A Brief Course in Brain Anatomy & Functional Neuroanatomy Part 2

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Acknowledgement:

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

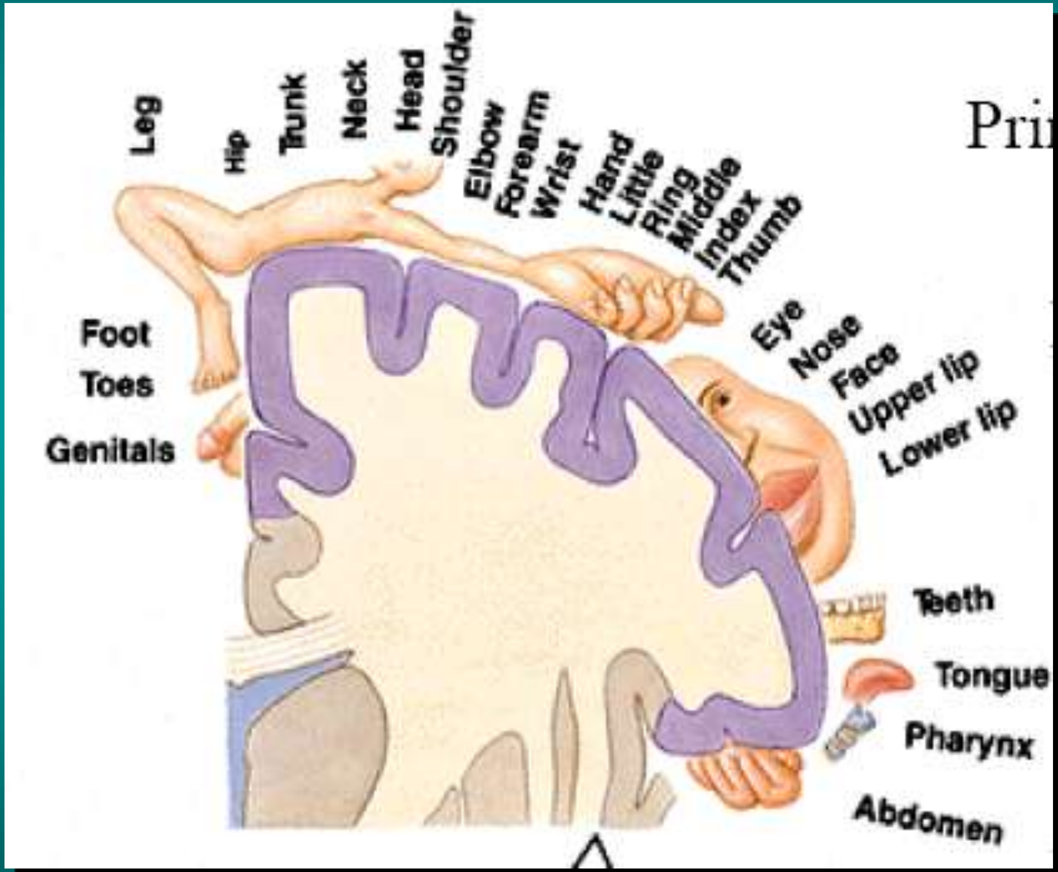
Parietal Lobe: Somatosensory System

- A collection of systems:
  Touch, pressure, temperature, pain
- Four somatotopic maps, two responsive to skin, two responsive to deep receptors

Parietal Lobe

- Anterior:
  - 2 –point threshold
  - Perception of passive movement
- Posterior
  - Ability to identify objects by touch
  - Knowledge or sense of one's own body and bodily condition
  - Body map: your body & space around it

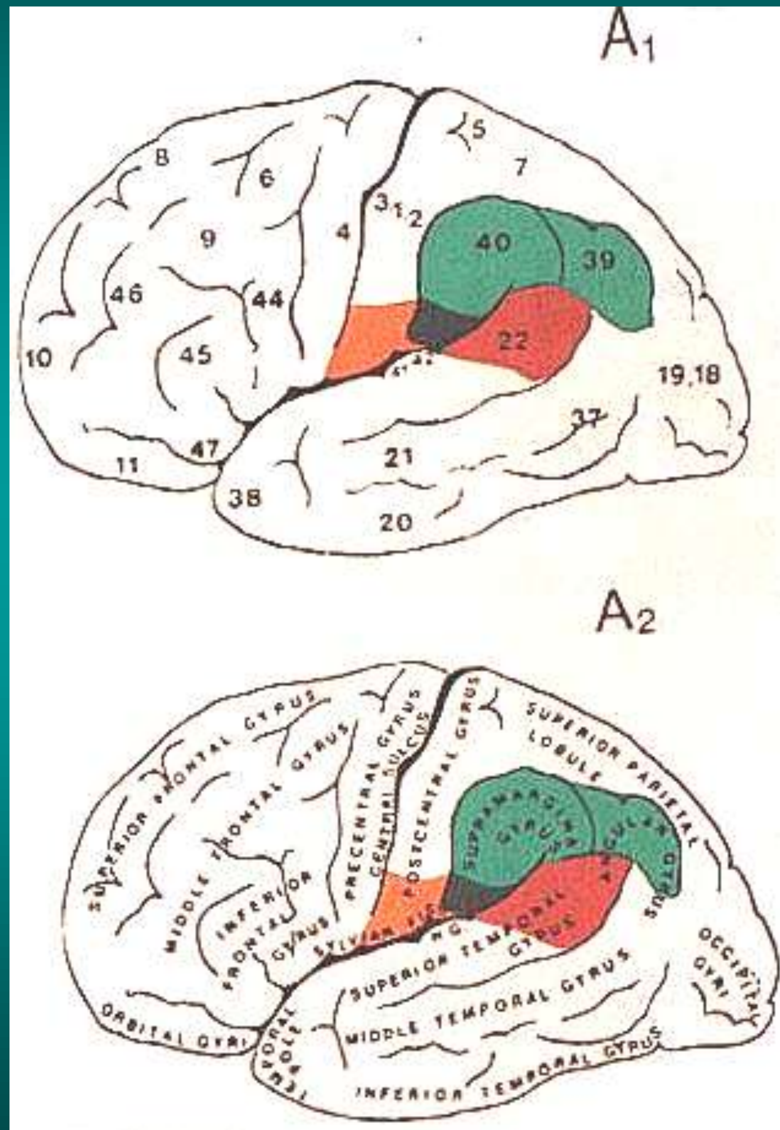
Primary Somatosensory Strip



Parietal Lobe Damage: Sensory

- **Tactile Agnosia (no recognition by touch)**
- **Anosognosia (lack klg of disease: denial of disability): 30% of stroke hemiplegia, right parietal**
- **Autopagnosia (unable to point to fingers)**
- **Contralateral Neglect**

Neuropsychological Manifestations of Parietal Lobe Lesions



Tranel, 1992

Neuropsychological Manifestations of Parietal Lobe Lesions

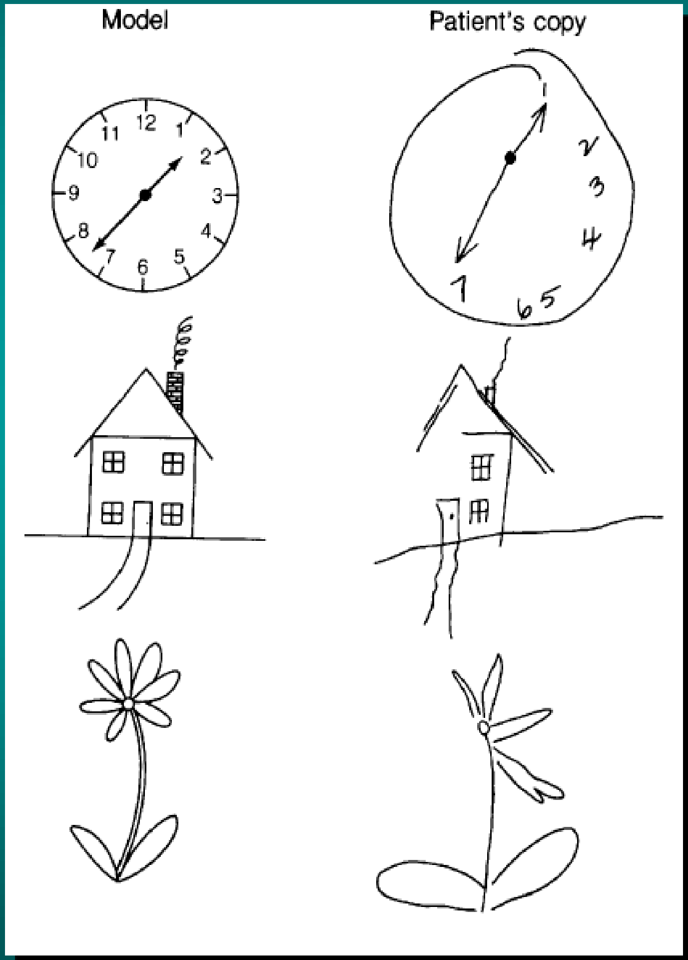
Temporoparietal Junction (including posterior superior temporal gyrus, 22, inferior 39,40)

- A) Left: Wernicke’s aphasia
- B) Right: Amusia, defective music recognition, ‘phonagnosia’ (familiarity of voice) (Capgras syndrome)
- C) Bilateral: auditory agnosia

Inferior Parietal Lobule (39,40)

- A) Left: Conduction aphasia, tactile agnosia
- B) Right: neglect, anosognosia, tactile agnosia, anosodiaphoria (indifference to disability)
- C) Balint’s syndrome (paralysis of gaze)

Left Visual Neglect



Posterior Parietal Lobe Damage: Motor 1

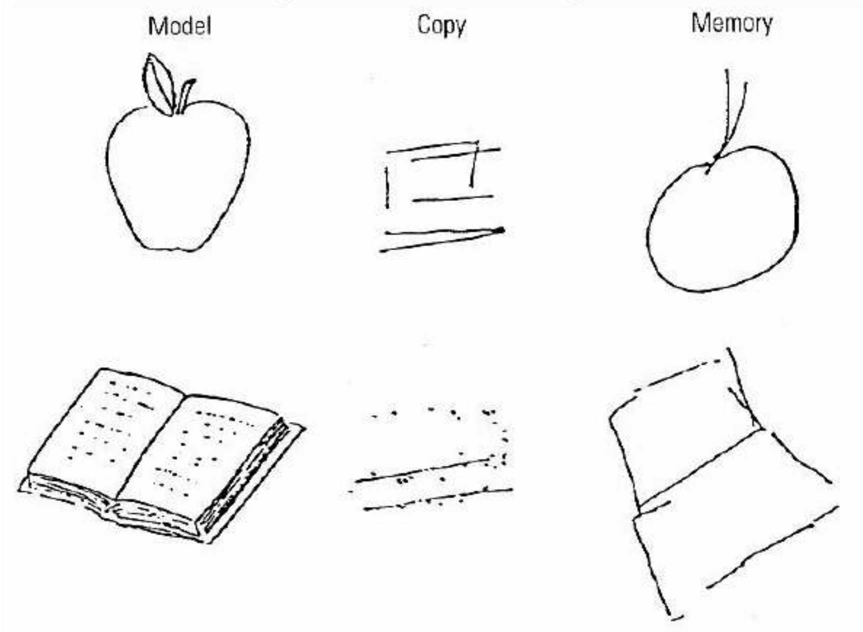
- Loss of skilled movement not due to motor weakness
- Left Hemisphere:

  Ideomotor apraxia: Unable to perform a goal motorically; Unable to copy a movement or to make a gesture (i.e. wave hello)

Ideomotor Apraxia:

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

Example of ideomotor apraxia:



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

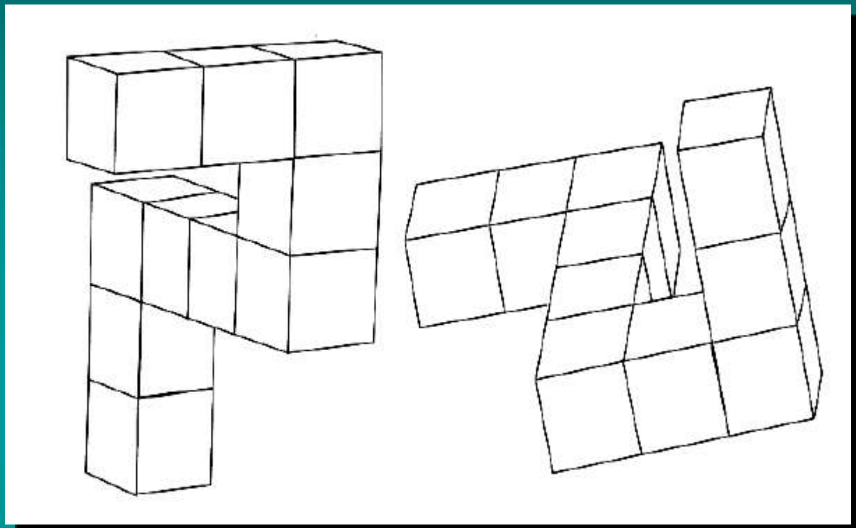
Inability to correctly imitate hand gestures and voluntarily pantomime tool use, e.g. pretend to brush one's hair; unable to copy model, but copy from memory

Posterior Parietal Lobe Damage: Motor 2

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

Mental Rotation



Left dominance for producing mental rotations

Right dominance for manipulating mental rotations

Laterality of Sensory Motor Systems

- LH = only contralateral sensory stimuli
- RH = both contralateral and ipsilateral sensory stimuli

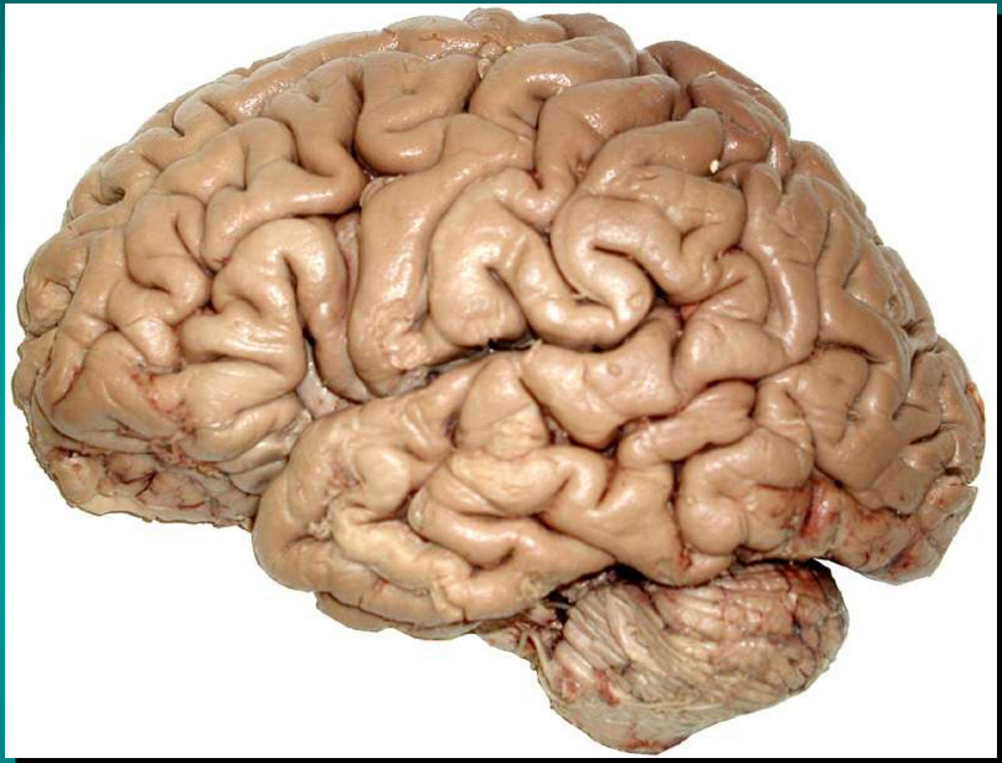
- LH = bilateral control over motor output
- RH = only contralaterally.

- LH = motor deftness for both hands,
- RH = motor deftness for the left hand.

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

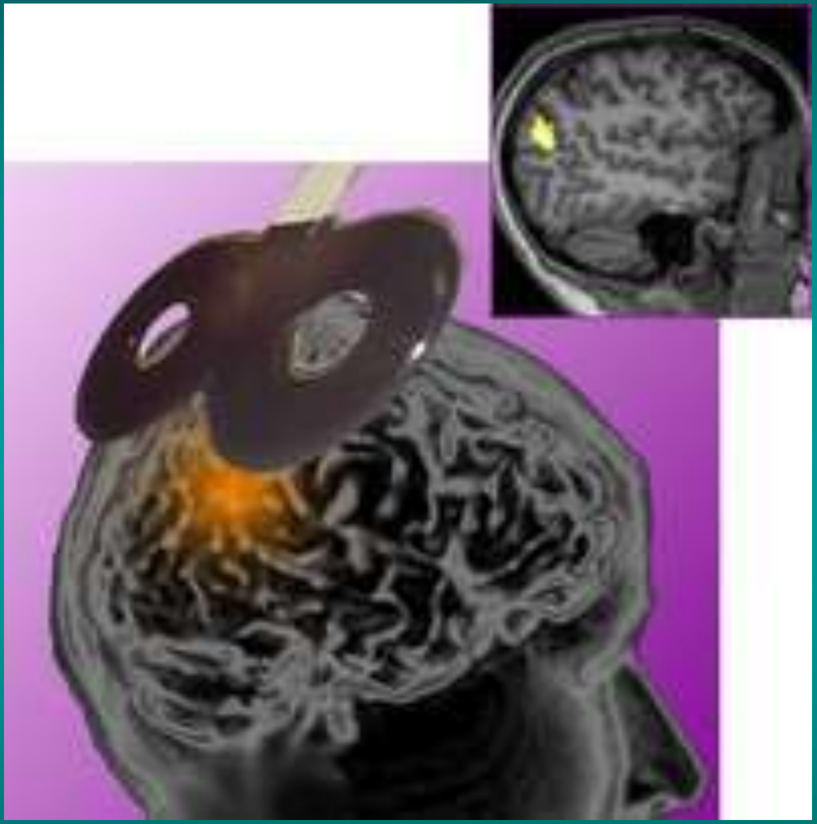
Somatosensory System II: Polysensory Areas



- Temporal-parietal-occipital junction

Right Temporoparietal junction: moral choice

The right temporoparietal junction (RTPJ) receives more blood than usual when we read about people's beliefs and intentions, particularly if we use the information to judge people negatively.

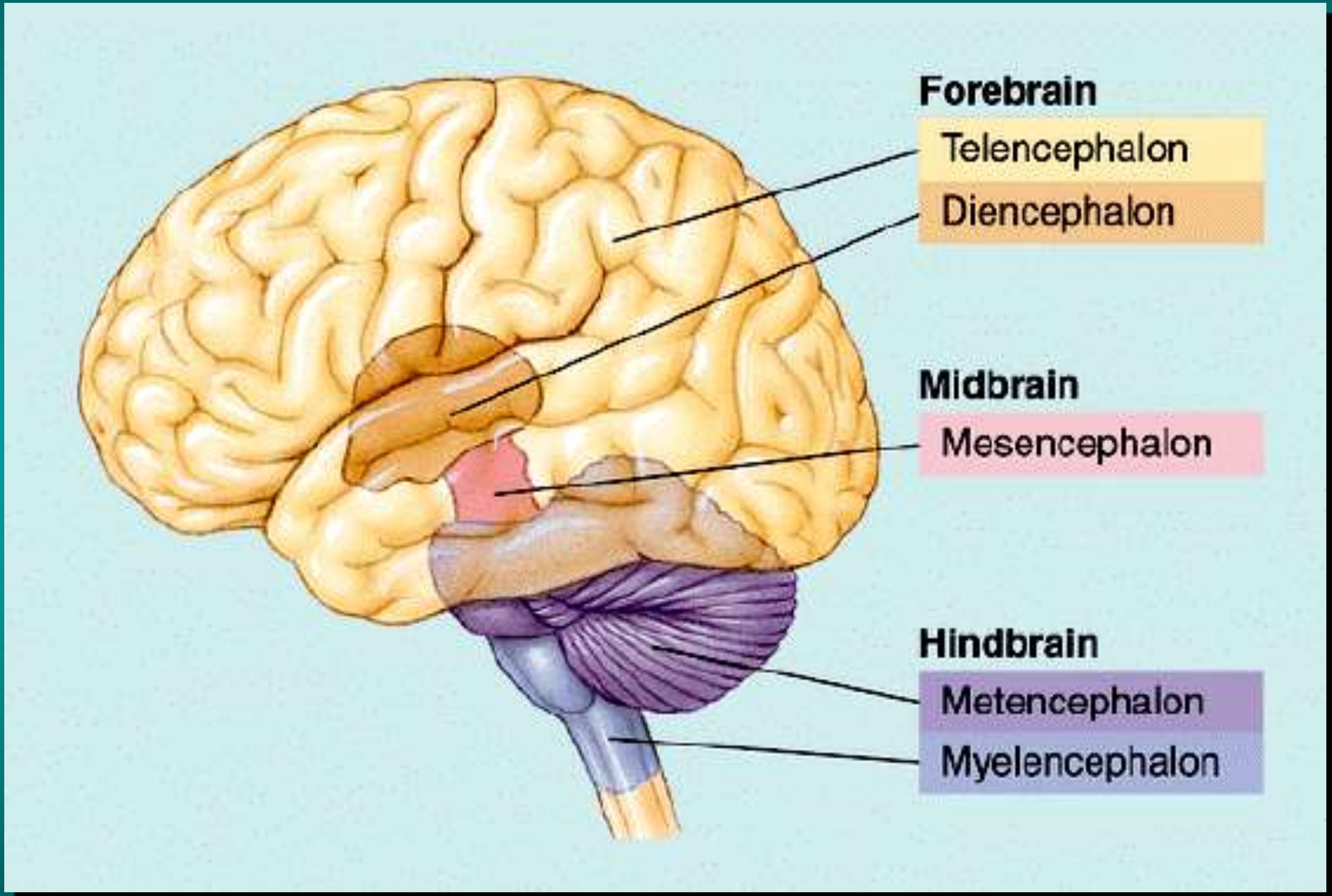


Premeditation. Subjects took less account of intention when their right temporoparietal junction was turned off.

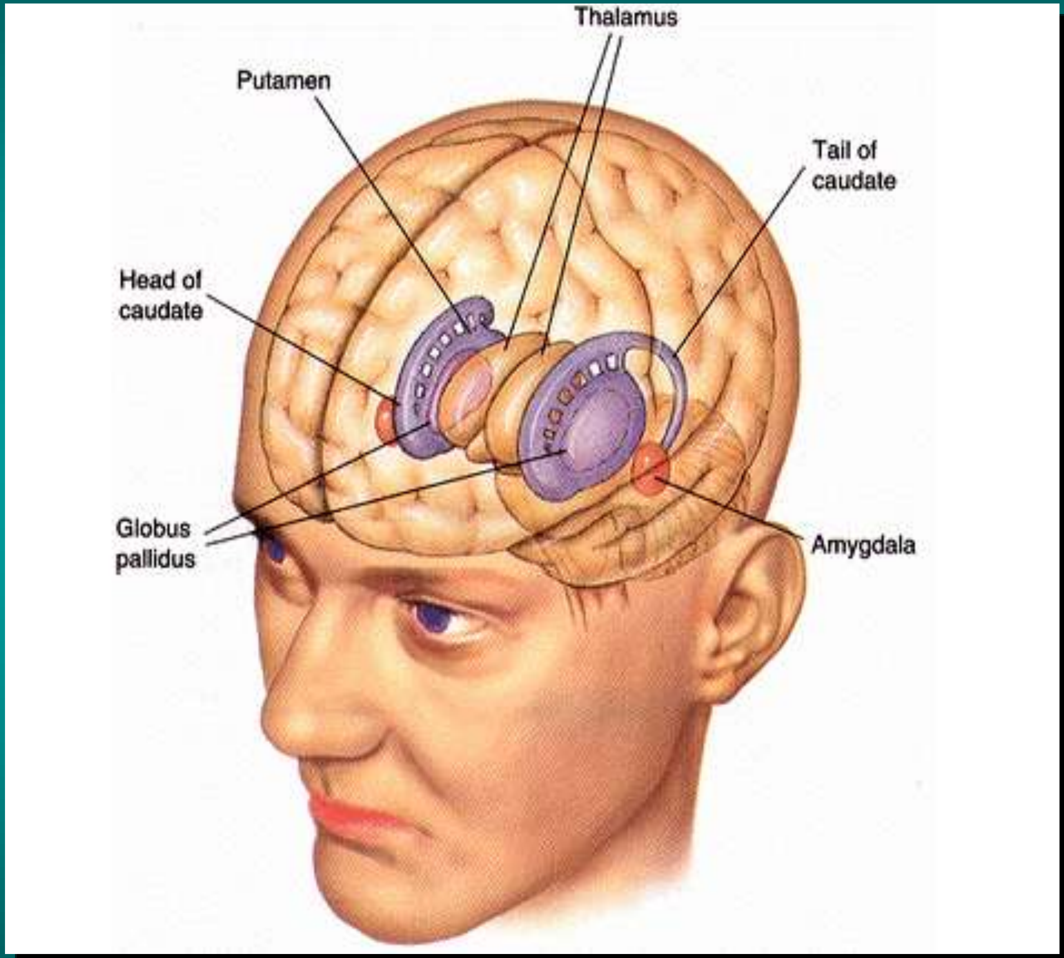
Precuneus (posteromedial parietal): the Self?

- Visuo-spatial imagery, episodic memory retrieval and self-processing operations, namely first-person perspective taking and an experience of agency.
- DMN: Displays the highest resting metabolic rates (hot spots) and are characterized by transient decreases in the tonic activity during engagement in non-self-referential goal-directed actions.
- Part of a medial prefrontal-mid-parietal neural network
- Supporting the mental representation of the self; network of the neural correlates of self-consciousness,
- Selective hypometabolism in the precuneus in a wide range of altered conscious states (sleep, drug-induced anesthesia and vegetative states).

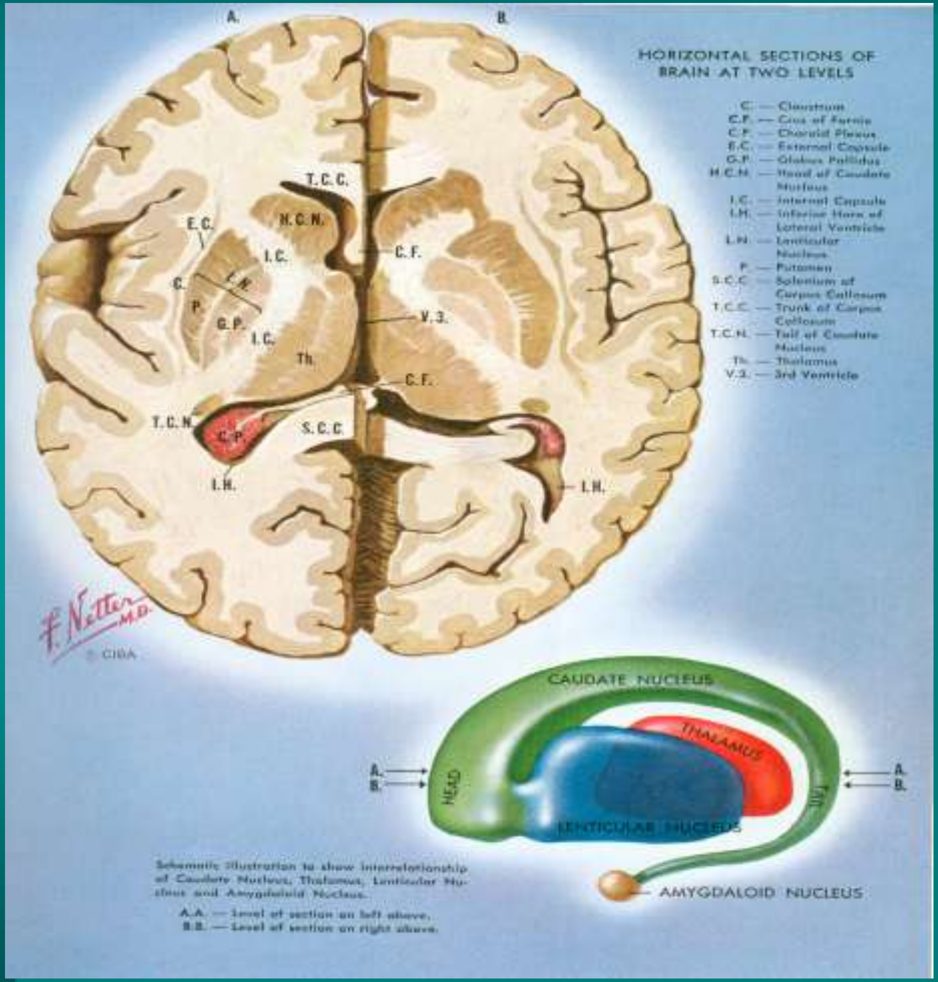
Subcortical Systems



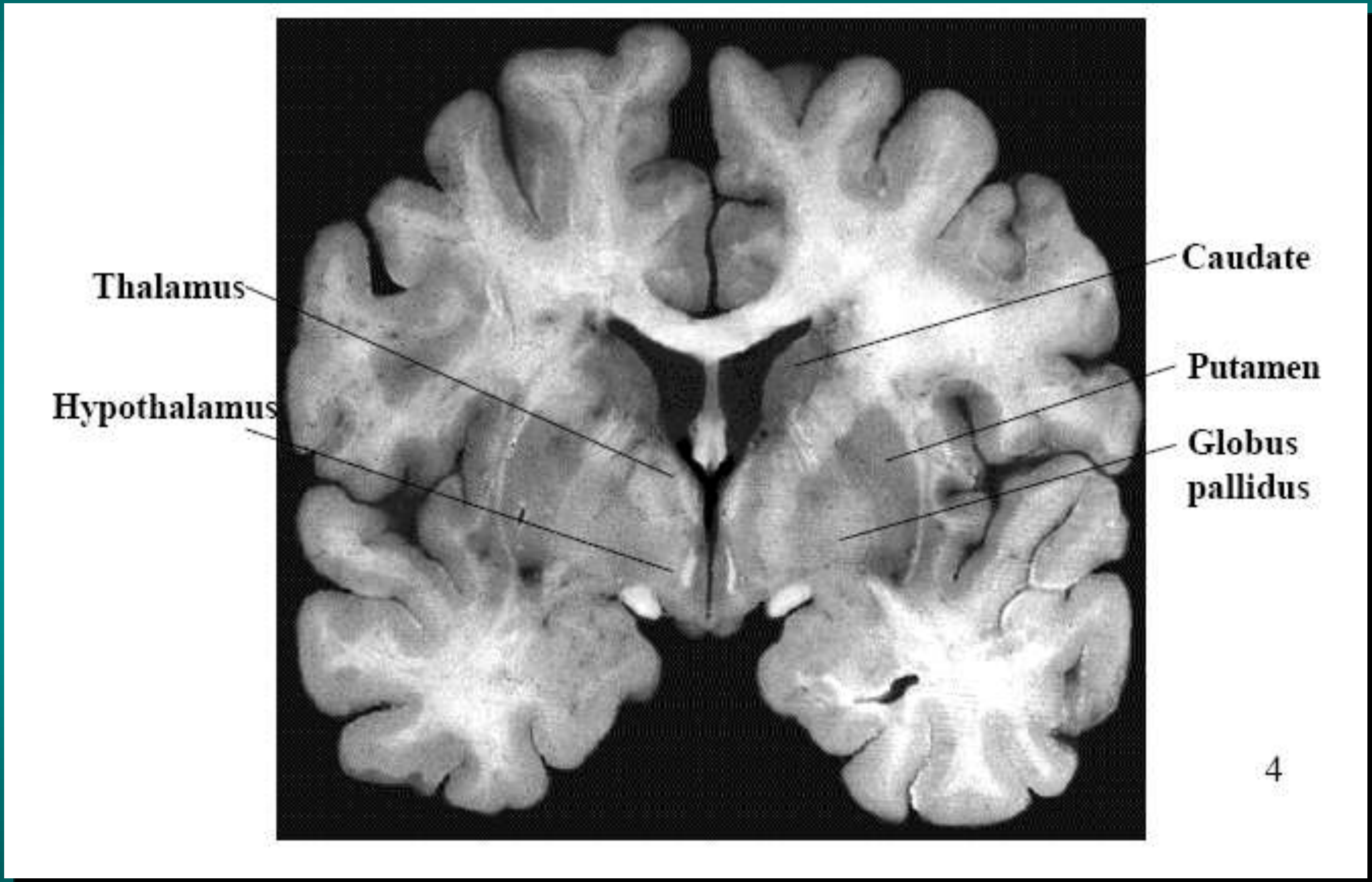
Subcortical 2



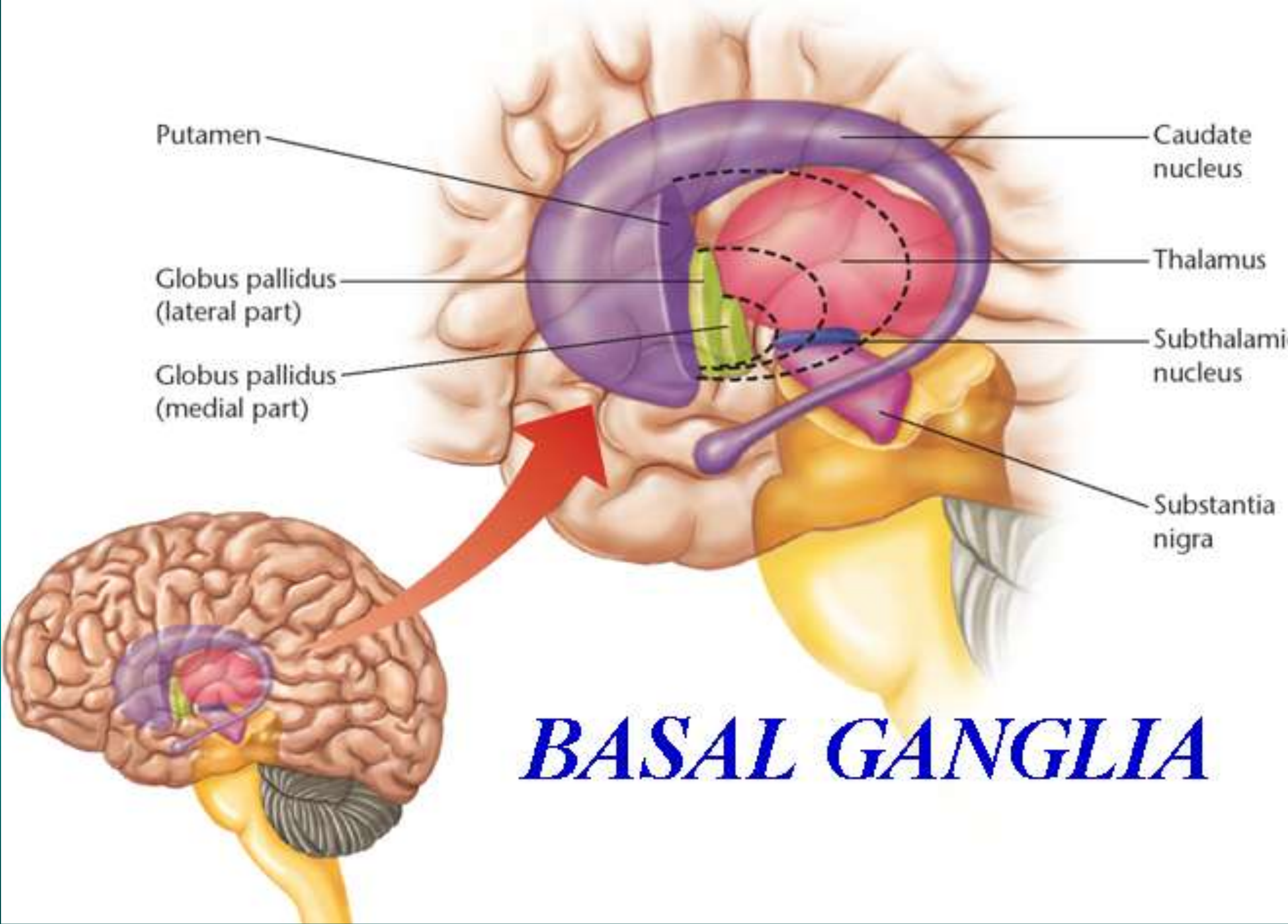
Basal Ganglia:
Globus Pallidus, Putamen, Caudate Nucleus

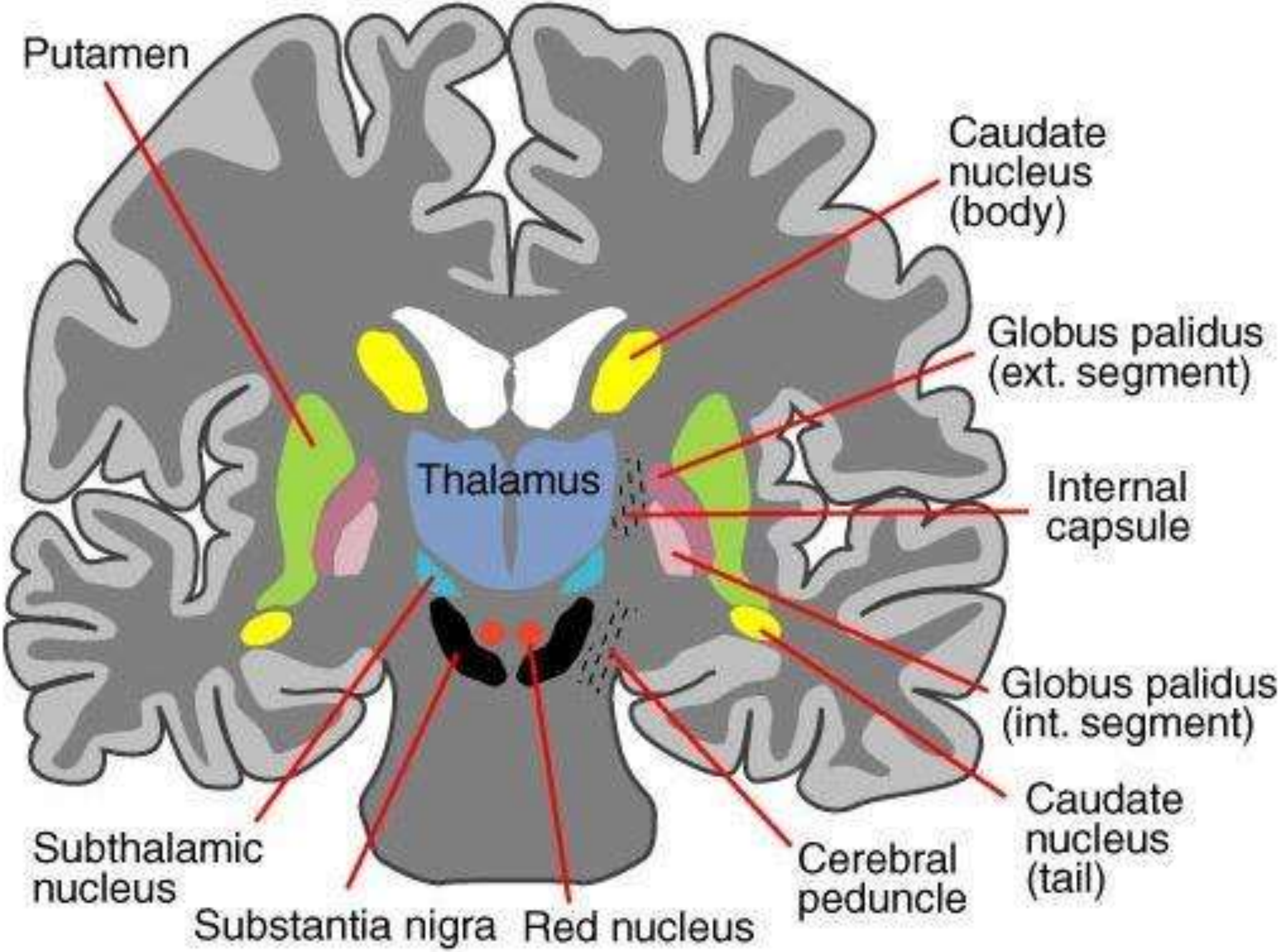


Basal Ganglia 2



BASAL GANGLIA




Putamen
Caudate nucleus (body)
Globus palidus (ext. segment)
Thalamus
Internal capsule
Globus palidus (int. segment)
Caudate nucleus (tail)
Subthalamic nucleus
Substantia nigra
Red nucleus
Cerebral peduncle

Motor functions of basal ganglia

- **Planning and programming of movement**, i.e.. an abstract thought is converted into voluntary action.

- It plays a role in **cognitive** processes. It is the major function of **caudate nucleus** which has connections with the frontal lobe.

- As a part of extra pyramidal system, it is required for the control of muscle tone and posture.

- Healthy basal ganglia inhibits **resting tremor**

Conditions of Motor Systems

EPS (Basal Ganglia)

1. Chorea (Huntington's, Syndenham's)
2. Athetosis (choreoathetosis in HD, Tardive dyskinesia when antipsychotics block DA receptors & make super-sensitive)
3. Hemiballismus (stroke)
4. Parkinson's vs Diffuse Lewy Body Dz (resting tremor, bradykinesia, truncal instability, dementia)

Cerebellum

1. Intention tremor
2. Ataxia (fall towards lesion, gait & trunk dystaxia, dysrhythmokinesia, dysdiadochokinesia, dysmetria)
3. Nystagmus
4. Dec tone ipsilaterally
5. Asthenia (tire easily)

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

<u>Paralysis agitans </u>(<u>Parkinson's disease</u>)

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

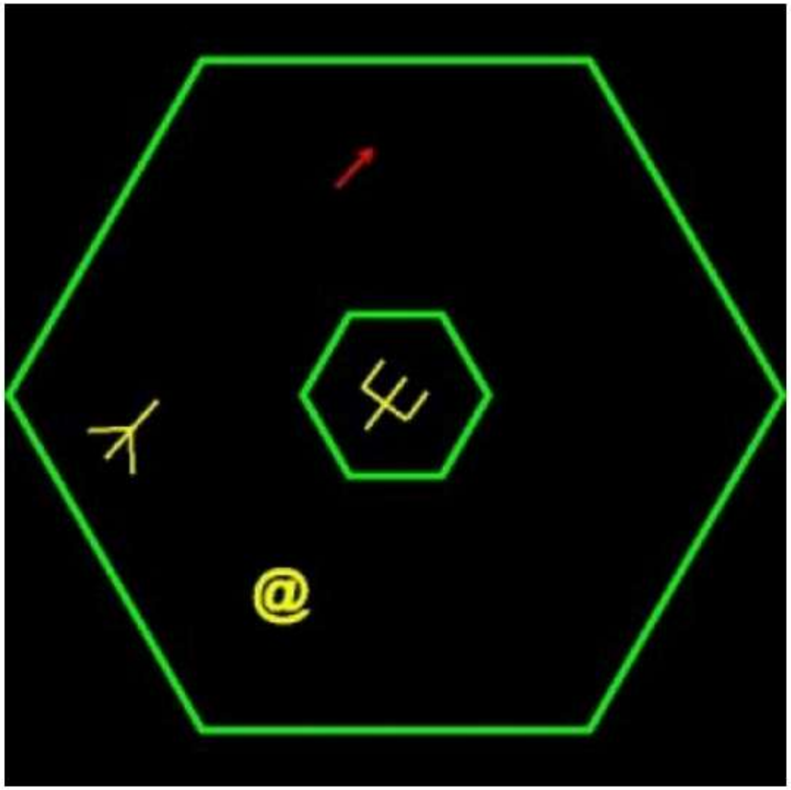
Disorders of basal ganglia

Huntington's chorea

- Caused by loss of GABA secreting neurons of striatum, that sends inhibitory impulse to globus pallidus & substantia nigra. The loss of inhibition cause
  - Flicking movements (at individual joints)
  - Distortional movements
- Ach secreting neurons of many parts of brain are lost. This causes
  - Dementia

Space Fortress

Space Fortress Video Game

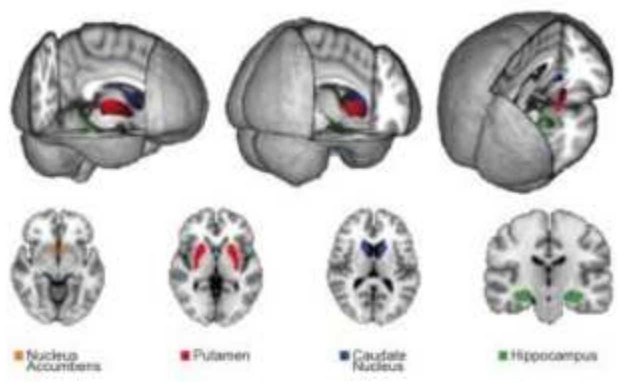


Caption: The video game Space Fortress, developed at the University of Illinois, can be manipulated to test various aspects of cognition.

Larger caudate nucleus and putamen and nucleus accumbens predict best players.

Your Brain on Video Games

Your Brain on Video Games



Caption: MRI scans reveal the brain structures analyzed in this study: nucleus accumbens (orange), putamen (red), caudate nucleus (blue), and hippocampus (green).

Striatum profoundly influence a person's ability to refine motor skills, learn new procedures, develop useful strategies and adapt to a quickly changing environment.

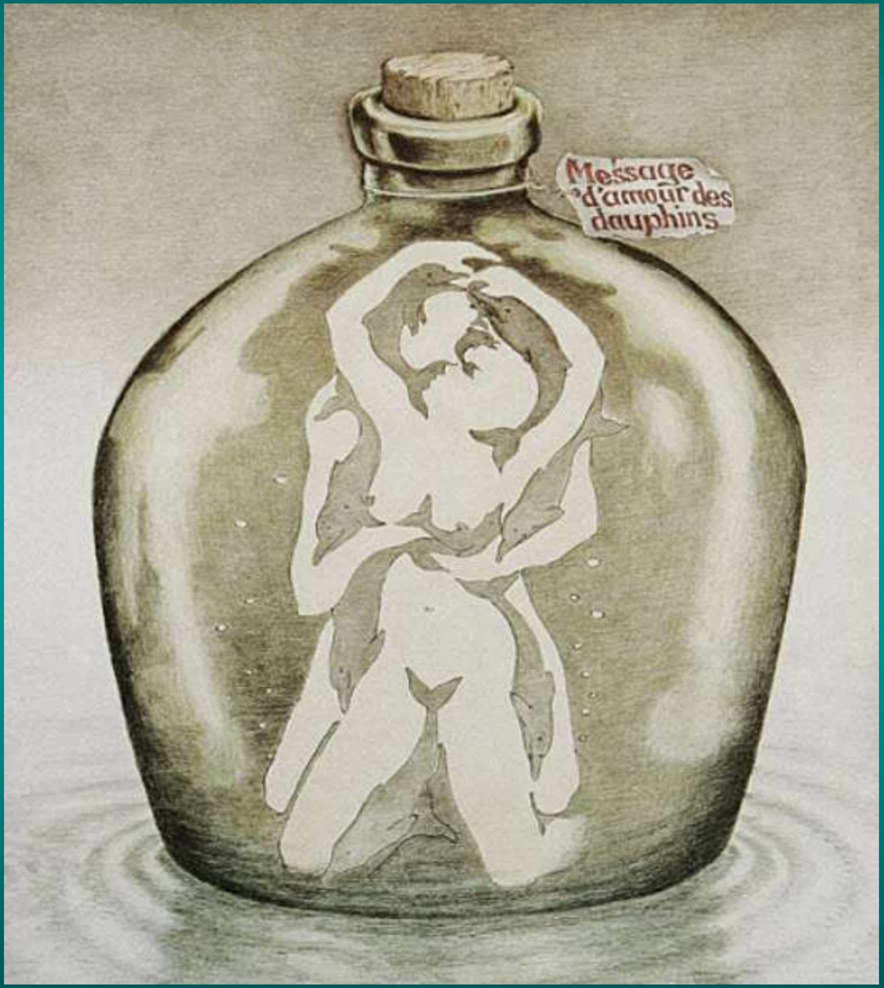
Caudate nucleus and putamen are Involved in motor learning and cognitive flexibility that allows one to quickly shift between tasks.

Nucleus accumbens processes emotions associated with reward or punishment.

Caudate Nucleus and Culture

- <u>In Americans, caudate nucleus </u>was likely to be activated <u>by dominant behavior</u>
- <u>In Japanese</u>, activated by <u>subordinate behavior</u>
- <u>Same region rewarding different pattterns of behavior depending on culture</u>

Effect of Experience on Vision: 2 Nudes or 10 Dolphins

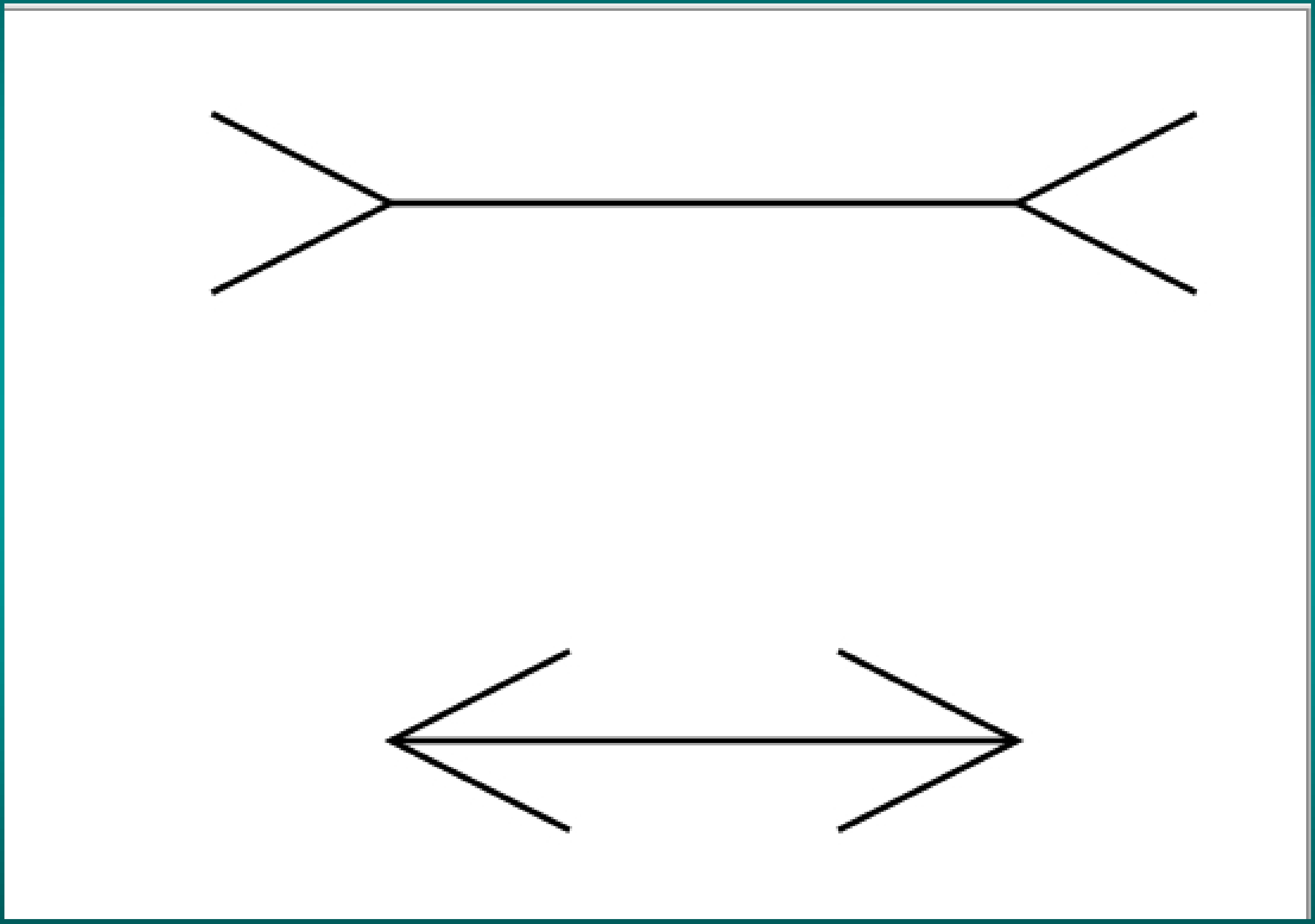


Young children see only 10 dolphins. Adults see two nude lovers embracing.

Effect of Cultural Experience on Visual Interpretation

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

Western vs. San of Kalahari



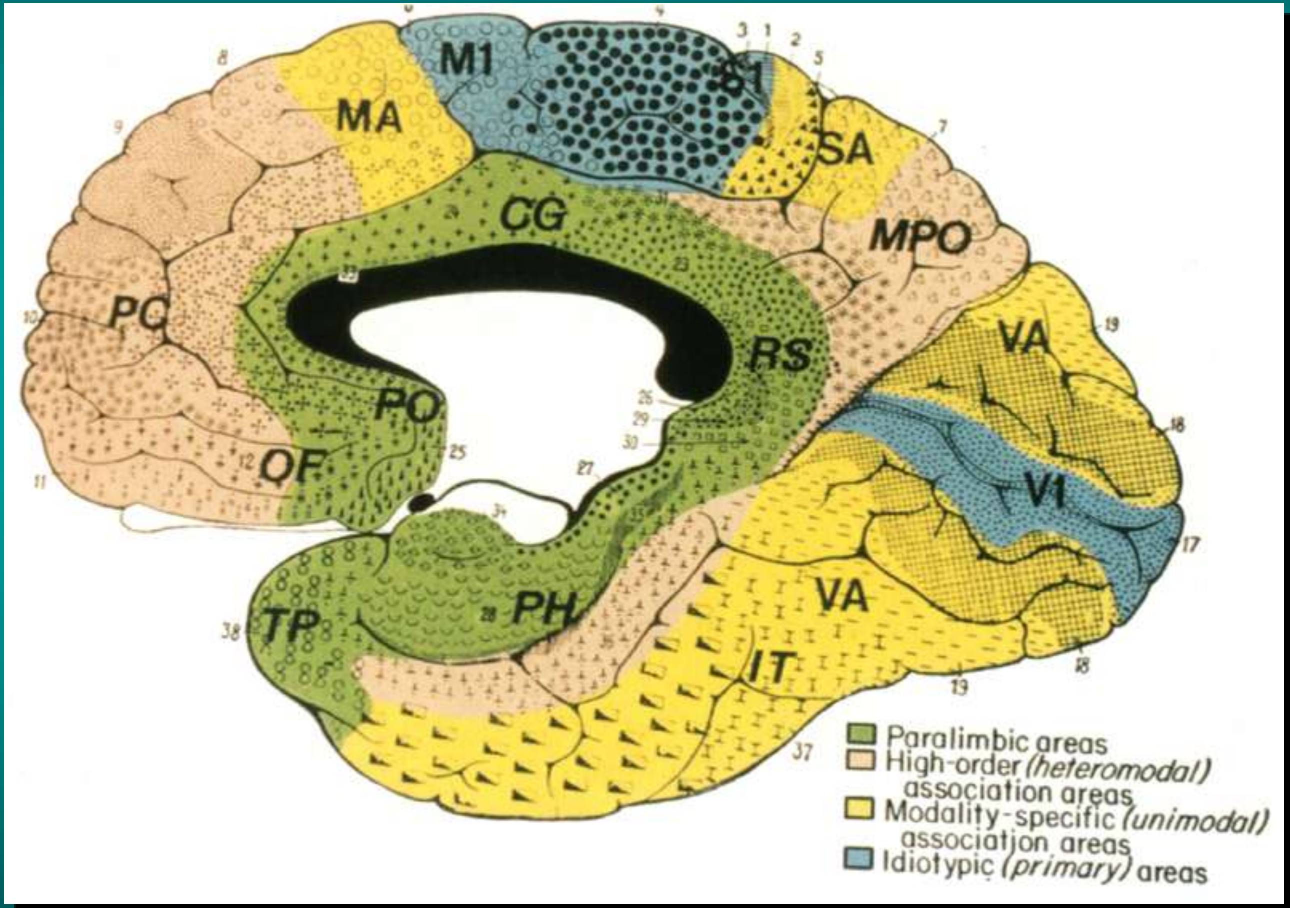
When kids grow up in an environment filled with right angles.

Medial Cortex: Internal State Systems

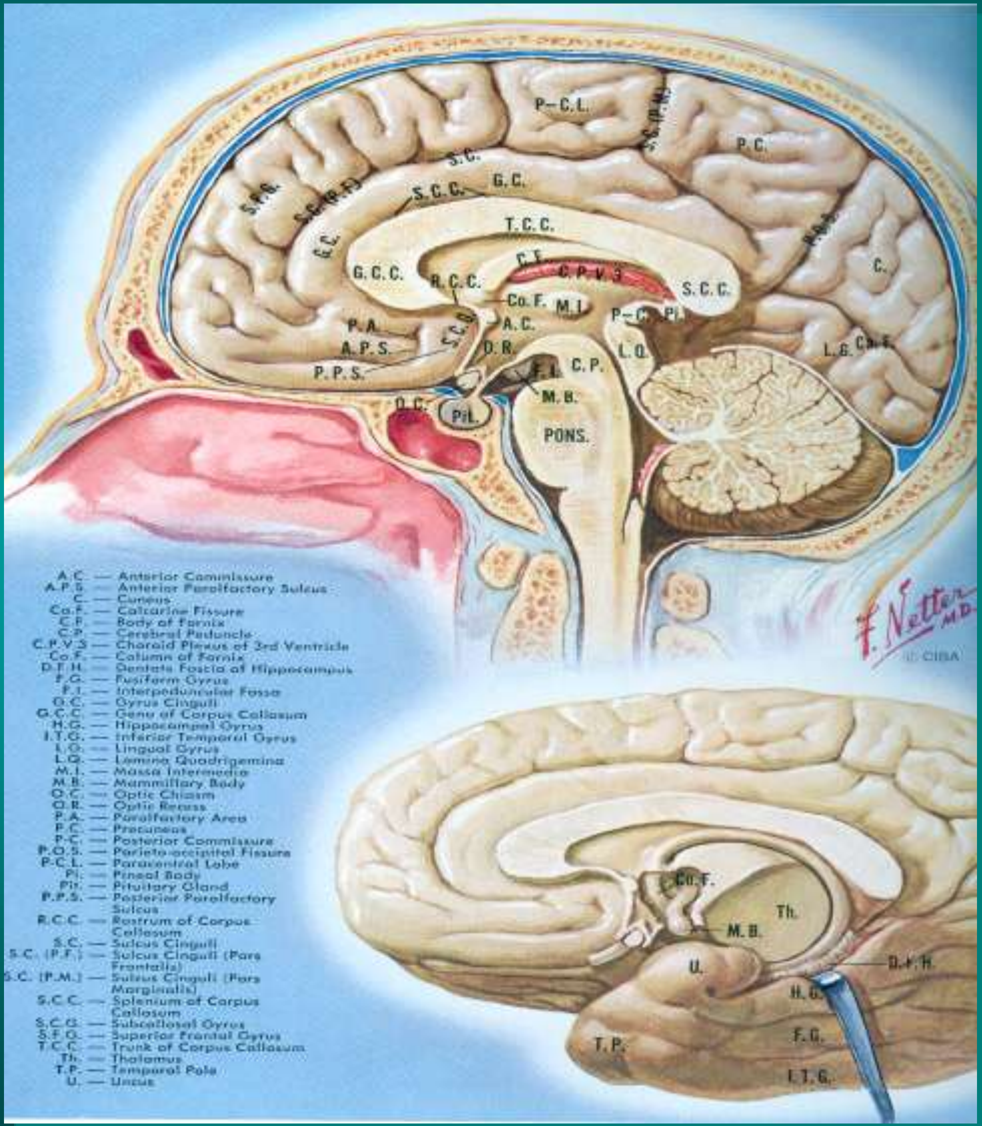
“Limbic Lobe”

1. memory
2. Emotion

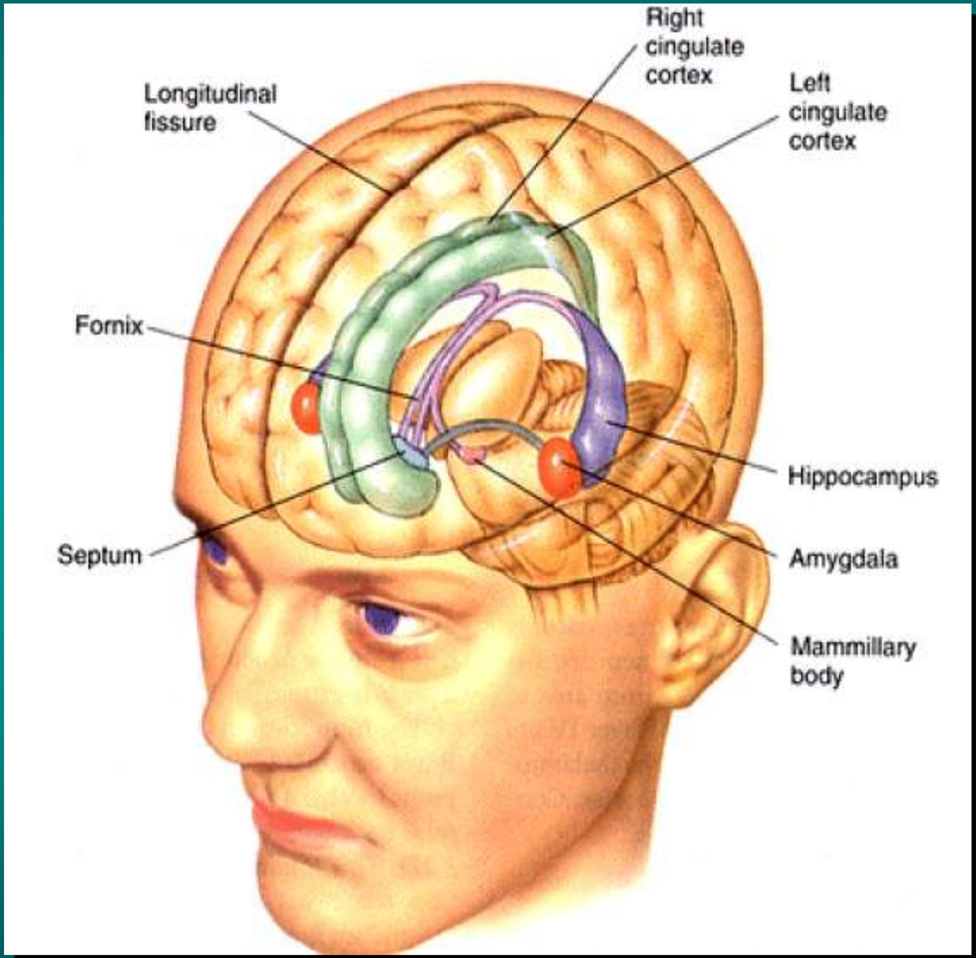
Part of Default Network



Medial Aspect



Limbic System



Components of limbic system

- The hypothalamus
- The subcortical structures
  - Septum
  - Paraolfactory area
  - Anterior nucleus of thalamus
  - Certain portions of basal ganglia
  - The hippocampus
  - The amygdala
- The cortical regions
  - Cortical regions between orbitofrontal & subcallosal gyrus
  - Cingulate gyrus, above the corpus callosum
  - Parahippocampal gyrus & uncus in the ventromedial temporal lobe

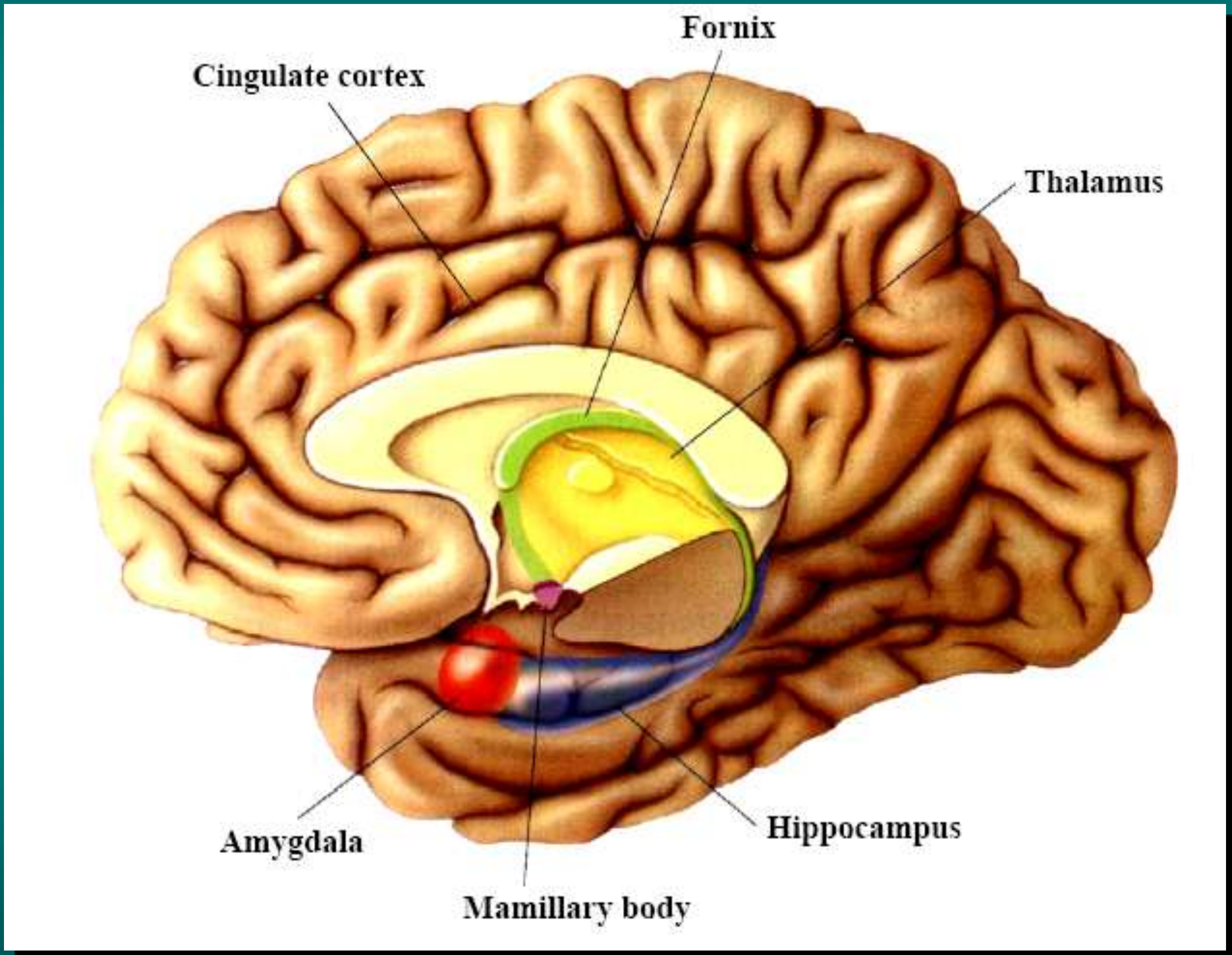
Functions of limbic system: remember the tiger

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

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

- Reward & punishment in learning & memory

Hippocampus and Amygdala



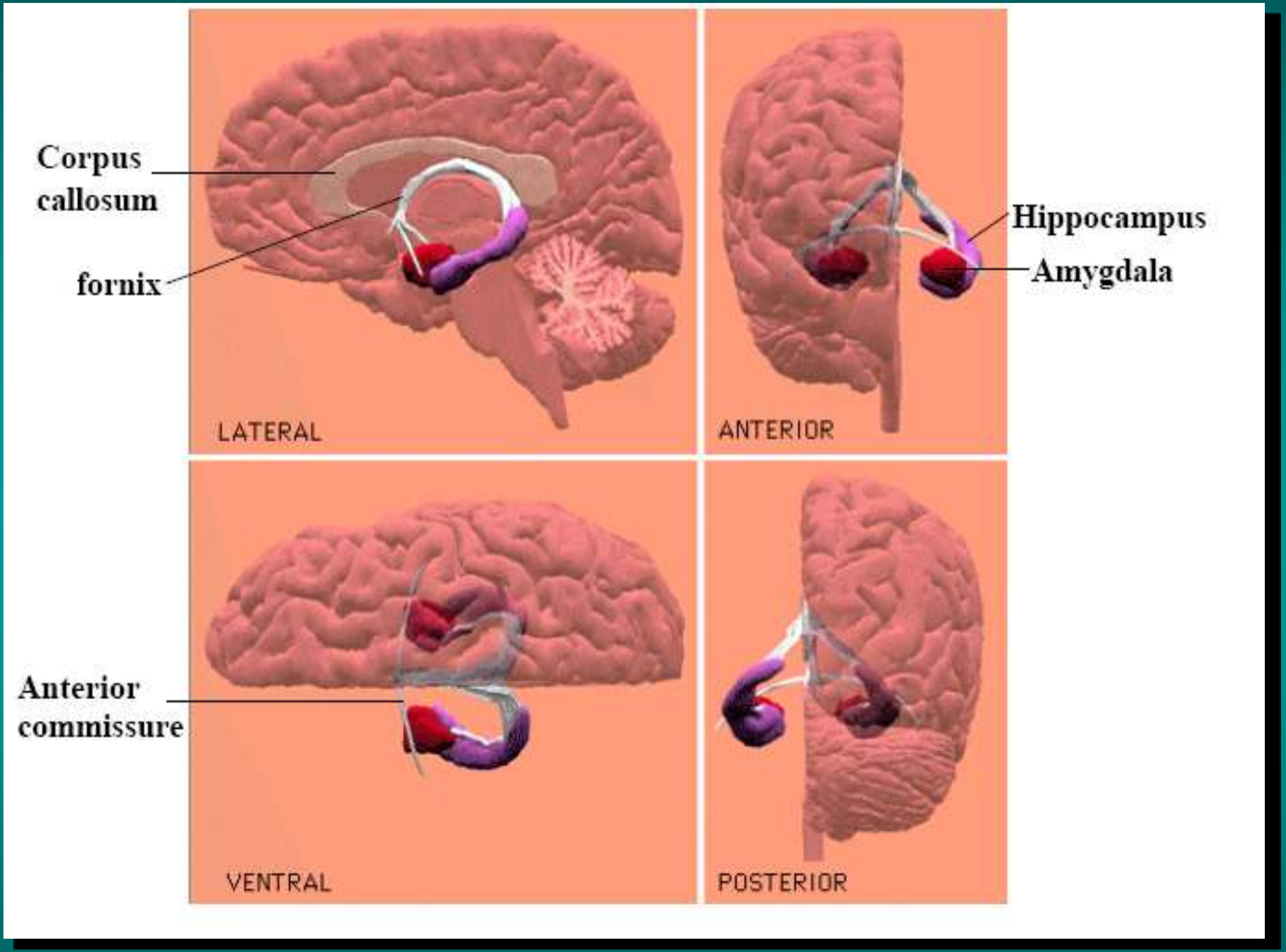
Functions of limbic system: Amygdala

Functions of the amygdala:

– A behavioral awareness area

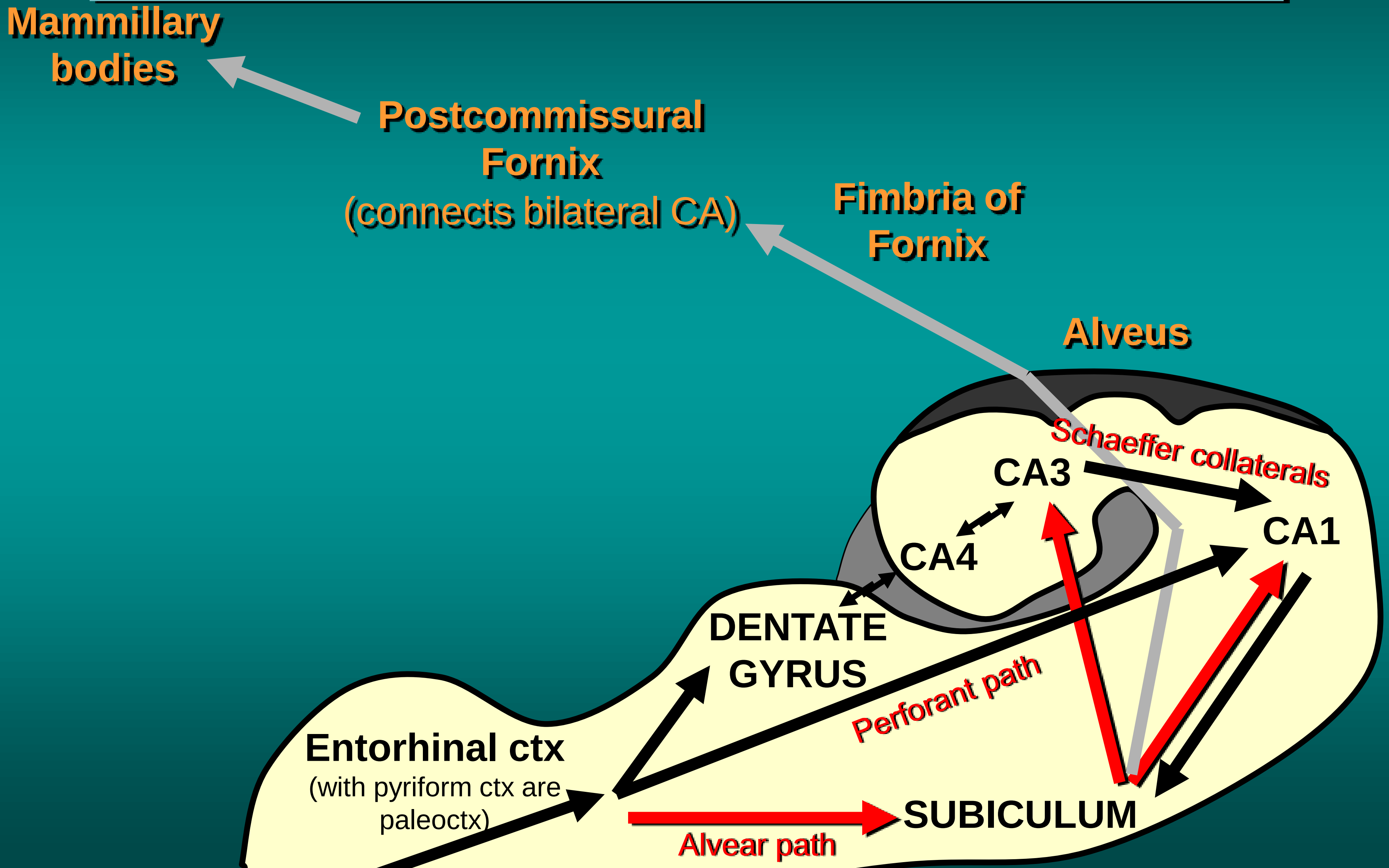
- Emotional response
- Receives information from limbic cortex & all other sensory cortex (visual, auditory etc) & sends information to hippocampus, thalamus & esp. hypothalamus
- ***Kluver-Bucy syndrome: (disorder of indiscrimination) visual agnosia, inappropriate food & sex***

Hippocampus: Index to memory database

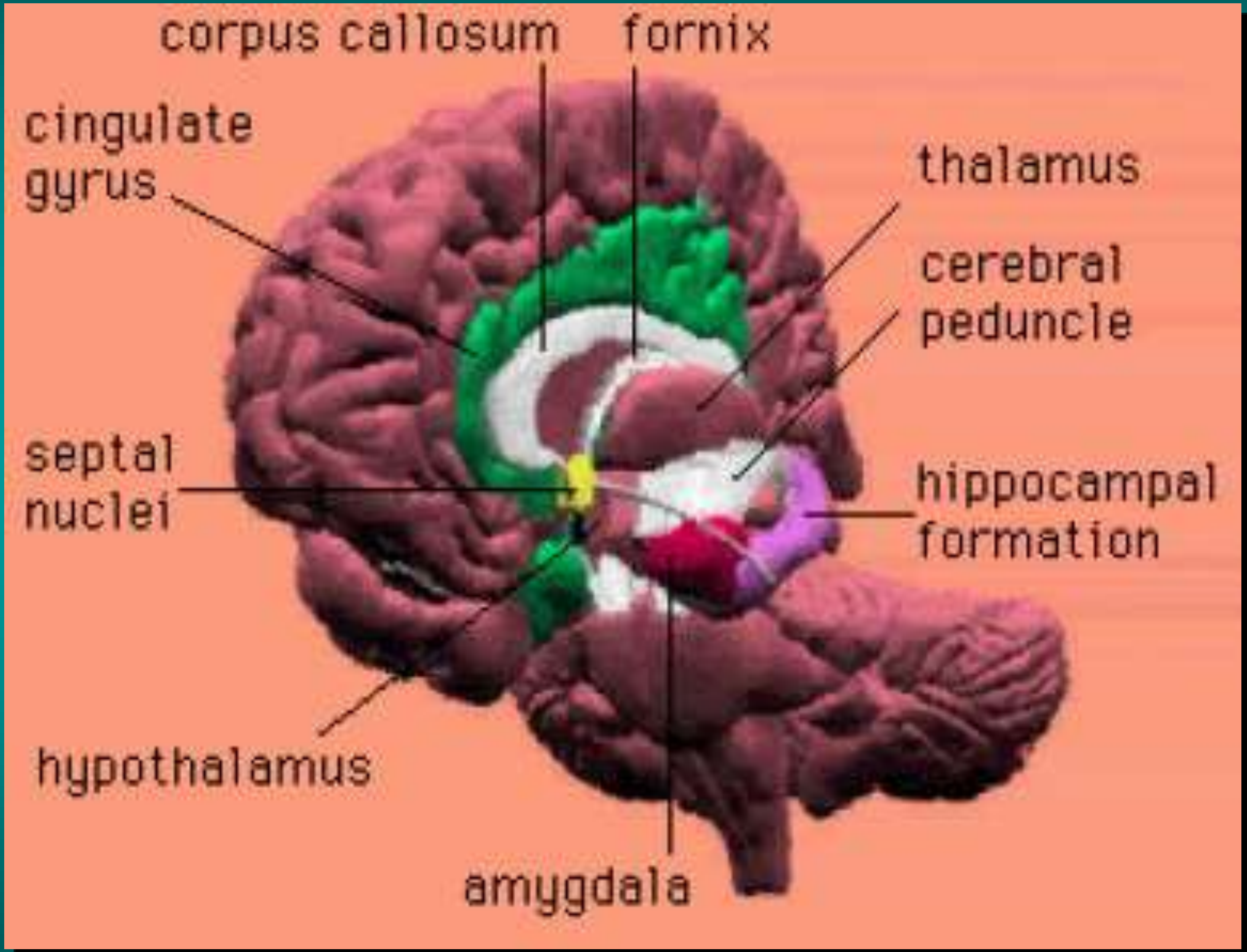


Major site of neurogenesis of stem cells

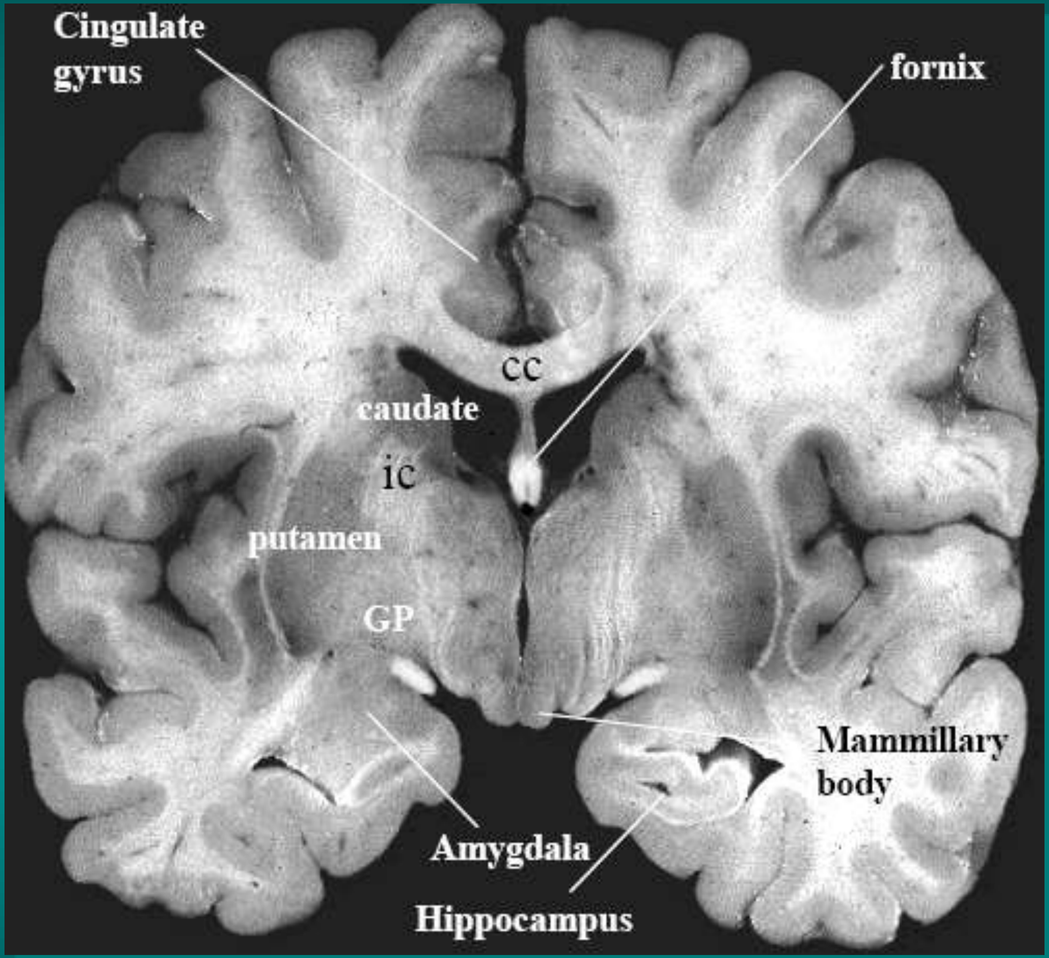
Hippocampus



Cingulate and Amygdala

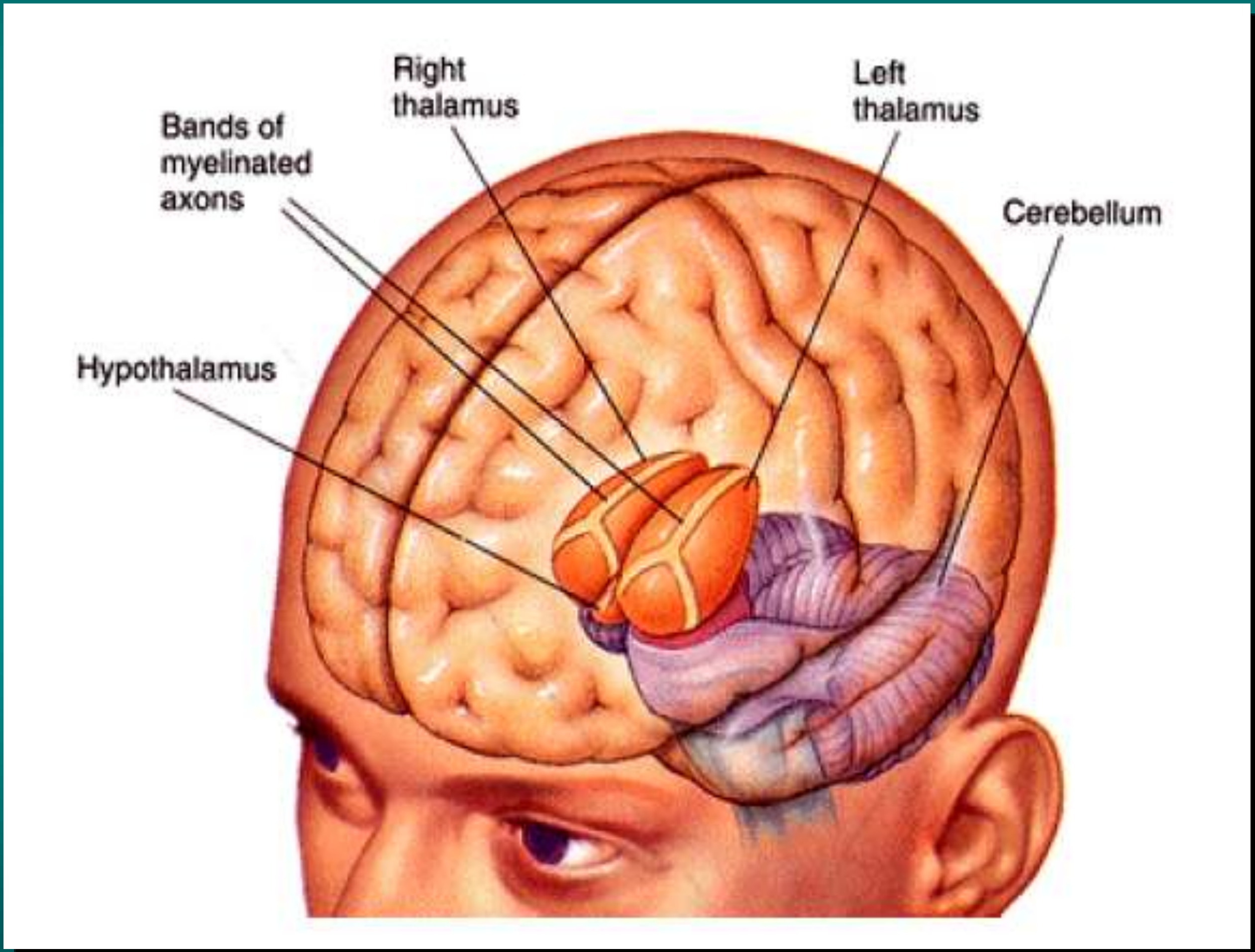


Mammillary Bodies



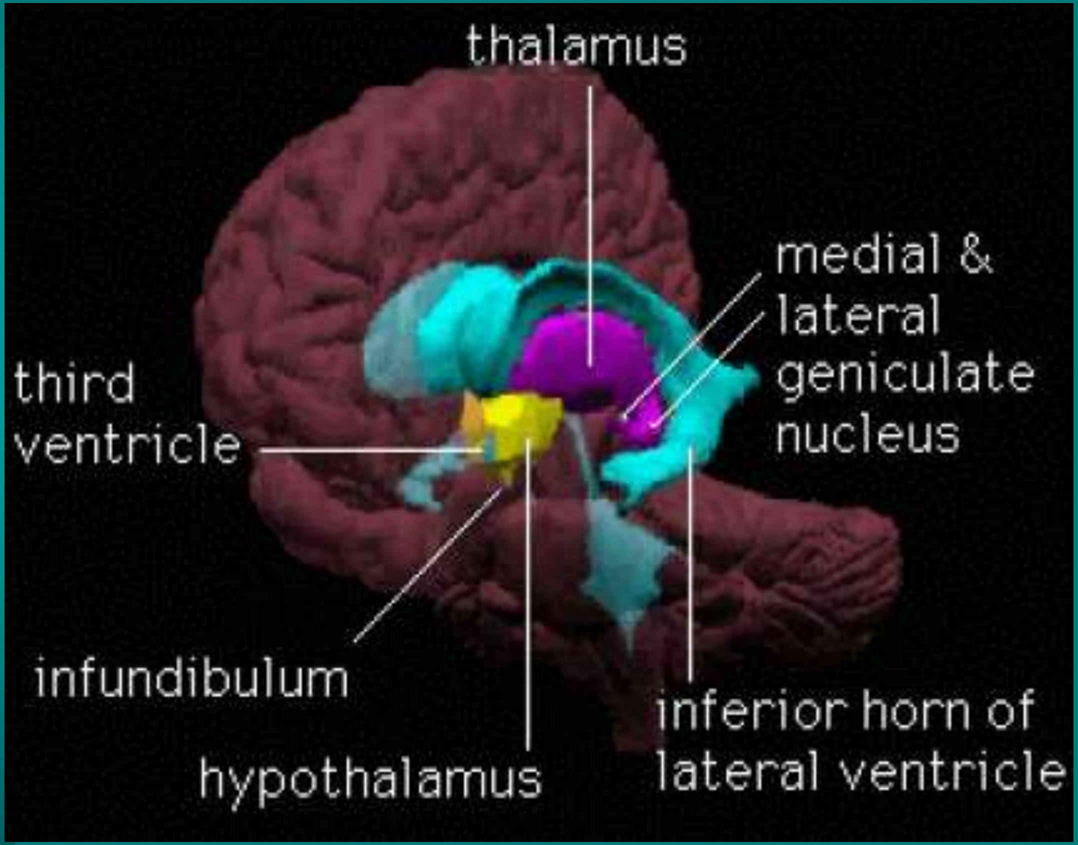
Anterograde Amnesia: Thiamine deficiency caused hemorrhages in Korsakoff’s Syndrome

Thalamus



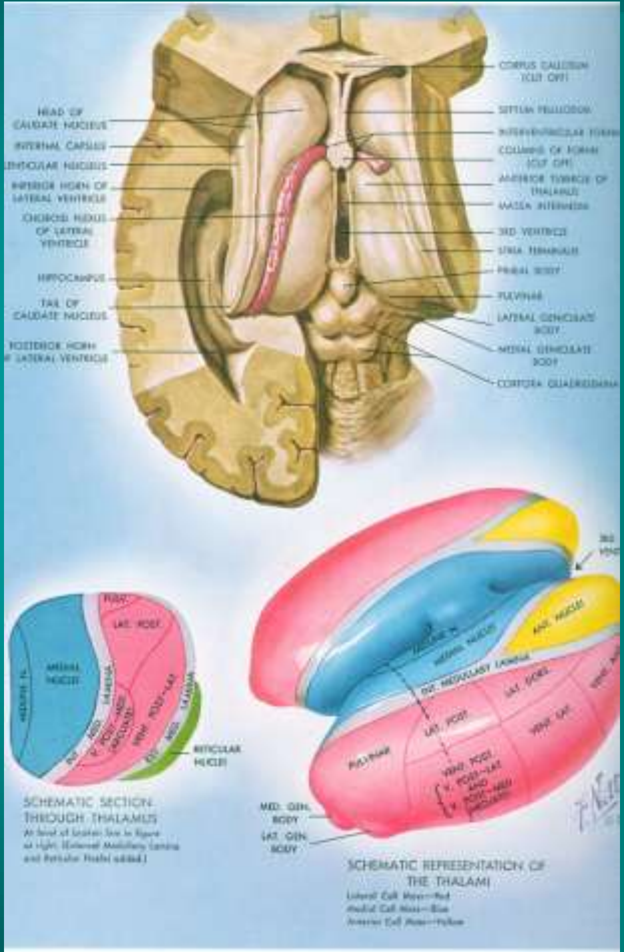
Right thalamus
Left thalamus
Bands of myelinated axons
Cerebellum
Hypothalamus

Thalamus 2



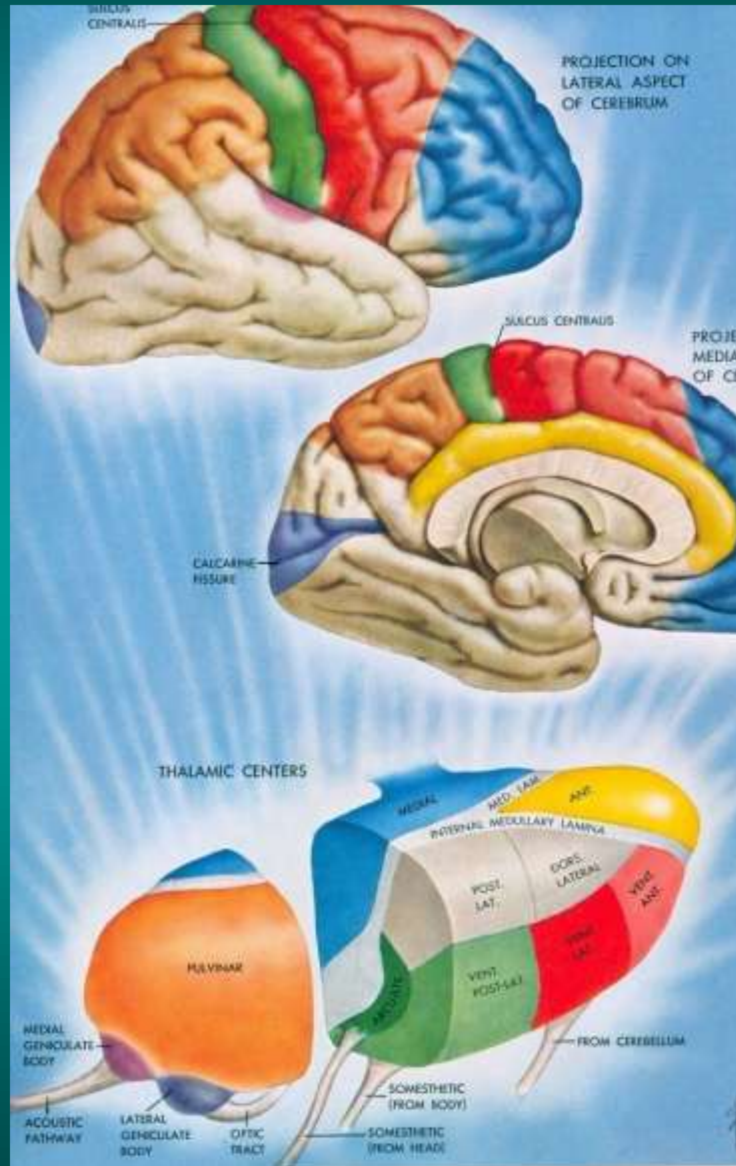
thalamus
medial & lateral geniculate nucleus
third ventricle
infundibulum
hypothalamus
inferior horn of lateral ventricle

Thalamus 3



HEAD OF CAUDATE NUCLEUS
INTERNAL CAPSULE
HIPPOCAMPUS
TAIL OF CAUDATE NUCLEUS
CORPUS CALLOSUM (CUT OFF)
3RD VENTRICLE
PULVINAR
LATERAL GENICULATE BODY
MEDIAL GENICULATE BODY
MEDIAL NUCLEI
LAT. POST.
PULVINAR
MED. GEN. BODY
LAT. GEN. BODY
RETICULAR NUCLEI
SCHEMATIC SECTION THROUGH THALAMUS
SCHEMATIC REPRESENTATION OF THE THALAMI

Thalamocortical Radiations



Thalamocortical Connections

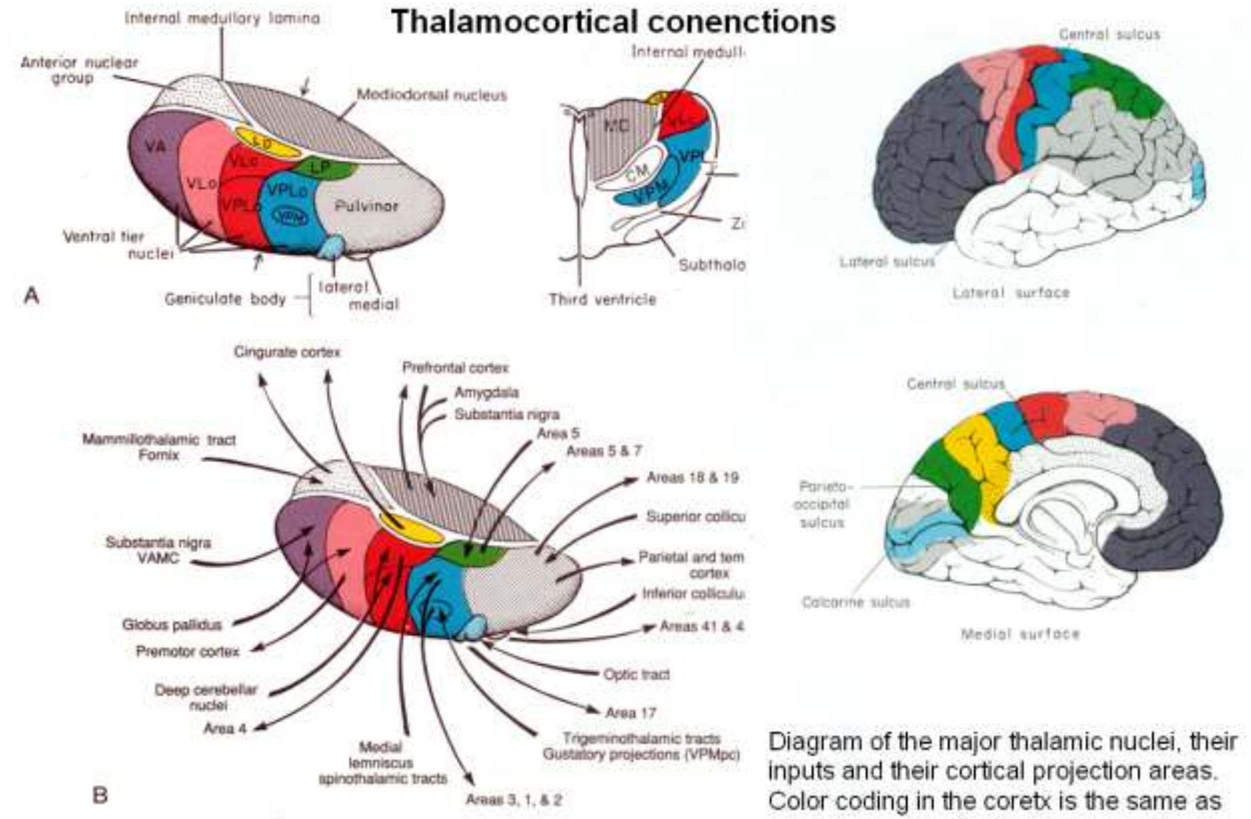
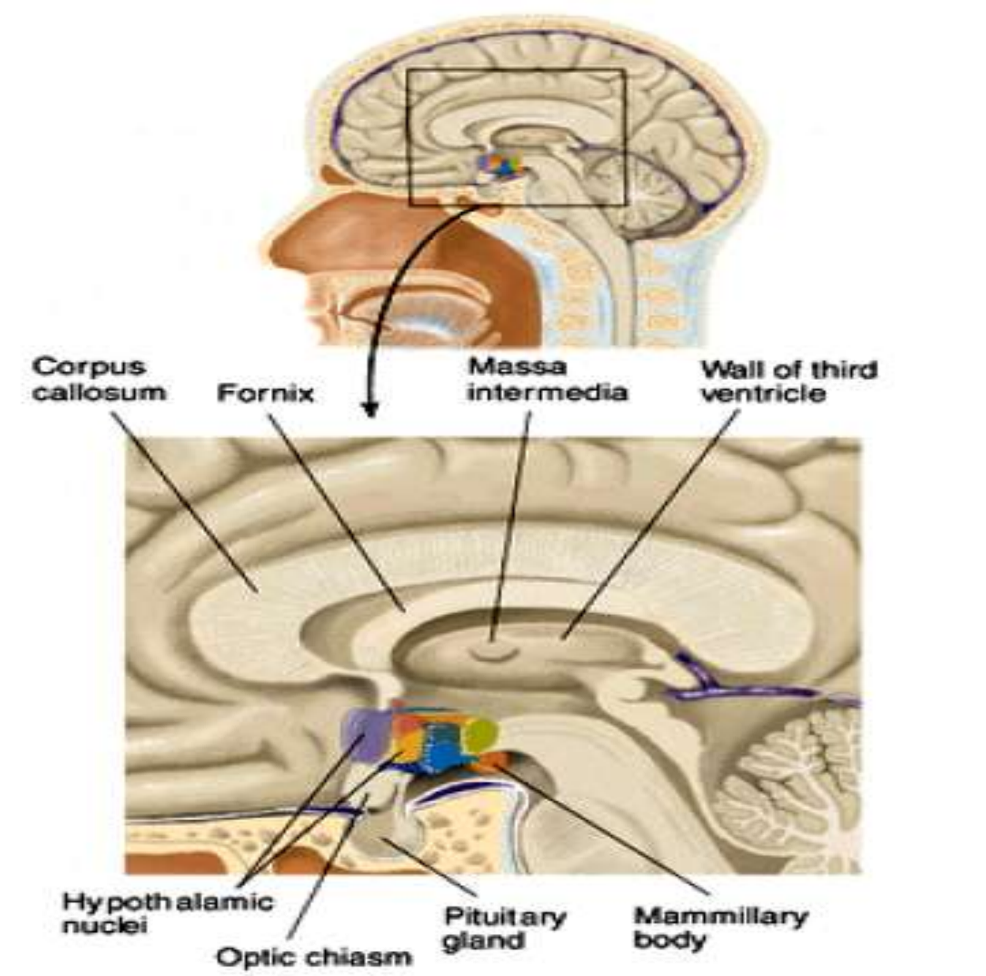
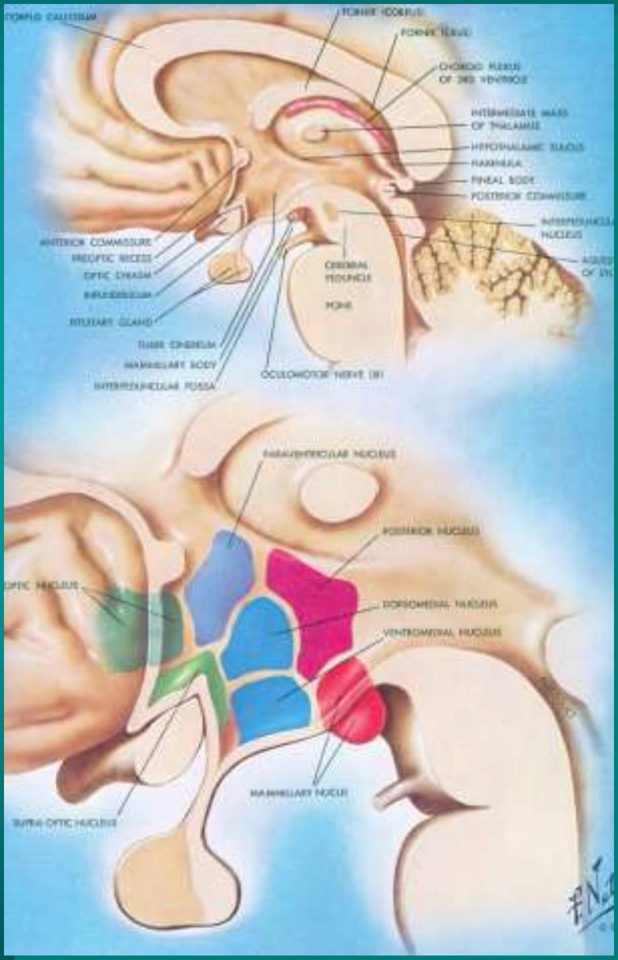


Diagram of the major thalamic nuclei, their inputs and their cortical projection areas. Color coding in the coretx is the same as for the thalamus (Carpenter, 1991)

Hypothalamus: Brain's Pharmacy

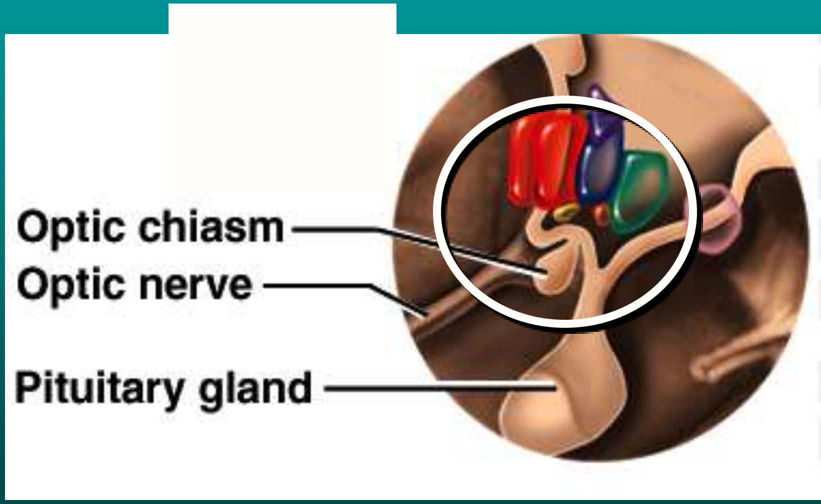


Hypothalamus 2



Diencephalon: Hypothalamus

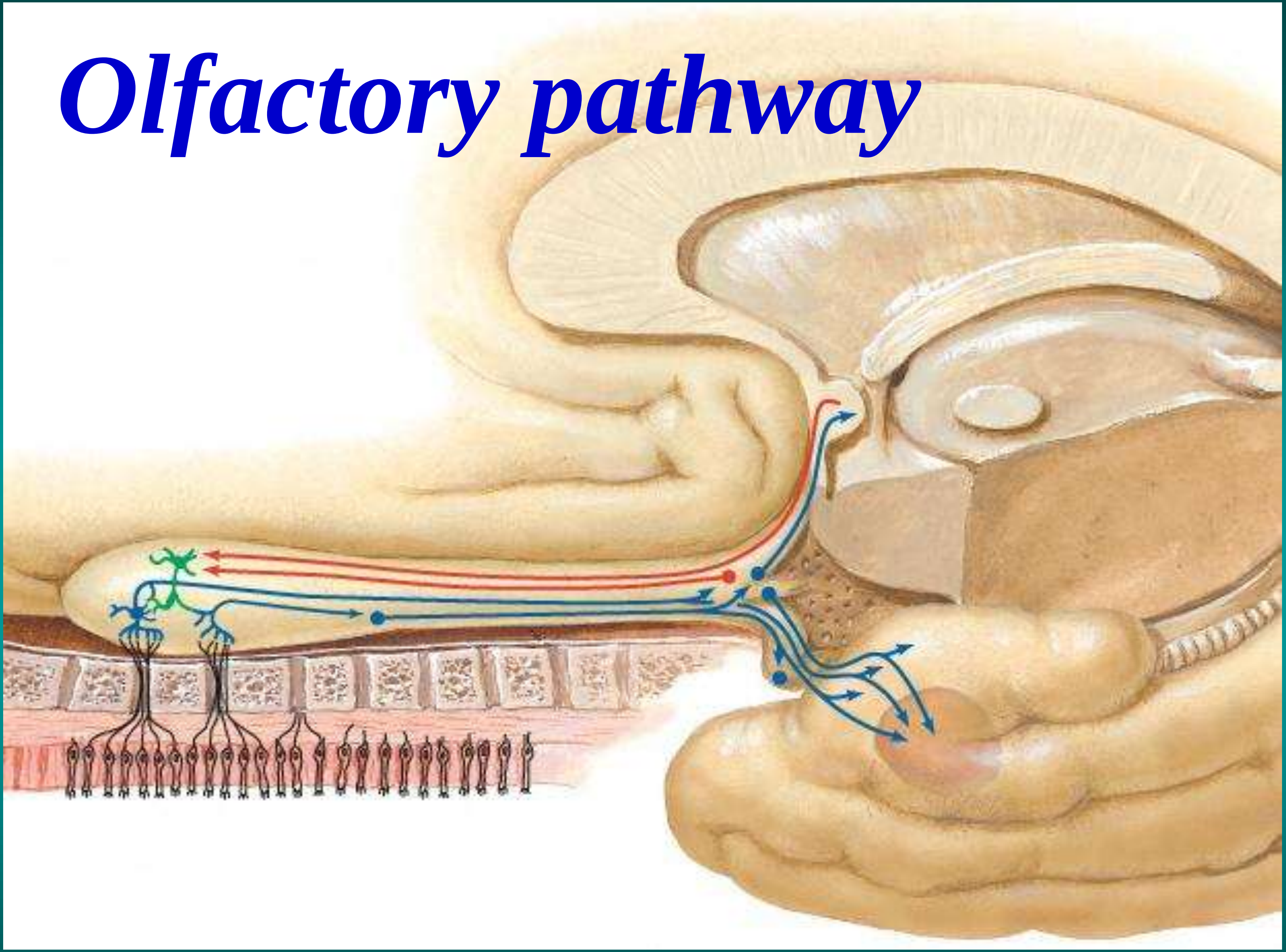
- Walls & floor of 3rd ventricle
- Functions: Secretes hormones that regulate **homeostasis.**
  - hormone secretion (pituitary)
  - autonomic NS control
  - thermoregulation (thermostat)
  - food & water intake (hunger & satiety)
  - sleep & circadian rhythms
  - memory (mammillary bodies)
  - emotional behavior
    - anger, aggression, fear,
    - pleasure, sex drive, orgasm



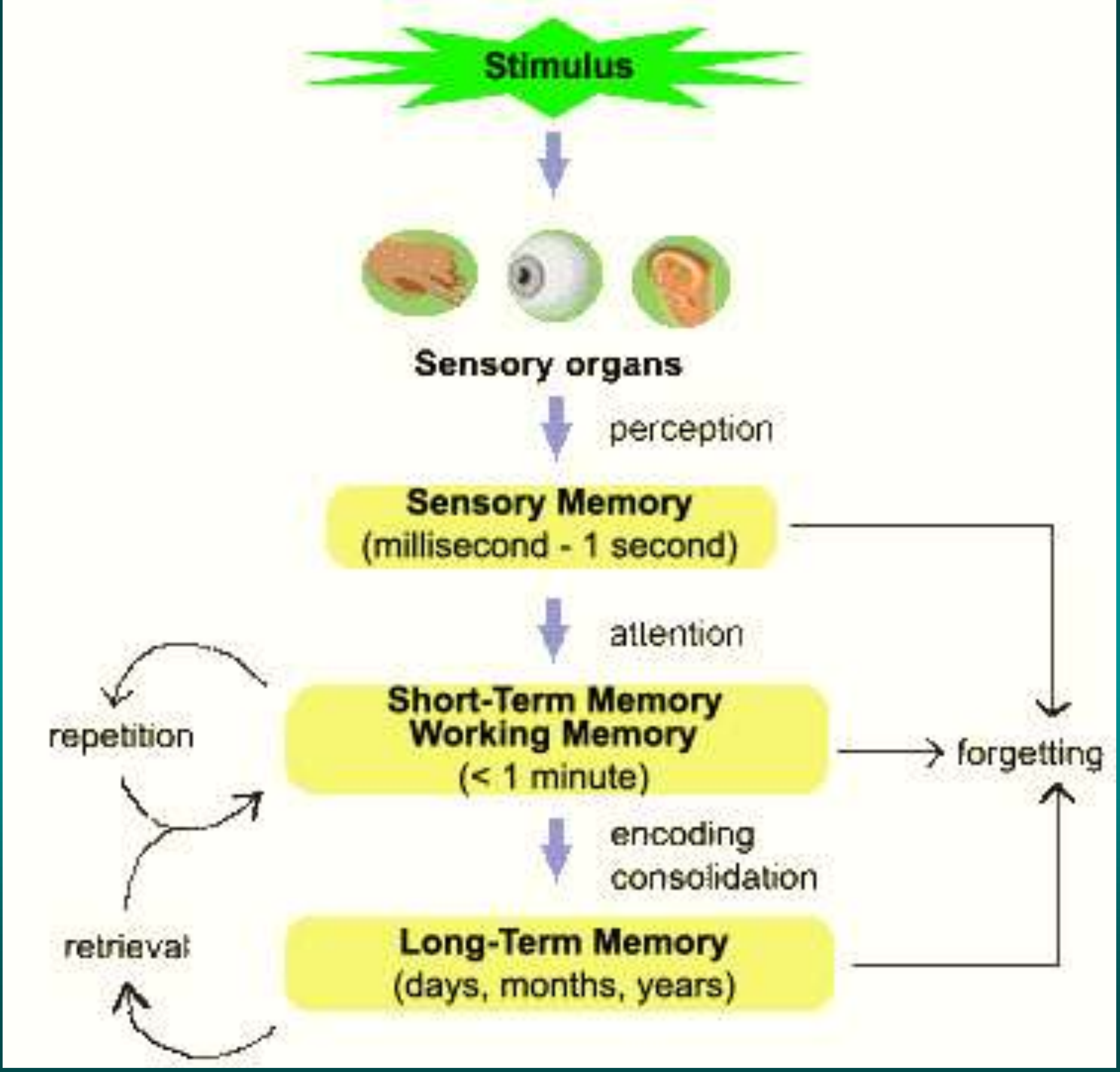
Diencephalon: Thalamus

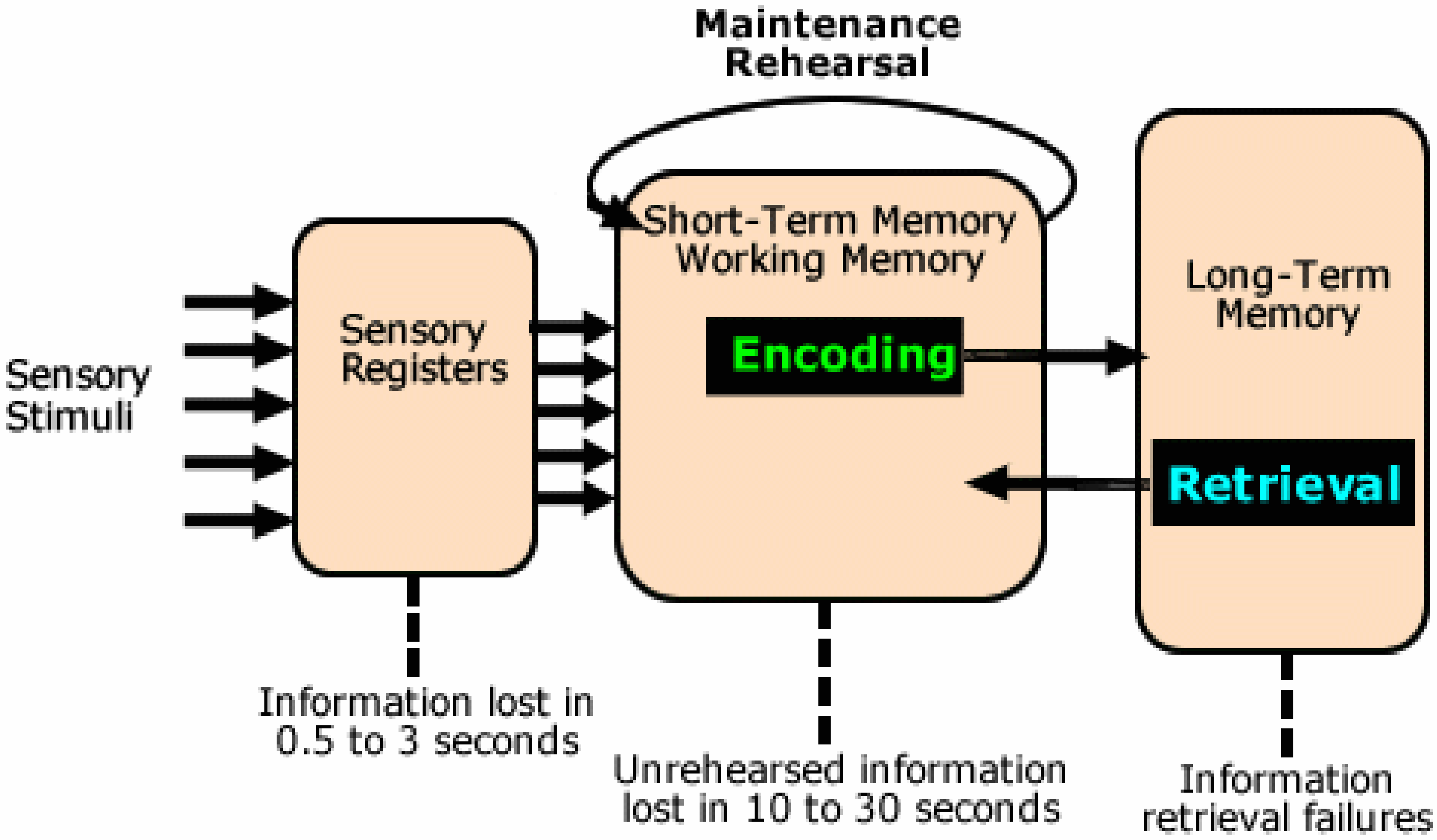
- Gateway to cortex
- Receives nearly all sensory information on its way to cerebral cortex
  - integrate & directs information to appropriate area
  - main output center for motor info leaving the cerebrum
- Interconnected to **limbic system** so involved in emotional & memory functions
  - Arousal, eye movements, taste, smell, hearing

Olfactory pathway

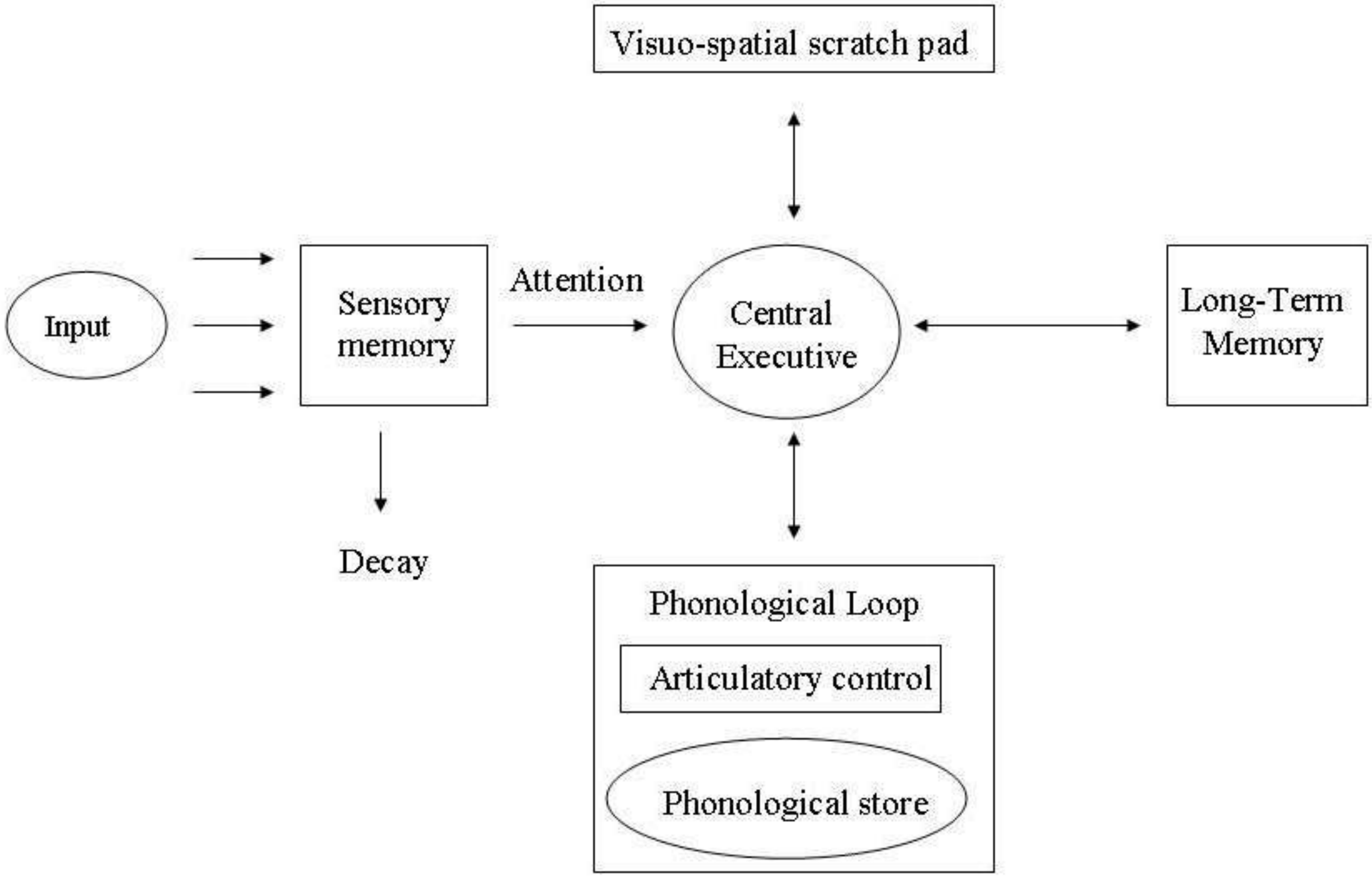


Also site of stem cell distribution in neurogenesis in pregnant women

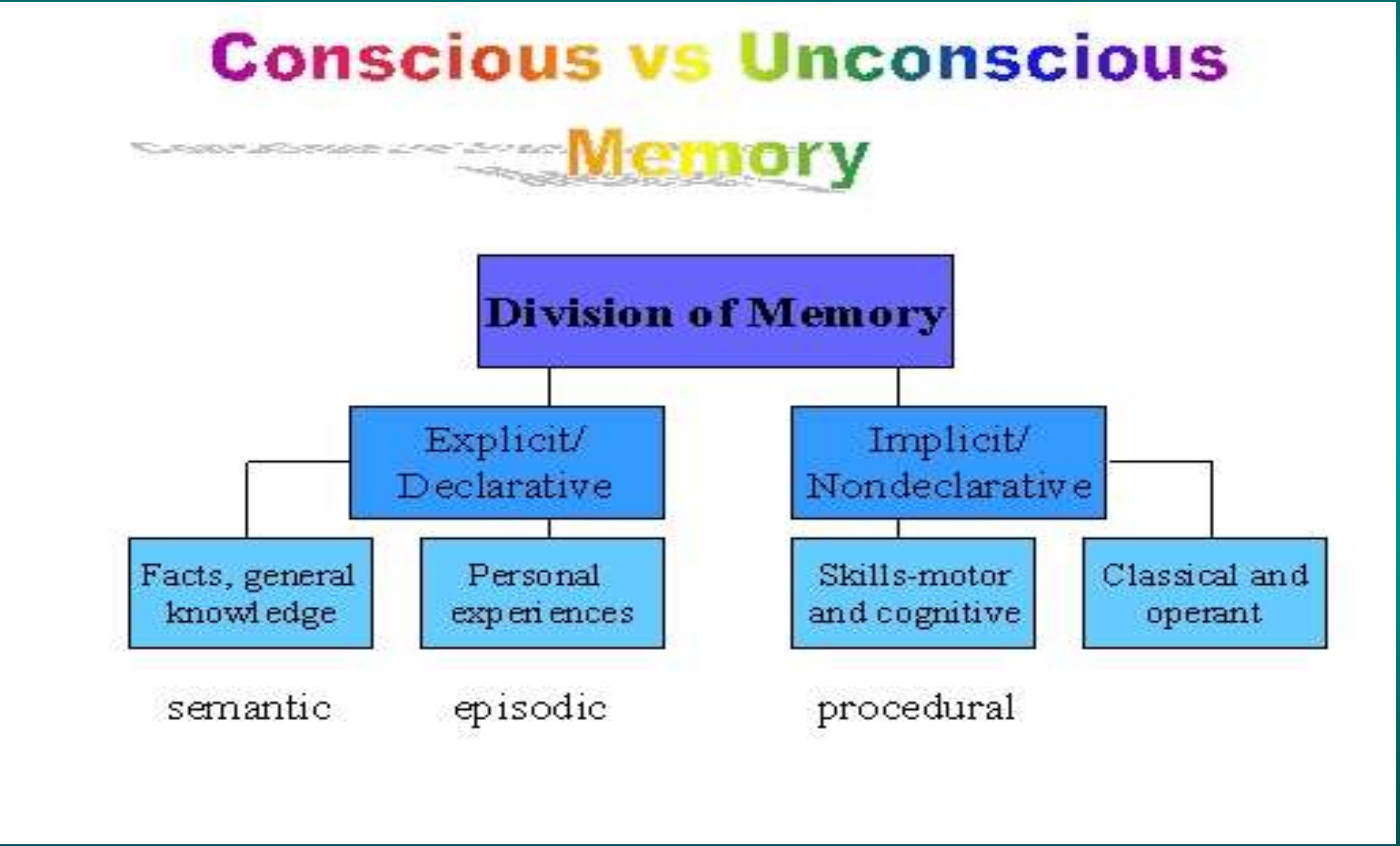

Stimulus
Sensory organs
perception
Sensory Memory
(millisecond - 1 second)
attention
Short-Term Memory
Working Memory
(< 1 minute)
repetition
forgetting
encoding
consolidation
retrieval
Long-Term Memory
(days, months, years)


Maintenance Rehearsal
Sensory Stimuli
Sensory Registers
Short-Term Memory Working Memory
Encoding
Long-Term Memory
Retrieval
Information lost in 0.5 to 3 seconds
Unrehearsed information lost in 10 to 30 seconds
Information retrieval failures

Working Memory Model (Baddeley and Hitch, 1974)



Memory Taxonomy



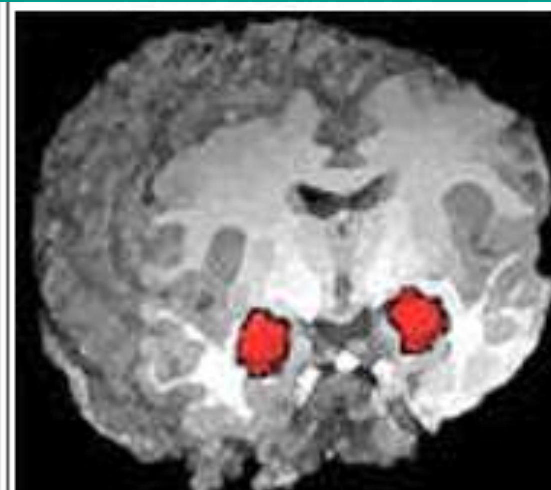
Memory & Emotion: William James (1890) & Maya Angelou

An impression may be so exciting emotionally as almost to leave a scar upon the cerebral tissues.

"I've learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel." –Maya Angelou

Amygdala: Flashbulb/traumatic memory

Challenger Space Shuttle
(NASA)



fMRI of Amygdalae
(NIMH)

Unanticipated, emotionally charged events can create vivid, detailed "Flashbulb Memories."

Flashbulb Memory:
My Daughter Lea at age 4 and Bambi's Mother

More facts of nature: All forest animals, to this very day, remember exactly where they were and what they were doing when they heard that Bambi's mother had been shot.

Flashbulb Memory : Nov. 22, 1963

CJV: 2 pm in classroom two at Mission San Luis Rey College

Flashbulb Memory : 1968

Flashbulb Memory : 9/11/2001

Sept 2002: 97% of Americans "can remember exactly where they were or what they were doing the moment they heard about the attacks"

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

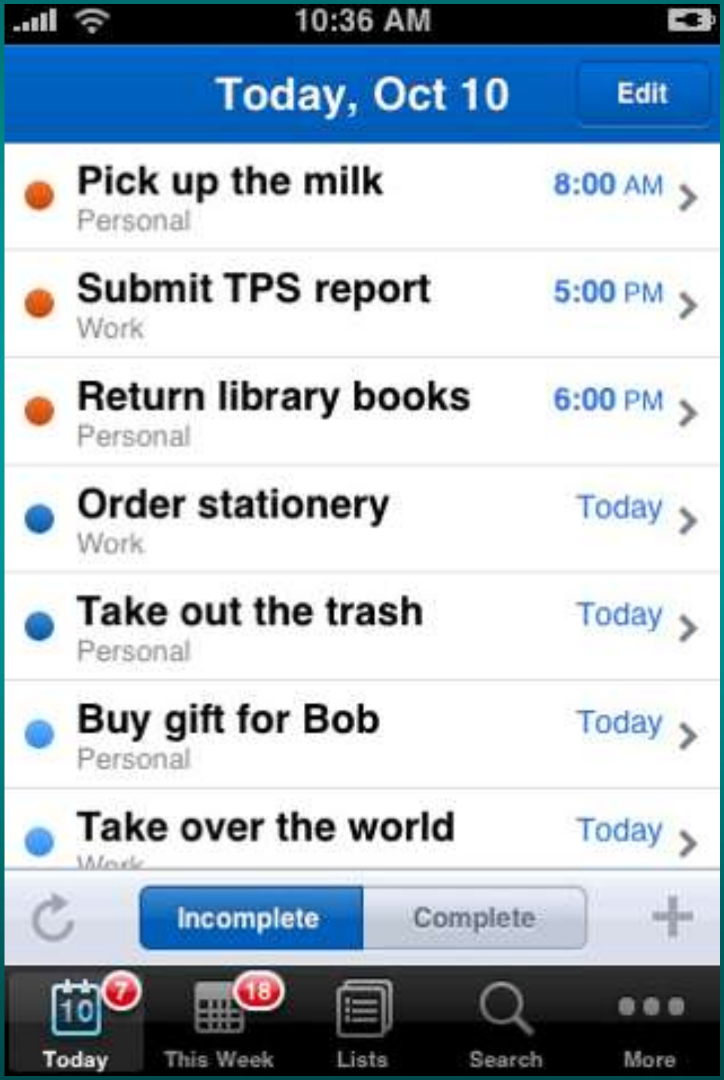
Working Memory

- Miller's Constant: 7 ± 2 in Psych. 101
- The capacity for <u>online storage and processing of information</u>
- <u>Highly correlated with Fluid IQ</u>
- <u>Attentional buffer that holds information while we process it</u>
  - Telephone number
  - Mental arithmetic
  - Recall of chess positions, bridge hands, music and baseball klg
  - Delayed response

Prospective Memory

- Remembering to remember

- Intention



Procedural Memory: Remembering how to…

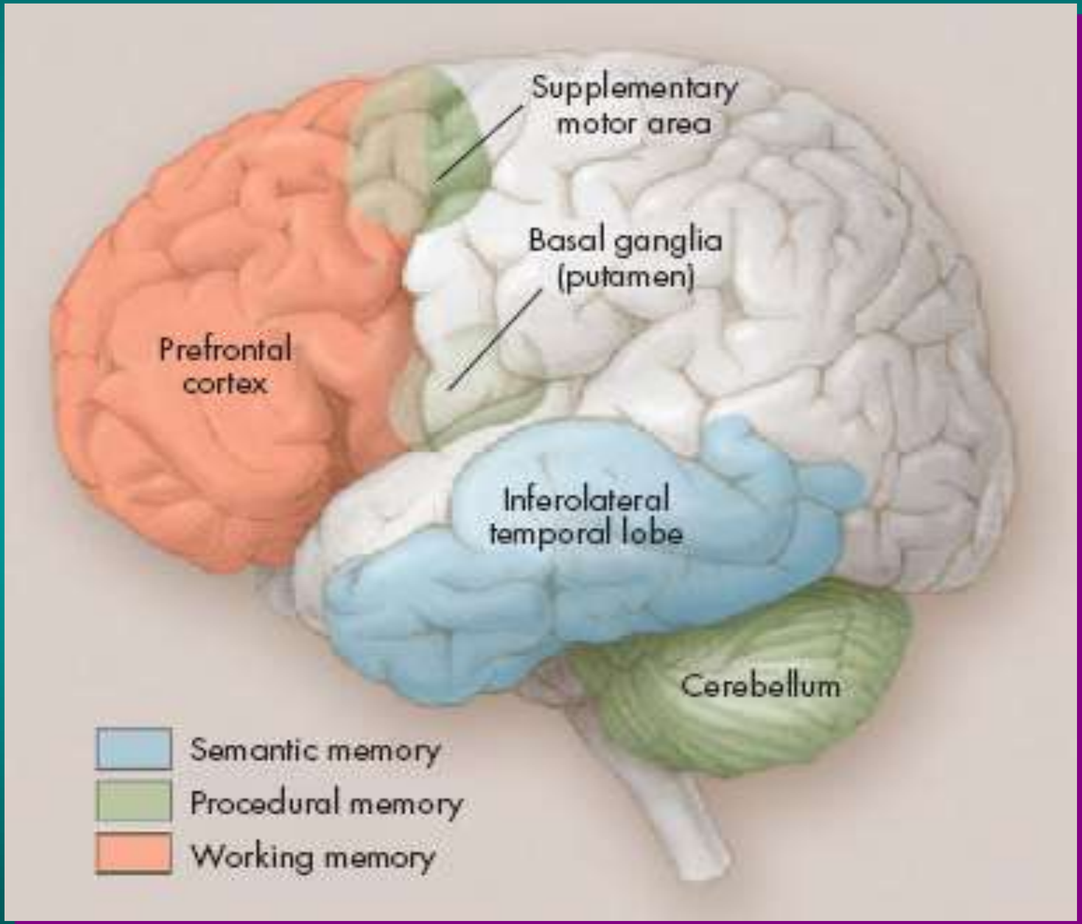
- Skills, habits
- Playing a musical instrument
- Playing sports
- Riding a bicycle, driving a car
- Reading mirror-reversed word
- Playing Chess, bridge
- Interpersonal Skills, Therapy behavior
- <u>Longest lasting</u>

Coming Up Next: Example of Procedural Memory

- Typewriting skills are procedural memory

Overlearned Memory

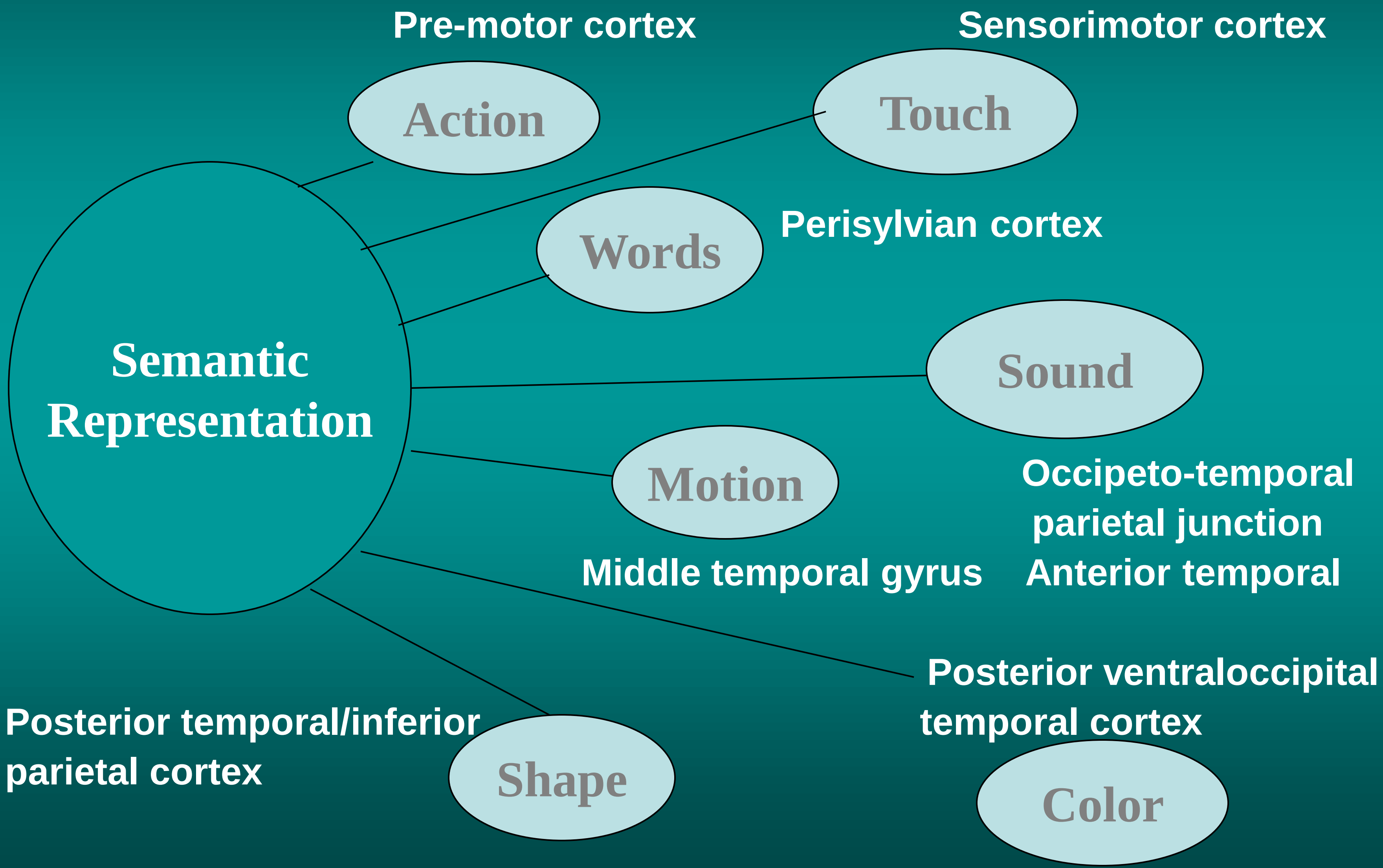
Memory and the Brain



Cortical Memory Structures

- <u>Hippocampus</u> – Acquisition of new factual knowledge
- <u>Primary association cortex</u> – Visual, auditory and somatosensory data
- <u>Non-medial temporal</u> – Retrieval of previously learned material e.g. autobiographical info, names, faces
- <u>Ventromedial frontal</u> – Memory traces linking facts and emotion
- <u>Dorsolateral frontal</u> – Recency and frequency memory. Working memory. Autobiog. memory

Locations of Semantic Memory



Topography of Semantic Knowledge: How Brain Stores Information

- Visual
- Verbal
  - Concrete
    - Nouns
      - Proper Nouns
        - Countries
        - People
      - Common Nouns
        - Animate
          - Animals
          - Fruits
        - Inanimate
          - Manipulable
          - Non-Manipulable
    - Verbs
  - Abstract

Other Known Categories: indoor / outdoor, vegetables

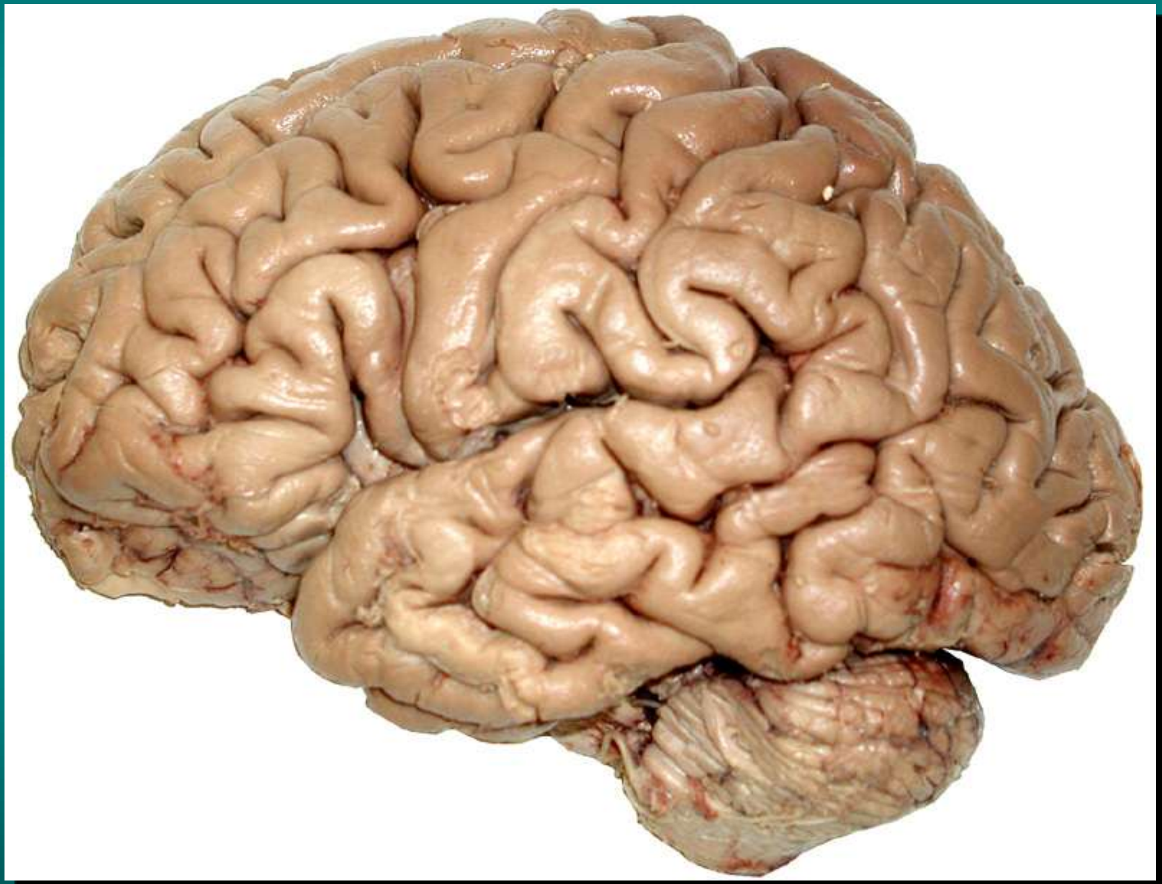
Frontal Action Systems

Three divisions of frontal cortex

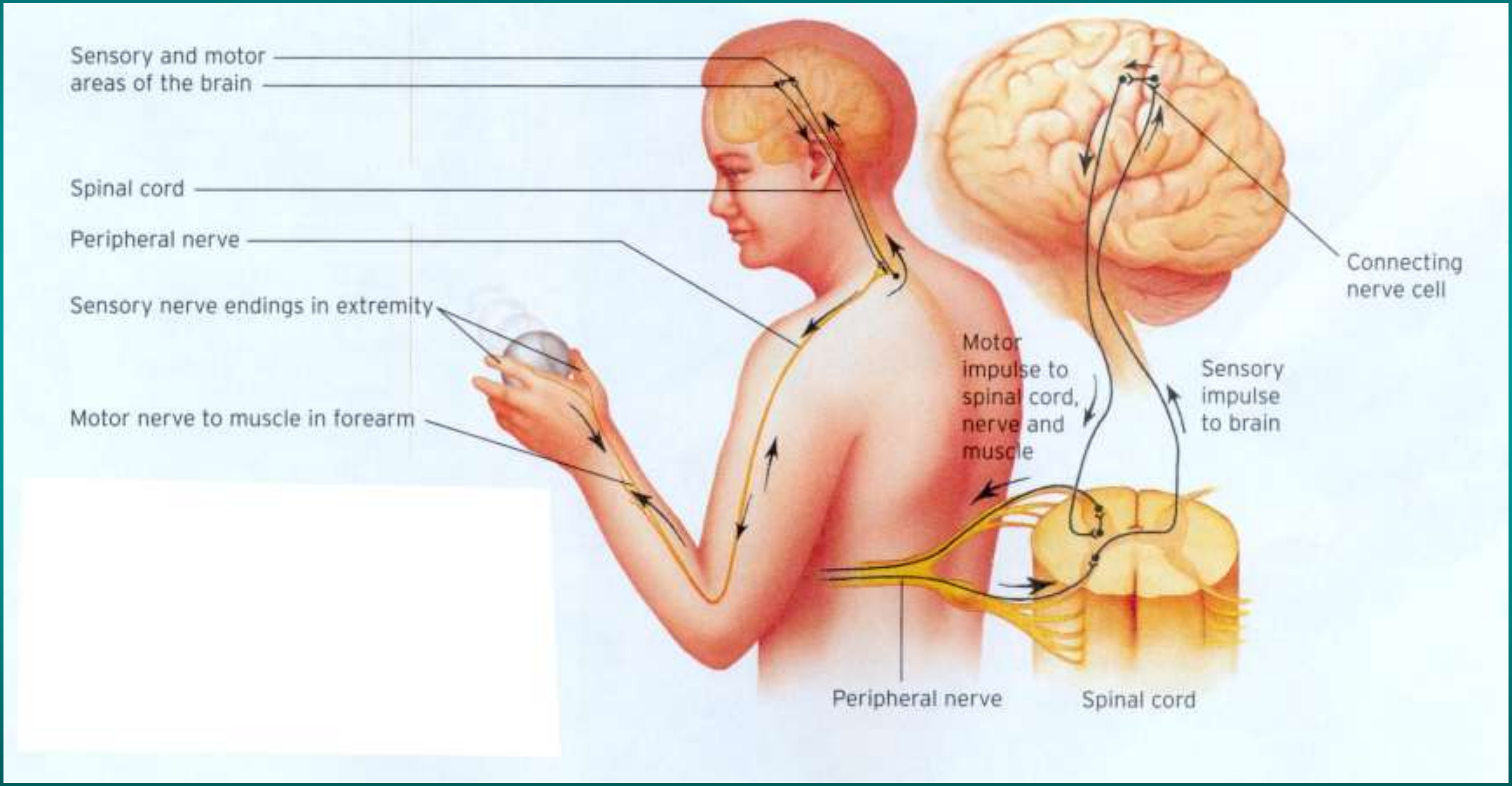
1. Primary motor

2. Premotor

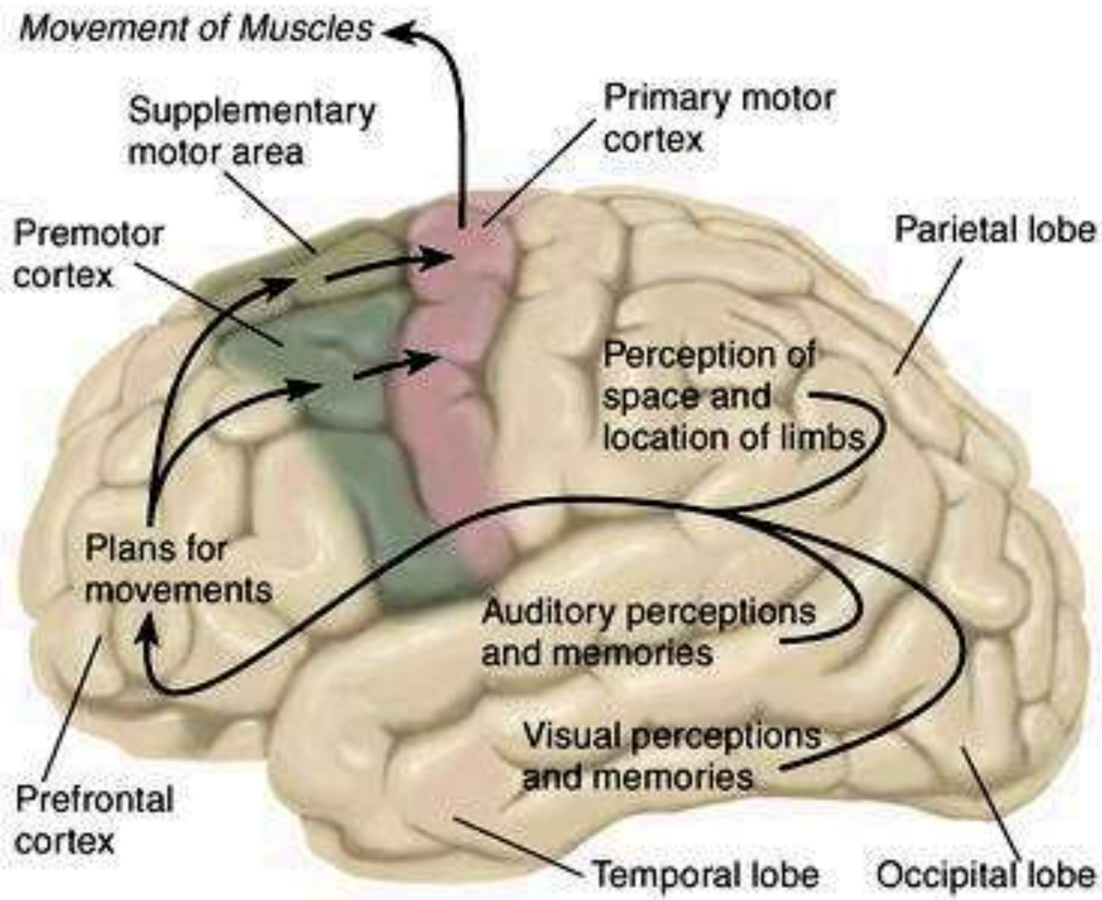
3. Prefrontal



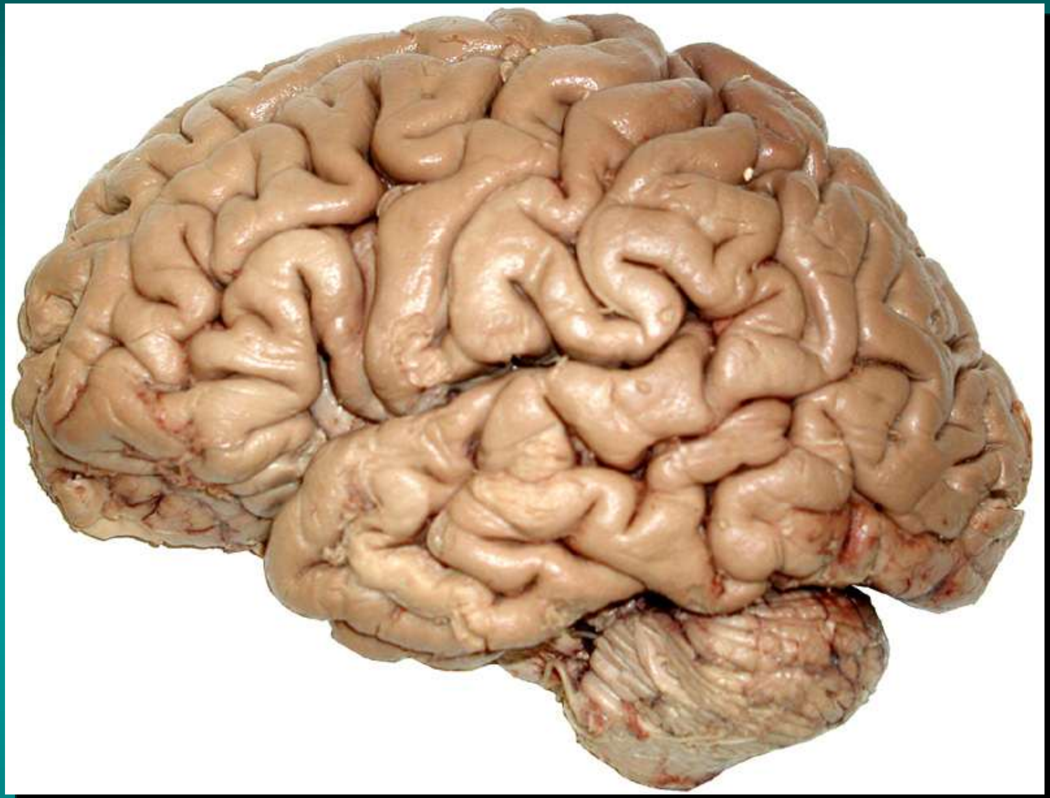
Control of Movement



► Cortical Control of Movement



Frontal: Primary Motor

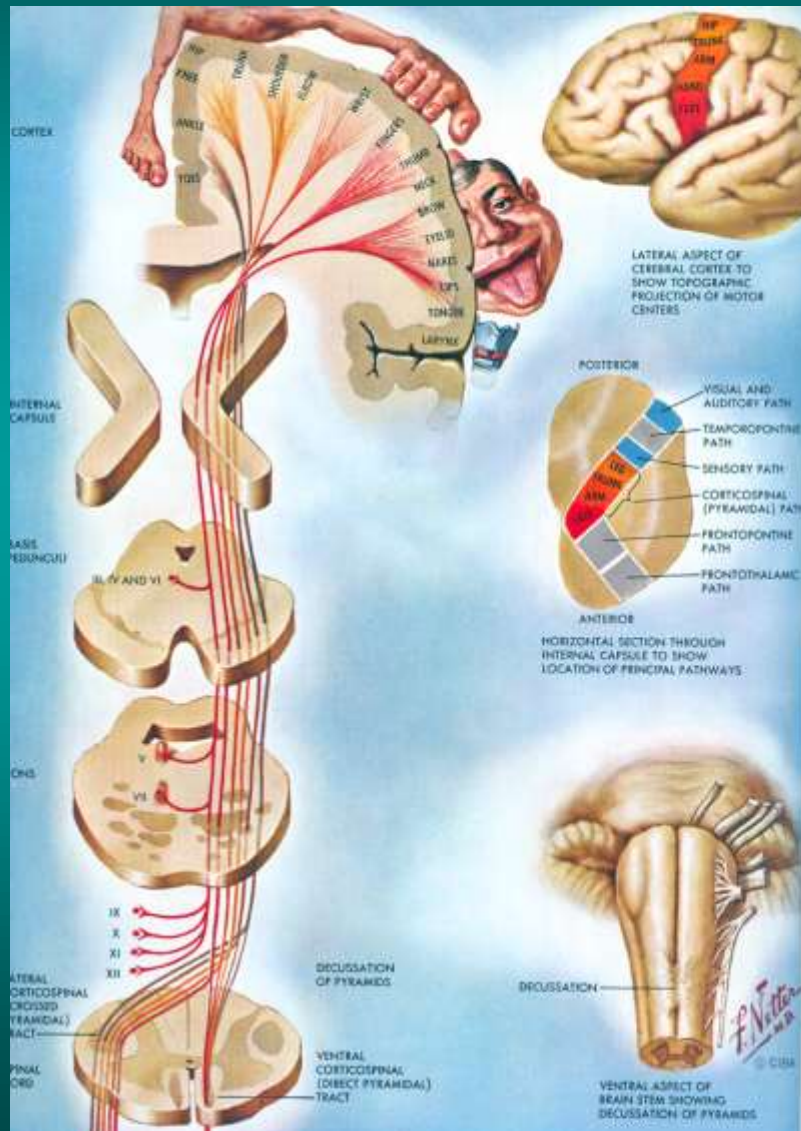


Primary Motor:

Execution of movement

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

Pyramidal System: Voluntary Movement



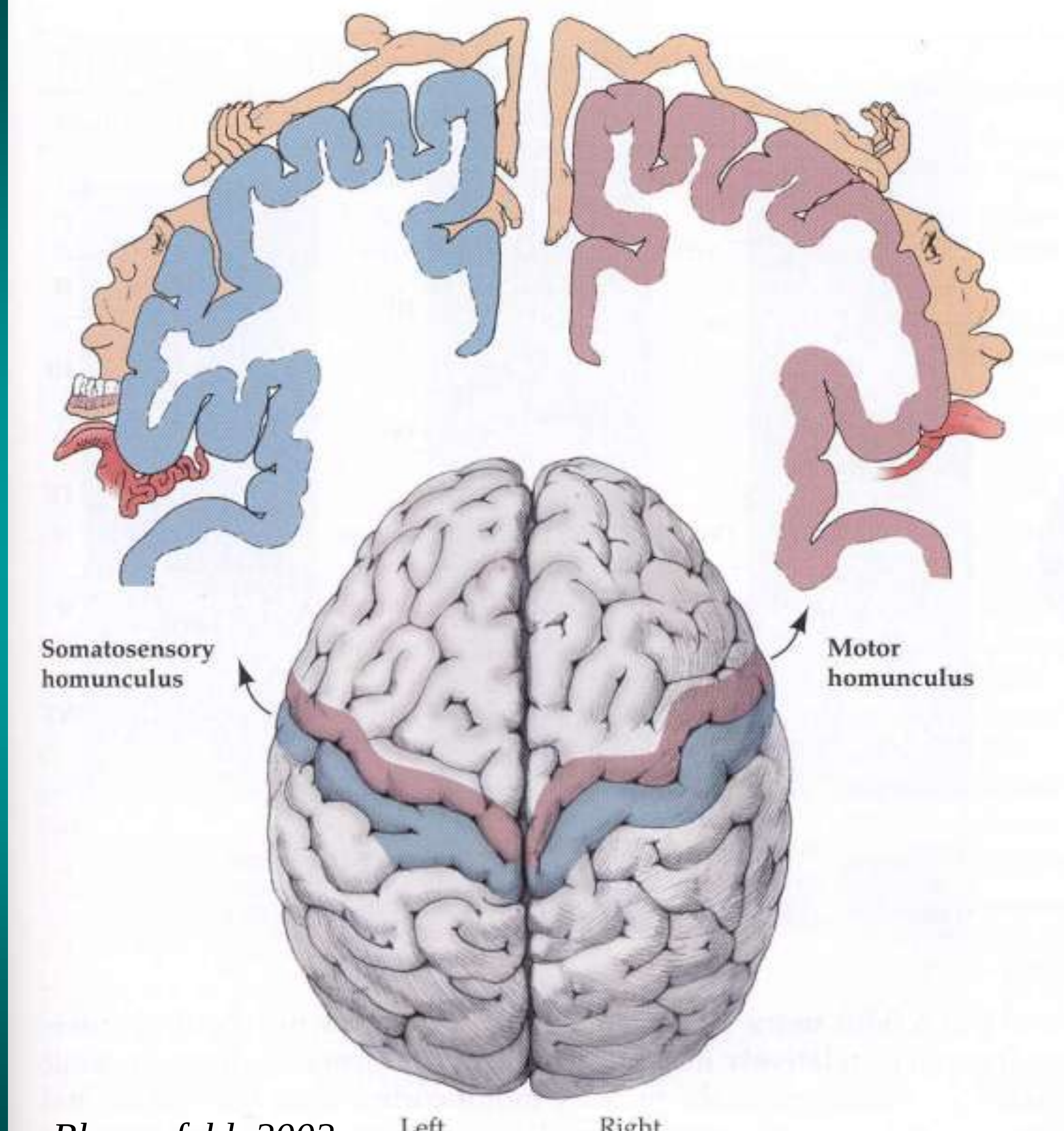
Motor Areas

Primary Motor Area (M I)

Premotor Area (PM)

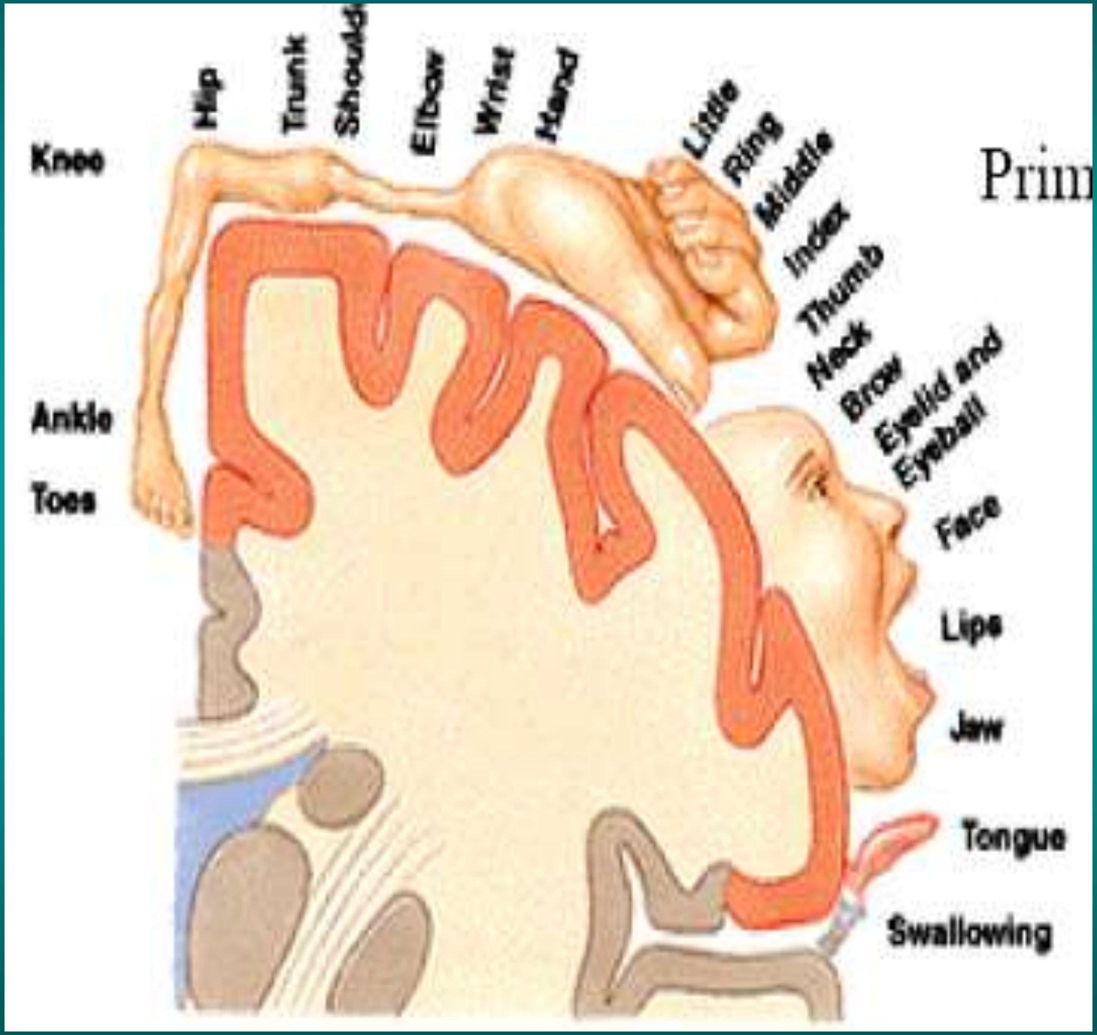
Supplementary Motor Area (SMA)

Frontal Eye Field (FEF)

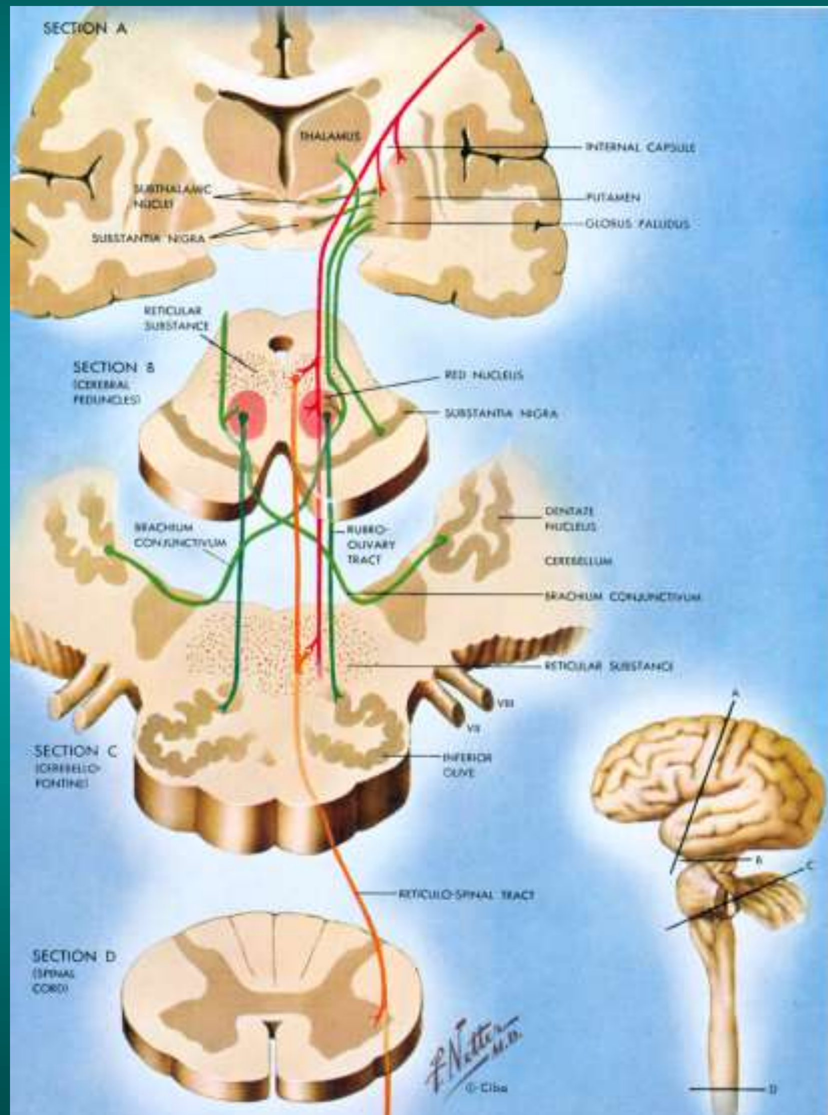


Blumenfeld, 2002

Primary Motor Strip



Extrapyramidal System: Involuntary Movement



Nonconscious Action

- 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 act; can veto

Apraxia

- Limb kinetic apraxia– breakdown of fine motor organisation of finger movements, so find it hard to copy meaningless hand movements, mimic proper gestures or use real objects flawlessly – Basal ganglia damage, supplementary motor area damage
- Ideomotor apraxia – unable to carry out motor acts to command, but often can do so spontaneously. Difficulty with selection, sequencing, spatial orientation and movements in meaningless and meaningful gestures, and demonstrating imaginary use of objects; dominant lobe. Perf. improves with imitation, and real object use - Inferior parietal and prefrontal damage. Callosal lesions can impair performance of one limb (usually the left)

Apraxia 2

- Ideational or conceptual apraxia – inability to carry out a complex sequence of co-ordinated movements even though each separate component of the sequence can be successfully performed. Inability to mime use of objects, or to even use the real objects. Thus possibly a disorder of semantic memory. – Left temporal lobe damage
- Oralbuccal apraxia – difficulty performing learned, skilled movements of face, lips, tongue, cheeks, larynx and pharynx on command – Inferior frontal region and insula, so commonly seen in Broca’s aphasia patients

Association Areas

Language Areas: 22, 39, 40, 44, 45

Posterior Parietal Association Area: *5, 7* (39, 40)
body image

Temporal Association Area: *20, 21, 37, 38* (22)
multisensory integration, conceptual ideation

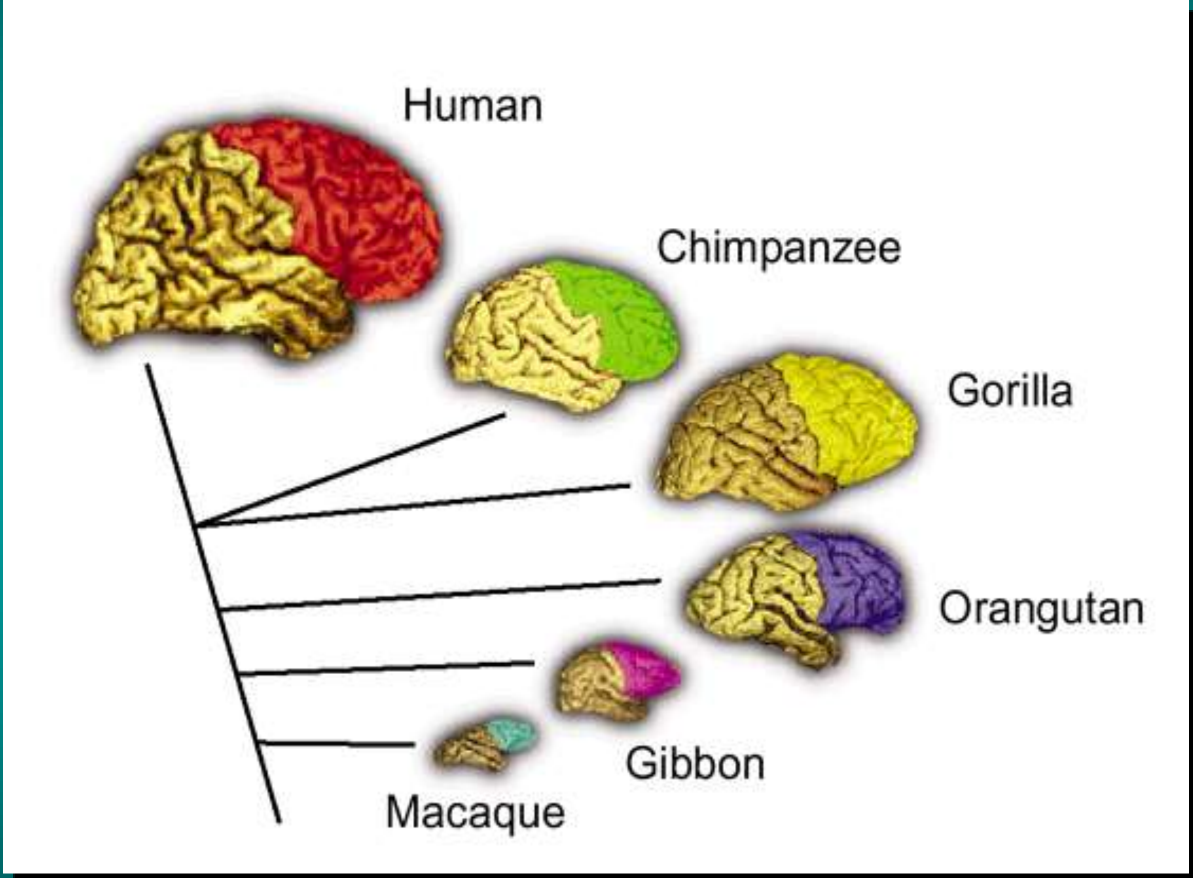
Prefrontal Association Area: 9, 10, 11, 12, 46, 47 (44,45) executive skills, judgment, planning, emotion-regulation

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.

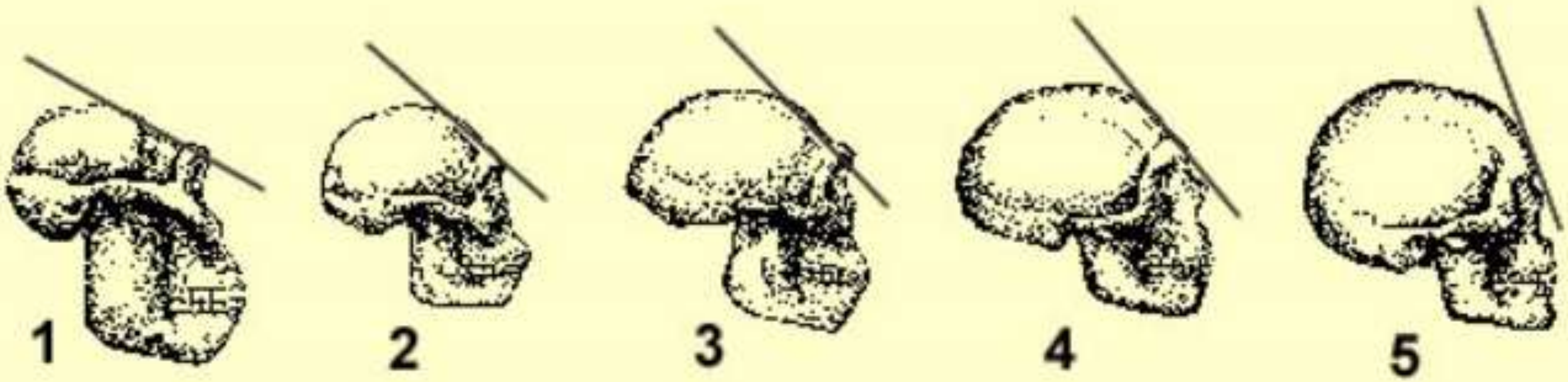
Evolution of Prefrontal Lobes:



30% in primates; humans greater white matter: greater neuronal connectivity

Forehead is the thing!

The high, straight forehead that characterizes modern humans, superceding the prominent brow ridges of our ancestors, is due to the expansion of the cortex, and especially the prefrontal cortex, in our species.



1. *Australopithecus robustus* 2. *Homo habilis* 3. *Homo erectus*
4. *Homo sapiens neanderthalensis* 5. *Homo sapiens sapiens*

Intelligence in 1955 = Larger Frontal Lobe
This Island Earth

Humans vs. Metalunan vs. Zagon

Prefrontal

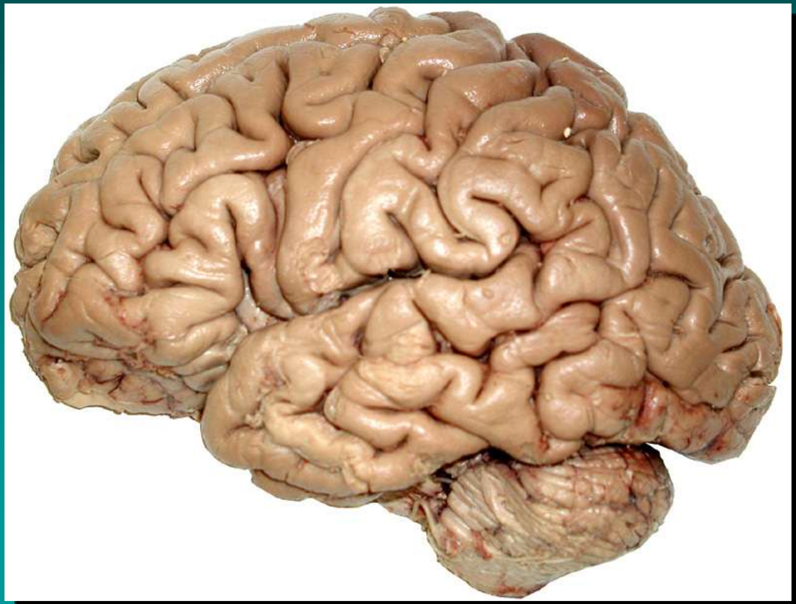
Pre-frontal

-->Three areas

- Dorsolateral
- Medial
- Orbital/Inferior

Artery:
- Anterior cerebral
- Middle cerebral

Vein:
- Superior sagittal sinus



Brodmann areas and Prefrontal Divisions

<table>
<tr><th>8</th><th>9</th><th>46</th><th>44</th><th>45</th><th>lateral 47</th><th>orbital 47</th><th>11</th><th>10</th></tr>
<tr><td colspan="6">dorsolateral</td><td colspan="2" rowspan="3">orbitofrontal, ventromedial, basal, orbital</td><td rowspan="3">frontopolar, anterior, rostral</td></tr>
<tr><td colspan="3">dorsolateral</td><td colspan="3" rowspan="2">ventrolateral</td></tr>
<tr><td>posterior dorsolateral</td><td colspan="2">mid-dorsolateral</td></tr>
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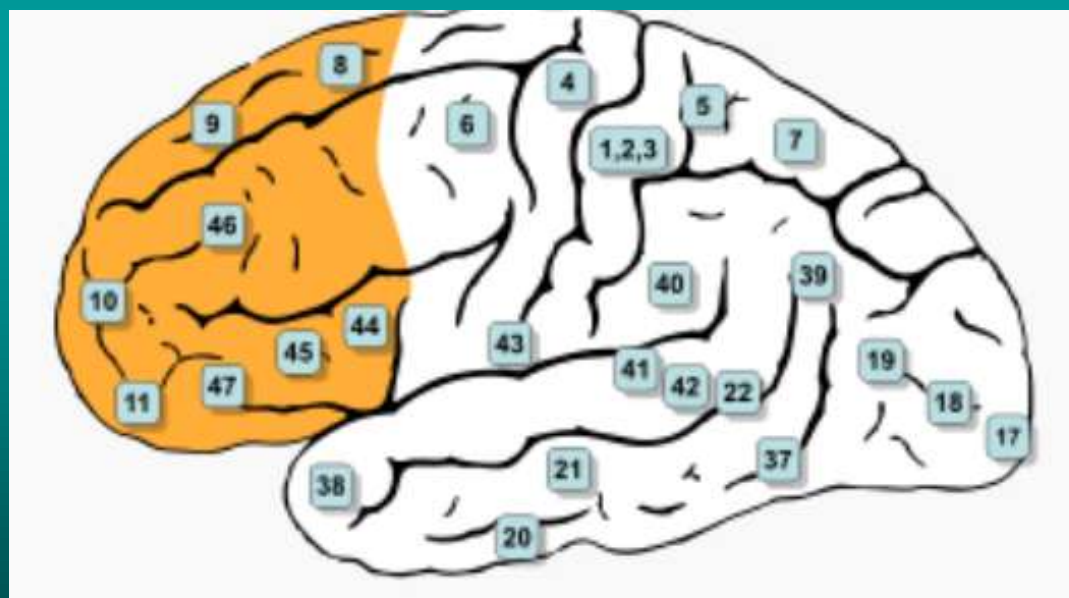
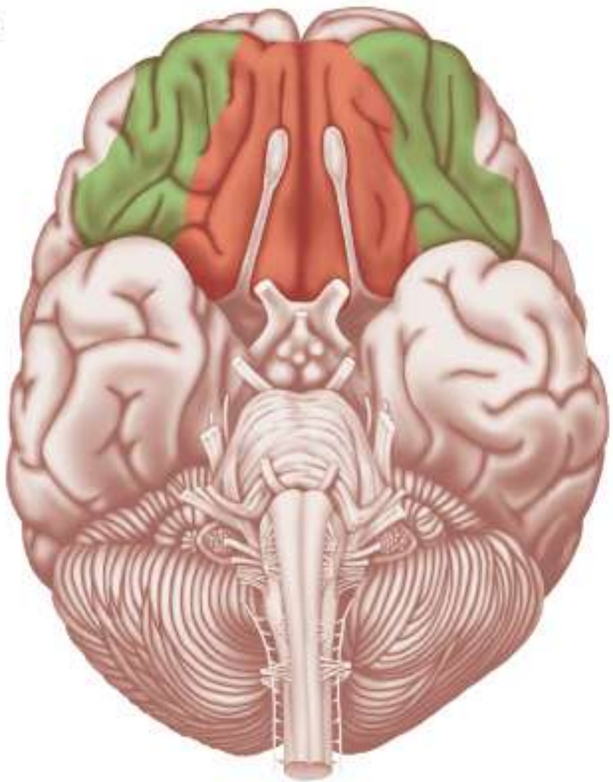
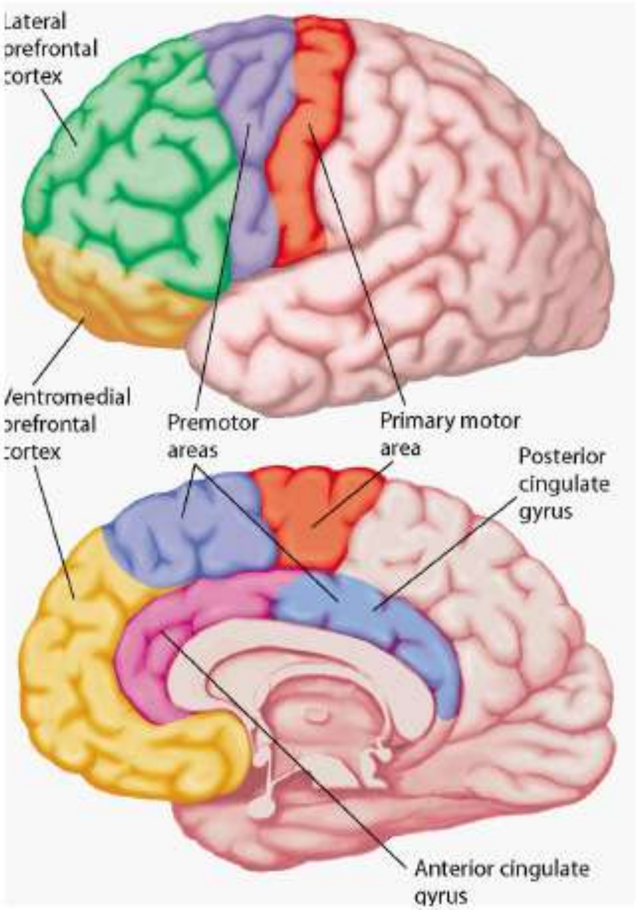


Frontal Lobe Divisions





The orbitofrontal cortex is divided into **ventromedial** (reddish in the anterior view: above and yellow in the convex-lateral and median-sagittal view) and the **lateral** orbitofrontal cortex (green)

Prefrontal Functions

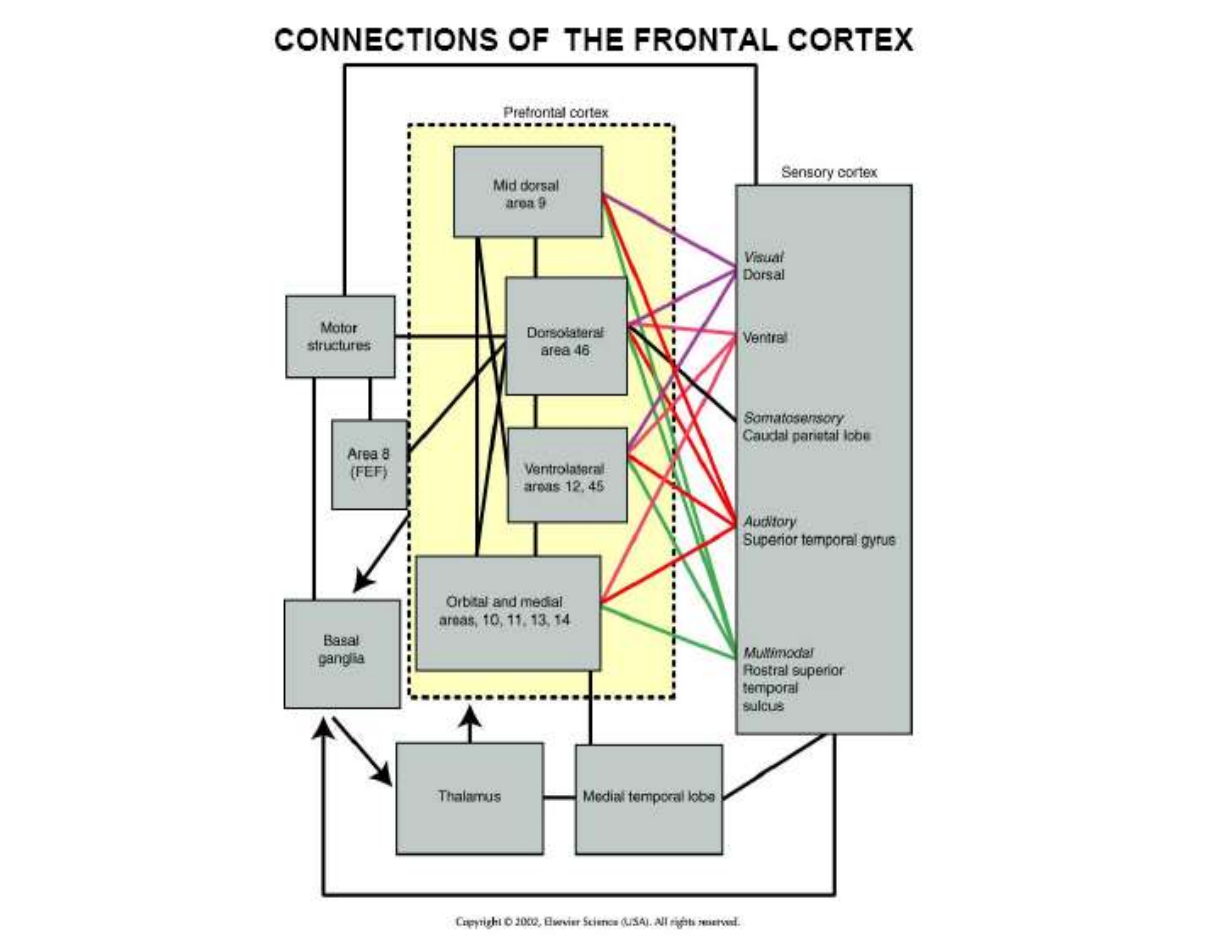
- Dorsolateral
  - higher cognitive functions, more complex, strategic thinking
  - working memory, planning, set shifting
  - response selection, inhibition
  - DLPFC and ACC are involved in difficult personal moral decisions, particularly when those decisions involve violating the rights of others
  - DL PFC appears to be critically involved in maintaining goal representation and in anticipating future affectively charged events

- Medial
  - Behavioral activation
  - VentroMedial: automatic, emotionally-mediated moral network that is centered in the right VMPFC.

Prefrontal Functions

- Orbital
  - behavioral inhibition
  - spontaneity
  - conscious odor awareness (right OFC)
  - social emotions activate the emotional states that are necessary for normal social decision making (normal = cooperation)
  - OFC subserves evaluation of reinforcers and learning of stimulus-incentive associations and thus plays a key role in the motivational control of goal-directed behavior.
- Medial OFC regions are critically implicated in reward monitoring,
- Lateral OFC regions are related to evaluation of punishment
- Resting activity in OFC and left PFC is associated with tendencies for approach-related behavior manifested through increased reward responsiveness

Frontal Lobe Connections



Attention Systems

- <u>Prefrontal</u>:
  - <u>Top-down control of intentional focus </u>(deficit = ADHD)

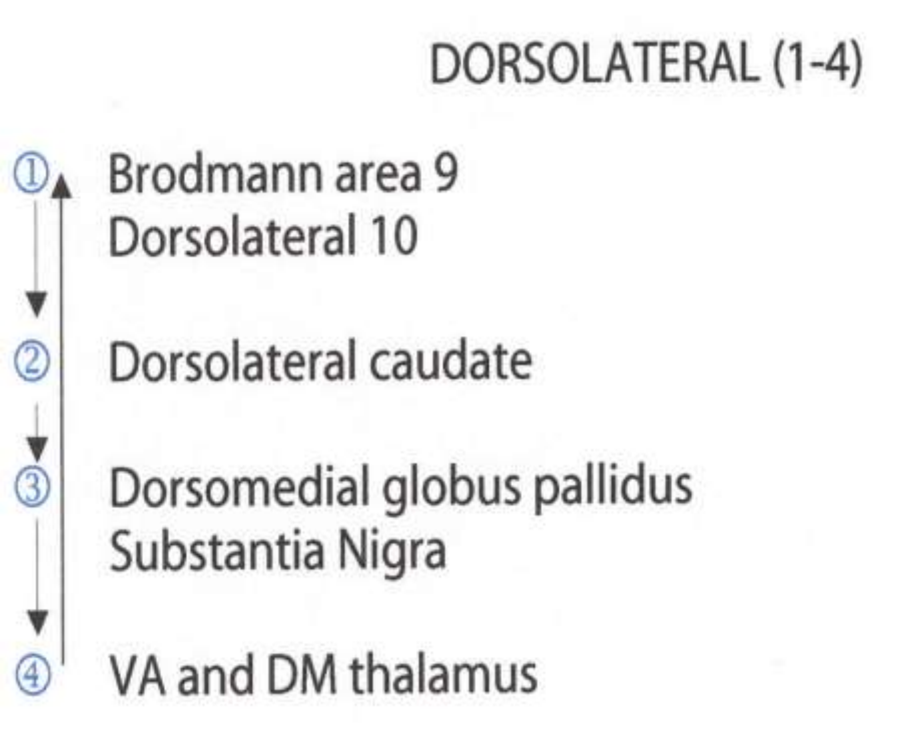
- <u>Parietal</u>:
  - <u>Bottom-up control of environmentally driven visual attentional orientation</u> (i.e. loud truck noise outside)

Sunscreen Choice and Medial Prefrontal

- Increased activity in the medial prefrontal cortex among individuals viewing and listening to public service announcement slides on the importance of using sunscreen strongly indicated that these people were more likely to increase their use of sunscreen the following week, even beyond the people's own expectations.
- From this region of the brain, we can predict for about three-quarters of the people whether they will increase their use of sunscreen beyond what they say they will do, vs. 50% of those saying they will.

Dorsolateral (Prefrontal) Loop

- Critical for executive function
- Dopamine plays a particularly important role in DL-PFC



Dorsolateral Damage

- Damage produces impaired:
  - Executive Functioning
  - Flexibility
  - Planning
  - Problem-solving
  - Goal-directed behavior
  - Poor Working Memory
- Poor test Performance:
  - Poor TMT
  - Poor WCST
  - Poor Category Test
  - Poor D-KEFS
  - Poor IVA

Left Dorsolateral Prefrontal & Pain

- Chronic Pain x 1 y:

Thinning of LDPFC

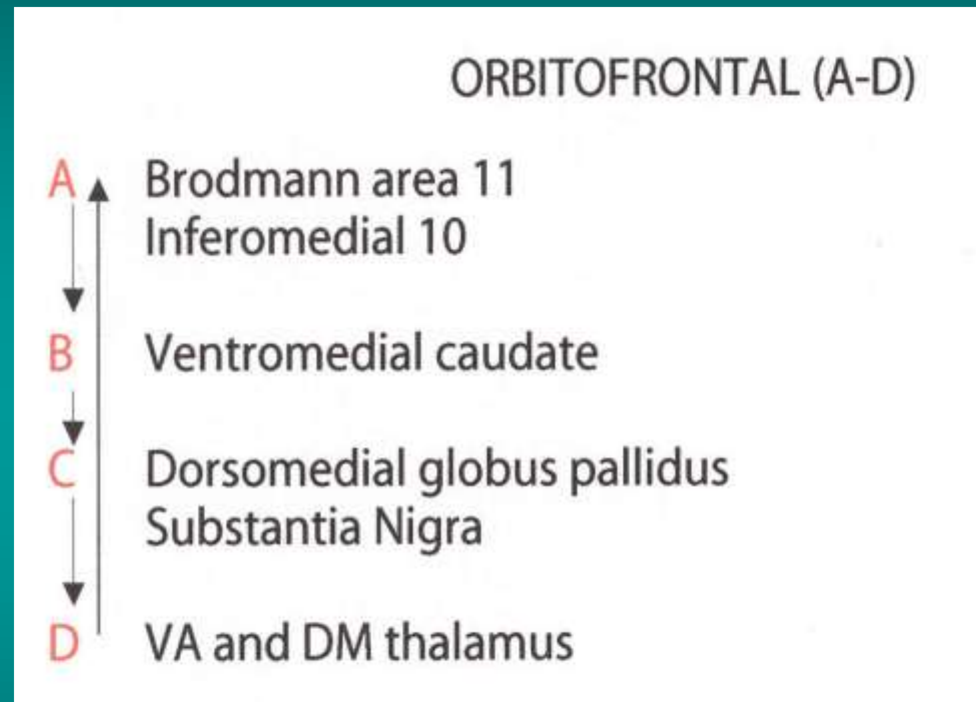
Abnormal activity on cognitive test in FMRI

Chiavo, 2011

- 6 months after pain relief: surgery or injections:
- Thickening of LDPFC
- Normalization of cognitive activity

Orbitofrontal (Limbic) Loop

- Involved in <u>social, emotional, & reward functioning</u>
- Decisions are made by <u>estimating the values of different outcomes</u> from incomplete info;
- Emotional Affective value of reinforcers
- Regulate <u>planning behavior associated with sensitivity to reward and punishment.</u>[
- <u>Substance abuse, drug expectancy, craving</u> and decision-making



Orbital Damage

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

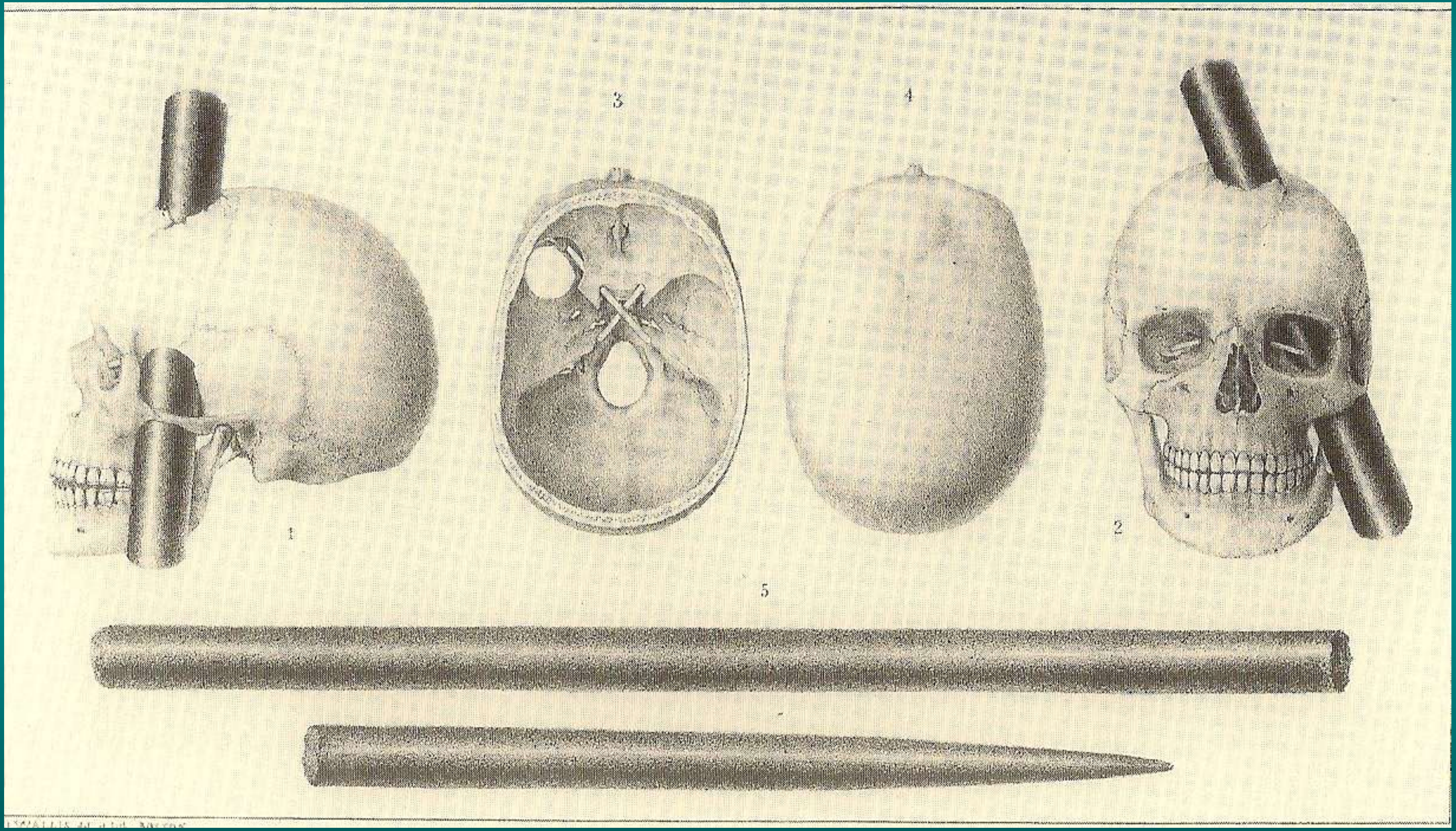
- Disinhibition:
  - swearing excessively, hypersexuality,
  - poor social interaction, compulsive gambling, drug use (including alcohol and tobacco),
  - poor empathizing ability

- FTD behaviors

Medial orbitofrontal cortex	Lateral orbitofrontal cortex
Personality change	**Personality change**
Anergy	Irritability
Anhedonia	Tactlessness
Neurovegetative changes	Fatuous euphoria
Hyper- or hypophagia	Impulsivity
Circadian dysfunction	Undue familiarity
Alimentary changes	**Environmental dependency**
Mood disorders	Utilization behavior
Depression	Imitation behavior
Dysphoria	**Mood disorders**
Obsessive-compulsive disorder	Lability
	Mania
	Obsessive-compulsive disorder

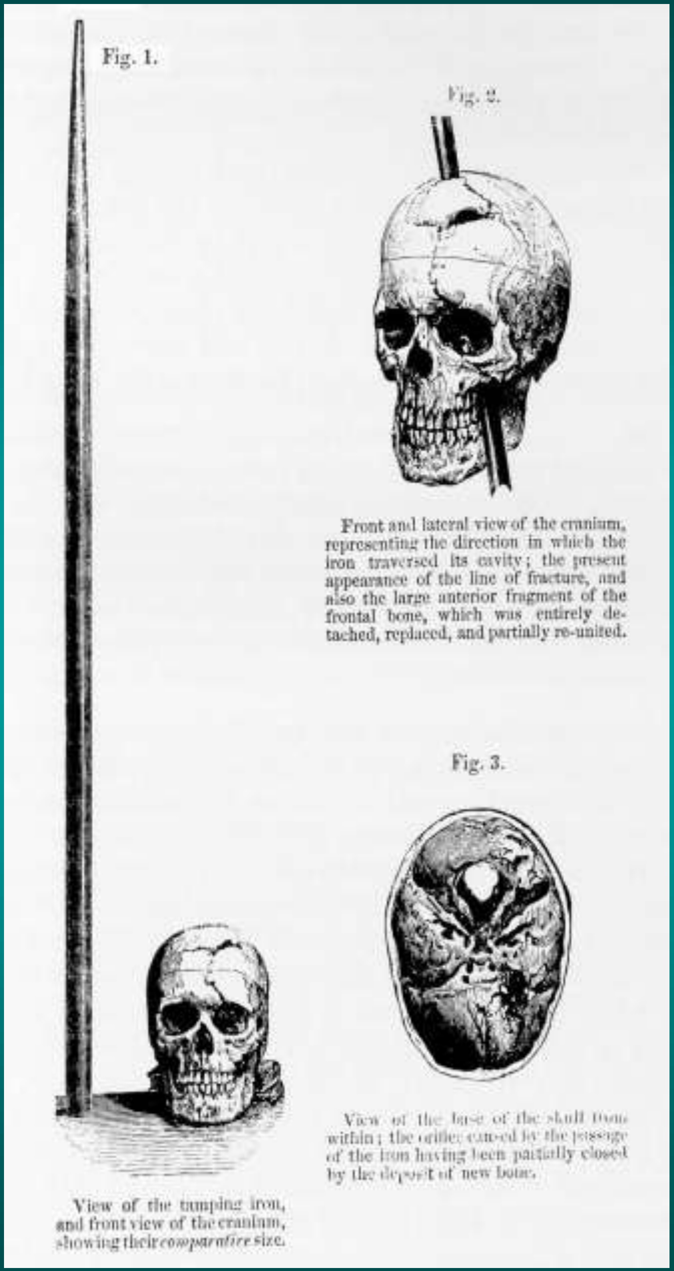
Mega & Cummings, 2001

1848: Most Famous Localization Case



Phineas Gage

(1823-1861, accident in 1848)



Phineas Gage: 1848

- 25-year-old foreman of a construction gang on Sept. 13, 1848, preparing a railroad bed outside Cavendish, Vt.
- As usual, he was using a pointed iron rod -- 3 feet, 7 inches long and 13 1/4 pounds -- to tamp gunpowder and sand into a hole drilled in the rock.
- But on that day, the mixture exploded, sending the rod through his left cheek and out through the top of his head.

Examined by John Harlow MD. Henry J. Bigelow MD. latter stated “no sequelae”

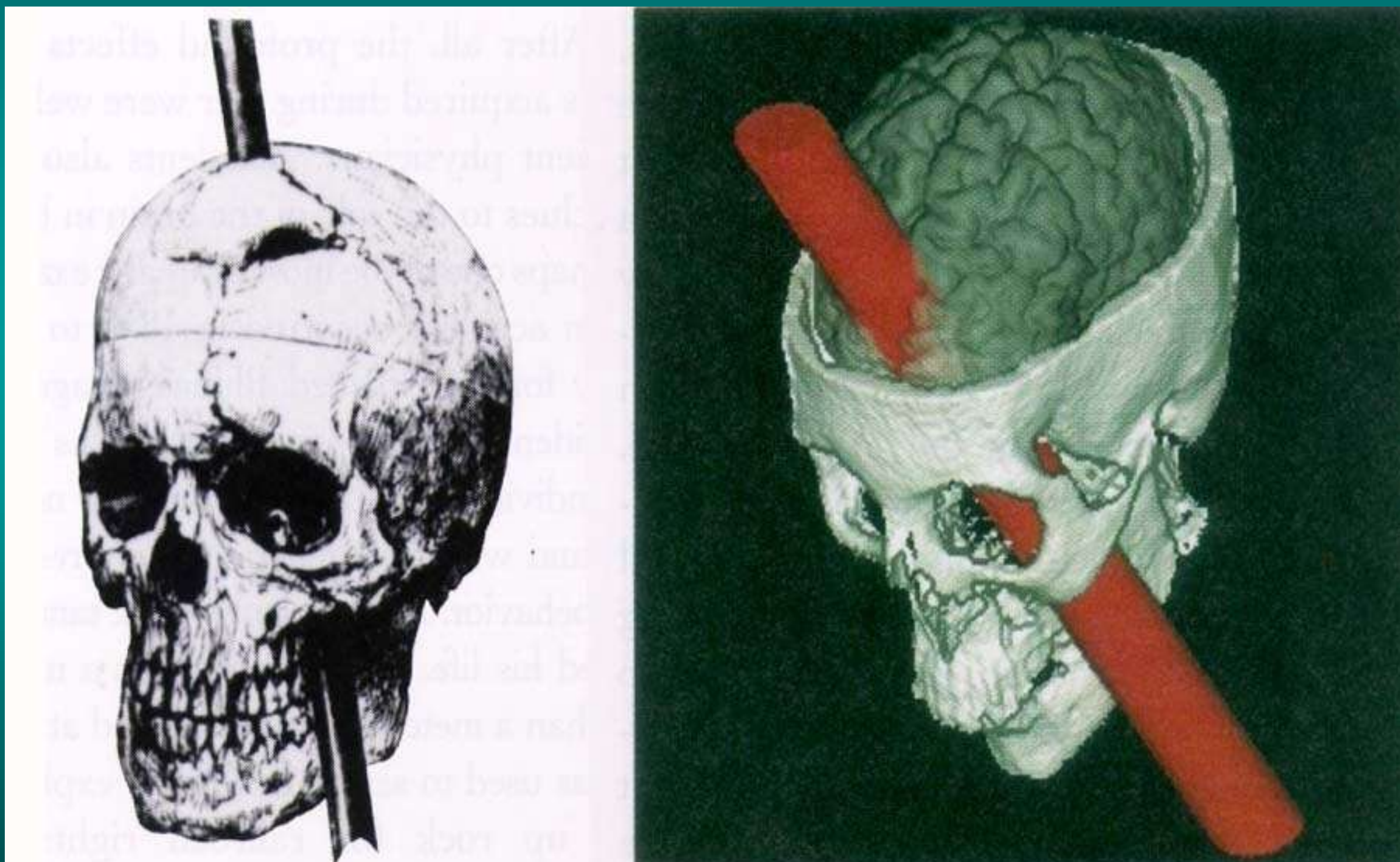
John Harlow MD describes Phineas in 1868

First to exam Phineas in 1848:
A phrenologist; but got Gage's skull and rod for Harvard in 1867.

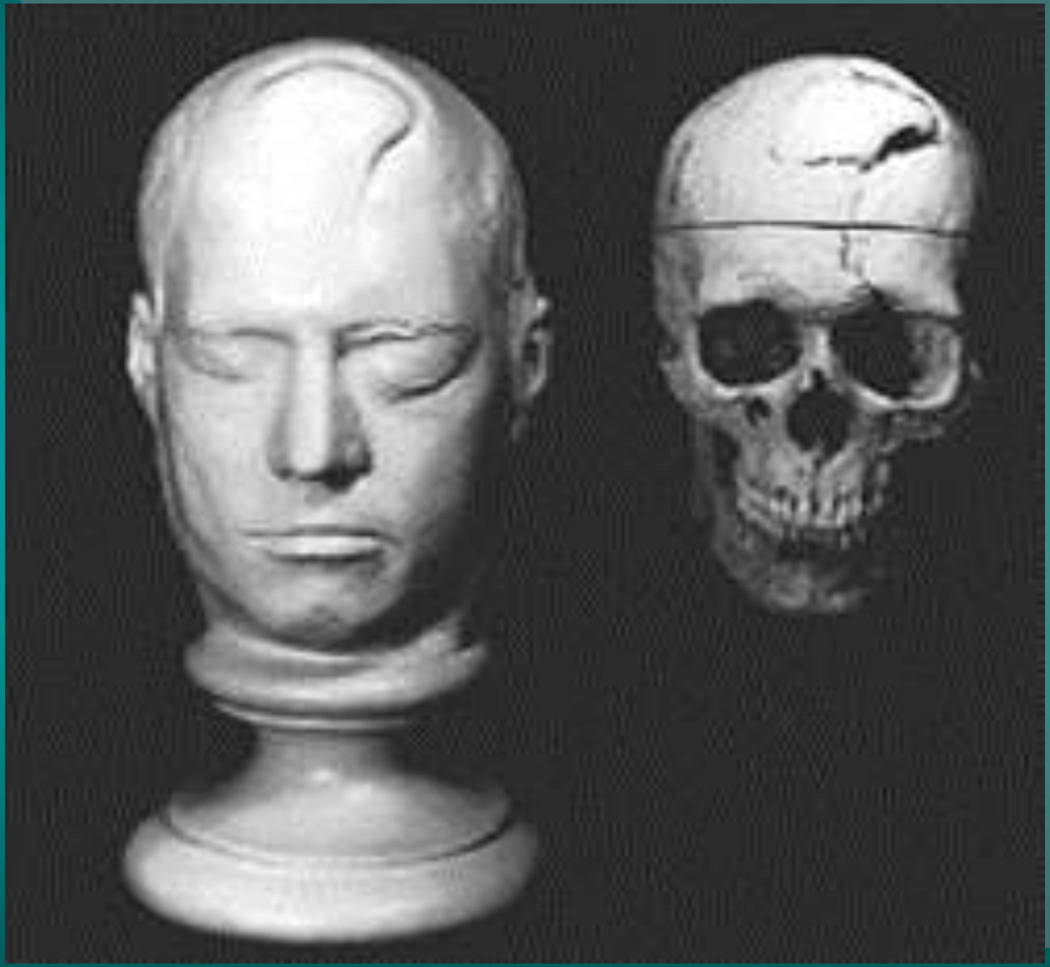
"His contractors, who regarded him as the most efficient and capable foreman in their employ previous to his injury, considered the change in his mind so marked that they could not give him his place again. He is fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operation, which are no sooner arranged than they are abandoned in turn for others appearing more feasible. In this regard, his mind was radically changed, so decidedly that his friends and acquaintances said he was "no longer Gage."

Phineas Gage's lesion reconstructed

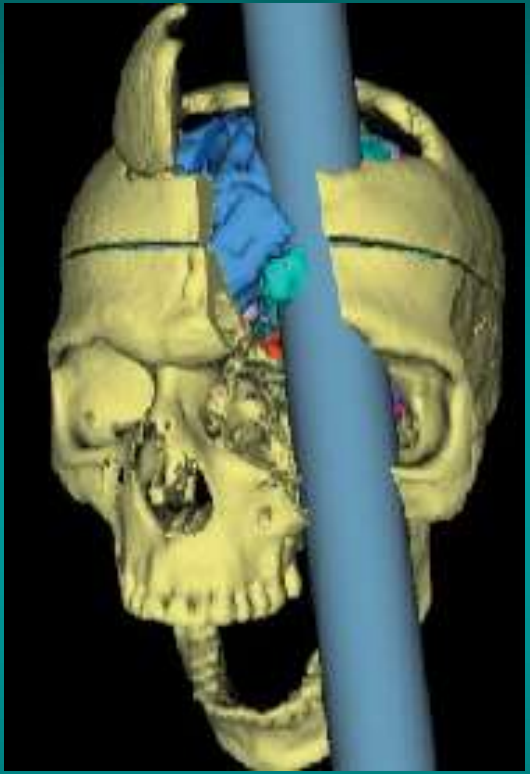
(H. Damasio and R. Frank, 1992)



Phineas Gage, 1848

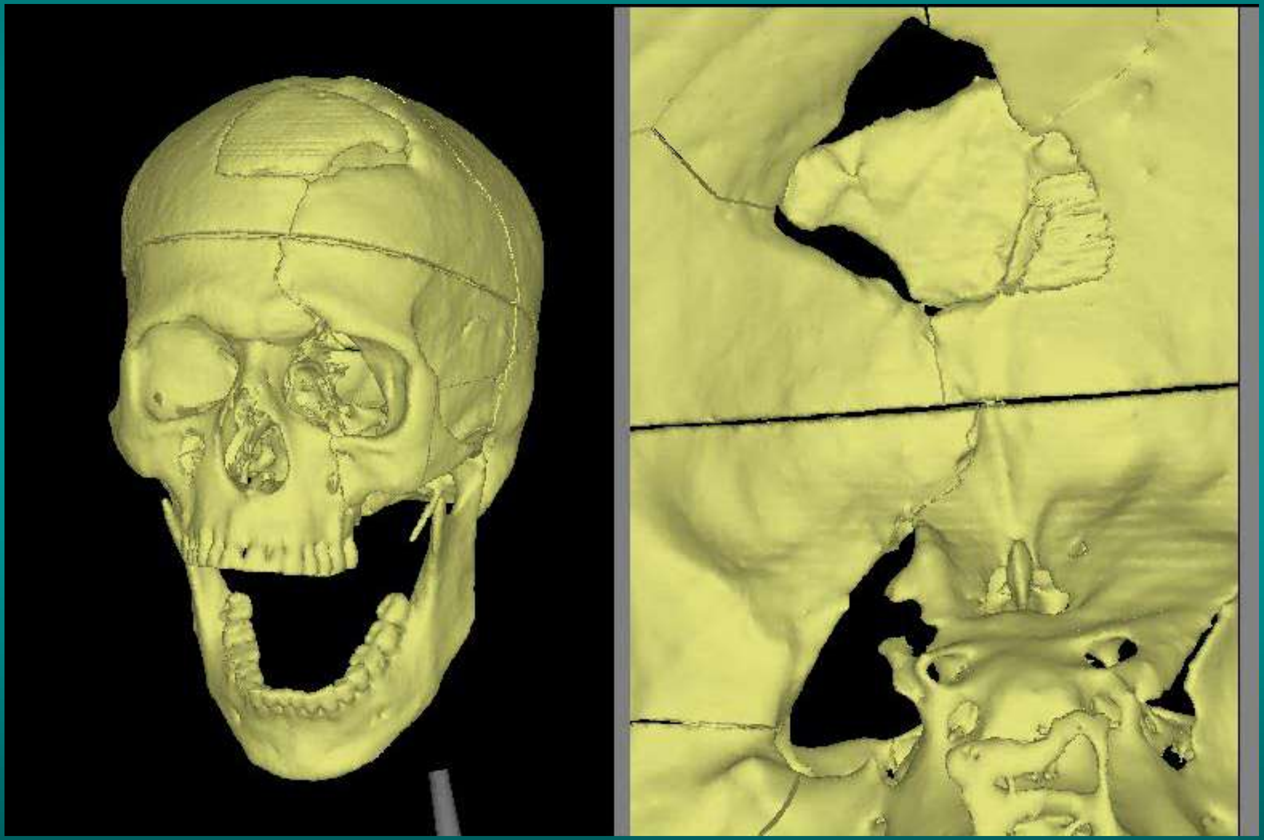


Life mask at Harvard Medical School's Warren Anatomical Museum

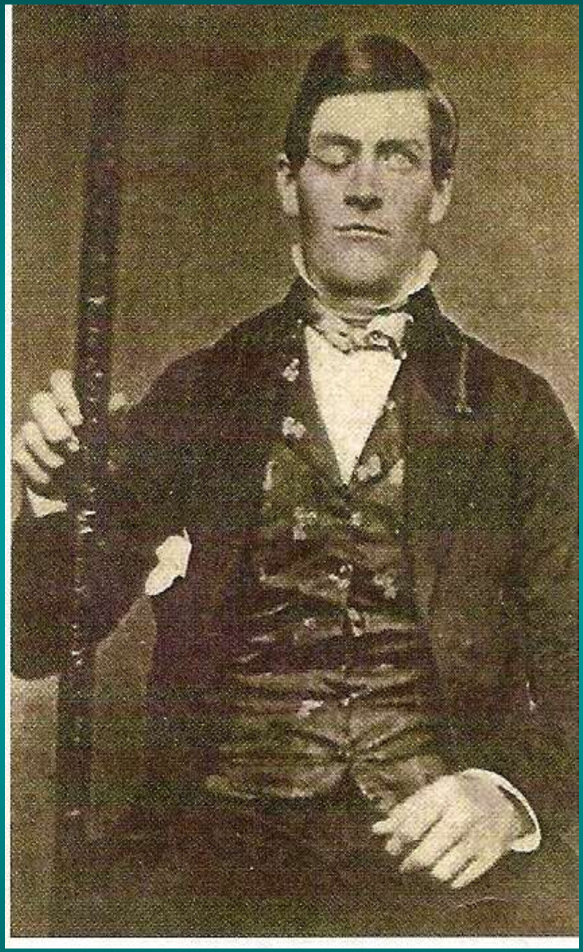


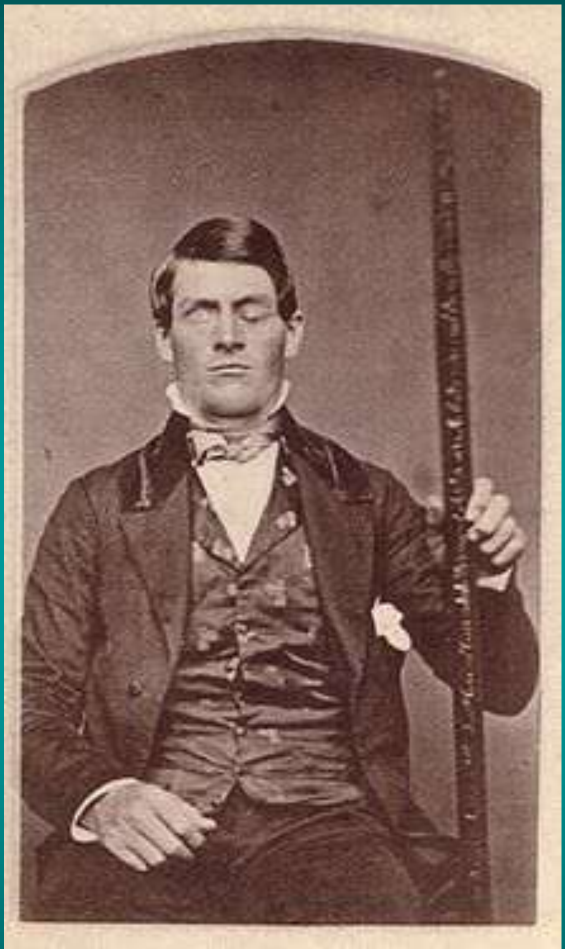
The image Peter Ratiu and Ion-Florin Talos published in the New England Journal of Medicine in 2004.

The Phineas Gage Event



Phineas Gage, 1848: Which is correct



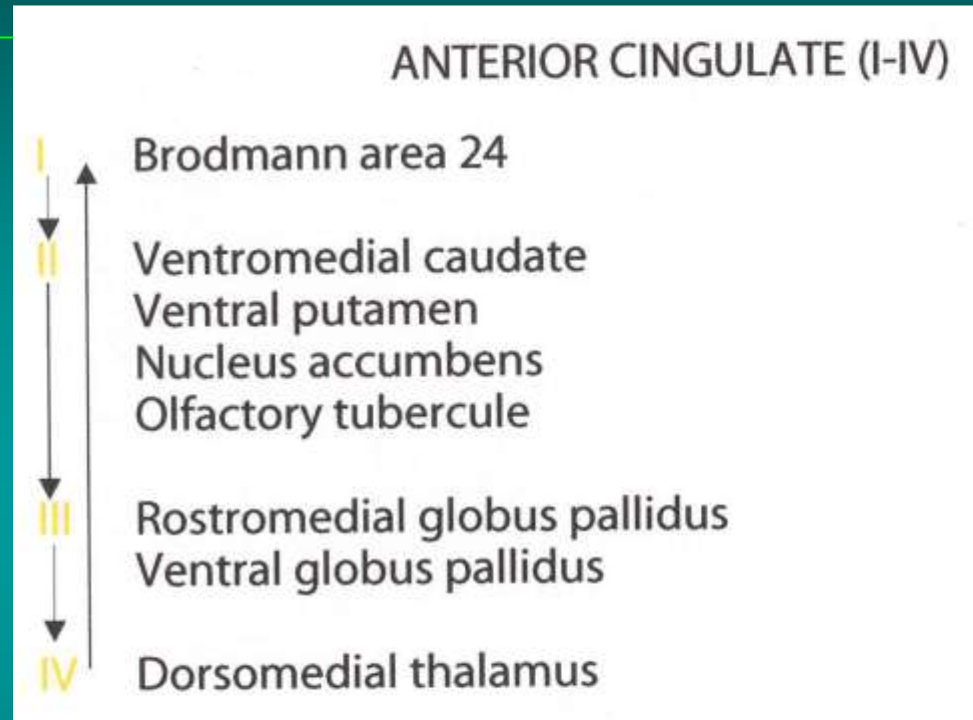


Phineas Gage

- Phineas gave lectures and exhibited himself and his tamping iron throughout New England;
- Worked as an ostler (stableman) at Jonathan Currier's Hanover Inn in Dartmouth, NH, for 18 months;
- Went to Valparaiso, Chile to work as a stage-coach driver.
- After about another 5-6 years Phineas became ill and returned, probably in 1859, to his family, then resident in San Francisco. After again regaining his health, his mother said he "was anxious to work" and did so as a farm laborer in Santa Clara County.
- In February 1860 he began to have epileptic seizures and only after they had begun did he become restless, dissatisfied with his employers, moving often from one job to another.
- The seizures became more frequent and he died in May 1860 of repeated attacks (*status epilepticus*).
- Phineas had survived his accident for eleven and a half years.
- *Odd Kind of Fame*, Malcolm Macmillan

Medial Frontal/Cingulate Loop

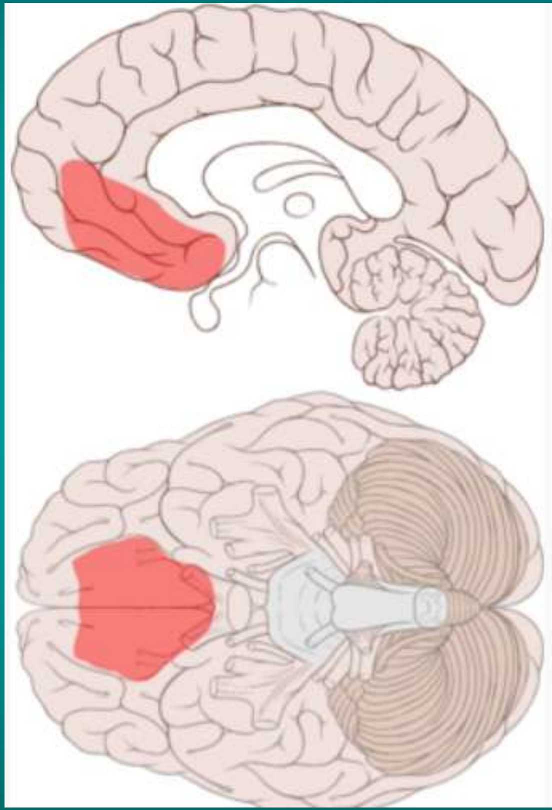
- Behavioral activation
- Others as self perception
- Damage results in
  - Akinetic mutism
  - Abulia
  - Impairments in spontaneous initiation of behavior
  - Sadness increases activation in depression relapsers



Chess Masters

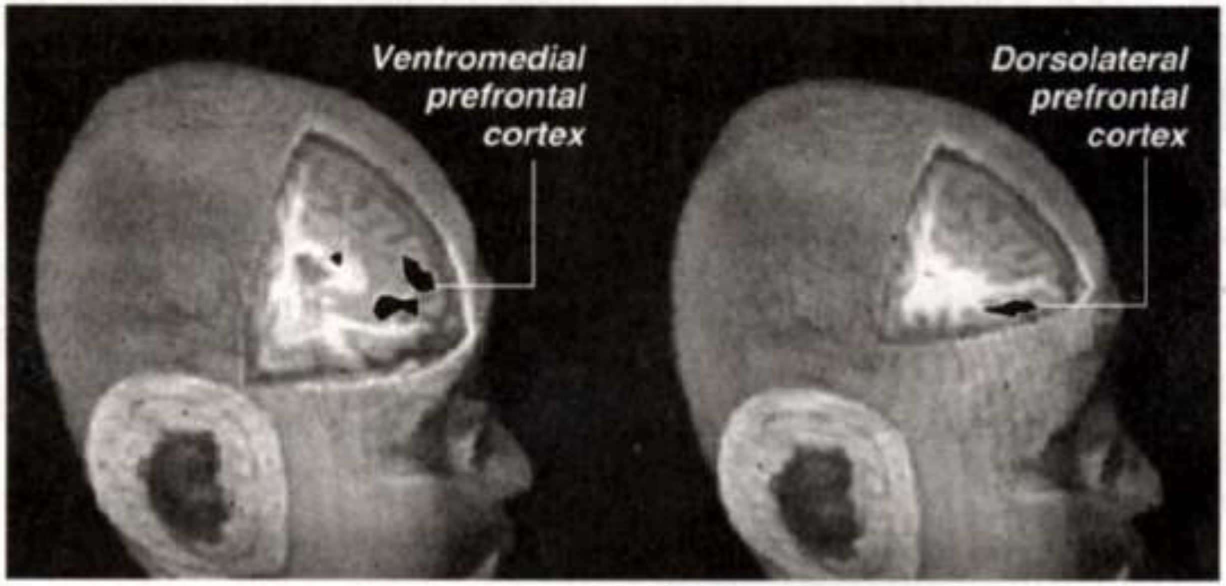
- Chess is not an intellectual activity based on analysis; decisions based immediate act of perceiving the board
- Using MEG, higher-rated chess players: activate the frontal and parietal areas when they look at the board (recalling information from long-term memory; recall of past board positions).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

Ventromedial PFC



- processing of risk and fear
- emotion regulation
- reactivating past emotional associations and events, therefore essentially mediating pathogenesis of PTSD
- Damasio’s somatic marker hypothesis: associations between mental objects and visceral (bodily) feedback - for use in natural decision making
- processing gender specific social cues.

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.

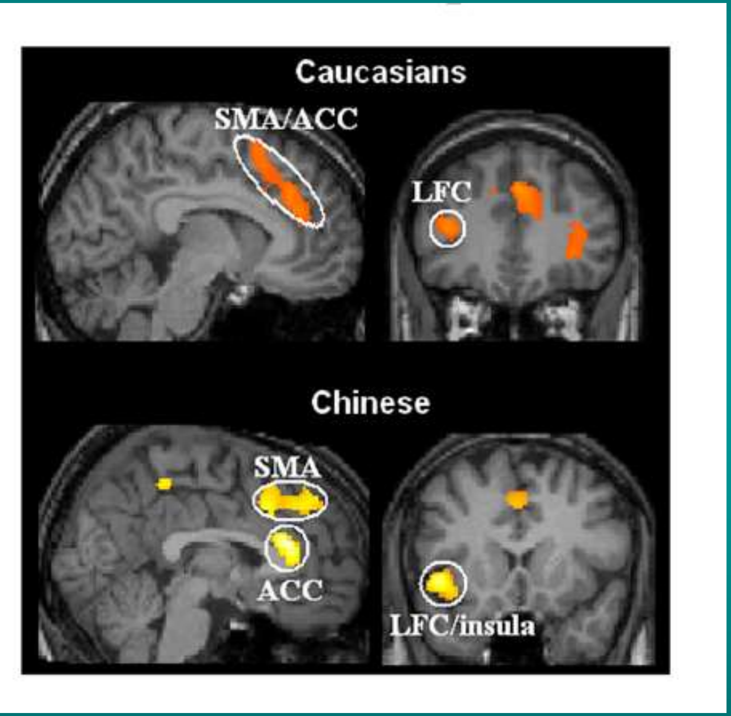
NEW YORK TIMES, Tuesday, April 20, 2004

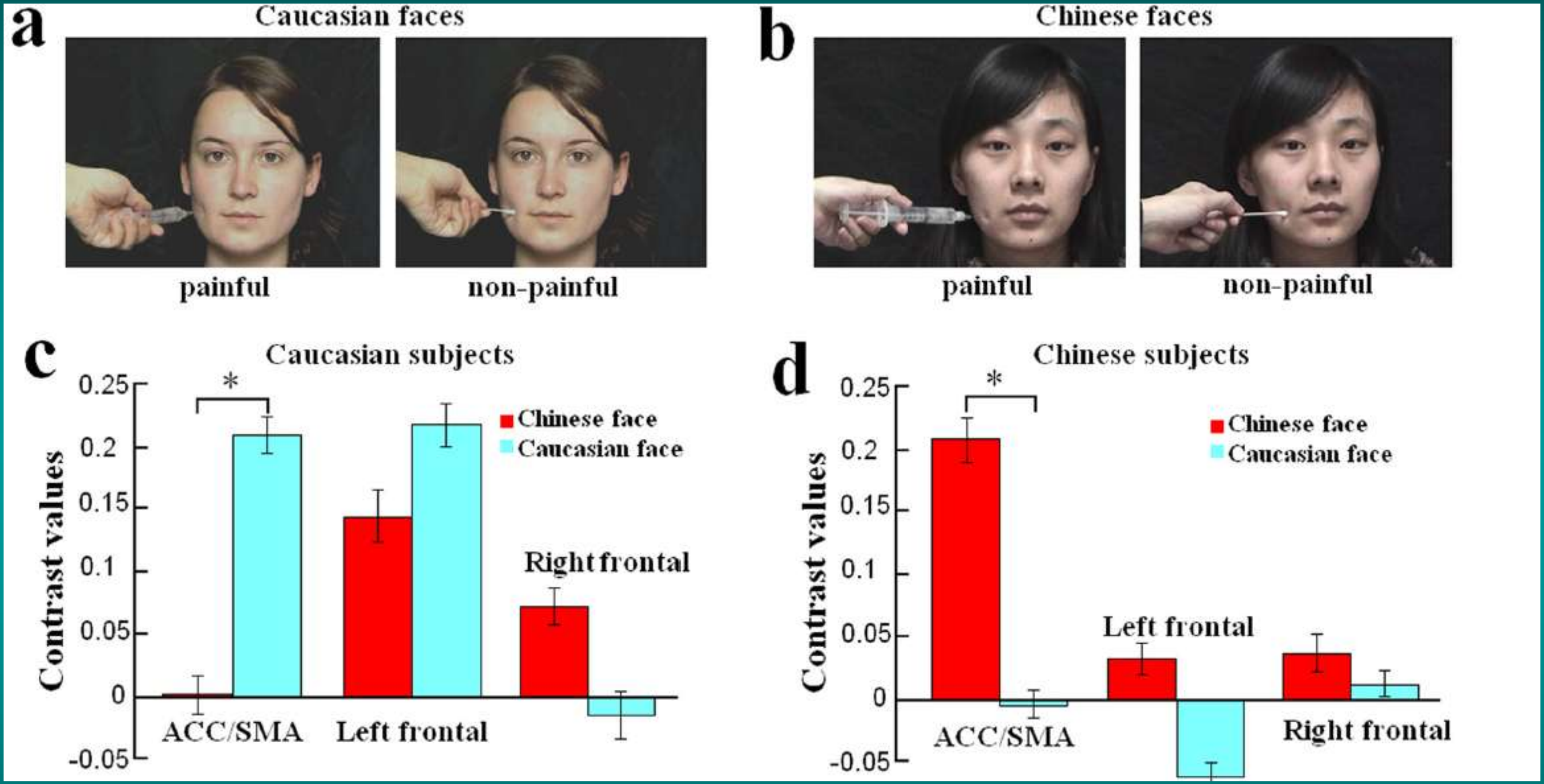
Ventromedial PFC

DL PFC

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

- In Group loyalty, empathy: evolution favored individuals who banded together = source of prejudice in brain activation
- Studies of q-tip vs. needle: if see done to loved one (not to stranger), SMA, ACC, and Insula activate (empathy)
- Similar for White seeing Black or Chinese




a
Caucasian faces
painful
non-painful
b
Chinese faces
painful
non-painful
c
Caucasian subjects
Contrast values
0.25
0.2
0.15
0.1
0.05
0
-0.05
*
Chinese face
Caucasian face
Right frontal
ACC/SMA
Left frontal
d
Chinese subjects
Contrast values
0.25
0.2
0.15
0.1
0.05
0
-0.05
*
Chinese face
Caucasian face
Left frontal
ACC/SMA
Right frontal

Social Rejection Hurts: Physical and Social Pain

- Brain systems that underlie social rejection developed by coopting brain circuits that support the affective component of physical pain
- Dorsal anterior cingulate (dACC) and anterior insula (AI): support the aversive quality of physical pain (the "affective" component), and also underlie the feeling of social rejection.
- Operculo-insular region [i.e., secondary somatosensory cortex (S2) and dorsal posterior insula (dpINS)]: support the somatic representation of physical pain, and are most closely aligned with the "sensory- discriminative" component, but are not activated by social rejection
- Rejection experiences may lead to various physical pain disorders (e.g., somatoform disorders; fibromyalgia),

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" and tend to respond to threatening situations with more aggression and are more sensitive to threatening facial expressions
- Anterior cingulate monitor(s) uncertainty and conflicts; capacity to tolerate uncertainty and conflicts

(Kanai et al., 2011

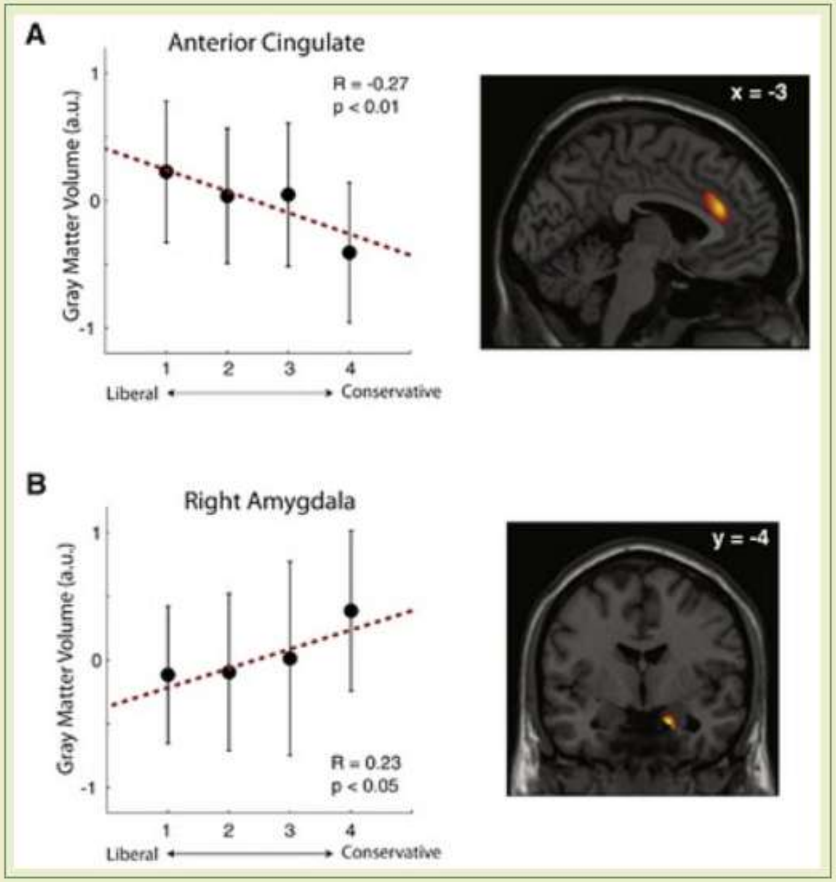
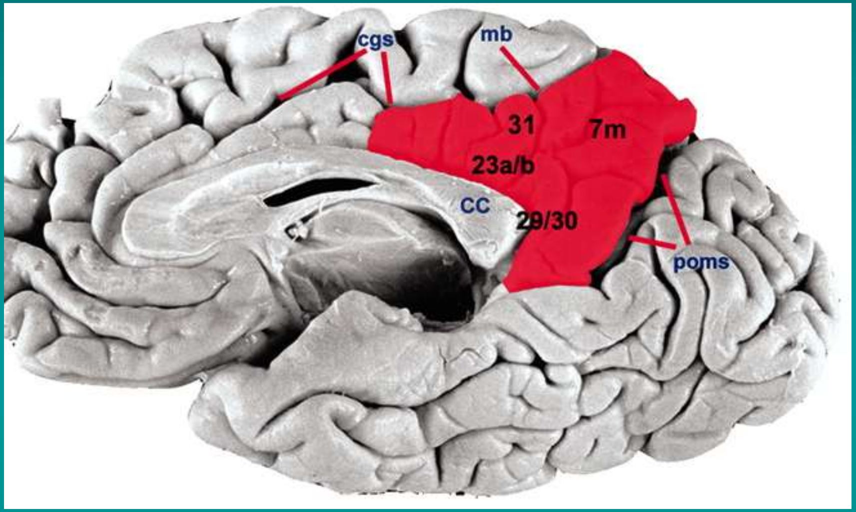


Figure 1 (Kanai et al., 2011). Individual Differences in Political Attitudes and Brain Structure. (A) Regions of the anterior cingulate where gray matter volume showed a correlation with political attitudes are shown overlaid on a T1-weighted MRI... A statistical threshold of $p < 0.05$,

Precuneus: Motivated (pro or con) reasoning, i.e. political choice



Other's Perspective:
"I Know You Are But What Am I?"

- Medial prefrontal cortex (MPFC) and the medial posterior parietal cortex (MPPC) are engaged during self-knowledge retrieval/self perception processes

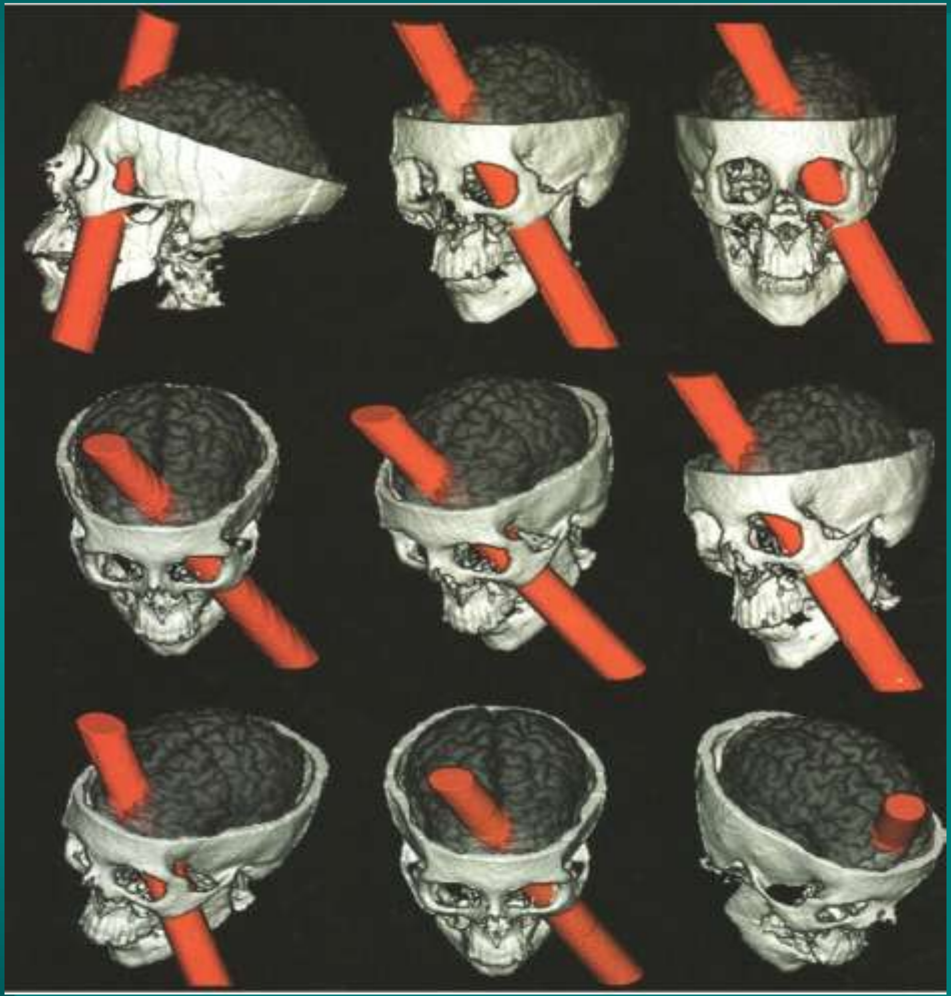
- Left temporal parietal junction = seeing other's point of view

- If attempt to see someone else's perspective, amygdala activation reduced

Phineas Gage: Ventromedial Prefrontal Damage

Before: responsible, well-mannered, well-liked, efficient worker

After: Not same person more impulsive?



Trolley Problem: 2 Scenarios

- Train heading toward five people who are going to die if you don't hit a switch, which makes the train veers onto a side track and kills only one person. 9 of 10 people confronted with this scenario say it's O.K. to hit the switch.
- Alternative: standing on a footbridge that spans the train tracks, and the only way you can save the five people is to push an obese man standing next to you off the footbridge so that his body stops the train. Under these circumstances, 9 of 10 people say it's not O.K. to kill one person to save five.

FMRI of Trolley Problem

- DL PFC active when subjects confronted the first trolley hypothetical, saving greatest number of lives.
- VM PFC active when subjects confronted the second trolley hypothetical, in which they tended to recoil at the idea of personally harming an individual

Morality in Brain

- Moral brain components are VMPFC and OFC/VL, amygdalae, and DLPFC

- The VMPFC ([BA]10-12, 25, 32 plus the frontopolar region of BA10) attaches moral and emotional value to social events, anticipates their future outcomes, and participates in ToM, empathy, and attribution

- The OFC/VL (BA47, parts of BA10-12 and 25, plus VL BA44), mediates socially aversive responses, changes responses based on feedback, and inhibits impulsive, automatic, or amygdalar responses.

Mendez, 2009

Morality in Brain 2

- The amygdalae mediate the response to threat and aversive social and moral learning. Fear and guilt responses.
- DLPFC can override this neuromoral network through the application of reasoned analysis to moral situations.

Ventromedial Frontal Damage

- Associated with emotional response; lack natural conflict between emotion and reason
- Individual with VMF damage were 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
- Impaired decision making; an impaired ability to determine the relative value of alternatives

Damasio, 2007, Nature

Ventromedial Damage: Sarcasm ↓↓

- Disrupt understanding sarcasm, understanding social cues, empathic response and emotion recognition.
- Extent of the right ventromedial lesion was significantly related understanding sarcasm. The worse the damage, the greater the impairment.

S.G. Shamay-Tsoory, 2009

FMRI & Frontal

- <u>DL</u>: cognitive load, complex thinking
- Anterior PF: morality judgments
- <u>VL OFC</u> activates when lying; more brain activation when lying (VL, DL) (& Amg activates); neither VL or Amg do in psychopaths
- <u>OF lesions (FTD)</u>: can’t lie well; tactless, blunt, unpleasant, can’t keep mouth shut
- <u>Volume reduction in anterior PF in psychopaths</u>

5 Factors & Brain

- Extraversion: Reward sensitivity: medial OFC

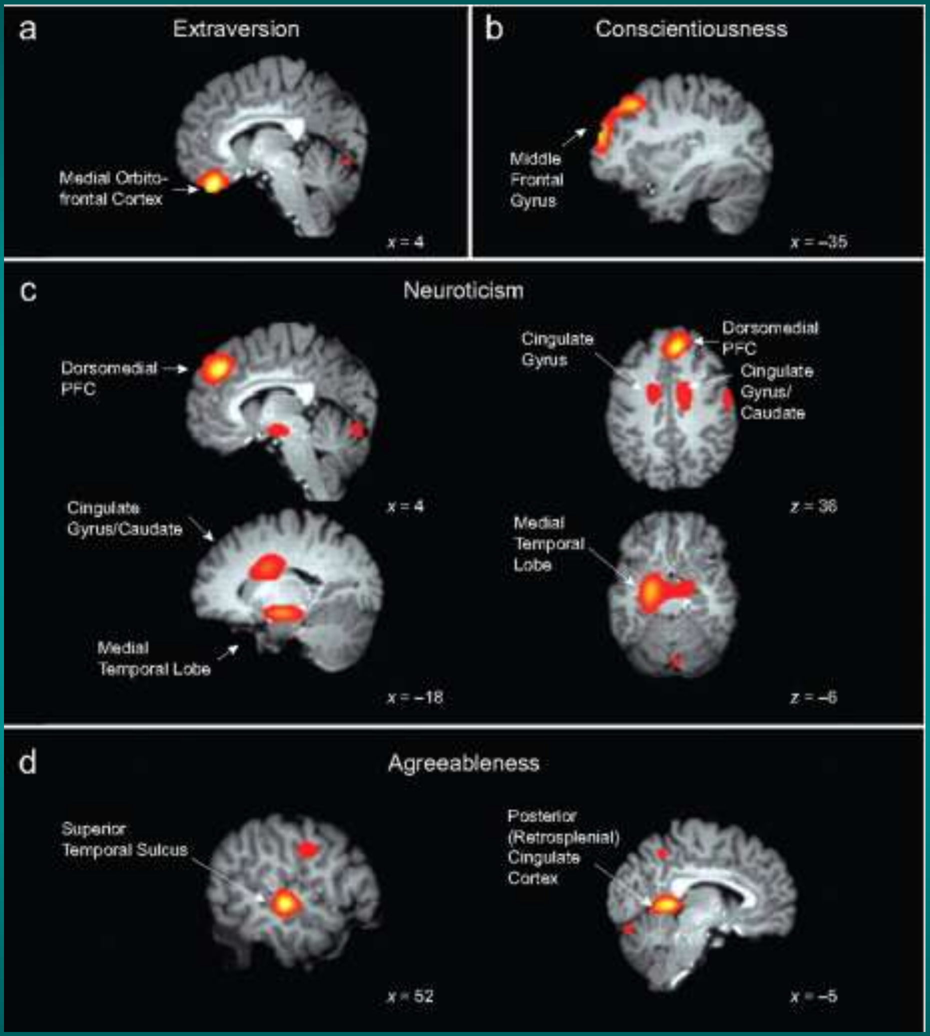
- Neuroticism: reduced volume in dorsomedial PFC and a part of left medial temporal lobe; related to cingulate

- Agreeableness: reduced volume in posterior left superior temporal sulcus and with increased volume in posterior cingulate cortex

- Conscientiousness: Associated positively with volume of the middle frontal gyrus in left lateral PFC

- Openness: only association with intelligence; associated with an area of parietal cortex

Brain regions in which local volume was significantly associated with (a) Extraversion, (b) Conscientiousness, (c) Neuroticism, and (d) Agreeableness.



DeYoung C G et al. Psychological Science 2010;0956797610370159

Psychological SCIENCE

Anatomic areas in morality network

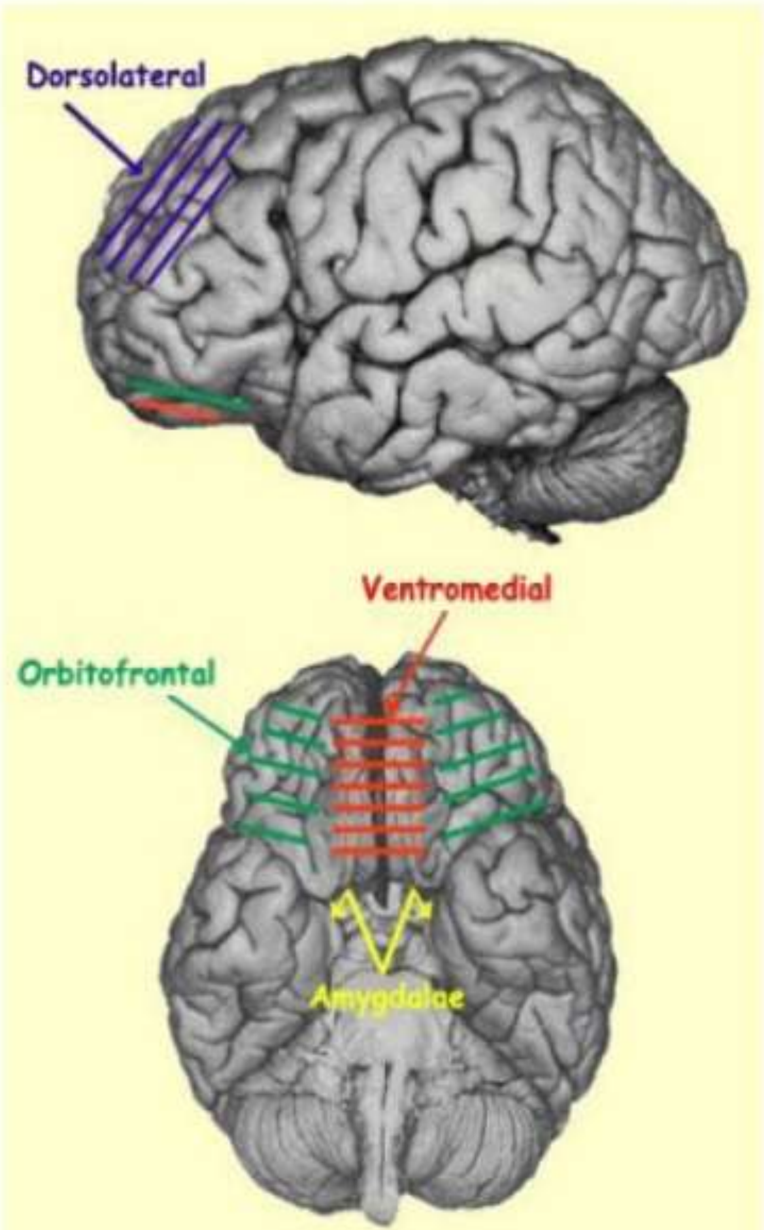


TABLE 4.
Sociopathic Acts among 16 Patients with Frontotemporal Dementia[145]

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.

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

- In 1977, Benjamin Libet devised cleverly designed experiments at the University of California, San Francisco, 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.

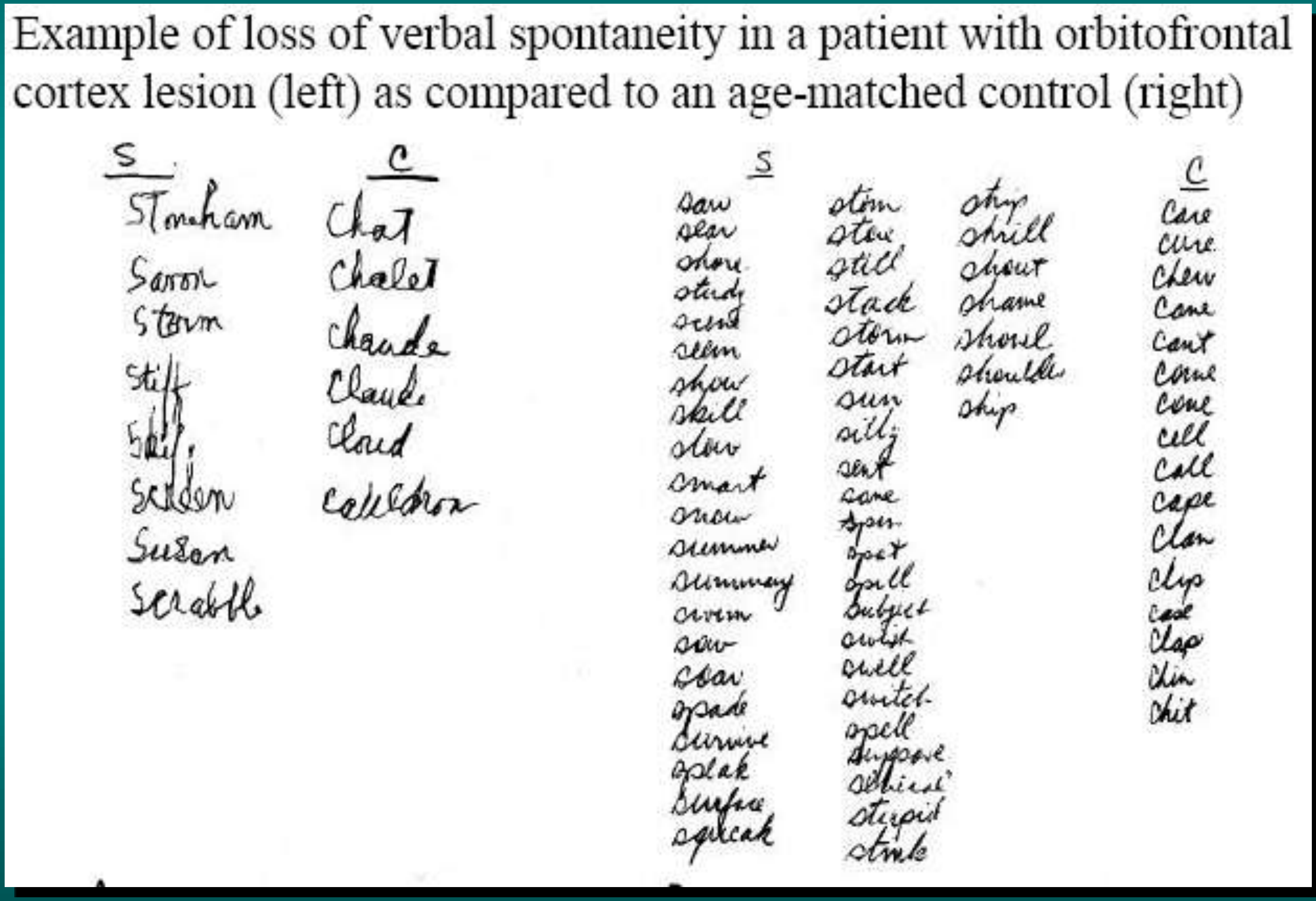
- Libet argued that this leaves 100 milliseconds for the conscious self to veto the brain's unconscious decision, or to give way to it -- suggesting, in the words of the neuroscientist Vilayanur S. Ramachandran, that we have not free will but "free won't."

Haynes repeats Libet

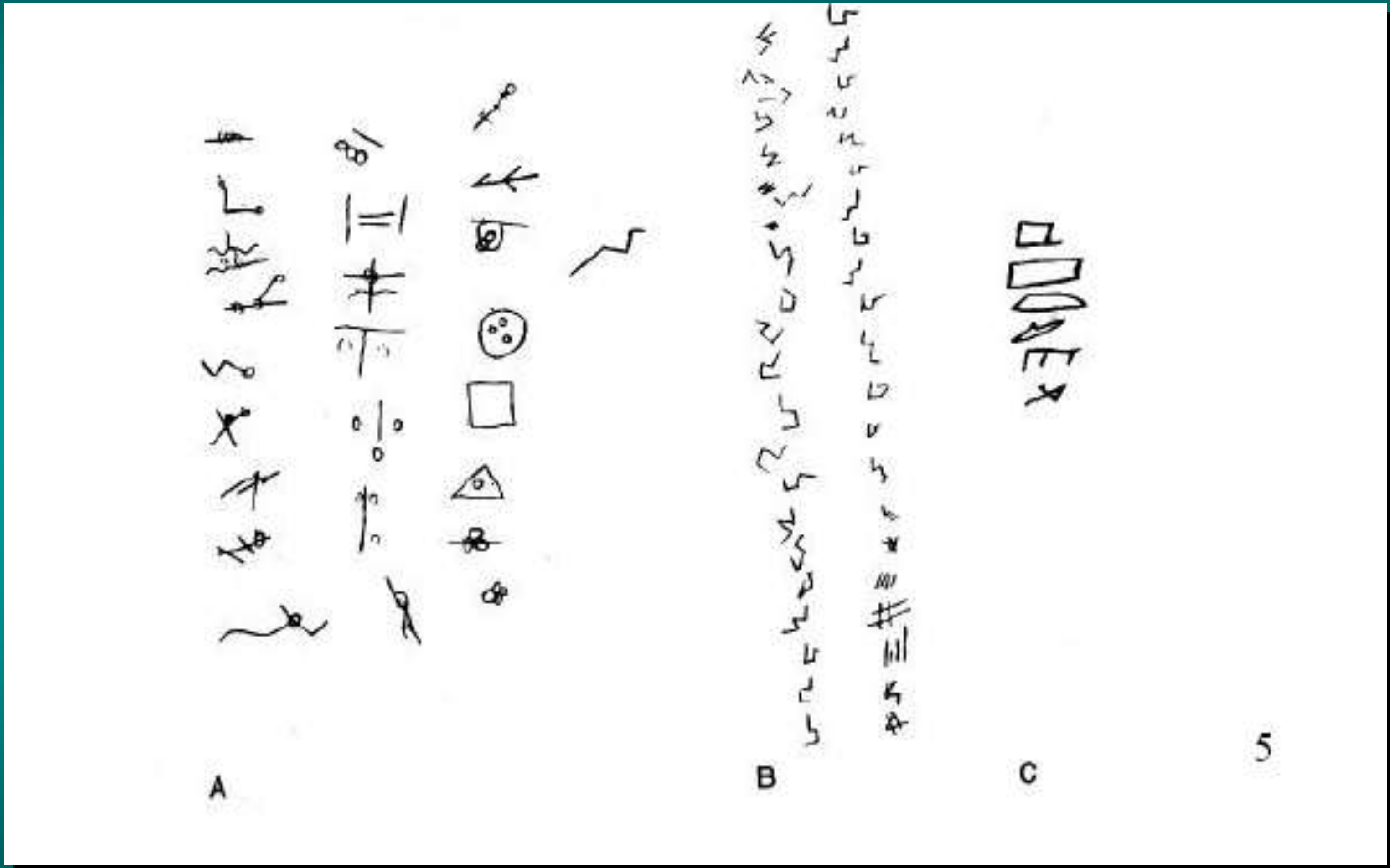
- In 2008, Dylan Haynes asked subjects to choose <u>to press right or left button under FMRI</u>

- <u>Strong prefrontal and parietal signals up to 10 seconds before subject consciously decided to act.</u>

Left Orbital frontal damage: Verbal Spontaneity



Right Orbital Frontal Damage: Design Fluency

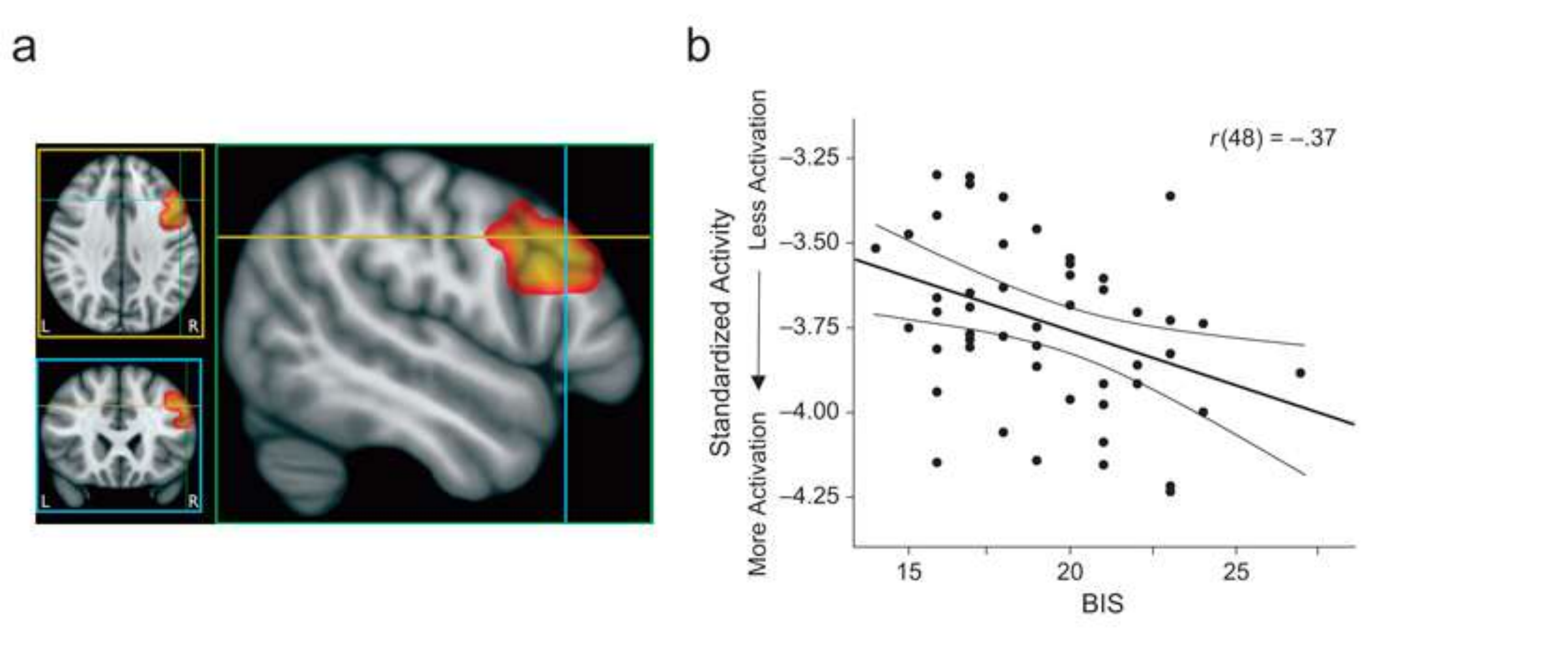


Control Patient

Right DL FPC ↓↓ & Behavioral Inhibition ↑↑

- Individuals with relatively greater EEG activity on the scalp overlying right PFC rated themselves as more behaviorally inhibited
- Evidence that more behaviorally inhibited individuals are characterized by tonic activity in right-posterior DLFPC.
- Taken with work showing that activation in this region predicts variation in threat-evoked anxiety (Dalton, Kalin, Grist, & Davidson, 2005), this observation provides compelling support for the hypothesis that DLPFC is a key constituent of the BIS (McNaughton & Corr, 2004).

Right DLFPC and Behavioral Inhibition



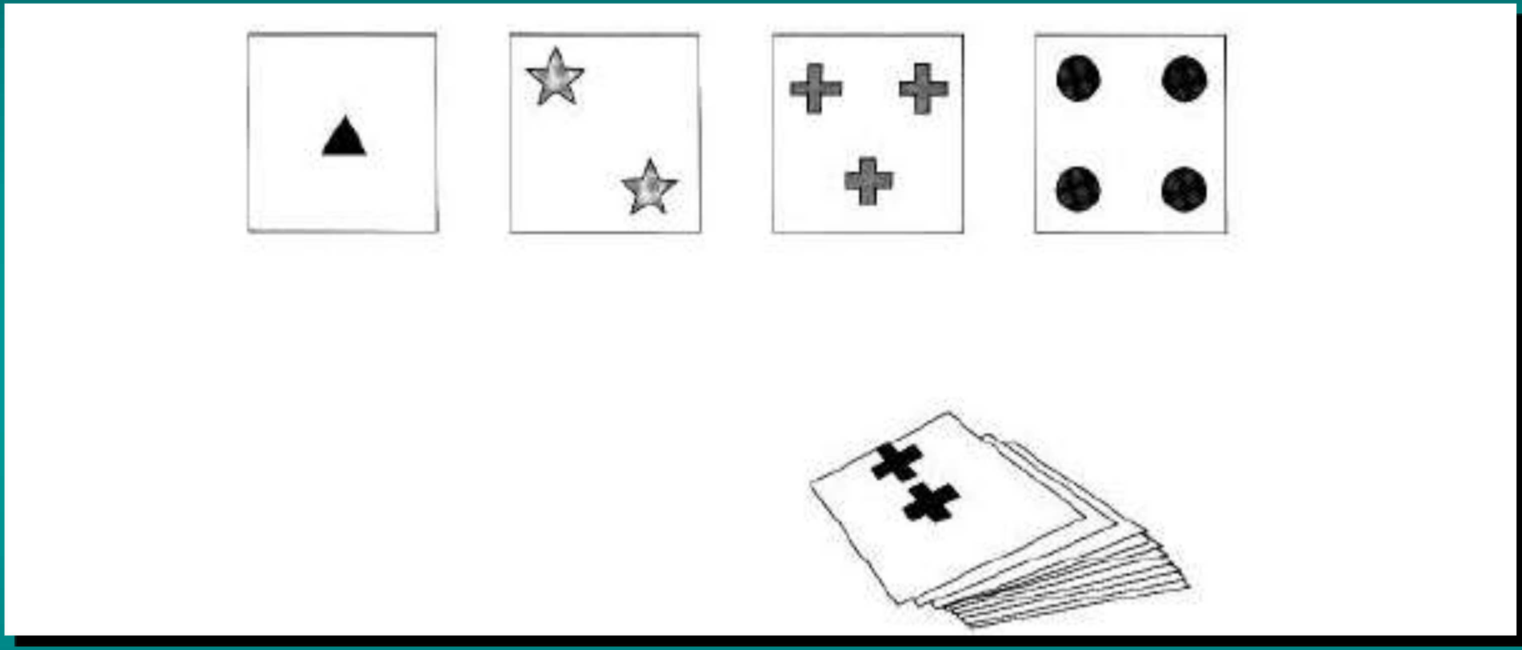
Relations between individual differences in behavioral inhibition and tonic activity in right-posterior dorsolateral prefrontal cortex (DLPFC). The images in (a) depict the results of the electroencephalography source modeling analyses. The scatter plot (b) depicts the peak correlation between scores on the Behavioral Inhibition System (BIS) scale and standardized activity in right-posterior DLPFC (area 9/46v),

SPECT Activation in Prefrontal

- <u>Bilateral frontal </u>hypo-oxygenation was found during <u>reading</u>
- <u>Right frontal </u>hyper-oxygenation during the <u>Continuous Performance Test</u>
- <u>Left frontal </u>hyper-oxygenation during the <u>Verbal Fluency Test</u>

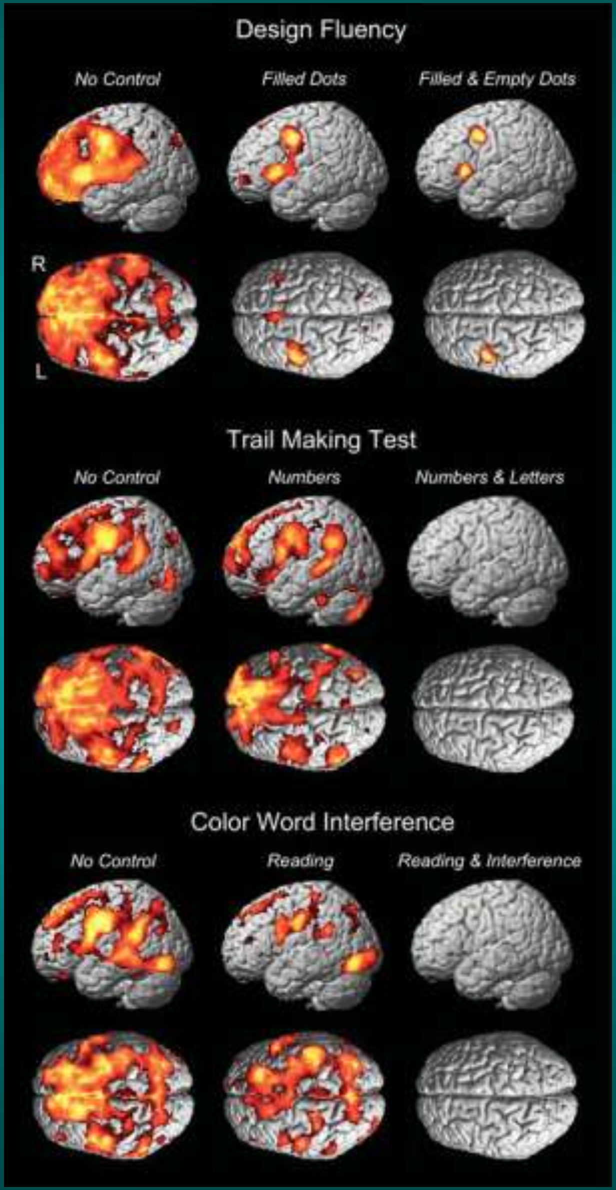
Fallgatter & Strik, 2004

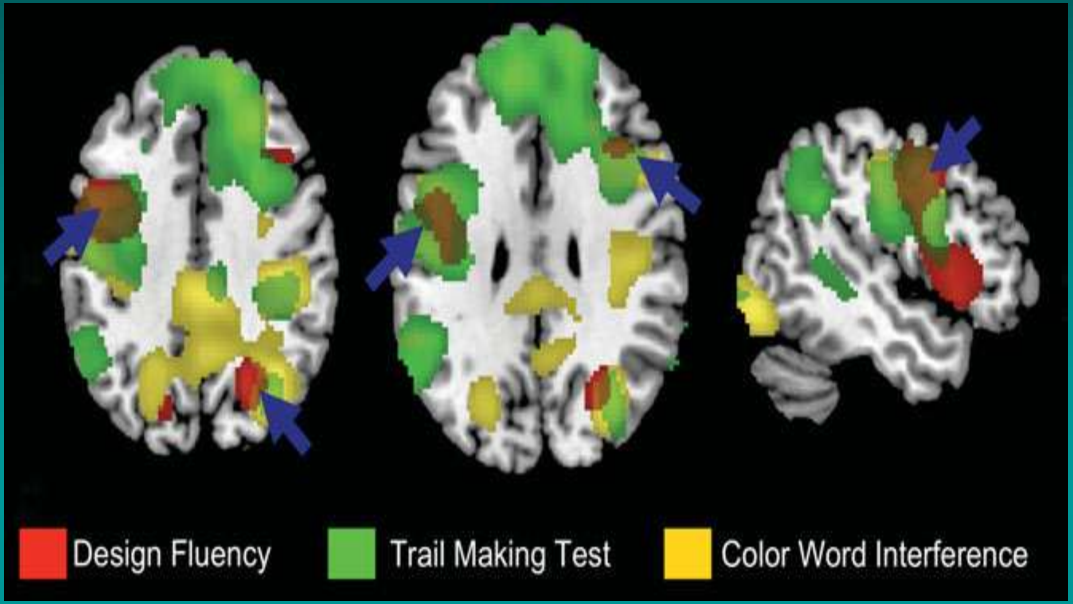
WCST: bilateral Ox increase in frontal brain regions



Behavioral perseveration in face of changing environmental demands

Design Fluency, TMT, CW Interference: Frontal & Parietal

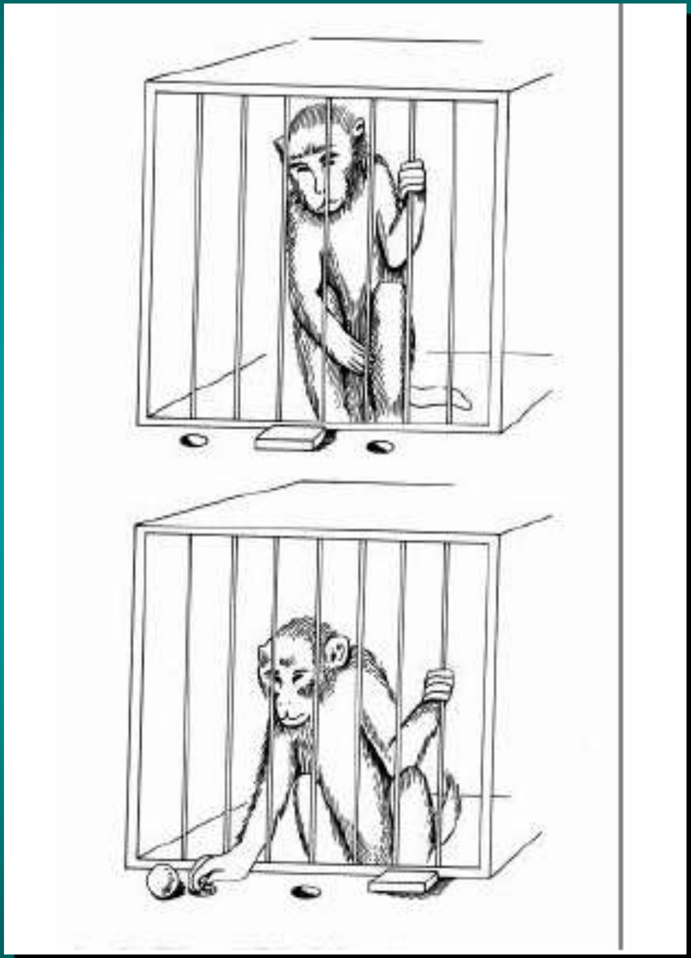




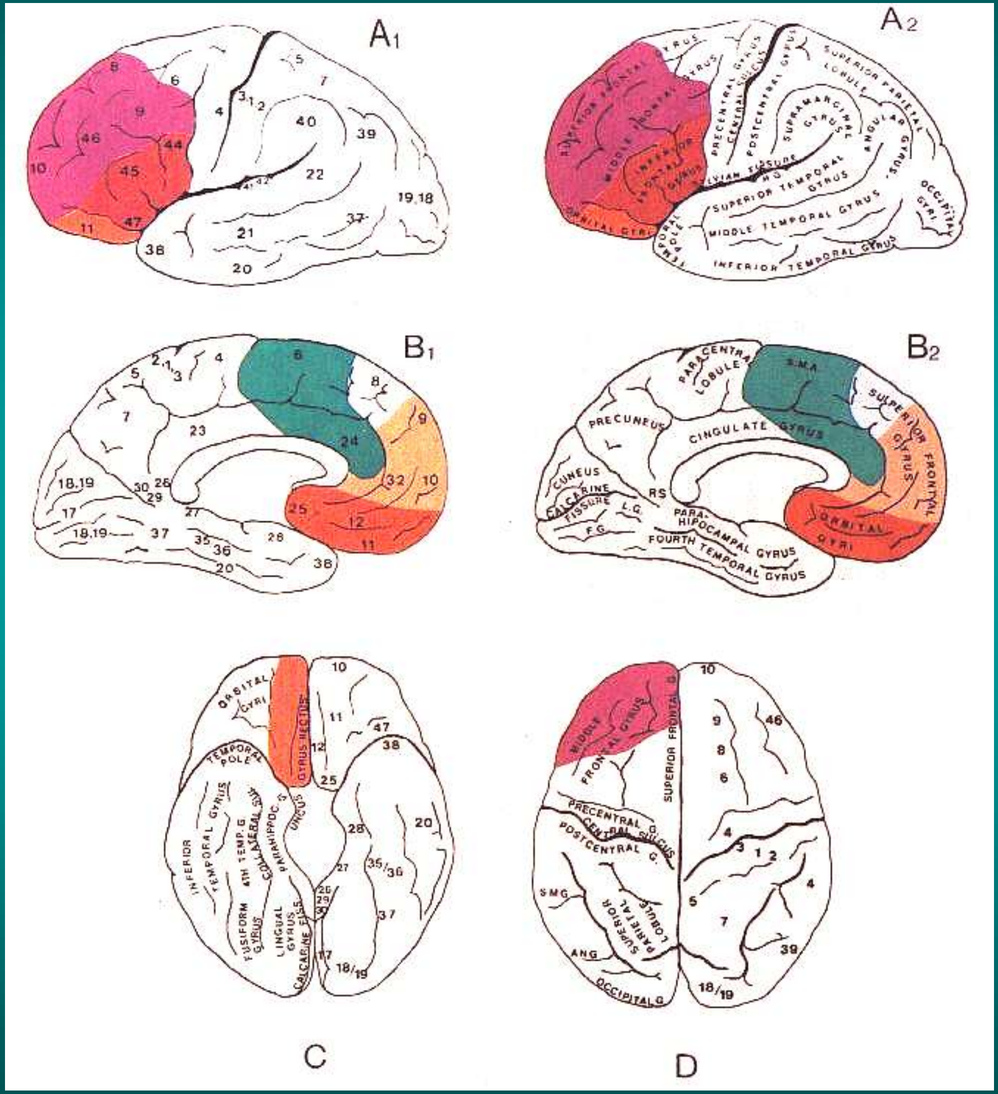
Design Fluency may be a better measure for assessing pure set-shifting ability (DL PFC) when controlling for component processes (motor speed and visual scanning).

J. Pa, et al., 2010

Prefrontal: Working Memory



Neuropsychological Manifestations of **Frontal Lesions** I



Neuropsychological Manifestations of **Frontal Lesions** I

Frontal Operculum (44,45,47)

A) Left: Broca's aphasia

B) Right: 'expressive' aprosodia

Superior Mesial (mesial 6, 24)

A) Left: akinetic mutism

B) Right: akinetic mutism

Bilateral lesions of mesial SMA (6) and anterior cingulate (24) produce more severe form of akinetic mutism

Tranel, 1992

Neuropsychological Manifestations of **Frontal Lobe** Lesions II

Inferior Mesial Region

A) Orbital Region (10, 11)

Lesions in this region produce disinhibition, altered social conduct, "acquired sociopathy", and other disturbances due to impairment in fronto-limbic relationships

B) Basal Forebrain (posterior extension of inferomesial region, including diagonal band of Broca, nucleus accumbens, septal nuclei, substantia innominata)

Lesions here produce prominent anterograde amnesia with confabulation (material specificity present, but relatively weak)

Tranel, 1992

Neuropsychological Manifestations of **Frontal Lobe** Lesions III

Dorsolateral Prefrontal Region (8,9,46)

Lesions in this region produce impairment in a variety of "executive" skills that cut across domains. Some degree of material-specificity is present, but relatively weak.

A) Fluency: impaired verbal fluency (left) or design fluency (right)

B) Memory impairments: defective recency judgment, metamemory defects, difficulties in memory monitoring

C) Impaired abstract concept formation and hypothesis testing

D) Defective planning, motor sequencing

E) Defective cognitive judgment and estimation

Tranel, 1992

Asymmetrical frontal brain activity and emotion

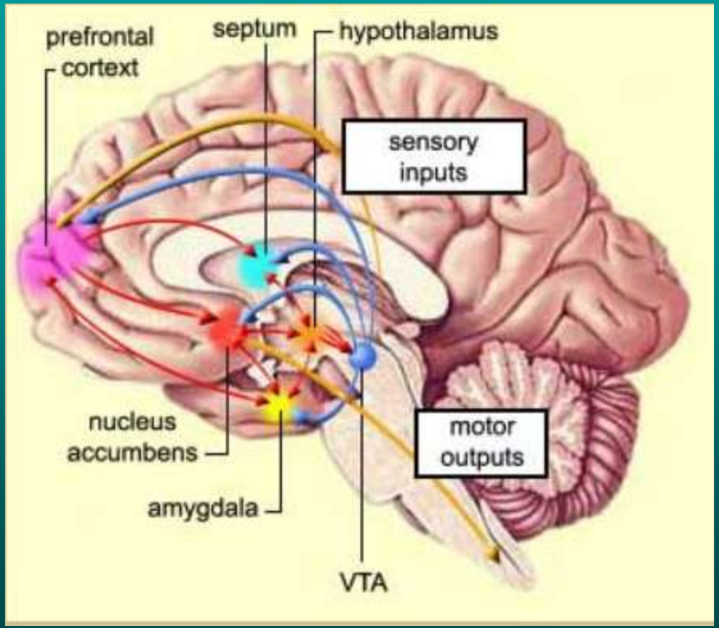
- Greater left frontal cortical activity is associated with approach motivation, which can be positive (e.g., enthusiasm) or negative in valence (e.g., anger).
- Valence model links negative affect (i.e. anger) to the right hemisphere
- Motivational direction model links approach-related emotions (anger) to the left hemisphere
- Anger activates left hemisphere.

Letter v. Semantic/Category Fluency

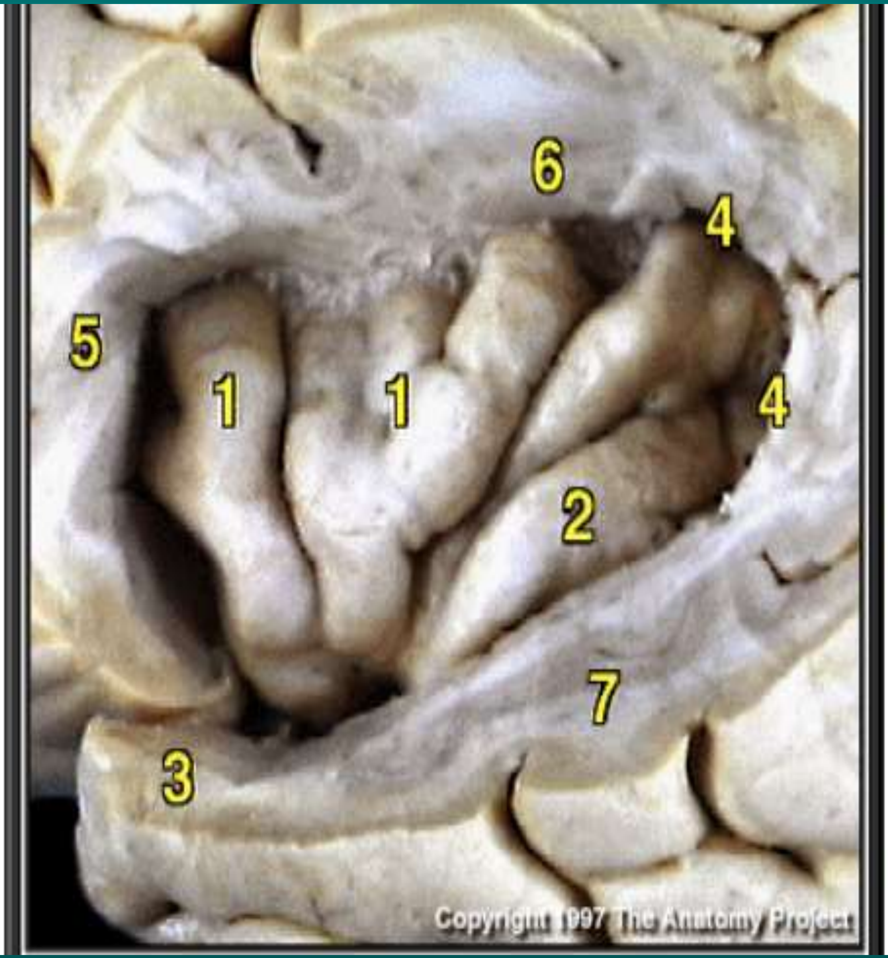
- Letter fluency requires more executive processes, as the patient tries to establish an organized lexical search strategy.
- Semantic/category fluency accesses more semantic/factual neural networks, a more temporal process.
- AD patients will often have diminished semantic fluency where letter fluency is intact.
- Poorer semantic fluency is considered typical of cortical dementias,
- Poorer phonemic fluency is more typical of subcortical processes.
- In R or LH epilepsy patients have decreased semantic fluency (even after surgery)

Nucleus Accumbens: Dopamine drug store

- <u>Reward, motivation and addiction</u>.
- Dependent drugs such as cocaine and nicotine trigger the release of dopamine; but not caffeine.
- Activation: drug paraphenalia, seeing newborn infant, grieving women

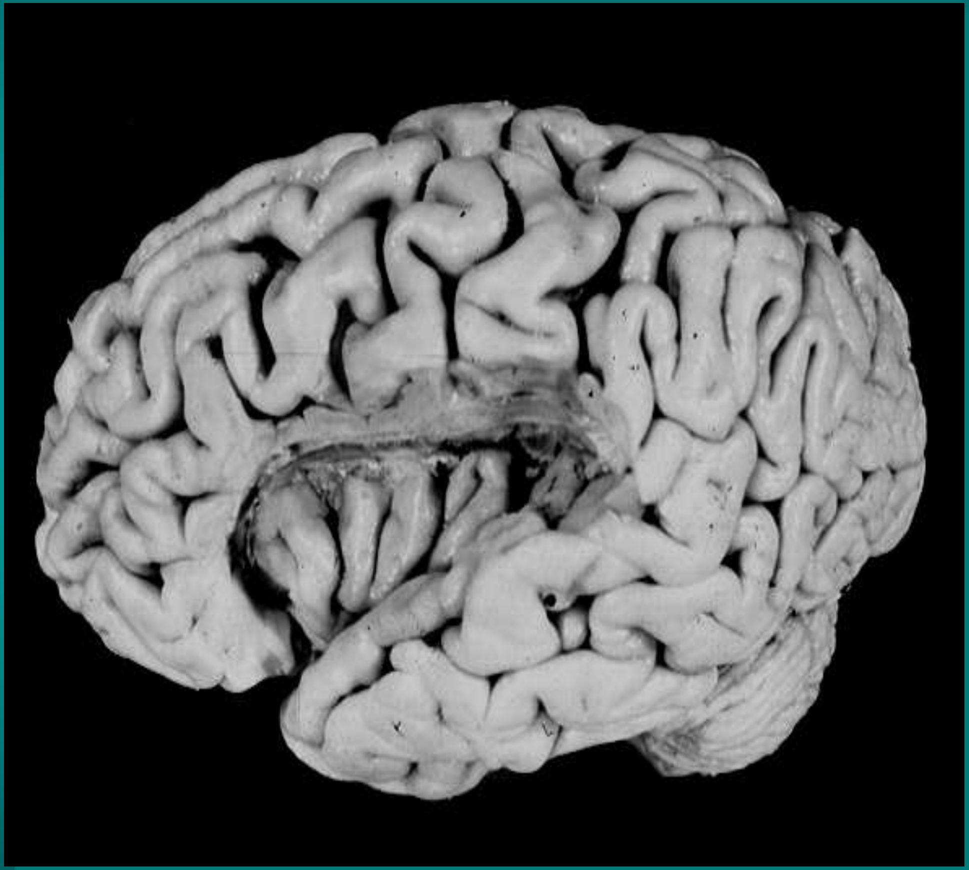


Insula: Gut Feelings; Operculum: Empathy



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,
Cravings,
Body states or sensations:
are recast as
social emotions, empathy,
emotional content of music,
instant smoking cessation

Insula

- Frontal insula: generation social emotions such as empathy, trust, guilt, embarrassment, love—even 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.
- **Gut feelings**: from bodily sensations
- Monitoring interactions within a social network
- Empathy for pain of others
- Affective component of physical pain
-

Evolution of predation in the brain

Evolution favored male brains who hunted well

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.

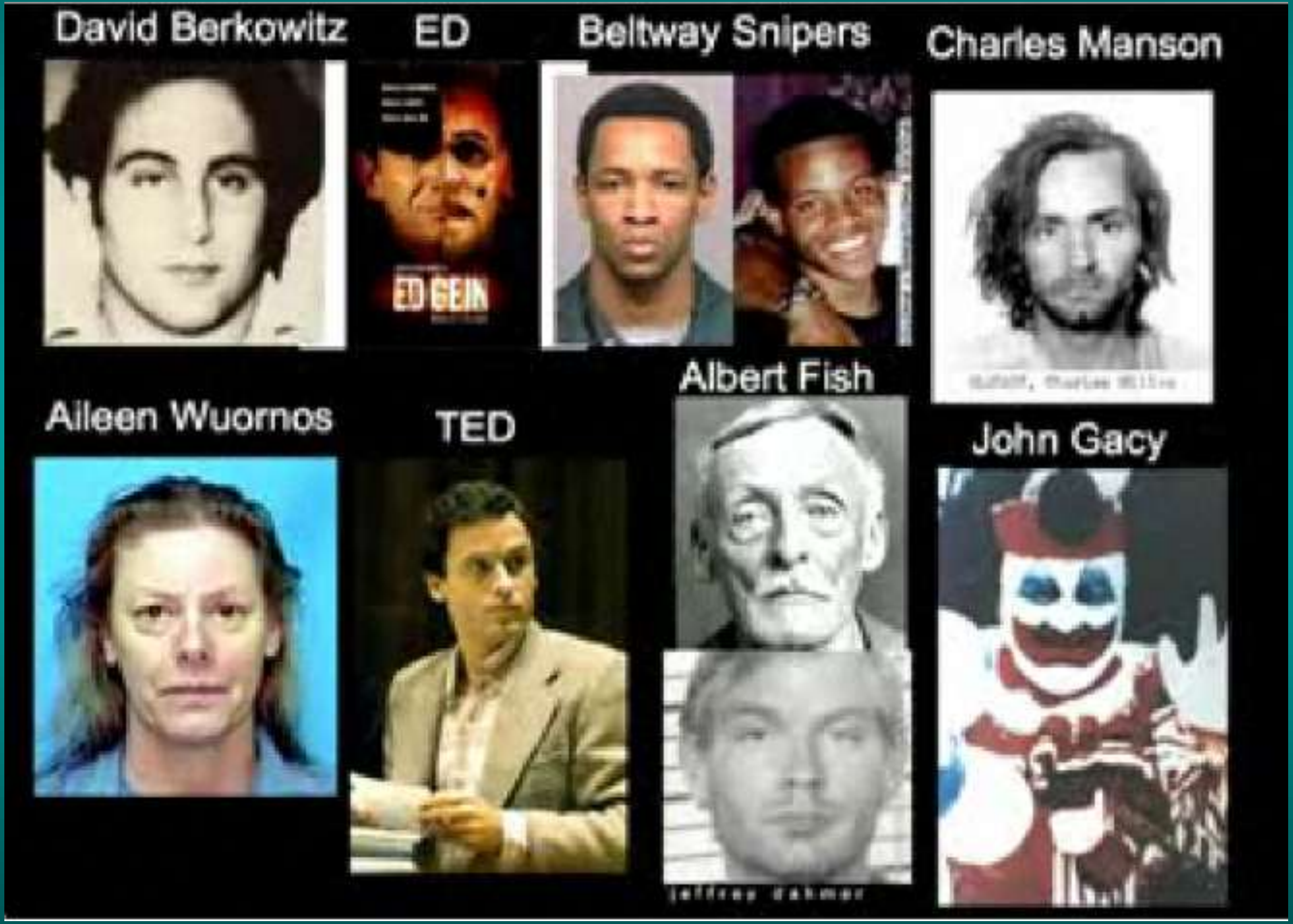
Neurobiology of Psychopathy

- Kiehl: a defect in what he calls "the paralimbic system," a network of brain regions, stretching from the 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).
- VM PF: push people off bridge in bridge paradigm
- They know right from wrong

Psychopathic Personality Disorder: Reduced Prefrontal Gray

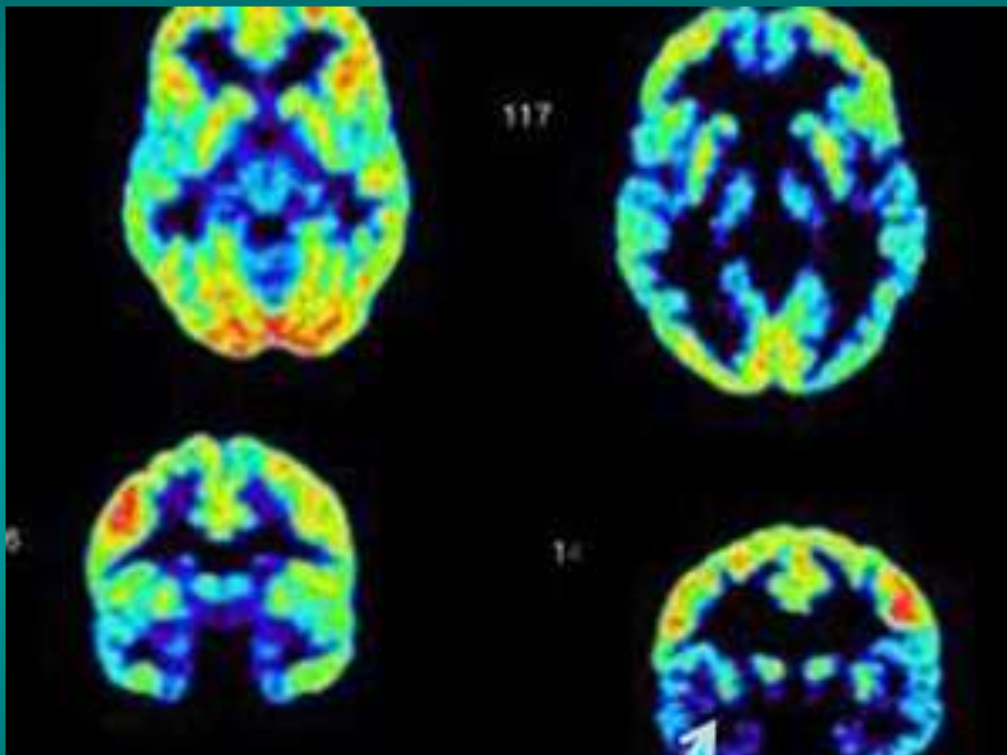
- Raine, 2000: 11.0% reduction in prefrontal gray matter volume
- May underlie the low arousal, poor fear conditioning, lack of conscience, and decision-making deficits that have been found to characterize antisocial, psychopathic behavior.

Psychopaths



Brains of James Fallon PhD and son (cousins of Lizzy Borden): Thwarted Sociopathy

Fallen's son   Fallen



Low Orbital Frontal Activation in Fallon

Fallon's brain (on the right) has dark patches in the orbital cortex. This is the area that Fallon says is involved with ethical behavior, moral decision-making and impulse control. The normal scan on the left is his son's.

James Fallen on Psychopathy: Need Combination of Factors

1 – Low Orbital Frontal activation pattern

2 - MAO-A gene (monoamine oxidase A):
high-aggression variant (low Serotonin),
Warrior gene

3 – Mother transmission to son
(X chromosome), too little Serotonin:
higher rates among males

3 – History of childhood abuse or
seeing lots of traumatic violence (i.e. war)

Psychopathy & FMRI

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

Psychopathy & FMRI 2

- <u>R insula, amygdala, and L anterior Temporal volume loss </u>(no visceral response to dead body)
- <u>Lateral OFC and R FPC </u>(lying inhibition) less active (due to genetics or non-use??)

Neurobiology of BPD

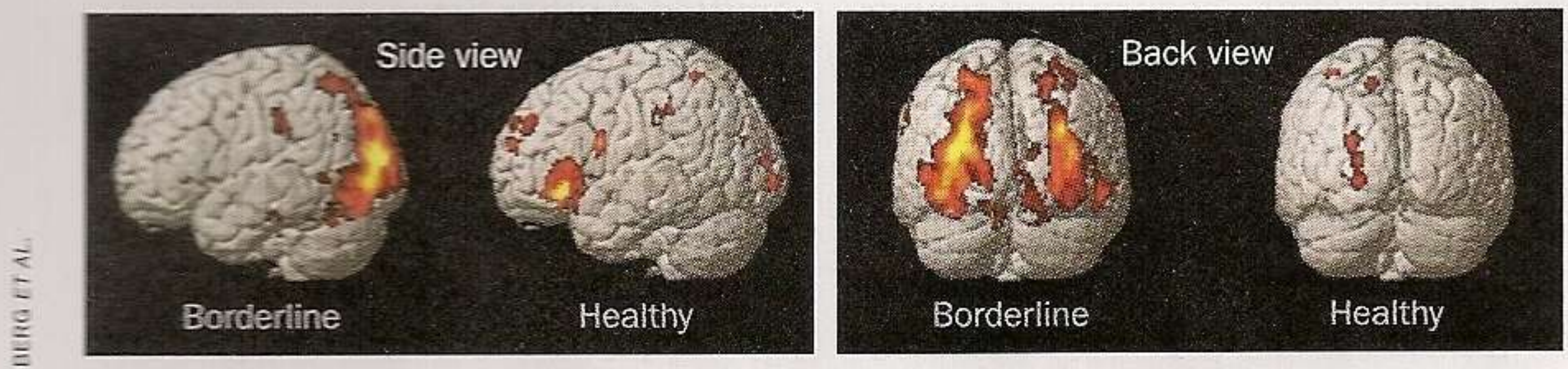
Early abuse & adaptation to adverse environment: fight-flight, aggression, alert to danger, stress response

- Frontal hypometabolism, smaller volume (less inhibition)
- Abnormal temporal metabolism
- Smaller hippocampal (16%) and amygdala (8%) volume
- Abnormal amygdala functioning
  - Elevated oxygenation bilaterally
  - Activates more quickly (irritability and anger↑)
  - Slower to baseline
- Reduced R/L Hemisphere integration, smaller Corpus Callosum
- Abrupt shifts to R Hemisphere negative emotional states

BPD and faster Visual Analysis

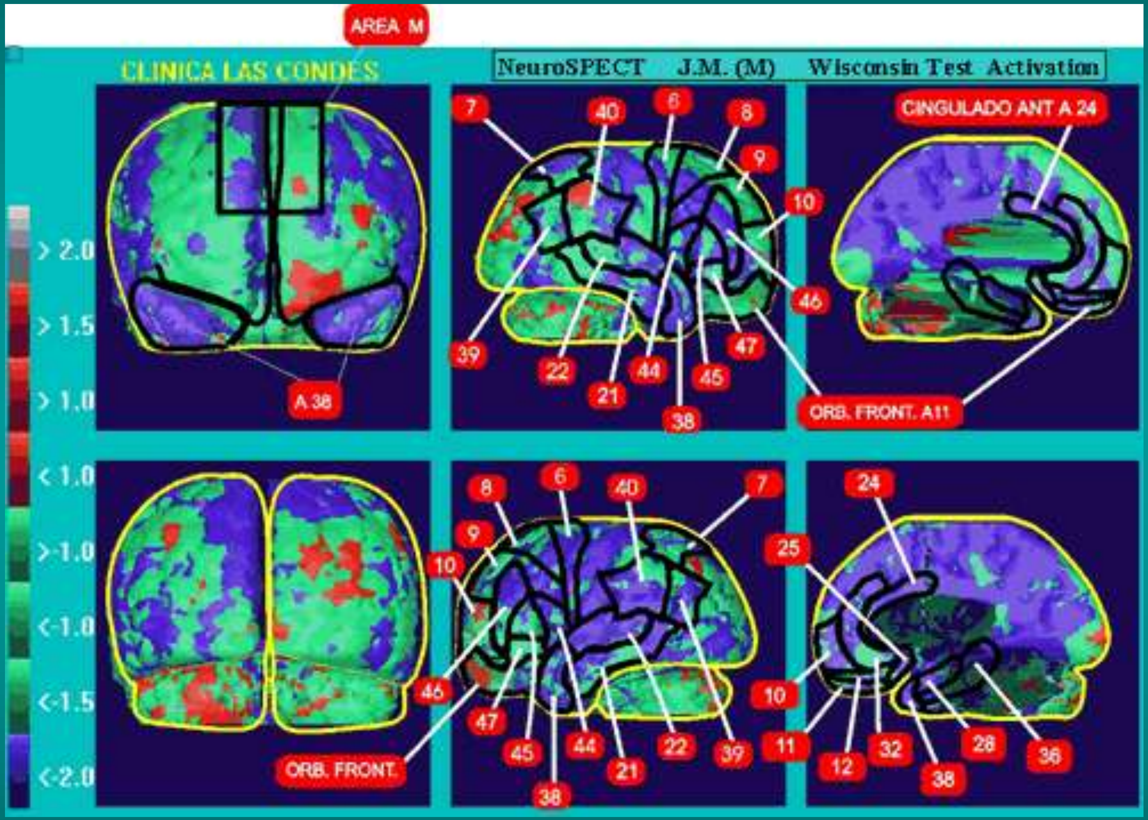
- FMRI: visual system and amygdyla activation
- Borderline personality disorder patients detect brief emotional expressions on others' faces that, typically, emotionally healthy people do not notice.
- Borderline patients may have a visual system that lets them see others' facial emotions through a high-powered lens.

Borderline Occipital Activation



While viewing disturbing images, patients with borderline personality disorder show greater activity in the brain's visual system than emotionally healthy volunteers.

BPD and frontal hypoperfusion



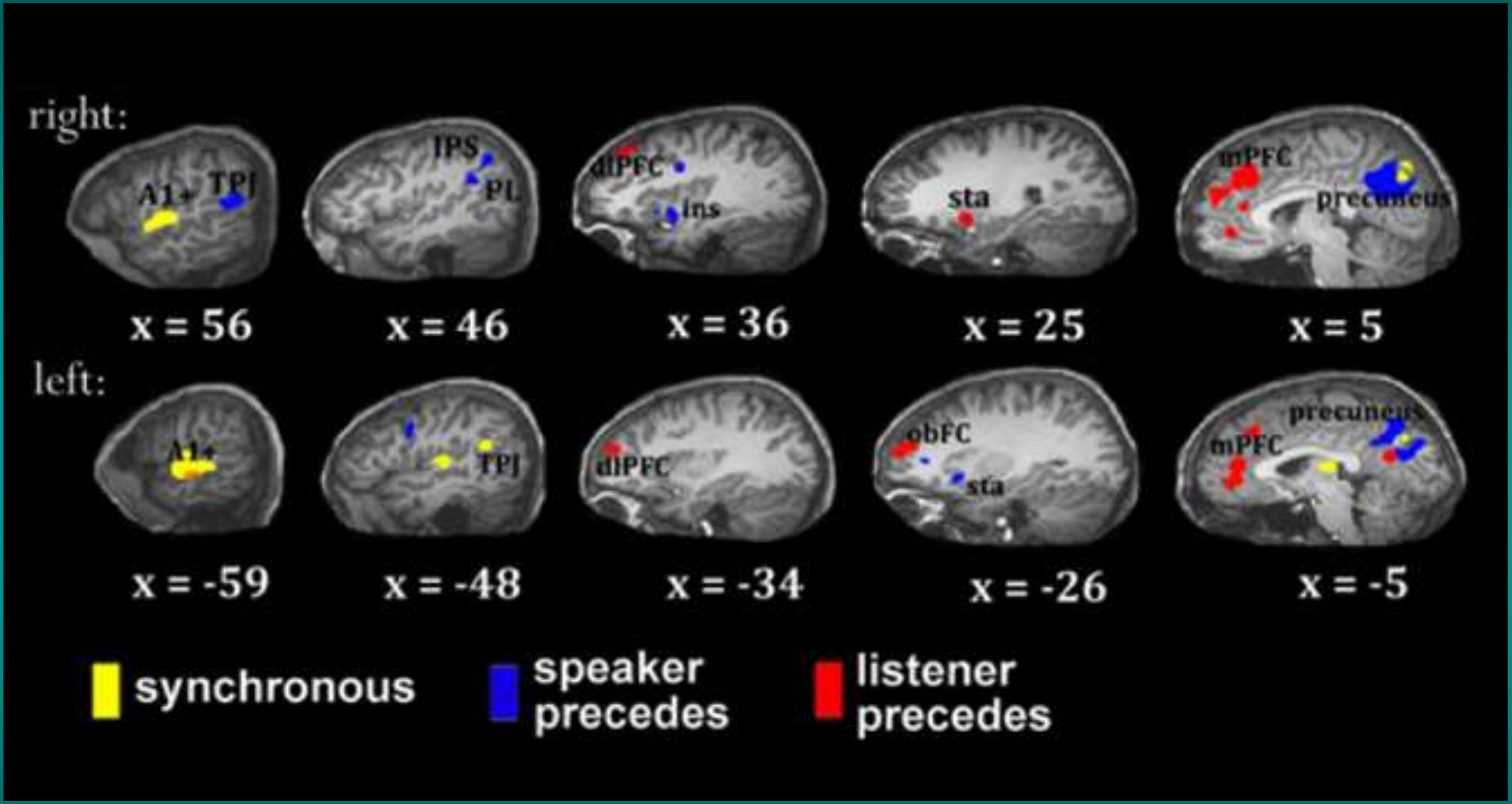
- Wisconsin Card Sorting Test. Same pt. Male Borderline Personality Disorder. , SPECT. There is extensive hypoperfusion of anterior cingulate gyri, area 24, both anterior temporal lobes, area 38, area 28, in the frontal lobes there is hypoperfusion in area 46 and 10. Paradoxically there is an overall hypoperfusion in both frontal lobes, in particular in both executive areas.

OCD vs. OCPD

- OCD:
  - Ego dystonic; don’t like sxs
  - They don’t like their obsessions & compulsions
  - Don’t present as obsessive
  - <u>Neurological disorder (BG & orbital frontal)</u>
  - Behavior therapy works (PET scan evidence)

- OCPD:
  - Ego syntonic: “what problem?”
  - Don’t do emotions, like histrionics don’t do facts
  - Higher in monozygotic
  - <u>DLPF executive deficits, left hemisphere detail orientation</u>
  - <u>Amygdala overactivation to objects</u>

Mind Meld:



When two people experience a deep connection, they're informally described as being on <u>the same wavelength</u>. There may be neurological truth to that. Brain scans of a speaker and listener showed their <u>neural activity synchronizing during storytelling</u>. The stronger their reported connection, the closer the coupling

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

Snakes in MRI machine: Bravery in ACC

- FMRI study of snakes coming toward your head: Fear vs. GSR; as long as these two disagree, you would act courageously. It is only when you scored high on both, sweat and fear, that you would succumb to cowardice.
- Subgenual anterior cingulate cortex (sgACC): location of bravery

  The sgACC was the only part of the brain whose activation went hand in hand with courageous acts. Bringing the snake closer to the head strongly activated the sgACC. The more the participants were afraid but did not succumb to fear, the more active was their sgACC.

  When they did succumb to fear, another region came into play: the amygdala.

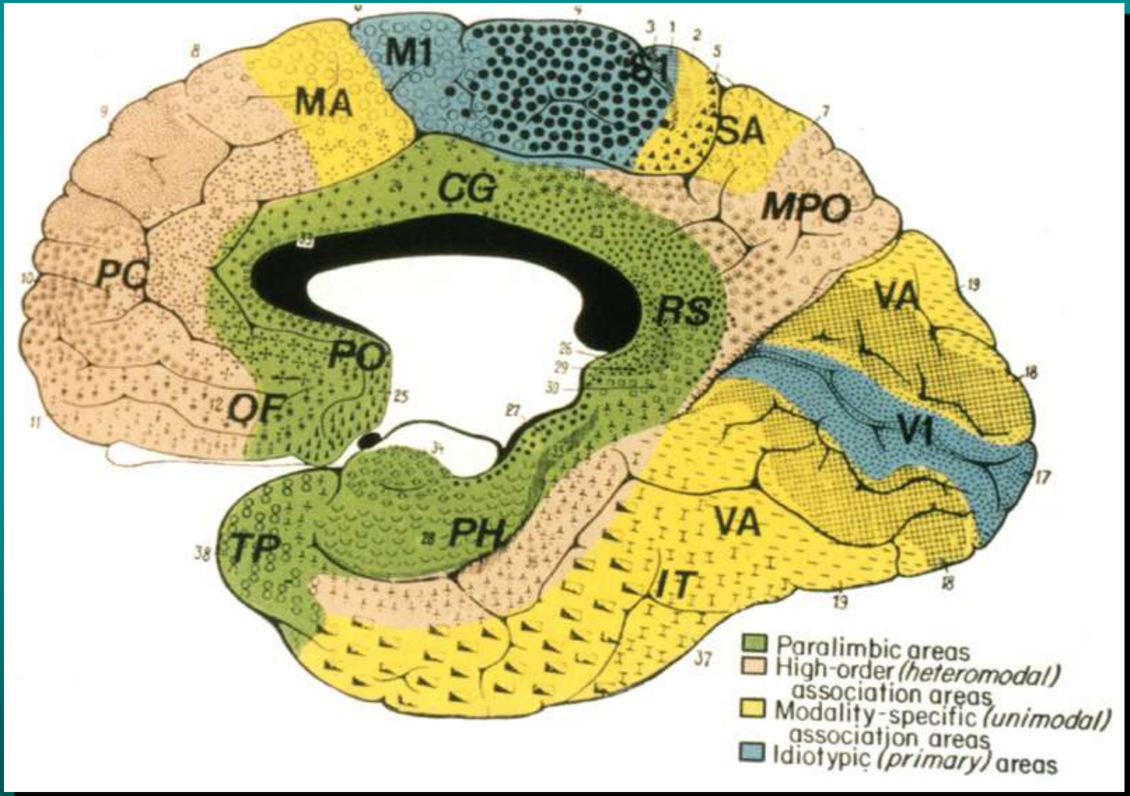
- Only a strongly active sgACC silenced the amygdala.

Emotional Control Systems

Amygdala

VMPFC

Posterior Cingulate



Dorsal Medial Frontal Cortex: Inhibitory Control

- Pulling back (finger from pressing a button) activates the dorsal medial frontal cortex (dmPFC), which did not show up when participants followed through and made the action.
- In addition, those who chose to stop the intended action most often showed greatest contrast in dmPFC activity.
- The capacity to withhold an action that we have prepared but reconsidered

M. Brass, 2007

Ventral Tegmental area, Romantic Love & Cocaine Rush

- People who had been experiencing <u>intense love for 20 years</u> and people who had been <u>in love for only months</u> showed similar <u>activation in the ventral tegmental area</u> of the brain - a region known to be activated during the intense, burning stages of early love.

- The same area is activated by the <u>rush of cocaine.</u>

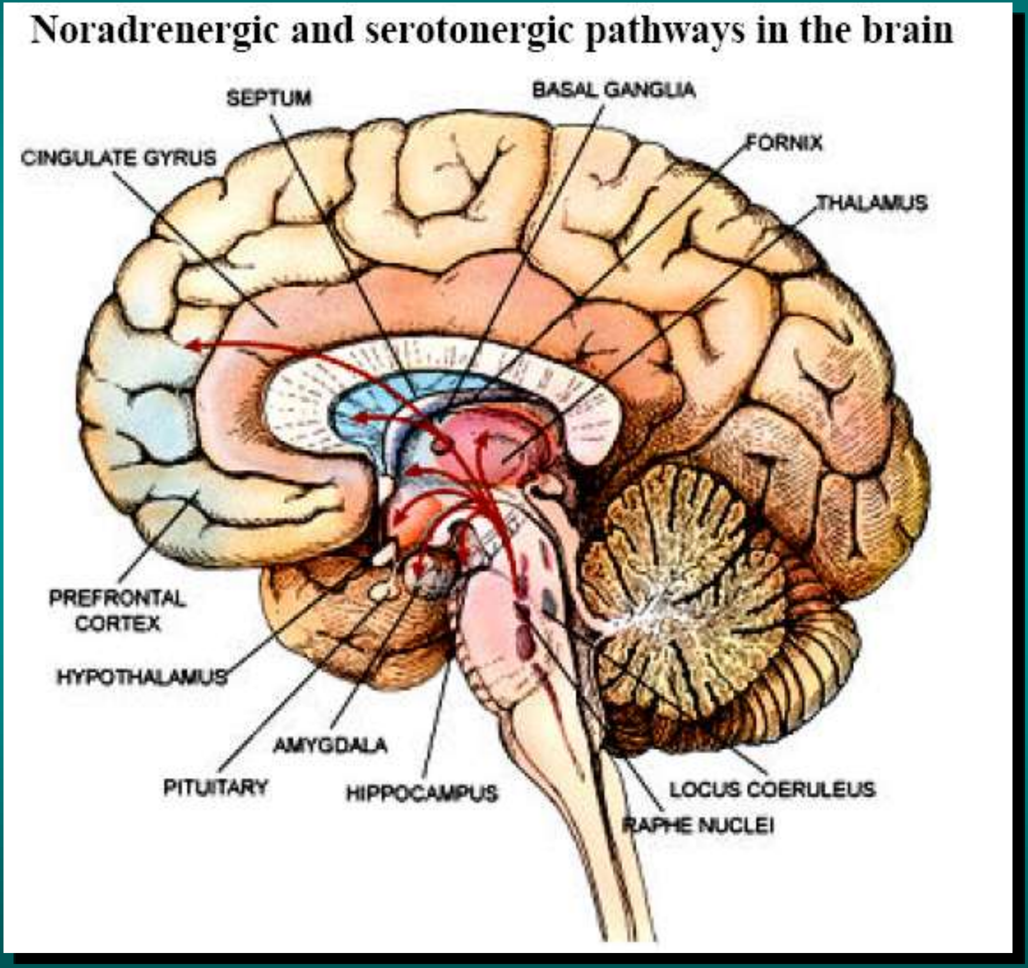
- People in long-term relationships showed higher levels of activity in a part of the brain associated with calmness and pain suppression, whereas people in love for shorter periods had higher activity in a region associated with obsession and anxiety.

Transcendence and the Right Parietal Lobe

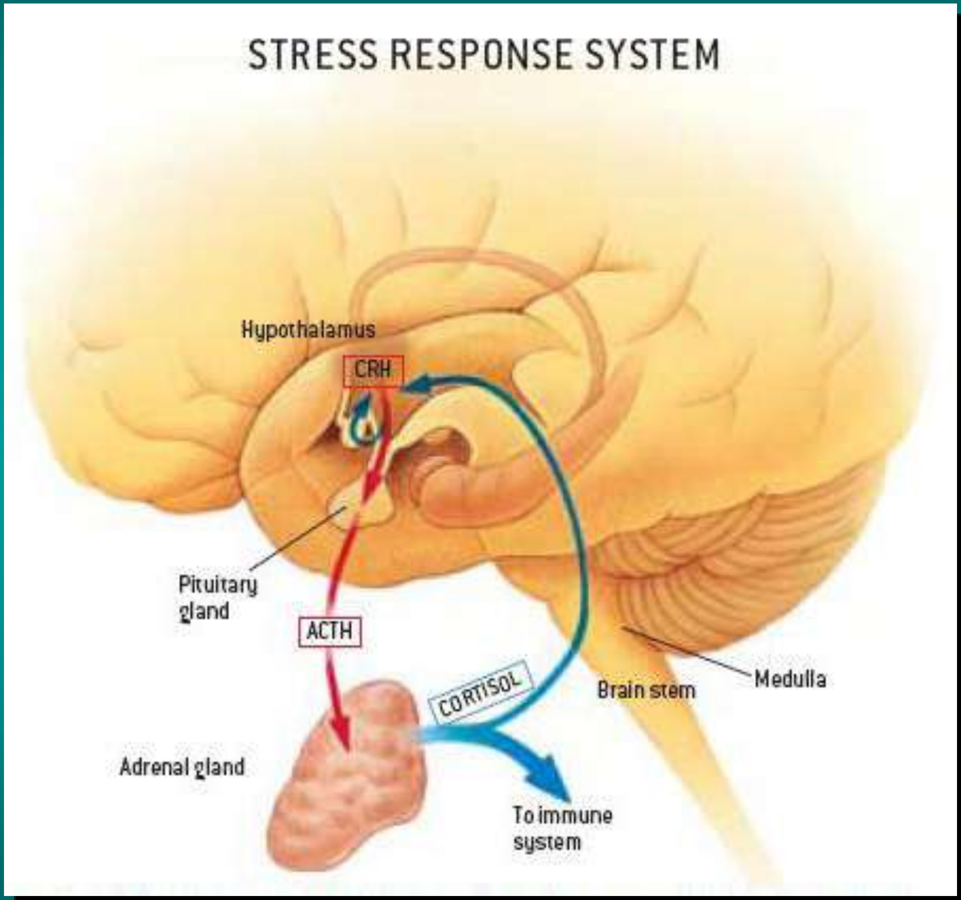
- A neuropsychological model that proposes <u>spiritual experiences associated with selflessness</u> are related to <u>decreased activity in the right parietal lobe.</u>

- People with injuries to the right parietal lobe of the brain reported higher levels of spiritual experiences, such as <u>transcendence</u>.
- Geschwind: epileptics have most conversions

Neuropeptide Pathways

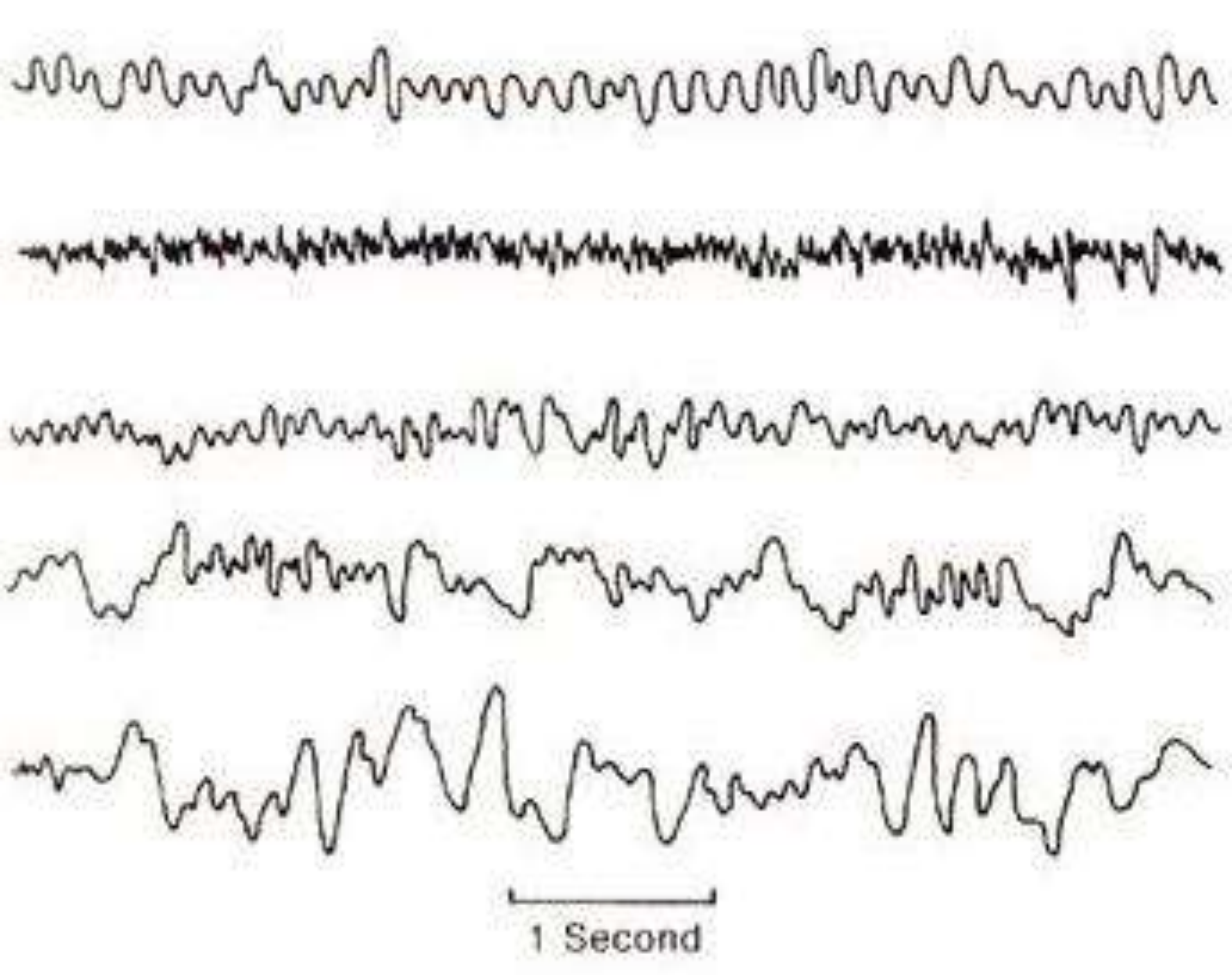


Hypothalamo-Pituitary-Adrenocortical (HPA) Axis



Controls reactions to stress

Brain waves



Alpha 8-13cps
(Relaxed state)

Beta 10-25cps
(Excited state)

Theta 4-7cps
(Drowsy)

Delta below 3.5cps
(Light sleep)

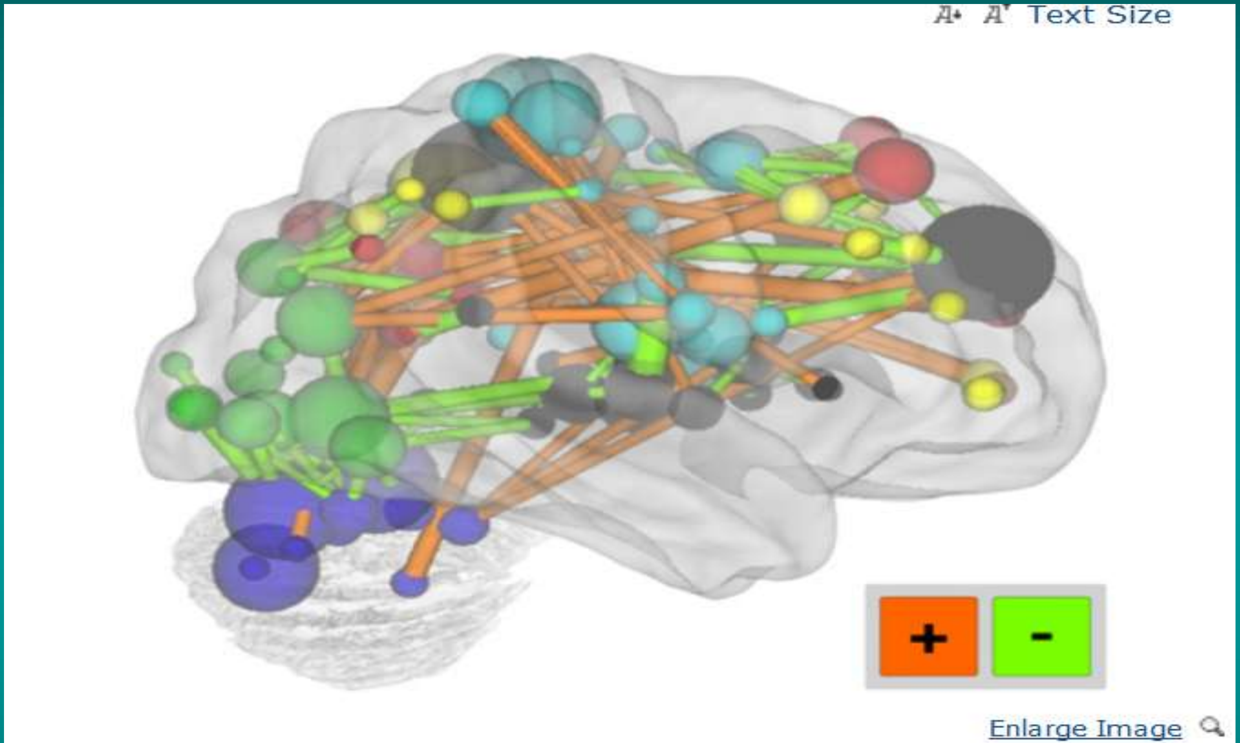
Delta
(Deep sleep)

Meditation and Brain Waves

- During meditation, theta waves were most abundant in the frontal and middle parts of the brain.
- Theta waves indicate deep relaxation and occur more frequently in highly experienced meditation practitioners. The source is probably frontal parts of the brain.
- Alpha waves were more abundant in the posterior parts of the brain during meditation than during simple relaxation. They are characteristic of wakeful rest: a universal sign of deep relaxation during meditation
- Delta waves are characteristic of sleep.
- Beta waves occur when the brain is working on goal-oriented tasks.

Lagopoulos, 2010

Growth curve for the brain,

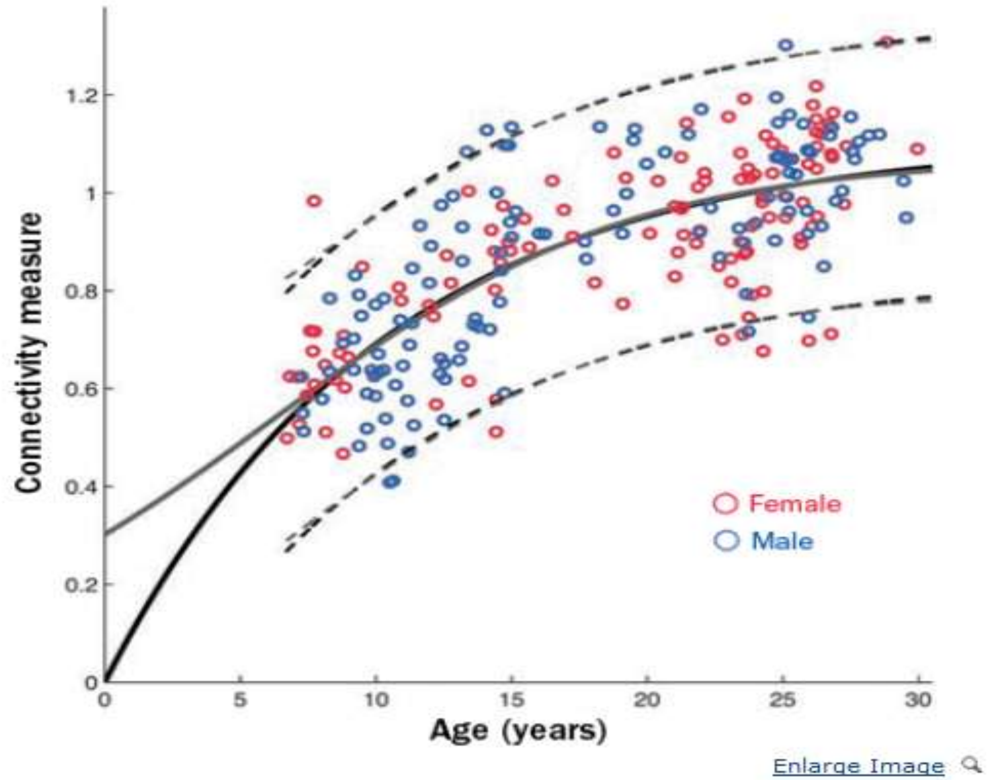


As the brain matures, some connections get stronger (orange) while others weaken (green). The sizes of the brain regions shown indicate their relative importance in predicting maturity.

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

Growth Curve

- How a typical brain's connections evolve with age
- Data from 238 volunteers of ages 7 to 30



The maturation scores for brains of 115 females (red) and 123 males (blue) between the ages of 7 and 30 years old were assembled into an average curve (black line), which shows that the brain changes quickly at young ages and levels off in the early 20s. (The gray solid line shows an alternate curve that also fits the data. Dashed lines mark the 95 percent prediction limits.)

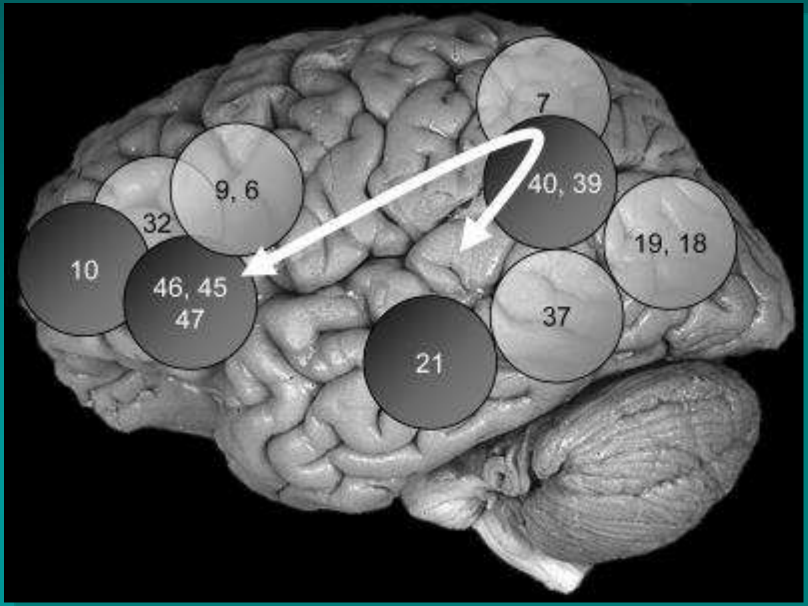
Nico Dosenbach and Bradley Schlaggar, Science, 2010

Growth Curve: a brain maturity test

- Links between brain regions that are physically close to each other get weaker with age, while specific long-range connections tend to get stronger.
- The overall organization switches from networks involving regions physically close to each other, which is the dominant motif in a child's brain, to networks that connect distant regions, the primary organizational principal in adult brains.
- Connections between the right anterior prefrontal cortex and the precuneus were the best predictors for overall brain maturity

- The test, by uncovering when and how brain maturity deviates from the norm, could be used to help diagnose and track neurological disorders such as Tourette’s syndrome, autism or schizophrenia.

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



In a review of 37 imaging studies related to intelligence, including their own, Richard Haier of the University of California, Irvine and Rex Jung of the University of New Mexico have uncovered evidence of a <u>distinct neurobiology of human intelligence</u>.

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

Brain energy metabolism: Mainly intrinsic

- Brain represents ~2% of the total body weight but accounts for 20% of all the energy consumed
- This high-energy consumption occurs in the resting state, a behavioral state characterized by quiet repose with either eyes closed or open, with or without visual fixation
- Brain activation: often increases of less than 5%
- 60–80% of overall brain energy consumption is devoted to glutamate cycling and, hence, neuronal signaling.
- The majority of brain energy consumption is devoted to functionally significant intrinsic activity.
- Lead to study of Intrinsic Connectivity Networks (ICNs), like DMN

Brain's Dark Energy: Default Mode Network

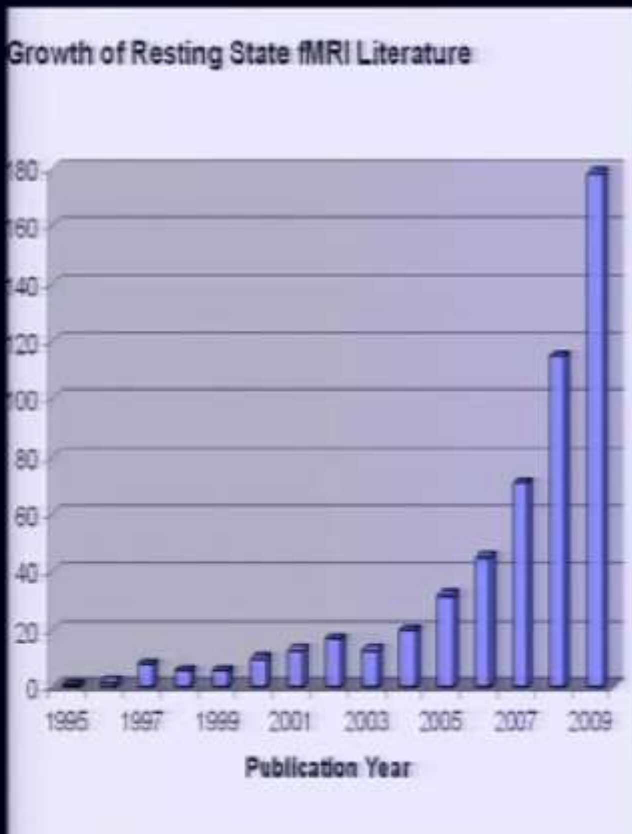
- Hans Berger, 1929: brain always active
- Mind at rest (daydreaming, asleep, anesthetized): 20 x energy consumption than when alert
- Default Mode Network (DMN): brain maintains high level of activity even when at rest
- Internal tasks such as daydreaming, envisioning the future, retrieving memories, and gauging others' perspectives.
- It is negatively correlated with brain systems that focus on external visual signals or goal activation.

Intrinsic connectivity network (ICN) fMRI methodology

- Resting state or ICN fMRI: technique maps temporally synchronous, spatially distributed, spontaneous low frequency (50.08 Hz) blood-oxygen level-dependent signal fluctuations at rest or, more accurately, in task-free settings.

New Research on Default Network

R-fMRI Total & Clinical Research



Disorder /condition	No. Studies
Alzheimer disorder	19
Schizophrenia	18
ADHD	14
Aging	12
Major depression	10
Anxiety disorders	8
Parkinson disorder	8
Multiple sclerosis	3
Coma	6
Tourette syndrome	2
Autism	5
Epilepsy	3
Callosotomy	2
Callosal agenesis	2

DMN: internal processing power

- 10 billion bits hit retina; 6 million bits per second via optic nerve; only 10,000 bits hit occipital areas; 100 bits in conscious visual perception; less 10% of synaptic connections in visual cortex devoted to external visual input
- 60-80 % of all brain energy occurs in circuits unrelated to any external events
- DMN makes constant predictions about outside environment

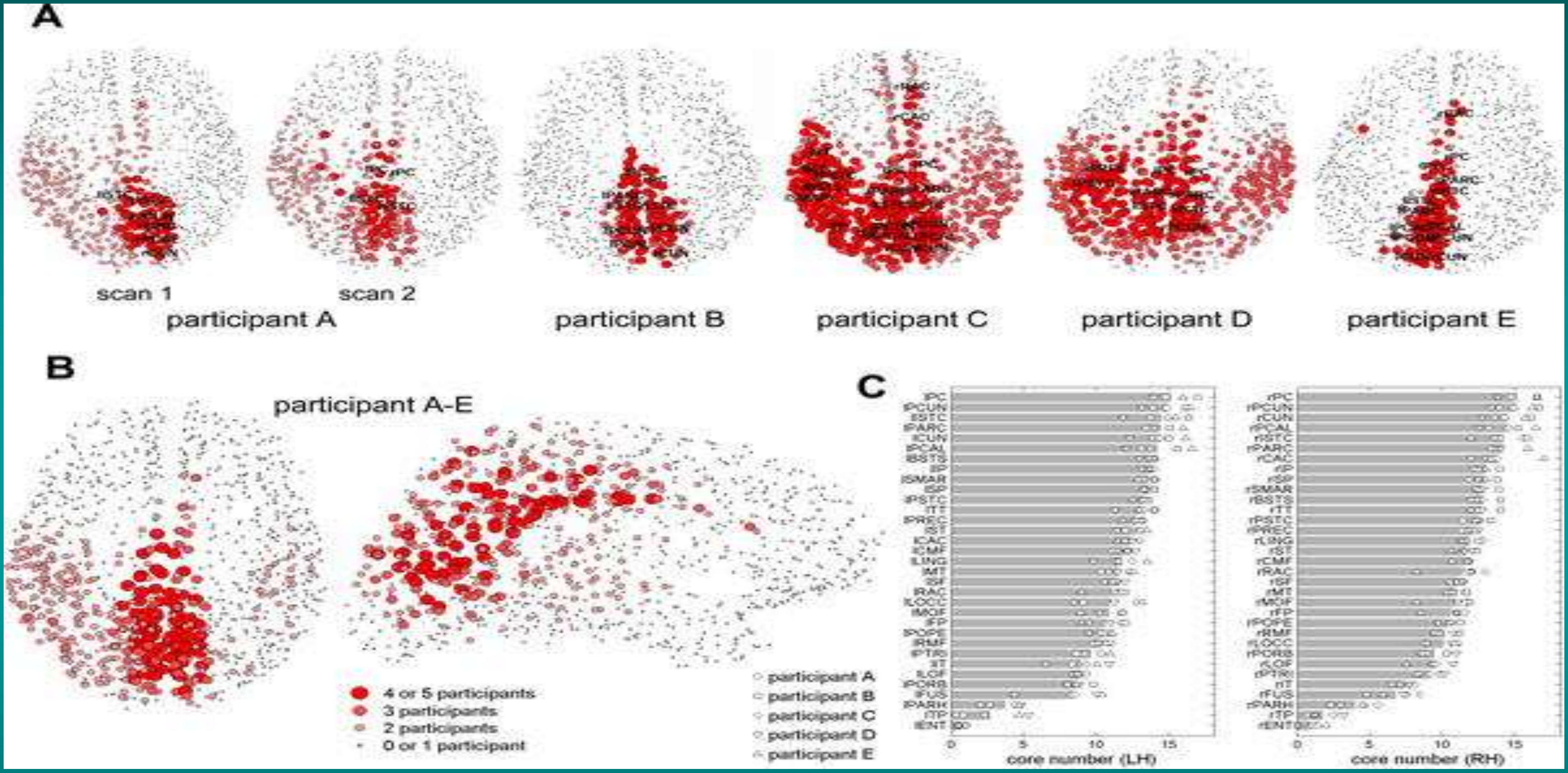
TPN: Dorsal Attention System

- The task-positive network TPN consists of regions routinely activated during goal-directed task performance.
- It includes a set of regions previously termed the “endogenous” or “dorsal attention system” (IPS, FEF) active during directed attention.
- In addition, the task-positive network includes dorsal-lateral and ventral prefrontal regions, insula, and SMA, activated by a variety of demanding cognitive tasks.
- TPN activation decreases activity in task-negative network

DMN Locations

- All show tight functional connectivity in the undirected brain (deactivated by(anticorrelated with) effortful cognitive task):
- Dorsal medial PFC
- Posterior Cingulate (PCC): hub
- Ventromedial PFC
- Lateral posterior Parietal
- Hippocampi

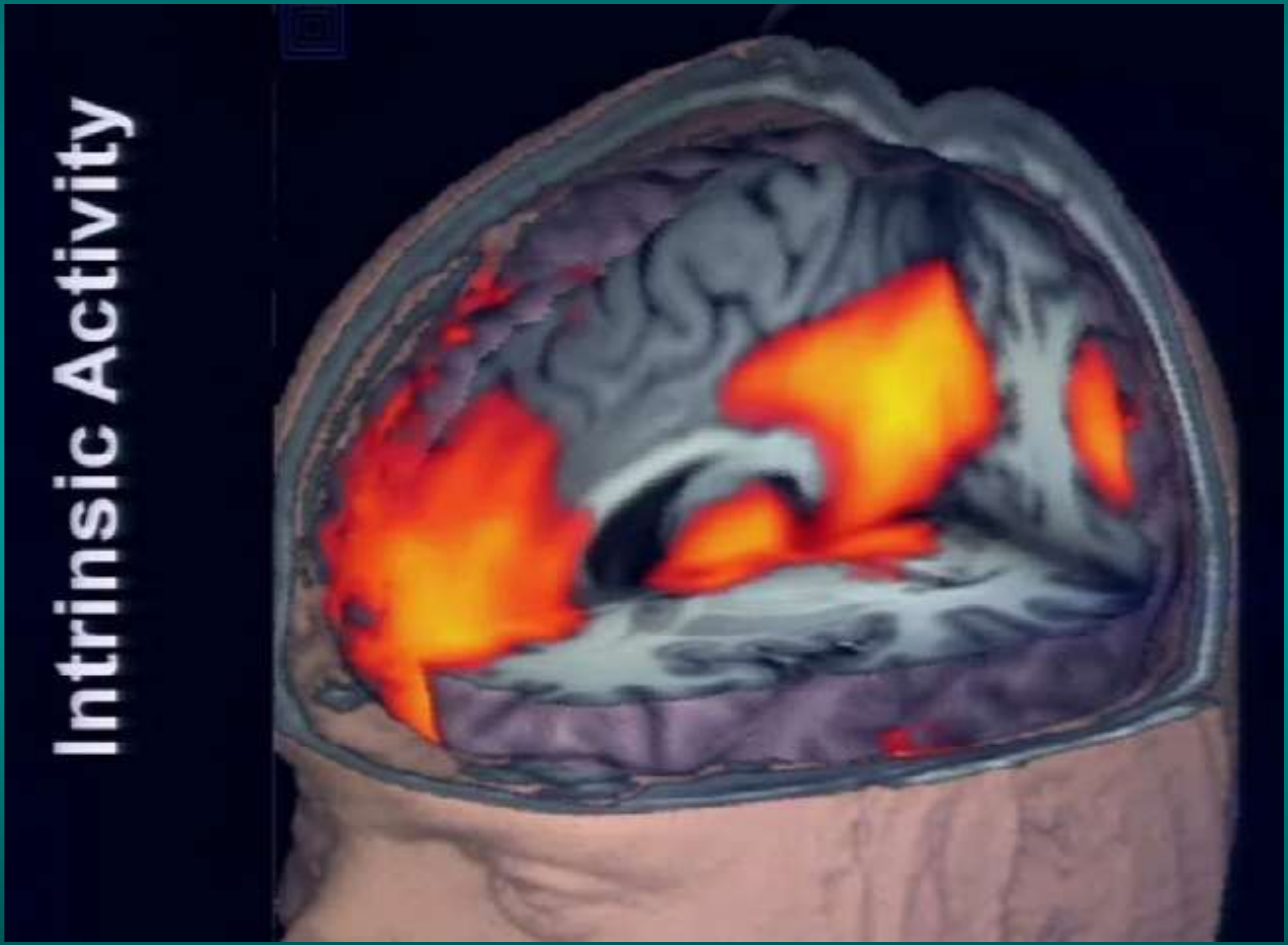
DMN: Structural Core of Human Cerebral Cortex

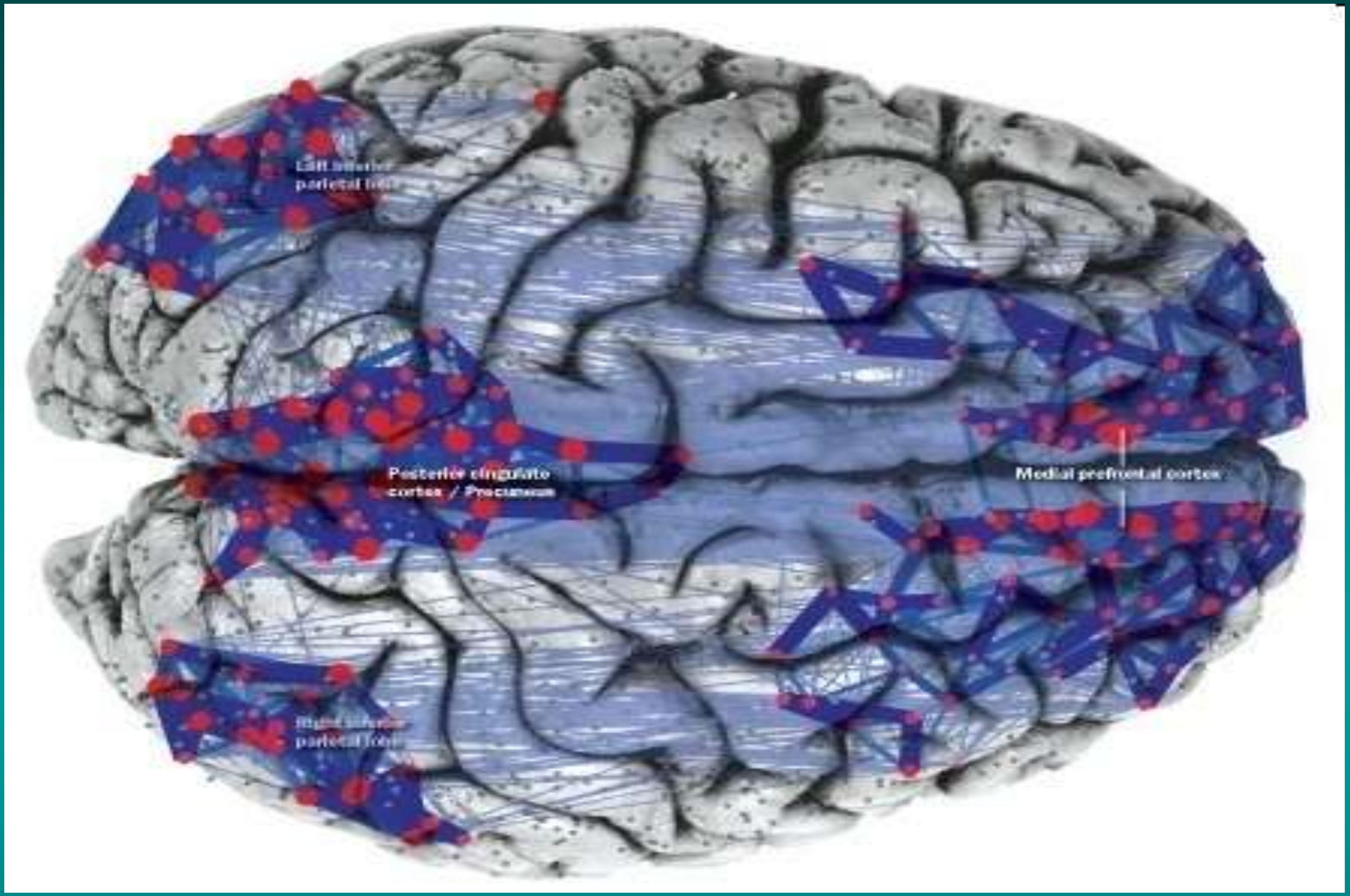


Dense network of cortico-cortical axonal pathways. Pathways within and across cortical hemispheres. Structural brain networks reveals a structural core within posterior medial & parietal cerebral cortex, as well as several distinct temporal and frontal modules. Brain regions that form the posterior components of the human default network.

Hagmann, et al., Plos Bio, 2008

FMRI of DMN locales

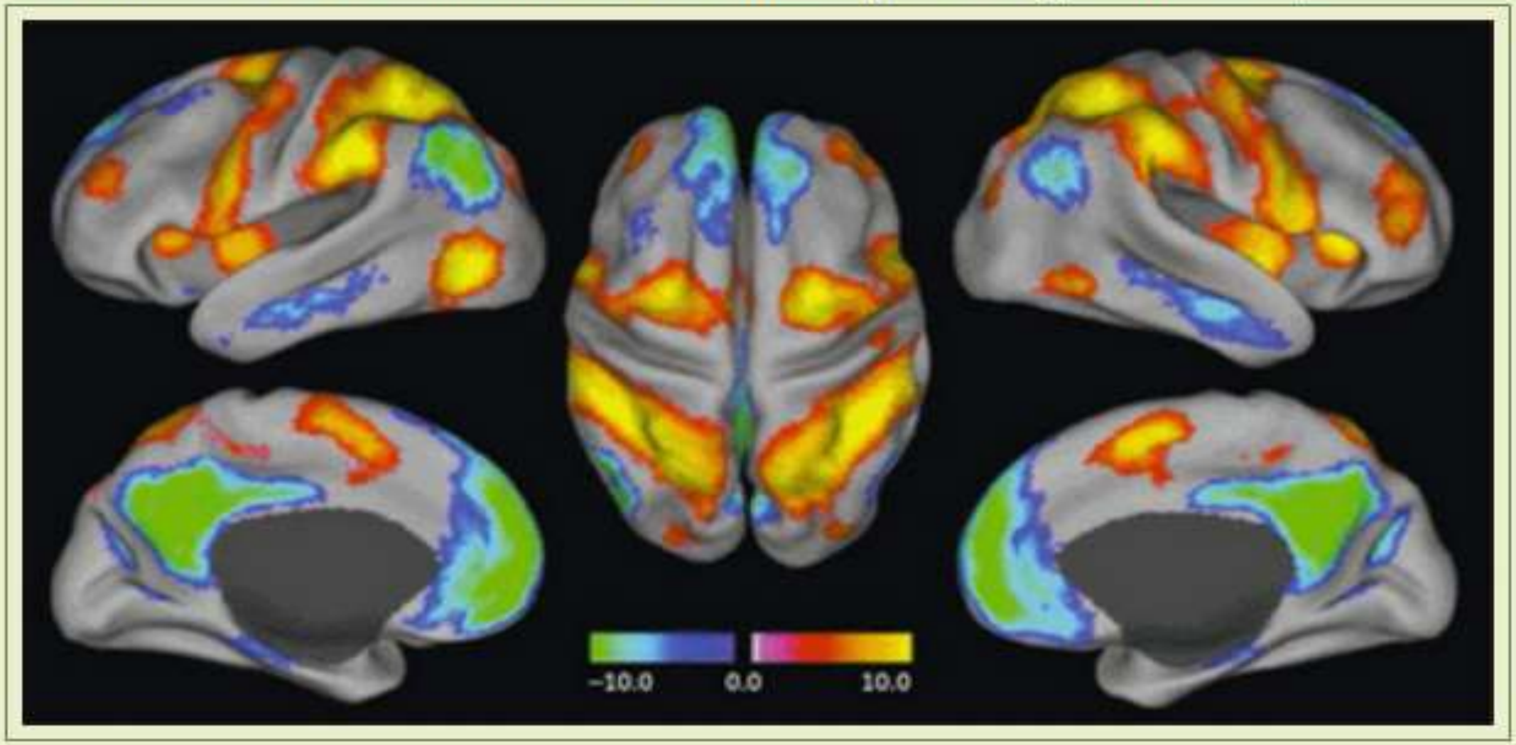




The brain's **<u>default mode network</u>** -- a series of connected areas that work hardest <u>when most of the brain is at rest</u> -- is active during daydreaming and mind-wandering. The default network <u>has two major hubs</u>, one in the <u>posterior cingulate cortex with the precuneus and one in the medial prefrontal cortex</u>.

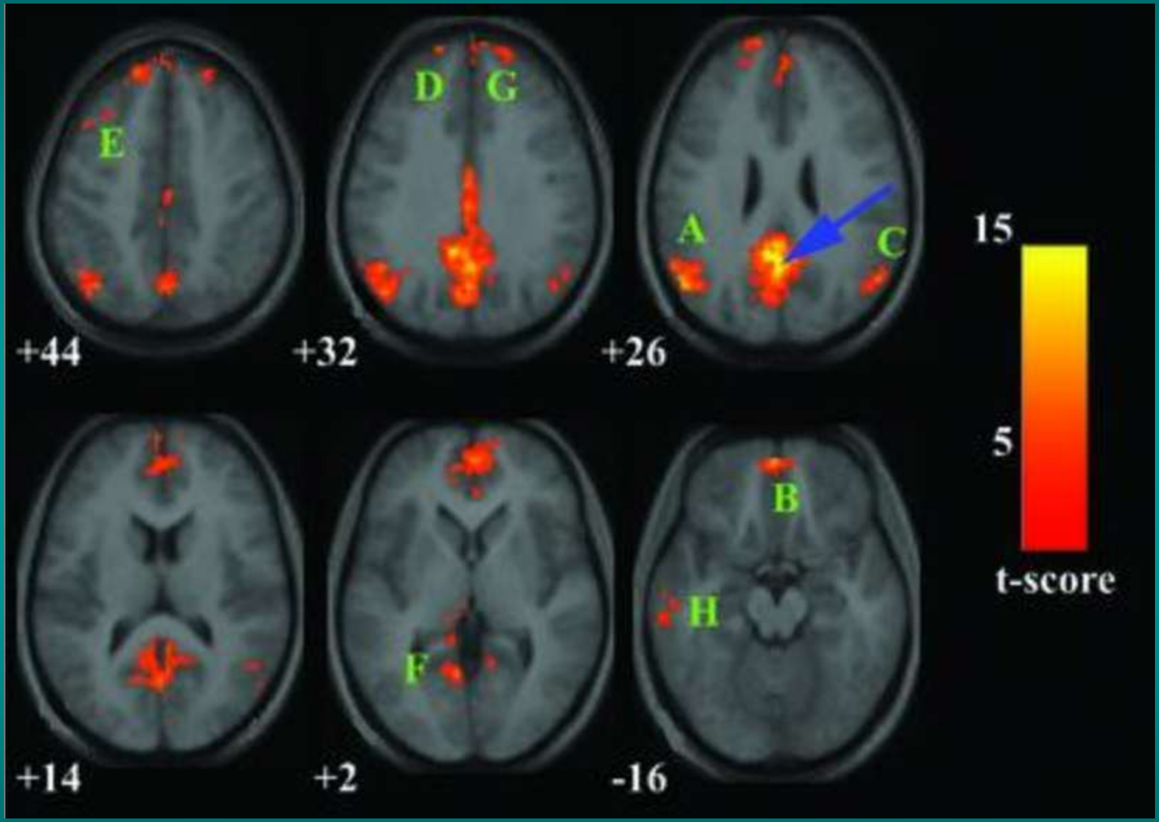
Olaf Sporns/Indiana Univ. (modified by J. Korenblat);
Brain photo: Omikron/photoresearchers

Default mode network illustrated below (in blue-green colors).



At rest, but active. fMRI images of a normal human brain at rest. The images reveal the highly organized nature of intrinsic brain activity, represented by correlated spontaneous fluctuations in the fMRI signal. Correlations are depicted by an arbitrary color scale. Positive correlations reside in areas known to increase activity during responses to controlled stimuli; negative correlations reside in areas that decrease activity under the same conditions. [from Raichle, 2006]

PCC (posterior cingulate cortex) connectivity: hub of DMN



As task difficulty increases, the ventral PCC shows reduced integration within the DMN and less anticorrelation with the cognitive control network (CCN) activated by the task. The dorsal PCC shows an opposite pattern, with increased DMN integration and more anticorrelation

PCC (hub of DMN) and Memory

- PCC: critical to the retrieval of episodic memories and semantic knowledge, and self-referential processing
- Among the earliest brain regions to show decreased metabolism in Alzheimer's disease
- There is neural connectivity between the PCC and medial temporal lobe regions, such as the entorhinal cortex and PHG, known to be key memory centers
- Default mode involves retrieval and manipulation of past events, in an effort to solve problems and develop future plans .

DMN or TPN

- During goal-oriented activity, the DMN is deactivated and another network, the task-positive network (TPN) is activated.
- It is thought that the default network (DMN) corresponds to task-independent introspection, or self-referential thought, while the TPN corresponds to action

Default Mode Network: functions of MPFC & PCC

- The <u>medial prefrontal cortex</u> is involved in <u>imagining, thinking about yourself and "theory of mind,"</u> which encompasses the ability to figure out what others think, feel or believe and to recognize that other people have different thoughts, feelings and beliefs from you.

- The <u>precuneus and PCC</u> are involved <u>in pulling personal memories from the brain's archives, visualizing yourself doing various activities and describing yourself.</u>

DMN

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

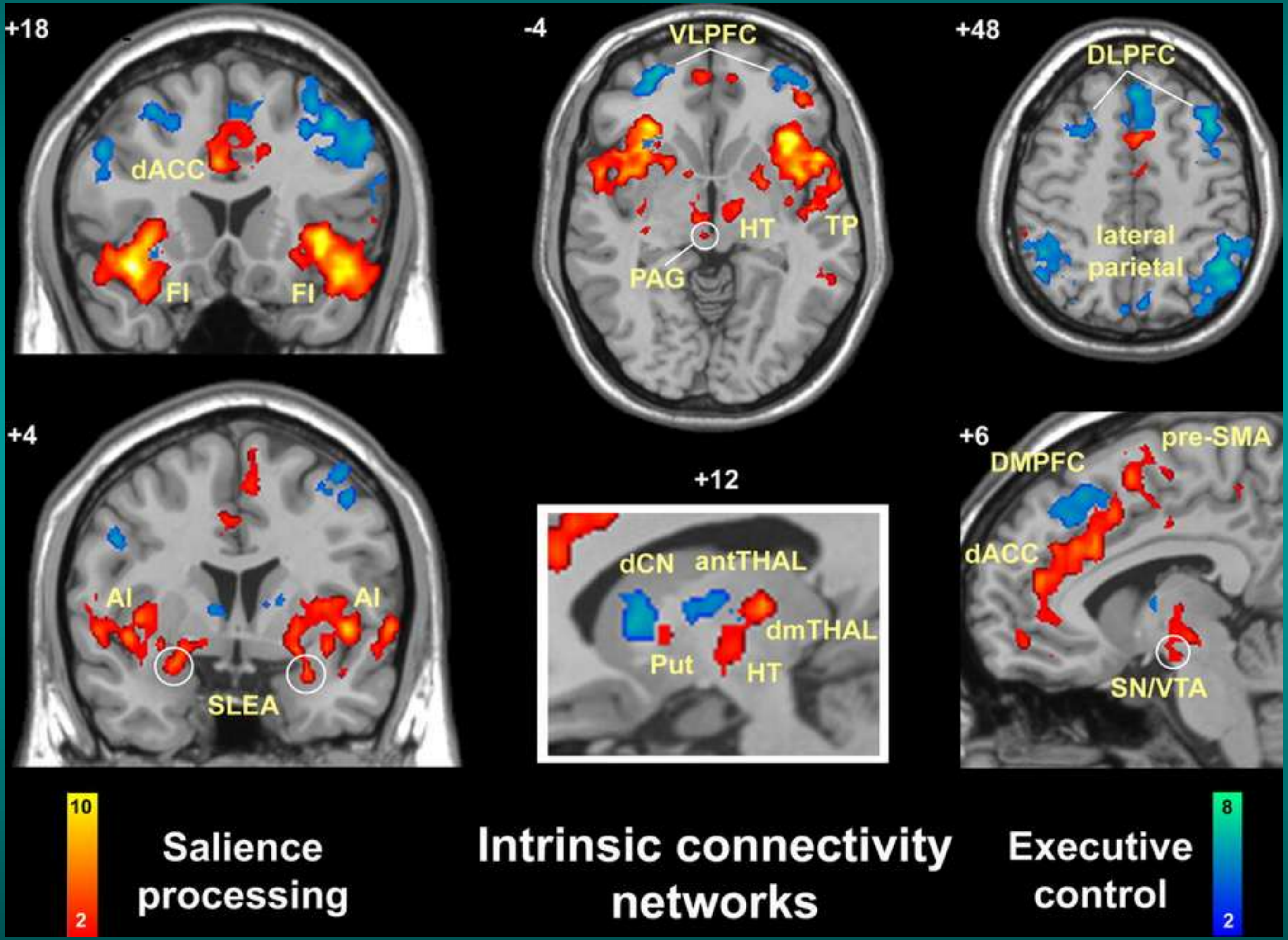
Salience Network (SAL)

- "Salience network," anchored by dorsal anterior cingulate (dACC) and orbital frontoinsular cortices (von Economo neurons) with robust connectivity to subcortical and limbic structures: interoceptive-autonomic processing/degree of personal salience (pain, uncertainty, and other threats to homeostasis)
- These regions coactivate in response to varied forms of salience, including the emotional dimensions of pain, empathy for pain, metabolic stress, hunger, or pleasurable touch, enjoyable "chills" to music, faces of loved ones or allies, anxiety, and social rejection.

Executive control network (ECN)

- “Executive-control network” that links <u>dorsolateral frontal and parietal</u> neocortices: <u>executive functioning</u>
- Sites include:
  - sustained attention and working memory (DLPFC, lateral parietal cortex),
  - response selection (dorsomedial frontal/pre-SMA),
  - response suppression (ventrolateral prefrontal cortex).

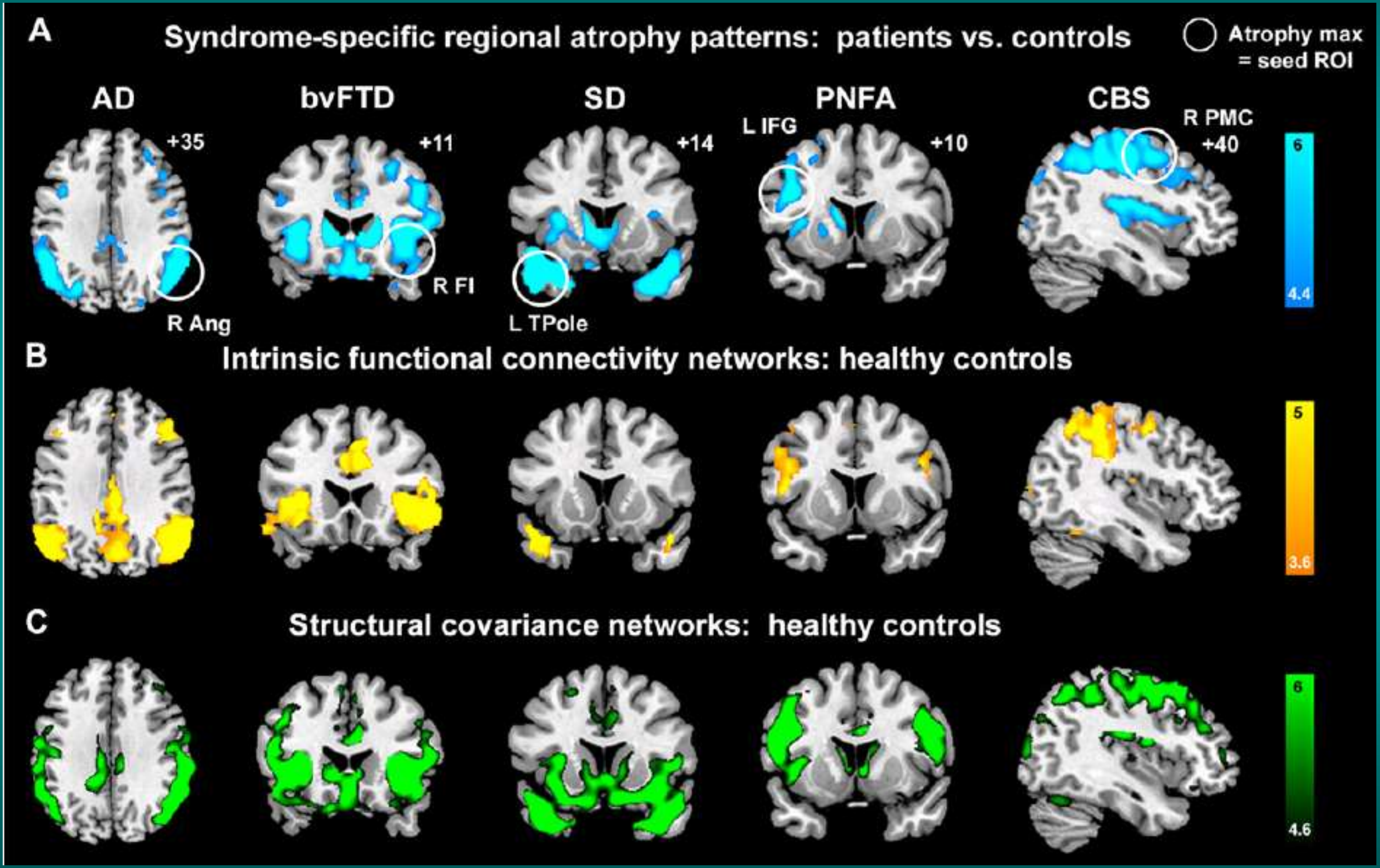
Salience vs. EF networks



FTD and Salience Network

- AD attacks DMN and FTD attacks salience network;
- Opposites ramps up: Salience revs up when DMN degenerates and vice versa
- Centrality of right frontoinsula in anchoring the Salience Network; frontoinsula features the peak brain-wide concentration of von Economo neurons, large bipolar Layer V projection neurons shown to undergo early, selective degeneration in bvFTD but not in Alzheimer’s disease

Convergent Syndromic Atrophy, Healthy ICN, and Healthy Structural Covariance Patterns



Five distinct clinical syndromes showed dissociable atrophy patterns,.

ICN detection of pathology

- Testing patients directly, ICN analysis has detected predictable connectivity reduction in:
  - Alzheimer’s disease,
  - prodromal Alzheimer’s asymptomatic individuals at risk for Alzheimer’s,
  - amyotrophic lateral
  - Sclerosis
  - Parkinson’s disease
  - bvFTD

Potential division of Networks

- **Visual**: occipital
- **Sensorimotor:** pre-post central gyrus
- **Auditory/memory:** auditory/temporal cortex
- **Language/spatial:** fronto-parietal, strongly lateralized in two hemispheres
- **SALience**(SAL): anterior Cingulate
- **Balance and co-ordination:** Cerebellum
- **Default Mode Network:** posterior cingulate, Angular gyrus
- **Executive Control Network**: dorsolateral, prefrontal + sup parietal

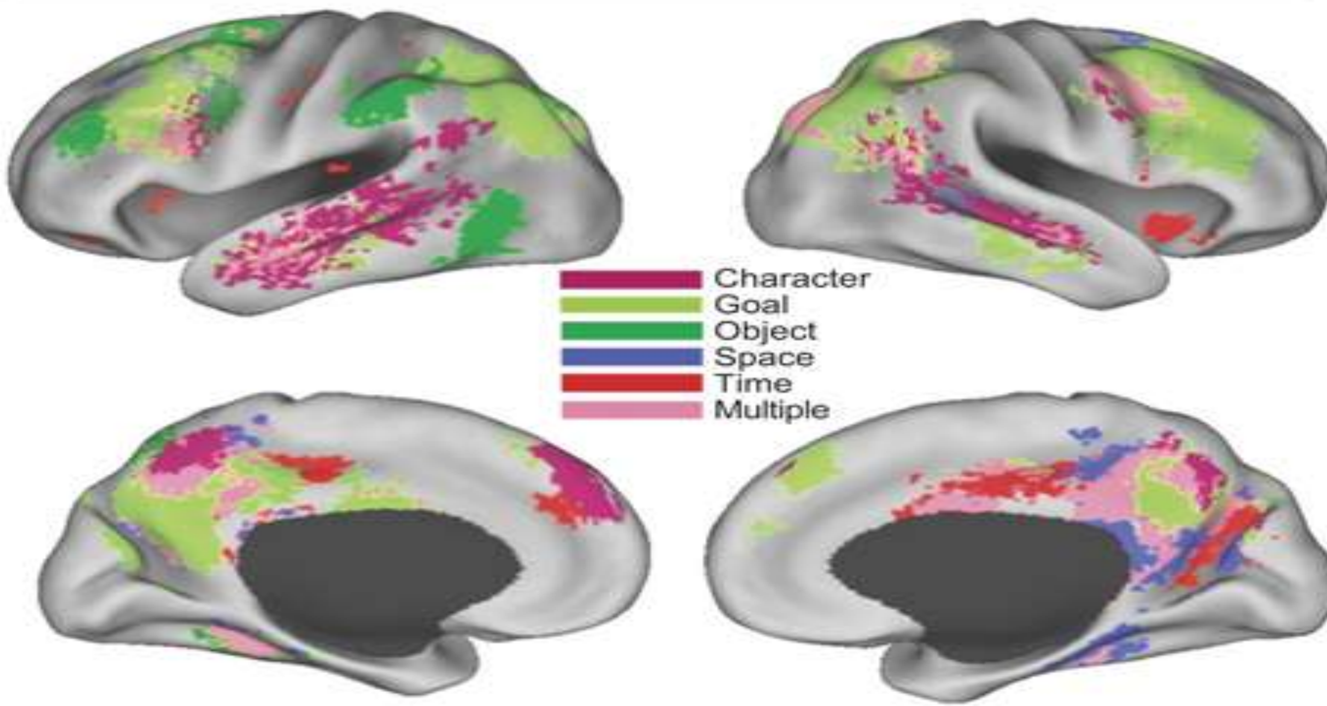
Developmentally based Networks

- **Visual** (calcerine sulcus)
- **Motor** (pre-central gyrus)
- **Auditory** (Heschel’s gyrus)
- **Syntax** (Inferior Frontal Gyrus)
- **Semantics** (temporal pole)
- **SALience** (Fronto Insula)
- **DMN** (Angular Gyrus)
- **ECN** (DLPFC)

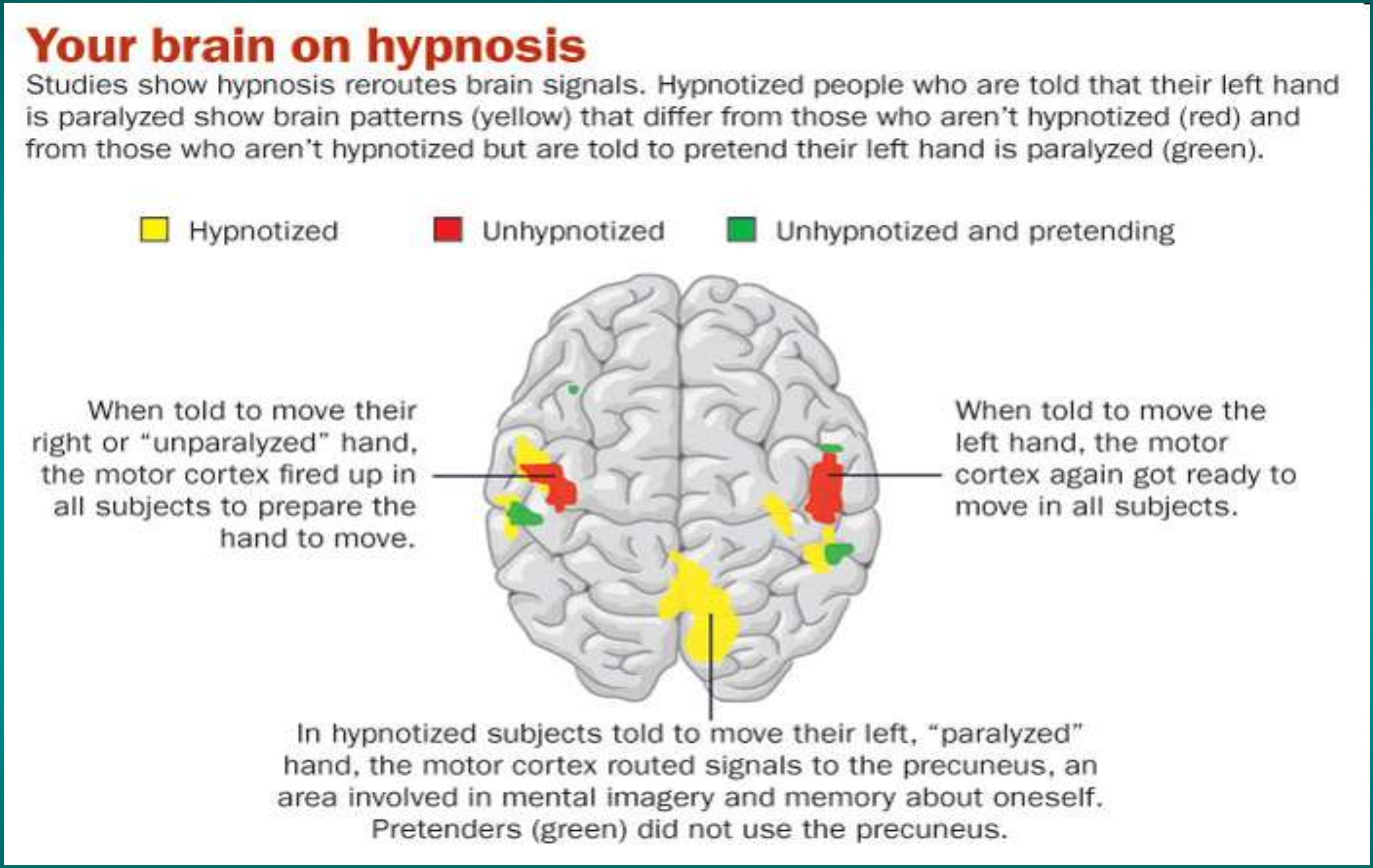
a

Clause	Cause	Character	Goal	Object	Space	Time
As soon as [Mrs. Logan] made a check mark on his paper,		•				•
[Raymond] hurried back to his desk.		•	•		•	
Nearing his desk,						
he crumpled the paper, seemingly without any disappointment or anxiety.	•		•	•		
His expression was one of "Well, that's that and I'm through."						
The teacher called to him pleasantly, "Did I grade your book?"	•	•	•			
Raymond answered with a negative shake of his head.		•	•			
He picked up his English workbook				•		
and returned to her desk.					•	
He walked briskly.						•
He laid his workbook on the desk.				•		

b



Hypnosis: Precuneus activation



Anterior cingulate less active during Stroop test

Where is the Second Brain?

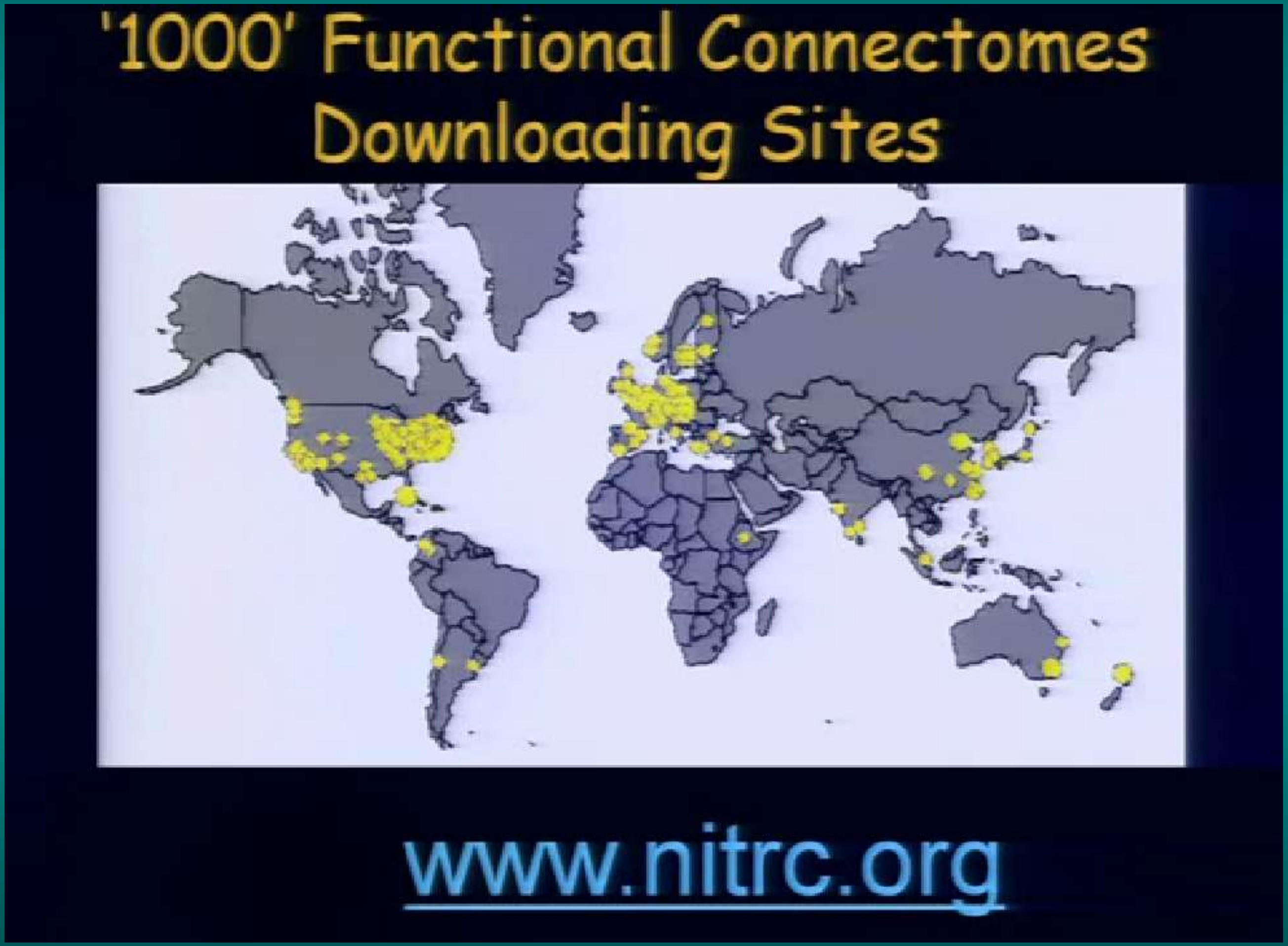
- The second brain contains some 100 million neurons, more than in either the spinal cord or the peripheral nervous system.

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 in the bowels.

- In mice, bacteria in gut can create behavioral anxiety.

1000 Functional Connections Data Site



Neuroimaging tools

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