Cognitive Neuroscience

Spring 2025

Type of Evaluation	Weightage (in %)	
Quiz 1	10 %	MCQs + short answers
Quiz 2	10 %	MCQs + short answers
Midterm	25 %	MCQs + short answers
In-class random quizzes	25 %	5 surprise class quizzes over the semester
End-term - Oral presentation	30 %	Viva/Oral – 15 minutes (student groups)
Experiment Participation	5% extra	Participate in experiments that are conducted in the Cognitive Science Lab

Grade	%
A	>= 88
A-	81-87.5
B	74-80.5
B-	66 -73.5
C	59-65.5
C-	52-58.5
D	40 – 51.5
F	Below 40

TAs

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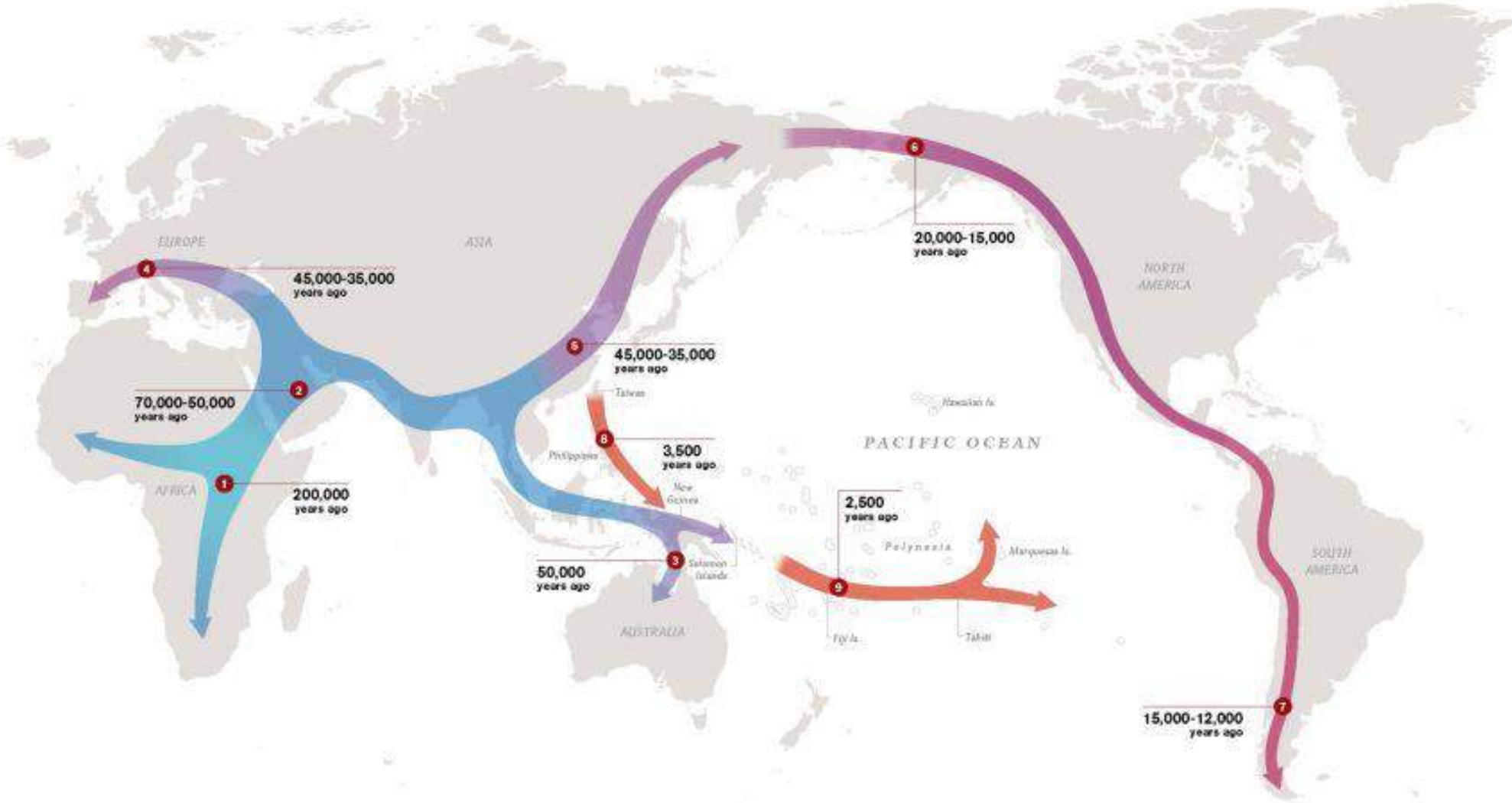


GLOBAL JOURNEY

Once modern humans began their migration out of Africa some 60,000 years ago, they kept going until they had spread to all corners of the Earth. How far and fast they went depended on climate, the pressures of population, and the invention of boats and other technologies. Less tangible qualities also sped their footsteps: imagination, adaptability, and an innate curiosity about what lay over the next hill.

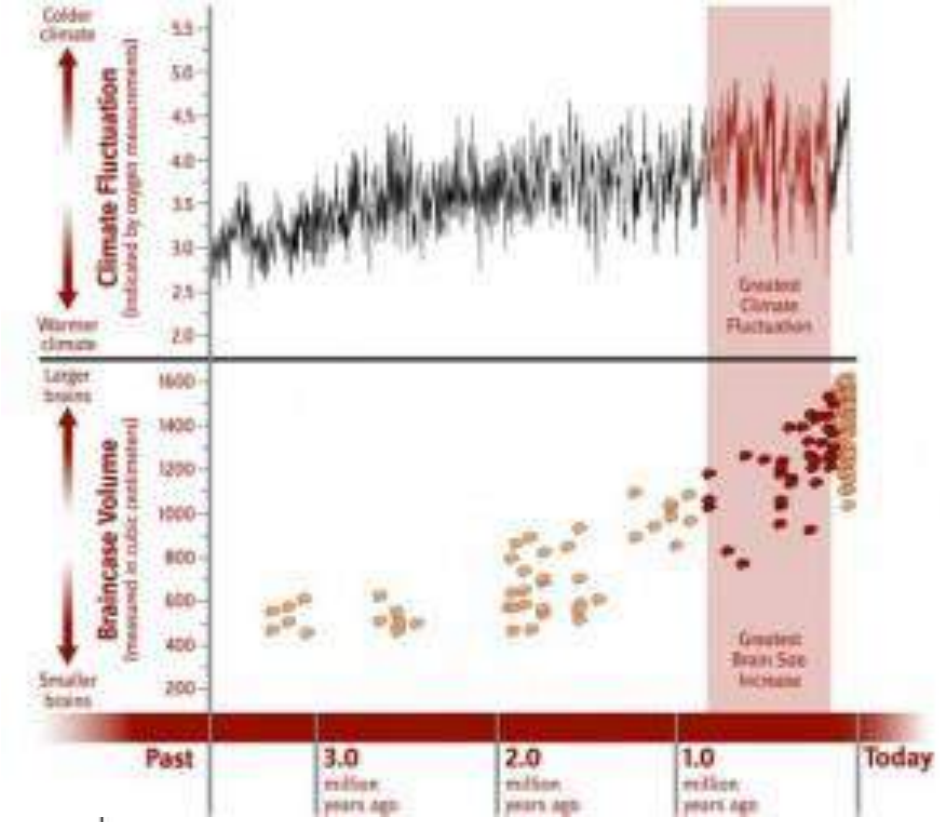
Generalized route with migration dates

200,000 50,000 20,000 2,500 years ago

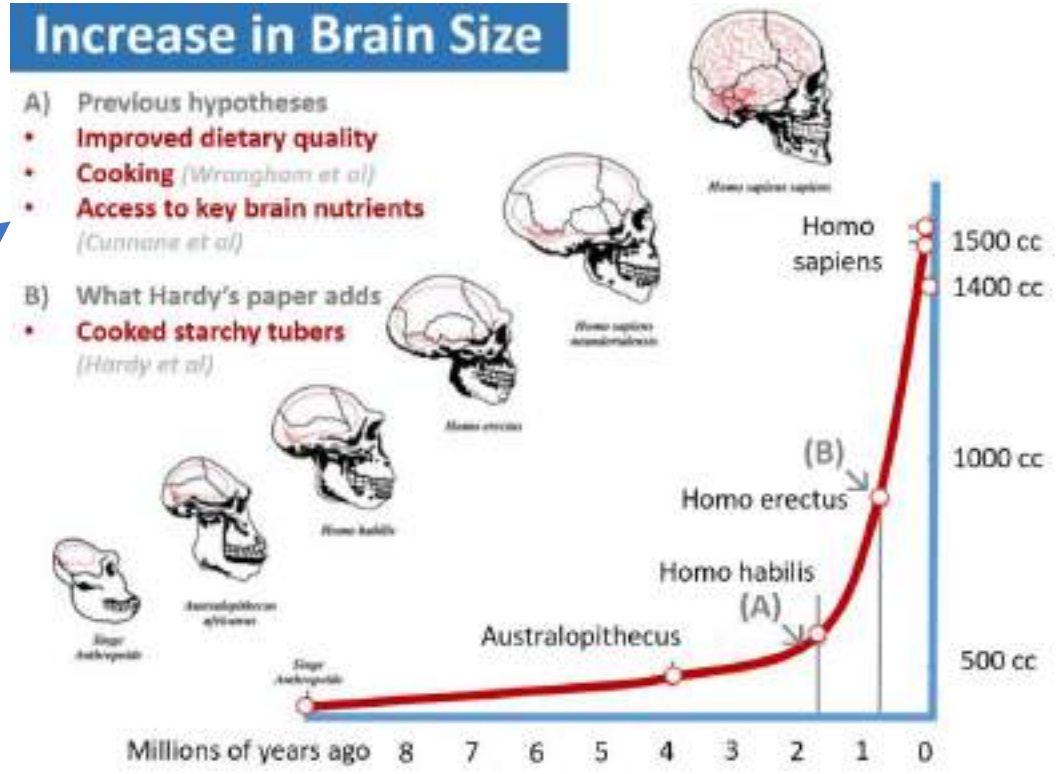
MAP: NATIONAL MAPPING
SOURCES: CHRIS STRINGER, NATURAL HISTORY MUSEUM, LONDON;
SPENCER WELLS, NG STAFF

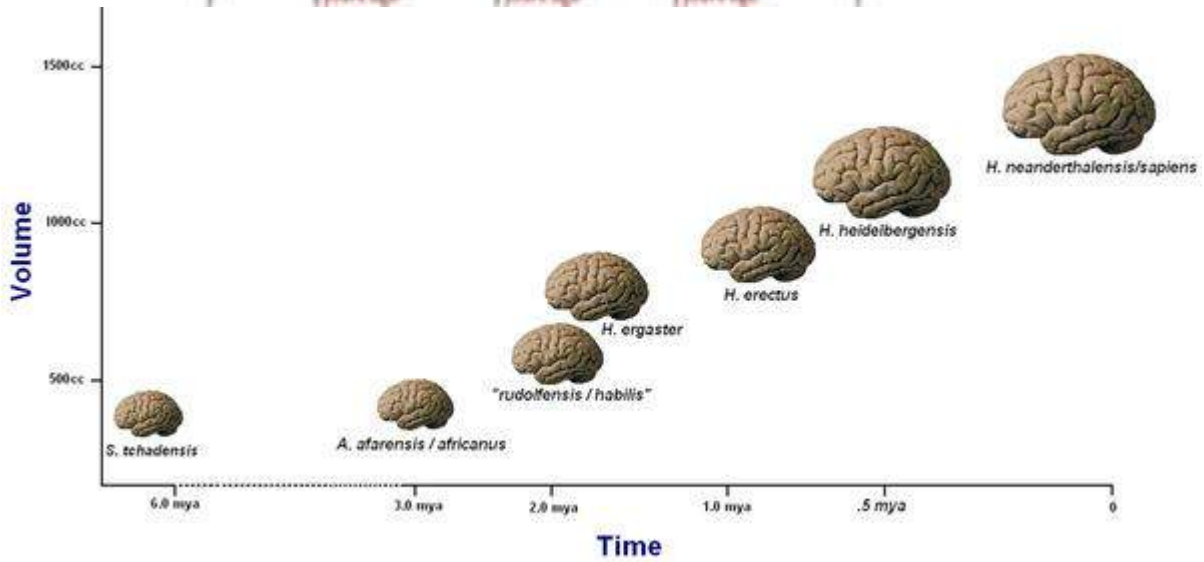
https://www.jstor.org/stable/full/10.1086/682587

[Kier Watson blog]

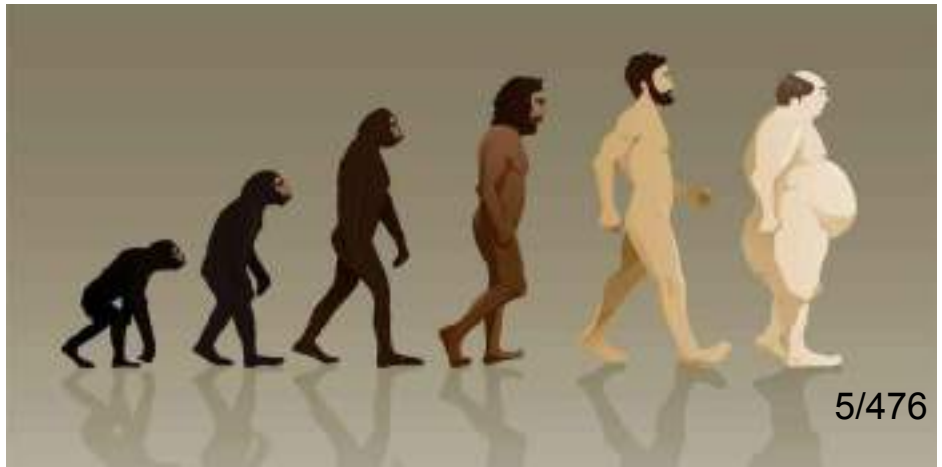


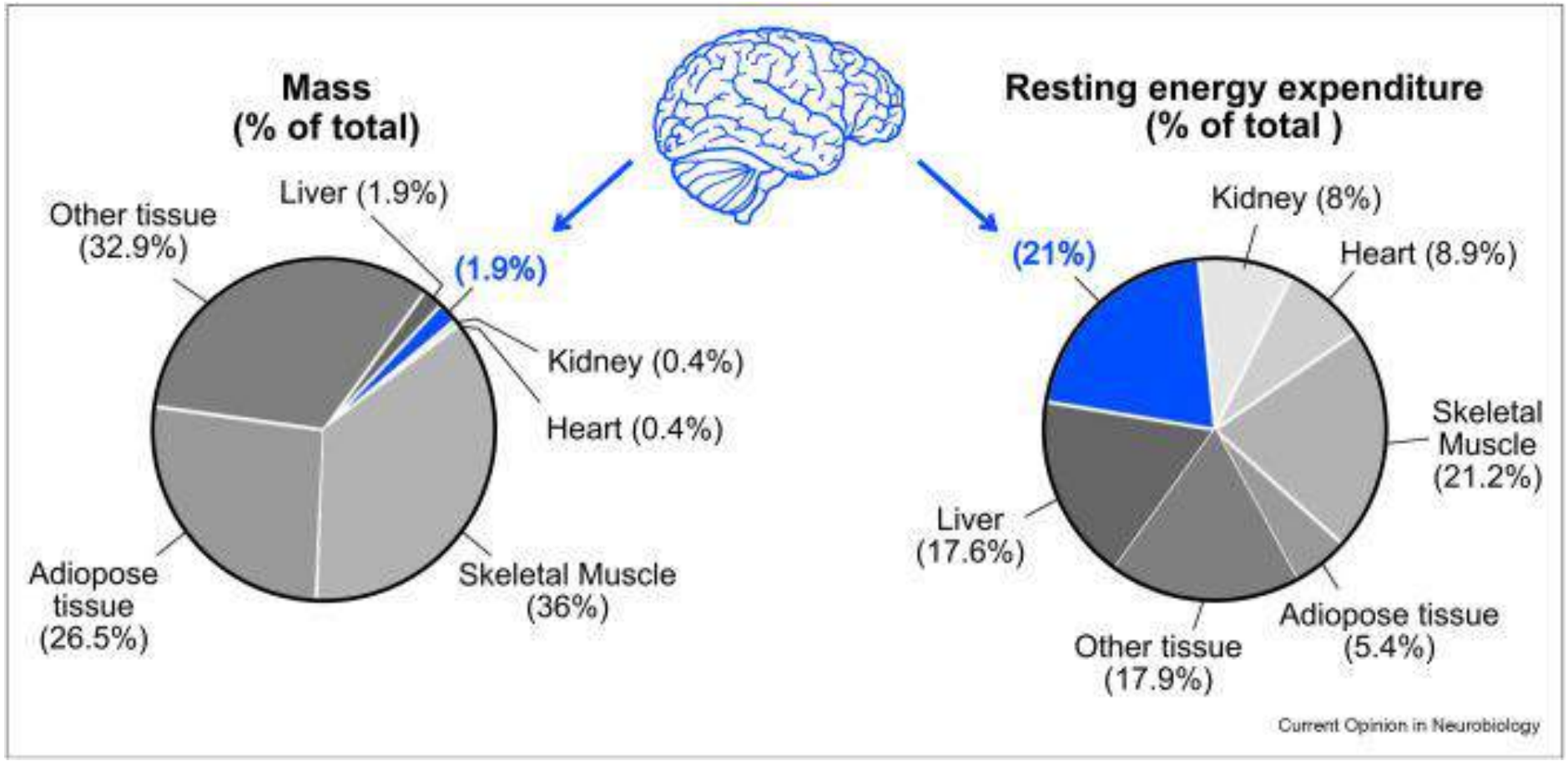
Why does this matter?





https://blogs.ntu.edu.sg/hg3040-2014-3/biological-evolution/increase-in-brain-size/





https://www.sciencedirect.com/science/article/pii/S0959438822001623

The brain accounts for about 20% of the body's energy consumption, despite only representing ~2% of its weight.

That's around 0.3 kilowatt hours (kWh) per day for an average adult, more than 100 times what the typical smartphone requires daily

How much energy do we expend thinking and using our brain?

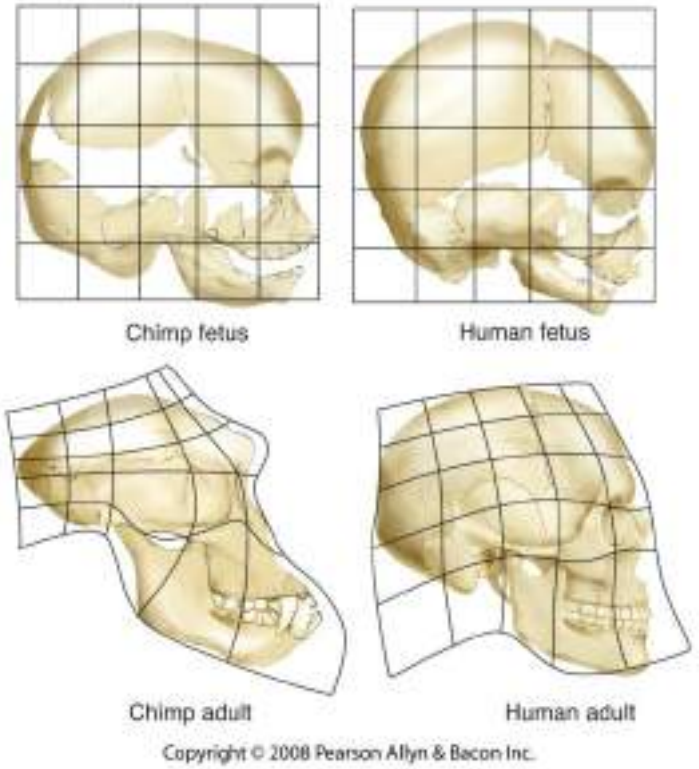
- What advantage does a larger brain, more neurons, offer?

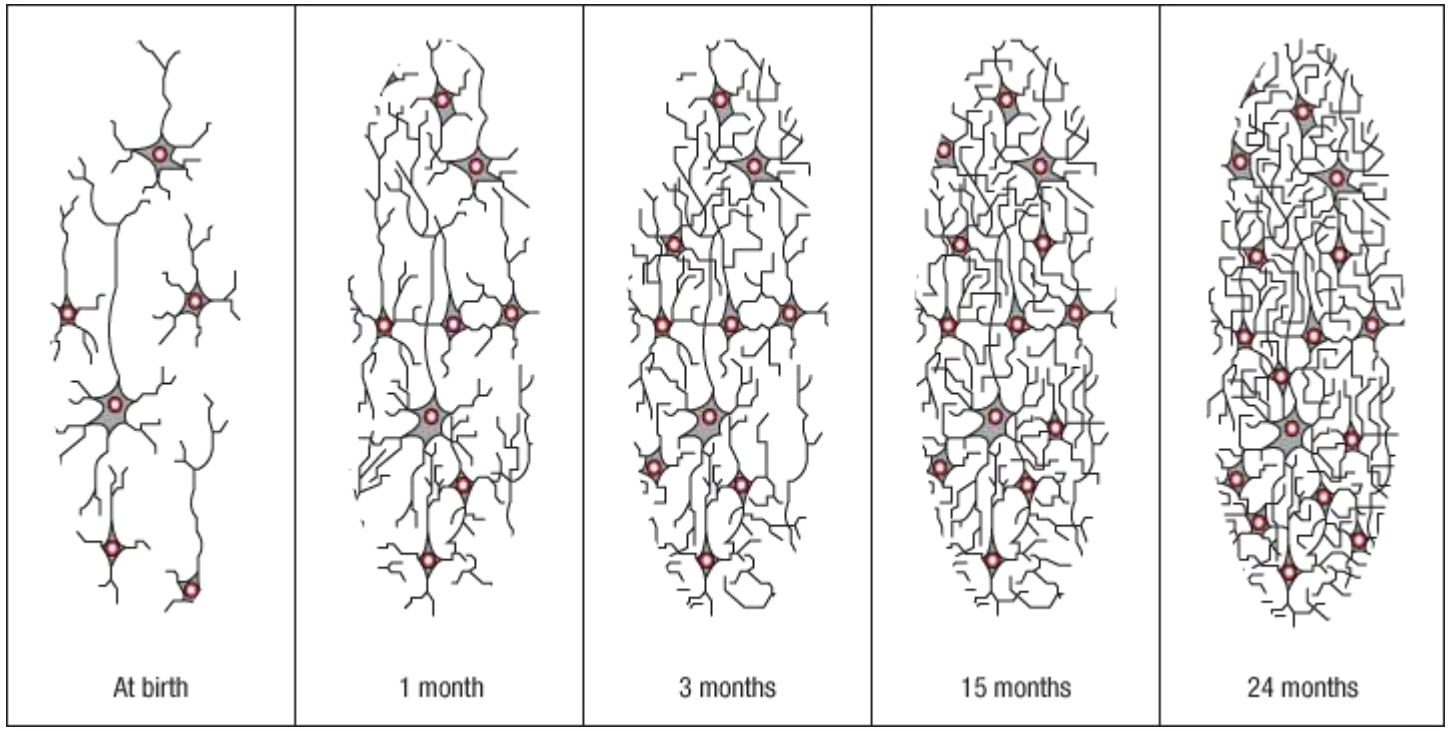
Evolution of human species

Large brains provide more memory capacity and the abilities to recognize patterns of events in the past and to plan for the future. Because an upright posture limits the size of a woman's birth canal and therefore the size of the head that can pass through it, much of the brain's growth must take place after birth, which means children require an extended period of parental care.

Our brains are 3 times larger than those of chimpanzees

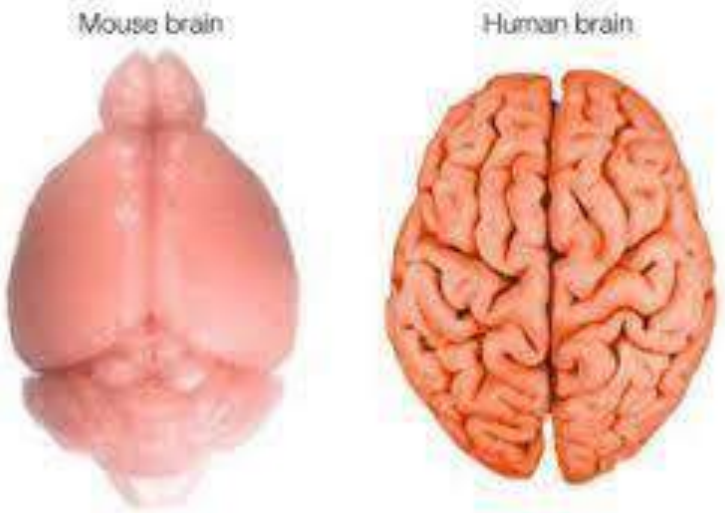
The grid lines indicate pattern of growth, showing much less change in the human skull from birth to adulthood

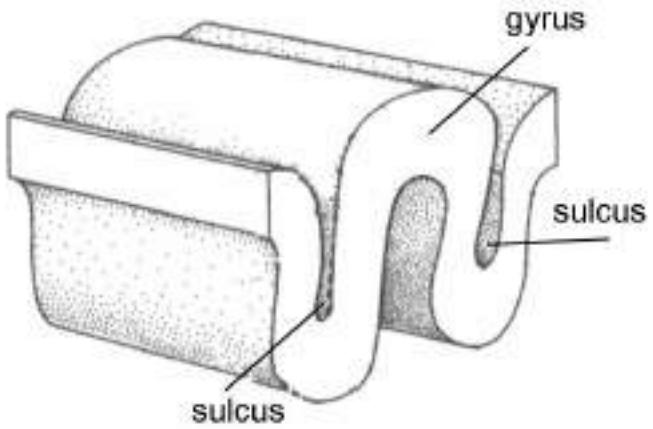




Synaptic pruning & synaptogenosis

- How does our brain accommodate high density of neurons in a limited space (skull)?
- ~86 billion neurons/interneurons
- ~86 billion non-neuron supporting cells (glial cells)

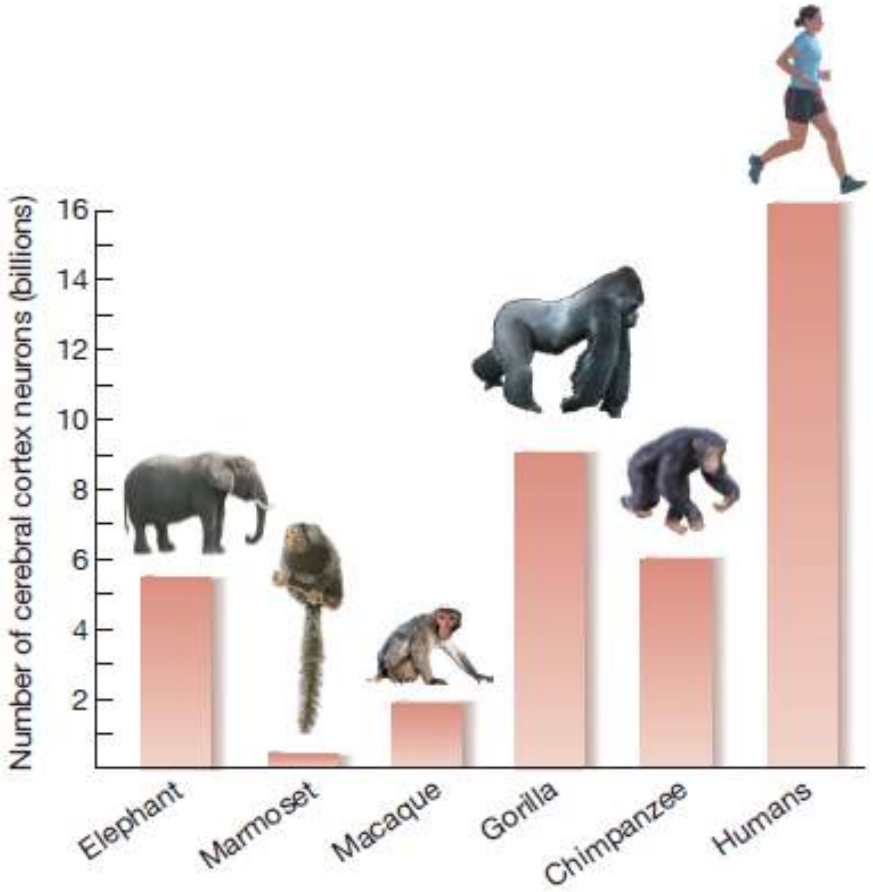




our brains contain many more neurons per gram

An increase in the number of **convolutions**—folds on the cerebral surface—has greatly increased the surface area of the *cerebral cortex*, the outermost layer of cerebral tissue

Species with more complex behaviors have brains with more neurons that are available for behavior, learning, remembering, reasoning, and making plans. Primate brains—especially large ones—contain many more neurons per gram than rodent brains and many more neurons in the cortex. Source: Herculano-Houzet, S., Marino, L. Brain Behav Evol 1998;51 230–238.

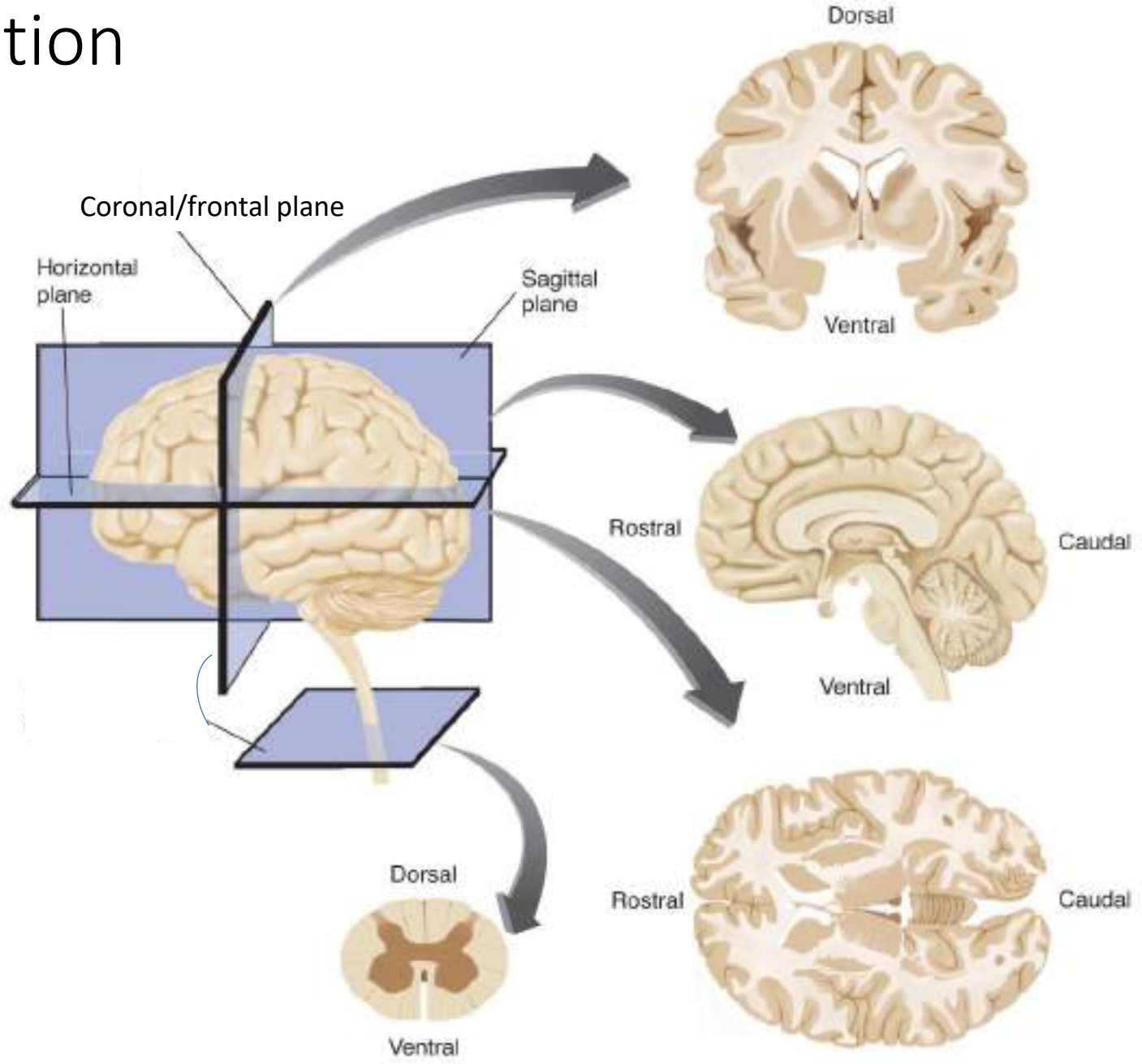


Humans have

- Larger surface area (especially cortical surface area)
- Higher neuronal density
- Higher ration of brain size to body size

Brain size → intelligence (non-linear relationship)
Humans → larger cerebral cortex (neocortex)
Elephants → larger cerebellum (trunk- sensory powerhouse)

Planes of section



Coronal section

Sagittal section

Horizontal section

Anatomical directions

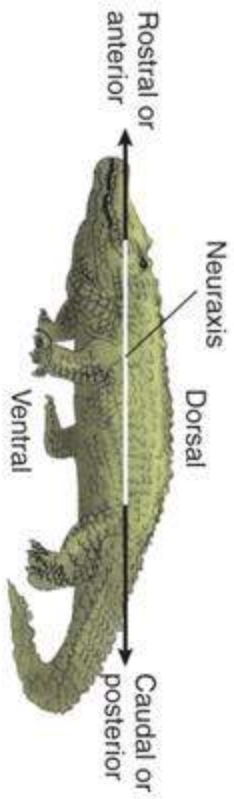
Neuraxis: An imaginary line drawn through the center of the length of the central nervous system, from the bottom of the spinal cord to the front of the forebrain

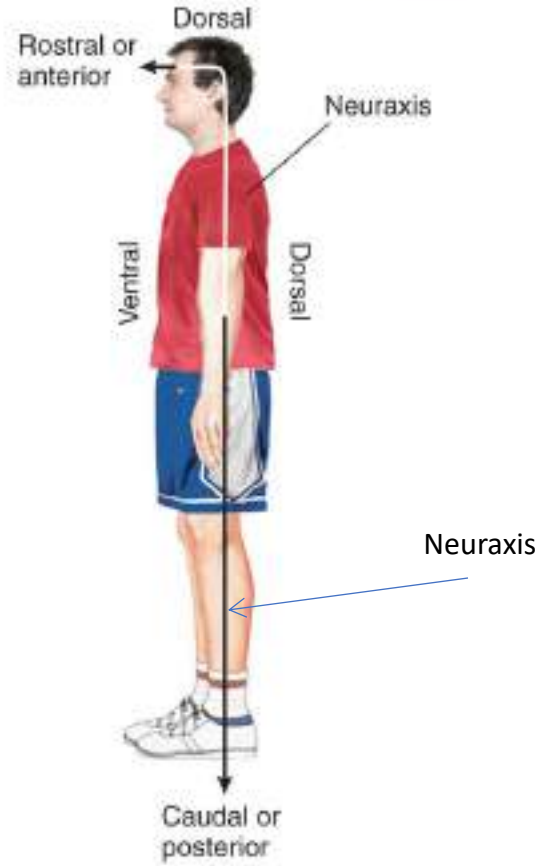
Dorsal: Towards the back

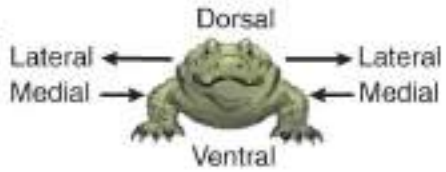
Ventral: Towards the belly

Ipsilateral: Located on the same side of the body.

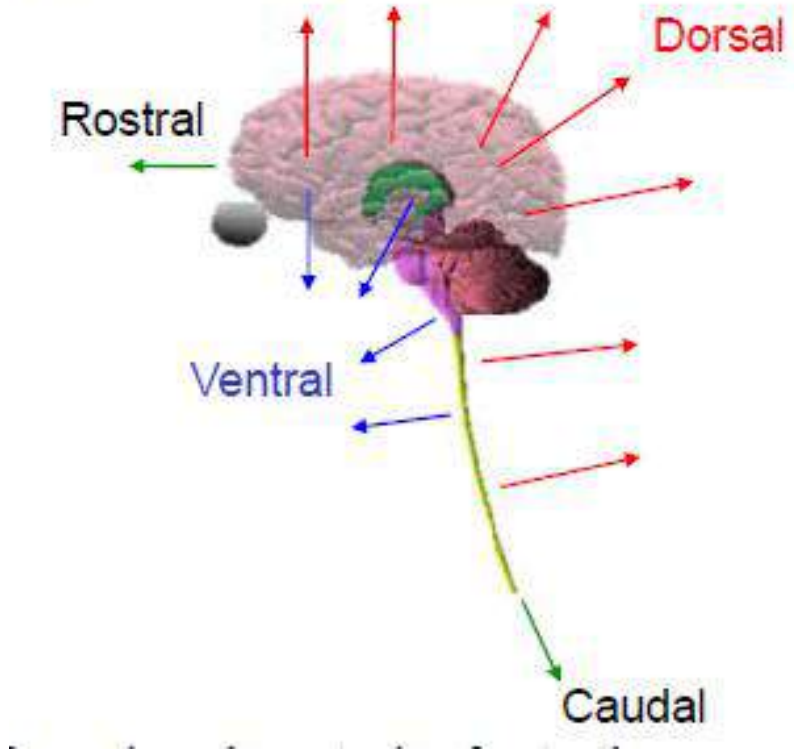
Contralateral: Located on opposite side of the body.

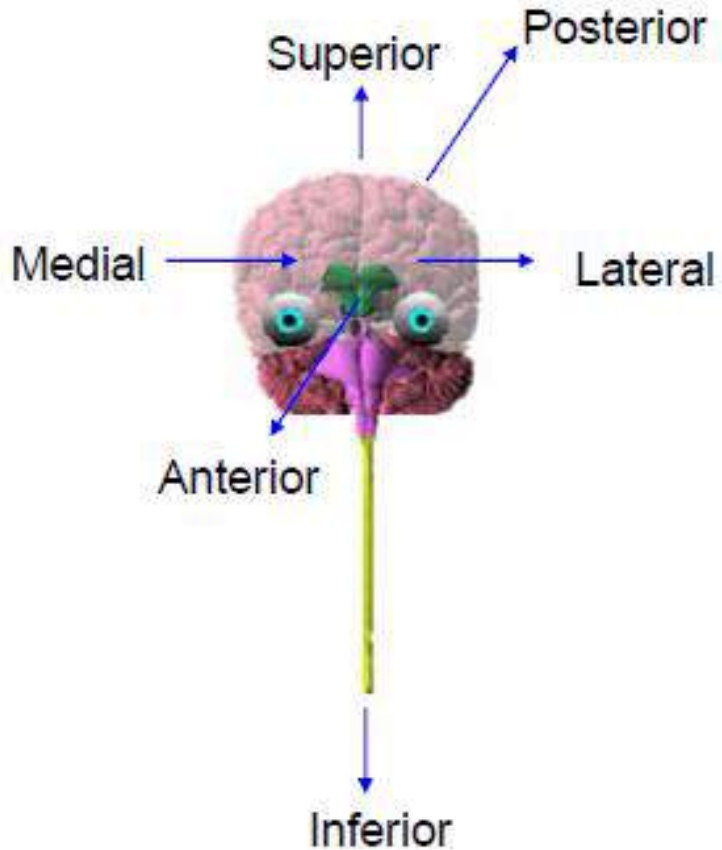


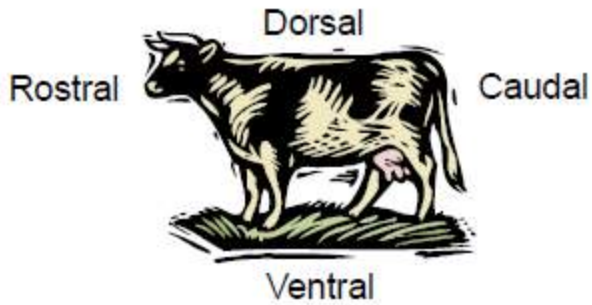


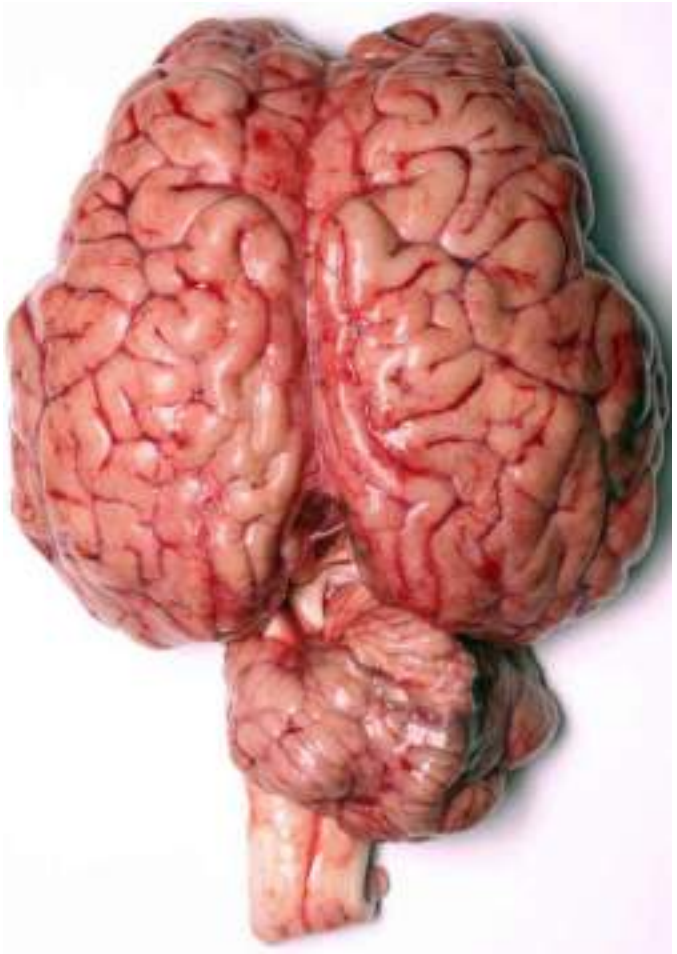


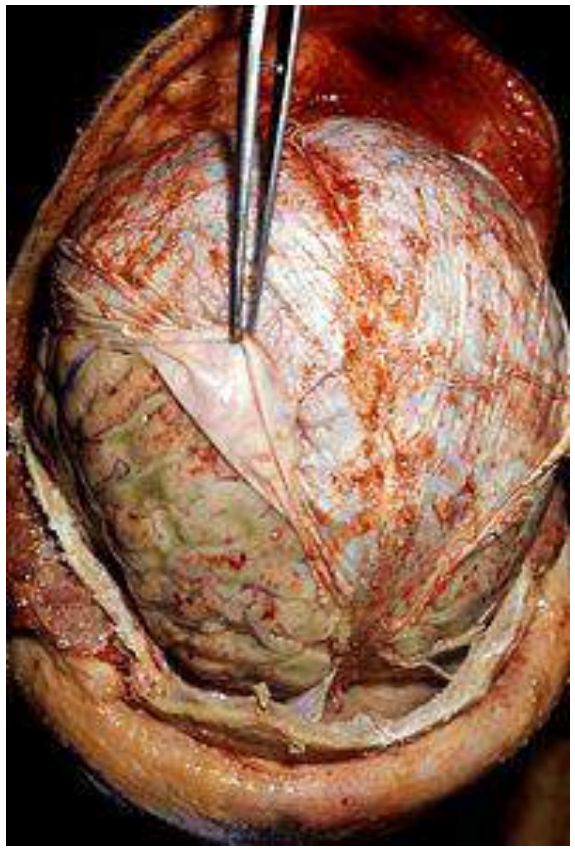
Orientation of CNS



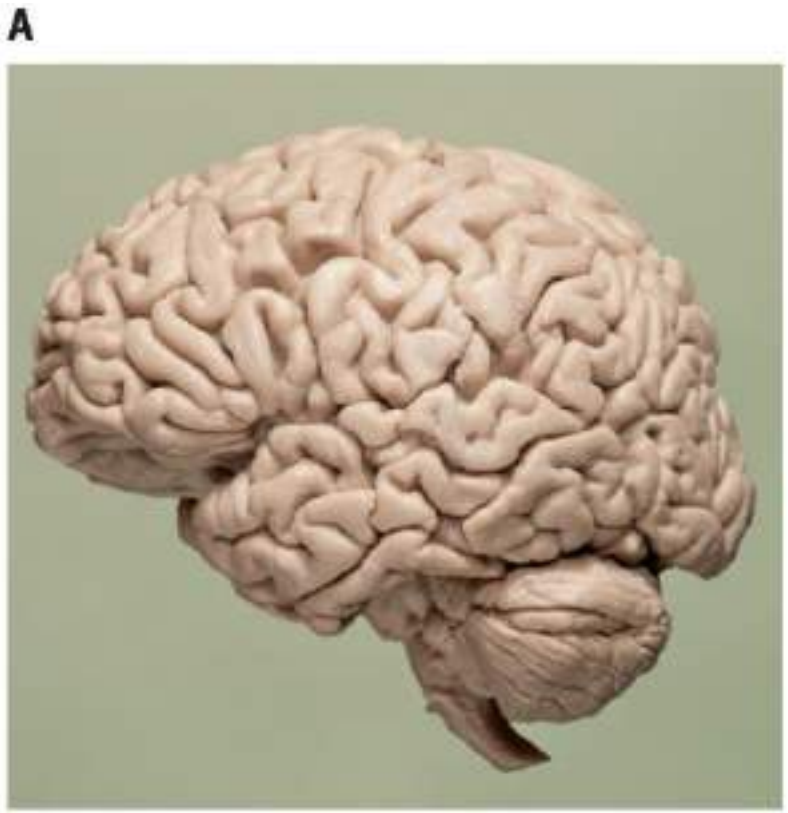


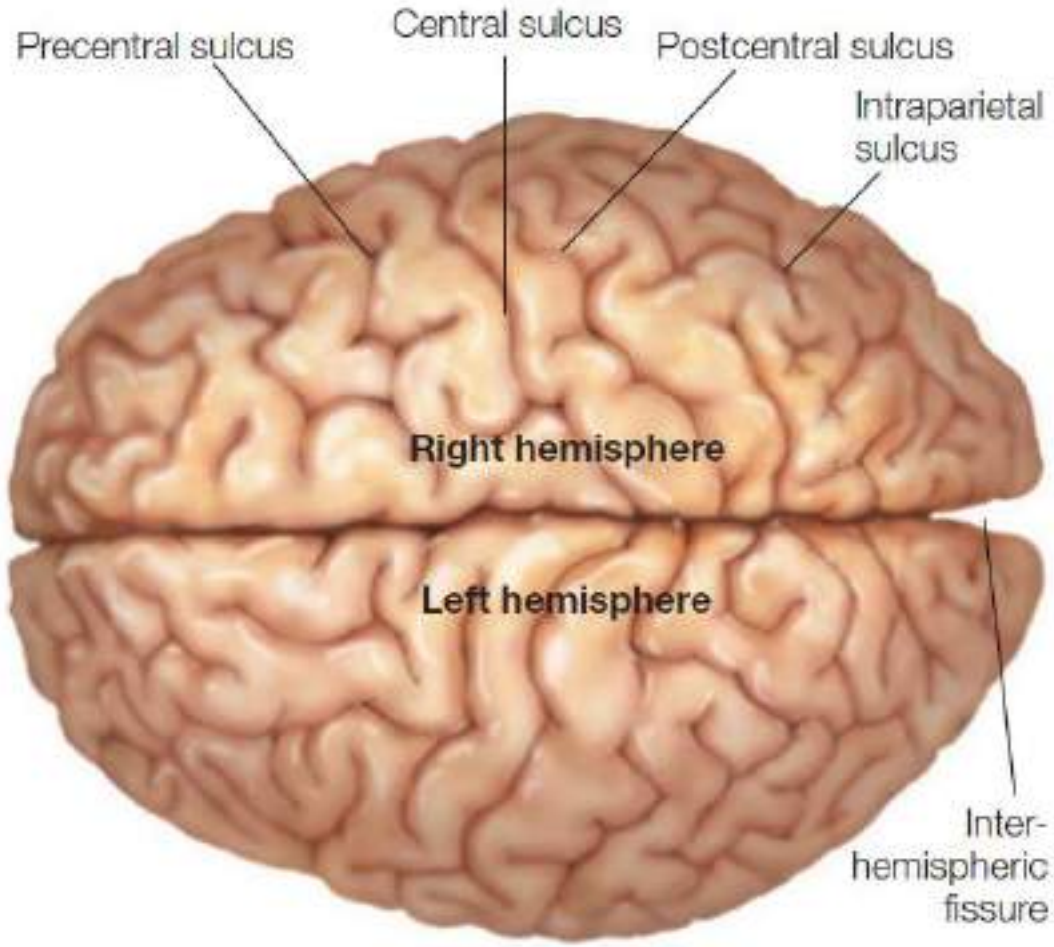


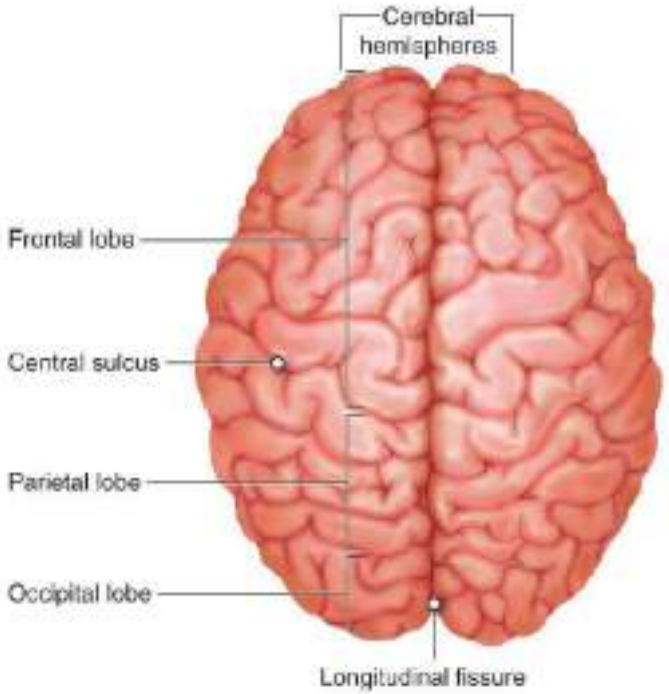


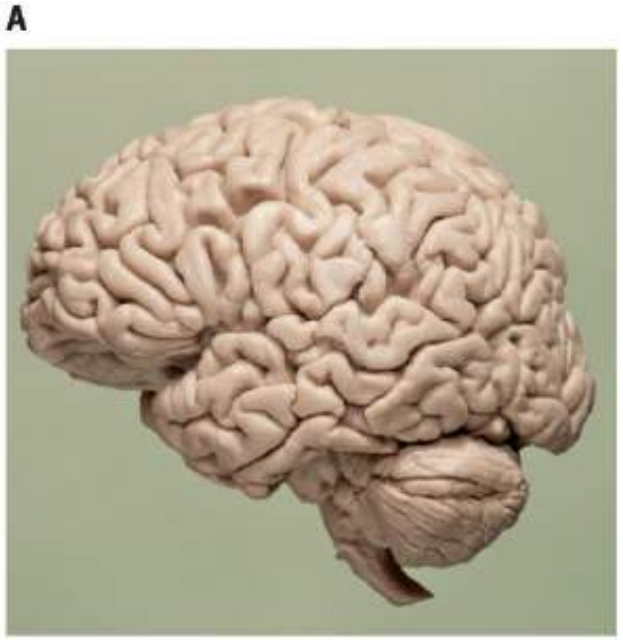


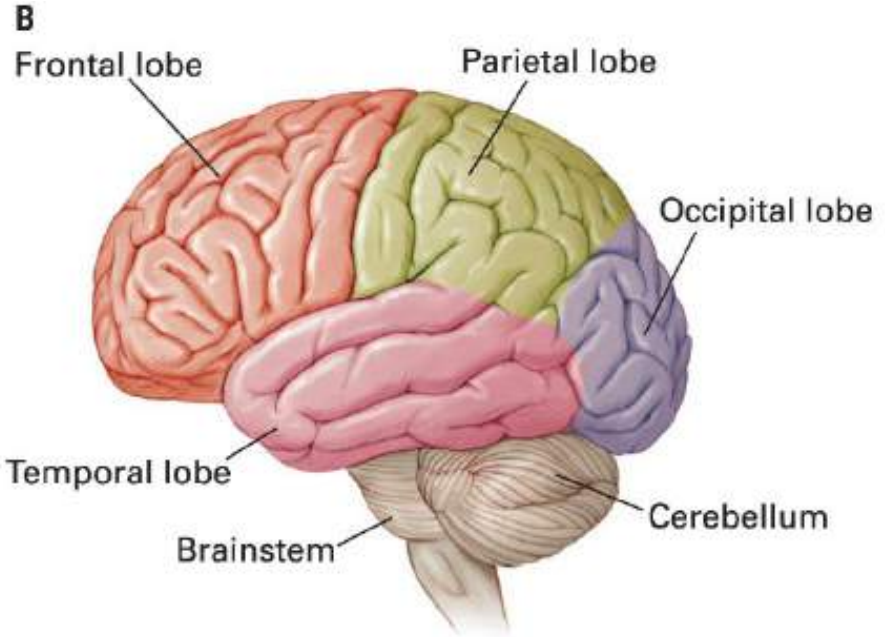
Reference points on the outer surface



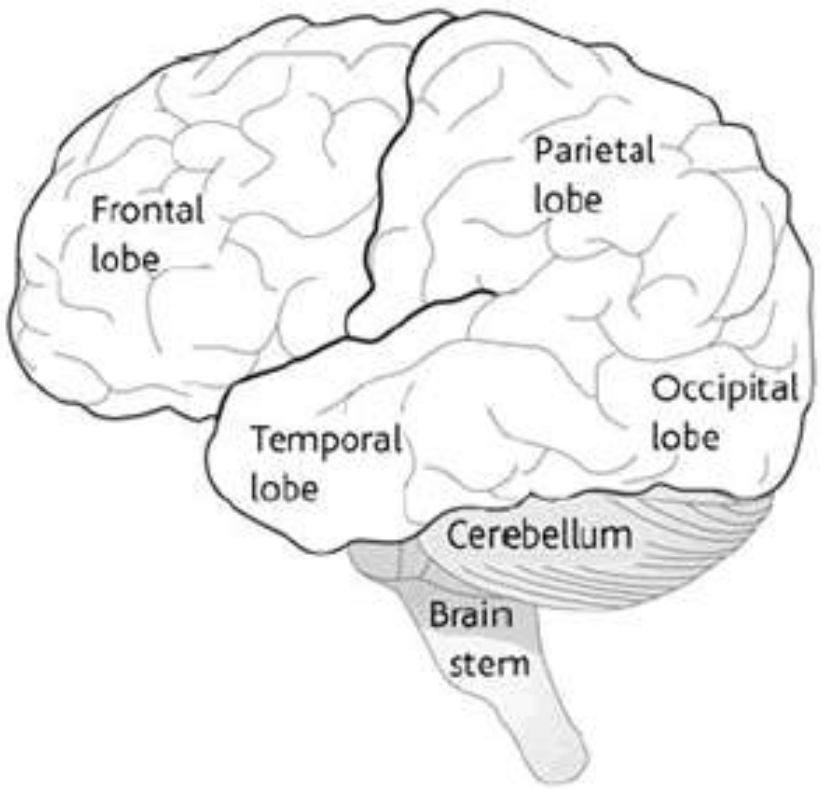


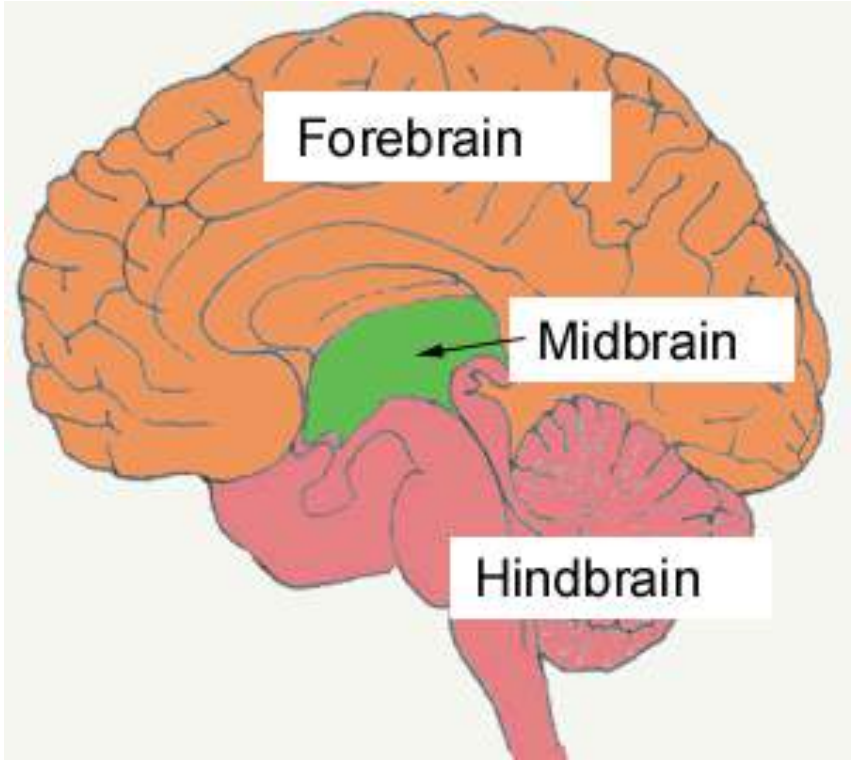






Major Divisions of the Brain





Forebrain – outer structures (frontal, temporal, parietal, occipital) – latest to evolve

Hindbrain – structures at the back (brain stem, cerebellum)

Midbrain – structures in the middle of the brain- cannot be seen for the outside – ancient in timescale (preserved across species)

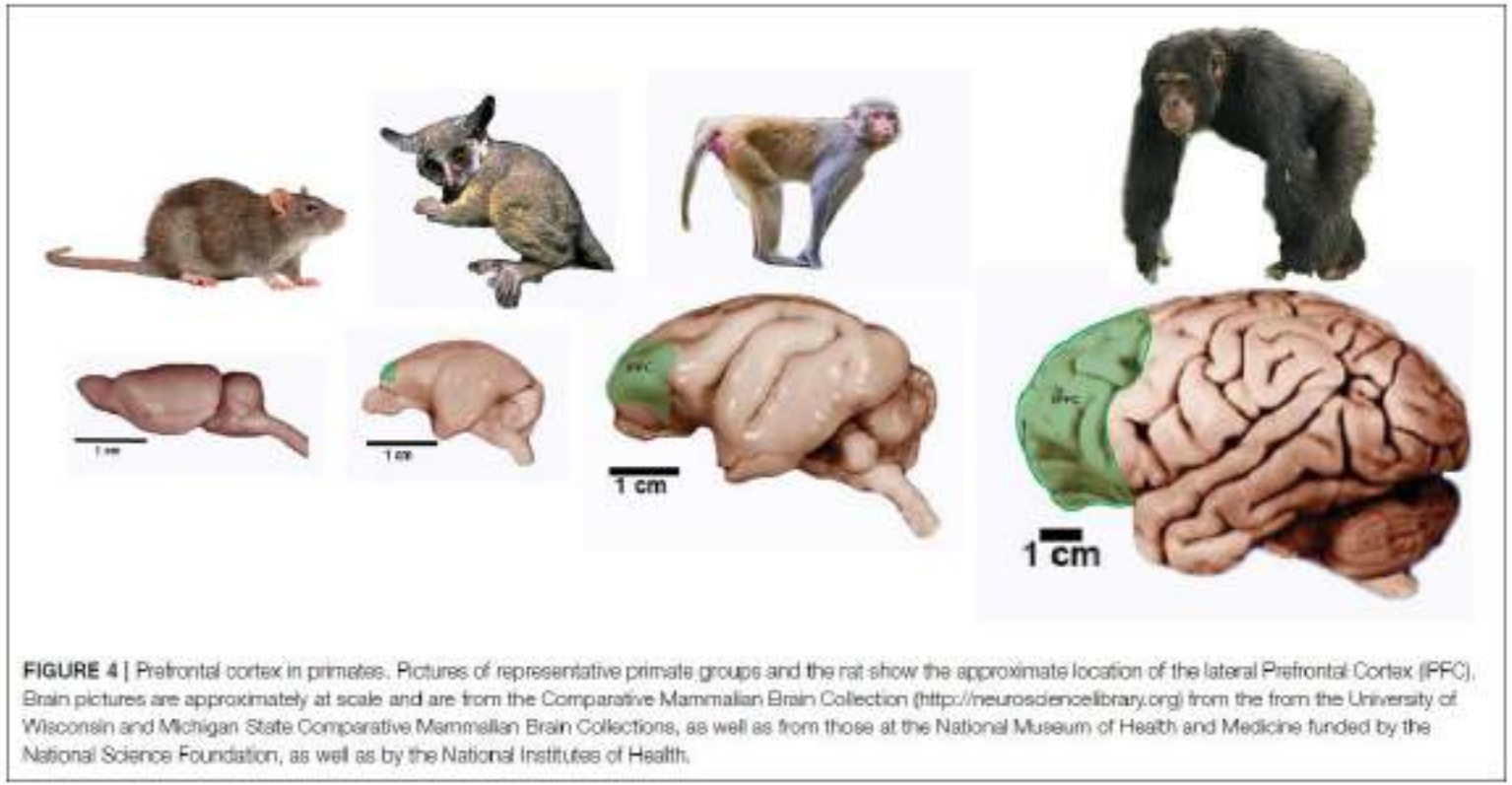
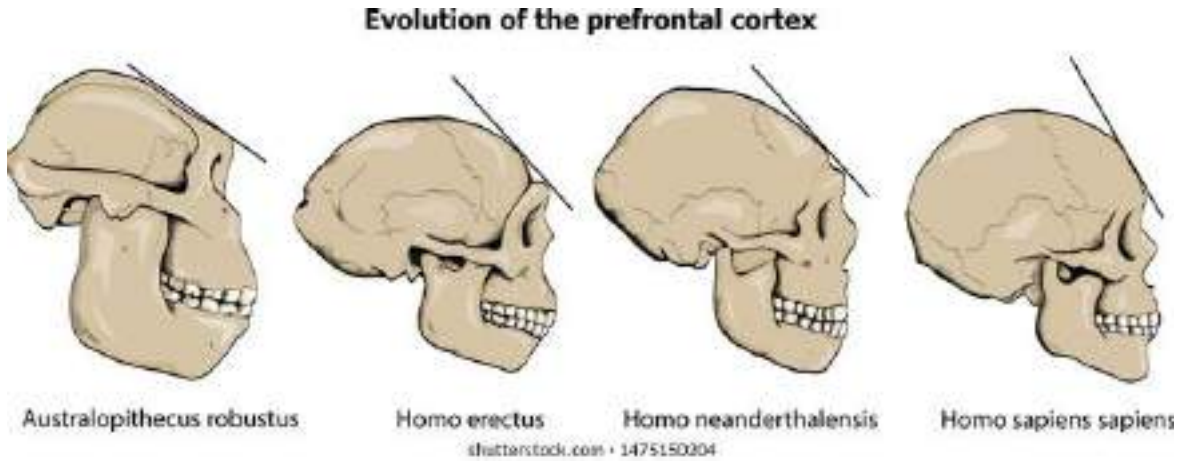
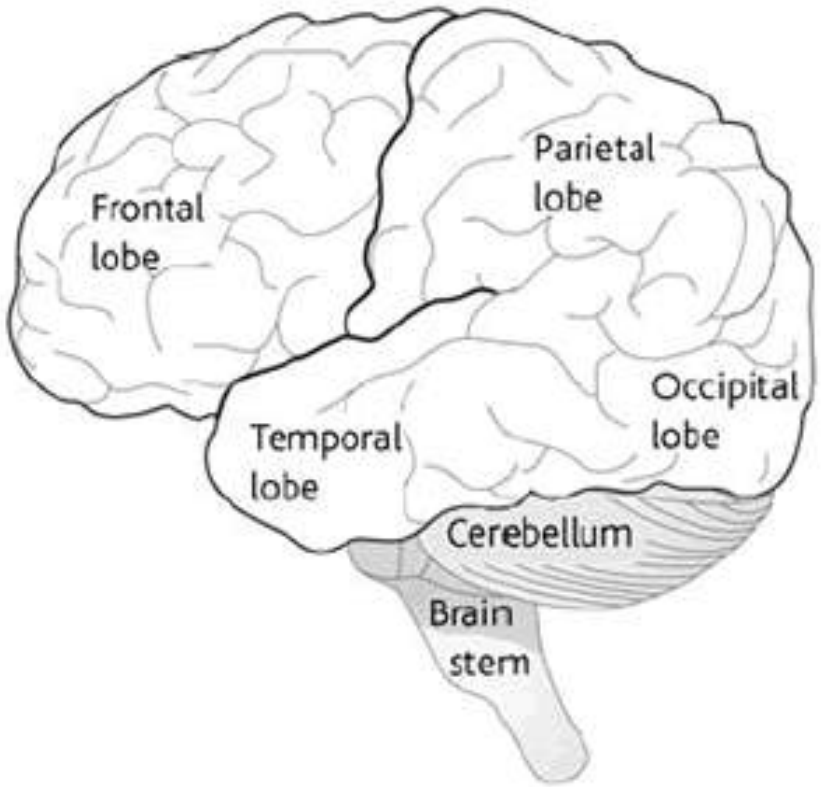


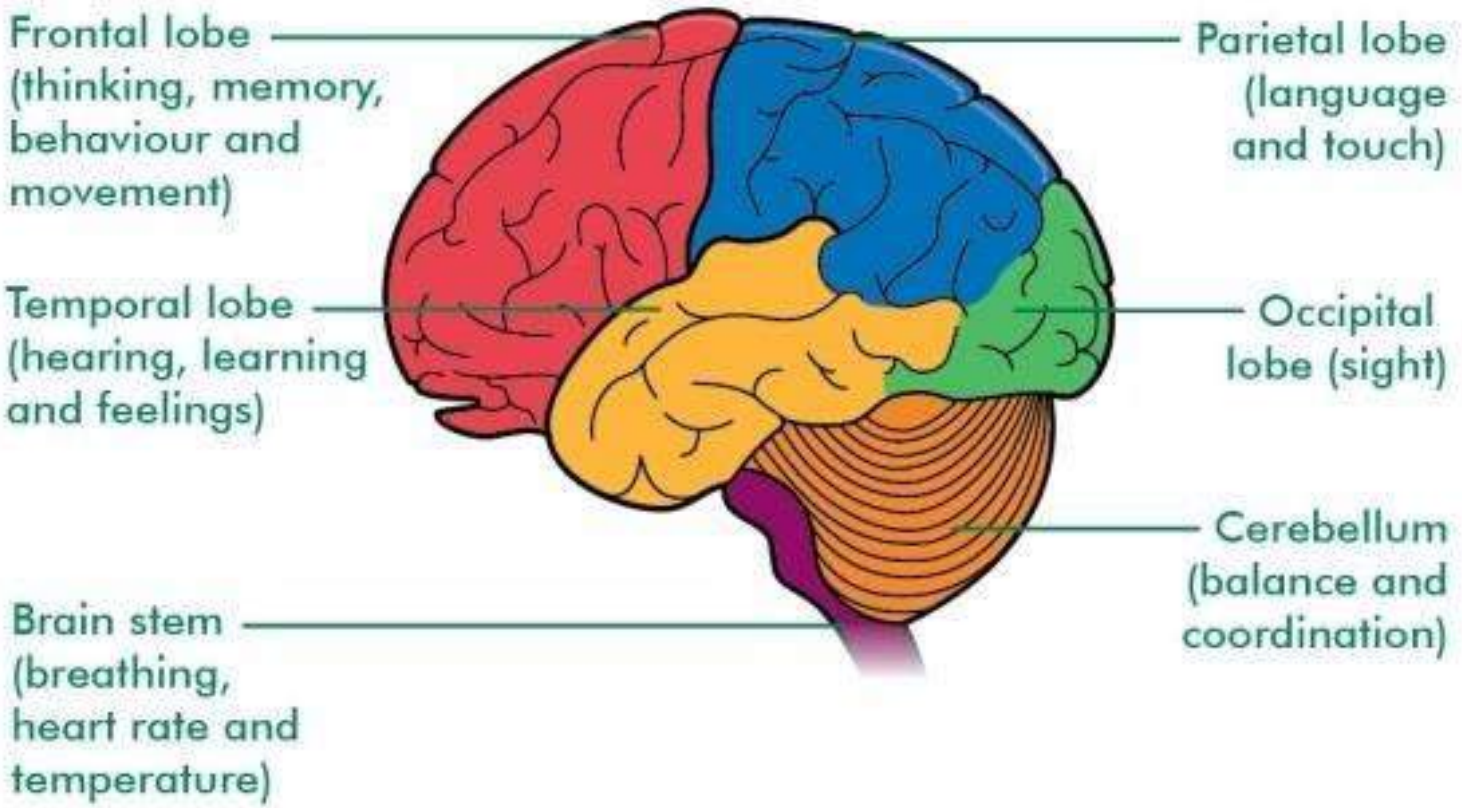
FIGURE 4 | Prefrontal cortex in primates. Pictures of representative primate groups and the rat show the approximate location of the lateral Prefrontal Cortex (PFC). Brain pictures are approximately at scale and are from the Comparative Mammalian Brain Collection (http://neurosciencelibrary.org) from the from the University of Wisconsin and Michigan State Comparative Mammalian Brain Collections, as well as from those at the National Museum of Health and Medicine funded by the National Science Foundation, as well as by the National Institutes of Health.

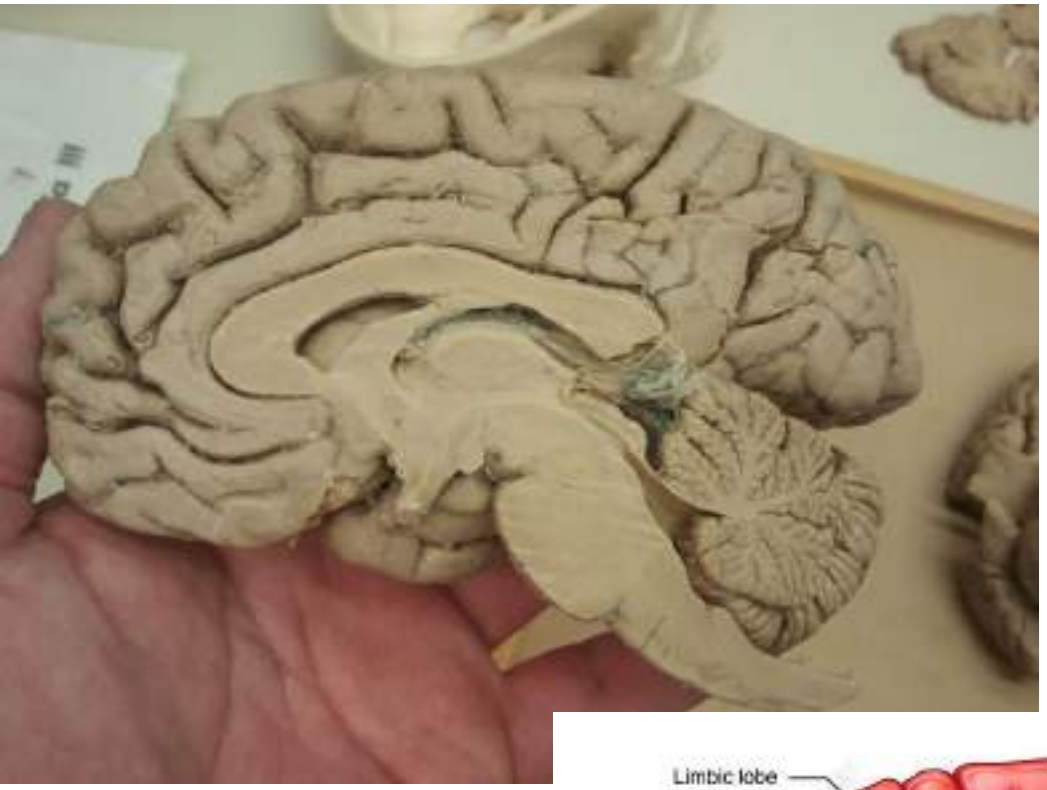


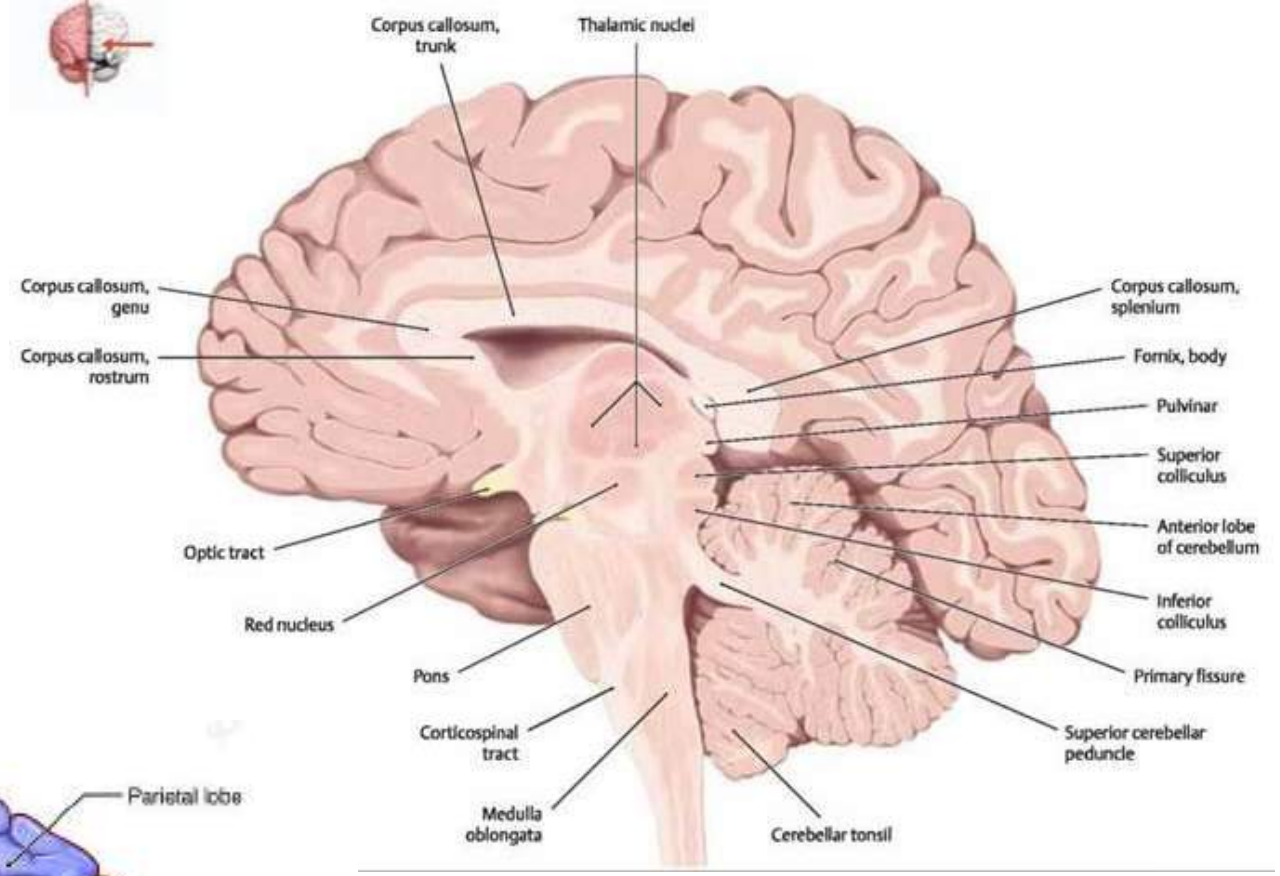
https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2021.591017/full

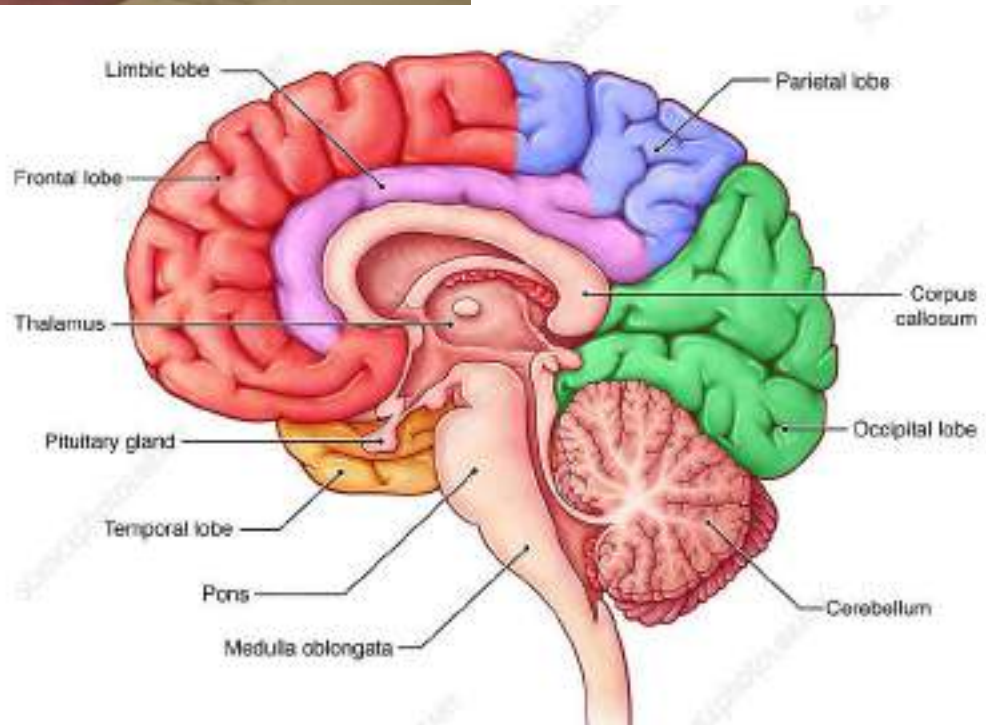
https://thebrain.mcgill.ca/flash/a/a_05/a_05_cr/a_05_cr_her/a_05_cr_her.html


Frontal lobe
Parietal lobe
Temporal lobe
Occipital lobe
Cerebellum
Brain stem

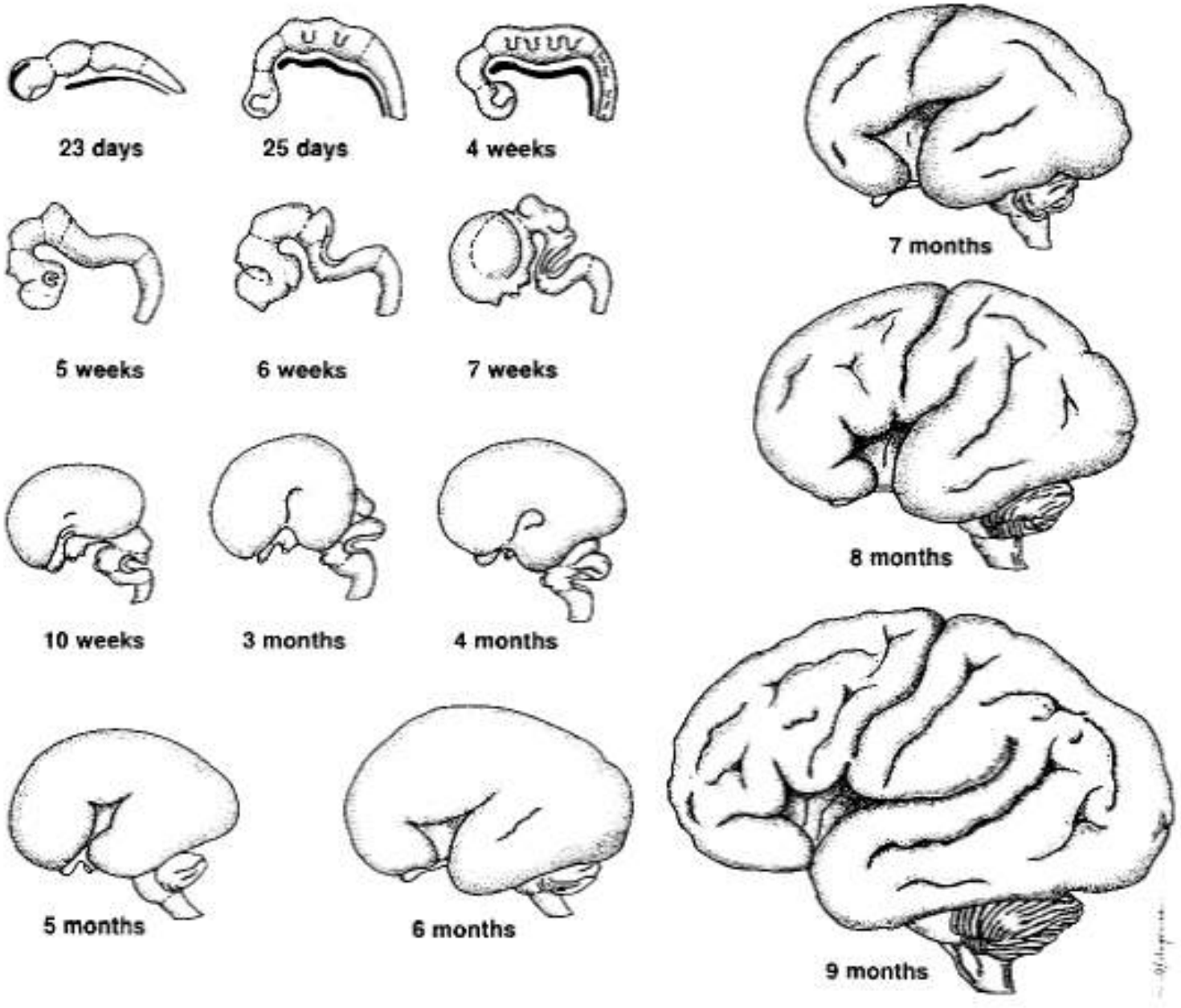

Frontal lobe (thinking, memory, behaviour and movement)
Parietal lobe (language and touch)
Temporal lobe (hearing, learning and feelings)
Occipital lobe (sight)
Cerebellum (balance and coordination)
Brain stem (breathing, heart rate and temperature)




Corpus callosum, trunk
Thalamic nuclei
Corpus callosum, genu
Corpus callosum, rostrum
Corpus callosum, splenium
Fornix, body
Pulvinar
Superior colliculus
Anterior lobe of cerebellum
Inferior colliculus
Primary fissure
Superior cerebellar peduncle
Optic tract
Red nucleus
Pons
Corticospinal tract
Medulla oblongata
Cerebellar tonsil


Limbic lobe
Parietal lobe
Frontal lobe
Thalamus
Corpus callosum
Occipital lobe
Pituitary gland
Temporal lobe
Pons
Cerebellum
Medulla oblongata

Development of the human nervous system begins around
the eighteenth day after conception



From conception to birth

Brain development continues after an animal is born. In fact, the human brain continues to develop for at least two decades. Every learning experience changes the brain.

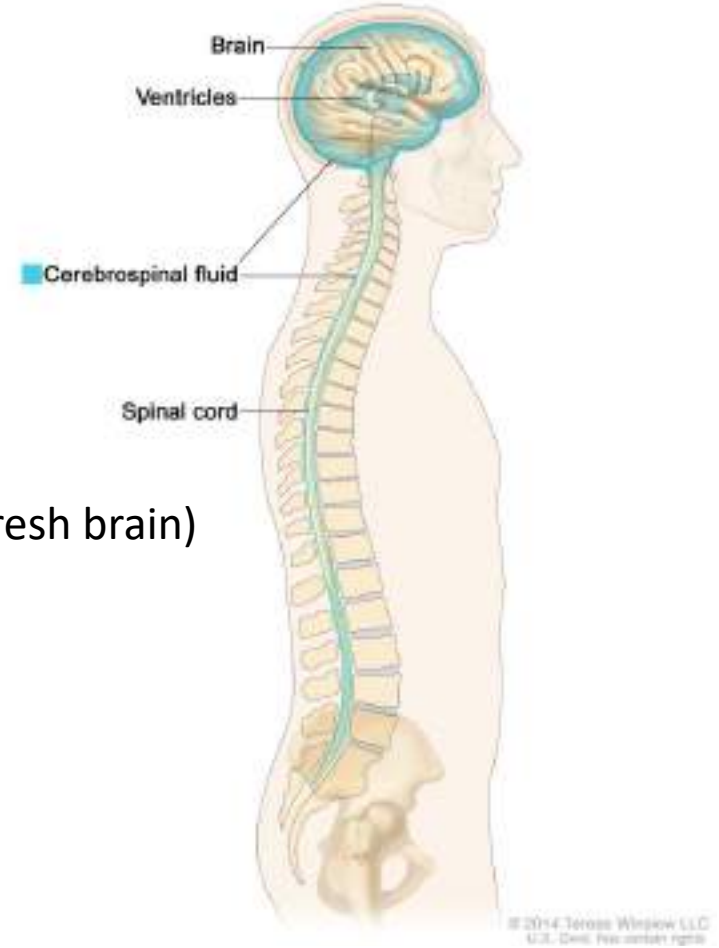
The last region to mature in the frontal cortex ~ 25 years

Legal age to drive or drink

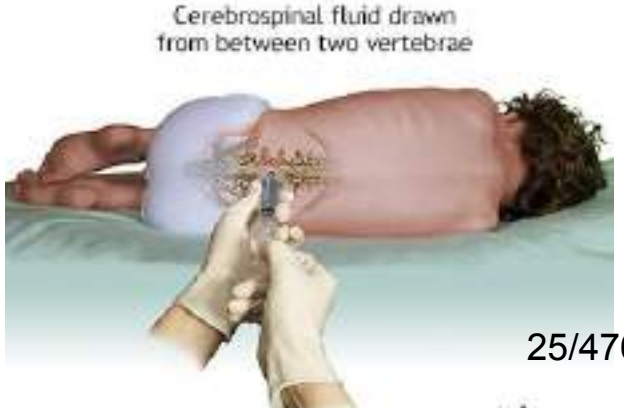
100 billion neurons

- How does your head and neck manage the weight of your brain?
- (1300-1400gms)

Cerebro-Spinal Fluid (CSF)

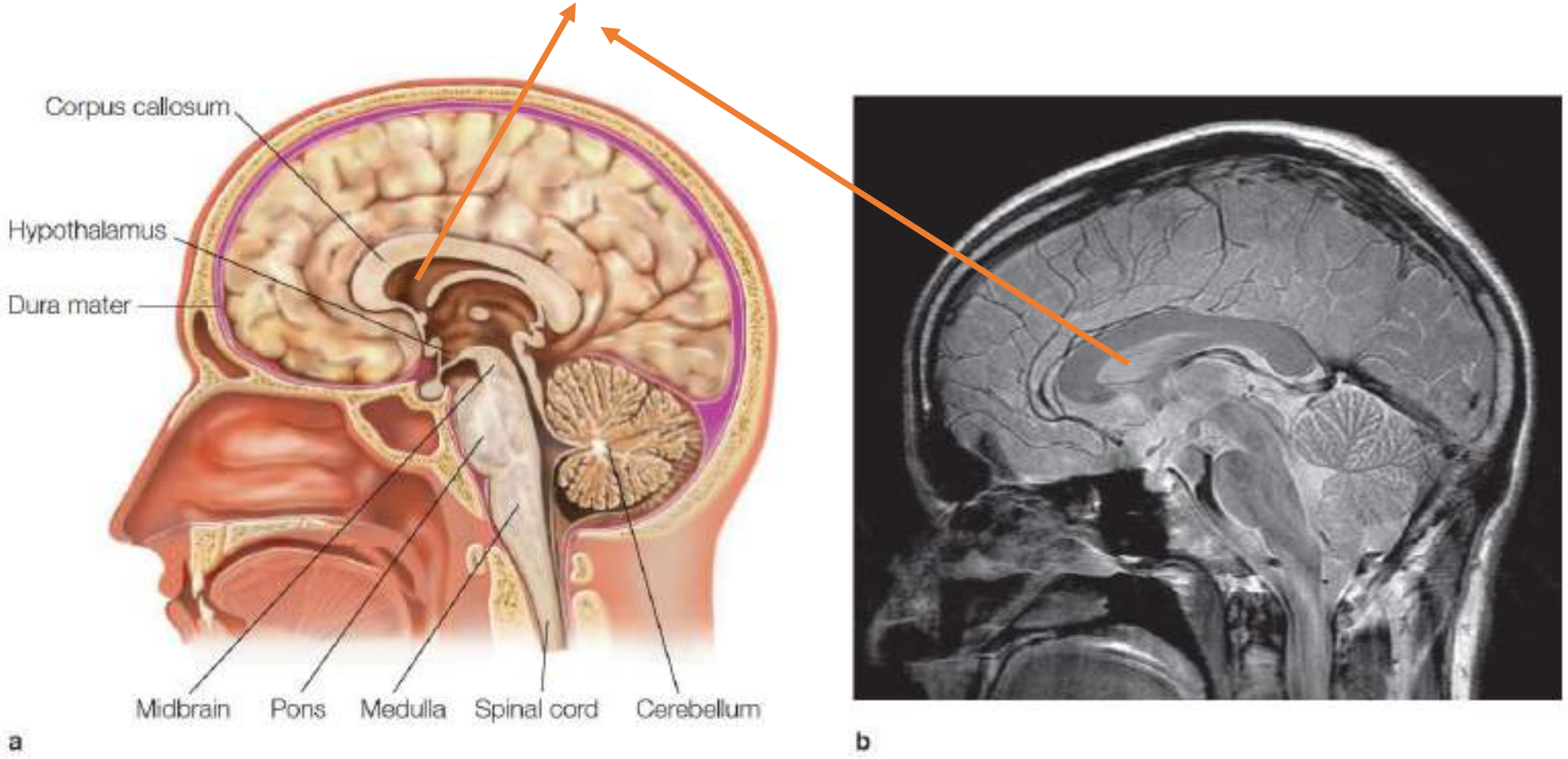


- ✓ A human brain cannot even support its own weight (extremely difficult to handle a fresh brain)
- ✓ An intact brain floats in CSF
- ✓ When floating, its weighs less, approx 80g!
- ✓ CSF also reduces the shock to the CNS due to sudden head movements and jolts.
- ✓ Total volume of CSF in brain – 125ml
- ✓ All of the CSF is replaced every six hours
- ✓ CSF is extracted to detect many infections in the brain



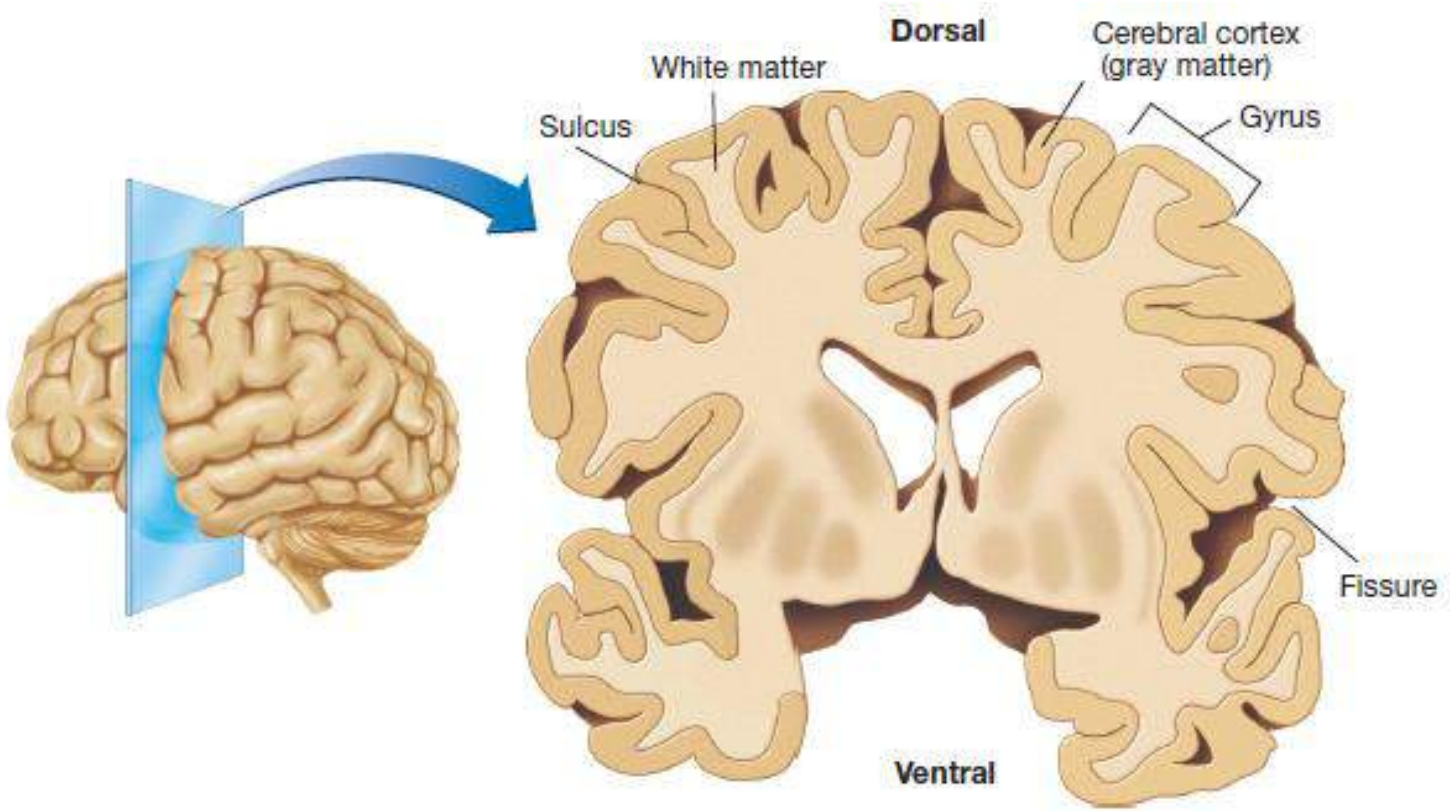
MRI Image

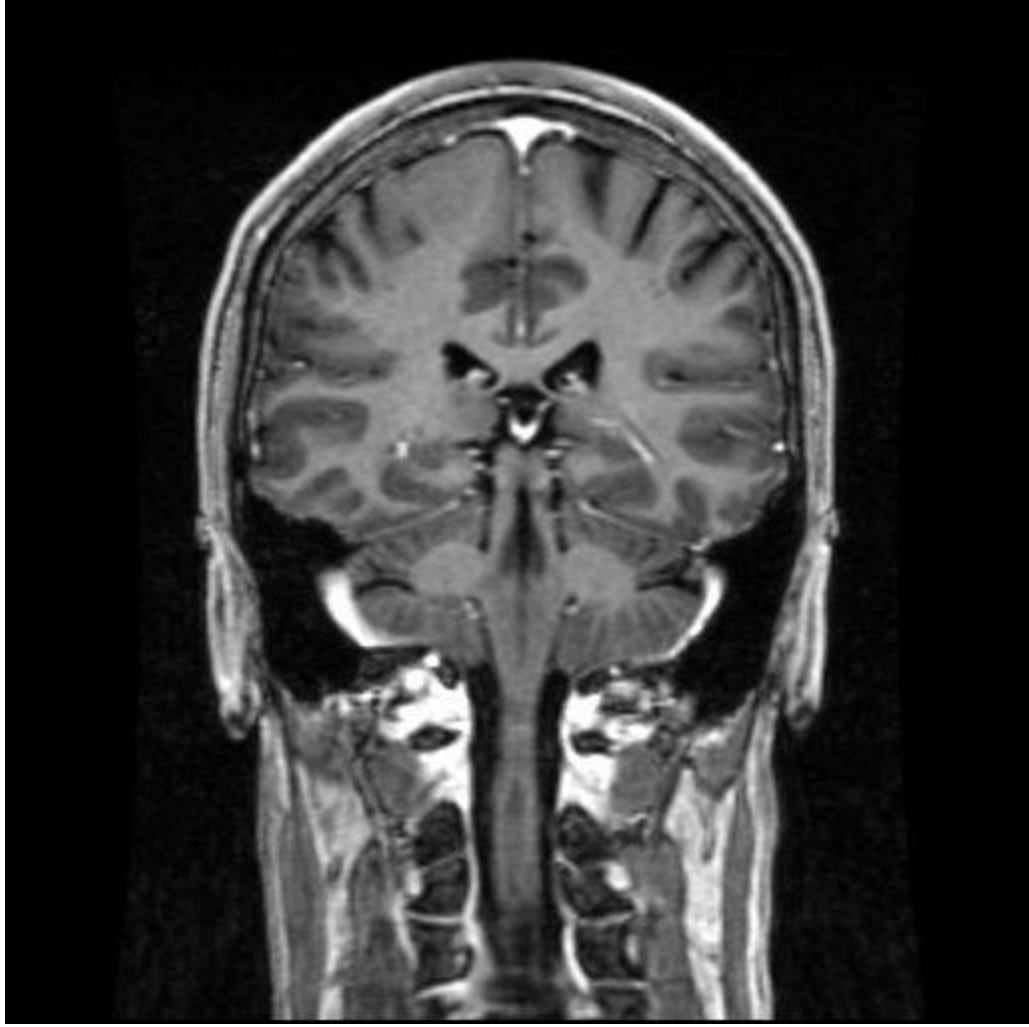
Ventricle (reference points)



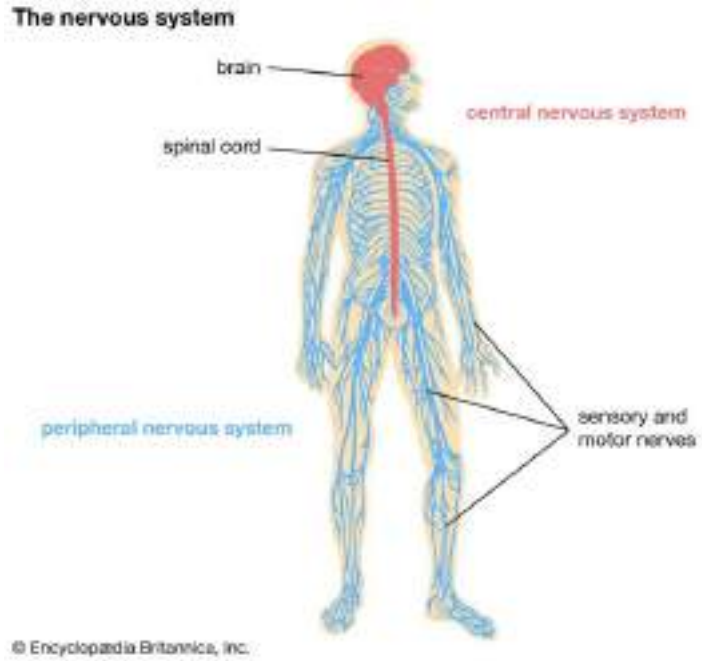
Gray matter **-** due to the grayish color of cell bodies (of neurons) that predominate the region

White matter: due to the whitish opaque color of the myelin (a protective covering on the neurons) that predominate this region

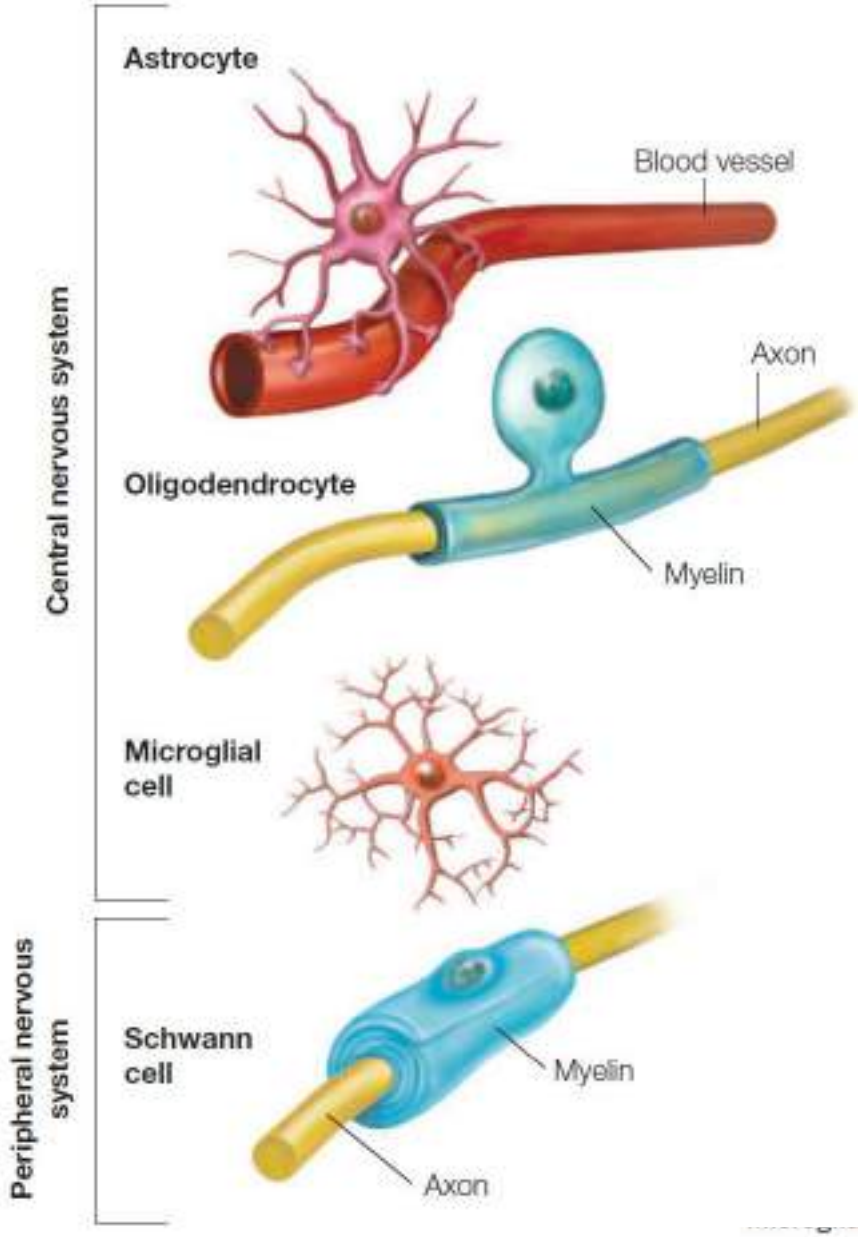




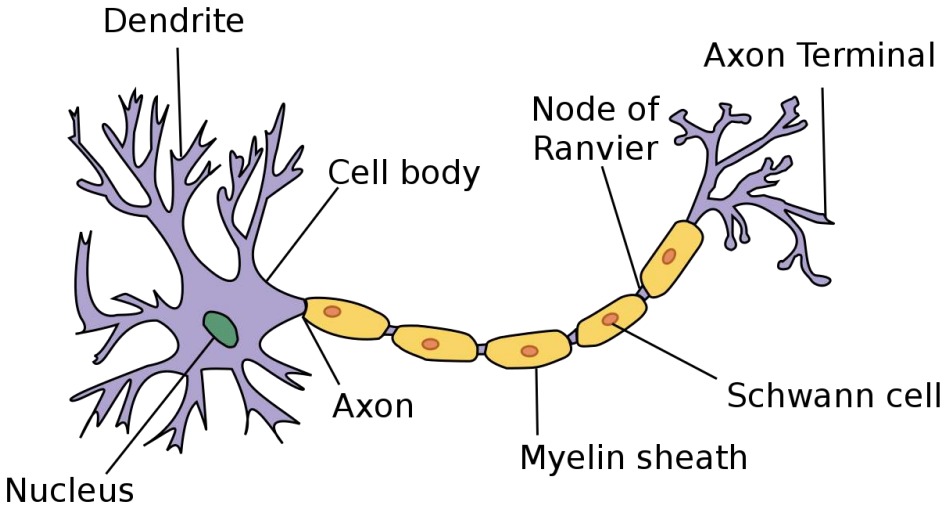
What gives the white color in the white matter seen in the MRI scans?



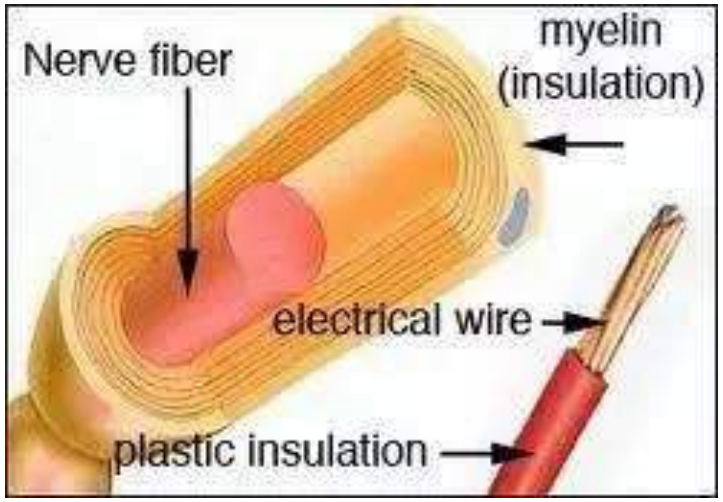
Glial cells (support neurons)



A
neuron



What is the function of the myelin sheath?

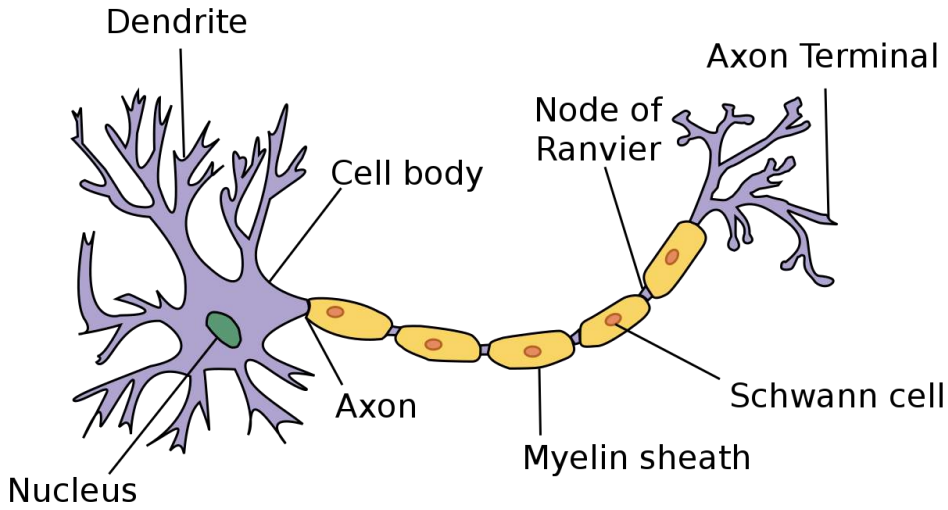


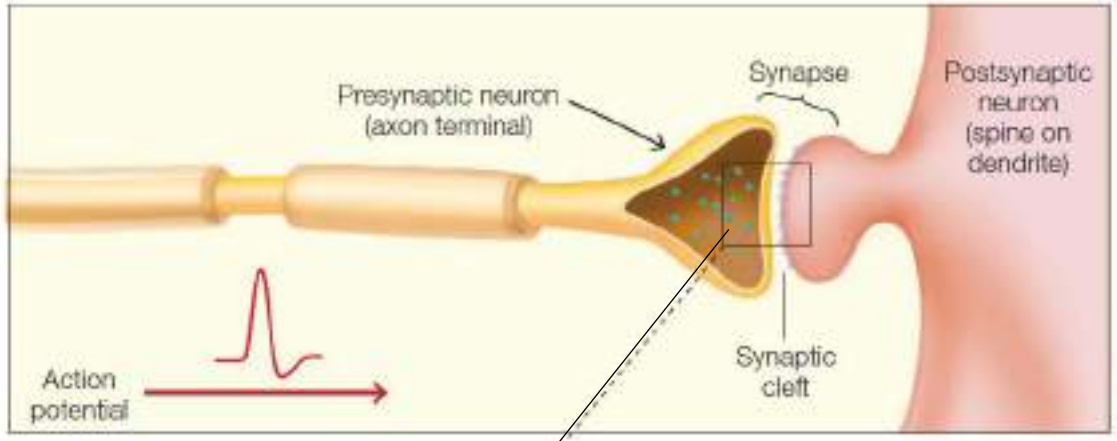
How does a neuron transmit a signal?

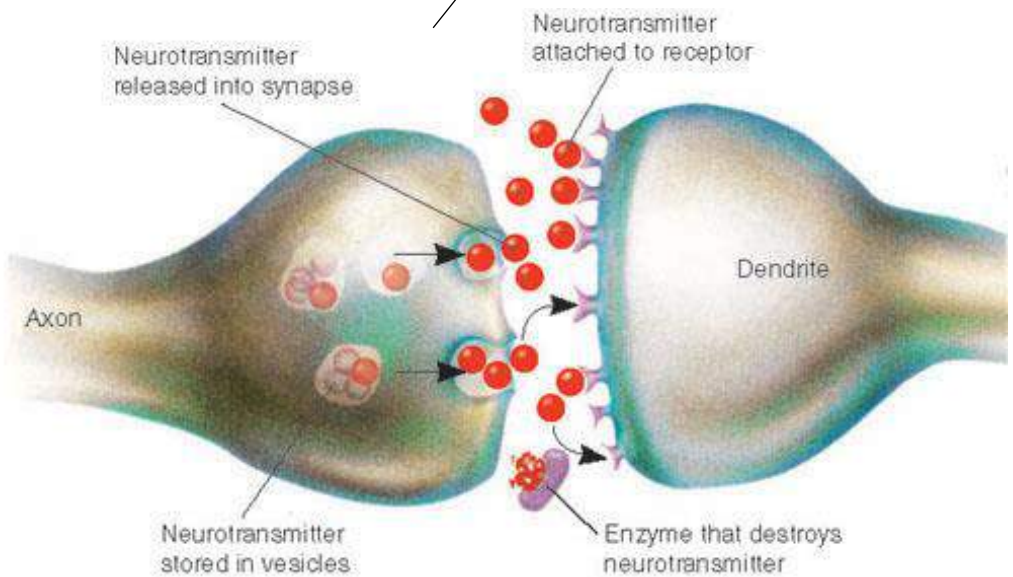
How does a neuron switch on?

Class 2
Neuronal Function

How does a neuron transmit a signal?

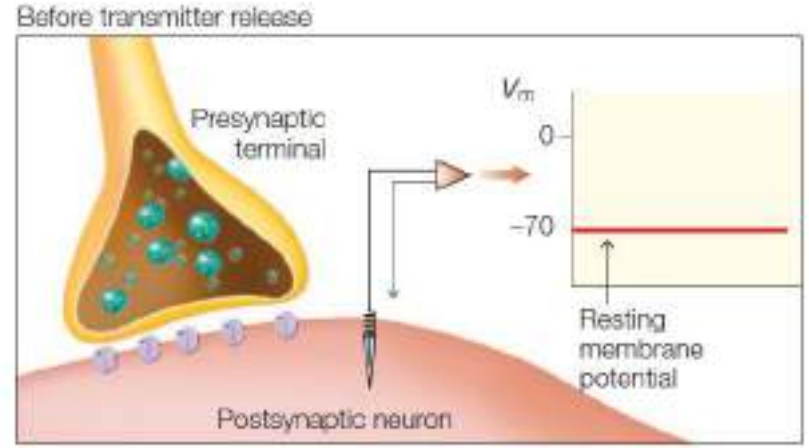






Synaptic cleft

a narrow gap of about 20 nanometers



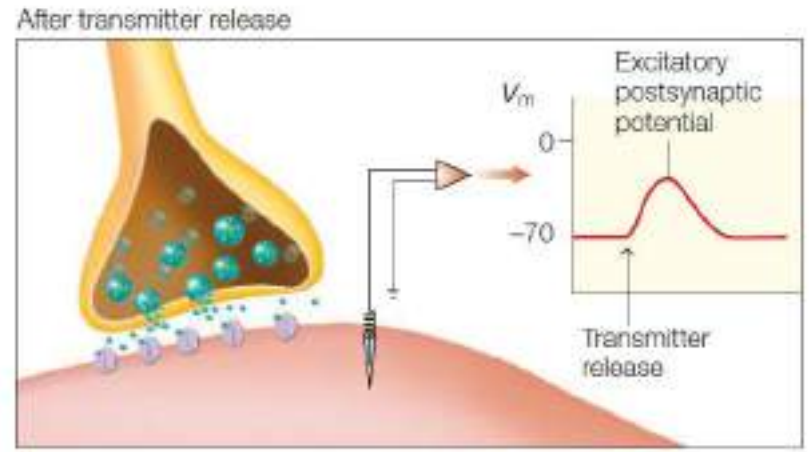
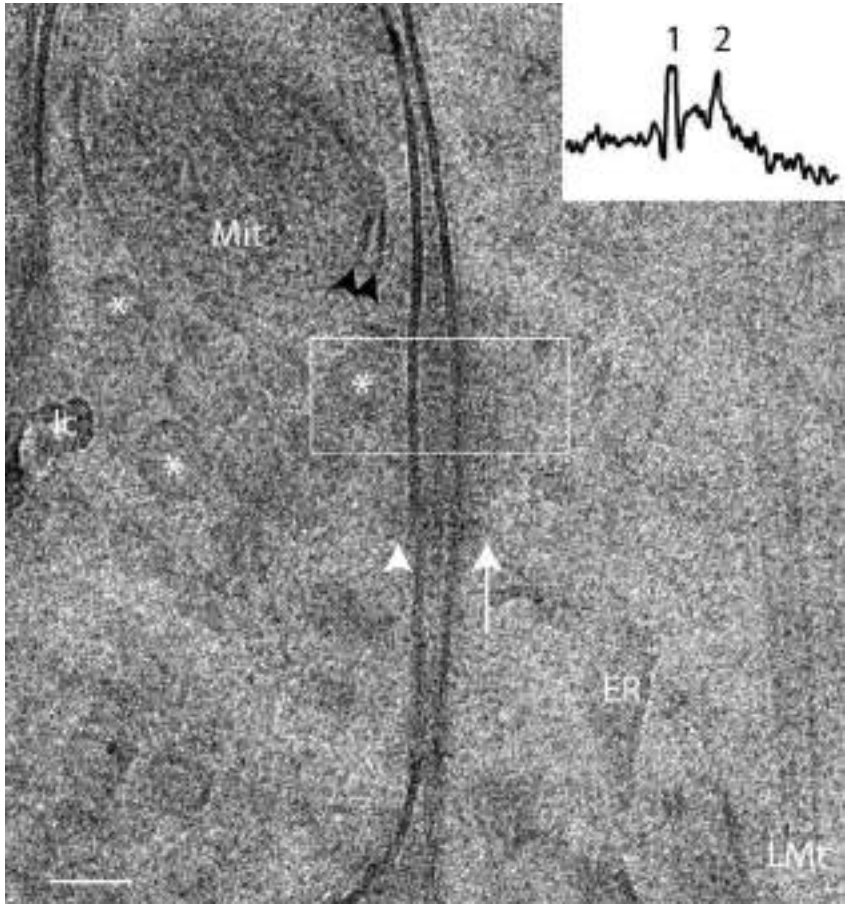
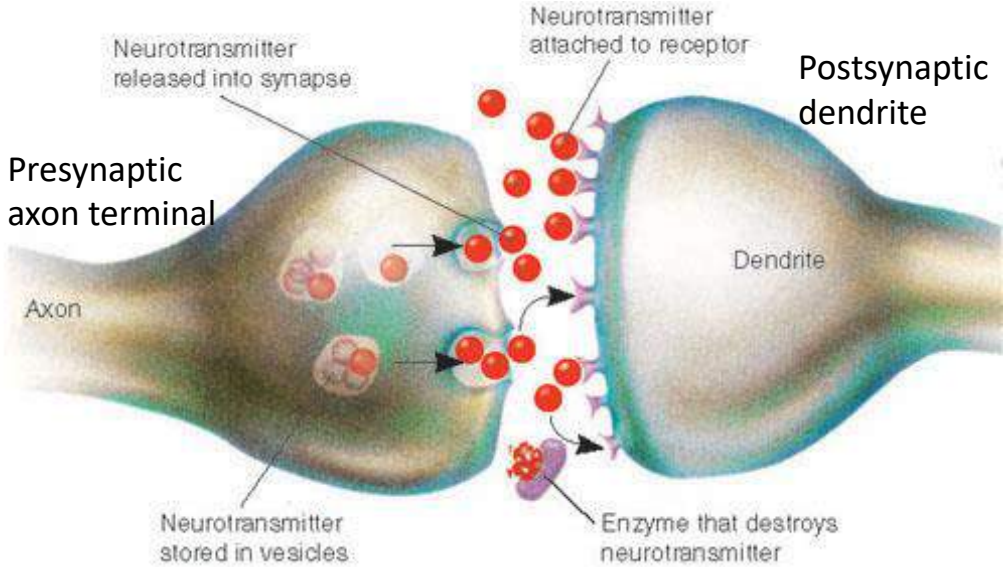


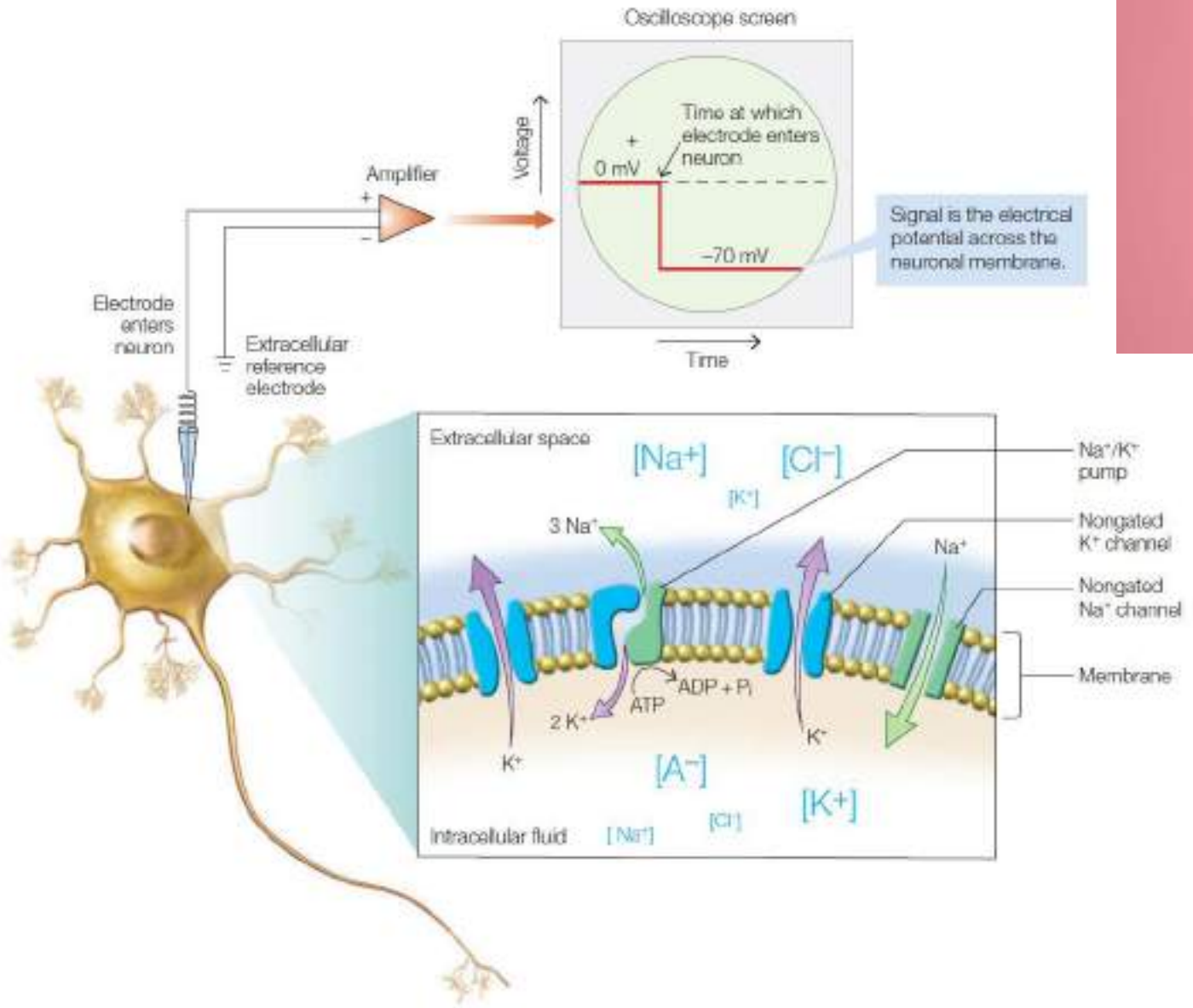
FIGURE 2.14 Neurotransmitter leading to a postsynaptic potential. The binding of neurotransmitter to the postsynaptic membrane receptors changes the membrane potential (V_m). These postsynaptic potentials can be either excitatory (depolarizing the membrane), as shown here, or inhibitory (hyperpolarizing the membrane).

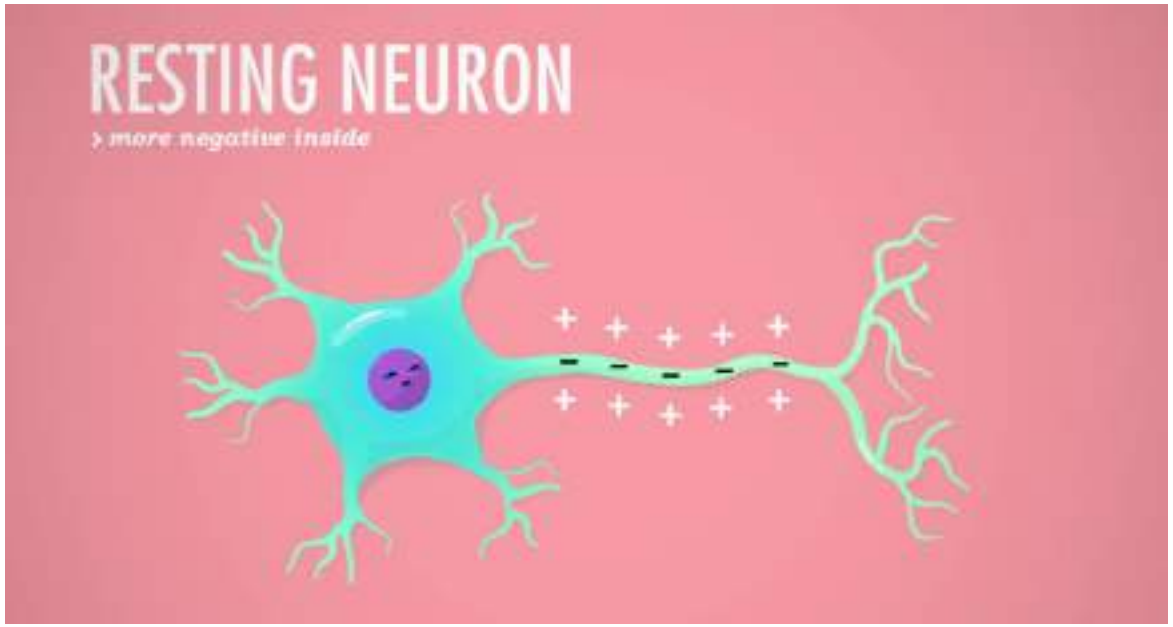
Synaptic cleft/gap



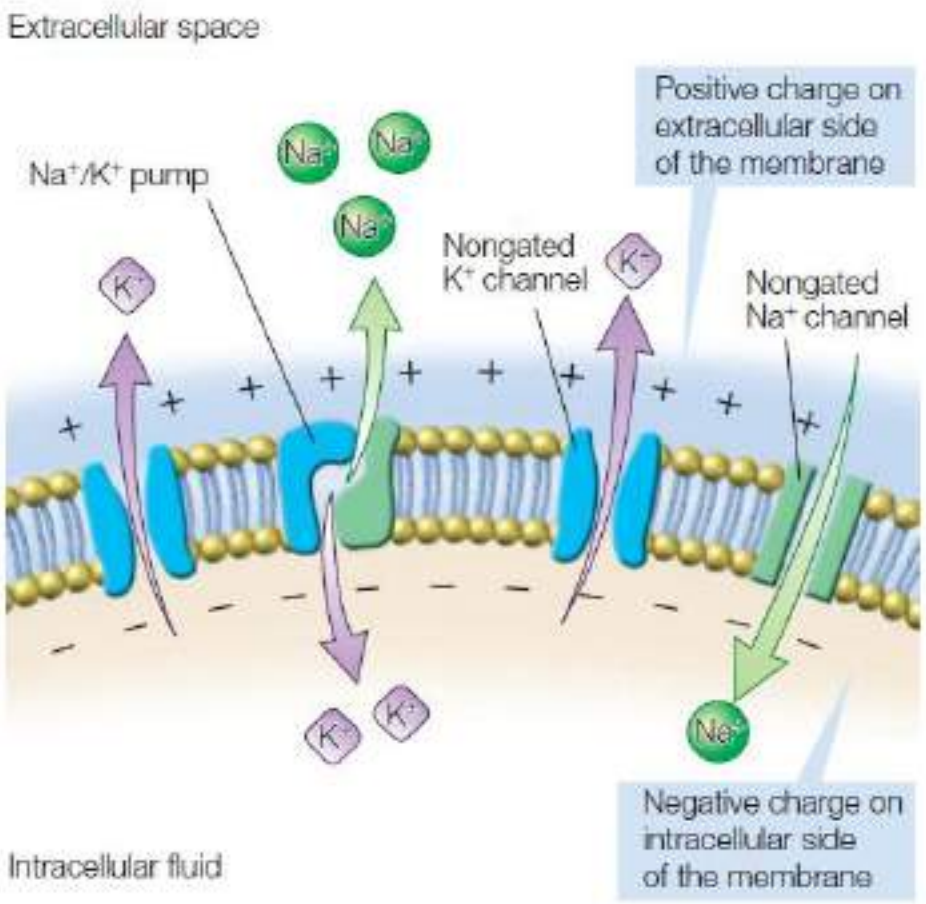


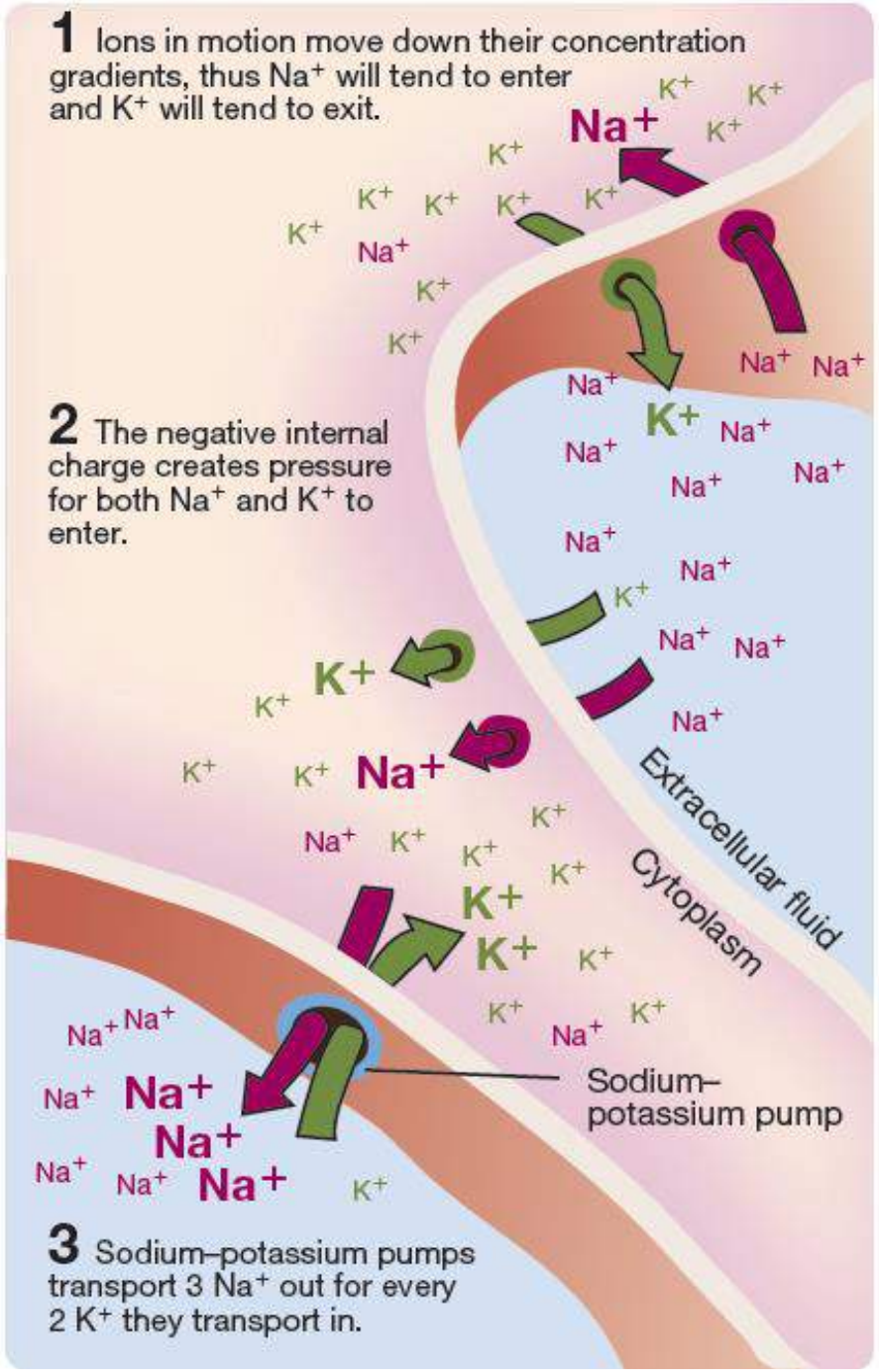
A neuron at rest



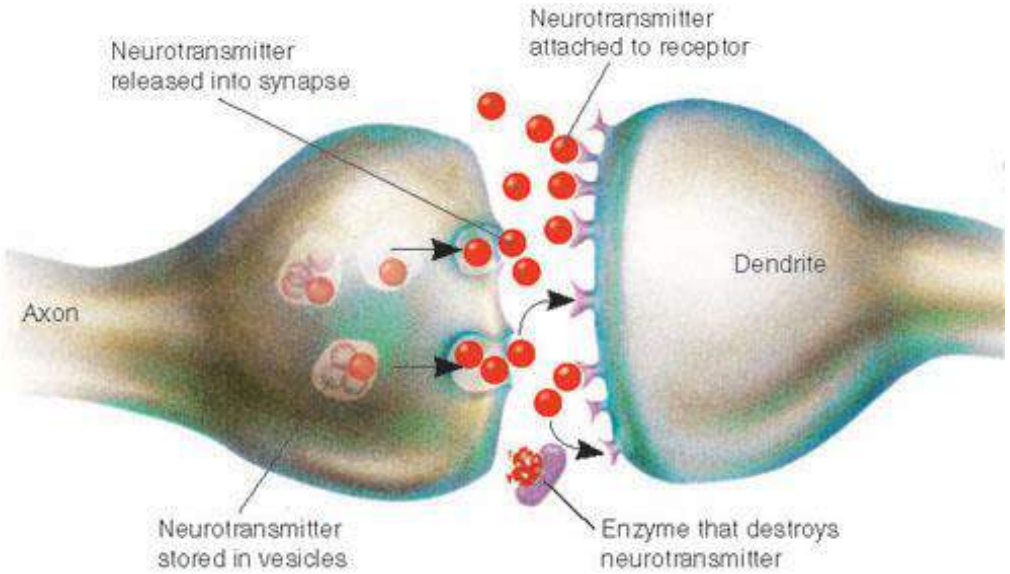


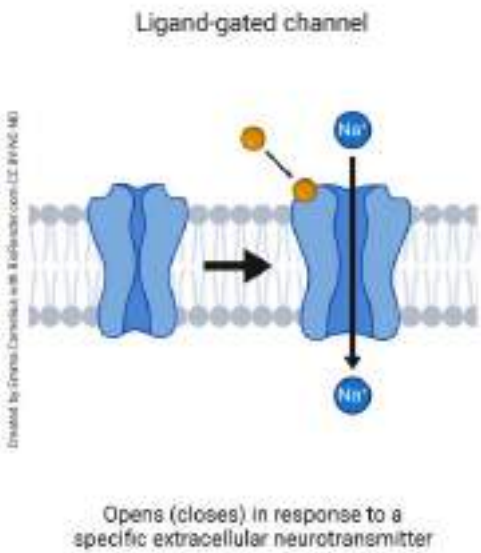
Na-K pump

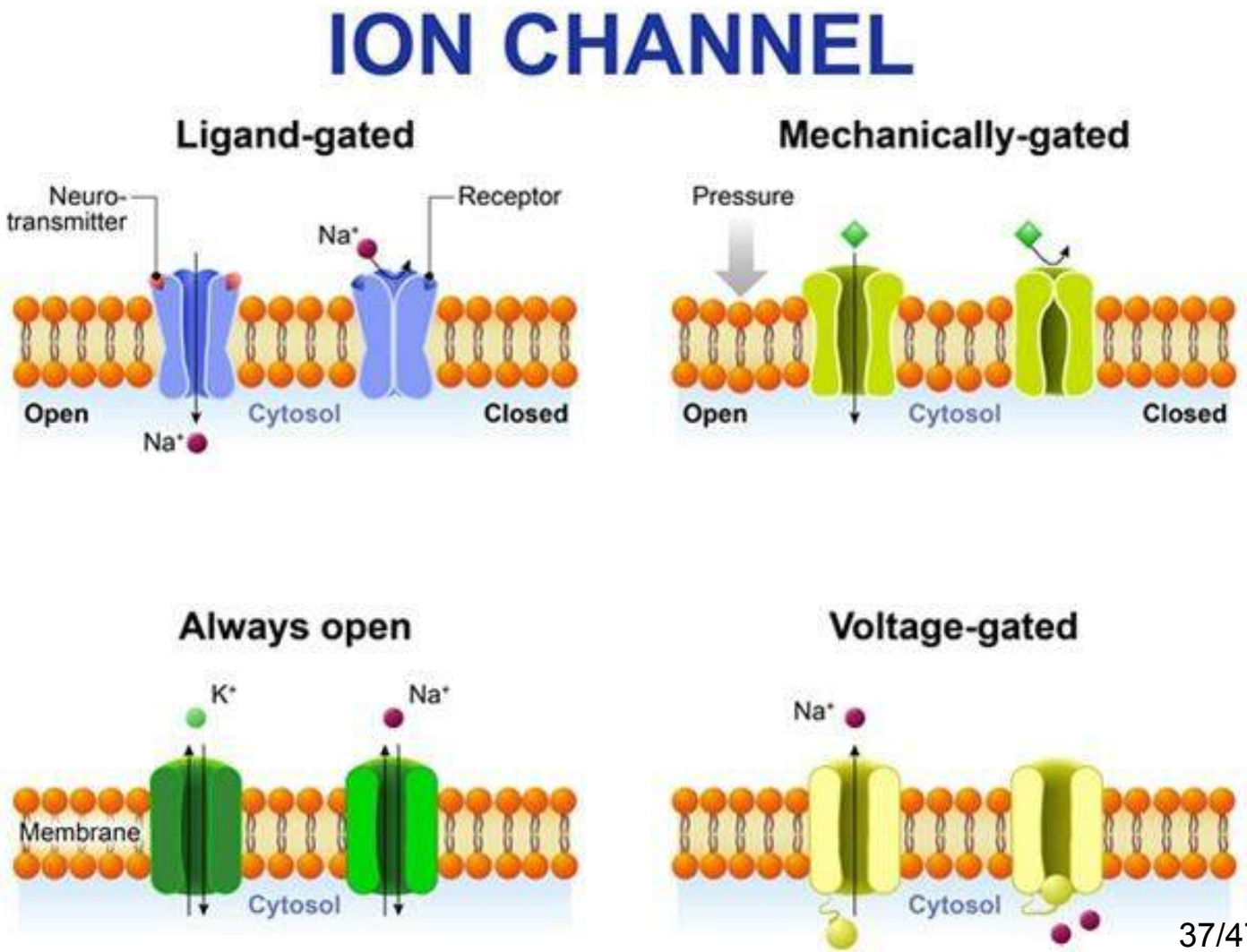

Extracellular space
Positive charge on extracellular side of the membrane
Na+/K+ pump
Nongated K+ channel
Nongated Na+ channel
Negative charge on intracellular side of the membrane
Intracellular fluid


1 Ions in motion move down their concentration gradients, thus Na+ will tend to enter and K+ will tend to exit.
2 The negative internal charge creates pressure for both Na+ and K+ to enter.
Extracellular fluid
Cytoplasm
Sodium–potassium pump
3 Sodium–potassium pumps transport 3 Na+ out for every 2 K+ they transport in.

https://uen.pressbooks.pub/anatomyphysiology2/chapter/ion-channels/

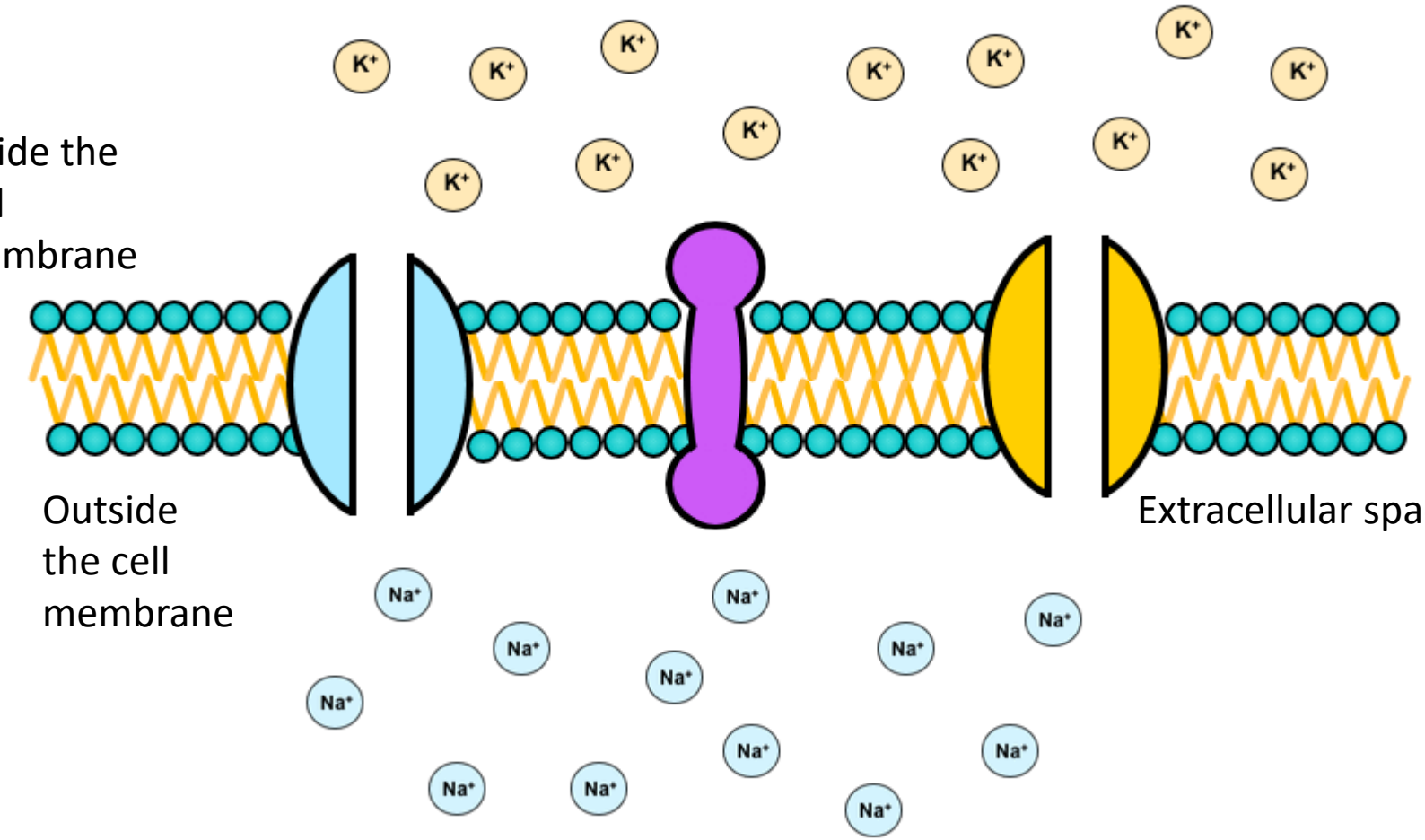






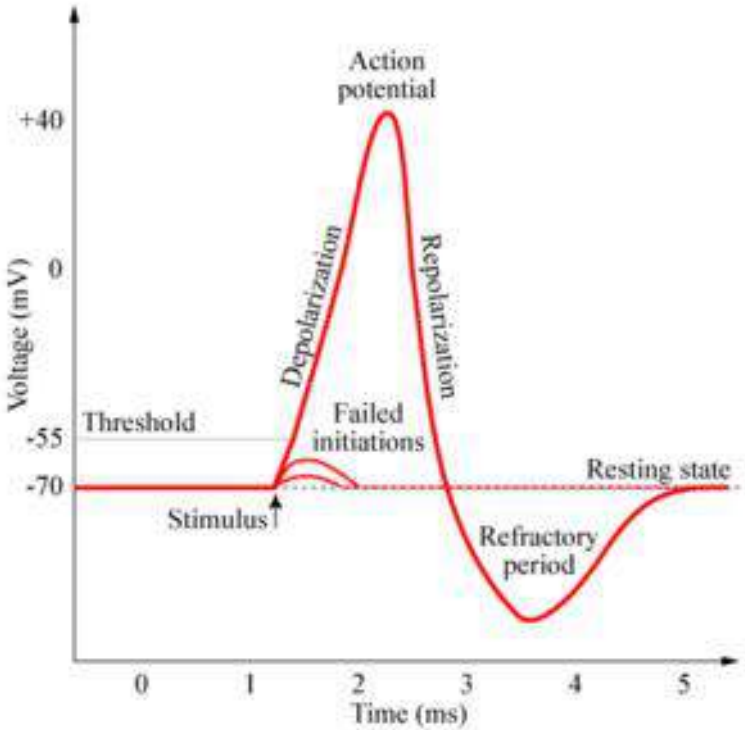
Depolarizace

Inside the cell membrane



Outside the cell membrane

Extracellular space

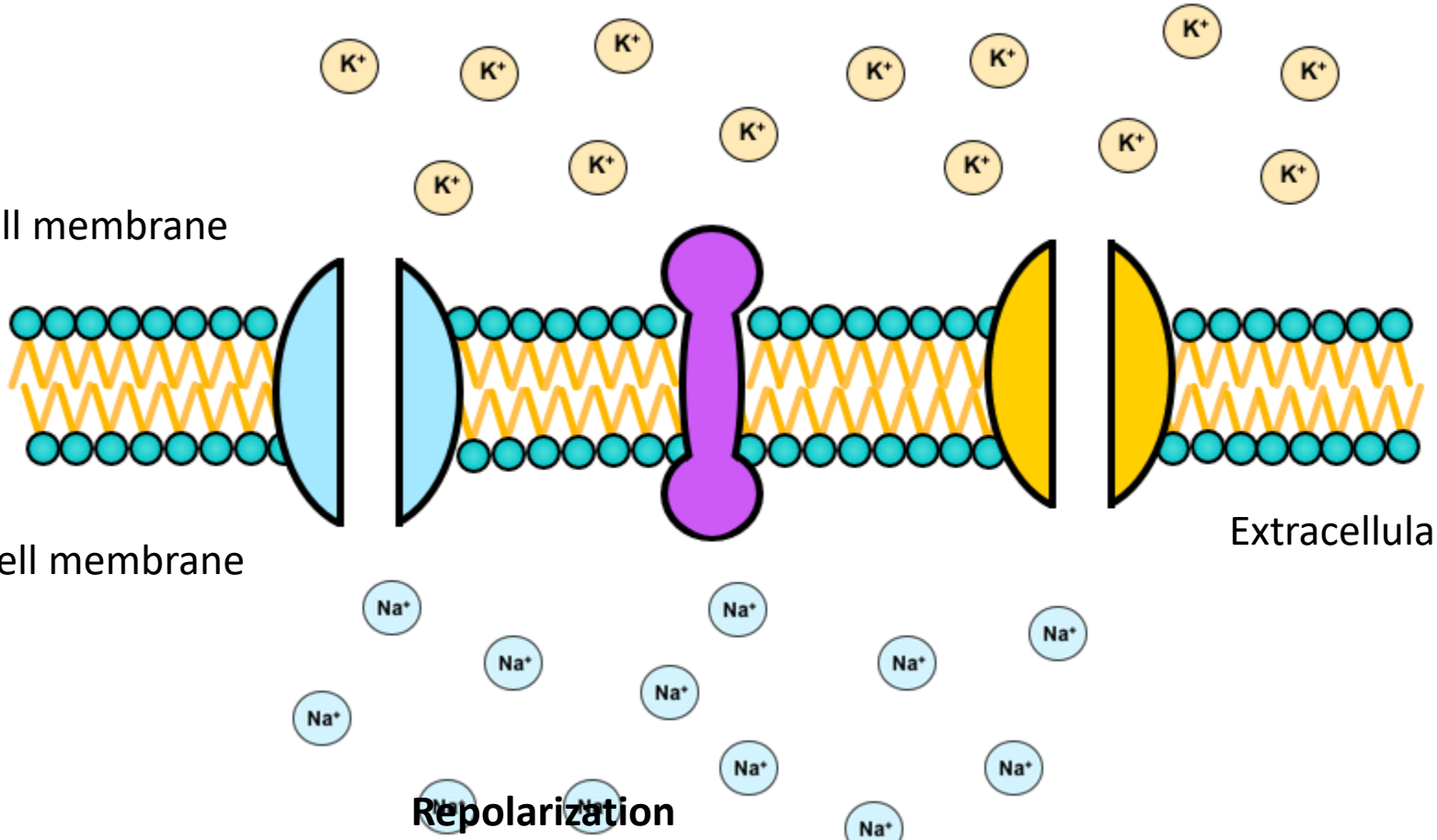


Because of the tension created by the resting membrane potential, the Na+ ions rush inside once the Na+ channels are opened

→ 1 millisecond

With too many + ions inside, the K+ gates open and K+ ions are pushed out to balance the electrostatic & concentration gradient

Depolarizace



Depolarization
Because of the tension created by the resting membrane potential, the Na+ ions rush inside once the Na+ channels are opened

1 millisecond

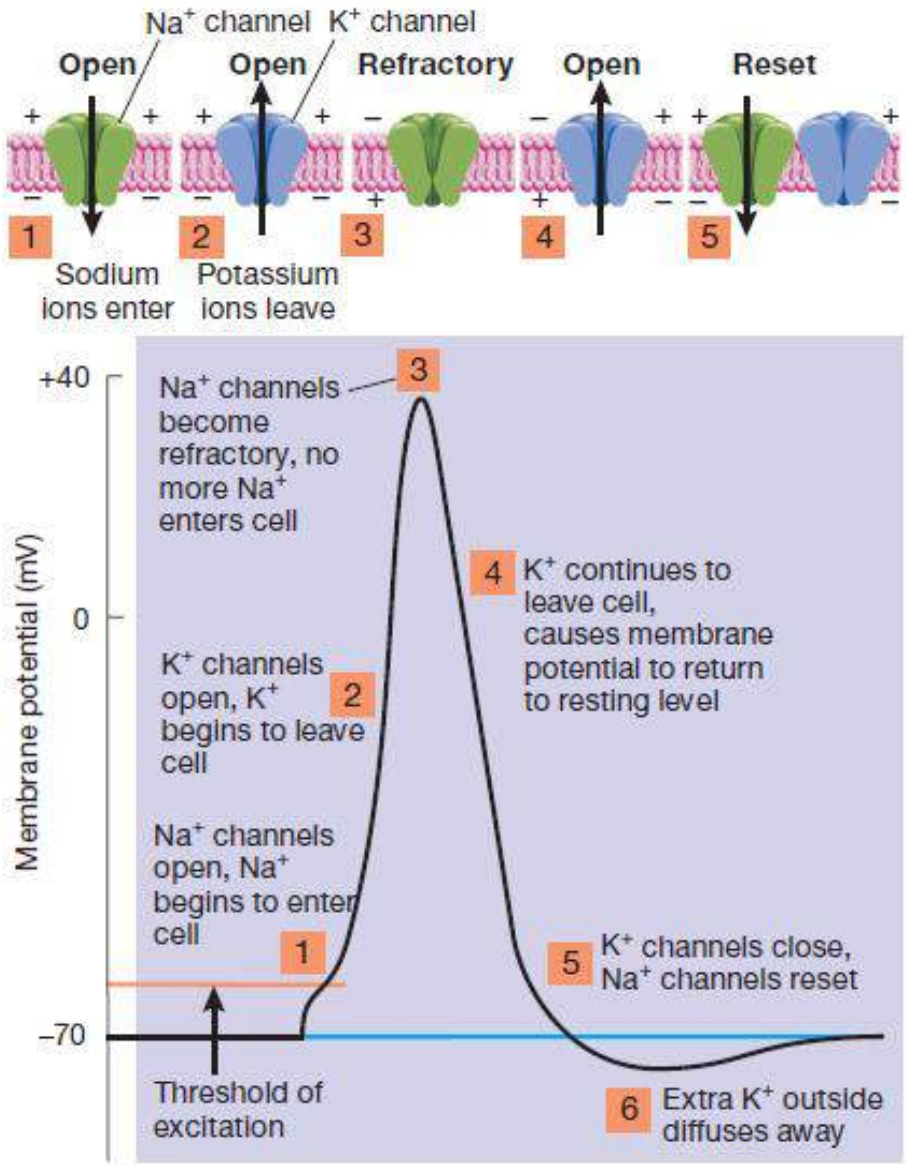
Repolarization
With too many + ions inside, the K+ gates open and K+ ions are pushed out to balance the electrostatic & concentration gradient

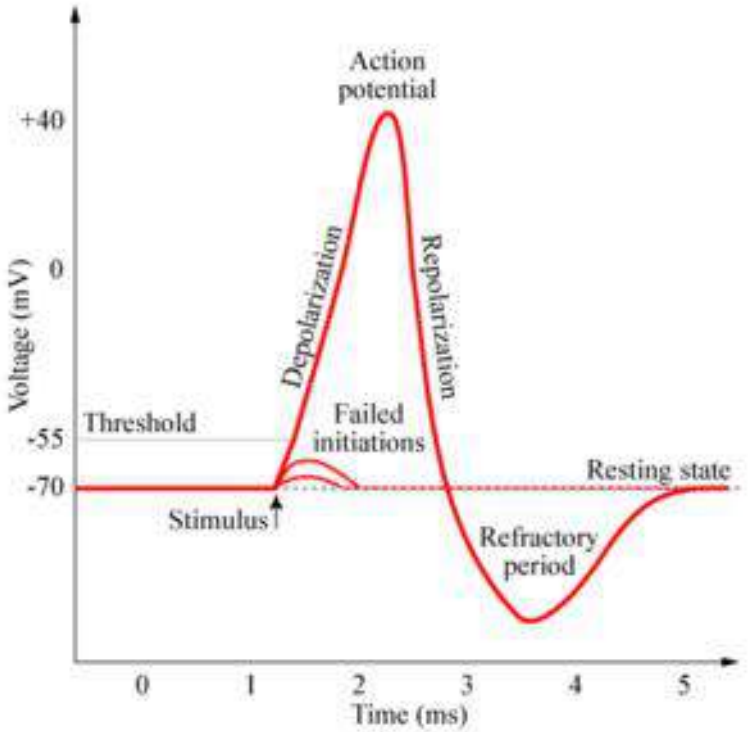
1 millisecond

Na/K pump

Resting membrane potential is restored

Dynamics of an Action Potential (AP)





The whole process takes about 2-3 msec

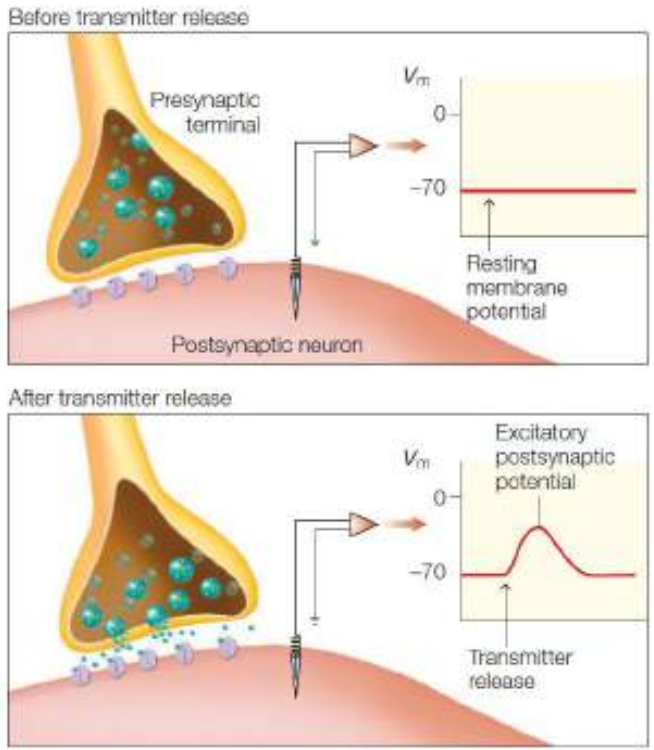
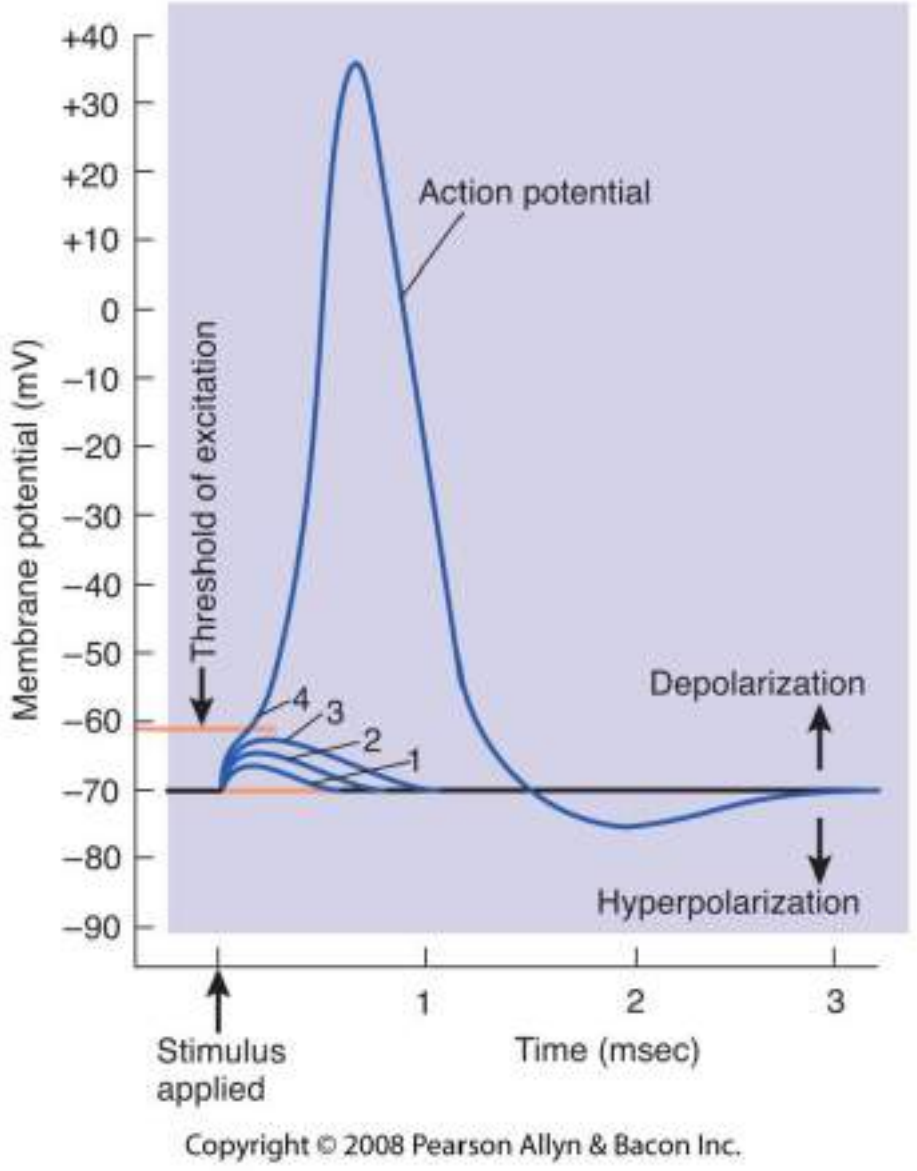
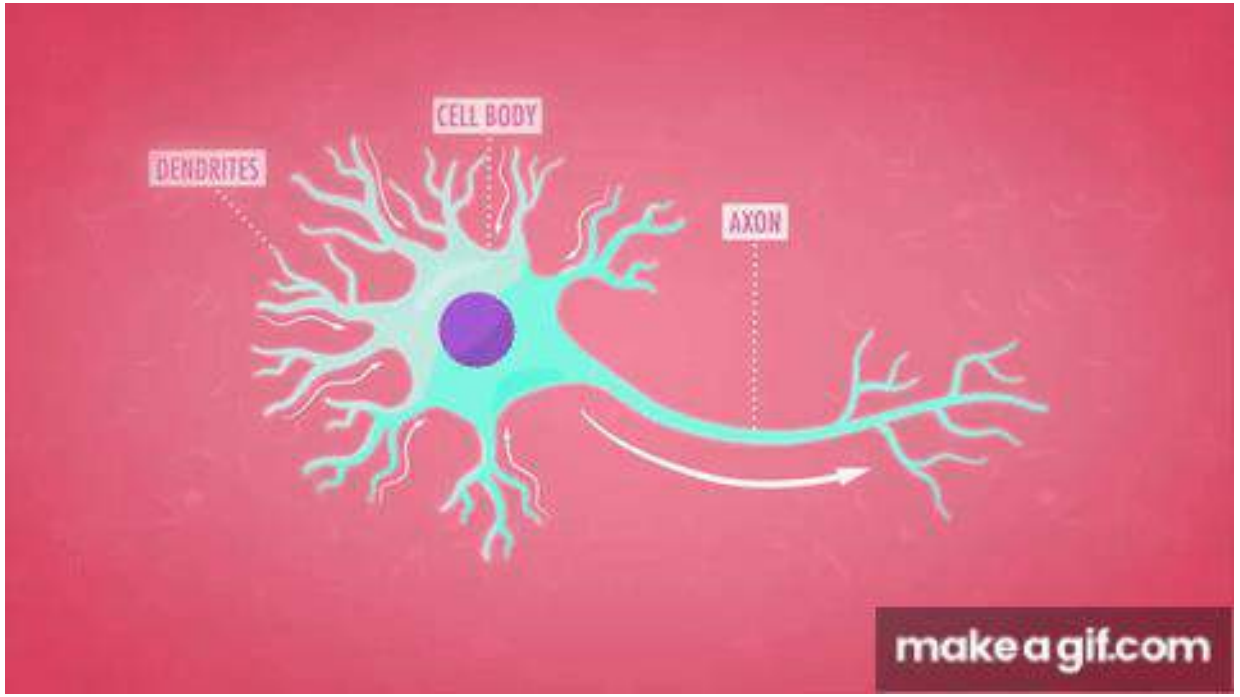


FIGURE 2.14 Neurotransmitter leading to a postsynaptic potential. The binding of neurotransmitter to the postsynaptic membrane receptors changes the membrane potential (V_m). These postsynaptic potentials can be either excitatory (depolarizing the membrane), as shown here, or inhibitory (hyperpolarizing the membrane).

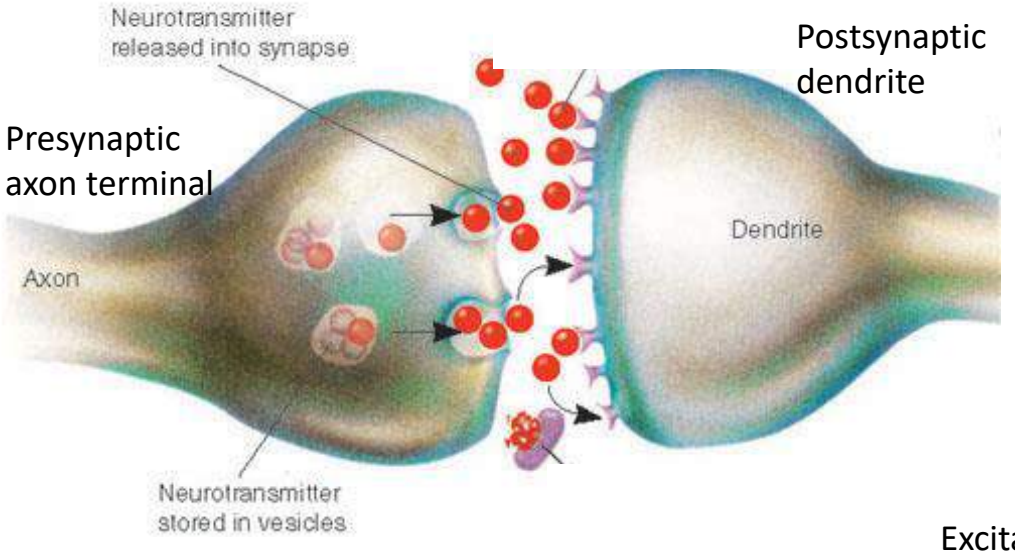
Action Potential (AP) in an axon

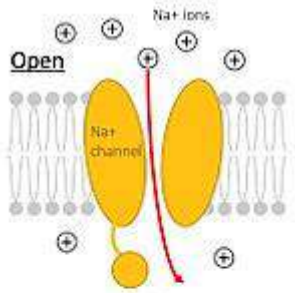
An action potential is an **all or none phenomenon**, i.e. only when depolarization crosses the threshold, an action potential occurs.



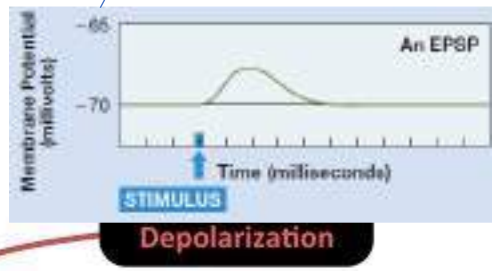


Threshold varies from -65mV to -55mV, across different brain regions

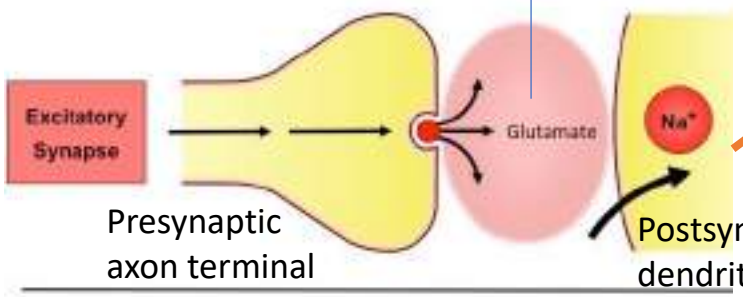




threshold



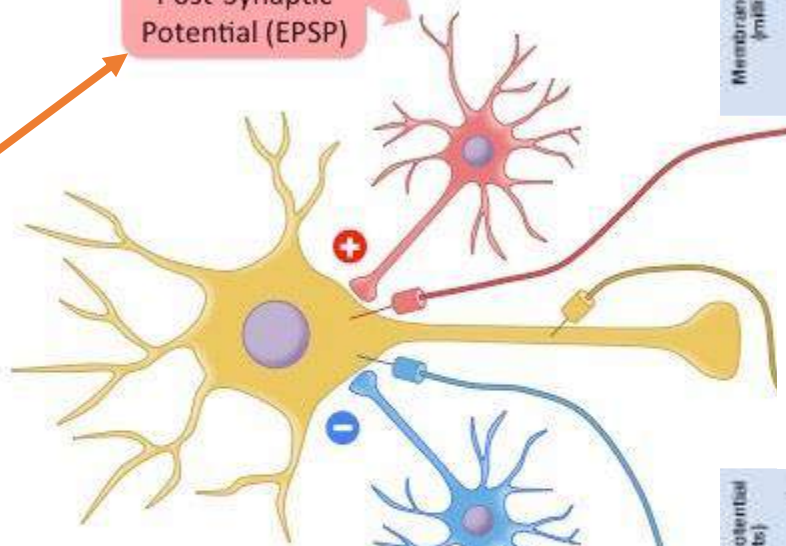
Excitatory neurotransmitter



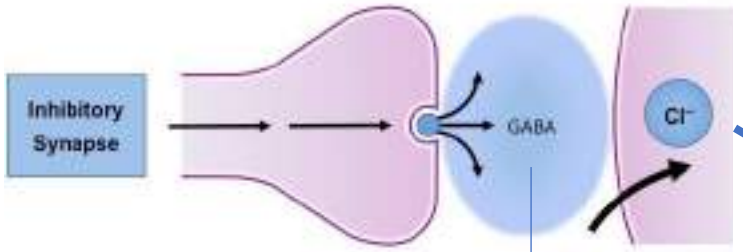
Presynaptic axon terminal

Postsynaptic dendrite

Excitatory Post-Synaptic Potential (EPSP)



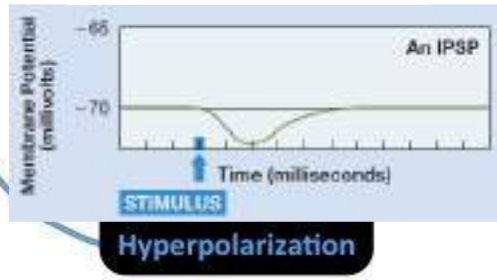
Ion channels/gates are specific to neurotransmitter molecules (shape/size). Depending on which type of ion channels are opened, the signal can be excitatory or inhibitory.



Presynaptic axon terminal

Postsynaptic dendrite

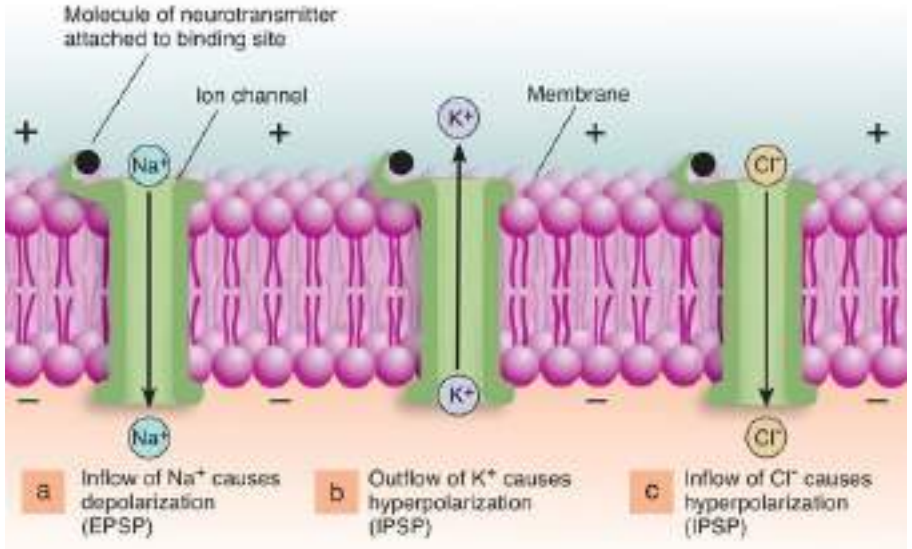
Inhibitory Post-Synaptic Potential (IPSP)



Inhibitory neurotransmitter

An action potential occurs if the combination of graded potentials exceeds a threshold

Postsynaptic potentials

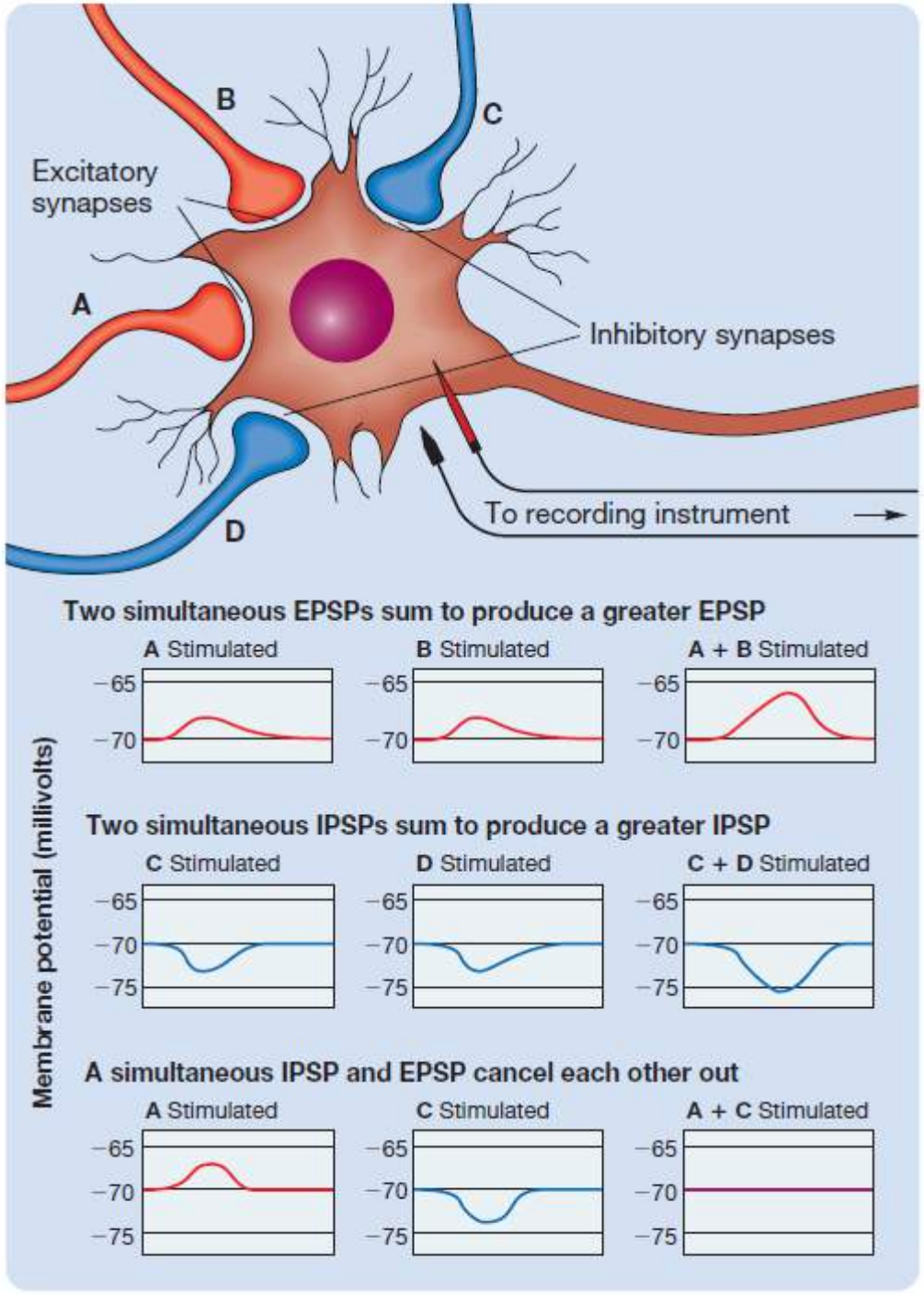


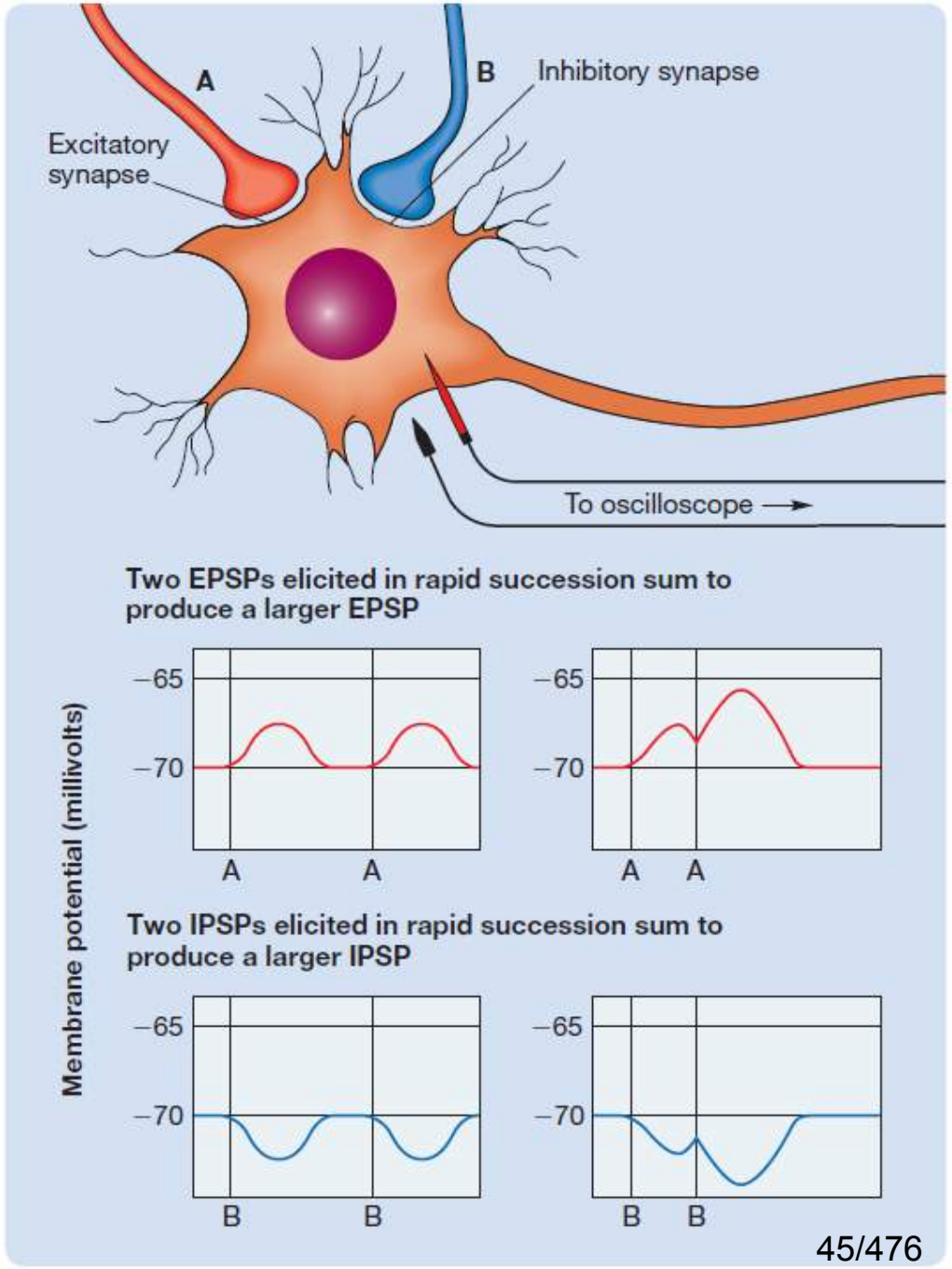
- ***Excitatory postsynaptic potential (EPSP):***
  - An excitatory depolarization of the postsynaptic membrane of a synapse caused by the liberation of a neurotransmitter by the terminal button.
  - Mainly due to the opening of Na^+ channels
  - Positive ions can enter or negative ions can leave the cell to cause a depolarization (Na^+ enter or A^- leave)
  -

- ***Inhibitory postsynaptic potential (IPSP):***
  - An inhibitory hyperpolarization of the postsynaptic membrane of a synapse caused by the liberation of a neurotransmitter by the terminal button
  - Due to the opening of K^+ or Cl^- channels
  - Positive ions can leave or negative ions can enter the cell to cause hyperpolarization (K^+ leave or Cl^- enter)

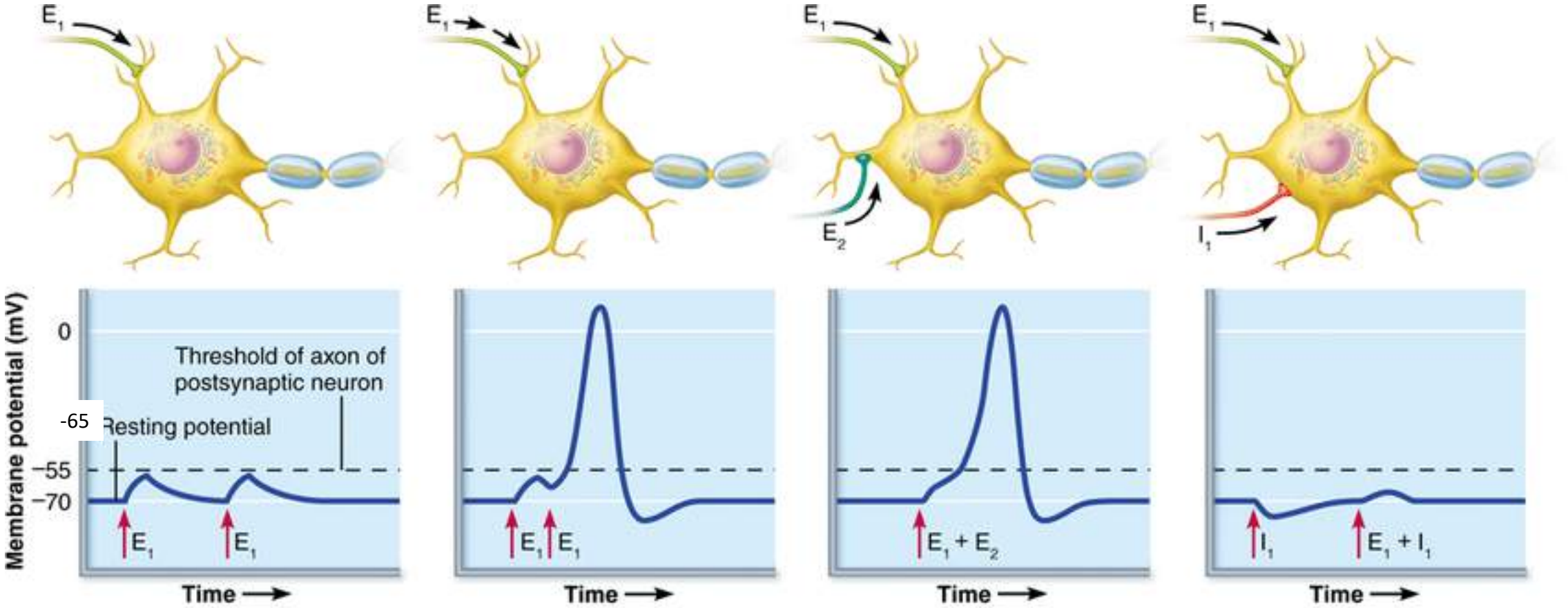
- How does a neuron know when to fire?

Graded Potential at dendrites





Factors that give rise to an action potential



(a) No summation: 2 stimuli separated in time cause EPSPs that do not add together.

(b) Temporal summation: 2 excitatory stimuli close in time cause EPSPs that add together.

(c) Spatial summation: 2 simultaneous stimuli at different locations cause EPSPs that add together.

(d) Spatial summation of EPSPs and IPSPs: Changes in membrane potential can cancel each other out.

Excitatory synapse 1 (E_1)

Excitatory synapse 2 (E_2)

Inhibitory synapse (I_1)

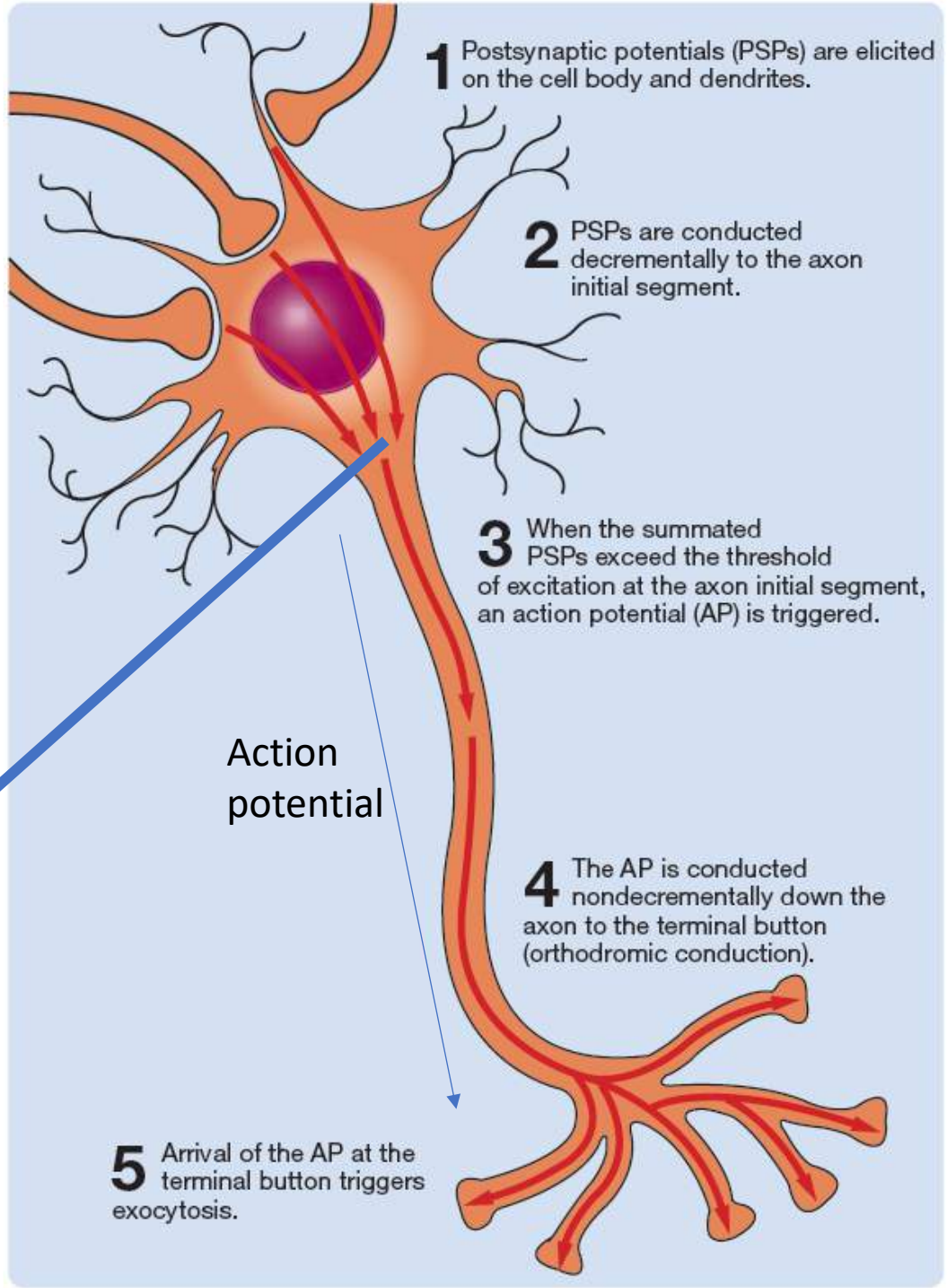
However,

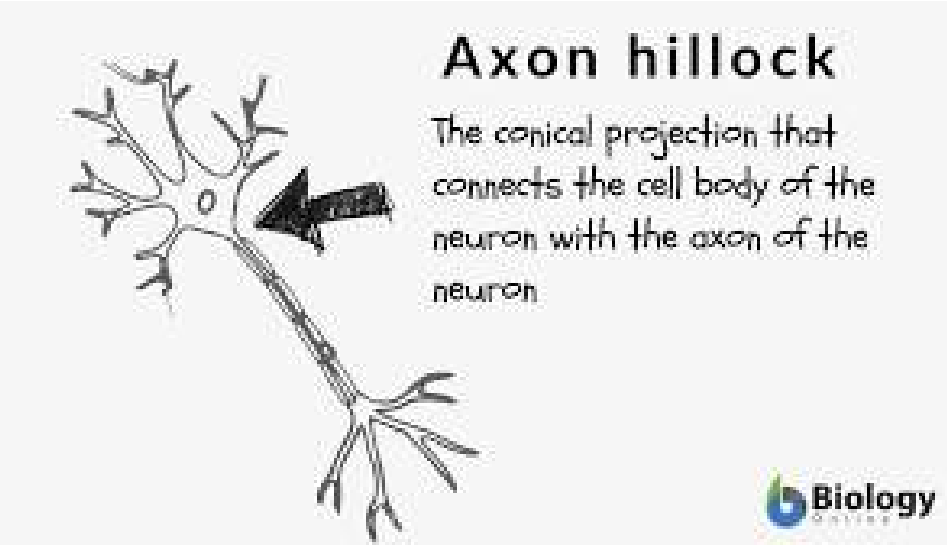
If EPSP > IPSP → AP is produced

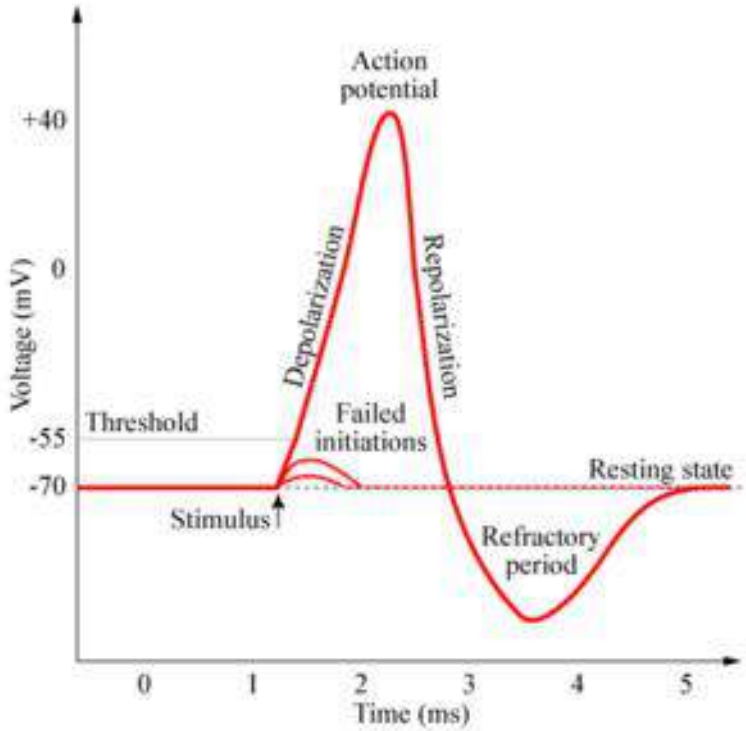
If EPSP < IPSP → no AP is produced

Graded potential

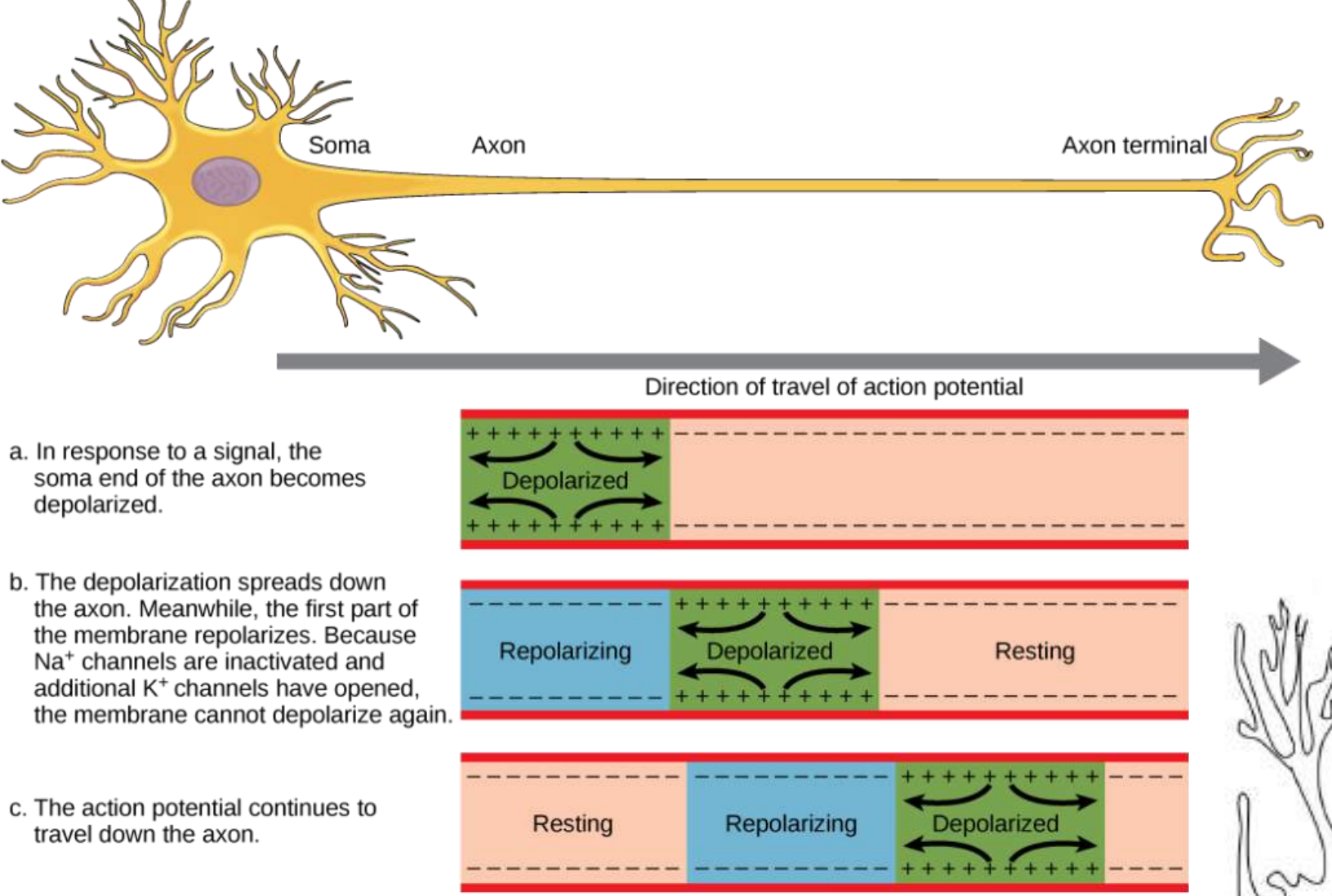
Voltage gated ion channels

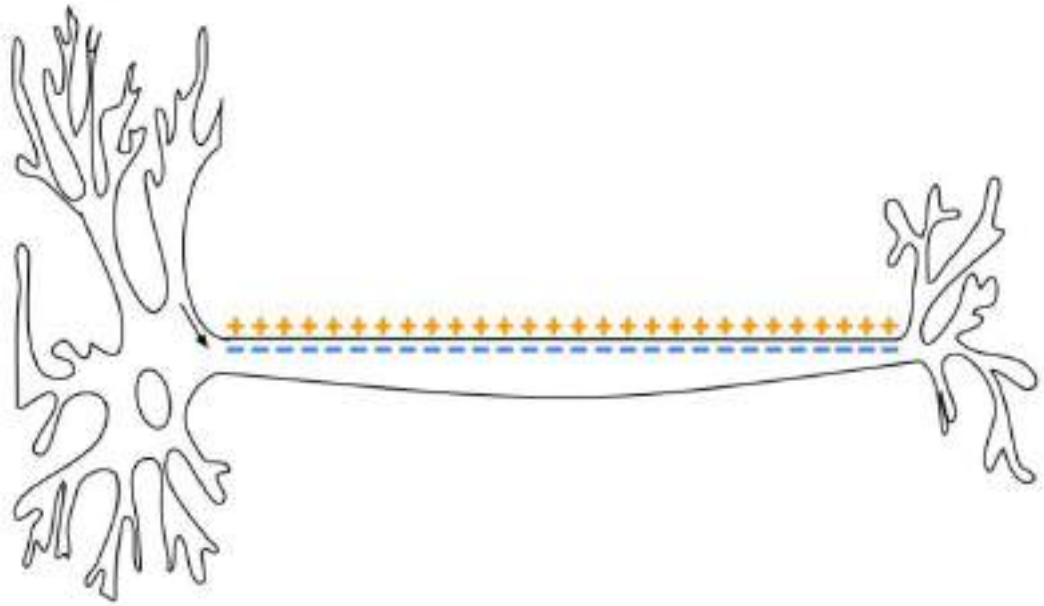




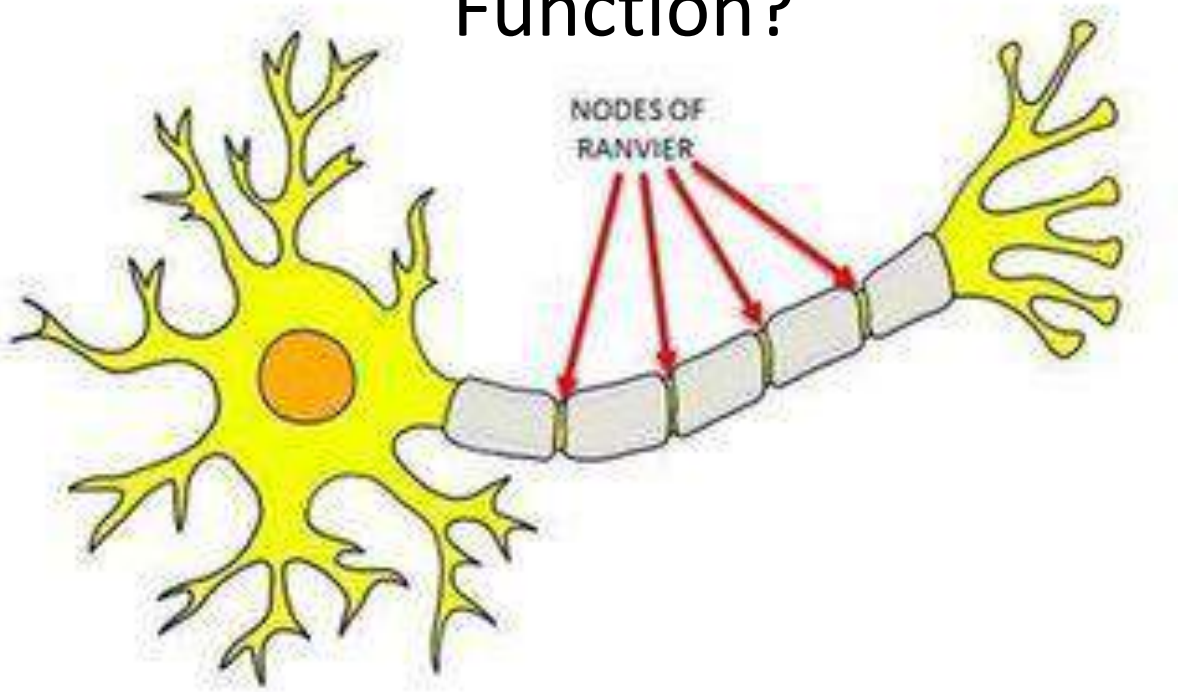


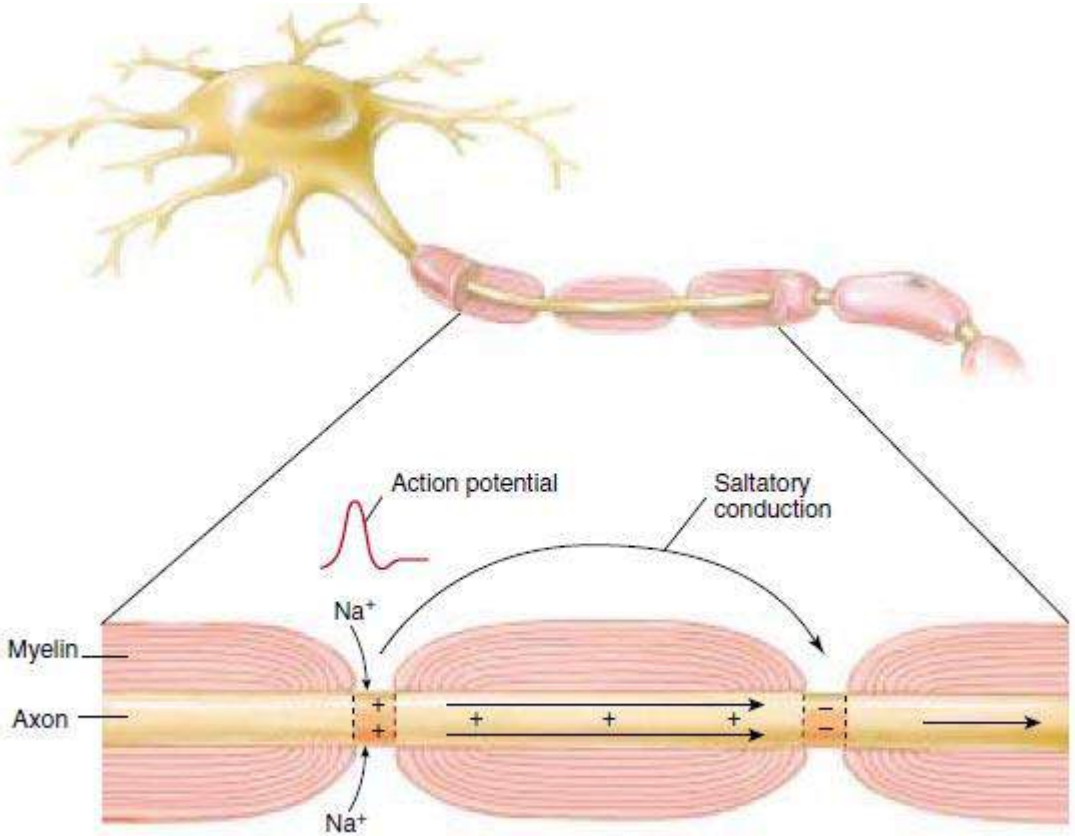
Propagation of an action potential

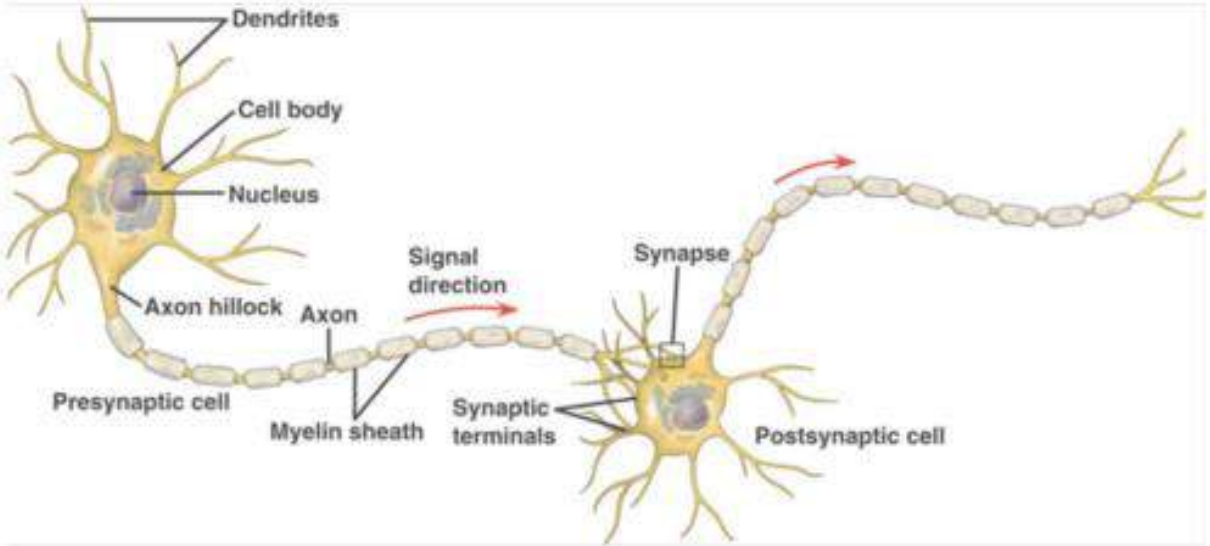


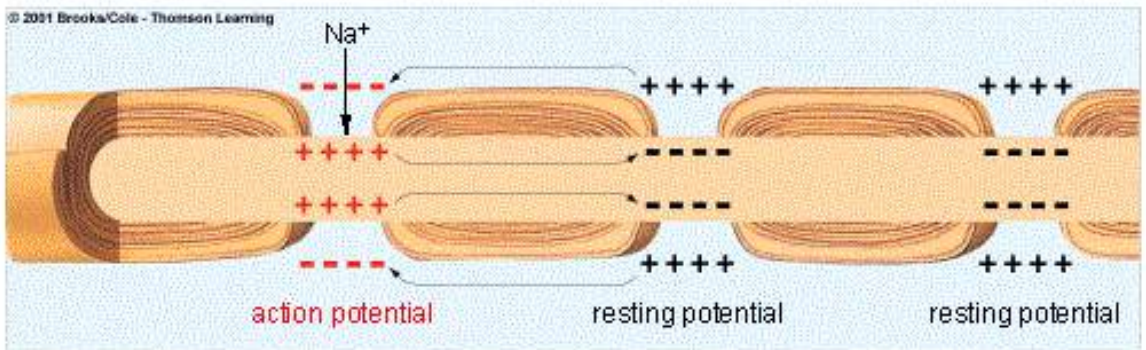


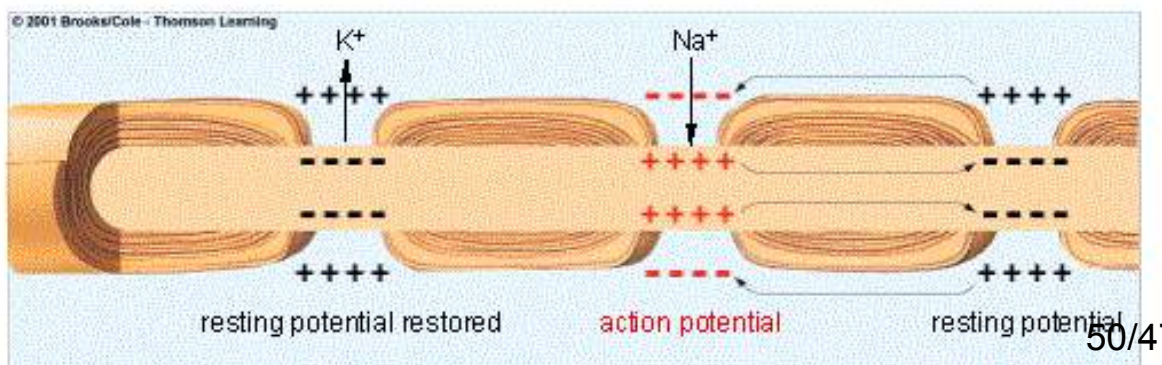
Function?





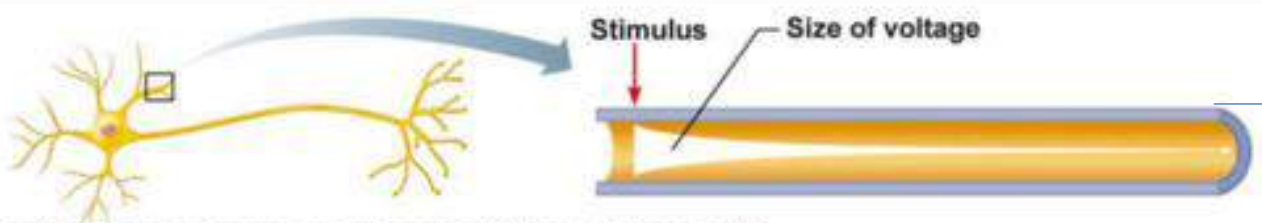




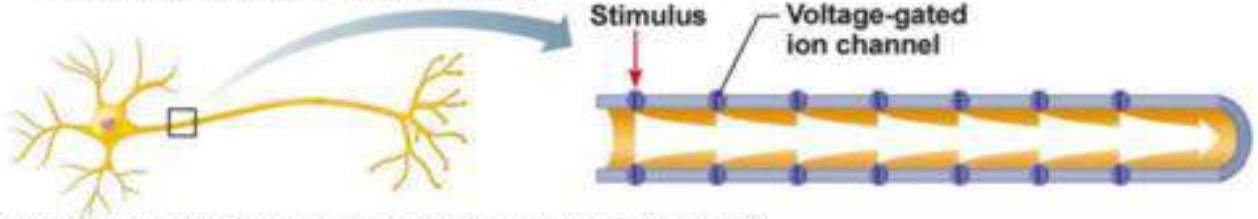


Saltatory conduction:

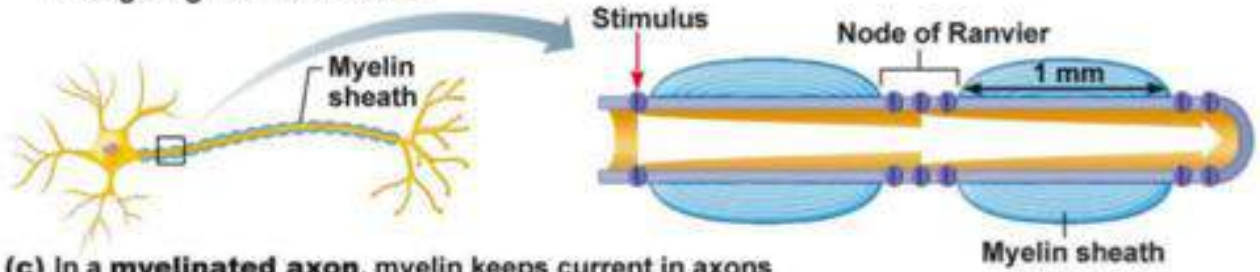
Conduction of action potentials by myelinated axons. The action potential appears to jump from one node of Ranvier to the next where it strengthens before it propagates further.



(a) In a **bare plasma membrane** (without voltage-gated channels), as on a dendrite, voltage decays because current leaks across the membrane.

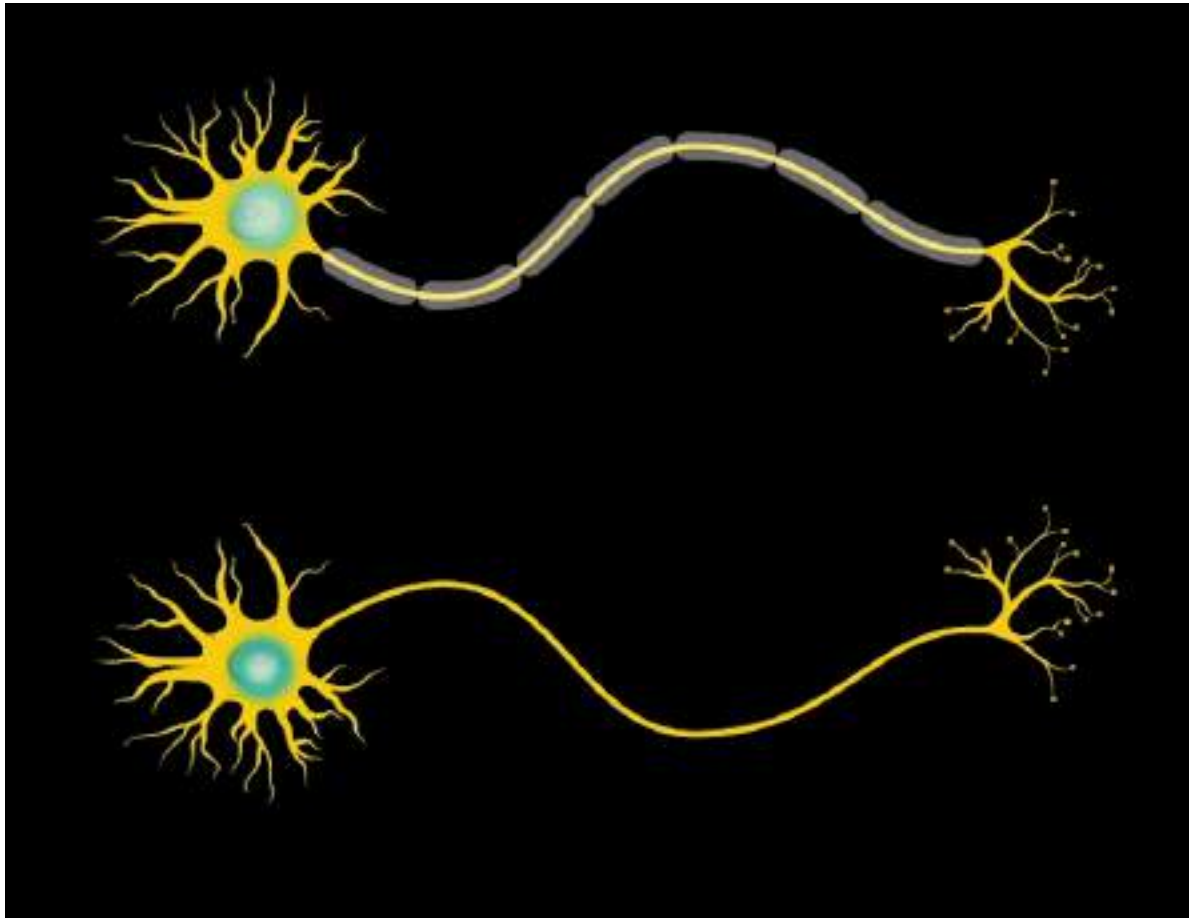


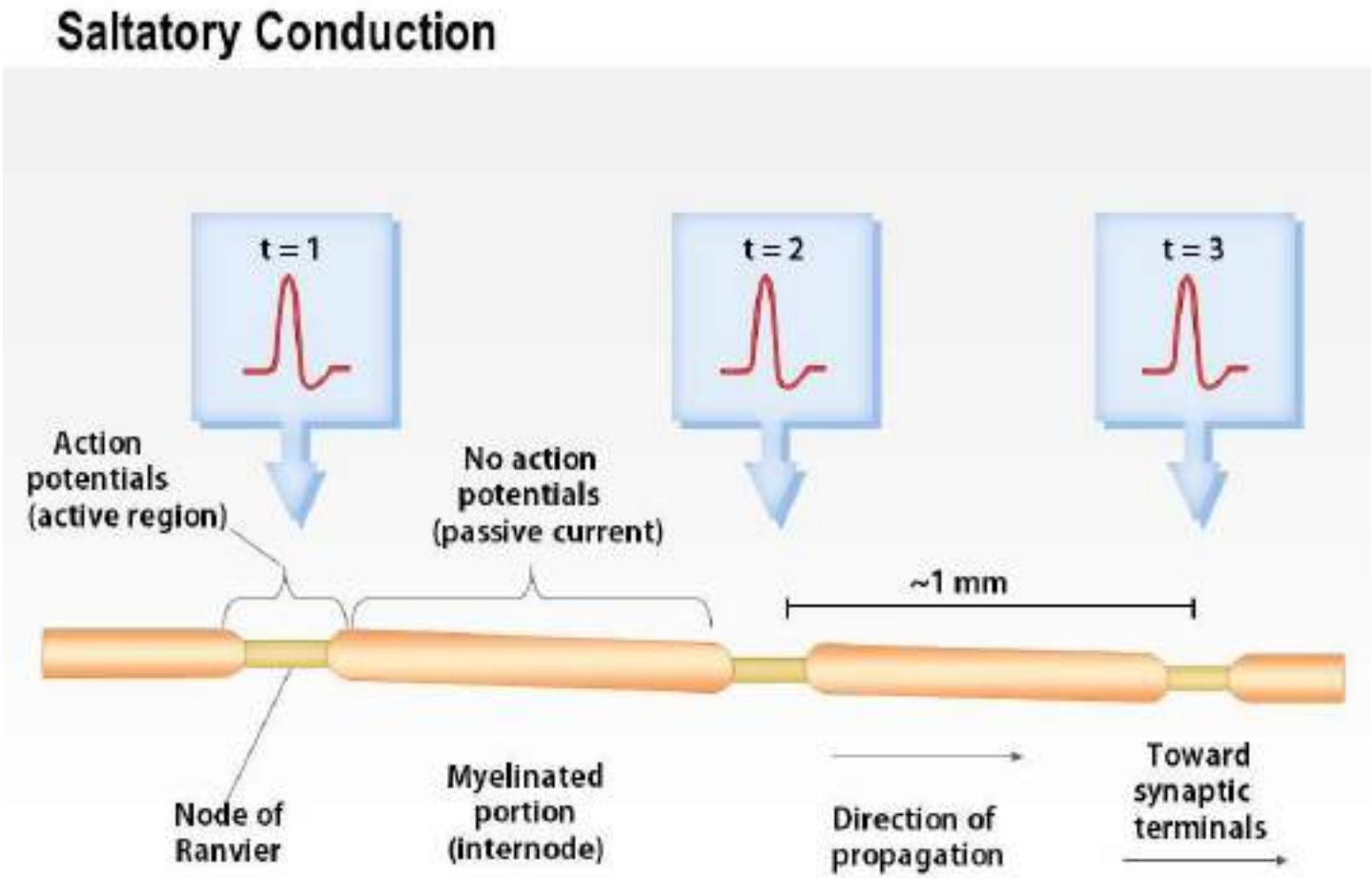
(b) In an **unmyelinated axon**, voltage-gated Na^+ and K^+ channels regenerate the action potential at each point along the axon, so voltage does not decay. Conduction is *slow* because movements of ions and of the gates of channel proteins take time and must occur before voltage regeneration occurs.



(c) In a **myelinated axon**, myelin keeps current in axons (voltage doesn't decay much). APs are generated *only* in the nodes of Ranvier and appear to jump *rapidly* from node to node.

In dendrites

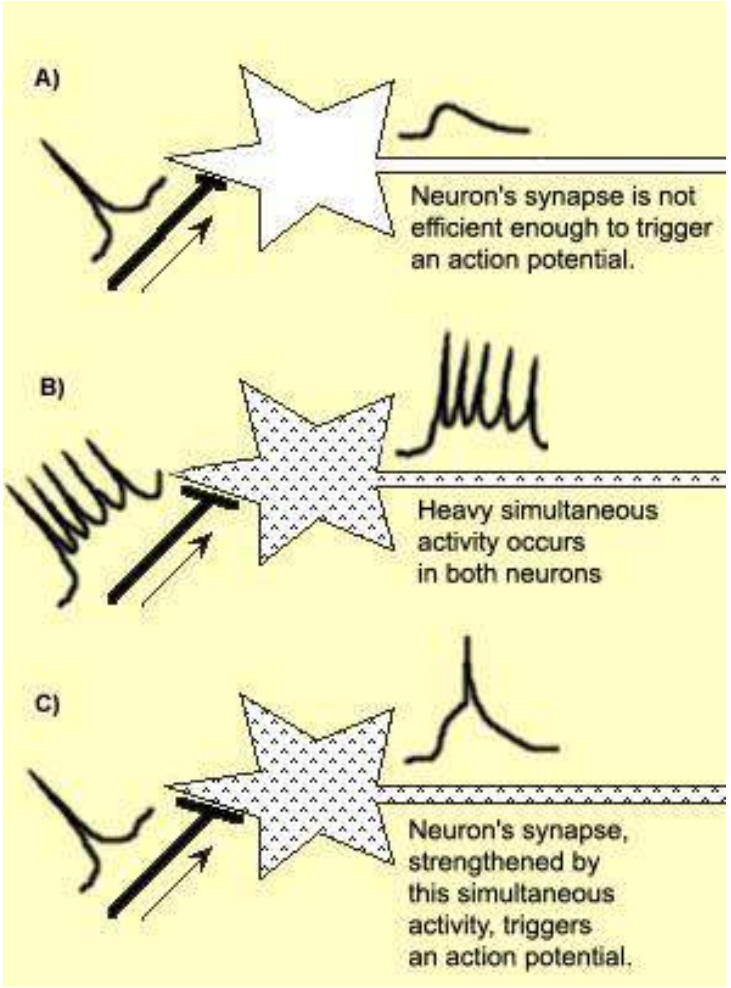




increases the conduction velocity of action potentials from 10 m/s in unmyelinated nerves to 150 m/s in myelinated nerves

- How do we understand that a neuron has undergone change or learning or had fired ?

Hebb's Rule



Donald Hebb

Neurons that fire together, wire together.

1. *Cooperativity*. More than one input must be active at the same time.
2. *Associativity*. Weak inputs are potentiated when co-occurring with stronger inputs.
3. *Specificity*. Only the stimulated synapse shows potentiation.

Long term potentiation (LTP) – strengthening of synapses

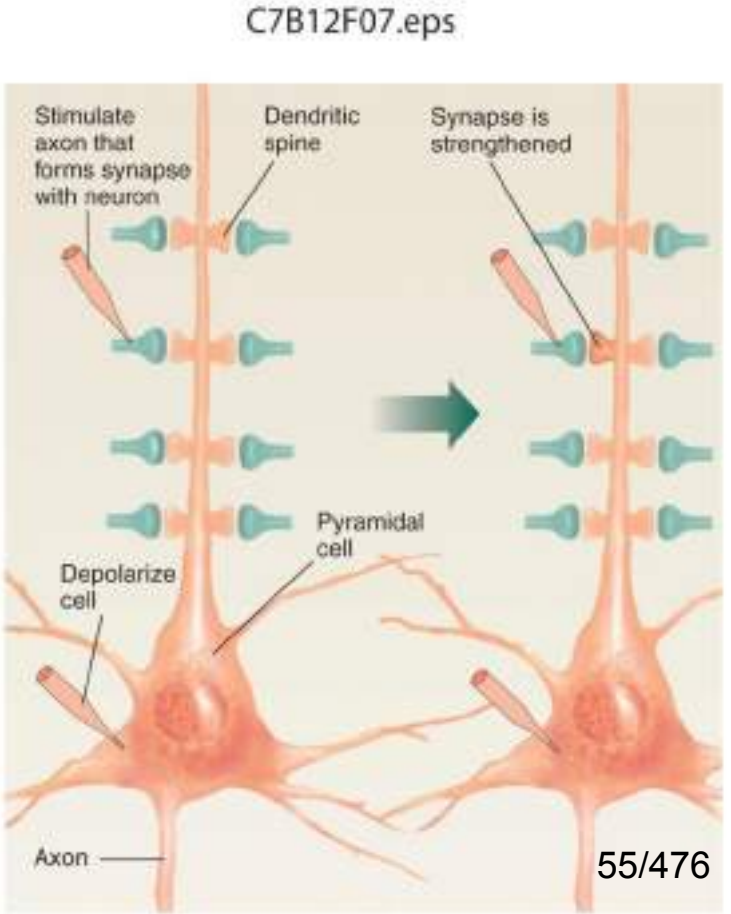
upto 3:30min

- The postsynaptic membrane needs to stay depolarized when the next incoming burst of neurotransmitters is released and continue to depolarize the postsynaptic cell.

- The pre-synaptic and postsynaptic terminals potentiate and their synapse is strengthened, so even a weak impulse in the pre-synaptic membrane can now activate the post synaptic cell.

Synaptic strengthening occurs when a post synaptic membrane becomes depolarized and before the depolarized fades, the next burst of neurotransmitter released fires another EPSPS in the post synaptic membrane

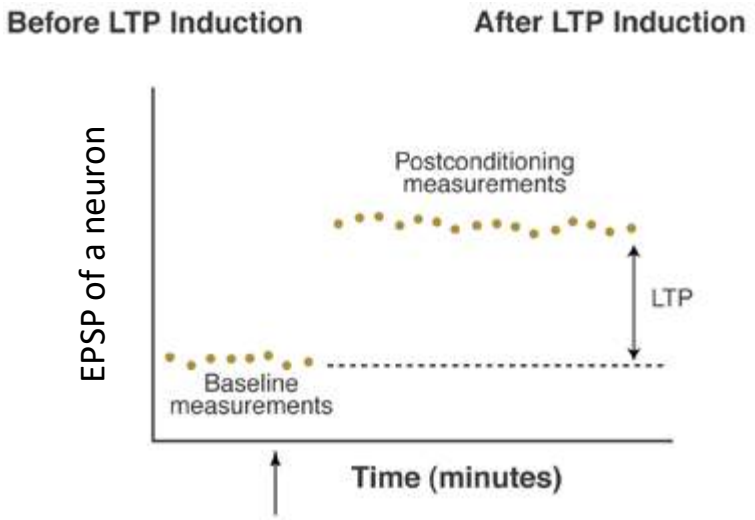
(while the membrane of the postsynaptic cell is still depolarized from a previous excitation)



Synaptic Plasticity

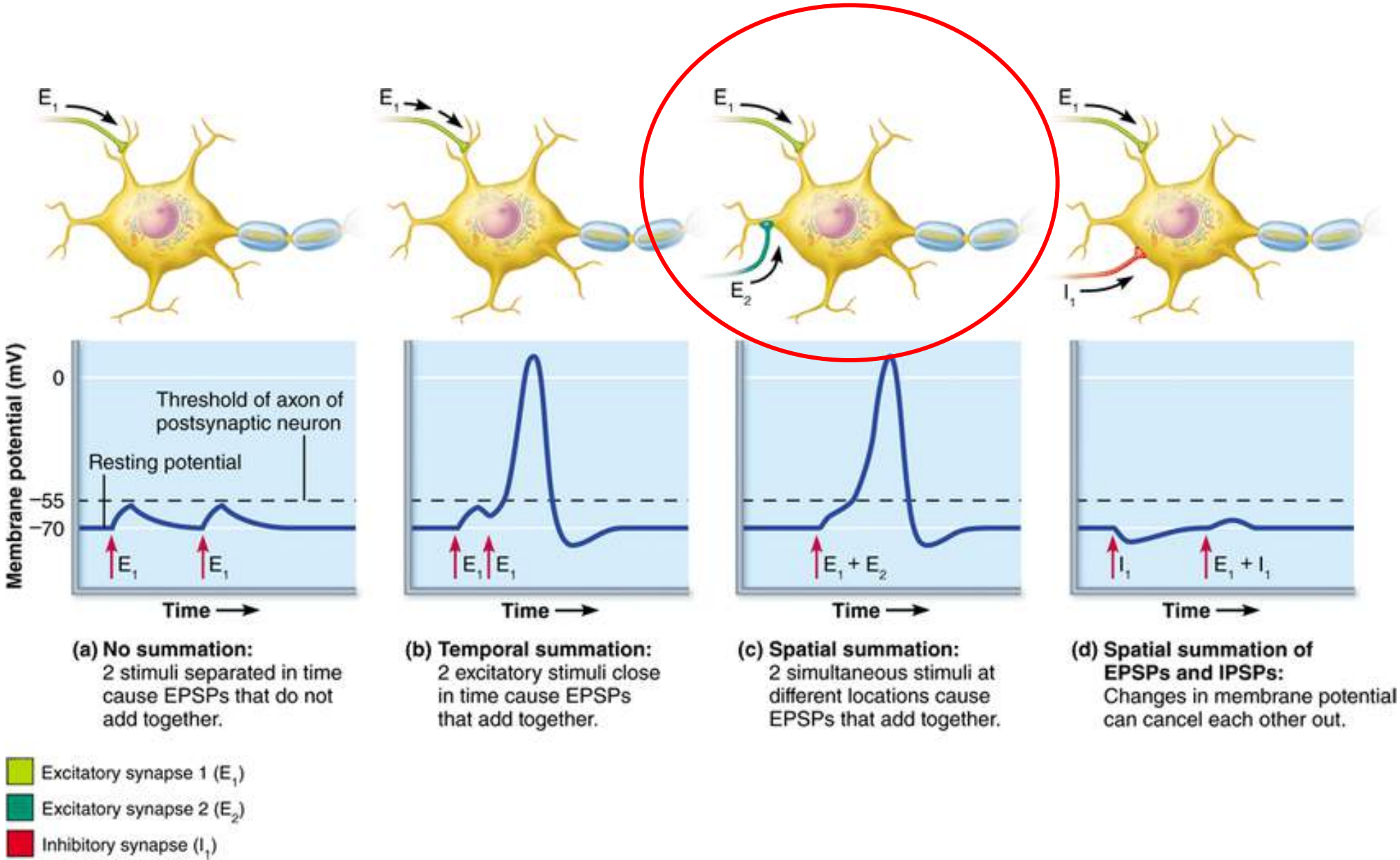
Long-term potentiation (LTP): (potentiate "strengthen")

- EPSPs (excitatory post synaptic potential):
  - High frequency stimulation increases the magnitude of post synaptic excitatory potentials in the postsynaptic neurons. This increase is called as LTP.
  - LTP can be induced by stimulating axons of presynaptic neurons (burst of approx. 100 pulses of electrical stimulation, delivered within a few seconds)
  - EPSPs in the postsynaptic neurons are recorded and if the activity is greater than it was before delivering the pulses, then LTP has occurred.



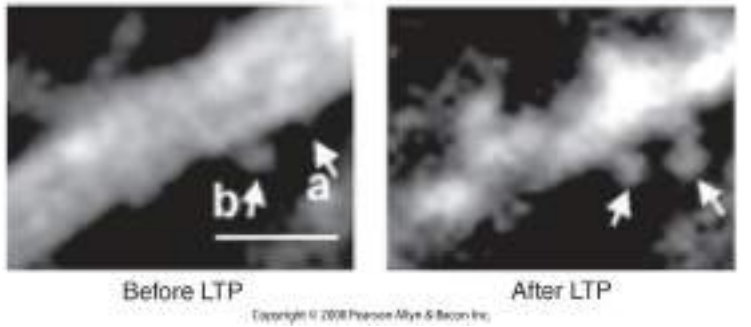
Applying strong electrical stimulation to entorhinal cortex neuron to release more neurotransmitter

Can neurons predict?

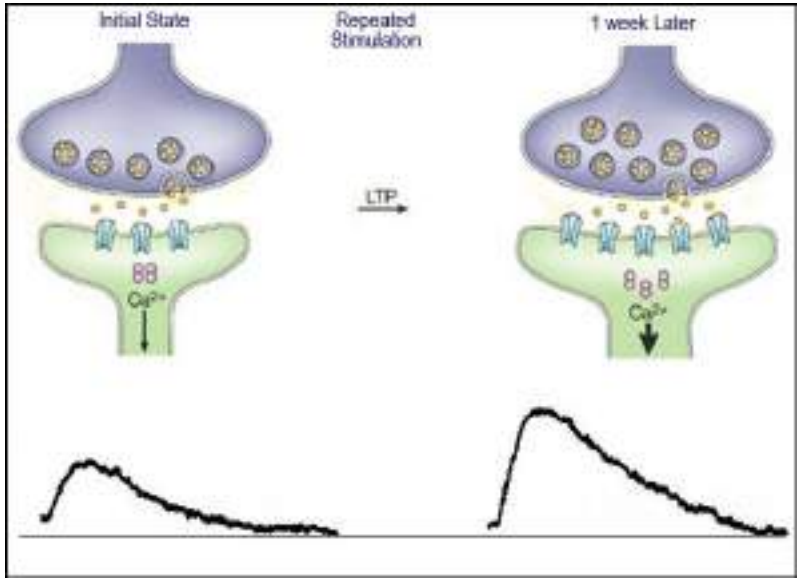


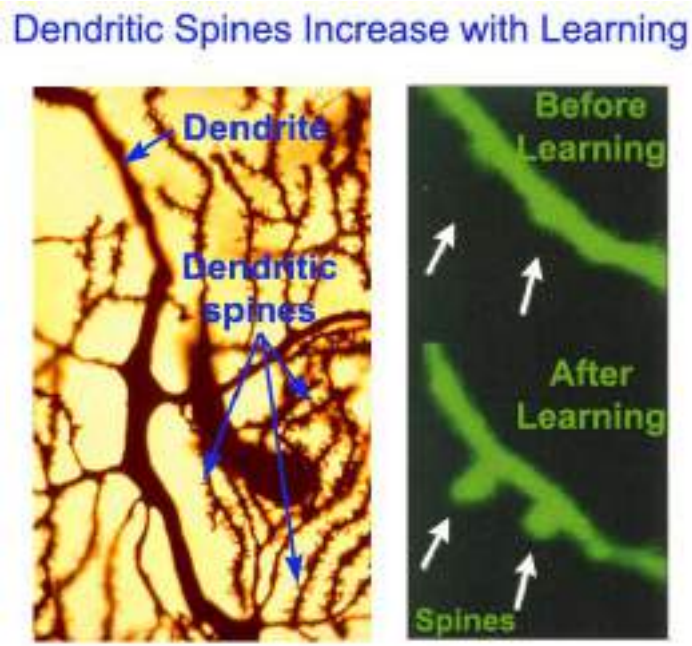
Measuring Synaptic Plasticity

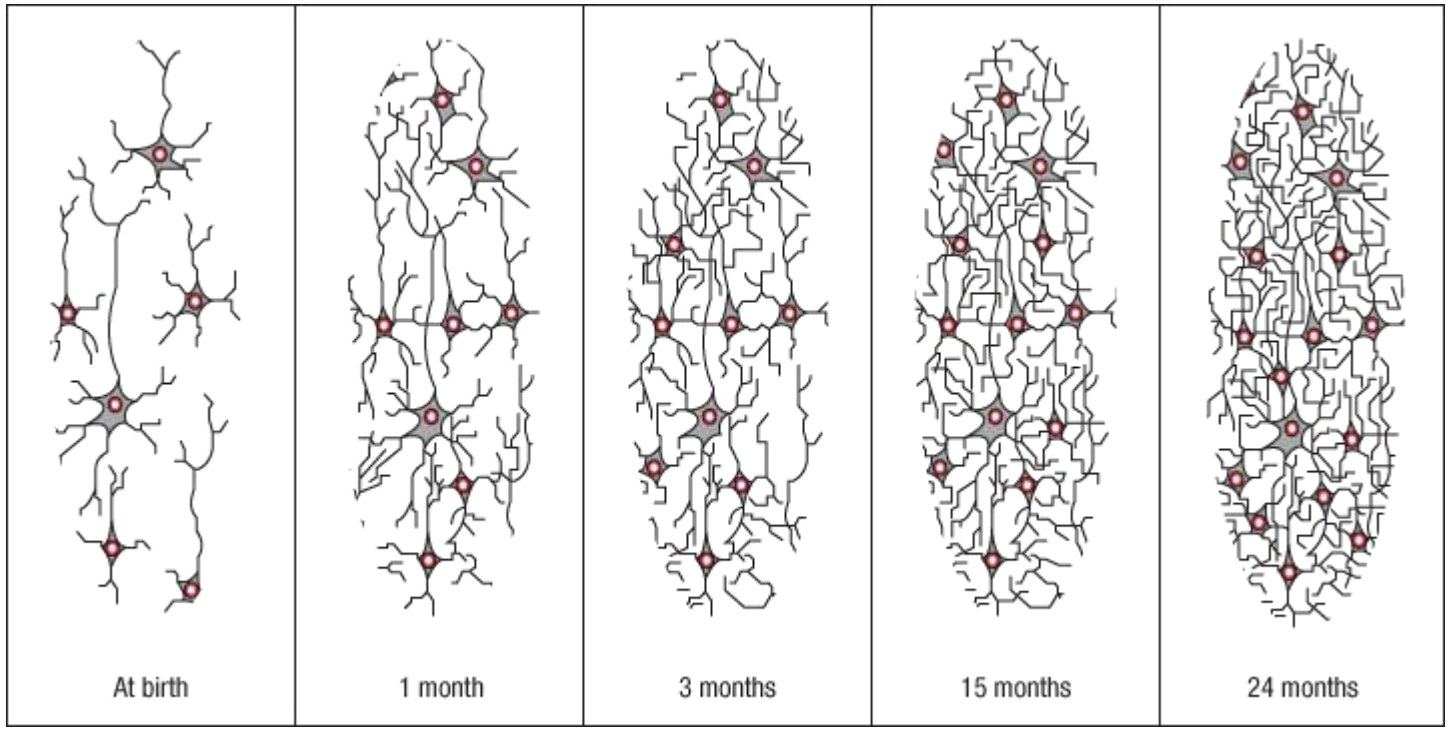
Insertion of receptors



- When synapses get strengthened, what changes occur that increase their strength?
  - More receptors on the postsynaptic membrane
  - More dendrites







Synaptic pruning & synaptogenosis

The unbearable slowness of being: Why do we live at 10 bits/s?

The unbearable slowness of being: Why do we live at 10 bits/s?: Neuron

https://arxiv.org/pdf/2408.10234

Neurotransmitters and Drugs

TABLE 3A.1

SOME NEUROTRANSMTTERS AND THEIR FUNCTIONS

Neurotransmitter	Function	Examples of Malfunctions
Acetylcholine (ACh)	Enables muscle action, learning, and memory.	With Alzheimer's disease, ACh-producing neurons deteriorate.
Dopamine	Influences movement, learning, attention, and emotion.	Excess dopamine receptor activity is linked to schizophrenia. Starved of dopamine, the brain produces the tremors and decreased mobility of Parkinson's disease.
Serotonin	Affects mood, hunger, sleep, and arousal.	Undersupply linked to depression. Prozac and some other antidepressant drugs raise serotonin levels.
Norepinephrine Or Noradrenaline	Helps control alertness and arousal.	Undersupply can depress mood.
GABA (gamma-aminobutyric acid)	A major inhibitory neurotransmitter.	Undersupply linked to seizures, tremors, and insomnia.
Glutamate	A major excitatory neurotransmitter; involved in memory.	Oversupply can overstimulate brain, producing migraines or seizures (which is why some people avoid MSG, monosodium glutamate, in food). (damage to the brain in stroke)

Since glutamate and GABA are found in very simple animals, it is speculated that these neurotransmitters may have been the first to evolve

Controls muscular movements, arousal, sleep, memory

coordinating movement, attention, learning and memory, prediction, reinforcement

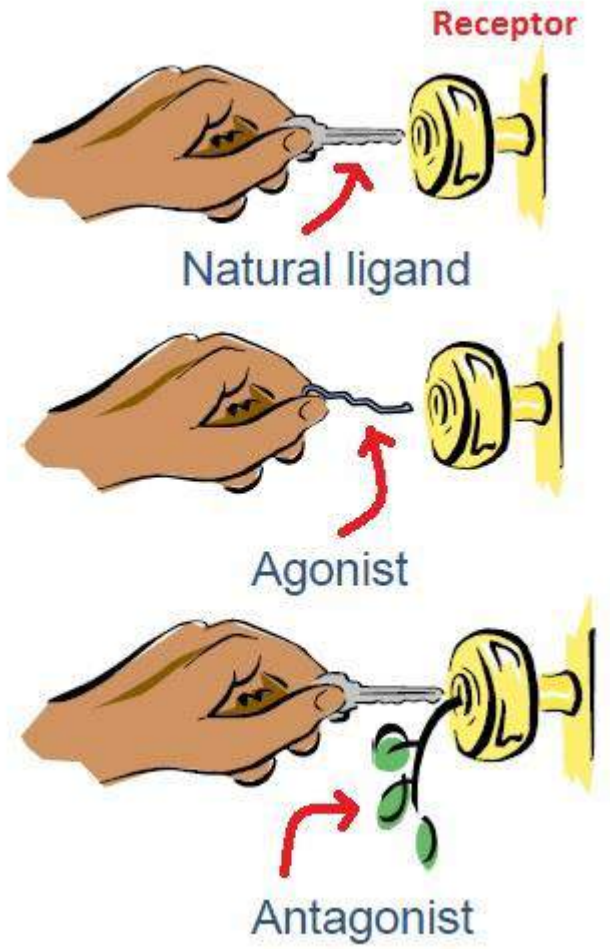
LSD and MDMA (ecstasy) release more serotonin or prevent reuptake of serotonin giving hallucinogenic effects

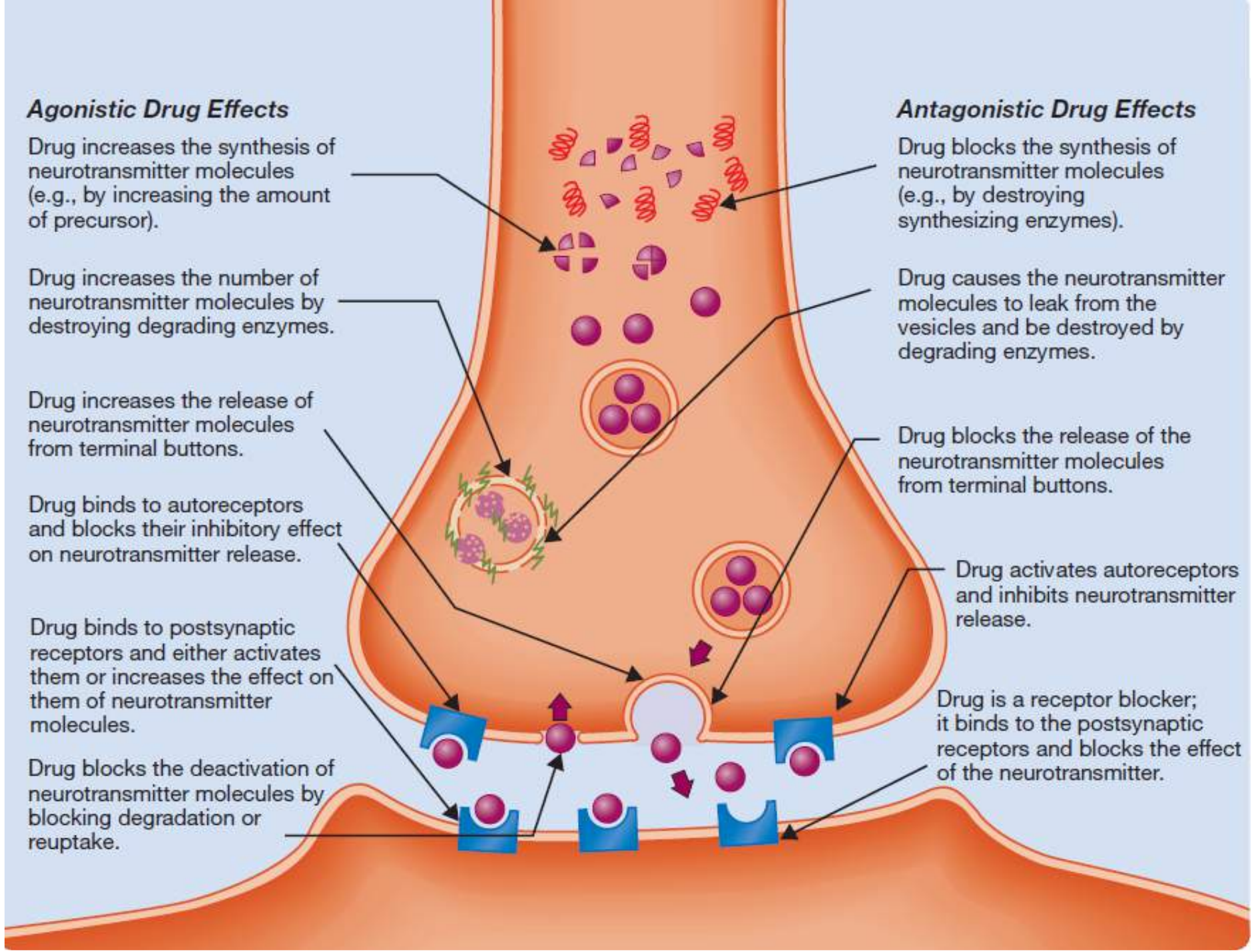
vigilance, attentiveness, high levels lead to euphoria

Found in Sleep meds, alcohol, anxiety meds, sedative

- Agonist:
  - A drug/chemical that facilitates that activates receptors on the postsynaptic cell and causes depolarization
  - Mimics the action is an excitatory neurotransmitter

- Antagonists:
  - A drug/chemical that blocks receptors on the postsynaptic cell and prevent depolarization
  - Prevents excitation of postsynaptic cell





Re-uptake of neurotransmitters

Neuro-peptides

- Released along with neurotransmitters
- Neuromodulators – regulate the sensitivity of presynaptic or postsynaptic receptors to the neurotransmitter
- E.g. endorphins (act like analgesics, diminish the perception of pain)
- E.g. Oxytocin (childbirth, maternal bonding, social interaction)
- Neuropeptides produce a slow but prolonged response at the postsynaptic cell
- Neurotransmitters produce a fast but short-term response in the post-synaptic cell

https://www.researchgate.net/publication/318305704_Difference_Between_Neuropeptides_and_Neurotransmitters

Lipid-based transmission

- Endocannabinoids – lipid (fat) based neurotransmitters - are naturally occurring substance in our body that produces a response similar to Marijuana or cannabis
- they are produced and released as needed and are not stored in synaptic vesicles.
- E.g. Anandamide – binds to endocannabinoid receptors
  - Reduces pain,
  - improves mood – bliss like feeling
- Paracetamol (fever drug) – produces similar effects in body but does not cross the blood-brain-barrier

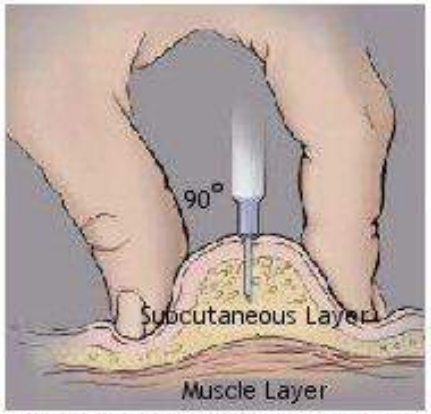
Routes of drug administration

Intravenous injection (IV)

- Injection into vein
- Enters bloodstream within few seconds
- Skill required to administer right dosage

Subcutaneous injection (SC)

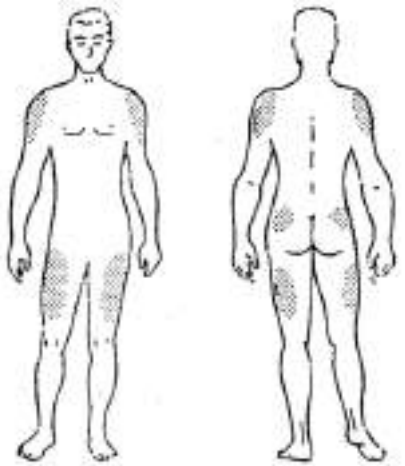
- Injected into the space beneath the skin.
- Useful for small amounts of drugs only (large amounts are painful).
- e.g. COVID vaccine



A subcutaneous injection into the fatty layer of tissue under the skin.

Intramuscular injection (IM) *(most older vaccinations)*

Injected into large muscles (of upper arm, thigh or buttocks)
Absorbed very slowly via capillary action into the bloodstream



Topical administration

Absorbed directly through skin
E.g. ointments, creams or patches

Routes of drug administration

Intranasal administration

- Inhaled by nasal cavity
- Shortest route to reach the brain
- Bypasses Blood-brain-barrier
- E.g. cocaine, anti-allergy

Inhalation

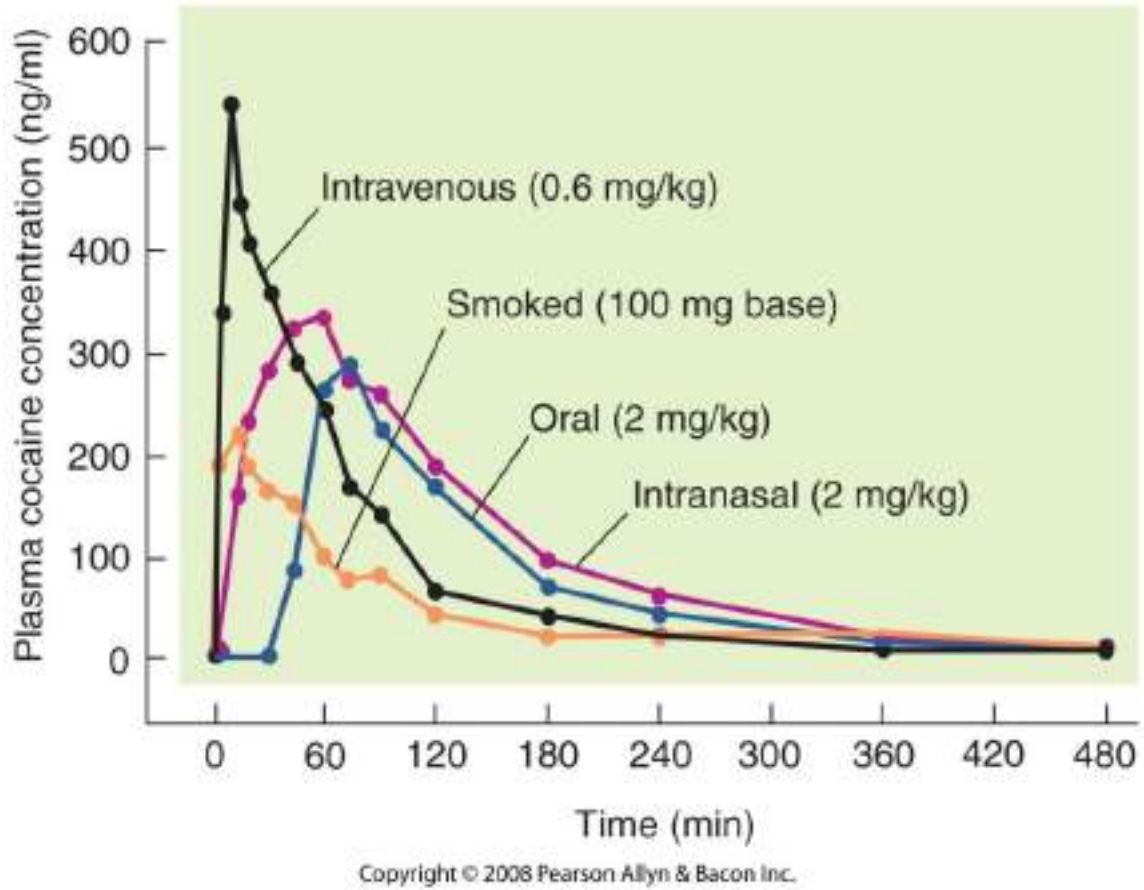
- Absorbed through lungs
- E.g. nicotine and marijuana smoking
- Very rapid entry into the brain since lungs to brain – mixes with blood
- E.g. tobacco, marijuana

Sublingual administration

- Drugs placed beneath the tongue
- Absorbed by capillaries that supply the mucous membrane in the mouth
- E.g. marijuana

Oral administration

- Not all drugs can be injected or inhaled. A few of them are consumed orally. The effect is slightly slower.
- E.g. medical drugs, alcohol



Cocaine absorption in the blood via different routes of administration

Effects of repeated drug administration

- **Dependance –** a regular usage of the drug is required to function normally

- **Tolerance** – over repeated use, larger amounts of the drug are required for it to be effective
    - It is body's mechanism to compensate for the effects of the drug in order to maintain body homeostasis
    - Reduced no. of receptors
    - Receptors become less sensitive to the drug molecules
    - Decrease receptor binding efficiency

- **Sensitization** – exact opposite of tolerance: same doses of drug produce larger and larger effects.
    - Reduced reuptake of the neurotransmitter by the pre-synaptic cell – the neurotransmitter is available for a longer time – increase in post-synaptic stimulation

- **Withdrawal symptoms** – a person who has developed tolerance for a drug will experience opposite effects of the drug if intake is suddenly stopped.
    - If drugs were creating an excitatory effect , withdrawal leads to less excitation – depressive like symptoms, fatigue, irritability, etc. E.g. dopamine withdrawal
    - If drugs were creating an inhibitory effect (GABAergic), withdrawal leads to more excitation – anxiety or restlessness. E.g. alcohol withdrawal

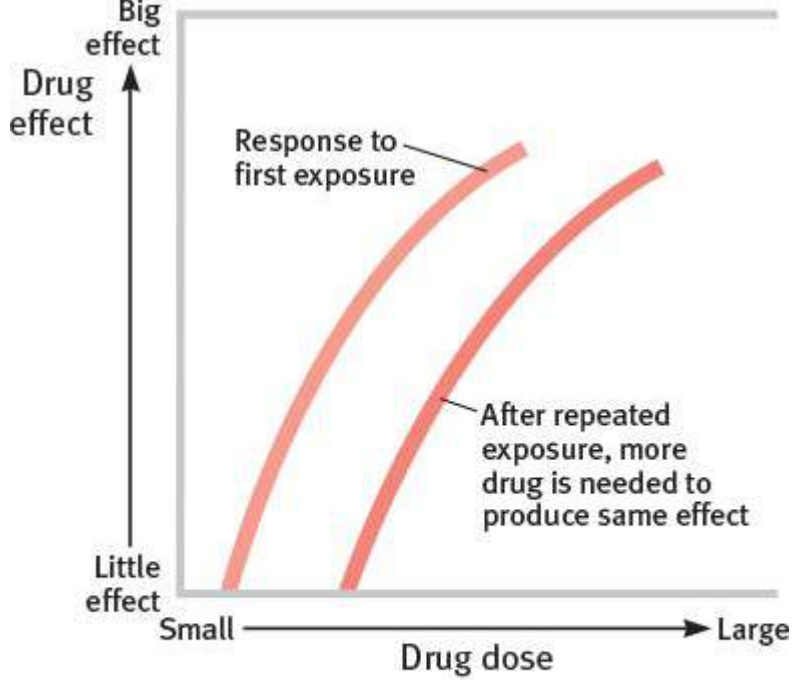
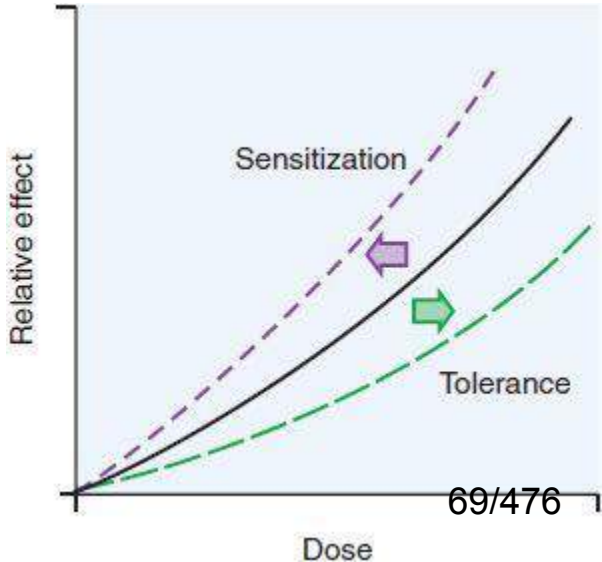


Figure 13.2
Myers/DeWall, *Psychology in Everyday Life*, 4e,
© 2017 Worth Publishers



Your roommate began the semester drinking one cup of coffee in the morning. Now you see that your roommate needs three cups to achieve the same level of alertness. Which effect of repeated administration has occurred?

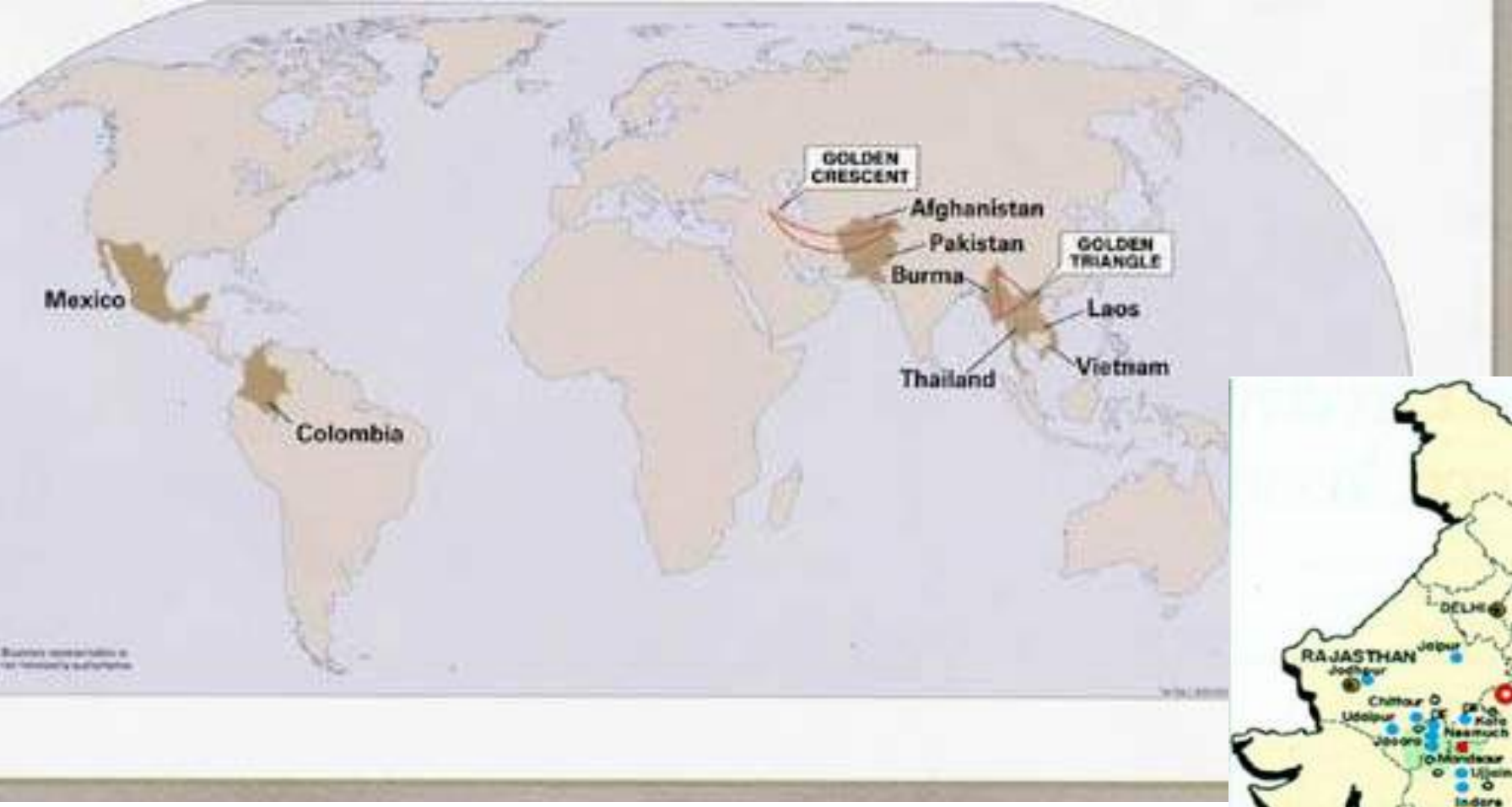
Tolerance

Withdrawal

Sensitization

Opiates

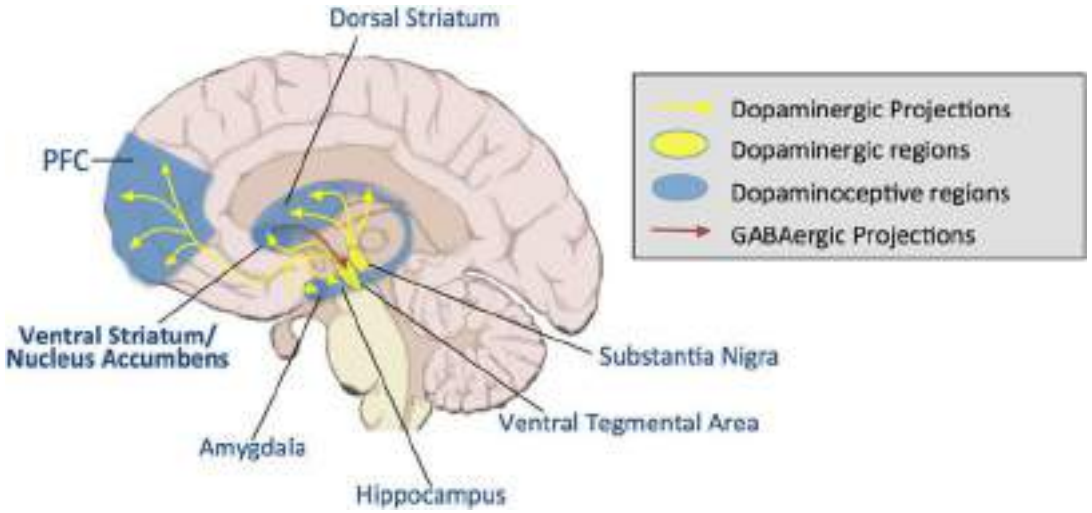
- Opium (dried sap) → morphine → heroin (higher ability to cross the blood brain barrier → more addictive)
- Poppy seeds (khas khas) contain negligible opium (consuming too many poppy seeds makes you drowsy)
- Heroin is snorted or taken intravenously, morphine - intravenous
- Opium – typically smoked



Opium has been consumed for thousands of years

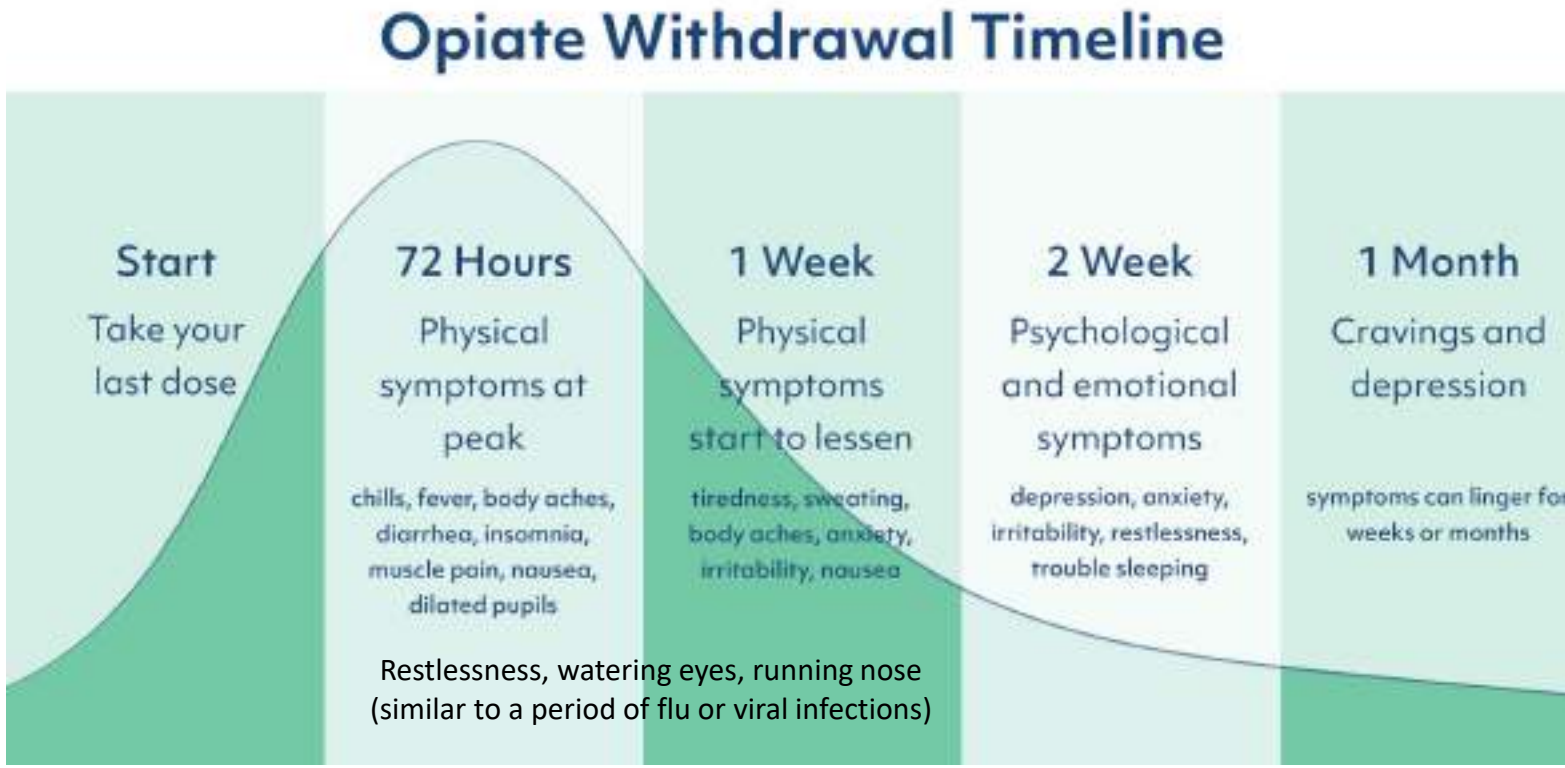
In India legal cultivation is permitted to farmers only in **Madhya Pradesh, Rajasthan and Uttar Pradesh**.

Opiates



- “heroin rush” is a wave intense pleasure that evolves into a state of serene, drowsy euphoria.
  - Morphine/heroin – increased dopamine release
  - At higher doses – serotonin is released (Wei et al., 2018)
  - Temporary decrease in norepinephrine levels
- Positives –
  - pain killer/analgesic – blocks endorphin/opioid receptors that carry pain signals from the PNS to the brain.
- Negative – high risk of addiction (tolerance → higher doses)
  - reinforce reward circuitry (any behaviour that causes pleasure is reinforced and repeated for more pleasure – drug seeking behaviour)
  - The addiction occurs due to activation of receptors in the NA and VTA
- Other effects – hypothermia, sedation

Opiates – withdrawal symptoms



- For gradual withdrawal – drugs that bind to same receptors as opium – produce less pleasure – dose is gradually lowered

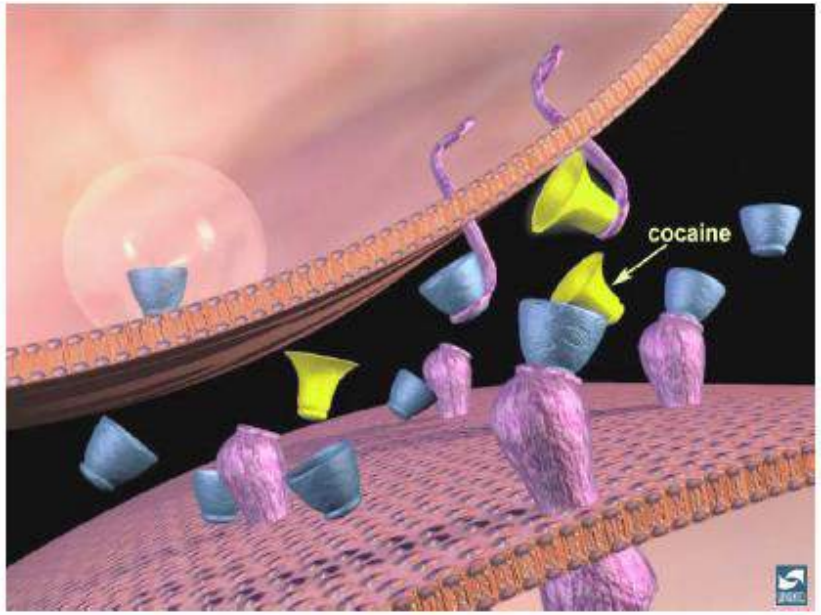
- Withdrawal is not as severe or difficult as alcohol (opium dependence can be over come gradually)

Cocaine

- Cocaine is prepared from the leaves of the coca shrub
- Grows primarily in western South America
- In olden times, coca paste was made directly from the leaves and eaten.
- Current form –highly processed - white powder – cocaine hydrochloride
- Impure residue after processing – Crack – cheap but potent
- Cocaine is typically snorted, smoked or taken intravenously

- First coca-cola recipe had cocaine in small amounts
- Now it has caffeine

Dopamine binding to receptors and uptake pumps in the nucleus accumbens: the action of cocaine



Cocaine binds to the uptake pumps and prevents them from transporting dopamine back into the neuron terminal. So more dopamine builds up in the synaptic space and causes a net increase in dopamine neurotransmission. This is the same general outcome as morphine, but morphine increased dopamine release from the terminal to produce more dopamine in the synaptic space.
Cocaine results in as much as a 10-fold increase in dopamine.

Cocaine blocks dopamine reuptake

Cocaine

- Cocaine blocks the reuptake of dopamine after it is released by the terminal buttons.
- Effects of cocaine –
  - euphoric, active and alert, talkative, friendly, feeling self-confident and powerful
  - have less than their usual desire for food and sleep

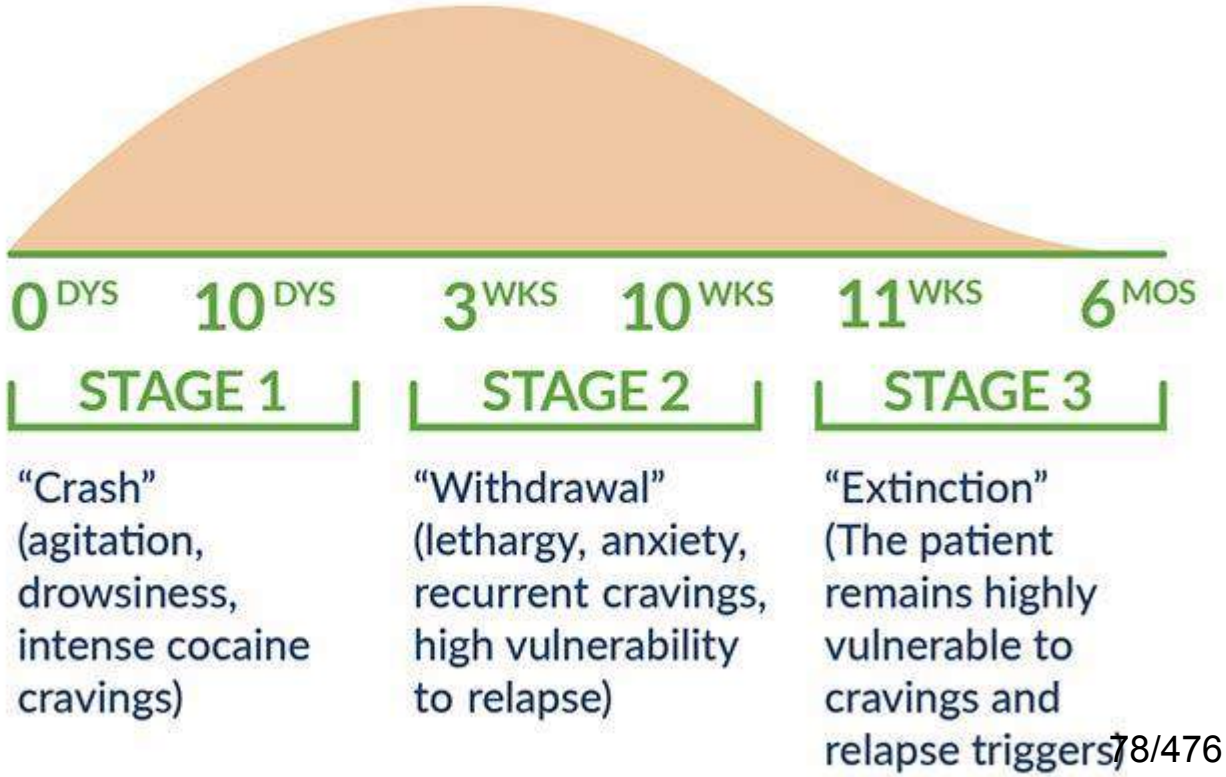
- Addictive – behaviour resulting in pleasure in reinforced (drug seeking)
  - cocaine sprees - binges in which extremely high levels of intake are maintained for periods of a day or two.
  - binging makes users increasingly tolerant to cocaine
  - psychotic behavior: hallucinations, delusions of persecution, mood disturbances, and repetitive behaviors.
  - These symptoms so closely resemble positive symptoms of schizophrenia that even a trained mental health professional cannot distinguish them unless he or she knows about the person's history of substance abuse.
  - This confirms that excessive dopaminergic activity causes these symptoms in schizophrenia as well

- Cocaine causes long-lasting suppression of both dopamine and serotonin neurons (Wei et al 2018)

  - Transgenerational epigenetic effects of cocaine consumption.
    - increased propensity for cocaine self-administration, the offspring of male rats given cocaine are more likely to display increases in anxiety- and depression-like behaviors

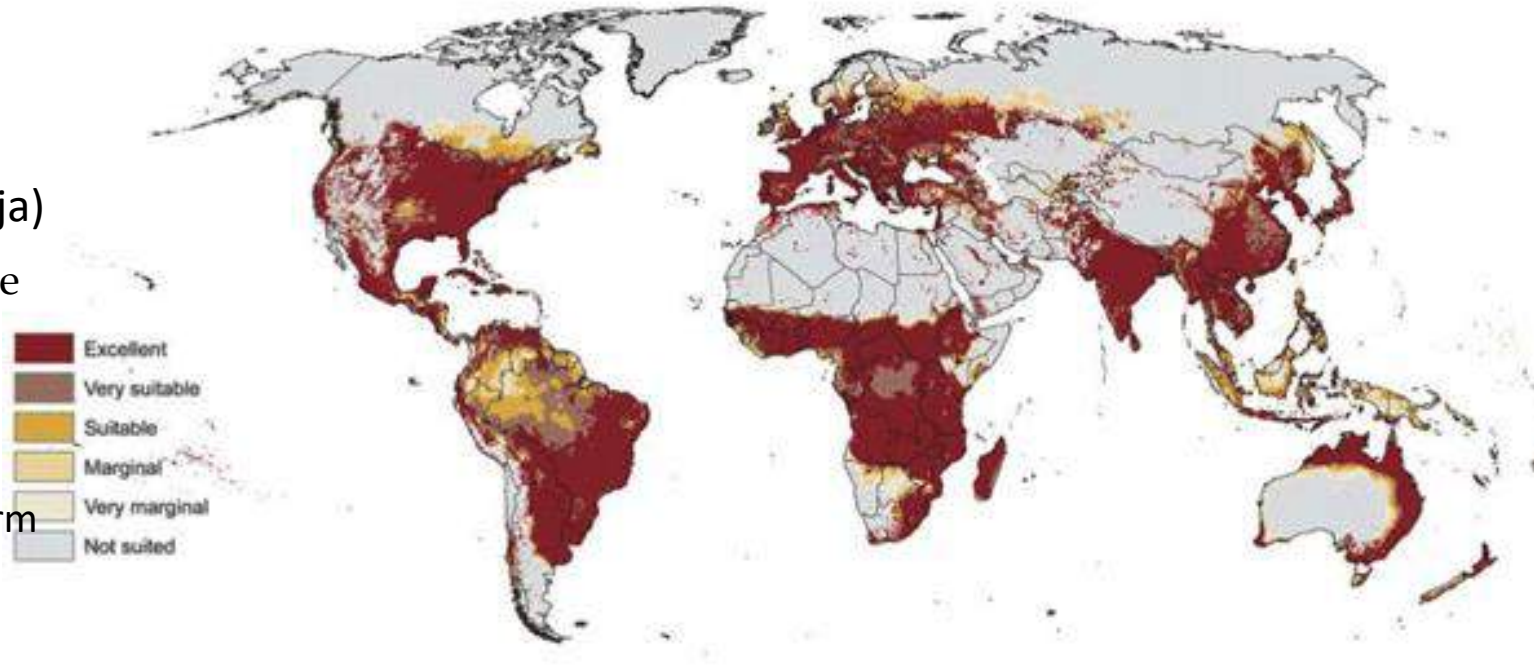
Cocaine withdrawal

- The withdrawal effects triggered by abrupt termination of a cocaine spree are relatively mild.
- Common cocaine withdrawal symptoms include a negative mood swing and insomnia.



Cannabis/Marijuana

- Dried flower buds of cannabis → marijuana (ganja)
- a sticky resin covering the leaves and flowers of the plant → extracted and dried → a dark corklike material '**hashish' (charas)**
- Weed, grass, pot
- Bhang- wet grinding of the leaves of the plant – this form has been consumed in India for more than 2000 years
- Mostly smoked

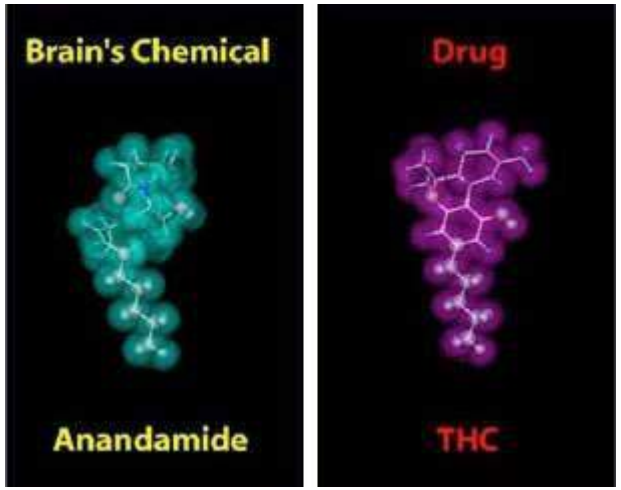


Written records of cannabis use go back 6,000 years in China, where its stems were used to make rope, its seeds were used as a grain, and its leaves and flowers were used for their psychoactive and medicinal effects

Cannabis Sativa

Marijuana effects

THC's chemical structure is similar to the brain chemical anandamide. Similarity in structure allows drugs to be recognized by the body and to alter normal brain communication.

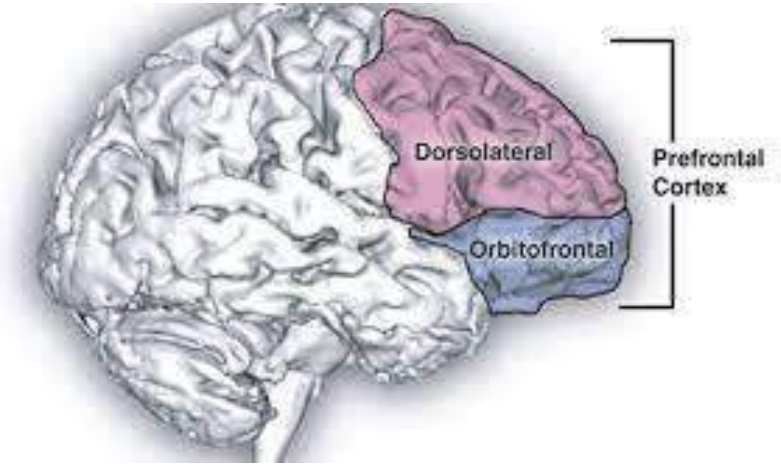


- THC (delta-9-tetrahydrocannabinol) is the main ingredient
- THC binds to the same receptors as anandaminde (endocannabinoid – naturally produce)
- Stimulates neurons in the reward system - high levels of dopamine released – addictive - down-regulation of cannabinoid receptors
- transgenerational epigenetic effects - increased vulnerability to stress-induced anxiety.

small doses of marijuana produce subtle effects -

- pleasant euphoria
- sense of relaxation.
- Other effects, which may vary dramatically among different people
  - include heightened sensory perception (e.g., brighter colours),
  - laughter
  - altered perception of time
  - increased appetite.

At high doses of marijuana



- Learning and memory is impaired (hippocampus - Chronic THC exposure may permanently damage hippocampal neurons.

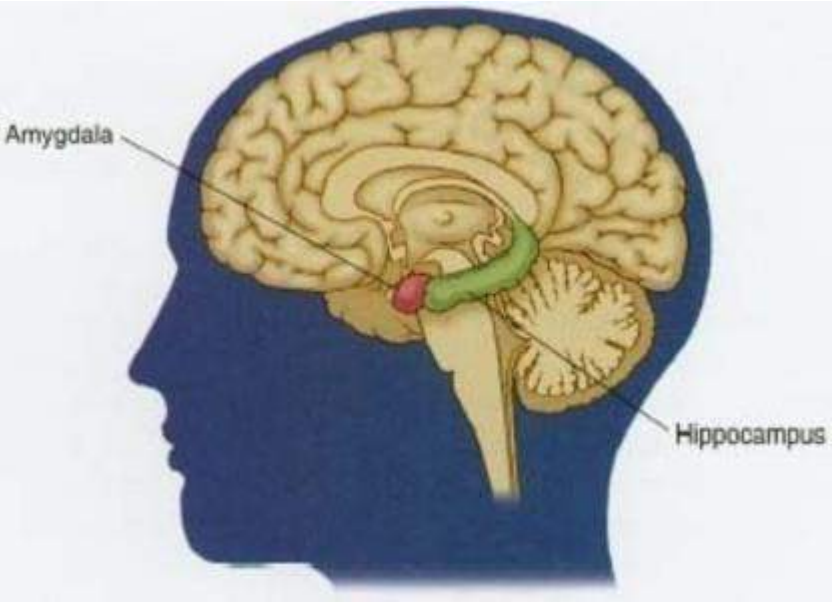
- impaired thinking - reduced ability to perform complicated tasks (orbitofrontal cortex)

- Speech becomes slurred
- Meaningful conversation becomes difficult.

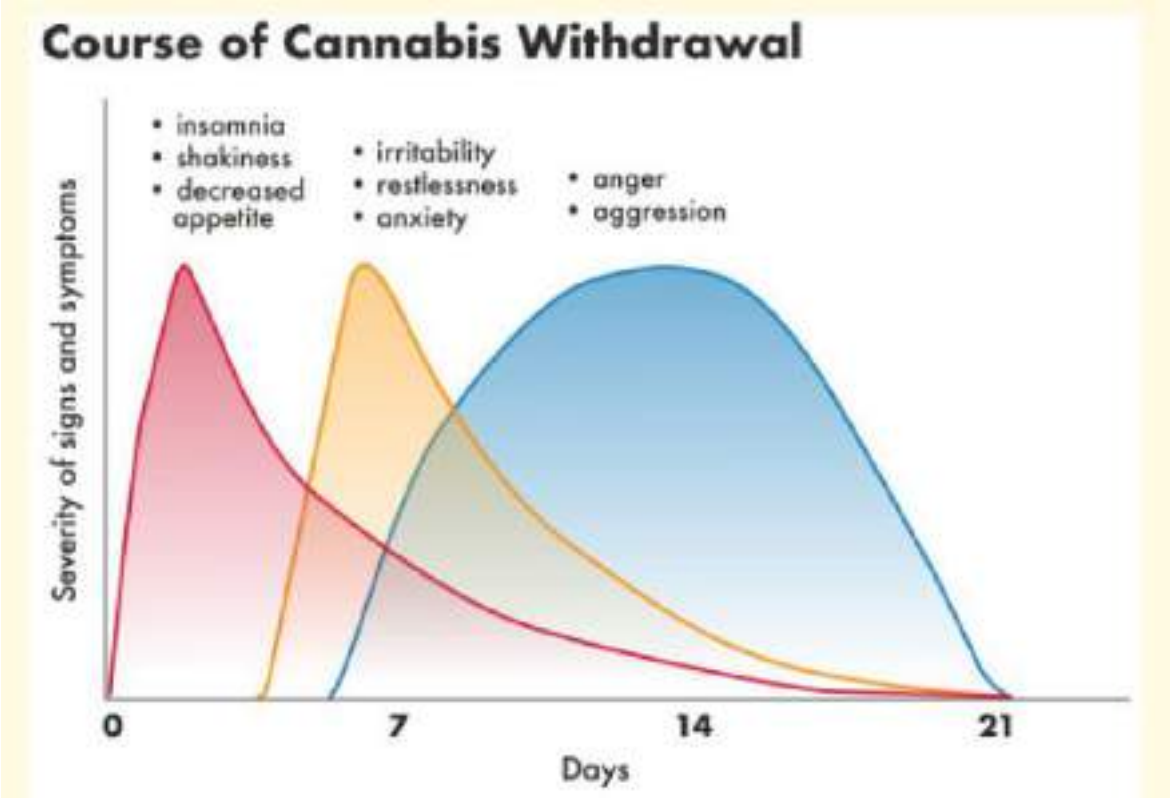
- Disruption of balance, posture, coordination, and reaction time, motor impairment (basal ganglia & cerebellum)

- A sense of unreality, emotional intensification, sensory distortion, feelings of paranoia,
- Acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity.

- Higher risk for multiple sclerosis (loss of myelin sheath)



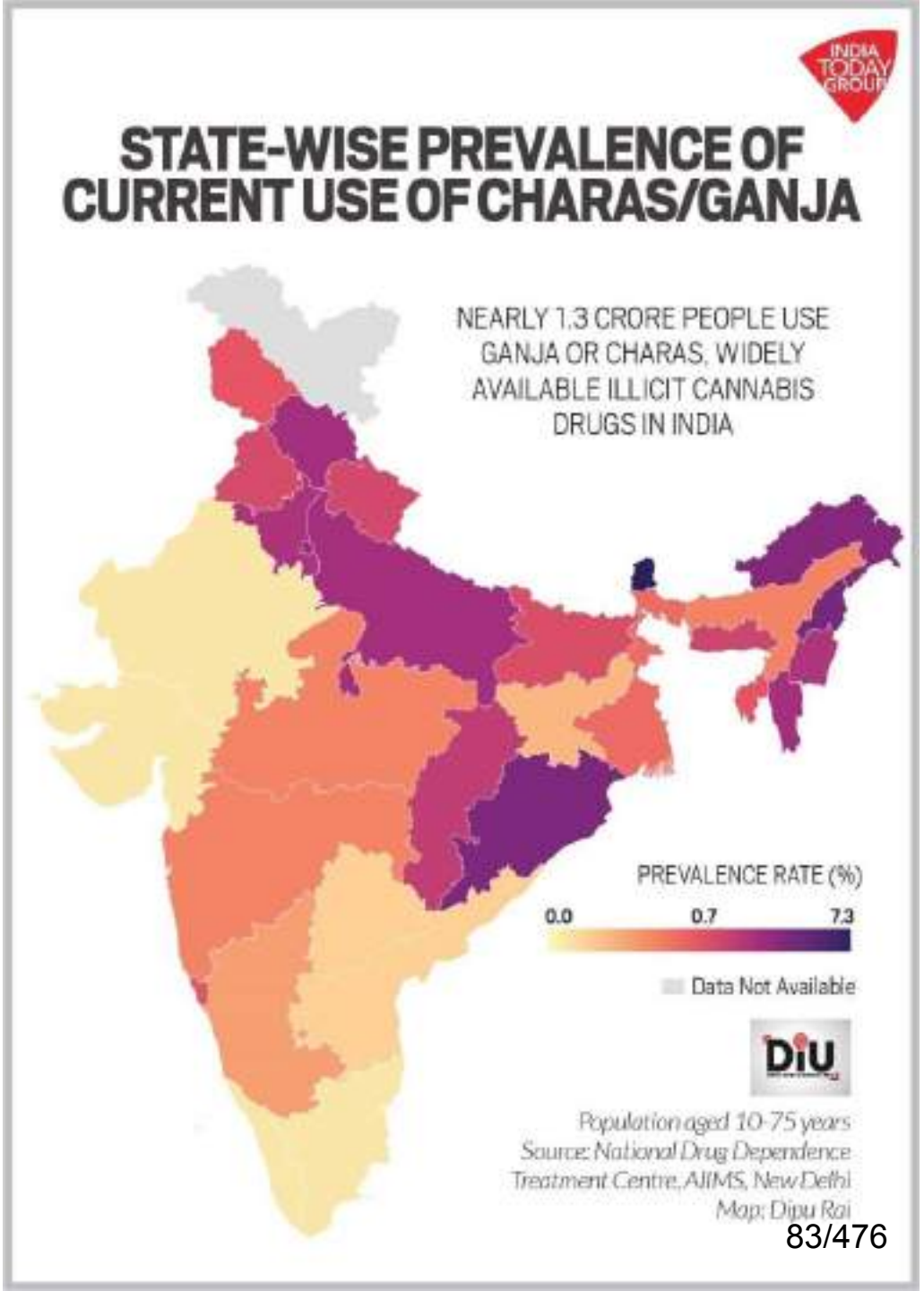
Cannabis Withdrawal

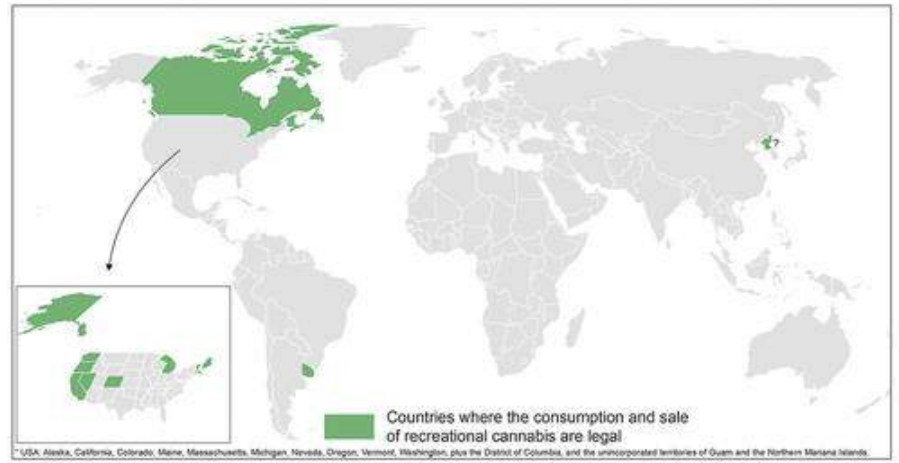


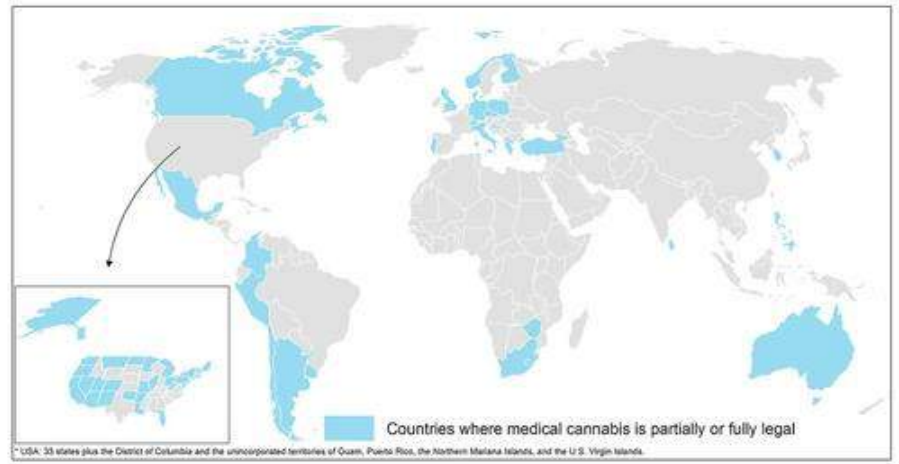
Cannabis in India

- Narcotic Drugs and Psychotropic Substances Act (1985) recognizes cannabis as a source of biomass, fiber, and high-value oil – can be cultivated for industrial use
  - GOI allows cultivation of cannabis with low THC content.
  - Bhang is not illegal - wet grinding of the leaves of the plant

- Bhang is banned in states of Maharashtra, Karnataka, Assam

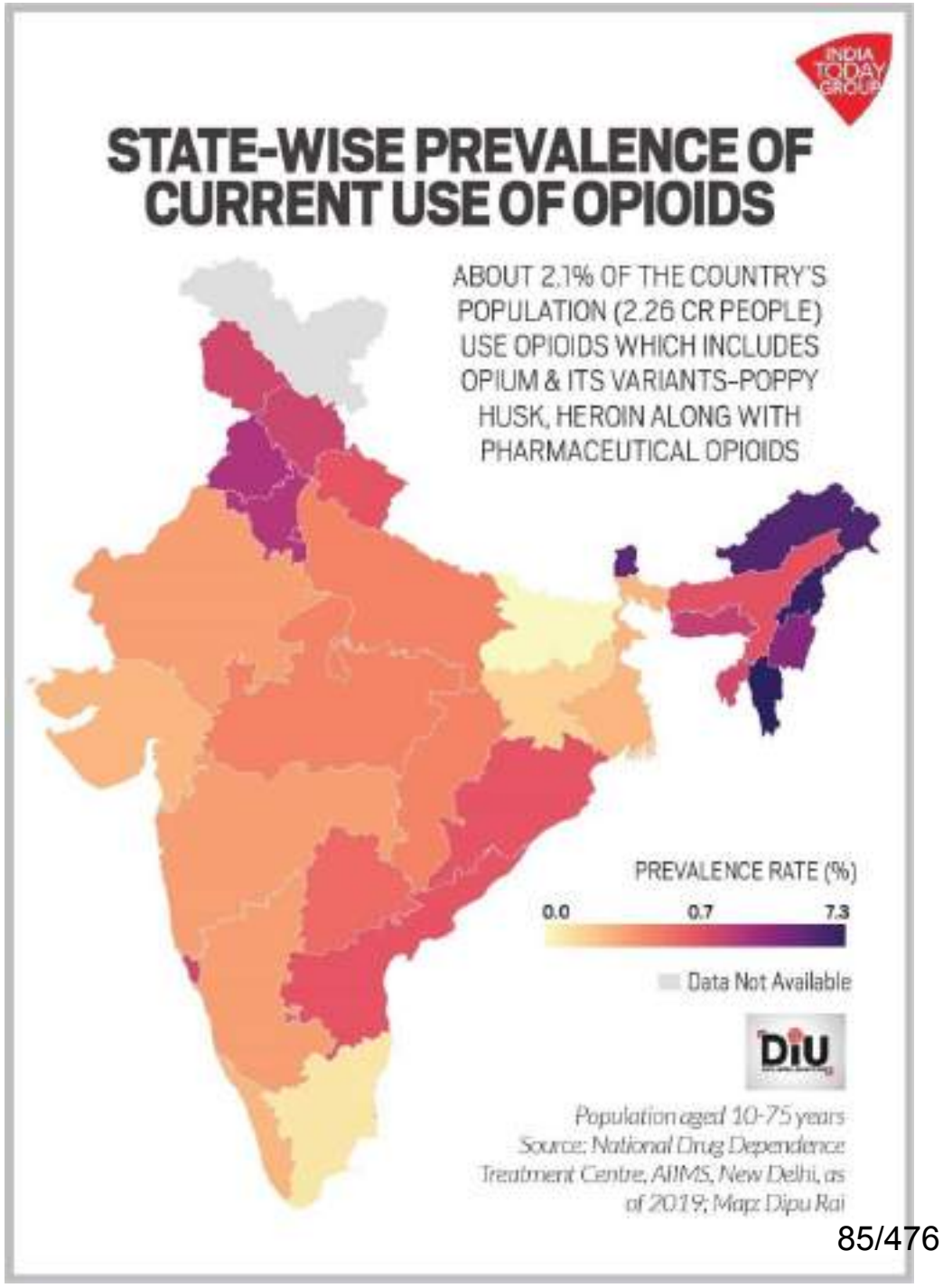






Sources: Research by Pierre-Arnaud Chouvy, January 2019

- All drugs discussed so far are illegal for consumption in India
  - Opium
  - Cocaine – doesn't grow in India
  - Cannabis



Why are SSRIs legal and MDMA/ecstasy illegal ?

3,4-Methylenedioxymethamphetamine (MDMA)

SEROTONIN is a chemical in the brain which affects a number of things, including mood. People suffering from clinical depression have lower than average levels of serotonin in their brains. Prozac gradually restores serotonin to its proper level, then maintains that level. It has no effect on mood in people who are not suffering from depression. Ecstasy, in contrast, releases a sudden excess or rush of serotonin which produces an elevated mood for several hours afterwards. In fact, the massive release of serotonin may leave nerve cells depleted and cause irreversible brain damage. Mood can be thought of as a light bulb and serotonin as the voltage which keeps it glowing. Too little voltage and it goes dim (depression). Prozac restores the voltage and brightness to normal. Ecstasy produces a blinding flash as the bulb burns out. Finally, prozac is a strictly controlled medicine, whereas the manufacture and sale of Ecstasy is unregulated and dangerous.

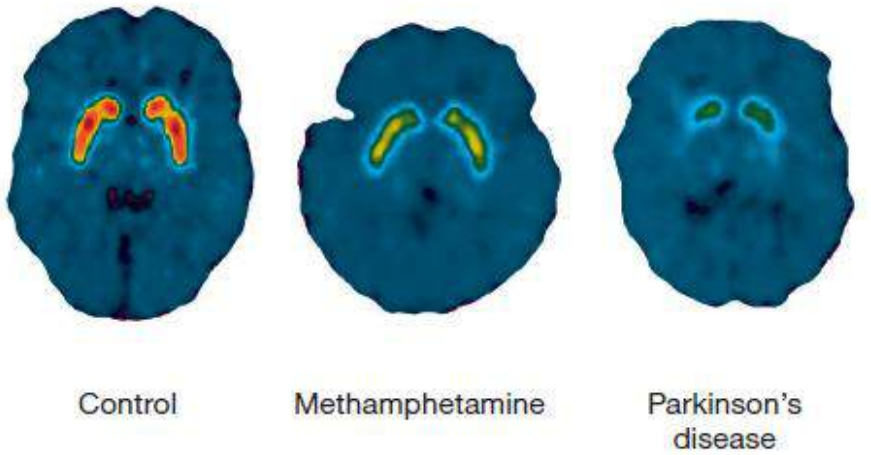
Dr A Simpson (Medical Director, Eli Lilly), Basingstoke, Hants
(Part of the group that manufactures Prozac)

SSRIs prevent "used" serotonin from being reabsorbed, allowing it to hang around the synapse longer than normal with the goal of correcting a chemical imbalance.

MDMA, on the other hand, actually causes your brain to pump out "extra" serotonin, producing the lovely feelings of "ecstasy" MDMA is known for.

https://www.theguardian.com/notesandqueries/query/0,,-2140,00.html

- Amphetamine/methamphetamine (meth) – synthetic drug
- inhibits the reuptake of dopamine and also stimulates the release of dopamine from terminal buttons.
- Meth can also damage terminals of serotonergic axons and trigger death of neurons in the cerebral cortex, striatum, and hippocampus
- Increased risk of Parkinson's disease



Legal stimulants

- Alcohol
- Tobacco (nicotine)
- Caffeine

Alcohol

- At low doses → mild euphoria, reduces anxiety
- At moderate doses → cognitive, perceptual, verbal, and motor impairment, loss of cognitive control, socially unacceptable behaviour
- At higher doses → stupor , unconsciousness, and if blood levels reach 0.5%, there is a risk of death

- Alcohol produces dependence and tolerance
- Addiction – to alleviate body pain and mental stress

- Withdrawal symptoms can be seen even after single bout of drinking
  - Nausea, headache, vomiting, tremors → hangover

- Withdrawal symptoms of moderate to heavy drinkers are severe

BAC	Predictable Effects
.02% to .04%	Lightheaded – Relaxation, sensation of warmth, "high," minor impairment of judgment
.05% to .07%	Buzzed– Relaxation, euphoria, lower inhibitions, minor impairment of reasoning and memory, exaggerated emotions (good and bad)
.08% to .10%	Legally Impaired – Euphoria, fatigue, impairment in balance, speech, vision, reaction time and hearing, judgment and self-control are impaired
.11% to .15%	Drunk – "High" reduced and depressive effects (anxiety, depression or unease) more pronounced, gross motor impairment, judgment and perception severely impaired
.16% to .19%	Very Drunk – Strong state of depression, nausea, disorientation, dizzy, increased motor impairment, blurred vision, judgment further impaired
.20% to .24%	Dazed and Confused – Gross disorientation to time and place, increased nausea and vomiting, may need assistance to stand/walk, impervious to pain, blackout likely
.25% to .30%	Stupor – All mental, physical and sensory functions are severely impaired, accidents very likely, little comprehension, may pass out suddenly
.31% and up	Coma – Level of surgical amnesia, onset of coma, possibility of acute alcohol poisoning, death respiratory arrest is likely in 50 % of drinkers

BAC – Blood Alcohol Concentration

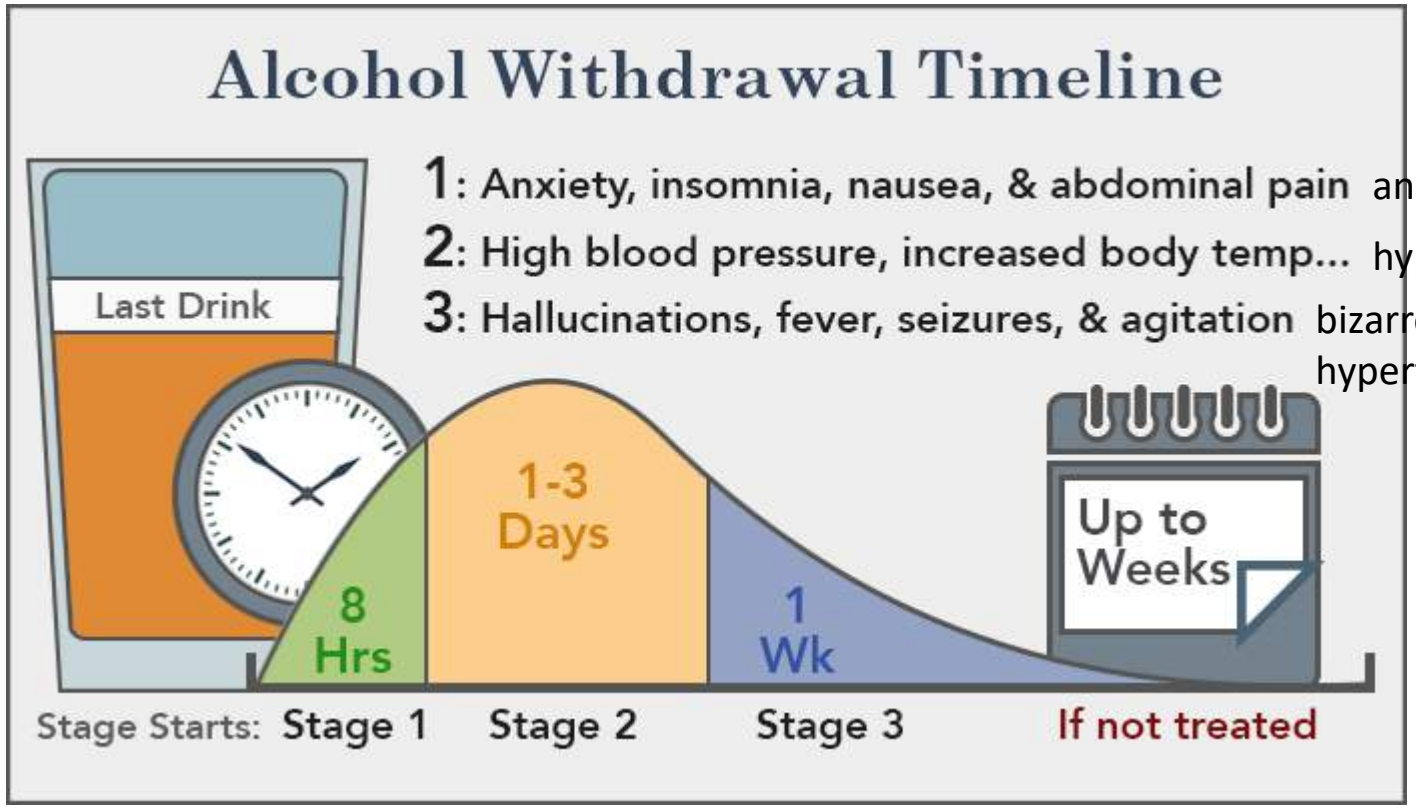
Effects of Alcohol addiction

- $GABA_A$ receptor – agonist – anxiolytic, sedative effect
- NMDA receptor (glutamate) - antagonist – disrupts learning and memory
  - Long term suppression of NMDA receptors makes them more sensitive to glutamate
  - Sudden withdrawal leads to spike in NMDA activity which can cause seizures
  - Drug controlled withdrawal – controlled dosage

- Fetal Alcohol Syndrome (FAS)→ Prenatal alcohol exposure (alcohol consumption by mother or father)
  - brain damage, intellectual disability, poor coordination, poor muscle tone, low birth weight, delayed growth, and/or physical deformity, birth defect

- alcohol consumption can produce *transgenerational epigenetic effects*

Korsakoff's syndrome (a neuropsychological disorder)
- by memory loss, sensory and motor dysfunction, and in advanced stages - severe dementia
- thiamine (vit B1) deficiency (inflammation of the gut lining due to excessive alcohol consumption, which reduces the body's ability to absorb vitamins and nutrients from the gut)
- general loss of cortical white and gray matter



and tachycardia (rapid heartbeat)

hyperactivity, insomnia, and hallucinations

bizarre delusions, disorientation, agitation, confusion, hyperthermia, and tachycardia.

Nicotine



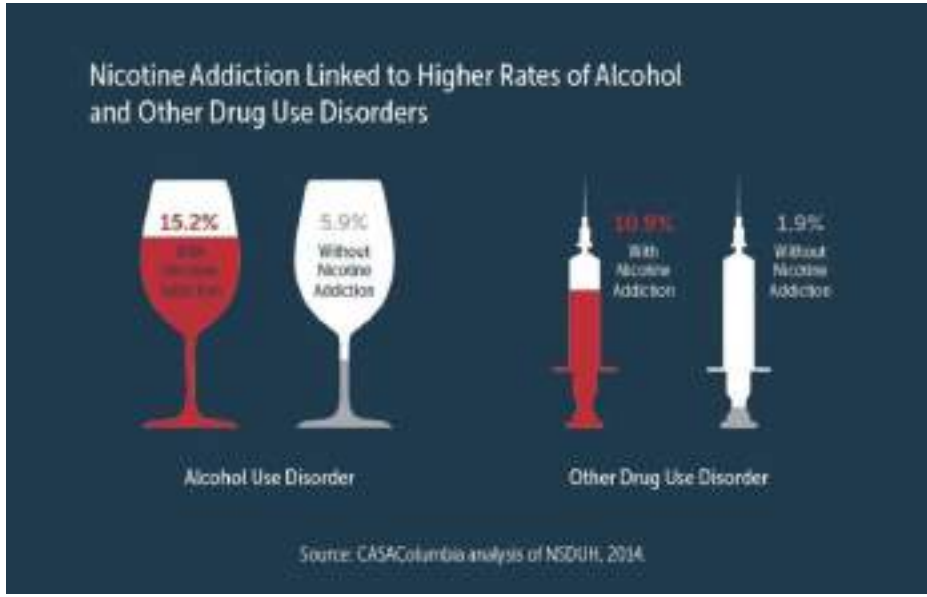

- Tobacco → major psychoactive ingredient → **nicotine**
- Nicotine → in lower quantities in tomato, potato, eggplant (brinjal), and green pepper, dark chocolate, tea
- two common methods of nicotine inhalation:
  - (1) **smoking**—inhaling the smoke from the burning of tobacco (e.g., *cigarettes, cigars*)
  - (2) **vaping**—inhaling a vapor that contains nicotine (e.g., *e-cigarettes*).
  - (3) chewing – especially in India

- Nicotinic receptors are also found in the brain (but fewer than those found at the neuromuscular junction)
  - Nicotine binds to nicotinic Ach receptors located on dopaminergic neurons in the VTA – increased release of dopamine in the Nucleus Accumbens → increased activity in prefrontal cortex, amygdala, hippocampus

- In the body, nicotine triggers the adrenal gland to release epinephrine - **stimulant**

- Short term effects of nicotine - Alertness, improved concentration, better memory, increased heart rate, loss of appetite
- Long term effects of nicotine – high blood pressure, hardening of arteries, respiratory disorders (smoking)

Nicotine – the gateway substance



- Mild drug → Does not produce a high, euphoria or any impairment like other drugs
- Because of the heightened alertness and concentration, performance improves → more frequent use
- Nicotine primes the brain towards addiction of other drugs including alcohol → makes it easier for other drugs of abuse to alter brain activity

- Develops tolerance and addiction
- Chronic tobacco use – respiratory infections, heart disease, risk of stroke, cancer of lungs, mouth, throat, or esophagus
- Individuals who live or work with smokers are also likely to develop heart disease and cancer
- Smoking during pregnancy increases the likelihood of miscarriage, stillbirth, early death of the child, psychiatric disorders during adolescence
- Higher cause of death than alcohol and other drugs

Nicotine Withdrawal

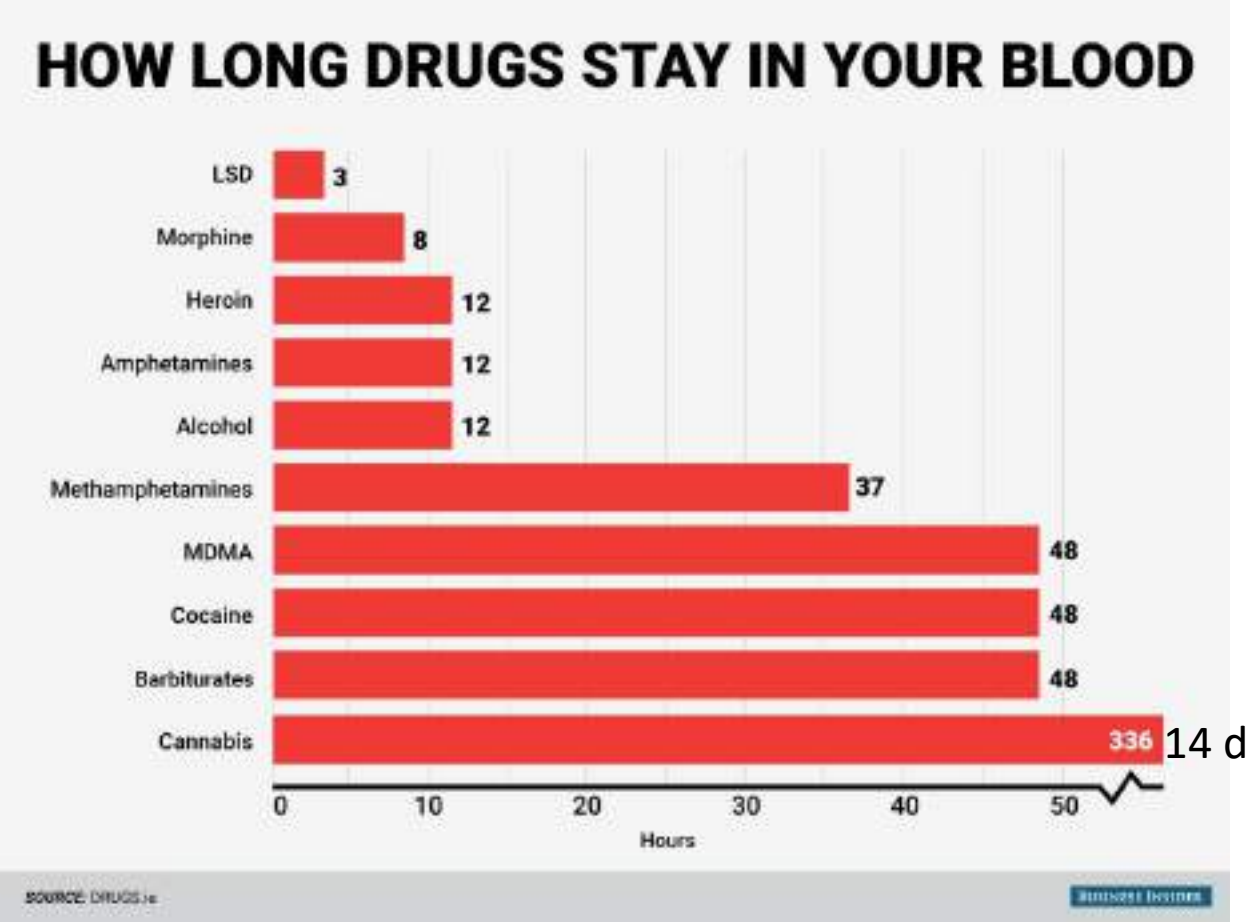
- Typical withdrawal effects, such as depression, anxiety, restlessness, irritability, constipation, and difficulties in sleeping and concentrating.
- Weight gain (increases appetite)

Insula’s role in addiction

- Insula is larger in smokers – plays a role in addiction
- Damage or stroke in the insula can suddenly halt addiction (without relapse or craving
- Patient N story (pg 622-623) helped to understand the role of insula in addiction

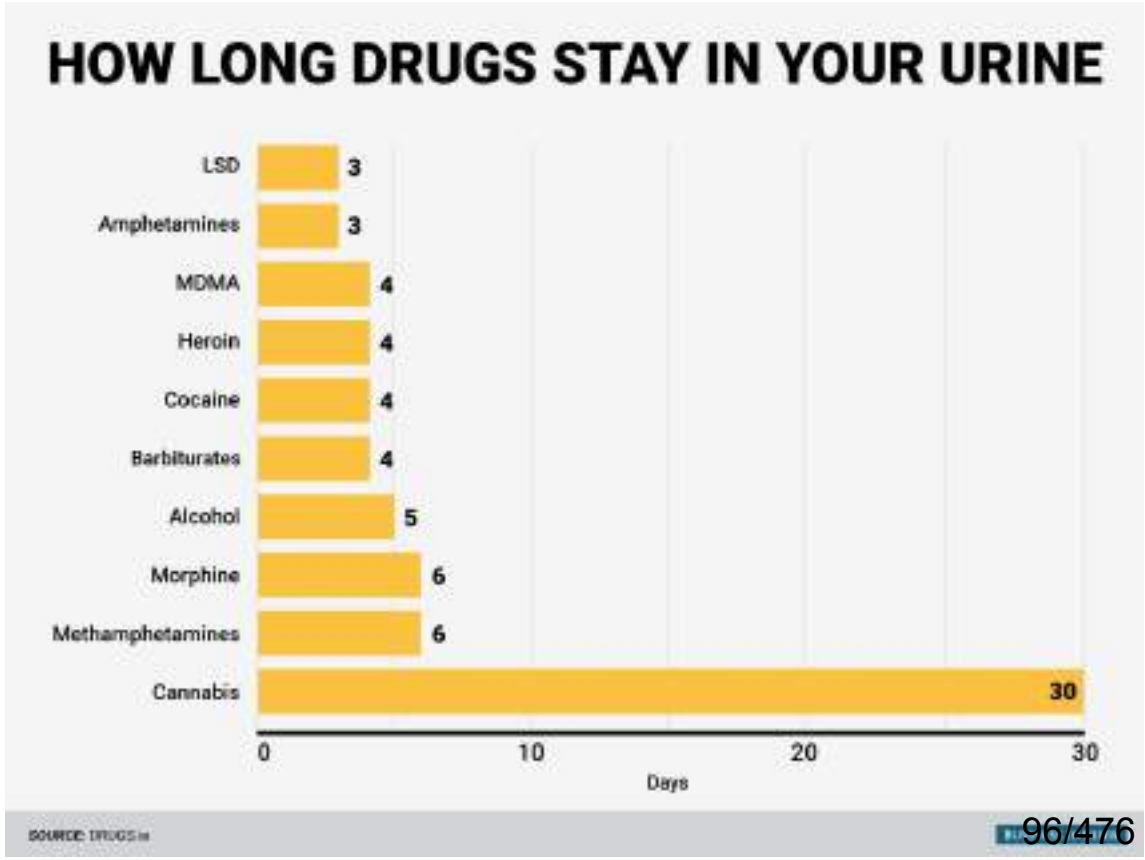
- Role for the insula →
  - conscious drug urges
  - translating bodily signals (perception of sensations inside the body) into conscious feelings,
  - behavioral biases during decision making that involves uncertain risk and reward.

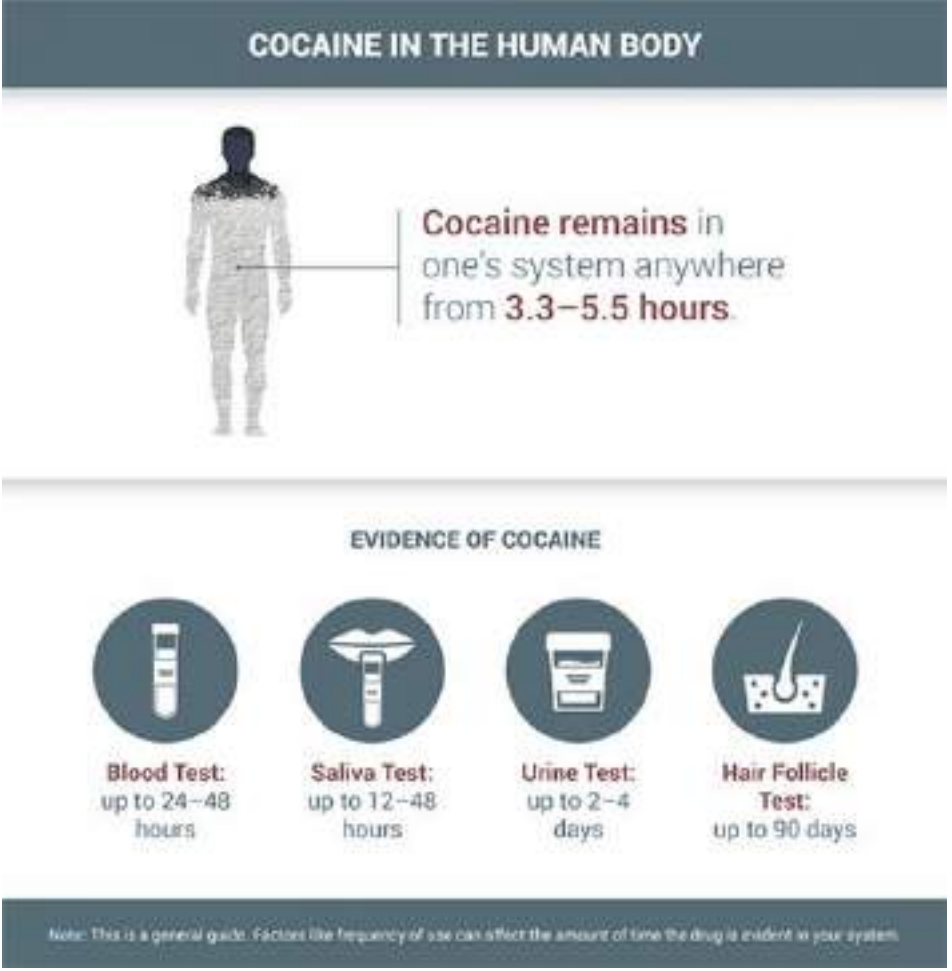
- In rat experiments – inhibitory drugs injected in insula help in nicotine deaddiction



14 days

After a single use of the drug/alcohol



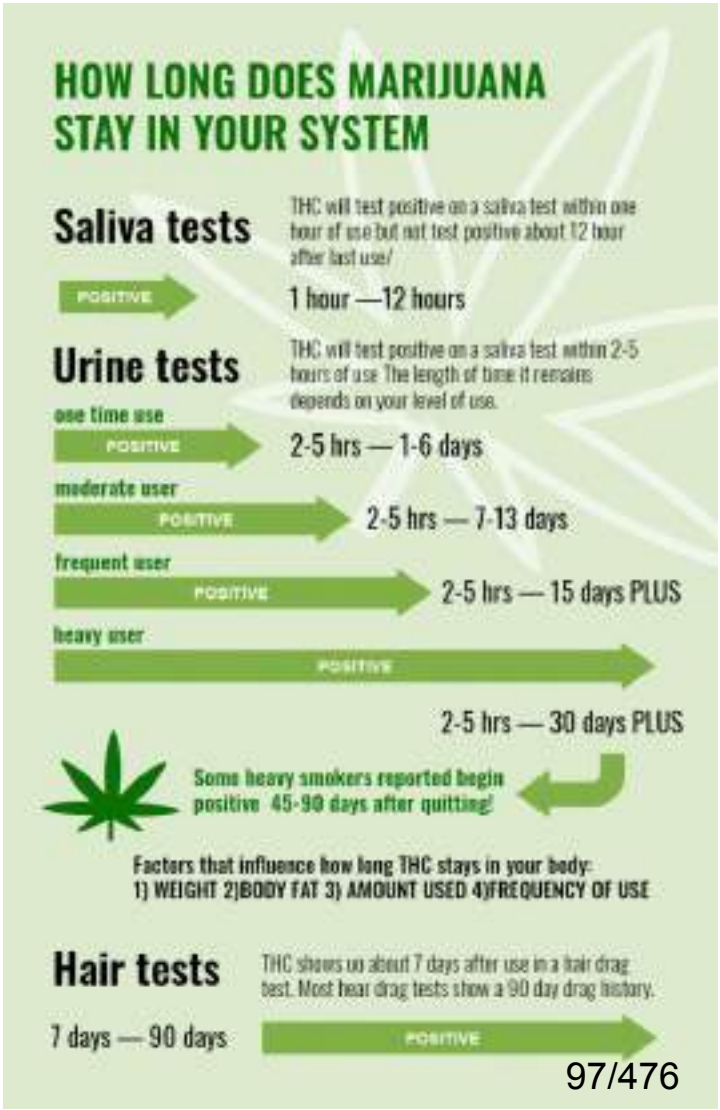

COCAINE IN THE HUMAN BODY
Cocaine remains in one's system anywhere from 3.3–5.5 hours.
EVIDENCE OF COCAINE
Blood Test: up to 24–48 hours
Saliva Test: up to 12–48 hours
Urine Test: up to 2–4 days
Hair Follicle Test: up to 90 days
Note: This is a general guide. Factors like frequency of use can affect the amount of time the drug is evident in your system.


Alcohol Detection Times
Breath up to 24 hrs
Urine 10 to 12 hrs
Blood up to 12 hrs
Saliva 1 to 5 days
Hair up to 90 days
verywell


How Long Does Heroin Stay in the System?
Testing Negative
• Urine : 2-7 Days
• Saliva : 5 Hrs
• Blood : 6 Hrs
• Hair : Up to 90 Days

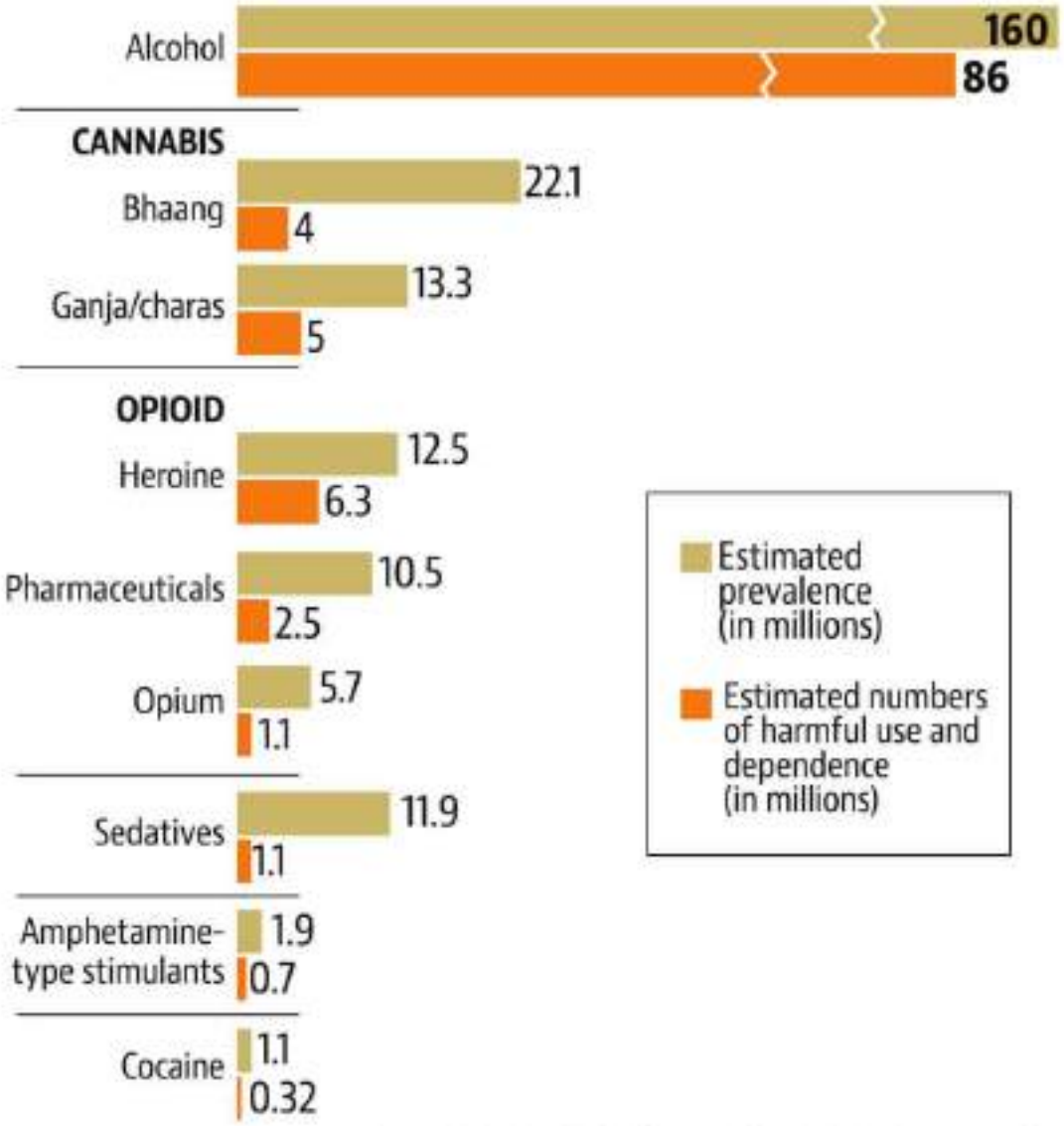
Nicotine


HAIR
SALIVA
URINE
BLOOD
90 DAYS
4 DAYS
4 DAYS
2-3 DAYS


HOW LONG DOES MARIJUANA STAY IN YOUR SYSTEM
Saliva tests
THC will test positive on a saliva test within one hour of use but not test positive about 12 hour after last use/
POSITIVE
1 hour —12 hours
Urine tests
THC will test positive on a saliva test within 2-5 hours of use The length of time it remains depends on your level of use.
one time use
POSITIVE
2-5 hrs — 1-6 days
moderate user
POSITIVE
2-5 hrs — 7-13 days
frequent user
POSITIVE
2-5 hrs — 15 days PLUS
heavy user
POSITIVE
2-5 hrs — 30 days PLUS
Some heavy smokers reported begin positive 45-90 days after quitting!
Factors that influence how long THC stays in your body:
1) WEIGHT 2)BODY FAT 3) AMOUNT USED 4)FREQUENCY OF USE
Hair tests
THC shows up about 7 days after use in a hair drug test. Most hear drug tests show a 90 day drug history.
7 days — 90 days
POSITIVE

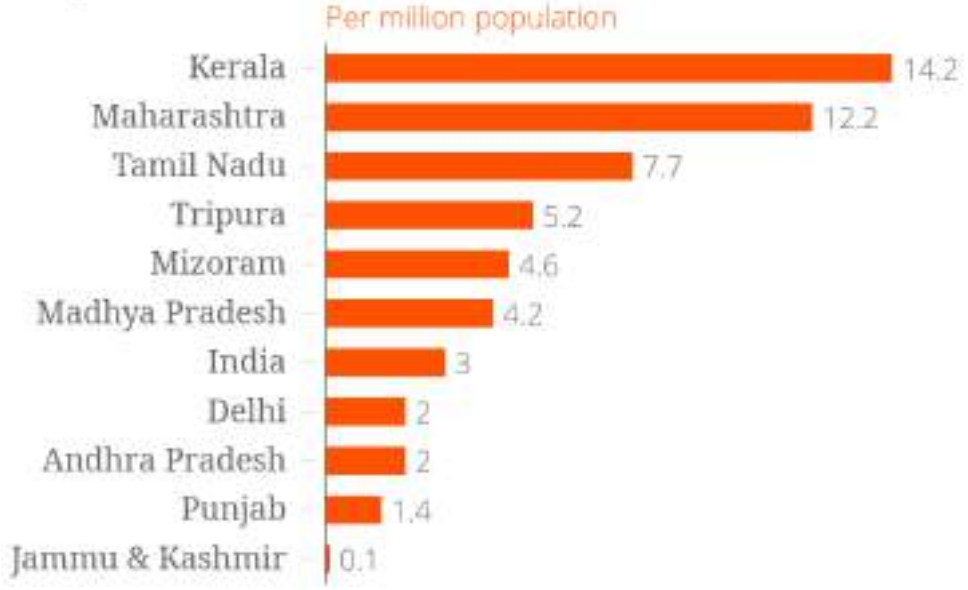
Scale of substance abuse in India

Alcohol is the most commonly used legal psychoactive substance, with about about 14.6% of population using it



(Source: Magnitude of Substance Abuse in India Report, 2019)

Drug addiction or abuse related suicides in some Indian states

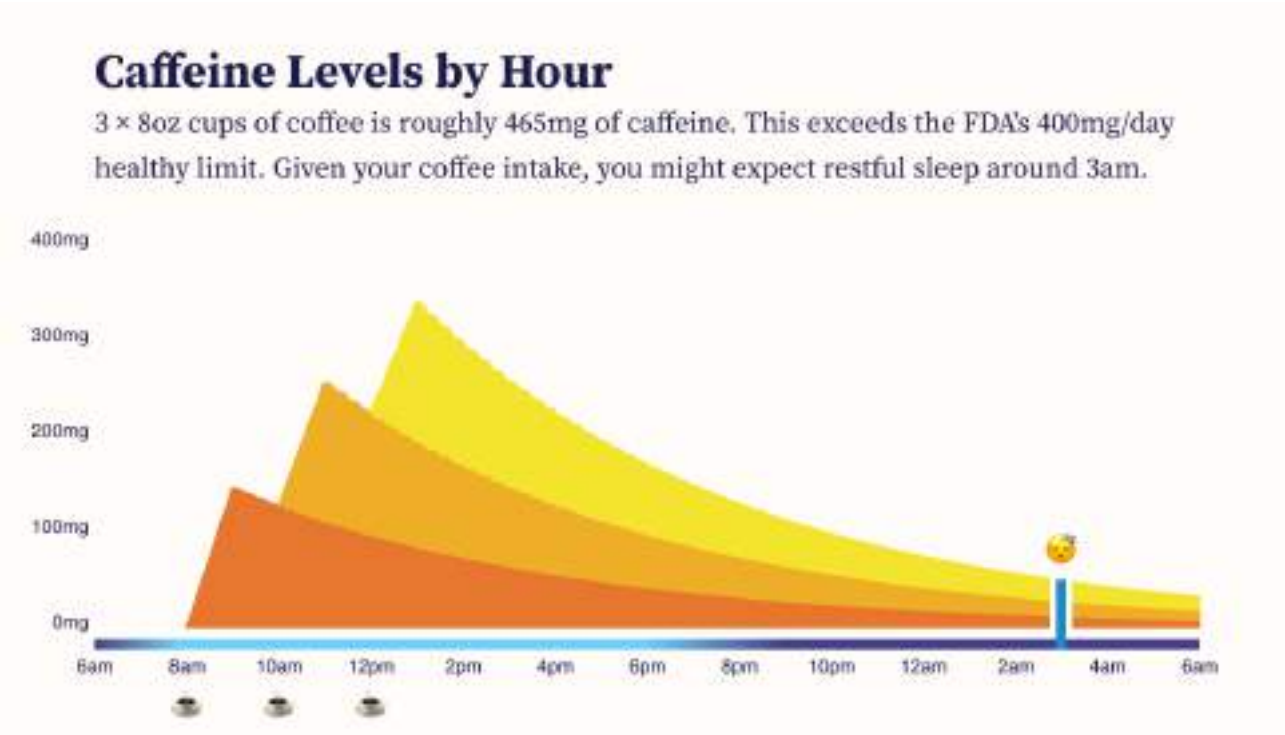


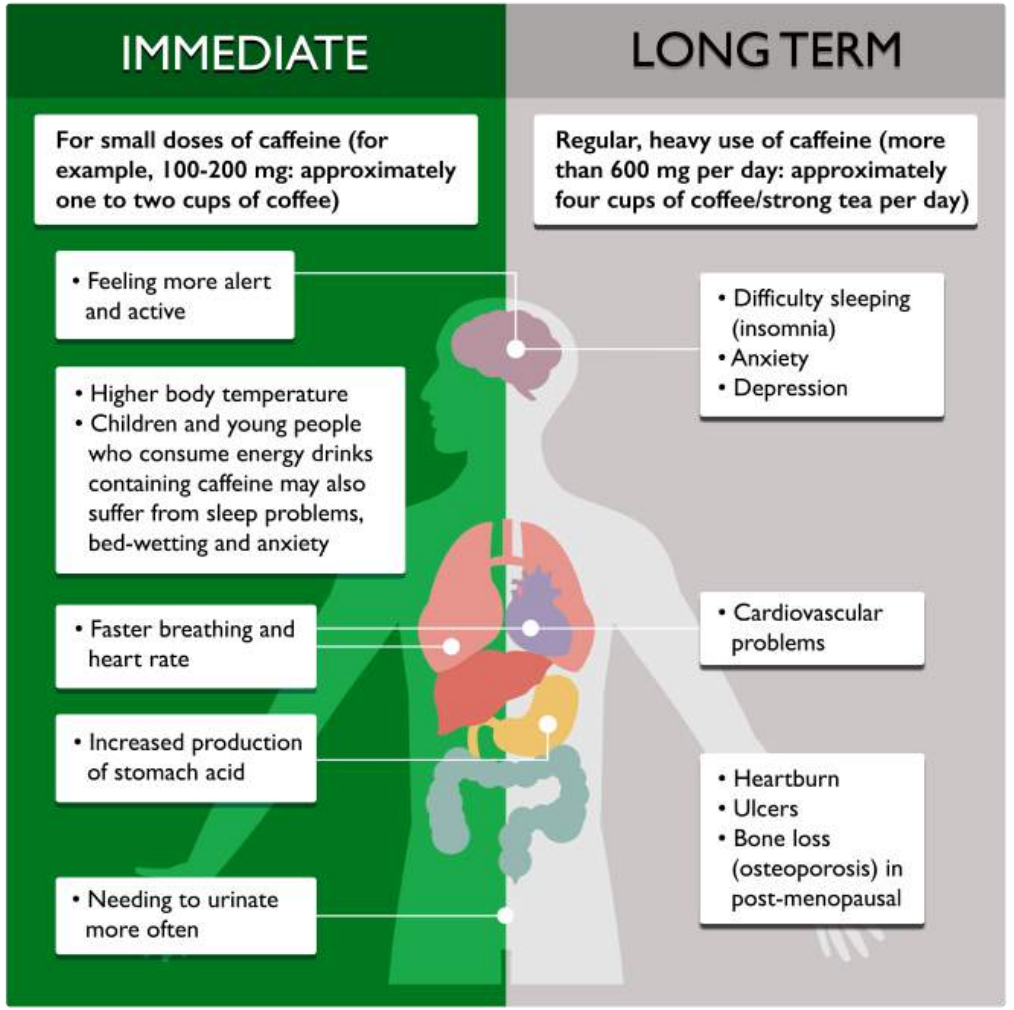
Data: Ministry of Social Justice and Empowerment

2014

Caffeine

- Stimulant – Makes you alert and active
- Caffeine can cross the blood brain barrier
- Mild use is helpful but chronic intake is harmful
- Effect persists for 4-6hrs
- Caffeine binds to
  - Increases dopamine and norepinephrine - addictive
  - Adenosine receptors antagonist – prevents sleepiness





Can cause dehydration

https://www.brown.edu/campus-life/health/services/promotion/content/what-are-effects-caffeine

Treatment for substance abuse

Behavioral therapies help patients:

- modify their attitudes and behaviors related to drug use
- persist with other forms of treatment, such as medication
- be productive in the family, at work, and in society
- increase healthy life skills

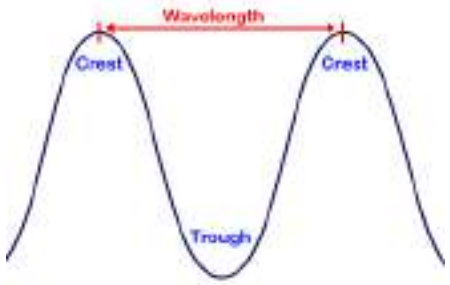
https://www.drugabuse.gov/

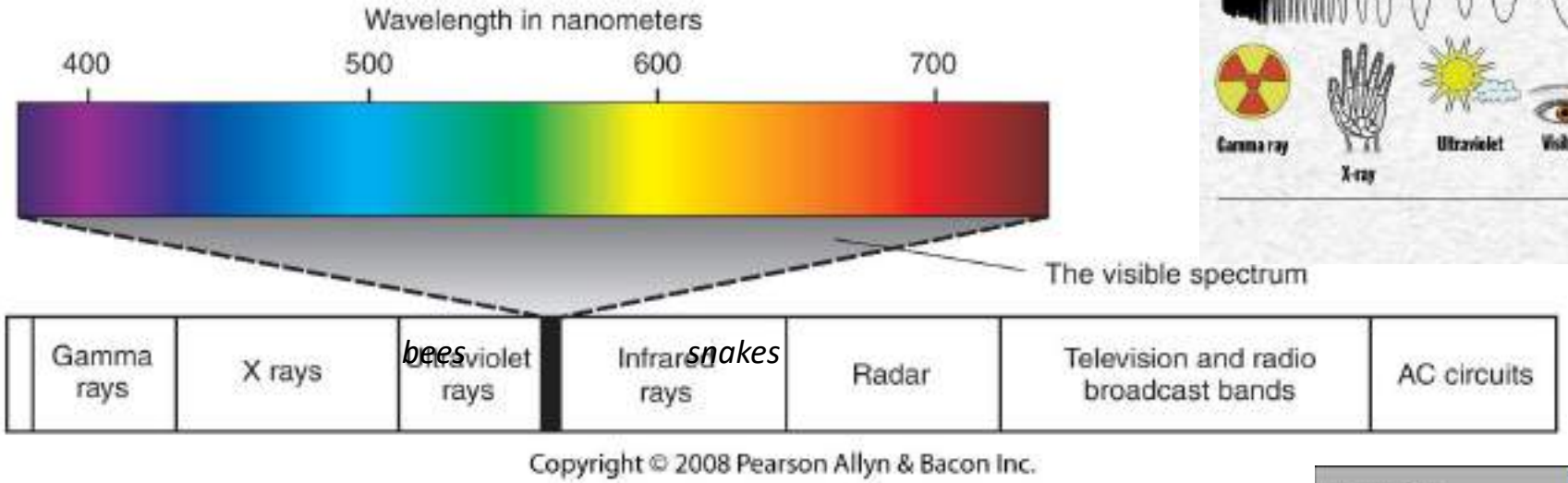
Gateway Foundation

- Any particular pattern of that you observed for legal vs illegal drugs (esp. related to neurotransmitters)?

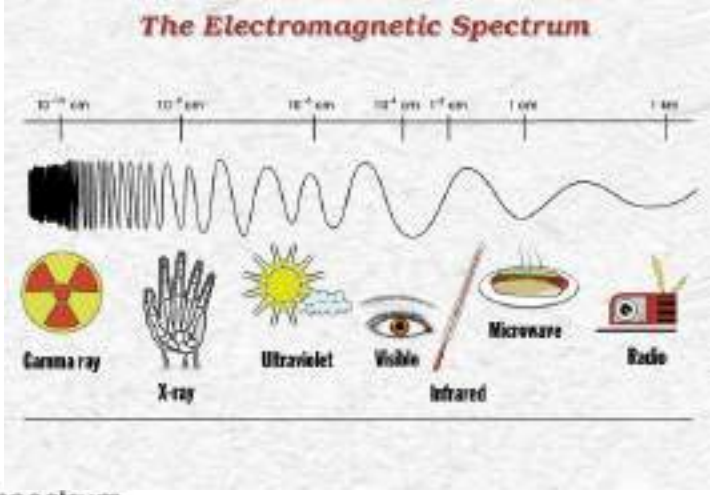
Vision

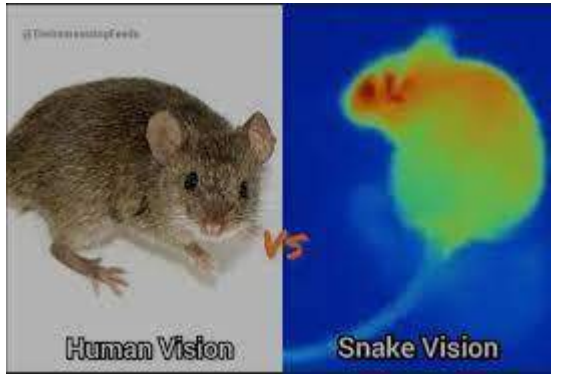
Our Visual stimulus





Copyright © 2008 Pearson Allyn & Bacon Inc.

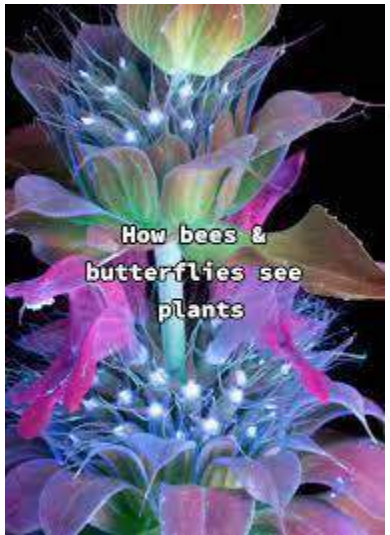




The ability to see ultraviolet (UV) helps guide bees to the pollen containing parts of flowers

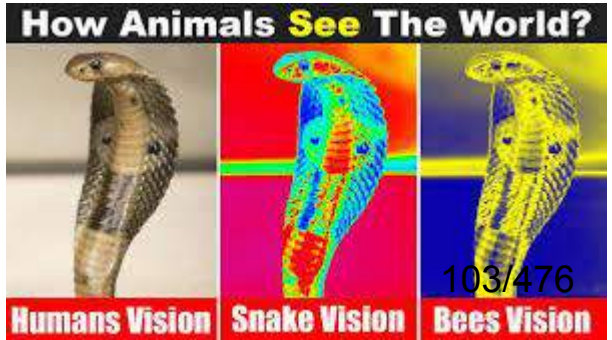
Human View
(No UV Sensitivity)

Bee View
(UV Sensitivity)



Human View
(No UV Sensitivity)

Dog View
(Some UV Sensitivity)



Anatomy of the eye

The iris gives the eye its characteristic color—blue, brown, or other.

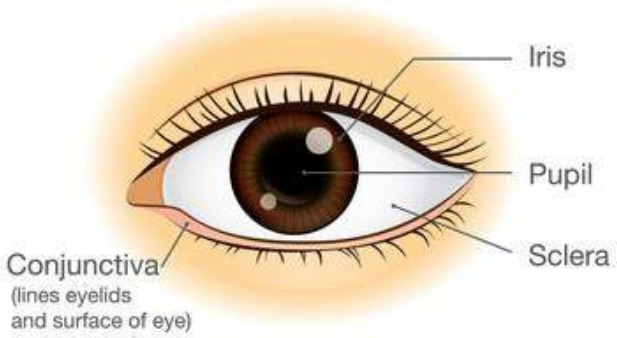
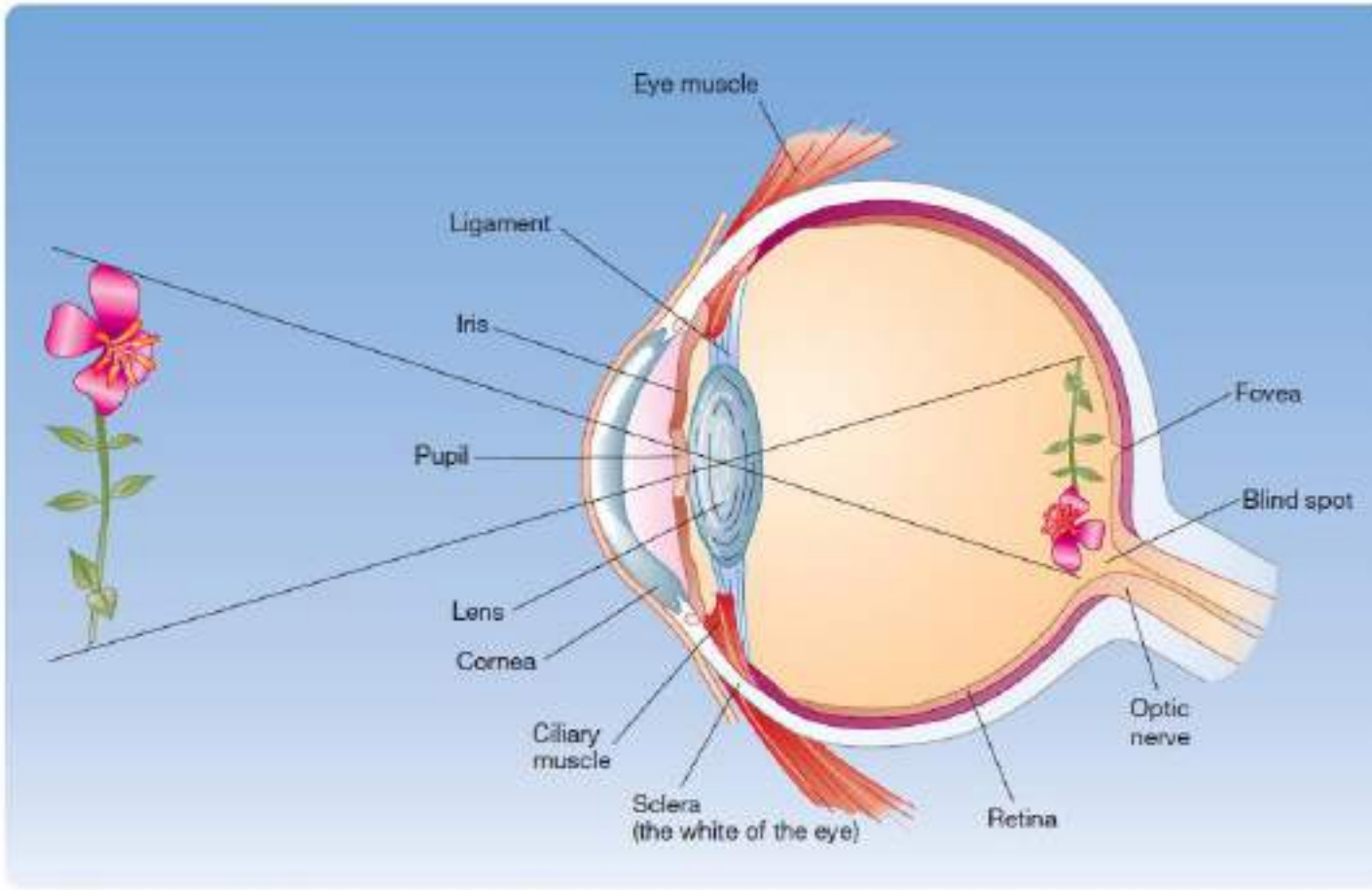


Figure 6.4 The human eye, a product of approximately 600 million years of evolution.

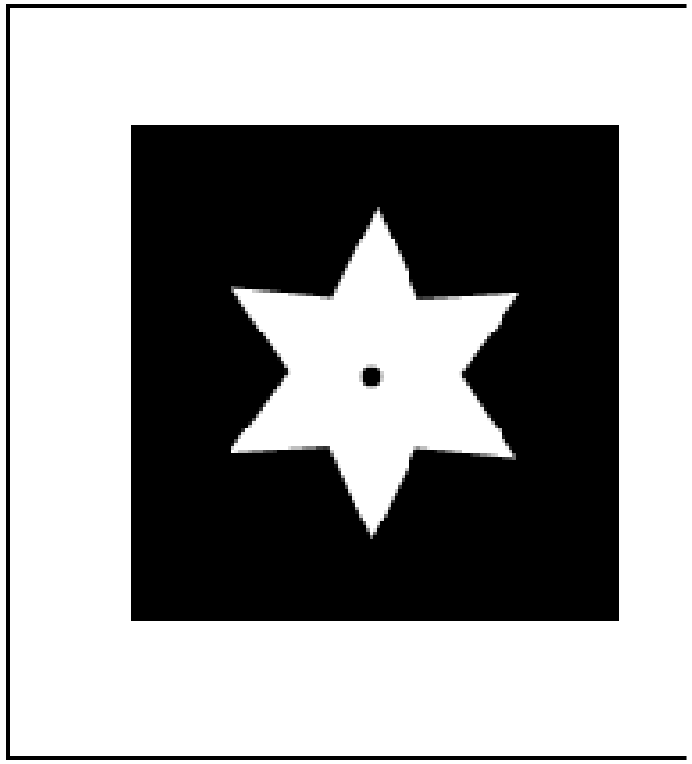


Based on Lamb, T. D., Collin, S. P., & Pugh, E. N. (2007). Evolution of the vertebrate eye: Opsins, photoreceptors, retina and eye cup. *Nature Reviews Neuroscience*, 8, 960–975.

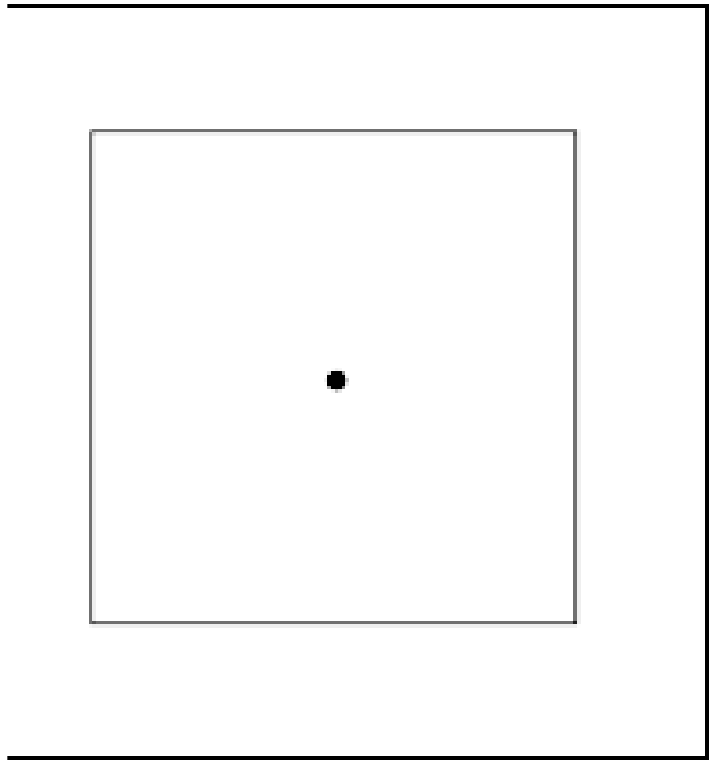
- Light enters the eye through the pupil, whose size is regulated by the iris.
- Light travels into the lens all the way to the retina

- **Fovea** – central region of the retina which contain only cones and mediates the most acute vision

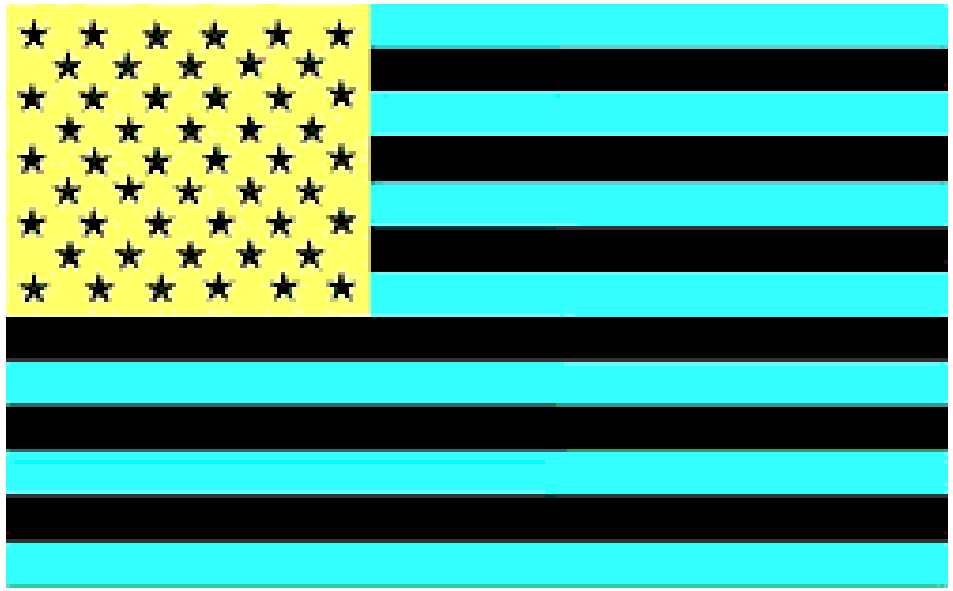
Look at the dot inside the star for 60 secs

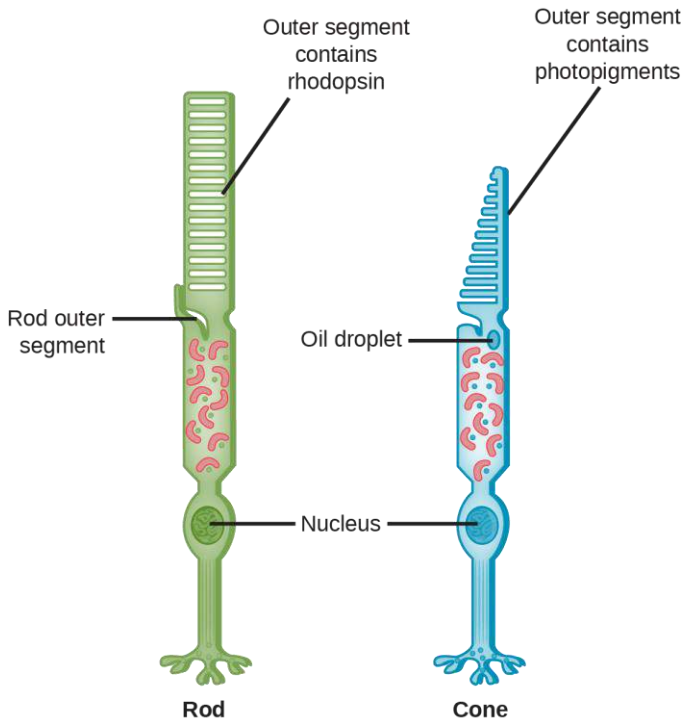


look at the dot inside the white box



Look at the flag for 60 secs and then look at the white/blank area



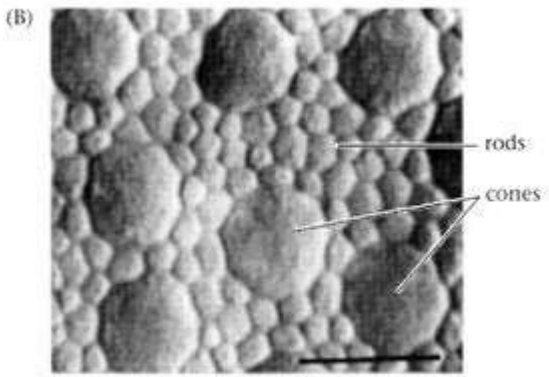


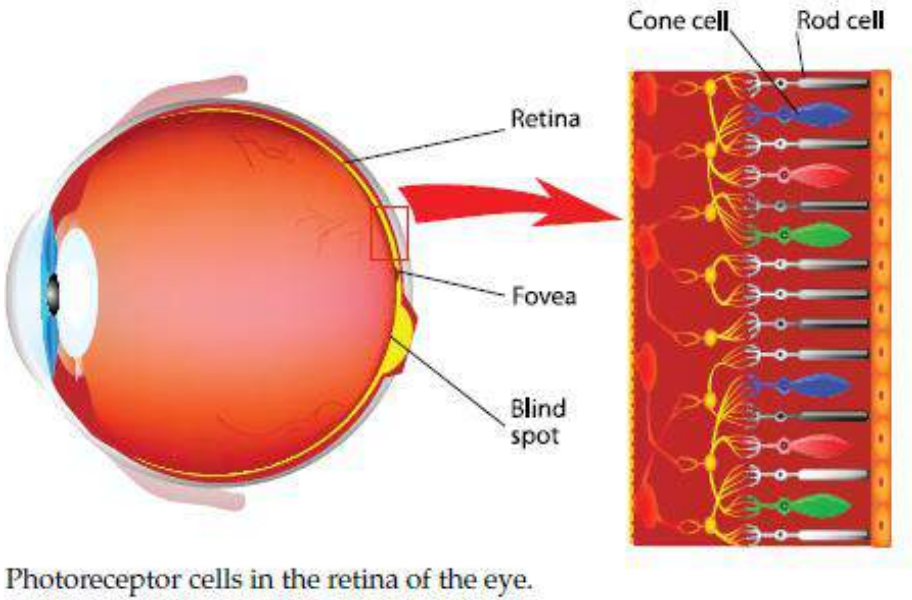
- Retina has two types of photoreceptors
  - **Rods** (12 million) – sensitive to light intensity (active in low light)
  - **Cones** (6 million) – sensitive to color/wavelength (active in normal daylight)

- Light passes through the transparent layers to the retina to stimulate the photoreceptors – rods/cones

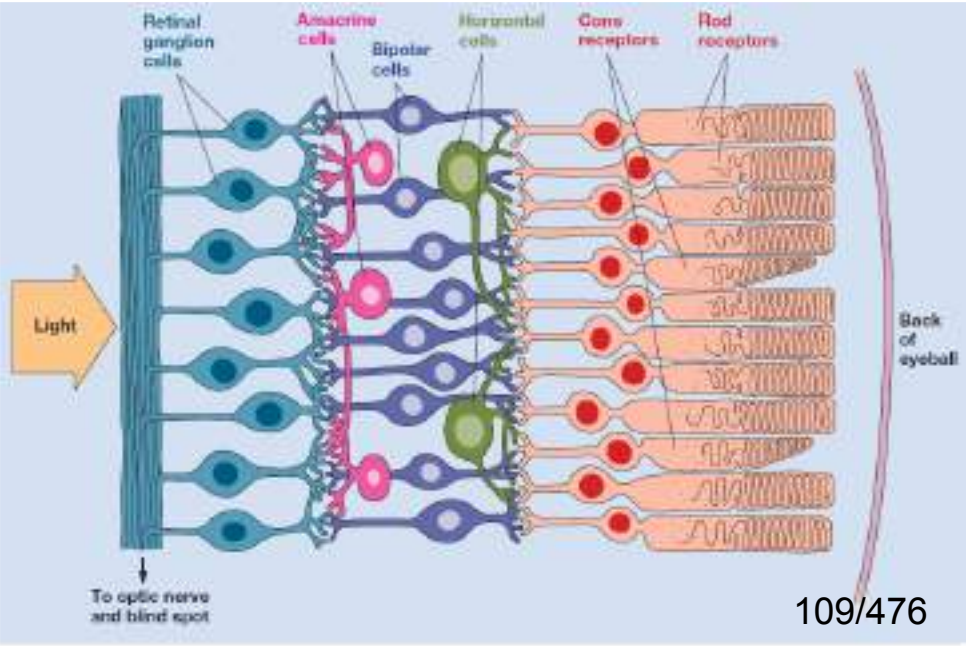
- Photoreceptors transduce light energy into electrical impulses (by release of different neurotransmitters)

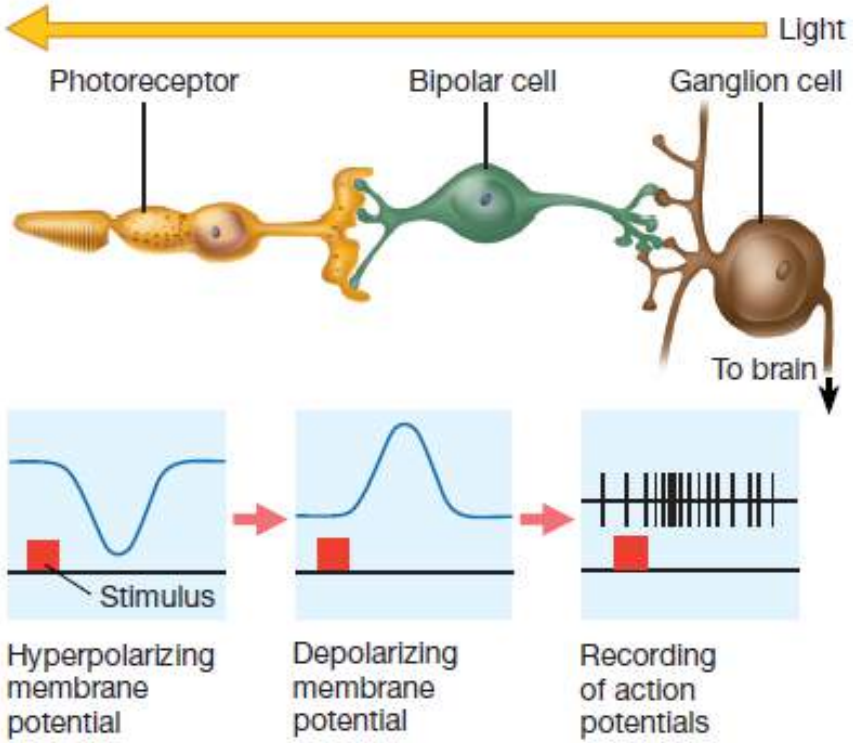
- Rods work in dim light conditions
- Cones function under good light intensity (daylight).

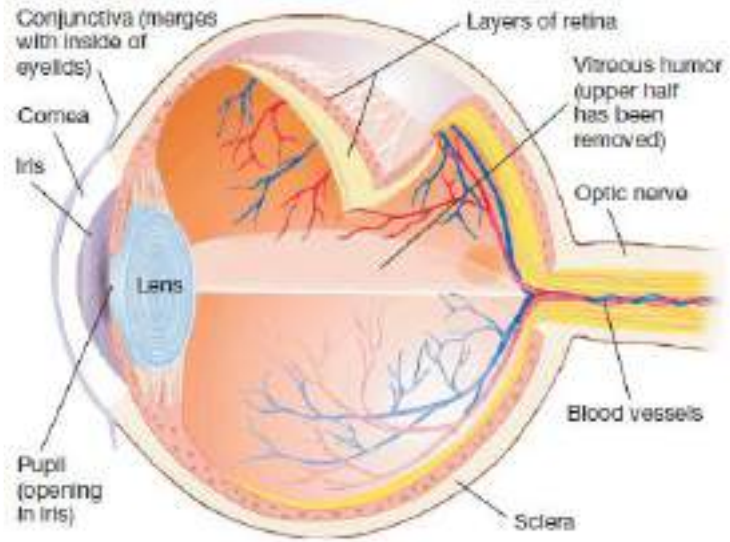




Photoreceptor cells in the retina of the eye.



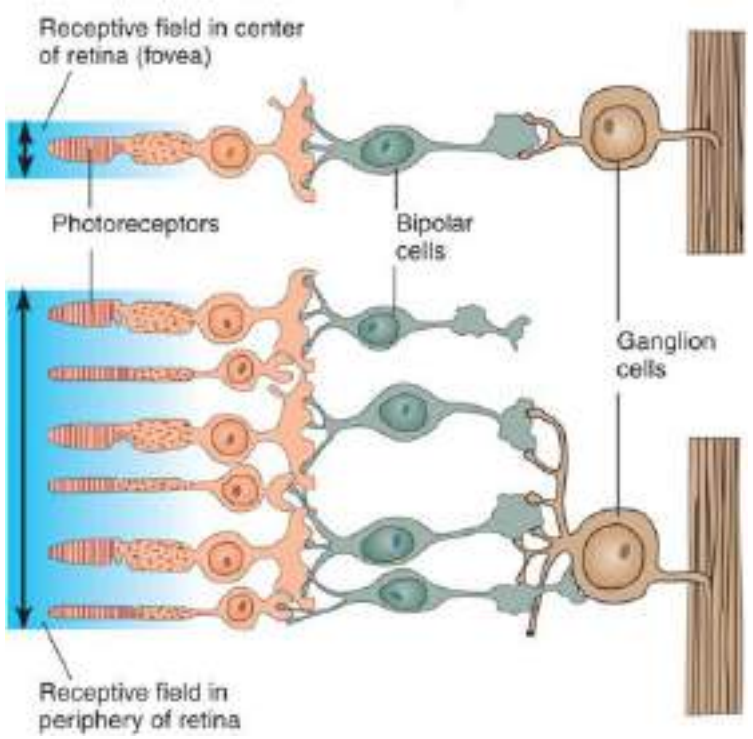




Neural circuitry in the retina

- Rods have rhodopsin that are turned off (hyperpolarized) when light falls on them. (detect light with closed eyelids)
- Cones have *photopigments* that are bleached (pigments change their color) when light falls on them. The bleaching causes hyperpolarization which changes the rate of glutamate neurotransmitter released.
- Hyperpolarization of the photoreceptor (PRs) results in reduced release of neurotransmitter (PRs are always ON and light falling on them reduces their activity or turns them OFF).
- Glutamate normally hyperpolarizes (inhibits) the bipolar cell. When light falls on the photoreceptors, the reduction of glutamate release results in depolarization (de-inhibits) of the bipolar cells. This depolarization causes the bipolar cells to excite the subsequent cells (ganglion cells) – increasing its firing rate
- The ganglion cell axons form the optic nerve

General versus peripheral acuity: ganglion cells in the fovea receive input from a smaller number of photoreceptors than in the periphery and hence provide more visual acuity



- Receptive field of a neuron is that part

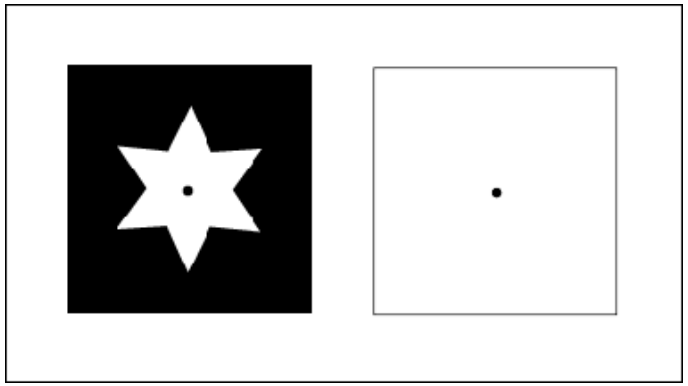
  of the visual field that the neuron “sees”

- If a neuron receives info. from PRs located in the fovea, its receptive field will be the fixation point – the point where the eye is looking.

- Fovea has equal no. of ganglion cells and cones, so the 1:1 ratio gives high acuity at the fixation point.

- The ratio decreases for the peripheral areas where the visual preciseness is less, i.e. more no. of PRs spread over a larger area are required to code information from the periphery.

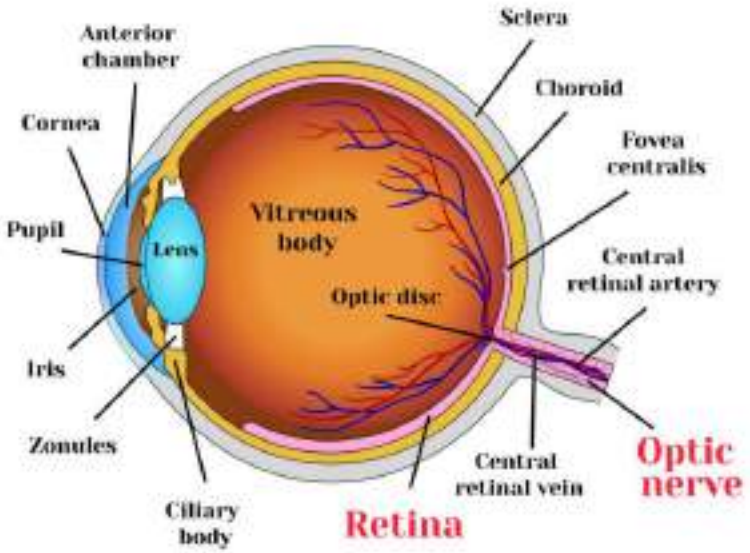
Afterimage



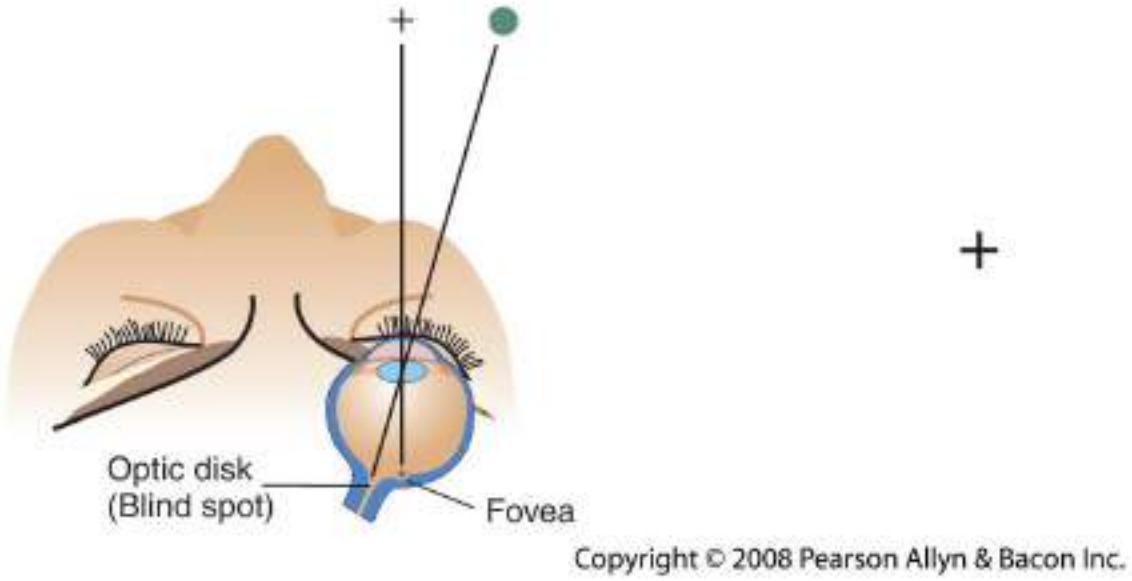
Negative afterimages - occur when the rods and cones, which are part of the retina, are overstimulated and become desensitized. This desensitization is strongest for cells viewing the brightest part of the image, but is weakest for those viewing the darkest. When you look away, the least depleted cells react strongest, and vice versa, and you see an image with colors that are the reverse of how the image originally appeared.

A positive afterimage ?

Blind Spot



Blind spot - small area of the retina where no receptors (no rods or cones) are present. This is where the optic nerve exits the eye carrying visual information to other brain areas.



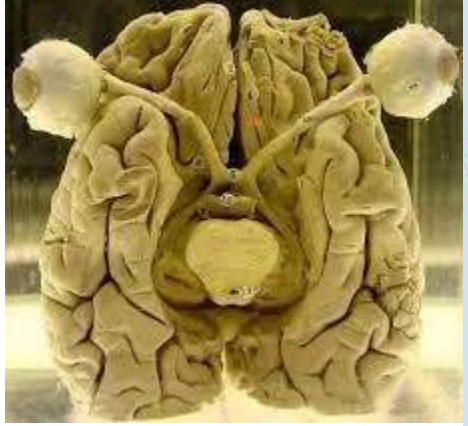
Check It Out

Your Blind Spot and Completion

First, prove to yourself that you do have areas of blindness that correspond to your retinal blind spots. Close your left eye and stare directly at the A below, trying as hard as you can to not shift your gaze. While keeping the gaze of your right eye fixed on the A, hold the text at different distances from you until the black dot to the right of the A becomes focused on your blind spot and disappears at about 13 centimeters (5 inches).

- If the blindsplot on the retina has no photoreceptors why don’t we see a black/blind/empty spot when we see the world?

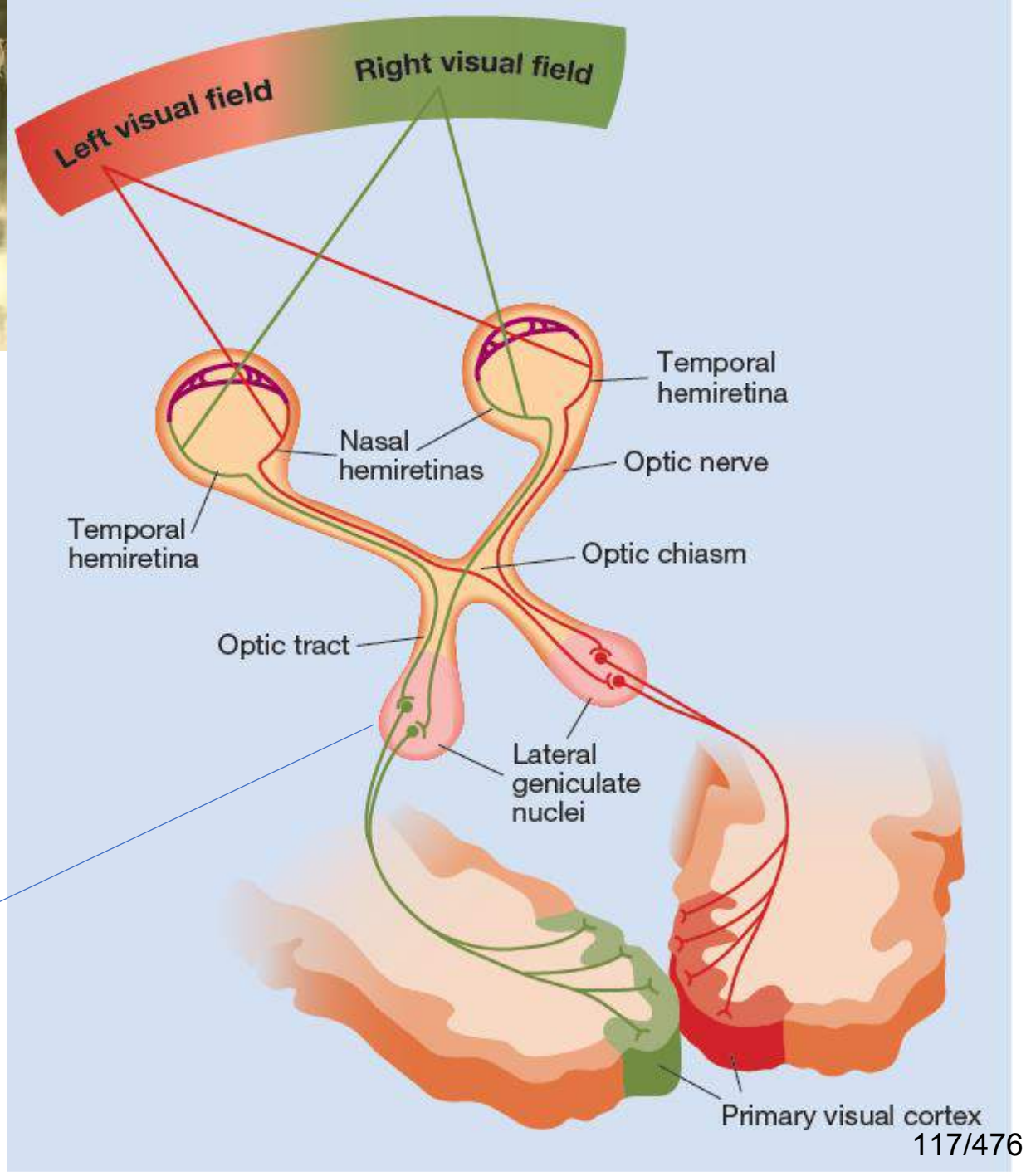
If each eye has a blind spot, why is there not a black hole in your perception of the world when you look at it with one eye? You will discover the answer by focusing on B with your right eye while holding the text at the same distance as before. Suddenly, the broken line to the right of B will become whole. Now focus on C at the same distance with your right eye. What do you see?



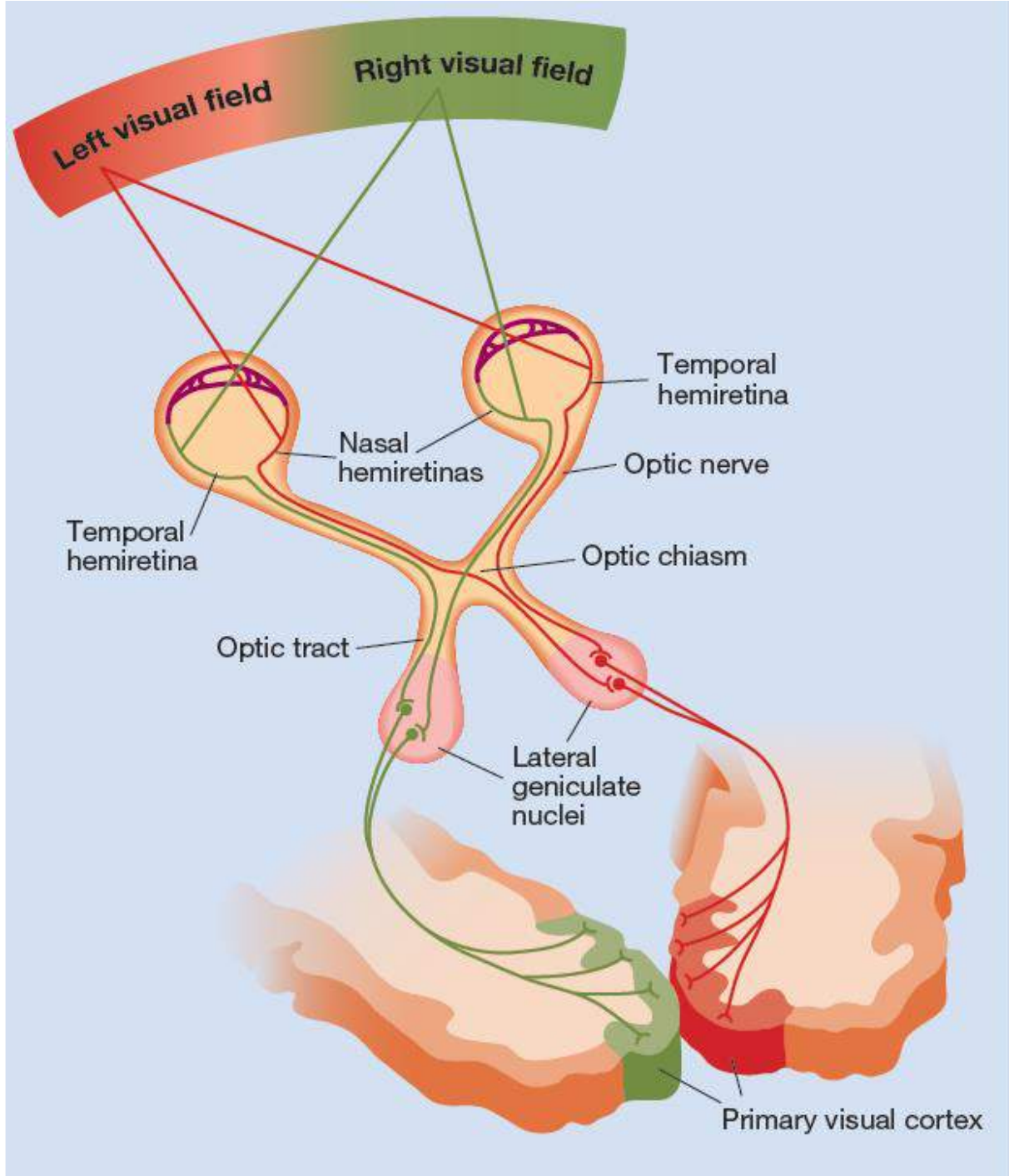
Information from retina via optic nerve → optic chiasm → LGN → primary visual cortex

- All information from the lateral (outer) side of a retina enters the ipsilateral optic tract
- All information from the nasal (inner) side of the retina crosses over at the chiasm and enters the contralateral optic tract.

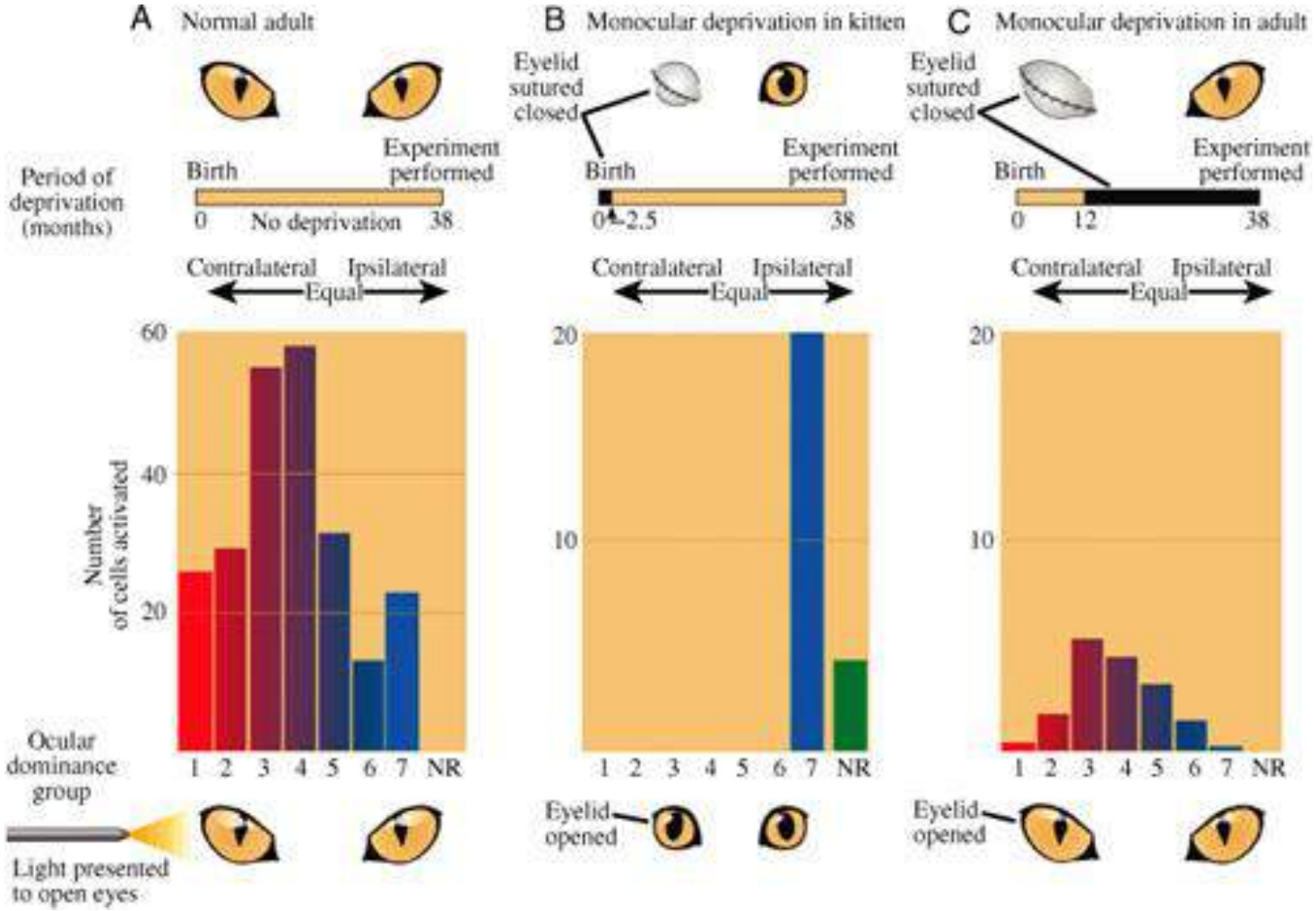
thalamus

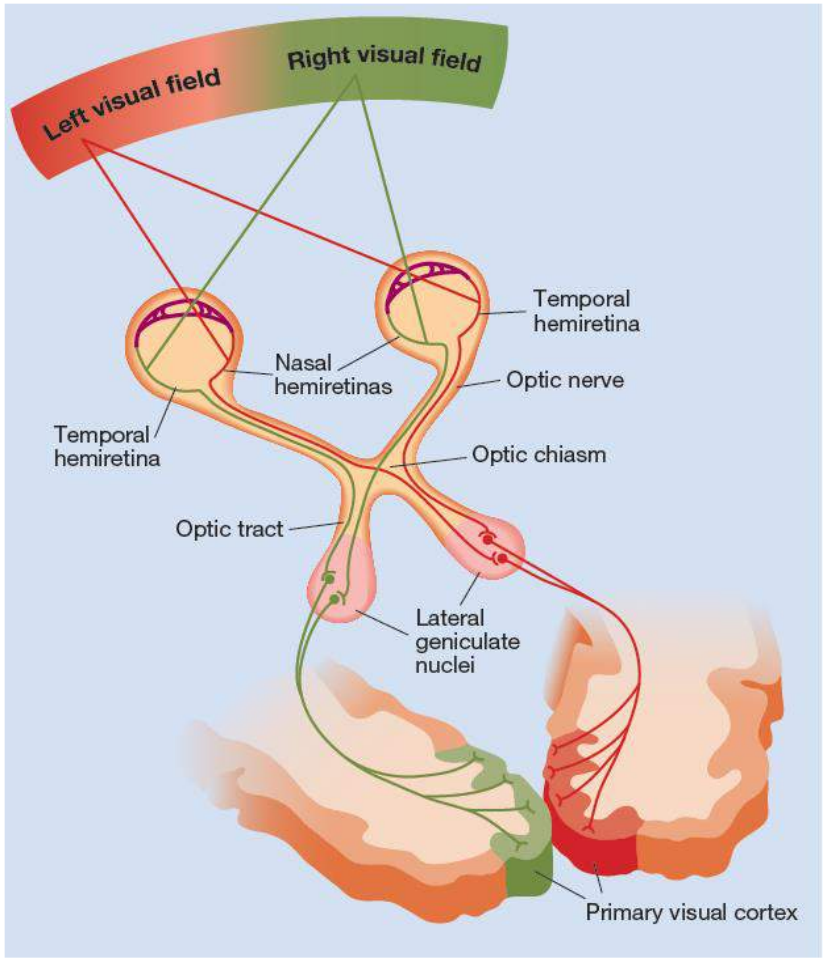


Visual fields and Primary visual pathway


Left visual field
Right visual field
Temporal hemiretina
Nasal hemiretinas
Optic nerve
Temporal hemiretina
Optic chiasm
Optic tract
Lateral geniculate nuclei
Primary visual cortex

Visual experience drives the wiring in the visual cortex





https://www.informit.com/articles/article.aspx?p=1431818

- How do we perceive depth?
- What allows us to perceive depth?

Depth perception

Veronica Lara/Shutterstock

Binocular cues help us to perceive depth.

Check It Out

The Position of Eyes

Here you see three animals whose eyes are on the front of their heads (a human, an owl, and a lion) and three whose eyes are on the sides of their heads (an antelope, a canary, and a squirrel). Why do a few vertebrate species have their eyes side-by-side on the front of the head while most species have one eye on each side?

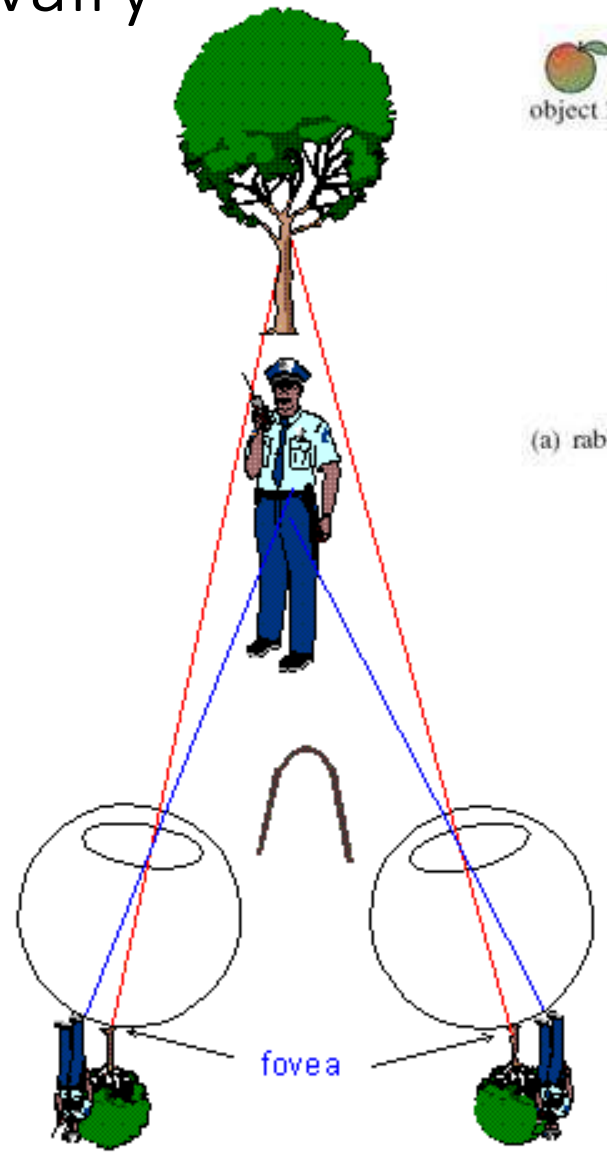
In general, predators tend to have the front-facing eyes because this enables them to accurately perceive how far away prey animals are; prey animals tend to have side-facing eyes because this gives them a larger field of vision and the ability to see predators approaching from most directions.

Top row from left: Guiziou Franck/Hemis/Alamy Stock Photo; Matthew Cuda/Alamy Stock Photo; C.K. Lorenz/Science Source
Bottom row from left: Naomi Engela Le Roux/123RF; Vasiliy Vishnevskiy/123RF; Colin Varndell/Nature Picture Library

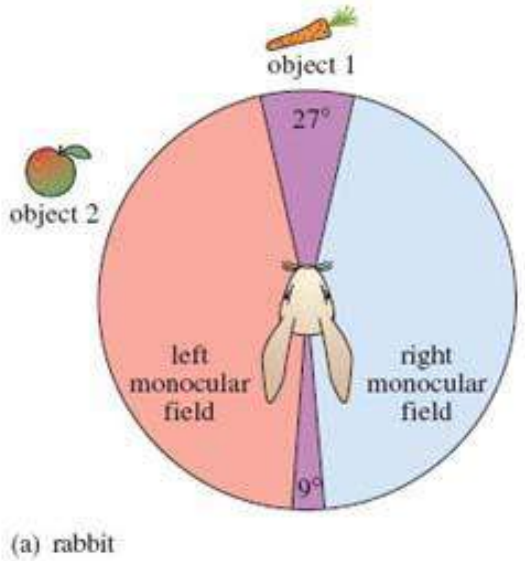
Binocular Disparity or Rivalry (Depth perception) 3D vision

The brain uses binocular disparity to extract depth information from the two-dimensional retinal images

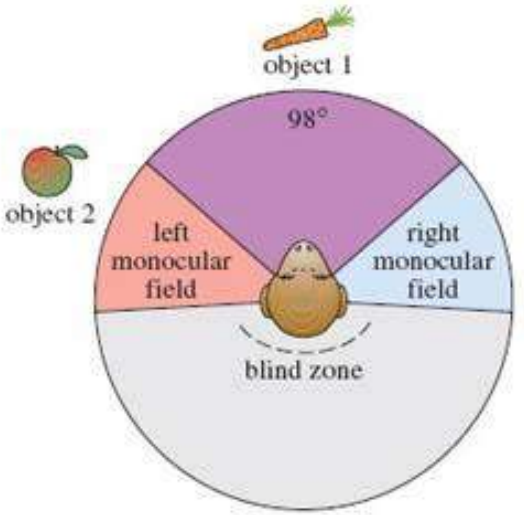
Both of your eyes perceive the same object at slightly different locations or at slightly different angles, but your brain can merge the two images into one 3-D image (stereoscopic vision)



Binocular Disparity



(a) rabbit



(b) monkey

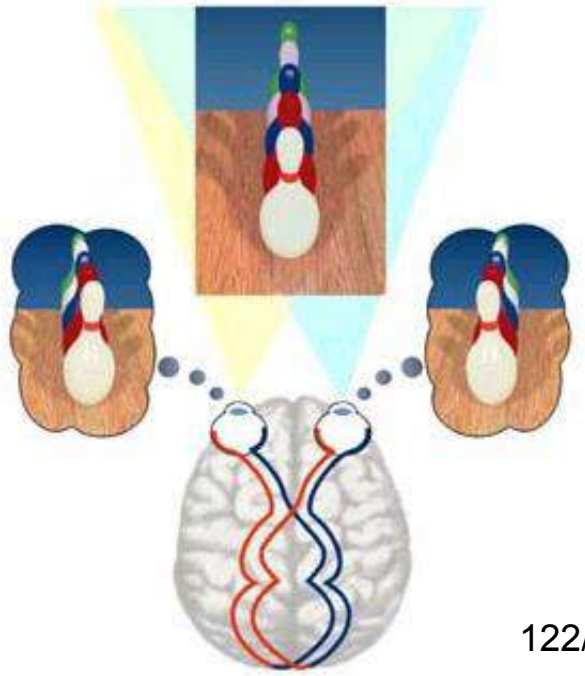
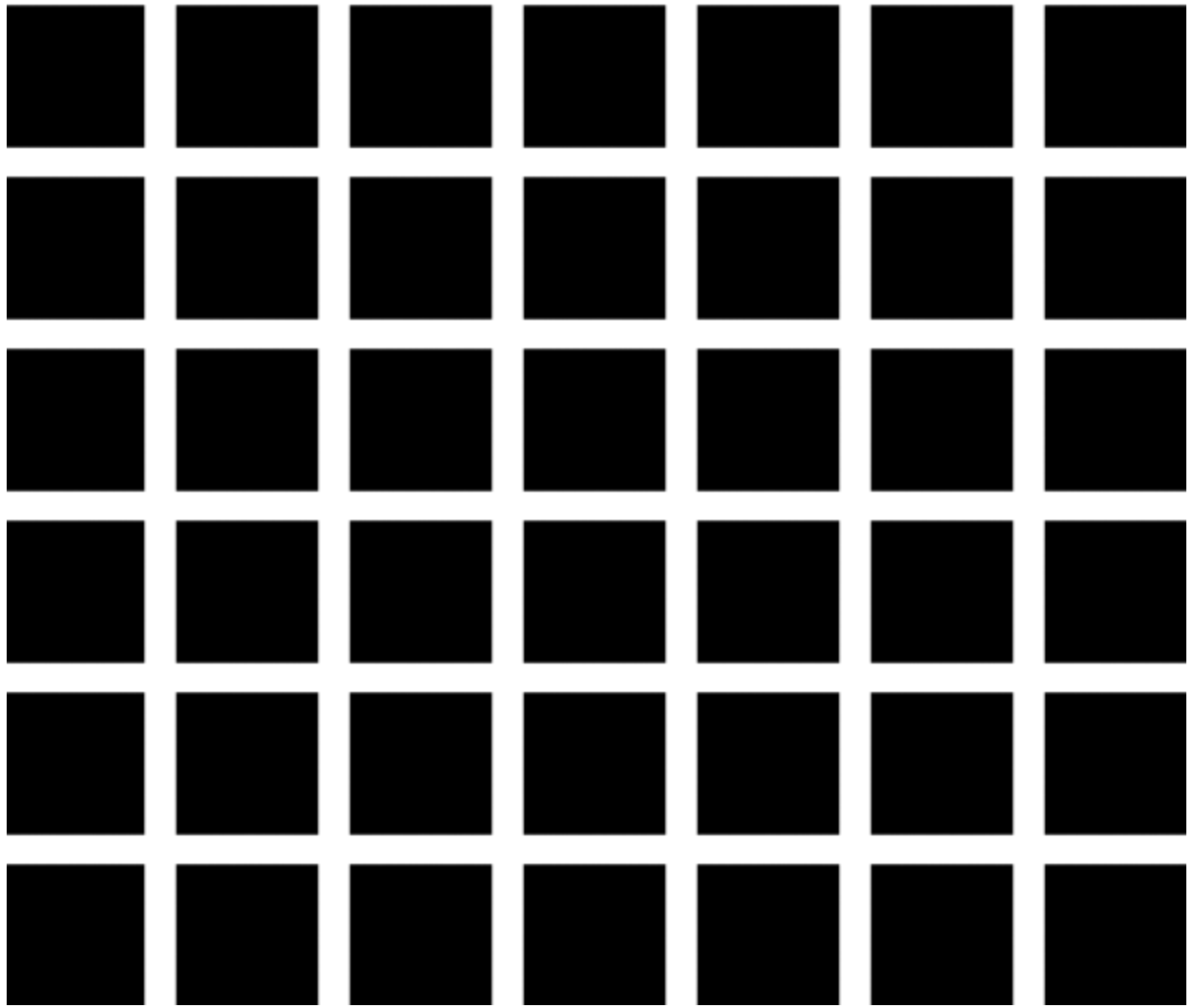
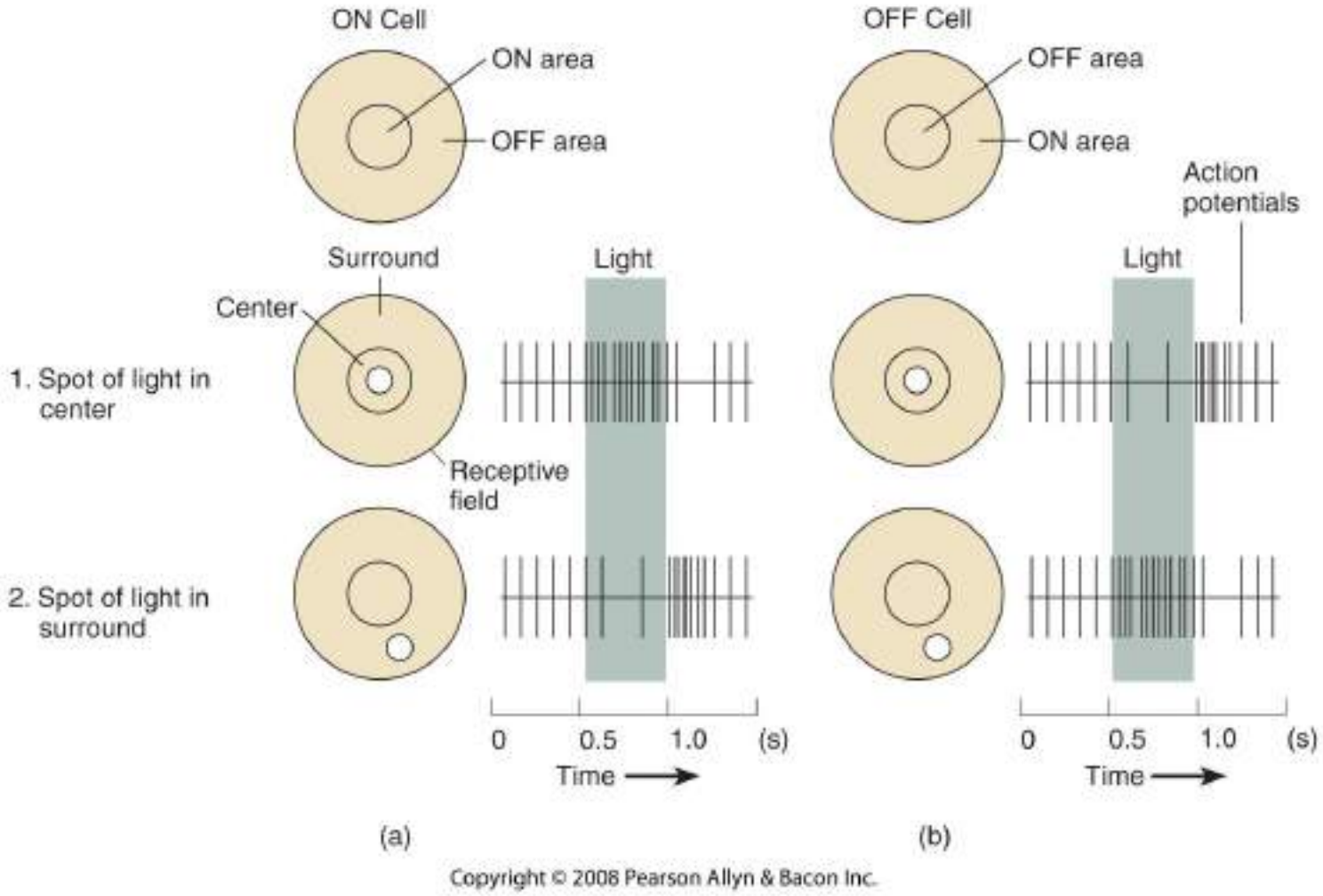


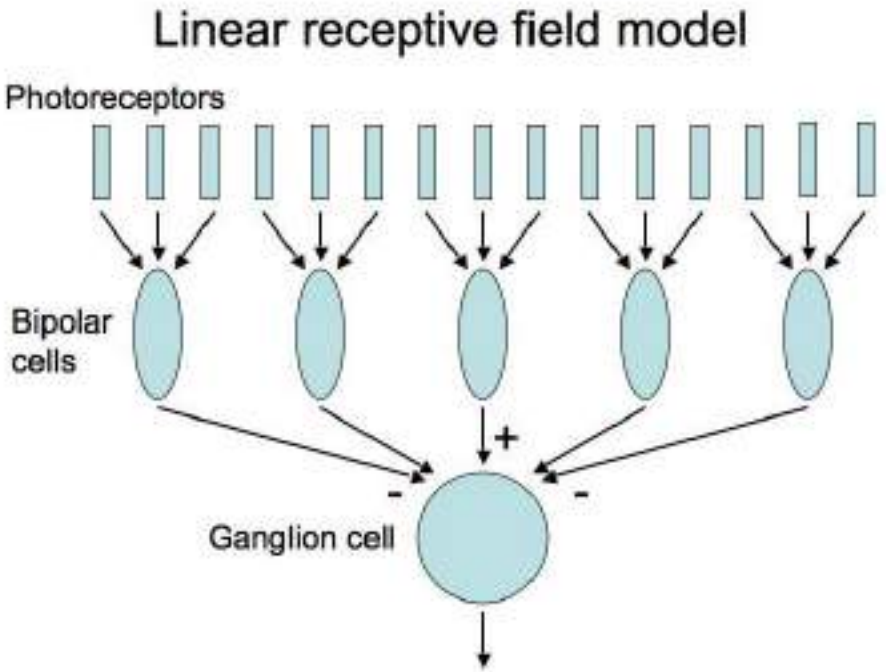
Figure ground perception

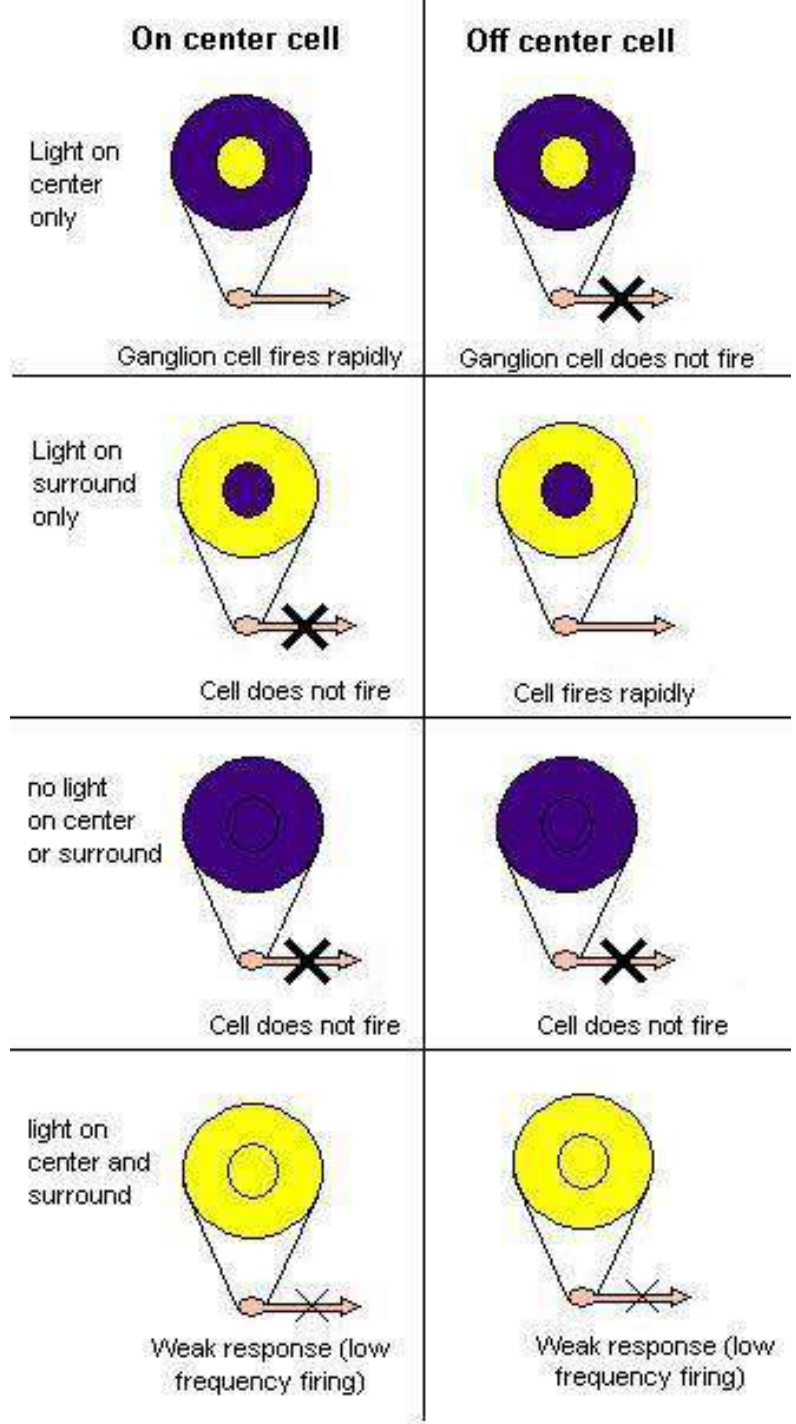


Coding light and dark

Retinal ganglion cells (circular receptive fields)






On center cell
Off center cell
Light on center only
Ganglion cell fires rapidly
Ganglion cell does not fire
Light on surround only
Cell does not fire
Cell fires rapidly
no light on center or surround
Cell does not fire
Cell does not fire
light on center and surround
Weak response (low frequency firing)
Weak response (low frequency firing)

Retinal ganglion cells respond to edges

Input image
(cornea)

"Neural image"
(retinal ganglion cells)

Center-surround receptive fields: emphasize edges.

Edge detection

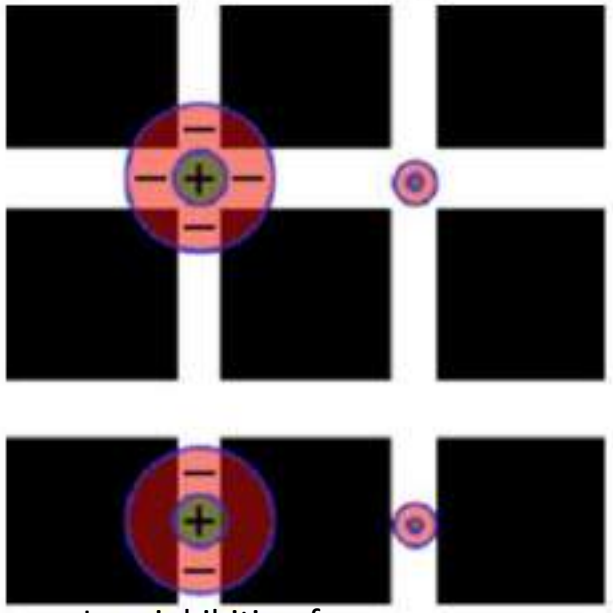
http://www.cns.nyu.edu/~david/courses/perception/lecturenotes/ganglion/ganglion.html

Hermann Grid Illusion is Due to Lateral Inhibition?

We see phantom dark spots at the intersections to the side of the focus of vision because .....

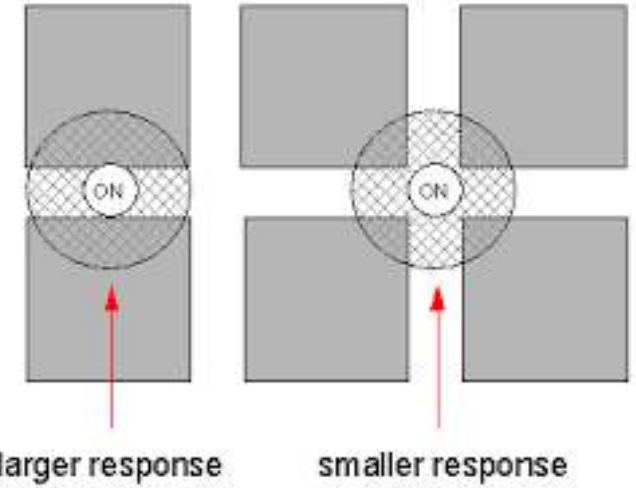
There is more lateral inhibition at the intersection than in the middle of a white bar.

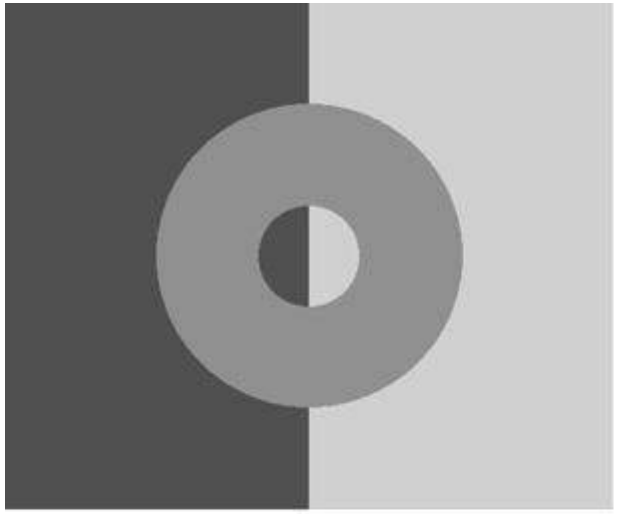
More inhibition from surrounding cells



Less inhibition from surrounding cells

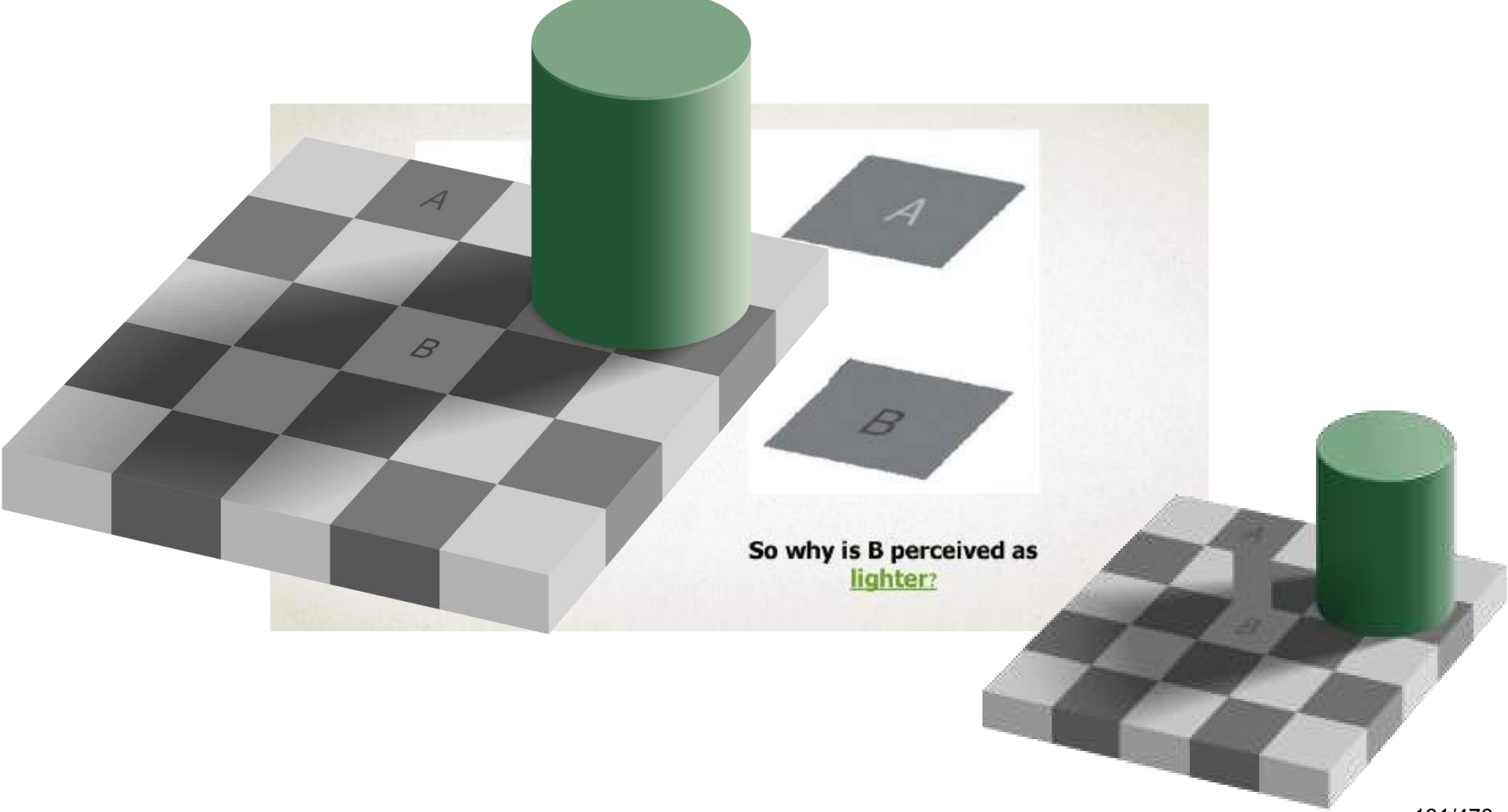
Receptive fields are smaller in the fovea (center of vision) than away from the fovea.





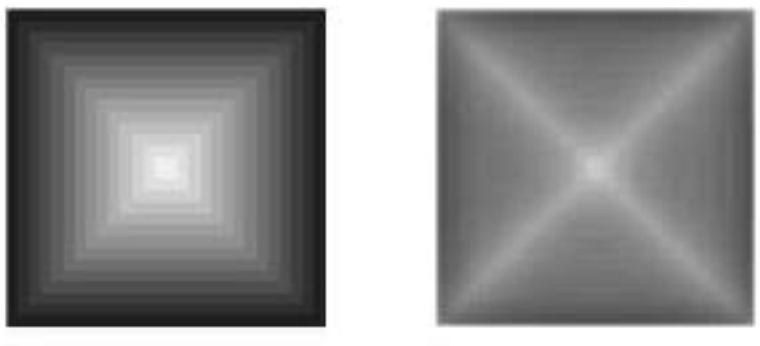
a

Variants on the Koffka ring.
(a) The ring appears almost uniform.
(b) When split, the two half-rings appear distinctly different.
(c) When shifted, the two half-rings appear quite different.

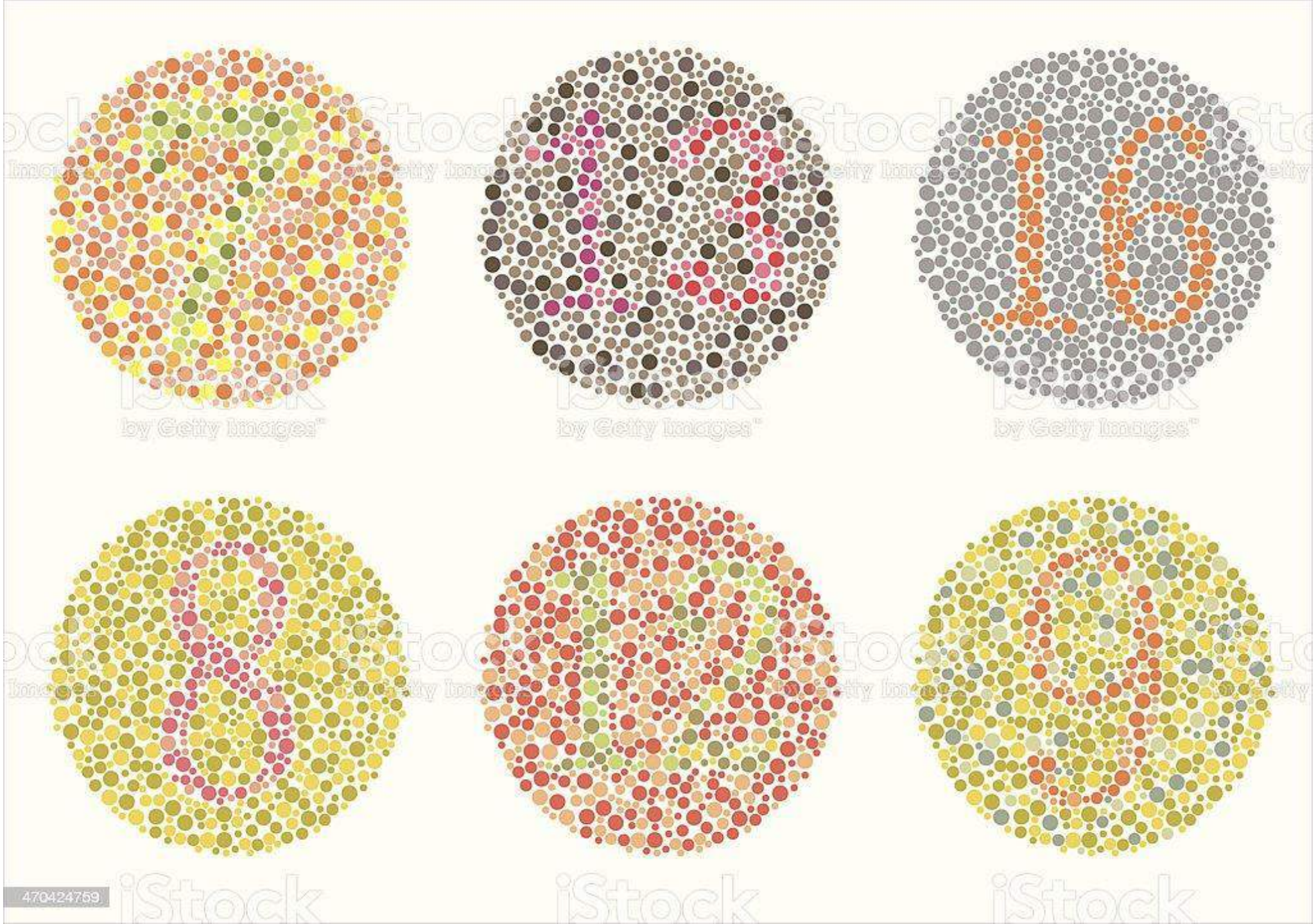

A
B
A
B
So why is B perceived as
lighter?

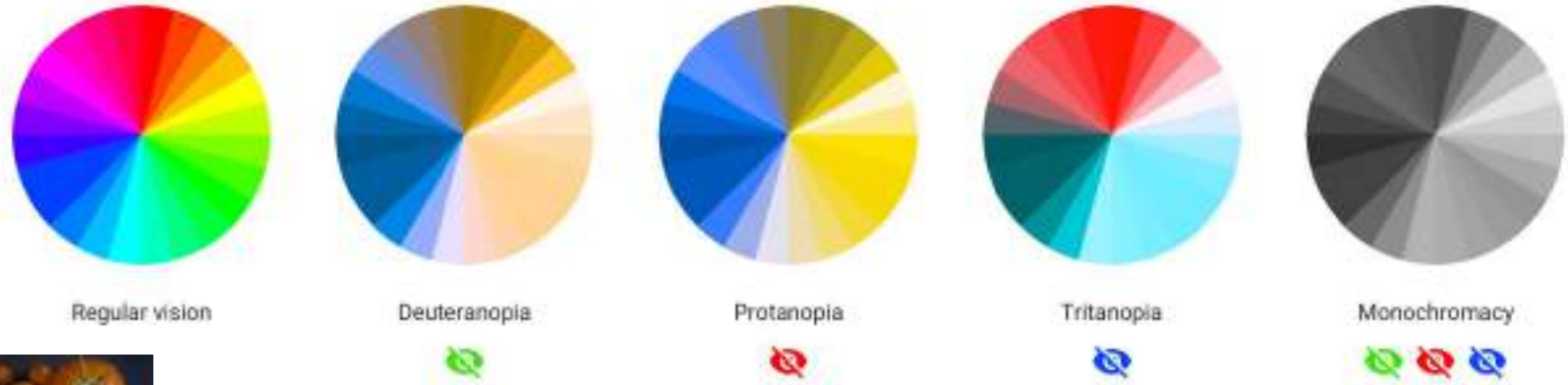
Simultaneous contrast

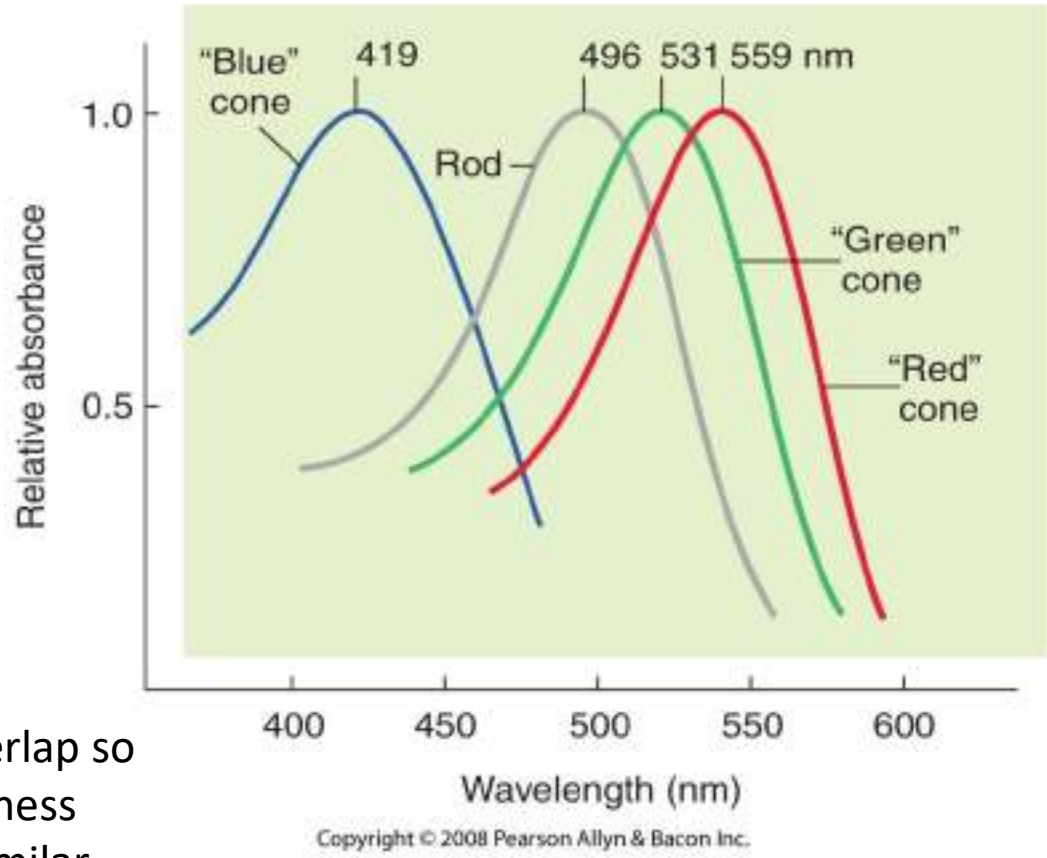
Center-on, surround-inhibit



Band pass filter


470424759

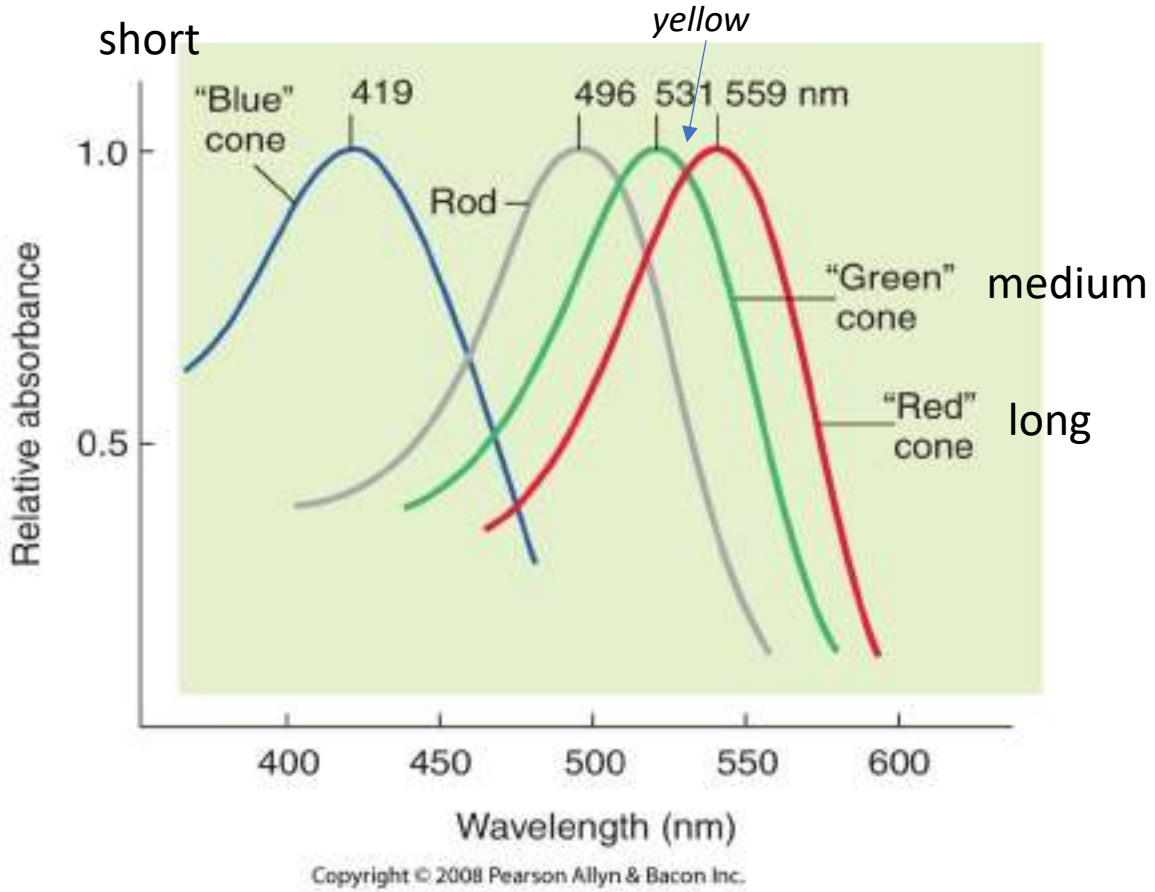


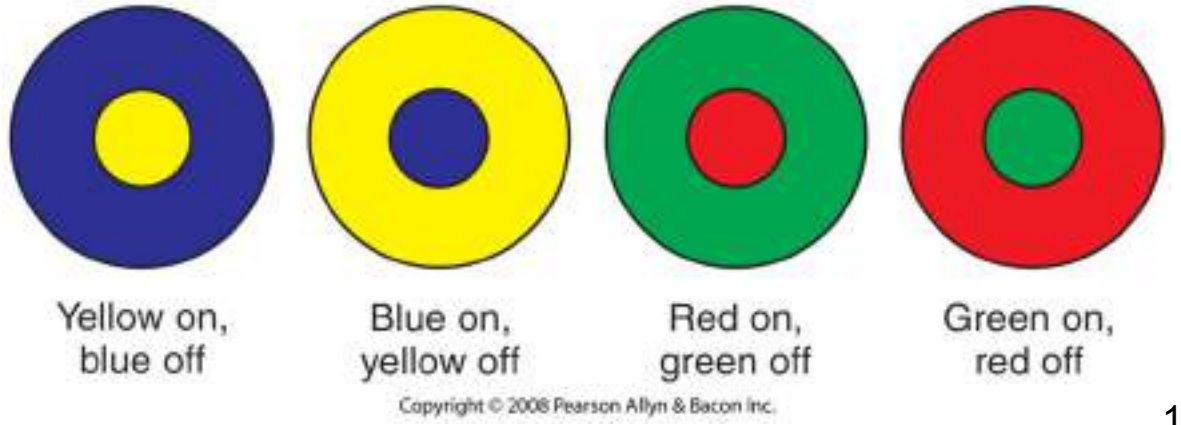


Red and green wavelengths overlap so their color blindness effects can be similar

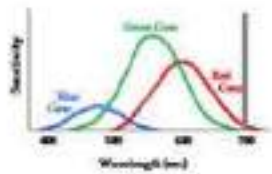
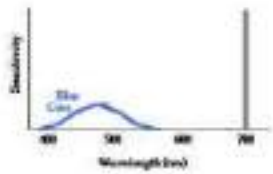
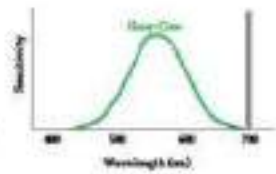
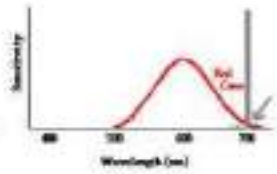
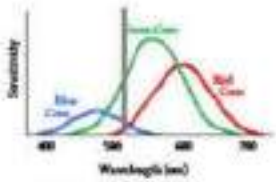
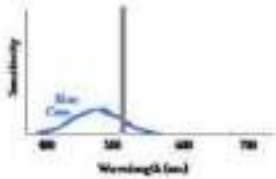
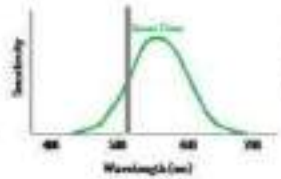
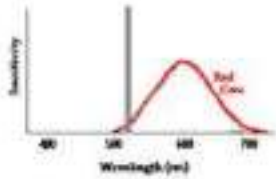
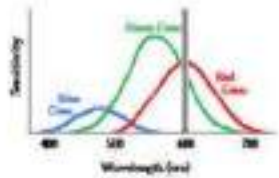
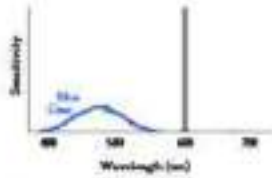
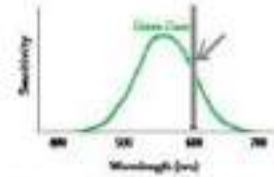
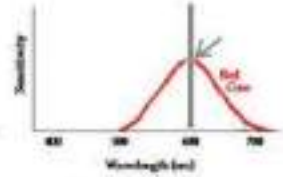
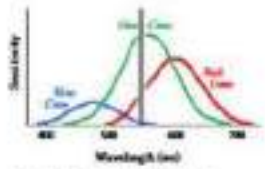
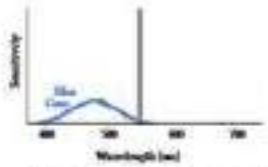
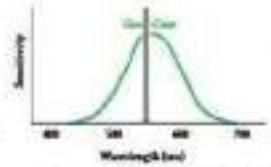
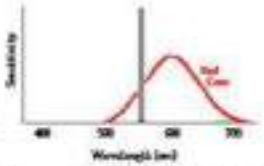
Color Coding

Retinal ganglion cells:
Opponent process coding

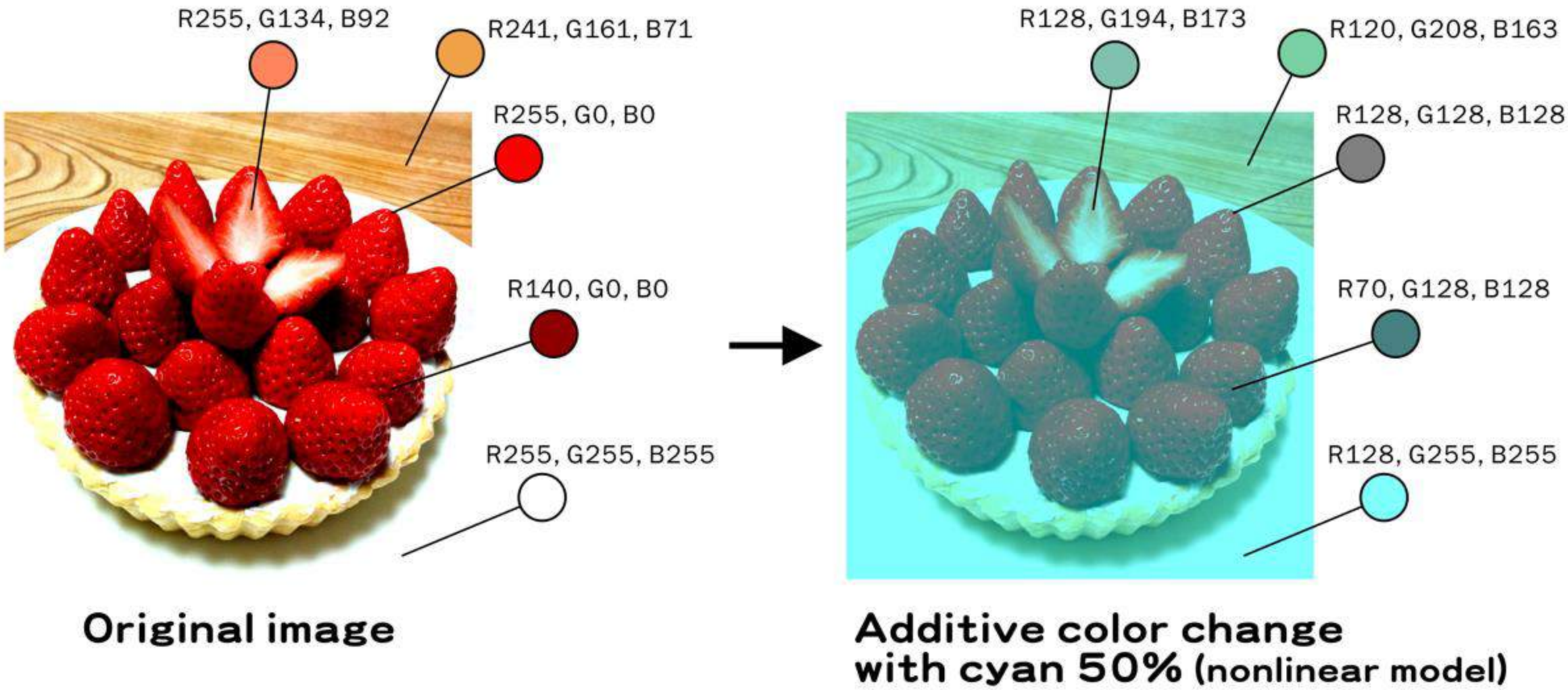




Let's do some color perception examples using the graph:

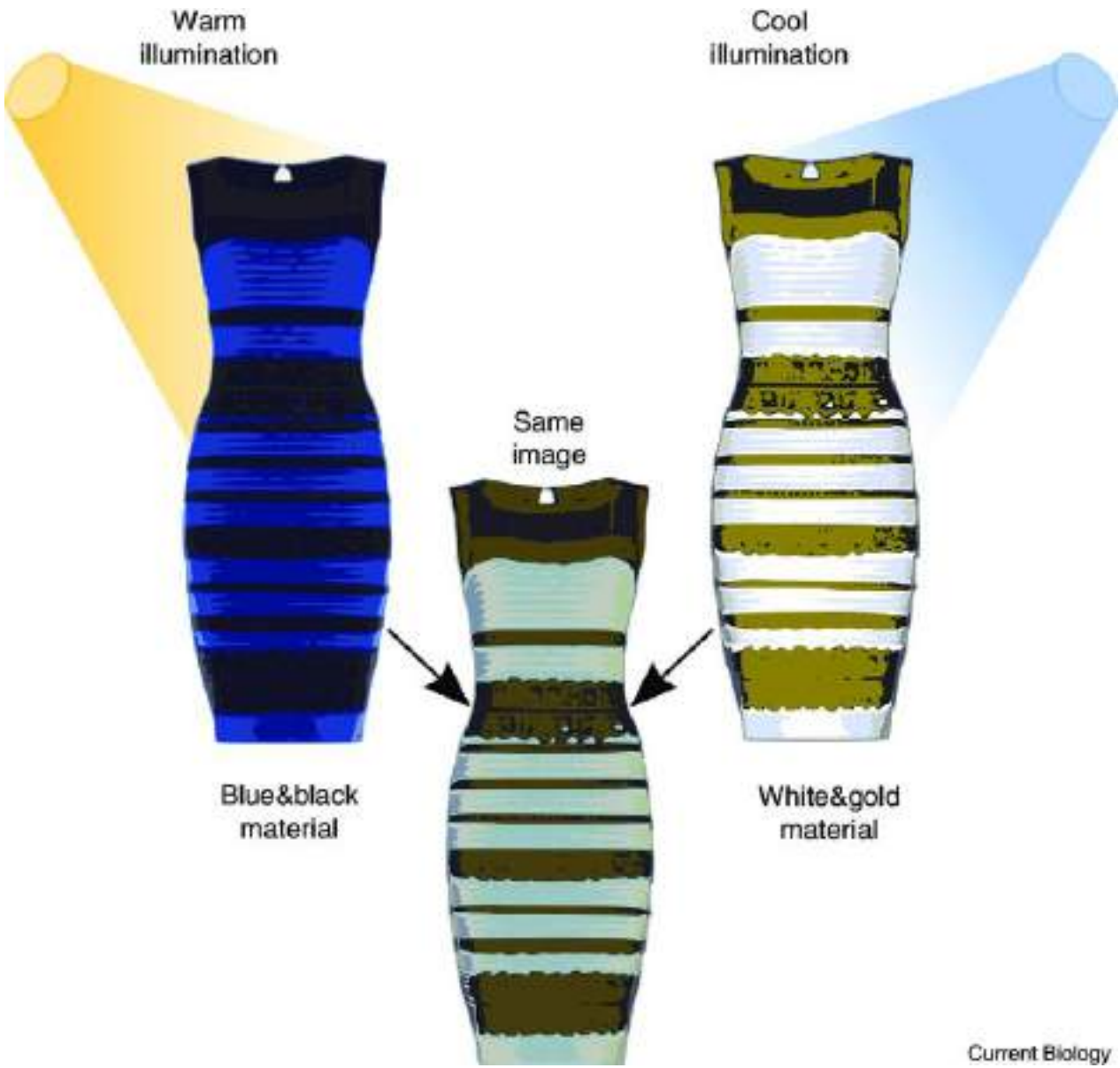
Wavelength of light shining at your eye	What the Blue Cone detects	What the Green Cone detects	What the Red Cone detects	What color the brain perceives
 A 700 nm light is shining (gray bar)	 The Blue Cone doesn't see it	 The Green Cone doesn't see it	 The Red Cone has a small signal	Only the Red Cone detected anything, so it must be **Red**
 A light of 510 nm (gray bar)	 Blue Cone detects some signal	 Green Cone has medium signal	 Red cone has a tiny signal	Blue and Red Cones detected a little, and Green detected a medium amount, so the color must be **Green**
 A 600 nm light (gray bar)	 The Blue Cone can't see it	 The Green Cone has a medium signal	 The Red Cone has a big signal	It's a lot of Red Cone, a medium amount of Green Cone, and no Blue Cone, so it must be **Orange**
 A 550 nm light (gray bar)	 Blue Cone detects a small signal	 Green Cone detects a large signal	 Red Cone detects a medium signal	It's a lot of Green Cone, a little bit Blue, and a medium amount of Red, so it must be **Yellow**

Yellowish green



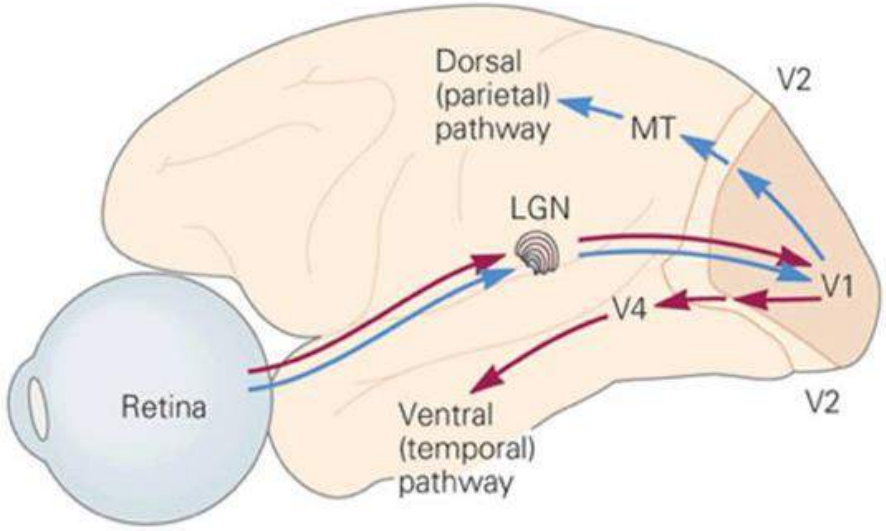
Original image

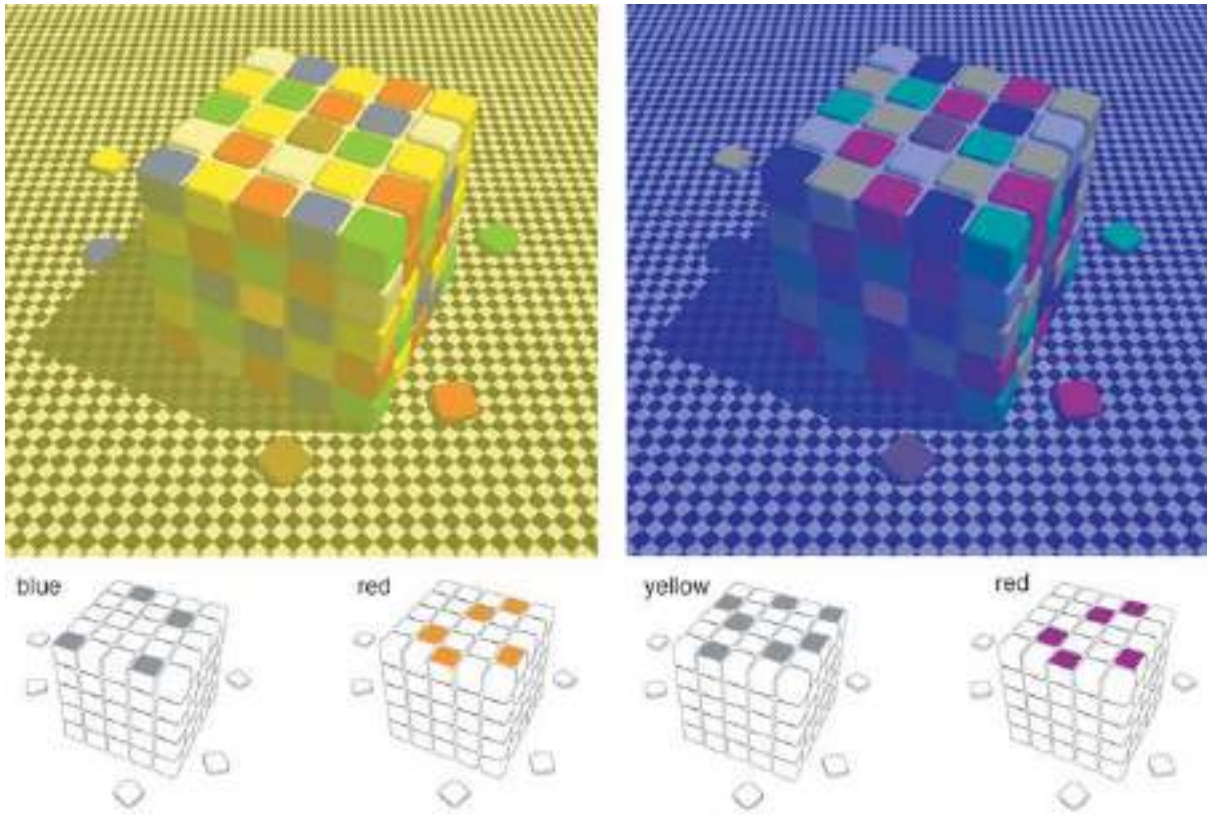
Additive color change with cyan 50% (nonlinear model)


Warm
illumination
Cool
illumination
Same
image
Blue&black
material
White&gold
material
Current Biology


NBC

Color constancy

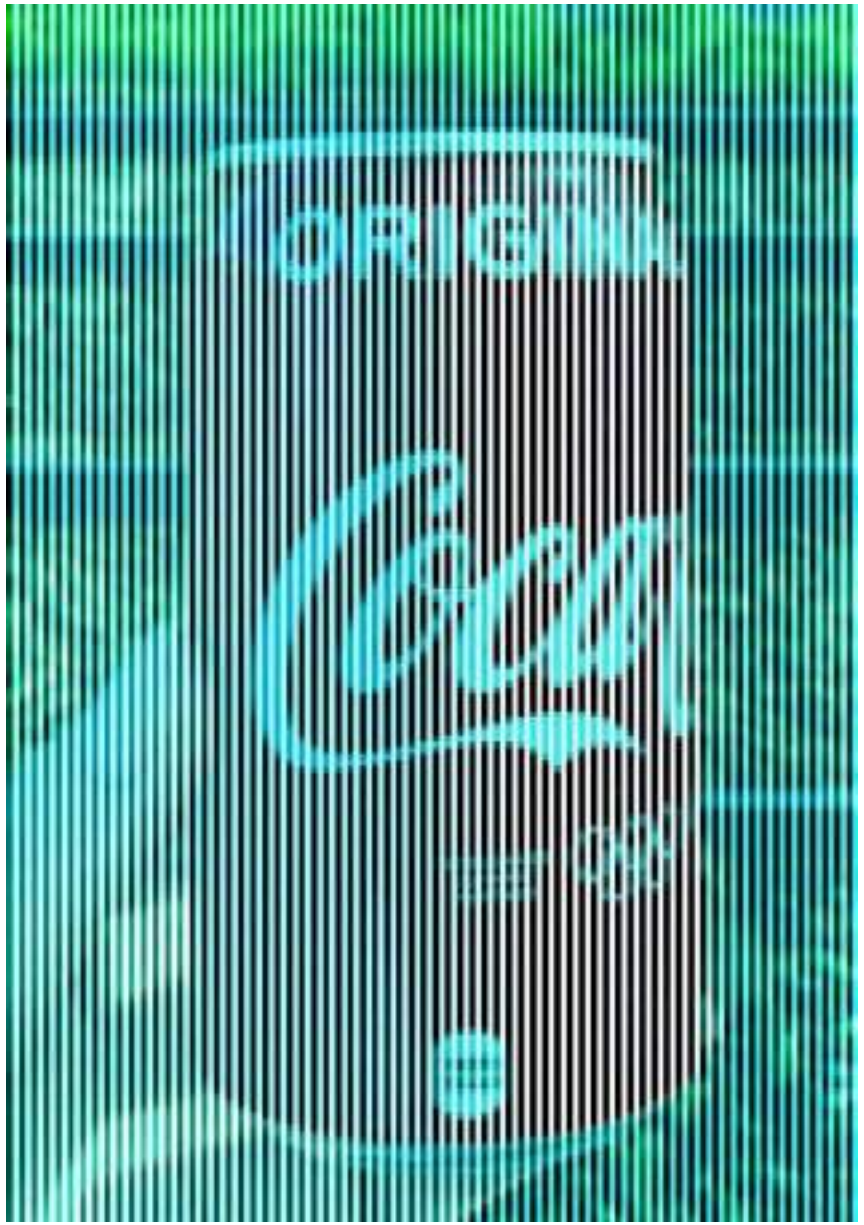


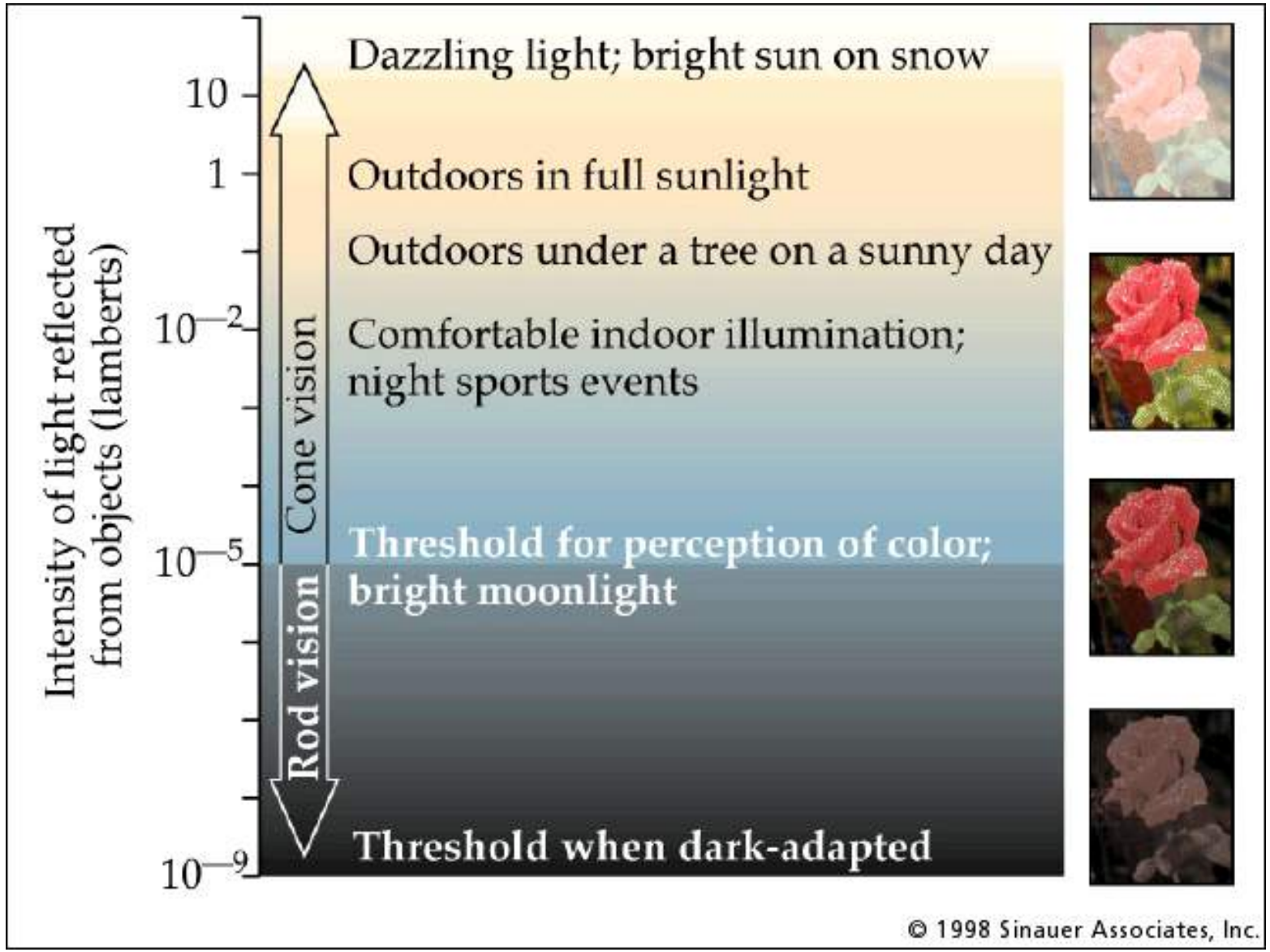


The relative constant appearance of the colors of objects viewed under varying lighting conditions

- Area V4 → perception of color and color constancy.
- Lesion in V4 area → Achromatopsia i.e. vision without color

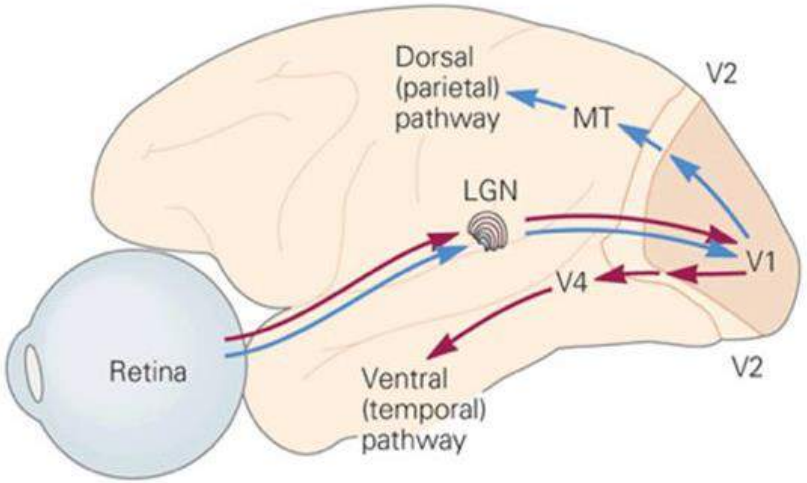

ORIGINAL


ORIGINAL

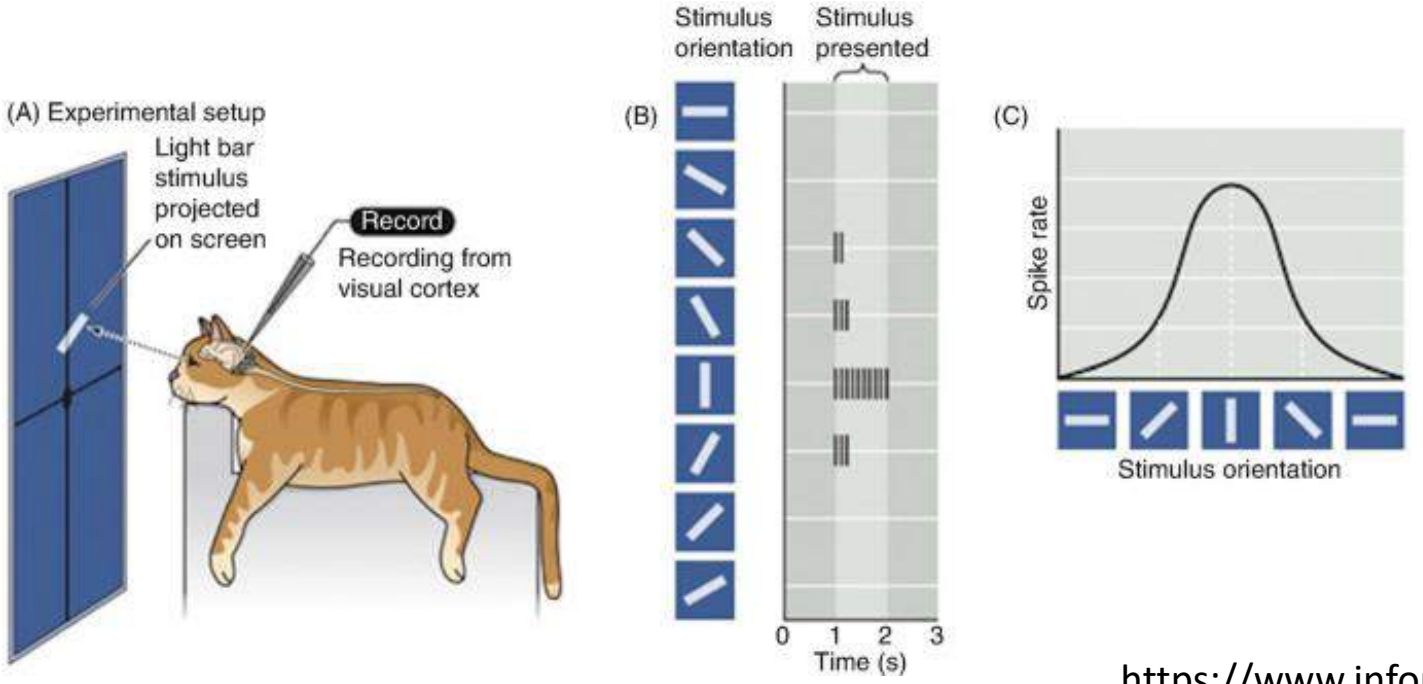

Intensity of light reflected from objects (lamberts)
10
1
10⁻²
10⁻⁵
10⁻⁹
Cone vision
Rod vision
Dazzling light; bright sun on snow
Outdoors in full sunlight
Outdoors under a tree on a sunny day
Comfortable indoor illumination; night sports events
Threshold for perception of color; bright moonlight
Threshold when dark-adapted
© 1998 Sinauer Associates, Inc.

Class 5
Vision

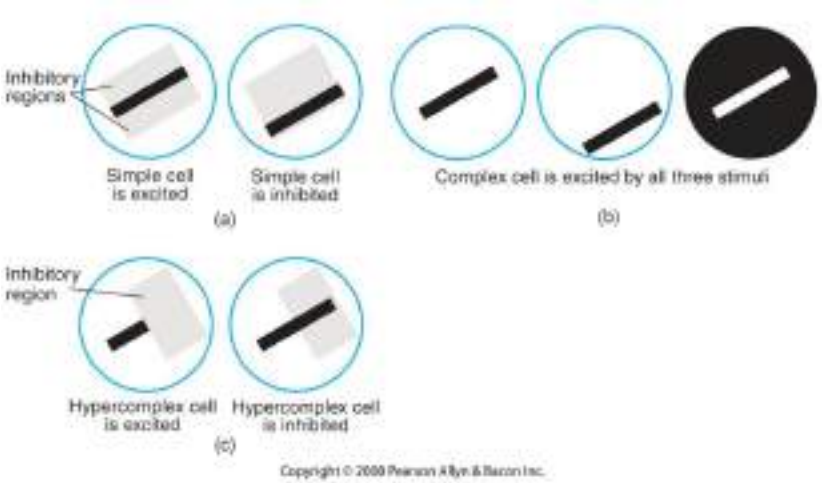
Orientation and movement (Area V1)



Hubel and Wiesel, 1959

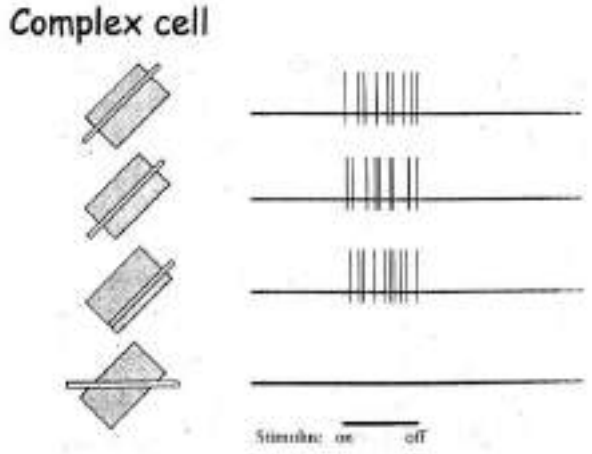


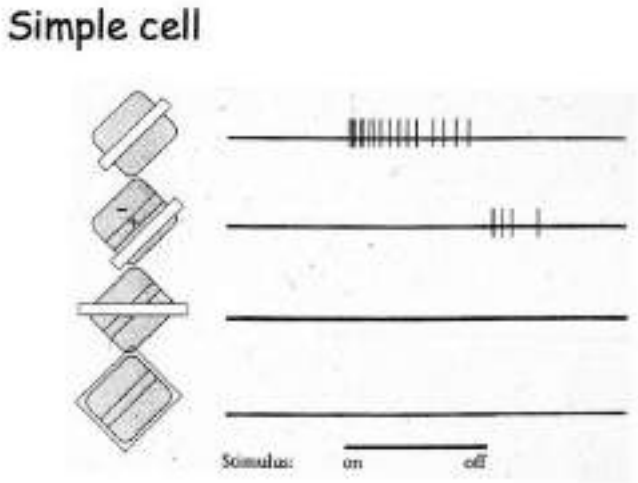
https://www.informit.com/articles/article.aspx?p=1431818

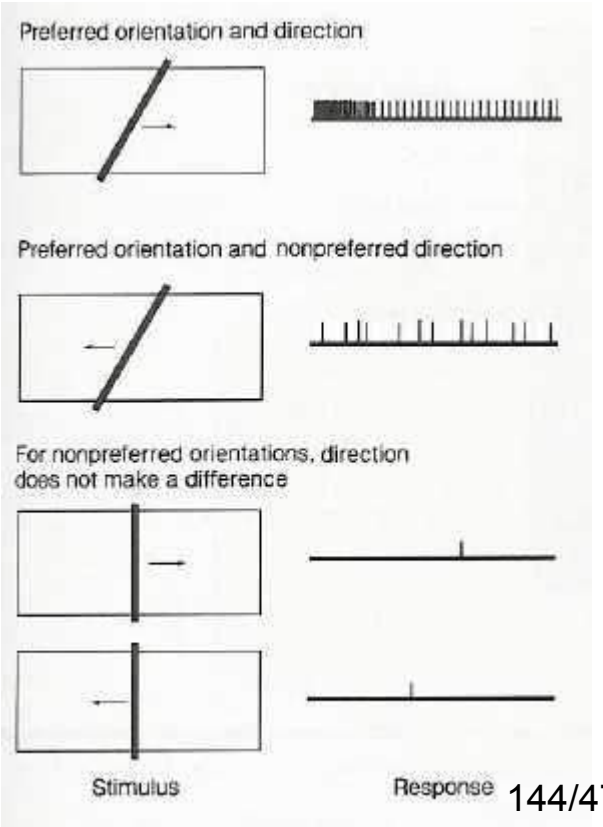


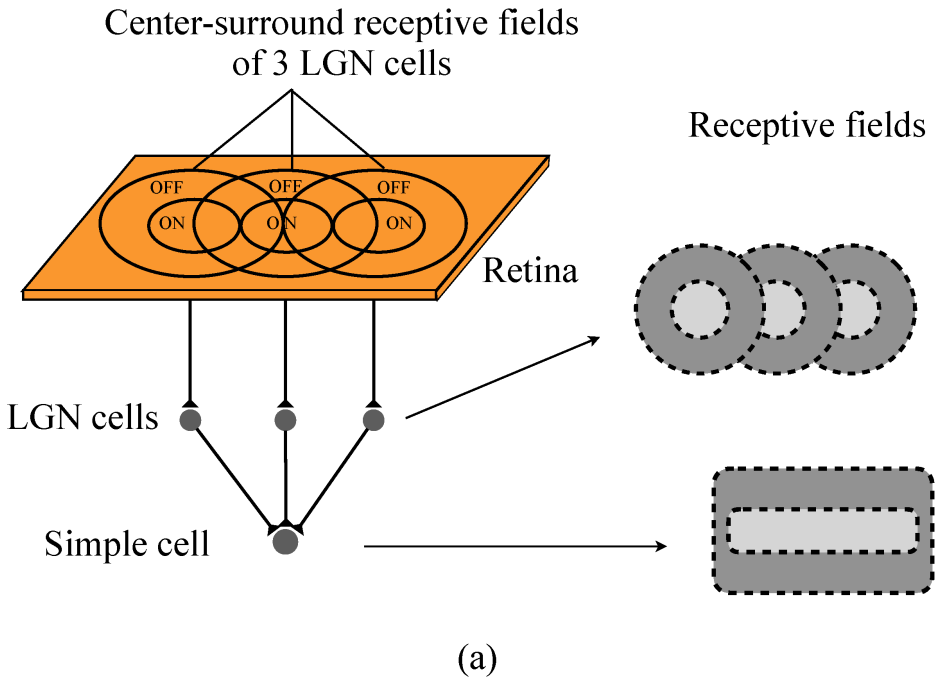
- **Simple cell**: sensitive to particular orientation of light
- **Complex cell**: sensitive to orientation and motion of light in a particular direction, esp. perpendicular to the orientation

  (movement detectors)
- **Hypercomplex cell**: sensitive to orientation and end of line

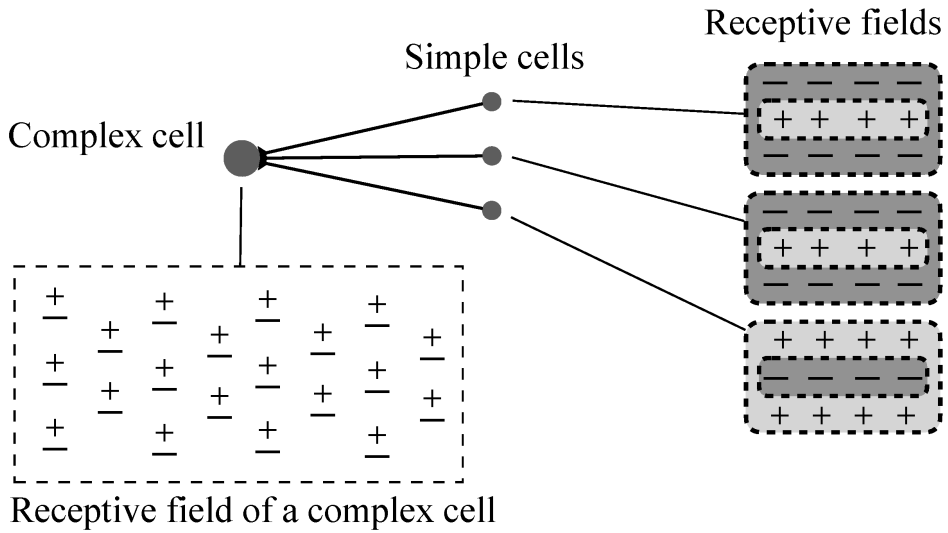






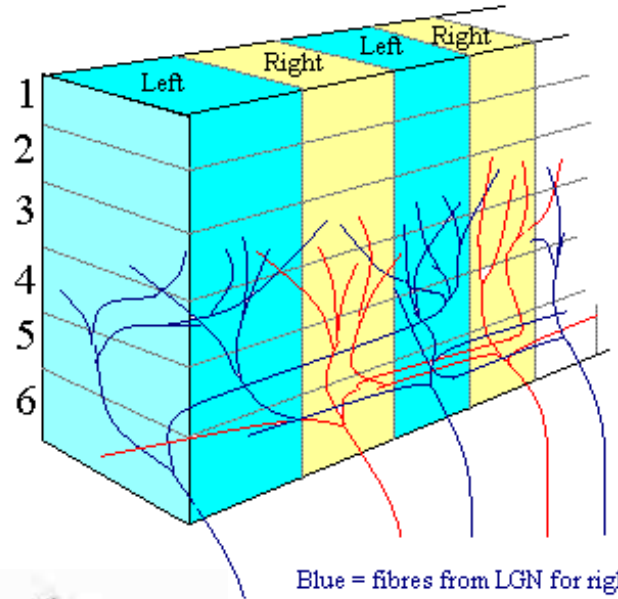


(a)



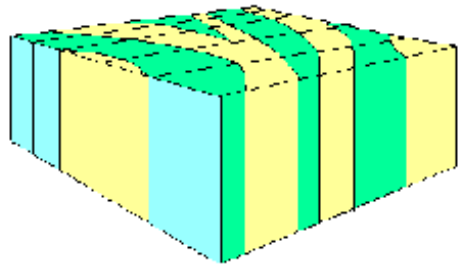
(b)

Cortical Columns

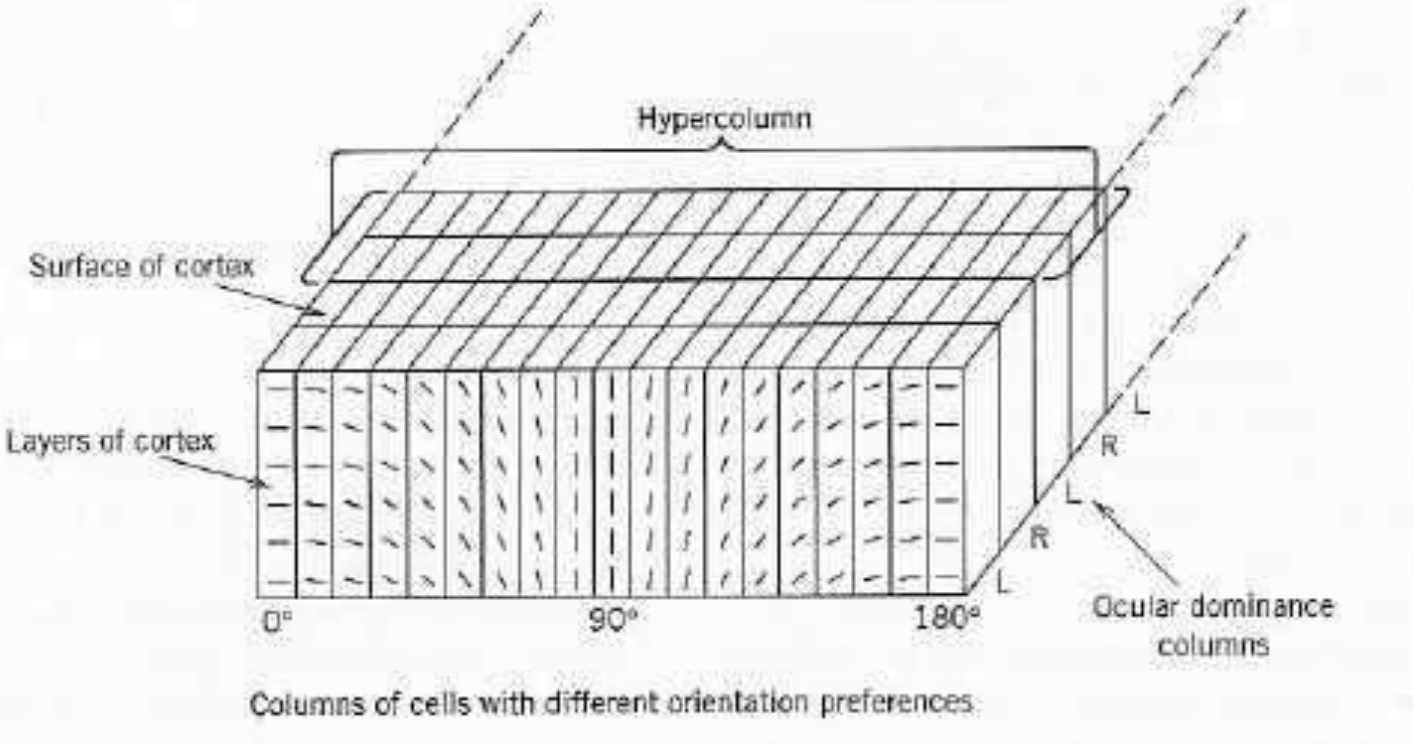


Blue = fibres from LGN for right eye

Red = fibres from LGN for left eye

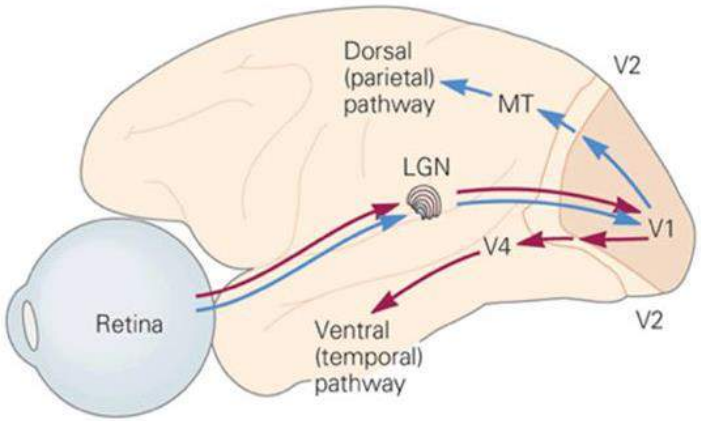


The columns are rather disorderly on the cortex and form a pattern like a finger print.



Columns of cells with different orientation preferences

Spatial frequency



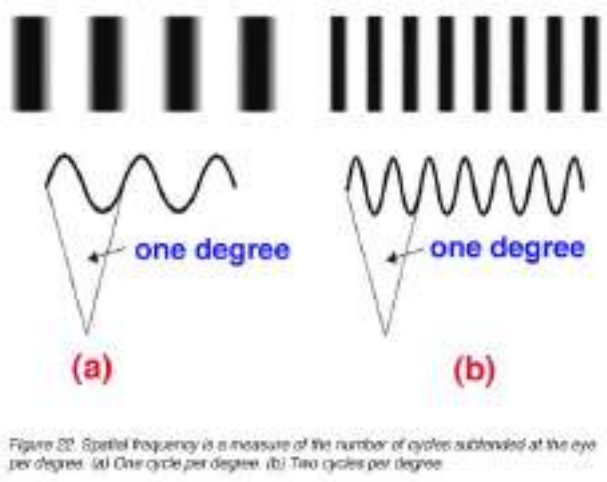


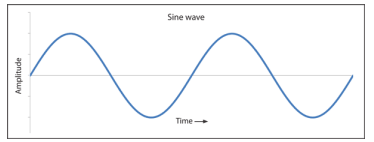
Figure 22. Spatial frequency is a measure of the number of cycles subtended at the eye per degree. (a) One cycle per degree. (b) Two cycles per degree.

Spatial frequency processing occurs in V1 (primary visual cortex)

Note: physical distance in visual physics is measured in units of visual angle. Cycles per degree of visual angle constitute spatial frequency

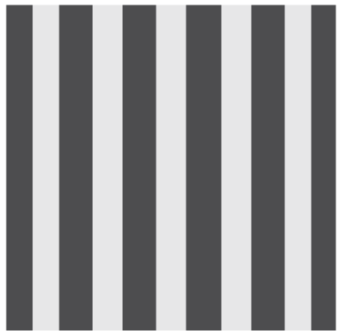
Object is too close to eyes

Sine wave grating



Object is far from eyes

Square wave grating



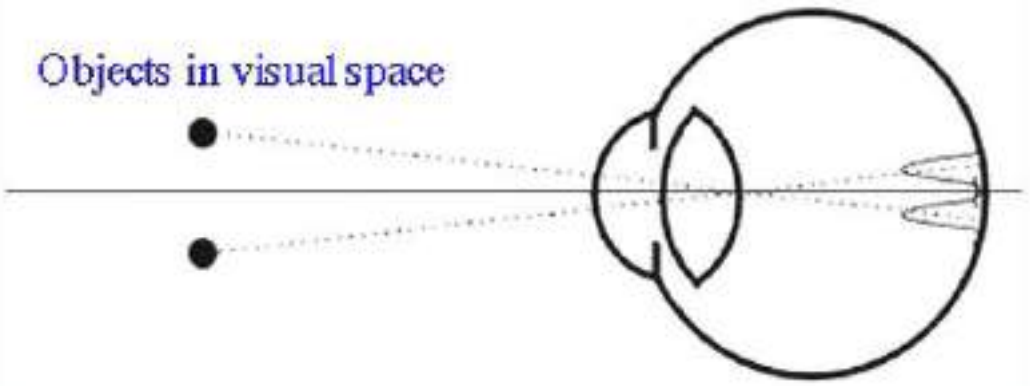
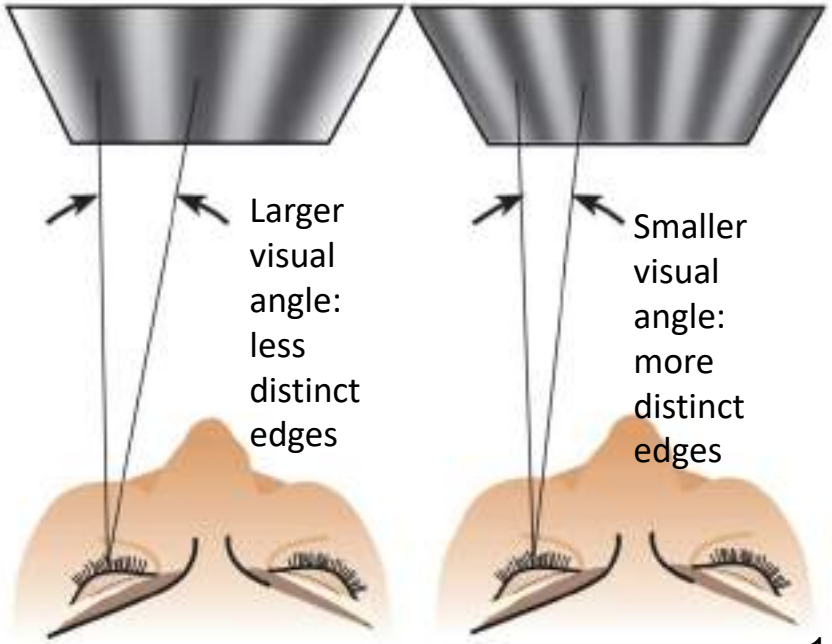


Figure 10. Two point sources and their point spread function at the back of the eye.



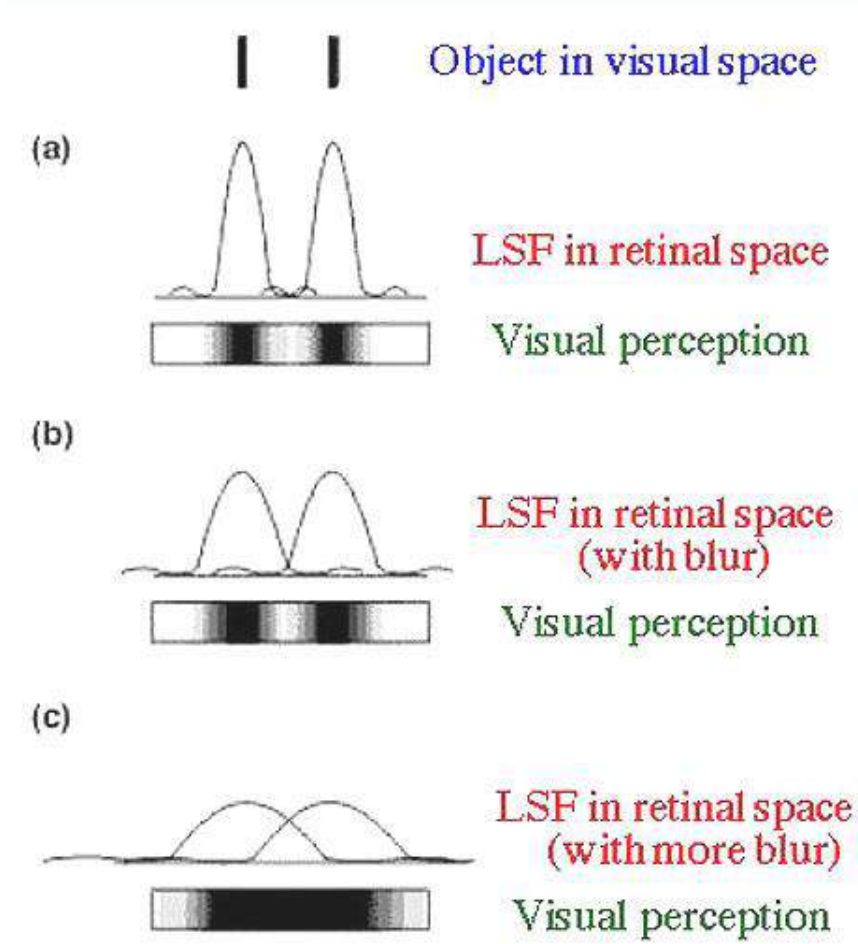


Figure 16. Line spread function (LSF) of two lines with varying amounts of blur. With increasing blur, the discrimination of the two lines is lost.

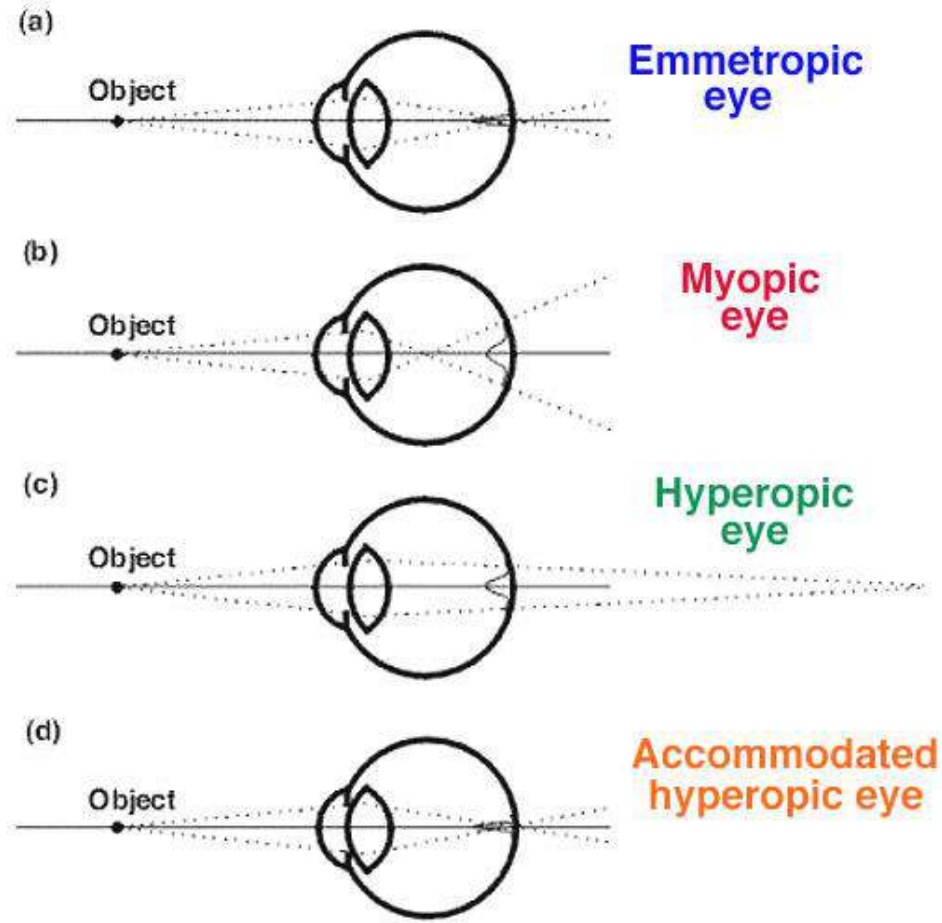
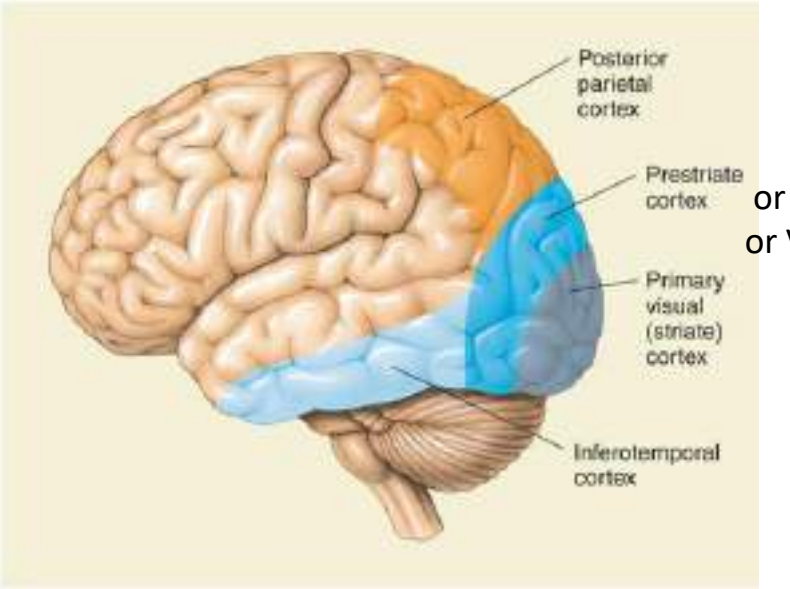


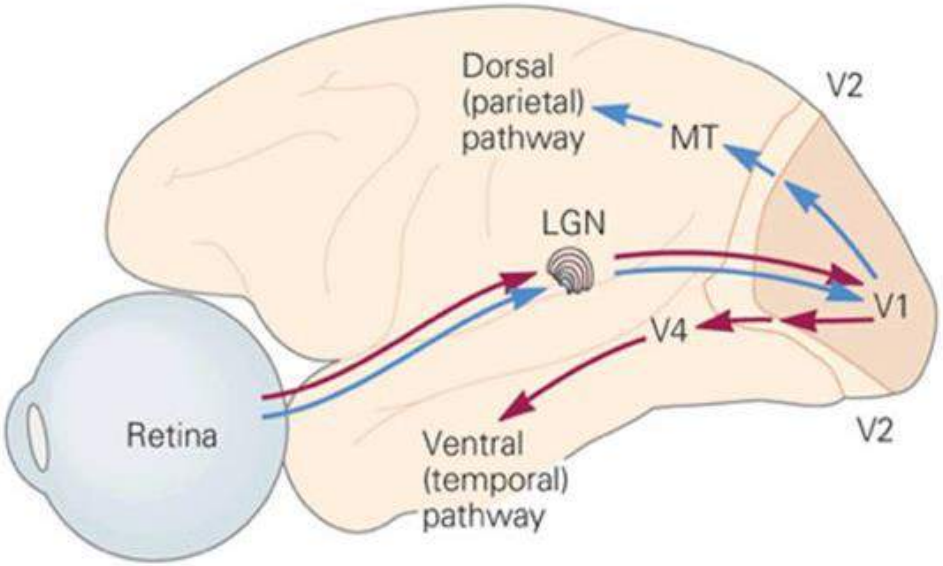
Figure 17. Point spread function at the back of the eye with different refractive errors.

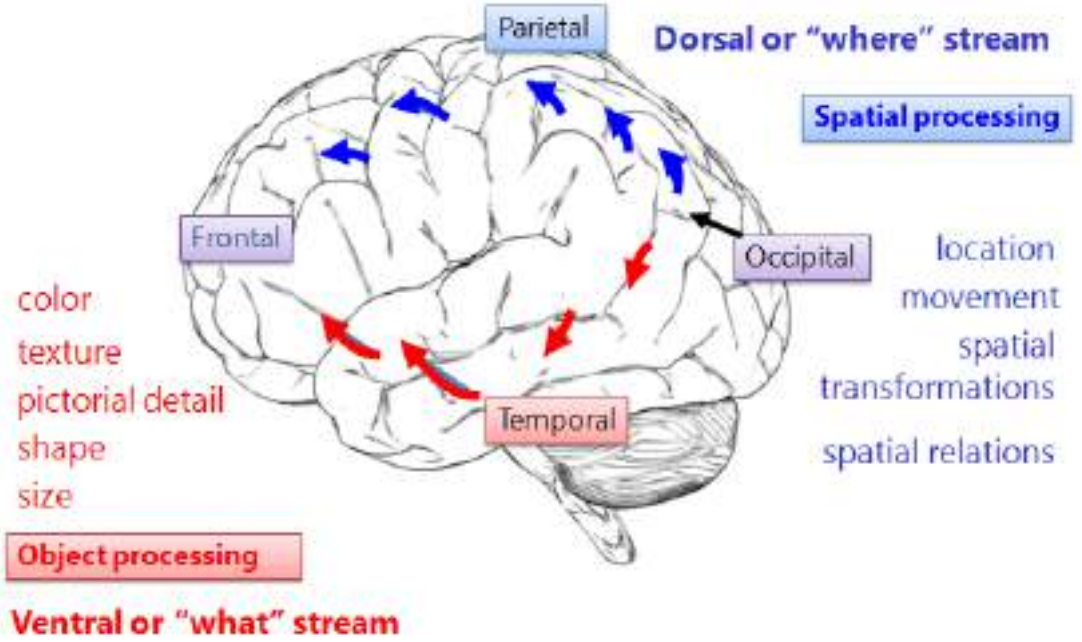
https://webvision.med.utah.edu/book/part-viii-psychophysics-of-vision/visual-acuity/

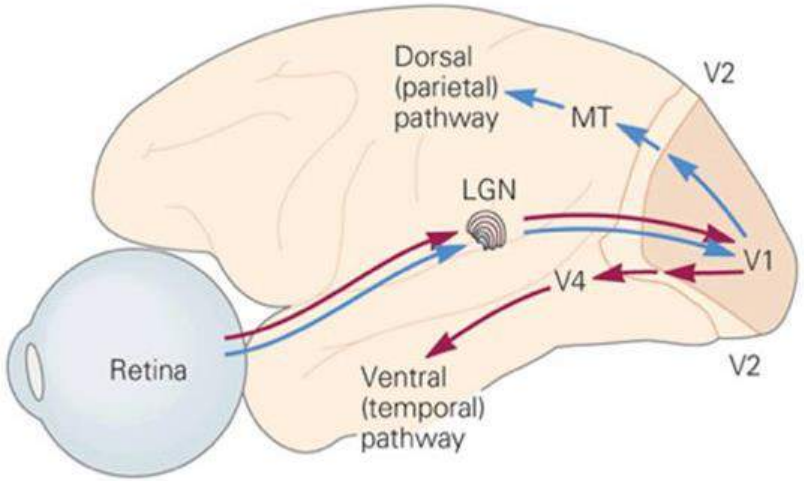
Visual pathway



or Extrastriate cortex
or Visual Association cortex







Dorsal Stream

middle temporal (MT)

medial superior temporal (MST)

V2
(thick stripes)
- Speed
- Direction
- Spatial frequency
- Temporal frequency

MT
- Speed
- Direction
- Spatial frequency
- Temporal frequency
- Local/Global motion

MST
- Expansions
- Contractions
- Rotations
- Translations
- Spirals
- Optic Flow

Parietal Regions
- Heading
- Optic flow
- Self motion
- Multi-modal integration

Primary Visual (Striate) Cortex

V1
- Speed
- Direction
- Spatial frequency
- Temporal frequency
- Orientation
- Color

Extrastriate cortex
(Second level of visual processing)

(Inferior temporal Cortex)

V2
(thin stripes, interstripes)
-Edges
-Illusory edges
- Border ownership
- Color

V4
- Angles
- Curvature
- Perceived color
- Kinetic contours
- Motion

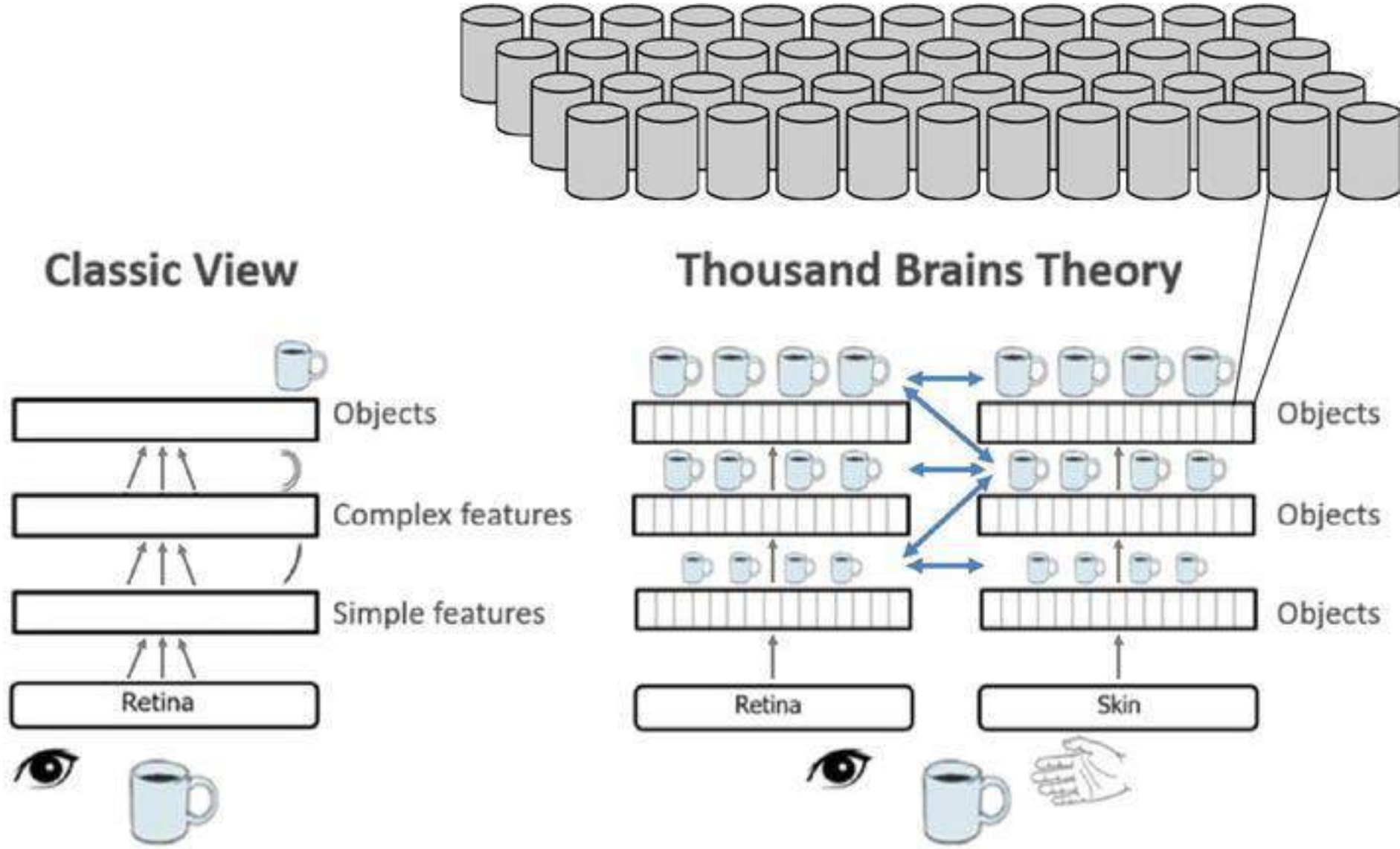
TEO/PIT
- Simple shapes

TE/AIT
- Complex shapes/ body parts
- Object recognition
- Object invariance

Ventral Stream

Visual Processing does not happen in isolation

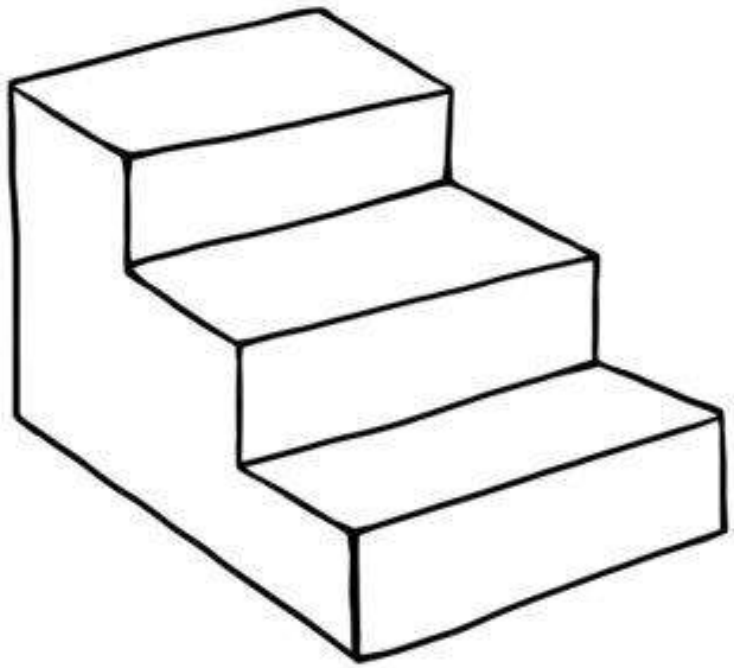
We still need neuroscientific data to confirm this theory



https://www.intechopen.com/chapters/86375

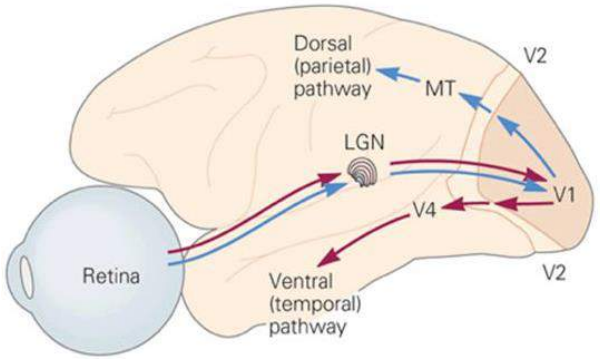
How do we resolve this conflict and see a stable perception?

How do we perceive 2D as 3D in our brain?




ERICH LESSING/ART RESOURCE

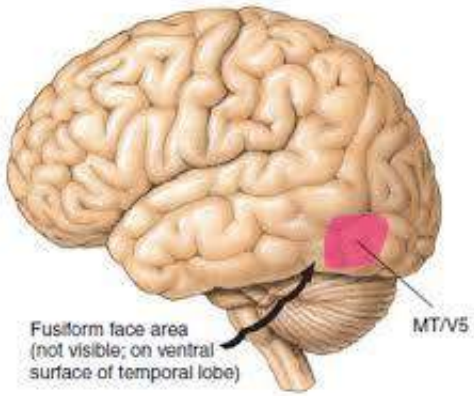
Perception of Form

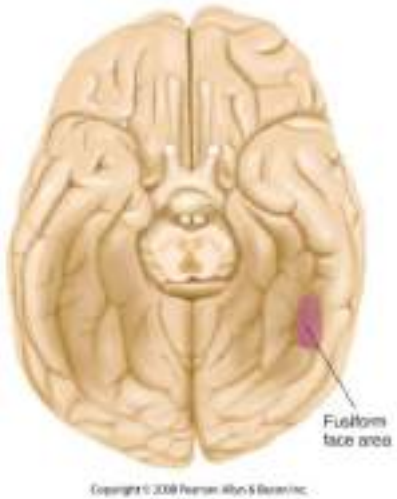


- ***Agnosia –*** *"failure to know"*

- ***Visual agnosia (damage to the ventral stream)***
  - Visual Agnosia video

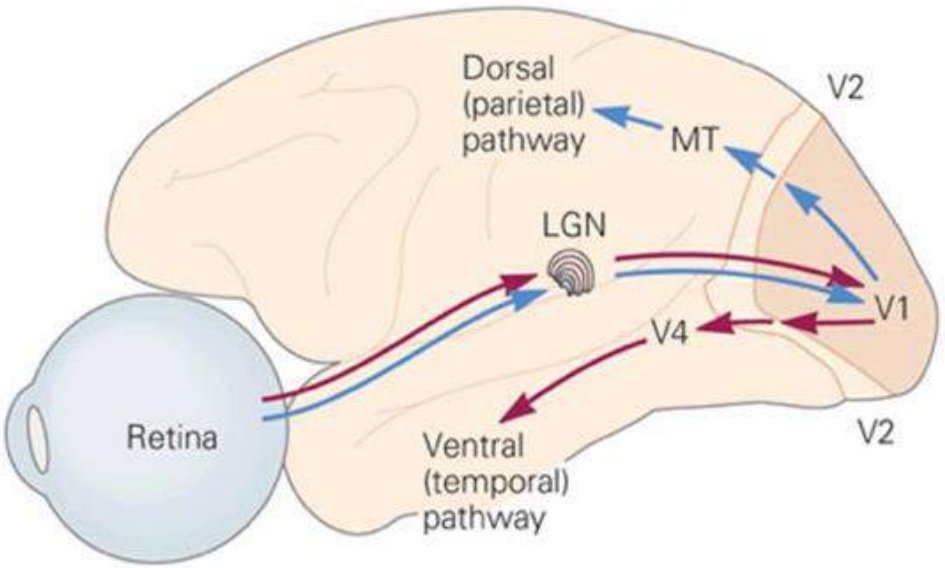
- ***Prosopagnosia (damage to fusiform area (FFA))***
  - Prosopagnosia video





Visual agnosia or prosopagnosia ?

Visual Agnosia

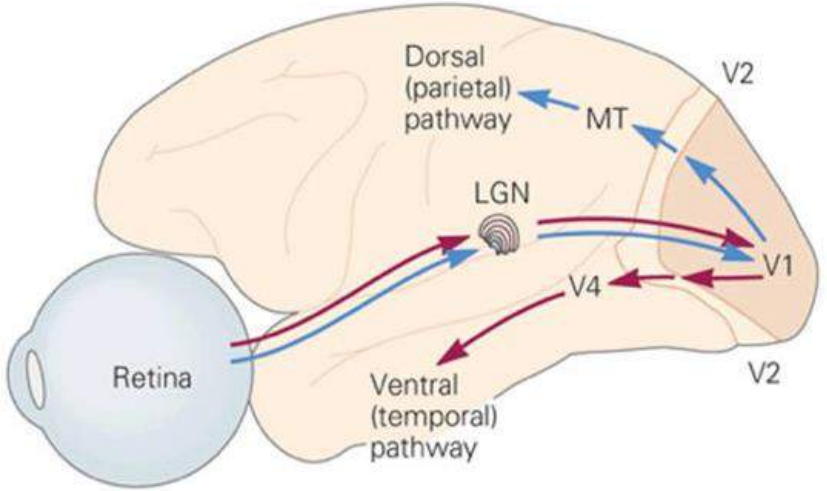


patient S. B., a 30-year-old man whose ventral stream was damaged extensively bilaterally by an infection when he was 3 years old. As a result, he was unable to recognize objects, faces, textures, or colors. However, he could perceive movement and could even catch a ball that was thrown to him. Furthermore, he could recognize other people's arm and hand movements that mimed common activities such as cutting something with a knife or brushing one's teeth, and he could recognize people he knew by their gait.

Blindsight

Perception without awareness

Damage to?



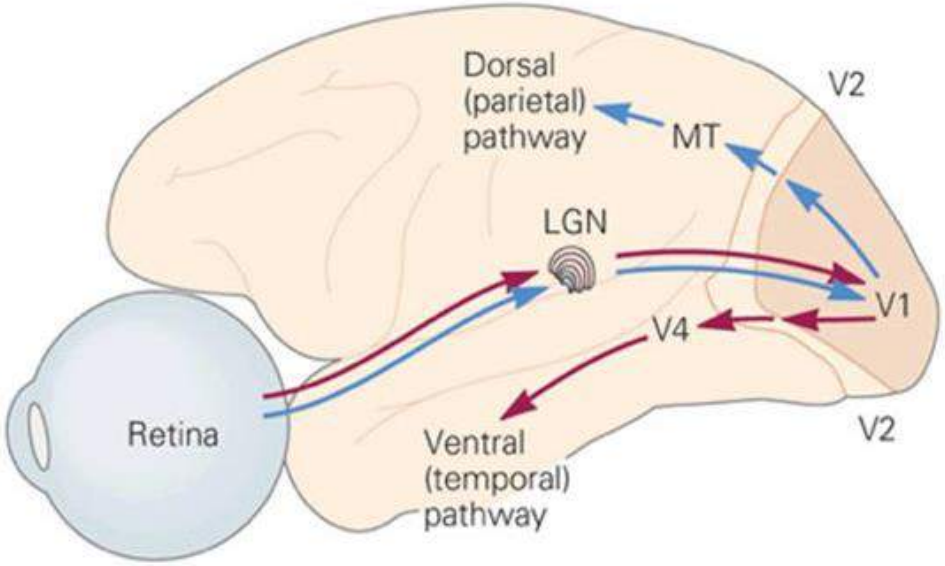
[Blindsight video]

The Case of D.B., the Man Confused by His Own Blindsight

D.B. had no awareness of "seeing" in his blind left field. Despite this apparent left-field blindness, he could accurately reach for visual stimuli in his left field and could accurately differentiate between a horizontal or diagonal line in his left field if forced to "guess." When he was questioned about his vision in his left field, his most usual response was that he saw nothing. When he was shown a video of his accurate left-field performance through his good, right field, he was astonished and insisted he was just guessing.

Perception of Movement

- Area V5 (Medial temporal (MT)) – responds to movement
- Damage to V5 - ***Akinetopsia*** – inability to perceive movement
- Form from motion: ability to perceive 3D forms
  - people with visual agnosia for objects can recognize actions (motion recognition) performed by those objects but cannot recognize the objects



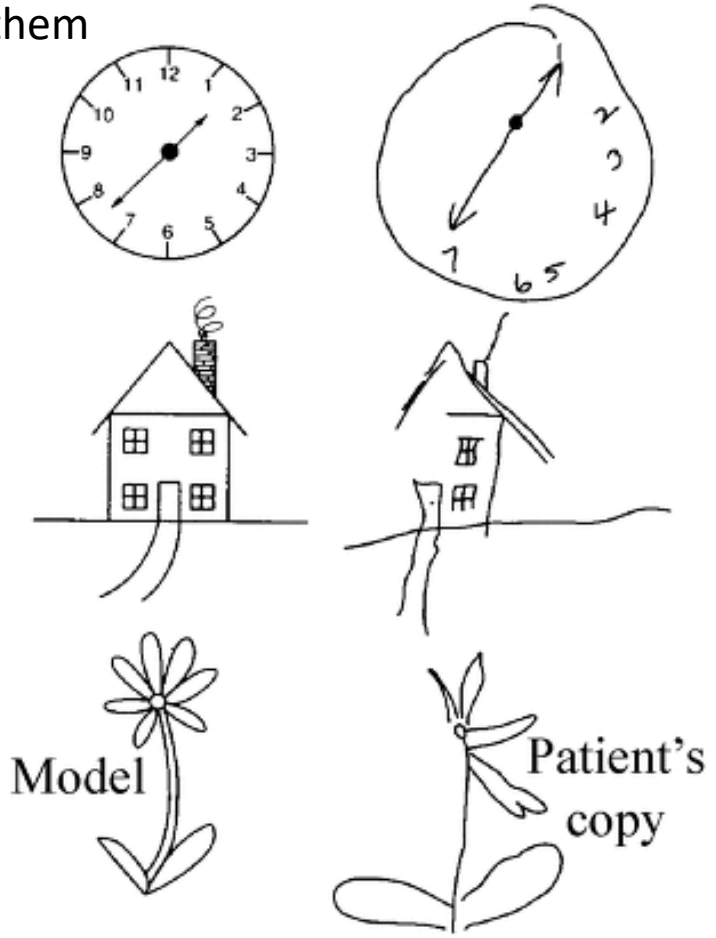
Patient L. M. had an almost total loss of movement perception. She was unable to cross a street without traffic lights because she could not judge the speed at which cars were moving. Although she could perceive movements, she found moving objects very unpleasant to look at. For example, while talking with another person, she avoided looking at the person's mouth because she found its movements very disturbing. When the investigators asked her to try to detect movements of a visual target in the laboratory, she said, "First the target is completely at rest. Then it suddenly jumps upwards and downwards" (Zihl et al., 1991, p. 22–44). She was able to see that the target was constantly changing its position, but she was unaware of any sensation of movement.

You can perceive objects but cannot act on them or interact with them

Hemispatial neglect

P.S. was presented simultaneously with two line drawings of a house, in one of which the left side was on fire. She judged that the drawings were identical; yet when asked to select which house she would prefer to live in, she reliably chose the house that was not burning.

One sided world



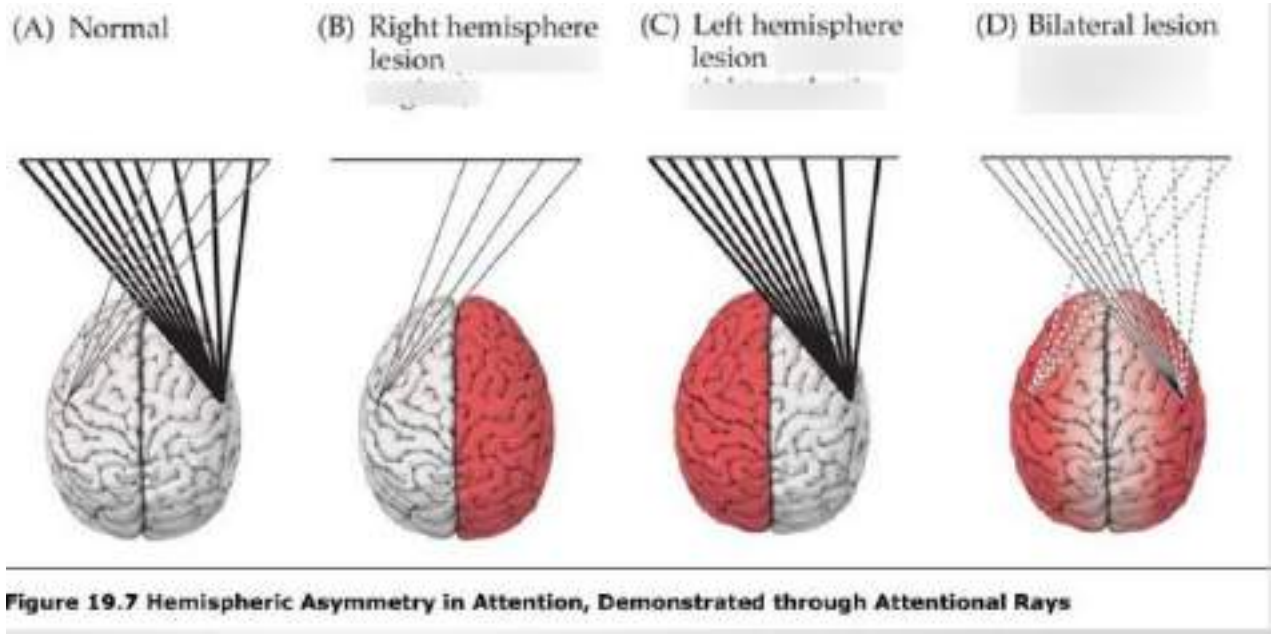
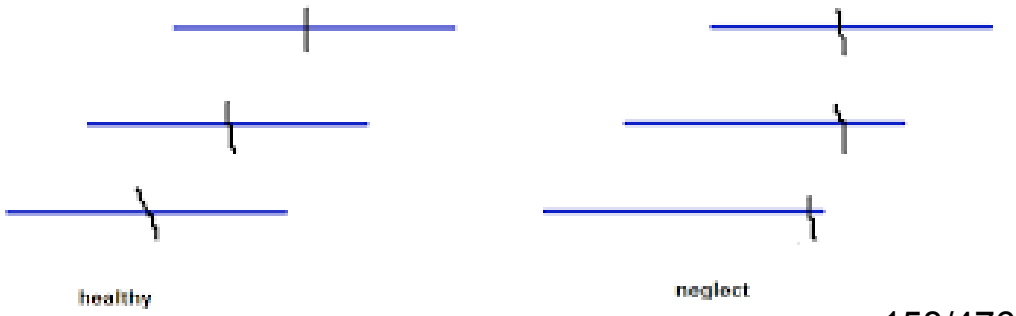
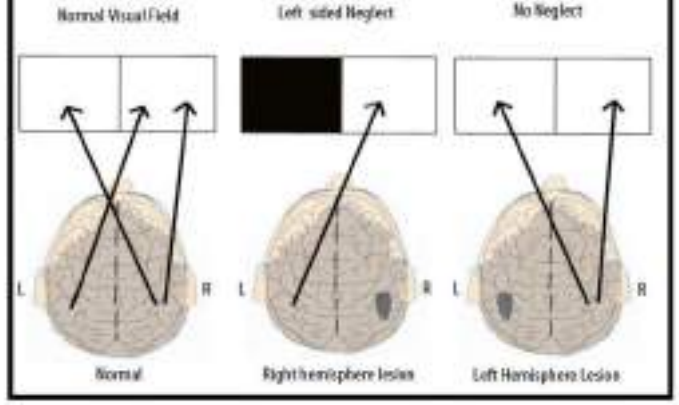
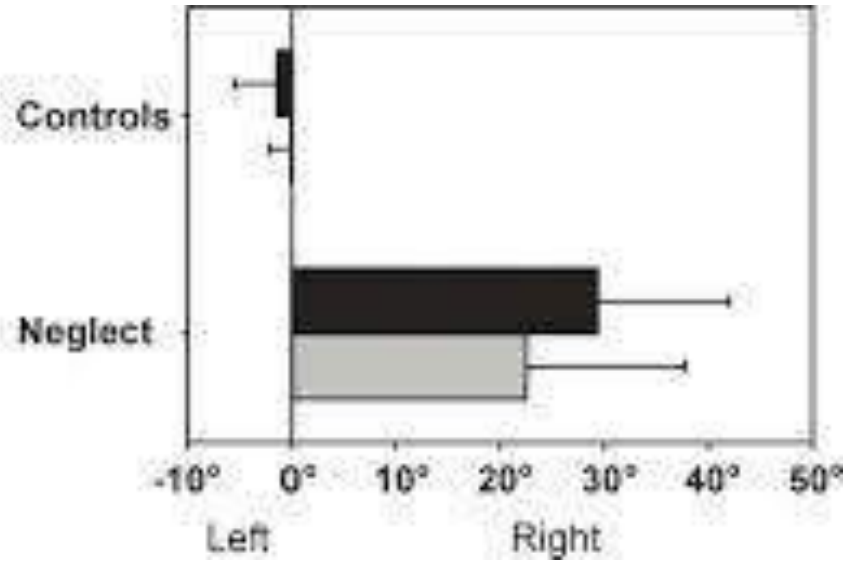


Figure 19.7 Hemispheric Asymmetry in Attention, Demonstrated through Attentional Rays



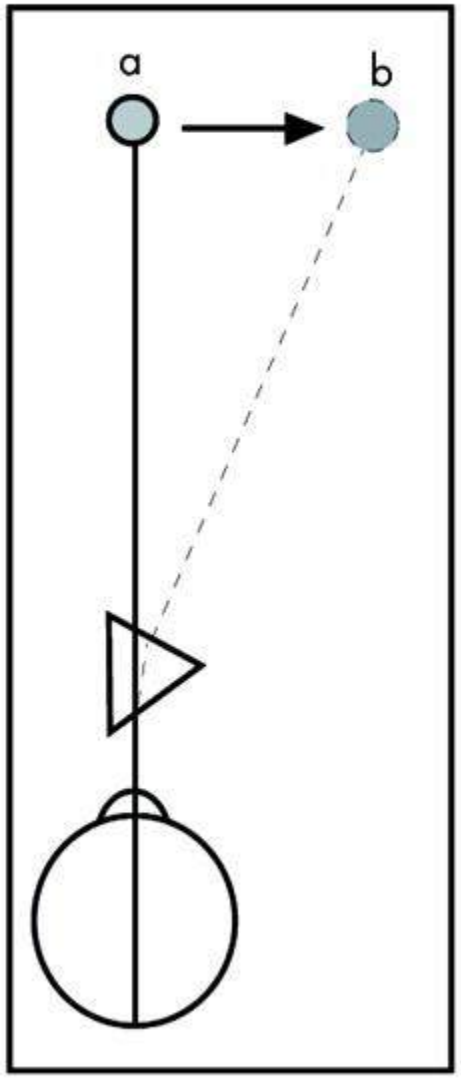


Right Left Right Left



The most prominent deficit in patients with spatial neglect is a bias of their active behaviour, i. e. a deviation of exploratory movements towards the right. When searching for targets, copying, or reading, the patients direct their eye and hand movements towards the ipsilesional side, leading to neglect of the contralesional side. The present study investigated whether spatial neglect is predominantly linked with such active behaviour or if it is obvious also without any explicit requirements, namely in the patients' spontaneous eye and head position. To address this issue we investigated the patients' spontaneous resting position while "doing nothing", i. e. just sitting and waiting for an experiment to start. Using magnetic search coil technique, we recorded spontaneous eye–in–head and head–on–trunk orientation in that waiting period in 24 patients with and without spatial neglect. In contrast to controls, neglect patients showed a marked deviation of spontaneous eye and head orientation of about 30° (= gaze position) towards the right. The findings strengthen the view that one component of the behaviour in neglect patients is due to a very elementary disturbance of spatial information processing. The deviation of eye and head may be understood as a pathological adjustment of the subject's normal resting position to a more rightward position. While the position in healthy subjects is in line with trunk orientation, this "default position" is shifted to a new origin in patients with spatial neglect.

Optical effect of rightward prism induced shift



Start of prism adaptation period

Prisms on

End of prism adaptation period

Prisms on

Post-adaptation (after effect)

Prisms off

- How does attention interact with vision?

Change blindness

Change blindness

Inattention Blindness

This is an example of what is called "inattention blindness" or "change blindness." The idea is that people often miss large changes in their visual field.

Visit the 'DIY' link on S:EI to test your change blindness

Change blindness is a surprising perceptual phenomenon that occurs when a change in a visual stimulus is introduced and the observer does not notice it. For example, observers often fail to notice major differences introduced into an image while it flickers off and on again. People's poor ability to detect changes has been argued to reflect fundamental limitations of human attention.

Source: Pavlov.tech

S:EI @ScienceEvidenceIntelligence

Inattention Blindness

A narrowed scope

Where drivers not using a hands-free cell phone looked.

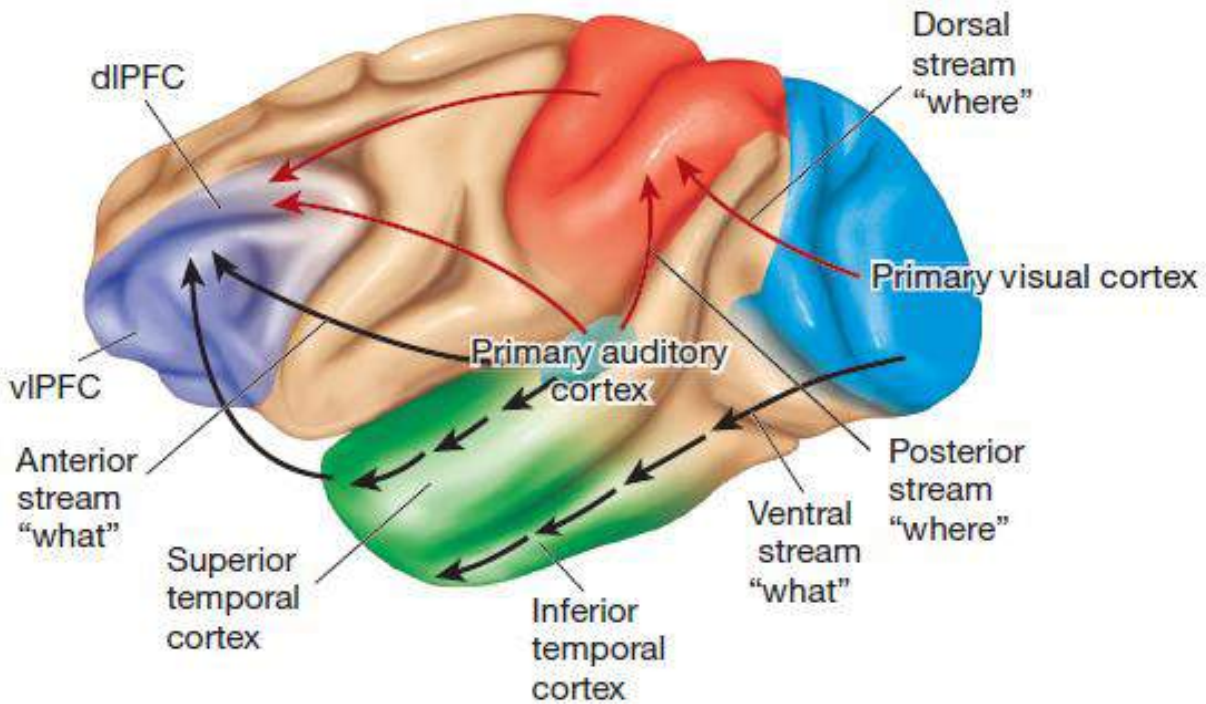
Where drivers using a hands-free cell phone looked.

Source: Transport Canada

Does perception need awareness?

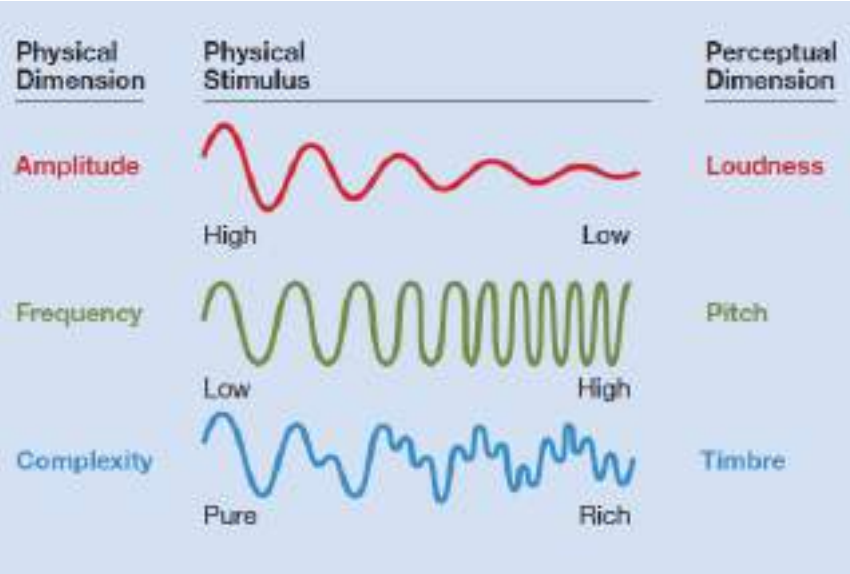
- In healthy normal brain

What would happen if someone becomes blind?



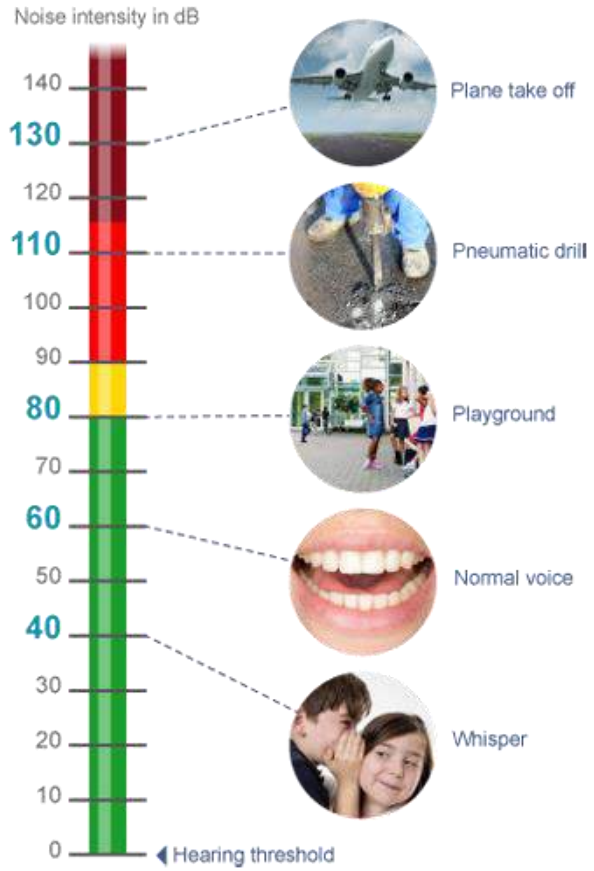
Enhanced responsiveness to auditory stimuli in blind people (auditory stimuli may engage the visual association areas in blind individuals)

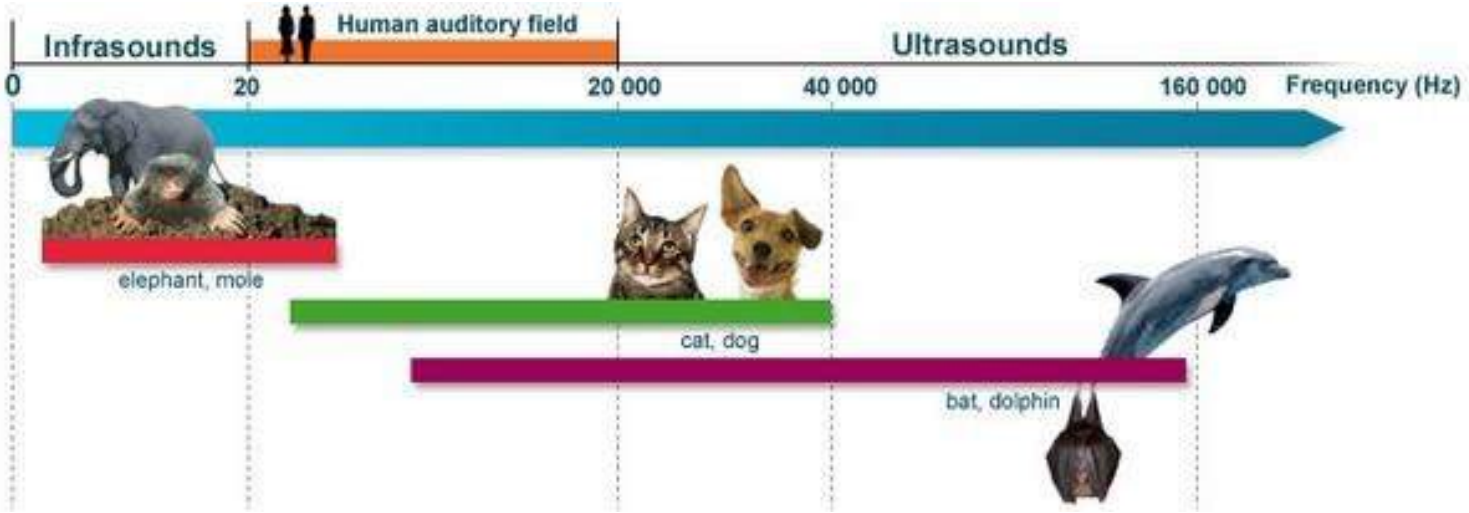
Audition



Decibels (dB)

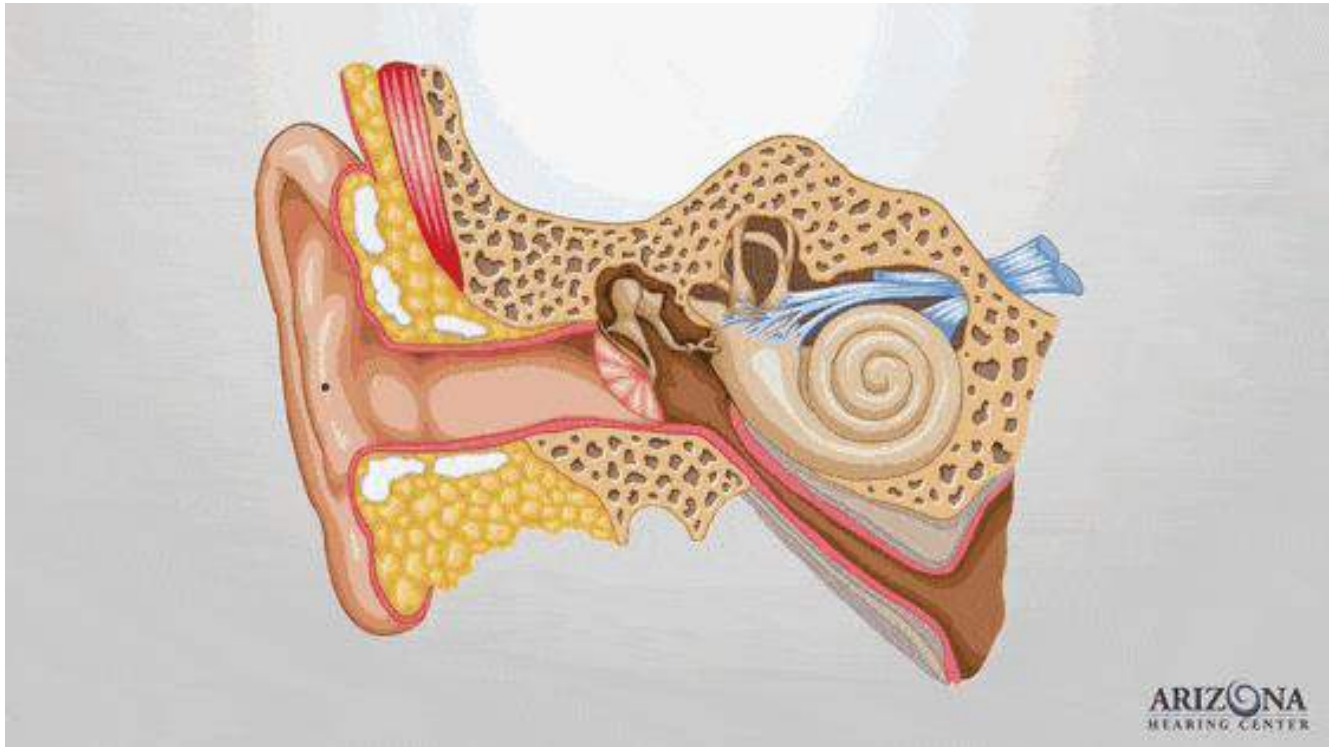
Hertz (Hz)

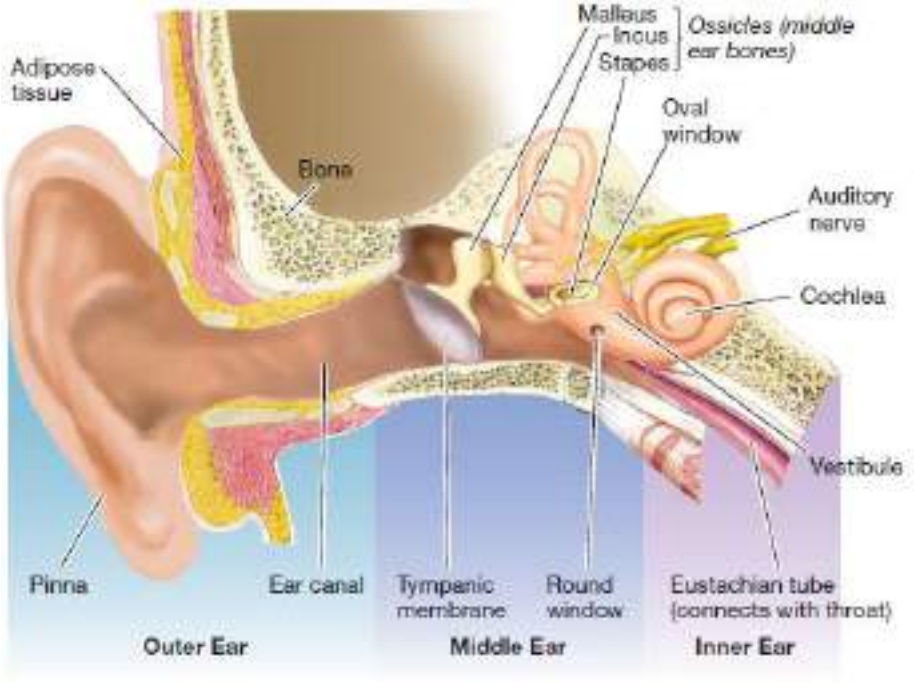


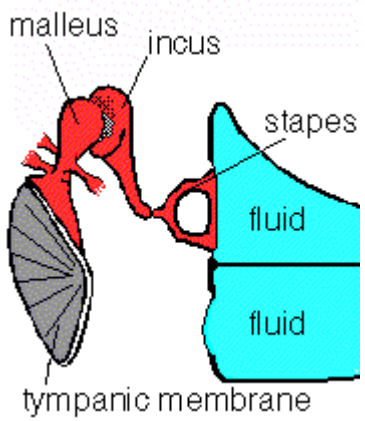


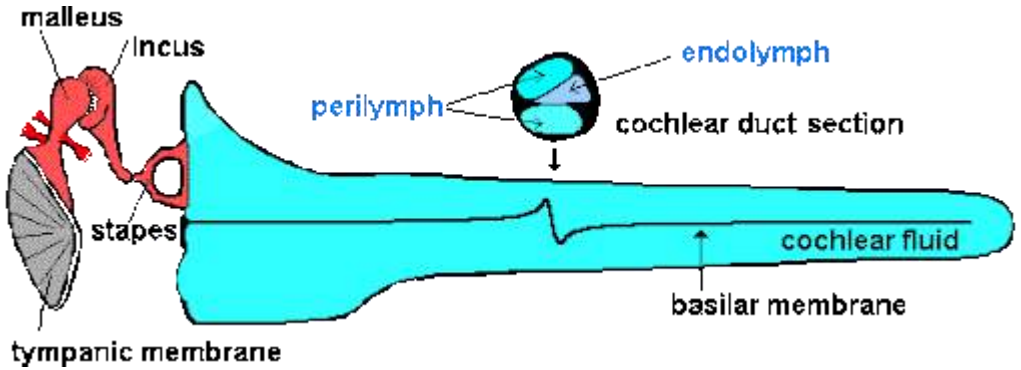
Humans are sensitive to vibrations between 20 and 20,000 times per second.
Most sensitive to 3000 Hz

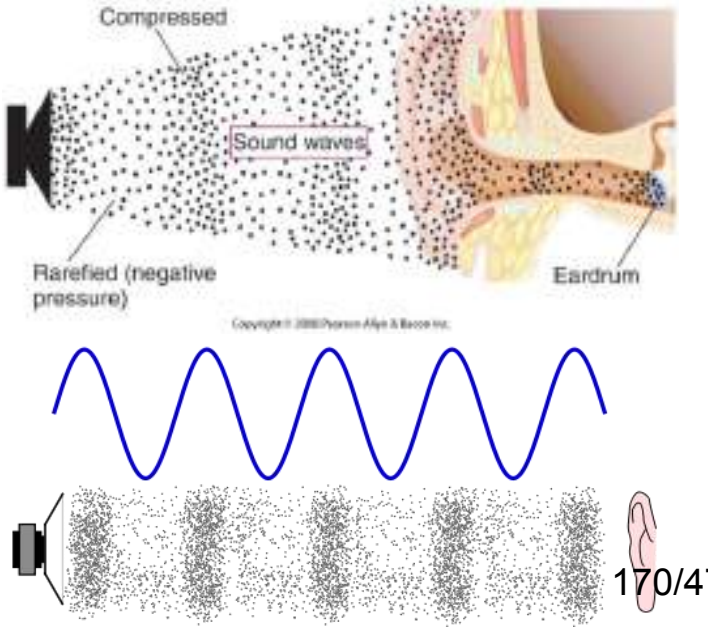
Anatomy of the ear







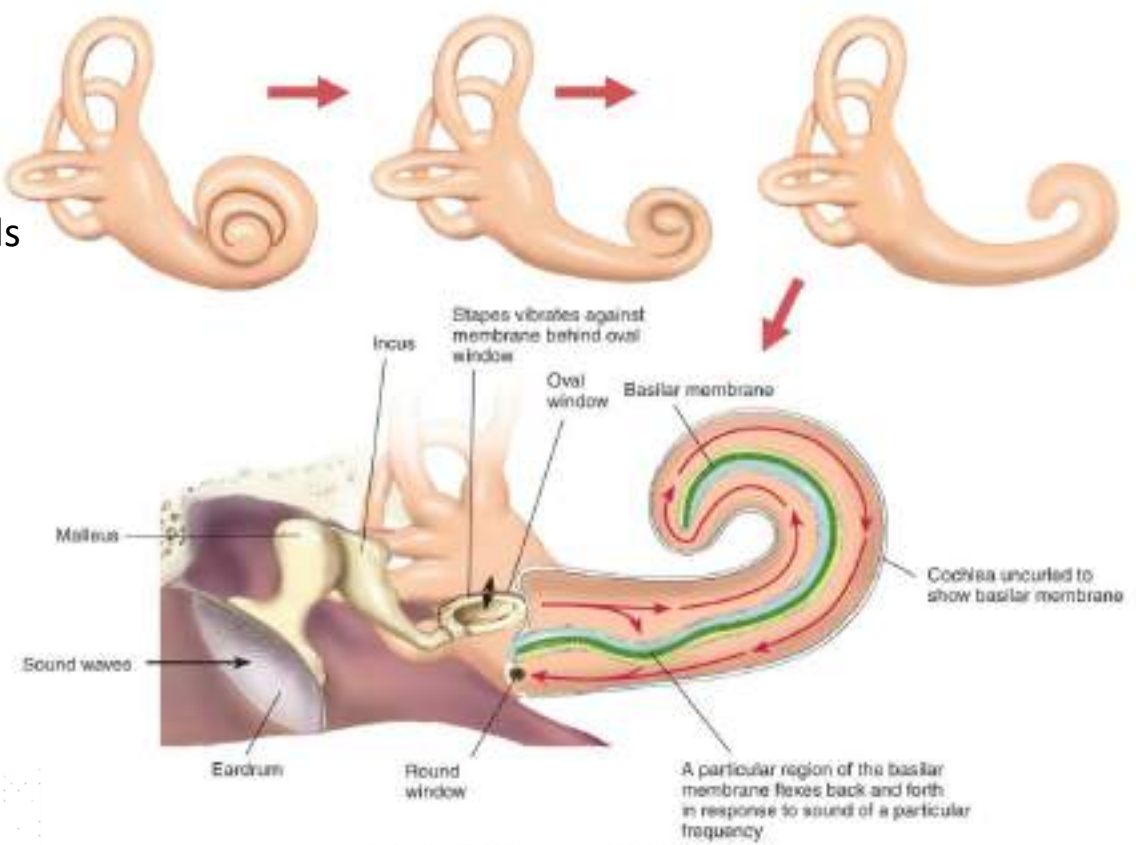


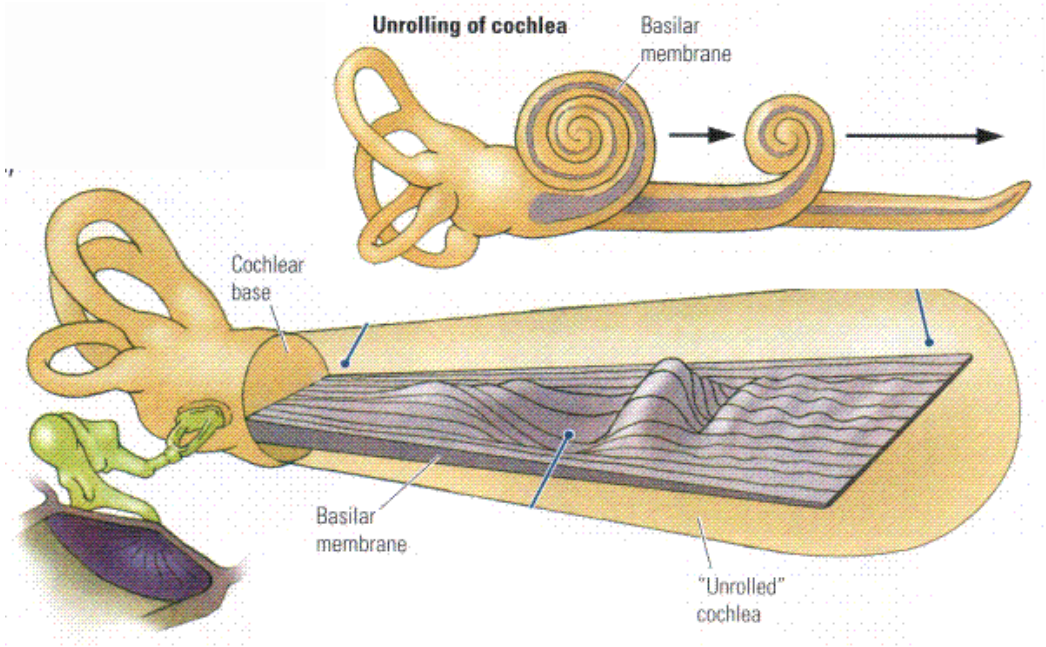


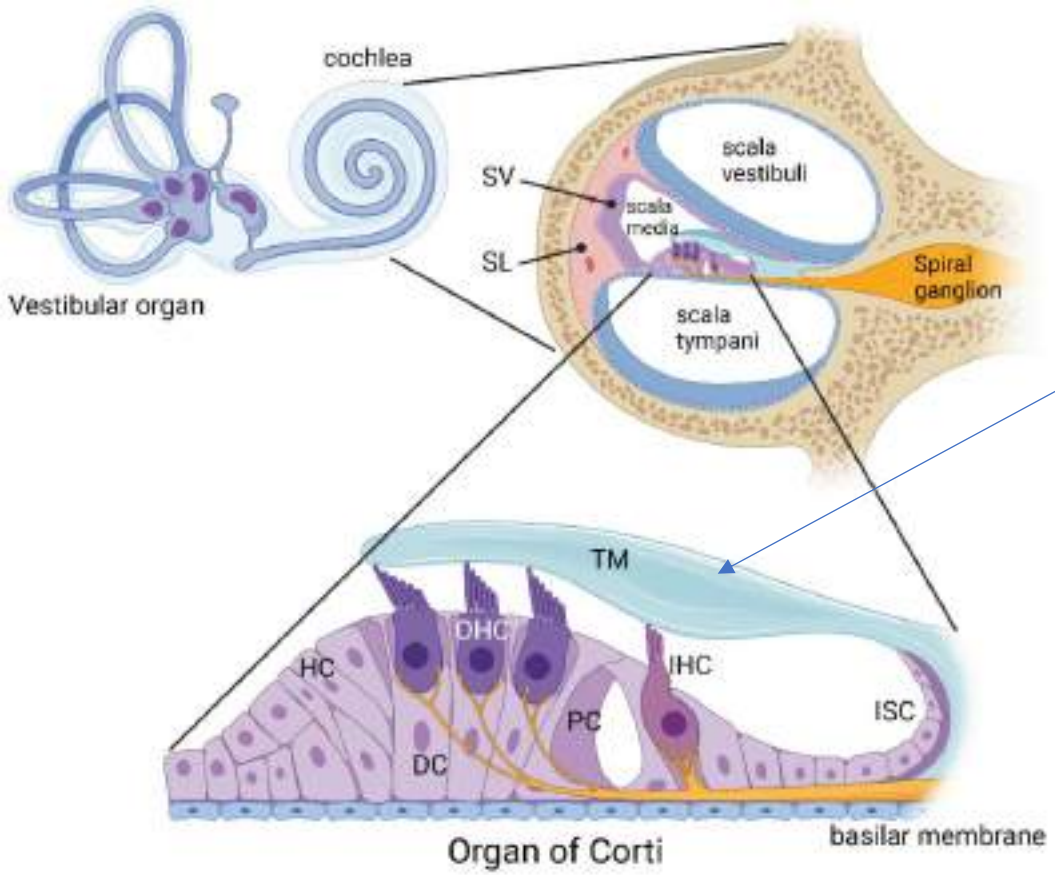
Sound transmitted from air is converted in to a forceful push by the ossicles to vibrate the fluid in the cochlea.

Kinetic energy (air)→ mechanical vibrations → liquid vibrations → electrical signals

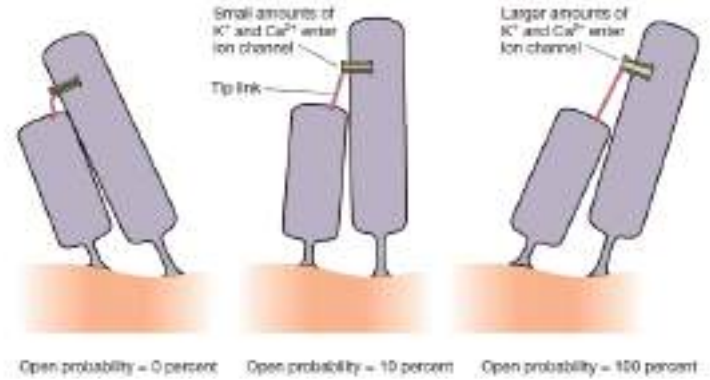
- In the absence of vibrations the cochlea is curled and no vibrations are transmitted in this position
- When the fluid vibrates, the pressure changes in the fluid produce vibrations in the basilar membrane
- High-frequency sounds cause the base of the membrane - the end nearest the oval window—to bend.
- Low frequency sounds flex the tip of the basilar membrane.

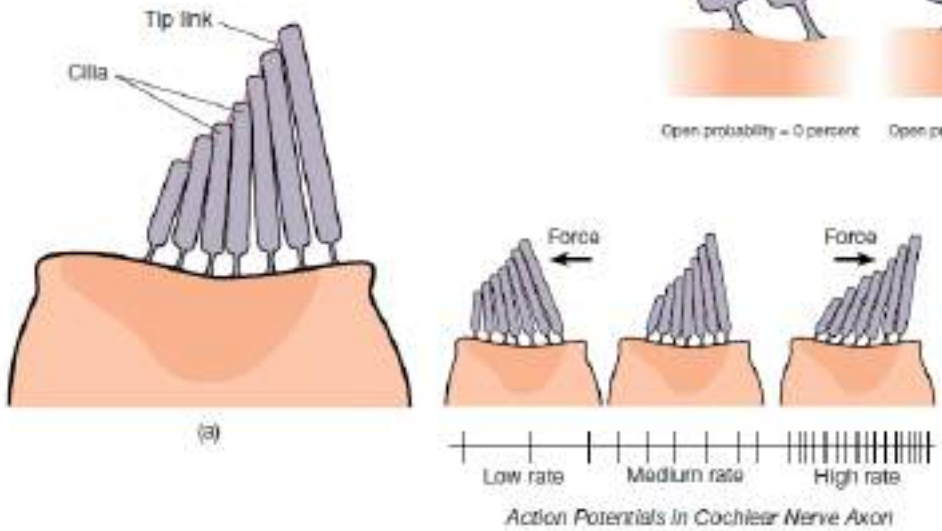






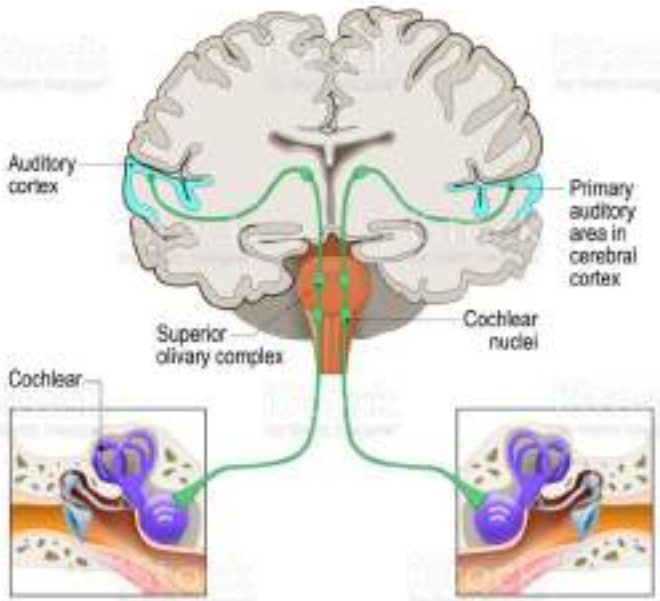
- The basilar membrane has hair cells which act as receptors
- Sound waves cause the basilar membrane to move relative to the **tectorial membrane (TM)**, which bends the cilia (eyelashes) of the hair cells.
- When the cilia bend towards the tallest one, the ion channels open, much like a trap door. This mechanism transduces mechanical energy into electrical impulses.
- The hair cells synapse on the auditory nerve that carries the signal to the brain

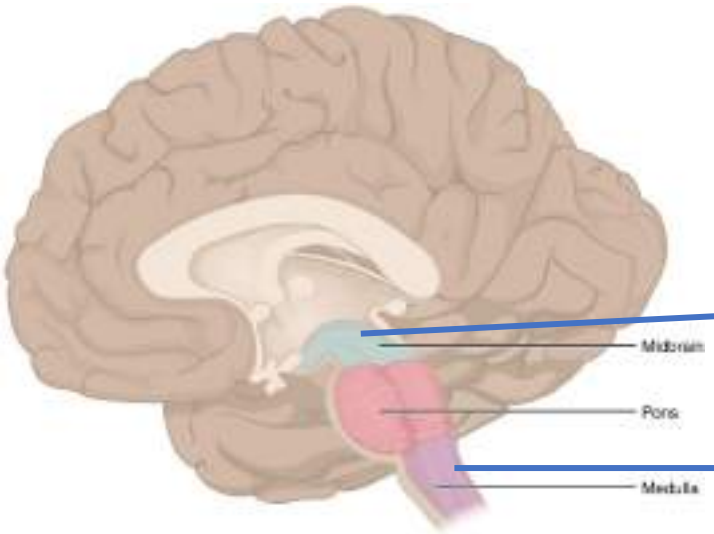


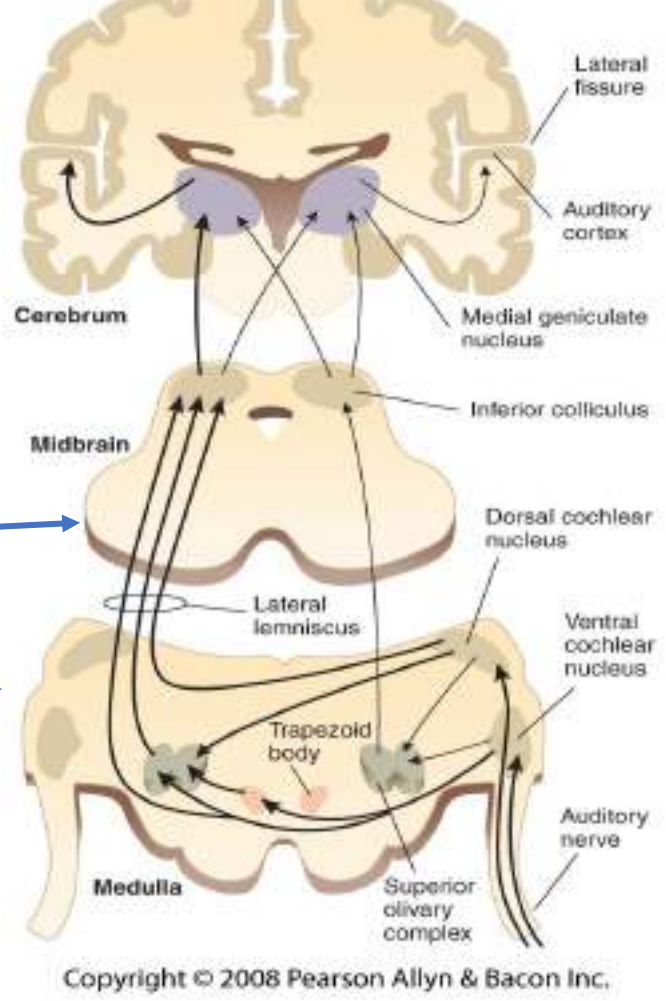


- Where should the sound signals go from the ear (auditory nerve)?

Auditory pathway







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- Auditory nerve → cochlear nucleus (medulla) → superior olivary nucleus (medulla) → inferior colliculus (midbrain) → MGN (thalamus) → primary auditory cortex (temporal lobe)

pathways of the auditory system are inherently complex, and they have many more synapses than the other senses

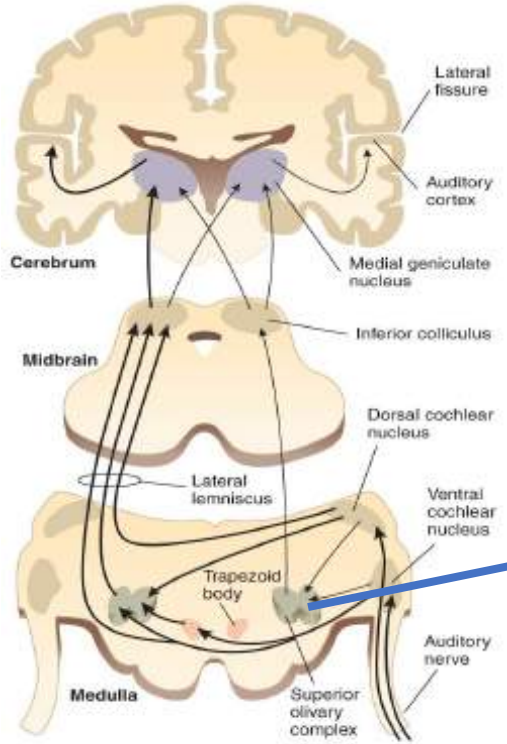
- The primary auditory cortex receives input from both ears and processes the quality of sound
  - More contralateral fibers than ipsilateral nerves

https://hearinghealthmatters.org/pathways/2017/contralateral-ear-effect-tests-central-auditory-function-introduction/

Perception of Spatial Location (in medulla)

Phase difference is calculated by the superior olivary complex

- If sound is located on one side, it will reach the other ear 180° out of phase
- If sound is located in front of us, it reaches both ears in the same phase (0 ° out of phase)



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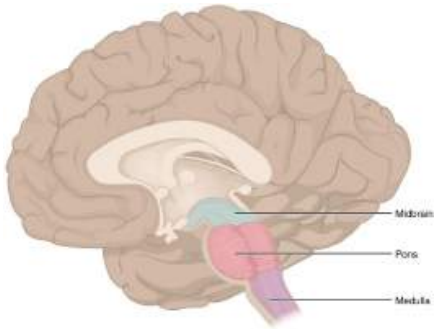
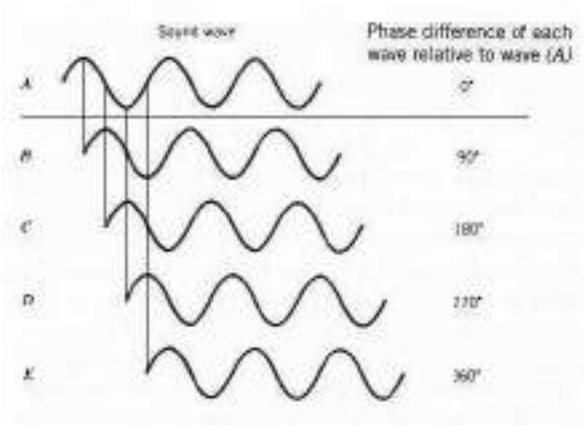
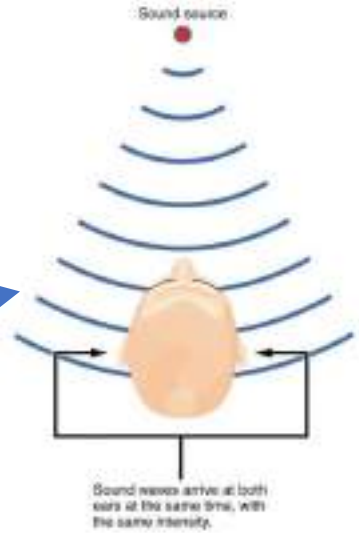
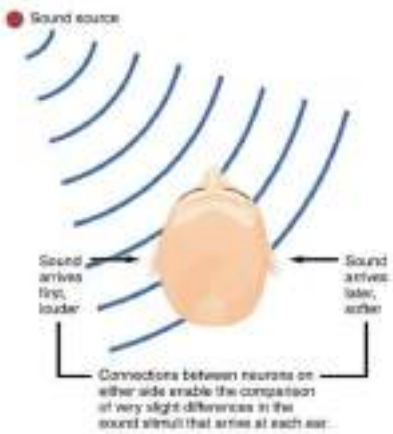
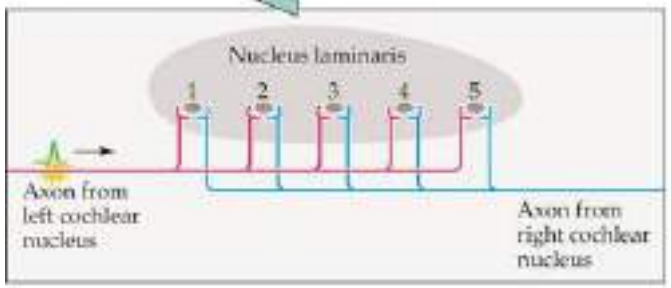


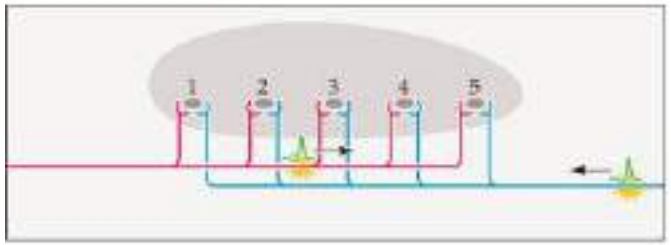


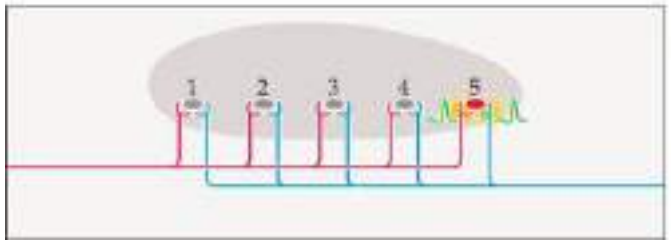




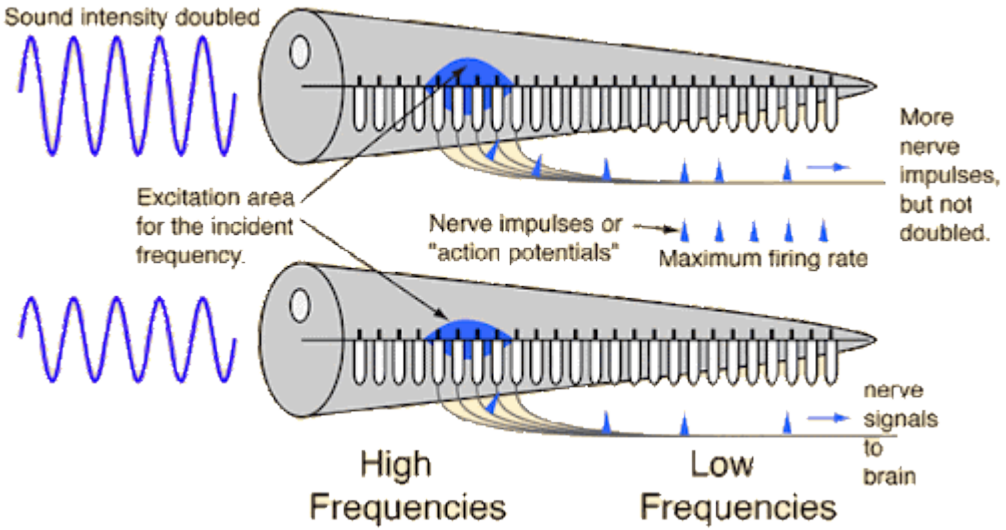
Coincidence detector circuit

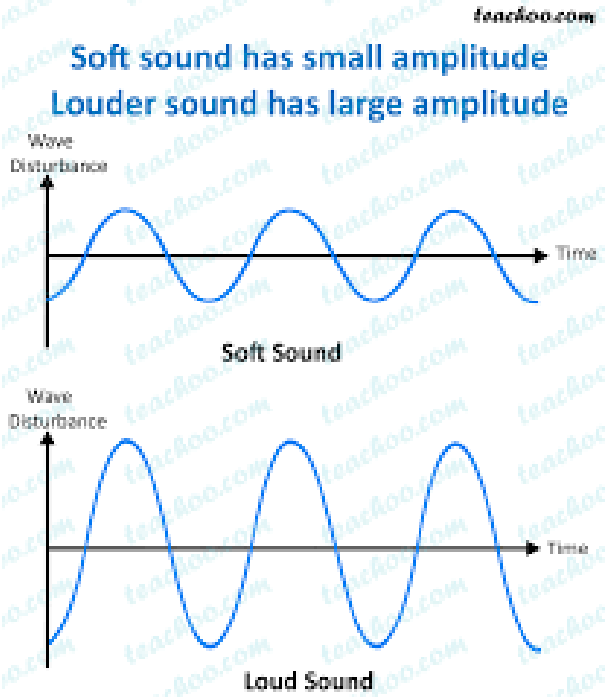






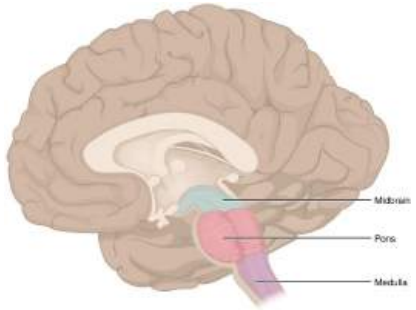
Perception of loudness



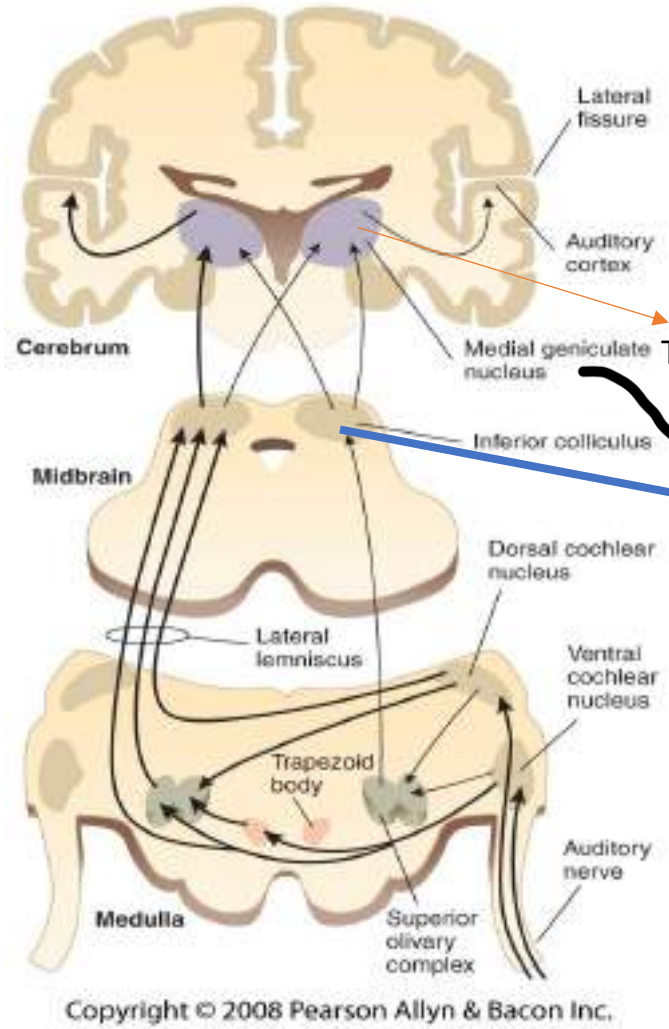


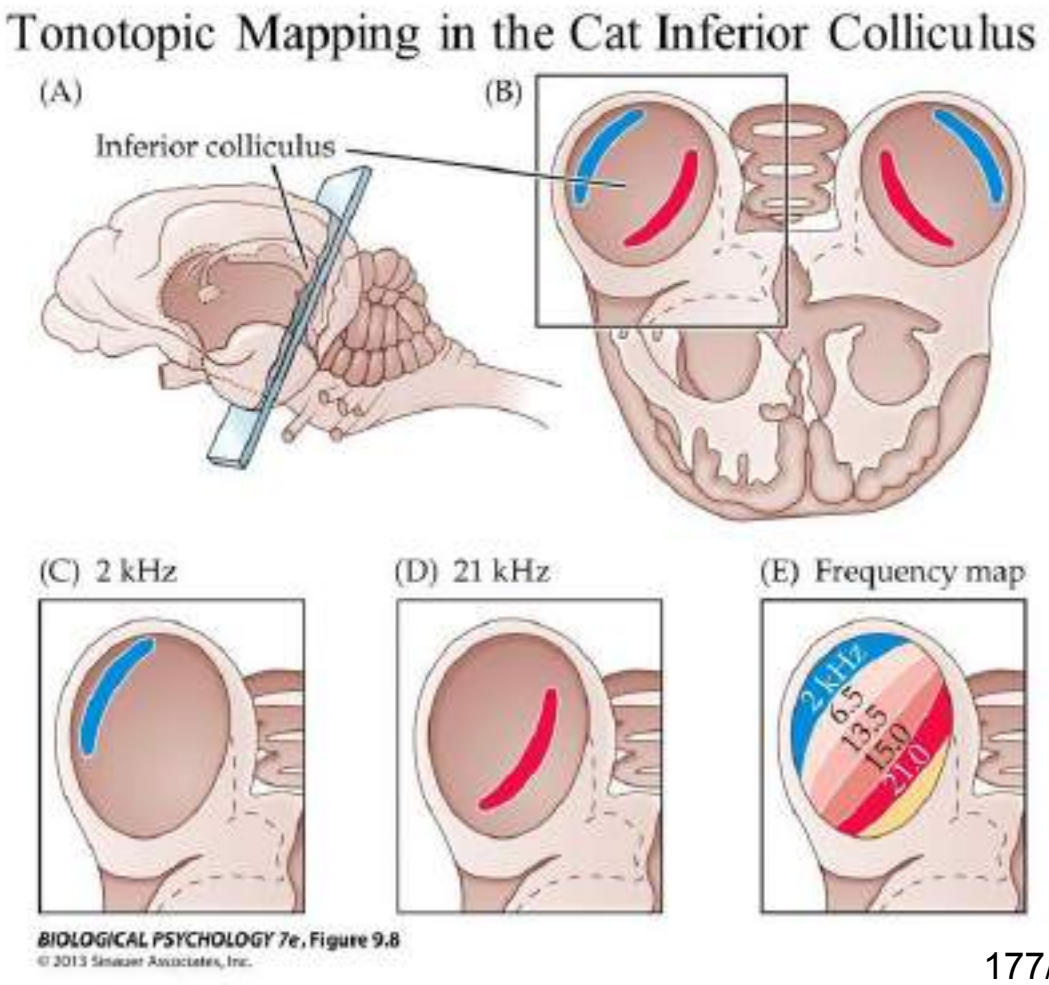
Louder sounds produce more intense vibrations of the eardrum and ossicles, which produce a more intense shearing force on the cilia of the auditory hair cells. As a result, these cells release more neurotransmitter, producing a higher rate of firing by the cochlear nerve axons

Loudness in not linear, it is logarithmic (twice the amplitude does not mean twice as loud)



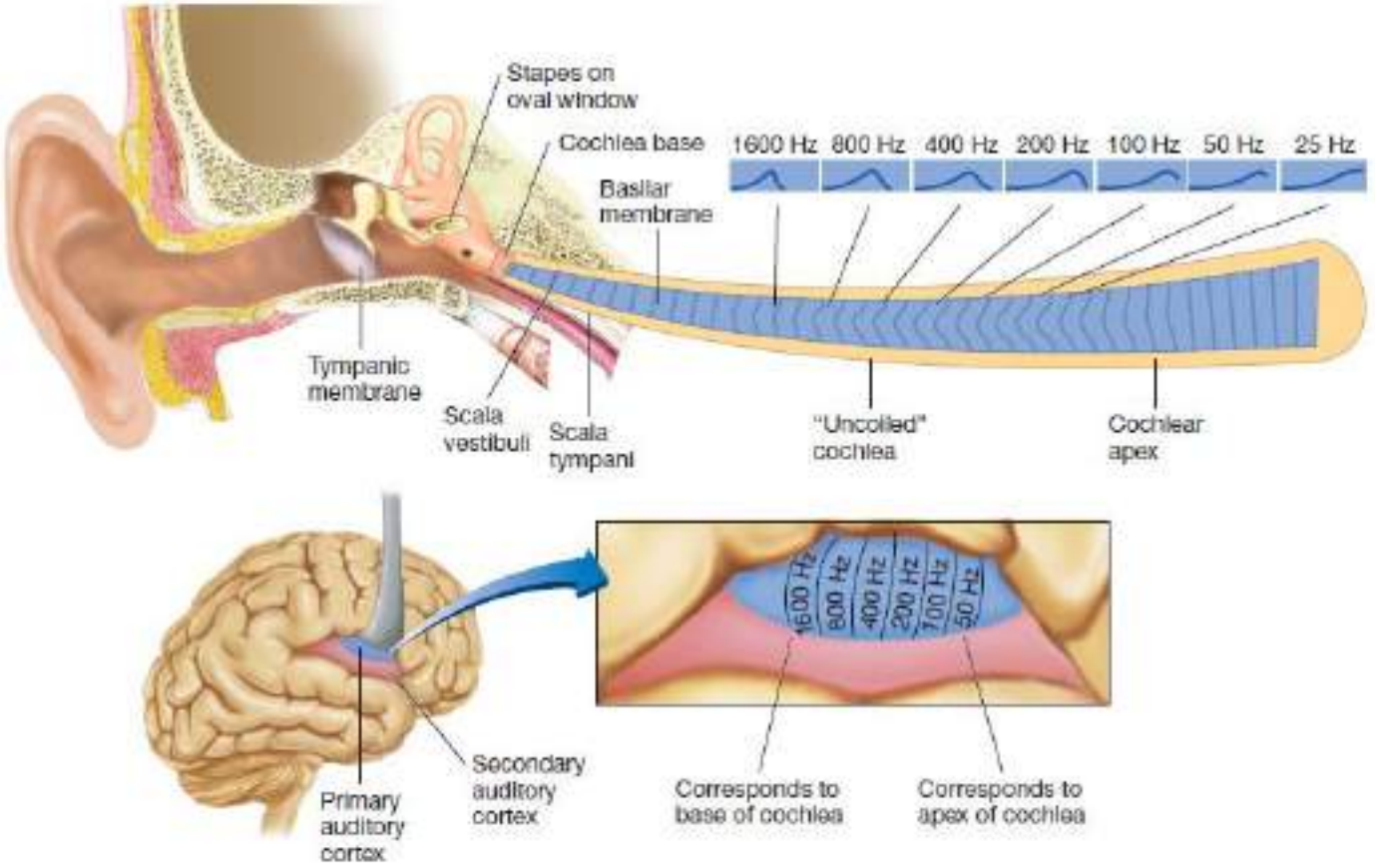
Rudimentary Sound perception in the Midbrain



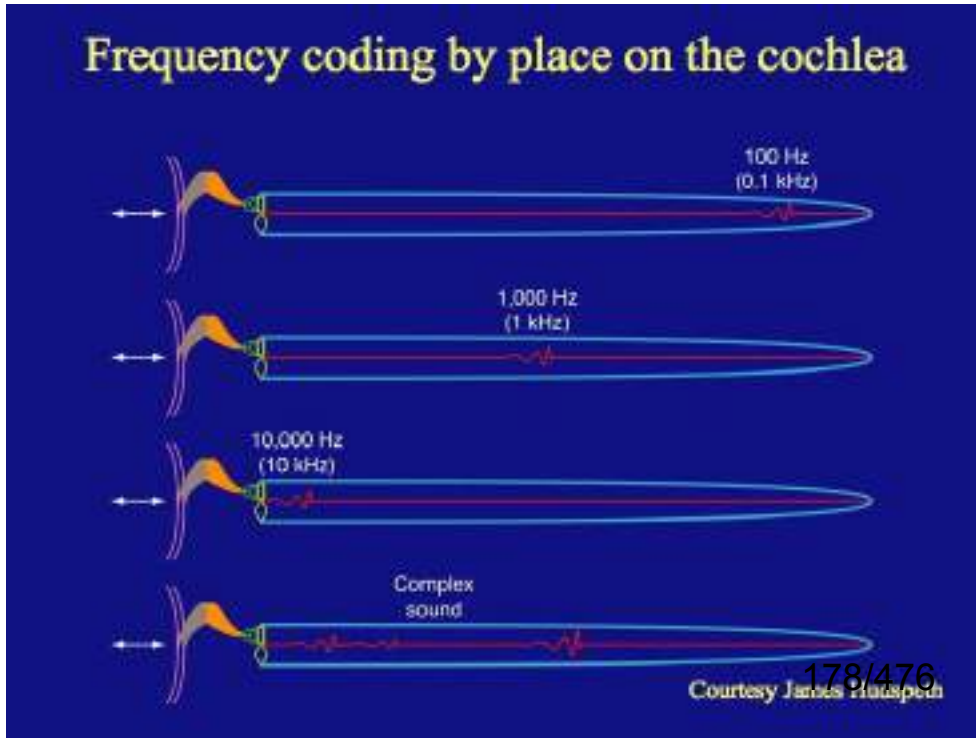


Frequency mapping

The frequency map (tonotopic representation) of the basilar membrane is preserved through processing in the subcortical structures and mapped in the primary auditory cortex.



Different frequencies are processed in their corresponding area of the auditory cortex



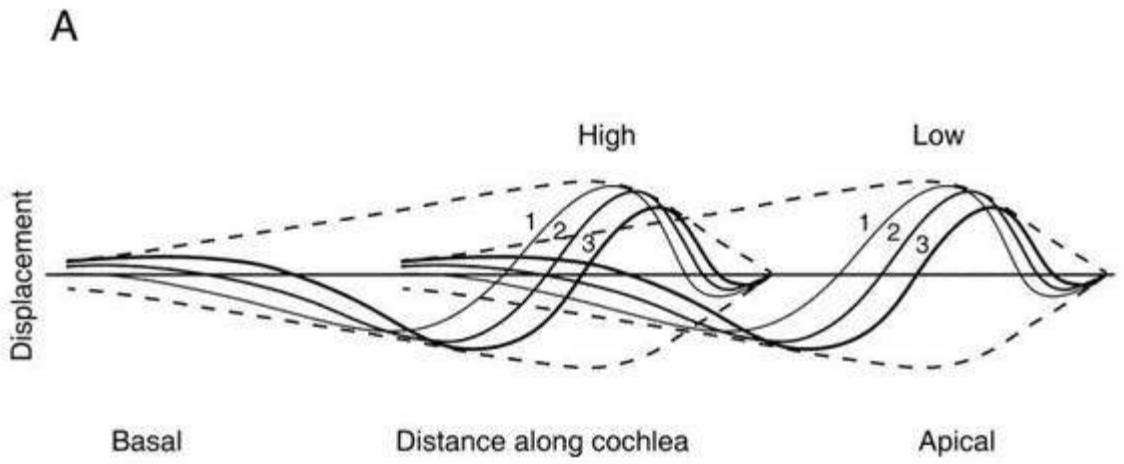
Perception of Pitch

- What happens when you combine frequencies?
- Which frequency do you really hear?

The case of the missing fundamental

Perception of timbre

When the basilar membrane is stimulated by complex sounds, different portions of the membrane respond to each of the overtones. This response produces a unique anatomically coded pattern of activity in the cochlear nerve, which is subsequently identified by circuits in the auditory association cortex



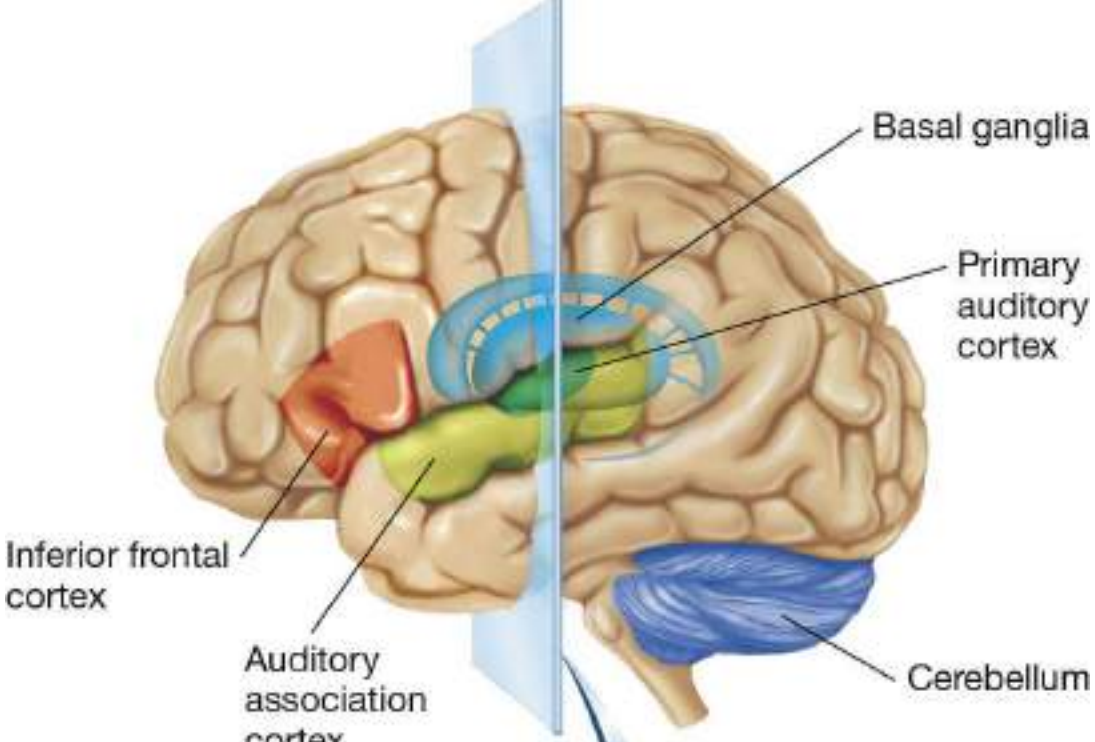
Special characteristics of neurons in the auditory pathway afford the processing of timbre.

e.g. hollow or solid door
e.g. different voices of friends

Music perception

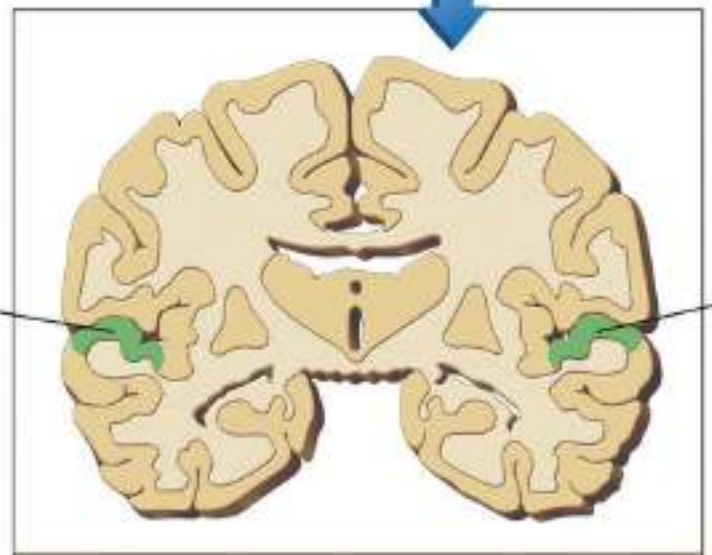
a melody is recognized by the relative intervals between its notes, not by their absolute value.

the inferior frontal cortex appears to be involved in recognition of harmony



the cerebellum and basal ganglia are involved in timing of musical rhythms, as they are in the timing of movements.

Heritability of musical abilities is high



the left auditory cortex appears to be involved in perception of rhythmic patterns that are superimposed on the rhythmic beat

right auditory cortex appears to be involved in perception of the underlying beat in music

Auditory processing disorder (APD)

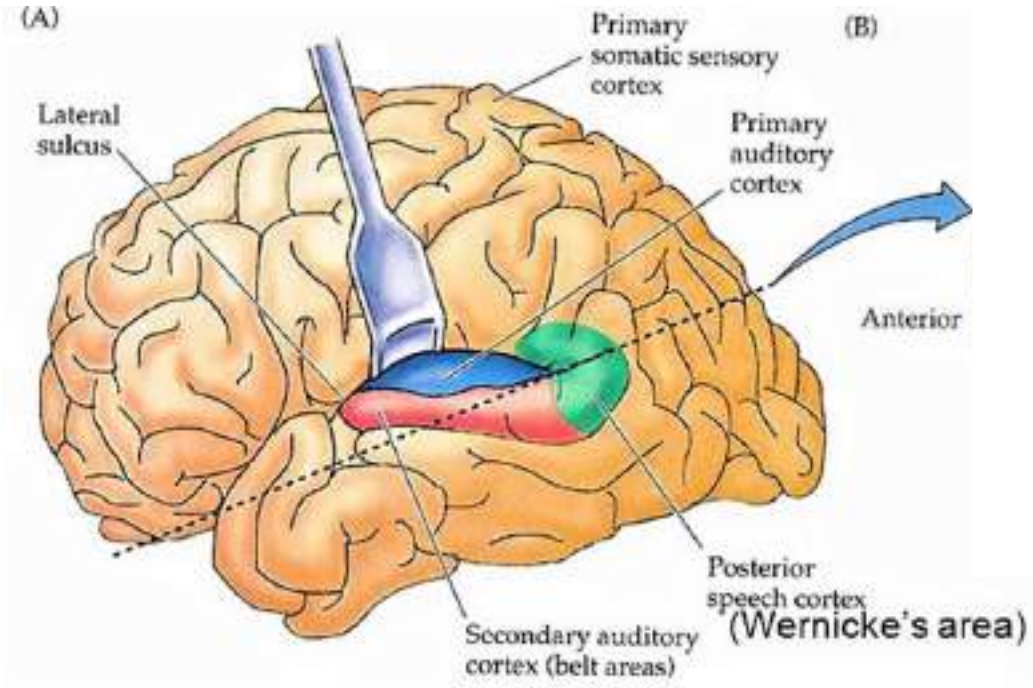
Someone says, "Please raise your hand," and you hear something like "Please haze your plan."

APD is a rare hearing problem that affects school-aged children.

- Auditory process matures fully by 13 years
- The child may grow out of the disorder once they reach that age.
- Listening skills usually develop as the auditory system matures.
- It usually takes around 12-15 years of age to have complete auditory processing maturity.

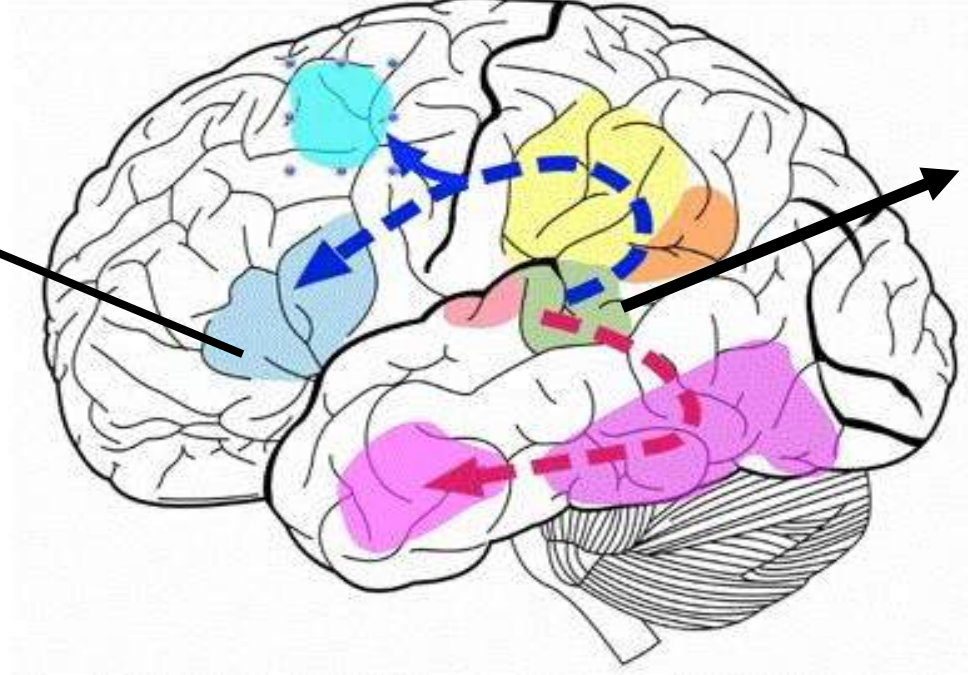
- Cause - genetic, brain trauma during childbirth, infection of the ear.
- Currently, APD is recognized as a “specific learning disability”

Auditory Pathways



Planning speech output

auditory comprehension



Dorsal pathway

auditory-motor integration

verbal repetition

sound localization

Ventral pathway

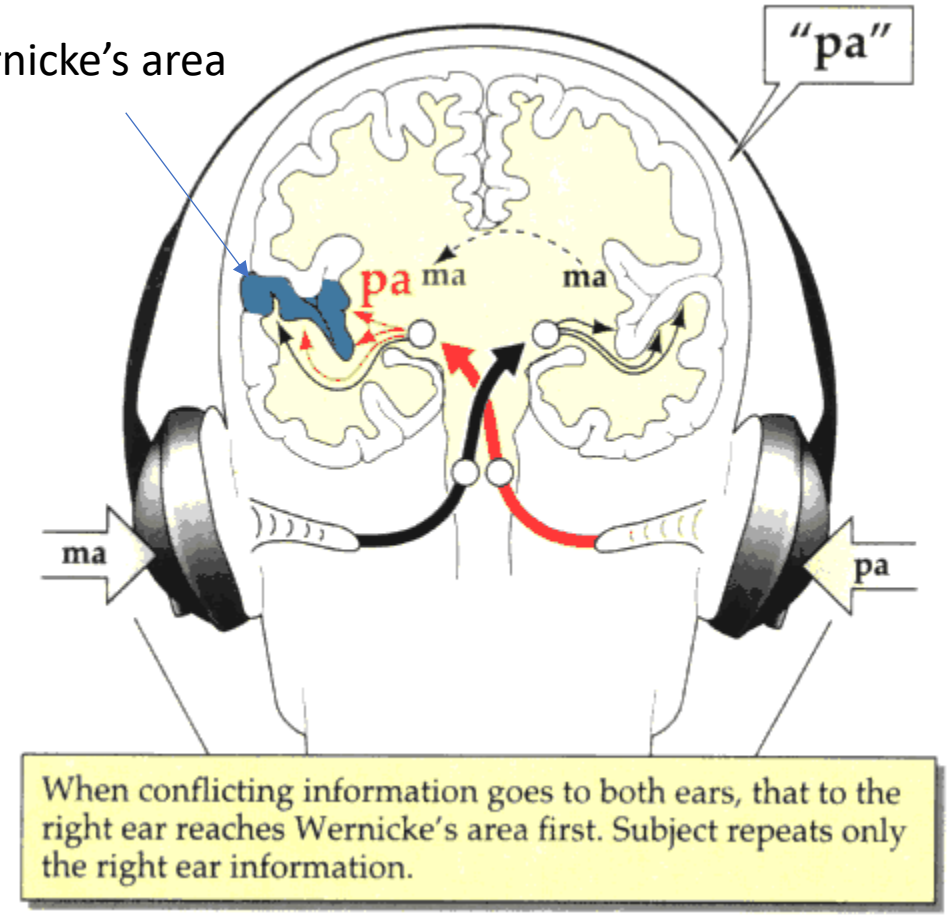
auditory-conceptual mapping

auditory comprehension

analysis of complex sounds

Asymmetries of the Auditory System

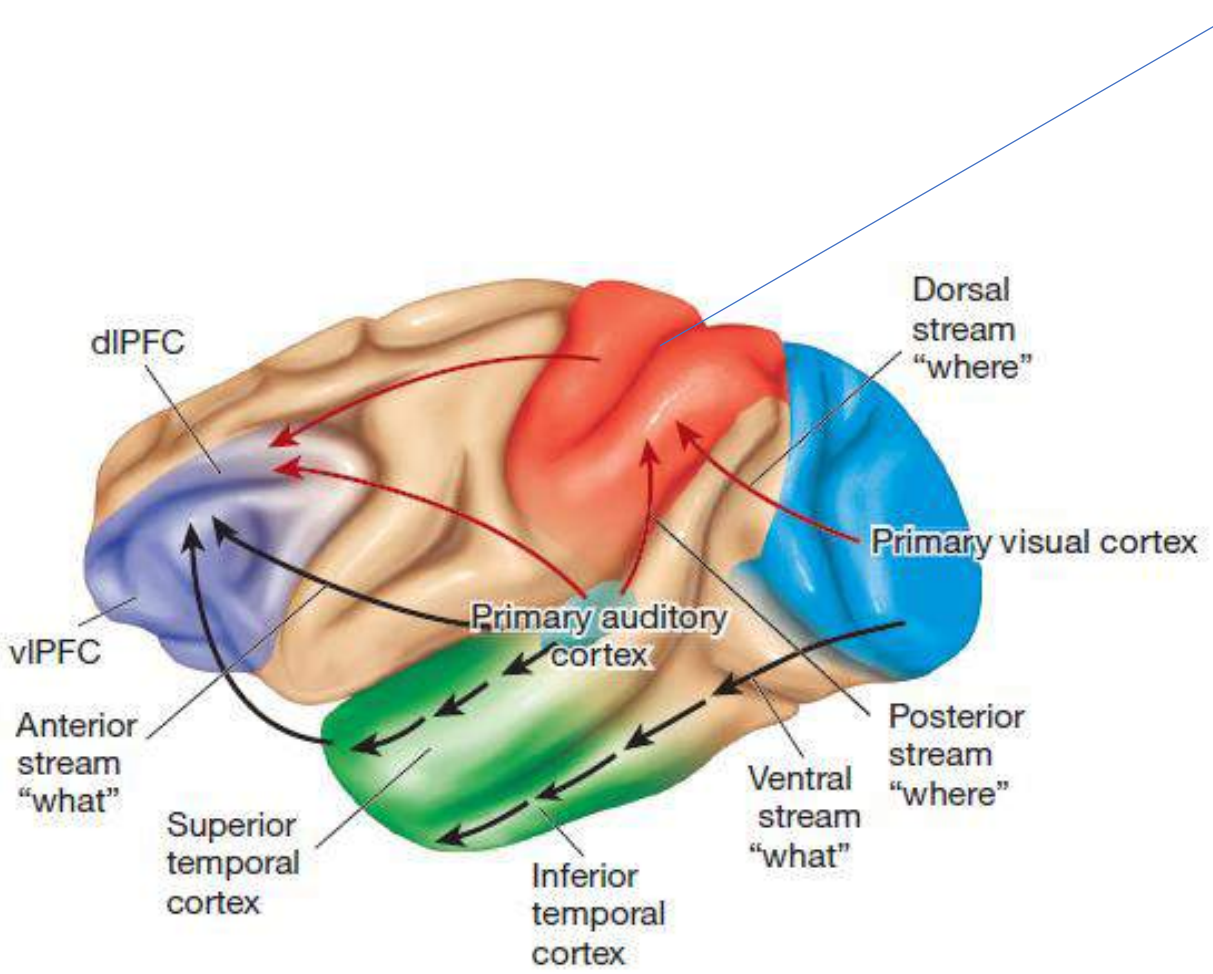
- In normally hearing individuals, anatomical and functional observations from the cochlea up to the cortex are in favor of a right ear advantage (REA), a feature hypothetically linked to the fact that in almost all right handed and most left handed people, speech is processed predominantly in the left cerebral hemisphere.
- Both afferent and efferent auditory pathways show asymmetrical features which suggests that competing signals from both ears are processed with a REA which enables the left hemisphere to process speech appropriately in difficult listening situations.
- Stimuli with complex speech-like acoustic properties, including rapid spectrotemporal changes, yield greater activation in auditory cortex over the left hemisphere, regardless of whether right ear, left ear, or binaural stimulation is used.
- The left hemisphere is specialized from birth for processing specific properties of speech and children exhibit the right ear advantage as early as the first year of life.



Right Ear Advantage

https://hearingreview.com/inside-hearing/research/remarkable-history-right-ear-advantage

Overlap of auditory and visual dorsal pathways



the visual and auditory "where" streams overlap in the parietal lobe.

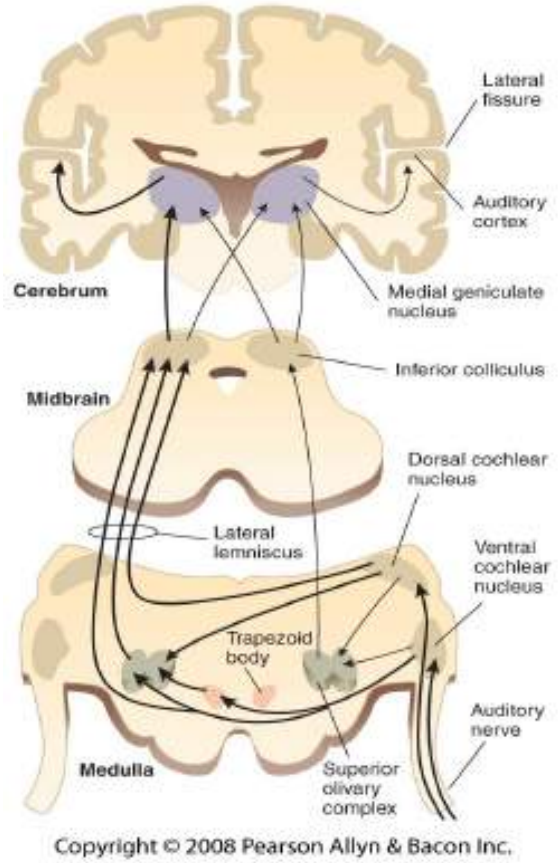
We can use the convergence of sight and sound to recognize which of several objects in the environment is making a noise.

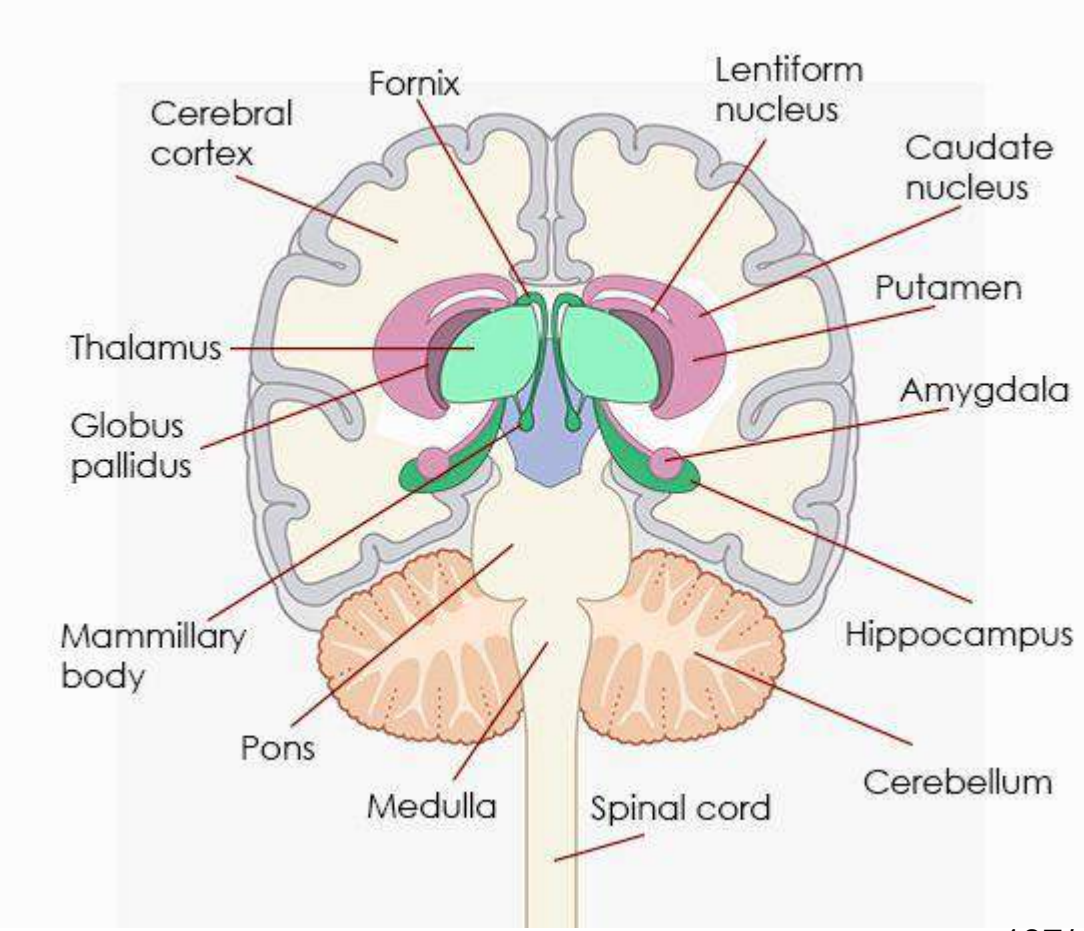
we can learn the association between the sight of an object and the sounds it makes – learning and memory

Enhanced responsiveness to auditory stimuli in blind people (auditory stimuli may engage the visual association areas in blind individuals)

- Can you detect additional information from sounds?

Auditory fear processing Thalamus → amygdala





Types of Deafness

trouble identifying sounds → damage to? → auditory 'what' pathway

difficulty localizing sounds → damage to ? → auditory 'where' pathway

Aging related deafness → damage to?→ basilar membrane neurons (esp high freq - "s," "f," and "t" sounds)

Noise (loud) induced hearing loss→ damage to the tympanic membrane or hair cells or base of basilar membrane that receives most signals first

Complete deafness → damage to ? → bilateral 'primary' auditory cortex

Congenital deafness → damage to ? → cochlea → cochlear implants

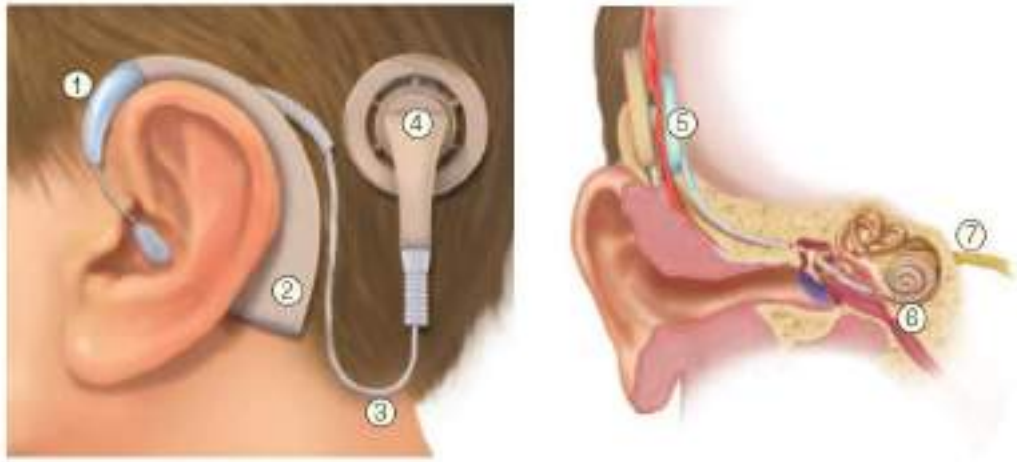
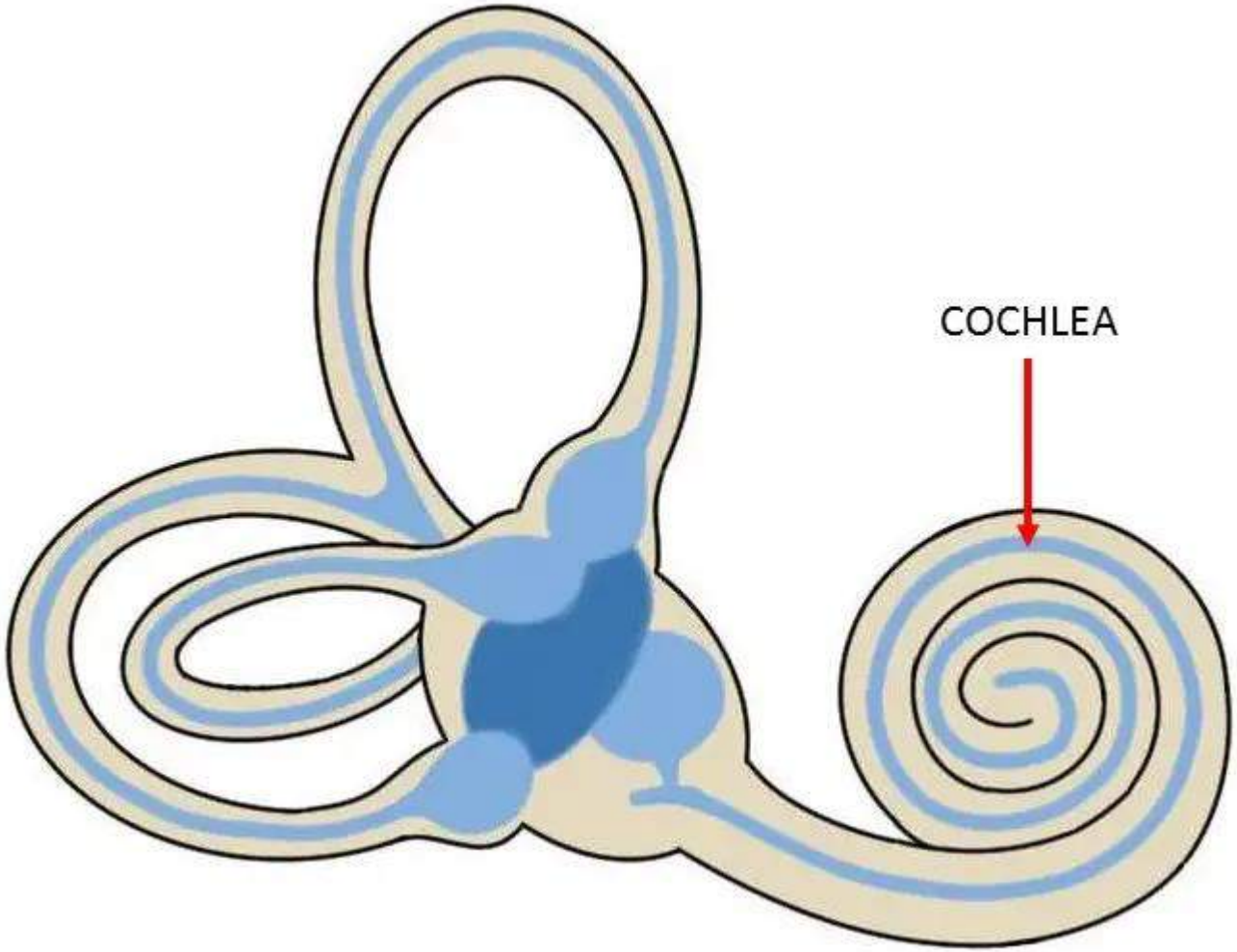


FIGURE 5.46 Cochlear implant.
Sound is picked up by a small microphone (1) located behind the ear and converted into an electrical signal. An external processor (2) converts the signals into complex digital representations of the sound, which travel by wire (3) to an external transmitter (4), which transmits them as radio waves to the internal processor (5). Here they are reconverted to electrical signals that travel by wire (6) to the cochlea, where 22 electrodes are placed. The electrodes stimulate the auditory nerve (7).

- What do these circular/angular canals do?



Vestibular System

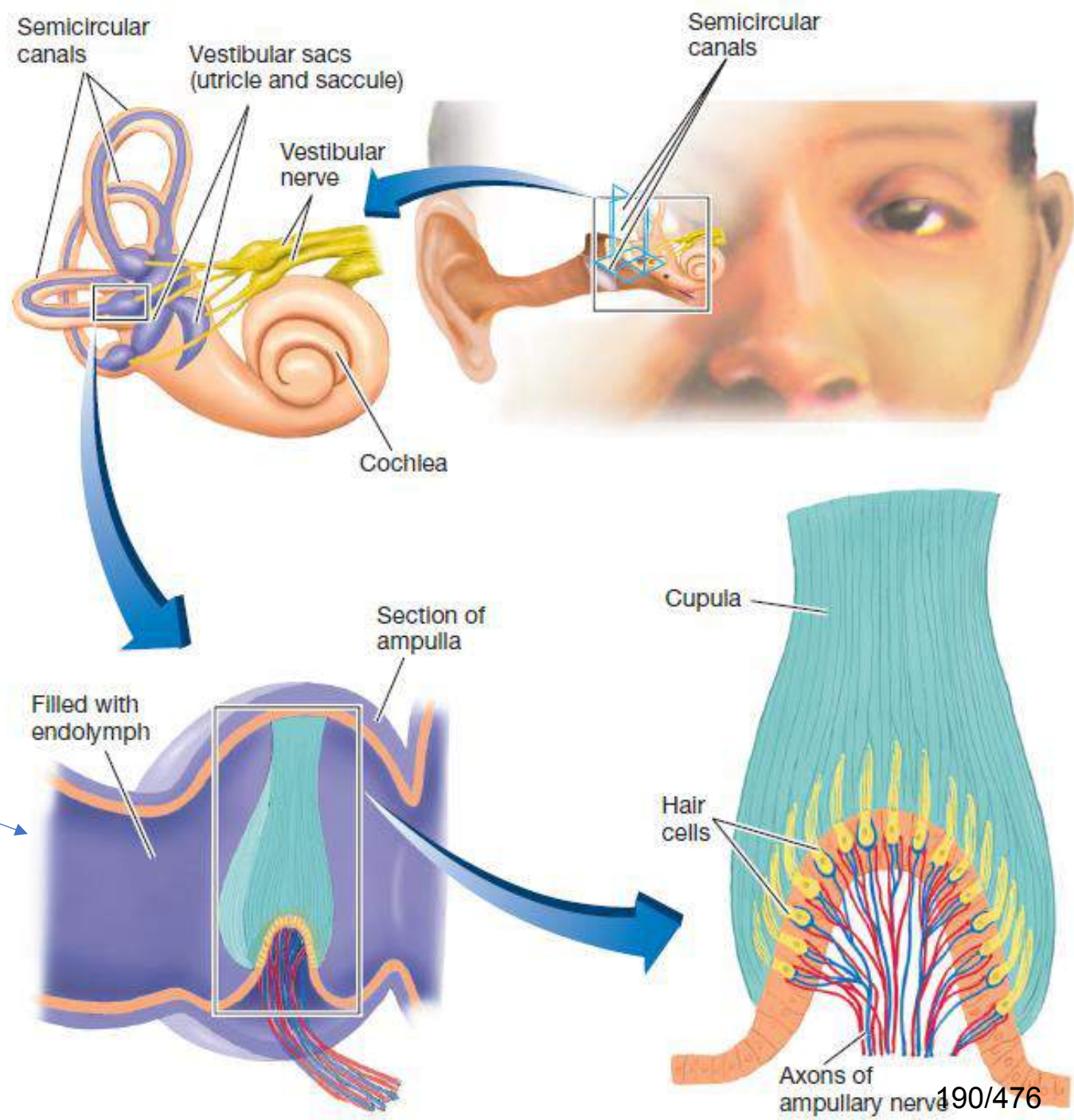
Function - balance, maintenance of the head in an upright position, and adjustment of eye movement to compensate for head movements.

Semi-circular canals

- Angular acceleration → electrical signals
- changes in the rotation of the head
- Arranged in a 3D manner

Vestibular Sacs

- force of gravity → electrical
- inform the brain about the head's orientation

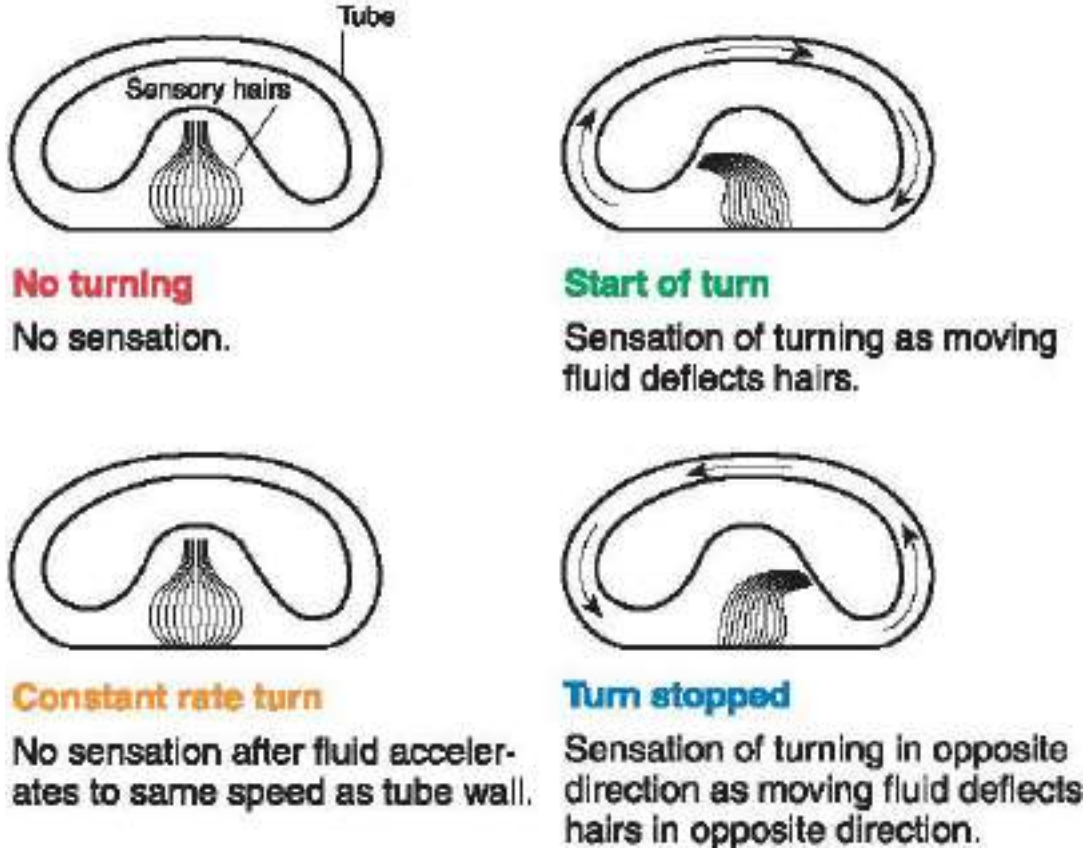


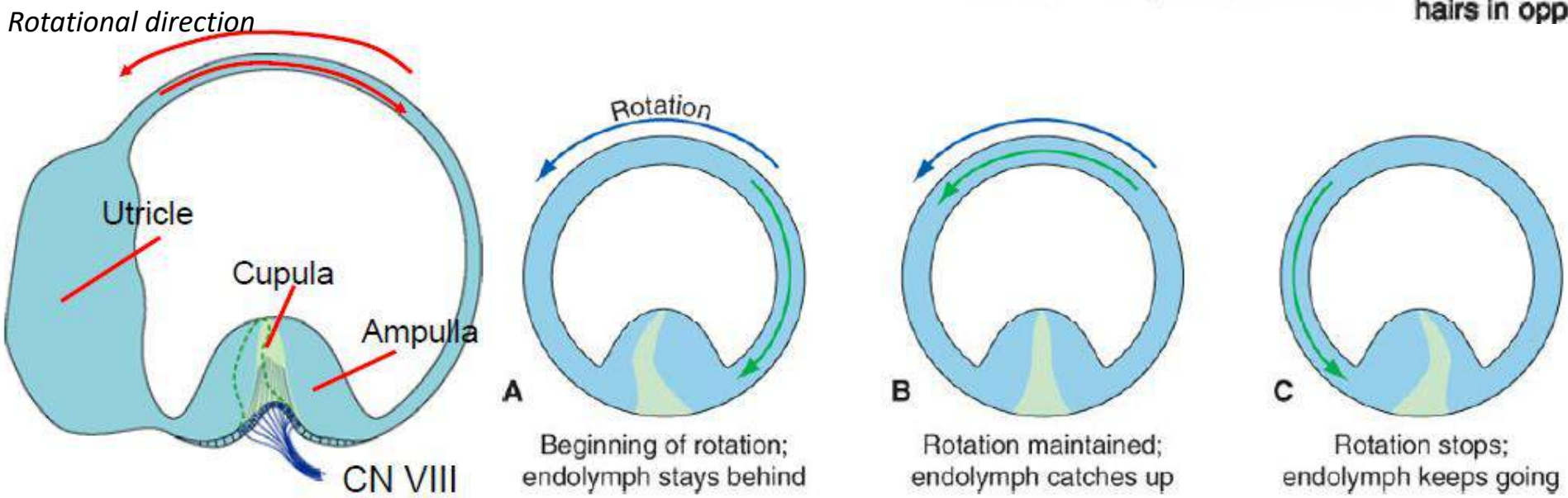
Working of semicircular canals

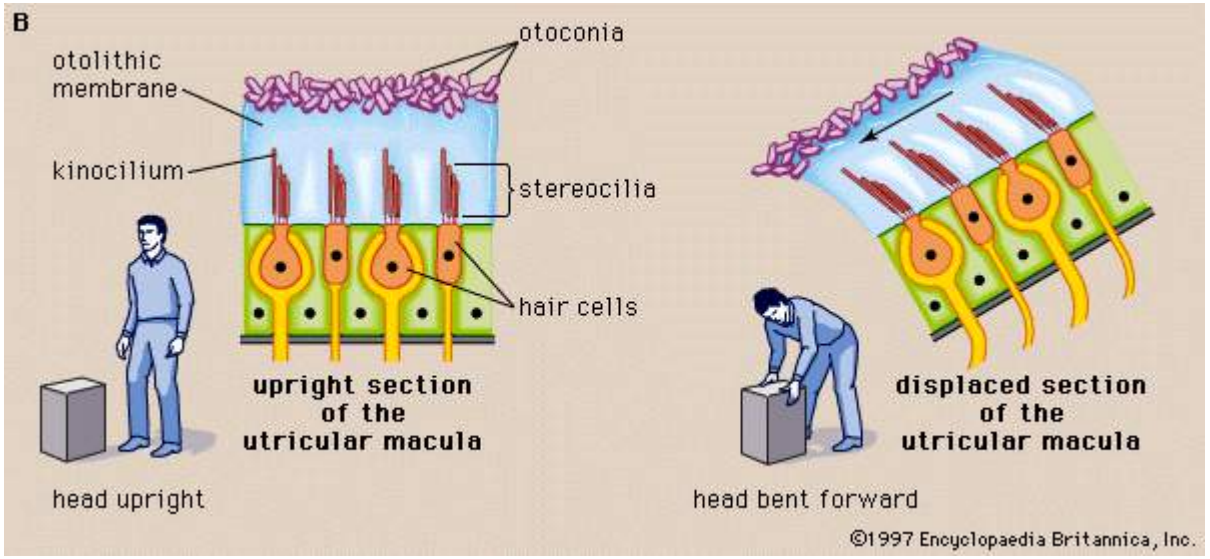
- Rotation of the head → fluid flows in the opposite direction → triggering receptor potentials in the hair cells

- Stimulation of the semi-circular canals can produce dizziness and rhythmic involuntary eye movements (nystagmus)

- Angular acceleration → electrical signals

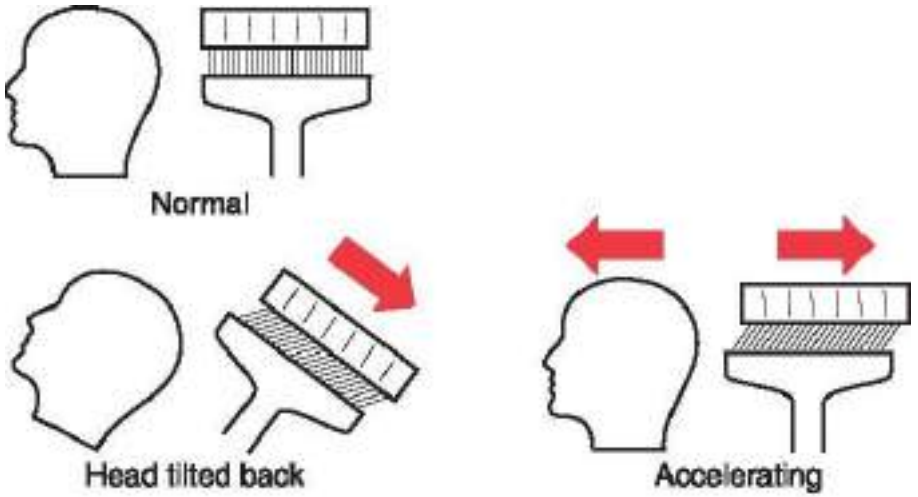






Working of vestibular sacs

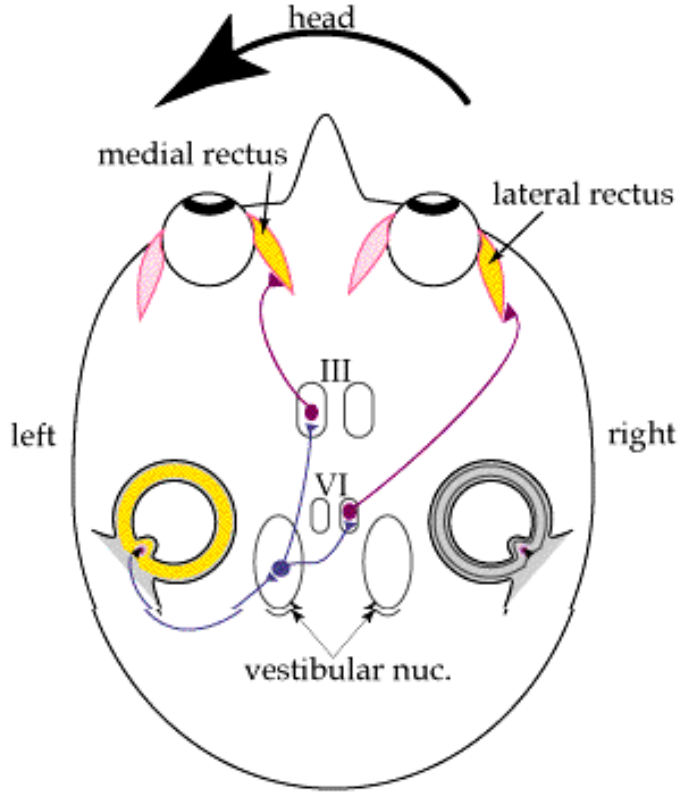
- The weight of the crystals causes the gelatinous mass to shift in position as the orientation of the head changes. This movement produces a shearing force on the cilia of the receptive hair cells
- Low frequency stimulation of the vestibular sacs can produce nausea



Vestibular Pathway:

- To prevent our vision from blurring while walking or running, the brain stem nuclei hold the head upright and control eye movements to compensate for sudden head movements

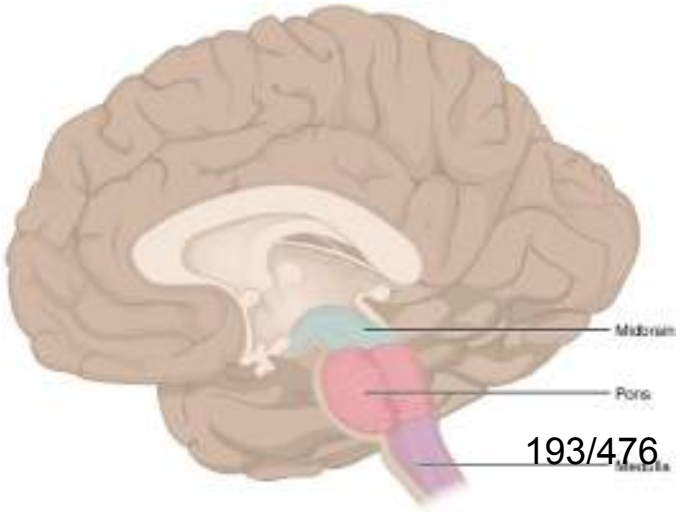
- Activity of vestibular pathway projections to the lower brain stem (medulla) can produce nausea and vomiting that may accompany motion sickness



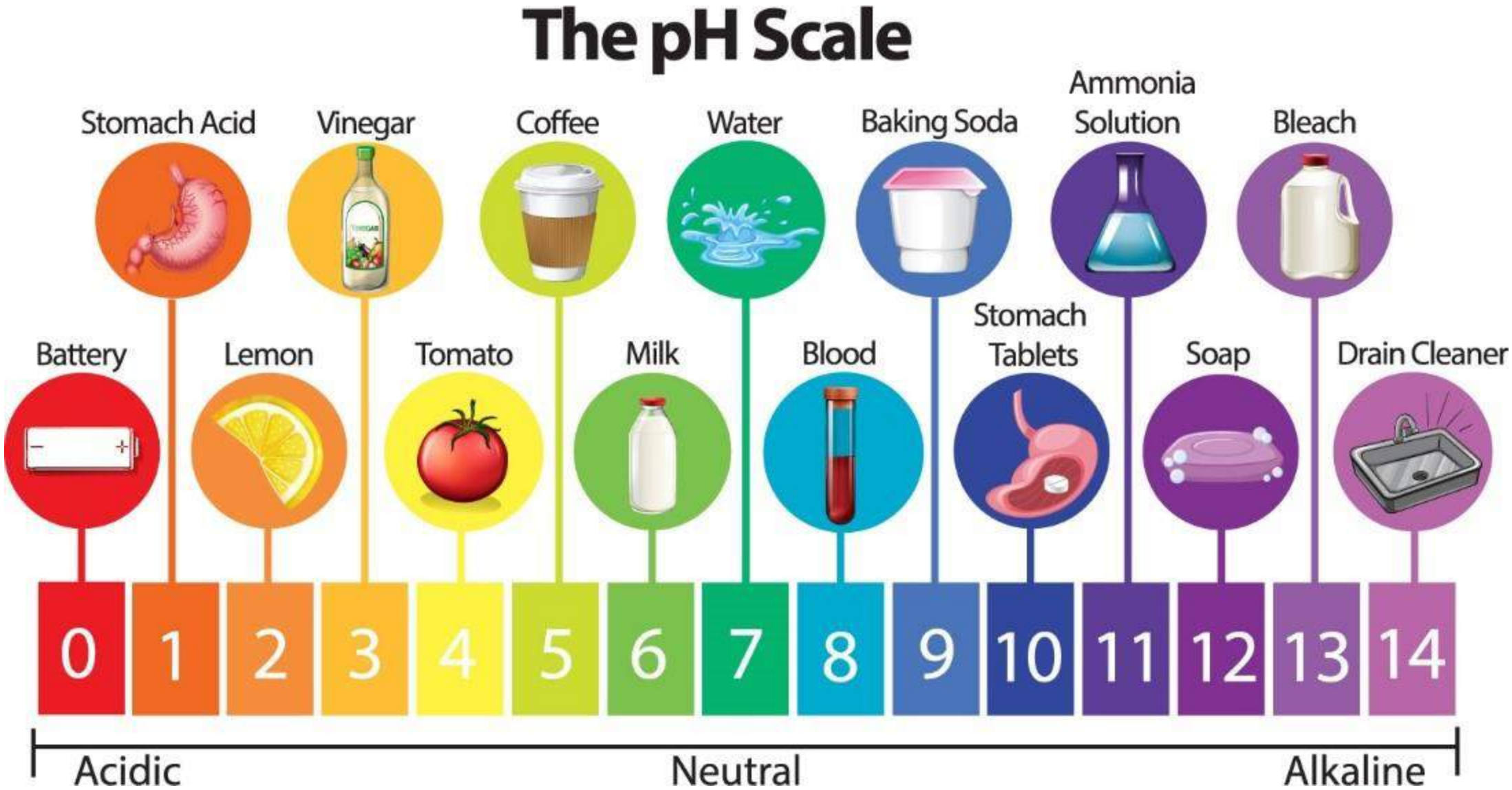
Connection of vestibular nuclei to eye movements

Functions of the vestibular system

- Balance
- Maintenance of head in an upright position
- Adjustment of eye movement to compensate for head movement



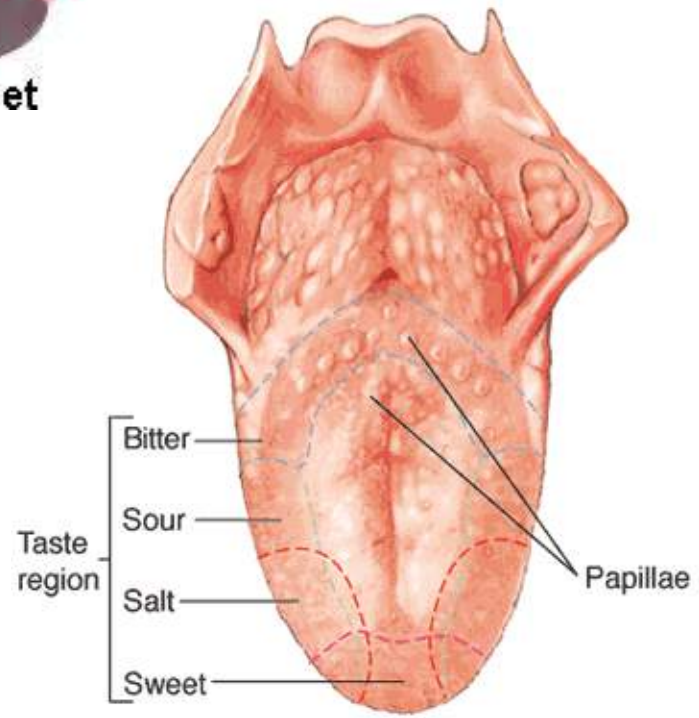
Olfaction
Gustation
Somatosenses


The pH Scale
Stomach Acid
Vinegar
Coffee
Water
Baking Soda
Ammonia Solution
Bleach
Battery
Lemon
Tomato
Milk
Blood
Stomach Tablets
Soap
Drain Cleaner
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
Acidic
Neutral
Alkaline

- Why do we have taste?
- Function?
- Covid effects?
- Why does food taste bland when you are sick?

Gustation

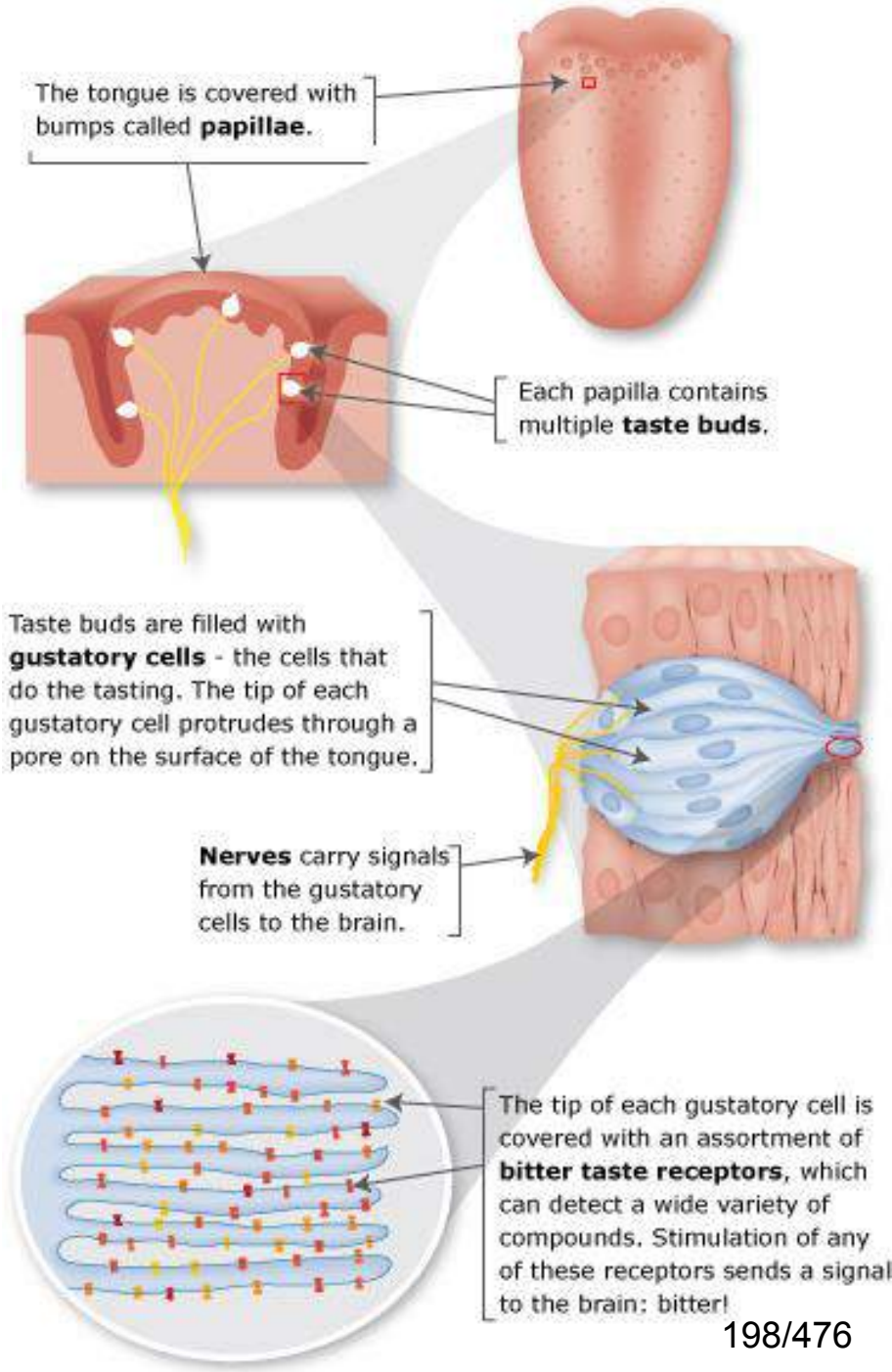
- Substance molecules act like chemicals that activate the taste receptors (chemoreceptors)
- There are 5 qualities of taste:
  1. Bitterness (alkaline, caffeine, polyphenols)
  2. Sourness (Acidic)
  3. Sweetness
  4. Saltiness
  5. Umami: (*Japanese word*) means good taste refers to the taste of monosodium glutamate (MSG), a substance that is found naturally and often used as flavor enhancer in Asian cuisine
     - Umami receptors detect the presence of glutamate, an amino acid found in proteins
- Sweet and salty tastes (amino acids) are preferred over sour (acidic) and bitter (alkaline) tastes
  - Foods that rot due to bacteria are acidic and therefore, taste sour
  - Alkaloids produced by plants to prevent them from being eaten by animals taste bitter



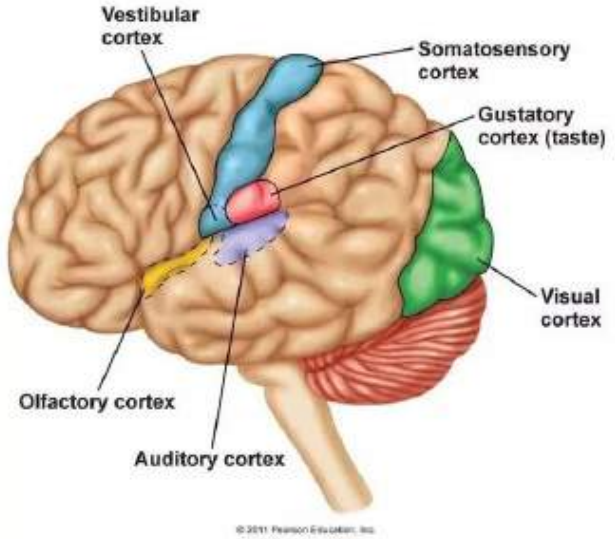
Umami
Fat???

Anatomy of taste buds:

- Papillae on the surface of the tongue contain taste buds
- Taste buds contain groups of 20-50 receptor cells arranged like segments of an orange
- Taste receptor cells are have a life span of only 10 days (renewed regularly)
  - If you burn your tongue you cannot taste food for a few days but you recover your tasting ability after a few days

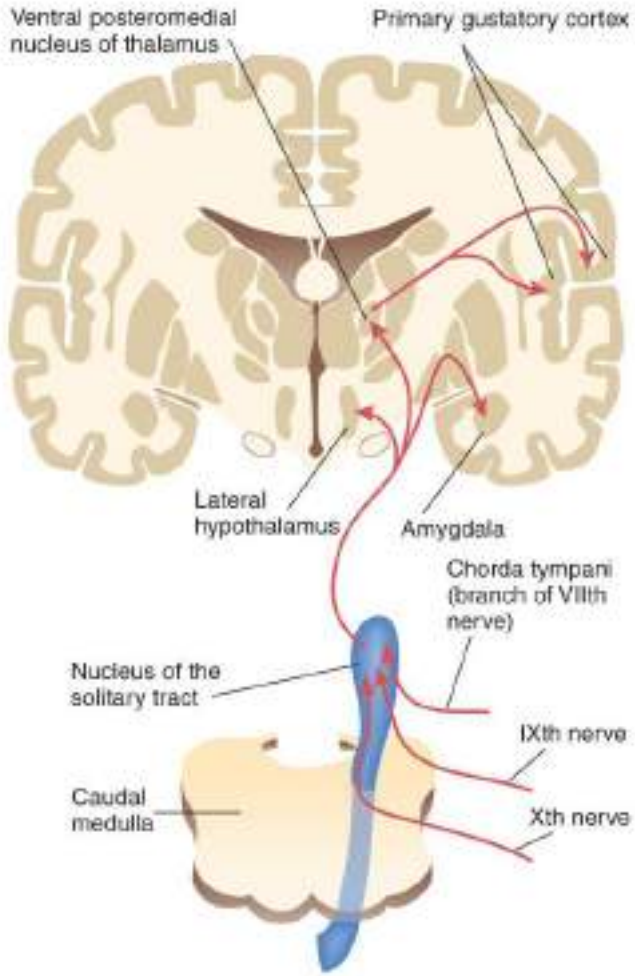


Gustatory Pathway



Gustatory cortex

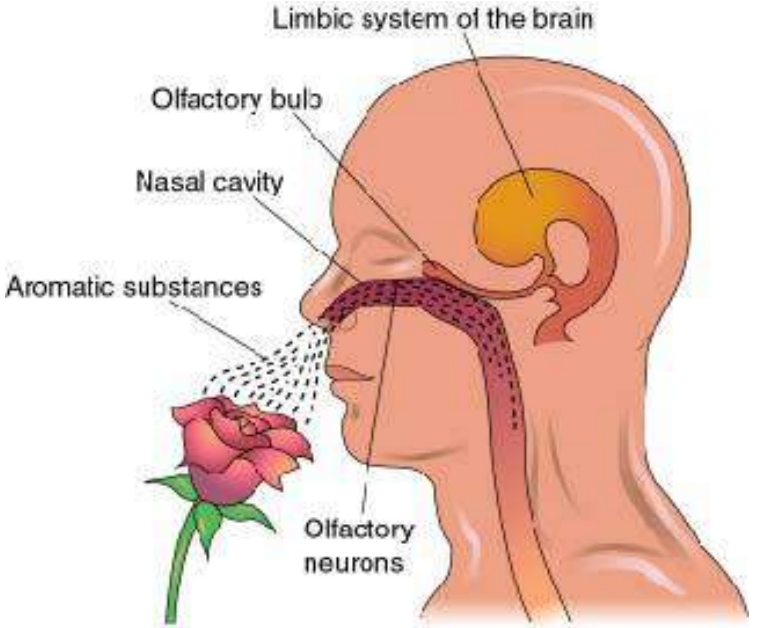
- Ipsilateral
- Different regions in the gustatory cortex code different tastes
- Gustatory information also reaches the amygdala and hypothalamus which may play a role in reinforcing a tastes and feelings of pleasure after eating preferred food
- The gustatory cortex also receives thermal, visceral, and nociceptive (painful) stimuli which plays a role in determining the palatability of food

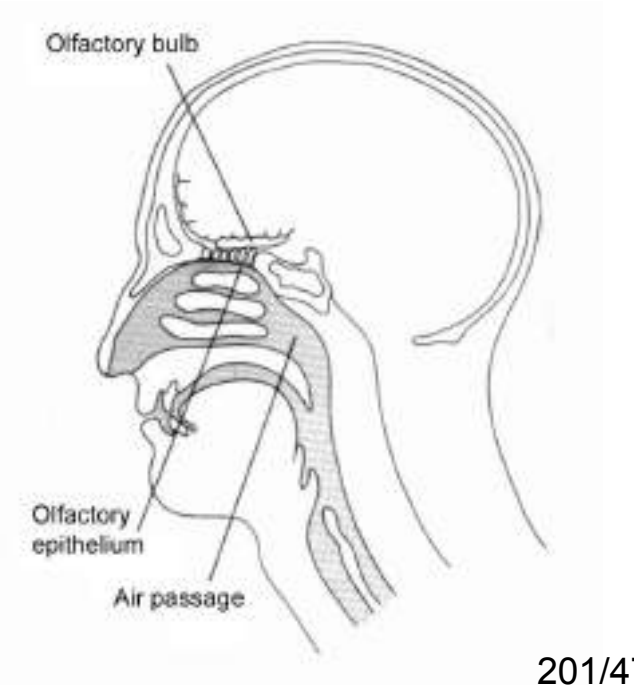


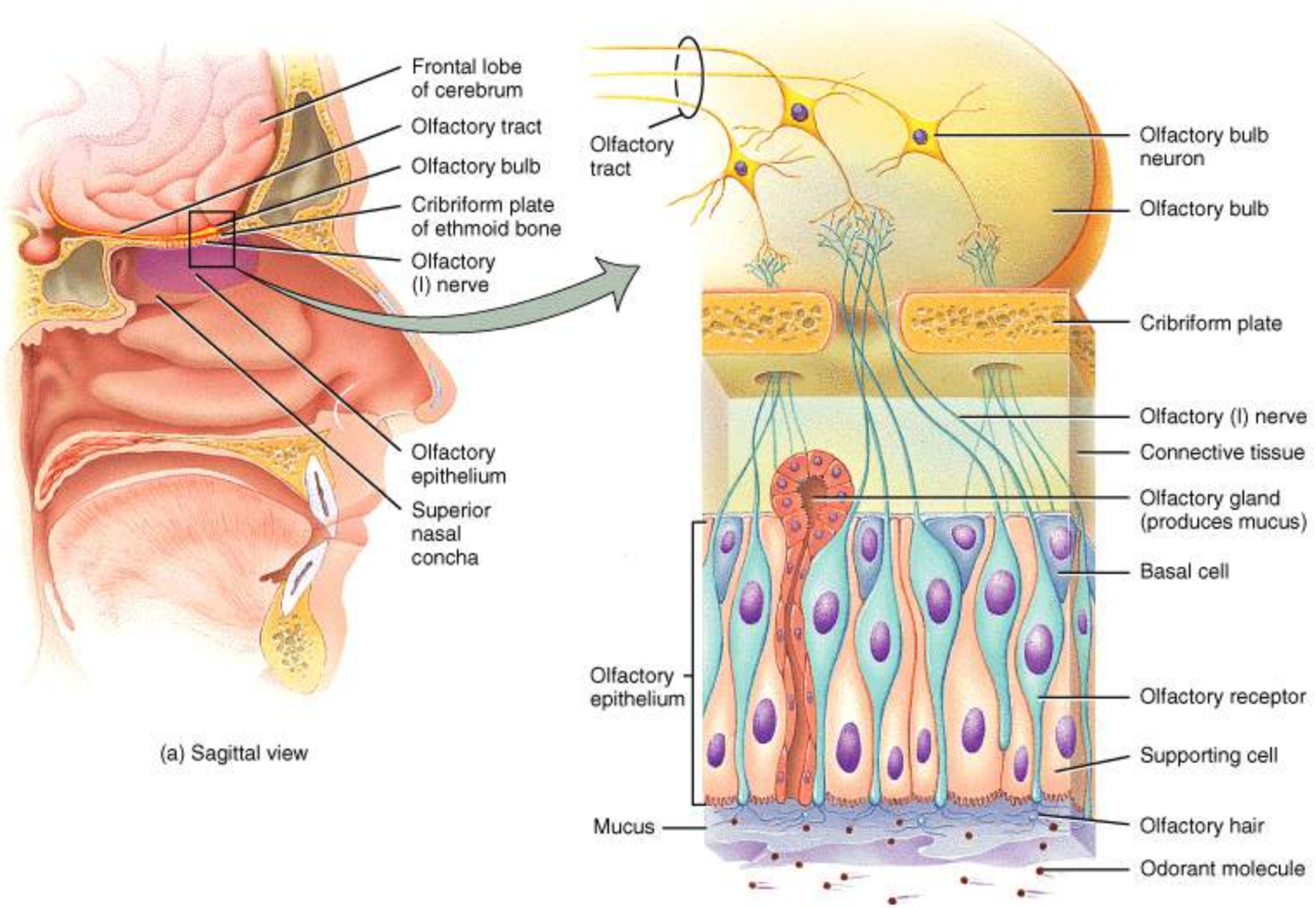
- What is purpose of smell?

Olfaction

- Another chemical sense that helps identify food and avoid spoiled/rotten food
- Taste is not a highly discriminating sense, and there is functional overlap between taste receptor cells. In contrast, odor is highly discriminating.
- Helps other species to track prey
- In humans, smells can evoke memories



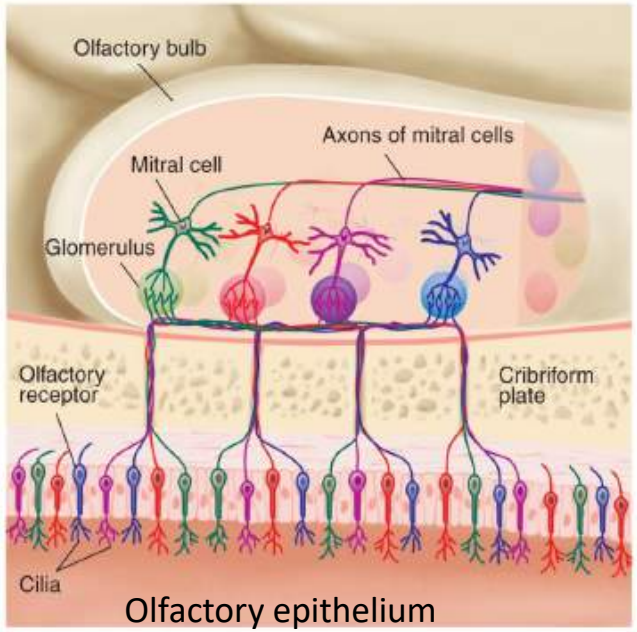




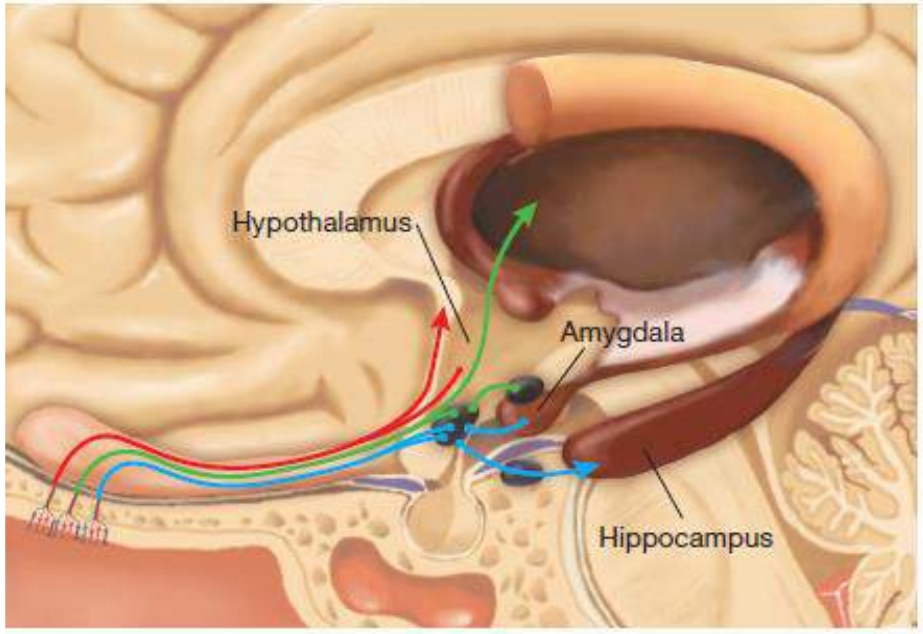
Anatomy of Olfactory System

- We have 6 million olfactory receptor cells on the mucous membrane (olfactory epithelium) inside our nose

- detect painful odorants such as ammonia



Olfactory receptor cells → glomerulus → mitral cells → amygdala (emotional valence) + hypothalamus (reception or rejection of food) + hippocampus (memories)



Encoding Odor

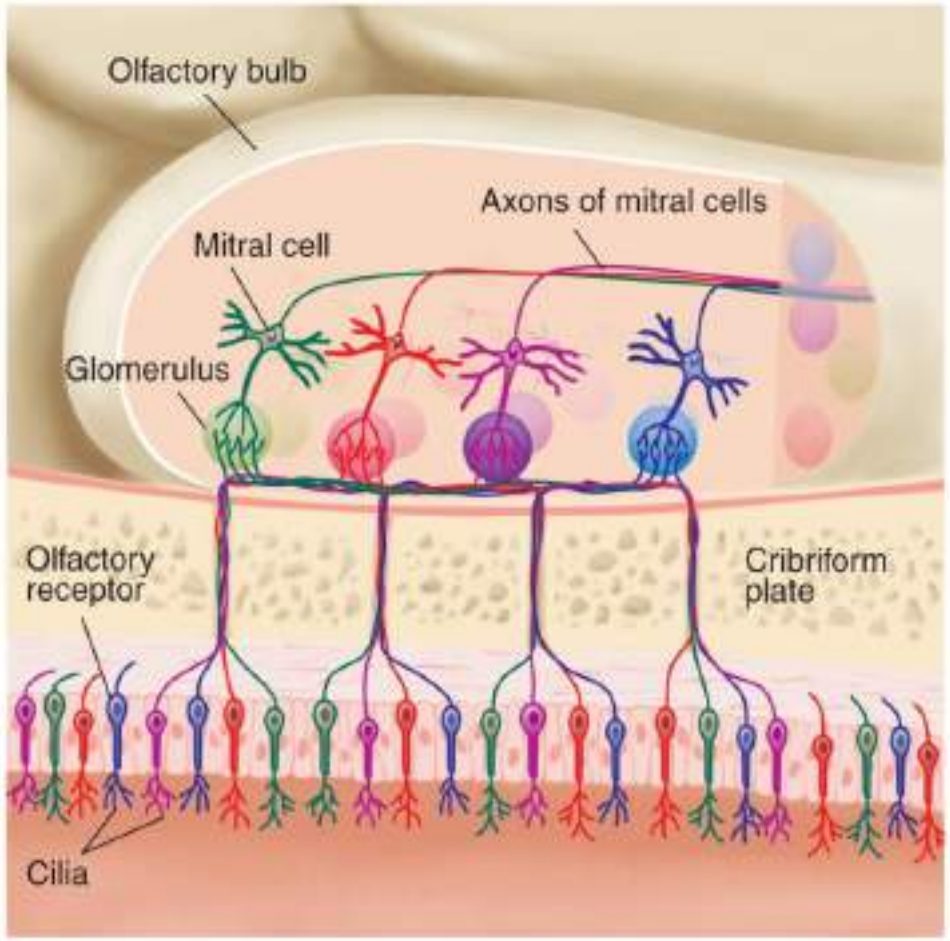
- Each glomerulus receives axons from specific type receptor cells that encode a specific odor.

- each glomerulus receives information from approximately 2,000 olfactory receptor cells detecting the same odor.

- Glomeruli can also inhibit activity in other glomeruli (more active inhibit less active glomeruli)
  - which is why we can mask odors (air fresheners, reuse old food with spices)

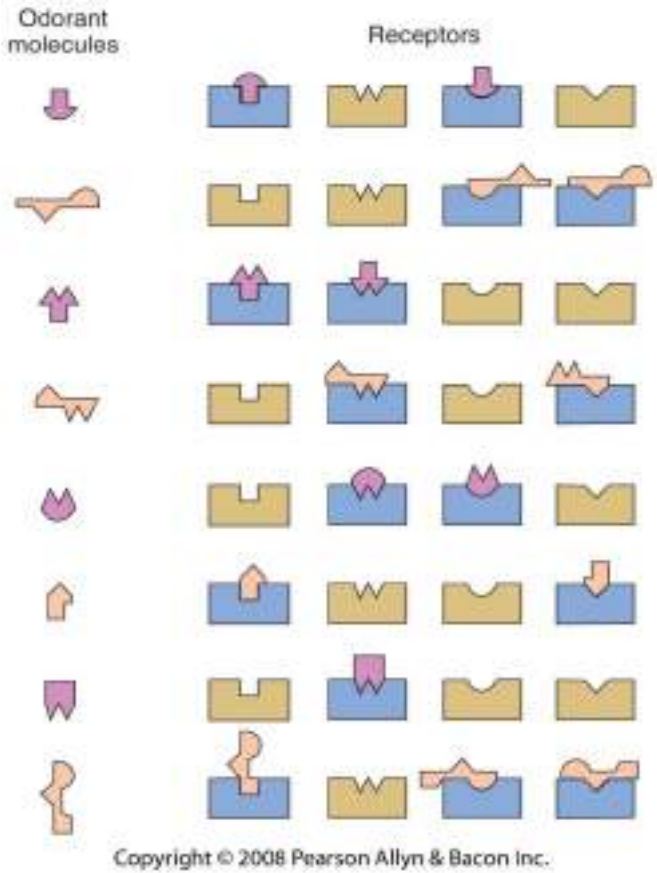
- Humans can recognize up to 10,000 different odors but with only

339 different olfactory receptors. How?



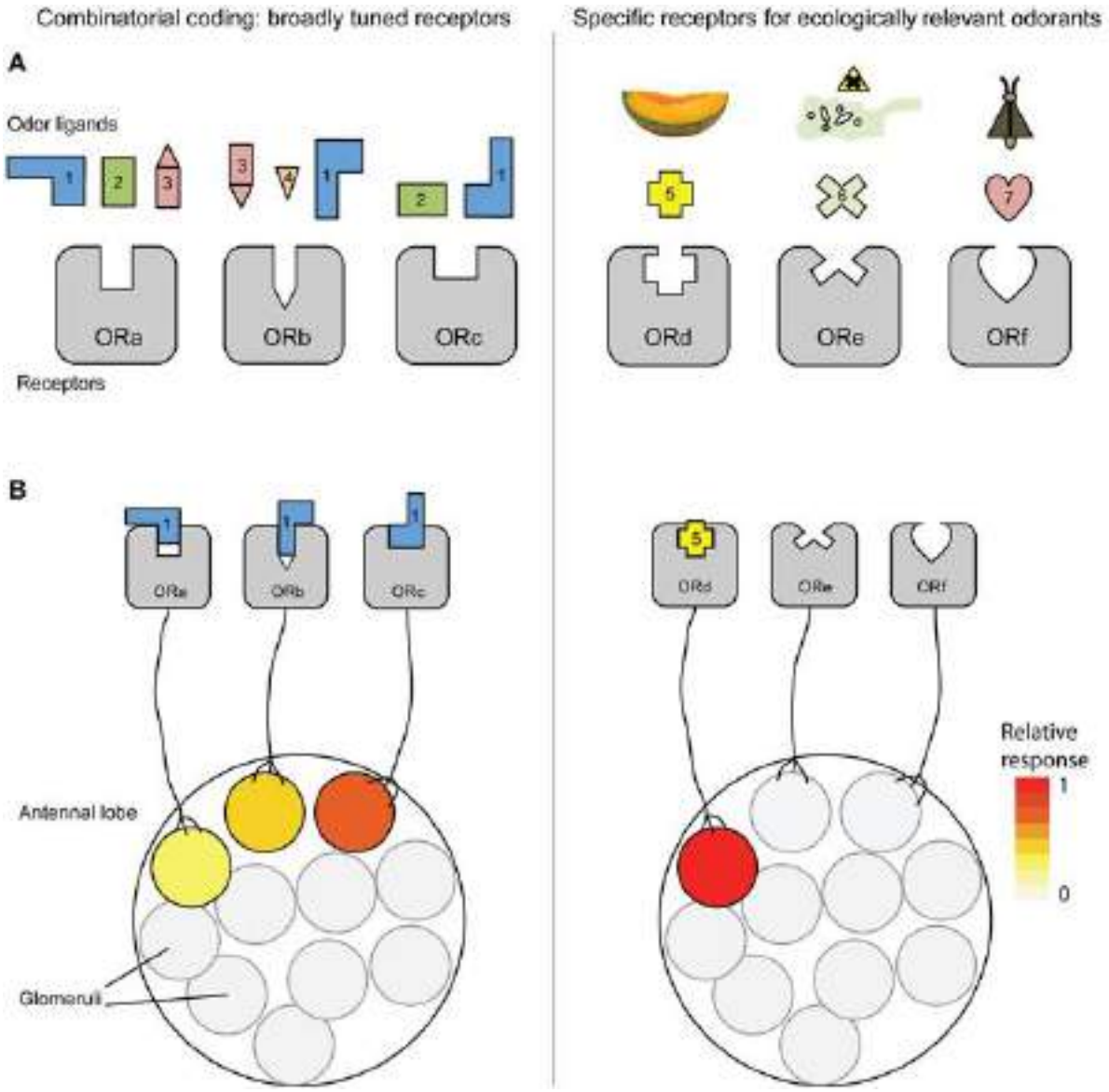
A hypothetical explanation of coding of olfactory information

Discriminating odor



e.g mint flowery sweet spice

-
- Identification of an odorant is a "lock and key” (different shapes and sizes of molecules) relationship between the odorant and the membrane receptor.
- Odorants bind to more than one receptor – high, moderate or weak binding
- Molecules of an odorant bind with olfactory receptors and open sodium channels and produce depolarizing receptor potentials
- Every odor creates a specific pattern of activation in different glomeruli
- Every pattern represents an odor which is identified by the olfactory cortex



Odorant receptors	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Description
A					●										rancid, sour, goat-like
B		●				●									sweet, herbal, woody
C	●			●	●		●			●	●				rancid, sour, sweaty
D		●			●	●									violet, sweet, woody
E	●			●	●		●	●		●	●	●			rancid, sour, repulsive
F				●	●		●			●					sweet, orange, rose
G	●			●	●		●	●		●		●		●	waxy, cheese, nut-like
H				●	●		●			●		●			fresh, rose, oily floral

MODIFIED AFTER LINDA BUCK AND COLLEAGUES IN CELL VOL 96, MARCH 5, 1999

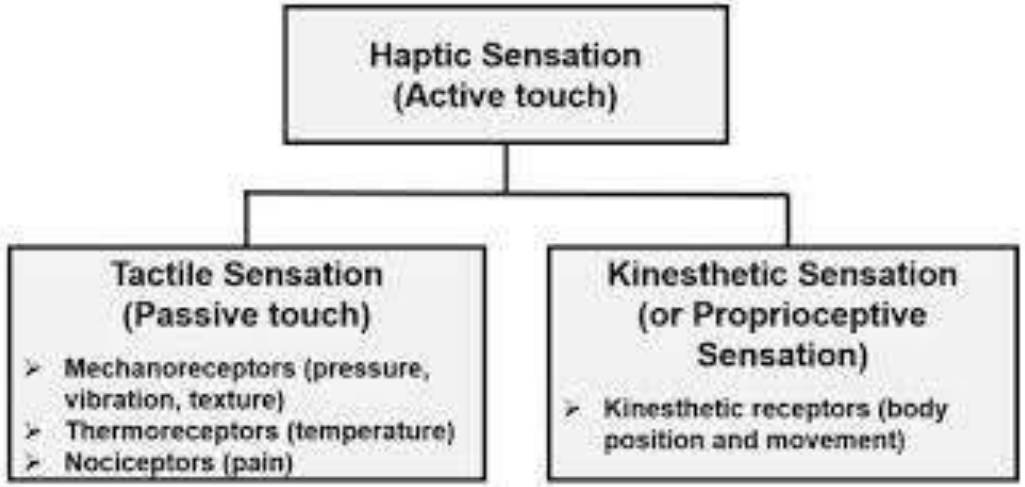
Flavour = olfaction + gustation.

- What is somatosense?
- Function?

Somatosenses

Somatosense	Function
Cutaneous Senses	Provide information from the surface of the body.
Proprioception	Provide information about location of body in space.
Kinesthesia	Provide information about movement of body though space.
Organic Senses	Provide information from in and around internal organs.

- Cutaneous (skin) senses respond to a range of stimuli (Tactile):
  - Pressure, Temperature, Vibration, Pain
- Kinesthetic & Proprioception senses
  - Muscle, skin, and joint movement
- Organic senses
  - Stomach ache, muscle cramps
  - Drinking hot/cold liquid down your throat



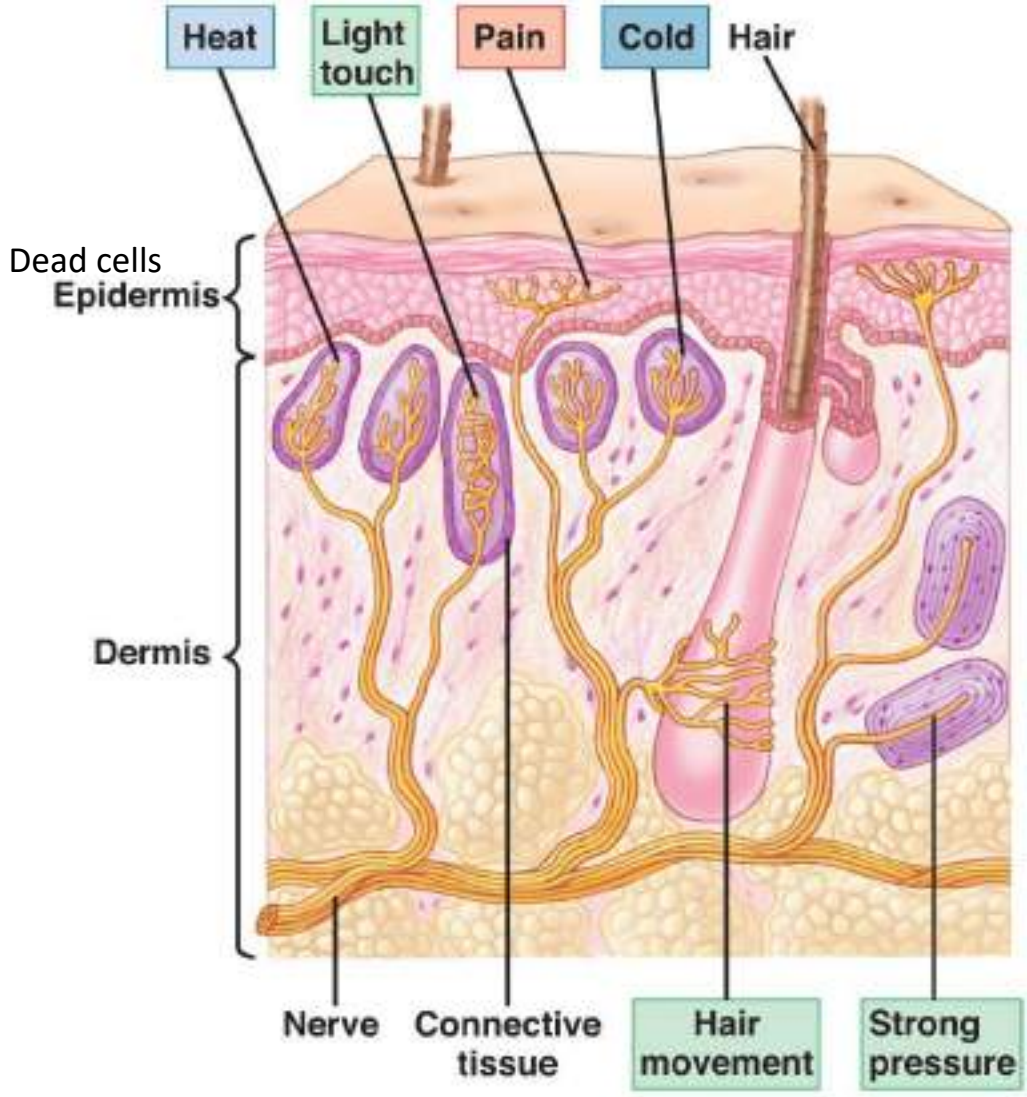
Skin Receptors

Hairless skin (glabrous skin) is found on our fingertips, palms and bottom of toes and feet

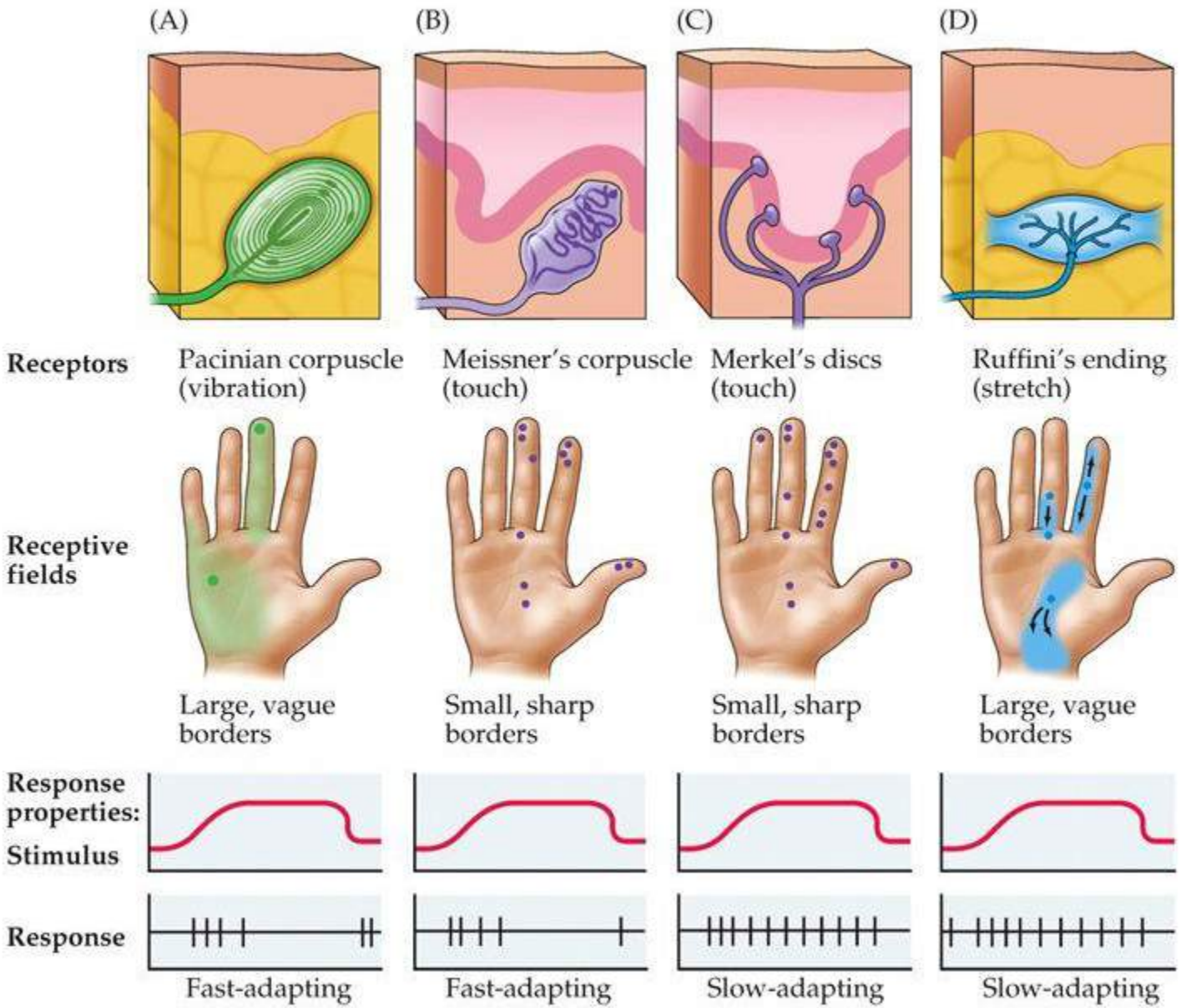
It has a complex mixture of receptors to explore the external environment with our palms and fingers – touching or holding objects

- Glabrous skin receptors
  - Free nerve endings – painful stimuli and temperature changes
  - Ruffini corpuscles – respond to pressure on skin
  - Pacinian - respond to rapid vibrations
  - Meissner's corpuscles – respond to low freq vibration and taps on the skin
  - Merkel endings – respond to touch and light pressures

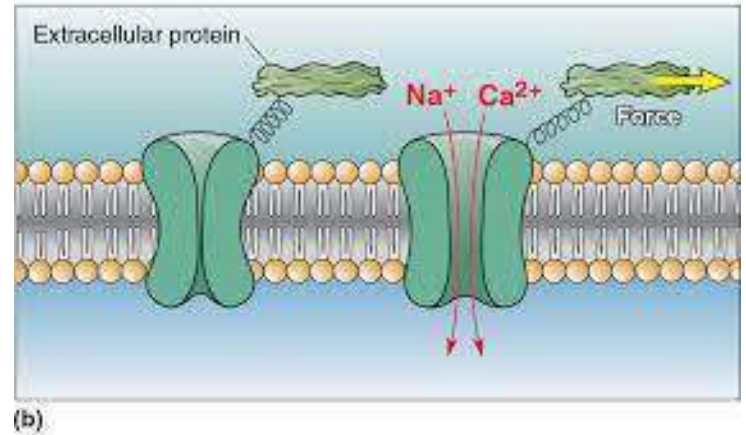
- Hairy skin receptors
  - Free nerve endings – at the base of hair shafts that detect movement of hair
  - Ruffini corpuscles – respond to pressure on skin
  - Pacinian - respond to rapid vibrations

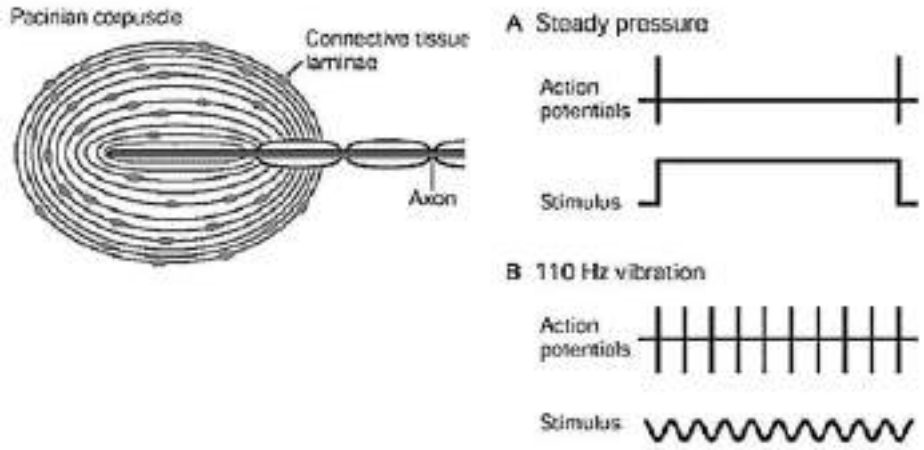


Properties of Skin Receptors Related to Touch

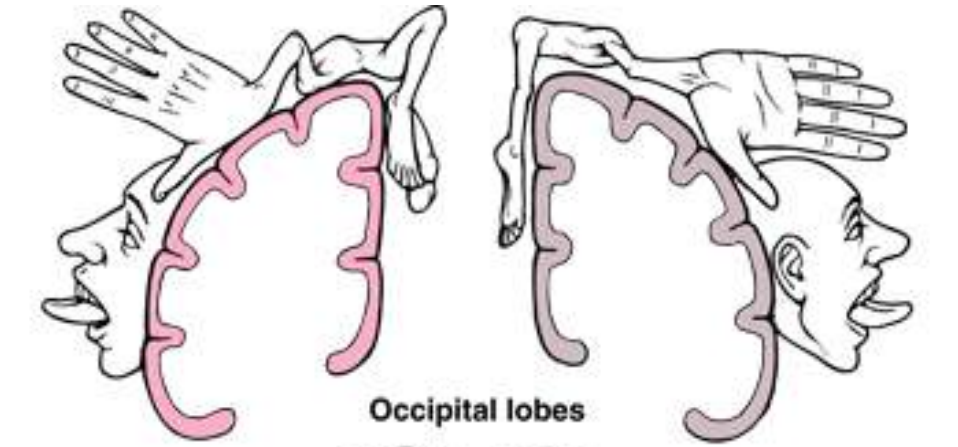


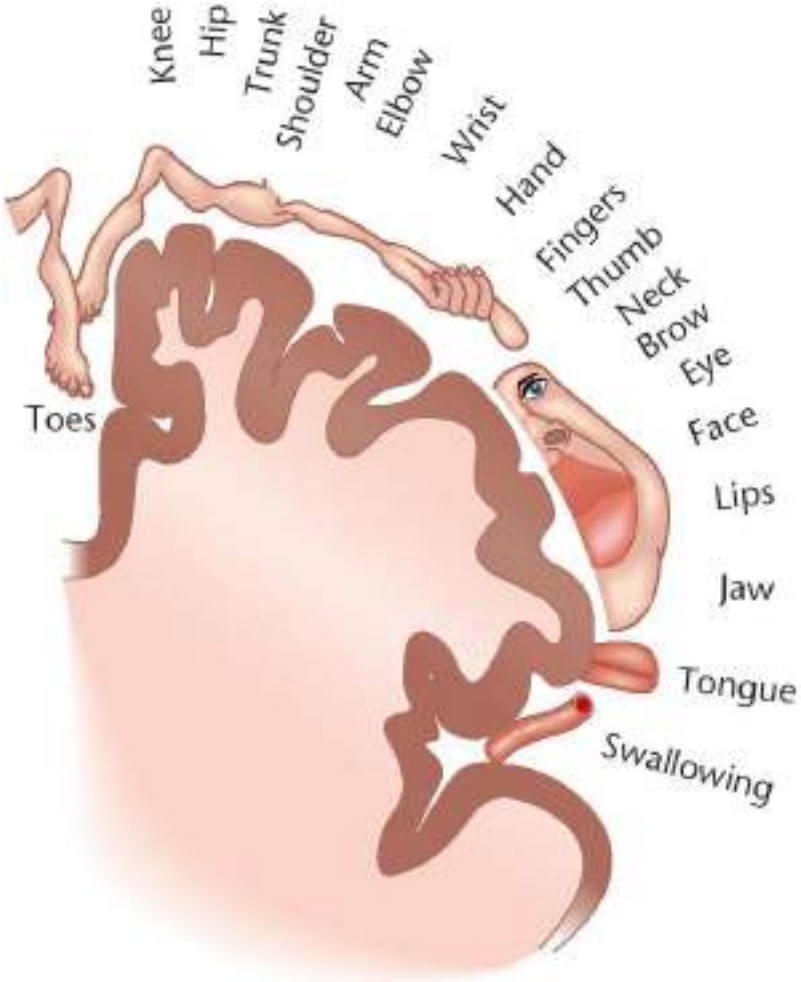
***BIOLOGICAL PSYCHOLOGY 7e*, Figure 8.13**

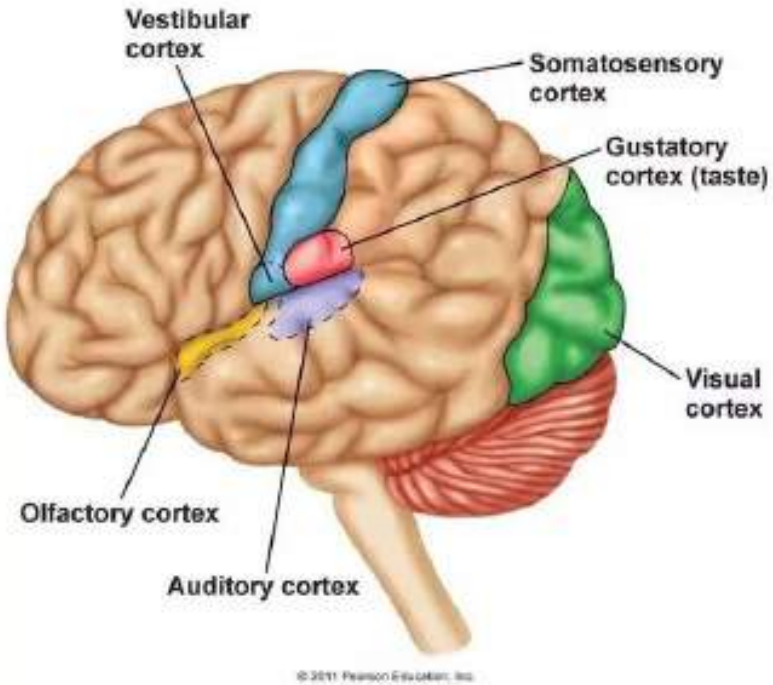


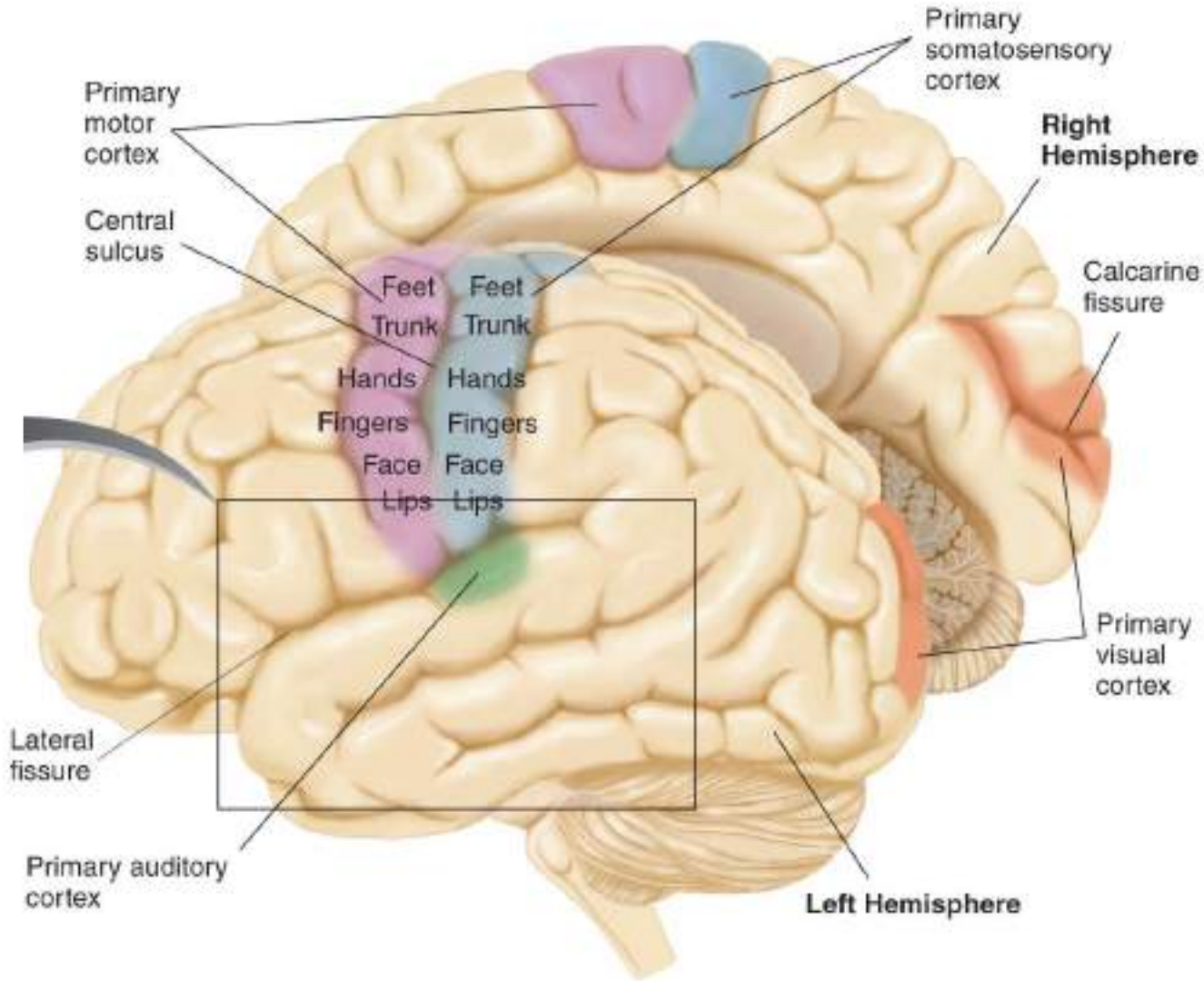


Homunculus – "little human"



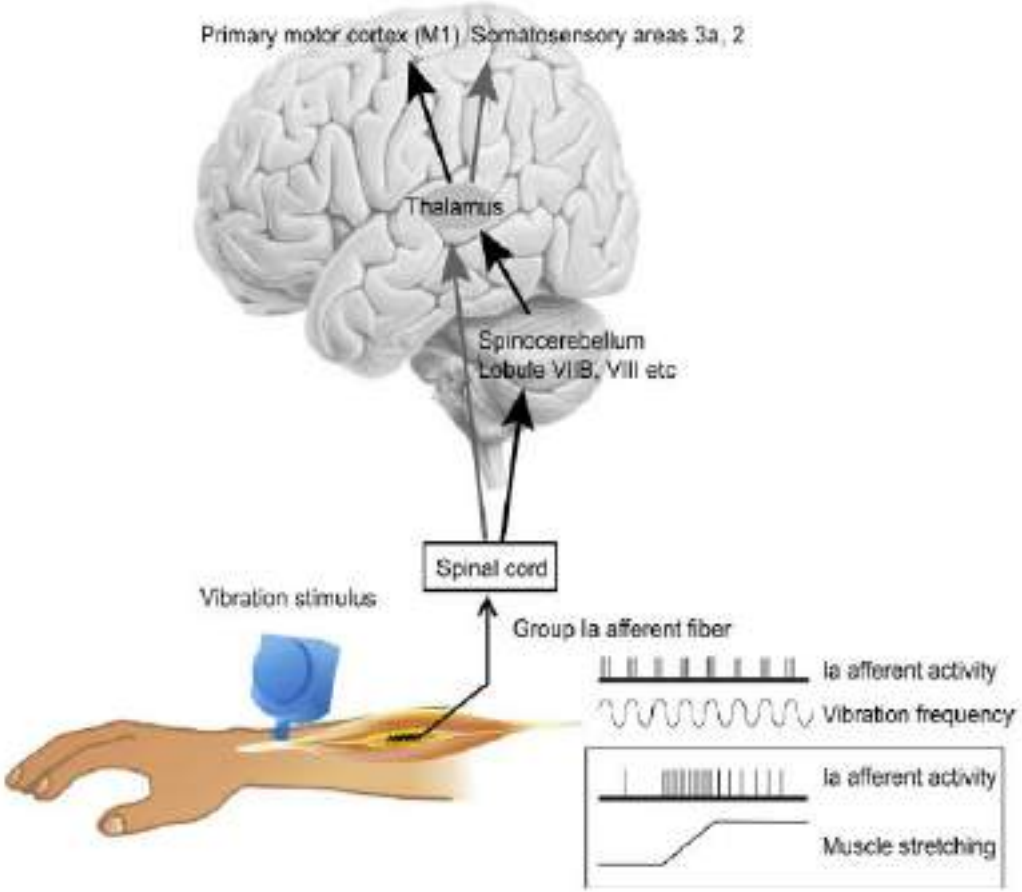






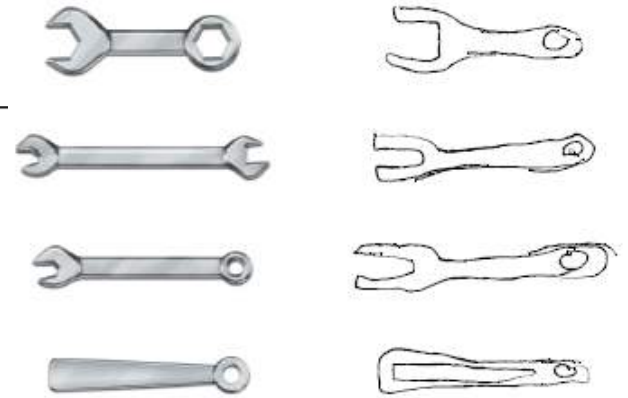
Perception of touch

- Mechanoreceptors respond to mechanical stimulation
- Dendrites of mechanoreceptors are stimulated by pressure and vibration on skin (mechanical energy → electrical energy)
- tactile sensation is localized- receptors are very specific to regions on the skin surface
- fingertips for precise movements like playing the violin need very accurate tactile and proprioceptive feedback
- corresponding contralateral hemispheres in such people allocate more cortex to accomplish such fine tasks

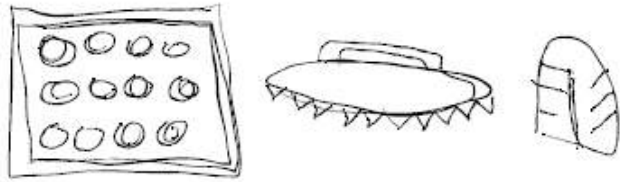


Tactile Agnosia

(a) Drawings of wrenches felt but not seen by M. T. Although the patient did not recognize the objects as wrenches, he was able to draw them accurately. (b) Drawings of objects felt but not seen by E. C. The patient could neither recognize the objects by touch nor draw them accurately.



(a)



Casette tape | Staple remover | Plug adaptor

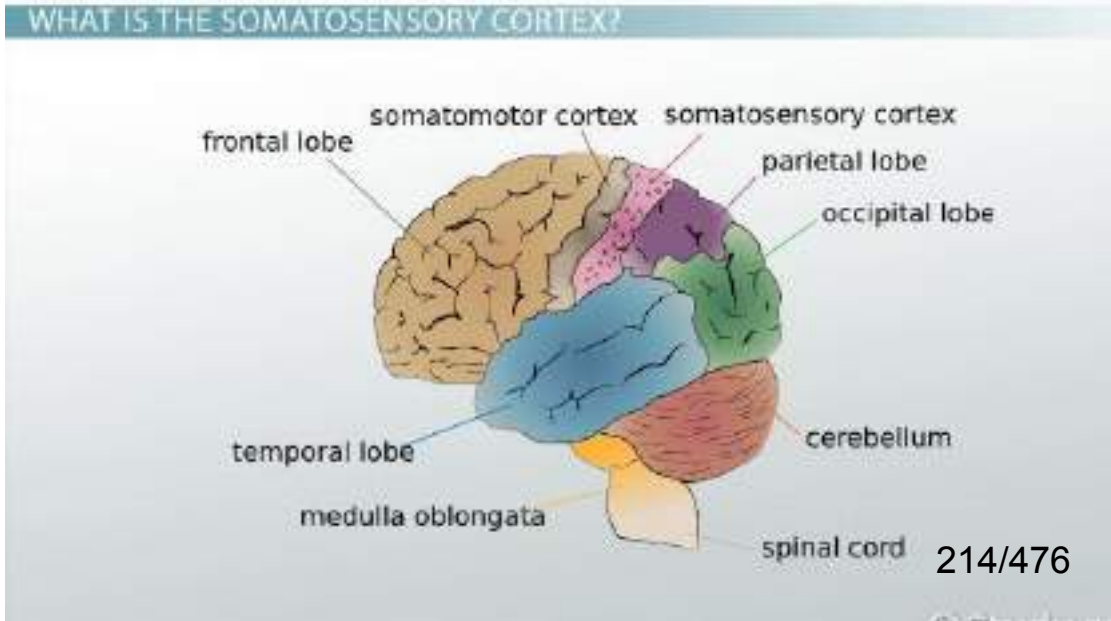
(b)

Tactile Agnosia (Astereognosis)

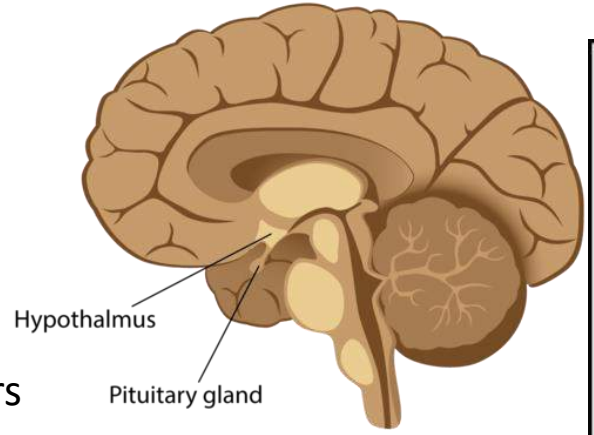
- Inability to identify object by touch (in the absence of visual input).
- Patient can name object by sight, draw object if asked to, and will reach for object if instructed to do so.

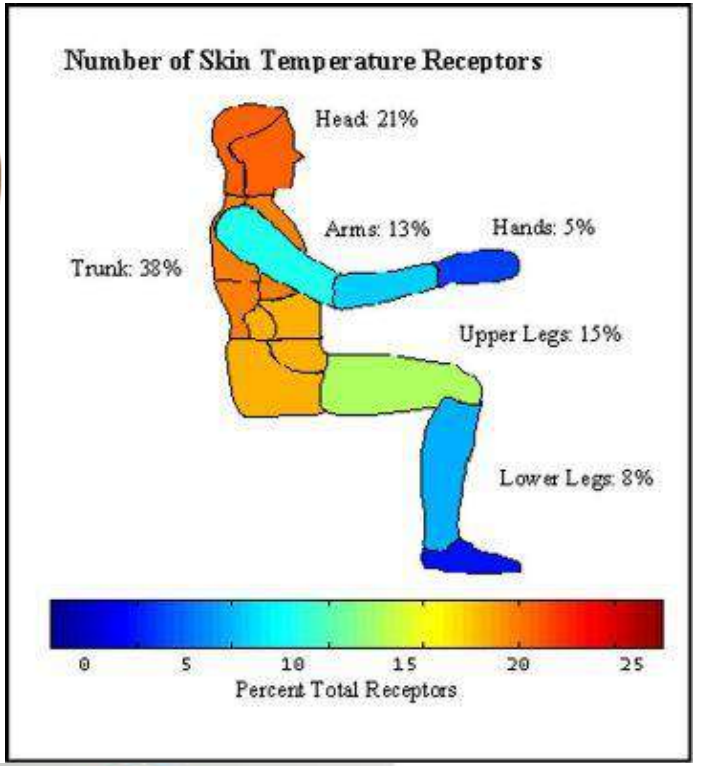
Tactile Agnosia – deficit in tactile perception

Damage to the somatosensory association cortex

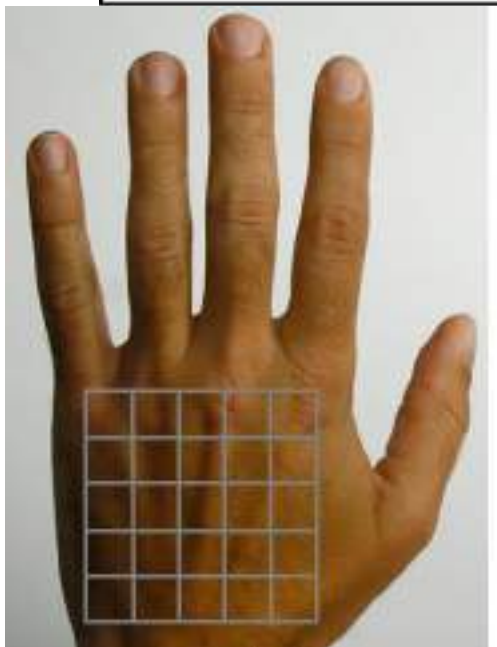


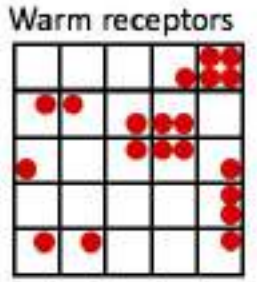
Perception of Temperature

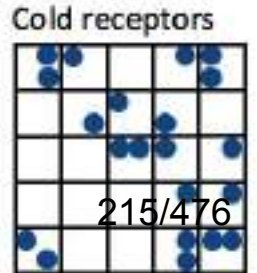


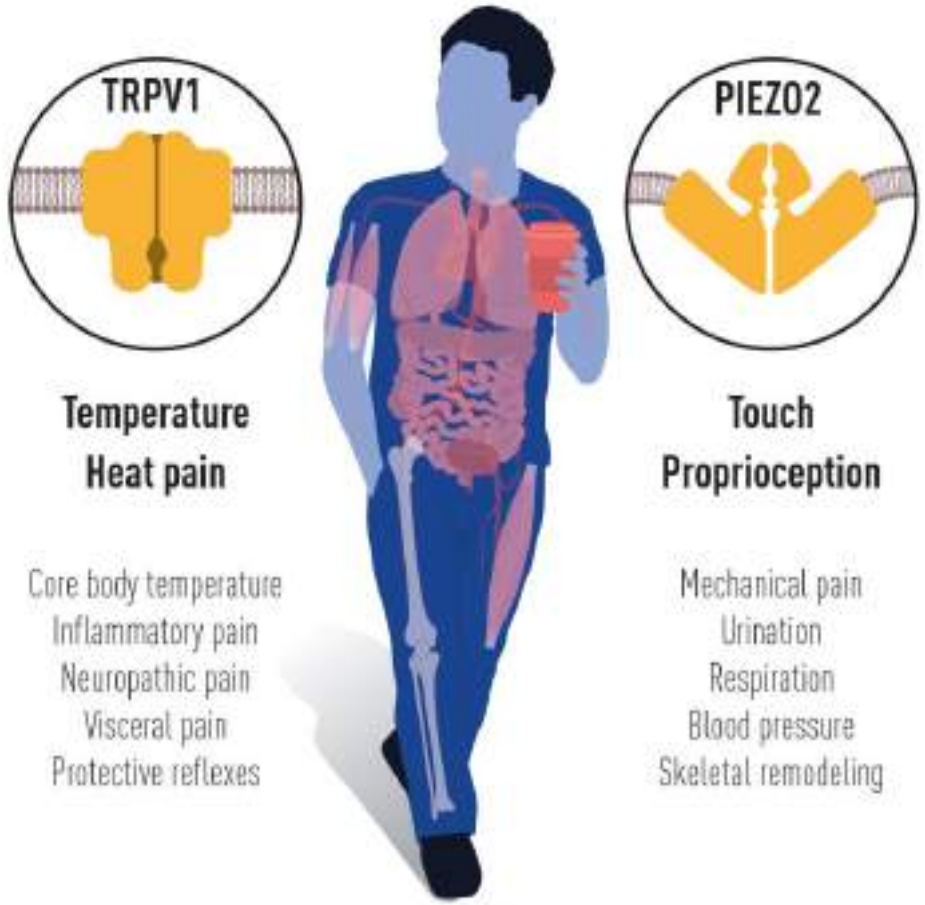


- Two types of thermal receptors – warmth and coolness receptors
- Humans can detect a wide range of temperatures
  - 8° C (noxious cold) to 52° C (noxious heat)
- Anterior hypothalamus → maintaining body temperature
- Our brain adjusts the core body temperature based predominantly upon feedback it receives from the temperature receptors in the torso and head
- Some chemicals can also produce the sensation of warmth or coolness – e.g. mint- coolness, capsaicin - heat
- Accomplished by free nerve endings

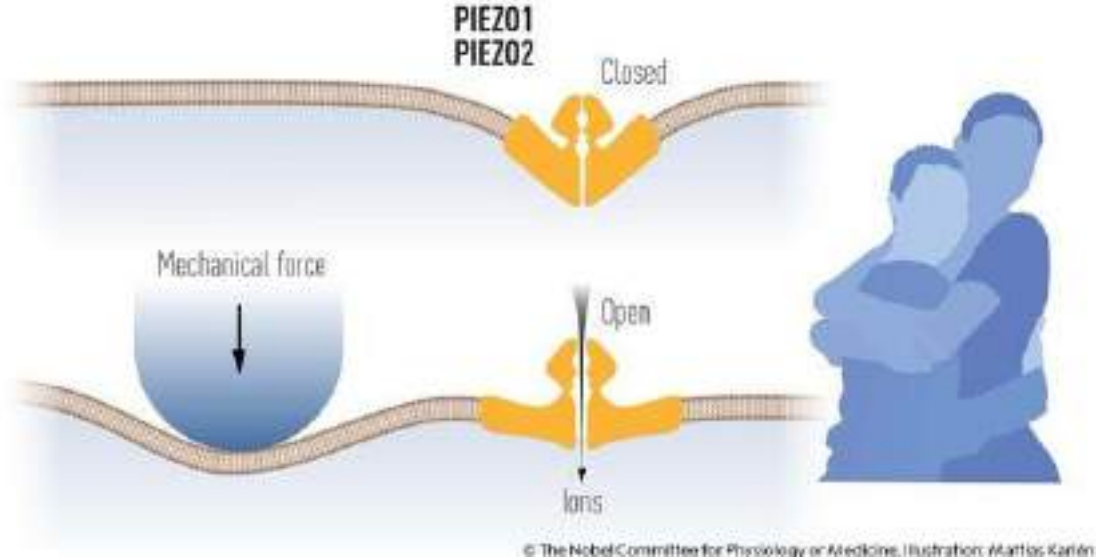


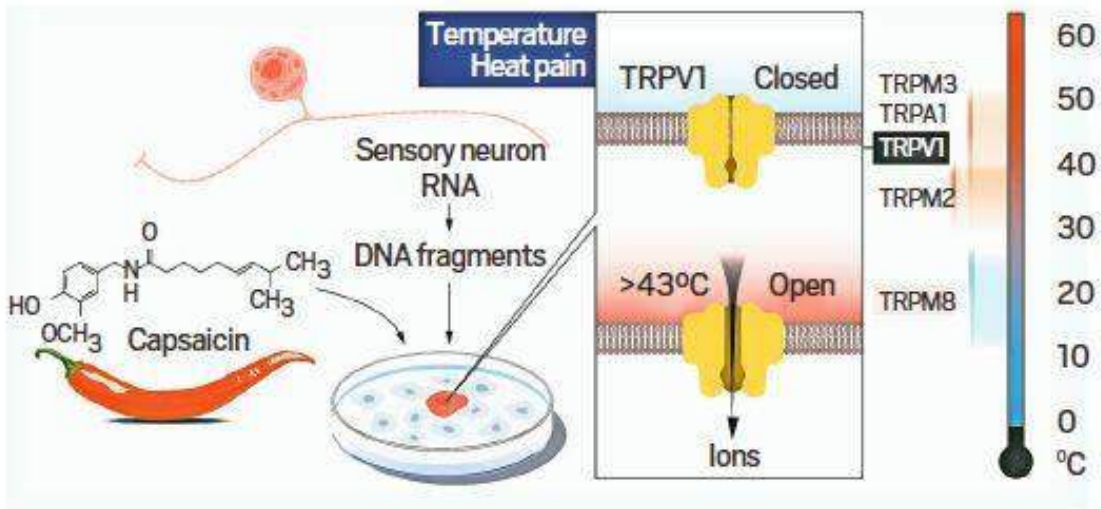






Nobel prize in Physiology/Medicine 2021 –

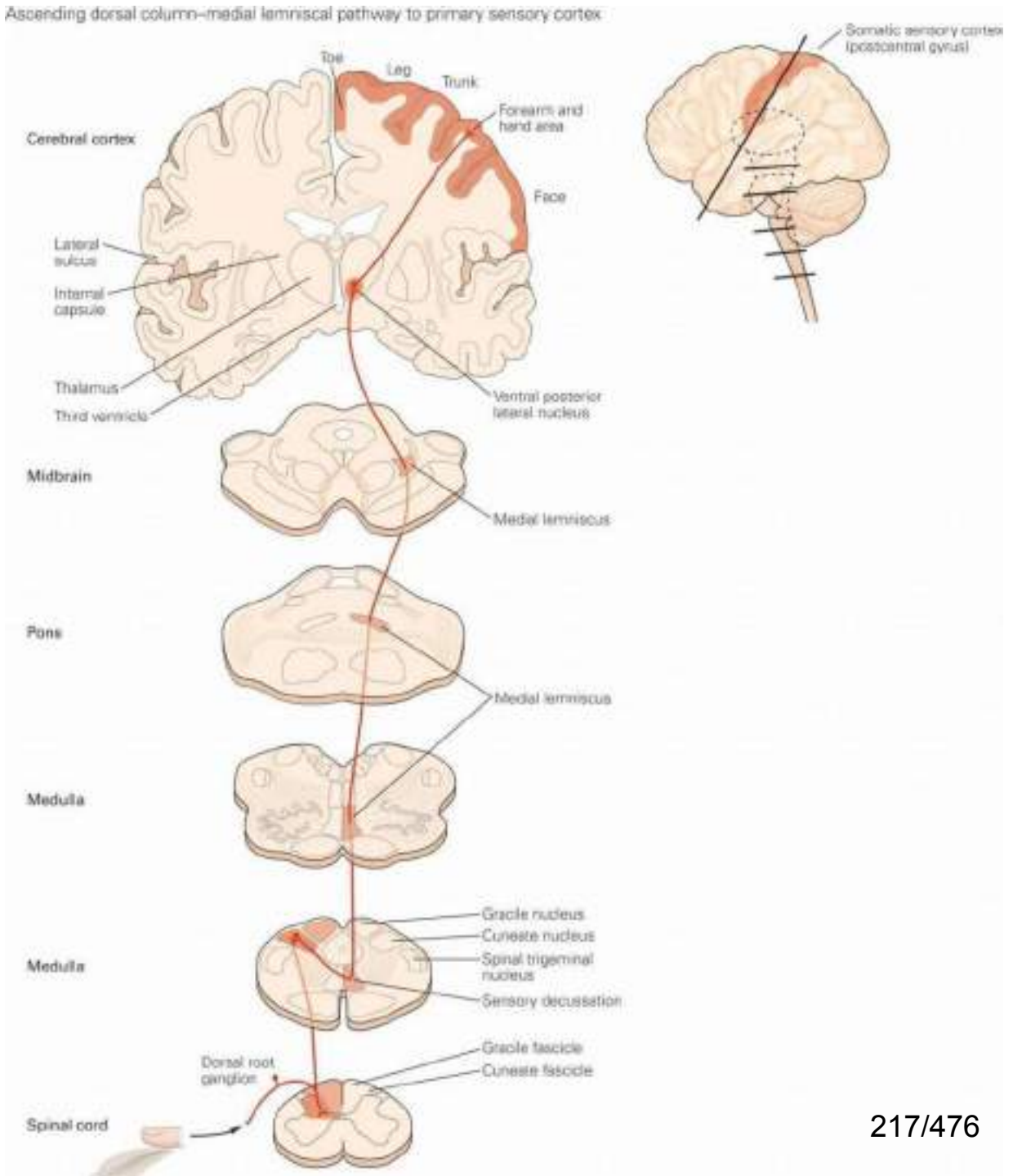




The discovery of the receptor TRPV1 paved the way to the unravelling of additional receptors, which together code for temperature sensation.
nobelprize.org

Perception of Pain

- 3 types of pain receptors
  1. Pain due to intense pressure – striking, excessive stretching or pinching of skin → high threshold
  2. Pain due to extremes of heat to acids and capsaicin (chili peppers) causing inflammation
  3. Pain due to internal injuries or disorders – migraine, damage to muscles, cancer, etc.
- Accomplished by free nerve endings



Types of pain

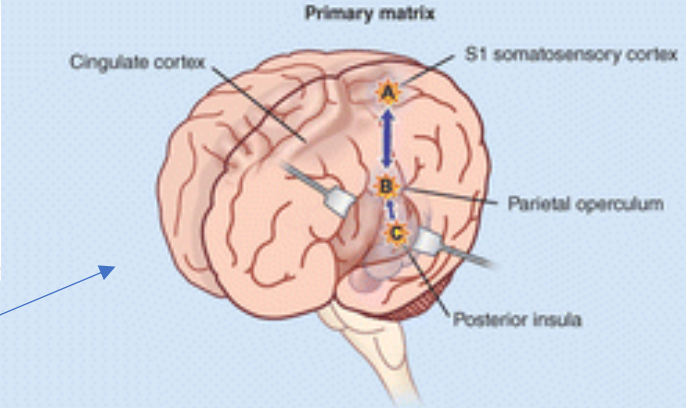
Effects of pain	Brain Regions Involved
Sensory component	Pathway from spinal cord to thalamus to primary/secondary somatosensory cortex
Immediate emotional consequences	Insular cortex, ACC, primary somato-sensory cortex
Long-term emotional consequences	Prefrontal cortex

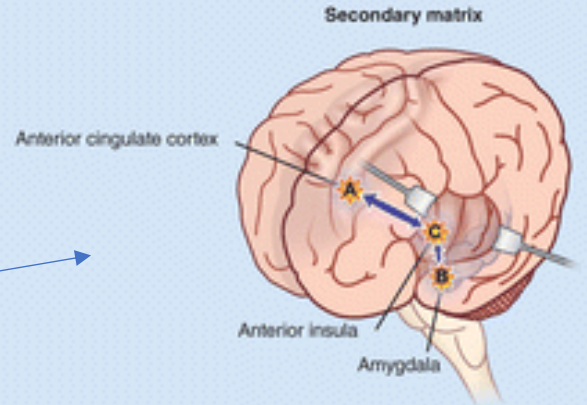
- Pain is a complex phenomenon
- Has 3 different perceptual and behavioral effects

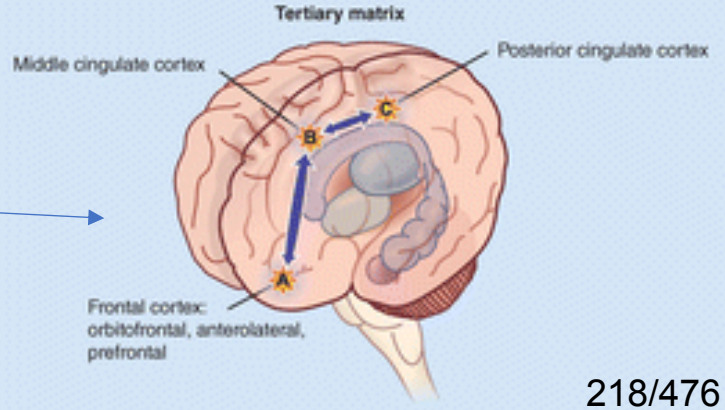
1. Sensory component
   - pure sensation of intensity of painful stimulus
   - Spinal nerves → thalamus → primary somatosensory cortex → secondary somatosensory cortex

2. Immediate emotional reaction
   - unpleasantness following the sensation
   - Spinal nerves → Thalamus → anterior cingulate cortex and insular cortex

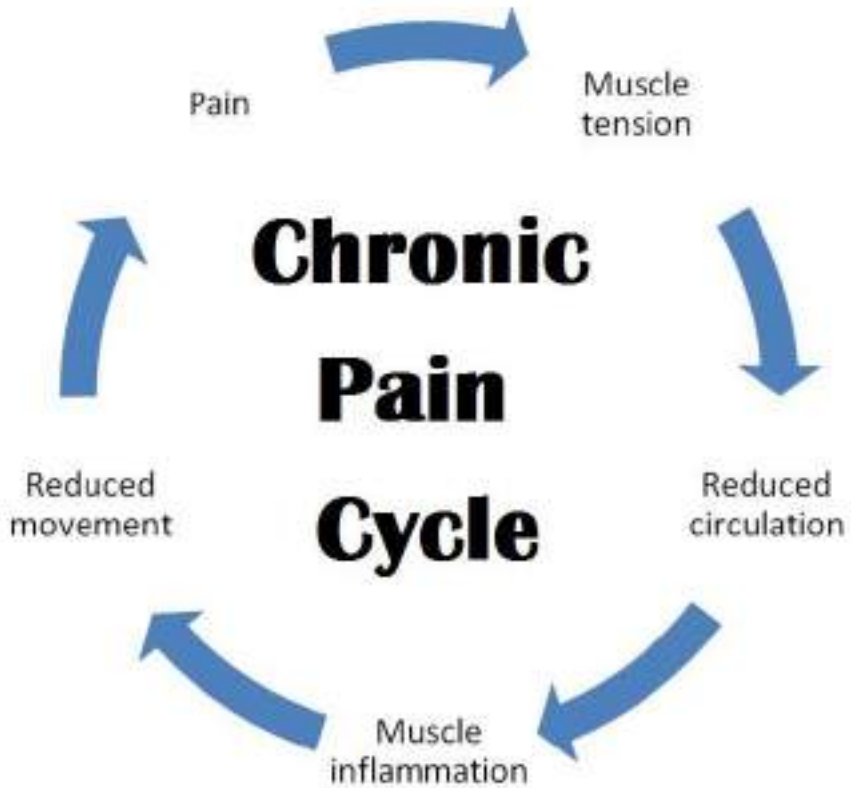
3. Long term emotional implications of chronic pain
   - Well being and comfort
   - Spinal nerves → Thalamus → frontal cortex







What is Chronic Pain?

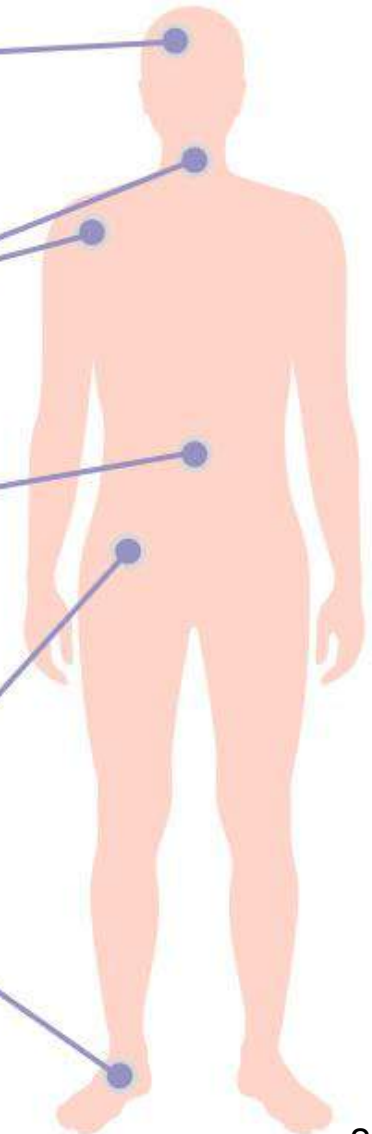


Nerve Pain (neuropathic pain, sciatica, diabetic neuropathy, etc.)

Muscle Pain (hips, legs, neck, shoulders, feet, etc.)

Mechanical/Compressive Pain (spinal cord compression, spinal disc degeneration, tumors, etc.)

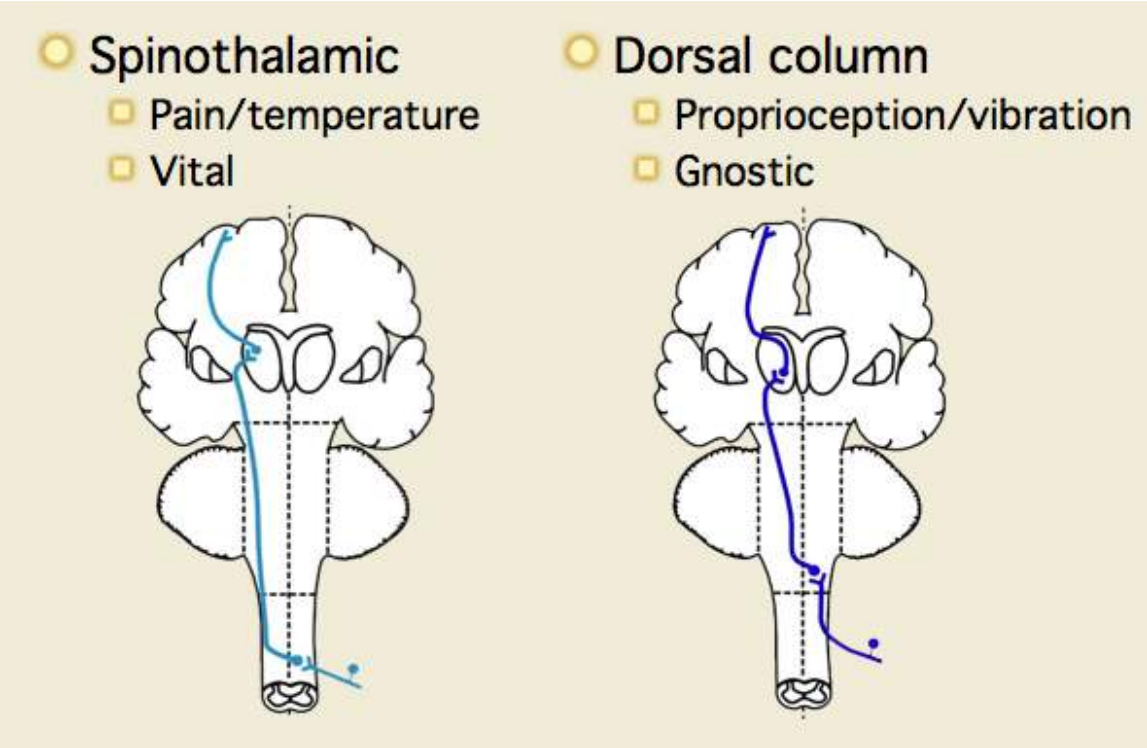
Inflammatory Pain (arthritis, infection, tissue injury, etc.)

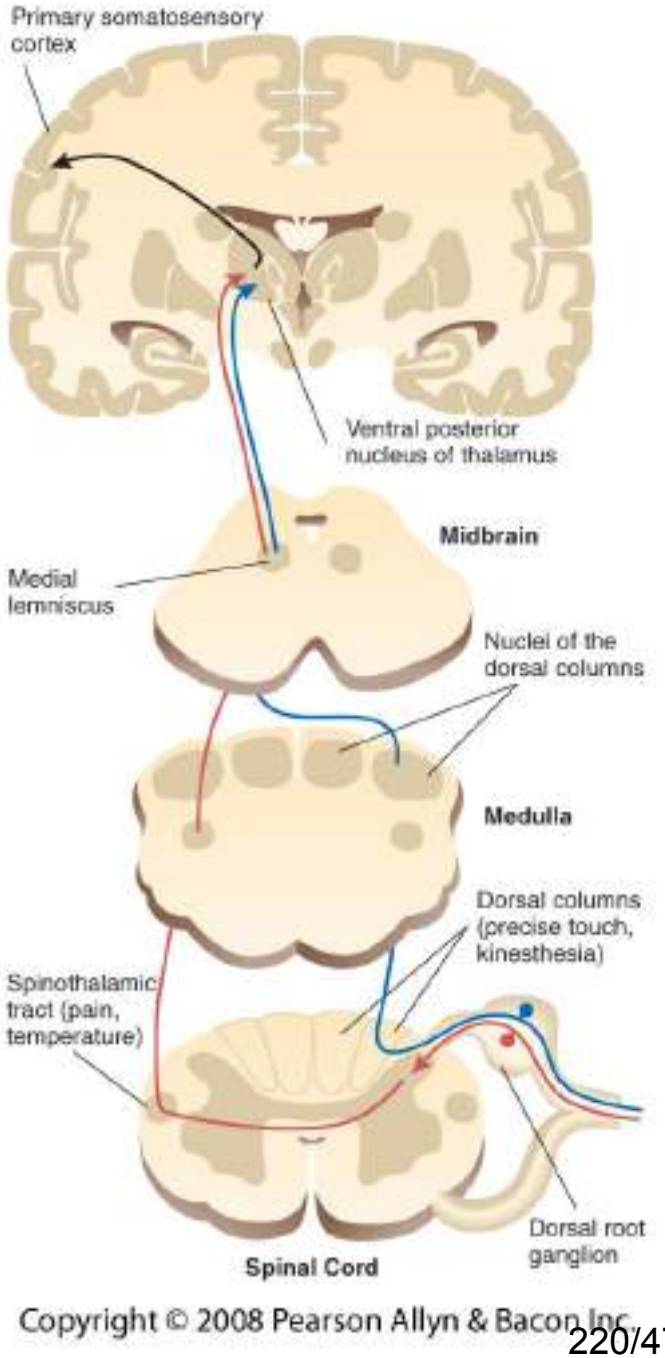


Somatosensory pathways

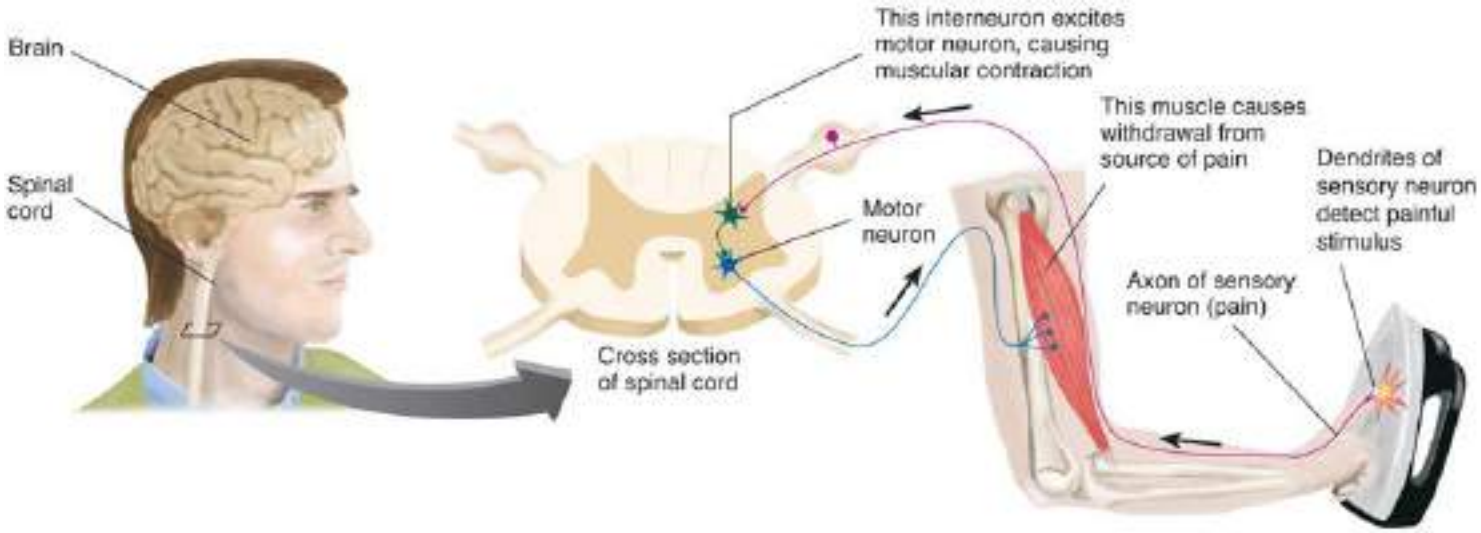
- Sensory information crosses the spinal cord at various levels to reach the contralateral hemisphere

Spinal cord injuries??

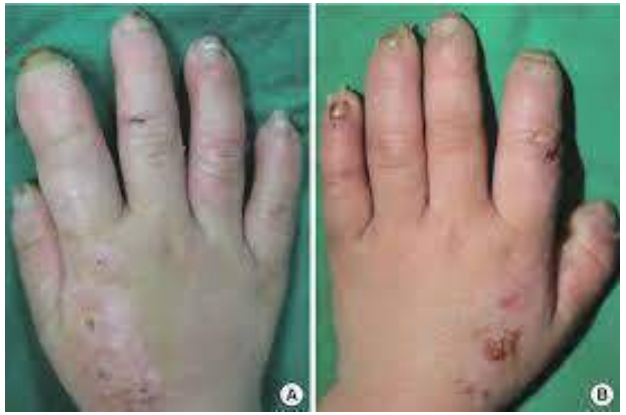




Simple withdrawal reflex



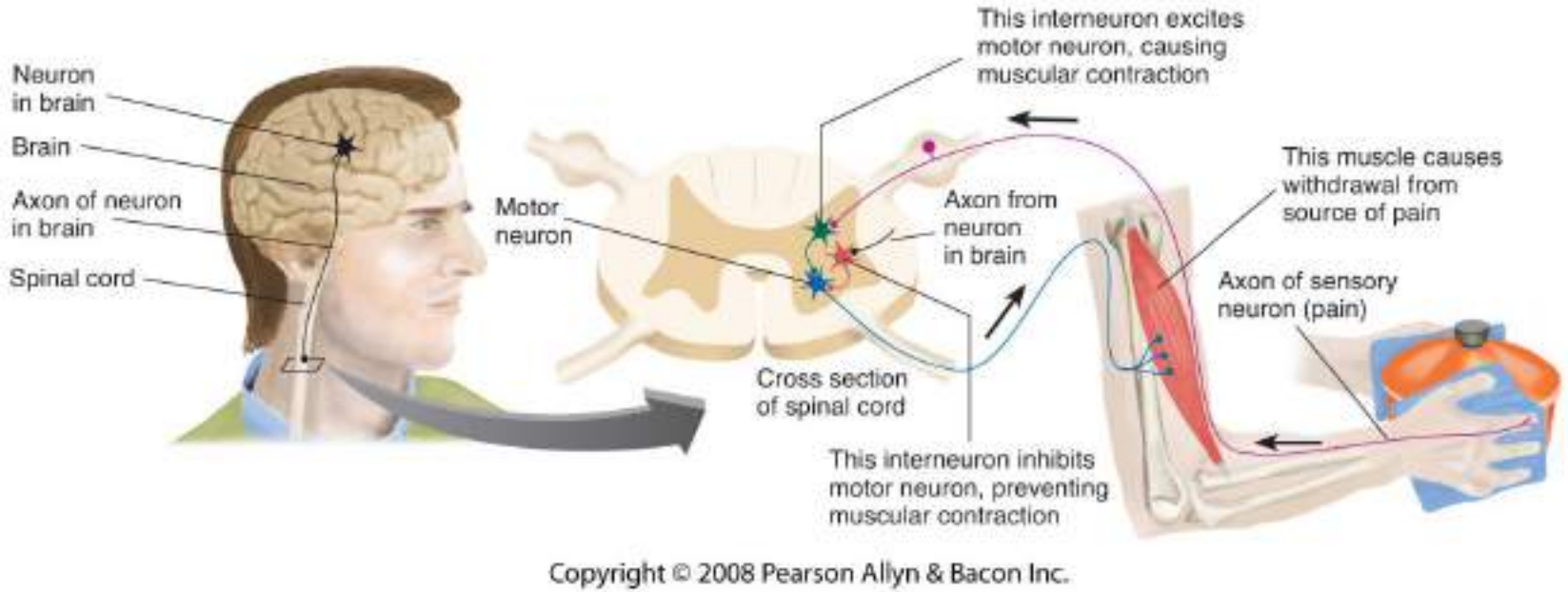
Congenital Insensitivity to Pain



The terminal boutons of the sensory neuron release a neurotransmitter that excites the interneuron, causing it to send messages down its axon. The terminal boutons of the interneuron release a neurotransmitter that excites the motor neuron. The axon of the motor neuron travels to join the muscle. When the motor neuron releases neurotransmitter, the muscle cells contract, causing the hand to move away from the hot object.

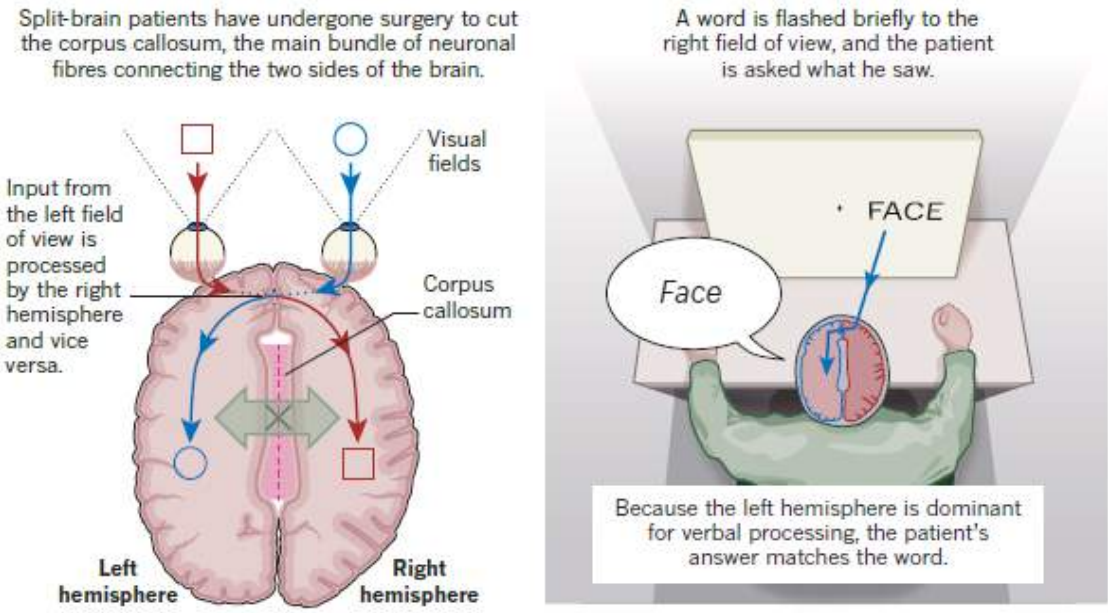
All synapses have **excitatory** effects

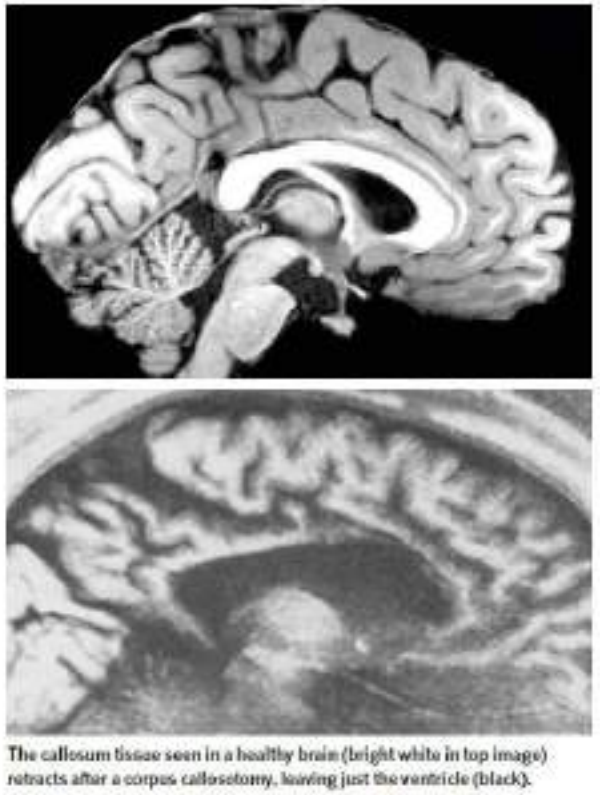
Preventing withdrawal reflex



The pain from the hot casserole increases the activity of excitatory synapses in the withdrawal reflex, which tends to cause the hand to pull away from the casserole. However, this excitation is counteracted by **inhibition**, supplied by the brain. The brain contains neural circuits that recognize what a disaster it would be if you dropped the casserole on the floor. These neural circuits send information to the spinal cord that prevents the withdrawal reflex from making you drop the casserole. The brain basically excites an inhibitory interneuron which decreases the activity of the motor neuron that was going to withdraw the muscle, i.e. blocks the withdrawal reflex. This is an example of two competing tendencies

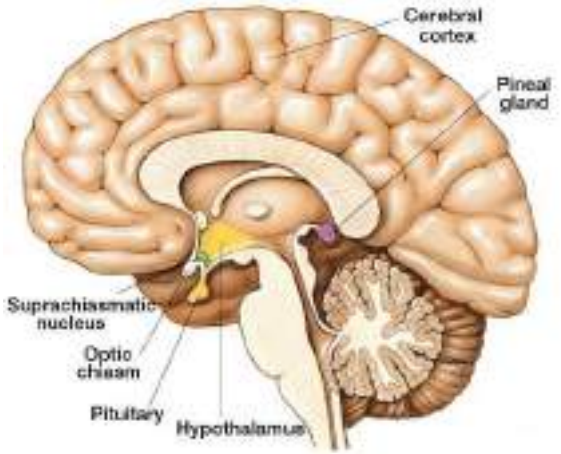
Split brain

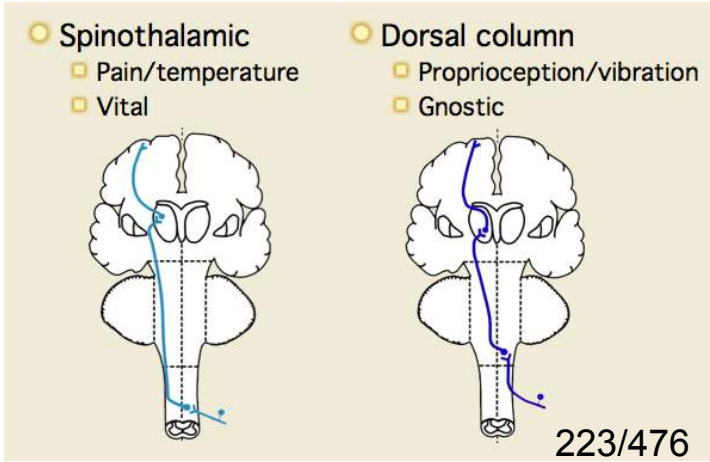


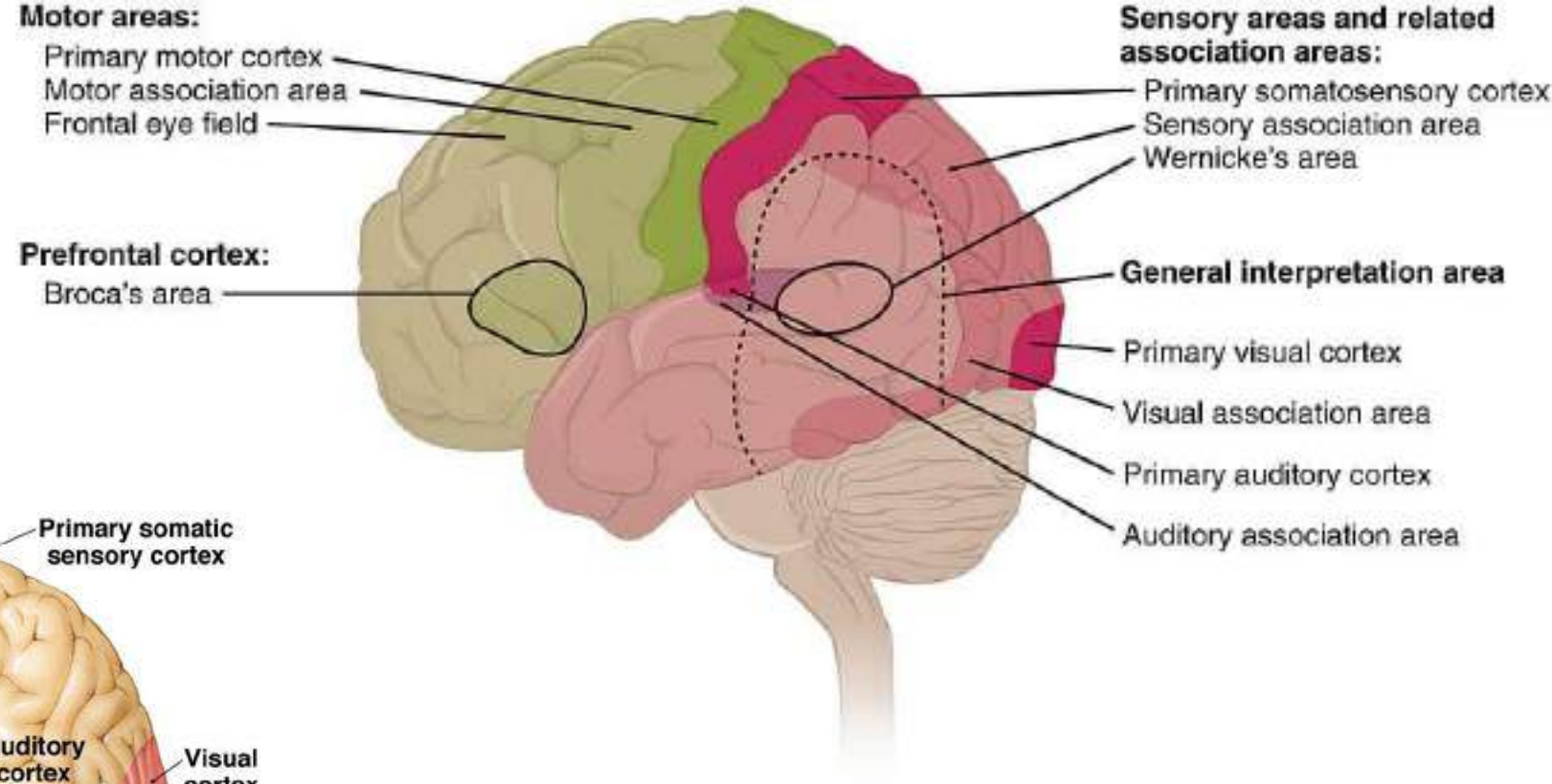

The callosum tissue seen in a healthy brain (bright white in top image) retracts after a corpus callosotomy, leaving just the ventricle (black).

Tactile and visual information reaches the contralateral hemispheres through nerves that cross over below the corpus collosum.

However, visual information in the right hemisphere travels to the language center in the left hemisphere via the corpus collosum







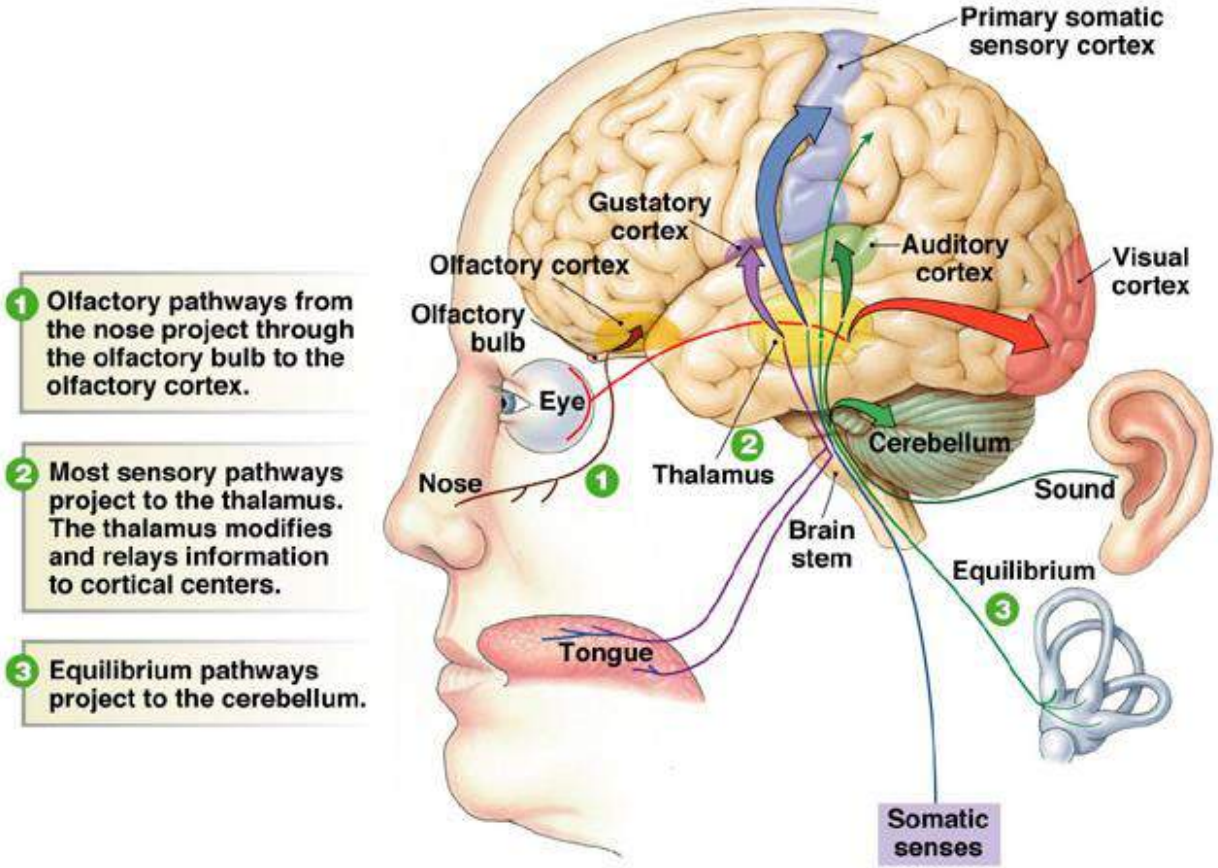
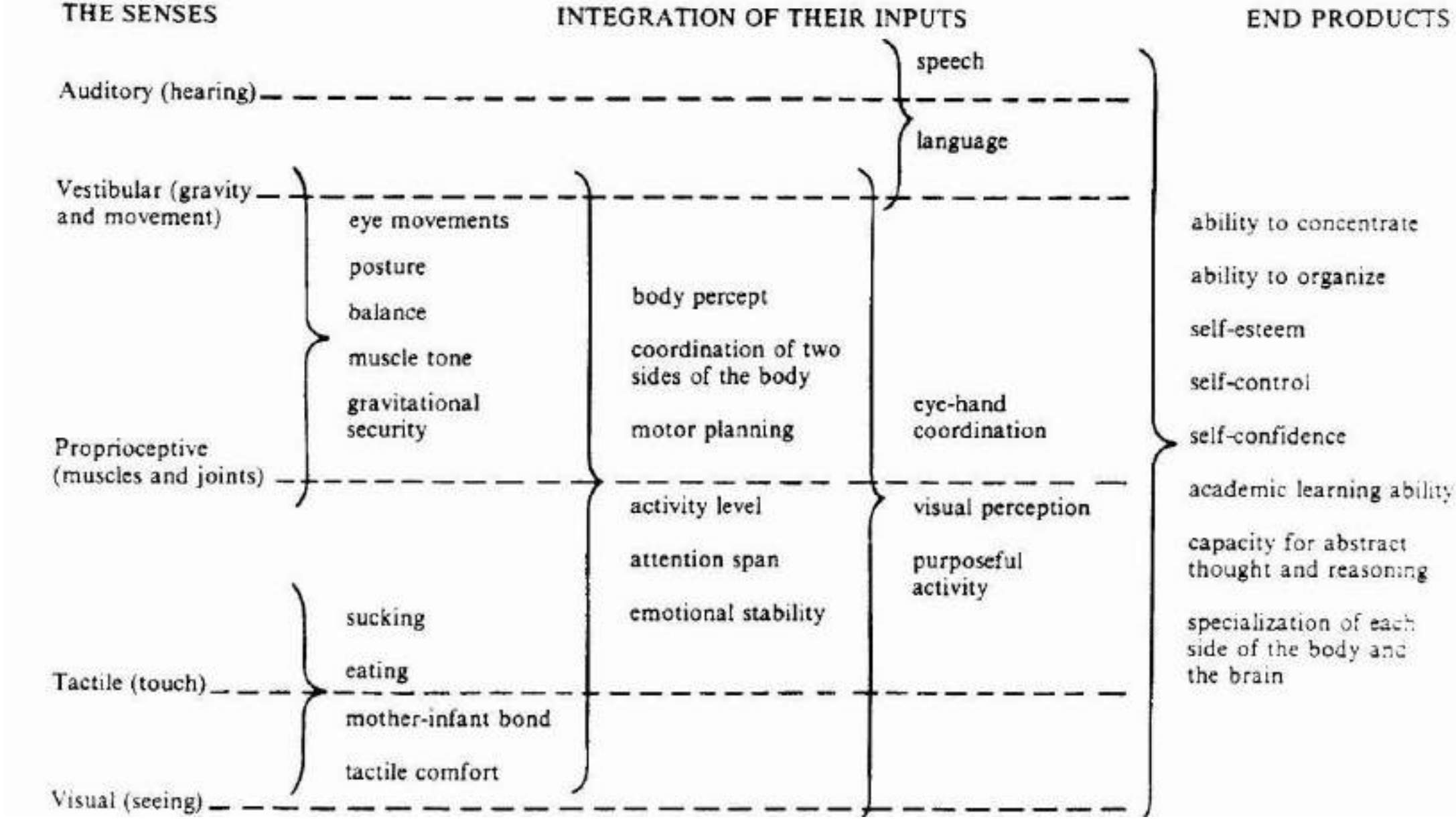
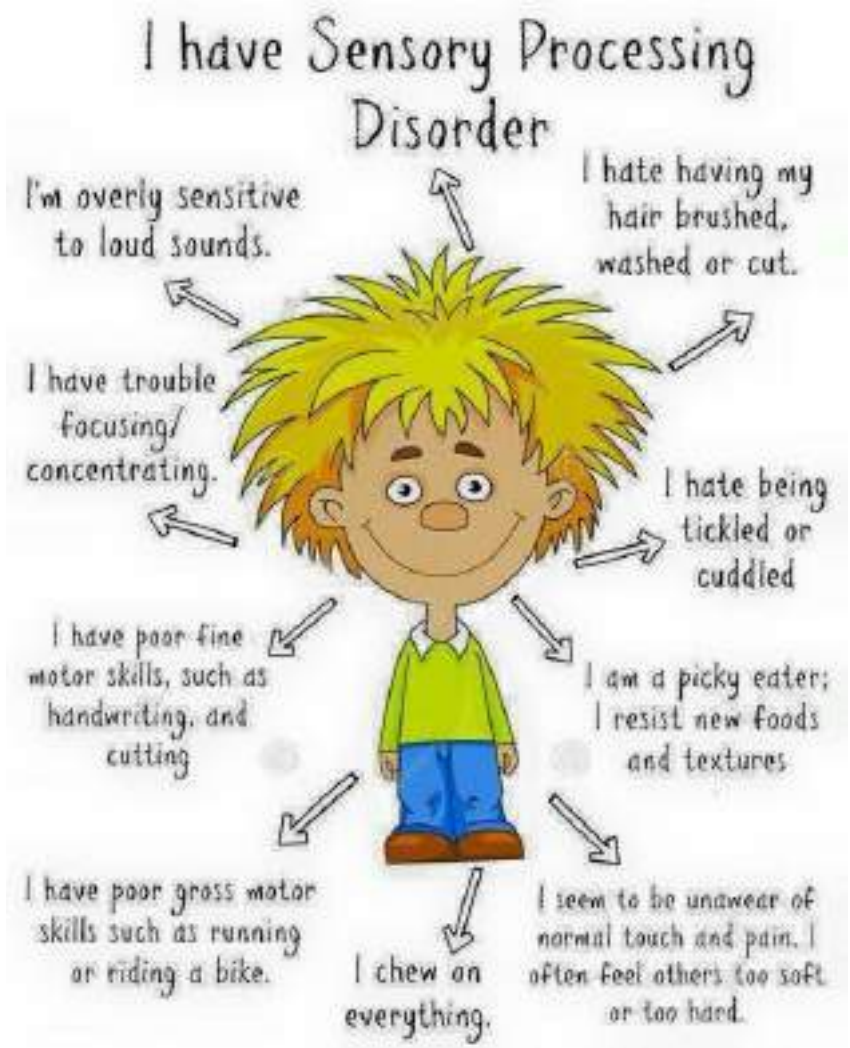


Fig. 10-4



https://www.griffinot.com/sensory-integration-sensory-processing/


I have Sensory Processing Disorder
I'm overly sensitive to loud sounds.
I hate having my hair brushed, washed or cut.
I have trouble focusing/ concentrating.
I hate being tickled or cuddled
I have poor fine motor skills, such as handwriting, and cutting
I am a picky eater; I resist new foods and textures
I have poor gross motor skills such as running or riding a bike.
I chew on everything.
I seem to be unaware of normal touch and pain. I often feel others too soft or too hard.

Treatment based on subtype of the

Sensory Processing Disorder

Sensory Modulation

Sensory Over Responsivity

Hypersensitive
dislike for textures (fabrics, foods, grooming products), discomfort towards normal sounds, lights, temperature, movements, smells, tastes

Sensory Under Responsivity

Hyposensitive
tardiness, sluggishness, slow reaction

Sensory Craver

fidgeting, impulsiveness, seeking or making loud, disturbing noises

Sensory Discrimination

Auditory: Did she say cat, cap, or pack?
Tactile: Is that a quarter or a nickel in my pocket?
Visual: Where is the key that looks like this?
Proprioceptive: How hard should I push this forward to move it, but not break the glass?
Vestibular: Which way am I turning?

Sensory Based Motor Disorder

Dyspraxia

slow and uncoordinated movements or poor handwriting, dropping objects, stumbling,

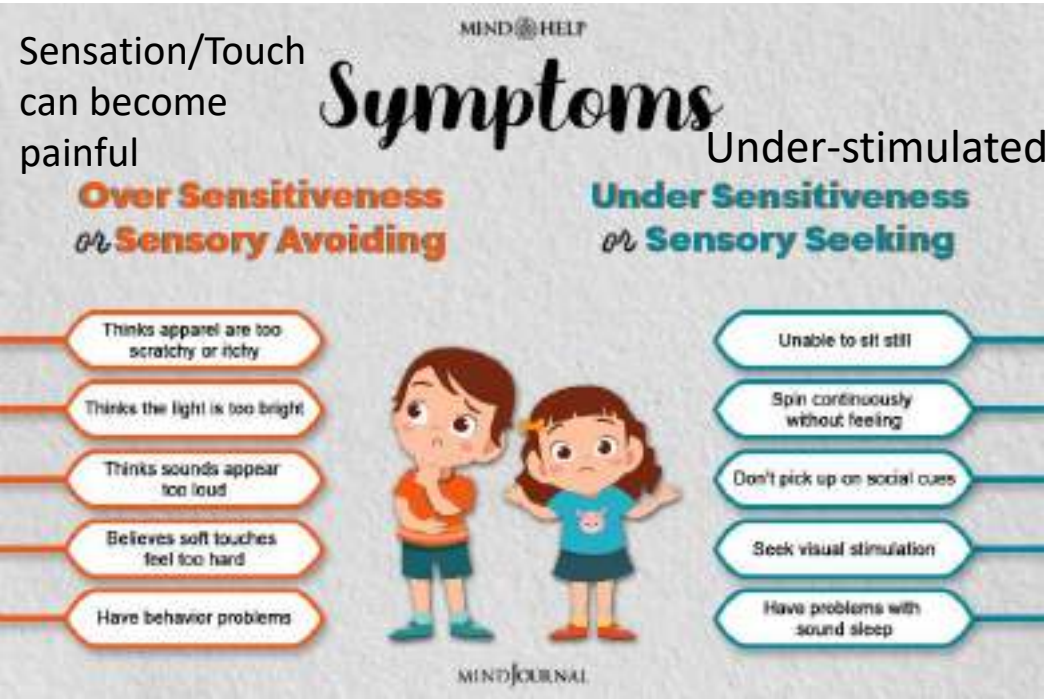
Dyspraxia is the inability or difficulty with three aspects of completing a motor action:
1) ideation,
2) sequencing, and/or
3) motor execution

Postural Disorders

- no internal motivation to move (e.g., run, jump, skip, hop)
- difficulty using both sides of the body simultaneously (e.g., catching a ball, rotating trunk to cross the midline of body needed to ride a bike or hit a baseball)
- challenges with following a moving object with eyes, noticing what happens around him using peripheral vision)
- inefficient vestibular (awareness of where he is in space)
- Inefficient proprioception (awareness of position of muscles and joints)

Commonly observed in Autism Spectrum Disorder (ADD, ADHD, Asperger's syndrome) and other developmental disabilities

Sensation/Touch can become painful



Under-stimulated

https://www.autism.org/sensory-integration/

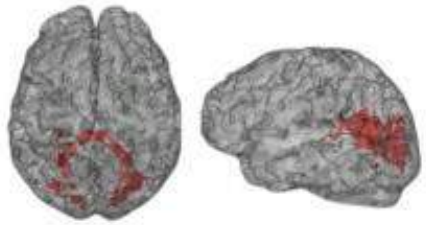
Mapping Sensory Processing Disorders in the Brain

Children with sensory processing disorders have decreased structural brain connectivity in specific sensory regions different than those in autism. Here's a closer look at the areas affected.

Sensory Processing Disorder only

Area Affected:

Splenium of the corpus callosum between left and right lateral occipital cortices



Autism Spectrum Disorder only

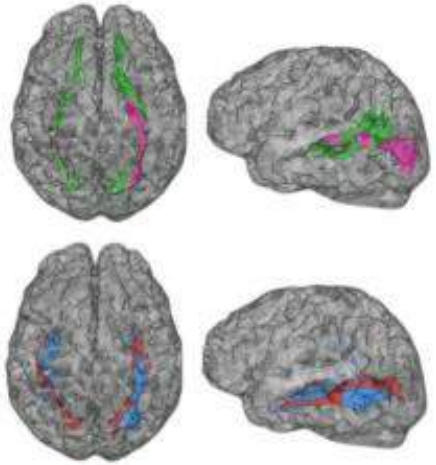
Areas Affected:

Inferior fronto-occipital fasciculus (IFOF)

Fusiform-amygdala

Inferior longitudinal fasiculus (ILF)

Fusiform-hippocampus

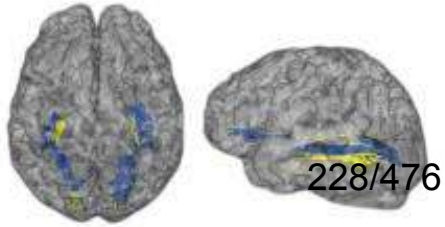


Autism Spectrum and Sensory Processing disorders

Areas Affected:

Posterior corona radiata (PCR)

Dorsal visual stream



https://www.ucsf.edu/news/2014/07/116196/kids-autism-sensory-processing-disorders-show-brain-wiring-differences

Example of activities a child can engage in to improve sensory discrimination

Children who have poor **sensory discrimination** need sensory-rich activities in the domain in which they have issues.

Visual: category games (e.g., find everything in the room that's a circle, while driving point to all food-related signs)

Interoceptive: Talk about how your body feels at times when you are happy versus worried. Say things such as, "I'm so happy, I can feel my heart beating fast!" or "I always feel nervous when I [fill in the blank]. My stomach feels like it is flipping over." That way the child will begin to understand the body sensations related to emotional content.

Auditory: Play the same-and-different game, "I'm going to say two words, and you tell me if they are the same or different. Then it will be your turn to try to trick me."

Proprioceptive: Play Simon Says or Mother May I? performing unusual, novel body movements.

Treatment for sensory processing problems is called sensory integration. The goal of sensory integration is to challenge a child in a fun, playful way so they can learn to respond appropriately and function more normally

Therapy video

Dance therapy

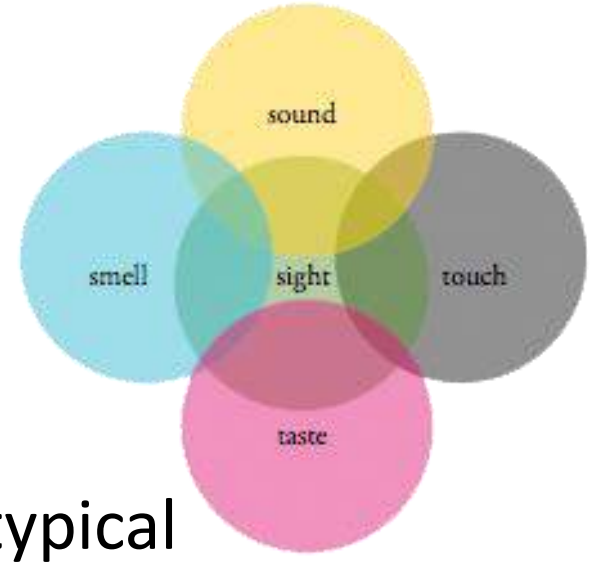
Repetitive movements
Costumes
Lights

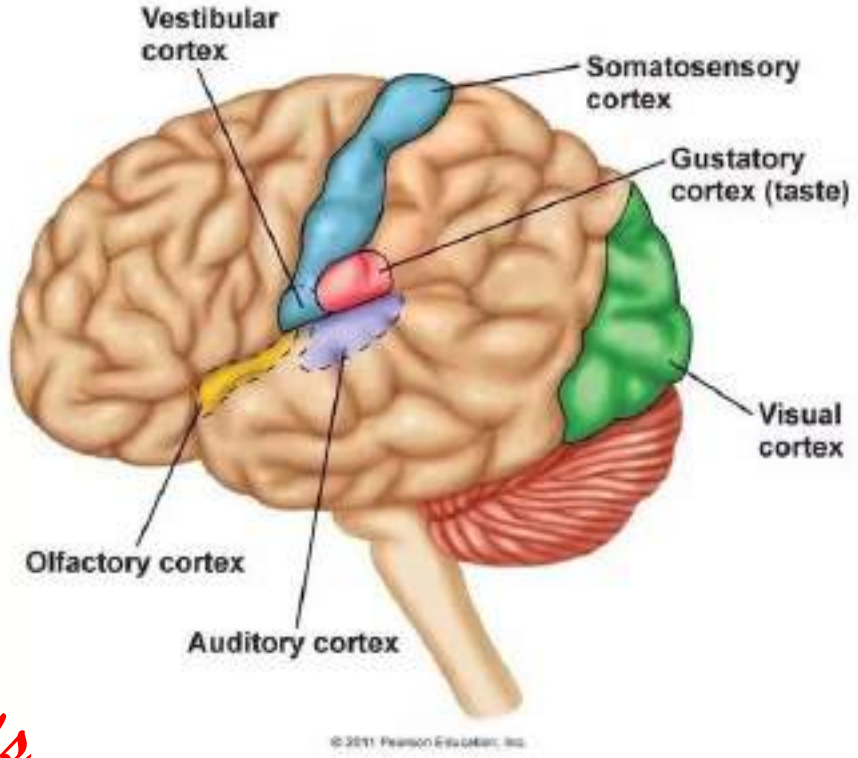
Art therapy

Concentration/engagement
Hand eye coordination
Sensitive touch

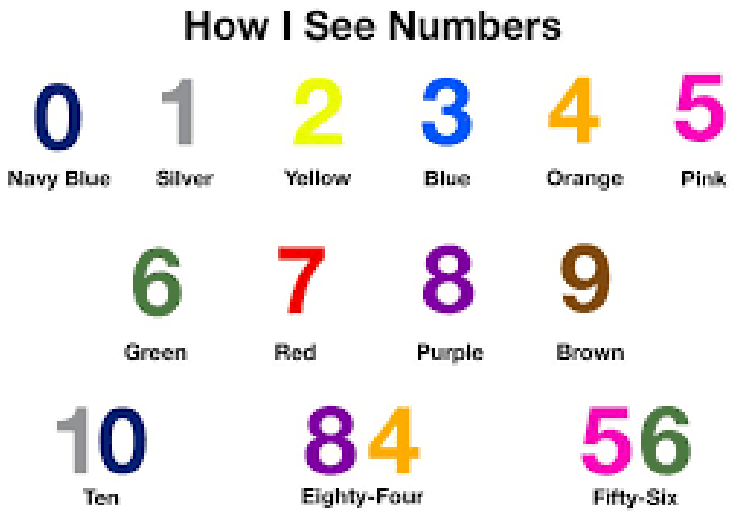
- Synesthesia?

Synesthesia





- Routing of senses is not typical

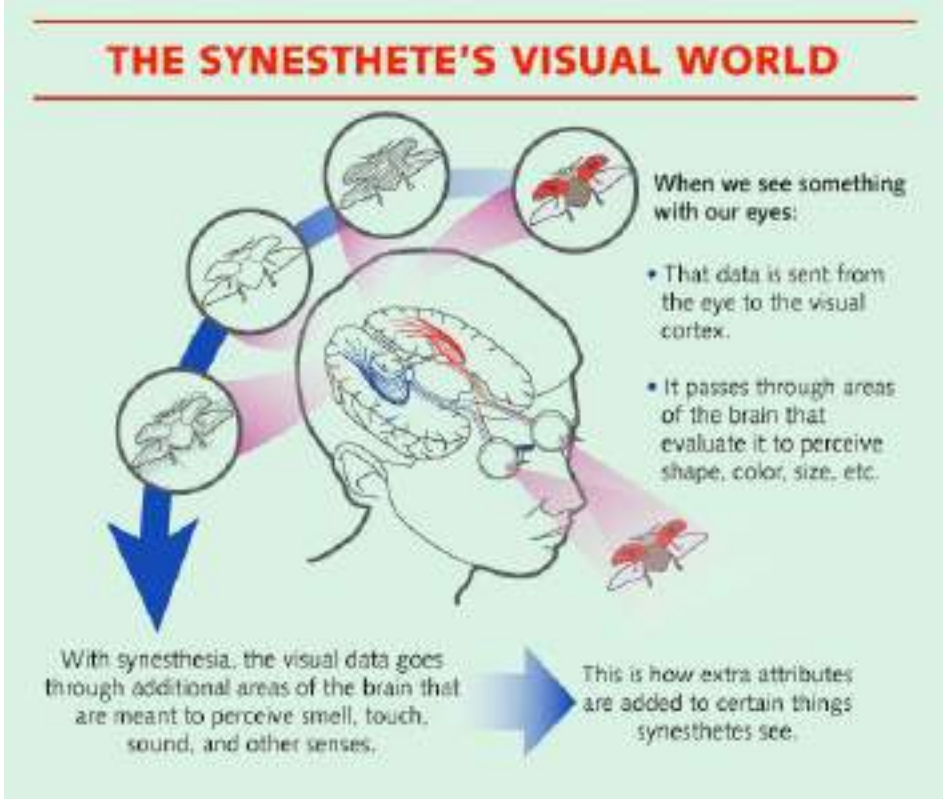


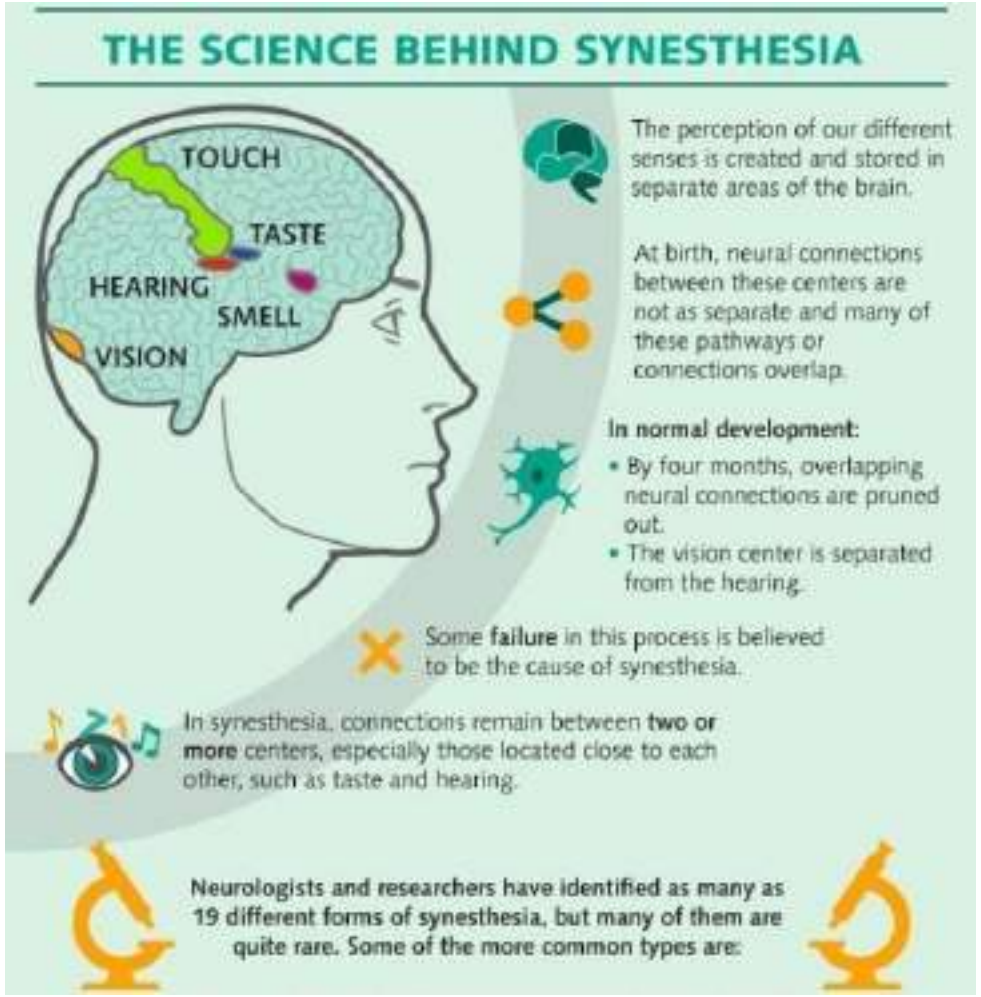
Tasty Words

Colorful Sounds

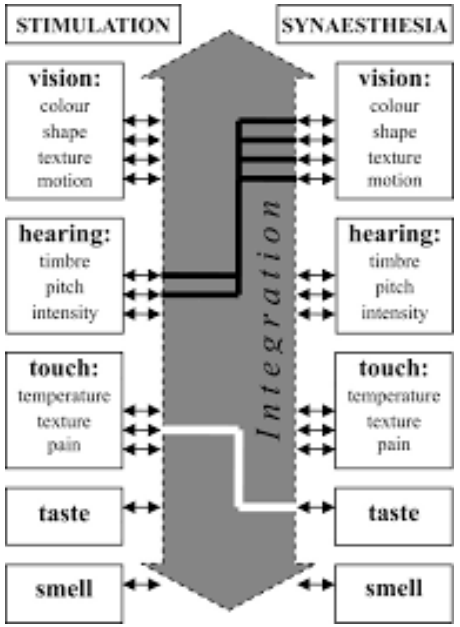
Synesthesia

Synaesthesia is thought to have a genetic component, since it often runs in families and is more common in women





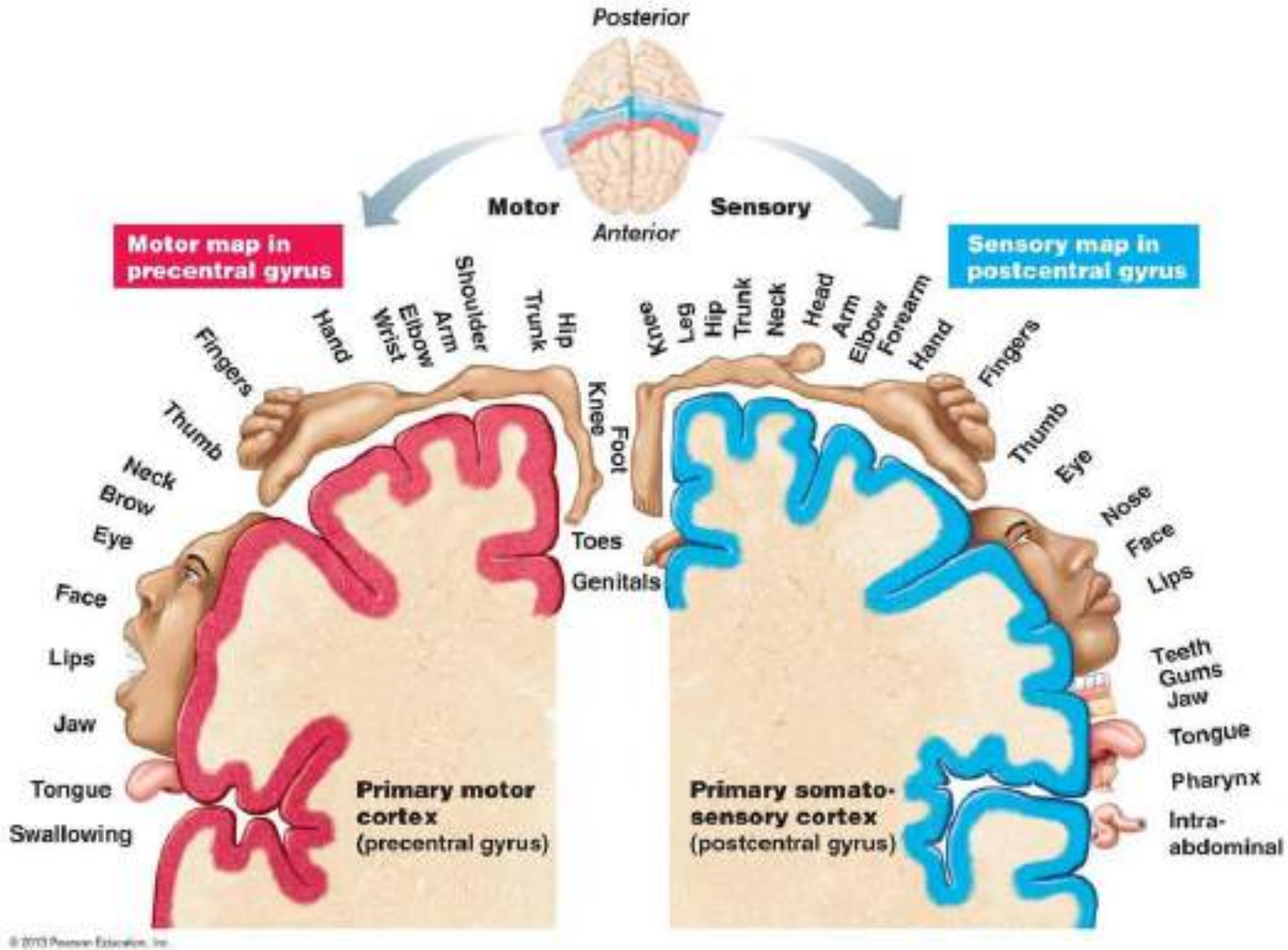
Emotions -> colors	Musical sounds -> colors	Sounds -> smells
Emotion -> smell	Odors -> colors	Sound -> temperatures
Emotion -> flavor	Orgasm -> colors	Sound -> touch
Emotion -> pain	Pain -> colors	Temperatures -> colors
Emotion -> smell	Pain -> flavor	Temperature -> flavors
Emotion -> temperature	Pain -> smell	Temperatures -> sounds
Emotion -> touch	Pain -> sound	Time units -> colors
Flavors -> colors	Personalities -> smells	Touch -> colors
Flavors -> sounds	Personalities -> touch	Touch -> emotions
Flavors -> temperatures	Personalities -> colors (auras)	Touch -> flavors
Flavors -> touch	Phoneme -> touch	Touch -> smell
General sounds -> colors	Phoneme -> flavor	Touch -> sounds
Graphemes -> colors	Phonemes -> colors	Touch -> temperatures
Grapheme -> flavor	Smells -> flavor	Vision -> flavors
Kinetics -> colors	Smells -> sounds	Vision -> kinetics
Kinetics -> sounds	Smells -> temperatures	Vision -> smells
Lexeme -> touch	Smells -> touch	Vision -> sounds
Musical notes -> colors	Sound -> flavors	Vision -> Temperatures
Musical notes -> flavors	Sounds -> kinetics	Vision -> touch

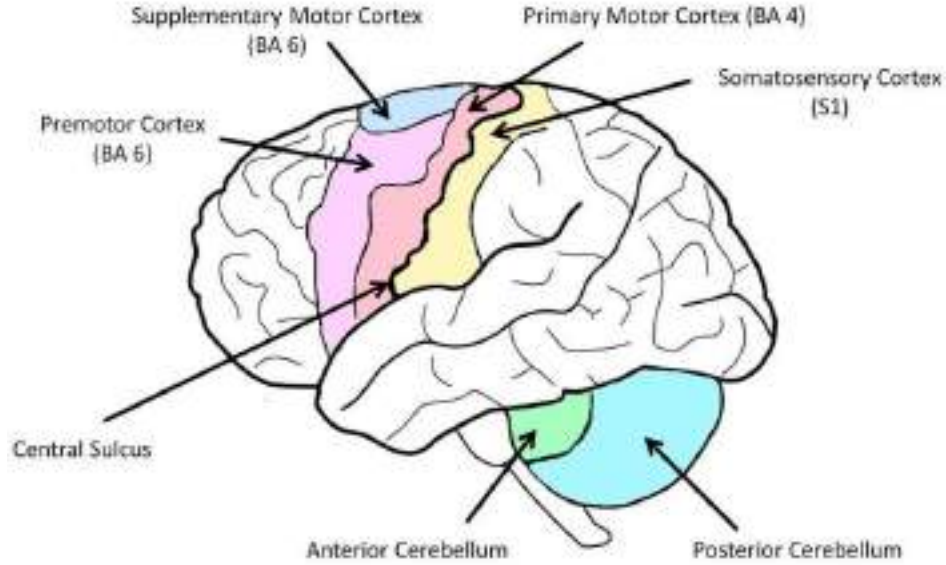


Hallucinations are a perception not based on sensory input, whereas illusions are a misinterpretation of a correct sensory input.

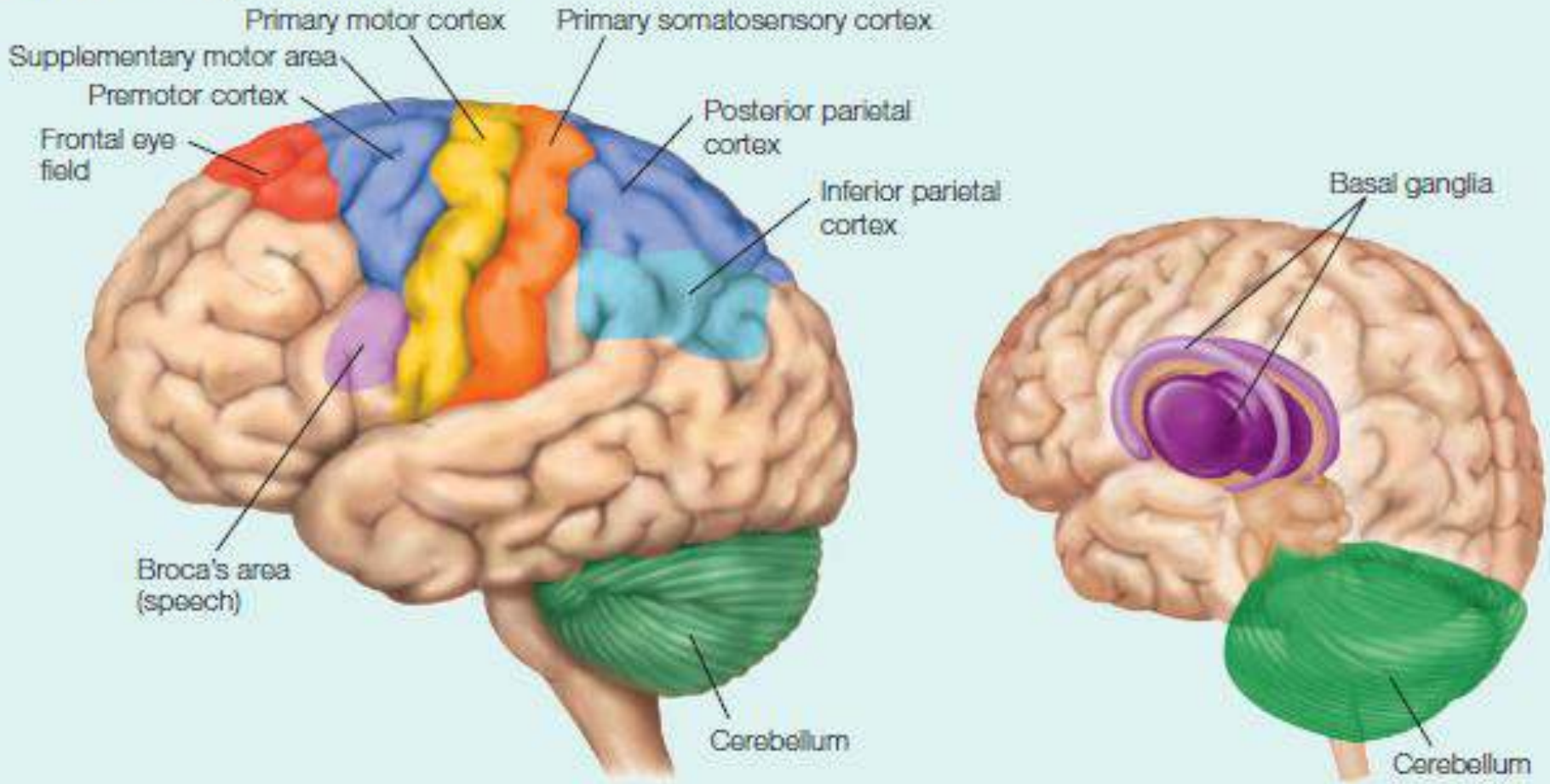
Synesthesia is not an illusion – it is an added perception to a stimulus (sound + color)

Movement and Navigation

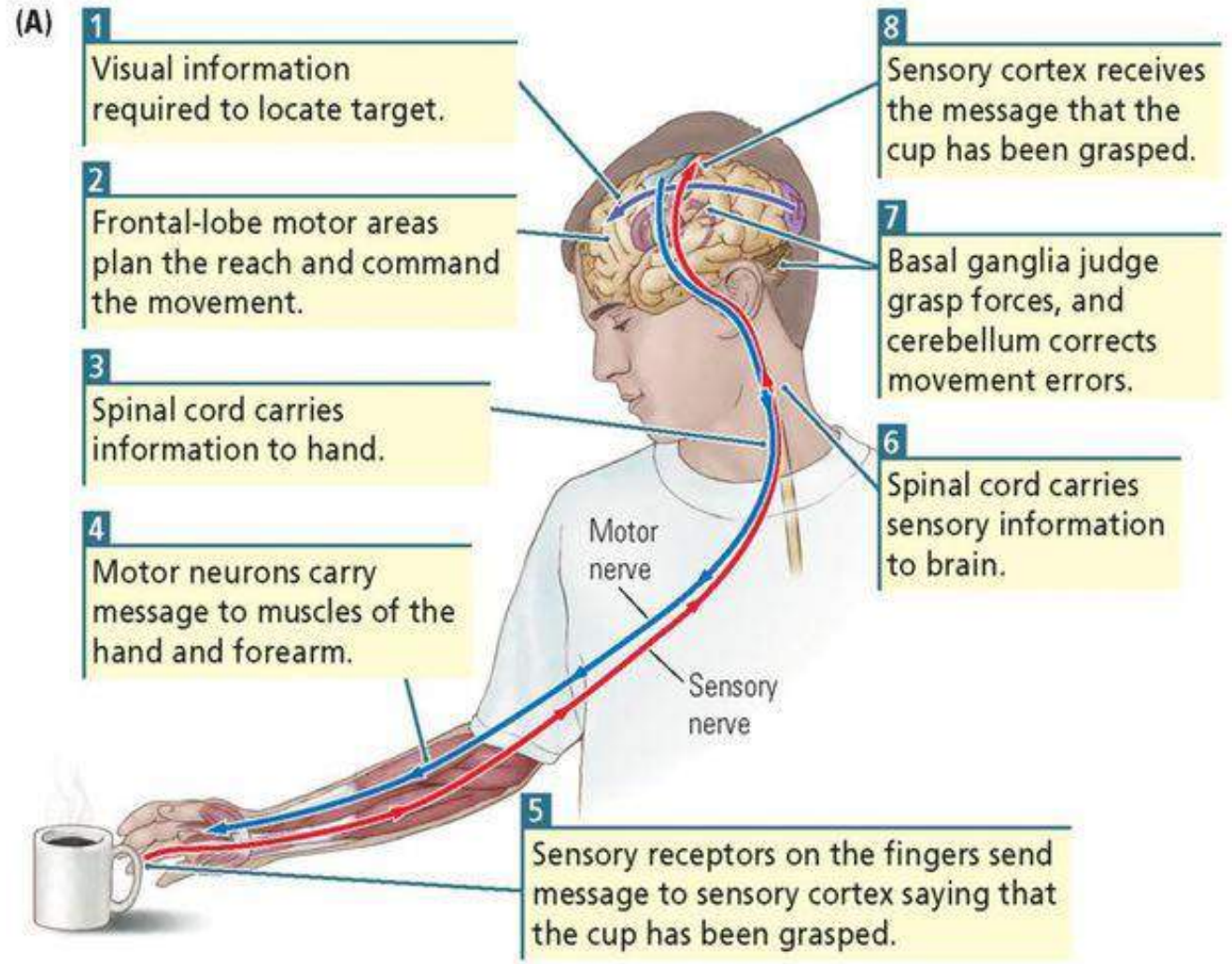

Posterior
Motor
Sensory
Anterior
Motor map in precentral gyrus
Sensory map in postcentral gyrus
Hand
Fingers
Thumb
Neck
Brow
Eye
Face
Lips
Jaw
Tongue
Swallowing
Wrist
Elbow
Arm
Shoulder
Trunk
Hip
Knee
Foot
Toes
Genitals
Leg
Knee
Hip
Trunk
Neck
Head
Arm
Elbow
Forearm
Hand
Fingers
Thumb
Eye
Nose
Face
Lips
Teeth
Gums
Jaw
Tongue
Pharynx
Intra-abdominal
Primary motor cortex (precentral gyrus)
Primary somato-sensory cortex (postcentral gyrus)

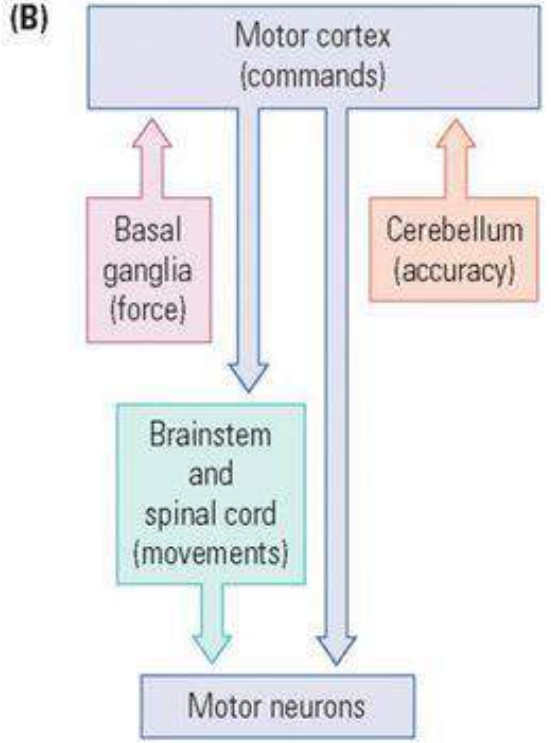

Supplementary Motor Cortex (BA 6)
Primary Motor Cortex (BA 4)
Somatosensory Cortex (S1)
Premotor Cortex (BA 6)
Central Sulcus
Anterior Cerebellum
Posterior Cerebellum

Anatomy of Action



Many cortical regions are involved in planning, control, and execution of movement. In addition, two major subcortical structures of the motor system are the cerebellum and the basal ganglia.





Biological Algorithm

Figure 9.1 The Motor System

Kolb/Whishaw: Fundamentals of Human Neuropsychology

Primary Somatosensory Cortex – receives sensory input

Frontal cortex – plans and decides action

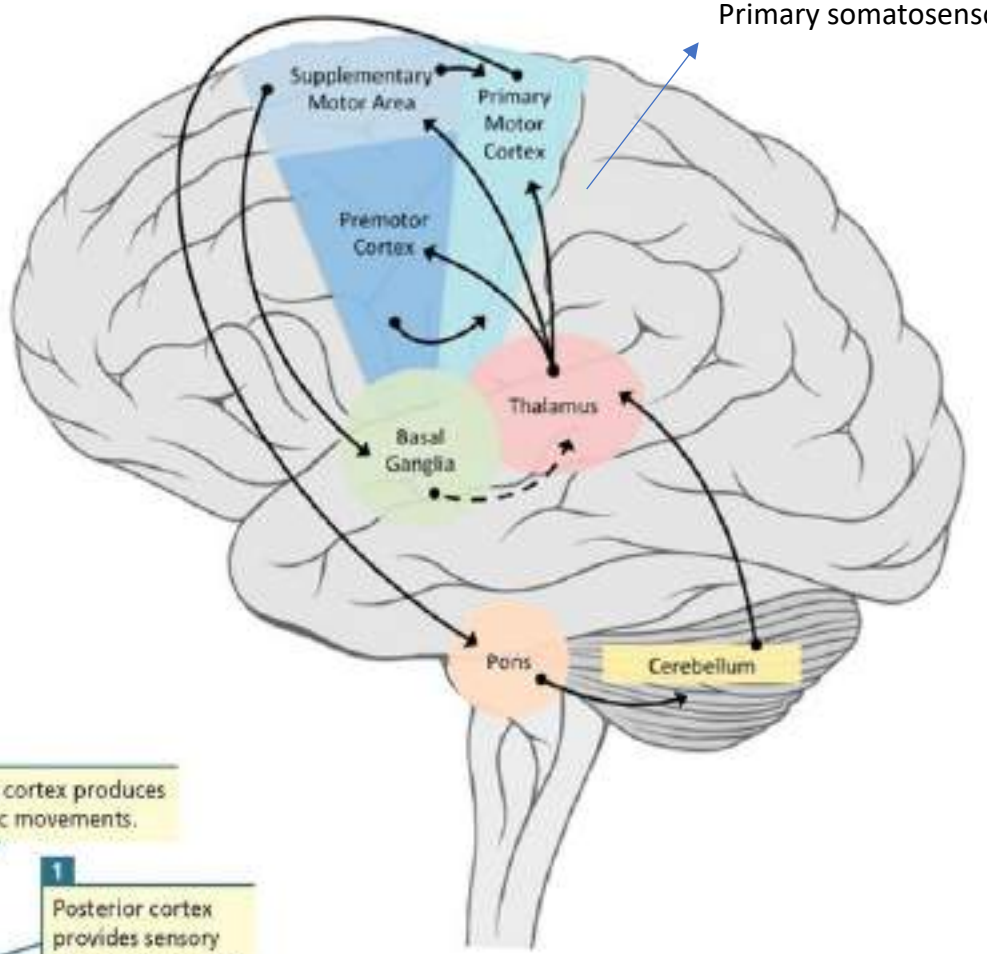
Premotor and Supplemental motor cortex – planning of movement

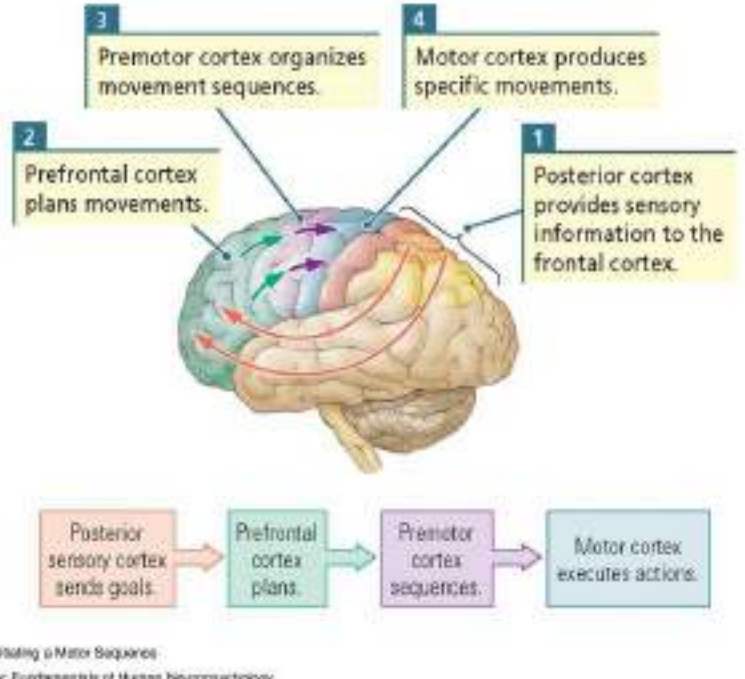
Primary motor cortex – execution of motor movement

Basal Ganglia – co-ordinates initiation/inhibition of movement

Cerebellum – corrects errors in movement based on visual/sensory feedback (coordination of ongoing movement)

Thalamus – relay center



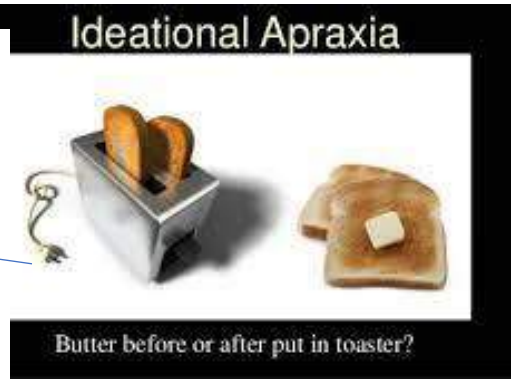


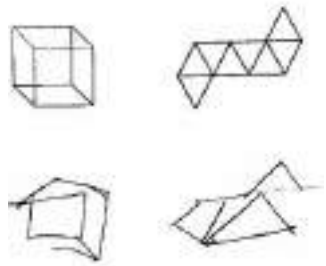
Damage to different parts of the motor circuit

Types of apraxia

- Ideomotor- inability to carry out a motor command, limb or buccofacial
- Ideational- inability to create a plan for or an idea of a specific movement
- Constructional- inability to draw or construct simple configurations
- Speech- impaired ability to speak
- Gait- impaired coordination of leg movements

Buccofacial apraxia -Unable to carry out facial and lip movements such as whistling, winking, coughing etc





Tactile Apraxia - deficit in tactile information for action

absence of movements, objects can be misidentified, hand movement to pick up object or imitate hand movements is impaired

Optic Apraxia -

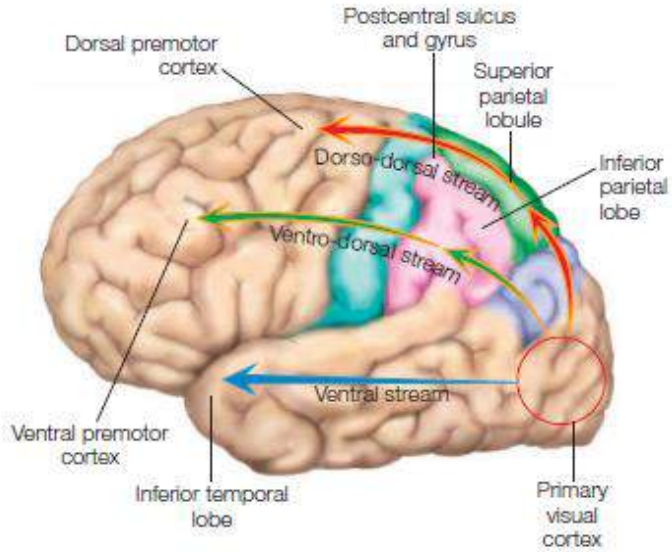


FIGURE 8.10 Proposed dorso-dorsal and ventro-dorsal processing streams, along with the ventral stream. Patients with lesions within the dorso-dorsal stream have optic ataxia while those with lesions to the ventro-dorsal stream have apraxia.

Comparing different types of apraxia

https://passtheot.com/apraxia-comparison/

The Case of G.O., the Man with Too Little Feedback

An infection had selectively destroyed the somatosensory nerves of G.O.'s arms. He had great difficulty performing intricate responses such as doing up his buttons or picking up coins, even under visual guidance. Other difficulties resulted from his inability to adjust his motor output in light of unanticipated external disturbances; for example, he could not keep from spilling a cup of coffee if somebody brushed against him. However, G.O.'s greatest problem was his inability to maintain a constant level of muscle contraction.

The result of his infection was that even simple tasks requiring a constant motor output to the hand required continual visual monitoring. For example, when carrying a suitcase, he had to watch it to reassure himself that he had not dropped it. However, even visual feedback was of little use to him in tasks requiring a constant force, tasks such as grasping a pen while writing or holding a cup. In these cases, he had no indication of the pressure that he was exerting on the object; all he saw was the pen or cup slipping from his grasp.

Sensory Feedback

Contralateral neglect

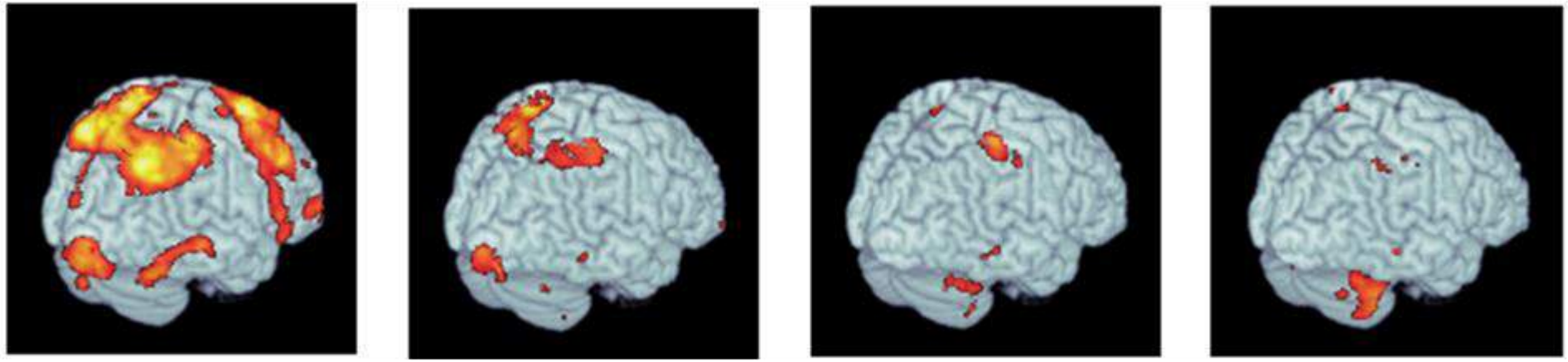
- posterior parietal cortex damage,
- Disturbed ability to respond to stimuli on the opposite side of (contralateral) the brain lesion
- No problems in simple sensory or motor activity

The Case of Mrs. S., the Woman Who Turned in Circles

After her stroke, Mrs. S. could not respond to things on her left—including objects and parts of her own body. For example, she often put makeup on the right side of her face but ignored the left.

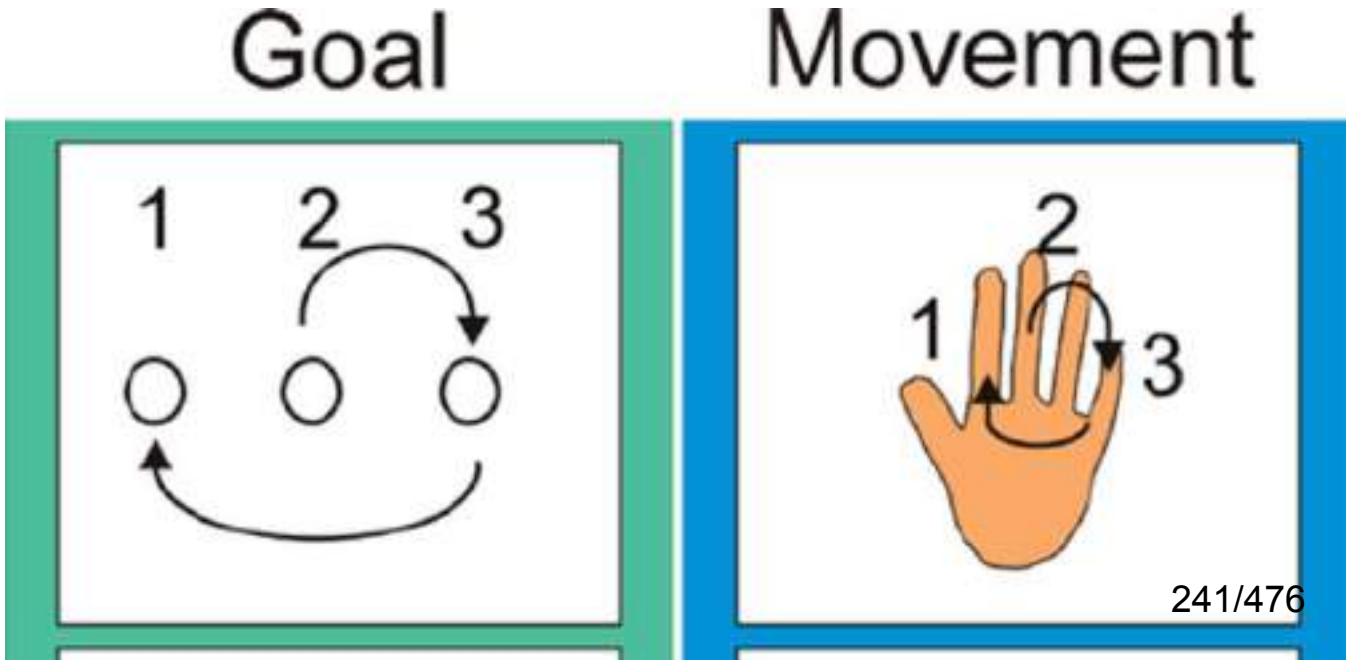
Mrs. S.'s left-side contralateral neglect created many problems for her, but a particularly bothersome one was that she had difficulty getting enough to eat. When a plate of food was put directly in front of her, she could see only the food on the right half of the plate, and she ate only that half, even if she was very hungry. However, Mrs. S. developed an effective way of getting more food. If she was still hungry after completing a meal, she turned her wheelchair to the right in a full circle until the remaining half of her meal appeared once more directly in front of her. Then, she ate that remaining food, or more precisely, she ate the right half of it. If she was still hungry after that, she turned once again in a circle to the right until the remaining quarter of her meal appeared, and she ate half of that . . . and so on.

Which brain regions have taken over?



seconds ⟶ minutes ⟶ hours

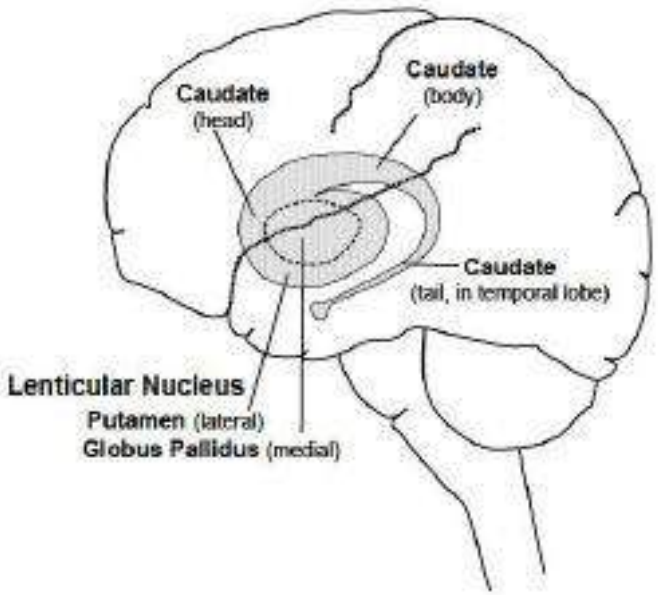
E.g. cycling, writing, driving, typing, etc.

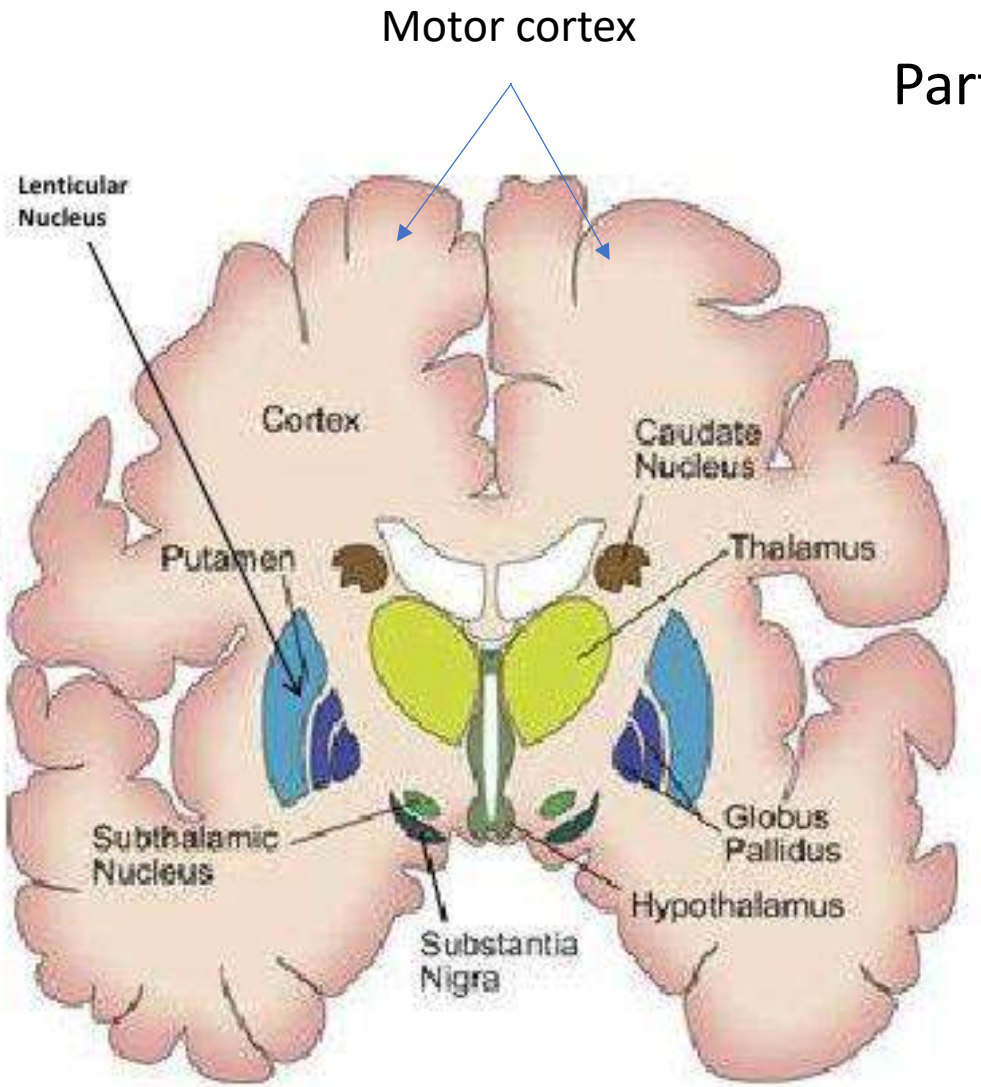


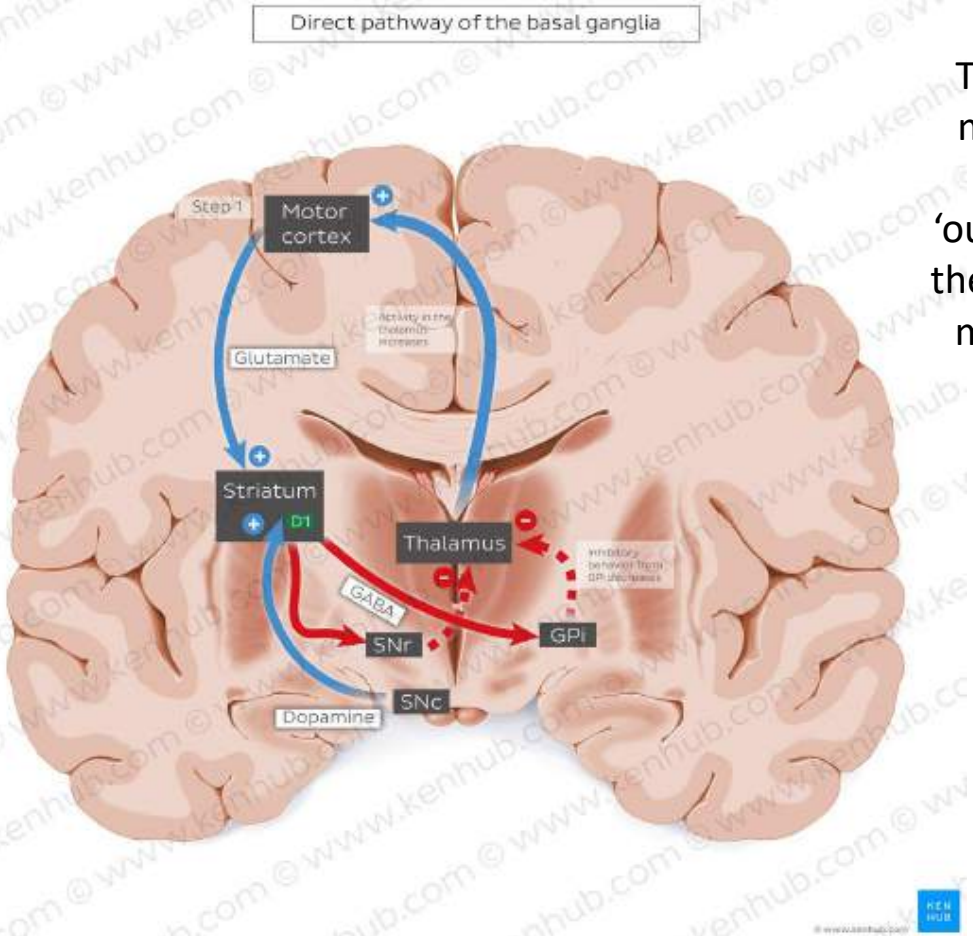
Parts of Basal ganglia

FUNCTIONAL DIVISIONS

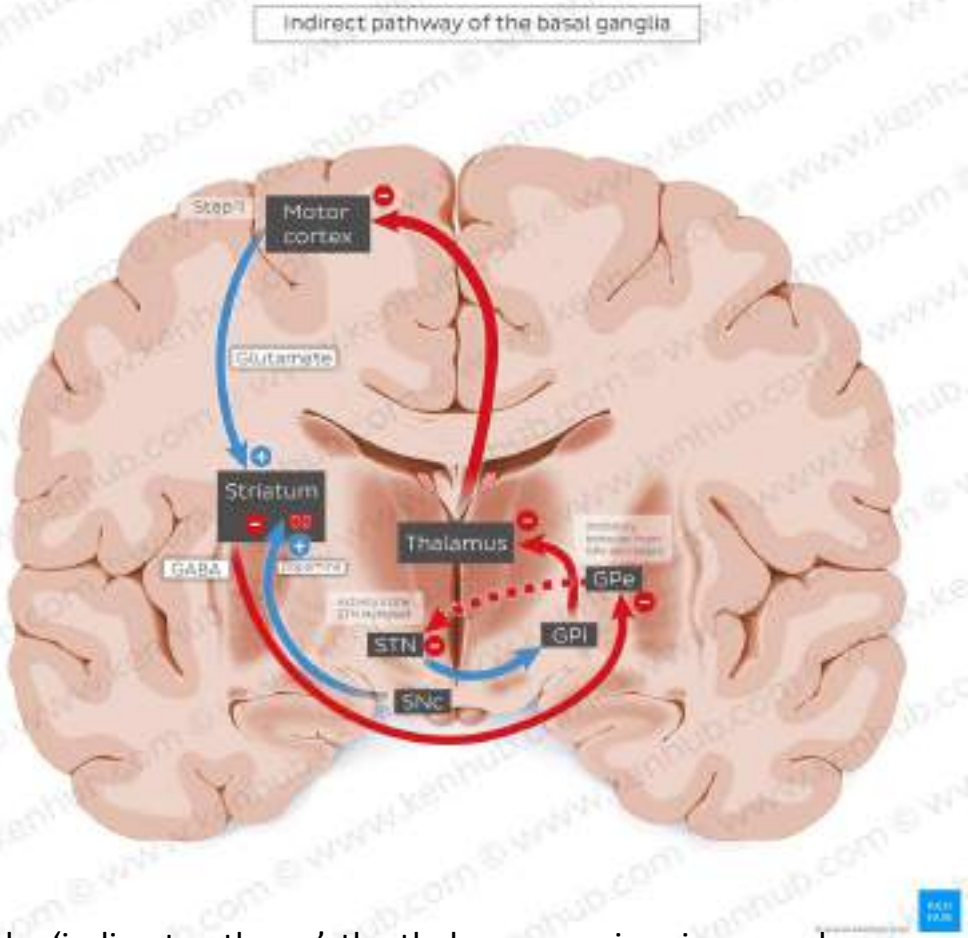
1. **Striatum**
   a. caudate nucleus
   b. putamen
2. **Pallidum**
   a. Globus Pallidus Interna (Gpi)
   b. Globus Pallidus Externa (Gpe)
3. **Thalamus**
4. **Subthalamic Nucleus**
5. **Substantia Nigra**







The direct pathway facilitates movement by decreasing the inhibition of basal ganglia 'outputs' to the thalamus, while the indirect pathway suppresses movements by increasing the inhibitory pathway.



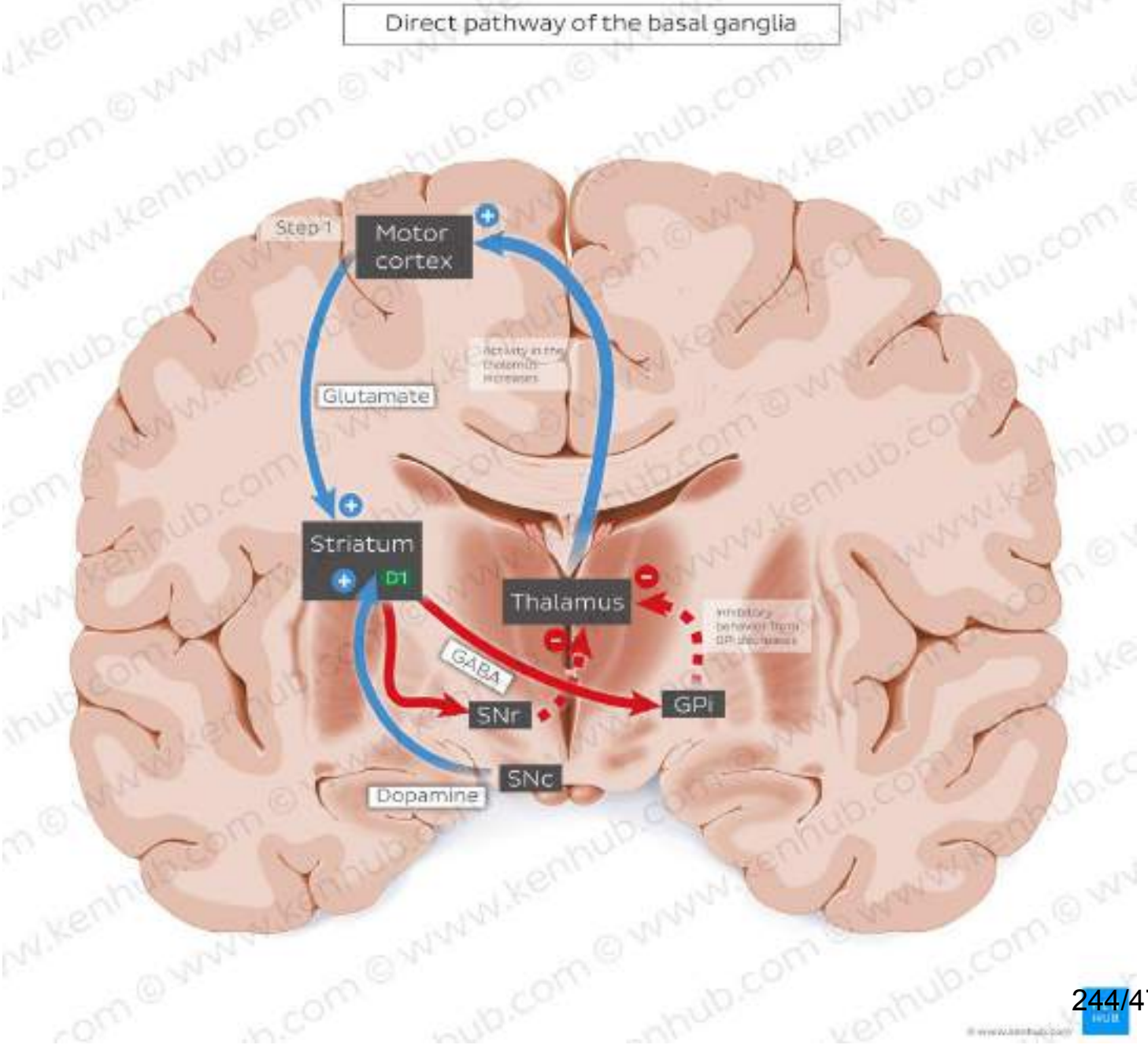
- In the 'direct pathway' striatal neurons disinhibit the thalamic neurons responsible for excitation of the pre-motor cortex. As such, activation of the direct pathway facilitates voluntary movements.
- Dopamine stimulates excitatory receptors (D_1 receptors) in the direct pathway (dopamine has an excitatory role)

- In the 'indirect pathway', the thalamus receives increased inhibition which reduces activity of pre-motor cortex. Activation of the indirect pathway suppresses voluntary movements.
- Dopamine stimulates inhibitory receptors (D_2 receptors) in the indirect pathway (dopamine has an inhibitory role)

Given that the direct and indirect pathways excite and attenuate movement, respectively, the net effect of dopamine is a facilitation of motor output

https://www.kenhub.com/en/library/anatomy/direct-and-indirect-pathways-of-the-basal-ganglia

Parkinson’s Disease



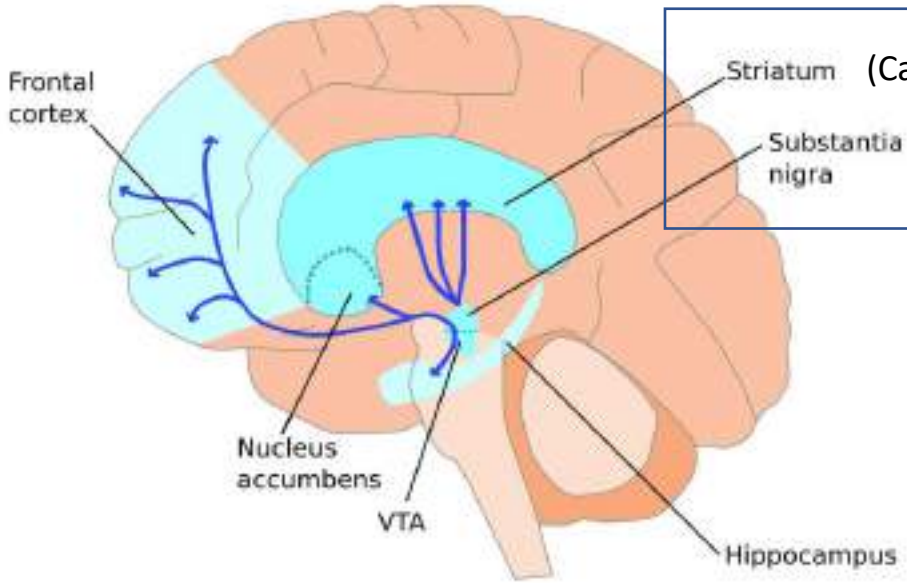
Parkinson's Disease

Cause:

- Genetic mutation (rare)– abnormal functioning of dopaminergic neurons
- 95% cases of Parkinson's do no have a genetic cause
- Degeneration of dopamine secreting neurons in basal ganglia (substantia nigra)
  - Toxins – affect cell functioning, metabolism
  - Head trauma
  - Advancing age
  - unrecognized infectious disorders
  - Chronic stress (exact role is yet to be determined)

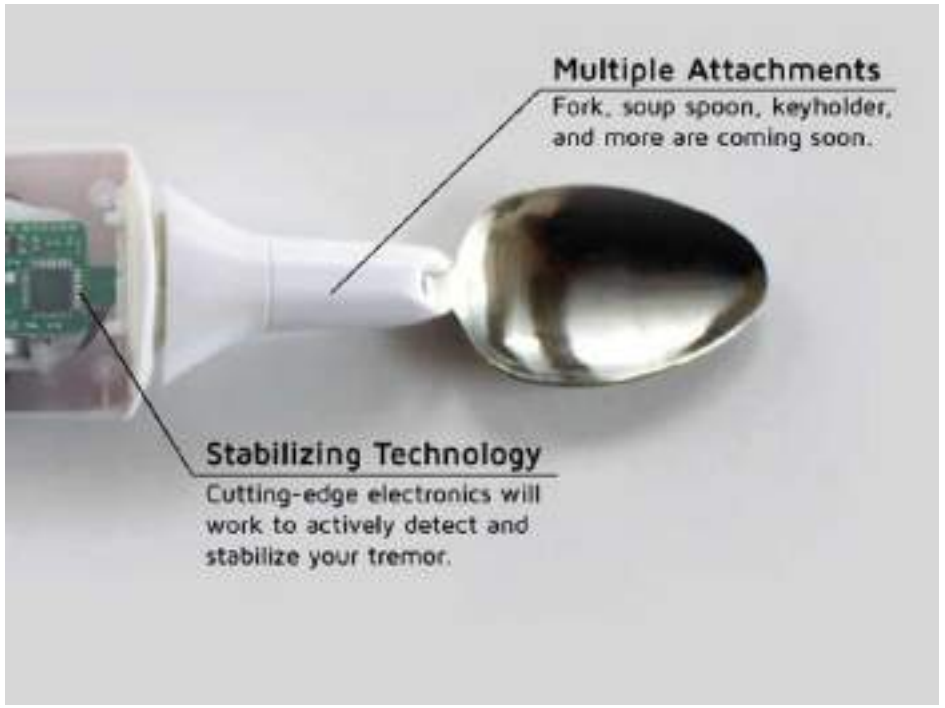
Symptoms:

Muscular rigidity
Slowness of movement
Resting tremor
Postural instability
Slowness of thought



Nigrostriatal pathway

ttps://www.youtube.com/watch?v=IHDFQfmkKlg&ab_channel=ButlerHospital



[Parkinson's Spoon Video]

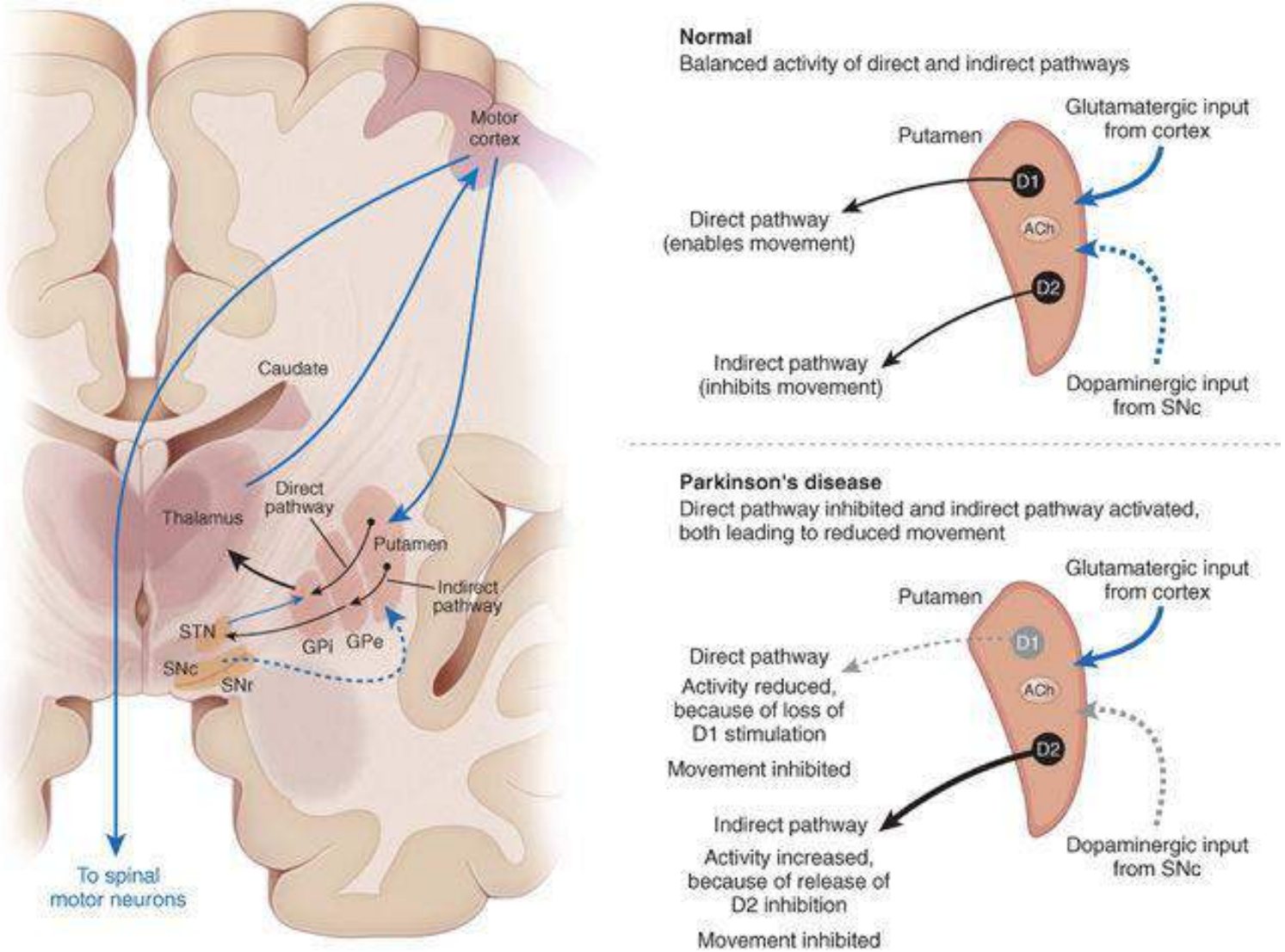


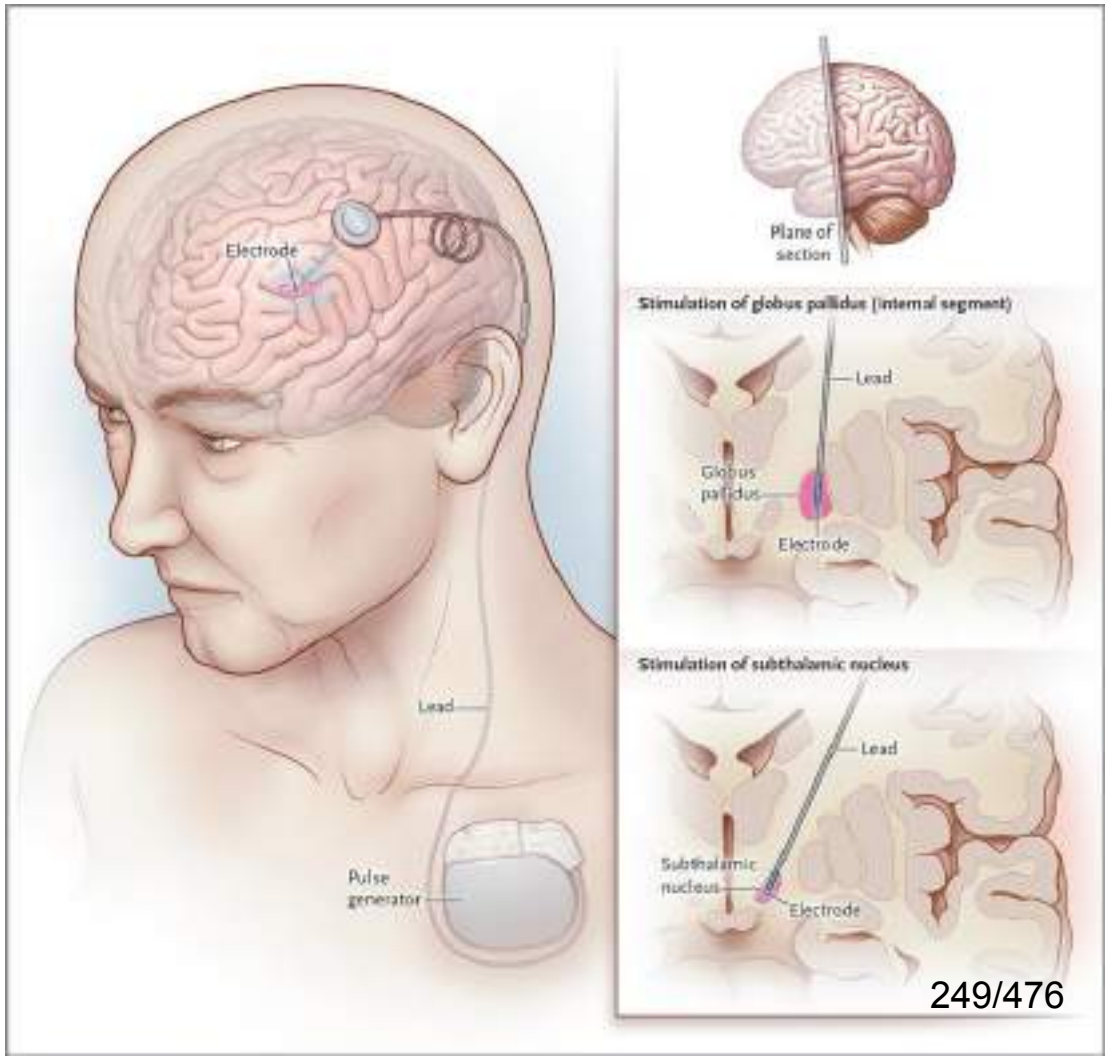
FIGURE 14-7. Effect of Parkinson's disease on dopaminergic pathways that regulate movement. Two principal pathways in the basal ganglia regulate movement: the direct pathway, which enables movement, and the indirect pathway, which inhibits movement. Dopamine stimulates the direct pathway and inhibits the indirect pathway, yielding a net bias that allows purposeful movement. Excitatory pathways are shown in *blue*, and inhibitory pathways are shown in *black*. The direct pathway signals from putamen to GPi to thalamus to cortex, while the indirect pathway signals from putamen to GPe to STN to GPi to thalamus to cortex. GPi, internal segment of the globus pallidus; GPe, external segment of the globus pallidus; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; STN, subthalamic nucleus. **Inset:** Both direct and indirect pathway neurons in the putamen receive inputs from the nigrostriatal dopaminergic system (*dotted blue arrow*) and from cortical glutamatergic systems (*solid blue arrow*), process these inputs in the context of local cholinergic influences (ACh), and transmit a GABAergic output (*not shown*). Degeneration of dopaminergic neurons in the substantia nigra results in understimulation of the direct (movement-enabling) pathway and underinhibition of the indirect (movement-inhibiting) pathway. The net result is a paucity of movement. *Dotted gray arrow* indicates decreased activity caused by understimulation, and *thick black arrow* indicates increased activity caused by underinhibition.

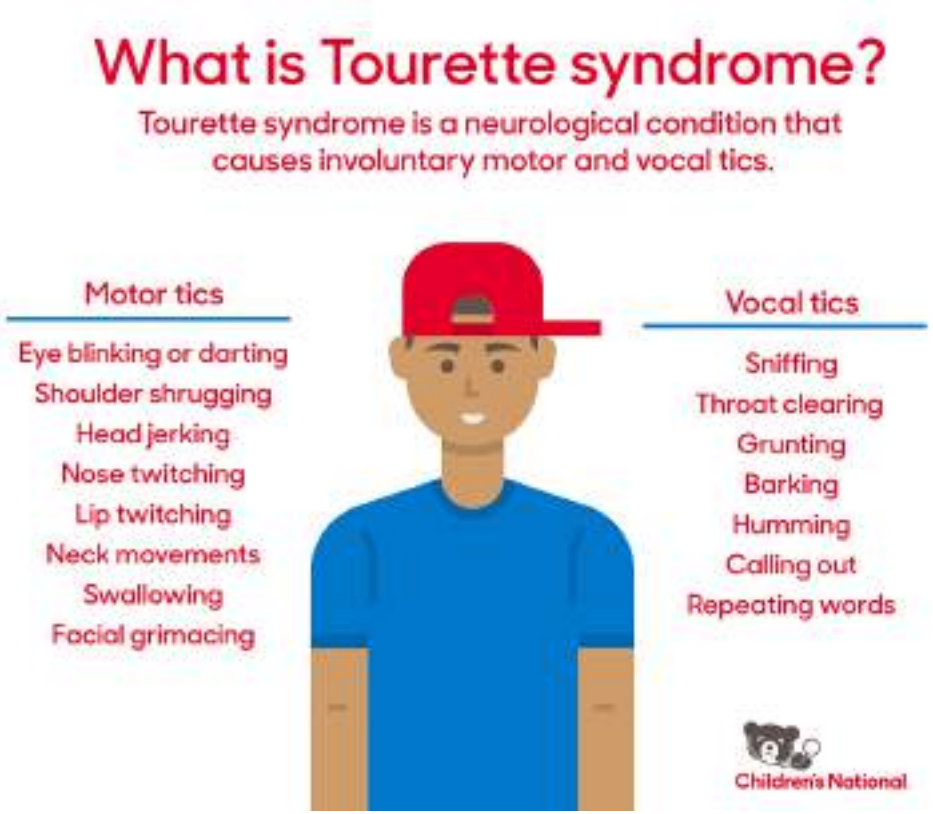
In the absence of dopamine, as seen in Parkinson's disease, there is an opposite net effect – suppression of motor output

- What could be treatment for Parkinson’s Disease?

Parkinson's Treatment (Reducing symptoms)

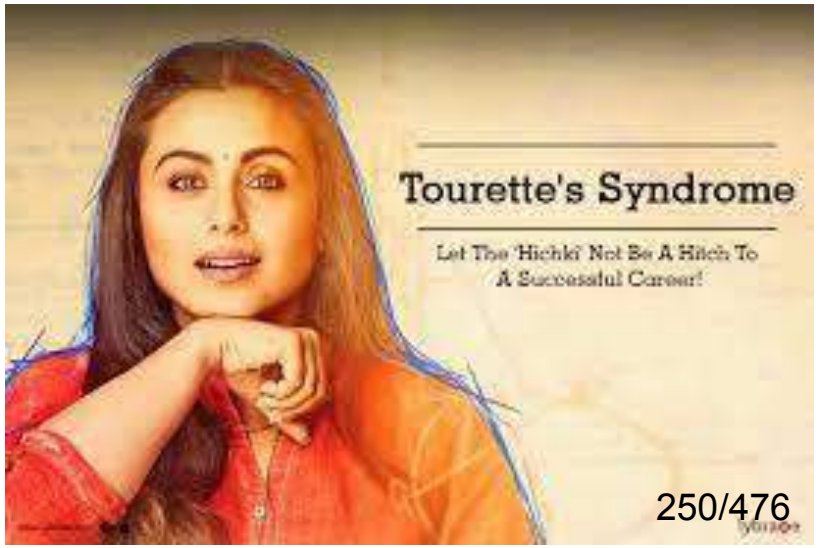
- Dopamine enhancing drugs (L-DOPA)
- Dopamine reuptake inhibitors
- Deep brain stimulation (via stereotaxic surgery)
- Inhibition of Globus Pallidus which sends inhibitory inputs to motor cortex via thalamus

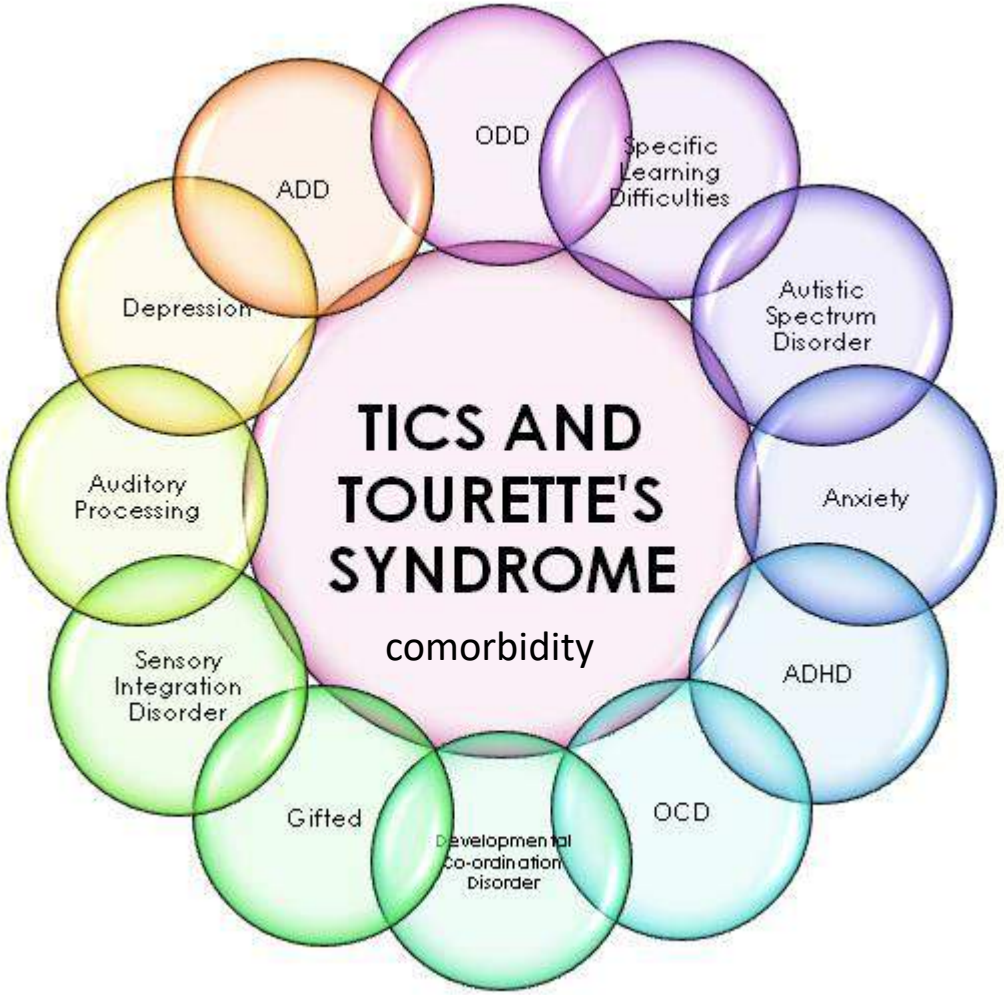




- Exact cause is unknown
- Neurodevelopmental (pregnancy, inhe
- Stress/anxiety can increase the tics

Excess of dopamine released in the caudate-putamen (basal ganglia) – that inhibits motor movements (motor movements not executed smoothly).





I have Tourette's syndrome,

which means that...

upbility
Publisher of Therapy Resources

- Five percent of children will start making tics at some point in their lives.
- Boys makes tics three or four times more often than girls.
- Tics are not 'bad habits' that can be stopped willingly.
- Tics are not caused by anxiety, stress, mental conflicts, or wrong family behaviour.
- Asking a child or a teenager to stop making tics is like asking an adult suffering from allergic rhinitis to stop sneezing.

What I want you to do is to:

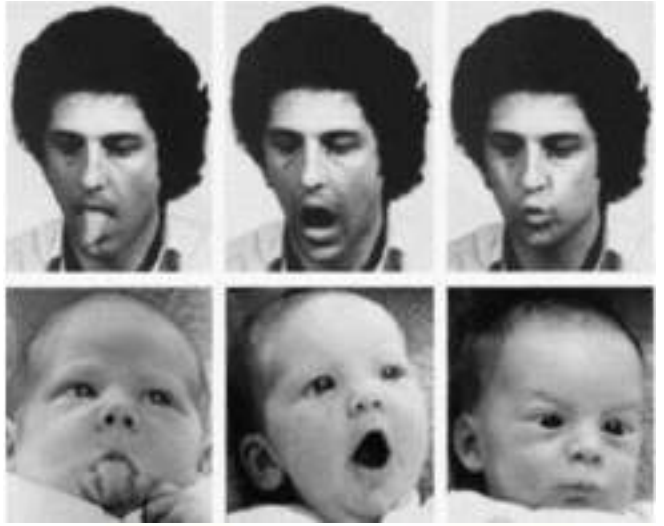
- stop scolding me. I don't do it on purpose.
- cease telling me that I have to stop these tics. You just make me more anxious.
- ignore my tics and look deep into my soul
- free me of any feeling of shame
- explain me what is wrong with me
- teach me relaxation techniques

How do we integrate our sensory world around us?

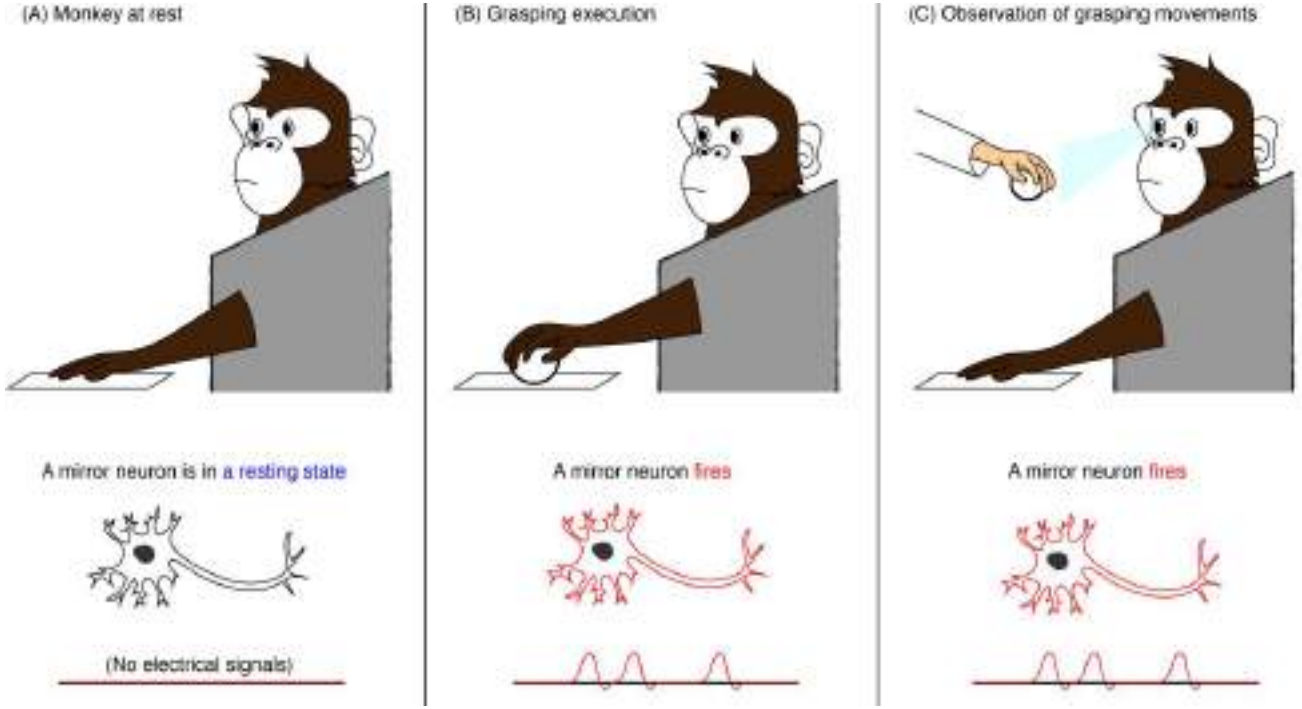
- Do neurons know what is happening outside the brain?
- Can vision, audition, and other sensory inputs make sense of the world?

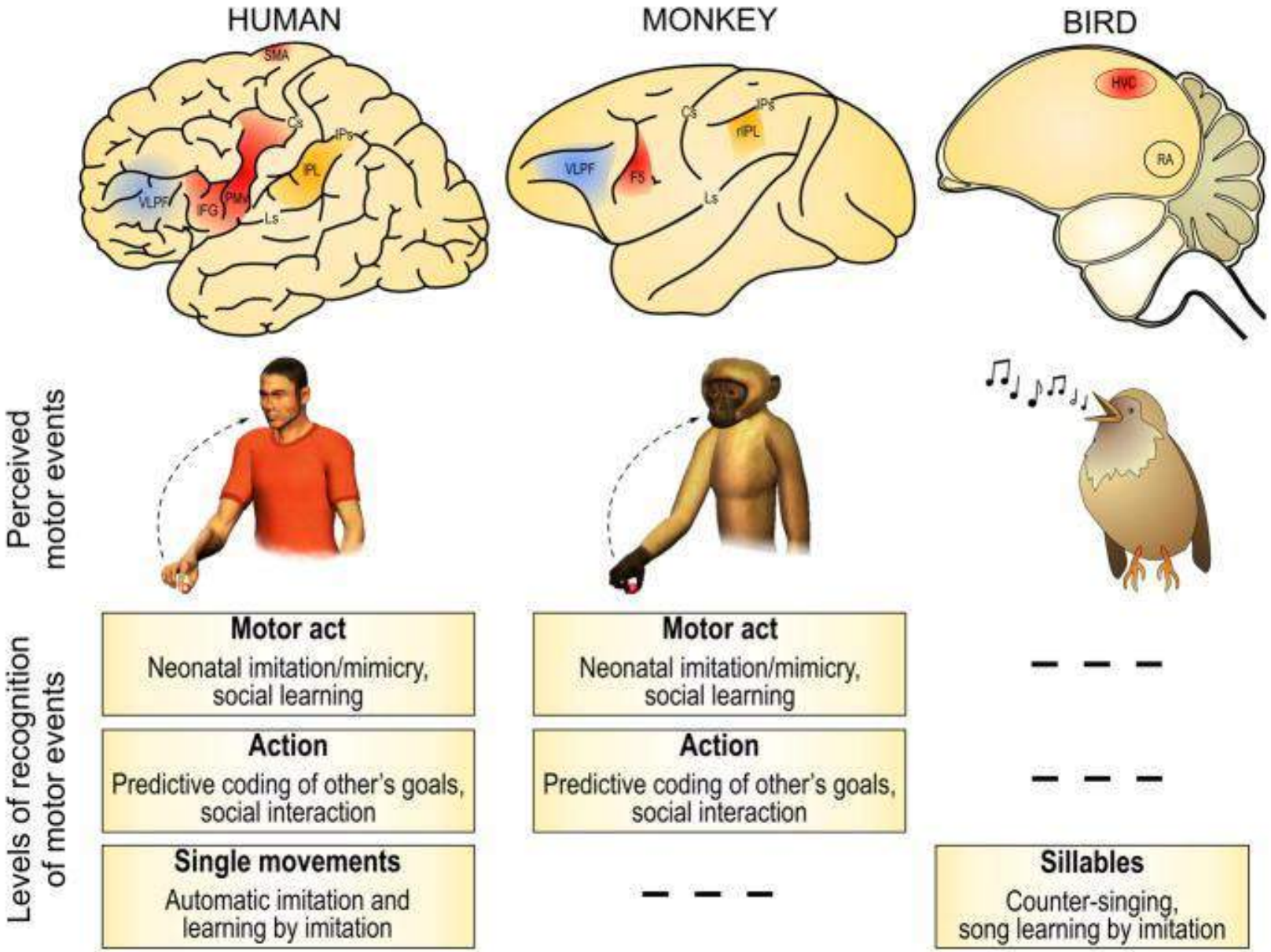
Mirror Neurons

- Our capacity to predict and imitate behaviour (understand actions of others)
- Allows us to mirror actions (learn by imitating others)
- Predict intention of a particular action
- Help us to empathize and understand others' emotions
- Important for social behaviour and interaction



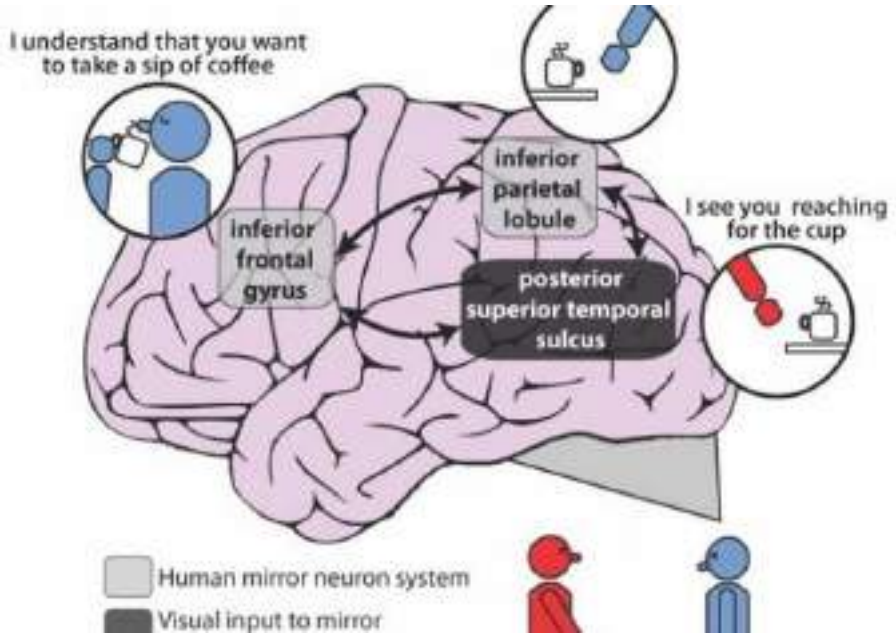
Neurons in the premotor cortex

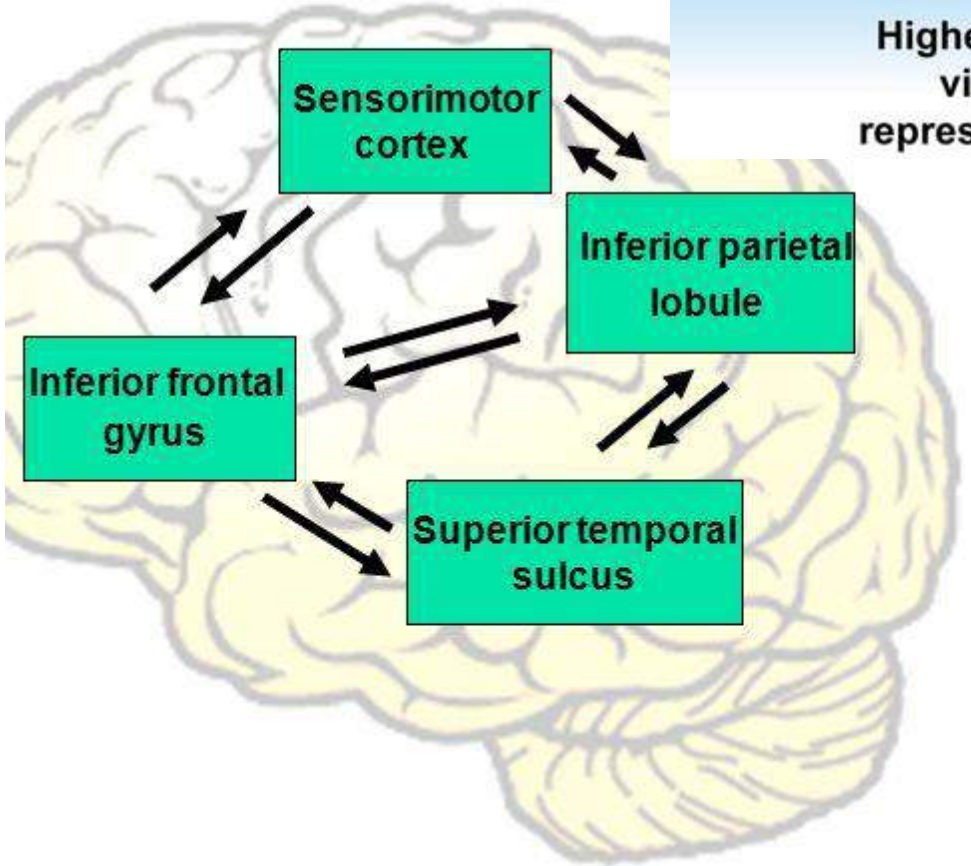


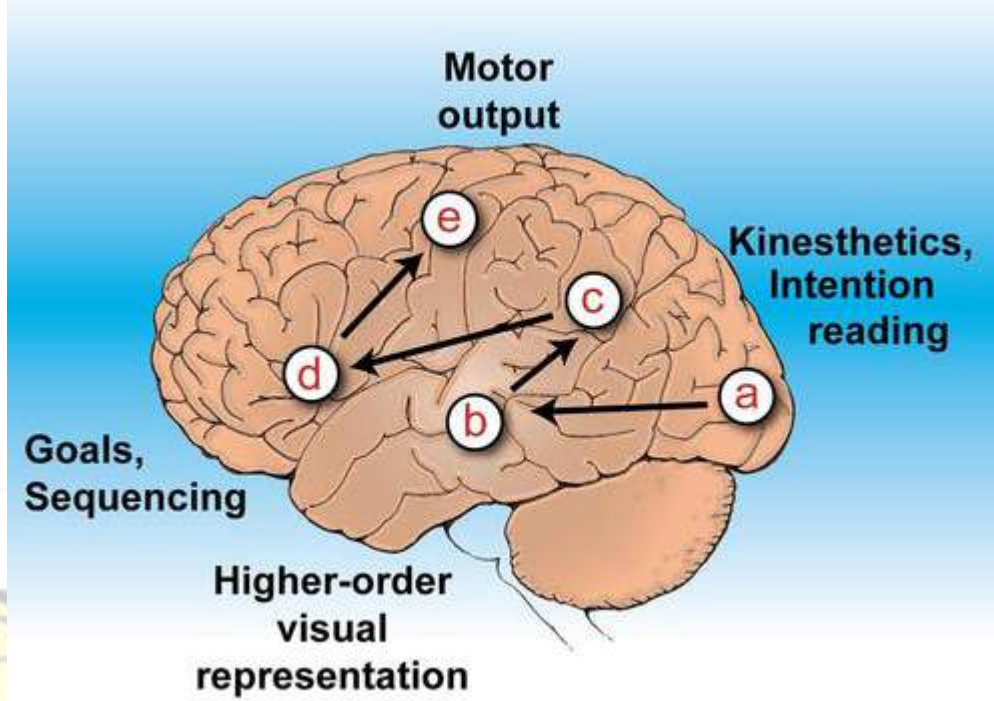


https://europepmc.org/article/PMC/3113469

The Mirror Neuron System







Phantom Limb

Mirror box

- A phantom limb is the sensation that an amputated or missing limb is still attached to the body and is moving appropriately with other body parts
- Most individuals with amputated limbs experience painful sensations from the nerve endings at the amputated site/ stump in an uncomfortable or unnatural position - pain, pressure, warmth, cold, wetness, itching, sweatiness, and prickliness

- Half cut afferent connections form neuromas – act as free nerve endings
  - Cut off afferent nerves carrying the sensation from the limb

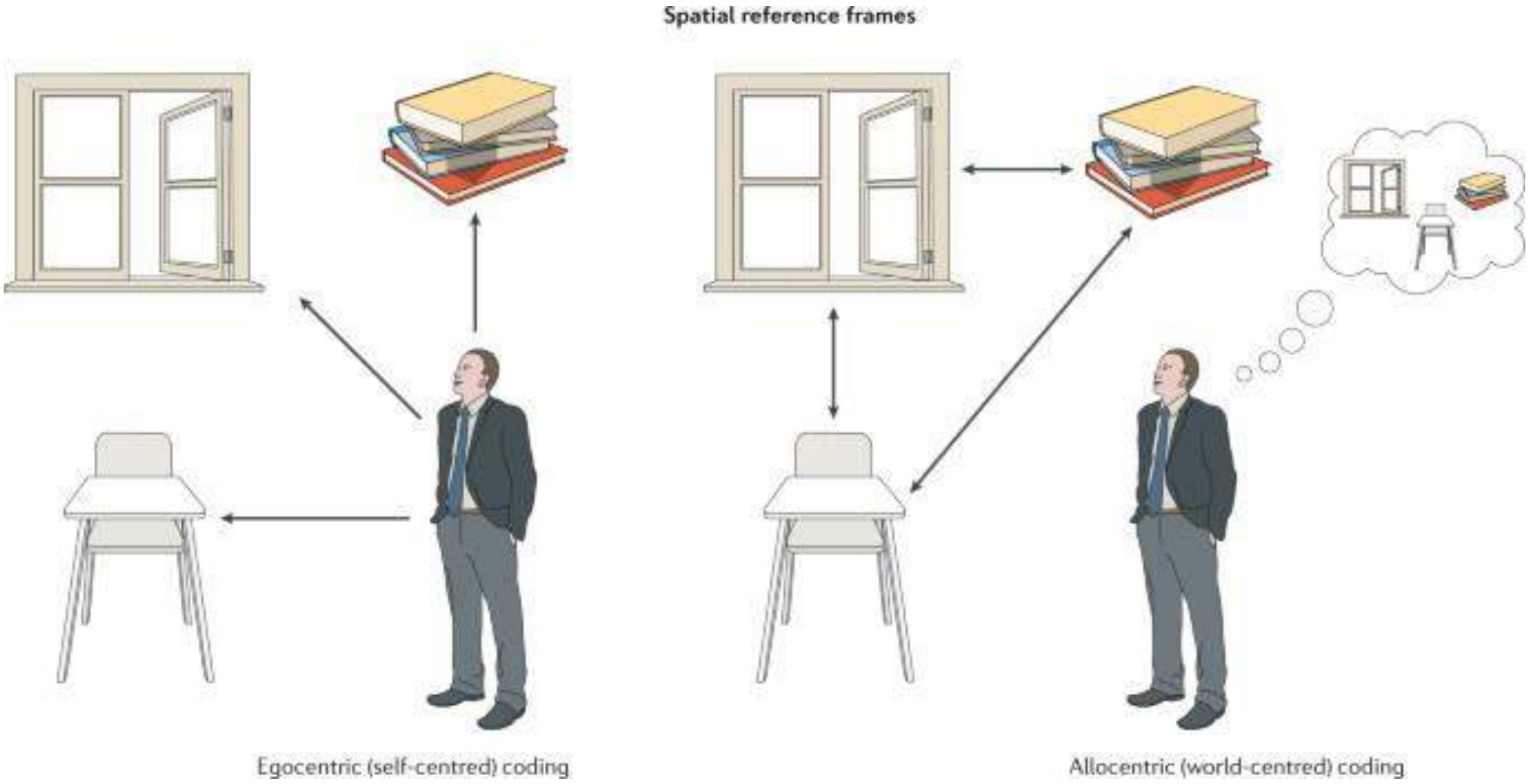
- Conflict between visual feedback and proprioceptive feedback
  - Mirror box therapy

[Rubber hand illusion]

- Treatments
  - Artificial visual feedback (Ramchandran's mirror box)
  - Massage
  - Acupuncture

How do we move in space?

Spatial Reference Frames



Parietal cortex
(WHERE pathway)

Hippocampus

Egocentric

Allocentric

Spatial learning

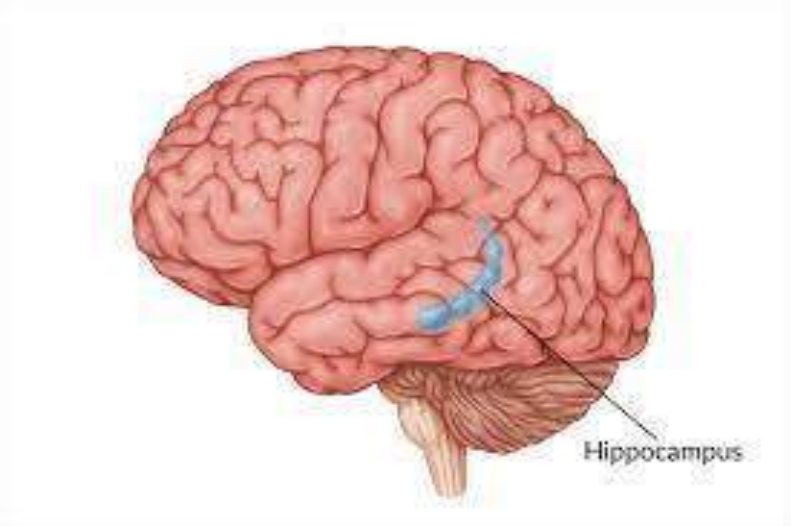
RESEARCH ARTICLE

Navigation-related structural change in the hippocampi of taxi drivers

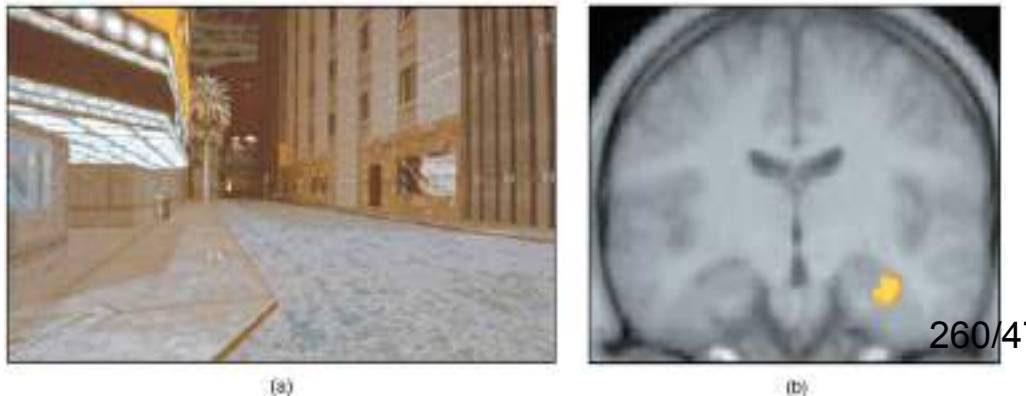
Eleanor A. Maguire, David G. Gadian, Ingrid S. Johnsrude, Catriona D. Good, John Ashburner, Richard S. J. Frackowiak, and Christopher D. Frith[†]

A PET scan study, revealed that the right hippocampus was activated when London taxi drivers described the routes.

- Bilateral temporal lobe damage results in severe impairment for spatial memories and navigation.



Virtual navigation also activates the hippocampus



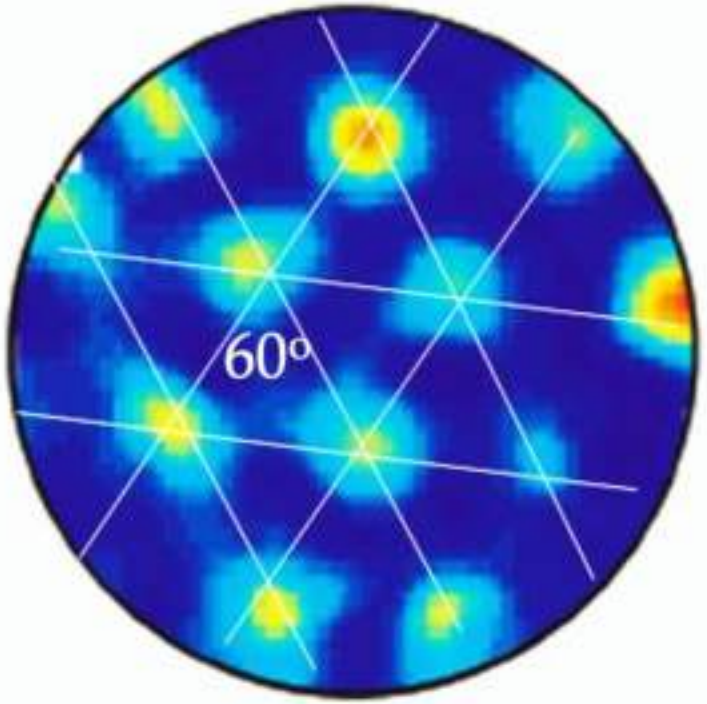
Elements of navigation
(the map metaphor)

Head directions cells

Ranck (1984)

no prize

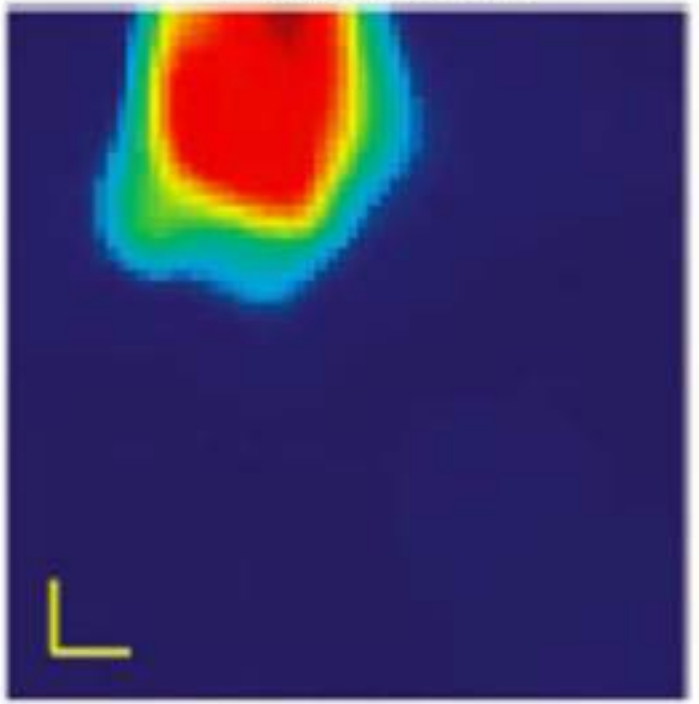
Grid cells



Moser group (2005)

Nobel Prize 2014

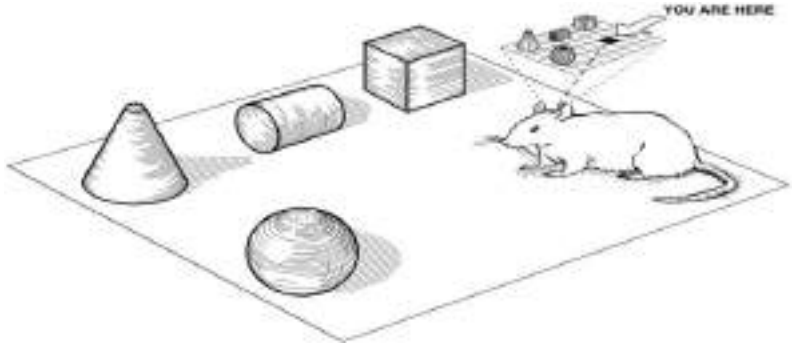
Place cells



O'Keefe (1971)

Nobel Prize 2014

Spatial navigation cell types



Examples of cell types with spatial tuning in the hippocampus and in parahippocampal cortices.

Grid cells fire in multiple spatial locations that form a triangular 'grid' of the environment

Head-direction cells fire throughout the environment but only when the animal is facing a specific direction.

Conjunctive cells fire in a triangular grid pattern only when the animal is facing a specific direction.

Boundary/border cells fire when the animal is located at a specific distance from a wall in the environment.

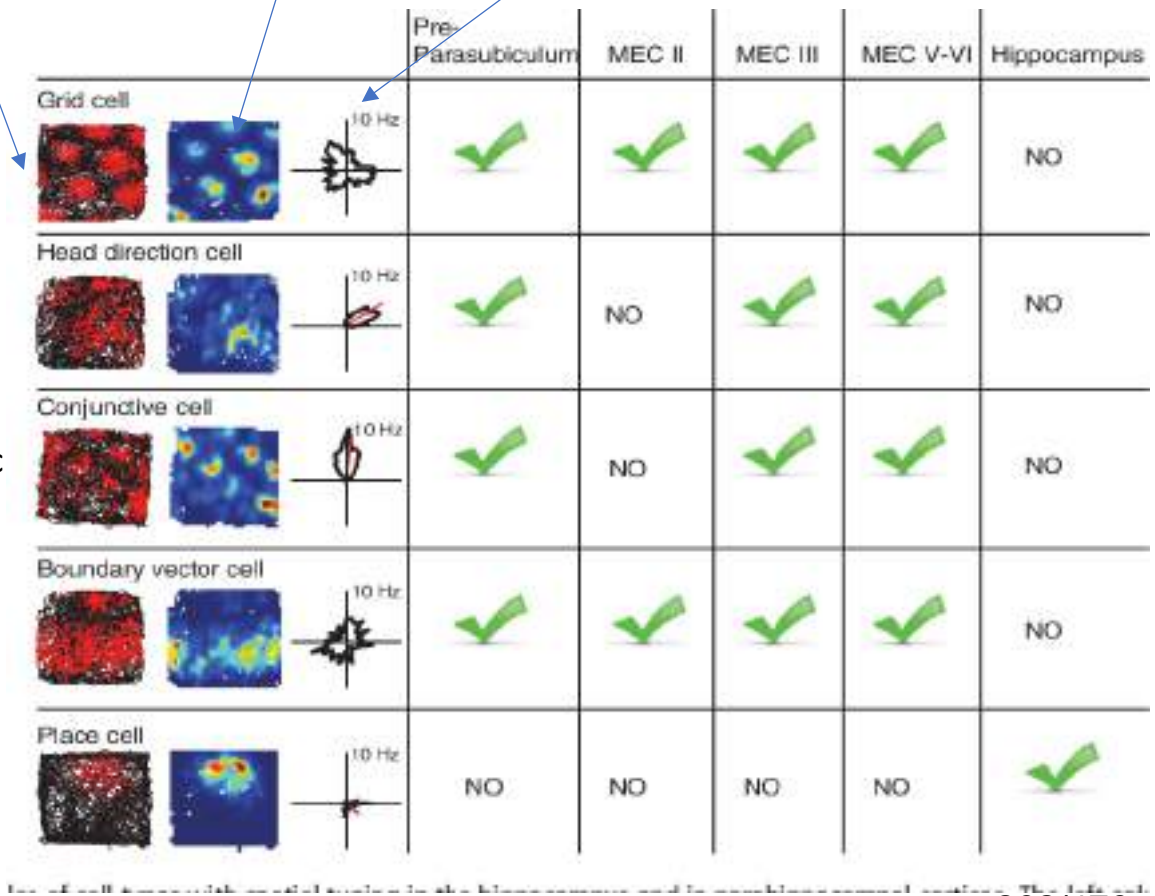
Place cells generally fire in a single or few locations within the environment, independent of the animal's head direction in the open field. These cells are found in the dentate gyrus, CA3, and CA1 of the hippocampus.

The spatial selectivity of each cell type is shown by plotting the location of each spike (in red) onto the trajectory of the animal (in black).

central panels are color-coded firing rate maps of the same arena with high firing rates in red and low firing rates in blue

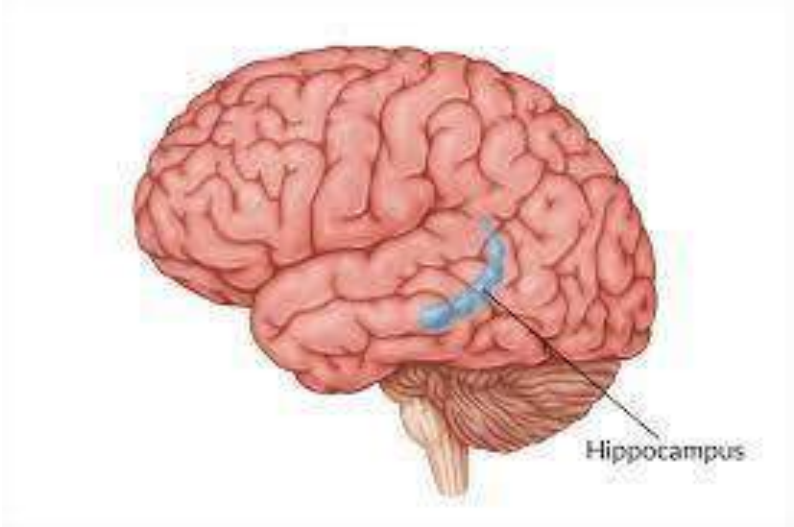
polar plots showing firing rate as a function of the head direction of the animal during exploration in the environment.

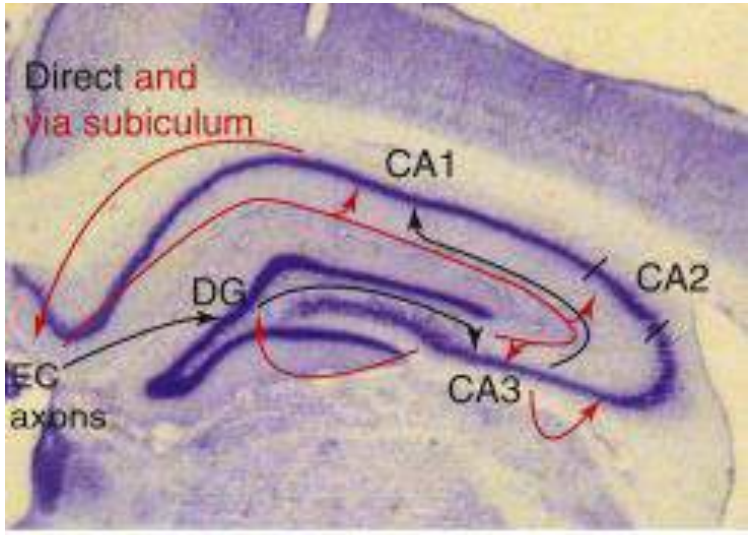
Specific Regions that surround the hippocampus



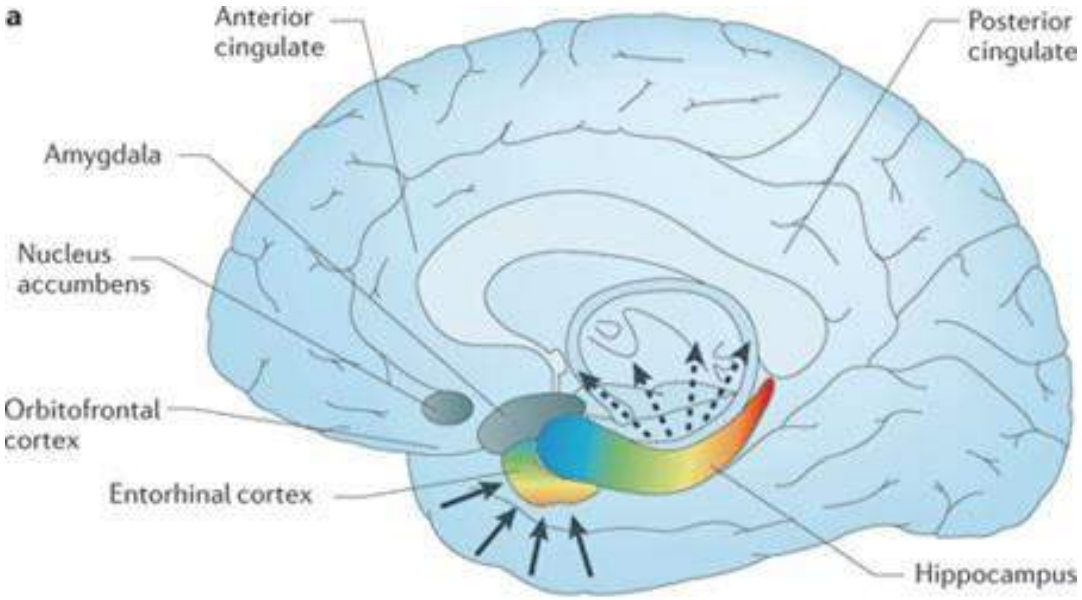
[Source + extra reading : Parallel and convergent processing]

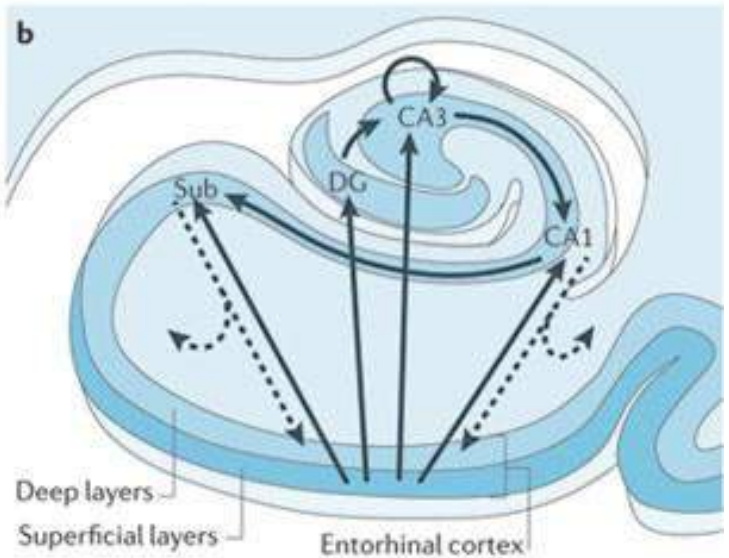
Hippocampus Means “Seahorse”



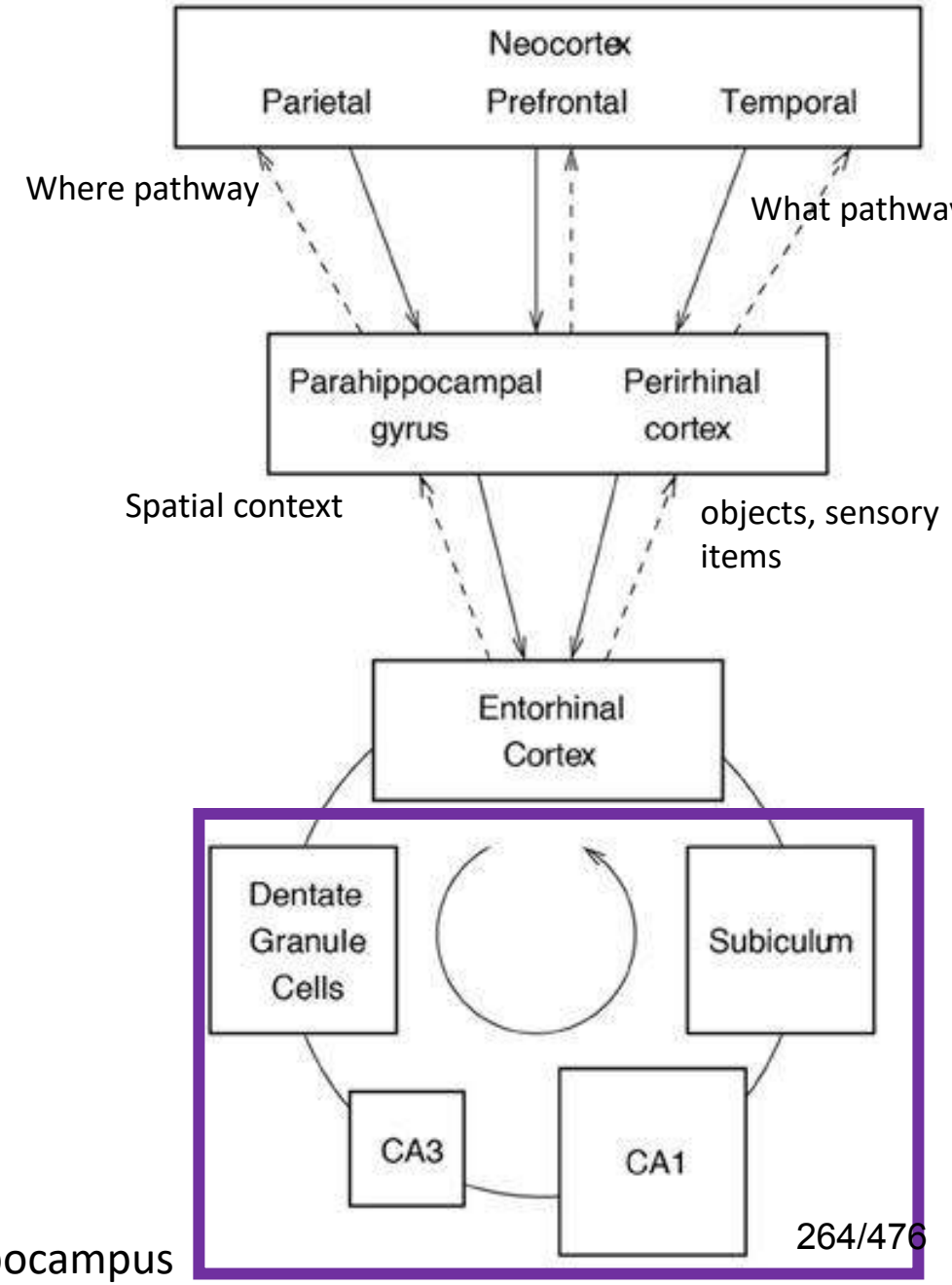


https://www.frontiersin.org/articles/10.3389/fnsys.2013.00074/full



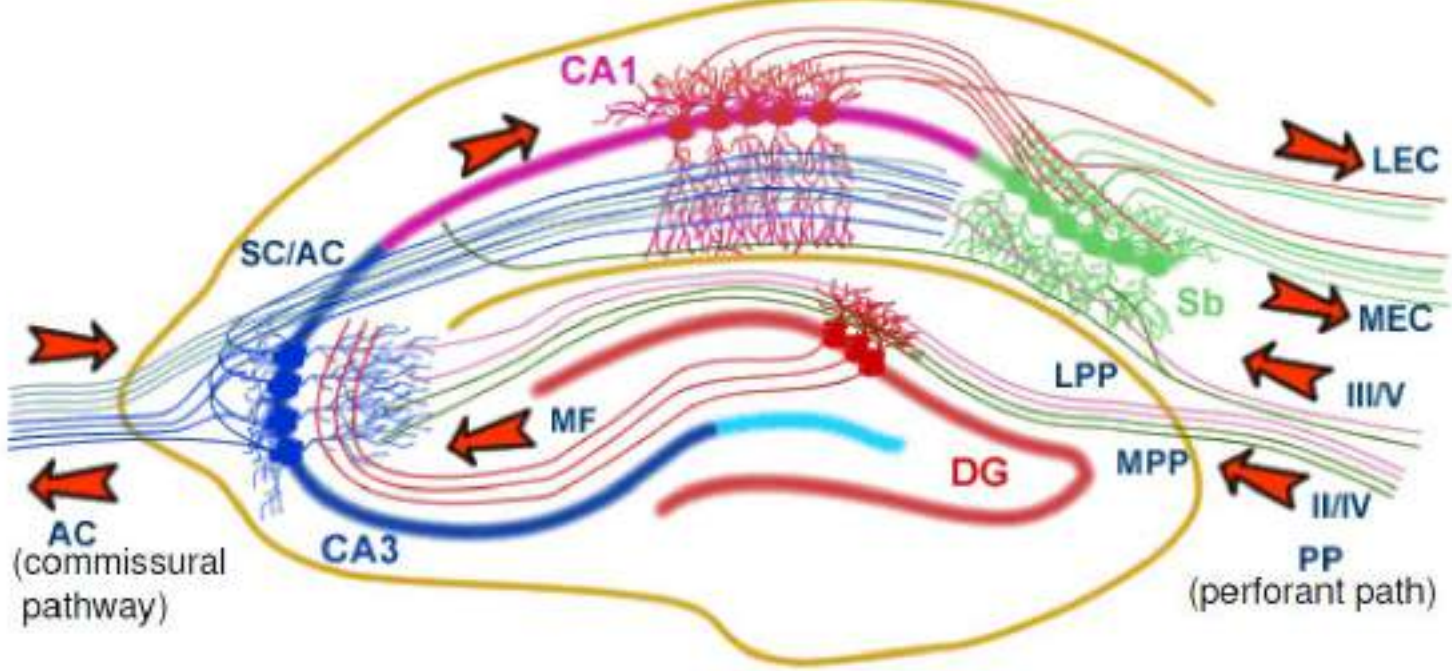


Nature Reviews | Neuroscience



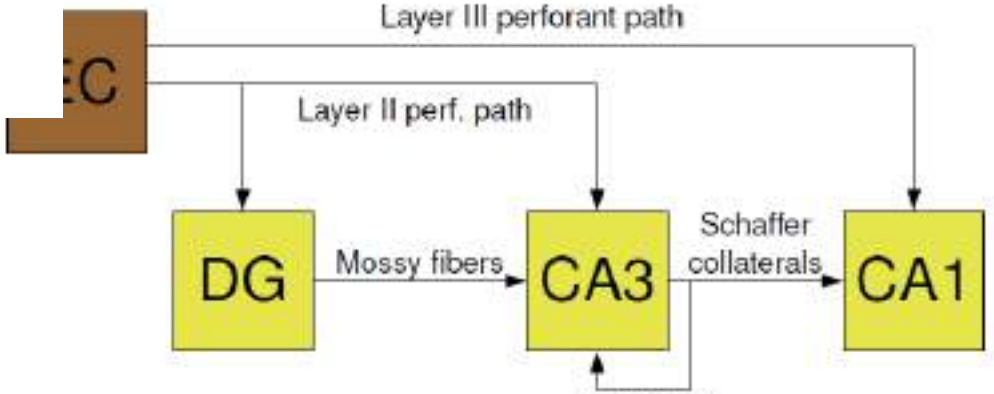
hippocampus

Hippocampal Autoassociative Network



The Hippocampal Network: The hippocampus forms a principally uni-directional network, with input from the Entorhinal Cortex (EC) that forms connections with the Dentate Gyrus (DG) and CA3 pyramidal neurons via the Perforant Path (PP - split into lateral and medial). CA3 neurons also receive input from the DG via the mossy fibres (MF). They send axons to CA1 pyramidal cells via the Schaffer Collateral Pathway (SC), as well as to CA1 cells in the contralateral hippocampus via the Associational Commissural pathway (AC). CA1 neurons also receive input directly from the Perforant Path and send axons to the Subiculum (Sb). These neuron in turn send the main hippocampal output back to the EC, forming a loop.

- Sparse coding/representation
- Autoassociative
- Information integrator (where, what, when)



The mossy fiber synapse is one of the largest and most powerful synapses in the brain.

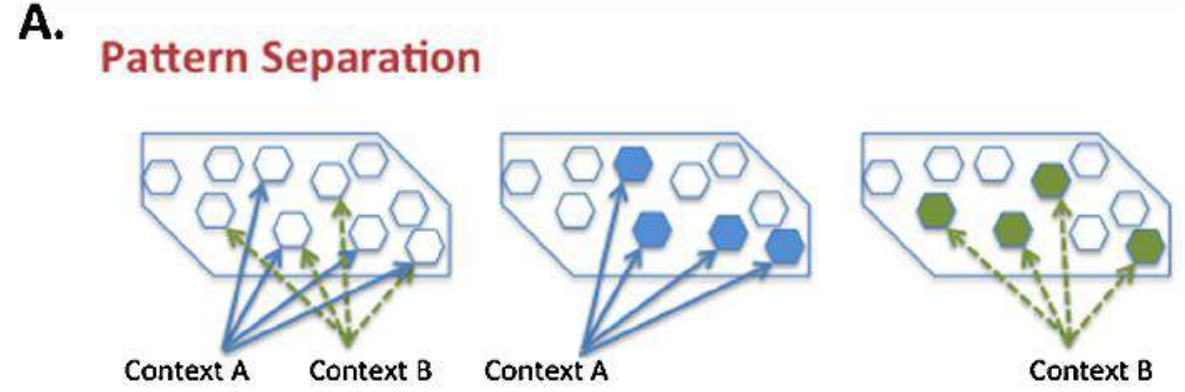
How do we differentiate very similar events?

- Let’s see if you can remember them

Old items - Target

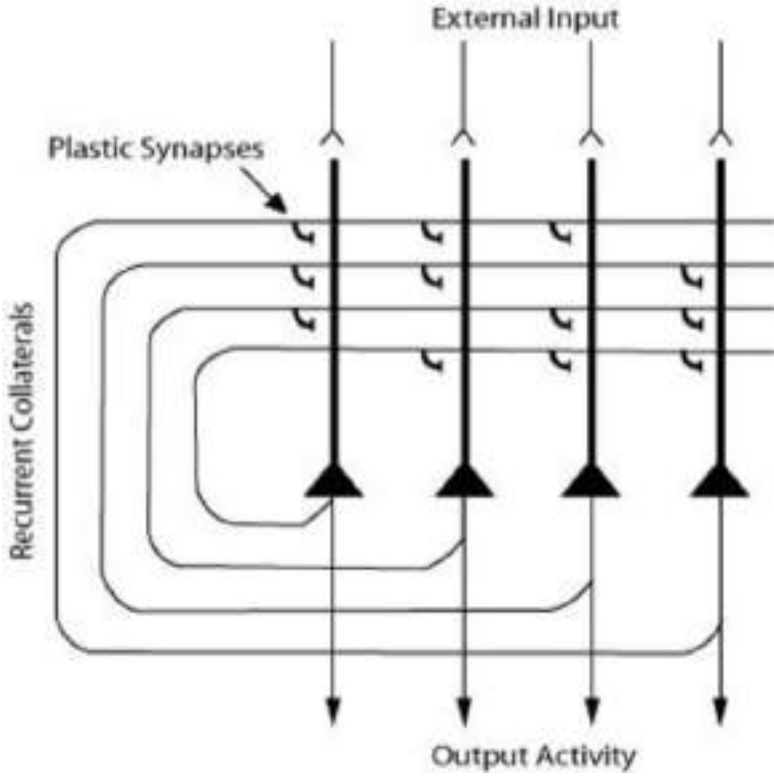
Similar items - Lures

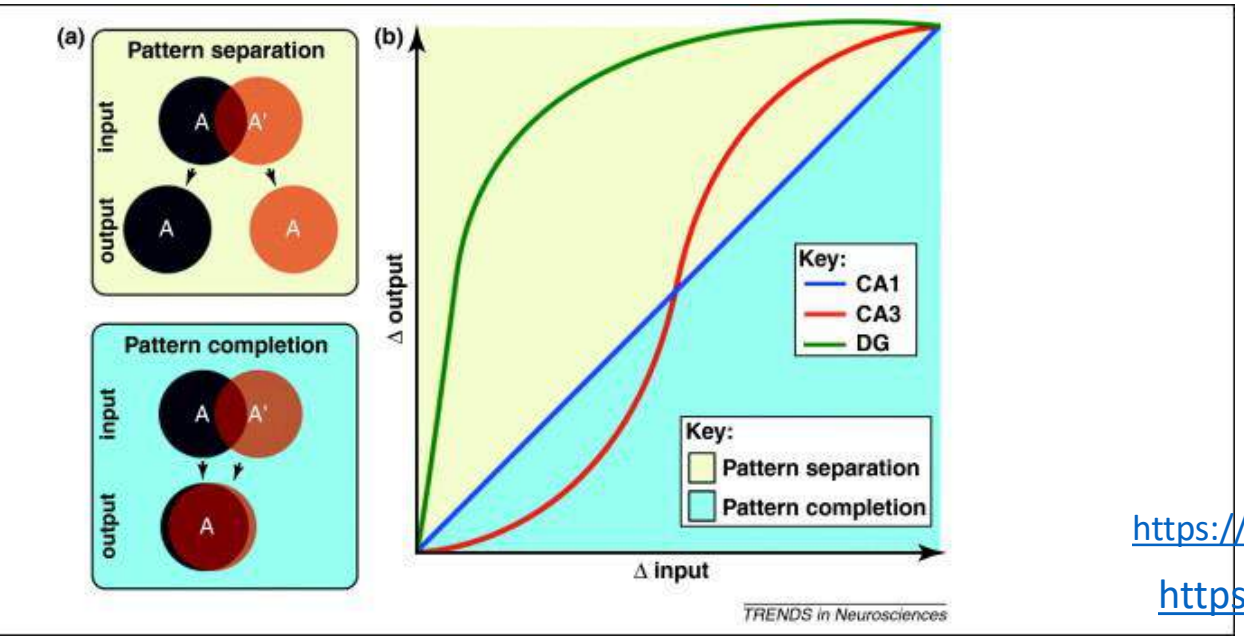
New items - Foils



Dentate Gyrus (DG)

(Cornu Ammonis 3) CA3



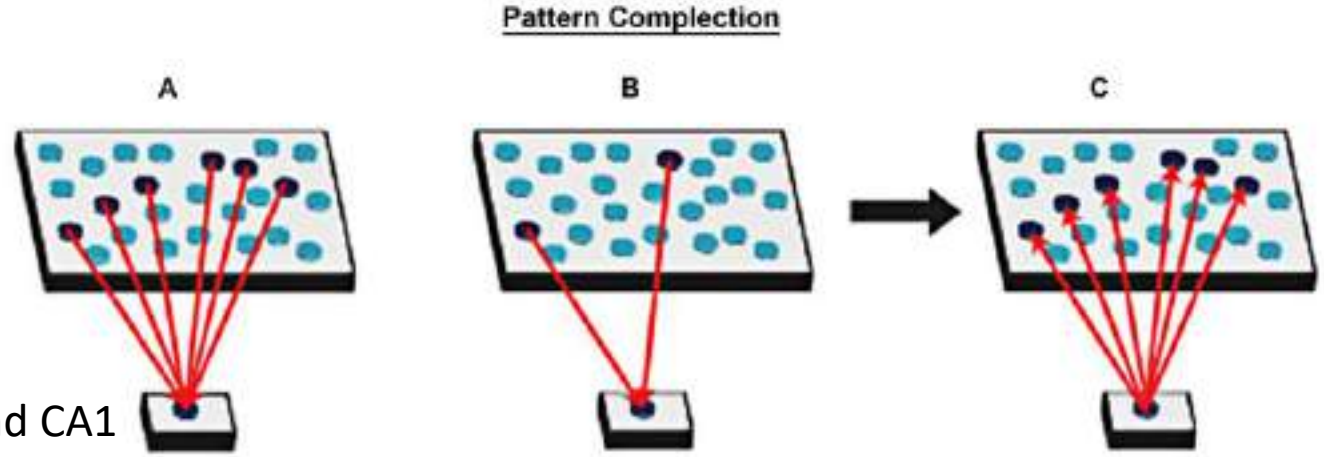


- Sparse coding/representation
- Autoassociative
- Information integrator (where, what, when) – by moving around in the world (every eye saccade gives you a different input of the world)

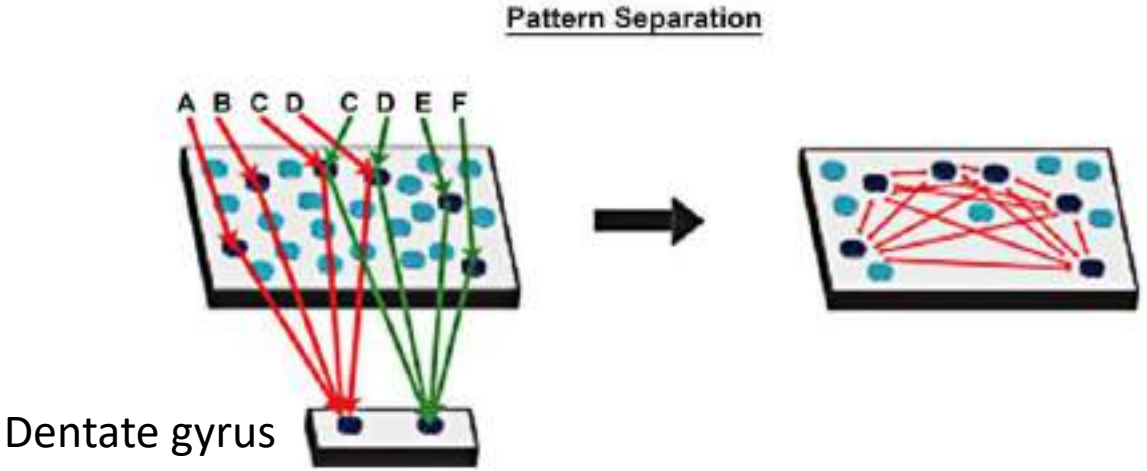
https://www.sciencedirect.com/science/article/abs/pii/S0301008215300186?via%3Dihub

https://www.sciencedirect.com/science/article/abs/pii/S0166223611001020

CA3 and CA1



Dentate gyrus



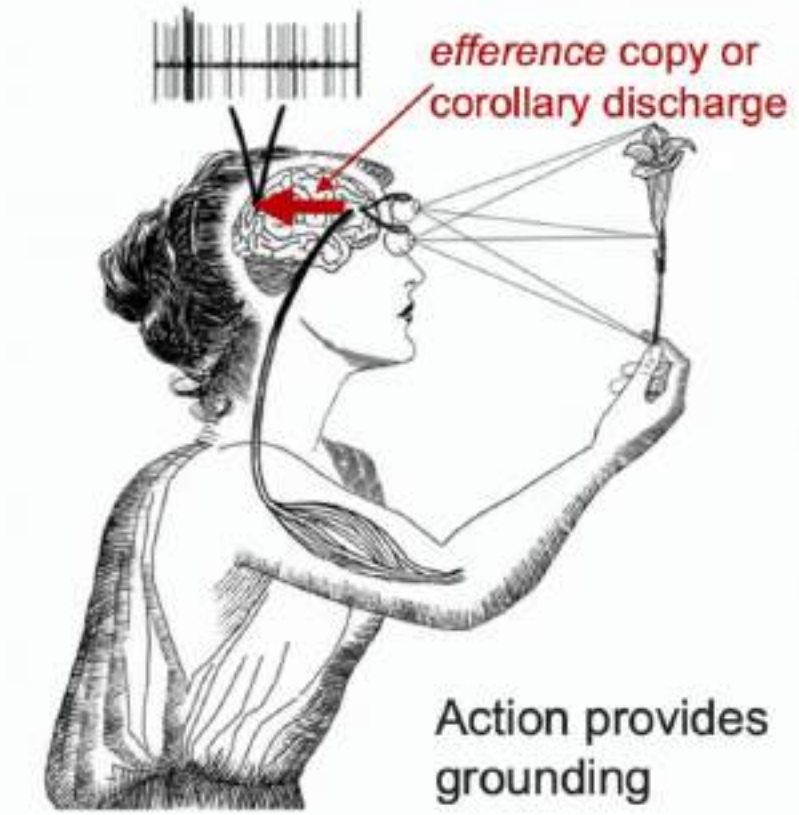
Pattern discrimination and completion are recognized as complementary processes, requiring a fine balance between establishing and dissociating new memories and reconstructing old ones

- How do you make sense of the world and understand how things operate in your environment

How do you find out whether the straw is broken or intact?

Inside-out framework

(internally organized, action based)



The brain learns by making predictions using movement and sensory input

Gyorgy Buzsaki

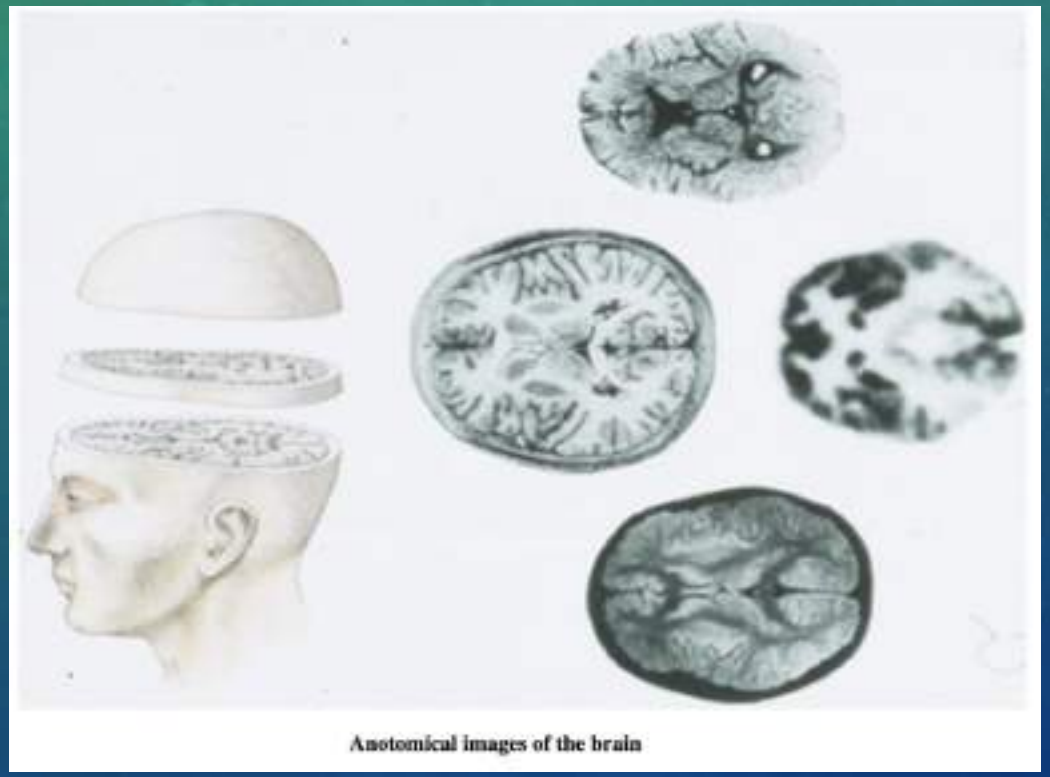
BRAIN RECORDING TECHNIQUES

COGNITIVE NEUROSCIENCE

NEUROIMAGING

- Choice of technique depends on what you want to study:
  - STRUCTURE vs FUNCTION
  - Temporal scales
  - Spatial scales
  - Invasive vs non-invasive
  - Aimed at inferring causation: brain stimulation or other methods to manipulate the activity of neurons (e.g. optogenetics)

ANATOMY (STRUCTURE)



Anatomical images of the brain

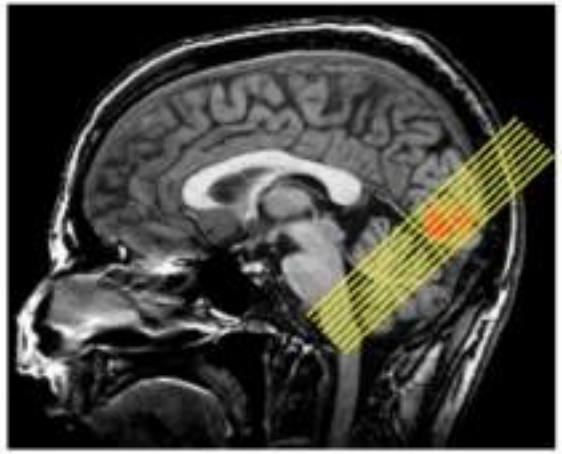
Source: David Heeger's lecture notes on perception

NEUROIMAGING

- CT & MRI give good static (still) images
  - MRI is better for soft tissues
- PET, fMRI, MEG, EEG are functional image techniques
  - PET scans are invasive due to the injection of tracers (short half-life radioactive isotopes)
  - fMRI is non-invasive with high spatial resolution but low temporal resolution
  - MEG/EEG are non-invasive with high temporal resolution
- ECoG (electrocorticography), LFP (local field potential), and single unit recordings are invasive – requires surgery and hence cognitive studies with these techniques are only done when surgery is required for clinical purposes (E.g. epilepsy, Parkinson's disease, etc)

FMRI

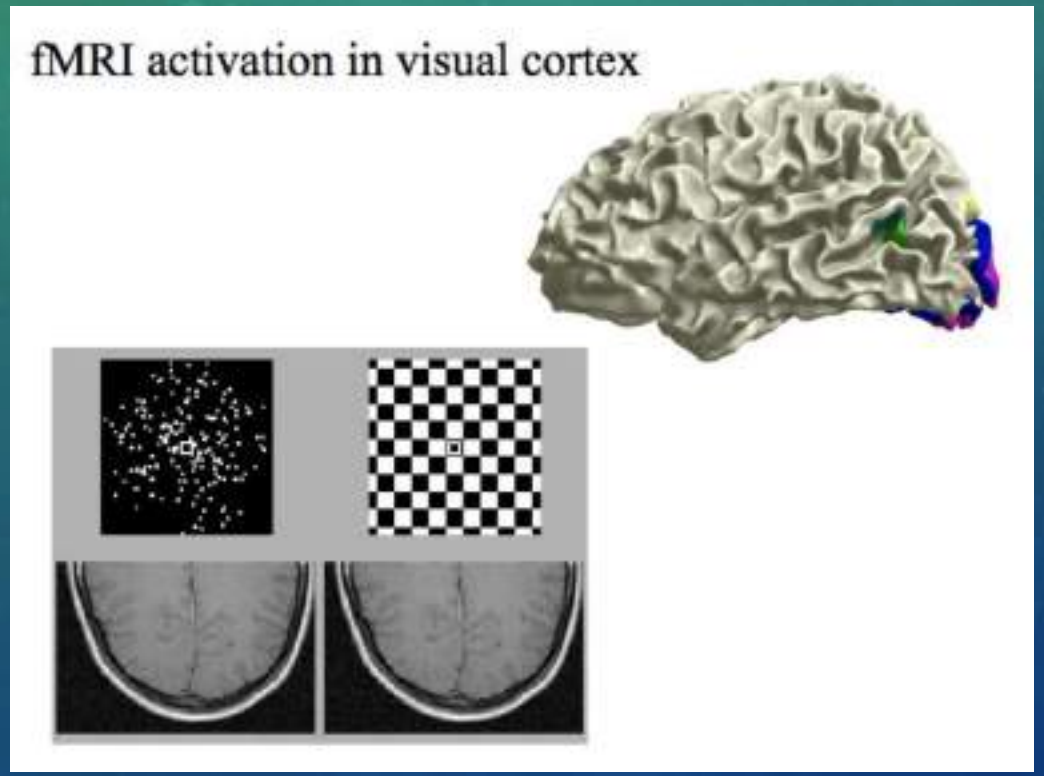
Functional magnetic resonance imaging



Revolution in psychology and neuroscience: >1000 papers published per month over the past 5 years!

Source: David Heeger's lecture notes on perception

FMRI



Motion perception activates area MT (or V5)

Source: David Heeger's lecture notes on perception

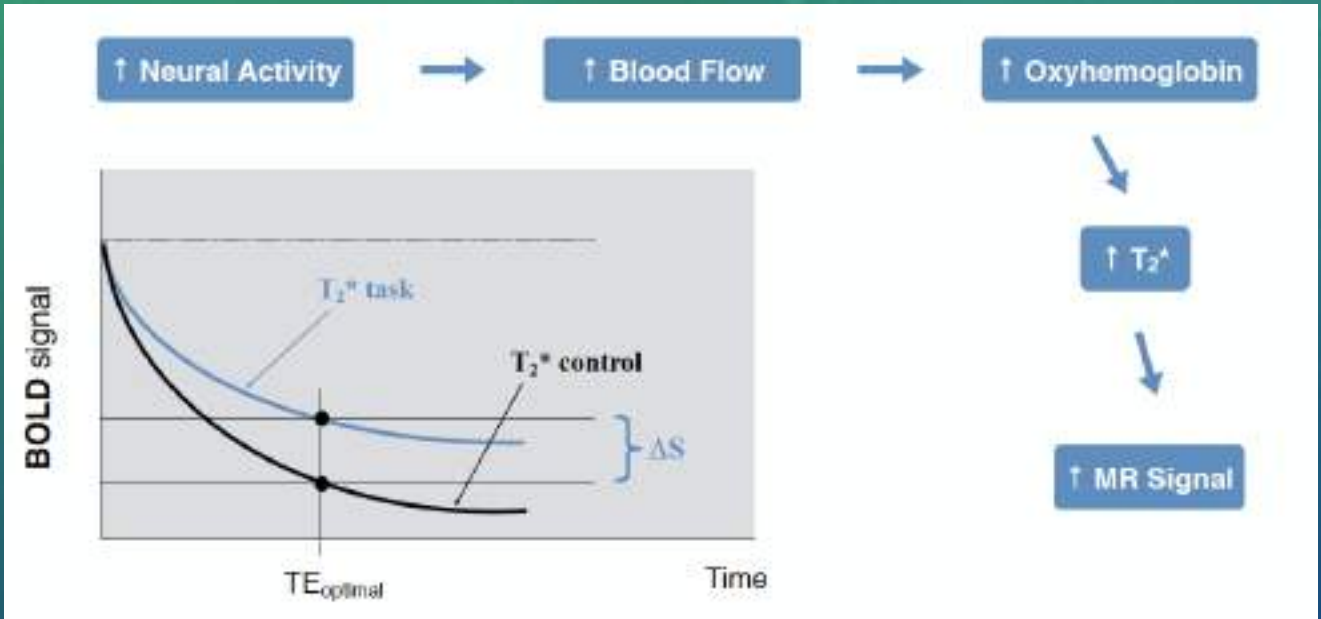
HOW DOES FMRI WORK?

- Essentially by measuring blood flow in the brain, due to the coupling between neuronal activity and hemodynamics (dynamics of blood flow). BOLD fMRI = Blood Oxygen Level Dependent functional MRI
- Specifically:

1. Flow of oxygenated blood to where it is needed in the brain (Roy & Sherrington, 1890)
2. Blood contains iron which is magnetic. Oxygenated and deoxygenated blood have different magnetic properties (Linus Pauling, 1930s).
3. MRI was invented in 1970s, based on the physics of magnetic resonances (1940s).
4. The MRI scanner was reprogramed to pick up differences in magnetization that take place when the oxygenated blood is shipped to where it is needed in the brain.

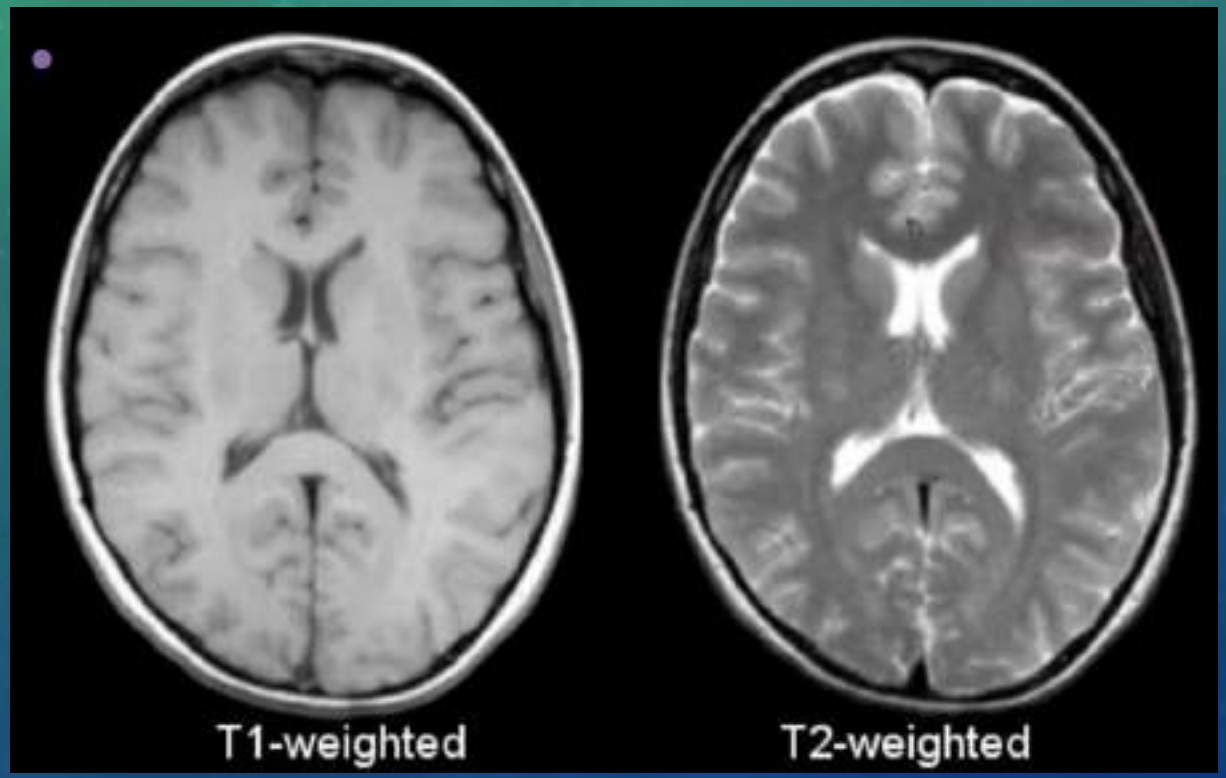
Source: David Heeger's lecture notes on perception

MECHANISM OF BOLD FMRI



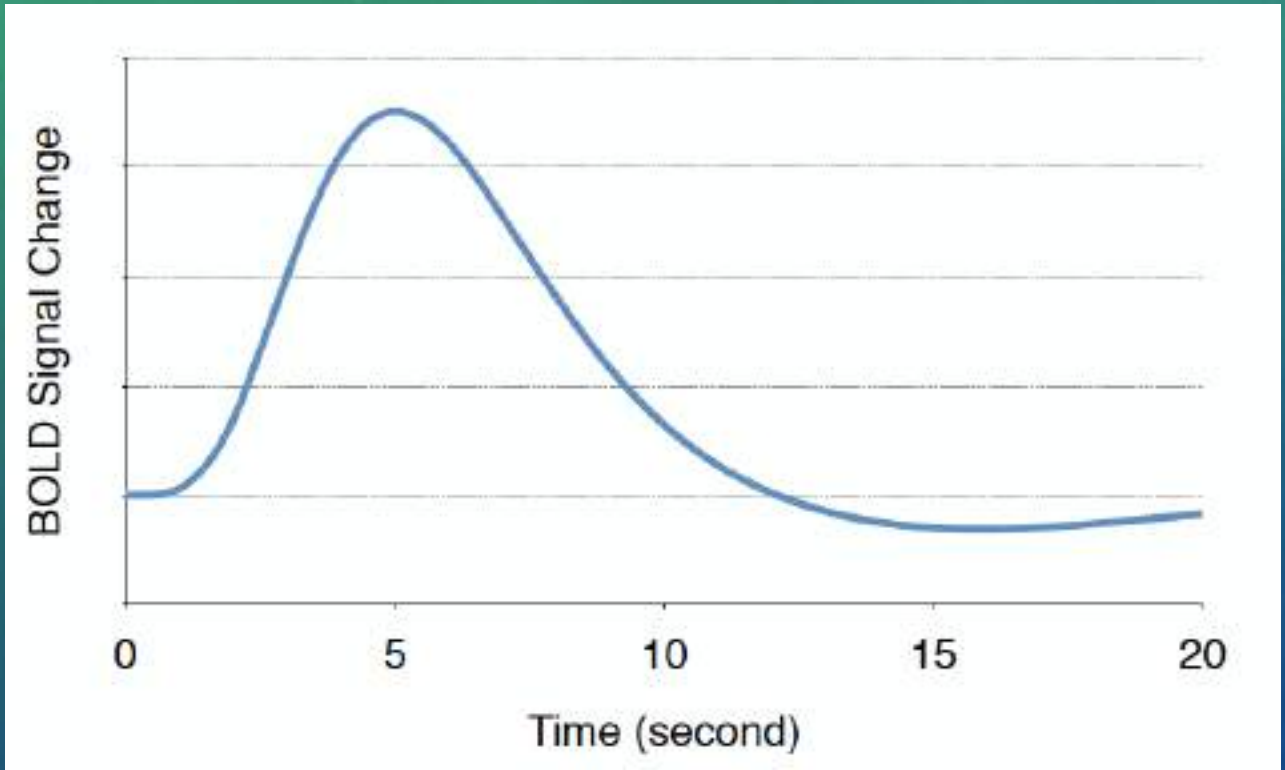
- BOLD primarily responds to concentration of deoxygenated hemoglobin which is paramagnetic and interferes with the MR signal making the local magnetic field inhomogeneous.
- MRI = RF pulse is applied to kick nuclei to higher magnetization levels and then removed to make nuclei “relax” to their original states. The energy emitted during this relaxation process is captured by a coil to recreate positions of the nuclei.
- fMRI - does the above by also measuring magnetic differences between oxygen-rich and oxygen-poor blood.

Source: Sunghyon Kyeong (Yonsei Univ)



https://case.edu/med/neurology/NR/MRI%20Basics.htm

HEMODYNAMIC RESPONSE AND THE CANONICAL HEMODYNAMIC RESPONSE FUNCTION



- Slow!
- The change in MR signal from neuronal activity = hemodynamic response.
- HRF = hemodynamic function is a model fit to many empirical observations of HR or a transfer function linking neural activity with fMRI signal, modeling neurovascular coupling
- *This hemodynamic response lags the generating neuronal activity by a few seconds*.
- Therefore, the temporal resolution of fMRI (several seconds) is poor relative to EEG or MEG (millisecond resolution).

https://andysbrainbook.readthedocs.io/en/latest/fMRI_Short_Course/Statistics/03_Stats_HRF_Overview.html is a useful reference

Source: Sunghyon Kyeong (Yonsei Univ)

HEMODYNAMIC RESPONSE

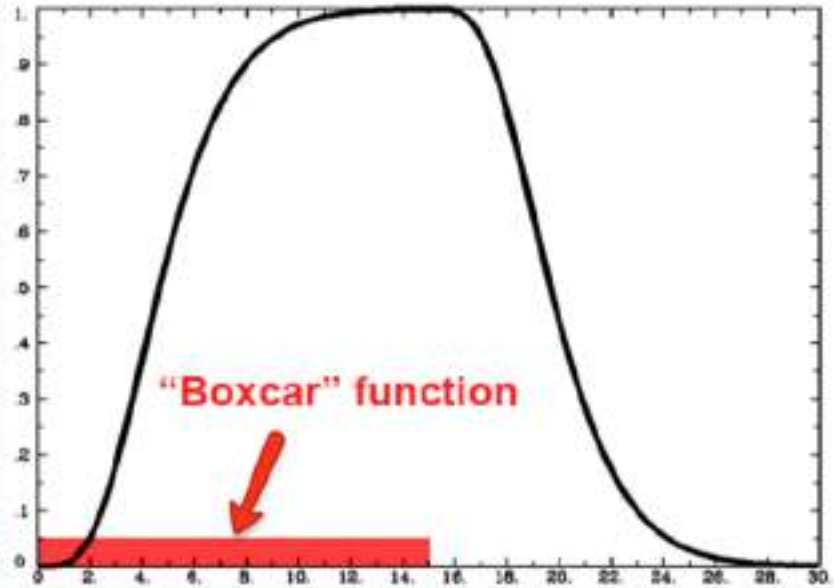
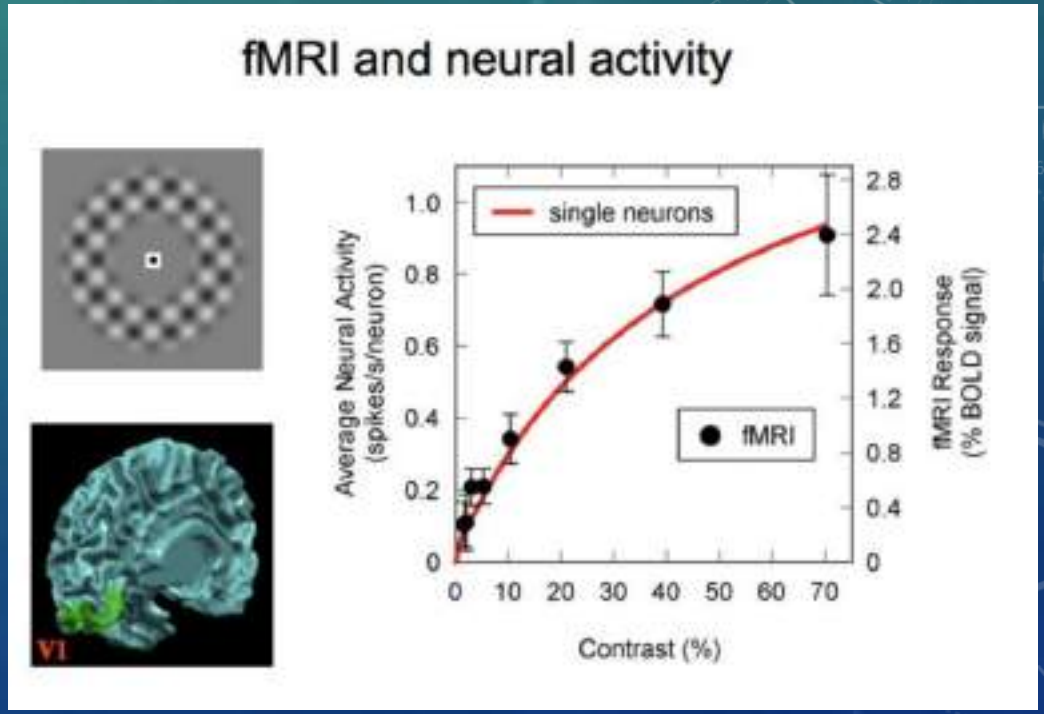


Illustration of the HRF generated by a boxcar stimulus lasting for fifteen seconds. Note that the BOLD signal begins descending back to baseline around the fifteen-second mark.

https://andysbrainbook.readthedocs.io/en/latest/fMRI_Short_Course/Statistics/03_Stats_HRF_Overview.html is a useful reference

SO IF IT MEASURES BLOOD FLOW, IS IT REALLY STRONGLY RELATED TO NEURONAL ACTIVITY?

- Although we know that fMRI works based on metabolic demands of increased neuronal activity, this process is not well understood and therefore, fMRI is only an indirect measue of neuronal activity.
- Nevertheless, there have been demonstrations that they are indeed tightly linked:



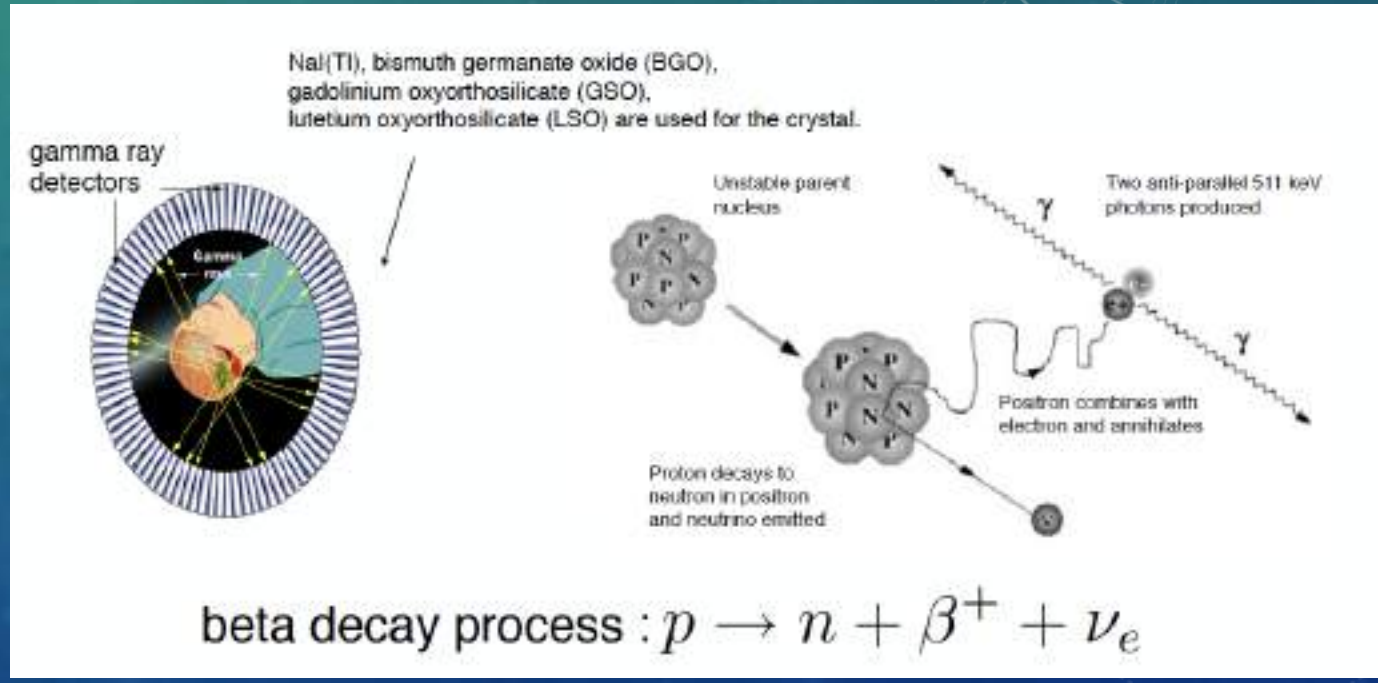
Source: David Heeger's lecture notes on perception

BOLD FMRI PROS AND CONS

- Pros: High spatial resolution (a few mm, laminar fMRI can even get sub-mm resolution), non-invasive
- Cons: Low temporal resolution (6-8 second lag from the triggering neuronal events), claustrophobia can be an issue, noise in the scanner, movement can influence recordings, etc

PET (POSITRON EMISSION TOMOGRAPHY)

- Hemodynamically based like fMRI, but can also detect glucose intake
- Invasive due to the use of radioactive tracers (i.e., small dose of radioactive substance added to water or sugar)
- Temporal resolution is poor (several seconds)
- Good spatial resolution (a few mm)



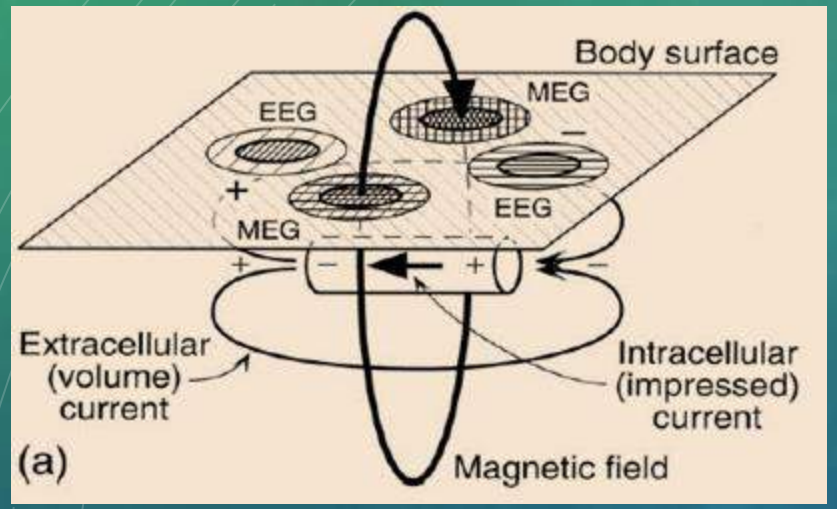
MEG: introduction

http://www.admin.ox.ac.uk/estates/capitalprojects/previouscapitalprojects/megscanner/

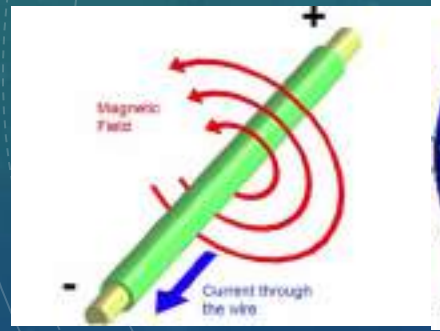
- **Magnetoencephalography**
- Direct external recordings of **magnetic fields** created by electrical currents in cortex
- Role of MEG in neuroimaging:
  - **Neural correlates** of cognitive/perceptual processes
  - **Localise** affected regions before surgery(?), determine regional and network functionality

Source: Linda Shi

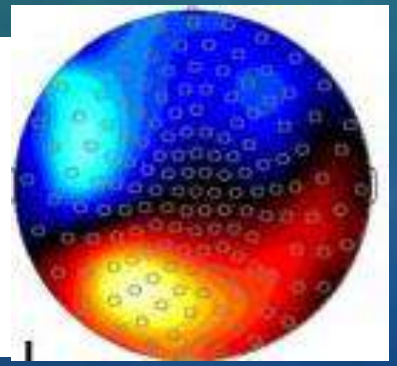
MEG: basis of the signal



Tiege & Zlobinski, 2006



http://www.youtube.com/watch?v=CPj4jJACeIs

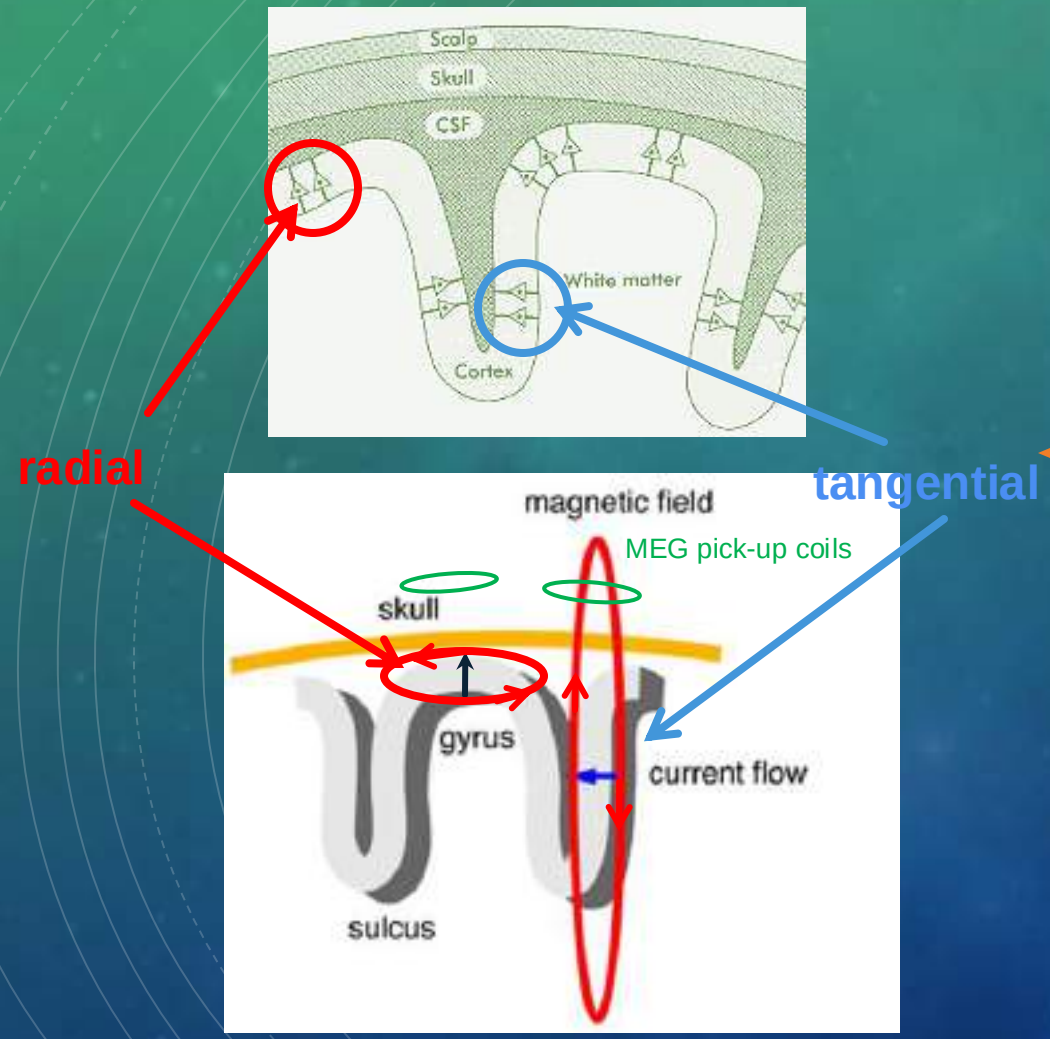


Ochi et al. 2011

- **large pyramidal neurons** in layer V of cortex, arranged in parallel, similarly-oriented, perpendicular to surface, fire synchronously
- Dipolar current flow generates a **magnetic field.**
  TRY IT: 'Right hand grip'!
- **10,000 to 50,000** active neurons required for detectable signal

Source: Linda Shi

MEG: tangential vs. radial



Tiege and Zlobinski, 2006

- MEG magnetic field **not distorted** by conductive properties of scalp/head
- MEG coil not sensitive to **perfectly radial sources**
- But in practice, only a **small proportion (<1%)** of cell populations are perfectly radial – i.e. on top of gyri

Source: Linda Shi

MEG: scale of magnetic field

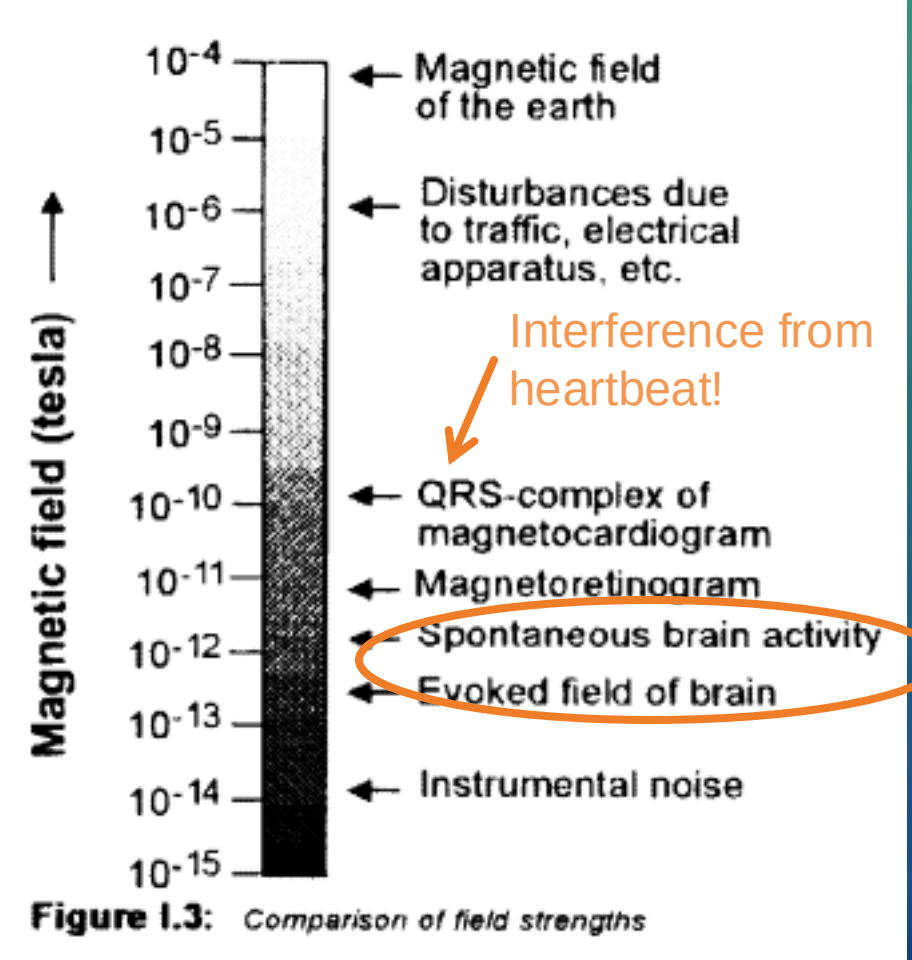


Figure I.3: *Comparison of field strengths*

- MEG signal is **tiny!**
- **Interference** from electrical equipment, traffic, the earth, participant's heartbeat etc.
- Requires **magnetically shield rooms** and **supersensitive magnetometers**

Source: Linda Shi

MEG: magnetically shielded room (MSR)

Brock & Sowman (2014)

- 3, 5 or 6 layers with different magnetic properties to protect from different frequencies of magnetic interference

Source: Linda Shi

MEG

- High temporal and spatial resolution
- Needs to be highly shielded, measuring really small magnetic fields generated by neuronal currents

EEG: introduction

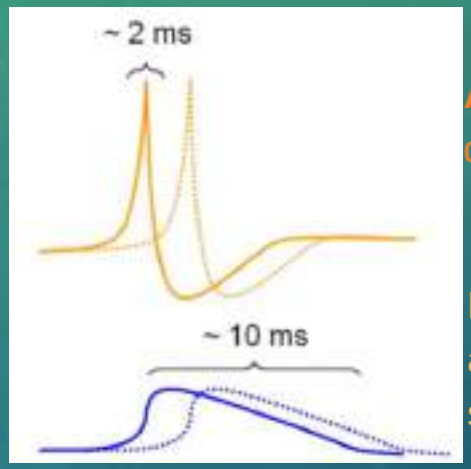
- **Electroencephalogram** (EEG) electrodes
- Scalp recording of **electrical activity** of cortex => waveform signals
- **Microvolts** (μV) – small!
- Role of EEG in neuroimaging:
  - Identify **neural correlates**
  - **Diagnose** epilepsy, sleep disorders, anaesthesia, coma, brain death

http://opencc.co.uk/blog/out-of-touch-manual-keypads-and-controllers-face-competition-from-new-hands-free-computer-interfaces/

Source: Linda Shi

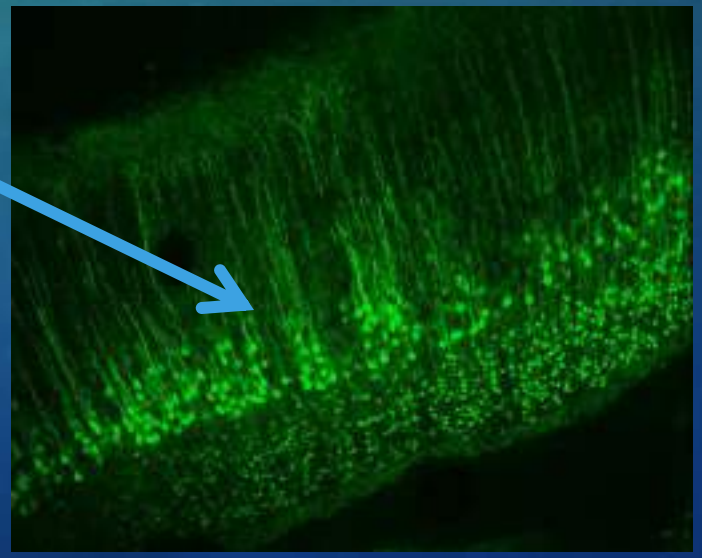
EEG: basis of the signal

- PSPs can be excitatory or inhibitory
- MEG/EEG reflects the **summation of synchronous PSPs** across a population of cells, at a point in time.
- **Large pyramidal neurons** in cortex layer V are:
  - ✓ arranged in parallel
  - ✓ similarly-oriented
  - ✓ perpendicular to surface
  - ✓ receive synchronous inputs



Action potentials are biphasic – do not summate

Postsynaptic potentials (PSPs) are monophasic – ideal for summation

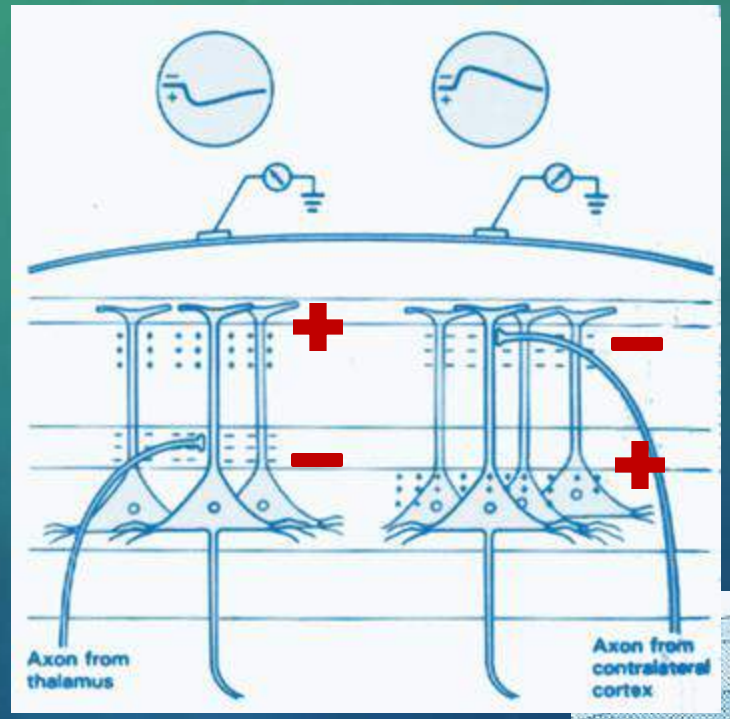


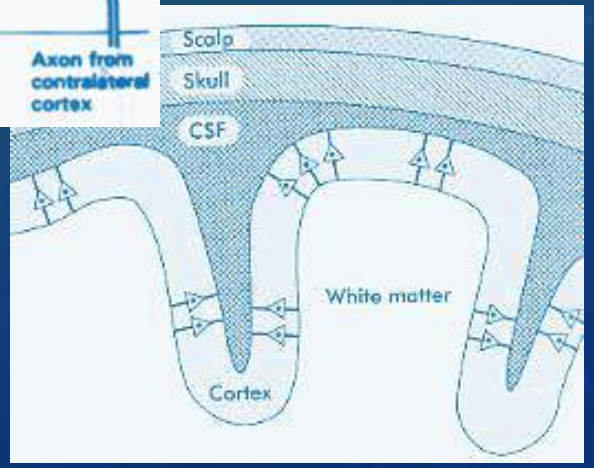
http://www.gensat.org/imagenavigator.jsp?imageID=29099

Source: Linda Shi

EEG: basis of the signal

- Dipole exists between soma and apical dendrites
- Potential behaves as if a **current flow**
- EEG electrodes on scalp detects net **positive** or net **negative** current flow from cortical neurons in both sulci and gyri



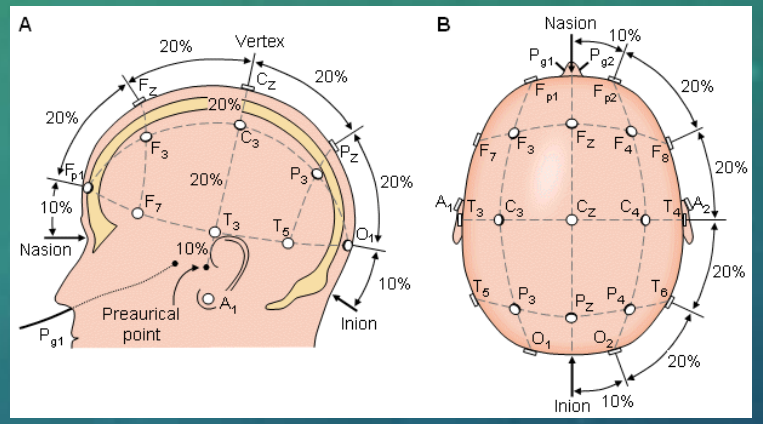


Kandel et al 1991. *Principles of Neural Science*

Source: Linda Shi

EEG: surface recordings

- **International** 10/20 or 10/10 system for placing electrodes:
  A: earlobes, **C:** central,
  P: parietal, **F:** frontal,
  O: occipital
- Low impedance 5-10kΩ
- Record **montages:**
  - **Bipolar** (electrodes connected to each other)
  - **Referential** (electrodes connected to one reference)

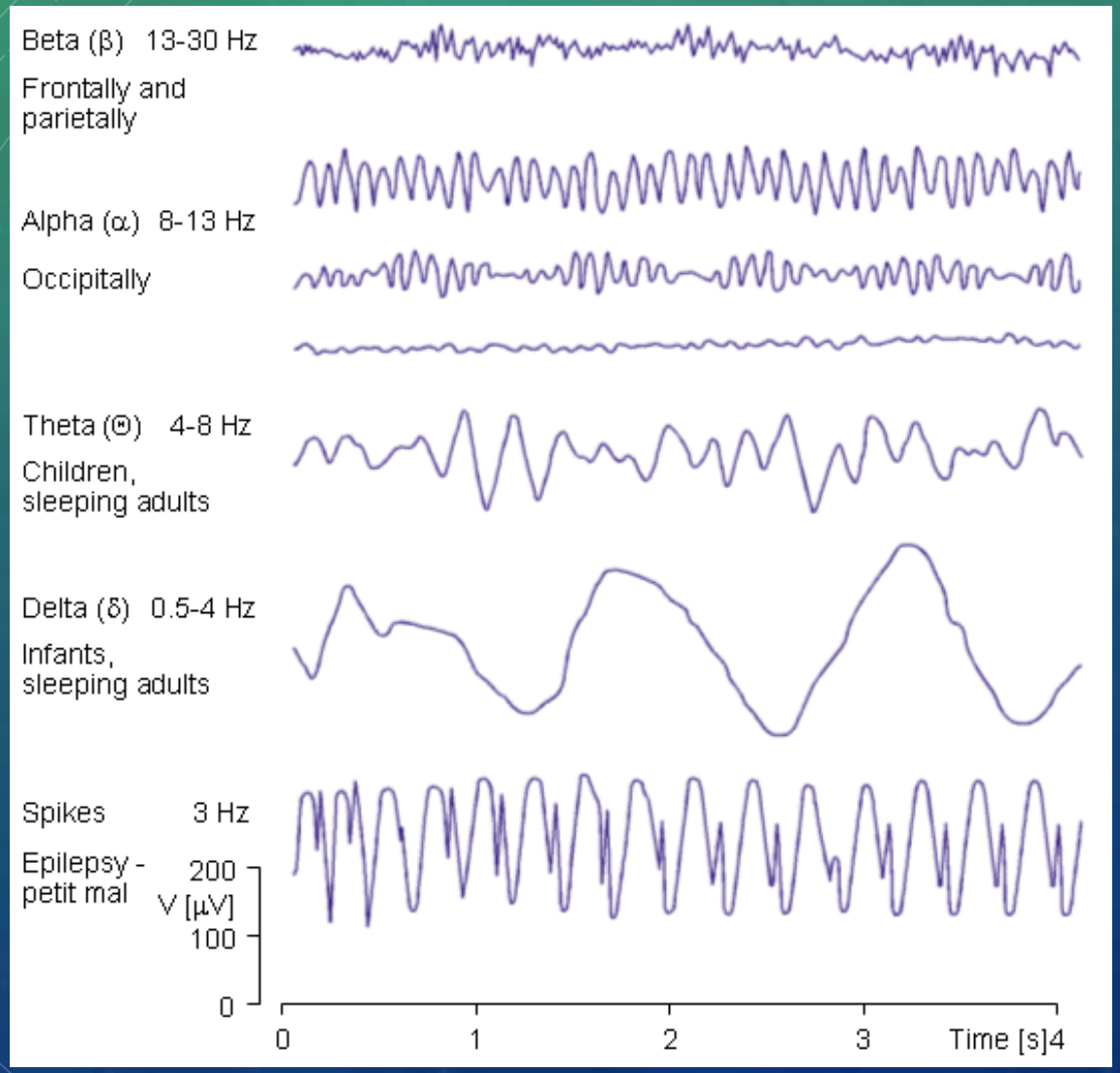


Malmivuo & Plonsey 1995.

http://www.lucid.ac.uk/news-and-events/blogs/how-to-study-language-why-do-we-put-electrodes-on-people-s-heads/

Source: Linda Shi

EEG: frequency spectrum



Tiege and Zlobinski, 2006

EEG vs. MEG

	EEG	MEG
Signal magnitude	10 mV (easily detectable) ✓	10 fT (magnetic shielding required)
Measurement	Secondary currents	Primary currents ✓
Signal purity	Distortion by skull/scalp	Little effect by skull/scalp ✓
Temporal resolution	~1ms	~1ms
Spatial resolution	~1cm	<1cm ✓
Experimental flexibility	Moves with subject ✓	Subject must remain stationary
Dipole orientation	Tangential and radial ✓	Tangential better

Source: Linda Shi

EEG/MEG advantages

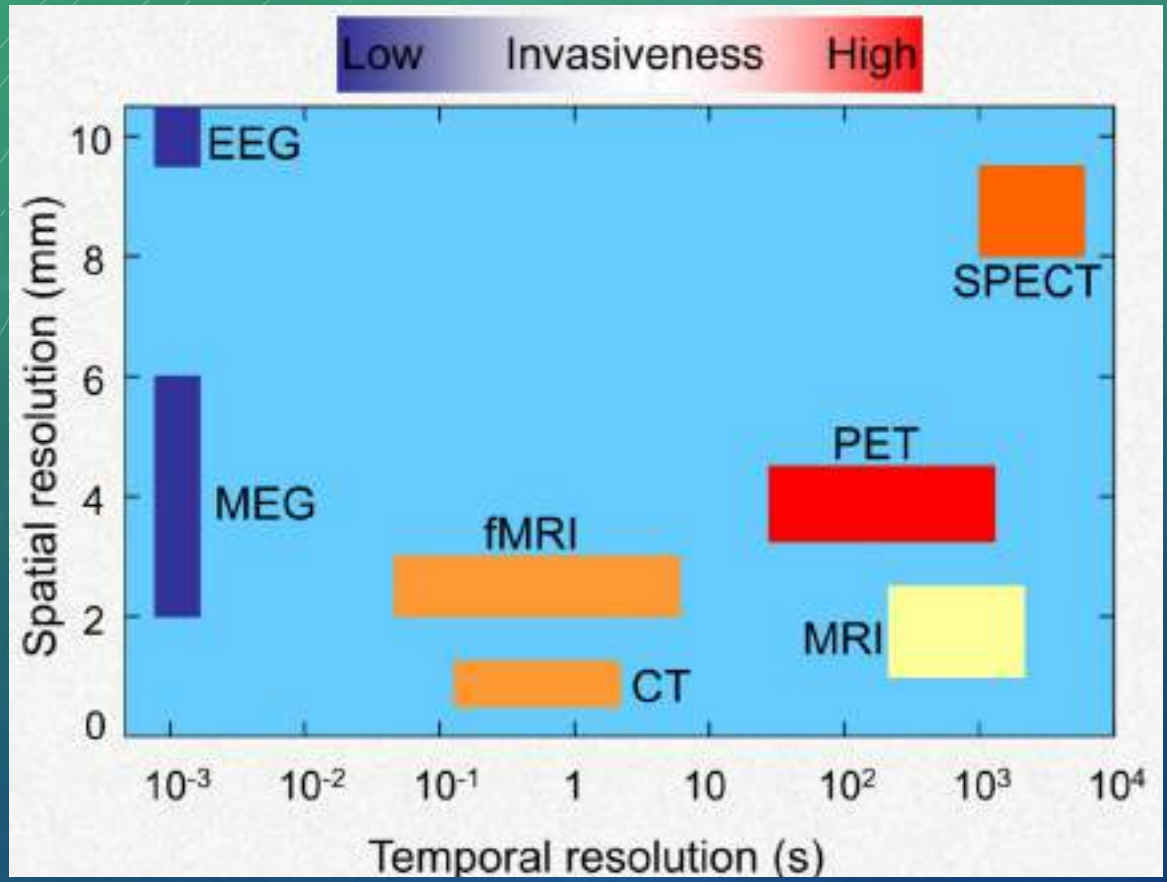
- ✓ **Non-invasive**
- ✓ **Direct** measurements of neuronal function (unlike fMRI)
- ✓ High **temporal resolution** (1ms or less, 1000x better than fMRI)
- ✓ Easy to use **clinically** (adults, children)
- ✓ **Quiet!** (can study auditory processing)
- ✓ **Affordable**, EEG is portable
- ✓ Subjects can perform tasks **sitting up** (more natural than MRI scanner)

https://www.colbertnewshub.com/2013/04/05/april-4-2013-dr-francis-collins/

https://medicalxpress.com/news/2015-02-brain-imaging-links-language-chromosome.html

Source: Linda Shi

EEG/MEG disadvantages

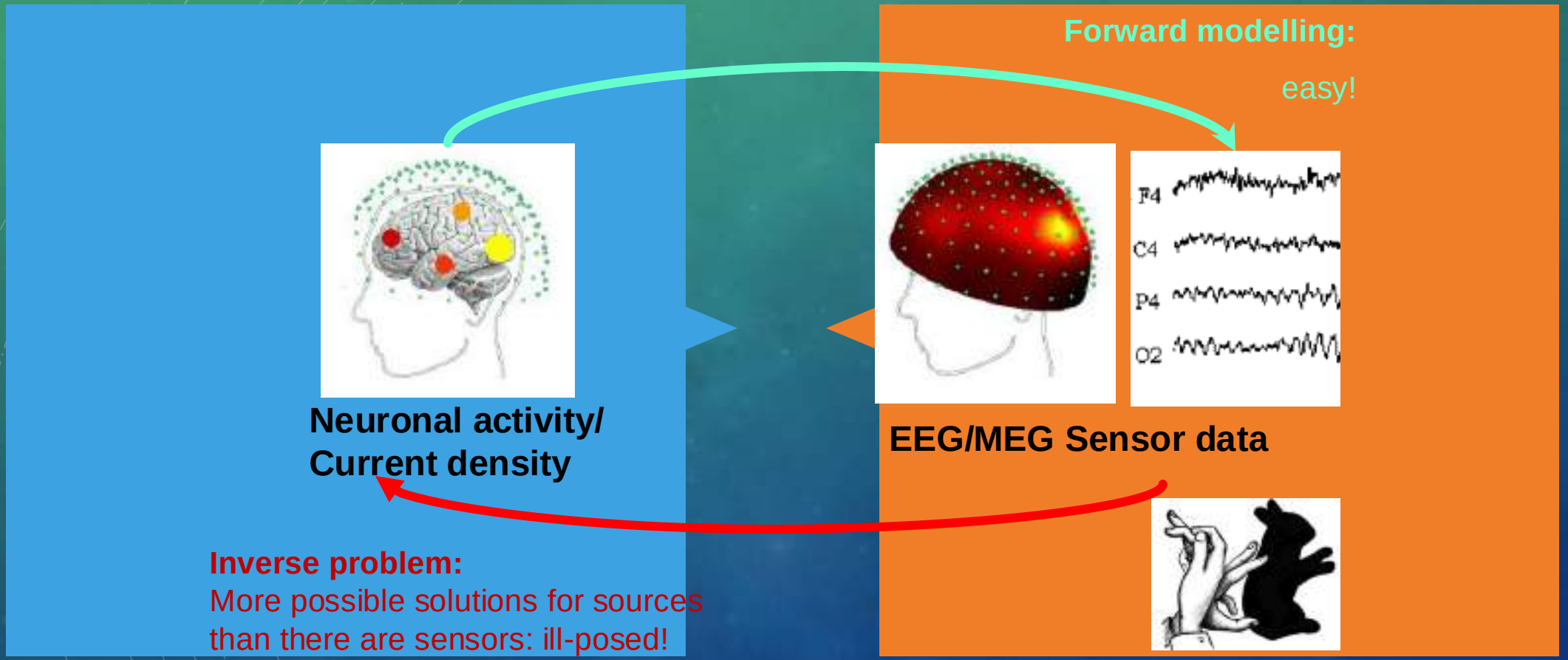


- Not as good **spatial localisation** as fMRI, MRI, CT
- **Sensitivity depth** only ~4cm (c.f. whole brain sensitivity of fMRI)
  - Sensitivity loss proportional to square of distance from sensor
- 3D Source reconstruction is ill-posed? **forward** and **inverse problems**

https://ngp.usc.edu/files/2013/06/Syed__EEG_MEG.pdf

Source: Linda Shi

Forward & inverse problems



→**SOLUTION:** Use forward models for inverse problem. Source localisation models and algorithms; iterative source reconstruction

Source: Linda Shi

SOME RESEARCH QUESTIONS: YOU PICK THE APPROPRIATE NEUROIMAGING TECHNIQUE

- I want to study whether I can predict the next word a participant intends to utter based on neural activity in Broca's region.
- fMRI? EEG? fMRI+EEG (simultaneous)? MEG?

SOME RESEARCH QUESTIONS: YOU PICK THE APPROPRIATE NEUROIMAGING TECHNIQUE

- Is the hippocampus involved in the representation of spatial information when participants remember the episodes of their lives?
- fMRI? EEG? MEG? LFP + single units?

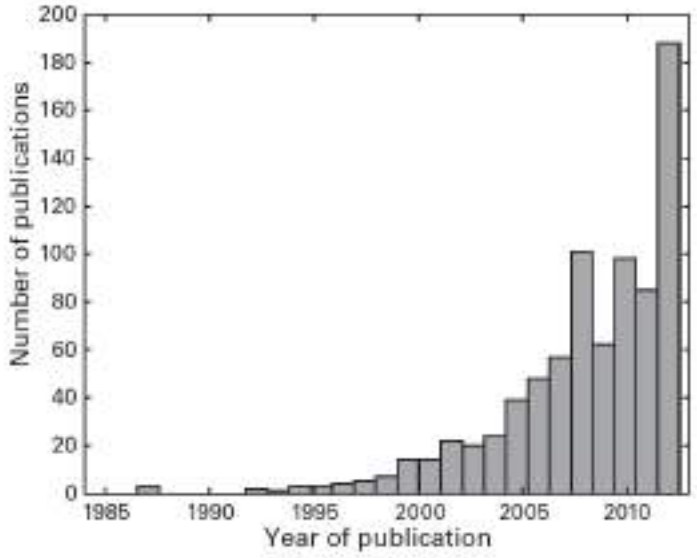
NEURAL APPROACHES SUMMARY

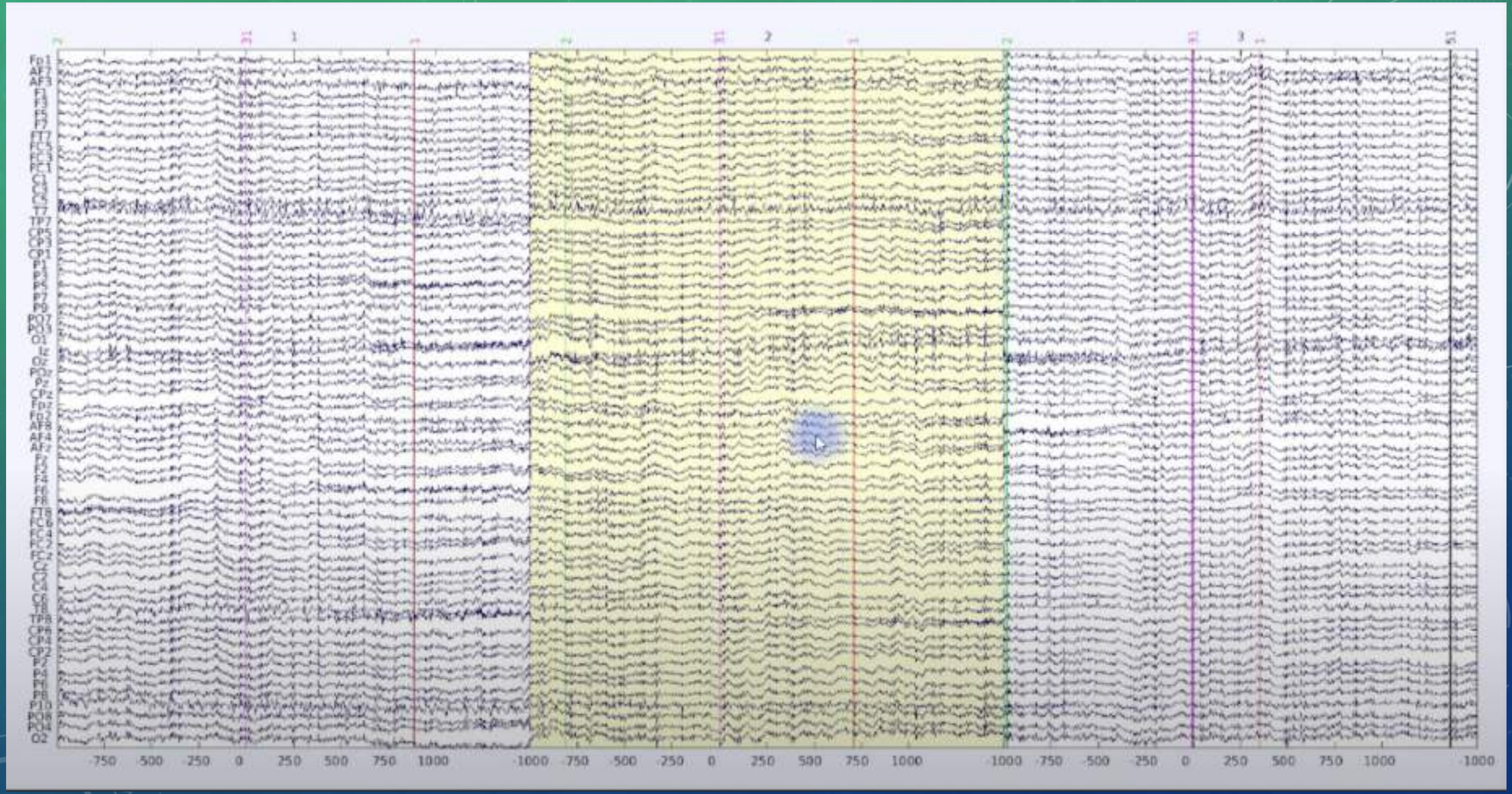
- Pay attention to spatial and temporal resolution of the neuroimaging technique you choose
- Choose a technique based on your research question (healthy vs clinical population, temporal and spatial resolution of the question!)

Search terms: Time-frequency/EEG/MEG/LFP

MORE ON EEG SIGNALS AND THEIR USE IN COGNITIVE NEUROSCIENCE

LET'S TAKE A SLIGHTLY DEEPER LOOK AT EEG



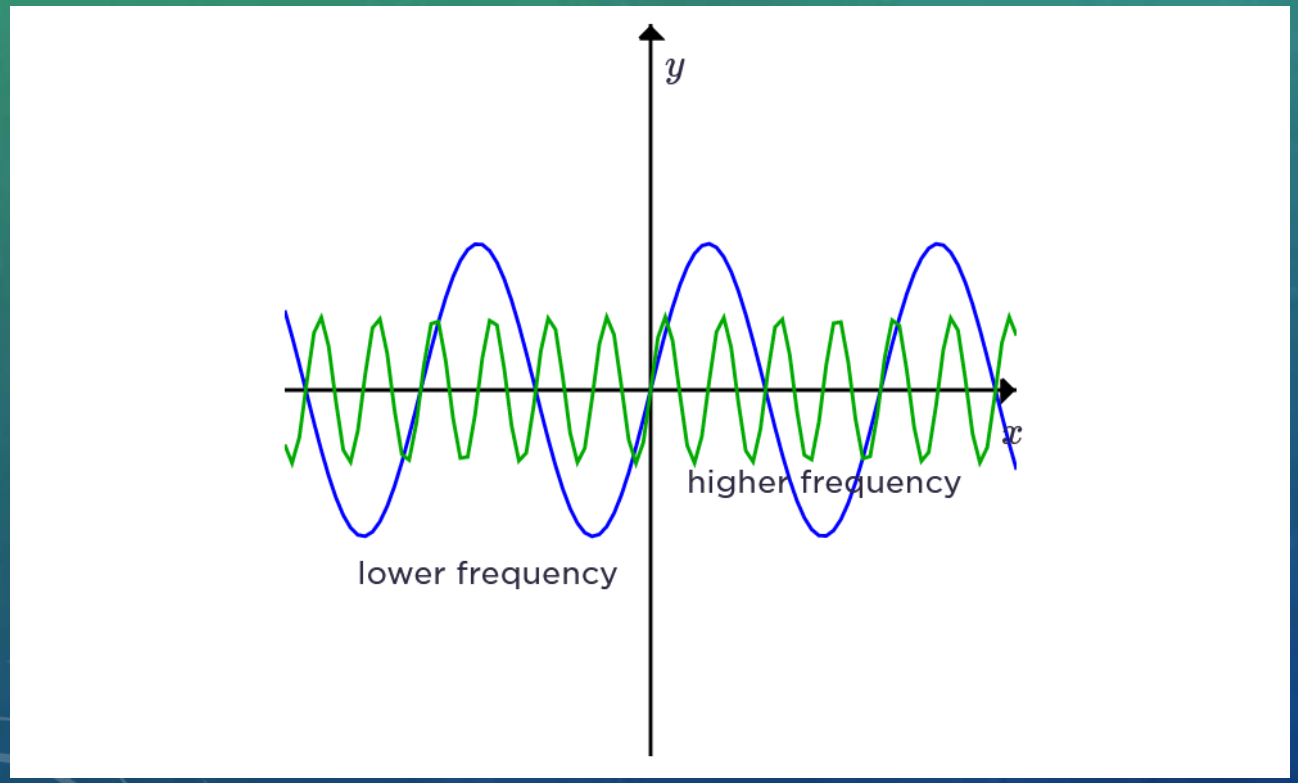


https://www.youtube.com/watch?v=Bmt89hHyxuM&ab_channel=MikeXCohen

OBSERVATIONS

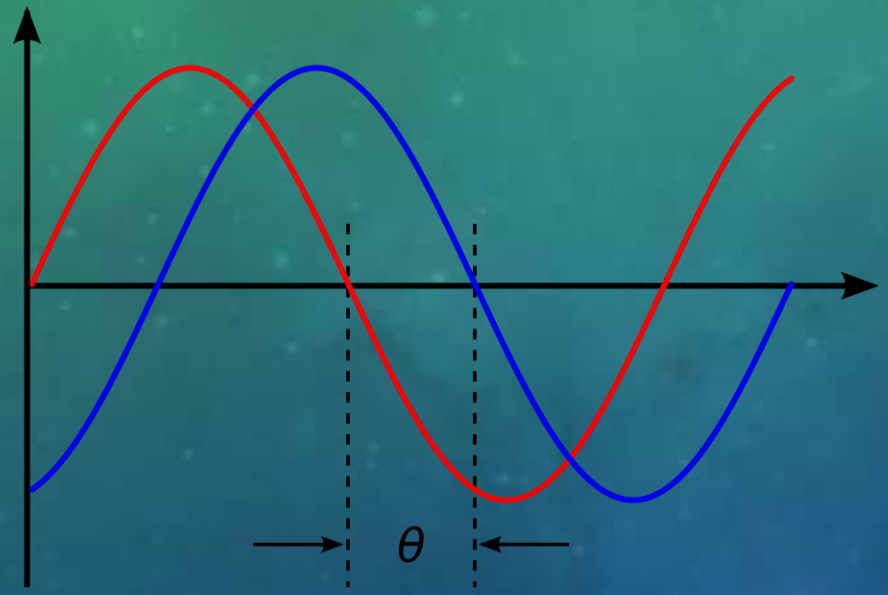
- Noisy
- Lots of common signals across channels
- From trial to trial, the signal on any single channel may look very different
- So how do we even use these signals to understand learning, memory, perception, etc??

SINUSOIDAL WAVES, FREQUENCY, WAVELENGTH



- What is the frequency of the blue wave?
- Green?
- Units?
- How do you measure wavelength?
- Which wave has the higher amplitude?

SINUSOIDAL WAVES, PHASE AND PHASE SHIFT/LAG



- Phase lag/difference/shift = how much does one wave "lag" or "lead" another wave?

FREQUENCY EXERCISE WITH SOUND

1 second

Delta/Theta – 4 Hz

Delta – 2 Hz

Higher theta – 6 Hz

Even higher theta – 8 Hz

HOW DO YOU GO FROM A MIXED SOUND TO THE INDIVIDUAL COMPONENTS?

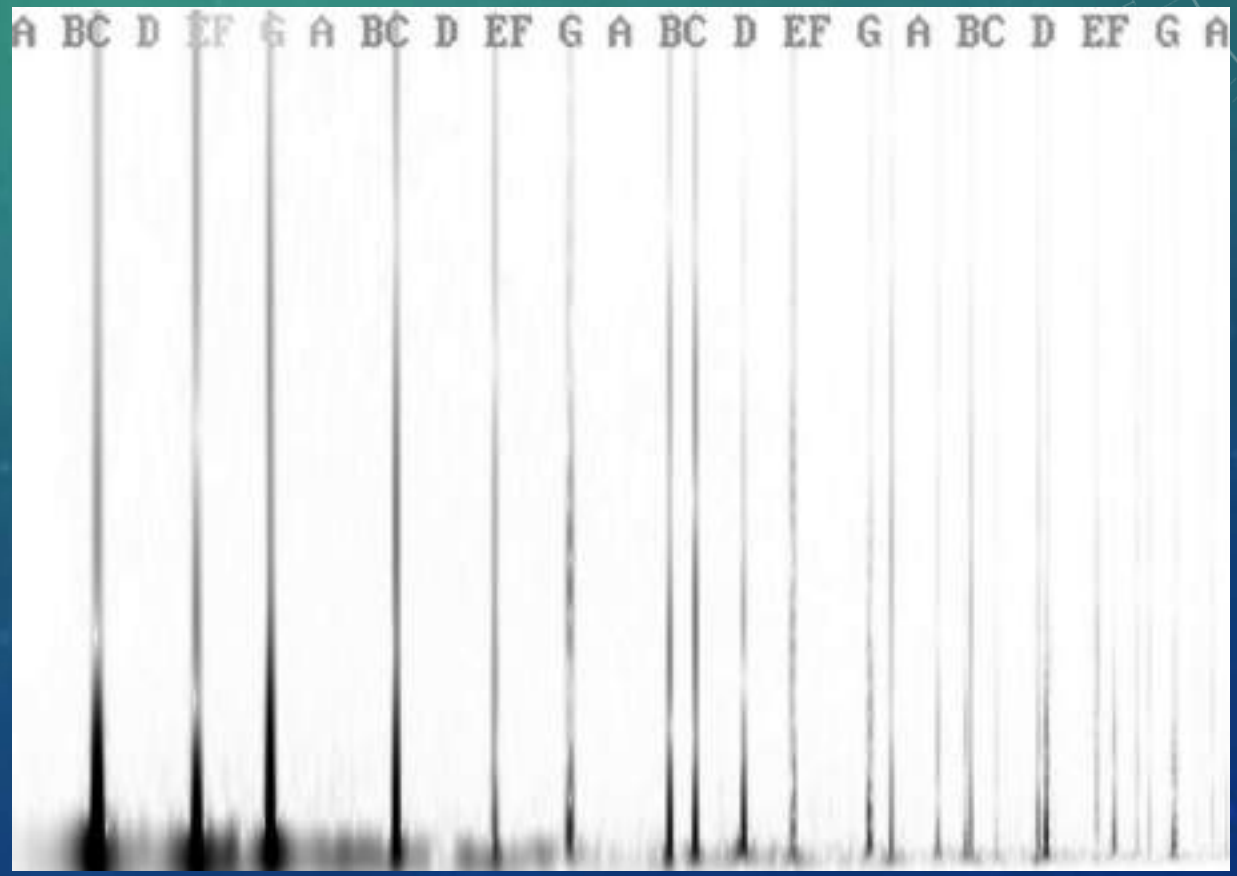
Time domain to frequency domain?

- Fourier transform
- A Fourier transform in my head?

Don't believe me? https://virtualpiano.net/

WHAT DO I DO IF I'M NOT A TRAINED MUSICIAN?

- Signal processing, use a computer!
- Let's try this now!

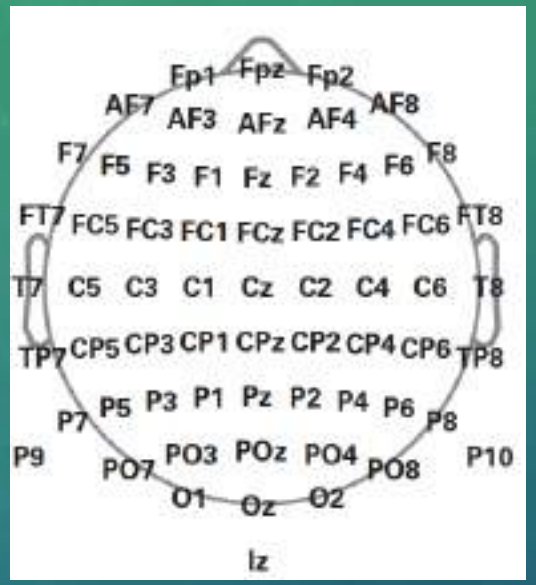


https://en.wikipedia.org/wiki/Fourier_transform

EEG DATA

- What is the dimensionality of the EEG data you will work with?

- Time
- Space (in the brain)
- Frequency
- Power and phase



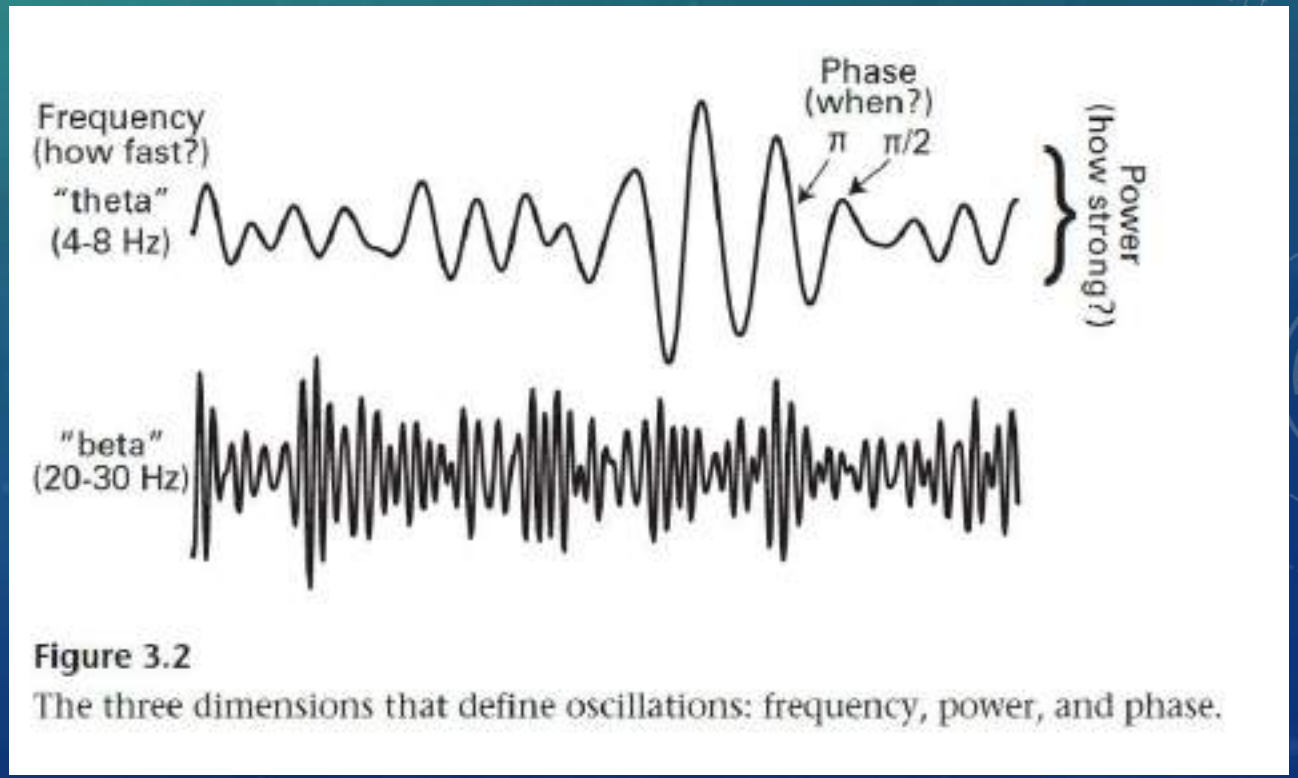


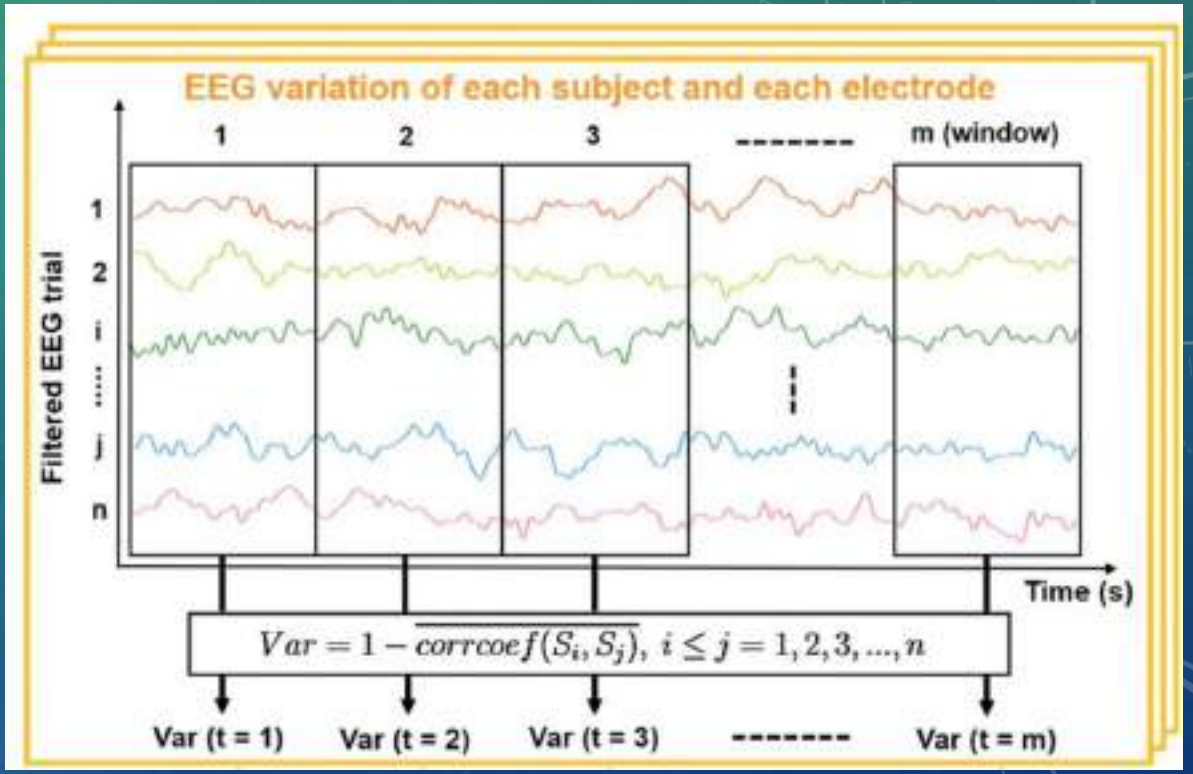
Figure 3.2
The three dimensions that define oscillations: frequency, power, and phase.

DEALING WITH NOISE

- Preprocessing (filtering)
- Averaging (over trials, over subjects, etc)

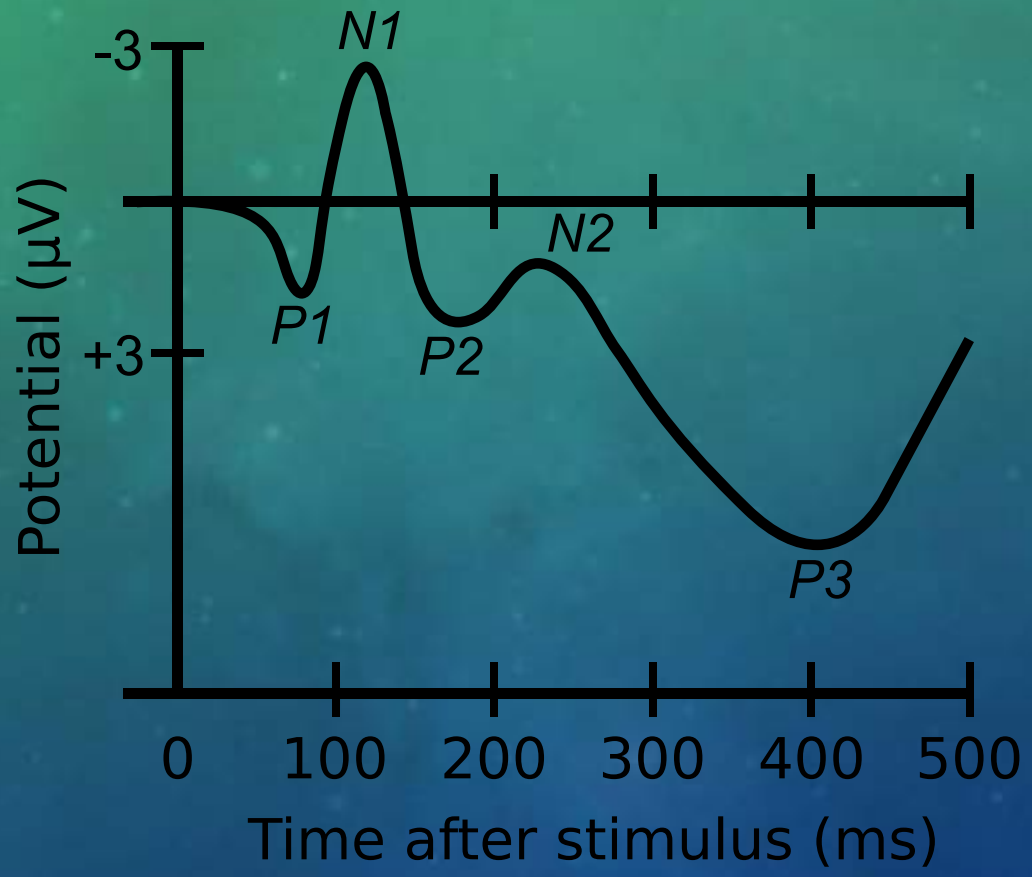
EVENT-RELATED POTENTIALS (ERPS)

- Variable across trials, electrodes, and subjects.
- Whether we want to discard this variability depends on the question.
- The variability itself is sometimes indicative of a brain's processing capabilities! (see Sheehan and Sreekumar, et al., 2018, Journal of Neuroscience).



https://www.biorxiv.org/content/10.1101/2021.10.29.465647v4.full

EVENT-RELATED POTENTIALS (ERPS)



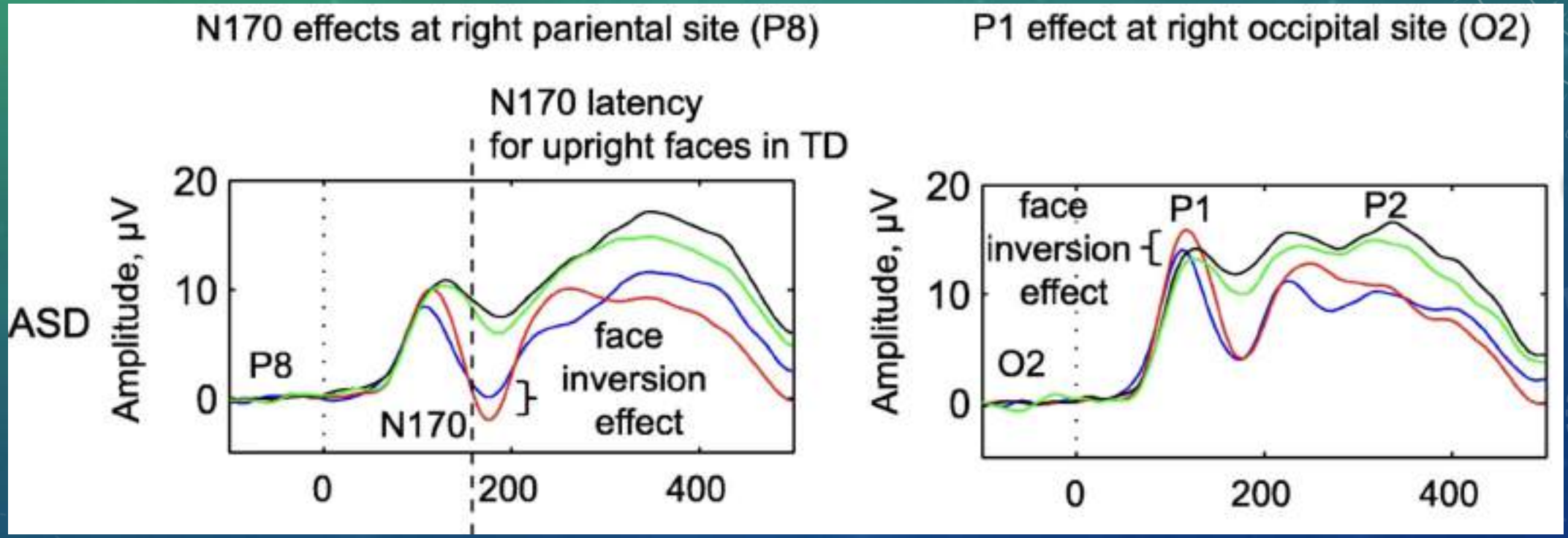
https://en.wikipedia.org/wiki/Event-related_potential

EVENT-RELATED POTENTIALS (ERPS)

- Depression: prolonged latency of P300, reduced amplitude.
- Visual processing: 70-80 ms positivity.
- Face-specific visual processing ERPs have been found!
- Big advantage: reliably study event-locked neural responses that are stable across individuals and indicate the precise time after stimulus at which certain information is processed in the brain.
- However, this technique requires averaging over many many trials.

https://en.wikipedia.org/wiki/Event-related_potential

EVENT-RELATED POTENTIALS (ERPS) EXAMPLE: N170 FACE PROCESSING



https://molecularautism.biomedcentral.com/articles/10.1186/s13229-018-0220-x/figures/1

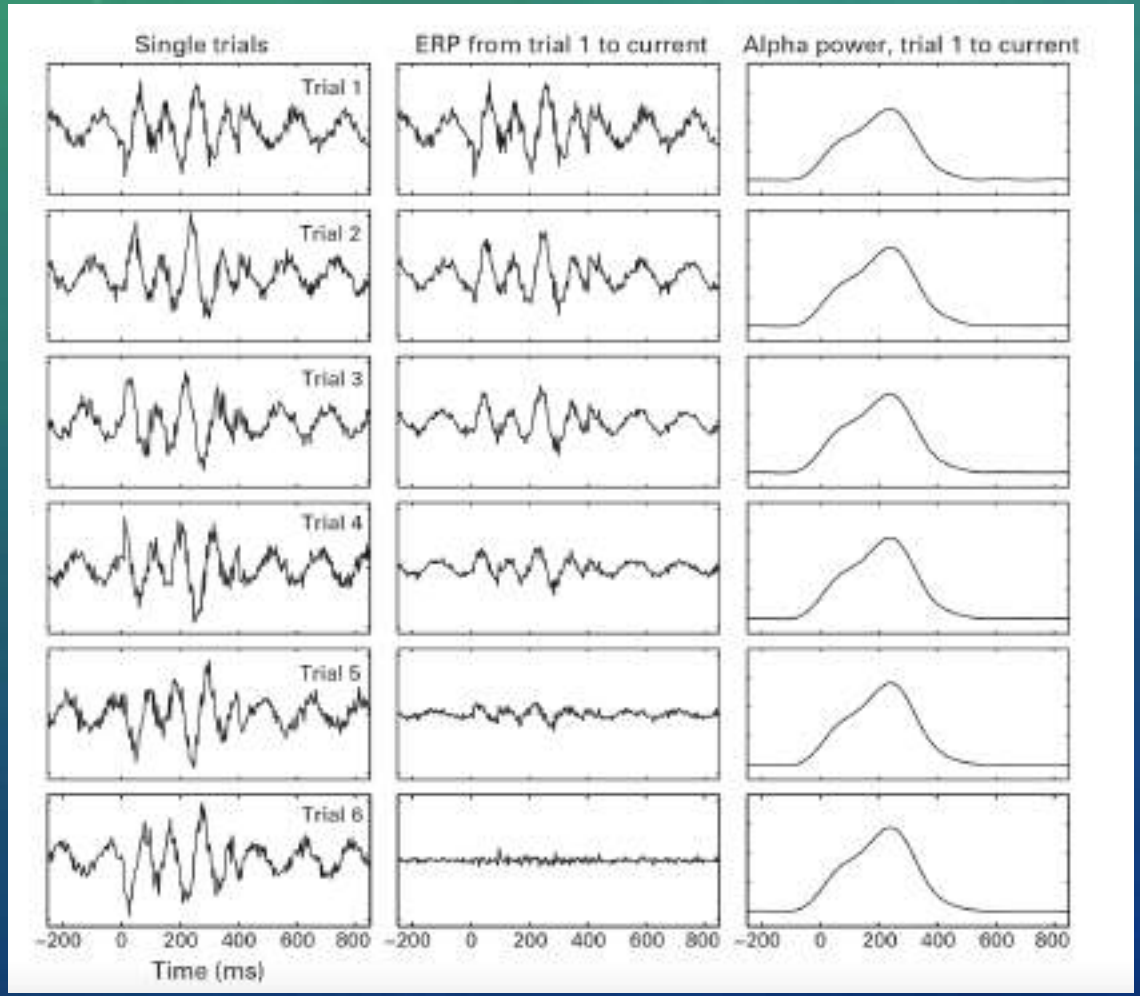
ADVANTAGES OF ERP

- Quick and simple to calculate
- No loss of temporal precision (just averaging the raw EEG signal with minimal preprocessing)
- Ideal for quick insights into condition differences
- No major theoretical assumptions

DISADVANTAGES OF ERP

- Not everything related to the task will show up in the ERP
- Many of the interesting phenomena are embedded in more complex dynamics across channels that are not apparent in the ERP

PHASE-LOCKED VS NON PHASE-LOCKED EVENT-RELATED SIGNALS – ONLY THE PHASE-LOCKED ONES WILL SHOW UP IN AN ERP!



Mike X Cohen "Analyzing neural time series data"

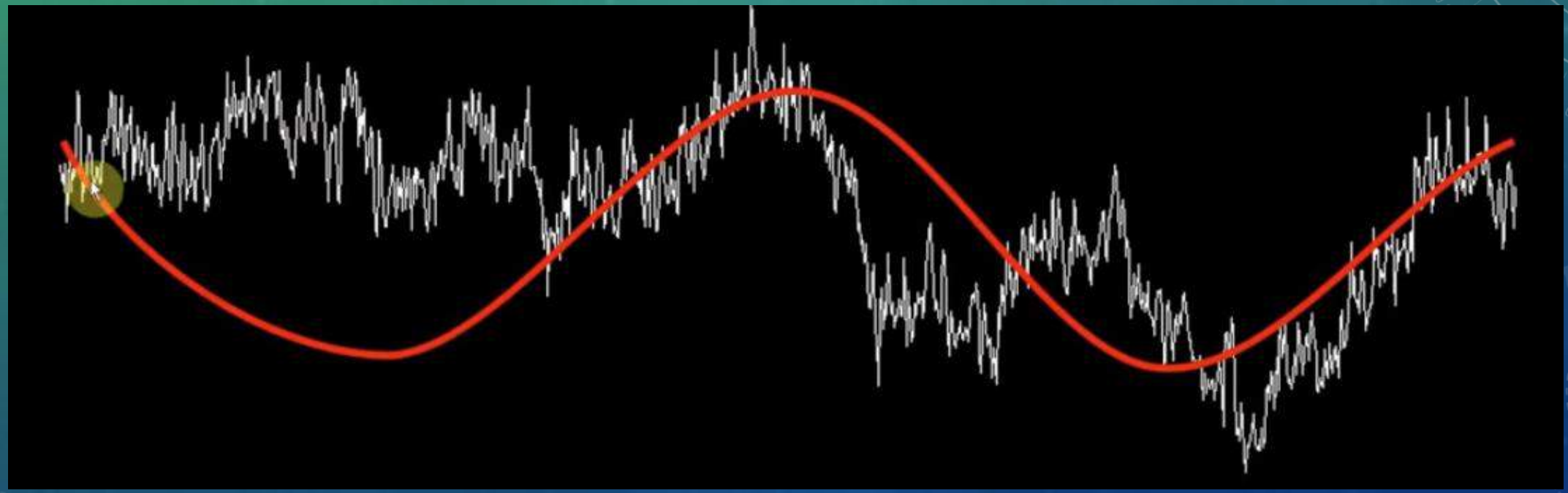
HOW ELSE CAN WE USE EEG SIGNALS TO STUDY COGNITION?

- Signal processing: break up into frequency bands of interest.
- Time-Frequency analyses and comparison between conditions.
- Single trial-level analyses.
- Communication between brain regions (I.e., electrodes).

FOURIER TRANSFORM

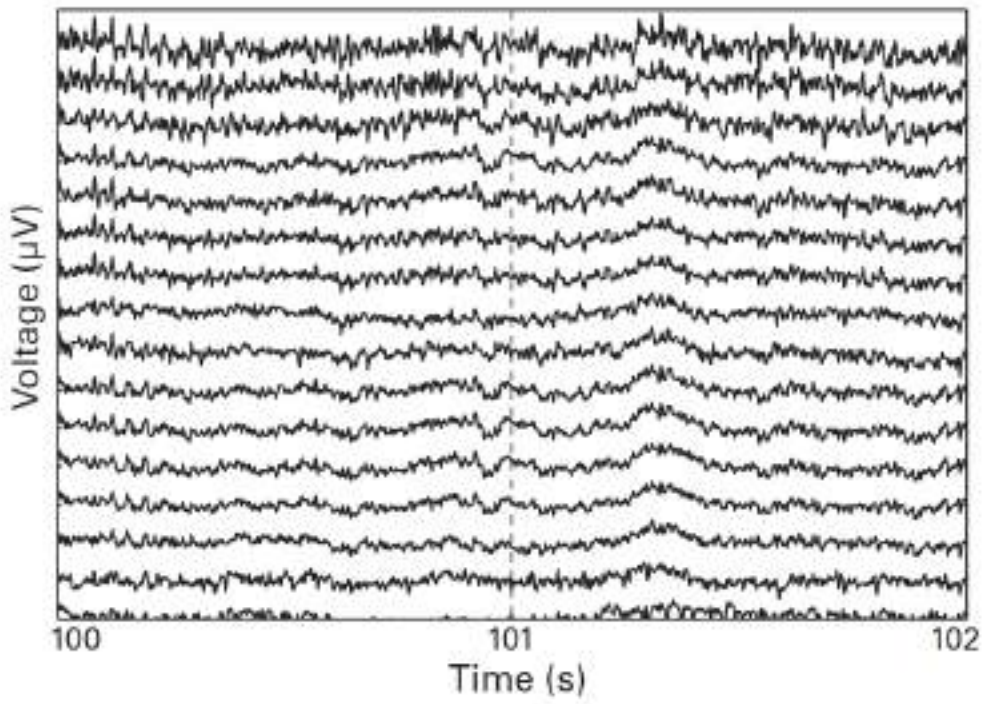
Any signal can be expressed as a combination of sine waves, each with its own freq, phase, and amplitude.

FOURIER TRANSFORM



https://www.youtube.com/watch?v=QBGjPtU_C6s&ab_channel=MikeXCohen

TIME-FREQUENCY BASICS



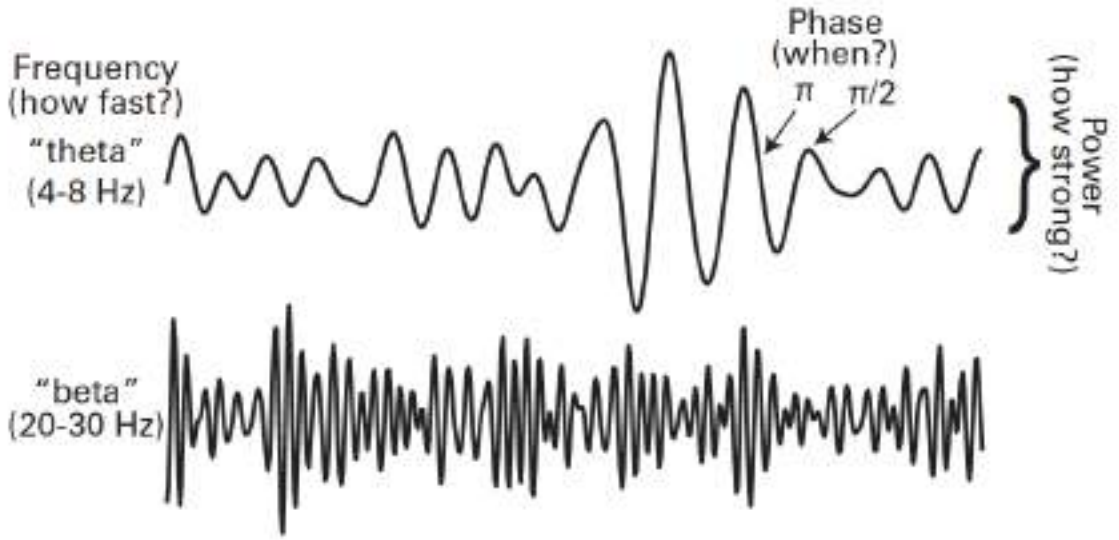


Figure 3.2
The three dimensions that define oscillations: frequency, power, and phase.

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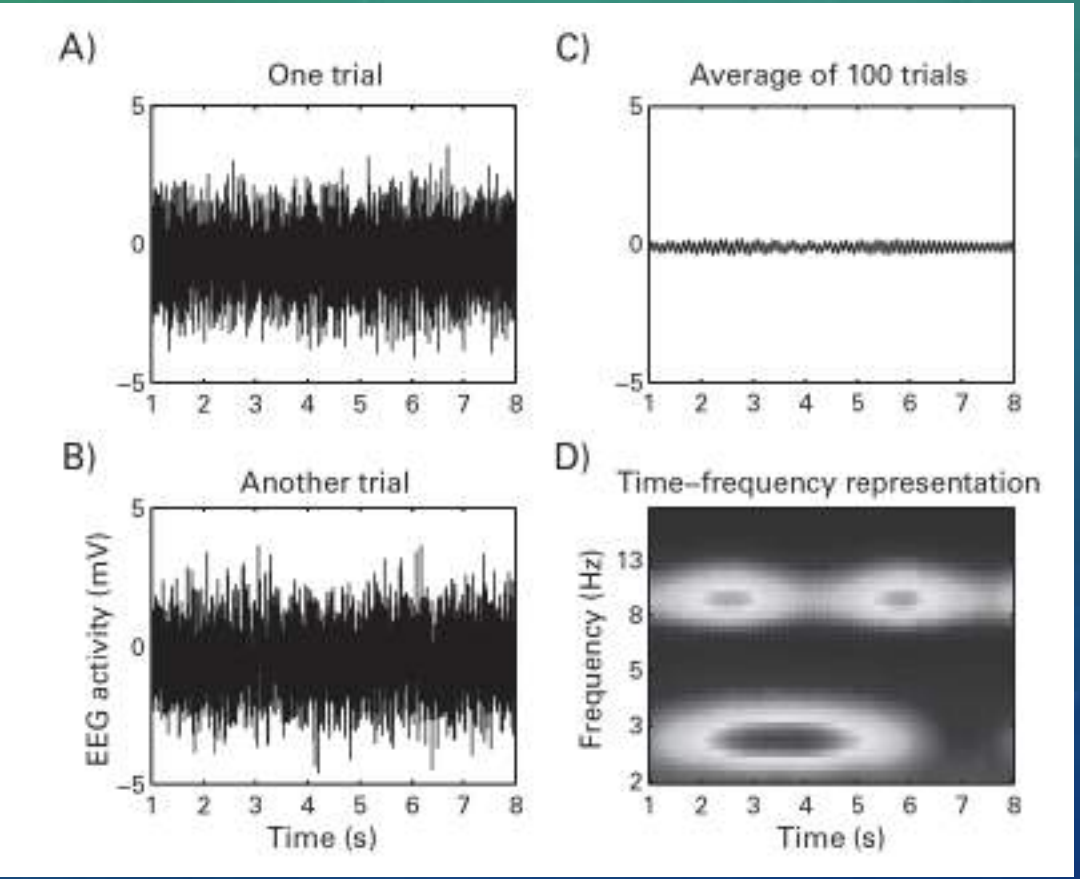
TIME-FREQUENCY BASICS



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TIME-FREQUENCY BASICS: MANY VIEWS OF THE SAME THING

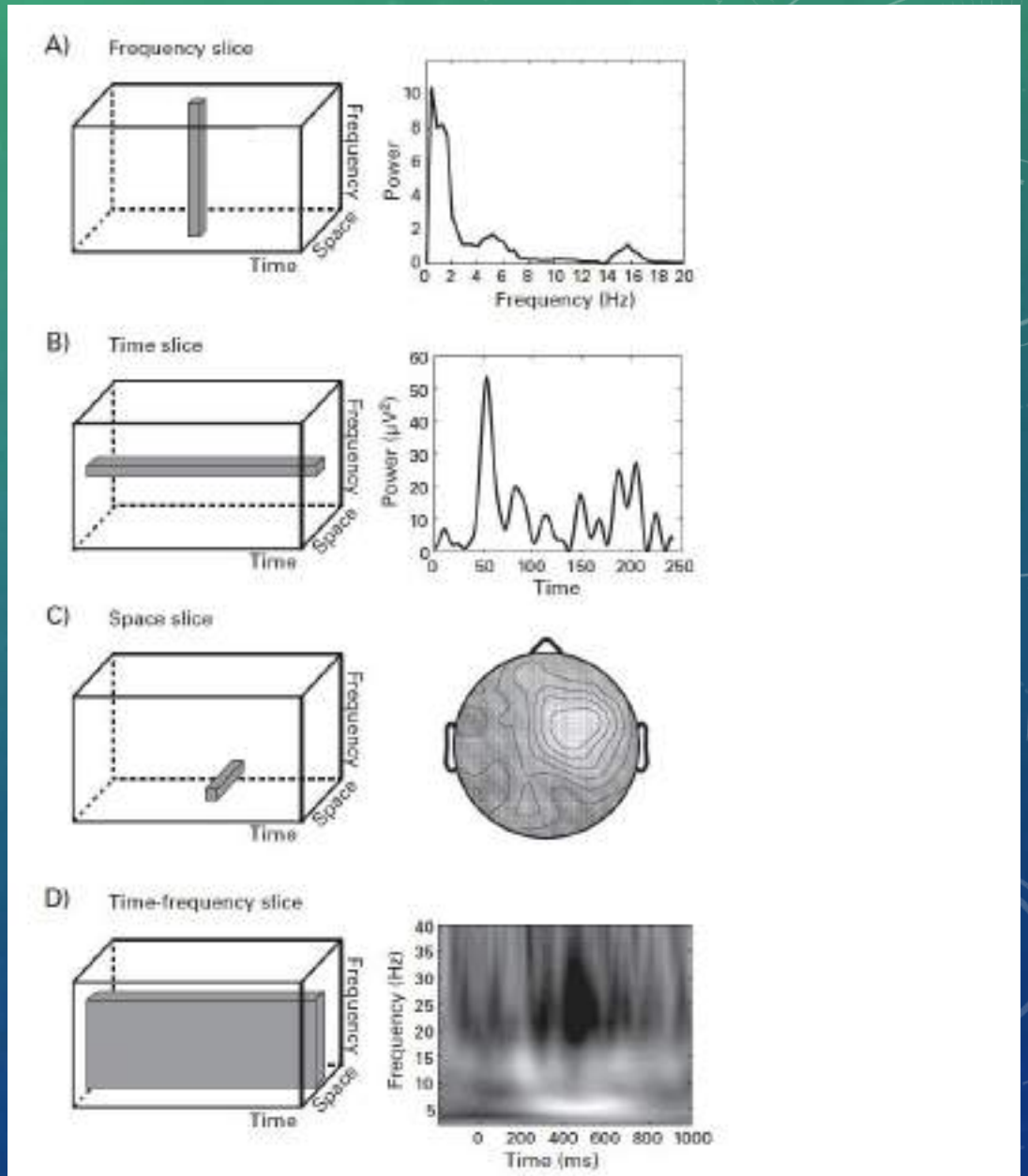

Figure 3.3
The data cube, containing information over time, frequency, and space, is difficult to view or conceptualize and therefore is sliced in different ways to illustrate 1-D or 2-D snapshots of the results.

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TIME-FREQUENCY ANALYSES IN PRACTICE

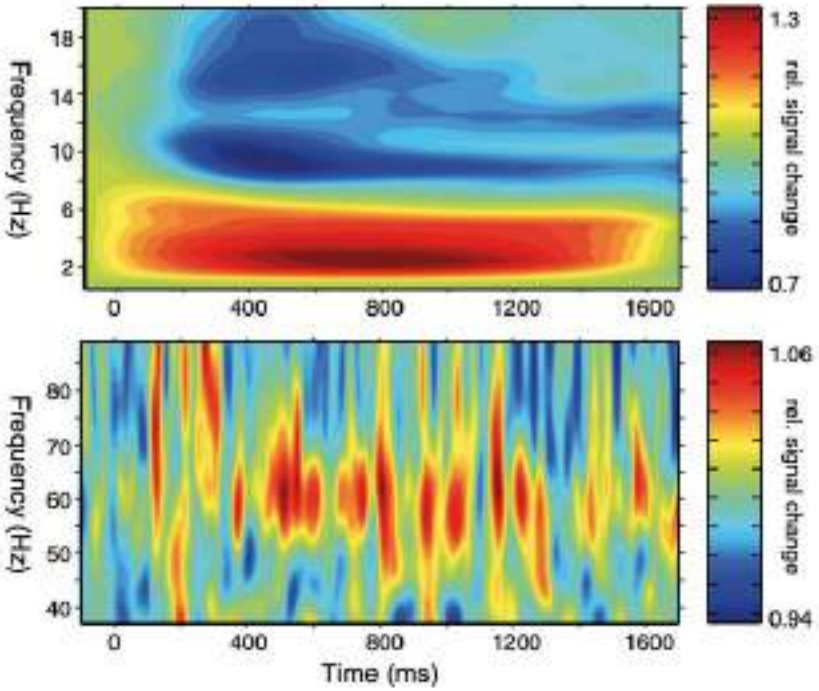
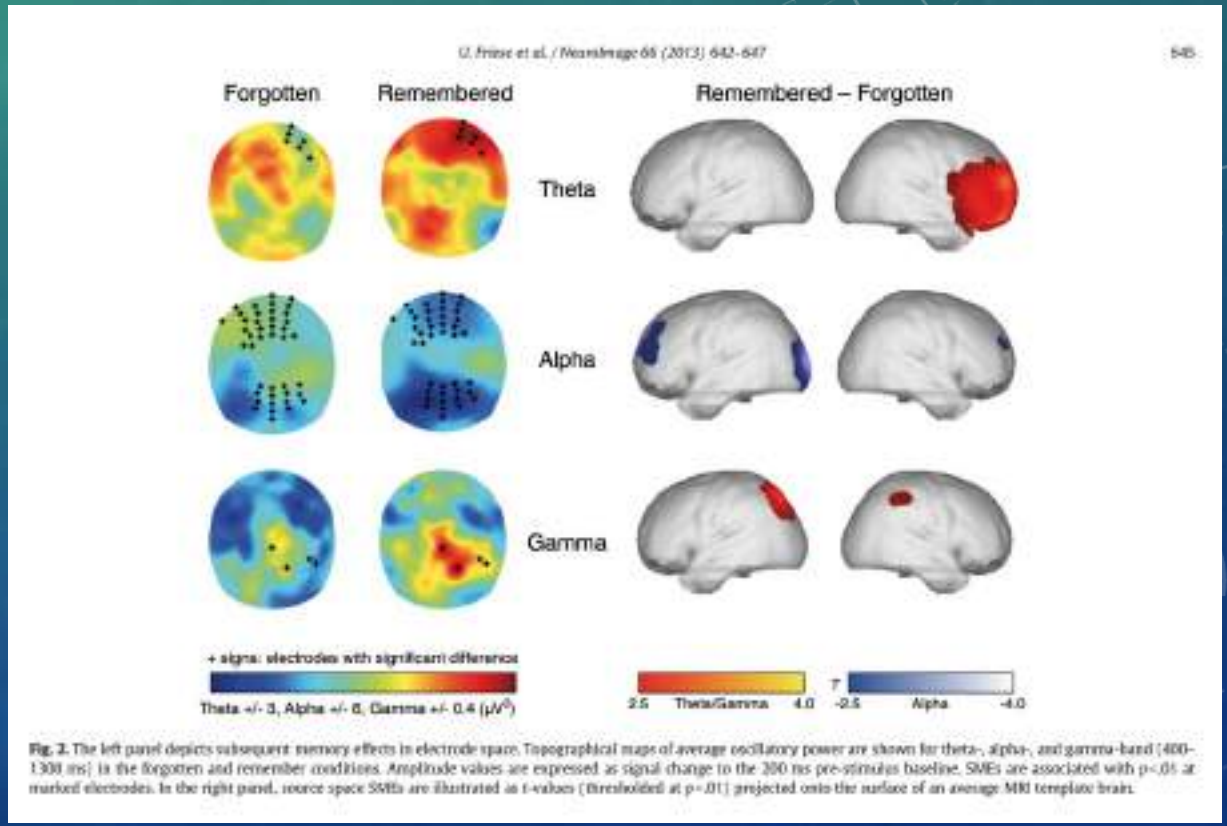


Fig. 1. Grand mean time-by-frequency plots of spectral power for frequencies up to 20 Hz and for the gamma range (40–100 Hz). Low frequency activity was averaged across all electrodes, gamma-band activity was averaged across parietal electrodes. Amplitude values are expressed as signal changes relative to the 200 ms pre-stimulus baseline.



https://pubmed.ncbi.nlm.nih.gov/23142278/

TIME-FREQUENCY LIMITATIONS

- Loss of temporal precision. Why?
- Time-frequency uncertainty effect in signal processing.

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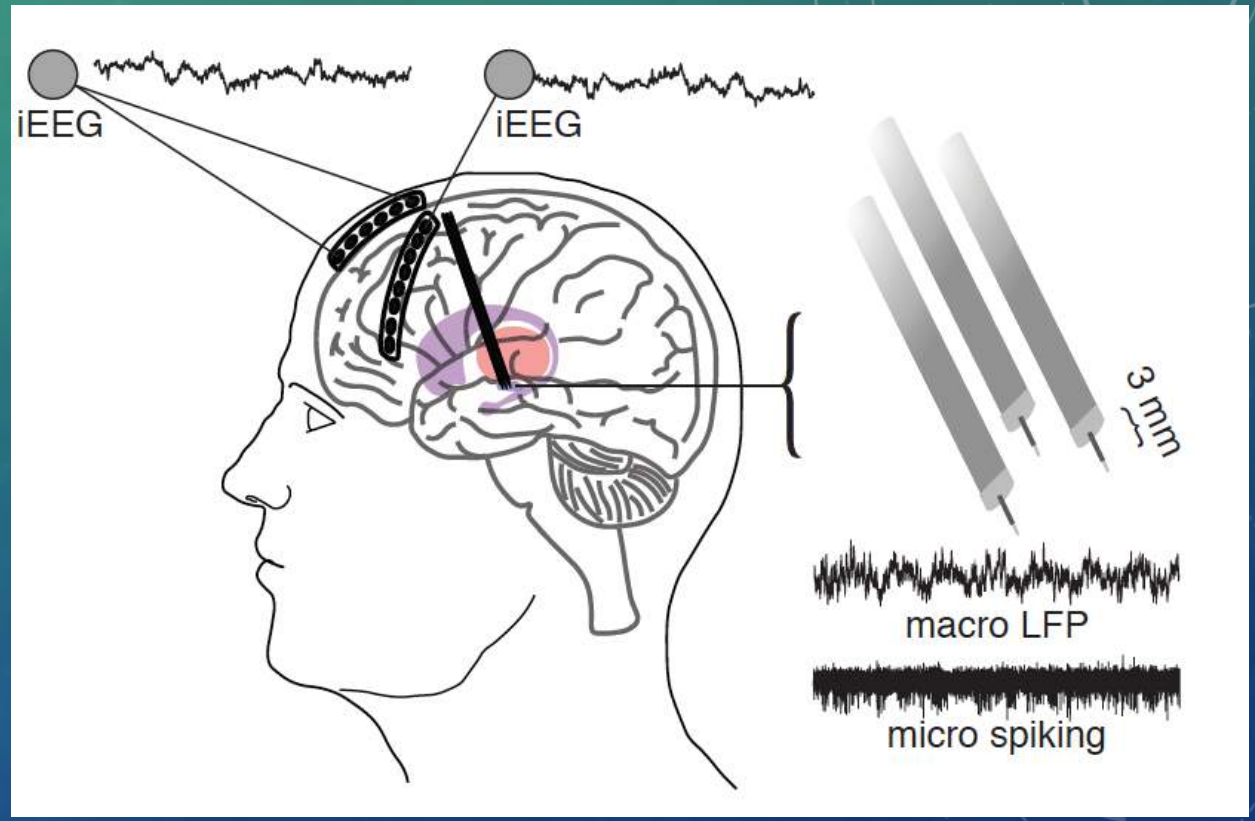
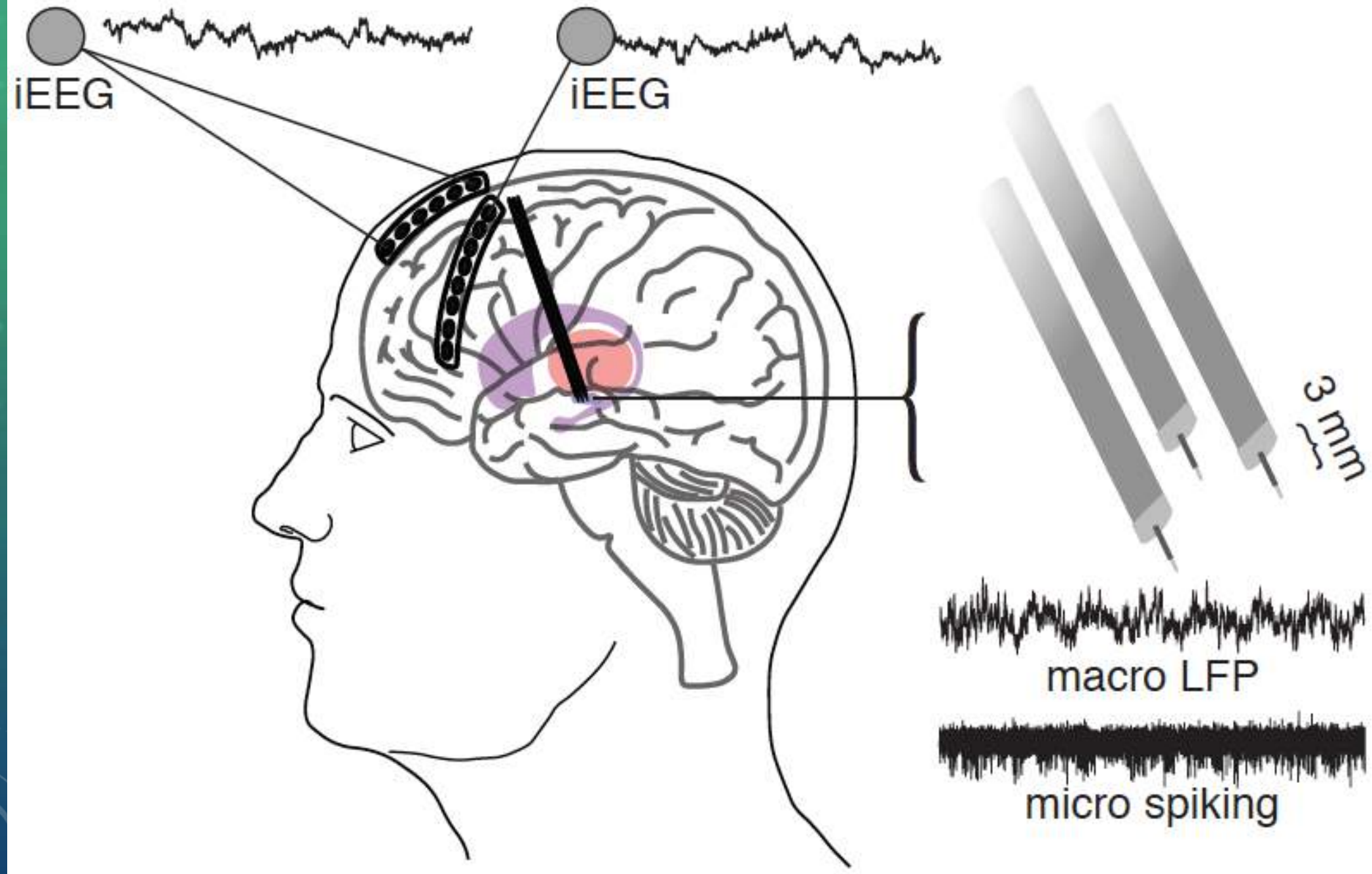
DOWNSIDES OF EEG

- Cannot be used for fine-grained spatial scales and a lot of interesting neural phenomena underlying cognition exist at the lower levels (e.g. Jennifer Aniston neurons?!) - discussed before (spatial vs temporal resolution).

ECOG, LFP, SINGLE-UNITS

- Invasive and can only be done with clinical populations
- Good spatial resolution (depends on electrode size)
- Excellent spatial source information compared to EEG/MEG (no source reconstruction modeling required)
- Excellent temporal resolution (ms and sub-ms)




iEEG
iEEG
3 mm
macro LFP
micro spiking

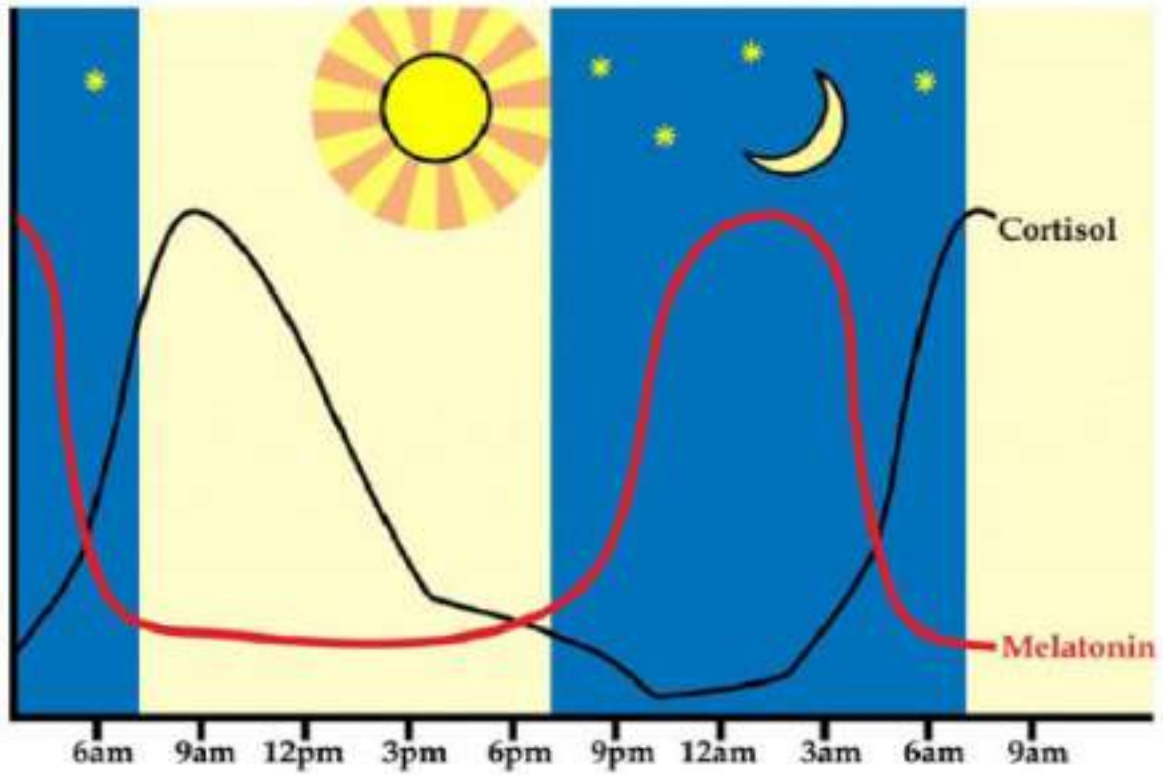
SUMMARY

- EEG is non-invasive, widely available, relatively easy to use.
- Signal processing required to deal with noise and other artifacts.
- Further analysis tools: ERPs, time-frequency, etc should be chosen depending on your research question.

Sleep

Circadian Rhythm?

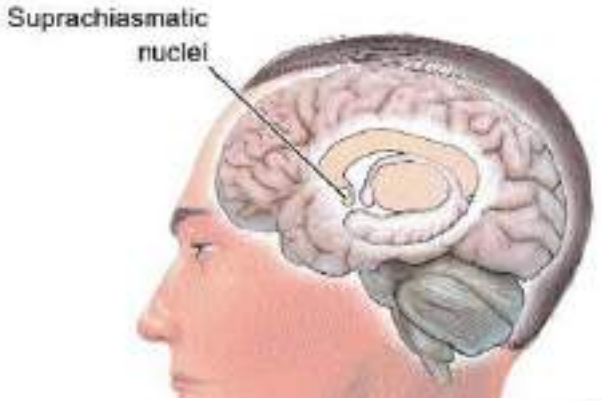
Circadian Rhythm



https://thoracicandsleep.com.au/blog/how-stress-and-the-circadian-rhythm-affect-sleep/

- How does our body maintain the circadian rhythm?

The Suprachiasmatic nucleus (SCN)



- SCN in the hypothalamus (atop the optic chiasm) controls the circadian rhythms - the sleep and wake cycles

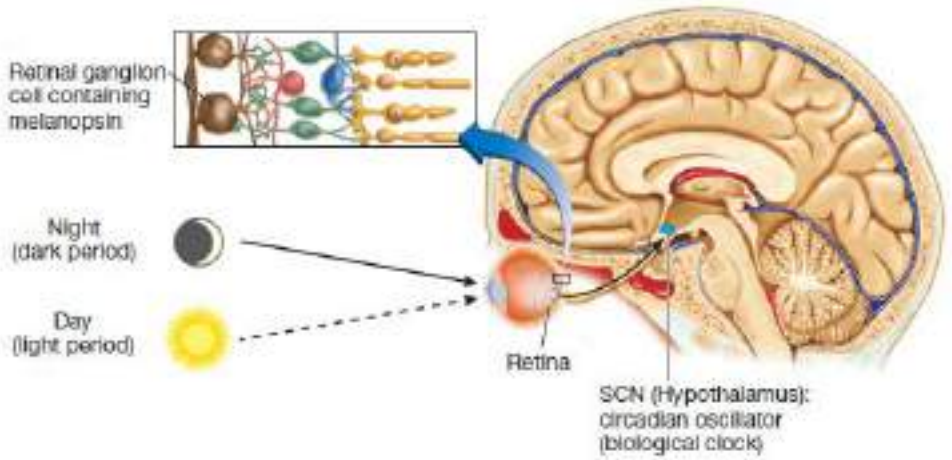
- *Melanopsin (photochemical in retina):*
  A photopigment present in the retinal ganglion cells transmit light information (day/night) to the SCN

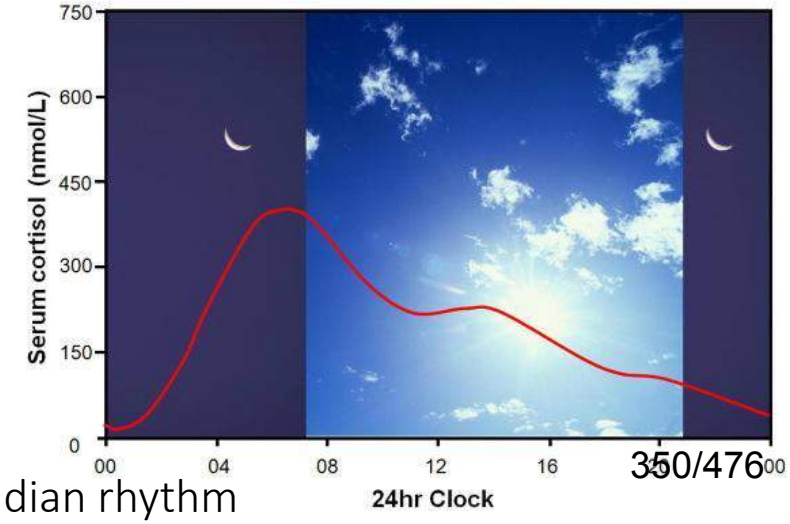
- SCN has specialized neurons that become active at different times during the day, thereby tracking the day and controlling the circadian rhythm (protein inside the neuron controls the circadian rhythm; when its levels reach a peak, it inhibits its own production, resetting the cycle.)

  - *Advanced Sleep phase syndrome*: person sleeps at 7:30pm and wakes up at 4:30am (4 hr advance in sleep & temp. cycles)

  - *Delayed Sleep phase syndrome*: person sleeps at 2am and wakes up at mid-morning (4 hr delay in sleep & temp. cycles)

    - Sleep habits, hormones, medication, not spending enough time in sunlight





Changes in cortisol levels according to circadian rhythm

Biological clock without sunlight?

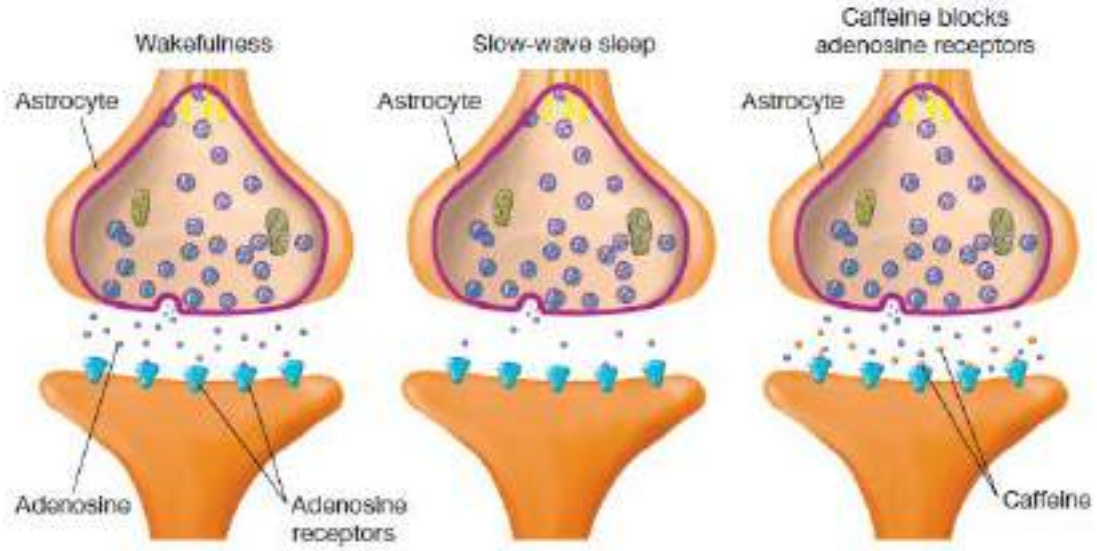
In presence of constant darkness or constant light, our rhythms are controlled by ***internal clocks*** (usually a 25 hrs cycle). It runs a little slower in the absence of an external resetting stimulus.

E.g. Scandinavian countries, north & south pole

Using artificial illumination (lights & lamps), we are able to delay bedtime and extend wake time, resulting in a 25 hrs internal clock instead of the natural 24 hrs biological clock

Physiological mechanisms of sleep and waking

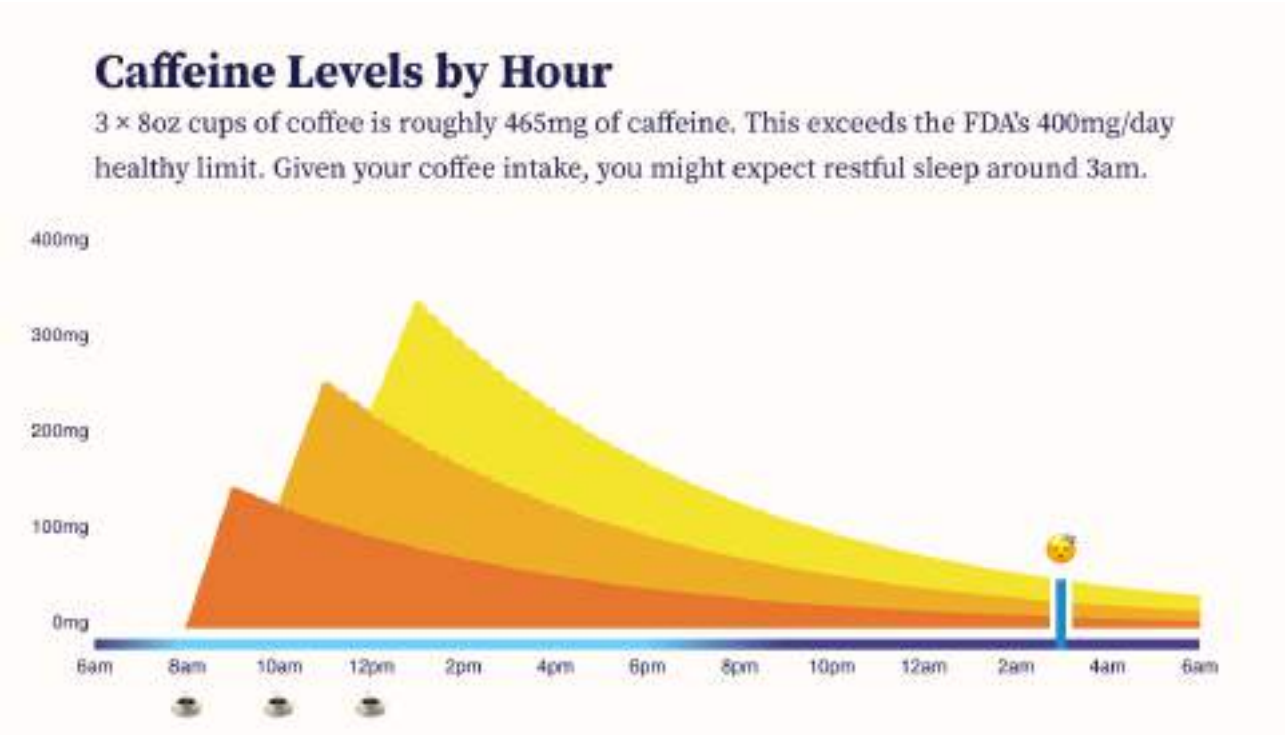
- Sleep, especially REM does not occur simply because neurons get tired, it occurs when a particular neural circuit gets more active
  - Brain is more active (no sleep) → more glucose → increase in adenosine (neuromodulator) levels → more delta activity during sleep (deeper sleep when you have been more active)
  - So basically, adenosine levels reflect the amount of sleep deprivation

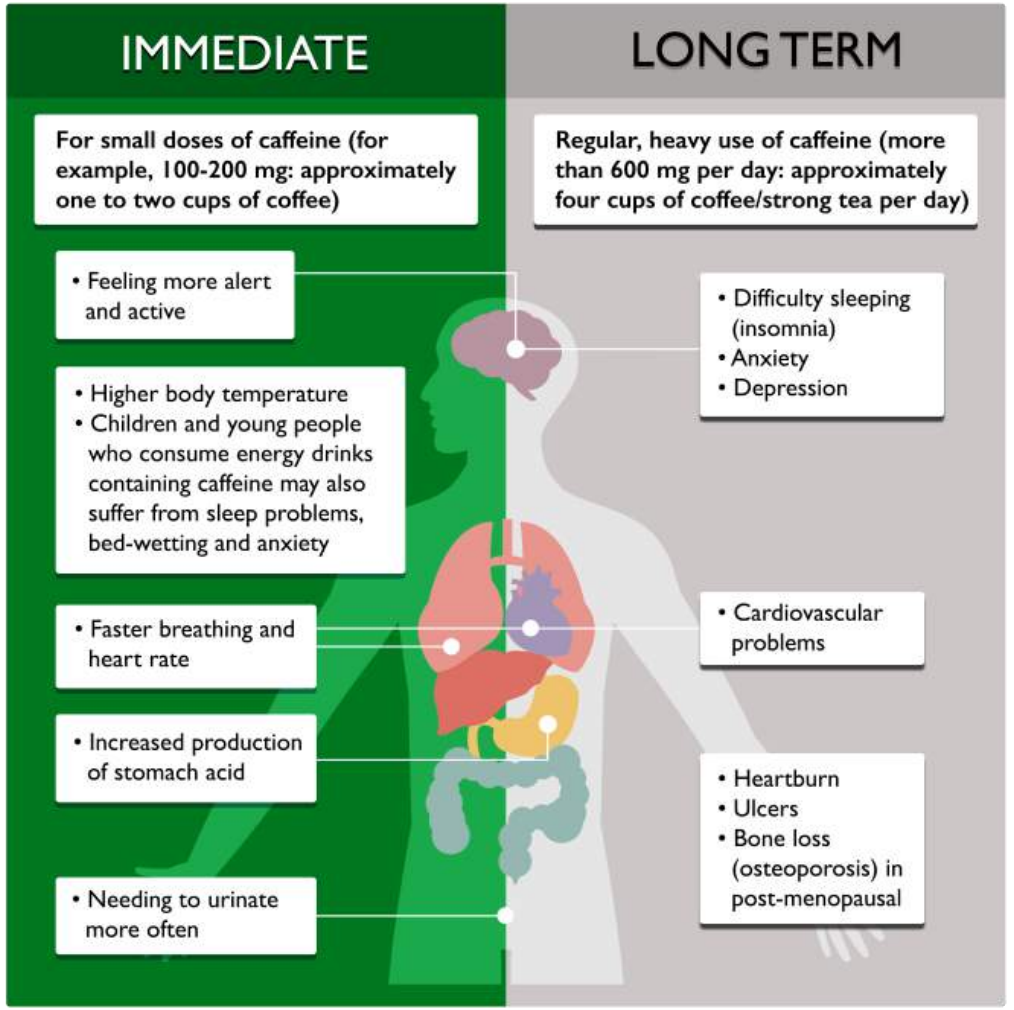


Adenosine accumulates during wakefulness and is reduced during slow-wave sleep. Caffeine blocks the adenosine receptors, preventing the inhibitory effect on neural activity and reducing the effects of sleep deprivation.

Caffeine

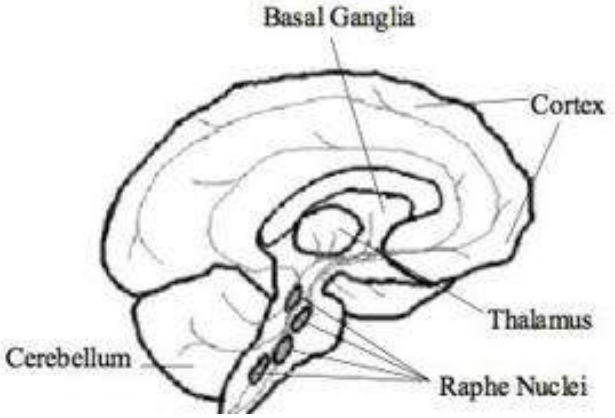
- Stimulant – Makes you alert and active
- Caffeine can cross the blood brain barrier
- Mild use is helpful but chronic intake is harmful
- Effect persists for 4-6hrs
- Caffeine binds to
  - Increases dopamine and norepinephrine - addictive
  - Adenosine receptors antagonist – prevents sleepiness



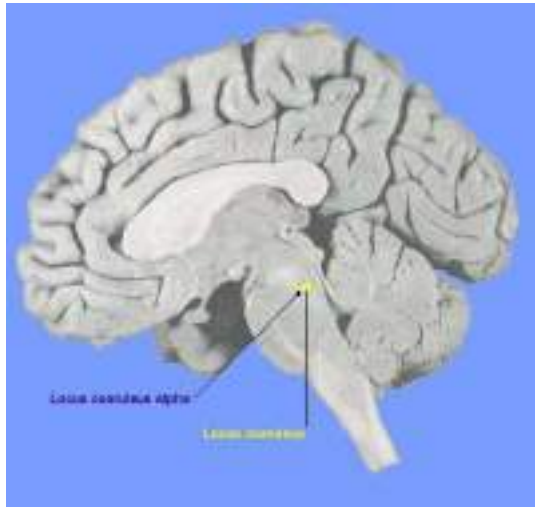


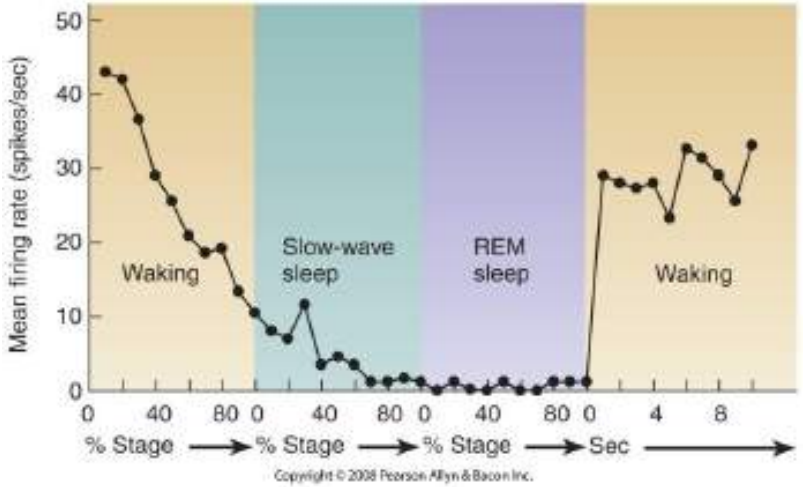
Can cause dehydration

https://www.brown.edu/campus-life/health/services/promotion/content/what-are-effects-caffeine



Neural control of Arousal

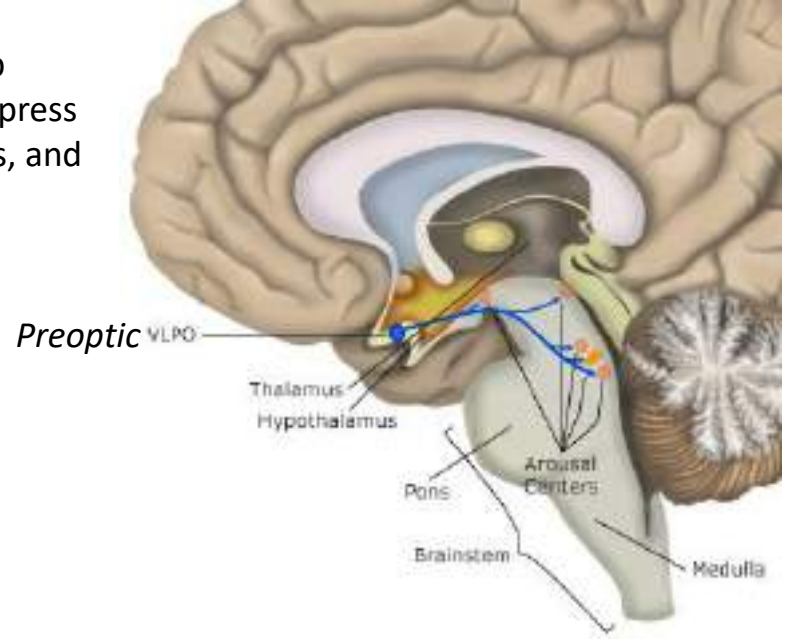




Arousal involves different circuits of neurons that secrete 5 different neurotransmitters which play a role in the animal's level of alertness and wakefulness.

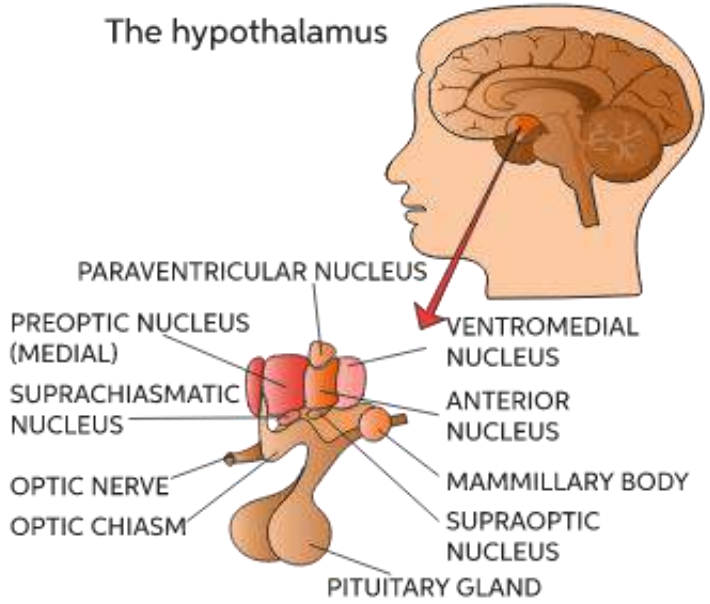
- *ACETYLCHOLINE: (midbrain/brainstem)* - overall activation and cortical desynchrony; sleep waves' desynchrony marks alertness/arousal.
- *NOREPINEPHRINE: (midbrain/brainstem)* - increases attentiveness or vigilance
- *HYPOCRETIN: (hypothalamus)* - excitatory, wakefulness promoting effect
- *SEROTONIN: (brainstem)* - locomotion and cortical arousal and are inactive during sleep
- *HISTAMINE: (hypothalamus)* – Histamine is involved in arousal, antihistamine (allergy) drugs cause drowsiness.

When our preoptic neurons (sleep neurons) become active, they suppress the activity of our arousal neurons, and we fall asleep



Neural control of Slow wave sleep (Onset of sleep)

- The activity of GABAergic neurons in the preoptic suppresses alertness and behavioral arousal and promotes sleep.
- SCN inhibits preoptic neurons during wakeful hours
- It has reciprocal inhibitory connections with the regions involved in arousal and wakefulness (SCN) , acts like a flip flop switch (i.e. both cannot be active at the same time)
- Destruction of the area causes insomnia
- This circuit is unstable in narcoleptic people

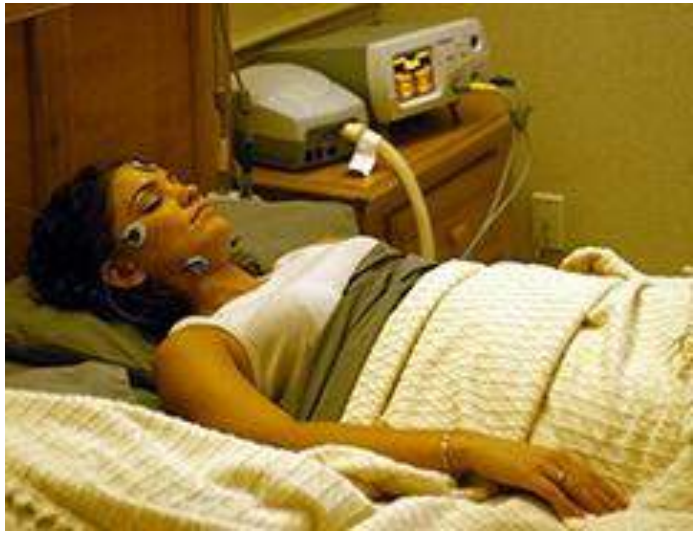


Neural Control of REM sleep (Deep sleep)

- REM sleep is controlled by levels of acetylcholine, higher the levels more the REM related activity.

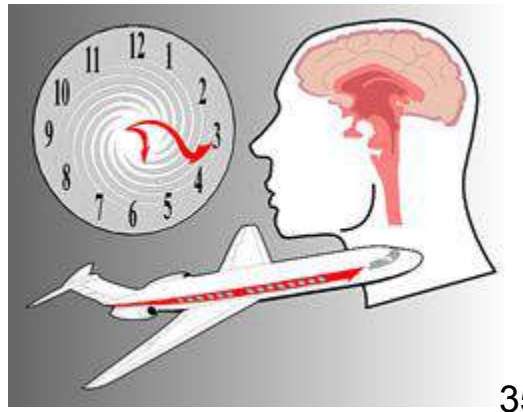
Sleep Activity (Polysomnography)

- Sleep research labs measure different physiological activity during sleep:
  - EEG – electro-encephalogram (brain activity)
  - ECG – electro-cardiogram (heart activity)
  - EMG – electro-myogram (muscle activity)
  - EOG – electro-occulogram (eye – movements)
  - EDA – electro-dermal activity (skin conductance)

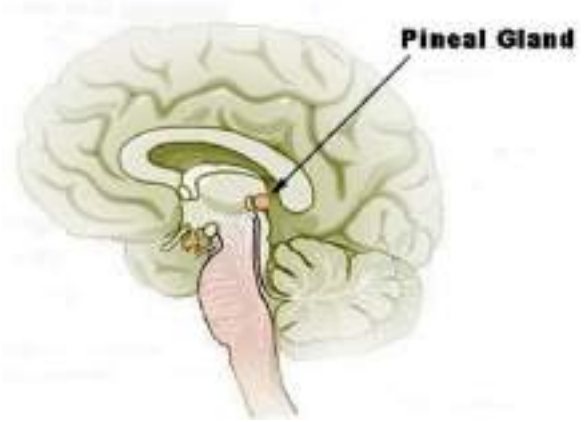


Changes in circadian rhythm

- Shift work and jet lag cause changes in circadian rhythms
- There is disparity between the sudden changes that SCN signals (external environment) and the internal clocks (internal environment)
- As a consequence, sleep and waking hours are affected
- To overcome jet lag or shift work, a strong zeitgeber should be provided before the low point in the circadian rhythm (i.e. when the person feels sleepy but it is day time) to advance the cycle



Control of seasonal rhythms



- ***Pineal gland*** **-** produces melatonin and plays a role in circadian and seasonal rhythms.

- ***Melatonin***

  A hormone secreted in response to darkness (levels rise in the evening bedtime) by the pineal body – promotes sleepiness - it puts you into a state of quiet wakefulness that helps promote sleep

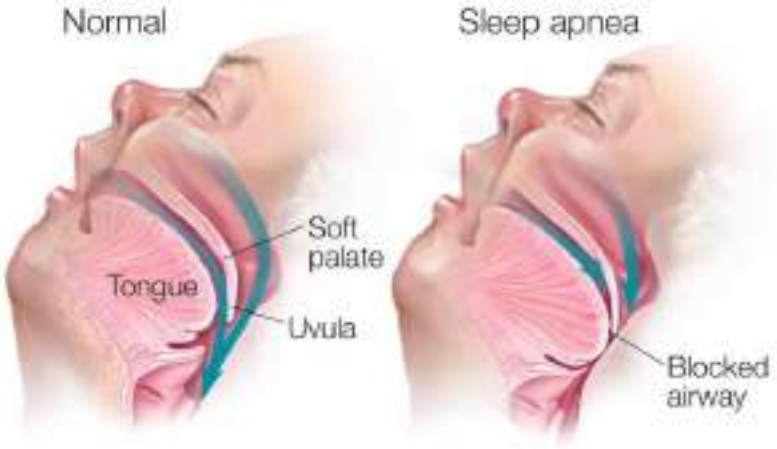
- Melatonin also tracks seasonal changes that alter the cycles in the circadian rhythm

- Stress, smoking, exposure to too much light at night (including blue light), not getting enough natural light during the day, shift work, and aging all affect melatonin production

- Melatonin is produced for a longer time in winter when nights are long, than in summer when nights are short. This may result seasonal changes in mood, seen especially in winter in countries closer to the north and south pole (~17 hour nights)
  - constantly tired, craving sugary foods, overeating, and over sleeping.

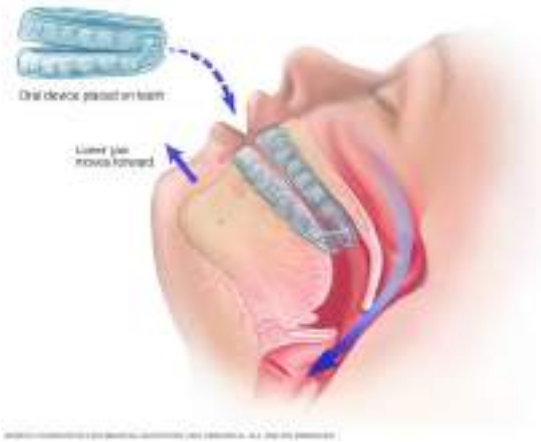
Disorders of Sleep

Sleep apnea



- Sleep hours required can differ from person to person (6-10hrs of sleep)
- Most sleep disorders can be controlled by drugs

- **<u>Insomnia</u>**
  - <u>Symptom:</u> Unable to sleep at night
  - ***Sleep apnea:*** inability to sleep and breathe at the same time (especially people who snore)
    - The person keep waking up during the night gasping for air and falls asleep again
    - Usually happens due to obstruction of airway, and is surgically treated



- **<u>REM sleep behavior disorder</u>**
  - Neurodegenerative disorder with some genetic component
  - <u>Symptom</u>: Patients fail to exhibit paralysis during REM sleep (muscle paralysis occurs in REM sleep)

- **<u>Slow Wave sleep problems</u>**
  - Maladaptive behaviors that occur during slow wave sleep, especially stage 4
  - Bedwetting, sleep walking, night terrors (all occur frequently in children)
  - Sleep walking in adults may be genetic
  - Sleep related eating disorder: eating during the night while asleep (sideffects of medications to treat insomnia)

Disorders of Sleep

- **<u>Narcolepsy:</u>**
  - A neurological disorder characterized by sleep at inappropriate times (however, consciousness is never lost)
  - Genetic disorder and influenced by environmental factors
  - Mutated gene causes destruction of ***hypocretin*** (neurotransmitter) neurons causing narcolepsy
  - Drugs can treat this condition

video
- <u>Symptom 1</u> – ***Sleep attack:*** An overwhelming urge to sleep at any time but more so in boring, monotonous conditions. It lasts for usually 2-5 minutes and the person wakes up refreshed

video
- <u>Symptom 2</u> – ***Cataplexy***: person suddenly wilts and jerks into a sleep. Muscles paralysis occurs at an inappropriate time and are usually triggered by laughter, anger or any strong emotional reaction.

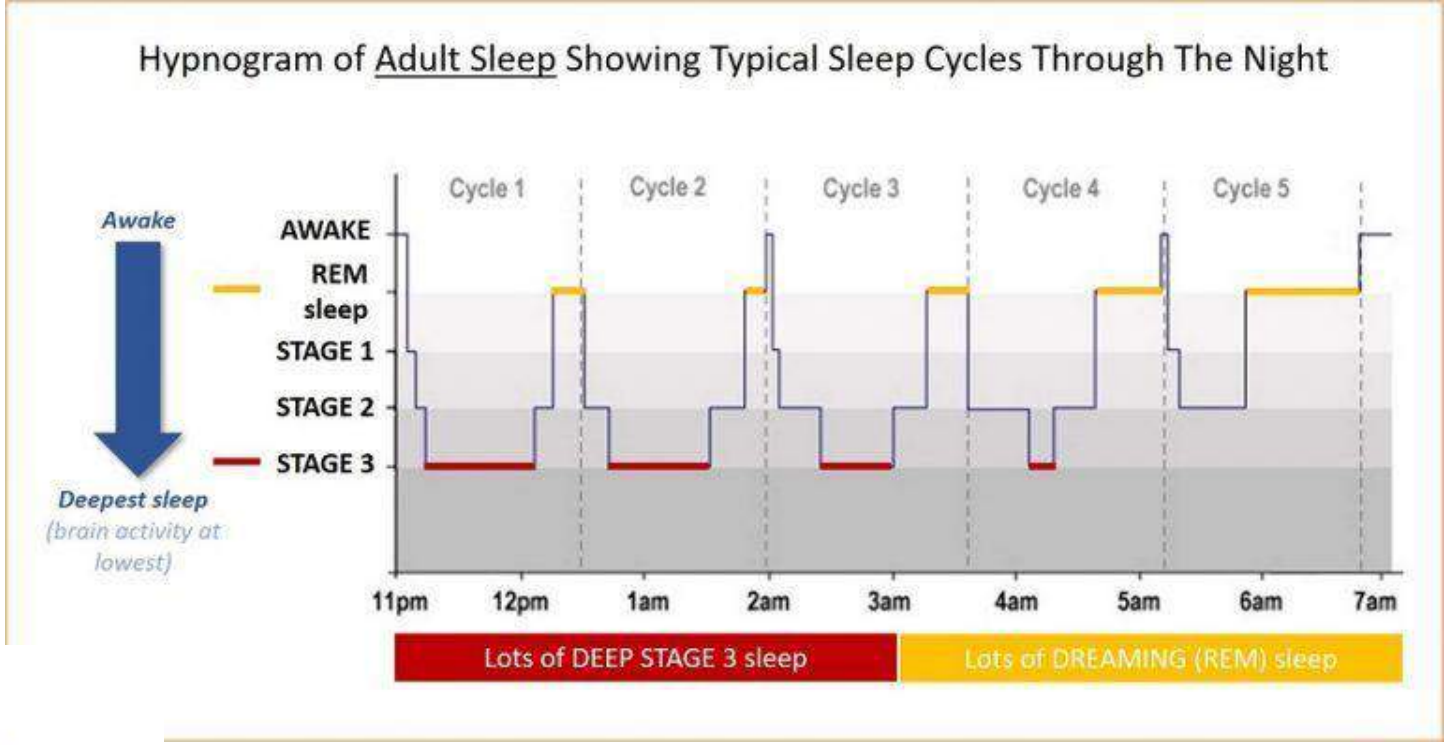
video
video
- <u>Symptom 3</u> – ***Sleep Paralysis***: inability to move just before the onset of sleep or upon waking up. The person can be snapped out of sleep paralysis by being touched or by calling out his/her name.

- <u>Symptom 4</u> – ***Hypnagogic hallucinations:*** person dreams while lying awake and paralyzed

- Sleep is a behavior
- Sleep is a change in consciousness

Stages of Sleep

An 8 hour sleep will contain
- 90 min cycles
- Each cycle has 20-30 min of REM sleep



STAGE 1
lightest (1-7 mins)

Light sleep right after you drift off, 1–5 minutes.

STAGE 2
light (10-25 mins)

Light sleep, your body relaxes, and it's best to wake up during this stage.

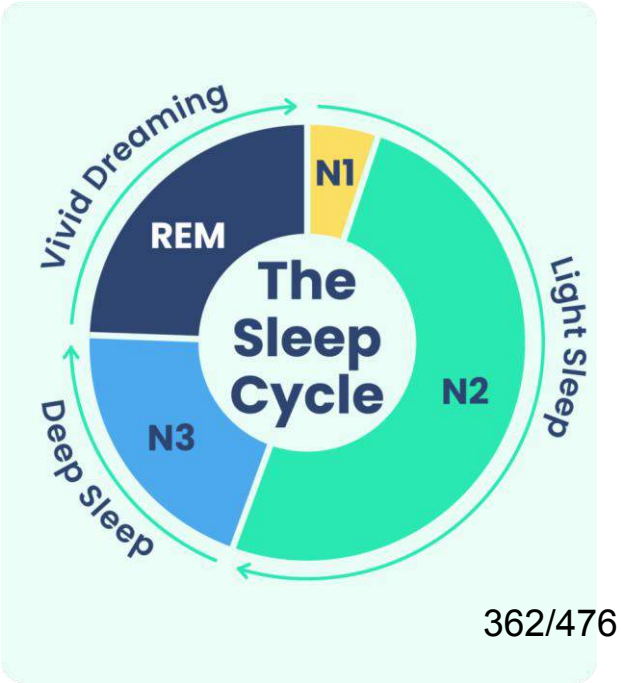
STAGE 3
deep sleep (20-40 mins)

Deep sleep, your brain and body recover, you'll wake up groggy.

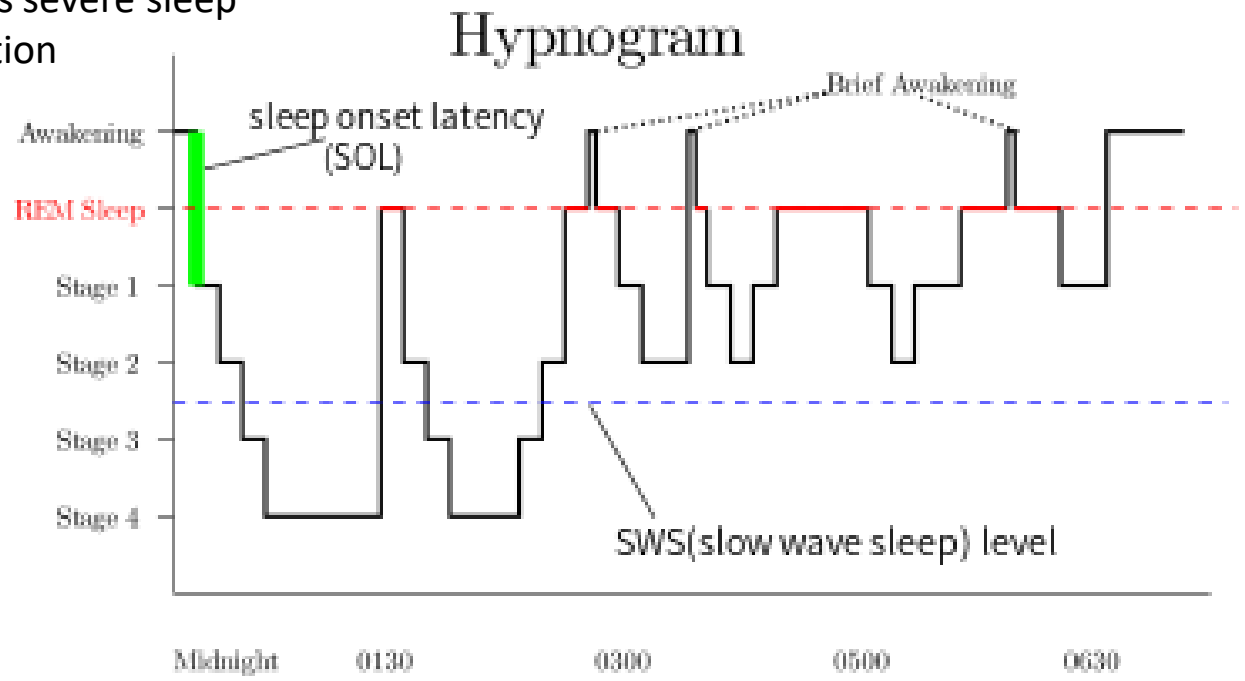
STAGE 4
REM (20-40 mins)

REM sleep populated by vivid dreams and a feeling of unrest upon awakening.

- A person appears alert and attentive when woken from REM sleep and are often able to narrate their dreams vividly.
- muscles and nerves become paralyzed in REM sleep but the brain is active

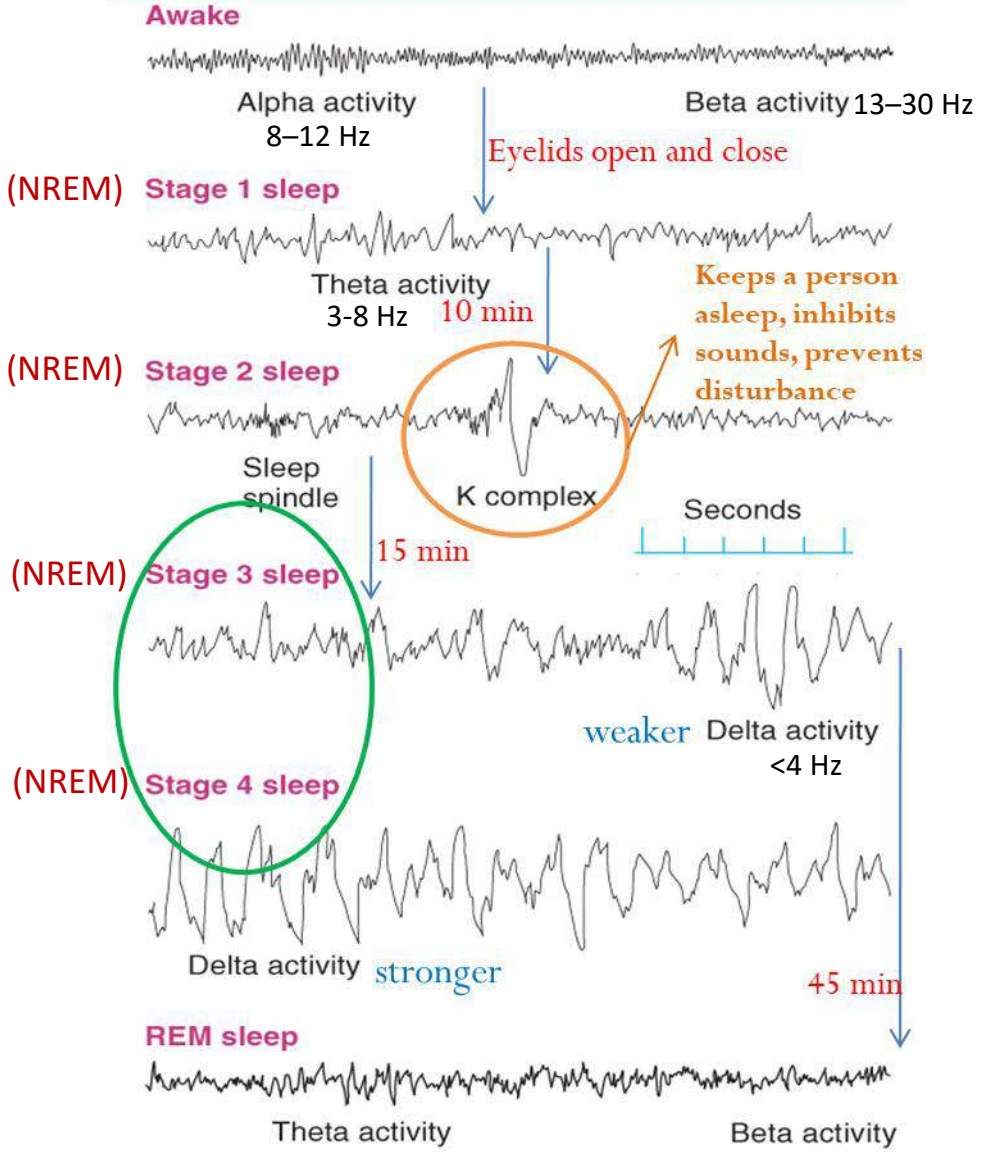


A SOL of < 5-10 minutes indicates severe sleep deprivation



Slow wave Sleep: Non-REM sleep, characterized by synchronized delta activity during deeper stages.

REM sleep: A period of desynchronized EEG activity during sleep, at which time dreaming, rapid eye movements, and muscular paralysis occur.

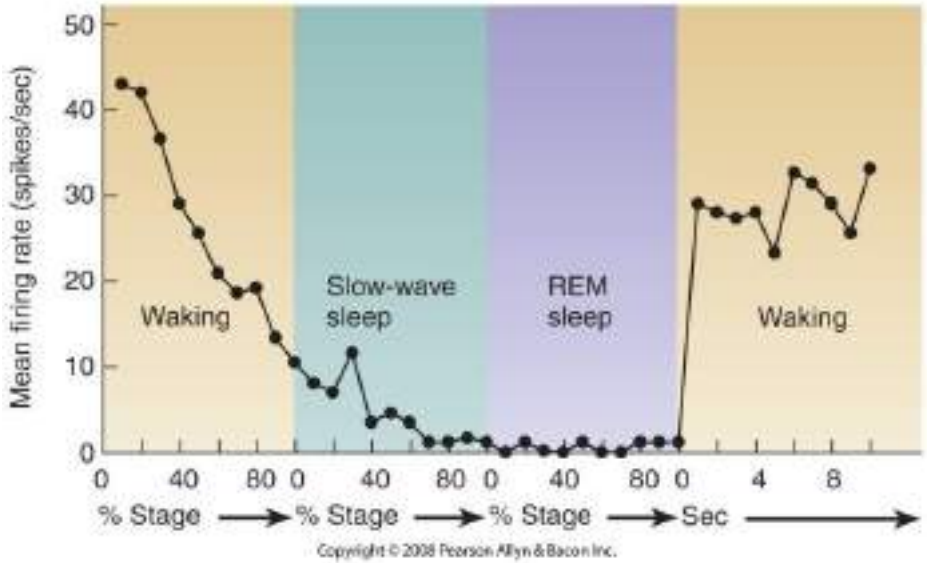


https://www.helpguide.org/harvard/biology-of-sleep-circadian-rhythms-sleep-stages.htm

Function of sleep?

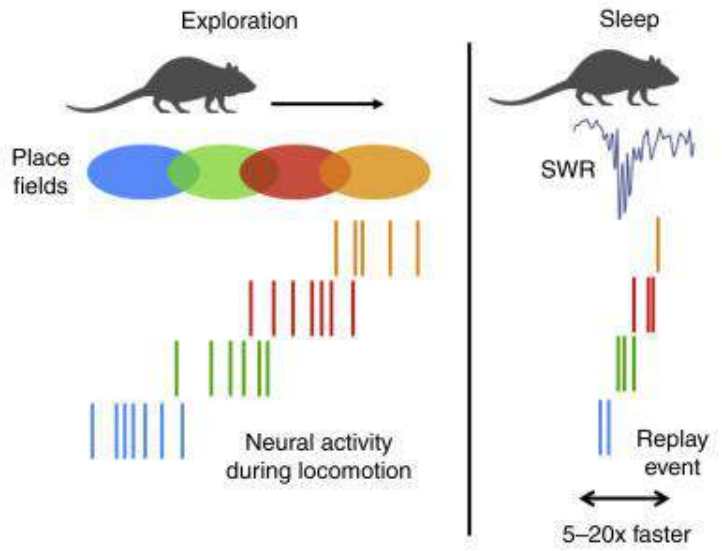
Why do we Sleep?

- ***Primary function of Slow wave sleep***: allows the brain to rest
- ***Primary function of REM sleep:*** "may" promote development and learning

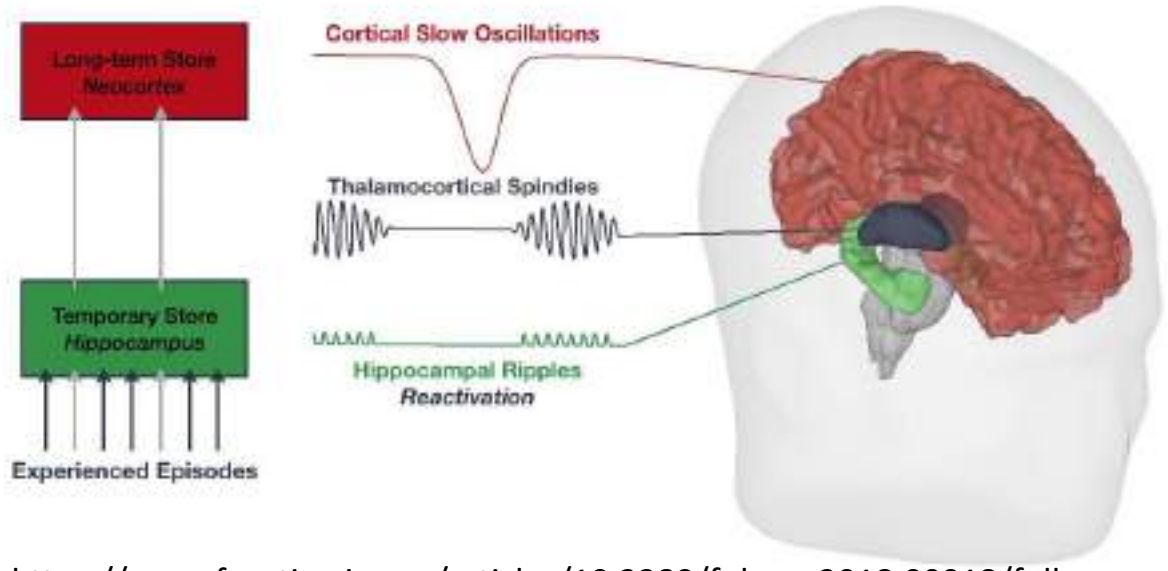


https://www.sciencedirect.com/science/article/pii/S0960982219310358

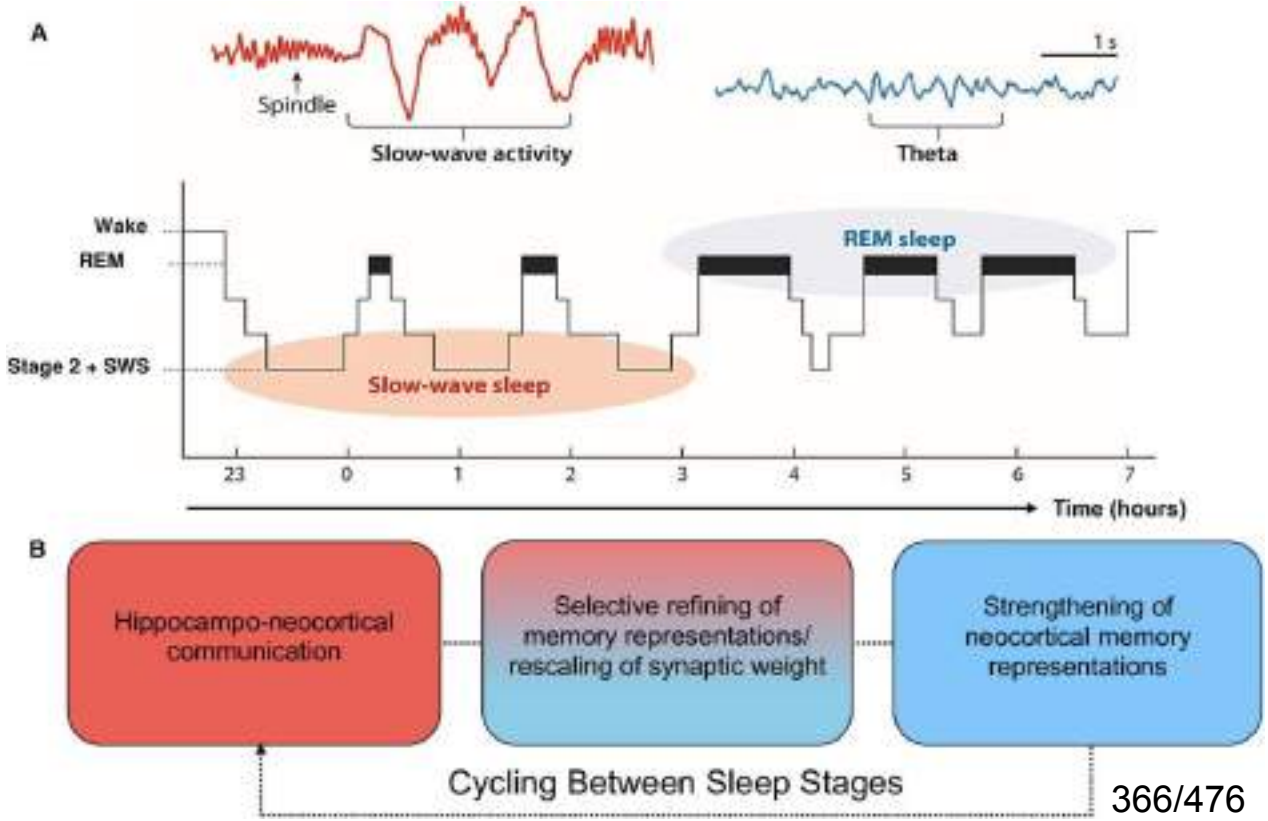
Functions of Sleep



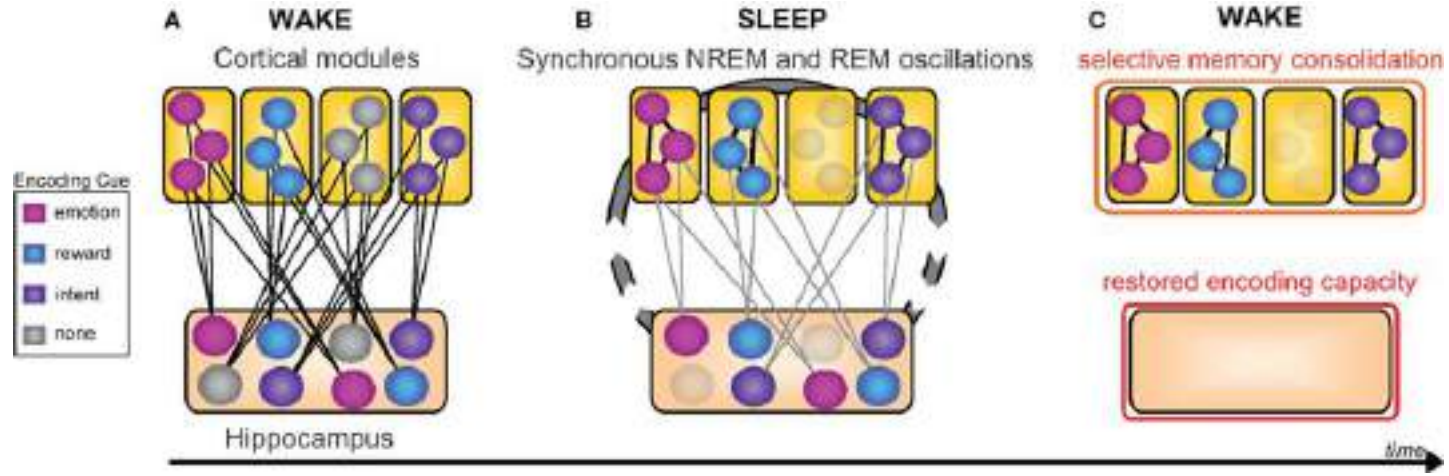
Slow Oscillation-Spindle-Ripple Coupling During Sleep Mediates Memory Consolidation

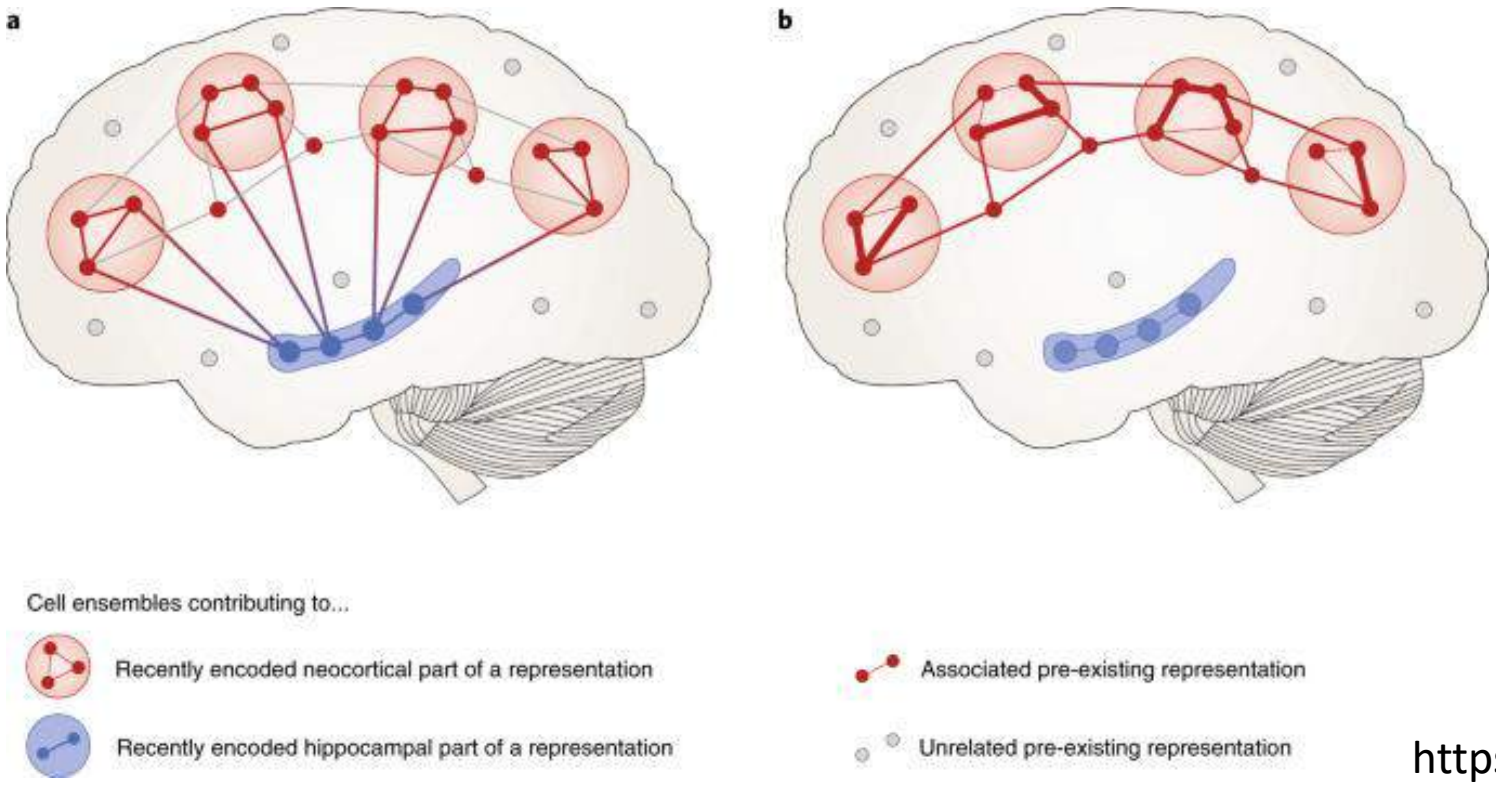


https://www.frontiersin.org/articles/10.3389/fnhum.2018.00018/full

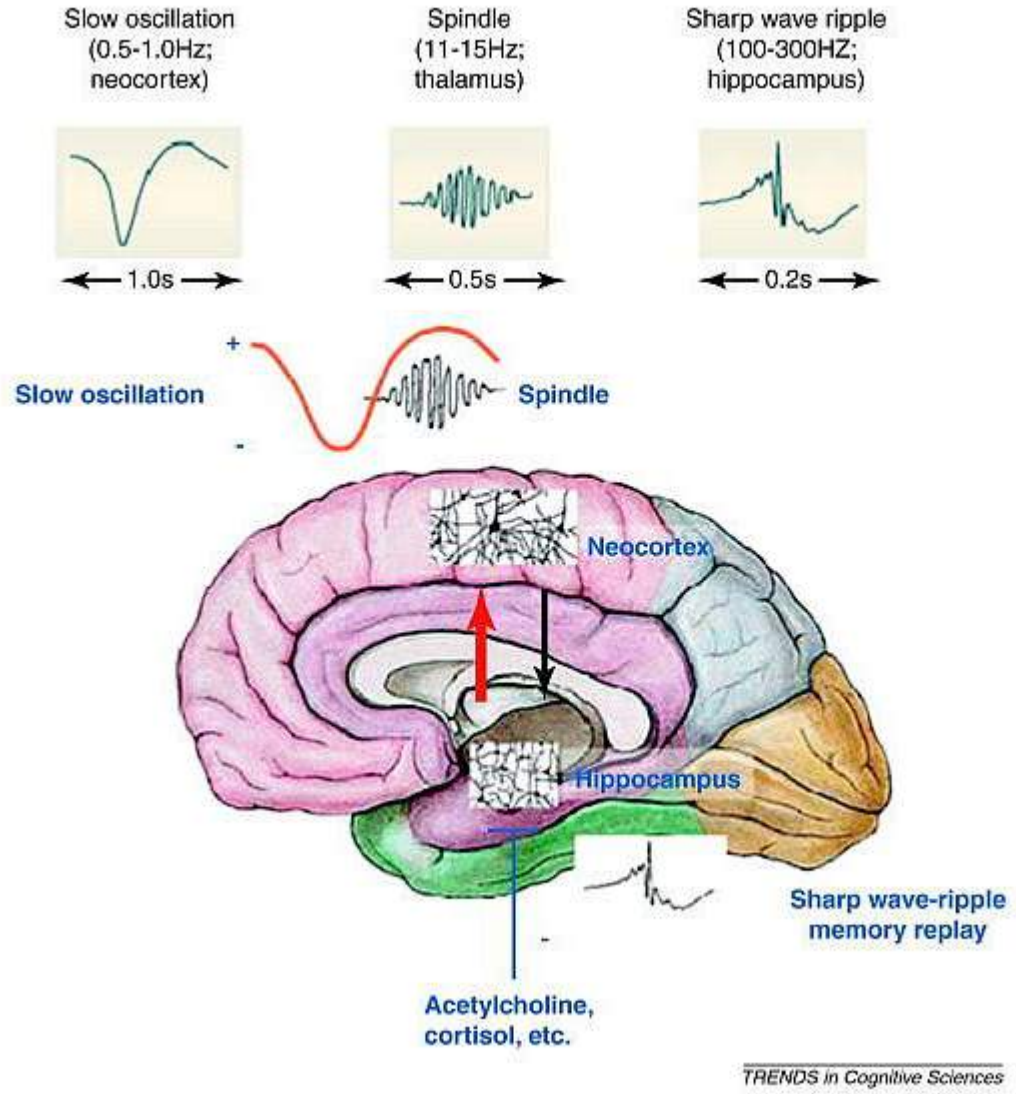


https://kevinbinz.com/2021/12/30/sharp-wave-ripples-and-memory-retrieval/

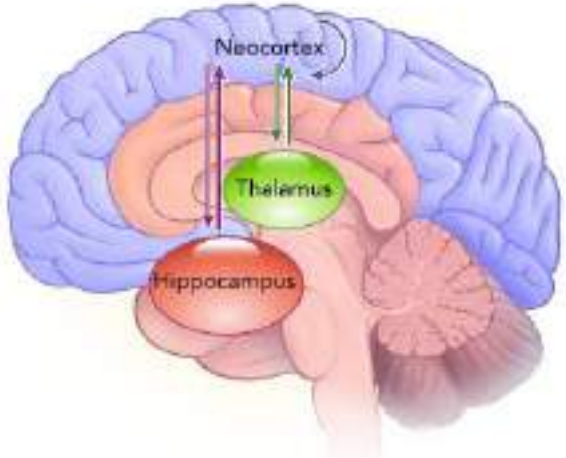




https://www.nature.com/articles/s41593-019-0467-3



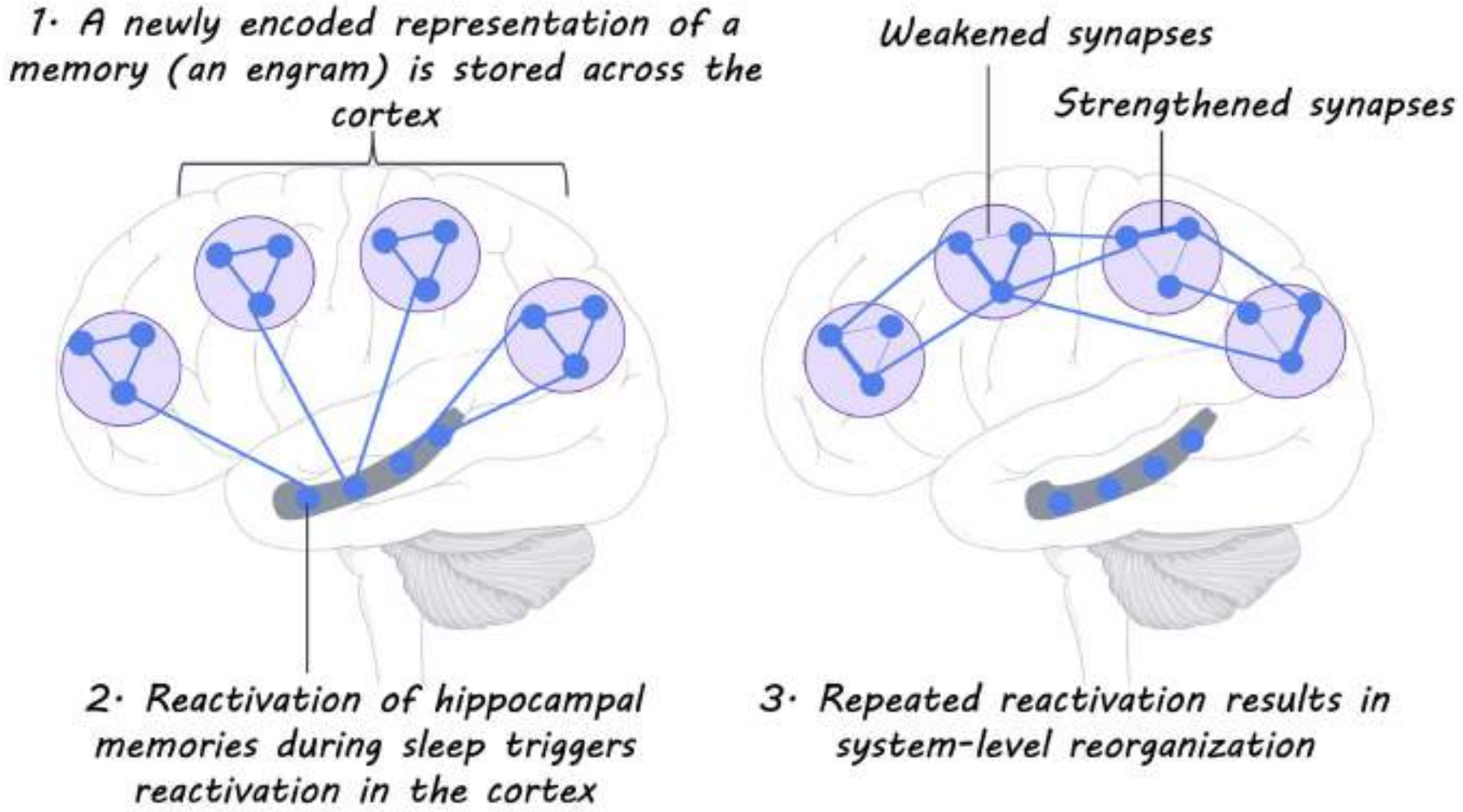
Figurative model of the interplay of neural oscillations/brain rhythms during NREM sleep. Slow oscillations in the neocortex temporally group neural activity in other brain structures such as thalamocortical spindles and hippocampal sharp wave ripples. The timing of spindles relative to the phase of the slow oscillation and the coordinated reactivation of hippocampal SWPRs underlie the transfer of previously learned information on the memory representation to the neocortex, reorganizing, consolidating, and possibly generalizing the memory content as it becomes hippocampus independent. During ongoing spindles, the thalamus performs sensory gating, thereby reducing external sensory input to the neocortex.



https://journals.sagepub.com/doi/abs/10.1177/1073858406292647?journalCode=nroa

https://journals.physiology.org/doi/epdf/10.1152/physiol.00004.2019

Sleep re-organizes memory networks

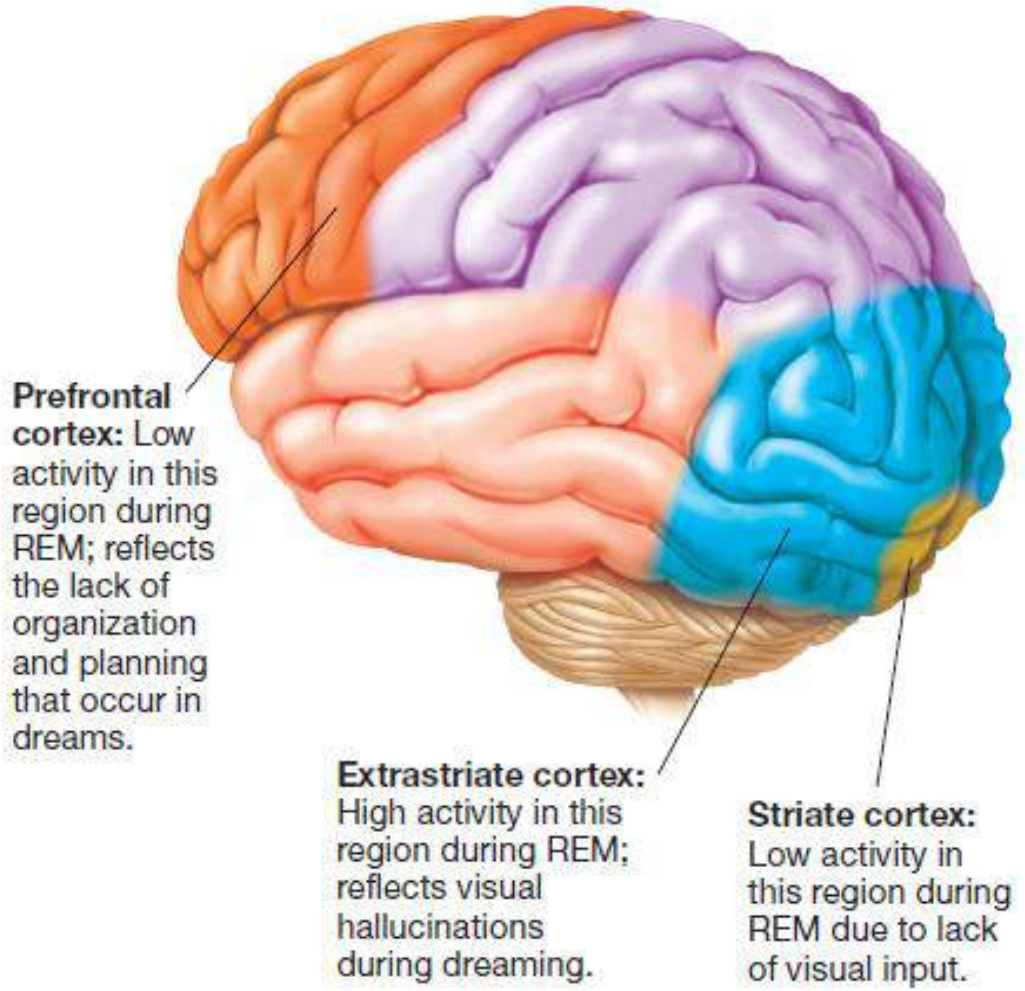


Forgetting?

https://www.brainpost.co/weekly-brainpost/2021/1/26/how-sleep-helps-us-remember-and-forget

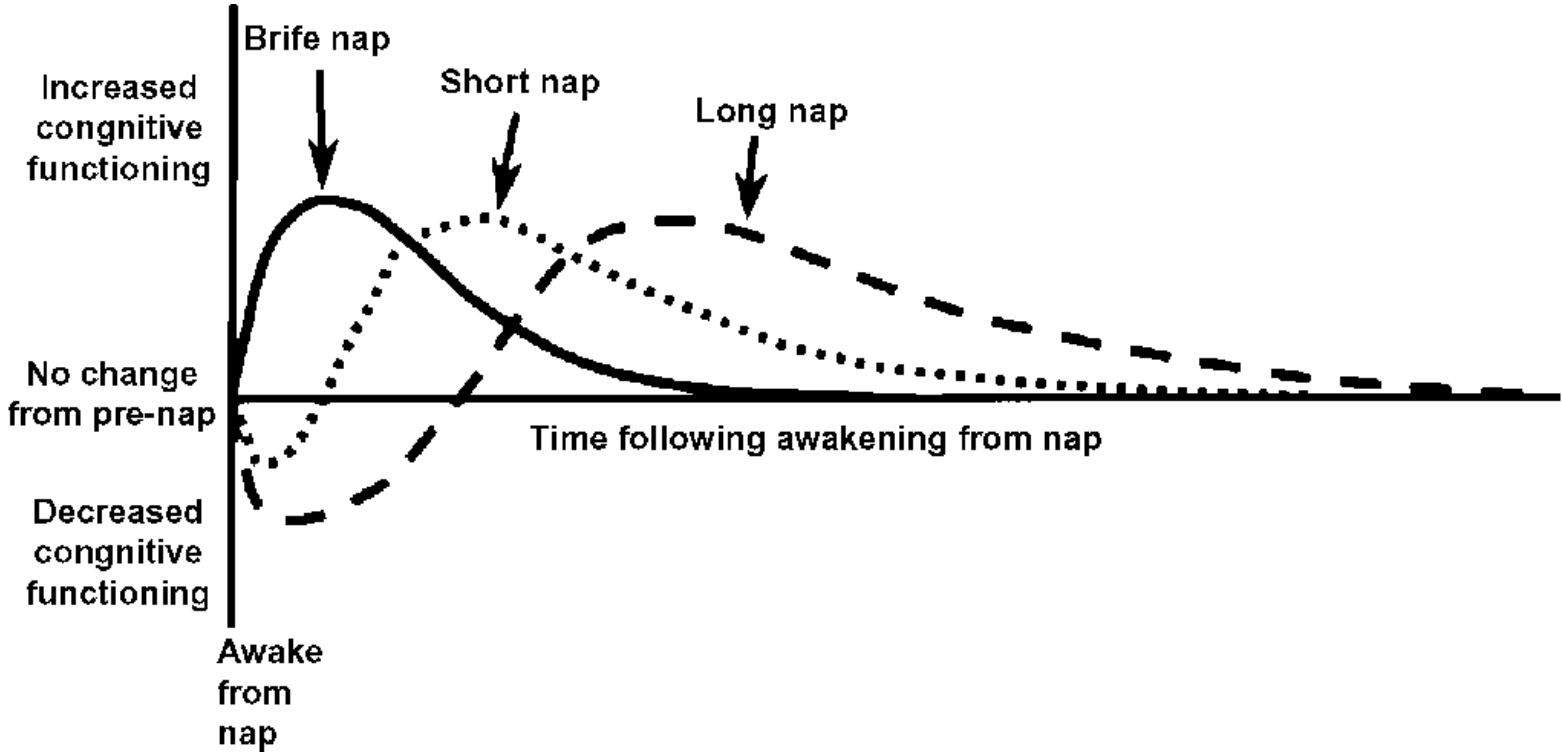
REM Activity in the Brain

Is dreaming simply an incidental consequence of REM sleep?



Dreams occur primarily during REM sleep

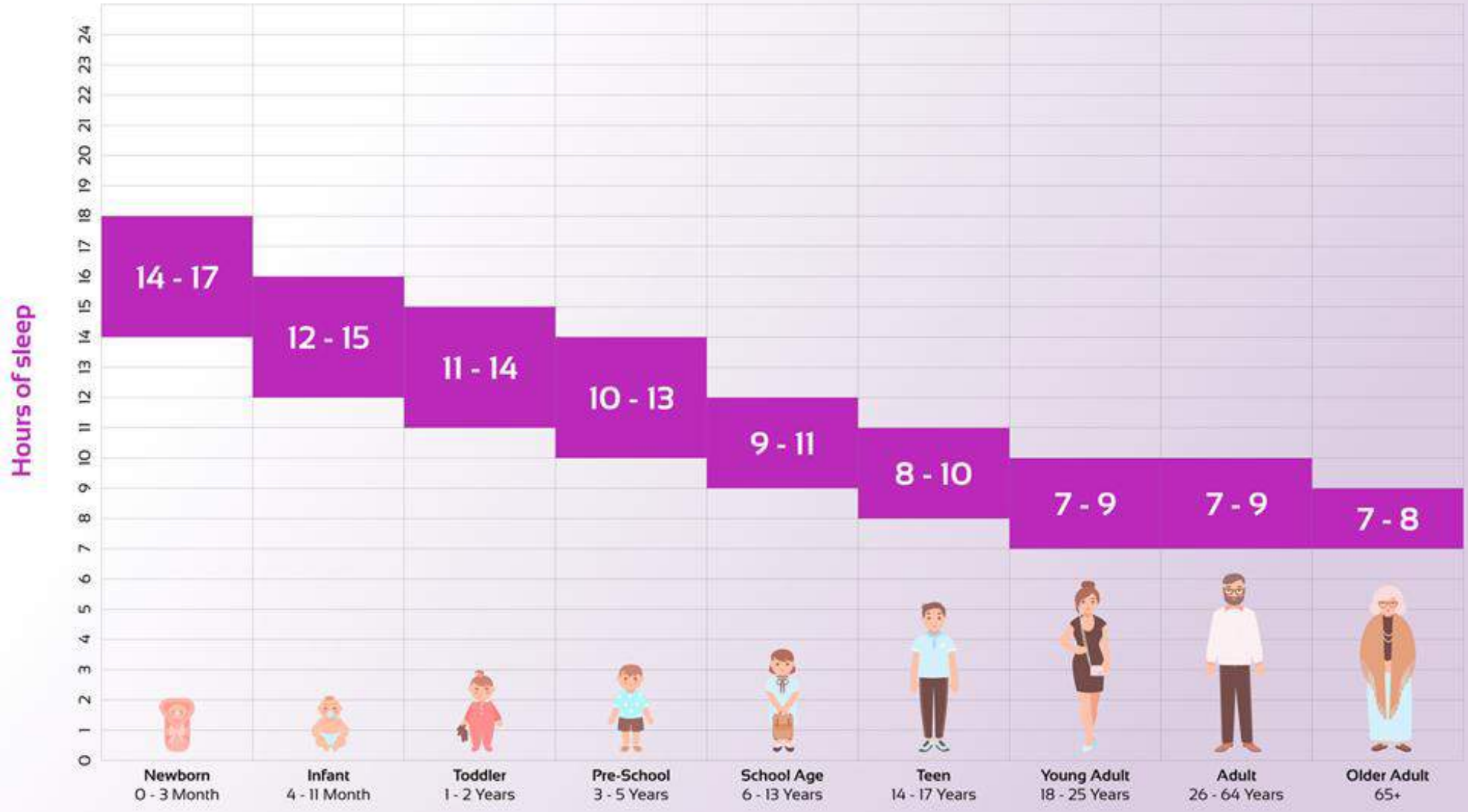
Day-time napping



- benefits of brief (5–15 min) naps are almost immediate after the nap and last a limited period (1–3 h).
- Longer naps (>30 min) can produce impairment from sleep inertia for a short period after waking but then produce improved cognitive performance for a longer period (up to many hours).
- early afternoon naps are beneficial – circadian rhythm

https://www.sciencedirect.com/science/article/abs/pii/B9780444537027000099?via%3Dihub

Recommended Sleep Times Duration



Source: Based on a table, published by National Sleep Foundation, https://www.sleepfoundation.org/

How Poor Sleep Impacts Cognitive Function

Short-Term

Effects of sleep deprivation can appear in the form of:

- Difficulty concentrating
- Decline in mood
- Impaired memory
- Visible signs of fatigue

Vs.

Long-Term

Sleep deprivation or fragmented sleep over long periods of time can result in:

- Poor work performance
- Cognitive decline
- Heightened risk of dementia

The Effects of Short-Term Vs. Long-Term Sleep Debt

Short-Term	Long-Term
Stress	Obesity
Increased Appetite	Diabetes
Irritability	Greater Risk of Cancer, Cardiovascular Disease, and Dementia
Learning Difficulties	

Effects of Sleep Deprivation?

Day 1

- Difficulty focusing eyes

Day 2

- Moodiness
- Difficulty focusing eyes

Day 3

- Irritability
- Memory lapses
- First hallucination

Day 4

- Hallucinations, with recognition that they were not real

Day 5 and onward

- Paranoia

Exercise to Improve Sleep

Find the Best Time of Day for Your Workout Routine.

Aerobic or resistance exercise in the morning may stimulate earlier melatonin release in the evening.

High-intensity exercise in the afternoon may promote sound sleep by reducing wakefulness.

Light resistance or aerobic exercise in the evening may help reduce nighttime awakenings.

https://www.sleepfoundation.org/physical-activity/exercise-and-sleep

Maintaining Circadian Rhythm

https://www.traywellness.com/blog/12-essential-tips-to-better-sleep-and-better-health

Quiz #5

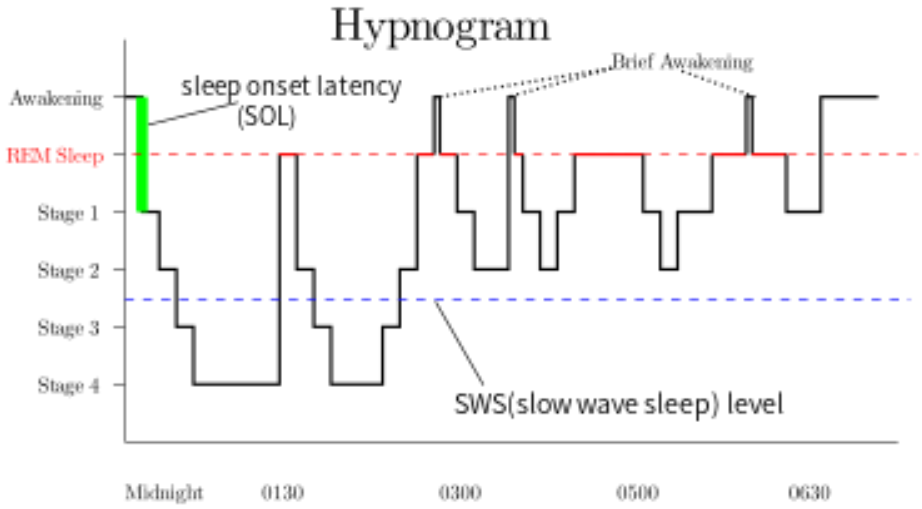
Q1. Stages of Sleep? Be specific (2)

Q2. Circadian Rhythm helps to regulate _____ & _____ levels in our body (2)

Q3. At which stage of sleep do hippocampus and cortex synchronize?

Stages of sleep

- ***Alpha activity:*** A smooth electrical activity of 8–12 Hz recorded from the brain; generally associated with a state of relaxation.
- ***Beta activity:*** Irregular electrical activity of 13–30 Hz recorded from the brain; generally associated with a state of arousal.
- ***Theta activity:*** EEG activity of 3.5-7.5 Hz that occurs intermittently during early stages of slow-wave and REM sleep, a transition between sleep and wakefulness.
- ***Delta activity:*** Regular, synchronous electrical activity of less than 4 Hz recorded from the brain; occurs during the deepest stages of slow-wave sleep.



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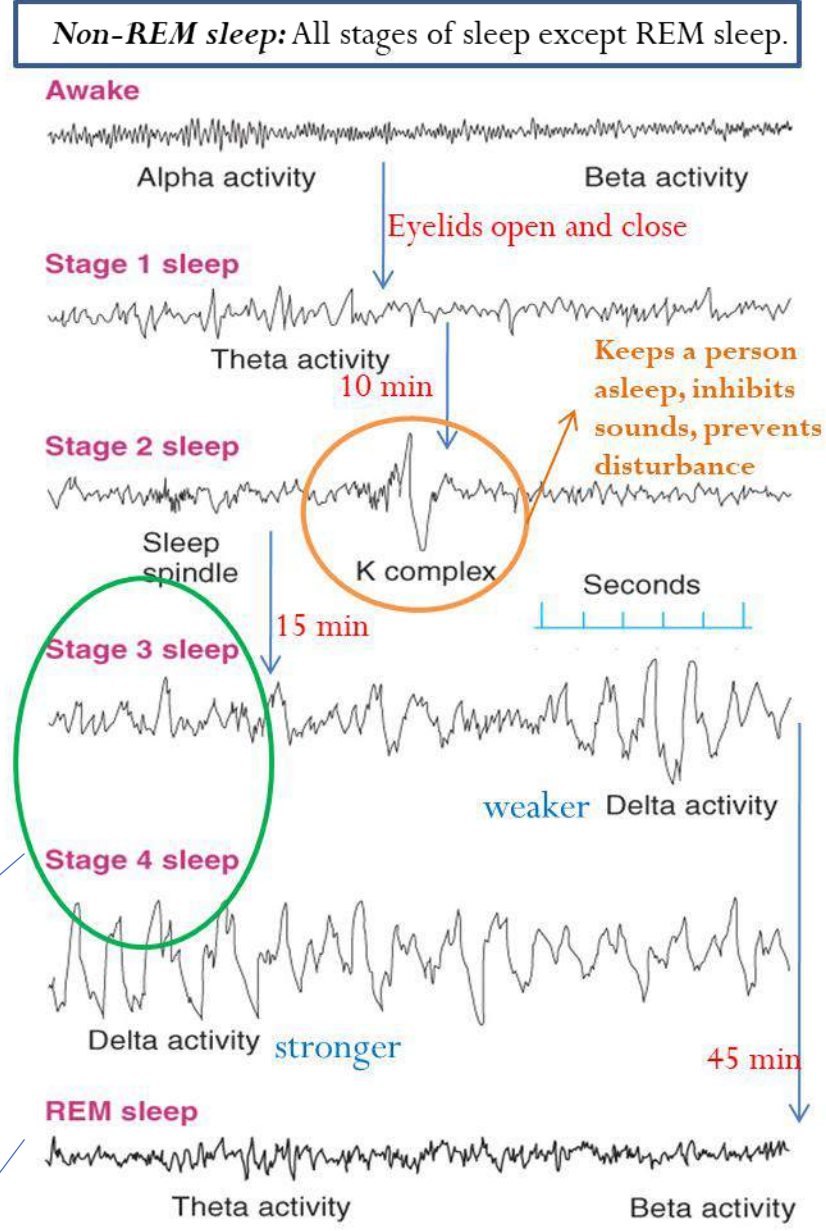
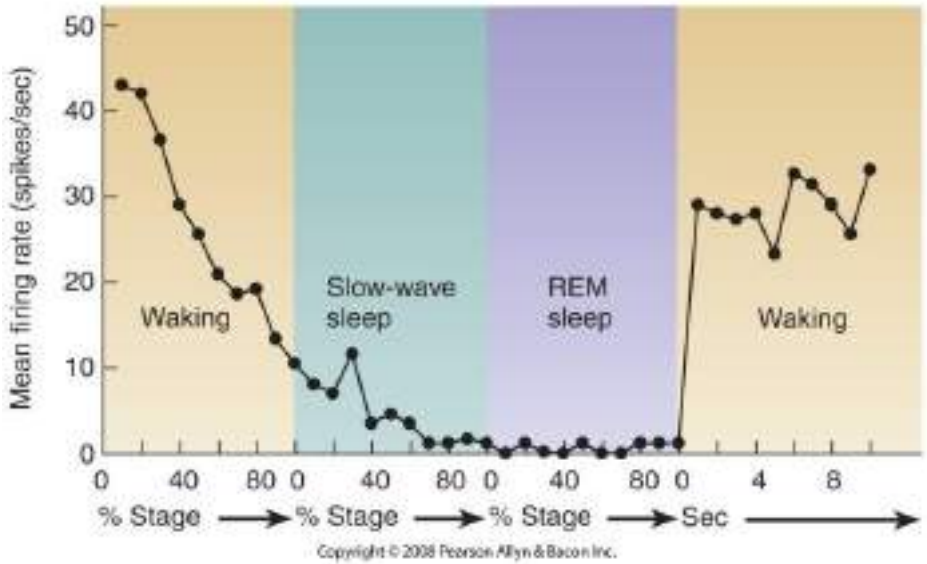


Behavioral description of sleep

- Sleep is a behavior
- Sleep is a change in consciousness

Why do we Sleep?

- No body can indefinitely resist the urge to sleep
- ***Primary function of Slow wave sleep***: allows the brain to rest
- ***Primary function of REM sleep:*** "may" promote development and learning

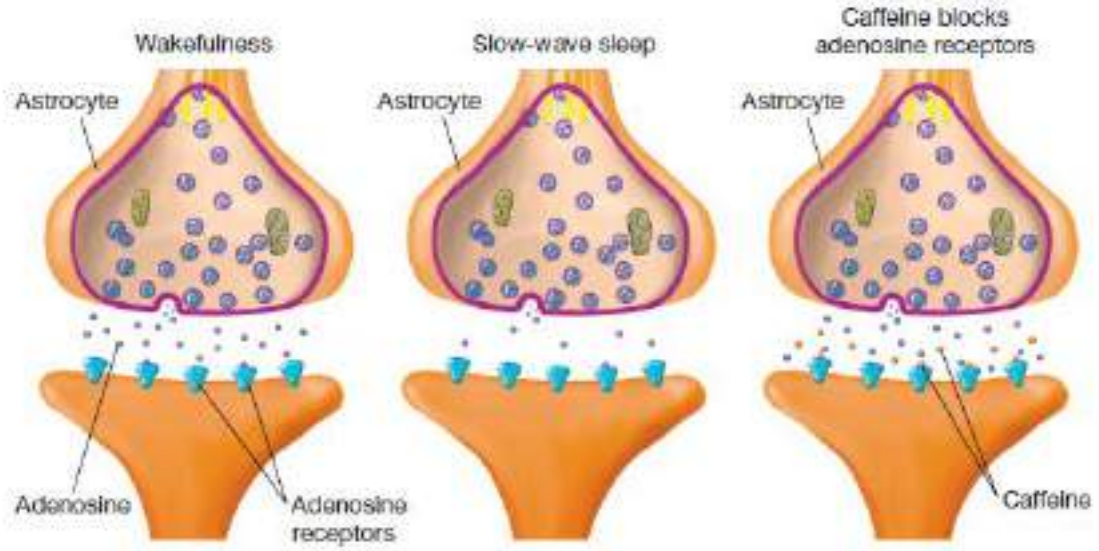


Functions of sleep

- Reactivation (stabilizing memory circuits)
- Creativity
- Stabilizing emotional circuits
- Dreams?

Physiological mechanisms of sleep and waking

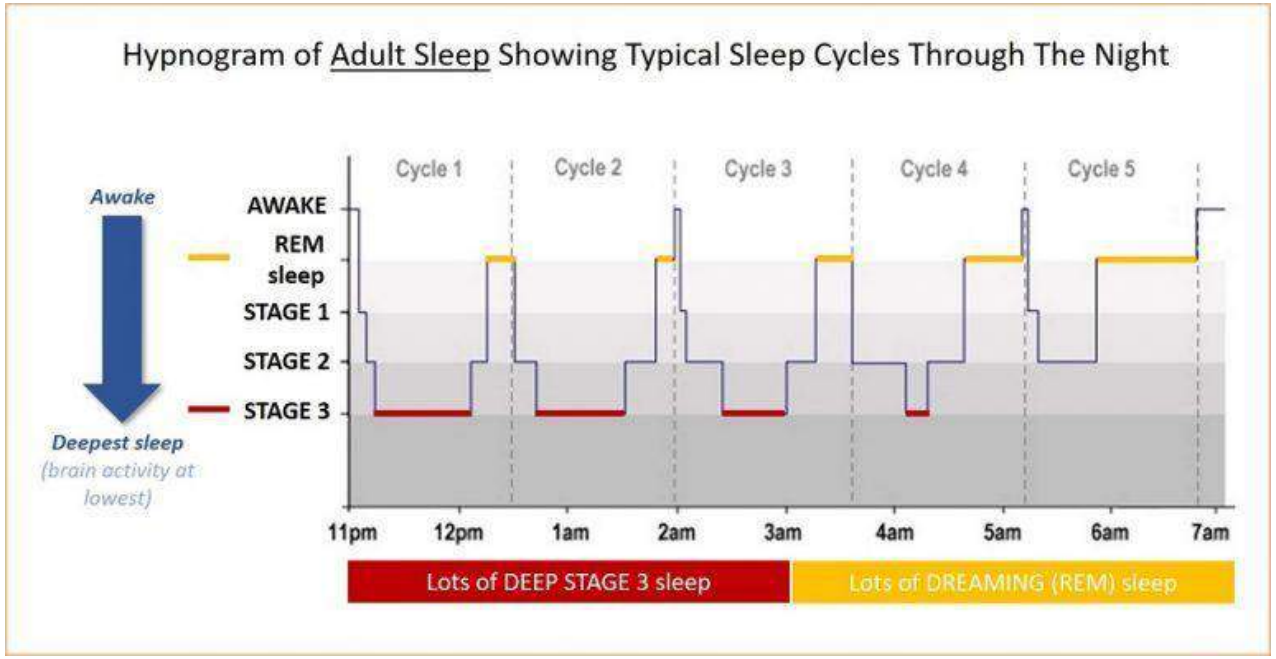
- Sleep, especially REM does not occur simply because neurons get tired, it occurs when a particular neural circuit gets more active
  - Brain is more active (no sleep) → more glucose → increase in adenosine (neuromodulator) levels → more delta activity during sleep (deeper sleep when you have been more active)
  - So basically, adenosine levels reflect the amount of sleep deprivation



Adenosine accumulates during wakefulness and is reduced during slow-wave sleep. Caffeine blocks the adenosine receptors, preventing the inhibitory effect on neural activity and reducing the effects of sleep deprivation.

REM Sleep

- REM is often called paradoxical sleep
- A person appears alert and attentive when woken from REM sleep and are often able to narrate their dreams vividly.
- An entire night's sleep alternates between REM and non REM sleep
- An 8 hour sleep will contain
  - 90 min cycles
  - Each cycle has 20-30 min of REM sleep



- During REM sleep our muscles and nerves become paralyzed but the brain activity and oxygen consumption accelerates

- ***Basic rest-activity cycle:***

  A 90-minute cycle (in humans) of waxing and waning alertness, controlled by a biological clock in the caudal brain stem; controls cycles of REM sleep and slow-wave sleep.

Functions of REM sleep

- ***Rebound phenomenon:***

  The increased frequency or intensity of a phenomenon after it has been temporarily suppressed; for example, the increase in REM sleep seen after a period of REM sleep deprivation.

- This rebound suggests a need for certain amount of REM sleep

- REM sleep is seen most in the active phase of brain development, especially in infants 70% of sleep is REM sleep.

- By late adulthood, it is less than 15%, thus REM sleep decreases with development

- Beyond development in adulthood, REM sleep may be responsible for the learning that occurs throughout life
  - Emotionally related information is consolidated and integrated with existing memories
  - Flush useless memories and loss of storage space
  - REM sleep of college students increased during exam time (i.e. the more you learn the more REM sleep you need)

Functions of slow-wave sleep

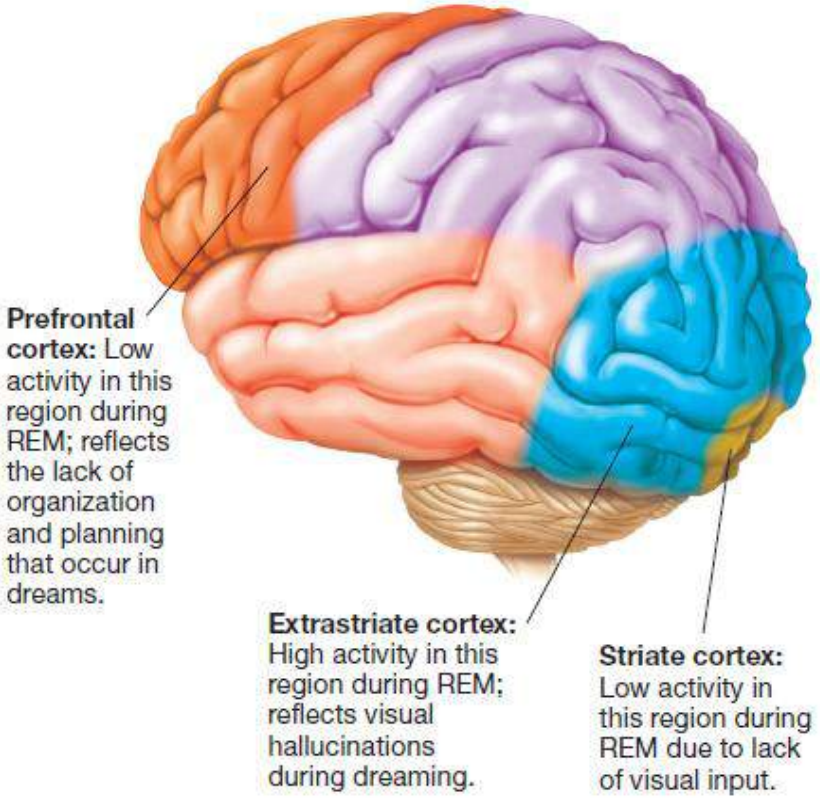
1. *Effects of sleep deprivation*
   - Restorative effects of sleep are more imp. for the brain than for the body
   - Sleep deprivation has no effect on physical exercise, however, their cognitive abilities are affected
   - During slow wave sleep, cerebral blood flow and metabolic rate increase
   - Regions of highest activity during waking have the lowest activity during sleep (i.e. the delta activity that signifies rest is the highest in these regions)
   - ***Fatal familial insomnia:*** inherited disorder that results in damage to thalamus causing deficits such an inattentiveness, insomnia may result in death over time

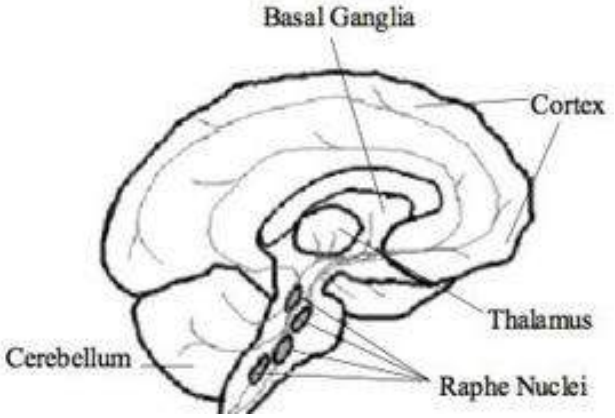
2. *Effects of exercise on sleep*
   - Exercising improves slow wave sleep (deep sleep)

3. *Effects of mental activity on sleep*
   - Tasks that demand more alertness and mental activity increase glucose metabolism in the brain
   - More delta activity is seen during sleep in those regions that have had more activity during daytime
   - Even without any physical exertion, a person may feel tired after heavy mental tasks

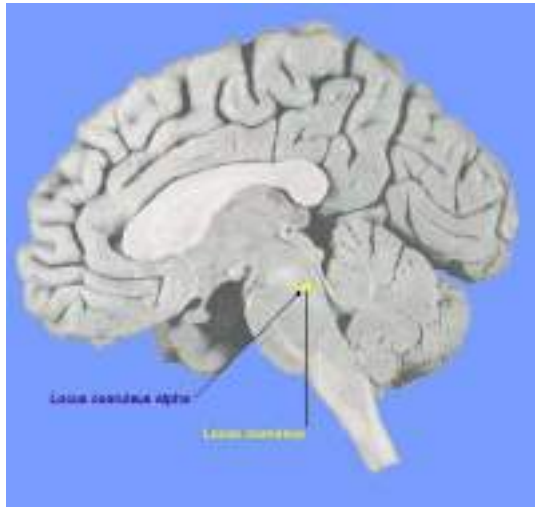
REM and Slow-Wave Sleep

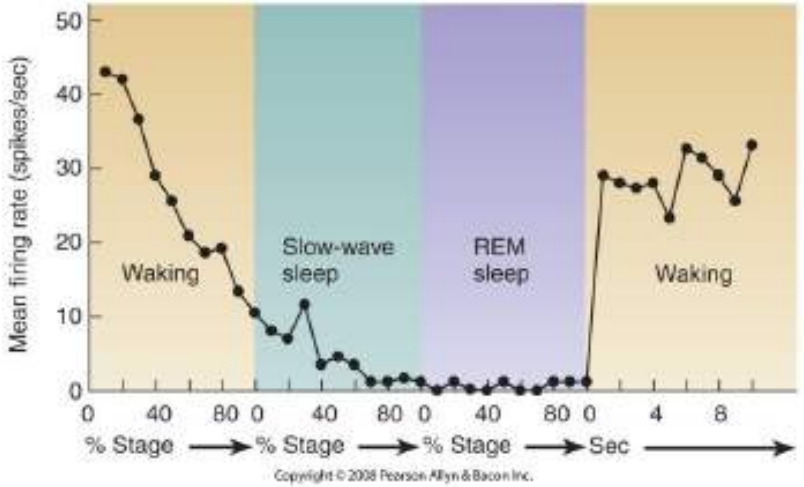
REM (Rapid Eye Movement) sleep	Slow Wave Sleep
EEG desynchrony (rapid, irregular waves)	EEG synchrony (slow waves)
Lack of muscle tone	Moderate muscle tone
Rapid eye movement (REM)	Slow or absent eye movement
Dreams	No dreams





Neural control of Arousal



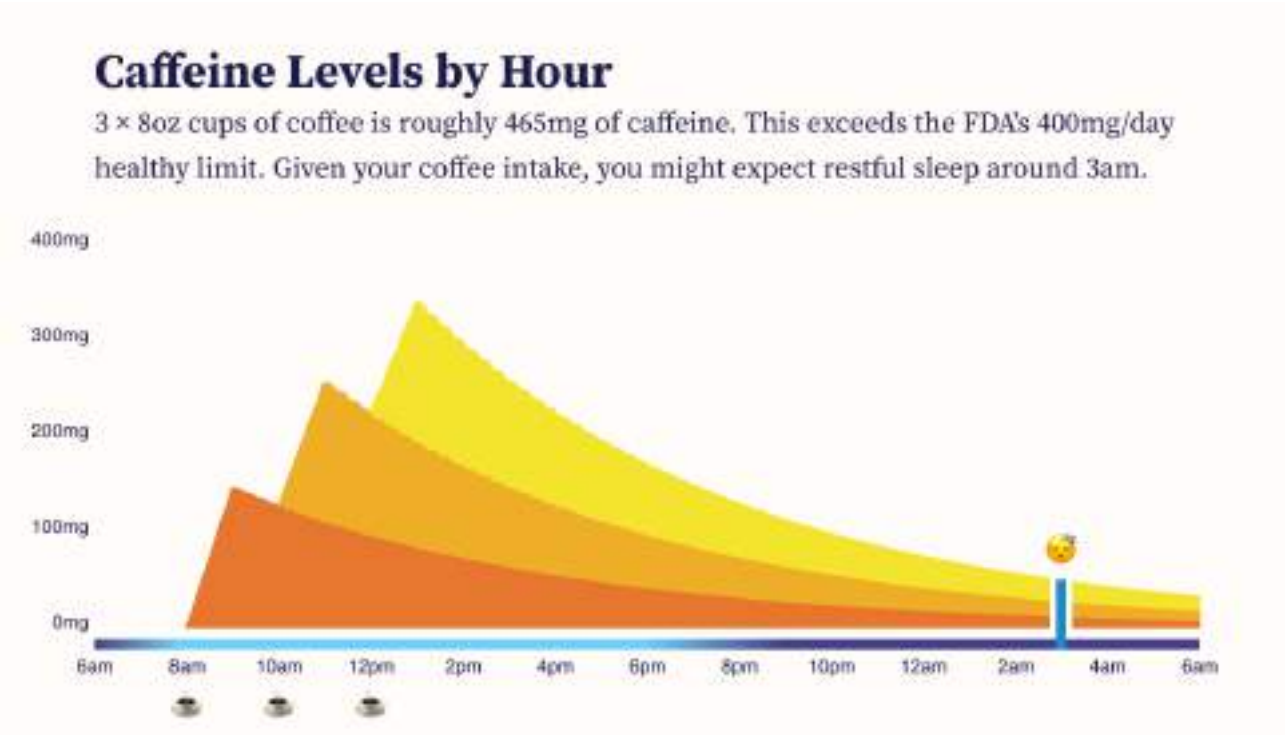


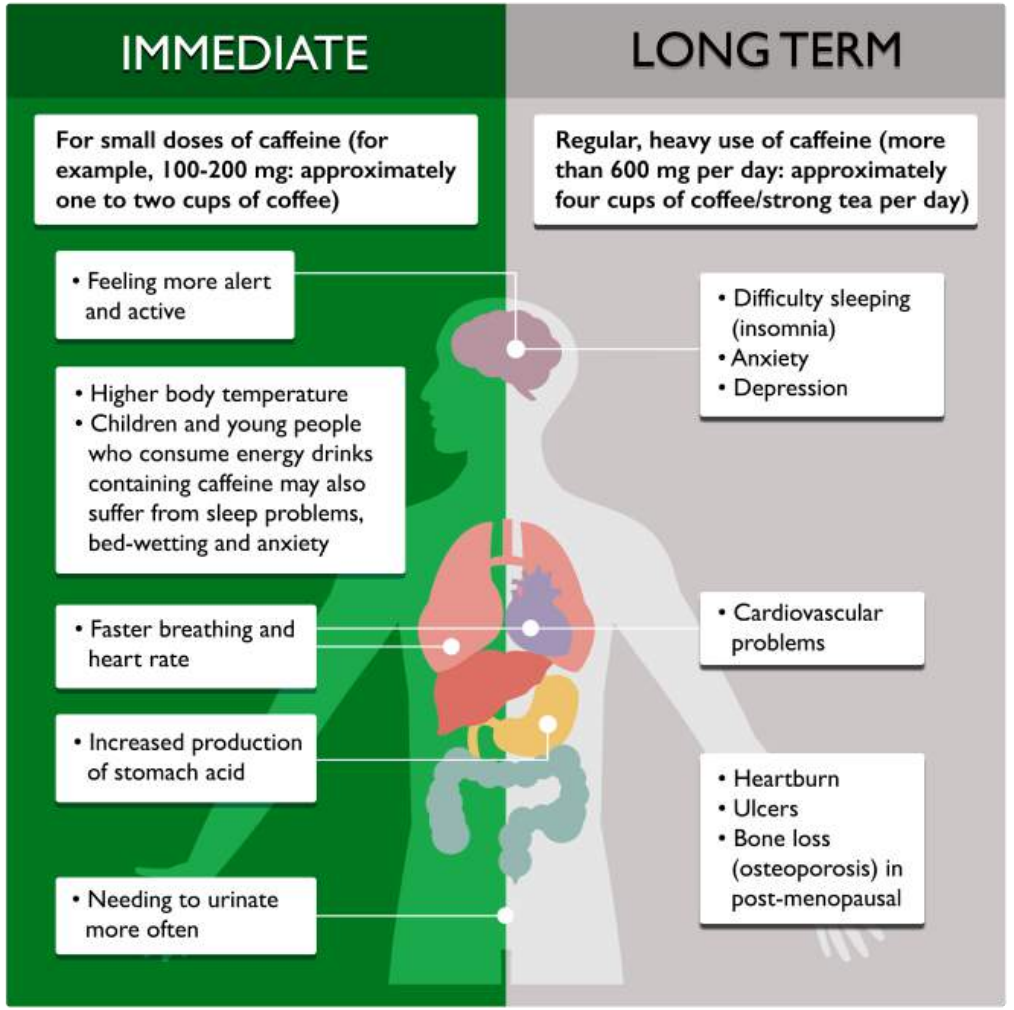
Arousal involves different circuits of neurons that secrete 5 different neurotransmitters which play a role in the animal's level of alertness and wakefulness.

- *ACETYLCHOLINE: (midbrain/brainstem)* - overall activation and cortical desynchrony; sleep waves' desynchrony marks alertness/arousal.
- *NOREPINEPHRINE: (midbrain/brainstem)* - increases attentiveness or vigilance
- *HYPOCRETIN: (hypothalamus)* - excitatory, wakefulness promoting effect
- *SEROTONIN: (brainstem)* - locomotion and cortical arousal and are inactive during sleep
- *HISTAMINE: (hypothalamus)* – Histamine is involved in arousal, antihistamine (allergy) drugs cause drowsiness.

Caffeine

- Stimulant – Makes you alert and active
- Caffeine can cross the blood brain barrier
- Mild use is helpful but chronic intake is harmful
- Effect persists for 4-6hrs
- Caffeine binds to
  - Increases dopamine and norepinephrine - addictive
  - Adenosine receptors antagonist – prevents sleepiness

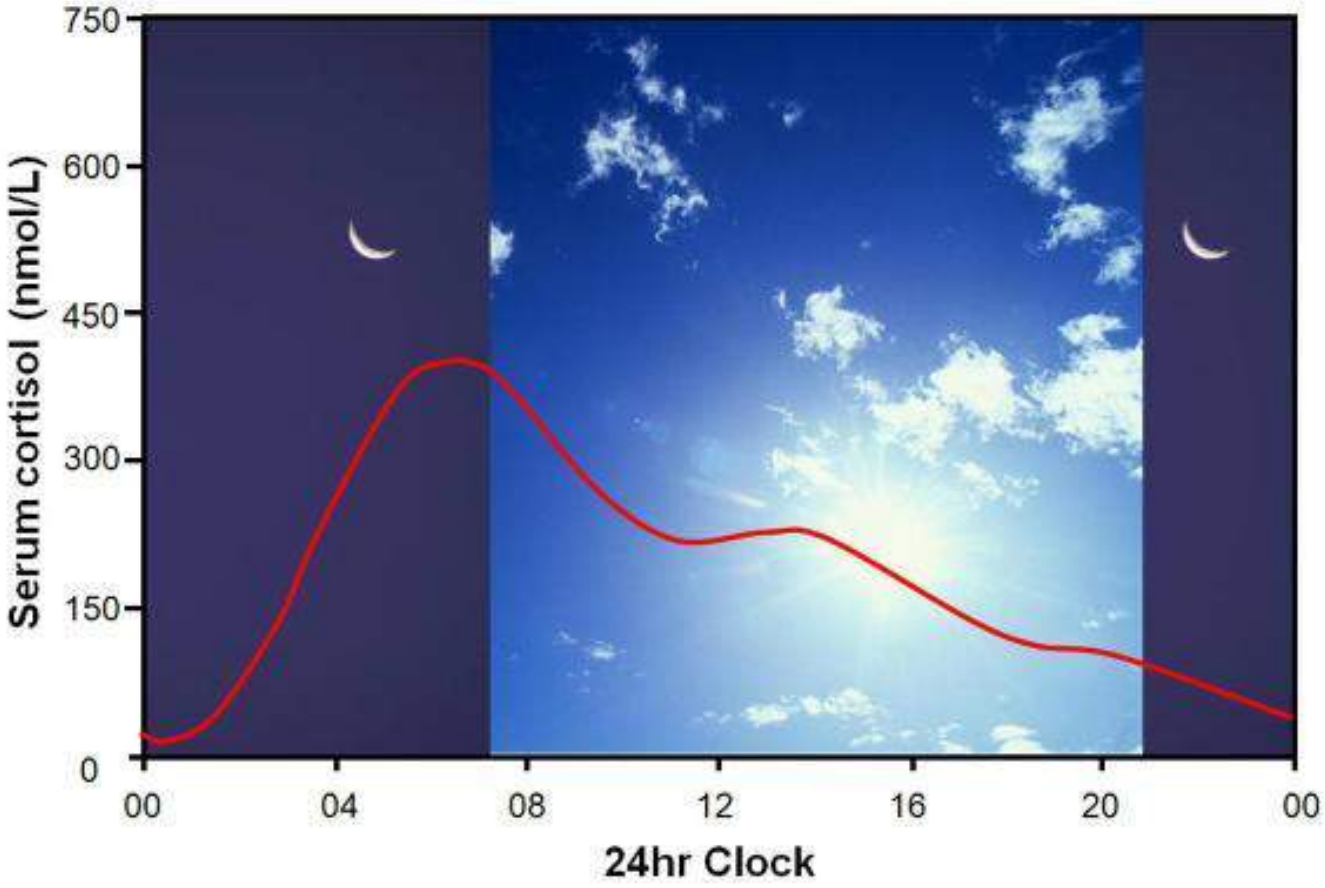




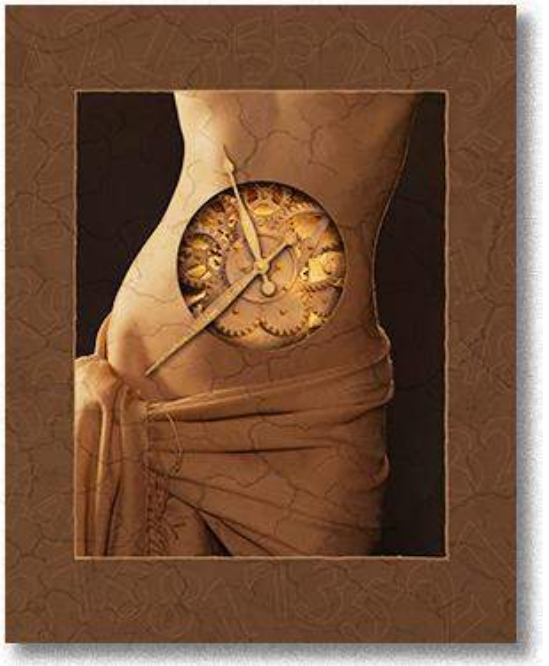
Can cause dehydration

https://www.brown.edu/campus-life/health/services/promotion/content/what-are-effects-caffeine

Changes in cortisol levels according to circadian rhythm



Biological Clock



- Our daily pattern of sleep and waking follows a 24hr cycle.

- ***Circadian rhythms***:

  A daily rhythmical change in behavior or physiological process (which is approx a 24 hr cycle governed or reset by zeitgebers)

- ***Zeitgebers*** *(light giver)* - An environmental agent or event that provides the cue for setting or resetting a biological clock or circadian rhythm

  (bright light, temperature, eating or drinking patterns, alarms)

- In presence of constant darkness or constant light, our rhythms are controlled by ***internal clocks*** (usually a 25 hrs cycle). It runs a little slower in the absence of an external resetting stimulus.
  - E.g. Scandinavian countries, north & south pole
  - Using artificial illumination (lights & lamps), we are able to delay bedtime and extend wake time, resulting in a 25 hrs internal clock instead of the natural 24 hrs biological clock

The Suprachiasmatic nucleus (SCN)

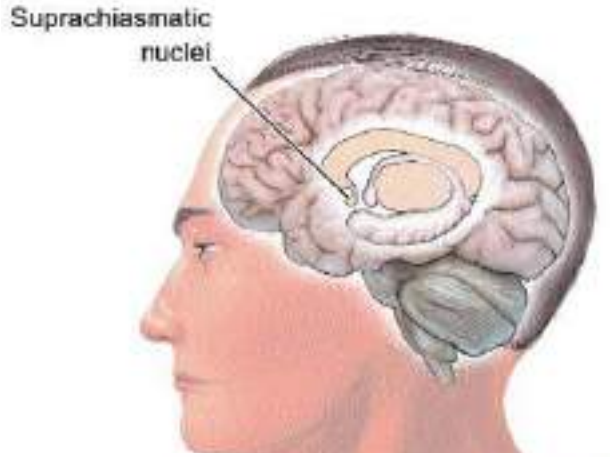
- SCN in the hypothalamus (atop the optic chiasm) controls the circadian rhythms

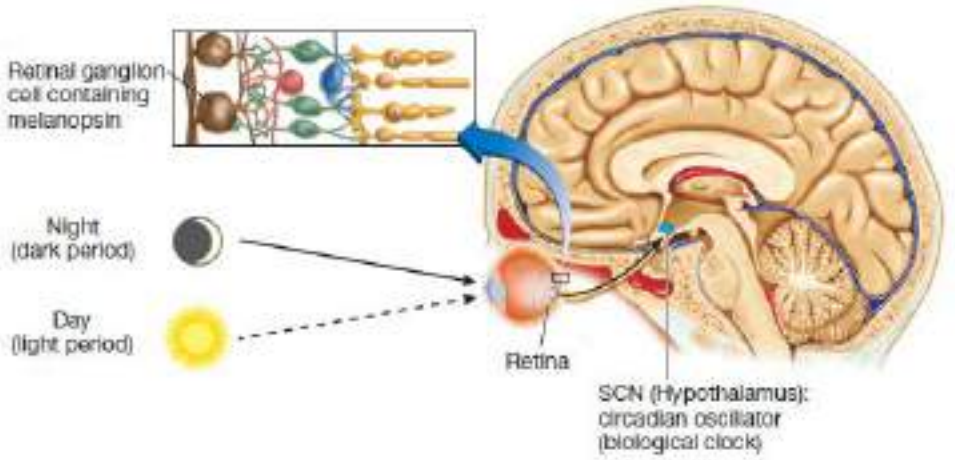
- SCN controls the sleep and wake cycles

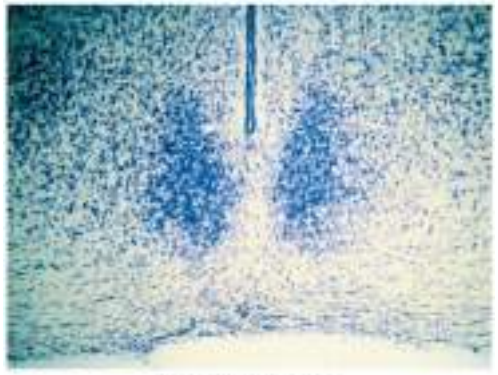
- *Melanopsin (photochemical in retina)*:
  A photopigment present in the retinal ganglion cells transmit light information (day/night) to the SCN

- SCN has specialized neurons that become active at different times during the day, thereby tracking the day and controlling the circadian rhythm (A protein inside the neuron controls the circadian rhythm; when its levels reach a peak, it inhibits its own production, resetting the cycle.)

- Mutation of gene involved in circadian rhythm may result in:
  - *Advanced Sleep phase syndrome*: person sleeps at 7:30pm and wakes up at 4:30am (4 hr advance in sleep & temp. cycles)
  - *Delayed Sleep phase syndrome*: person sleeps at 2am and wakes up at mid-morning (4 hr delay in sleep & temp. cycles

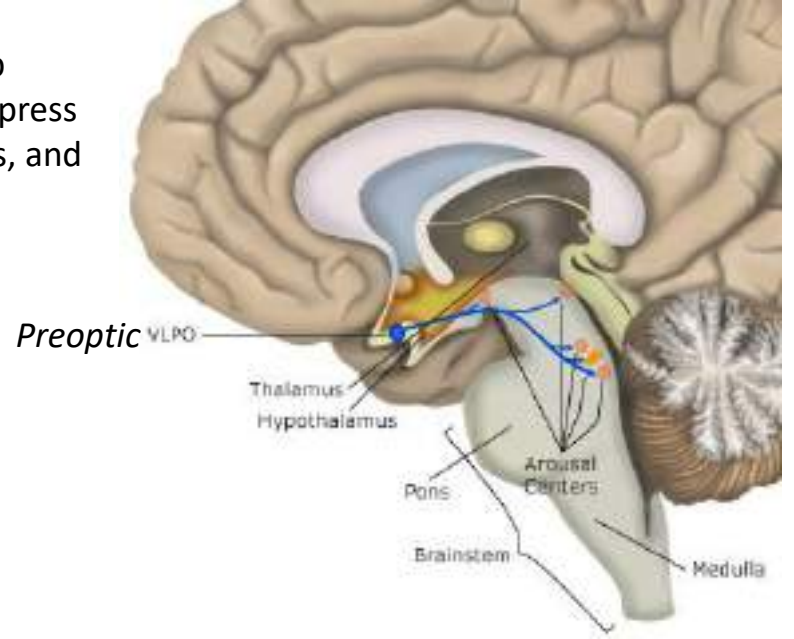






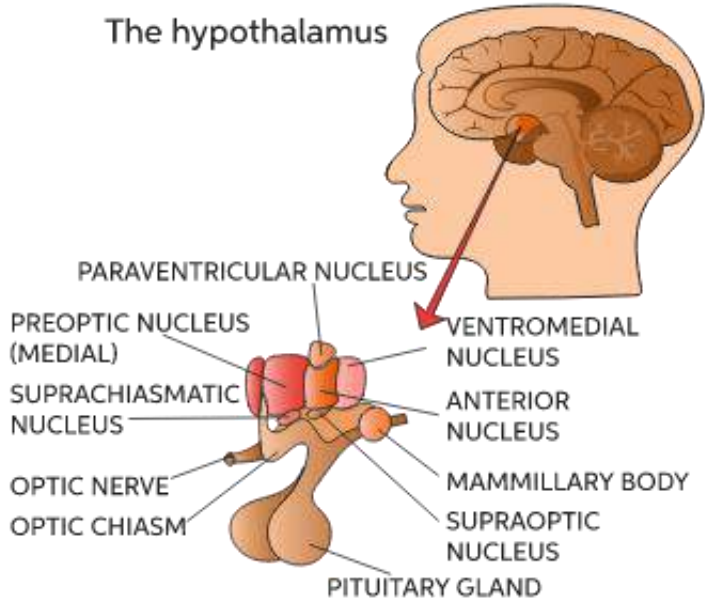
SCN in a rat's brain

When our preoptic neurons (sleep neurons) become active, they suppress the activity of our arousal neurons, and we fall asleep



Neural control of Slow wave sleep (Onset of sleep)

- The activity of GABAergic neurons in the preoptic suppresses alertness and behavioral arousal and promotes sleep.
- SCN inhibits preoptic neurons during wakeful hours
- It has reciprocal inhibitory connections with the regions involved in arousal and wakefulness (SCN) , acts like a flip flop switch (i.e. both cannot be active at the same time)
- Destruction of the area causes insomnia
- This circuit is unstable in narcoleptic people



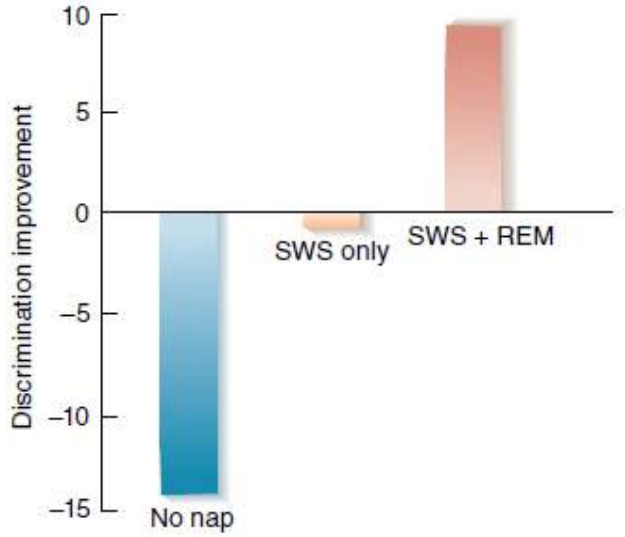
Neural Control of REM sleep (Deep sleep)

- REM sleep is controlled by levels of acetylcholine, higher the levels more the REM related activity.

Napping

- Short power naps
- Long naps indicate night sleep deprivation

Only after a 90-minute nap that included both slow-wave sleep and REM sleep was an improvement seen in the participants' performance on a nondeclarative visual discrimination task.



Over/Under sleeping

- More than 8-9 hours (over sleeping)
- Less than 6 hours (sleep deprivation)
- Moods can be dull – depressive moods
- Physical energy levels are lower
- Weight gain
- Risk for diabetes, heart diseases
- Risk for psychological illnesses
- Cognitive performance may not be optimal

PhD Balance

SLEEP HYGIENE

HEALTHY SLEEPING HABITS #PHDSTRONGERTOGETHER

STAY ON A CONSISTENT SLEEP-WAKE SCHEDULE

AVOID EATING OR WORKING IN YOUR BED

SLEEP IN A QUIET AND DARK ENVIRONMENT

AVOID ELECTRONIC DEVICES BEFORE BED TIME

ENGAGE IN RELAXING ACTIVITIES BEFORE BEDTIME

BE MINDFUL OF CAFFEINE INTAKE

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www.phdbalance.com


WHAT HAPPENS
WHEN YOU SLEEP
Memories are consolidated and stored (necessary for learning)
Maintain better mental health and physical health
What happens when you sleep
Ability to concentrate and pay attention is restored
Metabolism is regulated
Muscles repair and recover


WHAT HAPPENS
WHEN YOU DON'T SLEEP
Judgment and concentration are impared
Reaction time is slowed and more accidents occur
What happens when you don't sleep
Release of more appetite stimulating hormones that can consequently result in weight gain
Emotions are heightened, causing irritability, anger, and/or anxiety
Immune system is suppressed and increases risk of illness

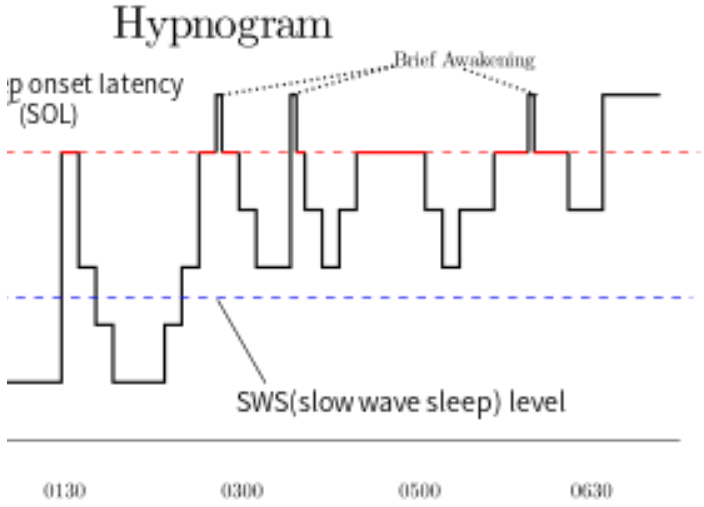
Stages of sleep

vity: A smooth electrical activity of 8–12 Hz recorded from the brain; generally
l with a state of relaxation.

ity: Irregular electrical activity of 13–30 Hz recorded from the brain; generally
l with a state of arousal.

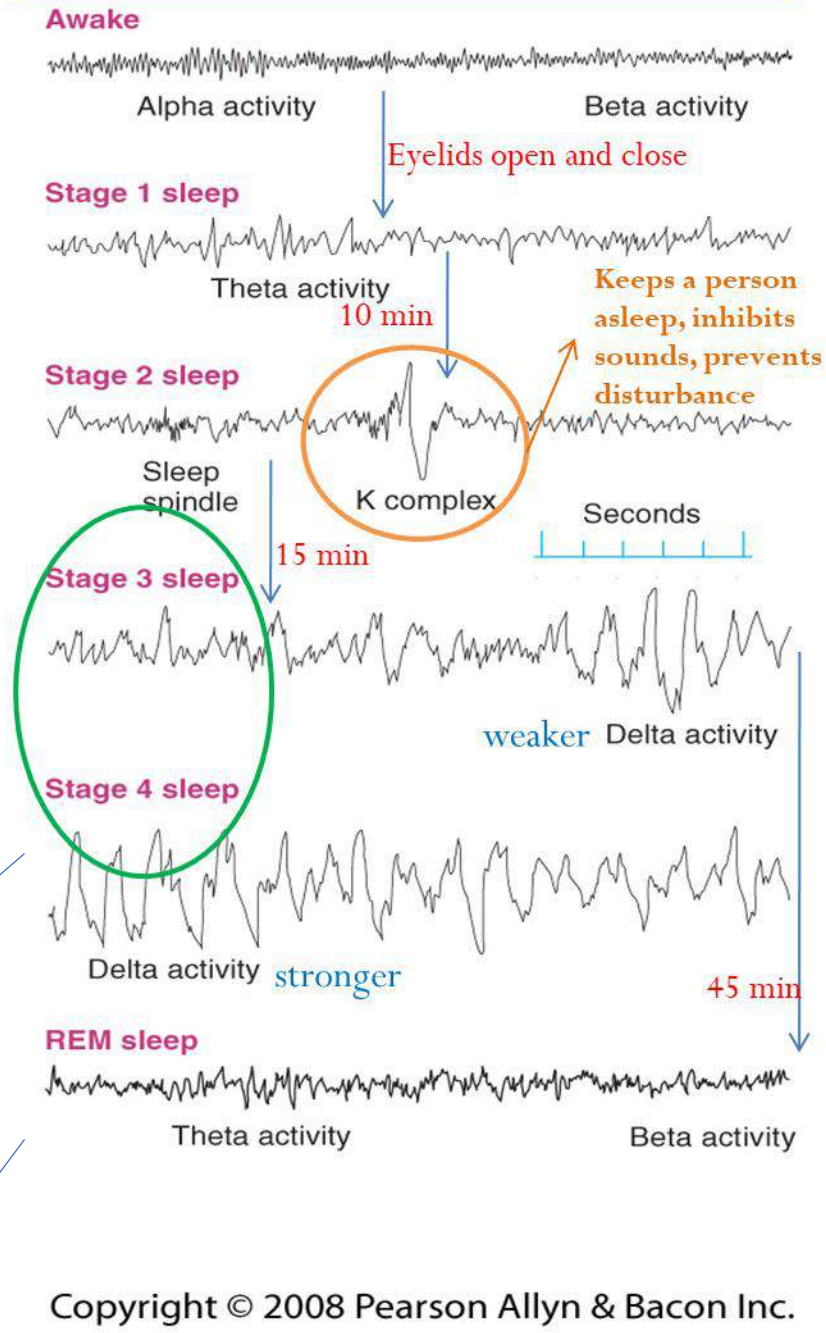
vity: EEG activity of 3.5-7.5 Hz that occurs intermittently during early stages of
and REM sleep, a transition between sleep and wakefulness.

vity: Regular, synchronous electrical activity of less than 4 Hz recorded from
occurs during the deepest stages of slow-wave sleep.



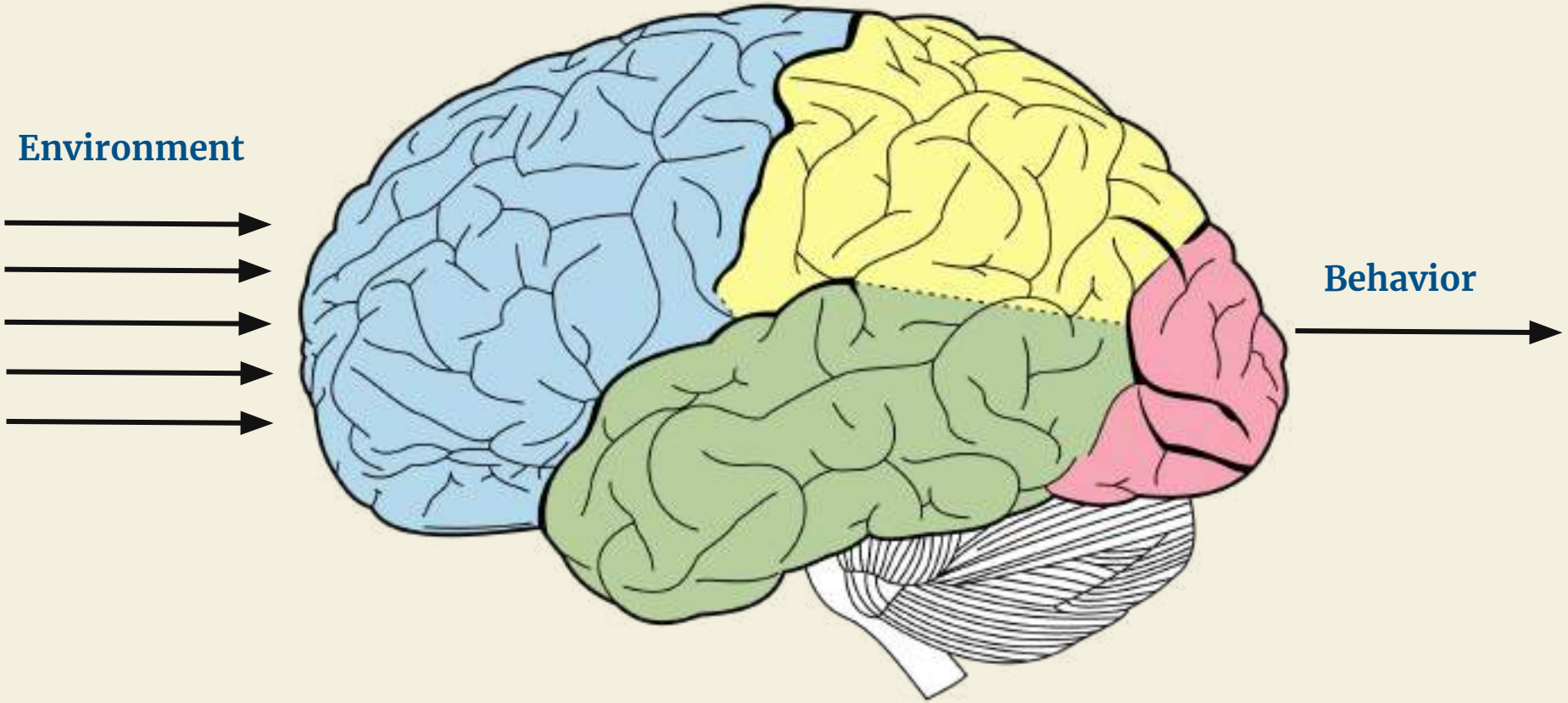
Slow wave Sleep: Non-REM sleep, characterized by synchronized delta activity during deeper stages.

REM sleep: A period of desynchronized EEG activity during sleep, at which time dreaming, rapid eye movements, and muscular paralysis occur.



Experiences and memory

Cognitive Neuroscience

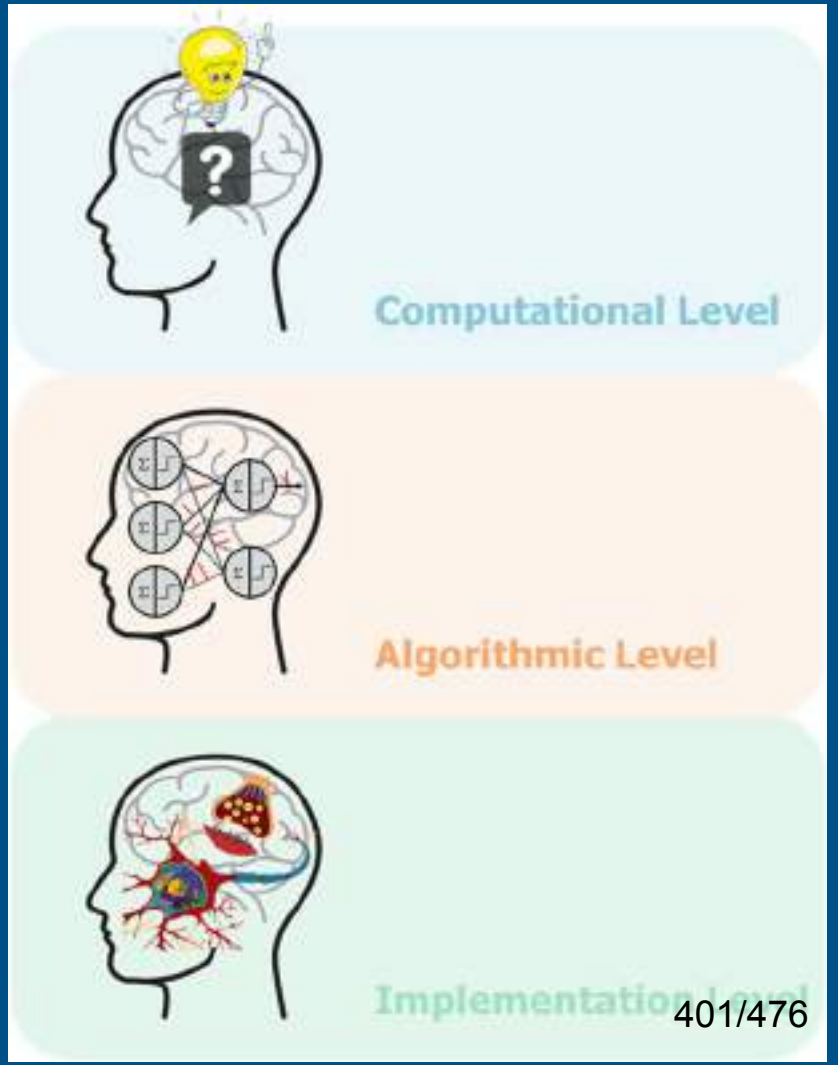

Environment
Behavior

Three levels of analysis

Why do the things work the way they do? What is the goal of the computation

What process does this computation follow? Representation and transformation

Where is this happening? Hardware



David Marr's theory of analysis

What is memory?

Ability to encode, store and retrieve information











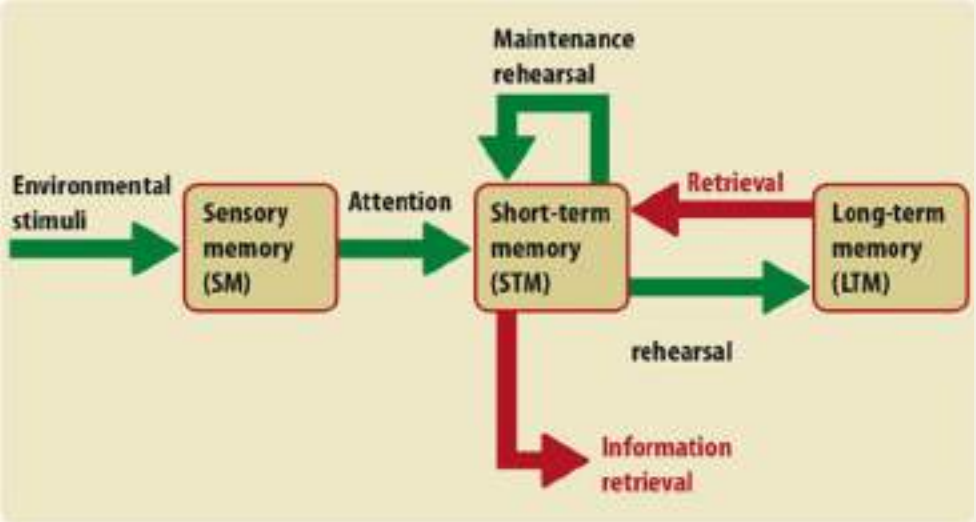

Types of memory

Sensory memory: around half second for visual info, 3-4 secs for auditory info

Short term memory: information we are currently aware of or thinking about. 20-30 seconds. Also called **working memory**

Long term memory: very large storage, can last a lifetime

Atkinson and Shiffrin's model (1968)



What processes or factors at encoding influence later memory performance?

- Attention
- Level of processing
- Salience
- Distinctive color
- Emotional arousal
- Organization
- Familiarity

We experience events that are way more dynamic and continuous than the “objects” you saw in the earlier demonstration. What might be happening in our brains that enable us to later remember these experiences as distinct episodes?

Event segmentation

- Ability to parse continuous experience into discrete events
- The demarcations that help distinguish one event from another is an event boundary
- Boundaries are hierarchically nested - fine and coarse boundaries

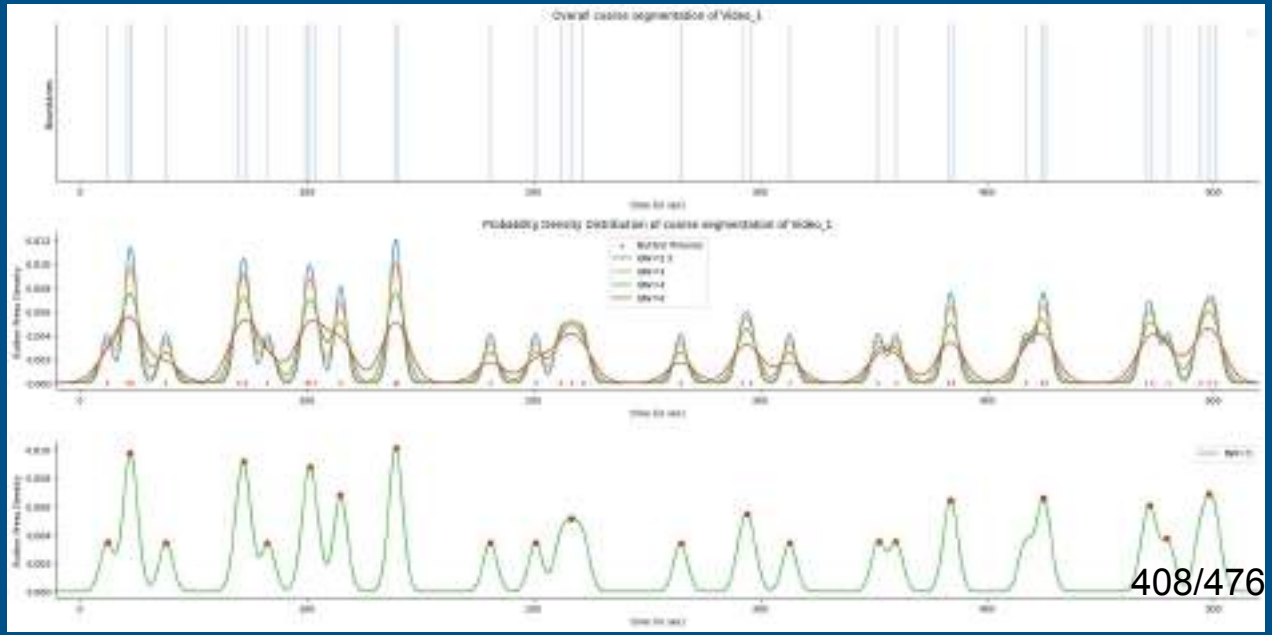
https://www.youtube.com/watch?v=jkKWwHs1Gq8

Now that we annotated.....

Segmentation agreement is computed across all individuals in a group

Basis for the norm

As close as ground truth

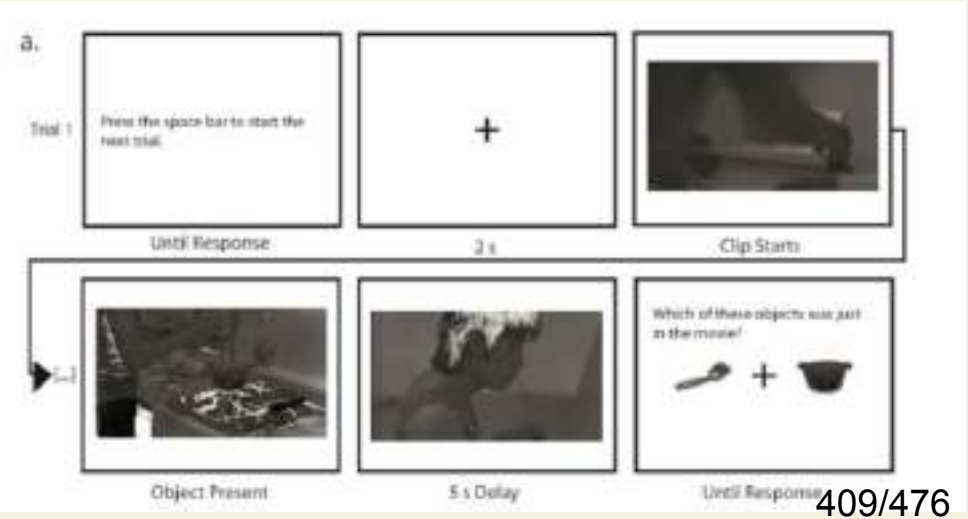


Consequences of segmentation on memory

Recognition memory

- Enhanced for items that appear close to boundary

  Boundary objects > non-boundary objects



Swallow et al (2009)

Memory recall test

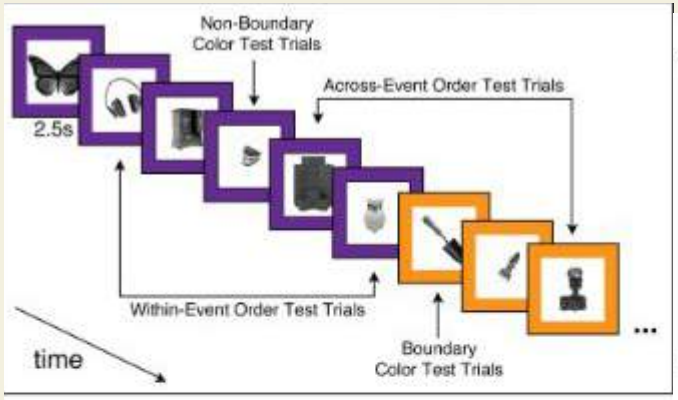
- Higher scores on recall when segmentation was closer to norm, which means identifying boundaries leads to better recall

Sargent et al (2013)

Associative memory test

- Better at for boundary items than items that come from within events

Heusser et al (2018)

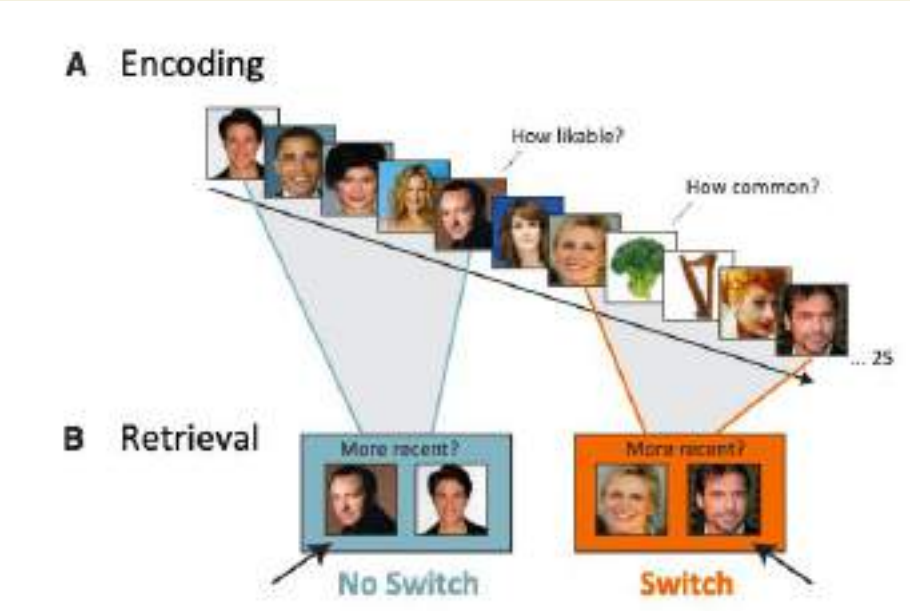


Temporal order memory task

- Recency discrimination task
- Better for within events

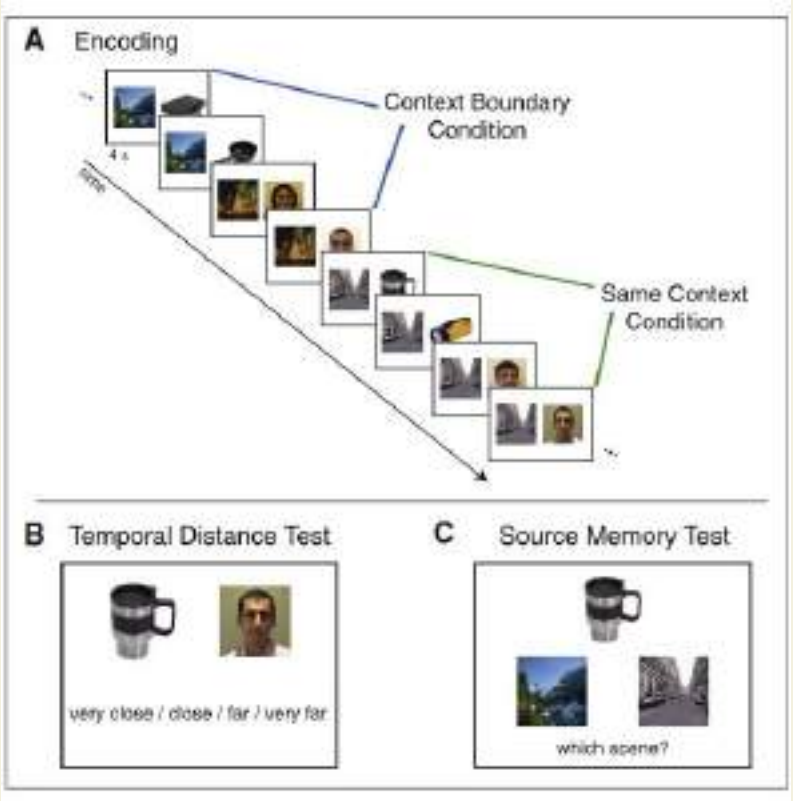
  And disrupted across boundaries

Dubrow and Davachi (2014)



Temporal proximity judgment task

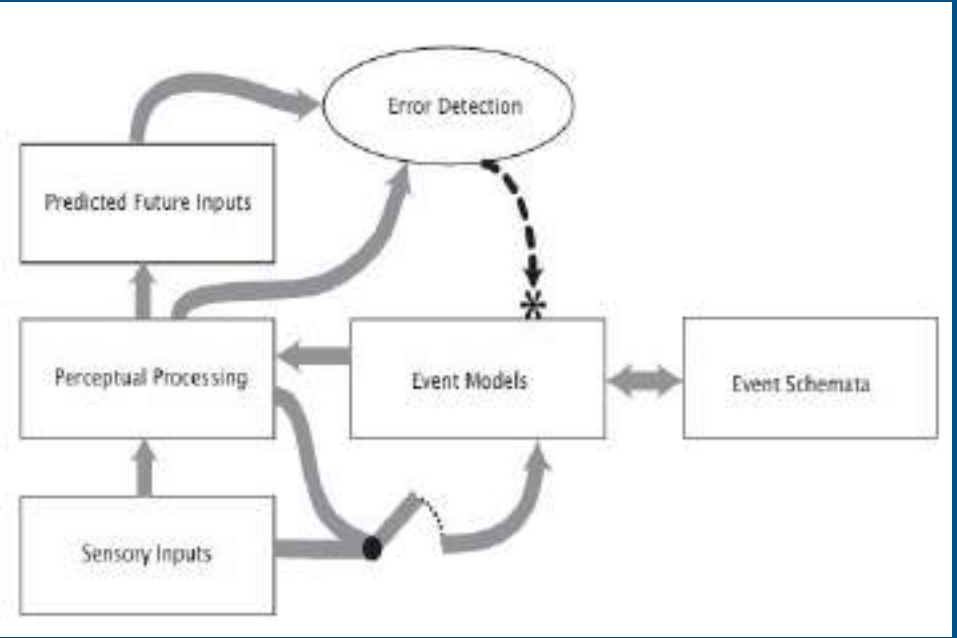
- Within event the closeness in proximity was accurately reported
- Items spanning a boundary are rated to have occurred further apart.



Ezzyat and Davachi, (2014)

Event segmentation theory

- A prediction error account of event segmentation
- Prior experience to form models of the world
- Event models - current, help predict upcoming changes
- When inaccurate, prediction errors occur



Examples

(Zacks, et al., 2007)

Context stability account

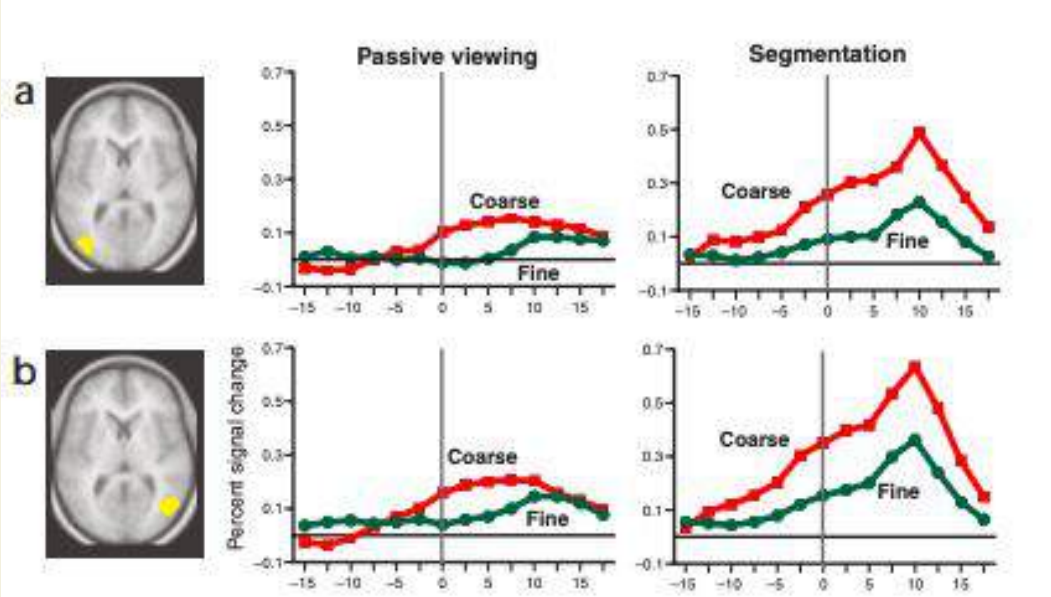
- Prediction error may not account for everything
- Contextual stability matters
- Fluctuations in contexts such as time, space, goal states, stimulus categories, background info and even internal states act like context

Clewett & Davachi (2017)

Is event segmentation automatic?

- Zacks et al., (2001)
- Evidence from fMRI study
- Passive vs active segmentation
- MT complex and FEF
- Brain processes correlated with event segmentation are a normal part of ongoing perception

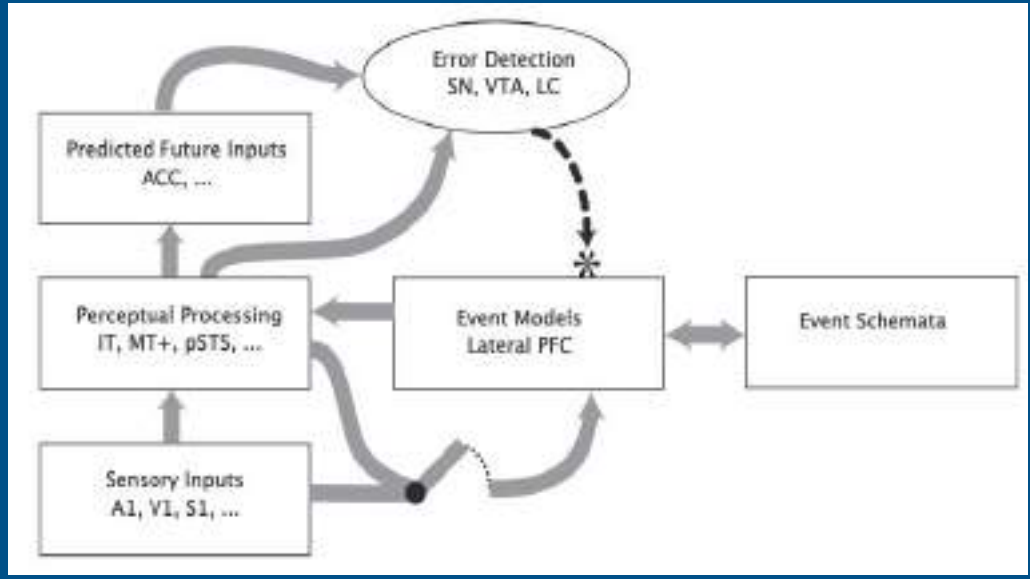
Overall segmentation leads to better memory



Time to link

Remember event models?

- Multimodal in nature
- Influenced by a combination of top-down and bottom-up processing.
- Instantiated in working memory
- Refreshed when predictions are not good anymore.



BUT where is the evidence?

Neural evidence

1. Activity in the PFC, MTL cortex, and ventral striatum showed fluctuations in the fMRI BOLD response that mirrored the event structure of a narrative as it unfolded (Ezzyat & Davachi, 2011). Decreased at event boundaries.

2. Greater activation in the mid hippocampus and vlPFC was observed for boundary items that were later serially recalled. Within-event serial recall was associated with stronger connectivity between the hippocampus and vmPFC (Dubrow & Davachi, 2016).

3. Segmentation agreement was significantly impaired in patients with lesions in vmPFC, dlPFC, RSP and the impairments were larger for coarse than for fine grain segmentation (Zacks. 2016).

Brodmann area 6
MT complex
FEF
posterior superior temporal sulcus (pSTS
MT+
hippocampus
posterior medial network (PMN)
posterior hippocampus (pHPC)
angular gyrus
posterior medial cortex(PMC)
parahippocmapal cortex
medial prefrontal cortex
middle temporal gyrus
hippocampus

What factors could affect segmentation?

- Age?
- Expertise?
- Familiarity?

Any questions?

EMOTIONS

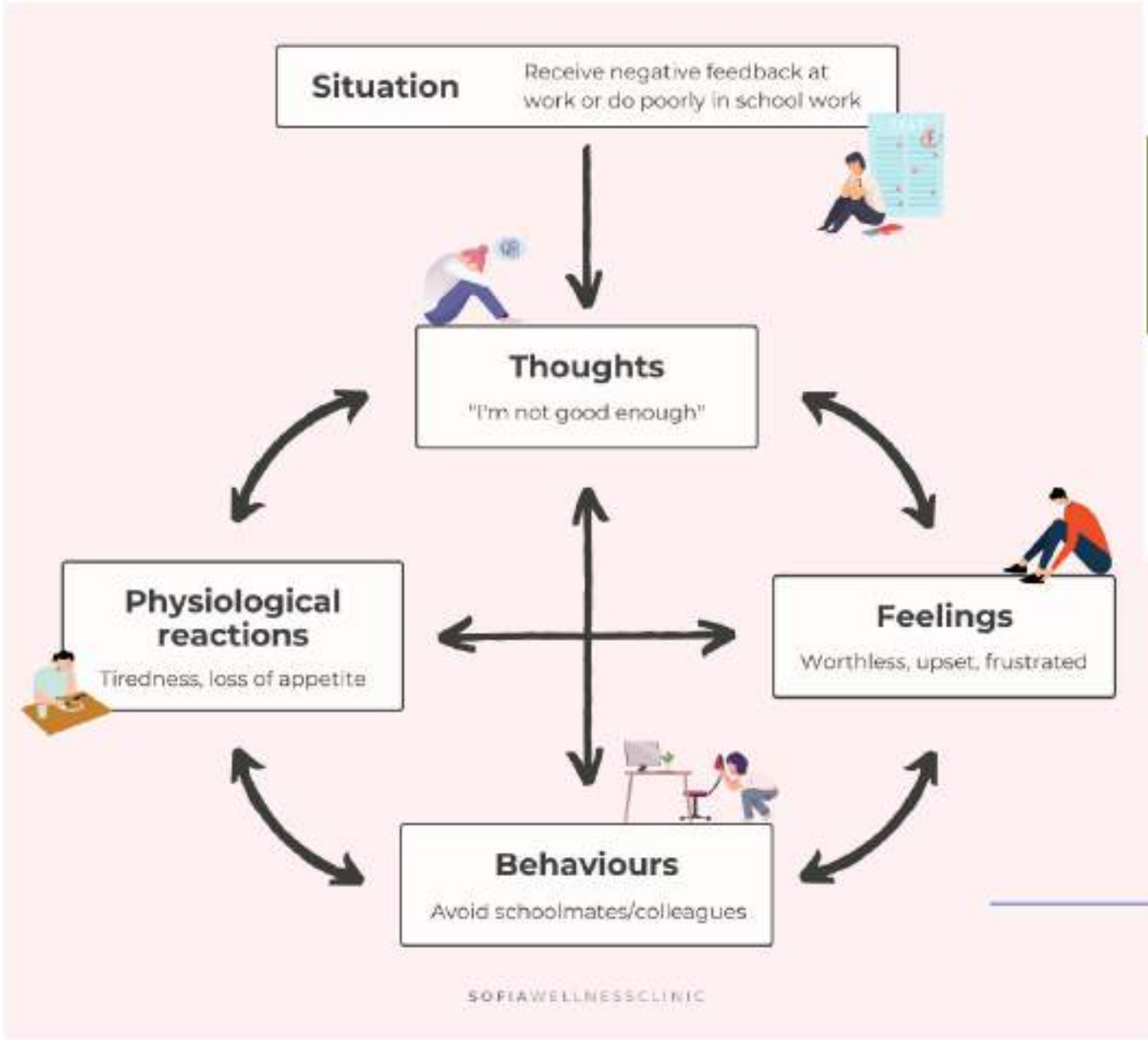
LET'S TALK EMOTIONS

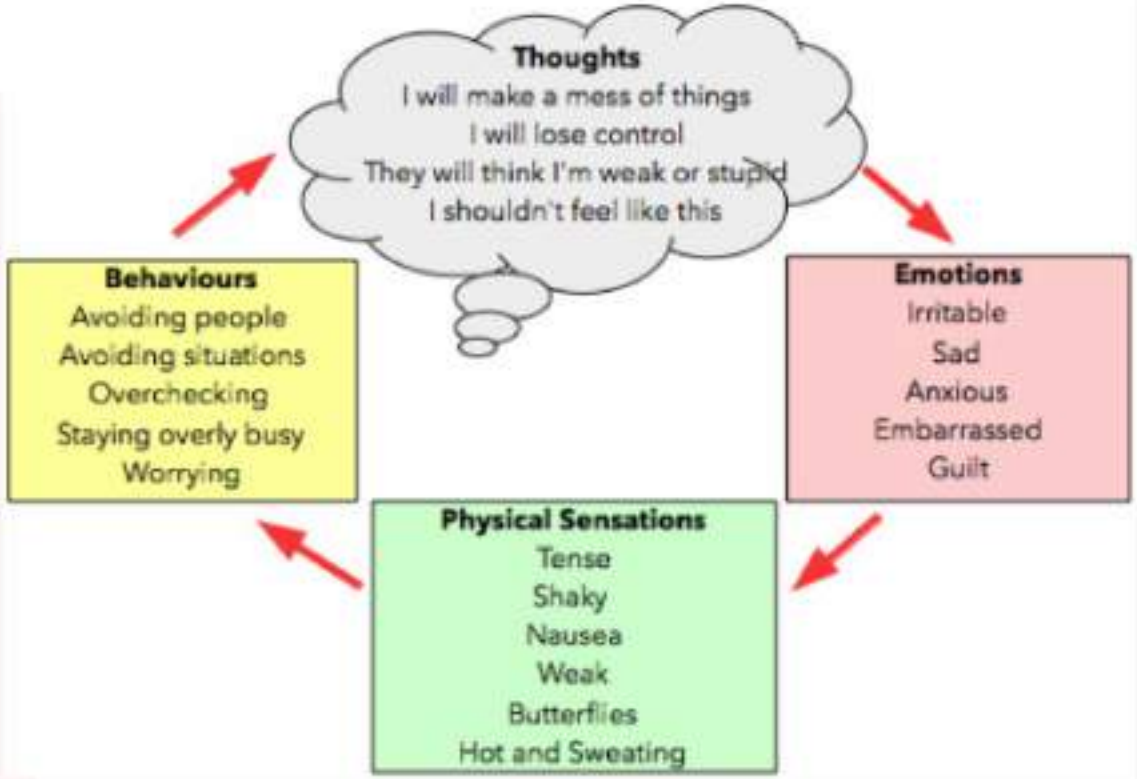
- What is an emotion
- What purpose do emotions serve?
- Are emotions Universal?

(Using book Morgan and King – Introduction to psychology for content of above mentioned topics)

RECOGNIZE THE EMOTIONS

- How do we recognize emotions
- Can we measure emotions?





Another way to look at the same situation?

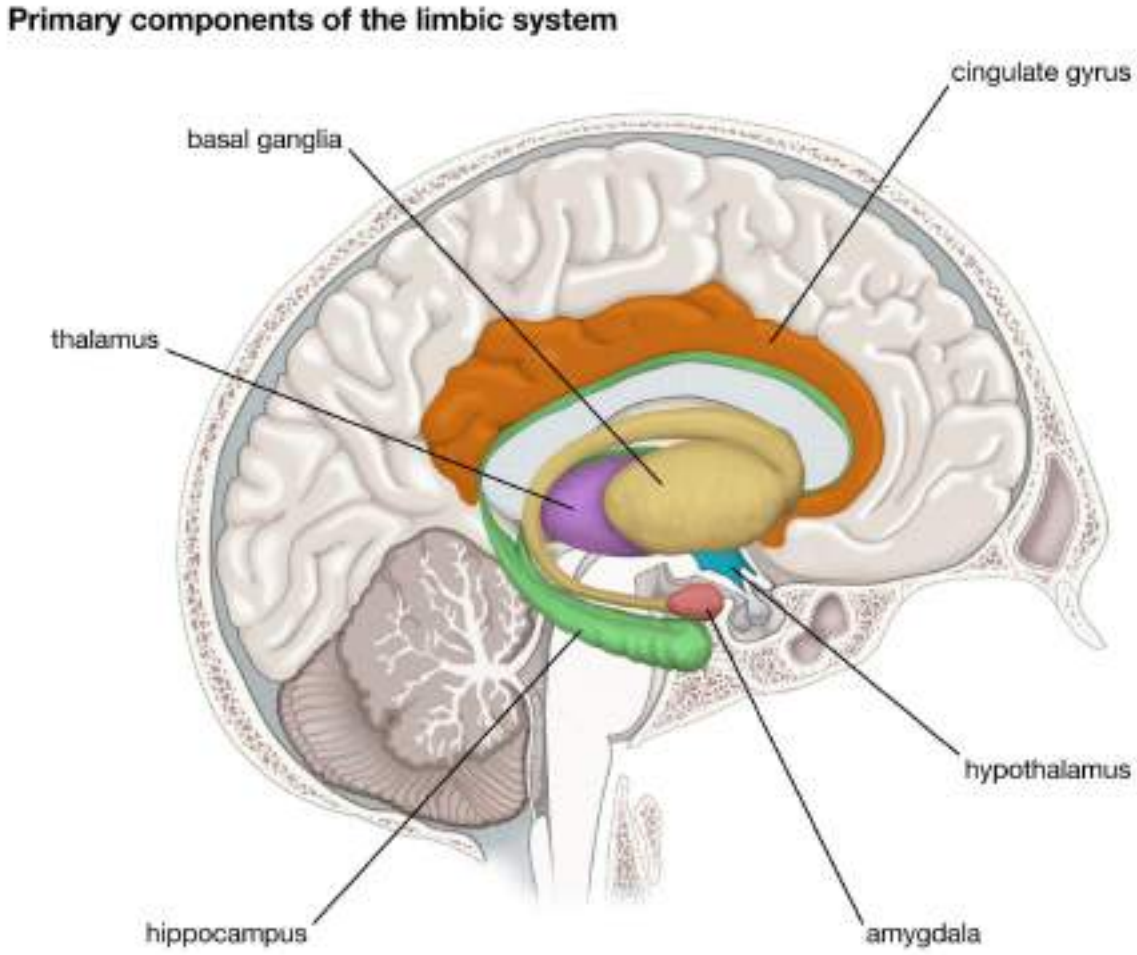
Emotion	Examples of Physiological Response (What a person might feel in their body)	Examples of Behavioral Expressions (What a person might notice in their behavior)
Joy	Inner calm, quiet confidence, dilated pupils, flushed skin, butterflies in the stomach	Smiling, relaxed stance, upbeat tone of voice, exuberance
Sadness	Ruminations, chest ache, listlessness, insomnia, deficient or excessive appetite	Crying, fatigue, withdrawn, detached
Fear	Rapid heartbeat, physical or internal trembling, need to fight or run, forebodings	Clenched chest, wide-open eyes, guarded stance
Anger	Elevated body temperature, sweating	Furrowed brow, heightened tone
Anticipation	Breathing at the top of the chest, tightness in the stomach, forebodings, sweating	Shaking, widened eyes
Surprise	Inability to focus, dazedness, speechlessness, disorientation	Raised brow, widened eyes, yelling, open mouth
Disgust	Need to flee, sense of revulsion, sickened	Curled lip, wrinkled nose

EMOTIONS AND THE BRAIN

The Limbic System

The **limbic system** (amygdala, hippocampus) regulates fear, anger, and pleasure.

- The **hypothalamus** connects emotions with physiological responses (e.g., heart rate).
- **The amygdala receives visual information directly from the thalamus**, allowing rapid emotional recognition before the visual cortex fully processes it.
- **Amygdala lesions impair the recognition of emotions, particularly fear.** However, individuals with amygdala damage can still **recognise emotions through tone of voice.**

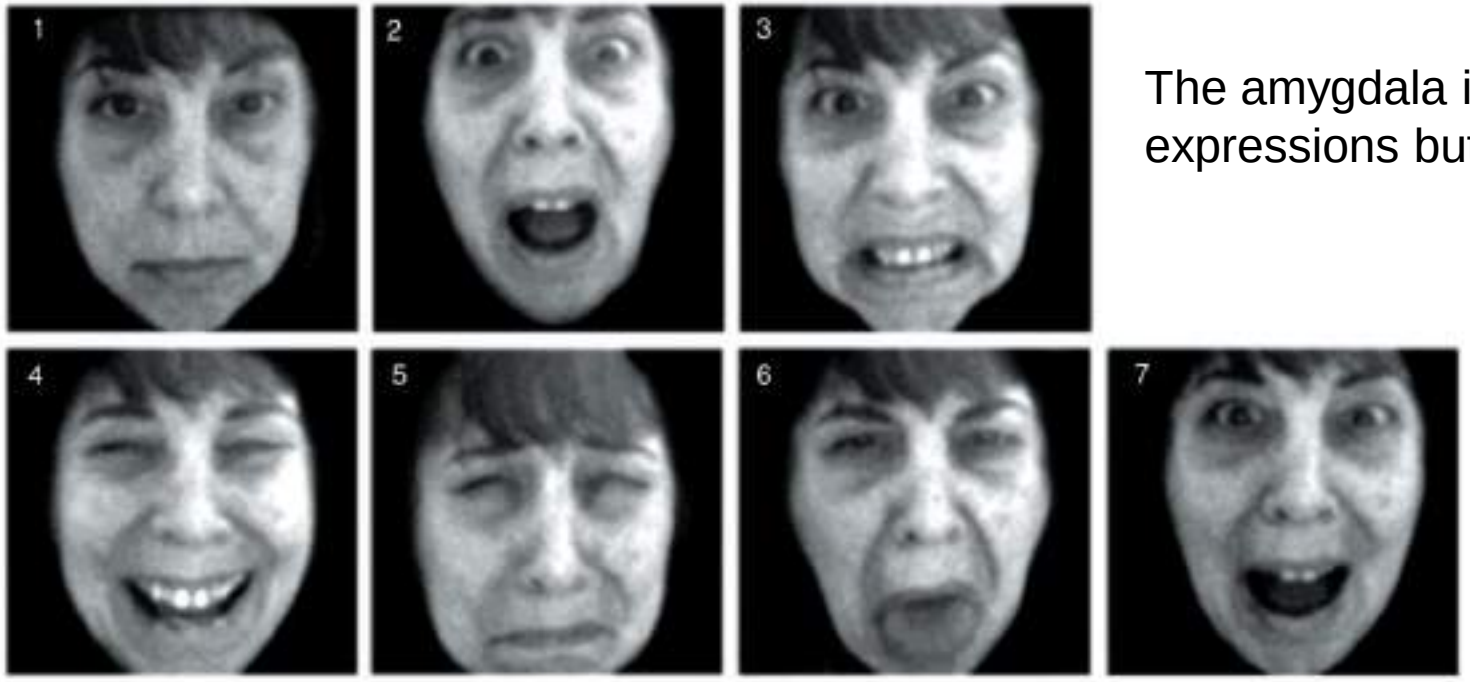


NEURAL BASIS OF EMOTION RECOGNITION

- We interpret emotions by **analysing facial expressions, tone of voice, and language.**
- **The right hemisphere** plays a dominant role in emotional comprehension, especially for facial expressions.
- Vision (Facial expressions) → Thalamus → Amygdala & Right Hemisphere
- Audition (Tone of voice) → Auditory Cortex → Right Hemisphere
- Both pathways contribute to understanding social cues and emotional states.

A woman (Patient SM) with bilateral amygdala lesion was unable to recognize expressions – not even her own. However, she had no problem producing facial expressions

Patient SM

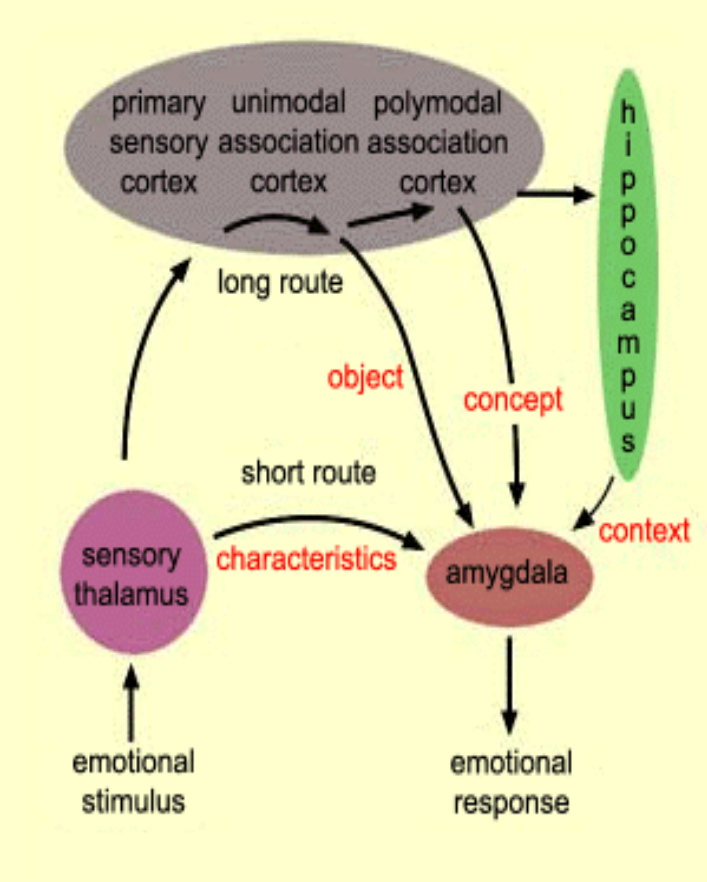


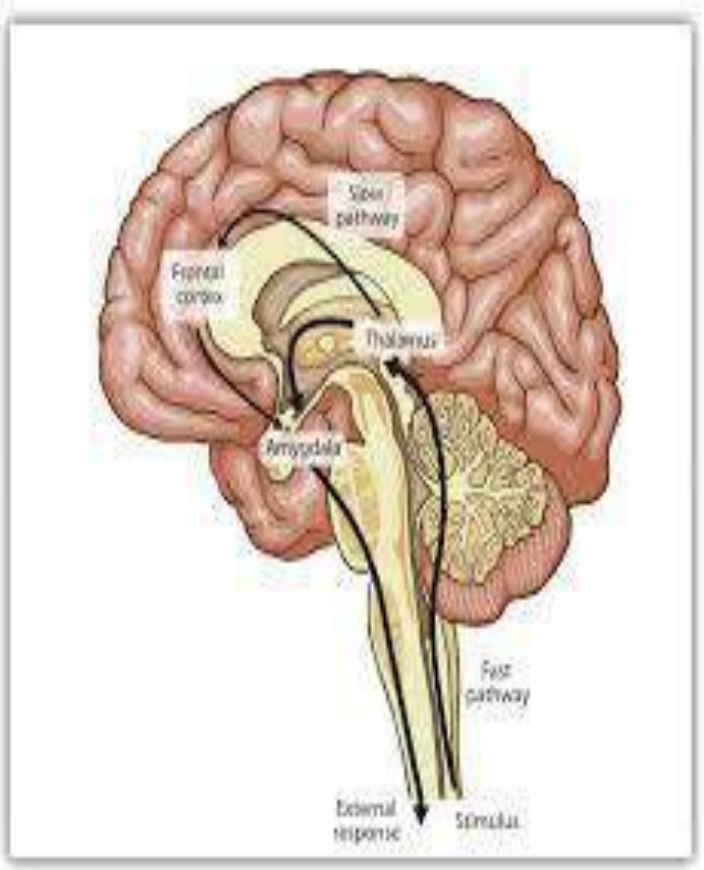
The amygdala is involved in recognizing expressions but not at producing them

In humans, patients whose amygdala had to be removed (due to seizures) showed less fear and were unable to associate fear to dangerous/threatening situations

FAST & SLOW ROUTES OF EMOTION PROCESSING

- 1. The Fast Route (Low Road) – Immediate Reaction
- 2. The Slow Route (High Road) – Thoughtful Processing





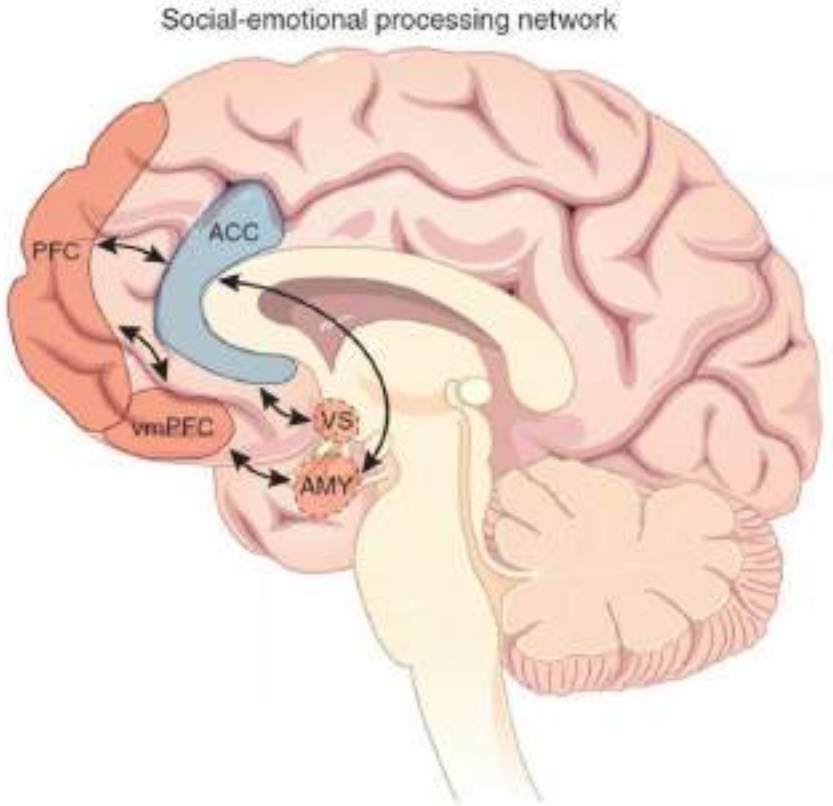
Cognitive control of emotions

Reappraisal - making a bad situation better (cognitively downregulating negative emotions)

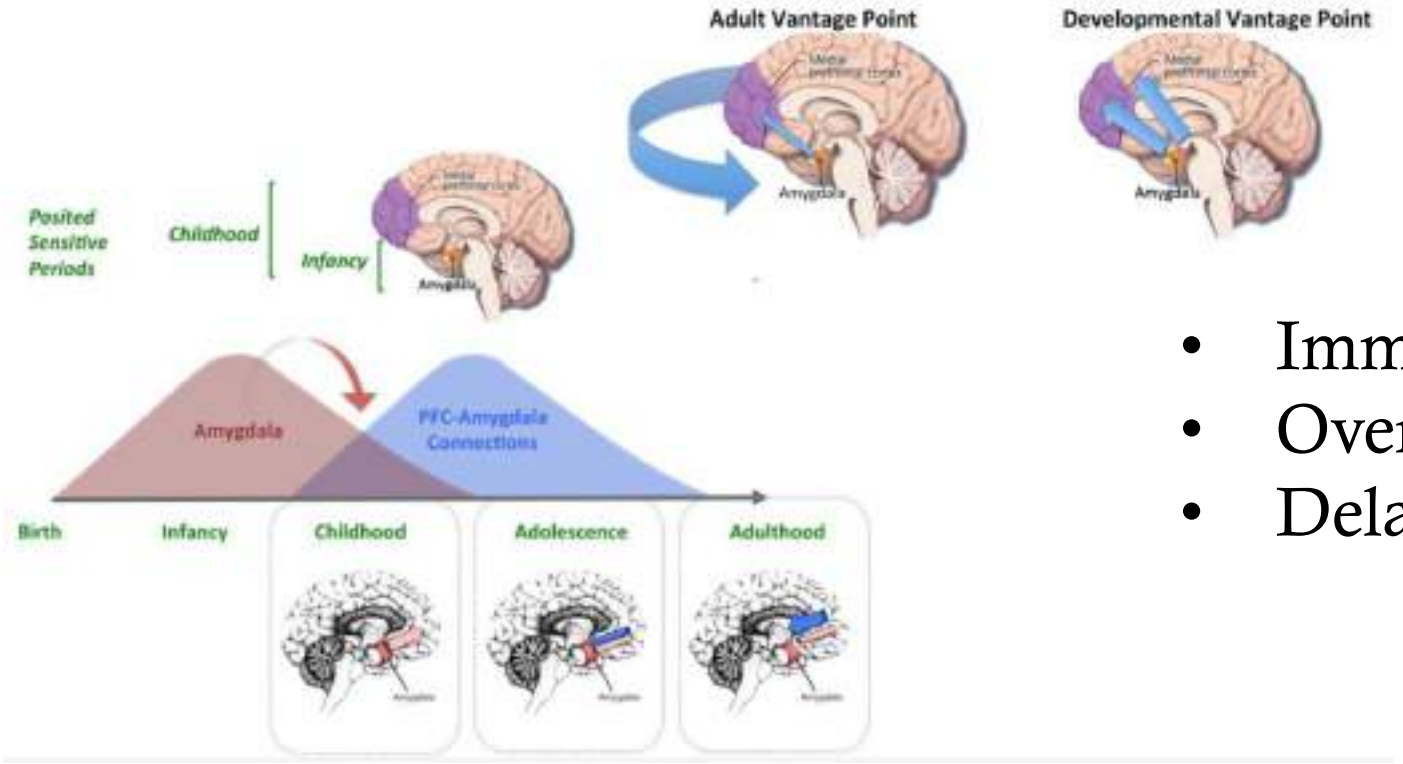
Suppression – inhibiting an emotion during an emotionally arousing situation (for instance, smiling when upset)

Negative upregulation - making a bad situation worse (cognitively upregulating negative emotions)

Not always healthy, because you have not addressed or reflected on the root cause of the problem.

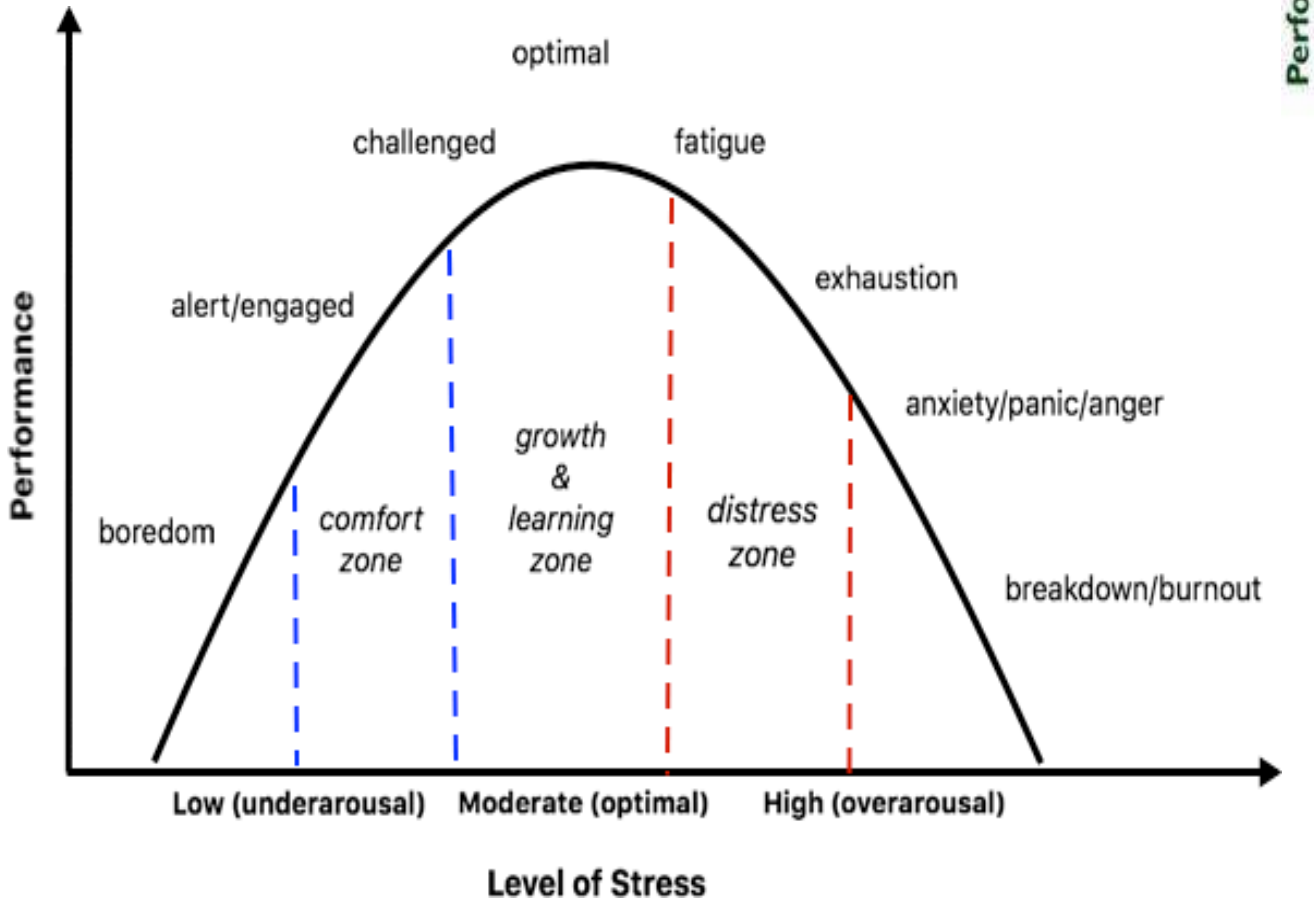


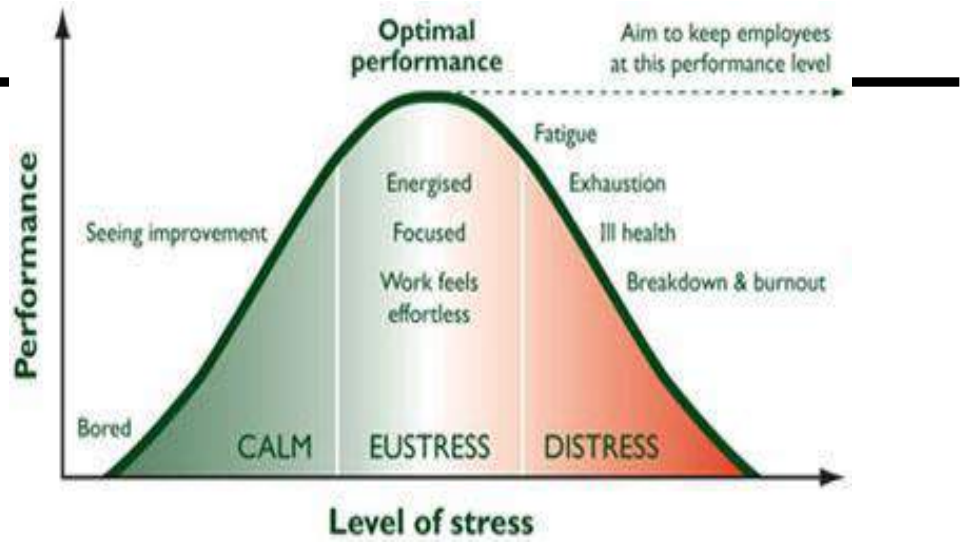
WHY ARE ADOLESCENTS MORE VULNERABLE TO EMOTIONS?



- Immature Prefrontal Cortex (PFC)
- Overactive Amygdala
- Delayed PFC-Amygdala Connectivity

What is stress?





Reticular Formation & Arousal:

- The **reticular formation (ARAS)** activates emotional states, affecting alertness and wakefulness.
- High arousal → Excitement or anxiety | Low arousal → Drowsiness or depression.

Arousal & Performance:

- **Inverted-U Hypothesis** (Yerkes-Dodson Law):

PHYSIOLOGY OF STRESS RESPONSE

Epinephrine

- nutrients stored in muscles converted into energy/glucose for strenuous activity

Norepinephrine

- Increases blood flow to the muscles by increasing heart rate and blood pressure

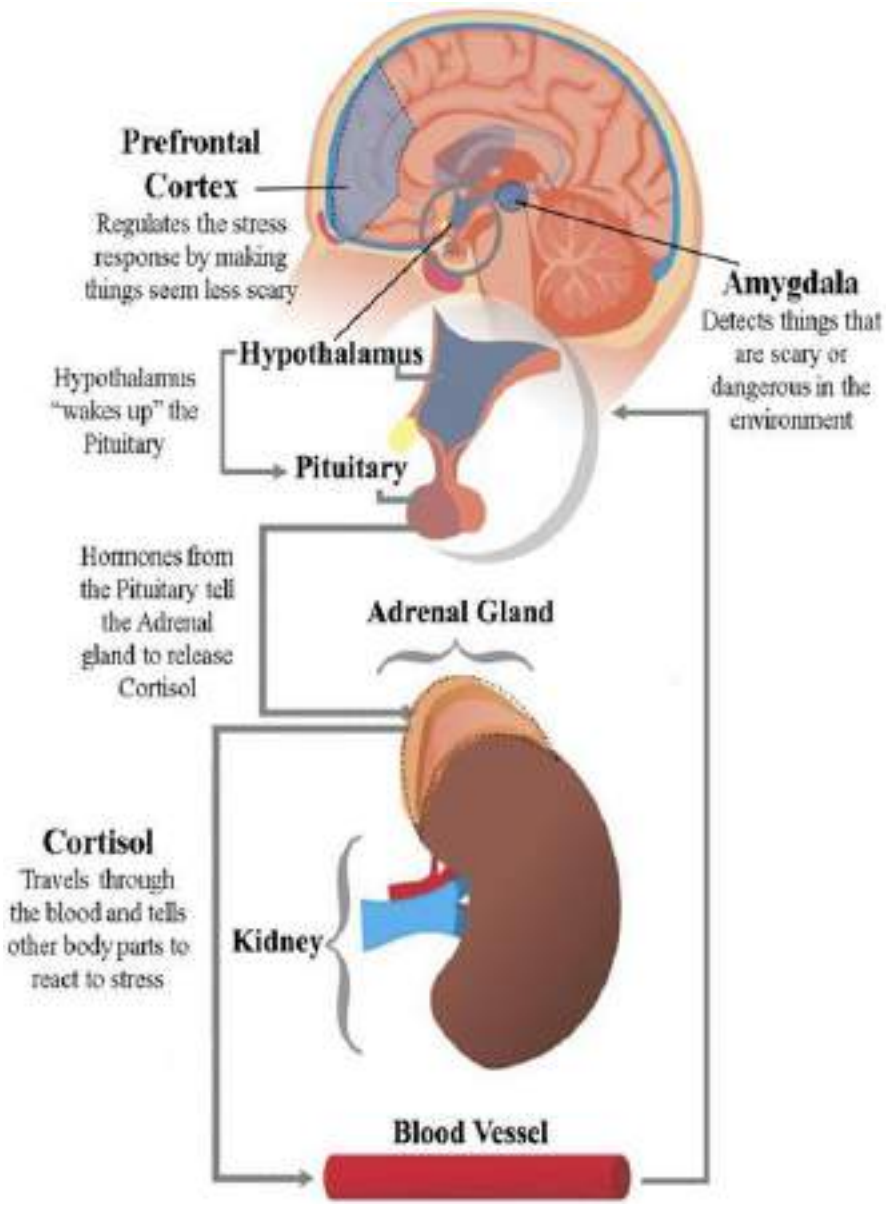
(which increases rate of cardiovascular disorders in the long term)

Cortisol *(glucocorticoid)* secreted by the adrenal gland breaks down proteins and converts it to glucose

- Convert fats into glucose
- Direct all energy to treat overcoming activity
- Results in less glucose sent to the brain

PVN (hypothalamus) ➐ CRH/CRF ➐ pituitary glands ➐ ACTH ➐ adrenal glands ➐ glucocorticoid

- ***PVN-*** *paraventricular nucleus of hypothalamus,*
- ***CRH*** *–Corticotropic Releasing Hormone (or Factor),*
- ***ACTH*** *–adrenocorticotropic hormone*



Stress & Learning

The stress-brain loop

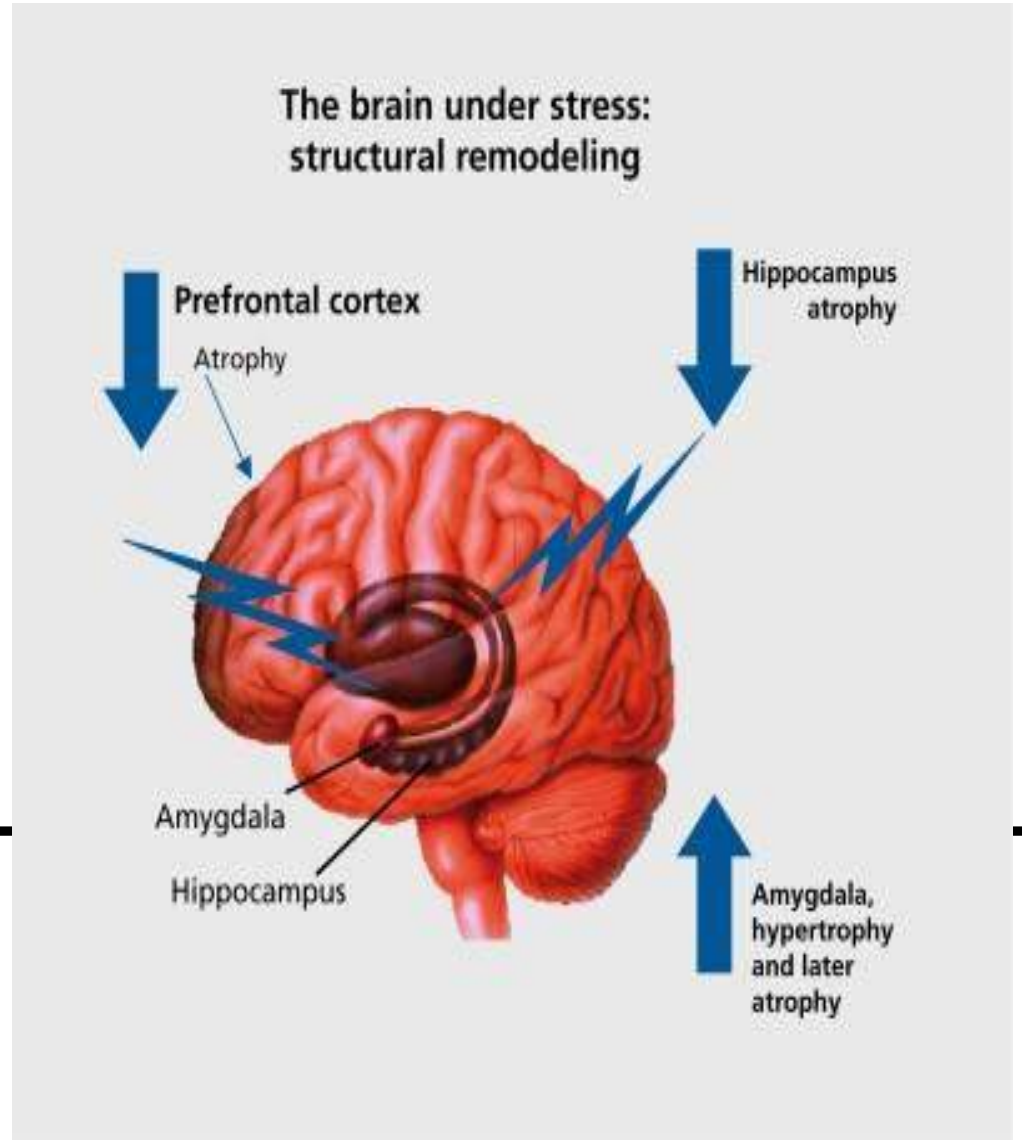
↓ Attention
↓ Perception
↓ Short-term memory
↓ Learning
↓ Word finding

Cellular changes in the hippocampus

Increases glucocorticoids

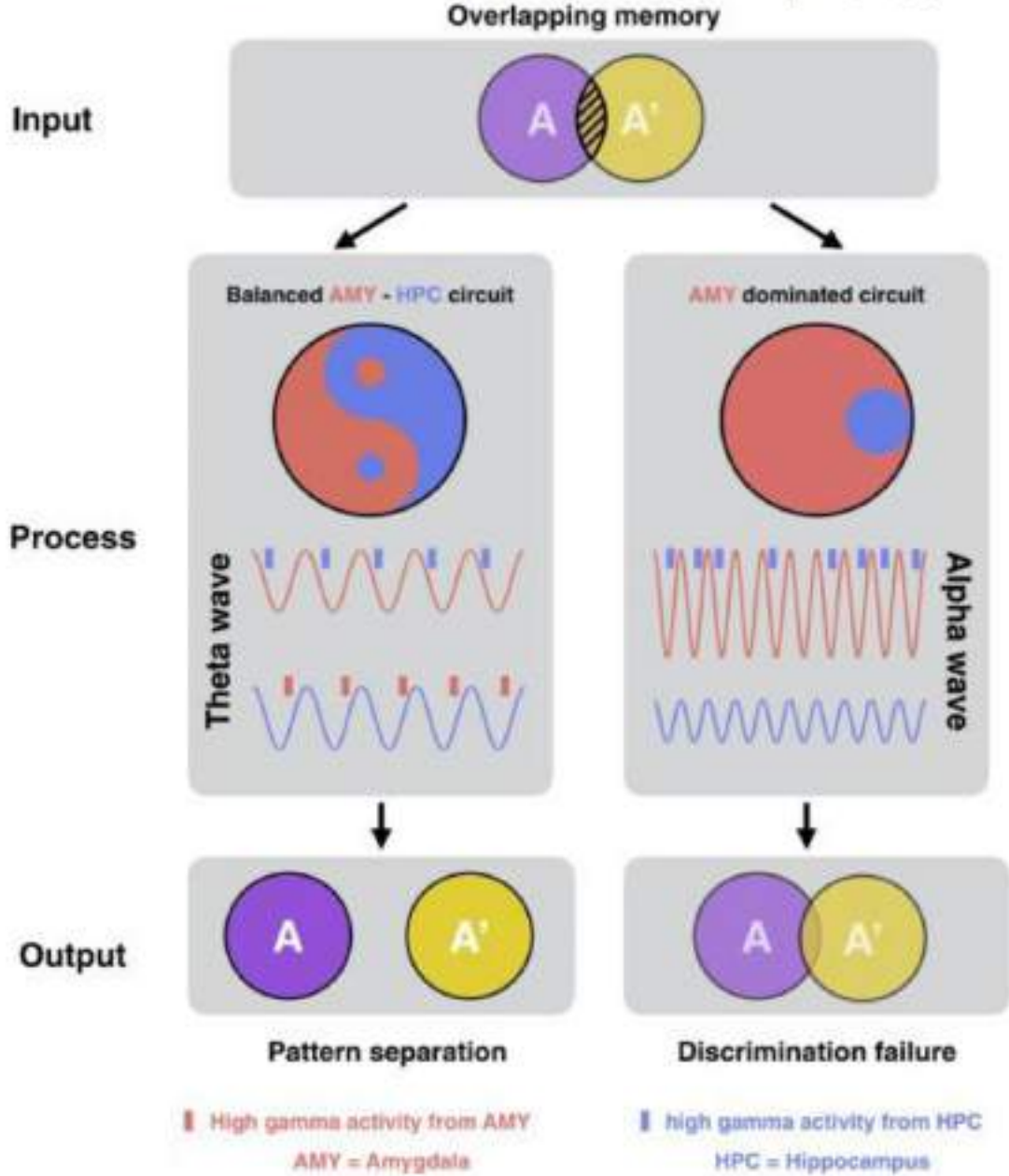
Chronic Stress
- Inadequate sleep
- Poor nutrition
- Emotional distress

Decreased regulation of cortisol



intracranial recordings in pre-surgical epilepsy patients

- Amygdala ⟷ Hippocampus (needed to remember emotional experiences)
- Bidirectional amygdala-hippocampal interactions support pattern separation (distinguish diff emotional experiences)
- Alpha synchrony disrupts mnemonic discrimination (context) and leads to overgeneralization errors
- Extreme emotional experiences (PTSD) – overgeneralization of memories/contexts



https://www.sciencedirect.com/science/article/pii/S0896627319302880

STRESS AND ANXIETY

- Can we use the words synonymously?

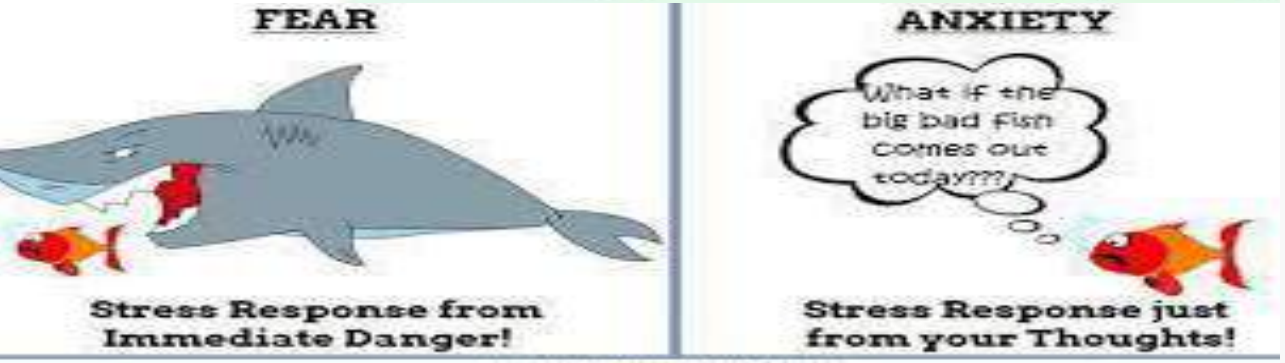
Stress

- Occurs as a response to a real threat
- It is the bodily response to a threat
- Goes away once the threat has passed
- Can have positive outcomes like motivation

Anxiety

- Can occur because of not very possible threats
- It is a feeling depicting your reaction to stress
- Continues even after the threat has passed
- Has negative outcomes and complicates life

MED vidi



Afferent and efferent connections

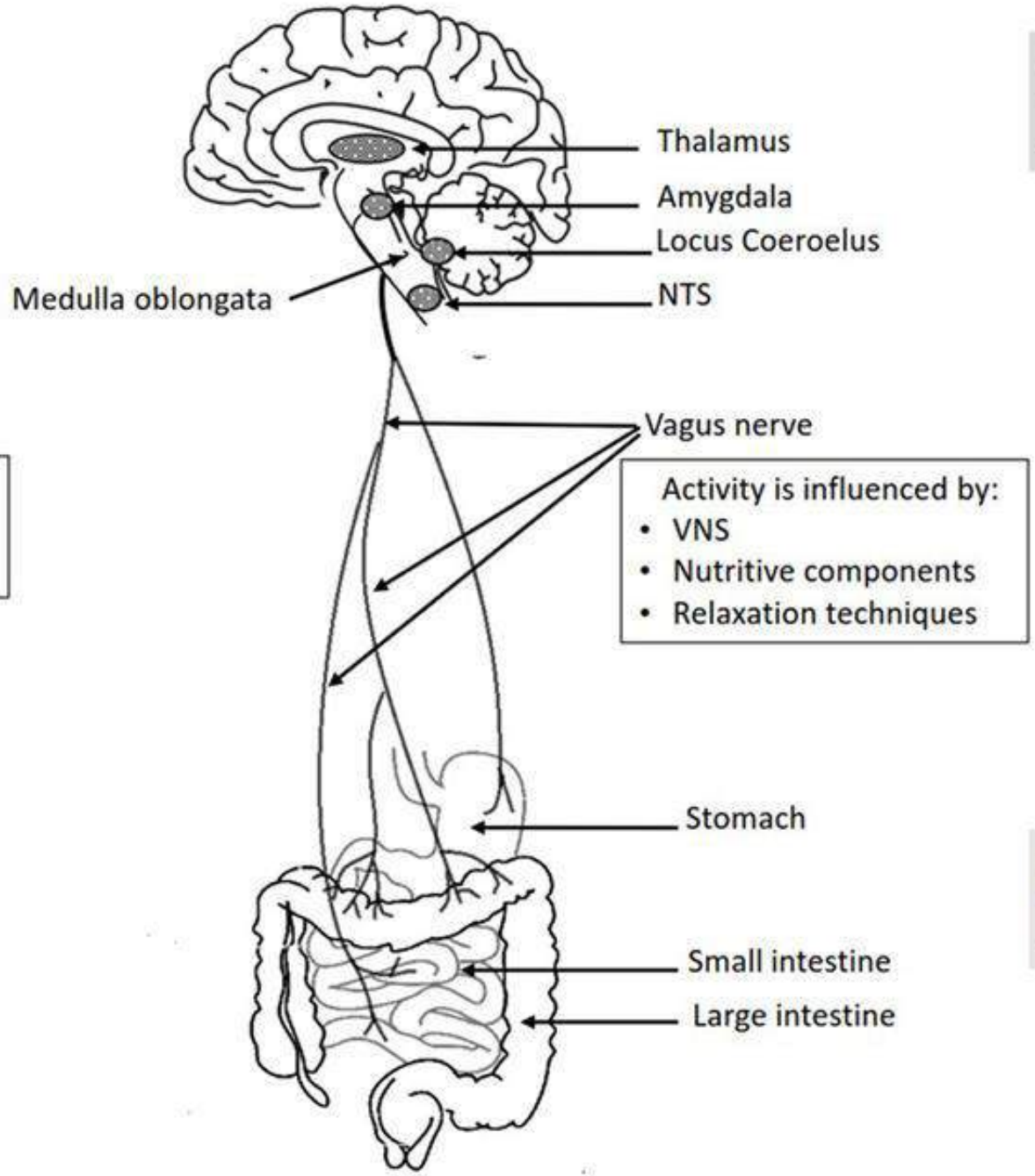
90% of vagus nerve fibers

- Imflammation
- Satiety (Hunger)
- Satiation (Fullness)
- Energy Metabolism

- Secretion of gastric acid and digestive enzymes
- Gastric capacity

10% of vagus nerve fibers

Anatomy



Disorders

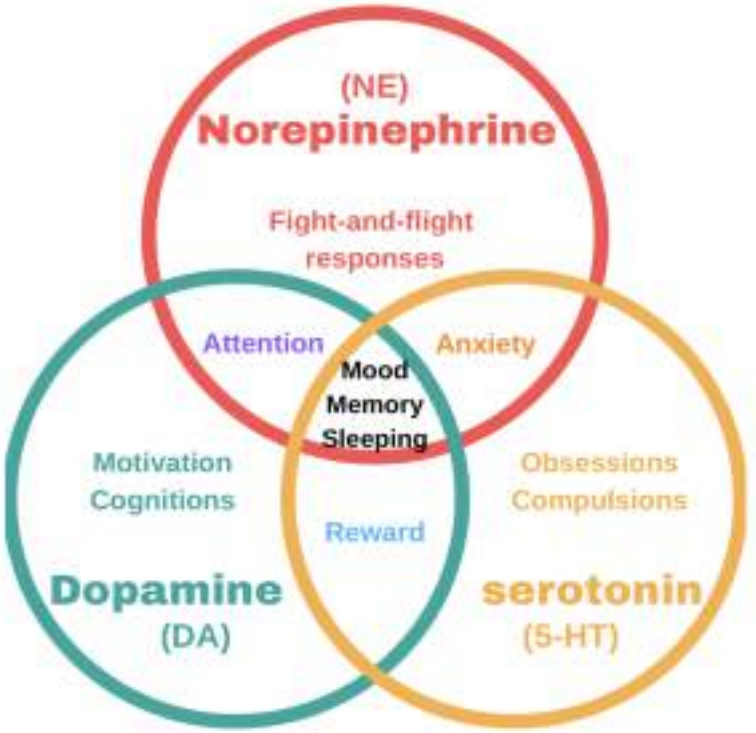
Psychiatric disorders
- Major depression
- PTSD

Inflammatory GI Disorders
- Ulcerative Colitis
- Crohn`s Desease

- What is the difference between mood and emotion?

NEUROTRANSMITTERS IN EMOTION & MOOD REGULATION

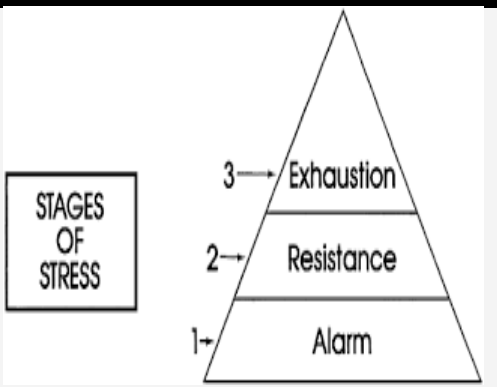
Neurotransmitter	Function in Emotion & Mood	Imbalance Effects
Serotonin (5-HT)	Regulates mood, anxiety, and emotional stability.	Low levels → Depression, anxiety, mood swings.
Dopamine (DA)	Reward, motivation, pleasure, and reinforcement learning.	Low levels → Anhedonia, lack of motivation (linked to depression). High levels → Euphoria, addiction.
Norepinephrine (NE)	Stress response, alertness, and arousal.	Low levels → Fatigue, lack of focus (seen in depression). High levels → Hyperarousal, anxiety.
GABA (Gamma-Aminobutyric Acid)	Inhibitory neurotransmitter, reduces excessive neural activity, promotes calmness.	Low levels → Anxiety, overthinking, panic disorders.
Glutamate	Excitatory neurotransmitter, essential for learning, memory, and emotional processing.	Excess → Neurotoxicity (linked to bipolar disorder, schizophrenia).
Endorphins	Natural painkillers, promote pleasure and stress relief.	Low levels → Increased pain sensitivity, emotional distress.
Oxytocin	Social bonding, trust, and empathy.	Low levels → Social withdrawal, difficulty forming relationships.



Key Differences Between Moods & Emotions

Aspect	Moods 🎭 (Longer-lasting) 🟦	Emotions ⚡ (Short-lived) 🟨
🕒 **Duration**	Lasts **minutes to hours** (sometimes days).	Lasts **seconds to minutes**.
⚡ **Provocation**	**Lowers the threshold** for experiencing emotions from the same family.	Triggered by a **specific event** and felt in isolation.
🎛️ **Modulation**	**Harder to regulate** because the cause is often unclear.	**Easier to regulate** if it's a single emotional reaction.
😶 **Expression**	No **distinct** nonverbal cues—may appear disengaged.	Has **universal facial expressions** (e.g., smiling for joy, frowning for sadness).
🔍 **Awareness**	Difficult to **identify exact triggers** causing the mood.	The **cause of the emotion is clear** and easily identifiable.

The 3 Phases of Stress



REST & DIGEST

ALARM PHASE

"Fight or flight response"
Effects last ~1 hour

- Heart races to give oxygen to the muscles and brain.
- The nervous system goes on high alert.
- All other body functions shut down.

RESISTANCE PHASE

- Cortisol queues brain to be on the look-out for additional threats.
- Parasympathetic system starts to return most your body to its pre-stress levels.
- Diverts some resources for next threat.
- Signs you're in this phase: irritability, frustration, and lack of focus.

RECOVERY

EXHAUSTION PHASE

"Burnout"

- Depleted bodily resources
- Decreased stress tolerance

YOU FEEL:

- Burned out
- Drained mentally, physically and emotionally
- Hopelessness
- Anxiety
- Depression
- High blood pressure
- Weakened immune system
- Chronic illness sets in

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- Chronic stress can lead to a range of disorders…..

EATING DISORDERS

Anorexia nervosa: (anorexia –"*loss of appetite*")

- A disorder that most frequently afflicts young women;
- exaggerated concern with being overweight that leads to excessive dieting and often compulsive exercising;
- can lead to starvation.

Bulimia nervosa:

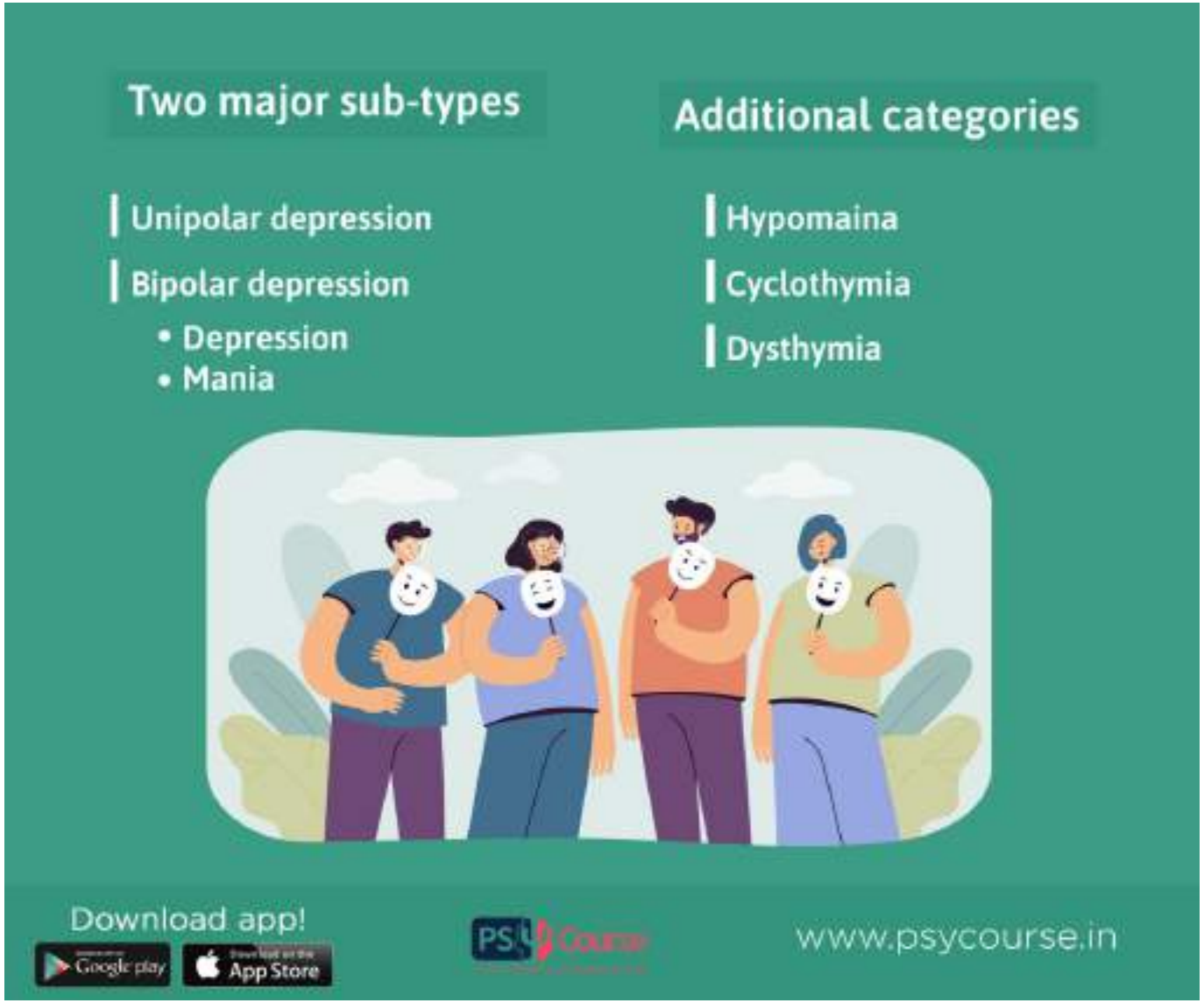
- Bouts of excessive hunger and eating; often followed by forced vomiting or purging with laxatives; sometimes seen in people with anorexia nervosa, to maintain a low body weight.

- Women are more likely to develop this disorder than men
- Possible causes:
    1. Excessive exercise or fasting
    2. OCD
    3. Social emphasis on slim women in industrialized societies
    4. Heredity or premature birth

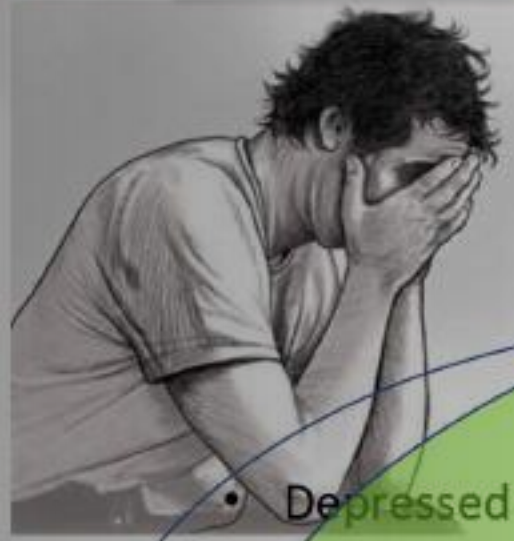
MOOD DISORDERS

- Affect –*" feelings or emotions"*
- Affect disorders are also known as *mood* disorders, characterized by disordered feelings

•***Extreme elation (mania)*** or ***extreme despair (depression)*** are common experiences of people with affect disorder when affect and reality are not interconnected.



Symptoms of Unipolar & Bipolar Disorders



Unipolar Depression

- Depressed mood all day
- Insomnia or hypersomnia
- Loss of interest in work and pleasurable activities
- Fatigue or loss of energy / headaches or backaches
- Retarded speech (severe cases)
- Inability to concentrate, indecisiveness, forgetful
- Indigestion/constipation/reduced appetite
- Feelings of worthlessness
- Suicidal thoughts

Bipolar Disorder

Manic State

- Euphoria/delusions/overexcited
- Decreased need for sleep
- Excess of pleasurable activities
- Energetic & excited
- Excessive talking
- Distractible, Incoherent, Irritable
- Inflated self esteem, grandiosity
- Unrealistic belief in abilities,
- High risk taking
- Over-confidence

Difference between sadness/feeling depressed and depression?

PTSD

THE SIGNS AND SYMPTOMS OF PTSD

- **Nightmares**
  Distressing dreams replaying the trauma.
- **Flashbacks**
  Intense re-experiencing of the traumatic event.
- **Emotional Numbness**
  Difficulty feeling emotions.
- **Avoidance**
  Steering clear of trauma-related reminders.
- **Hypervigilance**
  Heightened alertness and exaggerated reactions.
- **Sleep Issues**
  Trouble falling/staying asleep.
- **Negative Thoughts**
  Persistent negative beliefs about oneself or the world.
- **Difficulty Concentrating**
  Trouble focusing and maintaining attention.
- **Reduced Interest**
  Loss of interest in previously enjoyed activities.
- **Feelings of Hopelessness**
  Pervasive sense of despair.

WHITE LIGHT

RISK FACTORS FOR PTSD

WHITE LIGHT

1. **Previous Trauma Exposure**
   Multiple or severe past traumas increase PTSD risk by overwhelming coping mechanisms.
2. **Family History of Mental Health Disorders**
   A family history of conditions like anxiety or depression raises the likelihood of developing PTSD.
3. **Severity and Type of Trauma**
   Severe, direct, or high-intensity traumatic events have a higher risk of leading to PTSD.
4. **Lack of Social Support**
   Insufficient support from friends or family after a trauma can increase PTSD risk.
5. **Pre-existing Mental Health Conditions**
   Existing conditions such as anxiety or depression make individuals more vulnerable to PTSD.
6. **High Levels of Stress and Coping Style**
   Difficulty managing stress and maladaptive coping strategies contribute to PTSD development.
7. **Personal Vulnerability Factors**
   Traits like high neuroticism, poor emotional regulation, and low resilience increase susceptibility.
8. **Early Life Adversity**
   Childhood abuse, neglect, or other adverse experiences elevate the risk of PTSD later in life.

PTSD is not just about trauma exposure; cognitive processes play a major role in how trauma is encoded, interpreted, and recalled. These cognitive factors influence how people process traumatic memories and why PTSD symptoms persist.

Cognitive Factors in PTSD

1) Attentional Bias toward Threats 🚨

• People with PTSD hyper-focus on threat-related information.

• They misinterpret neutral or ambiguous situations as dangerous (e.g., loud noises → "I'm under attack").

• Example: A combat veteran may overreact to fireworks, perceiving them as gunfire.

2) Impaired Memory Processing 🧠

• Trauma memories in PTSD are often fragmented, disorganized, and intrusive.

• The hippocampus (memory center) has reduced activity, making it hard to differentiate past from present.

• Example: A PTSD patient may suddenly relive a traumatic event as if it is happening right now (flashbacks).

3) Overgeneralisation of Fear 😨

• The amygdala (fear center) becomes hyperactive, causing strong emotional reactions to non-threatening stimuli.

• Fear responses spread to similar but harmless situations.

• Example: Someone who survived a car accident may feel panic even in slow traffic, not just in high-speed situations.

4) Negative Cognitive Bias & Self-Blame 😞

• PTSD patients often have distorted thinking patterns such as:

• Self-blame: “I could have done something to prevent it.”

• Guilt: “It was my fault.”

• Helplessness: “I will never be safe again.”

• This reinforces avoidance behaviors and makes recovery difficult.

5) Avoidance & Thought Suppression 🚫

• PTSD patients avoid thinking about, talking about, or encountering anything related to trauma.

• Suppressing thoughts backfires, causing more intrusive thoughts and flashbacks.

• Example: A sexual assault survivor avoids crowds, loud music, or even certain clothes that remind them of the trauma.

"EMOTIONS SHAPE EVERY THOUGHT, DECISION, AND INTERACTION WE HAVE. WHEN NEUROTRANSMITTERS ARE IN BALANCE, THEY ALLOW US TO EXPERIENCE JOY, MOTIVATION, AND RESILIENCE. WHEN DYSREGULATED, THEY CAN LEAD TO MOOD DISORDERS THAT AFFECT LIVES PROFOUNDLY. UNDERSTANDING THE BRAIN'S CHEMISTRY ISN'T JUST NEUROSCIENCE—IT'S THE KEY TO EMPATHY, MENTAL HEALTH, AND EFFECTIVE TREATMENT."

Neurological Conditions

Causes of Damage to Brain

- Brain tumours
- Cerebrovascular disorders
- Brain injury
- Infections of the brain – Encephalitis, Meningitis
- Seizures
- Degenerative Disorders
- Schizophrenia

Tumors

- Tumor- A mass of cells whose growth is uncontrolled and that serves no useful function.

- Malignant tumor - A cancerous tumor that can cause harm; lacks a distinct border and may metastasize due to cancer elsewhere in the body.
  - Metastasis - The process by which cells break off of a tumor, travel through the vascular system, and grow elsewhere in the body.

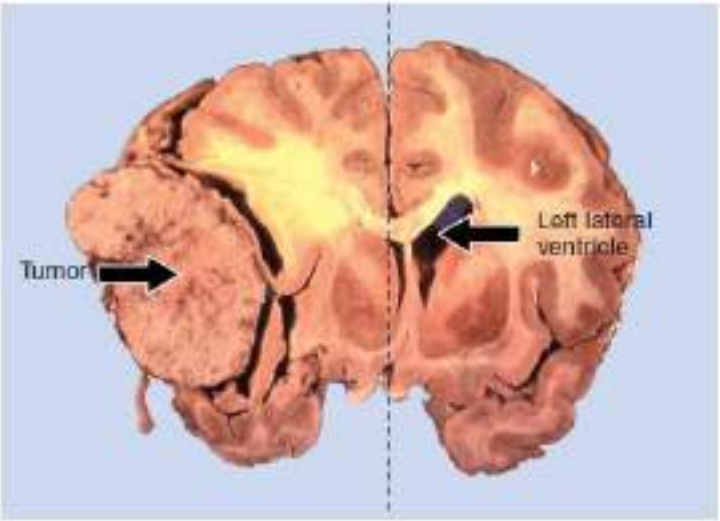
- Benign tumor - noncancerous tumor that does no harm; has a distinct border and cannot metastasize.

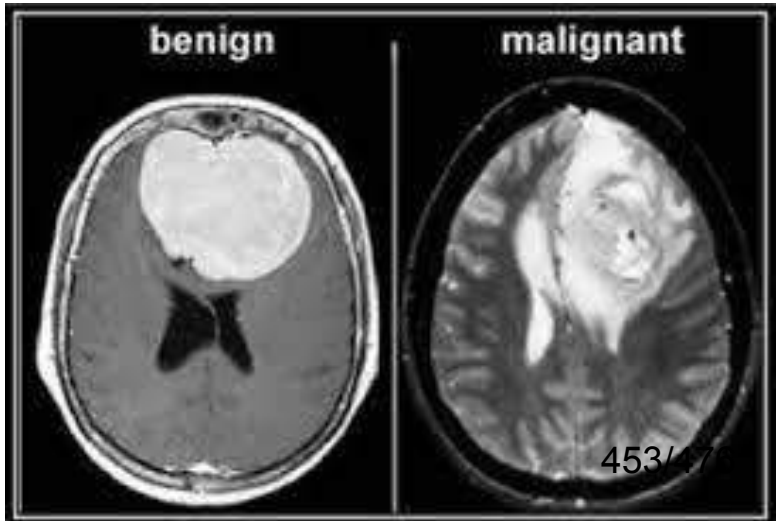
- Glioma - Tumors arising from glial cells – common form of malignant brain tumors

- Tumors do not arise from nerve cells or neurons because mature nerve cells do not divide.

- Tumors damage the brain by compressing the tissue and obstructing the flow of CSF

The photograph shows a slice of a human brain, showing how a large nonmalignant tumor (a meningioma) has displaced the right side of the brain toward the left. (The dashed line indicates the location of the midline.) The right lateral ventricle is almost completely occluded.
(Courtesy of A. D'Agostino, Good Samaritan Hospital, Portland, Oregon.)



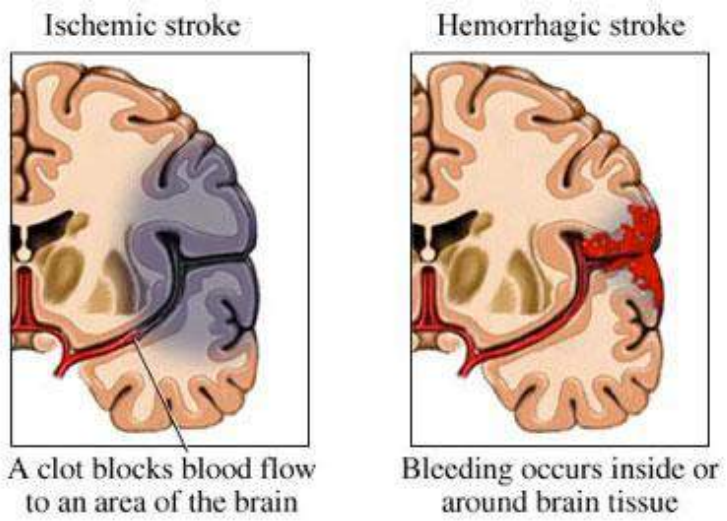


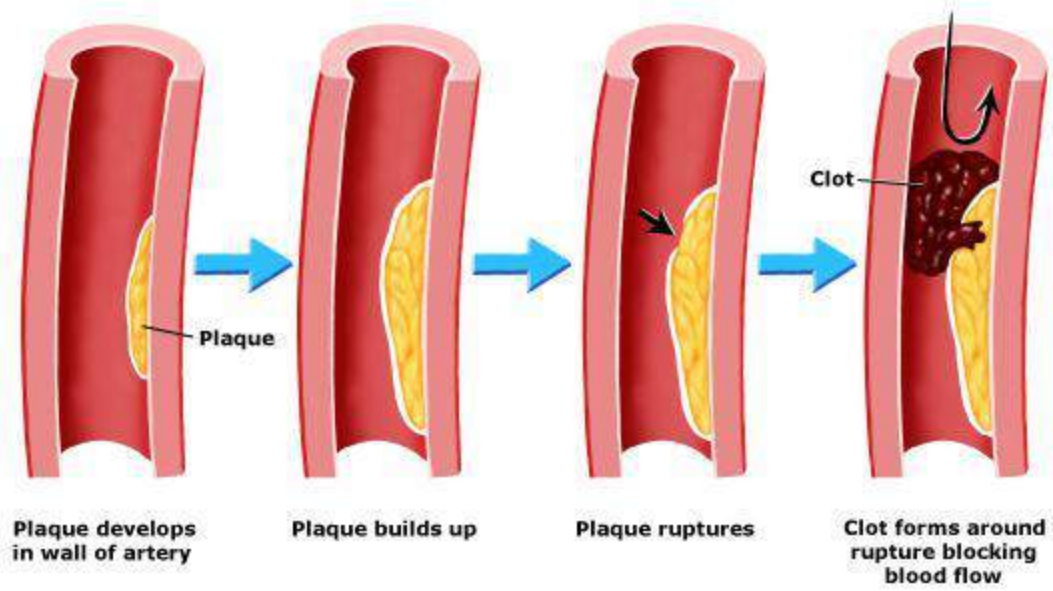
Cerebrovascular disorders

- Hemorrhagic strokes:
  - Bleeding within the brain
  - Blood vessels ruptured due to malformed blood vessels or due to hypertension
- Ischemic strokes
  - Obstruction of flow of blood leading to ischemia (loss of blood and therefore lack of glucose and oxygen)
  - NA-K pumps stop working in the absence of glucose/oxygen, and the Na ions rush in leading to excitotoxicity
  - Fat deposits inside arteries forming plaques – clots may form and break off and block arteries
  - Typically seen in high blood pressure, high cholesterol, diabetes

- Treatments:
  - The primary goal of treatment following a stroke is to save the tissue around the stroke from dying.

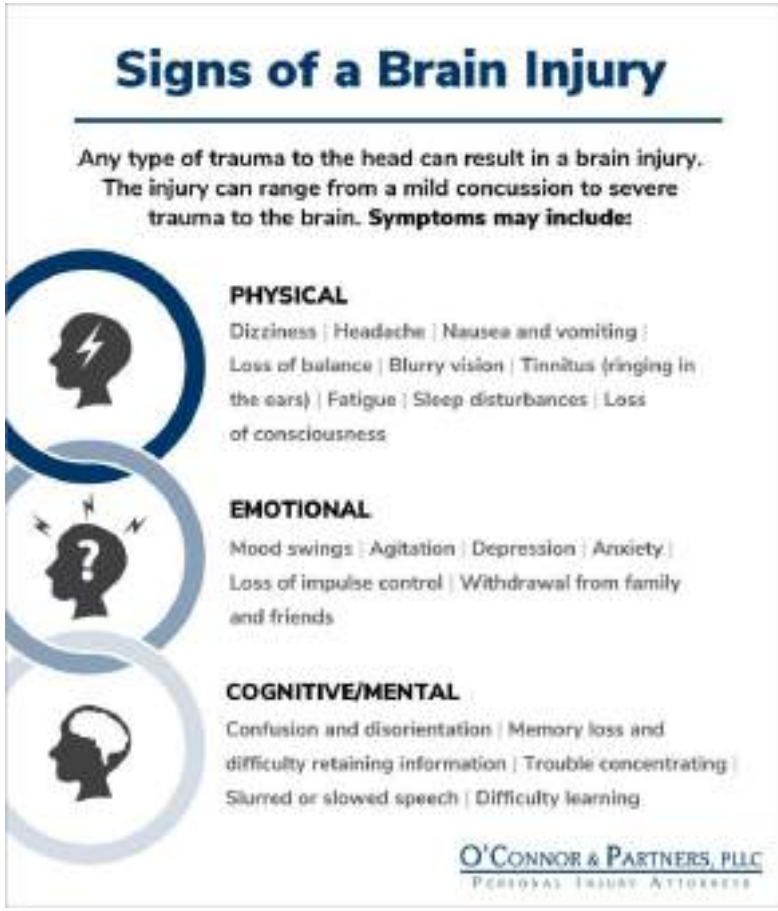
  - Drugs that dissolve clots in the blood vessels (prevent strokes)

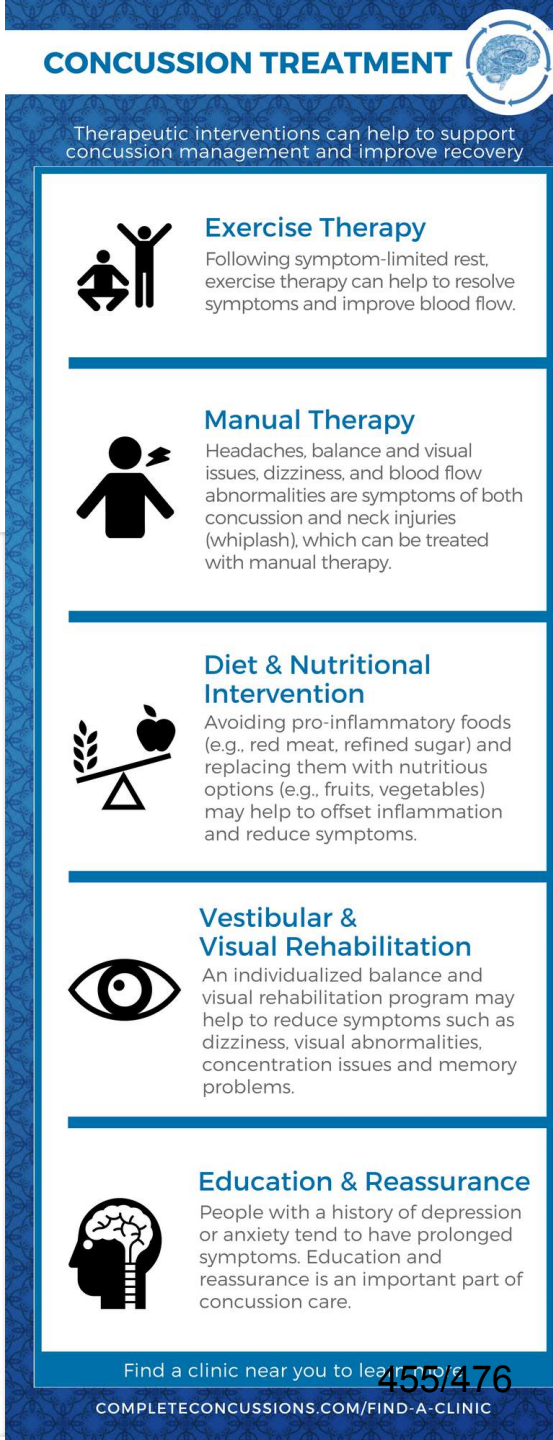




Traumatic Brain Injury

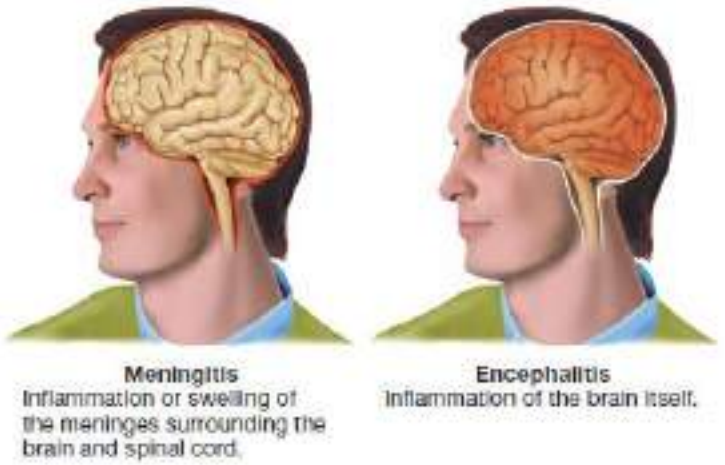
- Closed-head injury
  - Contusion (brain bangs against the skull) – opposite side of impact is injured
  - Bundles of axons can be torn and twisted, blood vessels can be ruptured (internal bleeding, seizures)
  - Cerebrospinal fluid can distort the walls of the ventricles
  - Chronic traumatic encephalopathy (CTE), a form of TBI, results in neurodegeneration due to repeated head trauma
    - E.g. American football players, boxers, rugby players, accidental fall, blow from a blunt object
    - Altered social behaviour, mood and cognitive impairment
    - Abnormal tau protein accumulates in the cortex of CTE patients – similar to Alzheimer's





Disorders caused by infectious diseases

- **Meningitis -** (inflammation of the meninges by bacterial or viral infections) medication may eliminate infections but brain damage is irreversible
- headache, a stiff neck
- depending on the severity of the disorder, convulsions, confusion or loss of consciousness, and sometimes death
- E.g. syphilis – sexually transmitted bacteria



COVID

Viral Infections

- Acute Anterior Poliomyelitis (polio) - Virus attacks motor areas in the brain including neurons of motor cortex and spinal cord resulting in varying structural abnormalities. (only legs or torso and legs leaving normal hands). However, the rest of the brain is not affected. (Polio vaccine)
- Rabies – animal bite (rabies vaccine given within a few hours)
- HIV – damage to synapses - mild cognitive impairment → dementia

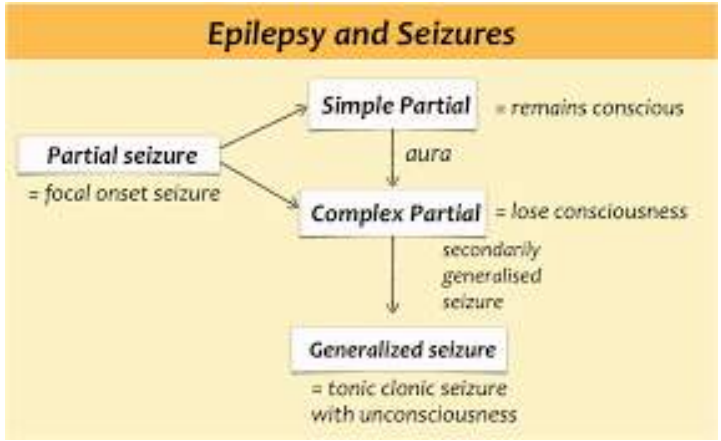
Encephalitis - inflammation due to viral infections

- Invades the entire brain
- Fever, nausea, irritability, convulsions, delirium followed by aphasia (loss of speech) or paralysis
- Herpes Simplex virus - can severely damage frontal and temporal lobes
- Viruses transmitted by mosquitoes (pick infectious agents from horses, birds and rodents)

Seizures

- A *seizure* is a period of sudden, excessive activity (glutamate) of cerebral neurons.

Causes –
- Scarring of tissue - injury, stroke, developmental abnormality, growing tumor, infection
- Fever
- Substance abuse withdrawal



I. Generalized seizures (with no apparent local onset)
   A. Tonic-clonic (grand mal)
   B. Absence (petit mal)
   C. Atonic (loss of muscle tone; temporary paralysis)

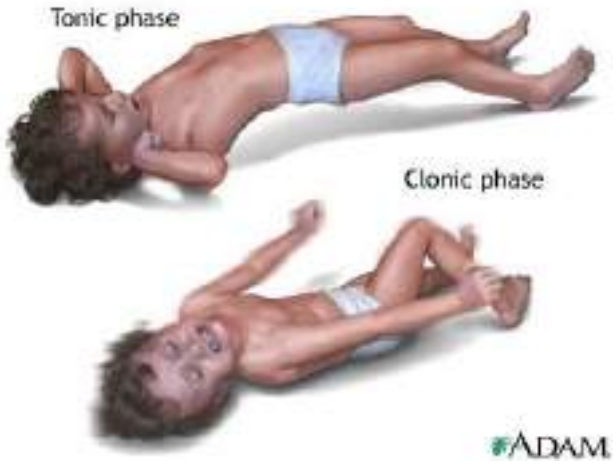
II. Partial seizures (starting from a focus)
   A. Simple (no major change in consciousness)
      1. Localized motor seizure
      2. Motor seizure, with progression of movements as seizure spreads along the primary motor cortex
      3. Sensory (somatosensory, visual, auditory, olfactory, vestibular)
      4. Psychic (forced thinking, fear, anger, etc.)
      5. Autonomic (e. g., sweating, salivating, etc.)
   B. Complex (with altered consciousness)
      Includes 1–5, as above

III. Partial seizures (simple or complex) evolving to a generalized seizure: Starts as simple partial seizure or a complex partial seizure, then becomes a grand mal seizure

Seizures

Convulsions - loss of both balance and consciousness.

- involve subtle changes of thought, mood, or behavior that are not easily distinguishable from normal ongoing activity.



1. Generalized Seizure

A. Tonic-Clonic Seizure

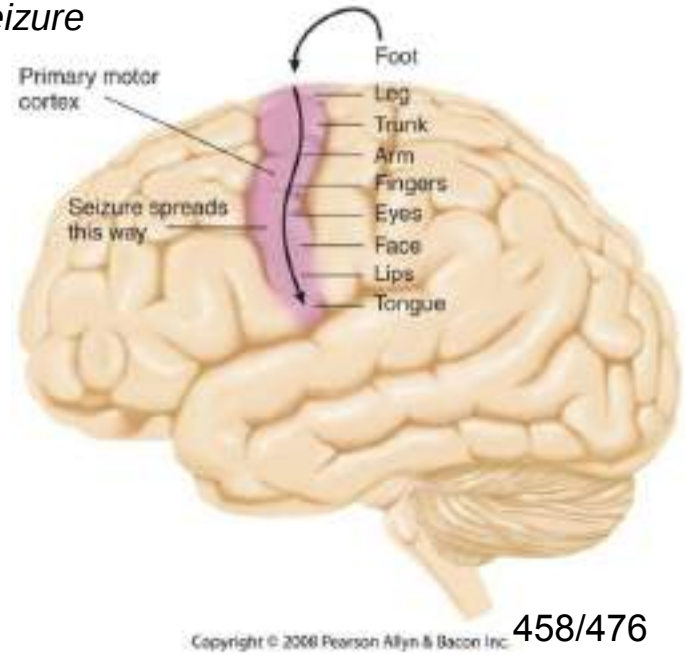
- ***Tonic phase*** - skeletal muscles contract, rigidity
- ***Clonic phase*** – tremors, rhythmic jerking movements.
- Hypoxia may also result in brain damage

B. Atonic Seizure - loss of muscle tone, temporary paralysis

C. Absence seizures - no convulsions;

- Ongoing activity end abruptly, → vacant look → sometimes fluttering eyelids
- loss of consciousness (extreme cases)
- Most common in children (around puberty)
- characterized by periods of inattention, which are not subsequently remembered.
- Affects performance in school

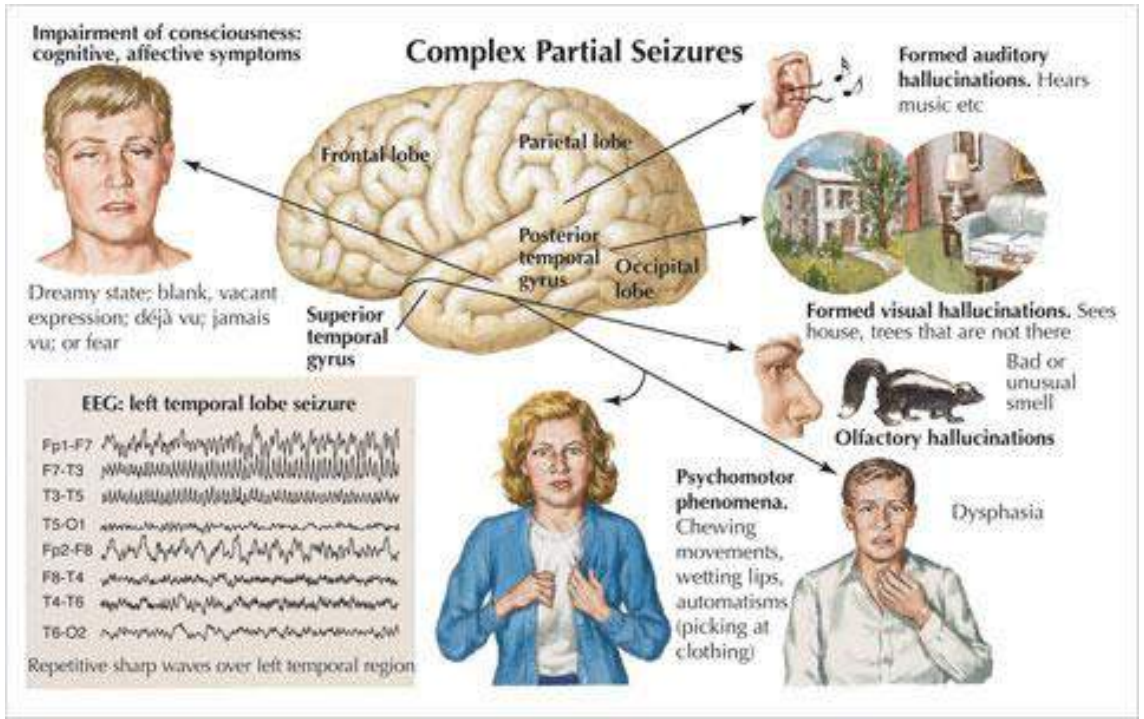
Spread of motor seizure

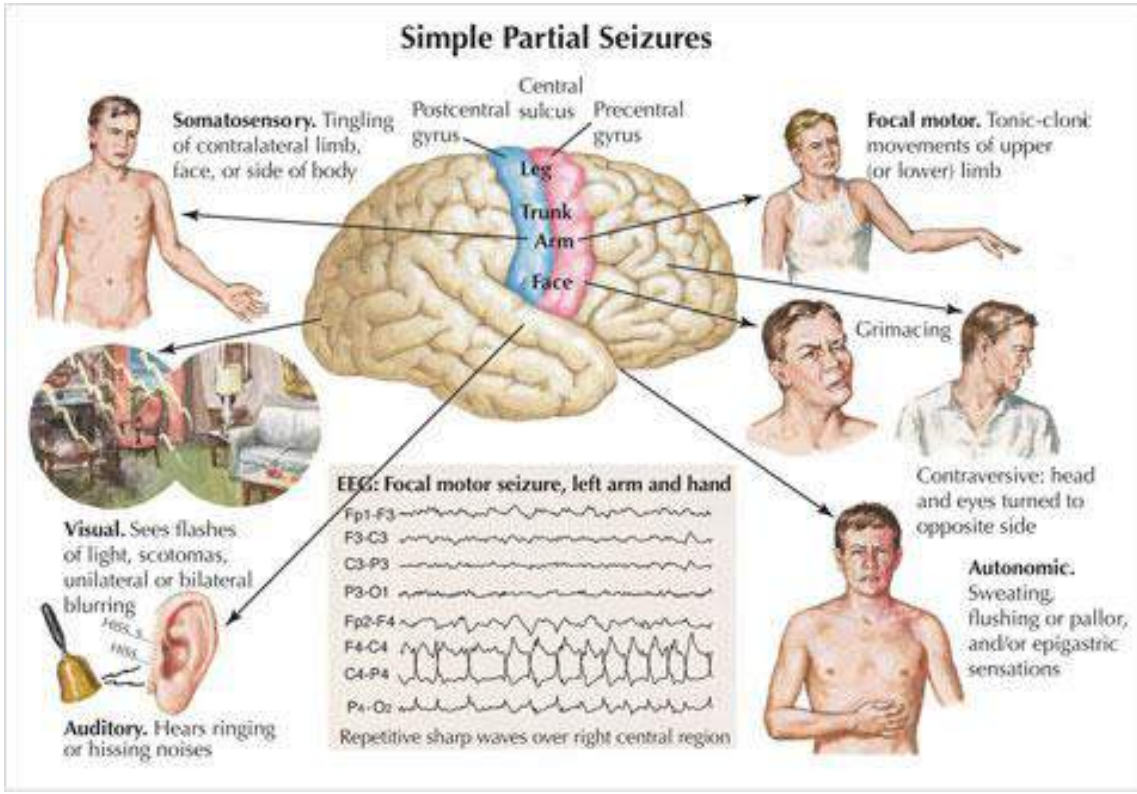


2. Partial Seizures (Focal Seizures)

begins at a focus and remains localized, not generalizing to the rest of the brain.

Type	Duration	Seizure Symptoms	Postictal (post-seizure) Symptoms
Simple Partial	90 seconds	No loss of consciousness. Sudden jerking sensory phenomena	Possible transient weakness or loss of sensation
Complex partial	1 to 2 minutes	May have aura , loss or altered consciousness Automatisms (such as lip smacking, picking at clothes, fumbling) Unaware of environment May wander	Amnesia for seizure events Mild to moderate confusion sleepy





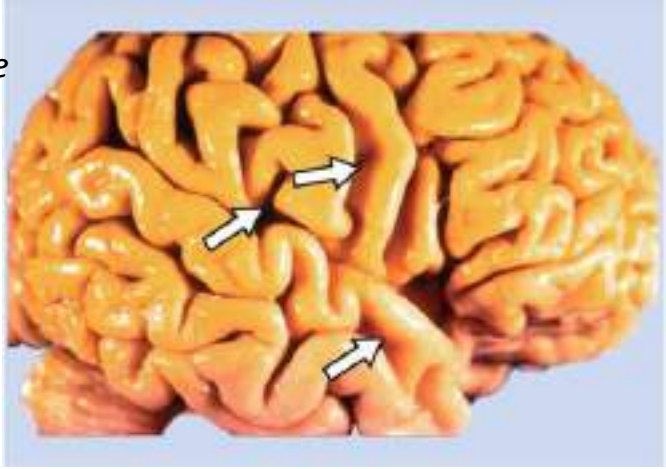
Seizures

No cure - frequency and severity of seizures can often be reduced by anticonvulsant medication

- GABAergic drugs
- Transcranial Magnetic Stimulation - repetitive pulses at low-frequency producing an inhibitory effect
- *Ketogenic diet* (a diet consisting of high levels of fat, moderate, levels of protein, and low levels of carbohydrates
  - reduces the amount of glutamate in the brain and enhances the synthesis of GABA, making it less likely for a seizure to occur.
  - reduce inflammation in the brain and inflammation due to infections like meningitis, encephalitis, or autoimmune disorders that can trigger seizures

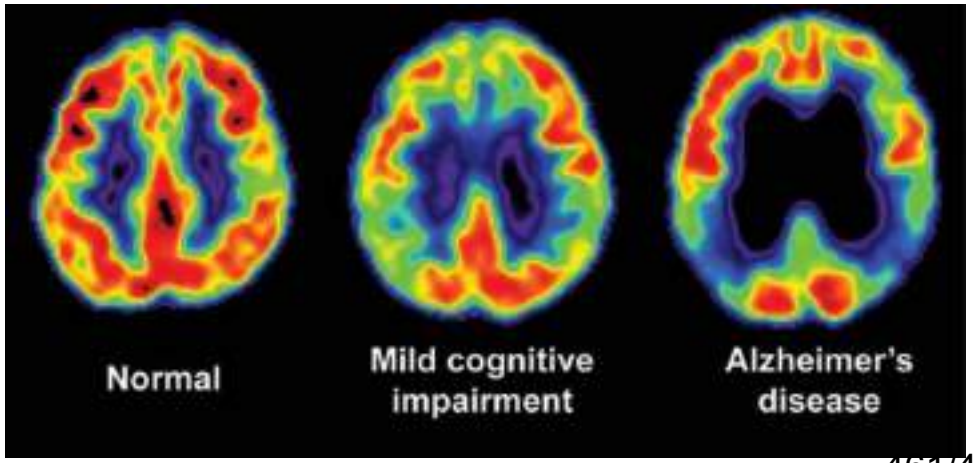
Alzheimer's Disease
Alzheimer's Dementia

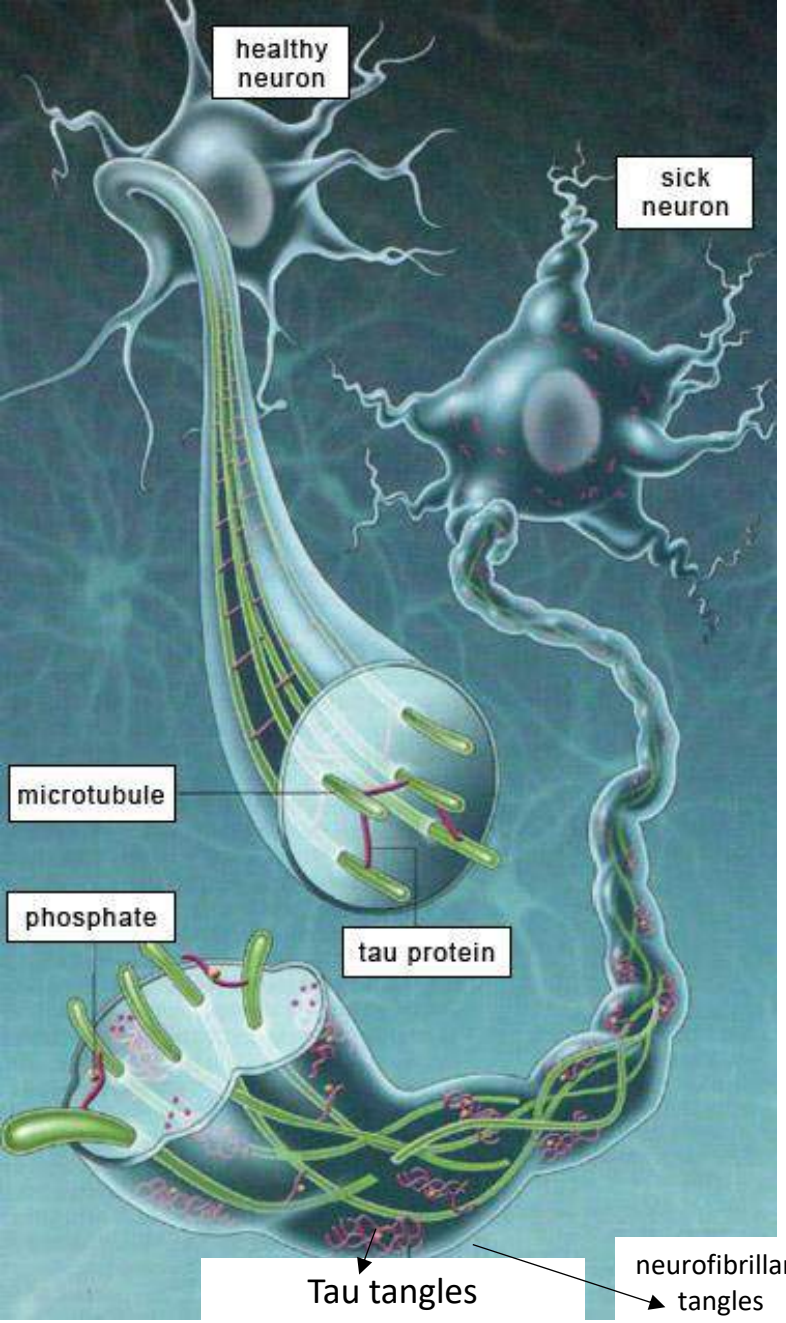
- *Sulci of temporal and parietal lobe are wide*
- *Loss of tissue*



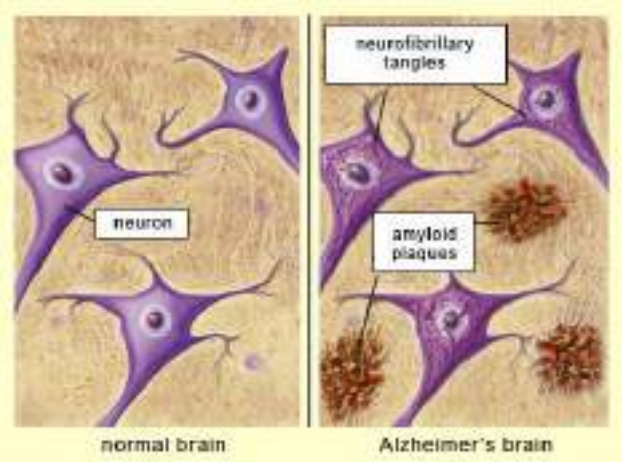
Symptoms:

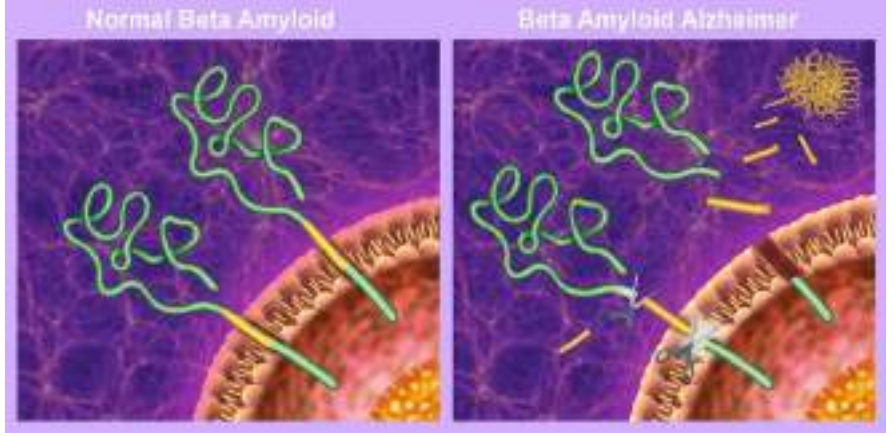
- Initially difficulty in remember names, appointments, faces, words – mild cognitive impairment (MCI)
- Progressive loss of memory, esp. Anterograde amnesia (inability to form new memories)
- Progressive loss of other cognitive functions – finances, planning, words, spatial disorientation, irritability, depression
- Severe cases (terminal illness) – loss of self-awareness, complete loss of memory, loss of bladder control, unable to bathe or wear clothes
- Typically occurs in older adults above the age of 65.
- As the case worsens, they are unable to handle their lives independently (emotionally and cognitively)





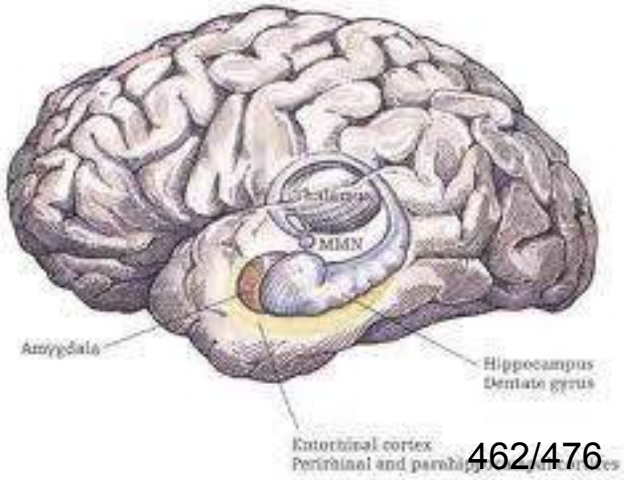
Tau protein normally plays a role in maintaining the overall structure of neurons



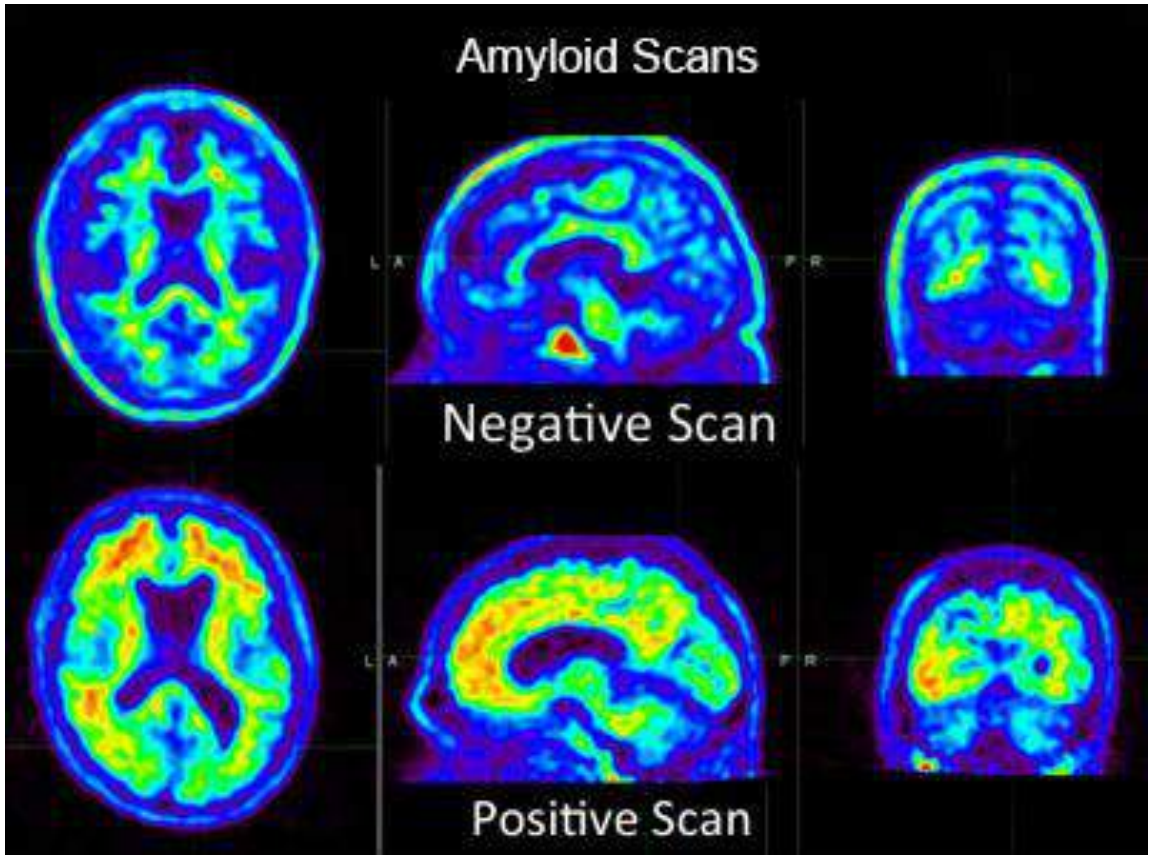


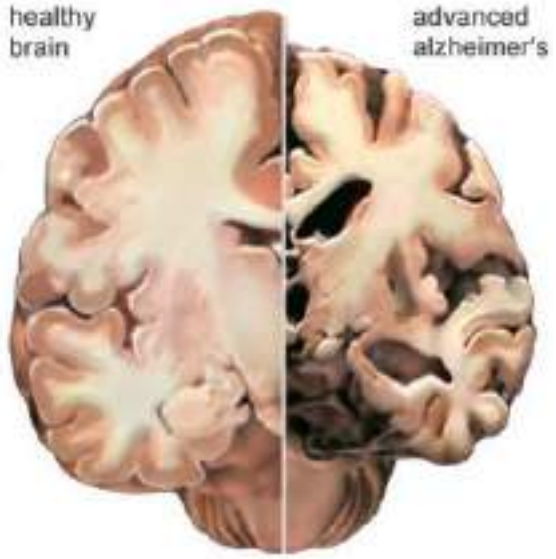
What happens inside the brain in Alzheimer's Disease ?

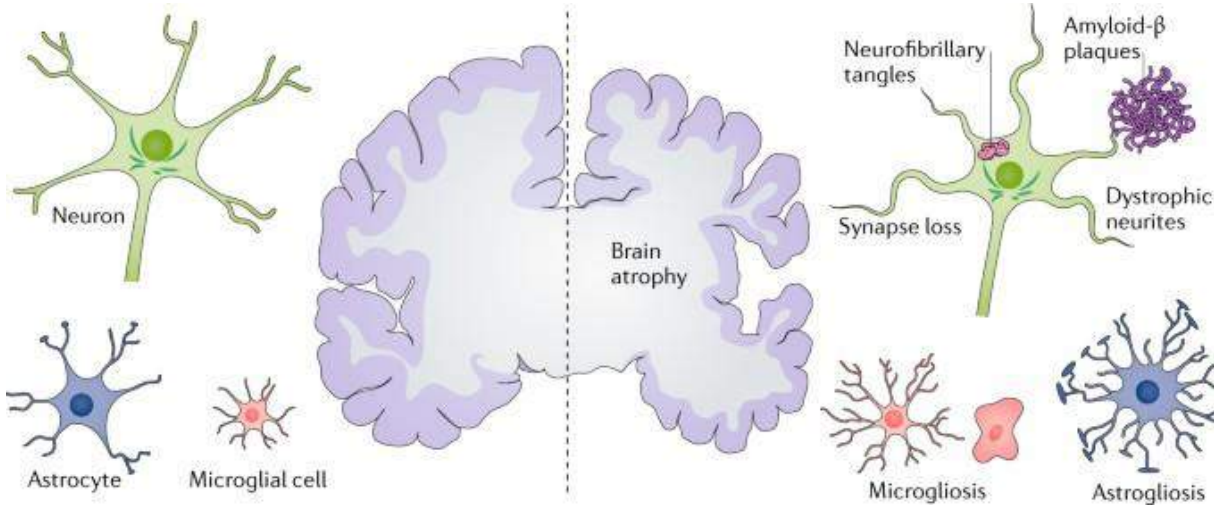
- Low levels of acetylcholine – memory encoding is affected
- Abnormal build-up of proteins in and around brain cells - neurofibrillary tangles (inside the neuron) and amyloid plaques (outside the neuron)
- Degeneration of cholinergic neurons is first seen in entorhinal cortex, hippocampus, amygdala (structures involved in various aspects of memory)
- Degeneration spreads across the brain over many years – dementia



Amyloid PET scan for Alzheimer's Disease







Cause of Alzheimer's Disease:

- Inheritance of mutated gene Apolipoprotein E (ApoE) – amyloid protein disintegrates
- most forms of Alzheimer's disease are sporadic, not hereditary
- Brain injury – amyloid plaques accumulate
- Obesity, hypertension, high cholesterol levels, and diabetes are also risk factors – high inflammation → high propensity to build amyloid plaques
- Level of education – lower cognitive activity

Treatment for Alzheimer's: (puzzling ….billions of research funds spent)

- Not curable
- Only progression can be slowed used drugs
- Keep your brain active (no retirement for the brain)
- Acetylcholinesterase inhibitors (donepezil, rivastigmine, and galantamine) – but symptomatic relief, cannot prevent degeneration
- NMDA antagonists (prevent excess Ca into acetylcholine neurons which cause cell death)
- Vaccines that prevent developments of antibodies in the immune system (which play a role in causing Alzheimer's)

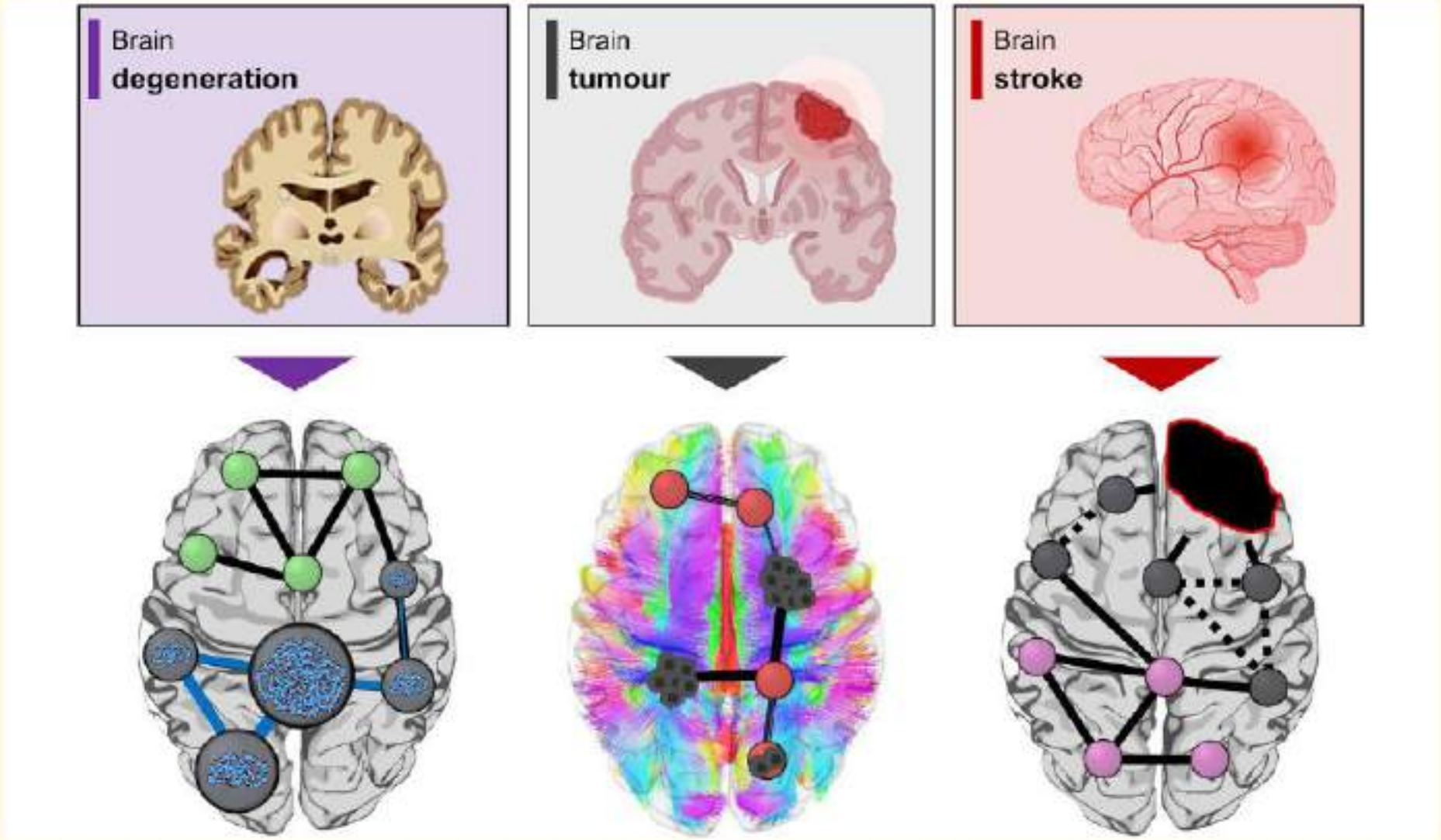
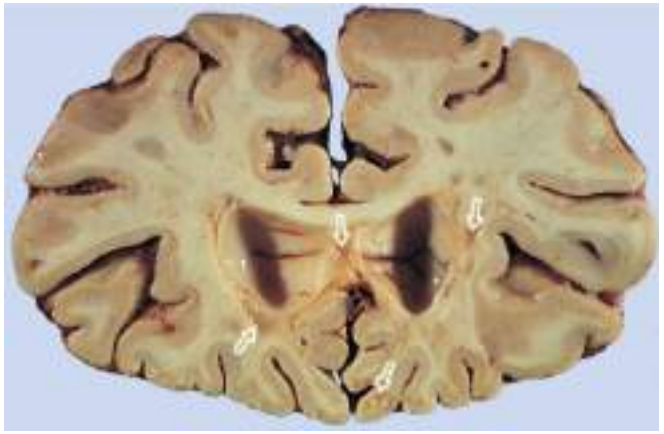


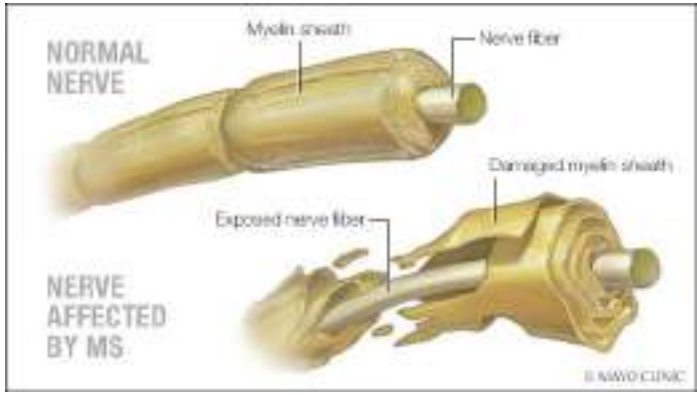
Figure 2 Brain connectivity across different neurological diseases. The brain connectome (both functional and structural) may represent a common substrate linking pathophysiological mechanisms to the clinical phenotypes of neurodegenerative diseases, gliomas and stroke. In neurodegenerative diseases, the connectome could serve as the biological substrate for the spread of misfolded proteins. In gliomas, tumour cells may spread along axonal pathways, suggesting that tumours growing in regions of high connectivity are more likely to recur, thus worsening prognosis. In stroke, connectivity diaschisis mechanisms have been described, indicating that the degree of disability after a stroke is more closely related to the lesion's impact on brain connectivity than to the size of the lesion.

Multiple sclerosis (MS)



sclerosis means "hardening"

- Symptoms:
  - Slowness in many abilities and cognitive skills degenerate.
  - In advanced MS – sensory disturbances, muscular weakness, numbness, tremor, and ataxia (loss of motor coordination).
  - Cognitive deficits and emotional changes occur in some patients
  - Appear in early to mid adulthood
  - Seen more in women
- Cause:
  - MS is an autoimmune demyelinating disease - slowing the transmission of electrical signals
  - loss of myelin (oligodendrocytes, white matter) in brain and spinal cord
    - In healthy individuals, remyelination of axons by oligodendrocytes and the generation of new oligodendroglia are both ongoing processes that occur throughout one's lifespan
  - Viral infection breaks down the immune system to attack its own myelin
  - Virus weakens the BBB allowing myelin to circulate in the blood stream
  - More prevalent in the cold regions where immunity due to cold is poor. People who have lived in cold countries during childhood have a higher probability of contracting the disease. (Risk factors - vit D deficiency, smoking)
  - Also seen in pregnant women whose first trimester falls during winter when susceptibility to viral infections is high.



- Treatment:
  - No cure – drugs that slows the progression of the disease by modulating the immune system

Amyotrophic lateral sclerosis (ALS)
Lou Gehrig's disease

- degenerative disorder that attacks spinal cord and cranial nerve motor neurons
- 5 in 100,000
- Symptoms spasticity (increased tension of muscles, causing stiff and awkward movements), exaggerated stretch reflexes, progressive weakness and muscular atrophy, and, finally, paralysis. The muscles that control eye movements are spared.
- Cognitive changes in executive function, working-memory, language and social cognition

In MS, the immune system is believed to attack nerve cells' protective coating, damaging the nerves and disrupting communication between the brain and body.

ALS causes voluntary motor neurons to decline and die, so they can no longer send messages to the muscles.

Cause – Neuroinflammation

- Only 10% cases of ALS are hereditary; rest are sporadic
- Risk factors – smoking, environmental toxins
- In genetic cases - increased extracellular levels of glutamate - impaired glutamate reuptake – excitotoxicity - cell death
- In sporadic cases - faulty programming of glutamate receptors – too many AMPA receptors – extra-excitation by glutamate – excitotoxicity – cell death

Treatment – Drugs that regulate glutamate levels

Stephen Hawking

SNc – Substantia Nigra

Meso = mid (brain)

1 Mesocortical Pathway

- VTA neurons project to cortex (CTX)
- Modulates cognitive functions and emotions
- Dysfunction in schizophrenia, ADHD and affective disorders

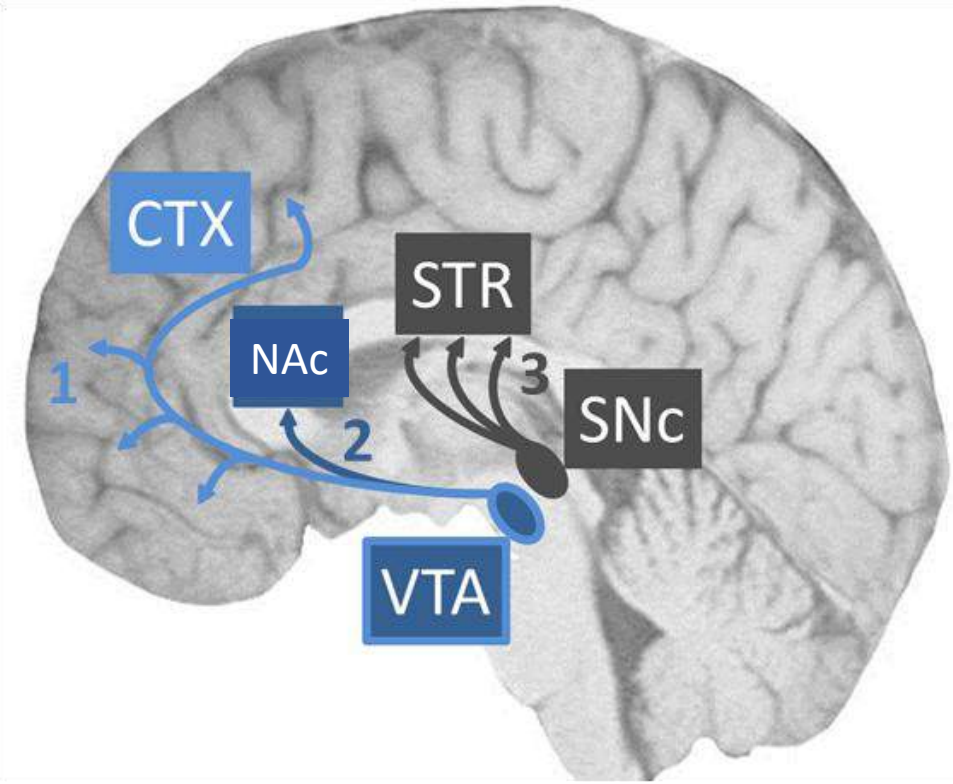
2 Mesolimbic Pathway

Reward pathway

- VTA neurons project to nucleus accumbens NAc
- Modulates motivation, reward and emotions
- Dysfunction in drug addiction, affective disorders and schizophrenia

3 Nigrostriatal Pathway

- SNc neurons project to striatum (STR)
- Controls motor function
- Degeneration causes motor symptoms in PD



Schizophrenia (SP)

- Schizophrenia "the splitting of psychic functions" - the breakdown of integration among emotion, thought, and action.

- attacks about 1 percent of individuals of all races and cultural groups, typically beginning in adolescence or early adulthood

- Schizophrenia is characterized by three categories of symptoms:

1. Positive symptoms
2. Negative symptoms
3. Cognitive symptom*s*

Positive symptoms

Due to excessive dopaminergic activity – as seen in substance abuse

- ***Delusions.*** Delusions of being controlled (e.g., "Martians are making me steal"), delusions of persecution (e.g.,"My mother is poisoning me"), or delusions of grandeur (e.g., "Narendra Modi admires my drawings").
- ***Hallucinations.*** Imaginary voices making critical comments or telling patients what to do.
- ***Inappropriate affect.*** Reacting with an inappropriate emotional response to positive or negative events.
- ***Disorganized speech or thought.*** Illogical thinking, peculiar associations among ideas, belief in supernatural forces.
- ***Odd behavior.*** Talking in rhymes, difficulty performing everyday tasks.

Negative symptoms

- *Affective flattening.* Diminished emotional expression
- *Avolition.* Reduction or absence of motivation.
- *Catatonia.* Remaining motionless, often in awkward positions for long periods.
- poverty of speech
- inability to experience pleasure (anhedonia)
- social withdrawal

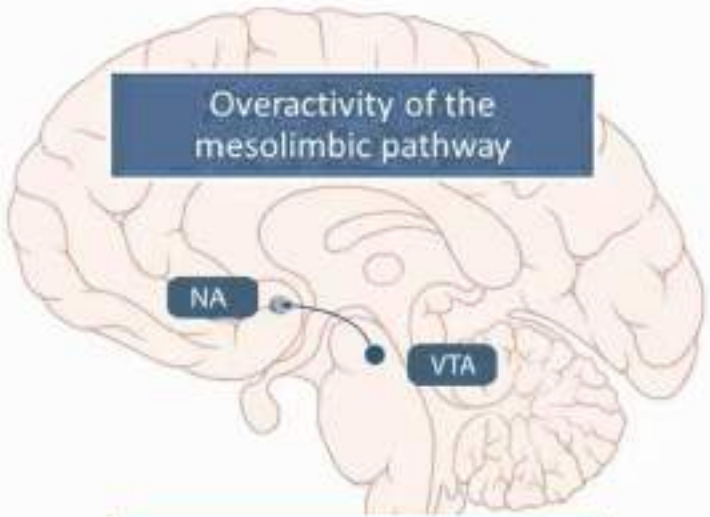
Due to degeneration or impaired development. Common in brain damage disorders, especially to frontal lobes

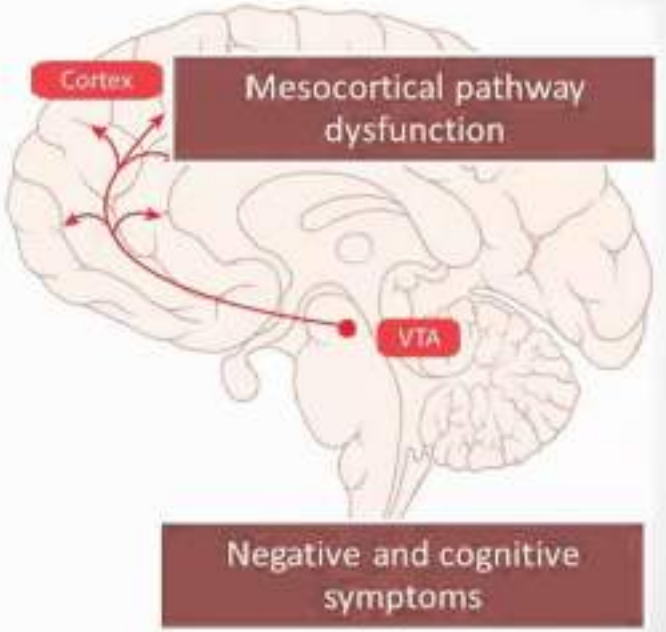
Cognitive symptoms

- difficulty sustaining attention
- low *psychomotor speed* (for example, in movements that include a cognitive element, such as reaction time, connecting numbers or letters in sequence, or alternating numbers and letters),
- deficits in learning and memory,
- poor abstract thinking, and poor problem solving

The frequent recurrence of any two of these symptoms for 1 month is currently sufficient for the diagnosis of schizophrenia—provided that one of the symptoms is delusions, hallucinations, or disorganized speech.

Dopamine Pathways Relevant to Schizophrenia Symptoms





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- Depression, anxiety, substance abuse, and smoking are also very common in schizophrenia.

- The symptoms of schizophrenia typically appear gradually, over a period of several years.
  1. first clinical symptoms of schizophrenia tend to be symptoms of depression,
  2. followed by social withdrawal (negative symptoms) and
  3. cognitive difficulties (cognitive symptoms),
  4. positive symptoms

Interview: Catatonic Schizophrenic

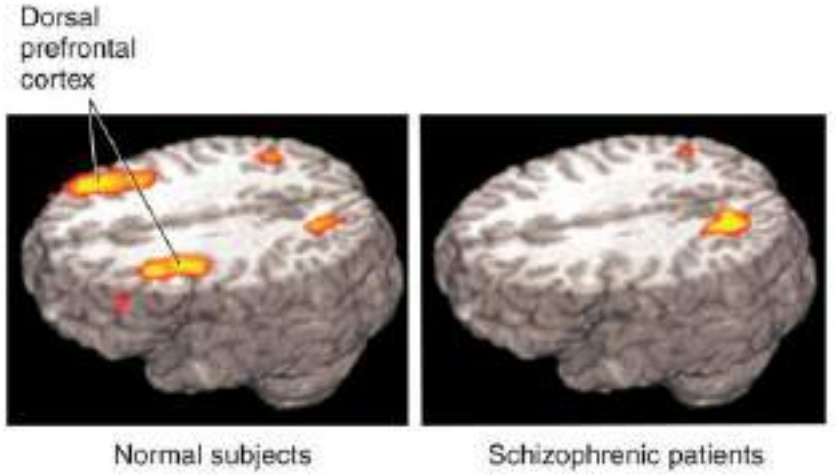
Psychiatric Interviews for Teaching: Psychosis

https://www.youtube.com/watch?v=iGH7hGkkMrU&ab_channel=NorthwesternMedicine

http://schizophrenia.com/diag.php#

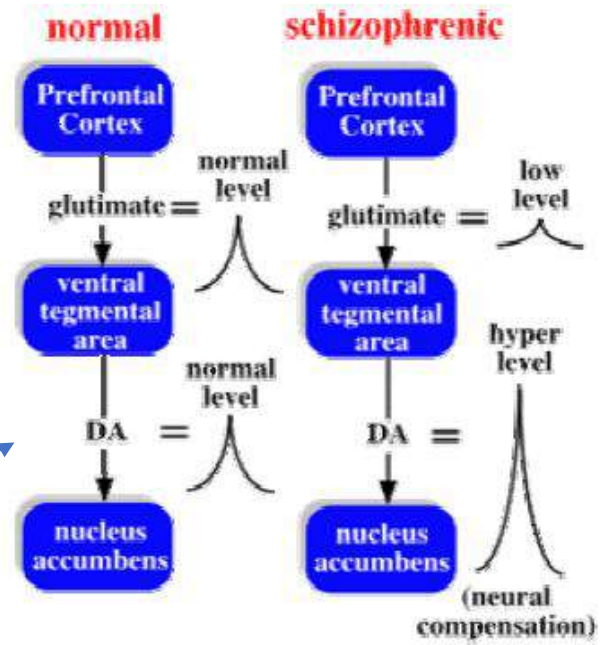
Hypofrontality in Schizophrenia

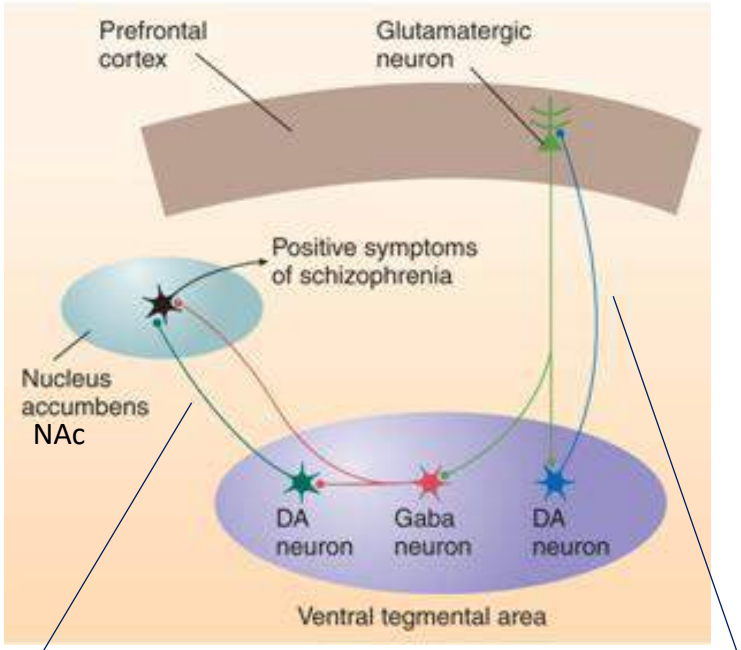
- Hypofrontality – structural changes in frontal lobe
  - fewer number of glutamate (NMDA) and dopamine receptors in the PFC
  - may be driven by prenatal environment (maternal viral infections)
  - may alter the brain development leading to smaller frontal regions and decreased activity during adolescence.



The schizophrenia network in the brain

- The prefrontal cortex (PFC) and excitatory (glutamatergic) and inhibitory (GABAergic) connections to the VTA
- Normally, at resting state, basal or spontaneous release of a neurotransmitter occurs constantly in the nervous system, independent of any environmental stimuli.
- Hypofrontality reduces the basal release of glutamate from the PFC to the VTA. This leads to lower basal release of dopamine in the VTA which in turn cause dopamine receptors in the VTA to become supersensitive, so they over react to environmental stimuli (neural compensation)
- Hypofrontality also lessens the inhibition from PFC to VTA, leading to hyperactivity in dopaminergic neurons from VTA to Nac.
- Thus overall, there is excess of dopamine released from VTA to NAc – resulting in positive symptoms (similar to those seen in substance abuse)
- The dopamine increase in NAc affects other brain areas it is connected to, especially amygdala, resulting in exaggerated positive symptoms (neutral faces look angry, delusions, etc.)
- Dopaminergic neurons also project back to the PFC – but due to hypofrontality (fewer dopamine receptors) the dopamine effect is low - the cause of negative and cognitive symptoms





What might cause schizophrenia?

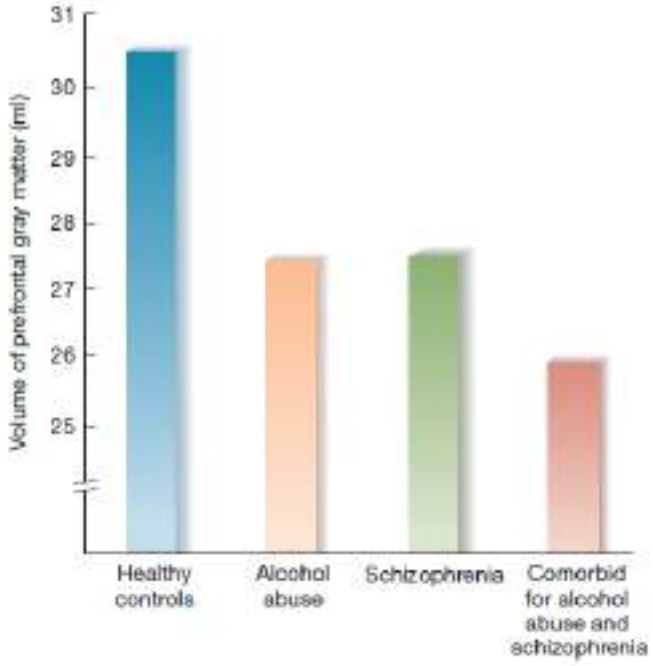
- Other factors that may play a role in schizophrenia susceptibility–
  - paternal age
  - maternal stress or malnutrition
  - prenatal infections (viral infections in mother)
  - urban birth or residing in an urban setting – higher rate of viral infections
  - childhood adversity
  - Substance abuse

co-morbidity of schizophrenia and substance abuse

- Schizophrenics also show hypo-frontality (reduced activity in the PFC)
  - High percentage of *co-morbidity* of schizophrenia and substance abuse
  - Hypo-frontality is correlated to schizophrenia & substance abuse (not causality)

Substance abuse – to compensate the excess of dopamine in the PFC, dopamine receptors reduce in number – resulting in hypofrontality - which appears to be causing of negative/cognitive symptoms in schizophrenia

The graph shows the volume of gray matter in the prefrontal cortex of healthy controls, patients who abuse alcohol, patients with schizophrenia, and patients comorbid for both disorders.
(Based on data from Mathalon et al., 2003.)



The graph shows the prevalence of schizophrenia during a 4- to 16-year follow-up period as a function of number of cigarettes smoked each day at age 18.
(Based on data from Weiser et al., 2004.)