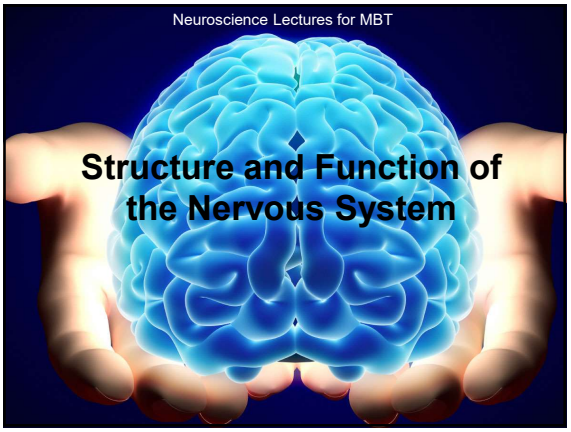
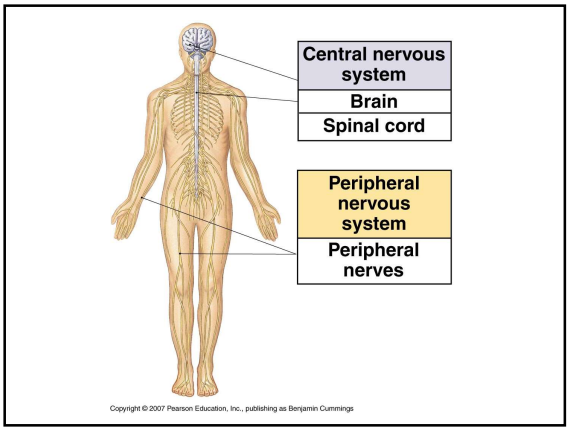
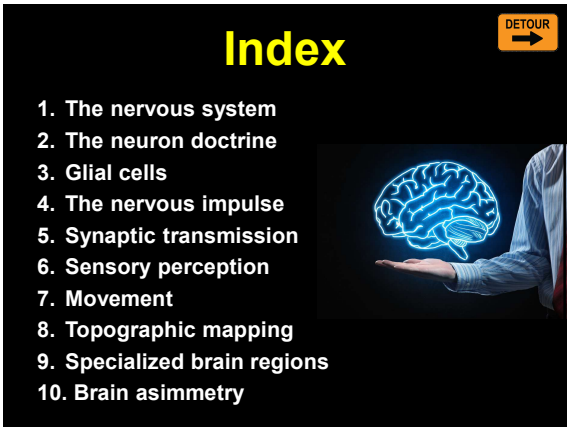
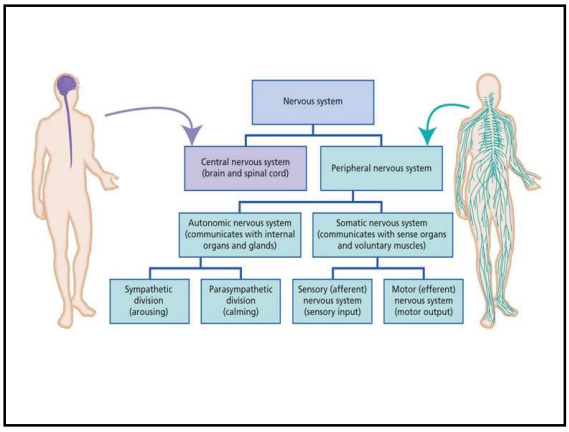
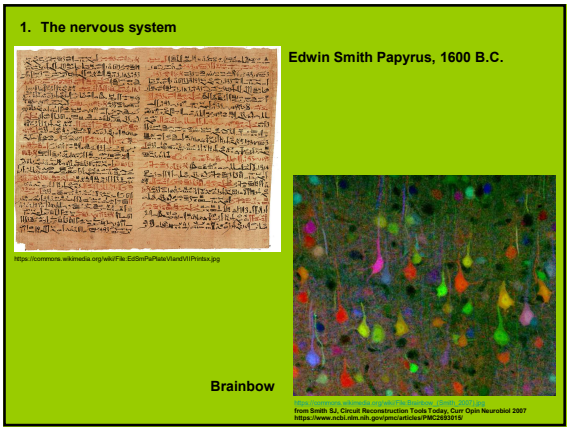
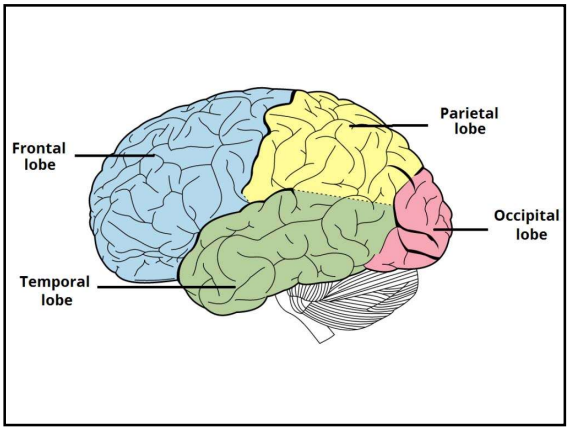

Neuroscience Lectures for MBT
Structure and Function of the Nervous System

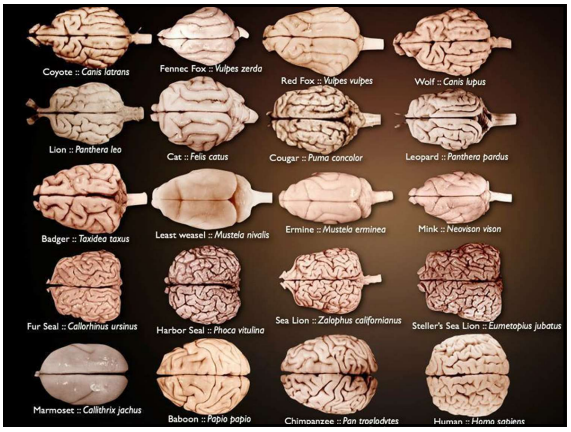

Central nervous system
Brain
Spinal cord
Peripheral nervous system
Peripheral nerves
Copyright © 2007 Pearson Education, Inc., publishing as Benjamin Cummings

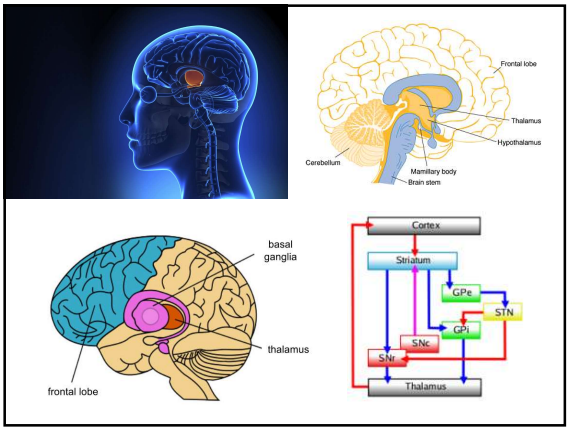

Index
DETOUR
1. The nervous system
2. The neuron doctrine
3. Glial cells
4. The nervous impulse
5. Synaptic transmission
6. Sensory perception
7. Movement
8. Topographic mapping
9. Specialized brain regions
10. Brain asimmetry

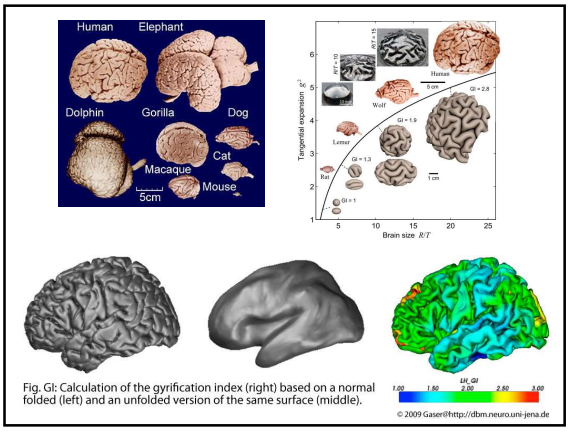

Nervous system
Central nervous system (brain and spinal cord)
Peripheral nervous system
Autonomic nervous system (communicates with internal organs and glands)
Somatic nervous system (communicates with sense organs and voluntary muscles)
Sympathetic division (arousing)
Parasympathetic division (calming)
Sensory (afferent) nervous system (sensory input)
Motor (efferent) nervous system (motor output)

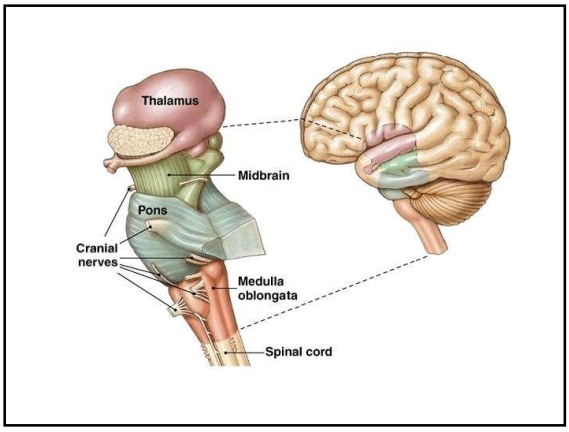

1. The nervous system
Edwin Smith Papyrus, 1600 B.C.
https://commons.wikimedia.org/wiki/File:EdSmPlaPlateVIandVIIPrintex.jpg
Brainbow
from Smith SJ. Circuit Reconstruction Tools Today. Curr Opin Neurobiol 2007
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2693015/

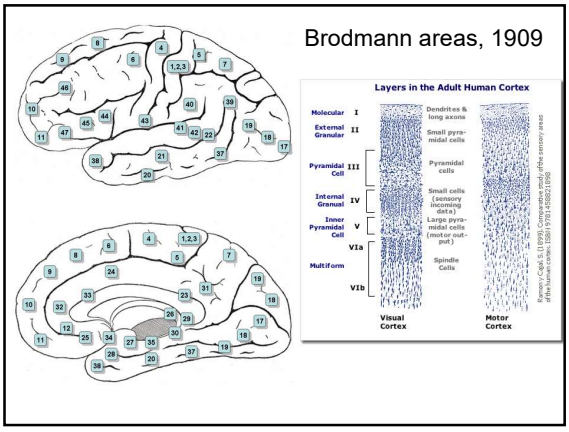

Frontal lobe
Parietal lobe
Occipital lobe
Temporal lobe

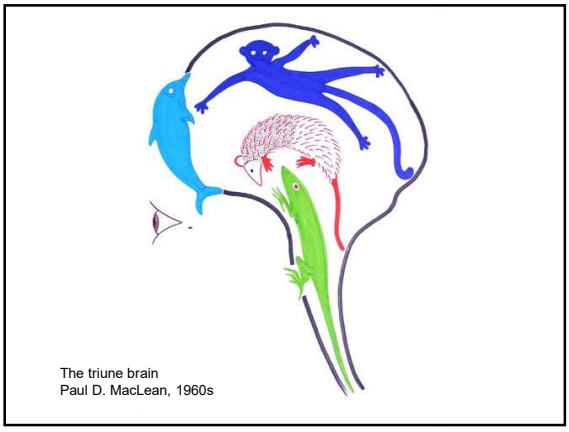

Coyote :: Canis latrans
Fennec Fox :: Vulpes zerda
Red Fox :: Vulpes vulpes
Wolf :: Canis lupus
Lion :: Panthera leo
Cat :: Felis catus
Cougar :: Puma concolor
Leopard :: Panthera pardus
Badger :: Taxidea taxus
Least weasel :: Mustela nivalis
Ermine :: Mustela erminea
Mink :: Neovison vison
Fur Seal :: Callorhinus ursinus
Harbor Seal :: Phoca vitulina
Sea Lion :: Zalophus californianus
Steller's Sea Lion :: Eumetopias jubatus
Marmoset :: Callithrix jachus
Baboon :: Papio papio
Chimpanzee :: Pan troglodytes
Human :: Homo sapiens

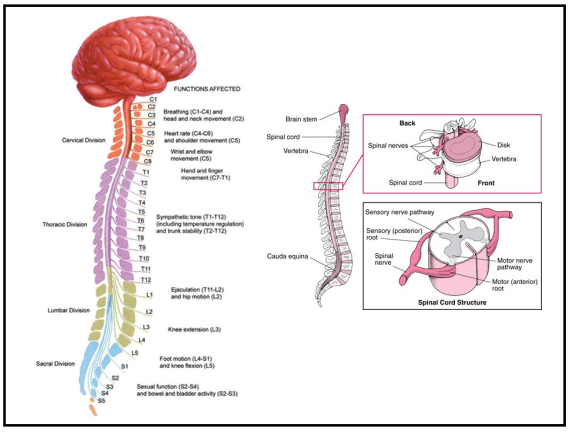

Frontal lobe
Thalamus
Hypothalamus
Cerebellum
Mamillary body
Brain stem
basal ganglia
thalamus
frontal lobe
Cortex
Striatum
GPe
STN
GPi
SNc
SNr
Thalamus

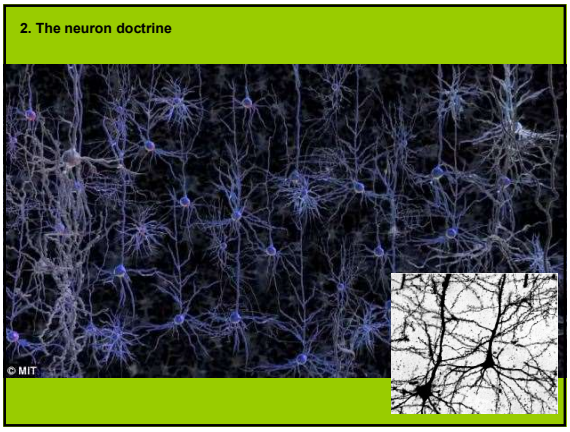

Human
Elephant
Dolphin
Gorilla
Dog
Cat
Macaque
Mouse
5cm
Tangential expansion
Brain size
Fig. GI: Calculation of the gyrification index (right) based on a normal folded (left) and an unfolded version of the same surface (middle).
© 2009 Gaser@http://dbm.neuro.uni-jena.de

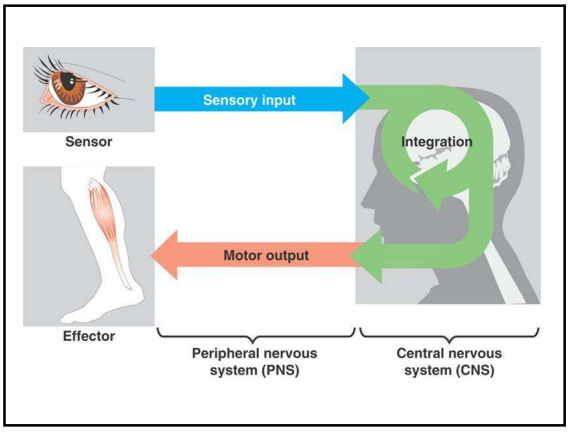

Thalamus
Midbrain
Pons
Cranial nerves
Medulla oblongata
Spinal cord

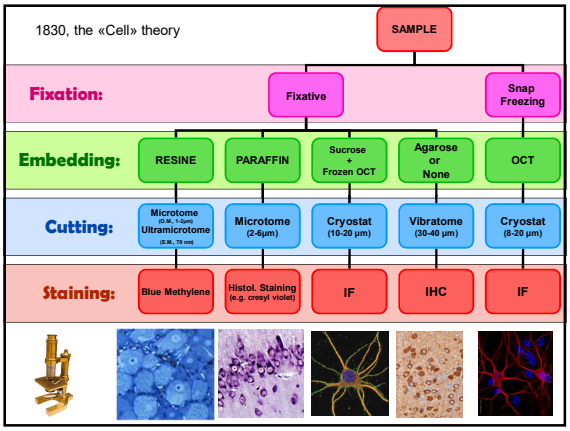

Brodmann areas, 1909
Layers in the Adult Human Cortex
Molecular I
External Granular II
Pyramidal Cell III
Internal Granual IV
Inner Pyramidal Cell V
VIa
Multiform
VIb
Visual Cortex
Motor Cortex

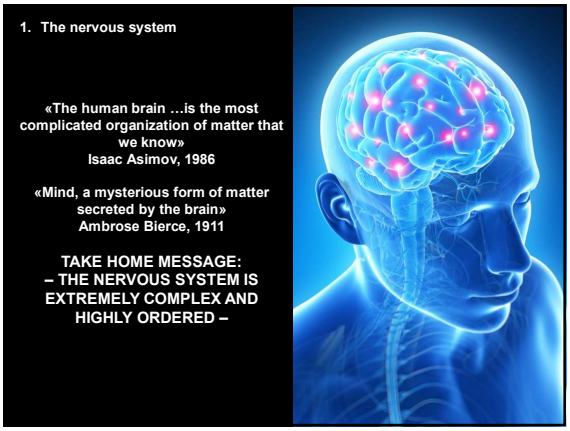

The triune brain
Paul D. MacLean, 1960s

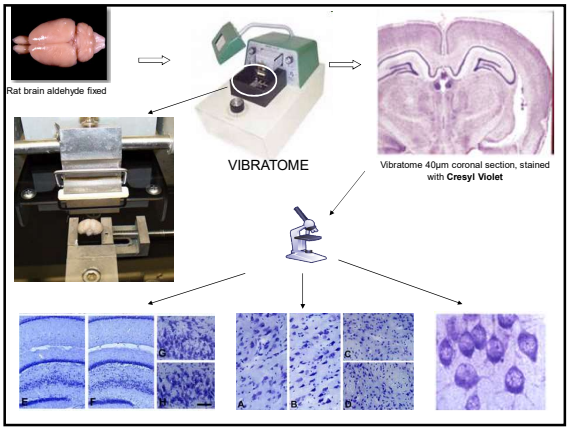

FUNCTIONS AFFECTED
Cervical Division
Thoracic Division
Lumbar Division
Sacral Division
Brain stem
Spinal cord
Vertebra
Cauda equina
Back
Spinal nerves
Disk
Vertebra
Spinal cord
Front
Sensory nerve pathway
Sensory (posterior) root
Spinal nerve
Motor nerve pathway
Motor (anterior) root
Spinal Cord Structure

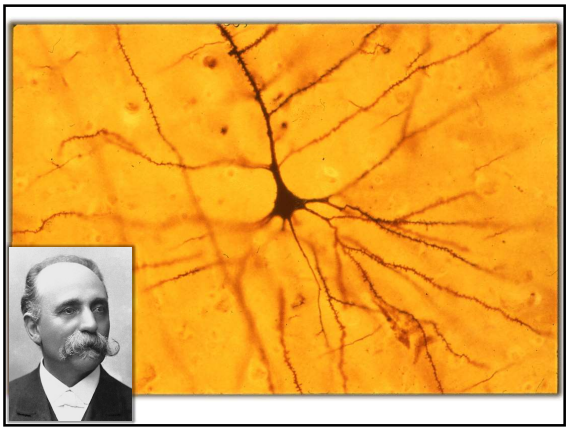

2. The neuron doctrine
© MIT

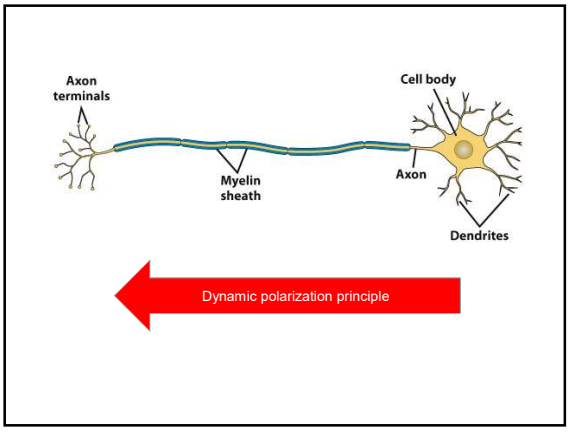

Sensory input
Sensor
Integration
Motor output
Effector
Peripheral nervous system (PNS)
Central nervous system (CNS)


1830, the «Cell» theory
SAMPLE
Fixation:
Fixative
Snap Freezing
Embedding:
RESINE
PARAFFIN
Sucrose + Frozen OCT
Agarose or None
OCT
Cutting:
Microtome Ultramicrotome
Microtome (2-6µm)
Cryostat (10-20 µm)
Vibratome (30-40 µm)
Cryostat (8-20 µm)
Staining:
Blue Methylene
Histol. Staining (e.g. cresyl violet)
IF
IHC
IF

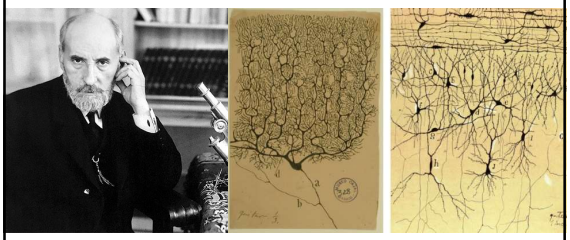

1. The nervous system
«The human brain …is the most complicated organization of matter that we know»
Isaac Asimov, 1986
«Mind, a mysterious form of matter secreted by the brain»
Ambrose Bierce, 1911
TAKE HOME MESSAGE:
– THE NERVOUS SYSTEM IS EXTREMELY COMPLEX AND HIGHLY ORDERED –


Rat brain aldehyde fixed
VIBRATOME
Vibratome 40µm coronal section, stained with Cresyl Violet



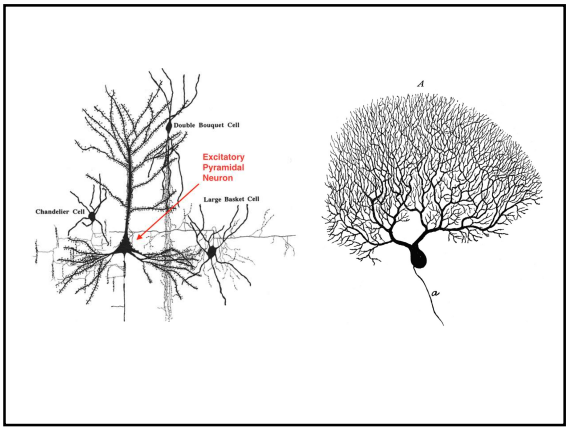


«Like the entomologist hunting for brightly coloured butterflies, my attention was drawn to the flower garden of the gray matter, which contained cells with delicate and elegant forms, the mysterious butterflies of the soul»
Santiago Ramòn y Cajal, 1894

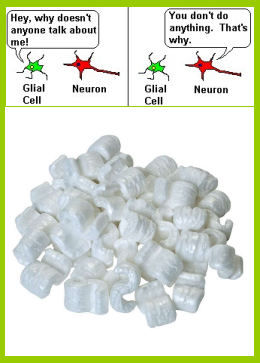


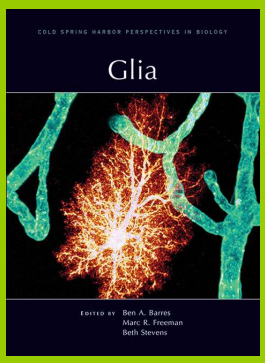
2. The neuron doctrine

TAKE HOME MESSAGE:
– NEURONS ARE THE FONDAMENTAL COMPONENTS OF THE NERVOUS SYSTEM –

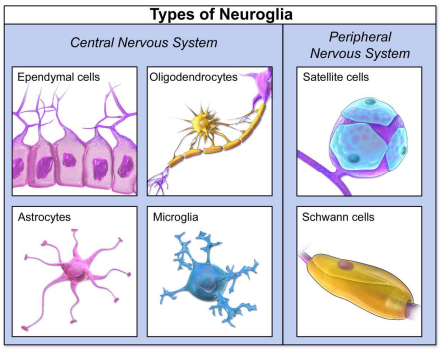


3. Glial cells





«This connective substance … is a kind of glue in which the nervous elements are planted»
Rudolph Virchow, 1856 («*nervenkitt*»)



Published in final edited form as:
Neuron. 2012 May 24; 74(4): 691–705. doi:10.1016/j.neuron.2012.03.026.

Microglia Sculpt Postnatal Neural Circuits in an Activity and Complement-Dependent Manner

Dorothy P Schafer[1], Emily K Lehrman[1,*], Amanda G Kautzman[1,*], Ryuta Koyama[1], Alan R Mardinly[2], Ryo Yamasaki[4], Richard M Ransohoff[4], Michael E Greenberg[2], Ben A Barres[2], and Beth Stevens[1]

…while past work has focused on the role of these cells during disease, recent imaging studies reveal dynamic interactions between microglia and synaptic elements in the healthy brain.
Despite these intriguing observations, the precise function of microglia at remodeling synapses and the mechanisms that underlie microglia-synapse interactions remain elusive…

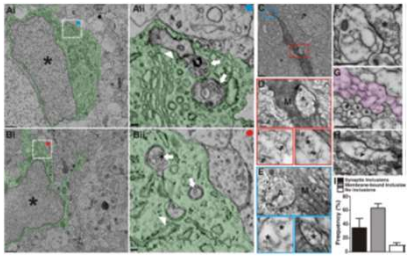
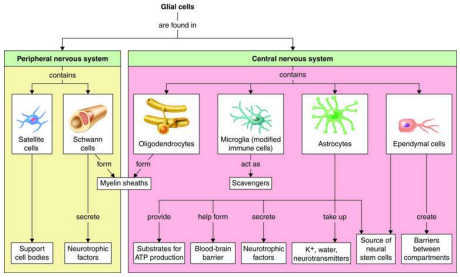


Figure 4. Microglia engulf presynaptic elements undergoing active synaptic pruning

Glial cells are critical partecipants in every major aspect of brain development, fucntion and disease
Ben Barres, 2008



Short Conceptual Overview

DETOUR

Marta Bolós, Juan Ramón Perea and Jesús Avila*

Alzheimer's disease as an inflammatory disease

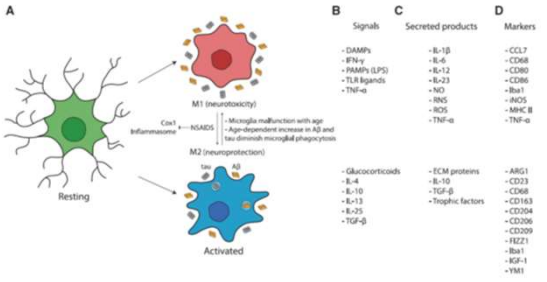
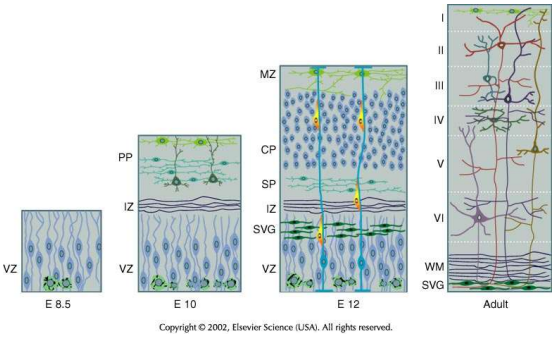


Figure 1: Diagram of polarization states of microglia.

Development of the cerebral cortex



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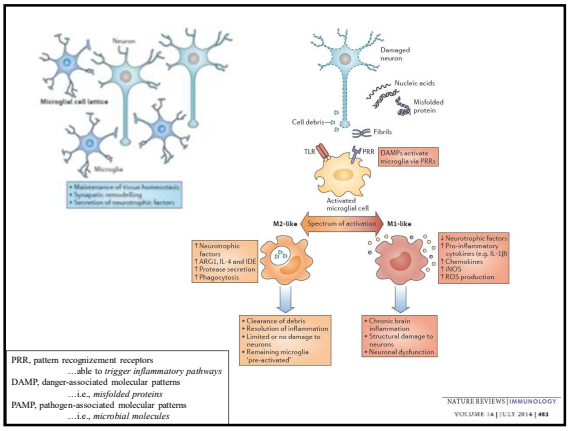
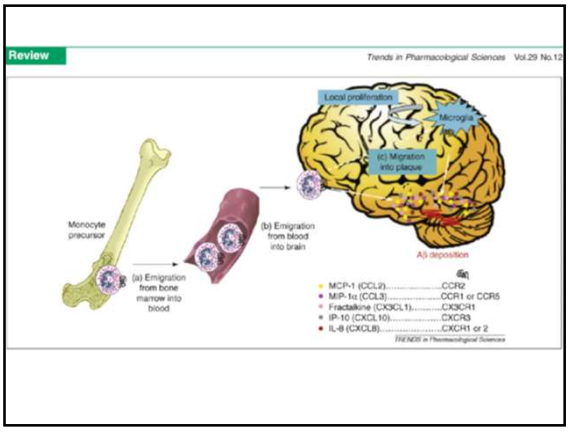
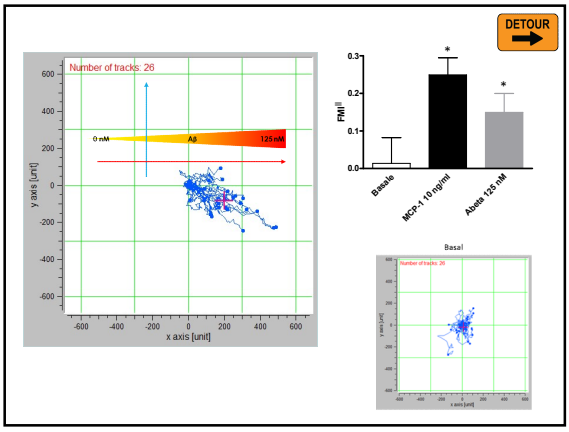
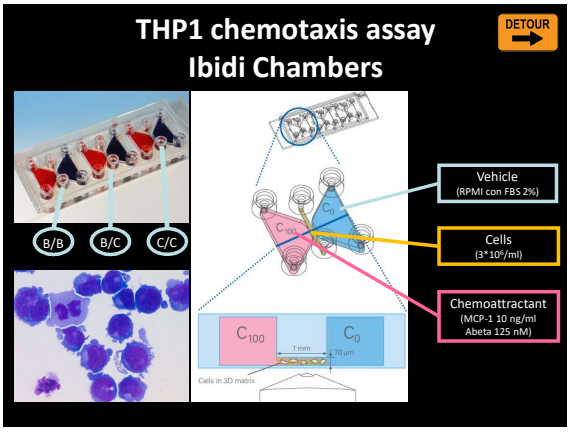
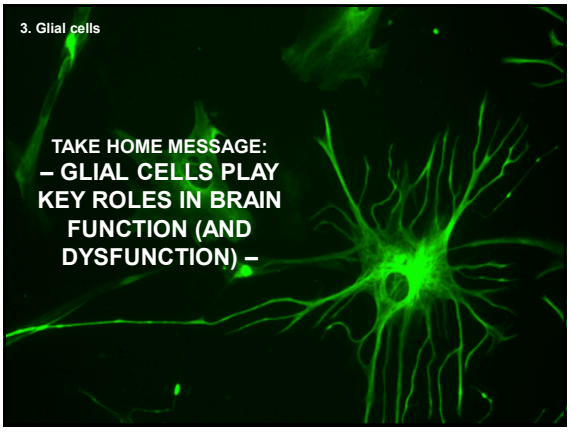
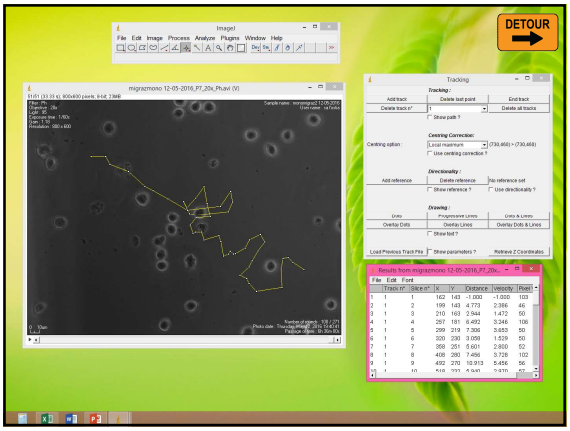


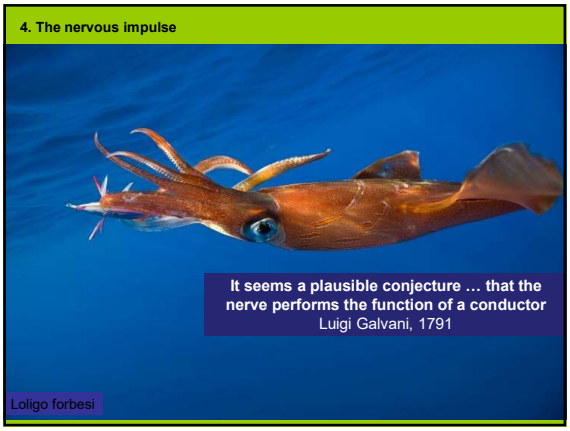

Review
Trends in Pharmacological Sciences Vol.29 No.12
Local proliferation
Microglia
(c) Migration into plaques
Monocyte precursor
(b) Emigration from blood into brain
Aβ deposition
(a) Emigration from bone marrow into blood
MCP-1 (CCL2)..... CCR2
MIP-1α (CCL3)..... CCR1 or CCR5
Fractalkine (CXXCL1)..... CX3CR1
IP-10 (CXCL10)..... CXCR3
IL-8 (CXCL8)..... CXCH1 or 2

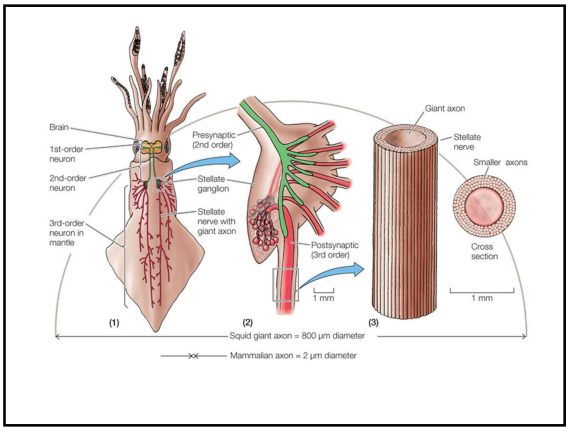

DETOUR
Number of tracks: 26
0 nM
Aβ
125 nM
y axis [unit]
x axis [unit]
FMI
Basale
MCP-1 10 ng/ml
Abeta 125 nM
Basal

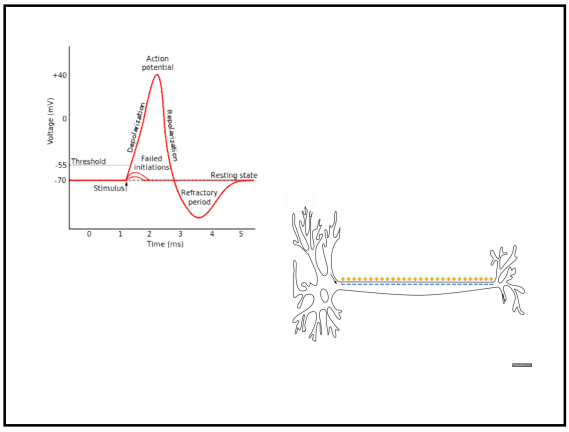

THP1 chemotaxis assay
Ibidi Chambers
DETOUR
B/B
B/C
C/C
Vehicle
(RPMI con FBS 2%)
Cells
(3*10⁵/ml)
Chemoattractant
(MCP-1 10 ng/ml
Abeta 125 nM)
C100
C0
1 mm
70 µm
Cells in 3D matrix

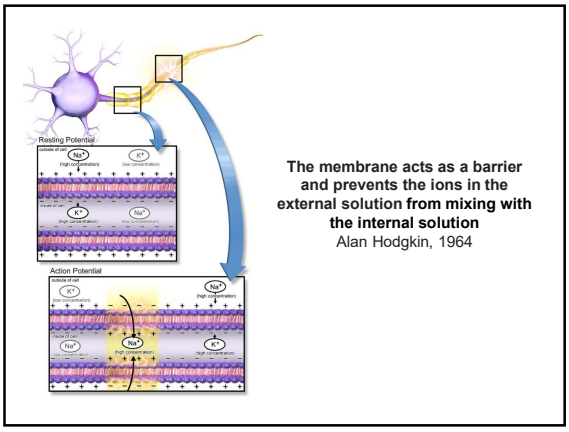

3. Glial cells
TAKE HOME MESSAGE:
– GLIAL CELLS PLAY KEY ROLES IN BRAIN FUNCTION (AND DYSFUNCTION) –


DETOUR

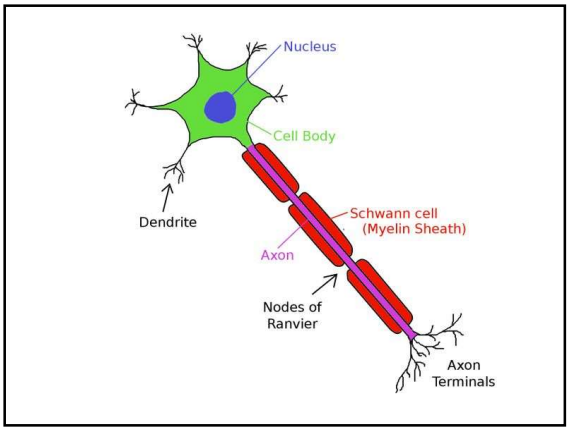

4. The nervous impulse
It seems a plausible conjecture … that the nerve performs the function of a conductor
Luigi Galvani, 1791
Loligo forbesi



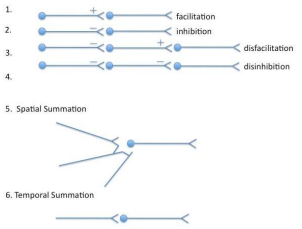


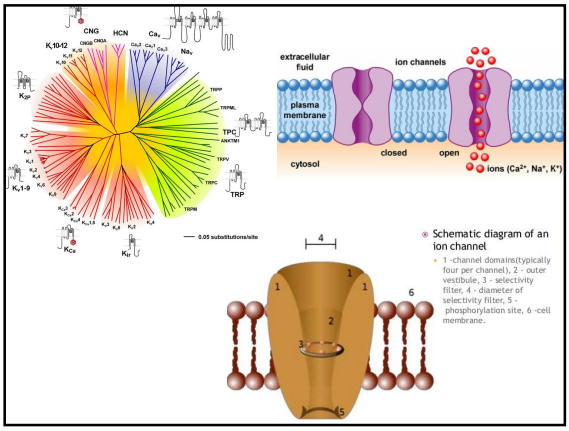


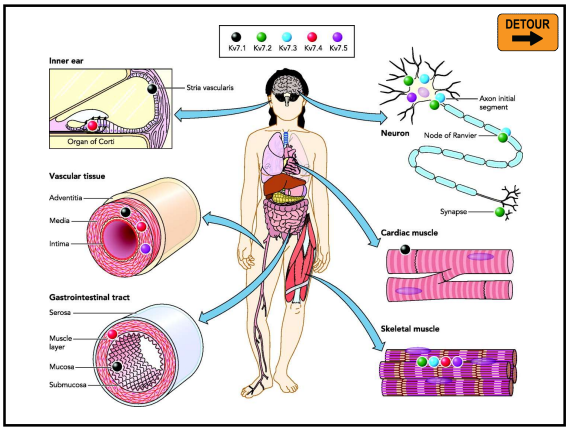
The membrane acts as a barrier and prevents the ions in the external solution from mixing with the internal solution
Alan Hodgkin, 1964



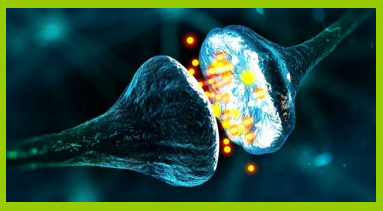
Summation, which includes both spatial and temporal summation, is the process that determines whether or not an action potential will be triggered by the combined effects of excitatory and inhibitory signals, both from multiple simultaneous inputs (spatial summation), and from repeated inputs (temporal summation). Depending on the sum total of many individual inputs, summation may or may not reach the threshold voltage to trigger an action potential





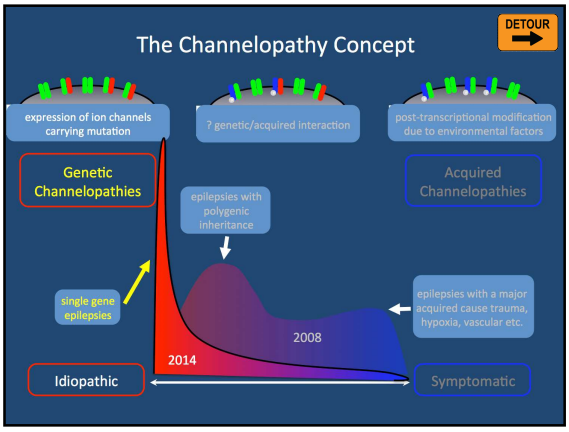


5. Synaptic transmission

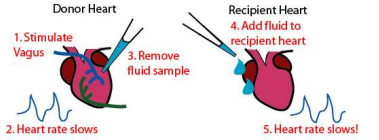


'In view of the probable importance of the … nexus between neuron and neuron it is convenient to have a name for it. The term introduced has been synapse.'

Charles Sherrington, 1906

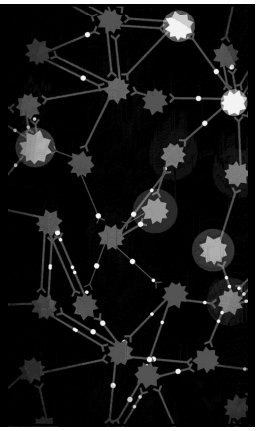


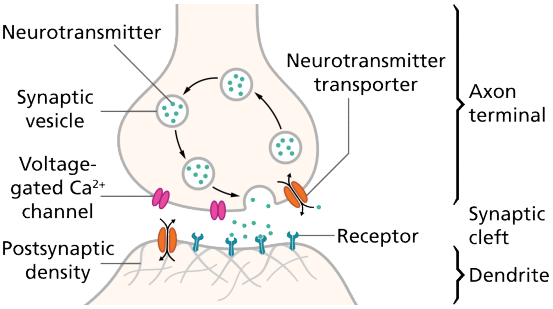
1921

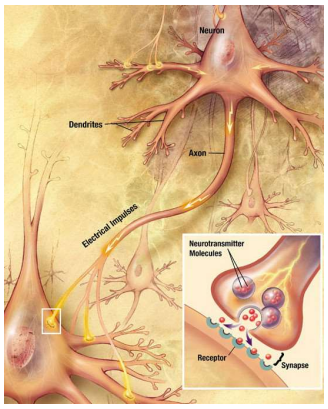


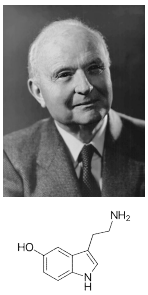
4. The nervous impulse

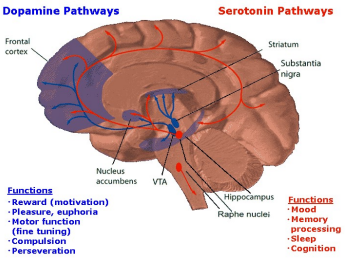
TAKE HOME MESSAGE:
– NEURONS PRODUCE ELECTRICAL SIGNALS THAT CARRY INFORMATION –

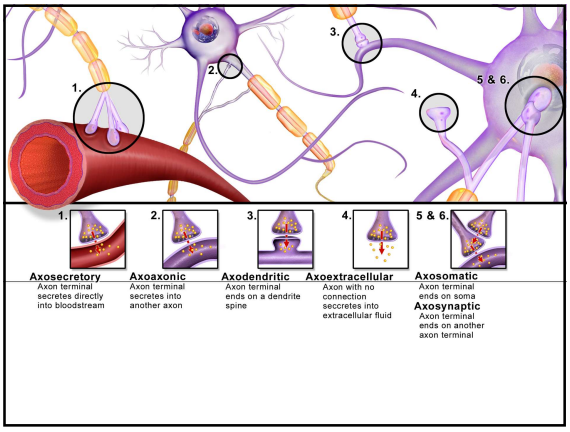


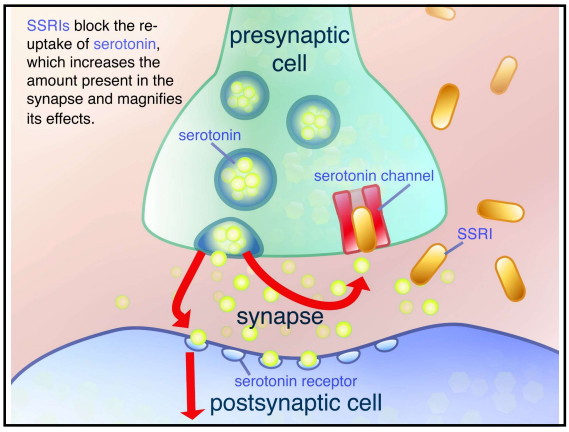






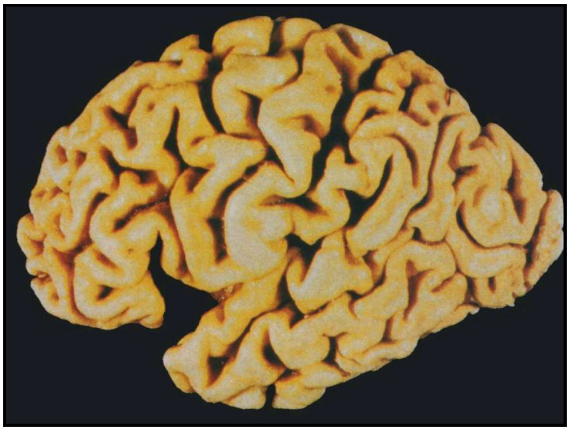


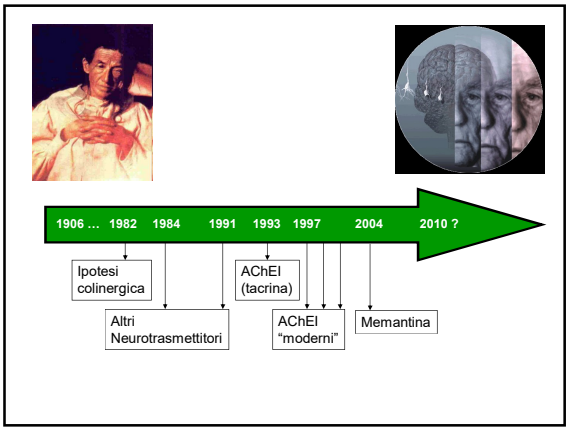




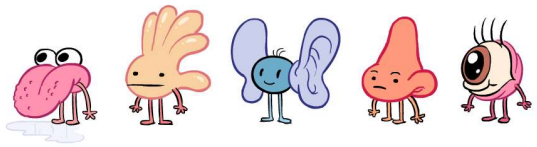
Major neurotransmitters:

- **Amino acids:** glutamate, aspartate, D-serine, γ-aminobutyric acid (GABA), glycine
- **Gasotransmitters:** nitric oxide (NO), carbon monoxide (CO), hydrogen sulfide (H_2S)
- **Monoamines:** dopamine (DA), norepinephrine (noradrenaline; NE, NA), epinephrine (adrenaline), histamine, serotonin (SER, 5-HT)
- **Trace amines**: phenethylamine, *N*-methylphenethylamine, tyramine, 3-iodothyronamine, octopamine, tryptamine, etc.
- **Peptides:** somatostatin, substance P, cocaine and amphetamine regulated transcript, opioid peptides
- **Purines:** adenosine triphosphate (ATP), adenosine
- Others: acetylcholine (ACh), anandamide, etc.



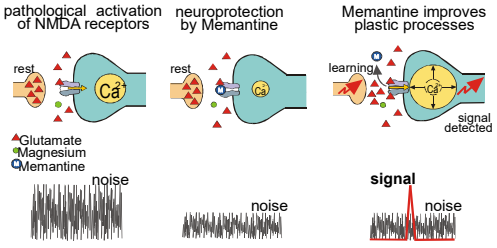


6. Sensory perception



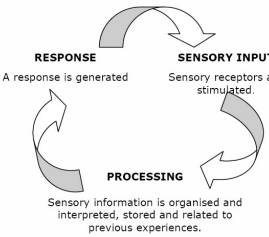
'All our knowledge begins with the senses, proceeds then to the understanding, and ends with reason.'
Immanuel Kant, 1787

Neurodegenerative Dementia + Memantine



Danysz and Parsons, 1999

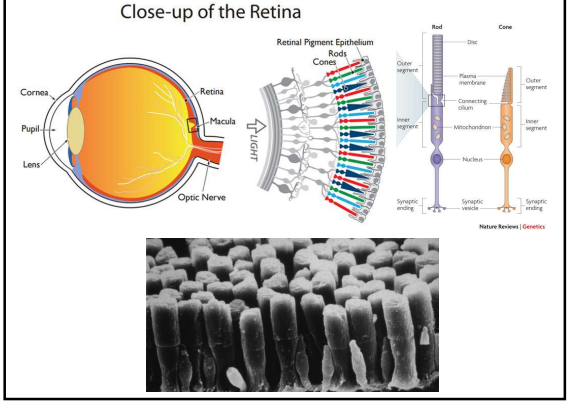
The senses are the windows through which information about the outside world enters the brain. **Each sense organ is specialized to detect data in the form of physical energy, which is then converted into electrical impulses that are sent to the brain, where they are processed and interpreted to generate a coherent experience of the world.**
Costandi Moheb. *50 Human Brain Ideas You Really Need to Know*

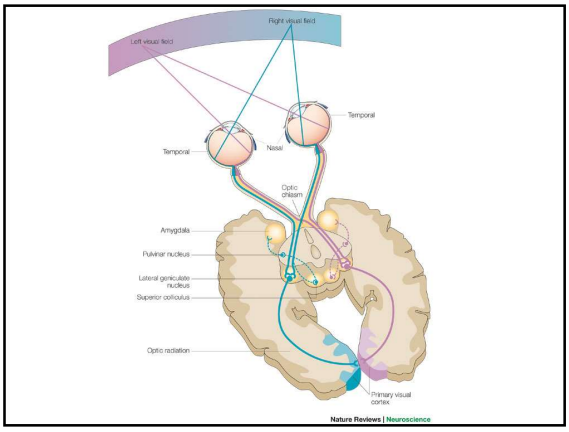


5. Synaptic transmission

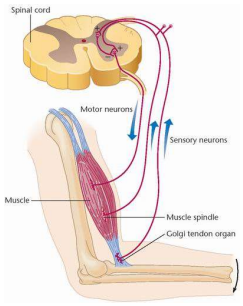
TAKE HOME MESSAGE:
– NEURONS COMMUNICATE WITH EACH OTHER THROUGH CHEMICAL SIGNALS –

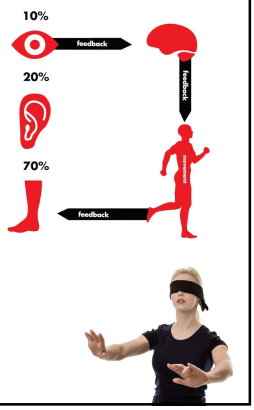
Close-up of the Retina

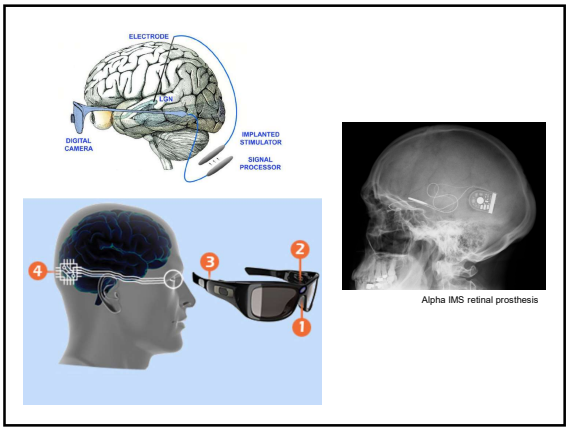




Proprioception: The 6th Sense

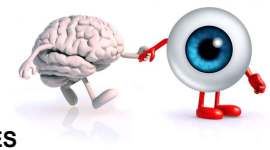




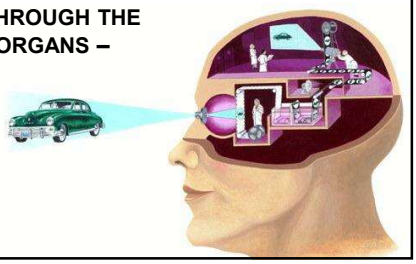


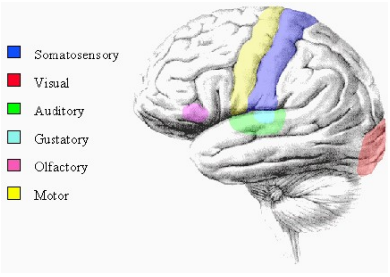
Alpha IMS retinal prosthesis

6. Sensory perception



TAKE HOME MESSAGE:
– THE BRAIN RECEIVES 'INPUTS' THROUGH THE SENSE ORGANS –

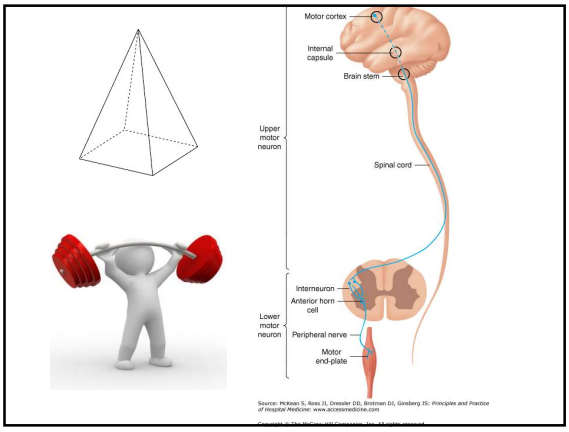


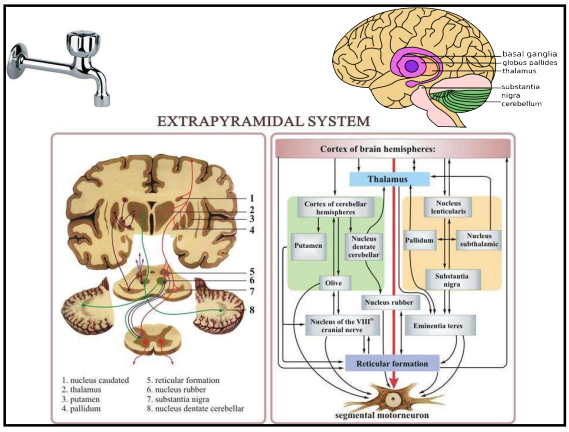


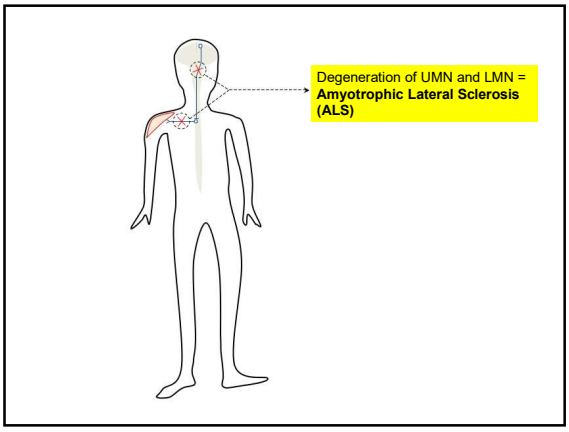
SYNESTHESIA
0123456789

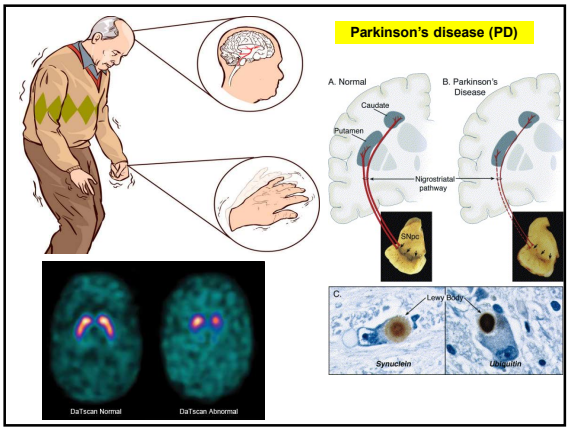
7. Movement

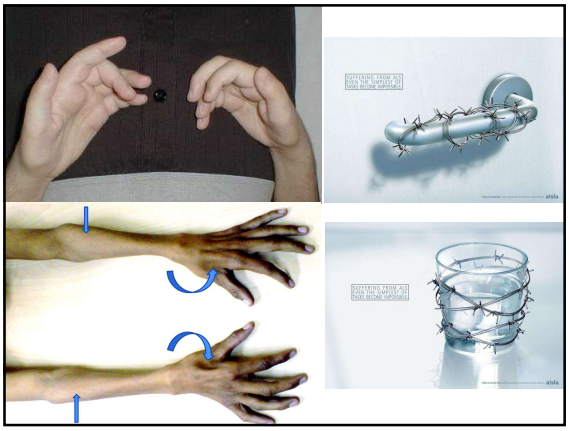
'We have a brain for one reason and one reason only, to produce adaptable and complex movements.'
Daniel Wolpert, 2011

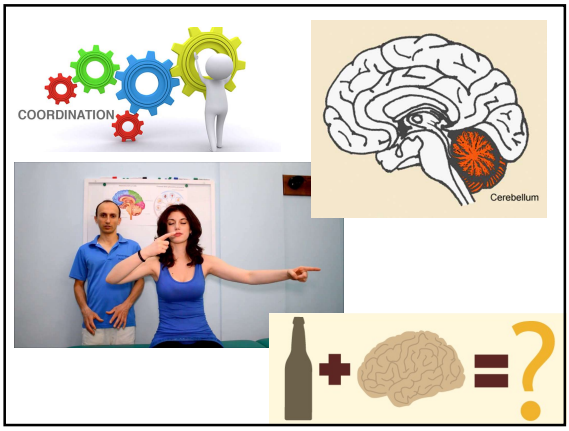

Motor cortex
Internal capsule
Brain stem
Upper motor neuron
Spinal cord
Interneuron
Anterior horn cell
Lower motor neuron
Peripheral nerve
Motor end-plate


basal ganglia
globus pallidus
thalamus
substantia nigra
cerebellum
EXTRAPYRAMIDAL SYSTEM
Cortex of brain hemispheres:
Thalamus
Cortex of cerebellar hemispheres
Nucleus lenticularis
Putamen
Nucleus dentate cerebellar
Pallidum
Nucleus subthalamic
Olive
Substantia nigra
Nucleus rubber
Nucleus of the VIII cranial nerve
Eminentia teres
Reticular formation
segmental motorneuron
1. nucleus caudated
2. thalamus
3. putamen
4. pallidum
5. reticular formation
6. nucleus rubber
7. substantia nigra
8. nucleus dentate cerebellar


Degeneration of UMN and LMN = **Amyotrophic Lateral Sclerosis (ALS)**


Parkinson's disease (PD)
A. Normal
B. Parkinson's Disease
Caudate
Putamen
Nigrostriatal pathway
SNpc
C.
Lewy Body
Synuclein
Ubiquitin
DaTscan Normal
DaTscan Abnormal

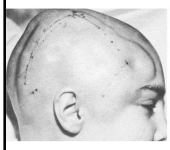


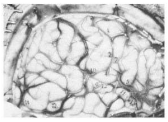

COORDINATION
Cerebellum

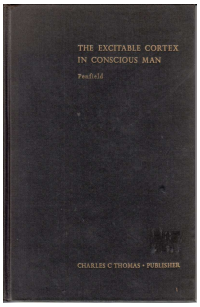
7. Movement

TAKE HOME MESSAGE:
– MOVEMENTS ARE THE MAIN OUTPUT OF THE BRAIN –

Electrical stimulation





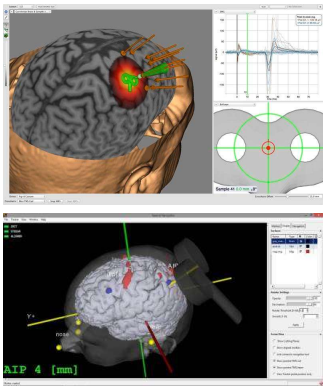


Pioneered by Penfield (1940s) while treating epilepsy patients

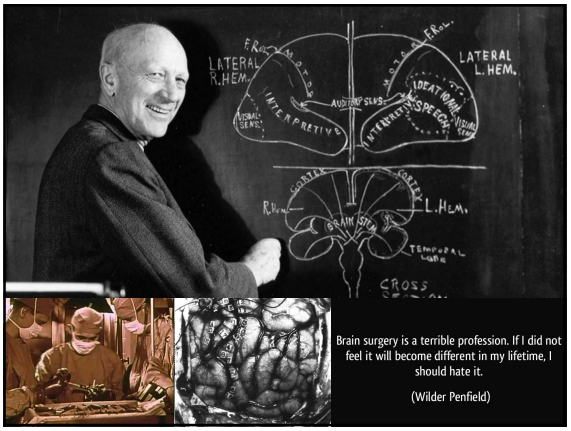
8. Topographic mapping

The brain is the organ of destiny. It holds within its humming mechanism secrets that will determine the future of the human race.

— *Wilder Penfield* —



DETOUR

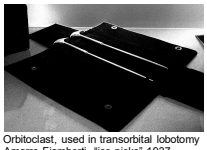


Brain surgery is a terrible profession. If I did not feel it will become different in my lifetime, I should hate it.

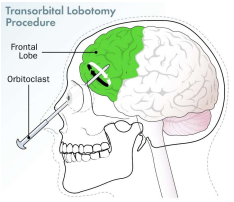
(Wilder Penfield)

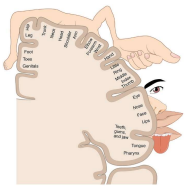
DETOUR

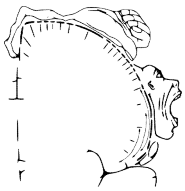
António Caetano de Abreu Freire Egas Moniz ,
Nobel prize 1949

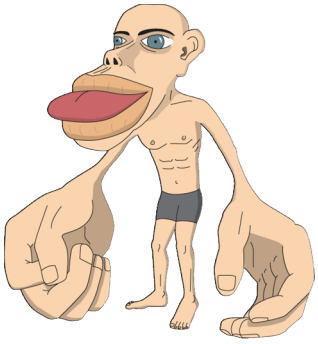


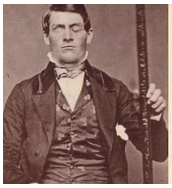
Orbitoclast, used in transorbital lobotomy
Amarro Fiamberti, "ice picks" 1937

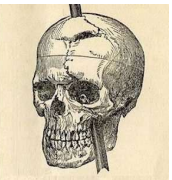


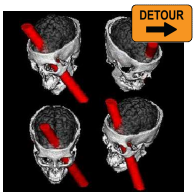










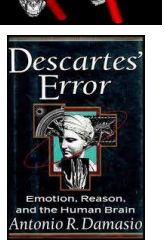


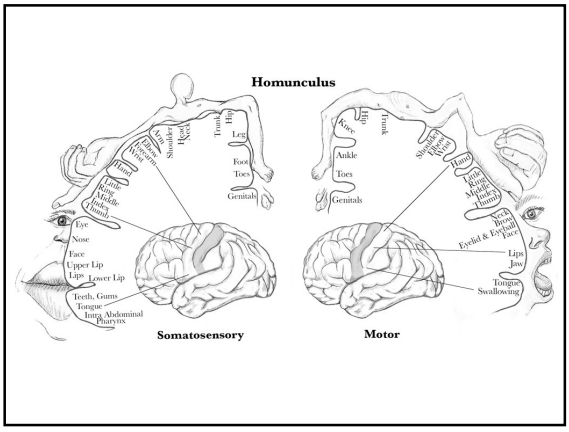
Phineas Gage 1848

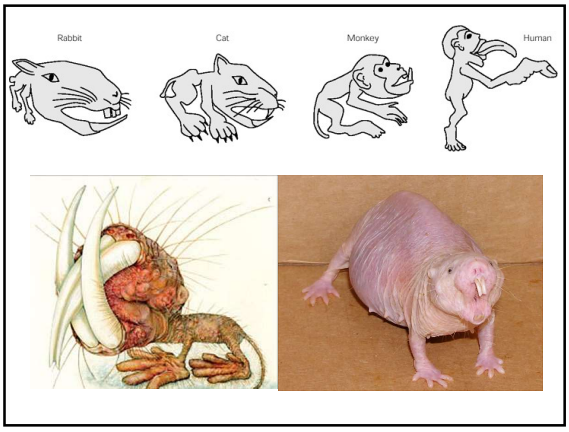
American Phrenological Journal 1851

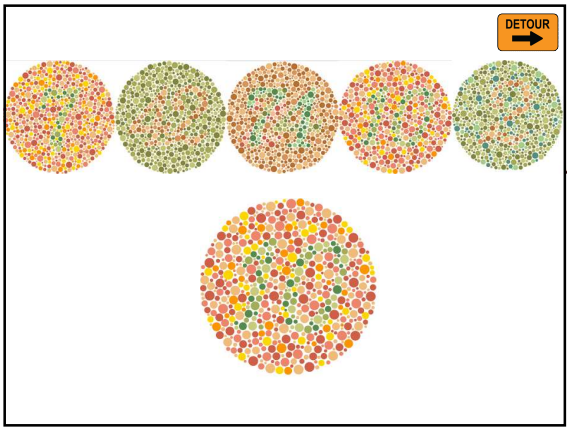
We are well acquainted with several of the leading men in the village where the above occurrence took place, and have been assured by them that the statement relative to the wound and recovery is correct. But that there was no difference in his mental manifestations after the recovery, is, however, not true.

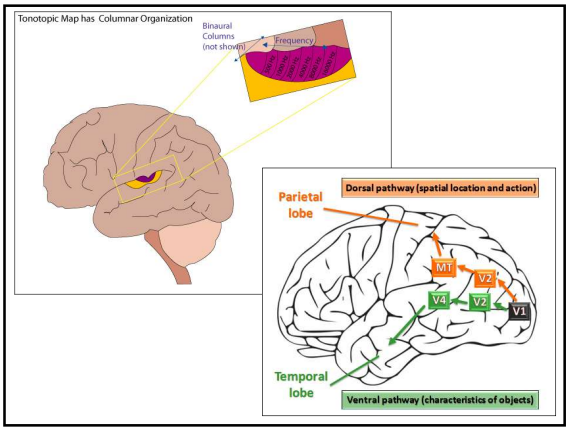
We have been informed by the best authority that after the man recovered, and while recovering, he was gross, profane, coarse, and vulgar, to such a degree that the society was intolerable to decent people. Before the injury he was quiet and respectful. If we remember correctly, the iron passed through the regions of the organs of Benevolence and Veneration, which left these organs without influence in his character, hence his profanity, and want of respect and kindness; giving the animal propensities absolute control in the character. The

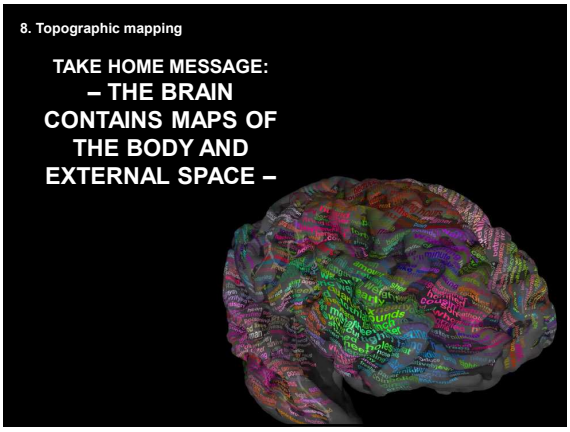





Rabbit
Cat
Monkey
Human


DETOUR

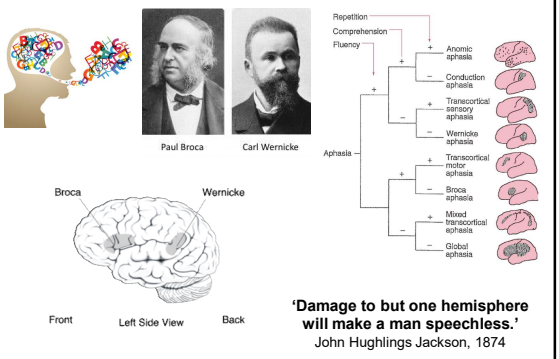

Tonotopic Map has Columnar Organization
Binaural Columns (not shown)
Frequency
Parietal lobe
Dorsal pathway (spatial location and action)
MT
V3
V4
V2
V1
Temporal lobe
Ventral pathway (characteristics of objects)


8. Topographic mapping
TAKE HOME MESSAGE:
– THE BRAIN CONTAINS MAPS OF THE BODY AND EXTERNAL SPACE –

DETOUR

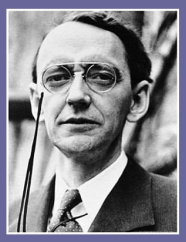
9. Specialized brain regions

Franz Joseph Gall (1758 – 1828)



'Damage to but one hemisphere will make a man speechless.'
John Hughlings Jackson, 1874

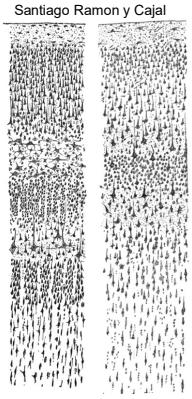
Biological Basis of Memory



Karl Lashley searched for a localized memory trace or *engram*

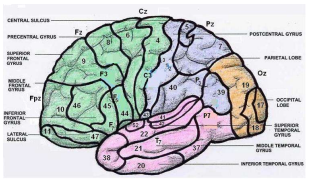
Found that maze-learning in rats was distributed throughout the brain

Santiago Ramon y Cajal



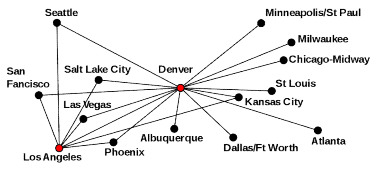
Visual cortex Motor cortex

'The great number of specially prepared structural areas suggests a special separation of individual functions.'
Korbinian Brodmann, 1909



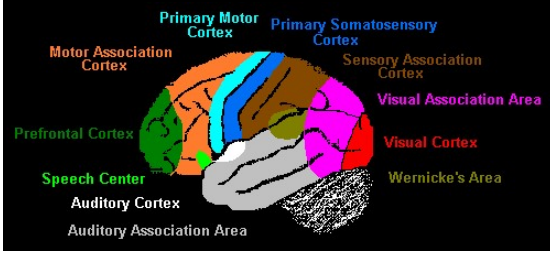
Functional modularity and distributive processing are not mutually exclusive, however. Indeed, the current view of how the brain works is a **combination of the two ideas**.
Neuroscientists now think that the brain operates as what they call a '**massively parallel distributed processor**', with multiple networks working together to generate thoughts and behaviour.

In other words, the brain does contain discrete areas specialized to perform specific functions, but individual specialized brain areas do not act on their own. Instead, each one can be thought of as **a node within a network** that is distributed throughout the brain or within particular regions.

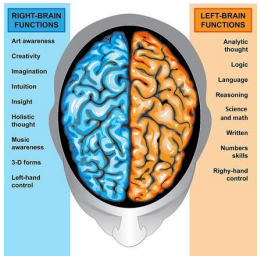


9. Specialized brain regions

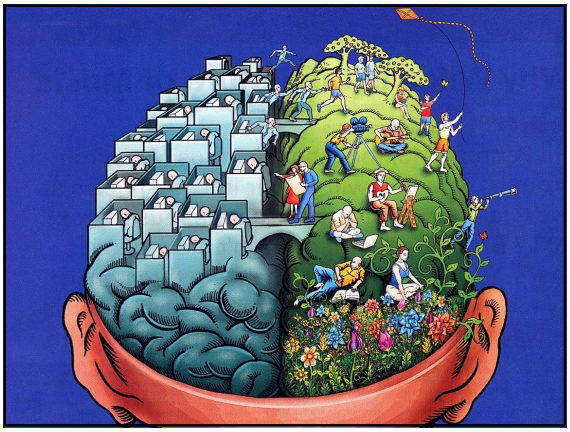
TAKE HOME MESSAGE:
– THE CORTEX CONTAINS DISTINCT AREAS FOR SPECIFIC FUNCTIONS –



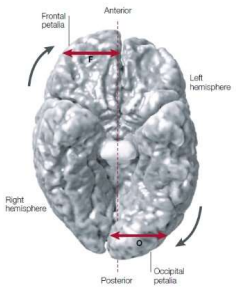
'There are two brains in the head … The one lying on the right side is the one that perceives; with the left one, we understand.'
Diocles, 4th century BC



10. Brain asimmetry



Morphological cerebral asymmetries of modern man, and non-human primates. Ann NY Acad. Sci. 1976

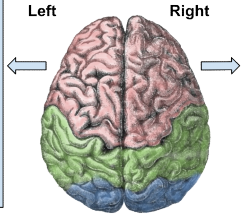


In evolutionary terms, brain asymmetries may be advantageous because they enable different tasks to be performed by each hemisphere in parallel, or simultaneously.

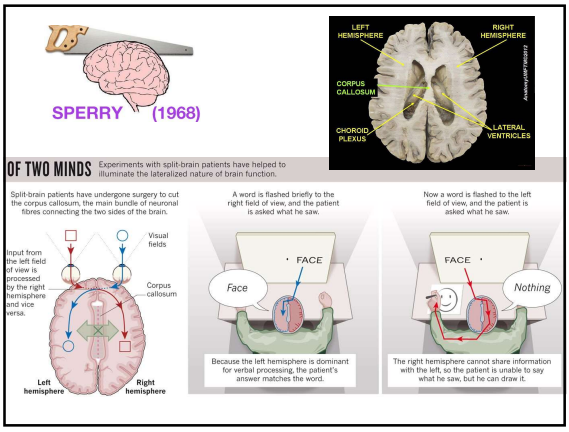
Yakovlevian brain torque

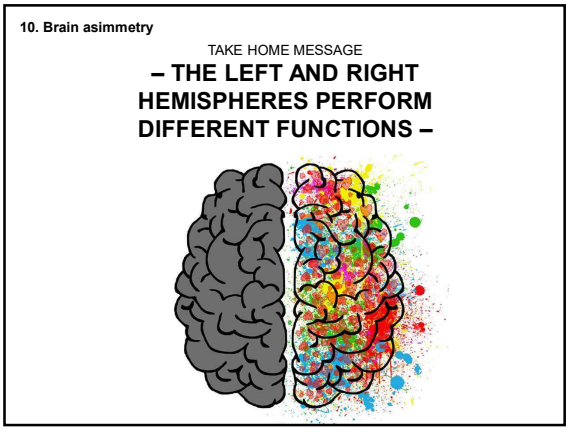
Brain Lateralization

Left	Right
• Analytical thought • Detail Oriented Perception • Ordered Sequencing • Rational Thought • Verbal • Cautious • Planning • Math/Science • Logic • Right Field Vision • Right Side Motor Skills	• Intuitive Thought, • Holistic perception • Random Sequencing • Emotional Thought • Non-verbal • Adventurous • Impulse • Creative Writing/Art • Imagination • Left Field Vision • Left Side Motor Skills



Normal view
Neglect and Anosognosia
Parietal lobe lesions
Cortical areas damaged
Symptoms:
• neglect
• extinction
• denial
• spatial orientation deficit
Unilateral Neglect and Awareness Deficits After Right Hemisphere Brain Damage


SPERRY (1968)
LEFT HEMISPHERE
RIGHT HEMISPHERE
CORPUS CALLOSUM
CHOROID PLEXUS
LATERAL VENTRICLES
OF TWO MINDS
Experiments with split-brain patients have helped to illuminate the lateralized nature of brain function.
Split-brain patients have undergone surgery to cut the corpus callosum, the main bundle of neuronal fibres connecting the two sides of the brain.
Input from the left field of view is processed by the right hemisphere and vice versa.
Visual fields
Corpus callosum
Left hemisphere
Right hemisphere
A word is flashed briefly to the right field of view, and the patient is asked what he saw.
FACE
Face
Because the left hemisphere is dominant for verbal processing, the patient's answer matches the word.
Now a word is flashed to the left field of view, and the patient is asked what he saw.
FACE
Nothing
The right hemisphere cannot share information with the left, so the patient is unable to say what he saw, but he can draw it.


10. Brain asimmetry
TAKE HOME MESSAGE
– THE LEFT AND RIGHT HEMISPHERES PERFORM DIFFERENT FUNCTIONS –