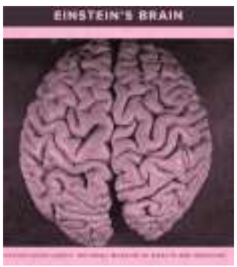
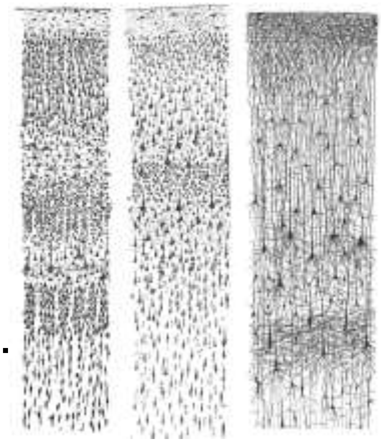
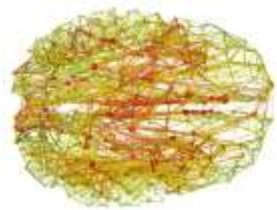
Welcome to Clinical anatomy of the head, neck and neuronal pathways

Lecture #7







Alemeh Zamani, Ph.D.

Department of Anatomy
MUNI, MED

Spring 2024

Future Lectures

Somatosensory and viscerosensory; pain pathways and connections of stress analgesia

Pathways of the somatomotor system, connections of the cerebellum and basal ganglia; spinal reflex motoric; eye movements

Arrangement and function of the autonomic nervous system

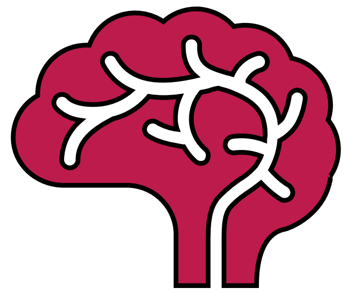
Today’s lecture will cover:

1- Nervous System Barriers

2- Plasticity and Regeneration of Nervous System

3- Visual and Auditory Pathways

4- Vestibular, Olfactory, and Gustatory Pathways



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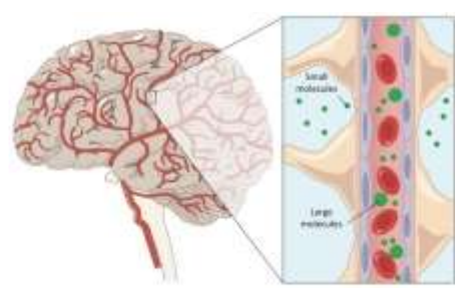
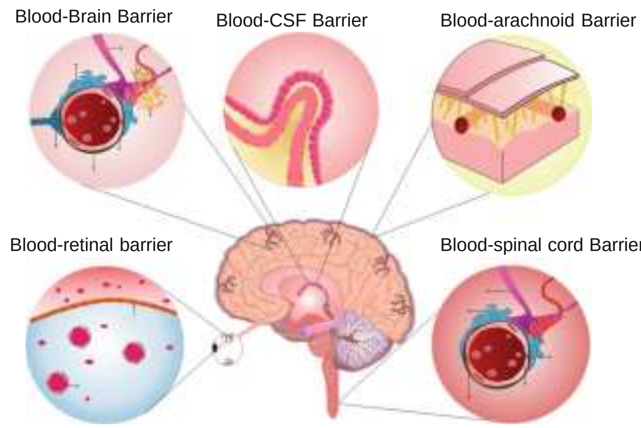


Nervous System Barriers

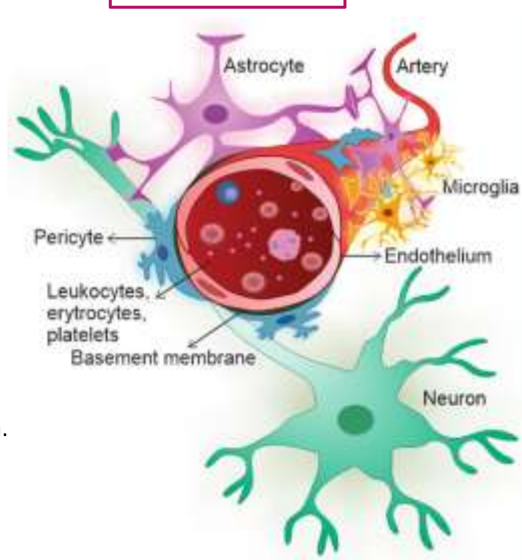
- Blood-Brain Barrier
- Blood-Spinal Cord Barrier
- Blood-Cerebrospinal Fluid Barrier
- Blood-Nerve Barrier
- Blood-DRG Barrier



Blood-Brain Barrier (BBB)

Neurovascular unit

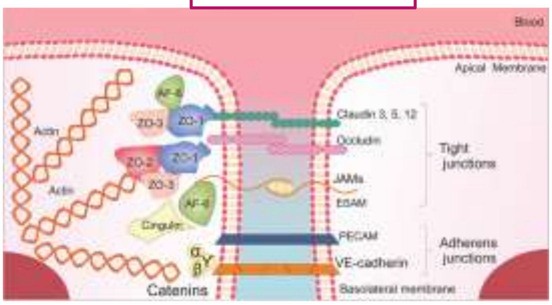
- BBB is formed by a tight monolayer of brain endothelial cells.
- Function of BBB is maintaining brain homeostasis by regulating transport to the brain.
- The plasticity of BBB is regulated within a dynamic system called Neurovascular unit.
- BBB represents a significant roadblock in delivering drugs to brain.



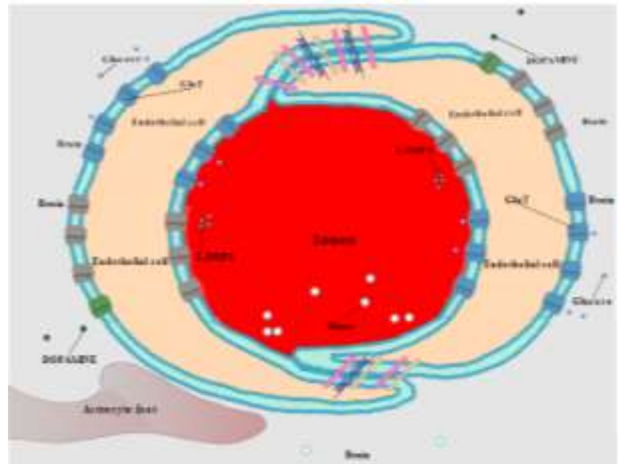
Blood-Brain Barrier -Tatiana Barichello

Blood-Brain Barrier

Junctional Proteins



Transporter Proteins



❖ Junctional proteins and transporters:

small inorganic molecules (O_2, CO_2, NO, and H_2O)

ions, peptides, amino acids, proteins, carbohydrates,

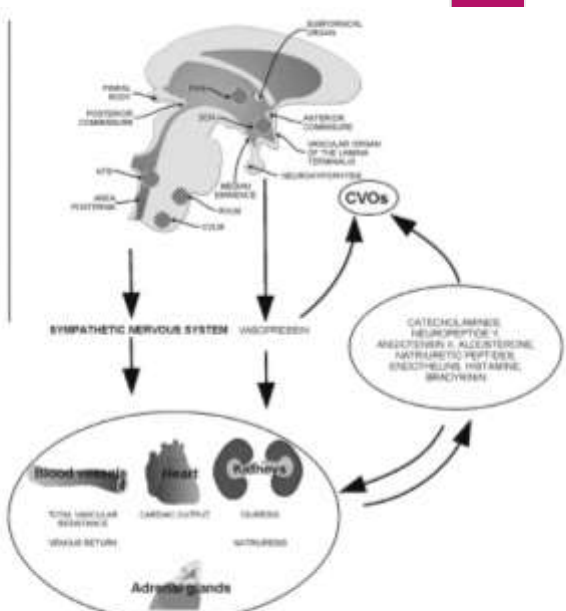
hormones, vitamins, etc.

Neuroscience Online, the Open-Access Neuroscience Electronic Textbook

Circumventricular organs (CVOs)

Non-barrier regions (hormonal control)

- Pituitary gland
- Median eminence
- Area postrema
- Preoptic recess
- Paraphysis
- Pineal gland
- Endothelium of choroid plexus



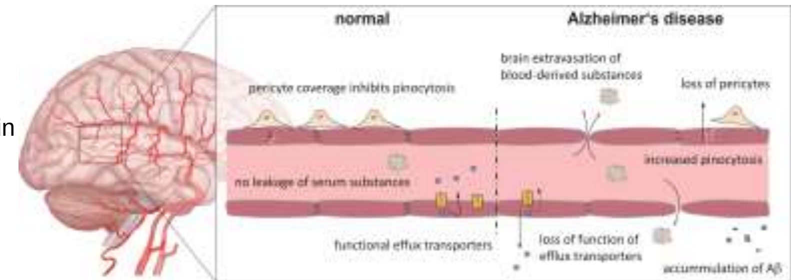
Ufnal, *Neuropeptides* 2014

Blood-Brain Barrier Dysfunction

Disruption of BBB can lead to:

- Changes in permeability
- Modulation of immune cell transport
- Trafficking of pathogens into the brain

Dysregulated BBB transport in Alzheimer's disease



BBB dysfunction is associated with neurological disorders:

Neurodegenerative diseases, Cerebrovascular diseases, Brain infections, Inflammatory diseases, Brain tumors, Neurotrauma, Mental or psychological stress

Storck, *Neuroforum* 2017

Blood-Spinal Cord Barrier (BSCB)

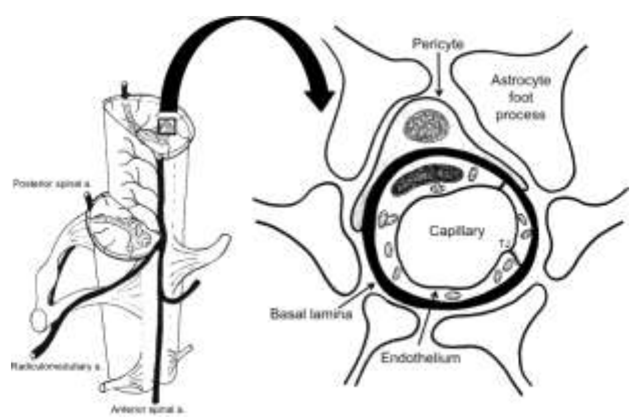
Composed of continuous type of microvessels

More permeable for cytokines and tracers compared to BBB:

- Lower level of occludin and ZO-1
- Less number of pericytes

Pathological conditions:

- Spinal cord injury
- Amyotrophic lateral sclerosis
- Radiation-induced myelopathy



Bartanusz, *Annals of Neurology*, 2011

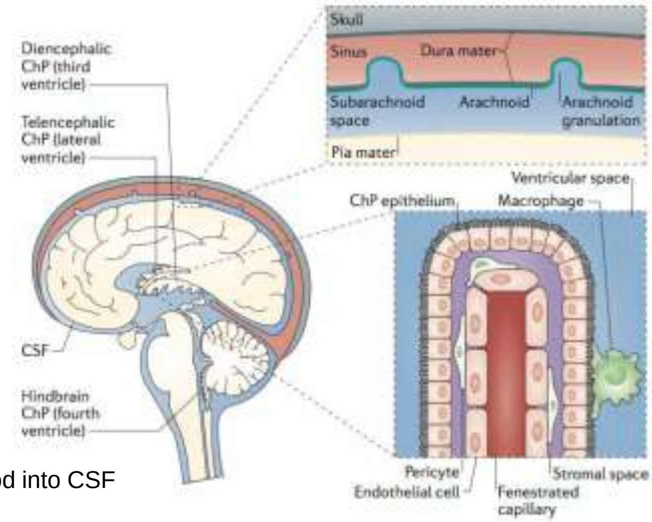
Blood-CSF Barrier

Epithelial cells of choroid plexus:

- Secrete cerebrospinal fluid (CSF)
- Form blood-CSF barrier

Role of blood-CSF barrier

- To restrict the passage of substances from blood into CSF



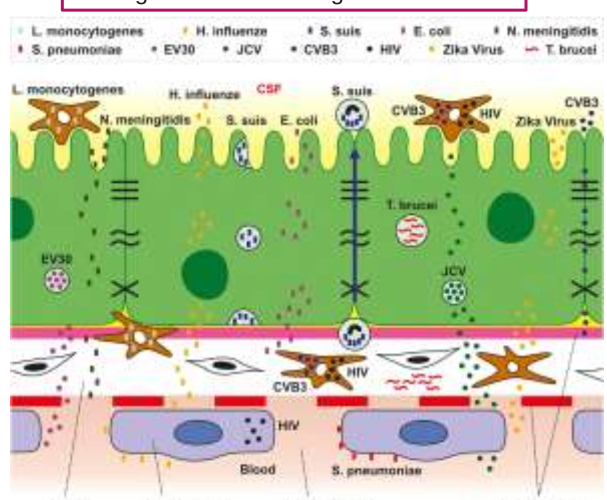
Lun, *Nature Reviews Neuroscience* 2015

Blood-CSF Barrier Dysfunction

Blood-CSF barrier permeability alteration:

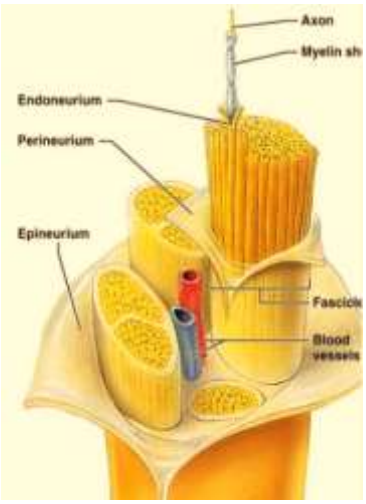
- Infectious disease
- Stroke
- Trauma
- Neurodegenerative disease
- Autoimmune disorders
- Tumors of choroid plexus
- Schizophrenia and chronic stress

Pathogen invasion through B-CSF barrier

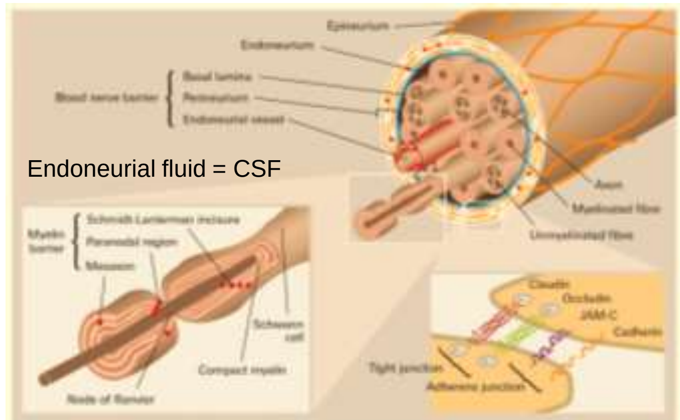


Solár, *Fluids Barriers CNS*, 2020

Blood-Nerve Barrier (BNB)



- Perineurial cells interaction with **Schwann cells** critical for nerve **development** and **regeneration**



Endoneurial fluid = CSF

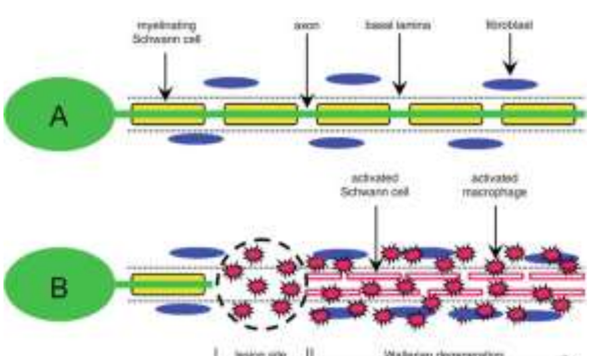
Blood-nerve exchange is maintained by endothelial cells of endoneurial vessels.

Reinhold, *Experimental neurology* 2020

Wallerian Degeneration

Injury of nerves and axons →

- Proliferation of Schwann cells
- Invasion of circulating macrophages
- Alteration of the blood-nerve barrier
- Changes in the endoneurial extracellular matrix
- Elevation of cytokine production

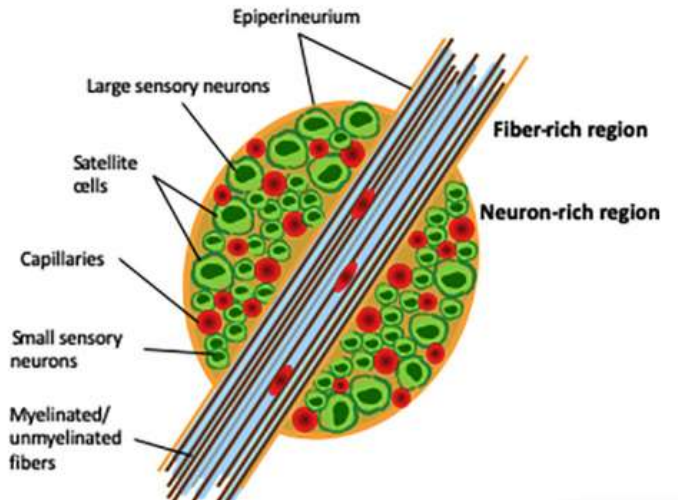


Blood-Dorsal Root Ganglion (DRG) Barrier

Present in DRG

- Somata of sensory nerves
- Nociceptive neurons

More permeable than the BNB



Peripheral nerve injury induces cellular and molecular changes in the DRG that contribute to induction and maintenance of neuropathic pain.

Reinhold, *Experimental neurology* 2020

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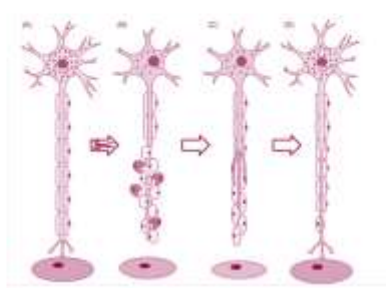


Plasticity and Regeneration of Nervous System

Brain never stops changing …

❖ Neuronal plasticity is defined as the ability of NS to modify the activity and organization of neuronal circuitry according to internal or external stimuli:

- Alterations in the level of the neurotransmitters
- Change in the protein content at synapses

Short-term and long-term potentiation and depression, milliseconds to hours or even longer

- Adaptational plasticity

Continuous adjustment in response to environmental challenges

- Reparation plasticity

Positive or negative changes during functional or structural recovery of damaged neuronal circuits

Reparation Plasticity

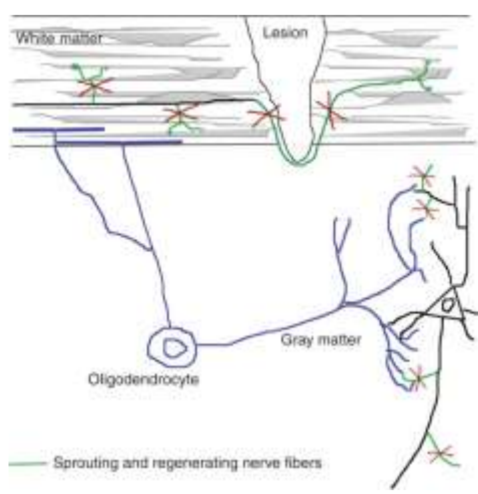
The correction of developmentally miswired neuronal connections or rehabilitation after stroke or traumatic brain injury depend crucially on the adult **brain's capacity for plasticity**.

Reaction to injury differs in neurons of CNS and PNS

Adult mammalian CNS has a limited regenerative capacity

CNS

- Damage to neurons, glial, and endothelial cells
- Breakdown of the blood-brain barrier
- Activation of glial cells and a robust inflammatory response



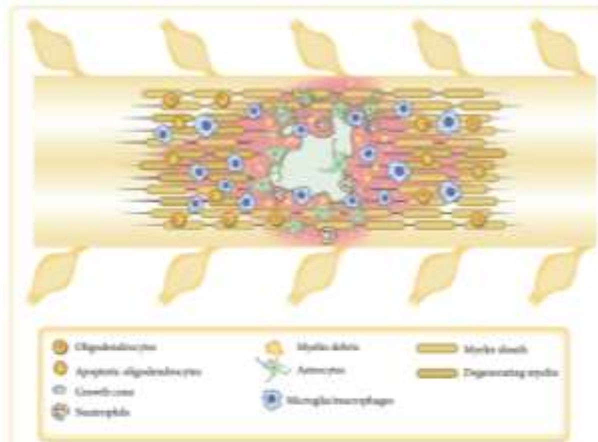
Silver, *Cold Spring Harb Prospect Biol* 2015

CNS Pathology after a Traumatic Injury

Glial environment of the adult CNS presents a major hurdle for successful axon regeneration

Inhibitory molecules for CNS regeneration:

- Chondroitin Sulfate Proteoglycans (from astroglial scar)
- Myelin-Associated Inhibitors (from oligodendrocytes)
- Inhibitory Signaling Pathways (Ibuprofen inhibits RhoA)



Pro-regenerative molecules

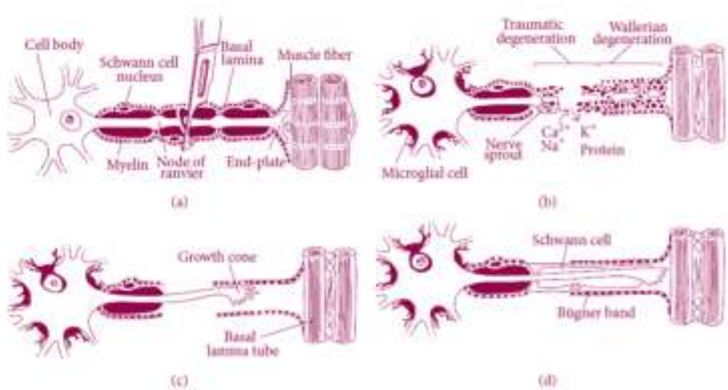
NGF, TGF-β, PDGF, EGF, BDNF, and oncomodulin

Mietto, *Mediators of Inflammation* 2015

Peripheral Nerve Pathology after a Traumatic Injury

Regeneration of PNS neurons depends on

- type of injury
- age of the organism
- localization and function of neurons



Schwann cells: overexpress a broad panel of inflammatory mediators

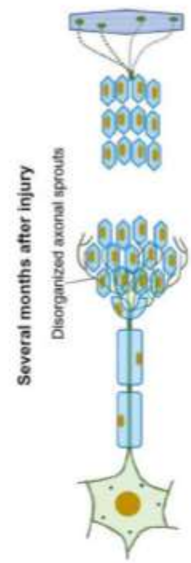
Macrophages: phagocytosis of cellular debris

Navarro, *Progress in Neurobiology* 2007

Cellular and molecular mechanisms during PNS regeneration

Regeneration-Associated Genes

- c-Jun
- activating transcription factor-3 (ATF-3)
- SRY-box containing gene 11 (Sox11)
- small proline-repeat protein 1A (SPRR1A)
- growth-associated protein-43 (GAP-43)
- CAP-23



❖ Neuroma = Result of disorganized growth of cone branches in an unsuccessful search of a receptor or endoneurial tube is not reached, = painful lump

Huebner, *Results Probl Cell Differ 2009*

Grinsell, *BioMed Research Internationall* 2014.

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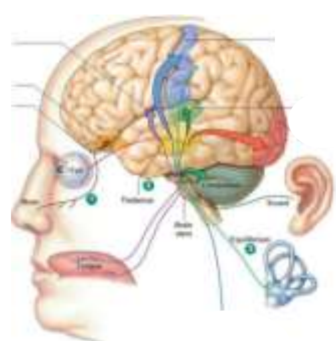
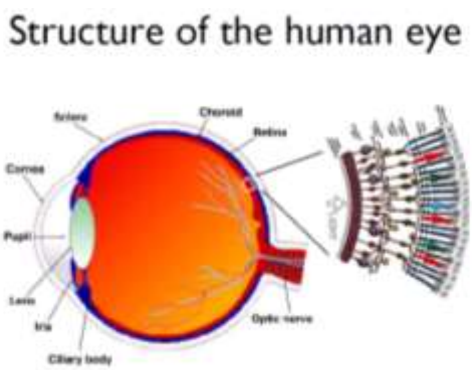
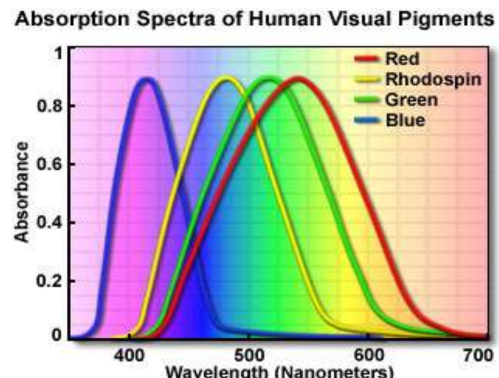


Visual Pathways

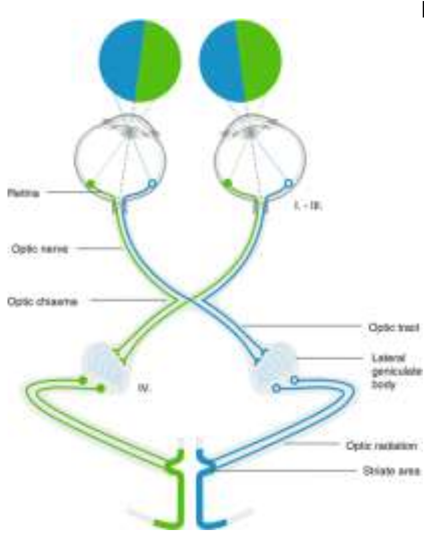
Perception of motion, depth, form and color



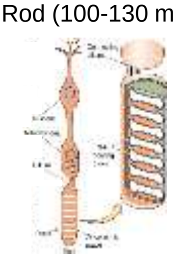


Boron, *Medical Physiology*, 2003

Neuronal elements of visual pathway



Rod (100-130 million)

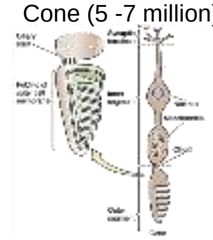


Scotopic vision

dim light

Rhodopsin

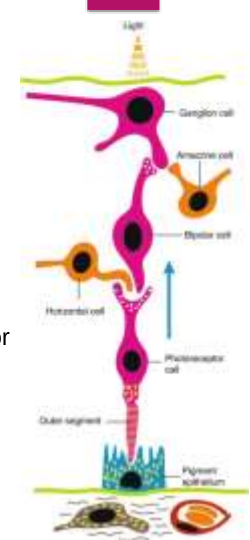
Cone (5 -7 million)



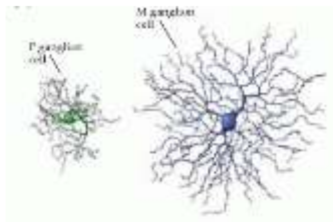
Photopic vision

perception of shape and color

Photopsin



Joukal, Anatomy of the Human Visual Pathway

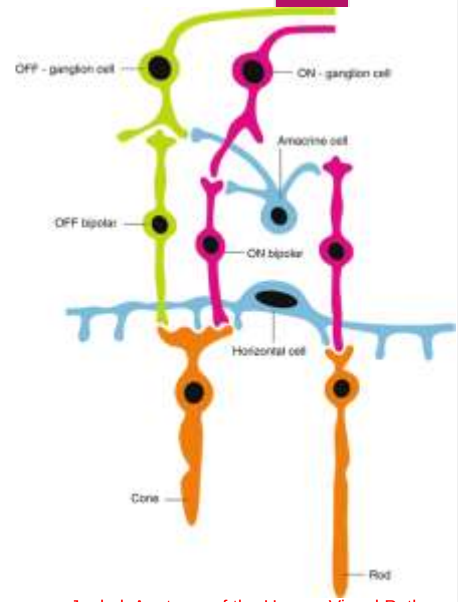


Neuronal elements of visual pathway

P cells (80%)
- ganglion cells that monitor cones
- color-specific
- terminate on P-neurons of the lateral geniculate body

M cells (10%)
- ganglion cells that monitor rods
- provide information about a general form of an object
- terminate on M-neurons of the lateral geniculate body

non-P non-M cells (10%)
- projection to subcortical nuclei, koniocellular cells of LGN



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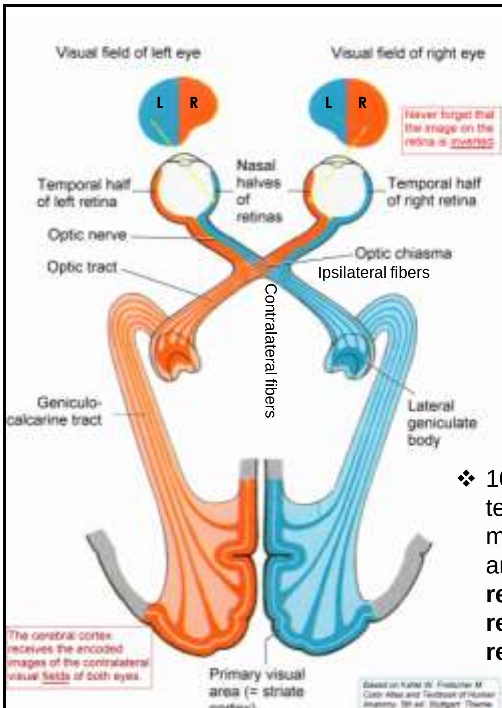
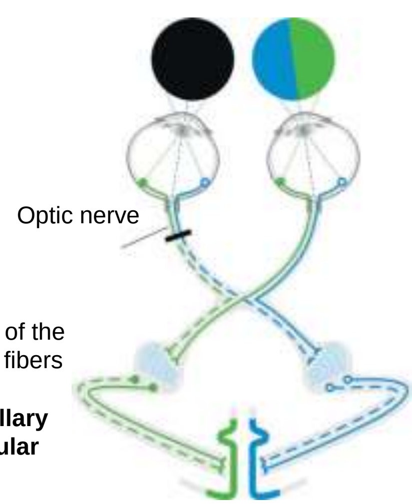


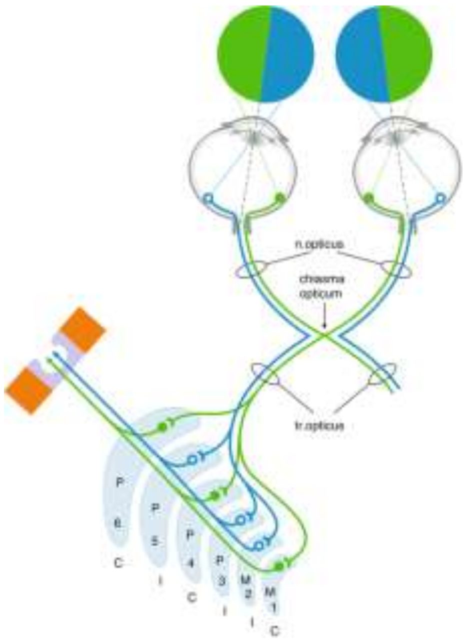
Pimary Visual Pathway

Monocular blindness



- ❖ 10% of axons at LGN terminate in the tectum of the mesencephalon.These fibers are important for **optic reflexes**, such as **pupillary reflex** or **vestibulo-ocular reflex**.

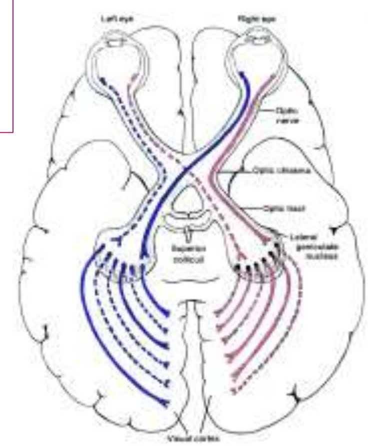
Joukal, Anatomy of the Human Visual Pathway



- ❖ Ipsilateral input enters layers 2,3 and 5 of LGN
- ❖ Contralateral input enters layers 1, 4 and 6 of LGN

Fibers crossing temporal lobe: inferior lateral fibers or **meyer's loop**

Fibers crossing parietal lobe: superior retinal fiber

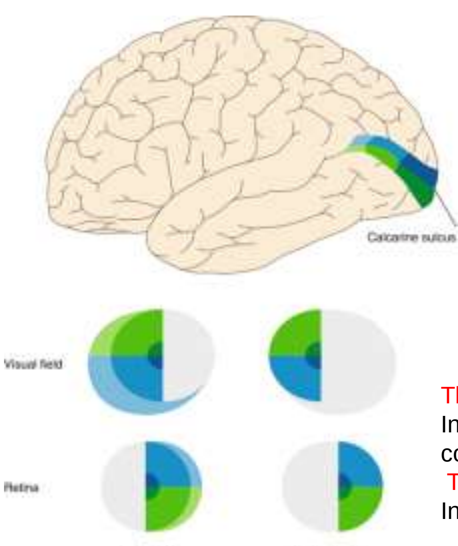


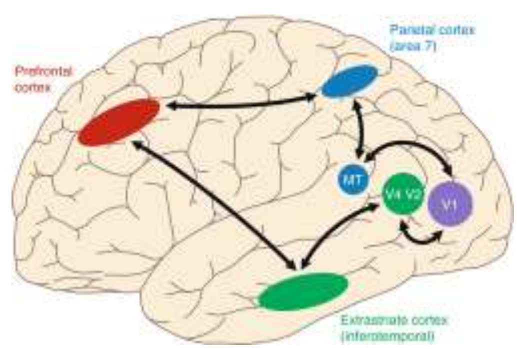
Joukal, Anatomy of the Human Visual Pathway

The Visual Cortex

Primary Visual Cortex

Extrastriate Visual Cortex





The ventral stream
Information about object identification including shape, contrast, and color, **"what" pathway**

The dorsal stream
Information about spatial features and movement, **"where" pathway**

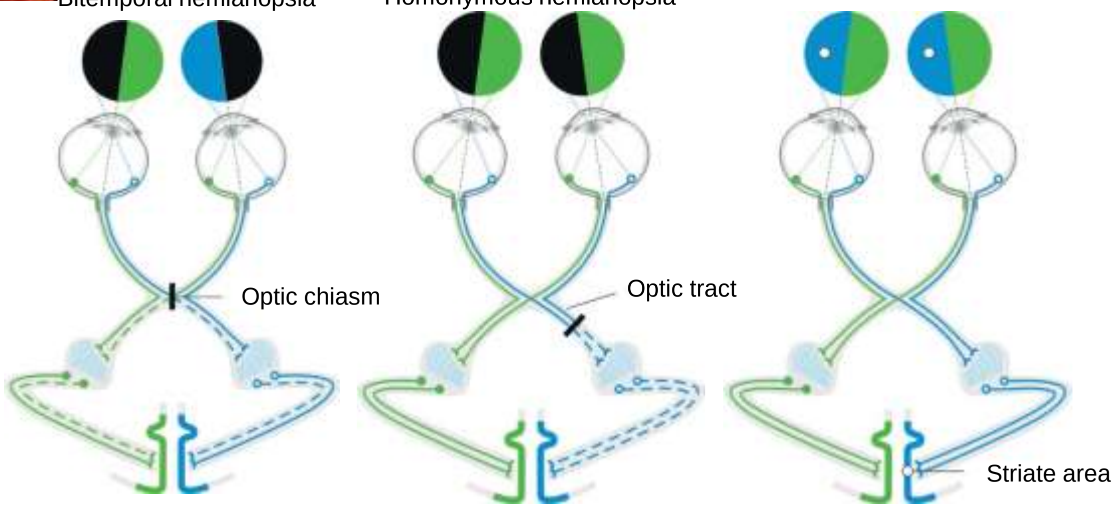
Joukal, Anatomy of the Human Visual Pathway

Lesions of the visual pathway

Bitemporal hemianopsia

Homonymous hemianopsia

Scotoma

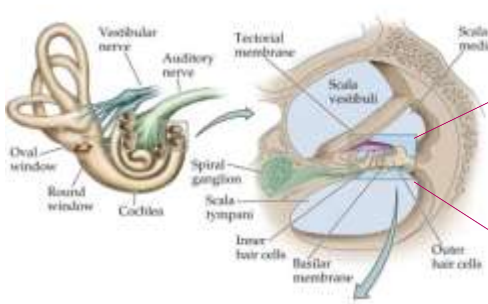


Joukal, Anatomy of the Human Visual Pathway

Auditory Pathways

The perception of sound; the most important means of communication

cross section of the cochlea



organ of Corti

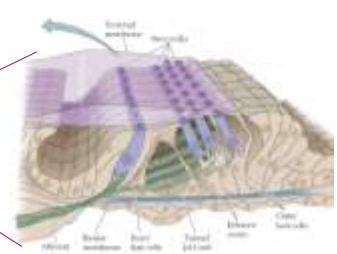
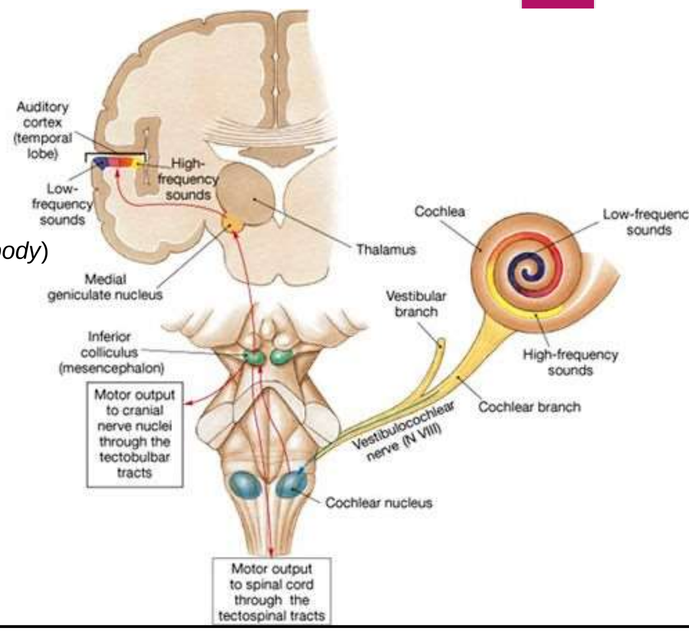


Diagram of the major auditory pathways

1st order neuron
- Spiral ganglion cells

2nd order neuron
- Dorsal cochlear nucleus
  → nucleus of lateral lemniscus
- Ventral cochlear nucleus:
  - VPCN → ?
  - AVCN → superior olivary nucleus (*trapezoid body*)



3rd order neuron
- nucleus of inferior colliculus

4th order neuron
- medial geniculate nucleus
(*brachium of inferior colliculus)*

Auditory pathway:

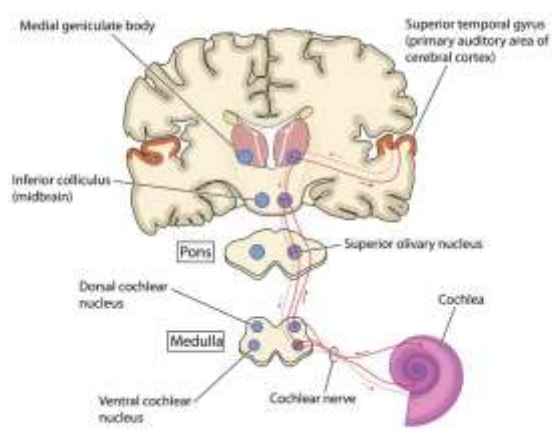
- Sensory hair cells
- Cochlear branch of vestibulocochlear nerve (C.N. VIII, Auditory Nerve):

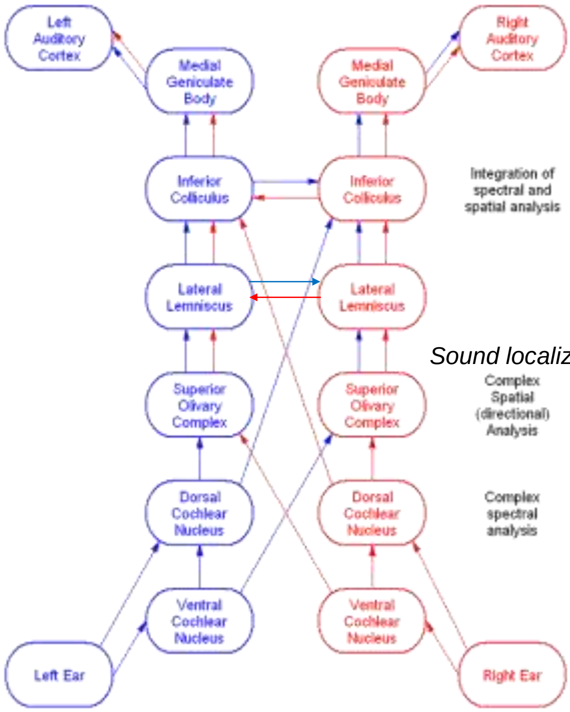
  Spiral ganglion cells →
- Brainstem: cochlear nucleus:

  DCN → nucleus of lateral lemniscus →

  VPCN → nucleus of inferior colliculus

  AVCN → superior olivary nucleus →
- Midbrain: nucleus of inferior colliculus →
- Thalamus: medial geniculate nucleus →
- Auditory cortex

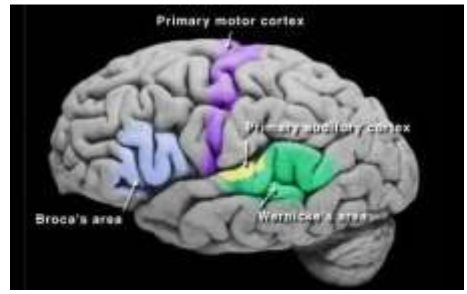




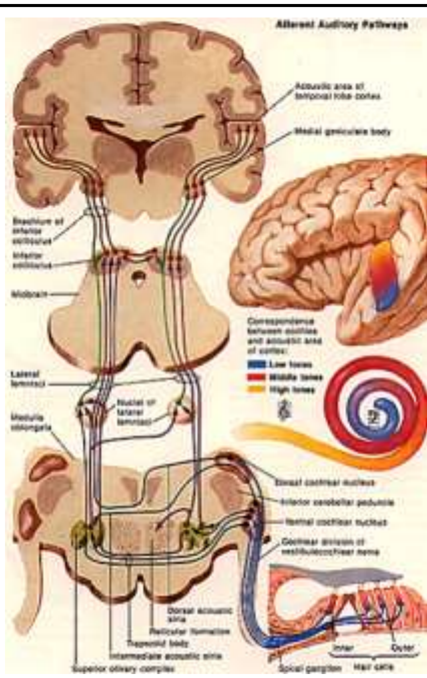
Sound localization

Auditory cortex

Temporal superior gyrus (Heschl gyrus)



In Wernicke's area speech is comprehended.



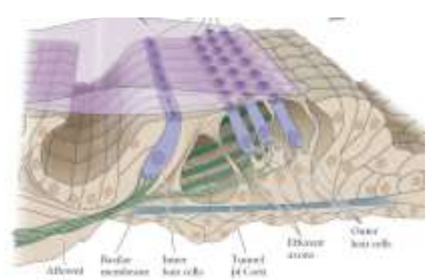
Ascending and Descending pathways

Two functionally significant features of ascending pathway:

- tonotopical organization
- bilateral projection

Descending pathway functions (superior olivary complex):

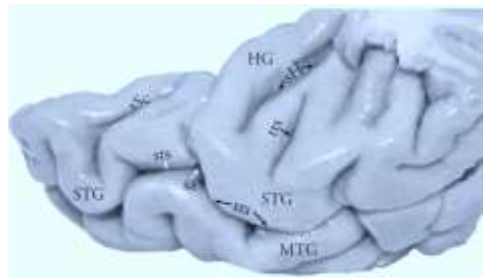
- feedback system processing ascending information
- enhance signals
- supress noise
- focus on a particular speaker
- inhibit other voices



Pathology

Bilateral lesions in cortical deafness

- Hearing impairments
- Impairments of speech comprehension
- Speech repetition impairment
- Impairment in recognition of familiar sounds and music



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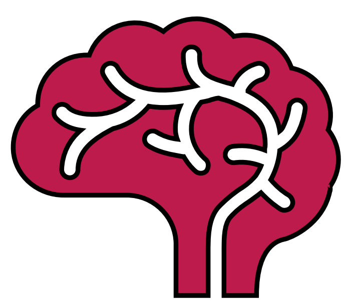


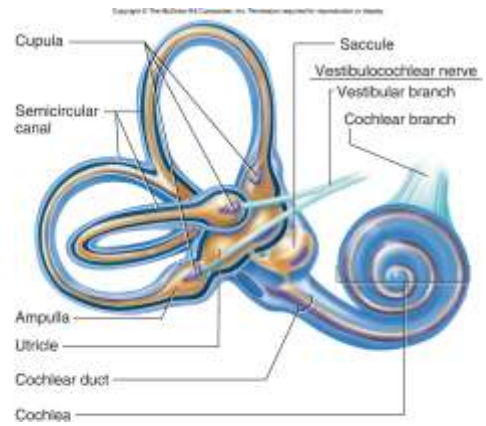
Vestibular Pathways

Vestibular information is used for:

- Control eye movements
- Maintain statice and dynamic equilibrium
- Conscious awareness of ourselves in “space”

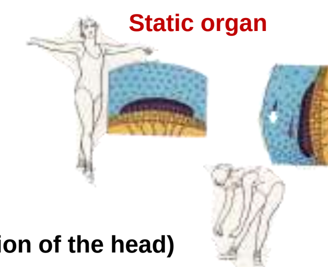
3 afferent sources:

- Eyes
- General proprioceptive receptors throughout the body
- Vestibular receptors in the inner ear



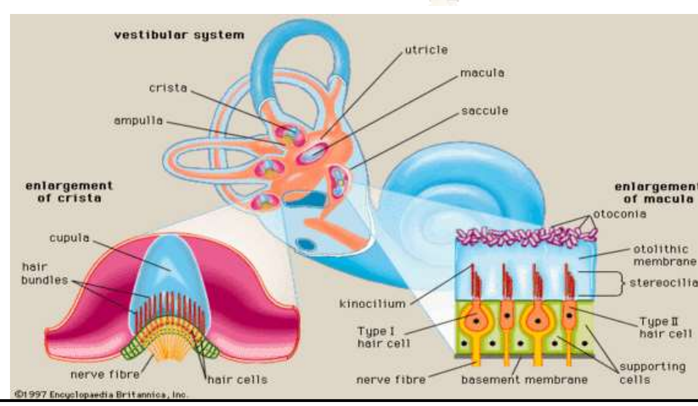
Vestibular Apparatus

Static organ

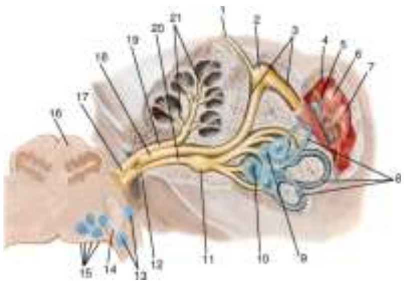


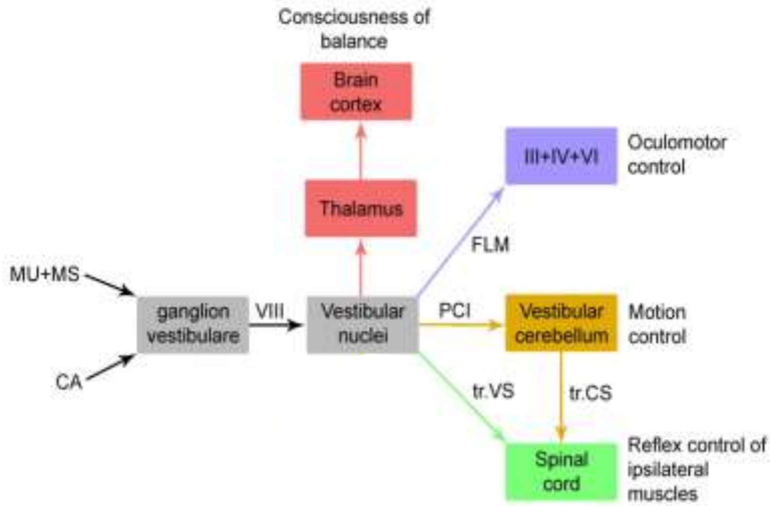
- **Receptors of static apparatus (linear acceleration- gravity)**
  - macula utriculi – orientation in horizontal position
  - macula sacculi – orientation in vertical position
- **Receptors of dynamic apparatus (angular acceleration- rotation of the head)**
  - cristae ampullares of semicircular ducts

Kinetic organ



Vestibular pathways





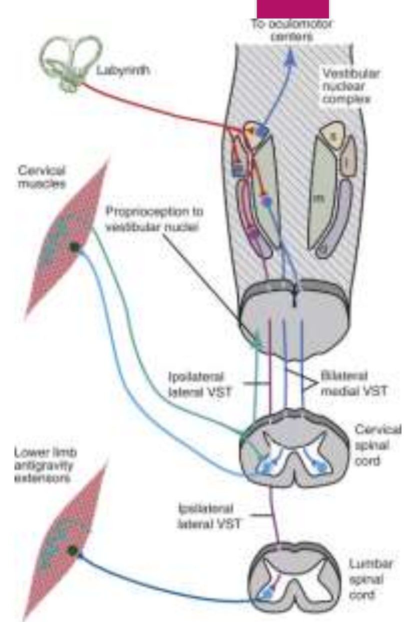
Connections with the spinal cord

To motoneurons that innervate axial and proximal limb muscles

- **Lateral vestibulospinal tract**
  - from lateral vestibular nucleus
  - uncrossed
  - terminating at all levels of the spinal cord
  - excitatory influences for extensors

Support body against gravity

- **Medial vestibulospinal tract**
  - from medial vestibular nucleus
  - uncrossed
  - terminates mainly at cervical levels
  - coordination of head position and eye movements

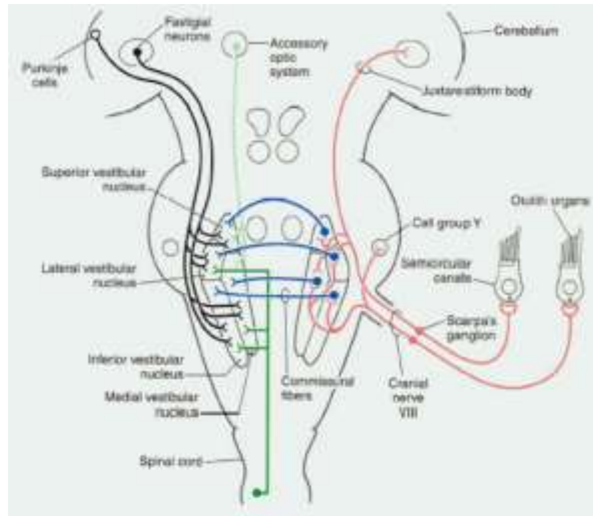


Marc, *Fundamental Neuroscience* 2013

Connections with the cerebellum

- Vestibular nucleus → inferior cerebellar peduncles → vestibulocerebellum (Fastigial nucleus)
- Fastigial nucleus → inferior cerebellar peduncles → vestibular nucleus (vestibulospinal tract)

Maintenance of balance



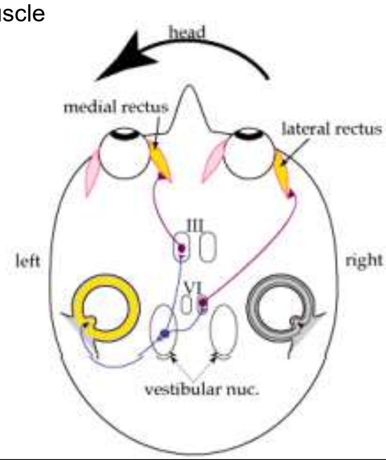
Connections with the brain stem

horizontal

Medial vestibular nucleus → CN VI → CN III / ventricle / CN IV → Eye's muscle

medial longitudinal fasciculus

Coordination of eye movements in response to head movements



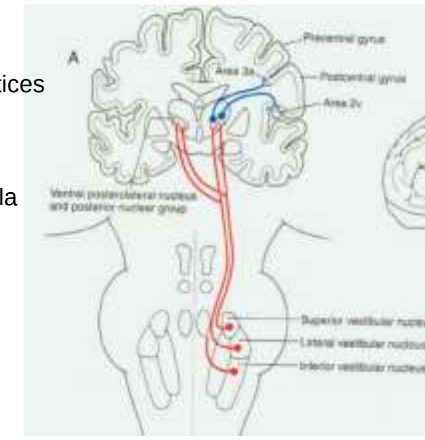
Connections with the cortex

Thalamus: Ventral posteromedial nucleus

No primary vestibular cortex

Distributed among several multisensory areas in the parietal and temporal cortices

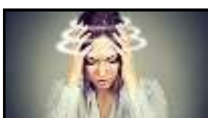
- Area 2v at the tip of the intraparietal sulcus
- Parieto-insular vestibular cortex (PIVC) at the posterior end of the insula
- Area 7 in the inferior parietal lobule



Natural stimulation of the vestibular system during head motion and locomotion is always **multisensory** (visual, vestibular, somatosensory)

Conscious perception of movement and gravity

Brant, Vestibular cortex: its locations, functions, and disorders



Vestibular Impairment

Disturbance in the body's balance system

Symptoms:

Dizziness, vertigo, nausea, vomiting, intolerance to head

motion, nystagmus, unsteady gait, and postural instability.

Acoustic Neuroma

Age-related dizziness and imbalance

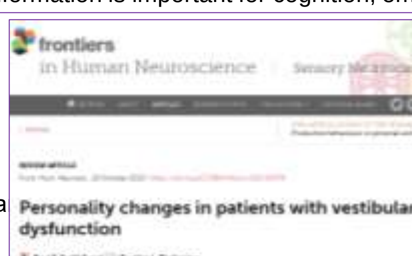
Bilateral Vestibular Hypofunction

Cortical representation of vestibular information is important for cognition, emotion and the sense of self.

Cognitive and emotional disorders

Symptoms:

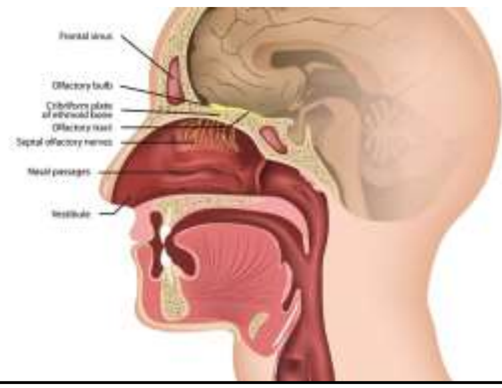
feeling “spaced out”, “body feeling stra


frontiers
in Human Neuroscience

Personality changes in patients with vestibular dysfunction

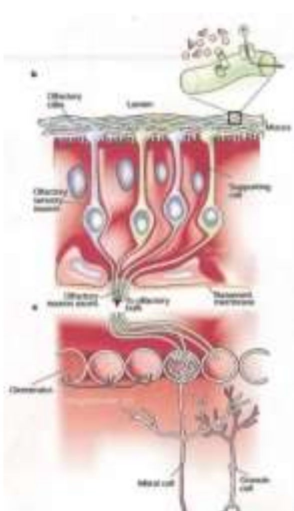
Olfactory Pathways

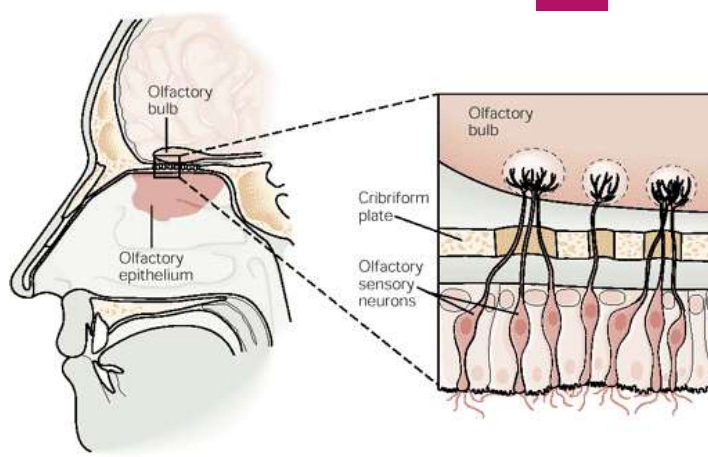
Humans are capable of discriminating a great variety of odors and flavors.



Olfactory Pathways

1st order neuron: bipolar olfactory neurons



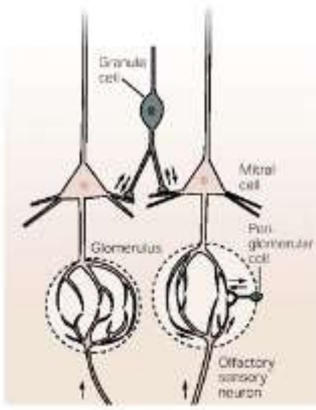


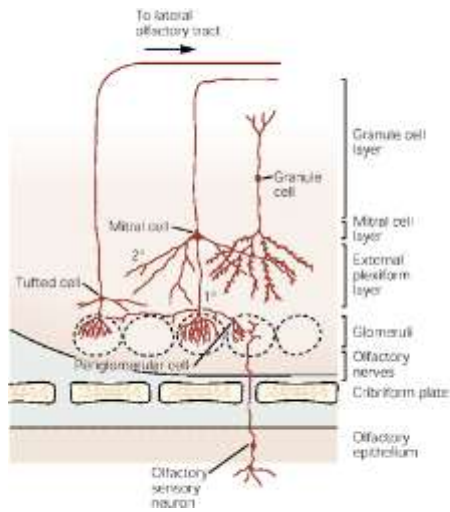
Olfactory neurons are distinctive among neurons in that they are short-lived, with an average life span of only 30-60 days, and are continuously replaced from the basal stem cell population.

Kandel, Samell and tatste; the chemical senses

Olfactory Pathways

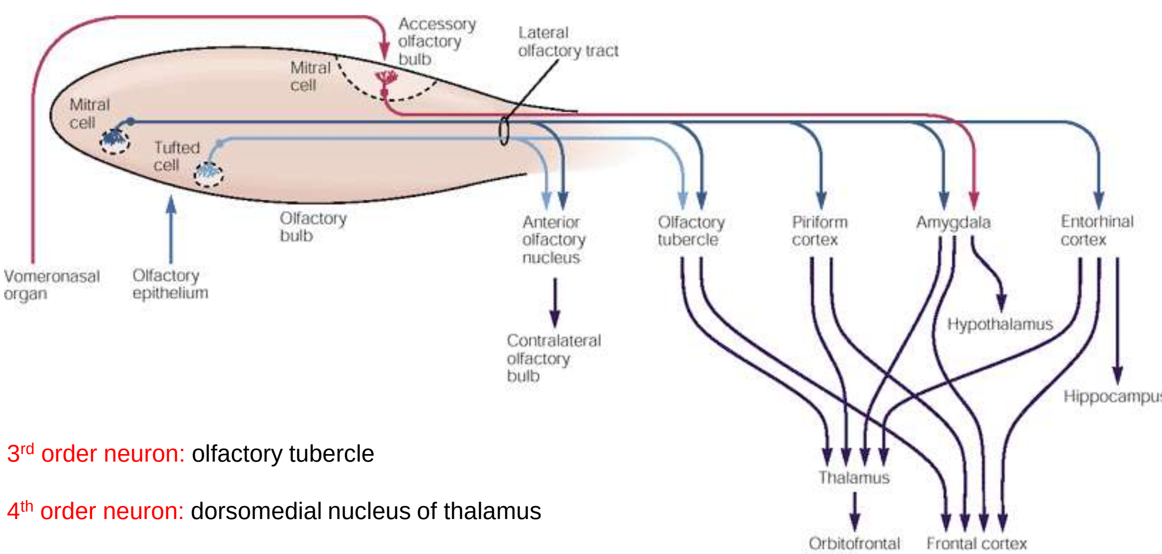
2nd order neuron: mitral cells ⟶ lateral olfactory tract





Olfactory Pathways

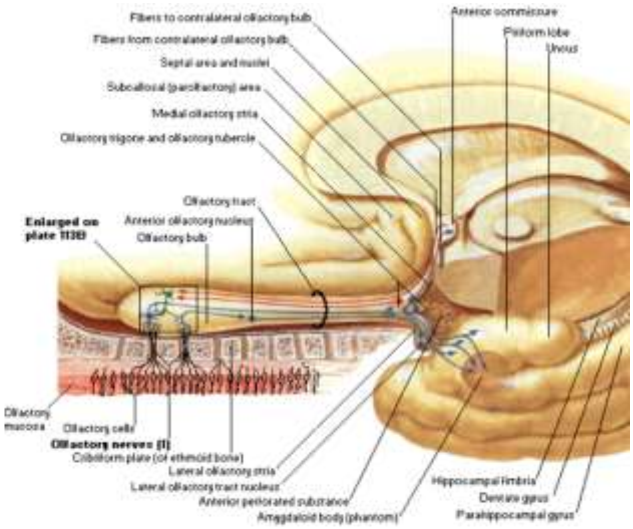
Olfactory information is processed in several regions of the cerebral cortex.



3rd order neuron: olfactory tubercle

4th order neuron: dorsomedial nucleus of thalamus

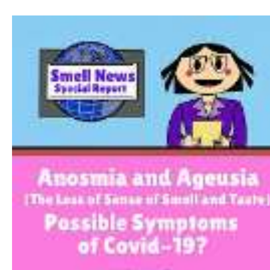
Olfactory Pathways



Olfactory nerve is divided to:

- Lateral olfactory stria
- Medial olfactory stria

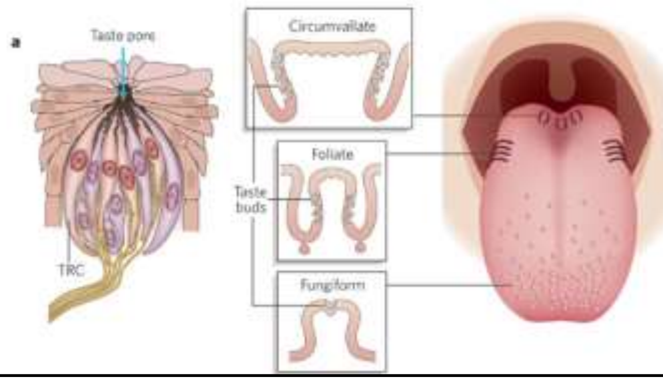
Pathology



Gustatory Pathways

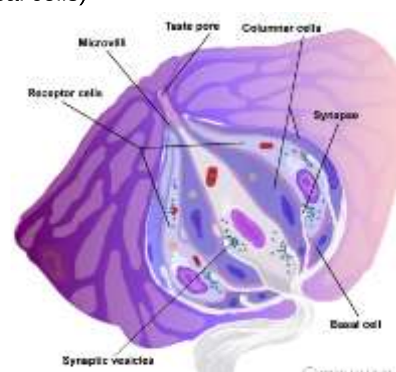
The distribution and types of human lingual papillae

Sense of taste



Taste buds

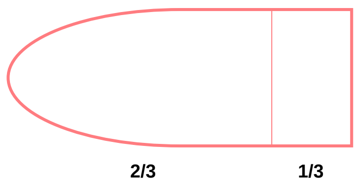
- receptor cells (replaced about every 9-10 days by differentiating basal cells)
- supportive columnar cells
- basal cells

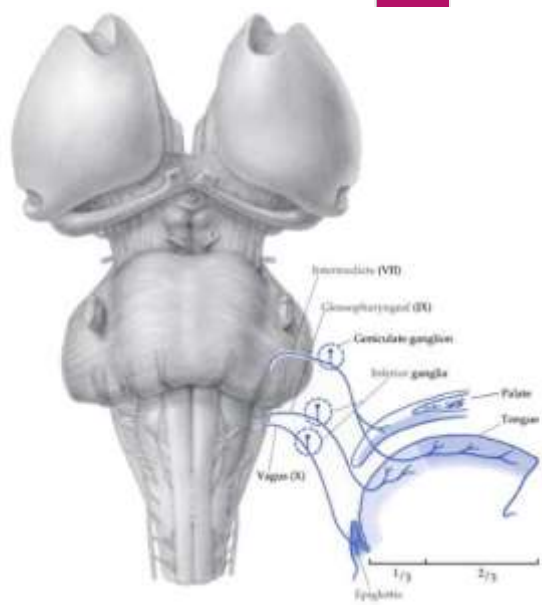


Gustatory pathway

1st order neuron

- CN VII (facial nerve) – geniculate ganglion (*chorda tympani)*
- CN IX (glossopharyngeal) – inferior ganglion of CN IX
- CN X (vagus)– nodose ganglion (inferior ganglion of CN X)

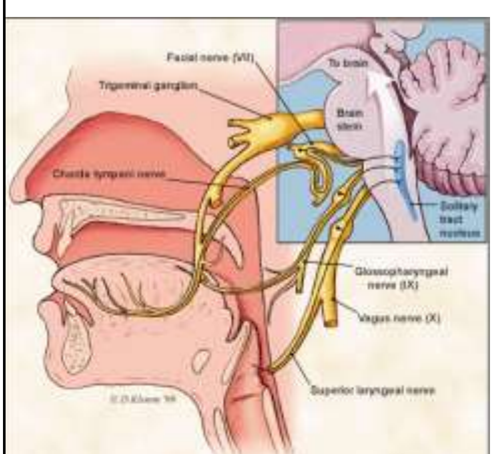


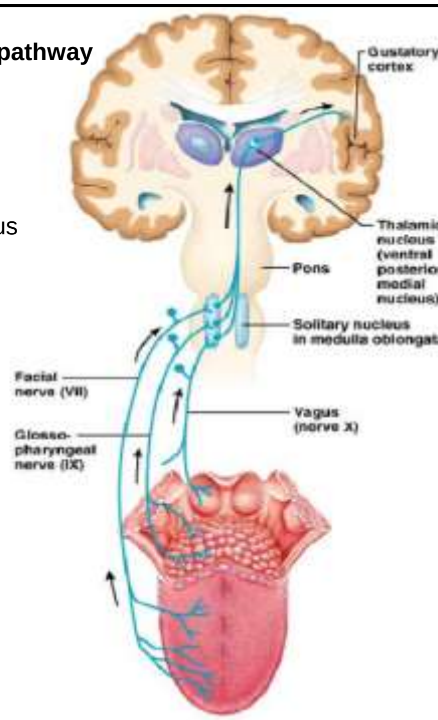


Gustatory pathway

2nd order neuron - rostral part of the solitary tract nucleus

3rd order neuron – ventral posteromedial nucleus of thalamus

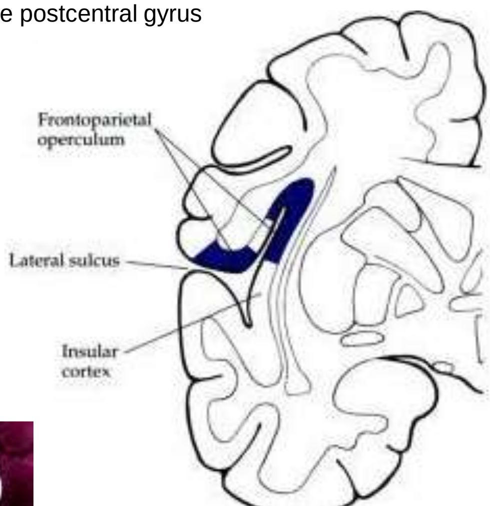


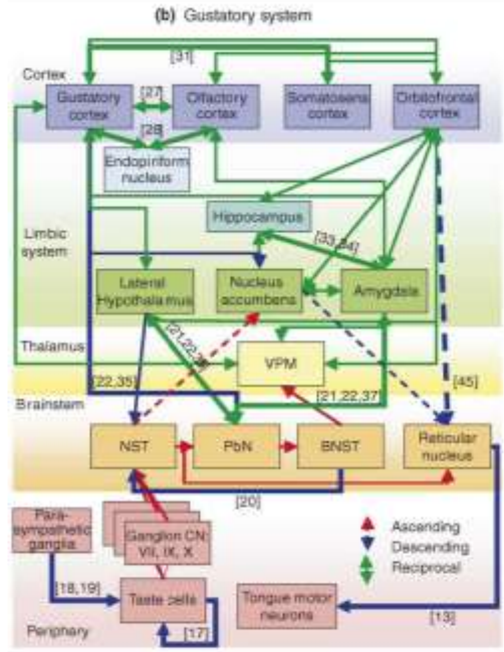


Gustatory pathway

Primary gustatory cortex

- a. 43 in the postcentral gyrus
- insula





Gustatory impairment

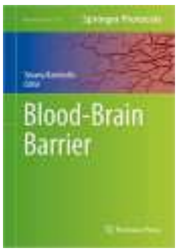
Gustatory dysfunctions:

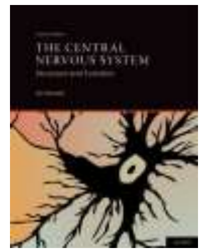
- quantitative disorders
  - a. Ageusia
  - b. Hypogeusia
  - c. hypergeusia
- qualitative disorders
  - a. Dysgeusia
  - b. phantogeusia

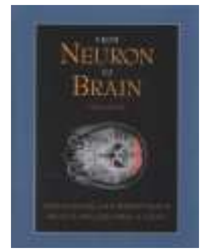
Oral sources of altered taste function are common and can be evaluated by a **dentist**.

Maheswaran, *J Pharm Bioallied Sci* 2014

Reading list







Thank you very much for your attention