billion cells:
  - 86 ± 8 billion neurons
  - 85 ± 10 billion glial cells.

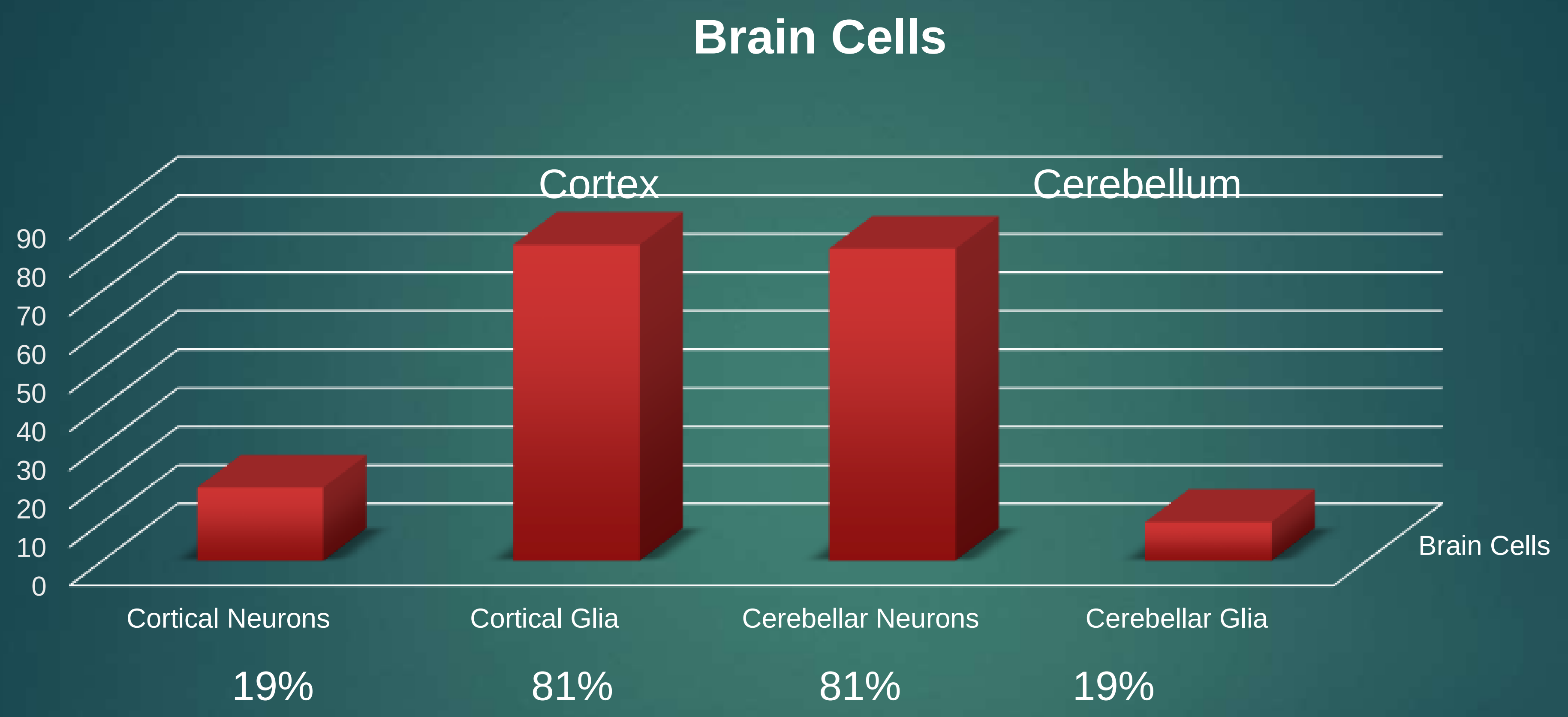
- Cerebral cortex: only 16 billion neurons
  - 19% of all neurons in the brain
  - 82% of total brain mass.
  - 61 billion glia; 16 billion neurons = 4 glia to 1 neuron

F. Azevedo et al., J. *Comp. Neurol*. 513:532–541, 2009

Number of Brain Cells 2

- Cerebellum: 69 billion cells:
  - 81% of all neurons
  - 10% of brain mass
- Glial cells are 50% of all brain cells.
- Gray: 6 billion neurons and 9 billion glia;
- White: 1.3 billion neurons and 20 billion glia
- Human brain is a linearly scaled-up primate brain, with just the expected number of neurons for a primate brain of its size,

Cortical Brain Cells: 170 Billion



Adult male human brain contains on average:

86 ± 8 billion neurons

85 ± 10 billion glial cells.

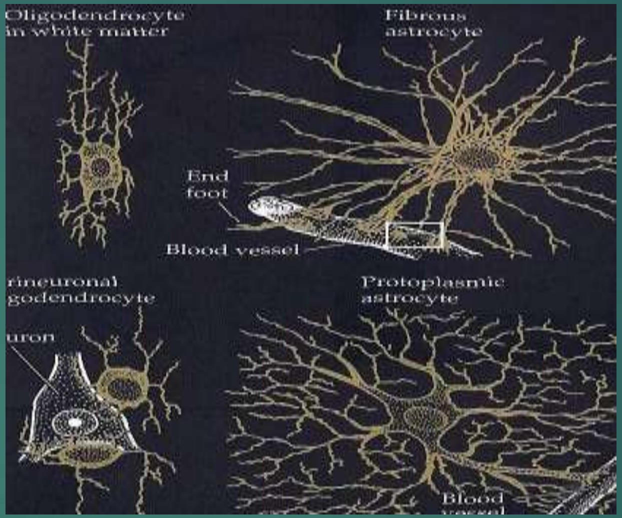
Cortex: 4 to 1 glia to neuron; Cerebellum: 4 to 1 neurons to glia

Suzana Herculano-Houzel conclusions:

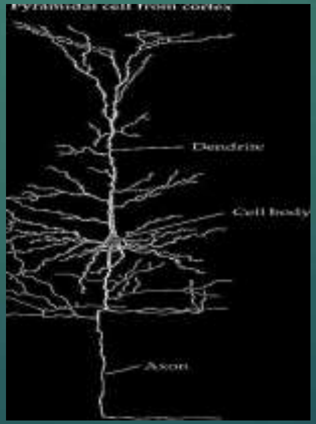
- Brains of 80 species analyzed
- A large brain does not necessarily have more neurons than a small one; some are more dense because their neurons are smaller on average
- Primate brains are much denser than other mammalian brains
- Birds appear to have the densest brains of all
- Humans do not have the most neurons: The African elephant has about three times as many, with a grand total of 257 billion
- Humans have 16 billion cortical neurons. The next runners-up, orangutans and gorillas, have nine billion cortical neurons; chimpanzees have six billion. The elephant brain, despite being three times larger than our own, has only 5.6 billion neurons in its cerebral cortex.
- Humans: the most cortical neurons

Brain: Cellular Organization

- Glia:

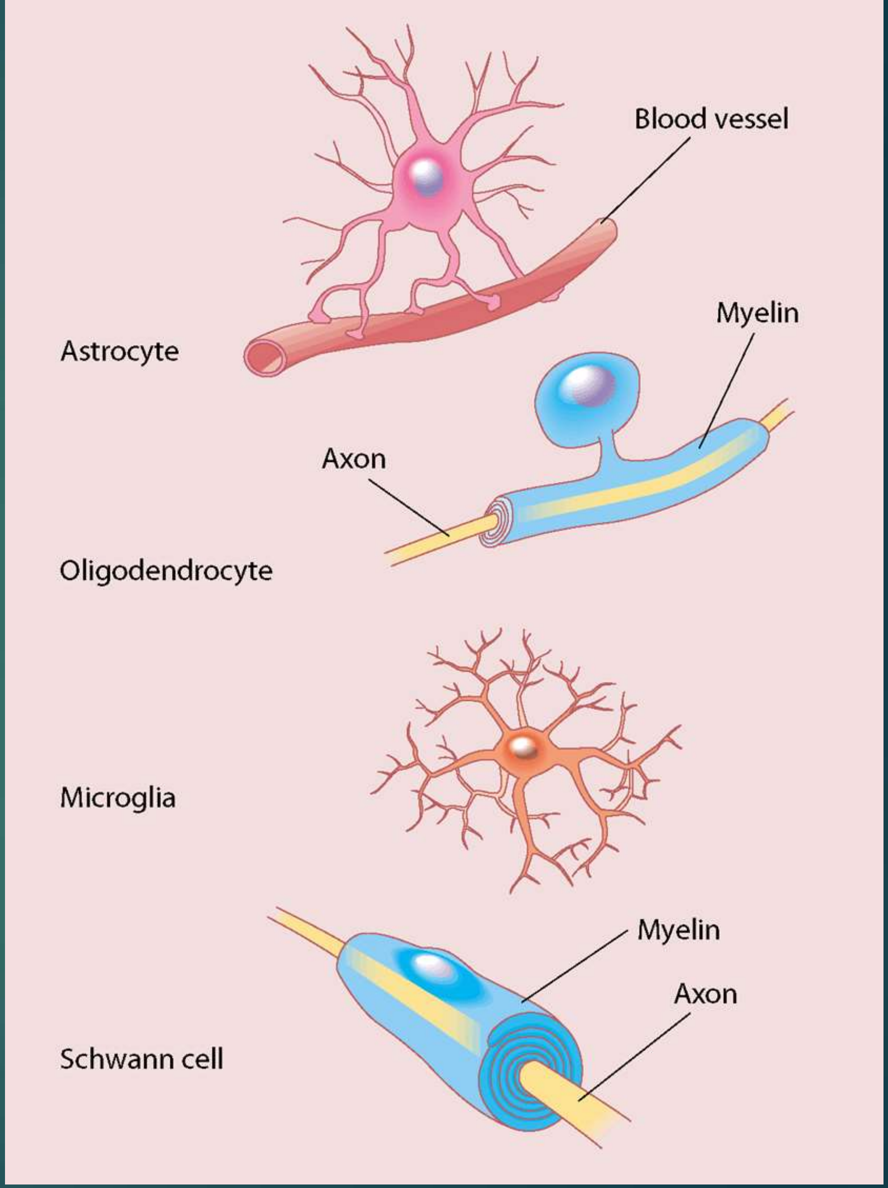


- Neurons:

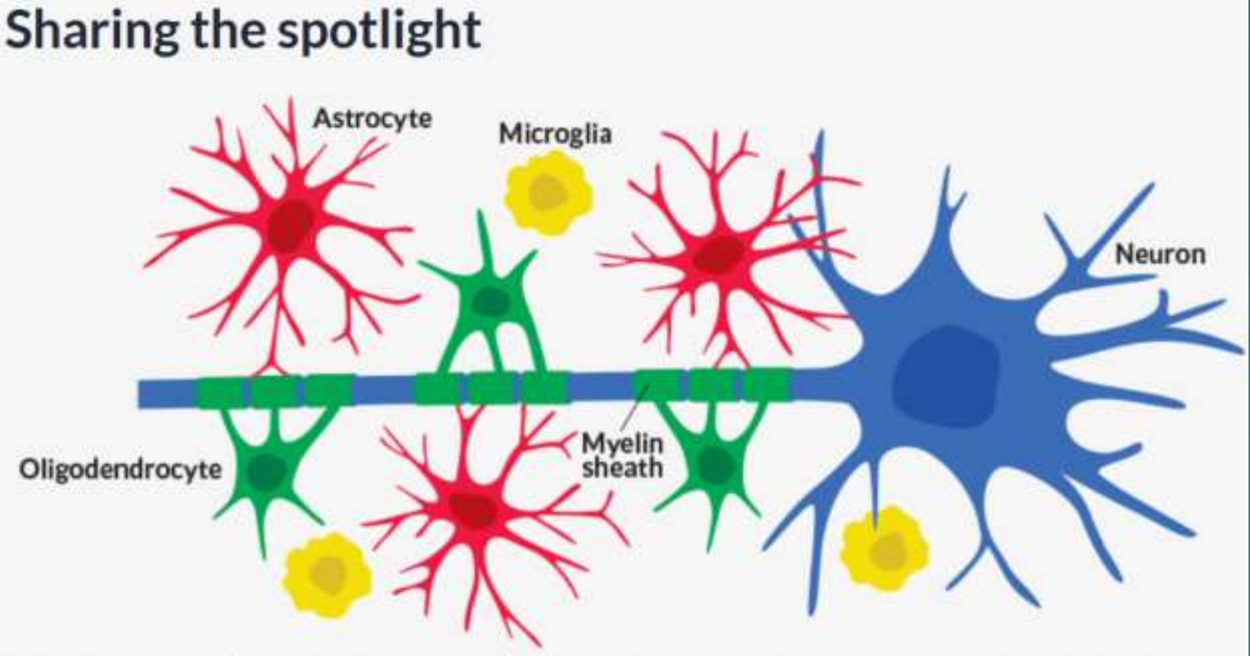


Glia are essential

- Support staff for neurons (named for the Greek term for “glue)
- Neuronal maintenance: feed, insulate (Myelin sheath), attack invaders
- Form blood-brain barrier
- Remove 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; speeding or slowing the electrical signals and strengthening neuron-to-neuron connections.



Three types of glial cells



Oligodendrocytes (green) and astrocytes (red) are glial cells that influence the way chemical and electrical signals travel from neuron to neuron (blue) and may shape the way information is stored. A third type of glia, microglia (yellow), help protect the brain.

1 - Tiny microglia puff up and kill invaders, using chemical warfare to kill infiltrators, while devouring dead and dying cells. Microglia also prune and clear away unnecessary nerve cell connections.

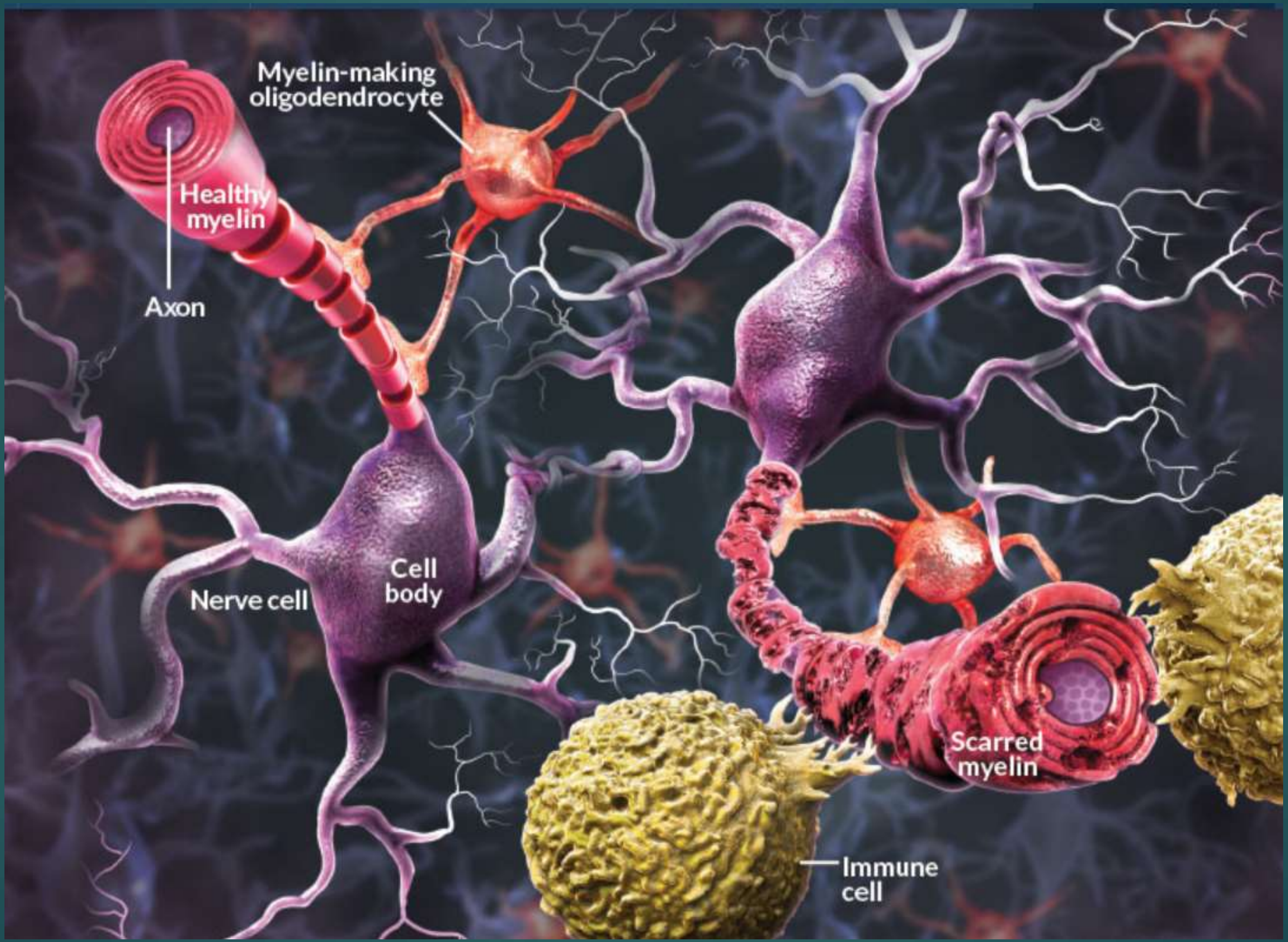
2 - Astrocytes nestle some of their pointed projections against synapses, playing a role in how neurons make connections. Other astrocyte projections connect to nearby capillaries, helping to bring oxygen-rich blood to the neurons.

3 - Oligodendrocytes, supports neurons by wrapping the neurons' long, wiry fibers called axons in myelin.

Astrocytes

- ~50% of brain cells: promote neuronal survival, stimulate synapse formation, and prune synapses.
- Wrap around synapses, influencing signaling and nerve birth and growth
- Call-and-response relationship with the blood that sustains them
- Respond to injury by producing proteins
- Transplantation of human astrocytes into mouse brains improved the animals' ability to learn and remember (see Han et al., 2013).
- When dysfunctional, implicated in many neurological and psychiatric disorders, such as epilepsy and schizophrenia
- Humans' superior learning and memory skills are at least in part due to glia. Astrocytes' release of brain chemicals, including glutamate, is essential to maintaining a rhythm of 25 to 60 surges/oscillations per second, essential for memory.

White Matter: Oligodendrocytes = Myelin makers



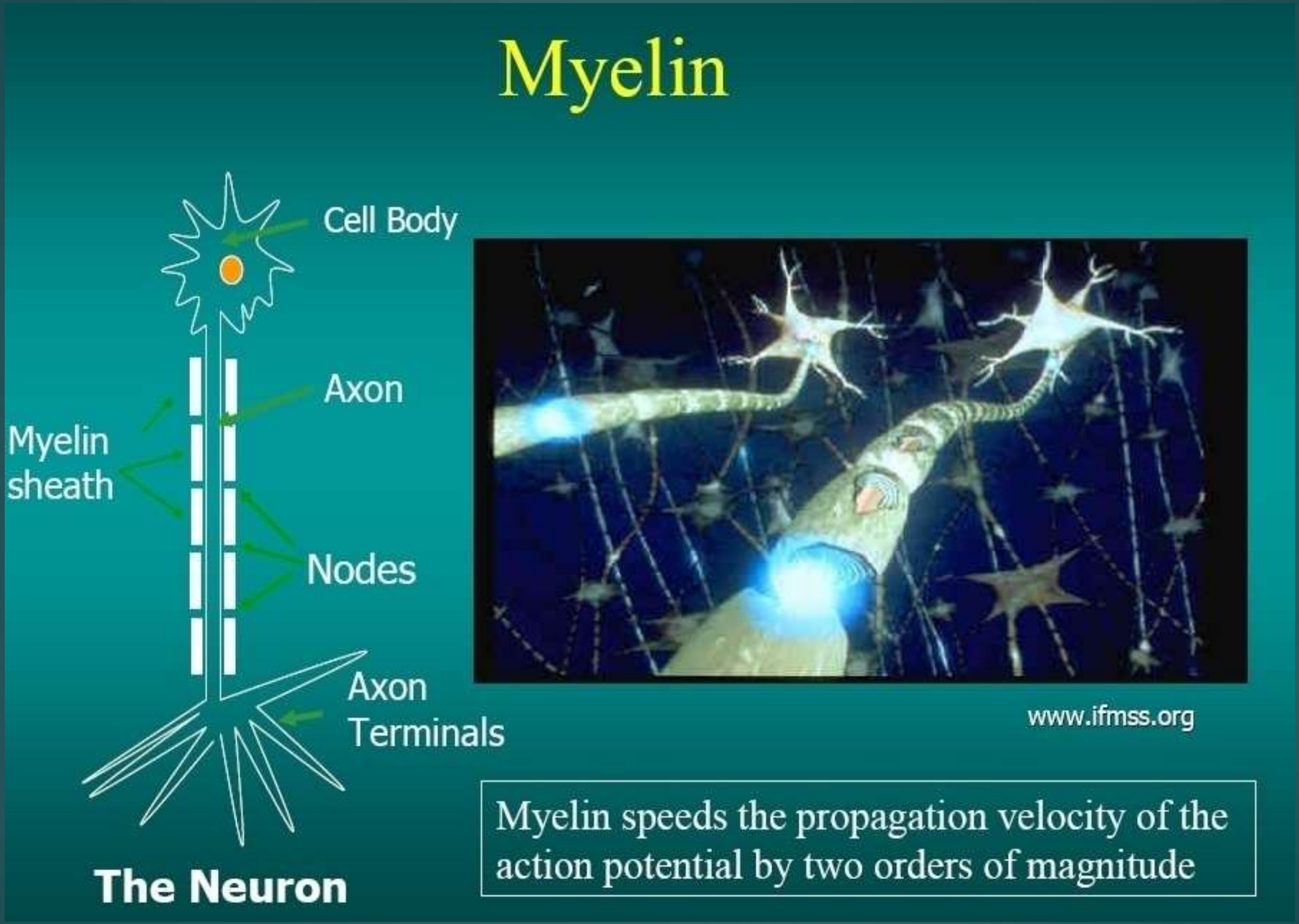
What happens to WM in MS

Oligodendrocytes

- Form myelin around neurons, substantially increase signal speed.
  - It takes a signal 30 milliseconds to cross from the left to the right side of the brain on myelinated axons.
  - A similar signal takes about 300 milliseconds on un-myelinated axons.
- Metabolic support for axons

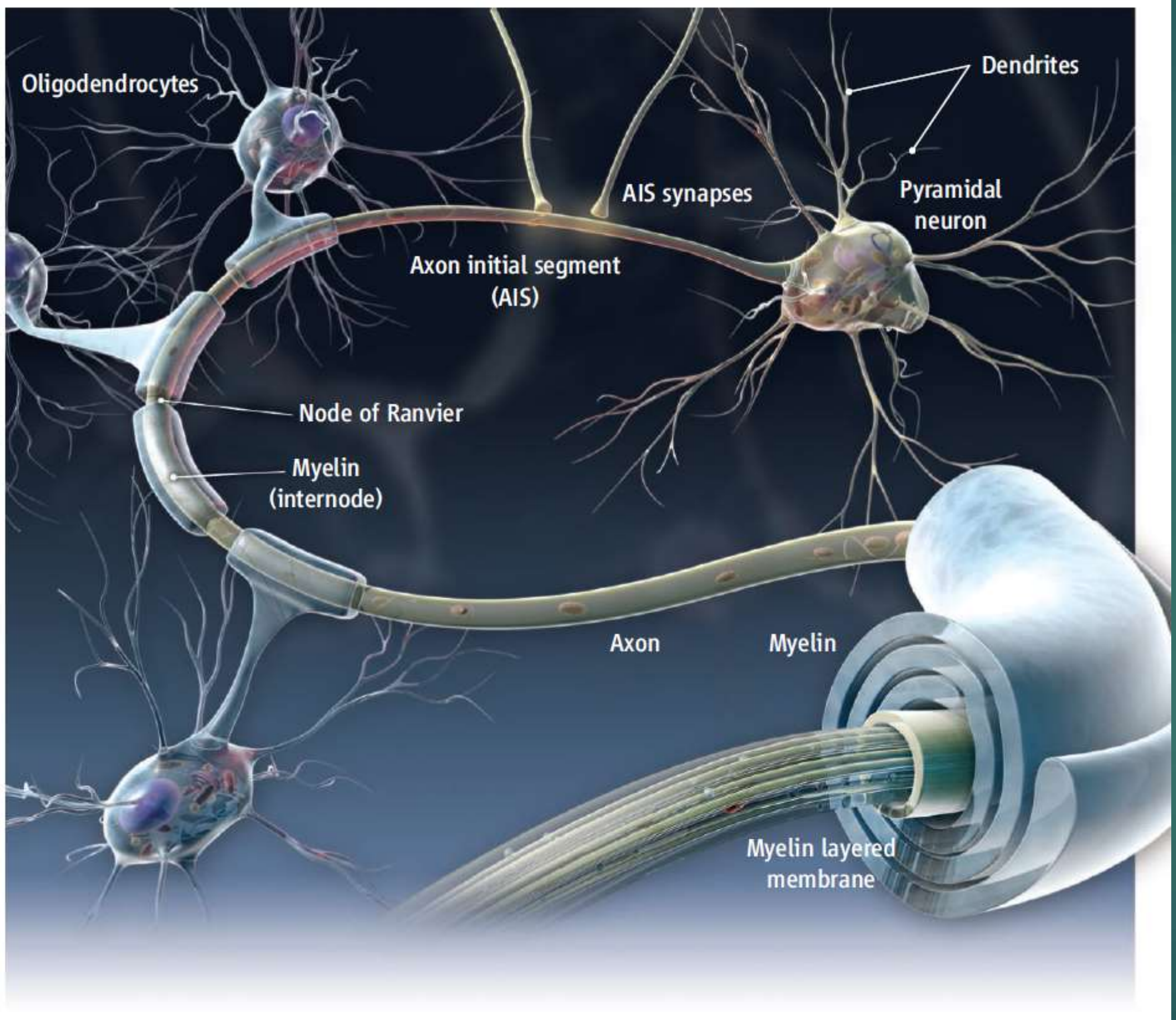
- Dysfunction: multiple sclerosis, amyotrophic lateral sclerosis and inhibition of repair after spinal cord injury
- Victims of childhood abuse have epigenetically altered oligodendrocyte function.

Myelin: 136,000 KM of Myelinated Axons

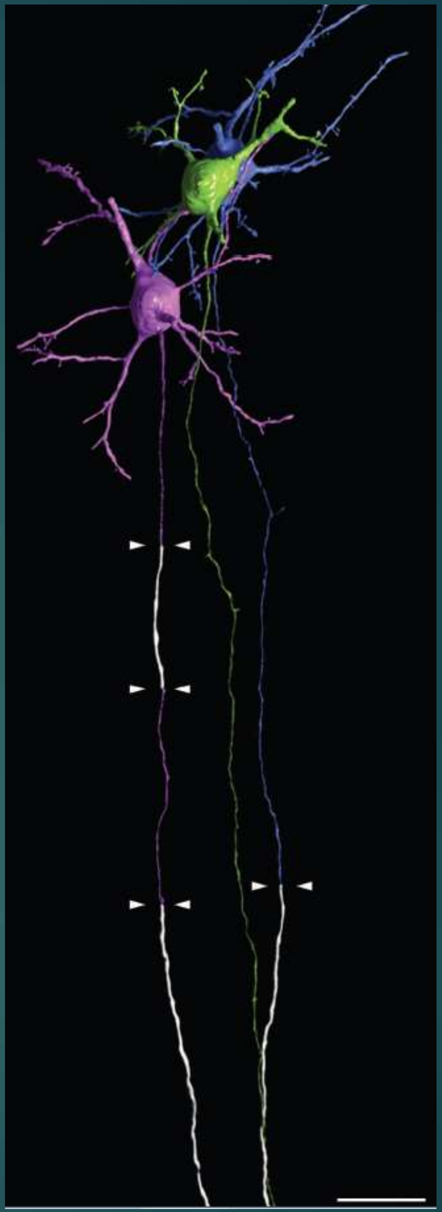


Mylenated speed: 100m/s; unmyelinated speed - less than 1m/s

Myelin: Oligodendrocytes



Intermittent myelination. Myelination of layer II/III pyramidal neurons of the cerebral cortex is illustrated, with a long axon initial segment and segments with variable lengths of unmyelinated axon.



Not all Axons are mylenated

Microglia

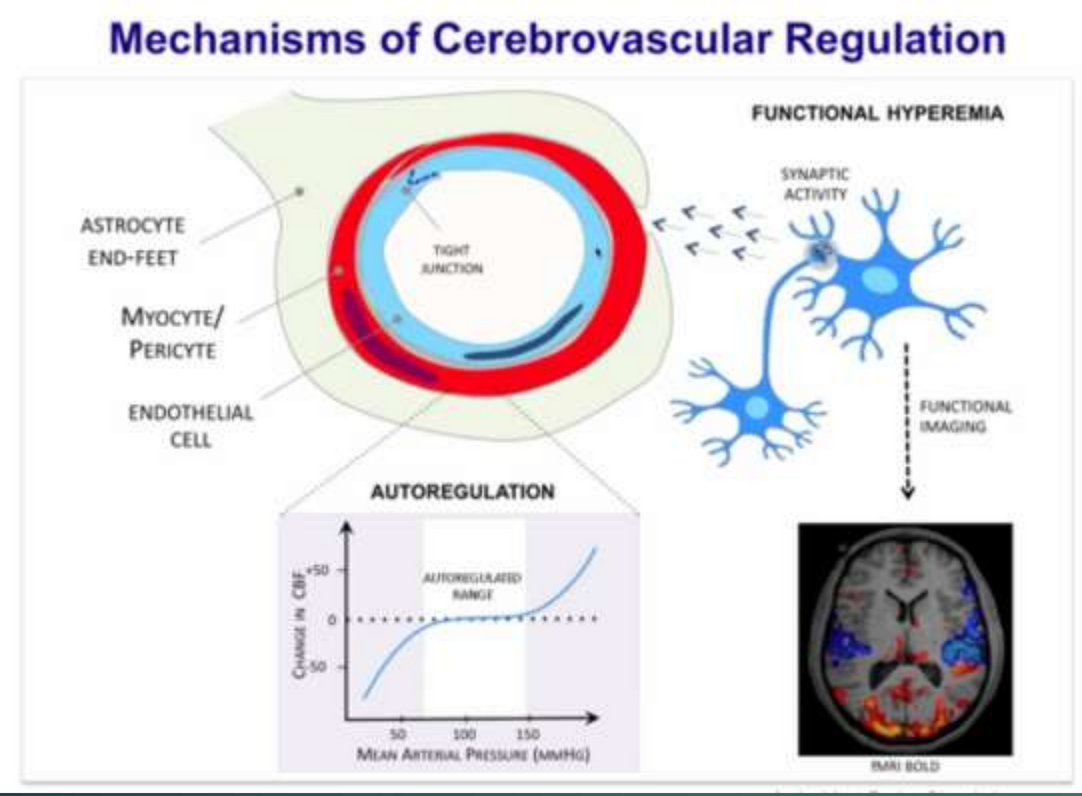
- Travel and respond to nervous system injury and infection
  - Monitor electrical activity in neurons and prune synaptic connections
  - Their dysfunction is involved in almost all nervous system diseases and in certain psychiatric conditions, including obsessive-compulsive disorder

Blood-Brain Barrier

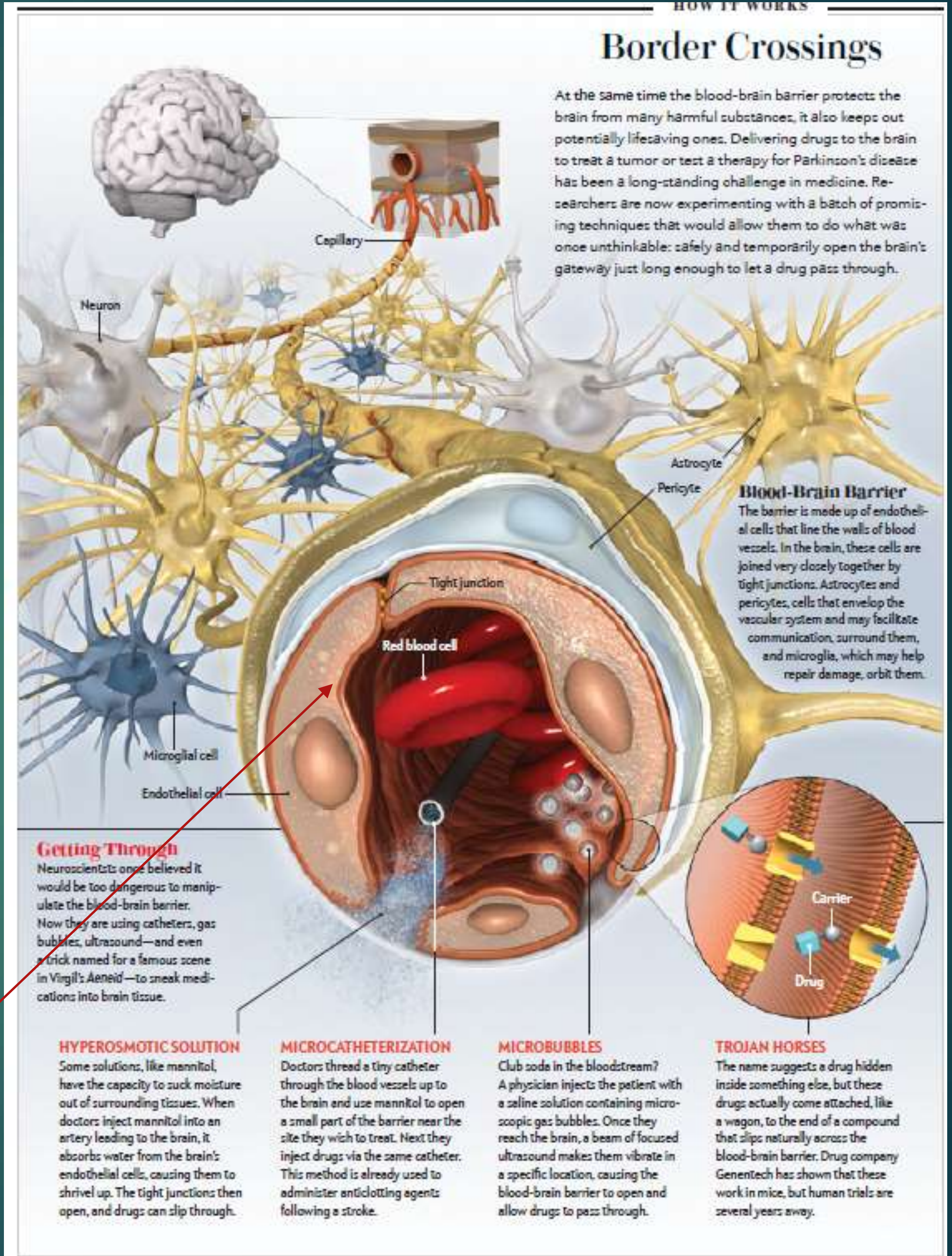
- Blood-brain barrier is tightly joined endothelium (thin layer of glial cells that lines the interior surface of blood vessels)

- Permeable to lipid-soluble materials (alcohol, O_2, CO_2, nicotine and anesthetics)

Blood Brain Barrier



BBB



Border Crossings

At the same time the blood-brain barrier protects the brain from many harmful substances, it also keeps out potentially lifesaving ones. Delivering drugs to the brain to treat a tumor or test a therapy for Parkinson's disease has been a long-standing challenge in medicine. Researchers are now experimenting with a batch of promising techniques that would allow them to do what was once unthinkable: safely and temporarily open the brain's gateway just long enough to let a drug pass through.

Blood-Brain Barrier

The barrier is made up of endothelial cells that line the walls of blood vessels. In the brain, these cells are joined very closely together by tight junctions. Astrocytes and pericytes, cells that envelop the vascular system and may facilitate communication, surround them, and microglia, which may help repair damage, orbit them.

Getting Through

Neuroscientists once believed it would be too dangerous to manipulate the blood-brain barrier. Now they are using catheters, gas bubbles, ultrasound—and even a trick named for a famous scene in Virgil's *Aeneid*—to sneak medications into brain tissue.

HYPEROSMOTIC SOLUTION

Some solutions, like mannitol, have the capacity to suck moisture out of surrounding tissues. When doctors inject mannitol into an artery leading to the brain, it absorbs water from the brain's endothelial cells, causing them to shrivel up. The tight junctions then open, and drugs can slip through.

MICROCATHETERIZATION

Doctors thread a tiny catheter through the blood vessels up to the brain and use mannitol to open a small part of the barrier near the site they wish to treat. Next they inject drugs via the same catheter. This method is already used to administer anticlotting agents following a stroke.

MICROBUBBLES

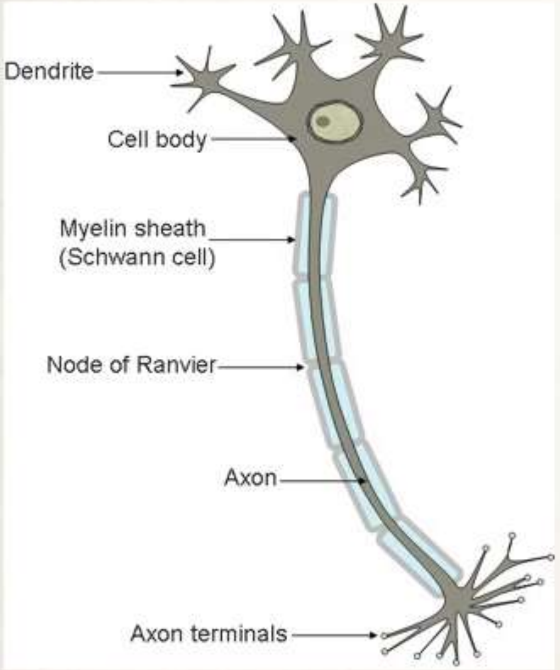
Club soda in the bloodstream? A physician injects the patient with a saline solution containing microscopic gas bubbles. Once they reach the brain, a beam of focused ultrasound makes them vibrate in a specific location, causing the blood-brain barrier to open and allow drugs to pass through.

TROJAN HORSES

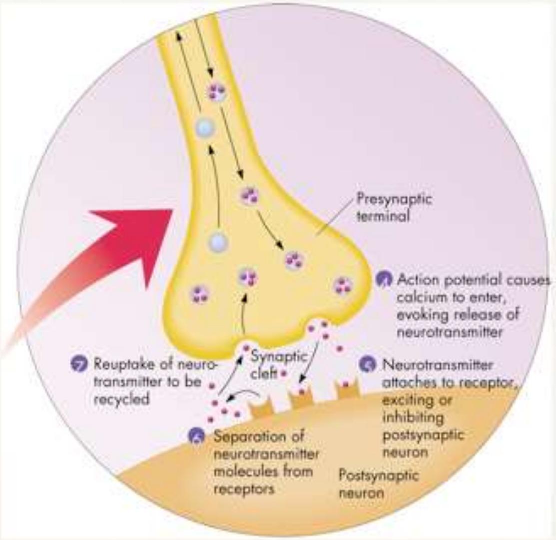
The name suggests a drug hidden inside something else, but these drugs actually come attached, like a wagon, to the end of a compound that slips naturally across the blood-brain barrier. Drug company Genentech has shown that these work in mice, but human trials are several years away.

The Least Brain Anatomy You Need to Know

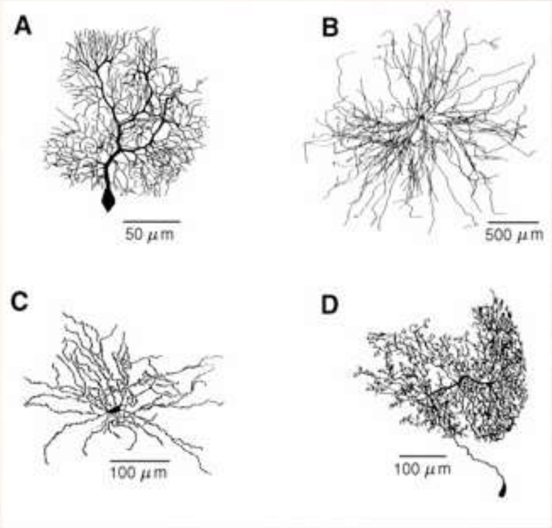
A ***neuron*** is a specialized brain cell



Neurons connect at ***synapses***

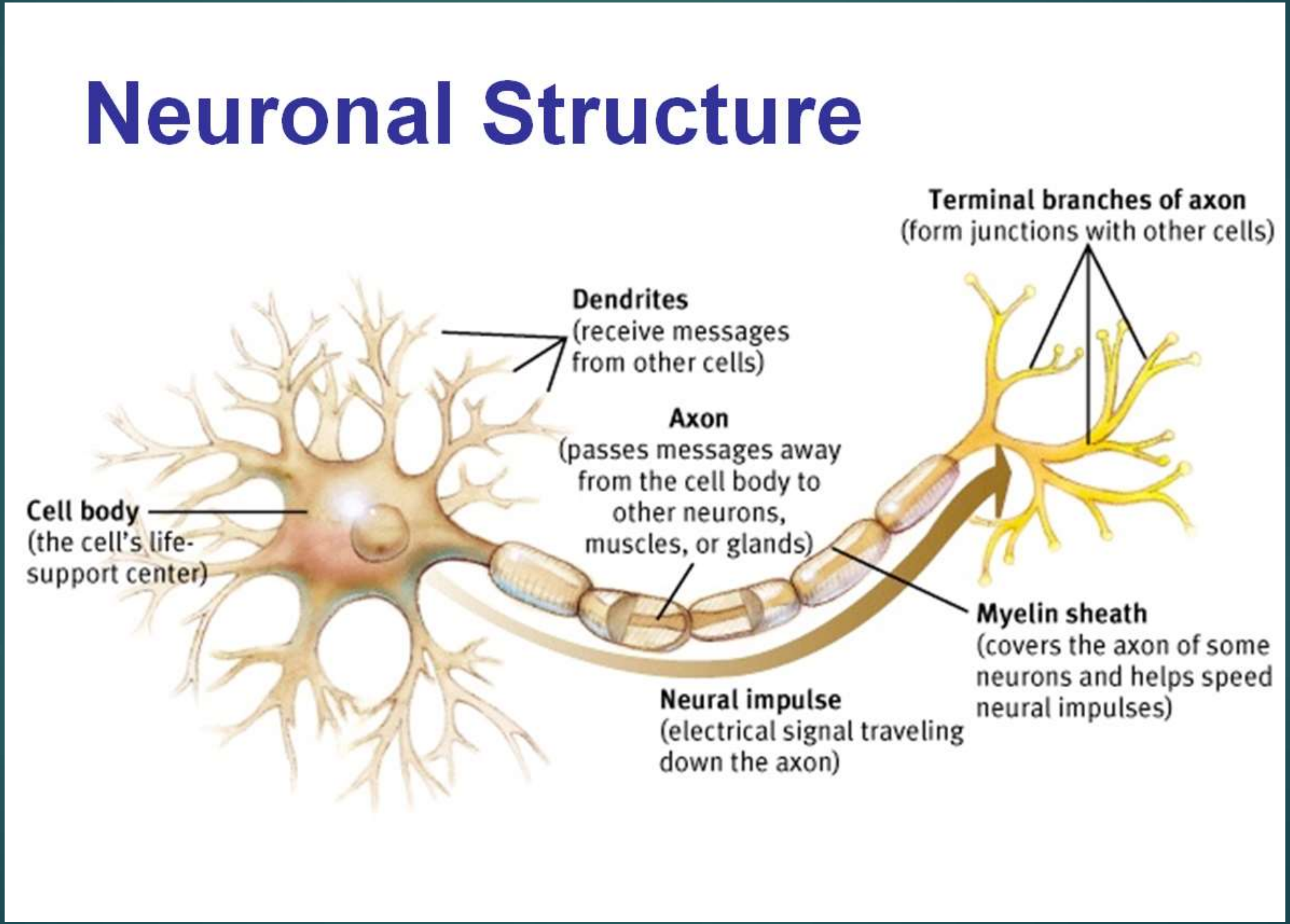


Neurons come in many ***varieties***



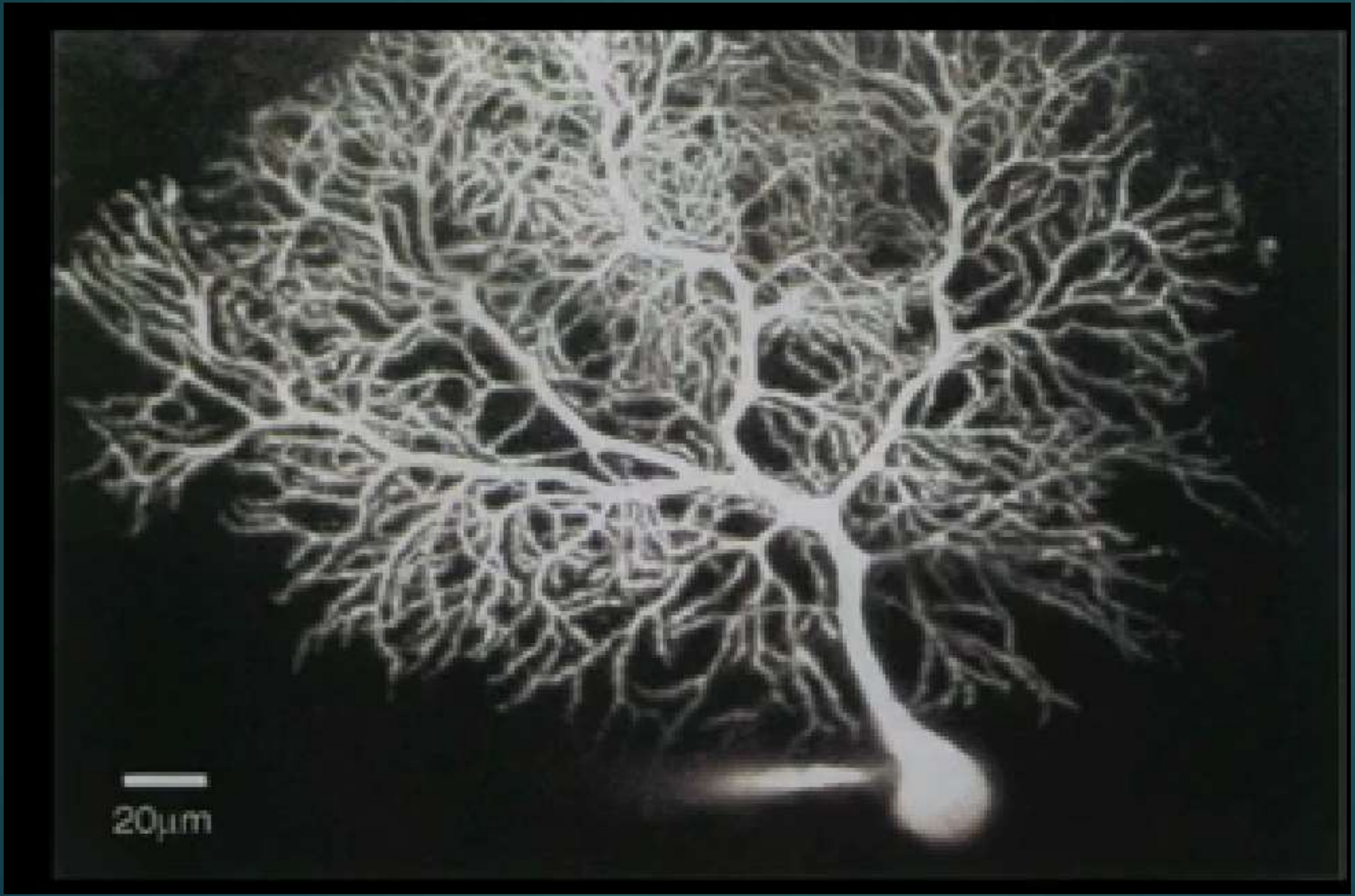
Neuron

Dendrites:
Receive info

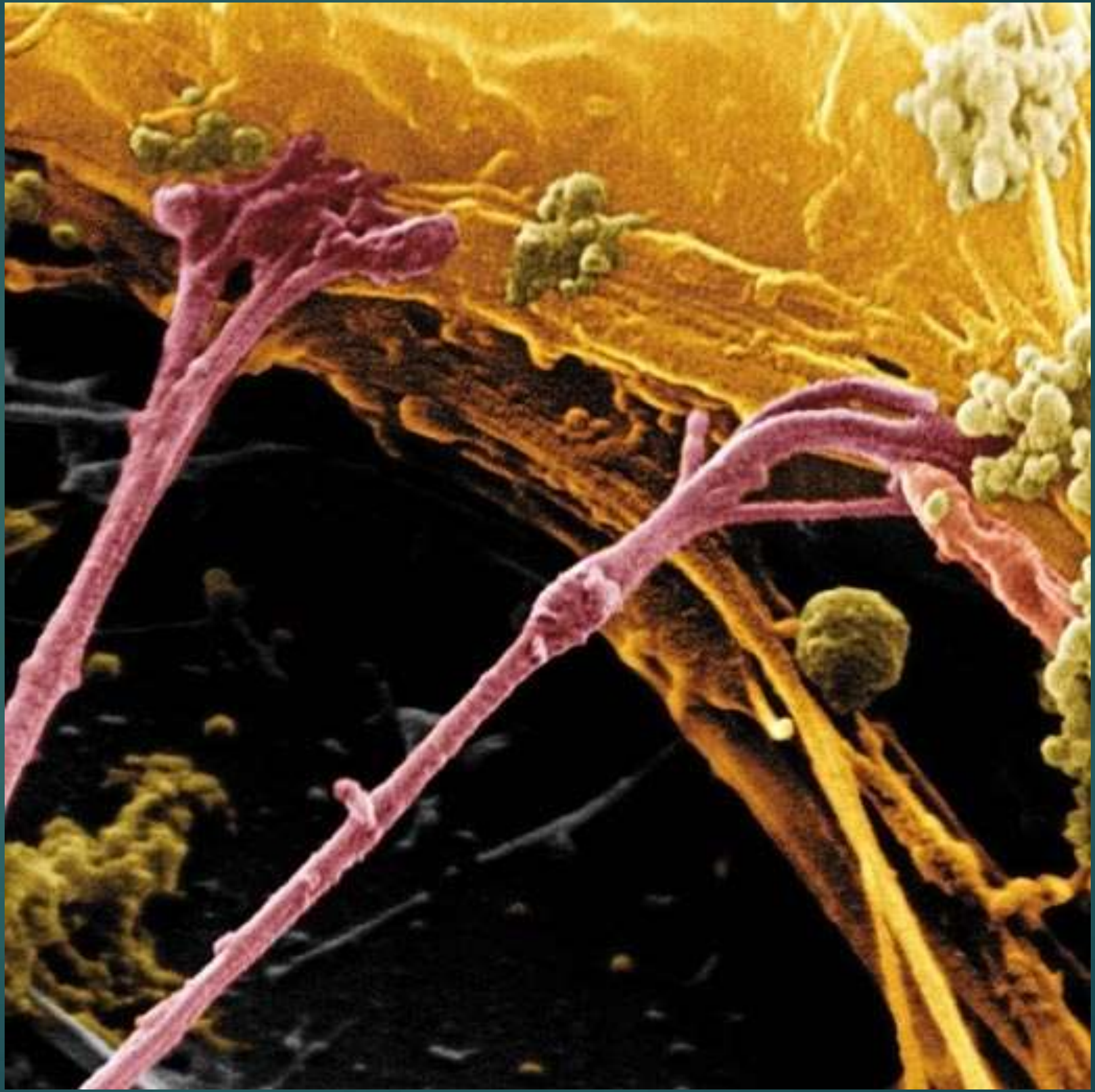


Axonal synapses:
Send info

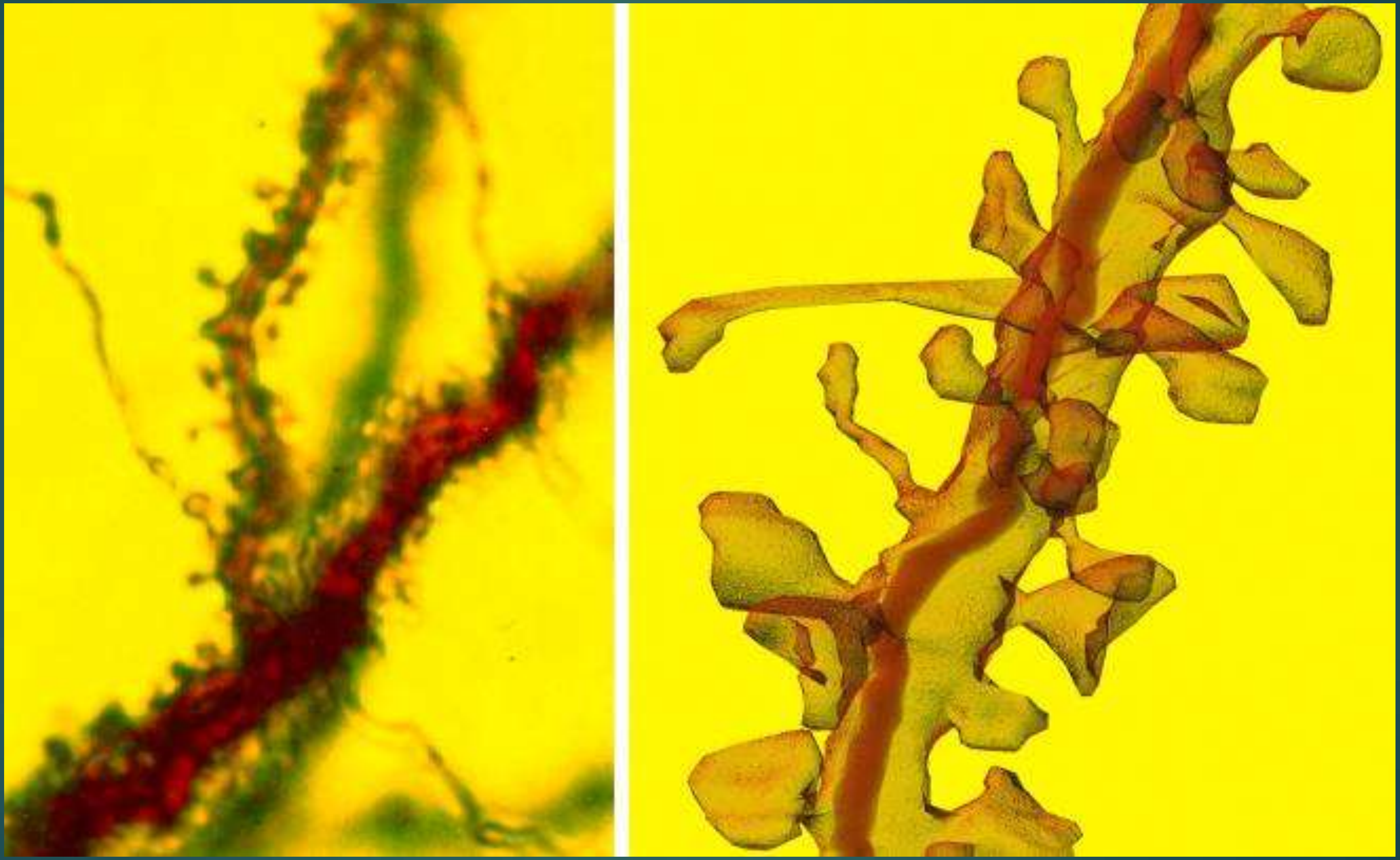
A Neuron



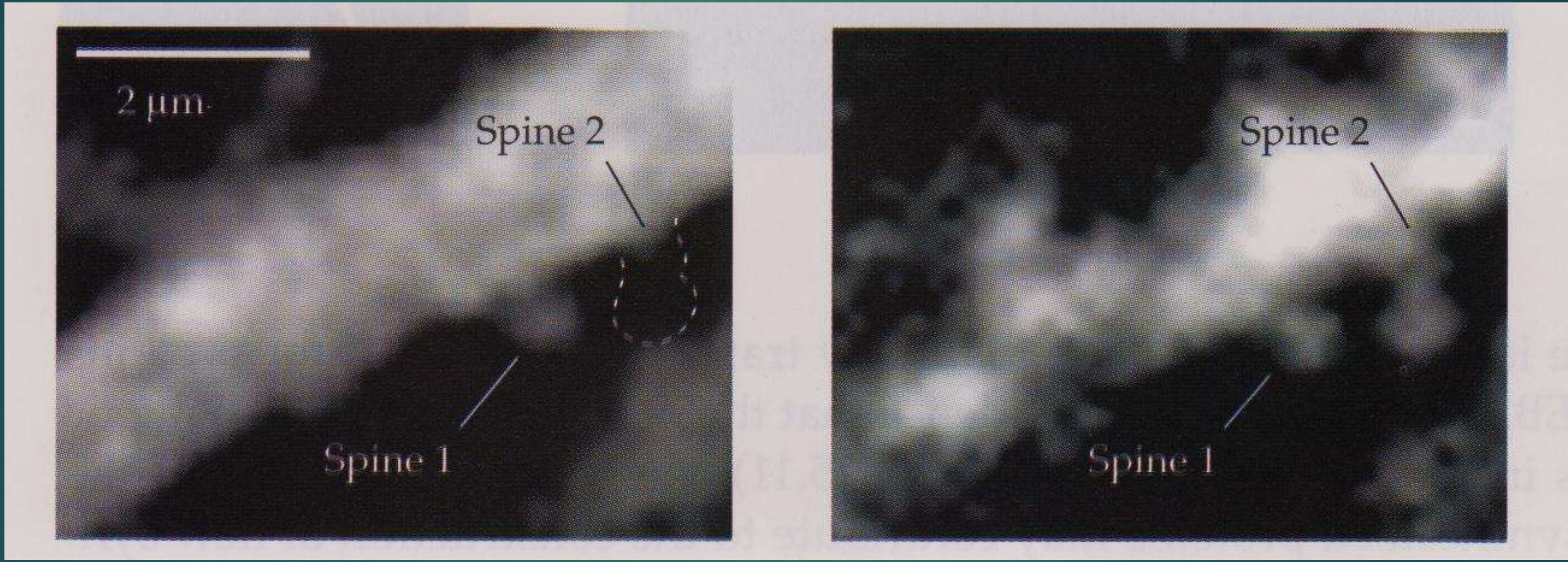
Dendrites



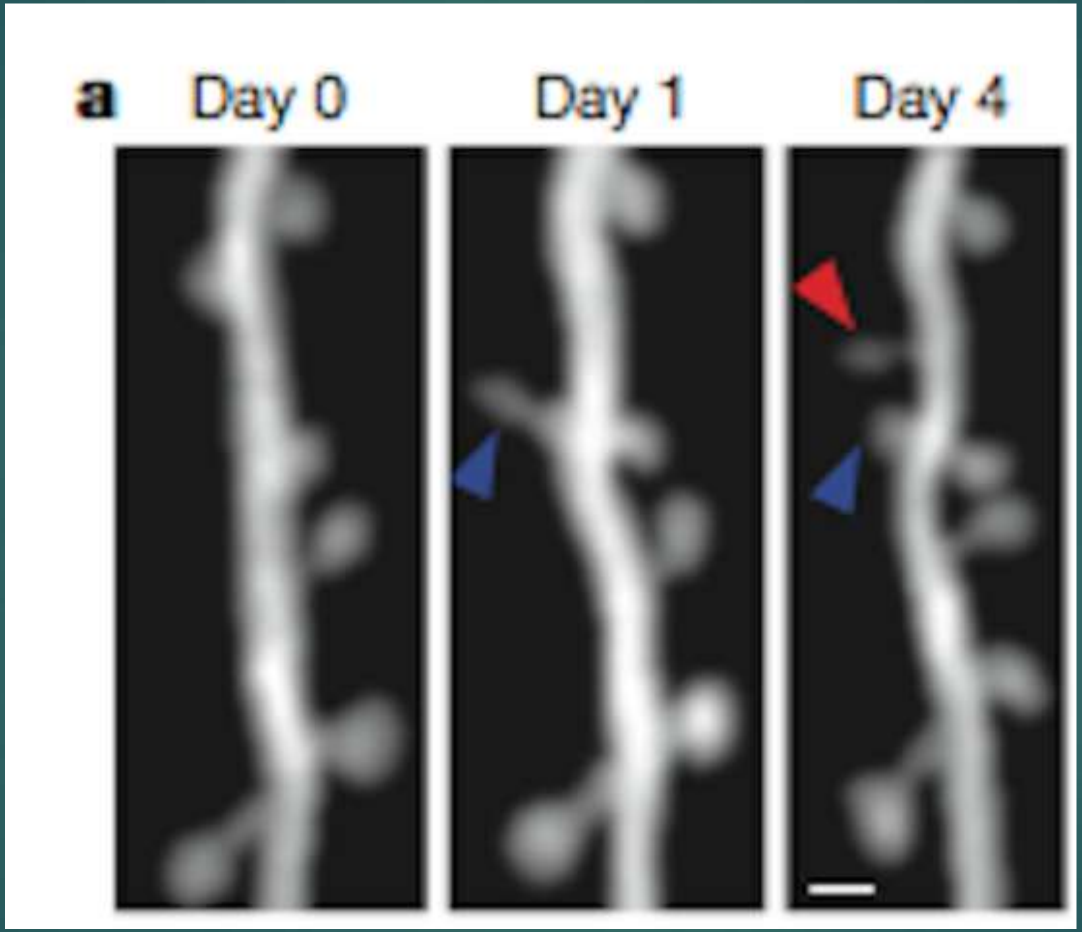
Dendrites: Electron Microscope



Dendritic Spine Growth: one-half hour



Physical basis of Neuroplasticity



2 dendrites grow in a mouse after 4 days of reaching for a seed

Increasing Size of Brain Body Maps

- Most brain areas: increased size via dendrite proliferation

- Learning braille:
  - > 2 hours of class, 5 days a week
  - > by 6 months, noticeable increase in parietal tactile area

- Basketball practice:
  - Increase in white matter in cerebellum with increased coordination

Pascual-Leone, R., et al. (1999)

Experience changes our brains: London Taxi Drivers

If you lived in London, and wanted to grow your hippocampus, which driving job would you choose?

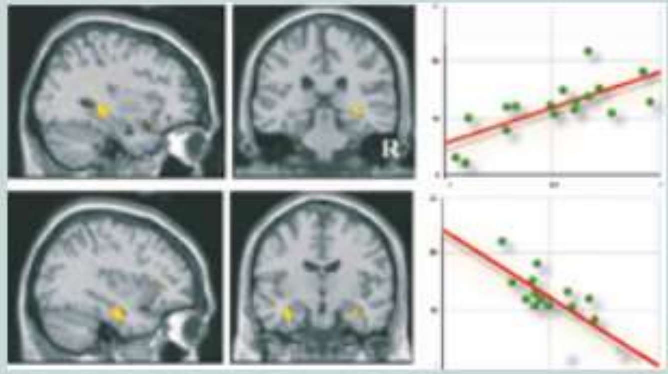
Knowledge exam: 3 of 10 pass

25,000 streets
1400 landmarks

Study of London Taxi cab drivers (vs. bus drivers): To earn their licenses, cab drivers in training spend three to four years driving around the city on mopeds, memorizing a labyrinth of 25,000 streets within a 10-kilometer radius of Charing Cross train station, as well as thousands of tourist attractions and hot spots. "The Knowledge" exams that only about 50 percent of hopeful pass.

Larger Right Posterior Hippocampus in London Taxi Drivers:

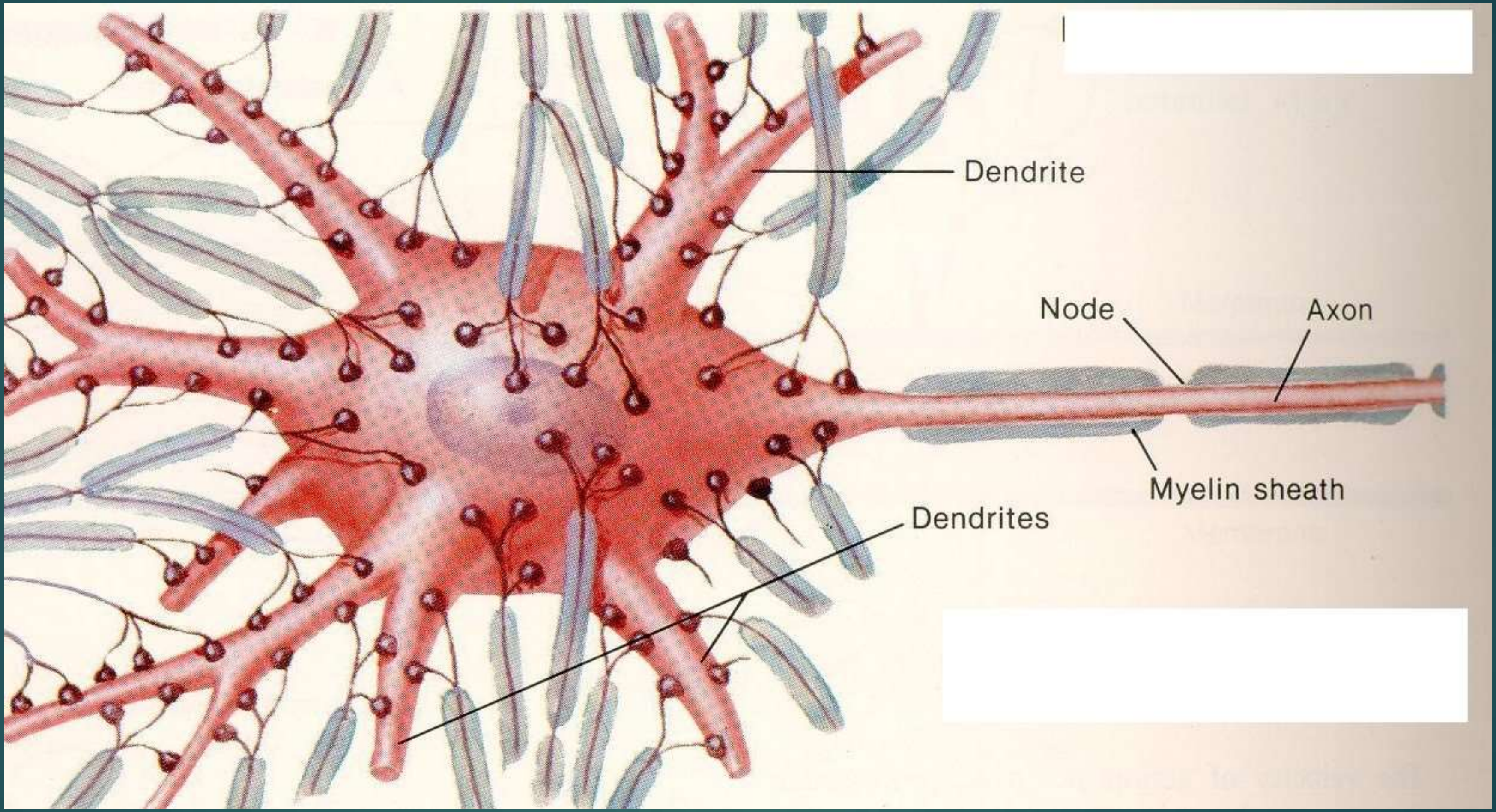
7% larger, but otherwise normal memory



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.

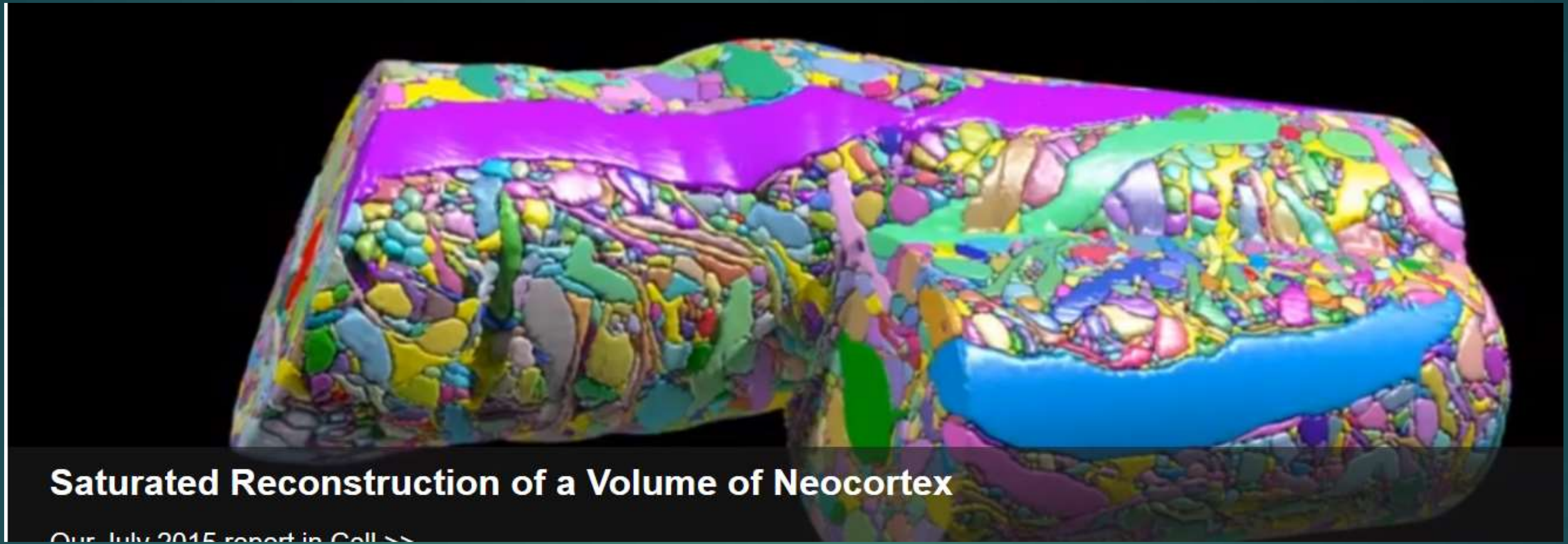
Enlarged the posterior hippocampus at the expense of the anterior

1000s of synapses per neuron



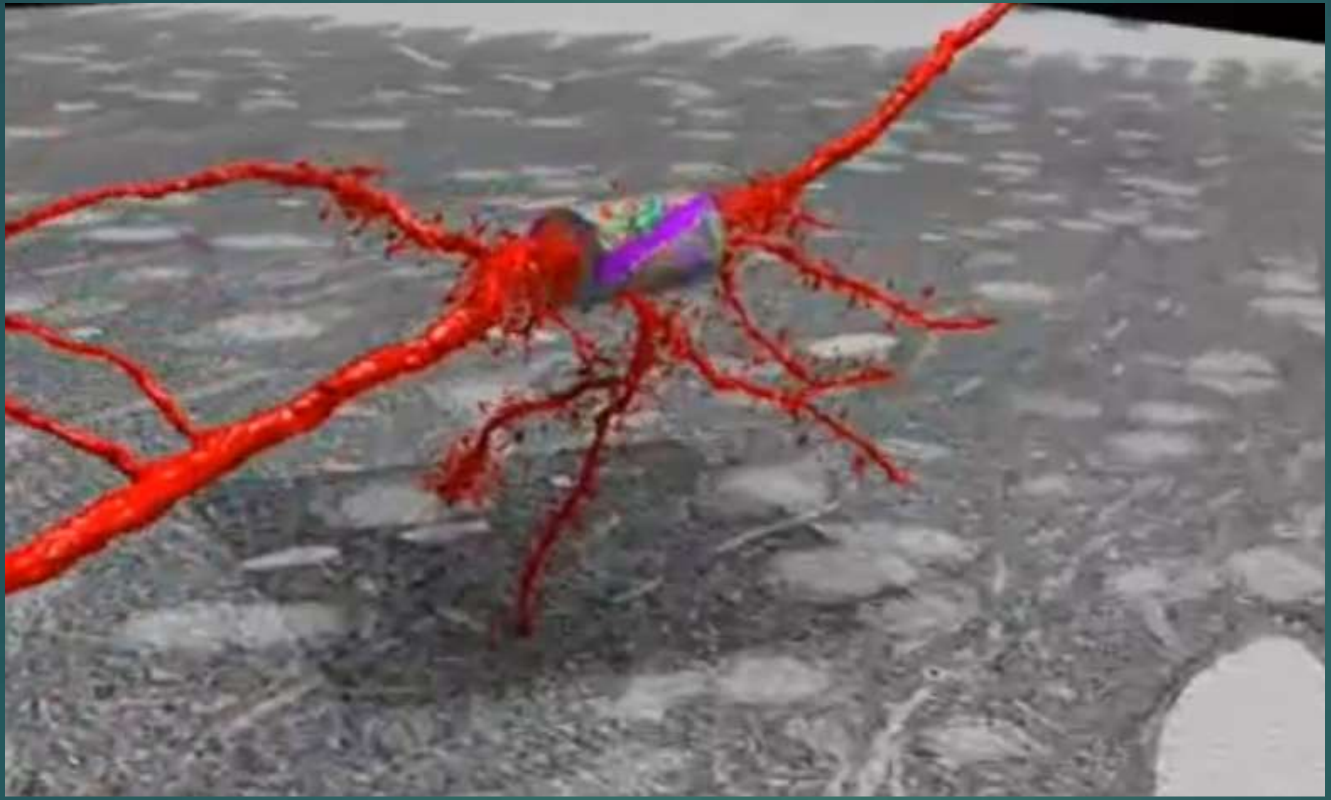
Data Estimate of brain capacity: 100-1000 terabytes of information

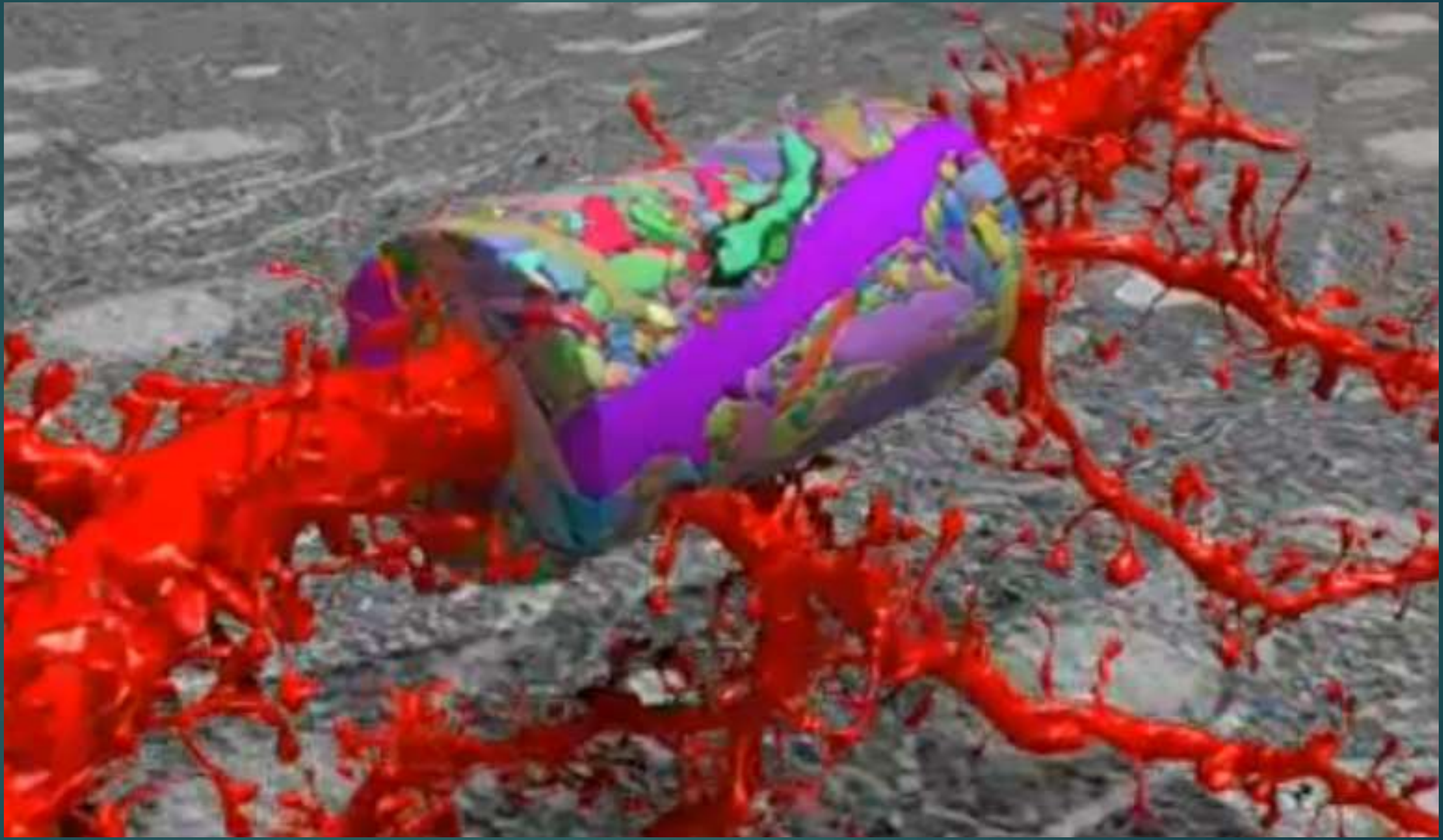
Jeff Lichtman from Harvard University 1 section of mouse brain



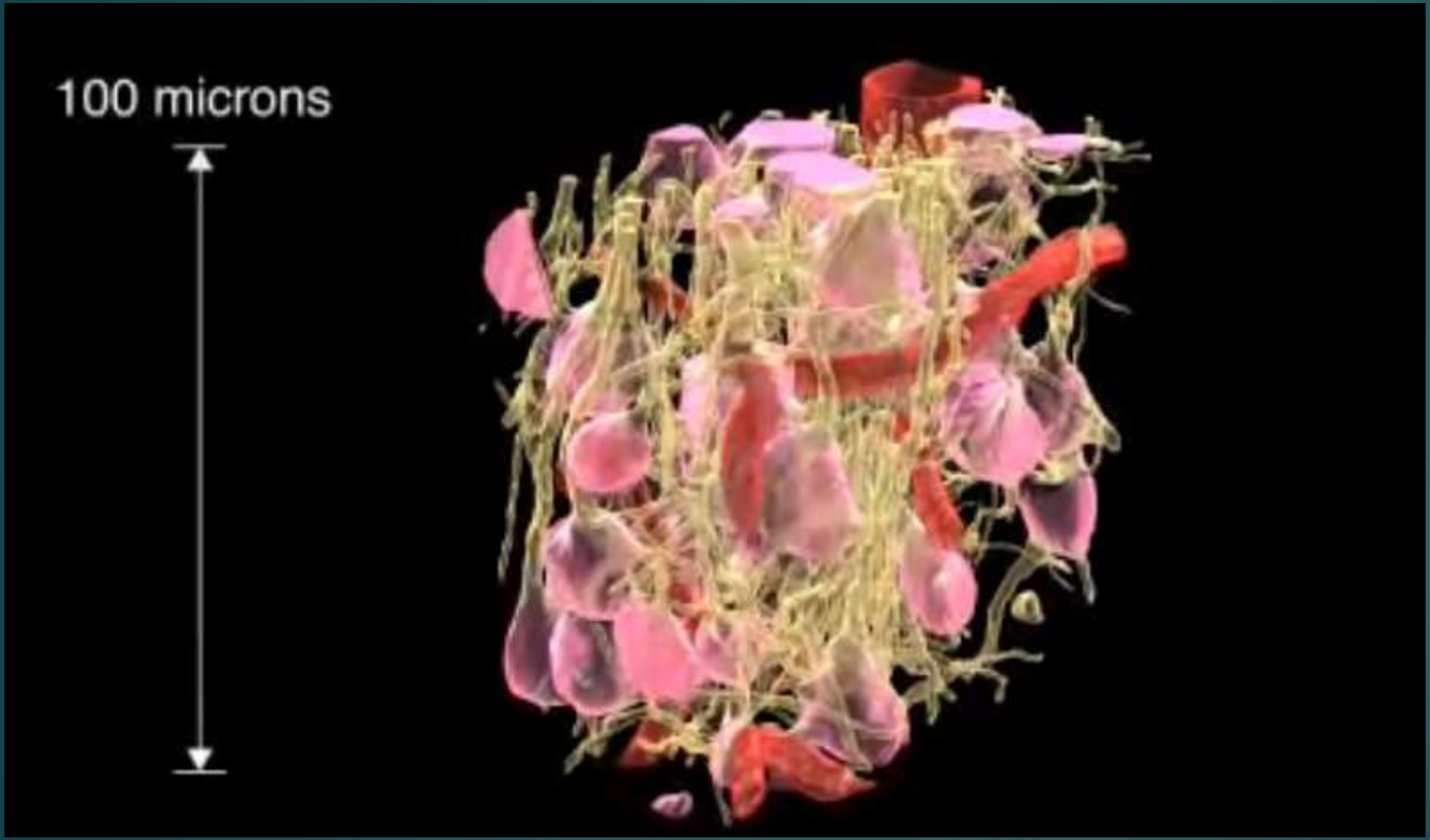
- Cylindrical EM reconstruction of a piece of mouse brain smaller than a grain of sand. In the center of this volume was the proximal shaft of a pyramidal cell apical dendrite surrounded by all manner of synaptic elements
- In this volume there are around 680 nerve fibers that can be resolved, together with 774 synapses. A key finding by Lichtman is that mere contact alone, does not a synapse make.
- Per mm, 33,000 sections

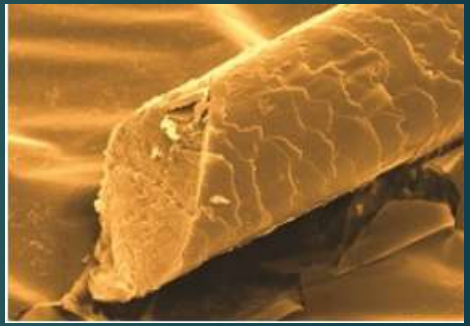
Crumb of mouse brain reconstructed in full detail





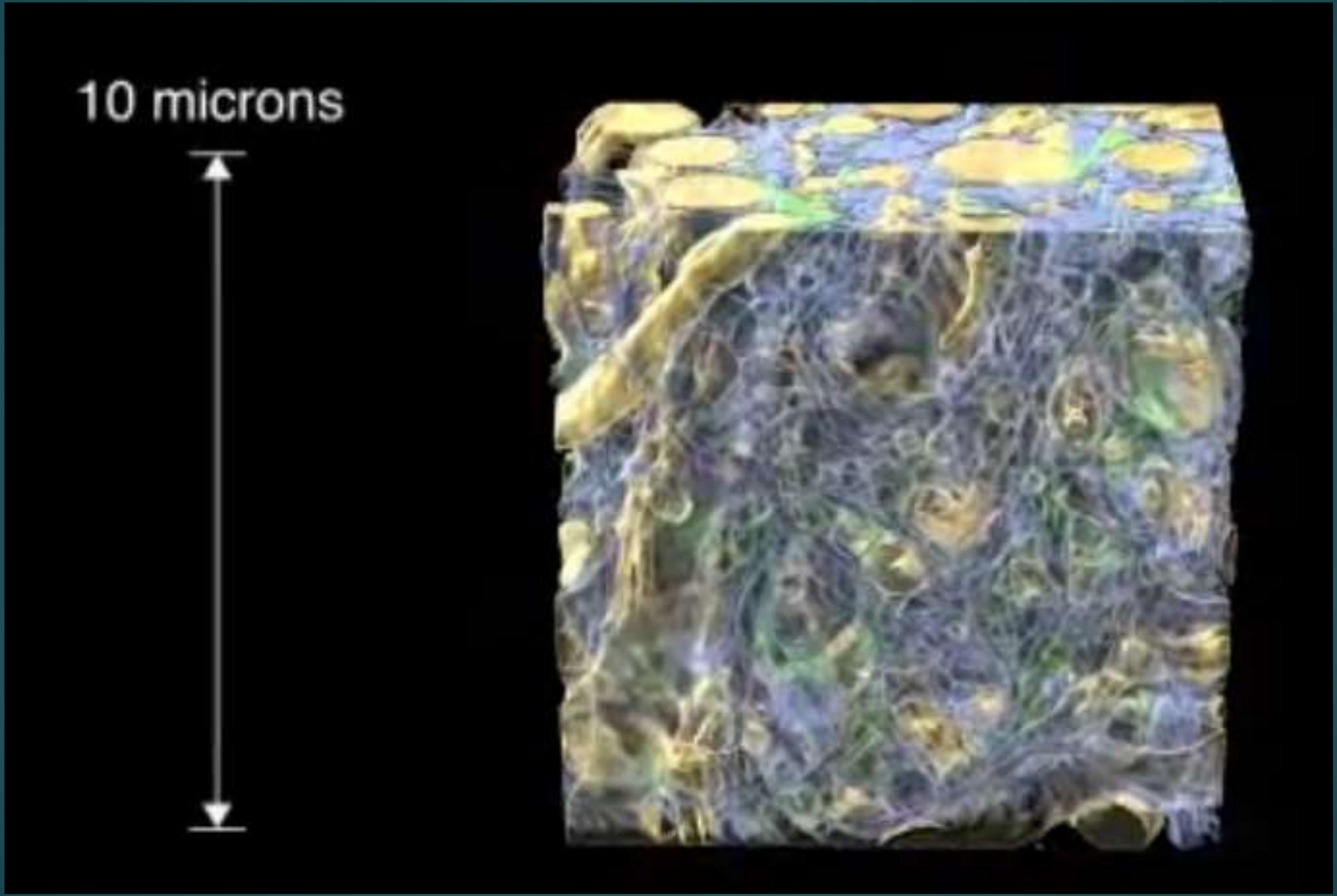
100 microns: pink = nerves; red = blood vessel; yellow = dendrites



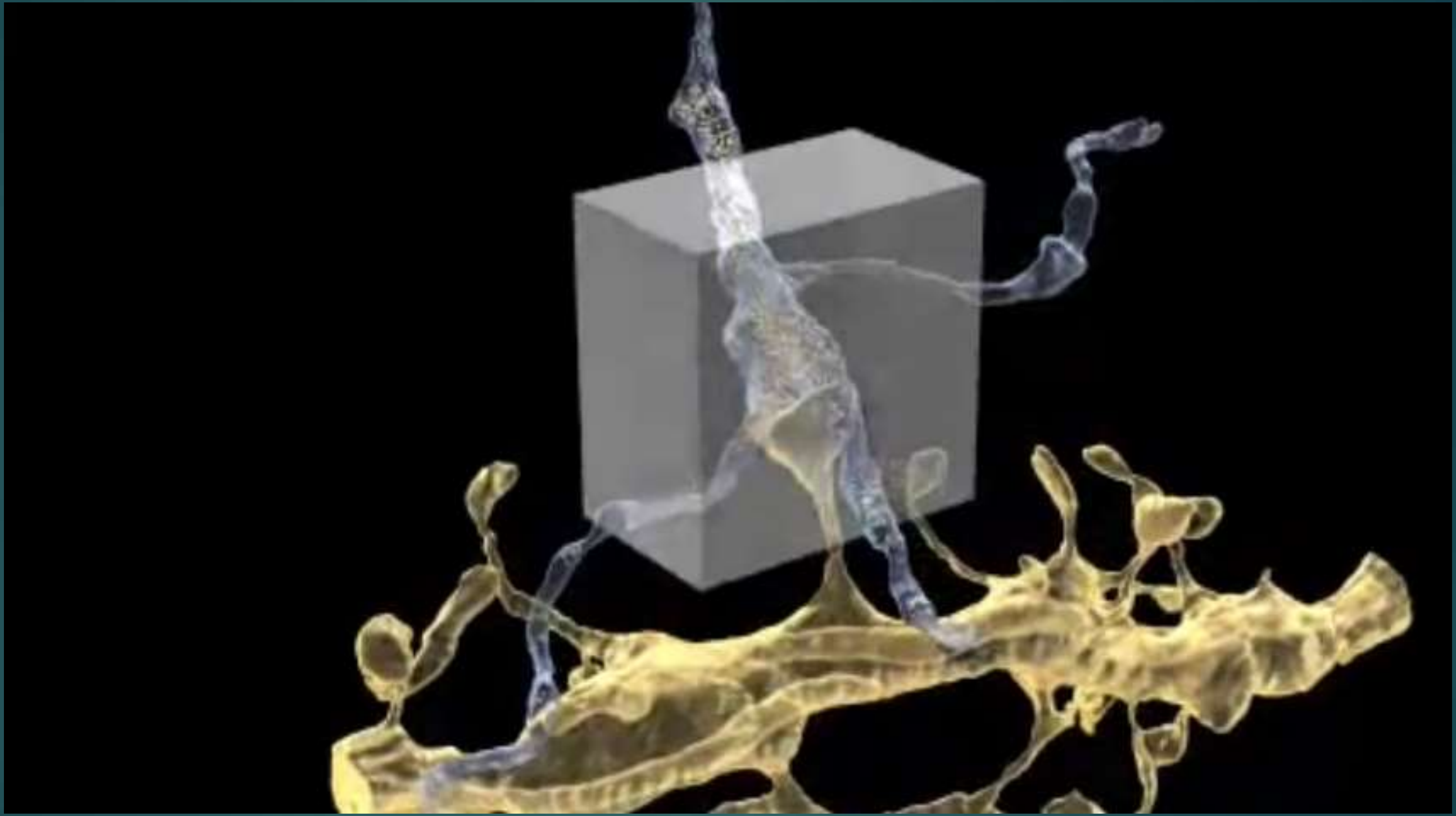


Human hair at 200x;
diameter of a hair, which
Is **40-50 microns** wide

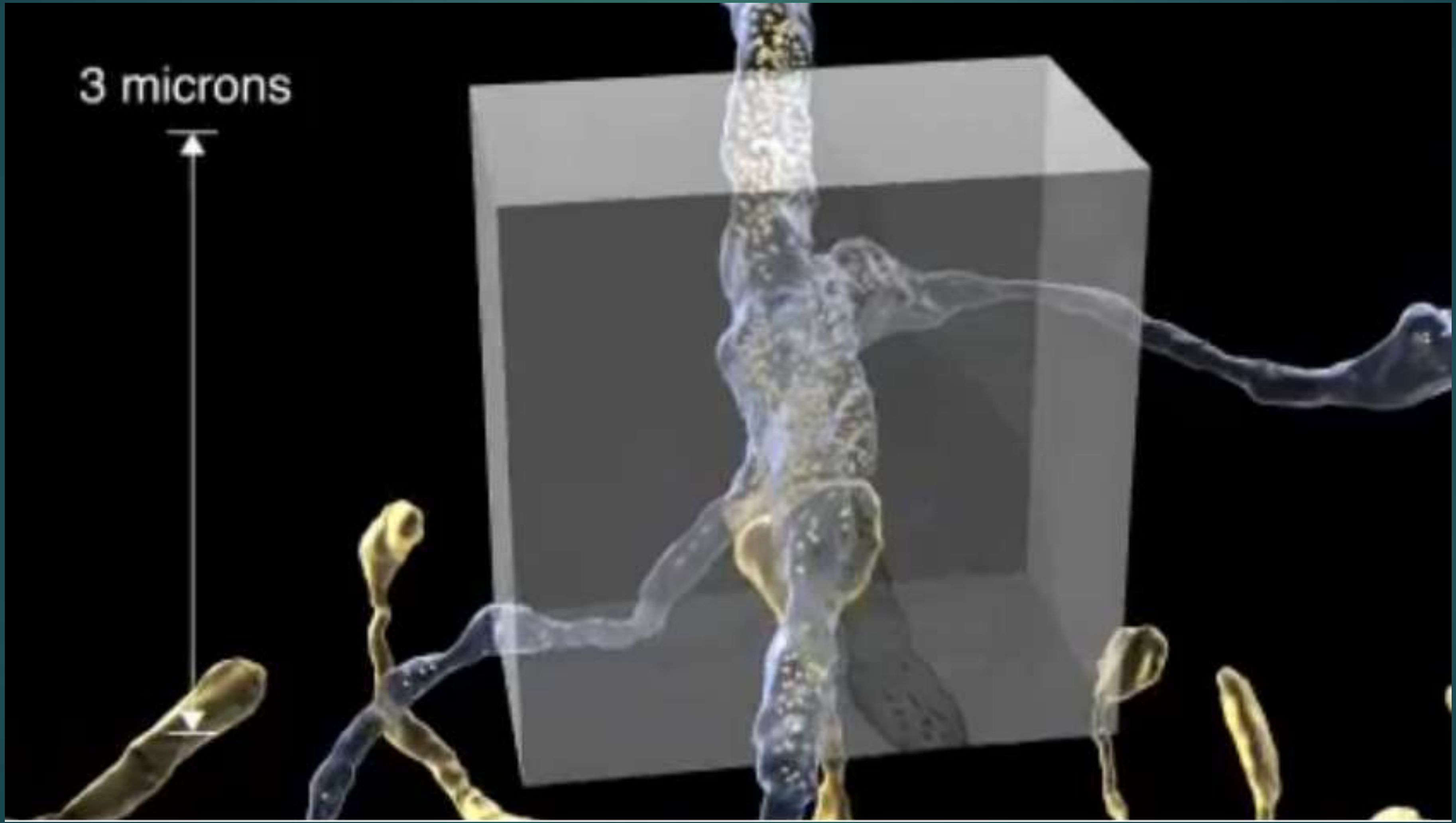
10 microns: yellow = dendrites; blue = axons



Yellow = dendrite

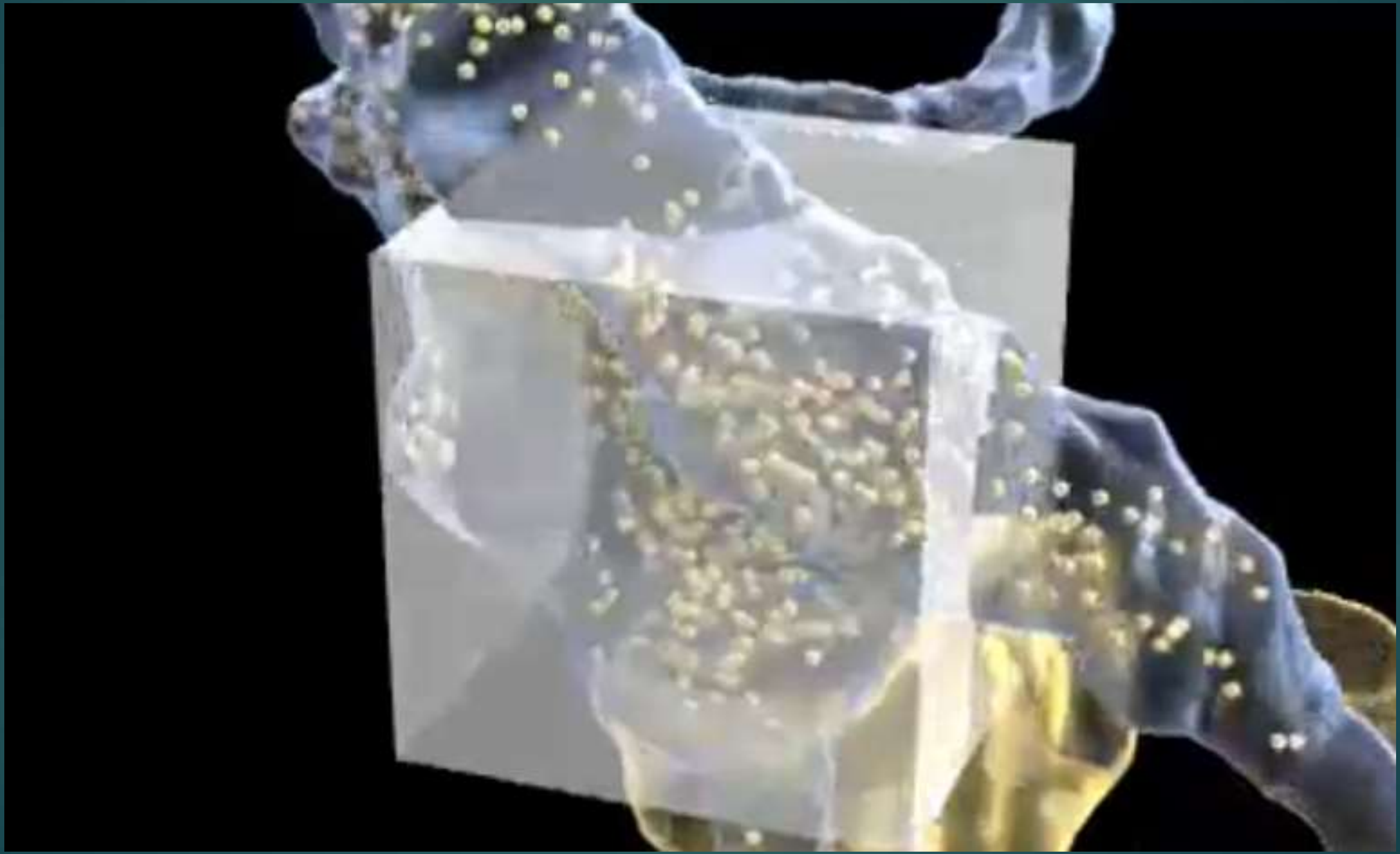


3 microns

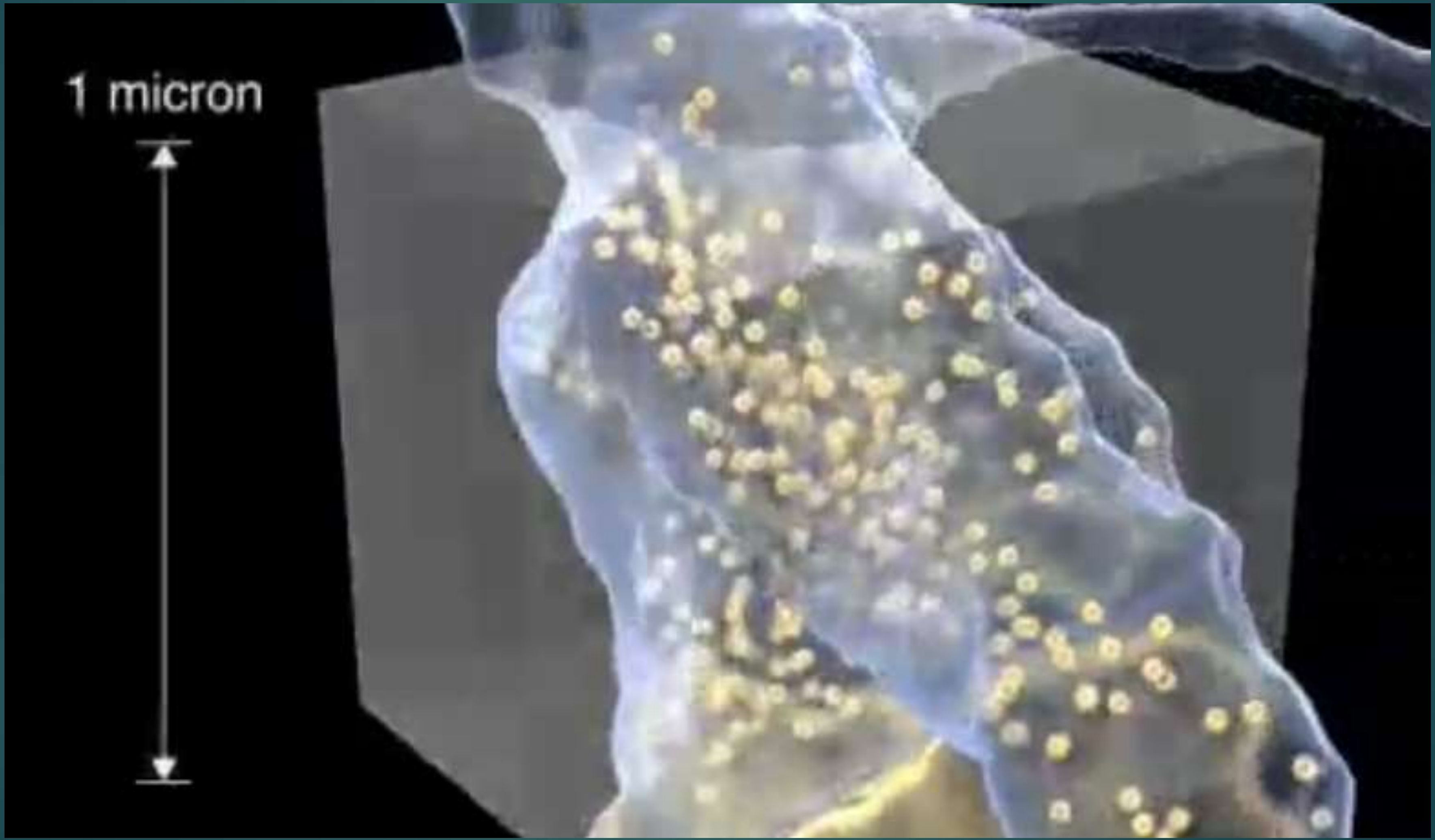


A synapse: dendrite meets axon

Synapse



1 micron

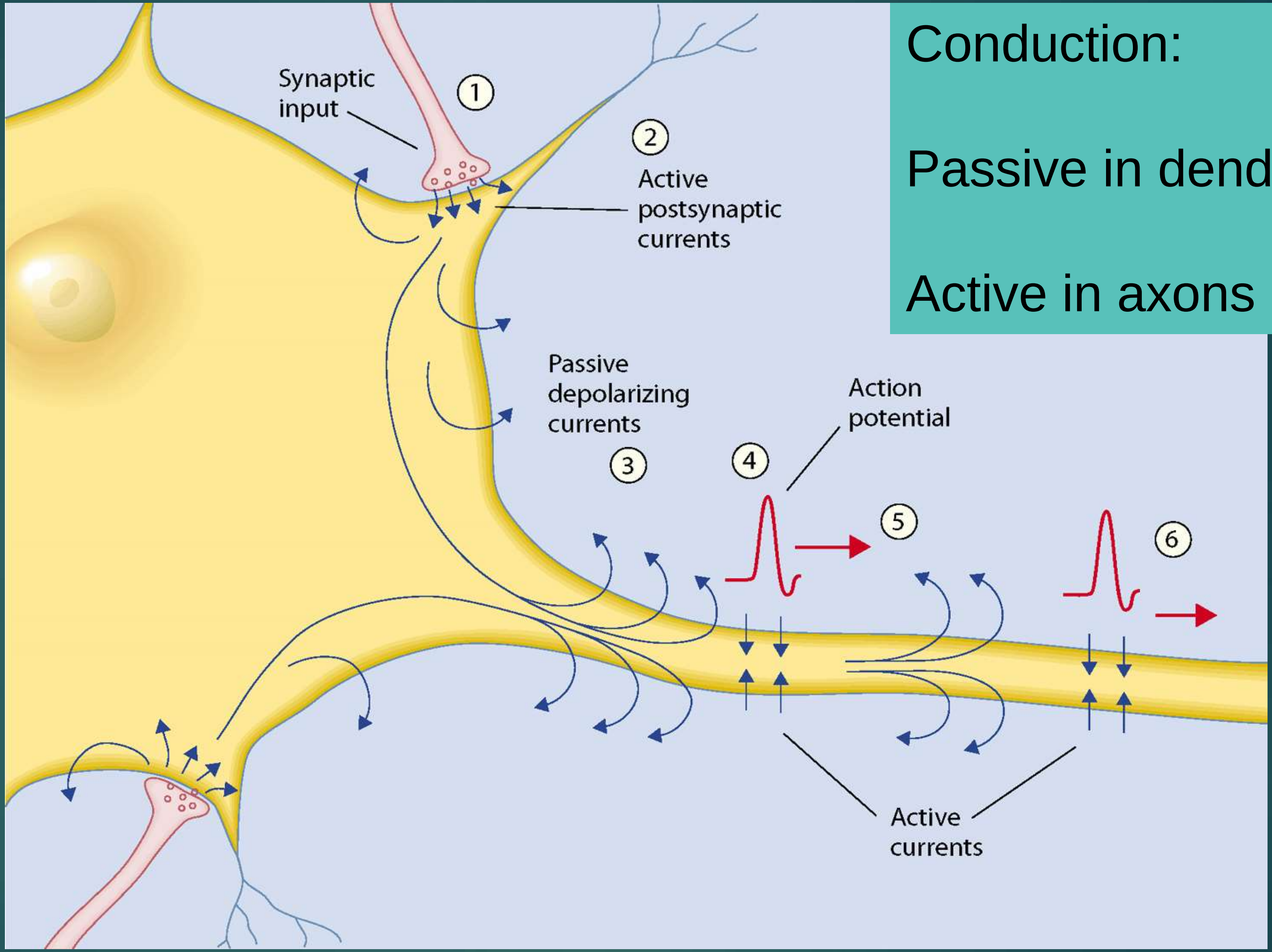


Neurotransmitter packets

Synapse

10 trillion of these synapses

Electrical signaling within neuron & across axon



Conduction:

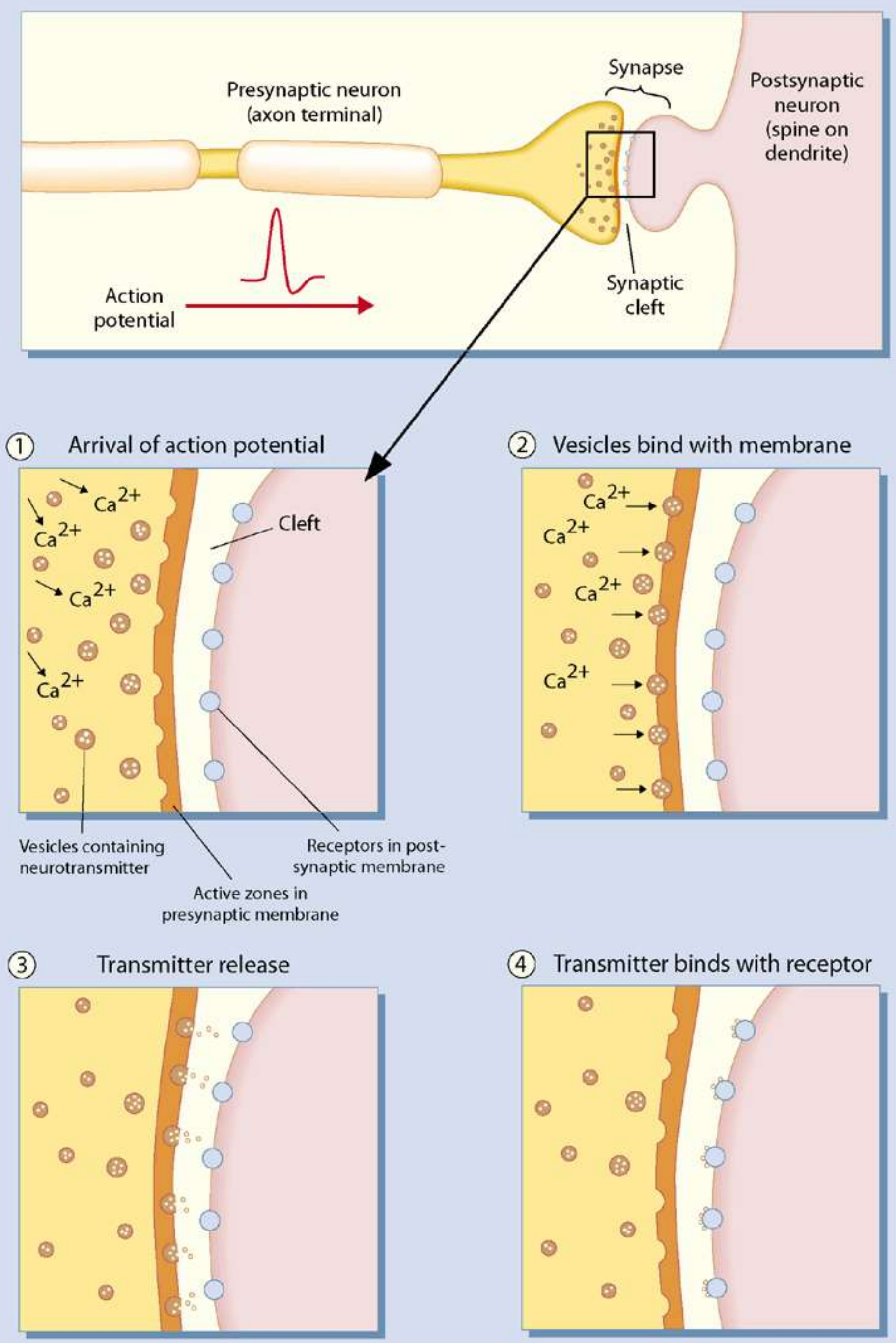
Passive in dendrites

Active in axons

Resting potential of neurons is -70mV; At rest, neurons have greater concentration Of NA+, Cl- & Ca2+ outside cell, and K+ inside cell.

Neurochemical transmission across the synapse

Axon to Dendrite



Neurotransmitters: 63 in brain

- Standard text: Stahl's *Essential Psychopharmacology*: Stephen M. Stahl (2013): 63 molecules
- Acetylcholine: arousal; diffuse; memory & attention; major projection area is the nucleus basalis of Meynert; 2 receptors (muscarinic & nicotinic)
  - anticholinergic drugs = negative cognitive effects
  - Aricept = antiacetylcholinesterase inhibitor
- Glutamate: most abundant excitatory; diffuse; NMDA receptor → LTP, synaptic plasticity, & neurogenesis = experience dependent memory; toxic if too much;
  - Memantine for AD
- GABA: the primary inhibitory (fast); diffuse; neuromodulation; memory, anxiety, sleep/arousal, attentional shift
  - anti-anxiety drugs

Neuromodulatory neurotransmitters 2

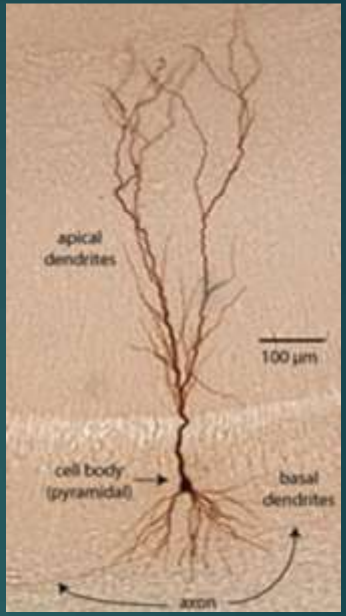
- Dopamine: neuromodulatory; alertness, anticipation; projections from substantia nigra, ventral tegmentum, hypothalamus;
  - 3 subsystems;
    - 1 – mesostriatal - Parkinsonism;
    - 2 – mesolimbic – reward, addictions; positive sxs in schizophrenia;
    - 3 – mesocortical – EF, WM, attention, motor initiation; neg. sxs of schizophrenia
- Norepinephrine: neuromodulatory; alertness, attentional shifting; mood; pain; reward from locus coeruleus & lateral tegmentum; involved in depression, bipolar, OCD;
  - ADHD meds increase it
- Serotonin: neuromodulatory: from raphe nuclei; involved in anxiety, depression, OCD, aggression, eating disorders, suicide; but S-less mouse (no depression)
  - Selective serotonin reuptake inhibitors, i.e. Prozac

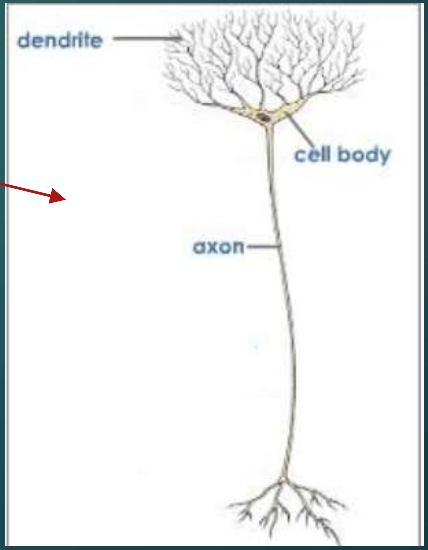
Cortex: 2 types of cells

- In humans, 90% of the cerebral cortex is neocortex.

- Neocortex contains two primary types of neurons:
  - excitatory pyramidal neurons (~80% of neocortical neurons)
    - 2 types of excitatory glutamatergic neurons
  - inhibitory interneurons (~20%)
    - 15 types of inhibitory GABAergic

- Pyramidal neurons are the primary excitation units of the mammalian prefrontal cortex and the corticospinal tract.





15 major types of interneurons

- each exhibited a characteristic pattern of connectivity with other interneuron types and pyramidal cells

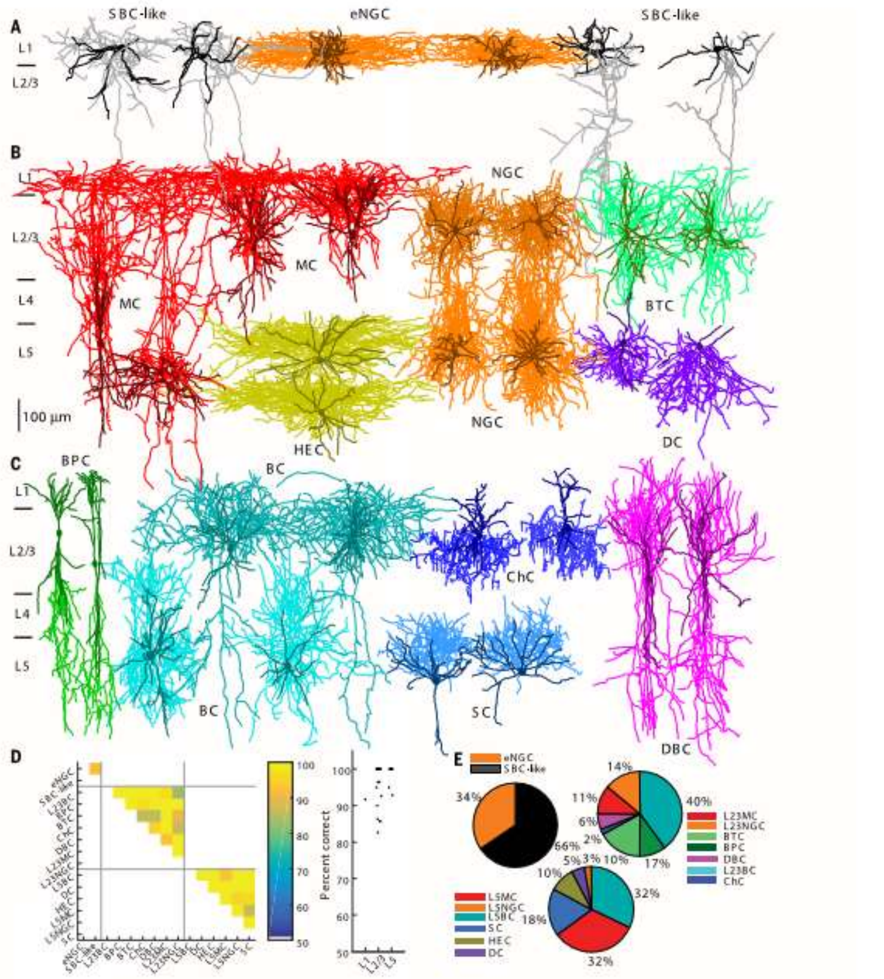
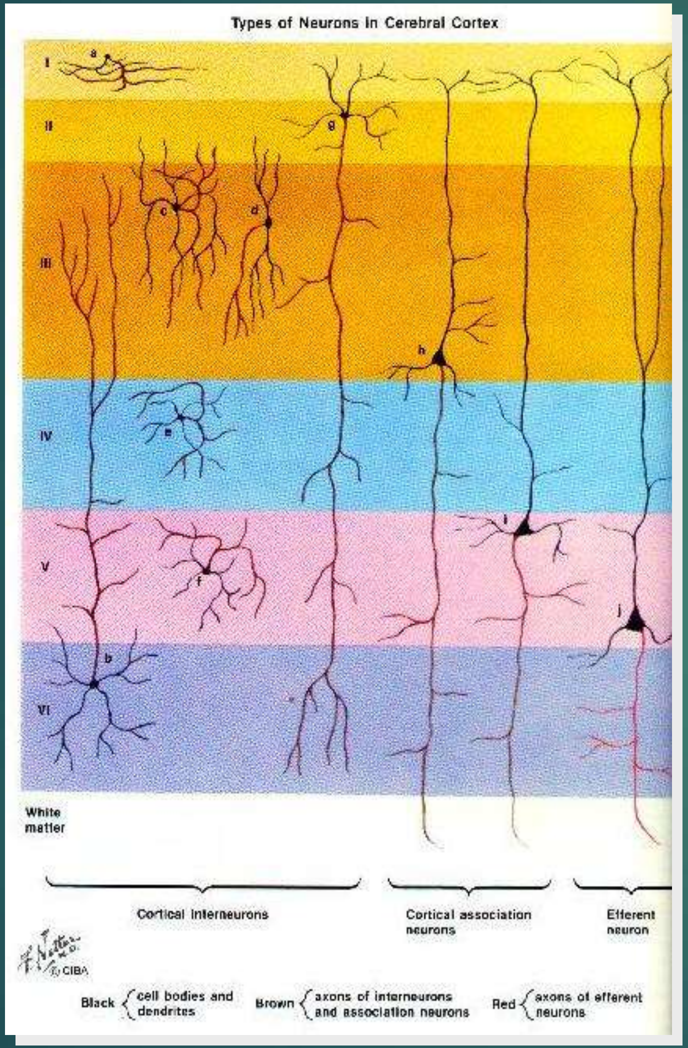
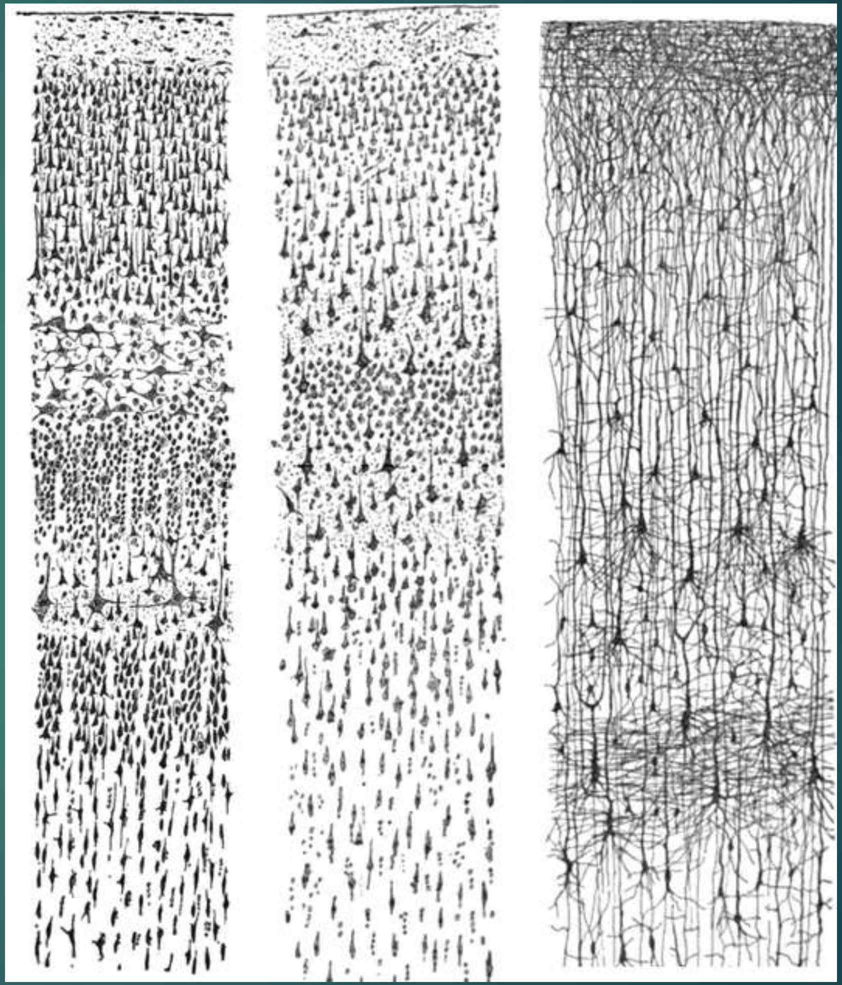


Fig. 1. Morphologically distinct GABAergic interneurons in L1, L23, and L5 of V1. (**A**) Two eNGCs (two middle; axon in dark orange and dendrite in brown) and four SBC-like cells. SBC-like cells on the left (two leftmost; axon in gray) have the axon arborizing mostly within layer 1, whereas SBC-like cells on the right (two rightmost; axon in gray) have the axon projecting mostly toward the deep layers. (**B**) Four MCs (both L23 and L5; axon in red and dendrite in dark red), four NGCs (L23 and L5; axon in orange and dendrite in brown), two HECs (axon in yellow and dendrite in dark yellow), two BTCs (axon in aquamarine and dendrite in green), and two DCs (axon in blue violet and dendrite in dark blue). (**C**) Two BPCs (axon in lime and dendrite in green), four BCs (both L23 and L5; axons in cyan and dendrite in dark cyan), two ChCs (axon in blue and dendrite in dark blue), two DBCs (axon in magenta and dendrite in purple), and two SCs (axon in dodge blue and dendrite in dark blue). (**D**) (Left) Cross-validated classification performance for each pair of cell types within a layer. (Right) Classification performance collapsed within each layer. (**E**) The proportion of each morphologically distinct type of interneurons.

Xiaolong Jiang, et al., Science, 2015

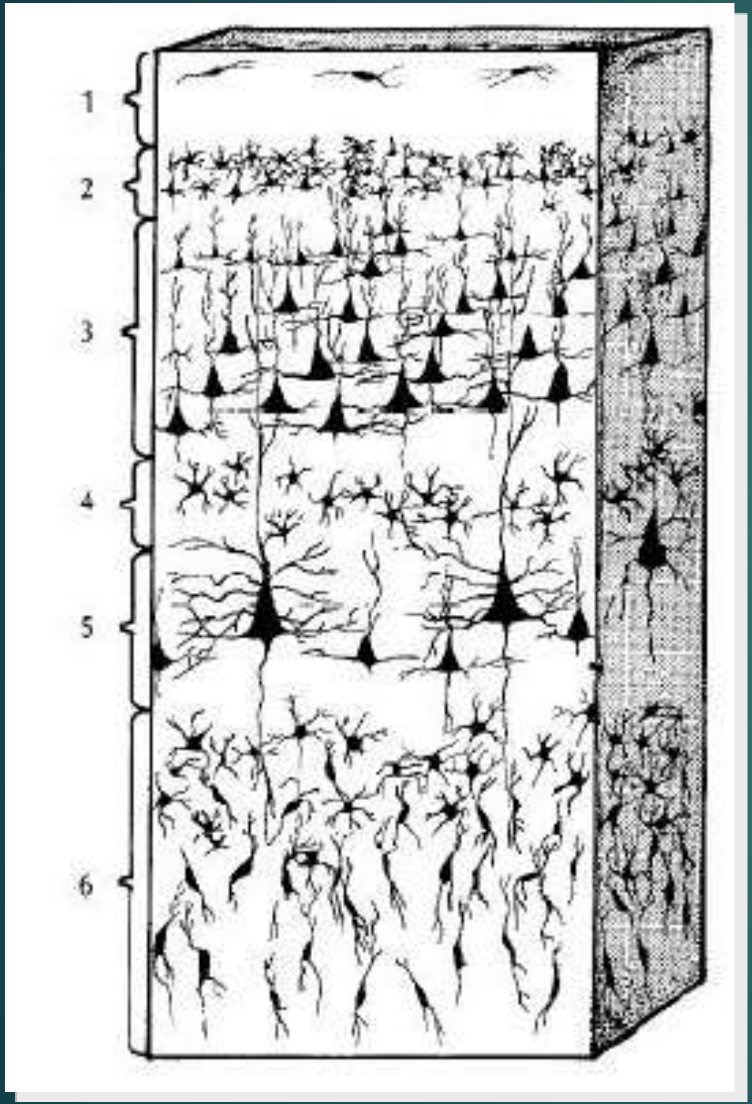
Cortical Layerization: 6 layers





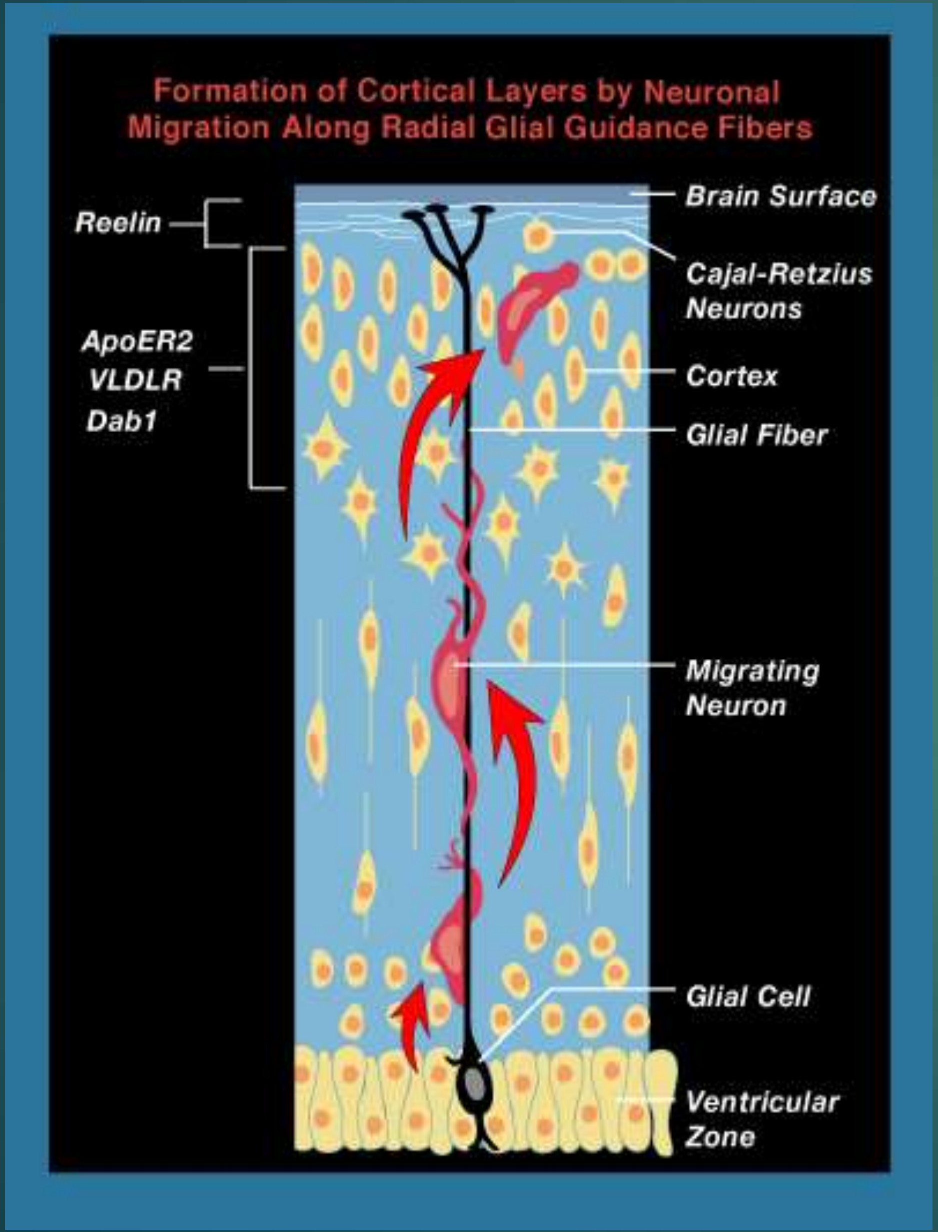
Limbic cortex has only 3 layers

Cortical Layer Organization



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

Neuronal Migration: Follow that Glial Cell

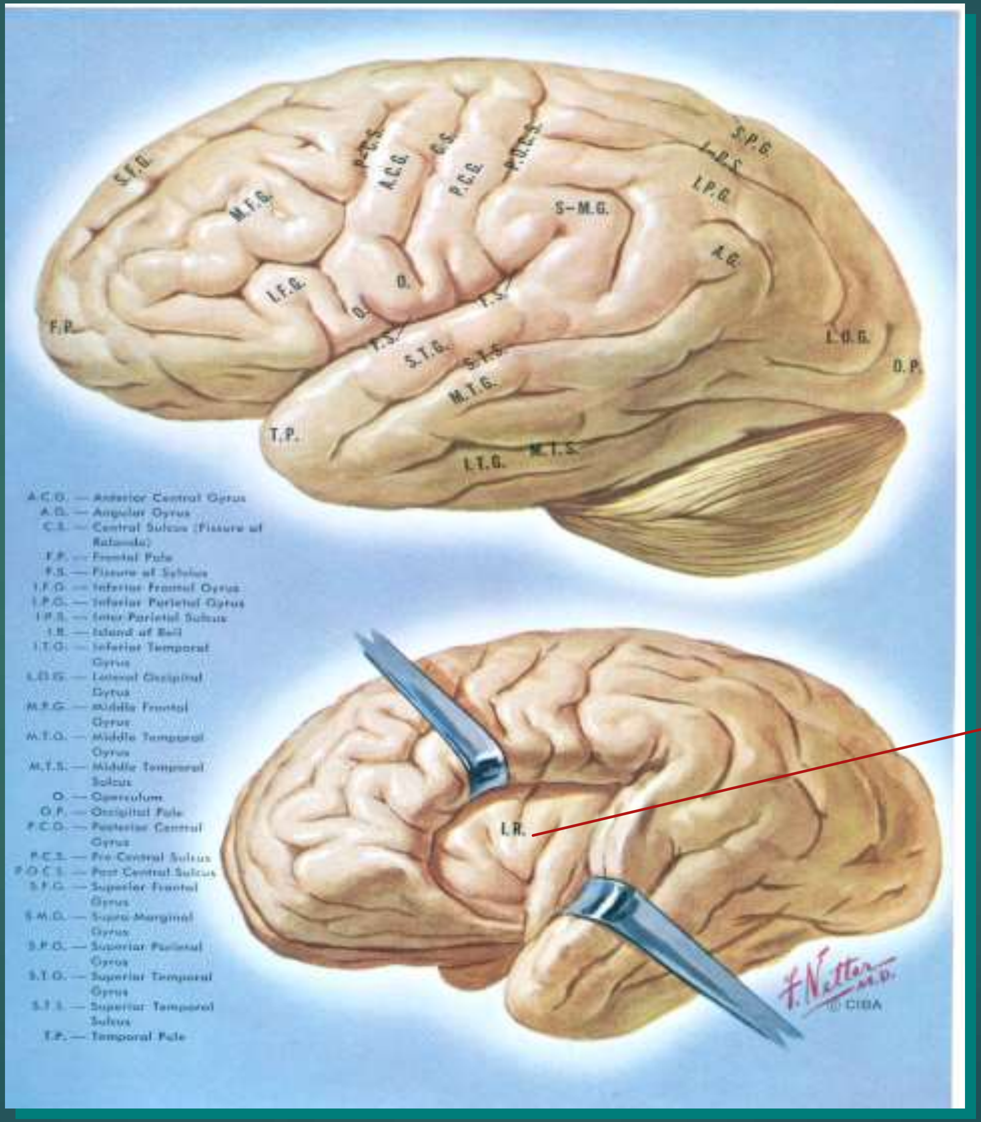


Radial glia –
Guide neuronal development

Cortical layers are created by neurons following glial fibers

Gyri = Hills

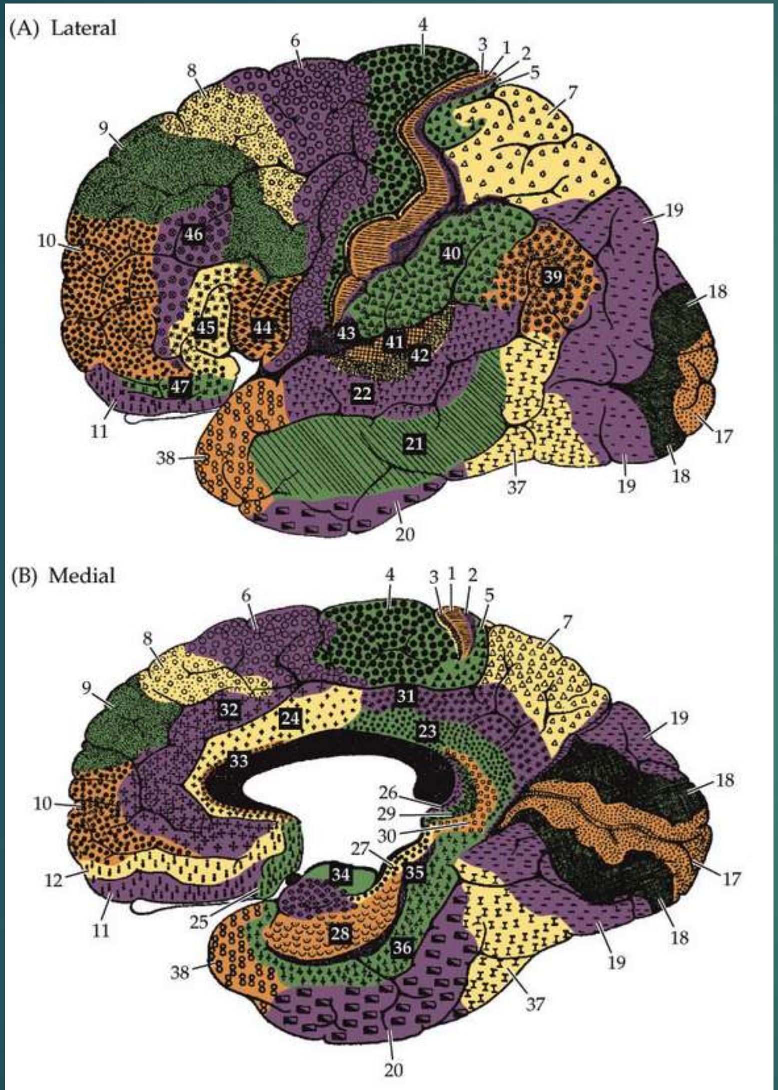
Sulci = Valleys

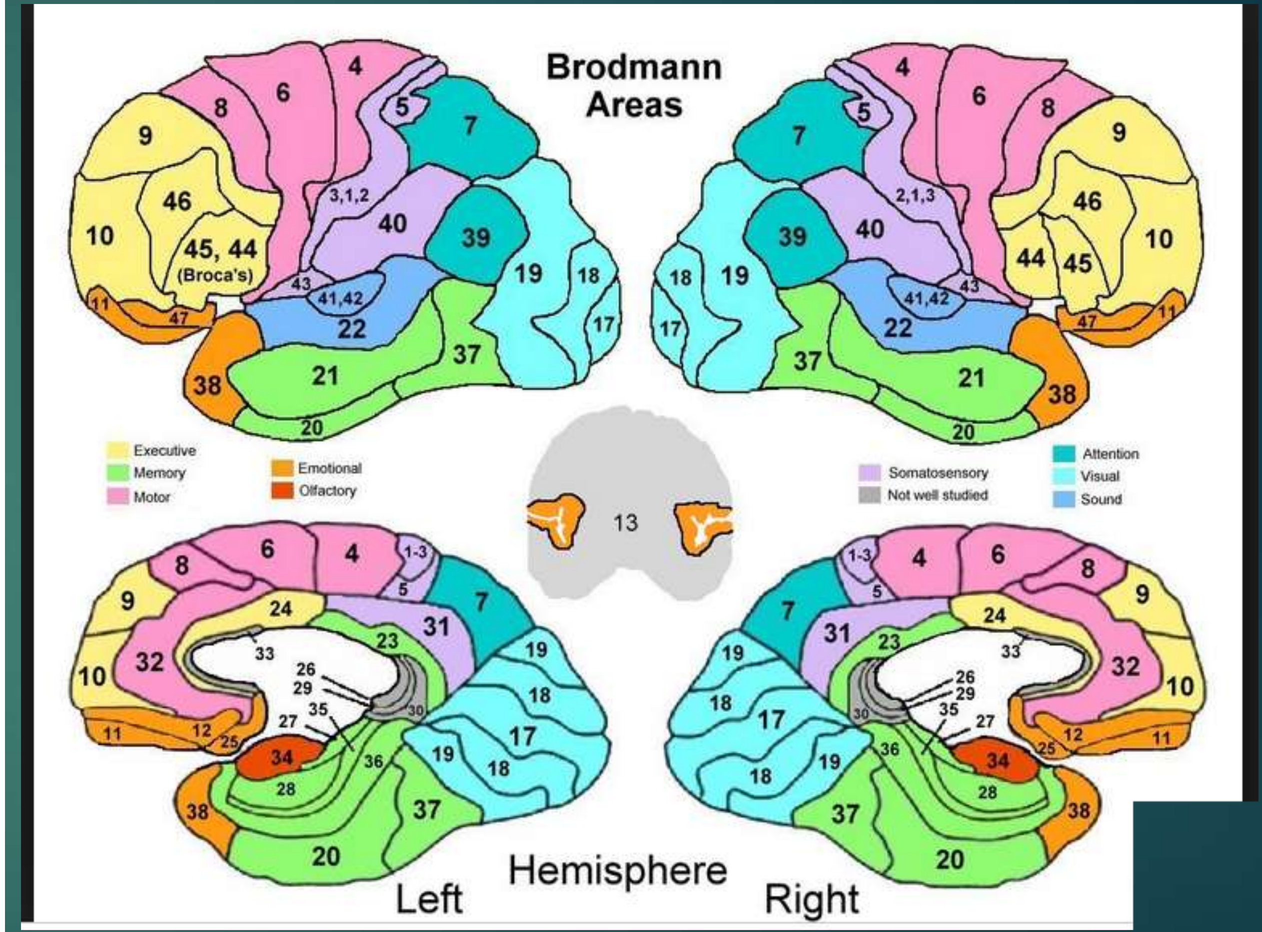


Insula

1909 Cytoarchitecture: Brodmann’s 52 Areas

Defined by its cytoarchitecture, or histological structure and organization of cells

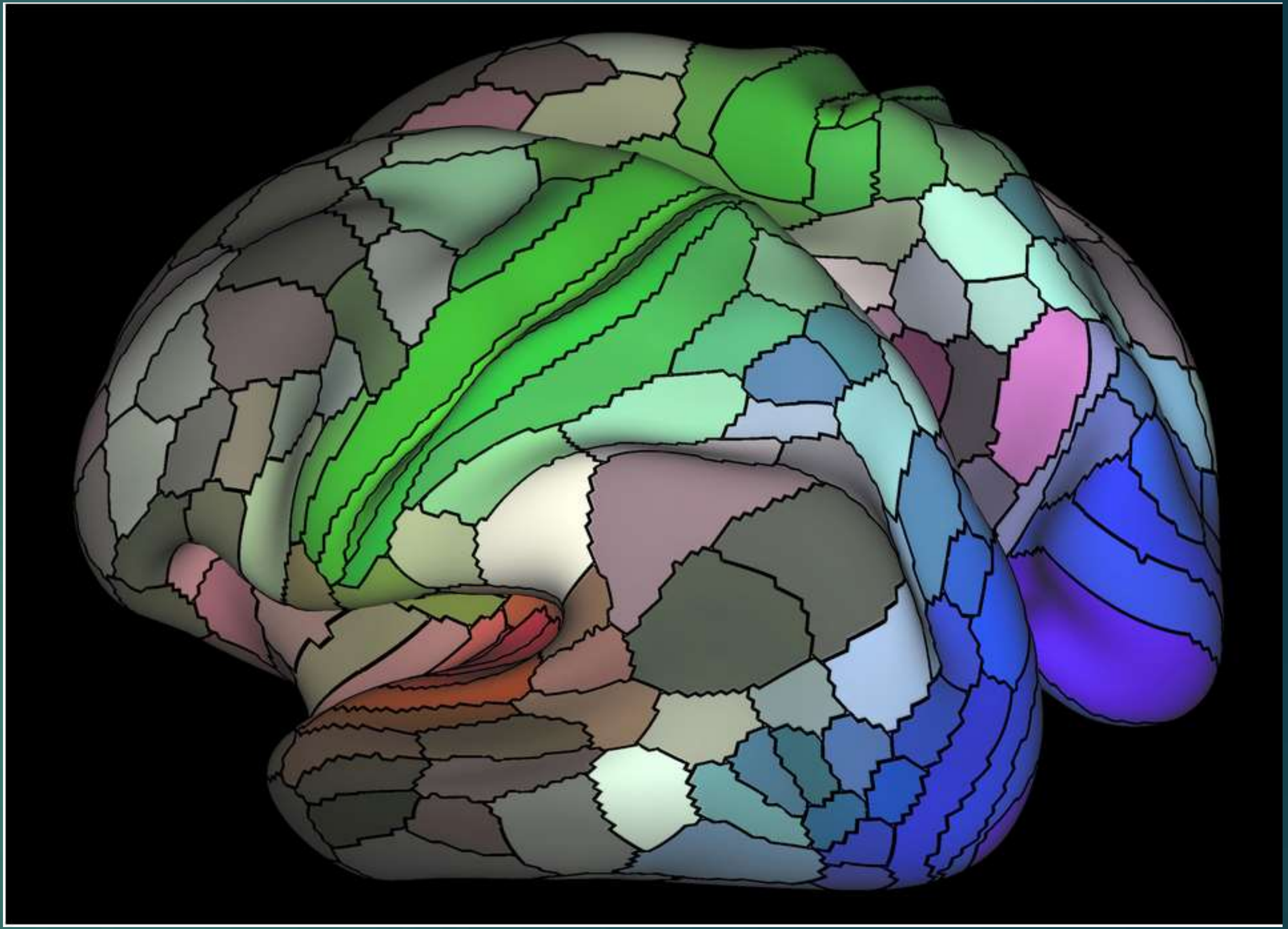




Korbinian Brodmann, 1909

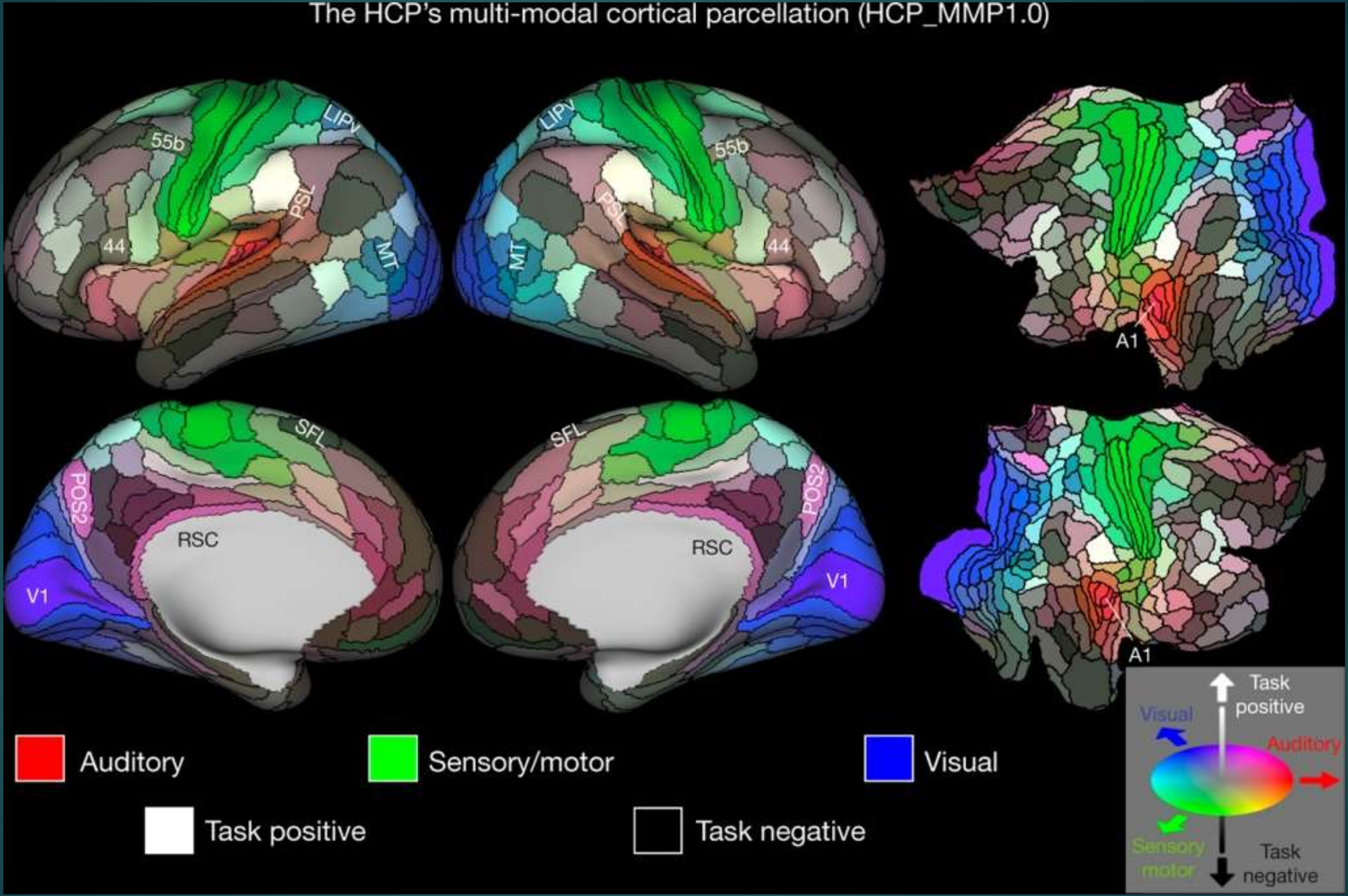
2016 Ultimate brain map: 180 areas per hemisphere

- Brain's cortex, or outer mantle, is composed of 180 distinct areas per hemisphere based on new imaging study of function, structure, & interconnectivity of each area in 100s of individuals. 97 new areas
- Areas connected to the three main senses - hearing (red), touch(green) vision (blue) and opposing cognitive systems (light and dark).
- The Human Connectome Project.



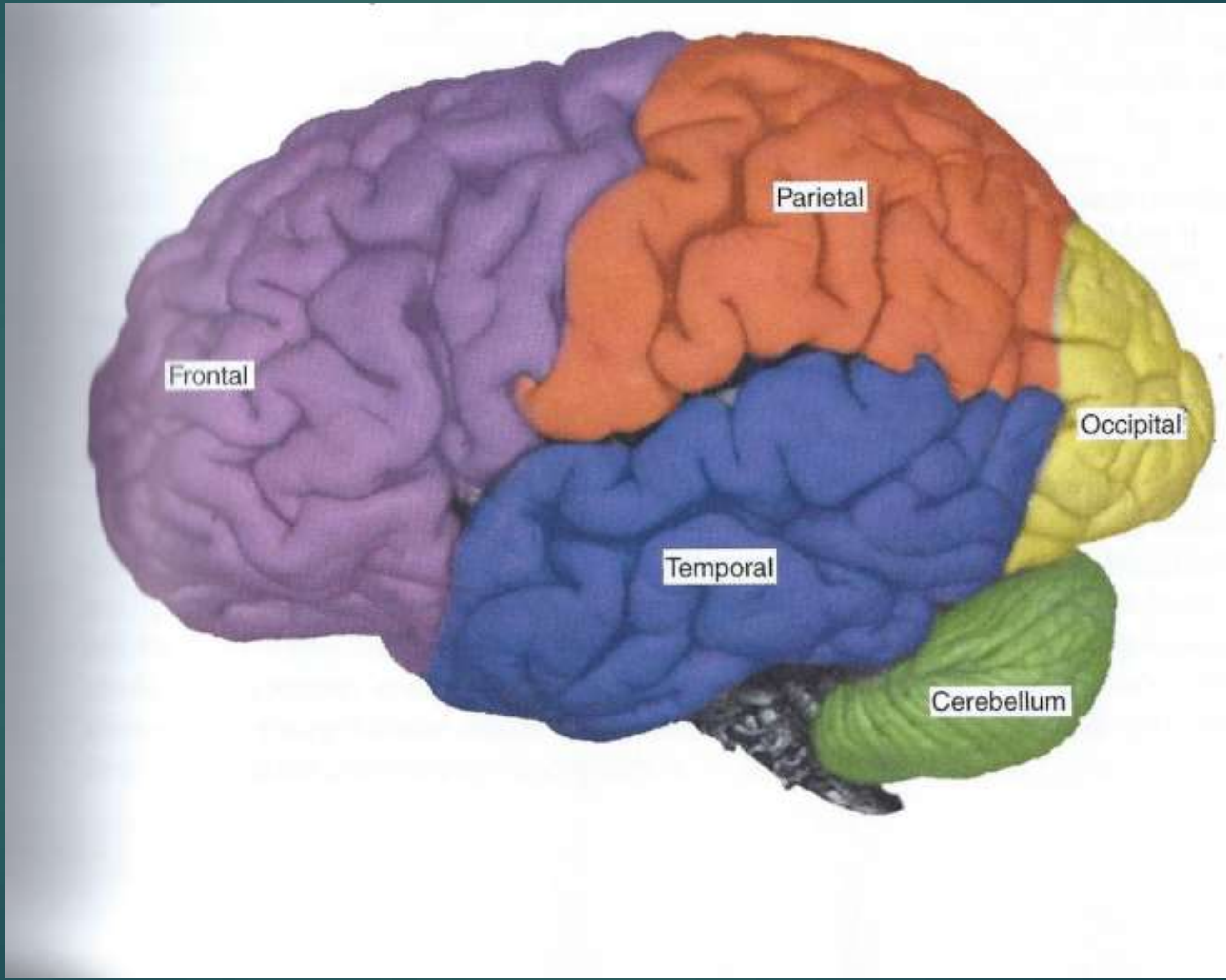
Replaces Boardman's areas

M F Glasser *et al.* *Nature* 1–8 (2016)



M F Glasser *et al. Nature* 1–8 (2016) doi:10.1038/nature18933

Brain's 4 lobes



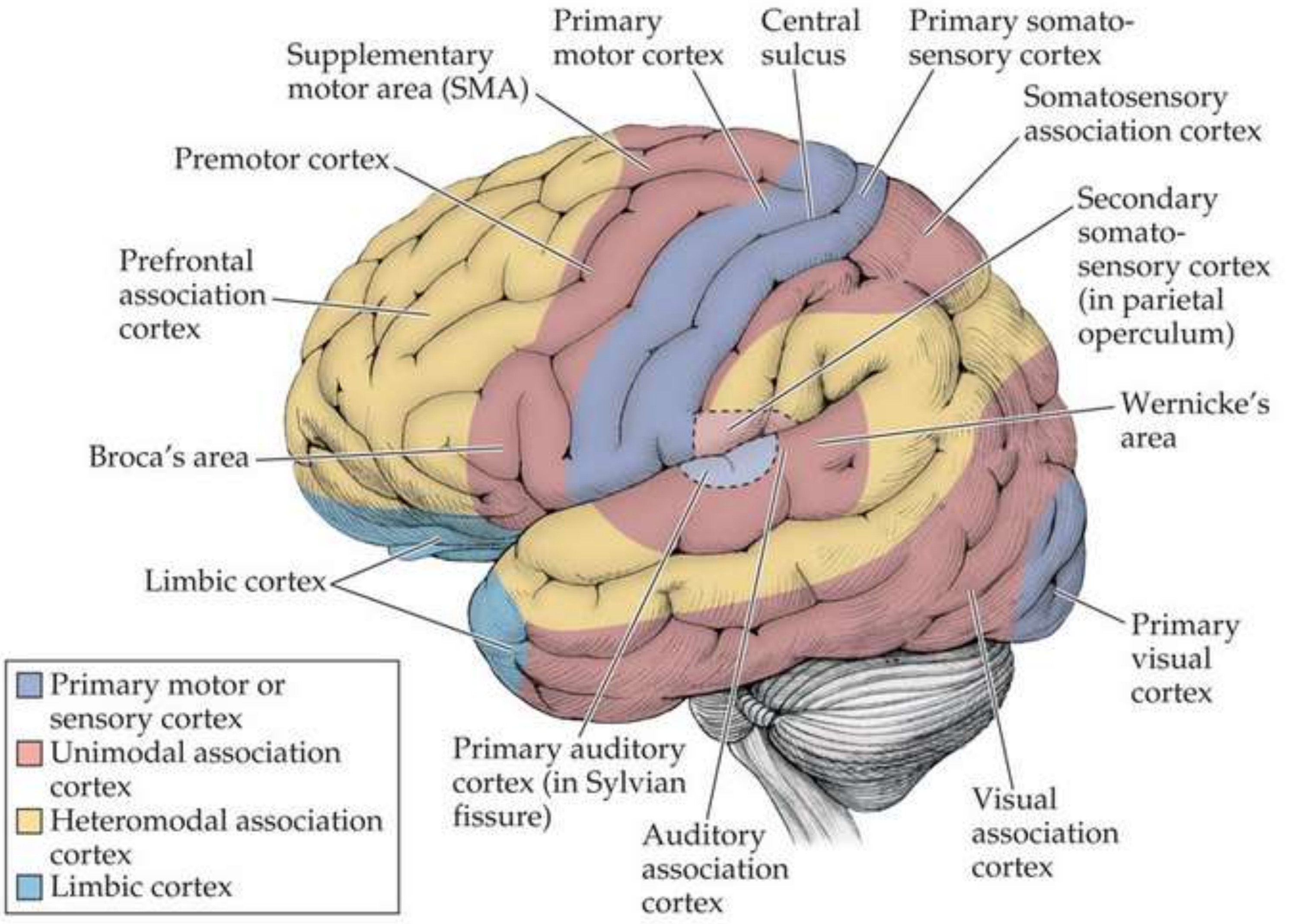
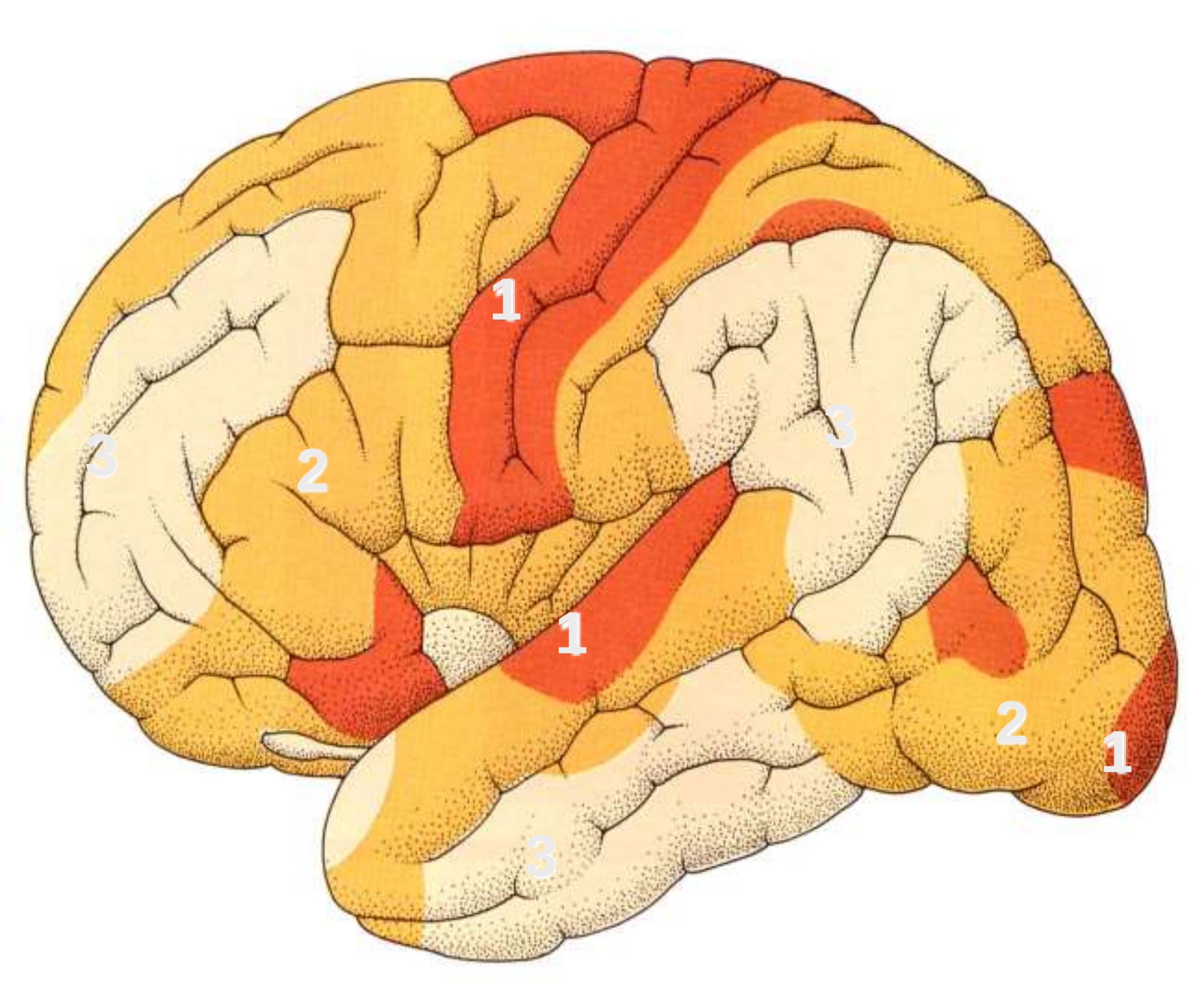


Figure 2.25 Association Cortex Lateral view of left hemisphere showing main areas of primary sensory and motor cortex,

Primary = direct perception; Unimodal Association = single perceptual processing
Heteromodal association (yellow)= multisensory, multimodal, higher cognitive processing

Order of Cortical Maturation



1 – Sensorimotor & primary areas; 2 – secondary areas; 3 – Association areas

Perception: Primary Sensory Areas

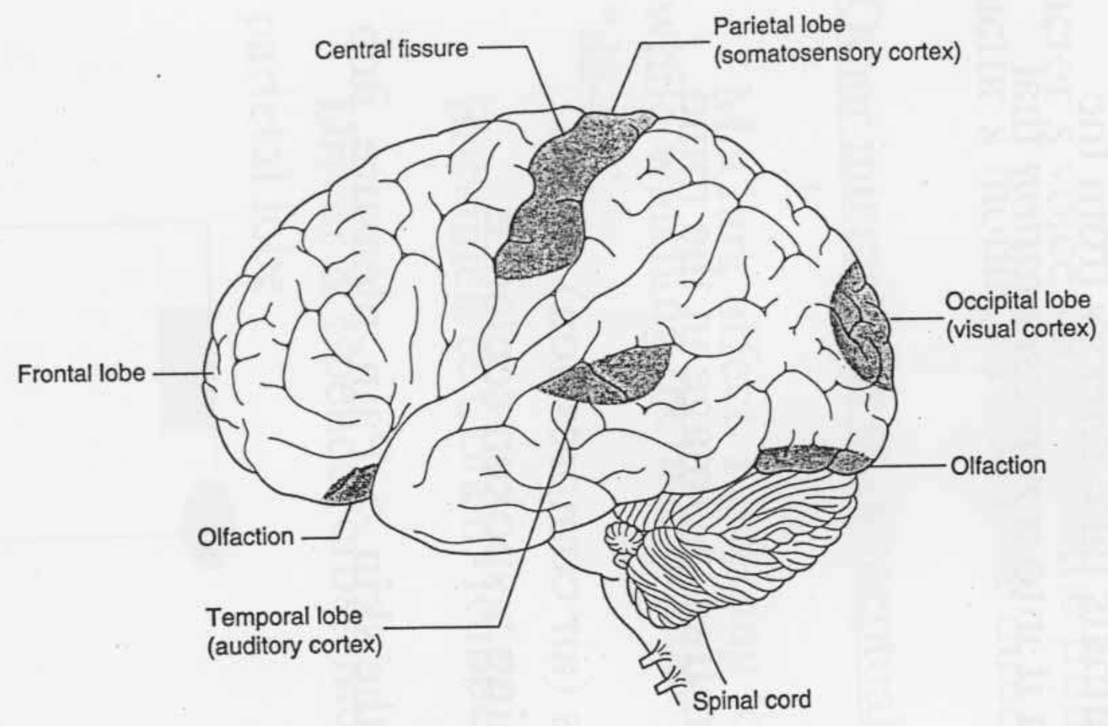
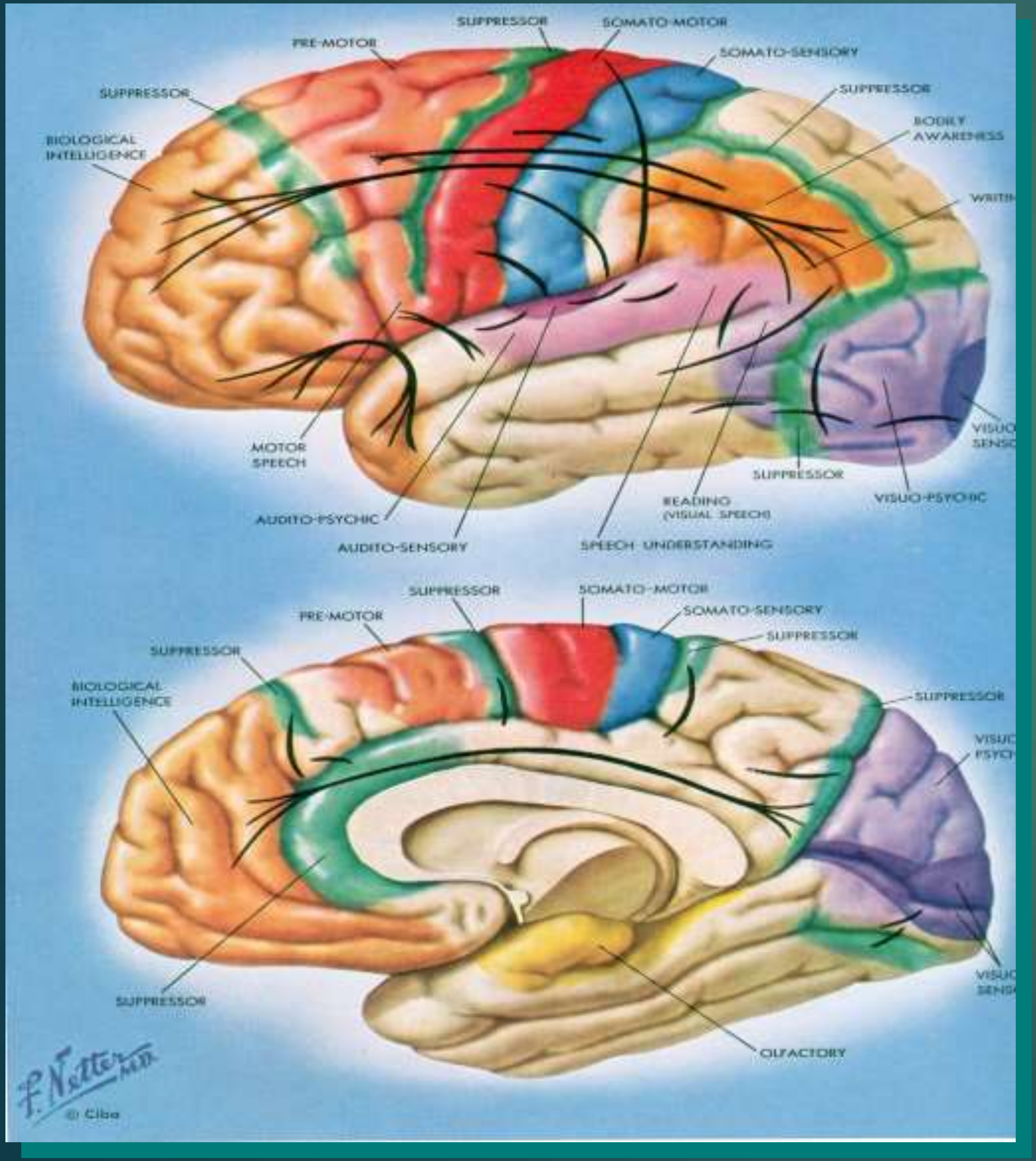
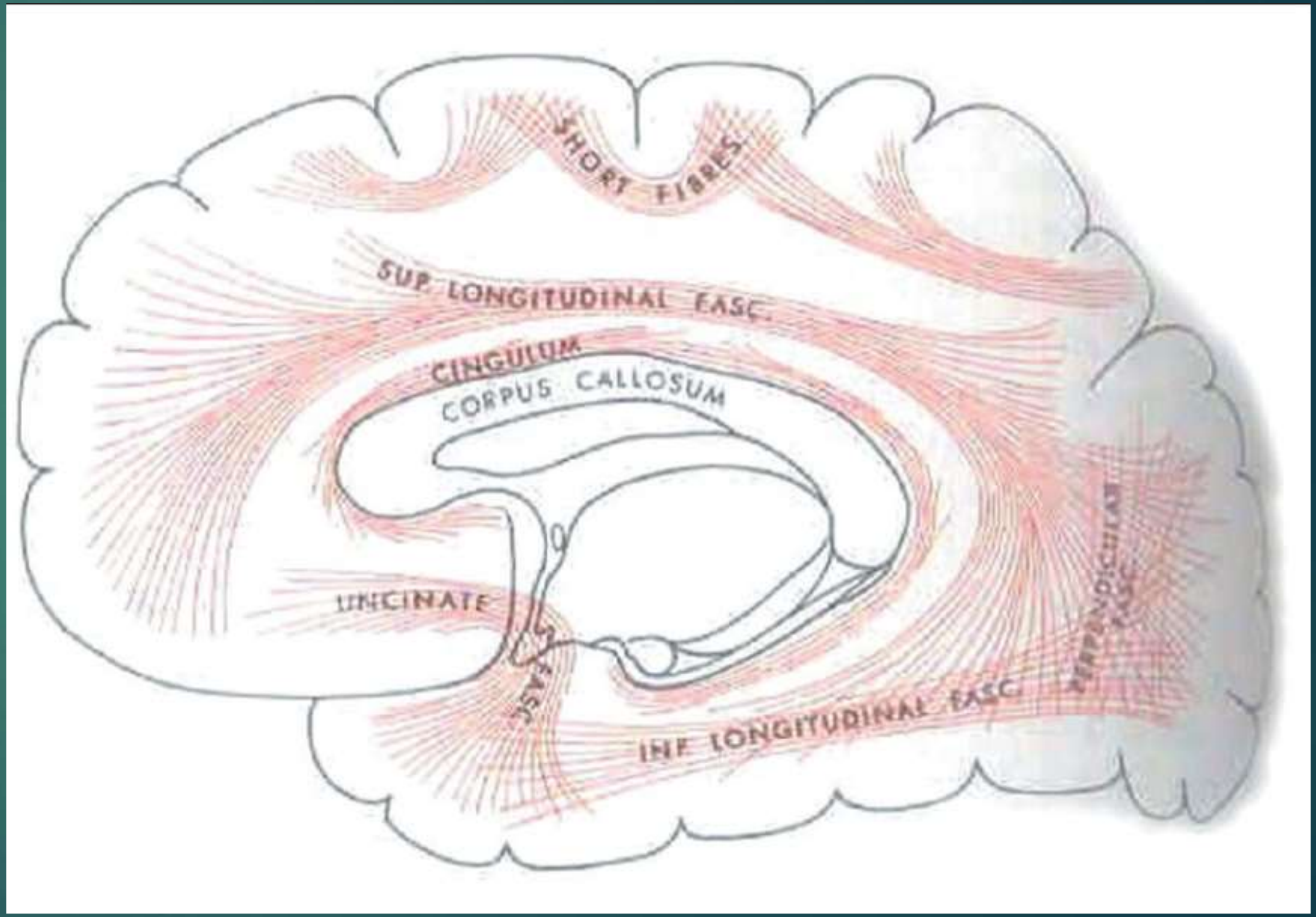


Figure 1.23
The human brain, showing the location of the primary receiving areas for the senses.

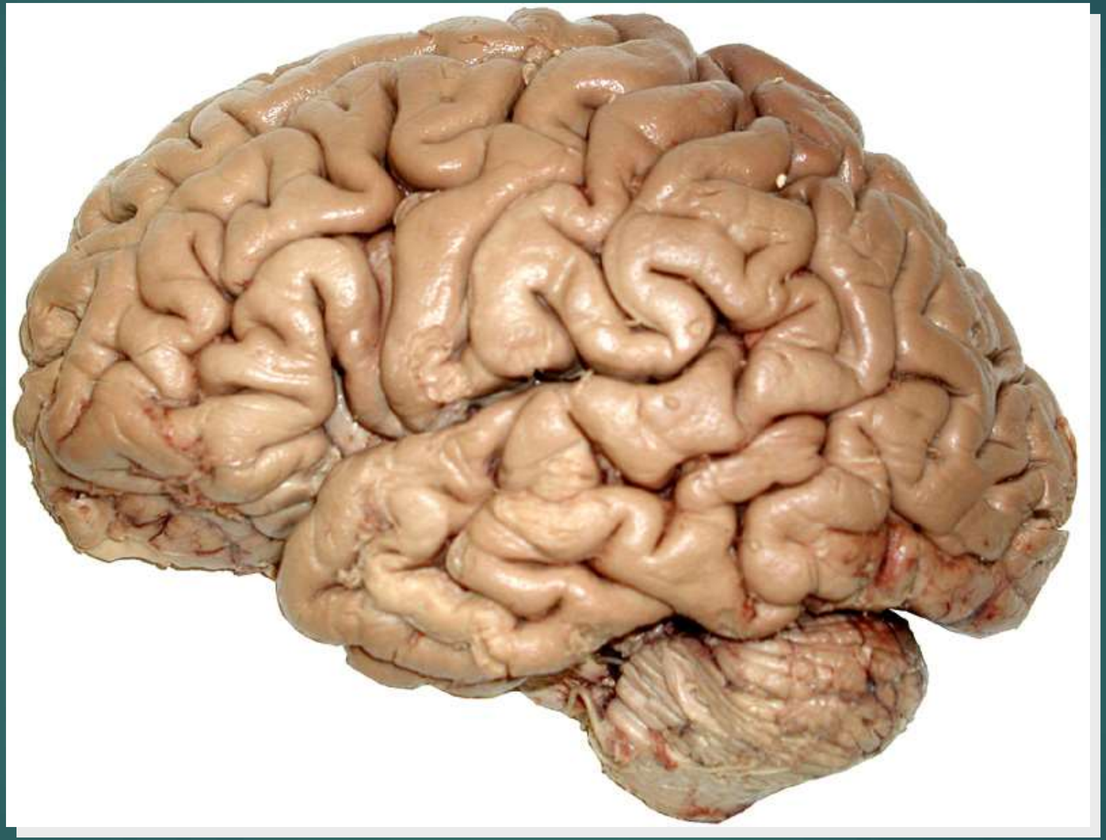
Senses: How we take energy from the environment & convert it into a representation that the mind can use

Cerebral fasciculi (long range axon connections)



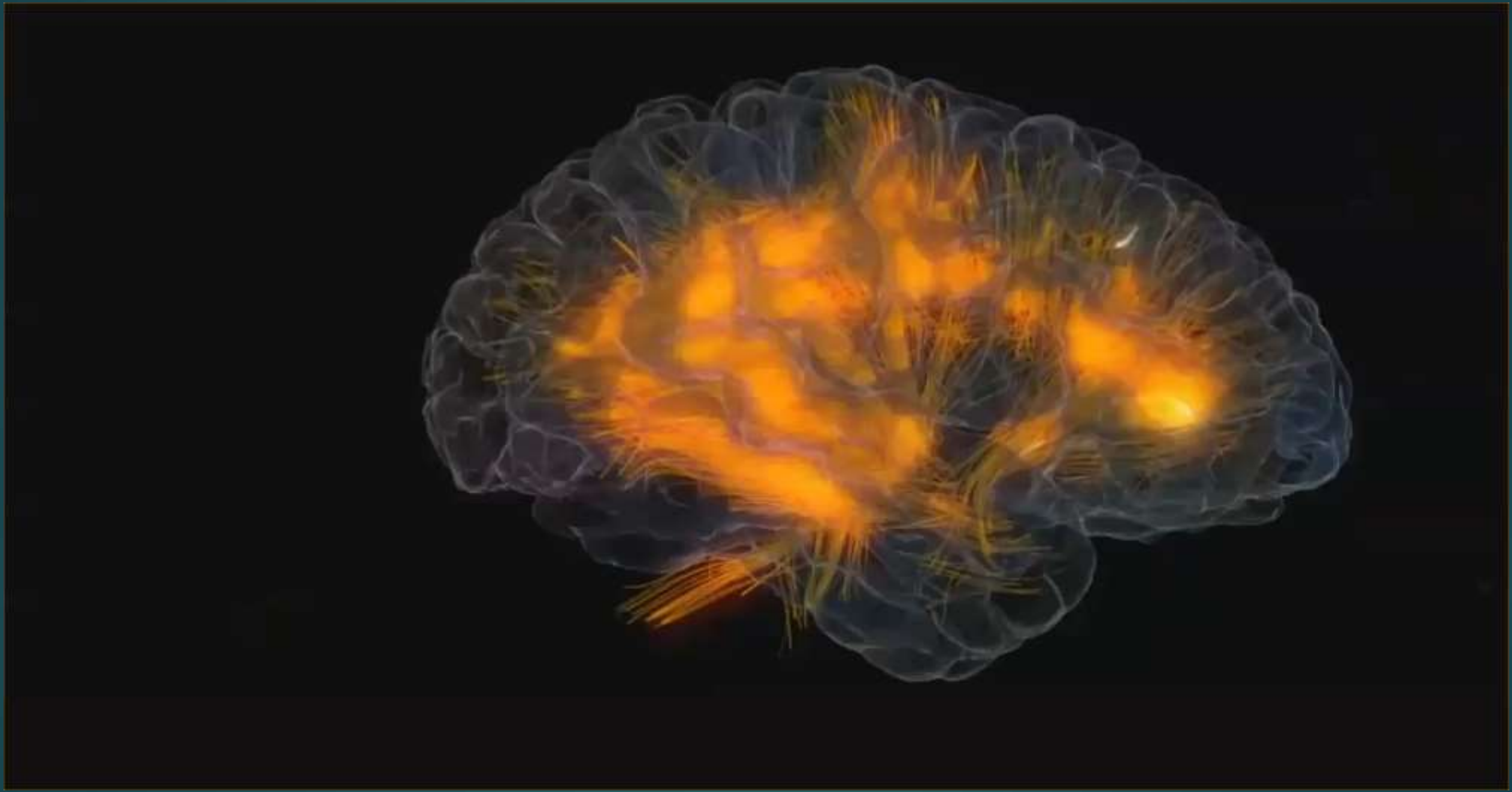


Human Brain



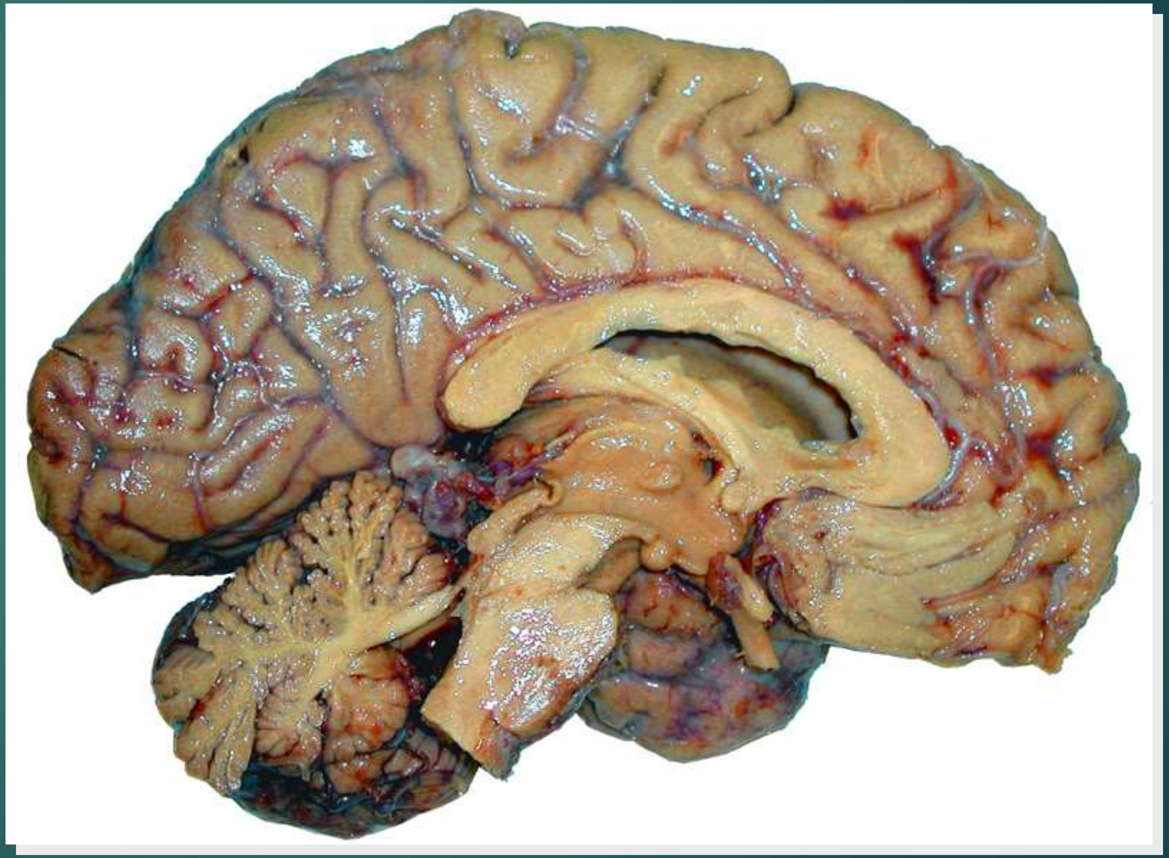
95%+ of human behavior is nonconscious

Electrical Storm: Brain activity in real time



Central Nervous System: CNS

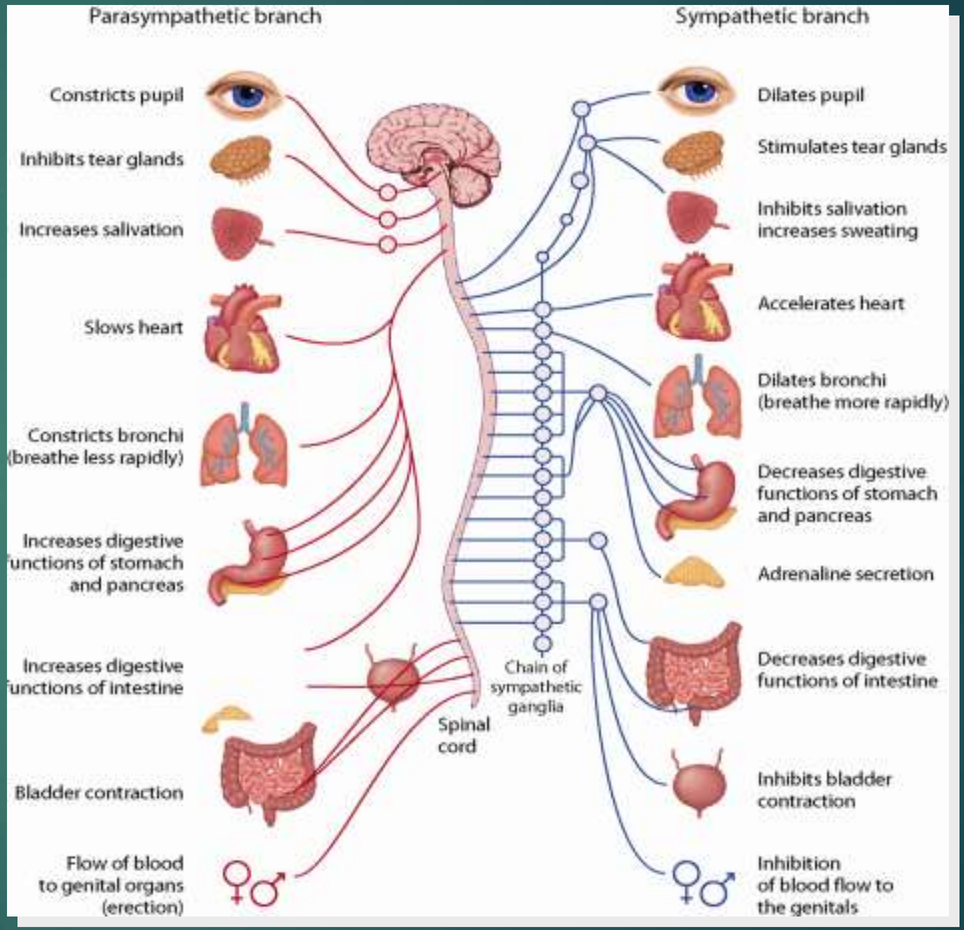
- Brain
- Spinal Cord



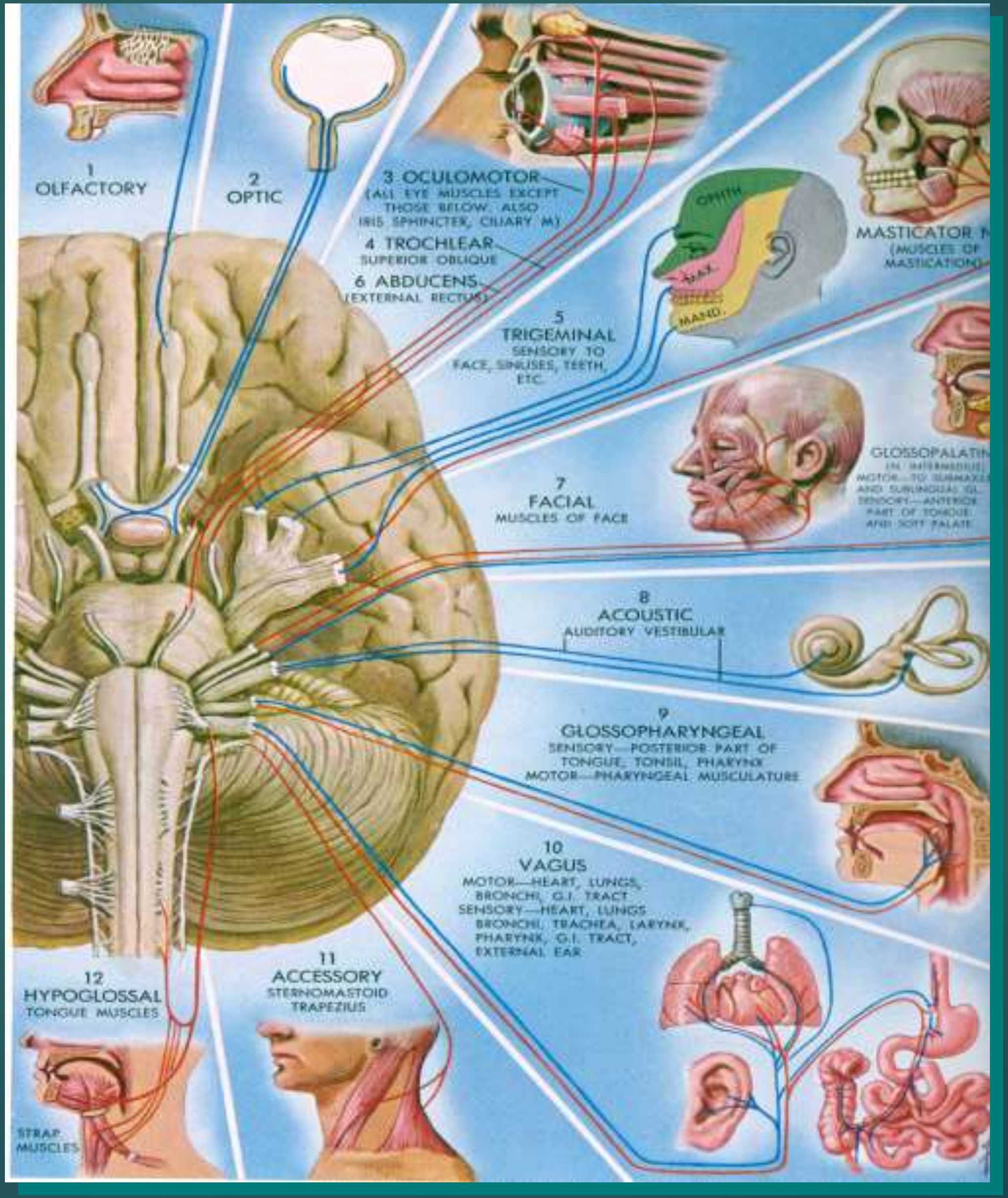
CNS and PNS

- Central nervous system (CNS):
  Brain

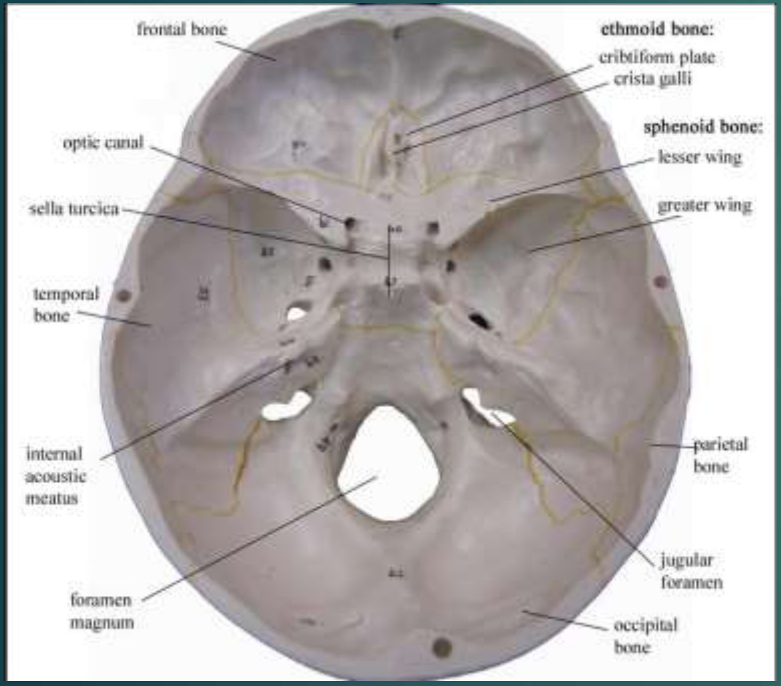
- Peripheral nervous system (PNS):
  Spinal Cord

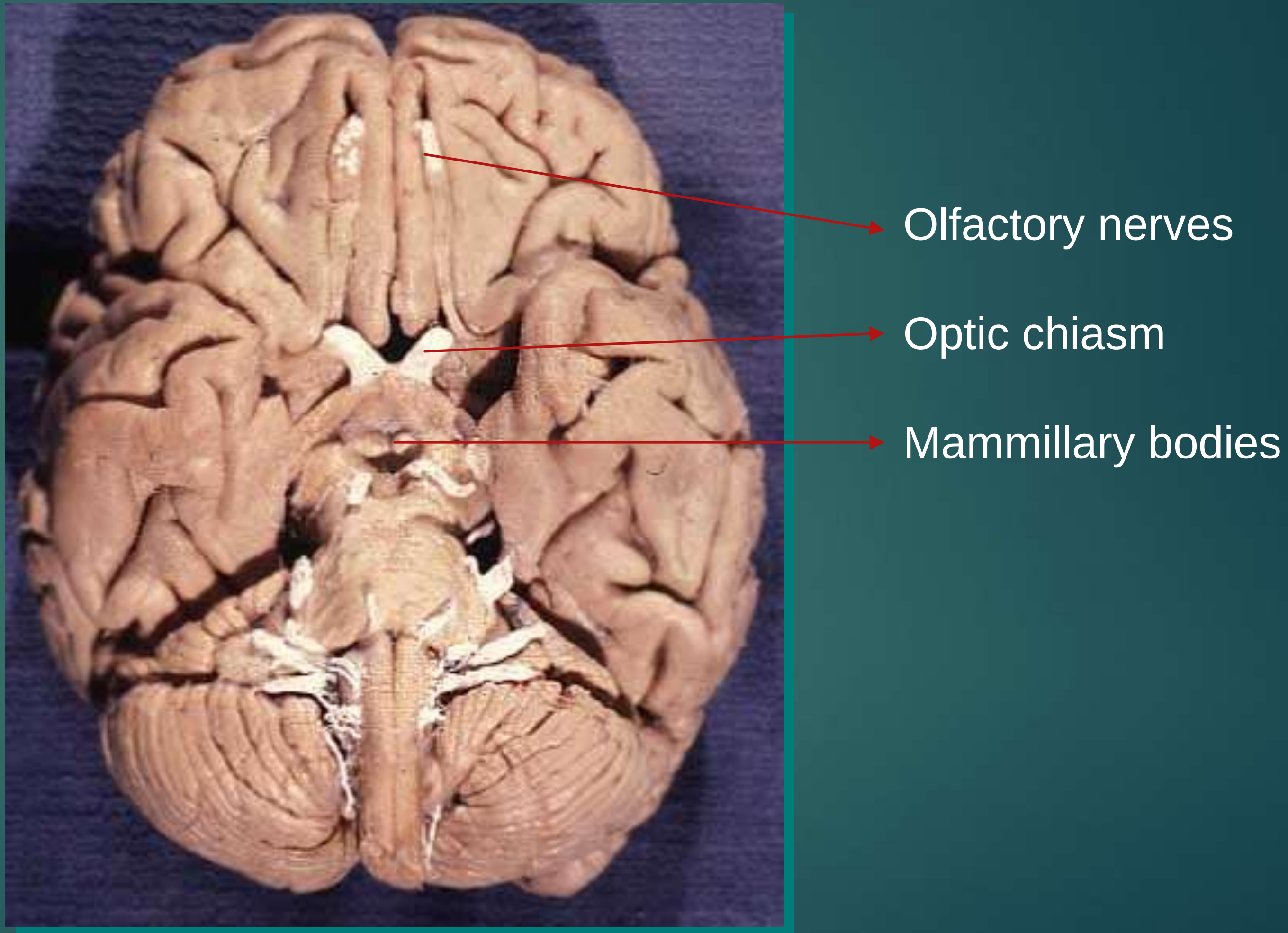


12 Cranial Nerves: domain of Neurology



Cranial Nerves stained white

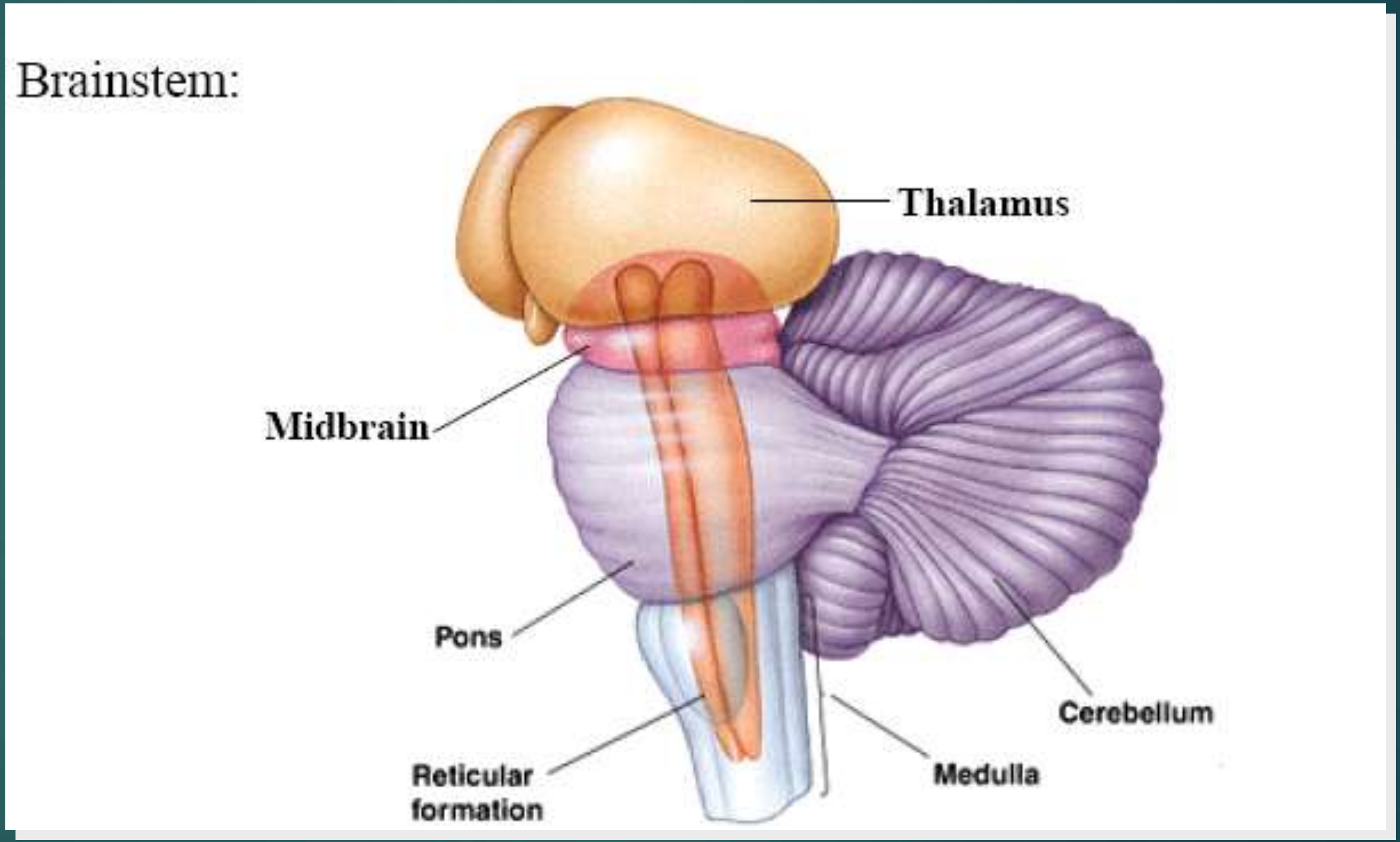




Brainstem

Automatic body functions: regulation of cardiac and respiratory function.

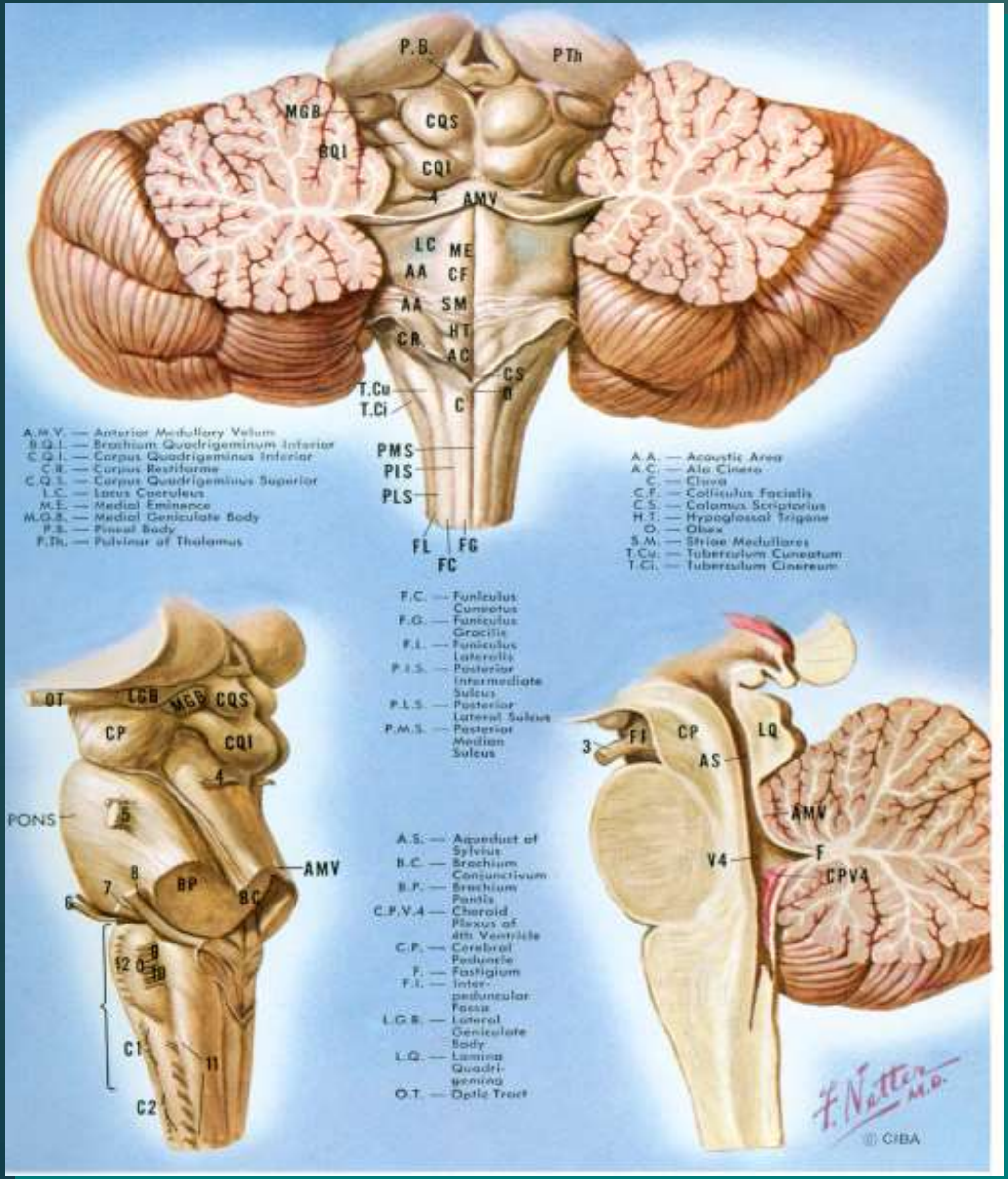
Damage = death

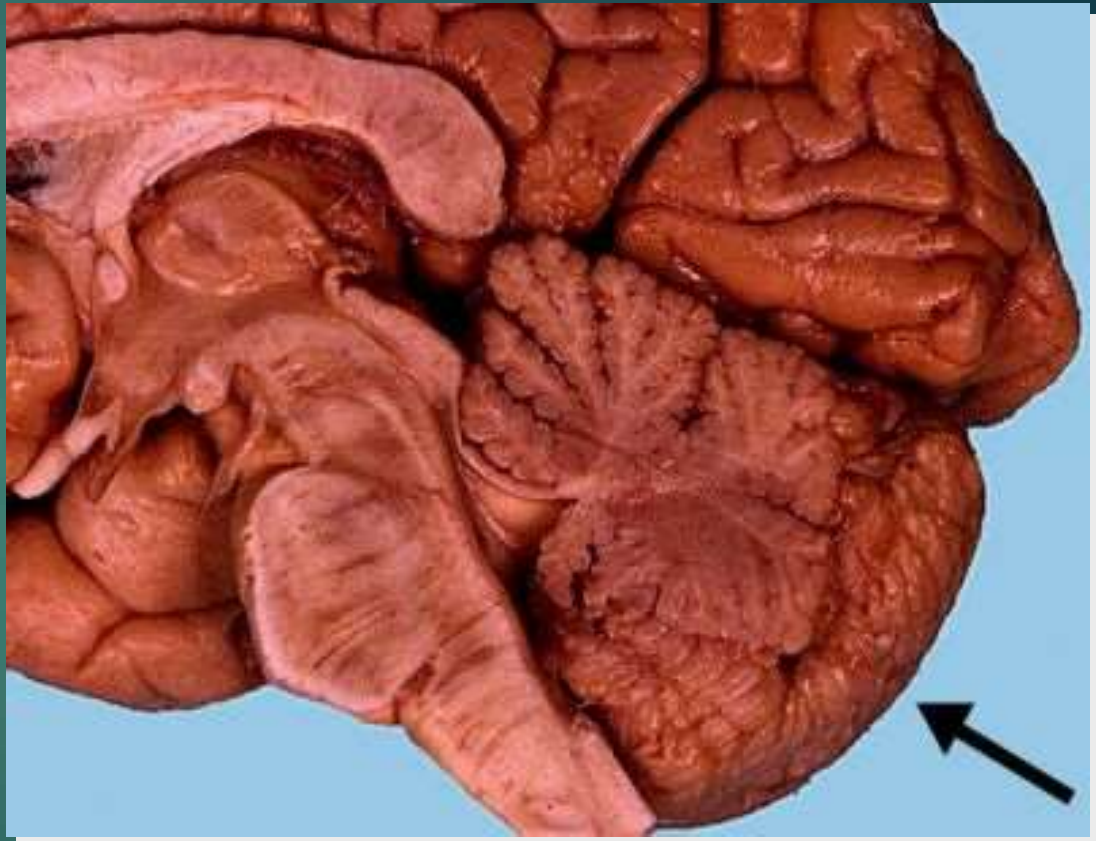


Brainstem

- Medulla (oblongata): life support (heart rate, blood pressure, gag reflex); decussation of afferent (sensory) and efferent (motor) pathways
- Pons: life support (sleep, heart rate, breathing), arousal (RAS = reticular activating system), & crossed afferent & efferent paths
- Cerebellum: motor control & coordination, balance, posture/equilibrium, implicit learning and memory

Cerebellum: 2 hemispheres





Classical Functions of cerebellum

- Does not initiate movement
- Equilibrium and balance
- Motor coordination
- Learned movement patterns

Cerebellum

- 80% of the 86 billion neurons (10% of the brain's total volume) in the human brain
- Involved in cognitive functions as well as motor functions
- More newly evolved areas of the cerebellum are involved in higher cognitive functions including:
  - language, inner speech,
  - higher-order rule formation,
  - attention,
  - verbal and visuospatial working memory
- Procedural memory: best predictor of ability to live independently

Procedural Memory:

Remembering how to…

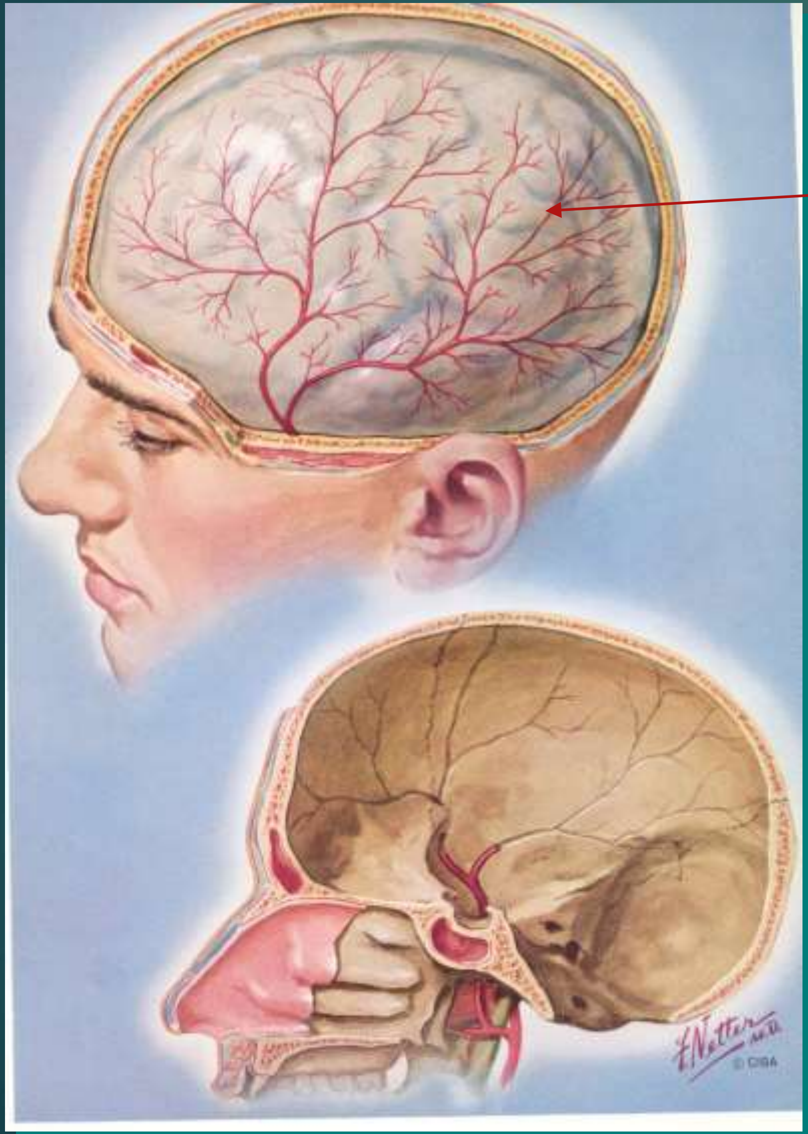
- Skills, habits
- Playing a musical instrument
- Playing sports
- Riding a bicycle, driving a car
- Reading mirror-reversed word
- Playing Chess, bridge
- Interpersonal Skills, Therapy behavior
- Longest lasting memory function

Coming Up Next:
Example of Procedural Memory

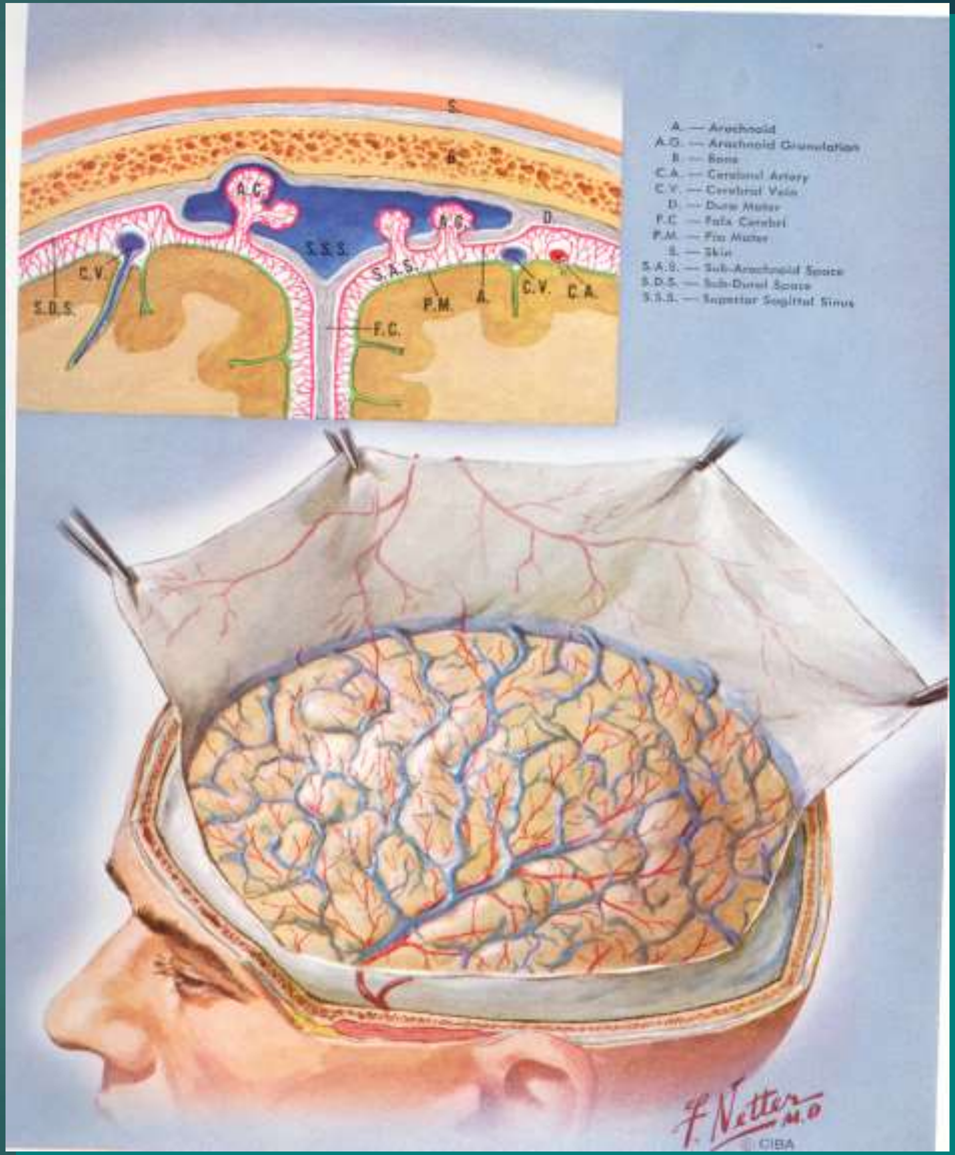
- Typewriting skills are procedural memory

Overlearned Memory

Meninges: Dura, Arachnoid, Pia

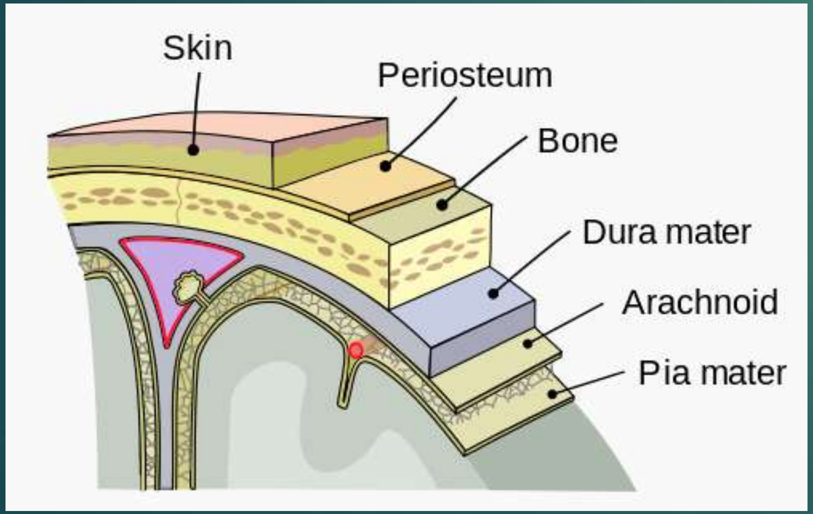


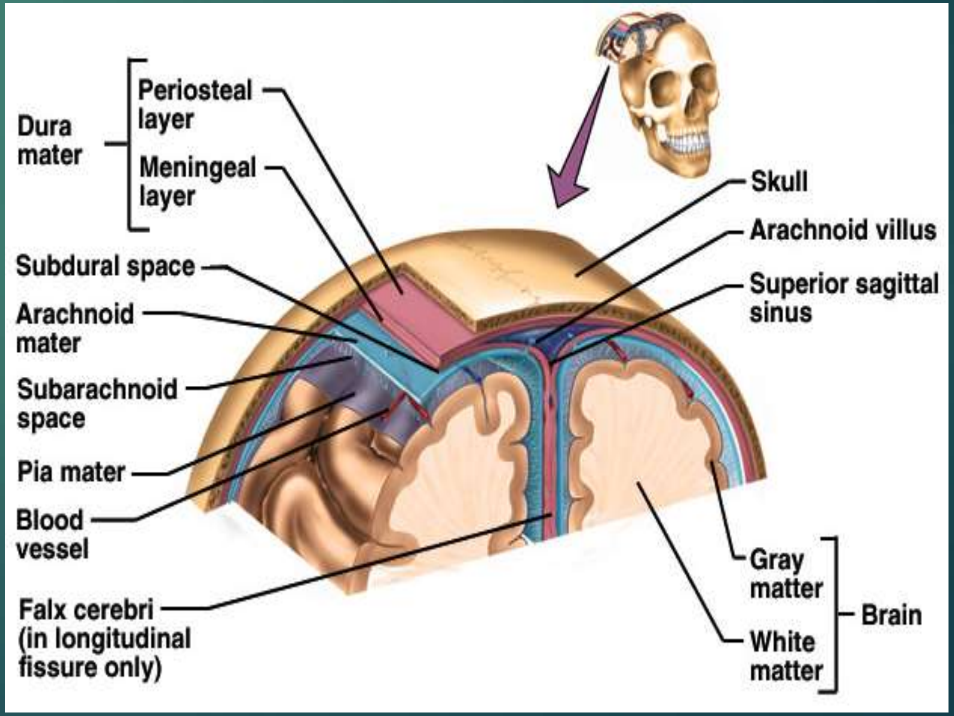
Dura



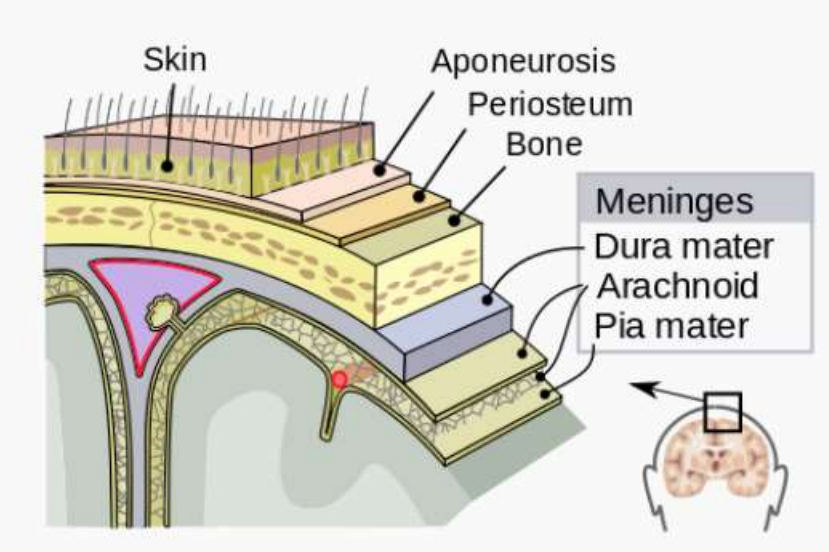
Meninges: Brain cover – 3 membranes

- 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





Brain coverings



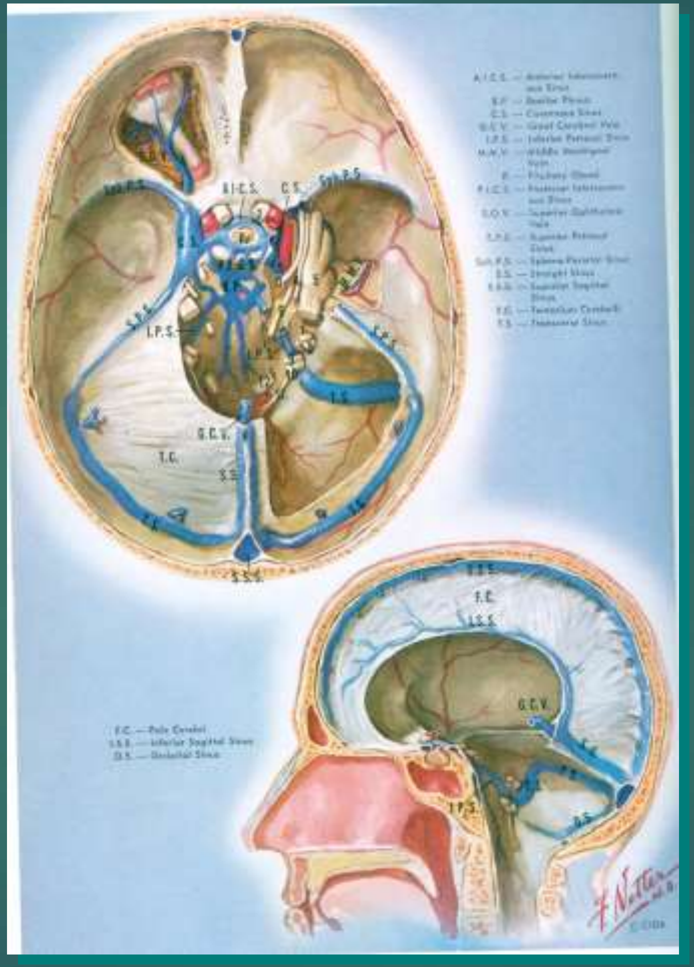
Meninges of the CNS

From right to left:

Scalp, Periosteum, Bone, Dura Mater, Arachnoid, Pia Mater, Brain

Venous Sinuses, Falx, Tentorium: Plastic like separators

Tentorium



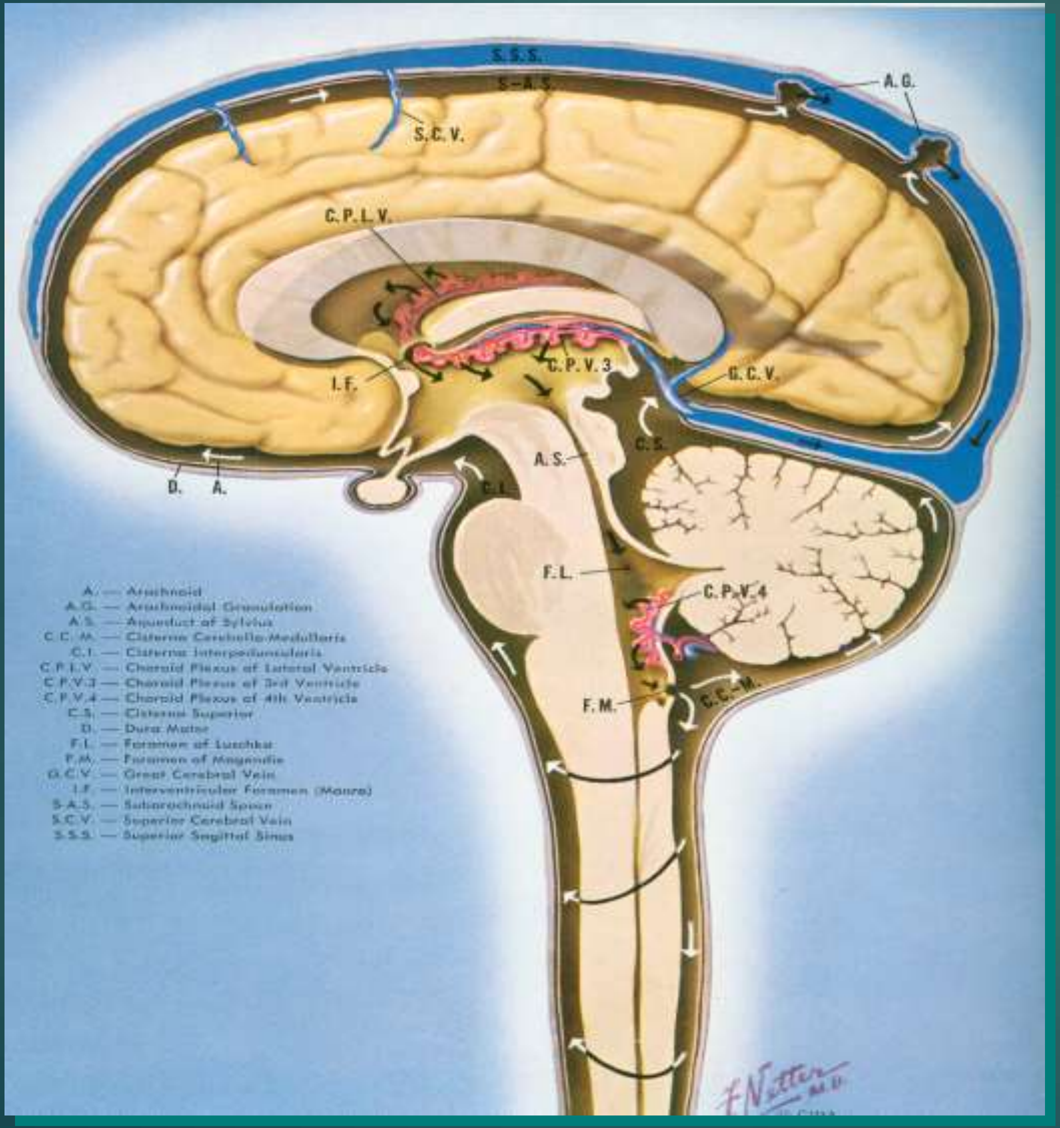
Falx

Dura creates 3 named falx: Falx cerebri (divides cortex), tentorium cerebelli (supports occipital lobes); falx cerebelli (separates cerebellum hemispheres)

Subdural Hematoma (bleed)

- Why not to go to sleep after head injury: Between the dura and arachnoid mater is the subdural space with many veins susceptible to injury (subdural hematoma)

Cerebral Spinal Fluid



Produced by choroid lexus

20 ml per hour; 500 ml per day
(turn over all 4-5 x day)

Total Volume: 125-150 ml

Provides buoyancy to brain

Hydrocephalus: increased CSF pressure due to interruption in the flow or reabsorption of CSF

Communicating = disrupted reabsorption

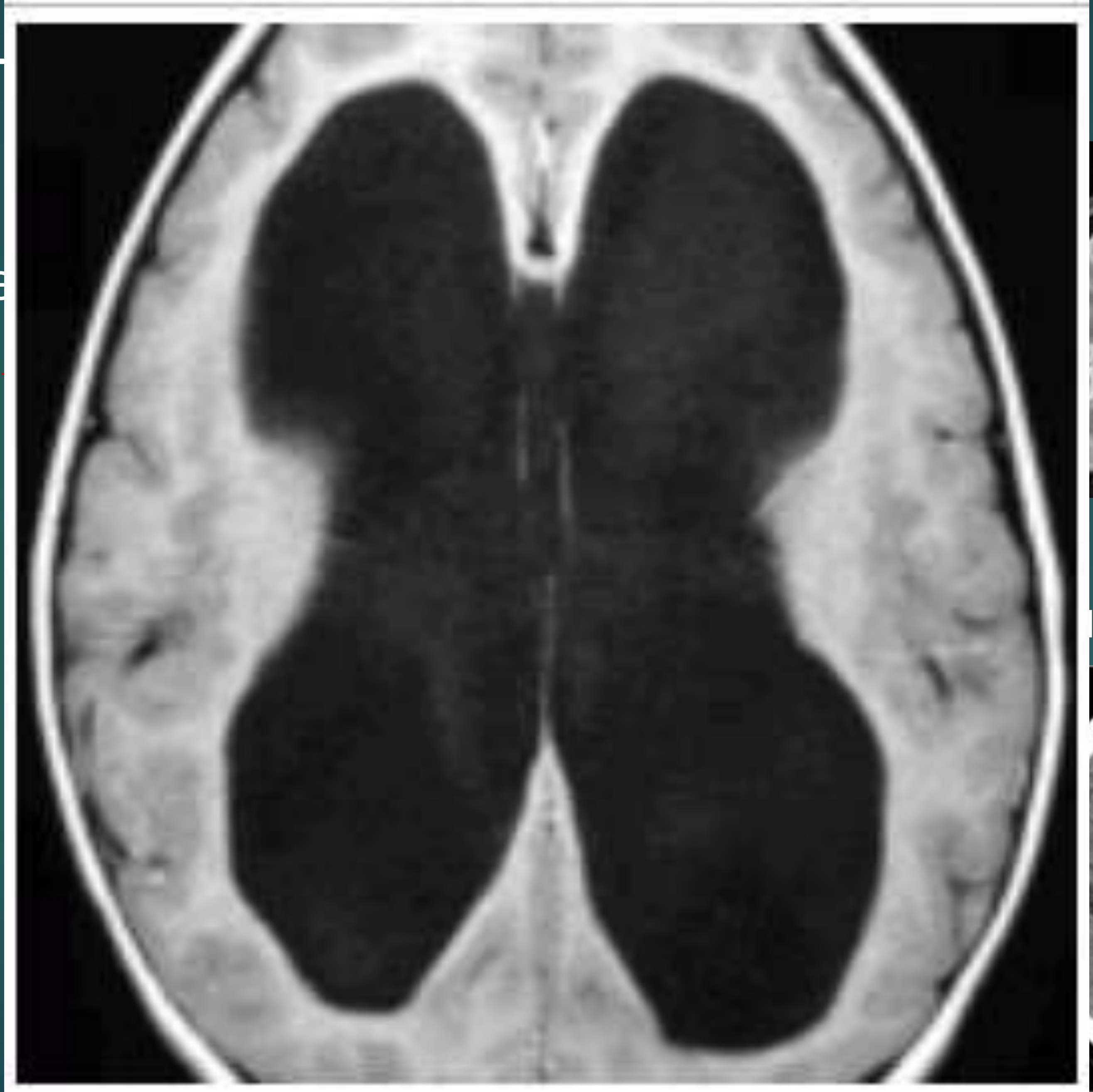
Noncommunicating = obstruction

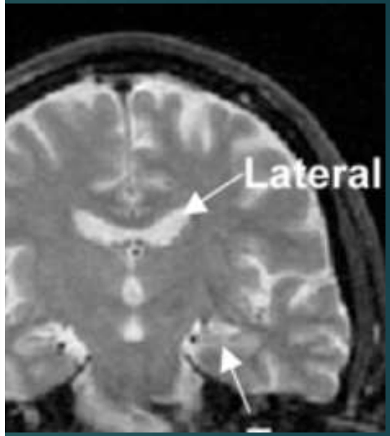
Ventricles: L

Late

3rd

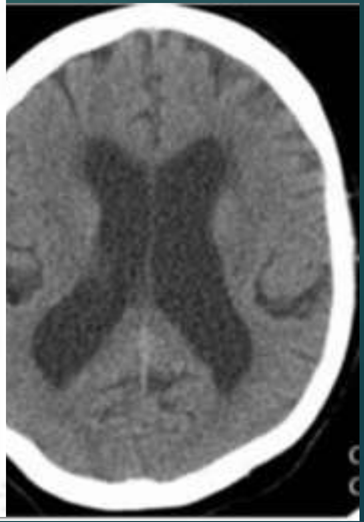
4th





Normal

ydrocephalus



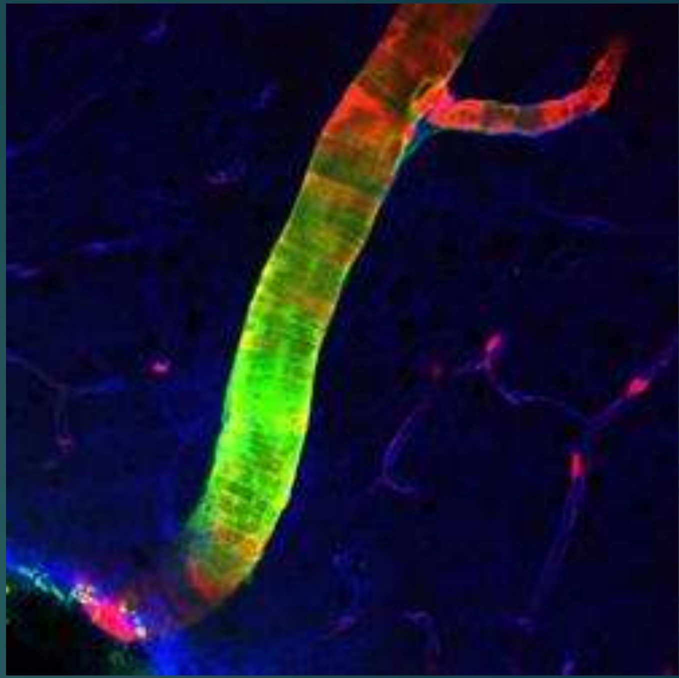
Cerebrospinal Fluid

- Clear liquid fills ventricles & bathes brain's external surface (in subarachnoid space)

- Brain produces & absorbs about 500 ml/day
  - produced by ependymal cells lining the ventricles
  - filtration of blood through choroid plexus
- CSF functions
  - buoyancy -- floats brain so it neutrally buoyant
  - protection -- cushions from hitting inside of skull
  - chemical stability -- rinses away wastes; Removes 50% of beta amyloid

Glymphatic System: Cleaning the Brain

Discovered in 2013



- Data from studies of mice, baboons, dogs & goats:
- Brain's interstitial space (fluid-filled area between cells) = 20% of brain volume
- Purpose = cleaning the brain's waste during sleep or anesthesia
- CSF flows on surface during day = 5%
- Swells up at night for CSF = 95% of flow at night between cells

Nedergaard, et al., 2013

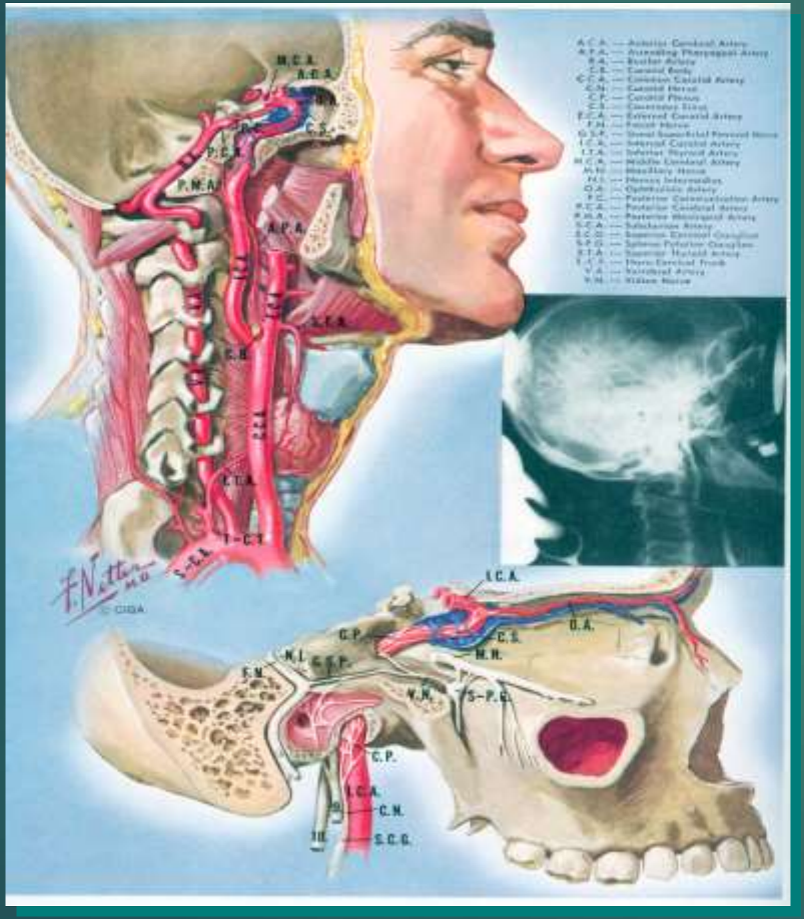
Glymphatic system 2

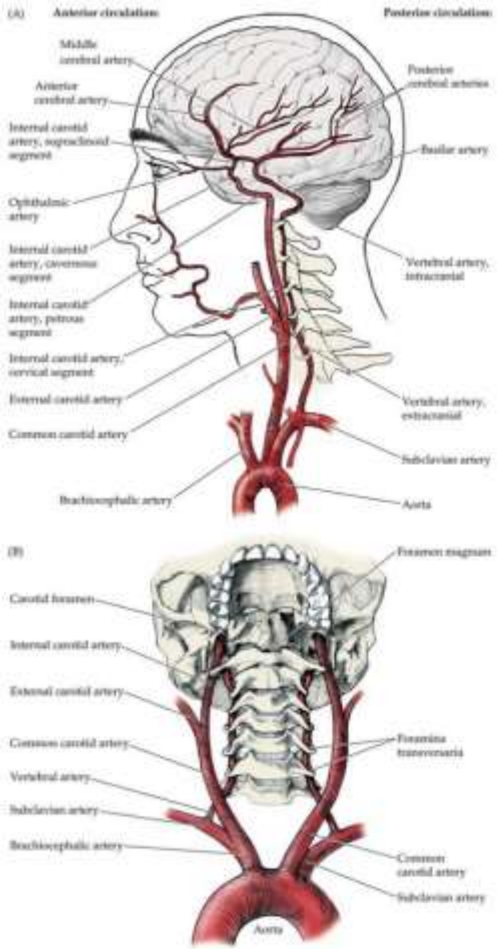
- Glymphatic system is more active while we sleep, can be damaged by stroke and trauma, and improves with exercise.
- astrocytes are key regulators of the glymphatic system
- Impaired by high use of alcohol
- low levels of alcohol consumption tamp down inflammation and helps the brain clear away toxins, incl. BA
- Animals that were exposed to low levels of alcohol consumption, analogous to approximately 2 ½ drinks per day, actually showed less inflammation in the brain and their glymphatic system was more efficient in moving CSF through the brain and removing waste

What is good for your heart is good for your brain

400 miles of blood vessels

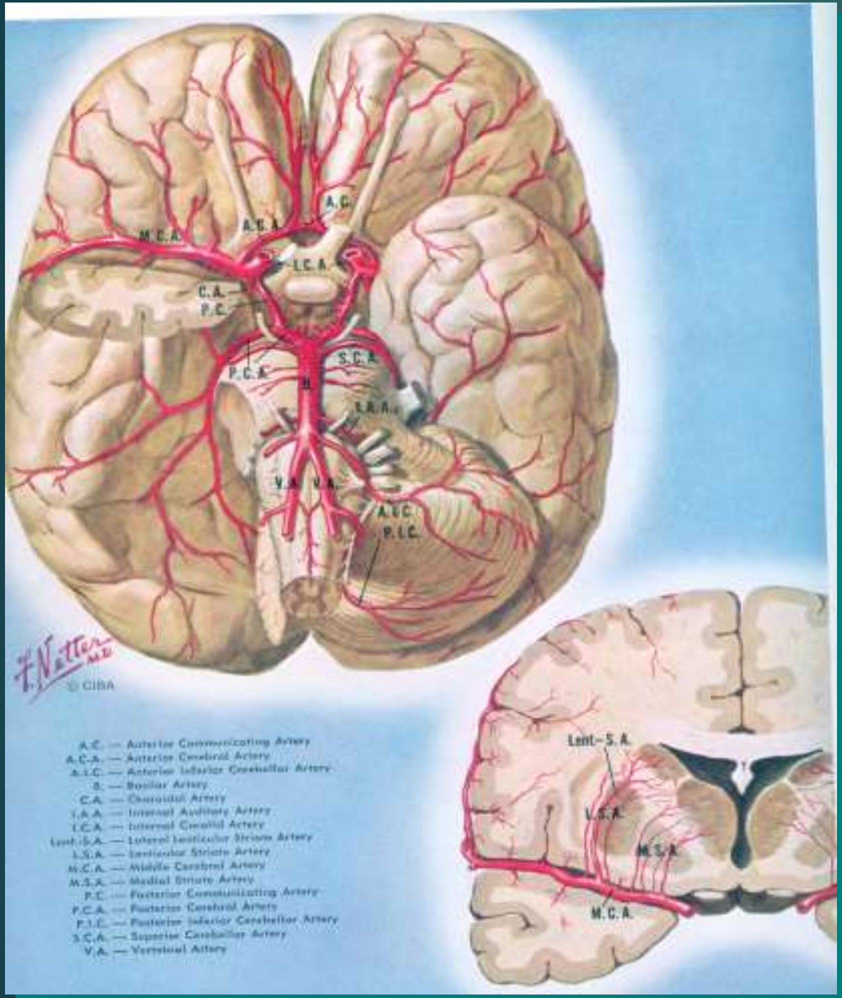
Brain's Blood Supply:
Internal Carotid, Basilar, Carotid, Vertebral Arteries

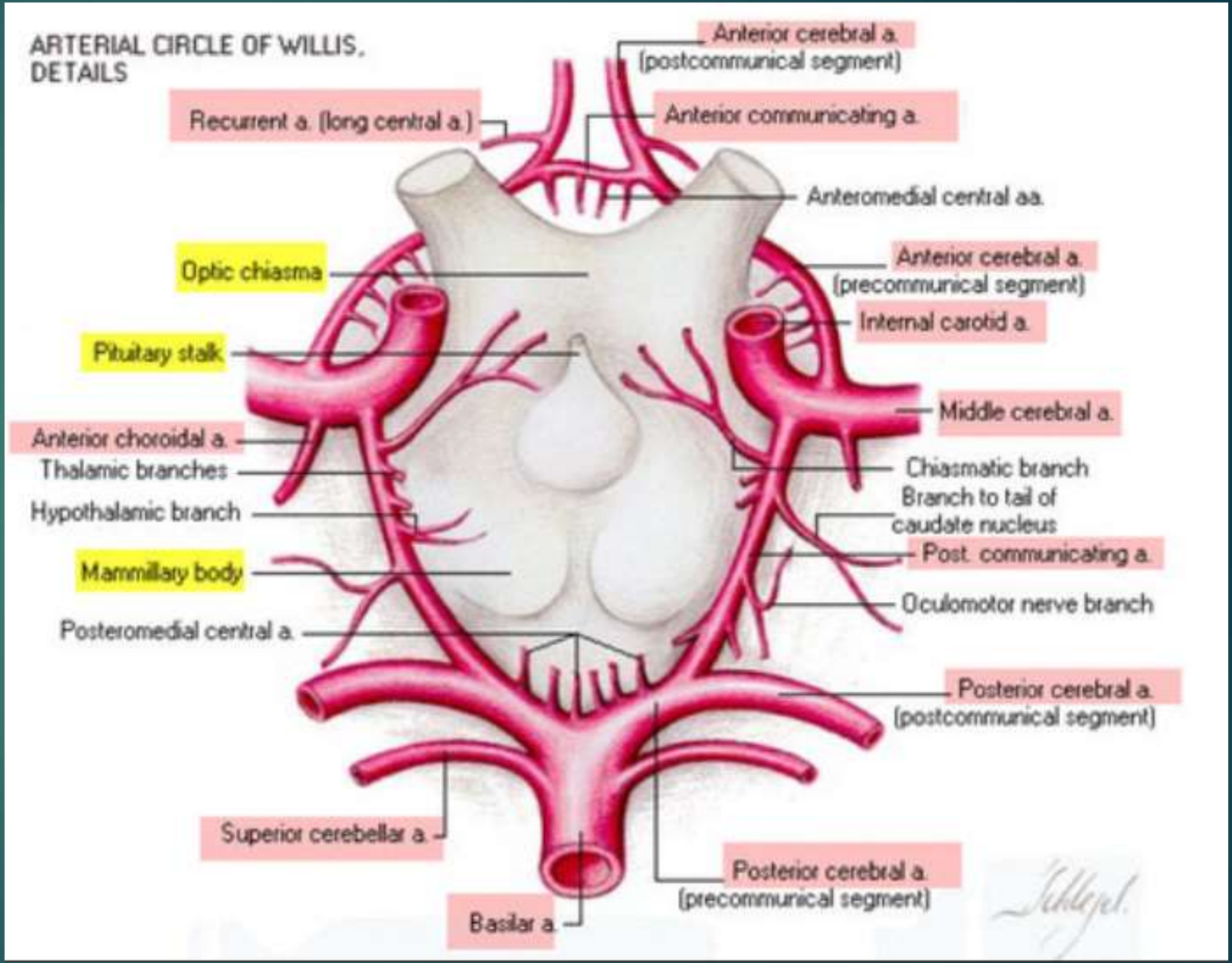




<u>Never let chiropractor do a neck adjustment</u>: basilar stroke

Circle of Willis





Venous System: removal of deoxygenated blood

Flow into series of sinuses in spaces left between meninges (dura)

Sinus = vein

Subdurals: vein breakage

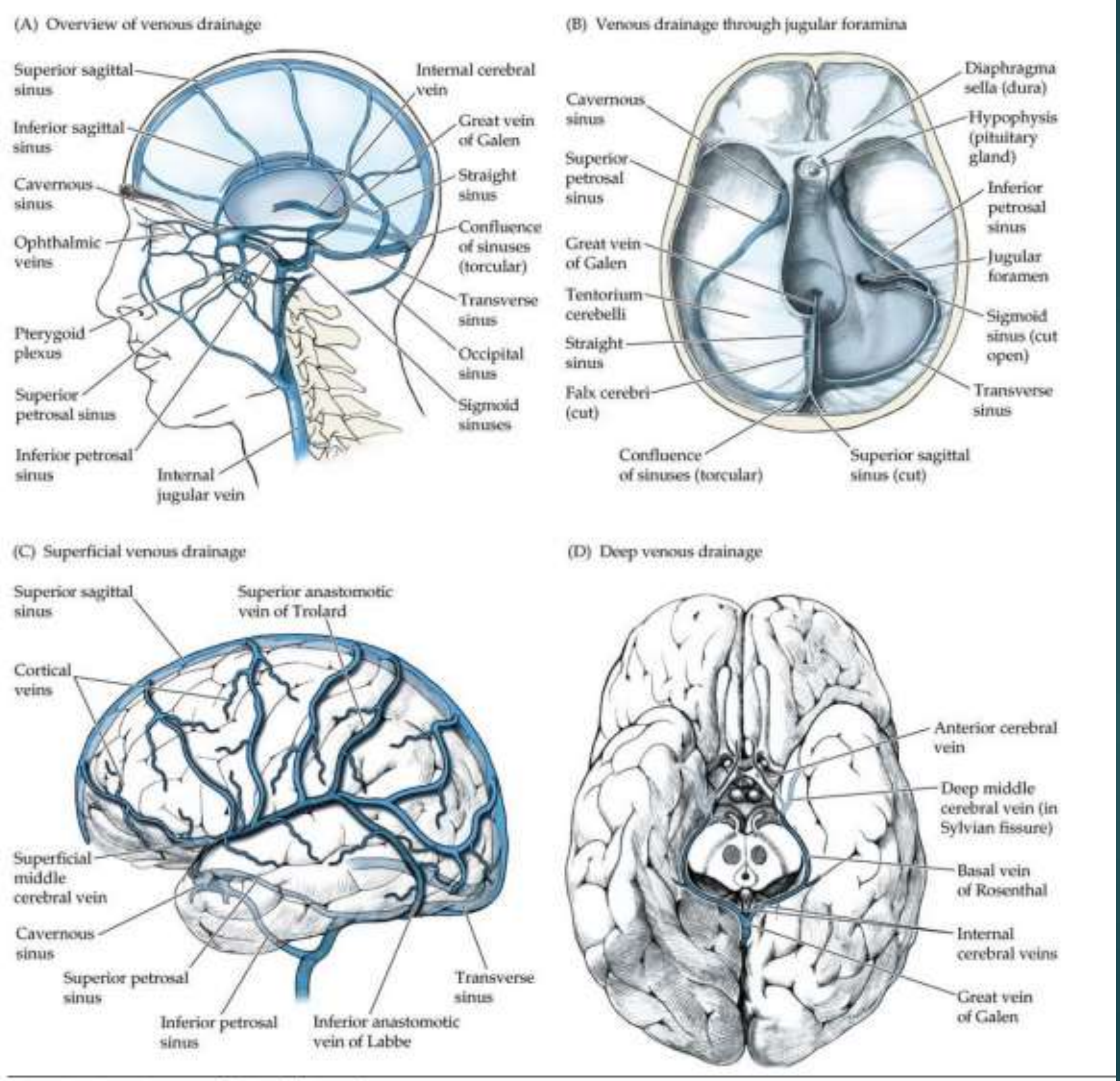
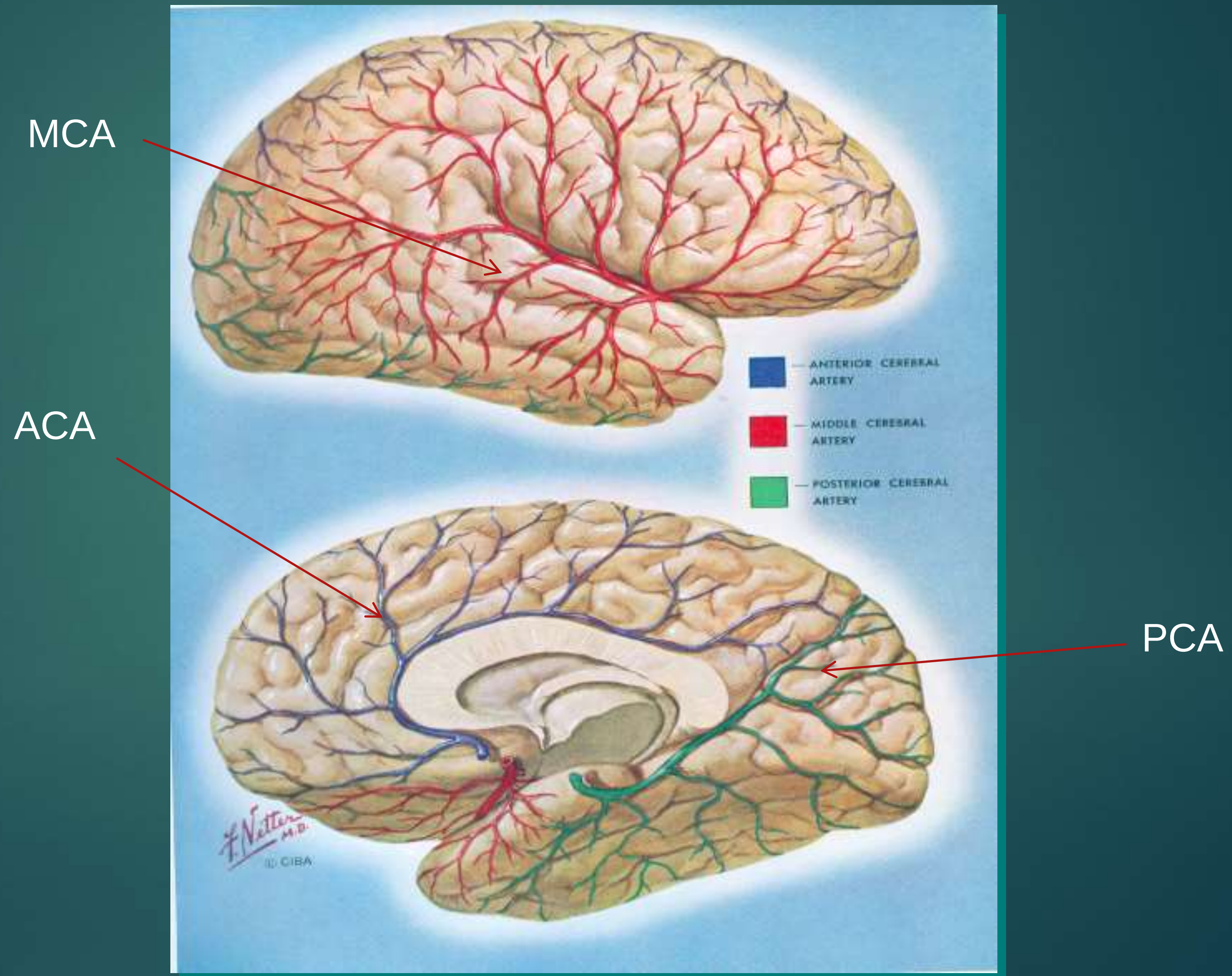


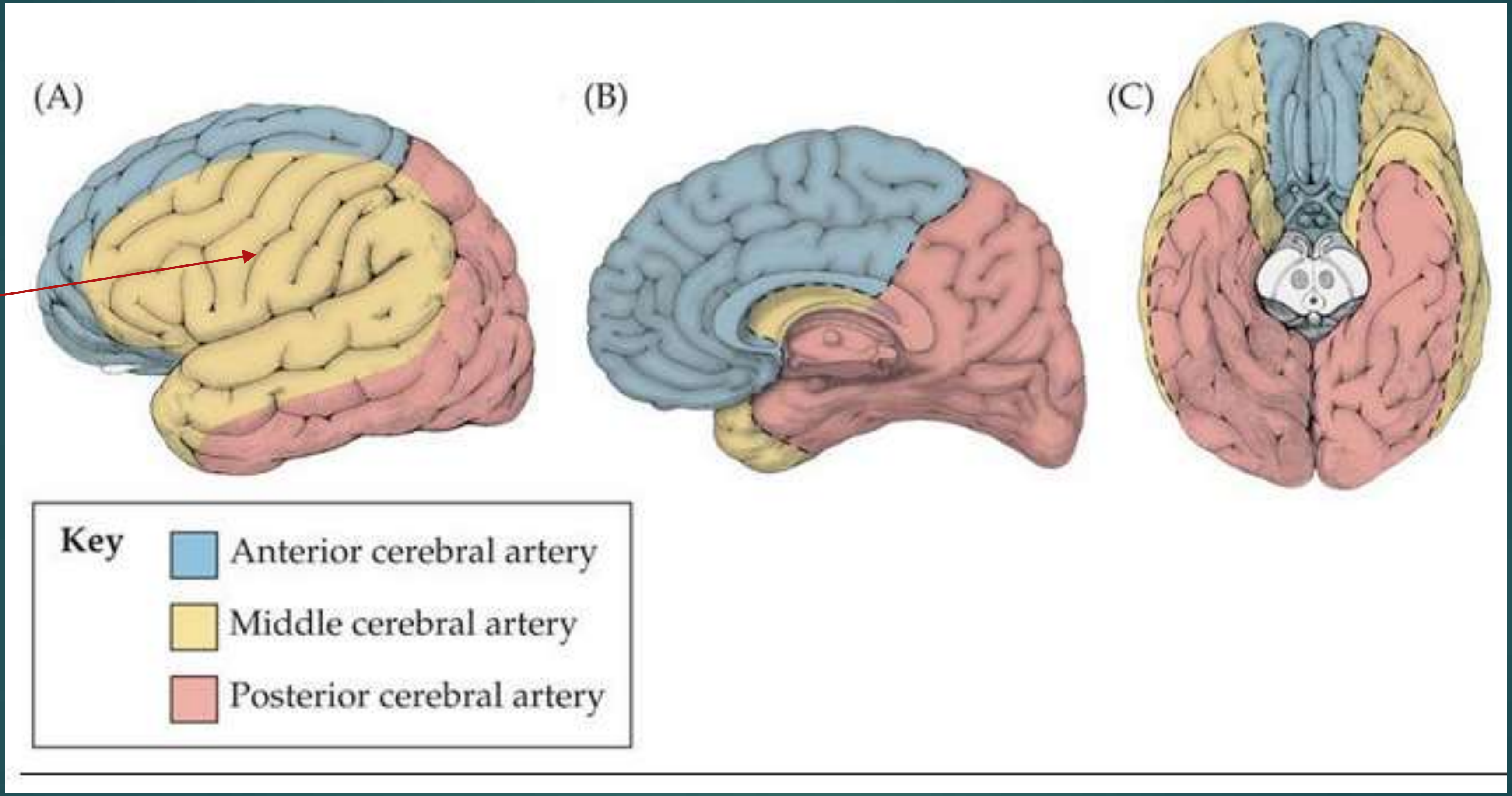
Figure 10.11 Venous Drainage of the Cerebral Hemispheres

Blood Supply 2: ACA, MCA, PCA

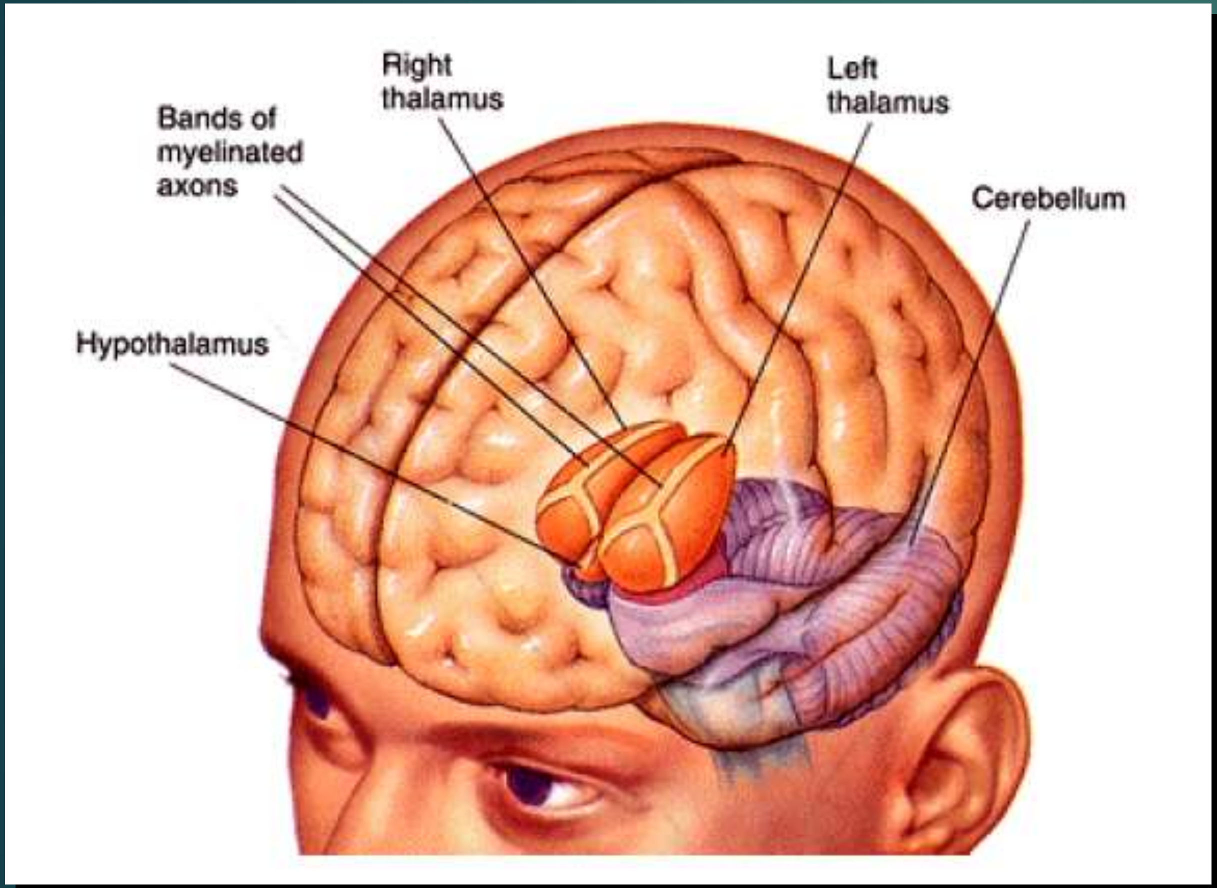


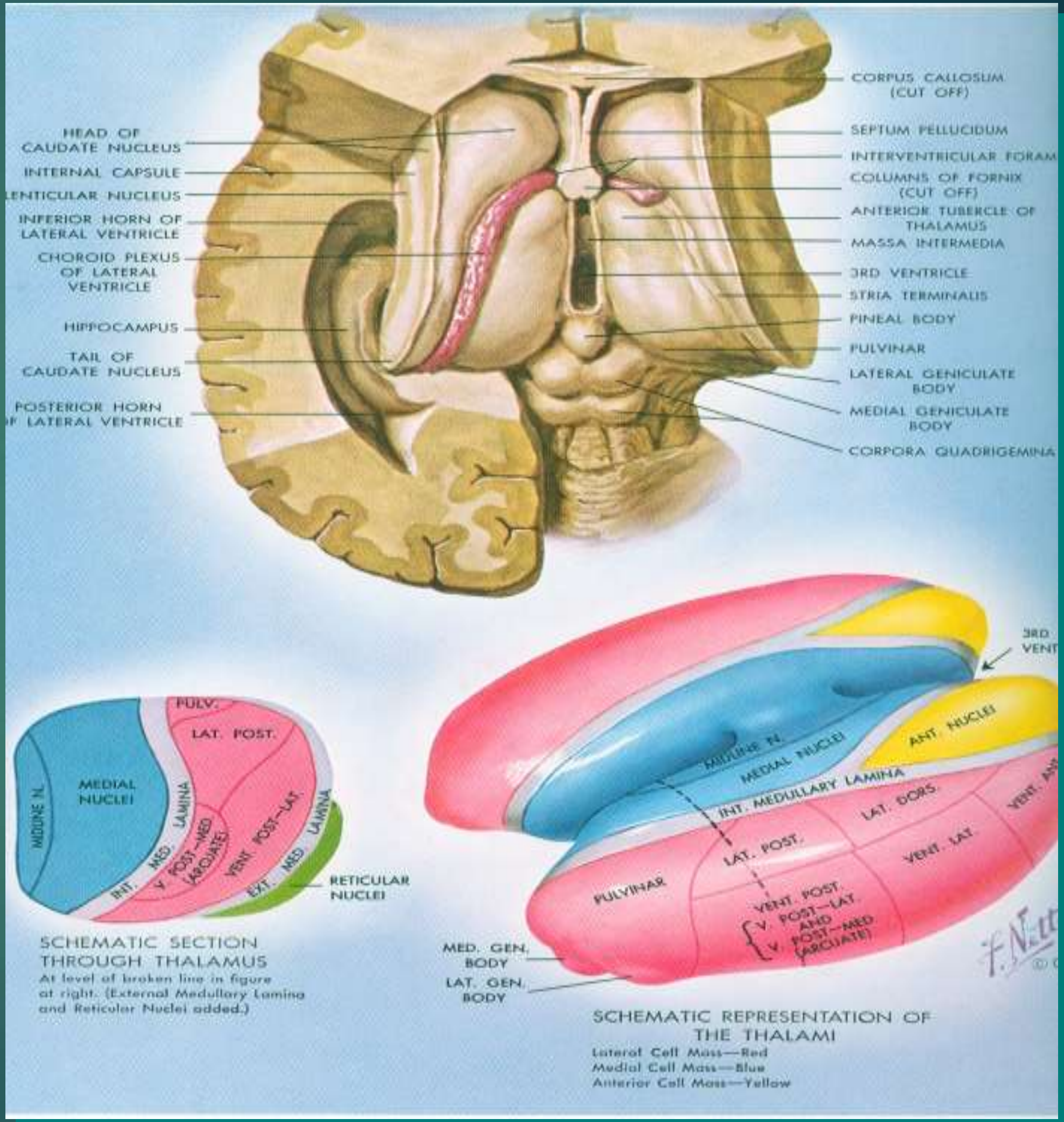
Artery Coverage Areas

Classic Stroke: Aphasia + hemiplegia



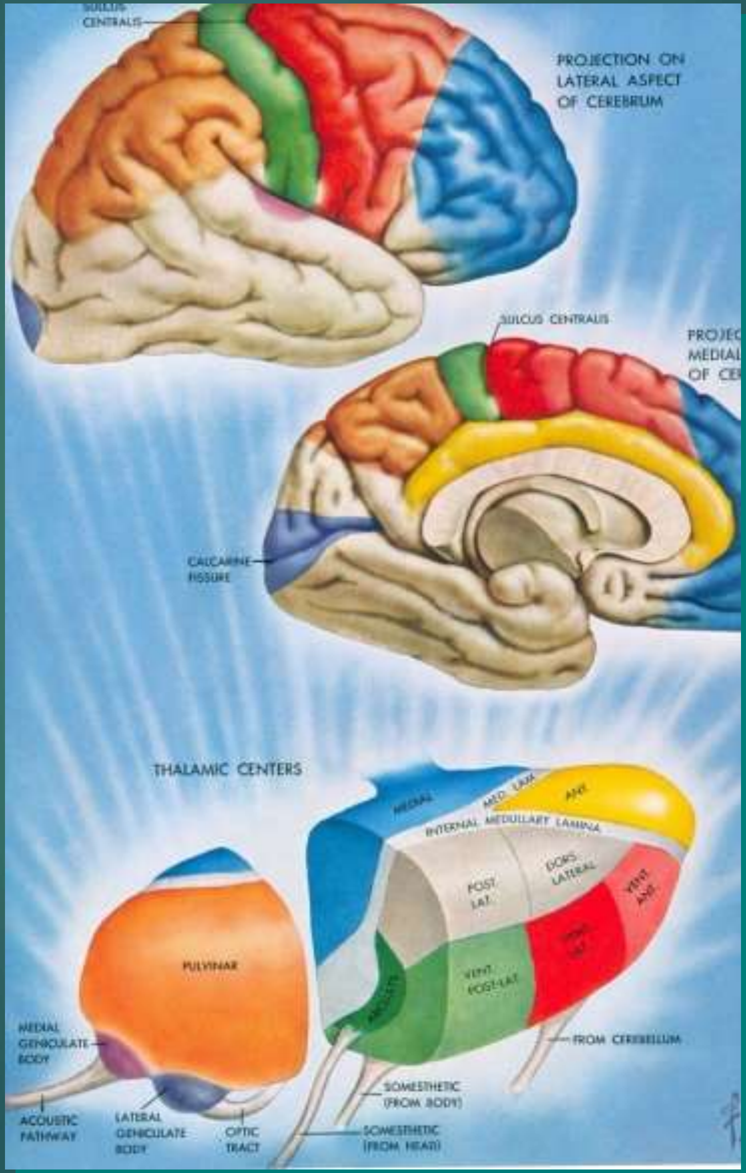
Thalamus: Sensory gateway





Sits on top of brain stem

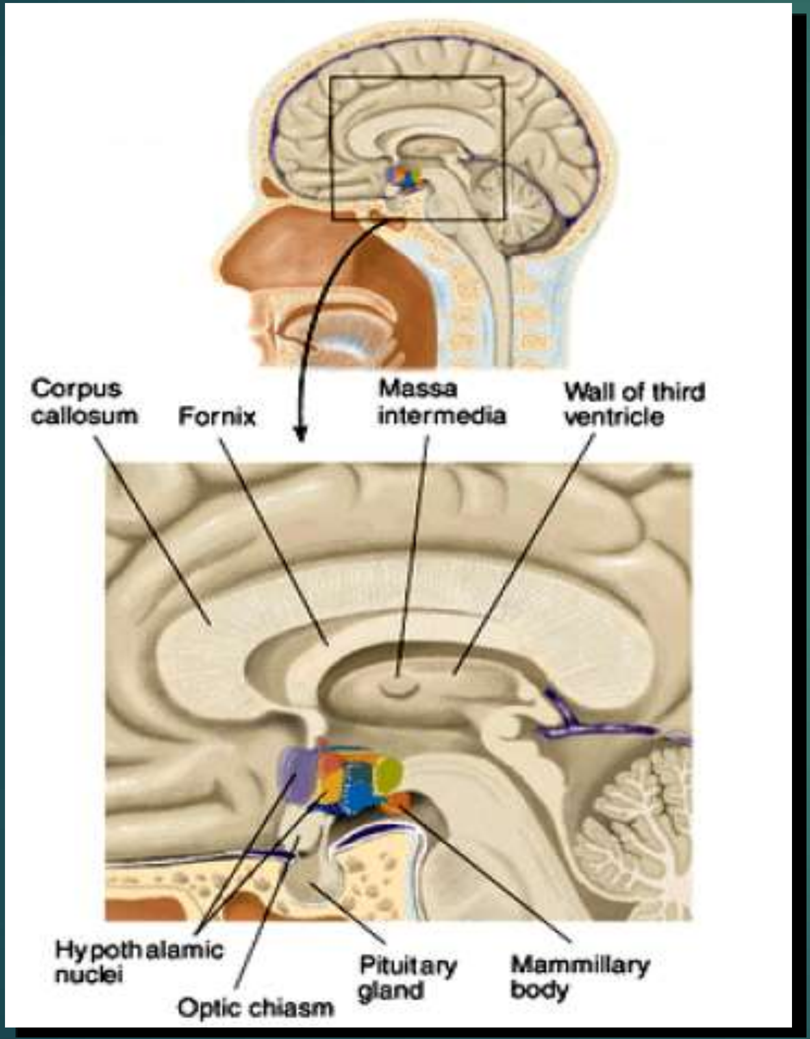
Thalamocortical Radiations



Thalamus

- Gateway/relay station for sensory input to cortex
- All afferent somatosensory neurons (except olfaction) pass through thalamus prior to reaching cortex.
  - integrate & directs information to appropriate area
  - main output center for motor info leaving the cerebrum
- Interconnected to **limbic system** so also involved in emotional & memory functions
  - Arousal, eye movements, taste, smell, hearing

Hypothalamus: Brain's Pharmacy



Below the Thalamus

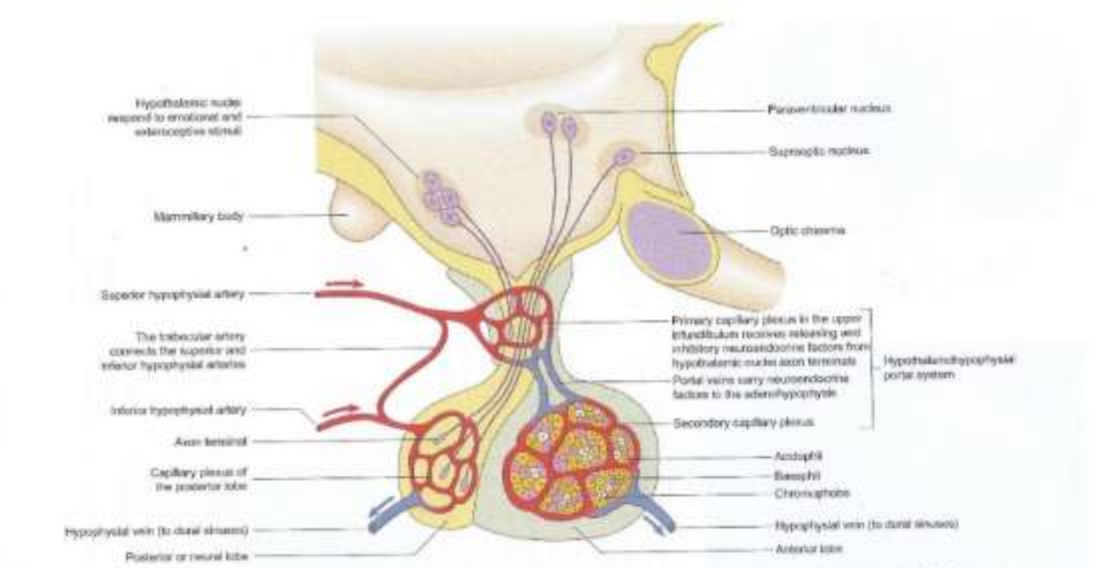
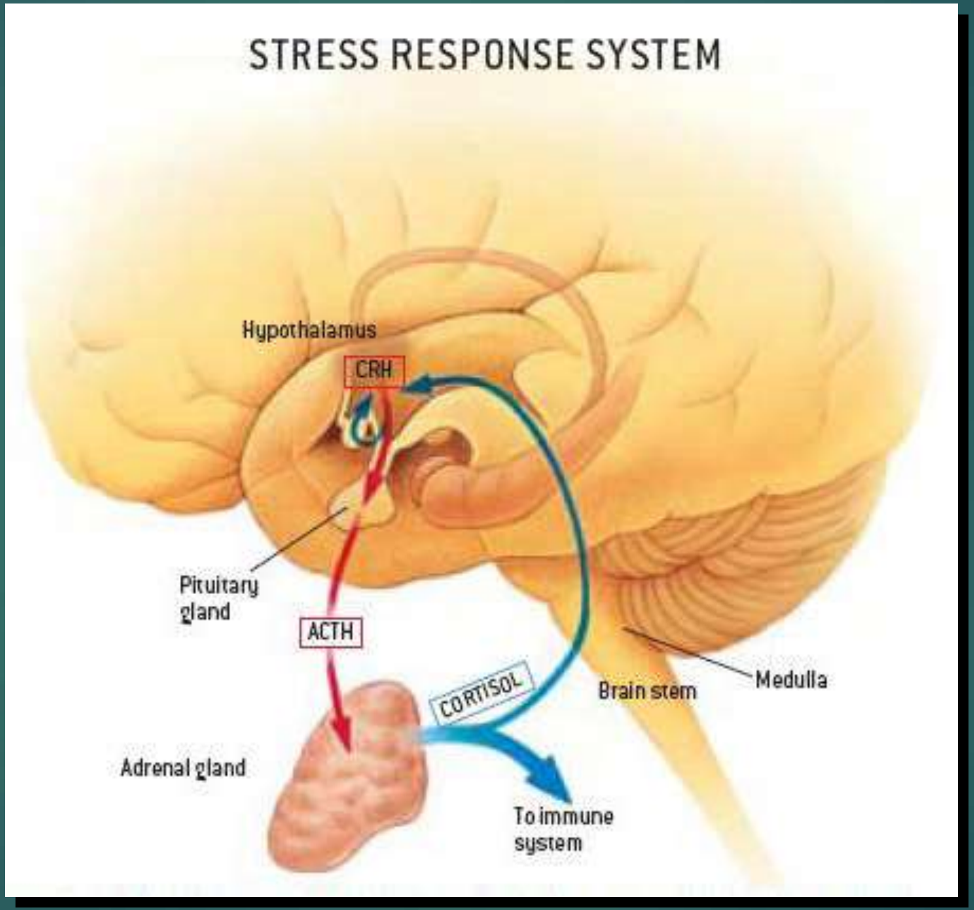


FIGURE 5.15 The hypothalamus (highlighted with dark blue circle) is a cluster of nuclei located immediately below and in front of each thalamus. The hypothalamus is important in regulating physiological and emotional processes and is closely connected with the pituitary gland. Source: Standring et al., *Gray's Anatomy*, 2008, Chapter 21, Figure 21.11.

- Whole-body homeostasis;
- Regulation of ANS
- Regulation of appetite, thirst, temperature, sexual arousal, fear & rage reactions
- HPA: Hypothalamo-pituitary-adrenocortical axis

Hypothalamo-Pituitary-Adrenocortical (HPA) Axis: Cortisol central



Controls reactions to stress

HPA: Hypothalamus-Pituitary-Adrenal Axis

- HPA is a neuroendocrine control system for initiation, regulation, & termination of glucocorticoid secretions in response to stress.
- Glucocorticoid receptors influence metabolic & inflammatory processes.
- Triggers release of CRH & vasopressin, which act on pituitary, which releases ACTH, which affects Adrenal cortex which releases cortisol
- Chronic stress = high cortisol levels (kills hippocampal cells)
- Affects depression, anxiety, and development of ACEs

Neurobiology of Childhood Abuse

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

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.

- Also economic hardship, and racism

- 60% have 1 ACE; 12% have 4 or more

Long term effects of early experience

- "The Long Shadow": Baltimore Beginning School Study: only 4 % of disadvantaged children earned college degrees by age 28.

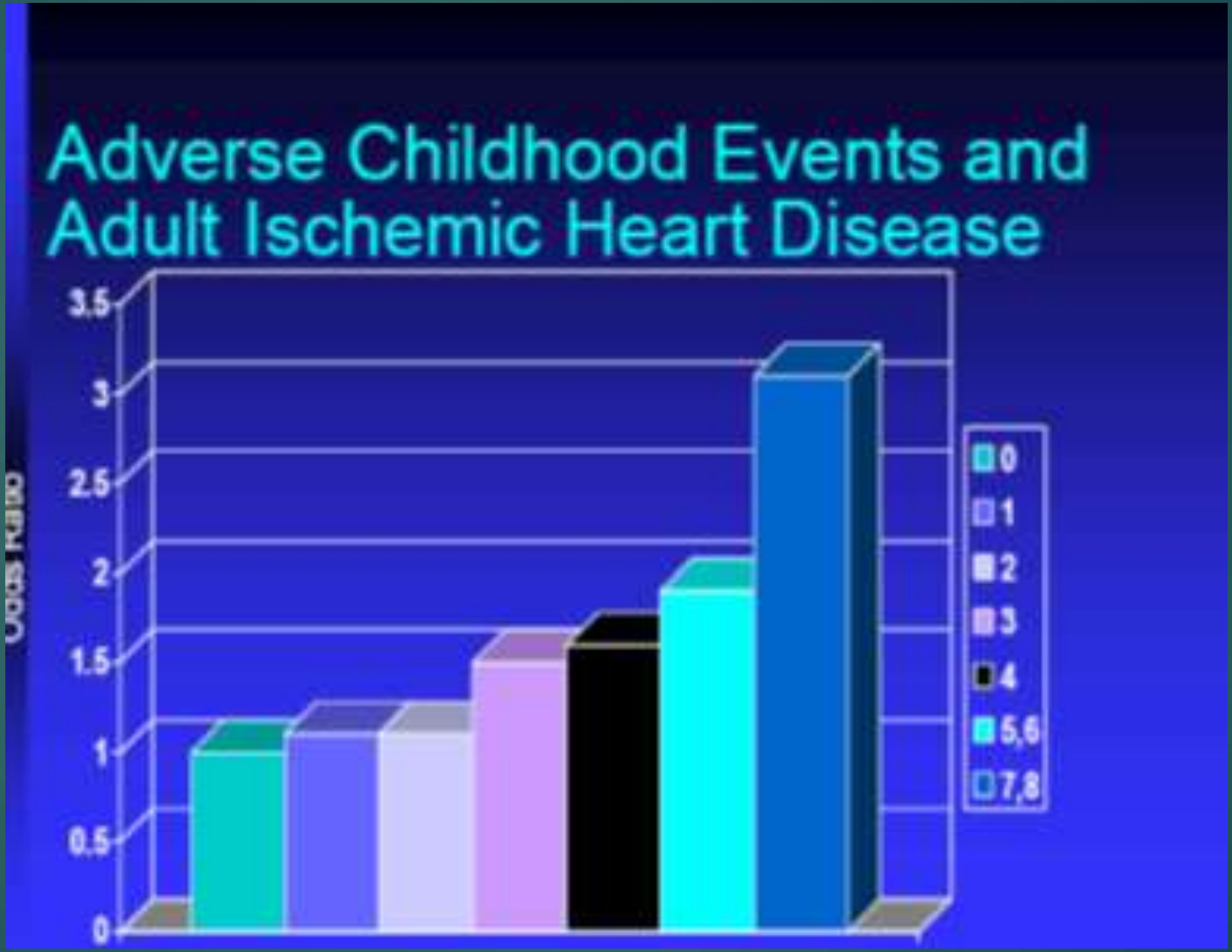
- Adverse Childhood Experience (ACEs) studies predict adult health and longevity

  - Felletti: ACEs are better predictors of adult medical status than most medical tests (COPD or hepatitis 2.5 x greater; Depression 4.5 x; Suicidality 12 x; 7+ score: 3 x lung CA, 3.5 x ischemic heart disease)

http://acestudy.org/

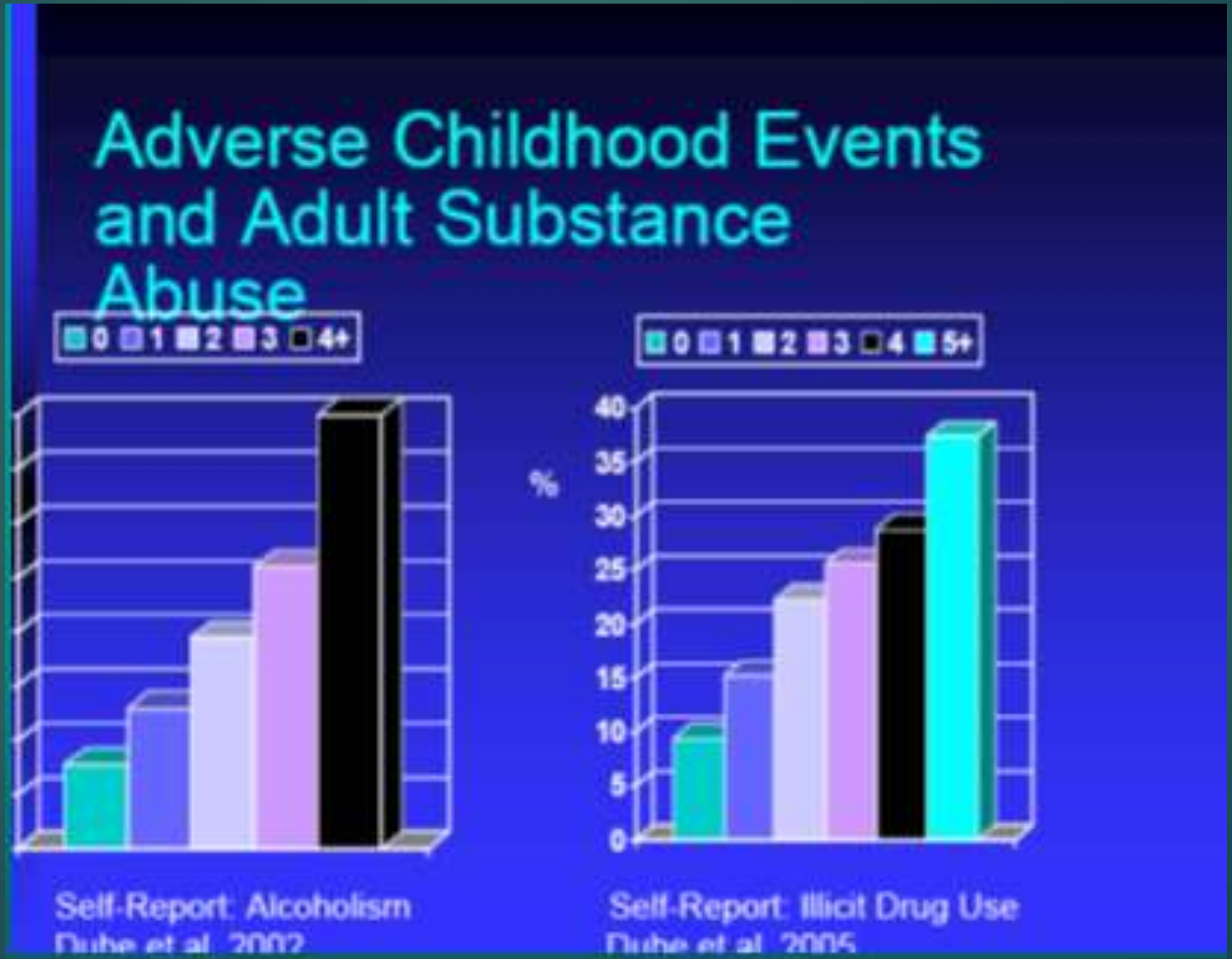
Adverse Childhood Events 1:
Adult Depression

Adverse Childhood Events 2:
Adult Heart Disease

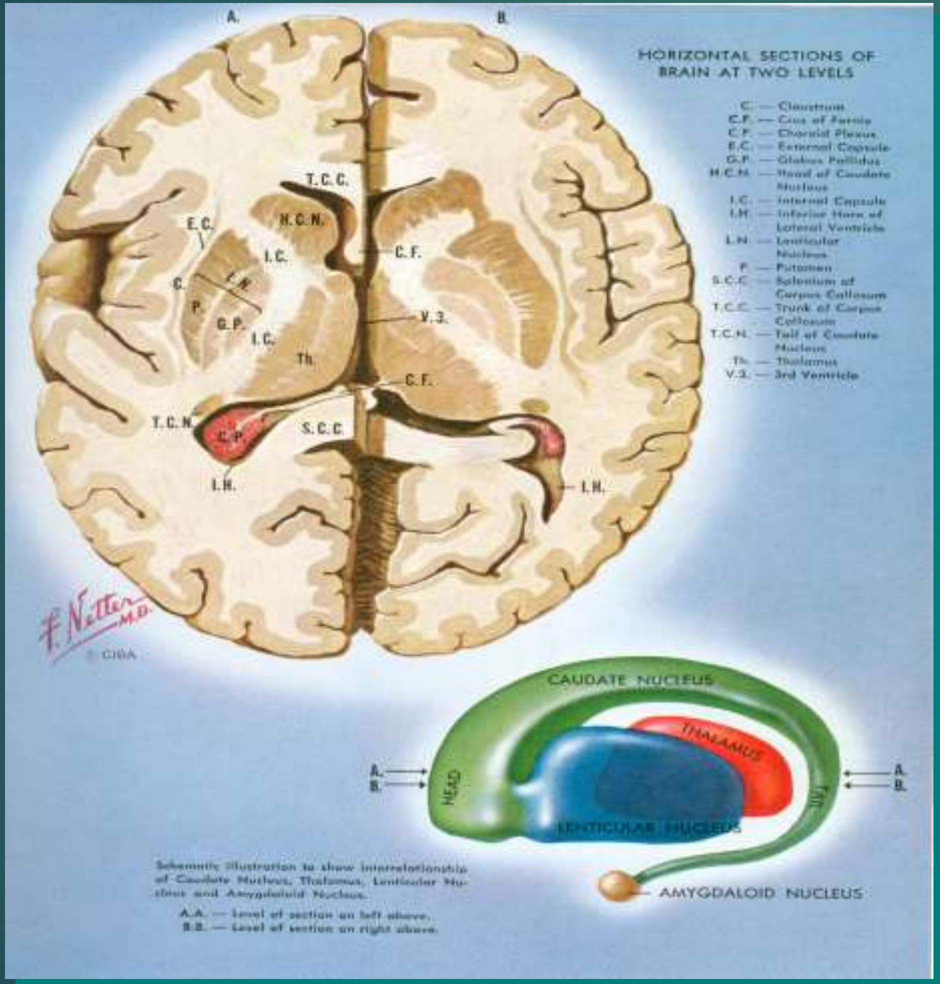


Having 6 or more ACES reduces life expectancy down to age 60.

Adverse Childhood Events 3: Substance Abuse



Basal Ganglia: Motor central



Pallidus
Putamen
Caudate Nucleus
Globus Pallidus
Substantia Nigra (SN)
Subthalamic Nucleus
Nucleus Accumbens (NA)

Major input = striatum (caudate Nucleus, putamen, NA)

Major output = Globus pallidus, SN

Motor functions of basal ganglia

- **Planning and programming of movement**, i.e.. an abstract thought is converted into voluntary action.
  - Dopamine signaling system center: **Everyday Clairvoyance: near-future predictions, prediction errors (**hop out of the way before the lion jumps)
  - **Cognitive** processes: cauda**te nucleus** has connections with the frontal lobe.
  - Muscle tone and posture.
- Healthy basal ganglia inhibits **resting tremor**

Basal Ganglia & Cerebellum: United

- Each has a unique learning mechanism.
- Basal ganglia: reward-driven learning and the gradual formation of habits.
- Cerebellum: more rapid and plastic learning in response to errors in performance.
- Both involved in procedural memory

Disorders of basal ganglia

Parkinson's disease (Paralysis agitans)

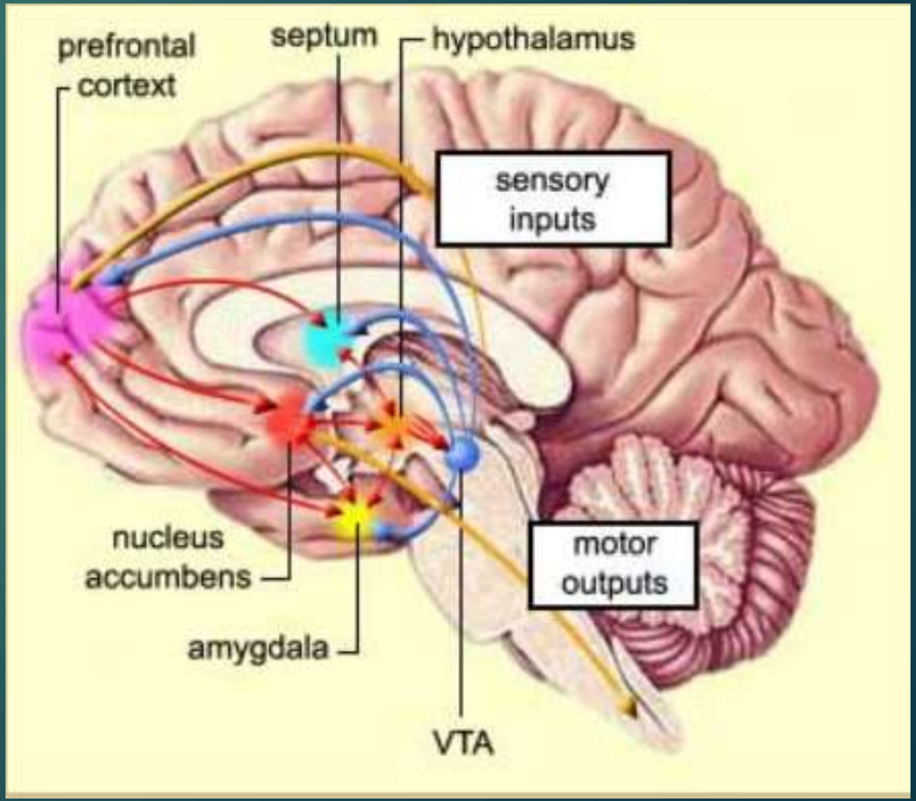
- Caused due to damage of dopaminergic neurons of Substantia Nigra, that sends inhibitory impulse to striatum
- Rigidity, Involuntary tremor (resting tremor), Akinesia (difficulty in initiating movements)
- Treatment with L-dopa

Huntington's chorea

- Loss of GABA secreting neurons of striatum (inhibitory impulses). The loss of inhibition cause distortional movements
- Acetylcholine secreting neurons of many parts of brain are lost. This causes dementia

Nucleus Accumbens: Dopamine drug store

- Fight, Flight, Eating, Sex
- Reward, motivation and addiction.
- Dependent drugs such as cocaine and nicotine trigger the release of dopamine; but not caffeine.
- Activation if you see:
  - drug paraphernalia,
  - newborn infant
  - grieving woman

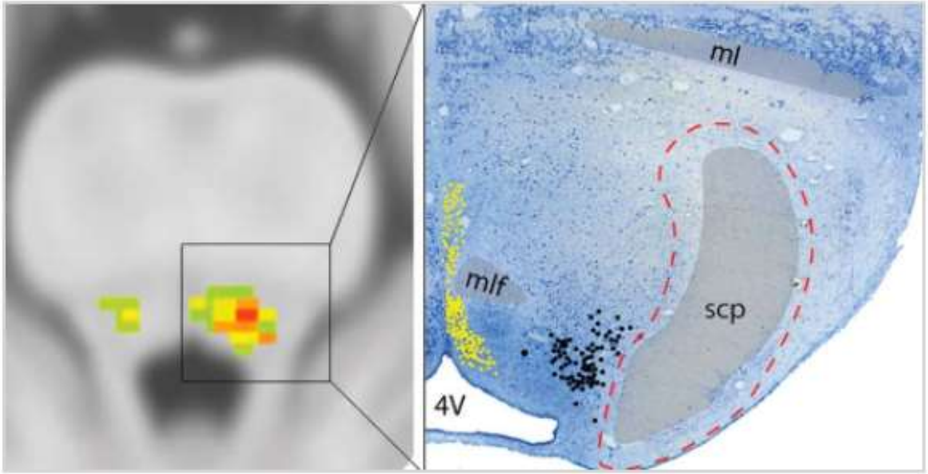


Consciousness: brainstem-cortex network

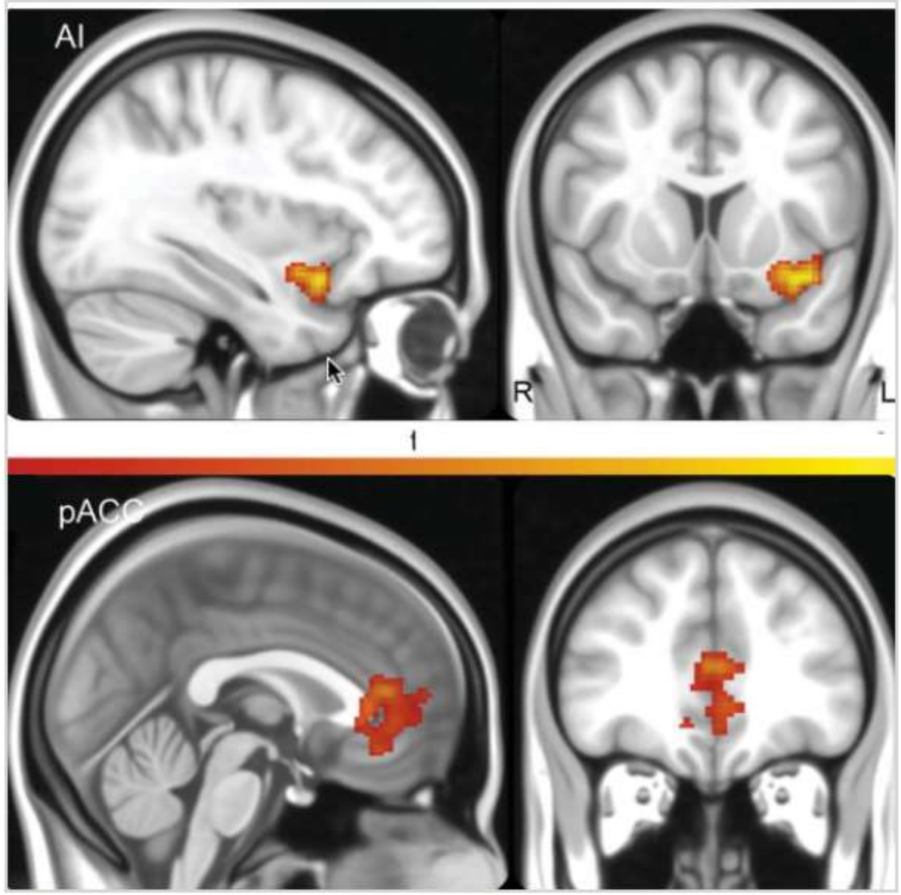
- Arousal and awareness are two critical components of consciousness. Arousal is likely regulated by the brainstem. Awareness is thought to reside in the cortex.
- Study: 36 patients with brainstem lesions, of which 12 led to coma and 24 did not. Mapping the injuries revealed that a small "coma-specific" area of the brainstem – the rostral dorsolateral pontine tegmentum – was significantly associated with coma
- Used the Human Connectome to identify which other parts of the brain were connected to these coma-causing lesions. Their analysis revealed two areas in the cortex that were significantly connected to the coma-specific region of the brainstem. One sat in the left, ventral, anterior insula (AI), the other in the pregenual anterior cingulate cortex (pACC). Both regions have been implicated previously in arousal and awareness.
- "consciousness network" was disrupted in patients with impaired consciousness.

David Fisher, et al., Neurology, 2016

Coma Central: Pontine Tegmentum & Anterior Insula & Cingulate



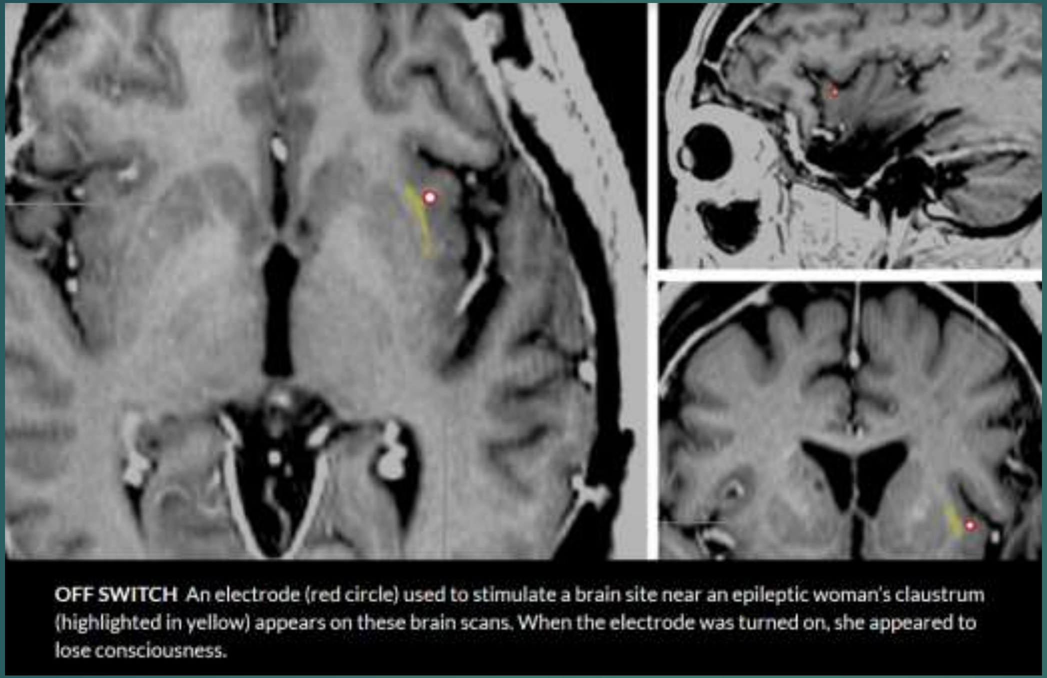
(Left) A coma-specific region in the left pontine tegmentum in the brainstem (red). (Right) Multiple nuclei implicated in arousal surround the coma-specific region, including the dorsal raphe (yellow dots), locus coeruleus (black dots), and parabrachial nucleus (red dashed line). (credit: David B. Fischer, MD et al./Neurology)



The coma-specific brainstem region is functionally connected to clusters in the anterior insula (AI) and pregenual anterior cingulate cortex (pACC). Voxels within these nodes were functionally connected to all 12 coma lesions, and were more functionally connected to coma lesions than control lesions. (credit: David B. Fischer, MD et al./Neurology)

David B. Fischer et al. A human brain network derived from coma-causing brainstem lesions. Neurology ® 2016;87:1–8

Claustrum: Consciousness Grand Central Station; "gate keeper" of neural information for consciousness awareness.



Single epileptic patient: deep electrode electrical stimulation of claustrum switched her consciousness on and off over 2 days; amnestic for uncs periods; every region of the cortex sends fibers to the claustrum; highest connectivity in the brain by regional volume

Mohamad Koubeissi, 2014

Unconsciousness: no brain internet

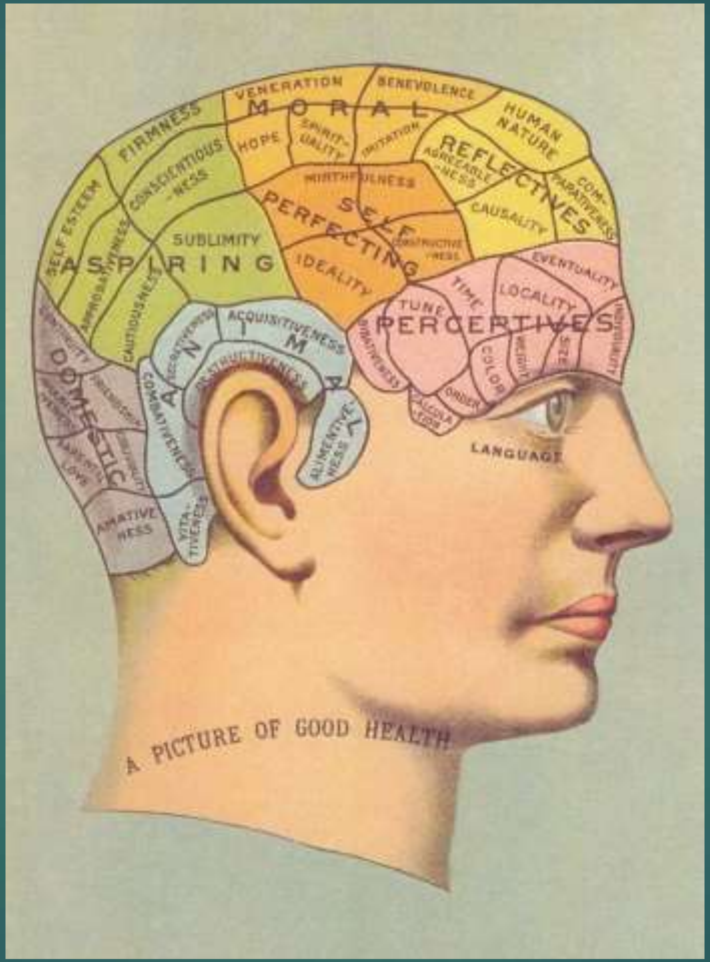
- Evidence that sensory networks in the brains of unconscious people remain locally functional, but intrabrain communication has broken down.
- The neighborhood's lights are on, in other words, but the brain's Internet and phone lines have all been cut.

- Unconsciousness is what happens when different parts of the brain can't connect: The signal simply dies.
- This also suggests that anesthetics work best when they cut those lines of communication.

Three Perspectives on Brain Functioning

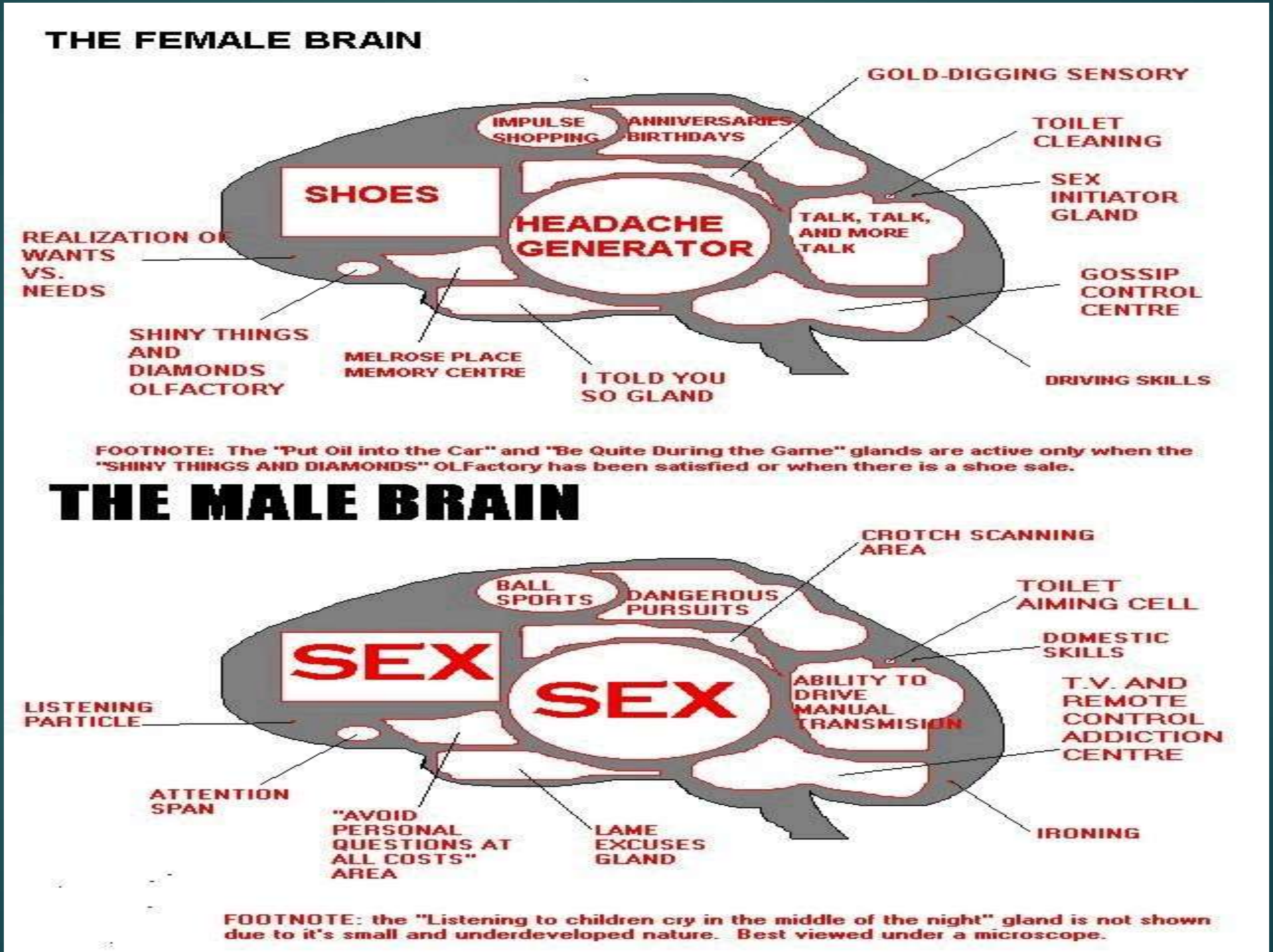
- Brain areas:
  - Functional Localization – domain specific processing areas: functional segregation is a principle of brain organization in humans.
  - General multiple demand processing areas
  - Connectivity network systems: Functional connectivity is defined as statistical dependencies among remote neurophysiological events.

Phrenological Model of Brain circa 1870

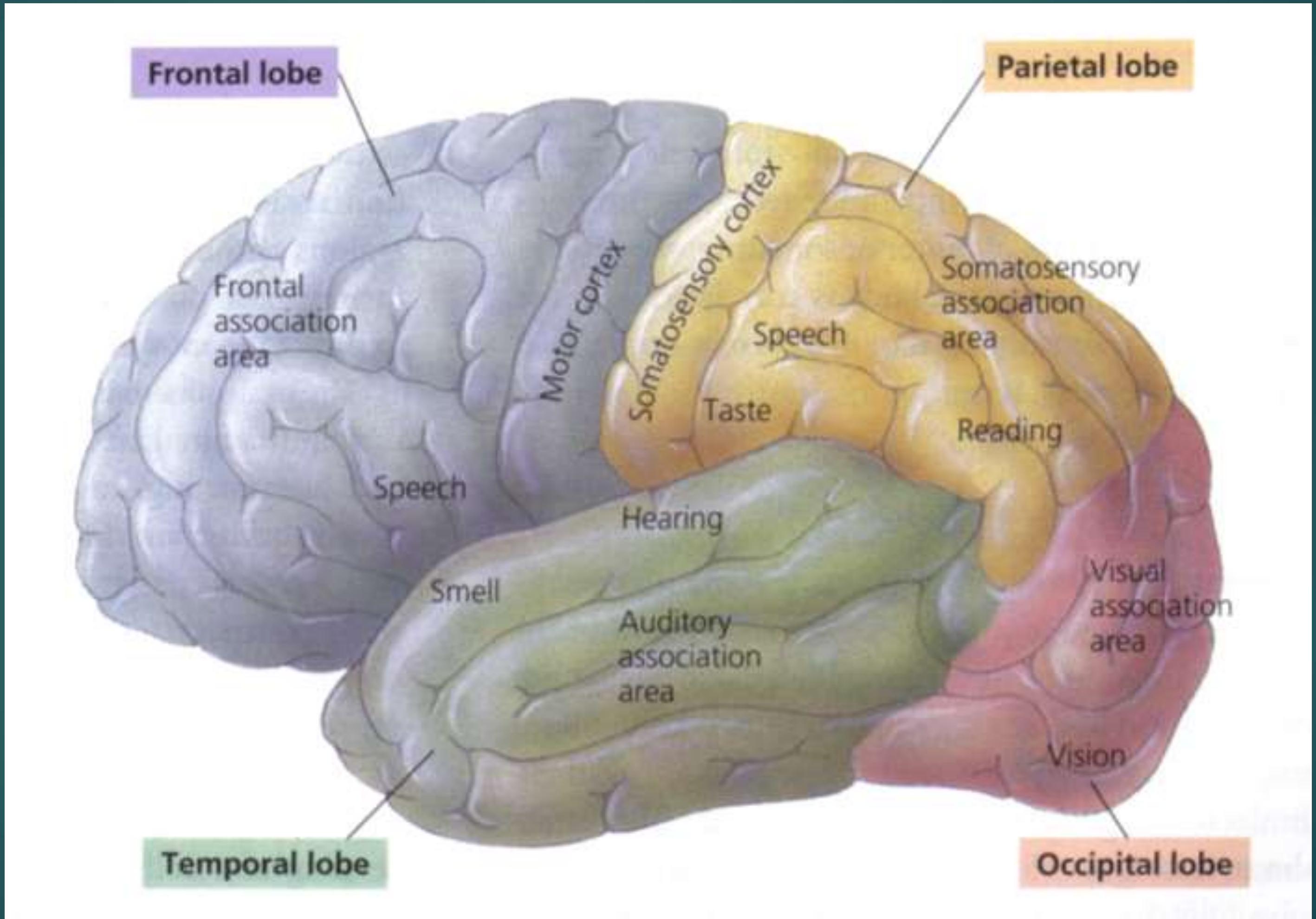


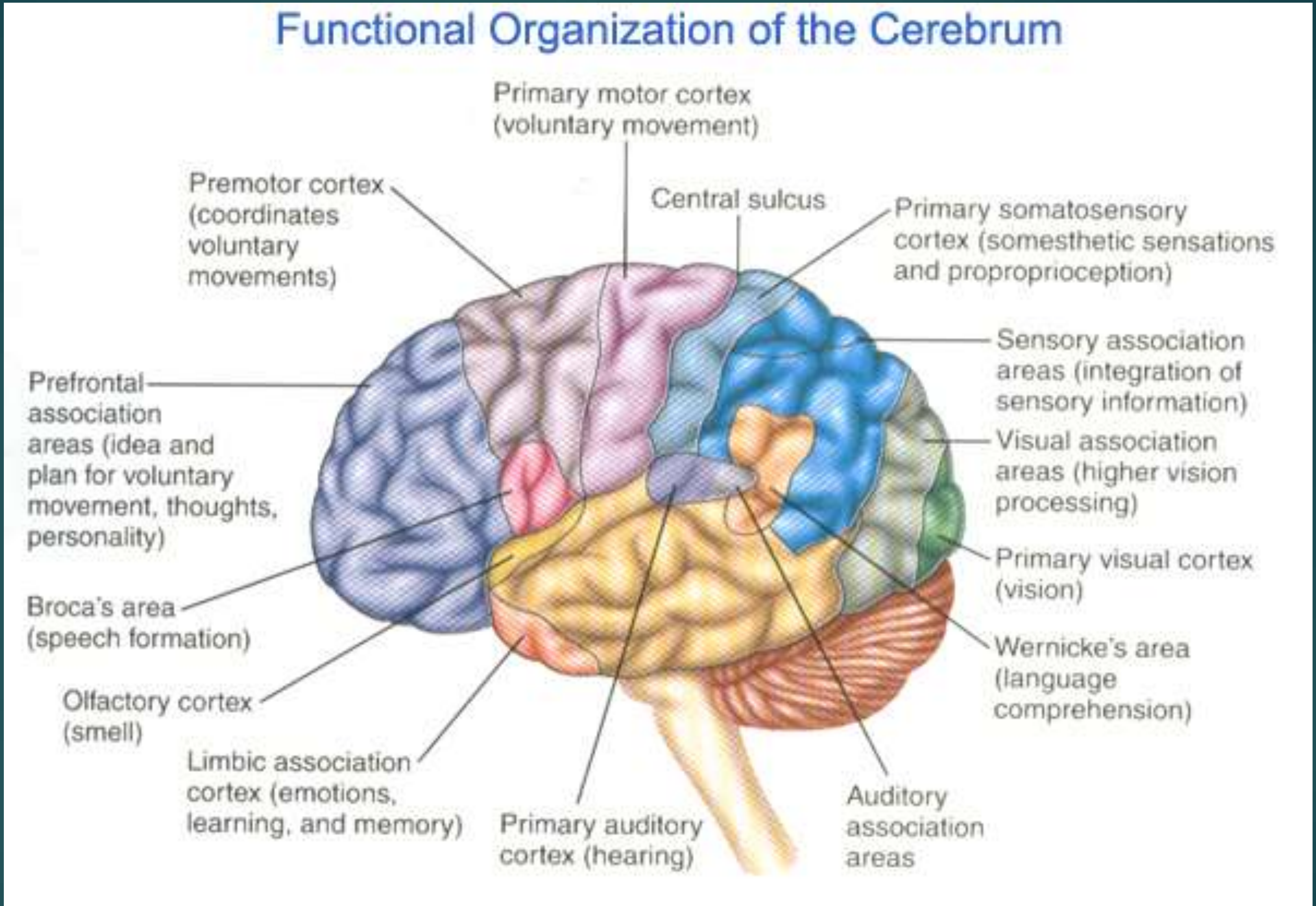
Phrenology had right idea – Functional Localization:
some brain areas are functionally specialized

Popular Conceptions of Localization

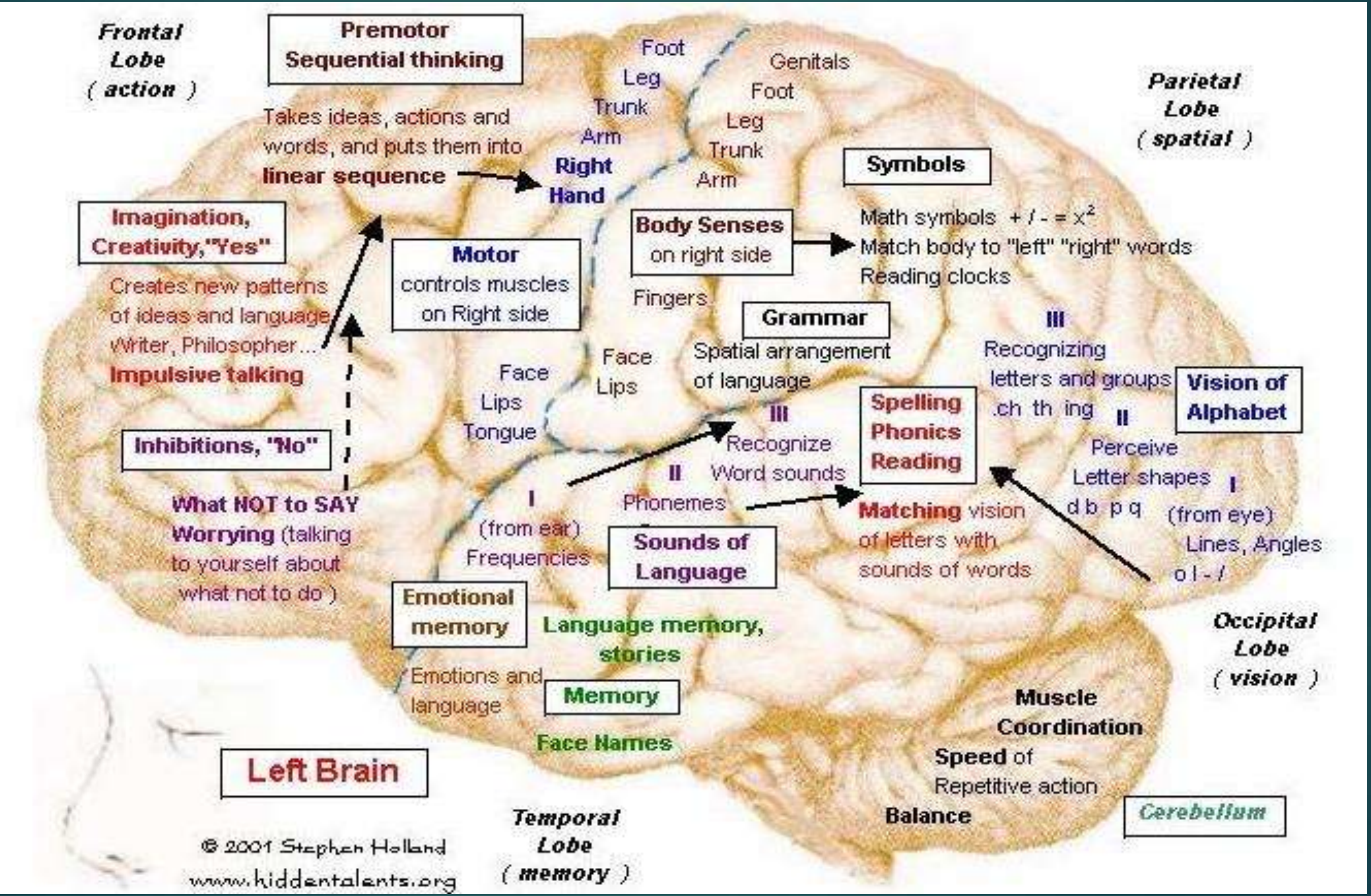


Neocortex: Regions of the cerebrum are specialized for different functions





Posterior brain produces stimulus-response reactions to environment (perception), the front brain facilitates decisions based on association and analysis (conception).


Frontal Lobe (action)
Premotor Sequential thinking
Takes ideas, actions and words, and puts them into linear sequence
Right Hand
Foot
Leg
Trunk
Arm
Genitals
Foot
Leg
Trunk
Arm
Parietal Lobe (spatial)
Symbols
Math symbols + / - = x²
Match body to "left" "right" words
Reading clocks
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
Fingers
Grammar
Spatial arrangement of language
Face
Lips
Tongue
Face
Lips
III
Recognizing letters and groups .ch th ing
Vision of Alphabet
Inhibitions, "No"
What NOT to SAY
Worrying (talking to yourself about what not to do)
III
Recognize
II Word sounds
Phonemes
I
(from ear)
Frequencies
Spelling Phonics Reading
II
Perceive Letter shapes
d b p q
I
(from eye)
Lines, Angles
o l - /
Matching vision of letters with sounds of words
Sounds of Language
Emotional memory
Language memory, stories
Emotions and language
Memory
Face Names
Occipital Lobe (vision)
Muscle Coordination
Speed of Repetitive action
Balance
Cerebellum
Left Brain
Temporal Lobe (memory)
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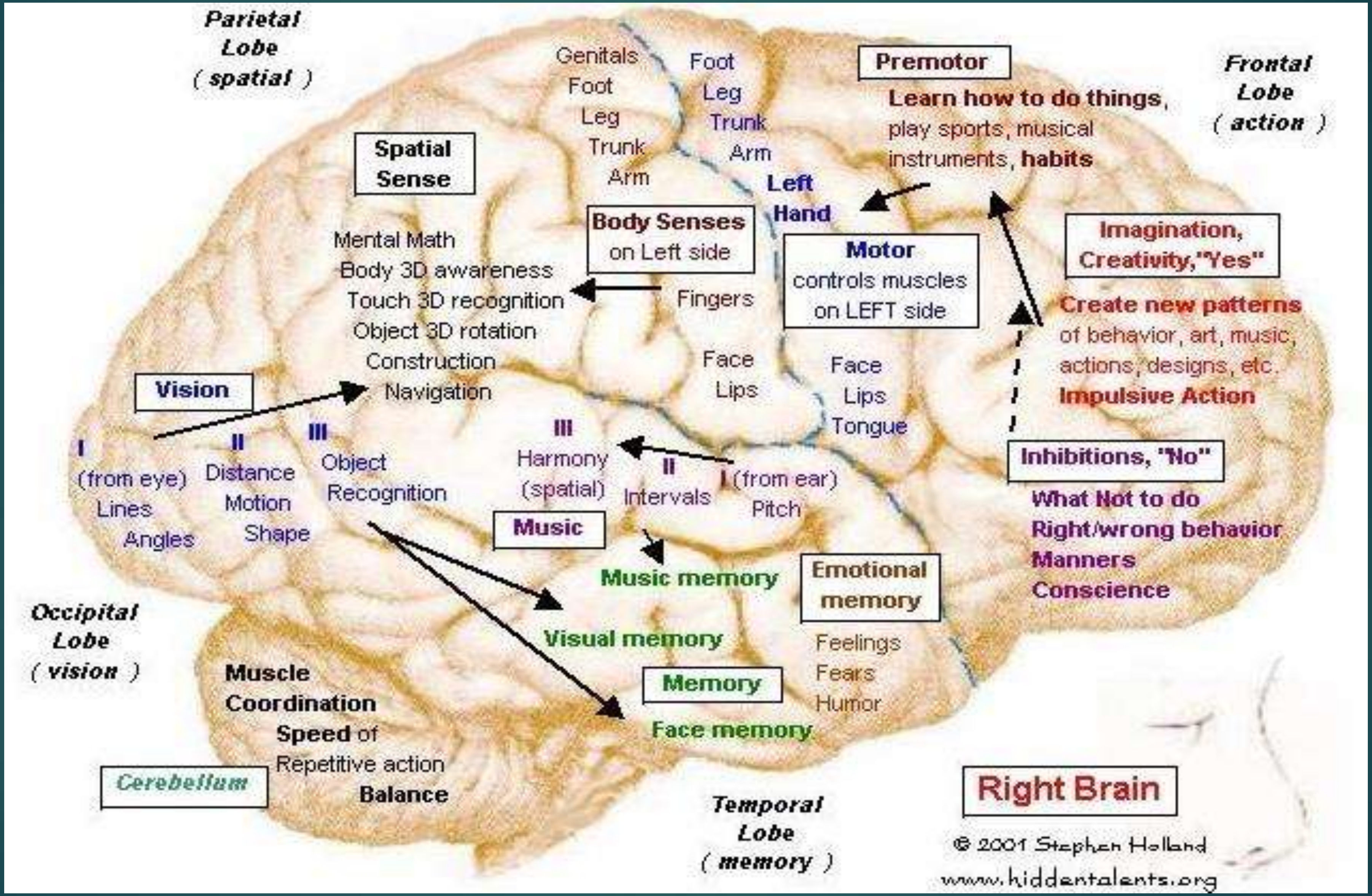
Parietal Lobe (spatial)
Frontal Lobe (action)
Occipital Lobe (vision)
Temporal Lobe (memory)
Genitals
Foot
Leg
Trunk
Arm
Foot
Leg
Trunk
Arm
Left Hand
Premotor
Learn how to do things, play sports, musical instruments, habits
Spatial Sense
Body Senses on Left side
Motor controls muscles on LEFT side
Imagination, Creativity,"Yes"
Mental Math
Body 3D awareness
Touch 3D recognition
Object 3D rotation
Construction
Navigation
Fingers
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
Music
Inhibitions, "No"
What Not to do
Right/wrong behavior
Manners
Conscience
Music memory
Emotional memory
Visual memory
Feelings
Fears
Humor
Memory
Face memory
Muscle Coordination
Speed of Repetitive action
Balance
Cerebellum
Right Brain
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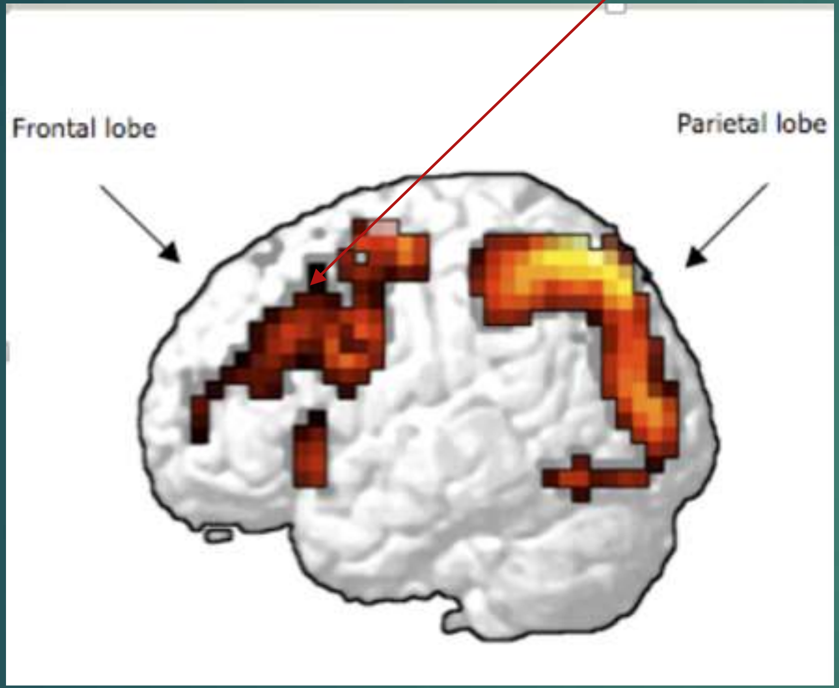
Major Areas of Cognition:
All cognitive processes involve multiregional networks

- Perception: vision, hearing, tactile, olfactory, taste
- Attention and concentration
- Memory
- Language
- Motor ability
- Visual Spatial ability
- Executive function: rational thinking, planning
- Social ability

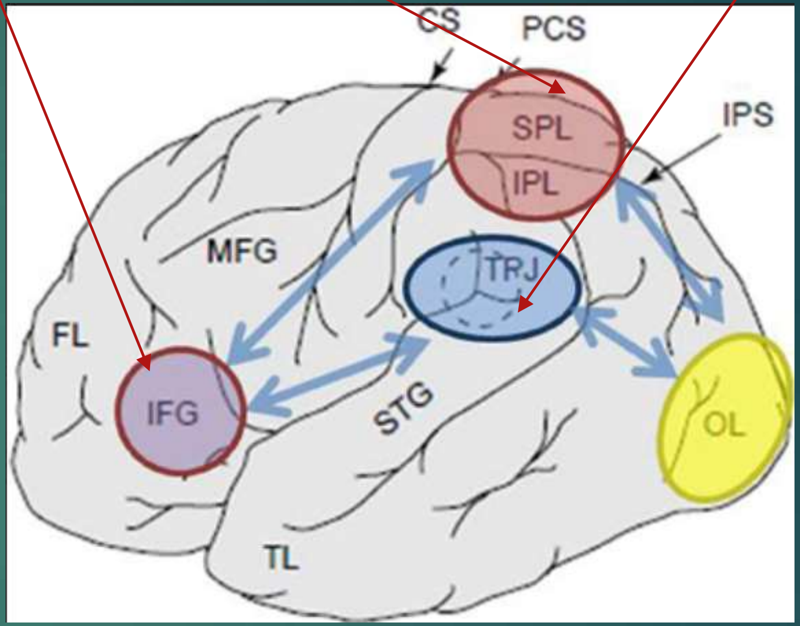
Attention = Prefrontal (goal) & Parietal (stimulus)

(top-down attentional orienting; task relevance)

bottom-up orienting: stimulus demand



Kingberg, et al., 2002



S. Shomstein, 2012

Attention can be controlled by:

- intentions/expectation/goal direction of the observer as well as by
- salience of the external physical stimulus

Attention and Concentration

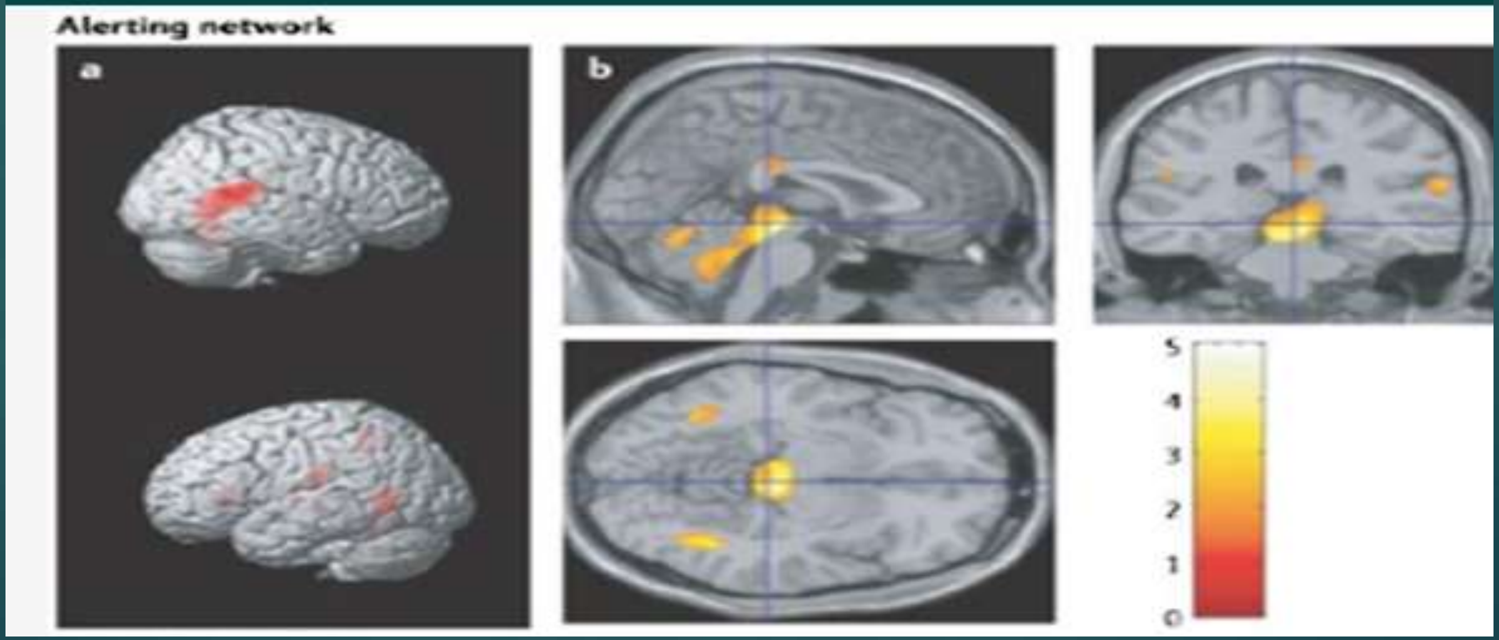
Three attentional networks:

- Alerting – Bottom Up modulation (memory-free, and reactive): awake
- Orienting – Sensory Domain Specific: sound of truck going by
- Executive control – Top down modulation (memory-dependent, or anticipatory): focusing on task

Alerting: Bottom Up Modulation

- Achieving and maintaining an alert state in preparation for incoming stimuli (RAS)
- Locus coeruleus (pons), right frontal and parietal cortex

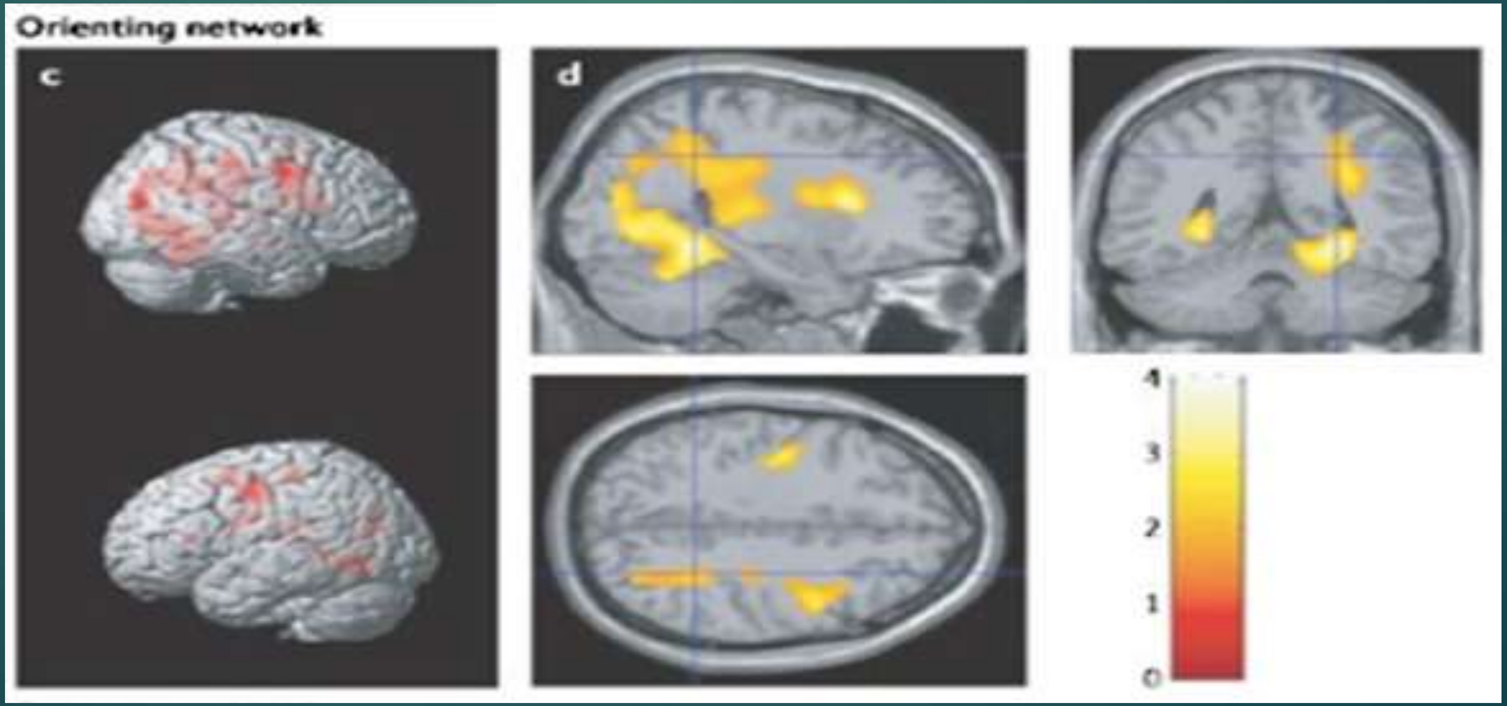
- Modulator: Norepinephrine



Orienting: Sensory Domain Specific

- Selectively focusing on one sensory stimuli, i.e. hear truck outside
- Superior Parietal & Temporal Parietal Junction

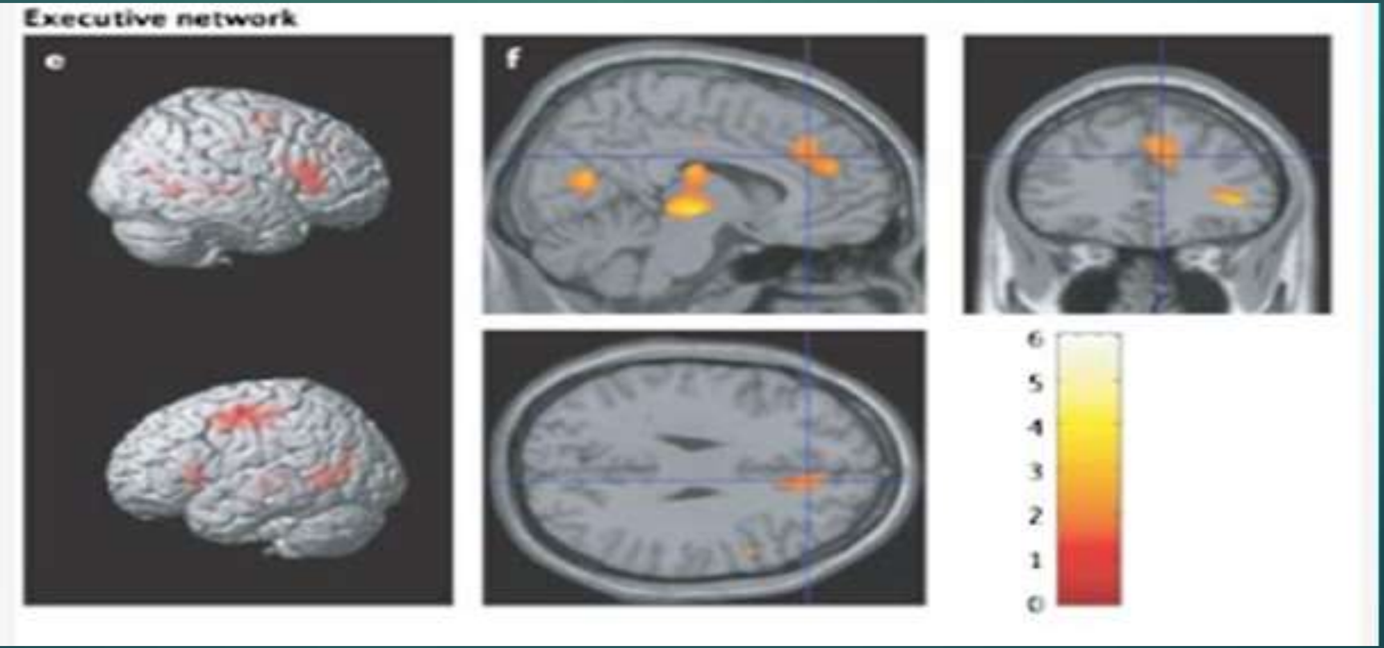
- Modulation: Acetylcholine



Executive Attention: Top Down Modulation

- Monitoring and resolving conflicts in planning, error detection and overcoming habitual actions
- Anterior Cingulate, Lateral ventral Prefrontal, Basal Ganglia

- Modulator: Dopamine



Brain as Swiss army knife: Domain Specific Areas of the Brain

Special purpose, domain specific processors (localized functional areas):

- Classic: Vision, Touch, Motor Control, anger & fear (Amygdala) areas
- Face recognition
- Color
- Regions of space
- Visual motion
- Body parts (but not faces)
- Hearing sounds with pitch
- Hearing sounds without pitch
- Speech
- Understanding the meaning of a sentence
- Understanding mental states of others
- Voice recognition

141 functions: $1400

Modular/specialized brain areas

- There are domain-specific regions (i.e. Broca for language).
- Tailored to solve particular problems of longstanding importance to our species
- Proof of functional specialties of these areas:
  - activation on fMRI for normal function and
  - lesion studies for pathology

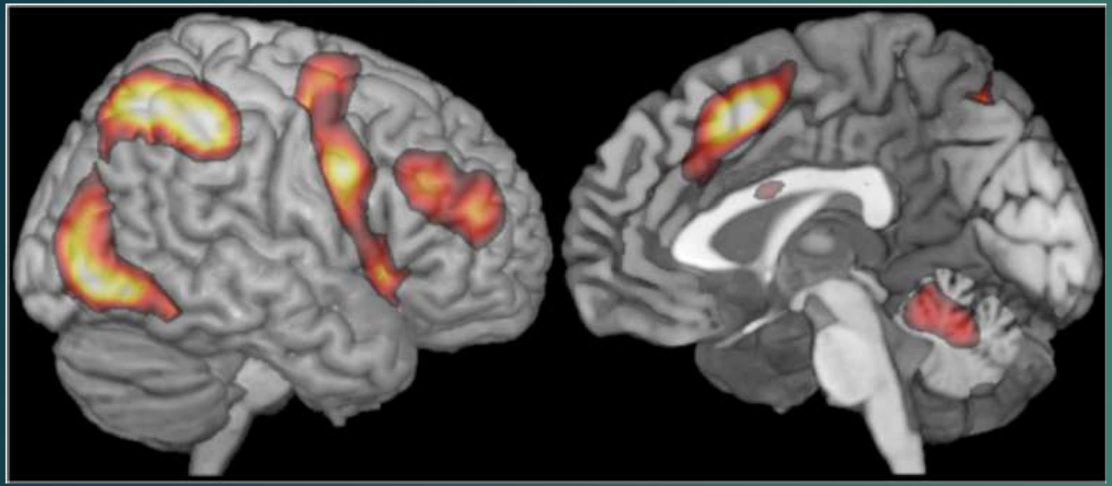
Multiple-demand (MD) system:
Functionally general regions

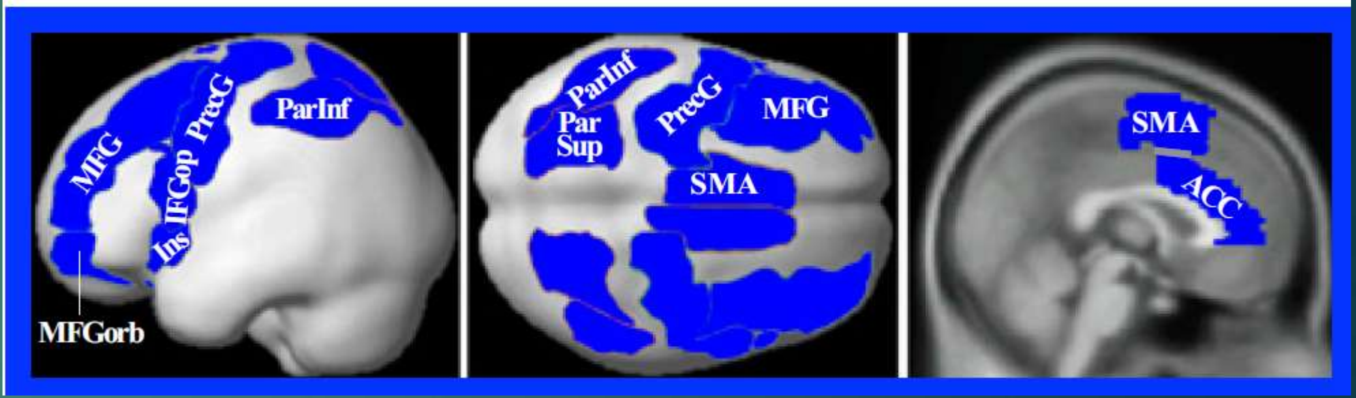
- There are also a set of functionally general regions that endow us with the cognitive flexibility necessary to solve novel problems.

- Study: Seven diverse demanding cognitive tasks produced overlapping activation at the individual-subject level in a number of frontal and parietal brain regions

Evelina Fedorenko, et al., 2013

Multiple Demand Processors: 7 prefrontal/parietal areas





- Problems used: Localization, math, multisource interference tasks, spatial and verbal WM, Stroop
- Opposite of Default Mode Network (DMN) areas: medial temporal lobe, parts of the medial prefrontal cortex, the posterior cingulate cortex, and the precuneus

Distributed & Parallel Processing Networks: Connectivity networks

- Ways brain is neuroanatomical organized into networks:
  - Extensive neuron to neuron connections
  - Neurotransmitter systems
  - Functional areas organized via heteromodal connections
  - White matter fiber tracts – short to distant
  - Multiple processing networks: i.e. semantic memory, language, attention, etc.
  - Hub regions, i.e. expressive, receptive
  - Connectivity networks

Dynamic networks model

- Brain isn't just functionally modular. While certain regions are specialized to process certain types of information and are active during certain tasks, they are all part of distributed functional networks.

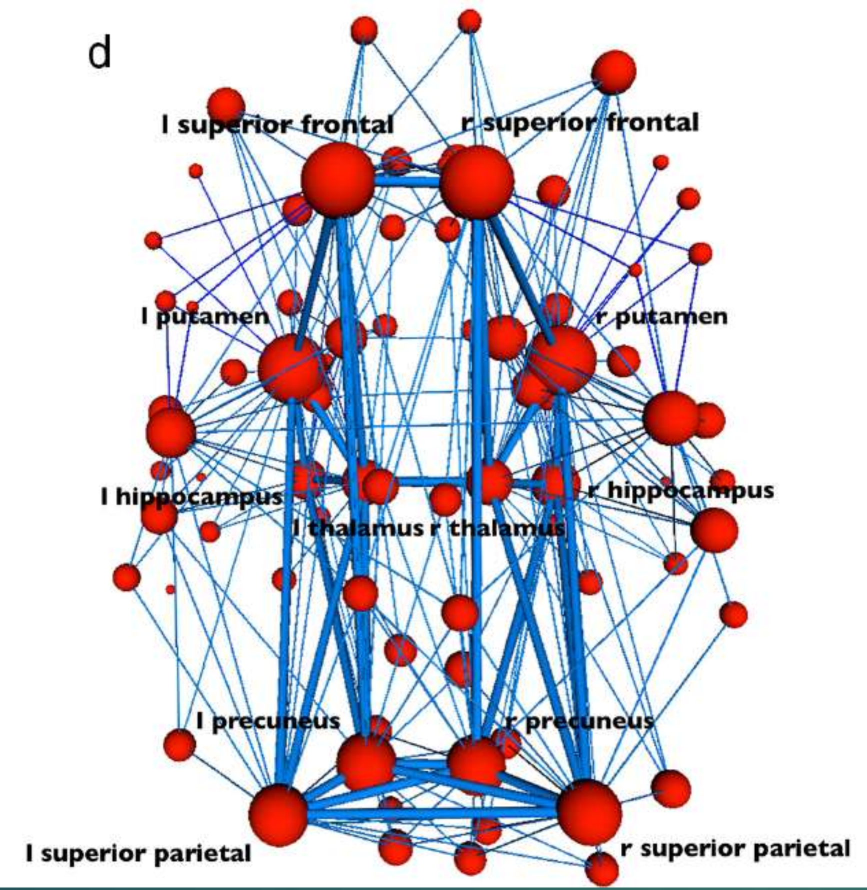
- The CNS is an integrated, wide, dynamic network made up of cortical functional epicenters connected by both short-local and large-scale white matter fibers.

- Brain function results from parallel streams of information dynamically modulated within an interactive, multimodal, and widely distributed circuit.

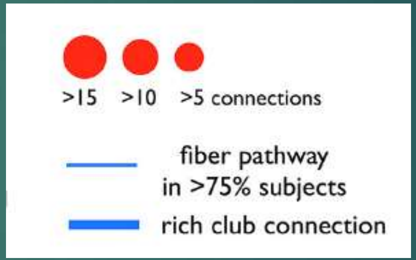
Rich World Organization

- Brain Hubs: Some regions have a high degree, low clustering, short path length, high centrality and participation in multiple communities across the network,
- Brain hubs form a "rich club," characterized by a tendency for high-degree nodes to be more densely connected among themselves than nodes of a lower degree.
- There is a group of 12 strongly interconnected bihemispheric hub regions, comprising the precuneus, superior frontal, superior parietal cortex, subcortical hippocampus, putamen, and thalamus.

12 Rich World Hubs: central areas and freeways

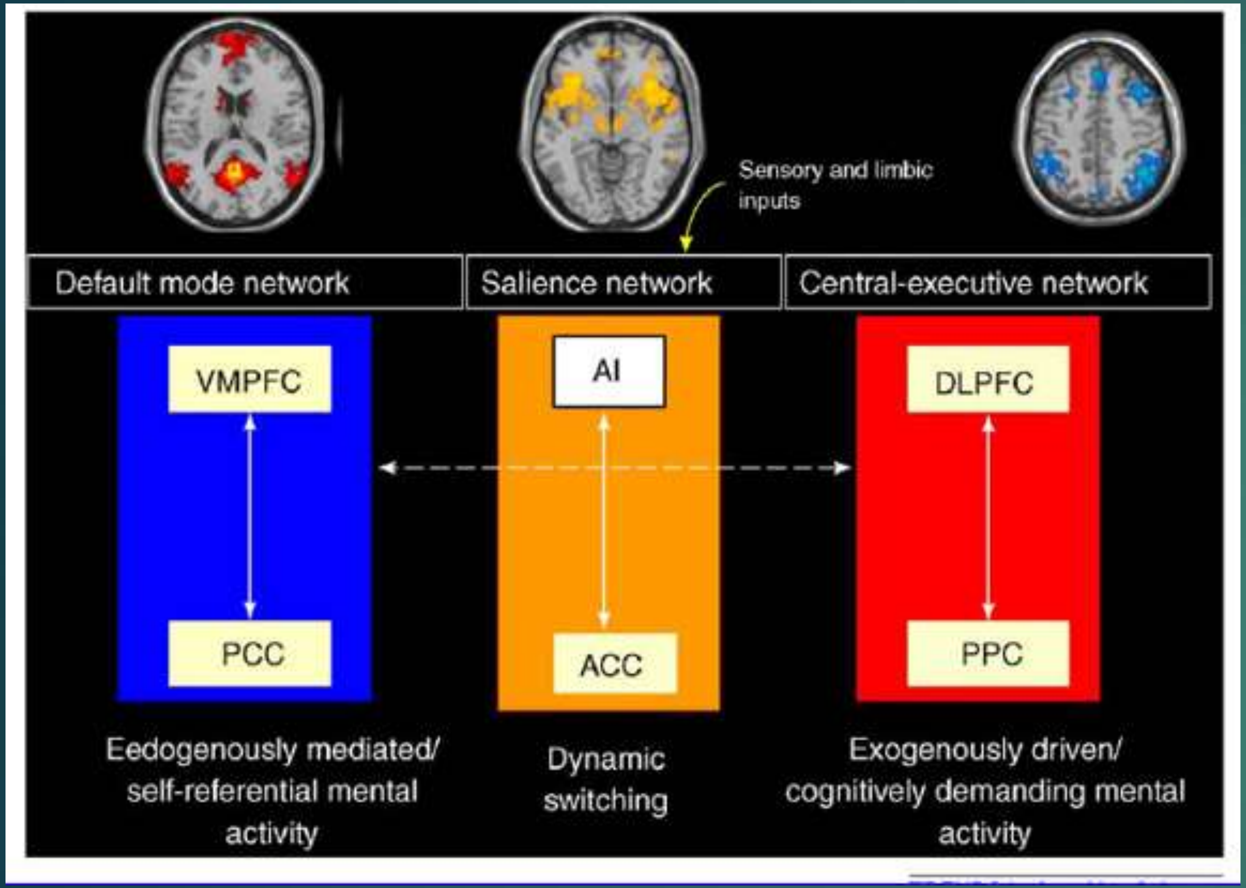


Bilateral frontoparietal regions, including precuneus, superior frontal and parietal cortex, hippocampus, thalamus, and putamen are individually central & also densely interconnected, together forming a rich club.



Connections between rich-club regions (dark blue) and connections from rich-club nodes to the other regions of the brain network (light blue). The figure shows that almost all regions of the brain have at least one link directly to the rich club. Brain lesions that damage one of the rich club hubs will have more serious behavioral effects (3x more) than damage to non-hub area.

Major Connectivity Networks



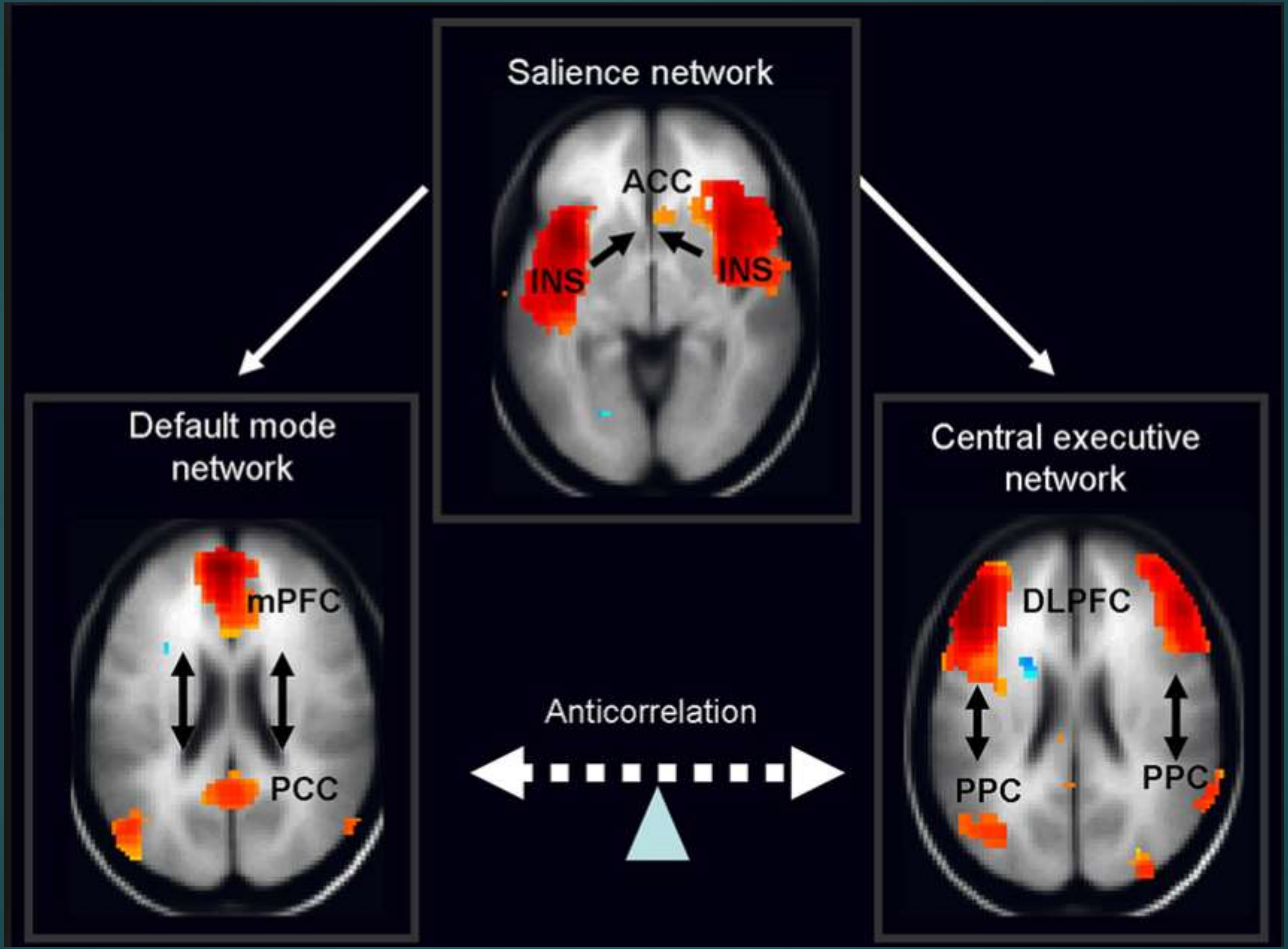
3 major networks:

DMN: day dreaming, self reference

Salience: earliest cortical signal of behaviorally salient events, such as errors. Interoceptive awareness, emotional responses, &
empathic processes.

Central Executive: higher-order cognitive and attentional control

3 Major Networks



Disease Conditions = Impaired Functional Connectivity

- Alzheimer’s: decreased connectivity
- Autism: altered connectivity
- Depression: abnormal connectivity
- Schizophrenia: disrupted networks
- ADHD: Altered "small networks" and Thalamus changes
- Aging brain: disruption of brain systems and motor network
- Epilepsy: disruption and decrease/increase in connectivity
- Parkinson's disease: altered connectivity
- Obsessive Compulsive Disorder: increase/decrease in connectivity
- Pain Disorder: altered connectivity

Dysconnectivity is a transdiagnostic brain-based phenotype in individuals with psychiatric disorders.

- Frontotemporal connectivity has been implicated in a range of mental illnesses including schizophrenia, conduct disorder, as well as anxiety.
- Study: clinical symptoms as well as cognitive function in 6487 individuals aged 8 to 21 years from November 1, 2009, to November 30, 2011; n = 784; neuroimaging
- Findings: significant association with general psychopathology levels and cognition. (Proxies of critical adult-life indicators)
- A brain white matter pattern reflecting frontotemporal connectivity and crossing fibers in the uncinate fasciculus was the most associated feature for both traits; UF is most heritable & longest to maturation. Hypothesized to subserve a limbic temporo-amygdala-orbitofrontal network critically involved in integration of emotional states with cognition and behavior.

Dag Alnæs, et. Al., JAMA Psych, 2018

Dysconnectivity 2

- he component reflects a distinct frontotemporal pattern reflecting crossing fibers at the intersection between the uncinate fasciculus and the inferior fronto-occipital fasciculus.
- Both the general psychopathology (16%) and cognitive (18%) factor were heritable and showed a negative genetic correlation.
- Dysconnectivity of limbic temporo-amygdala-orbitofrontal pathways is a transdiagnostic brain-based phenotype in individuals with increased susceptibility and symptoms of psychiatric disorders.

Commonality of many psychiatric disorders: DMN hyperactivity

- Metaanalysis: major depressive disorder, bipolar disorder, social anxiety disorder, obsessive-compulsive disorder, or posttraumatic stress disorder, as well as healthy control
- Most common behavior = negative thinking
- The most common difference in white matter structure that — present in every emotional disorder — was disruption in a region of the brain that connects different parts of the "default-mode network," which is responsible for passive thoughts not focused on a particular task.
- That area is the left superior longitudinal fasciculus. The superior longitudinal fasciculus, or SLF, also connects the default-mode network and the cognitive control network, which is important in task-based thinking and planning and tends to work in alternation with the default-mode network. The constant negative thoughts or ruminations associated with most emotional disorders appear to be due to a hyperactive default-mode network
- If the part of the brain that helps rein in the default-mode network isn't as well-connected through the SLF, this could explain why people with emotional disorders have such a hard time modulating or gaining control of their negative thoughts

Hemispheric Lateralization

Hemispheric Asymmetry: Dominant (Left) Hemisphere

Hemispheric Size Differences:

- LH denser, more gray matter relative to WM
- Frontal operculum area larger (more sulcal surface area)
- Inferior parietal lobe larger
- Insula larger
- Medial temporal larger
- Neocortex thicker
- Occipital lobe wider
- Occipital horn of later ventricle longer
- Planum temporale (BA 22) larger
- Sylvian fissure longer
- TP cortex larger

Asymmetry: Nondominant (Right)

- RH is larger and slightly heavier
- Heschl’s gyri larger
- Convexity of frontal operculum larger
- Frontal lobe wider
- Medial geniculate nucleus larger

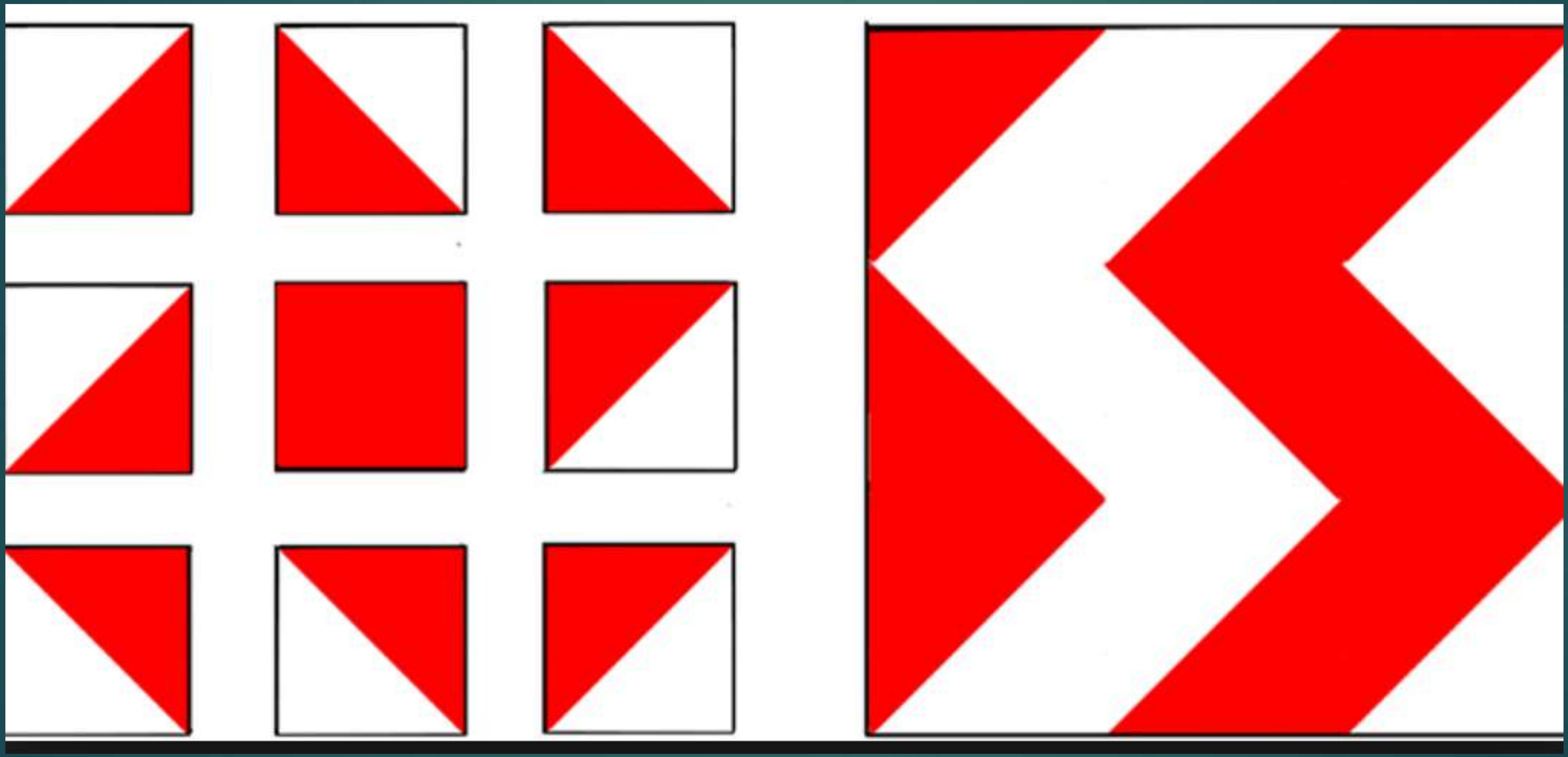
Functional Asymmetries

Function	Left Dominant	Right Dominant
Attention	Speech sounds	Left hemispace: all senses
Auditory	Language/speech	Music
		Nonlanguage Sounds
Language	Expressive/receptive	Prosody of speech
	Verbal comprehension	Prosody comprehension
	Spontaneous speech	Expressive prosody
	Repetition	Repetition of prosody
	Reading, Writing	Emotional expression
		Sarcasm; Jokes
Memory	Verbal Memory	Spatial/visual memory
	Word lists	Faces
	Stories	Spatial location
	Word-pairs	

Functional Asymmetries

Function	Left Dominant	Right Dominant
Motor/movement	Right side of body	Left side of body
	Mouth Movements	
	Complex movements	Movement in spatial patterns
Tactile	Braille	
	Tactile Patterns	
Visual/spatial	Printed letter/words	Faces
	Geometric patterns	
	Geometry	
	Mental rotation of shapes	
	Spatial orientation	

Block Design test: bihemispheric spatial ability



LH: detail orientation RH: maintaining the gestalt

Right Hemisphere Language Processes

- Nouns for which image is available (tree)
- Emotional content (love)
- Symbolic or pictorial word form (kanji, pictorial logos); pictographic reading
- Distantly verbal related material (journey, life)
- Better at semantic (meaning) than lexical (word or not)
- Metaphor appreciation
- Context processing
- Sarcasm
- Humor
- Prosody

Musical abilities and the hemispheres

- LH:
  - Rhythm
  - Absolute pitch (if present)
  - Musicians’ ability to analyze chord structures
  - Discrimination of local melody cues
- RH:
  - Pitch, melody, intensity, harmony, etc.
  - Appreciation of chord harmony
  - Timbre discrimination
  - Melody recognition

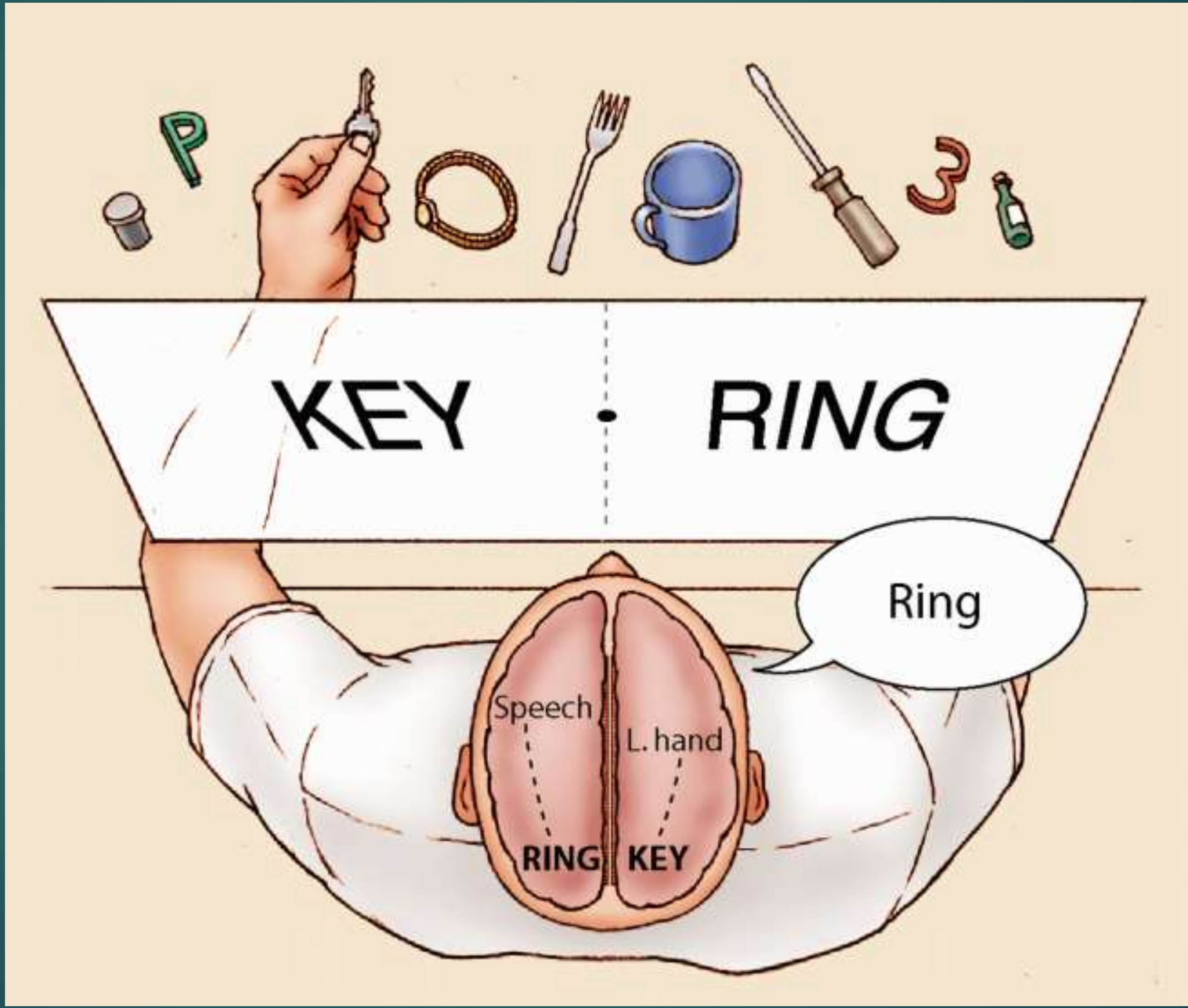
Evidence from results of brain lesions/surgery, from dichotic listening experiments, from Wada test experiments, and from imaging

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, i.e. first sight of word “age”
- Lateralization develops with age
  - trauma creates more problems in males since females have more communication between hemisphere (corpus callosum is thicker posteriorly in women)
- Remember: both hemispheres used simultaneously in almost all behaviors

Split brain (corpus callosum cut) effects:
RH does not know what left hand does

Speech is controlled by LH; has no access to left hand info



W. W. Norton

Brain Asymmetries: handedness & language

- 90% of people are right-handed
- 95% of right-handers are left hemisphere dominant for speech
- 80% of left handers are left dominant for language
- Larger protrusions of the right frontal lobe and the left occipital lobe (in all hominids).
- Structures involved in language processing are larger in the left hemisphere than in the right.
  - Broca's area in the left frontal lobe is larger

Approach/Avoidance in Left handers

- Approach motivation is computed mainly in the left hemisphere of the brain
  - If anterior left frontal lesion, depression
- Withdrawal motivation in the right hemisphere.
  - If anterior right frontal, impulsivity
- This is reversed in left-handers.

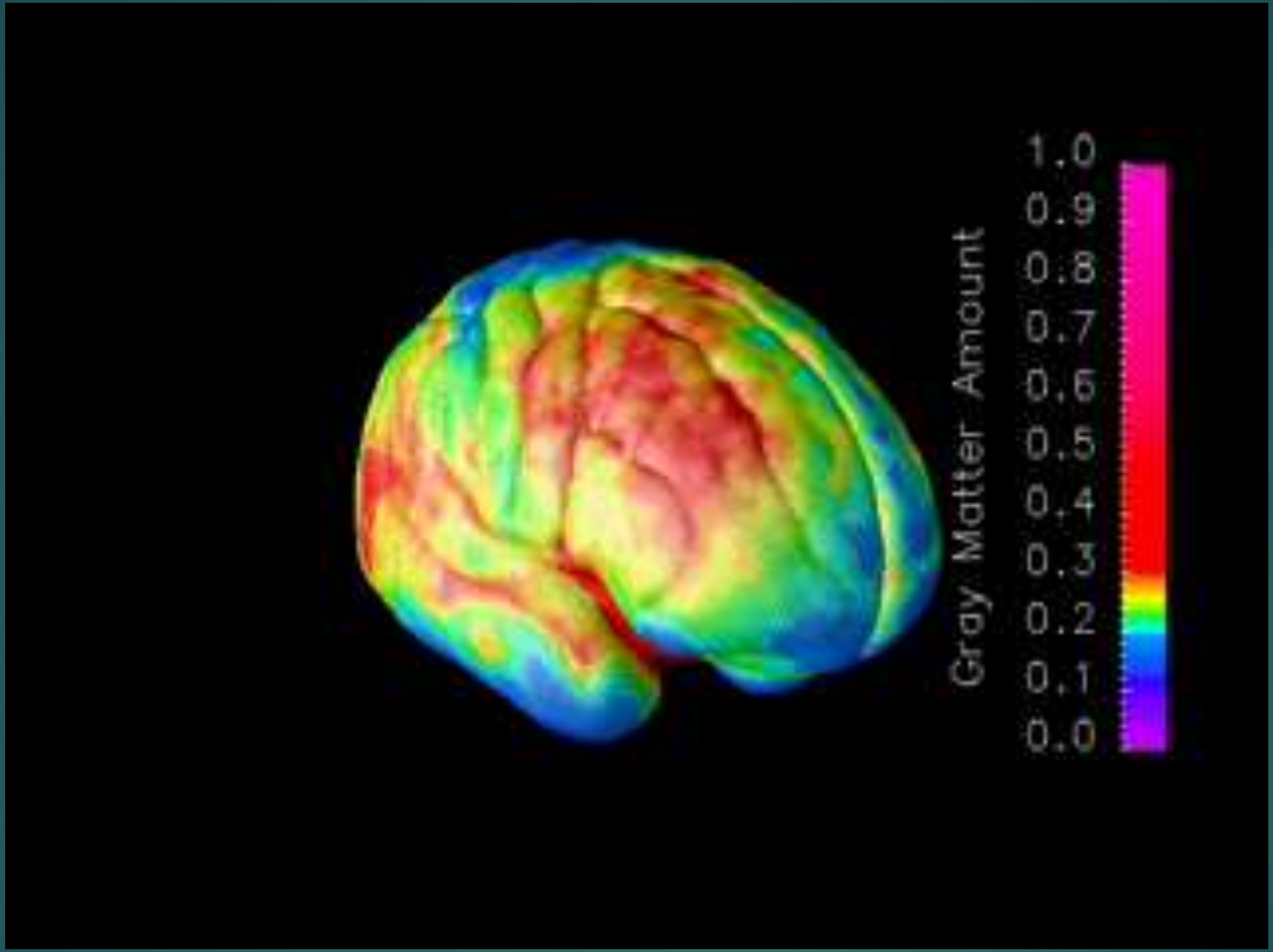
Brookshire and Casasanto, 2012

Brain Development

Toddlers: Practice makes Permanent

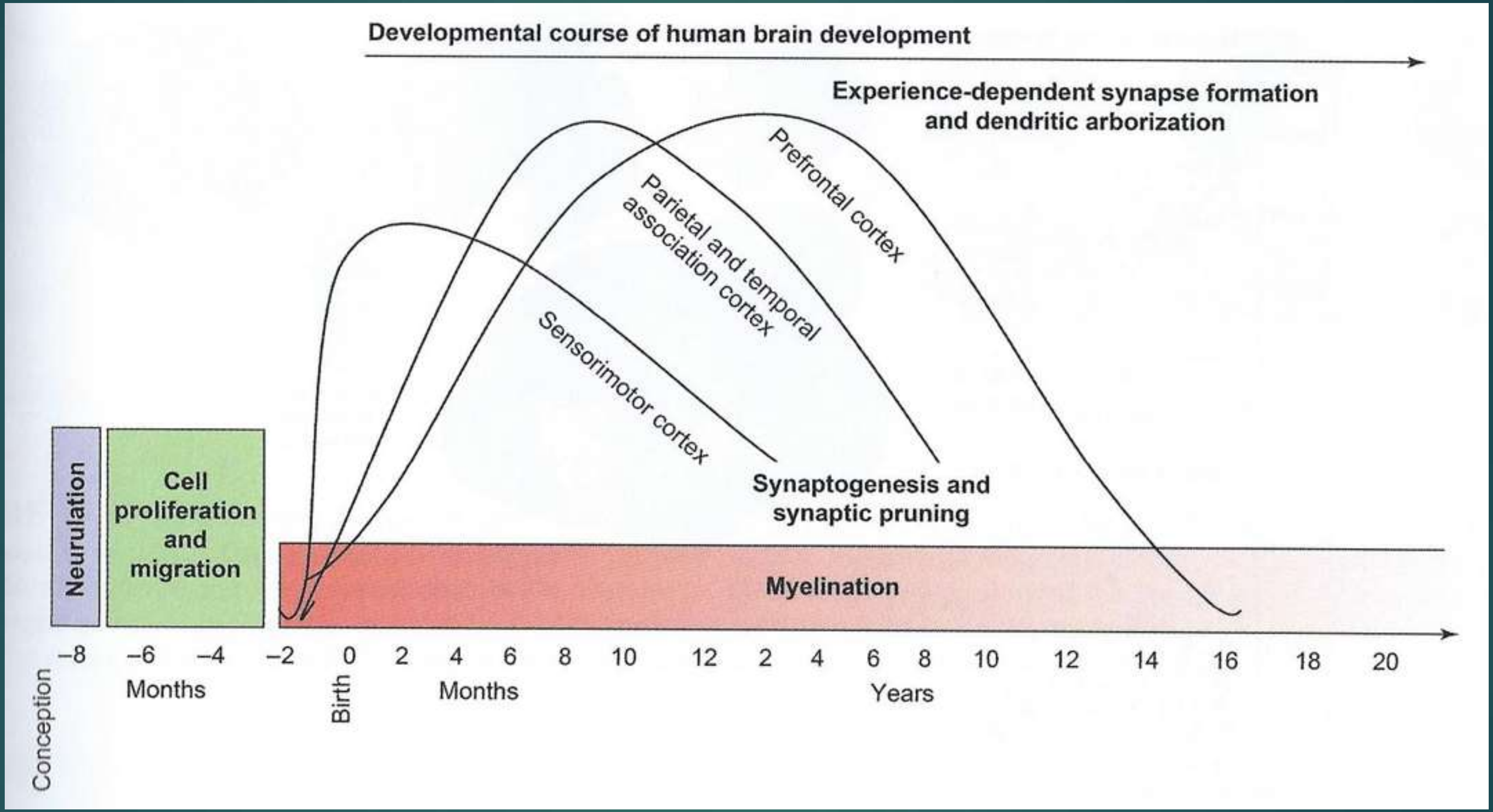
- By eight months of age, the average infant, living in a stimulating, secure and loving environment, will have sparked 500 trillion synaptic connections.
- By the age of two, an infant has developed around 1000 trillion of these connections; twice as many neurons as parents
- Synaptic connections have reached their highest density (10,000 synapses per neuron) by age 3.
- A 3-year-old toddler's brain is twice as active as an adult's brain.
- Age 4 is most metabolically active period: use of 43% of metabolic output (vs. adult = 20% of metabolic output of body)

Teen Brain: age 5 to 21



Lose 50% of all synaptic connections;
Motor areas first, frontal last

The Great Pruning: A leaner brain is a better brain



Intellectually challenged have significantly more synaptic connections than gifted do; as do autistic; but schizophrenia, ADHD = too much pruning, atrophy.

Complement System of immune system

- Immune system Complement pruning has been found in
  - Normal adolescent brain maturation
  - In schizophrenia,
    - excessive activity of the complement system results in inappropriate pruning length –
    - more C4 present, the higher the risk of developing schizophrenia:
    - excessive levels of the protein could lead to over pruning and to the thinning out of brain tissue that appears to coincide with the worsening of schizophrenia symptoms
  - In memory disorders: Pathogens induce complement activation (C3) and result in in presynaptic terminal loss in hippocampus resulting in memory loss:
    - Amyloid plaques in Alzheimer's
    - HIV
    - West Nile virus infections
    - Results in presynaptic terminal loss in hippocampus resulting in memory loss

Brain Maturation ages 5-20

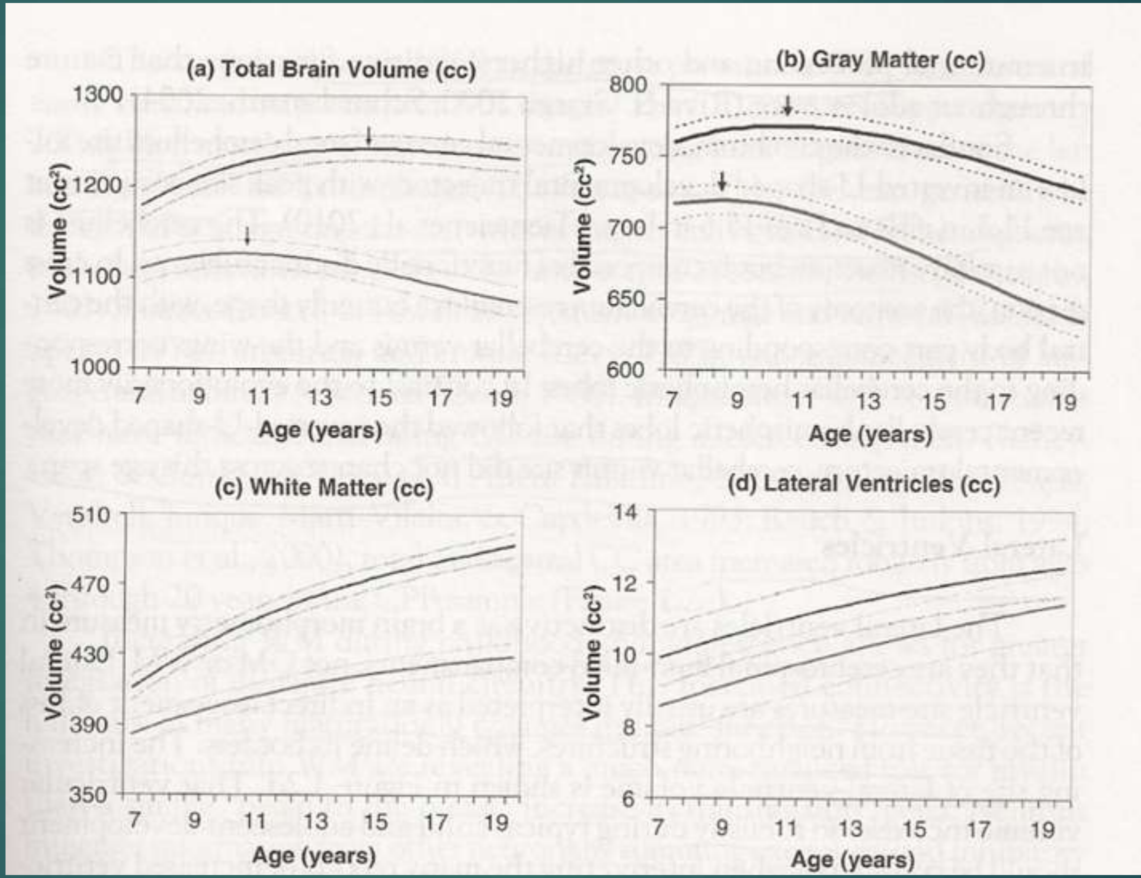
- Pruning away of synapses to neurons that are not used
- Increase in amount of white matter relative to grey neurons
- Increase in myelination of axons, which then can transfer information 1000s of times faster
- This improved connectivity of fewer more specialized neurons and networks creates behavioral maturity
- Crucial decision making frontal lobes are the last to mature
- Females are 2 years ahead in this maturation process.
- High variability: can fully mature at 13 or 30

Brain Component Development

Brain Volume

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

Correlation with improved language, reading, inhibition, & memory functions



GM decrease

Ventricle increase

Major Adolescent Brain Changes

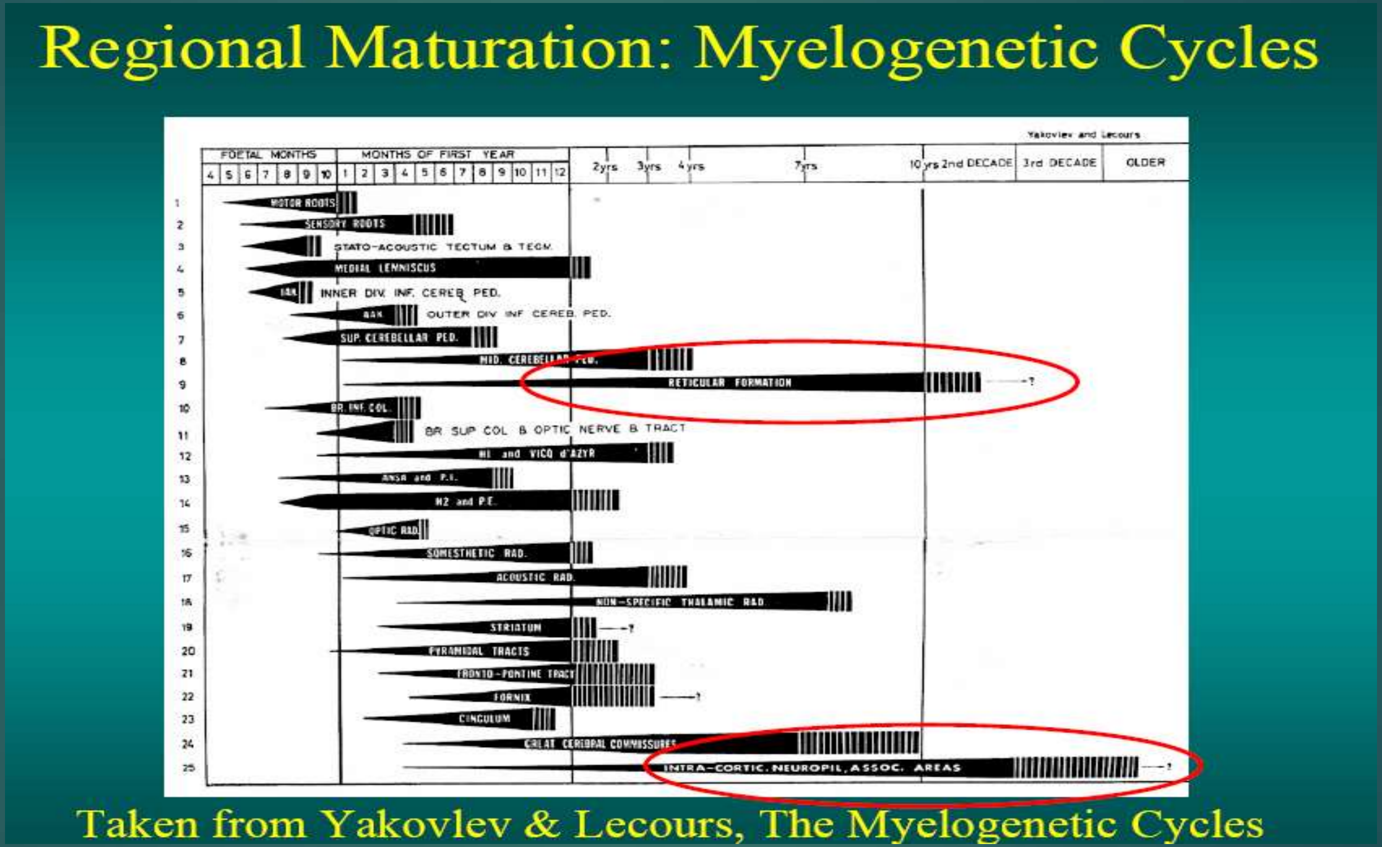
- Major synaptic pruning (loss of 50% of synaptic connections in the brain); but autistic brains have only 16% loss

- Maturation of frontal and limbic regions

- 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); hypersensitivity to reward which leads to risker behavior

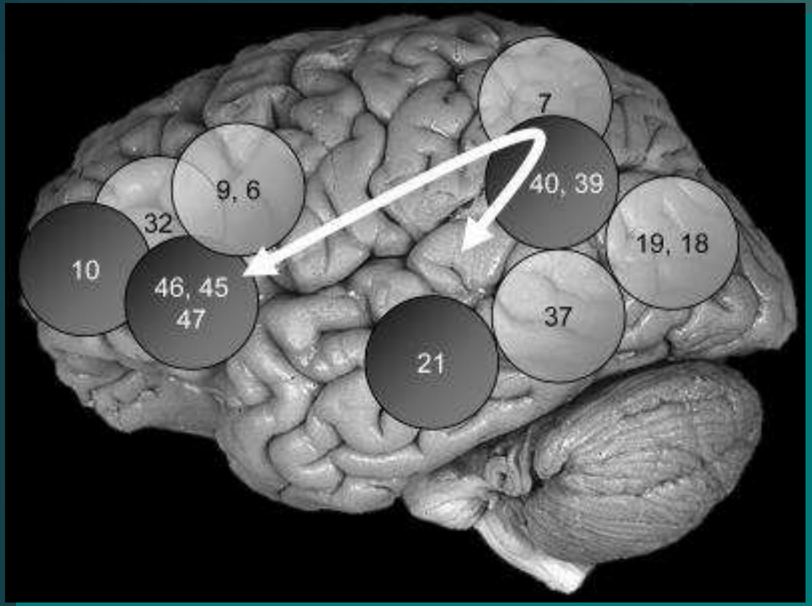
<u>Myelin</u> Sheets on Axons Mature Slowly in Frontal Lobes; may increase into 30s.



<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

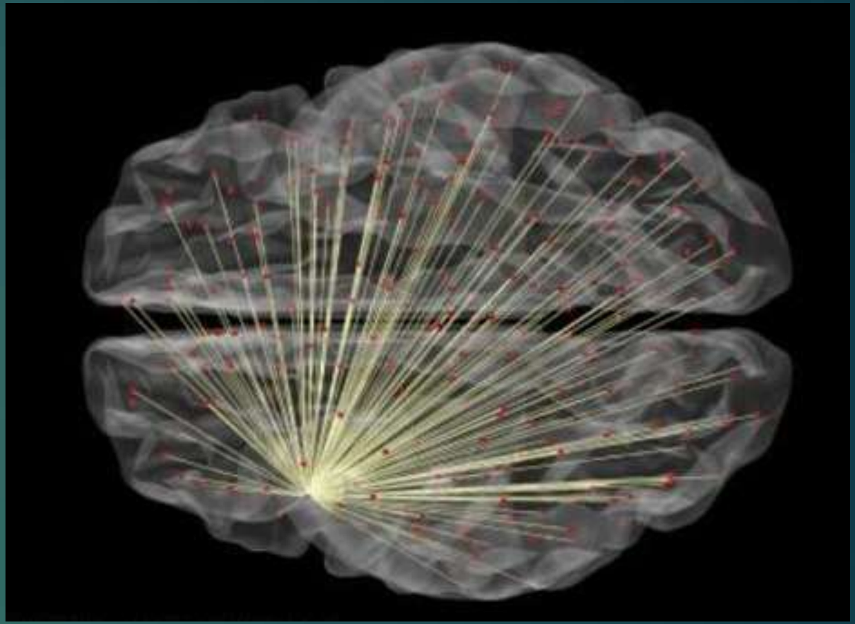
P-FIT: Parieto-Frontal Integration Theory: Biological basis of IQ



Dark Grey: Left Hem

Light Grey: Right Hem

Arcuate Fasiculus: connector



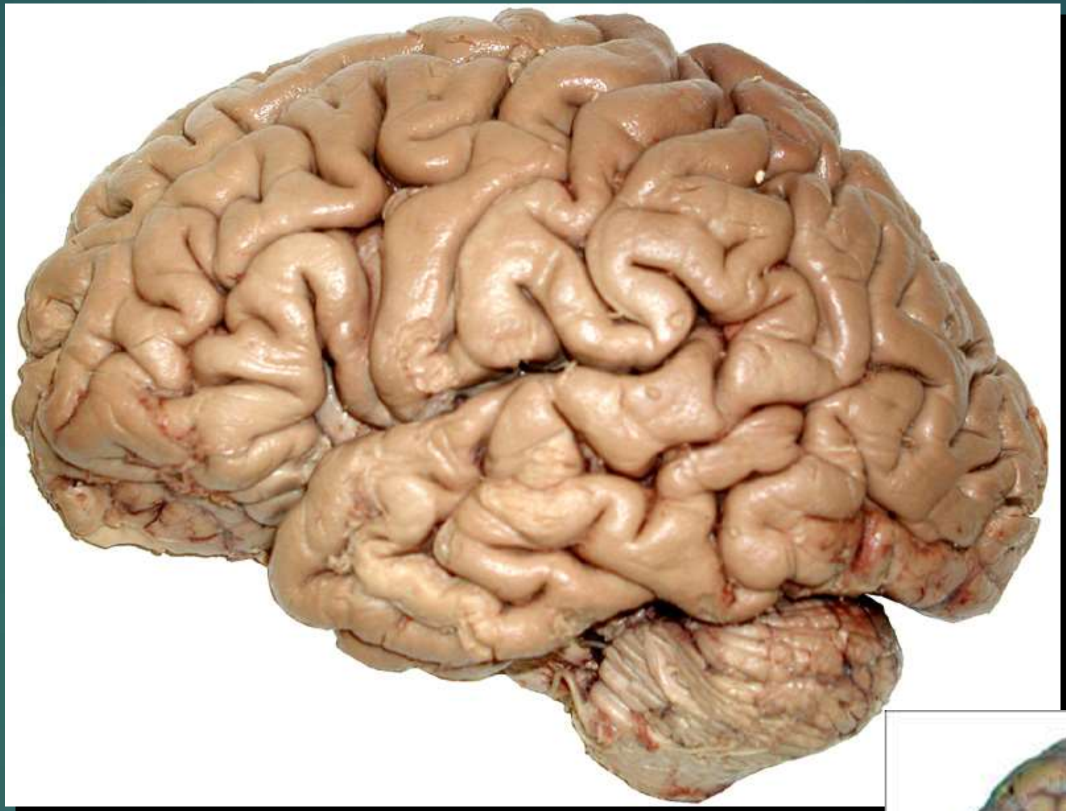
Their Parieto-Frontal Integration Theory (P-FIT) identifies a brain network related to intelligence, one that primarily involves areas in the frontal and the parietal lobes:

High intelligence probably requires *undisrupted information transfer among the involved brain regions along white matter fibers*

10% of Fluid IQ: Connectivity to Left DLPFC: goal monitoring

Three Main Functional Systems

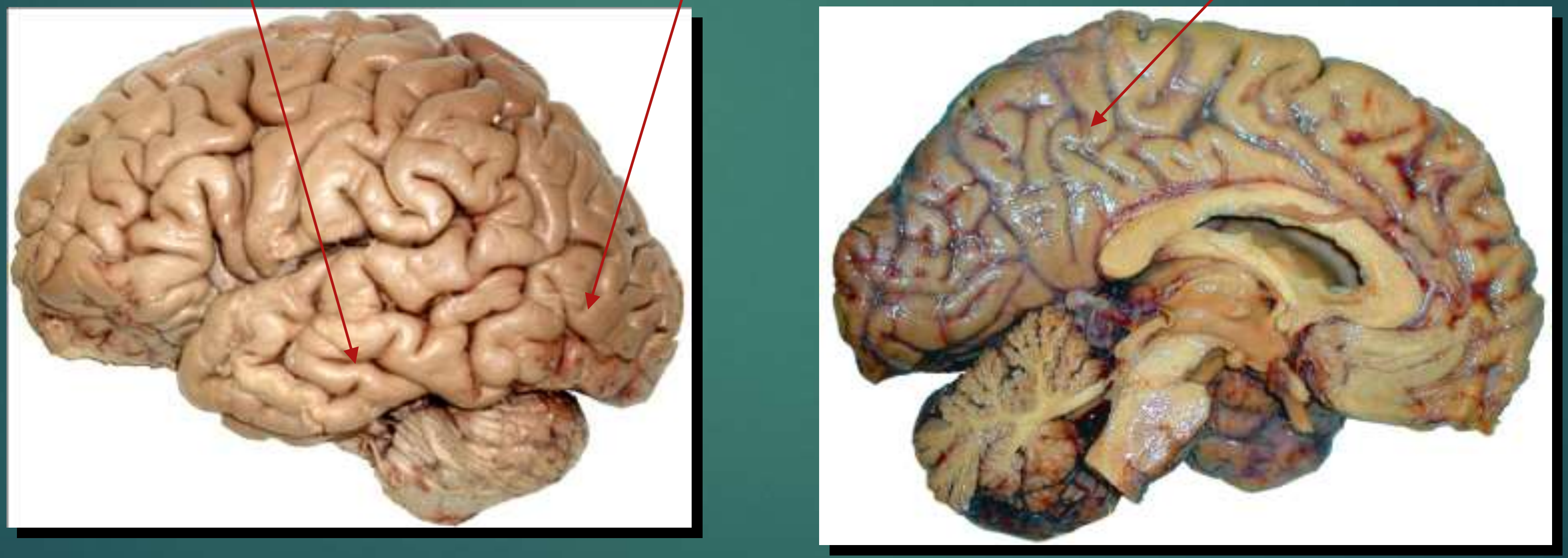
Frontal:
Action



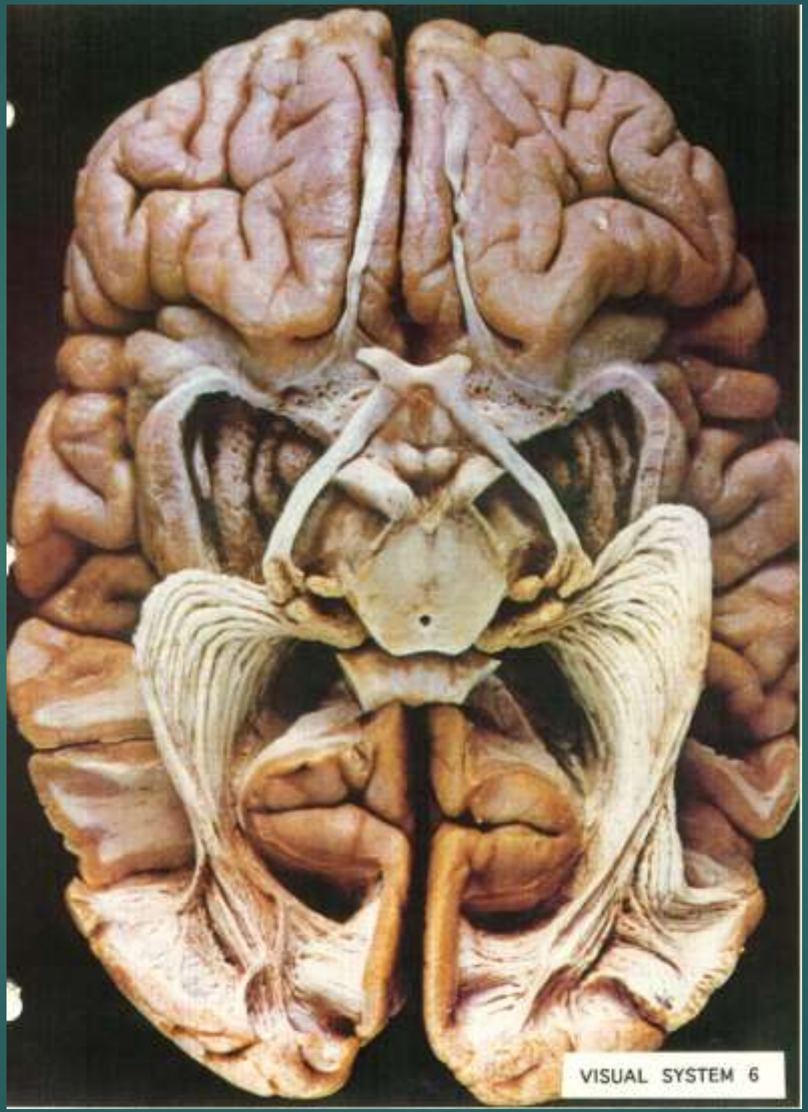
Posterior:
Sensory

Medial:
Internal States

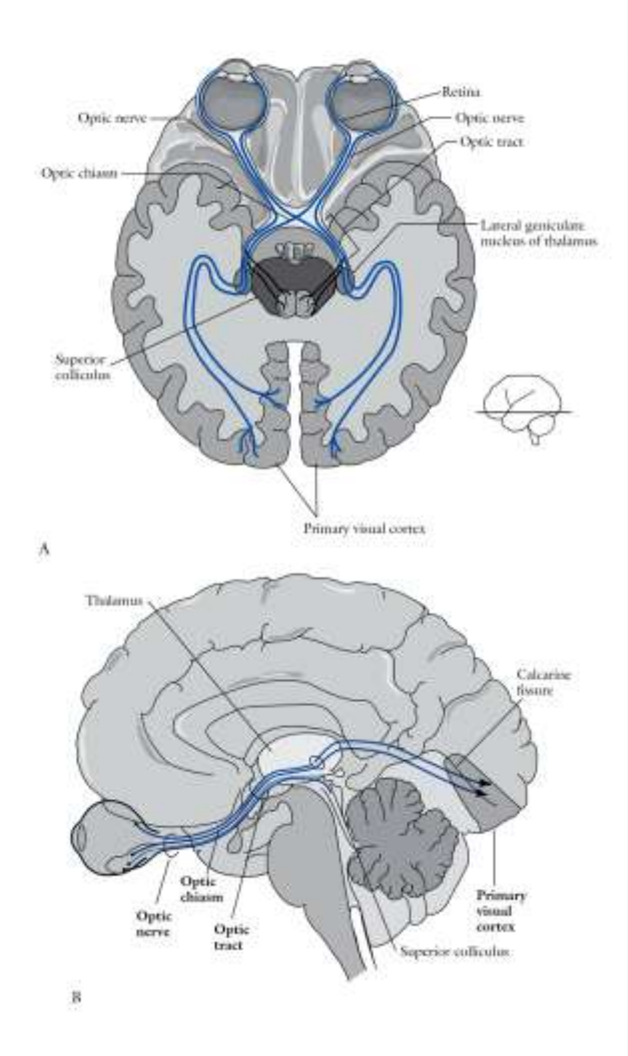
Posterior Sensory Systems

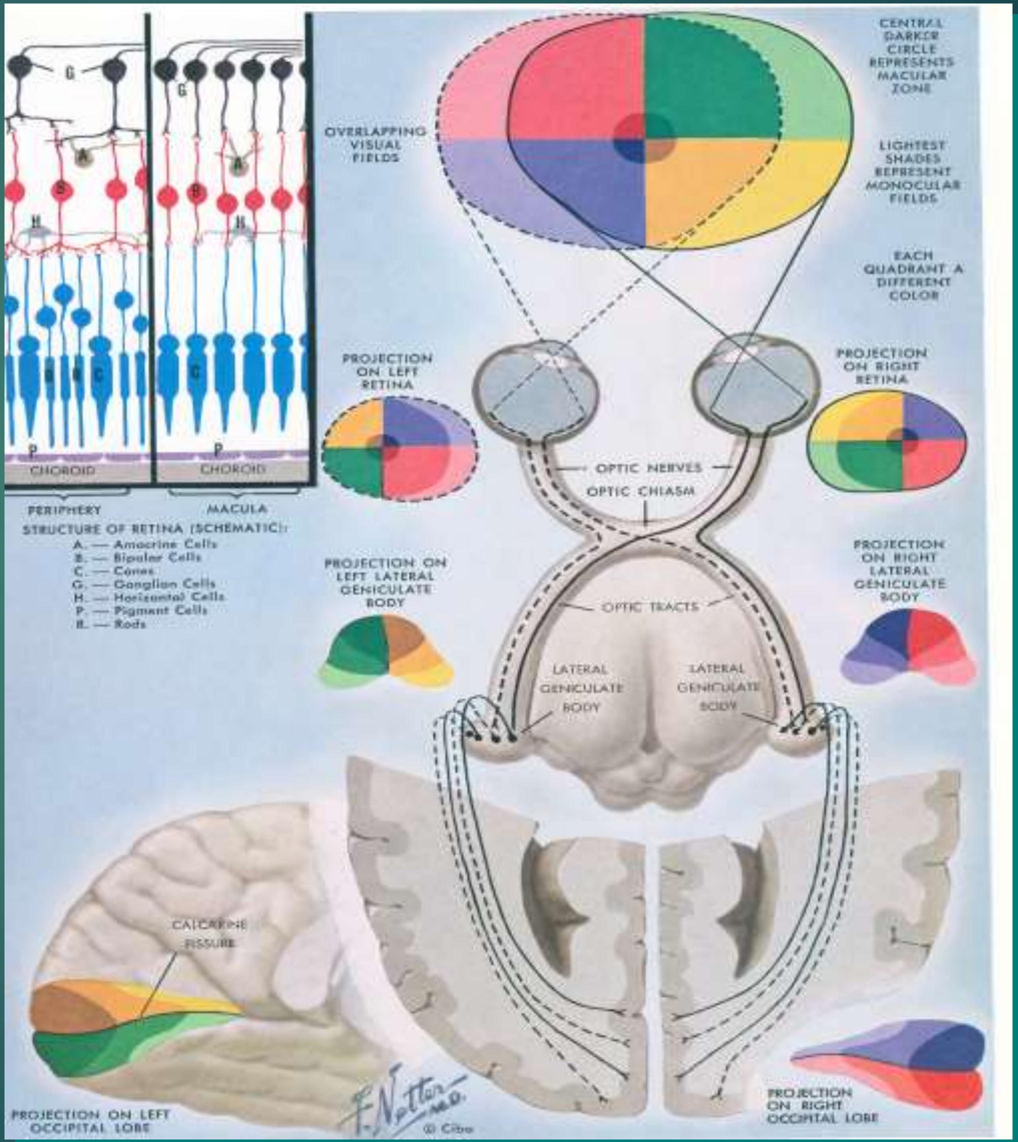


Visual system

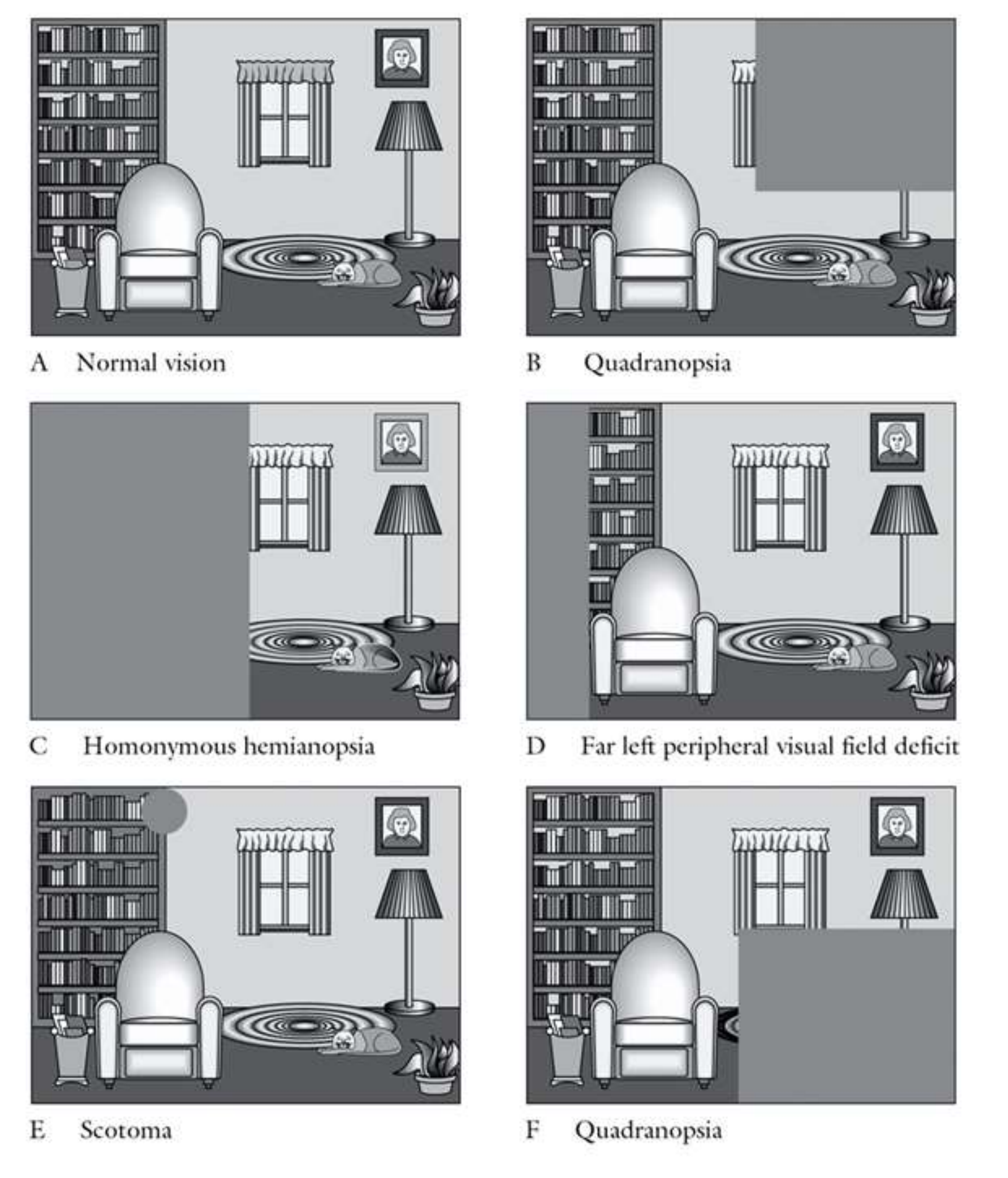


Visual System

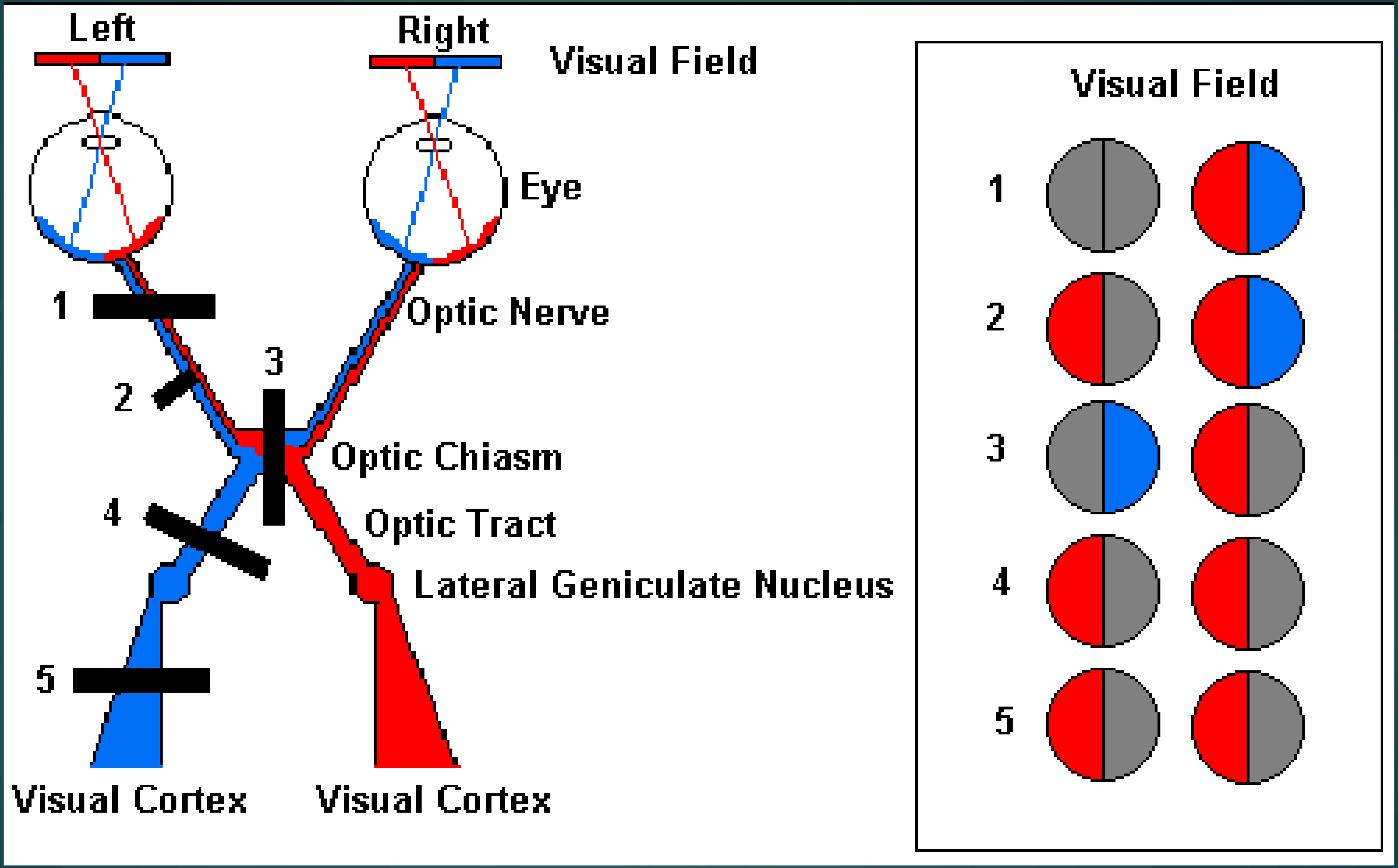




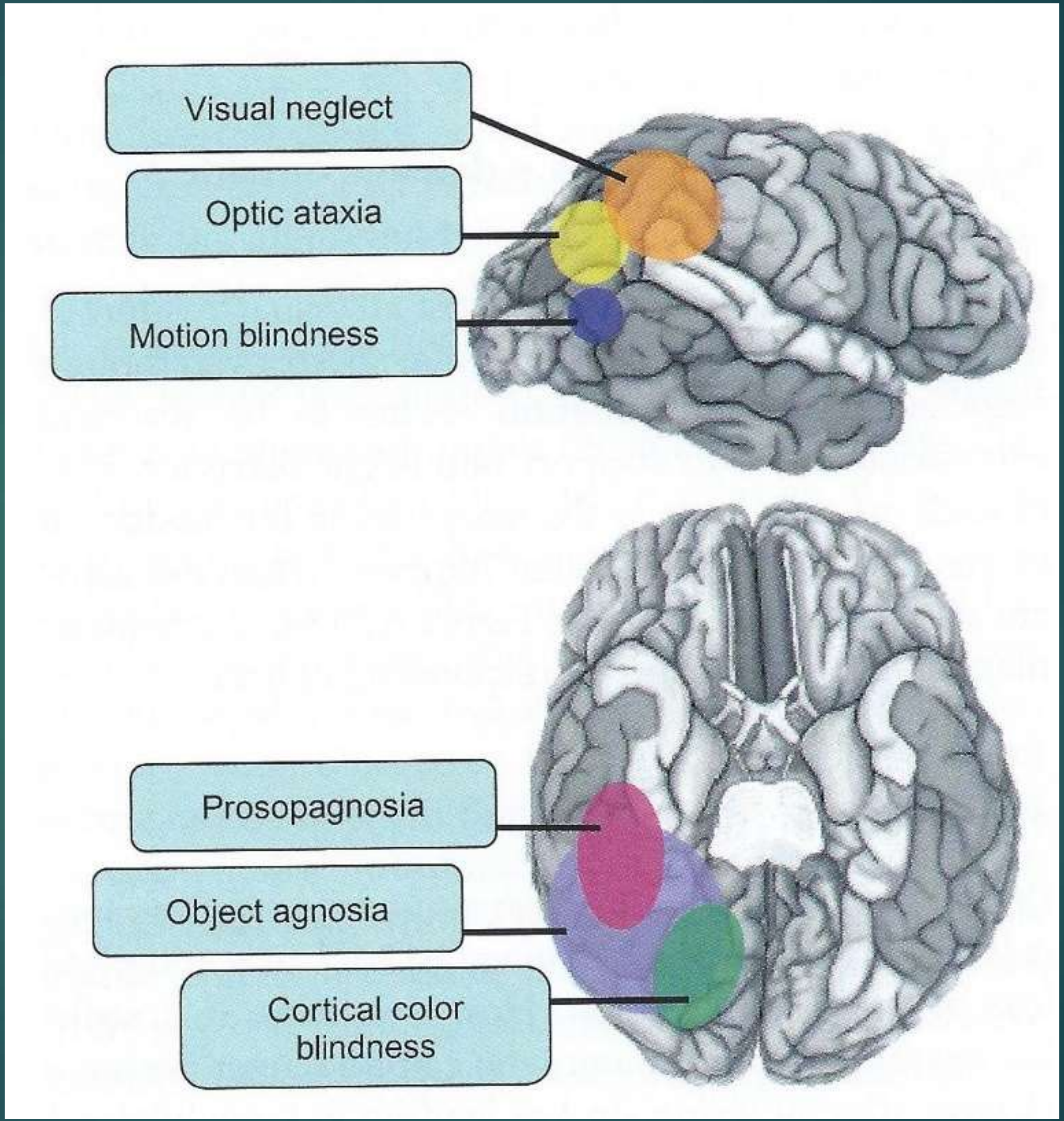
Visual Field Cuts



Lesions at different sites of visual pathway



Neuroanatomy of Visual Deficits in occipital & temporal areas



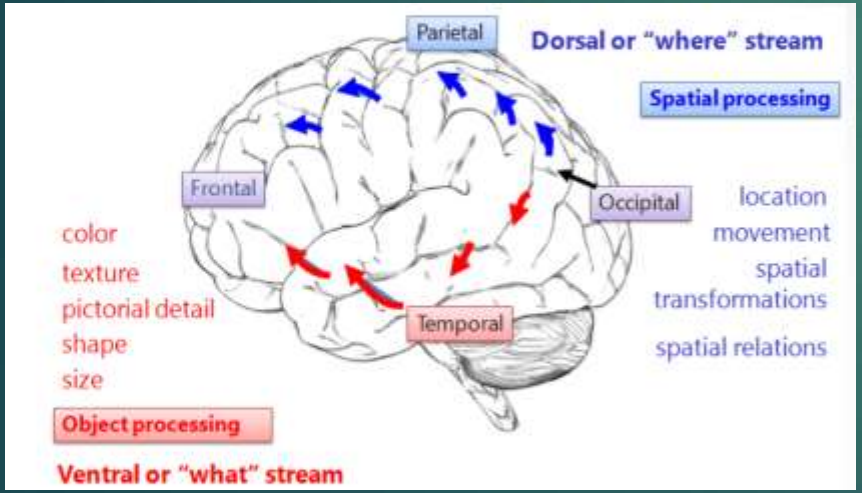
Right Hemisphere

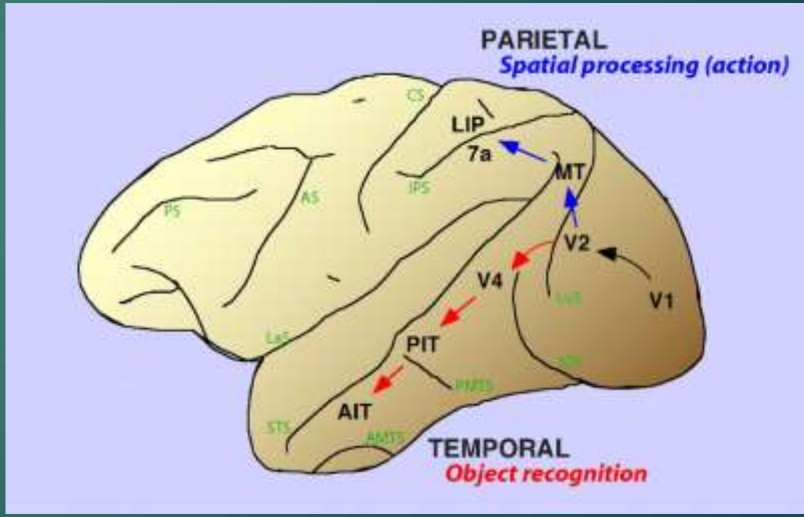
Left Hemisphere

4 Posterior Visual Pathways

1 Ventral (lower) Visual Pathway (what): Occipital-Temporal: object recognition, item based memory, complex visual discrimination

2 Dorsal (higher) Visual Pathway: (where) (action, spatial processing) Occipital-Parietal pathway via STS: spatial vision, visuomotor integration





Lateral intraparietal sulcus (LIP) contains neurons that produce enhanced activation when attention is moved toward a stimulus

STS Pathway: social nonverbal communication

- 3. Superior Temporal Sulcus stream
  - Specialized movement: visual analysis of movement of body parts (hands) & biological objects
  - Perception of social nonverbal communication cues
  - Complex visuoconstructional processing
  - Functions: analysis of body movements for nonverbal communication (STS); analysis of moving body (STS)

Fourth Temporal Pathway: When, temporal order

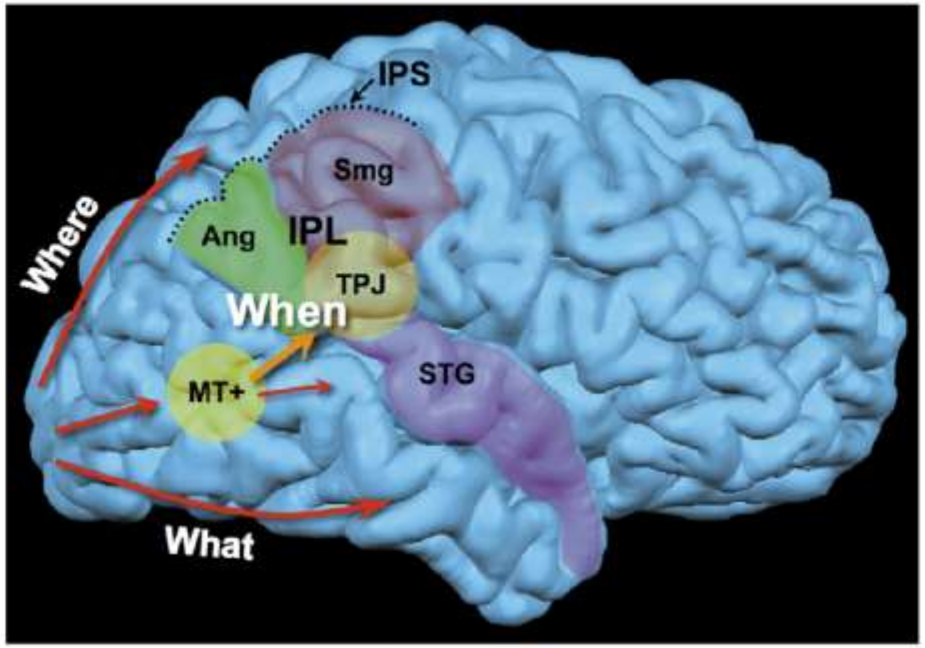
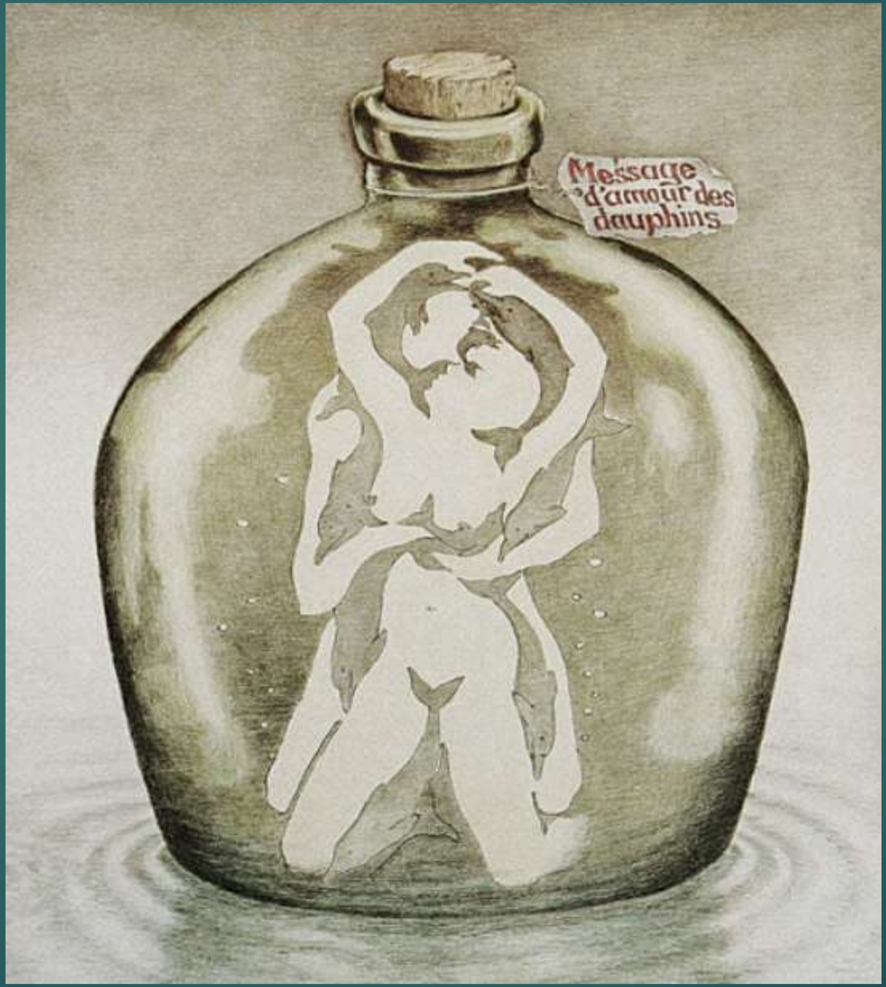


Figure 3. The *when* pathway. The *when* pathway is represented in the brain. This pathway is lateralized in the right hemisphere. Information from the primary visual cortex (V1) travels along the dorsal pathway (spatial perception, determining *where* objects are) or the ventral pathway (object recognition, determining *what* objects are), according to the classical subdivision that has been proposed based on animal models [1]. A third pathway coming from V1 is dedicated to using time information to identify objects (e.g. determining when objects appeared or disappeared). Here, the temporoparietal junction (TPJ; considered the most common substrate of neglect [16]) is identified as a core anatomical locus, within the inferior parietal lobe (IPL); however, the *when* pathway is likely to include a bigger network of areas, including the right angular gyrus (Ang), the supramarginal gyrus (Smg) and the posterior superior temporal sulcus (included in the superior temporal gyrus, STG). All these areas are often involved in the cortical lesion of right parietal patients. The intraparietal sulcus (IPS) separates the IPL from the superior parietal lobe (not labeled). The middle temporal area MT+ is reported in yellow (also called the motion area, highly specialized in detecting and discriminating moving stimuli).

LTPJ: temporal order judgment; Wernicke's aphasia - integration of the order within and/or between phonemes or more generally in auditory temporal order judgment

Battelli et al., 2008

Effect of Experience on Vision:
2 Nudes or 10 Dolphins



Young children see only 10 dolphins. Adults see two nude lovers embracing.

Effect of Cultural Experience on Visual Interpretation

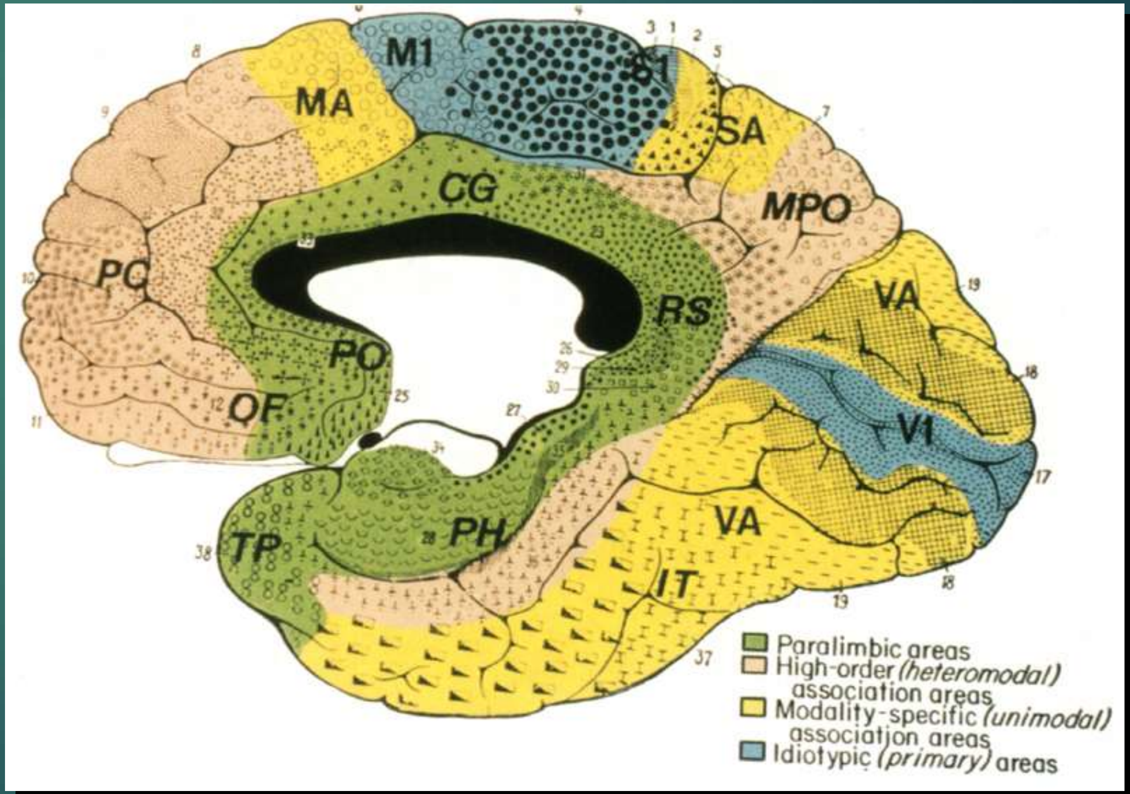
Westerners see people inside a room; African villagers see family outside

Limbic System: Emotional Control

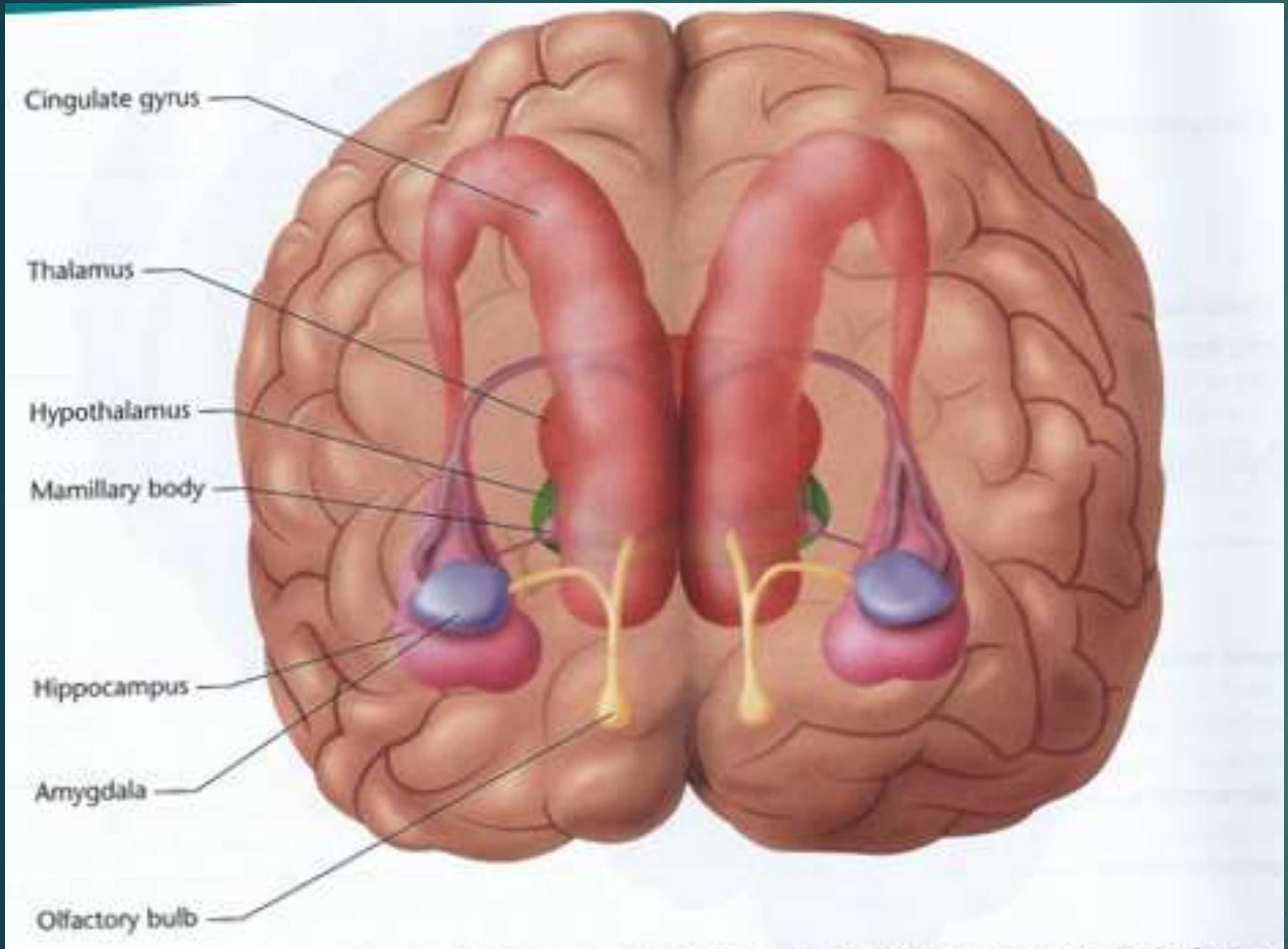
Amygdala

Ventral Medial PFC

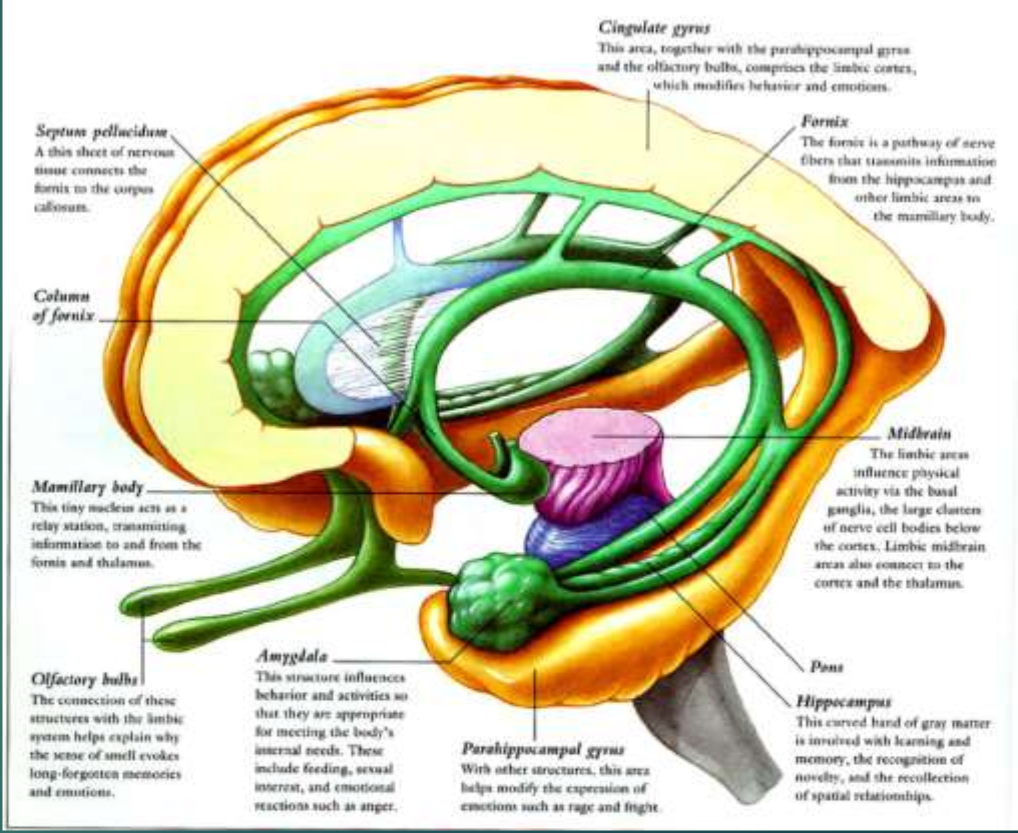
Posterior Cingulate



Limbic System



The limbic system is a set of subcortical structures that form a border (or limbus) around the brainstem



Functions of limbic system: remember the tiger

- Affective nature of sensory sensation – “pleasant or unpleasant”, “reward or punishment” or “satisfaction or aversion”, threat assessment

- Behaviors associated with pleasant & unpleasant stimulus – Rage & tameness

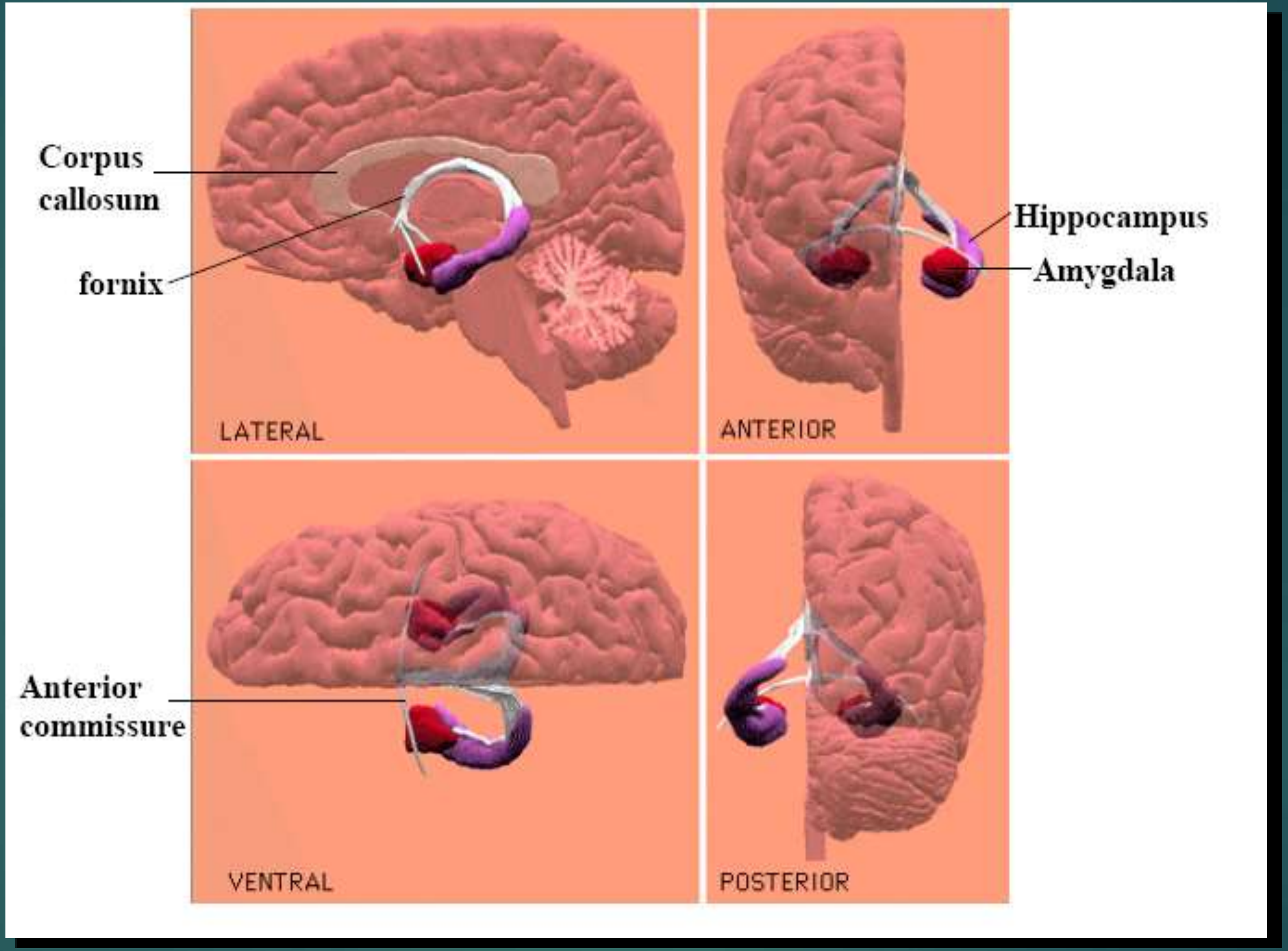
- Reward & punishment in learning & memory

Amygdala: Processing of motivationally relevant stimuli

- Classic interpretation: fear response
- Function: processing events that are related to what a person cares about at the moment

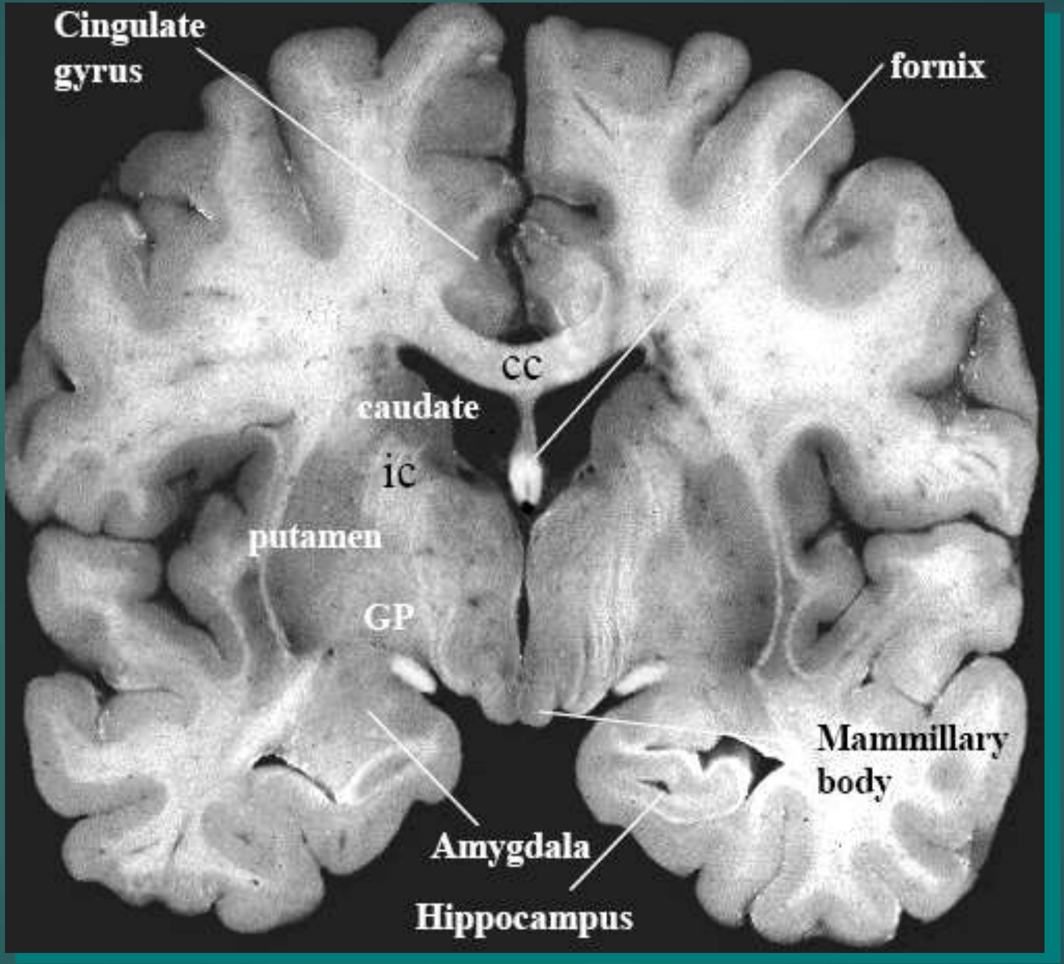
- Stimulus relevance for the goals and motivations of the perceiver.
  - Threat response (50 ms vs. 600ms for csness = 12 x faster)
  - scary situation or frightening image.
  - food if hungry
  - people if empathic

Hippocampus: Memory index



Major site of neurogenesis of stem cells

Mammillary Bodies



Anterograde Amnesia:
Thiamine deficiency caused hemorrhages in Korsakoff’s Syndrome

Temporal Lobes

Temporal Lobe Functions

- Language:
  - human speech sound frequencies;
  - pitch, timbre, music melodies;
  - Wernicke's area - verbal comprehension (spoken, written)

- Visual perception:
  - object recognition,
  - Fusiform face area (FFA): face;
  - Parahippocampal place area (PPA): geographic scene; places

- Semantic knowledge of words & word reading; Visual and semantic aspects of language

Temporal Lobe Functions 2

- Perception of different facial features & body movements with nonverbal communication cues & social behaviors (recognizing a smirk)
- Declarative & episodic (person/time specific) memory
- Olfactory & Emotional processing; Theory of Mind

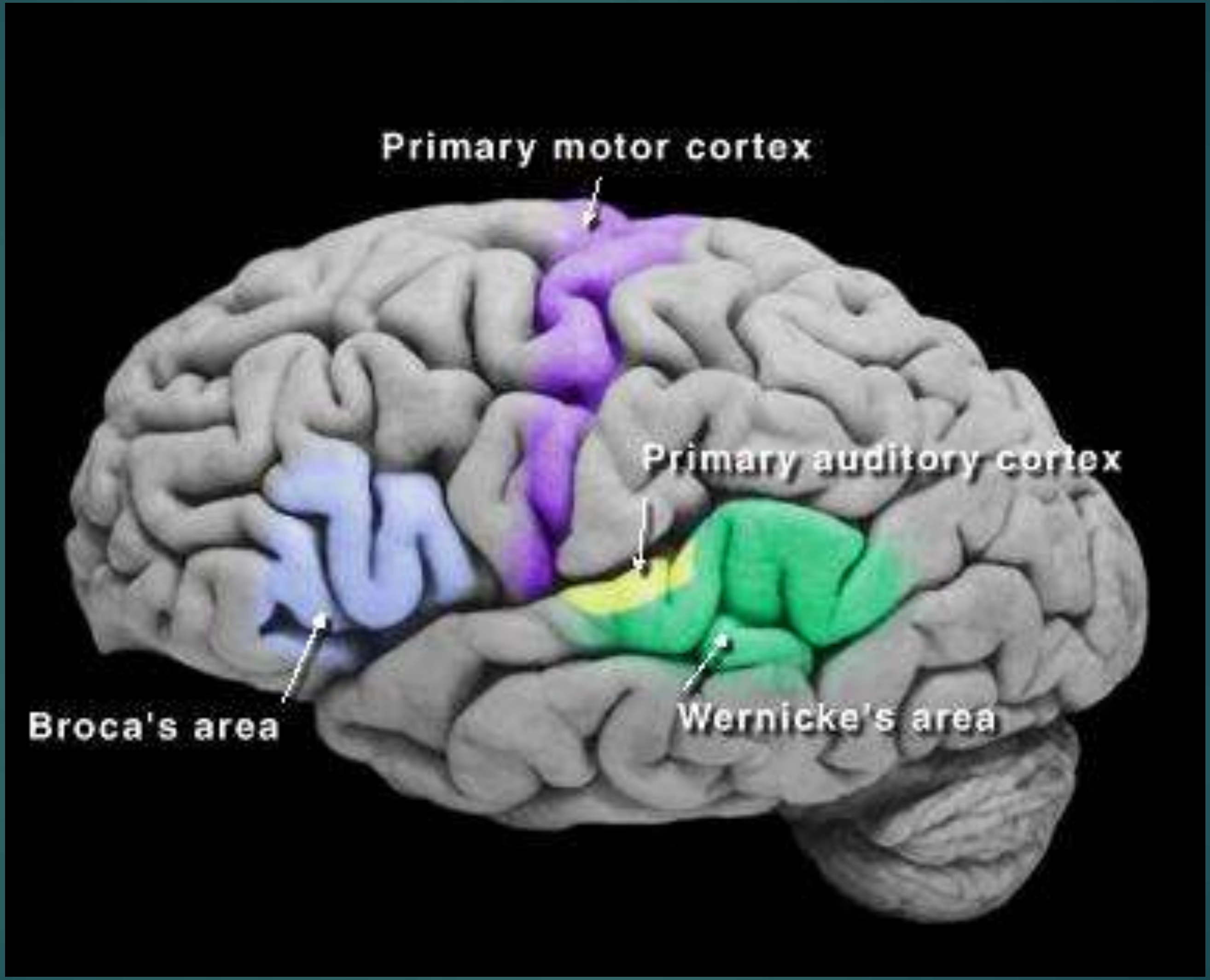
Temporal Lobe Damage: the agnosias – loss of meaning of things

- Apperceptive agnosia: inability to recognize objects, copy, or match objects.
- Associative (Visual Object) Agnosia: failure to recognize visually presented objects despite having intact perception of that object (recognition without meaning) (Sacks: *Man who mistook his wife for a hat*)
- Prosopagnosia: inability to recognize faces
- Olfactory agnosia: inability to recognize smell
- Auditory sensation/perception (cortical deafness to receptive aphasia)
- Social cue apperception
- RT resection: loss of left visual field bias in face viewing

Temporal Lobe Impairments

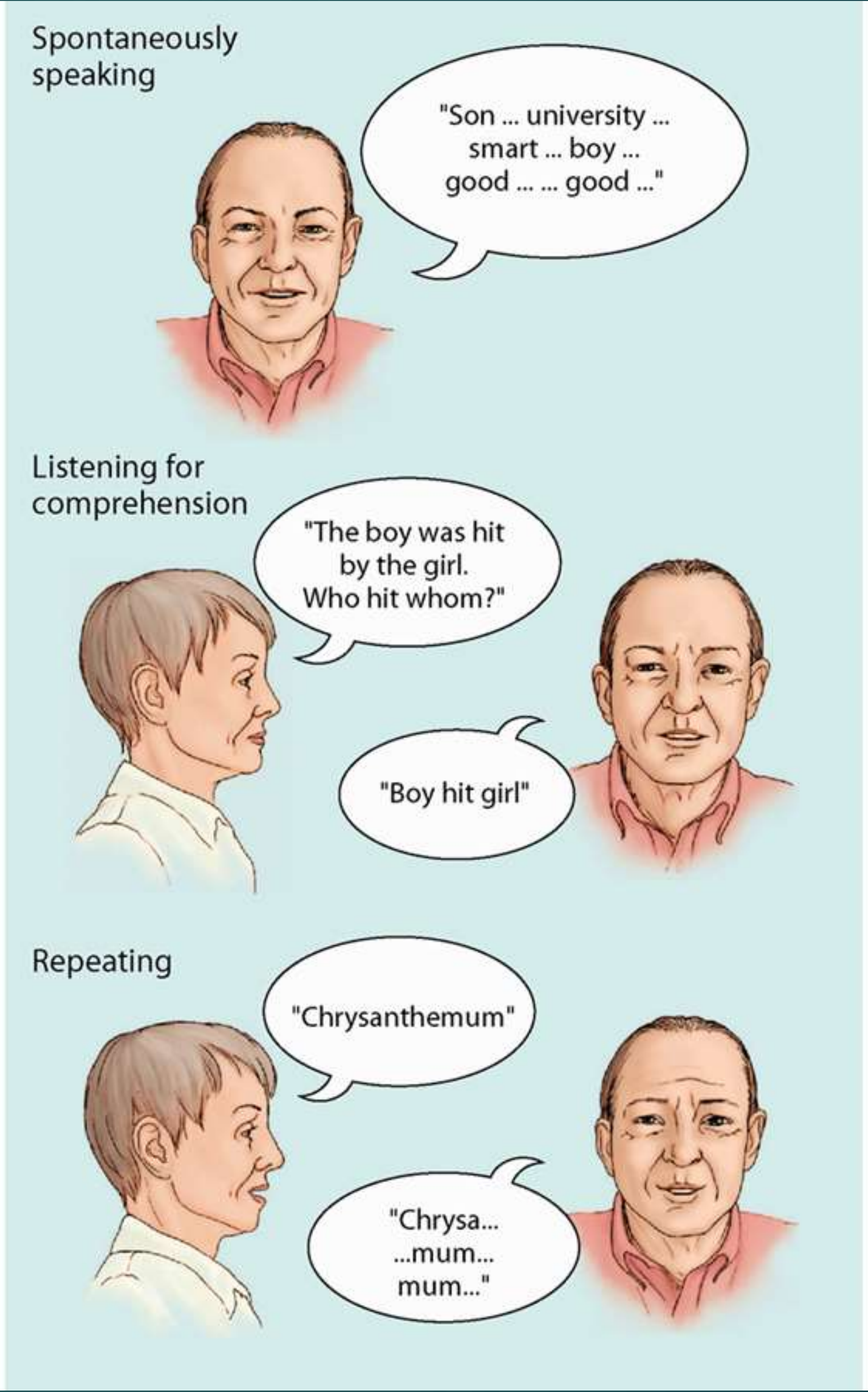
- Declarative (esp. episodic) memory: Anterograde and retrograde Amnesia
- Altered personality or affective behavior (focus on minutiae, religious preoccupation, paranoia, aggressiveness)
- Altered sexual behavior (Kluver-Bucy syndrome)

Temporal Lobe Language function of brain



BA 41, 42, 22

Broca’s aphasia



Broca’s aphasia

M.E. Cinderella...poor...um 'dopted her...scrubbed floor, um, tidy...poor, um... 'dopted...Si-sisters and mother...ball. Ball, prince um, shoe...

Examiner Keep going.

M.E. Scrubbed and uh washed and un...tidy, uh, sisters and mother, prince, no, prince, yes. Cinderella hooked prince. (Laughs.) Um, um, shoes, um, twelve o'clock ball, finished.

Examiner So what happened in the end?

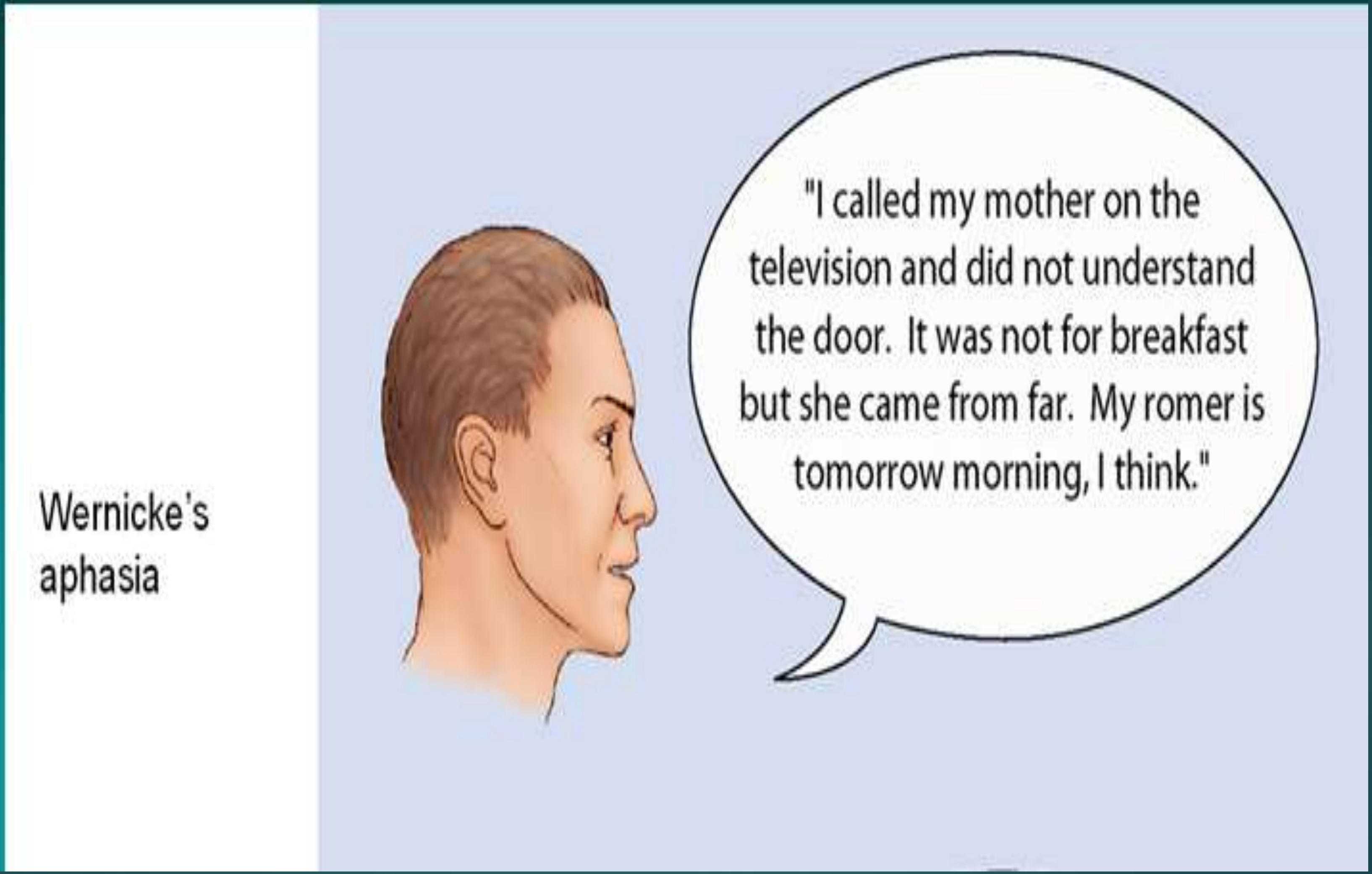
M.E. Married.

Examiner How does he find her?

M.E. Um, Prince, um, happen to, um...Prince, and Cinderalla meet, um met um met.

Examiner What happened at the ball? They didn't get married at the ball.

M.E. No, um, no...I don't know. Shoe, um found shoe...


Wernicke's aphasia
"I called my mother on the television and did not understand the door. It was not for breakfast but she came from far. My romer is tomorrow morning, I think."

Wernicke’s aphasia

Examiner Yeah, what's happening there?

C.B. I can't tell you what that is, but I know what it is, but I don't now where it is. But I don't know what's under. I know it's you couldn't say it's ... I couldn't say what it is. I couldn't say what that is. This shu-- that should be right in here. That's very bad in there. Anyway, this one here, and that, and that's it. This is the getting in here and that's the getting around here, and that, and that's it. This is getting in here and that's the getting around here, this one and one with this one. And this one, and that's it, isn't it? I don't know what else you'd want.

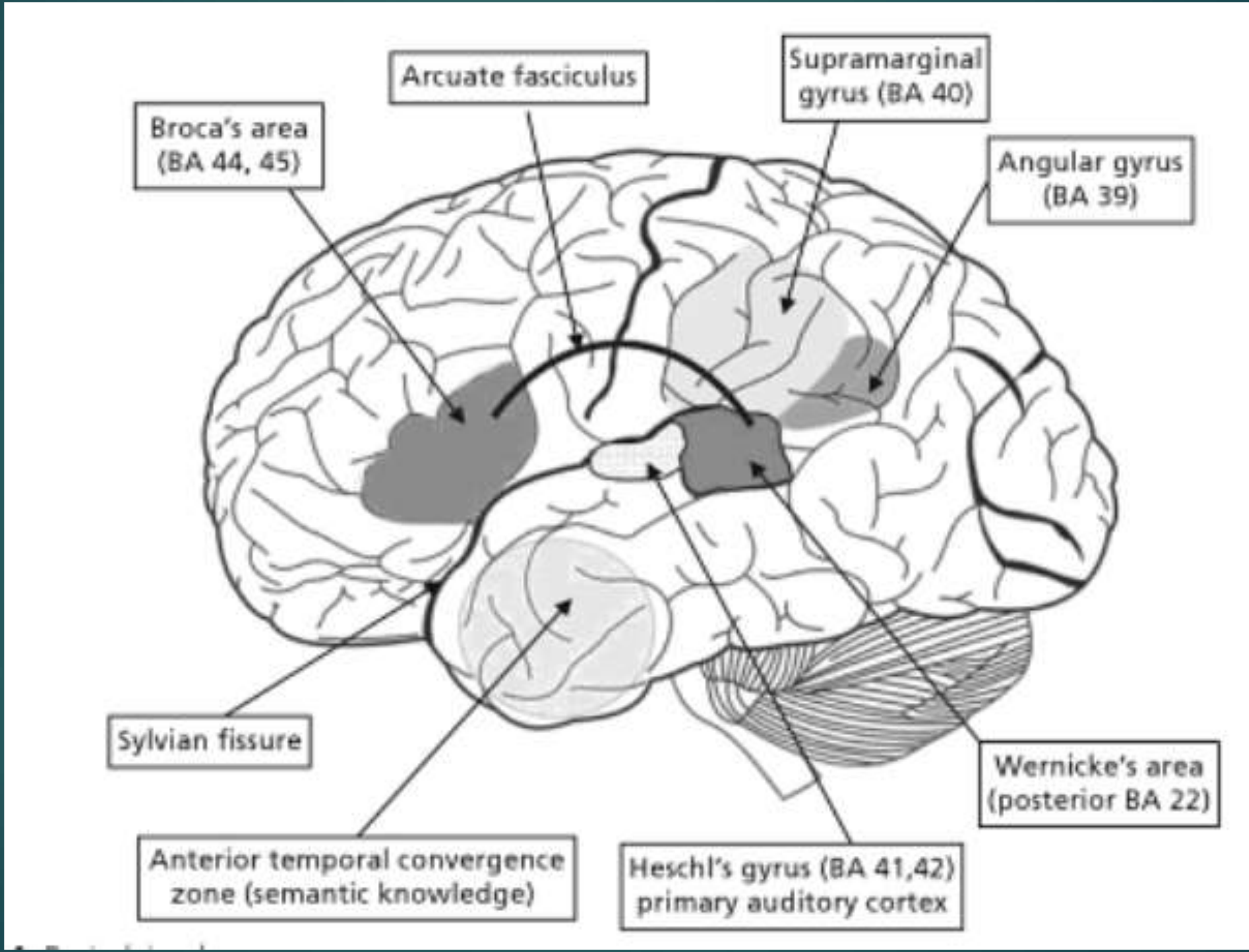
Neuroanatomy of Language

- Language is a distributed brain system

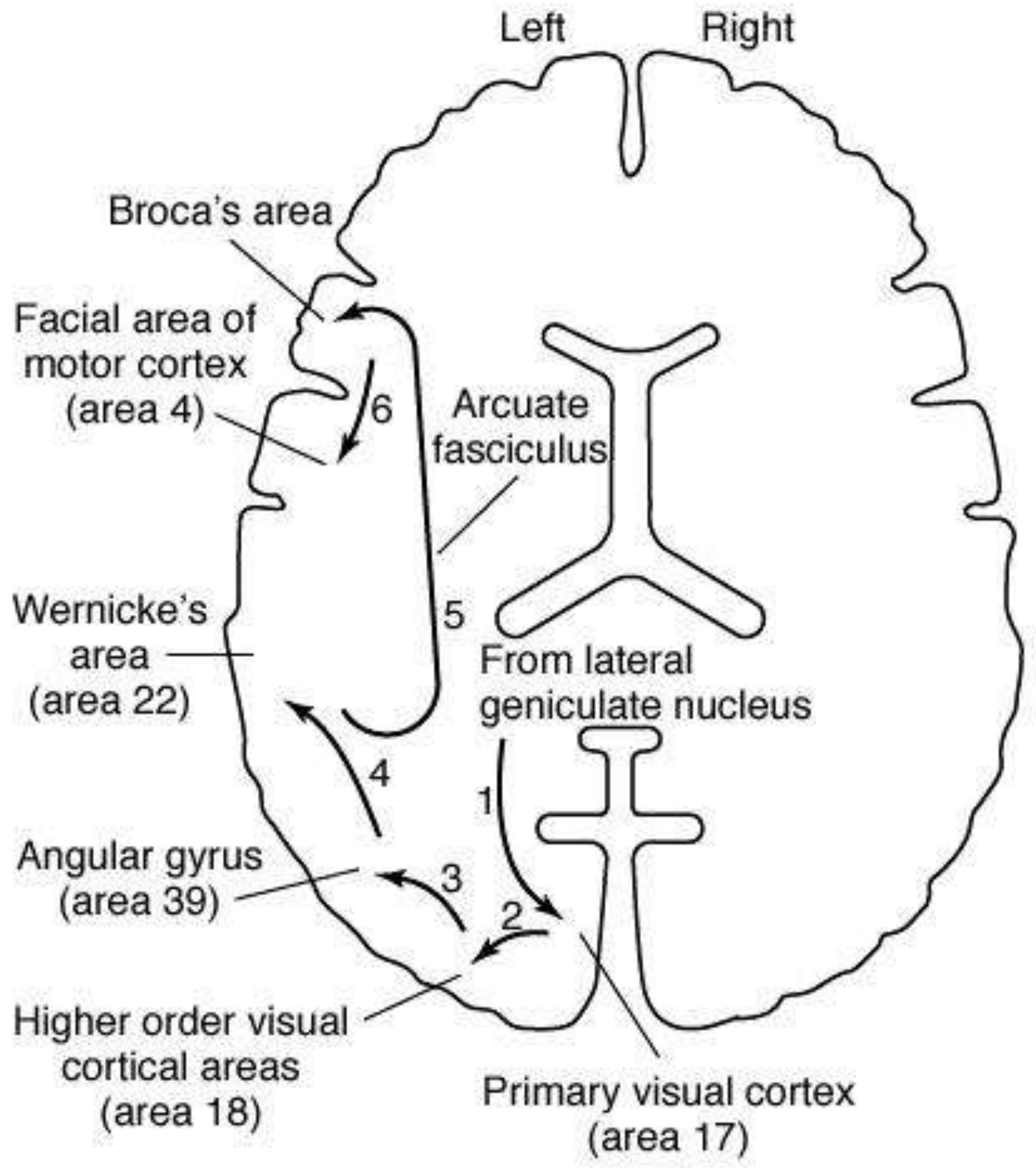
- Left hemisphere is language dominant in 95% of right handers & in 60-70% of left handers.

- Language areas: Broca's (BA 44/45), arcuate fasciculus, Supramarginal gyrus (BA 40), Angular gyrus (BA 39), Wernicke's (posterior BA 22), Heschl's gyrus (BA 41,42; primary auditory cortex), anterior temporal convergence zone (semantic klg)

Multiple Language Areas



Speaking a seen word requires 6 areas



Visual & Auditory Word Processing

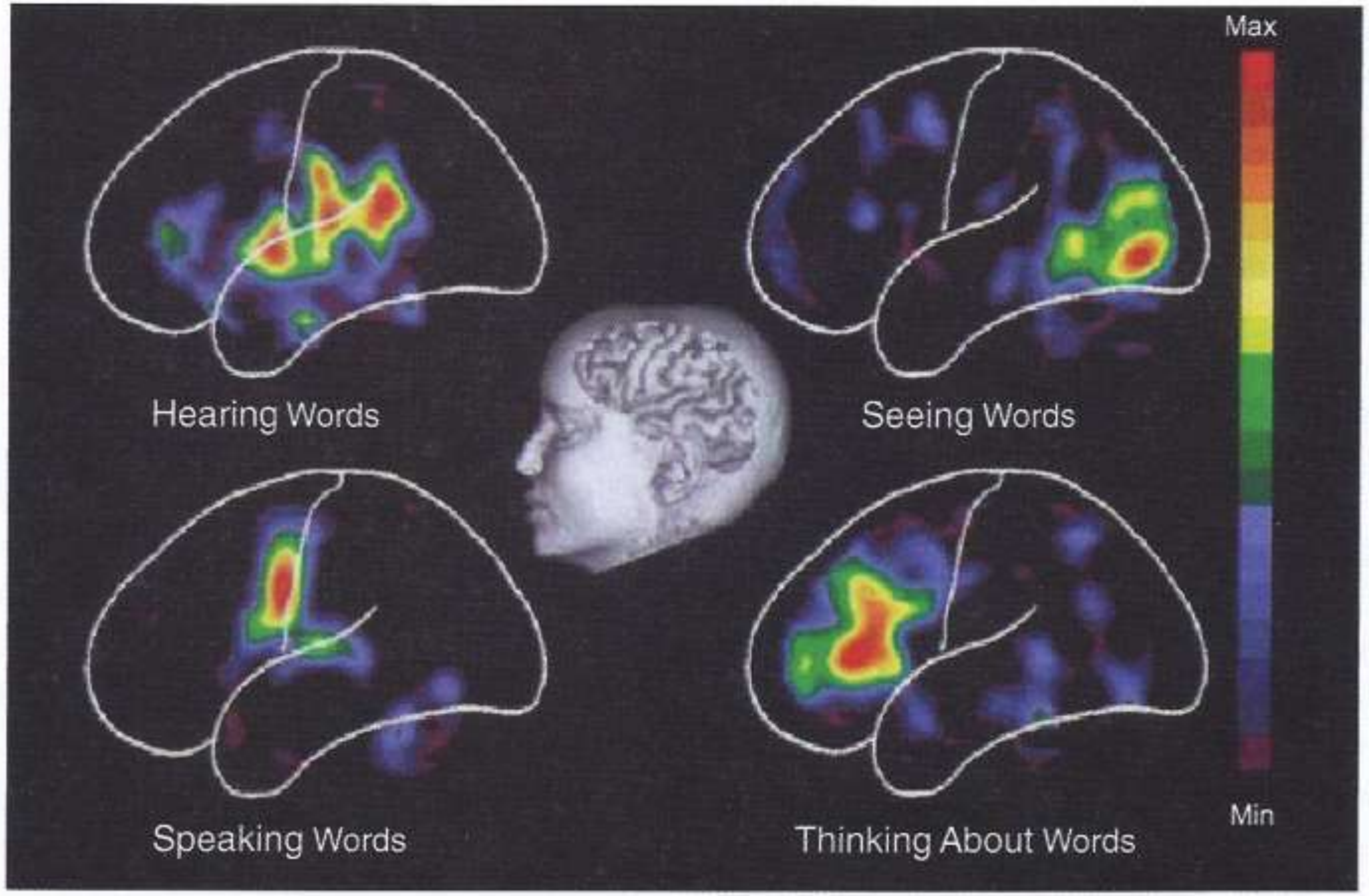
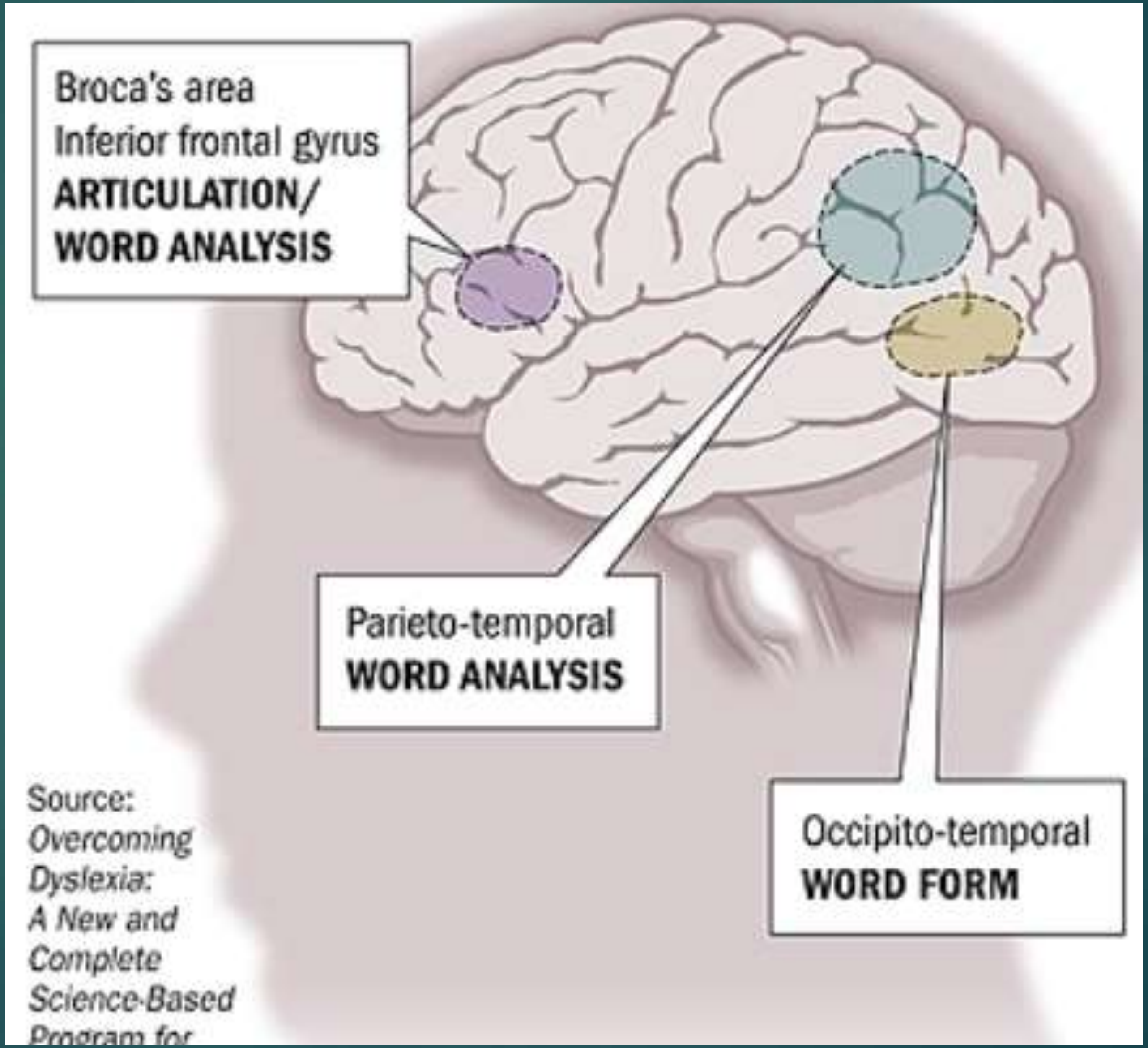


FIGURE 4.30 A classical PET finding: visual versus auditory brain activity. Early PET scans showing different speaking, seeing, hearing, and internally generating words (Posner and Raichle, 1994). Notice that visual, auditory, motoric, and speech production regions appear to be activated. However, the surrounding brain outline (white lines) is only approximate. In more recent brain images, the functional activity would be superimposed upon a structural MRI of the same subject's brain. *Source*: Posner and Raichle, 1994.

Reading Harry Potter: sentence reading activates all brain areas

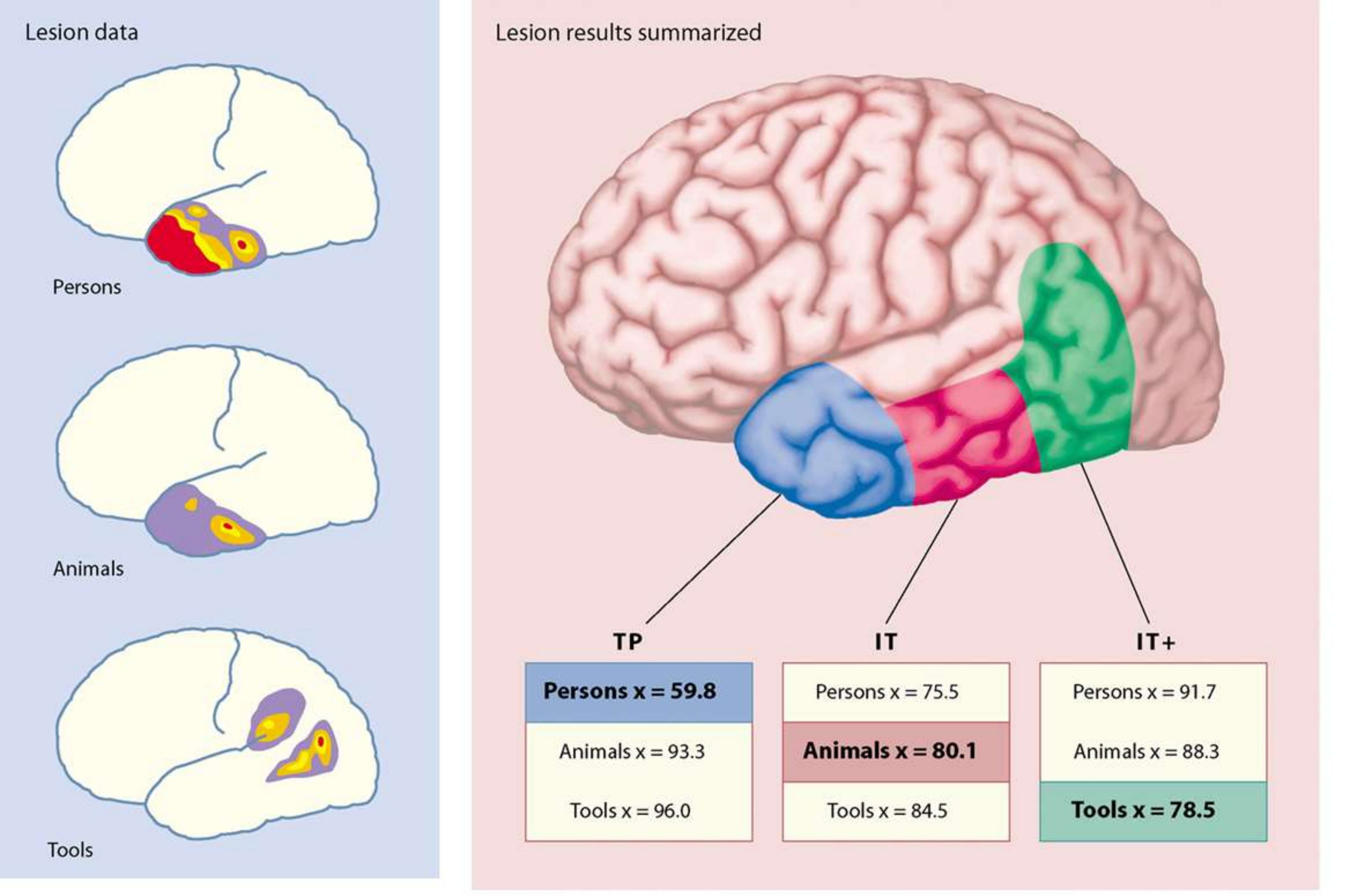
- Statistical model is able to classify which of two novel passages of the story is being read with an accuracy of 74% based on neural activity while reading.
- Brain areas involved:
  - Angular Gyrus: lexical semantics (bilateral); physical motions of story characters
  - Fusiform Gyrus
  - Inferior frontal: high level word integration (right); semantics of individual words (left); Physical motions of story characters; dialog among story characters (right)
  - Inferior temporal
  - Middle temporal: semantics of individual words (bilateral), identities of different story characters
  - Superior temporal: sentence length (L), syntax (R); semantics of individual words (R); Physical motions of story characters; identities of different story characters , protagonist's perspective (right)
  - Temporal pole: high level word integration (bilateral)
  - Occipital: word length (left Visual Word Form Area)
  - Precentral Gyrus
  - Precuneus
  - Temporal Parietal Junction: sentence length/syntax (left & esp. right); dialog among story characters (right)
  - Supplementary Motor Gyrus

Reading System: 3 areas



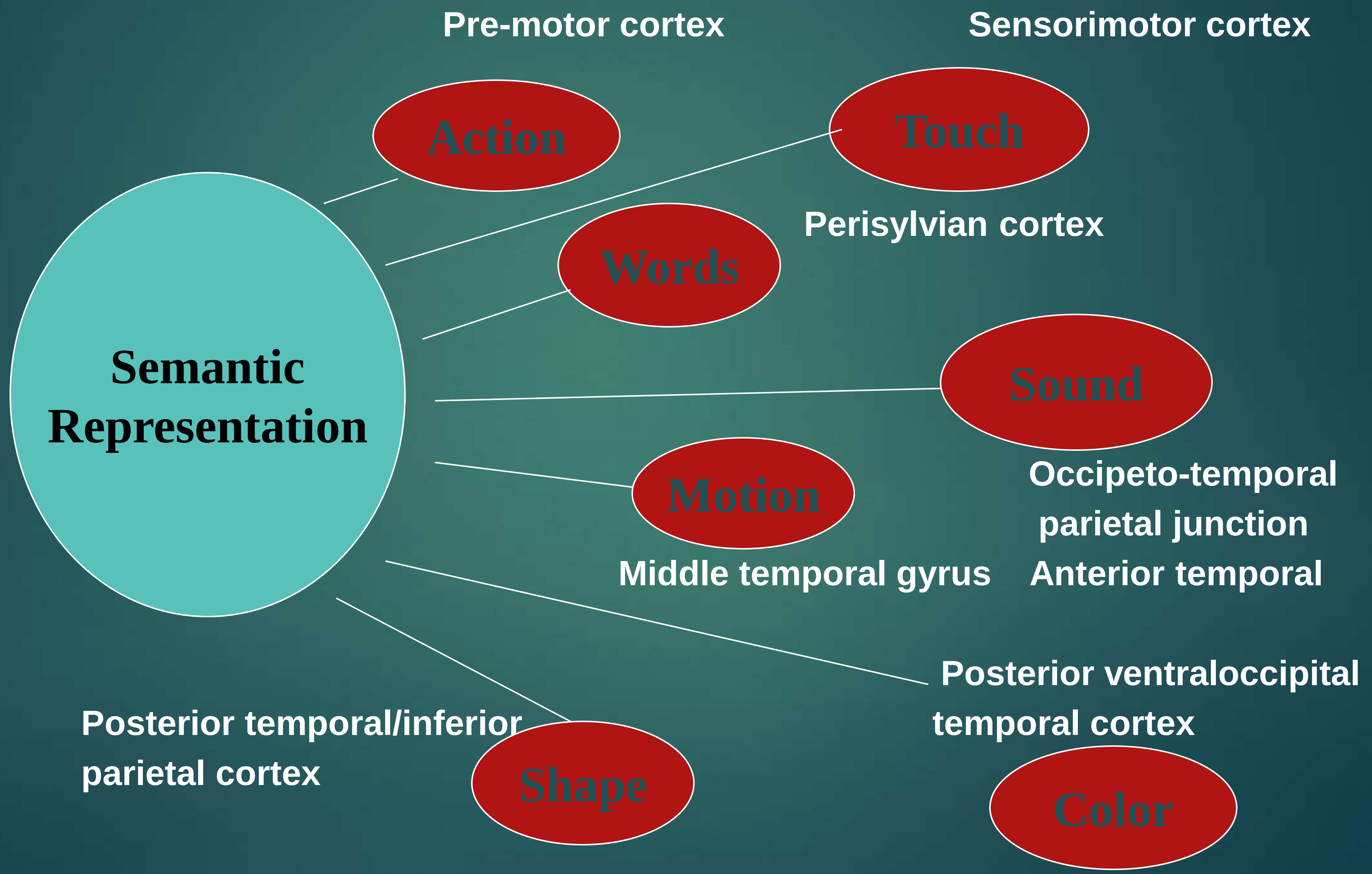
Historical (1996) view of Semantic Knowledge:

Location of people, animals and tools: lesion based

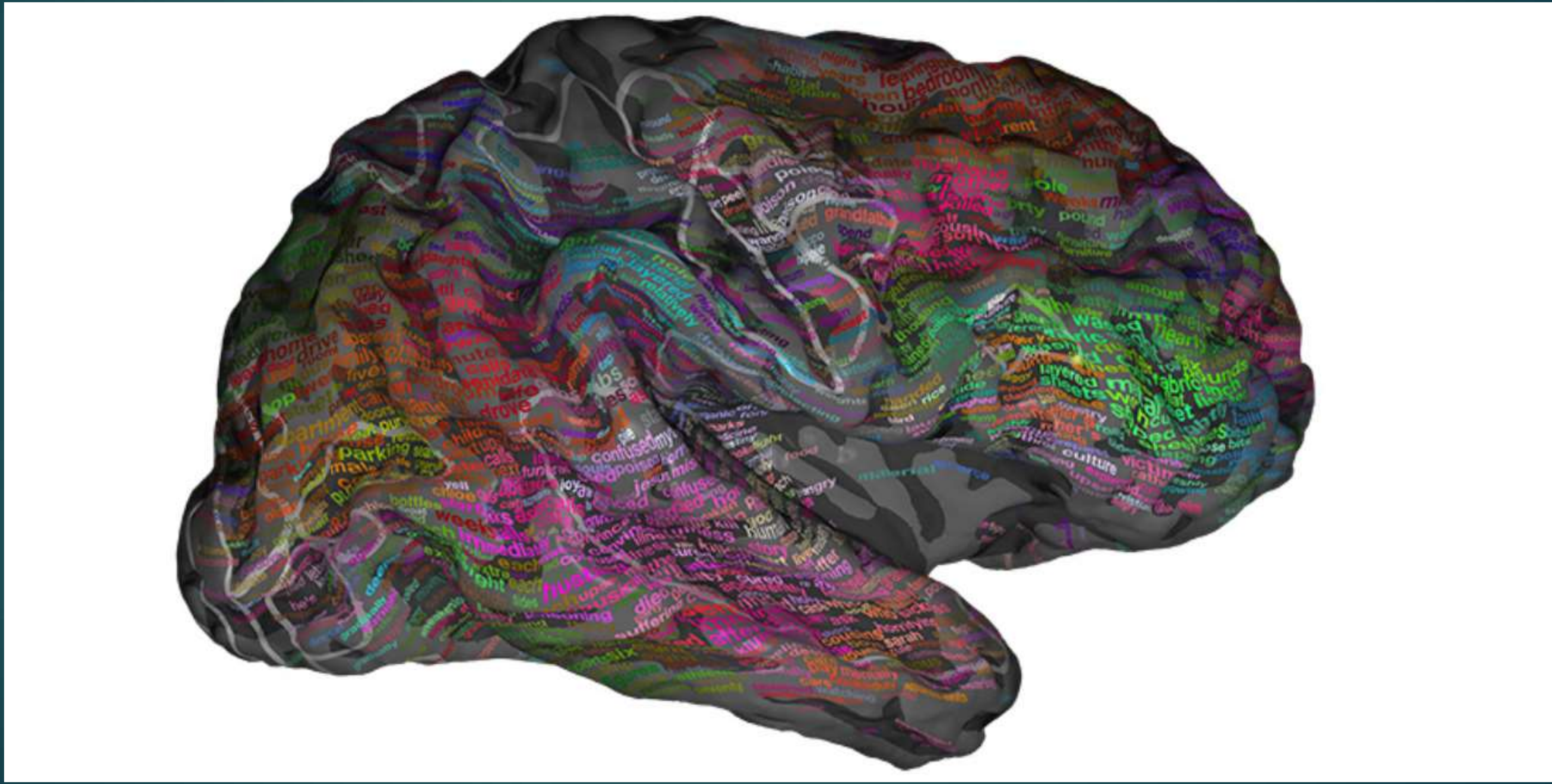


Location of brain lesions that are correlated with selective deficits in anming persons, animals or tools (Damasio et al., 1996).

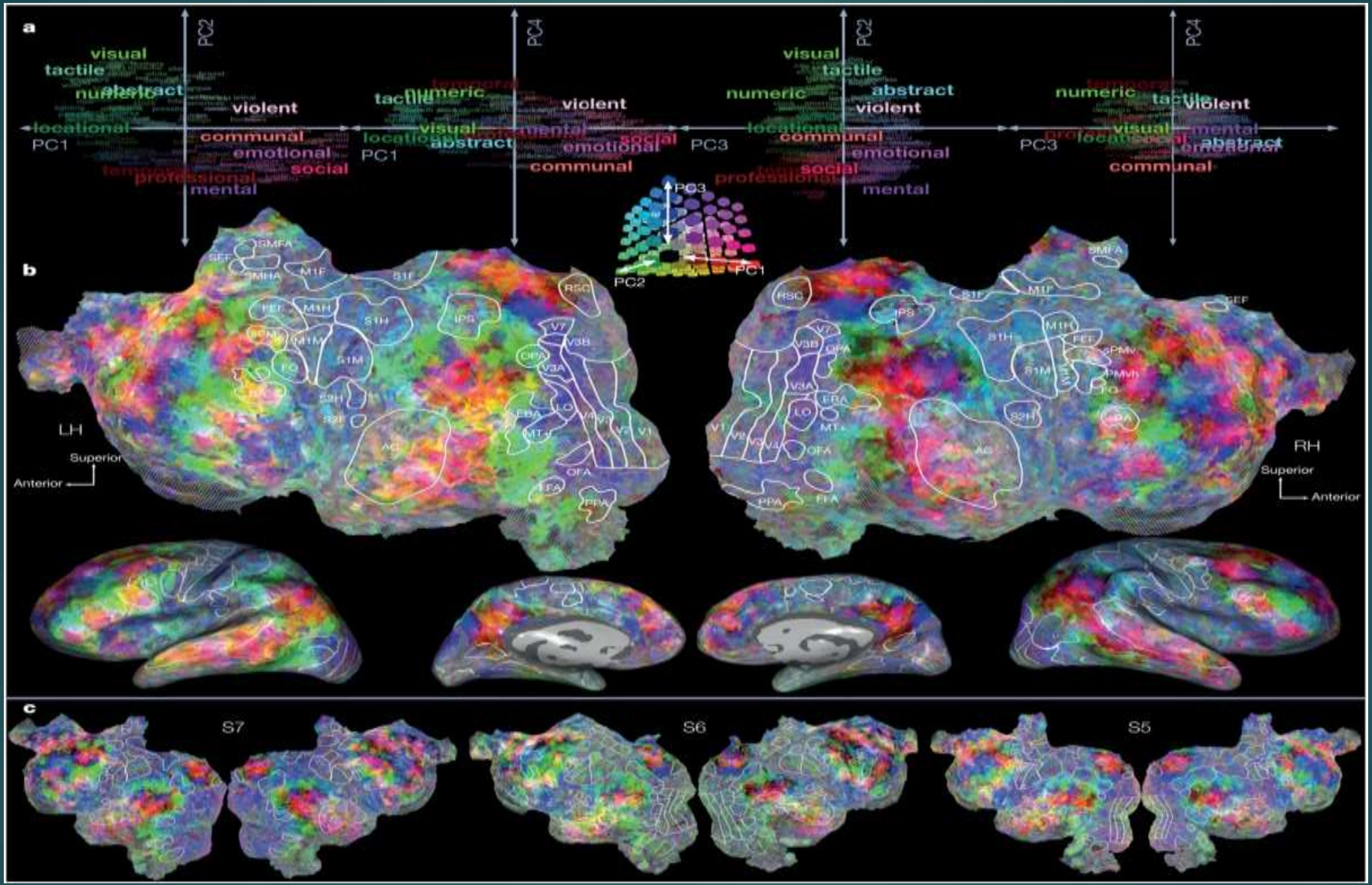
Locations of Semantic Memory (via stroke effects)



Meaning in the Brain: Listening to narrative stories – areas activated by meaning



Language everywhere: Principal components of voxel-wise semantic models



Semantic representation is bihemispheric

A G Huth *et al. Nature* **532,** 453–458 (2016) doi:10.1038/nature17637

Naming Errors: Ubiquitous

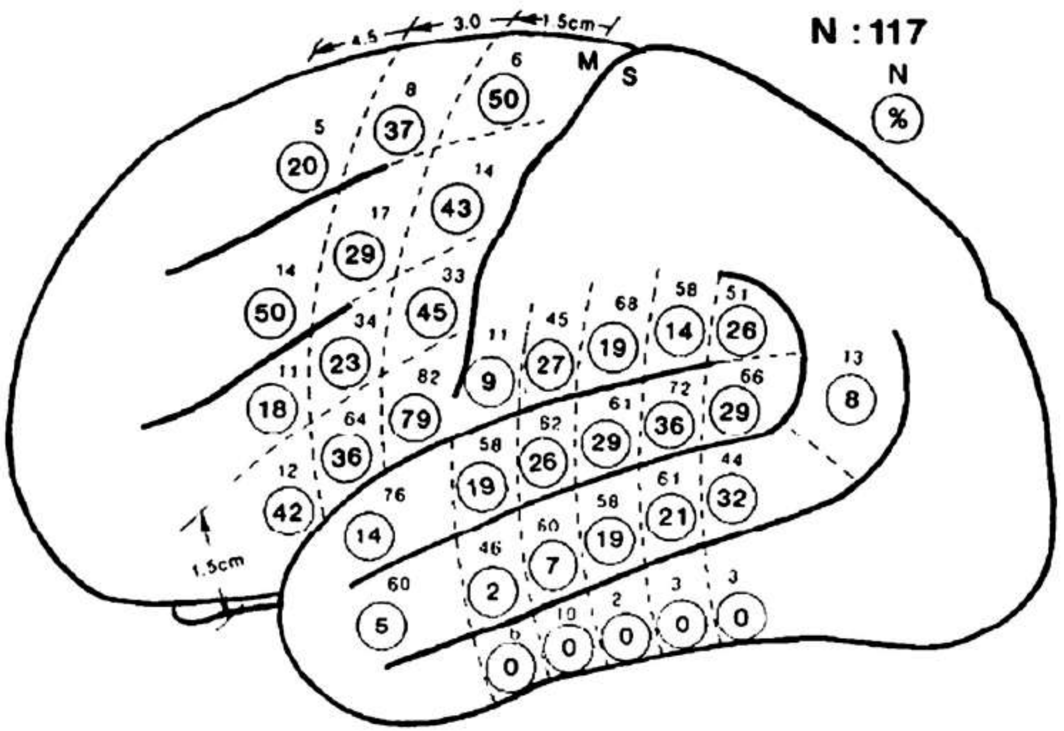
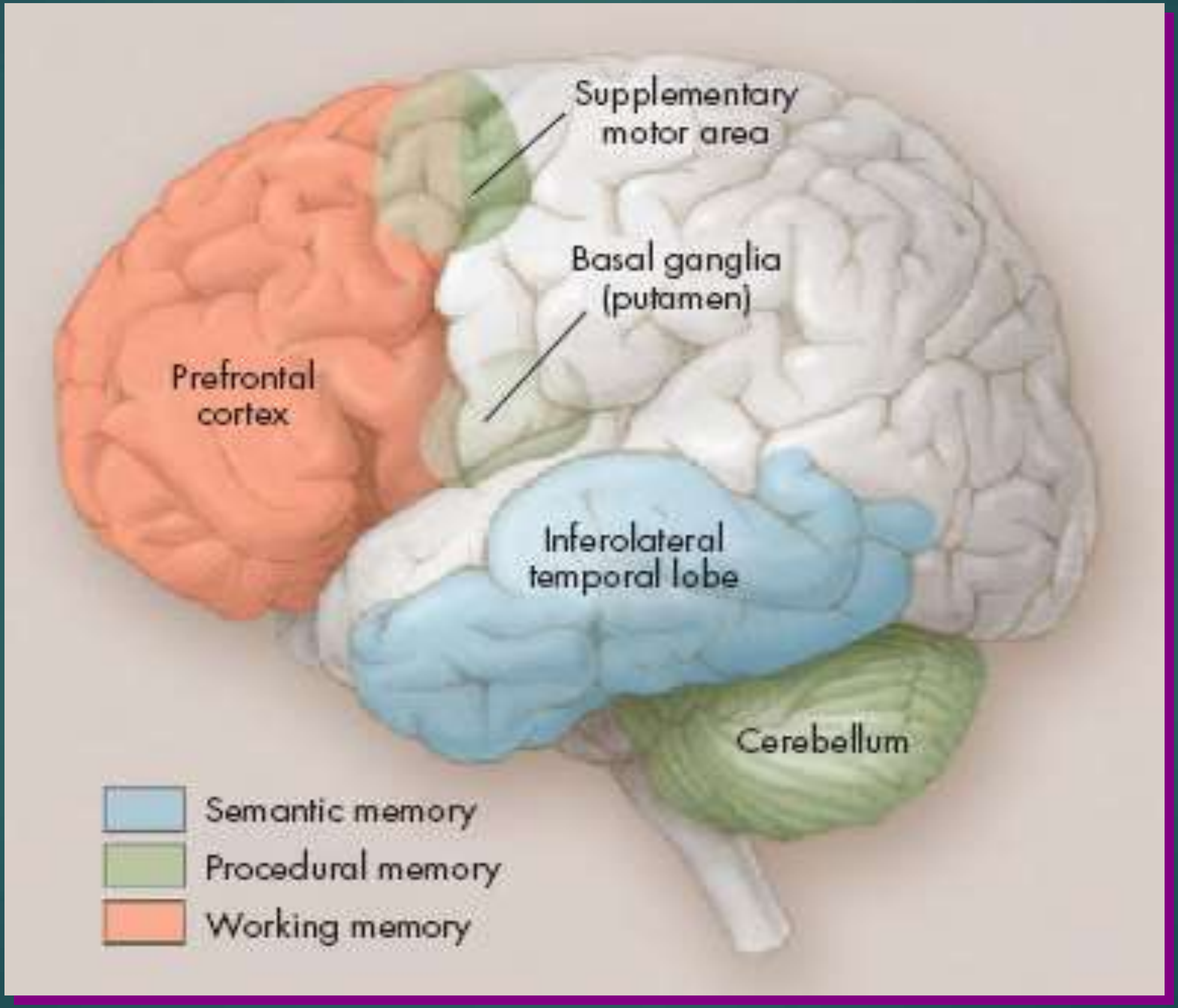


Fig. 4. Intraoperative stimulation data demonstrating individual variability of cortical sites essential for naming in the left, dominant hemisphere in 117 patients (from Steinmetz and Seitz 1991; data from Ojemann et al. 1989). Numbers in the circles are percentages of patients with an evoked naming error following stimulation of that area; numbers above the circles are numbers of patients stimulated in that area (reproduced with permission from *Neuropsychologia*).

Multiple Memory Systems



Memory Localization Summary

- **Rhinal cortex**
  - Formation of new long-term explicit memories
- **Hippocampus**
  - Formation of long-term verbal/spatial memory
- **Amygdala**
  - Enhanced Memory for emotional experiences.
- **Inferotemporal Cortex**
  - Storage location for sensory memories
- **Striatum & Cerebellum**
  - Storage location for procedural memories.
- **Prefrontal Cortex**
  - Search strategies for Encoding & Retrieval

Types of Memory & examples

- Explicit (Factual) Memory: name, birth date
- Episodic (Personal) Memory: first kiss
- Working (Brief, Temporary) Memory: phone #
- Prospective Memory: remember to buy milk
- Procedural (How to…) Memory: piano, tennis

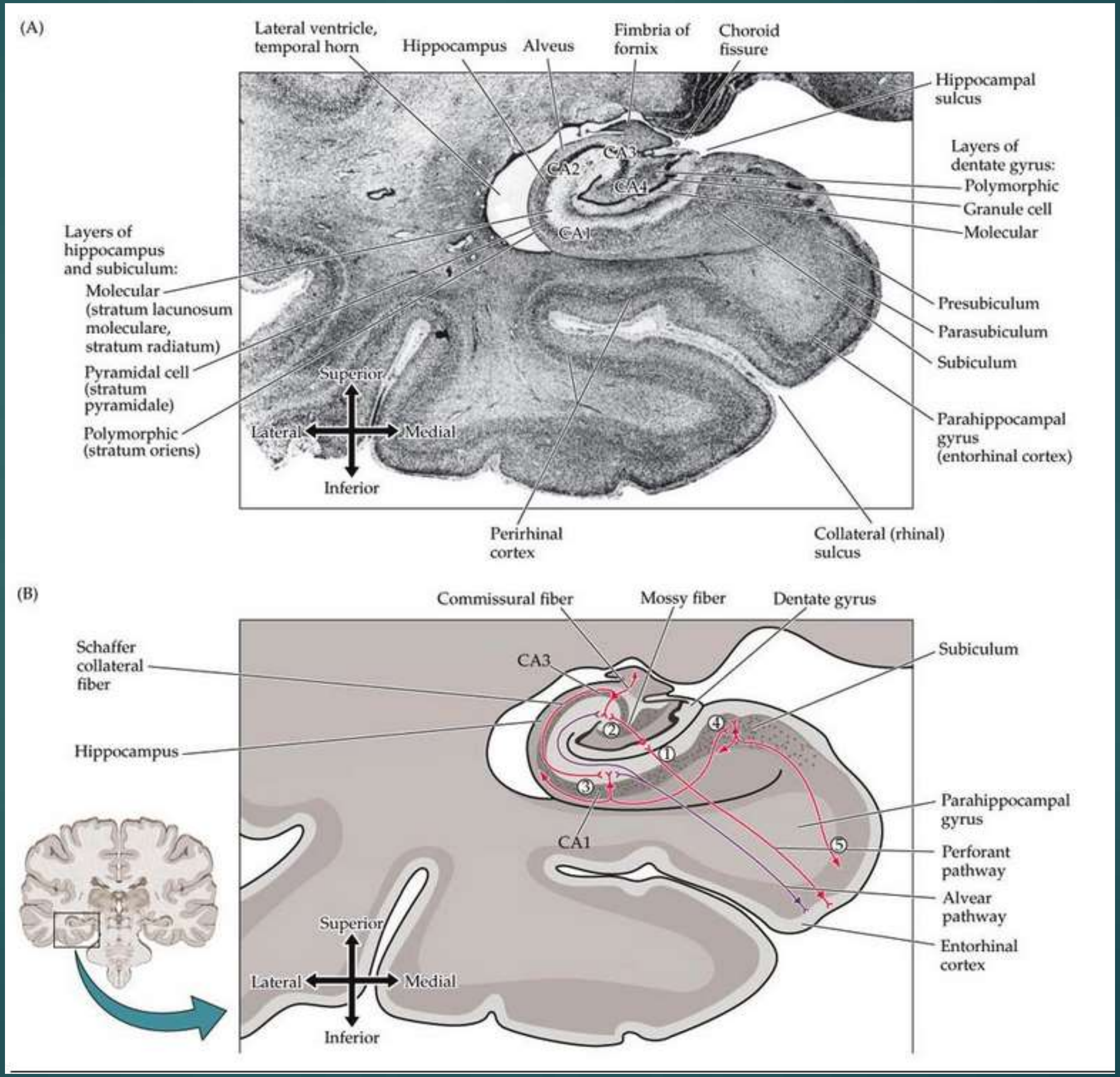
Hardware vs. Software

- Brain = Your hardware
- Experience/Memory = Your software (via neuroplasticity)
- Neuroplasticity: experience produces constant neurological changes: new synapses, new dendrites

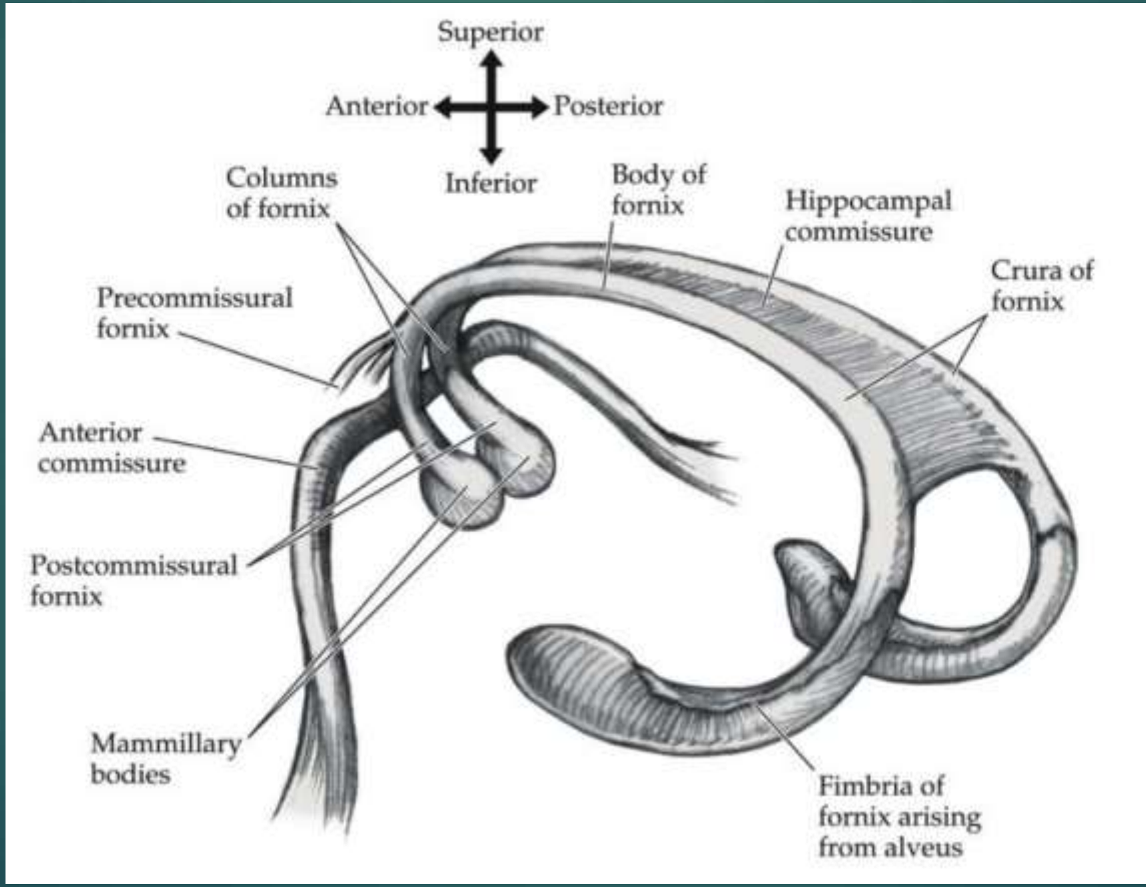
Neuroplasticity: creation of memory

- 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); phantom limb; phantom limb

Hippocampus



Mammillary Bodies & Fornix



Summary of Anatomy of Memory & Amnesia

- Memory is a distributed function of brain

- Amnesia is associate with medial temporal, thalamic & basal forebrain damage which affects integrity of 2 memory systems

- Functional impairment of both circuits is necessary for severe amnesia; Less severe forms of memory deficit can result from more restricted lesions that affect only 1 circuit.

Place & Grid Hippocampal Cells: Inner GPS

- Grid cells in entorhinal cortex of hippocampus (certain locations spaced at regular intervals); place cells in hippocampus (specific spot)
- Navigation is a memory. Cells that identify location, time and distance provide a framework — scaffolding onto which memories are placed.
- Functions:
  - "Place" cells: map, localization, navigation - brain cells fire off regular signals as animals move around in space, partially forming an internal map of the environment.
  - "Speed" cells: Speed cells make up about 15 percent of all cells in the entorhinal cortex: how fast you move
  - "Time" cells: these cells stay tuned to distance or time, or both. About 40 percent of grid cells detected both time and distance.

B. Kraus et al., Neuron, 2015

Memory Systems

Conscious Unconscious

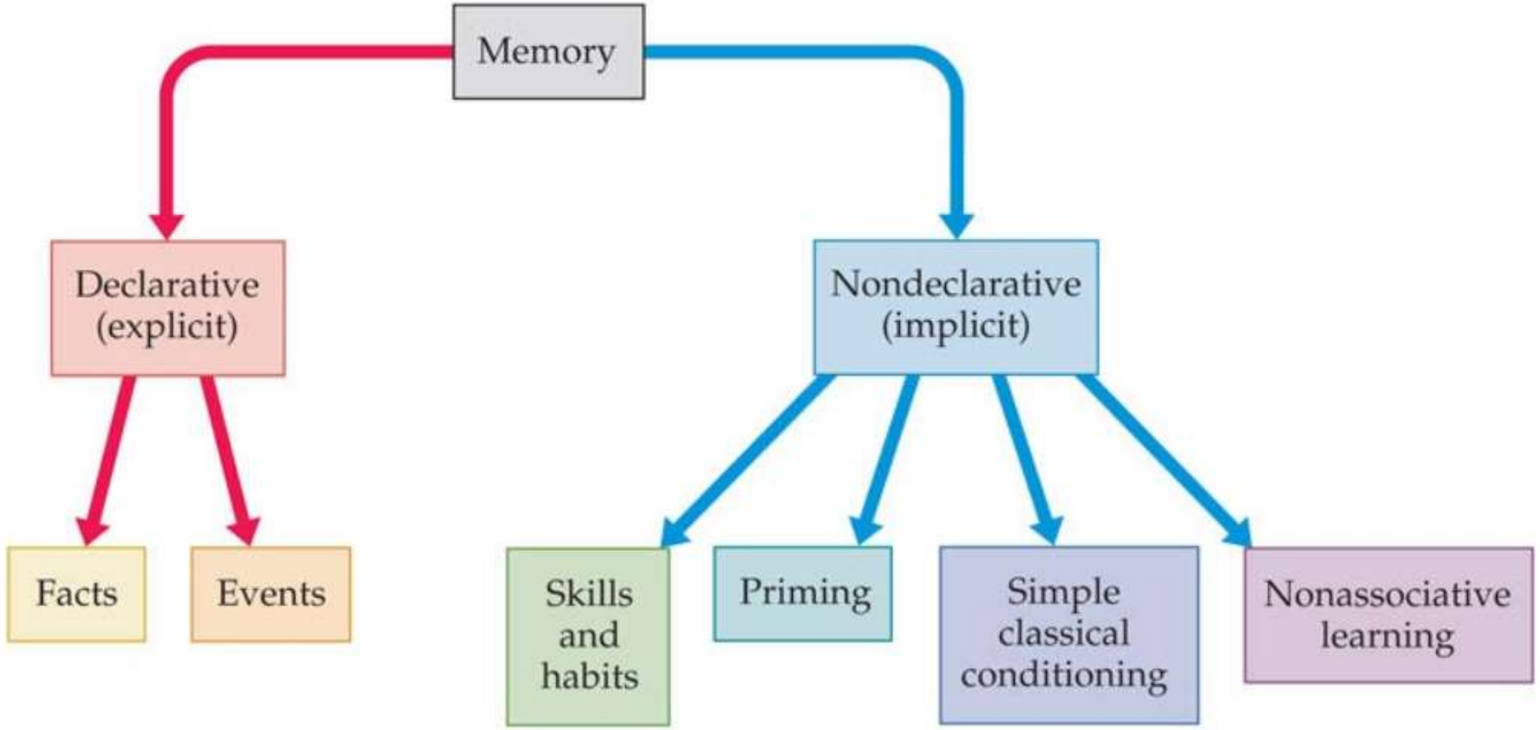
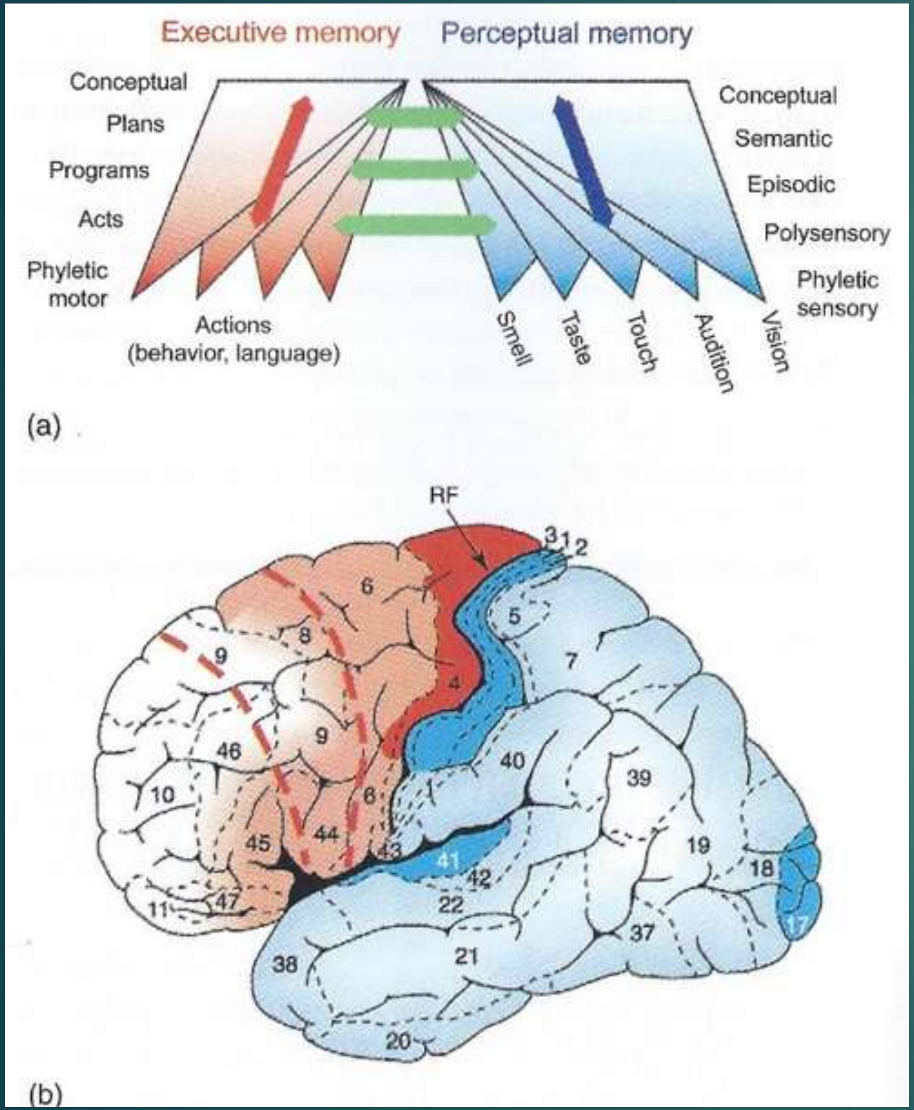


Figure 18.15 Classification of Memory (After Squire LR, and Zola-Morgan S. 1991. The medial temporal lobe memory system. *Science* 253: 1380–1385.)

Semantic Episodic Procedural

Personal

Fuster: All memories are individual networks



Memory is stored in many different regions by means of synaptic connections.

Posterior cortex houses sensory memory systems;

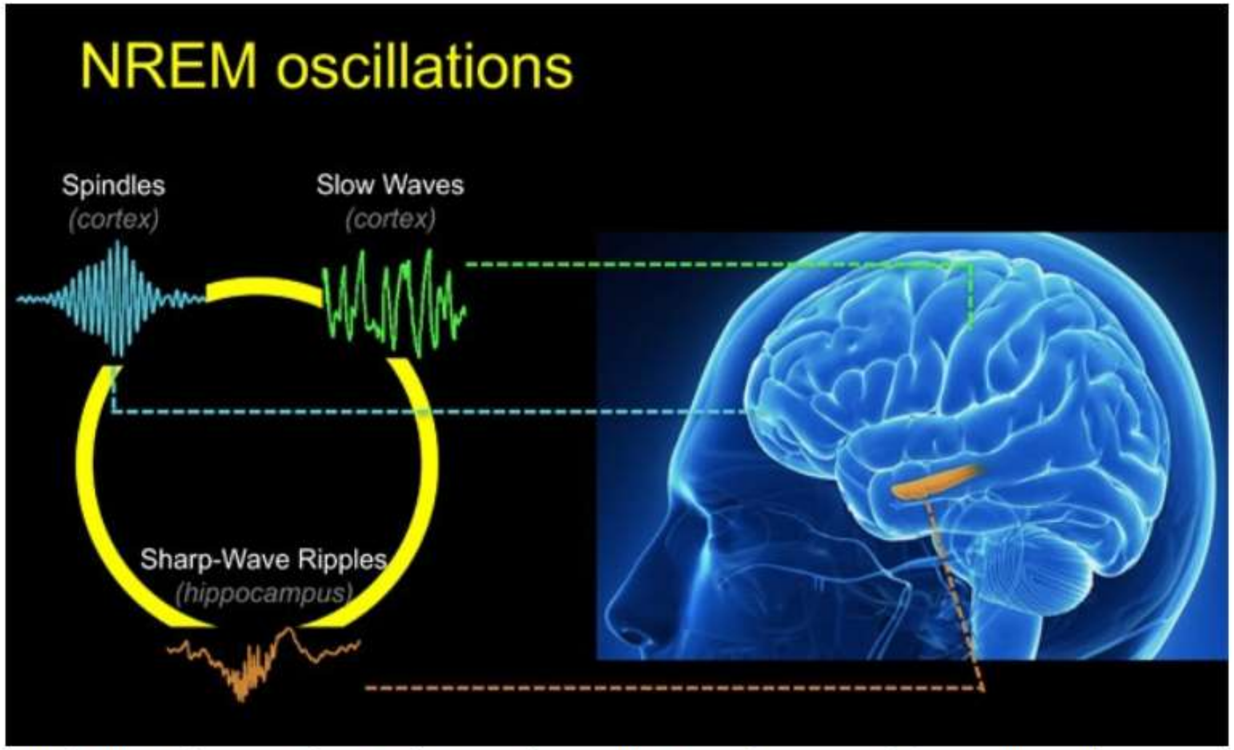
Frontal cortex houses executive and motor memories.

Hippocampal region is involved with episodic memory.

Subcortical areas like BG and cerebellum are involved in motor learning

J. Fuster, Cortex and Mind, 2003

STM to LTM transfer during NREM sleep



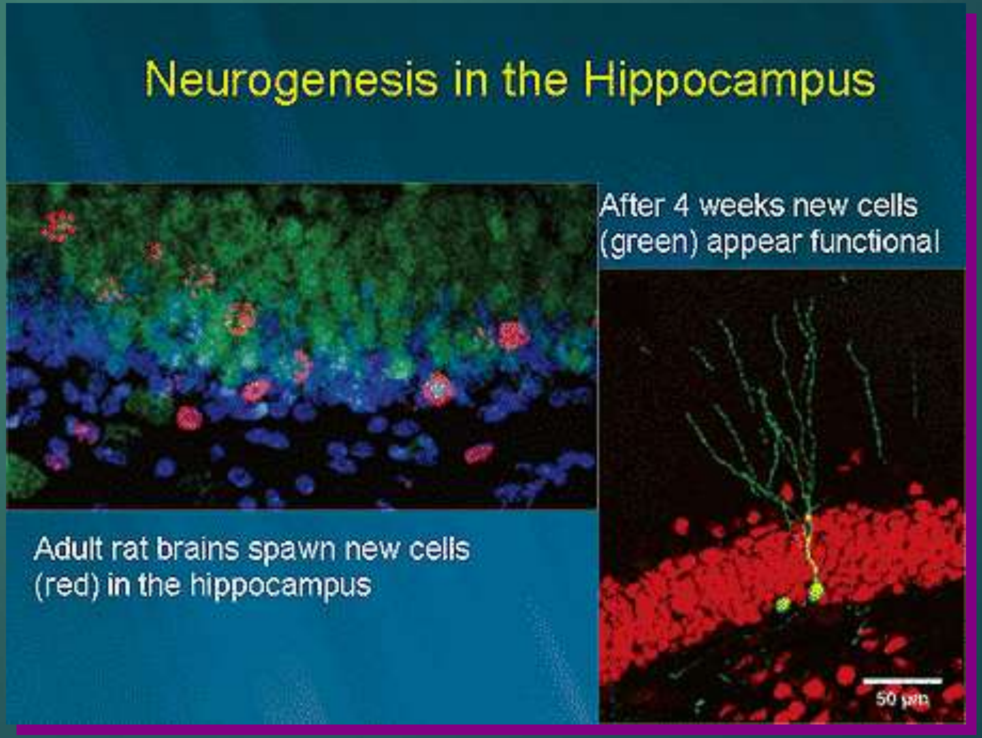
Synchronous Sleep. Coordination between three oscillations—hippocampal sharp-wave ripples, spindles, and slow waves—is crucial for consolidating memories while we sleep. [Courtesy of the Walker lab.]

The more out of synch the two oscillations were, the worse the person performed on the memory task. Increases with age due to atrophy of medial prefrontal cortex

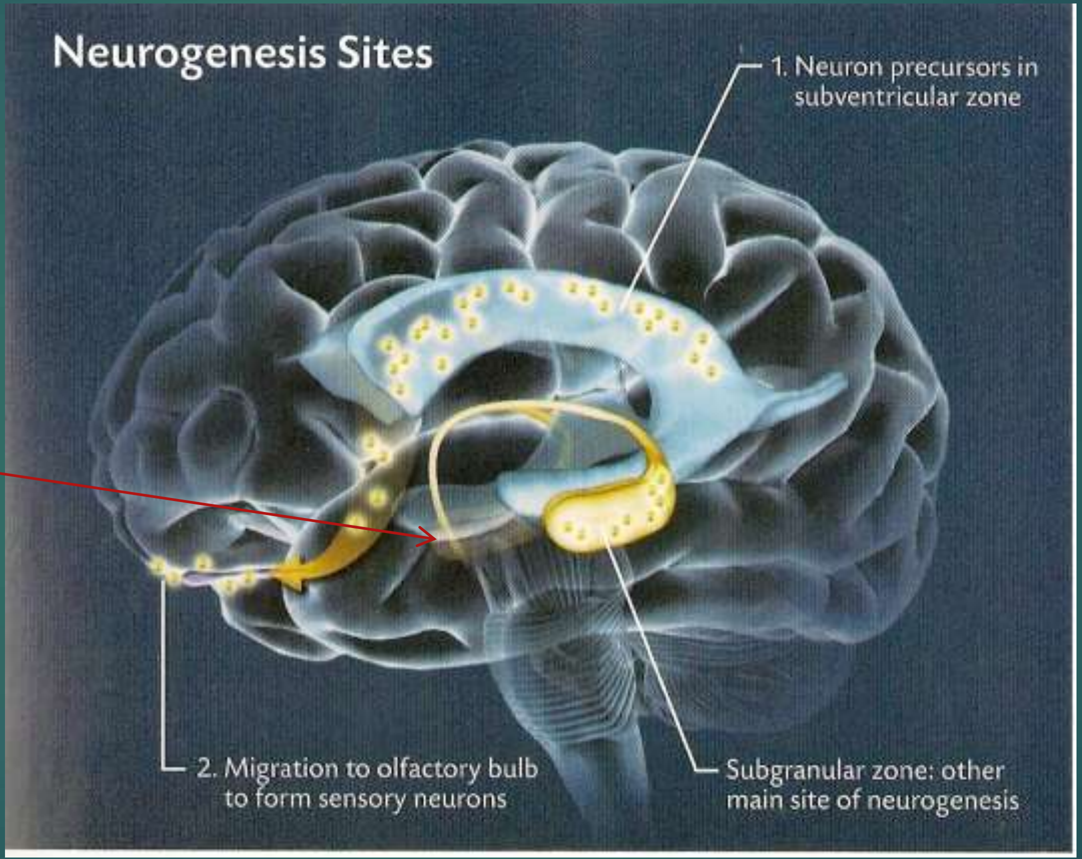
- Aging disrupts the neural activity that solidifies memories during sleep.
- Alzheimer's pathology also alters memory-consolidating neuronal waves during sleep.
- Skimping on sleep kills neurons in mice and pumps up p-tau.
- Non-rapid eye movement sleep makes up about 80 percent of our sleeping hours.
- During NREM sleep, a trio of neuronal oscillations coordinates to consolidate memories formed during the day when these both align with the hippocampal sharp wave, then the brain is poised to convert short-term memories to long-term ones
- Sleep loss increases BA & Tau.

Neurogenesis

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



Neurogenesis: 3 major sites



Interneurons in Striatum

1400 new neurons per day, enough to replace all the neurons in the dentate gyrus of the hippocampus over a lifetime; needed for new memories

Function of Neurogenesis

- Most stem cells die

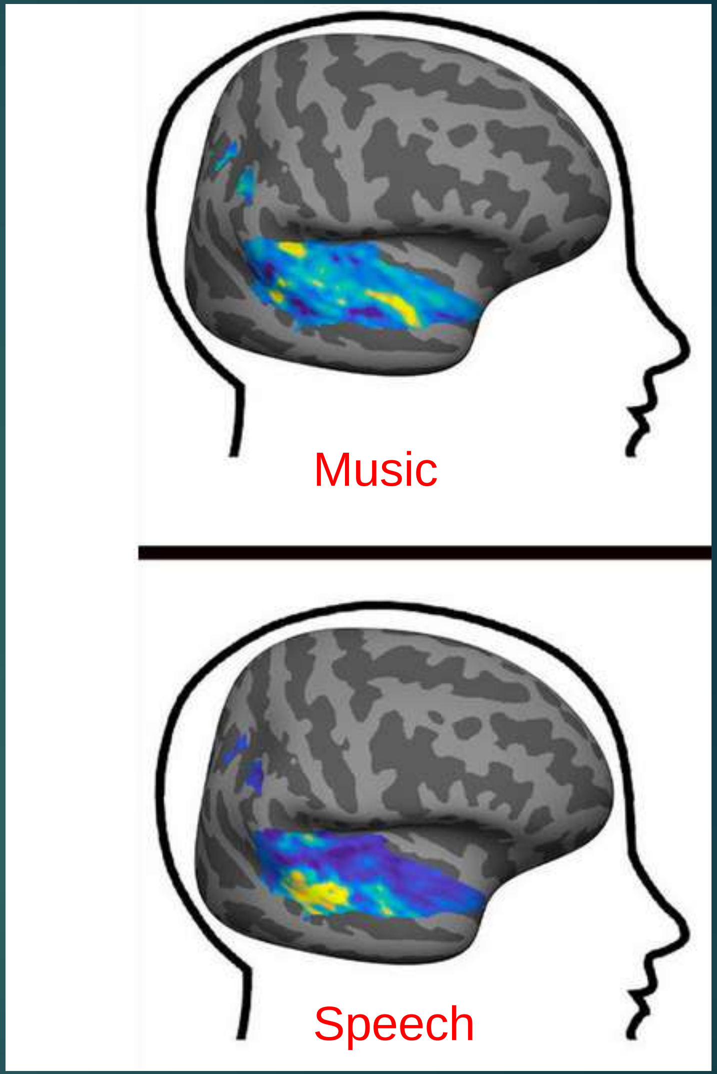
- Those involved in new learning survive

- Decreased by: Increased by:
  - Stress (Cortisol) Environmental enrichment
  - Depression Exercise
  - Aging Antidepressants
  - Alzheimer's Alzheimer's
  - Seizures

Nancy Kanwisher, MIT: domain specific processors

Unique Music network

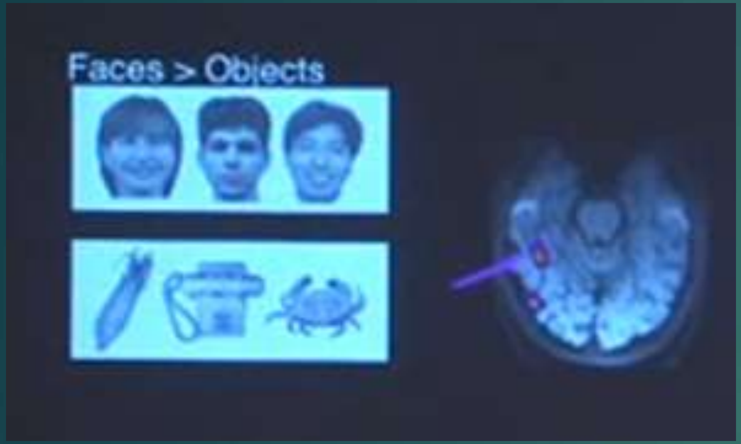
- Music and speech selectivity concentrate in distinct regions of non-primary auditory cortex
- There are neural pathways that react almost exclusively to the sound of music — any music, and not to any other sound.
- Speech and music circuits are in different parts of the brain's sprawling auditory cortex, where all sound signals are interpreted, and that each is largely deaf to the other's sonic cues
- Brain gives specialized treatment to music recognition, that it regards music as fundamental a category as speech



Sam Norman-Haignere, Nancy G. Kanwisher, and Josh H. McDermott, Neuron, 2016

Fusiform Face Area (FFA): Face Recognition

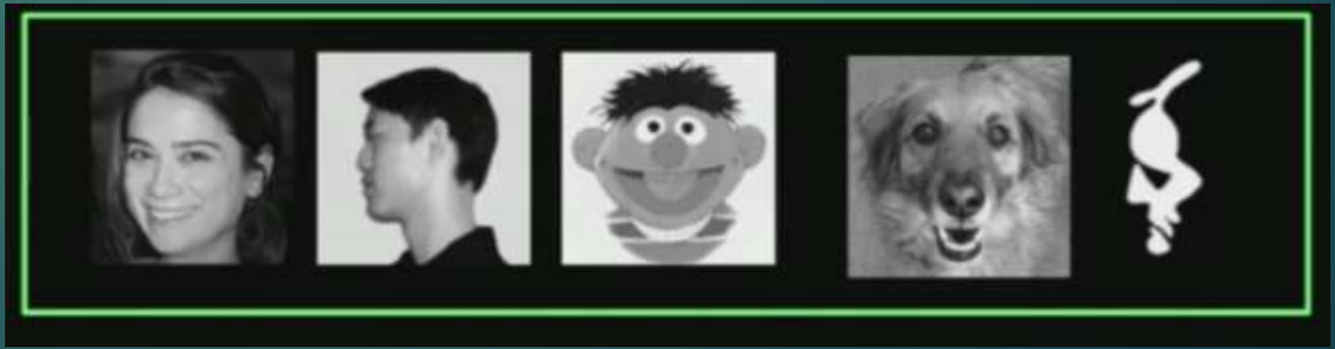
Brain regions for face vs. object recognition



Genetic: Face perceptual abilities are inherited

Also chess boards in expert chess players

No correlation between IQ & face recognition



Confirmed in epileptic pt with 2 electrodes on FFA

Nancy Kanwisher at MIT

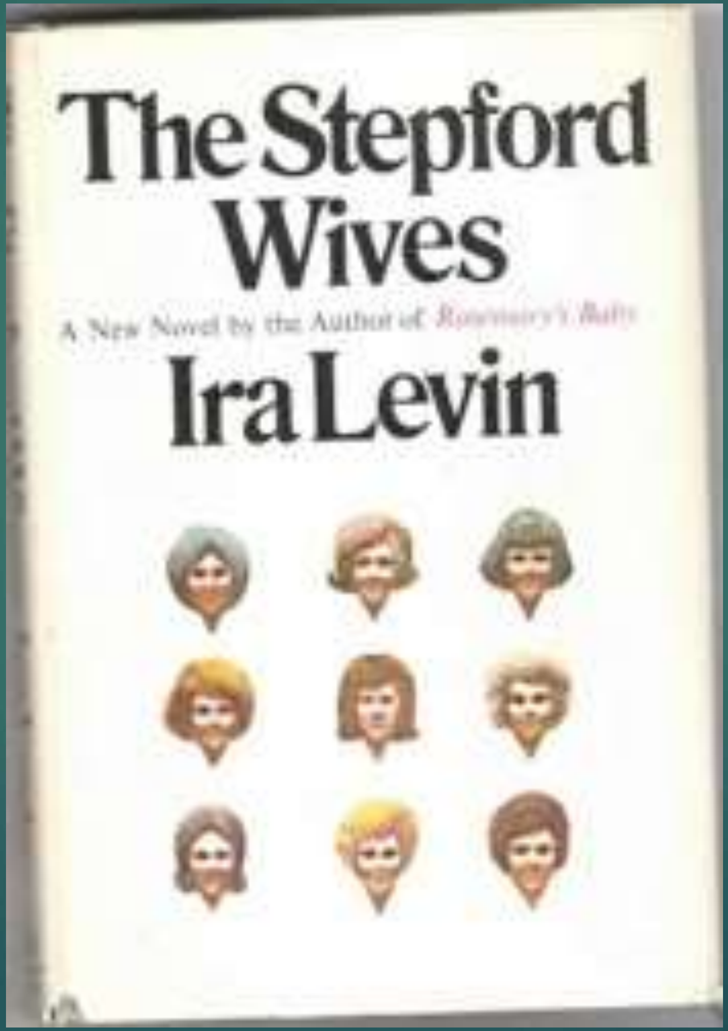
Amygdala beats FFA

- Amygdala has faster face processing than the FFA; faster than blink of an eye (33ms)

- Flashes of faces result in a response from the amygdala, initiating an emotional response, sometimes without even activating the FFA at all.

Capgras Syndrome:

A loved one has been stolen by a doppelganger



Capgras Syndrome: The trouble with disconnections

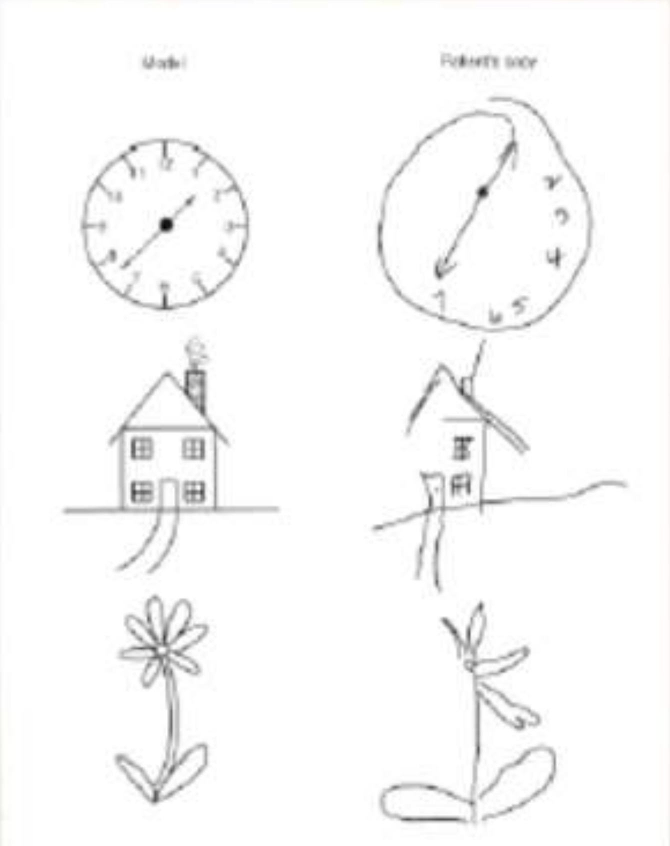
I know your face, but you are not familiar

- V. S. Ramachandran: a disconnection between
  - the FFA (visual face recognition↑↑) and
  - the limbic system (amygdala and hippocampus) (emotional familiarity↓↓)

- Visual, not auditory, circuit: When wife calls on the phone and he hears her voice, he instantly recognizes her. Yet if she walks in the room after that call, he is again convinced that she is an impostor.

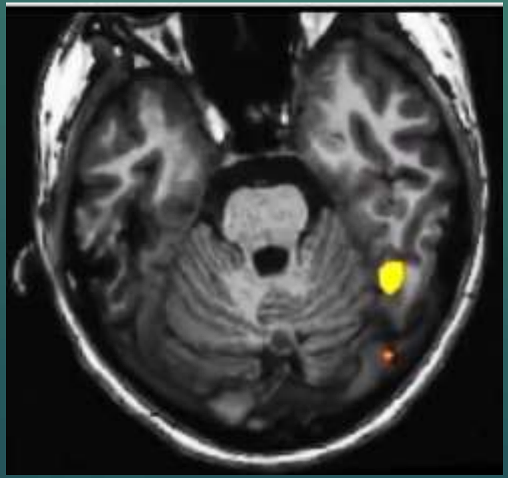
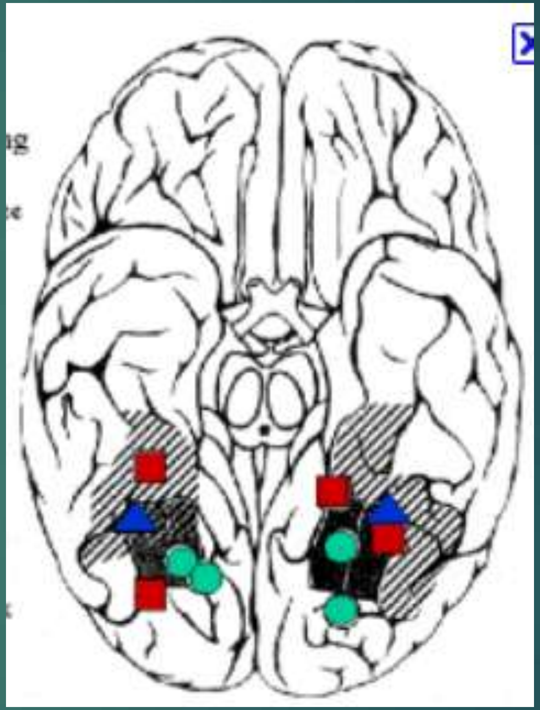
The *fusiform face area*

The *right posterior parietal cortex*



Fusiform Face Area in right Temporal lobe:
facial identity

- Fusiform face area (FFA):
  - Perception of unchanging (identity) aspects of human face
  - Only upright faces

Blue & Red

Upside down faces: very difficult

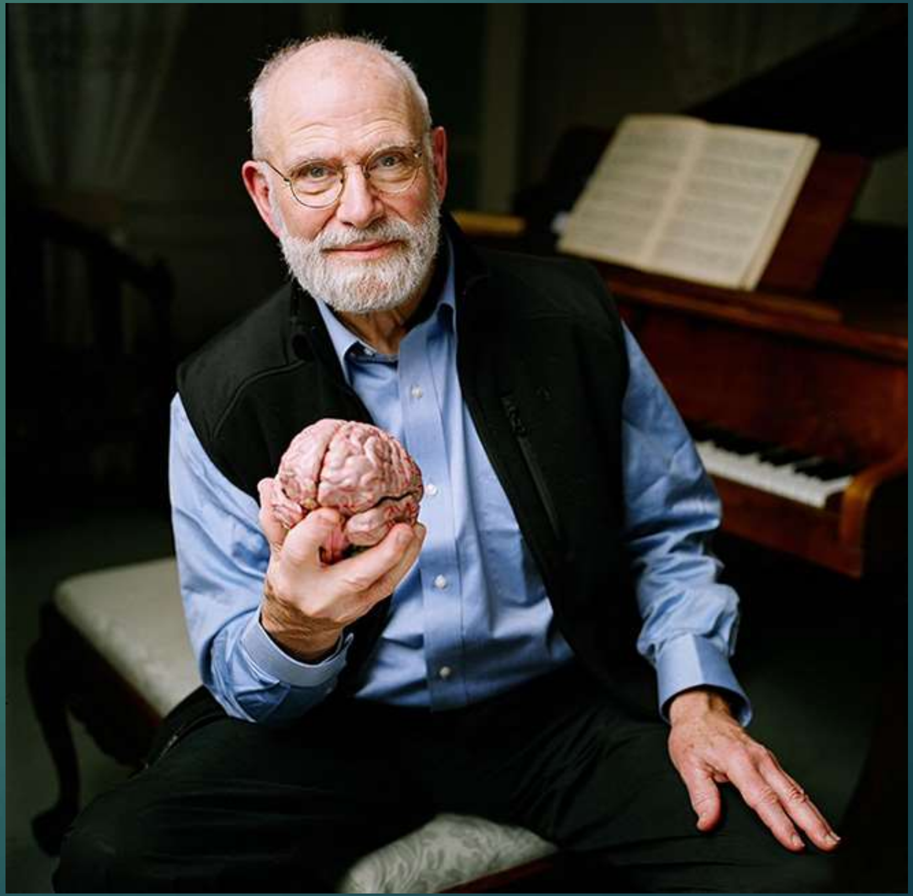
Right side up: Easy

Prosopagnosia or Face Blindness

- Patients are unable to recognize faces consciously
- Patient isn't blind (can still read a book); can not recognize faces by looking at people.
- There are also super-recognizers who do not forget faces and recognize people from childhood pictures (http://prosopagnosiaresearch.org/super-recogniser
- Typical people tend to focus on the eyes; some people with prosopagnosia avoid the eye region, and instead look at the mouth & spent less time on the eyes, yet it also turned out that super-recognizers spent more time viewing the nose - suggesting that it is the center of the face, rather than the eye region, that is optimal for facial identity recognition.

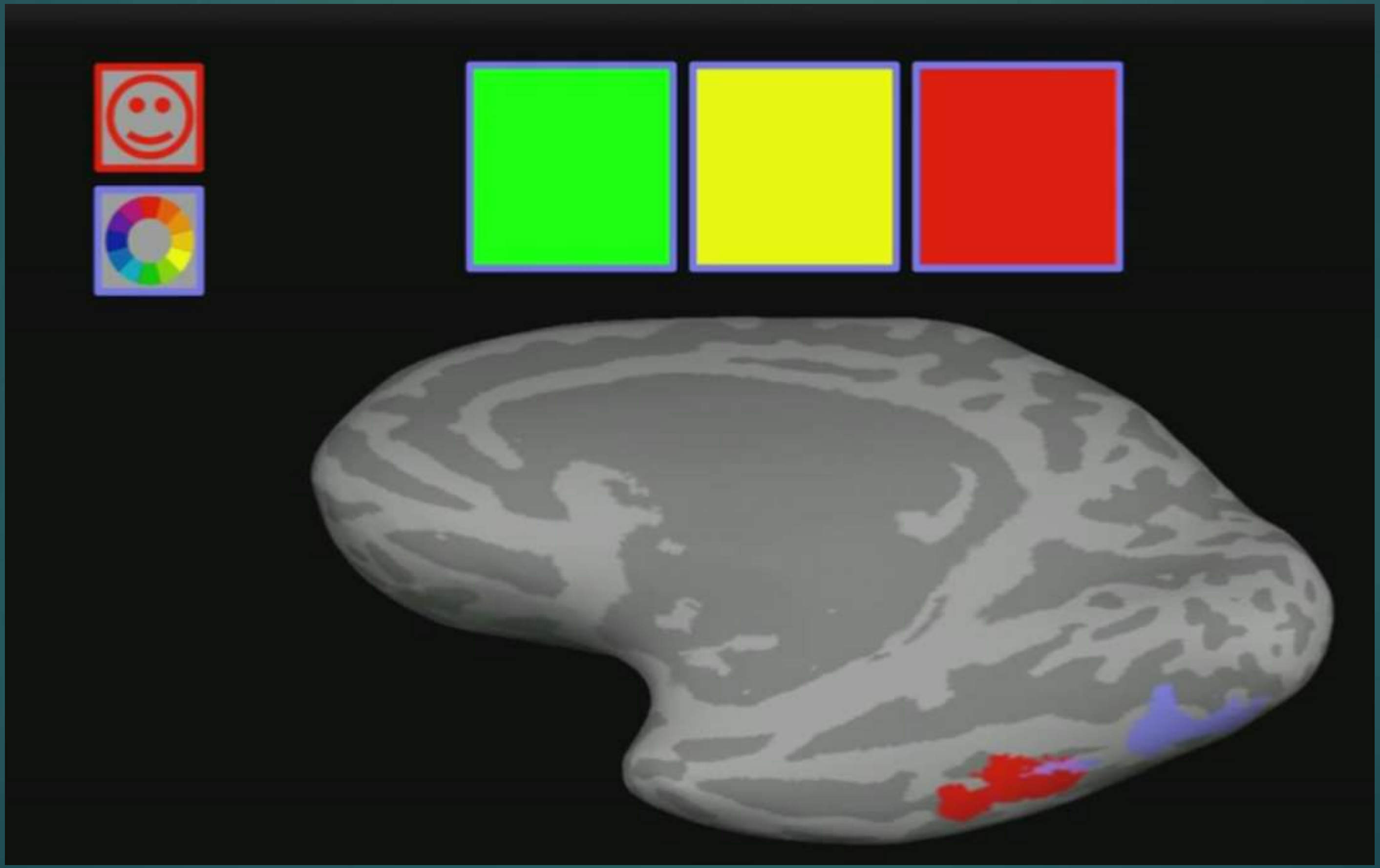
Oliver Sacks, MD

- *The Man who Mistook his Wife for A Hat*
- Face Blind (prosopagnosia)
- As is Jane Goodall

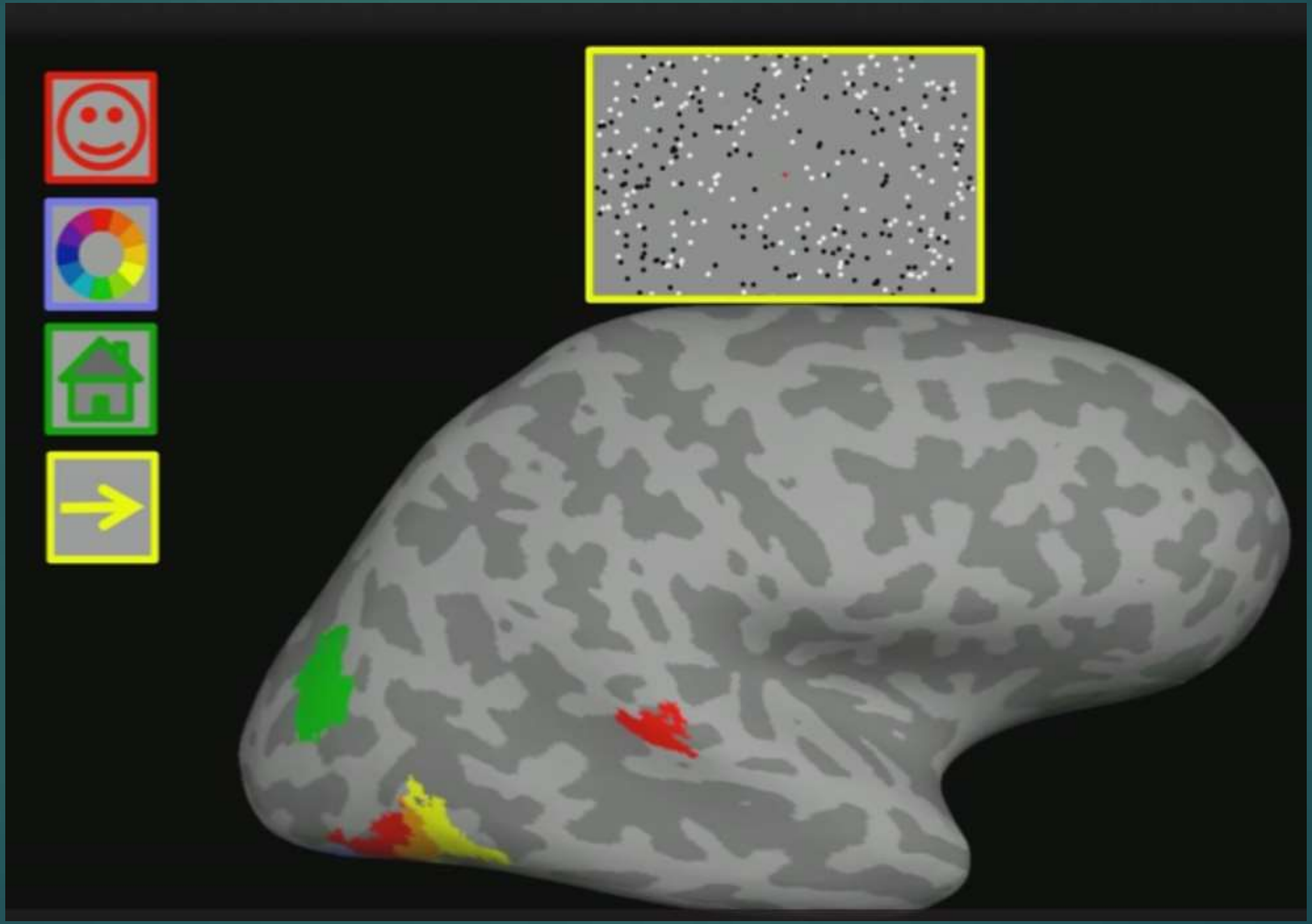


http://www.faceblind.org/facetests/index.php

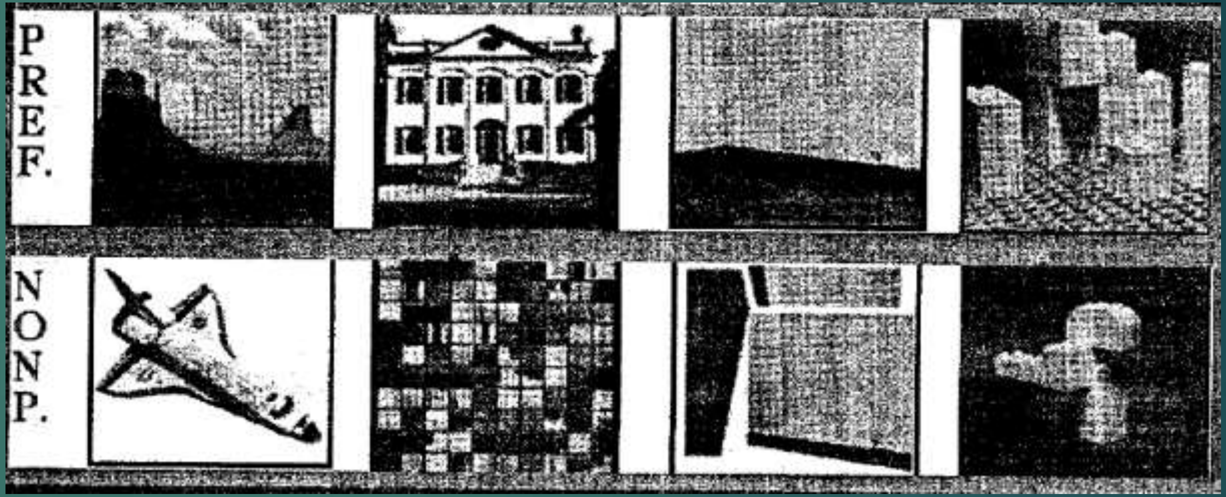
Color Processing Area



Visual Motion area

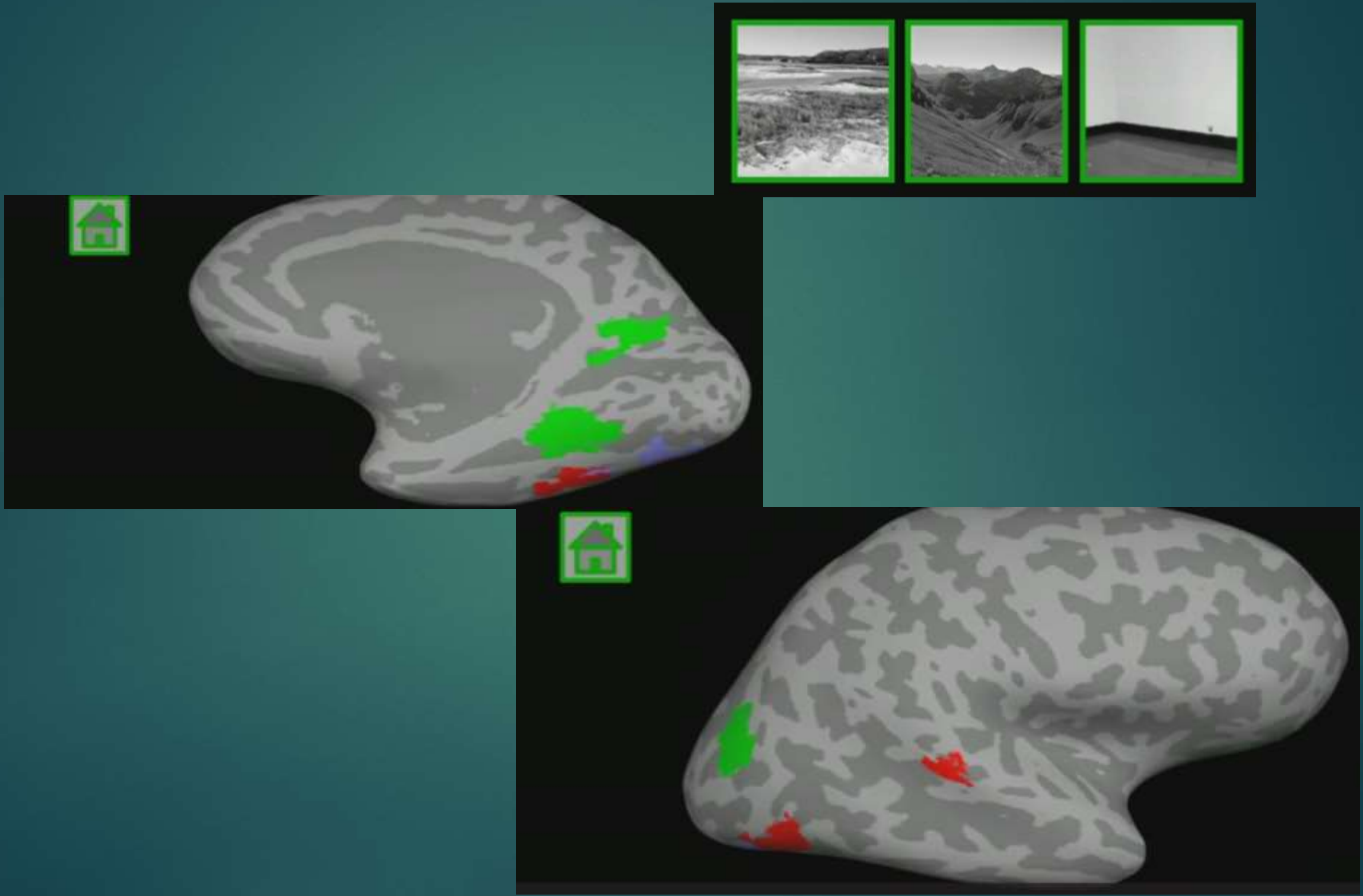


Parahippocamal gyrus: Recognition of places/spatial layout

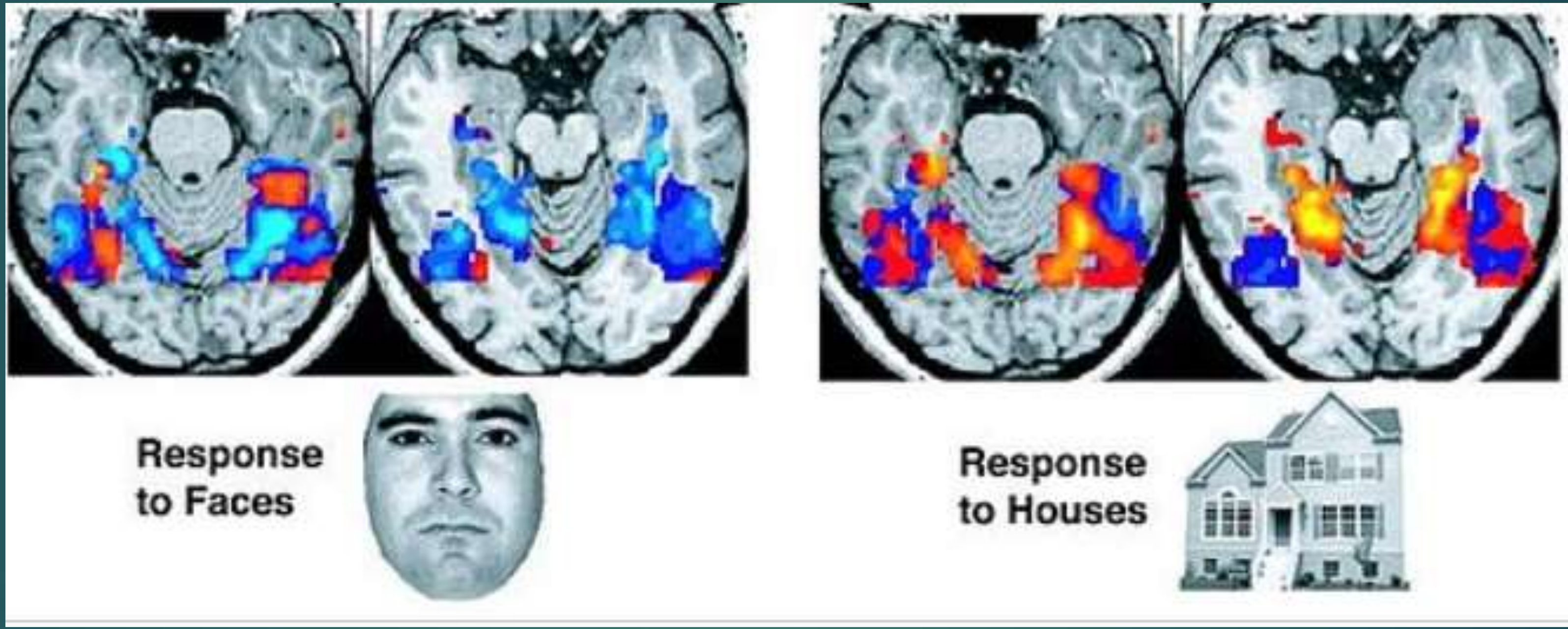


Parahippocampal place area (PPA):
Place area of brain: Recognition of spatial layouts

PPA: Place area

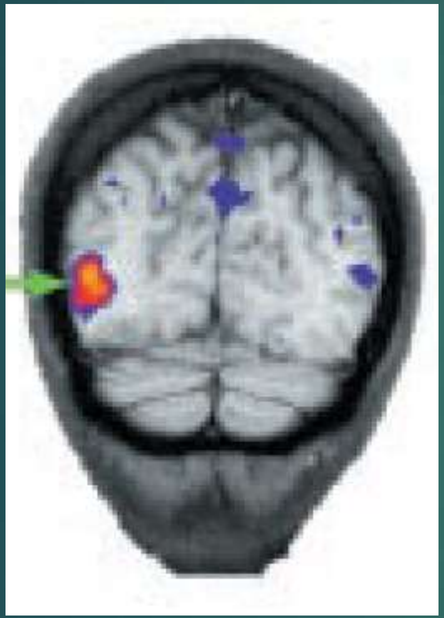


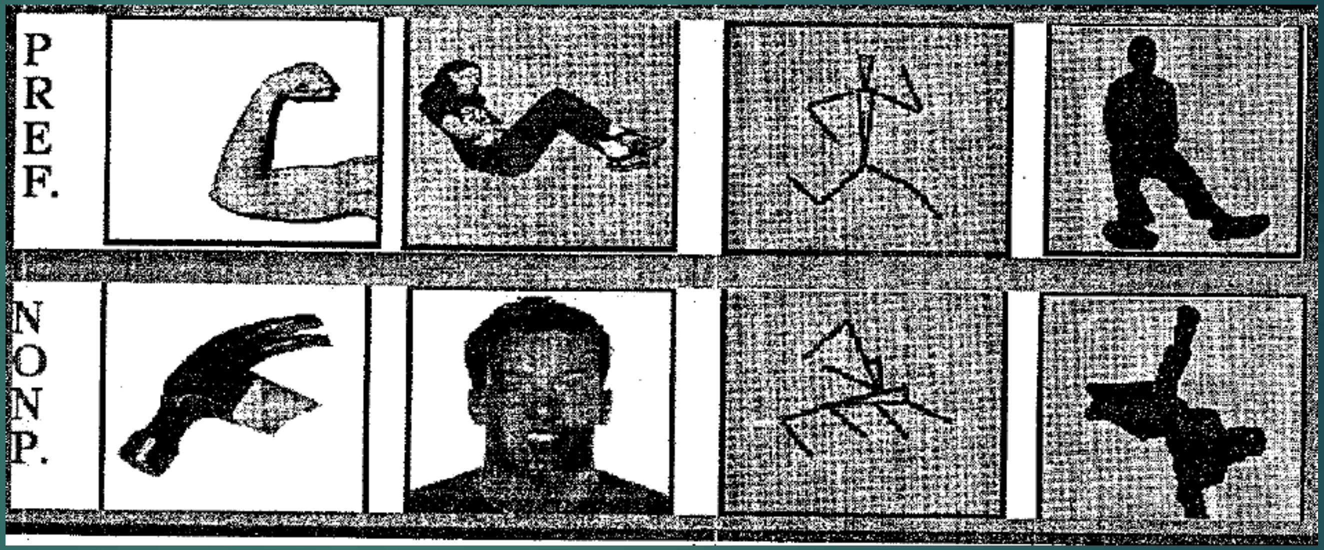
Method for communication with pts with locked in syndrome: focus on a face or a house



YES NO

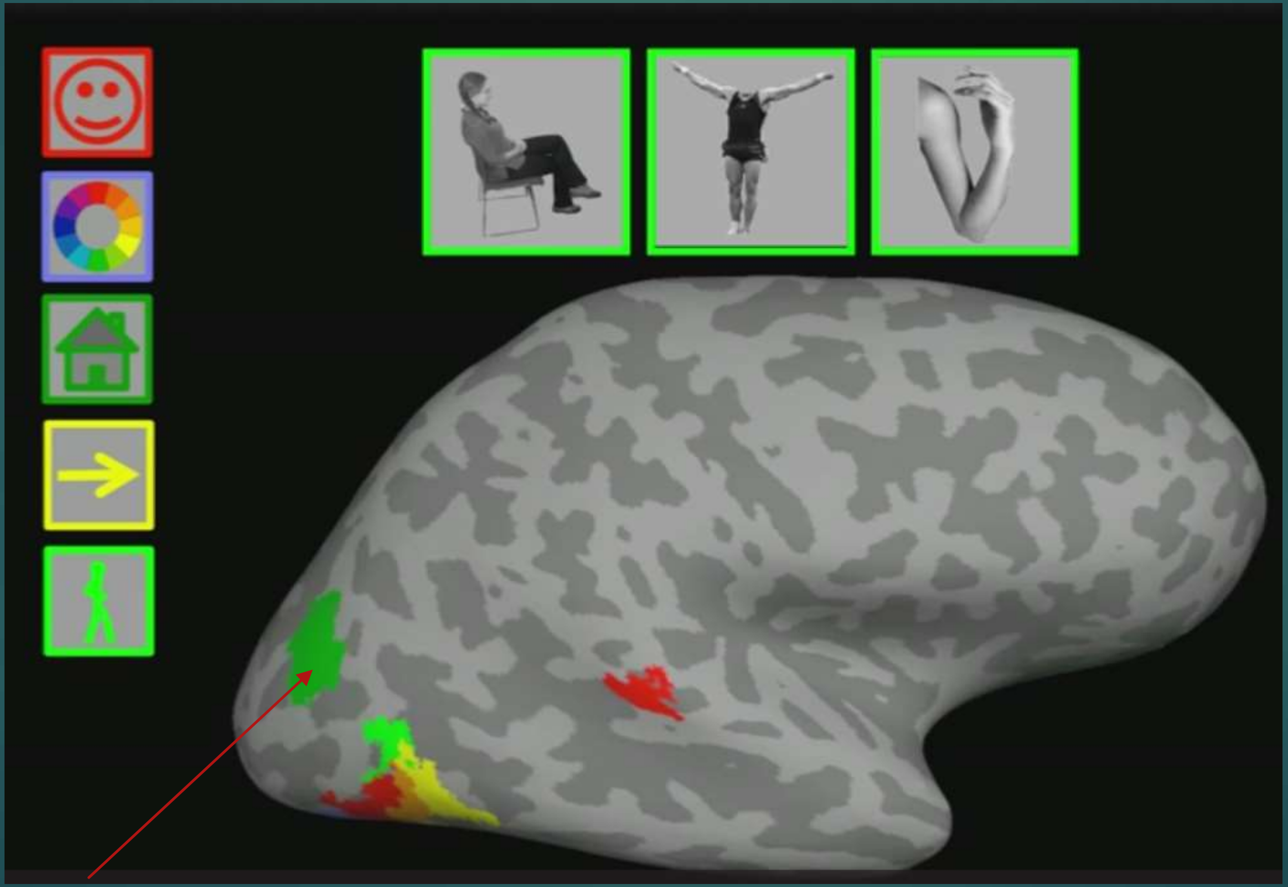
Extrastriatal Body Area





EBA: Only responds to bodies and body parts

Body Parts Area



EBA

Reduced connectivity between the left fusiform body area and the extrastriate body area in anorexia nervosa

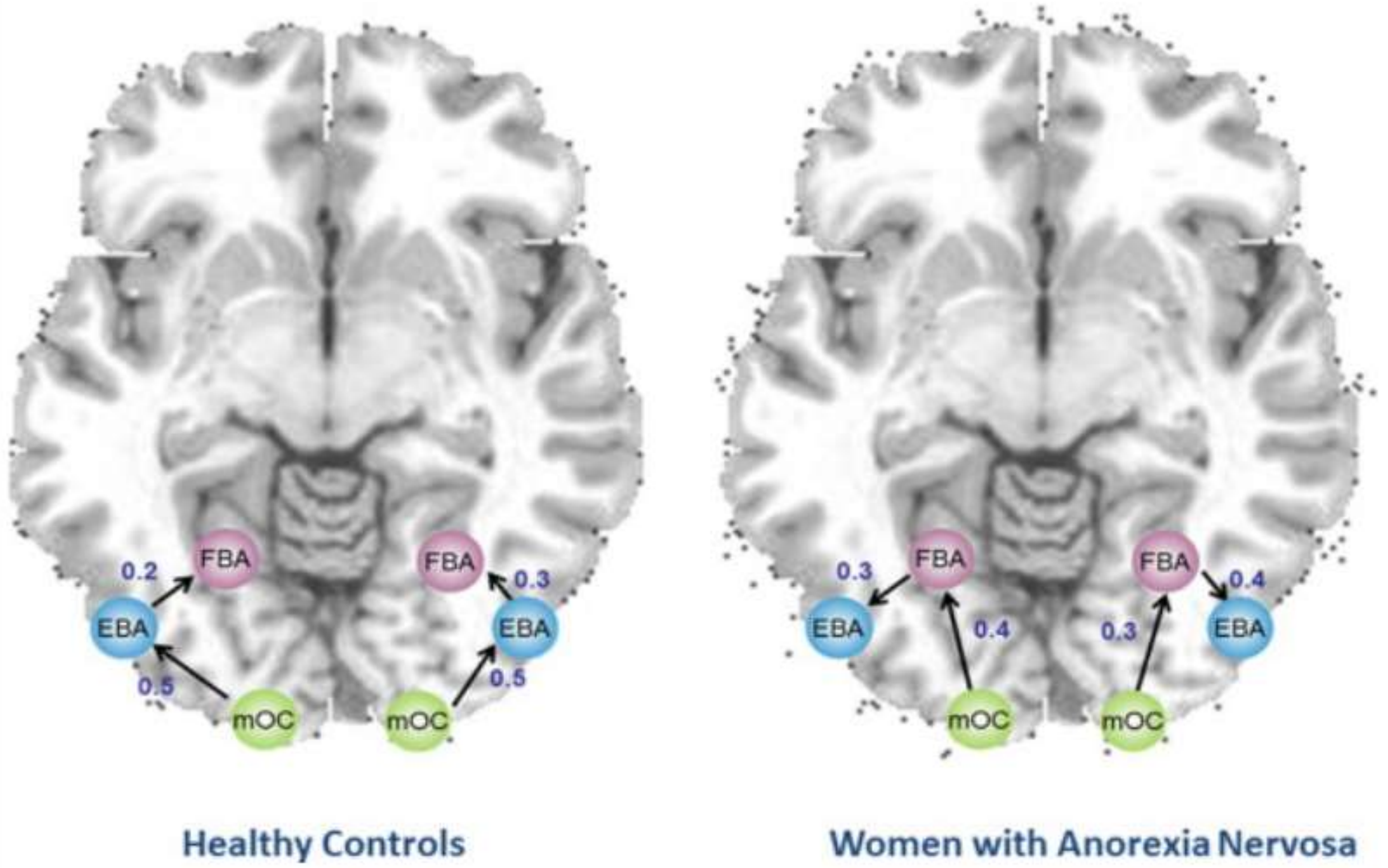
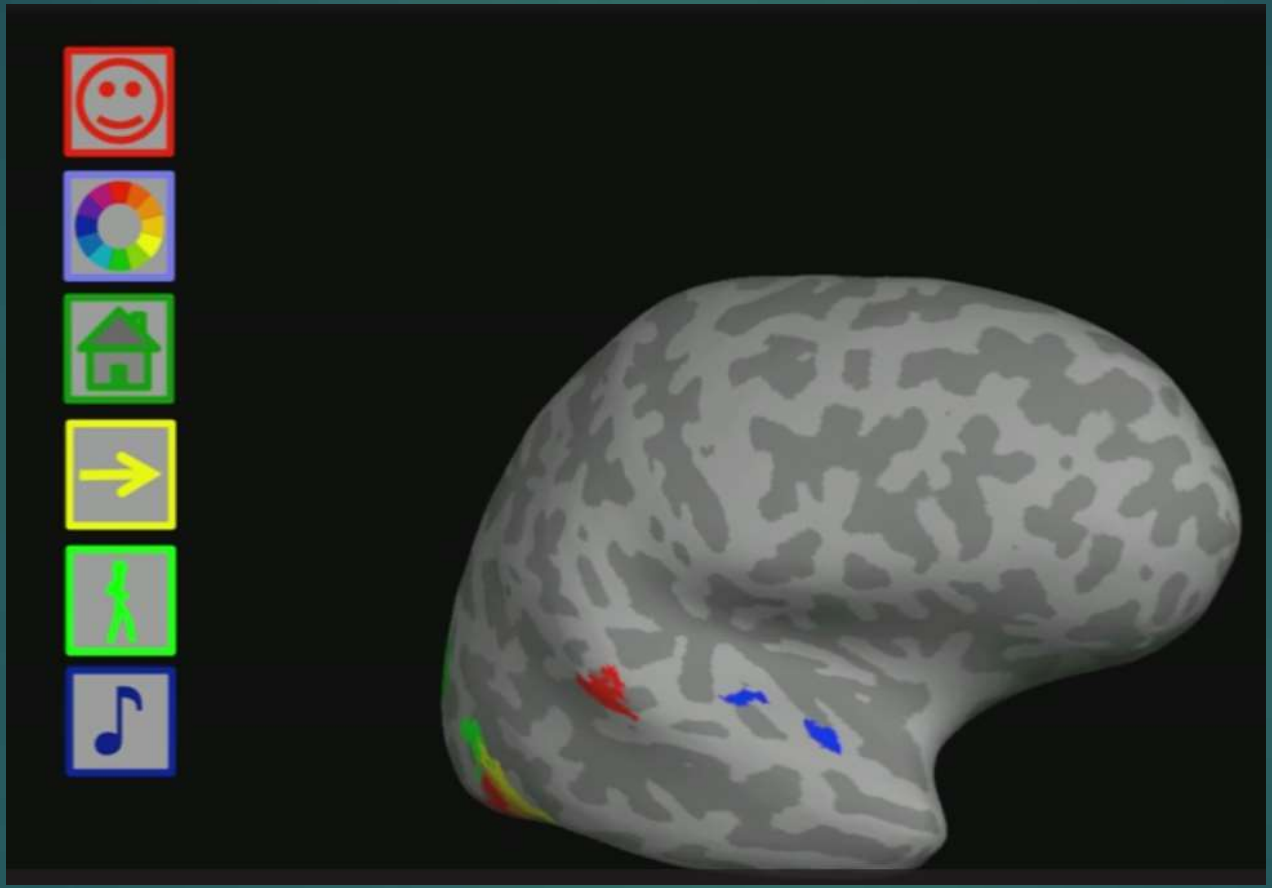


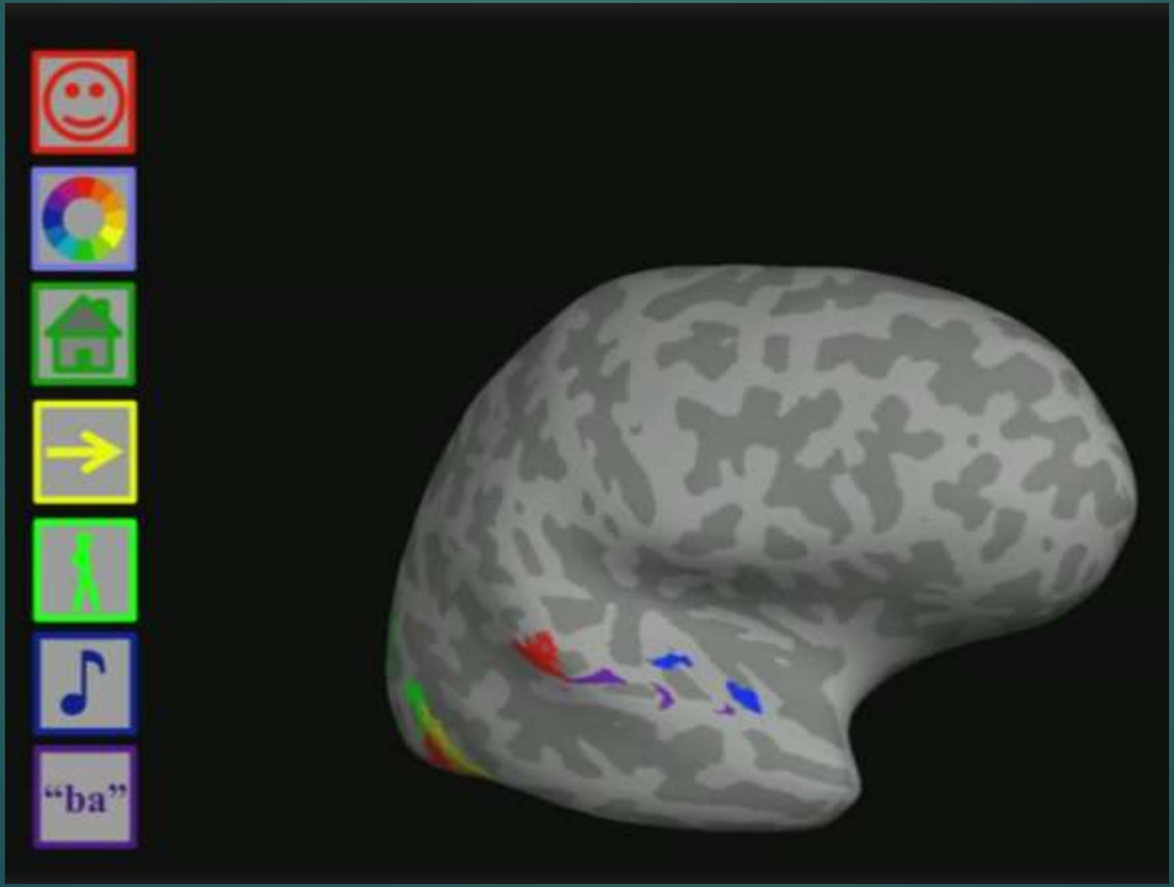
Fig. 3. Connection strength in the model chosen by the Bayes Model Selection procedure for healthy controls and women with AN.

Hearing pitch area

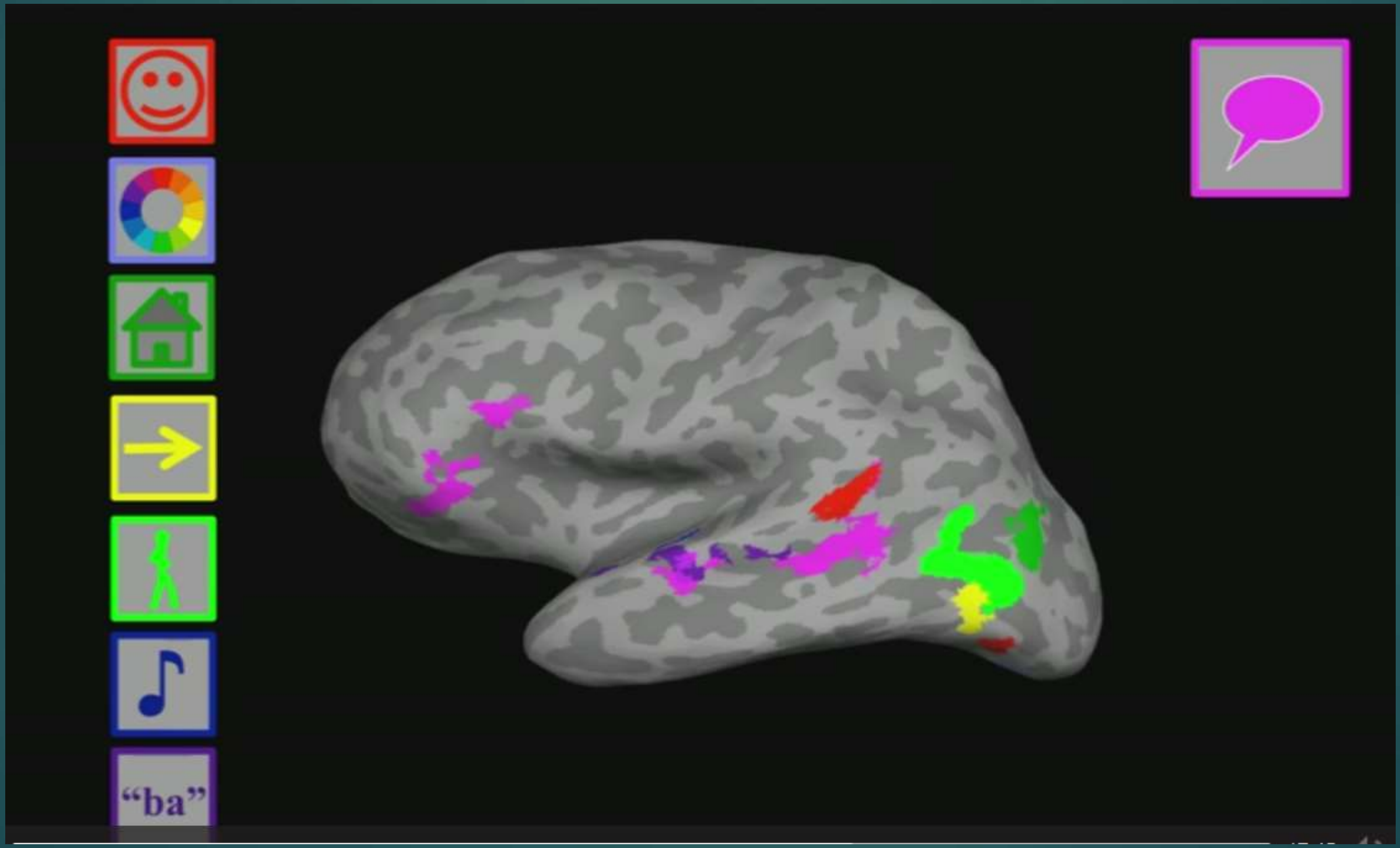


Sounds with pitch i.e. police siren

Speech Sound area



Language regions



Visual Word Area: Reading is experience dependent

FFA

VWFA
Left ventral occipitotemporal cortex

PPA

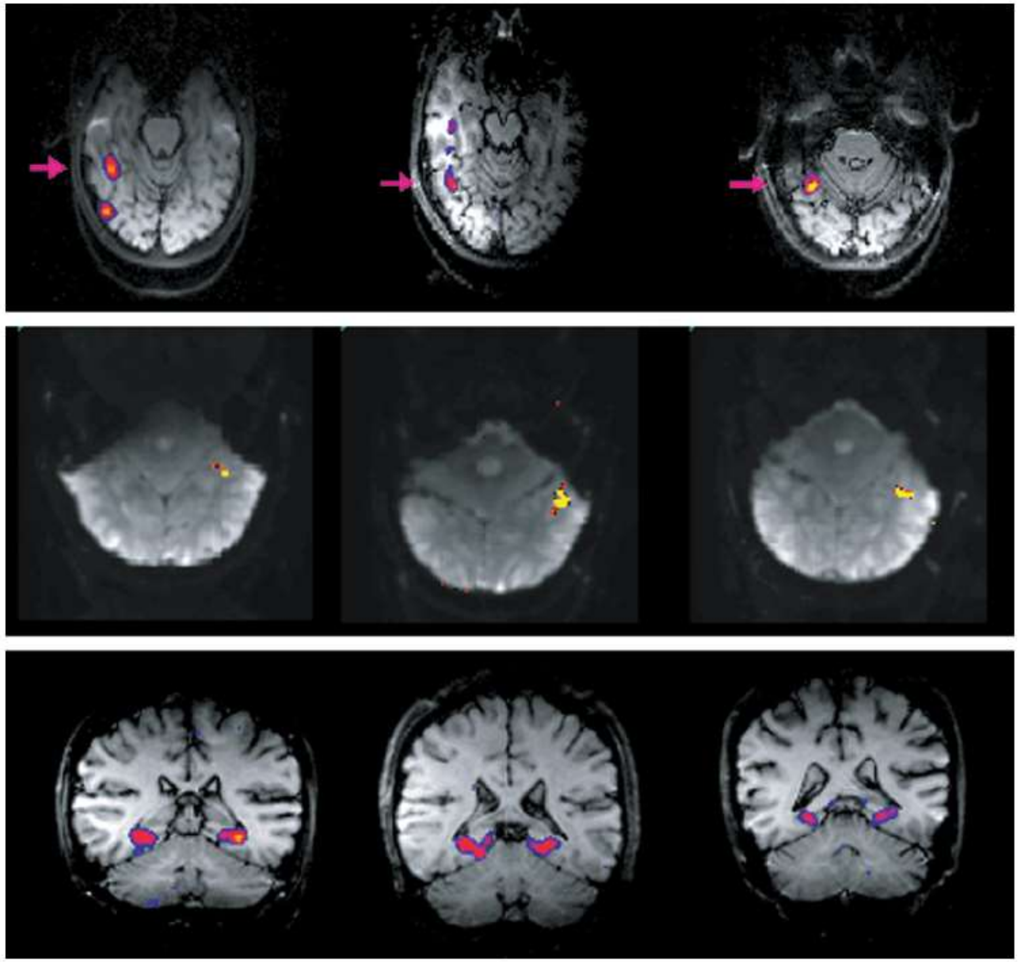


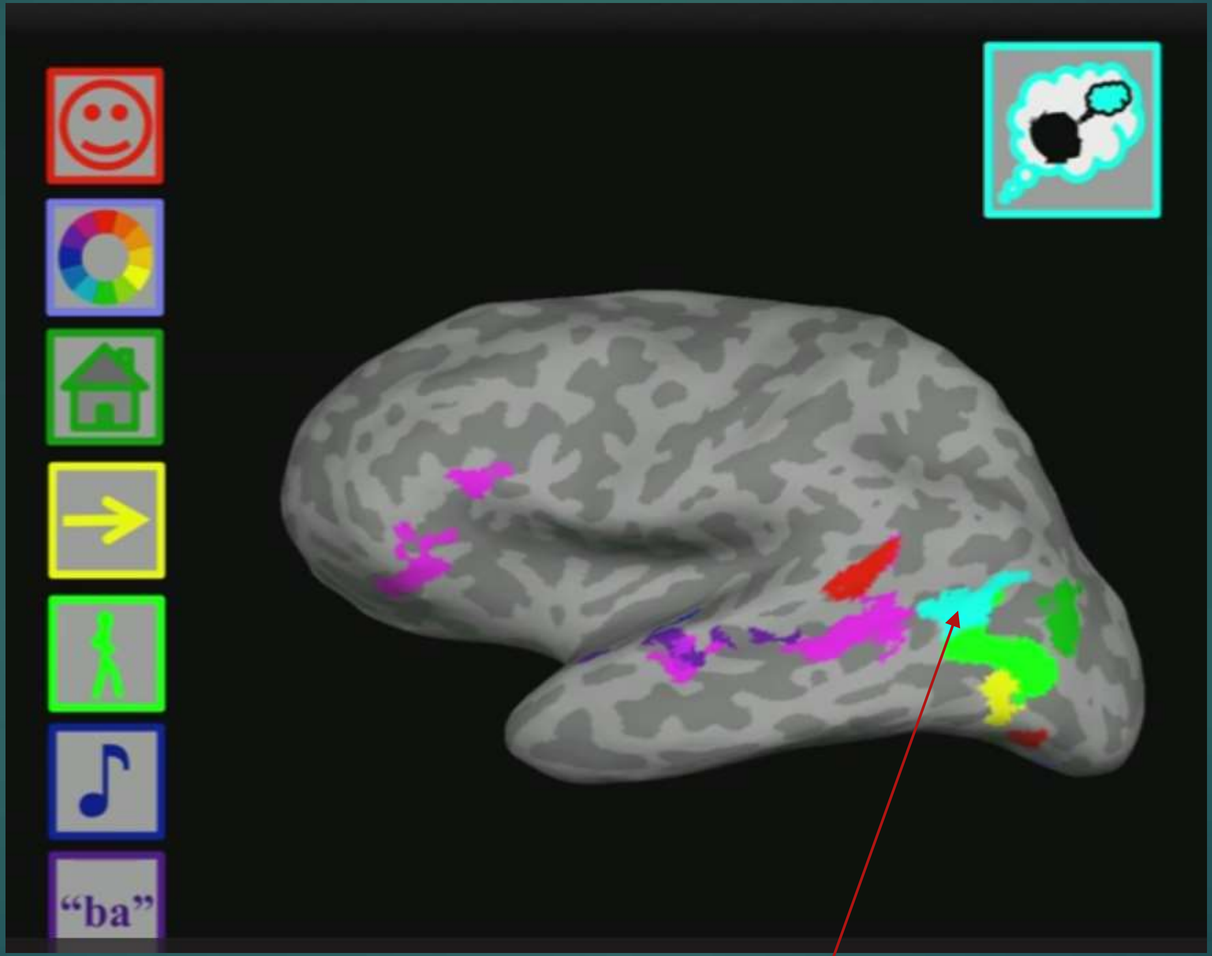
Fig. 6. Three of the functionally specific regions that have been discovered using the individual-subjects functional ROI approach. Top panel: the fusiform face area (FFA), which is defined by a higher response to faces than objects shown in three individual subjects (data from Kanwisher et al. 1997). Middle panel: a word and letter-string selective region, which is defined by its higher response to visually presented words than line drawings of objects shown in three individual subjects (data from Baker et al. 2007). Lower panel: the parahippocampal place area (PPA) which is defined by a higher response to scenes than objects shown in three individual subjects (data from Epstein et al. 1999).

Faces

Visual Words based on <u>experience: literacy changes the brain</u>

Scenes

Thinking about thoughts of others



Other's Thoughts

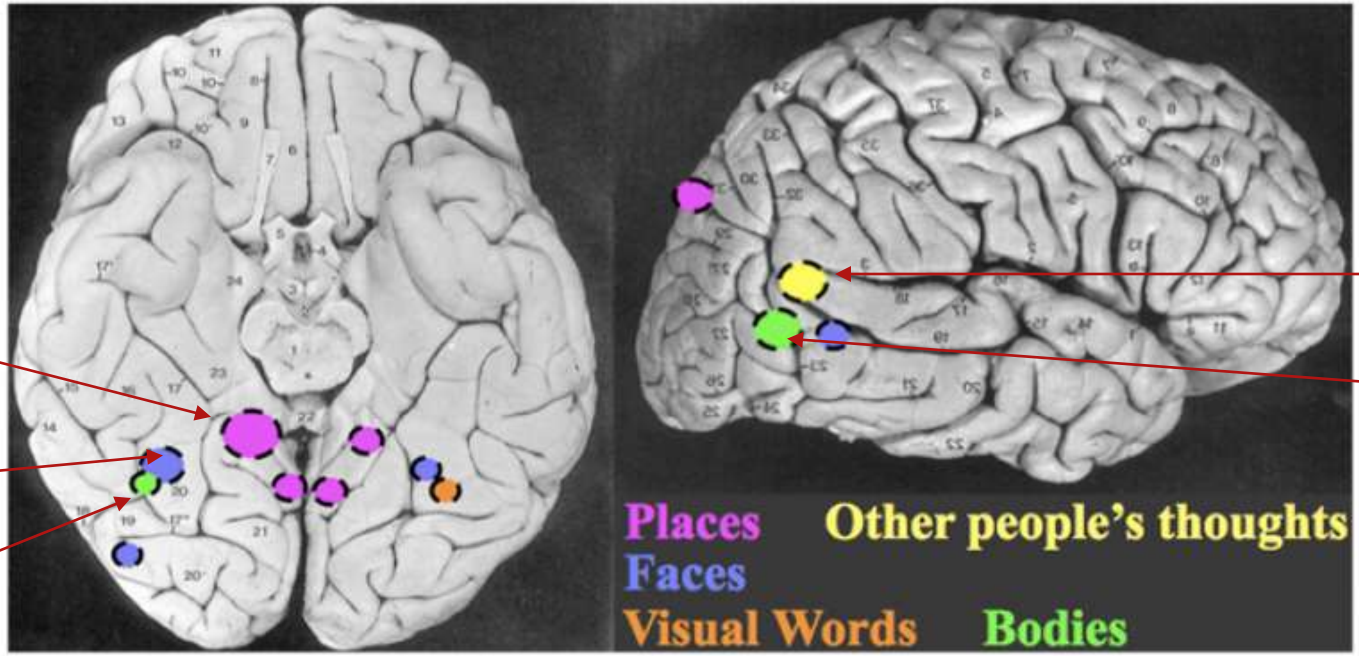
Summary - Functionally specific areas:
Faces, Places, Bodies, Visual Words, Thoughts

Ventral Visual Pathway:

PPA

FFA

EBA



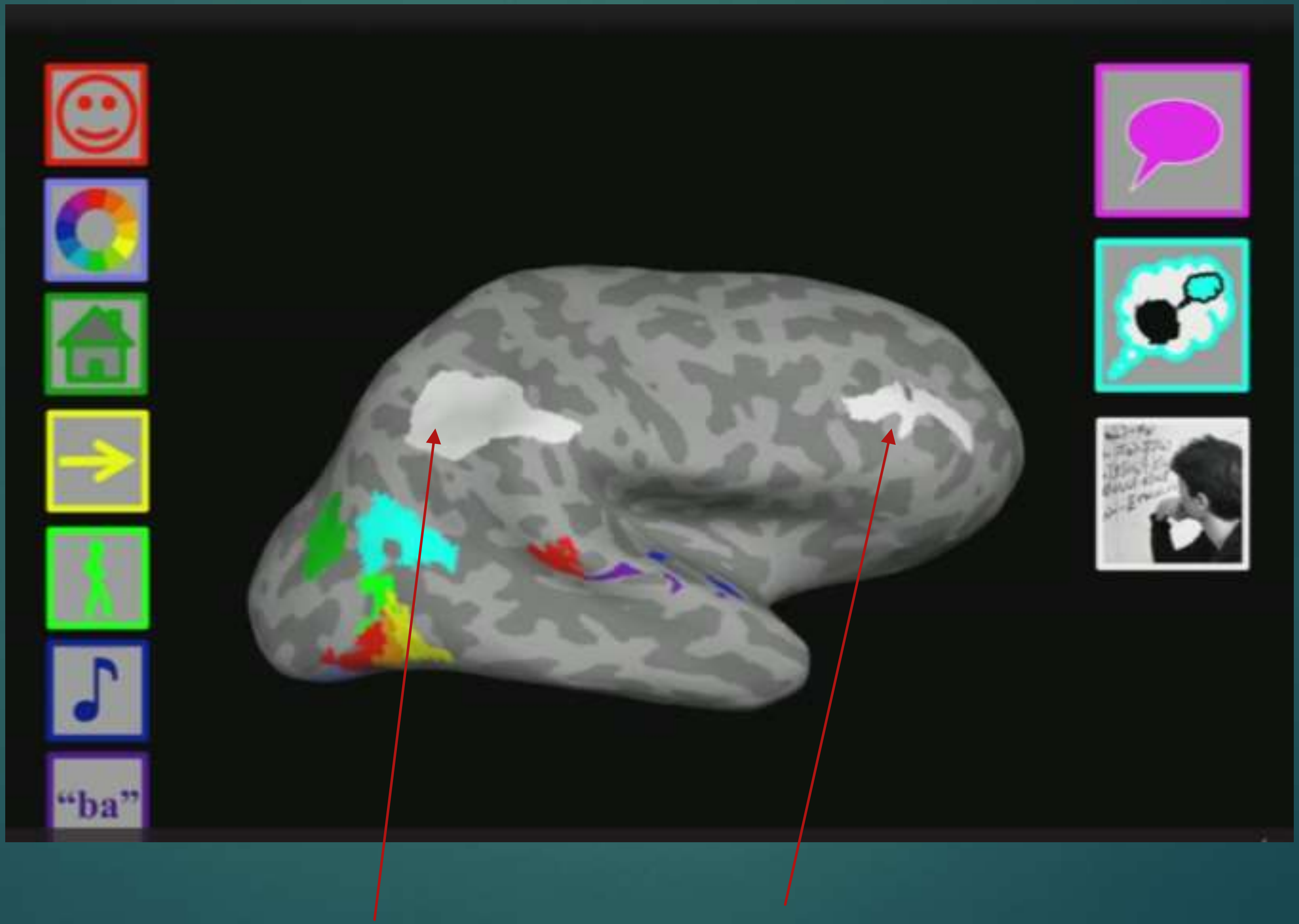
rTPJ

EBA

Fig. 1. This schematic diagram indicates the approximate size and location of regions in the human brain that are engaged specifically during perception of faces (blue), places (pink), bodies (green), and visually presented words (orange), as well as a region that is selectively engaged when thinking about another person's thoughts (yellow). Each of these regions can be found in a short functional scan in essentially all normal subjects.

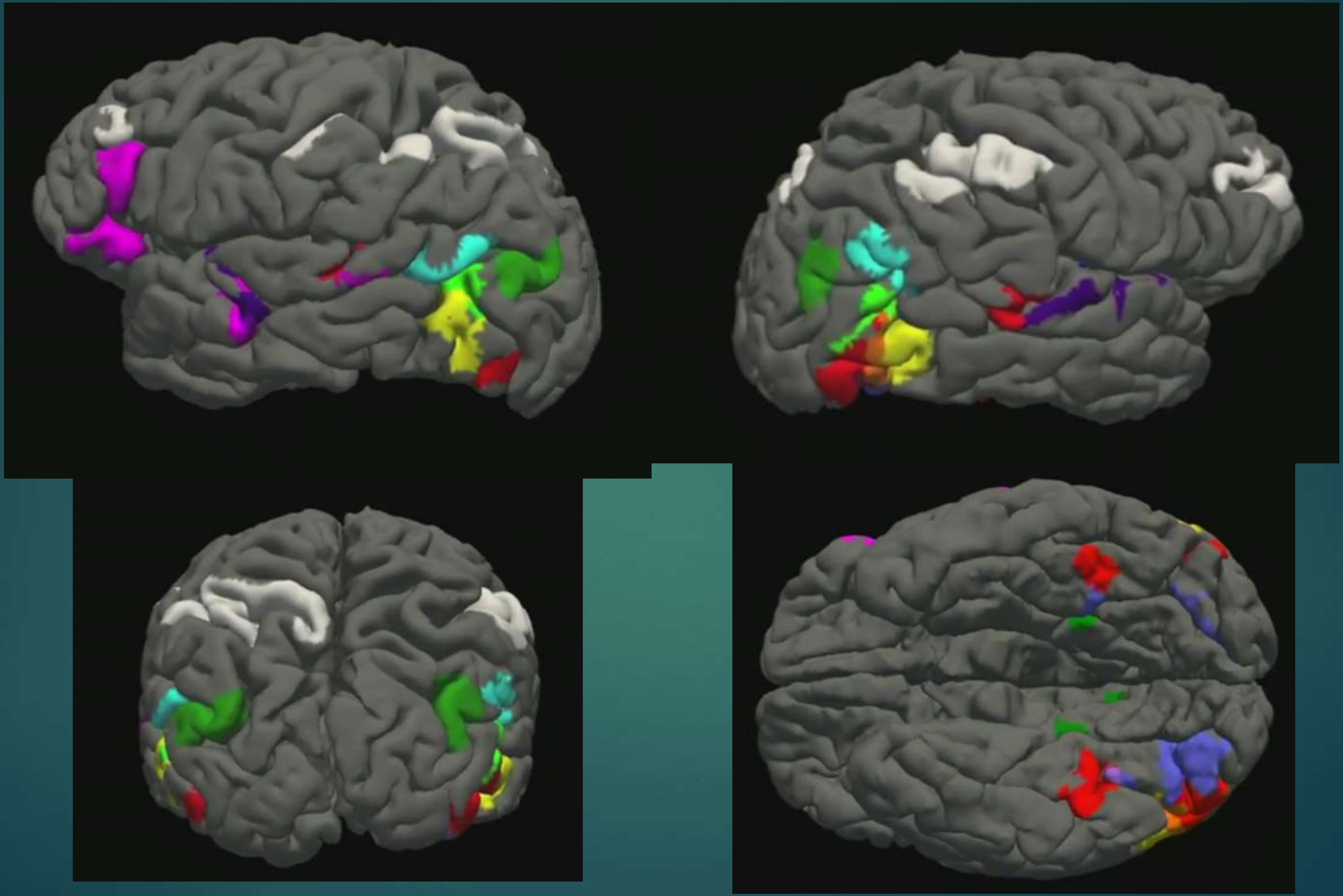
Nancy Kanwisher1, 2010

General Purpose Processors



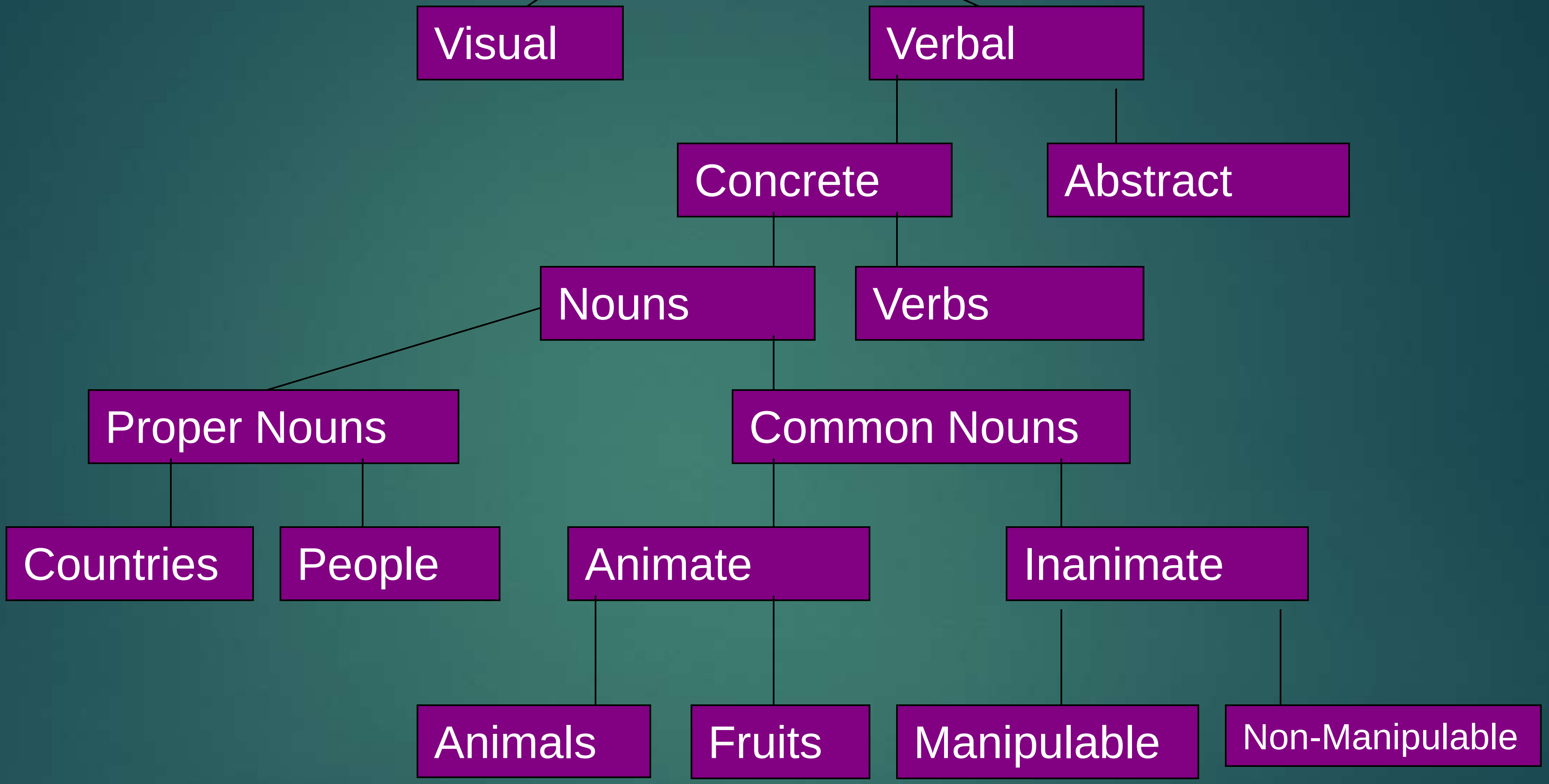
Respond to any difficult mental task

Same places in everyone: genetic



Based on stroke pts

Topography of Semantic Knowledge: How Brain Stores Information from Lesions/Strokes



Other Known Categories: indoor / outdoor, vegetables

Parietal Lobes: Major change in brain of Homo sapiens

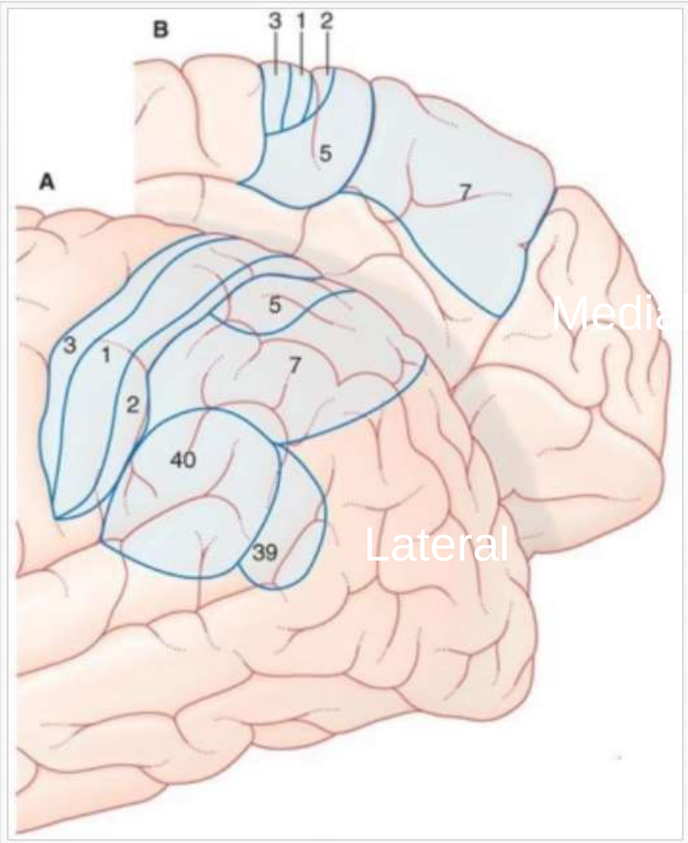


Figure 4: Brodmann areas. A (lateral), B (medial). Somatosensory cortex (Areas 3,1,2); Somatosensory association area (Area 5); Posterior parietal cortex (Area 7); Angular gyrus (Area 39); Supramarginal gyrus (Area 40)[8]

Postcentral sulcus:

3,1,2 - Somatosensory cortex

Superior Sulcus:

5 - Somatosensory Association area

7 - Posterior parietal cortex (incl. dorsal path)

Inferior Parietal Lobule (IPL or ventral PC):

39 - Angular gyrus

40 - Supramarginal gyrus

Superior Parietal: sensory-motor integration, body schema, spatial processing; spatial maps
Inferior Parietal: Spatial attention, integration of tactile sensation, self awareness

Functions of Anterior Parietal Cortex

- BA 1, 2, 3, 43: Somatosensory processing
- Primary & unimodal somatosensory:
  - Tactile, muscle, joint, vibration, vestibular, 2 pt. discrimination
  - Body sense
  - Visual object recognition

- Classical sxs of PL lesions: tactile discrimination and stereognosis (tactile object recognition) deficits;

- Severe anterior lesion = sensory loss, complete anesthesia; resemble deafferentated states

Functions of Posterior Parietal Cortex

- BA 5, 7, 39, 40: Dorsal "where" Pathway of visual processing
- BA 5 & 7 (heteromodal, superior P): guided movement (praxis), spatial WM
- BA 39 & 40: high level integration of visual stimuli & language functions (reception & reading);
- arithmetic functions (borrowing & math involving spatial aspect; IPL)
  - Inferior parietal: linguistically mediated calculations, like multiplication
  - Intraparietal sulcus: on-line computations, like subtraction

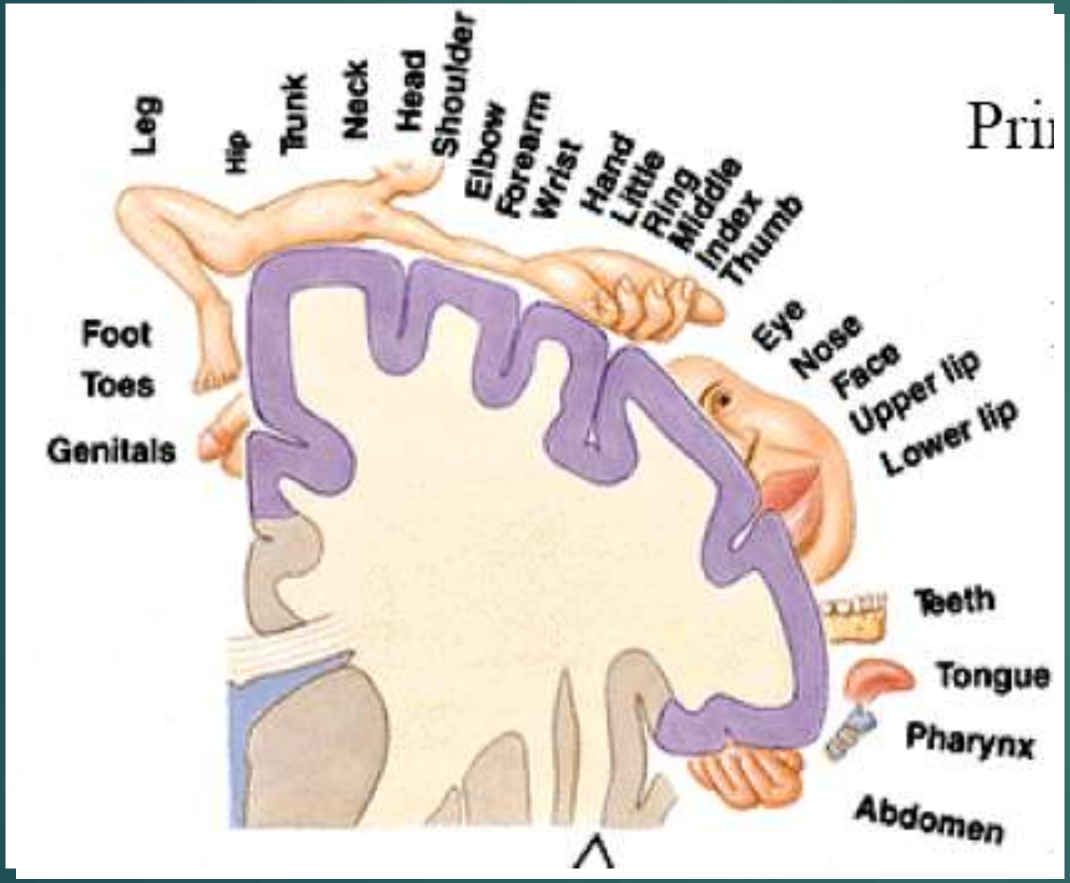
Posterior Parietal

- Spatial orientation, attention, navigation (medial P; posterior CG)
  - Spatial attention
    - Route following
    - L- R discrimination
    - Spatial rotation (Interparietal sulcus)
- Constructional ability
  - Drawing
- Auditory & visual working memory

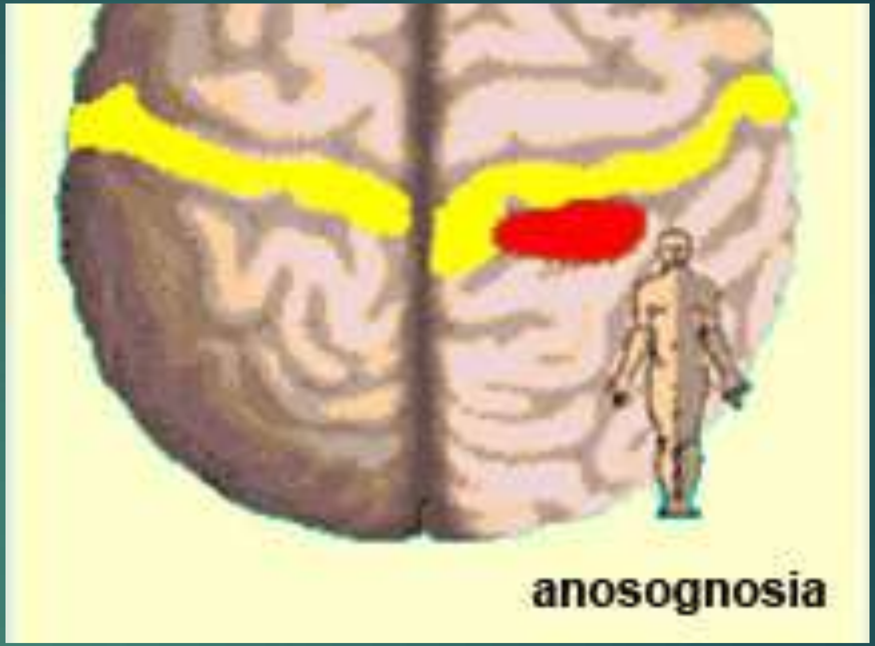
- Body map: your body & space around it

- Supramarginal gyrus: attribute a sense of "this belongs to me" to body parts; stimulating close to it produces out of body experience; transgenders do not activate sexual areas (breast) of gender they do not identify with (breast is "not self")

Primary Somatosensory Strip



Anosognosia: Right Parietal



Anosognosia:

impaired or lack awareness of illness, denial of disability

Present in chronic alcoholics, schizophrenia, Bipolars

Why we need law allowing involuntary psychiatric hospitalization

Anosognosia

- Impaired or lack awareness of illness, denial of disability:
- 30% of stroke hemiplegia
- Believed to be the single largest reason why individuals do not take their medications
- 50 % schizophrenia, 40 % bipolar disorder.
- Also impaired limb denial, “alien limb”

Left Hemineglect: Right Hemisphere

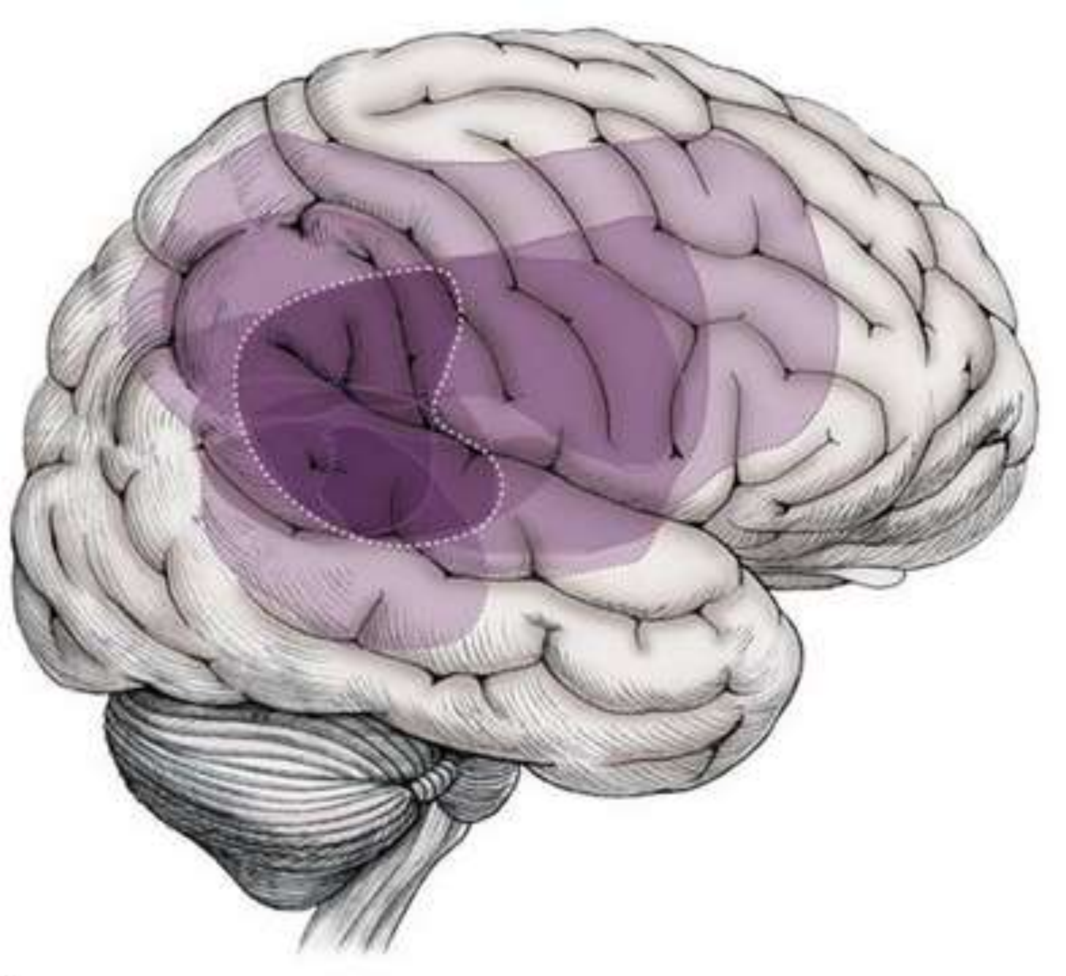
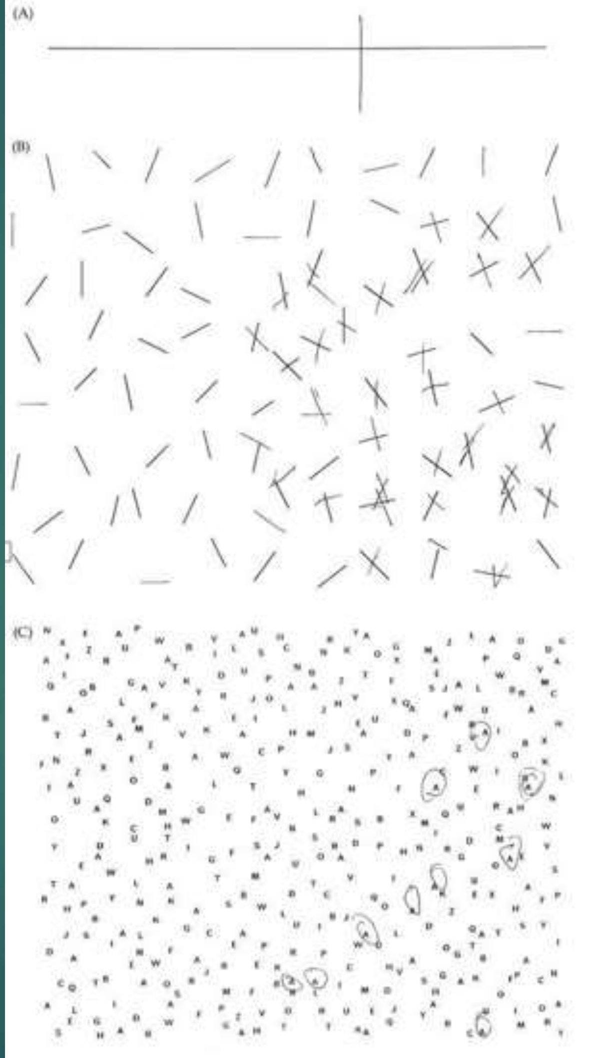
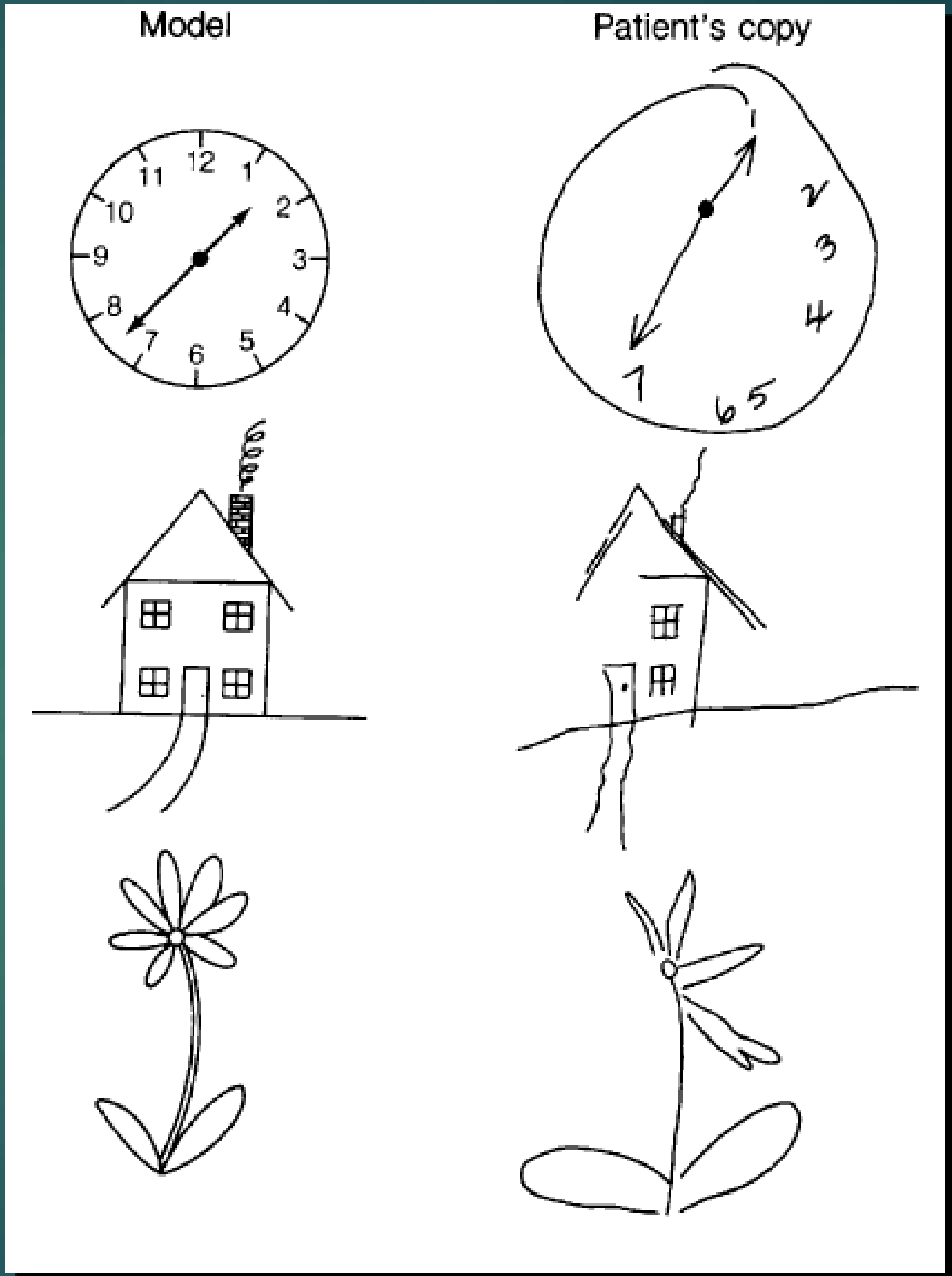


Figure 19.8 Lesions Causing Left Hemineglect Lateral view of right h



Left Visual Neglect



Agnosias: loss of the meaning of a perception

- Auditory agnosias – inability to recognize sounds

- Visual agnosias – inability to recognise familiar objects
  - Prosopagnosia – inability to recognise faces
  - Agnostic alexia – inability to read
  - Color agnosia – inability to retrieve color information e.g. what color are bananas
  - Object agnosia – inability to name objects
  - Simultiagnosia – inability to recognise a whole image although individual details are recognised

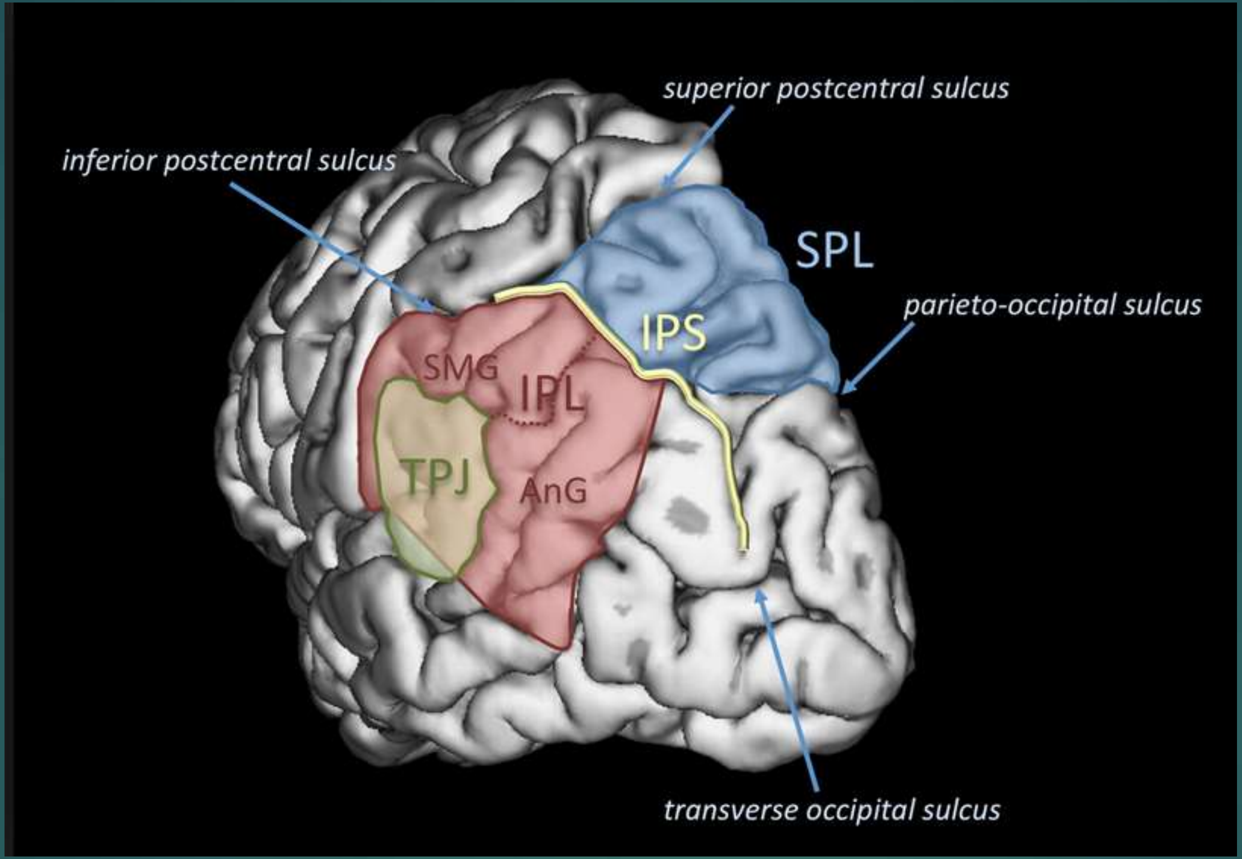
Posterior Parietal Lobe Dysfunctions

- Apraxia (inability to do an action to command)

- Disturbances of sensory perception:
  - Astereognosia (inability to recognize objects by feel); Agraphesthesia (inability to identify letters or numbers on fingers); Atopognosia (inability to localize by touch); Abarognosia (inability to match weights)

- Disturbance of body image:
  - tactile extinction,
  - Spatial neglect,
  - anosognosia,
  - denial of hemiparesis,
  - asomatognosia (forgetting, ignoring, denying, disowning, or misperceiving the body (entirely or partially) (Request for surgical removal: “It’s not part of me”)
  - finger agnosia

TPJ: temporoparietal junction

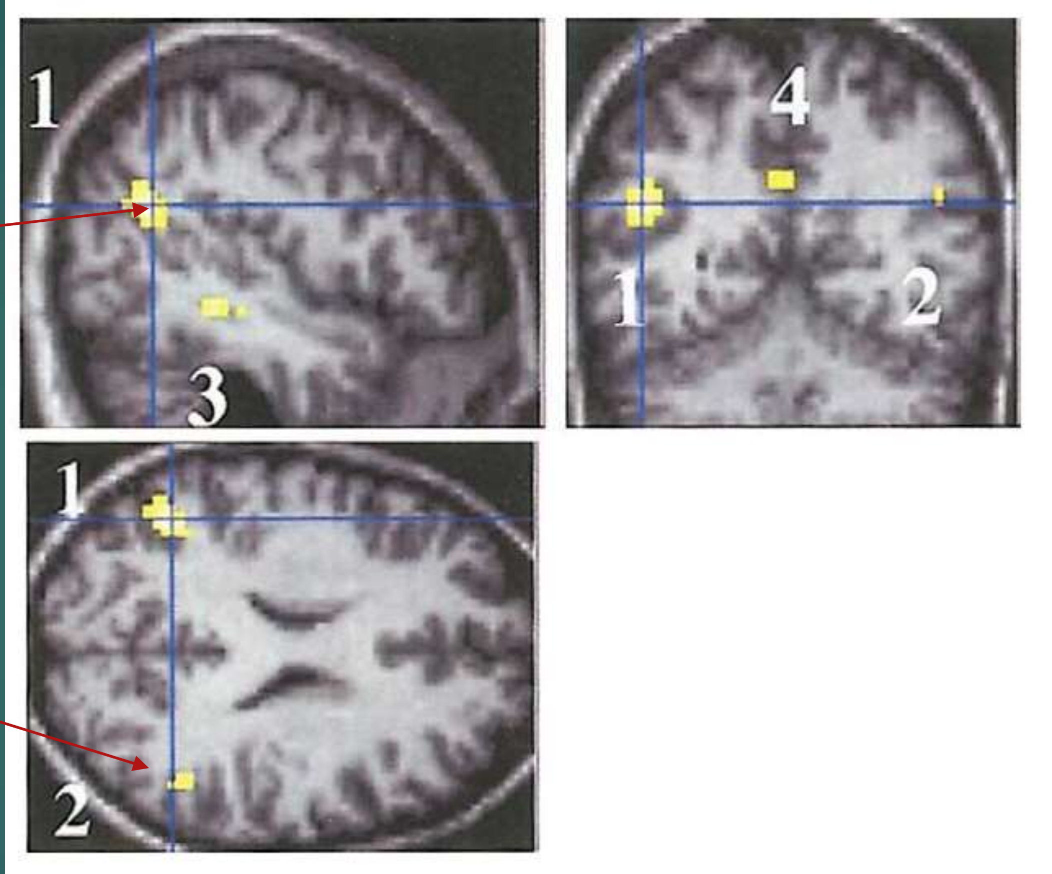


Language comprehension (left)
& music comprehension & theory of mind (right)

rTPJ: Reading Thoughts, Theory of Mind

left TPJ
verbal

rTPJ
pictures



Reading stories that describe or imply a <u>character's goals and beliefs</u>

Theory of mind vs. mechanical inference stories. Crosshair marks the most significant voxel in the left TPJ

Saxe & Kanwisher, 2003

Temporal Parietal Junction (bilateral VPC):
Theory of Mind (think about what others are thinking)

"I know you think you understand what you thought I said, but I don't think you realize that what you heard is not what I meant."

rTPJ is critical for representing mental state information, irrespective of whether it is about oneself or others.

Lower RTPJ activation: harsh, outcome-based judgments of accidents
(e.g., she *poisoned* her friend; deliberate murder)
Higher RTPJ activation: more lenient belief-based judgments
(e.g., she *thought* the poison was sugar; accident)

RTPJ allows a person to *identify* harmful actions as being either deliberate or inadvertent.

AutismSD: atypical, only outcome-based moral judgments, blame even for accidental outcome

Psychopaths: more likely to "forgive" accidental harms; blunted response to harmful outcome

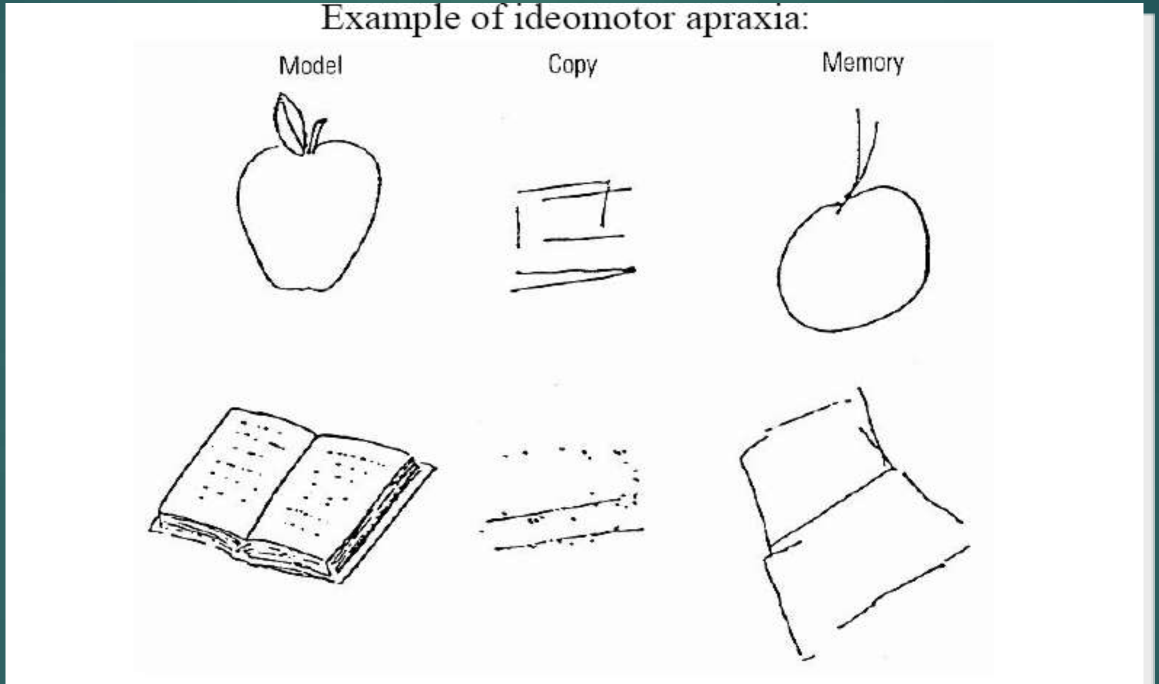
Mind blindness: rTPJ in autism

- “Mindblindness”= deficits in representing mental states
- RTPJ was the only mentalizing region that responded atypically in autistics
- Less activity of rTPJ correlated with most socially impaired.

M. V. Lombardo et al., 2011; (Happé, 1995).

Ideomotor Apraxia:

Loss of knowledge about how to perform skilled movements (i.e. tools), impaired gesture discrimination; predictor of disability



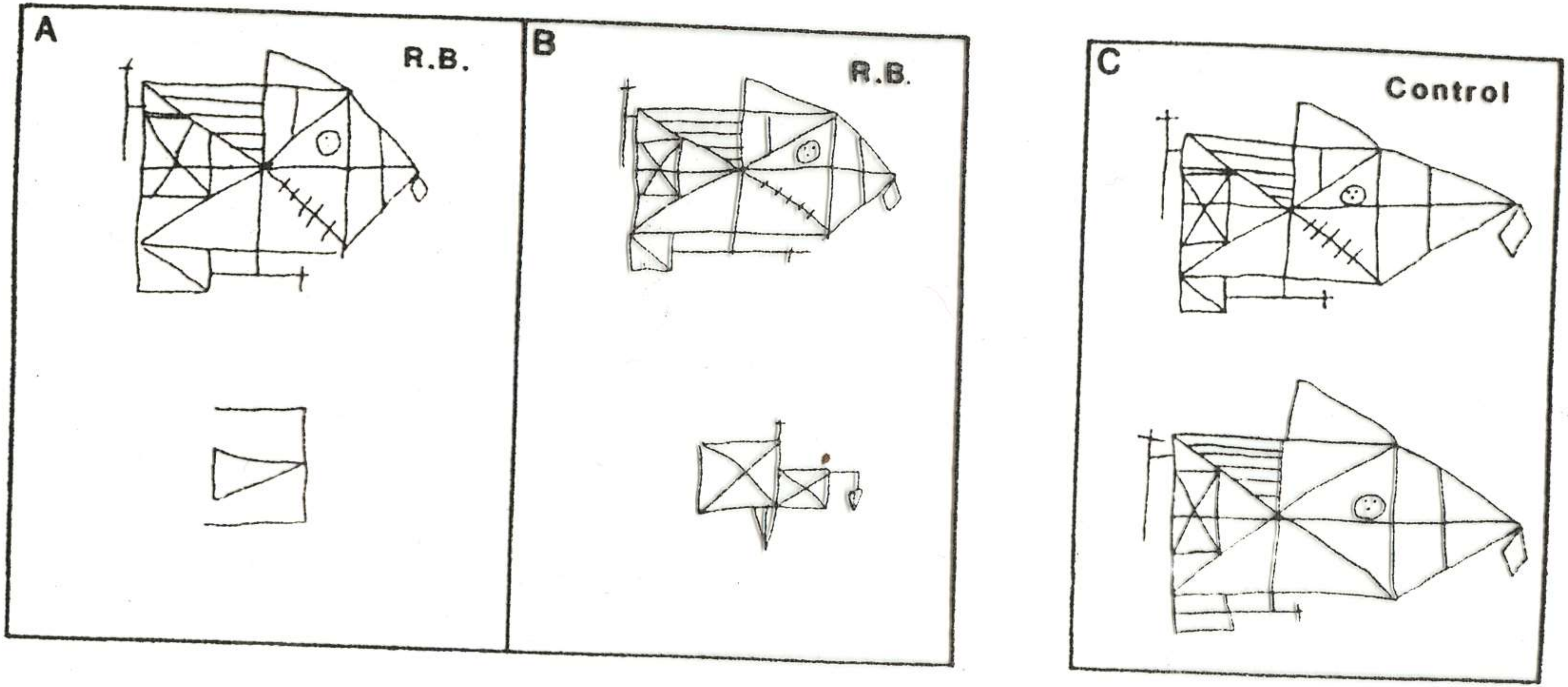
Patient unable to copy models, but does better from memory when prompted to do so.

Inability to correctly imitate hand gestures and voluntarily pantomime tool use, e.g. pretend to brush one's hair; unable to copy model, but can copy from memory

Posterior Parietal Lobe Damage

Right Hemisphere (Gestalt):

- Visuoconstructive: Inability to assemble, build, or draw. Will produce very distorted drawings
- Inability to mentally manipulate objects (mental rotations, arithmetic)
- Loss of gestalt on Block Design or RCF


A
R.B.
B
R.B.
C
Control

Chess Mastery

- Chess is not an intellectual activity based on analysis
- Immediate act of pattern recognition (perceiving the board)
- Using MEG, higher-rated chess players: activate the frontal and parietal areas when they look at the board (recalling information from long-term memory; recall of past board positions).
- Lower-ranked players activate medial temporal areas (seeing the board as something new).

Phantom Limb

FIGURE 5.17 Sources of phantom sensation for one person Stimulation in the areas marked on the cheek produced phantom sensations of digits 1 (thumb), 2, 4, and 5. Stimulation on the shoulder also evoked phantom sensations of digits 1, 2, 3, and 5. *(Based on Figure 5.29 from* Phantoms in the Brain *by V. S. Ramachandran, M.D., PhD, and Sandra Blakeslee. Copyright © 1998 by V. S. Ramachandran and Sandra Blakeslee. Reprinted by permission of HarperCollins Publishers and authors.)*

Brain fills in holes: Finger removal & arm deafferentation

- Michael Merzenich, UCSF, 1984:
- Microelectrodes to map sensory cortex:
  - mapped hand in monkey, removed a finger;
  - months later, brain map for missing finger was gone & replaced by maps for 2 adjacent fingers
- First evidence of brain reorganization: neuroplasticity

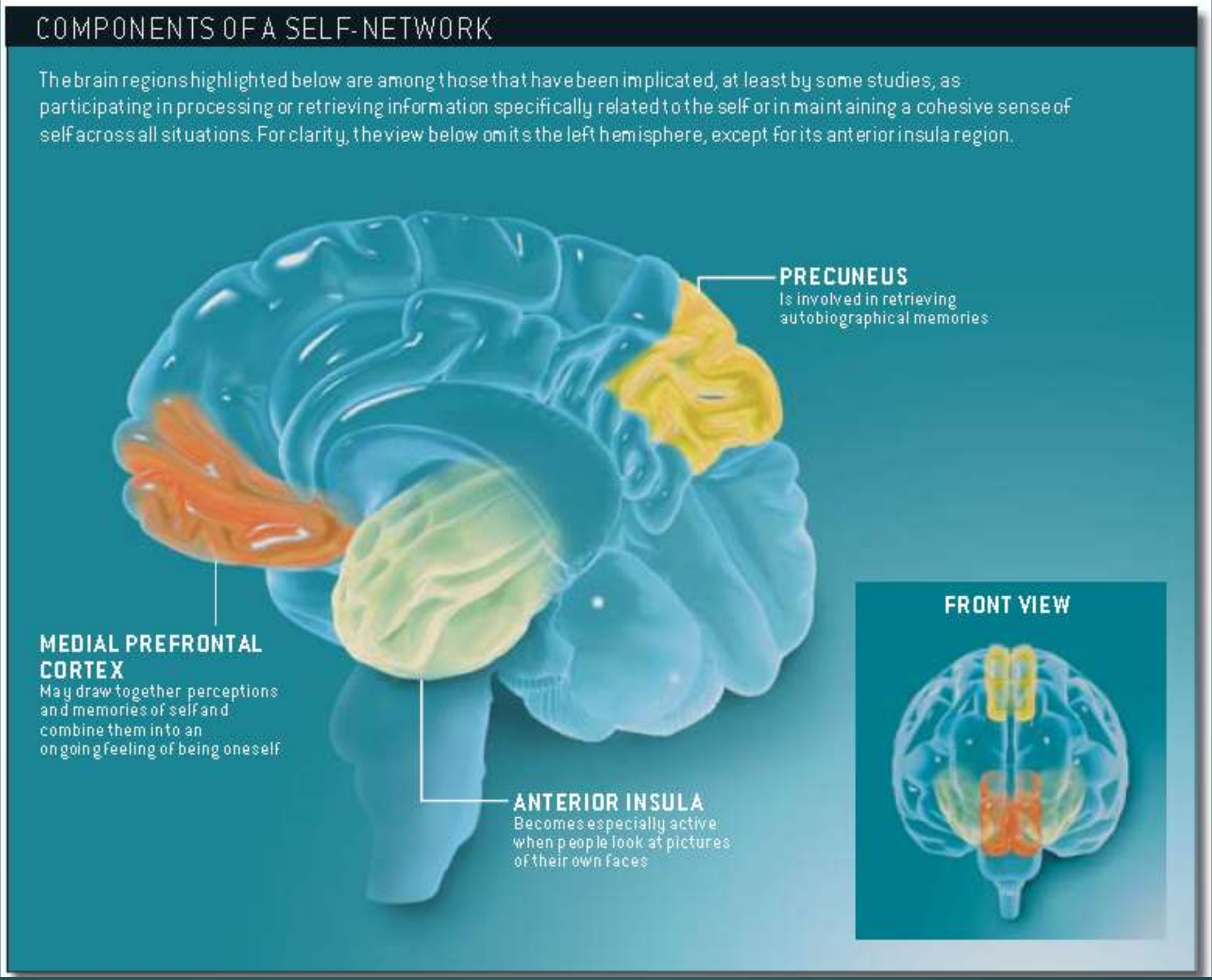
- Tim Pons, 1991: first proof that neurons in face map invaded area of missing arm map; 14 mm of arm map reorganized to process sensory input from face
- Lead to Ramachandran's 1992 work on phantom limbs: brain hallucinates a missing limb

Blind use visual areas of brain for tactile processing

- Congenitally blind reading Braille: activation of primary visual area from tactile sensation = radical reorganization of brain
- Tactile processing pathways usually linked in the secondary somatosensory area are rerouted in blind subjects to the ventral occipital cortical regions originally reserved for visual shape discrimination.
- Used TMS to prove causal link.

•N Sadato, A Pascual-Leone, et al., 1998

Self Network: MFC, Precuneus, ACC



Functions of the Precuneus

- Precuneus is major evolutionary advance of Homo sapiens
- Right - Control of spatial aspects of motor behavior; execution of spatially guided behavior
- Shifting spatial attention/tracking of different targets in space and between different object features, and in motor imagery tasks
- Visually goal-directed hand movements (optic ataxia)
- Mental imagery (visual rotation, deductive reasoning, music processing; virtual reality)
- Episodic memory retrieval; R - regeneration of contextual autobiographic memory

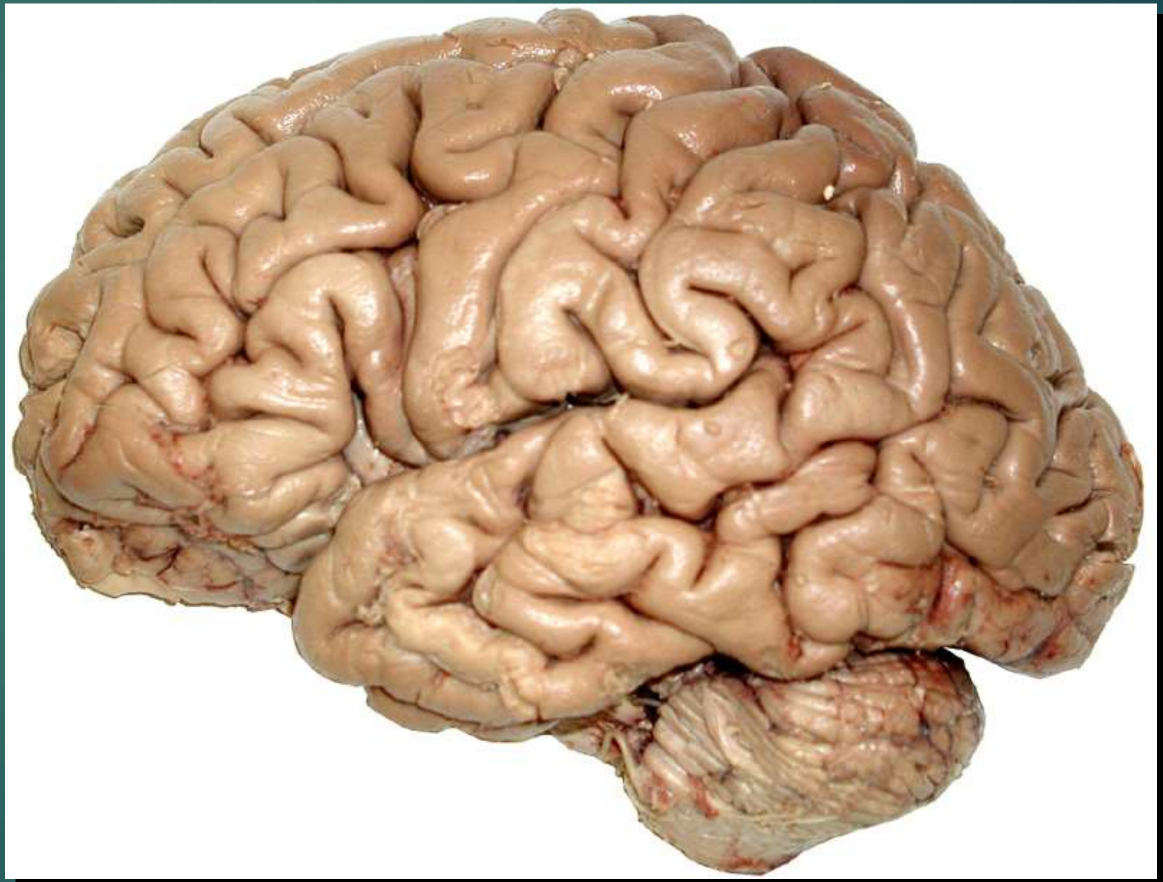
Precuneus (& ACC) & Self Perception/Processing

- Precuneus: neural network supporting the mental representation of the self.
- Personal identity and past personal experiences
- Self versus non-self representation:
  - self-referential judgments,
  - first- versus third-person perspective taking,
  - perceived agency
  - mind reading/social cognition (TOM - judgments requiring empathy)
  - Description of your own personality traits and physical appearance
- Major part of the DMN: All of these structures show high activity during rest, mind wandering, and conditions of stimulus-independent thought

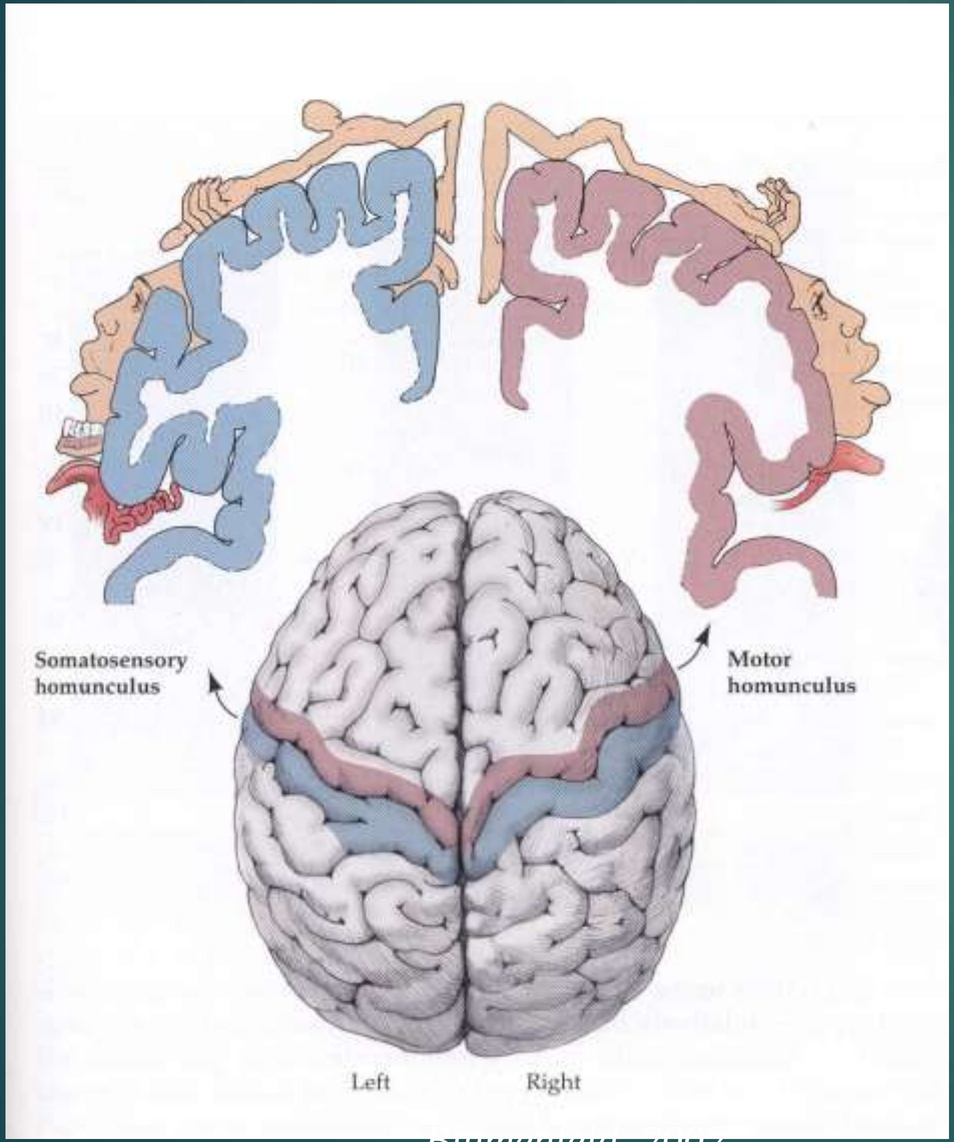
Frontal Action Systems

Three divisions of frontal cortex

1. Primary motor
2. Premotor
3. Prefrontal

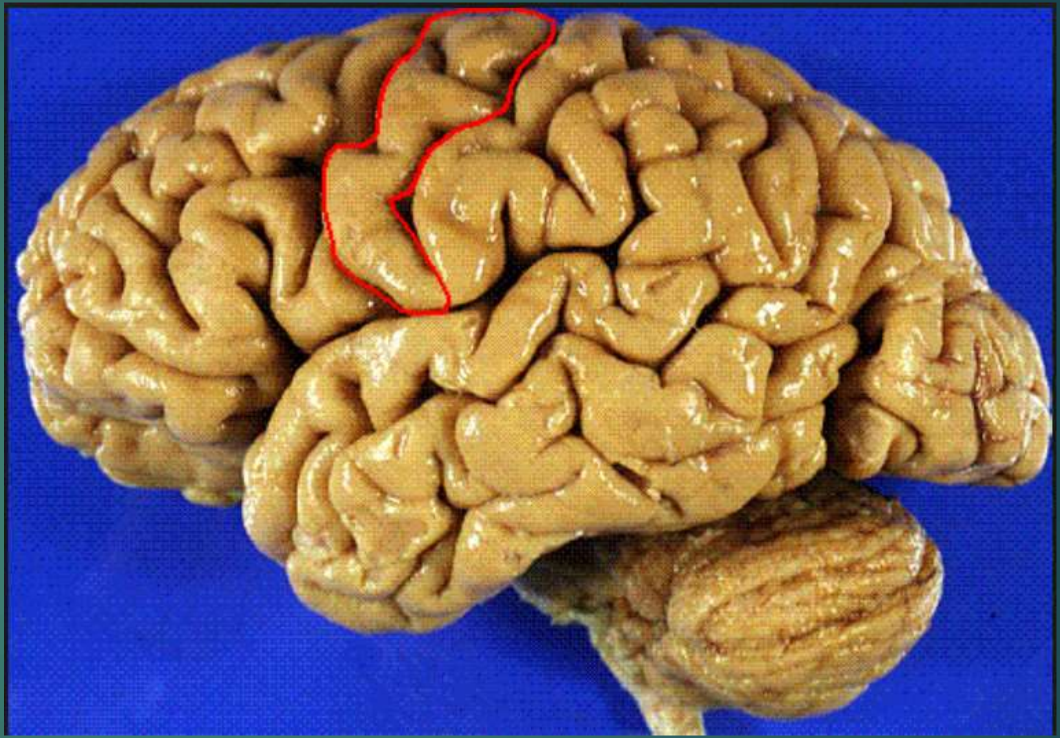


Primary Motor Strip



Blumenfeld, 2002

Frontal: Primary Motor



Primary Motor (BA 4) - Precentral Gyrus:

Execution of movement

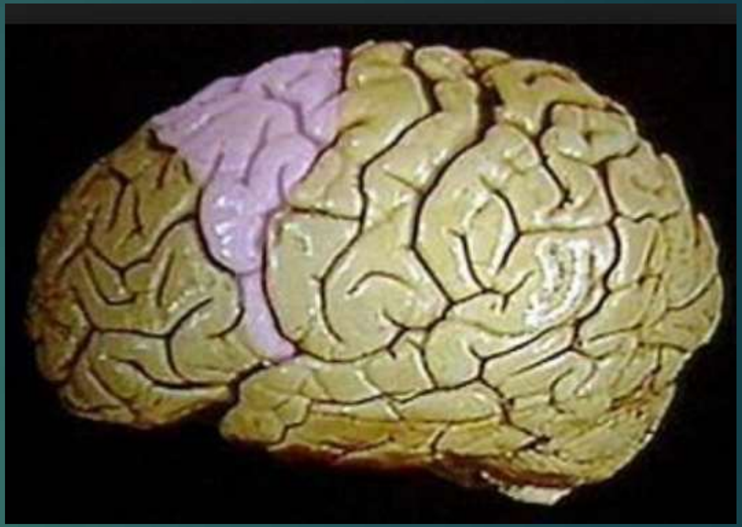
- Massive descending projections to spinal cord
- Damage => pronounced weakness in affected body parts; hemiplegia
- Stimulation => simple movement in small muscle groups

Nonconscious Action: You can only veto

- Brain registers sensory events immediately. Takes half a second to become conscious of them.
- Returning a tennis serve:
  - 0 ms: attention
  - 70 ms: body memory (BG, parietal)
  - 250 ms: action plan (premotor)
  - 355 ms: sending signals to body (motor)
  - 500 ms: 1st conscious awareness; can veto action

Premotor Cortex

- Premotor Cortex (BA 6, 8): premotor & medial supplementary motor
- BA 8 = frontal eye fields
- Heteromodal
- Motor Planning



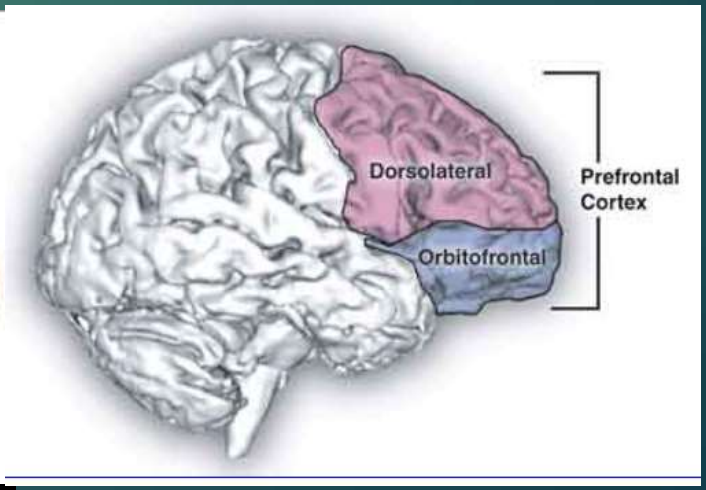
Supplementary Motor Area: Sequencing

- Supplementary motor area is involved in sequence processing.
- Plays a crucial role in domain-general sequence processes, contributing to the integration of sequential elements into higher-order representations regardless of the nature of such elements (e.g., motor, temporal, spatial, numerical, linguistic, etc.).
- SMA regions play a domain-general role. support sequence operations in a variety of cognitive domains that, albeit different, share an inherent sequence processing. These include action, time and spatial processing, numerical cognition, music and language processing, and working memory.
- SMA regions mediate integration of sequential elements into representations.
- SMA regions encode ordinal and temporal properties of a sequence.
- Pre-SMA, rather than SMA-proper, is implicated in sequence operations.

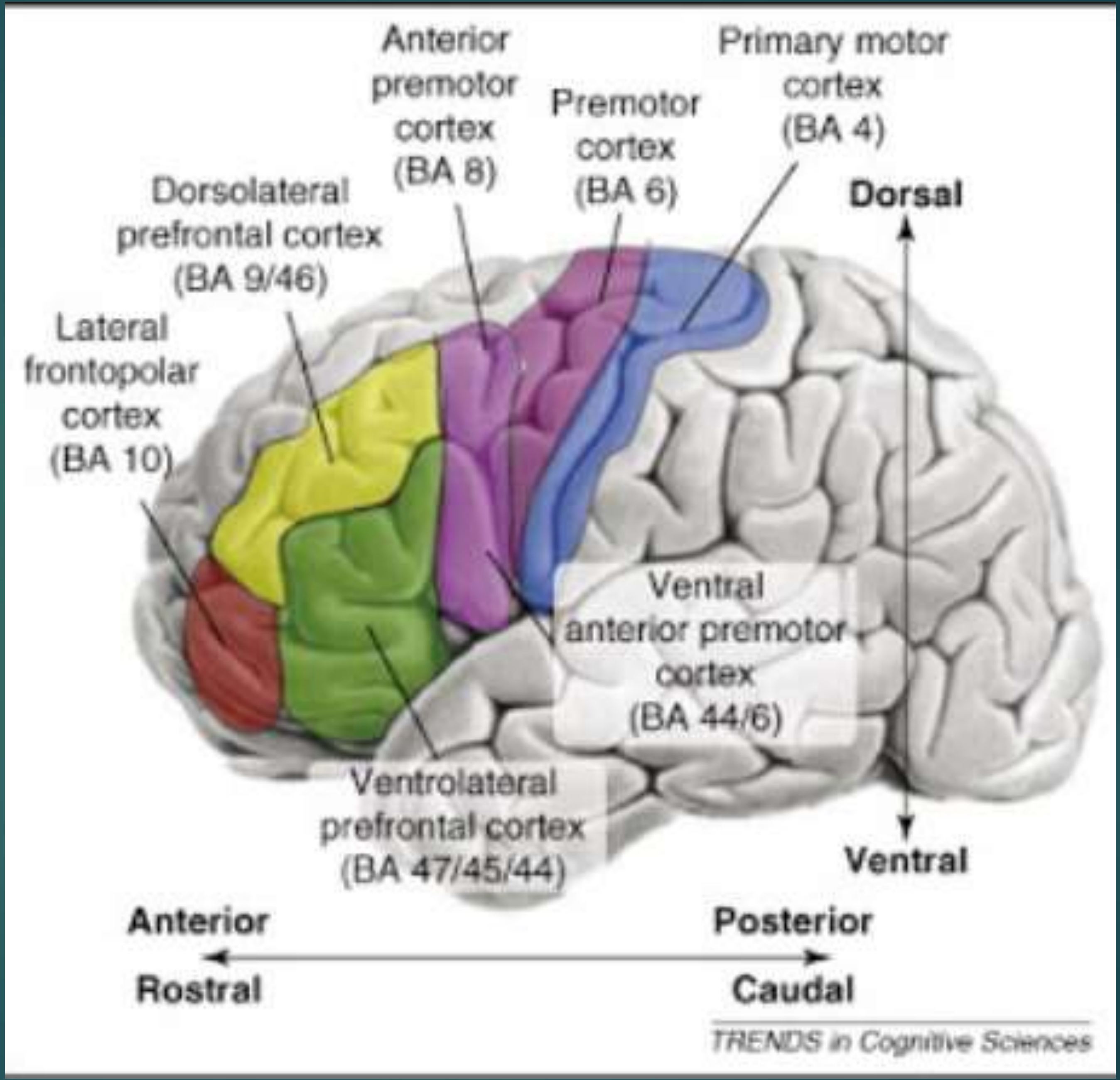
Prefrontal: All Roads Lead to Rome

Massive projections to frontal lobe from many brain areas including unimodal and polymodal sensory systems, limbic structures, and subcortical systems.

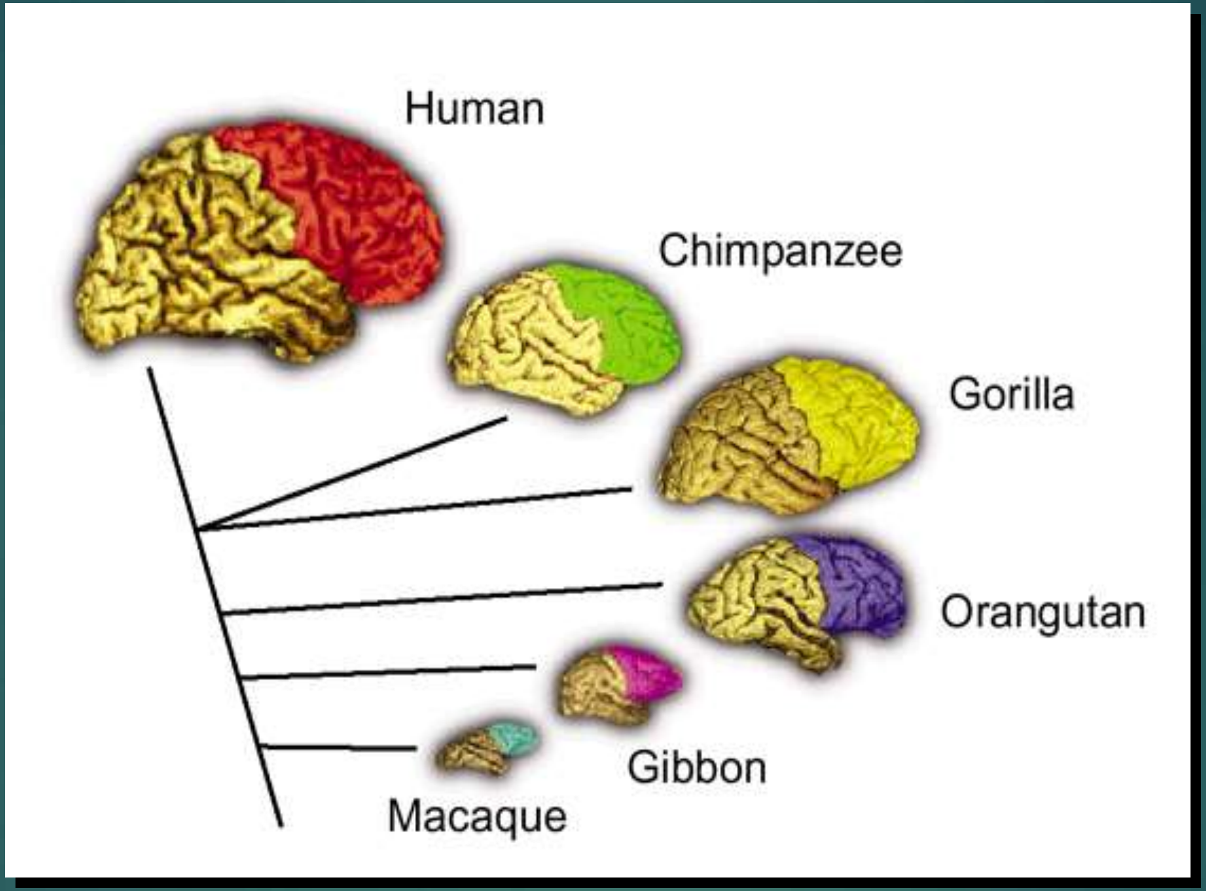
Good position for integrating information from many sources in the brain and to use this information in reasoning, decision making, and planning.



Frontal Lobe

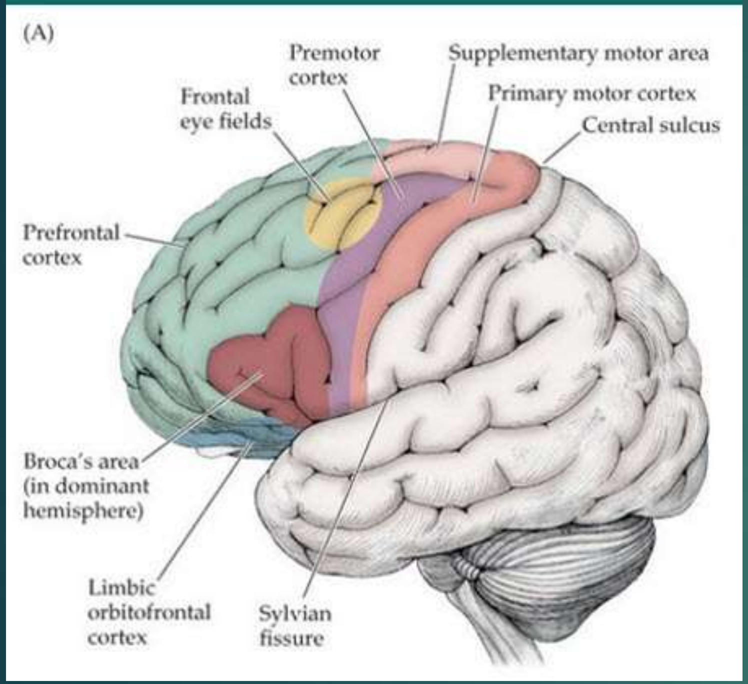


Evolution of Prefrontal Lobes: Humans do not have larger frontal lobes

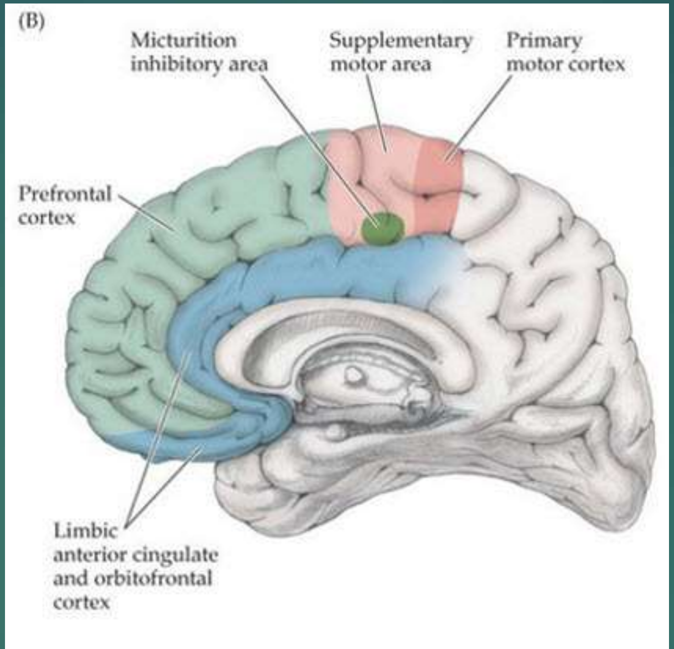


35% in all primates; humans greater white matter: greater frontal gyral white matter; greater connectivity

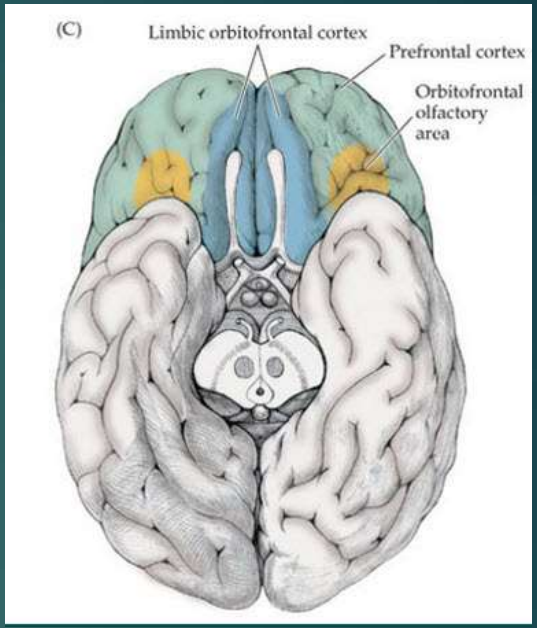
Frontal Lobe Divisions: 3 Divisions



1 – Dorsolateral



2 – Medial



3 - Orbitofrontal

Prefrontal Area: General Executive

- Organization of incoming information
- Response selection, problem solving (executive functioning)
- Maintenance of set/goal
- Behavioral flexibility
- Working Memory
- Other:
  - Speech Production
  - Self regulation and impulse control
  - Initiation and inhibition of environmental exploration
  - ToM
  - Empathy
  - Social Cognition

Frontal/Executive Skills

- Frontal lobes are critical for high level executive functions.
- Phylogentically youngest brain region; last to fully develop
- Frontal lobes are involved in extensive cortico-cortico networks with parietal systems for attention, proprioception & visuomotor response to environment, and with temporal systems for memory and emotions.
- Involved in all modulation and volitional control of perceptual, emotional, and action systems

Frontal Functions

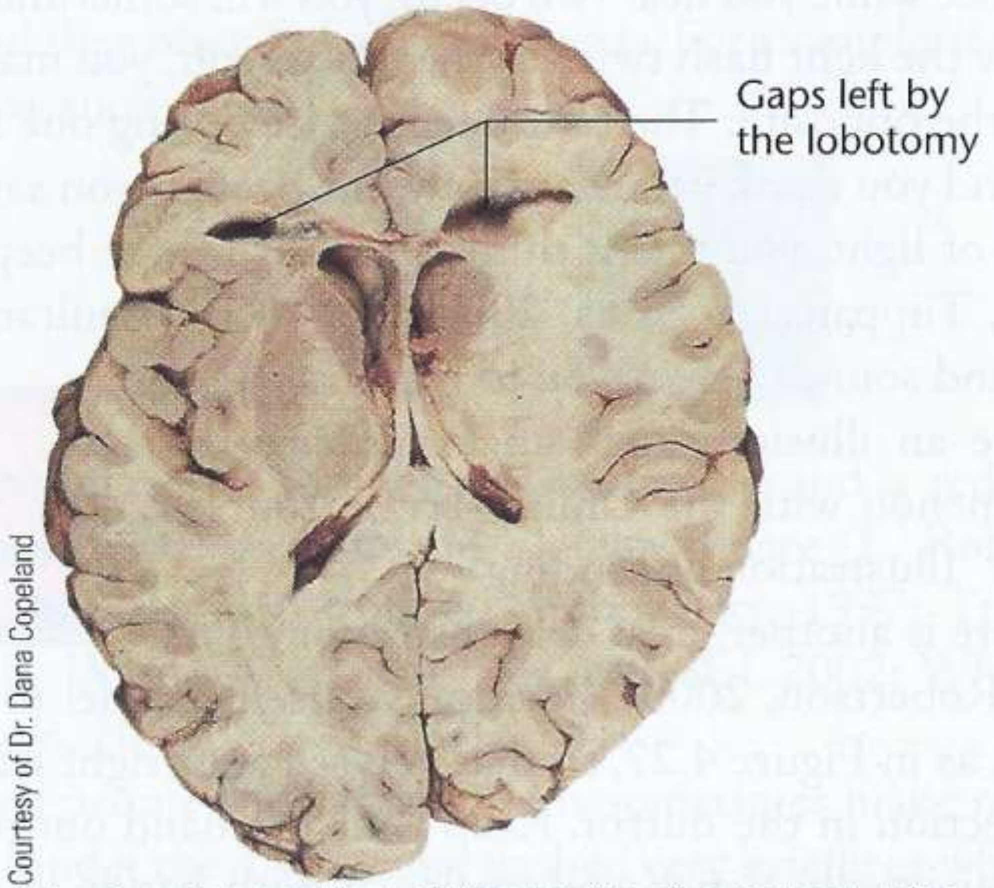
TABLE 19.8 Some Functions of the Frontal Lobes

RESTRAINT	INITIATIVE	ORDER
Judgment	Curiosity	Abstract reasoning
Foresight	Spontaneity	Working memory
Perseverance	Motivation	Perspective taking
Delaying gratification	Drive	Planning
Inhibiting socially	Creativity	Insight
inappropriate responses	Shifting cognitive set	Organization
Self-governance	Mental flexibility	Sequencing
Concentration	Personality	Temporal order

TABLE 19.9 Apparently Contradictory Behavior Seen in Frontal Lobe Syndromes

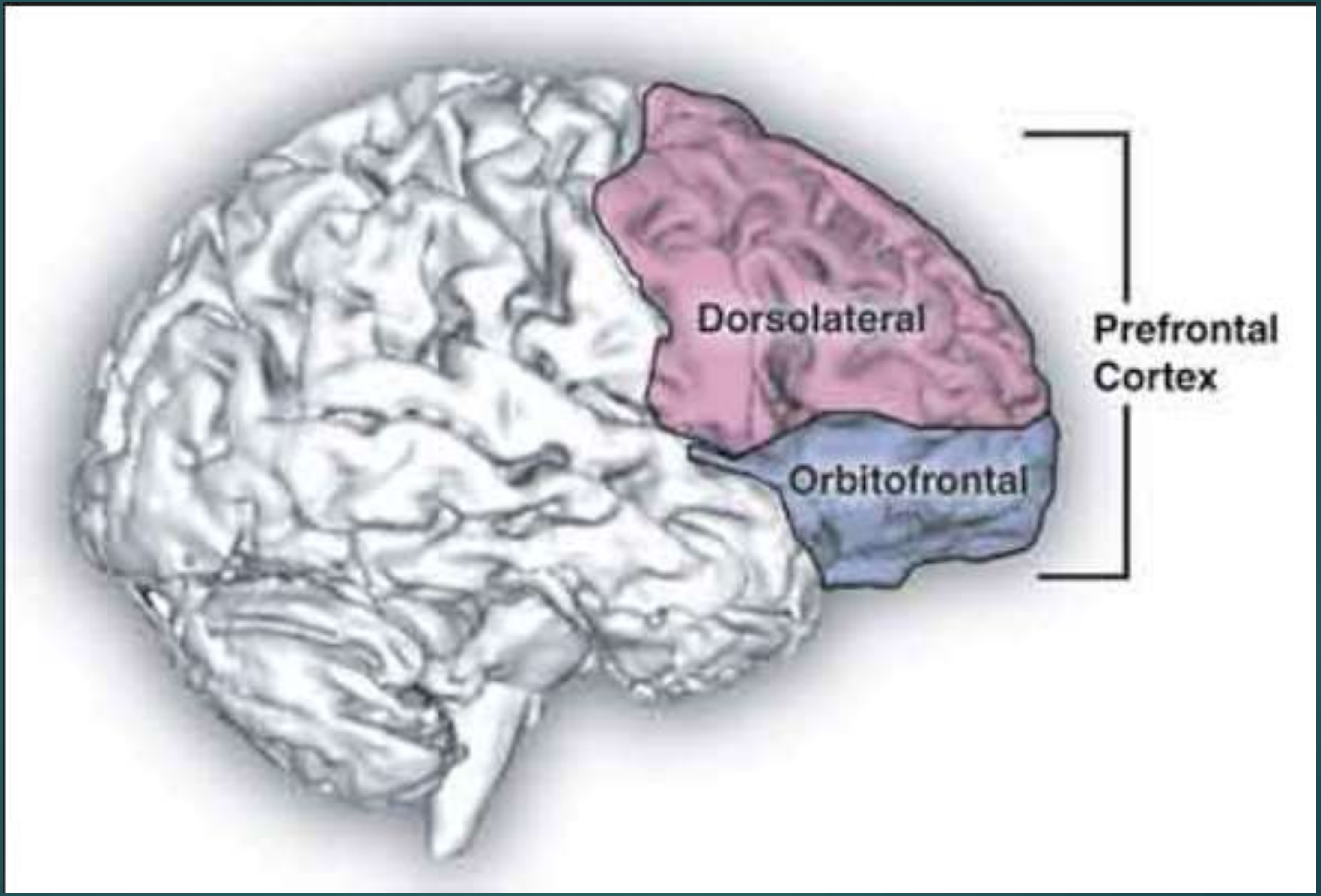
Apathetic indifference	vs.	Explosive emotional lability
Abulia	vs.	Environmental dependency
Akinesia	vs.	Distractibility
Perseveration	vs.	Impersistence
Mutism	vs.	Confabulation
Depression	vs.	Mania
Hyposexuality	vs.	Hypersexuality

Prefrontal Lobotomy: Only Nobel Prize in Psychiatry



A horizontal section of the brain of a person who had a prefrontal lobotomy many years earlier. The two holes in the frontal cortex are the visible results of the operation.

Dorsolateral PFC



Dorsolateral Functions: cognition

- Cognitive-executive functions:
  - Working memory
  - Attention
  - Problem Solving
  - Maintenance of behavioral goals
  - Divergent thinking
  - Planning, future prediction
  - Set Shifting
  - Response selection & inhibition
  - Moral decision making
  - Gain maintenance

Frontal Damage

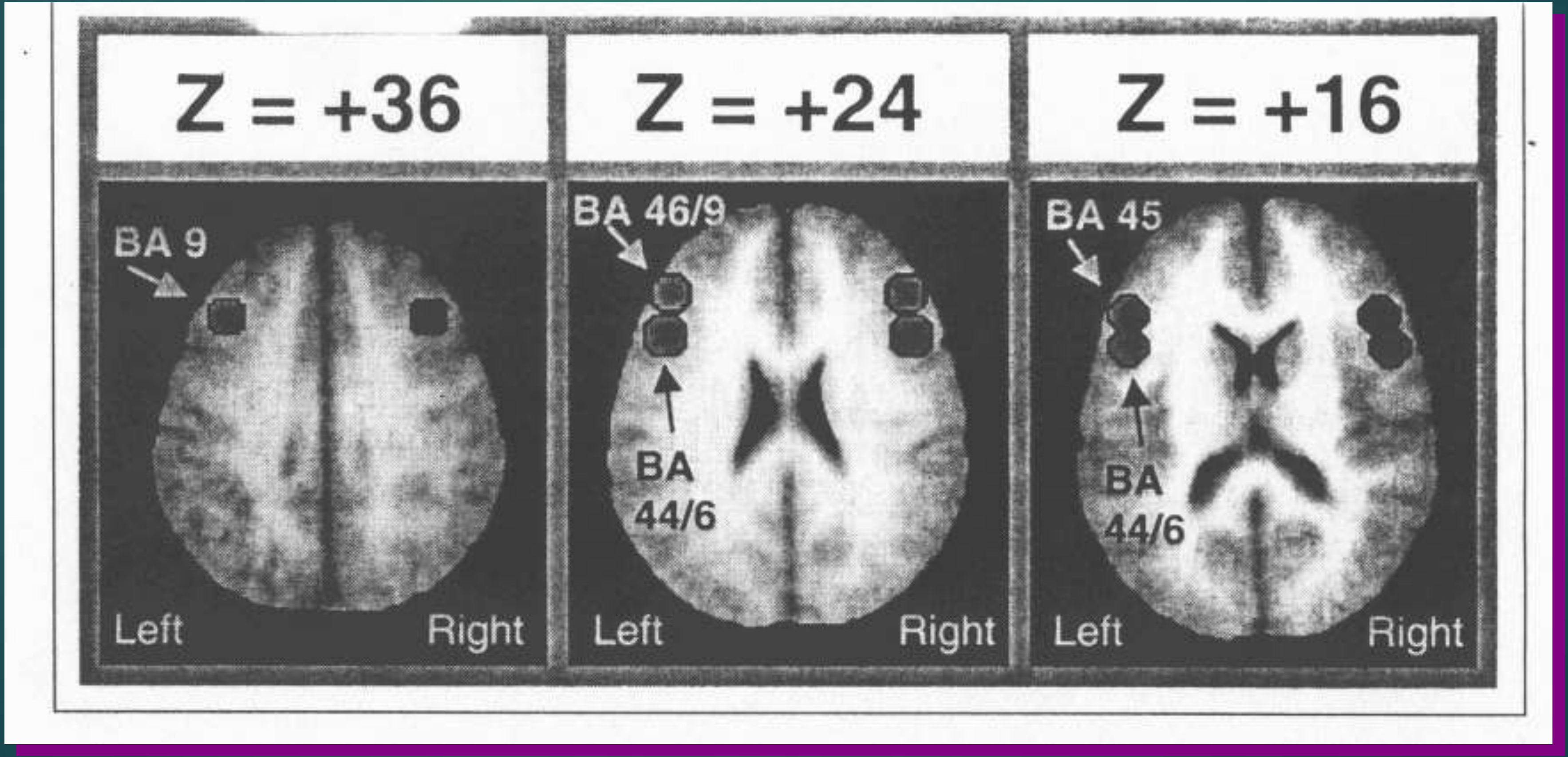
- Concrete problem solving, esp. for divergent than convergent thinking
- Poor insight and judgment
- Environmental dependency
- Slow learning: reduced WM, less efficient retrieval strategies, temporal sequence deficit
- Blunted emotions/apathy or anger outbursts
- Expressive aphasia

Working Memory

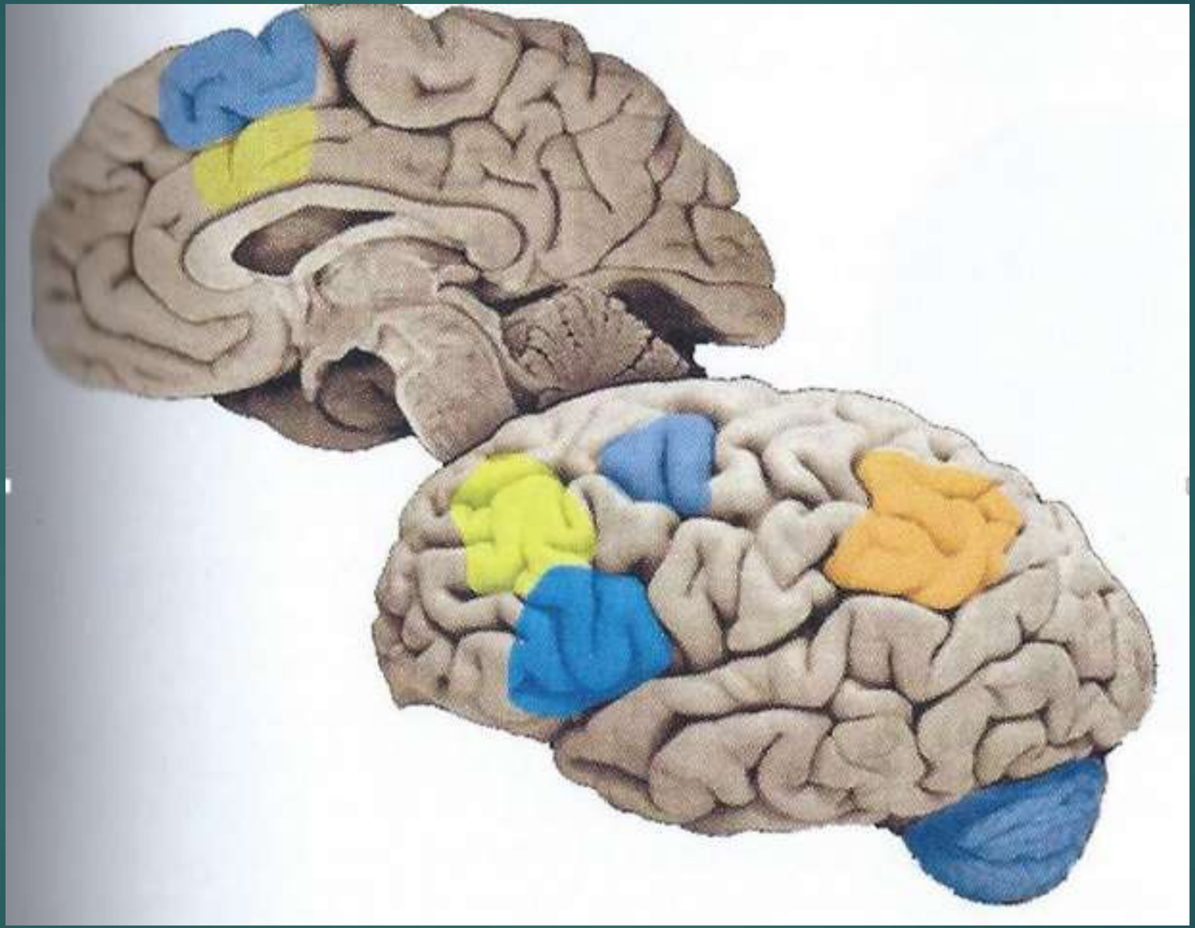
- Miller's Constant: 7 ± 2 in Psych. 101
- Limited capacity system for temporary online storage and manipulation of information
- Highly correlated with Fluid IQ (problem solving); Good WM requires optimal dopamine function
- Attentional buffer that holds information while we process it
  - Telephone number
  - Mental arithmetic
  - Recall of chess positions, bridge hands, music and baseball klg
  - Delayed response

Working Memory: Frontal neuroanatomy

Area 46 & 9: Spatial location WM -- where
Area 45: Visual feature WM – what
Area 44: Linguistic WM

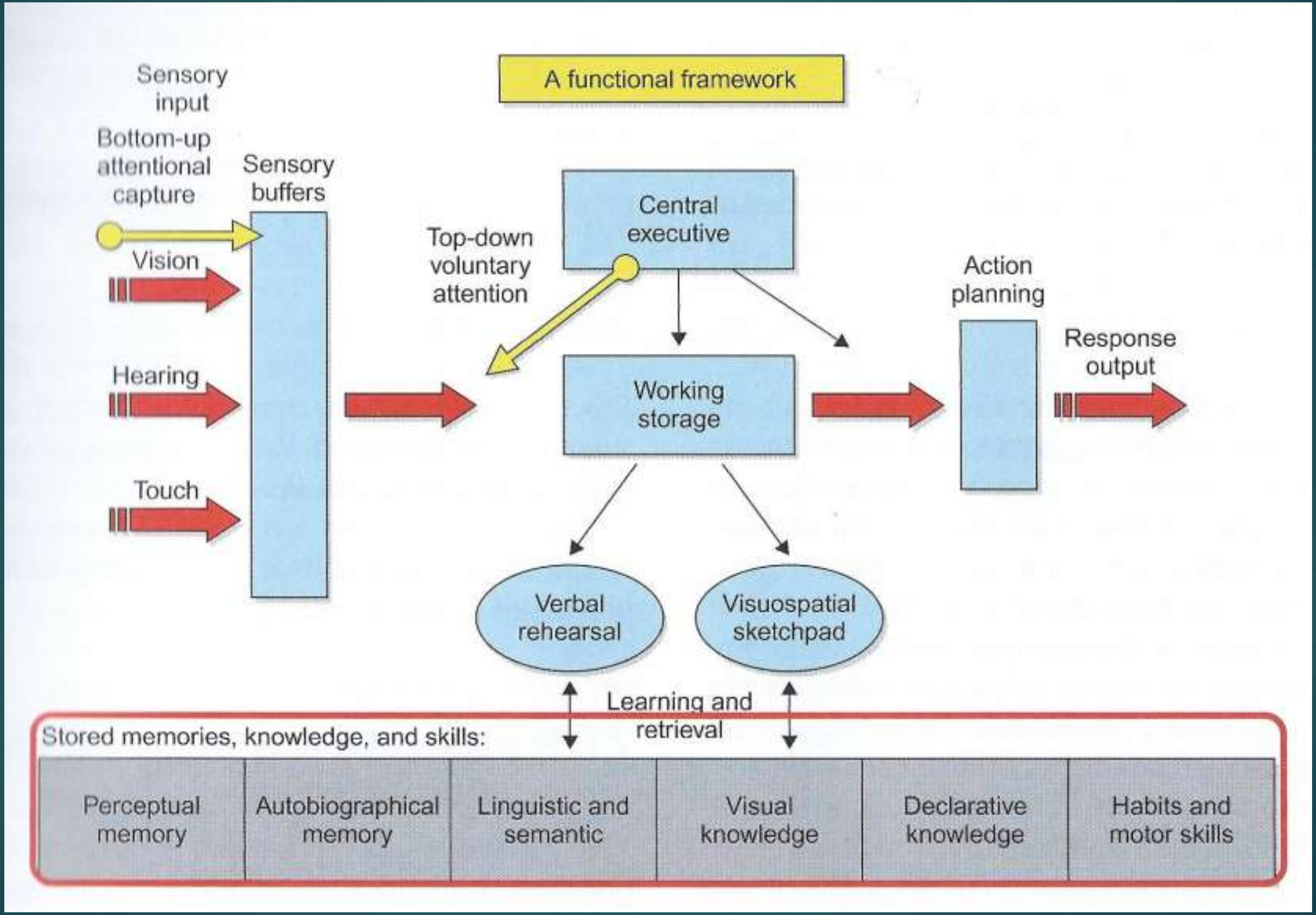


Working Memory: Frontal & Parietal Network



Brain wave synchronization between DLPF and posterior parietal circuit carries content-specific information that produces visual working memory.

Working Memory



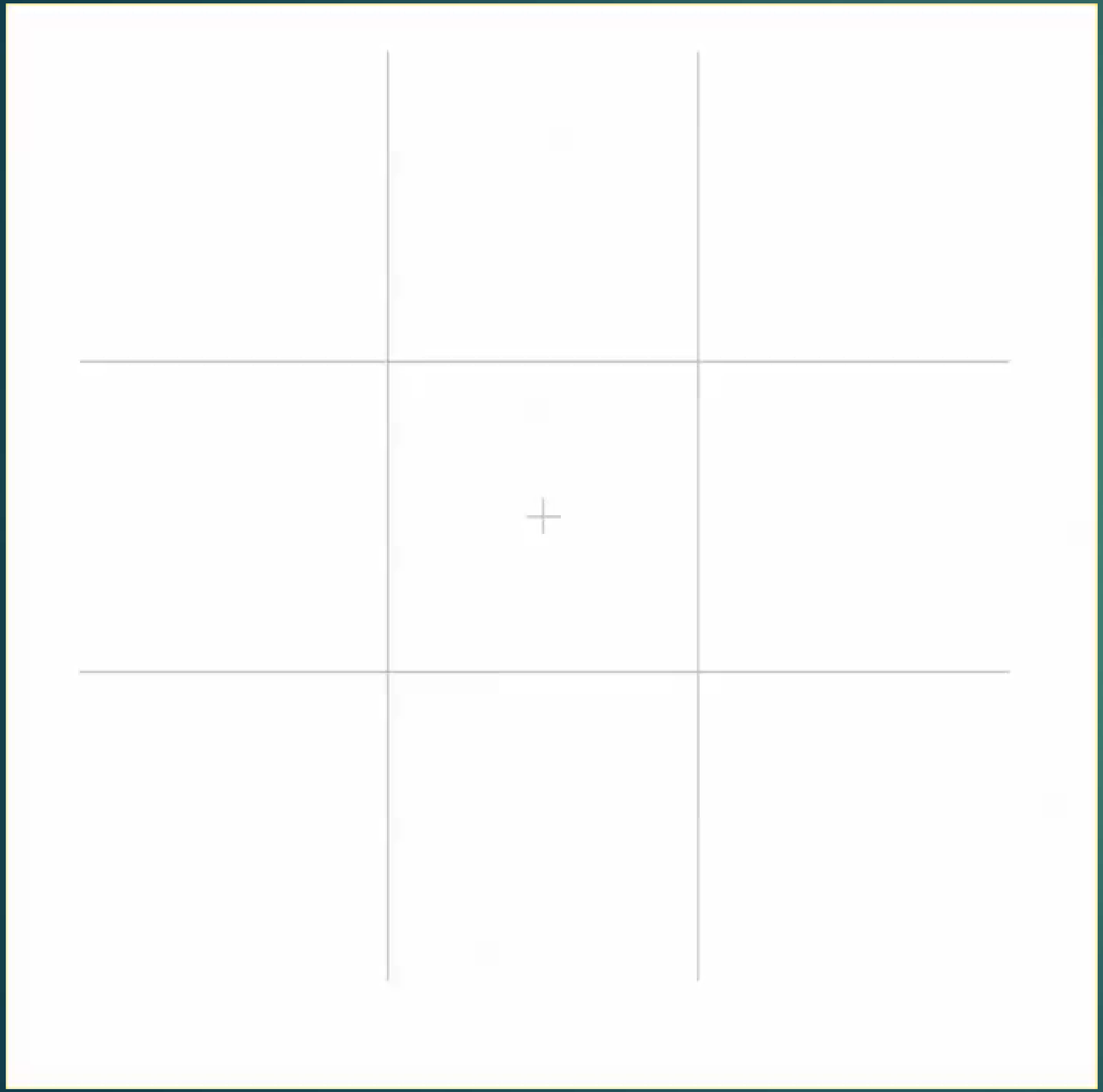
Choking Up: WM & Stereotype Threat

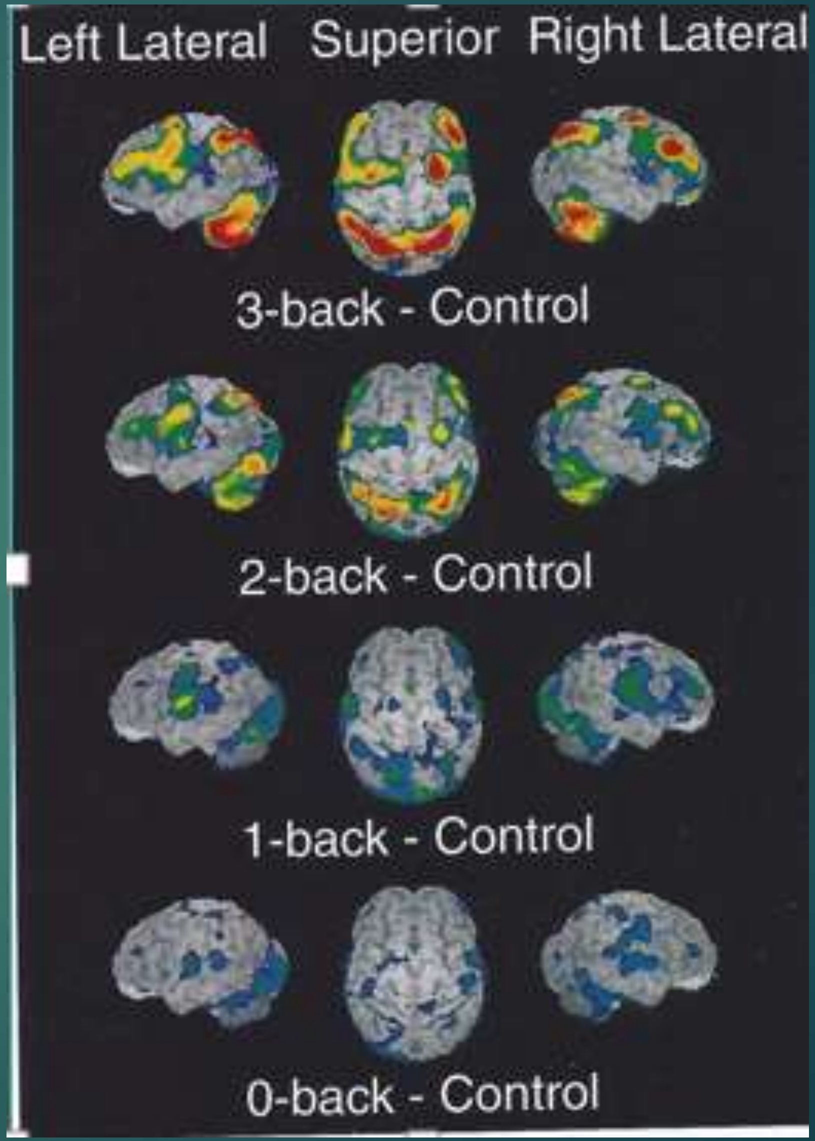
- Stereotype threat is a disruptive concern that occurs when people know that if they perform poorly, they will confirm a negative self-relevant stereotype
- In response to this threat, people underperform compared with their potential, thereby confirming the stereotype
- When older adults (60+) are confronted with negative stereotypes about age-related cognitive declines, they underperform on memory tests

- Neuroanatomy: choking up due to amygdala (threat detection) interfering with WM in prefrontal cortex; people who do not choke up have appropriate disconnect between amygdala and PFC
- Treatment: writing/journaling for 5 minutes about feelings or worries before test (B+ vs B-)

Claude Steele; Sian Beilock

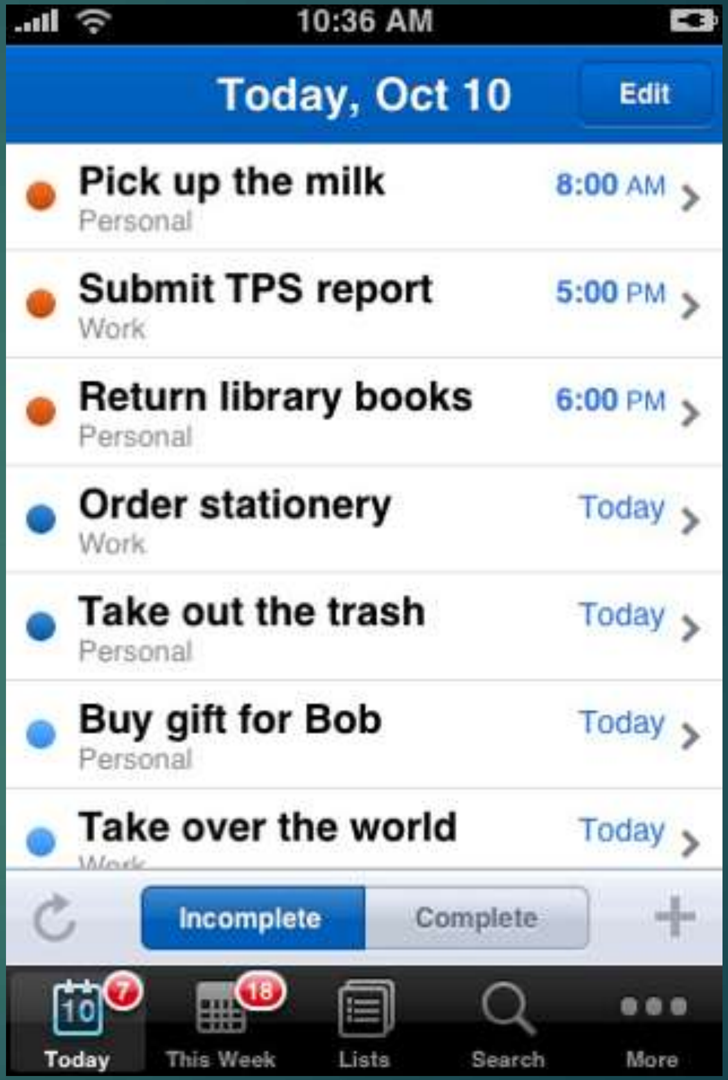
N Back Game: Harder, more regions utilized



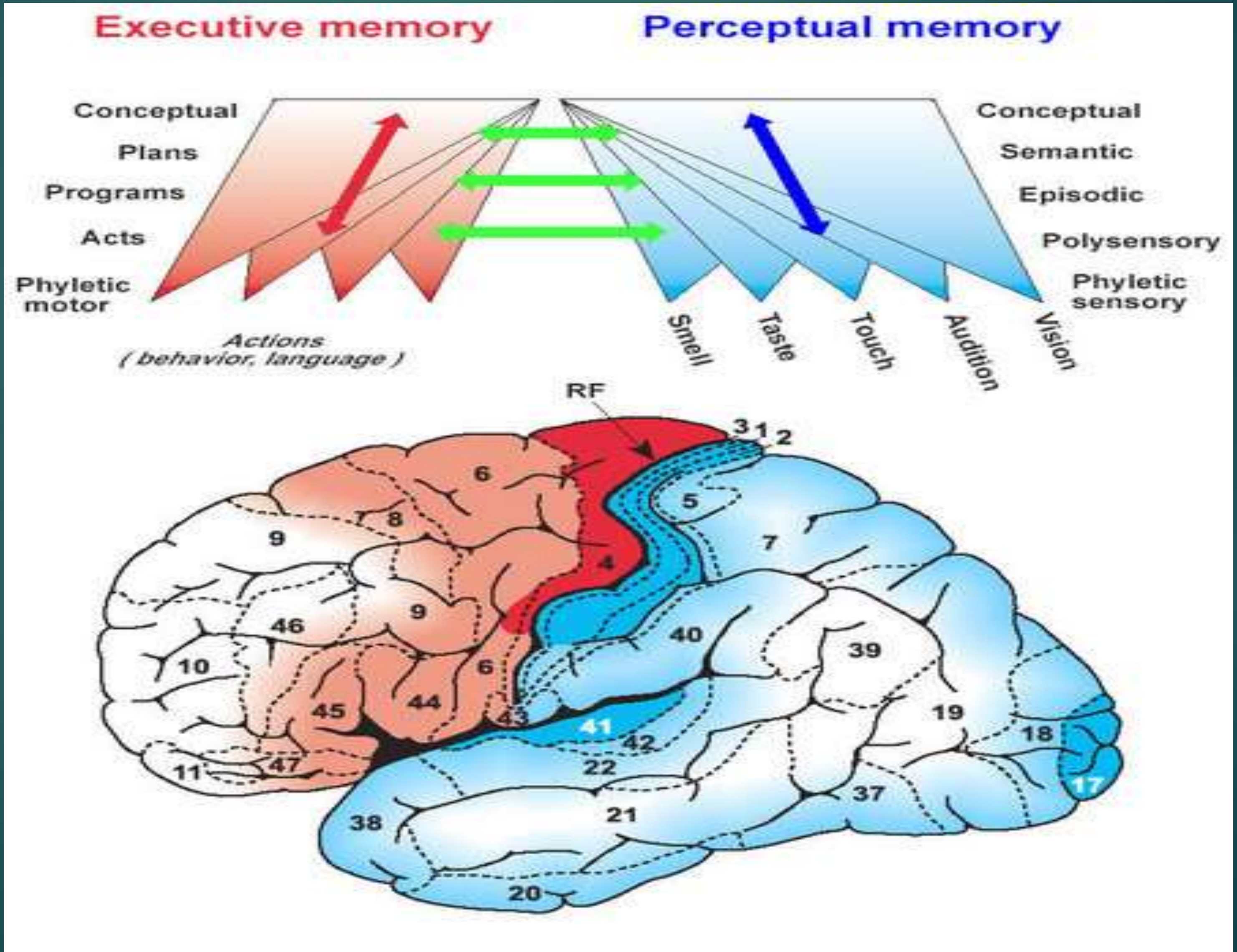


Prospective Memory

- Remembering to remember
- Intention



Frontal Memory:
Action memory, motor plan memory, concept memory



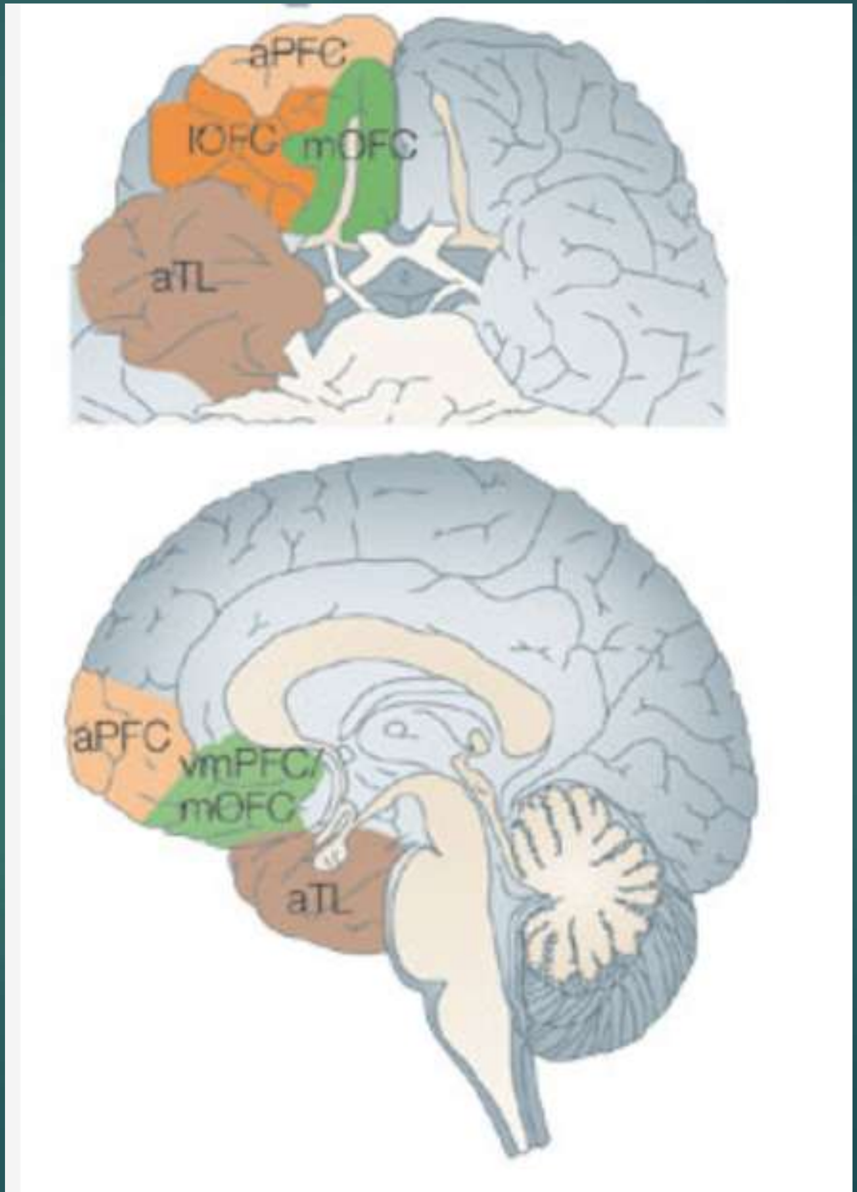
Frontal Memory Disorders

- Reduced Working Memory
- Sensitivity to interference effects
- Reduced search/retrieval of information
- Impaired source memory
- Impaired serial/temporal order
- Deficient metamemory (knowledge of own memory)
- Primacy effect: increase
- Confabulation
- Intrusions/Omissions
- Failure to release from proactive interference

Thinking Fast & Slow – Daniel Kahneman

System 1: Hot (Go) System/Default	System 2: Cool (Know) System
Emotional	Cognitive
Stereotypic	Calculating
Automatic	Effortful
Frequent	Infrequent
Reflexive	Reflective (deliberative, logical)
Nonconscious	Conscious
Fast	Slow
Amygdala & Ventral Striatum	Prefrontal
Develops Early	Develops Later
Accentuated by Stress	Attenuated by Stress
Stimulus Control	Self-Control

Ventromedial/Orbitofrontal



Orbital Frontal Cortex (OFC): how rewarding is a reward

- Conscious evaluation of rewards (medial OFC) and punishments (lateral OFC)
- Rapid evaluation of cost/benefits of behavioral responses to environment, esp. social
- OFC = Valence meter (pleasant-to-unpleasant, good-to-bad feelings)
- Evaluation of reinforcers and learning of stimulus-incentive associations; a key role in the motivational control of goal-directed behavior
- Can send a 'stop' signal to other brain regions concerned with more automatic movements (i.e. OCD)

Junichi Chikazoe, et al., 2014

OFC: affective coloring of experience

- Medial OFC represents approach tendency (reward monitor)

- Lateral OFC is inhibitory;
  - avoidance tendency (punishment evaluation: risk, fear)
  - recognizing cues of social conflict, such as when someone disapproves of a choice.

Orbitofrontal/ventromedial function

- Behavior inhibition
- Emotional regulation
- Reward monitoring
- Personality
- Olfaction (conscious odor awareness (right OFC))

Damage to OFC: Significantly alters interpersonal behavior

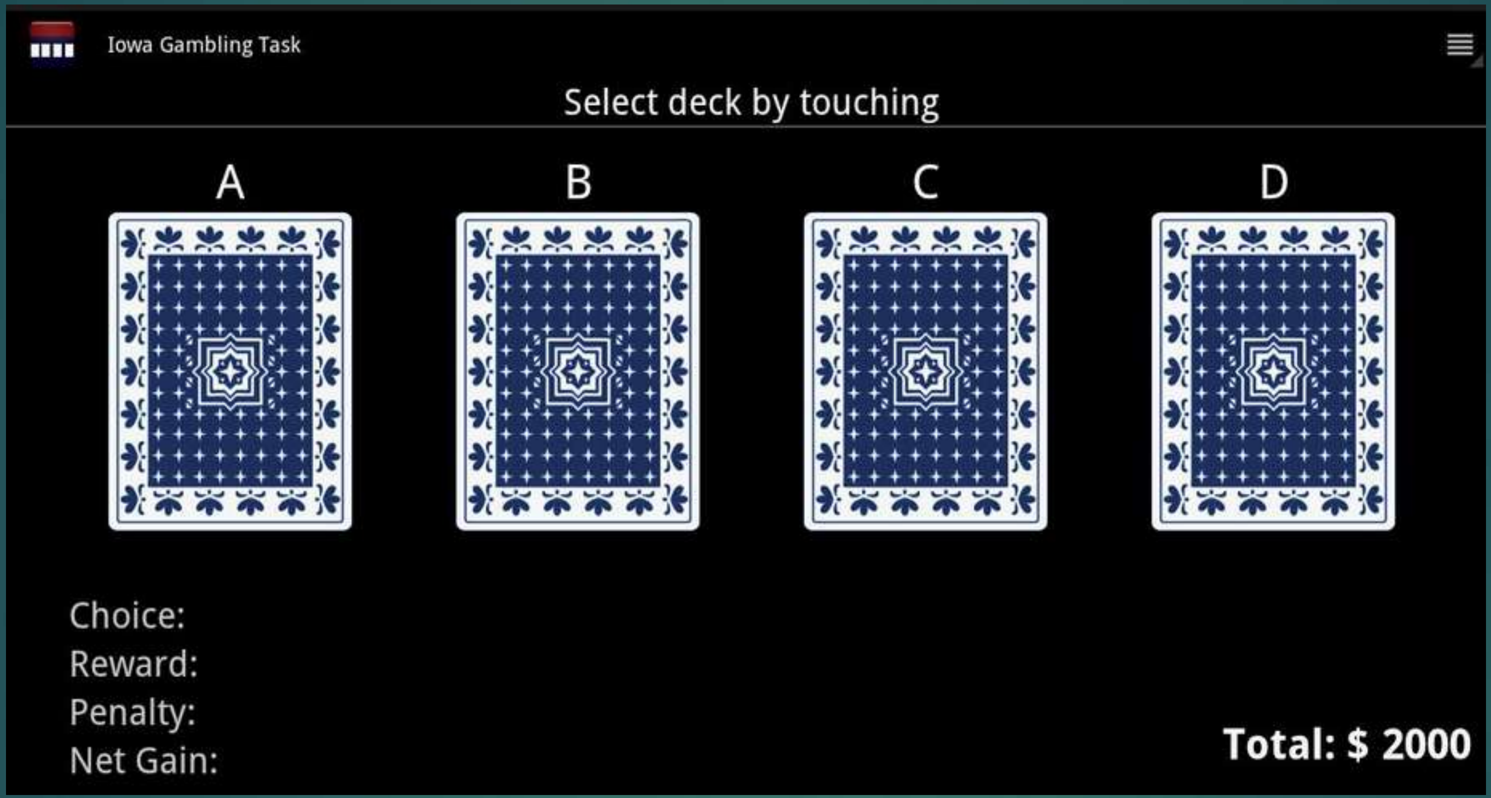
- Pedophile case
- Abnormal social behavior and violations of social norms
- Cannot see how behavior might be viewed negatively by others & be socially punished
- Bilateral damage: impaired identification of self conscious emotions (no embarrassment, shame)
- Unilateral right damage: impaired recognition of anger & disgust

OFC Tumor:
Is Mr. Spock's rationality the ideal

- 1982: Pt. E.: model father, corporate manager, 97%tile IQ
- Then behavior change; considered a "malingerer"; fired from job, wife divorced him.
- He walked into neurologist Antonio Damasio's office: bilateral mOFC tumor diagnosed & removed
- No emotional reaction (no GSR) to scenes of mutilation
- Now: pathological indecision: Use of blue or black pen, where to park
- Discovery: human decision making requires emotions to function correctly
- Damasio's Somatic Marker Theory: Iowa Gambling Test

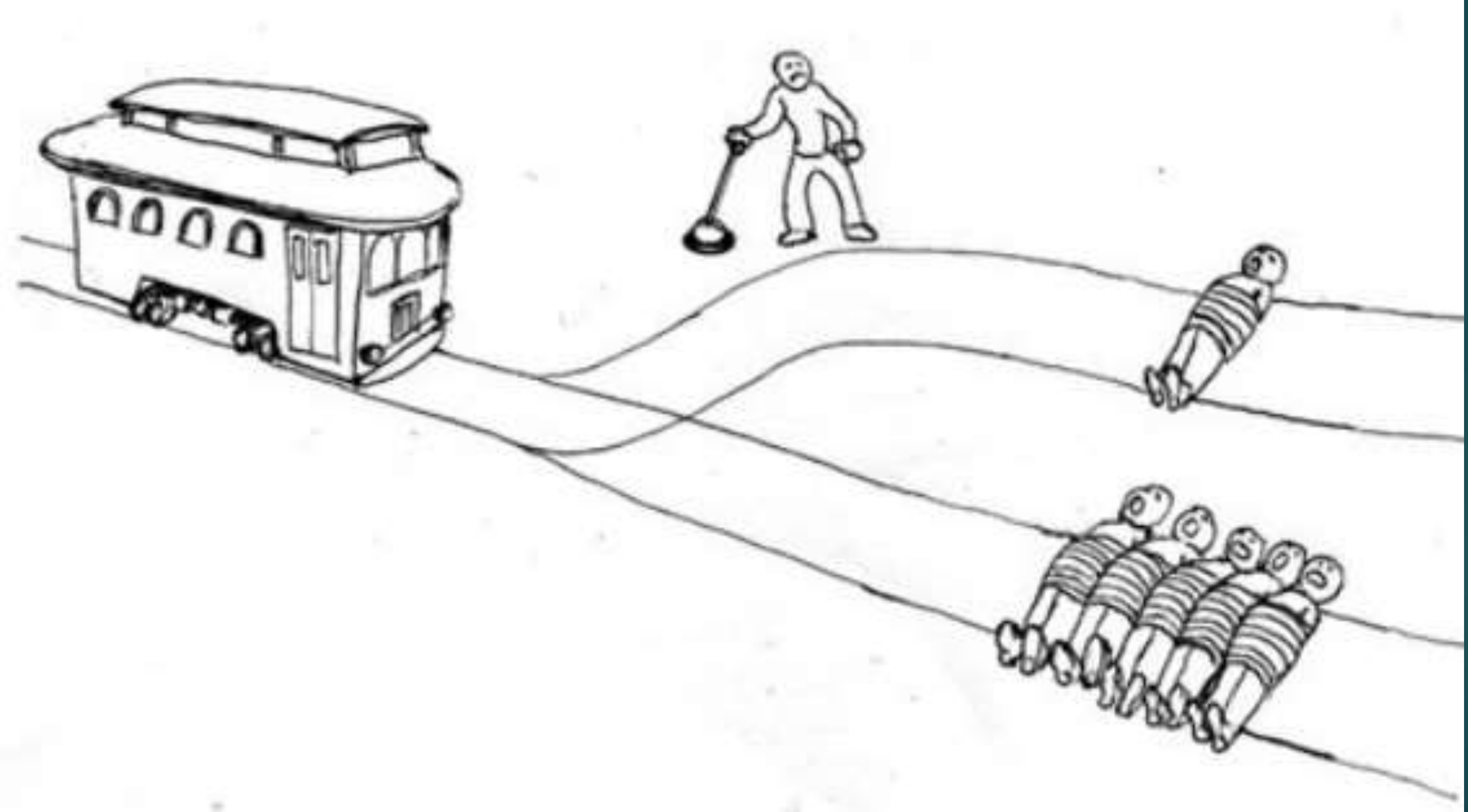
(A. R. Damasio, Tranel, & Damasio, 1990; Eslinger & Damasio, 1985)

Iowa Gambling Task: 2 decks lose consistently



Normals stop using bad decks quickly; vmPFC damaged never learn negative consequence

Trolley Problem 1: DL PFC active



9 of 10 people confronted with this scenario say it's O.K. to hit the switch.

Trolley Problem 2: vmPFC active

9 of 10 people say it's not O.K. to kill one person to save five;
Individuals with vmPFC damage 3x more likely to push the person off; low level of empathic concern; 60% will smother a baby to save 50 people

OFC Damage

- Disorganized; Poor goal directed behavior (apathy, disorganization)
- Behaviorally disinhibited, impulsive
- Behave hedonistically
- No social concern for feelings or rights of others; loss of empathy
- Emotionally disregulated
- Anosmia
- *Witzelsucht* or hollow, inappropriate jocularity (laugh at a funeral)
- Altered emotional experience (blunt or labile)
- Impaired decision making, lack of self monitoring

- bvFTD

Orbital Damage

- Damage produces:
  - Disinhibition
  - Hyperactivity
  - Emotional lability
  - Aggressiveness
  - Reduce self-awareness
  - Mood disorders
  - Poor Iowa Gambling Test

- Disinhibition:
  - swearing excessively, hypersexuality,
  - poor social interaction, compulsive gambling, drug use (including alcohol and tobacco),
  - poor empathizing ability

- bvFTD behaviors

OFC Damage

- Deficits in emotion recognition, both in facial and vocal modes
- Ventral damage: impaired facial emotion recognition, nonverbal vocal expressions of emotion
- Bilateral damage: impaired identification of self conscious emotions (embarrassment, shame)
- Unilateral right damage: impaired recognition of anger & disgust
- Poorer matching of emotion expressions (facial, hand, body expressions)

vmPFC Damage

- VMPFC damage: strongest predictor of empathic deficits
- 3 x more likely to advocate throwing a person to certain death in front of a runaway train to keep it from killing five other people.
- 5 x more likely to advocate smothering one’s baby to save others
- Predicts future alcoholism and psychopathy

Damasio, 2007; Amitai Shenhav and Joshua D. Greene, 2010

Recognition of facial emotion & Botoxin:
automatic mirroring of facial expressions

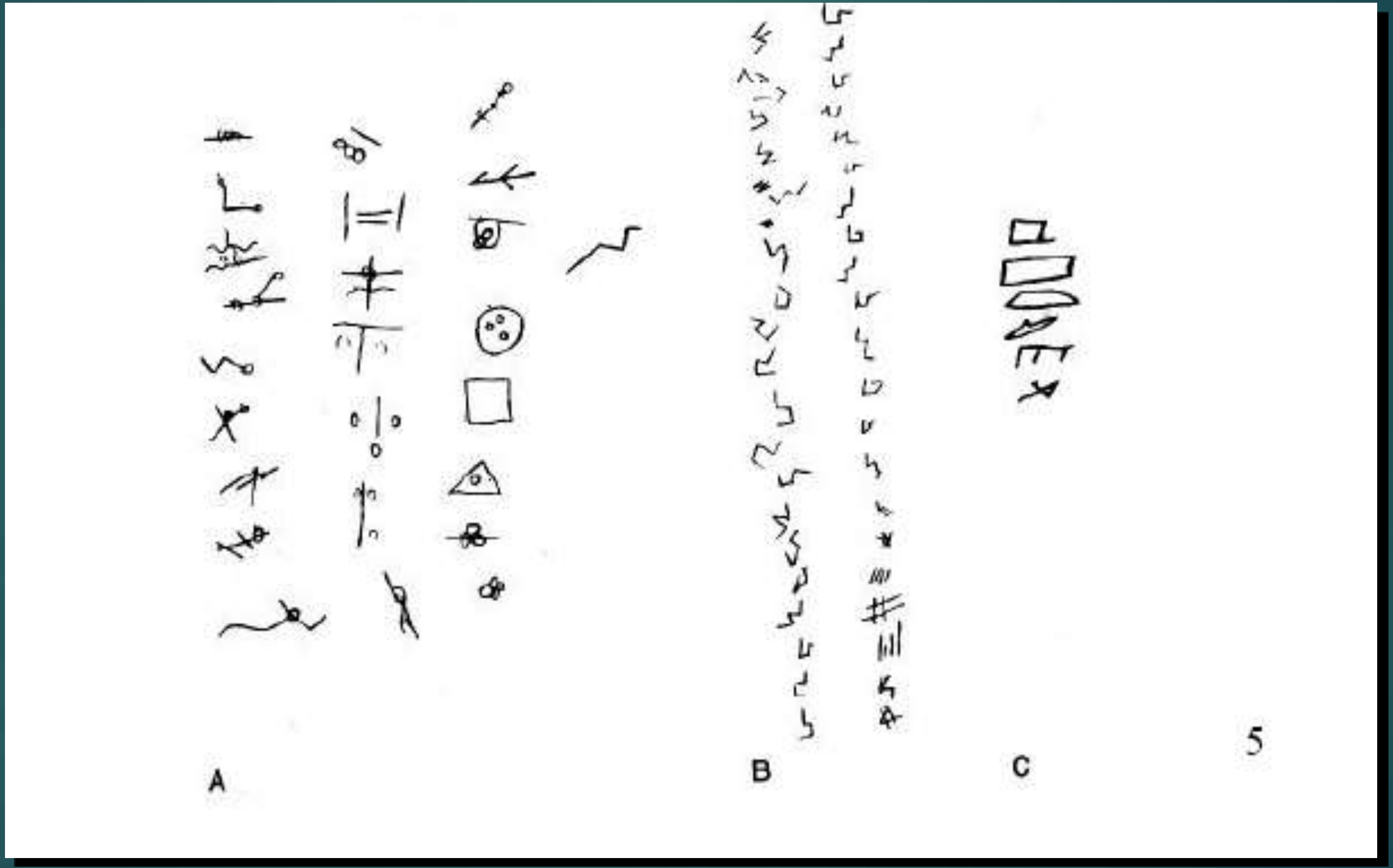
- People are sensitive to recognizing emotions in others. We automatically mirror the emotions of others.
- We form same emotional facial features when viewing an emotion on another person's face
- Women who have had facial wrinkles removed with botulin (more paralyzed facial muscles) are less able to identify feelings in others; other people are less able to read their feelings as well.

ADHD & OCD: Differential neuroanatomy for inhibition

- Patients with ADHD showed disorder-contrasting multimodal structural and functional abnormalities in bilateral basal ganglia/insula, which were decreased in Grey matter volume and function in patients with ADHD relative to those with OCD (and controls).
- In OCD patients, they were enhanced relative to controls. Patients with OCD showed disorder-specific reduced function and structure in rostral and dorsal anterior cingulate/medial prefrontal cortex, whereas patients with ADHD showed disorder-specific underactivation predominantly in the right ventrolateral prefrontal cortex. Ventromedial prefrontal GMV reduction was shared in both disorders relative to controls.
- **Conclusions and Relevance** Shared impairments in inhibitory control, rather than representing a transdiagnostic endophenotype in ADHD and OCD, were associated with disorder-differential functional and structural abnormalities.
- Patients with ADHD show smaller and underfunctioning ventrolateral prefrontal/insular-striatal regions
- Patients with OCD show larger and hyperfunctioning insular-striatal regions that may be poorly controlled by smaller and underfunctioning rostro/dorsal medial prefrontal regions.

Luke J. Norman, et al., 2016

Right Orbital Frontal Damage: Design Fluency



Control: unique designs

Patient: repetitive

Anatomic areas in morality network

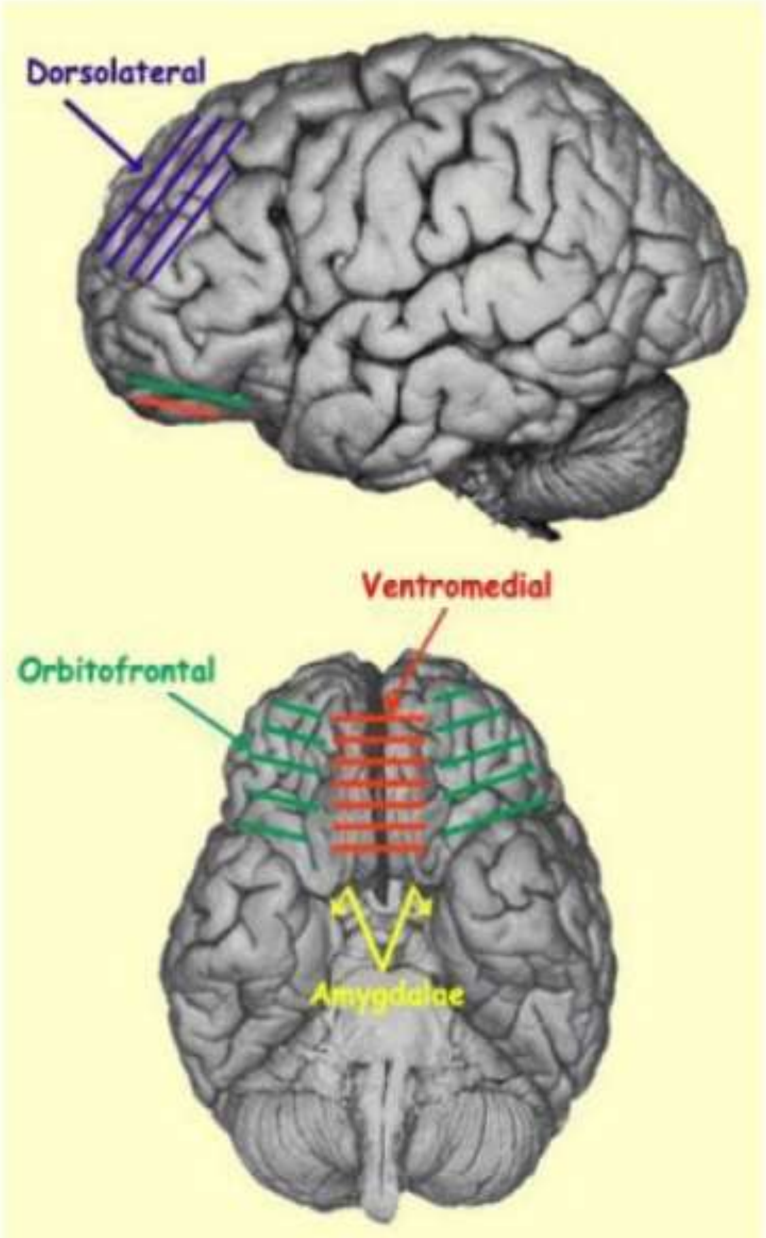


TABLE 4.
Sociopathic Acts among 16 Patients with Frontotemporal Dementia[145]

Number	*Type*
3	Unsolicited sexual approach or touching
3	Traffic violations including hit-and-run accidents
2	Physical assaults
1	Shoplifting
1	Deliberate non-payment of bills
1	Pedophilia
1	Indecent exposure in public
1	Urination in inappropriate public places
1	Stealing food
1	Eating food in grocery store stalls
1	Breaking and entering into others' homes

Mendez MF. *CNS Spectr*. Vol 14, No 11. 2009.

Kent Kiehl, PhD & his 1100 Psychopaths

Kent Kiehl in front of the semi-trailer that houses a portable MRI scanner at the Western New Mexico Correctional Facility.

Neurocriminology:
Neurobiology of Psychopathy

- Kiehl: a defect in "the paralimbic system," (orbital frontal cortex to the posterior cingulate cortex) that are involved in processing emotion, inhibition, and attentional control.

- At the neural level, individuals with psychopathy show atypical responding within the amygdala and ventromedial prefrontal cortex (vmPFC).

Neurobiology of Psychopathy 2

- More psychopathic, less dense, underdeveloped limbic system; rely less on emotion in moral decision making
- VM PF: push people off bridge in bridge paradigm
- They know right from wrong
- Respond more from thinking than emotion
- Low activation of anterior cingulate in tests of impulsivity predicts recidivism (doubles chance of rearrest)

Psychopathy & FMRI

- Amygdala: 17% smaller in psychopaths; psychopaths are hypolimbic (emotionally deactivated)
- White collar psychopaths & serial killers: better prefrontal (EF)
- VL OFC activates with lying in normals, not in Psychopaths; check temporary-employment agencies
- Limbic, Anterior Cingulate, Orbital Frontal activation when experience event of negative emotional response in normals; not in Psychopaths

Meta-analysis of child abuse brain effects

- Children from low-income households:
  - smaller and slower growth in parietal and frontal gray matter volumes, related to greater behavior problems.
- Most consistent gray matter abnormalities: ventrolateral prefrontal-limbic-temporal regions
- Child Abuse: associated with abnormalities in the right orbitofrontal-temporo-limbic regions that form the paralimbic system,
- Left inferior prefrontal volume was negatively correlated with sexual abuse severity.

Lena Lim et al., AJP, 2014

Meta-analysis of child abuse brain effects 2

- Amygdala volumes: inversely associated with time spent in institutions and positively associated with age at adoption in severely deprived children/adolescents (i.e. Romanian orphanages).

- Hippocampal volumes were negatively correlated with duration and severity of childhood maltreatment.

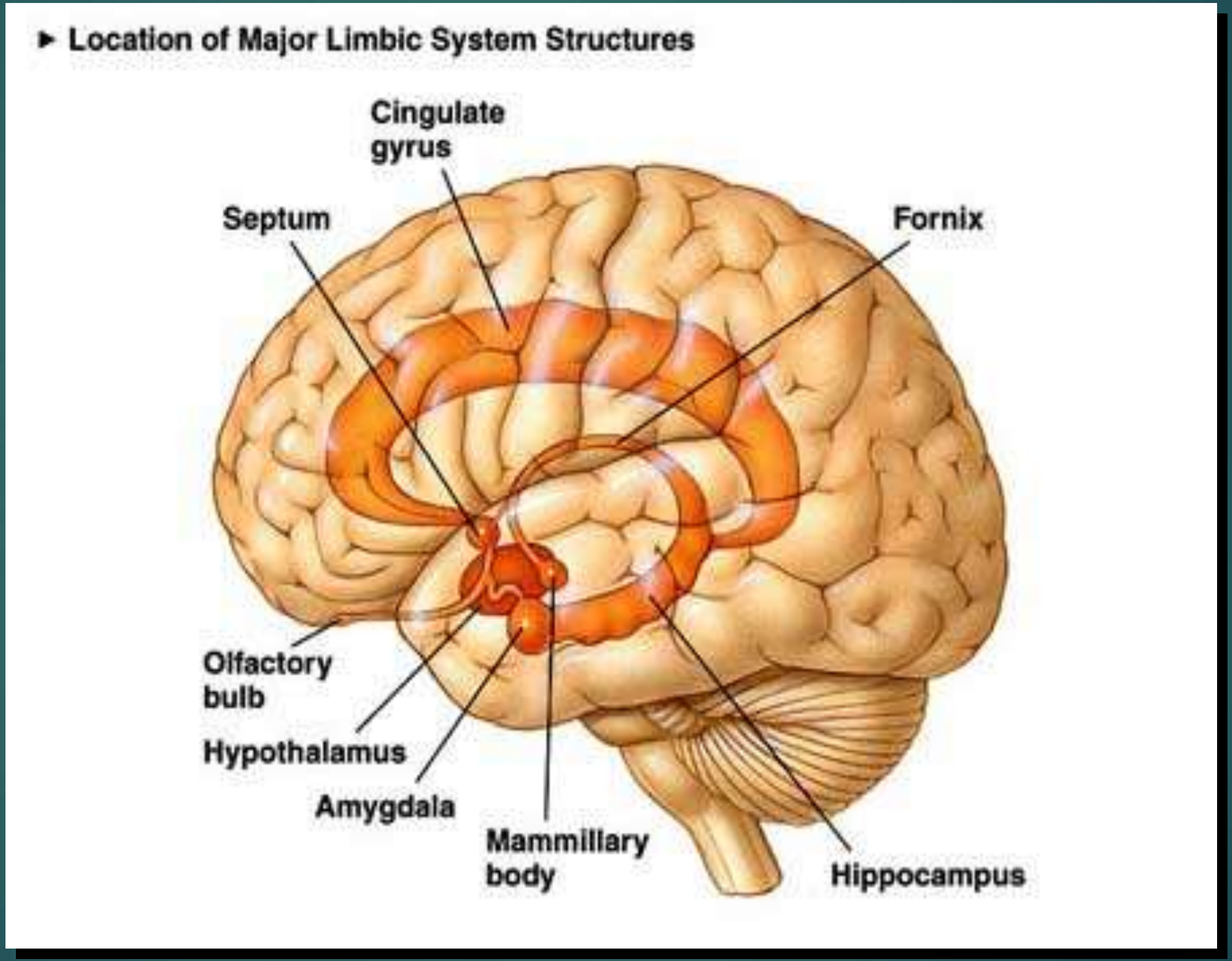
- Left and right occipital volumes were negatively correlated with the duration of the childhood sexual abuse that occurred before age 12.

- Predominantly right amygdala and insula hyperresponsiveness to negative facial expressions in maltreated children/adolescents and adults

Use Tylenol: Physical pain, social rejection & existential dread

- Pain perception & DACC & insula: both real physical and social rejection
- 1000 mg of Tylenol decreases real pain, social rejection, & uncertainty; and distrust in BPD
- Latest: Rather than just being a pain reliever, acetaminophen can be seen as an all-purpose emotion reliever. Feel less pleasure also.
- But not helpful for back pain or sleep.

Cingulate Gyrus



Conflict Resolution circuit; Salience network

Cingulate Gyrus: Truth or Consequence

- Location: Collar around Corpus Callosum

- Functions:
  - Flags response conflict
  - error detection
  - anticipation of tasks
  - motivation
  - modulation of emotional responses
  - Social cognition
  - Bravery: Only a strongly active ACC silences the amygdala

- Coactivation with DLPFC (which then corrects behavior)

Cingulate

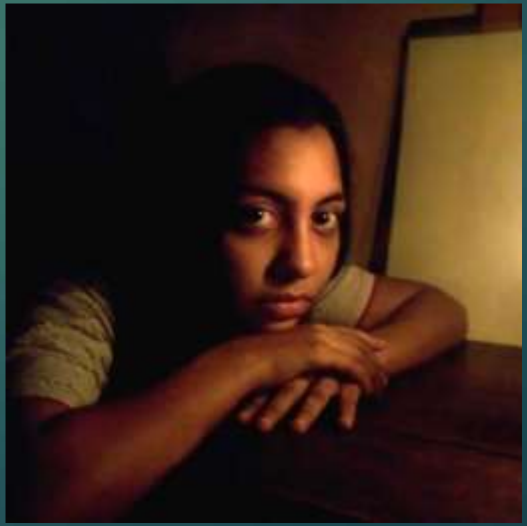
- Receives information about a stimulus, selects an appropriate response, monitors the action, and adapts behavior if there is a violation of expectancy

- Self-monitoring: such as noticing bodily sensations of pain and hunger or recognizing that one has made a mistake.

- Low activation AC in psychopaths predicts recidivism

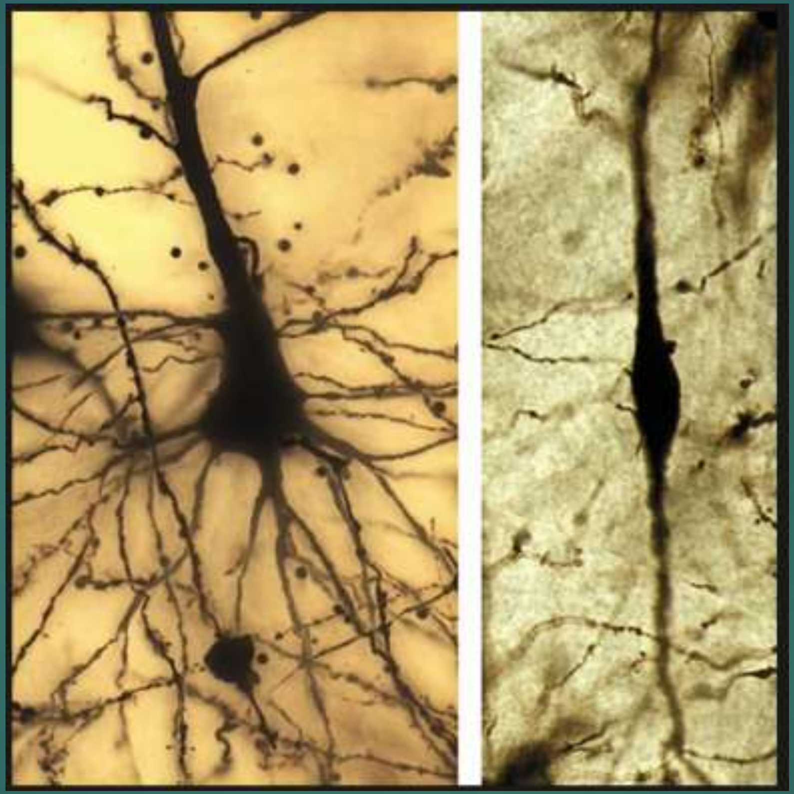
- Damage: OCD, akinetic mutism, ADHD, depression, psychopathy

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



Von Economo Neurons: Brain Cells for Socializing?

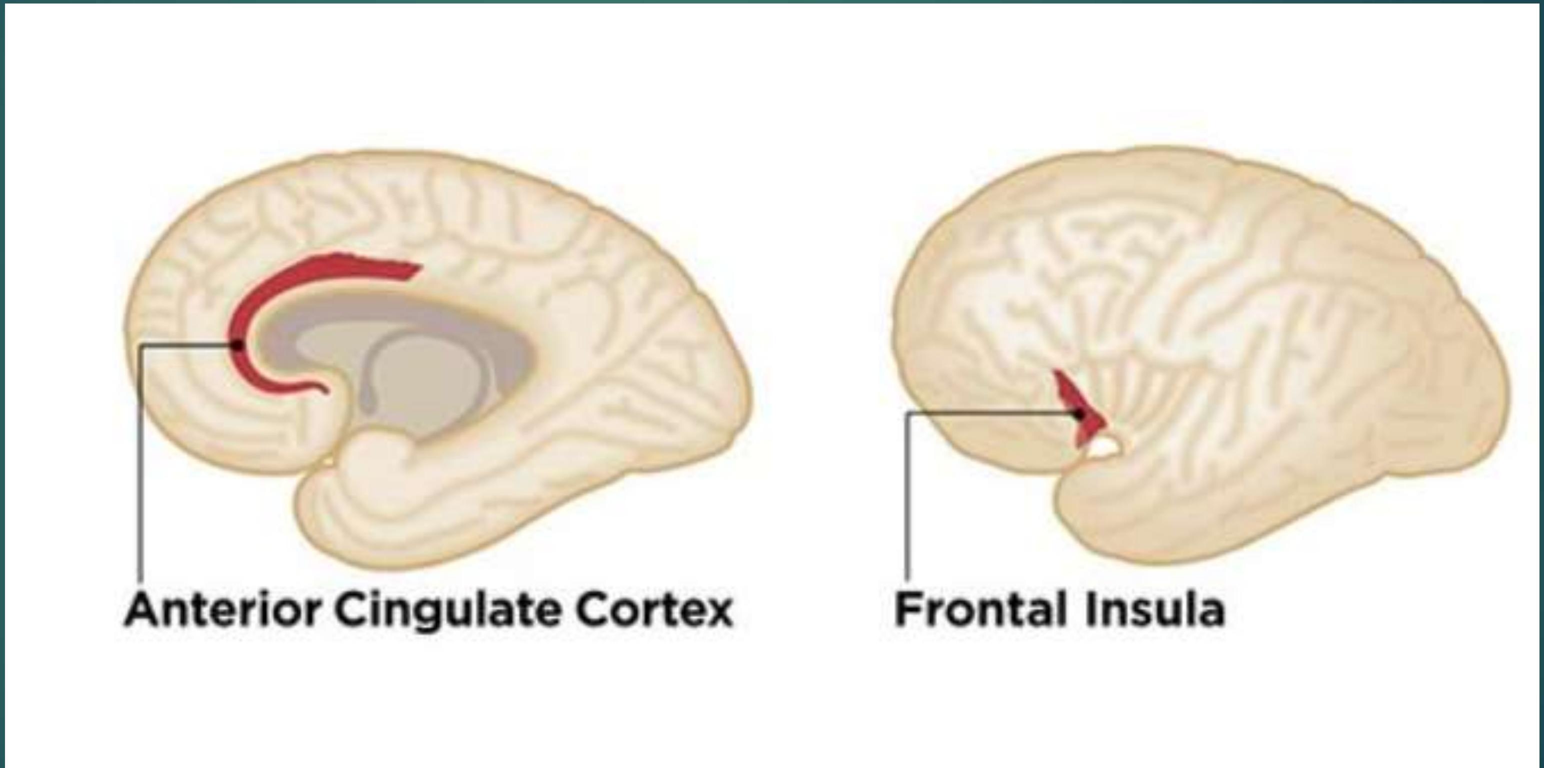
Von Economo Neurons



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 & Frontal Insula



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

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.
- The volume of Von Economo neurons is correlated with increased encephalization.
- Evolved to speed information around a big brain
- bvFTD targets ACC and Insula: 70 percent of VENs destroyed

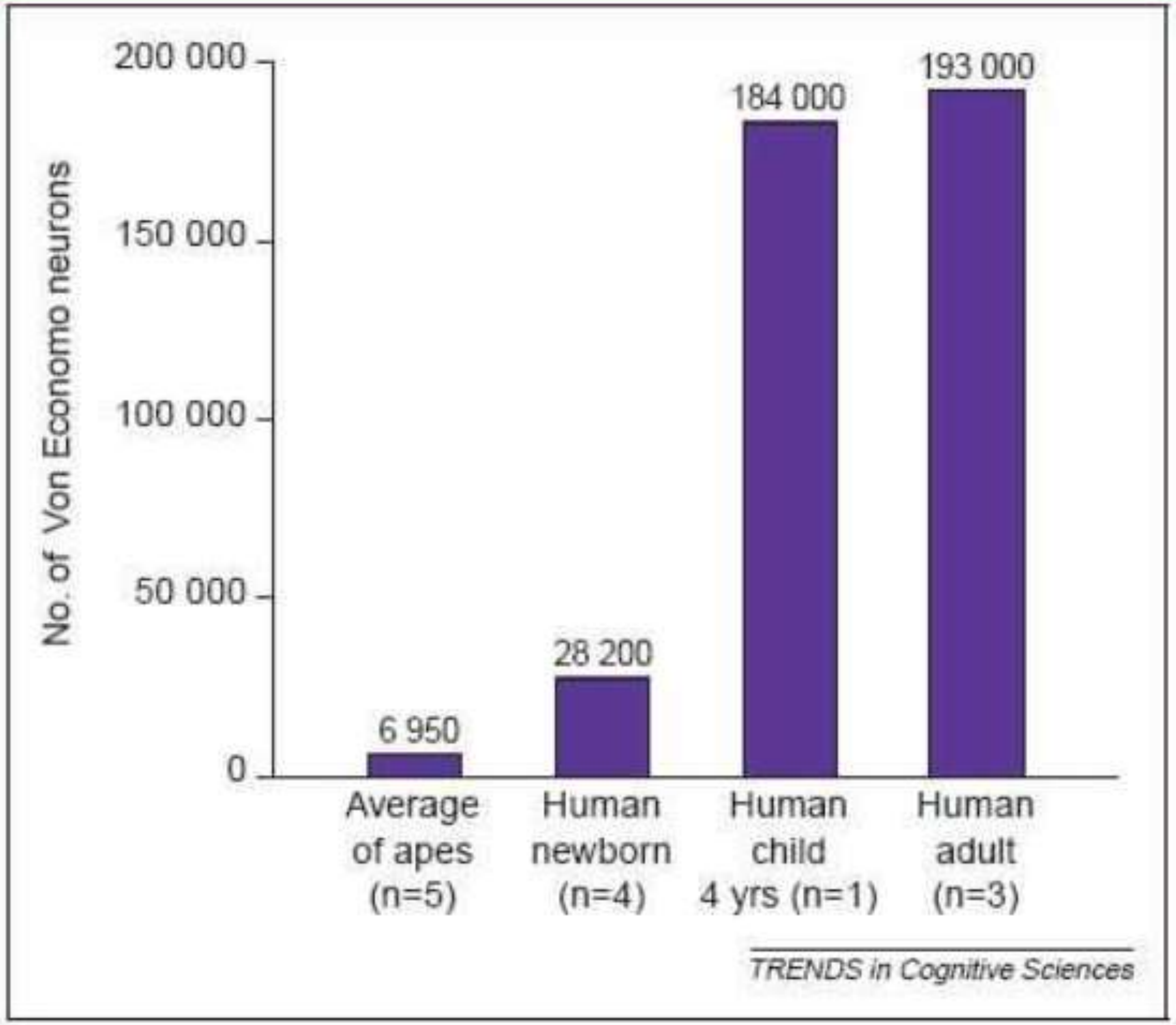


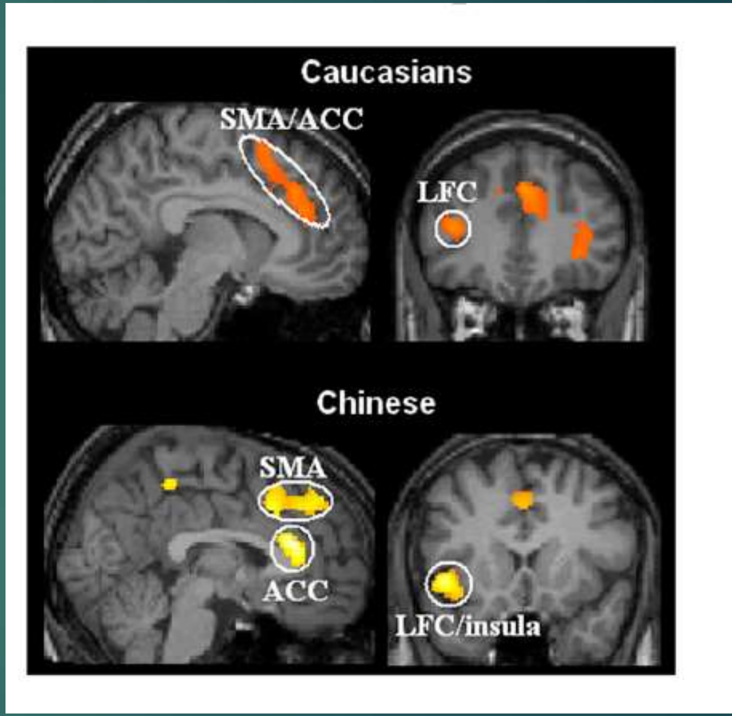
Figure 2. Comparison of Von Economo neuron numbers. Total number of VENs in FI (total of right and left hemispheres) is shown for apes, human neonates, a four-year-old child, and an adult human. The number of subjects is given in parentheses. The data are stereological counts by the authors on brains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

Loyalty & Empathy & Prejudice in the In Group:
Do You Feel My Pain?

- People show more empathy to own group.

- ACC mainly contributes to the affective component of empathy

- ACC & FI activate when witnessing someone in pain



Small right ACC size predicts lack of embarrassment in bvFTD

- Self-conscious emotions: embarrassment, pride and guilt; Are felt in the context of others' imagined reactions.
- In a Karaoke experiment of FTD, the degree to which the singers were not embarrassed in hearing themselves sing "My Girl", the smaller the ACC.
- Those with damage in the right ACC were least likely to feel embarrassment.
- Embarrassment may have evolved to motivate us to repair social bonds that become strained when we fall short of expectations.

V. Strumm, et al., 2011

Minority Report (crime prediction): Low anterior cingulate

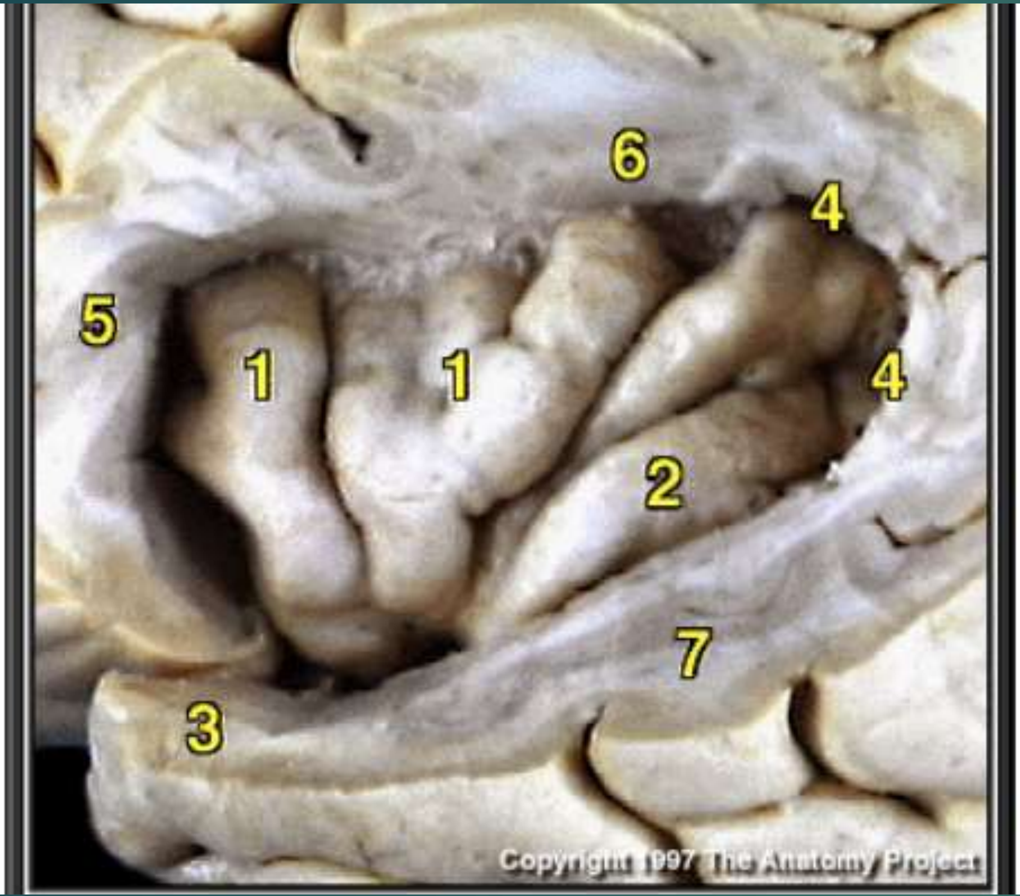
- Low activity in the anterior cingulate cortex = twice as likely to commit another offense

- Men with a smaller amygdala are three times more likely to commit violence three years later.

- Omega-3 supplements in the diets of young offenders—reduces serious offending by about 35%.

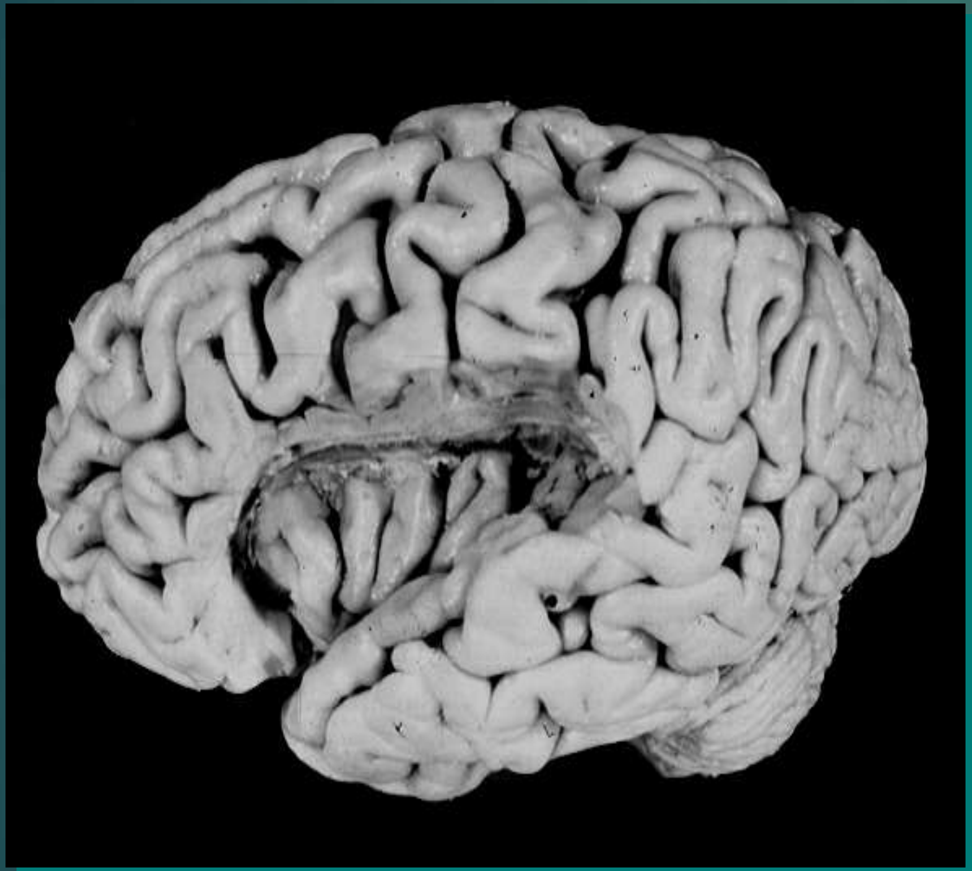
Kiehl, 2013

Insula: Gut Feelings; & Frontal Operculum: Empathy



1. Short gyri of insula
2. Long gyrus of insula
3. Superior temporal gyrus
4. Circular sulcus of insula
5. Frontal operculum
6. Frontoparietal operculum
7. Temporal operculum

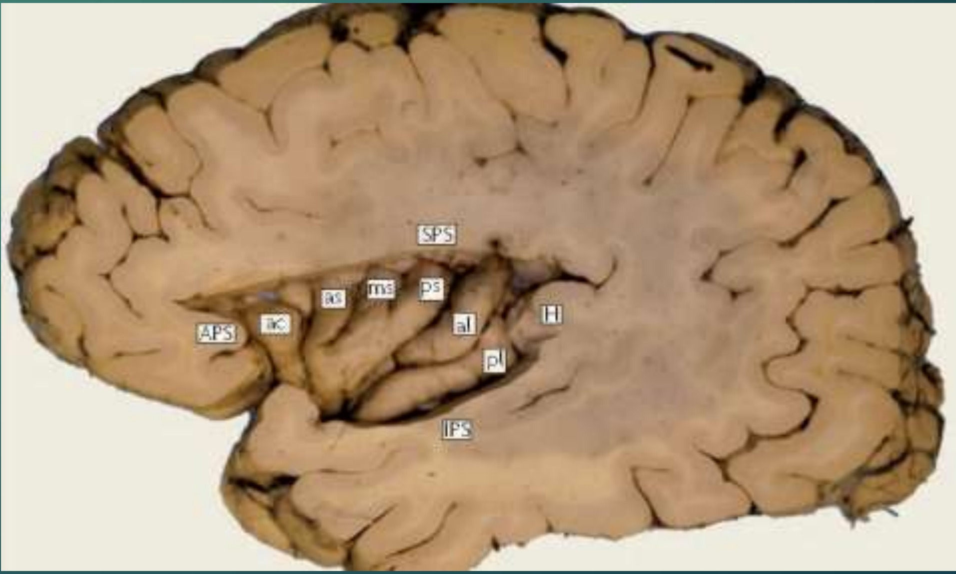
Insula



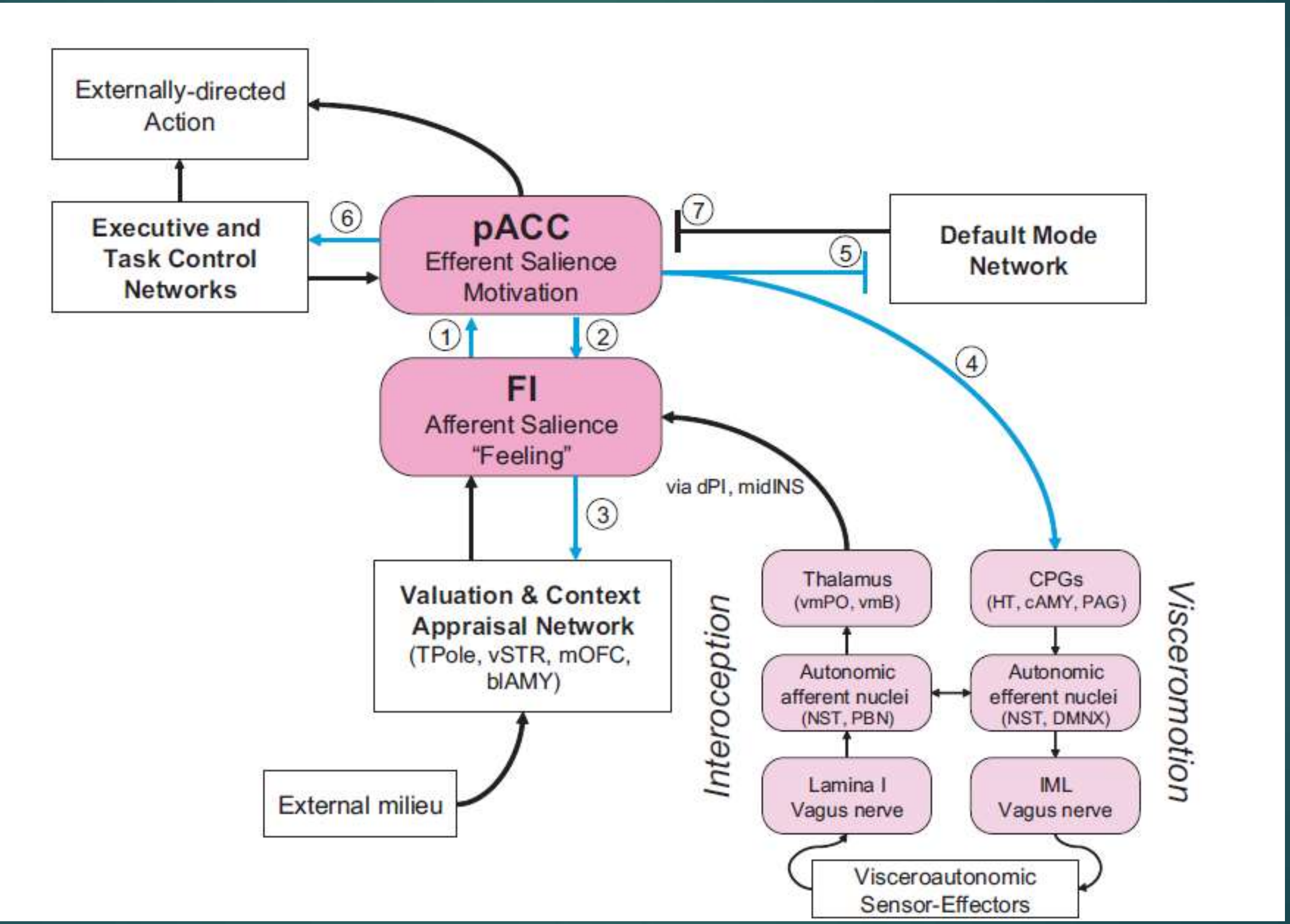
- Gut reactions
- Disgust
- Food & drug cravings
- Body states or sensations: are recast as social emotions, empathy
- von Economo neuron site

Insula: Self awareness of sensation

- Thirst, dyspnea, 'air hunger', sensual touch, itch, penile stimulation, sexual arousal, coolness, warmth, exercise, heartbeat, winetasting (in sommeliers), distension of the bladder, stomach, rectum or esophagus.



Salience Network Central: pACC & FI



bvFTD central

W. Seeley, et al., 2011

Insula

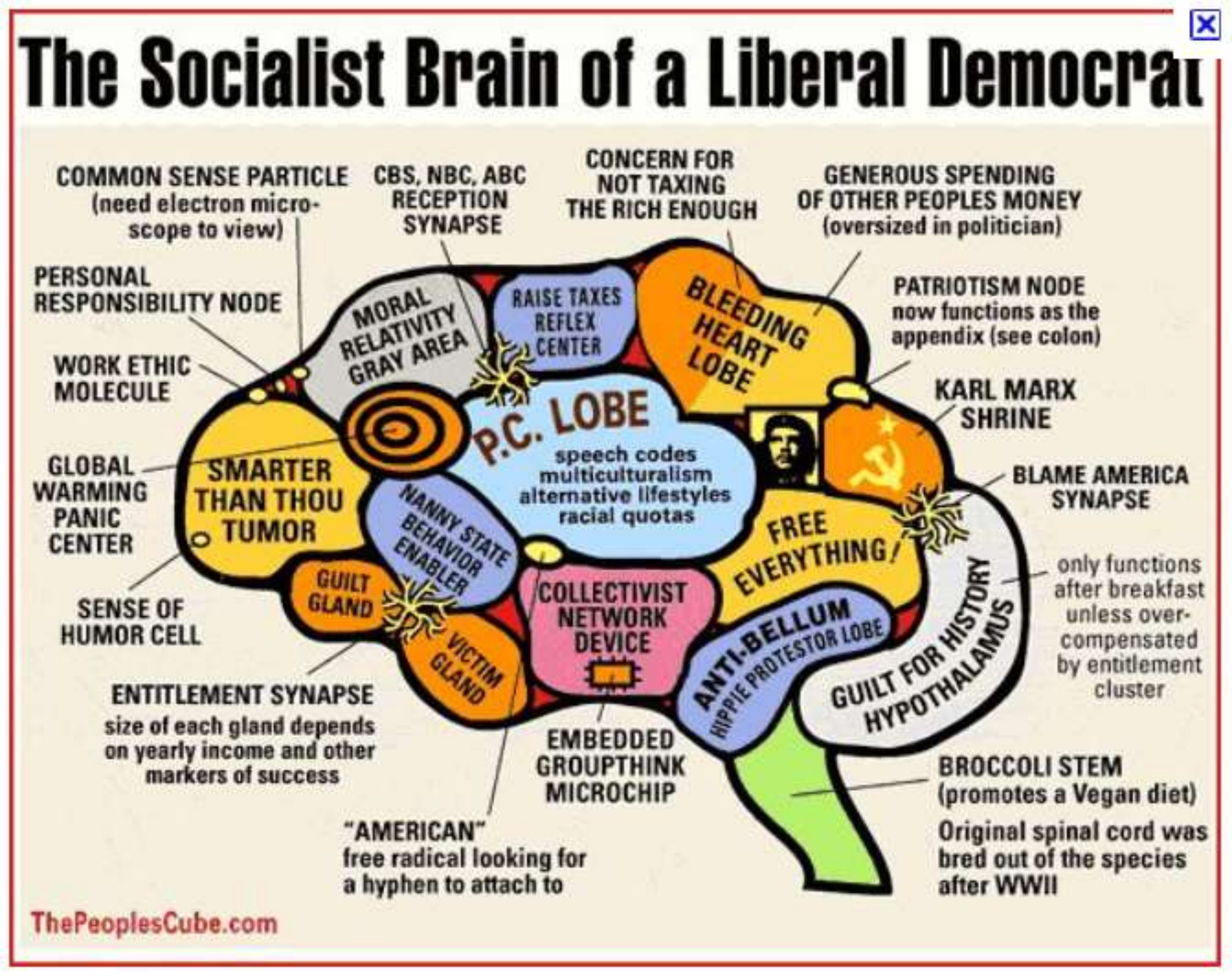
- Frontal insula: generation social emotions such as empathy, trust, guilt, embarrassment, love, a sense of humor.
- Activation: when a mother hears a crying baby, or when someone scrutinizes a face to determine the other person's intentions.
- Monitoring interactions within a social network
- Empathy for pain of others
- Disgust awareness
- Affective component of physical pain

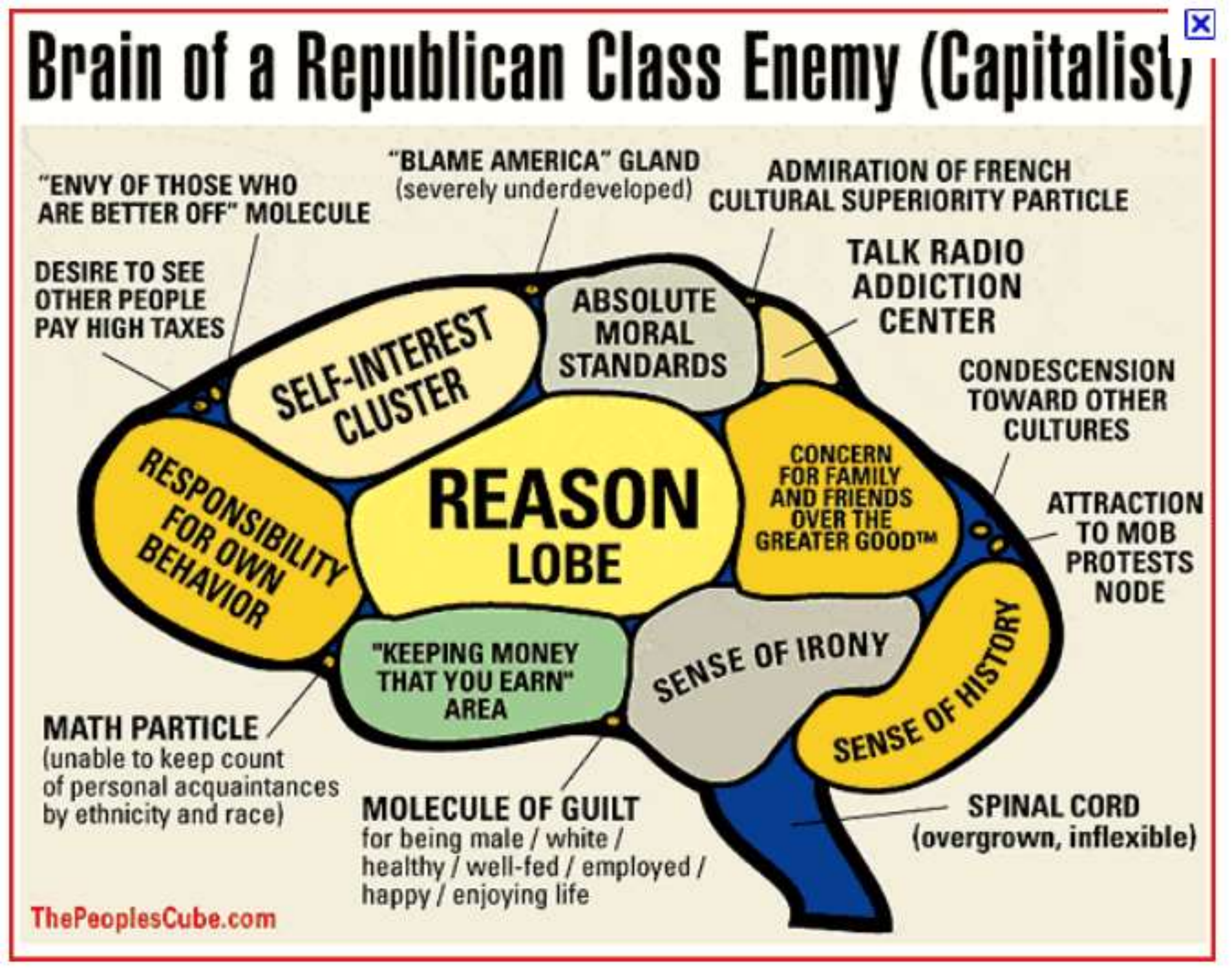
Evidence for Mirror Neuron system for emotions: Disgust

- Insula triggered both for
  - experiencing disgust feelings
  - recognition of disgust in others

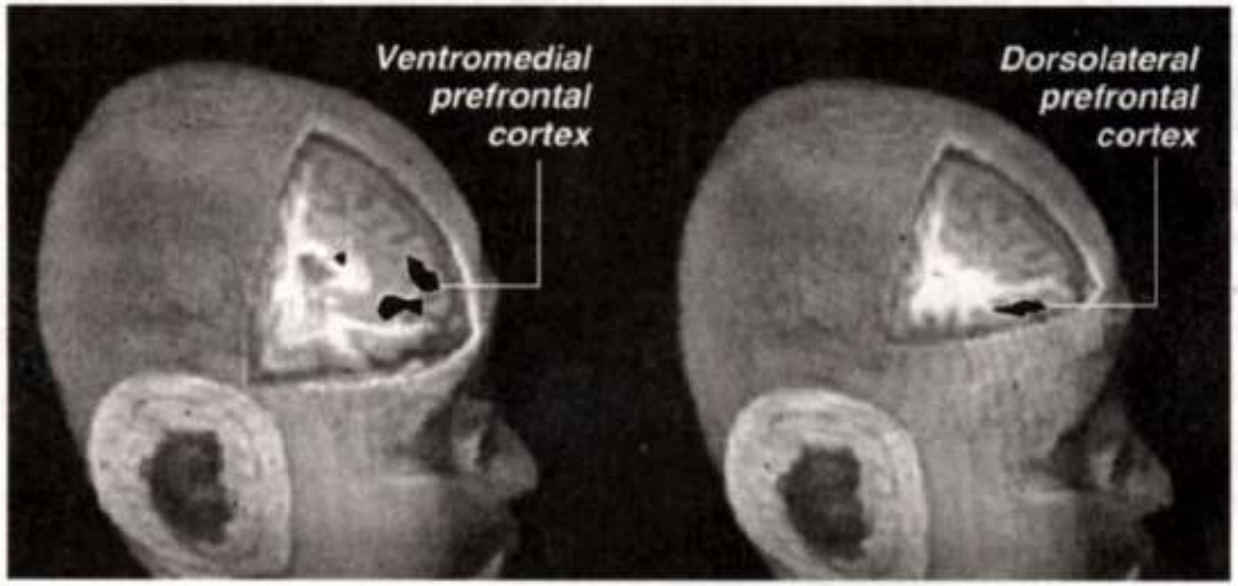
- Insula activates
  - Olfactory: if smell rotten odors
  - Visual: mutilation, contamination, putrification; watch a movie of rotten food (visceral sense of nausea)
  - Watch a film of facial disgust in others
  - Or even imagination of above

Brain Functioning in Congressional Behavior




Brain of a Republican Class Enemy (Capitalist)
"ENVY OF THOSE WHO ARE BETTER OFF" MOLECULE
"BLAME AMERICA" GLAND (severely underdeveloped)
ADMIRATION OF FRENCH CULTURAL SUPERIORITY PARTICLE
DESIRE TO SEE OTHER PEOPLE PAY HIGH TAXES
TALK RADIO ADDICTION CENTER
SELF-INTEREST CLUSTER
ABSOLUTE MORAL STANDARDS
CONDESCENSION TOWARD OTHER CULTURES
RESPONSIBILITY FOR OWN BEHAVIOR
REASON LOBE
CONCERN FOR FAMILY AND FRIENDS OVER THE GREATER GOOD™
ATTRACTION TO MOB PROTESTS NODE
"KEEPING MONEY THAT YOU EARN" AREA
SENSE OF IRONY
SENSE OF HISTORY
MATH PARTICLE (unable to keep count of personal acquaintances by ethnicity and race)
MOLECULE OF GUILT for being male / white / healthy / well-fed / employed / happy / enjoying life
SPINAL CORD (overgrown, inflexible)
ThePeoplesCube.com

USING M.R.I. MACHINES TO SEE PARIZANSHIP ON THE BRAIN



MY GUY The voter reacts to the candidate of his own party in the emotional, reflexive area of his brain, the ventromedial prefrontal cortex.

THE OTHER GUY Here, the voter reacts to the other party's candidate in the rational, cognitive area of his brain, the dorsolateral prefrontal cortex.

NEW YORK TIMES, Tuesday, April 20, 2004

Ventromedial PFC (react to own party; emotional reaction)

DL PFC (other party; think rational)

Warning: Disgusting Image coming

How Your Brain Reacts to Disgusting Images Reveals Your Political Affiliation

- Emotion of disgust has evolved as a response to offensive foods that may cause harm to the organism.
- Reaction to a single disgusting image could predict a person's political leanings with 95% accuracy (amygdala and BG)
- Large amygdala = "more sensitive to disgust“

- Anterior cingulate monitor(s) uncertainty and conflicts; capacity to tolerate uncertainty and conflicts

P. Read Montague et al., 2014

Disgust 2

- Negatively correlated with aggression (disgust leads to avoidance).
- People who are more sensitive to disgust tend to find their own in-group more attractive and tend to have more negative attitudes toward other groups. individuals who are prone to physical disgust will also be prone to moral disgust
- That was true even though the neural predictors didn't necessarily agree with participants' conscious rating of those disturbing pictures
- Disgust = Evolutionary defense against environmental threats

Conservatives have larger right amygdala

95-98% identification of conservatives with 1 single mutilated body image, independent of conscious opinion;

Conservatives have more negativity bias. Political ideology is highly heritable, almost as heritable as height.

Woo-Young Ahn, et al., Current Biology 2014

Liberal vs. Conservative in the brain: Fear containment

- Liberalism = increased gray matter volume in the anterior cingulate cortex
- Conservatism = increased volume of the right amygdala
- Large amygdala = "more sensitive to disgust“
- Anterior cingulate monitor(s) uncertainty and conflicts; capacity to tolerate uncertainty and conflicts

Kanai et al., 2011

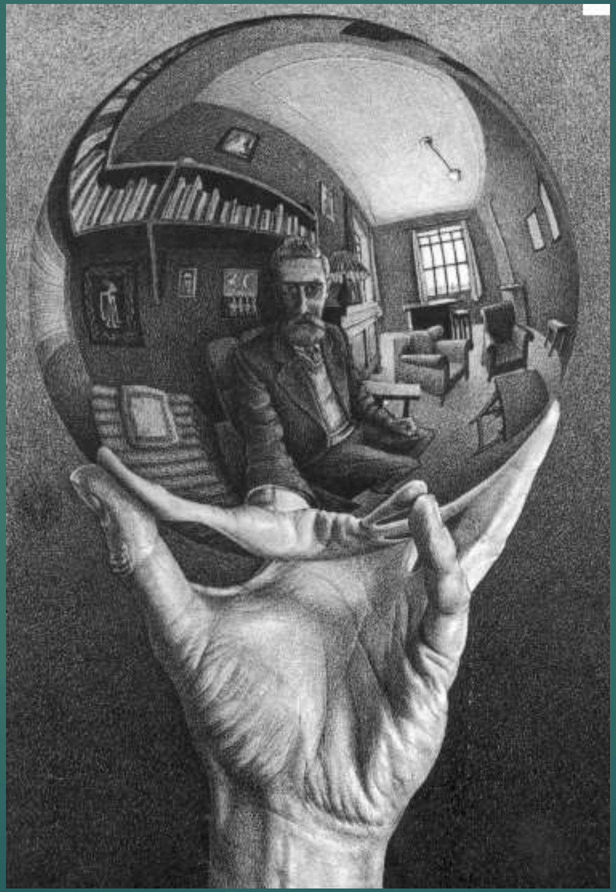
Liberals

- Own more books and travel-related memorabilia
- More open and novelty seeking
- Liberals were reluctant to harm a living thing or act unfairly

Conservatives:

- Linger 15 % longer on repellent images, such as car wrecks and excrement
- Possess more cleaning and organizational items
- Fundamentally more anxious
- Typically desire stability, structure and clear answers even to complicated questions
- People of all political persuasions became more conservative in the wake of the terrorist attacks.
- Asking Republicans to imagine that they possessed superpowers and were impermeable to injury made them more liberal.

Mirror Neurons



Monkey See, Monkey Do

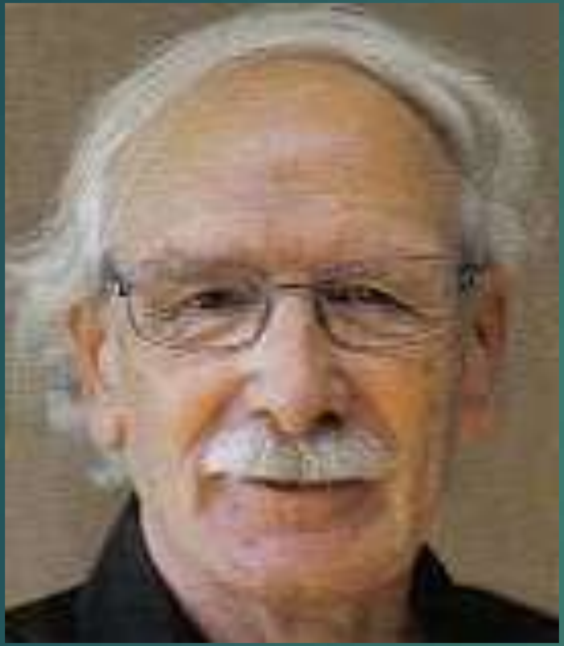
Mirror Neurons:

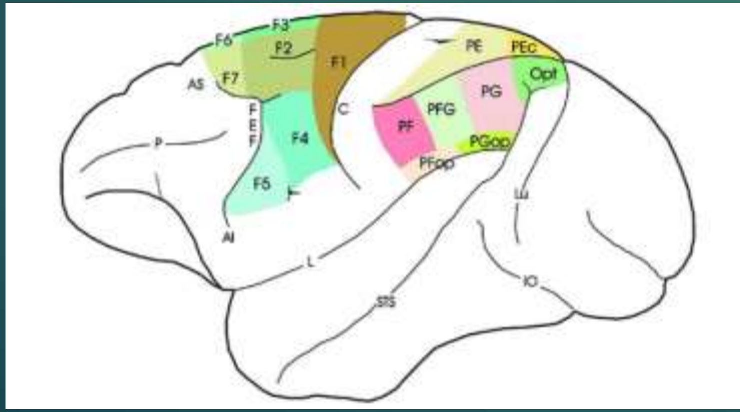
Understanding by an observer without any cognitive mediation

Dr. Rizzolatti:

"Mirror neurons allow us to grasp the minds of others not through conceptual reasoning but through direct simulation. By feeling, not by thinking."

Giacomo Rizzolatti 1937-





- 1992: describes mirror neurons in area F5 of monkey premotor cortex
- Premotor area neurons that discharge both when the monkey does a particular action and when it observes another individual (monkey or human) doing a similar action
- The discovery was initially sent to *Nature* but was rejected for its "lack of general interest"

(Di Pellegrino et al. 1992, Gallese et al. 1996, Rizzolattiet al. 1996a).

Mirror Neurons: Visual motor system & empathy

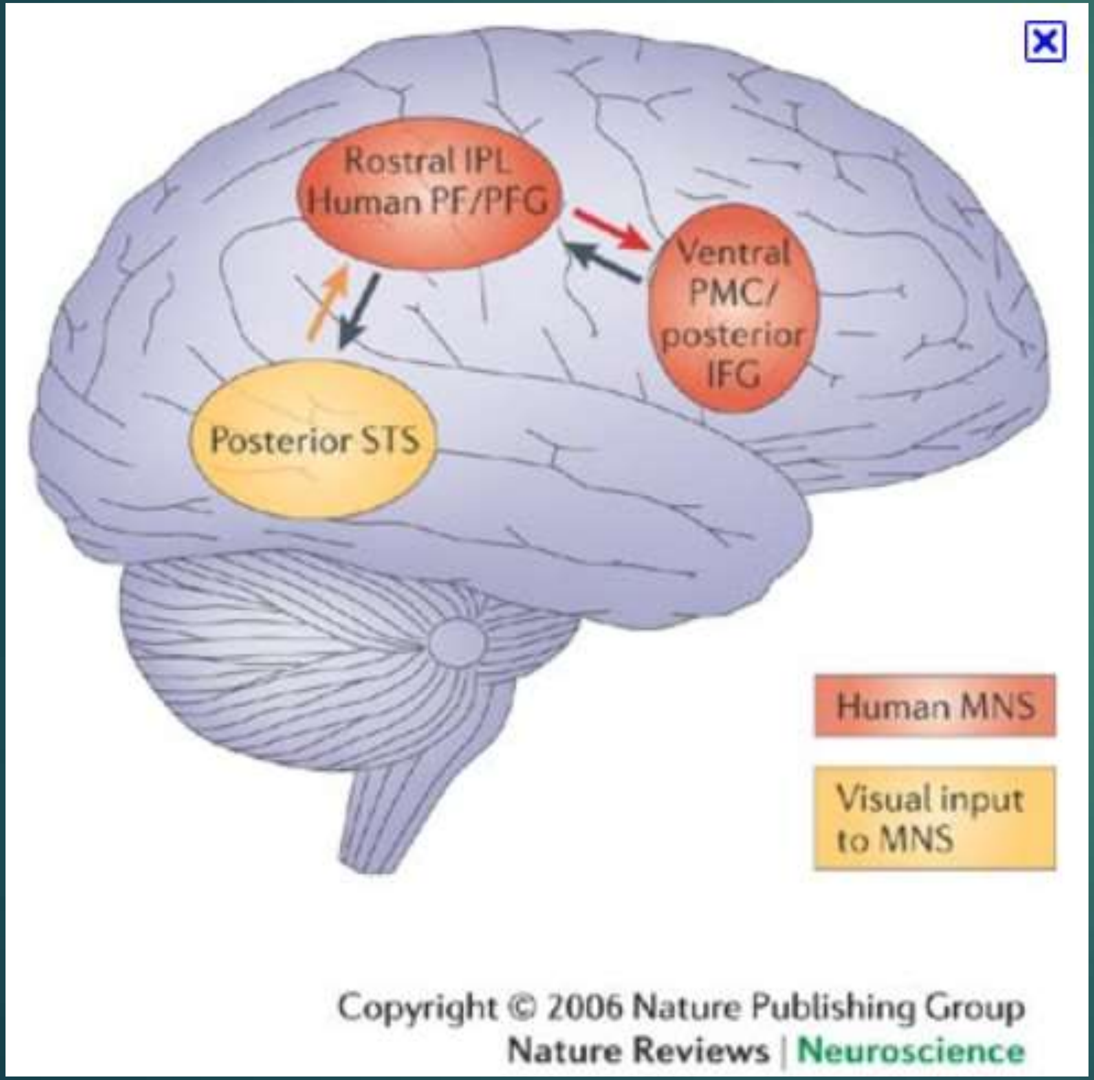
Class of visuomotor neurons, originally discovered in area F5 of the monkey premotor cortex, that discharge both when the monkey does a particular action and when it observes another individual (monkey or human) doing a similar action

Where: Rostral part of the inferior parietal, ventral premotor, primary motor;

Mirror neurons are at the basis of:
- action understanding,
- mediate imitation
- gestural speech understanding
- assessment of complex social situations (aka intuition).

Can mirror: touch, movement, emotions, intentions

Mirror Neurons: Gandhi neurons: dissolve the barrier between you and me



rIPL encodes specific actions, whether they are executed or passively observed

STS: superior temporal sulcus

Social Brain & Orbital Frontal

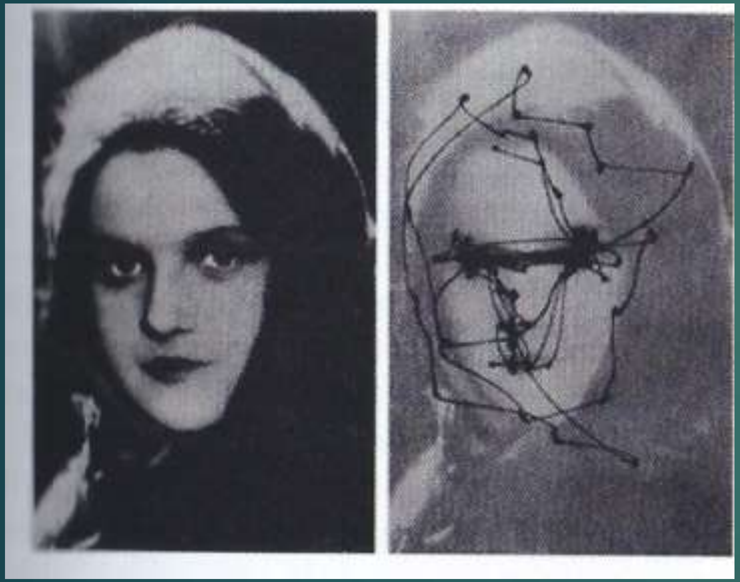
- Intentionality, or Theory of Mind, is the ability to explain and predict the behavior of others by attributing to them intentions and mental states

- Orbital prefrontal cortex volume correlates with intentionality

- Size of each individual's social network is linearly related to the neural volume in individual's orbital prefrontal cortex.

Joanne L. Powell, et al., 2012

Eye Gaze:
Significant key to social interactions



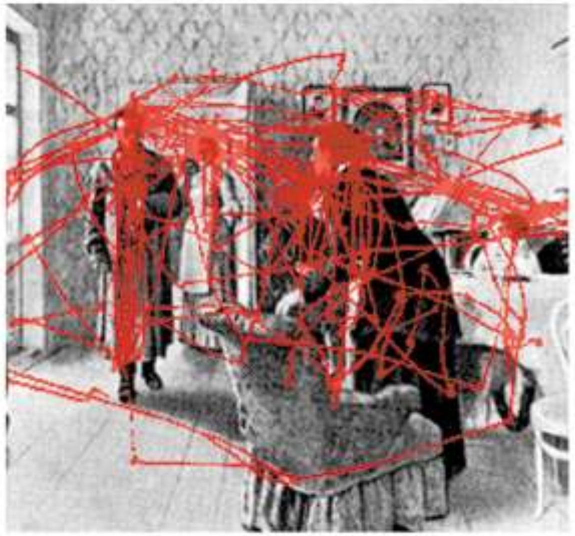
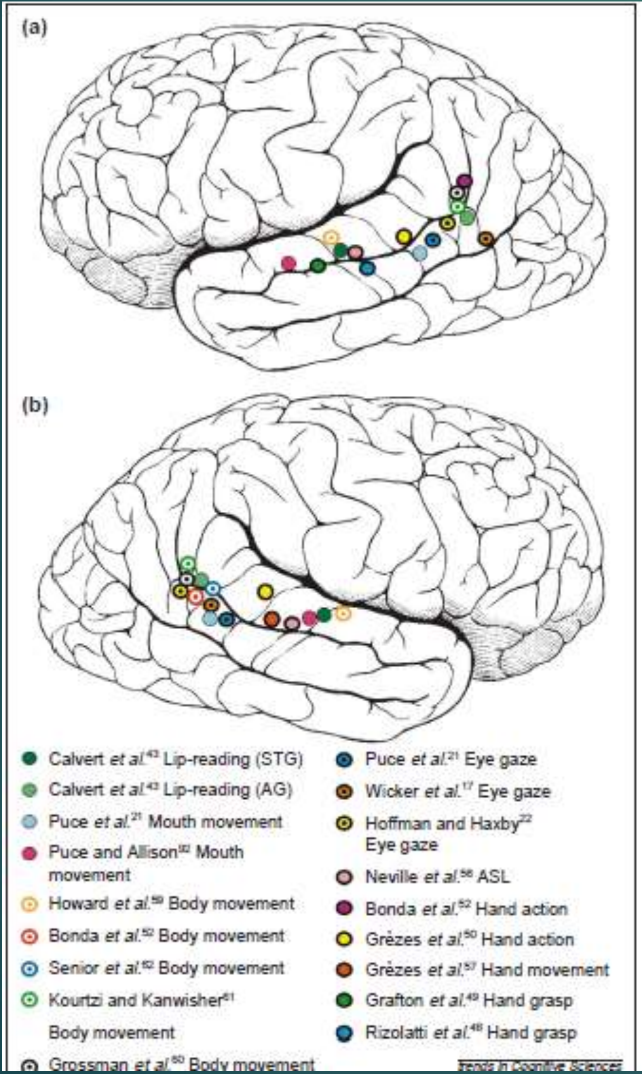


Fig. 1. Eye movement scanpath (in red) of a person viewing a painting by Rein; note the tendency to fixate on the faces. Adapted from Yarbus (*Eye Movements and Vision*, Plenum, New York, 1967).

STS: Superior Temporal Sulcus



Activated:

- Lip reading
- Mouth movement
- Body movement
- Eye gaze
- ASL
- Hand movement
- Hand grasp

T. Allison, et al., 2000

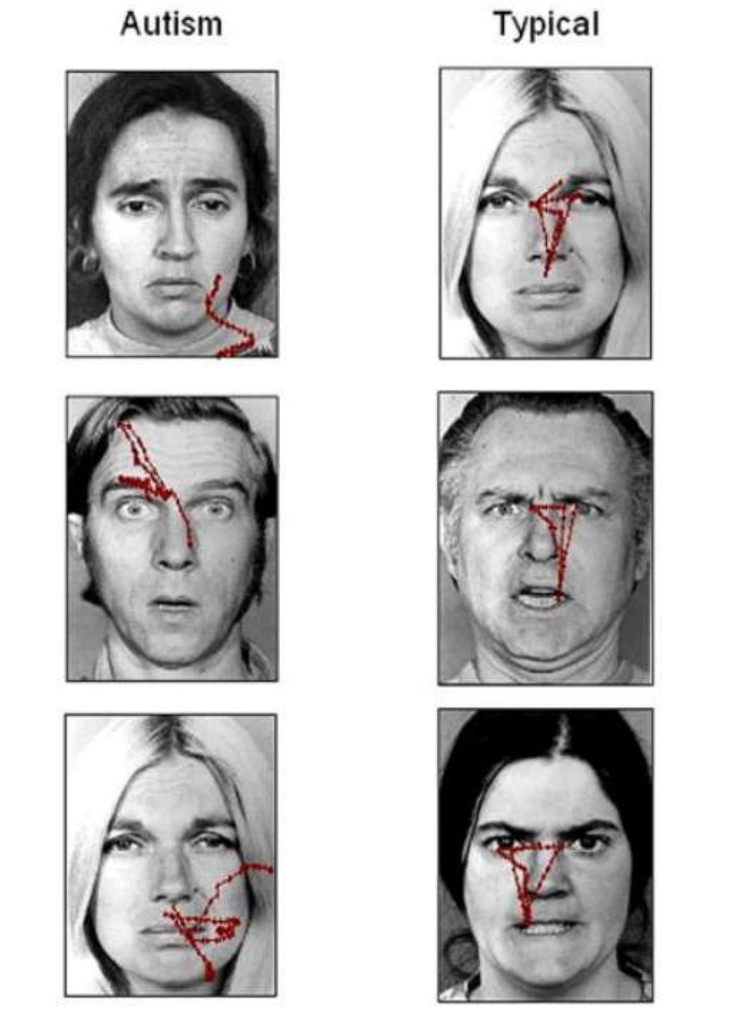
STS: Grasping the Intentions of Others

- STS region is activated by movements of the eyes, mouth, hands and body:

- The posterior STS region:
  - biological motion & intentionality of an action
  - goals of others via gaze shifting or reaching-to-grasp

- In autism, dysfunction in the right STS is strongly and specifically correlated with the level of social impairment exhibited.

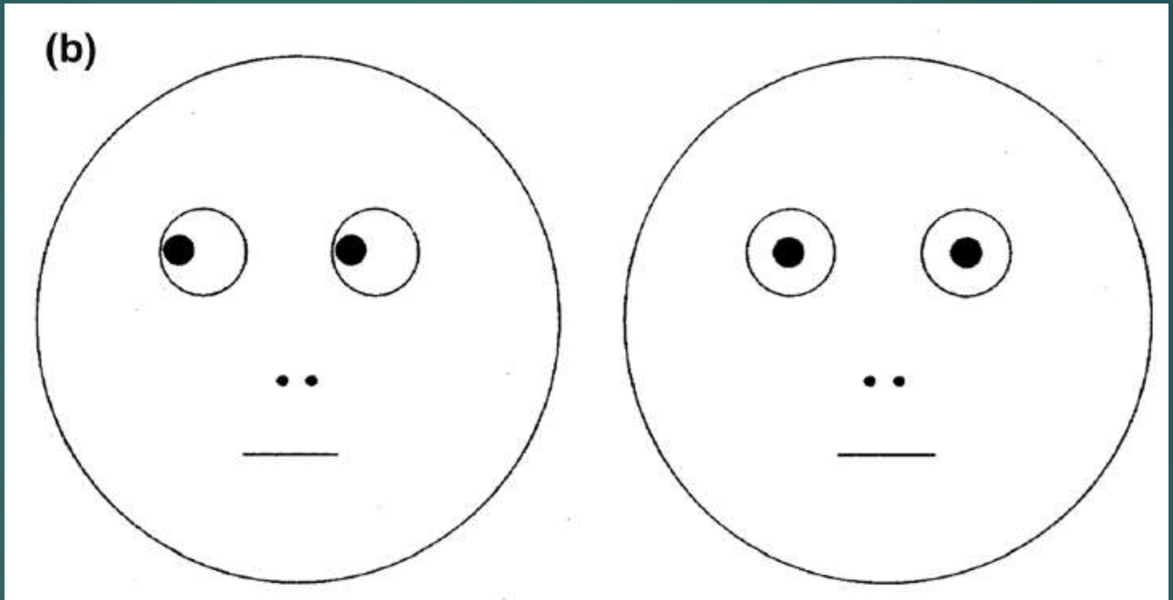
Autism: Deficit in social eye tracking



- Neurologically normal focus on the eyes, nose and mouth).
- Individuals with autism did not look at the eyes
- Using gaze information to infer mental states and intentions is consistently impaired even in high-functioning adults with autism

Pelphrey et al. (2002).

Autism: Able to perceive the direction of gaze



- When asked ‘which one is looking at you?’, autistic children score as well as normal children.

Autism: Can do gaze following, but not it's meaning

When asked which candy 'Charlie' prefers, most normal children point to the Polo Mints, but autistic children are less likely to do so.

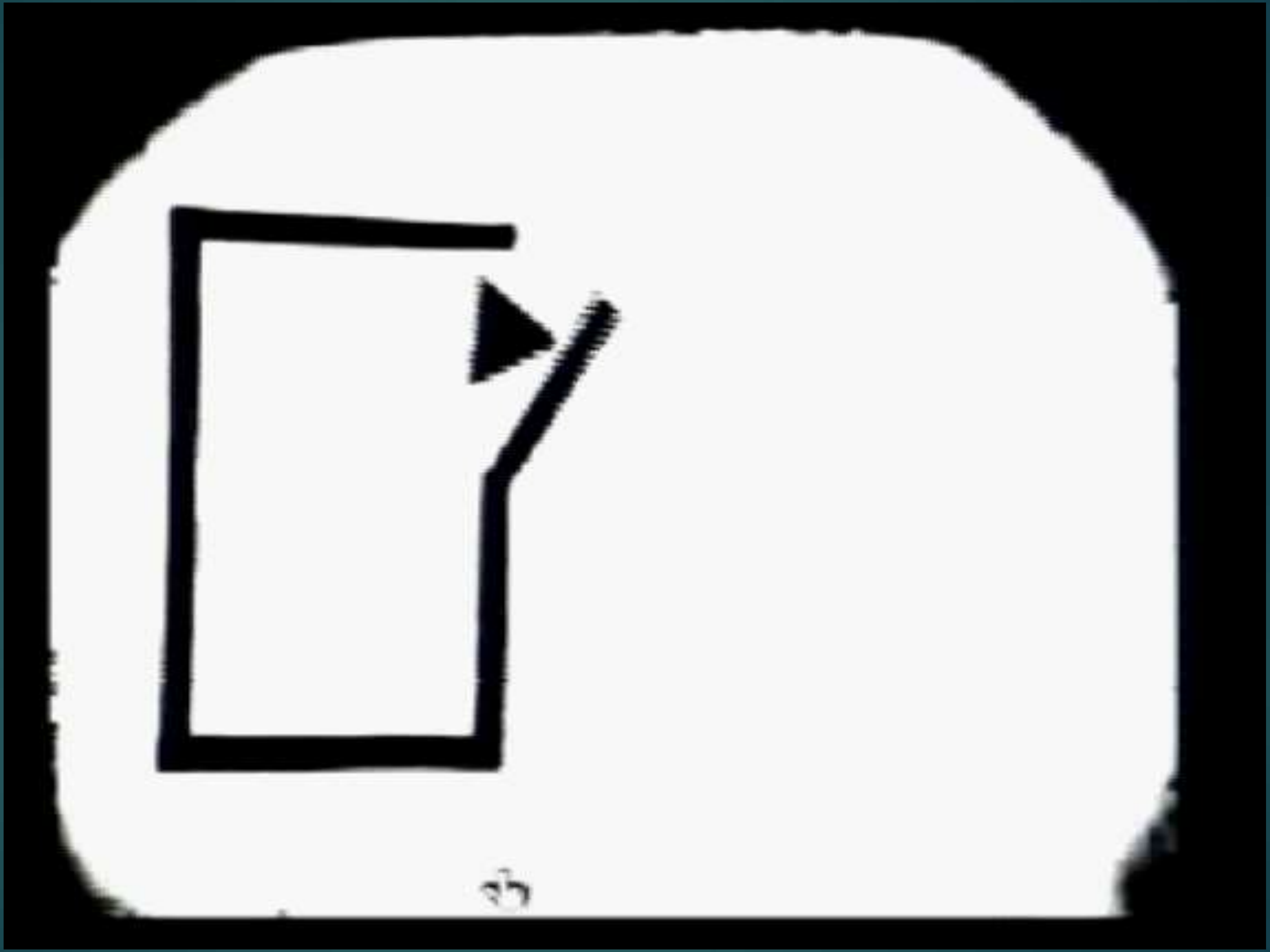
ToM: Theory of Mind

- The term 'theory of mind' (ToM) was coined in by Premack and Woodruff in 1978 in relation to chimpanzees' capacity for deception
- ToM: Other individuals possesses a mind just like one's own.
- ToM is the ability to attribute mental states to others and thus forms the very basis of social interaction and communication.

Premack & Woodruff 1978).

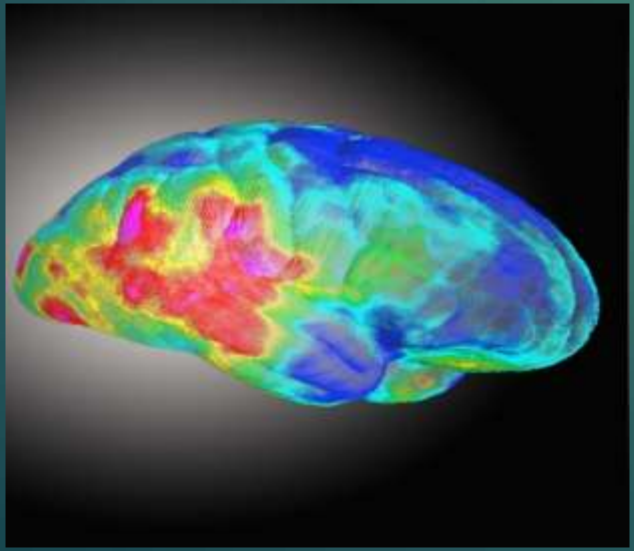
Neural circuits of ToM

- Medial prefrontal cortex (mPFC),
- Posterior superior temporal sulcus (pSTS),
- Precuneus and amygdala/temporopolar cortex
- RTPJ



Heider-Simmel Animation

William's Syndrome: Social ++



- Neurodevelopmental disorder
- Intellectual disability
- Unusually cheerful demeanor and ease with strangers
- Severe VS deficits

William's Syndrome: No Social Fear

- Gregarious, Increased empathy, no social fear
- Positive interpersonal facial perceptual bias
- Inability to detect social danger
- Reduced Amygdala activation to social danger cues (faces)
- Increased activation in the MNS (Inf PFC, bilateral IPL, and right STS)

(Hoeft et al, 2007)

Social areas of brain: predominantly right hemisphere

- Social Self Monitoring: right medial & orbital frontal
- Detection of sarcasm: right parahippocampal
- Embarrassment: right pregenual anterior cingulate
- Ability to track dynamically changing emotions: right OFC

Transcendence and the Right Parietal Lobe

- A neuropsychological model that proposes spiritual experiences associated with selflessness are related to decreased activity in the right parietal lobe.
- People with injuries to the right parietal lobe of the brain reported higher levels of spiritual experiences, such as transcendence.
- Norman Geschwind: epileptics have most conversions

Libet: Does Mind Control the Brain (Free Will ?)

- In 1977, Benjamin Libet devised cleverly designed experiments at the UCSF, that detected activity in the motor cortex of subjects nearly half a second before they became conscious of their decision to press a button.

- This suggested to many that free will was an illusion.

- Libet also showed that there is a brief window of time in which the conscious mind can still veto an action before it is taken.

- These and other experiments reinforced the notion that much of what goes on in our brain takes place outside of conscious awareness

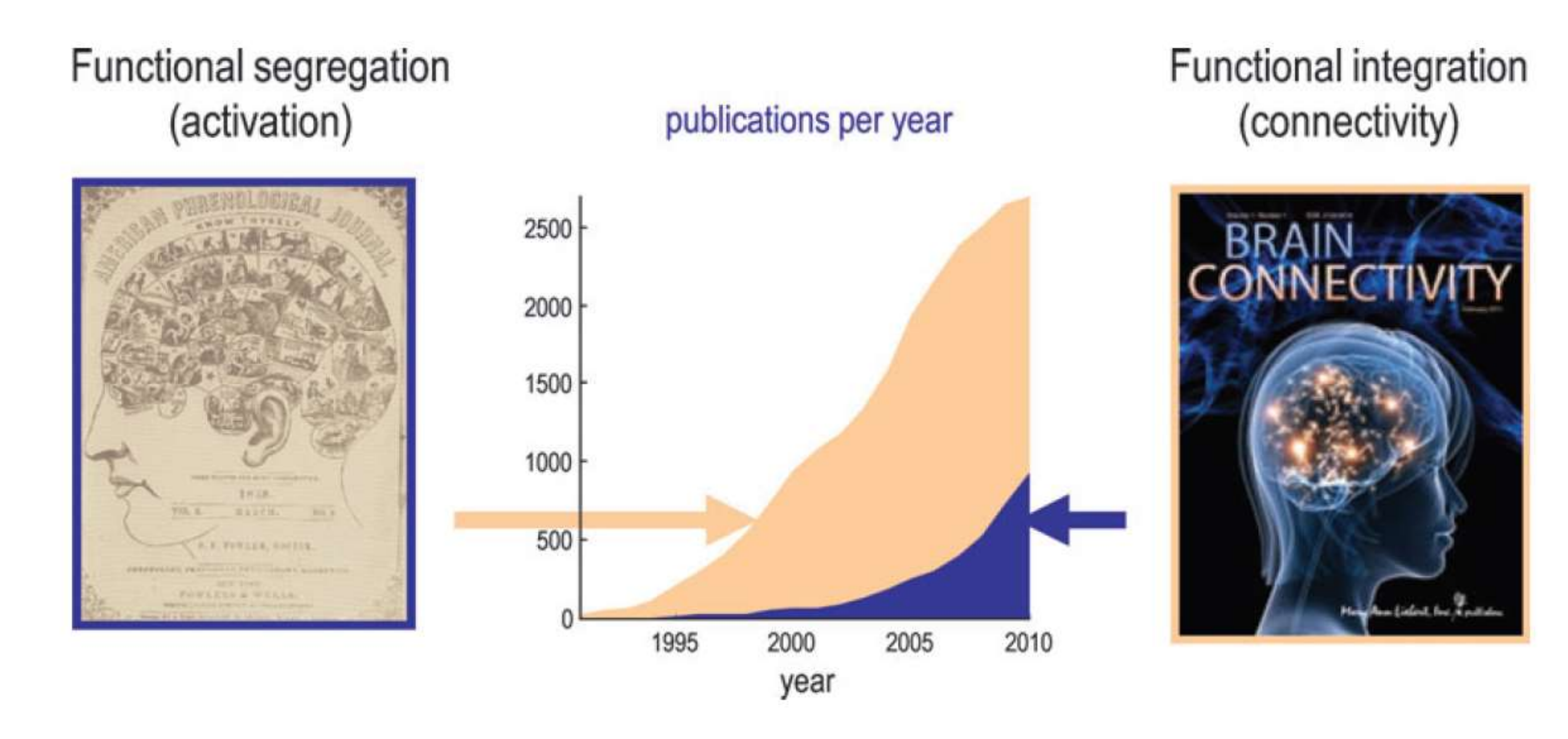
Not Free Will but Free Won’t: 100 ms to say no

- Libet told subjects to move their fingers whenever they felt like it. Libet detected brain activity suggesting a readiness to move the finger half a second before the actual movement and about 400 milliseconds before people became aware of their conscious intention to move their finger.

- Libet argued that this leaves 100 milliseconds for the conscious self to veto the brain's unconscious decision, or to give way to it -- suggesting, in the words of the neuroscientist Vilayanur S. Ramachandran, that we do not have free will but "free won't."“

- See *Free Will* by Sam Harris: we are not in control of our thoughts or our actions: all determined by prior experience & nonconscious processing

Growing Research on Connectivity



Intrinsic Connectivity Networks (ICNs): Brain Networks (8-14 in all)

- Default Mode Network (DMN)
- Task-Positive Network TPN (or Executive Control Network)
- Salience Network (SN)
- Valuation & Context Appraisal Network
- Spatial Attention Network

(Beckmann et al., 2005; Damoiseaux et al., 2006; Dosenbach et al., 2007; Seeley et al., 2009).

3 Major Networks: SN, CEN, DMN

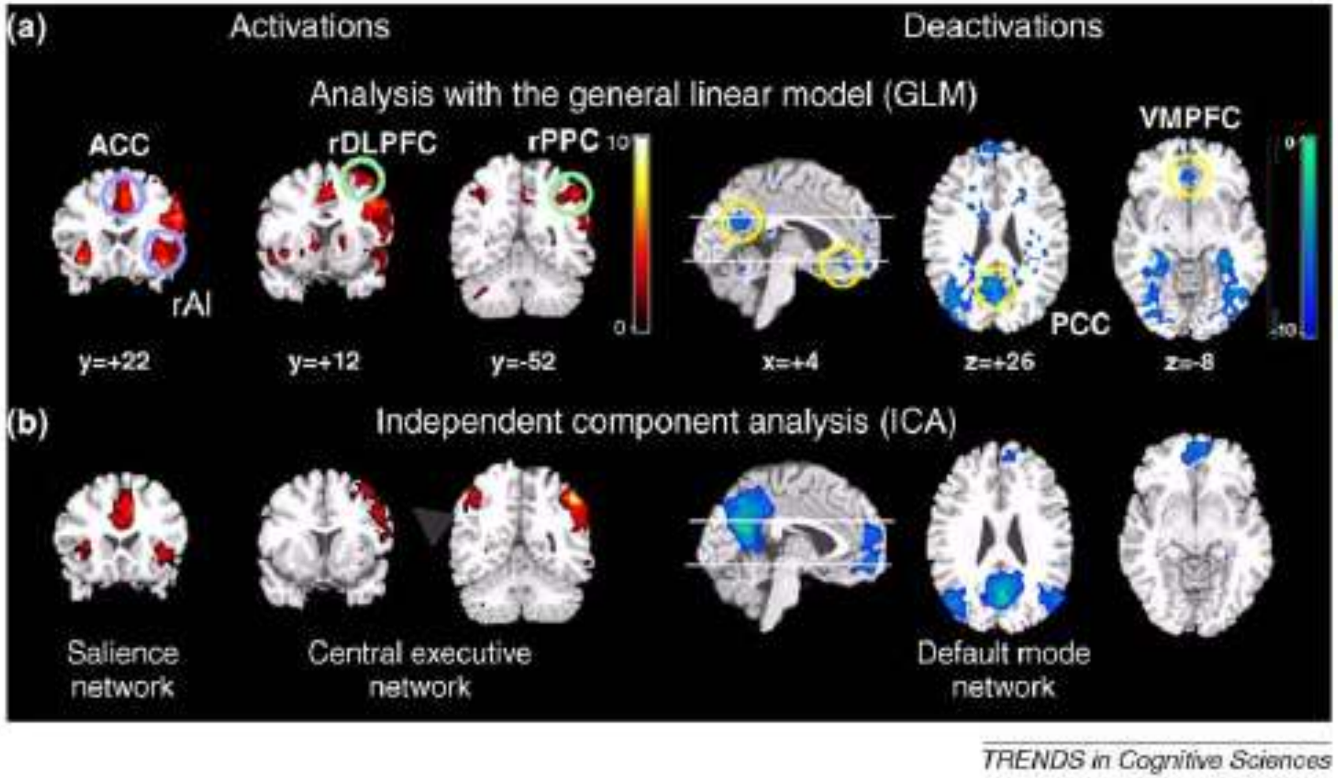


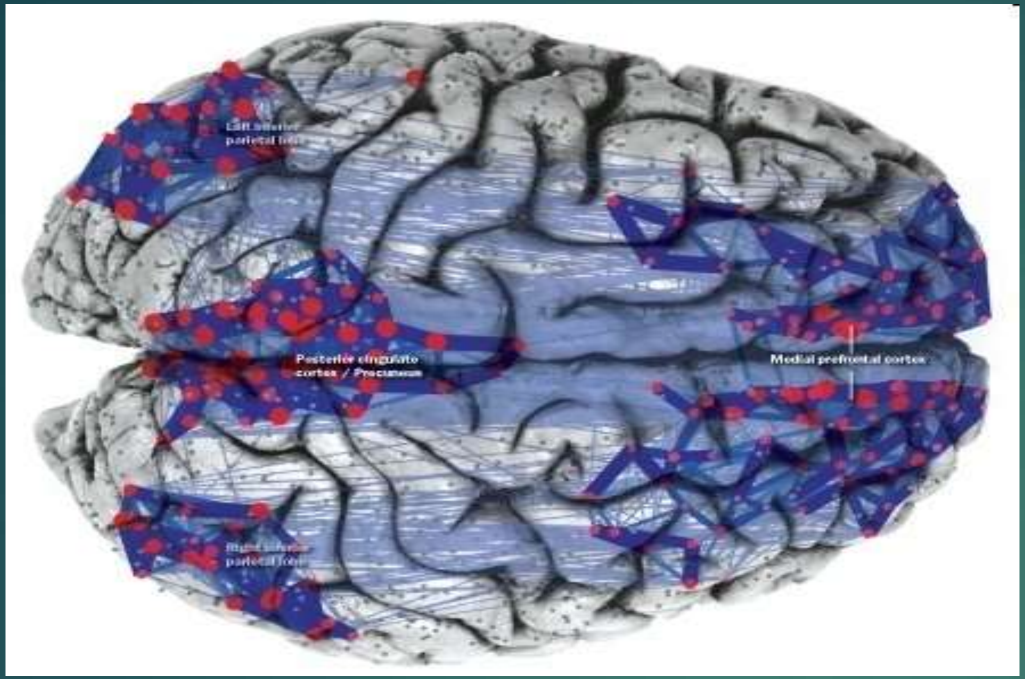
Figure 6. Three major functional networks in the human brain identified using converging methodologies. Task-related activation patterns in the central-executive and salience networks, and deactivation patterns in the default-mode network during an auditory event segmentation task. Activation and deactivation patterns can be decomposed into distinct subpatterns. **(a)** Analysis with the general linear model revealed regional activations (left) in the right AI and ACC (blue circles) and the DLPFC and PPC (green circles), and deactivations (right) in the ventromedial (VM)PFC and PCC. **(b)** Independent component analysis provided converging evidence of spatially distinct networks. From left to right: salience network (rAI and ACC), central-executive network (rDLPFC and rPPC), and default-mode network (VMPFC and PCC). (Reproduced with permission from [129].)

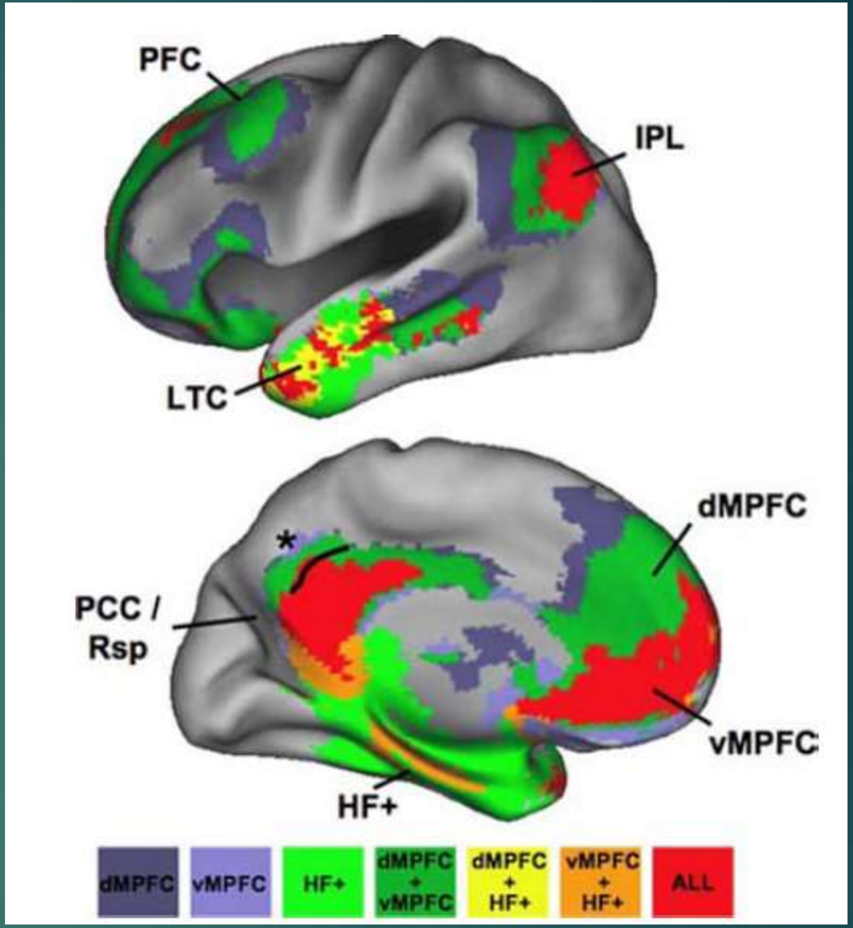
Brain's Dark Energy: Default Mode Network

- Hans Berger, 1929: brain always active
- Brain activation for thinking: often increases of less than 5%
- 60–80% of overall brain energy consumption is devoted to neuronal signaling, to functionally significant intrinsic activity, in circuits unrelated to any external events

Marcus Raichle: Default Mode Network, 2001

- Marcus Raichle coined "default-mode" in 2001
- DMN: distributed network that is active when the brain is resting and that powers down during focused mental tasks.
- Activates during daydreaming, self-referential thought , envisioning the future, retrieving memories, and gauging others' perspectives.
- Interacting subsystems: vmPFC, PCC, IPL, LTC, dmPFC, Hippo (no sensory or motor areas; all connect to Hippo)





The brain's **default mode network**.
The default network has two major hubs: posterior cingulate cortex/precuneus and medial prefrontal cortex.
Subsystems: vmPFC, PCC, IPL, LTC, dmPFC, Hippo

Olaf Sporns/Indiana Univ. (modified by J. Korenblat);

Default Mode Network

- Default Mode Network (DMN): brain maintains high level of activity even when at rest
- Mind "at rest" (daydreaming, asleep, anesthetized): 20 x energy consumption than when alert/attention-demanding tasks
- Lead to study of Intrinsic Connectivity Networks (ICNs), like DMN

DMN: automated information processing

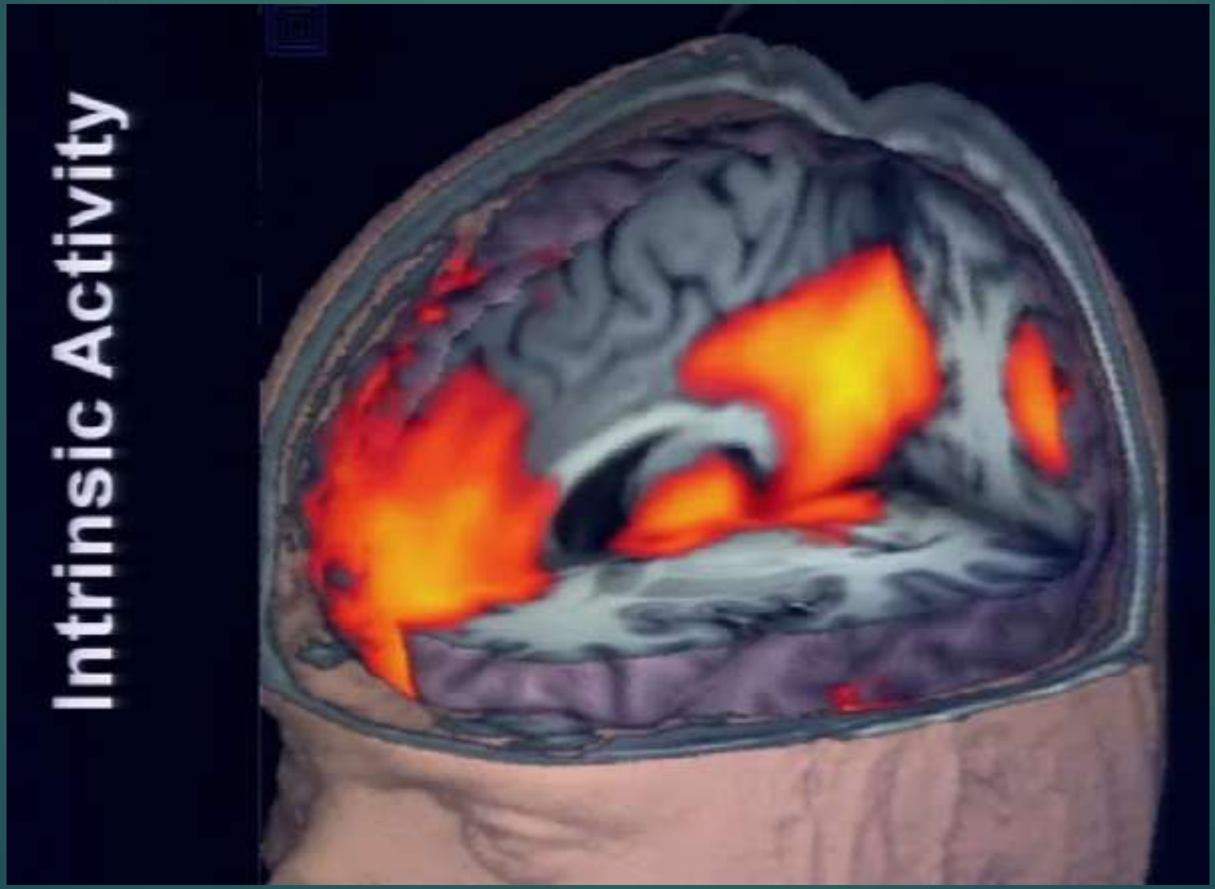
- DMN Functions: daydreaming, thinking about the past, planning for the future, and creativity
- Abnormal activity in the DMN has been linked to an array of disorders including Alzheimer's disease, schizophrenia, attention-deficit/hyperactivity disorder (ADHD) and disorders of consciousness.
- DMN: switch to 'autopilot' once we are familiar with a task.
- During the task acquisition stage, the dorsal attention network, which has been associated with the processing of attention-demanding information, was more active.
- During task application stage, where participants utilized learned rules from memory, the DMN was more active.

Vatansever, D, et al., 2017

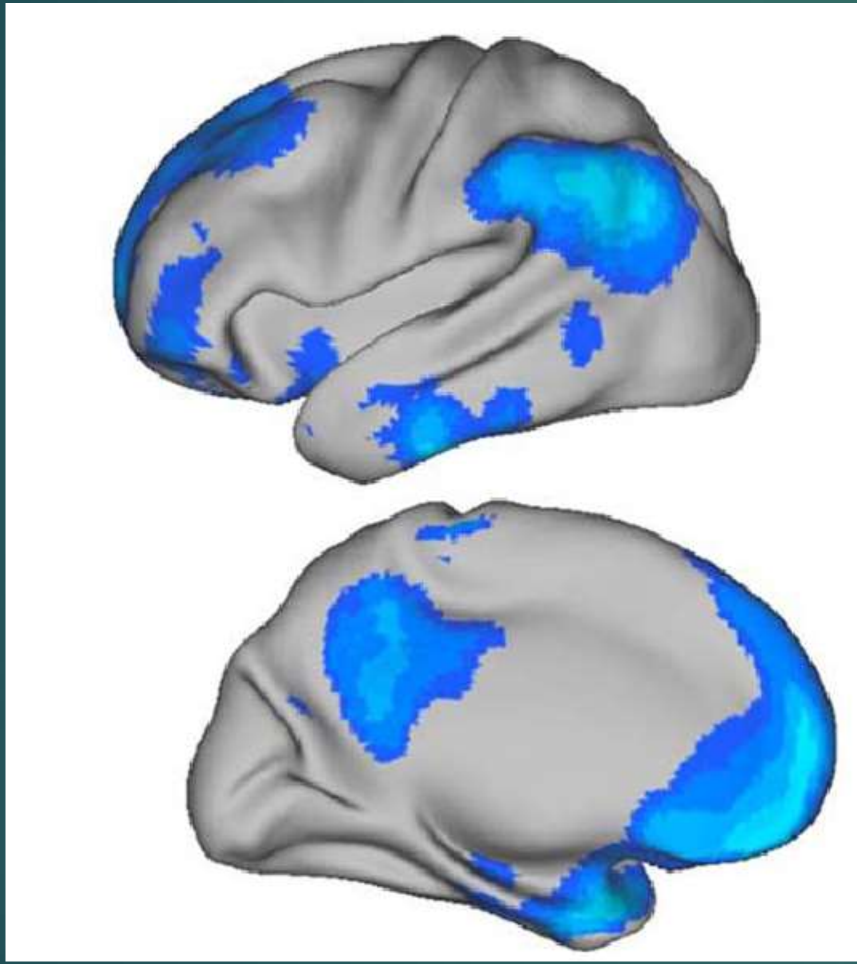
DMN 2

- During the application stage, the stronger the relationship between activity in the DMN and in regions of the brain associated with memory, such as the hippocampus, the faster and more accurately the volunteer was able to perform the task. This suggested that during the application stage, the participants could efficiently respond to the task using the rule from memory.
- DMN: It is essentially like an autopilot that helps us make fast decisions when we know what the rules of the environment are, i.e. when driving on autopilot.
- Daniel Kahneman's fast intuitive system: significant correlation between this network and hippocampal connectivity and individual differences in the participants' ability to make automated, fast, and accurate responses i.e., when rapidly selecting appropriate responses under predictable behavioral contexts.

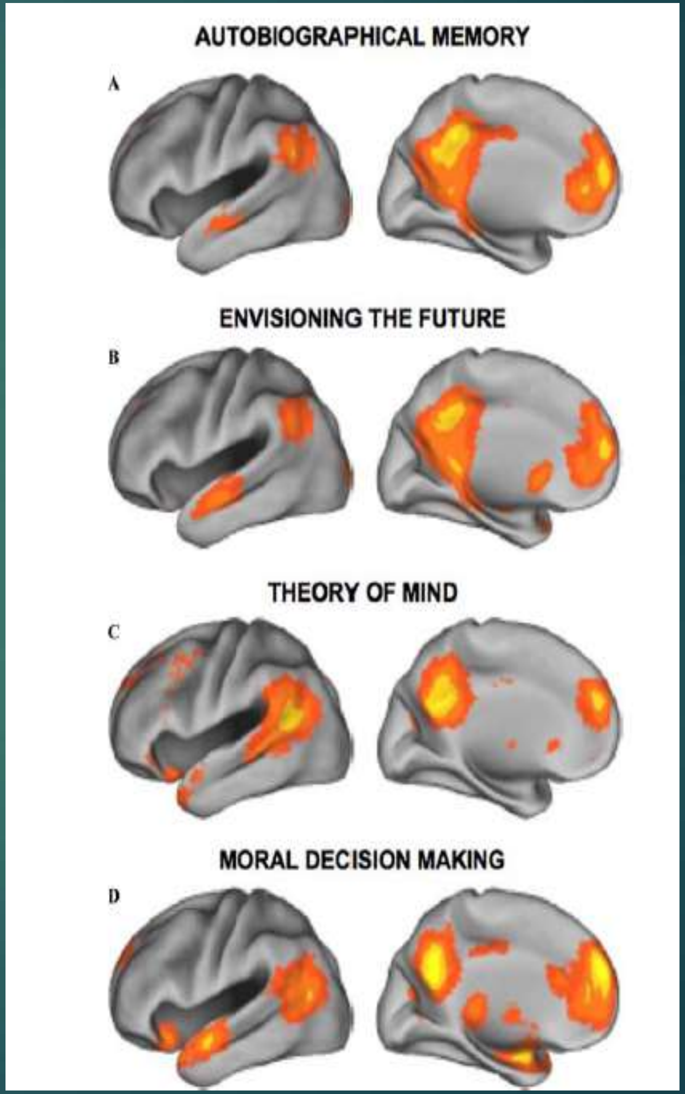
FMRI of DMN locales



DMN sites



Shulman et al. (1997; reanalyzed in Buckner et al. 2005).



Frequent mind wandering correlates with most active DMN

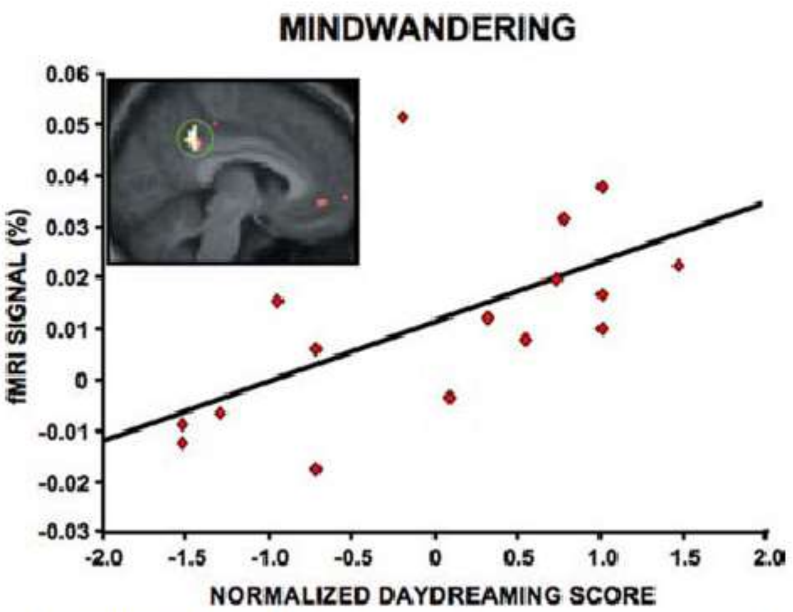


FIGURE 9. The default network is most active in individuals who report frequent mindwandering, suggesting a functional role in spontaneous cognition. Activity estimates are plotted for 16 subjects from PCC/Rsp (region shown in insert) from a task contrast conducive to encouraging mindwandering. The activity within this region is significantly correlated with individual self-reports of daydreaming obtained outside the scanner. Adapted from data published in Mason et al. (2007).

Functions of Default Network: Mind wandering

- self- awareness,
- creative incubation,
- improvisation and evaluation,
- memory consolidation,
- autobiographical planning,
- goal driven thought,
- future planning,

- retrieval of deeply personal memories,
- reflective consideration of the meaning o
events and experiences,
- simulating the perspective of another person,
- evaluating the implications of self and others' emotional reactions,
- moral reasoning,
- reflective compassion

(Singer and Schonbar, 1961; Singer, 1964b; Singer, 1966, 1974, 1975, 1993, 2009; Wang et al., 2009; Baars, 2010; Baird et al., 2011, 2012; Kaufman and Singer, 2011; Stawarczyk et al., 2011; Immordino-Yang et al., 2012; Kaufman, 2013).

2017: Two DMN networks

- Using multivariate pattern analysis, the researchers identified two reliable and distinct mind-wandering patterns:
  - one that linked connectivity within the default-mode network and positive habitual experiences and
  - another that linked connectivity between the posterior cingulate cortex and the medial prefrontal cortex with spontaneous off-task thoughts.
- The findings indicate that mind wandering is not a unitary construct but is instead multidimensional in its content, neural basis, and functional outcomes.

Network Seesaw: Either DMN or CEN - Anticorrelation

- Central Executive: The task-positive network is active when you're actively engaged in a task, focused on it, and undistracted
- DMN: The task-negative network is active when your mind is wandering; this is the daydreaming mode. Daydreaming can lead to creativity
- These two attentional networks operate like a seesaw in the brain: when one is active the other is not.
- Switch between daydreaming and attention is controlled by the insula, the attentional switch

Meditation: DMN shows decreased activation

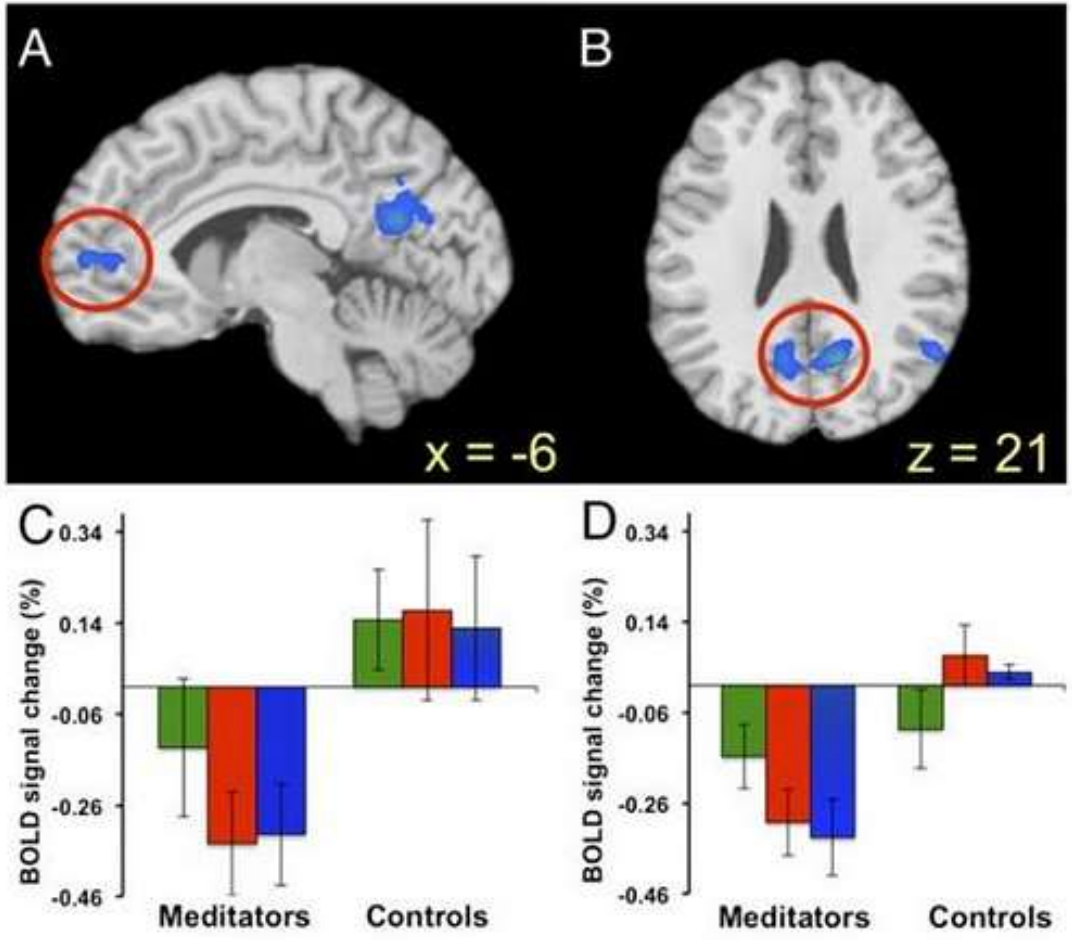


Fig. 1. Experienced meditators demonstrate decreased DMN activation during meditation. Brain activation in meditators > controls is shown, col-

Salience Network: FI & pACC

- Activate in response to varied forms of social salience:
  - emotional dimensions of pain
  - empathy for pain
  - metabolic stress, hunger, or pleasurable touch
  - enjoyable "chills" to music
  - faces of loved ones or allies
  - social rejection
  - anxiety

- Damage = U curve tuning: too low = social insensitivity, poor social skills; too high = anxiety

Salience Network

- SN = FTD central
- Medial (reward) to lateral (punishment)
- Not knowledge, but evaluation/application;
- Damage = failure to access rule, not absence of rule
- Dorsal damage: Cortical Basal Degeneration (CBD) – more apathetic
- Ventral damage: FTD/Pick’s

Two Opposing Networks: DMN & SN

- Posterior 'Default Mode Network' (atrophied in AD, but enhanced in bvFTD).

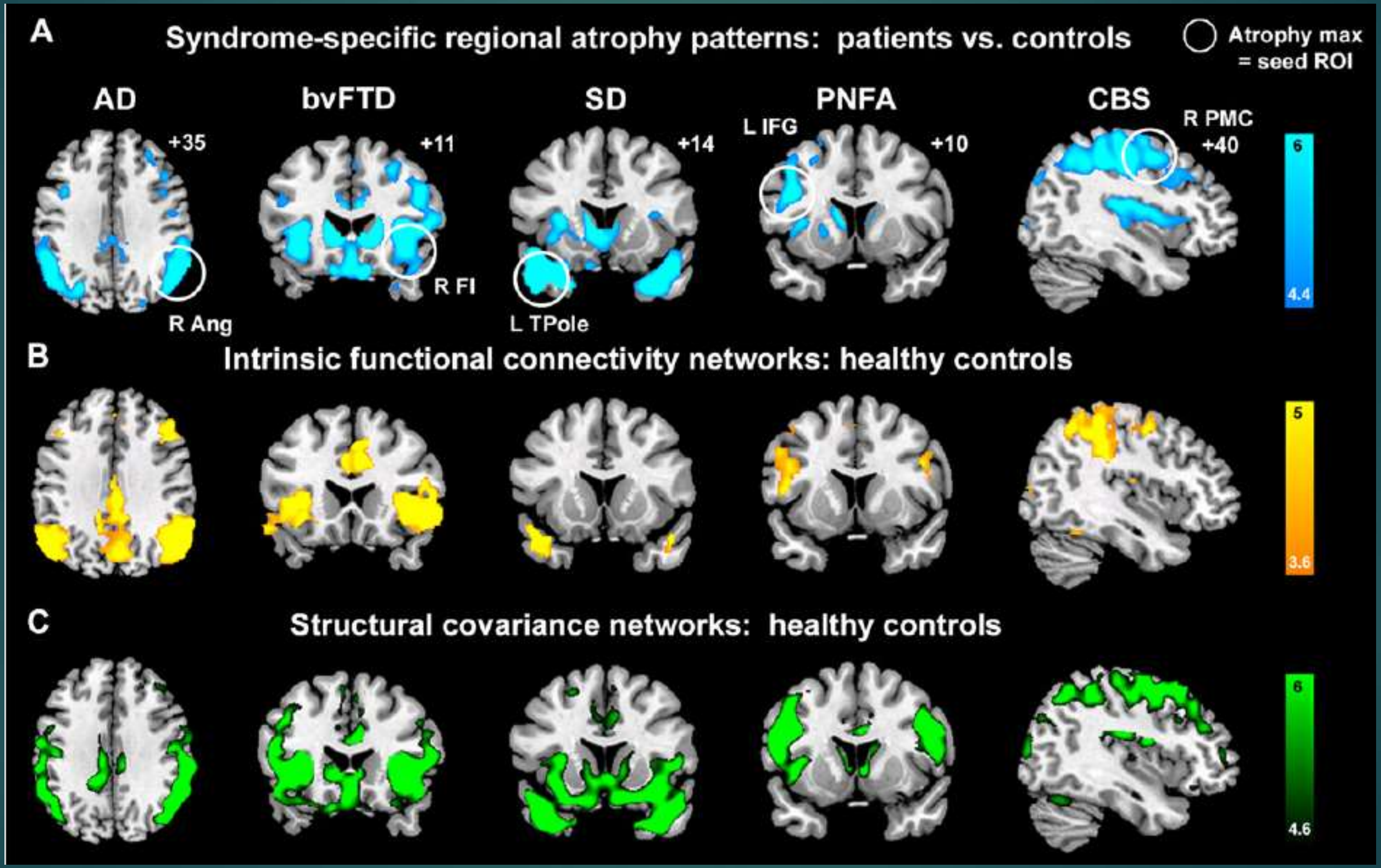
- Anterior 'Salience Network' (atrophied in bvFTD, but enhanced in AD)

- These networks exhibit an anti-correlated relationship with each other in the healthy brain.

Impairment of DMN

- Autism: Reduced DMN activity
- Schizophrenia: Overactive DMN
- Old age: Impaired control of entering and leaving the DMN.
- AD atrophied areas exactly match DMN areas
- Can tell 30 seconds ahead by watching DMN if error is about to be made: DMN takes over

Syndromic Atrophy: Five distinct clinical syndromes showed dissociable atrophy patterns.



Alterations in connectivity within large-scale CNS networks, including the DMN, can be used to phenotype CNS diseases.

Where is the Second Brain?

- The second brain contains some 100 million neurons, more than in either the spinal cord or the peripheral nervous system.

Second Brain

- The enteric nervous system, the second brain consists of sheaths of neurons embedded in the walls of the alimentary canal, which measures about nine meters end to end from the esophagus to the anus.
- Own reflexes and senses
- 90 percent of the fibers in the vagus carry information one way from the gut to the brain
- The enteric nervous system uses more than 30 neurotransmitters, just like the brain, and 95 percent of the body's serotonin is found and used in the bowels.
- Bowels carries at least 160 bacterial species (3 lbs., 100 trillion cells). Together, our collective guts have just under 3.3 million bacterial genes, more than 150 times as many as reside in our own genomes.
- Excess salt in stomach produces poorer memory independent of HTN

Fundamental Reference Library

- Principles of Neural Science, 5e – by Eric R. Kandel, J. Schwartz, et al. (2012) (1760 p)
- *Fundamentals of Human Neuropsychology* - B. Kolb & I. Whishaw (2008)
- *Neuropsychological Assessment, 5e* – Muriel Lezak, D. Howieson, E. Bigler & D. Tranel (2012) (1200p)
- *Clinical Neuropsychology: A Pocket Handbook For Assessment* - P. Snyder, P. Nussbaum, D. Robins (eds.) (2005)
- *The Little Black Book of Neuropsychology* – M. Schoenberg & J. Scott, (eds.)
- *Clinical Neuropsychology* - K. Heilman and E. Valenstein (2011)
- *Clinical Neuropsychology Study Guide and Board Review* – K. Stucky, M. Kirkwood, J. Donders (2013)
- * *Neuroanatomy Through Clinical Cases* by H. Blumenfeld, 2e, (2011)

Fundamental Reference Library 2

- *Clinical Neuroanatomy: A Neurobehavioral Approach* – A. Foundas & J. (2011)
- *Principles of Behavioral and Cognitive Neurology* - M. Mesulam (2000)
- *Adams and Victor's Principles of Neurology*, 10th Ed. - A. Ropper, M. Samuels & J. Klein (2014)
- *The Little Black Book of Neurology*, 5e - O. Zaidat & A. Lerner (2008)
- *A Compendium of Neuropsychological Tests: Administration, Norms, and Commentary*, 3e – E. Strauss, E.Sherman, & O. Spreen (2006)
- *Handbook of Normative Data for Neuropsychological Assessment*, 2e – M. Mitrushina, K. Boone, J. Razani, L. D'Elia (2005)

Neuroanatomy Books

- * *Neuroanatomy Through Clinical Cases* by Blumenfeld
- *Neuroanatomy - Fix*
- *Neuroanatomy: An Atlas of Structures, Sections, and Systems* by Haines
- *The Human Brain: An Introduction to Its Functional Anatomy* by Nolte
- *Atlas of Morphology and Functional Anatomy of the Brain* by Scarabino, Salvolini, Salle, Duvernoy, Rabischong
- *Netter's Concise Neuroanatomy* by Rubin and Safdieh
- *Atlas of Neuroanatomy and Neurophysiology (Sections from the Netter Collection of Medical Illustrations),* text by Hansen and Koeppen, illustrations by Netter, Craig, Perkins
- *Neuroanatomy: Draw It to Know It* by Fisch
- *Atlas of the Human Brain* by Mai, Paxinos, Voss
- *Clinical Neuroanatomy* by Waxman
- *Neuroanatomy for the Neuroscientist* by Jacobson and Marcus

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