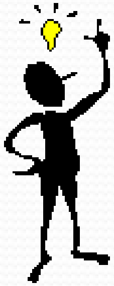
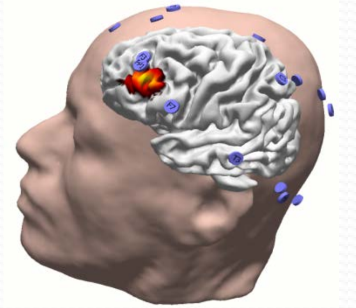
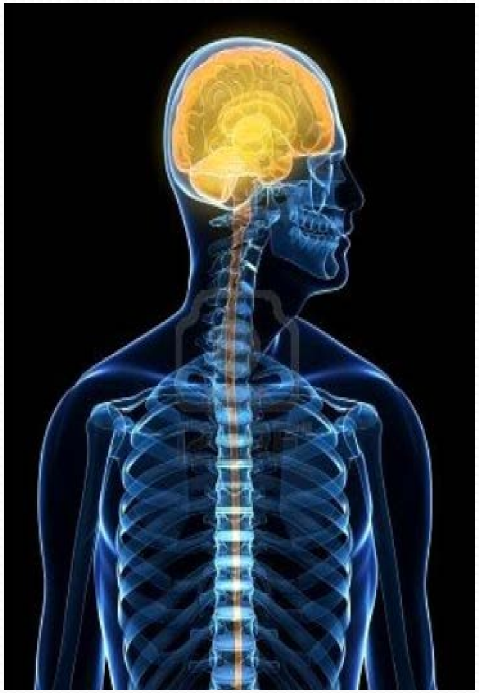


How the Brain Works





- The brain is the master organ of the body. It is a soft mass of supportive tissues and nerves connected to the spinal cord that interprets the information it gets in order to monitor and regulate your body. The brain takes in all information relating to the body's internal and external environments, and it produces the appropriate responses.

- The brain controls your ability to think, talk, feel, see, hear, remember things, within other functions.

- Some of the nerves in the brain go right to the eyes, ears and other parts of the head. Other nerves connect the brain with other parts of the body through the spinal cord to control personality, senses and body functions from breathing to walking.

The Brain...

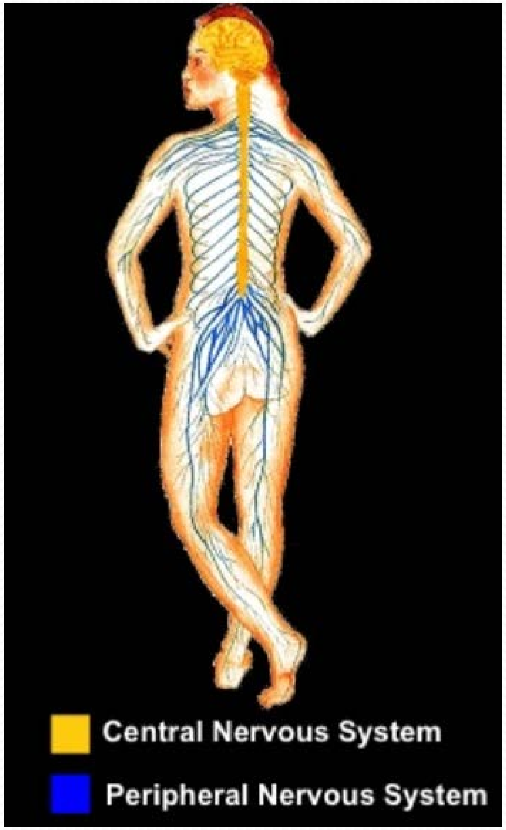
- It is the most important organ in your body.
- The adult brain weights an average of 1.4 Kg (3.08 lbs.) or about <u>2% of the total body weight.</u>
- It is a highly organized **ORGAN**.
- Contains approximately <u>100 billion neurons</u>. These neurons make up the most complex and highly organized structure on earth.
- The brain of an adult human <u>uses around 20% of its body energy (oxygen consumption).</u>

Note: The brain can stay alive for 4 to 6 minutes without oxygen.

Nervous System: Anatomical Subdivisions

- Central nervous system (CNS)
  - Brain & Spinal cord enclosed in bony coverings

- Peripheral nervous system (PNS)-connects everything to the brain and spinal cord.
  - Sensory neurons
  - Motor neurons
  - Interneurons



- The Nervous System is the control center for the entire body.

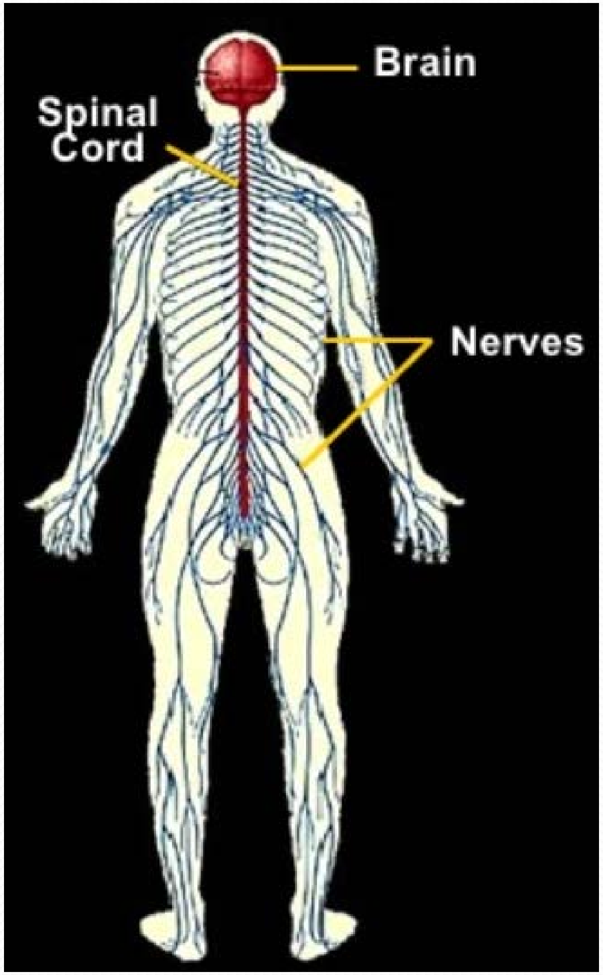
- The brain uses information it receives from your nerves to coordinate all of your actions and reactions.

Note: EEG Scalp Potentials can measure the reactions of your nervous system with a high temporal resolution.

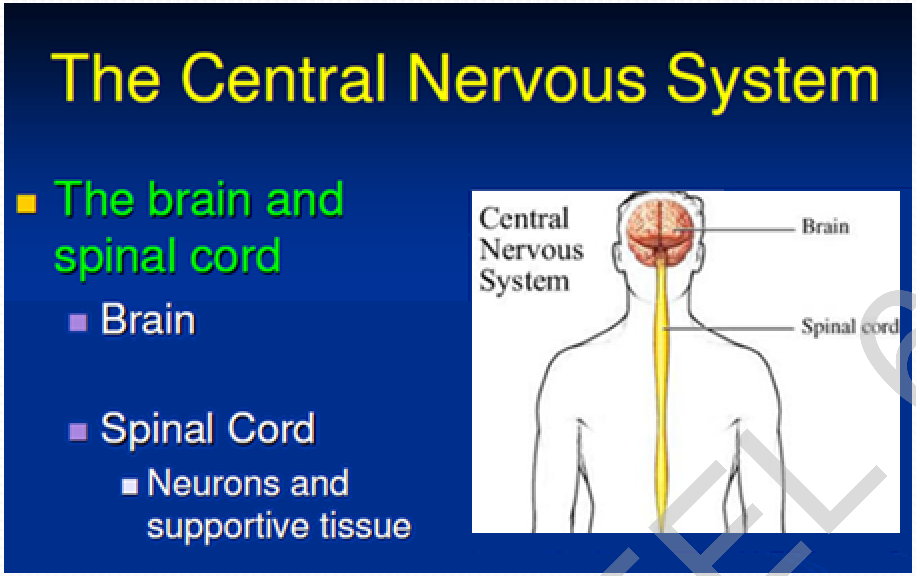
3 Kinds of Neurons (PNS)

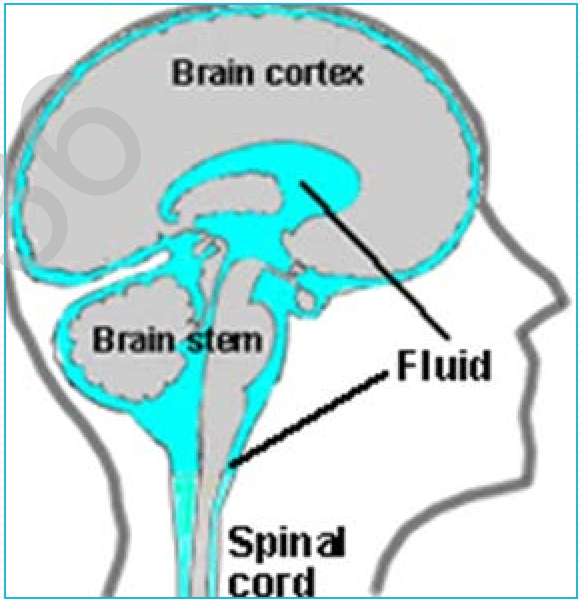
- Sensory neurons—sensory receptors to CNS
- Motor neurons—CNS to muscles and organs
- Interneurons—Connections within CNS

Note: They all connect CNS to the body



Central Nervous System

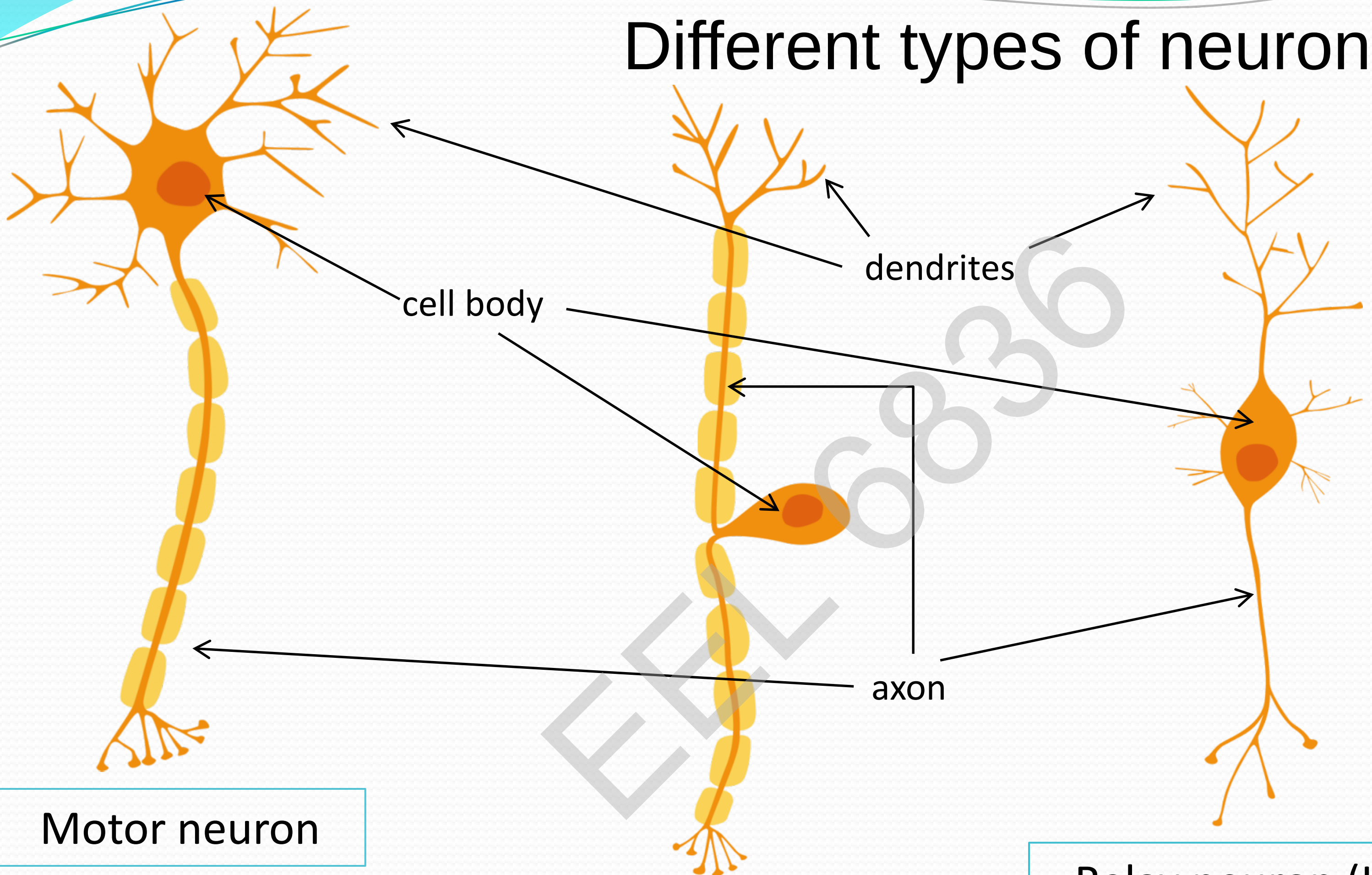




Human Central Nervous System (**CNS**):

- Constituents: Brain + Spinal Cord + Nerves going to muscles and sensory organs.
- Cerebrospinal fluid (CSF): clear liquid surrounding brain & spinal cord and filling brain cavities. (protects the brain from mechanical injury by acting as a shock absorber).
- Nerve cells (neurons): 10^{10} nerve cells with perhaps 10^{14} or more interconnections.

Different types of neurons



Motor neuron

sends signals to your muscles to tell them to move

Sensory neuron

sends signals from your organs

Relay neuron (Interneuron)

connects neurons to other neurons

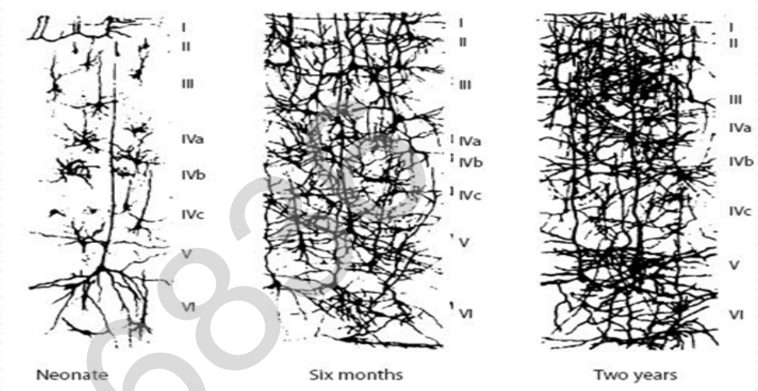
Cell Interconnections

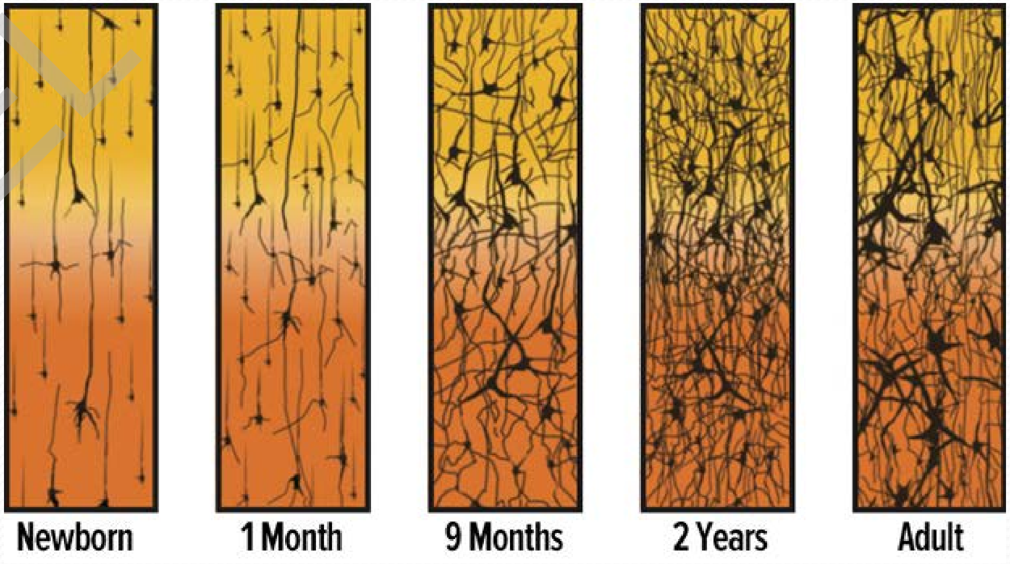
- The brain learns and forms memories by strengthening synapses that are used a lot and weakening those that are used less often.

- As our brains mature, the brain changes and adapts.

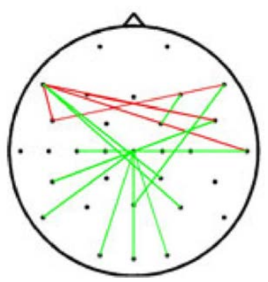
- Between birth and ages 2-3 your brain makes lots of new synapses.

- The more the dendrites and connections are formed with the brain cells connected, the more memory storage data and thinking ability will be possessed.



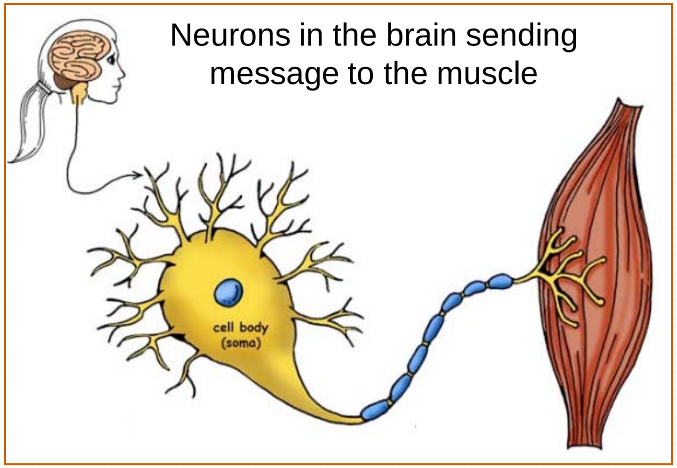


CHARACTERISTICS OF NERVE CELLS / NEURONS



- A neuron is just another name for a nerve cell.
- The human brain contains at least 100 billion neurons.
- Neurons can send messages at up to 200 miles per hour.
- Neurons communicate with each other by using Action Potentials (APs), which is a small pulse of electrical activity.

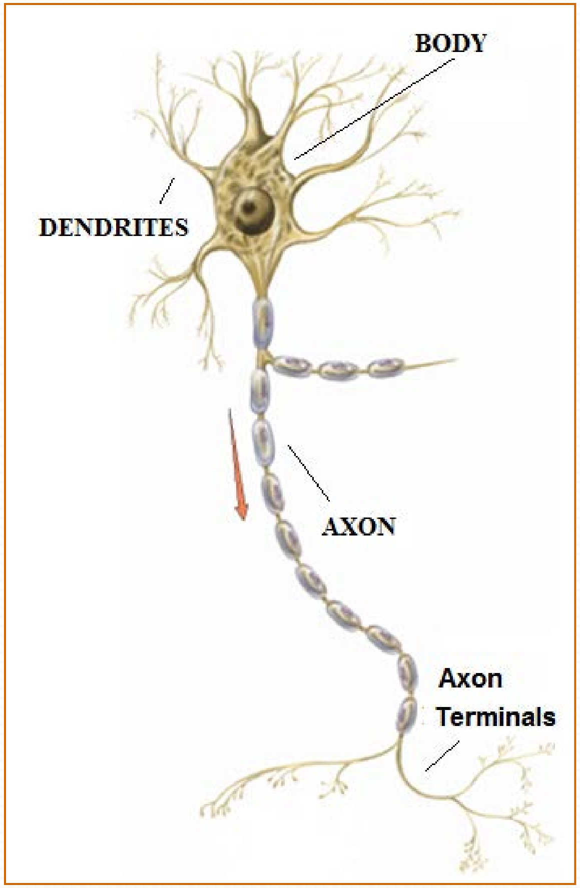
Example: If you pinch yourself, nerve cells send messages to the brain. Those signals are electric, so electricity is needed for neurons to work.



Neurons are cells, so they are microscopic. The largest are about 0.1mm (100 microns) in diameter. Smallest (0.004 mm).

Structure of a Neuron

- Body = membrane containing nucleus, also called soma
- Axon
  - terminates on other nerve cells connecting to other neuron's dendrites
  - transmits output to other dendrites of other neurons (rapid conduction)
- Dendrites
  - receive the signal from other neuron's axons
- Synapse
  - Connection axon

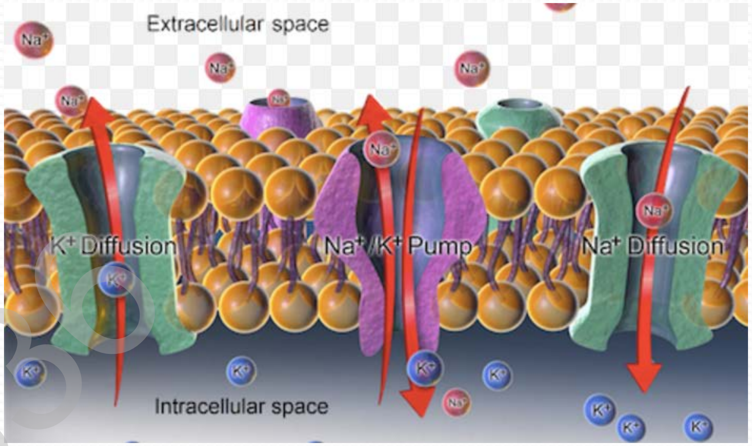


Biochemical components (ions):

Sodium (Na+), Potassium(K+), Chloride(CL-)

Note: In the human brain each nerve is connected to approximately 10,000 other nerves, mostly to dendrite connections.

Brain Potentials



- All potentials result from ions moving across membranes.
- Two forces on ions: Diffusion (from high to low concentration); Electrical (toward opposite charge and away from like charge).
- Each ion that can flow through channels reaches equilibrium between two forces.
- Equilibrium potential for each ion determined by Nernst Equation.
- K+ make - potentials; Na+ make + potentials.

Nernst Equation

Nernst Equilibrium Potential:

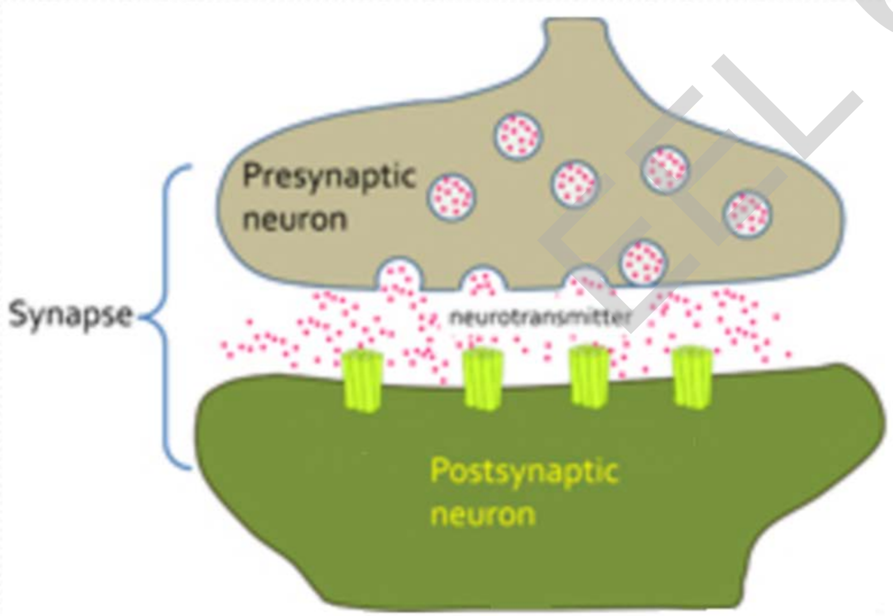
E_{K+} = +58 mV $\log_{10}$ ([K+] outside/[K+] inside).

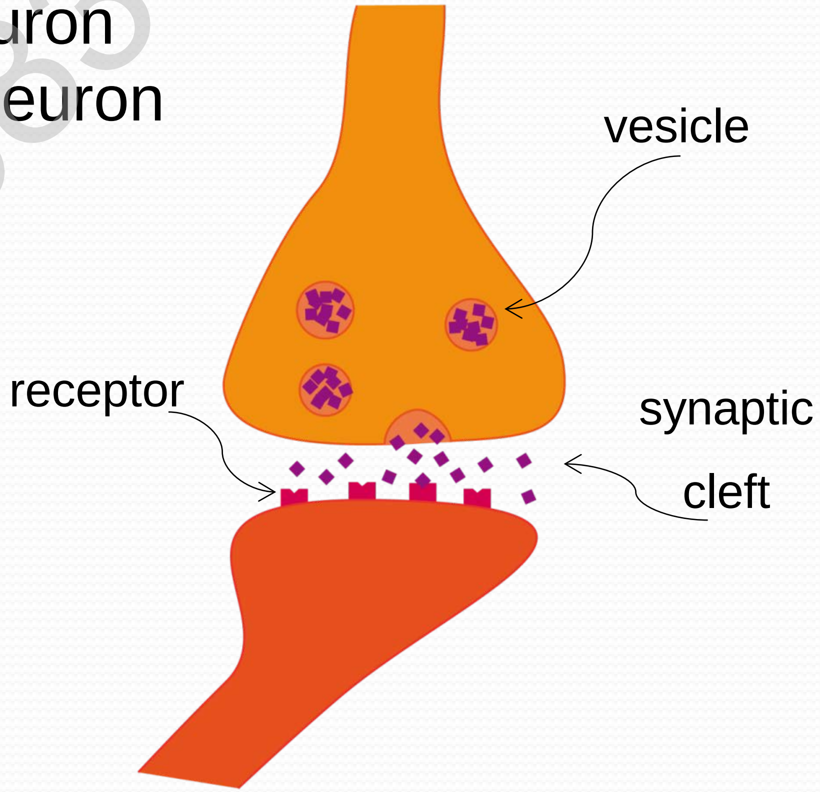
(+58 mV for room temperature, squid axon).

- E_{K+} = 58 mV $\log_{10}$ 1/20 = -75 mV.
- E_{Na+} = 58 mV $\log_{10}$ 10/1 = + 58 mV.
- E_{Cl-} = -58 mV $\log_{10}$ 15 = -68 mV.
- E_{Ca++} = +58 mV $\log_{10}$ 10,000 = +220 mV.

Synapses Between Two Neurons

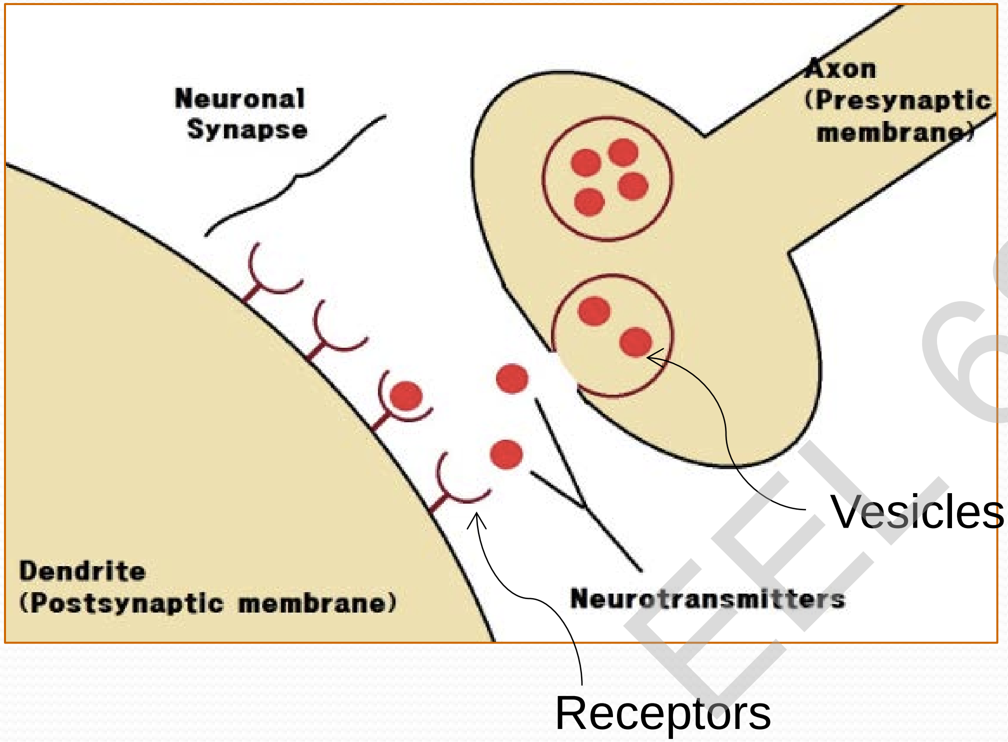
- Signals cross between neurons at the synapse.
- First, neuron in path releases neurotransmitter onto second neuron that responds to it.
  - 1st neuron is presynaptic neuron
  - 2nd neuron is postsynaptic neuron



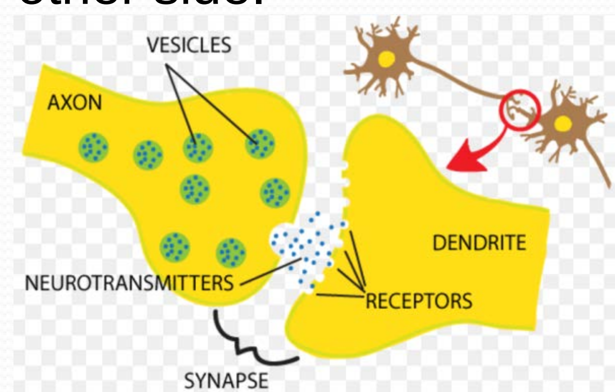


Note: Synapses are the control switches of the nervous system

Chemical Synapse Structure



- Presynaptic neurons have synaptic vesicles with neurotransmitters and postsynaptic have receptors.
- Vesicles release neurotransmitters into the synaptic cleft.
- Neurotransmitters diffuse across the cleft and binds to receptors on the other side.

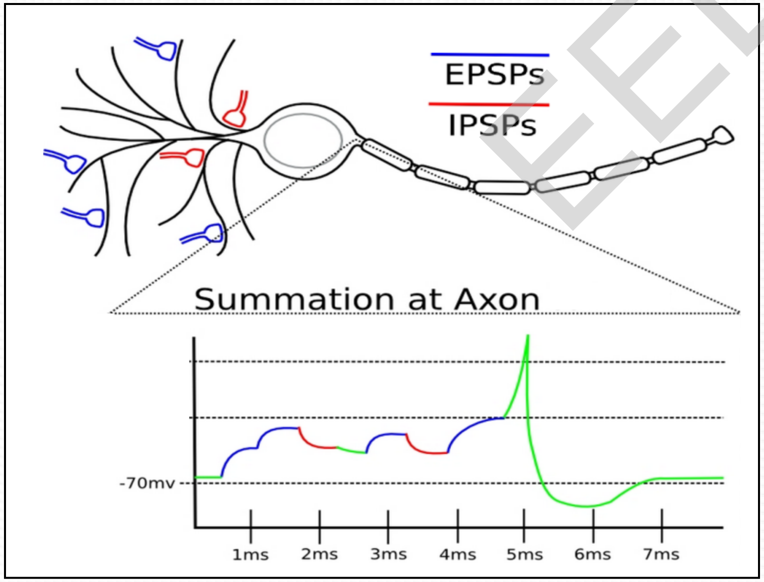


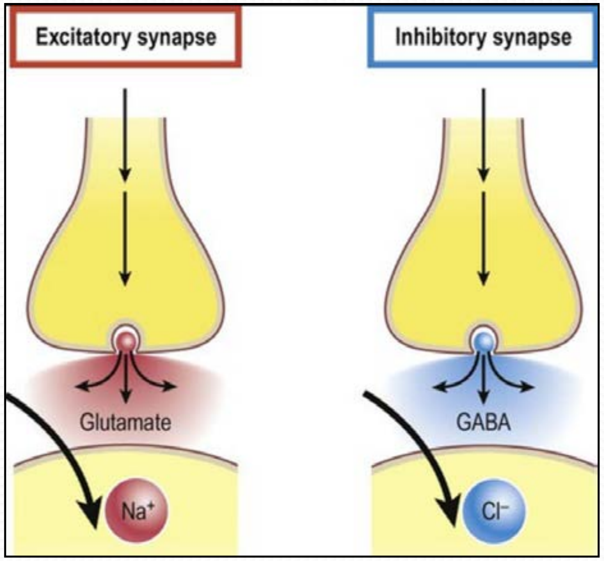
Once enough receptors have neurotransmitters bound to them, the signal is transmitted…

Postsynaptic Potentials

- Excitatory postsynaptic potentials (EPSP)
  - a positive voltage change causing postsynaptic cell to be more likely to fire
    - result from Na+ flowing into the cell

- Inhibitory postsynaptic potentials (IPSP)
  - a negative voltage change causing postsynaptic cell to be less likely to fire (hyperpolarize)
    - result of K+ leaving the cell

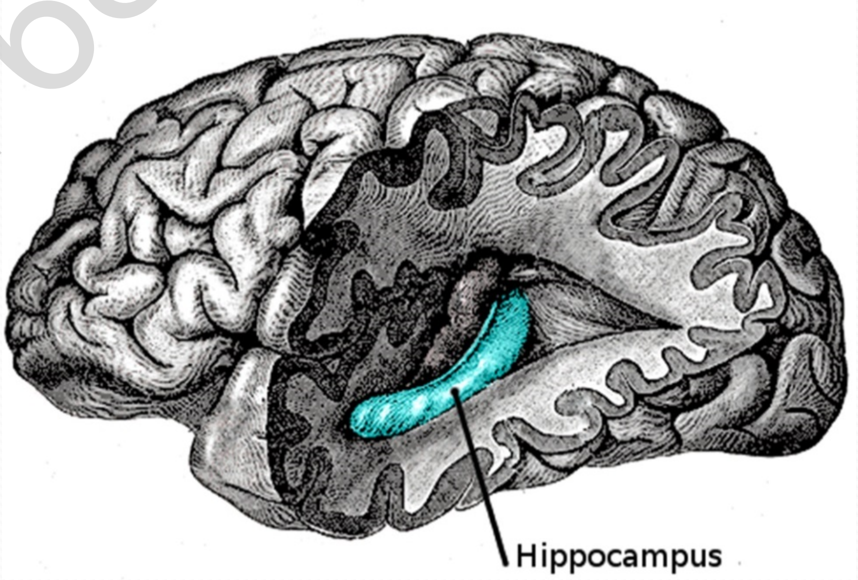




Neuron Reproduction:

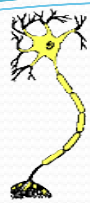
Unlike most other cells, neurons cannot regrow after damage (except neurons from the hippocampus).

***Fortunately, there are about 100 billion neurons in the brain.



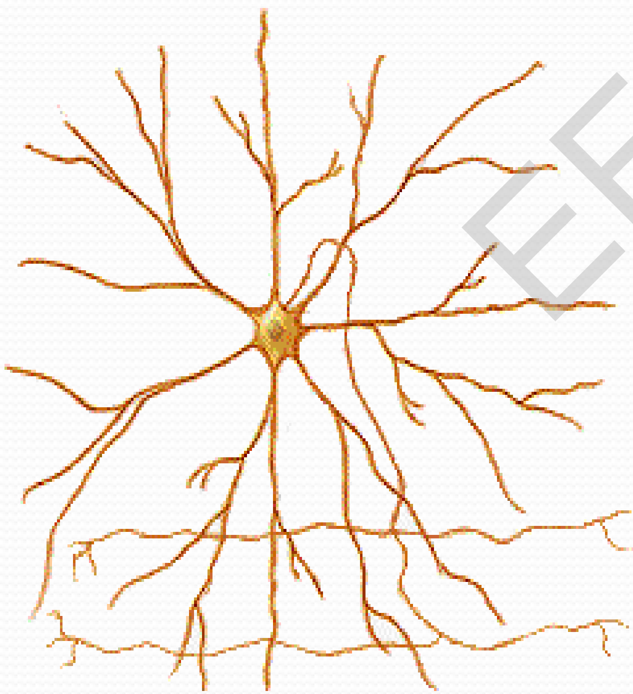
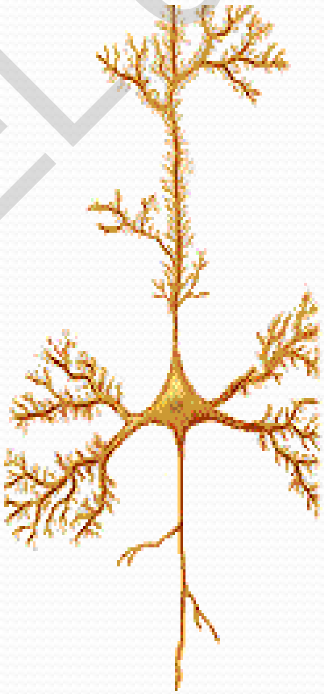
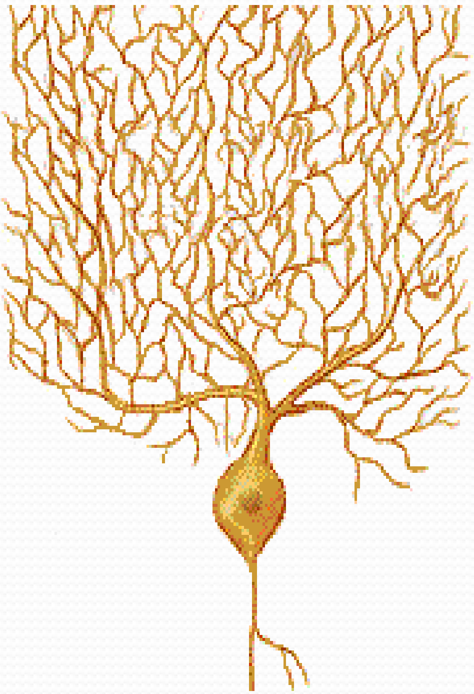
Interesting Fact:
Old person has perhaps ≈ 1/3 of the neurons at the time of birth => continuous loss of neurons

- Most ancient part of the cortex
- LTP was first discovered to occur in
- this region



Brain Cells

- There are <u>different types of neurons</u>. They all carry <u>electro-chemical</u> nerve signals, but <u>differ in structure</u> (the number of processes, or axons, emanating from the cell body) and are found in different parts of the body.
- The brain and spinal cord are made up of many cells, including **neurons and glial cells.**

Brain Cells

1) Neurons

- Neurons typically consist of dendrites that receive information, a cell body, and an axon used to transmit information throughout the nervous system.

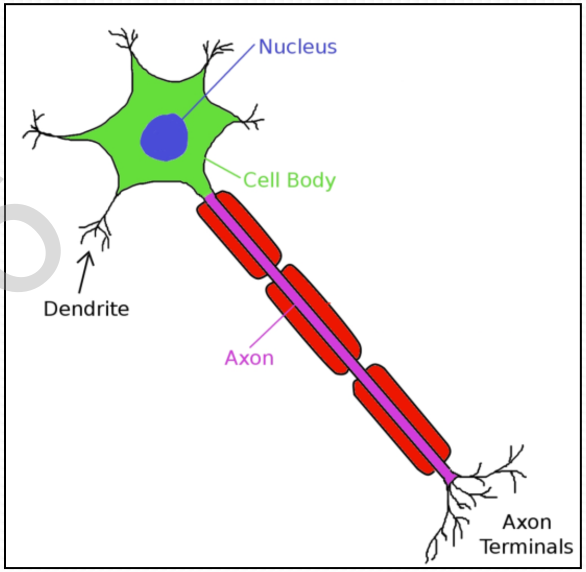
- Neurons send and receive electro-chemical signals to and from the brain and nervous system. There are about 100 billion neurons in the brain.

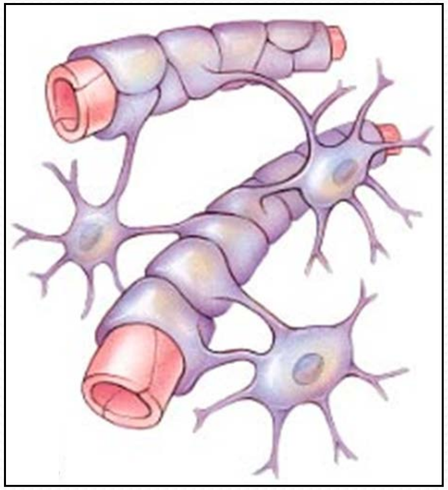
2) Glial cells

- There are many more glial cells than neurons; they provide support functions for the neurons, and are far more numerous than neurons.

- Glial cells have multiple functions, which include repairing the Central Nervous System (CNS), and regulating the biochemical balance of the brain.

Neuron

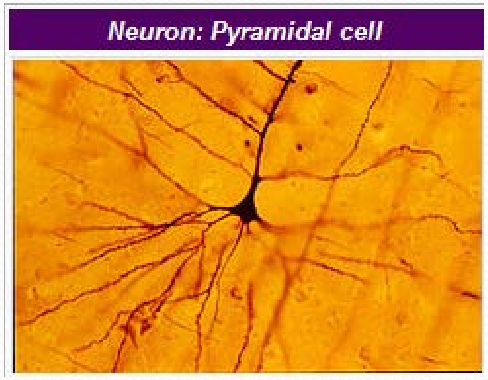




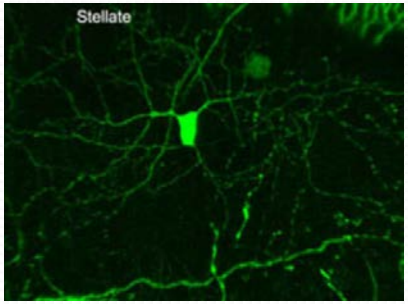
Glial cells

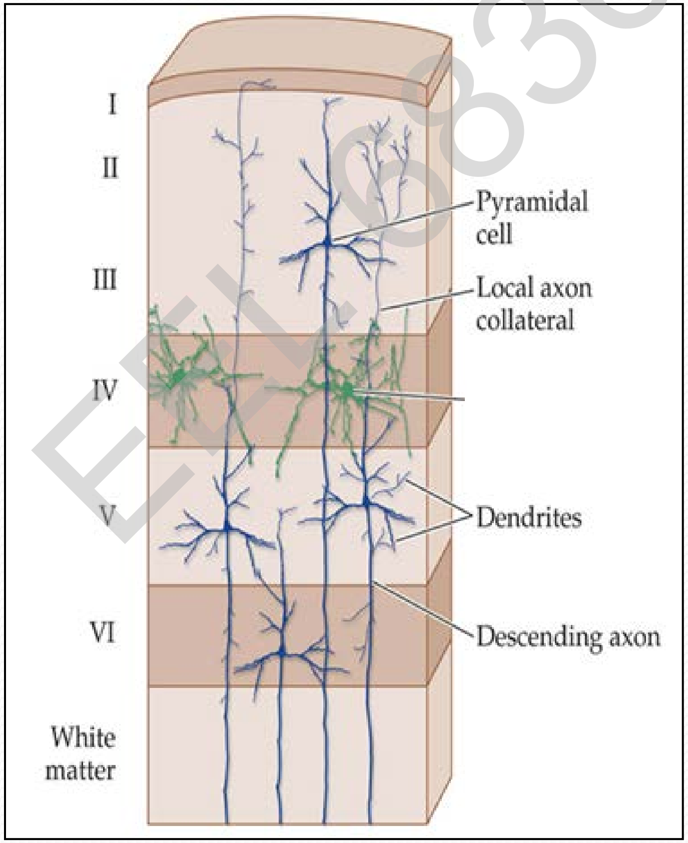
Cells of the cerebral cortex

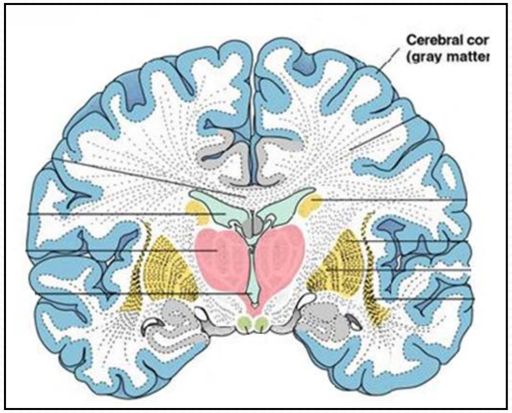
1) Pyramidal cells



2) Stellate cells: multiple dendrites with short axons







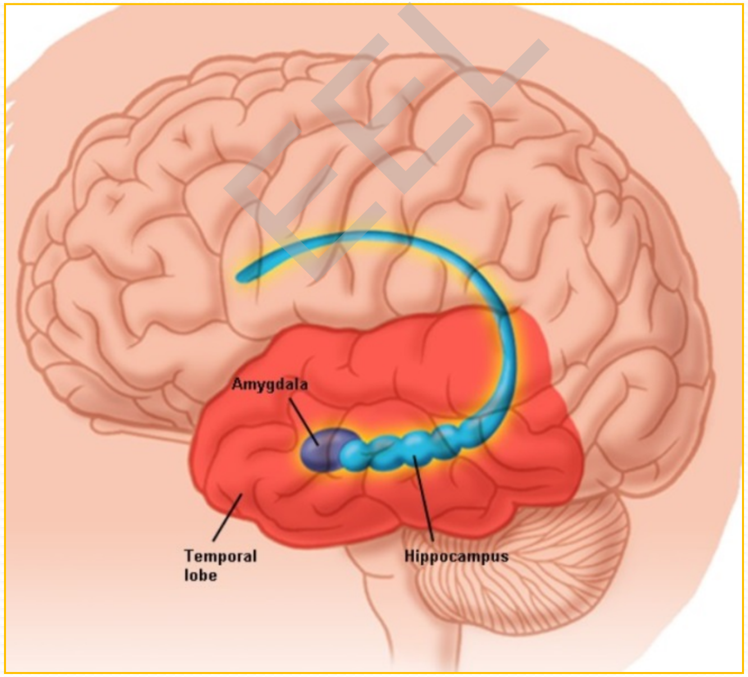
Cerebral cortex:

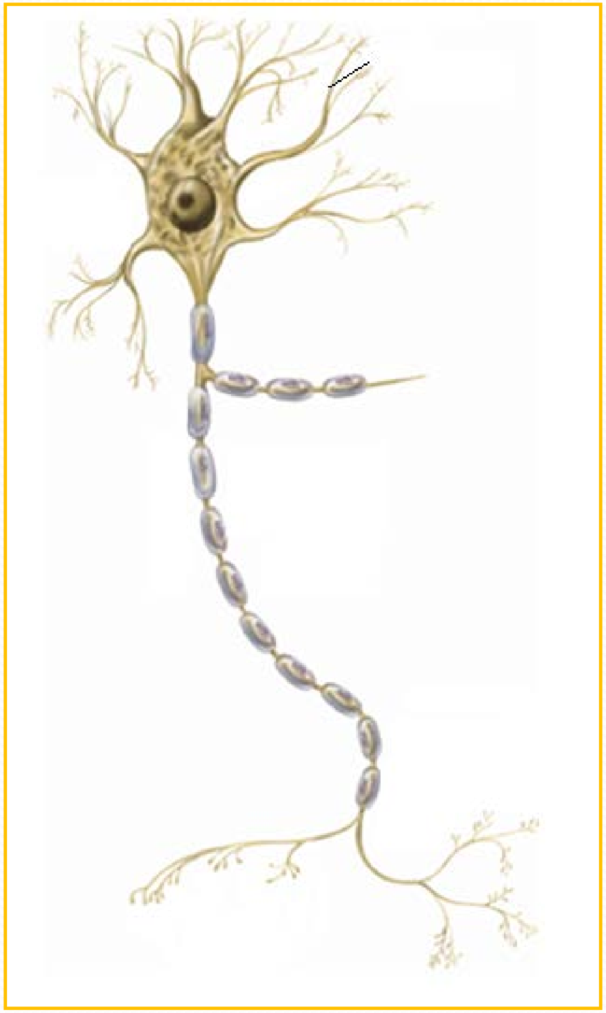
- Thin layer of gray matter
- <u>2-4 mm thick</u>

Pyramidal cells

- Pyramidal cells are neurons found in the cerebral cortex. **These are responsible for the generation of EEG signals**.

- Pyramidal neurons (pyramidal cells) are a type of neuron found in areas of the brain including cerebral cortex, the hippocampus, and in the amygdala.

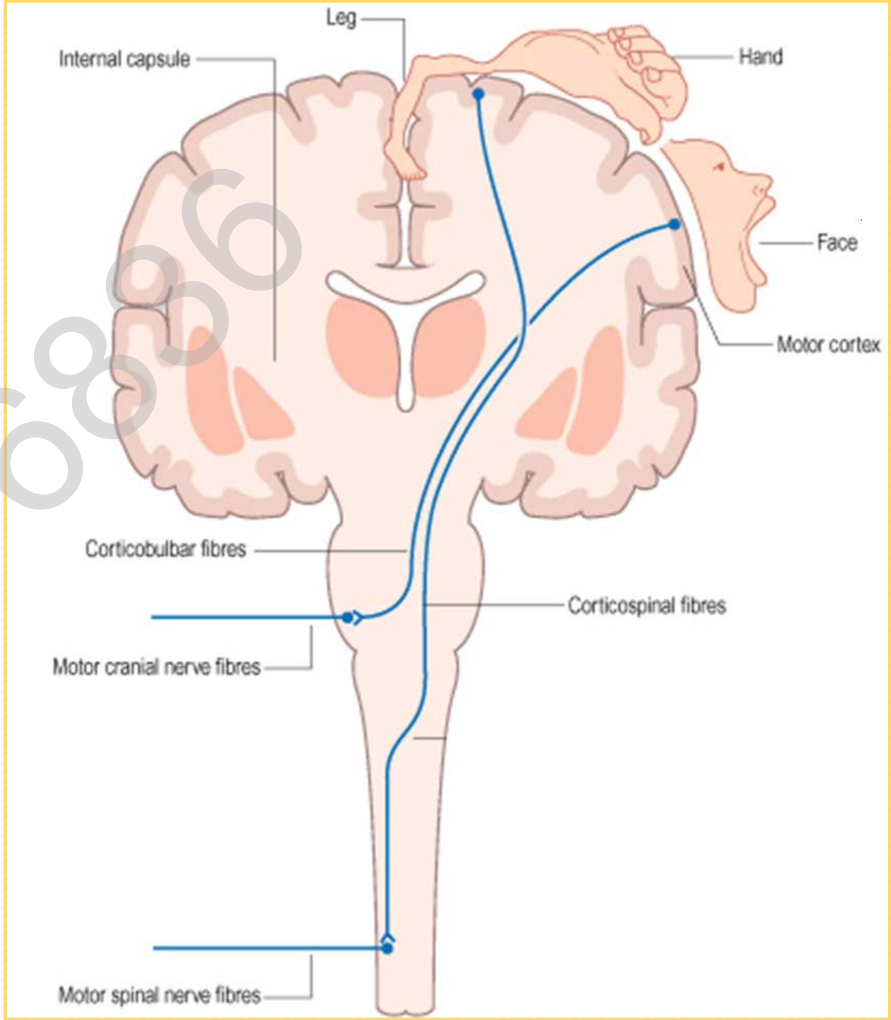




Pyramidal Cells

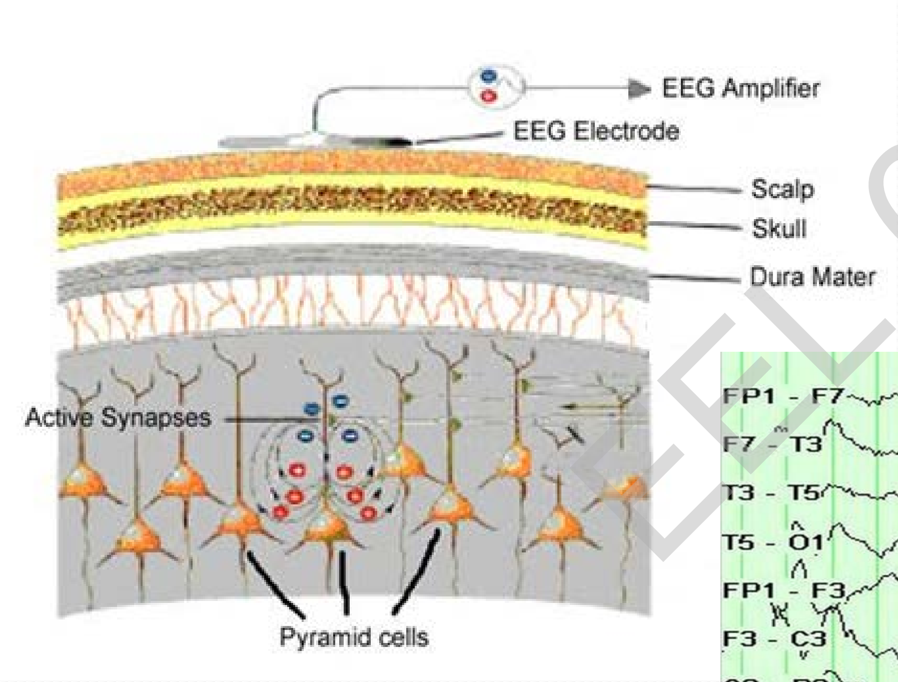
- Pyramidal neurons are the <u>primary excitation units</u> of the mammalian prefrontal cortex and the corticospinal tract.

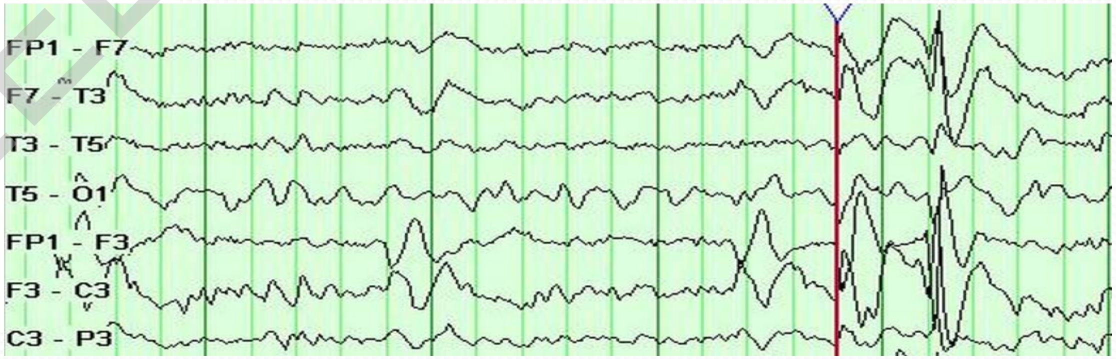
- What makes a pyramidal neuron unique is how the dendrites are arranged and the fact that both the <u>axon and dendrites undergo extensive branching.</u>



Pyramidal Cells

- The voltage volume generated by pyramidal cells is weak: only 20 to 100 microvolts after amplification on the order of ten thousand times.

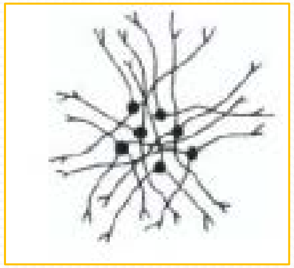




*We need to fire several millions of Neurons to get a spike in the EEG recordings.

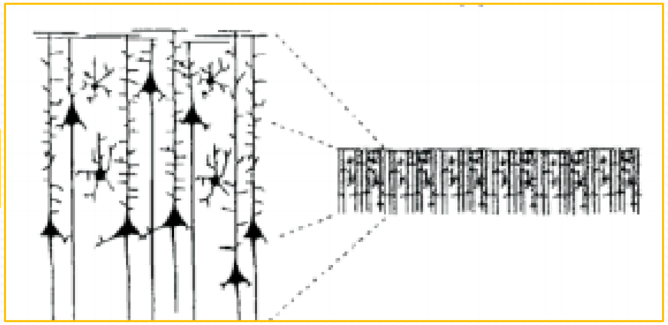
Pyramidal Cells Properties

- A single neural event is too small to be detected on the scalp.
- Action potentials (APs) do not add up – too short.
- EPSPs/IPSPs sum up in time through synchronization, and in space due to cortical architecture (open/closed electrical fields). □
- No EEG generated due to closed fields in glial cells and subcortical structures.



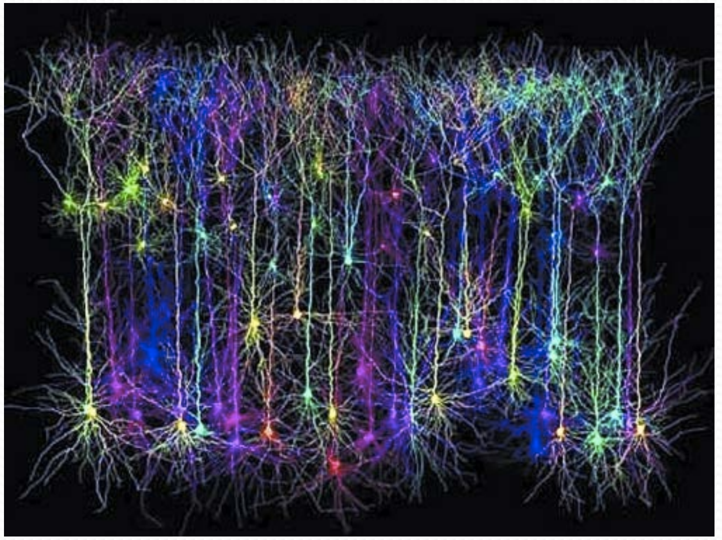
glial cells

Pyramidal cells



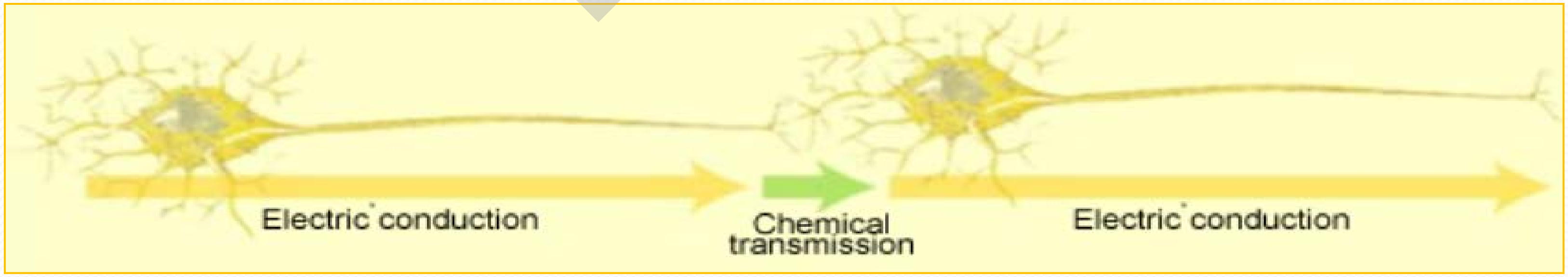
Pyramidal Cells Properties (cont.)

- Long apical dentrite perpendicular to the surface of the cortex.
- Axons run perpendicular to the cortical surface and travel to sites outside the cerebral cortex.
- Aligned in parallel.
- Synchronized in activity.
- They received synchronous input from subcortical and cortical sources.

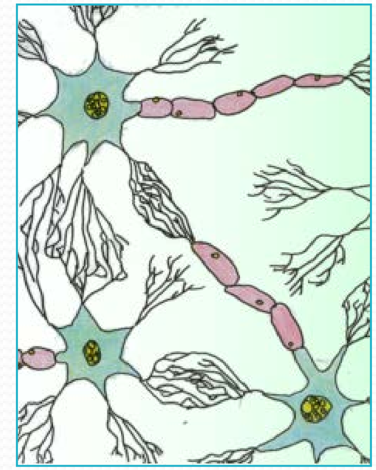


MODEL OF COMMUNICATIONS AMONG NEURONS

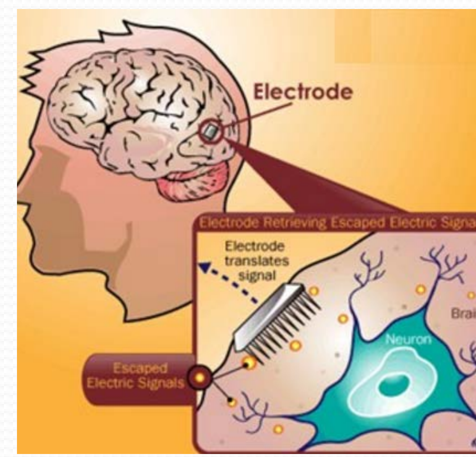
- Nerve impulses have a domino effect.
- Each neuron receives an impulse and must pass it on to the next neuron and make sure the correct impulse continues on its path.
- Through a chain of chemical events, the dendrites (part of a neuron) pick up an impulse that's shuttled through the axon and transmitted to the next neuron.
- The entire impulse passes through a neuron in about seven milliseconds (7 ms) — faster than a lightning strike.



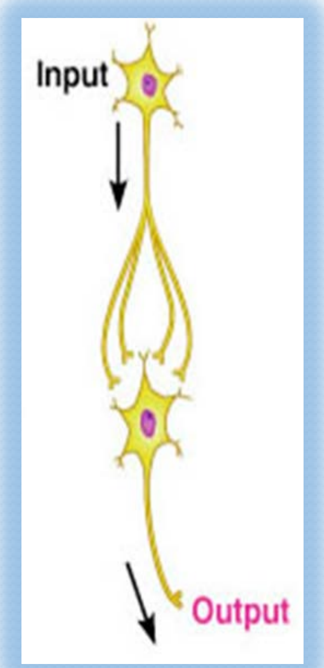
Properties of the Neurons



- Excitability (irritability)
  - ability to respond to changes in the body and external environment called stimuli
- Conductivity
  - development of action potentials (APs)
  - produce traveling electrical signals
- Synaptic linkage
  - when electrical signal reaches the end of a nerve fiber, a chemical neurotransmitter is released



Neurons properties (cont.)



Neurons are very responsive to stimuli due to APs.

Action potentials, or nerve impulses, are:

--Electrical impulses conducted along the length of axons.

--Always the same regardless of stimulus.

--The underlying functional feature of the nervous system.

Definitions

Voltage (V) – measure of potential energy between two points generated by a charge separation.

(Voltage = Potential Difference = Potential)

Current (I) – Flow of electrical charge

Resistance (R) – Tendency to oppose the current

Units: V (volt), I (ampere), R (ohm)

Conductor – Substance with low electrical resistance.

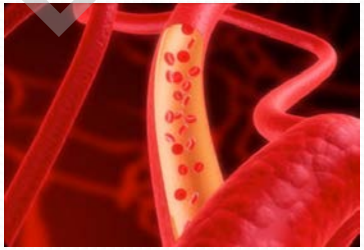
Associated Electrical Concepts

Voltage:

- the potential of current that flows from one point to another.
- It is a relative measure.

Current:

- number of charged particles (ions) that flow in a given time.



Resistance:

- resistance to the movement of charges.

Ohm’s Law

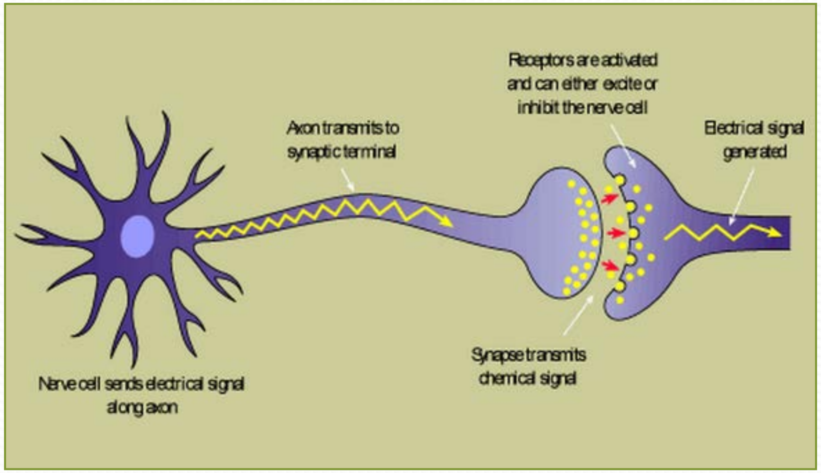
The relationship between voltage, current, and resistance is defined by Ohm’s Law

$$\text{Current (I)} = \frac{\text{Voltage (V)}}{\text{Resistance (R)}}$$

$$I(ion) = g(ion)(Vm\text{-}Ei)$$

- Ionic current (I_{ion})
- Ion's conductance (g_{ion})
- Membrane potential - the ion's equilibrium potential (V_m - E_{ion})

- In the body, electrical current is the flow of ions (rather than free electrons) across membranes.
- A Potential Difference exists when there is a difference in the numbers of + and – ions on either side of the membrane.

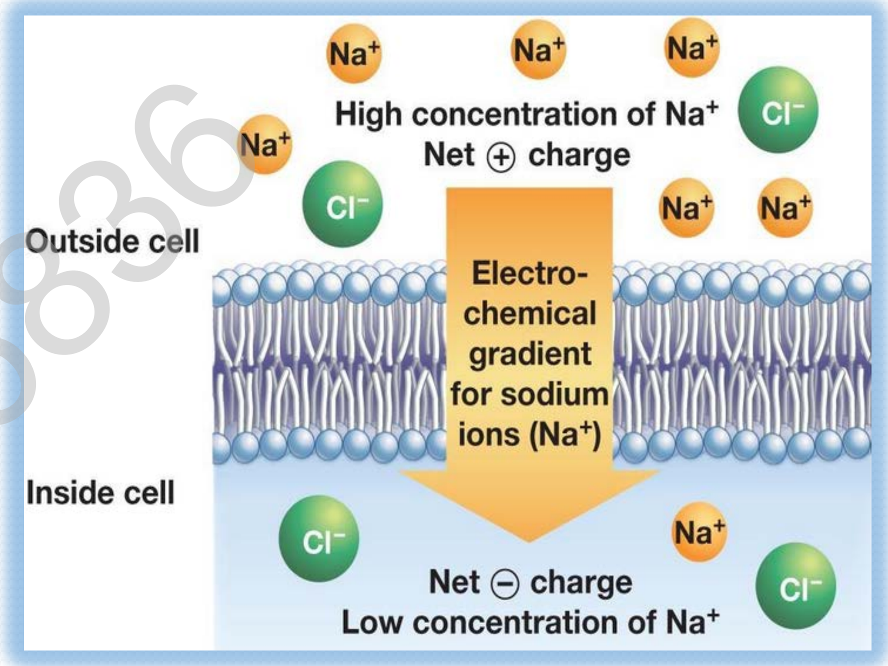


CHARACTERISTICS OF THE SIGNAL TRANSMISSION BETWEEN NEURONS

- Binary output over time. Cell either transmits or not.
- After a cell fires, it can not fire again for a short period of several ms, known as the refractory period.
- Neuron activation = chain-like process = a neuron is activated by other activated neurons and, in turn, activates other neurons.

Voltage Generators

- When gated ion channels open, ions diffuse across the membrane following their electrochemical gradients.
- This movement of charge is an electrical current and can create voltage change across the membrane.

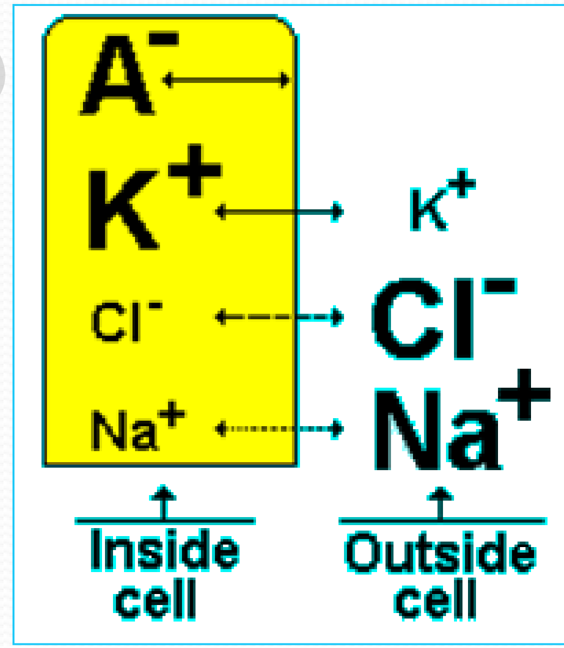


Voltage (V) = Current (I) x Resistance (R)

- Ion movement (flow) along electrochemical gradients underlies all the electrical phenomena in neurons.
- Ions move from a high concentration to a low concentration.

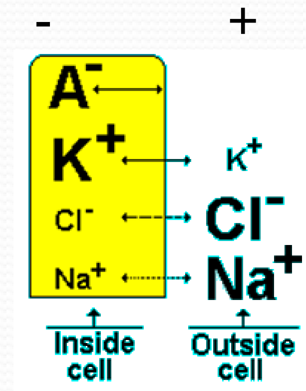
Polarization of the neuron's membrane

- When a neuron is not stimulated; it's just sitting with no impulse to carry or transmit; its membrane is polarized.
- **Sodium** Na+ **is on the outside, and potassium** K+ **is on the inside.**
- Electrical charge on the outside of the membrane is positive while the electrical charge on the inside of the membrane is negative.
- The outside of the cell contains excess sodium ions (Na+); the inside of the cell contains excess potassium ions (K+).



\-   +

Note: (Ions are atoms of an element with a positive or negative charge.)



How can the charge inside the cell be negative if the cell contains positive ions (K+)?

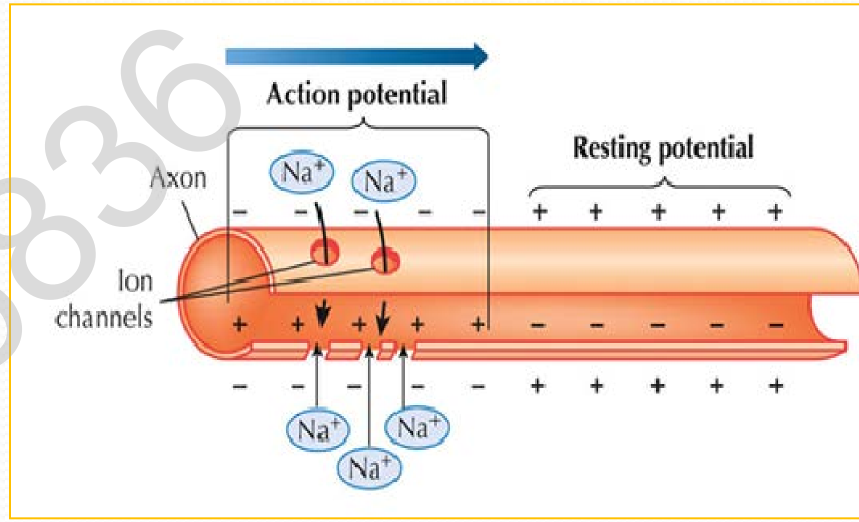
<u>Answer:</u>

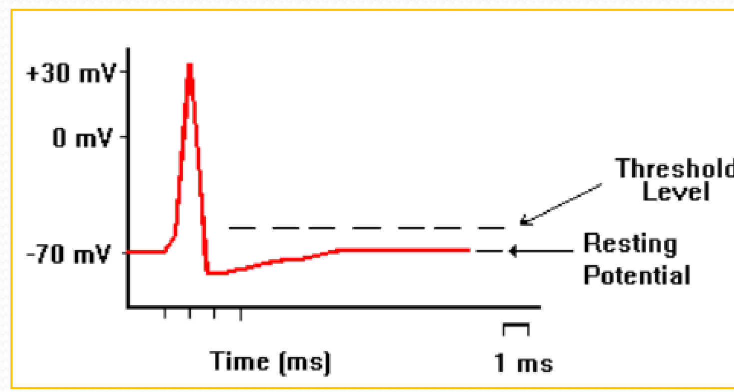
In addition to the K+, negatively charged protein and nucleic acid molecules also inhabit the cell; therefore, the inside is negative as compared to the outside.

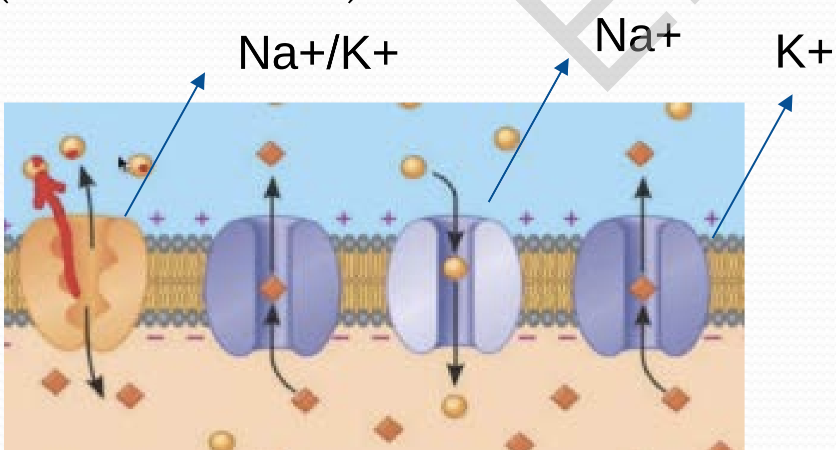
There are Na+/K+ pumps on the membrane that pump the Na+ back outside and the K+ back inside.

Resting potential

- It gives the neuron a break.
- When the neuron is inactive and polarized, it's said to be at its resting potential. It remains this way until a stimulus comes along.
- The resting membrane potential of a neuron is about -70 mV (mV=millivolt)





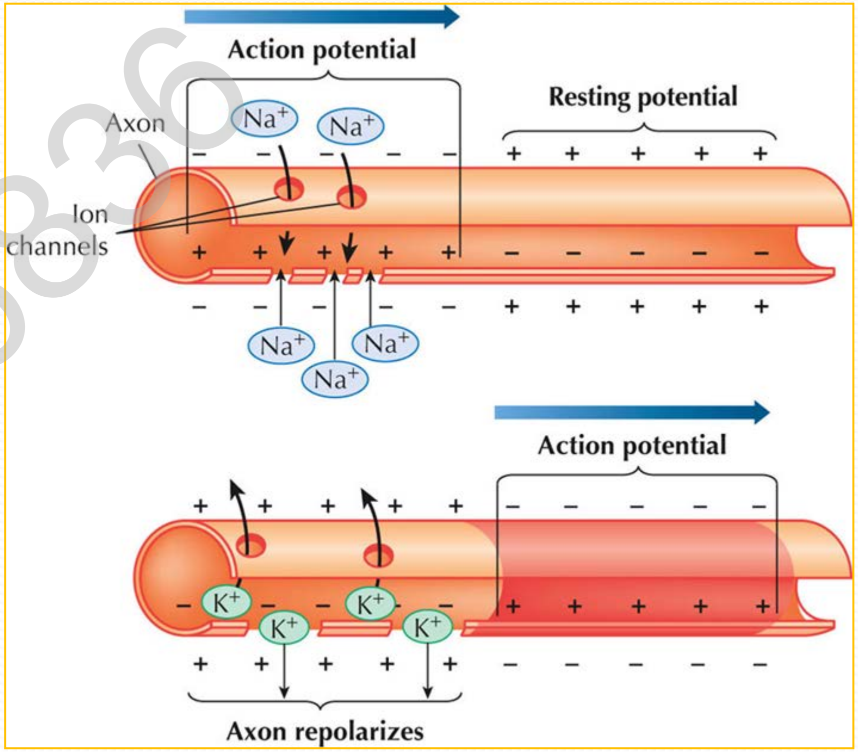


Action potential

- **Sodium ions** Na+ **move inside the membrane.**

- When a stimulus reaches a resting neuron, the gated ion channels on the resting neuron's membrane open suddenly and allow the Na+ that was on the outside of the membrane to go rushing into the cell.

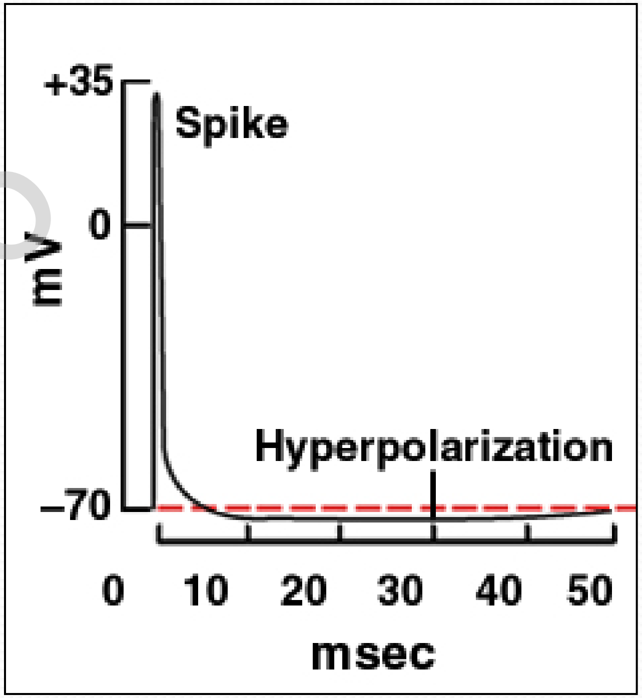
- Neuron goes from being polarized to being depolarized.



Action Potentials

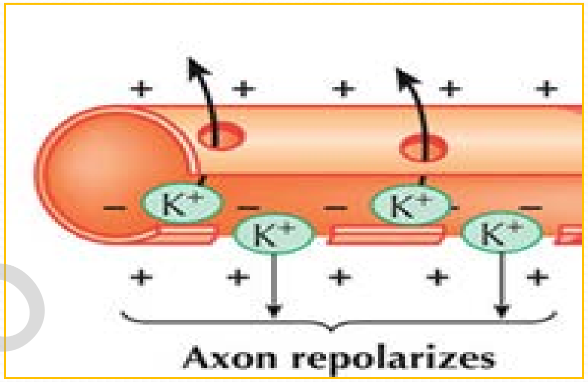
- Called a spike.

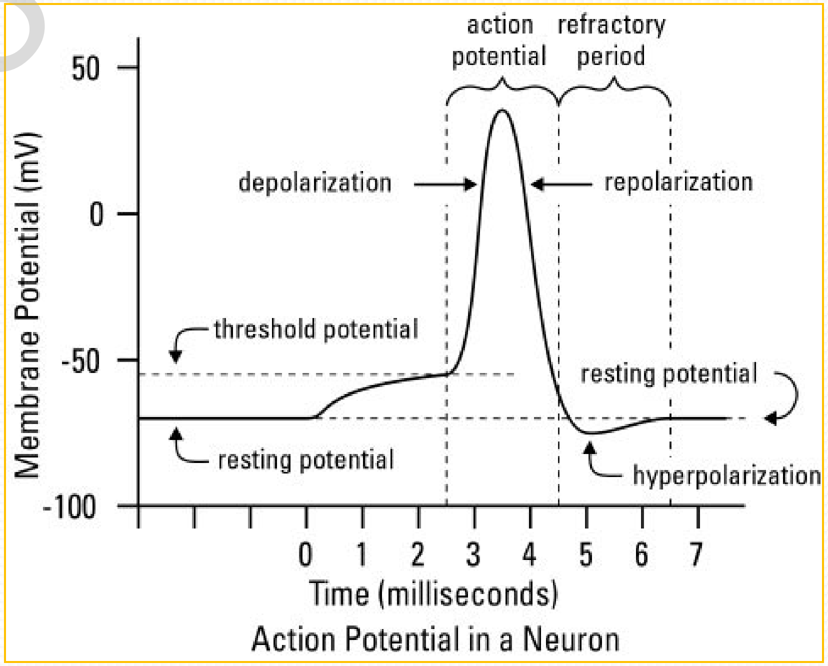
- Characteristics of **AP**
  - follows an all-or-none law.
    - voltage gates either open or don't
  - Non-decremental (do not get weaker with distance).
  - Irreversible (once started goes to completion and can not be stopped).



Repolarization

- **Potassium ions move outside, and sodium ions stay inside the membrane.**
- After the inside of the cell becomes flooded with Na+, the gated ion channels on the inside of the membrane open to allow the K+ to move to the outside of the membrane.
- With K+ moving to the outside, the membrane's repolarization restores electrical balance, although it's opposite of the initial polarized membrane that had Na+ on the outside and K+ on the inside. Just after the K+ gates open, the Na+ gates close; otherwise, the membrane couldn't repolarize.



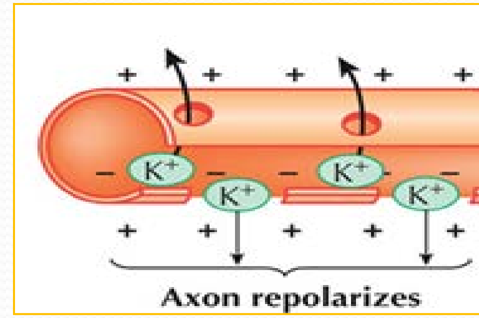


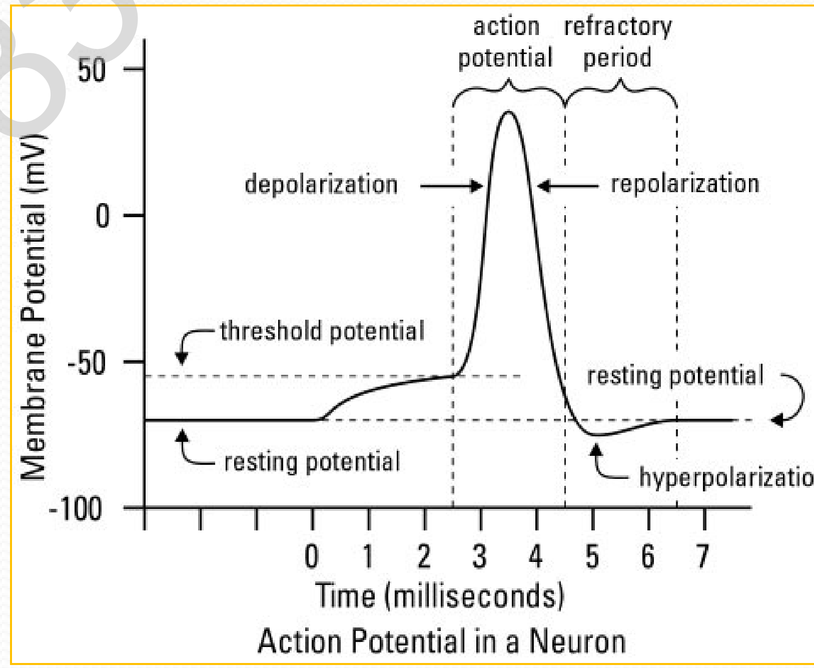
Hyperpolarization

- <u>**More potassium ions are on the outside than there are sodium ions on the inside.**</u>

- When the K+ gates finally close, <u>the neuron has slightly more K+ on the outside than it has Na+ on the inside.</u> This causes the membrane potential to drop slightly lower than the resting potential, and the membrane is said to be hyperpolarized because it has a greater potential.

- This period doesn't last long. After the impulse has traveled through the neuron, the action potential is over, and the cell membrane returns to normal (that is, the resting potential).





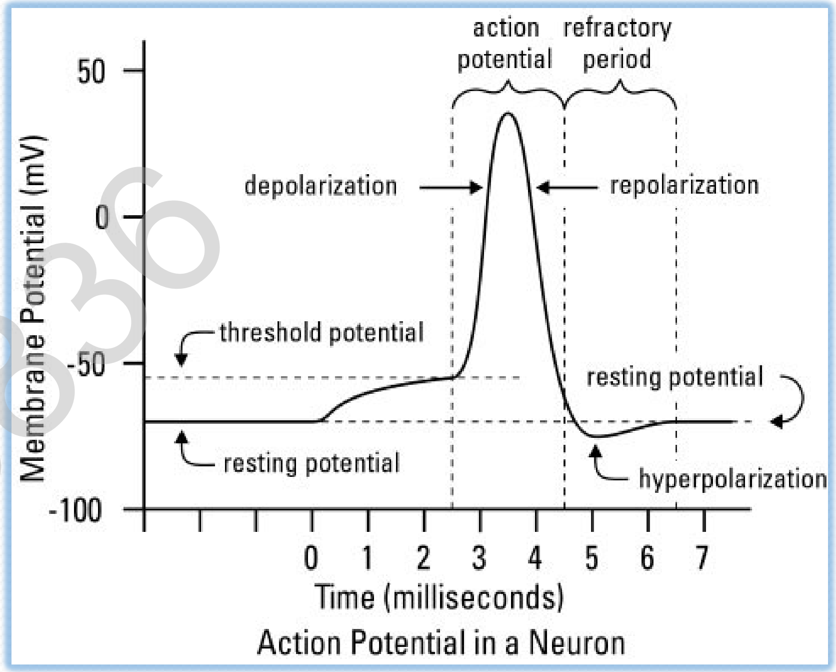
Refractory Period

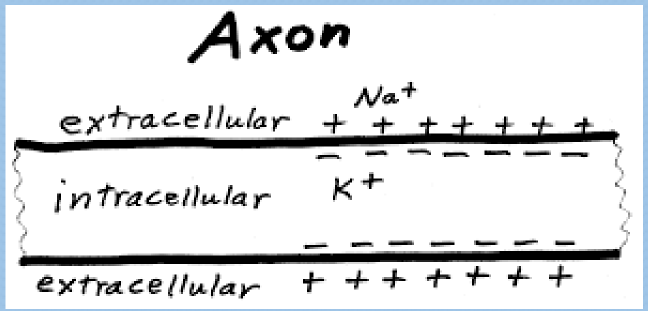
- **It puts everything back to normal: Potassium returns inside, sodium returns outside.**

- The refractory period is when the Na+ and K+ are returned to their original sides: Na+ on the outside and K+ on the inside.

- While the neuron is busy returning everything to normal, it doesn't respond to any incoming stimuli.

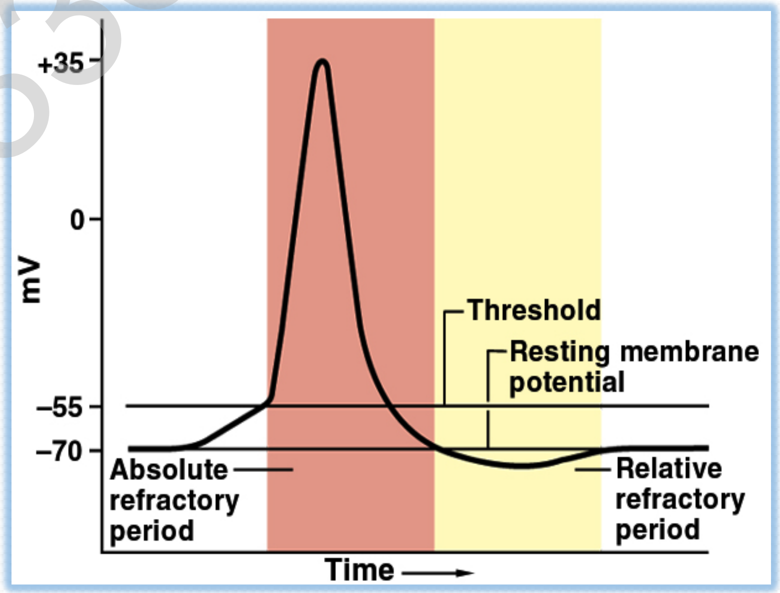
- After the Na+/K+ pumps return the ions to their rightful side of the neuron's cell membrane, the neuron is back to its normal polarized state and stays in the resting potential until another impulse comes along.



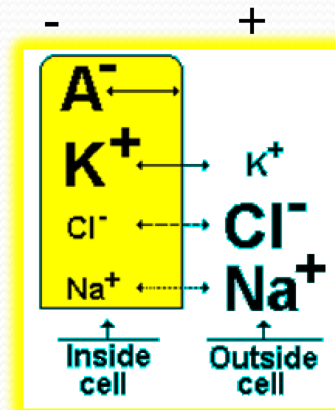


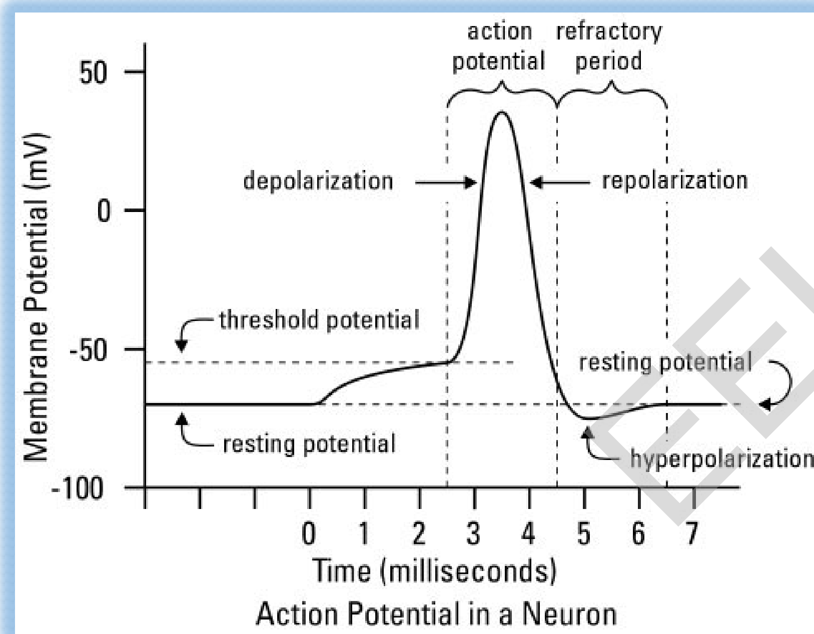
Refractory Period (cont.)

- Period of resistance to stimulation.
- Absolute refractory period
  - as long as Na^+ gates are open
  - no stimulus will trigger **AP**
- Relative refractory period
  - as long as K^+ gates are open
  - only especially strong stimulus will trigger new **AP**



During steady state

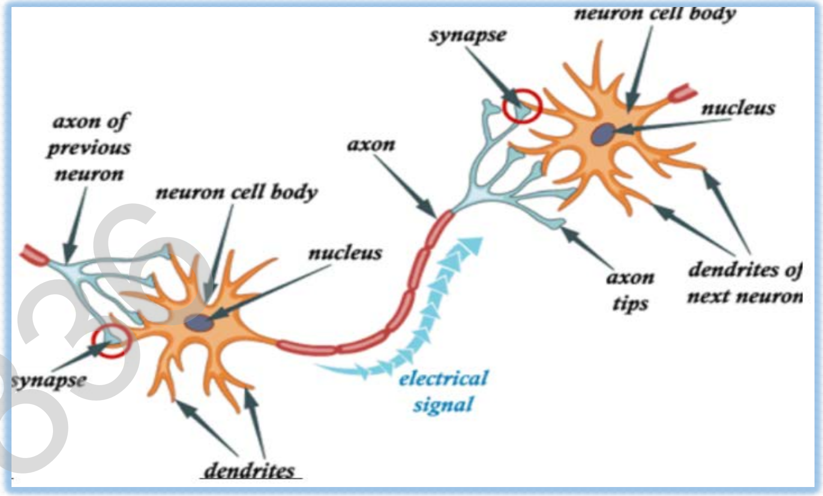


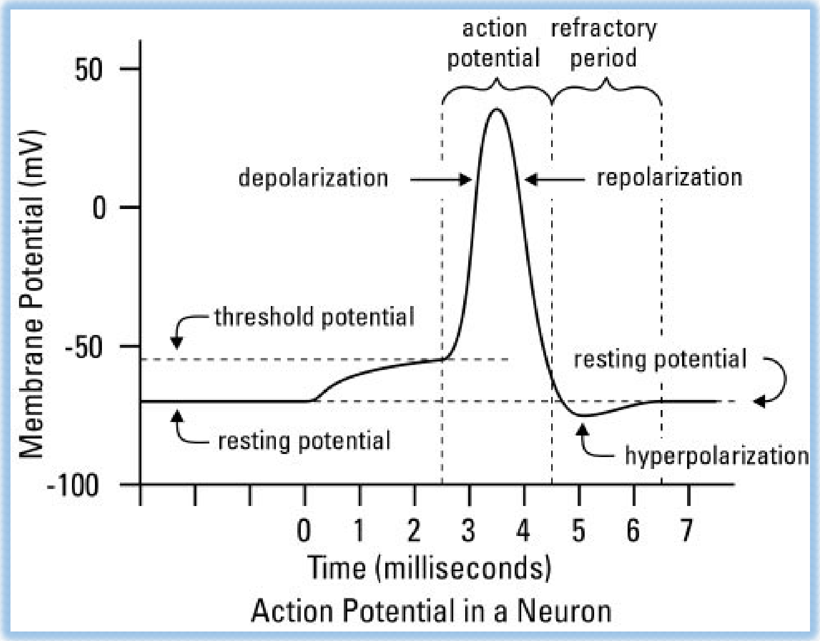


- Body membrane maintains balance K^+, Na^+, Cl^+ (Potassium, Sodium, Chloride).
- Sodium/K+ pump continuously passes Na+ out of the cell and K+ into the cell => dynamical chemical equilibrium (resting/steady state of a neuron).
- Inside Neuron: High concentration of K^+, low concentration of Na^+, Cl (in extra cellular region: vice versa)

During stimulation

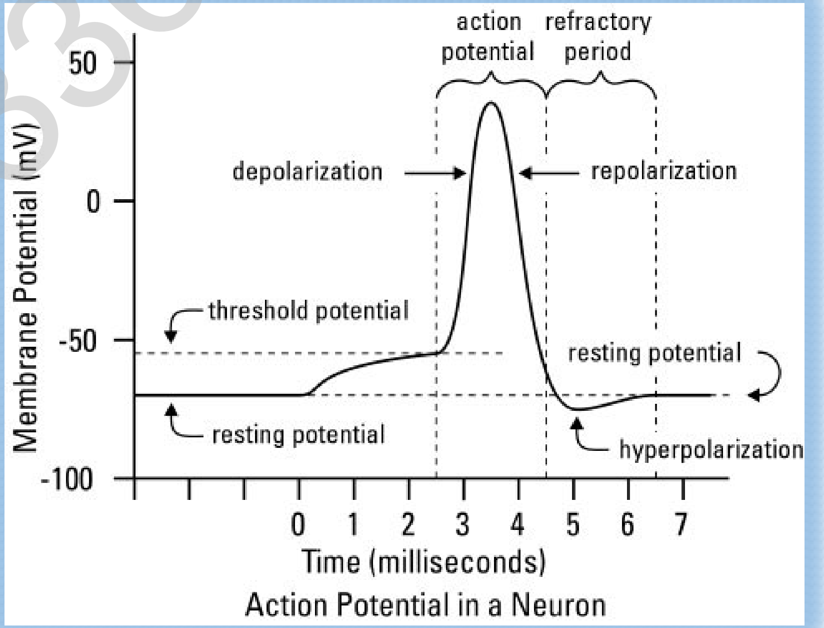
- Occurs due to synaptic inputs through synaptic gaps (dendrites).
- **Soma**: sums inputs received by the dendrites. If sufficient input received -> cell fires, i.e. transmits a signal over its axon to other cells.
- Impulse travels via axon.
- When impulse arrives at the terminal of an axon, Na+ channels open => neurotransmitter molecules enter the synaptic gap passing to the dendrites of other neurons.
- Impulse can be **excitatory** or **inhibitory**.





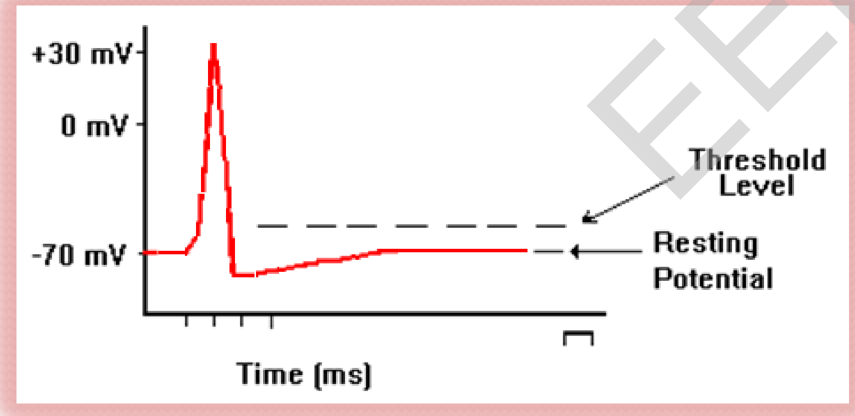
During Depolarization

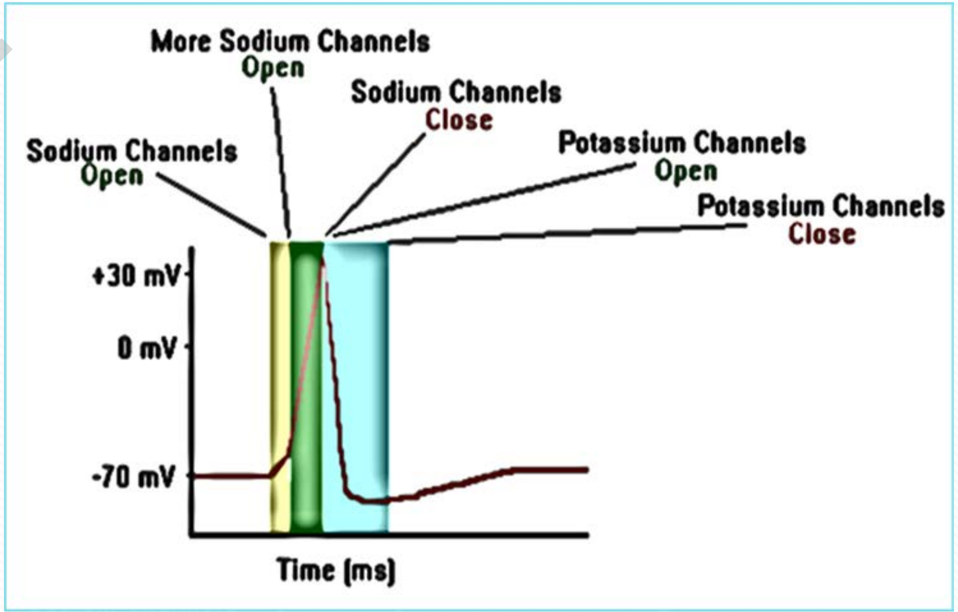
- <u>Action potential is an explosion of electrical activity </u>that is created by a **depolarizing current**.
- A stimulus causes the resting potential to move toward 0 mV.
- When the depolarization reaches about -55 mV a neuron will fire an action potential.
- This is the **Threshold**. If the neuron does not reach this critical threshold level, <u>then no Action Potential will fire.</u>



Firing model

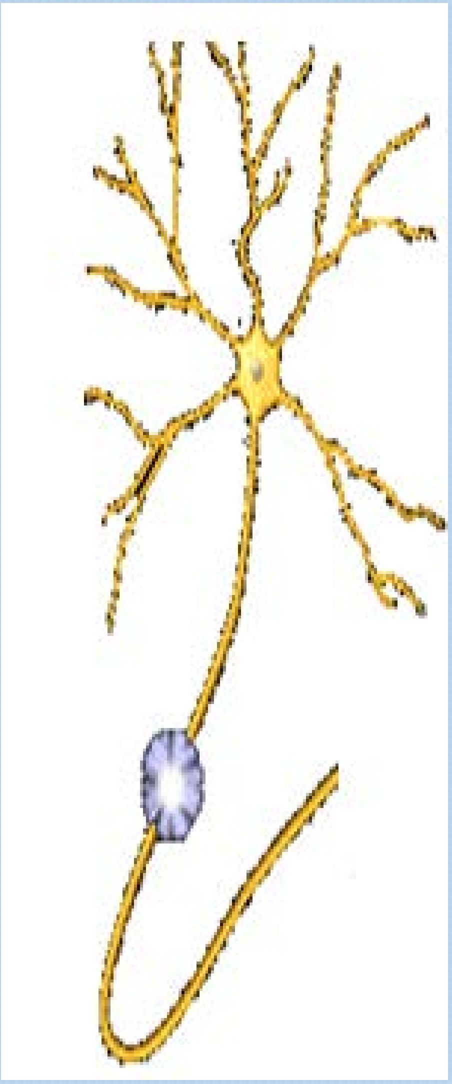
- When N fires, output is referred as a spike (not the same as the EEG spikes)
- N fires if threshold exceeded (-55 mV)
- State vector of N: expressed its output as a function of time *X(t)*
- Since binary activation: X(t) can only be 0 or 1
- X(t) ε (0 , 1) => bistable space "ALL OR NONE" principle
- <u>Action potential of a fixed sized will always fire</u>; for any given neuron, <u>the size of the Action Potential is always the same.</u>





Electrical Potentials & Currents

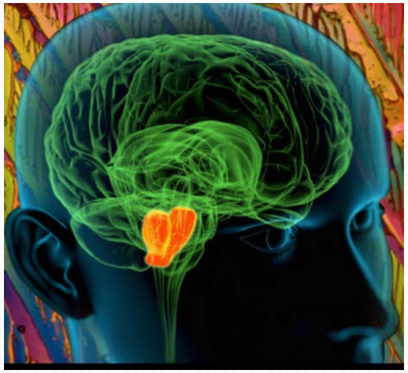
- Neuron pathway is not a continuous "wire" but a series of separate cells.
- Neuronal communication is based on mechanisms for producing electrical potentials & currents.
  - electrical potential - difference in concentration of charged particles between different parts of the cell.
  - electrical current - flow of charged particles from one point to another within the cell.
- Living cells are polarized
  - resting membrane potential is -70 mV with a relatively negative charge on the inside of nerve cell membranes.

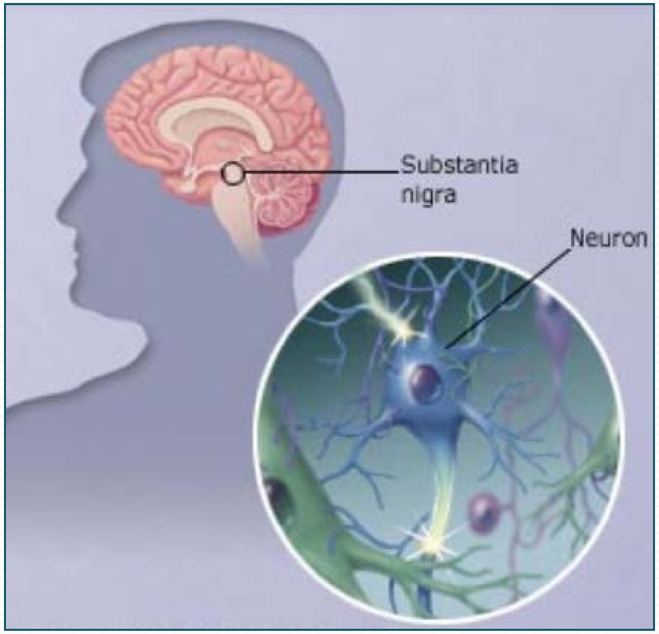


Diseases of the Nervous system

- Alzheimer’s Disease (AD)
- Parkinson’s Disease (PD)
- Epilepsy

Parkinson Disease





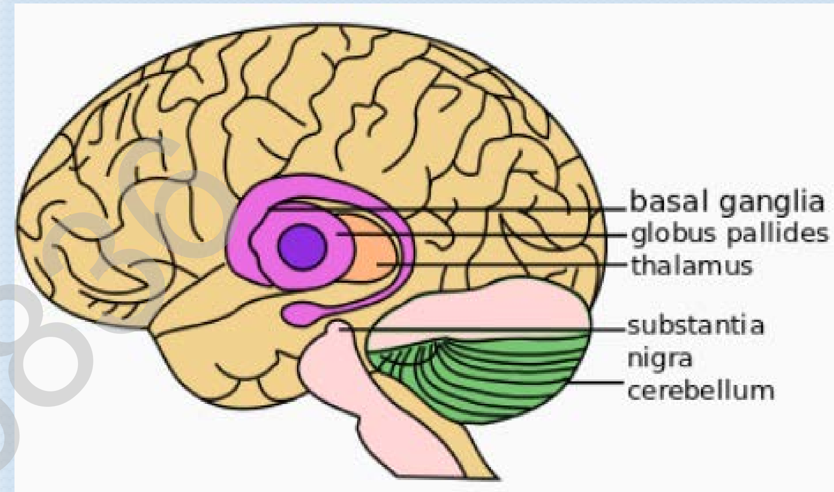
- Progressive loss of motor function beginning in 50's or 60's -- no recovery
  - degeneration of dopamine-releasing neurons in substantia nigra.
  - involuntary muscle contractions
    - facial rigidity, slurred speech, illegible handwriting, etc.
- Treatment: drugs and physical therapy
  - At present, there is no cure for PD, but a variety of medications provide dramatic relief from the symptoms.

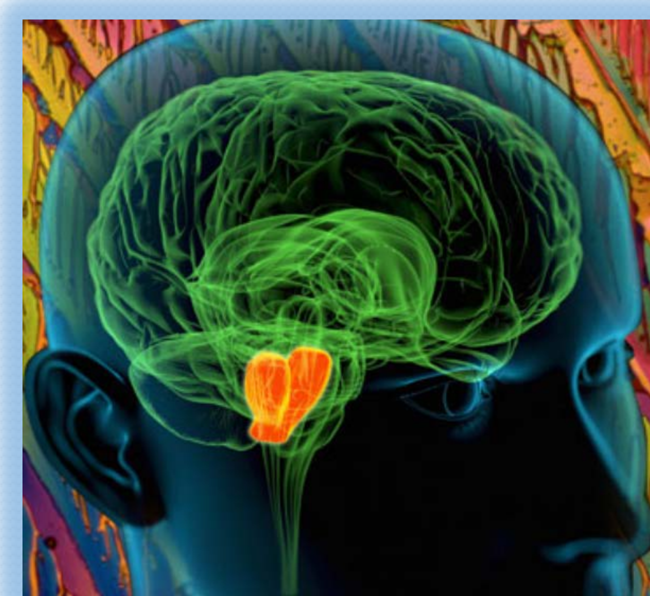
Parkinson Disease

- **Surgery: Deep Brain Stimulation**

- Electrodes can be implanted into different areas of the brain -- the globus pallidus, the thalamus, among others.
- Electric pulses stimulate the brain to help reduce a patient's rigidity, tremors, and bradykinesia.

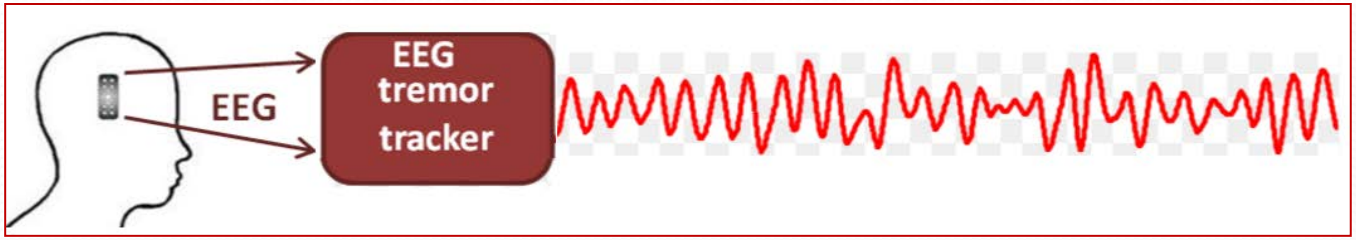
- It doesn't stop the progression of PD or affect other symptoms.

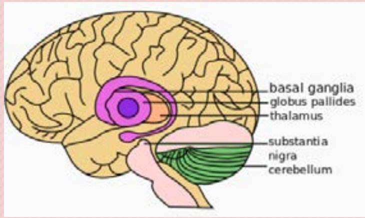




Parkinson Disease- EEG

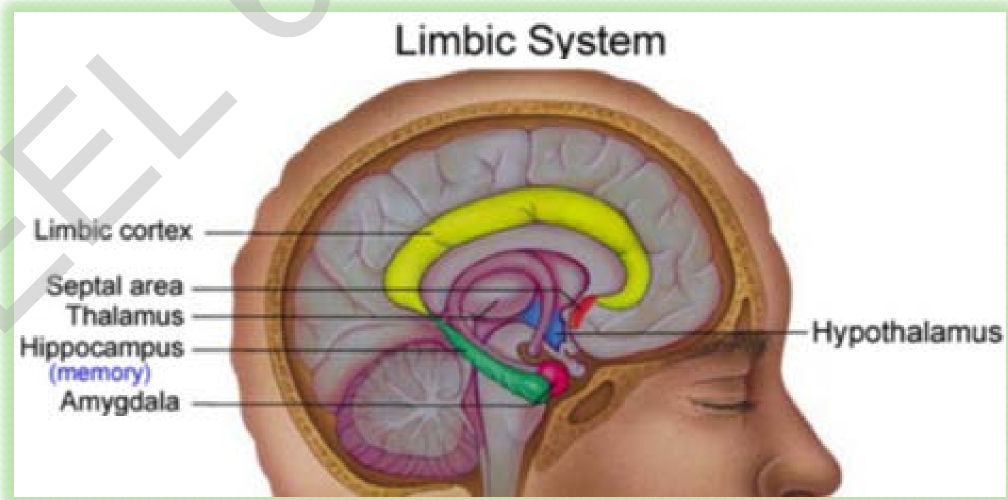
- *Identification* of EEG biomarkers will aid in characterizing pre-clinical brain signal changes in PD and allow earlier clinical trials of new PD therapies.
- It has been shown that quantifying *EEG rhythms* could provide an important biomarker for PD patients.
- A slowing of EEG frequencies correlates with a decline of cognition. An increase of low spectral powers <8 Hz (delta and theta) and a decrease in the "fast" frequency bands >8 Hz (alpha, beta, and gamma) are spectral markers of PD-related cognitive decline.
- Topographically, occipital, parietal, and temporal regions show the higher significance.





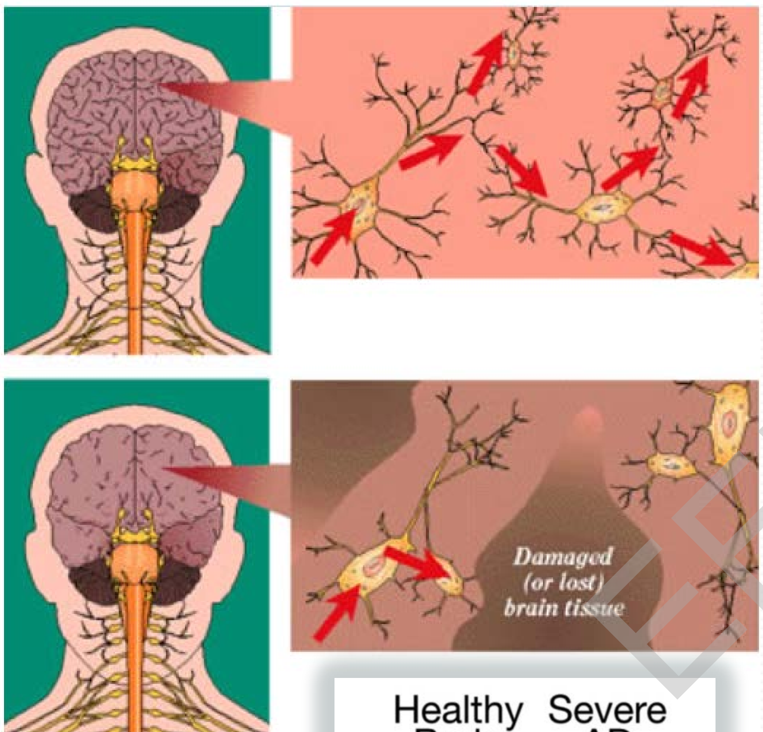
Alzheimer’s Disease

- The <u>most common form of dementia among older people </u>is Alzheimer’s Disease (AD), which initially involves the parts of the brain that control <u>thought, memory, and language</u>.
- Although scientists are learning more every day, right now they still do not know what causes <u>AD, and there is no cure</u>.
- The number of people with the disease doubles every 5 years beyond age 65.

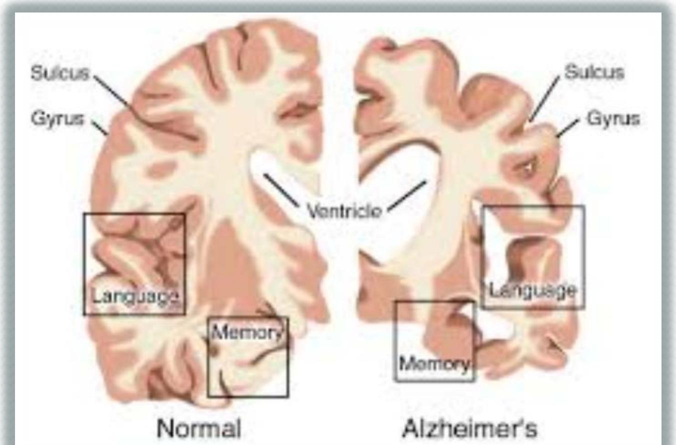


- EEG of an Alzheimer’s disease patient usually shows a <u>decrease</u> in Alpha and Beta (8-30Hz) waves as well as an <u>increase</u> in Delta and Theta waves.(1-7 Hz).

Alzheimer’s Disease



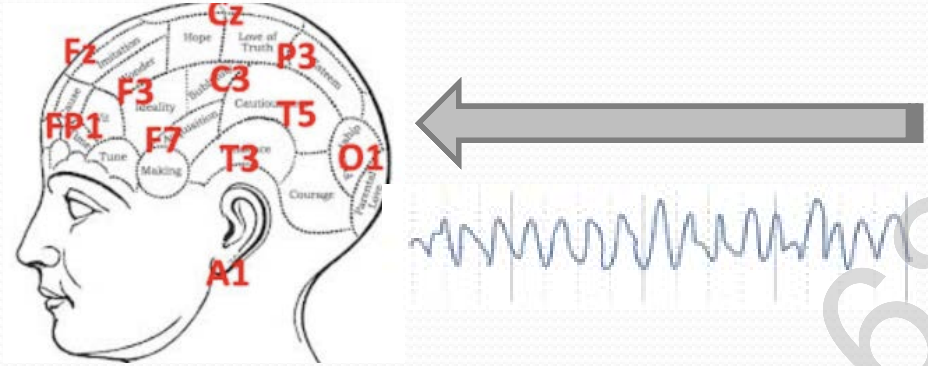
- An early, accurate diagnosis of AD helps patients and their families plan for the future.
- It gives them time to discuss care while the patient can still take part in making decisions.
- Early diagnosis will also offer the best chance to treat the symptoms of the disease.



Alzheimer's Disease-EEG

- Slowing of EEG: an increase of power in low frequencies (delta and theta band, 0.5–8Hz) and a decrease of power in higher frequencies (alpha and beta, 8–30Hz, and gamma, 30–100Hz). To quantify these changes in spectral power, Fourier transforms have been applied.
- The EEG of MCI and AD patients seems to be more regular than of age-matched control subjects. Complexity measures have been used to quantify this reduction in EEG complexity such as: Entropy, fractal dimension, among others.
- Numerous studies have reported decreased EEG synchrony in MCI and AD patients under resting conditions ("spontaneous EEG"). Measures have been applied to quantify this loss such as: correlation coefficient, coherence, among others.

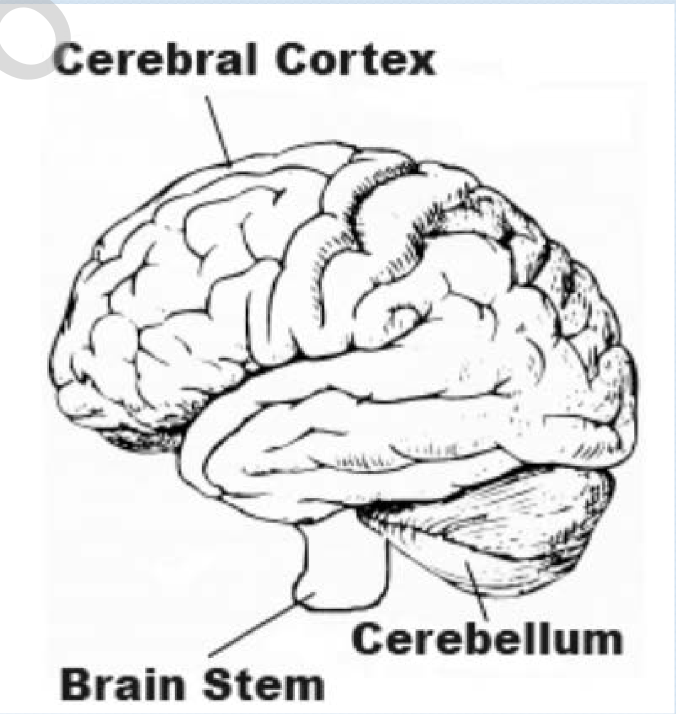
The Brain…



- The brain is <u>not a uniform material</u>. It is a mass of gray and white matter.
- The brain is made up of <u>many different areas</u>, each having a <u>particular structure and function</u>.
- The brain is <u>protected by several bones</u>.

COMPONENTS OF THE BRAIN

- **Cerebrum:** consists of the left and right cerebral hemispheres.
- **Cerebellum:** structure located behind the brain stem.
- **Brain stem:** lowest section of the brain and it is connected to the spinal cord.

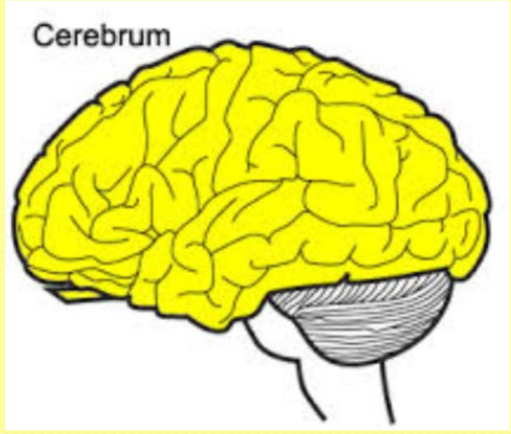


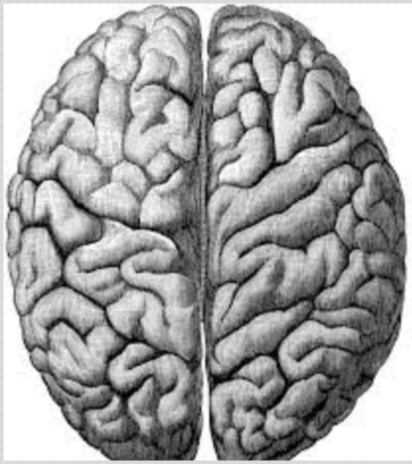
Cerebrum

- The cerebral hemispheres of the brain make up the largest part of your brain. 85% of the weight of a human brain.

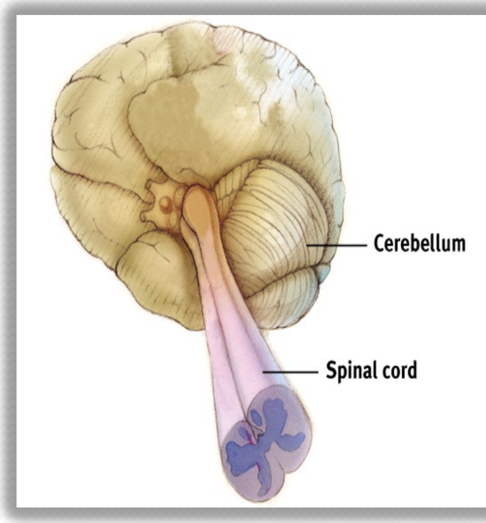
- The outer part is called the cerebral cortex.

- It is often referred to as "gray matter." It is associated with higher mental functions, almost fills the entire brain cavity. It determines intelligence, personality, and thinking.

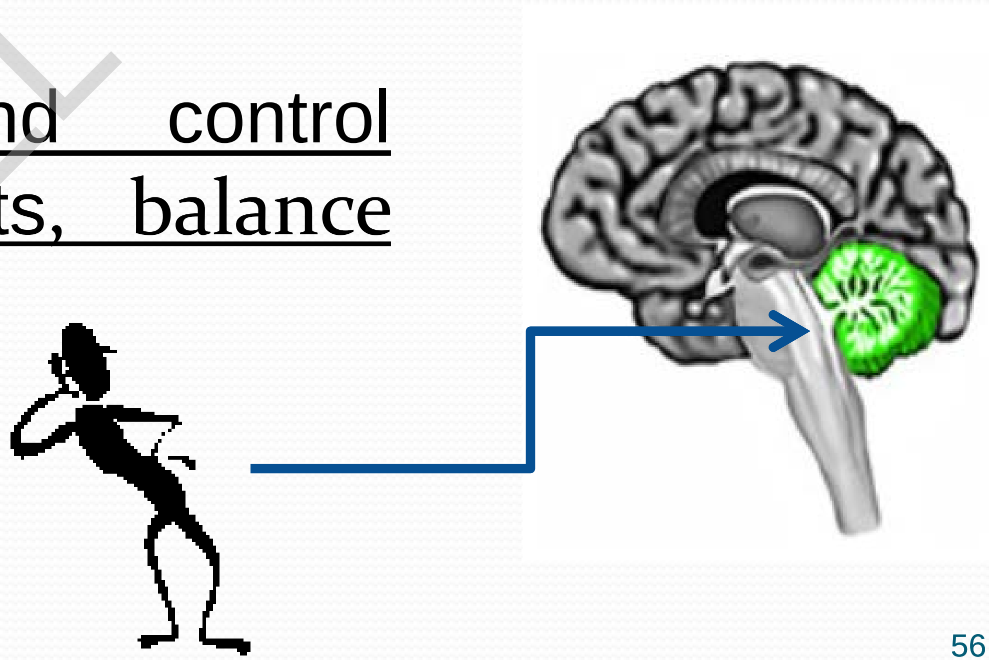




The Cerebellum



- It is about the size of a pear.
- The word "cerebellum" comes from the Latin word for "<u>little brain</u>."
- It <u>coordinates and control voluntary movements, balance and coordination</u>.

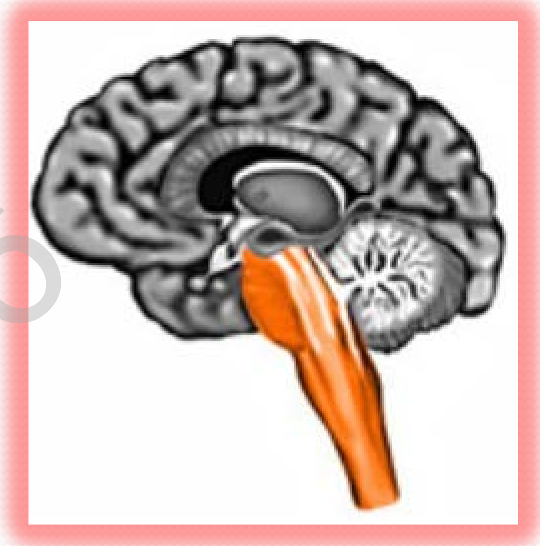


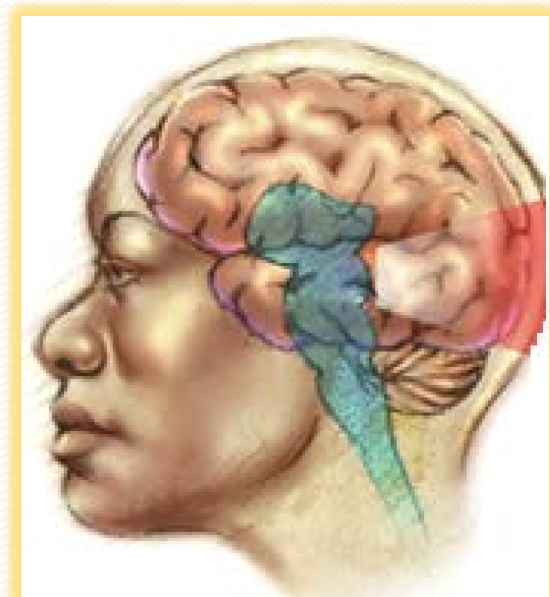
Brain Stem

- It controls <u>breathing and circulation</u> and <u>connects the cerebrum and cerebellum to the spinal column.</u>

- <u>Provides the main motor and sensory functions to the face and neck through the cranial nerves.</u>

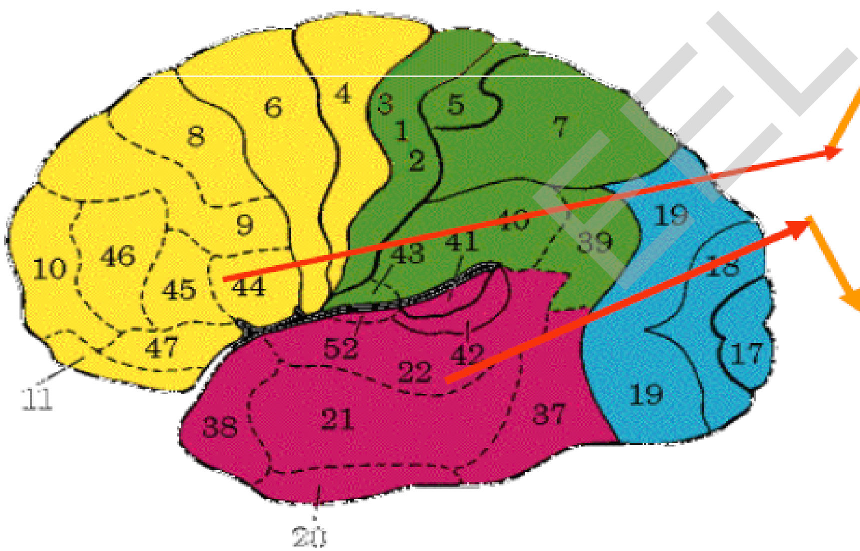
- It is responsible for <u>automatic survival functions</u> such as heartbeat, digestion, and keeping your body alive while you sleep.





Functional Localization Throughout History

- Arround Mids 1800:
- Paul Broca (1861) & Carl Wernicke (1874) set the fundamentals for the Language Functionality of the Brain



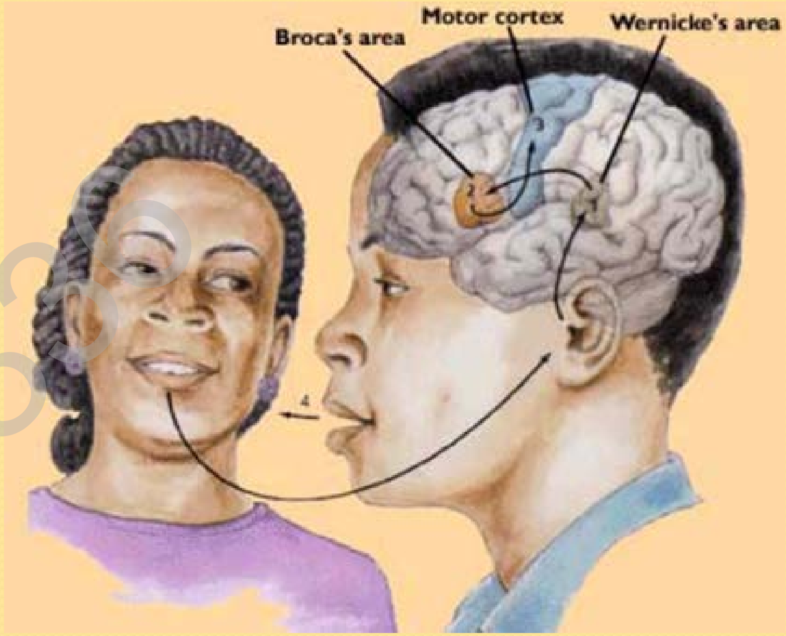
Broca's area = BA 44,45,47
Left frontal lobe. Damage results in poor and slow speech

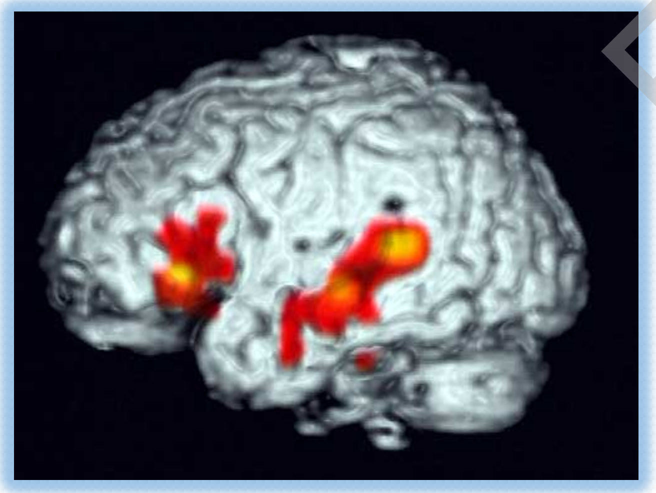
Wernicke's area = BA 21,22,39
Left temporal lobe. Damage results in failure to understand language

Eloquent Cortex

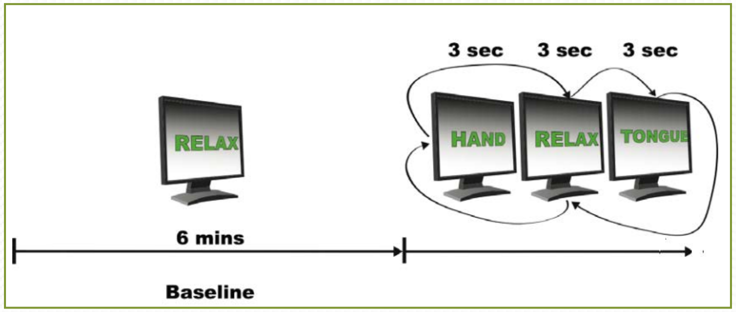
Wernicke's area (central language area): Difficulty speaking understandably and comprehending speech; confusion between left and right; difficulty reading, writing, naming objects, and calculating.

Broca's area (speech): Difficulty speaking and sometimes writing.



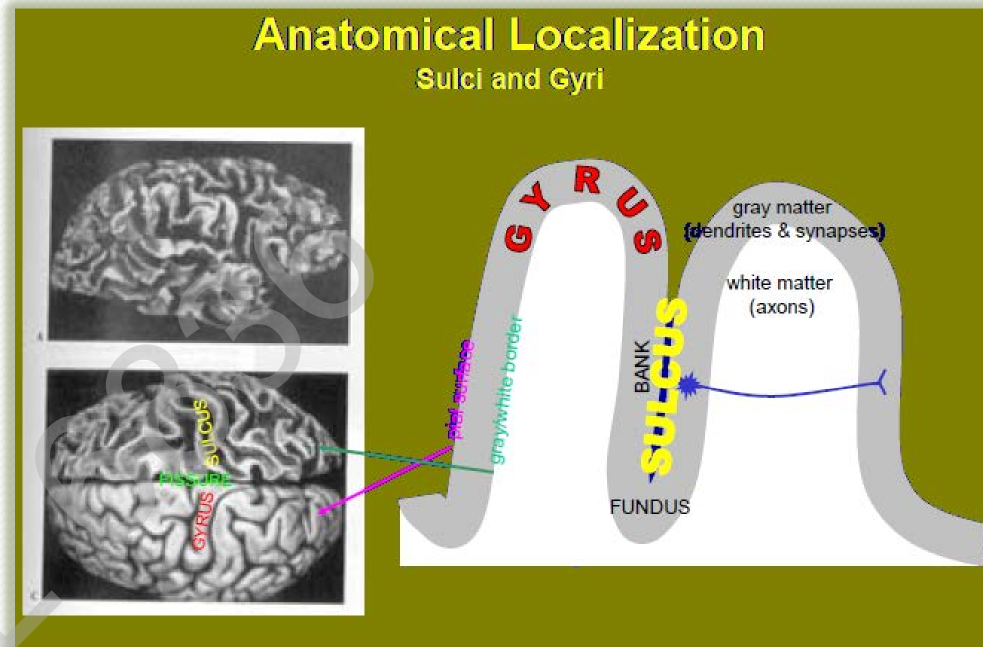


fMRI Language Areas



EEG Mapping

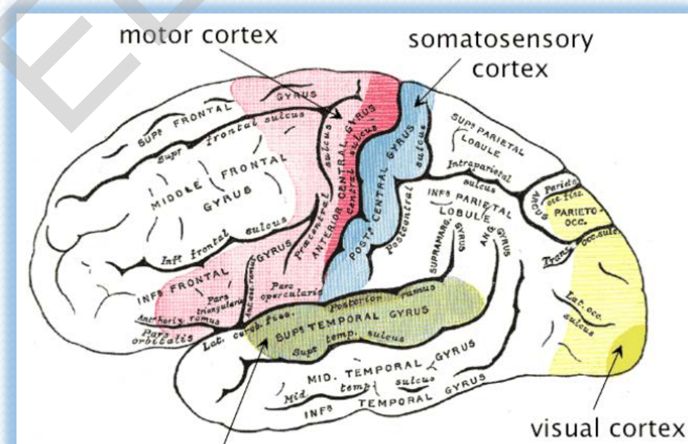
Cerebral Cortex

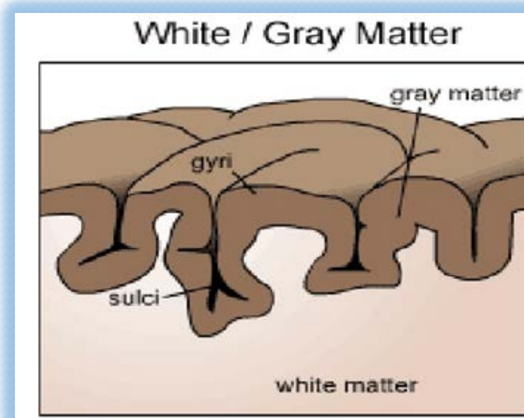


- The outermost layer of the cerebral hemisphere which is composed of gray matter. Both hemispheres are able to analyze sensory data, perform memory functions, learn new information, form thoughts and make decisions.
- The cortical thickness and intelligence are associated.

- Somatosensory cortex is thicker in migraine sufferers.

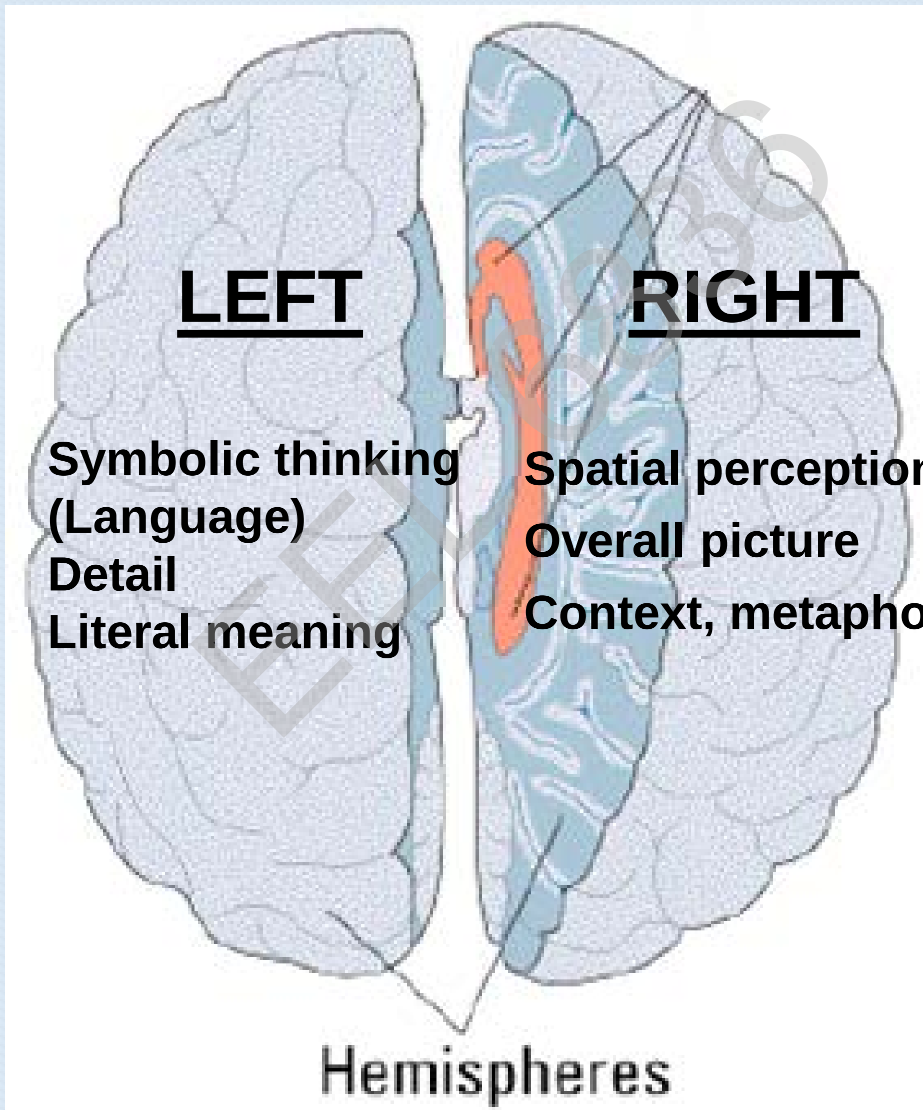
- Average thickness of the cerebral cortex: **approximately 2.5 mm**





Hemispheric Specialization

Left temporal Lobe - Mainly involved in <u>verbal memory</u> (i.e., memory for words and names).



Right Temporal Lobe - Mainly involved in <u>visual memory</u> (i.e., memory for pictures and faces).

**90% of population is Right-handed.

Hemispheric Specialization

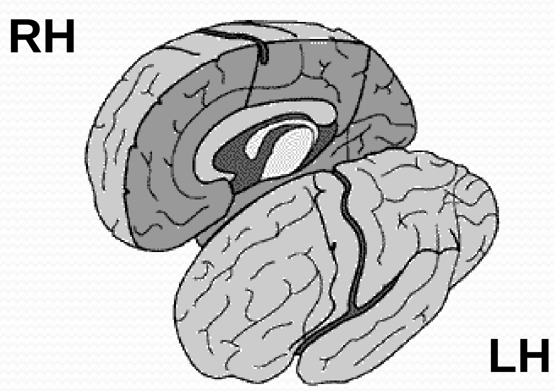
- **Left Hemisphere:** Sequential Analysis: systematic, logical interpretation of information. Interpretation and production of symbolic information: language, mathematics, abstraction and reasoning. Memory stored in a language format. **Most people are LH dominant for language.**

- **Right Hemisphere:** Holistic Functioning: processing multi-sensory input simultaneously to provide "holistic" picture of one's environment. Visual spatial skills. Holistic functions such as dancing and gymnastics are coordinated by the right hemisphere. Memory is stored in auditory, visual and spatial modalities.

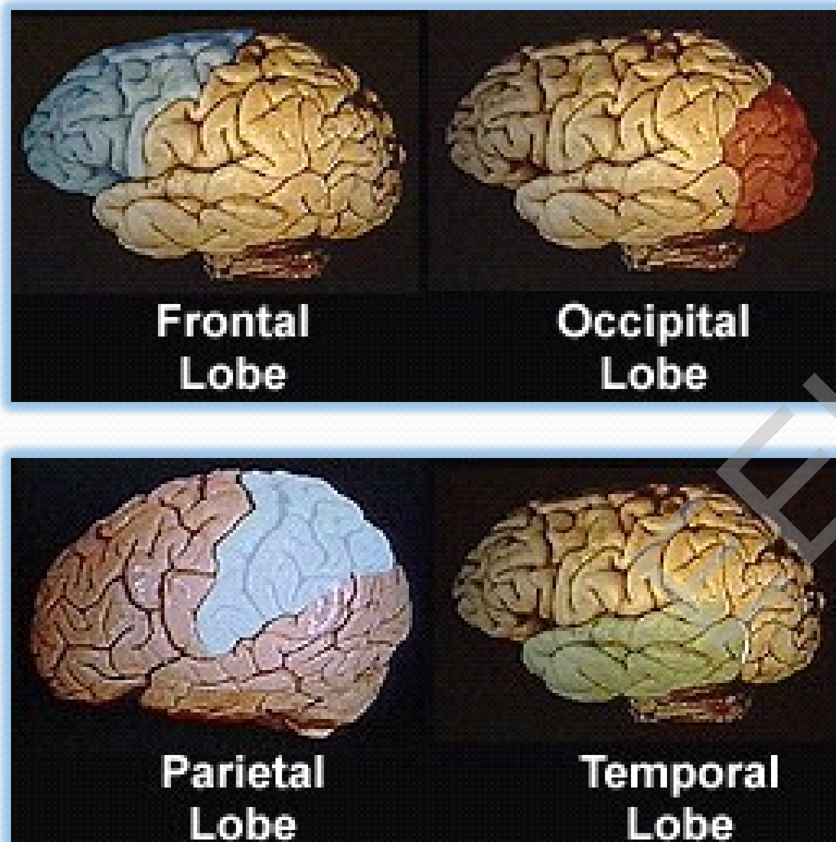
EEG/ERP: Mapping Hemispheres

Reduced alpha power (8-12 Hz):

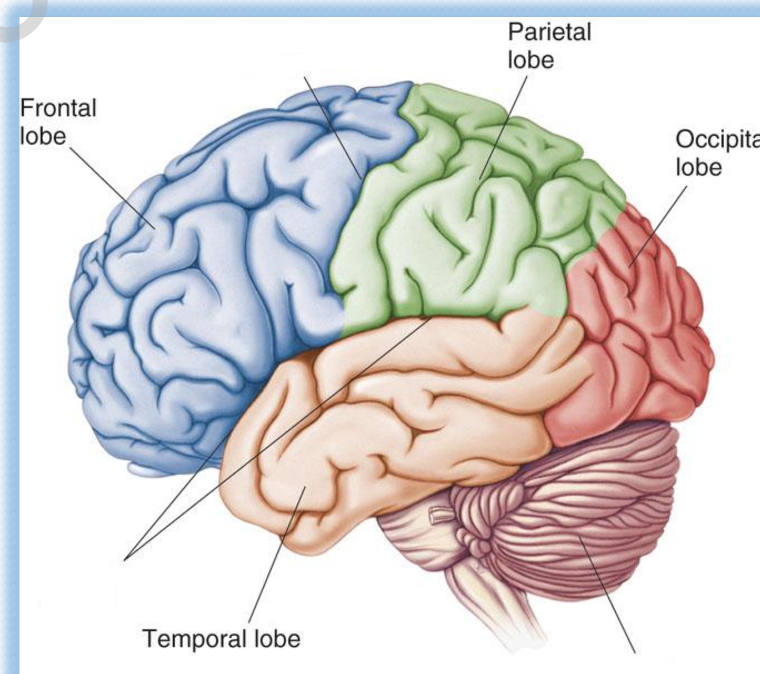
Increased neural activity.



Four Lobes of the Cerebral Cortex

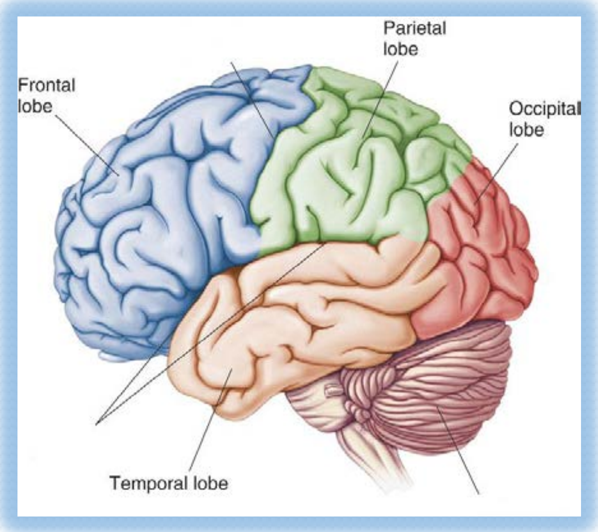


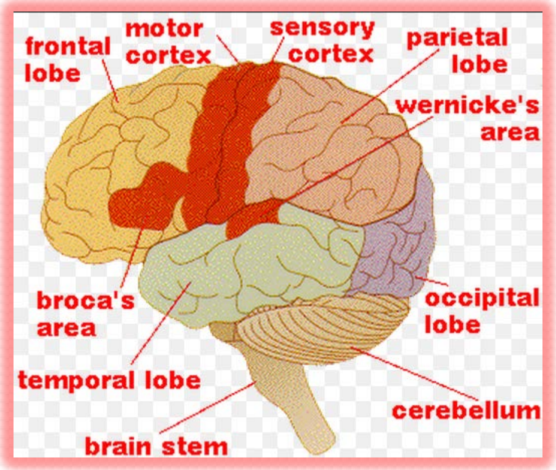
Frontal (Forehead to top) → Motor Cortex
Parietal (Top to rear) → Sensory Cortex
Occipital (Back) → Visual Cortex
Temporal (Above ears) → Auditory Cortex



Brain Regions Functionality

- **Frontal Lobe:**
  - Cognition and memory.
  - Prefrontal area: The ability to concentrate, attend and elaboration of thoughts.
  - Movement.
  - Motor Cortex : voluntary motor activity.
  - Premotor Cortex: storage of motor patterns and voluntary activities.
  - Language: motor speech.
- **Parietal Lobe:** Processing of sensory input, sensory discrimination.
- **Occipital Lobe**: Primary visual reception area. Primary visual association area: Allows for visual interpretation.
- **Temporal Lobe:** Auditory receptive area and association areas. Expressed behavior. Language: Receptive speech. Memory: Information retrieval.

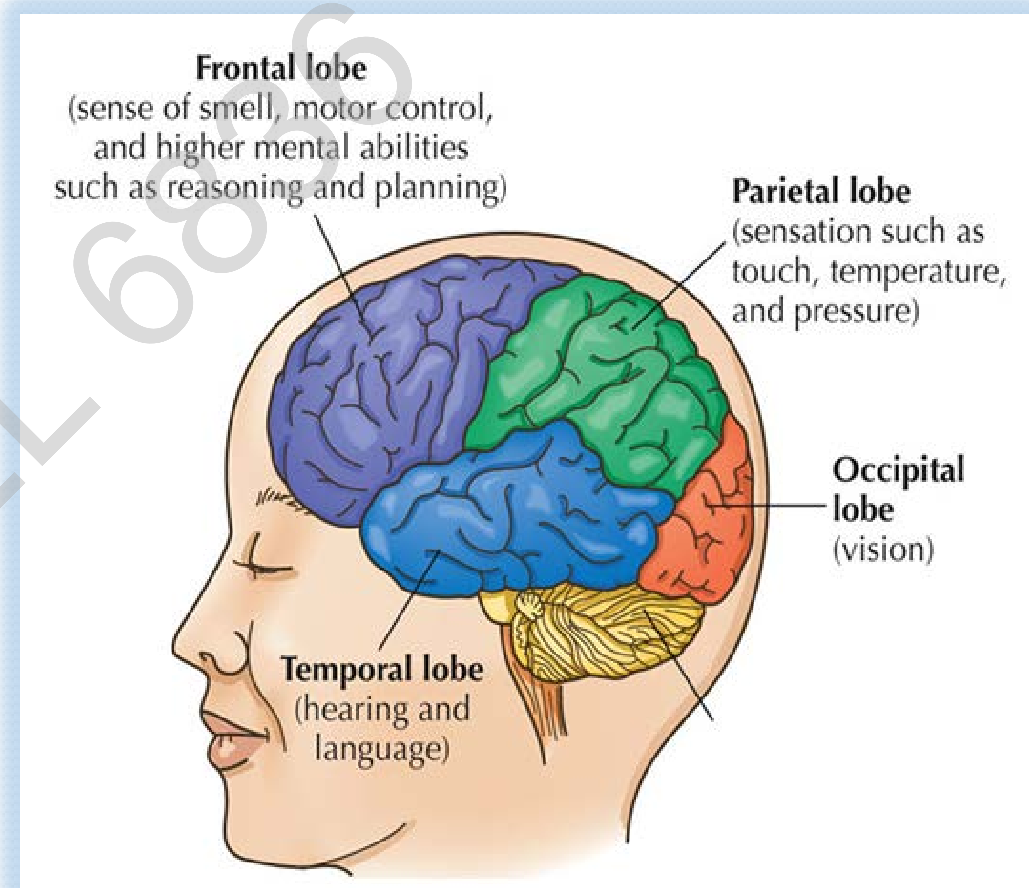




Brain Functionality (cont.)

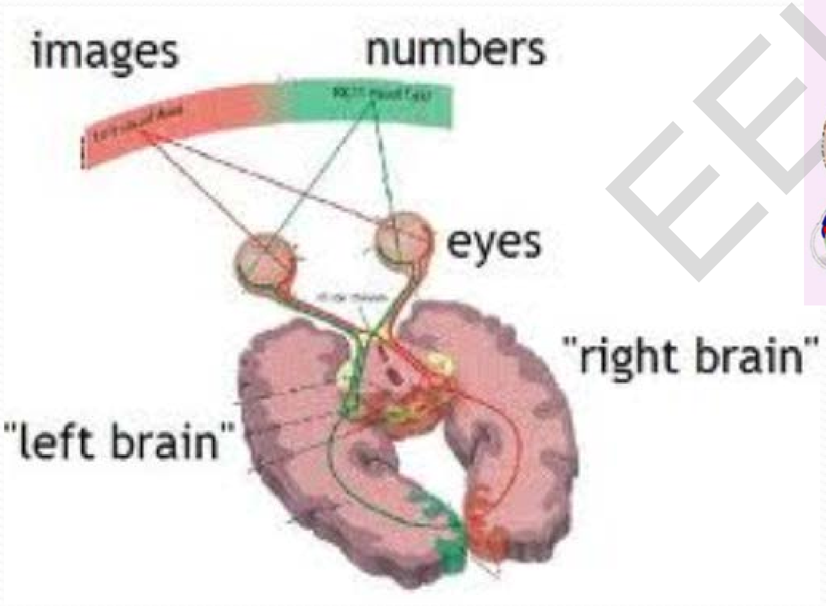
- The overall goal of the neurosurgeon is to maintain blood flow and oxygen to all parts of the brain, thus minimizing the damage and increasing the prospect of survival and recovery.

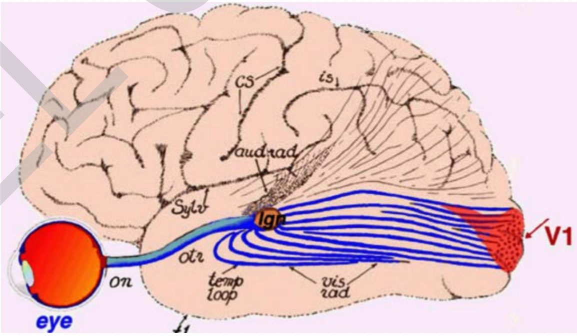
- If there is damage in any region, the functionality is gone.



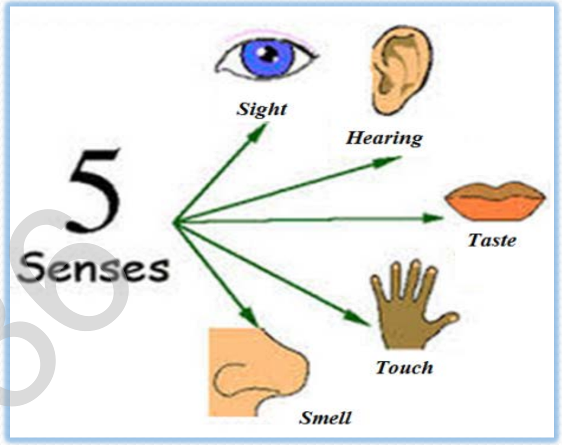
Visual Cortex

- Humans are primarily visual creatures.
- Brain regions not adjacent to one another are connected by long tracts of cellular projections called axons.





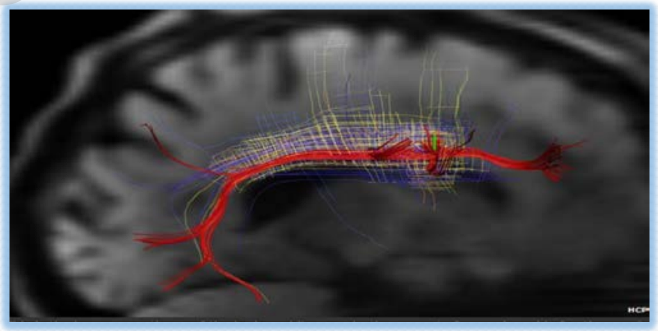
Enigma of seeing



- 75% of the information humans receive about our environment comes from our sight, making it the most 'important' of the five senses.

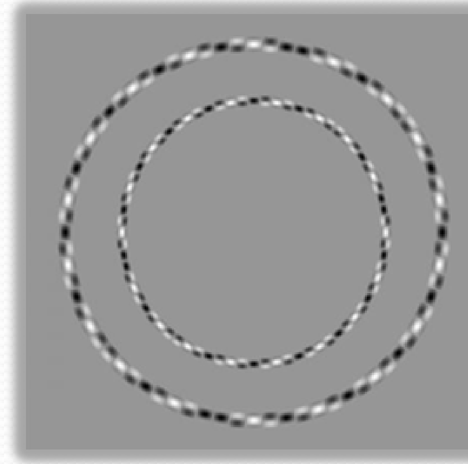
- The vision depends, on the EYES to see and on the BRAIN to make sense of what we see.

- The brain receives electrical impulses (stimuli) from our eyes which are interpreted as SIGHT, but the brain adds memory and interpretation.



- Sometimes the brain is deceived by information received from the eyes.
- Visual illusions are caused when differences occur between our perceptions or expectations and the image seen by the eye.

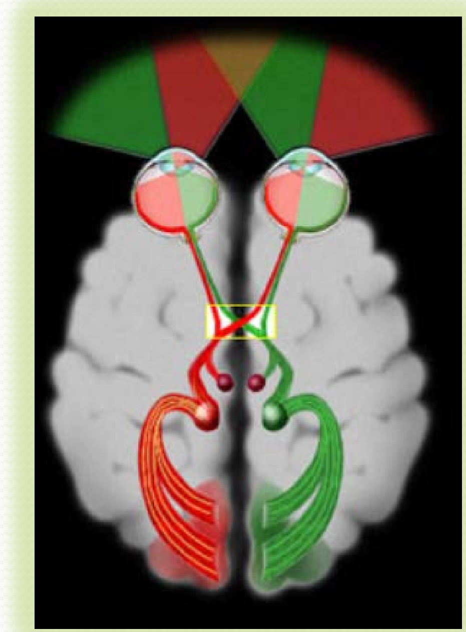
Physiological illusions



- Physiological illusions are the effects on the eyes or brain of prolonged stimulation of a specific type: brightness, tilt, color, movement. It is a physiological imbalance that alters perception.

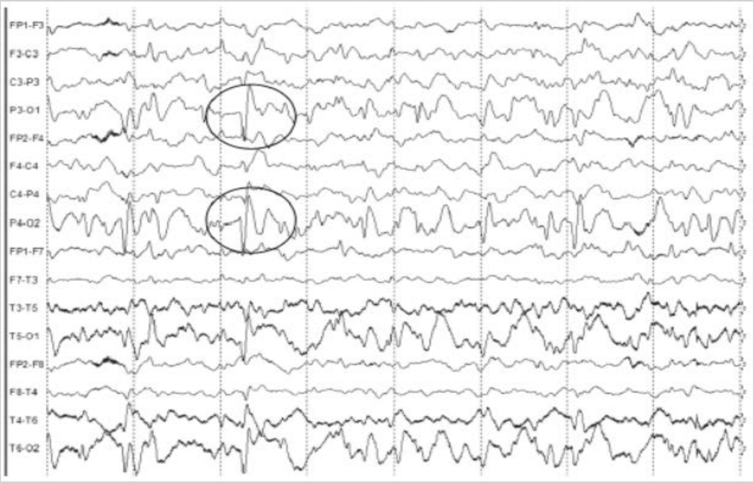
- The eyes and the brain have an interesting relationship. What we see is transferred to the brain and then the brain tells us exactly what our eyes transmitted is not the real case.

- One type of optical illusion is the physiological illusion. This type of illusion includes afterimages. Afterimages are really not "there," but the brain perceives them as being real because the brain was over stimulated.



Visual illusions

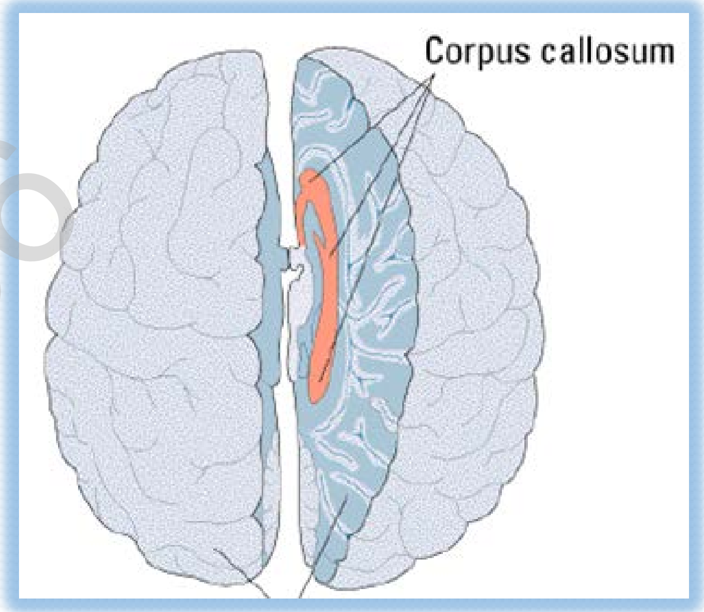
- Stimuli have individual dedicated neural paths in the early stages of visual processing and that repetitive stimulation of one or a few channels causes a physiological imbalance that alters perception.
- Optical illusions are characterized by visually perceived images that differ from objective reality.
- The information gathered by the eye is processed in the brain to give a percept that differs from the object being imaged.
- EEG responds to the optical illusion (Pz and Poz) have negative peaks. Latency and amplitude are different from regular VEP.
- Visual Illusions have a <u>smaller Latency</u> and <u>higher amplitude</u>.



Corpus Callosum

A <u>deep channel divides the cerebrum into two halves</u>, known as the left and right hemispheres. The two hemispheres look mostly symmetrical yet it has been shown that <u>each side functions slightly different than the other.</u>

The <u>**corpus callosum**</u> is a bundle of axons which connects these two hemispheres.



- Millions of axons connecting the brain's hemispheres.
- Provides a <u>pathway for communication.</u>
- Sometimes used to treat severed epilepsy.

Split Brain Patients

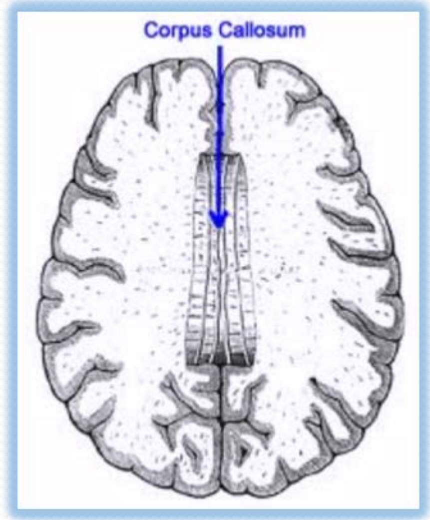
In the 1960s, surgeon Joe Bogen discovered that splitting the brain in half by cutting the nerves that connect the two hemispheres, the corpus callosum, reduced the intensity of epileptic seizures in monkeys without any major side-effects. He decided to use this surgical procedure on humans.

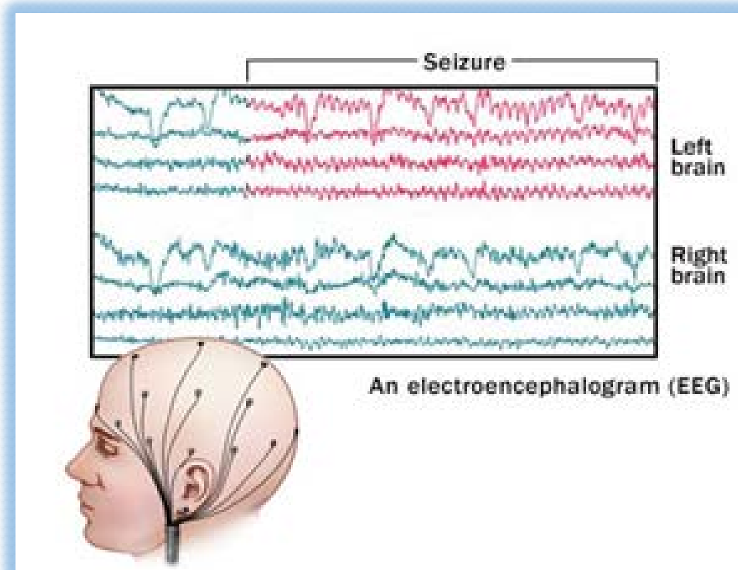
- Epileptic patients had corpus callosum cut to reduce seizures in the brain.
- Seizures reduced.
- Some side effects: Affected abilities related to naming objects in the left visual field.

Corpus Callosum

The corpus callosum helps the hemispheres share information, but it also contributes to the spread of seizure impulses from one side of the brain to the other. A corpus callosotomy is an operation that cuts the corpus callosum, interrupting the spread of seizures from hemisphere to hemisphere.

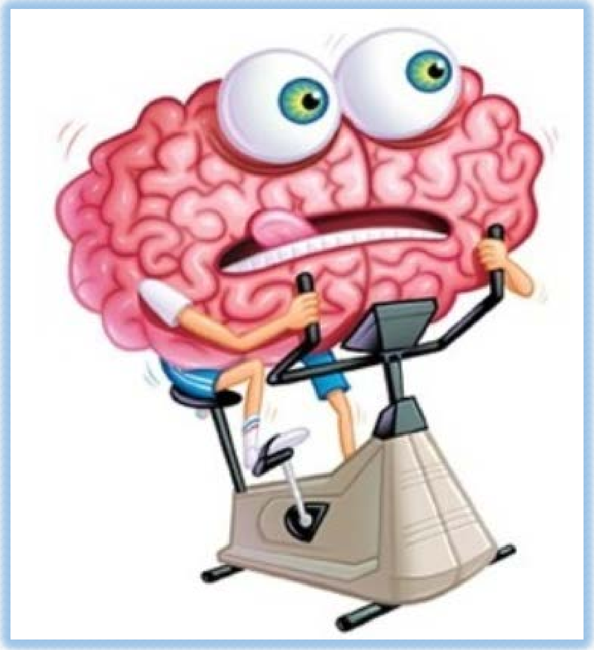
Seizures generally do not completely stop after this procedure (they continue on the side of the brain in which they originate). However, the seizures usually become less severe, as they cannot spread to the opposite side of the brain.





Brain Plasticity

- The ability of the brain to reorganize neural pathways based on new experiences.
- Persistent functional changes in the brain represent new knowledge.
- Age dependent component.



The brain's ability to remain flexible, alert, responsive and solution-oriented is due to its lifelong capacity for plasticity. **Before, it was thought that only infant brains were plastic.**

The brain is physically modified through strengthening, and elimination of existing connections, and the growth of new ones.

Why should I care about the brain?

Your brain is like your PC with one ***REALLY*** big difference. You can back up all the information on your PC. We ***DO NOT*** have a restore button. Once the neurons in our brains that held a particular memory or knew how to speak are gone we can't get them back. There is no restore button.

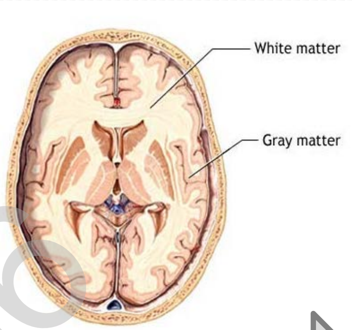
…..*Treat your brain well, you only get one.*

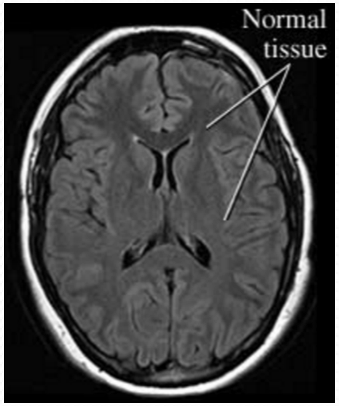
Brain Tissue

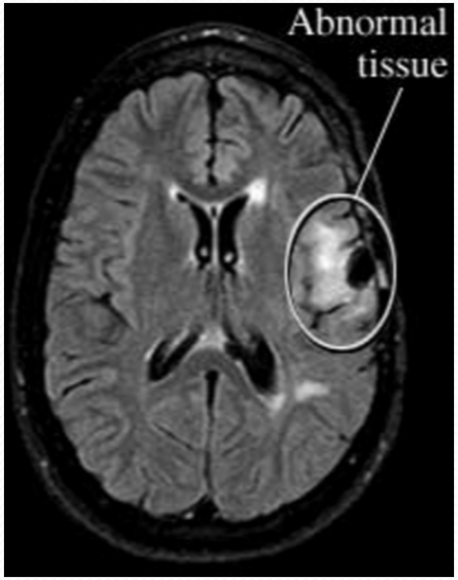
- Brain tissue is divided into two types:
  grey matter (GM) and white matter (WM).

- GM is made up of the cell bodies of nerve cells, dendrites, and axon terminals.

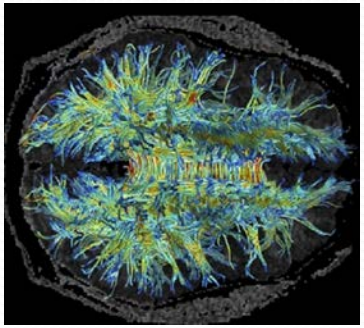
- WM is made up of the long filaments that extend from the cell bodies - the "telephone wires" of the neuronal network, transmitting the electrical signals that carry the messages between neurons.







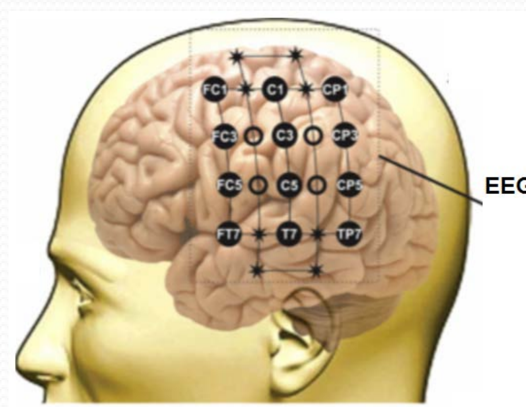
GM+WM+CSF=1500-1700 ml (avg)

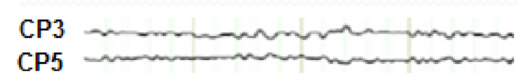


WM (fiber tracts)

MRI

- What is an MRI?
  - Magnetic resonance imaging is an image of the structure of the brain. Intense magnetic fields and radio waves are used to make images of the inside of the head.
  - Produces no radiation.
  - Provides a detail view of the brain in different dimensions.
  - Safe, painless, and non-invasive.
  - No special preparation.

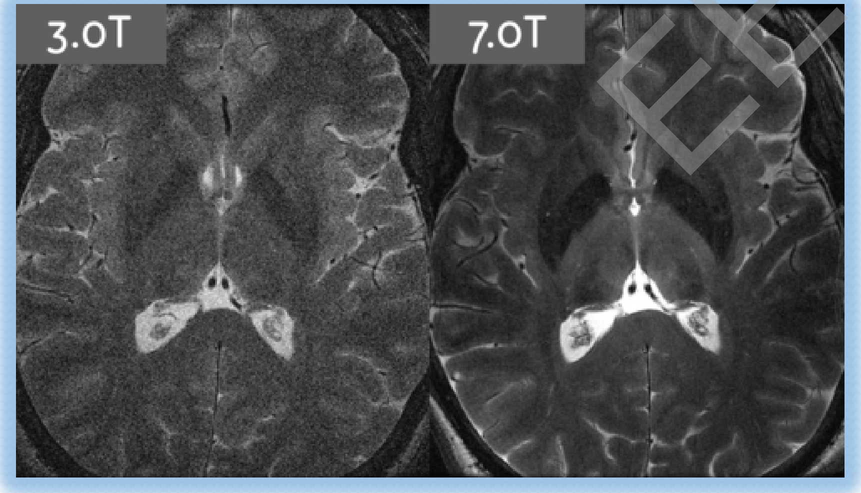




MRI

MRI machines look like a large block with a tube running through the middle of the machine, called the bore of the magnet.

MCH Philips 1.5 T

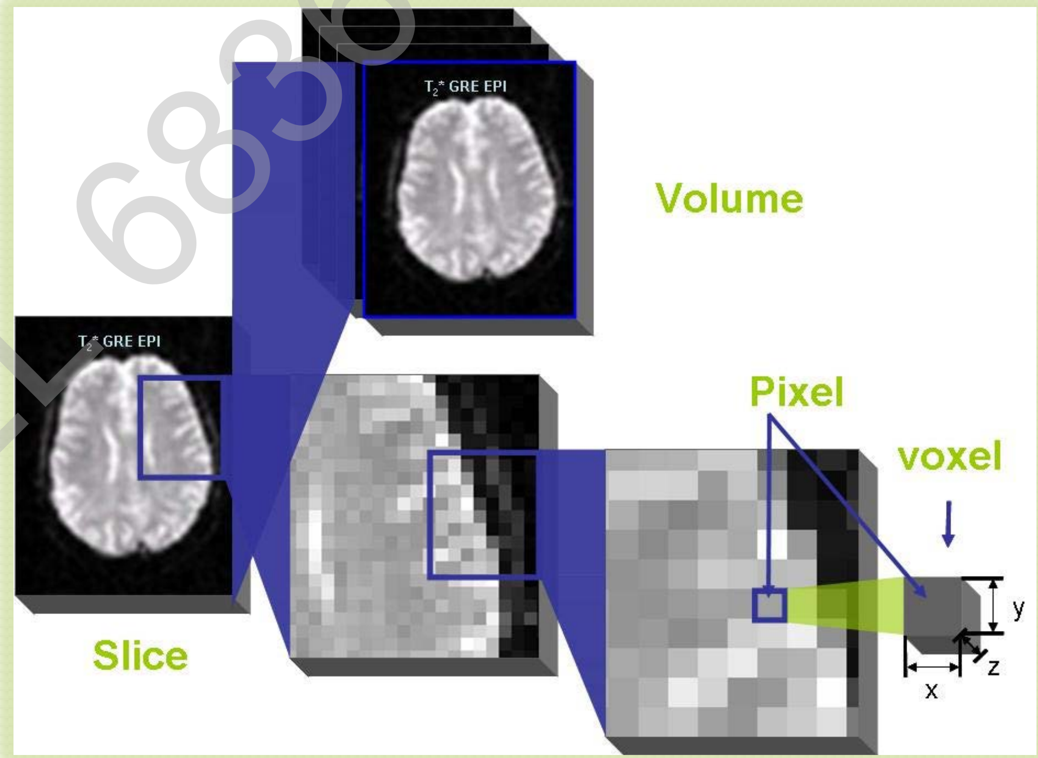


The bore is where the patient is located for the duration of the scan.

MRI Parameters

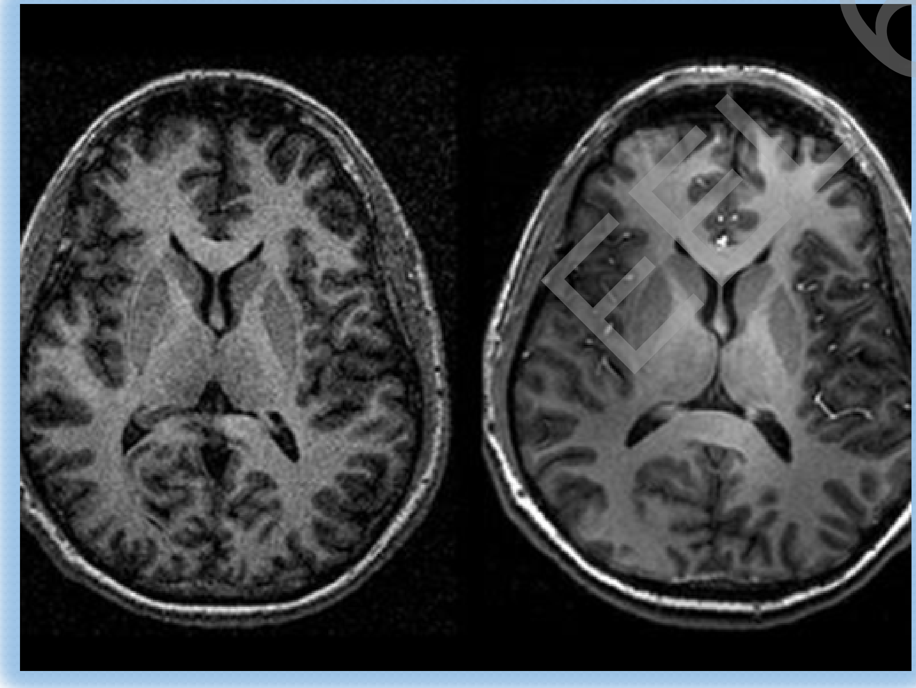
- The relationship between volume, slice and a voxel in an image.

- In general, voxels carry the same color-intensity properties as pixels.



MRI Components

- T1-weighted: most useful
- It provides grey/white/CSF delineation
- Acquisition: 5-10 minutes
- Excellent for demonstrating anatomy



MRI Basics:

•Components: Magnet, antenna, PC, software

•Magnet “ON” and “OFF” to change directions in the magnetic field

•Water molecules spin around, they give pulse in a form of Radio waves.

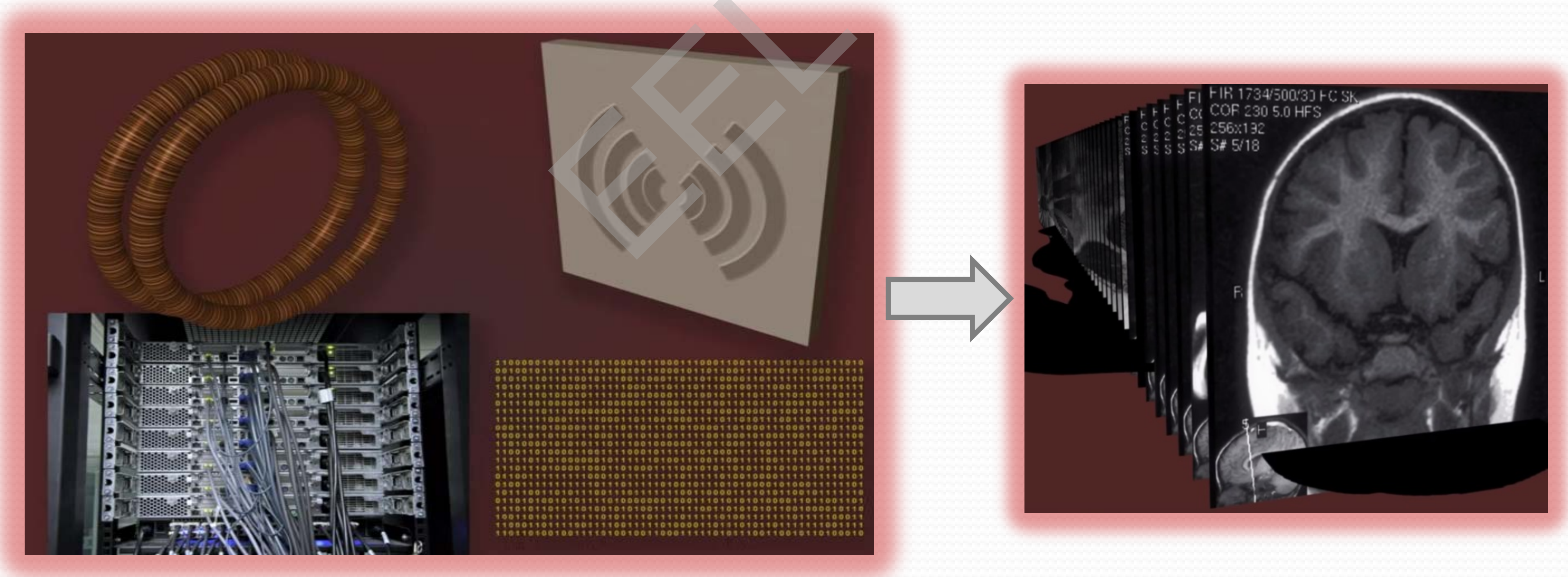
•Antenna will collect data and detect radio signal when water molecules spin.

•Pictures out of the radio signal.

MRI (cont.)

- The MRI machine picks points in the patients head, decides what type of tissue the points define, then compiles the points into 2 dimensional and 3 dimensional images.

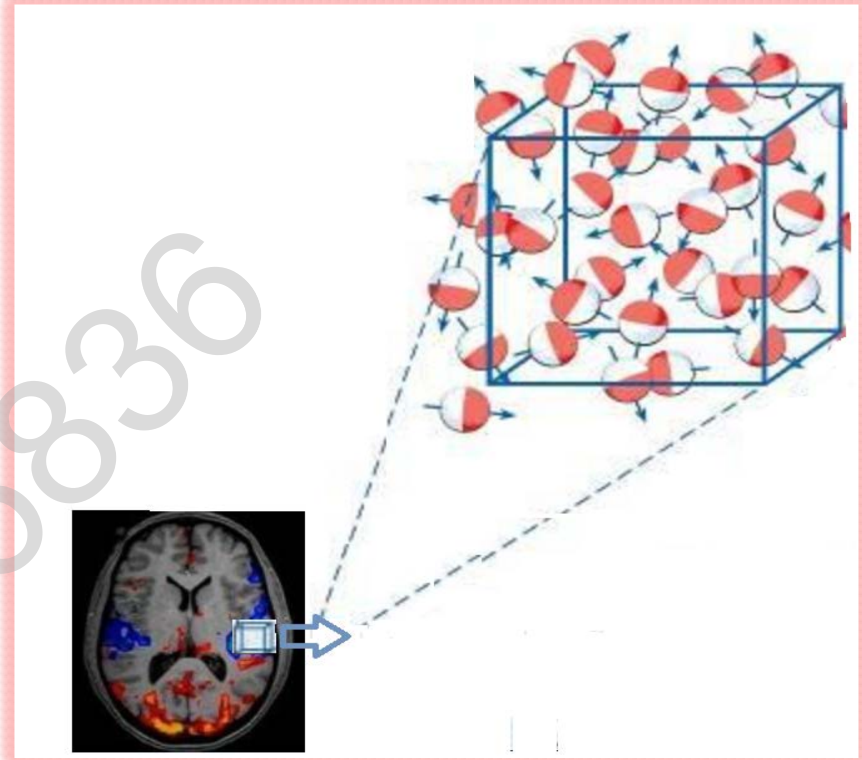
- Once the 3 dimensional image is created, the MRI machine creates a model of the tissue.

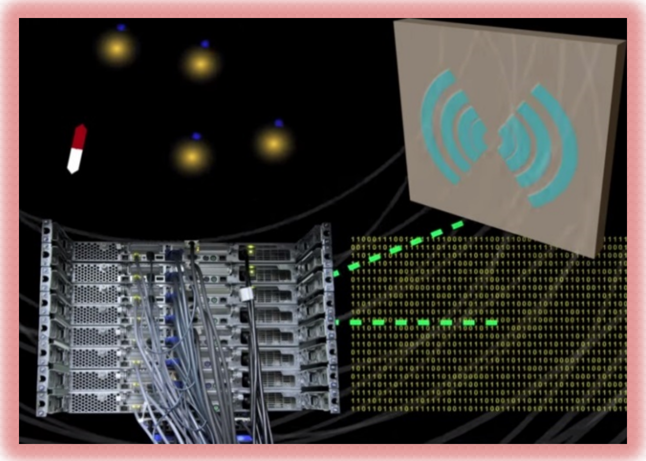


MRI (cont.)

The tissues with the help of the magnetic field send a signal to the computer.

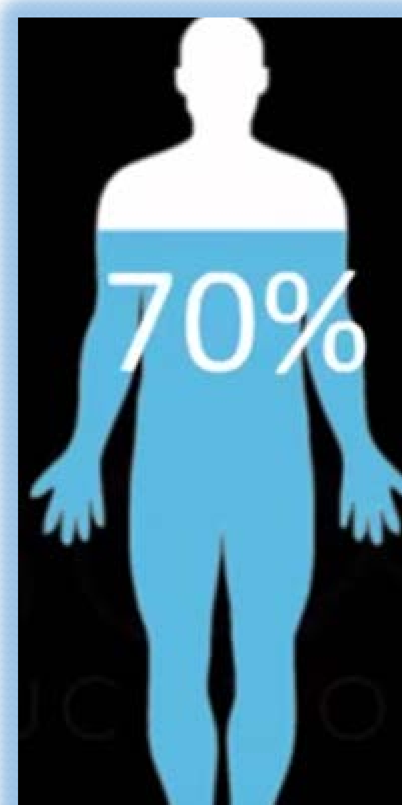
The different signals are sent and modified into images that the clinicians can evaluate, and label as normal or abnormal.

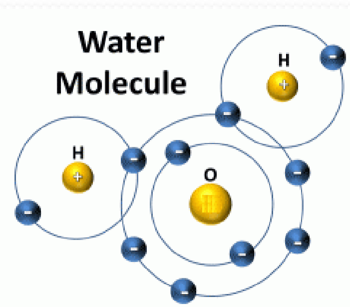


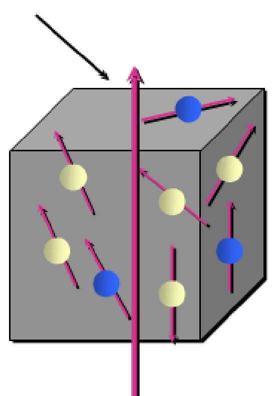


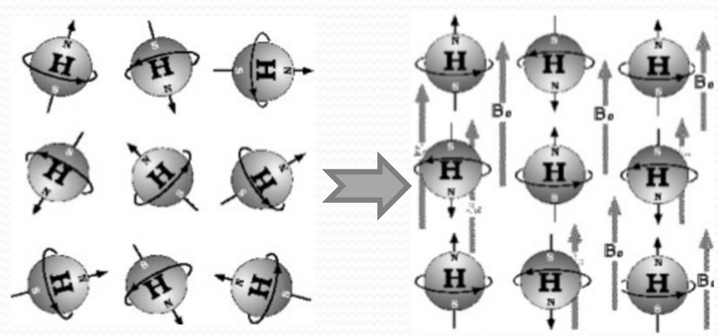
What does the image represent?

- For every unit volume of tissue, there is a number of cells, these cells contain water molecules, each water molecule contain one oxygen and two hydrogen atoms.
- Different tissues thus produce different images based on the amount of their hydrogen atoms producing a signal.
- Moving proton induces a signal in the RF antenna(irritates and responds).
- Signal is picked up and sent to the computer system.









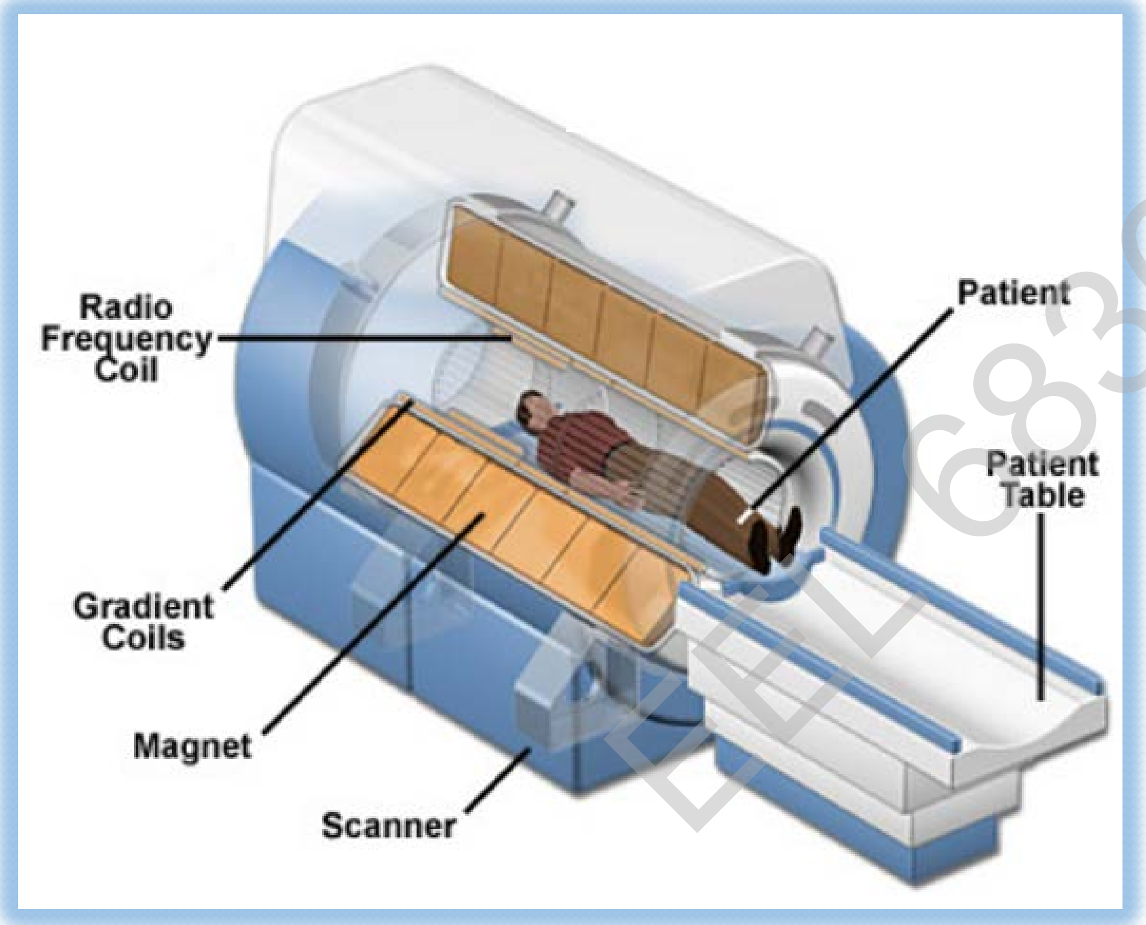
MRI Frequency

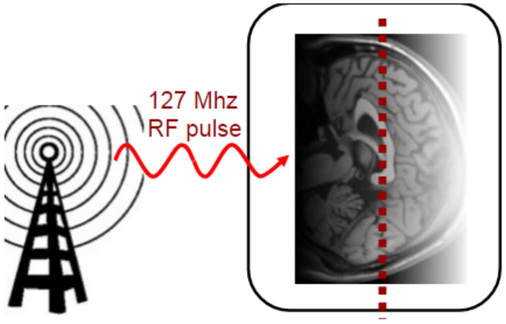
- MRI involves the absorption and emission of energy by nuclei(H+) at a specific resonant *(Larmor) frequency.*
- Larmor frequency scales directly with main magnetic field strength (Bo), and for clinical MRI lies in the range of tens to hundreds of MHz.
- These frequencies are part of the electromagnetic spectrum commonly used for radio transmission.

1.5 T= 63.9 Mhz

3.0T=127.8 MHz

MRI

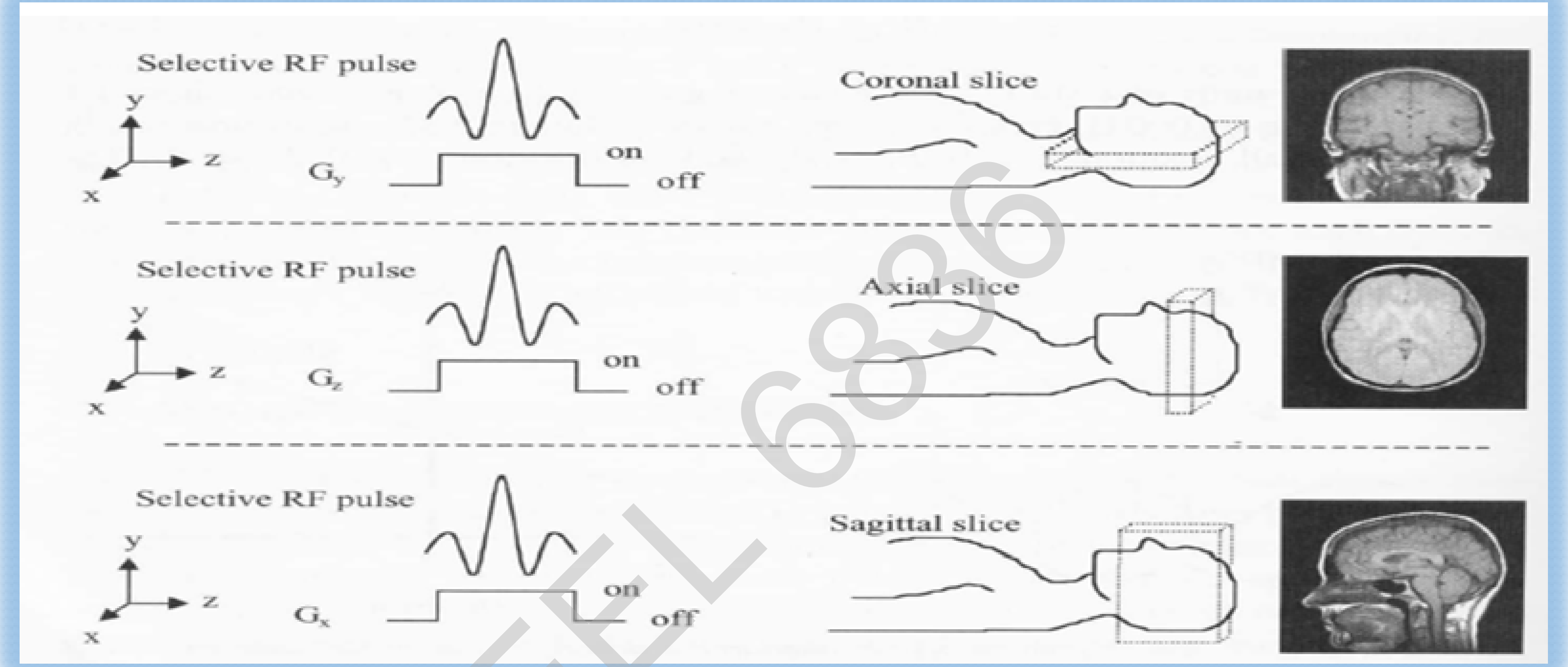




The MR signal in MRI is produced by the process of resonance, which is the result of radiofrequency coils.

- Two electromagnetic coils: transmitter and receiver coils generate and receive electromagnetic fields.
- Atomic nuclei of interest in MRI studies have their own resonant frequencies, in the radiofrequency portion of the electromagnetic spectrum.

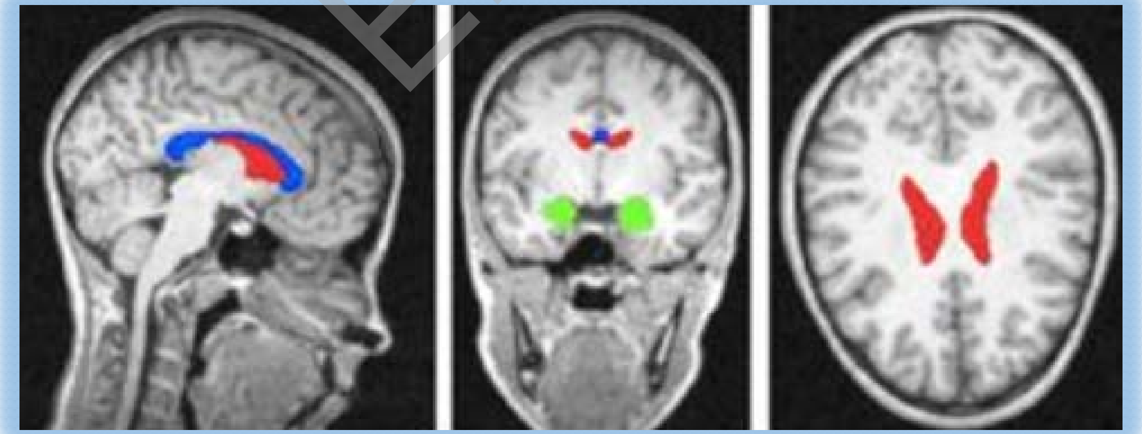
MRI (cont.)



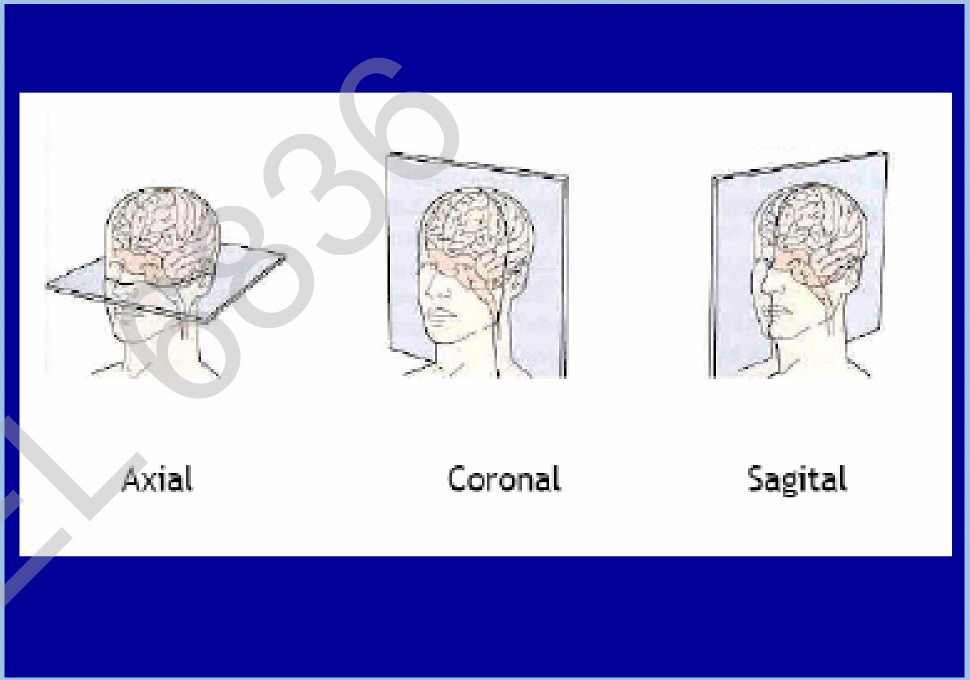
- The RF pulses are applied through a coil that is specific to the part of the body being scanned.
- When Radio waves are turned off, protons realign and in doing so, send out radio signals which are picked up by receivers.
- Protons in different tissue types produce different signals.
- Signals from millions of protons in the brain can create a detailed image of the brain tissue.

MRI Imaging Planes

- **CORONAL, AXIAL, SAGITAL**
- The brain, like all biological structures, is 3 dimensional. Any point on or inside the brain can be localized on three "axes" or "planes" - the x, y and z axes or planes.
- The brain is often cut ("sectioned") into pieces for further study. These slices are usually made in one of three planes: the coronal plane, the horizontal plane or the sagittal plane.



MRI Imaging Planes

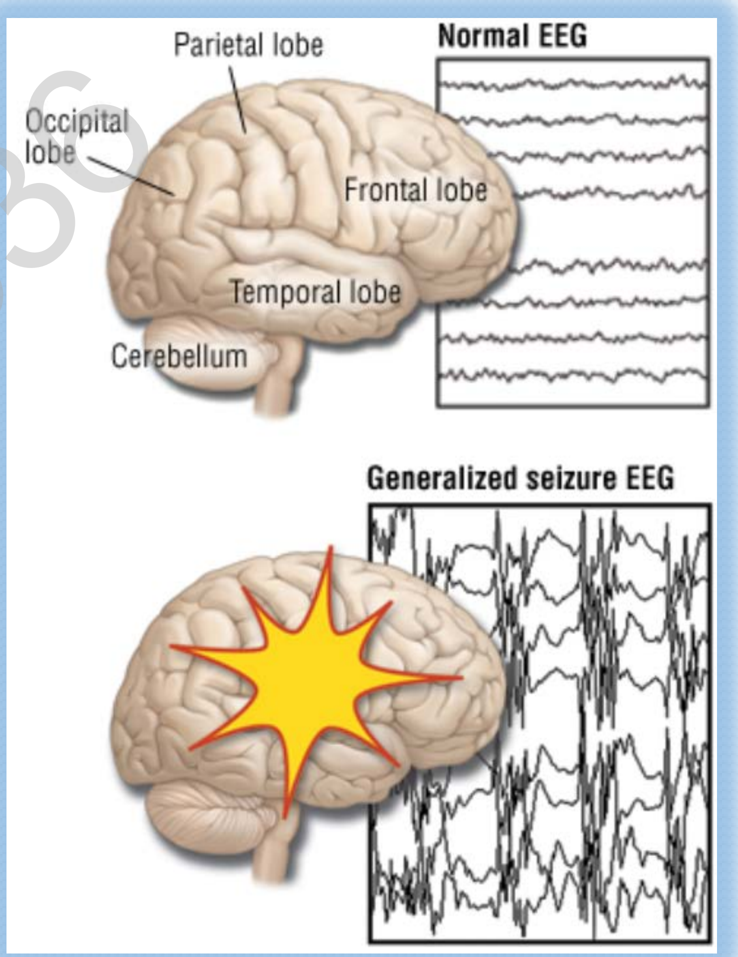


When analyzing medical images, please note that sometimes the left side of the picture is the right side of the patient. This does not always apply, but doctors need to be certain before making any assessment.

Surgical Candidates Selection Criteria

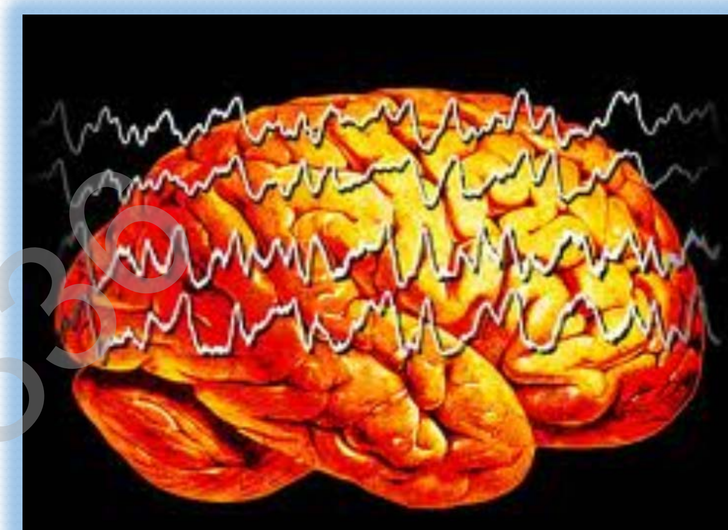
- Seizures can be well controlled with appropriate medication. <u>However, **20-30%** of patients with epilepsy are refractory to all forms of medical therapy</u>.

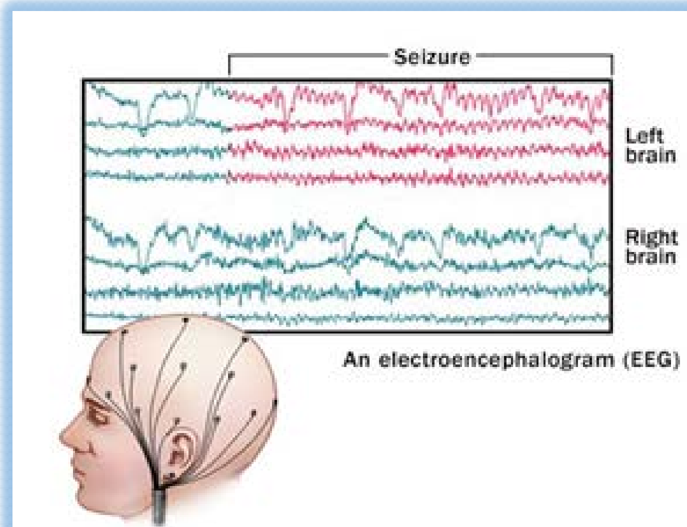
- Another group of patients who might benefit from a surgery are those whose seizures may be relatively well controlled but who have certain characteristic <u>presentations or lesions</u> that strongly suggest surgical intervention might be curative.



Surgery Outcome

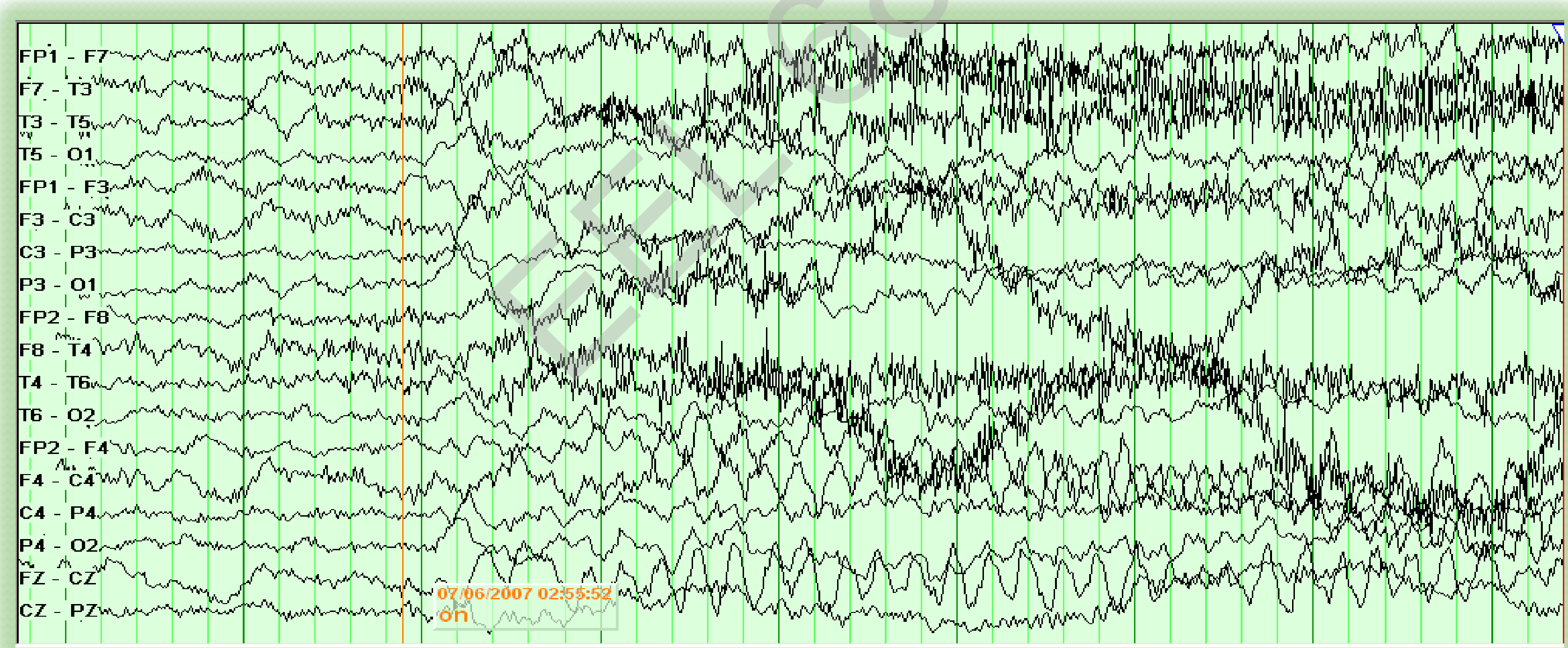
- Overall, the single most important determinant of a successful surgical outcome is <u>patient selection</u>.
- This requires <u>detailed pre-surgical evaluation</u> in order to select the most appropriate treatment from a variety of surgical options.
- <u>Evaluation includes:</u>
  - <u>seizure type</u>
  - <u>frequency</u>
  - <u>site of onset</u>
  - <u>psychosocial functioning</u>
  - <u>degree of disability</u>





Seizure

- There are many **types of seizures** and different forms of epilepsy.
- A seizure is defined as a change in behavior associated with excessive electrical discharge from the central nervous system.

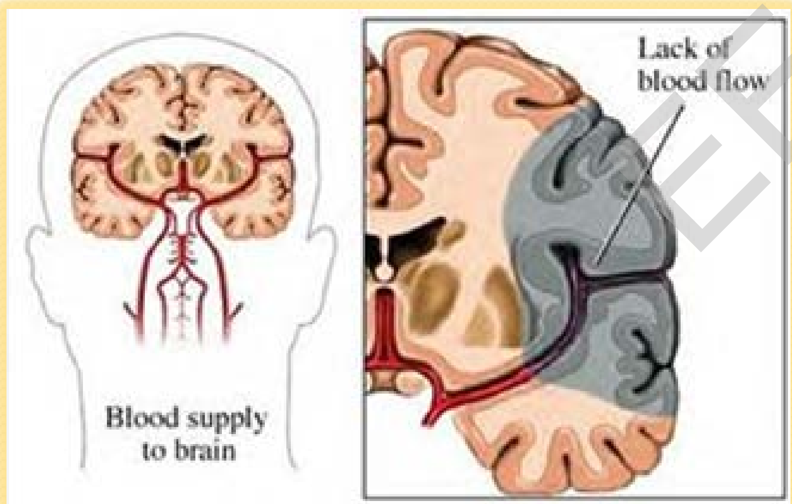


Scalp EEG containing the transition from interictal to ictal state.

Epilepsy (cont.)

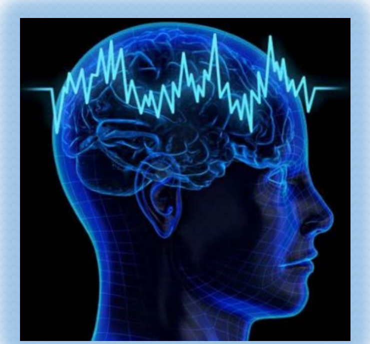
- If too many brain cells are sending signals at the same time, it causes an overload, and a person may pass out.

- A classification, divides the clinical epilepsies into **idiopathic and symptomatic** forms based upon their presumed etiologies.



Status epilepticus is either a seizure lasting longer than 30 minutes or repeated seizures without a return to normal in between them. It is most common in children younger than 2 years. It could damage the brain because of the lack of oxygen to the brain.

Classification of Epileptic Syndromes



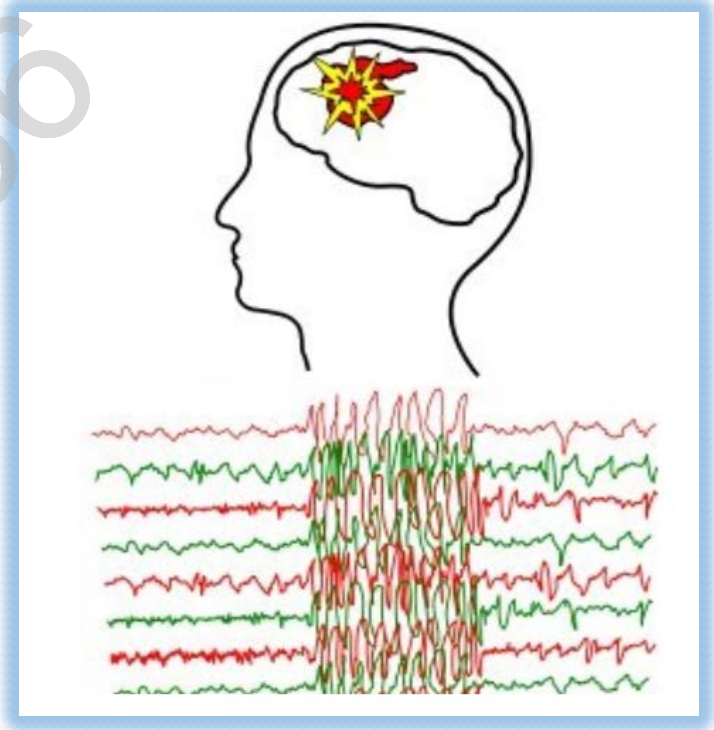
- Idiopathic forms include some of the generalized seizure types that do not have a prominent genetic component. Seizures that occur without an identifiable cause in a patient with entirely normal findings on neurologic examination and of normal intelligence. Unknown cause. Normal background EEG activity.

- Symptomatic forms are those caused by a recognized central nervous system lesion (brain damage). Interictal background EEG frequencies that are slower than normal.

Note: The ability to place a patient in one or another of the syndromic categories has the advantage of providing a basis for predicting long term prognosis.

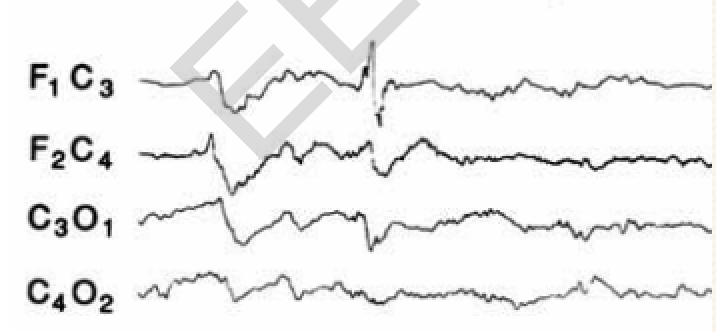
Seizures in Children

- A seizure occurs when the brain functions abnormally, resulting in a change in movement, attention, or level of awareness.
- Different types of seizures may occur in different parts of the brain and may be localized (affect only a part of the body) or widespread (affect the whole body). Seizures may occur for many reasons, especially in children.
- Seizures in newborns may be very different than seizures in toddlers, school-aged children, and adolescents.
- Seizures, especially in a child who has never had one, can be frightening to the parents.



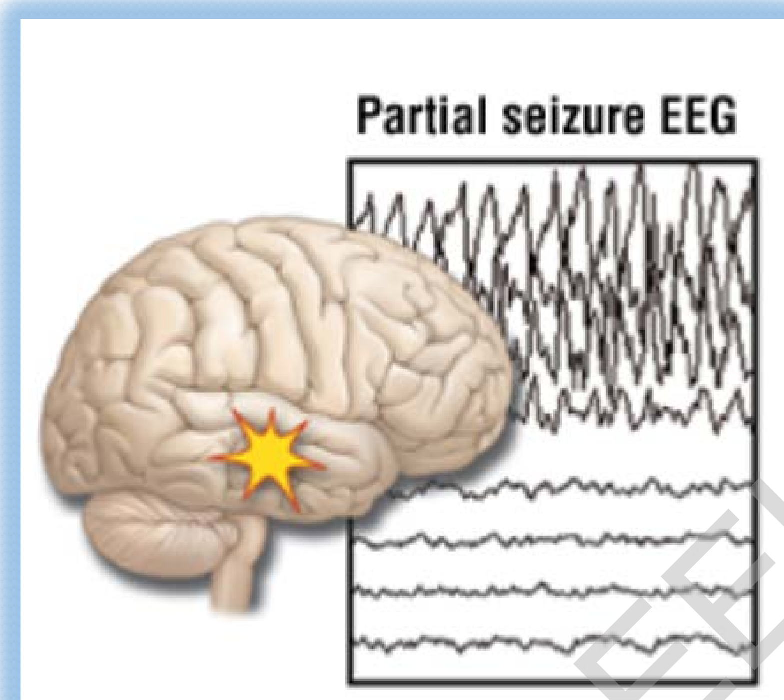
Types of seizures

- **Neonatal seizures** occur within 28 days of birth. Most occur soon after the child is born. They may be due to a large variety of conditions. Persistent focal abnormalities suggest focal structural lesions: EEG Sharp waves, Voltage asymmetry and Focal slow.



Note: *It may be difficult to determine if a newborn is actually seizing, because they often do not have convulsions. Instead, their eyes appear to be looking in different directions. They may have lip smacking or periods of no breathing.*

Partial Seizures

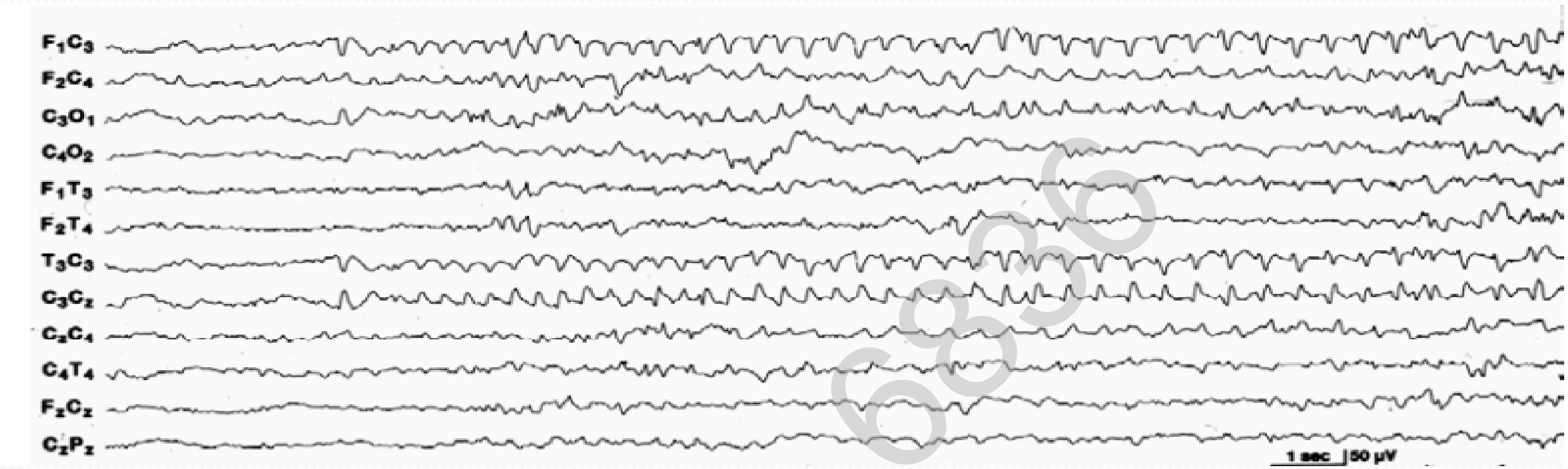


Partial seizures involve only a part of the brain and therefore only a part of the body.

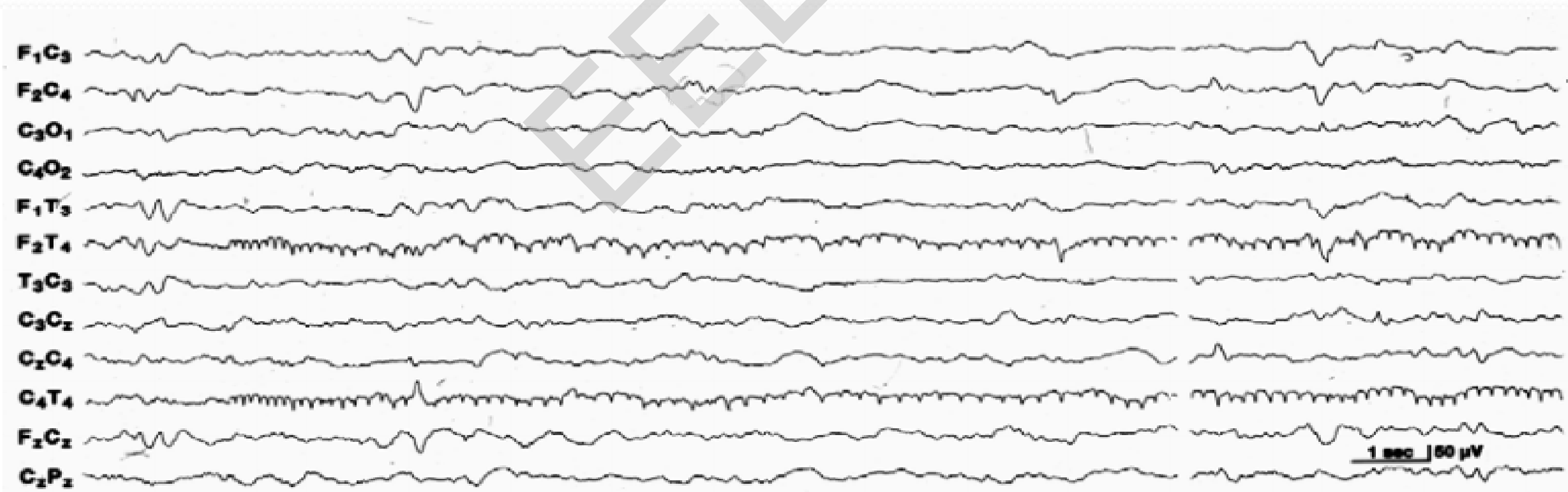
Simple partial seizures have a motor (movement) component that is located in one portion of the body. Children with these seizures remain awake and alert.

Complex partial seizures are similar, except that the child is not aware of what is going on. Frequently, children with this type of seizure repeat an activity, such as clapping, throughout the seizure. They have no memory of this activity. After the seizure ends, the child is often disoriented in a state known as the postical period.

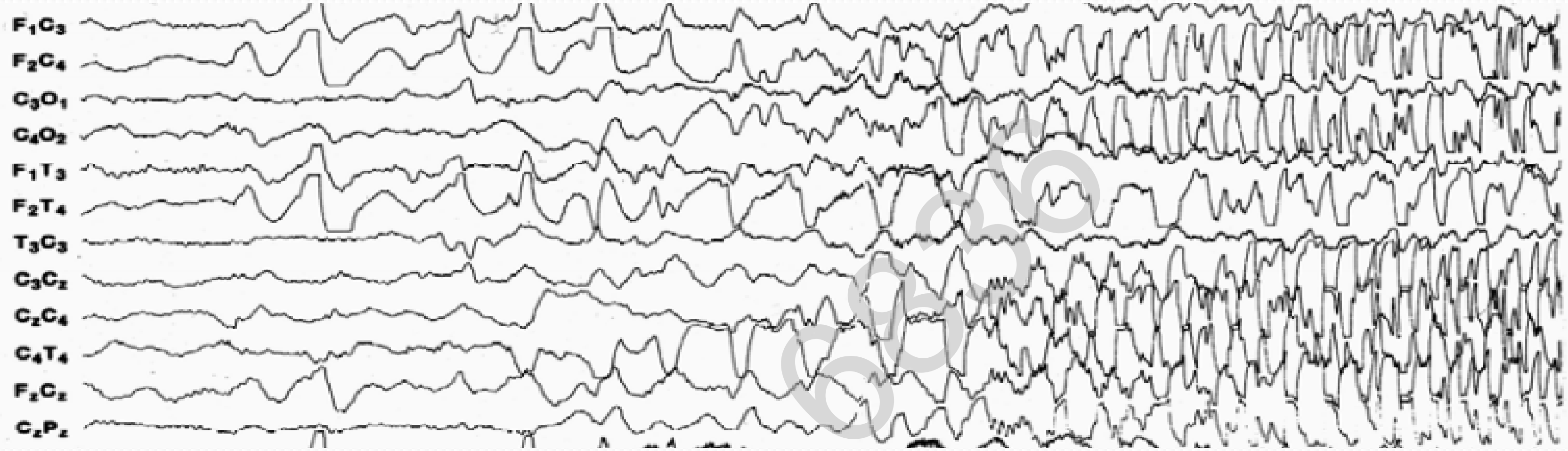
Central Onset of Electrical Seizure Activity



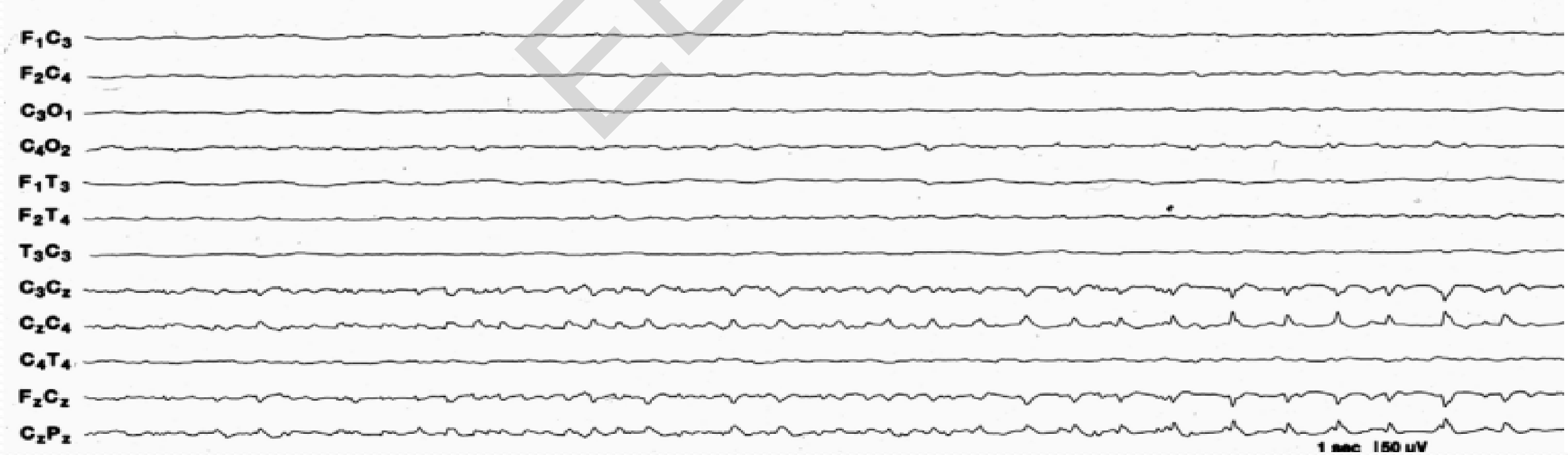
Central Onset of Electrical Seizure Activity



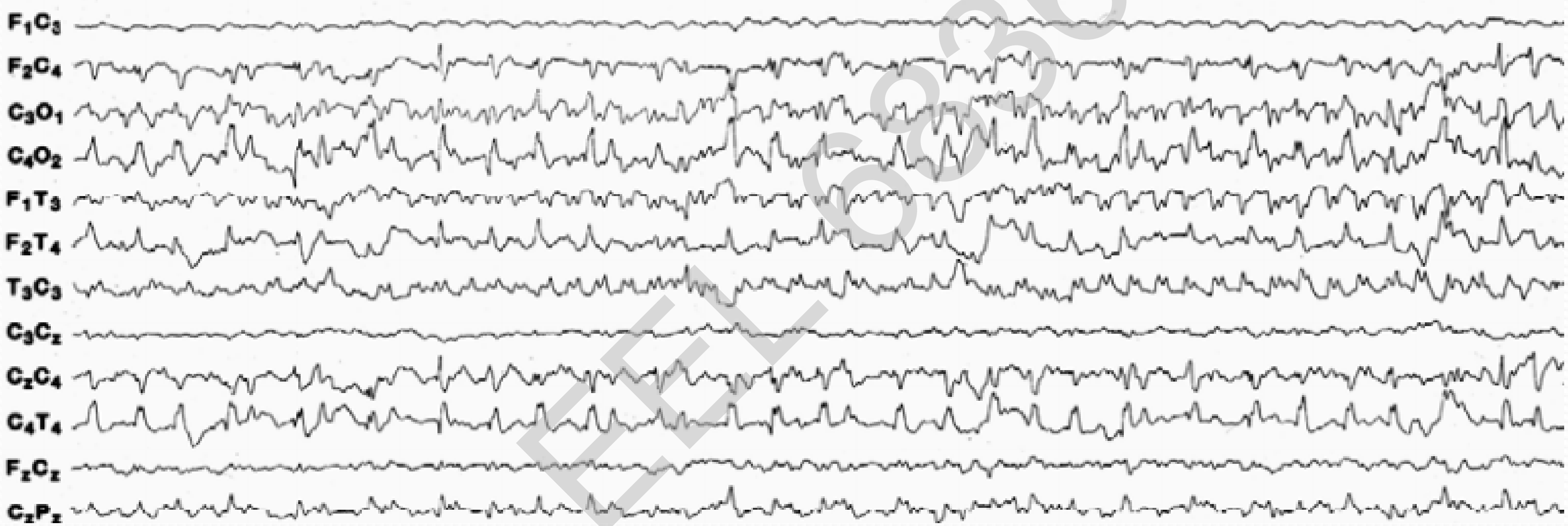
Frontal Onset of Electrical Seizure Activity



Midline Central Onset of Electrical Seizure Activity

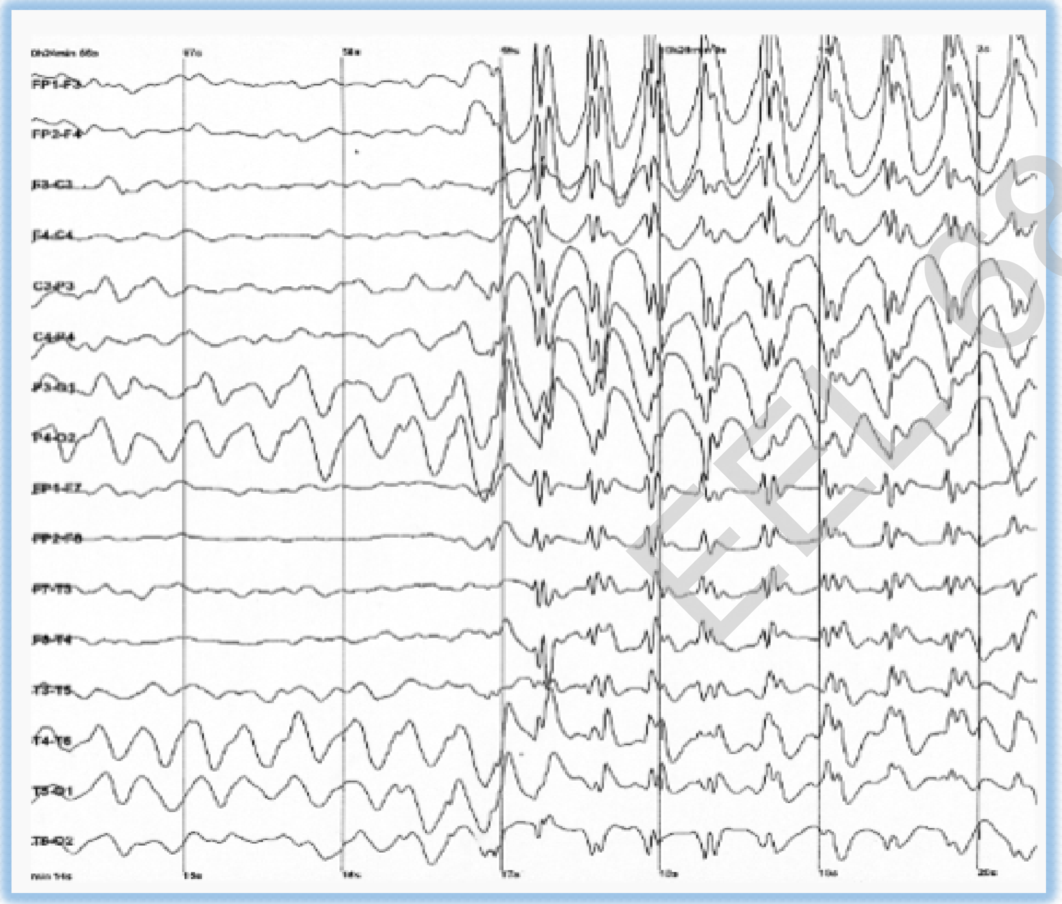


Multifocal Electrical Seizure Activity

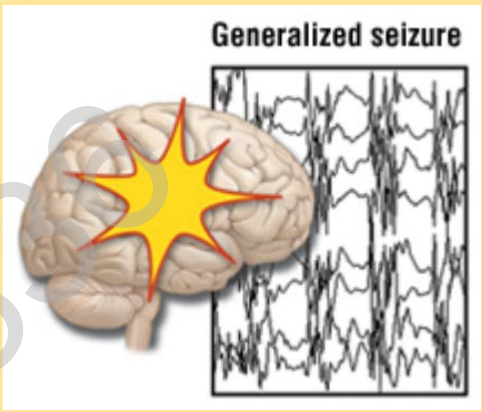


Types of seizures (cont.)

Generalized seizure



Maximal spikes amplitudes in the frontal regions



Generalized seizures:

Involve a much larger portion of the brain.

They are grouped into 2 types:

- convulsive (muscle jerking)
- Non-convulsive with several subgroups.

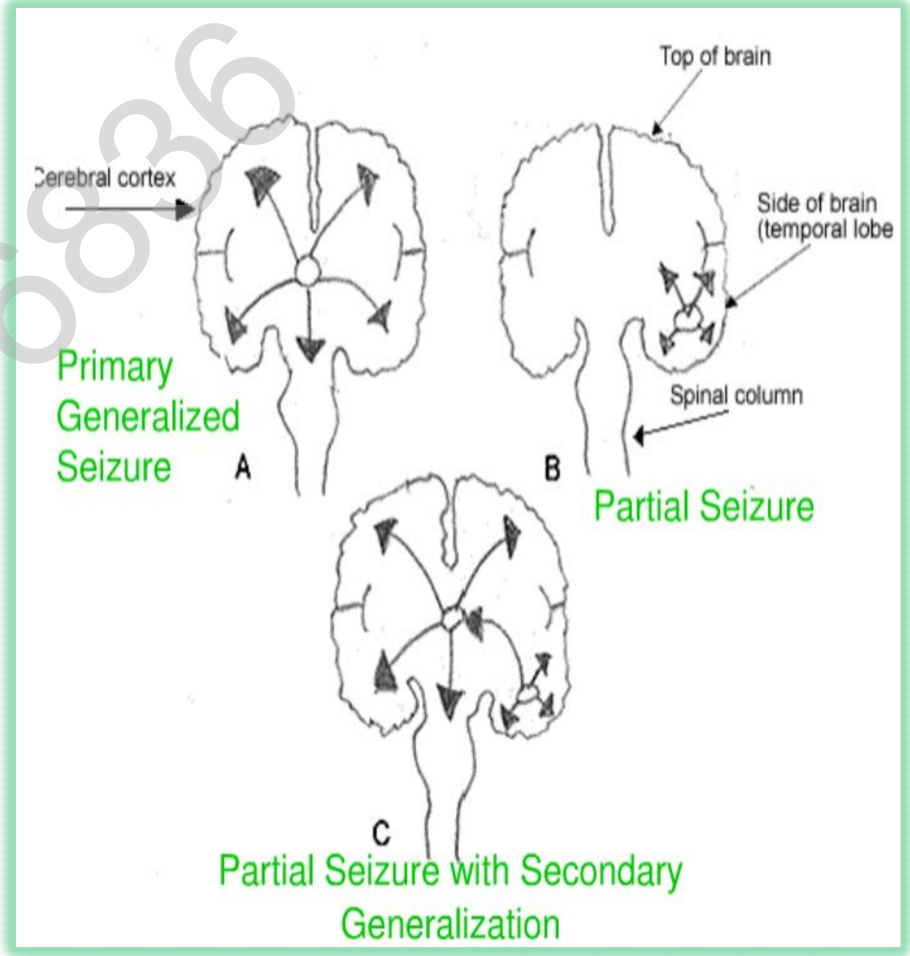
Types of seizures (cont.)

Convulsive seizures are noted by uncontrollable muscle jerking lasting for a few minutes-usually less than 5 followed by a period of drowsiness that is called the post-ictal period.

-**Tonic seizures** result in continuous muscle contraction in the arms and legs.

-**Absence seizures** are short episodes during which the child stares or eye blinks, with no apparent awareness of their surroundings. EEG generalized 3-Hz spike-and-wave complexes

These episodes usually do not last longer than a few seconds and start and stop abruptly.



Types of Epilepsy

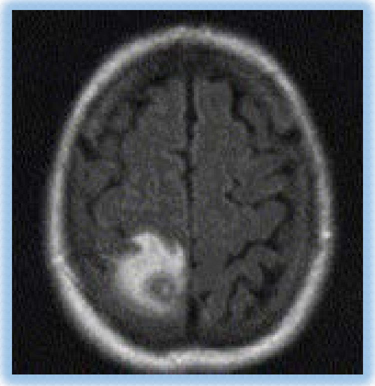
- **Temporal lobe epilepsy**, is the most common type of epilepsy in teens and adults, the area where the seizures start (called the seizure focus) is located within the temporal lobe.

- **Extratemporal** means the tissue is located in an area of the brain other than the temporal lobe. The frontal lobe is the most common extratemporal site for seizures. In some cases, tissue may be removed from more than one area/lobe of the brain.

Cortical resection is an operation to resect, or cut away, brain tissue that contains a seizure focus.

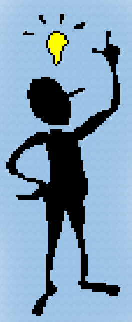
Major surgical Questions

The goal of epilepsy surgery is to identify an abnormal area of cortex from which the seizures originate and remove it without causing any significant functional impairment.



The primary components of the pre-surgical evaluation includes:

-detailed clinical history and physical examination,
-advanced neuro-imaging,
-video-EEG monitoring,
-neuropsychological testing and assessment of psychosocial functioning.

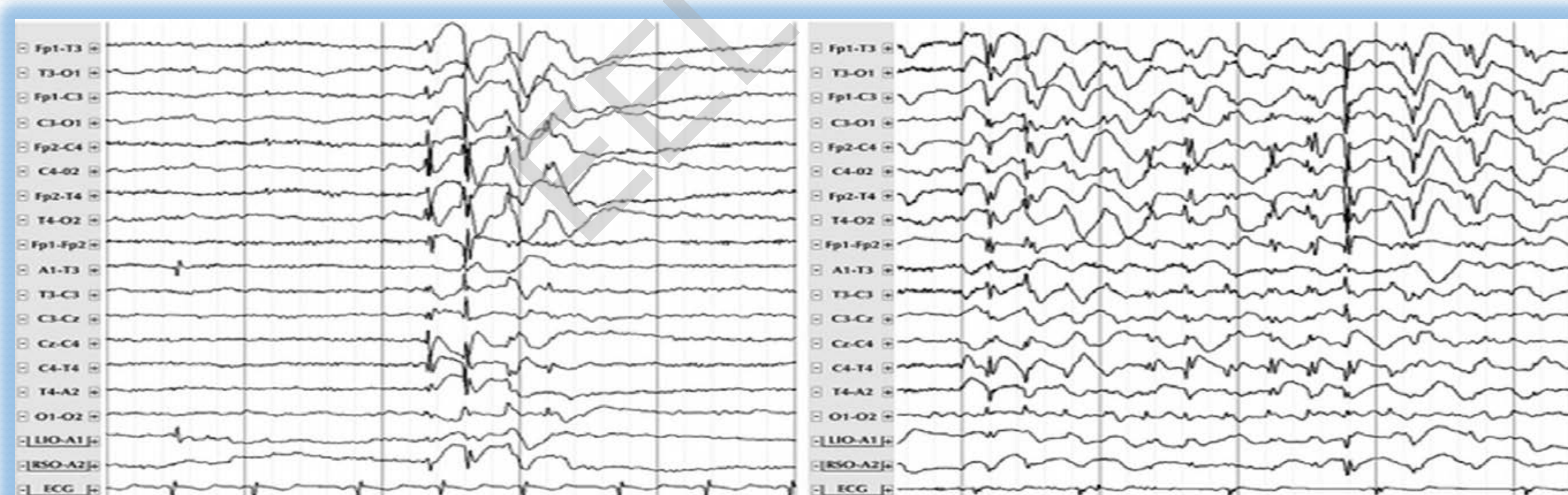


The major surgical questions one hopes to answer with this evaluation are:

1) Are the seizures focal or generalized?
2) If focal, are they temporal or extra-temporal in origin?
3) Is there a lesion associated with the seizures?
4) If surgery is undertaken what functional deficits, if any, might be anticipated?

EEG and Epilepsy

- Electroencephalographic (EEG) investigation remains the <u>most important aspect of the pre-surgical evaluation.</u>
- Analysis of selected EEG activity between events (interictal) or of specific activity during events (ictal) can provide <u>evidence of focal electrical dysfunction</u>.

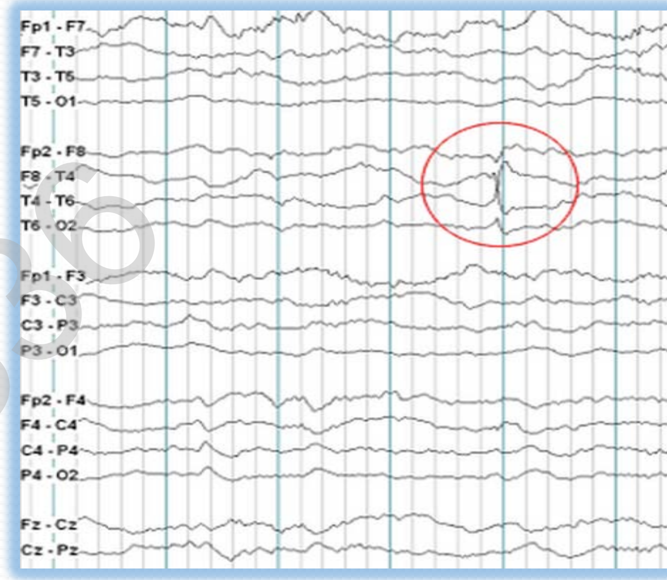


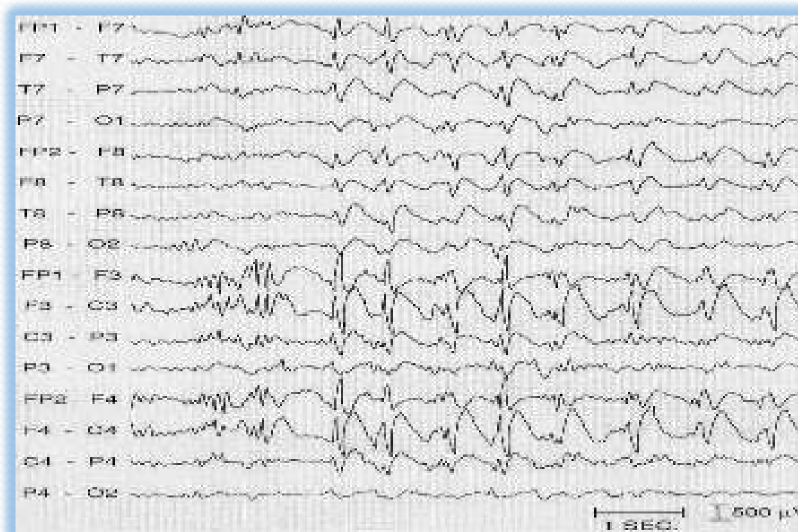
interictal ictal

EEG and Epilepsy

- Certain <u>interictal EEG abnormalities</u> (spike and slow wave complexes) can be of <u>localizing value</u>, it is considered extremely important to record the EEG with concomitant <u>videotape</u> during the spontaneous occurrence of the patient's events.

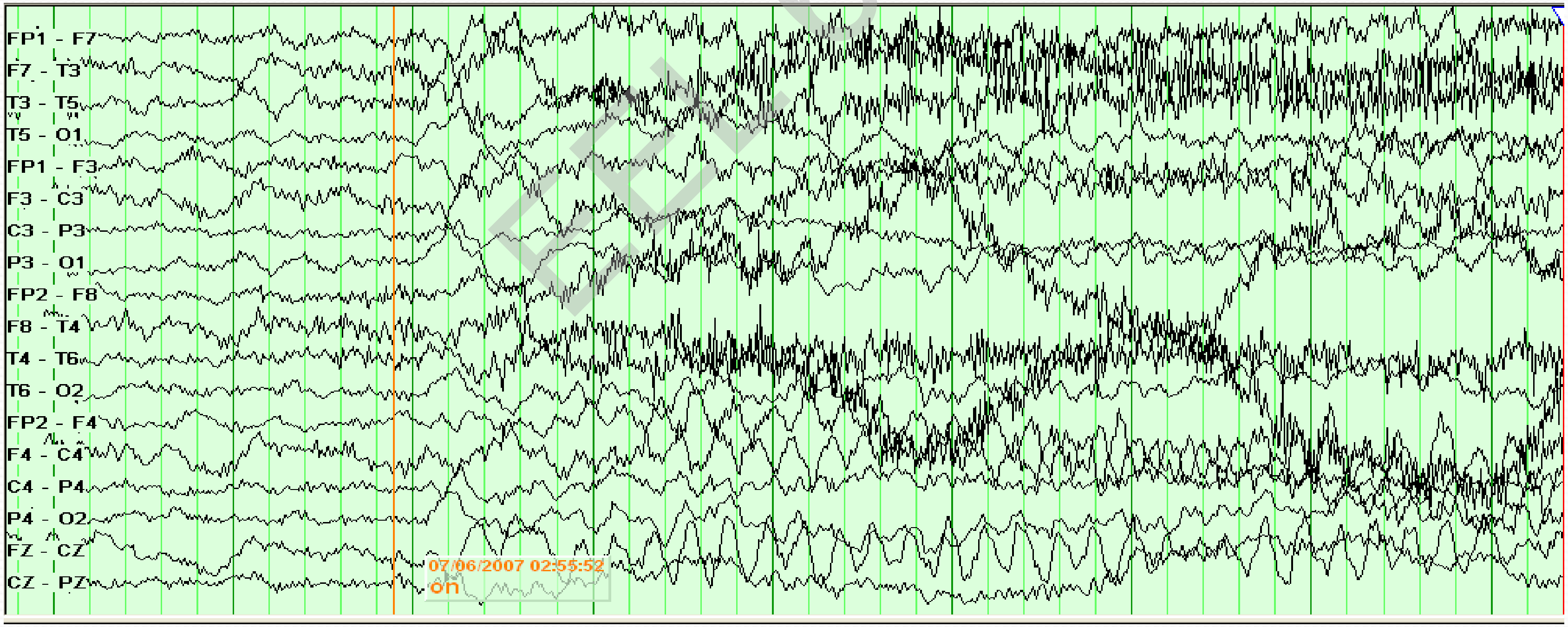
- Video/EEG monitoring can continuously record the EEG over a 24 hour period which allows for <u>careful inspection of the record during</u> any event.



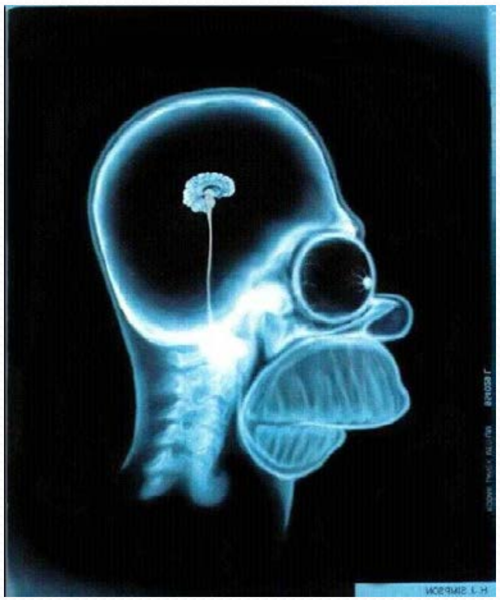


Epileptic Focus

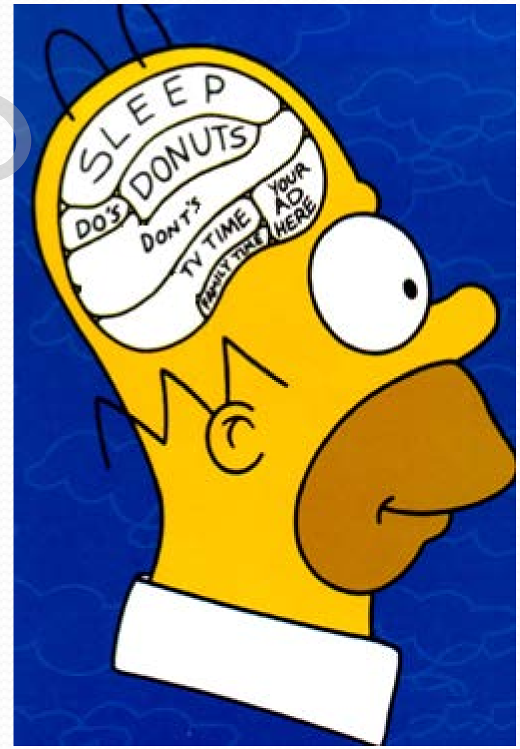
<u>EEG activity at the very beginning of the seizure</u> before spread to adjacent areas is most important in terms of localization.



Structural MRI vs. *Functional* MRI

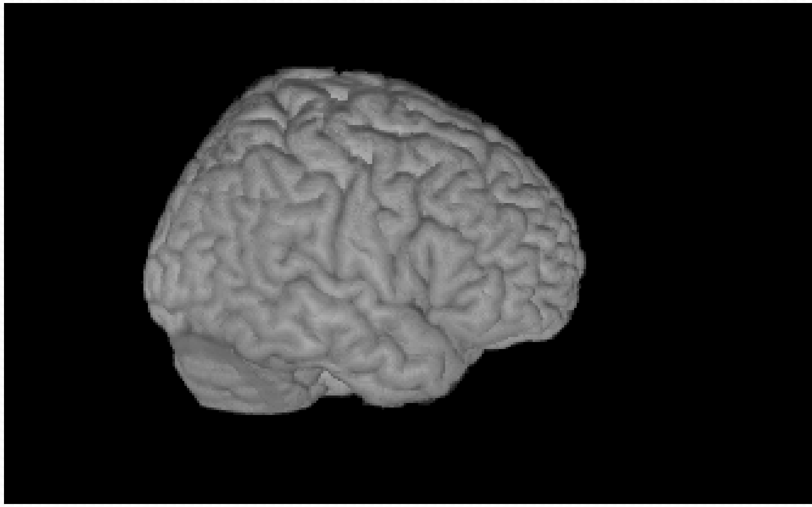


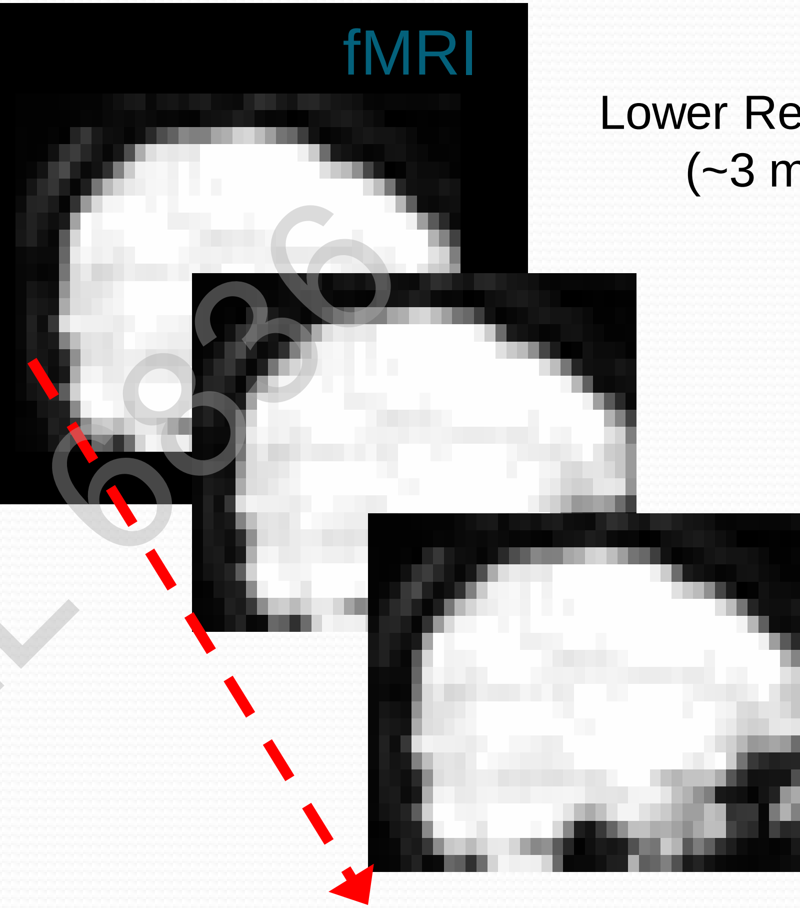
***Structural* MRI reveals brain <u>anatomy</u>.**



***Functional* MRI (fMRI) reveals brain <u>function</u>.**

MRI vs. fMRI





Lower Resolution
(~ 3 mm^3)

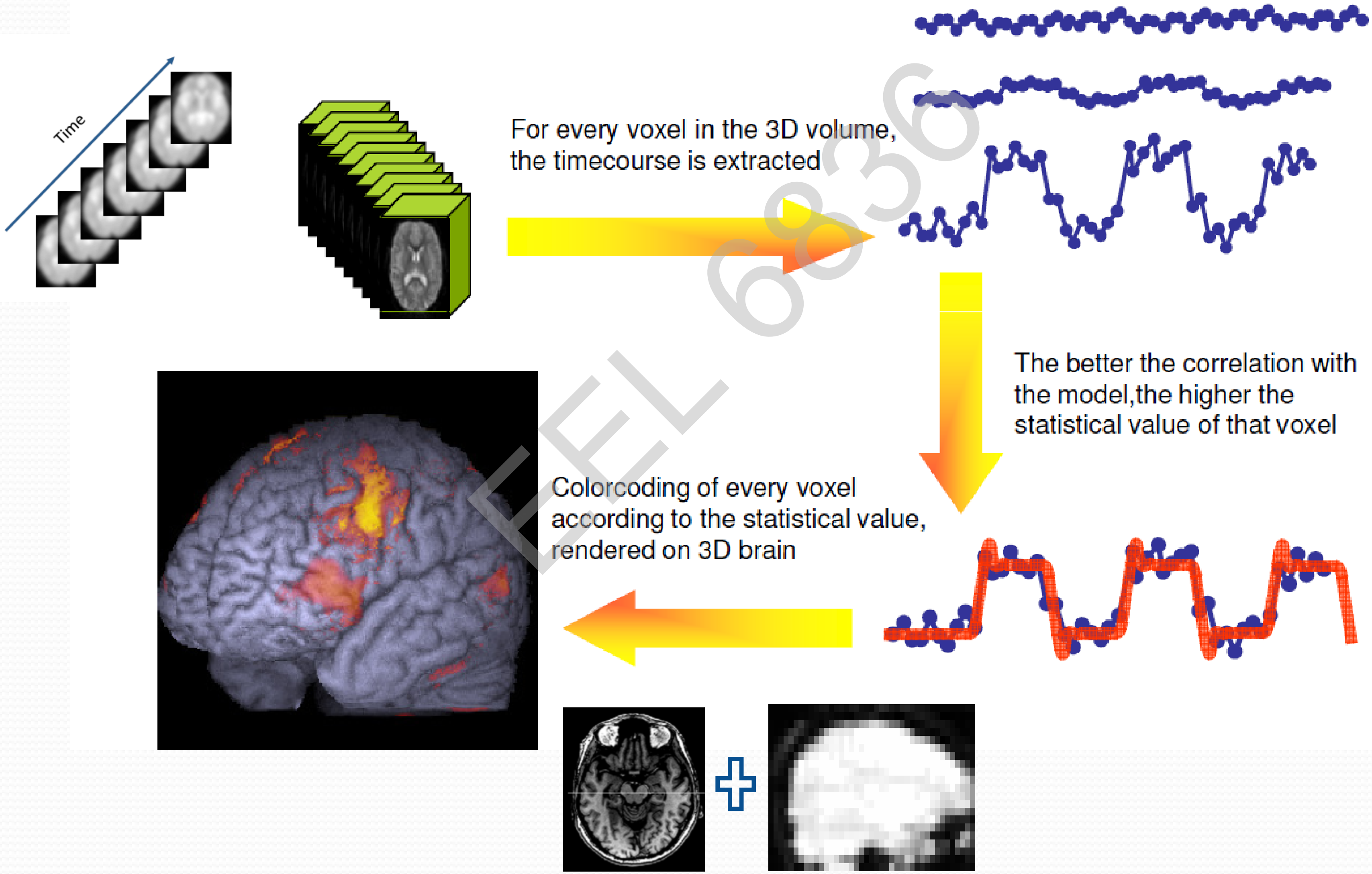
Only one image collected
(one full head volume)

High Resolution
(<1 mm^3)

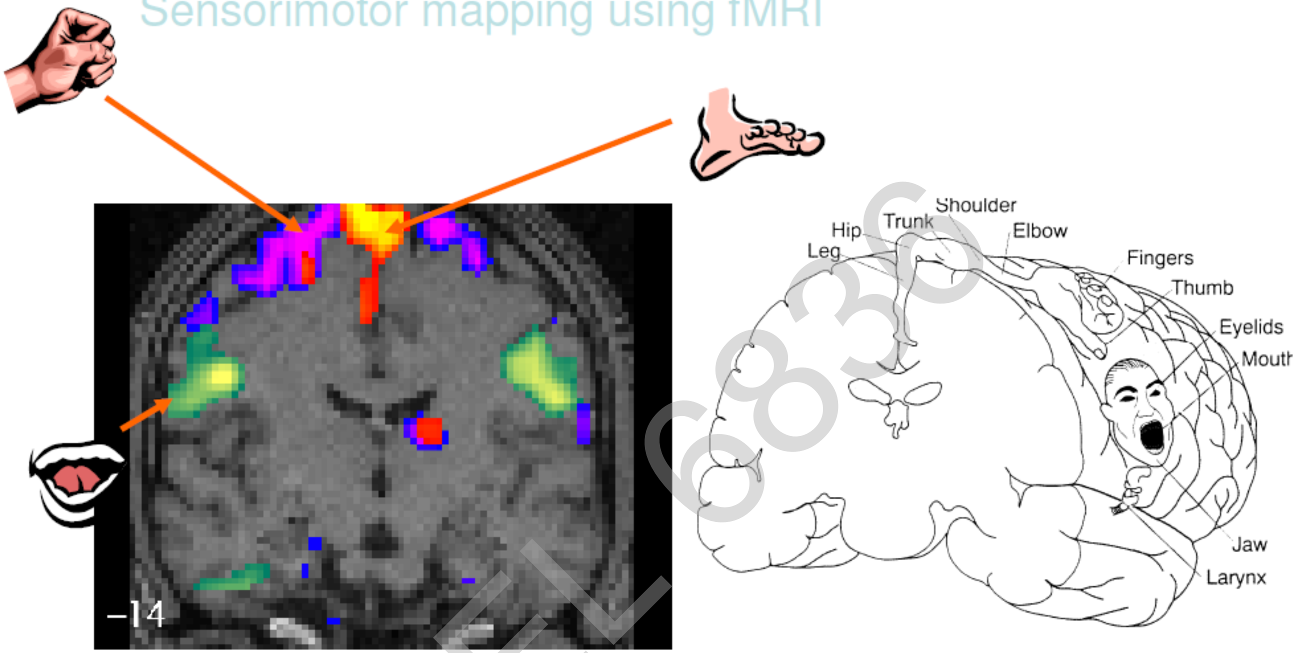
…

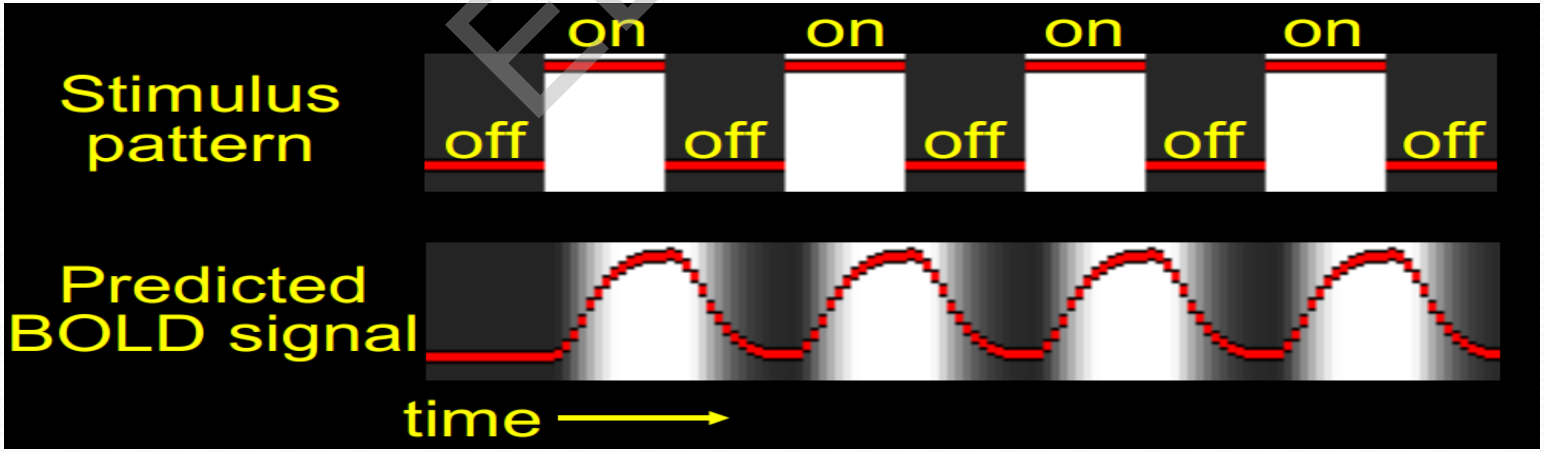
Series of several images collected over time
(e.g., 1 full head volume every 2 seconds over the course of several minutes)

fMRI data analysis overview

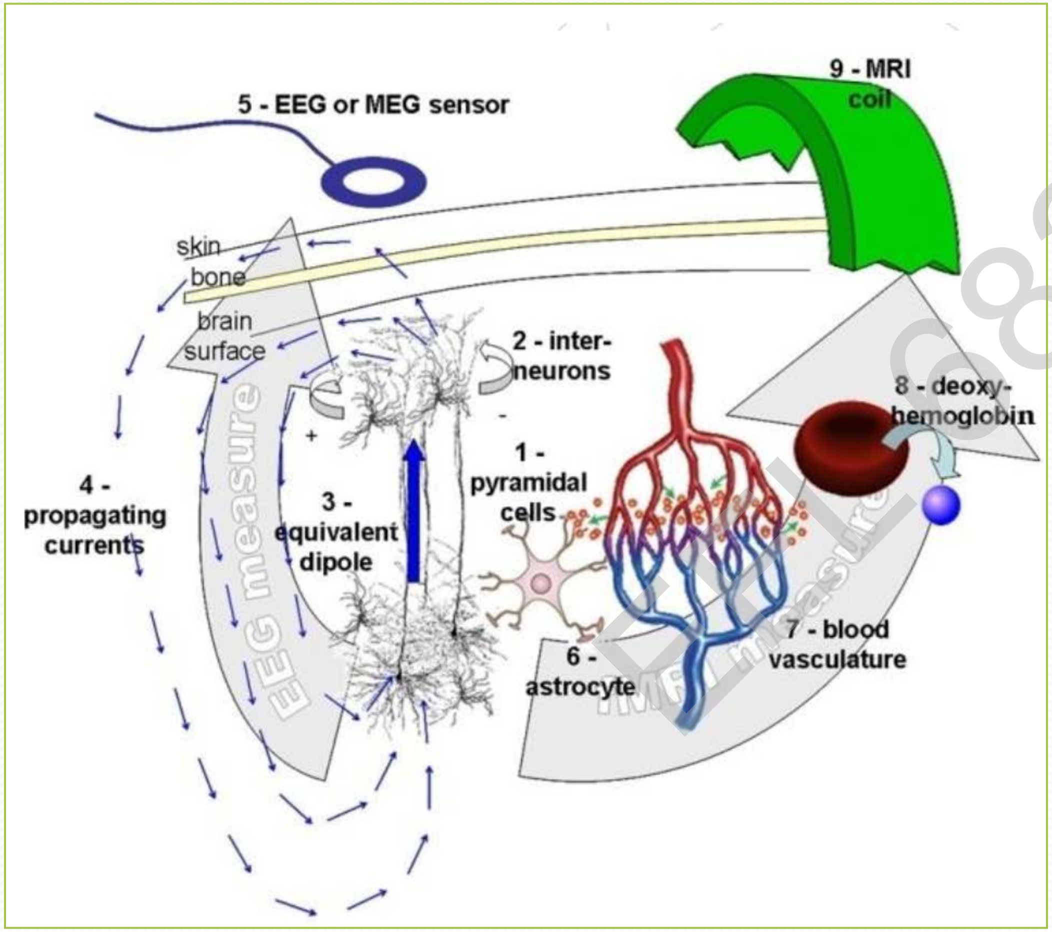


Sensorimotor mapping using fMRI



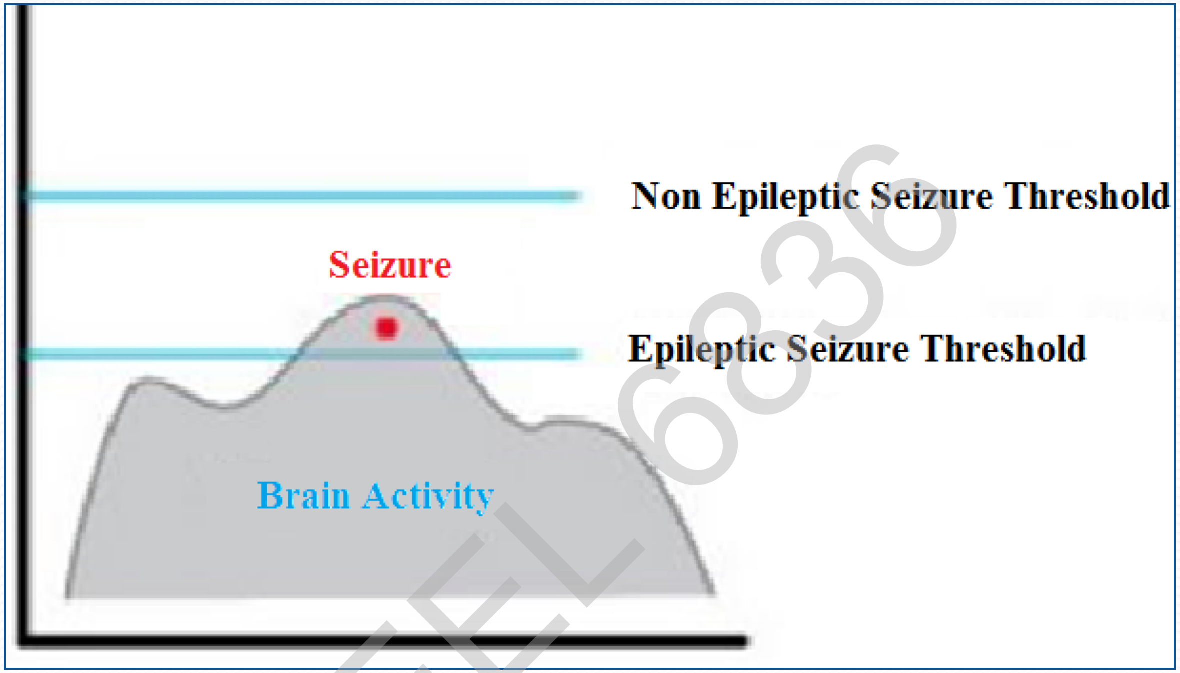


fMRI Integration of Modalities



- fMRI is complementary to EEG, but they measure different things (electrical activity vs. metabolic changes).
- fMRI can capture whole-brain changes in metabolic activity related to brain activity with good spatial resolution (~1 mm) but it is rather slow temporally (~1 s.)

Seizure Threshold



<u>Seizure threshold:</u> Minimum stimulation required to trigger a seizure.

Stimulation could be:
Electrical or magnetic stimulation
Chemical compound that stimulates the brain
External stimulus such as: noise and flashing lights

Drugs will raise the seizure threshold, so the brain will be less excitable.